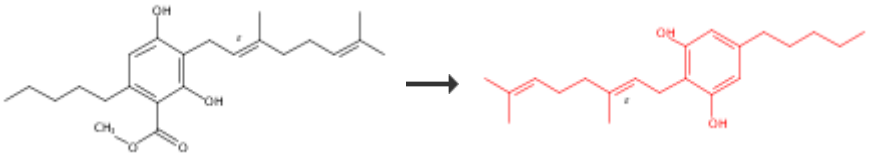
1. Single Step



90%

Overview

Steps/Stages

1.1 R:LiCl, S:DMSO, S:H_2O, 4 h, reflux

Notes

Reactants: 1, Reagents: 1, Solvents: 2, Steps: 1, Stages: 1, Most stages in any one step: 1

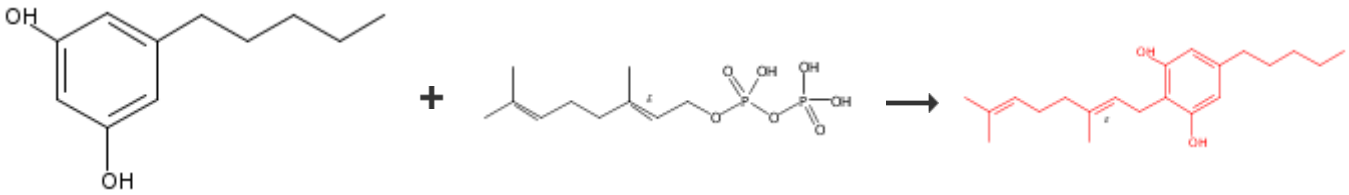
References

Synthesis of phytocannabinoids including a decarboxylation step

By Reekie, Tristan et al

From PCT Int. Appl., 2019033168, 21 Feb 2019

2. Single Step



Overview

Steps/Stages

1.1 R:Tris buffer, R:$MgCl_2$, 25°C, pH 9

Notes

biotransformation, buffered solution, enzymic, recombinant NphB (prenyltransferase from Streptomyces sp. strain CL190) used, regioselective, Reactants: 2, Reagents: 2, Steps: 1, Stages: 1, Most stages in any one step: 1

References

Chemoenzymatic syntheses of prenylated aromatic small molecules using Streptomyces prenyltransferases with relaxed substrate specificities

By Kumano, Takuto et al

From Bioorganic & Medicinal Chemistry, 16(17), 8117-8126; 2008

Reaction Protocol

Procedure

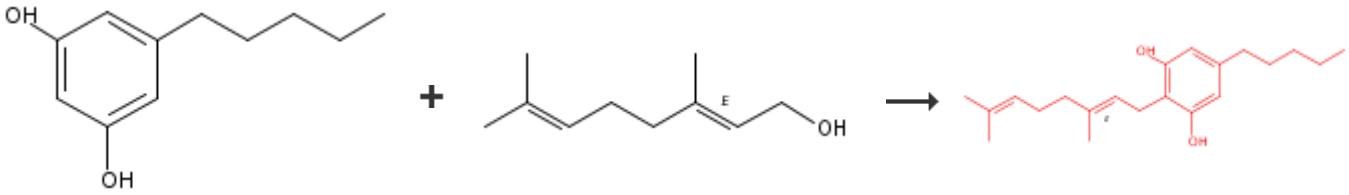
1. Carry out the NphB-catalyzed reaction in 50 mM Tris-HCl (pH 9.0), containing 5 mM $MgCl_2$, 5 mM olivetol, 5 mM geranyl diphosphate (GPP), 1 mg/ml NphB, in a total volume of 60 µl.
2. Incubate the reaction mixtures at 25 °C overnight and extract with 200 µl ethyl acetate.

View more...

Available Experimental Data ^{1}H NMR, ^{13}C NMR, HRMS

View with MethodsNow

3. Single Step



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Overview

Steps/Stages

1.1 C:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

Notes

Reactants: 2, Catalysts: 1, Solvents: 1, Steps: 1, Stages: 1, Most stages in any one step: 1

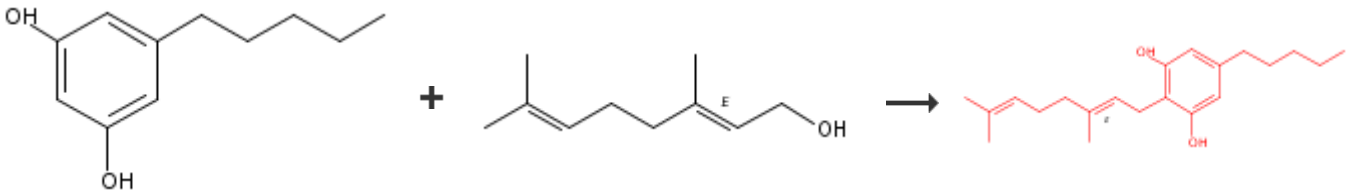
References

Methods for the manufacture of cannabinoid prodrugs, pharmaceutical formulations and their use

By Peet, Richard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017216362, 21 Dec 2017

4. Single Step



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Overview

Steps/Stages

Notes

1.1 C:*p*-$MeC_6H_4SO_3H$, $S:CHCl_3$, 12 h, rt

in the dark, Reactants: 2, Catalysts: 1, Solvents: 1, Steps: 1, Stages: 1, Most stages in any one step: 1

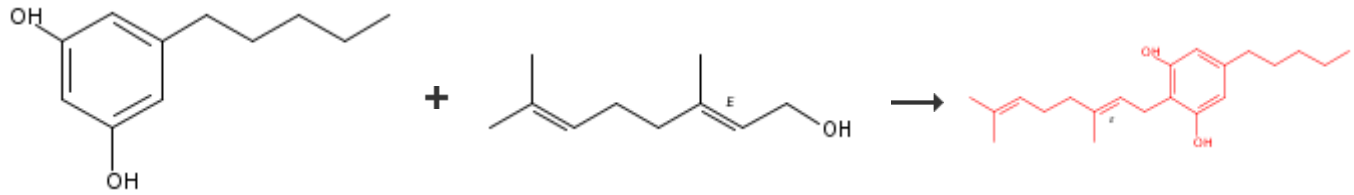
References

Chemoenzymatic synthesis of tetrahydrocannabivarin, carnnabivarin, and cannabinol

By Kavarana, Malcolm J. and Peet, Richard C.

From U.S. Pat. Appl. Publ., 20170283837, 05 Oct 2017

5. Single Step



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Overview

Steps/Stages

1.1 R:*p*-$MeC_6H_4SO_3H$, $S:CHCl_3$, 12 h, rt

Notes

in the dark, Reactants: 2, Reagents: 1, Solvents: 1, Steps: 1, Stages: 1, Most stages in any one step: 1

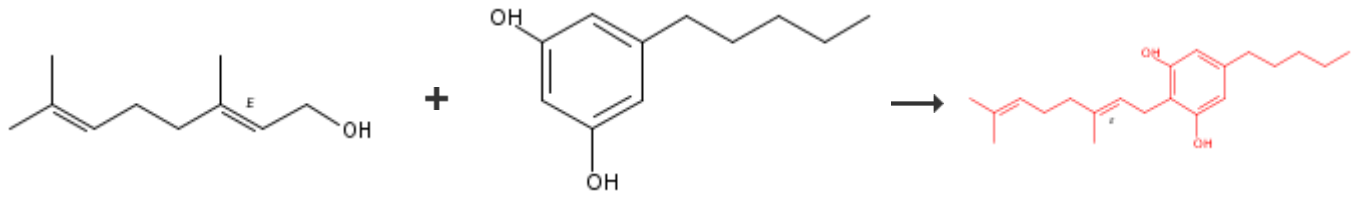
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

6. Single Step



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Overview

Steps/Stages

Notes

1.1 C:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

literature preparation, in the dark, Reactants: 2, Catalysts: 1, Solvents: 1, Steps: 1, Stages: 1, Most stages in any one step: 1

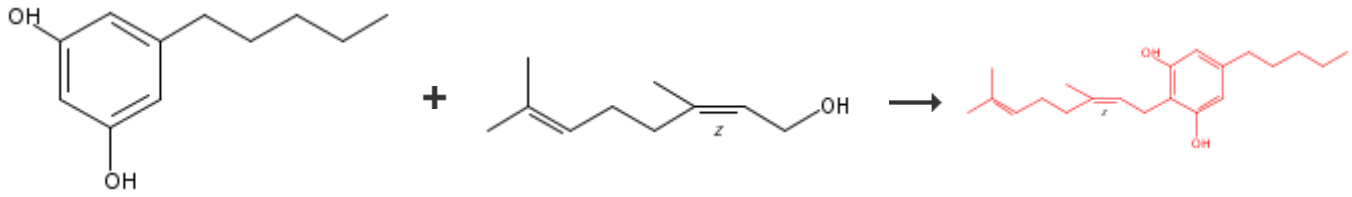
References

Chemoenzymic synthesis of cannabinoids

By Winnicki, Robert and Donsky, Marc

From PCT Int. Appl., 2014134281, 04 Sep 2014

7. Single Step



Overview

Steps/Stages

1.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$

Notes

IN THE DARK, Reactants: 2, Reagents: 1, Solvents: 1, Steps: 1, Stages: 1, Most stages in any one step: 1

References

Cannabinerolic acid, a cannabinoid from Cannabis sativa

By Taura, Futoshi et al

From Phytochemistry, 39(2), 457-8; 1995

8. Single Step

Overview

Steps/Stages

Notes

1.1 C:BF_3-Et_2O, C:SiO_2, S:CH_2Cl_2

Reactants: 1, Catalysts: 2, Solvents: 1, Steps: 1, Stages: 1, Most stages in any one step: 1

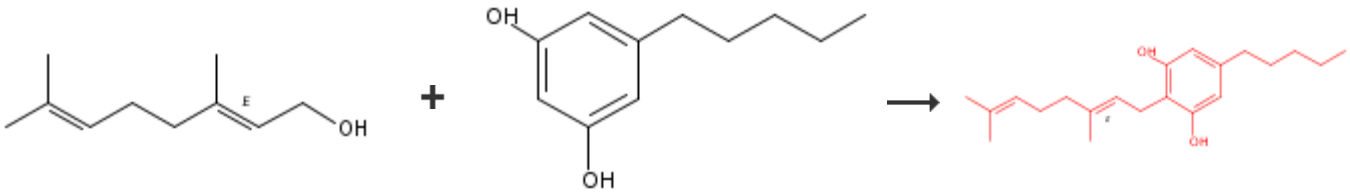
References

Boron trifluoride etherate on alumina - a modified Lewis acid reagent. An improved synthesis of cannabidiol

By Baek, Seung Hwa et al

From Tetrahedron Letters, 26(8), 1083-6; 1985

9. Single Step



29%

Overview

Steps/Stages

Notes

Reactants: 2, Reagents: 3, Solvents: 2, Steps: 1, Stages: 2, Most stages in any one step: 2

1.1 R:BF_3-Et_2O, R:Al_2O_3, S:CH_2Cl_2

1.2 R:$NaHCO_3$, S:H_2O

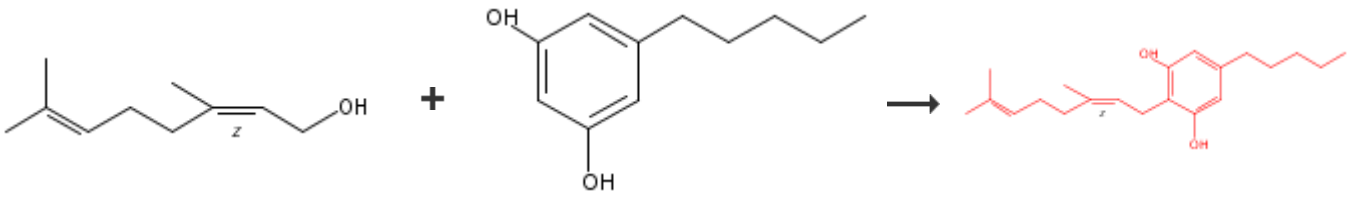
References

Boron trifluoride etherate on alumina - a modified Lewis acid reagent(V) a convenient single-step synthesis of cannabinoids

By Baek, Seung-Hwa et al

From Bulletin of the Korean Chemical Society, 16(3), 293-6; 1995

10. Single Step



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Overview

Steps/Stages

Notes

1.1 R:BF_3-Et_2O, R:Al_2O_3, S:CH_2Cl_2

1.2 R:$NaHCO_3$, S:H_2O

Reactants: 2, Reagents: 3, Solvents: 2, Steps: 1, Stages: 2, Most stages in any one step: 2

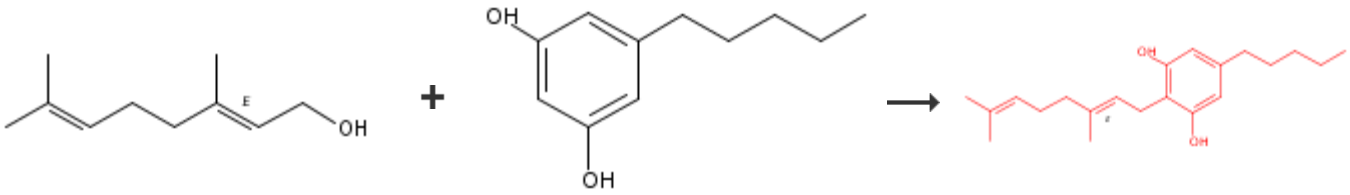
References

Boron trifluoride etherate on alumina - a modified Lewis acid reagent(V) a convenient single-step synthesis of cannabinoids

By Baek, Seung-Hwa et al

From Bulletin of the Korean Chemical Society, 16(3), 293-6; 1995

11. Single Step



Overview

Steps/Stages

1.1 S:Decalin

Notes

Classification: Condensation; C-Alkylation; Regioselective; Allylic; # Conditions: decalin; 36h, Reactants: 2, Solvents: 1, Steps: 1, Stages: 1, Most stages in any one step: 1

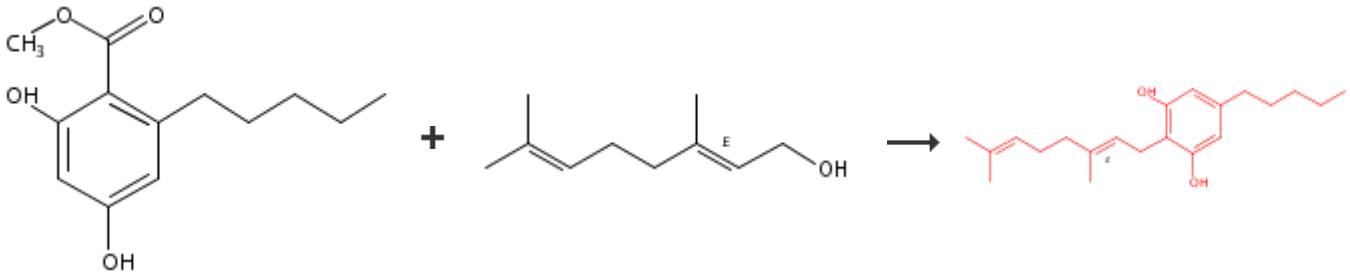
References

Structure and synthesis of cannabigerol, a new hashish constituent

By Gaoni, Y. and Mechoulam, R.

From Proceedings of the Chemical Society, London, (Mar.), 82; 1964

12. 2 Steps



Overview

Steps/Stages

Notes

1.1 R:BF_3-Et_2O, S:$CHCl_3$, 0.25 h, -20°C

2.1 R:LiCl, S:DMSO, S:H_2O, 4 h, reflux

Reactants: 2, Reagents: 2, Solvents: 3, Steps: 2, Stages: 2, Most stages in any one step: 1

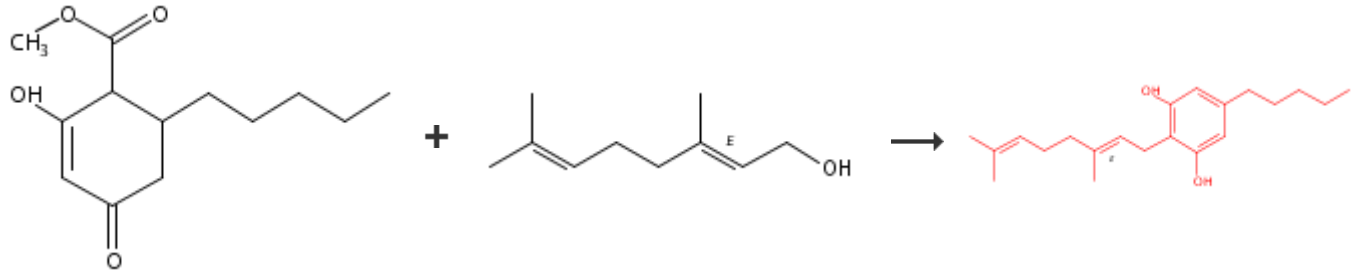
References

Synthesis of phytocannabinoids including a decarboxylation step

By Reekie, Tristan et al

From PCT Int. Appl., 2019033168, 21 Feb 2019

13. 2 Steps



[Step 2.1]

Overview

Steps/Stages

1.1 R:Br_2, S:DMF, 90 min, cooled; 80°C → 160°C; 10 h, 160°C

2.1 C:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

Notes

Reactants: 2, Reagents: 1, Catalysts: 1, Solvents: 2, Steps: 2, Stages: 2, Most stages in any one step: 1

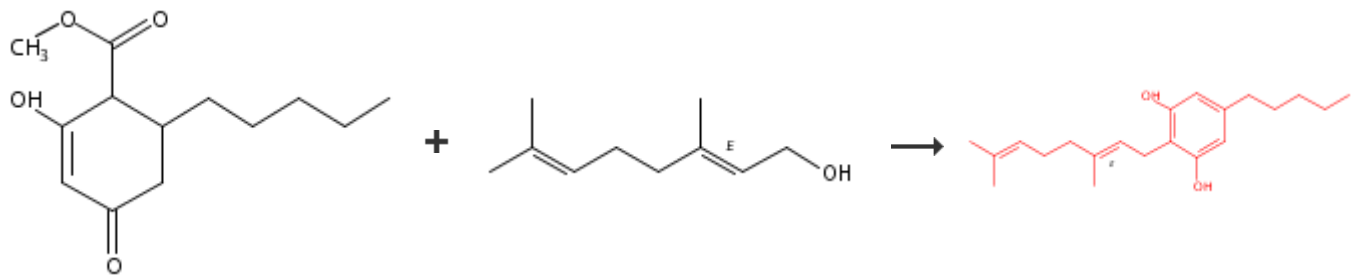
References

Methods for the manufacture of cannabinoid prodrugs, pharmaceutical formulations and their use

By Peet, Richard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017216362, 21 Dec 2017

14. 2 Steps



[Step 2.1]

Overview

Steps/Stages

1.1 R:Br_2, S:DMF, 90 min, cooled; 80°C; 80°C → 160°C; 10 h, 160°C
2.1 C:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

Notes

2) in the dark, Reactants: 2, Reagents: 1, Catalysts: 1, Solvents: 2, Steps: 2, Stages: 2, Most stages in any one step: 1

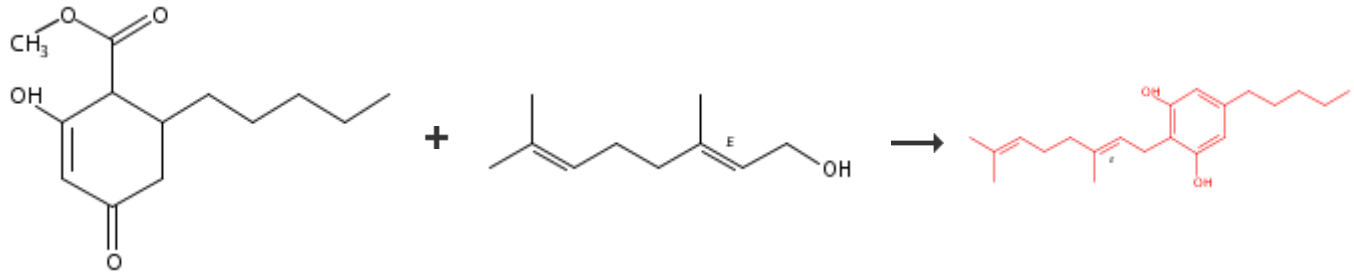
References

Chemoenzymatic synthesis of tetrahydrocannabivarin, carnnabivarin, and cannabinol

By Kavarana, Malcolm J. and Peet, Richard C.

From U.S. Pat. Appl. Publ., 20170283837, 05 Oct 2017

15. 2 Steps



[Step 2.1]

Overview

Steps/Stages

1.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

2.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

Notes

2) in the dark, Reactants: 2, Reagents: 2, Solvents: 2, Steps: 2, Stages: 2, Most stages in any one step: 1

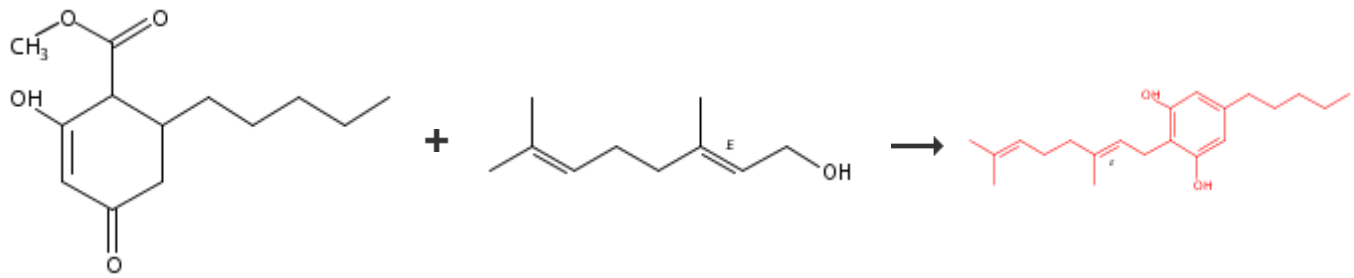
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

16. 2 Steps



[Step 2.1]

Overview

Steps/Stages

1.1 R:Br_2, S:DMF, cooled; 90 min, 80°C; 10 min, 80°C → 160°C

2.1 C:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

Notes

2) literature preparation, in the dark, Reactants: 2, Reagents: 1, Catalysts: 1, Solvents: 2, Steps: 2, Stages: 2, Most stages in any one step: 1

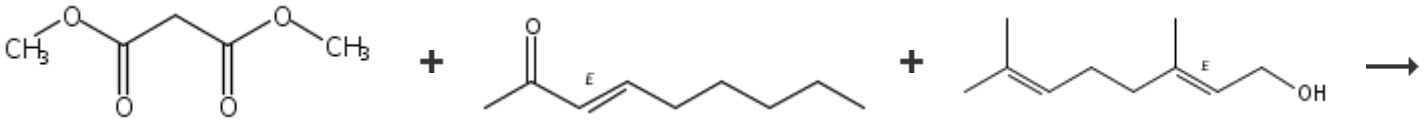
References

Chemoenzymic synthesis of cannabinoids

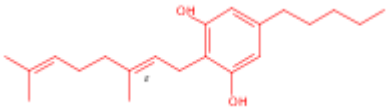
By Winnicki, Robert and Donsky, Marc

From PCT Int. Appl., 2014134281, 04 Sep 2014

17. 3 Steps



[Step 2.1]



Overview

Steps/Stages

1.1 R:Na, S:MeOH, 0°C; 8 h, reflux

1.2 R:Br_2, S:DMF, 0°C; 1 h, 20°C; 16 h, 20°C → 80°C; cooled

1.3 R:$Na_2S_2O_3$, S:H_2O

2.1 R:BF_3-Et_2O, S:$CHCl_3$, 0.25 h, -20°C

3.1 R:LiCl, S:DMSO, S:H_2O, 4 h, reflux

Notes

Reactants: 3, Reagents: 5, Solvents: 5, Steps: 3, Stages: 5, Most stages in any one step: 3

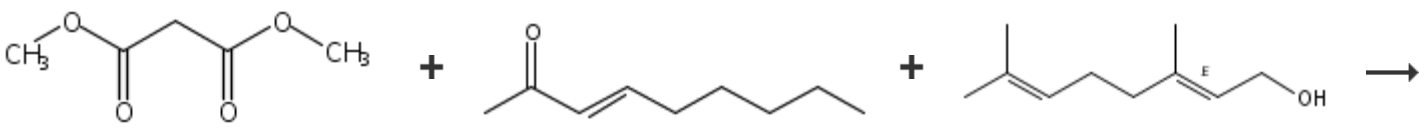
References

Synthesis of phytocannabinoids including a decarboxylation step

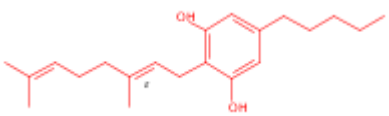
By Reekie, Tristan et al

From PCT Int. Appl., 2019033168, 21 Feb 2019

18. 3 Steps



[Step 3.1]



Overview

Steps/Stages

1.1 R:NaOMe, S:MeOH, rt; 3 h, reflux

2.1 R:Br_2, S:DMF, 90 min, cooled; 80°C → 160°C; 10 h, 160°C
3.1 C:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

Notes

Reactants: 3, Reagents: 2, Catalysts: 1, Solvents: 3, Steps: 3, Stages: 3, Most stages in any one step: 1

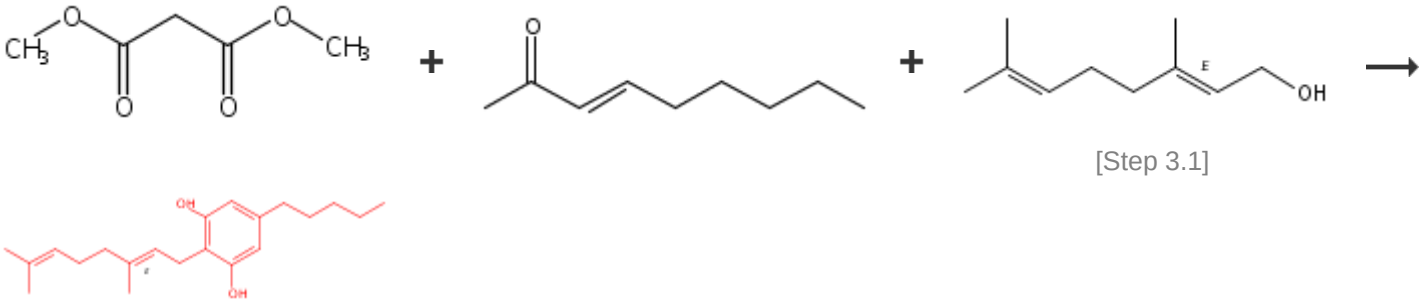
References

Methods for the manufacture of cannabinoid prodrugs, pharmaceutical formulations and their use

By Peet, Richard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017216362, 21 Dec 2017

19. 3 Steps



Overview

Steps/Stages

1.1 R:NaOMe, S:MeOH, S:H_2O, rt; 3 h, reflux

2.1 R:Br_2, S:DMF, 90 min, cooled; 80°C; 80°C → 160°C; 10 h, 160°C
3.1 C:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

Notes

3) in the dark, Reactants: 3, Reagents: 2, Catalysts: 1, Solvents: 4, Steps: 3, Stages: 3, Most stages in any one step: 1

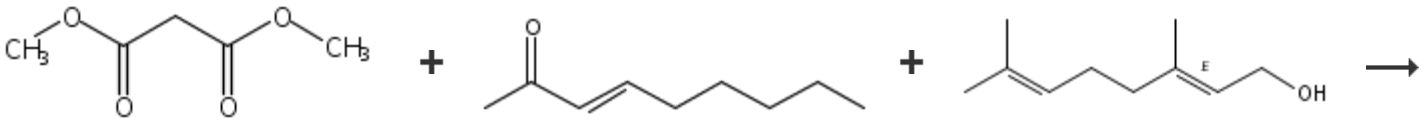
References

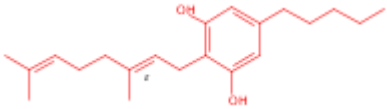
Chemoenzymatic synthesis of tetrahydrocannabivarin, carnnabivarin, and cannabinol

By Kavarana, Malcolm J. and Peet, Richard C.

From U.S. Pat. Appl. Publ., 20170283837, 05 Oct 2017

20. 3 Steps





Overview

Steps/Stages

1.1 R:NaOMe, S:MeOH, rt; 3 h, reflux; reflux → rt

1.2 R:H_2O, rt

2.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

3.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

Notes

3) in the dark, Reactants: 3, Reagents: 4, Solvents: 3, Steps: 3, Stages: 4, Most stages in any one step: 2

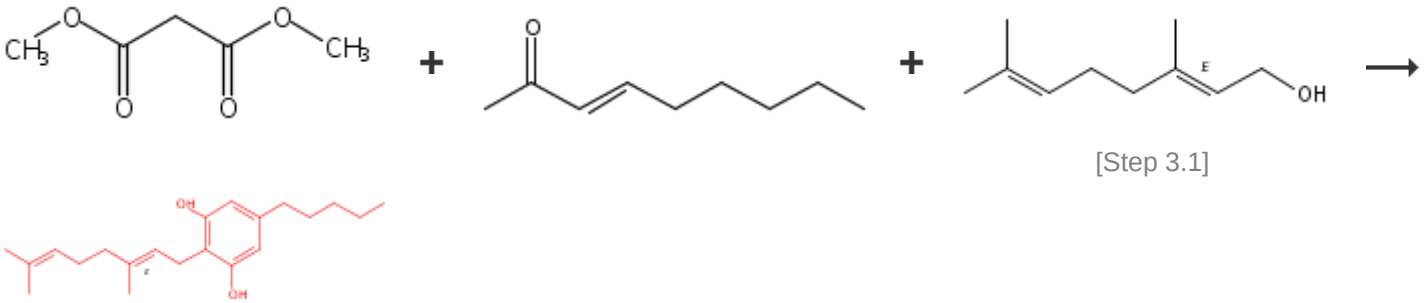
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

21. 3 Steps



[Step 3.1]

Overview

Steps/Stages

1.1 R:NaOMe, S:MeOH, rt; 3 h, reflux; reflux → rt

1.2 R:HCl, S:H_2O, rt, pH 4

2.1 R:Br_2, S:DMF, cooled; 90 min, 80°C; 10 min, 80°C → 160°C

3.1 C:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

Notes

3) literature preparation, in the dark, Reactants: 3, Reagents: 3, Catalysts: 1, Solvents: 4, Steps: 3, Stages: 4, Most stages in any one step: 2

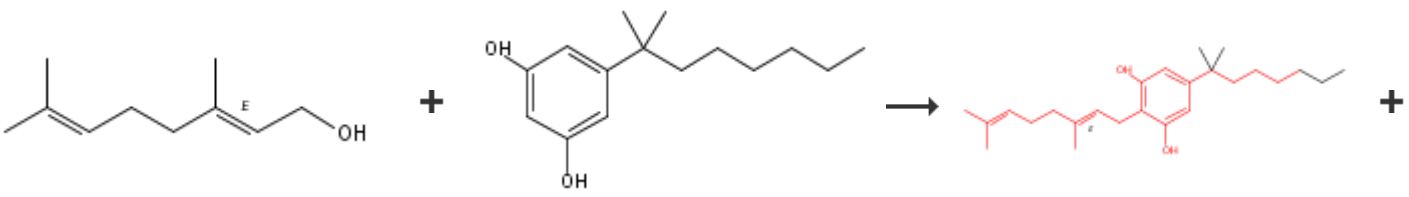
References

Chemoenzymic synthesis of cannabinoids

By Winnicki, Robert and Donsky, Marc

From PCT Int. Appl., 2014134281, 04 Sep 2014

22. Single Step



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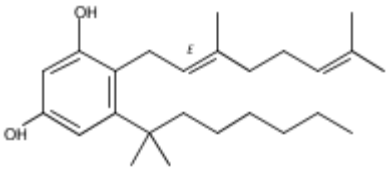

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Overview

Steps/Stages

1.1 R:BF_3-Et_2O, R:Al_2O_3, S:CH_2Cl_2

1.2 R:$NaHCO_3$, S:H_2O

Notes

Reactants: 2, Reagents: 3, Solvents: 2, Steps: 1, Stages: 2, Most stages in any one step: 2

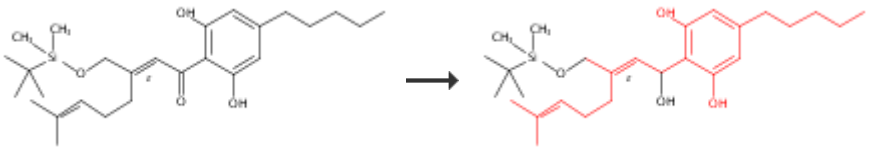
References

Boron trifluoride etherate on alumina - a modified Lewis acid reagent(V) a convenient single-step synthesis of cannabinoids

By Baek, Seung-Hwa et al

From Bulletin of the Korean Chemical Society, 16(3), 293-6; 1995

23. Single Step



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Overview

Steps/Stages

1.1 R:$NaBH_4$, S:H_2O, S:MeOH

Notes

Reactants: 1, Reagents: 1, Solvents: 2, Steps: 1, Stages: 1, Most stages in any one step: 1

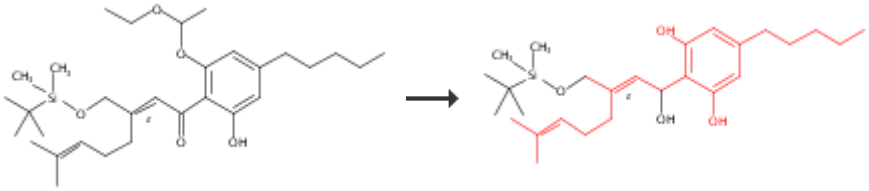
References

Synthesis of (±)-nor-Δ9-cis-6a,10a-THC-carboxylic acid (THC = tetrahydrocannabinol)

By Tius, Marcus A. and Gu, Xueqin

From Journal of the Chemical Society, Chemical Communications, (16), 1171-3; 1989

24. 2 Steps



Overview

Steps/Stages

1.1 R:AcOH, R:H_2O, S:H_2O, S:THF

2.1 R:$NaBH_4$, S:H_2O, S:MeOH

Notes

1) AcOH:THF:H2O, 1:1:1, Reactants: 1, Reagents: 3, Solvents: 3, Steps: 2, Stages: 2, Most stages in any one step: 1

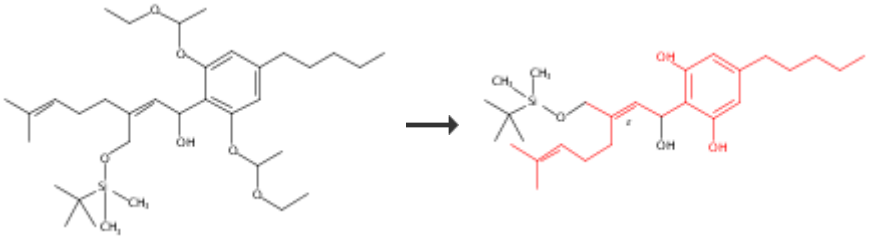
References

Synthesis of (±)-nor-Δ9-cis-6a,10a-THC-carboxylic acid (THC = tetrahydrocannabinol)

By Tius, Marcus A. and Gu, Xueqin

From Journal of the Chemical Society, Chemical Communications, (16), 1171-3; 1989

25. 3 Steps



Overview

Steps/Stages

1.1 R:$C_5H_{10}N(O=)CN=NC(=O)NC_5H_{10}$, R:*t*-BuOMgBr

2.1 R:AcOH, R:H_2O, S:H_2O, S:THF

3.1 R:$NaBH_4$, S:H_2O, S:MeOH

Notes

2) AcOH:THF:H2O, 1:1:1, Reactants: 1, Reagents: 5, Solvents: 3, Steps: 3, Stages: 3, Most stages in any one step: 1

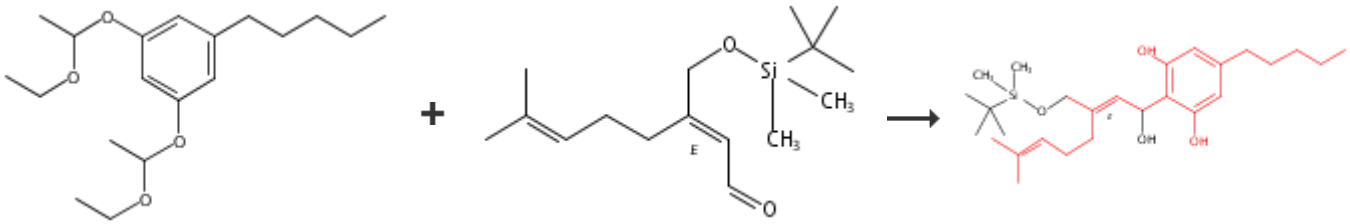
References

Synthesis of (±)-nor-Δ9-cis-6a,10a-THC-carboxylic acid (THC = tetrahydrocannabinol)

By Tius, Marcus A. and Gu, Xueqin

From Journal of the Chemical Society, Chemical Communications, (16), 1171-3; 1989

26. 4 Steps



Overview

Steps/Stages

1.1 R:BuLi, S:THF

1.2

2.1 R:$C_5H_{10}N(O=)CN=NC(=O)NC_5H_{10}$, R:*t*-BuOMgBr

3.1 R:AcOH, R:H_2O, S:H_2O, S:THF

4.1 R:$NaBH_4$, S:H_2O, S:MeOH

Notes

3) AcOH:THF:H2O, 1:1:1, Reactants: 2, Reagents: 6, Solvents: 3, Steps: 4, Stages: 5, Most stages in any one step: 2

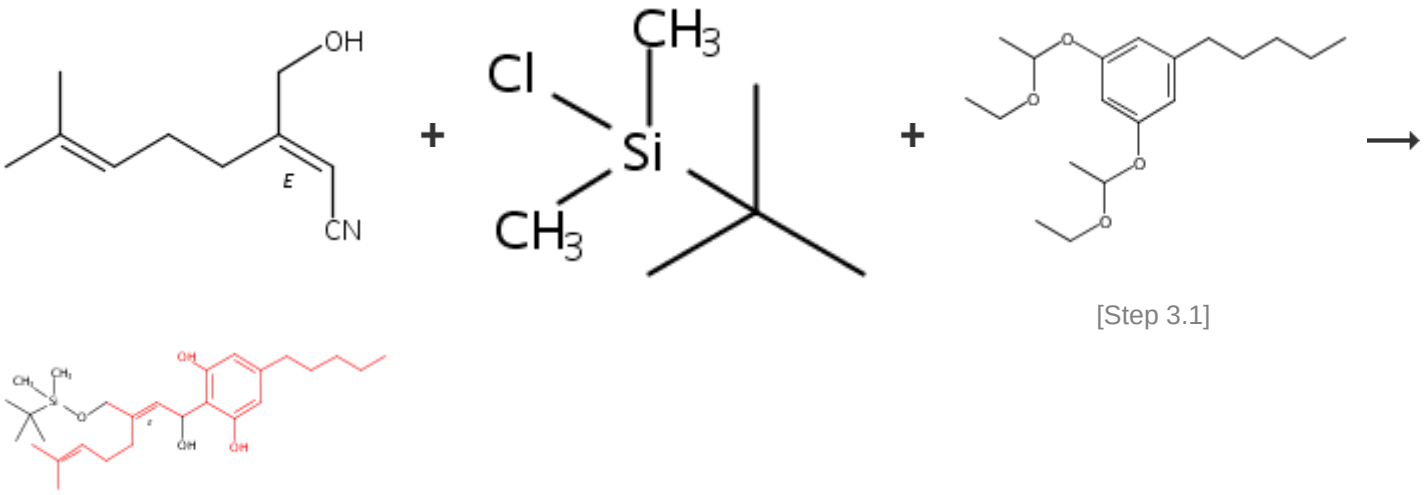
References

Synthesis of (±)-nor-Δ9-cis-6a,10a-THC-carboxylic acid (THC = tetrahydrocannabinol)

By Tius, Marcus A. and Gu, Xueqin

From Journal of the Chemical Society, Chemical Communications, (16), 1171-3; 1989

27. 6 Steps



[Step 3.1]

Overview

Steps/Stages

Notes

1.1

2.1 R:AlH(Bu-*i*)$_2$, S:Et$_2$O

3.1 R:BuLi, S:THF

3.2

4.1 R:$C_5H_{10}N(O=)CN=NC(=O)NC_5H_{10}$, R:*t*-BuOMgBr

5.1 R:AcOH, R:H_2O, S:H_2O, S:THF

6.1 R:$NaBH_4$, S:H_2O, S:MeOH

5) AcOH:THF:H2O, 1:1:1, Reactants: 3, Reagents: 7, Solvents: 4, Steps: 6, Stages: 7, Most stages in any one step: 2

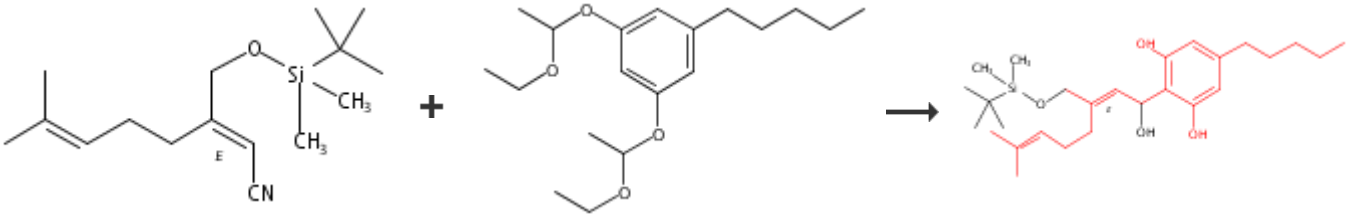
References

Synthesis of (±)-nor-Δ9-cis-6a,10a-THC-carboxylic acid (THC = tetrahydrocannabinol)

By Tius, Marcus A. and Gu, Xueqin

From Journal of the Chemical Society, Chemical Communications, (16), 1171-3; 1989

28. 5 Steps



[Step 2.1]

Overview

Steps/Stages

1.1 R:AlH(Bu-*i*)$_2$, S:Et$_2$O

2.1 R:BuLi, S:THF

2.2

3.1 R:$C_5H_{10}N(O=)CN=NC(=O)NC_5H_{10}$, R:*t*-BuOMgBr

4.1 R:AcOH, R:H_2O, S:H_2O, S:THF

5.1 R:$NaBH_4$, S:H_2O, S:MeOH

Notes

4) AcOH:THF:H2O, 1:1:1, Reactants: 2, Reagents: 7, Solvents: 4, Steps: 5, Stages: 6, Most stages in any one step: 2

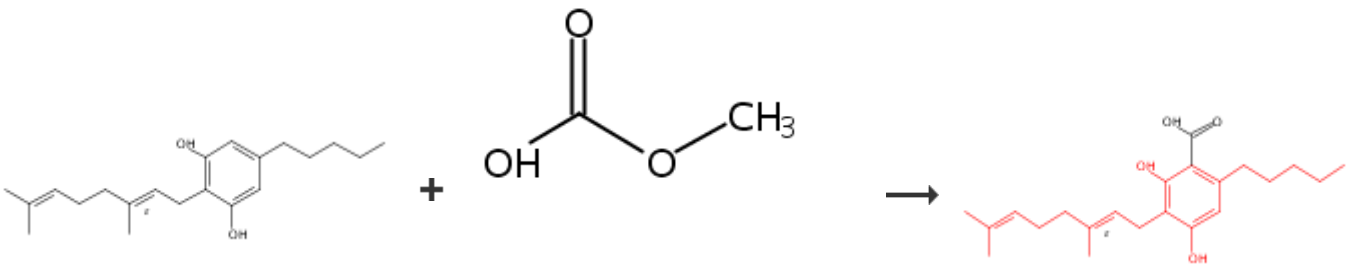
References

Synthesis of (±)-nor-Δ9-cis-6a,10a-THC-carboxylic acid (THC = tetrahydrocannabinol)

By Tius, Marcus A. and Gu, Xueqin

From Journal of the Chemical Society, Chemical Communications, (16), 1171-3; 1989

29. Single Step



• 1/2 Mg

90%

Overview

Steps/Stages

1.1 S:DMF, 1 h, 120°C

1.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

Notes

alternative preparation gave lower yield, LH-20 Sephadex resin, LH-20 lipophilic resin, Reactants: 2, Reagents: 1, Solvents: 4, Steps: 1, Stages: 2, Most stages in any one step: 2

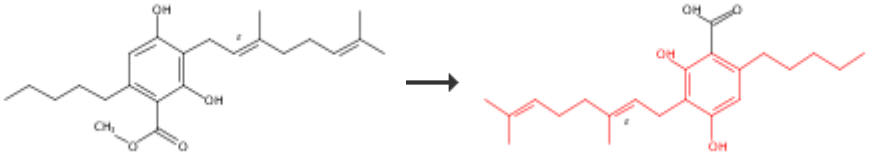
References

Bioreactor and process for the enzymatic biosynthesis of cannabinoids

By Peet, Richard and Sun, Mingyang

From U.S. Pat. Appl. Publ., 20160053220, 25 Feb 2016

30. Single Step



80%

Overview

Steps/Stages

1.1 R:Cs_2CO_3, R:PhSH, S:DMF, 24 h, 85°C

1.2 R:HCl, S:H_2O, cooled, pH 3

Notes

alternate reaction conditions gave lower yield, Reactants: 1, Reagents: 3, Solvents: 2, Steps: 1, Stages: 2, Most stages in any one step: 2

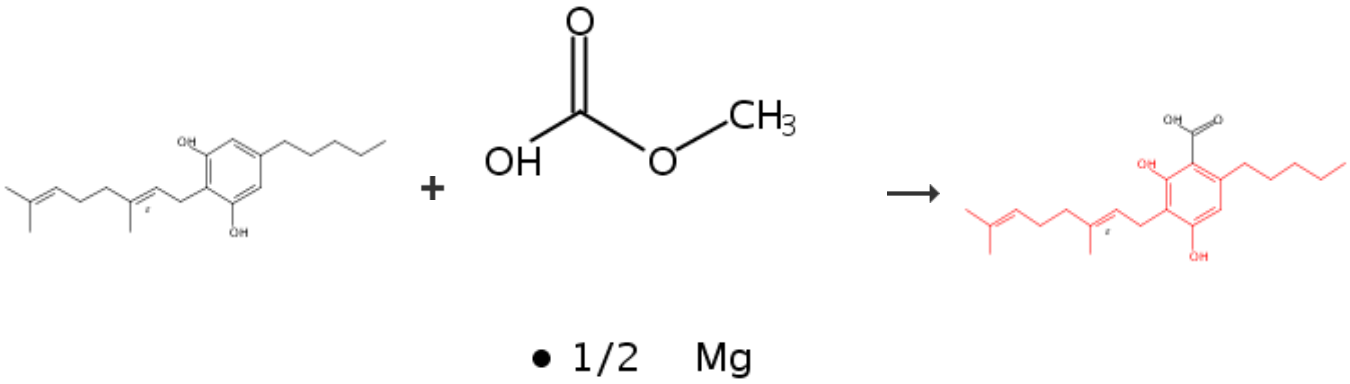
References

Synthesis of phytocannabinoids including a demethylation step

By Reekie, Tristan et al

From PCT Int. Appl., 2019033164, 21 Feb 2019

31. Single Step



• 1/2 Mg

Overview

Steps/Stages

1.1 S:DMF, 1 h, 120°C

1.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

Notes

alternative preparation shown,conversion = 40%, Reactants: 2, Reagents: 1, Solvents: 4, Steps: 1, Stages: 2, Most stages in any one step: 2

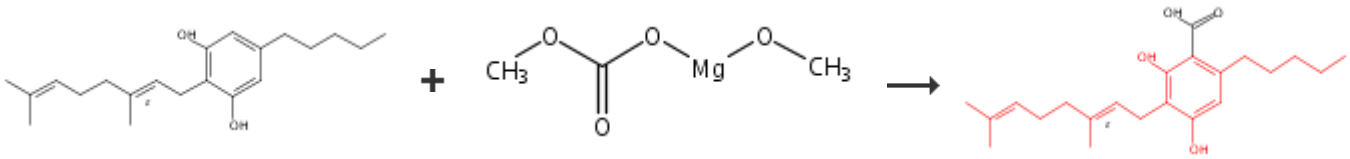
References

Methods for the manufacture of cannabinoid prodrugs, pharmaceutical formulations and their use

By Peet, Richard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017216362, 21 Dec 2017

32. Single Step



Overview

Steps/Stages

1.1 S:DMF, 1 h, 120°C

1.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

Notes

conversion, 40%, alternative preparation shown, Reactants: 2, Reagents: 1, Solvents: 4, Steps: 1, Stages: 2, Most stages in any one step: 2

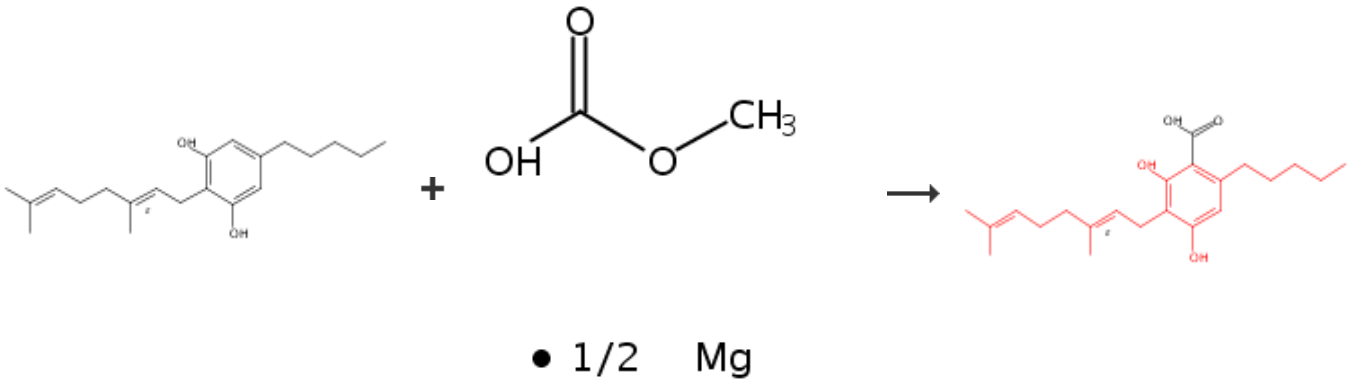
References

Chemoenzymatic synthesis of tetrahydrocannabivarin, carnnabivarin, and cannabinol

By Kavarana, Malcolm J. and Peet, Richard C.

From U.S. Pat. Appl. Publ., 20170283837, 05 Oct 2017

33. Single Step



Overview

Steps/Stages

1.1 S:DMF, 1 h, 120°C

1.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

Notes

conversion = 40%,alternative preparation shown, Reactants: 2, Reagents: 1, Solvents: 4, Steps: 1, Stages: 2, Most stages in any one step: 2

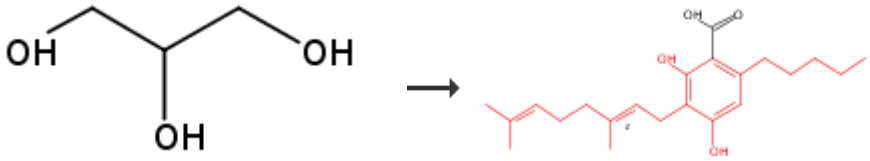
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

34. Single Step

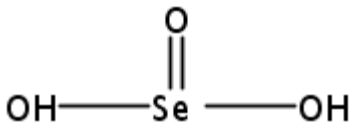


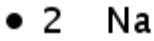
Overview

Steps/Stages

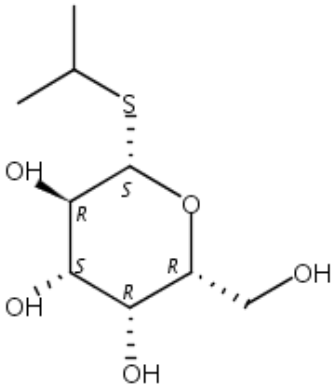
Notes

1.1 R:





R:



R:NaOH, R:H_2SO_4, S:H_2O, 37°C, pH 7

biotransformation, enzymic, fermentation, alternate reaction conditions also shown, Reactants: 1, Reagents: 4, Solvents: 1, Steps: 1, Stages: 1, Most stages in any one step: 1

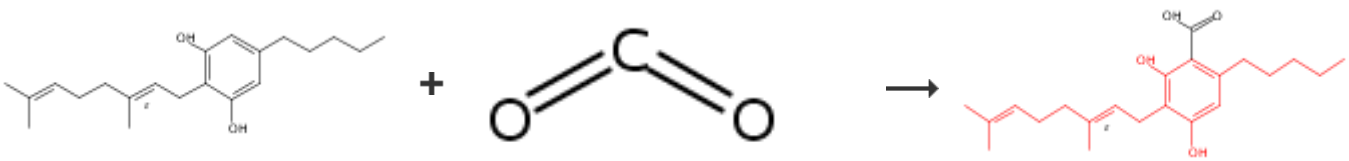
References

Engineered metabolic pathways for the in-vivo or in-vitro biosynthesis of polyketides

By Gonzalez, Ramon et al

From PCT Int. Appl., 2017020043, 02 Feb 2017

35. Single Step



38%

Overview

Steps/Stages

1.1 R:$Mg(OMe)_2$, S:DMF, rt → 50°C; 3 h, 50°C; 50°C → rt

1.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, rt, pH 2

Notes

alternative preparation shown,conversion = 85%, Reactants: 2, Reagents: 2, Solvents: 4, Steps: 1, Stages: 2, Most stages in any one step: 2

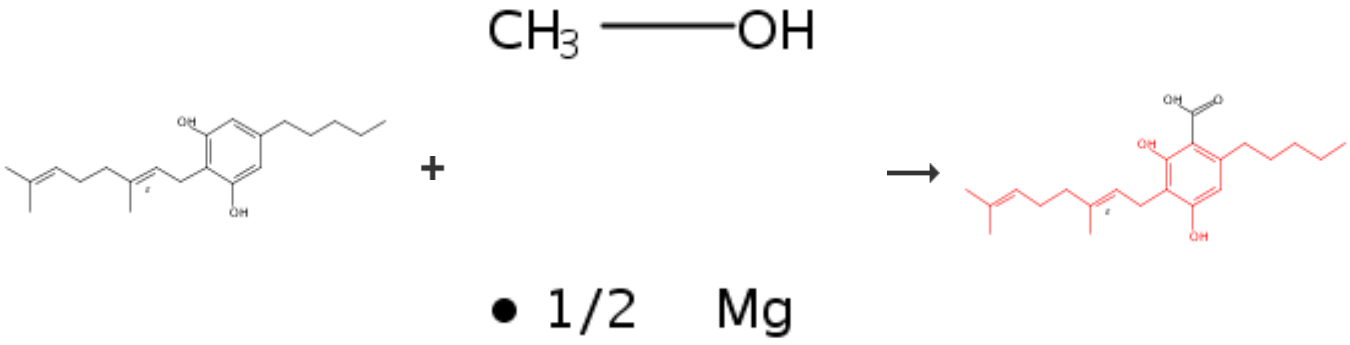
References

Methods for the manufacture of cannabinoid prodrugs, pharmaceutical formulations and their use

By Peet, Richard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017216362, 21 Dec 2017

36. Single Step



38%

Overview

Steps/Stages

1.1 R:CO_2, cooled; 50°C; 3 h, 50°C; 50°C → rt

1.2 R:HCl, S:H_2O, rt, pH 2

Notes

conversion, 85%, sealed vessel used, alternative preparation shown, Reactants: 2, Reagents: 2, Solvents: 1, Steps: 1, Stages: 2, Most stages in any one step: 2

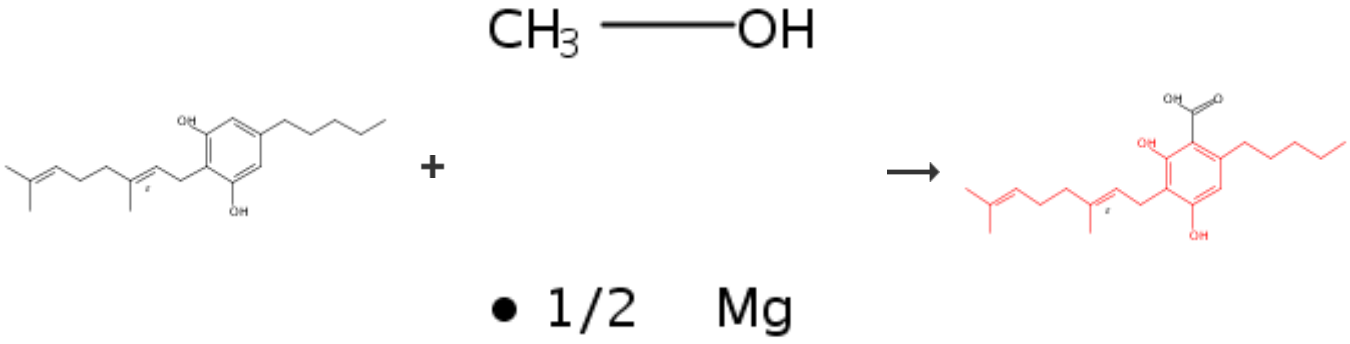
References

Chemoenzymatic synthesis of tetrahydrocannabivarin, carnnabivarin, and cannabinol

By Kavarana, Malcolm J. and Peet, Richard C.

From U.S. Pat. Appl. Publ., 20170283837, 05 Oct 2017

37. Single Step



38%

Overview

Steps/Stages

Notes

1.1 S:H_2O, cooled; 50°C; 3 h, 50°C; 50°C → rt

1.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, rt, pH 2

conversion = 85%,alternative preparation shown,reaction in a sealed pressure vessel, Reactants: 2, Reagents: 1, Solvents: 3, Steps: 1, Stages: 2, Most stages in any one step: 2

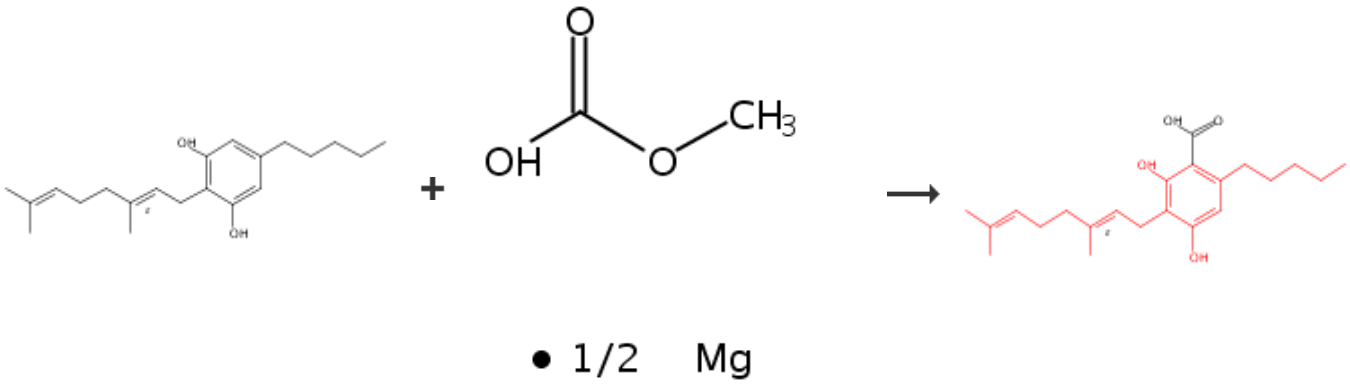
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

38. Single Step



38%

Overview

Steps/Stages

1.1 rt → 50°C; 3 h, 50°C; 50°C → rt

1.2 R:HCl, S:H_2O, S:MeOH, S:$CHCl_3$, rt, pH 2

Notes

conversion, 85%, alternative preparation shown, sealed vessel used, Reactants: 2, Reagents: 1, Solvents: 3, Steps: 1, Stages: 2, Most stages in any one step: 2

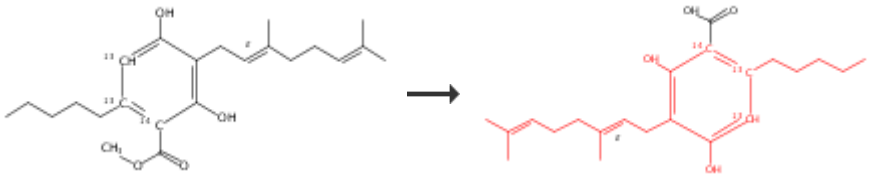
References

Chemoenzymic synthesis of cannabinoids

By Winnicki, Robert and Donsky, Marc

From PCT Int. Appl., 2014134281, 04 Sep 2014

39. Single Step



Overview

Steps/Stages

1.1 R:LiSPr, S:$(Me_2N)_3P=O$

1.2 R:HCl, S:H_2O

Notes

Reactants: 1, Reagents: 2, Solvents: 2, Steps: 1, Stages: 2, Most stages in any one step: 2

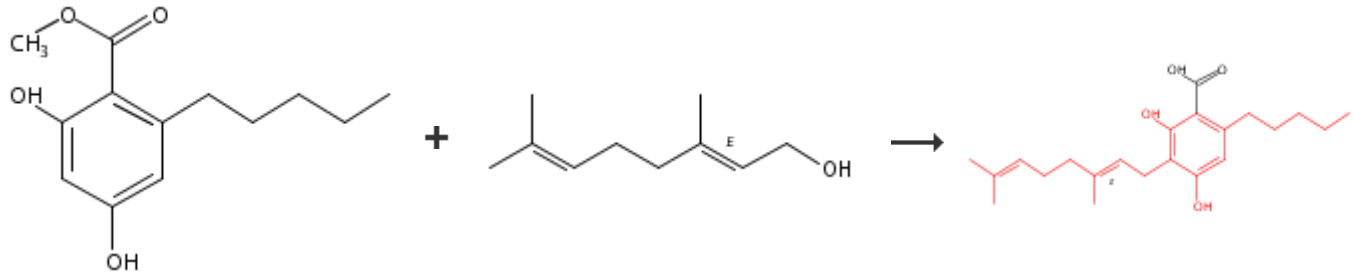
References

Synthesis of [5,6-13C2,1-14C]olivetolic acid, methyl [1'-13C]olivetolate and [5,6-13C2,1-14C]cannabigerolic acid

By Porwoll, Joseph P. and Leete, Edward

From Journal of Labelled Compounds and Radiopharmaceuticals, 22(3), 257-71; 1985

40. 2 Steps



Overview

Steps/Stages

1.1 R:BF_3-Et_2O, S:$CHCl_3$, 0.25 h, -20°C

2.1 R:Cs_2CO_3, R:PhSH, S:DMF, 24 h, 85°C

2.2 R:HCl, S:H_2O, cooled, pH 3

Notes

2) alternate reaction conditions gave lower yield, Reactants: 2, Reagents: 4, Solvents: 3, Steps: 2, Stages: 3, Most stages in any one step: 2

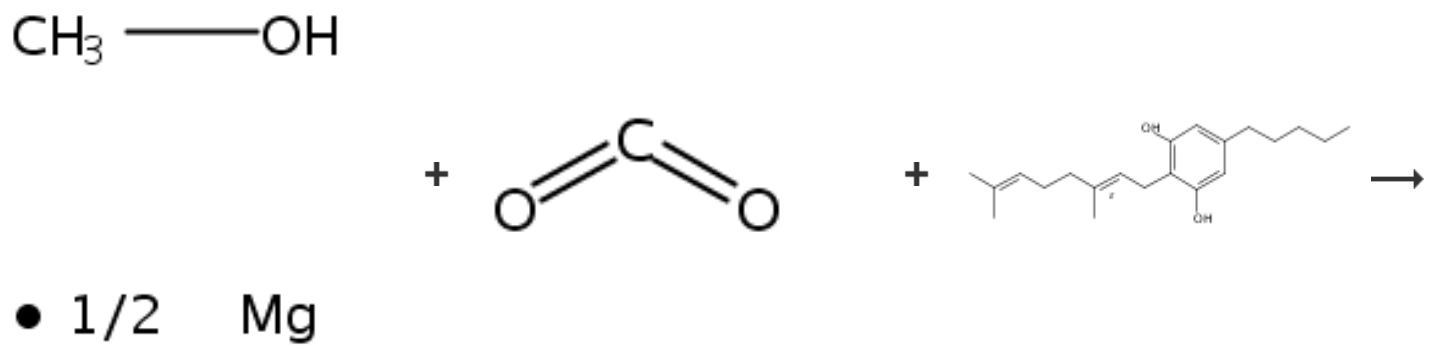
References

Synthesis of phytocannabinoids including a demethylation step

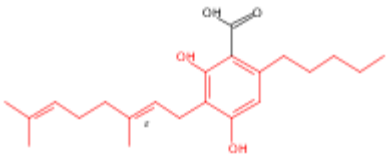
By Reekie, Tristan et al

From PCT Int. Appl., 2019033164, 21 Feb 2019

41. 2 Steps



[Step 2.1]



Overview

Steps/Stages

1.1 S:DMF, 140°C
2.1 S:DMF, 1 h, 120°C

2.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

Notes

2) alternative preparation shown,conversion = 40%, Reactants: 3, Reagents: 1, Solvents: 4, Steps: 2, Stages: 3, Most stages in any one step: 2

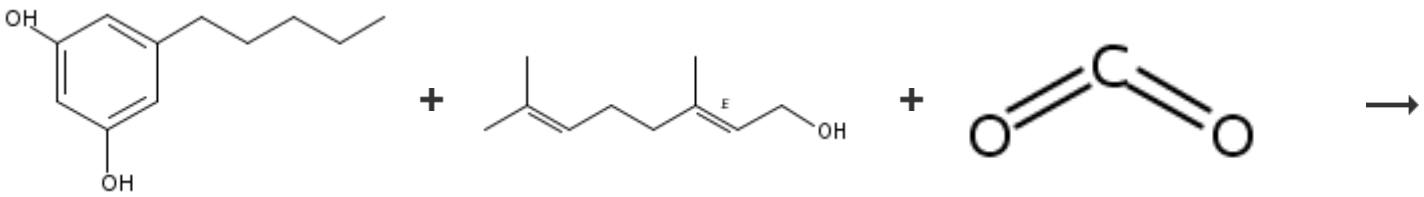
References

Methods for the manufacture of cannabinoid prodrugs, pharmaceutical formulations and their use

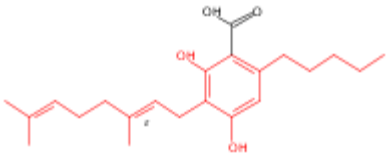
By Peet, Richard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017216362, 21 Dec 2017

42. 2 Steps



[Step 2.1]



Overview

Steps/Stages

1.1 C:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

2.1 R:$Mg(OMe)_2$, S:DMF, rt → 50°C; 3 h, 50°C; 50°C → rt

2.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, rt, pH 2

Notes

2) alternative preparation shown,conversion = 85%, Reactants: 3, Reagents: 2, Catalysts: 1, Solvents: 4, Steps: 2, Stages: 3, Most stages in any one step: 2

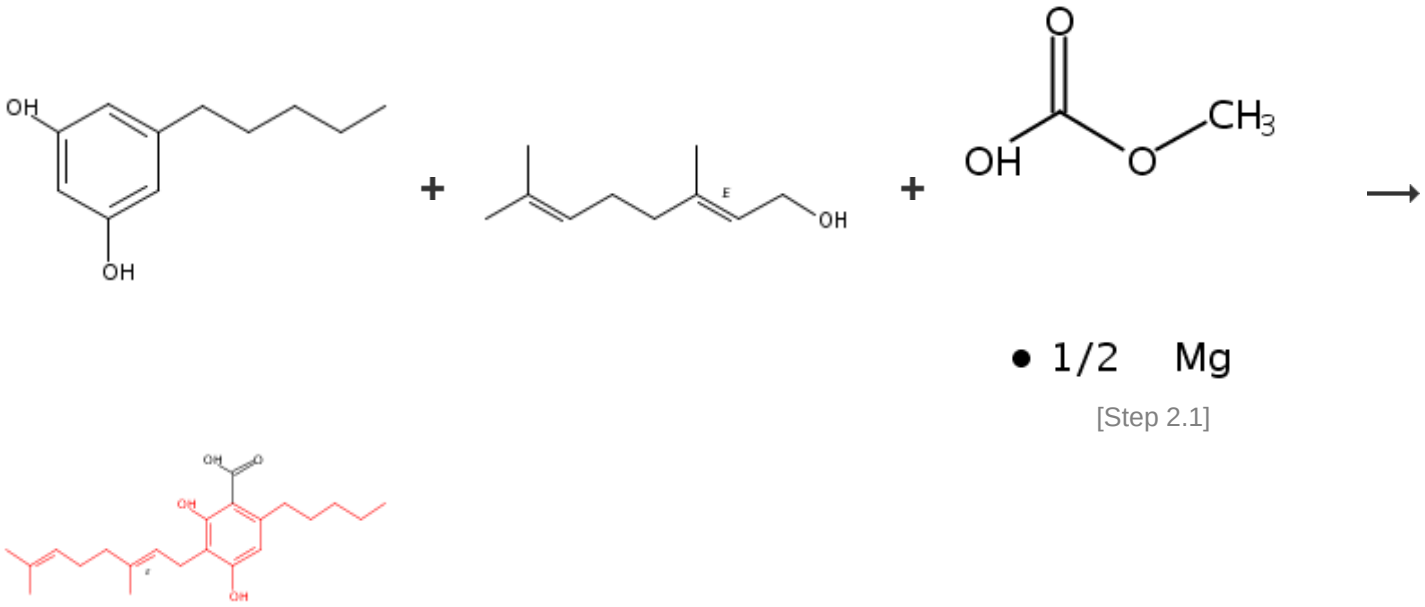
References

Methods for the manufacture of cannabinoid prodrugs, pharmaceutical formulations and their use

By Peet, Richard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017216362, 21 Dec 2017

43. 2 Steps



Overview

Steps/Stages

1.1 C:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
2.1 S:DMF, 1 h, 120°C

2.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

Notes

2) alternative preparation shown,conversion = 40%, Reactants: 3, Reagents: 1, Catalysts: 1, Solvents: 4, Steps: 2, Stages: 3, Most stages in any one step: 2

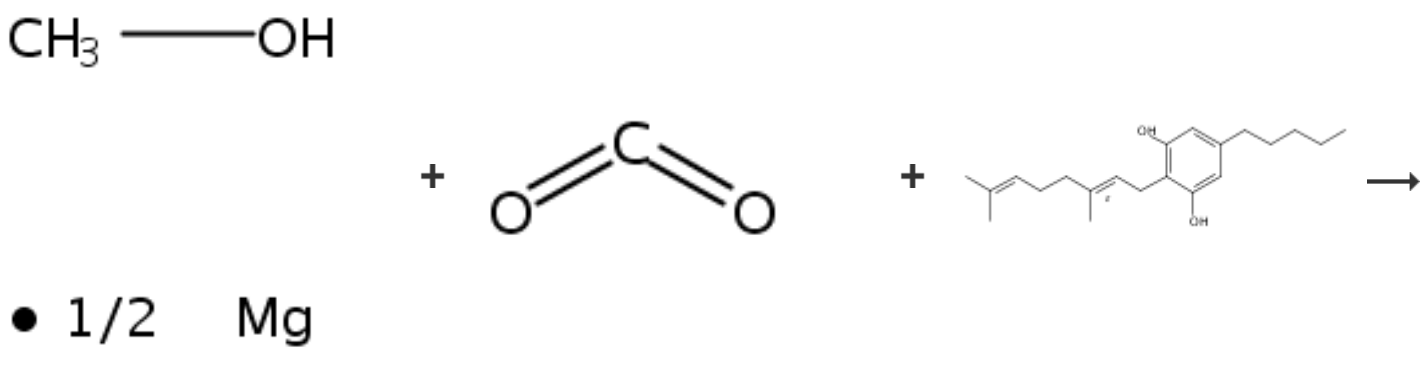
References

Methods for the manufacture of cannabinoid prodrugs, pharmaceutical formulations and their use

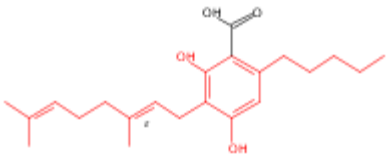
By Peet, Richard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017216362, 21 Dec 2017

44. 2 Steps



[Step 2.1]



Overview

Steps/Stages

1.1 S:DMF, 140°C
2.1 S:DMF, 1 h, 120°C

2.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

Notes

1) exothermic, 2) conversion, 40%, alternative preparation shown, Reactants: 3, Reagents: 1, Solvents: 4, Steps: 2, Stages: 3, Most stages in any one step: 2

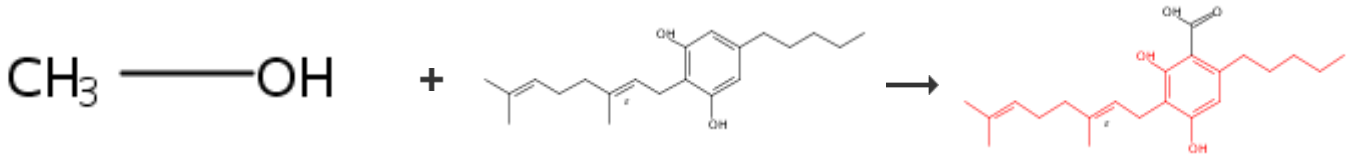
References

Chemoenzymatic synthesis of tetrahydrocannabivarin, carnnabivarin, and cannabinol

By Kavarana, Malcolm J. and Peet, Richard C.

From U.S. Pat. Appl. Publ., 20170283837, 05 Oct 2017

45. 2 Steps



[Step 2.1]

Overview

Steps/Stages

1.1 R:Mg, S:MeOH, cooled

2.1 R:CO_2, cooled; 50°C; 3 h, 50°C; 50°C → rt

2.2 R:HCl, S:H_2O, rt, pH 2

Notes

2) conversion, 85%, sealed vessel used, alternative preparation shown, Reactants: 2, Reagents: 3, Solvents: 2, Steps: 2, Stages: 3, Most stages in any one step: 2

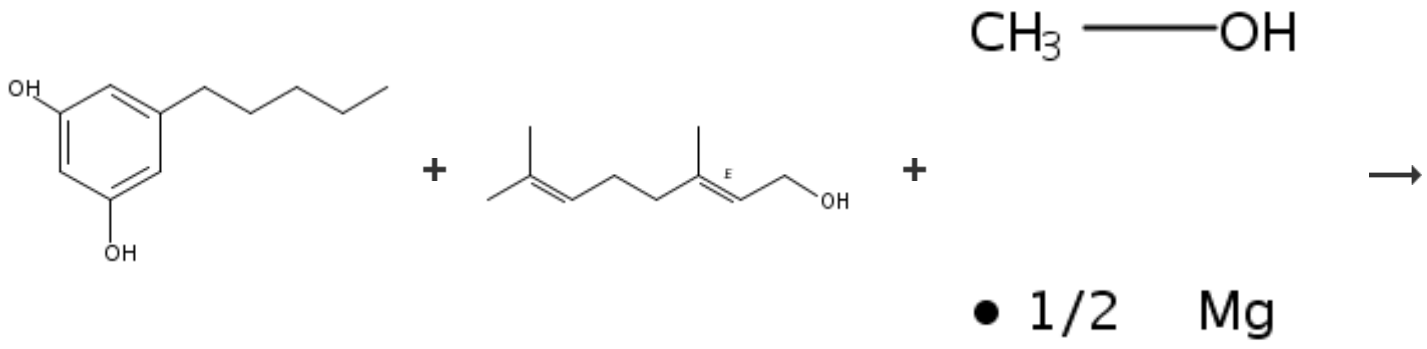
References

Chemoenzymatic synthesis of tetrahydrocannabivarin, carnnabivarin, and cannabinol

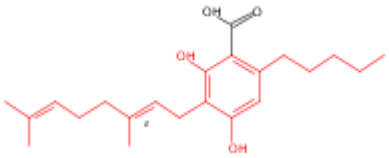
By Kavarana, Malcolm J. and Peet, Richard C.

From U.S. Pat. Appl. Publ., 20170283837, 05 Oct 2017

46. 2 Steps



[Step 2.1]



Overview

Steps/Stages

1.1 C:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

2.1 R:CO_2, cooled; 50°C; 3 h, 50°C; 50°C → rt

2.2 R:HCl, S:H_2O, rt, pH 2

Notes

1) in the dark, 2) conversion, 85%, sealed vessel used, alternative preparation shown, Reactants: 3, Reagents: 2, Catalysts: 1, Solvents: 2, Steps: 2, Stages: 3, Most stages in any one step: 2

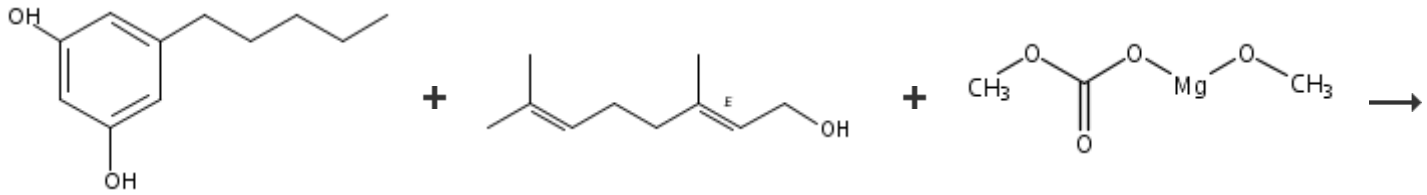
References

Chemoenzymatic synthesis of tetrahydrocannabivarin, carnnabivarin, and cannabinol

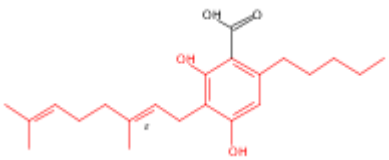
By Kavarana, Malcolm J. and Peet, Richard C.

From U.S. Pat. Appl. Publ., 20170283837, 05 Oct 2017

47. 2 Steps



[Step 2.1]



Overview

Steps/Stages

Notes

1.1 C:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
2.1 S:DMF, 1 h, 120°C

2.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

1) in the dark, 2) conversion, 40%, alternative preparation shown, Reactants: 3, Reagents: 1, Catalysts: 1, Solvents: 4, Steps: 2, Stages: 3, Most stages in any one step: 2

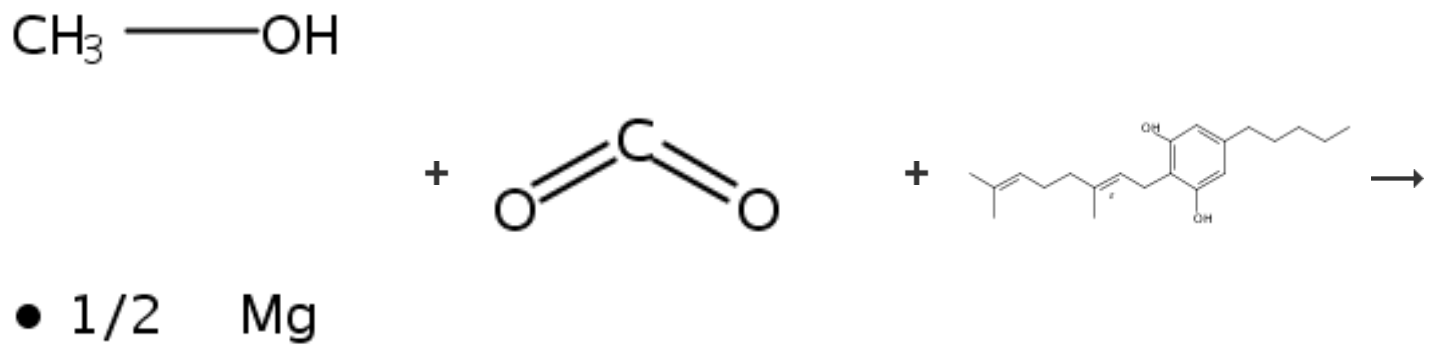
References

Chemoenzymatic synthesis of tetrahydrocannabivarin, carnnabivarin, and cannabinol

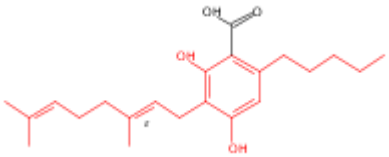
By Kavarana, Malcolm J. and Peet, Richard C.

From U.S. Pat. Appl. Publ., 20170283837, 05 Oct 2017

48. 2 Steps



[Step 2.1]



Overview

Steps/Stages

1.1 S:DMF, 140°C
2.1 S:DMF, 1 h, 120°C

2.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

Notes

1) exothermic reaction, 2) conversion = 40%,alternative preparation shown, Reactants: 3, Reagents: 1, Solvents: 4, Steps: 2, Stages: 3, Most stages in any one step: 2

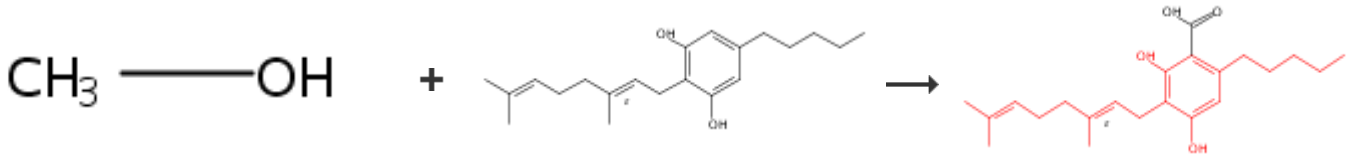
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

49. 2 Steps



[Step 2.1]

Overview

Steps/Stages

1.1 R:Mg, S:MeOH, rt
2.1 S:H_2O, cooled; 50°C; 3 h, 50°C; 50°C → rt

2.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, rt, pH 2

Notes

2) conversion = 85%,alternative preparation shown,reaction in a sealed pressure vessel, Reactants: 2, Reagents: 2, Solvents: 3, Steps: 2, Stages: 3, Most stages in any one step: 2

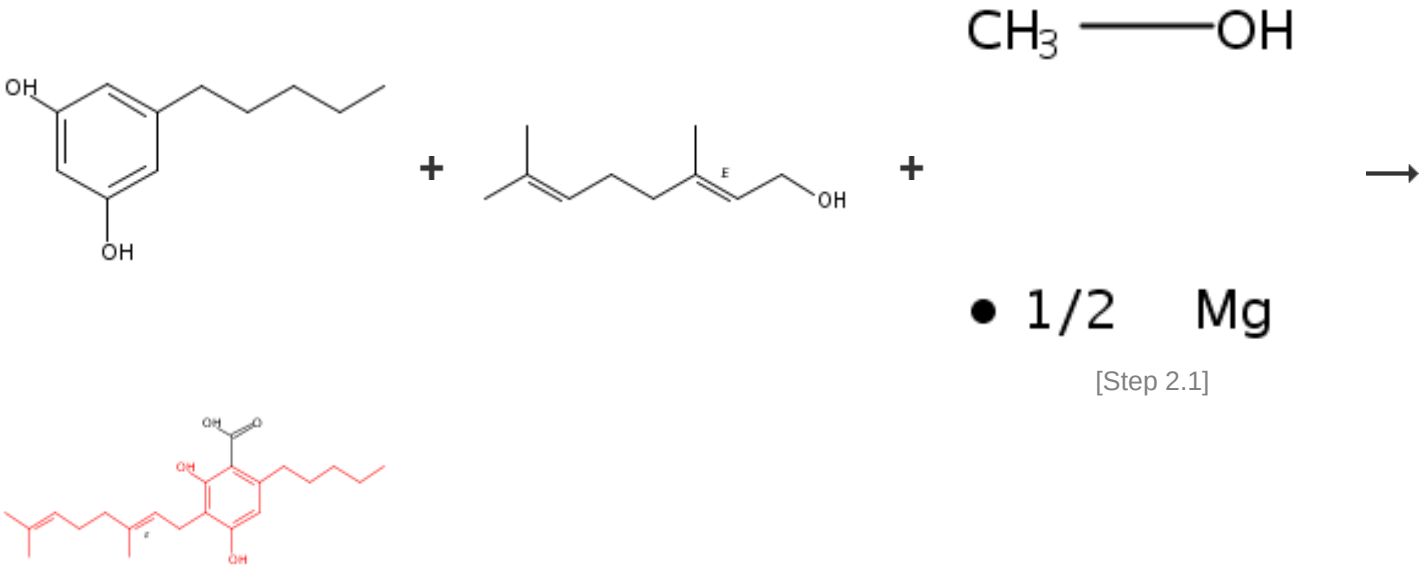
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

50. 2 Steps



[Step 2.1]

Overview

Steps/Stages

1.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
2.1 S:H_2O, cooled; 50°C; 3 h, 50°C; 50°C → rt

2.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, rt, pH 2

Notes

1) in the dark, 2) conversion = 85%,alternative preparation shown,reaction in a sealed pressure vessel, Reactants: 3, Reagents: 2, Solvents: 3, Steps: 2, Stages: 3, Most stages in any one step: 2

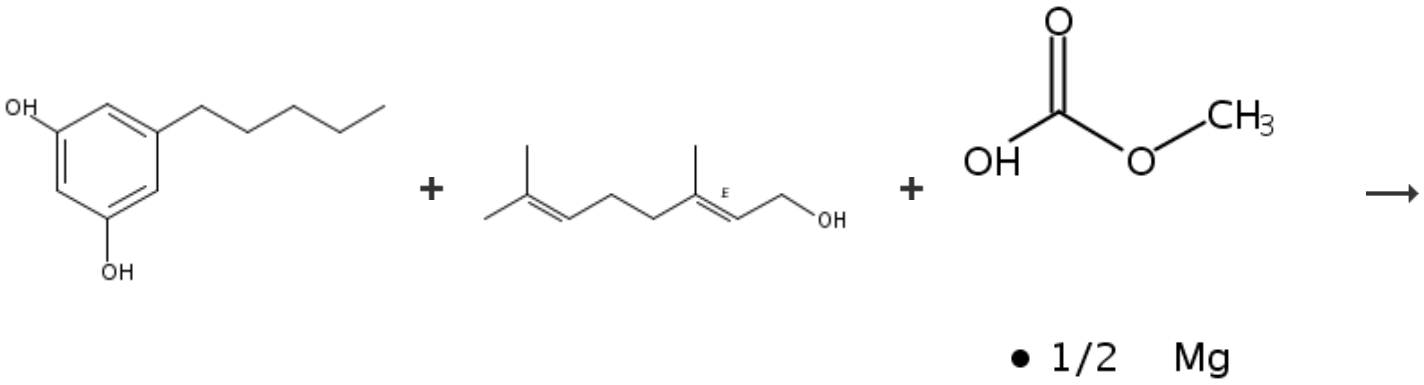
References

Biosynthesis of cannabinoid prodrugs

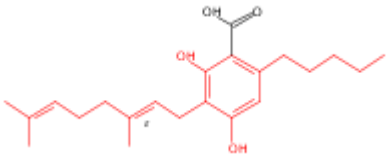
By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

51. 2 Steps



[Step 2.1]



Overview

Steps/Stages

1.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
2.1 S:DMF, 1 h, 120°C

2.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

Notes

1) in the dark, 2) conversion = 40%,alternative preparation shown, Reactants: 3, Reagents: 2, Solvents: 4, Steps: 2, Stages: 3, Most stages in any one step: 2

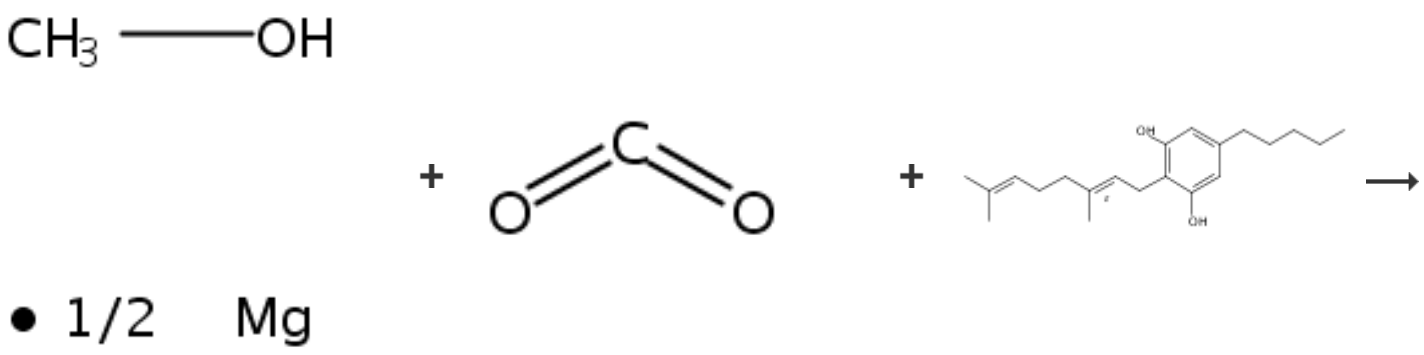
References

Biosynthesis of cannabinoid prodrugs

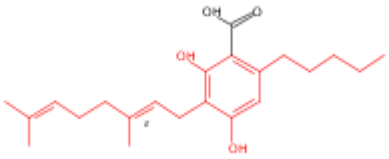
By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

52. 2 Steps



[Step 2.1]



Overview

Steps/Stages

1.1 S:DMF
2.1 S:DMF, 1 h, 120°C

2.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

Notes

1) exothermic, 2) alternative preparation gave lower yield, LH-20 Sephadex resin, LH-20 lipophilic resin, Reactants: 3, Reagents: 1, Solvents: 4, Steps: 2, Stages: 3, Most stages in any one step: 2

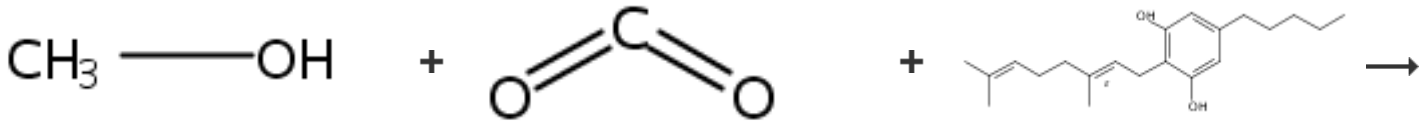
References

Bioreactor and process for the enzymatic biosynthesis of cannabinoids

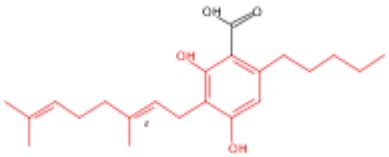
By Peet, Richard and Sun, Mingyang

From U.S. Pat. Appl. Publ., 20160053220, 25 Feb 2016

53. 2 Steps



[Step 2.1]



Overview

Steps/Stages

1.1 R:Mg, S:MeOH, rt
1.2 S:DMF, 140°C
2.1 rt → 50°C; 3 h, 50°C; 50°C → rt

2.2 R:HCl, S:H_2O, S:MeOH, S:$CHCl_3$, rt, pH 2

Notes

1) literature preparation, exothermic (stage 2), 2) conversion, 85%, alternative preparation shown, sealed vessel used, Reactants: 3, Reagents: 2, Solvents: 4, Steps: 2, Stages: 4, Most stages in any one step: 2

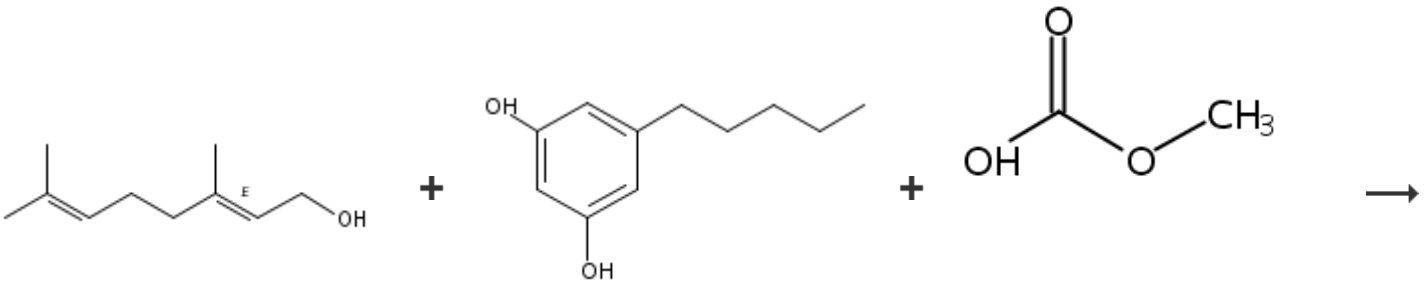
References

Chemoenzymic synthesis of cannabinoids

By Winnicki, Robert and Donsky, Marc

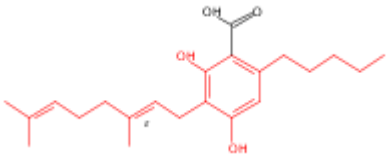
From PCT Int. Appl., 2014134281, 04 Sep 2014

54. 2 Steps



• 1/2 Mg

[Step 2.1]



Overview

Steps/Stages

1.1 C:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
2.1 rt → 50°C; 3 h, 50°C; 50°C → rt

2.2 R:HCl, S:H_2O, S:MeOH, S:$CHCl_3$, rt, pH 2

Notes

1) literature preparation, in the dark, 2) conversion, 85%, alternative preparation shown, sealed vessel used, Reactants: 3, Reagents: 1, Catalysts: 1, Solvents: 3, Steps: 2, Stages: 3, Most stages in any one step: 2

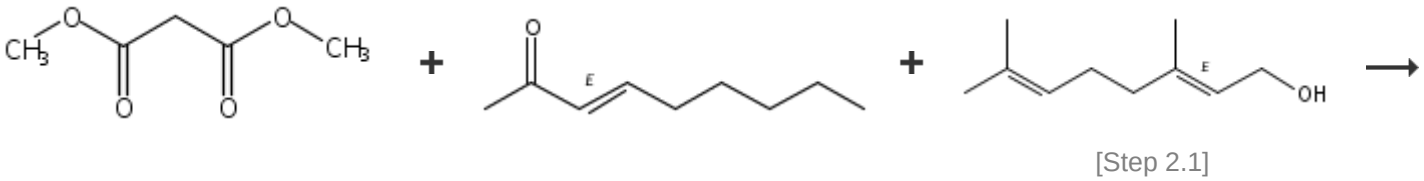
References

Chemoenzymic synthesis of cannabinoids

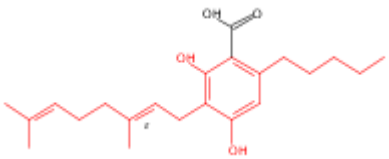
By Winnicki, Robert and Donsky, Marc

From PCT Int. Appl., 2014134281, 04 Sep 2014

55. 3 Steps



[Step 2.1]



Overview

Steps/Stages

Notes

1.1 R:Na, S:MeOH, 0°C; 8 h, reflux

1.2 R:Br_2, S:DMF, 0°C; 1 h, 20°C; 16 h, 20°C → 80°C; cooled

1.3 R:$Na_2S_2O_3$, S:H_2O

2.1 R:BF_3-Et_2O, S:$CHCl_3$, 0.25 h, -20°C

3.1 R:Cs_2CO_3, R:PhSH, S:DMF, 24 h, 85°C

3.2 R:HCl, S:H_2O, cooled, pH 3

3) alternate reaction conditions gave lower yield, Reactants: 3, Reagents: 7, Solvents: 4, Steps: 3, Stages: 6, Most stages in any one step: 3

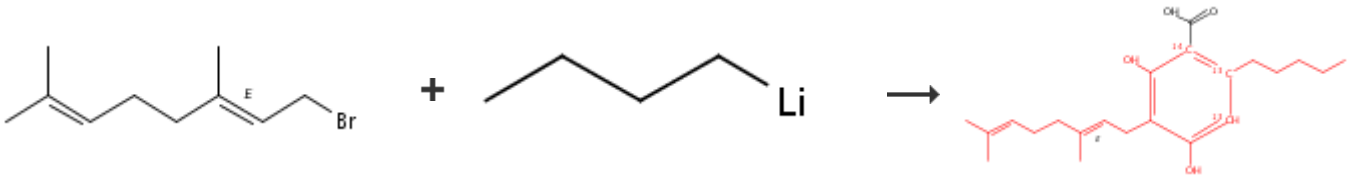
References

Synthesis of phytocannabinoids including a demethylation step

By Reekie, Tristan et al

From PCT Int. Appl., 2019033164, 21 Feb 2019

56. 2 Steps



Overview

Steps/Stages

1.1 R:Benzene

1.2 R:HCl, S:H_2O

2.1 R:LiSPr, S:$(Me_2N)_3P{=}O$

2.2 R:HCl, S:H_2O

Notes

Reactants: 2, Reagents: 3, Solvents: 2, Steps: 2, Stages: 4, Most stages in any one step: 2

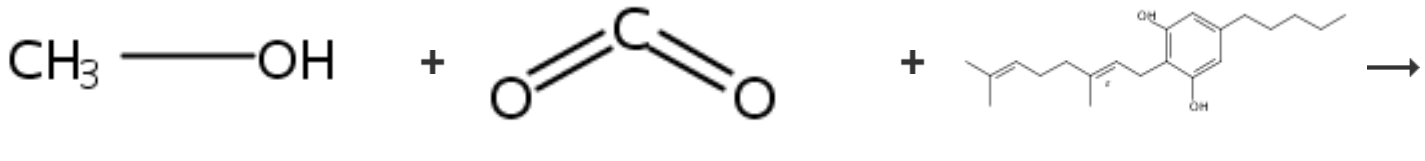
References

Synthesis of [5,6-13C2,1-14C]olivetolic acid, methyl [1'-13C]olivetolate and [5,6-13C2,1-14C]cannabigerolic acid

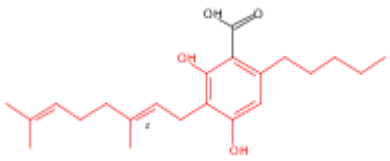
By Porwoll, Joseph P. and Leete, Edward

From Journal of Labelled Compounds and Radiopharmaceuticals, 22(3), 257-71; 1985

57. 3 Steps



[Step 2.1] [Step 3.1]



Overview

Steps/Stages

1.1 R:Mg, S:MeOH, cooled
2.1 S:DMF, 140°C
3.1 S:DMF, 1 h, 120°C

3.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

Notes

3) alternative preparation shown,conversion = 40%, Reactants: 3, Reagents: 2, Solvents: 4, Steps: 3, Stages: 4, Most stages in any one step: 2

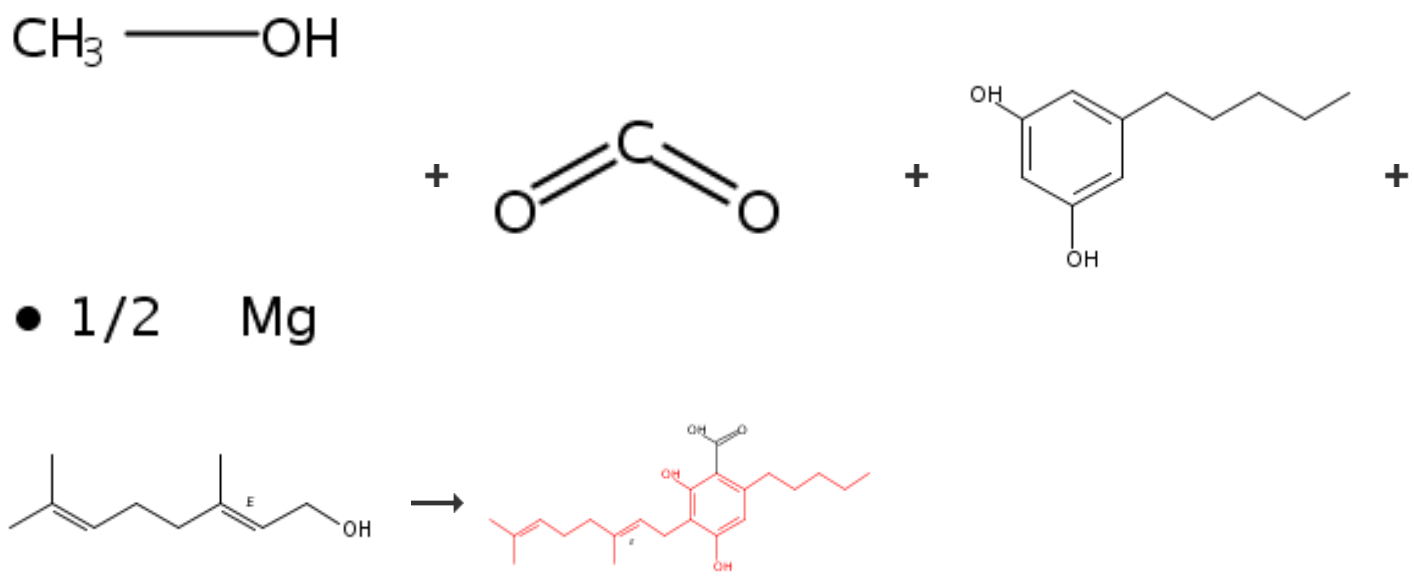
References

Methods for the manufacture of cannabinoid prodrugs, pharmaceutical formulations and their use

By Peet, Richard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017216362, 21 Dec 2017

58. 3 Steps (Converging)



Overview

Steps/Stages

1.1 S:DMF, 140°C
1.1 C:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
2.1 S:DMF, 1 h, 120°C

2.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

Notes

alternative preparation shown,conversion = 40%, Reactants: 4, Reagents: 1, Catalysts: 1, Solvents: 4, Steps: 3, Stages: 4, Most stages in any one step: 2

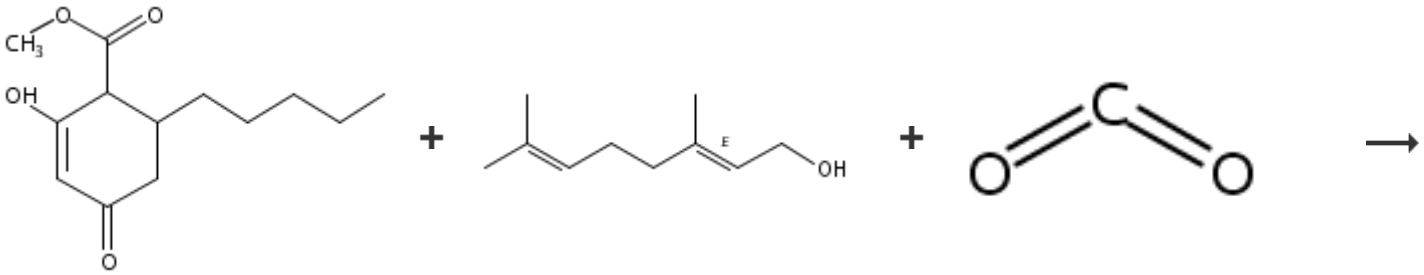
References

Methods for the manufacture of cannabinoid prodrugs, pharmaceutical formulations and their use

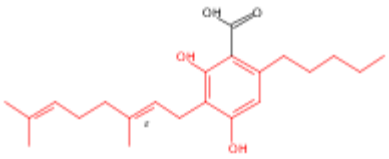
By Peet, Richard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017216362, 21 Dec 2017

59. 3 Steps



[Step 2.1] [Step 3.1]



Overview

Steps/Stages

1.1 R:Br_2, S:DMF, 90 min, cooled; 80°C → 160°C; 10 h, 160°C
2.1 C:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

3.1 R:$Mg(OMe)_2$, S:DMF, rt → 50°C; 3 h, 50°C; 50°C → rt

3.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, rt, pH 2

Notes

3) alternative preparation shown,conversion = 85%, Reactants: 3, Reagents: 3, Catalysts: 1, Solvents: 4, Steps: 3, Stages: 4, Most stages in any one step: 2

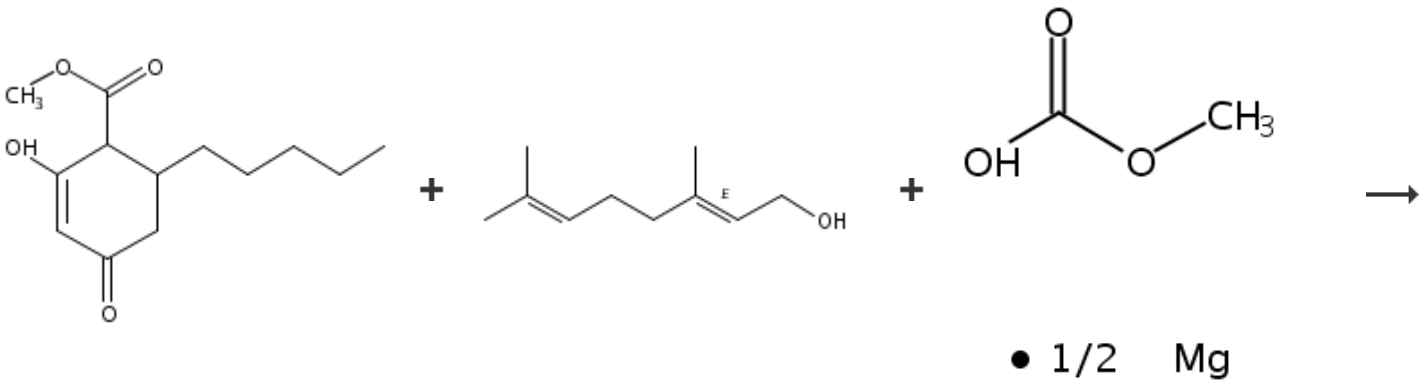
References

Methods for the manufacture of cannabinoid prodrugs, pharmaceutical formulations and their use

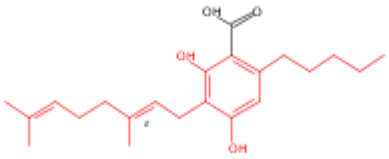
By Peet, Richard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017216362, 21 Dec 2017

60. 3 Steps



[Step 2.1] [Step 3.1]



Overview

Steps/Stages

1.1 R:Br_2, S:DMF, 90 min, cooled; 80°C → 160°C; 10 h, 160°C
2.1 C:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
3.1 S:DMF, 1 h, 120°C

3.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

Notes

3) alternative preparation shown,conversion = 40%, Reactants: 3, Reagents: 2, Catalysts: 1, Solvents: 4, Steps: 3, Stages: 4, Most stages in any one step: 2

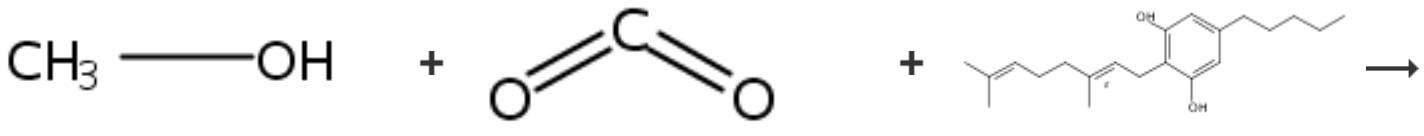
References

Methods for the manufacture of cannabinoid prodrugs, pharmaceutical formulations and their use

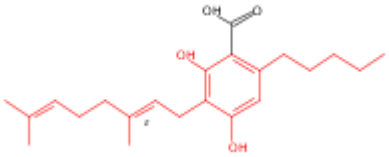
By Peet, Richard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017216362, 21 Dec 2017

61. 3 Steps



[Step 2.1] [Step 3.1]



Overview

Steps/Stages

1.1 R:Mg, S:MeOH, cooled
2.1 S:DMF, 140°C
3.1 S:DMF, 1 h, 120°C

3.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

Notes

2) exothermic, 3) conversion, 40%, alternative preparation shown, Reactants: 3, Reagents: 2, Solvents: 4, Steps: 3, Stages: 4, Most stages in any one step: 2

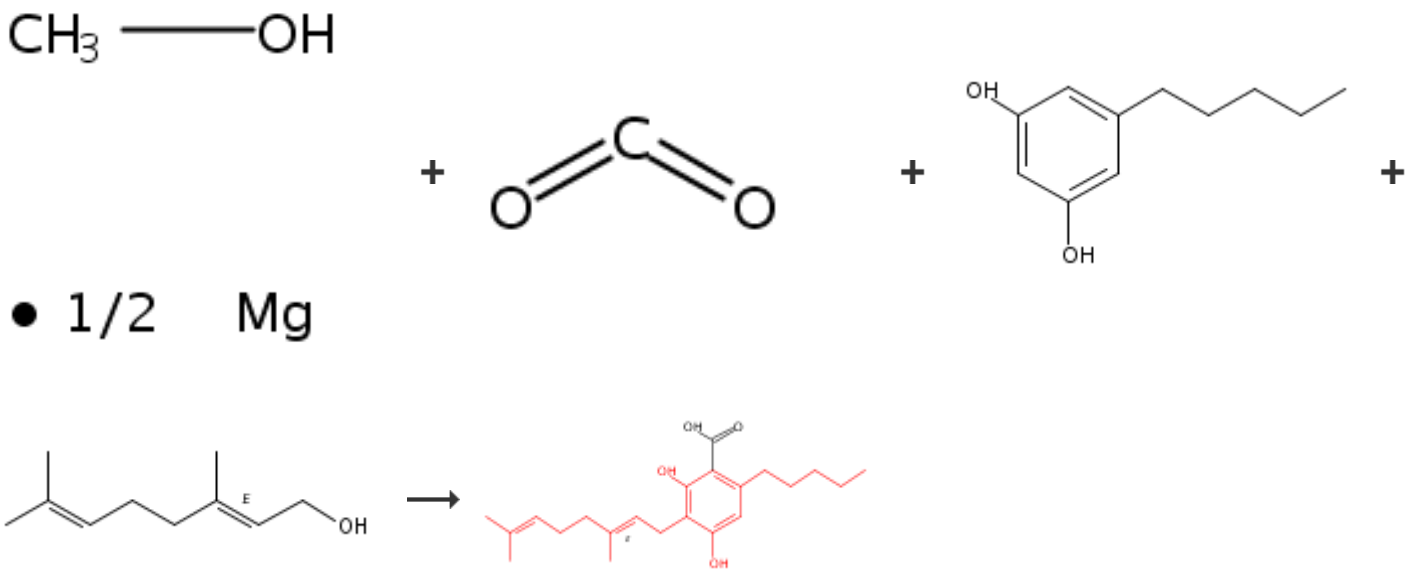
References

Chemoenzymatic synthesis of tetrahydrocannabivarin, carnnabivarin, and cannabinol

By Kavarana, Malcolm J. and Peet, Richard C.

From U.S. Pat. Appl. Publ., 20170283837, 05 Oct 2017

62. 3 Steps (Converging)



Overview

Steps/Stages

1.1 S:DMF, 140°C
1.1 C:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
2.1 S:DMF, 1 h, 120°C

2.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

Notes

exothermic, in the dark, conversion, 40%, alternative preparation shown, Reactants: 4, Reagents: 1, Catalysts: 1, Solvents: 4, Steps: 3, Stages: 4, Most stages in any one step: 2

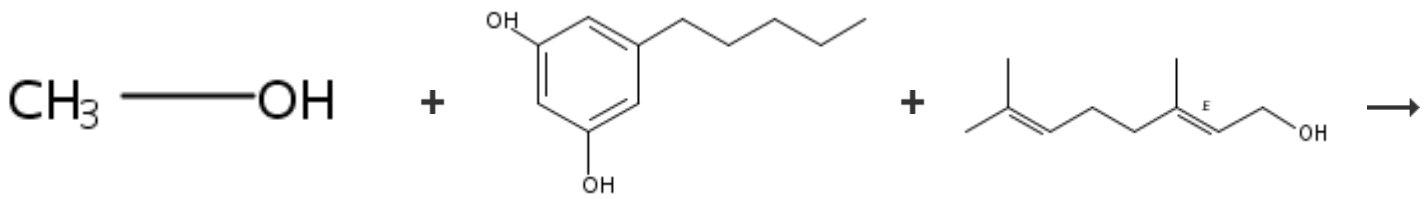
References

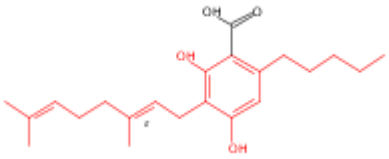
Chemoenzymatic synthesis of tetrahydrocannabivarin, carnnabivarin, and cannabinol

By Kavarana, Malcolm J. and Peet, Richard C.

From U.S. Pat. Appl. Publ., 20170283837, 05 Oct 2017

63. 3 Steps (Converging)





Overview

Steps/Stages

1.1 R:Mg, S:MeOH, cooled

1.1 C:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

2.1 R:CO_2, cooled; 50°C; 3 h, 50°C; 50°C → rt

2.2 R:HCl, S:H_2O, rt, pH 2

Notes

in the dark, conversion, 85%, sealed vessel used, alternative preparation shown, Reactants: 3, Reagents: 3, Catalysts: 1, Solvents: 3, Steps: 3, Stages: 4, Most stages in any one step: 2

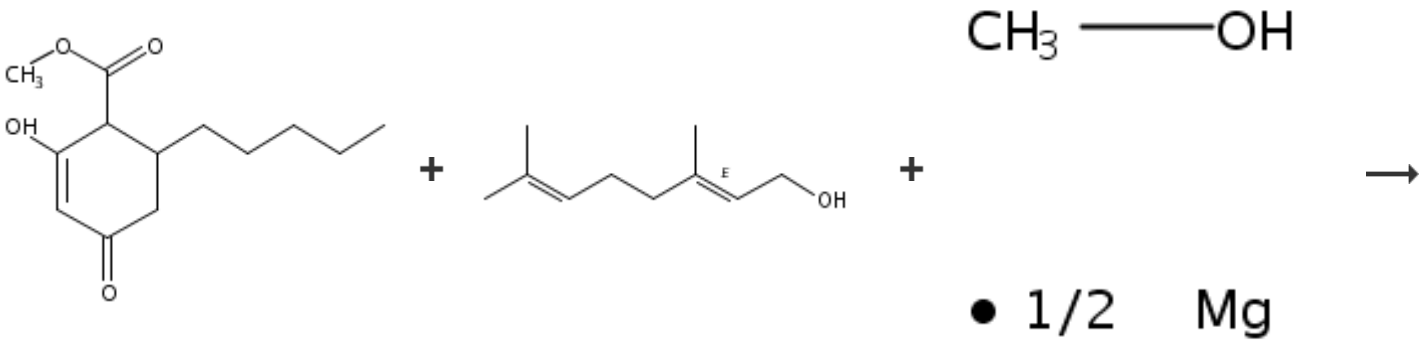
References

Chemoenzymatic synthesis of tetrahydrocannabivarin, carnnabivarin, and cannabinol

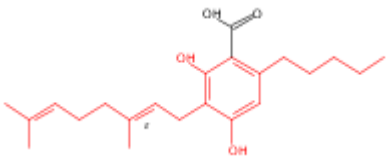
By Kavarana, Malcolm J. and Peet, Richard C.

From U.S. Pat. Appl. Publ., 20170283837, 05 Oct 2017

64. 3 Steps



[Step 2.1] [Step 3.1]



Overview

Steps/Stages

Notes

1.1 R:Br_2, S:DMF, 90 min, cooled; 80°C; 80°C → 160°C; 10 h, 160°C
2.1 C:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

3.1 R:CO_2, cooled; 50°C; 3 h, 50°C; 50°C → rt

3.2 R:HCl, S:H_2O, rt, pH 2

2) in the dark, 3) conversion, 85%, sealed vessel used, alternative preparation shown, Reactants: 3, Reagents: 3, Catalysts: 1, Solvents: 3, Steps: 3, Stages: 4, Most stages in any one step: 2

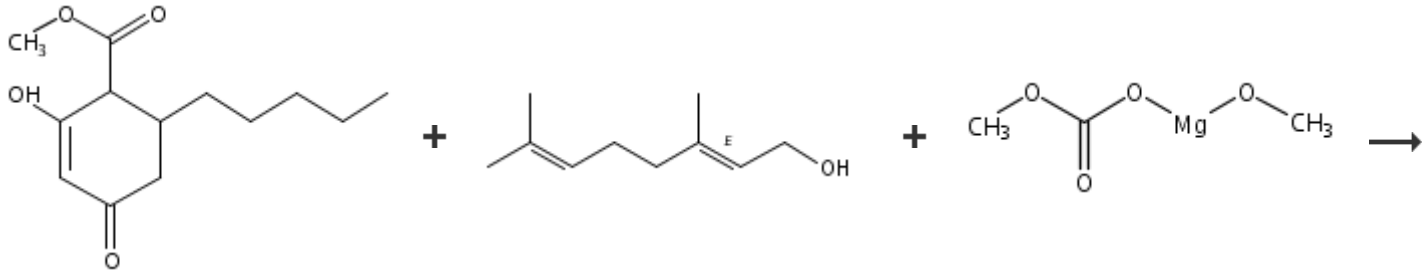
References

Chemoenzymatic synthesis of tetrahydrocannabivarin, carnnabivarin, and cannabinol

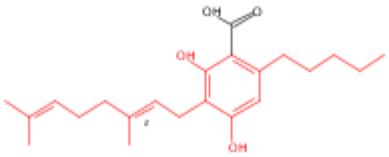
By Kavarana, Malcolm J. and Peet, Richard C.

From U.S. Pat. Appl. Publ., 20170283837, 05 Oct 2017

65. 3 Steps



[Step 2.1] [Step 3.1]



Overview

Steps/Stages

1.1 R:Br_2, S:DMF, 90 min, cooled; 80°C; 80°C → 160°C; 10 h, 160°C
2.1 C:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
3.1 S:DMF, 1 h, 120°C

3.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

Notes

2) in the dark, 3) conversion, 40%, alternative preparation shown, Reactants: 3, Reagents: 2, Catalysts: 1, Solvents: 4, Steps: 3, Stages: 4, Most stages in any one step: 2

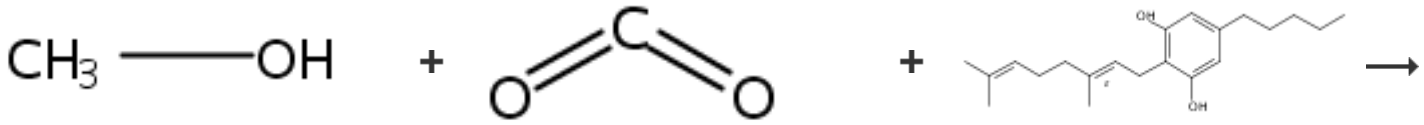
References

Chemoenzymatic synthesis of tetrahydrocannabivarin, carnnabivarin, and cannabinol

By Kavarana, Malcolm J. and Peet, Richard C.

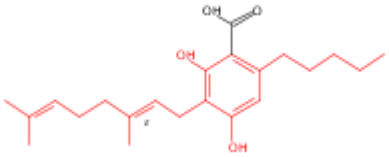
From U.S. Pat. Appl. Publ., 20170283837, 05 Oct 2017

66. 3 Steps



[Step 2.1]

[Step 3.1]



Overview

Steps/Stages

1.1 R:Mg, S:MeOH, rt
2.1 S:DMF, 140°C
3.1 S:DMF, 1 h, 120°C

3.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

Notes

2) exothermic reaction, 3) conversion = 40%,alternative preparation shown, Reactants: 3, Reagents: 2, Solvents: 4, Steps: 3, Stages: 4, Most stages in any one step: 2

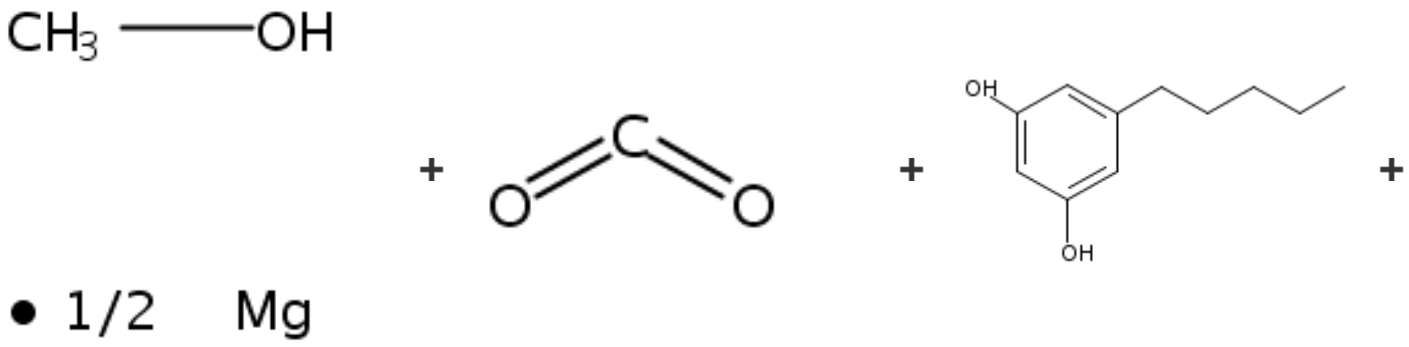
References

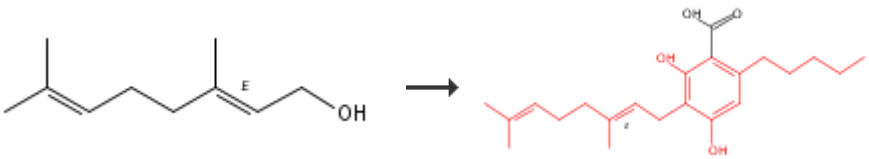
Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

67. 3 Steps (Converging)





Overview

Steps/Stages

Notes

1.1 S:DMF, 140°C

1.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
2.1 S:DMF, 1 h, 120°C

2.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

exothermic reaction, in the dark, conversion = 40%,alternative preparation shown, Reactants: 4, Reagents: 2, Solvents: 4, Steps: 3, Stages: 4, Most stages in any one step: 2

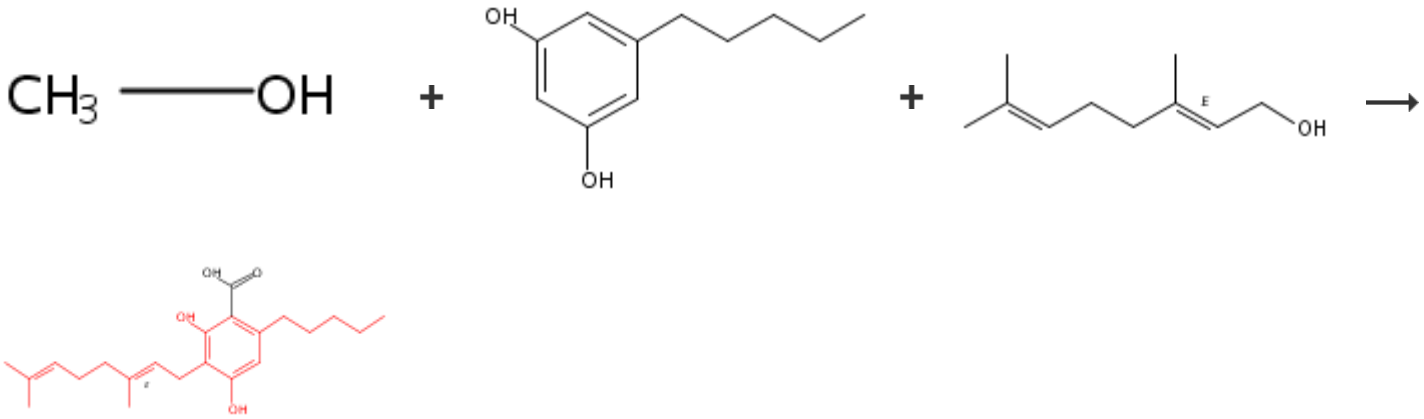
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

68. 3 Steps (Converging)



Overview

Steps/Stages

1.1 R:Mg, S:MeOH, rt

1.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
2.1 S:H_2O, cooled; 50°C; 3 h, 50°C; 50°C → rt

2.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, rt, pH 2

Notes

in the dark, conversion = 85%,alternative preparation shown,reaction in a sealed pressure vessel, Reactants: 3, Reagents: 3, Solvents: 3, Steps: 3, Stages: 4, Most stages in any one step: 2

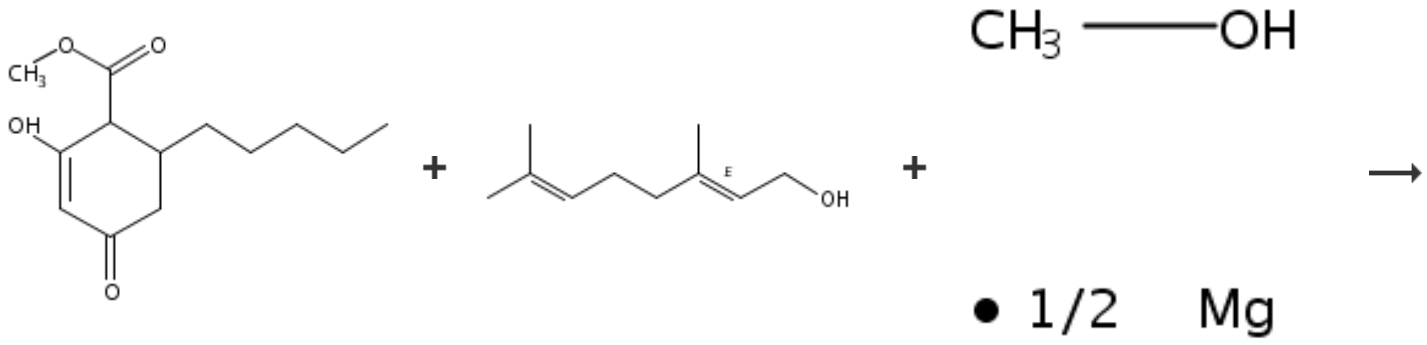
References

Biosynthesis of cannabinoid prodrugs

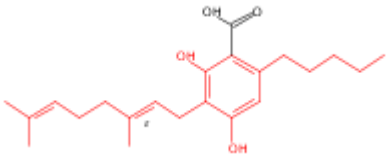
By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

69. 3 Steps



[Step 2.1] [Step 3.1]



Overview

Steps/Stages

1.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

2.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

3.1 S:H_2O, cooled; 50°C; 3 h, 50°C; 50°C → rt

3.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, rt, pH 2

Notes

2) in the dark, 3) conversion = 85%,alternative preparation shown,reaction in a sealed pressure vessel, Reactants: 3, Reagents: 3, Solvents: 4, Steps: 3, Stages: 4, Most stages in any one step: 2

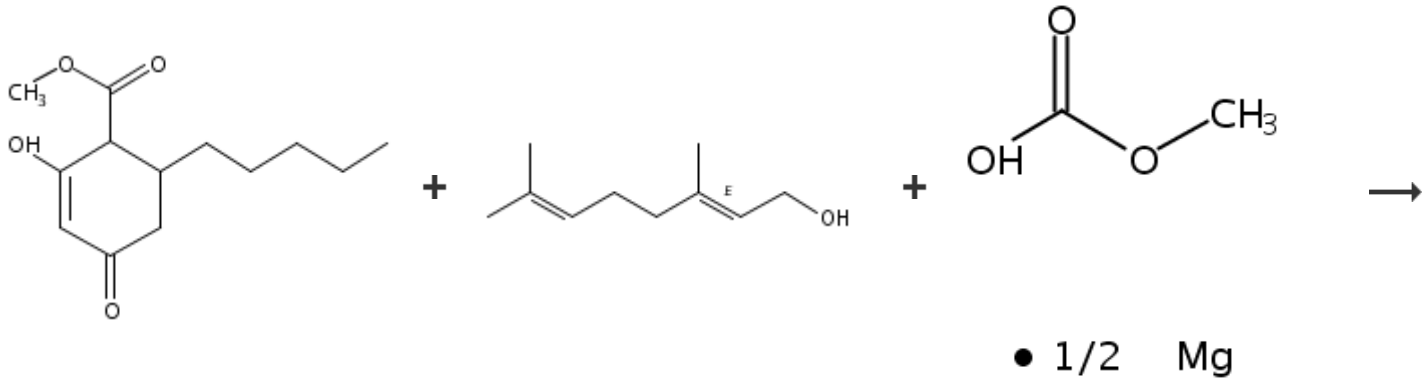
References

Biosynthesis of cannabinoid prodrugs

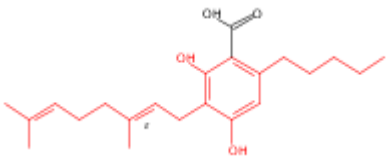
By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

70. 3 Steps



[Step 2.1] [Step 3.1]



Overview

Steps/Stages

1.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

2.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

3.1 S:DMF, 1 h, 120°C

3.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

Notes

2) in the dark, 3) conversion = 40%,alternative preparation shown, Reactants: 3, Reagents: 3, Solvents: 4, Steps: 3, Stages: 4, Most stages in any one step: 2

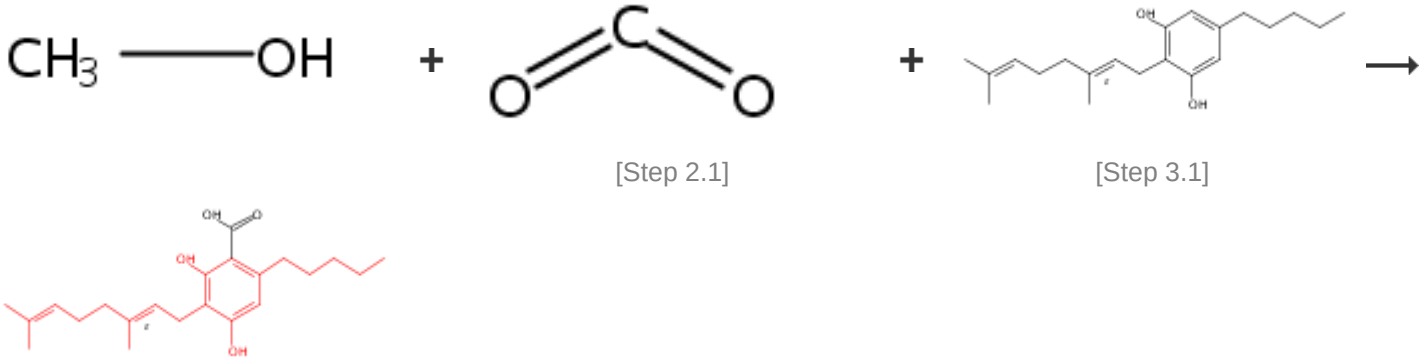
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

71. 3 Steps



Overview

Steps/Stages

1.1 R:Mg, rt

2.1 S:DMF

3.1 S:DMF, 1 h, 120°C

3.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

Notes

2) exothermic, 3) alternative preparation gave lower yield, LH-20 Sephadex resin, LH-20 lipophilic resin, Reactants: 3, Reagents: 2, Solvents: 4, Steps: 3, Stages: 4, Most stages in any one step: 2

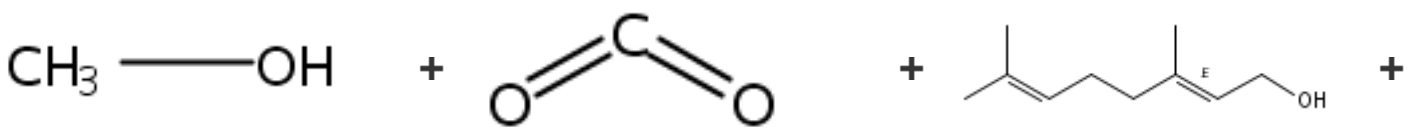
References

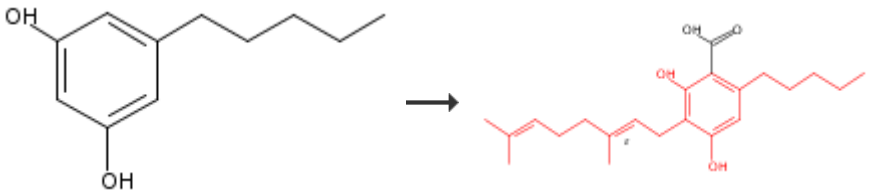
Bioreactor and process for the enzymatic biosynthesis of cannabinoids

By Peet, Richard and Sun, Mingyang

From U.S. Pat. Appl. Publ., 20160053220, 25 Feb 2016

72. 3 Steps (Converging)





Overview

Steps/Stages

1.1 R:Mg, S:MeOH, rt
1.2 S:DMF, 140°C
1.1 C:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
2.1 rt → 50°C; 3 h, 50°C; 50°C → rt

2.2 R:HCl, S:H_2O, S:MeOH, S:$CHCl_3$, rt, pH 2

Notes

literature preparation, exothermic (stage 2), literature preparation, in the dark, conversion, 85%, alternative preparation shown, sealed vessel used, Reactants: 4, Reagents: 2, Catalysts: 1, Solvents: 4, Steps: 3, Stages: 5, Most stages in any one step: 2

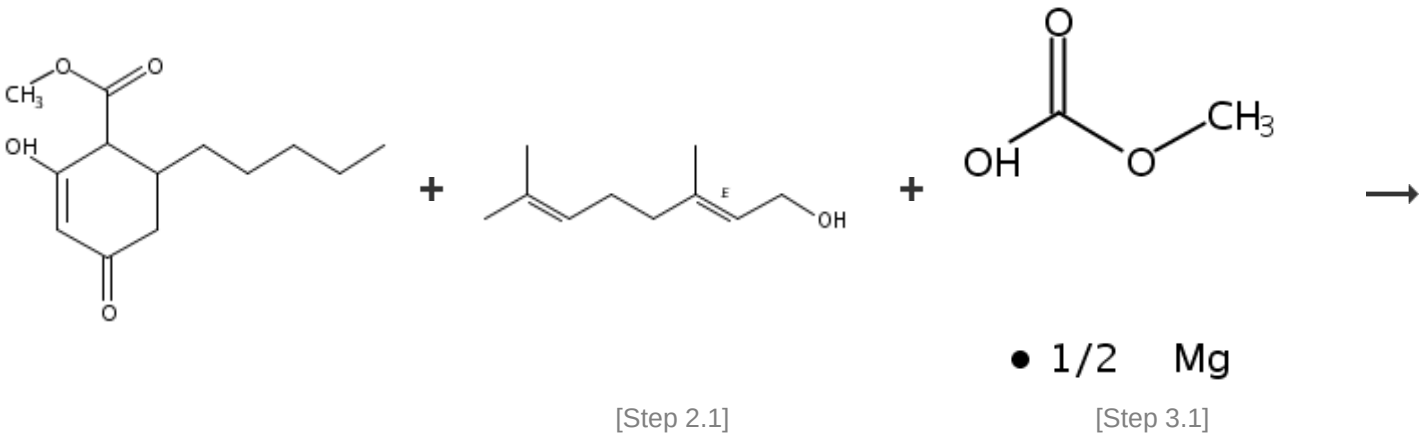
References

Chemoenzymic synthesis of cannabinoids

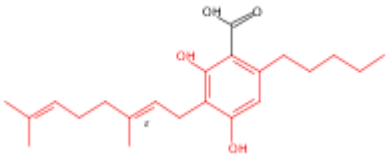
By Winnicki, Robert and Donsky, Marc

From PCT Int. Appl., 2014134281, 04 Sep 2014

73. 3 Steps



[Step 2.1] [Step 3.1]



Overview

Steps/Stages

Notes

1.1 R:Br_2, S:DMF, cooled; 90 min, 80°C; 10 min, 80°C → 160°C
2.1 C:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
3.1 rt → 50°C; 3 h, 50°C; 50°C → rt

3.2 R:HCl, S:H_2O, S:MeOH, S:$CHCl_3$, rt, pH 2

2) literature preparation, in the dark, 3) conversion, 85%, alternative preparation shown, sealed vessel used, Reactants: 3, Reagents: 2, Catalysts: 1, Solvents: 4, Steps: 3, Stages: 4, Most stages in any one step: 2

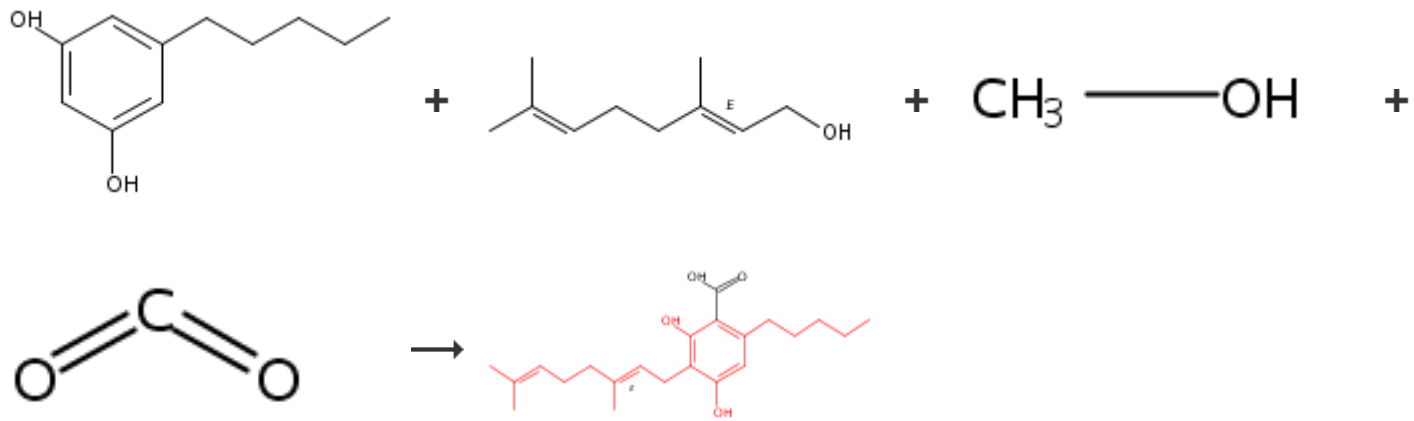
References

Chemoenzymic synthesis of cannabinoids

By Winnicki, Robert and Donsky, Marc

From PCT Int. Appl., 2014134281, 04 Sep 2014

74. 4 Steps (Converging)



Overview

Steps/Stages

1.1 C:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

1.1 R:Mg, S:MeOH, cooled
2.1 S:DMF, 140°C
3.1 S:DMF, 1 h, 120°C

3.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

Notes

alternative preparation shown,conversion = 40%, Reactants: 4, Reagents: 2, Catalysts: 1, Solvents: 4, Steps: 4, Stages: 5, Most stages in any one step: 2

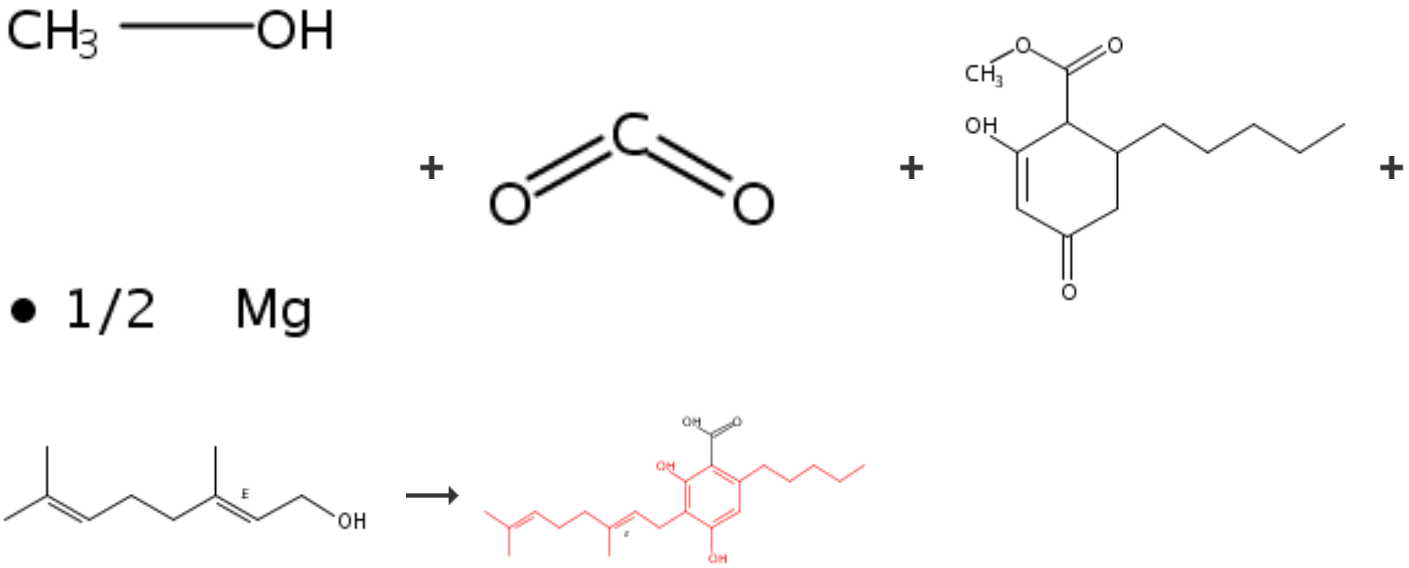
References

Methods for the manufacture of cannabinoid prodrugs, pharmaceutical formulations and their use

By Peet, Richard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017216362, 21 Dec 2017

75. 4 Steps (Converging)



Overview

Steps/Stages

1.1 S:DMF, 140°C

1.1 R:Br_2, S:DMF, 90 min, cooled; 80°C → 160°C; 10 h, 160°C
2.1 C:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
3.1 S:DMF, 1 h, 120°C

3.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

Notes

alternative preparation shown,conversion = 40%, Reactants: 4, Reagents: 2, Catalysts: 1, Solvents: 4, Steps: 4, Stages: 5, Most stages in any one step: 2

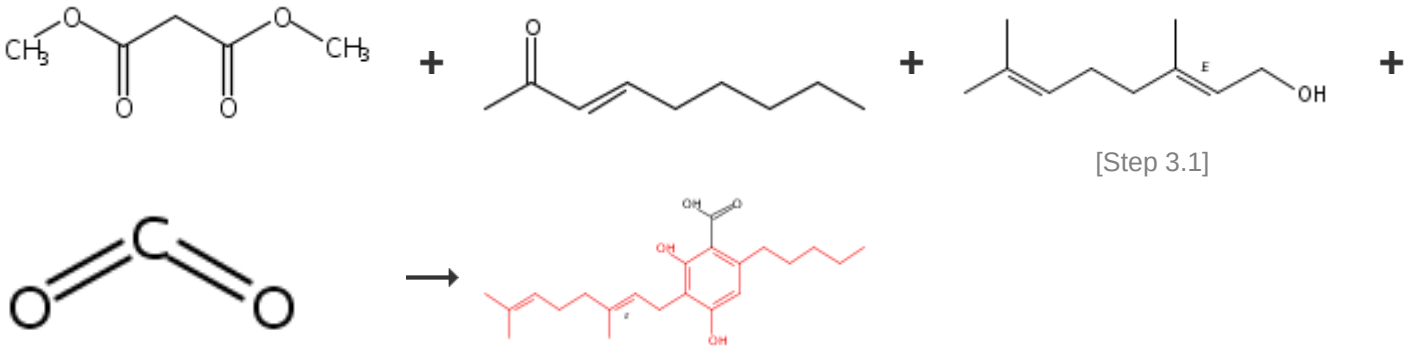
References

Methods for the manufacture of cannabinoid prodrugs, pharmaceutical formulations and their use

By Peet, Richard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017216362, 21 Dec 2017

76. 4 Steps



[Step 3.1]

[Step 4.1]

Overview

Steps/Stages

Notes

1.1 R:NaOMe, S:MeOH, rt; 3 h, reflux

2.1 R:Br_2, S:DMF, 90 min, cooled; 80°C → 160°C; 10 h, 160°C
3.1 C:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

4.1 R:$Mg(OMe)_2$, S:DMF, rt → 50°C; 3 h, 50°C; 50°C → rt

4.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, rt, pH 2

4) alternative preparation shown,conversion = 85%, Reactants: 4, Reagents: 4, Catalysts: 1, Solvents: 4, Steps: 4, Stages: 5, Most stages in any one step: 2

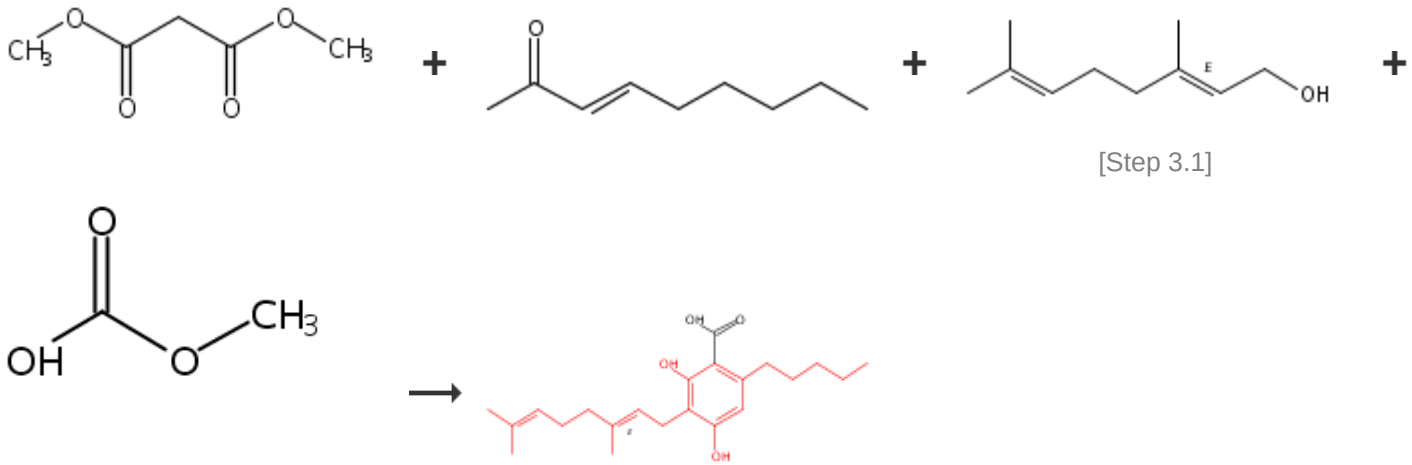
References

Methods for the manufacture of cannabinoid prodrugs, pharmaceutical formulations and their use

By Peet, Richard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017216362, 21 Dec 2017

77. 4 Steps



Overview

Steps/Stages

1.1 R:NaOMe, S:MeOH, rt; 3 h, reflux

2.1 R:Br_2, S:DMF, 90 min, cooled; 80°C → 160°C; 10 h, 160°C
3.1 C:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
4.1 S:DMF, 1 h, 120°C

4.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

Notes

4) alternative preparation shown,conversion = 40%, Reactants: 4, Reagents: 3, Catalysts: 1, Solvents: 4, Steps: 4, Stages: 5, Most stages in any one step: 2

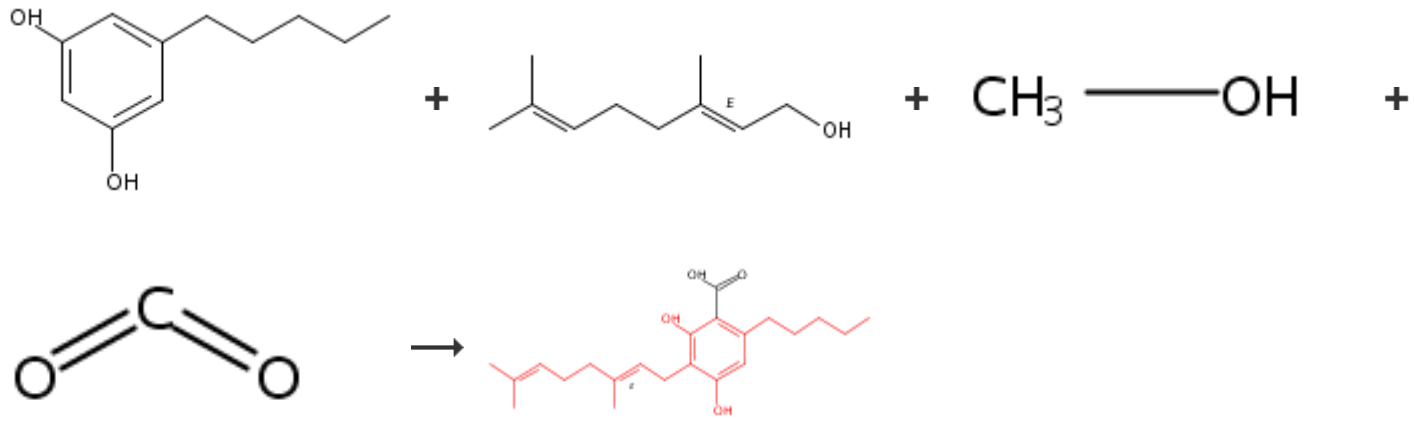
References

Methods for the manufacture of cannabinoid prodrugs, pharmaceutical formulations and their use

By Peet, Richard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017216362, 21 Dec 2017

78. 4 Steps (Converging)



Overview

Steps/Stages

1.1 C:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

1.1 R:Mg, S:MeOH, cooled
2.1 S:DMF, 140°C
3.1 S:DMF, 1 h, 120°C

3.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

Notes

in the dark, exothermic, conversion, 40%, alternative preparation shown, Reactants: 4, Reagents: 2, Catalysts: 1, Solvents: 4, Steps: 4, Stages: 5, Most stages in any one step: 2

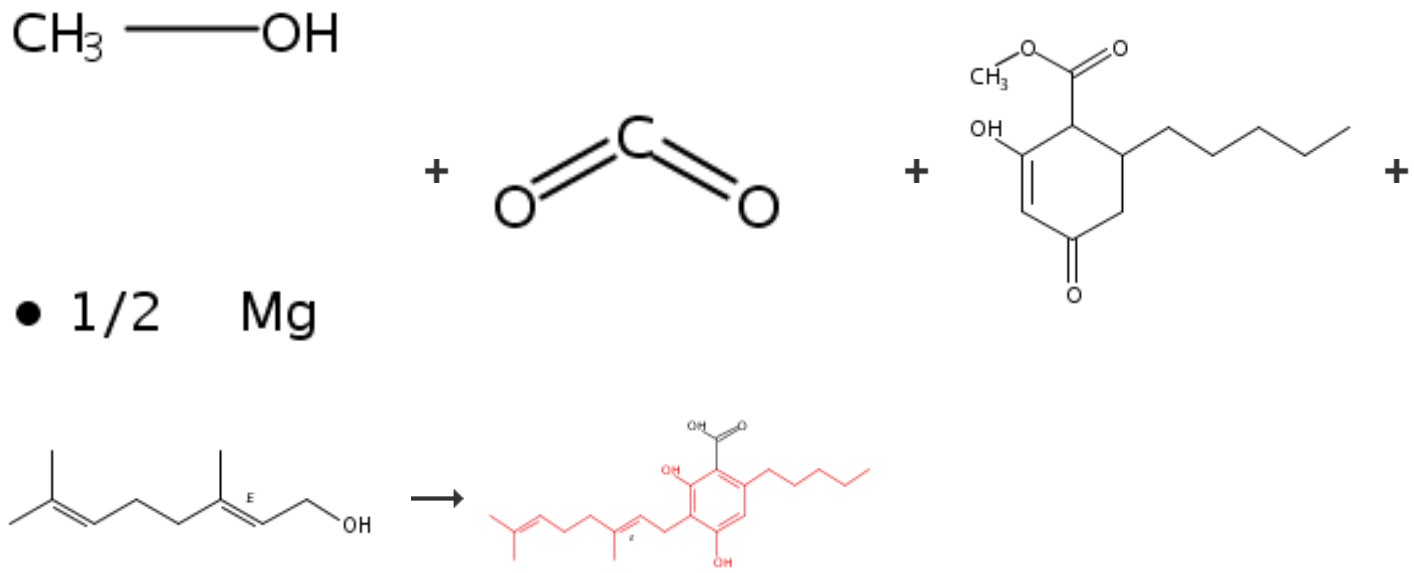
References

Chemoenzymatic synthesis of tetrahydrocannabivarin, carnnabivarin, and cannabinol

By Kavarana, Malcolm J. and Peet, Richard C.

From U.S. Pat. Appl. Publ., 20170283837, 05 Oct 2017

79. 4 Steps (Converging)



Overview

Steps/Stages

1.1 S:DMF, 140°C

1.1 R:Br_2, S:DMF, 90 min, cooled; 80°C; 80°C → 160°C; 10 h, 160°C
2.1 C:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
3.1 S:DMF, 1 h, 120°C

3.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

Notes

exothermic, in the dark, conversion, 40%, alternative preparation shown, Reactants: 4, Reagents: 2, Catalysts: 1, Solvents: 4, Steps: 4, Stages: 5, Most stages in any one step: 2

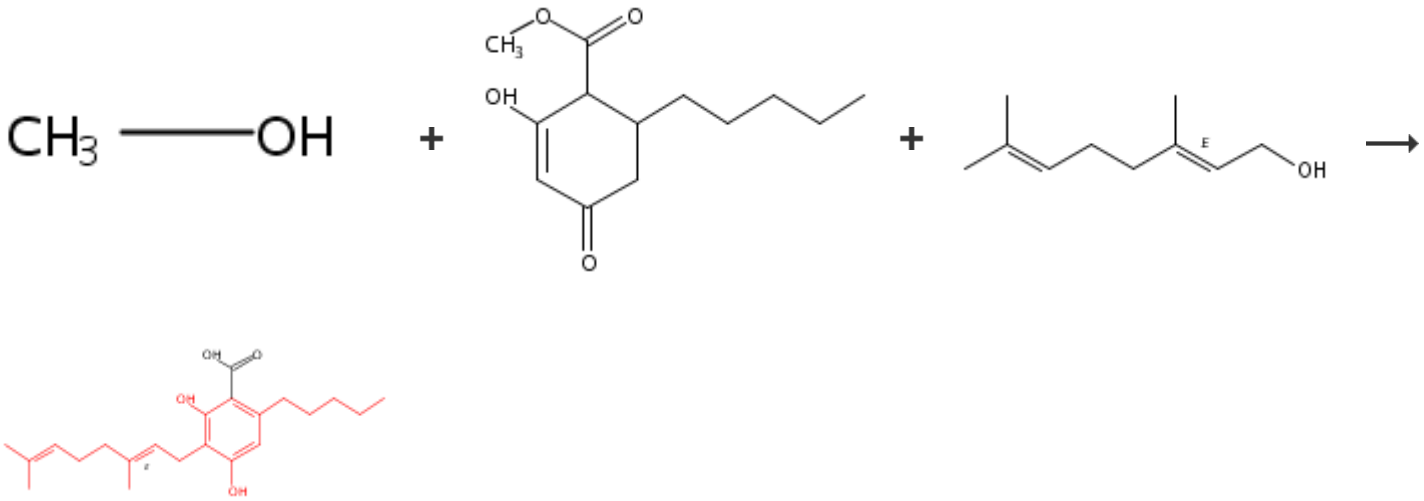
References

Chemoenzymatic synthesis of tetrahydrocannabivarin, carnnabivarin, and cannabinol

By Kavarana, Malcolm J. and Peet, Richard C.

From U.S. Pat. Appl. Publ., 20170283837, 05 Oct 2017

80. 4 Steps (Converging)



Overview

Steps/Stages

1.1 R:Mg, S:MeOH, cooled

1.1 R:Br_2, S:DMF, 90 min, cooled; 80°C; 80°C → 160°C; 10 h, 160°C
2.1 C:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

3.1 R:CO_2, cooled; 50°C; 3 h, 50°C; 50°C → rt

3.2 R:HCl, S:H_2O, rt, pH 2

Notes

in the dark, conversion, 85%, sealed vessel used, alternative preparation shown, Reactants: 3, Reagents: 4, Catalysts: 1, Solvents: 4, Steps: 4, Stages: 5, Most stages in any one step: 2

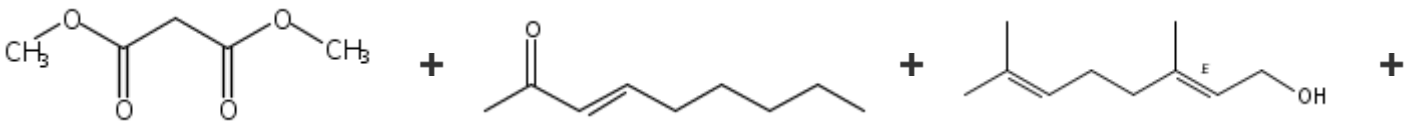
References

Chemoenzymatic synthesis of tetrahydrocannabivarin, carnnabivarin, and cannabinol

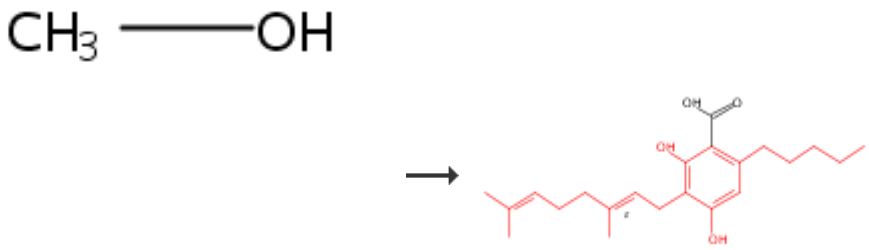
By Kavarana, Malcolm J. and Peet, Richard C.

From U.S. Pat. Appl. Publ., 20170283837, 05 Oct 2017

81. 4 Steps



[Step 3.1]



- 1/2 Mg

[Step 4.1]

Overview

Steps/Stages

1.1 R:NaOMe, S:MeOH, S:H_2O, rt; 3 h, reflux

2.1 R:Br_2, S:DMF, 90 min, cooled; 80°C; 80°C → 160°C; 10 h, 160°C

3.1 C:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

4.1 R:CO_2, cooled; 50°C; 3 h, 50°C; 50°C → rt

4.2 R:HCl, S:H_2O, rt, pH 2

Notes

3) in the dark, 4) conversion, 85%, sealed vessel used, alternative preparation shown, Reactants: 4, Reagents: 4, Catalysts: 1, Solvents: 4, Steps: 4, Stages: 5, Most stages in any one step: 2

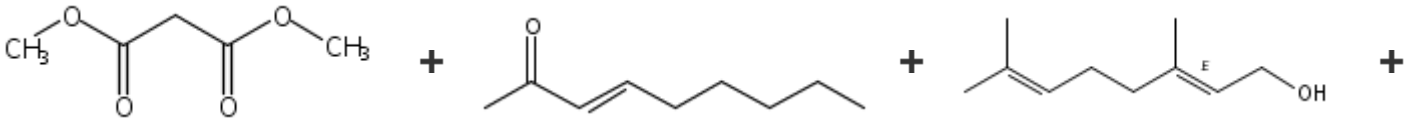
References

Chemoenzymatic synthesis of tetrahydrocannabivarin, carnnabivarin, and cannabinol

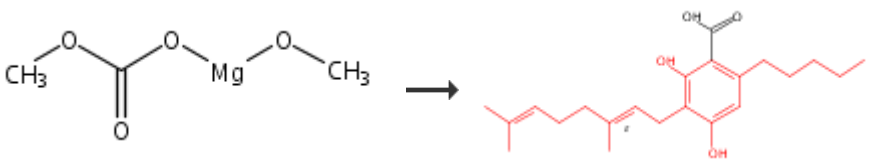
By Kavarana, Malcolm J. and Peet, Richard C.

From U.S. Pat. Appl. Publ., 20170283837, 05 Oct 2017

82. 4 Steps



[Step 3.1]



[Step 4.1]

Overview

Steps/Stages

Notes

1.1 R:NaOMe, S:MeOH, S:H_2O, rt; 3 h, reflux

2.1 R:Br_2, S:DMF, 90 min, cooled; 80°C; 80°C → 160°C; 10 h, 160°C
3.1 C:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
4.1 S:DMF, 1 h, 120°C

4.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

3) in the dark, 4) conversion, 40%, alternative preparation shown, Reactants: 4, Reagents: 3, Catalysts: 1, Solvents: 4, Steps: 4, Stages: 5, Most stages in any one step: 2

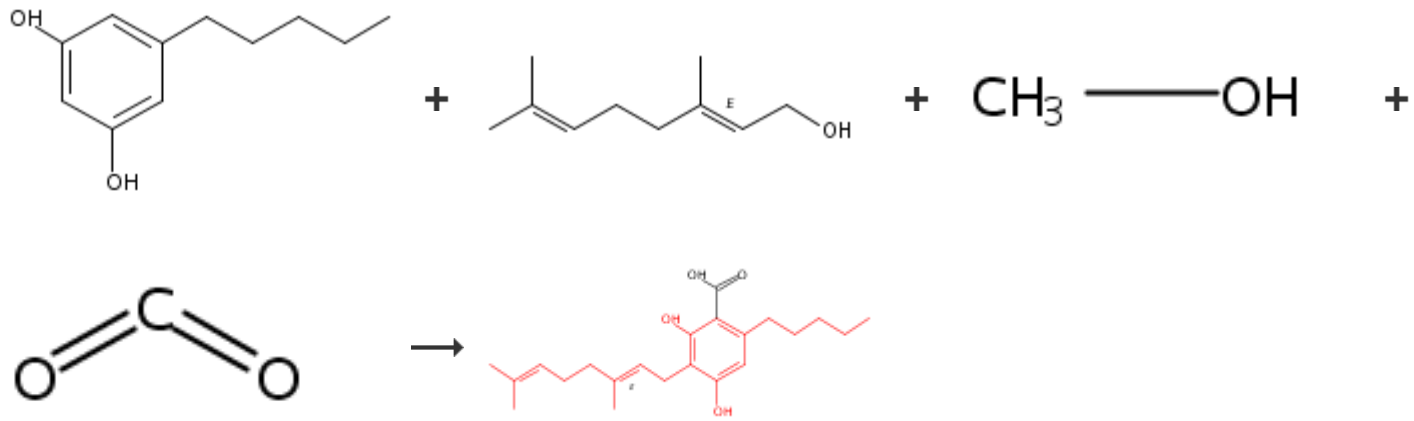
References

Chemoenzymatic synthesis of tetrahydrocannabivarin, carnnabivarin, and cannabinol

By Kavarana, Malcolm J. and Peet, Richard C.

From U.S. Pat. Appl. Publ., 20170283837, 05 Oct 2017

83. 4 Steps (Converging)



Overview

Steps/Stages

1.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

1.1 R:Mg, S:MeOH, rt
2.1 S:DMF, 140°C
3.1 S:DMF, 1 h, 120°C

3.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

Notes

in the dark, exothermic reaction, conversion = 40%,alternative preparation shown, Reactants: 4, Reagents: 3, Solvents: 4, Steps: 4, Stages: 5, Most stages in any one step: 2

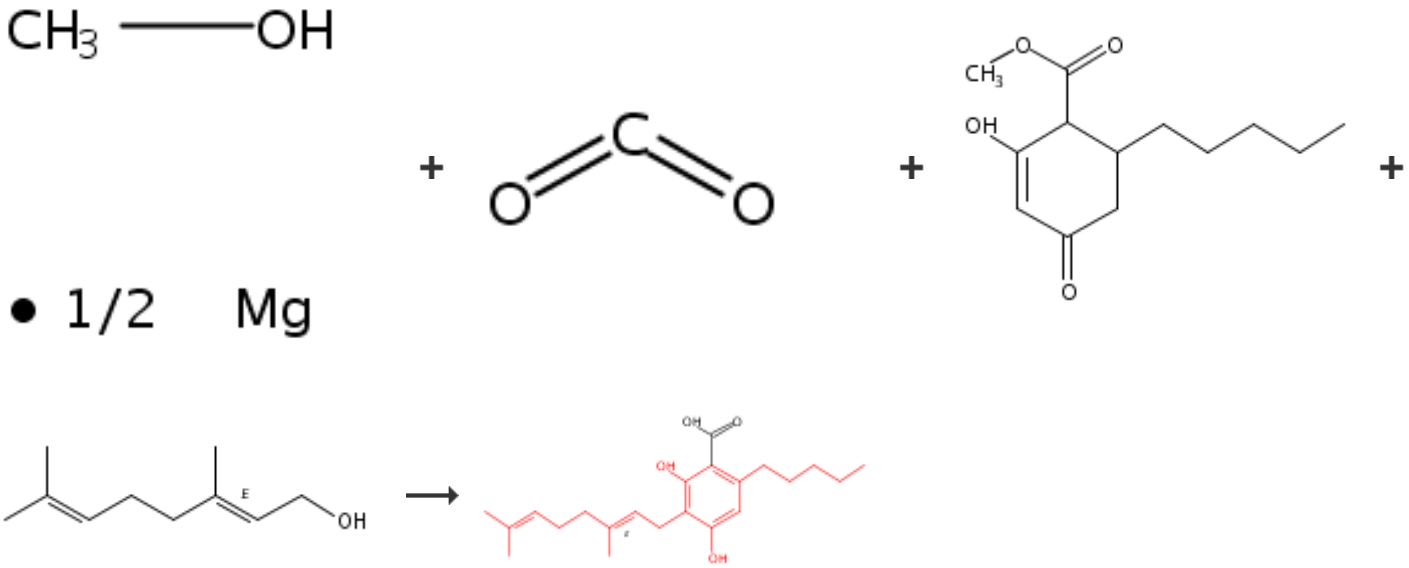
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

84. 4 Steps (Converging)



Overview

Steps/Stages

1.1 S:DMF, 140°C

1.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

2.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

3.1 S:DMF, 1 h, 120°C

3.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

Notes

exothermic reaction, in the dark, conversion = 40%,alternative preparation shown, Reactants: 4, Reagents: 3, Solvents: 4, Steps: 4, Stages: 5, Most stages in any one step: 2

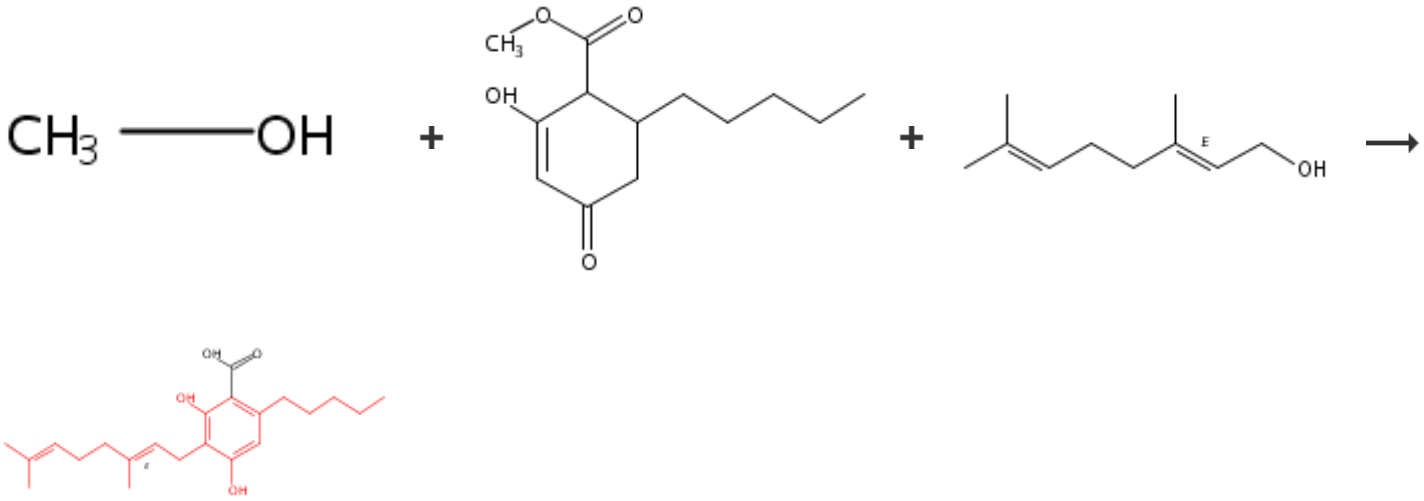
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

85. 4 Steps (Converging)



Overview

Steps/Stages

Notes

1.1 R:Mg, S:MeOH, rt

1.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

2.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
3.1 S:H_2O, cooled; 50°C; 3 h, 50°C; 50°C → rt

3.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, rt, pH 2

in the dark, conversion = 85%,alternative preparation shown,reaction in a sealed pressure vessel, Reactants: 3, Reagents: 4, Solvents: 4, Steps: 4, Stages: 5, Most stages in any one step: 2

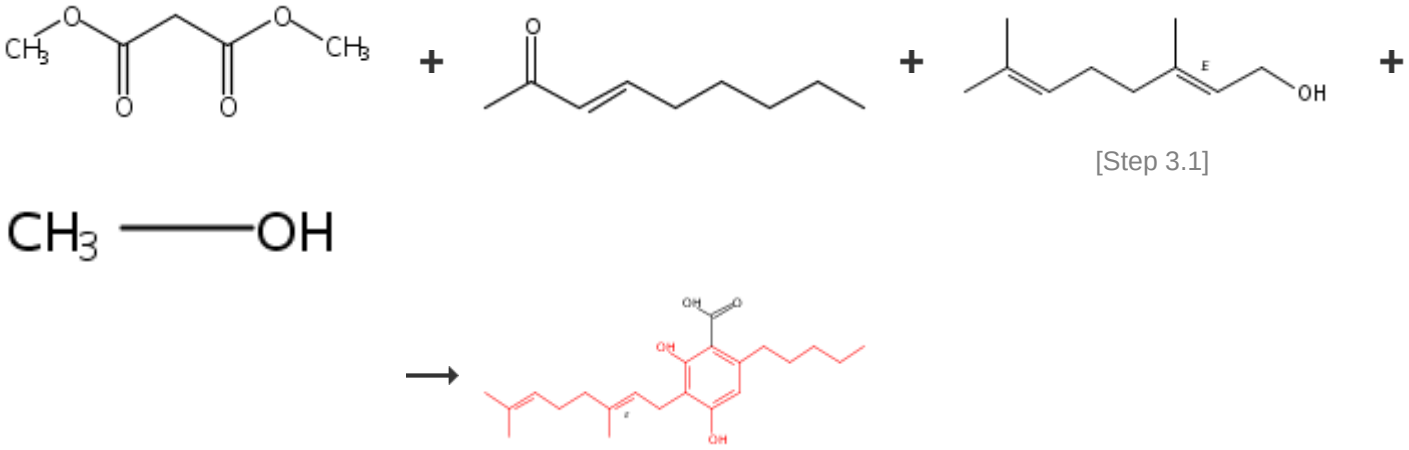
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

86. 4 Steps



[Step 4.1]

Overview

Steps/Stages

1.1 R:NaOMe, S:MeOH, rt; 3 h, reflux; reflux → rt

1.2 R:H_2O, rt

2.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

3.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
4.1 S:H_2O, cooled; 50°C; 3 h, 50°C; 50°C → rt

4.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, rt, pH 2

Notes

3) in the dark, 4) conversion = 85%,alternative preparation shown,reaction in a sealed pressure vessel, Reactants: 4, Reagents: 5, Solvents: 4, Steps: 4, Stages: 6, Most stages in any one step: 2

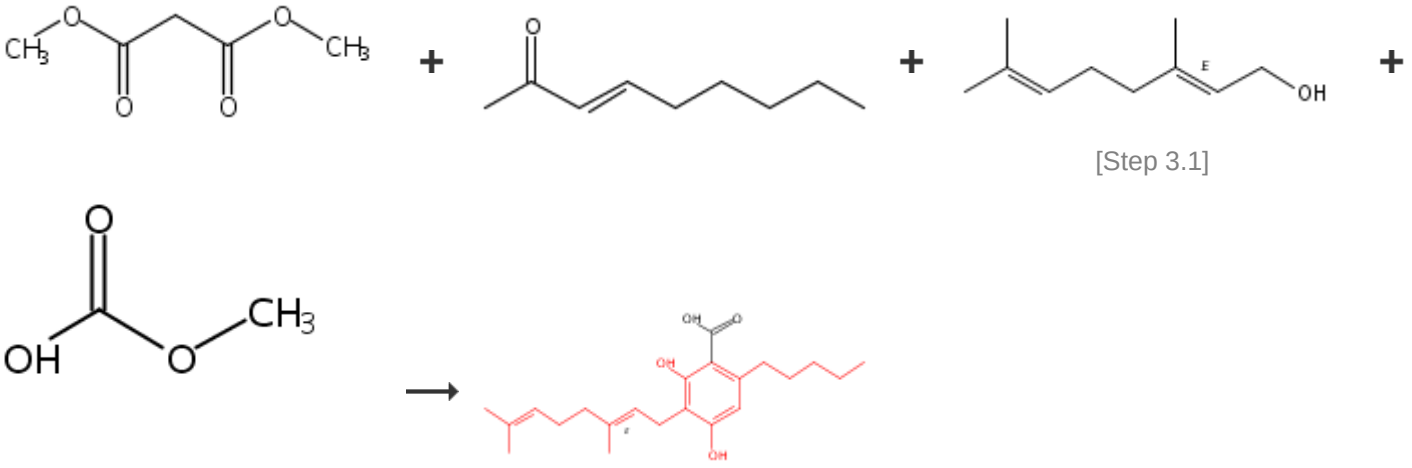
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

87. 4 Steps



[Step 3.1]

- 1/2 Mg

[Step 4.1]

Overview

Steps/Stages

1.1 R:NaOMe, S:MeOH, rt; 3 h, reflux; reflux → rt

1.2 R:H_2O, rt

2.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

3.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

4.1 S:DMF, 1 h, 120°C

4.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

Notes

3) in the dark, 4) conversion = 40%,alternative preparation shown, Reactants: 4, Reagents: 5, Solvents: 4, Steps: 4, Stages: 6, Most stages in any one step: 2

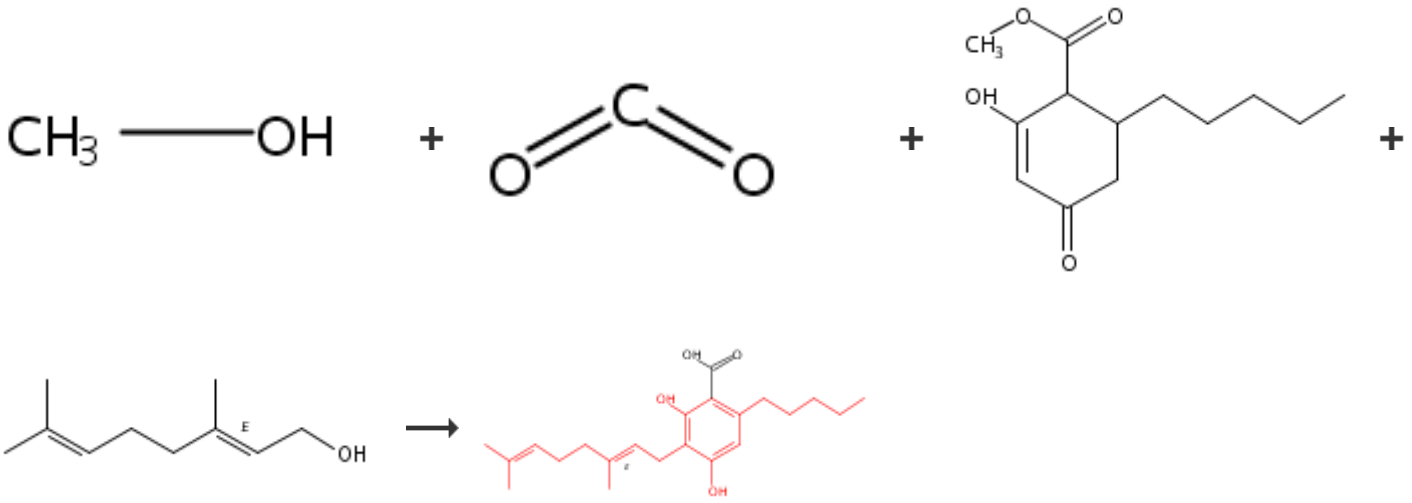
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

88. 4 Steps (Converging)



Overview

Steps/Stages

1.1 R:Mg, S:MeOH, rt
1.2 S:DMF, 140°C

1.1 R:Br_2, S:DMF, cooled; 90 min, 80°C; 10 min, 80°C → 160°C
2.1 C:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
3.1 rt → 50°C; 3 h, 50°C; 50°C → rt

3.2 R:HCl, S:H_2O, S:MeOH, S:$CHCl_3$, rt, pH 2

Notes

literature preparation, exothermic (stage 2), literature preparation, in the dark, conversion, 85%, alternative preparation shown, sealed vessel used, Reactants: 4, Reagents: 3, Catalysts: 1, Solvents: 4, Steps: 4, Stages: 6, Most stages in any one step: 2

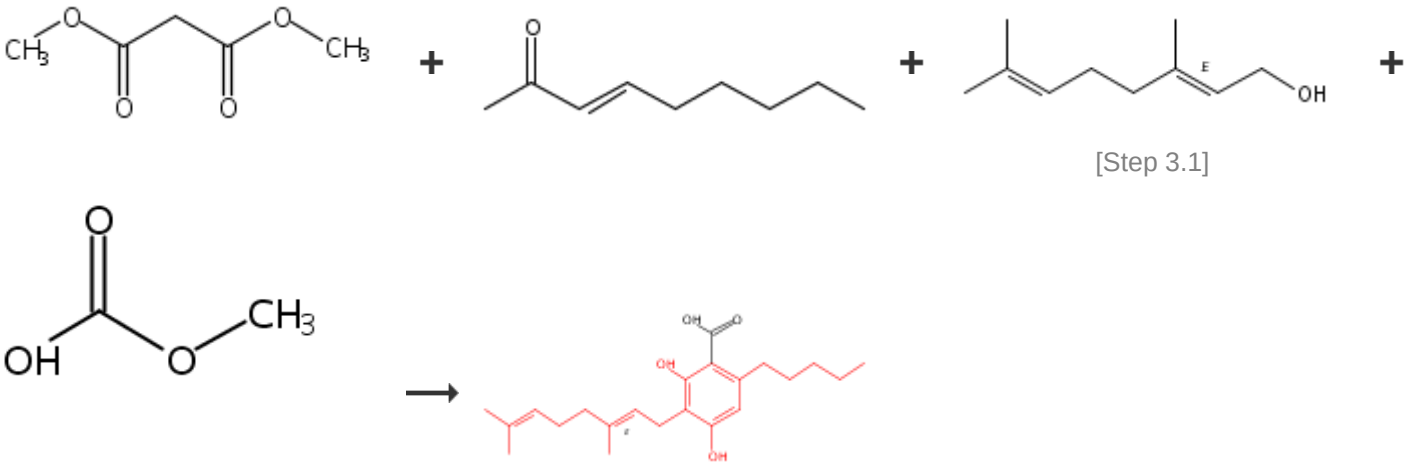
References

Chemoenzymic synthesis of cannabinoids

By Winnicki, Robert and Donsky, Marc

From PCT Int. Appl., 2014134281, 04 Sep 2014

89. 4 Steps



[Step 3.1]

- 1/2 Mg

[Step 4.1]

Overview

Steps/Stages

1.1 R:NaOMe, S:MeOH, rt; 3 h, reflux; reflux → rt

1.2 R:HCl, S:H_2O, rt, pH 4

2.1 R:Br_2, S:DMF, cooled; 90 min, 80°C; 10 min, 80°C → 160°C
3.1 C:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
4.1 rt → 50°C; 3 h, 50°C; 50°C → rt

4.2 R:HCl, S:H_2O, S:MeOH, S:$CHCl_3$, rt, pH 2

Notes

3) literature preparation, in the dark, 4) conversion, 85%, alternative preparation shown, sealed vessel used, Reactants: 4, Reagents: 3, Catalysts: 1, Solvents: 4, Steps: 4, Stages: 6, Most stages in any one step: 2

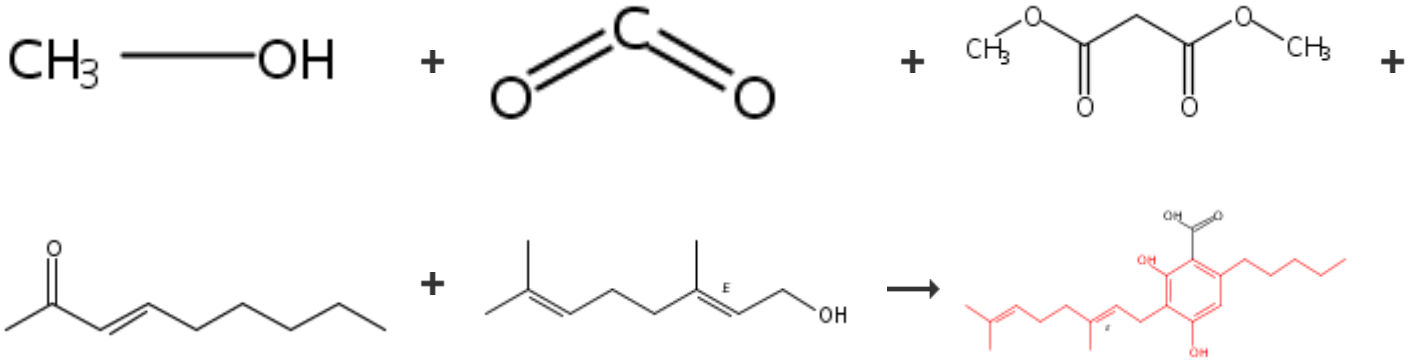
References

Chemoenzymic synthesis of cannabinoids

By Winnicki, Robert and Donsky, Marc

From PCT Int. Appl., 2014134281, 04 Sep 2014

90. 6 Steps (Converging)



Overview

Steps/Stages

1.1 R:Mg, S:MeOH, cooled
2.1 S:DMF, 140°C

1.1 R:NaOMe, S:MeOH, rt; 3 h, reflux

2.1 R:Br_2, S:DMF, 90 min, cooled; 80°C → 160°C; 10 h, 160°C
3.1 C:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
4.1 S:DMF, 1 h, 120°C

4.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

Notes

alternative preparation shown,conversion = 40%, Reactants: 5, Reagents: 4, Catalysts: 1, Solvents: 4, Steps: 6, Stages: 7, Most stages in any one step: 2

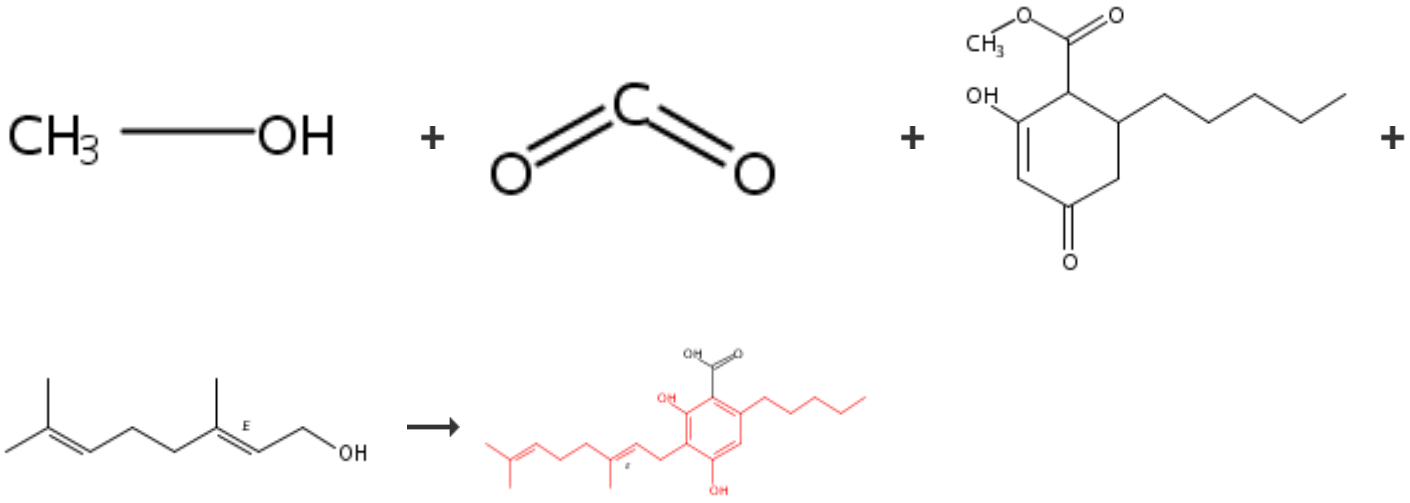
References

Methods for the manufacture of cannabinoid prodrugs, pharmaceutical formulations and their use

By Peet, Richard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017216362, 21 Dec 2017

91. 5 Steps (Converging)



Overview

Steps/Stages

Notes

1.1 R:Mg, S:MeOH, cooled
2.1 S:DMF, 140°C

1.1 R:Br_2, S:DMF, 90 min, cooled; 80°C → 160°C; 10 h, 160°C
2.1 C:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
3.1 S:DMF, 1 h, 120°C

3.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

alternative preparation shown,conversion = 40%, Reactants: 4, Reagents: 3, Catalysts: 1, Solvents: 4, Steps: 5, Stages: 6, Most stages in any one step: 2

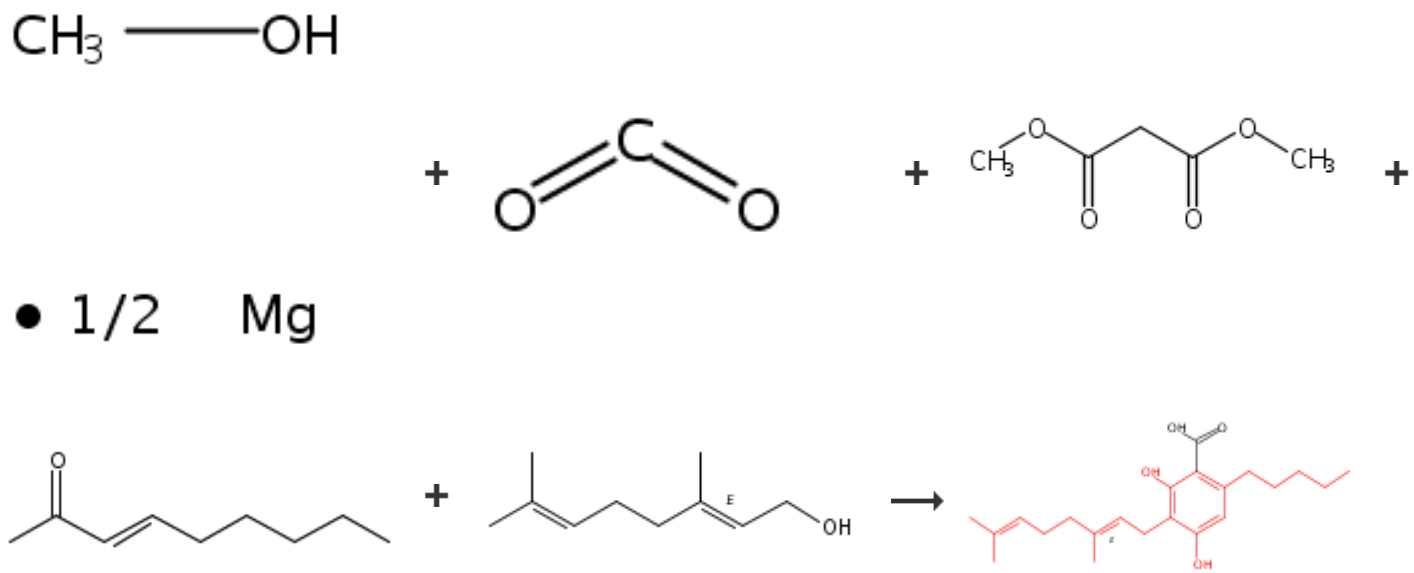
References

Methods for the manufacture of cannabinoid prodrugs, pharmaceutical formulations and their use

By Peet, Richard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017216362, 21 Dec 2017

92. 5 Steps (Converging)



Overview

Steps/Stages

1.1 S:DMF, 140°C

1.1 R:NaOMe, S:MeOH, rt; 3 h, reflux

2.1 R:Br_2, S:DMF, 90 min, cooled; 80°C → 160°C; 10 h, 160°C
3.1 C:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
4.1 S:DMF, 1 h, 120°C

4.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

Notes

alternative preparation shown,conversion = 40%, Reactants: 5, Reagents: 3, Catalysts: 1, Solvents: 4, Steps: 5, Stages: 6, Most stages in any one step: 2

References

Methods for the manufacture of cannabinoid prodrugs, pharmaceutical formulations and their use

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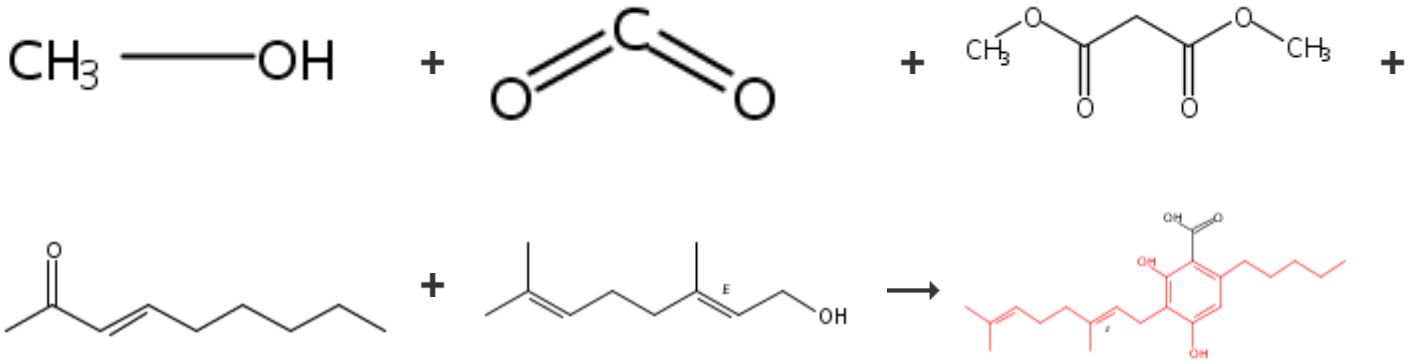
From PCT Int. Appl., 2017216362, 21 Dec 2017

93. 6 Steps (Converging)



Overview

Steps/Stages

1.1 R:Mg, S:MeOH, cooled
2.1 S:DMF, 140°C

1.1 R:NaOMe, S:MeOH, S:H_2O, rt; 3 h, reflux

2.1 R:Br_2, S:DMF, 90 min, cooled; 80°C; 80°C → 160°C; 10 h, 160°C
3.1 C:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
4.1 S:DMF, 1 h, 120°C

4.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

Notes

exothermic, in the dark, conversion, 40%, alternative preparation shown, Reactants: 5, Reagents: 4, Catalysts: 1, Solvents: 4, Steps: 6, Stages: 7, Most stages in any one step: 2

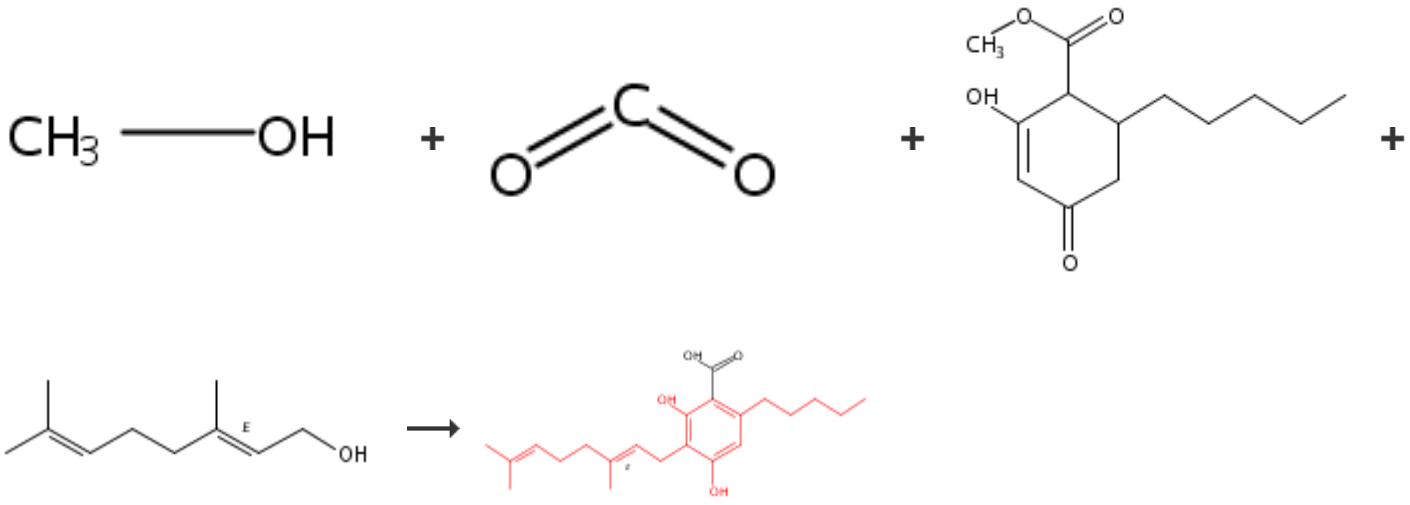
References

Chemoenzymatic synthesis of tetrahydrocannabivarin, carnnabivarin, and cannabinol

By Kavarana, Malcolm J. and Peet, Richard C.

From U.S. Pat. Appl. Publ., 20170283837, 05 Oct 2017

94. 5 Steps (Converging)



Overview

Steps/Stages

Notes

1.1 R:Mg, S:MeOH, cooled
2.1 S:DMF, 140°C

1.1 R:Br_2, S:DMF, 90 min, cooled; 80°C; 80°C → 160°C; 10 h, 160°C
2.1 C:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
3.1 S:DMF, 1 h, 120°C

3.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

exothermic, in the dark, conversion, 40%, alternative preparation shown, Reactants: 4, Reagents: 3, Catalysts: 1, Solvents: 4, Steps: 5, Stages: 6, Most stages in any one step: 2

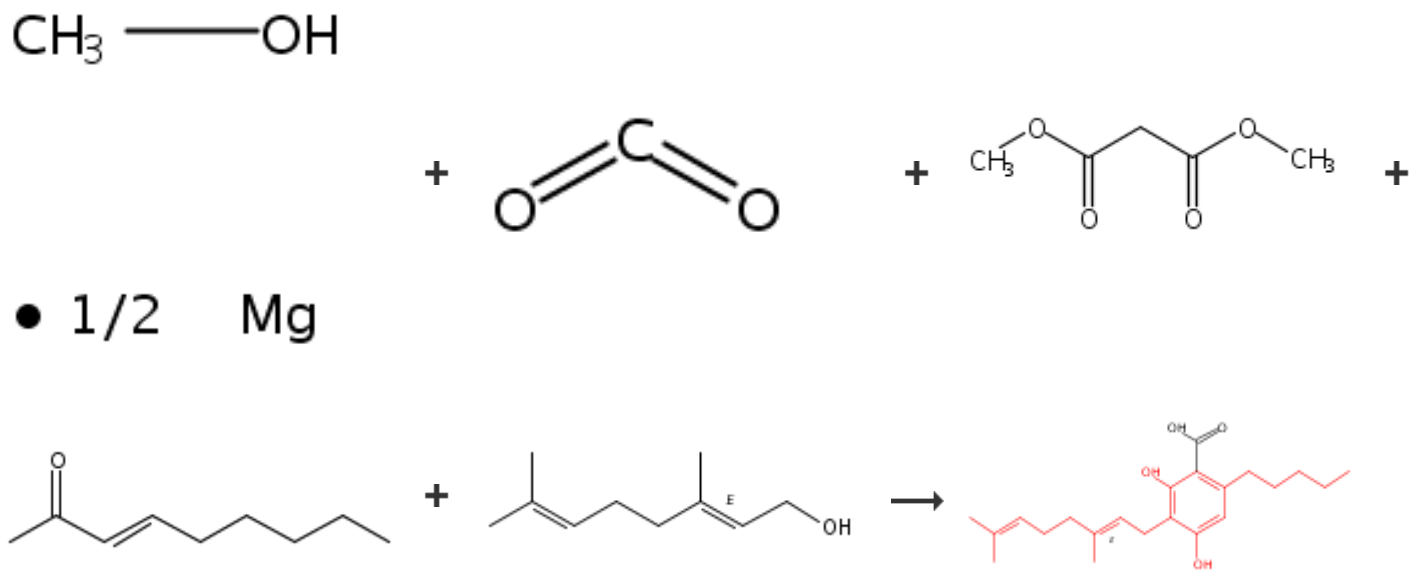
References

Chemoenzymatic synthesis of tetrahydrocannabivarin, carnnabivarin, and cannabinol

By Kavarana, Malcolm J. and Peet, Richard C.

From U.S. Pat. Appl. Publ., 20170283837, 05 Oct 2017

95. 5 Steps (Converging)



Overview

Steps/Stages

1.1 S:DMF, 140°C

1.1 R:NaOMe, S:MeOH, S:H_2O, rt; 3 h, reflux

2.1 R:Br_2, S:DMF, 90 min, cooled; 80°C; 80°C → 160°C; 10 h, 160°C
3.1 C:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
4.1 S:DMF, 1 h, 120°C

4.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

Notes

exothermic, in the dark, conversion, 40%, alternative preparation shown, Reactants: 5, Reagents: 3, Catalysts: 1, Solvents: 4, Steps: 5, Stages: 6, Most stages in any one step: 2

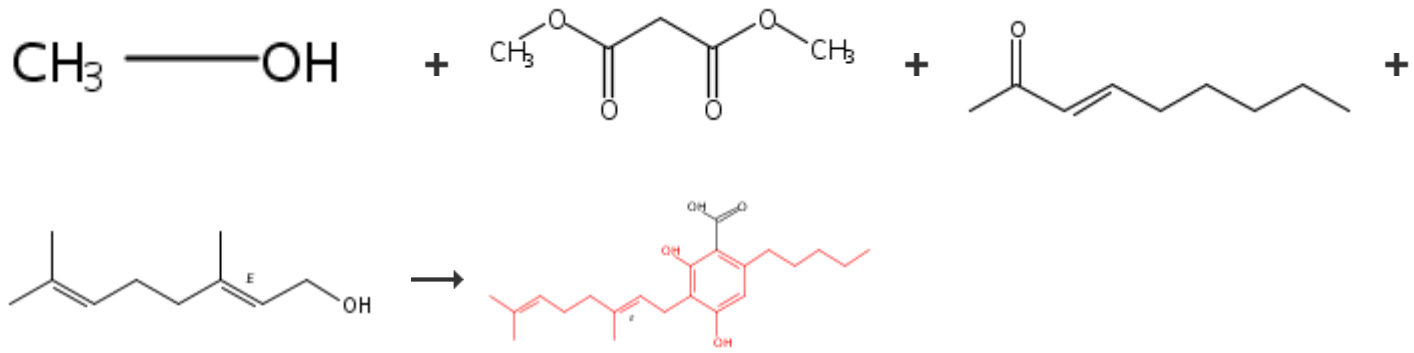
References

Chemoenzymatic synthesis of tetrahydrocannabivarin, carnnabivarin, and cannabinol

By Kavarana, Malcolm J. and Peet, Richard C.

From U.S. Pat. Appl. Publ., 20170283837, 05 Oct 2017

96. 5 Steps (Converging)



Overview

Steps/Stages

1.1 R:Mg, S:MeOH, cooled

1.1 R:NaOMe, S:MeOH, S:H_2O, rt; 3 h, reflux

2.1 R:Br_2, S:DMF, 90 min, cooled; 80°C; 80°C → 160°C; 10 h, 160°C

3.1 C:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

4.1 R:CO_2, cooled; 50°C; 3 h, 50°C; 50°C → rt

4.2 R:HCl, S:H_2O, rt, pH 2

Notes

in the dark, conversion, 85%, sealed vessel used, alternative preparation shown, Reactants: 4, Reagents: 5, Catalysts: 1, Solvents: 4, Steps: 5, Stages: 6, Most stages in any one step: 2

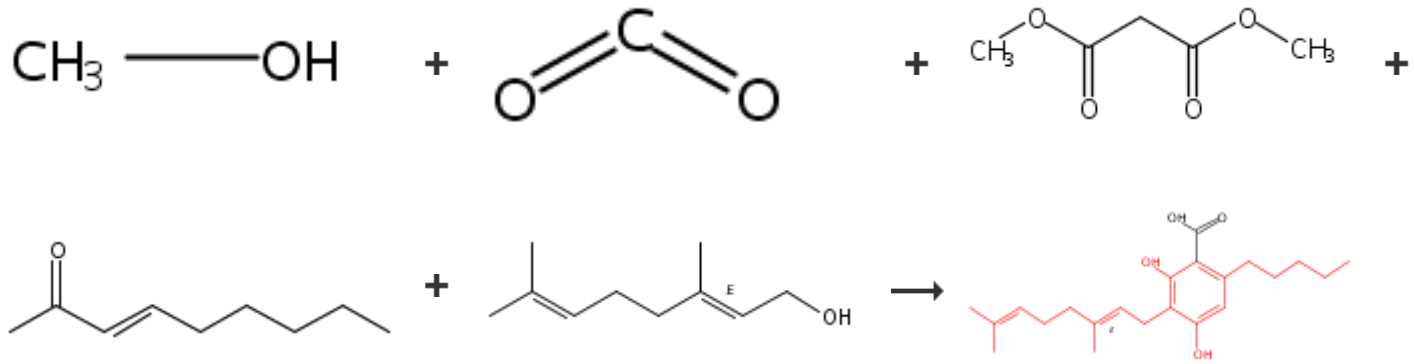
References

Chemoenzymatic synthesis of tetrahydrocannabivarin, carnnabivarin, and cannabinol

By Kavarana, Malcolm J. and Peet, Richard C.

From U.S. Pat. Appl. Publ., 20170283837, 05 Oct 2017

97. 6 Steps (Converging)



Overview

Steps/Stages

Notes

1.1 R:Mg, S:MeOH, rt
2.1 S:DMF, 140°C

1.1 R:NaOMe, S:MeOH, rt; 3 h, reflux; reflux → rt

1.2 R:H_2O, rt

2.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

3.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
4.1 S:DMF, 1 h, 120°C

4.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

exothermic reaction, in the dark, conversion = 40%,alternative preparation shown, Reactants: 5, Reagents: 6, Solvents: 4, Steps: 6, Stages: 8, Most stages in any one step: 2

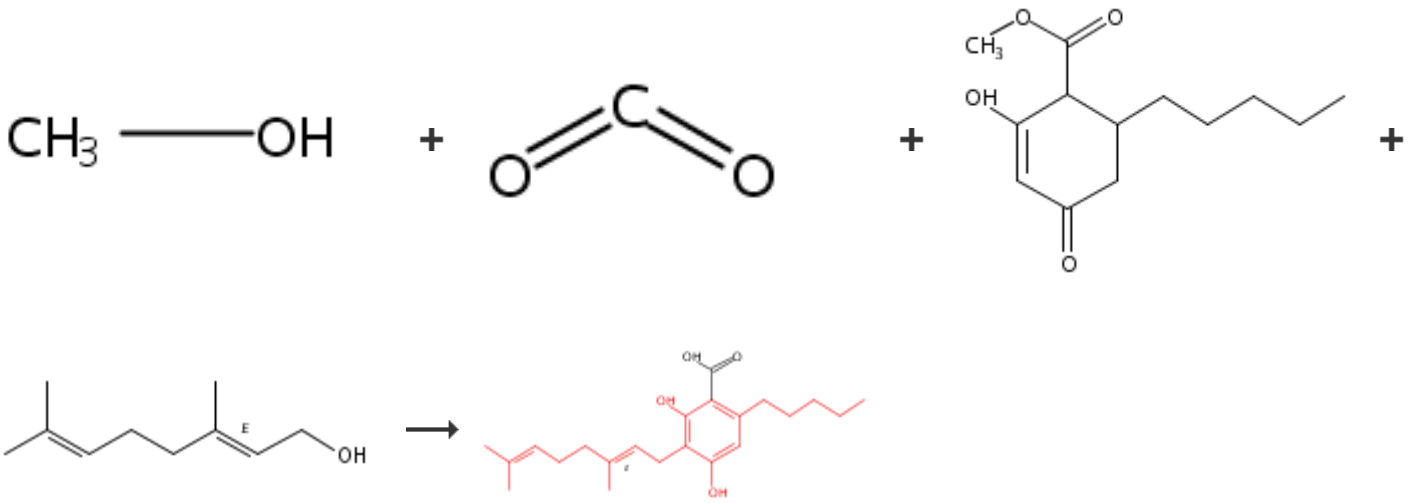
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

98. 5 Steps (Converging)



Overview

Steps/Stages

1.1 R:Mg, S:MeOH, rt
2.1 S:DMF, 140°C

1.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

2.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
3.1 S:DMF, 1 h, 120°C

3.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

Notes

exothermic reaction, in the dark, conversion = 40%,alternative preparation shown, Reactants: 4, Reagents: 4, Solvents: 4, Steps: 5, Stages: 6, Most stages in any one step: 2

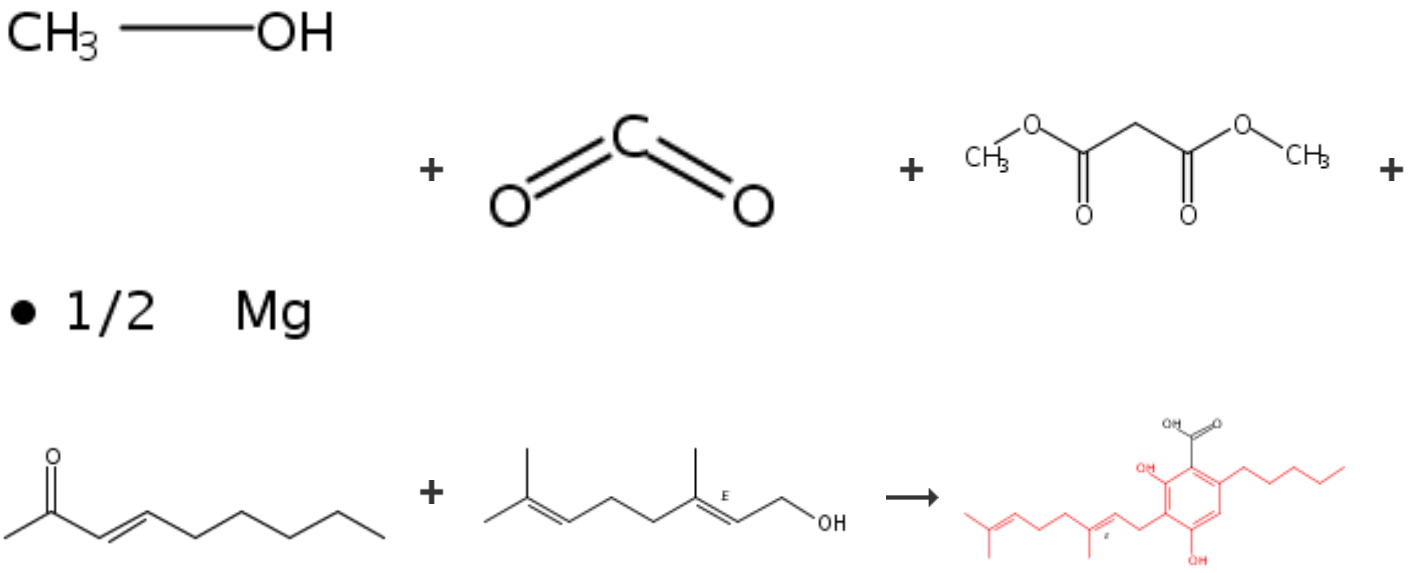
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

99. 5 Steps (Converging)



• 1/2 Mg

Overview

Steps/Stages

1.1 S:DMF, 140°C

1.1 R:NaOMe, S:MeOH, rt; 3 h, reflux; reflux → rt

1.2 R:H_2O, rt

2.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

3.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

4.1 S:DMF, 1 h, 120°C

4.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

Notes

exothermic reaction, in the dark, conversion = 40%,alternative preparation shown, Reactants: 5, Reagents: 5, Solvents: 4, Steps: 5, Stages: 7, Most stages in any one step: 2

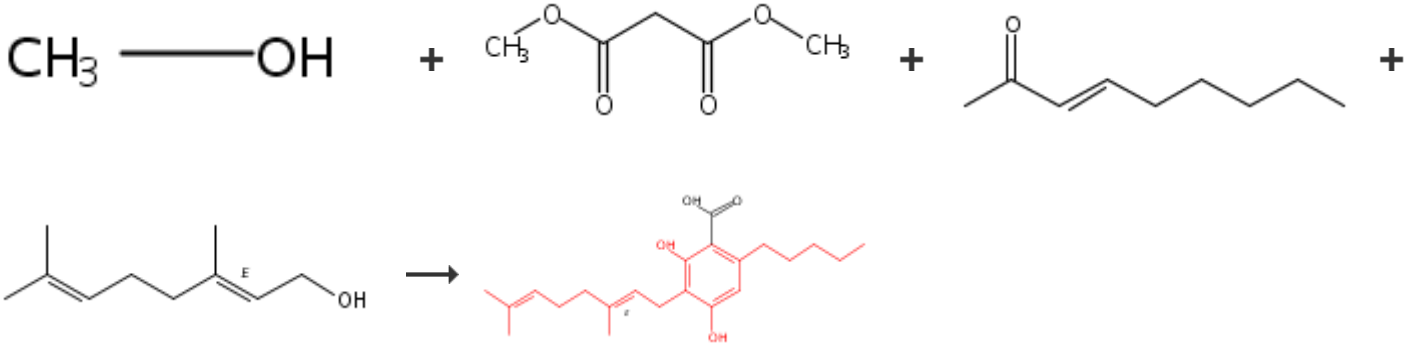
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

100. 5 Steps (Converging)



Overview

Steps/Stages

Notes

1.1 R:Mg, S:MeOH, rt

1.1 R:NaOMe, S:MeOH, rt; 3 h, reflux; reflux → rt

1.2 R:H_2O, rt

2.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

3.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
4.1 S:H_2O, cooled; 50°C; 3 h, 50°C; 50°C → rt

4.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, rt, pH 2

in the dark, conversion = 85%,alternative preparation shown,reaction in a sealed pressure vessel, Reactants: 4, Reagents: 6, Solvents: 4, Steps: 5, Stages: 7, Most stages in any one step: 2

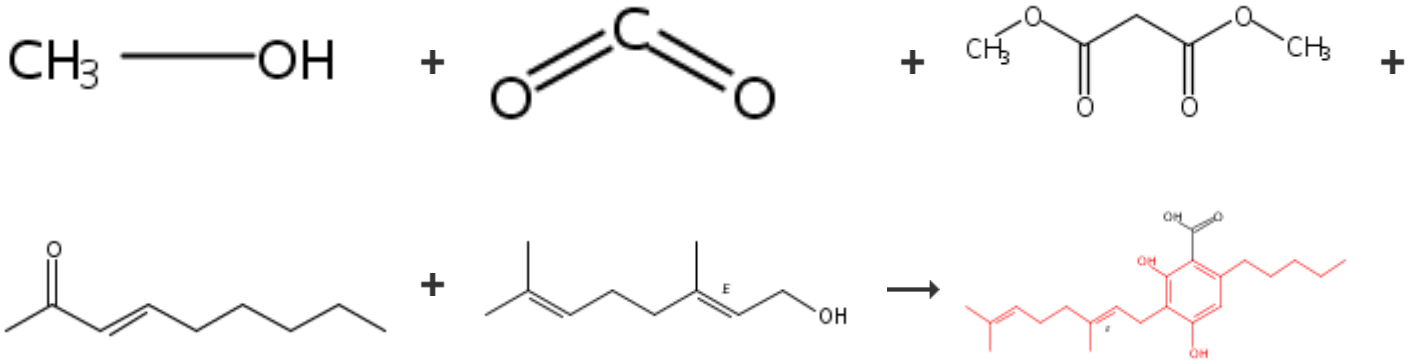
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

101. 5 Steps (Converging)



Overview

Steps/Stages

1.1 R:Mg, S:MeOH, rt
1.2 S:DMF, 140°C

1.1 R:NaOMe, S:MeOH, rt; 3 h, reflux; reflux → rt

1.2 R:HCl, S:H_2O, rt, pH 4

2.1 R:Br_2, S:DMF, cooled; 90 min, 80°C; 10 min, 80°C → 160°C
3.1 C:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
4.1 rt → 50°C; 3 h, 50°C; 50°C → rt

4.2 R:HCl, S:H_2O, S:MeOH, S:$CHCl_3$, rt, pH 2

Notes

literature preparation, exothermic (stage 2), literature preparation, in the dark, conversion, 85%, alternative preparation shown, sealed vessel used, Reactants: 5, Reagents: 4, Catalysts: 1, Solvents: 4, Steps: 5, Stages: 8, Most stages in any one step: 2

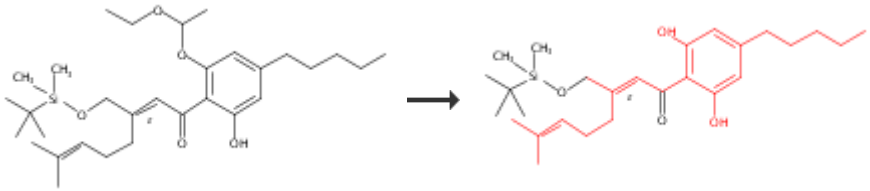
References

Chemoenzymic synthesis of cannabinoids

By Winnicki, Robert and Donsky, Marc

From PCT Int. Appl., 2014134281, 04 Sep 2014

102. Single Step



Overview

Steps/Stages

1.1 R:AcOH, R:H_2O, S:H_2O, S:THF

Notes

AcOH:THF:H2O, 1:1:1, Reactants: 1, Reagents: 2, Solvents: 2, Steps: 1, Stages: 1, Most stages in any one step: 1

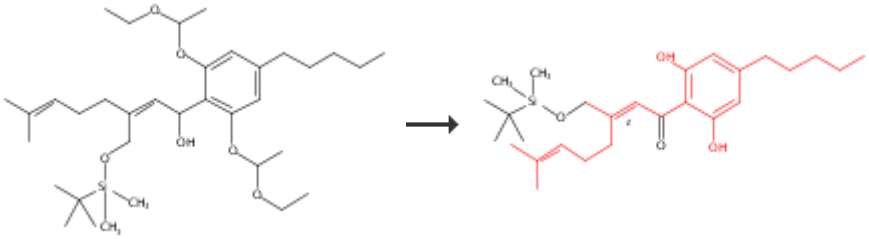
References

Synthesis of (±)-nor-Δ9-cis-6a,10a-THC-carboxylic acid (THC = tetrahydrocannabinol)

By Tius, Marcus A. and Gu, Xueqin

From Journal of the Chemical Society, Chemical Communications, (16), 1171-3; 1989

103. 2 Steps



Overview

Steps/Stages

1.1 R:$C_5H_{10}N(O=)CN=NC(=O)NC_5H_{10}$, R:*t*-BuOMgBr

2.1 R:AcOH, R:H_2O, S:H_2O, S:THF

Notes

2) AcOH:THF:H2O, 1:1:1, Reactants: 1, Reagents: 4, Solvents: 2, Steps: 2, Stages: 2, Most stages in any one step: 1

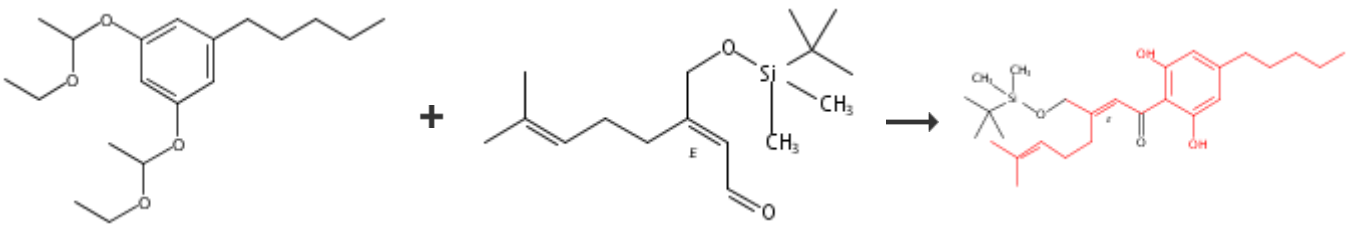
References

Synthesis of (±)-nor-Δ9-cis-6a,10a-THC-carboxylic acid (THC = tetrahydrocannabinol)

By Tius, Marcus A. and Gu, Xueqin

From Journal of the Chemical Society, Chemical Communications, (16), 1171-3; 1989

104. 3 Steps



Overview

Steps/Stages

1.1 R:BuLi, S:THF

1.2

2.1 R:$C_5H_{10}N(O=)CN=NC(=O)NC_5H_{10}$, R:*t*-BuOMgBr

3.1 R:AcOH, R:H_2O, S:H_2O, S:THF

Notes

3) AcOH:THF:H2O, 1:1:1, Reactants: 2, Reagents: 5, Solvents: 2, Steps: 3, Stages: 4, Most stages in any one step: 2

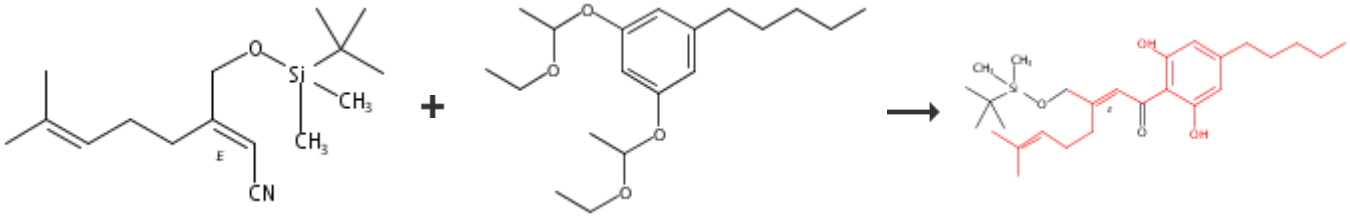
References

Synthesis of (±)-nor-Δ9-cis-6a,10a-THC-carboxylic acid (THC = tetrahydrocannabinol)

By Tius, Marcus A. and Gu, Xueqin

From Journal of the Chemical Society, Chemical Communications, (16), 1171-3; 1989

105. 4 Steps



[Step 2.1]

Overview

Steps/Stages

1.1 R:AlH(Bu-*i*)$_2$, S:Et_2O

2.1 R:BuLi, S:THF

2.2

3.1 R:$C_5H_{10}N(O=)CN=NC(=O)NC_5H_{10}$, R:*t*-BuOMgBr

4.1 R:AcOH, R:H_2O, S:H_2O, S:THF

Notes

4) AcOH:THF:H2O, 1:1:1, Reactants: 2, Reagents: 6, Solvents: 3, Steps: 4, Stages: 5, Most stages in any one step: 2

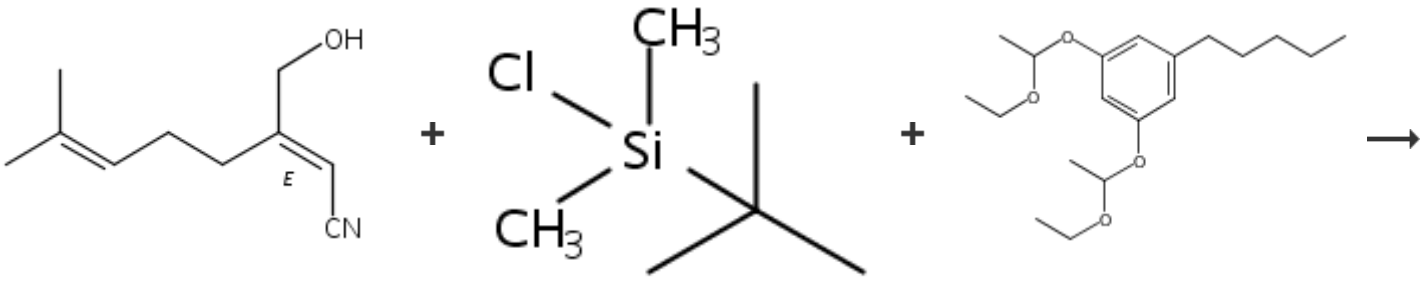
References

Synthesis of (±)-nor-Δ9-cis-6a,10a-THC-carboxylic acid (THC = tetrahydrocannabinol)

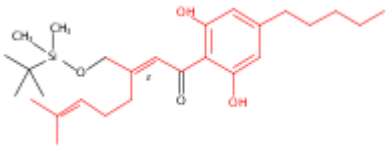
By Tius, Marcus A. and Gu, Xueqin

From Journal of the Chemical Society, Chemical Communications, (16), 1171-3; 1989

106. 5 Steps



[Step 3.1]



Overview

Steps/Stages

1.1

2.1 R:AlH(Bu-*i*)$_2$, S:Et$_2$O

3.1 R:BuLi, S:THF

3.2

4.1 R:C$_5$H$_{10}$N(O=)CN=NC(=O)NC$_5$H$_{10}$, R:*t*-BuOMgBr

5.1 R:AcOH, R:H$_2$O, S:H$_2$O, S:THF

Notes

5) AcOH:THF:H2O, 1:1:1, Reactants: 3, Reagents: 6, Solvents: 3, Steps: 5, Stages: 6, Most stages in any one step: 2

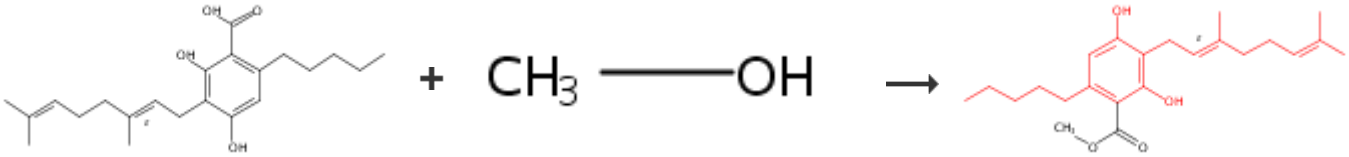
References

Synthesis of (±)-nor-Δ9-cis-6a,10a-THC-carboxylic acid (THC = tetrahydrocannabinol)

By Tius, Marcus A. and Gu, Xueqin

From Journal of the Chemical Society, Chemical Communications, (16), 1171-3; 1989

107. Single Step



70%

Overview

Steps/Stages

1.1 R:DCC, C:*p*-MeC$_6$H$_4$SO$_3$H, S:MeOH, 40 min, rt

Notes

Reactants: 2, Reagents: 1, Catalysts: 1, Solvents: 1, Steps: 1, Stages: 1, Most stages in any one step: 1

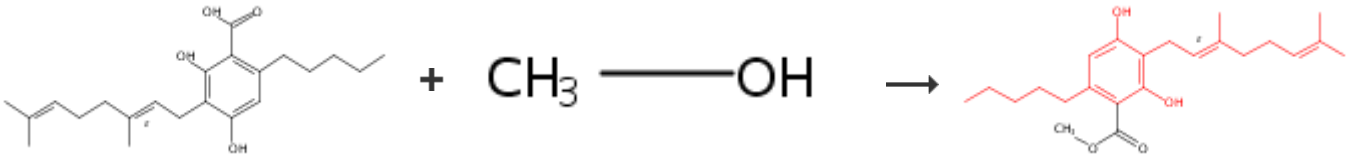
References

Preparation of cannabigerol derivatives as PPAR-γ agonists and therapeutic uses thereof

By Appendino, Giovanni et al

From Eur. Pat. Appl., 2913321, 02 Sep 2015

108. Single Step



70%

Overview

Steps/Stages

1.1 R:DCC, C:*p*-$MeC_6H_4SO_3H$, S:MeOH, 40 min, rt
1.2 S:PhMe, 1 h, -18°C

Notes

Reactants: 2, Reagents: 1, Catalysts: 1, Solvents: 2, Steps: 1, Stages: 2, Most stages in any one step: 2

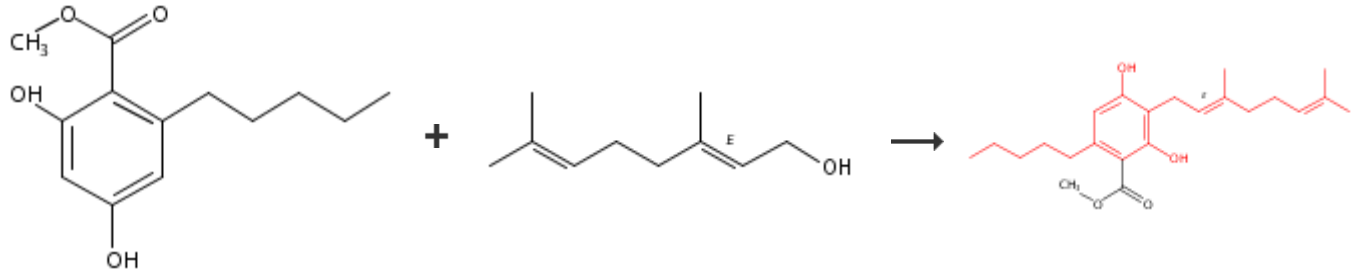
References

Preparation of cannabigerol derivatives as PPAR-γ agonists and therapeutic uses thereof

By Appendino, Giovanni et al

From PCT Int. Appl., 2015128200, 03 Sep 2015

109. Single Step



40%

Overview

Steps/Stages

1.1 R:BF_3-Et_2O, S:$CHCl_3$, 0.25 h, -20°C

Notes

Reactants: 2, Reagents: 1, Solvents: 1, Steps: 1, Stages: 1, Most stages in any one step: 1

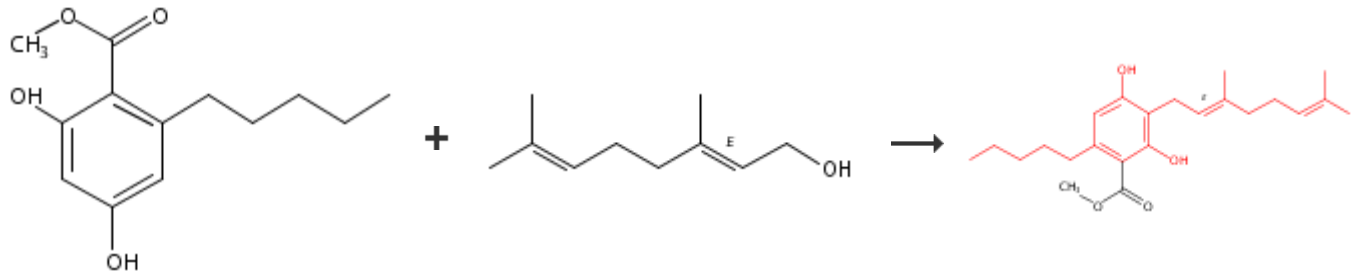
References

Synthesis of phytocannabinoids including a decarboxylation step

By Reekie, Tristan et al

From PCT Int. Appl., 2019033168, 21 Feb 2019

110. Single Step



40%

Overview

Steps/Stages

1.1 R:BF_3-Et_2O, S:$CHCl_3$, 0.25 h, -20°C

Notes

Reactants: 2, Reagents: 1, Solvents: 1, Steps: 1, Stages: 1, Most stages in any one step: 1

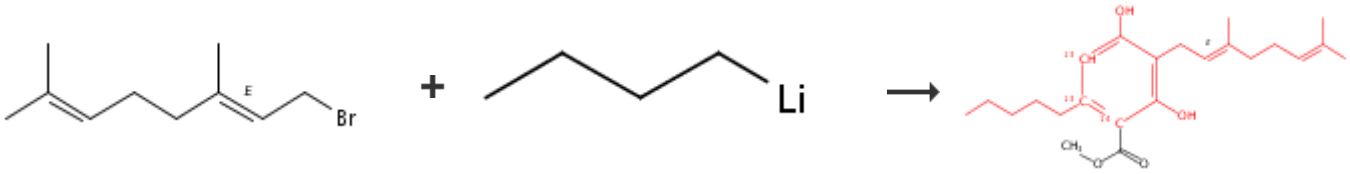
References

Synthesis of phytocannabinoids including a demethylation step

By Reekie, Tristan et al

From PCT Int. Appl., 2019033164, 21 Feb 2019

111. Single Step



Overview

Steps/Stages

1.1 R:Benzene

1.2 R:HCl, S:H_2O

Notes

Reactants: 2, Reagents: 2, Solvents: 1, Steps: 1, Stages: 2, Most stages in any one step: 2

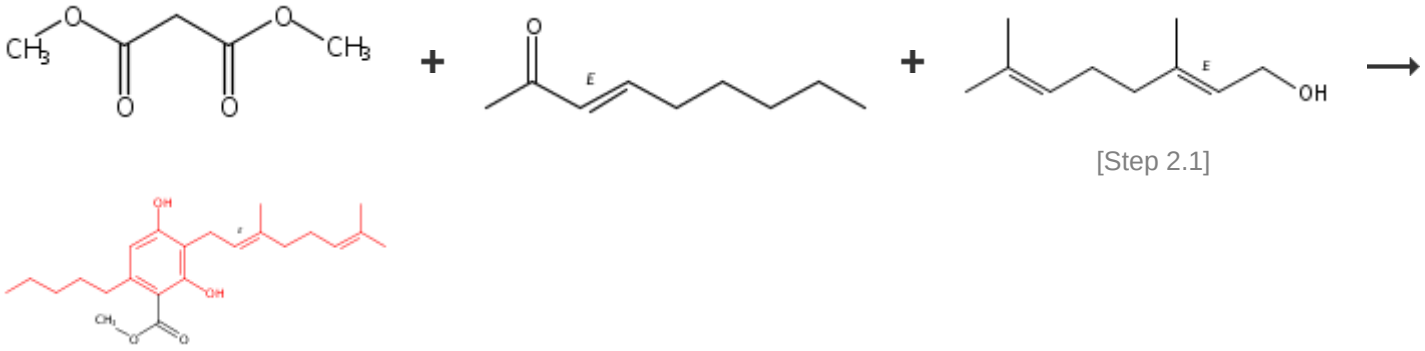
References

Synthesis of [5,6-13C2,1-14C]olivetolic acid, methyl [1'-13C]olivetolate and [5,6-13C2,1-14C]cannabigerolic acid

By Porwoll, Joseph P. and Leete, Edward

From Journal of Labelled Compounds and Radiopharmaceuticals, 22(3), 257-71; 1985

112. 2 Steps



[Step 2.1]

Overview

Steps/Stages

Notes

1.1 R:Na, S:MeOH, 0°C; 8 h, reflux

1.2 R:Br_2, S:DMF, 0°C; 1 h, 20°C; 16 h, 20°C → 80°C; cooled

1.3 R:$Na_2S_2O_3$, S:H_2O

2.1 R:BF_3-Et_2O, S:$CHCl_3$, 0.25 h, -20°C

Reactants: 3, Reagents: 4, Solvents: 4, Steps: 2, Stages: 4, Most stages in any one step: 3

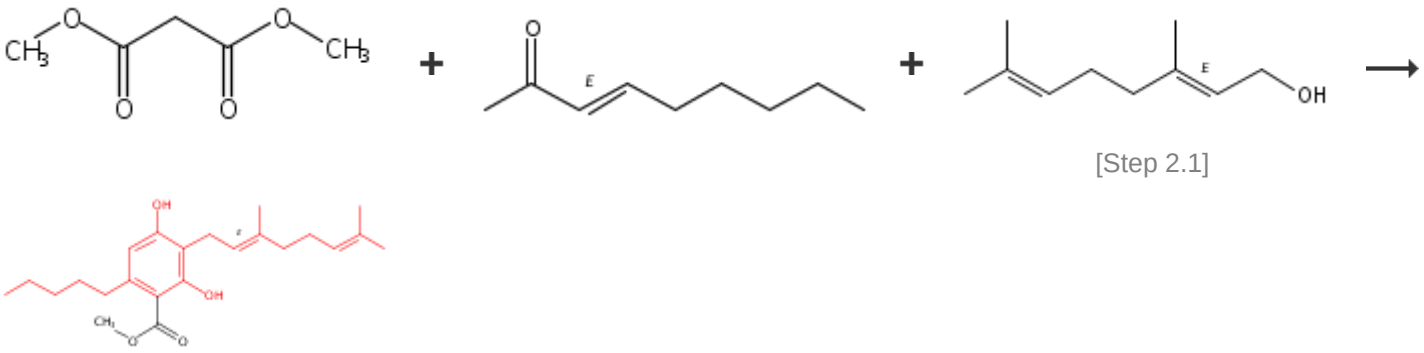
References

Synthesis of phytocannabinoids including a decarboxylation step

By Reekie, Tristan et al

From PCT Int. Appl., 2019033168, 21 Feb 2019

113. 2 Steps



[Step 2.1]

Overview

Steps/Stages

1.1 R:Na, S:MeOH, 0°C; 8 h, reflux

1.2 R:Br_2, S:DMF, 0°C; 1 h, 20°C; 16 h, 20°C → 80°C; cooled

1.3 R:$Na_2S_2O_3$, S:H_2O

2.1 R:BF_3-Et_2O, S:$CHCl_3$, 0.25 h, -20°C

Notes

Reactants: 3, Reagents: 4, Solvents: 4, Steps: 2, Stages: 4, Most stages in any one step: 3

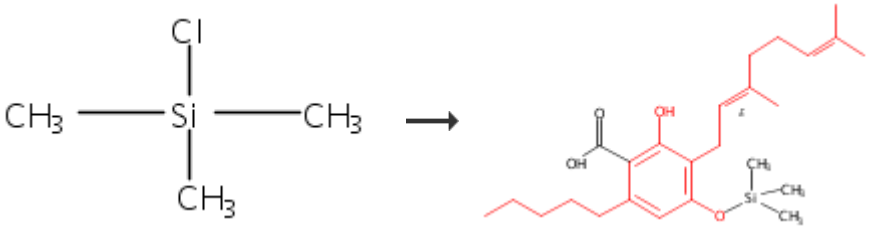
References

Synthesis of phytocannabinoids including a demethylation step

By Reekie, Tristan et al

From PCT Int. Appl., 2019033164, 21 Feb 2019

114. Single Step



Overview

Steps/Stages

Notes

1.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

1.2 R:NaCl, S:H_2O

unspecified reactant used in stage 1, regioselective, Reactants: 1, Reagents: 2, Solvents: 2, Steps: 1, Stages: 2, Most stages in any one step: 2

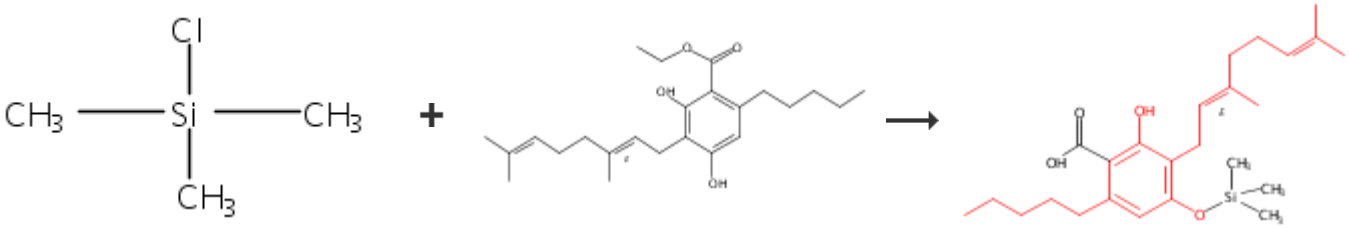
References

Methods for the manufacture of cannabinoid prodrugs, pharmaceutical formulations and their use

By Peet, Richard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017216362, 21 Dec 2017

115. Single Step



Overview

Steps/Stages

1.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

1.2 R:NaCl, S:H_2O

1.3

Notes

unspecified reagent used for acidic hydrolysis in stage 3,alternative preparation shown, regioselective, Reactants: 2, Reagents: 2, Solvents: 2, Steps: 1, Stages: 3, Most stages in any one step: 3

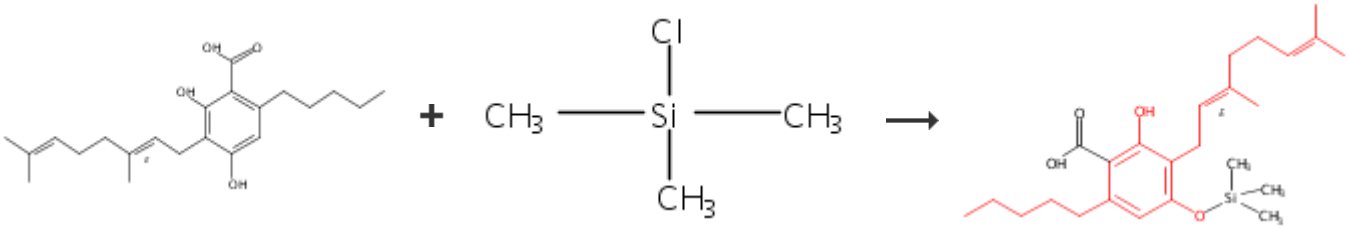
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

116. Single Step



Overview

Steps/Stages

1.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

1.2 R:NaCl, S:H_2O

Notes

alternative preparation shown, regioselective, Reactants: 2, Reagents: 2, Solvents: 2, Steps: 1, Stages: 2, Most stages in any one step: 2

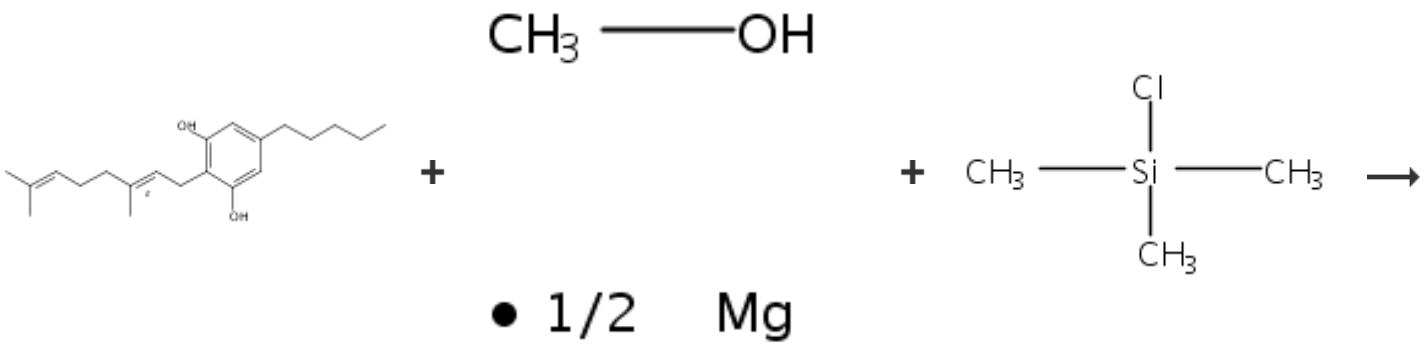
References

Biosynthesis of cannabinoid prodrugs

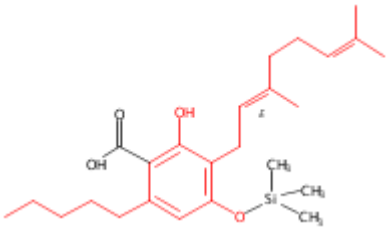
By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

117. 2 Steps



[Step 2.1]



Overview

Steps/Stages

1.1 S:H_2O, cooled; 50°C; 3 h, 50°C; 50°C → rt

1.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, rt, pH 2

2.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

2.2 R:NaCl, S:H_2O

Notes

1) conversion = 85%,alternative preparation shown,reaction in a sealed pressure vessel, 2) alternative preparation shown, regioselective, Reactants: 3, Reagents: 3, Solvents: 4, Steps: 2, Stages: 4, Most stages in any one step: 2

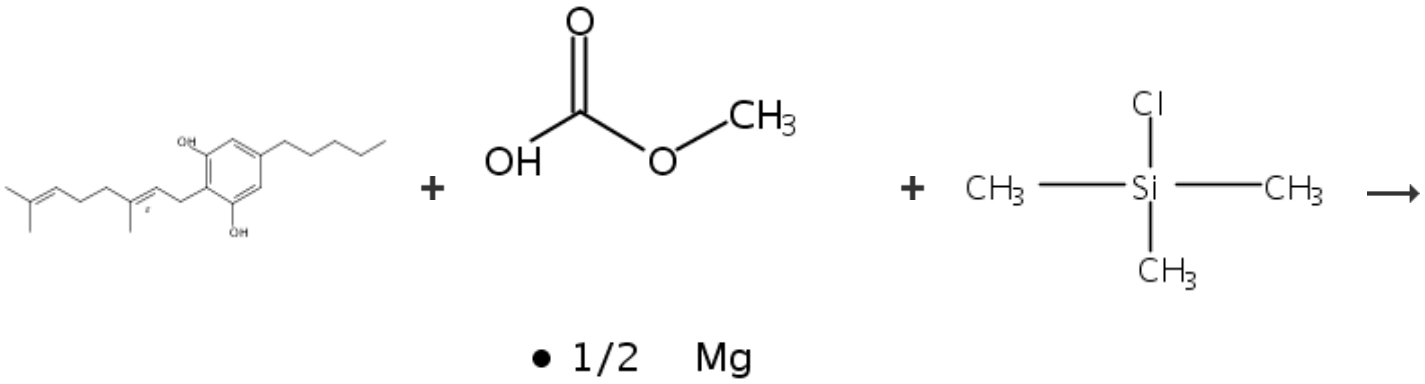
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

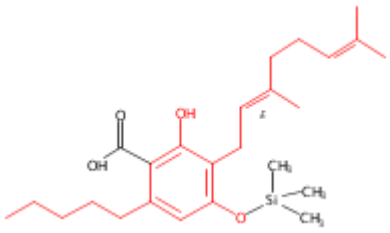
From PCT Int. Appl., 2017181118, 19 Oct 2017

118. 2 Steps



• 1/2 Mg

[Step 2.1]



Overview

Steps/Stages

1.1 S:DMF, 1 h, 120°C

1.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

2.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

2.2 R:NaCl, S:H_2O

Notes

1) conversion = 40%,alternative preparation shown, 2) alternative preparation shown, regioselective, Reactants: 3, Reagents: 3, Solvents: 5, Steps: 2, Stages: 4, Most stages in any one step: 2

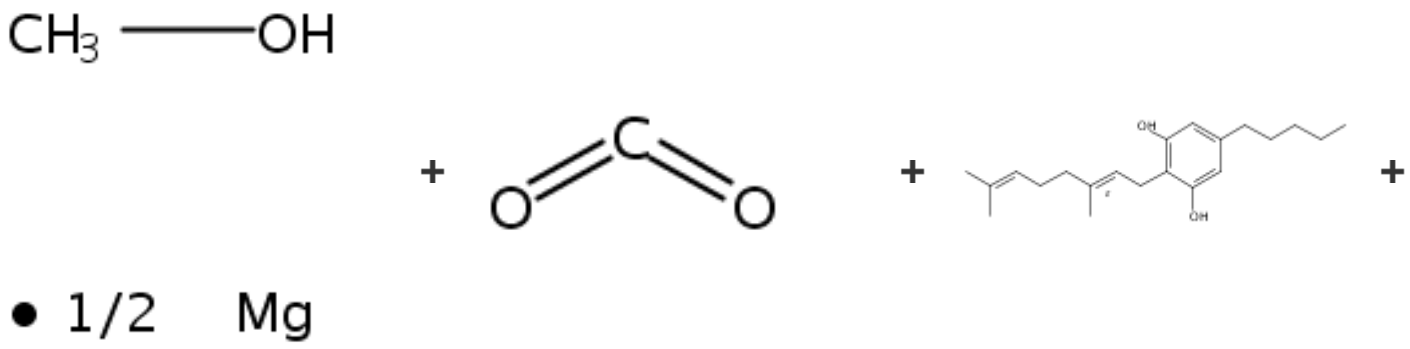
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

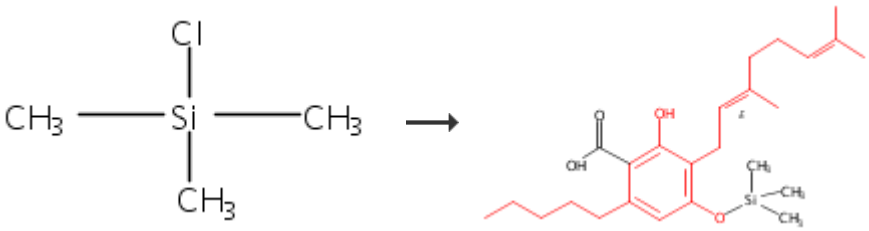
From PCT Int. Appl., 2017181118, 19 Oct 2017

119. 3 Steps



• 1/2 Mg

[Step 2.1]



[Step 3.1]

Overview

Steps/Stages

1.1 S:DMF, 140°C
2.1 S:DMF, 1 h, 120°C

2.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

3.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

3.2 R:NaCl, S:H_2O

Notes

1) exothermic reaction, 2) conversion = 40%,alternative preparation shown, 3) alternative preparation shown, regioselective, Reactants: 4, Reagents: 3, Solvents: 5, Steps: 3, Stages: 5, Most stages in any one step: 2

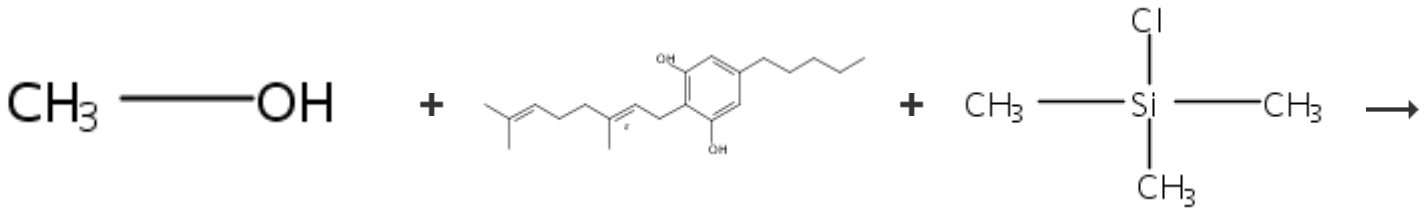
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

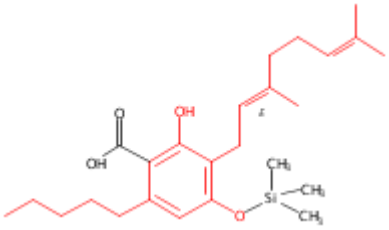
From PCT Int. Appl., 2017181118, 19 Oct 2017

120. 3 Steps



[Step 2.1]

[Step 3.1]



Overview

Steps/Stages

Notes

1.1 R:Mg, S:MeOH, rt
2.1 S:H_2O, cooled; 50°C; 3 h, 50°C; 50°C → rt
2.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, rt, pH 2
3.1 R:1H-Imidazole, S:CH_2Cl_2, cooled
3.2 R:NaCl, S:H_2O

2) conversion = 85%,alternative preparation shown,reaction in a sealed pressure vessel, 3) alternative preparation shown, regioselective, Reactants: 3, Reagents: 4, Solvents: 4, Steps: 3, Stages: 5, Most stages in any one step: 2

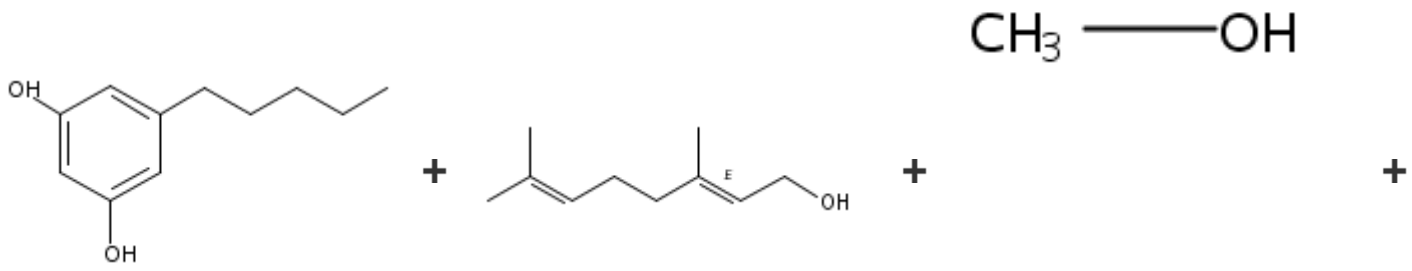
References

Biosynthesis of cannabinoid prodrugs

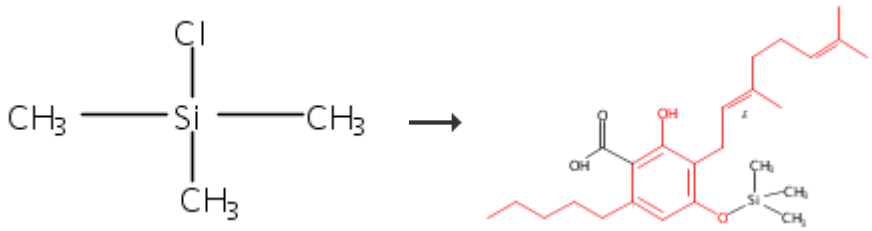
By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

121. 3 Steps



[Step 2.1]



[Step 3.1]

Overview

Steps/Stages

1.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
2.1 S:H_2O, cooled; 50°C; 3 h, 50°C; 50°C → rt
2.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, rt, pH 2
3.1 R:1H-Imidazole, S:CH_2Cl_2, cooled
3.2 R:NaCl, S:H_2O

Notes

1) in the dark, 2) conversion = 85%,alternative preparation shown,reaction in a sealed pressure vessel, 3) alternative preparation shown, regioselective, Reactants: 4, Reagents: 4, Solvents: 4, Steps: 3, Stages: 5, Most stages in any one step: 2

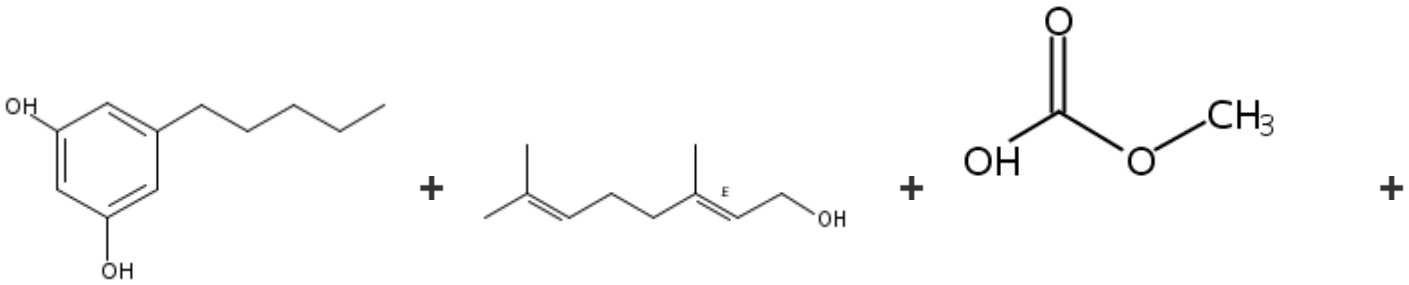
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

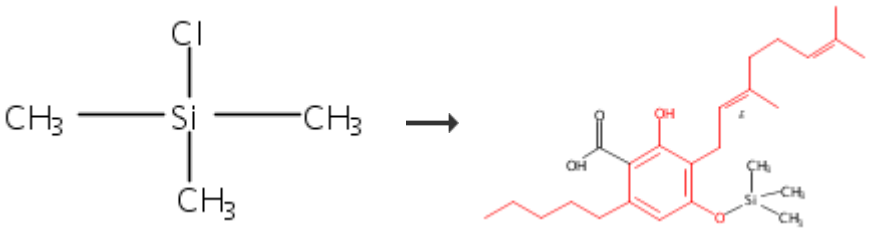
From PCT Int. Appl., 2017181118, 19 Oct 2017

122. 3 Steps



• 1/2 Mg

[Step 2.1]



[Step 3.1]

Overview

Steps/Stages

1.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
2.1 S:DMF, 1 h, 120°C

2.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

3.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

3.2 R:NaCl, S:H_2O

Notes

1) in the dark, 2) conversion = 40%,alternative preparation shown, 3) alternative preparation shown, regioselective, Reactants: 4, Reagents: 4, Solvents: 5, Steps: 3, Stages: 5, Most stages in any one step: 2

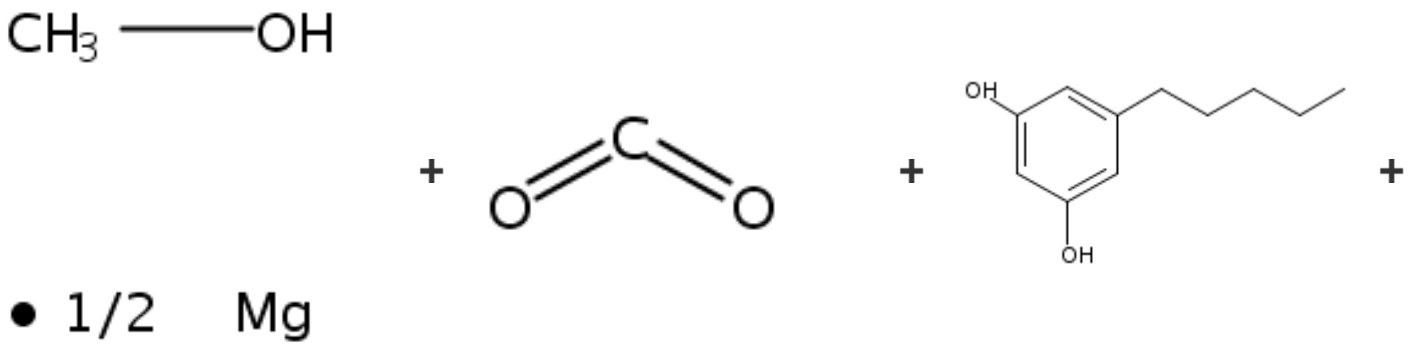
References

Biosynthesis of cannabinoid prodrugs

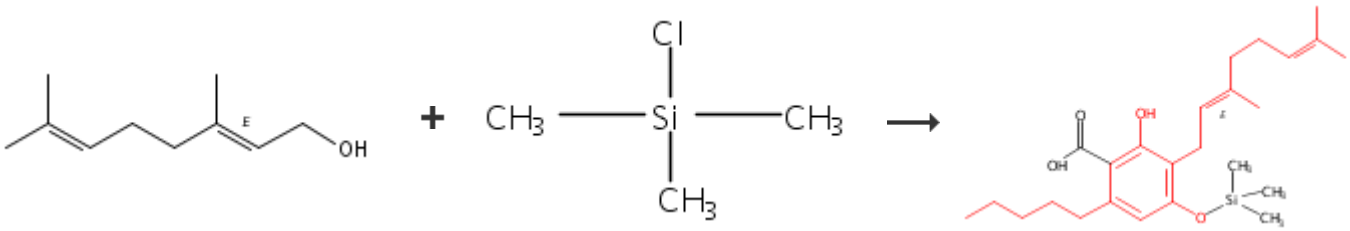
By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

123. 4 Steps (Converging)



• 1/2 Mg



Overview

Steps/Stages

1.1 S:DMF, 140°C

1.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
2.1 S:DMF, 1 h, 120°C

2.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

3.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

3.2 R:NaCl, S:H_2O

Notes

exothermic reaction, in the dark, conversion = 40%,alternative preparation shown, alternative preparation shown, regioselective, Reactants: 5, Reagents: 4, Solvents: 5, Steps: 4, Stages: 6, Most stages in any one step: 2

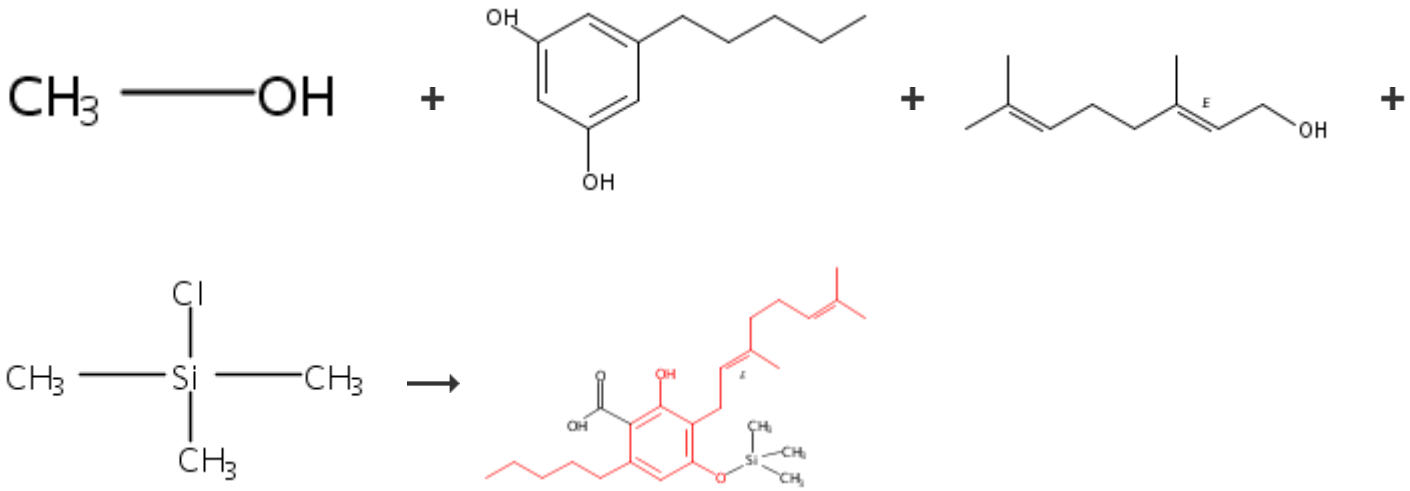
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

124. 4 Steps (Converging)



Overview

Steps/Stages

Notes

1.1 R:Mg, S:MeOH, rt

1.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
2.1 S:H_2O, cooled; 50°C; 3 h, 50°C; 50°C → rt

2.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, rt, pH 2

3.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

3.2 R:NaCl, S:H_2O

in the dark, conversion = 85%,alternative preparation shown,reaction in a sealed pressure vessel, alternative preparation shown, regioselective, Reactants: 4, Reagents: 5, Solvents: 4, Steps: 4, Stages: 6, Most stages in any one step: 2

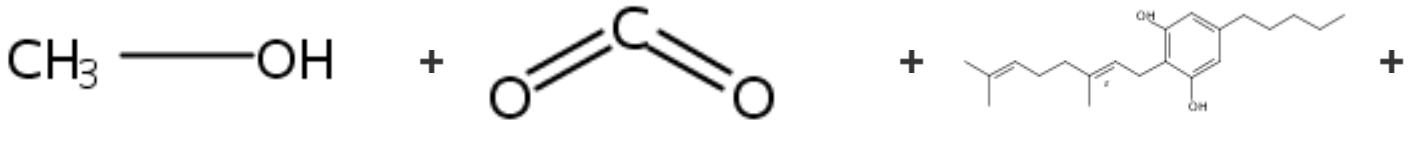
References

Biosynthesis of cannabinoid prodrugs

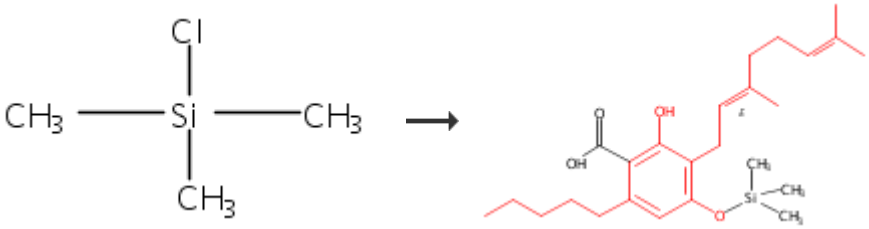
By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

125. 4 Steps



[Step 2.1] [Step 3.1]



[Step 4.1]

Overview

Steps/Stages

1.1 R:Mg, S:MeOH, rt
2.1 S:DMF, 140°C
3.1 S:DMF, 1 h, 120°C

3.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

4.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

4.2 R:NaCl, S:H_2O

Notes

2) exothermic reaction, 3) conversion = 40%,alternative preparation shown, 4) alternative preparation shown, regioselective, Reactants: 4, Reagents: 4, Solvents: 5, Steps: 4, Stages: 6, Most stages in any one step: 2

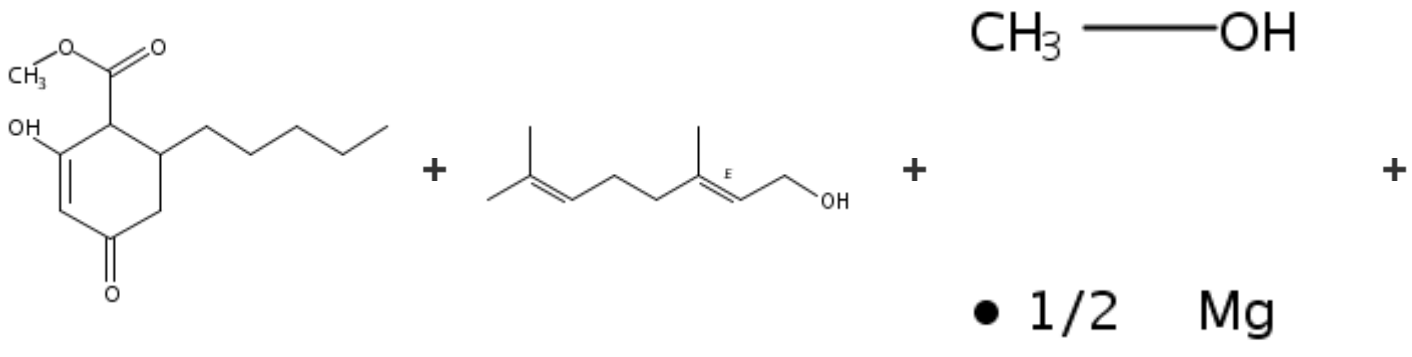
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

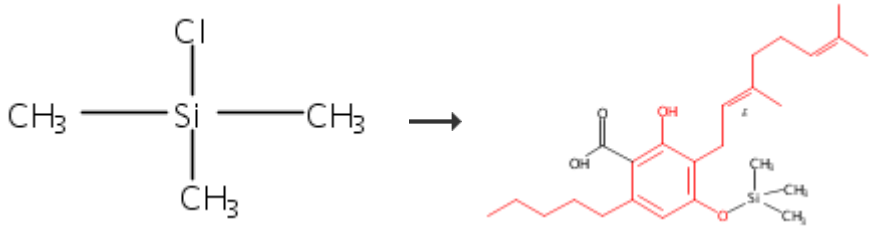
From PCT Int. Appl., 2017181118, 19 Oct 2017

126. 4 Steps



[Step 2.1]

[Step 3.1]



[Step 4.1]

Overview

Steps/Stages

1.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

2.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

3.1 S:H_2O, cooled; 50°C; 3 h, 50°C; 50°C → rt

3.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, rt, pH 2

4.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

4.2 R:NaCl, S:H_2O

Notes

2) in the dark, 3) conversion = 85%,alternative preparation shown,reaction in a sealed pressure vessel, 4) alternative preparation shown, regioselective, Reactants: 4, Reagents: 5, Solvents: 5, Steps: 4, Stages: 6, Most stages in any one step: 2

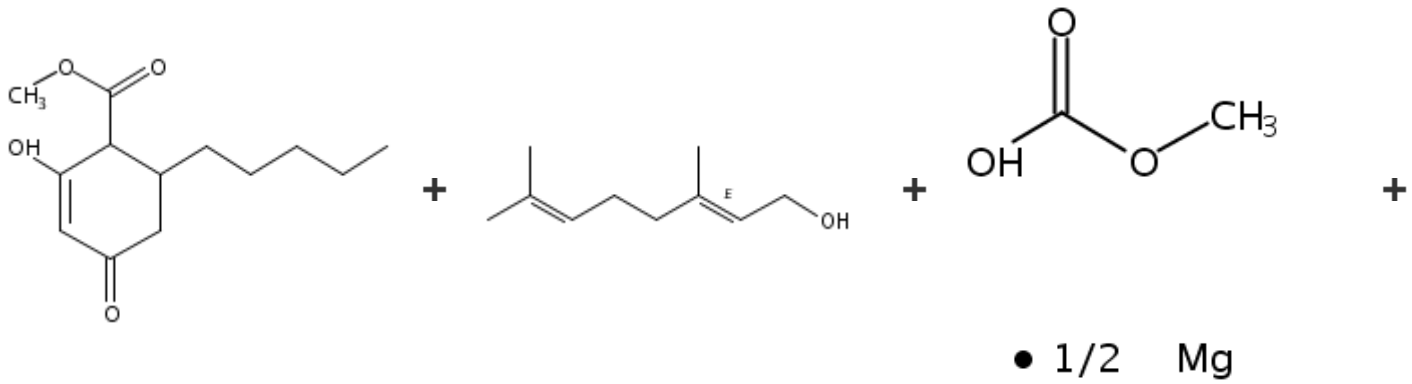
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

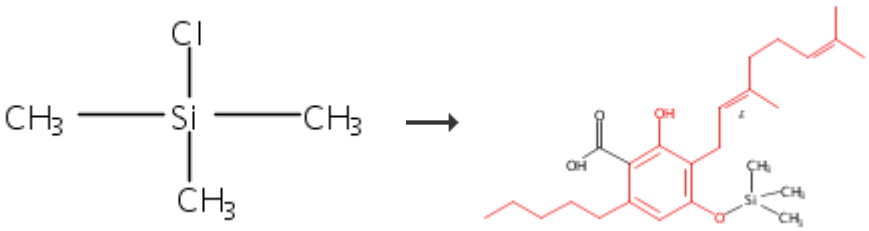
From PCT Int. Appl., 2017181118, 19 Oct 2017

127. 4 Steps



[Step 2.1]

[Step 3.1]



[Step 4.1]

Overview

Steps/Stages

1.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

2.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

3.1 S:DMF, 1 h, 120°C

3.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

4.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

4.2 R:NaCl, S:H_2O

Notes

2) in the dark, 3) conversion = 40%,alternative preparation shown, 4) alternative preparation shown, regioselective, Reactants: 4, Reagents: 5, Solvents: 5, Steps: 4, Stages: 6, Most stages in any one step: 2

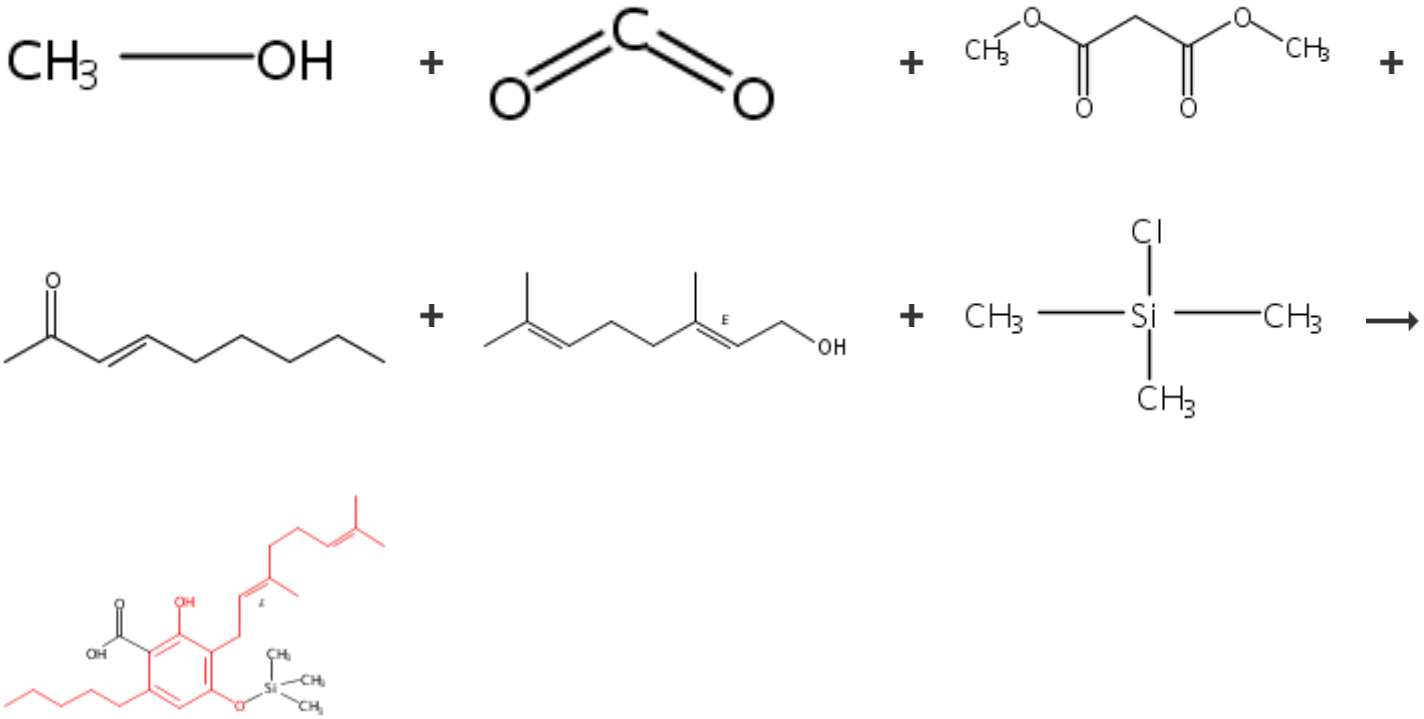
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

128. 7 Steps (Converging)



Overview

Steps/Stages

Notes

1.1 R:Mg, S:MeOH, rt
2.1 S:DMF, 140°C

1.1 R:NaOMe, S:MeOH, rt; 3 h, reflux; reflux → rt

1.2 R:H_2O, rt

2.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

3.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
4.1 S:DMF, 1 h, 120°C

4.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

5.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

5.2 R:NaCl, S:H_2O

exothermic reaction, in the dark, conversion = 40%,alternative preparation shown, alternative preparation shown, regioselective, Reactants: 6, Reagents: 8, Solvents: 5, Steps: 7, Stages: 10, Most stages in any one step: 2

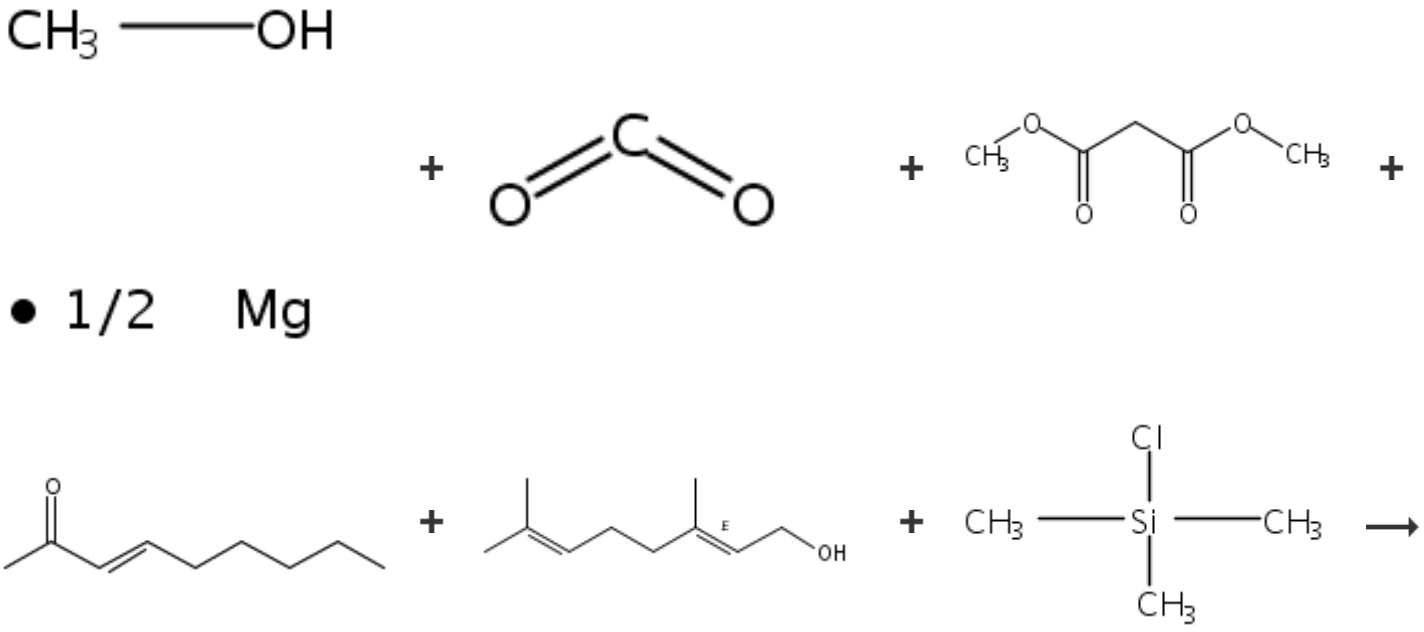
References

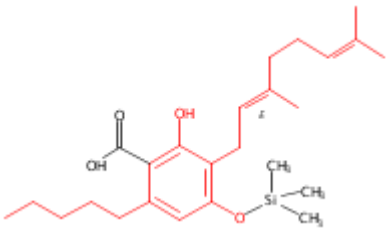
Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

129. 6 Steps (Converging)





Overview

Steps/Stages

Notes

1.1 S:DMF, 140°C

1.1 R:NaOMe, S:MeOH, rt; 3 h, reflux; reflux → rt

1.2 R:H_2O, rt

2.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

3.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
4.1 S:DMF, 1 h, 120°C

4.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

5.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

5.2 R:NaCl, S:H_2O

exothermic reaction, in the dark, conversion = 40%,alternative preparation shown, alternative preparation shown, regioselective, Reactants: 6, Reagents: 7, Solvents: 5, Steps: 6, Stages: 9, Most stages in any one step: 2

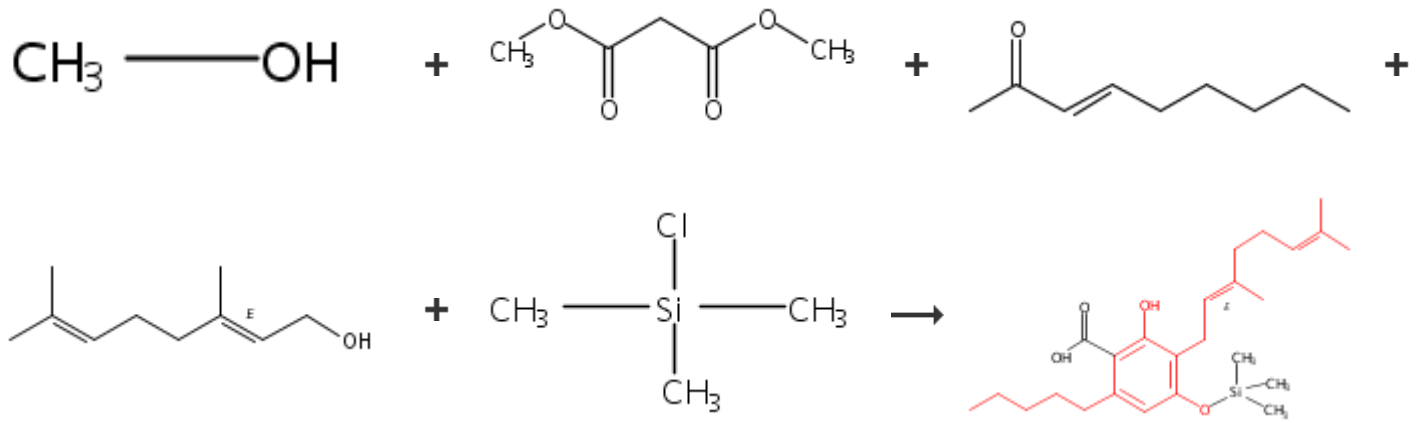
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

130. 6 Steps (Converging)



Overview

Steps/Stages

1.1 R:Mg, S:MeOH, rt

1.1 R:NaOMe, S:MeOH, rt; 3 h, reflux; reflux → rt

1.2 R:H_2O, rt

2.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

3.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
4.1 S:H_2O, cooled; 50°C; 3 h, 50°C; 50°C → rt

4.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, rt, pH 2

5.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

5.2 R:NaCl, S:H_2O

Notes

in the dark, conversion = 85%,alternative preparation shown,reaction in a sealed pressure vessel, alternative preparation shown, regioselective, Reactants: 5, Reagents: 8, Solvents: 5, Steps: 6, Stages: 9, Most stages in any one step: 2

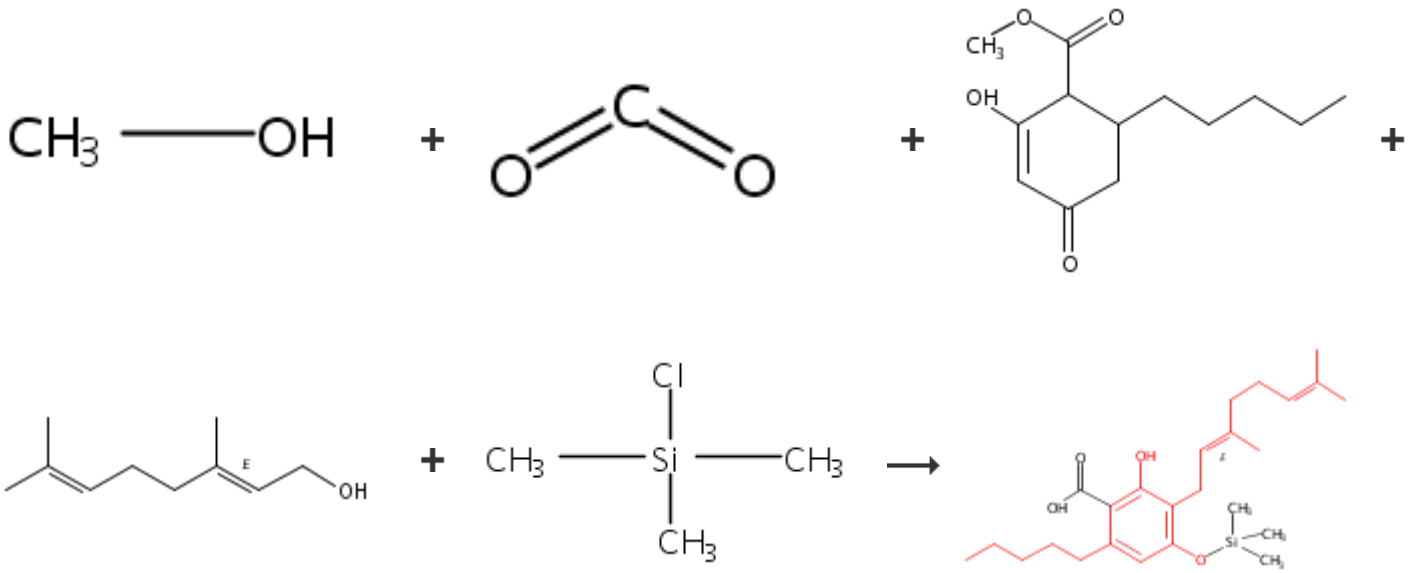
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

131. 6 Steps (Converging)



Overview

Steps/Stages

1.1 R:Mg, S:MeOH, rt
2.1 S:DMF, 140°C

1.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

2.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
3.1 S:DMF, 1 h, 120°C

3.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

4.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

4.2 R:NaCl, S:H_2O

Notes

exothermic reaction, in the dark, conversion = 40%,alternative preparation shown, alternative preparation shown, regioselective, Reactants: 5, Reagents: 6, Solvents: 5, Steps: 6, Stages: 8, Most stages in any one step: 2

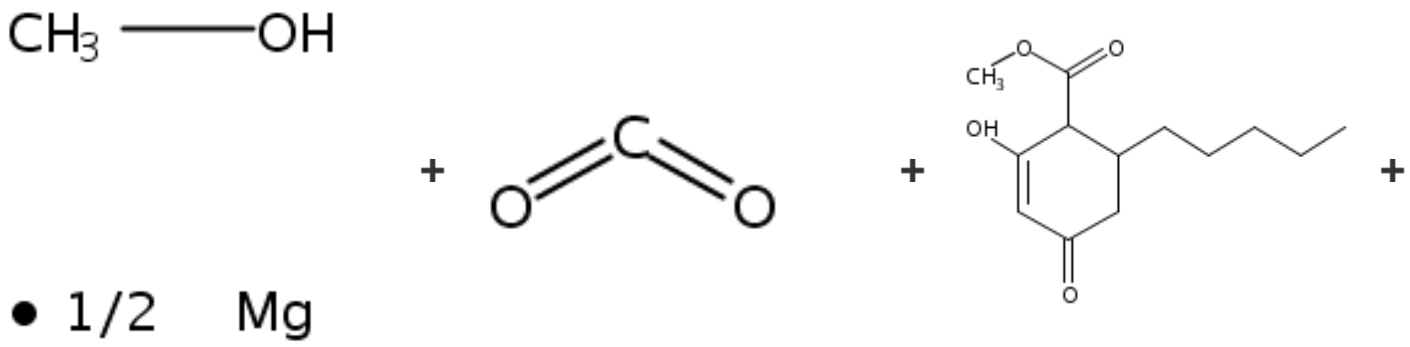
References

Biosynthesis of cannabinoid prodrugs

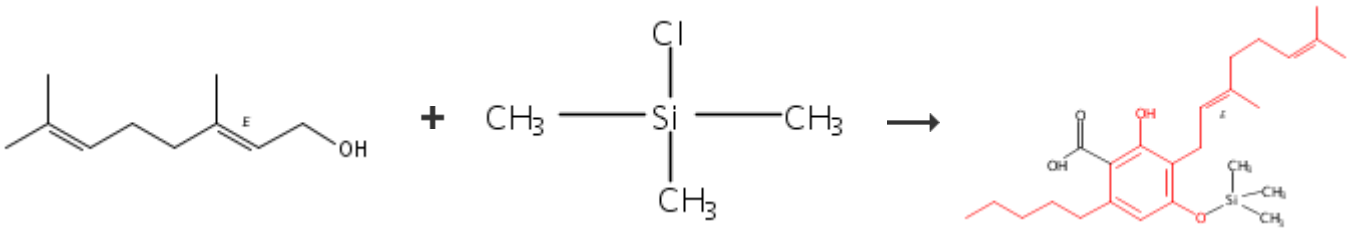
By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

132. 5 Steps (Converging)



- 1/2 Mg



Overview

Steps/Stages

1.1 S:DMF, 140°C

1.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

2.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

3.1 S:DMF, 1 h, 120°C

3.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

4.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

4.2 R:NaCl, S:H_2O

Notes

exothermic reaction, in the dark, conversion = 40%,alternative preparation shown, alternative preparation shown, regioselective, Reactants: 5, Reagents: 5, Solvents: 5, Steps: 5, Stages: 7, Most stages in any one step: 2

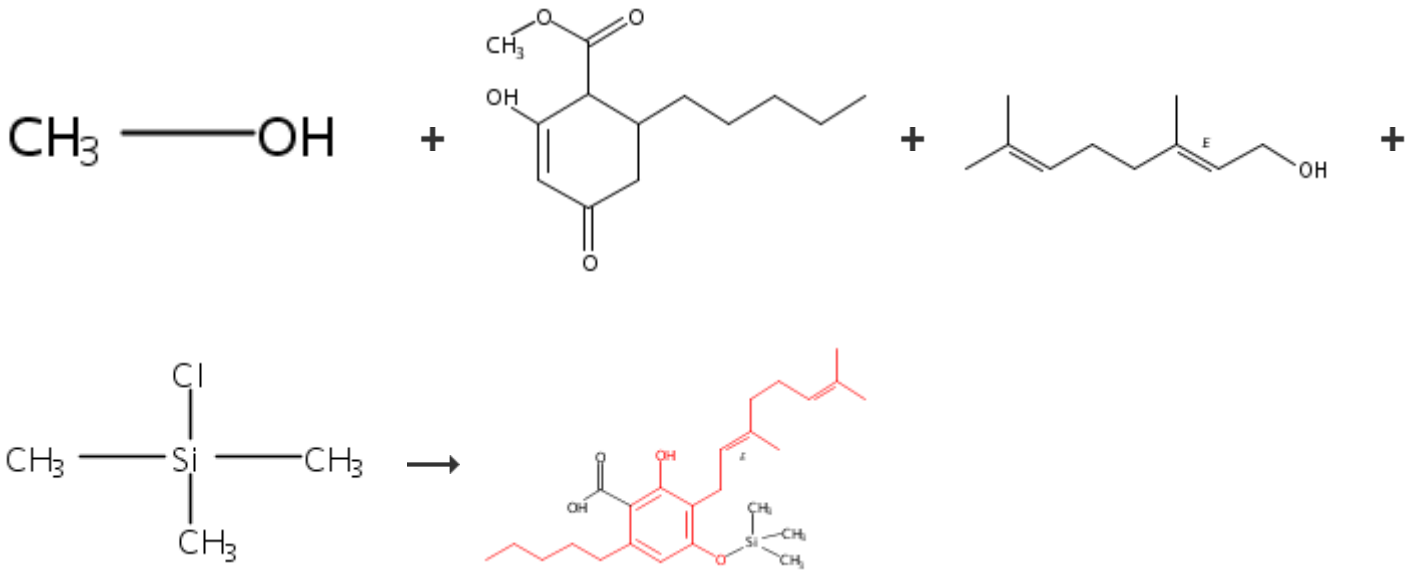
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

133. 5 Steps (Converging)



Overview

Steps/Stages

Notes

1.1 R:Mg, S:MeOH, rt

1.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

2.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
3.1 S:H_2O, cooled; 50°C; 3 h, 50°C; 50°C → rt

3.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, rt, pH 2

4.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

4.2 R:NaCl, S:H_2O

in the dark, conversion = 85%,alternative preparation shown,reaction in a sealed pressure vessel, alternative preparation shown, regioselective, Reactants: 4, Reagents: 6, Solvents: 5, Steps: 5, Stages: 7, Most stages in any one step: 2

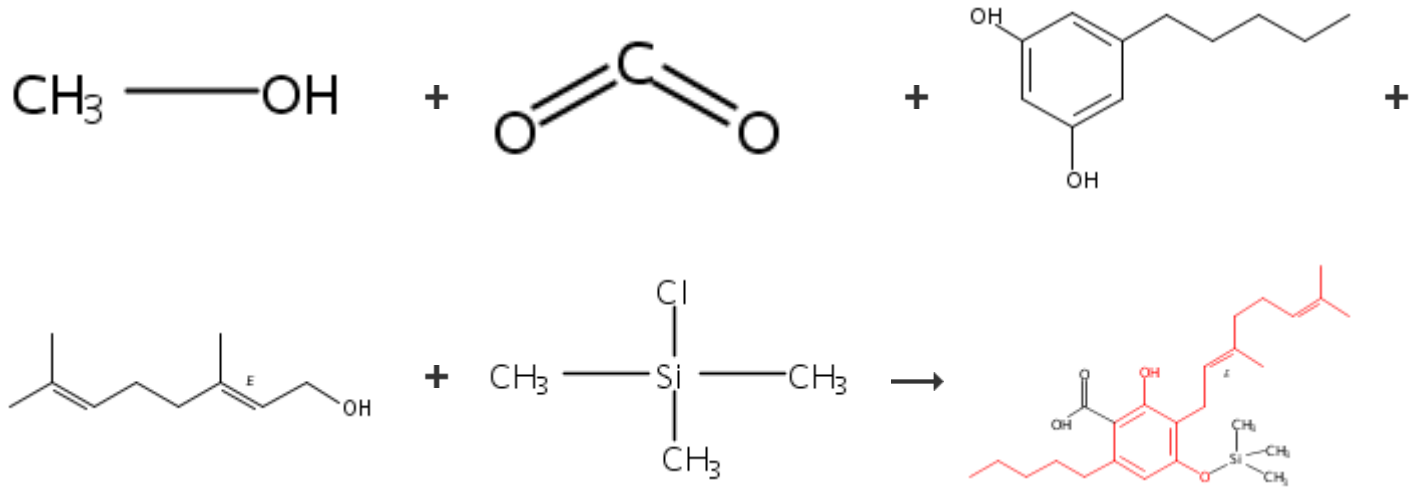
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

134. 5 Steps (Converging)



Overview

Steps/Stages

1.1 R:Mg, S:MeOH, rt
2.1 S:DMF, 140°C

1.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
2.1 S:DMF, 1 h, 120°C

2.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

3.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

3.2 R:NaCl, S:H_2O

Notes

exothermic reaction, in the dark, conversion = 40%,alternative preparation shown, alternative preparation shown, regioselective, Reactants: 5, Reagents: 5, Solvents: 5, Steps: 5, Stages: 7, Most stages in any one step: 2

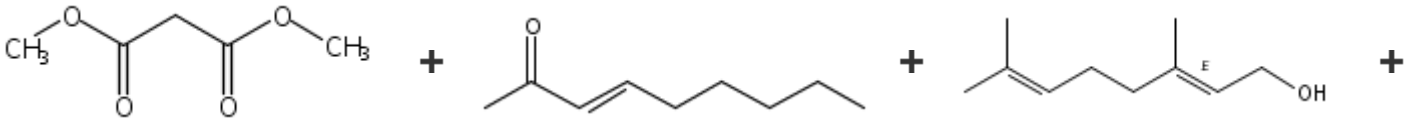
References

Biosynthesis of cannabinoid prodrugs

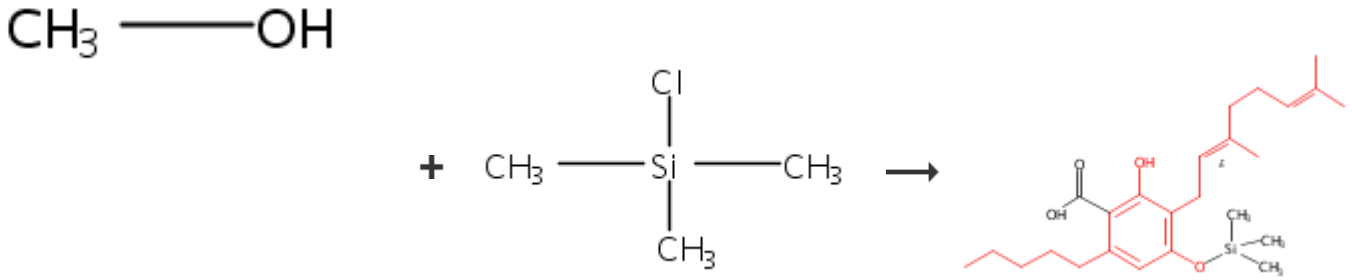
By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

135. 5 Steps



[Step 3.1]



• 1/2 Mg

[Step 4.1] [Step 5.1]

Overview

Steps/Stages

1.1 R:NaOMe, S:MeOH, rt; 3 h, reflux; reflux → rt

1.2 R:H_2O, rt

2.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

3.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

4.1 S:H_2O, cooled; 50°C; 3 h, 50°C; 50°C → rt

4.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, rt, pH 2

5.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

5.2 R:NaCl, S:H_2O

Notes

3) in the dark, 4) conversion = 85%,alternative preparation shown,reaction in a sealed pressure vessel, 5) alternative preparation shown, regioselective, Reactants: 5, Reagents: 7, Solvents: 5, Steps: 5, Stages: 8, Most stages in any one step: 2

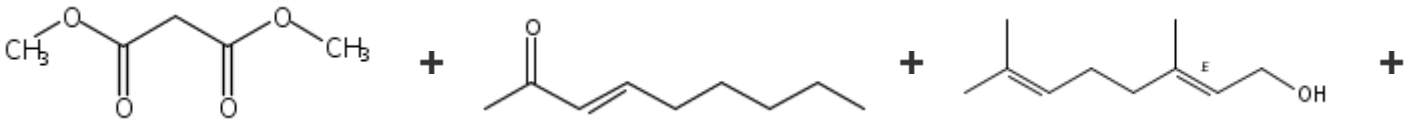
References

Biosynthesis of cannabinoid prodrugs

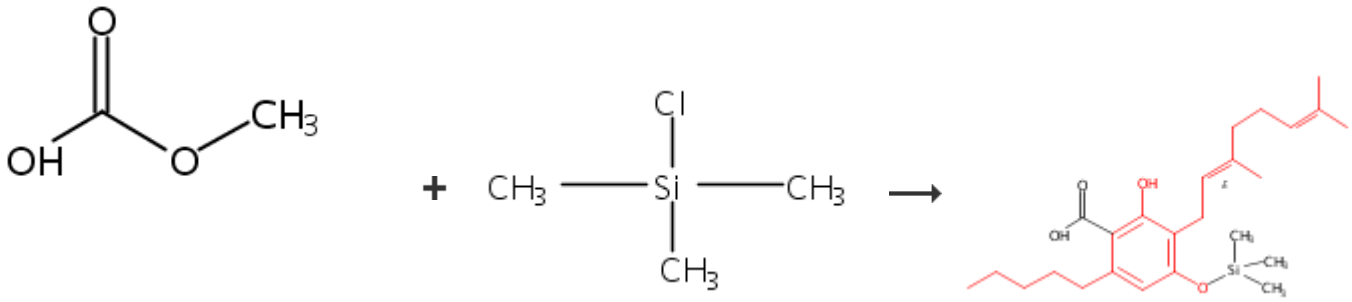
By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

136. 5 Steps



[Step 3.1]



- 1/2 Mg

[Step 4.1] [Step 5.1]

Overview

Steps/Stages

1.1 R:NaOMe, S:MeOH, rt; 3 h, reflux; reflux → rt

1.2 R:H_2O, rt

2.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

3.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

4.1 S:DMF, 1 h, 120°C

4.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

5.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

5.2 R:NaCl, S:H_2O

Notes

3) in the dark, 4) conversion = 40%,alternative preparation shown, 5) alternative preparation shown, regioselective, Reactants: 5, Reagents: 7, Solvents: 5, Steps: 5, Stages: 8, Most stages in any one step: 2

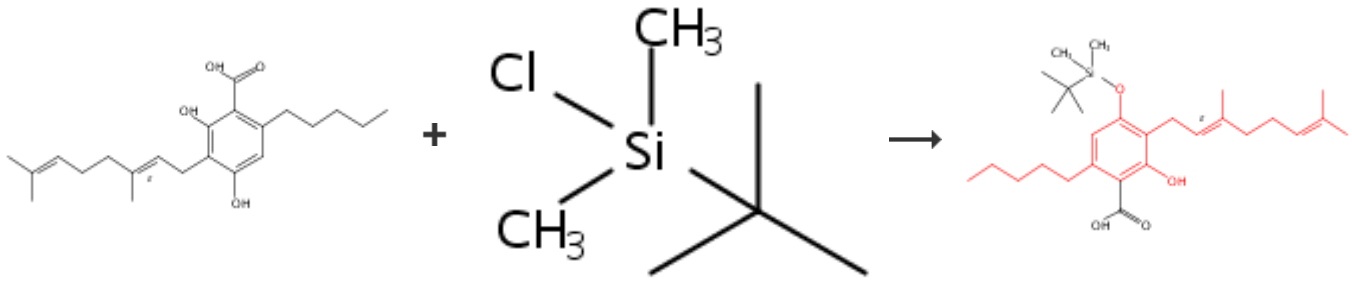
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

137. Single Step



Overview

Steps/Stages

Notes

1.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

1.2 R:NaCl, S:H_2O

regioselective, Reactants: 2, Reagents: 2, Solvents: 2, Steps: 1, Stages: 2, Most stages in any one step: 2

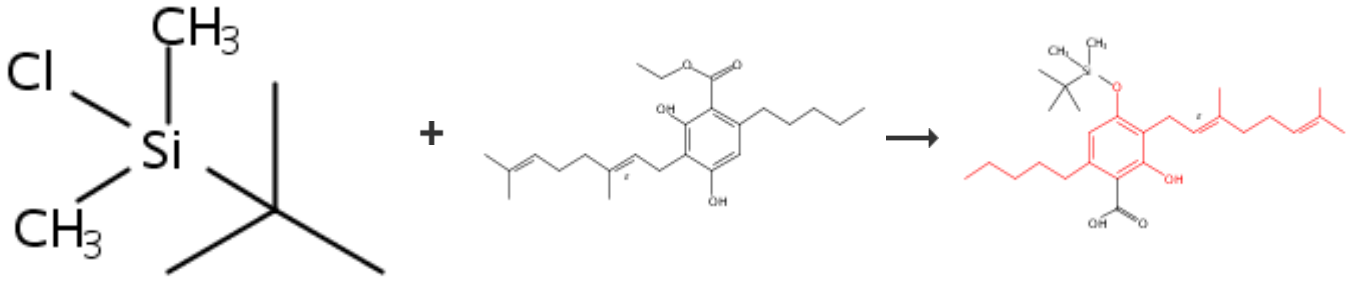
References

Methods for the manufacture of cannabinoid prodrugs, pharmaceutical formulations and their use

By Peet, Richard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017216362, 21 Dec 2017

138. Single Step



Overview

Steps/Stages

1.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

1.2 R:NaCl, S:H_2O

1.3

Notes

unspecified reagent used for acidic hydrolysis in stage 3,alternative preparation shown, regioselective, Reactants: 2, Reagents: 2, Solvents: 2, Steps: 1, Stages: 3, Most stages in any one step: 3

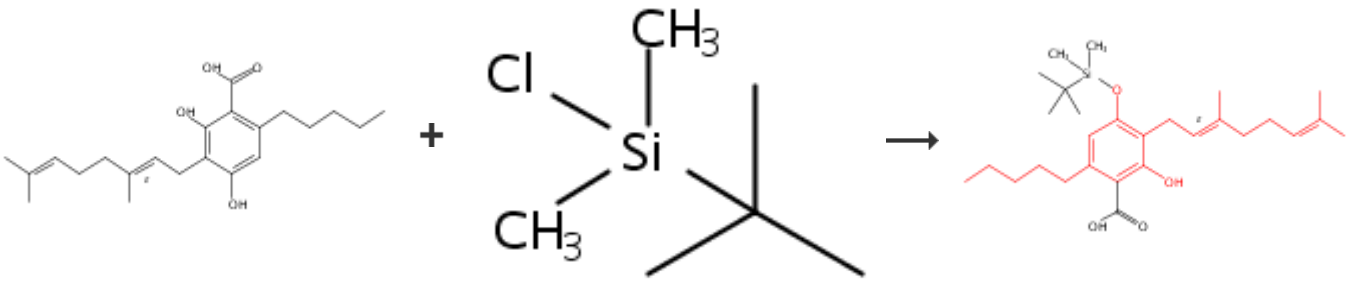
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

139. Single Step



Overview

Steps/Stages

1.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

1.2 R:NaCl, S:H_2O

Notes

alternative preparation shown, regioselective, Reactants: 2, Reagents: 2, Solvents: 2, Steps: 1, Stages: 2, Most stages in any one step: 2

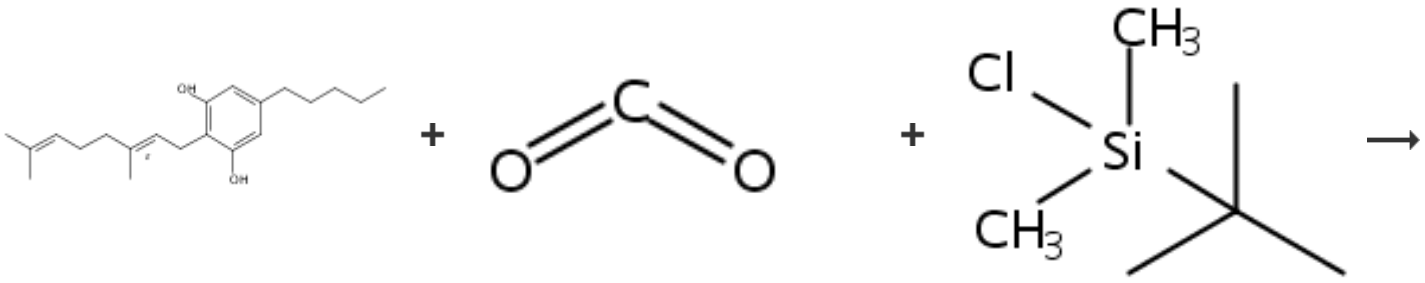
References

Biosynthesis of cannabinoid prodrugs

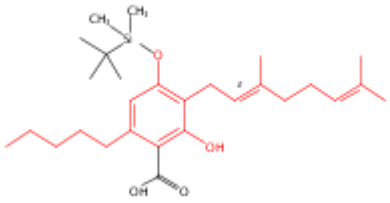
By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

140. 2 Steps



[Step 2.1]



Overview

Steps/Stages

1.1 R:$Mg(OMe)_2$, S:DMF, rt → 50°C; 3 h, 50°C; 50°C → rt

1.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, rt, pH 2

2.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

2.2 R:NaCl, S:H_2O

Notes

1) alternative preparation shown,conversion = 85%, 2) regioselective, Reactants: 3, Reagents: 4, Solvents: 5, Steps: 2, Stages: 4, Most stages in any one step: 2

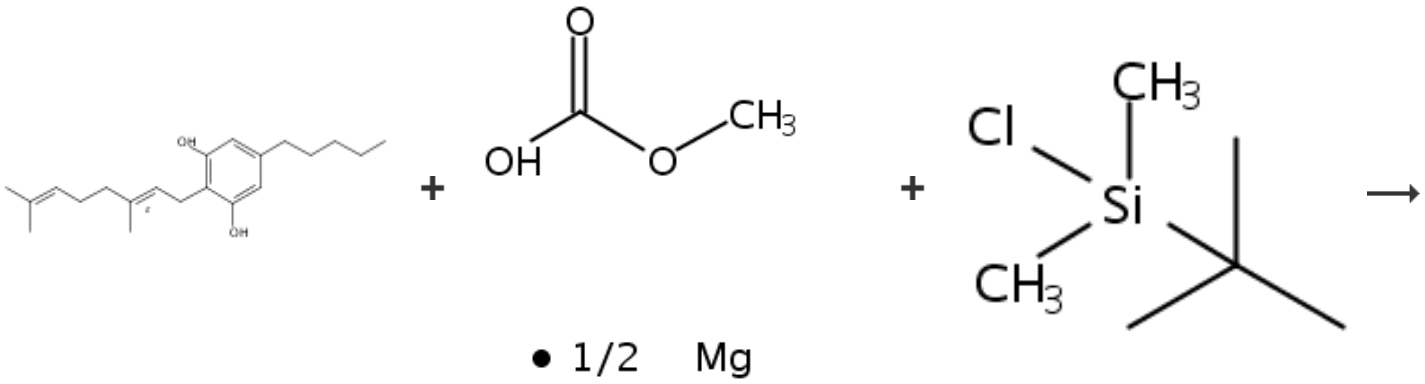
References

Methods for the manufacture of cannabinoid prodrugs, pharmaceutical formulations and their use

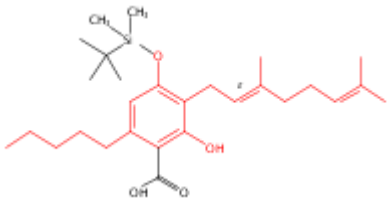
By Peet, Richard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017216362, 21 Dec 2017

141. 2 Steps



[Step 2.1]



Overview

Steps/Stages

1.1 S:DMF, 1 h, 120°C

1.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

2.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

2.2 R:NaCl, S:H_2O

Notes

1) alternative preparation shown,conversion = 40%, 2) regioselective, Reactants: 3, Reagents: 3, Solvents: 5, Steps: 2, Stages: 4, Most stages in any one step: 2

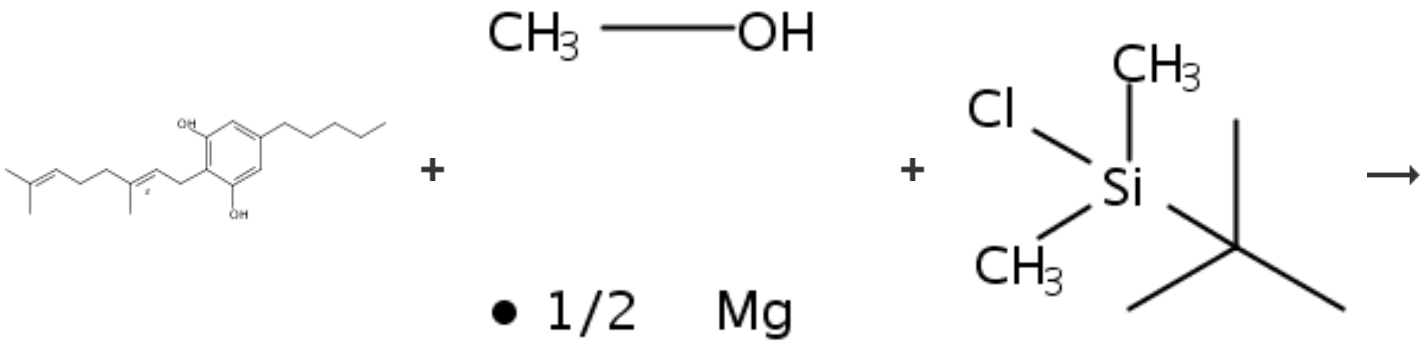
References

Methods for the manufacture of cannabinoid prodrugs, pharmaceutical formulations and their use

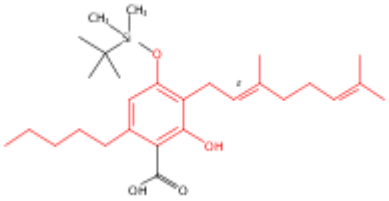
By Peet, Richard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017216362, 21 Dec 2017

142. 2 Steps



[Step 2.1]



Overview

Steps/Stages

1.1 S:H_2O, cooled; 50°C; 3 h, 50°C; 50°C → rt

1.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, rt, pH 2

2.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

2.2 R:NaCl, S:H_2O

Notes

1) conversion = 85%,alternative preparation shown,reaction in a sealed pressure vessel, 2) alternative preparation shown, regioselective, Reactants: 3, Reagents: 3, Solvents: 4, Steps: 2, Stages: 4, Most stages in any one step: 2

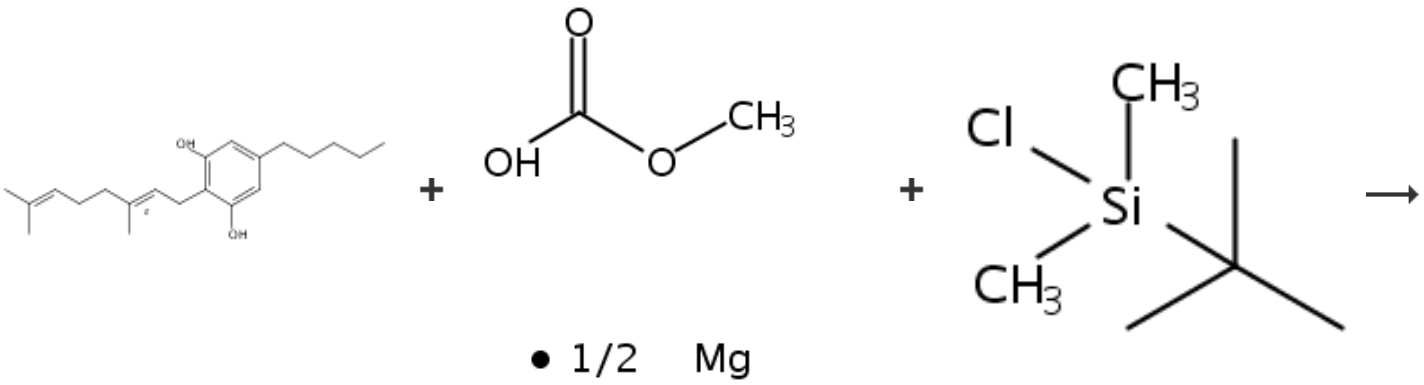
References

Biosynthesis of cannabinoid prodrugs

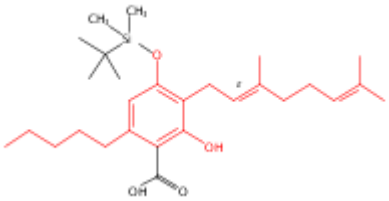
By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

143. 2 Steps



[Step 2.1]



Overview

Steps/Stages

Notes

1.1 S:DMF, 1 h, 120°C

1.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

2.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

2.2 R:NaCl, S:H_2O

1) conversion = 40%,alternative preparation shown, 2) alternative preparation shown, regioselective, Reactants: 3, Reagents: 3, Solvents: 5, Steps: 2, Stages: 4, Most stages in any one step: 2

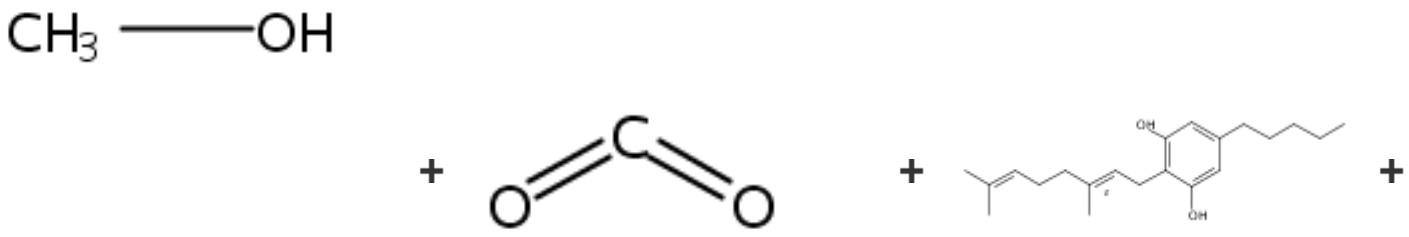
References

Biosynthesis of cannabinoid prodrugs

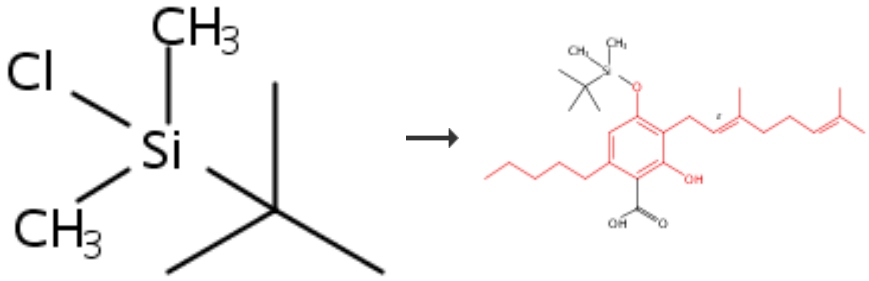
By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

144. 3 Steps



[Step 2.1]



[Step 3.1]

Overview

Steps/Stages

1.1 S:DMF, 140°C
2.1 S:DMF, 1 h, 120°C

2.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

3.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

3.2 R:NaCl, S:H_2O

Notes

2) alternative preparation shown,conversion = 40%, 3) regioselective, Reactants: 4, Reagents: 3, Solvents: 5, Steps: 3, Stages: 5, Most stages in any one step: 2

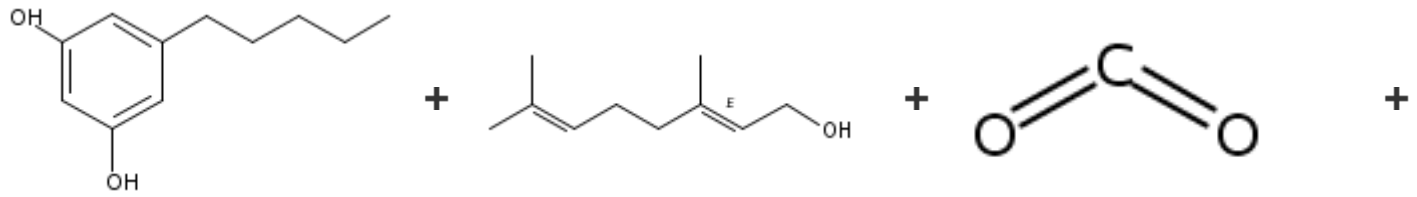
References

Methods for the manufacture of cannabinoid prodrugs, pharmaceutical formulations and their use

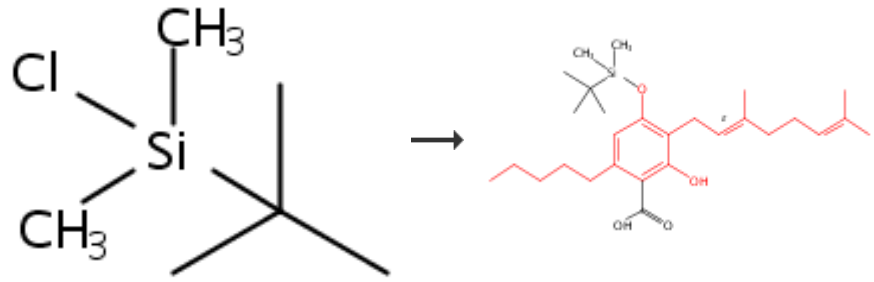
By Peet, Richard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017216362, 21 Dec 2017

145. 3 Steps



[Step 2.1]



[Step 3.1]

Overview

Steps/Stages

1.1 C:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

2.1 R:$Mg(OMe)_2$, S:DMF, rt → 50°C; 3 h, 50°C; 50°C → rt

2.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, rt, pH 2

3.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

3.2 R:NaCl, S:H_2O

Notes

2) alternative preparation shown,conversion = 85%, 3) regioselective, Reactants: 4, Reagents: 4, Catalysts: 1, Solvents: 5, Steps: 3, Stages: 5, Most stages in any one step: 2

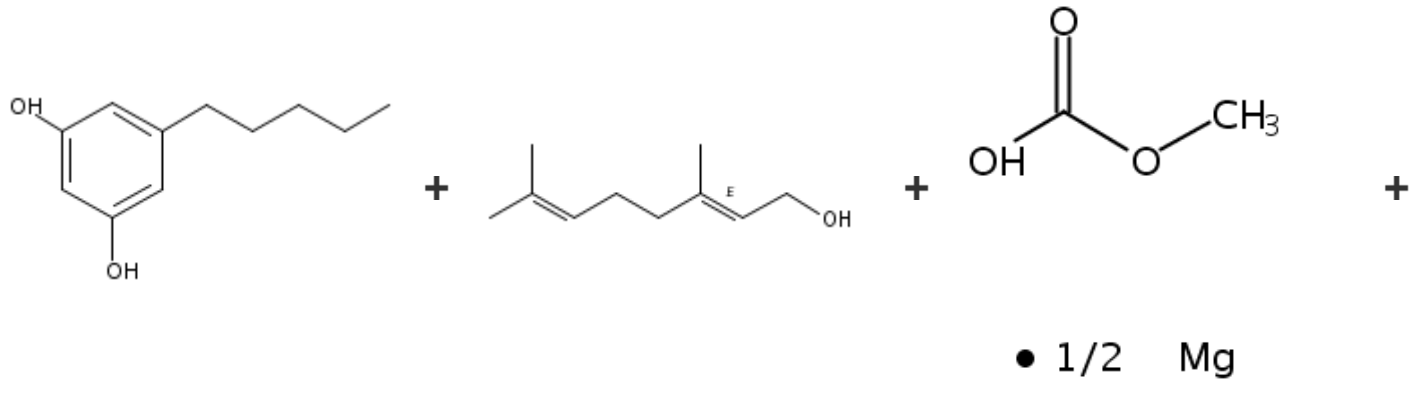
References

Methods for the manufacture of cannabinoid prodrugs, pharmaceutical formulations and their use

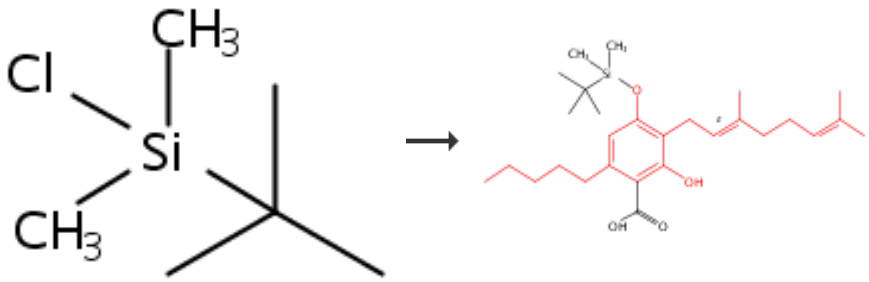
By Peet, Richard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017216362, 21 Dec 2017

146. 3 Steps



[Step 2.1]



[Step 3.1]

Overview

Steps/Stages

1.1 C:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
2.1 S:DMF, 1 h, 120°C

2.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

3.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

3.2 R:NaCl, S:H_2O

Notes

2) alternative preparation shown,conversion = 40%, 3) regioselective, Reactants: 4, Reagents: 3, Catalysts: 1, Solvents: 5, Steps: 3, Stages: 5, Most stages in any one step: 2

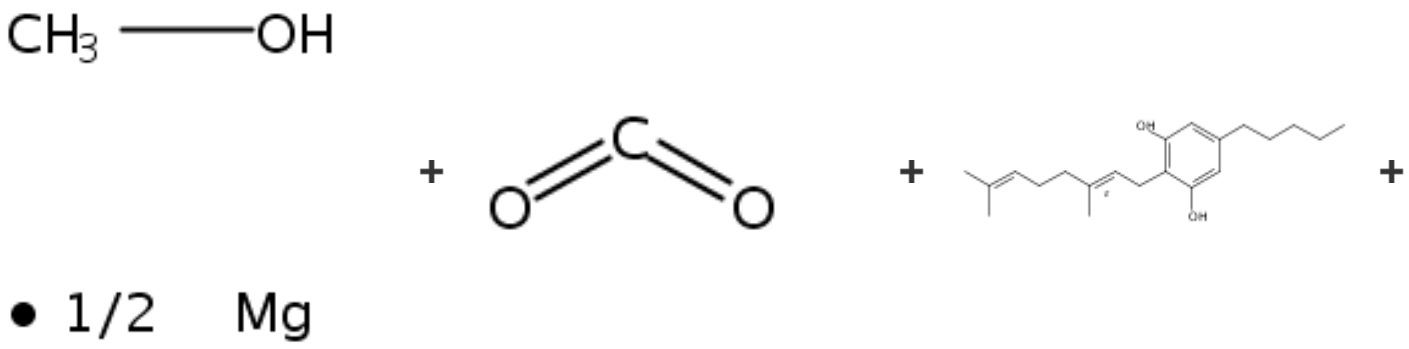
References

Methods for the manufacture of cannabinoid prodrugs, pharmaceutical formulations and their use

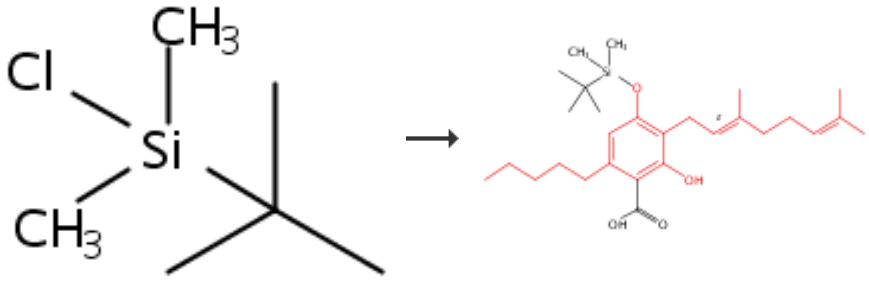
By Peet, Richard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017216362, 21 Dec 2017

147. 3 Steps



[Step 2.1]



[Step 3.1]

Overview

Steps/Stages

1.1 S:DMF, 140°C
2.1 S:DMF, 1 h, 120°C

2.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

3.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

3.2 R:NaCl, S:H_2O

Notes

1) exothermic reaction, 2) conversion = 40%,alternative preparation shown, 3) alternative preparation shown, regioselective, Reactants: 4, Reagents: 3, Solvents: 5, Steps: 3, Stages: 5, Most stages in any one step: 2

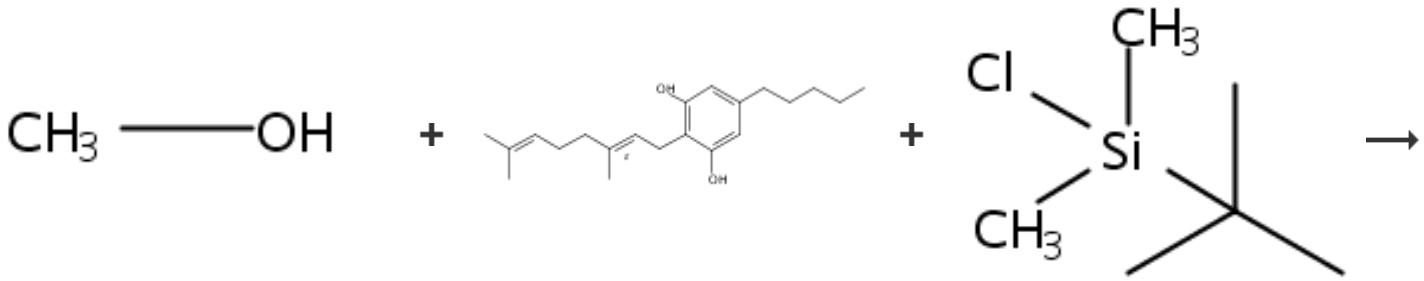
References

Biosynthesis of cannabinoid prodrugs

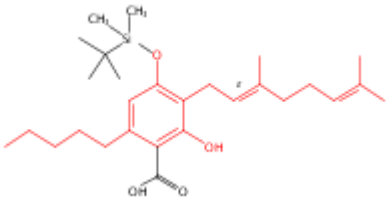
By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

148. 3 Steps



[Step 2.1] [Step 3.1]



Overview

Steps/Stages

1.1 R:Mg, S:MeOH, rt
2.1 S:H_2O, cooled; 50°C; 3 h, 50°C; 50°C → rt

2.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, rt, pH 2

3.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

3.2 R:NaCl, S:H_2O

Notes

2) conversion = 85%,alternative preparation shown,reaction in a sealed pressure vessel, 3) alternative preparation shown, regioselective, Reactants: 3, Reagents: 4, Solvents: 4, Steps: 3, Stages: 5, Most stages in any one step: 2

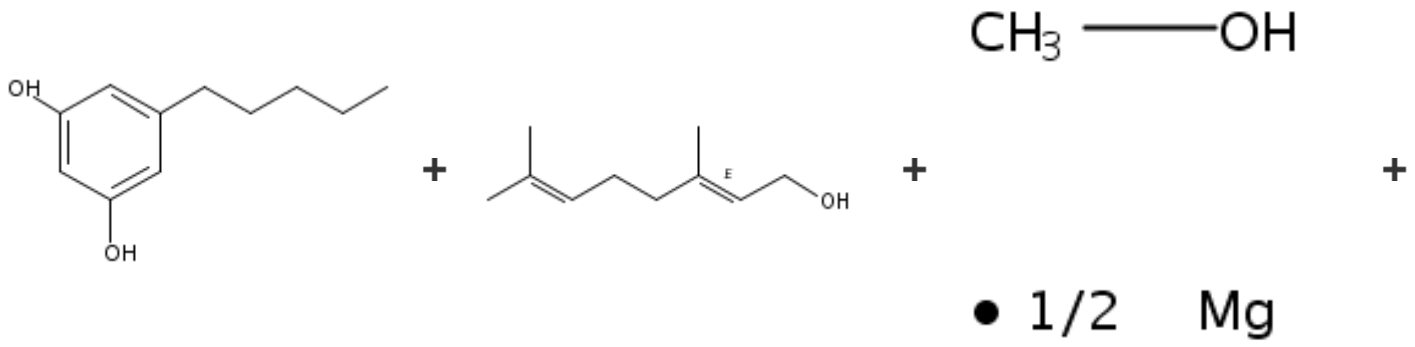
References

Biosynthesis of cannabinoid prodrugs

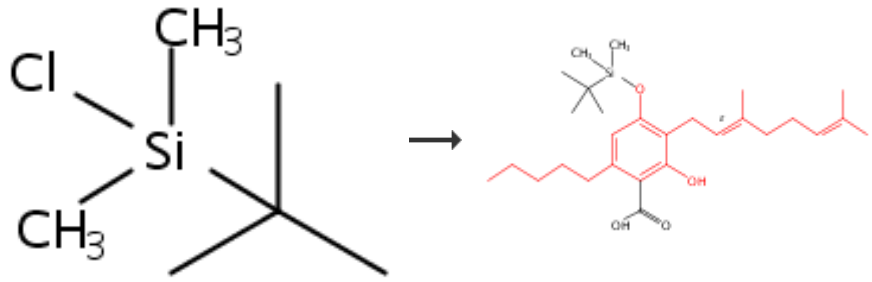
By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

149. 3 Steps



[Step 2.1]



[Step 3.1]

Overview

Steps/Stages

1.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

2.1 S:H_2O, cooled; 50°C; 3 h, 50°C; 50°C → rt

2.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, rt, pH 2

3.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

3.2 R:NaCl, S:H_2O

Notes

1) in the dark, 2) conversion = 85%,alternative preparation shown,reaction in a sealed pressure vessel, 3) alternative preparation shown, regioselective, Reactants: 4, Reagents: 4, Solvents: 4, Steps: 3, Stages: 5, Most stages in any one step: 2

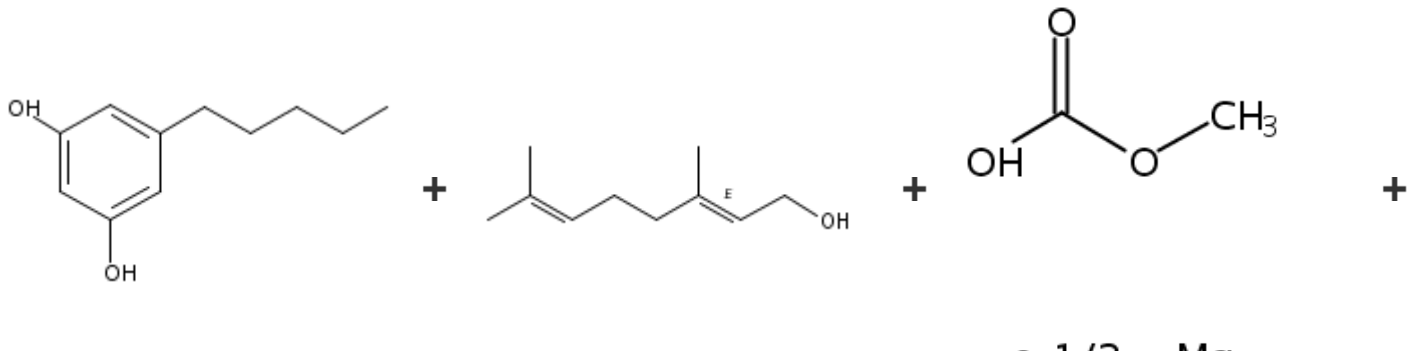
References

Biosynthesis of cannabinoid prodrugs

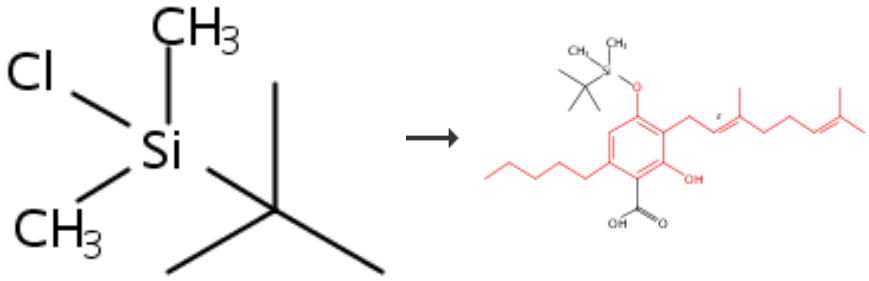
By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

150. 3 Steps



[Step 2.1]



[Step 3.1]

Overview

Steps/Stages

1.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
2.1 S:DMF, 1 h, 120°C

2.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

3.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

3.2 R:NaCl, S:H_2O

Notes

1) in the dark, 2) conversion = 40%,alternative preparation shown, 3) alternative preparation shown, regioselective, Reactants: 4, Reagents: 4, Solvents: 5, Steps: 3, Stages: 5, Most stages in any one step: 2

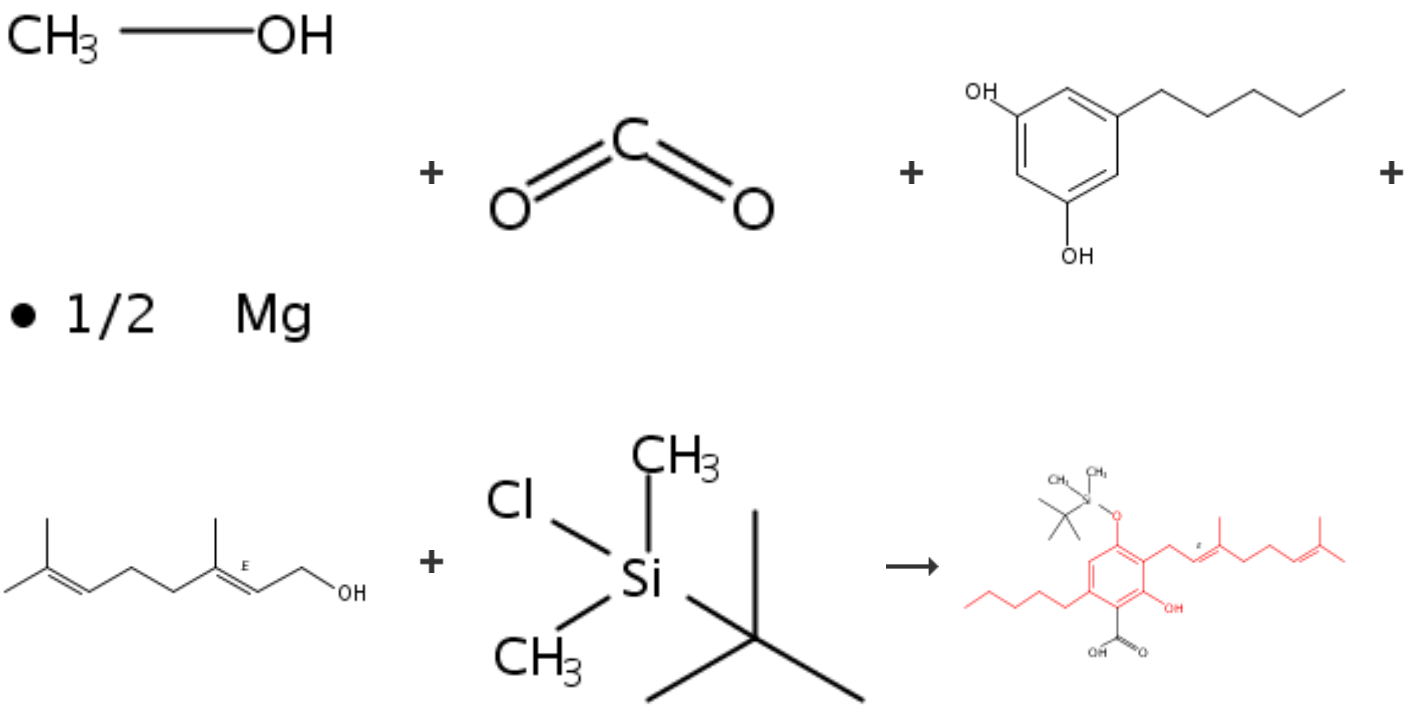
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

151. 4 Steps (Converging)



Overview

Steps/Stages

Notes

1.1 S:DMF, 140°C
1.1 C:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
2.1 S:DMF, 1 h, 120°C

2.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

3.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

3.2 R:NaCl, S:H_2O

alternative preparation shown,conversion = 40%, regioselective, Reactants: 5, Reagents: 3, Catalysts: 1, Solvents: 5, Steps: 4, Stages: 6, Most stages in any one step: 2

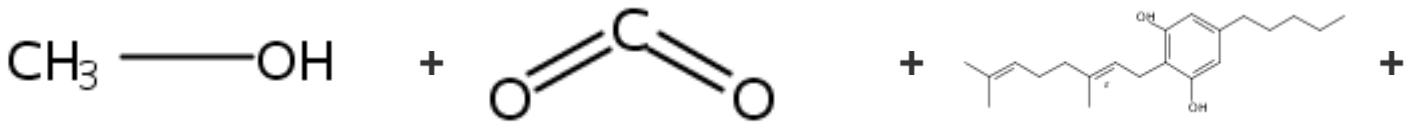
References

Methods for the manufacture of cannabinoid prodrugs, pharmaceutical formulations and their use

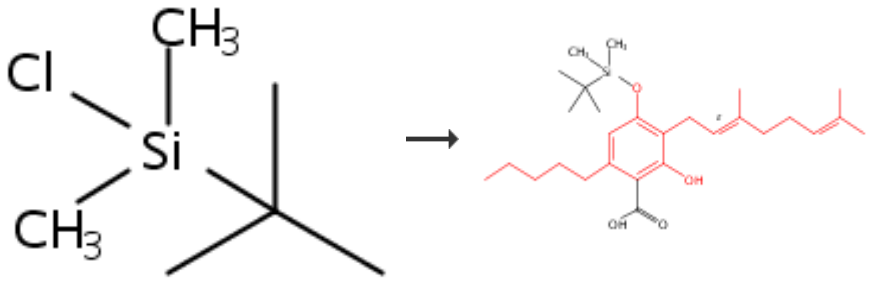
By Peet, Richard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017216362, 21 Dec 2017

152. 4 Steps



[Step 2.1] [Step 3.1]



[Step 4.1]

Overview

Steps/Stages

1.1 R:Mg, S:MeOH, cooled
2.1 S:DMF, 140°C
3.1 S:DMF, 1 h, 120°C

3.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

4.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

4.2 R:NaCl, S:H_2O

Notes

3) alternative preparation shown,conversion = 40%, 4) regioselective, Reactants: 4, Reagents: 4, Solvents: 5, Steps: 4, Stages: 6, Most stages in any one step: 2

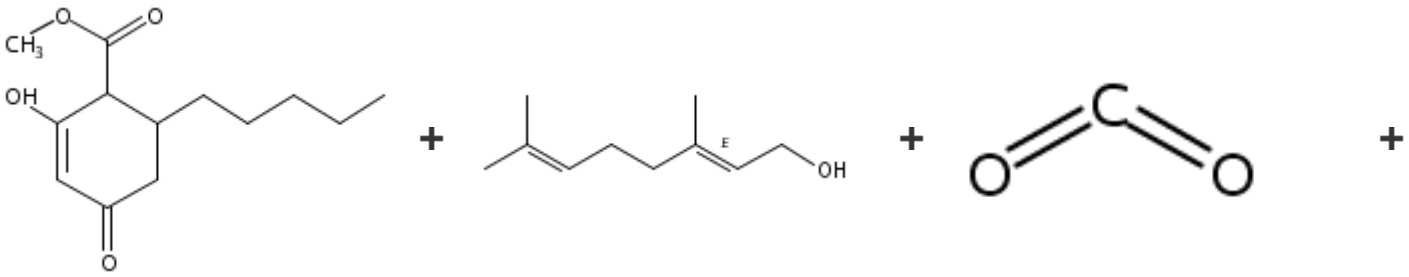
References

Methods for the manufacture of cannabinoid prodrugs, pharmaceutical formulations and their use

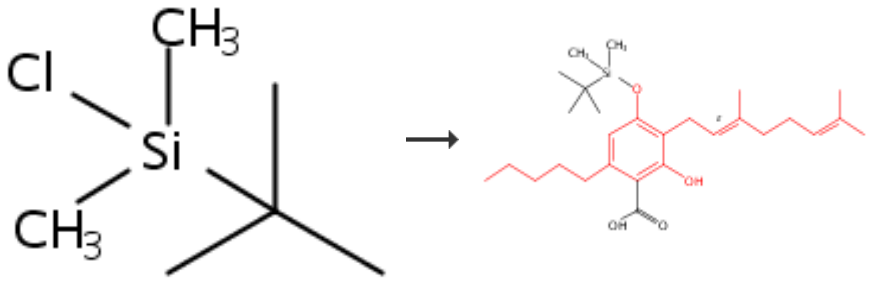
By Peet, Richard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017216362, 21 Dec 2017

153. 4 Steps



[Step 2.1] [Step 3.1]



[Step 4.1]

Overview

Steps/Stages

1.1 R:Br_2, S:DMF, 90 min, cooled; 80°C → 160°C; 10 h, 160°C

2.1 C:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

3.1 R:$Mg(OMe)_2$, S:DMF, rt → 50°C; 3 h, 50°C; 50°C → rt

3.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, rt, pH 2

4.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

4.2 R:NaCl, S:H_2O

Notes

3) alternative preparation shown,conversion = 85%, 4) regioselective, Reactants: 4, Reagents: 5, Catalysts: 1, Solvents: 5, Steps: 4, Stages: 6, Most stages in any one step: 2

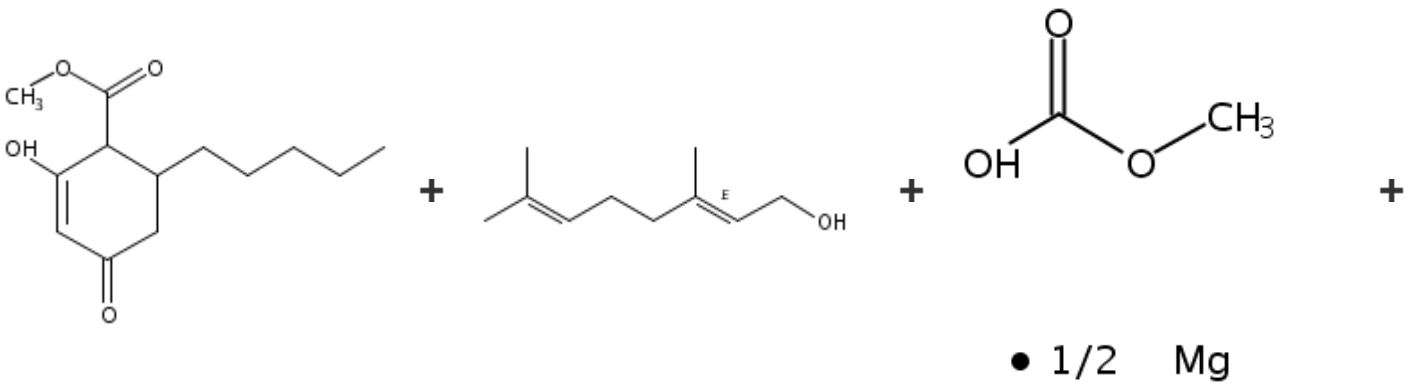
References

Methods for the manufacture of cannabinoid prodrugs, pharmaceutical formulations and their use

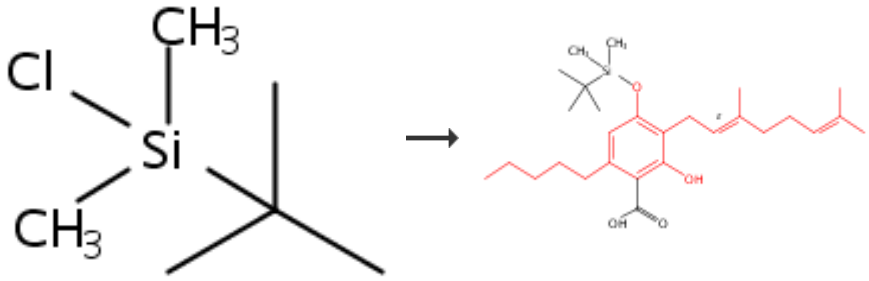
By Peet, Richard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017216362, 21 Dec 2017

154. 4 Steps



[Step 2.1] [Step 3.1]



[Step 4.1]

Overview

Steps/Stages

1.1 R:Br_2, S:DMF, 90 min, cooled; 80°C → 160°C; 10 h, 160°C
2.1 C:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
3.1 S:DMF, 1 h, 120°C

3.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

4.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

4.2 R:NaCl, S:H_2O

Notes

3) alternative preparation shown,conversion = 40%, 4) regioselective, Reactants: 4, Reagents: 4, Catalysts: 1, Solvents: 5, Steps: 4, Stages: 6, Most stages in any one step: 2

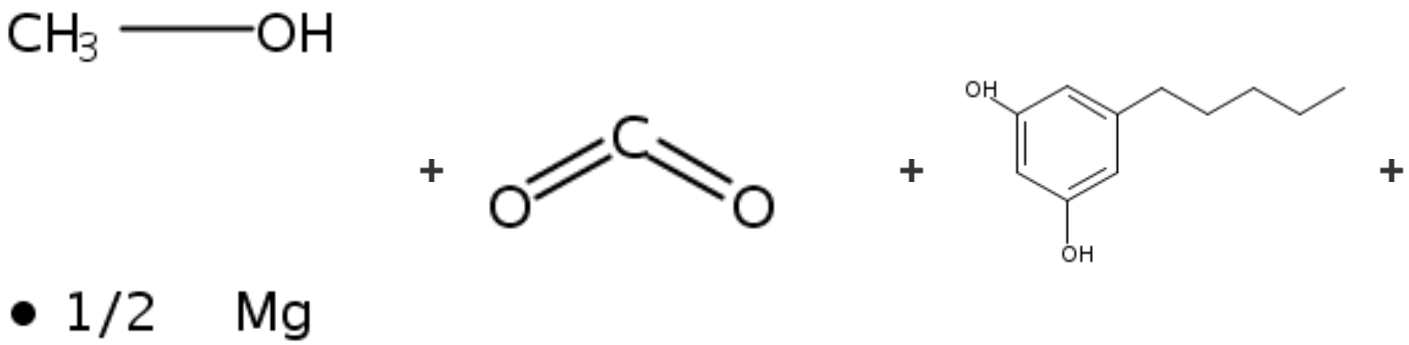
References

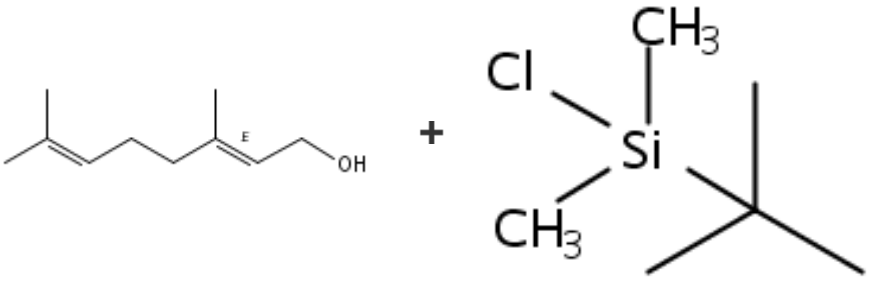
Methods for the manufacture of cannabinoid prodrugs, pharmaceutical formulations and their use

By Peet, Richard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017216362, 21 Dec 2017

155. 4 Steps (Converging)





Overview

Steps/Stages

1.1 S:DMF, 140°C

1.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
2.1 S:DMF, 1 h, 120°C

2.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

3.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

3.2 R:NaCl, S:H_2O

Notes

exothermic reaction, in the dark, conversion = 40%,alternative preparation shown, alternative preparation shown, regioselective, Reactants: 5, Reagents: 4, Solvents: 5, Steps: 4, Stages: 6, Most stages in any one step: 2

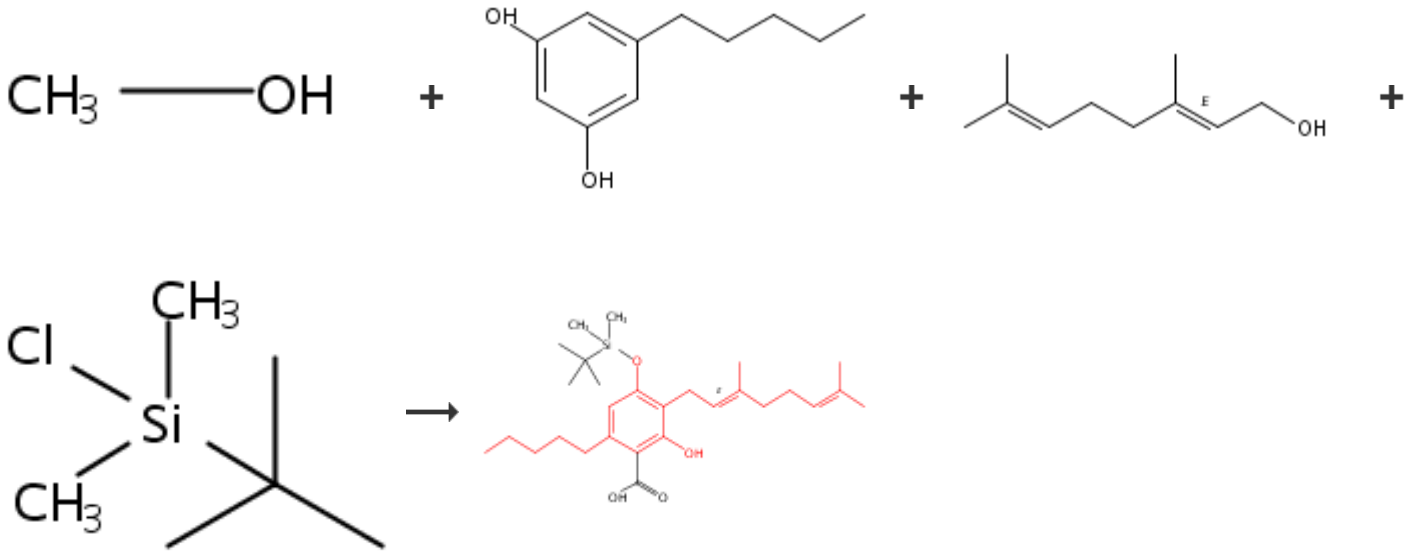
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

156. 4 Steps (Converging)



Overview

Steps/Stages

1.1 R:Mg, S:MeOH, rt

1.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
2.1 S:H_2O, cooled; 50°C; 3 h, 50°C; 50°C → rt

2.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, rt, pH 2

3.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

3.2 R:NaCl, S:H_2O

Notes

in the dark, conversion = 85%,alternative preparation shown,reaction in a sealed pressure vessel, alternative preparation shown, regioselective, Reactants: 4, Reagents: 5, Solvents: 4, Steps: 4, Stages: 6, Most stages in any one step: 2

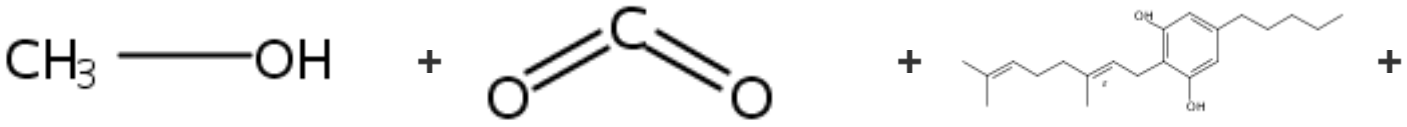
References

Biosynthesis of cannabinoid prodrugs

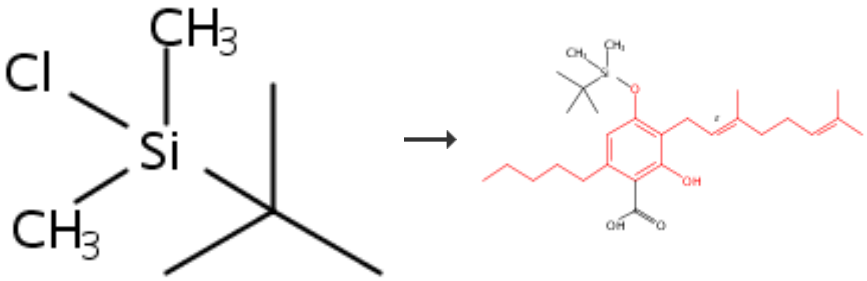
By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

157. 4 Steps



[Step 2.1] [Step 3.1]



[Step 4.1]

Overview

Steps/Stages

1.1 R:Mg, S:MeOH, rt
2.1 S:DMF, 140°C
3.1 S:DMF, 1 h, 120°C

3.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

4.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

4.2 R:NaCl, S:H_2O

Notes

2) exothermic reaction, 3) conversion = 40%,alternative preparation shown, 4) alternative preparation shown, regioselective, Reactants: 4, Reagents: 4, Solvents: 5, Steps: 4, Stages: 6, Most stages in any one step: 2

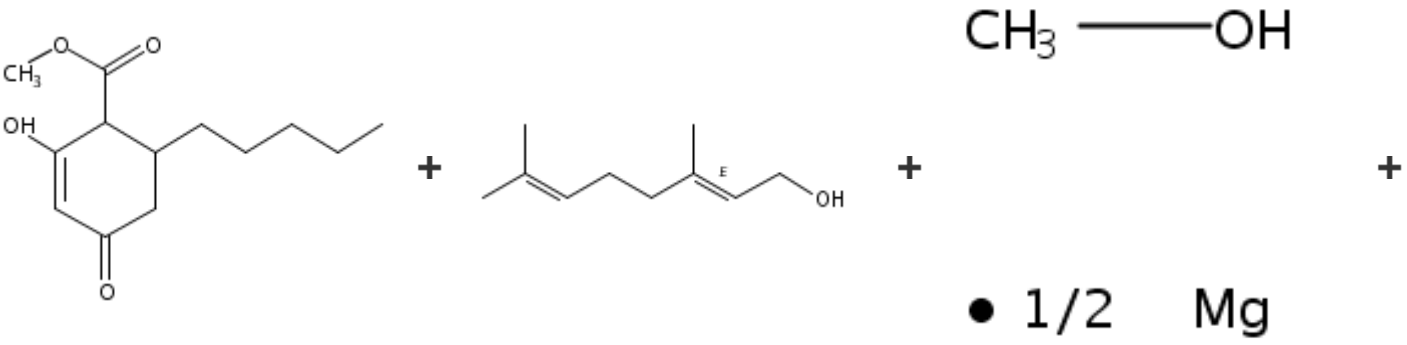
References

Biosynthesis of cannabinoid prodrugs

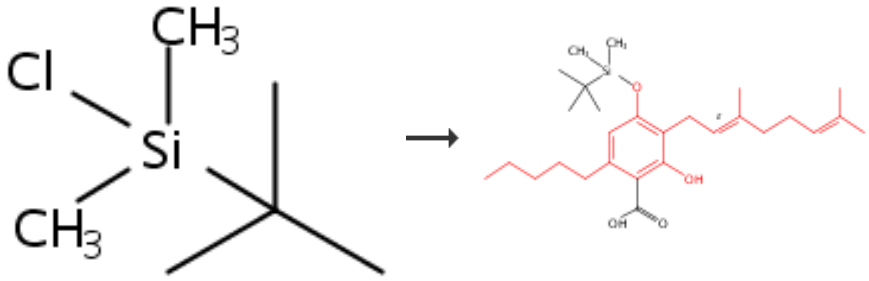
By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

158. 4 Steps



[Step 2.1] [Step 3.1]



[Step 4.1]

Overview

Steps/Stages

1.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

2.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

3.1 S:H_2O, cooled; 50°C; 3 h, 50°C; 50°C → rt

3.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, rt, pH 2

4.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

4.2 R:NaCl, S:H_2O

Notes

2) in the dark, 3) conversion = 85%,alternative preparation shown,reaction in a sealed pressure vessel, 4) alternative preparation shown, regioselective, Reactants: 4, Reagents: 5, Solvents: 5, Steps: 4, Stages: 6, Most stages in any one step: 2

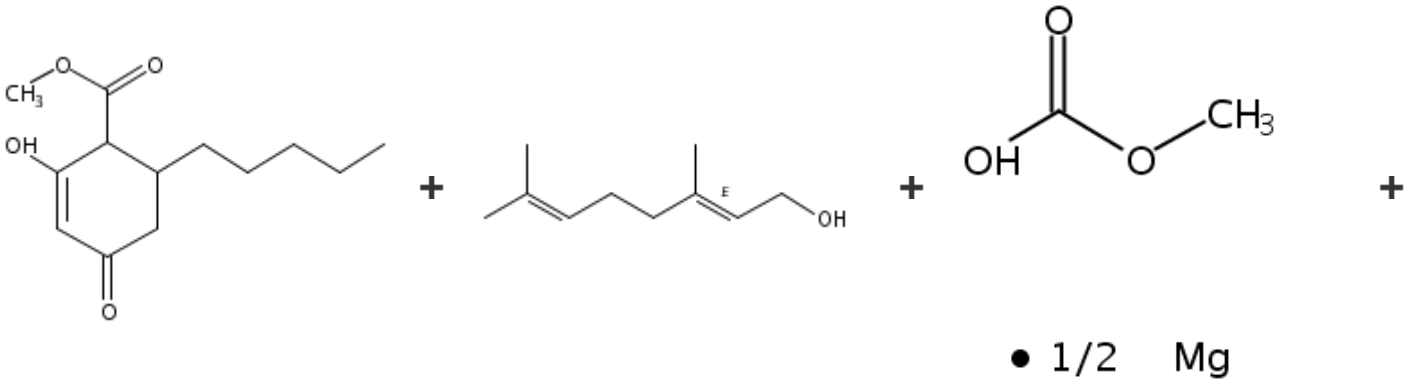
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

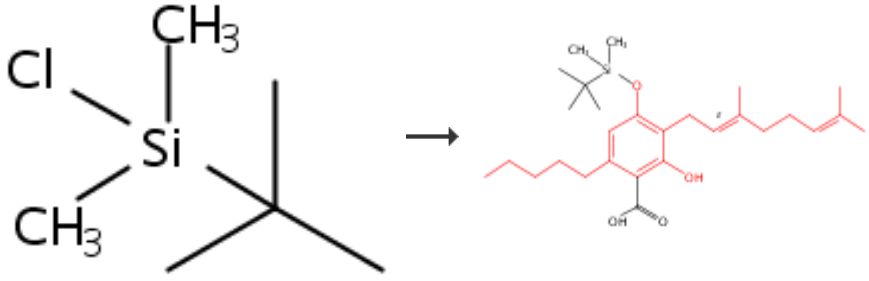
From PCT Int. Appl., 2017181118, 19 Oct 2017

159. 4 Steps



[Step 2.1]

[Step 3.1]



[Step 4.1]

Overview

Steps/Stages

Notes

1.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

2.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

3.1 S:DMF, 1 h, 120°C

3.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

4.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

4.2 R:NaCl, S:H_2O

2) in the dark, 3) conversion = 40%,alternative preparation shown, 4) alternative preparation shown, regioselective, Reactants: 4, Reagents: 5, Solvents: 5, Steps: 4, Stages: 6, Most stages in any one step: 2

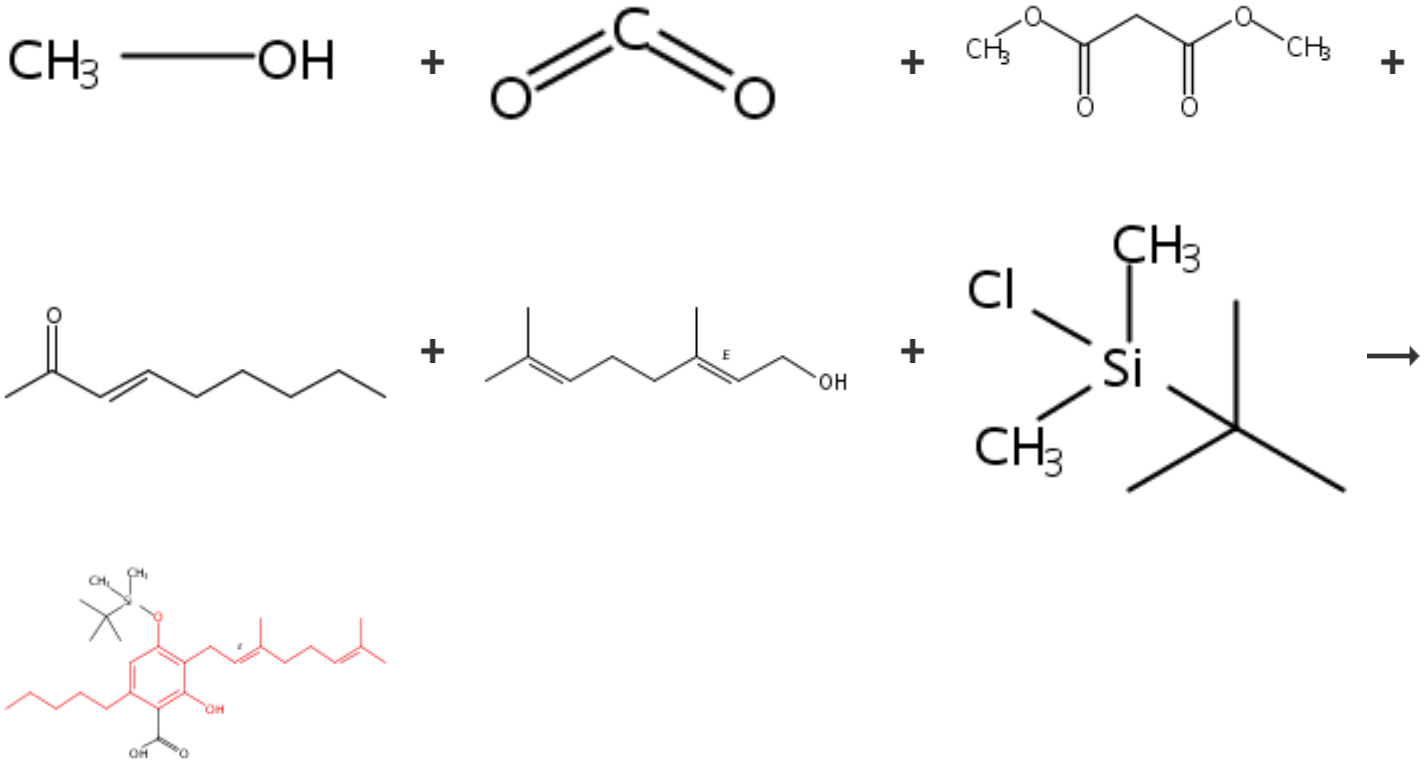
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

160. 7 Steps (Converging)



Overview

Steps/Stages

Notes

1.1 R:Mg, S:MeOH, cooled
2.1 S:DMF, 140°C

1.1 R:NaOMe, S:MeOH, rt; 3 h, reflux

2.1 R:Br_2, S:DMF, 90 min, cooled; 80°C → 160°C; 10 h, 160°C
3.1 C:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
4.1 S:DMF, 1 h, 120°C

4.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

5.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

5.2 R:NaCl, S:H_2O

alternative preparation shown,conversion = 40%, regioselective, Reactants: 6, Reagents: 6, Catalysts: 1, Solvents: 5, Steps: 7, Stages: 9, Most stages in any one step: 2

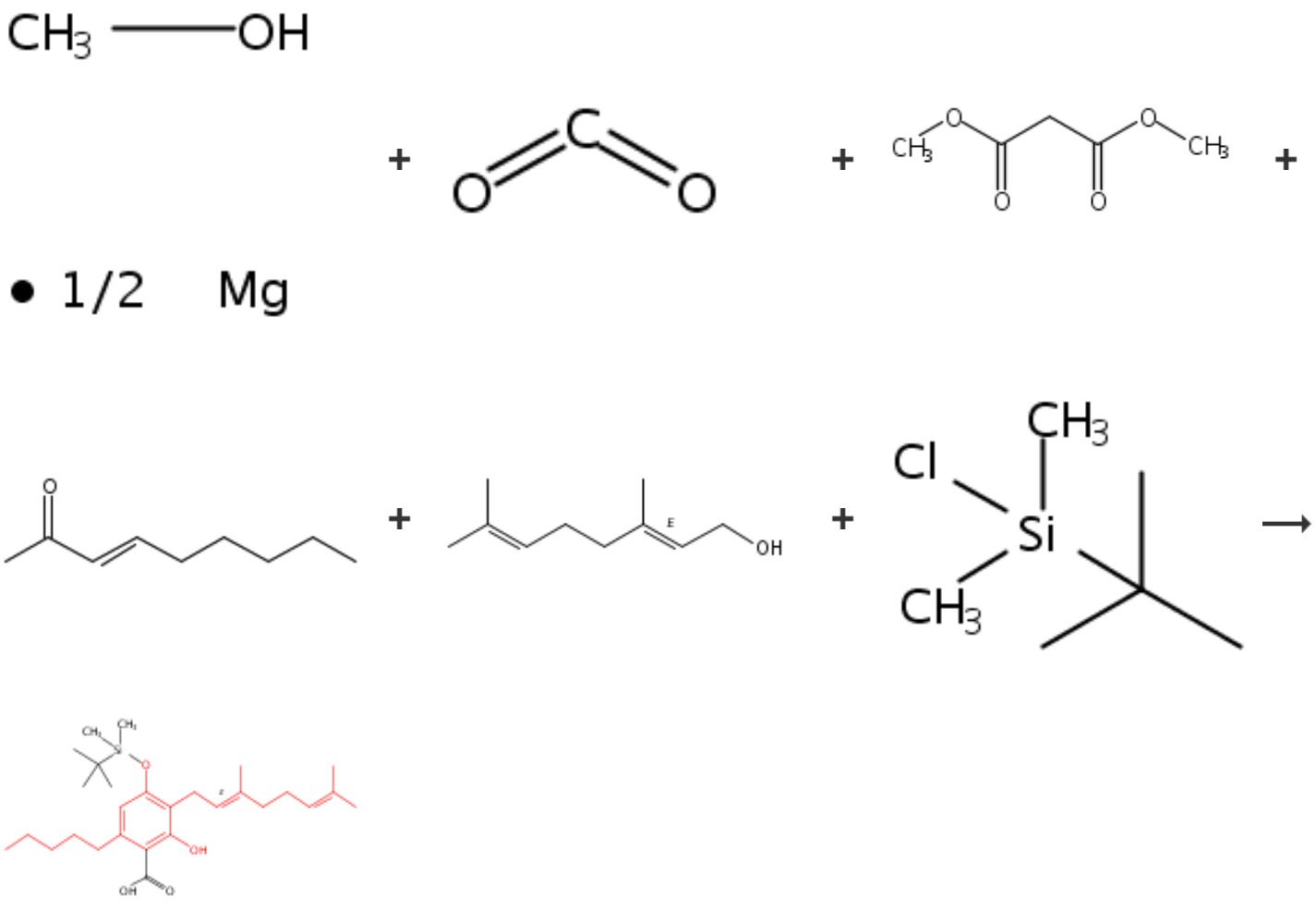
References

Methods for the manufacture of cannabinoid prodrugs, pharmaceutical formulations and their use

By Peet, Richard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017216362, 21 Dec 2017

161. 6 Steps (Converging)



Overview

Steps/Stages

Notes

1.1 S:DMF, 140°C

1.1 R:NaOMe, S:MeOH, rt; 3 h, reflux

2.1 R:Br_2, S:DMF, 90 min, cooled; 80°C → 160°C; 10 h, 160°C
3.1 C:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
4.1 S:DMF, 1 h, 120°C

4.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

5.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

5.2 R:NaCl, S:H_2O

alternative preparation shown,conversion = 40%, regioselective, Reactants: 6, Reagents: 5, Catalysts: 1, Solvents: 5, Steps: 6, Stages: 8, Most stages in any one step: 2

References

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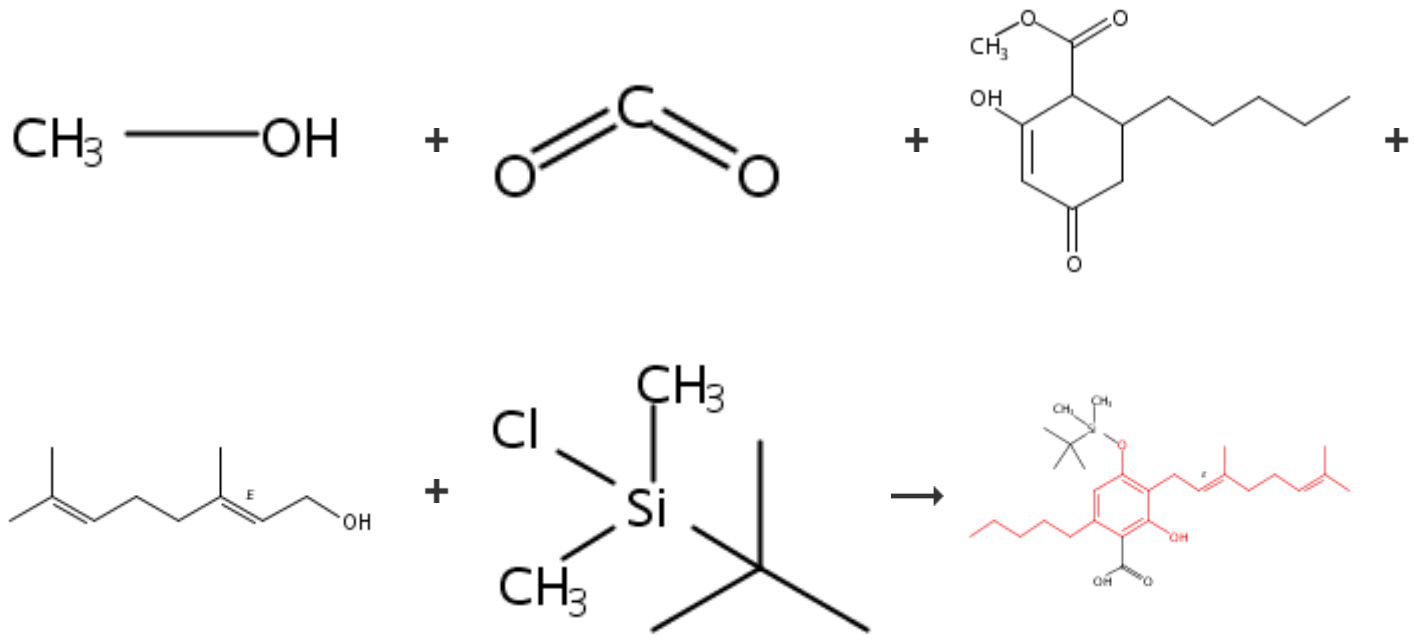
By Peet, Richard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017216362, 21 Dec 2017

162. 6 Steps (Converging)



Overview

Steps/Stages

1.1 R:Mg, S:MeOH, cooled
2.1 S:DMF, 140°C

1.1 R:Br_2, S:DMF, 90 min, cooled; 80°C → 160°C; 10 h, 160°C
2.1 C:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
3.1 S:DMF, 1 h, 120°C

3.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

4.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

4.2 R:NaCl, S:H_2O

Notes

alternative preparation shown,conversion = 40%, regioselective, Reactants: 5, Reagents: 5, Catalysts: 1, Solvents: 5, Steps: 6, Stages: 8, Most stages in any one step: 2

References

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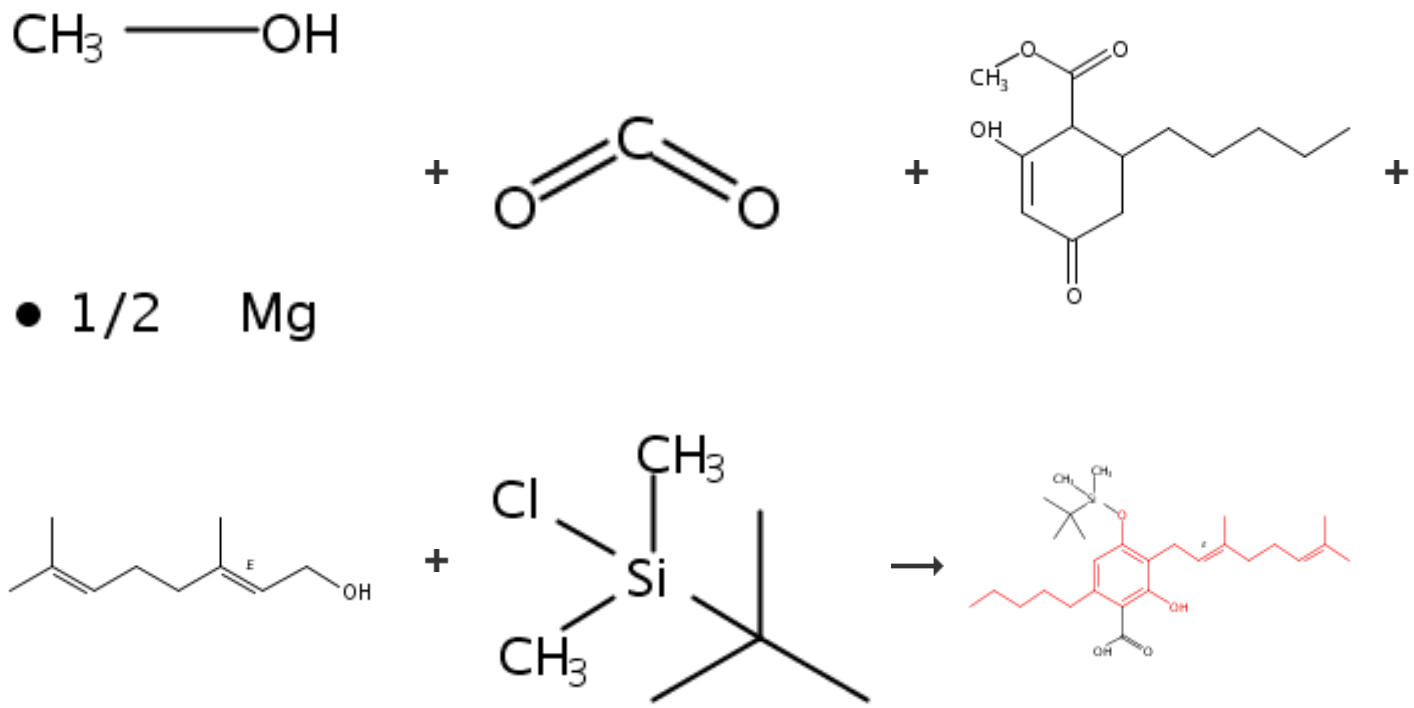
By Peet, Richard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017216362, 21 Dec 2017

163. 5 Steps (Converging)



Overview

Steps/Stages

1.1 S:DMF, 140°C

1.1 R:Br_2, S:DMF, 90 min, cooled; 80°C → 160°C; 10 h, 160°C
2.1 C:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
3.1 S:DMF, 1 h, 120°C

3.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

4.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

4.2 R:NaCl, S:H_2O

Notes

alternative preparation shown,conversion = 40%, regioselective, Reactants: 5, Reagents: 4, Catalysts: 1, Solvents: 5, Steps: 5, Stages: 7, Most stages in any one step: 2

References

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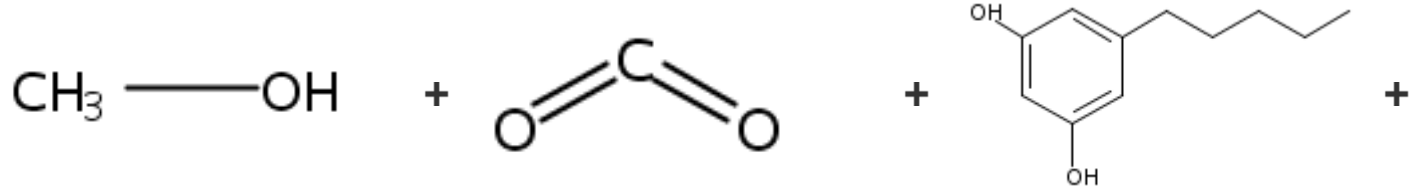
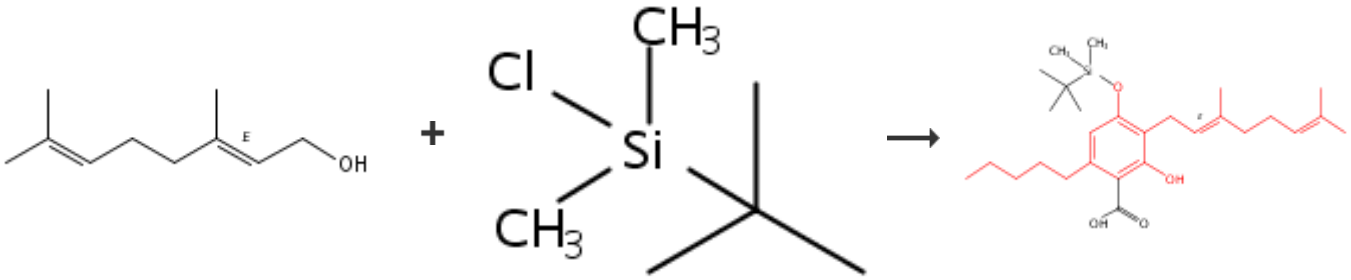
By Peet, Richard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017216362, 21 Dec 2017

164. 5 Steps (Converging)





Overview

Steps/Stages

1.1 R:Mg, S:MeOH, cooled
2.1 S:DMF, 140°C
1.1 C:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
2.1 S:DMF, 1 h, 120°C

2.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

3.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

3.2 R:NaCl, S:H_2O

Notes

alternative preparation shown,conversion = 40%, regioselective, Reactants: 5, Reagents: 4, Catalysts: 1, Solvents: 5, Steps: 5, Stages: 7, Most stages in any one step: 2

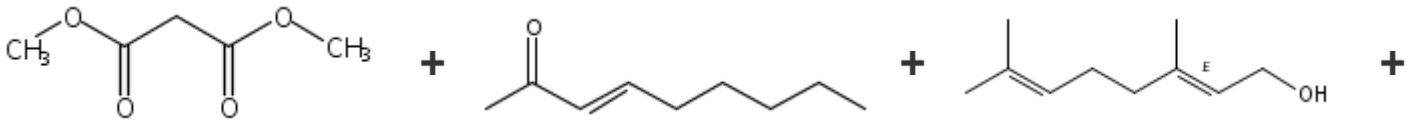
References

Methods for the manufacture of cannabinoid prodrugs, pharmaceutical formulations and their use

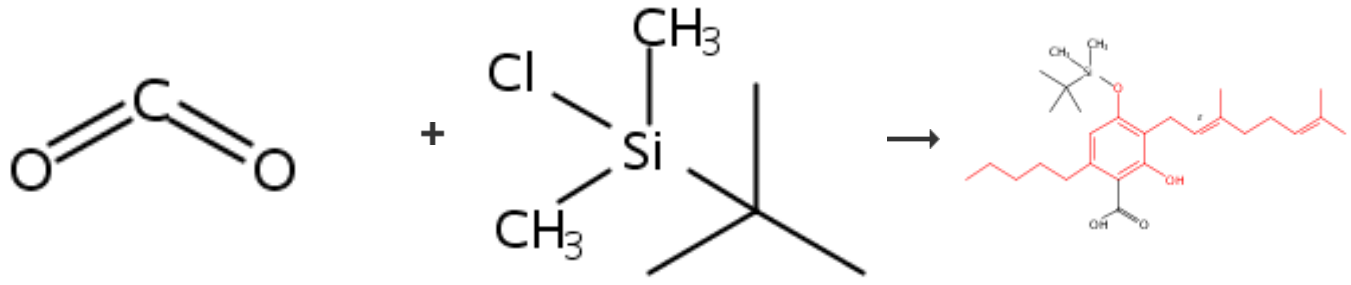
By Peet, Richard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017216362, 21 Dec 2017

165. 5 Steps



[Step 3.1]



[Step 4.1] [Step 5.1]

Overview

Steps/Stages

Notes

1.1 R:NaOMe, S:MeOH, rt; 3 h, reflux

2.1 R:Br_2, S:DMF, 90 min, cooled; 80°C → 160°C; 10 h, 160°C
3.1 C:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

4.1 R:$Mg(OMe)_2$, S:DMF, rt → 50°C; 3 h, 50°C; 50°C → rt

4.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, rt, pH 2

5.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

5.2 R:NaCl, S:H_2O

4) alternative preparation shown,conversion = 85%, 5) regioselective, Reactants: 5, Reagents: 6, Catalysts: 1, Solvents: 5, Steps: 5, Stages: 7, Most stages in any one step: 2

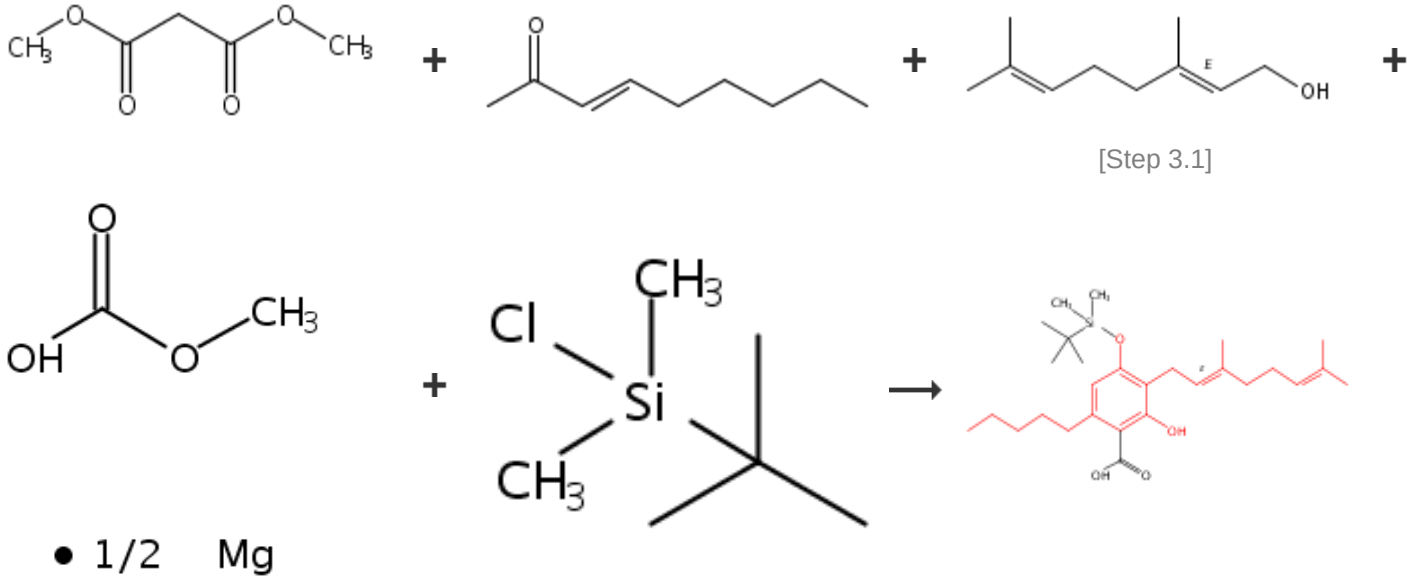
References

Methods for the manufacture of cannabinoid prodrugs, pharmaceutical formulations and their use

By Peet, Richard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017216362, 21 Dec 2017

166. 5 Steps



Overview

Steps/Stages

1.1 R:NaOMe, S:MeOH, rt; 3 h, reflux

2.1 R:Br_2, S:DMF, 90 min, cooled; 80°C → 160°C; 10 h, 160°C
3.1 C:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
4.1 S:DMF, 1 h, 120°C

4.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

5.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

5.2 R:NaCl, S:H_2O

Notes

4) alternative preparation shown,conversion = 40%, 5) regioselective, Reactants: 5, Reagents: 5, Catalysts: 1, Solvents: 5, Steps: 5, Stages: 7, Most stages in any one step: 2

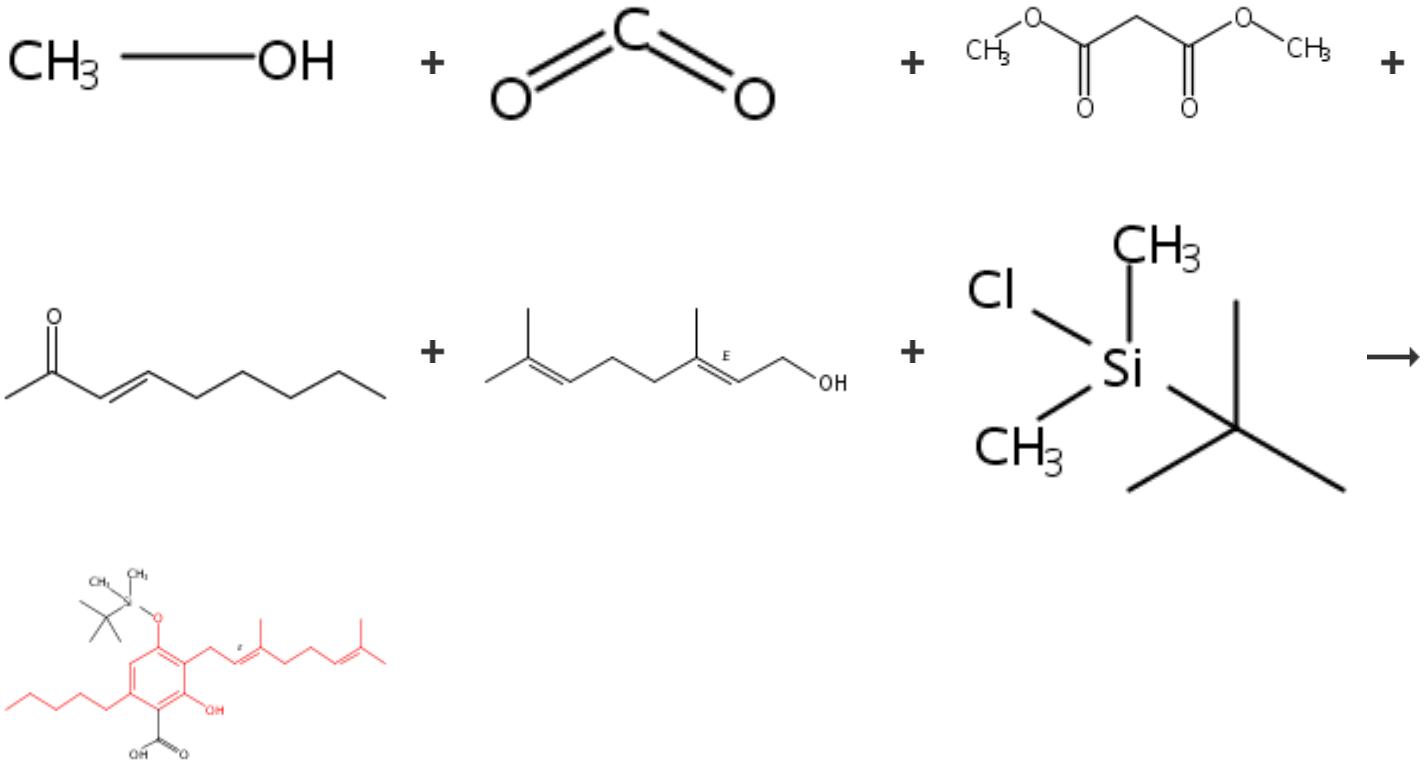
References

Methods for the manufacture of cannabinoid prodrugs, pharmaceutical formulations and their use

By Peet, Richard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017216362, 21 Dec 2017

167. 7 Steps (Converging)



Overview

Steps/Stages

1.1 R:Mg, S:MeOH, rt
2.1 S:DMF, 140°C

1.1 R:NaOMe, S:MeOH, rt; 3 h, reflux; reflux → rt

1.2 R:H_2O, rt

2.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

3.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
4.1 S:DMF, 1 h, 120°C

4.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

5.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

5.2 R:NaCl, S:H_2O

Notes

exothermic reaction, in the dark, conversion = 40%,alternative preparation shown, alternative preparation shown, regioselective, Reactants: 6, Reagents: 8, Solvents: 5, Steps: 7, Stages: 10, Most stages in any one step: 2

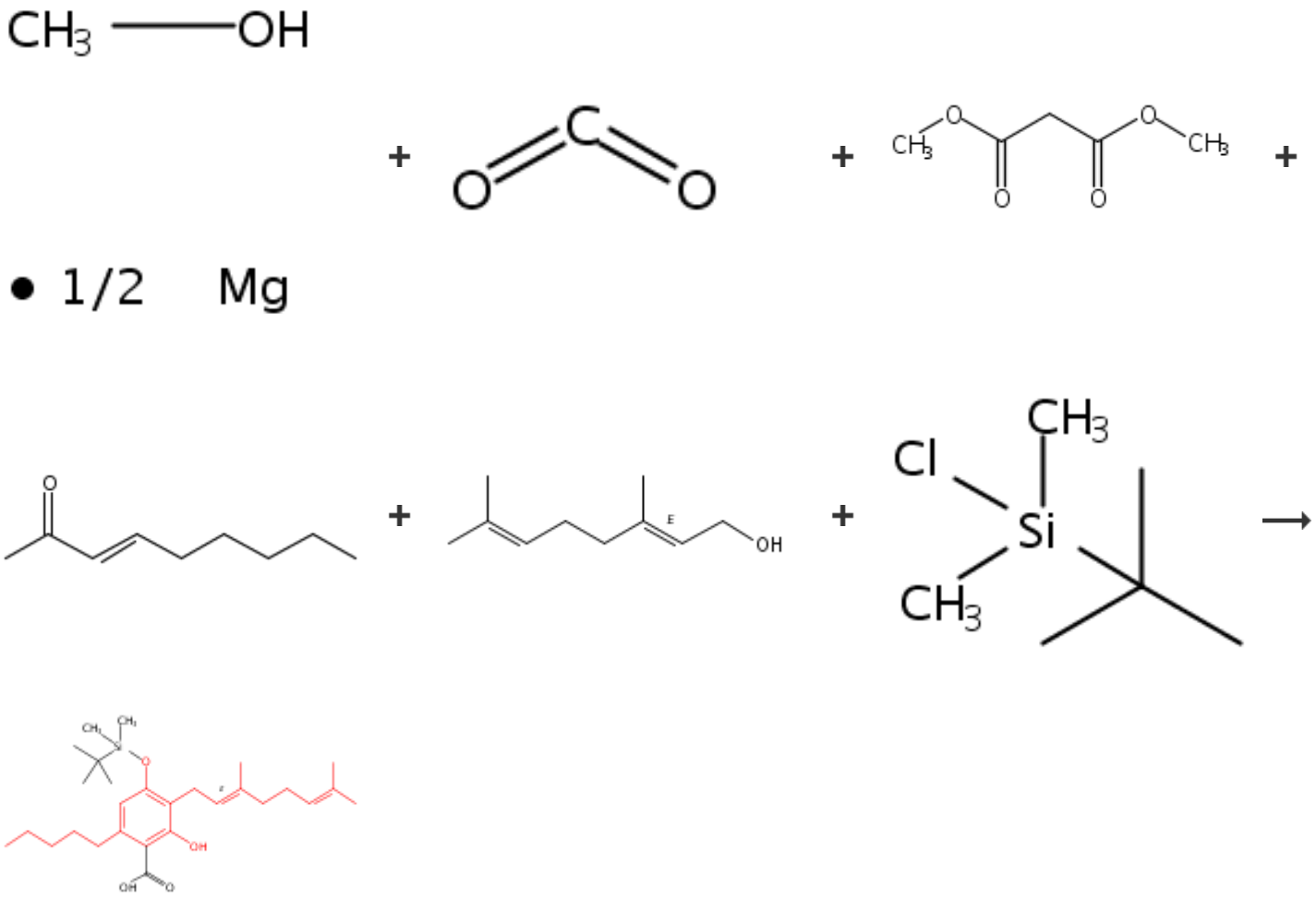
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

168. 6 Steps (Converging)



Overview

Steps/Stages

1.1 S:DMF, 140°C

1.1 R:NaOMe, S:MeOH, rt; 3 h, reflux; reflux → rt

1.2 R:H_2O, rt

2.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

3.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

4.1 S:DMF, 1 h, 120°C

4.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

5.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

5.2 R:NaCl, S:H_2O

Notes

exothermic reaction, in the dark, conversion = 40%,alternative preparation shown, alternative preparation shown, regioselective, Reactants: 6, Reagents: 7, Solvents: 5, Steps: 6, Stages: 9, Most stages in any one step: 2

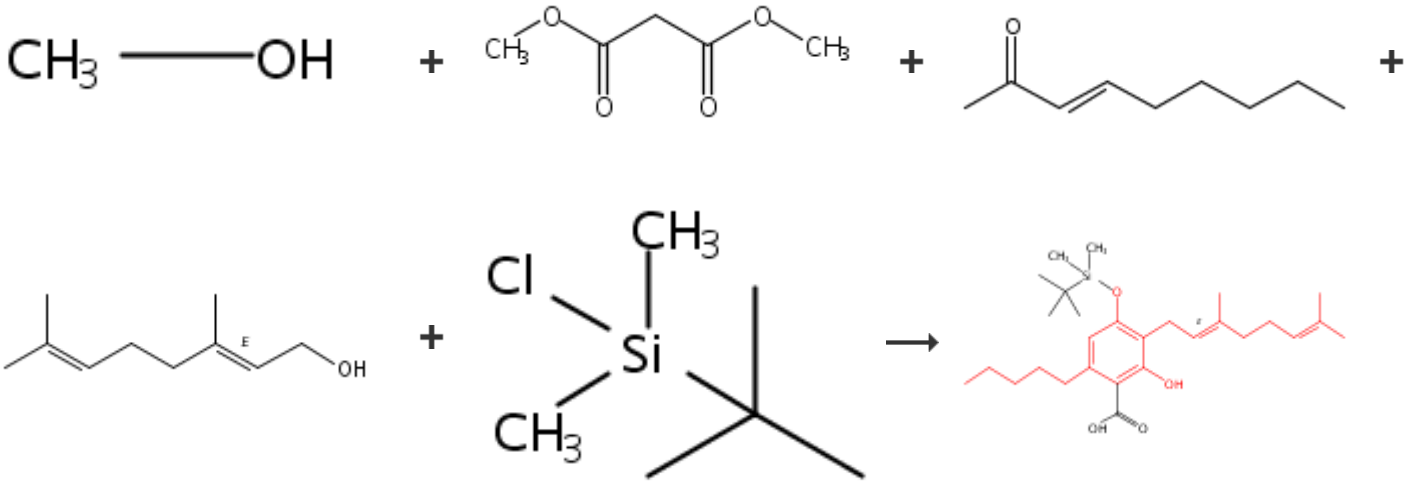
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

169. 6 Steps (Converging)



Overview

Steps/Stages

1.1 R:Mg, S:MeOH, rt

1.1 R:NaOMe, S:MeOH, rt; 3 h, reflux; reflux → rt

1.2 R:H_2O, rt

2.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

3.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

4.1 S:H_2O, cooled; 50°C; 3 h, 50°C; 50°C → rt

4.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, rt, pH 2

5.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

5.2 R:NaCl, S:H_2O

Notes

in the dark, conversion = 85%,alternative preparation shown,reaction in a sealed pressure vessel, alternative preparation shown, regioselective, Reactants: 5, Reagents: 8, Solvents: 5, Steps: 6, Stages: 9, Most stages in any one step: 2

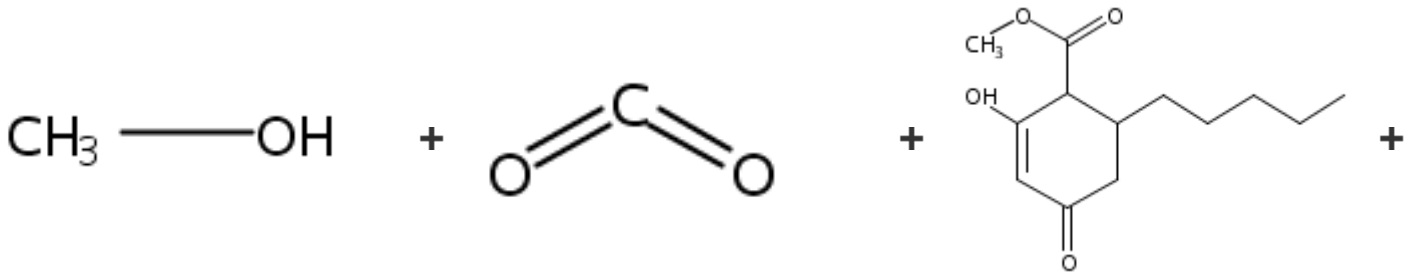
References

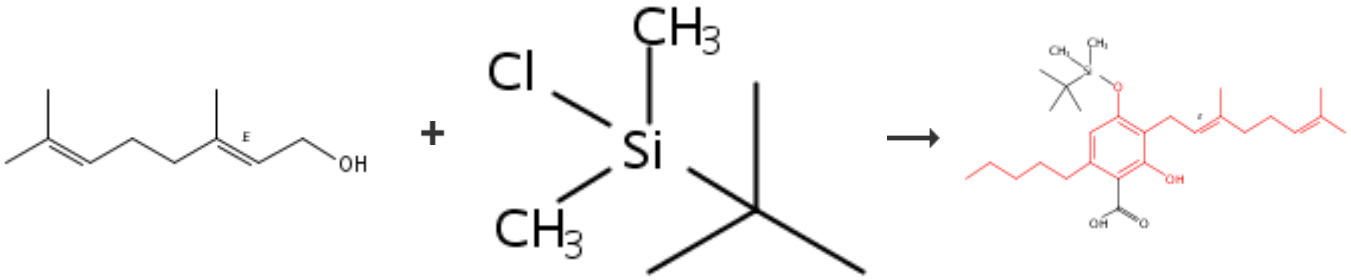
Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

170. 6 Steps (Converging)





Overview

Steps/Stages

1.1 R:Mg, S:MeOH, rt
2.1 S:DMF, 140°C

1.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

2.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
3.1 S:DMF, 1 h, 120°C

3.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

4.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

4.2 R:NaCl, S:H_2O

Notes

exothermic reaction, in the dark, conversion = 40%,alternative preparation shown, alternative preparation shown, regioselective, Reactants: 5, Reagents: 6, Solvents: 5, Steps: 6, Stages: 8, Most stages in any one step: 2

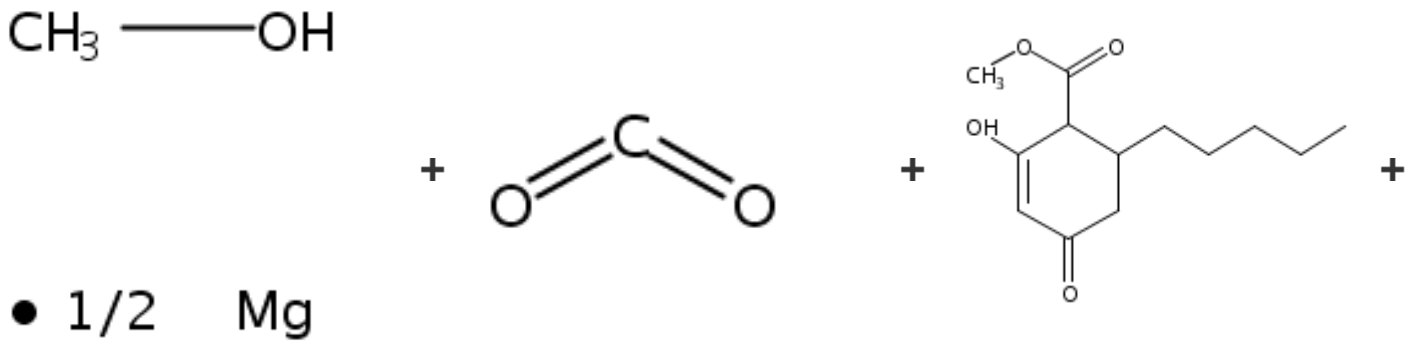
References

Biosynthesis of cannabinoid prodrugs

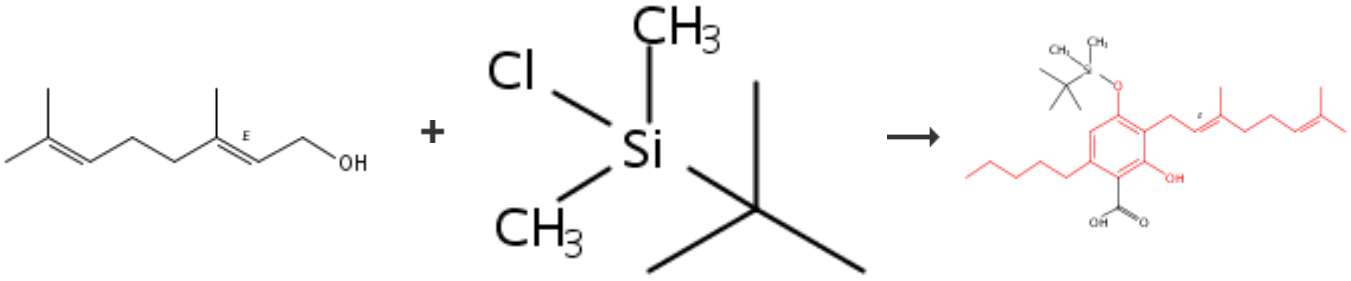
By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

171. 5 Steps (Converging)



- 1/2 Mg



Overview

Steps/Stages

1.1 S:DMF, 140°C

1.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

2.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

3.1 S:DMF, 1 h, 120°C

3.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

4.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

4.2 R:NaCl, S:H_2O

Notes

exothermic reaction, in the dark, conversion = 40%,alternative preparation shown, alternative preparation shown, regioselective, Reactants: 5, Reagents: 5, Solvents: 5, Steps: 5, Stages: 7, Most stages in any one step: 2

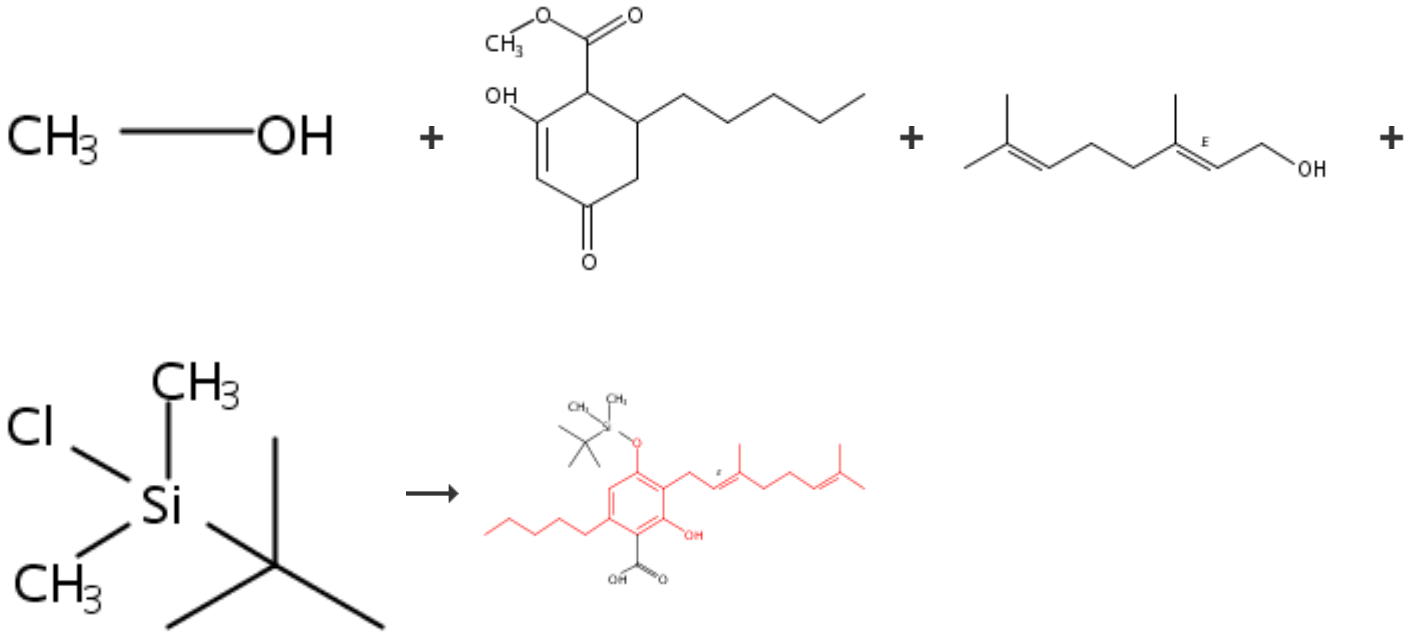
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

172. 5 Steps (Converging)



Overview

Steps/Stages

1.1 R:Mg, S:MeOH, rt

1.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

2.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

3.1 S:H_2O, cooled; 50°C; 3 h, 50°C; 50°C → rt

3.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, rt, pH 2

4.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

4.2 R:NaCl, S:H_2O

Notes

in the dark, conversion = 85%,alternative preparation shown,reaction in a sealed pressure vessel, alternative preparation shown, regioselective, Reactants: 4, Reagents: 6, Solvents: 5, Steps: 5, Stages: 7, Most stages in any one step: 2

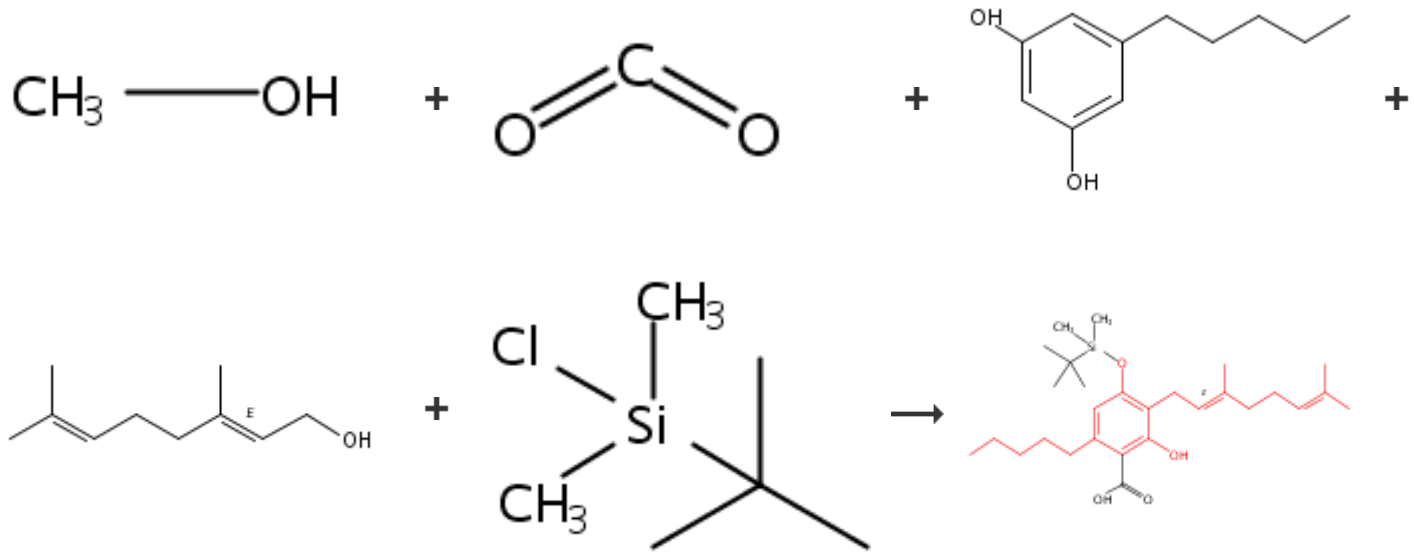
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

173. 5 Steps (Converging)



Overview

Steps/Stages

1.1 R:Mg, S:MeOH, rt
2.1 S:DMF, 140°C

1.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
2.1 S:DMF, 1 h, 120°C

2.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

3.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

3.2 R:NaCl, S:H_2O

Notes

exothermic reaction, in the dark, conversion = 40%,alternative preparation shown, alternative preparation shown, regioselective, Reactants: 5, Reagents: 5, Solvents: 5, Steps: 5, Stages: 7, Most stages in any one step: 2

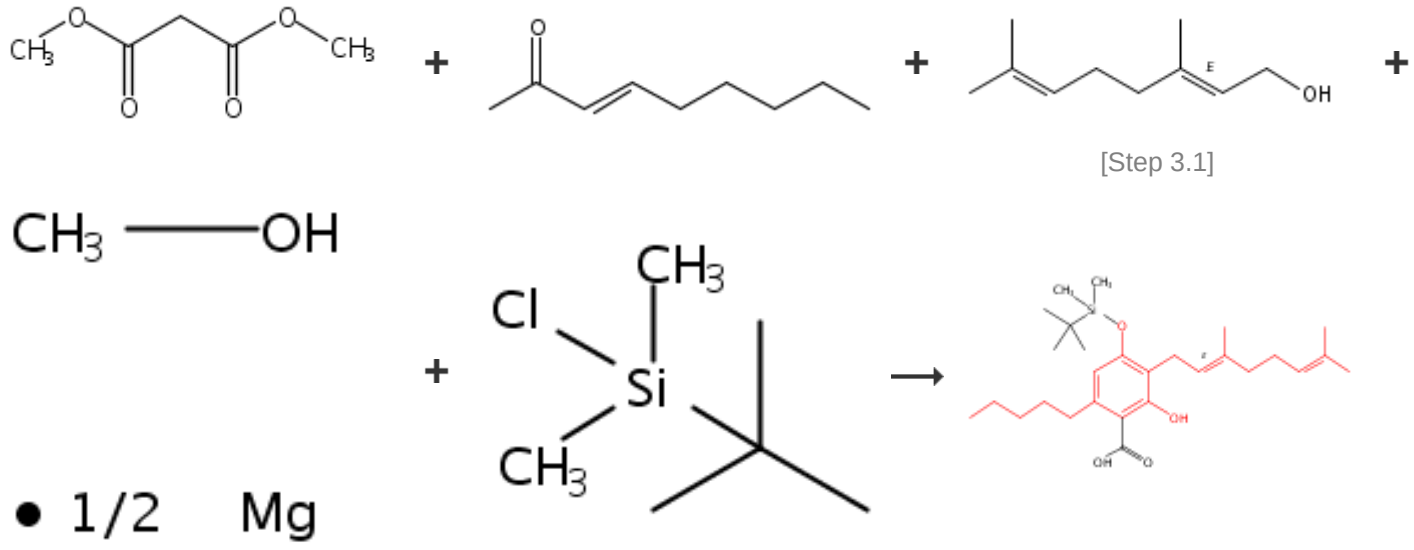
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

174. 5 Steps



[Step 3.1]

[Step 4.1] [Step 5.1]

Overview

Steps/Stages

1.1 R:NaOMe, S:MeOH, rt; 3 h, reflux; reflux → rt

1.2 R:H_2O, rt

2.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

3.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

4.1 S:H_2O, cooled; 50°C; 3 h, 50°C; 50°C → rt

4.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, rt, pH 2

5.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

5.2 R:NaCl, S:H_2O

Notes

3) in the dark, 4) conversion = 85%,alternative preparation shown,reaction in a sealed pressure vessel, 5) alternative preparation shown, regioselective, Reactants: 5, Reagents: 7, Solvents: 5, Steps: 5, Stages: 8, Most stages in any one step: 2

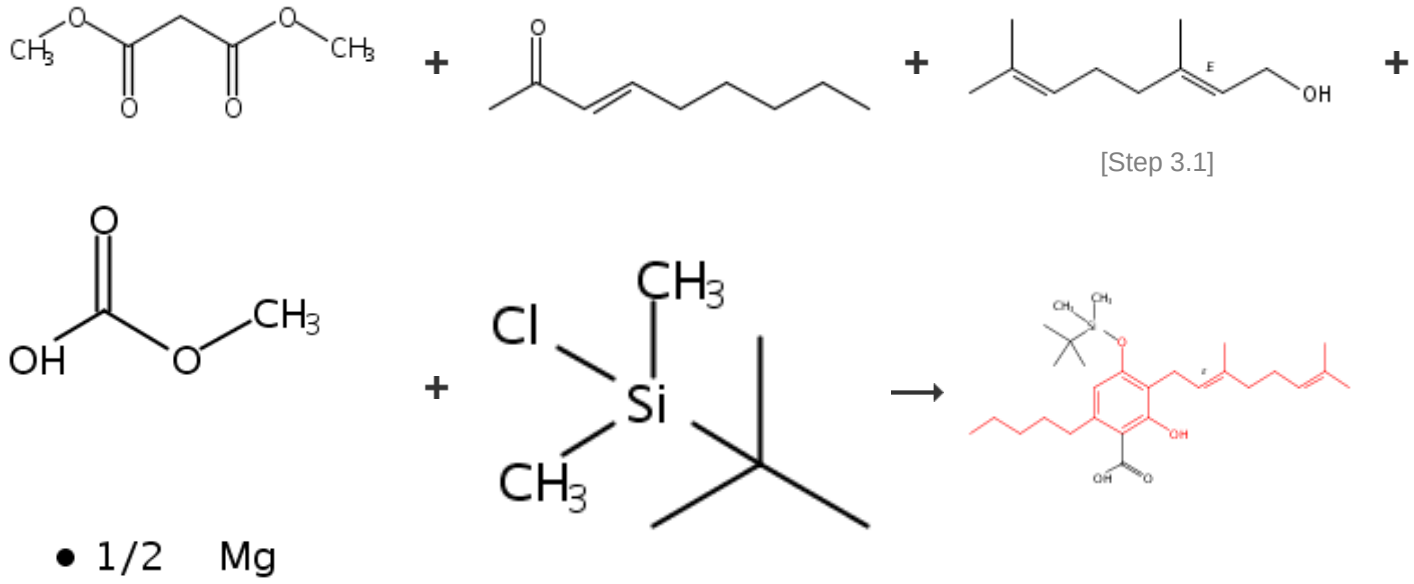
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

175. 5 Steps



Overview

Steps/Stages

Notes

1.1 R:NaOMe, S:MeOH, rt; 3 h, reflux; reflux → rt

1.2 R:H_2O, rt

2.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

3.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

4.1 S:DMF, 1 h, 120°C

4.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

5.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

5.2 R:NaCl, S:H_2O

3) in the dark, 4) conversion = 40%,alternative preparation shown, 5) alternative preparation shown, regioselective, Reactants: 5, Reagents: 7, Solvents: 5, Steps: 5, Stages: 8, Most stages in any one step: 2

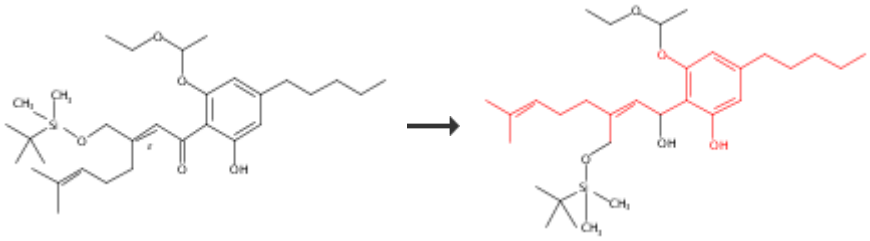
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

176. Single Step



94%

Overview

Steps/Stages

1.1 R:$NaBH_4$

Notes

Reactants: 1, Reagents: 1, Steps: 1, Stages: 1, Most stages in any one step: 1

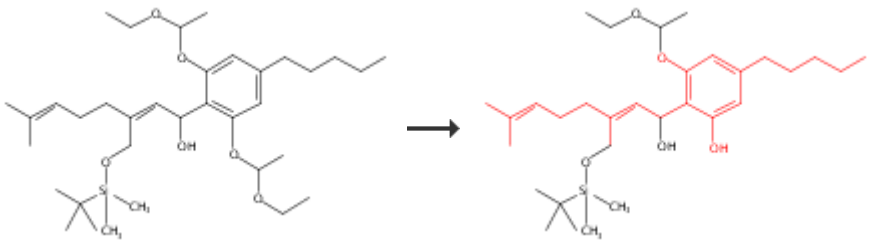
References

Synthesis of (±)-nor-Δ9-cis-6a,10a-THC-carboxylic acid (THC = tetrahydrocannabinol)

By Tius, Marcus A. and Gu, Xueqin

From Journal of the Chemical Society, Chemical Communications, (16), 1171-3; 1989

177. 2 Steps



Overview

Steps/Stages

1.1 R:$C_5H_{10}N(O=)CN=NC(=O)NC_5H_{10}$, R:*t*-BuOMgBr

2.1 R:$NaBH_4$

Notes

Reactants: 1, Reagents: 3, Steps: 2, Stages: 2, Most stages in any one step: 1

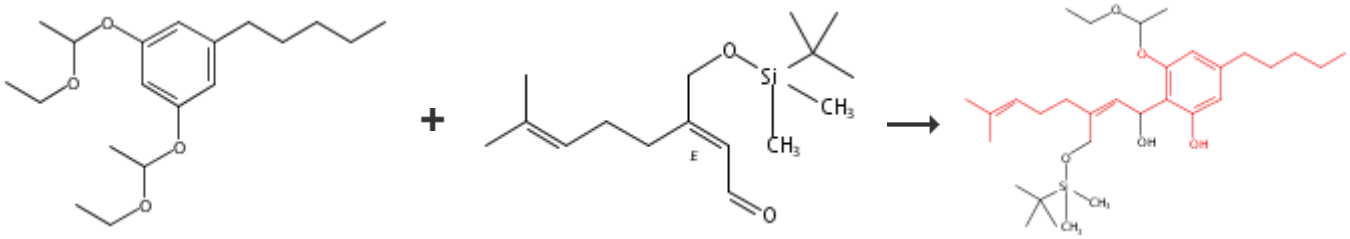
References

Synthesis of (±)-nor-Δ9-cis-6a,10a-THC-carboxylic acid (THC = tetrahydrocannabinol)

By Tius, Marcus A. and Gu, Xueqin

From Journal of the Chemical Society, Chemical Communications, (16), 1171-3; 1989

178. 3 Steps



Overview

Steps/Stages

1.1 R:BuLi, S:THF

1.2

2.1 R:$C_5H_{10}N(O=)CN=NC(=O)NC_5H_{10}$, R:*t*-BuOMgBr

3.1 R:$NaBH_4$

Notes

Reactants: 2, Reagents: 4, Solvents: 1, Steps: 3, Stages: 4, Most stages in any one step: 2

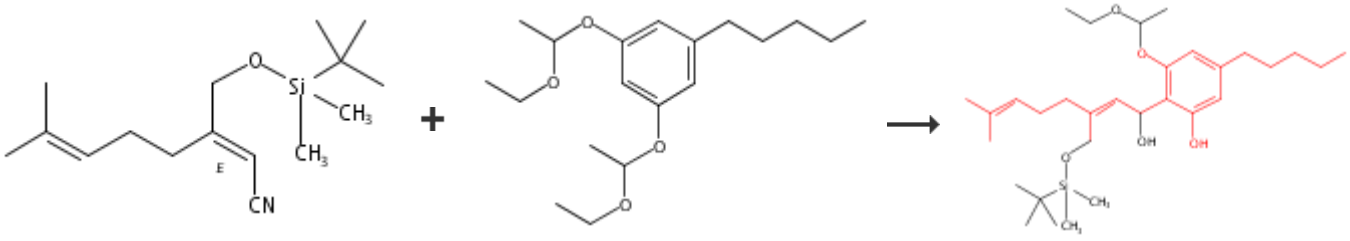
References

Synthesis of (±)-nor-Δ9-cis-6a,10a-THC-carboxylic acid (THC = tetrahydrocannabinol)

By Tius, Marcus A. and Gu, Xueqin

From Journal of the Chemical Society, Chemical Communications, (16), 1171-3; 1989

179. 4 Steps



[Step 2.1]

Overview

Steps/Stages

1.1 R:AlH(Bu-*i*)$_2$, S:Et$_2$O

2.1 R:BuLi, S:THF

2.2

3.1 R:C$_5$H$_{10}$N(O=)CN=NC(=O)NC$_5$H$_{10}$, R:*t*-BuOMgBr

4.1 R:NaBH$_4$

Notes

Reactants: 2, Reagents: 5, Solvents: 2, Steps: 4, Stages: 5, Most stages in any one step: 2

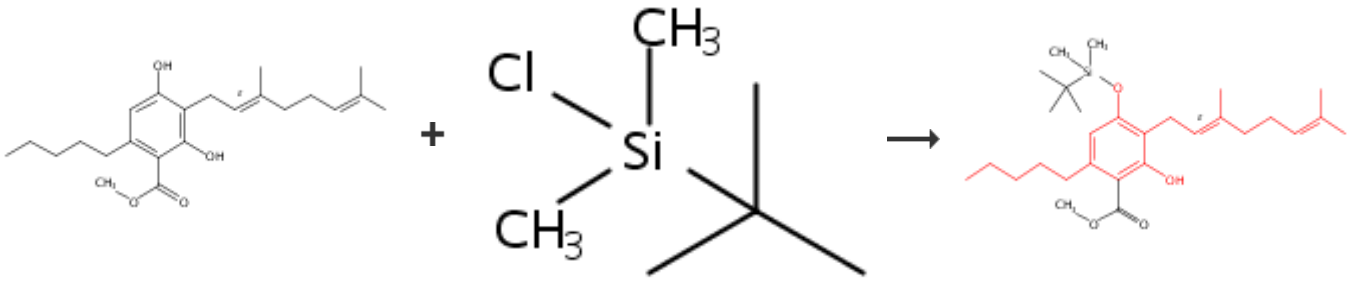
References

Synthesis of (±)-nor-Δ9-cis-6a,10a-THC-carboxylic acid (THC = tetrahydrocannabinol)

By Tius, Marcus A. and Gu, Xueqin

From Journal of the Chemical Society, Chemical Communications, (16), 1171-3; 1989

180. Single Step



Overview

Steps/Stages

1.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

1.2 R:NaCl, S:H_2O

Notes

regioselective, Reactants: 2, Reagents: 2, Solvents: 2, Steps: 1, Stages: 2, Most stages in any one step: 2

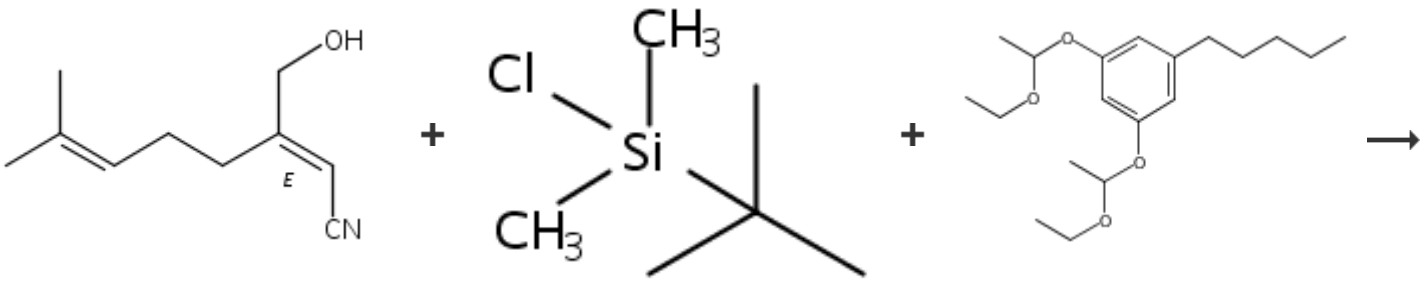
References

Methods for the manufacture of cannabinoid prodrugs, pharmaceutical formulations and their use

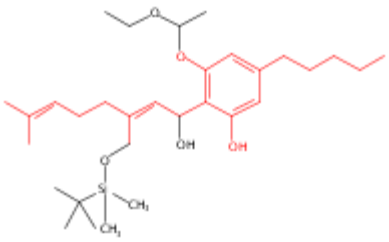
By Peet, Richard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017216362, 21 Dec 2017

181. 5 Steps



[Step 3.1]



Overview

Steps/Stages

1.1

2.1 R:AlH(Bu-*i*)$_2$, S:Et$_2$O

3.1 R:BuLi, S:THF

3.2

4.1 R:C$_5$H$_{10}$N(O=)CN=NC(=O)NC$_5$H$_{10}$, R:*t*-BuOMgBr

5.1 R:NaBH$_4$

Notes

Reactants: 3, Reagents: 5, Solvents: 2, Steps: 5, Stages: 6, Most stages in any one step: 2

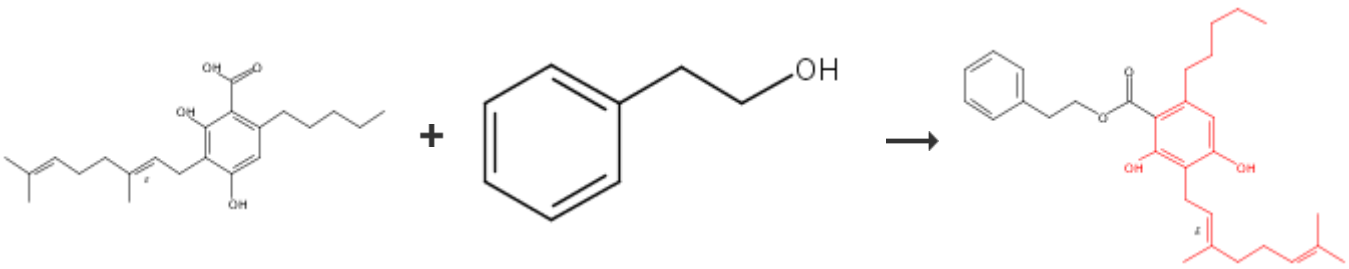
References

Synthesis of (±)-nor-Δ9-cis-6a,10a-THC-carboxylic acid (THC = tetrahydrocannabinol)

By Tius, Marcus A. and Gu, Xueqin

From Journal of the Chemical Society, Chemical Communications, (16), 1171-3; 1989

182. Single Step



32%

Overview

Steps/Stages

1.1 R:PPh$_3$, R:N$_2$(CO$_2$CHMe$_2$)$_2$, S:CH$_2$Cl$_2$, cooled; 16 h, rt

Notes

Mitsunobu esterification, Reactants: 2, Reagents: 2, Solvents: 1, Steps: 1, Stages: 1, Most stages in any one step: 1

References

Antibacterial Cannabinoids from Cannabis sativa: A Structure-Activity Study

By Appendino, Giovanni et al

From Journal of Natural Products, 71(8), 1427-1430; 2008

Experimental Procedure

Mitsunobu Esterification of Pre-cannabinoids (synthesis of 3g as an example). To a cooled (ice bath) solution of **3a** (360 mg, 1.1 mmol) in dry CH_2Cl_2 (4 mL) were added sequentially phenethyl alcohol (92 µL, 0.76 mmol, 0.75 molar equiv), triphenylphosphine (TPP) (220 mg, 0.84 mmol, 0.80 molar equiv), and diisopropyldiazodicarboxylate (DIAD) (228 µL, 1.1 mmol, 1 molar equiv). At the end of the addition, the cooling bath was removed, and the reaction was stirred at room temperature. After 16 h, the reaction was worked up by evaporation, and the residue was dissolved in toluene and cooled at 4 °C overnight to remove most of the TPPO-dihydro DIAD adduct. The filtrate was evaporated and purified by gravity column chromatography on silica gel (10 g, petroleum ether as eluant) to afford 126 mg (32%) of **3g**. **Pre-cannabigerol Phenethyl Ester (3g):** colorless foam, yield 126 mg (32%) IR ν^{KBr}_{max} 3746, 3513, 3313, 1715, 1589, 1421, 1274, 1164, 980, 804, 690 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 12.08 (1H, s), 7.25 (5H, m), 6.02 (1H, s), 5.98 (1H, s), 5,25 (1H, br t, *J* = 7.0 Hz), 5.01 (1H, br t, *J* = 6.5 Hz), 4.56 (2H, t, *J* = 6.6 Hz), 3.40 (2H, d, *J* = 7.3 Hz), 3.1 (2H, t, *J* = 6.6 Hz), 2.7 (2H, t, *J* = 6.6 Hz), 2.05 (4H, m), 1.79 (3H, s), 1.65 (3H, s), 1.57 (3H, s), 1.24 (6H, m), 0.88 (3H, t, *J* = 7.1 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.1 (s), 162.7 (s), 159.5 (s), 148.8 (s), 139.1 (s), 137.4 (d), 132.1 (s), 128.8 (d), 126.8 (d), 125.9 (d), 121.5 (d), 111.5 (s), 110.8 (s), 65.8 (t), 39.8 (t), 36.6 (t), 35.0 (t), 32.0 (t), 31.5 (t), 26.5 (t), 25.8 (q), 22.2 (t), 17.8 (q), 16.3 (q), 14.2 (q); CIMS *m/z* [M + H] 465 [$C_{30}H_{40}O_4$ + H].

Reaction Protocol

Procedure

1. Add phenethyl alcohol (92 µL, 0.76 mmol, 0.75 molar equivalents), triphenylphosphine (TPP) (220 mg, 0.84 mmol, 0.80 molar equivalents) and diisopropyldiazodicarboxylate (DIAD) (228 µL, 1.1 mmol, 1 molar equivalent) to a cooled (ice bath) solution of pre-cannabinoids (1.1 mmol) in dry CH_2Cl_2 (4 ml).
2. At the end of the addition, remove the cooling bath.

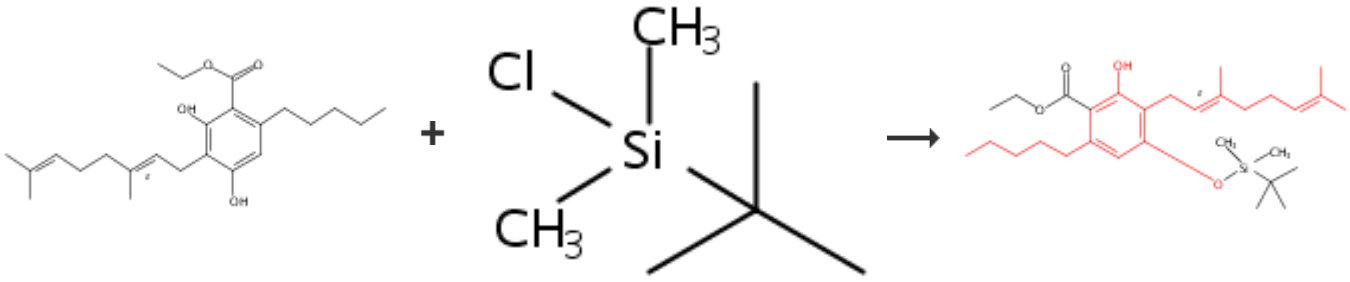
View more...

Available Experimental Data

^1H NMR, ^{13}C NMR, IR, Mass Spec, State

View with MethodsNow

183. Single Step



Overview

Steps/Stages **Notes**

1.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

1.2 R:NaCl, S:H_2O

regioselective, Reactants: 2, Reagents: 2, Solvents: 2, Steps: 1, Stages: 2, Most stages in any one step: 2

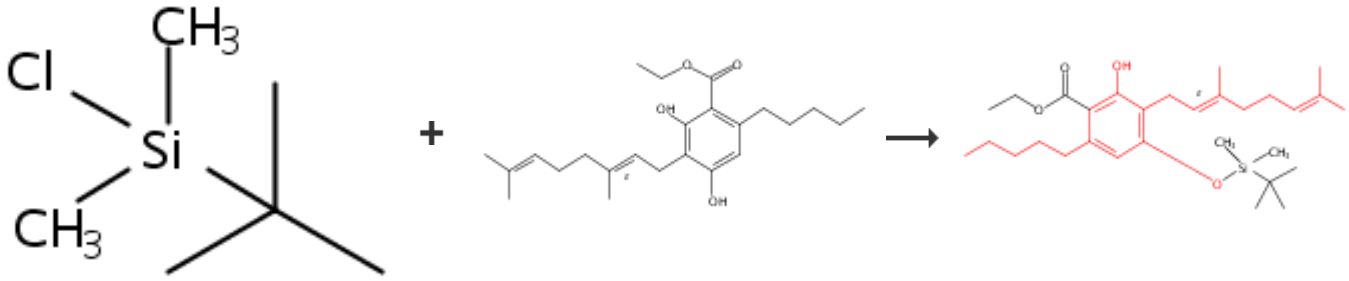
References

Methods for the manufacture of cannabinoid prodrugs, pharmaceutical formulations and their use

By Peet, Richard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017216362, 21 Dec 2017

184. Single Step



Overview

Steps/Stages

1.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

1.2 R:NaCl, S:H_2O

Notes

regioselective, Reactants: 2, Reagents: 2, Solvents: 2, Steps: 1, Stages: 2, Most stages in any one step: 2

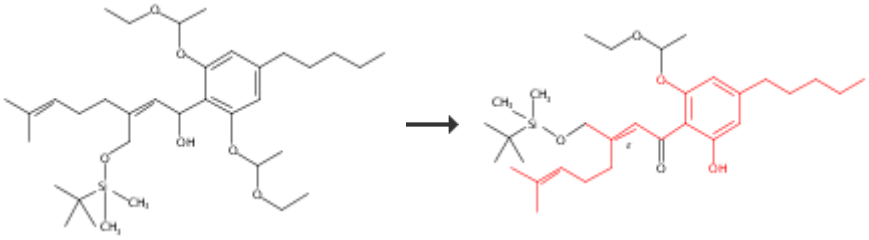
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

185. Single Step



79%

Overview

Steps/Stages

Notes

1.1 R:$C_5H_{10}N(O=)CN=NC(=O)NC_5H_{10}$, R:*t*-BuOMgBr

Reactants: 1, Reagents: 2, Steps: 1, Stages: 1, Most stages in any one step: 1

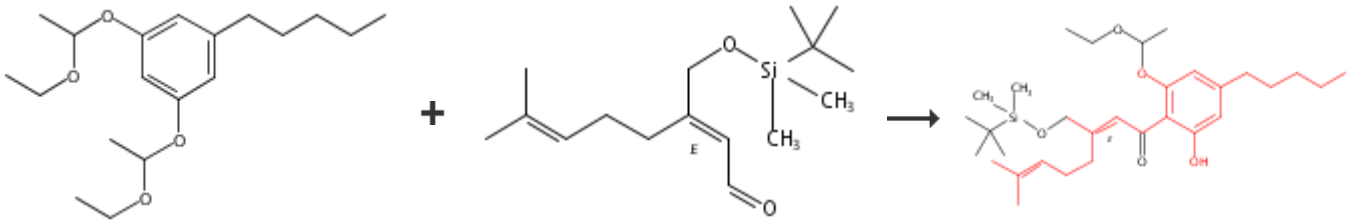
References

Synthesis of (±)-nor-Δ9-cis-6a,10a-THC-carboxylic acid (THC = tetrahydrocannabinol)

By Tius, Marcus A. and Gu, Xueqin

From Journal of the Chemical Society, Chemical Communications, (16), 1171-3; 1989

186. 2 Steps



Overview

Steps/Stages

1.1 R:BuLi, S:THF

1.2

2.1 R:$C_5H_{10}N(O=)CN=NC(=O)NC_5H_{10}$, R:*t*-BuOMgBr

Notes

Reactants: 2, Reagents: 3, Solvents: 1, Steps: 2, Stages: 3, Most stages in any one step: 2

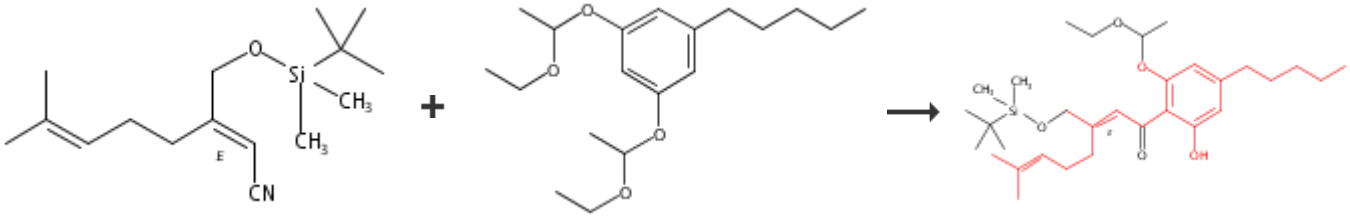
References

Synthesis of (±)-nor-Δ9-cis-6a,10a-THC-carboxylic acid (THC = tetrahydrocannabinol)

By Tius, Marcus A. and Gu, Xueqin

From Journal of the Chemical Society, Chemical Communications, (16), 1171-3; 1989

187. 3 Steps



[Step 2.1]

Overview

Steps/Stages

Notes

1.1 R:AlH(Bu-*i*)$_2$, S:Et$_2$O

2.1 R:BuLi, S:THF

2.2

3.1 R:C$_5$H$_{10}$N(O=)CN=NC(=O)NC$_5$H$_{10}$, R:*t*-BuOMgBr

Reactants: 2, Reagents: 4, Solvents: 2, Steps: 3, Stages: 4, Most stages in any one step: 2

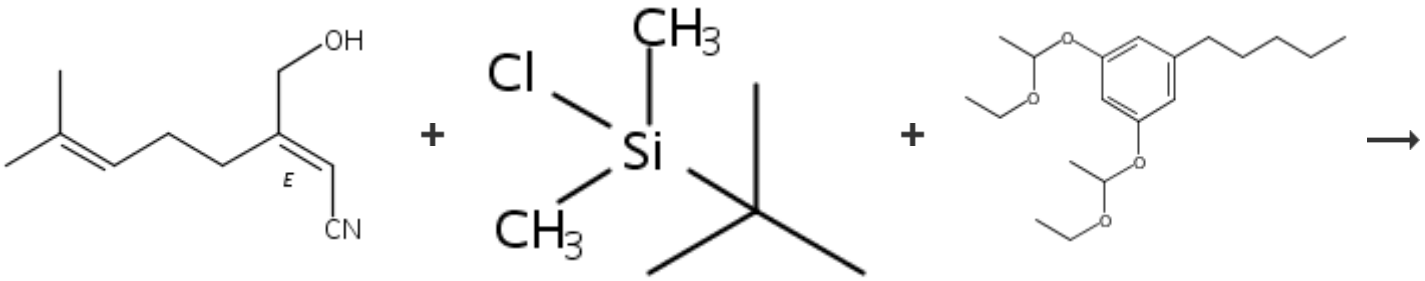
References

Synthesis of (±)-nor-Δ9-cis-6a,10a-THC-carboxylic acid (THC = tetrahydrocannabinol)

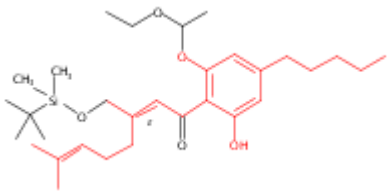
By Tius, Marcus A. and Gu, Xueqin

From Journal of the Chemical Society, Chemical Communications, (16), 1171-3; 1989

188. 4 Steps



[Step 3.1]



Overview

Steps/Stages

1.1

2.1 R:AlH(Bu-*i*)$_2$, S:Et$_2$O

3.1 R:BuLi, S:THF

3.2

4.1 R:C$_5$H$_{10}$N(O=)CN=NC(=O)NC$_5$H$_{10}$, R:*t*-BuOMgBr

Notes

Reactants: 3, Reagents: 4, Solvents: 2, Steps: 4, Stages: 5, Most stages in any one step: 2

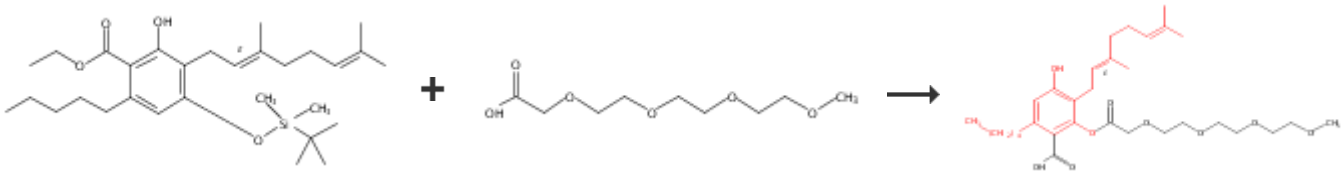
References

Synthesis of (±)-nor-Δ9-cis-6a,10a-THC-carboxylic acid (THC = tetrahydrocannabinol)

By Tius, Marcus A. and Gu, Xueqin

From Journal of the Chemical Society, Chemical Communications, (16), 1171-3; 1989

189. Single Step



Overview

Steps/Stages

1.1 R:DCC, C:4-DMAP, S:CH_2Cl_2, rt; overnight, rt

1.2 R:Bu_4N^+ •F^-, S:CH_2Cl_2, -15°C

Notes

alternative preparation shown,other reagent carbonyldiimidazole may be used in stage 1 and triethylamine trihydrofluoride in stage 2, Reactants: 2, Reagents: 2, Catalysts: 1, Solvents: 1, Steps: 1, Stages: 2, Most stages in any one step: 2

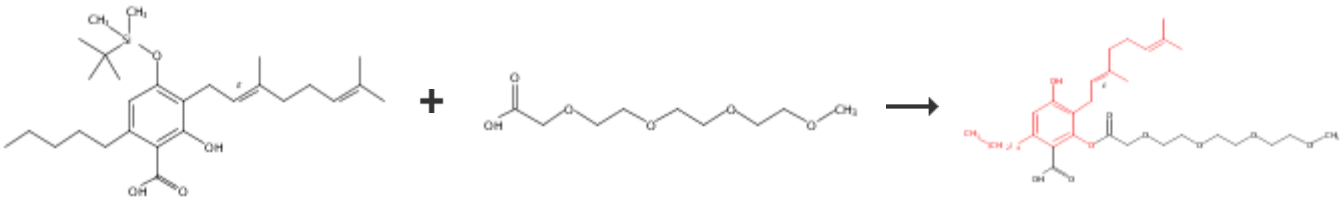
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

190. Single Step



Overview

Steps/Stages

1.1 R:DCC, C:4-DMAP, S:CH_2Cl_2, rt; overnight, rt

1.2 R:Bu_4N^+ •F^-, S:CH_2Cl_2, -15°C

Notes

alternative preparation shown,other reagent carbonyldiimidazole may be used in stage 1 and triethylamine trihydrofluoride in stage 2, Reactants: 2, Reagents: 2, Catalysts: 1, Solvents: 1, Steps: 1, Stages: 2, Most stages in any one step: 2

References

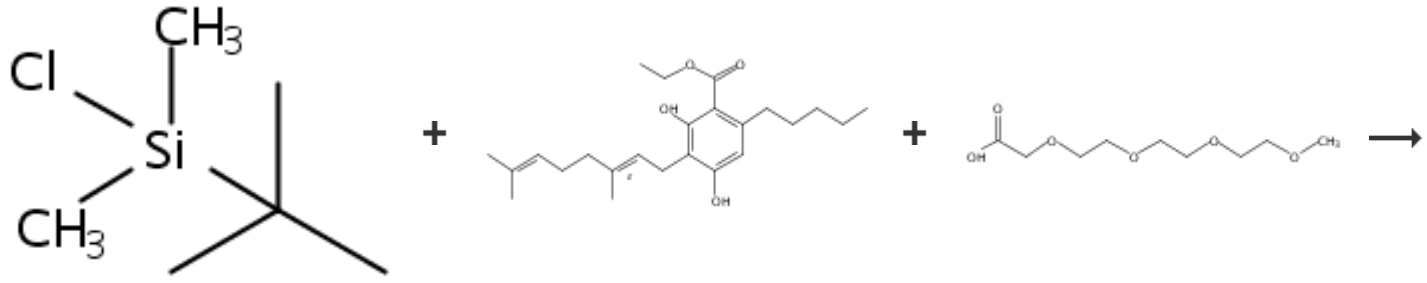
Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

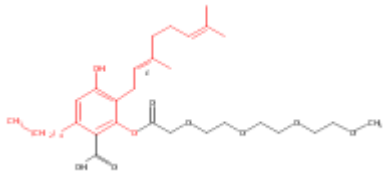
From PCT Int. Appl., 2017181118, 19 Oct 2017

CASREACT ®: Copyright © 2019 American Chemical Society. All Rights Reserved. CASREACT contains reactions from CAS and from: ZIC/VINITI database (1974-1999) provided by InfoChem; INPI data prior to 1986; Biotransformations database compiled under the direction of Professor Dr. Klaus Kieslich; organic reactions, portions copyright 1996-2006 John Wiley & Sons, Ltd., John Wiley and Sons, Inc., Organic Reactions Inc., and Organic Syntheses Inc. Reproduced under license. All Rights Reserved.

191. 2 Steps



[Step 2.1]



Overview

Steps/Stages

1.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

1.2 R:NaCl, S:H_2O

2.1 R:DCC, C:4-DMAP, S:CH_2Cl_2, rt; overnight, rt

2.2 R:$Bu_4N^+ \cdot F^-$, S:CH_2Cl_2, -15°C

Notes

1) regioselective, 2) alternative preparation shown,other reagent carbonyldiimidazole may be used in stage 1 and triethylamine trihydrofluoride in stage 2, Reactants: 3, Reagents: 4, Catalysts: 1, Solvents: 2, Steps: 2, Stages: 4, Most stages in any one step: 2

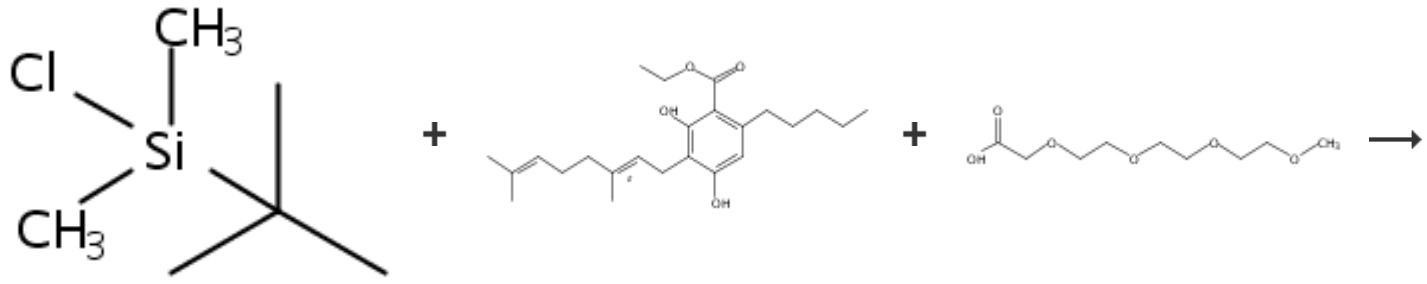
References

Biosynthesis of cannabinoid prodrugs

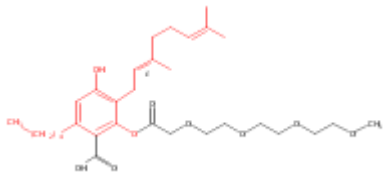
By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

192. 2 Steps



[Step 2.1]



Overview

Steps/Stages

Notes

1.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

1.2 R:NaCl, S:H_2O

1.3

2.1 R:DCC, C:4-DMAP, S:CH_2Cl_2, rt; overnight, rt

2.2 R:Bu_4N^+ •F^-, S:CH_2Cl_2, -15°C

1) unspecified reagent used for acidic hydrolysis in stage 3,alternative preparation shown, regioselective, 2) alternative preparation shown,other reagent carbonyldiimidazole may be used in stage 1 and triethylamine trihydrofluoride in stage 2, Reactants: 3, Reagents: 4, Catalysts: 1, Solvents: 2, Steps: 2, Stages: 5, Most stages in any one step: 3

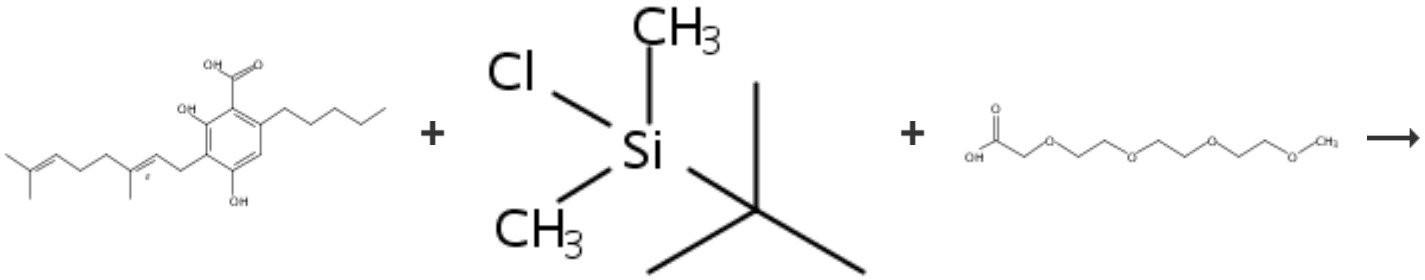
References

Biosynthesis of cannabinoid prodrugs

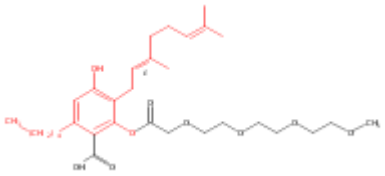
By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

193. 2 Steps



[Step 2.1]



Overview

Steps/Stages

1.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

1.2 R:NaCl, S:H_2O

2.1 R:DCC, C:4-DMAP, S:CH_2Cl_2, rt; overnight, rt

2.2 R:Bu_4N^+ •F^-, S:CH_2Cl_2, -15°C

Notes

1) alternative preparation shown, regioselective, 2) alternative preparation shown,other reagent carbonyldiimidazole may be used in stage 1 and triethylamine trihydrofluoride in stage 2, Reactants: 3, Reagents: 4, Catalysts: 1, Solvents: 2, Steps: 2, Stages: 4, Most stages in any one step: 2

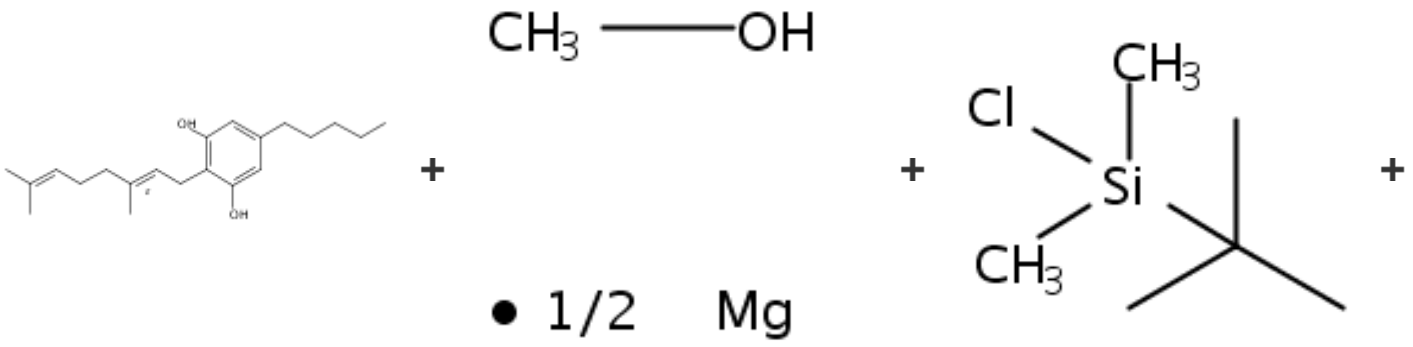
References

Biosynthesis of cannabinoid prodrugs

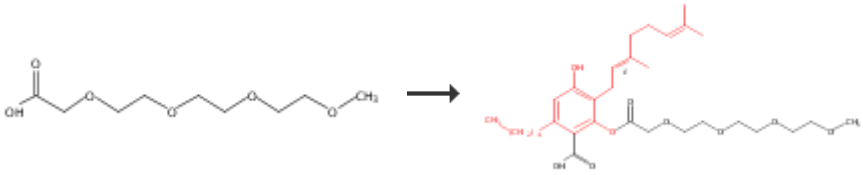
By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

194. 3 Steps



[Step 2.1]



[Step 3.1]

Overview

Steps/Stages

1.1 S:H_2O, cooled; 50°C; 3 h, 50°C; 50°C → rt

1.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, rt, pH 2

2.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

2.2 R:NaCl, S:H_2O

3.1 R:DCC, C:4-DMAP, S:CH_2Cl_2, rt; overnight, rt

3.2 R:Bu_4N^+ •F^-, S:CH_2Cl_2, -15°C

Notes

1) conversion = 85%,alternative preparation shown,reaction in a sealed pressure vessel, 2) alternative preparation shown, regioselective, 3) alternative preparation shown,other reagent carbonyldiimidazole may be used in stage 1 and triethylamine trihydrofluoride in stage 2, Reactants: 4, Reagents: 5, Catalysts: 1, Solvents: 4, Steps: 3, Stages: 6, Most stages in any one step: 2

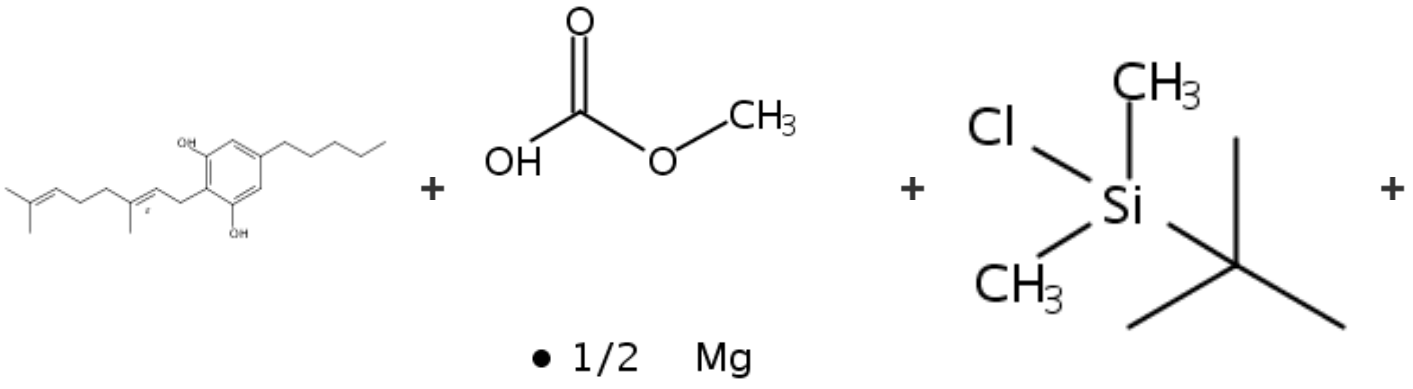
References

Biosynthesis of cannabinoid prodrugs

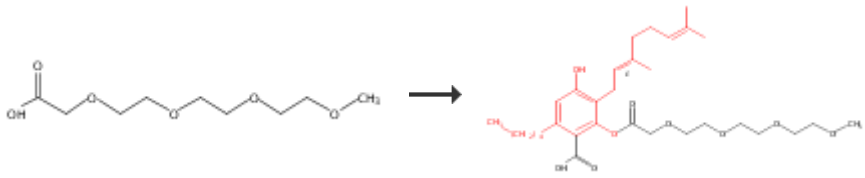
By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

195. 3 Steps



[Step 2.1]



[Step 3.1]

Overview

Steps/Stages

1.1 S:DMF, 1 h, 120°C

1.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

2.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

2.2 R:NaCl, S:H_2O

3.1 R:DCC, C:4-DMAP, S:CH_2Cl_2, rt; overnight, rt

3.2 R:$Bu_4N^+ \cdot F^-$, S:CH_2Cl_2, -15°C

Notes

1) conversion = 40%,alternative preparation shown, 2) alternative preparation shown, regioselective, 3) alternative preparation shown,other reagent carbonyldiimidazole may be used in stage 1 and triethylamine trihydrofluoride in stage 2, Reactants: 4, Reagents: 5, Catalysts: 1, Solvents: 5, Steps: 3, Stages: 6, Most stages in any one step: 2

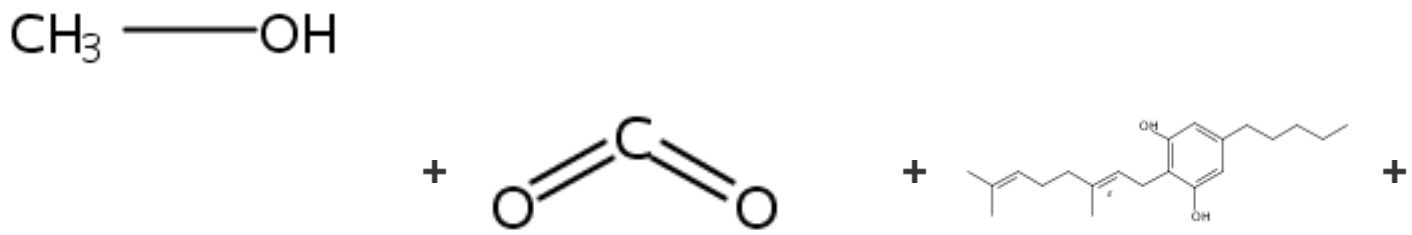
References

Biosynthesis of cannabinoid prodrugs

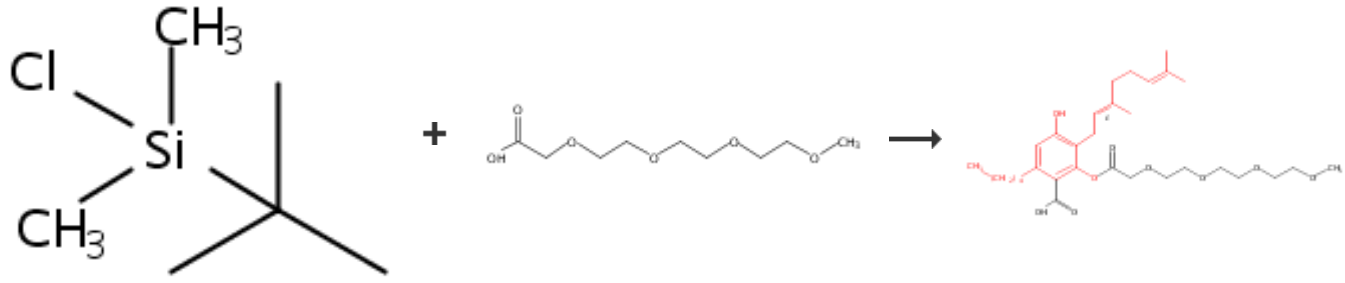
By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

196. 4 Steps



[Step 2.1]



[Step 3.1] [Step 4.1]

Overview

Steps/Stages

Notes

1.1 S:DMF, 140°C
2.1 S:DMF, 1 h, 120°C

2.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

3.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

3.2 R:NaCl, S:H_2O

4.1 R:DCC, C:4-DMAP, S:CH_2Cl_2, rt; overnight, rt

4.2 R:Bu_4N^+ •F^-, S:CH_2Cl_2, -15°C

1) exothermic reaction, 2) conversion = 40%,alternative preparation shown, 3) alternative preparation shown, regioselective, 4) alternative preparation shown,other reagent carbonyldiimidazole may be used in stage 1 and triethylamine trihydrofluoride in stage 2, Reactants: 5, Reagents: 5, Catalysts: 1, Solvents: 5, Steps: 4, Stages: 7, Most stages in any one step: 2

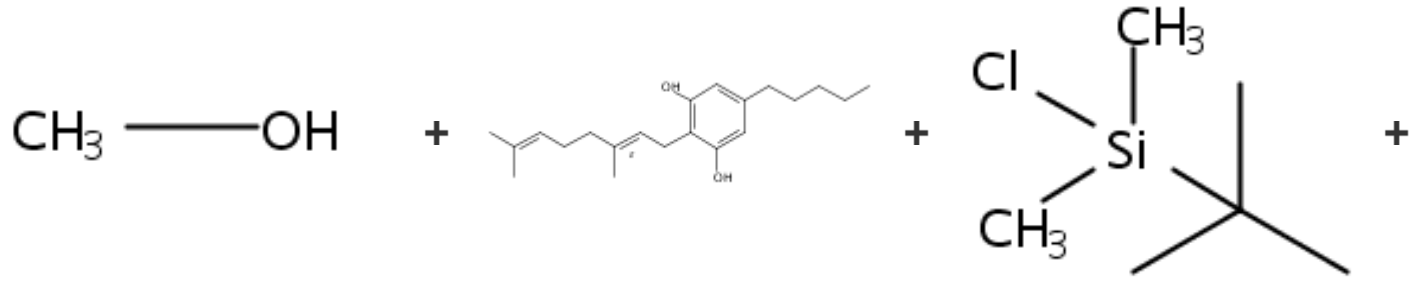
References

Biosynthesis of cannabinoid prodrugs

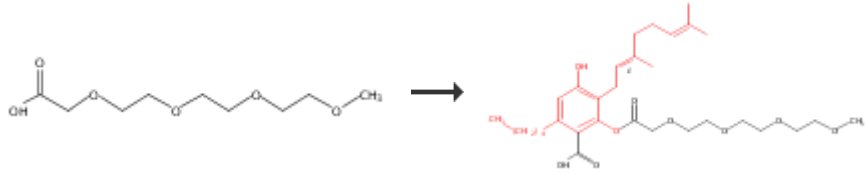
By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

197. 4 Steps



[Step 2.1] [Step 3.1]



[Step 4.1]

Overview

Steps/Stages

1.1 R:Mg, S:MeOH, rt
2.1 S:H_2O, cooled; 50°C; 3 h, 50°C; 50°C → rt

2.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, rt, pH 2

3.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

3.2 R:NaCl, S:H_2O

4.1 R:DCC, C:4-DMAP, S:CH_2Cl_2, rt; overnight, rt

4.2 R:Bu_4N^+ •F^-, S:CH_2Cl_2, -15°C

Notes

2) conversion = 85%,alternative preparation shown,reaction in a sealed pressure vessel, 3) alternative preparation shown, regioselective, 4) alternative preparation shown,other reagent carbonyldiimidazole may be used in stage 1 and triethylamine trihydrofluoride in stage 2, Reactants: 4, Reagents: 6, Catalysts: 1, Solvents: 4, Steps: 4, Stages: 7, Most stages in any one step: 2

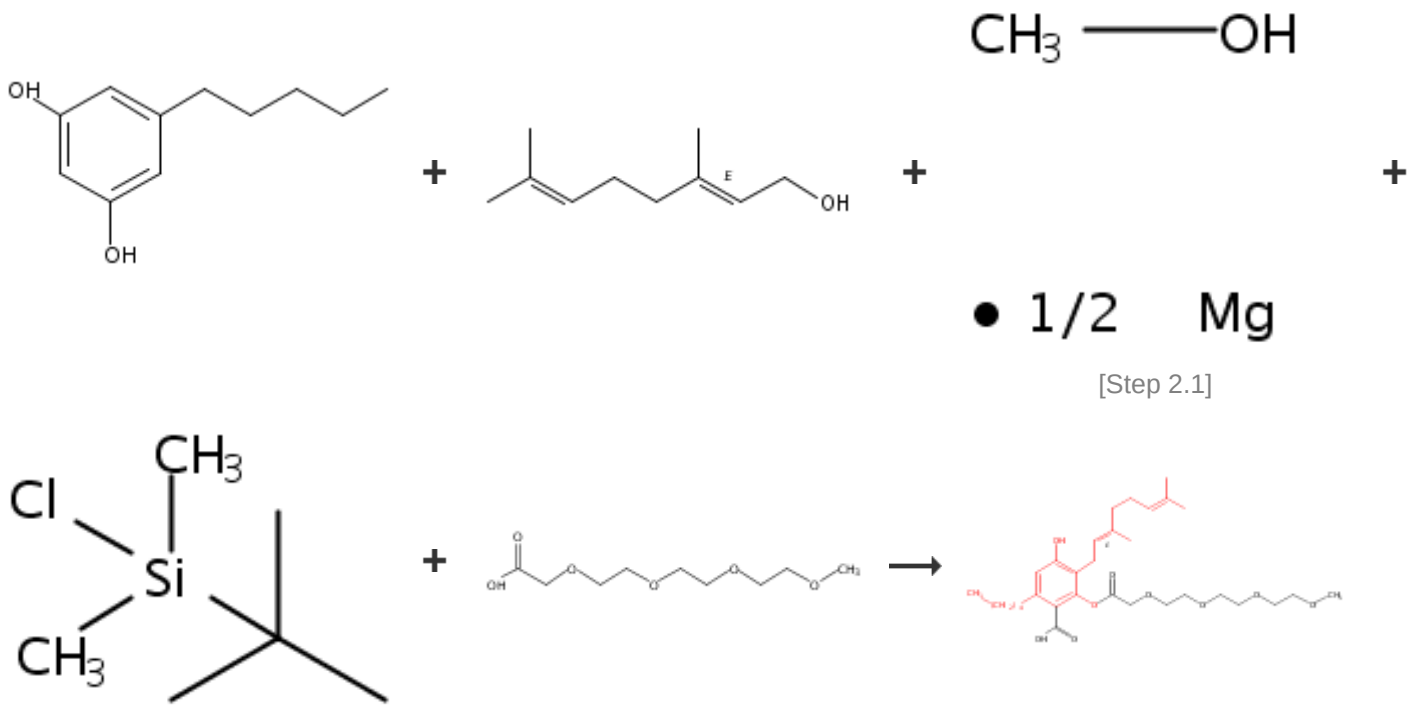
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

198. 4 Steps



Overview

Steps/Stages

1.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

2.1 S:H_2O, cooled; 50°C; 3 h, 50°C; 50°C → rt

2.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, rt, pH 2

3.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

3.2 R:NaCl, S:H_2O

4.1 R:DCC, C:4-DMAP, S:CH_2Cl_2, rt; overnight, rt

4.2 R:$Bu_4N^+ \cdot F^-$, S:CH_2Cl_2, -15°C

Notes

1) in the dark, 2) conversion = 85%,alternative preparation shown,reaction in a sealed pressure vessel, 3) alternative preparation shown, regioselective, 4) alternative preparation shown,other reagent carbonyldiimidazole may be used in stage 1 and triethylamine trihydrofluoride in stage 2, Reactants: 5, Reagents: 6, Catalysts: 1, Solvents: 4, Steps: 4, Stages: 7, Most stages in any one step: 2

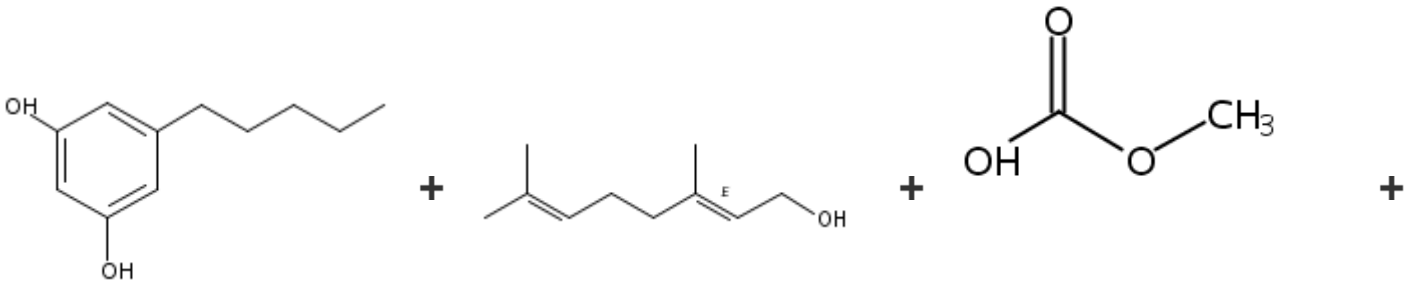
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

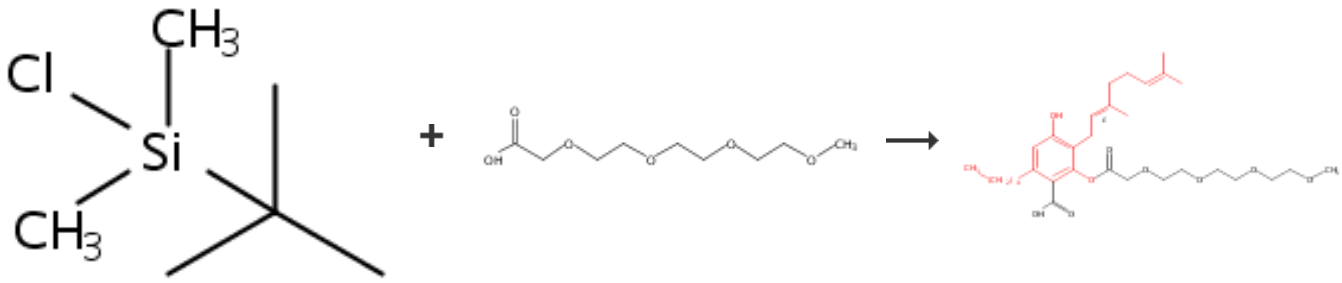
From PCT Int. Appl., 2017181118, 19 Oct 2017

199. 4 Steps



• 1/2 Mg

[Step 2.1]



[Step 3.1]

[Step 4.1]

Overview

Steps/Stages

1.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

2.1 S:DMF, 1 h, 120°C

2.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

3.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

3.2 R:NaCl, S:H_2O

4.1 R:DCC, C:4-DMAP, S:CH_2Cl_2, rt; overnight, rt

4.2 R:$Bu_4N^+ \cdot F^-$, S:CH_2Cl_2, -15°C

Notes

1) in the dark, 2) conversion = 40%,alternative preparation shown, 3) alternative preparation shown, regioselective, 4) alternative preparation shown,other reagent carbonyldiimidazole may be used in stage 1 and triethylamine trihydrofluoride in stage 2, Reactants: 5, Reagents: 6, Catalysts: 1, Solvents: 5, Steps: 4, Stages: 7, Most stages in any one step: 2

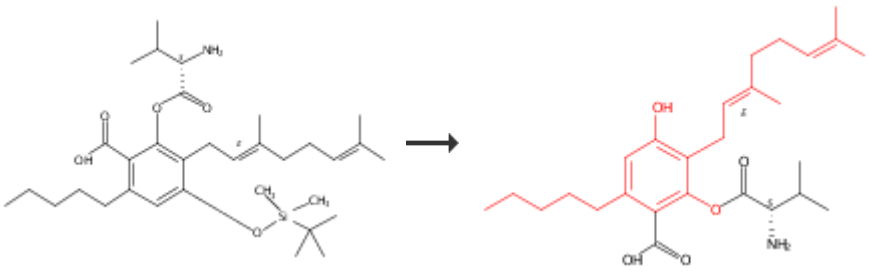
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

200. Single Step



Overview

Steps/Stages

1.1 R:Bu_4N^+ •F^-, S:CH_2Cl_2, -15°C

Notes

Reactants: 1, Reagents: 1, Solvents: 1, Steps: 1, Stages: 1, Most stages in any one step: 1

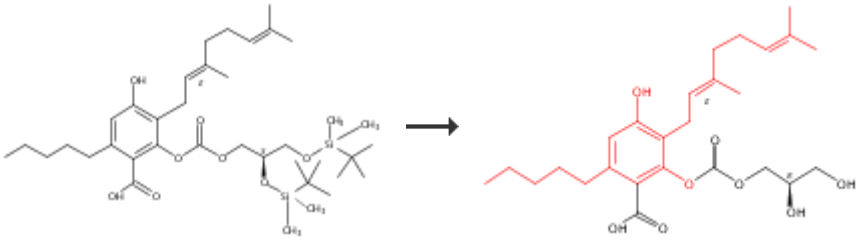
References

Methods for the manufacture of cannabinoid prodrugs, pharmaceutical formulations and their use

By Peet, Richard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017216362, 21 Dec 2017

201. Single Step



Overview

Steps/Stages

1.1 R:Et_3N •3HF, S:CH_2Cl_2, -15°C; 65 h, 5°C

1.2 R:$NaHCO_3$, S:H_2O, S:AcOEt, 0°C

Notes

Reactants: 1, Reagents: 2, Solvents: 3, Steps: 1, Stages: 2, Most stages in any one step: 2

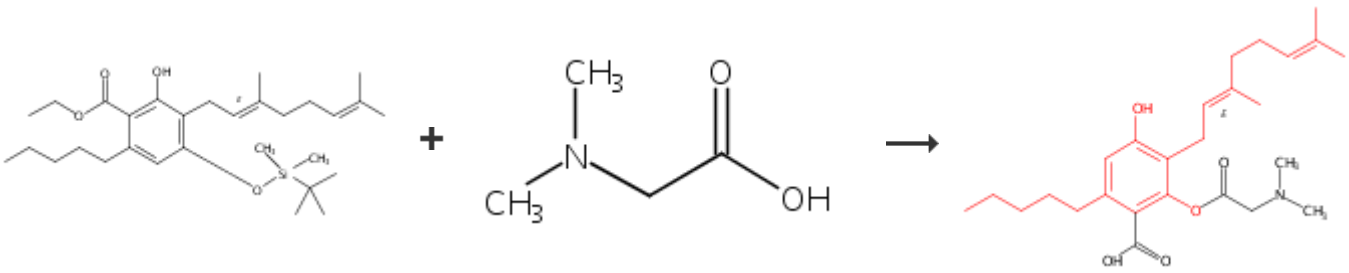
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

202. Single Step



Overview

Steps/Stages

1.1 R:DCC, C:4-DMAP, S:CH_2Cl_2, rt; overnight, rt

1.2 R:$Bu_4N^+ \bullet F^-$, S:CH_2Cl_2, -15°C

Notes

alternative preparation shown,other reagent triethylamine trihydrofluoride may be used in stage 2, Reactants: 2, Reagents: 2, Catalysts: 1, Solvents: 1, Steps: 1, Stages: 2, Most stages in any one step: 2

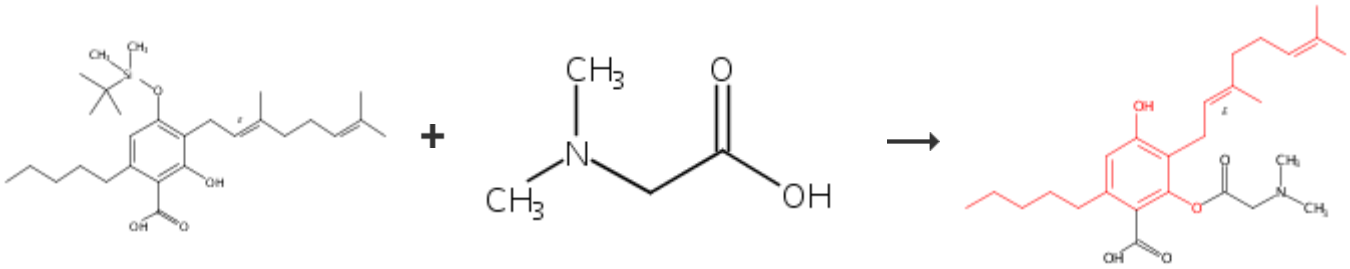
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

203. Single Step



Overview

Steps/Stages

1.1 R:DCC, C:4-DMAP, S:CH_2Cl_2, rt; overnight, rt

1.2 R:$Bu_4N^+ \bullet F^-$, S:CH_2Cl_2, -15°C

Notes

alternative preparation shown,other reagent triethylamine trihydrofluoride may be used in stage 2, Reactants: 2, Reagents: 2, Catalysts: 1, Solvents: 1, Steps: 1, Stages: 2, Most stages in any one step: 2

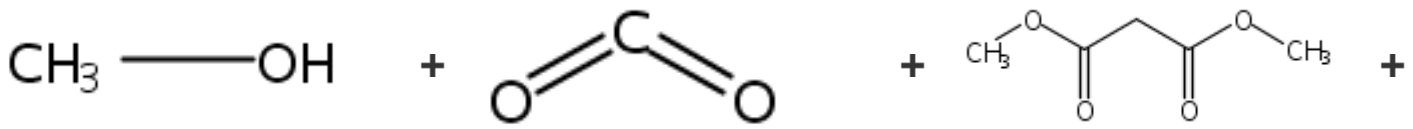
References

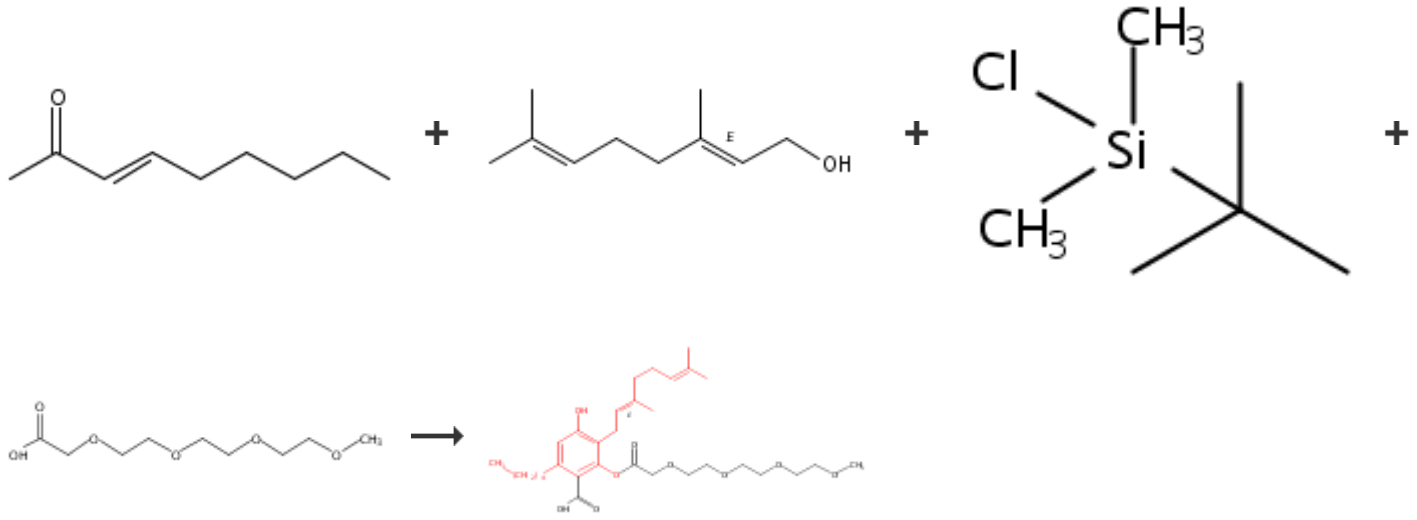
Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

204. 8 Steps (Converging)





Overview

Steps/Stages

1.1 R:Mg, S:MeOH, rt
2.1 S:DMF, 140°C

1.1 R:NaOMe, S:MeOH, rt; 3 h, reflux; reflux → rt

1.2 R:H_2O, rt

2.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

3.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
4.1 S:DMF, 1 h, 120°C

4.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

5.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

5.2 R:NaCl, S:H_2O

6.1 R:DCC, C:4-DMAP, S:CH_2Cl_2, rt; overnight, rt

6.2 R:Bu_4N^+ •F^-, S:CH_2Cl_2, -15°C

Notes

exothermic reaction, in the dark, conversion = 40%,alternative preparation shown, alternative preparation shown, regioselective, alternative preparation shown,other reagent carbonyldiimidazole may be used in stage 1 and triethylamine trihydrofluoride in stage 2, Reactants: 7, Reagents: 10, Catalysts: 1, Solvents: 5, Steps: 8, Stages: 12, Most stages in any one step: 2

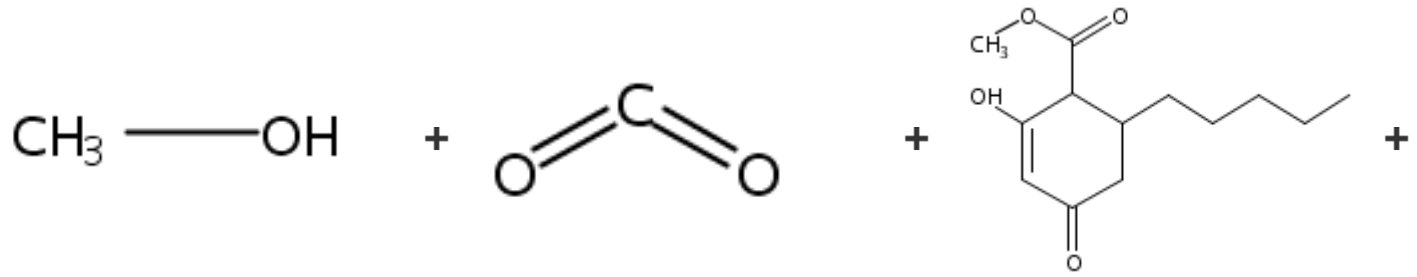
References

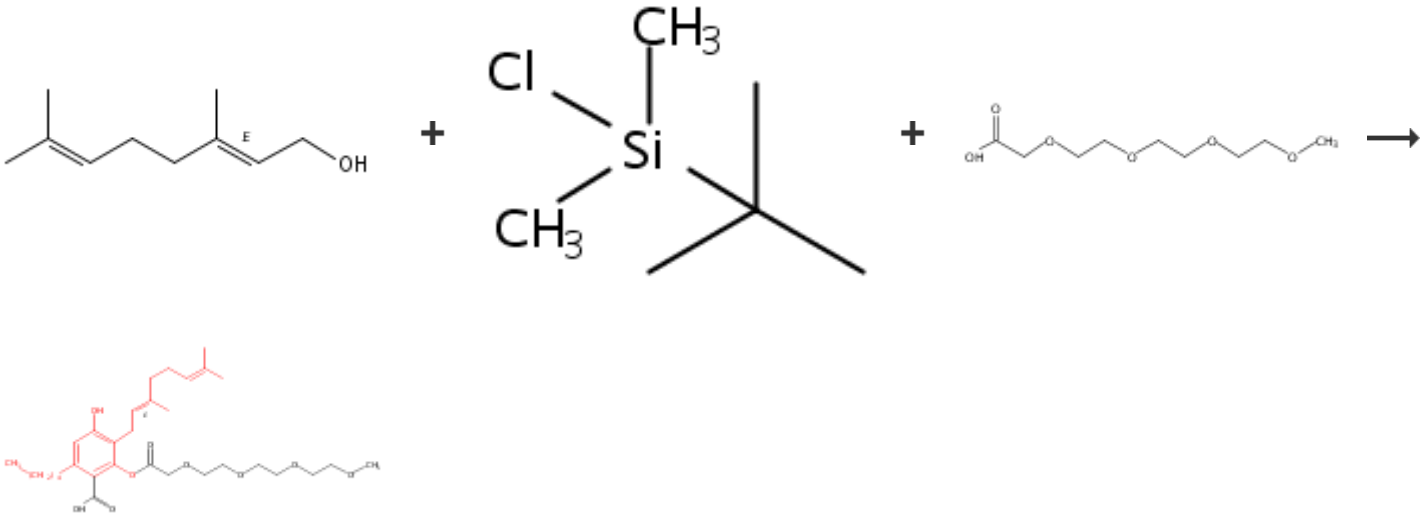
Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

205. 7 Steps (Converging)





Overview

Steps/Stages

1.1 R:Mg, S:MeOH, rt
2.1 S:DMF, 140°C

1.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

2.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
3.1 S:DMF, 1 h, 120°C

3.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

4.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

4.2 R:NaCl, S:H_2O

5.1 R:DCC, C:4-DMAP, S:CH_2Cl_2, rt; overnight, rt

5.2 R:$Bu_4N^+ \cdot F^-$, S:CH_2Cl_2, -15°C

Notes

exothermic reaction, in the dark, conversion = 40%,alternative preparation shown, alternative preparation shown, regioselective, alternative preparation shown,other reagent carbonyldiimidazole may be used in stage 1 and triethylamine trihydrofluoride in stage 2, Reactants: 6, Reagents: 8, Catalysts: 1, Solvents: 5, Steps: 7, Stages: 10, Most stages in any one step: 2

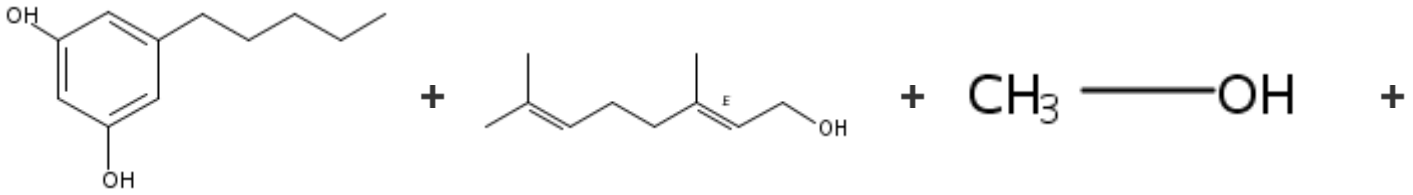
References

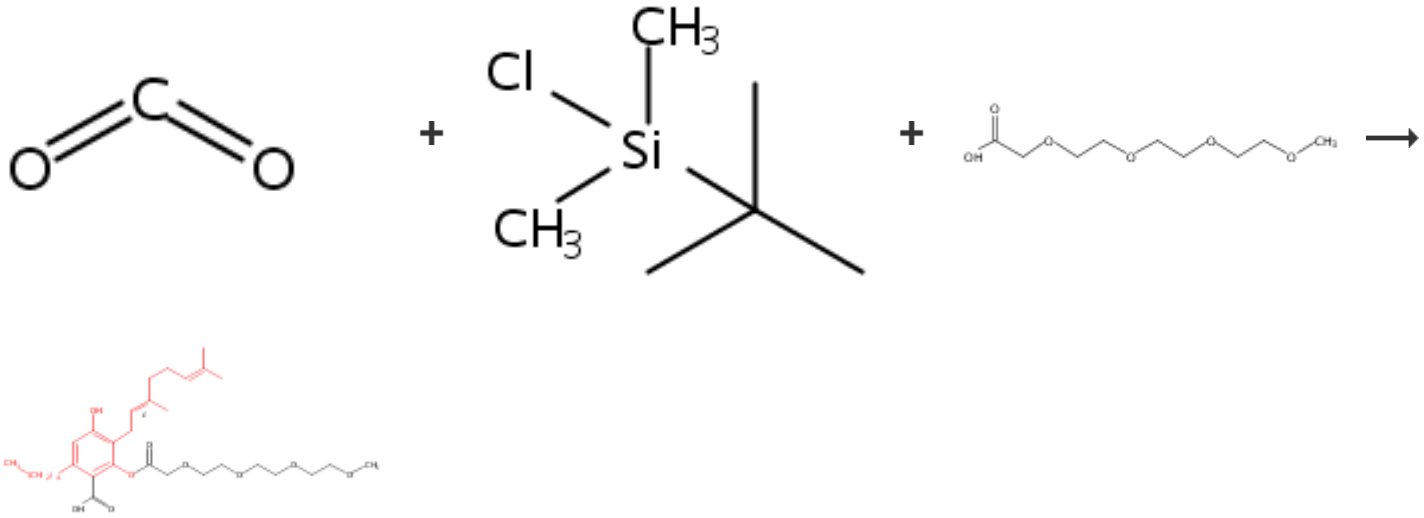
Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

206. 6 Steps (Converging)





Overview

Steps/Stages

1.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

1.1 R:Mg, S:MeOH, rt
2.1 S:DMF, 140°C
3.1 S:DMF, 1 h, 120°C

3.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

4.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

4.2 R:NaCl, S:H_2O

5.1 R:DCC, C:4-DMAP, S:CH_2Cl_2, rt; overnight, rt

5.2 R:$Bu_4N^+ \cdot F^-$, S:CH_2Cl_2, -15°C

Notes

in the dark, exothermic reaction, conversion = 40%,alternative preparation shown, alternative preparation shown, regioselective, alternative preparation shown,other reagent carbonyldiimidazole may be used in stage 1 and triethylamine trihydrofluoride in stage 2, Reactants: 6, Reagents: 7, Catalysts: 1, Solvents: 5, Steps: 6, Stages: 9, Most stages in any one step: 2

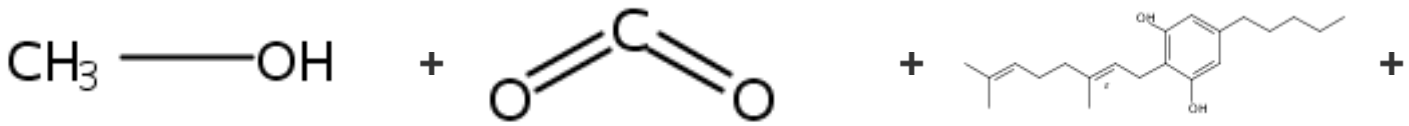
References

Biosynthesis of cannabinoid prodrugs

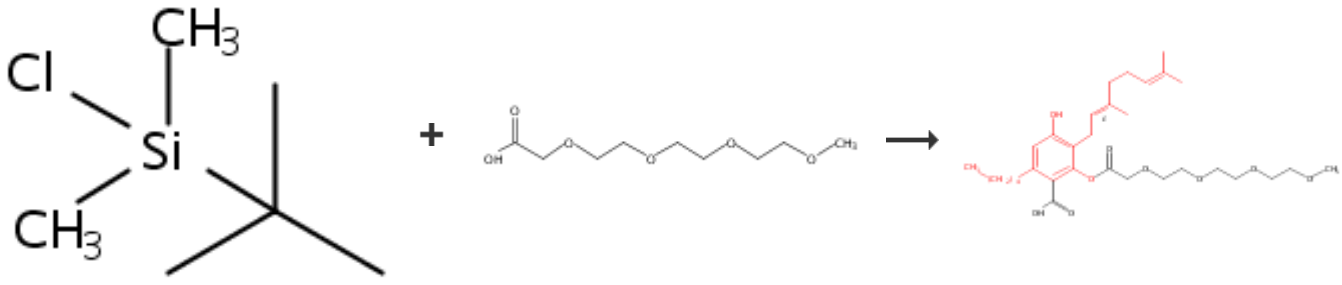
By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

207. 5 Steps



[Step 2.1] [Step 3.1]



[Step 4.1] [Step 5.1]

Overview

Steps/Stages

1.1 R:Mg, S:MeOH, rt
2.1 S:DMF, 140°C
3.1 S:DMF, 1 h, 120°C

3.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

4.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

4.2 R:NaCl, S:H_2O

5.1 R:DCC, C:4-DMAP, S:CH_2Cl_2, rt; overnight, rt

5.2 R:$Bu_4N^+ \bullet F^-$, S:CH_2Cl_2, -15°C

Notes

2) exothermic reaction, 3) conversion = 40%,alternative preparation shown, 4) alternative preparation shown, regioselective, 5) alternative preparation shown,other reagent carbonyldiimidazole may be used in stage 1 and triethylamine trihydrofluoride in stage 2, Reactants: 5, Reagents: 6, Catalysts: 1, Solvents: 5, Steps: 5, Stages: 8, Most stages in any one step: 2

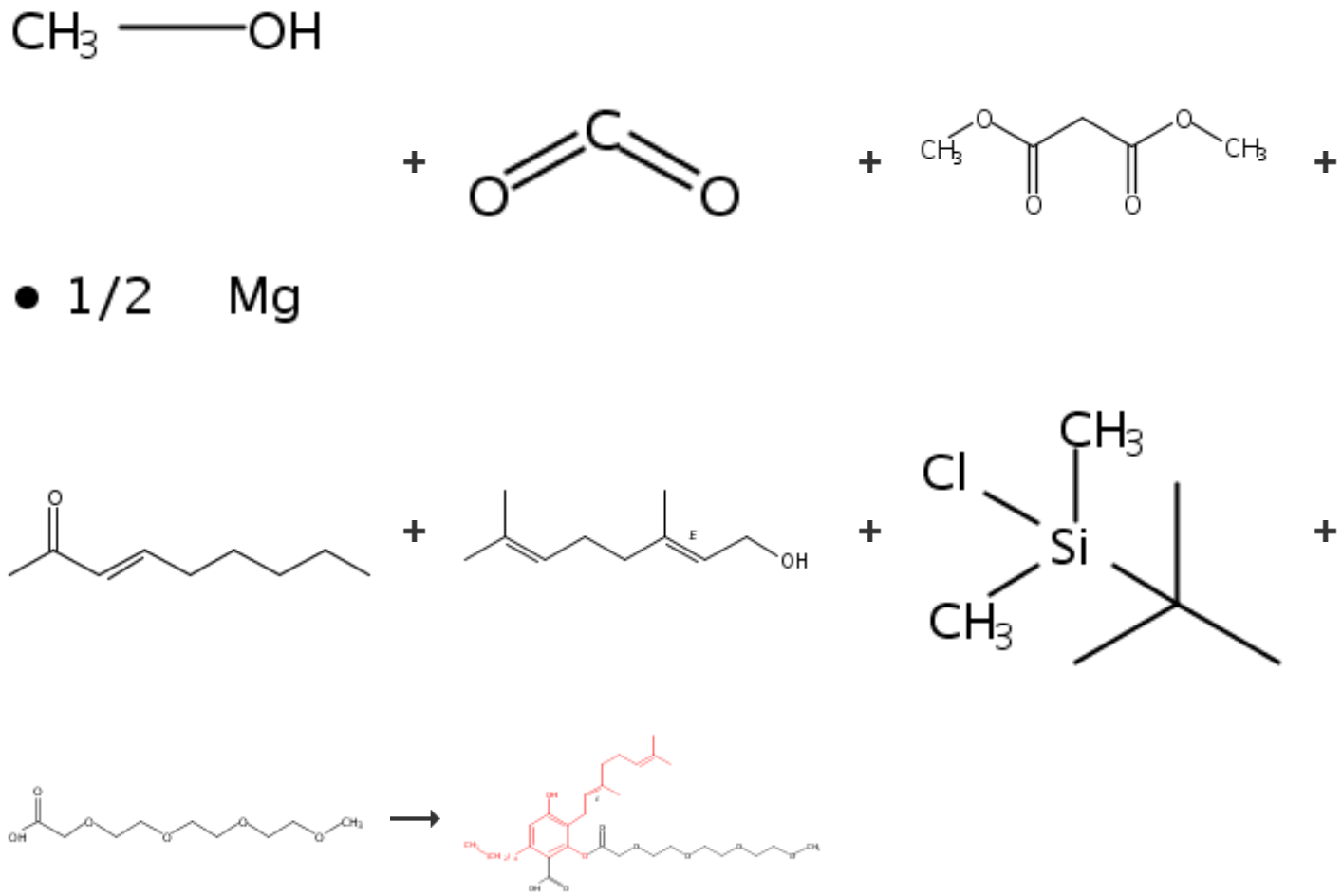
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

208. 7 Steps (Converging)



Overview

Steps/Stages

Notes

1.1 S:DMF, 140°C

1.1 R:NaOMe, S:MeOH, rt; 3 h, reflux; reflux → rt

1.2 R:H_2O, rt

2.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

3.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

4.1 S:DMF, 1 h, 120°C

4.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

5.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

5.2 R:NaCl, S:H_2O

6.1 R:DCC, C:4-DMAP, S:CH_2Cl_2, rt; overnight, rt

6.2 R:Bu_4N^+ •F^-, S:CH_2Cl_2, -15°C

exothermic reaction, in the dark, conversion = 40%,alternative preparation shown, alternative preparation shown, regioselective, alternative preparation shown,other reagent carbonyldiimidazole may be used in stage 1 and triethylamine trihydrofluoride in stage 2, Reactants: 7, Reagents: 9, Catalysts: 1, Solvents: 5, Steps: 7, Stages: 11, Most stages in any one step: 2

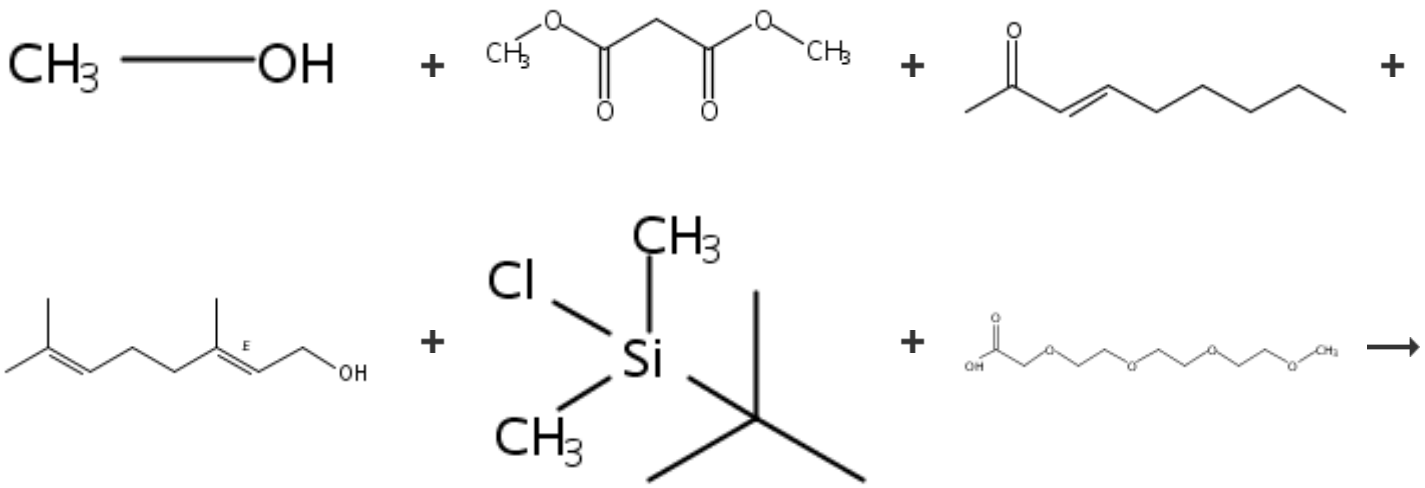
References

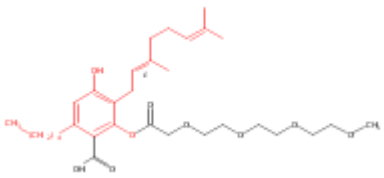
Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

209. 7 Steps (Converging)





Overview

Steps/Stages

Notes

1.1 R:Mg, S:MeOH, rt

1.1 R:NaOMe, S:MeOH, rt; 3 h, reflux; reflux → rt

1.2 R:H_2O, rt

2.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

3.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

4.1 S:H_2O, cooled; 50°C; 3 h, 50°C; 50°C → rt

4.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, rt, pH 2

5.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

5.2 R:NaCl, S:H_2O

6.1 R:DCC, C:4-DMAP, S:CH_2Cl_2, rt; overnight, rt

6.2 R:Bu_4N^+ •F^-, S:CH_2Cl_2, -15°C

in the dark, conversion = 85%,alternative preparation shown,reaction in a sealed pressure vessel, alternative preparation shown, regioselective, alternative preparation shown,other reagent carbonyldiimidazole may be used in stage 1 and triethylamine trihydrofluoride in stage 2, Reactants: 6, Reagents: 10, Catalysts: 1, Solvents: 5, Steps: 7, Stages: 11, Most stages in any one step: 2

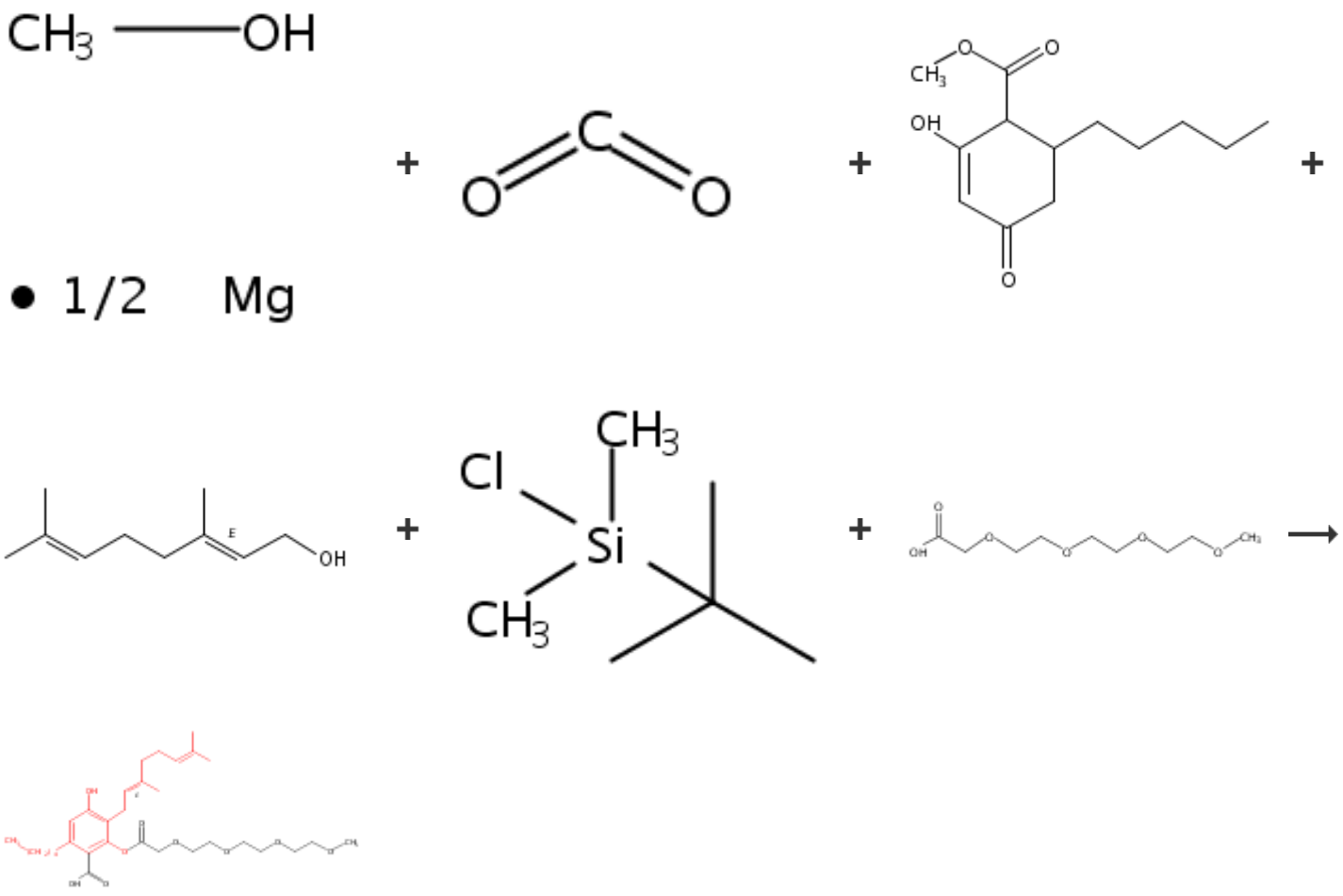
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

210. 6 Steps (Converging)



Overview

Steps/Stages

Notes

1.1 S:DMF, 140°C

1.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

2.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

3.1 S:DMF, 1 h, 120°C

3.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

4.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

4.2 R:NaCl, S:H_2O

5.1 R:DCC, C:4-DMAP, S:CH_2Cl_2, rt; overnight, rt

5.2 R:$Bu_4N^+ \bullet F^-$, S:CH_2Cl_2, -15°C

exothermic reaction, in the dark, conversion = 40%,alternative preparation shown, alternative preparation shown, regioselective, alternative preparation shown,other reagent carbonyldiimidazole may be used in stage 1 and triethylamine trihydrofluoride in stage 2, Reactants: 6, Reagents: 7, Catalysts: 1, Solvents: 5, Steps: 6, Stages: 9, Most stages in any one step: 2

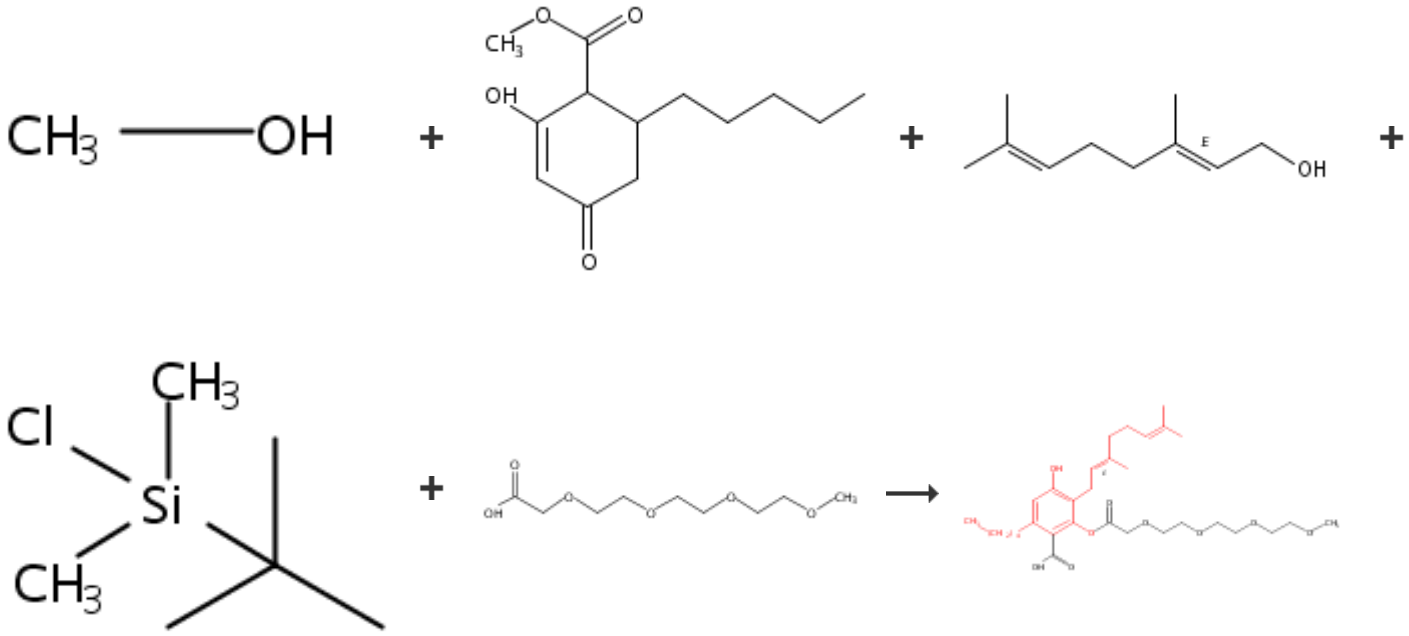
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

211. 6 Steps (Converging)



Overview

Steps/Stages

Notes

1.1 R:Mg, S:MeOH, rt

1.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

2.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

3.1 S:H_2O, cooled; 50°C; 3 h, 50°C; 50°C → rt

3.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, rt, pH 2

4.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

4.2 R:NaCl, S:H_2O

5.1 R:DCC, C:4-DMAP, S:CH_2Cl_2, rt; overnight, rt

5.2 R:Bu_4N^+ •F^-, S:CH_2Cl_2, -15°C

in the dark, conversion = 85%,alternative preparation shown,reaction in a sealed pressure vessel, alternative preparation shown, regioselective, alternative preparation shown,other reagent carbonyldiimidazole may be used in stage 1 and triethylamine trihydrofluoride in stage 2, Reactants: 5, Reagents: 8, Catalysts: 1, Solvents: 5, Steps: 6, Stages: 9, Most stages in any one step: 2

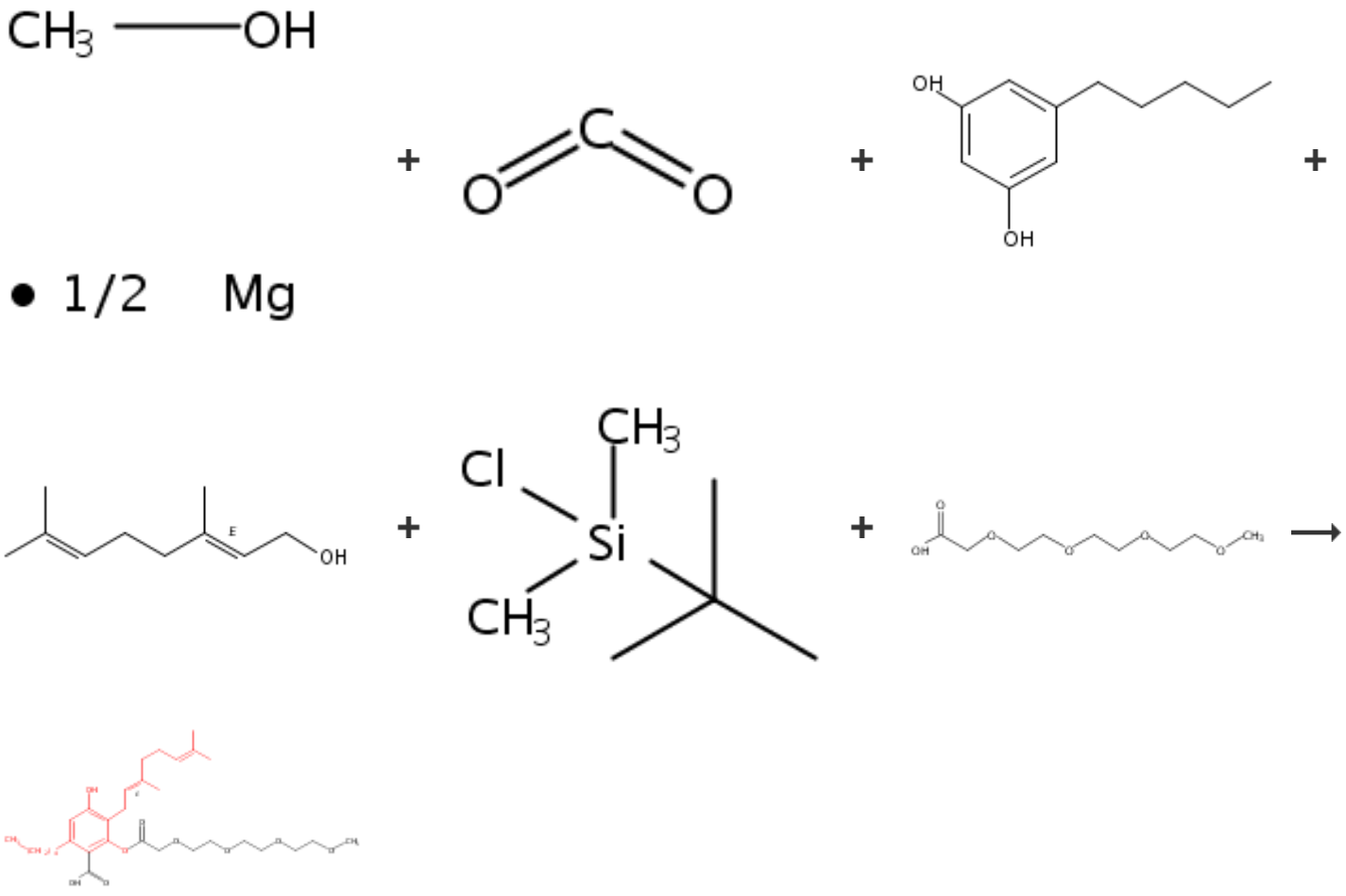
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

212. 5 Steps (Converging)



Overview

Steps/Stages

Notes

1.1 S:DMF, 140°C

1.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
2.1 S:DMF, 1 h, 120°C

2.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

3.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

3.2 R:NaCl, S:H_2O

4.1 R:DCC, C:4-DMAP, S:CH_2Cl_2, rt; overnight, rt

4.2 R:$Bu_4N^+ \bullet F^-$, S:CH_2Cl_2, -15°C

exothermic reaction, in the dark, conversion = 40%,alternative preparation shown, alternative preparation shown, regioselective, alternative preparation shown,other reagent carbonyldiimidazole may be used in stage 1 and triethylamine trihydrofluoride in stage 2, Reactants: 6, Reagents: 6, Catalysts: 1, Solvents: 5, Steps: 5, Stages: 8, Most stages in any one step: 2

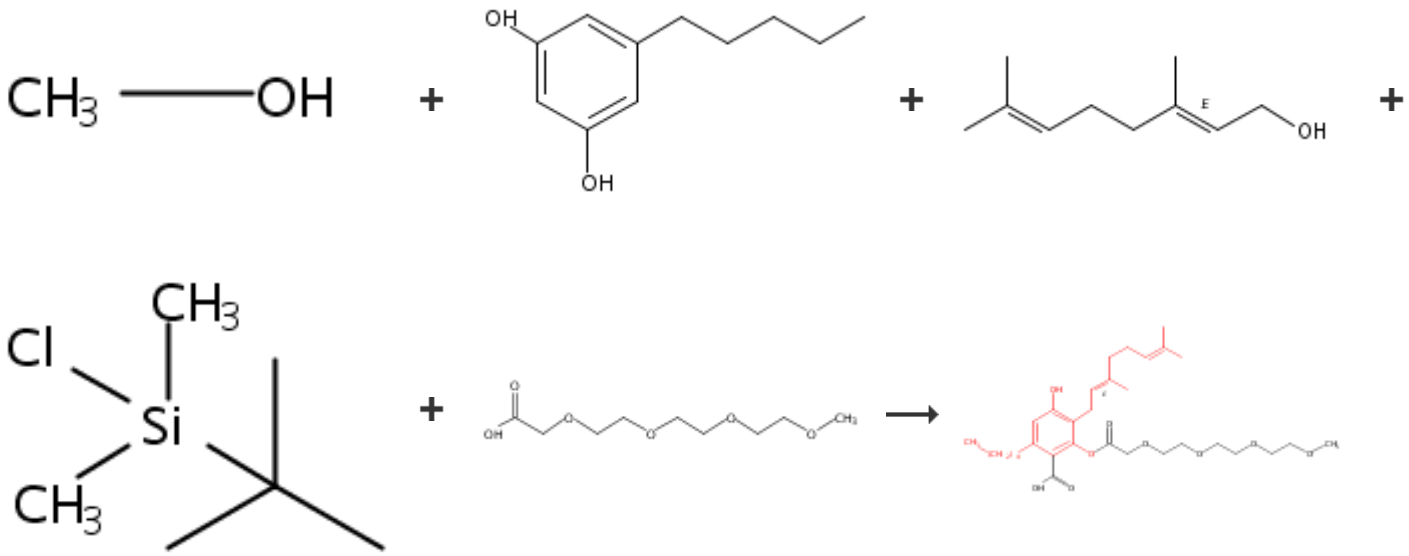
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

213. 5 Steps (Converging)



Overview

Steps/Stages

1.1 R:Mg, S:MeOH, rt

1.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
2.1 S:H_2O, cooled; 50°C; 3 h, 50°C; 50°C → rt

2.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, rt, pH 2

3.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

3.2 R:NaCl, S:H_2O

4.1 R:DCC, C:4-DMAP, S:CH_2Cl_2, rt; overnight, rt

4.2 R:$Bu_4N^+ \bullet F^-$, S:CH_2Cl_2, -15°C

Notes

in the dark, conversion = 85%,alternative preparation shown,reaction in a sealed pressure vessel, alternative preparation shown, regioselective, alternative preparation shown,other reagent carbonyldiimidazole may be used in stage 1 and triethylamine trihydrofluoride in stage 2, Reactants: 5, Reagents: 7, Catalysts: 1, Solvents: 4, Steps: 5, Stages: 8, Most stages in any one step: 2

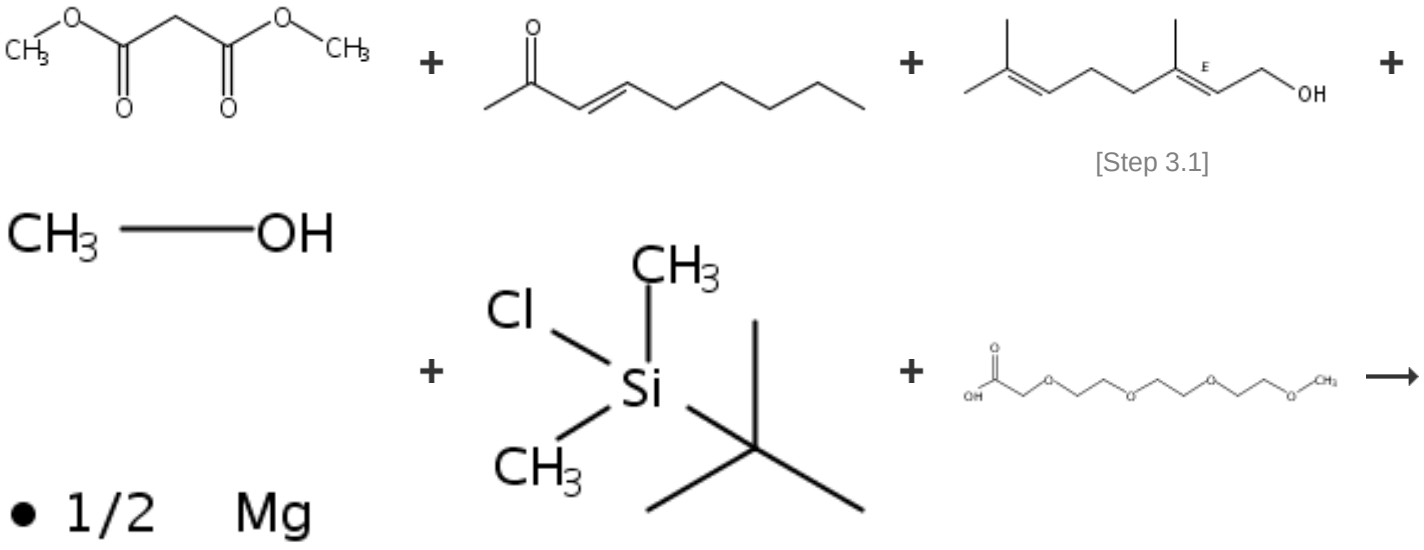
References

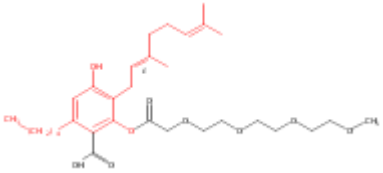
Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

214. 6 Steps





Overview

Steps/Stages

1.1 R:NaOMe, S:MeOH, rt; 3 h, reflux; reflux → rt

1.2 R:H_2O, rt

2.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

3.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

4.1 S:H_2O, cooled; 50°C; 3 h, 50°C; 50°C → rt

4.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, rt, pH 2

5.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

5.2 R:NaCl, S:H_2O

6.1 R:DCC, C:4-DMAP, S:CH_2Cl_2, rt; overnight, rt

6.2 R:$Bu_4N^+ \cdot F^-$, S:CH_2Cl_2, -15°C

Notes

3) in the dark, 4) conversion = 85%,alternative preparation shown,reaction in a sealed pressure vessel, 5) alternative preparation shown, regioselective, 6) alternative preparation shown,other reagent carbonyldiimidazole may be used in stage 1 and triethylamine trihydrofluoride in stage 2, Reactants: 6, Reagents: 9, Catalysts: 1, Solvents: 5, Steps: 6, Stages: 10, Most stages in any one step: 2

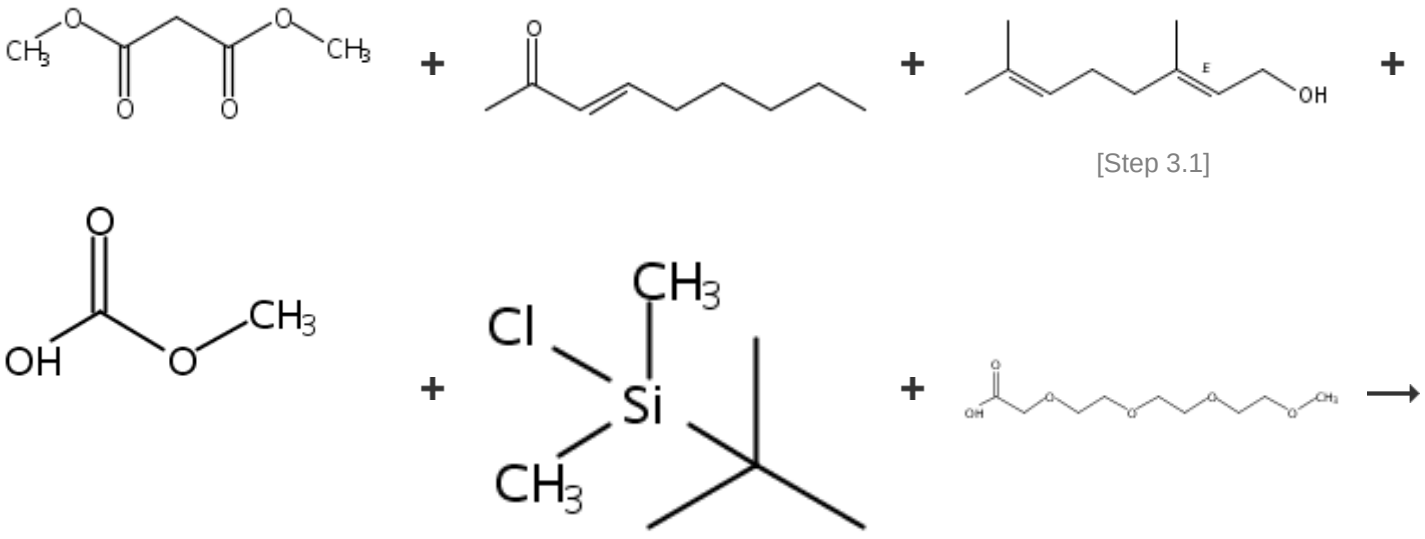
References

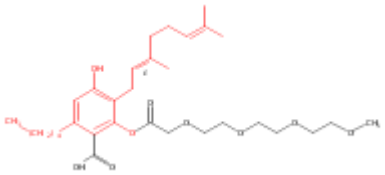
Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

215. 6 Steps





Overview

Steps/Stages

1.1 R:NaOMe, S:MeOH, rt; 3 h, reflux; reflux → rt

1.2 R:H_2O, rt

2.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

3.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

4.1 S:DMF, 1 h, 120°C

4.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

5.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

5.2 R:NaCl, S:H_2O

6.1 R:DCC, C:4-DMAP, S:CH_2Cl_2, rt; overnight, rt

6.2 R:$Bu_4N^+ \cdot F^-$, S:CH_2Cl_2, -15°C

Notes

3) in the dark, 4) conversion = 40%,alternative preparation shown, 5) alternative preparation shown, regioselective, 6) alternative preparation shown,other reagent carbonyldiimidazole may be used in stage 1 and triethylamine trihydrofluoride in stage 2, Reactants: 6, Reagents: 9, Catalysts: 1, Solvents: 5, Steps: 6, Stages: 10, Most stages in any one step: 2

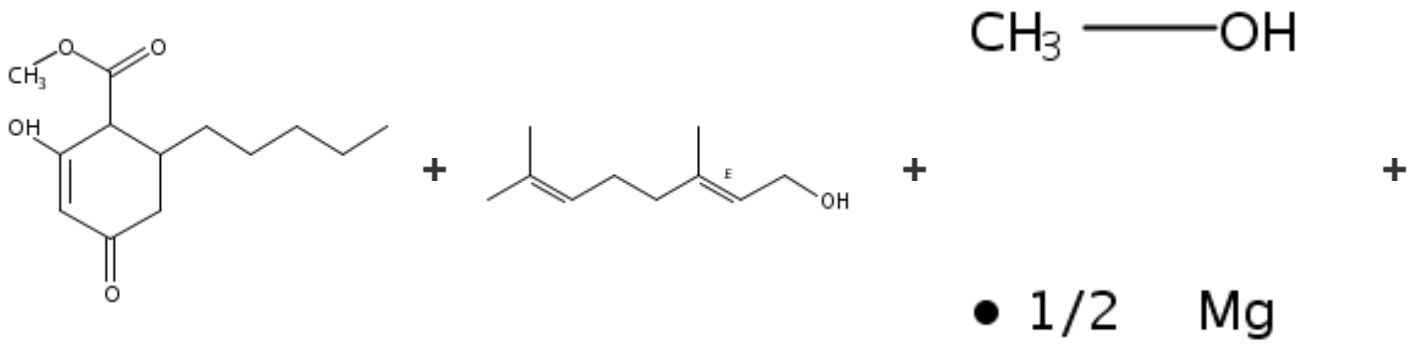
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

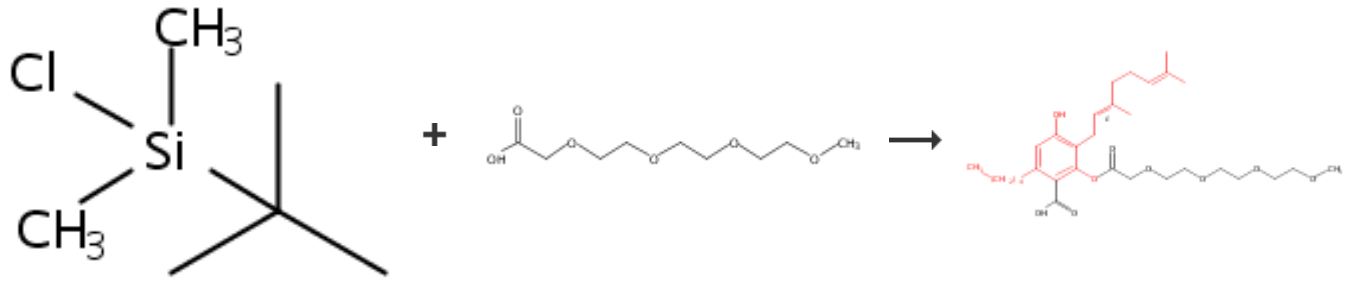
From PCT Int. Appl., 2017181118, 19 Oct 2017

216. 5 Steps



[Step 2.1]

[Step 3.1]



[Step 4.1]

[Step 5.1]

Overview

Steps/Stages

1.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

2.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

3.1 S:H_2O, cooled; 50°C; 3 h, 50°C; 50°C → rt

3.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, rt, pH 2

4.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

4.2 R:NaCl, S:H_2O

5.1 R:DCC, C:4-DMAP, S:CH_2Cl_2, rt; overnight, rt

5.2 R:Bu_4N^+ •F^-, S:CH_2Cl_2, -15°C

Notes

2) in the dark, 3) conversion = 85%,alternative preparation shown,reaction in a sealed pressure vessel, 4) alternative preparation shown, regioselective, 5) alternative preparation shown,other reagent carbonyldiimidazole may be used in stage 1 and triethylamine trihydrofluoride in stage 2, Reactants: 5, Reagents: 7, Catalysts: 1, Solvents: 5, Steps: 5, Stages: 8, Most stages in any one step: 2

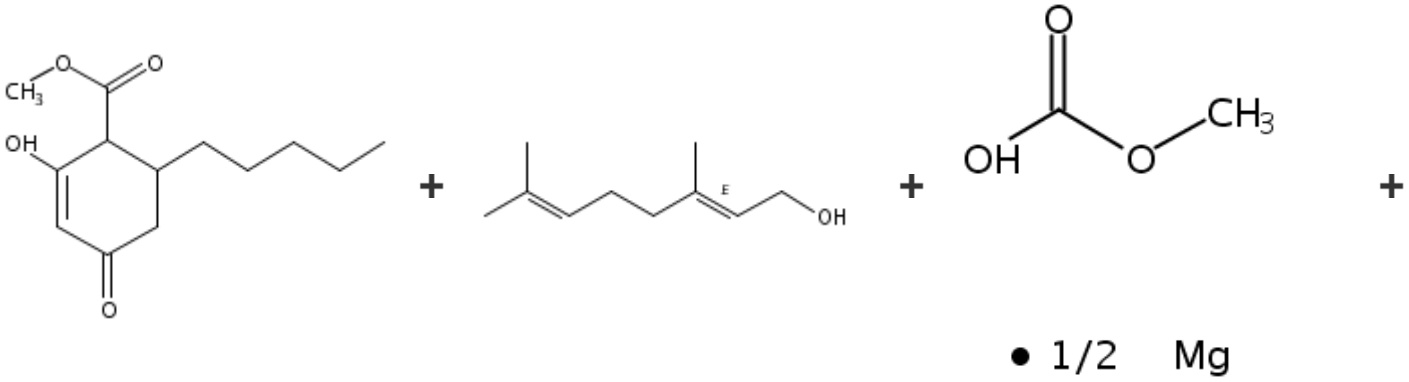
References

Biosynthesis of cannabinoid prodrugs

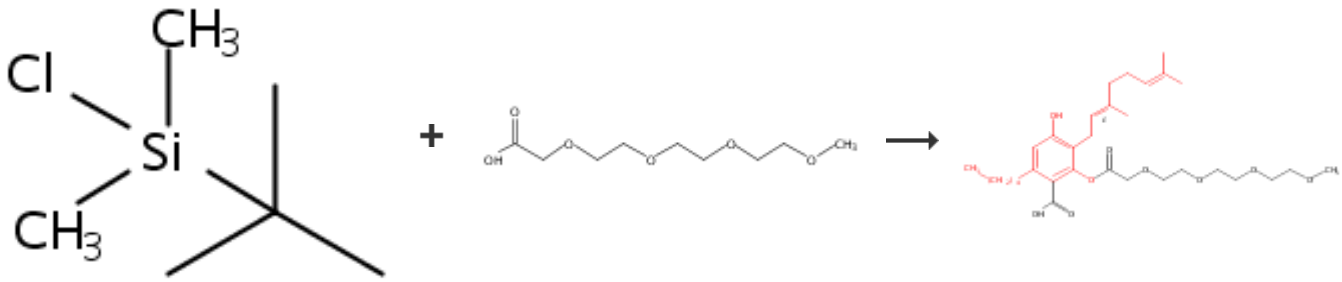
By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

217. 5 Steps



[Step 2.1] [Step 3.1]



[Step 4.1] [Step 5.1]

Overview

Steps/Stages

1.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

2.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

3.1 S:DMF, 1 h, 120°C

3.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

4.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

4.2 R:NaCl, S:H_2O

5.1 R:DCC, C:4-DMAP, S:CH_2Cl_2, rt; overnight, rt

5.2 R:Bu_4N^+ •F^-, S:CH_2Cl_2, -15°C

Notes

2) in the dark, 3) conversion = 40%,alternative preparation shown, 4) alternative preparation shown, regioselective, 5) alternative preparation shown,other reagent carbonyldiimidazole may be used in stage 1 and triethylamine trihydrofluoride in stage 2, Reactants: 5, Reagents: 7, Catalysts: 1, Solvents: 5, Steps: 5, Stages: 8, Most stages in any one step: 2

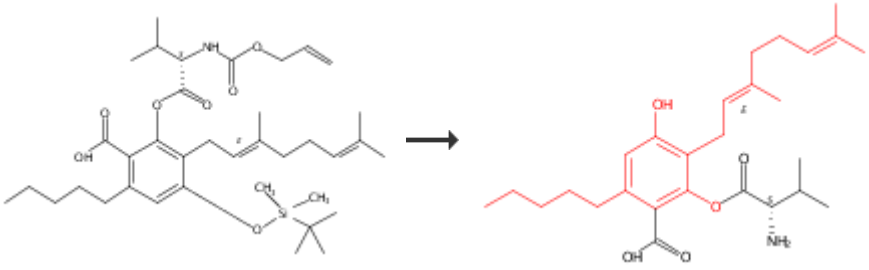
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

218. 2 Steps



Overview

Steps/Stages

1.1 R:$PhSiH_3$, C:$Pd(PPh_3)_4$, S:MeOH, S:CH_2Cl_2, rt

2.1 R:$Bu_4N^+ \bullet F^-$, S:CH_2Cl_2, -15°C

Notes

Reactants: 1, Reagents: 2, Catalysts: 1, Solvents: 2, Steps: 2, Stages: 2, Most stages in any one step: 1

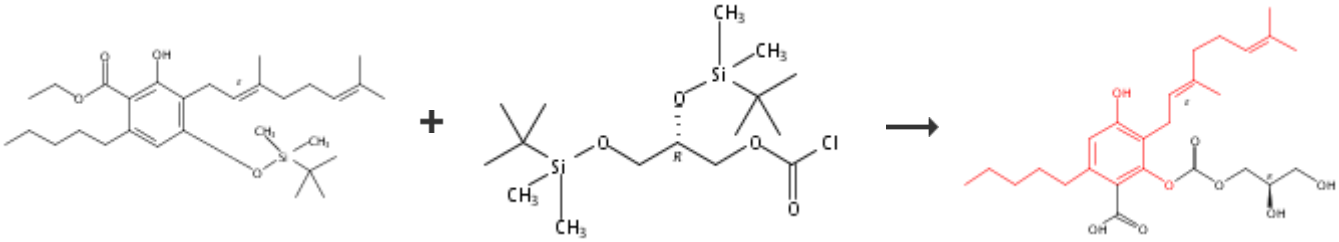
References

Methods for the manufacture of cannabinoid prodrugs, pharmaceutical formulations and their use

By Peet, Richard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017216362, 21 Dec 2017

219. 2 Steps



Overview

Steps/Stages

1.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

2.1 R:$Et_3N \bullet 3HF$, S:CH_2Cl_2, -15°C; 65 h, 5°C

2.2 R:$NaHCO_3$, S:H_2O, S:AcOEt, 0°C

Notes

1) alternative preparation shown, Reactants: 2, Reagents: 3, Solvents: 3, Steps: 2, Stages: 3, Most stages in any one step: 2

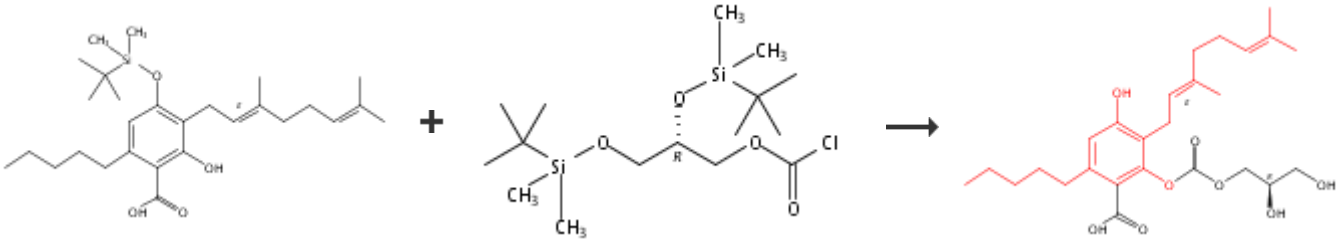
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

220. 2 Steps



Overview

Steps/Stages

1.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

2.1 R:Et_3N •3HF, S:CH_2Cl_2, -15°C; 65 h, 5°C

2.2 R:$NaHCO_3$, S:H_2O, S:AcOEt, 0°C

Notes

1) alternative preparation shown, Reactants: 2, Reagents: 3, Solvents: 3, Steps: 2, Stages: 3, Most stages in any one step: 2

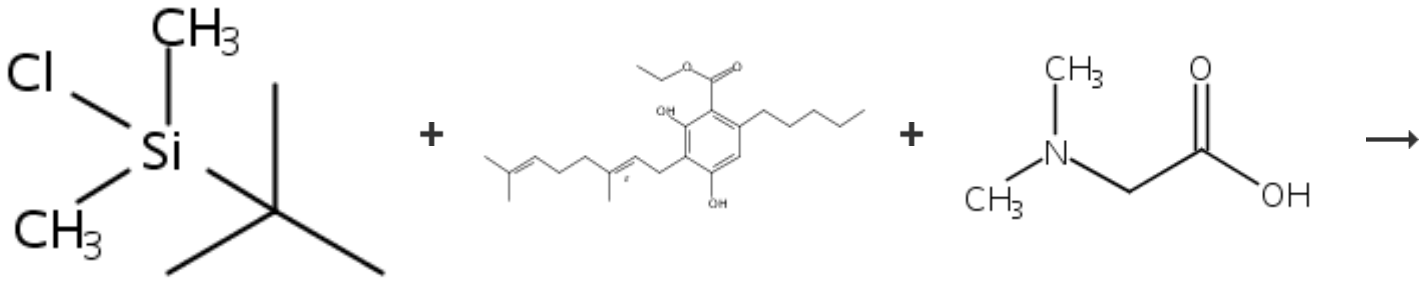
References

Biosynthesis of cannabinoid prodrugs

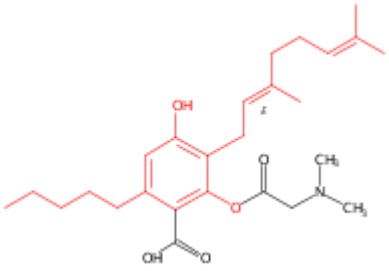
By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

221. 2 Steps



[Step 2.1]



Overview

Steps/Stages

1.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

1.2 R:NaCl, S:H_2O

2.1 R:DCC, C:4-DMAP, S:CH_2Cl_2, rt; overnight, rt

2.2 R:Bu_4N^+ •F^-, S:CH_2Cl_2, -15°C

Notes

1) regioselective, 2) alternative preparation shown,other reagent triethylamine trihydrofluoride may be used in stage 2, Reactants: 3, Reagents: 4, Catalysts: 1, Solvents: 2, Steps: 2, Stages: 4, Most stages in any one step: 2

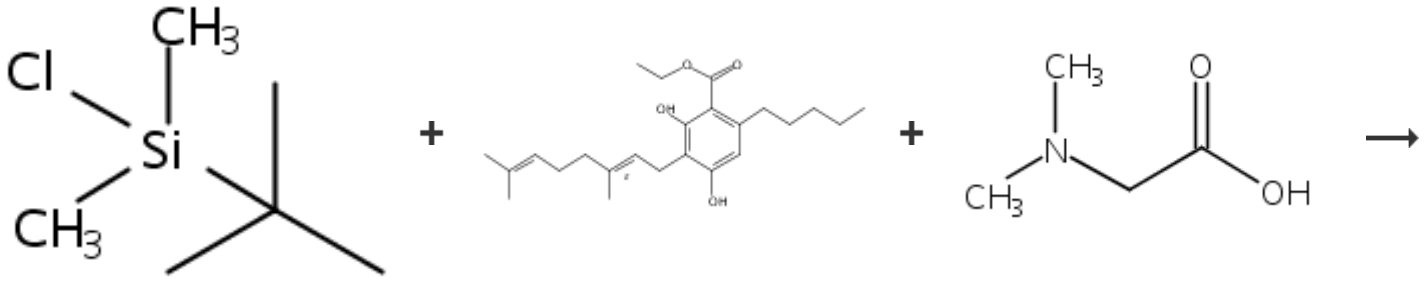
References

Biosynthesis of cannabinoid prodrugs

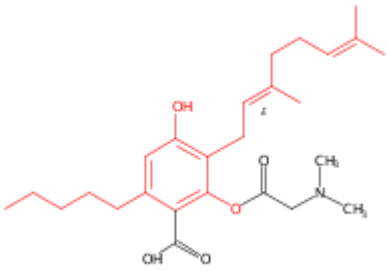
By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

222. 2 Steps



[Step 2.1]



Overview

Steps/Stages

1.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

1.2 R:NaCl, S:H_2O

1.3

2.1 R:DCC, C:4-DMAP, S:CH_2Cl_2, rt; overnight, rt

2.2 R:Bu_4N^+ •F^-, S:CH_2Cl_2, -15°C

Notes

1) unspecified reagent used for acidic hydrolysis in stage 3,alternative preparation shown, regioselective, 2) alternative preparation shown,other reagent triethylamine trihydrofluoride may be used in stage 2, Reactants: 3, Reagents: 4, Catalysts: 1, Solvents: 2, Steps: 2, Stages: 5, Most stages in any one step: 3

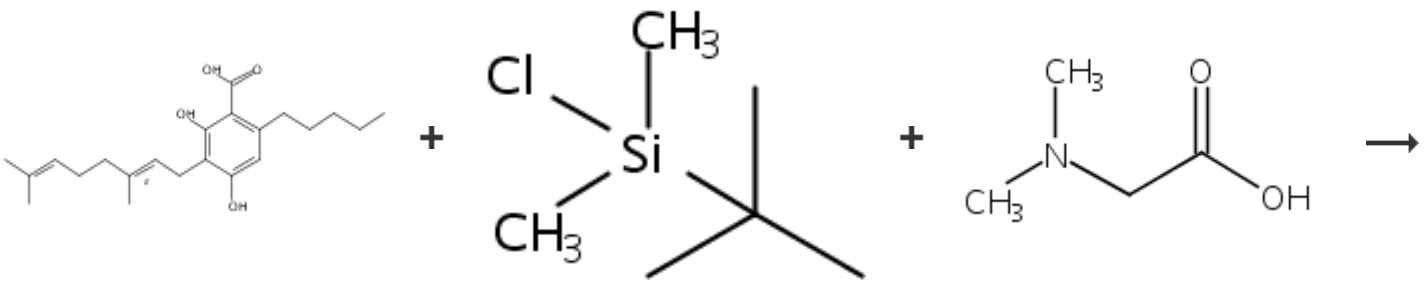
References

Biosynthesis of cannabinoid prodrugs

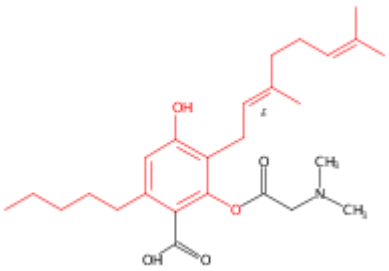
By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

223. 2 Steps



[Step 2.1]



Overview

Steps/Stages

1.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

1.2 R:NaCl, S:H_2O

2.1 R:DCC, C:4-DMAP, S:CH_2Cl_2, rt; overnight, rt

2.2 R:Bu_4N^+ •F^-, S:CH_2Cl_2, -15°C

Notes

1) alternative preparation shown, regioselective, 2) alternative preparation shown,other reagent triethylamine trihydrofluoride may be used in stage 2, Reactants: 3, Reagents: 4, Catalysts: 1, Solvents: 2, Steps: 2, Stages: 4, Most stages in any one step: 2

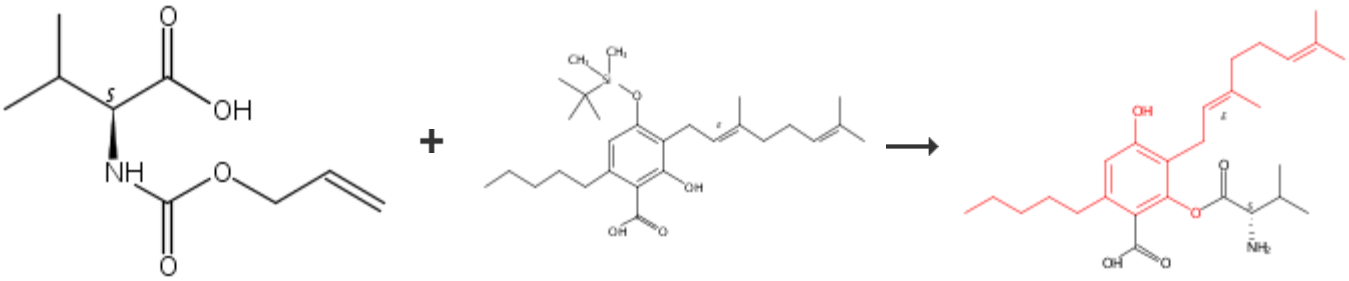
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

224. 3 Steps



Overview

Steps/Stages

1.1 R:DCC, R:4-DMAP, S:CH_2Cl_2, rt

1.2 S:CH_2Cl_2, rt; overnight, rt

2.1 R:$PhSiH_3$, C:$Pd(PPh_3)_4$, S:MeOH, S:CH_2Cl_2, rt

3.1 R:Bu_4N^+ •F^-, S:CH_2Cl_2, -15°C

Notes

Reactants: 2, Reagents: 4, Catalysts: 1, Solvents: 2, Steps: 3, Stages: 4, Most stages in any one step: 2

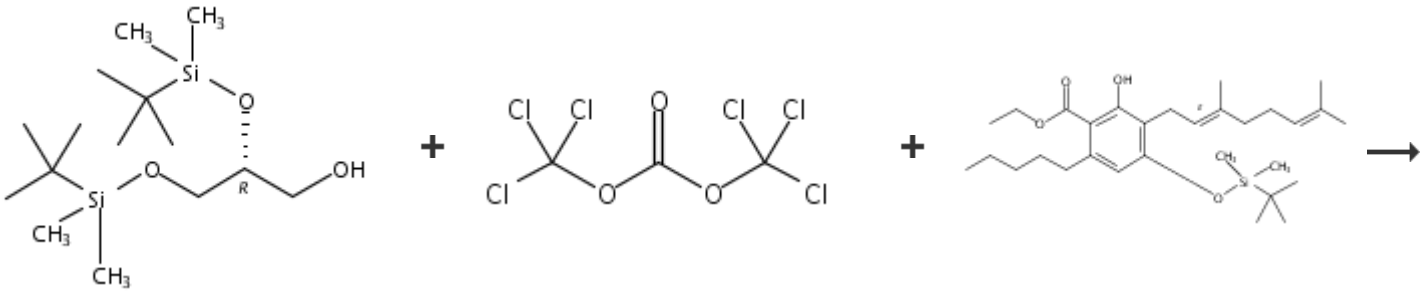
References

Methods for the manufacture of cannabinoid prodrugs, pharmaceutical formulations and their use

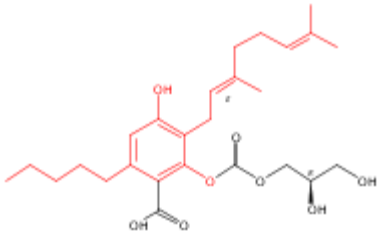
By Peet, Richard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017216362, 21 Dec 2017

225. 3 Steps



[Step 2.1]



Overview

Steps/Stages

1.1 R:Et_3N, S:CH_2Cl_2, 3-5 h, 0°C

2.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

3.1 R:Et_3N •3HF, S:CH_2Cl_2, -15°C; 65 h, 5°C

3.2 R:$NaHCO_3$, S:H_2O, S:AcOEt, 0°C

Notes

2) alternative preparation shown, Reactants: 3, Reagents: 3, Solvents: 3, Steps: 3, Stages: 4, Most stages in any one step: 2

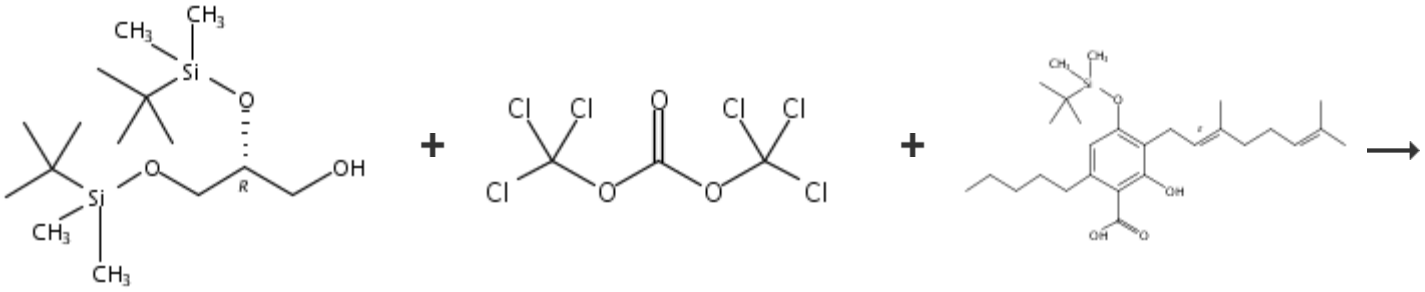
References

Biosynthesis of cannabinoid prodrugs

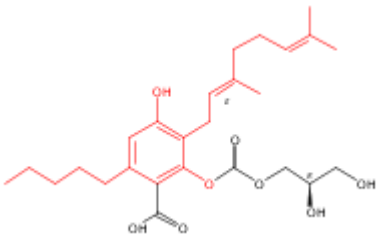
By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

226. 3 Steps



[Step 2.1]



Overview

Steps/Stages

1.1 R:Et_3N, S:CH_2Cl_2, 3-5 h, 0°C

2.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

3.1 R:Et_3N •3HF, S:CH_2Cl_2, -15°C; 65 h, 5°C

3.2 R:$NaHCO_3$, S:H_2O, S:AcOEt, 0°C

Notes

2) alternative preparation shown, Reactants: 3, Reagents: 3, Solvents: 3, Steps: 3, Stages: 4, Most stages in any one step: 2

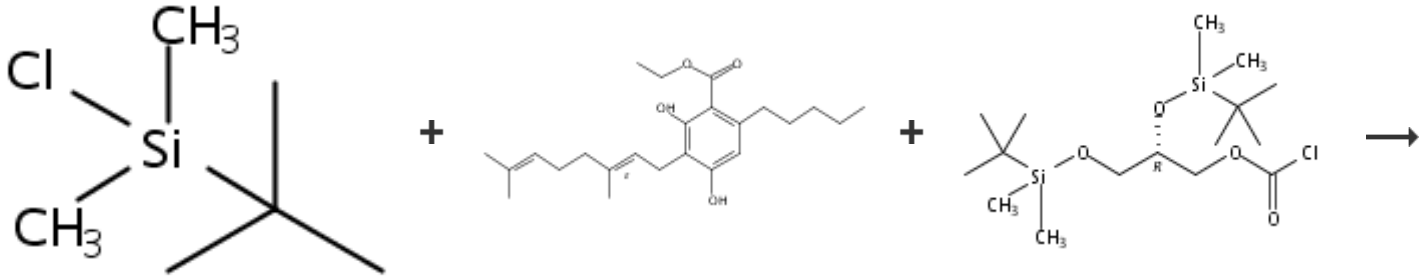
References

Biosynthesis of cannabinoid prodrugs

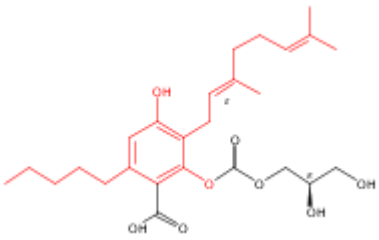
By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

227. 3 Steps



[Step 2.1]



Overview

Steps/Stages

1.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

1.2 R:NaCl, S:H_2O

2.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

3.1 R:Et_3N •3HF, S:CH_2Cl_2, -15°C; 65 h, 5°C

3.2 R:$NaHCO_3$, S:H_2O, S:AcOEt, 0°C

Notes

1) regioselective, 2) alternative preparation shown, Reactants: 3, Reagents: 5, Solvents: 3, Steps: 3, Stages: 5, Most stages in any one step: 2

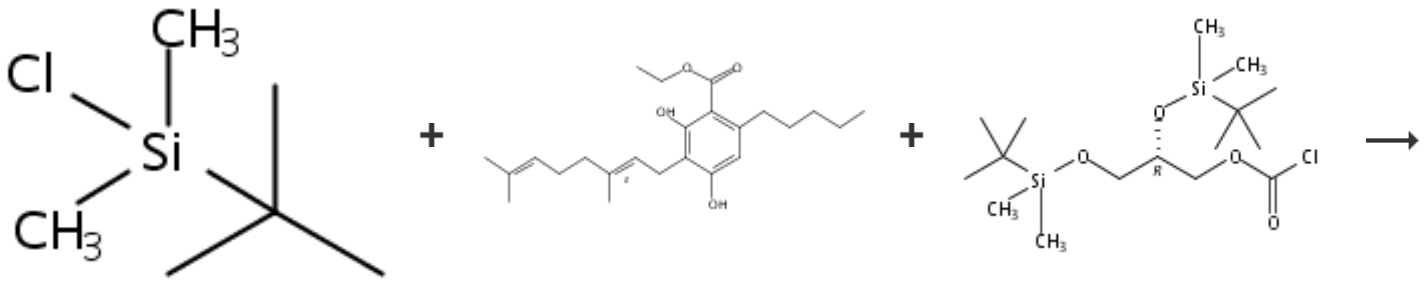
References

Biosynthesis of cannabinoid prodrugs

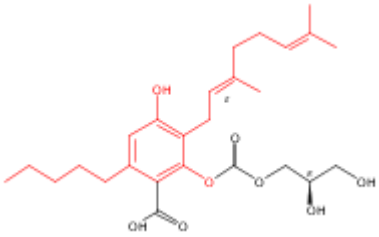
By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

228. 3 Steps



[Step 2.1]



Overview

Steps/Stages

1.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

1.2 R:NaCl, S:H_2O

1.3

2.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

3.1 R:Et_3N •3HF, S:CH_2Cl_2, -15°C; 65 h, 5°C

3.2 R:$NaHCO_3$, S:H_2O, S:AcOEt, 0°C

Notes

1) unspecified reagent used for acidic hydrolysis in stage 3,alternative preparation shown, regioselective, 2) alternative preparation shown, Reactants: 3, Reagents: 5, Solvents: 3, Steps: 3, Stages: 6, Most stages in any one step: 3

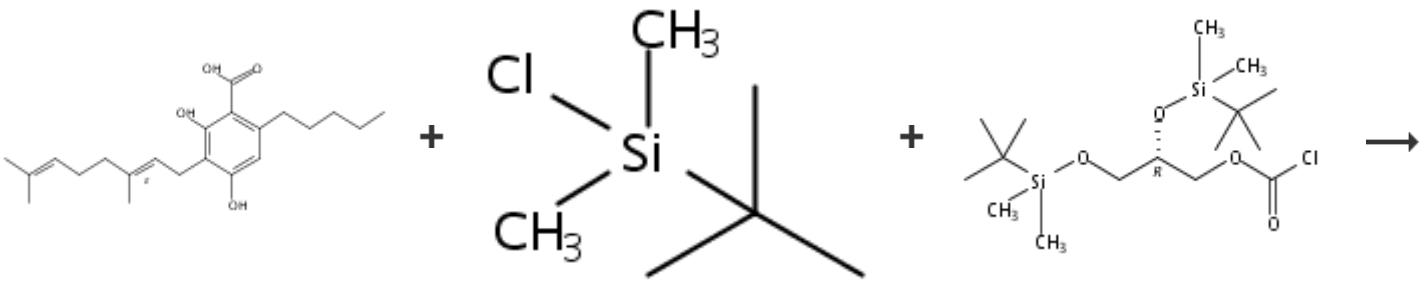
References

Biosynthesis of cannabinoid prodrugs

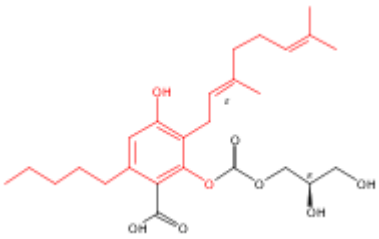
By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

229. 3 Steps



[Step 2.1]



Overview

Steps/Stages

1.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

1.2 R:NaCl, S:H_2O

2.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

3.1 R:Et_3N •3HF, S:CH_2Cl_2, -15°C; 65 h, 5°C

3.2 R:$NaHCO_3$, S:H_2O, S:AcOEt, 0°C

Notes

1) alternative preparation shown, regioselective, 2) alternative preparation shown, Reactants: 3, Reagents: 5, Solvents: 3, Steps: 3, Stages: 5, Most stages in any one step: 2

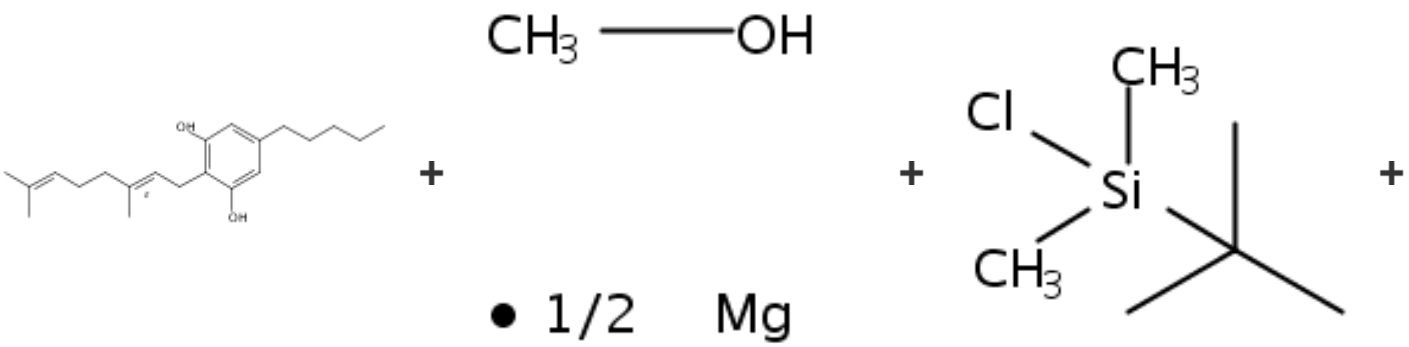
References

Biosynthesis of cannabinoid prodrugs

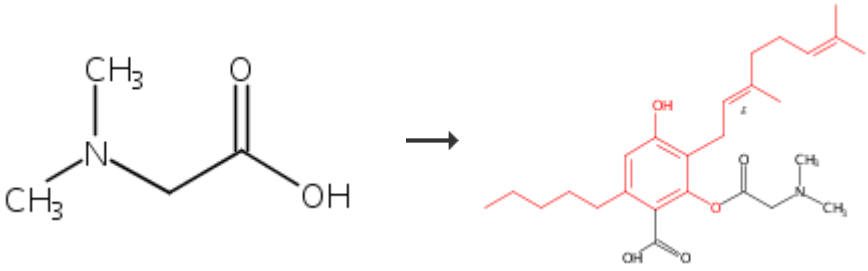
By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

230. 3 Steps



[Step 2.1]



[Step 3.1]

Overview

Steps/Stages

Notes

1.1 S:H_2O, cooled; 50°C; 3 h, 50°C; 50°C → rt

1.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, rt, pH 2

2.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

2.2 R:NaCl, S:H_2O

3.1 R:DCC, C:4-DMAP, S:CH_2Cl_2, rt; overnight, rt

3.2 R:Bu_4N^+ •F^-, S:CH_2Cl_2, -15°C

1) conversion = 85%,alternative preparation shown,reaction in a sealed pressure vessel, 2) alternative preparation shown, regioselective, 3) alternative preparation shown,other reagent triethylamine trihydrofluoride may be used in stage 2, Reactants: 4, Reagents: 5, Catalysts: 1, Solvents: 4, Steps: 3, Stages: 6, Most stages in any one step: 2

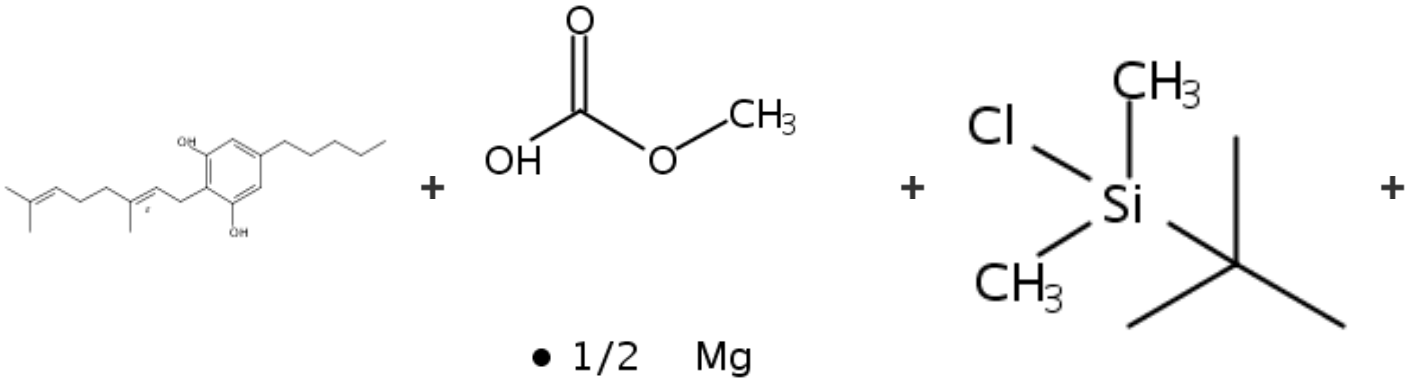
References

Biosynthesis of cannabinoid prodrugs

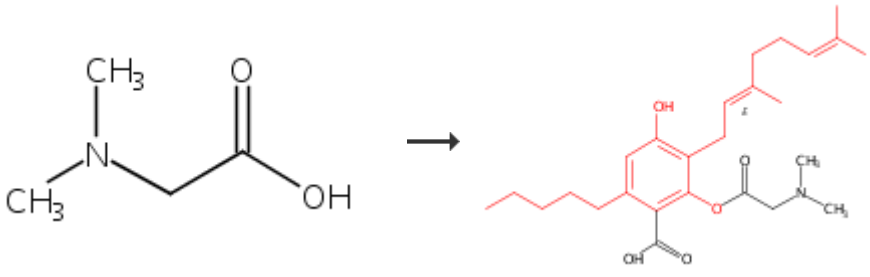
By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

231. 3 Steps



[Step 2.1]



[Step 3.1]

Overview

Steps/Stages

Notes

1.1 S:DMF, 1 h, 120°C

1.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

2.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

2.2 R:NaCl, S:H_2O

3.1 R:DCC, C:4-DMAP, S:CH_2Cl_2, rt; overnight, rt

3.2 R:Bu_4N^+ •F^-, S:CH_2Cl_2, -15°C

1) conversion = 40%,alternative preparation shown, 2) alternative preparation shown, regioselective, 3) alternative preparation shown,other reagent triethylamine trihydrofluoride may be used in stage 2, Reactants: 4, Reagents: 5, Catalysts: 1, Solvents: 5, Steps: 3, Stages: 6, Most stages in any one step: 2

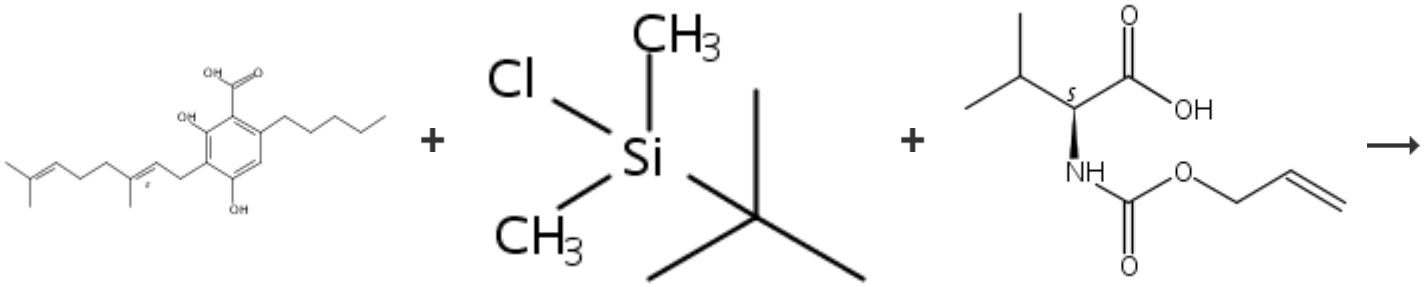
References

Biosynthesis of cannabinoid prodrugs

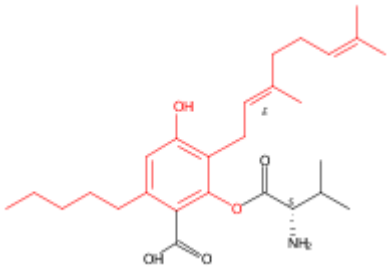
By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

232. 4 Steps



[Step 2.1]



Overview

Steps/Stages

1.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

1.2 R:NaCl, S:H_2O

2.1 R:DCC, R:4-DMAP, S:CH_2Cl_2, rt

2.2 S:CH_2Cl_2, rt; overnight, rt

3.1 R:$PhSiH_3$, C:$Pd(PPh_3)_4$, S:MeOH, S:CH_2Cl_2, rt

4.1 R:Bu_4N^+ •F^-, S:CH_2Cl_2, -15°C

Notes

1) regioselective, Reactants: 3, Reagents: 6, Catalysts: 1, Solvents: 3, Steps: 4, Stages: 6, Most stages in any one step: 2

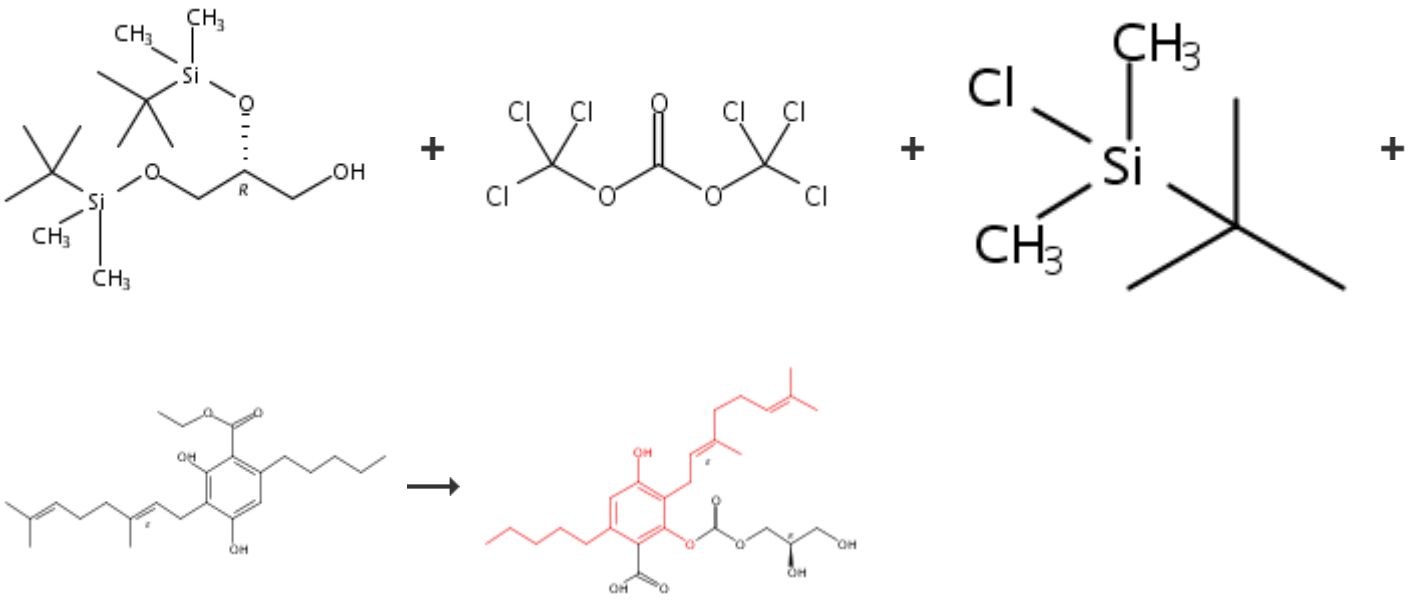
References

Methods for the manufacture of cannabinoid prodrugs, pharmaceutical formulations and their use

By Peet, Richard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017216362, 21 Dec 2017

233. 4 Steps (Converging)



Overview

Steps/Stages

1.1 R:Et_3N, S:CH_2Cl_2, 3-5 h, 0°C

1.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

1.2 R:NaCl, S:H_2O

2.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

3.1 R:Et_3N •3HF, S:CH_2Cl_2, -15°C; 65 h, 5°C

3.2 R:$NaHCO_3$, S:H_2O, S:AcOEt, 0°C

Notes

regioselective, alternative preparation shown, Reactants: 4, Reagents: 5, Solvents: 3, Steps: 4, Stages: 6, Most stages in any one step: 2

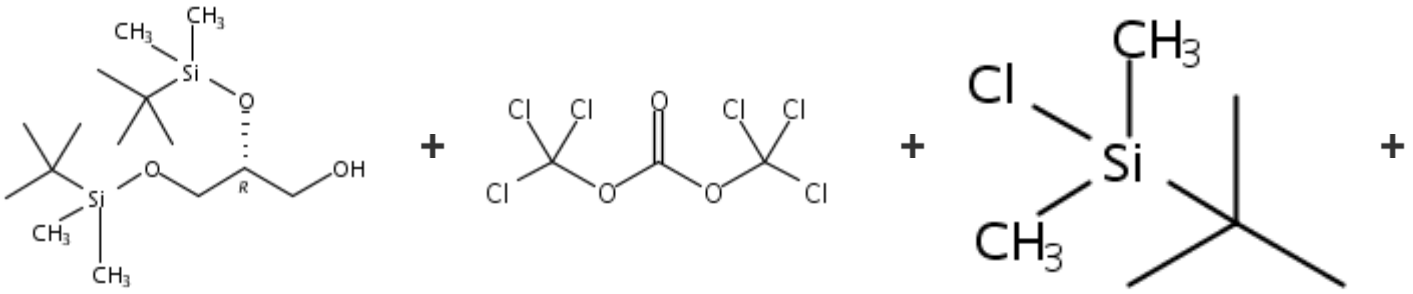
References

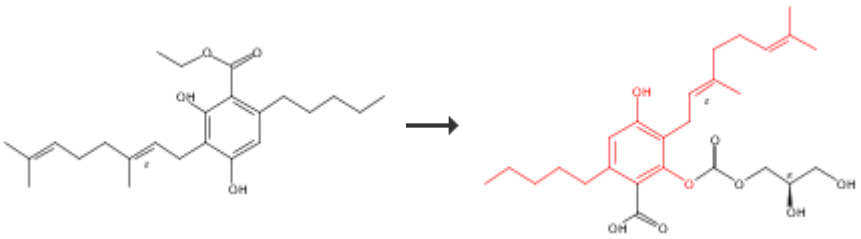
Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

234. 4 Steps (Converging)





Overview

Steps/Stages

1.1 R:Et_3N, S:CH_2Cl_2, 3-5 h, 0°C

1.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

1.2 R:NaCl, S:H_2O

1.3

2.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

3.1 R:Et_3N •3HF, S:CH_2Cl_2, -15°C; 65 h, 5°C

3.2 R:$NaHCO_3$, S:H_2O, S:AcOEt, 0°C

Notes

unspecified reagent used for acidic hydrolysis in stage 3,alternative preparation shown, regioselective, alternative preparation shown, Reactants: 4, Reagents: 5, Solvents: 3, Steps: 4, Stages: 7, Most stages in any one step: 3

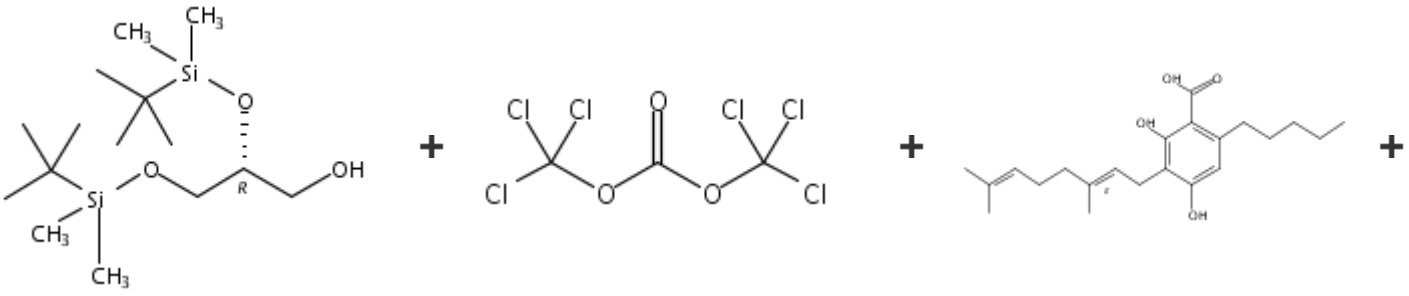
References

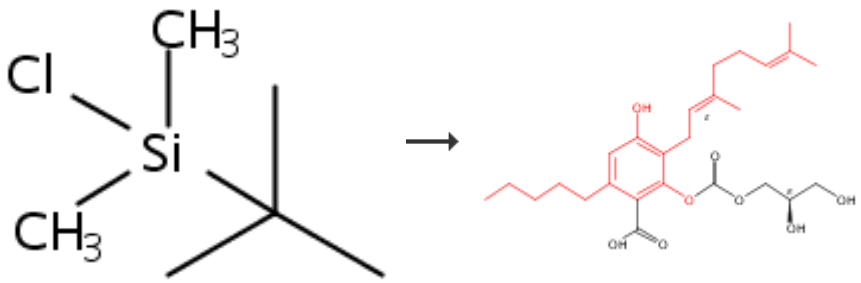
Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

235. 4 Steps (Converging)





Overview

Steps/Stages

Notes

1.1 R:Et_3N, S:CH_2Cl_2, 3-5 h, 0°C

1.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

1.2 R:NaCl, S:H_2O

2.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

3.1 R:Et_3N •3HF, S:CH_2Cl_2, -15°C; 65 h, 5°C

3.2 R:$NaHCO_3$, S:H_2O, S:AcOEt, 0°C

alternative preparation shown, regioselective, alternative preparation shown, Reactants: 4, Reagents: 5, Solvents: 3, Steps: 4, Stages: 6, Most stages in any one step: 2

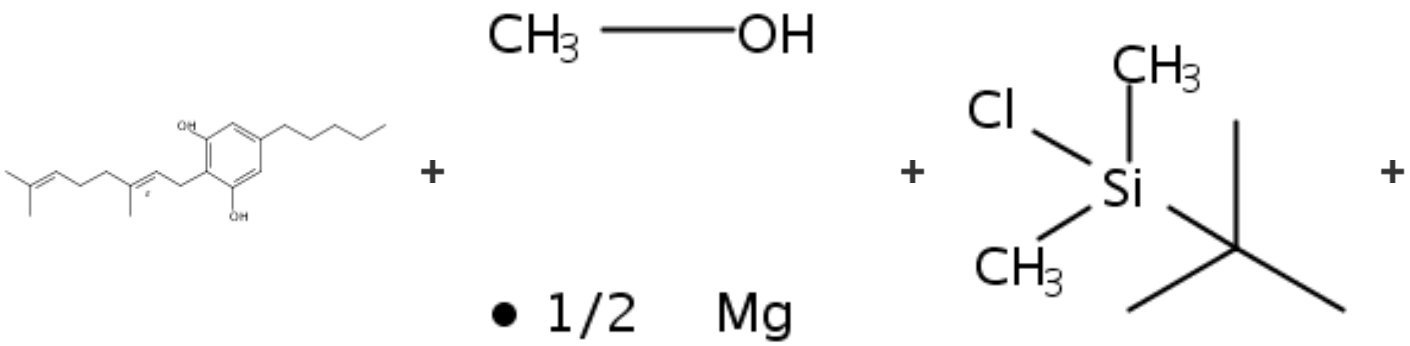
References

Biosynthesis of cannabinoid prodrugs

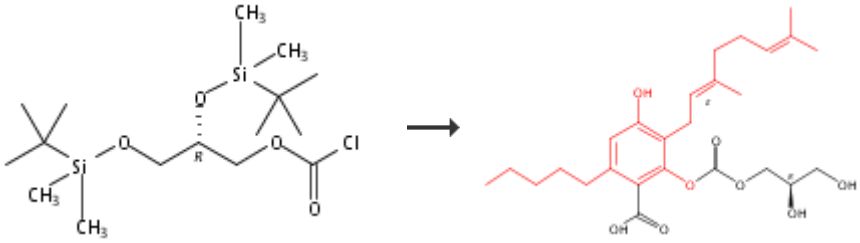
By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

236. 4 Steps



[Step 2.1]



[Step 3.1]

Overview

Steps/Stages

1.1 S:H_2O, cooled; 50°C; 3 h, 50°C; 50°C → rt

1.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, rt, pH 2

2.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

2.2 R:NaCl, S:H_2O

3.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

4.1 R:Et_3N •3HF, S:CH_2Cl_2, -15°C; 65 h, 5°C

4.2 R:$NaHCO_3$, S:H_2O, S:AcOEt, 0°C

Notes

1) conversion = 85%,alternative preparation shown,reaction in a sealed pressure vessel, 2) alternative preparation shown, regioselective, 3) alternative preparation shown, Reactants: 4, Reagents: 6, Solvents: 5, Steps: 4, Stages: 7, Most stages in any one step: 2

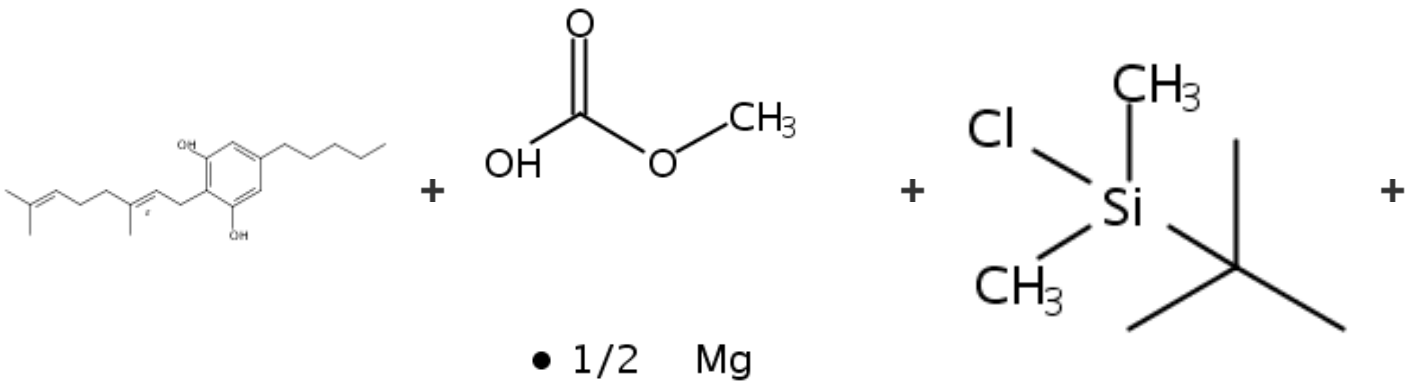
References

Biosynthesis of cannabinoid prodrugs

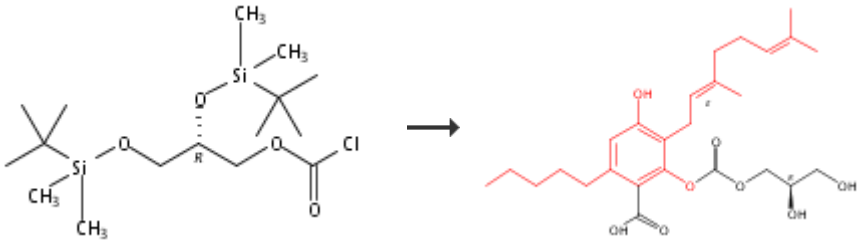
By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

237. 4 Steps



[Step 2.1]



[Step 3.1]

Overview

Steps/Stages

1.1 S:DMF, 1 h, 120°C

1.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

2.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

2.2 R:NaCl, S:H_2O

3.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

4.1 R:Et_3N •3HF, S:CH_2Cl_2, -15°C; 65 h, 5°C

4.2 R:$NaHCO_3$, S:H_2O, S:AcOEt, 0°C

Notes

1) conversion = 40%,alternative preparation shown, 2) alternative preparation shown, regioselective, 3) alternative preparation shown, Reactants: 4, Reagents: 6, Solvents: 6, Steps: 4, Stages: 7, Most stages in any one step: 2

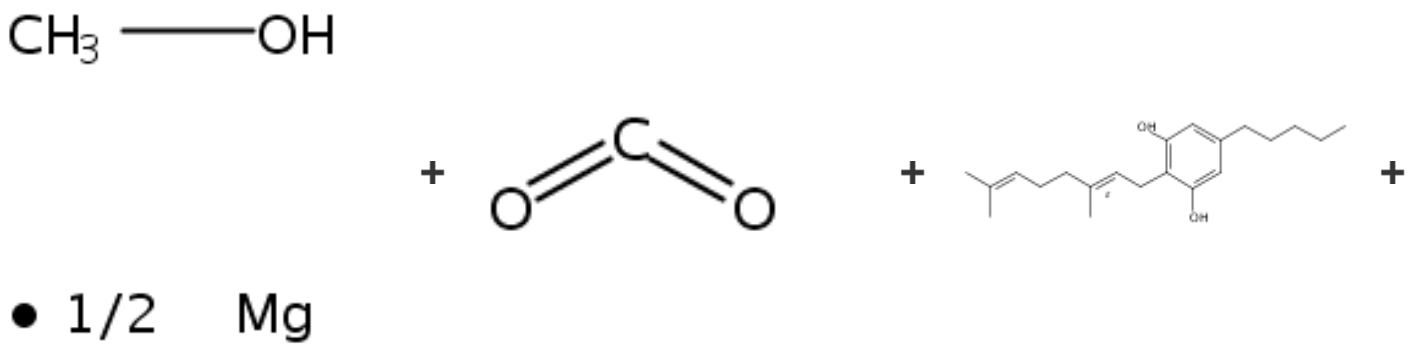
References

Biosynthesis of cannabinoid prodrugs

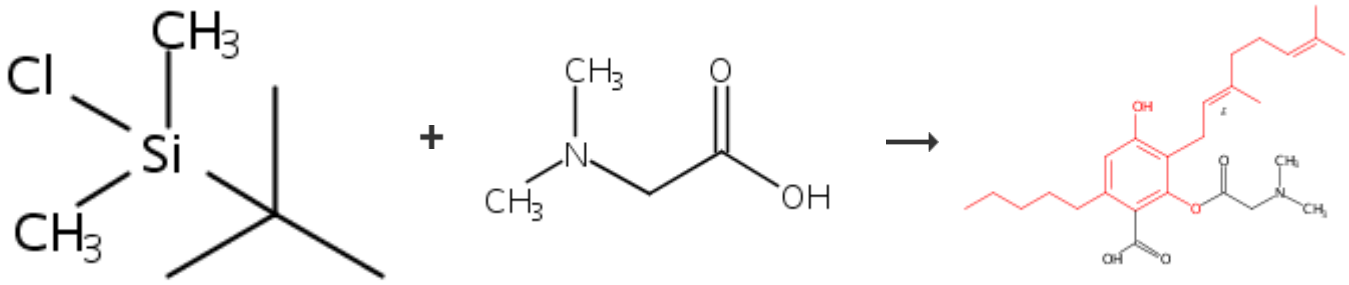
By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

238. 4 Steps



[Step 2.1]



[Step 3.1] [Step 4.1]

Overview

Steps/Stages

1.1 S:DMF, 140°C
2.1 S:DMF, 1 h, 120°C

2.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

3.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

3.2 R:NaCl, S:H_2O

4.1 R:DCC, C:4-DMAP, S:CH_2Cl_2, rt; overnight, rt

4.2 R:$Bu_4N^+ \bullet F^-$, S:CH_2Cl_2, -15°C

Notes

1) exothermic reaction, 2) conversion = 40%,alternative preparation shown, 3) alternative preparation shown, regioselective, 4) alternative preparation shown,other reagent triethylamine trihydrofluoride may be used in stage 2, Reactants: 5, Reagents: 5, Catalysts: 1, Solvents: 5, Steps: 4, Stages: 7, Most stages in any one step: 2

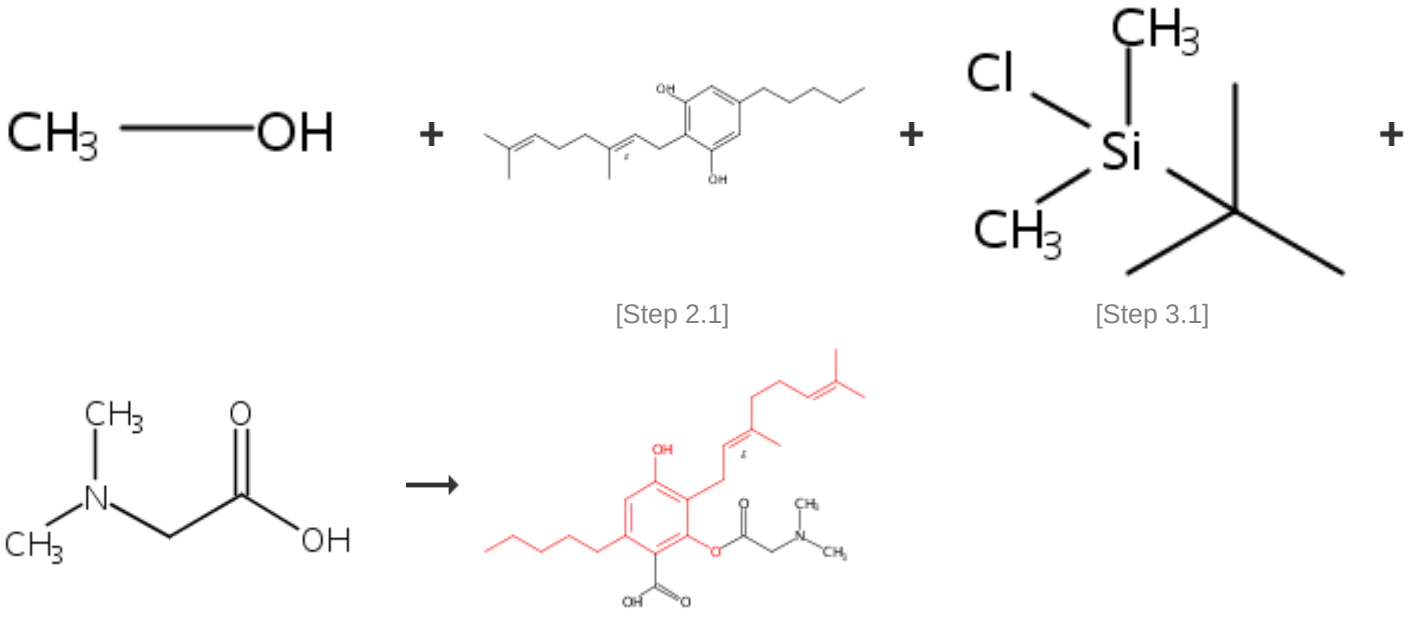
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

239. 4 Steps



[Step 2.1] [Step 3.1]

[Step 4.1]

Overview

Steps/Stages

Notes

1.1 R:Mg, S:MeOH, rt

2.1 S:H_2O, cooled; 50°C; 3 h, 50°C; 50°C → rt

2.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, rt, pH 2

3.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

3.2 R:NaCl, S:H_2O

4.1 R:DCC, C:4-DMAP, S:CH_2Cl_2, rt; overnight, rt

4.2 R:$Bu_4N^+ \bullet F^-$, S:CH_2Cl_2, -15°C

2) conversion = 85%,alternative preparation shown,reaction in a sealed pressure vessel, 3) alternative preparation shown, regioselective, 4) alternative preparation shown,other reagent triethylamine trihydrofluoride may be used in stage 2, Reactants: 4, Reagents: 6, Catalysts: 1, Solvents: 4, Steps: 4, Stages: 7, Most stages in any one step: 2

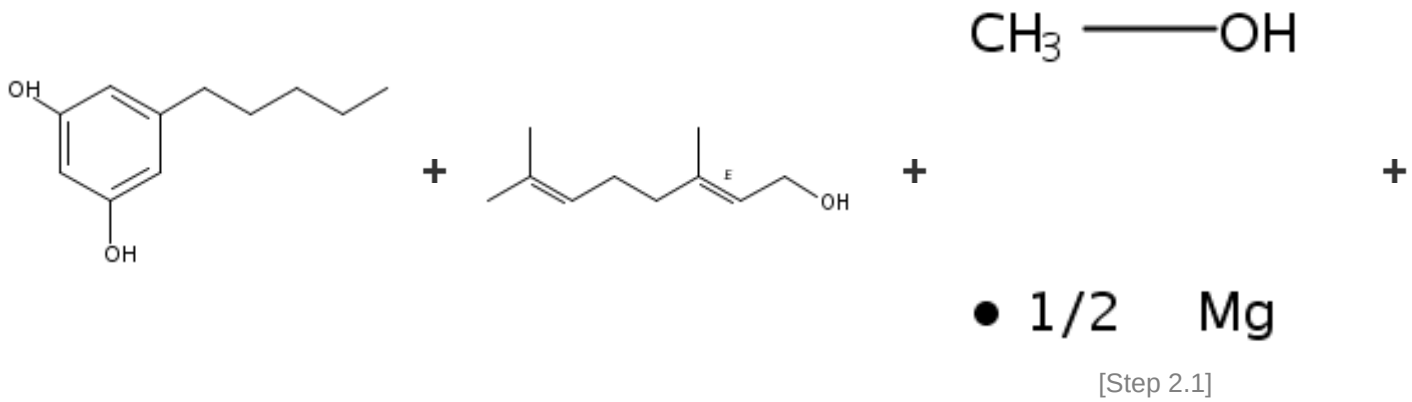
References

Biosynthesis of cannabinoid prodrugs

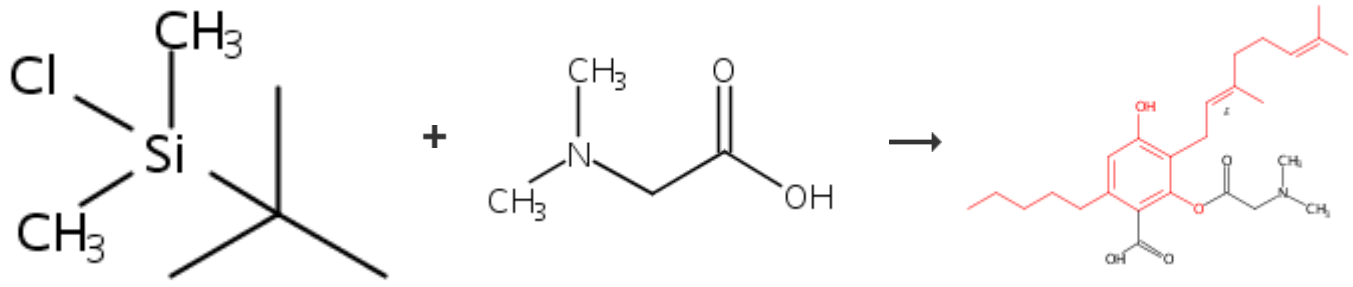
By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

240. 4 Steps



[Step 2.1]



[Step 3.1] [Step 4.1]

Overview

Steps/Stages **Notes**

1.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
2.1 S:H_2O, cooled; 50°C; 3 h, 50°C; 50°C → rt
2.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, rt, pH 2
3.1 R:1H-Imidazole, S:CH_2Cl_2, cooled
3.2 R:NaCl, S:H_2O
4.1 R:DCC, C:4-DMAP, S:CH_2Cl_2, rt; overnight, rt
4.2 R:$Bu_4N^+ \cdot F^-$, S:CH_2Cl_2, -15°C

1) in the dark, 2) conversion = 85%,alternative preparation shown,reaction in a sealed pressure vessel, 3) alternative preparation shown, regioselective, 4) alternative preparation shown,other reagent triethylamine trihydrofluoride may be used in stage 2, Reactants: 5, Reagents: 6, Catalysts: 1, Solvents: 4, Steps: 4, Stages: 7, Most stages in any one step: 2

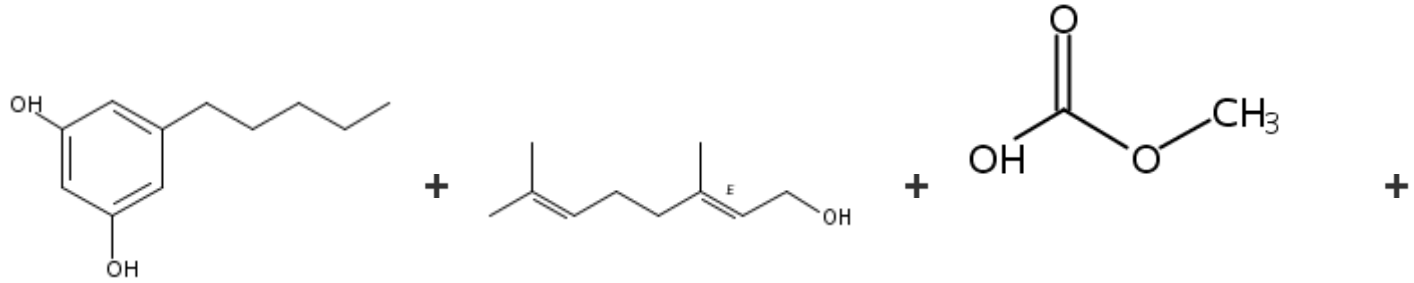
References

Biosynthesis of cannabinoid prodrugs

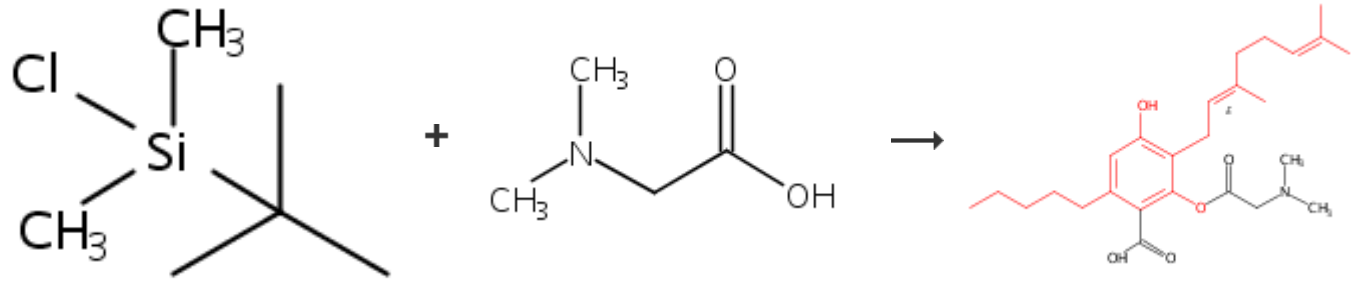
By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

241. 4 Steps



[Step 2.1]



[Step 3.1] [Step 4.1]

Overview

Steps/Stages **Notes**

1.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
2.1 S:DMF, 1 h, 120°C

2.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

3.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

3.2 R:NaCl, S:H_2O

4.1 R:DCC, C:4-DMAP, S:CH_2Cl_2, rt; overnight, rt

4.2 R:$Bu_4N^+ \cdot F^-$, S:CH_2Cl_2, -15°C

1) in the dark, 2) conversion = 40%,alternative preparation shown, 3) alternative preparation shown, regioselective, 4) alternative preparation shown,other reagent triethylamine trihydrofluoride may be used in stage 2, Reactants: 5, Reagents: 6, Catalysts: 1, Solvents: 5, Steps: 4, Stages: 7, Most stages in any one step: 2

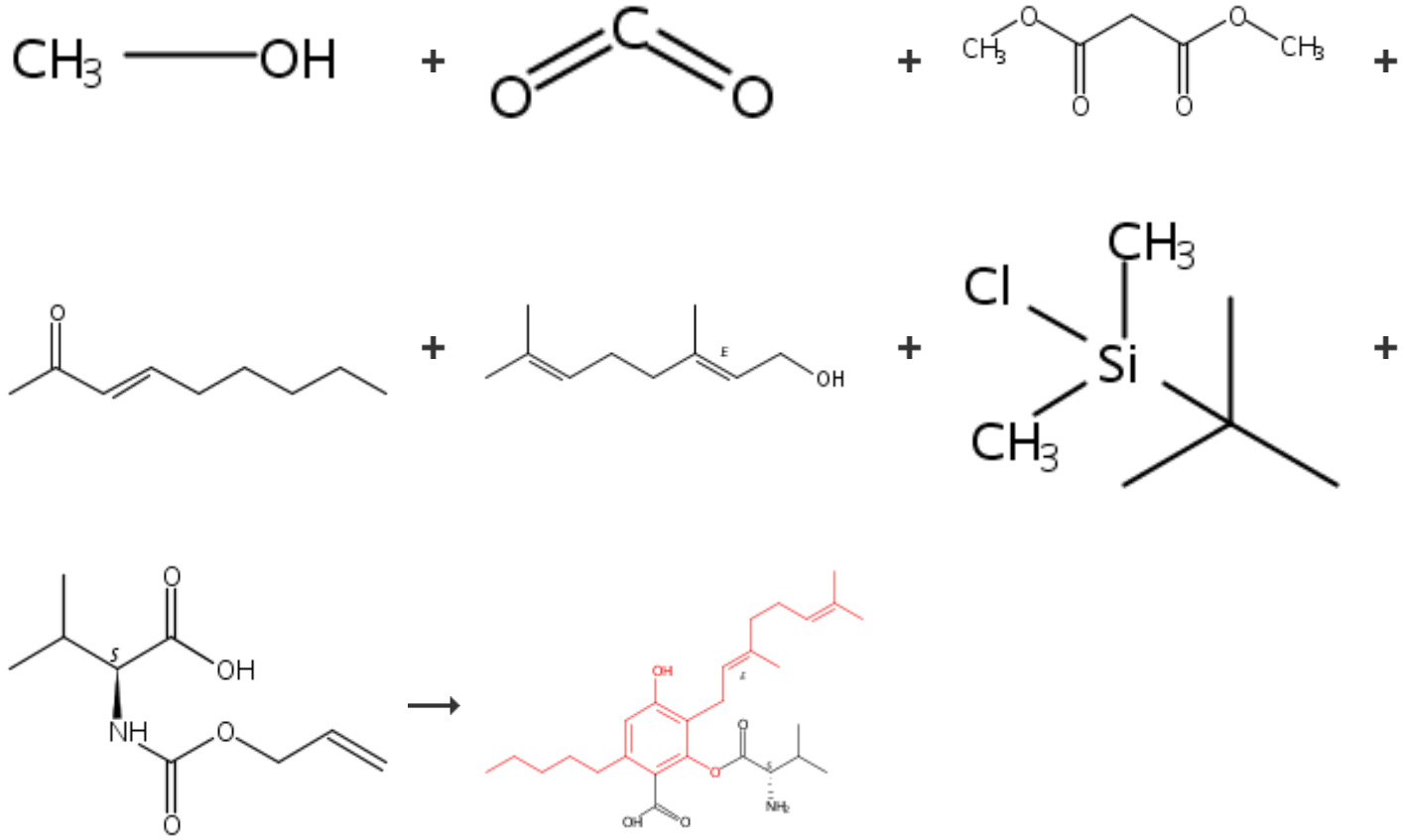
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

242. 10 Steps (Converging)



Overview

Steps/Stages

Notes

1.1 R:Mg, S:MeOH, cooled
2.1 S:DMF, 140°C

1.1 R:NaOMe, S:MeOH, rt; 3 h, reflux

2.1 R:Br_2, S:DMF, 90 min, cooled; 80°C → 160°C; 10 h, 160°C
3.1 C:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
4.1 S:DMF, 1 h, 120°C

4.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

5.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

5.2 R:NaCl, S:H_2O

6.1 R:DCC, R:4-DMAP, S:CH_2Cl_2, rt
6.2 S:CH_2Cl_2, rt; overnight, rt

7.1 R:$PhSiH_3$, C:$Pd(PPh_3)_4$, S:MeOH, S:CH_2Cl_2, rt

8.1 R:$Bu_4N^+ \bullet F^-$, S:CH_2Cl_2, -15°C

alternative preparation shown,conversion = 40%, regioselective, Reactants: 7, Reagents: 10, Catalysts: 2, Solvents: 5, Steps: 10, Stages: 13, Most stages in any one step: 2

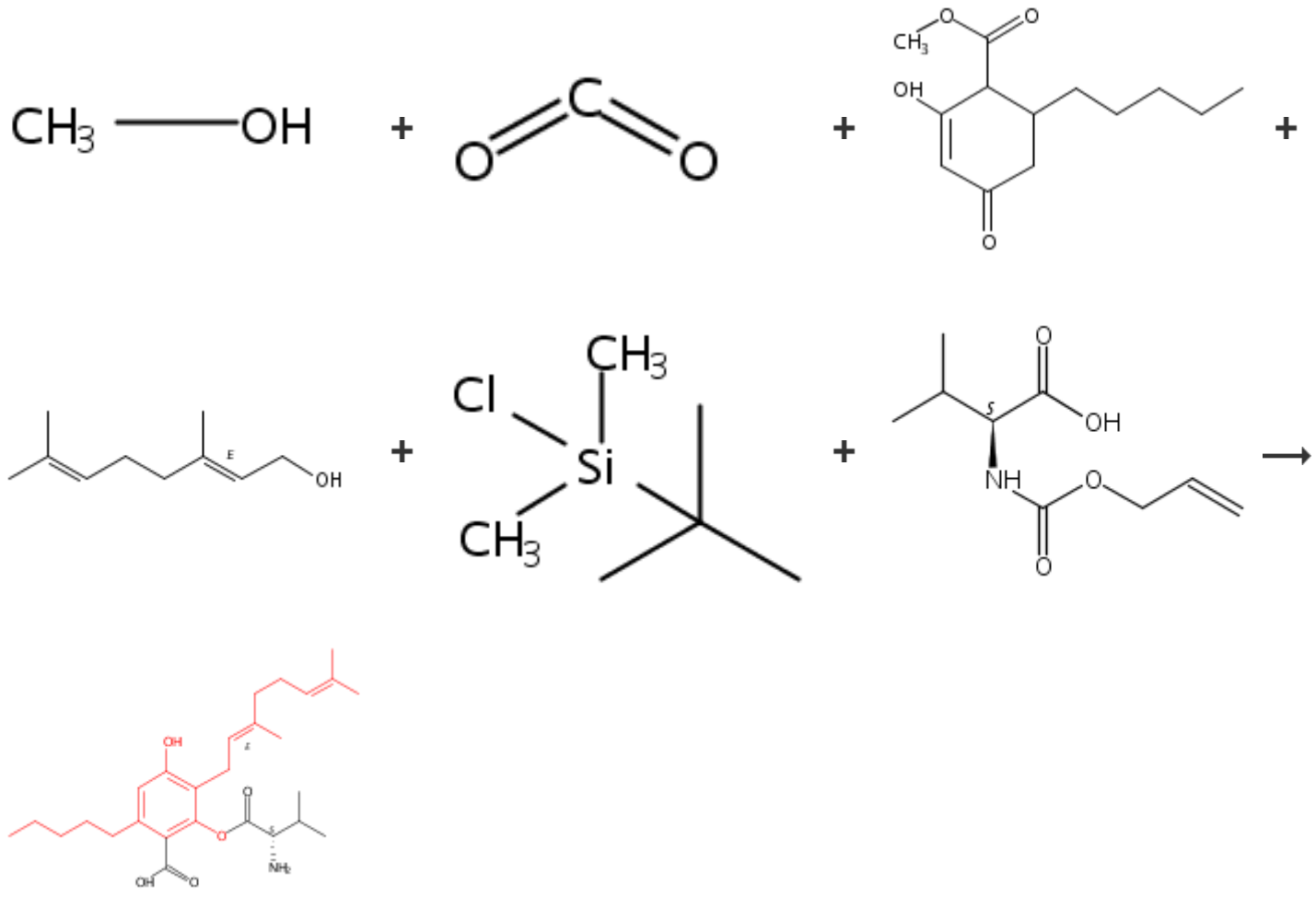
References

Methods for the manufacture of cannabinoid prodrugs, pharmaceutical formulations and their use

By Peet, Richard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017216362, 21 Dec 2017

243. 9 Steps (Converging)



Overview

Steps/Stages

1.1 R:Mg, S:MeOH, cooled
2.1 S:DMF, 140°C

1.1 R:Br_2, S:DMF, 90 min, cooled; 80°C → 160°C; 10 h, 160°C
2.1 C:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
3.1 S:DMF, 1 h, 120°C

3.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

4.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

4.2 R:NaCl, S:H_2O

5.1 R:DCC, R:4-DMAP, S:CH_2Cl_2, rt
5.2 S:CH_2Cl_2, rt; overnight, rt

6.1 R:$PhSiH_3$, C:$Pd(PPh_3)_4$, S:MeOH, S:CH_2Cl_2, rt

7.1 R:$Bu_4N^+ \cdot F^-$, S:CH_2Cl_2, -15°C

Notes

alternative preparation shown,conversion = 40%, regioselective, Reactants: 6, Reagents: 9, Catalysts: 2, Solvents: 5, Steps: 9, Stages: 12, Most stages in any one step: 2

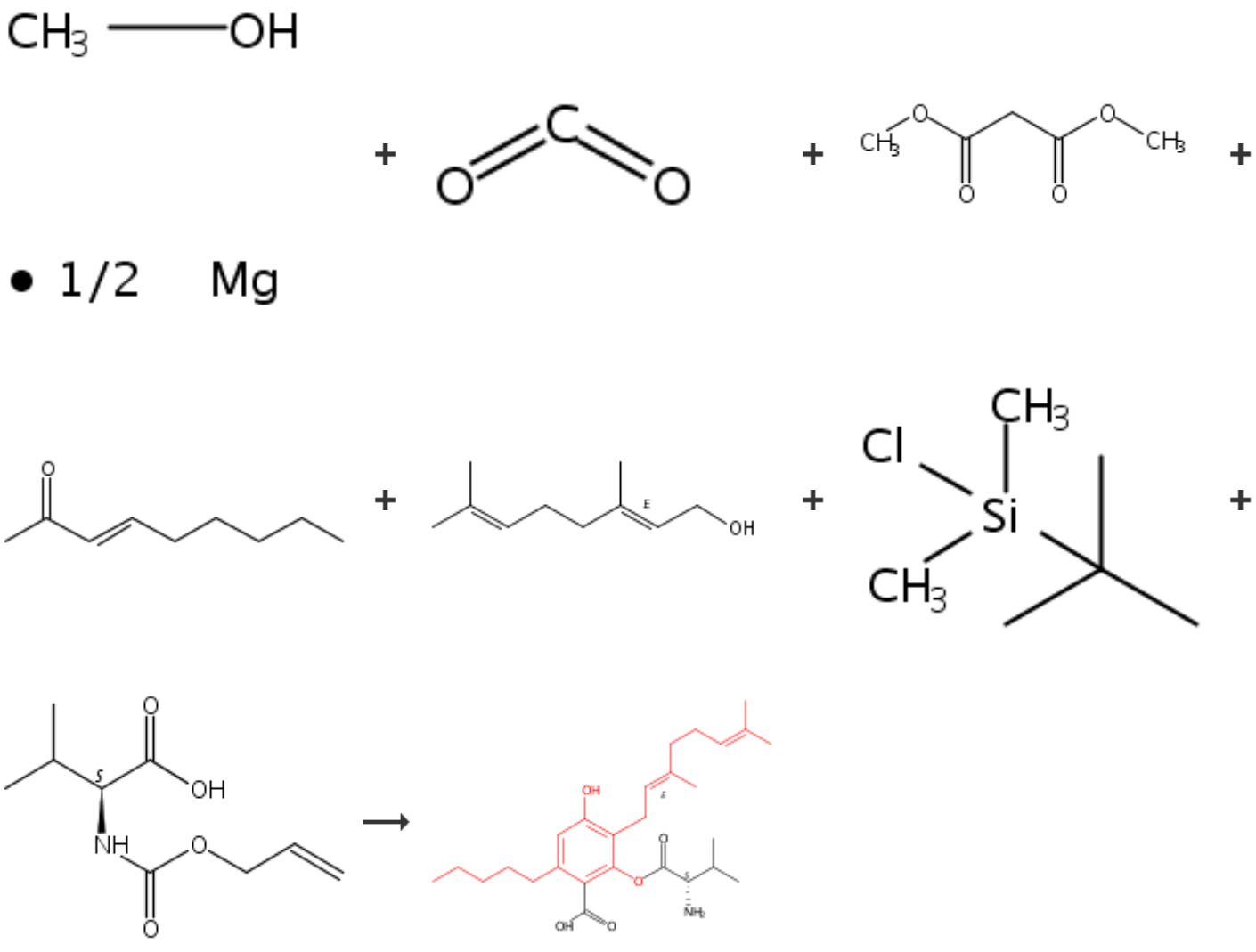
References

Methods for the manufacture of cannabinoid prodrugs, pharmaceutical formulations and their use

By Peet, Richard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017216362, 21 Dec 2017

244. 9 Steps (Converging)



Overview

Steps/Stages

1.1 S:DMF, 140°C

1.1 R:NaOMe, S:MeOH, rt; 3 h, reflux

2.1 R:Br_2, S:DMF, 90 min, cooled; 80°C → 160°C; 10 h, 160°C

3.1 C:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

4.1 S:DMF, 1 h, 120°C

4.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

5.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

5.2 R:NaCl, S:H_2O

6.1 R:DCC, R:4-DMAP, S:CH_2Cl_2, rt

6.2 S:CH_2Cl_2, rt; overnight, rt

7.1 R:$PhSiH_3$, C:$Pd(PPh_3)_4$, S:MeOH, S:CH_2Cl_2, rt

8.1 R:$Bu_4N^+ \cdot F^-$, S:CH_2Cl_2, -15°C

Notes

alternative preparation shown,conversion = 40%, regioselective, Reactants: 7, Reagents: 9, Catalysts: 2, Solvents: 5, Steps: 9, Stages: 12, Most stages in any one step: 2

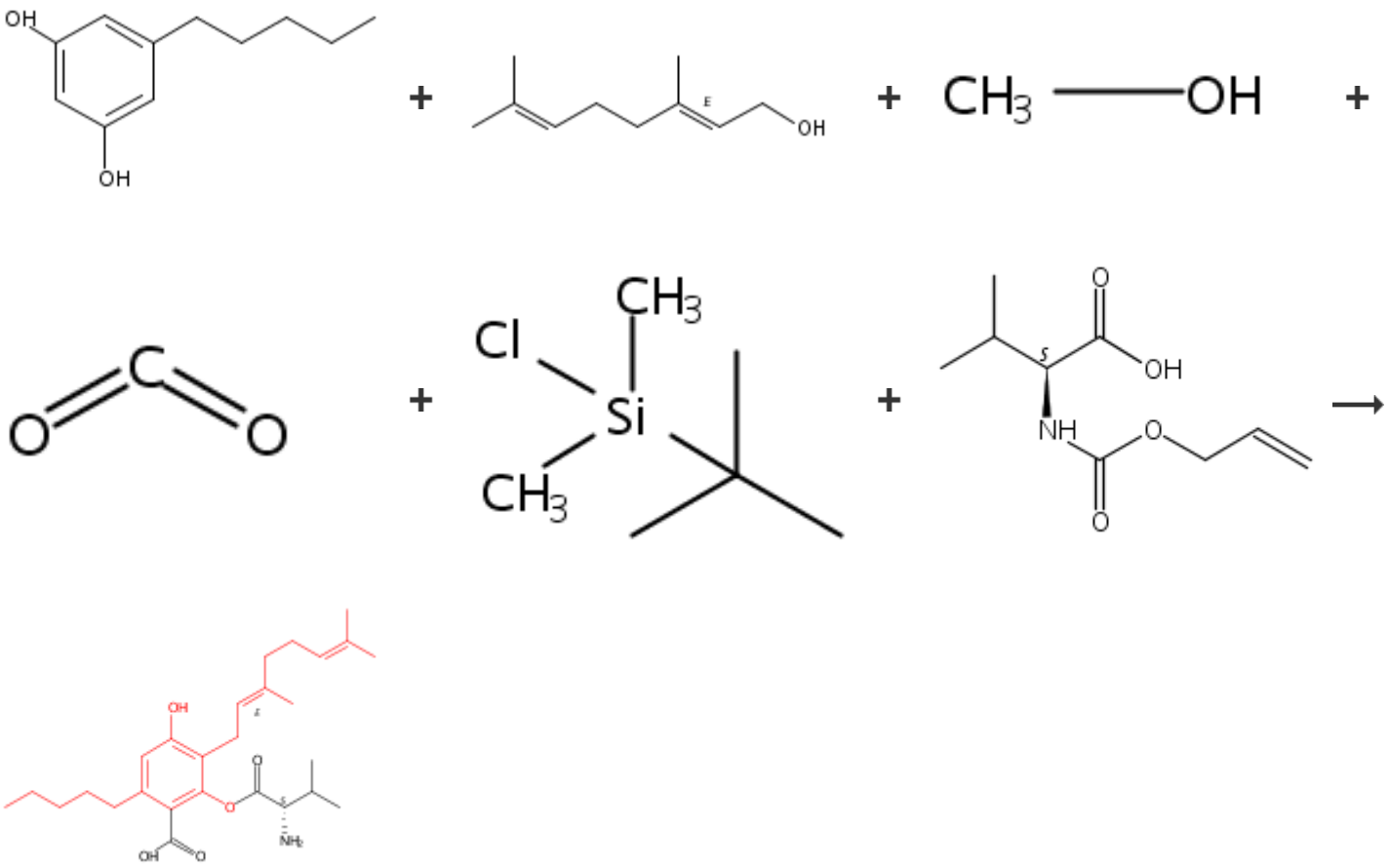
References

Methods for the manufacture of cannabinoid prodrugs, pharmaceutical formulations and their use

By Peet, Richard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017216362, 21 Dec 2017

245. 8 Steps (Converging)



Overview

Steps/Stages

1.1 C:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

1.1 R:Mg, S:MeOH, cooled
2.1 S:DMF, 140°C
3.1 S:DMF, 1 h, 120°C

3.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

4.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

4.2 R:NaCl, S:H_2O

5.1 R:DCC, R:4-DMAP, S:CH_2Cl_2, rt
5.2 S:CH_2Cl_2, rt; overnight, rt

6.1 R:$PhSiH_3$, C:$Pd(PPh_3)_4$, S:MeOH, S:CH_2Cl_2, rt

7.1 R:$Bu_4N^+ \bullet F^-$, S:CH_2Cl_2, -15°C

Notes

alternative preparation shown,conversion = 40%, regioselective, Reactants: 6, Reagents: 8, Catalysts: 2, Solvents: 5, Steps: 8, Stages: 11, Most stages in any one step: 2

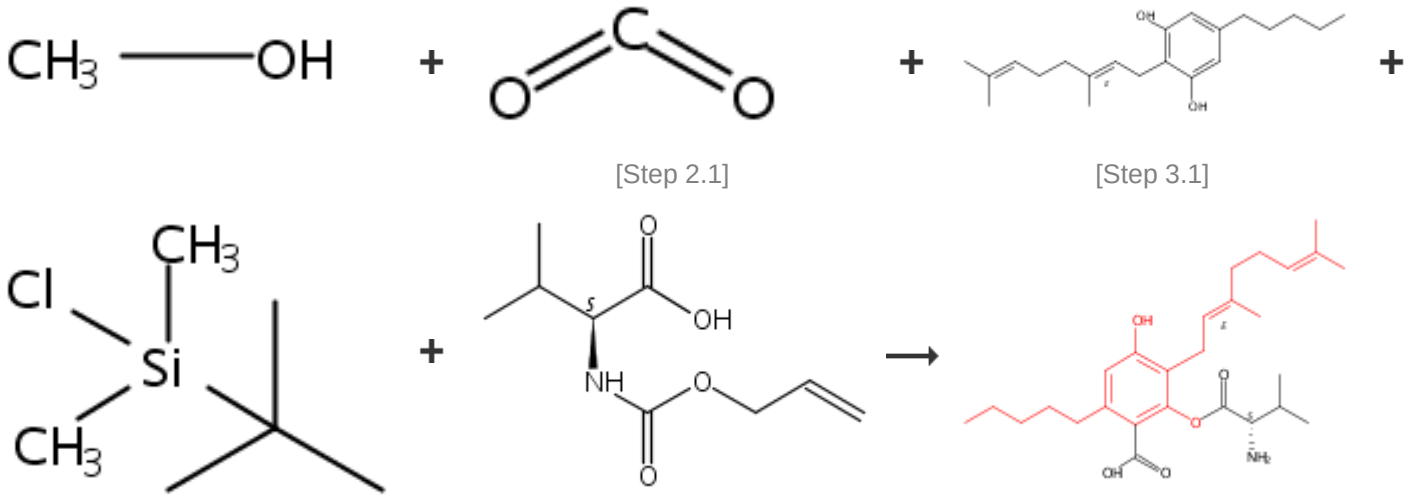
References

Methods for the manufacture of cannabinoid prodrugs, pharmaceutical formulations and their use

By Peet, Richard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017216362, 21 Dec 2017

246. 7 Steps



[Step 2.1] [Step 3.1] [Step 4.1] [Step 5.1]

Overview

Steps/Stages

Notes

1.1 R:Mg, S:MeOH, cooled
2.1 S:DMF, 140°C
3.1 S:DMF, 1 h, 120°C

3.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

4.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

4.2 R:NaCl, S:H_2O

5.1 R:DCC, R:4-DMAP, S:CH_2Cl_2, rt
5.2 S:CH_2Cl_2, rt; overnight, rt

6.1 R:$PhSiH_3$, C:$Pd(PPh_3)_4$, S:MeOH, S:CH_2Cl_2, rt

7.1 R:$Bu_4N^+ \cdot F^-$, S:CH_2Cl_2, -15°C

3) alternative preparation shown,conversion = 40%, 4) regioselective, Reactants: 5, Reagents: 8, Catalysts: 1, Solvents: 5, Steps: 7, Stages: 10, Most stages in any one step: 2

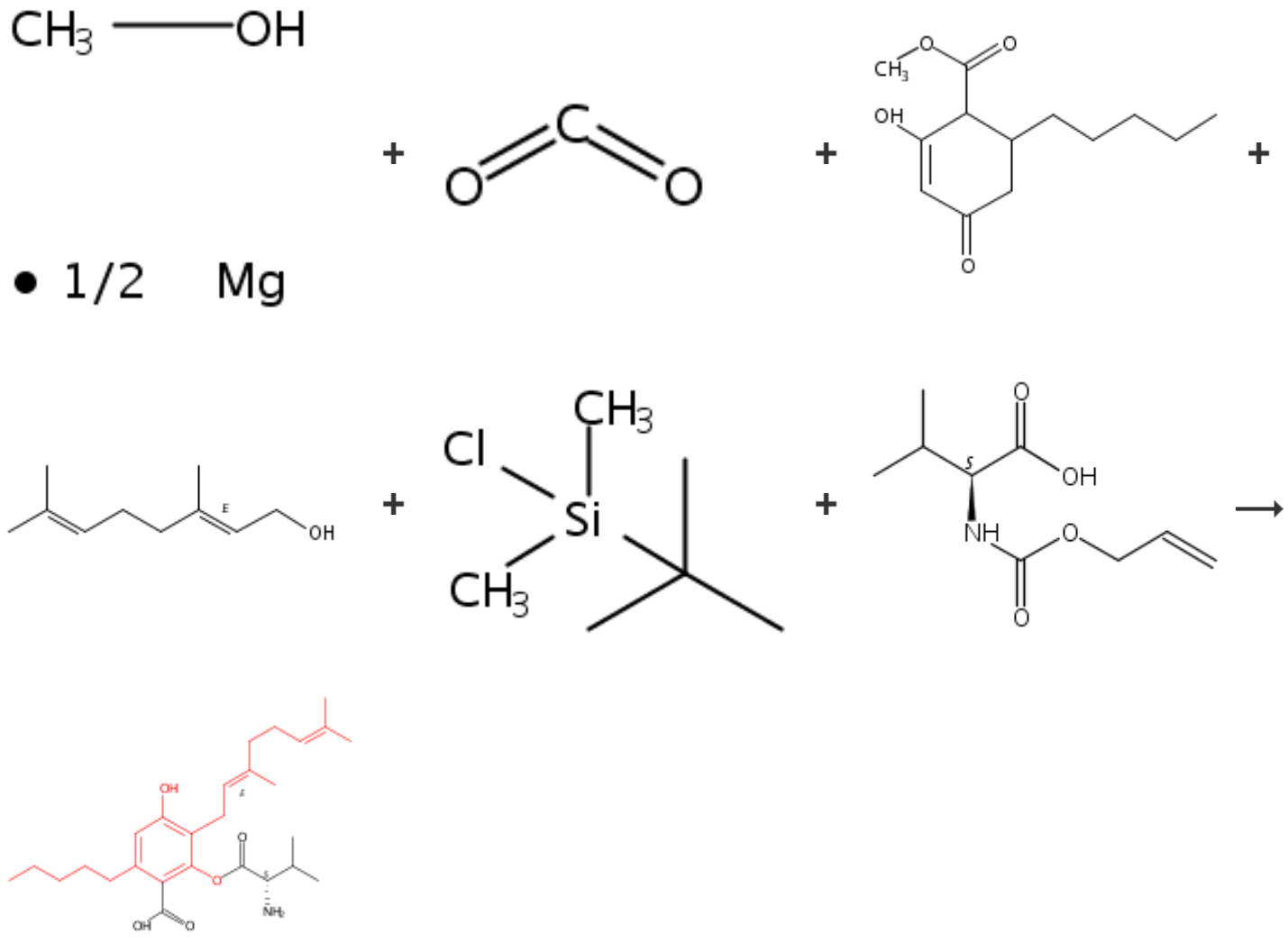
References

Methods for the manufacture of cannabinoid prodrugs, pharmaceutical formulations and their use

By Peet, Richard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017216362, 21 Dec 2017

247. 8 Steps (Converging)



Overview

Steps/Stages

Notes

1.1 S:DMF, 140°C

1.1 R:Br_2, S:DMF, 90 min, cooled; 80°C → 160°C; 10 h, 160°C
2.1 C:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
3.1 S:DMF, 1 h, 120°C

3.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

4.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

4.2 R:NaCl, S:H_2O

5.1 R:DCC, R:4-DMAP, S:CH_2Cl_2, rt
5.2 S:CH_2Cl_2, rt; overnight, rt

6.1 R:$PhSiH_3$, C:$Pd(PPh_3)_4$, S:MeOH, S:CH_2Cl_2, rt

7.1 R:$Bu_4N^+ \cdot F^-$, S:CH_2Cl_2, -15°C

alternative preparation shown,conversion = 40%, regioselective, Reactants: 6, Reagents: 8, Catalysts: 2, Solvents: 5, Steps: 8, Stages: 11, Most stages in any one step: 2

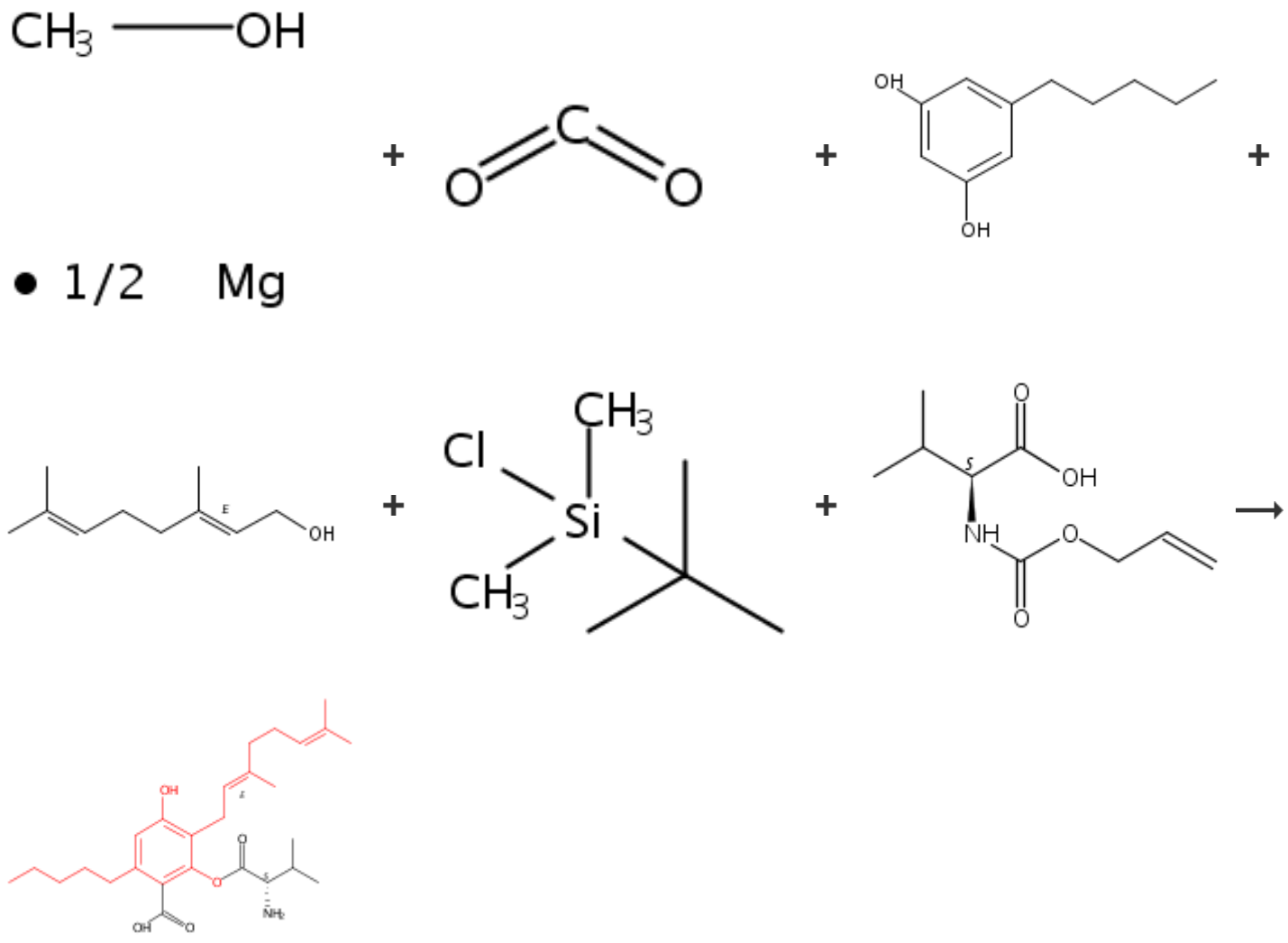
References

Methods for the manufacture of cannabinoid prodrugs, pharmaceutical formulations and their use

By Peet, Richard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017216362, 21 Dec 2017

248. 7 Steps (Converging)



Overview

Steps/Stages

Notes

1.1 S:DMF, 140°C
1.1 C:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
2.1 S:DMF, 1 h, 120°C

2.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

3.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

3.2 R:NaCl, S:H_2O

4.1 R:DCC, R:4-DMAP, S:CH_2Cl_2, rt
4.2 S:CH_2Cl_2, rt; overnight, rt

5.1 R:$PhSiH_3$, C:$Pd(PPh_3)_4$, S:MeOH, S:CH_2Cl_2, rt

6.1 R:$Bu_4N^+ \cdot F^-$, S:CH_2Cl_2, -15°C

alternative preparation shown,conversion = 40%, regioselective, Reactants: 6, Reagents: 7, Catalysts: 2, Solvents: 5, Steps: 7, Stages: 10, Most stages in any one step: 2

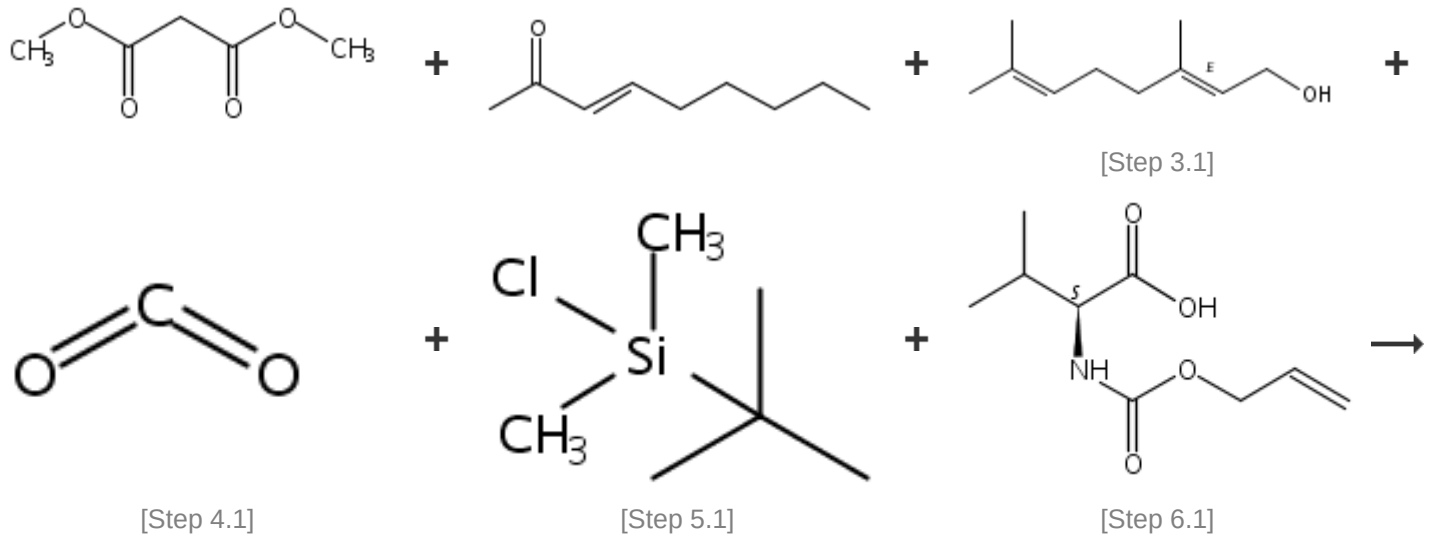
References

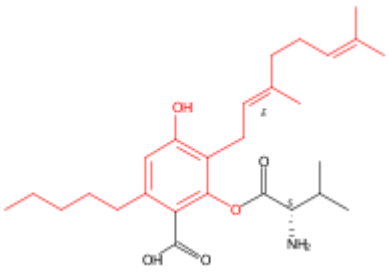
Methods for the manufacture of cannabinoid prodrugs, pharmaceutical formulations and their use

By Peet, Richard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017216362, 21 Dec 2017

249. 8 Steps





Overview

Steps/Stages

Notes

1.1 R:NaOMe, S:MeOH, rt; 3 h, reflux

2.1 R:Br_2, S:DMF, 90 min, cooled; 80°C → 160°C; 10 h, 160°C
3.1 C:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

4.1 R:$Mg(OMe)_2$, S:DMF, rt → 50°C; 3 h, 50°C; 50°C → rt

4.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, rt, pH 2

5.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

5.2 R:NaCl, S:H_2O

6.1 R:DCC, R:4-DMAP, S:CH_2Cl_2, rt
6.2 S:CH_2Cl_2, rt; overnight, rt

7.1 R:$PhSiH_3$, C:$Pd(PPh_3)_4$, S:MeOH, S:CH_2Cl_2, rt

8.1 R:$Bu_4N^+ \cdot F^-$, S:CH_2Cl_2, -15°C

4) alternative preparation shown,conversion = 85%, 5) regioselective, Reactants: 6, Reagents: 10, Catalysts: 2, Solvents: 5, Steps: 8, Stages: 11, Most stages in any one step: 2

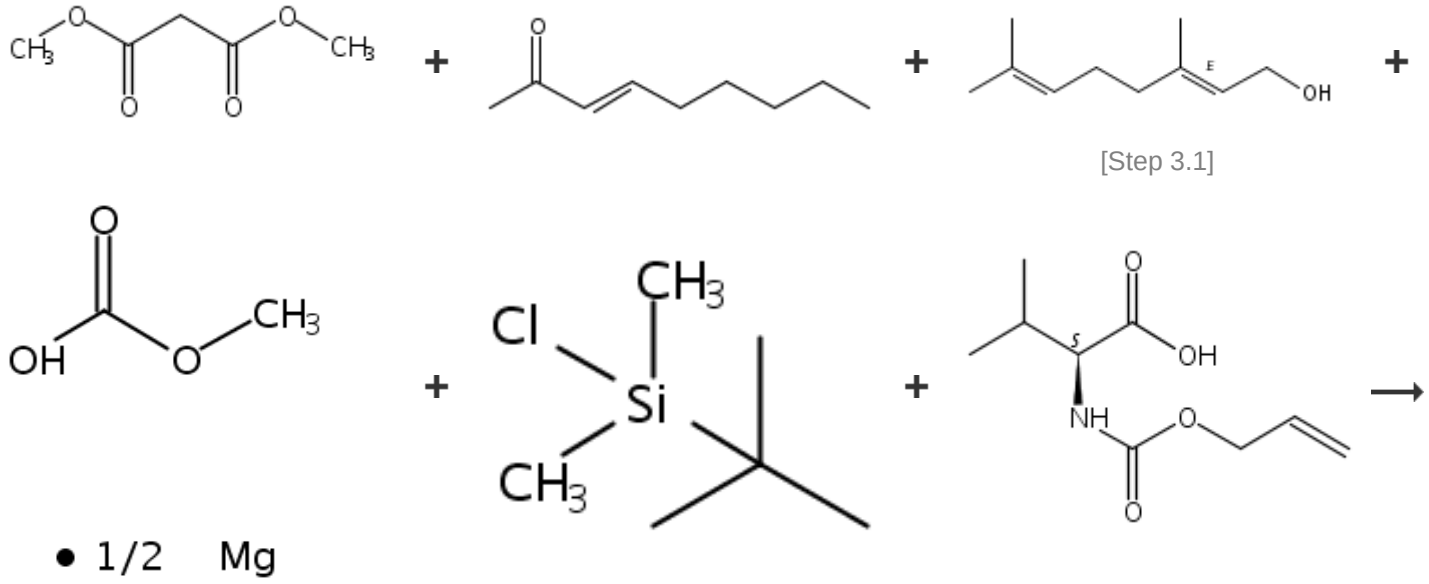
References

Methods for the manufacture of cannabinoid prodrugs, pharmaceutical formulations and their use

By Peet, Richard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017216362, 21 Dec 2017

250. 8 Steps

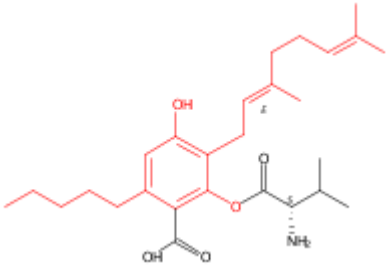


[Step 3.1]

[Step 4.1]

[Step 5.1]

[Step 6.1]



Overview

Steps/Stages

Notes

1.1 R:NaOMe, S:MeOH, rt; 3 h, reflux

2.1 R:Br_2, S:DMF, 90 min, cooled; 80°C → 160°C; 10 h, 160°C

3.1 C:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

4.1 S:DMF, 1 h, 120°C

4.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

5.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

5.2 R:NaCl, S:H_2O

6.1 R:DCC, R:4-DMAP, S:CH_2Cl_2, rt

6.2 S:CH_2Cl_2, rt; overnight, rt

7.1 R:$PhSiH_3$, C:$Pd(PPh_3)_4$, S:MeOH, S:CH_2Cl_2, rt

8.1 R:$Bu_4N^+ \cdot F^-$, S:CH_2Cl_2, -15°C

4) alternative preparation shown,conversion = 40%, 5) regioselective, Reactants: 6, Reagents: 9, Catalysts: 2, Solvents: 5, Steps: 8, Stages: 11, Most stages in any one step: 2

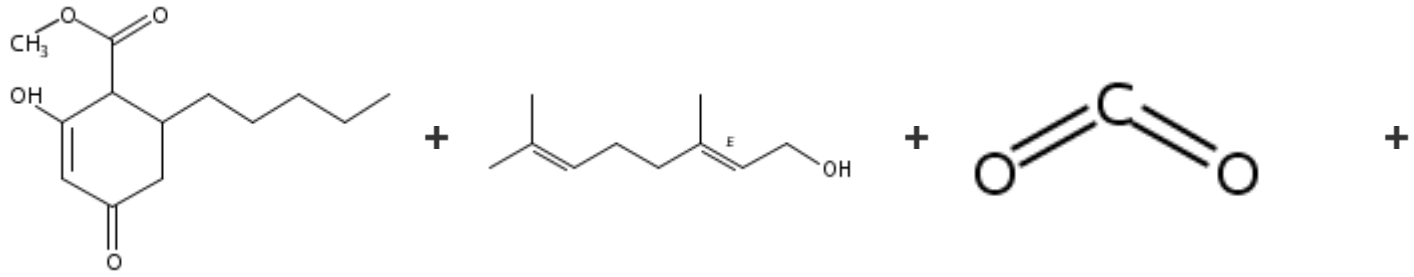
References

Methods for the manufacture of cannabinoid prodrugs, pharmaceutical formulations and their use

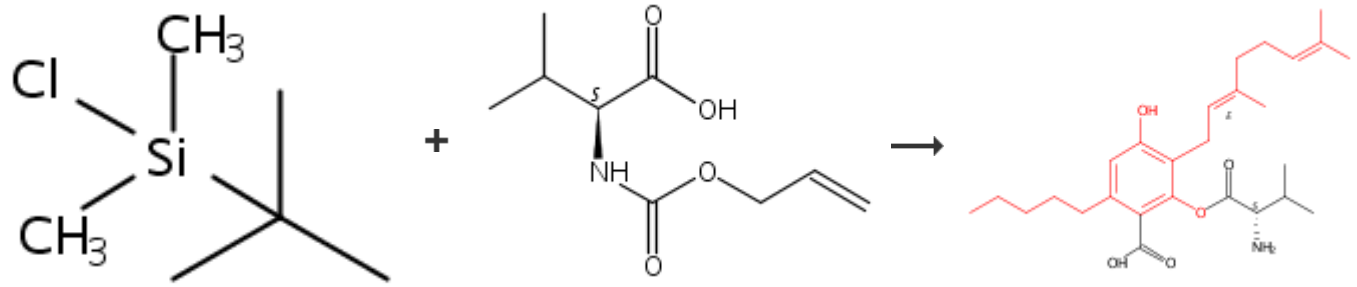
By Peet, Richard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017216362, 21 Dec 2017

251. 7 Steps



[Step 2.1] [Step 3.1]



[Step 4.1] [Step 5.1]

Overview

Steps/Stages **Notes**

1.1 R:Br_2, S:DMF, 90 min, cooled; 80°C → 160°C; 10 h, 160°C
2.1 C:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

3.1 R:$Mg(OMe)_2$, S:DMF, rt → 50°C; 3 h, 50°C; 50°C → rt

3.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, rt, pH 2

4.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

4.2 R:NaCl, S:H_2O

5.1 R:DCC, R:4-DMAP, S:CH_2Cl_2, rt
5.2 S:CH_2Cl_2, rt; overnight, rt

6.1 R:$PhSiH_3$, C:$Pd(PPh_3)_4$, S:MeOH, S:CH_2Cl_2, rt

7.1 R:$Bu_4N^+ \bullet F^-$, S:CH_2Cl_2, -15°C

3) alternative preparation shown,conversion = 85%, 4) regioselective, Reactants: 5, Reagents: 9, Catalysts: 2, Solvents: 5, Steps: 7, Stages: 10, Most stages in any one step: 2

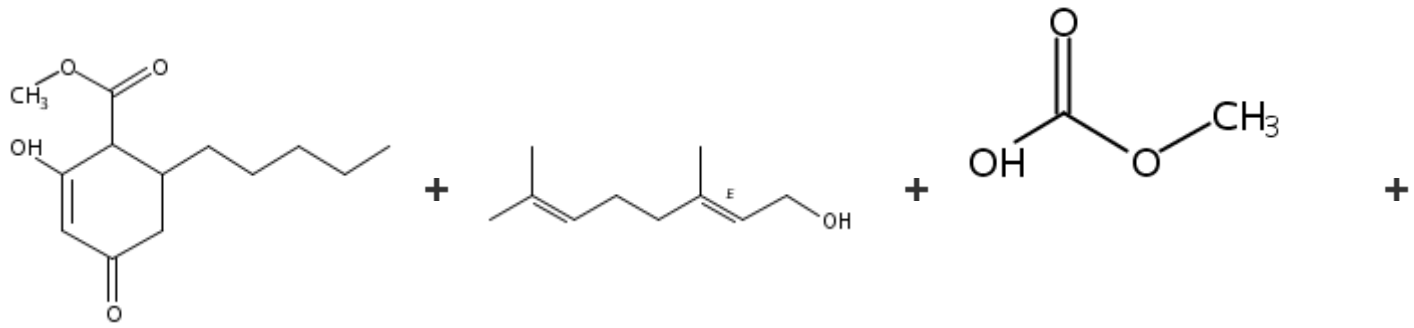
References

Methods for the manufacture of cannabinoid prodrugs, pharmaceutical formulations and their use

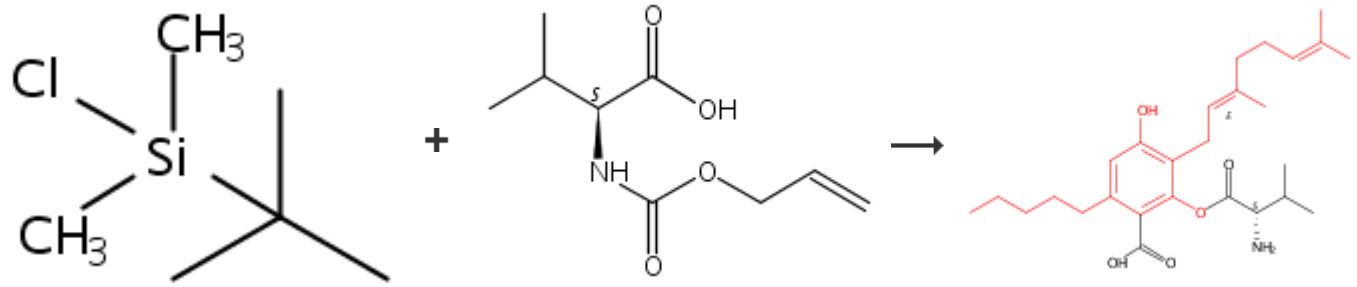
By Peet, Richard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017216362, 21 Dec 2017

252. 7 Steps



[Step 2.1] [Step 3.1]



[Step 4.1] [Step 5.1]

Overview

Steps/Stages **Notes**

1.1 R:Br_2, S:DMF, 90 min, cooled; 80°C → 160°C; 10 h, 160°C
2.1 C:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
3.1 S:DMF, 1 h, 120°C

3.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

4.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

4.2 R:NaCl, S:H_2O

5.1 R:DCC, R:4-DMAP, S:CH_2Cl_2, rt
5.2 S:CH_2Cl_2, rt; overnight, rt

6.1 R:$PhSiH_3$, C:$Pd(PPh_3)_4$, S:MeOH, S:CH_2Cl_2, rt

7.1 R:$Bu_4N^+ \cdot F^-$, S:CH_2Cl_2, -15°C

3) alternative preparation shown,conversion = 40%, 4) regioselective, Reactants: 5, Reagents: 8, Catalysts: 2, Solvents: 5, Steps: 7, Stages: 10, Most stages in any one step: 2

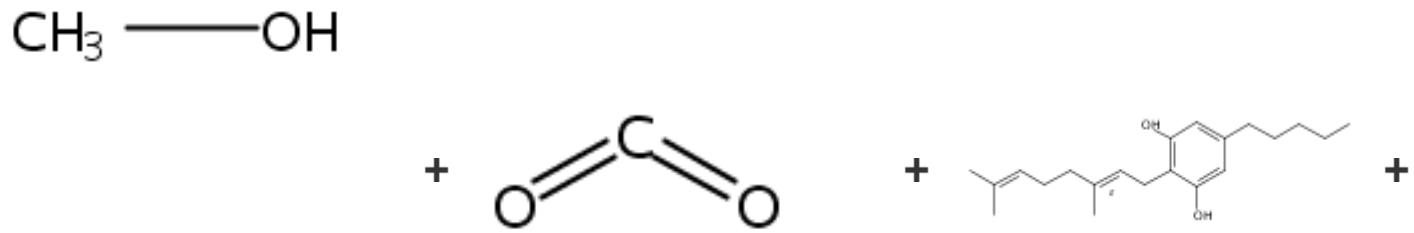
References

Methods for the manufacture of cannabinoid prodrugs, pharmaceutical formulations and their use

By Peet, Richard C. and Kavarana, Malcolm J.

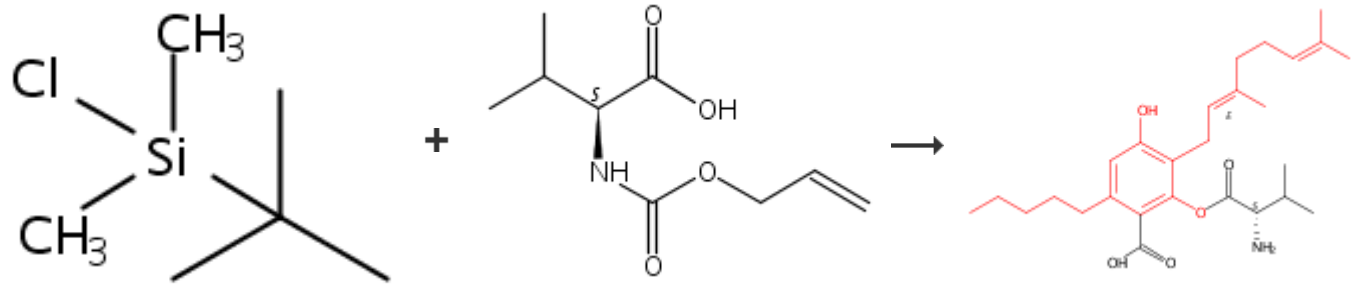
From PCT Int. Appl., 2017216362, 21 Dec 2017

253. 6 Steps



• 1/2 Mg

[Step 2.1]



[Step 3.1] [Step 4.1]

Overview

Steps/Stages **Notes**

1.1 S:DMF, 140°C
2.1 S:DMF, 1 h, 120°C

2.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

3.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

3.2 R:NaCl, S:H_2O

4.1 R:DCC, R:4-DMAP, S:CH_2Cl_2, rt
4.2 S:CH_2Cl_2, rt; overnight, rt

5.1 R:$PhSiH_3$, C:$Pd(PPh_3)_4$, S:MeOH, S:CH_2Cl_2, rt

6.1 R:$Bu_4N^+ \cdot F^-$, S:CH_2Cl_2, -15°C

2) alternative preparation shown,conversion = 40%, 3) regioselective, Reactants: 5, Reagents: 7, Catalysts: 1, Solvents: 5, Steps: 6, Stages: 9, Most stages in any one step: 2

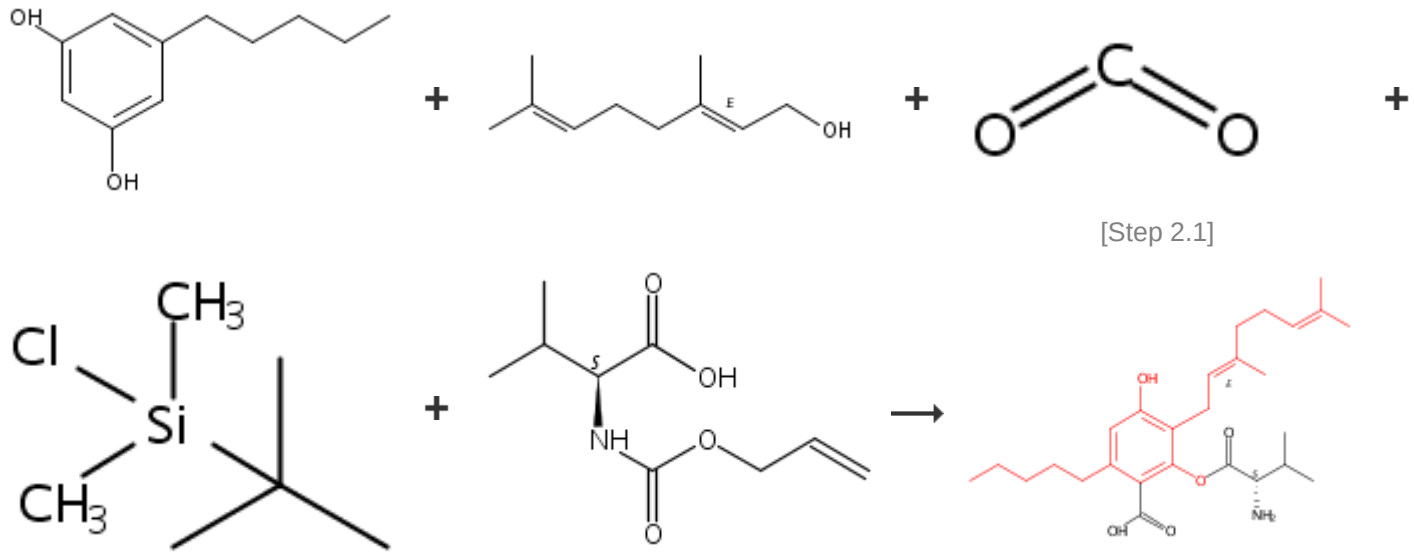
References

Methods for the manufacture of cannabinoid prodrugs, pharmaceutical formulations and their use

By Peet, Richard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017216362, 21 Dec 2017

254. 6 Steps



Overview

Steps/Stages

1.1 C:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

2.1 R:$Mg(OMe)_2$, S:DMF, rt → 50°C; 3 h, 50°C; 50°C → rt

2.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, rt, pH 2

3.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

3.2 R:NaCl, S:H_2O

4.1 R:DCC, R:4-DMAP, S:CH_2Cl_2, rt
4.2 S:CH_2Cl_2, rt; overnight, rt

5.1 R:$PhSiH_3$, C:$Pd(PPh_3)_4$, S:MeOH, S:CH_2Cl_2, rt

6.1 R:$Bu_4N^+ \cdot F^-$, S:CH_2Cl_2, -15°C

Notes

2) alternative preparation shown,conversion = 85%, 3) regioselective, Reactants: 5, Reagents: 8, Catalysts: 2, Solvents: 5, Steps: 6, Stages: 9, Most stages in any one step: 2

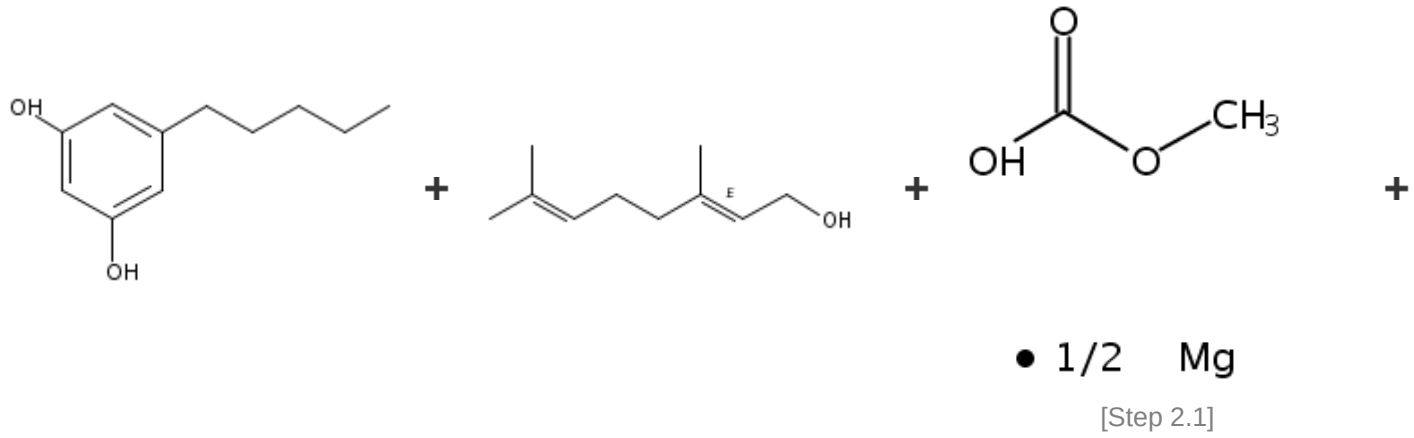
References

Methods for the manufacture of cannabinoid prodrugs, pharmaceutical formulations and their use

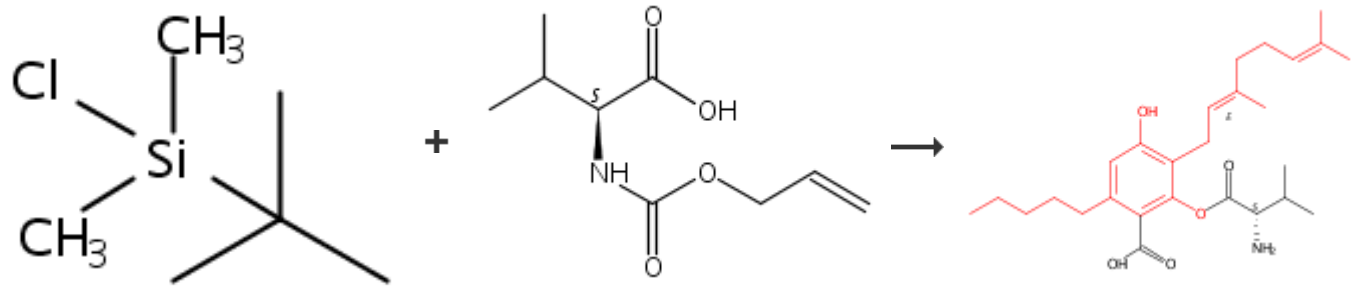
By Peet, Richard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017216362, 21 Dec 2017

255. 6 Steps



[Step 2.1]



[Step 3.1] [Step 4.1]

Overview

Steps/Stages

1.1 C:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
2.1 S:DMF, 1 h, 120°C

2.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

3.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

3.2 R:NaCl, S:H_2O

4.1 R:DCC, R:4-DMAP, S:CH_2Cl_2, rt
4.2 S:CH_2Cl_2, rt; overnight, rt

5.1 R:$PhSiH_3$, C:$Pd(PPh_3)_4$, S:MeOH, S:CH_2Cl_2, rt

6.1 R:Bu_4N^+ •F^-, S:CH_2Cl_2, -15°C

Notes

2) alternative preparation shown,conversion = 40%, 3) regioselective, Reactants: 5, Reagents: 7, Catalysts: 2, Solvents: 5, Steps: 6, Stages: 9, Most stages in any one step: 2

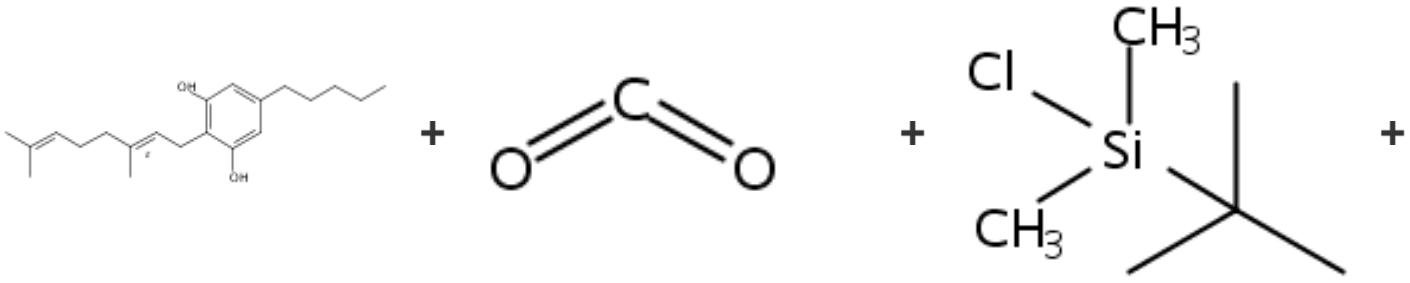
References

Methods for the manufacture of cannabinoid prodrugs, pharmaceutical formulations and their use

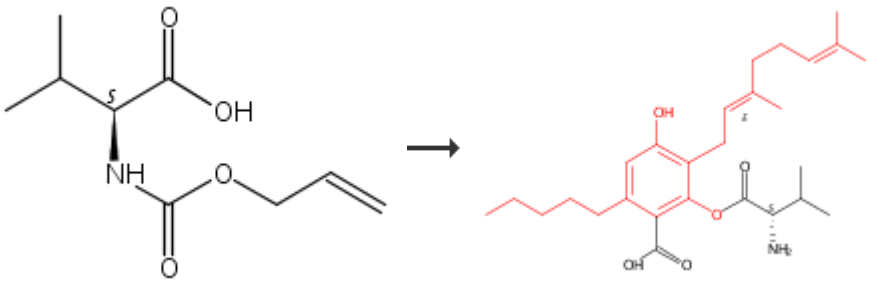
By Peet, Richard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017216362, 21 Dec 2017

256. 5 Steps



[Step 2.1]



[Step 3.1]

Overview

Steps/Stages

1.1 R:$Mg(OMe)_2$, S:DMF, rt → 50°C; 3 h, 50°C; 50°C → rt

1.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, rt, pH 2

2.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

2.2 R:NaCl, S:H_2O

3.1 R:DCC, R:4-DMAP, S:CH_2Cl_2, rt
3.2 S:CH_2Cl_2, rt; overnight, rt

4.1 R:$PhSiH_3$, C:$Pd(PPh_3)_4$, S:MeOH, S:CH_2Cl_2, rt

5.1 R:$Bu_4N^+ \cdot F^-$, S:CH_2Cl_2, -15°C

Notes

1) alternative preparation shown,conversion = 85%, 2) regioselective, Reactants: 4, Reagents: 8, Catalysts: 1, Solvents: 5, Steps: 5, Stages: 8, Most stages in any one step: 2

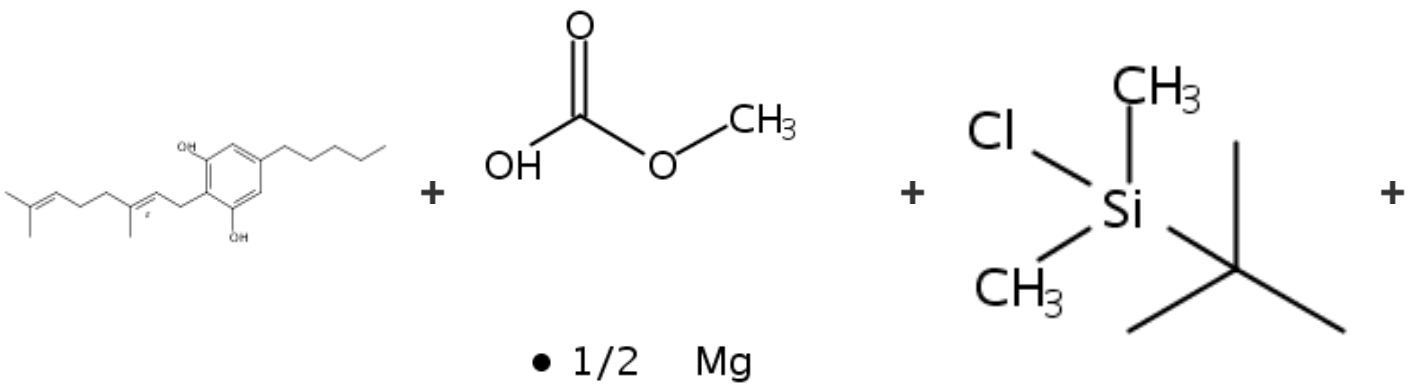
References

Methods for the manufacture of cannabinoid prodrugs, pharmaceutical formulations and their use

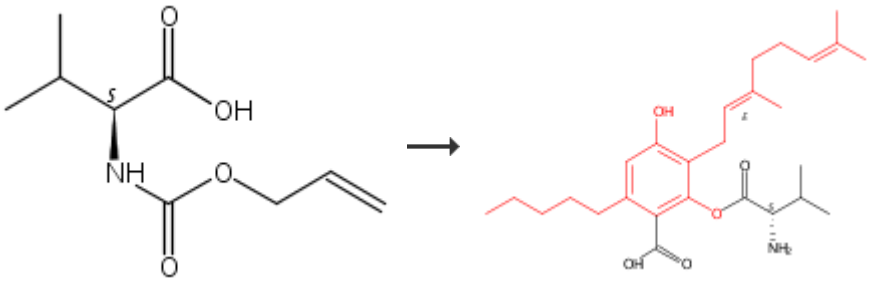
By Peet, Richard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017216362, 21 Dec 2017

257. 5 Steps



[Step 2.1]



[Step 3.1]

Overview

Steps/Stages

1.1 S:DMF, 1 h, 120°C

1.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

2.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

2.2 R:NaCl, S:H_2O

3.1 R:DCC, R:4-DMAP, S:CH_2Cl_2, rt

3.2 S:CH_2Cl_2, rt; overnight, rt

4.1 R:$PhSiH_3$, C:$Pd(PPh_3)_4$, S:MeOH, S:CH_2Cl_2, rt

5.1 R:Bu_4N^+ •F^-, S:CH_2Cl_2, -15°C

Notes

1) alternative preparation shown,conversion = 40%, 2) regioselective, Reactants: 4, Reagents: 7, Catalysts: 1, Solvents: 5, Steps: 5, Stages: 8, Most stages in any one step: 2

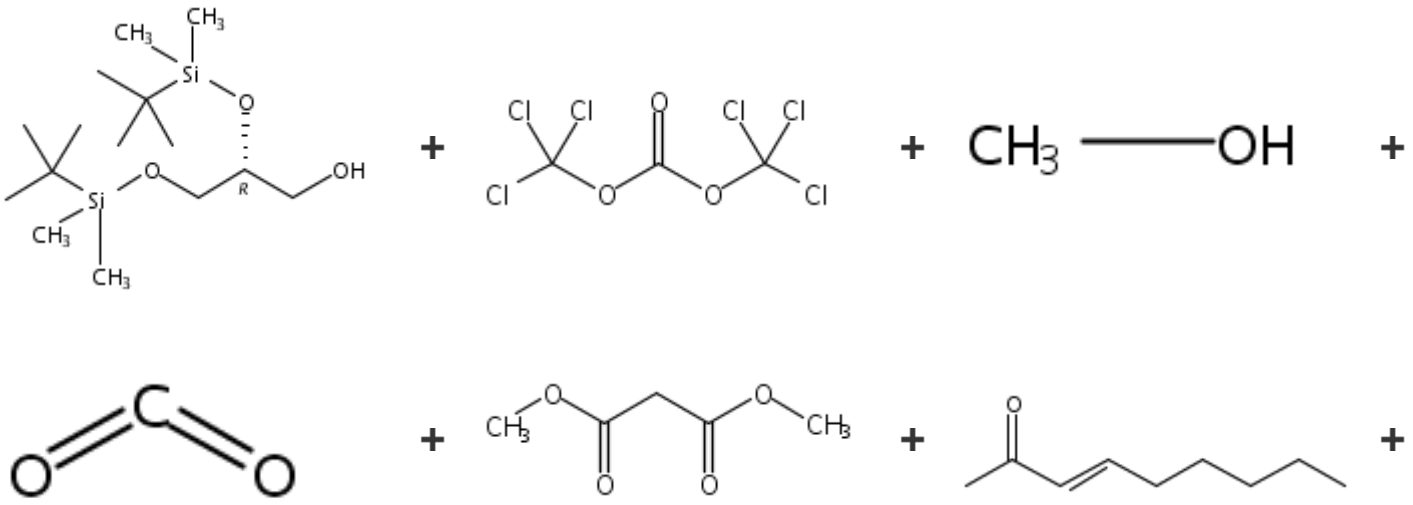
References

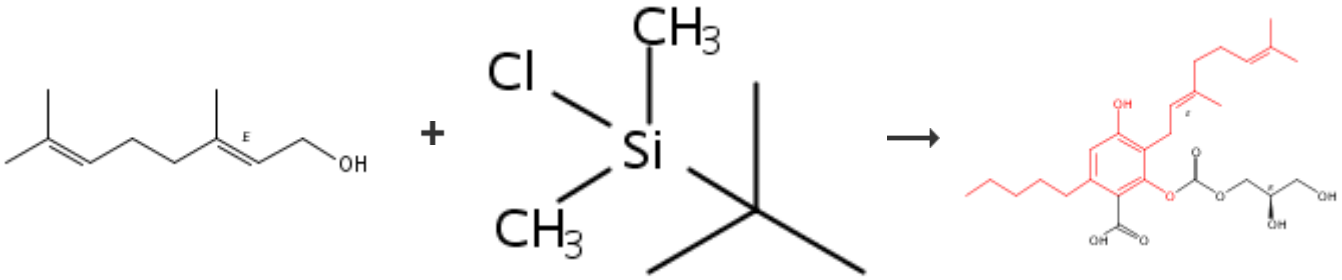
Methods for the manufacture of cannabinoid prodrugs, pharmaceutical formulations and their use

By Peet, Richard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017216362, 21 Dec 2017

258. 10 Steps (Converging)





Overview

Steps/Stages

1.1 R:Et_3N, S:CH_2Cl_2, 3-5 h, 0°C

1.1 R:Mg, S:MeOH, rt
2.1 S:DMF, 140°C

1.1 R:NaOMe, S:MeOH, rt; 3 h, reflux; reflux → rt

1.2 R:H_2O, rt

2.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

3.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
4.1 S:DMF, 1 h, 120°C

4.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

5.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

5.2 R:NaCl, S:H_2O

6.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

7.1 R:Et_3N •3HF, S:CH_2Cl_2, -15°C; 65 h, 5°C

7.2 R:$NaHCO_3$, S:H_2O, S:AcOEt, 0°C

Notes

exothermic reaction, in the dark, conversion = 40%,alternative preparation shown, alternative preparation shown, regioselective, alternative preparation shown, Reactants: 8, Reagents: 11, Solvents: 6, Steps: 10, Stages: 14, Most stages in any one step: 2

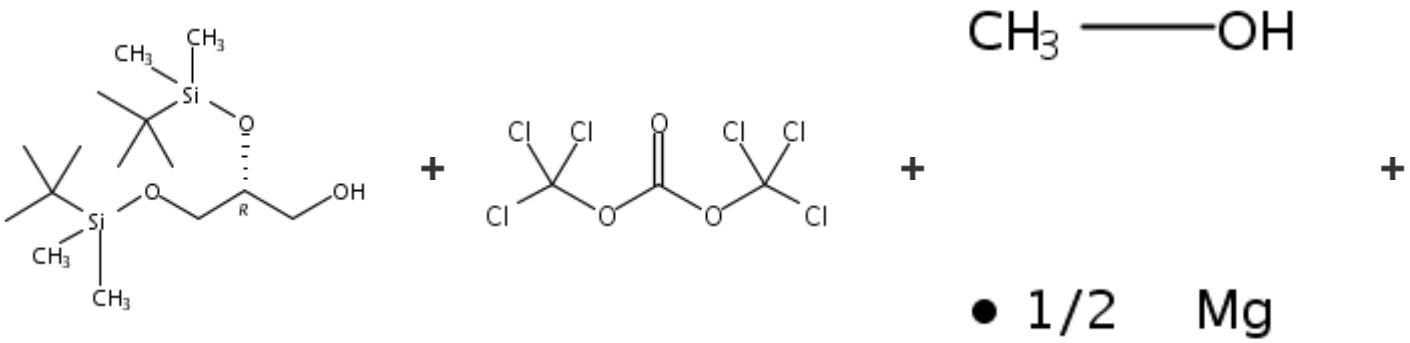
References

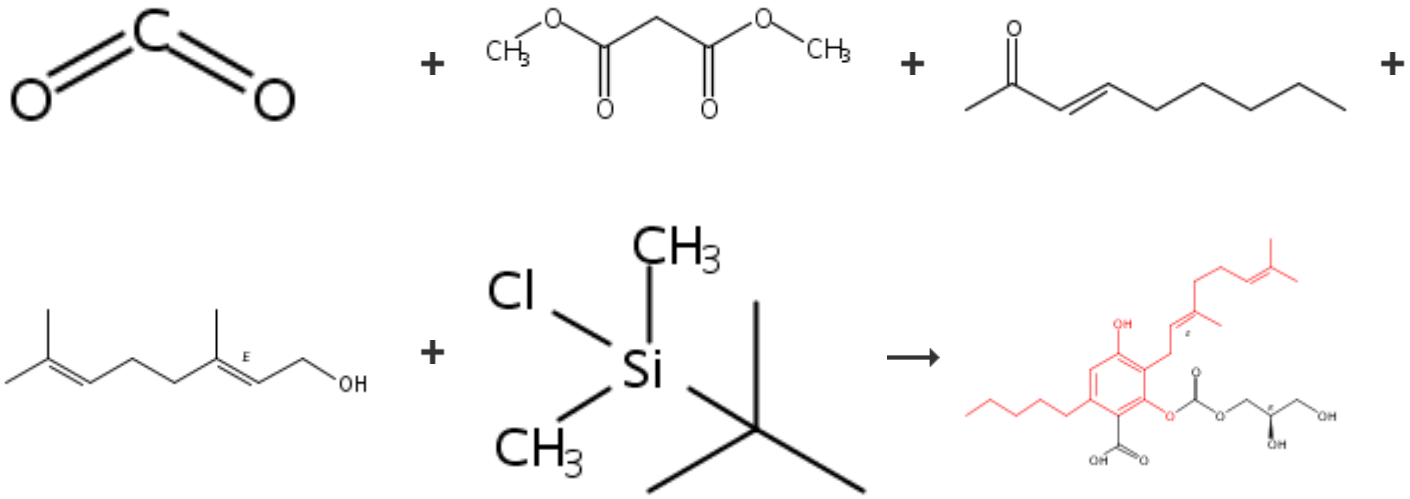
Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

259. 9 Steps (Converging)





Overview

Steps/Stages

1.1 R:Et_3N, S:CH_2Cl_2, 3-5 h, 0°C
1.1 S:DMF, 140°C

1.1 R:NaOMe, S:MeOH, rt; 3 h, reflux; reflux → rt

1.2 R:H_2O, rt

2.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

3.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
4.1 S:DMF, 1 h, 120°C

4.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

5.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

5.2 R:NaCl, S:H_2O

6.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

7.1 R:Et_3N •3HF, S:CH_2Cl_2, -15°C; 65 h, 5°C

7.2 R:$NaHCO_3$, S:H_2O, S:AcOEt, 0°C

Notes

exothermic reaction, in the dark, conversion = 40%,alternative preparation shown, alternative preparation shown, regioselective, alternative preparation shown, Reactants: 8, Reagents: 10, Solvents: 6, Steps: 9, Stages: 13, Most stages in any one step: 2

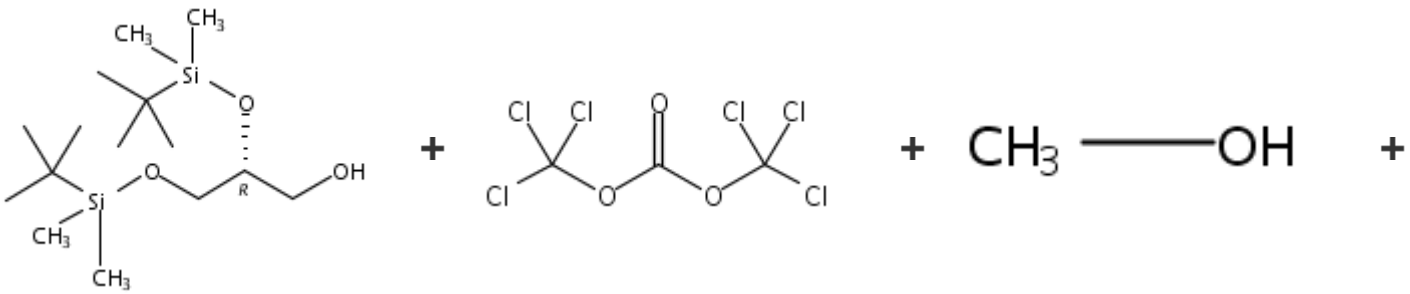
References

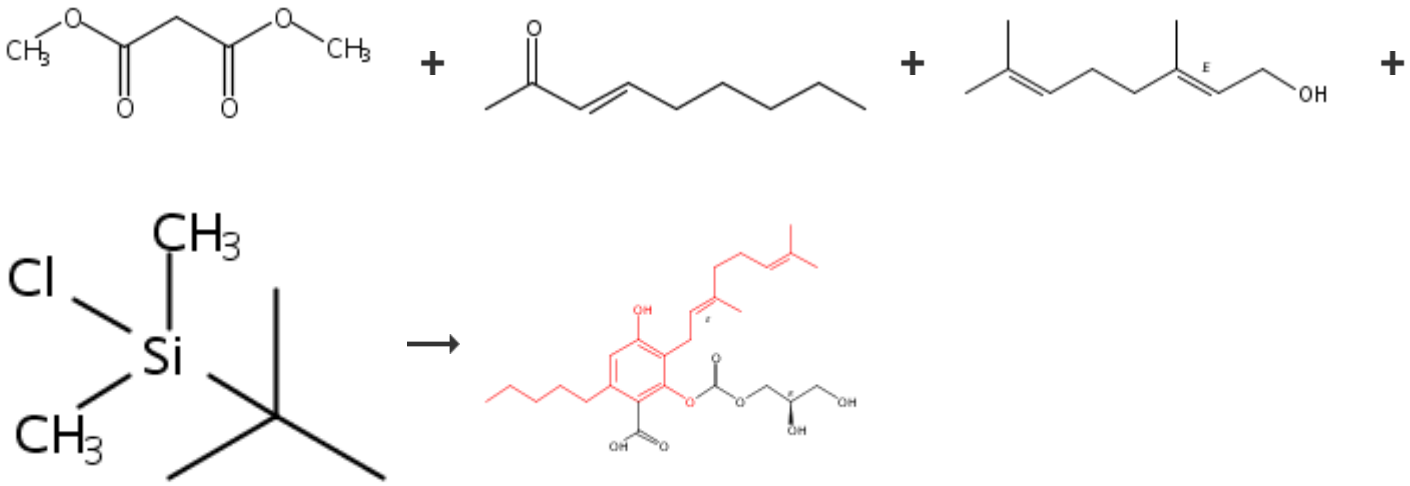
Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

260. 9 Steps (Converging)





Overview

Steps/Stages

1.1 R:Et_3N, S:CH_2Cl_2, 3-5 h, 0°C

1.1 R:Mg, S:MeOH, rt

1.1 R:NaOMe, S:MeOH, rt; 3 h, reflux; reflux → rt

1.2 R:H_2O, rt

2.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

3.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
4.1 S:H_2O, cooled; 50°C; 3 h, 50°C; 50°C → rt

4.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, rt, pH 2

5.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

5.2 R:NaCl, S:H_2O

6.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

7.1 R:Et_3N •3HF, S:CH_2Cl_2, -15°C; 65 h, 5°C

7.2 R:$NaHCO_3$, S:H_2O, S:AcOEt, 0°C

Notes

in the dark, conversion = 85%,alternative preparation shown,reaction in a sealed pressure vessel, alternative preparation shown, regioselective, alternative preparation shown, Reactants: 7, Reagents: 11, Solvents: 6, Steps: 9, Stages: 13, Most stages in any one step: 2

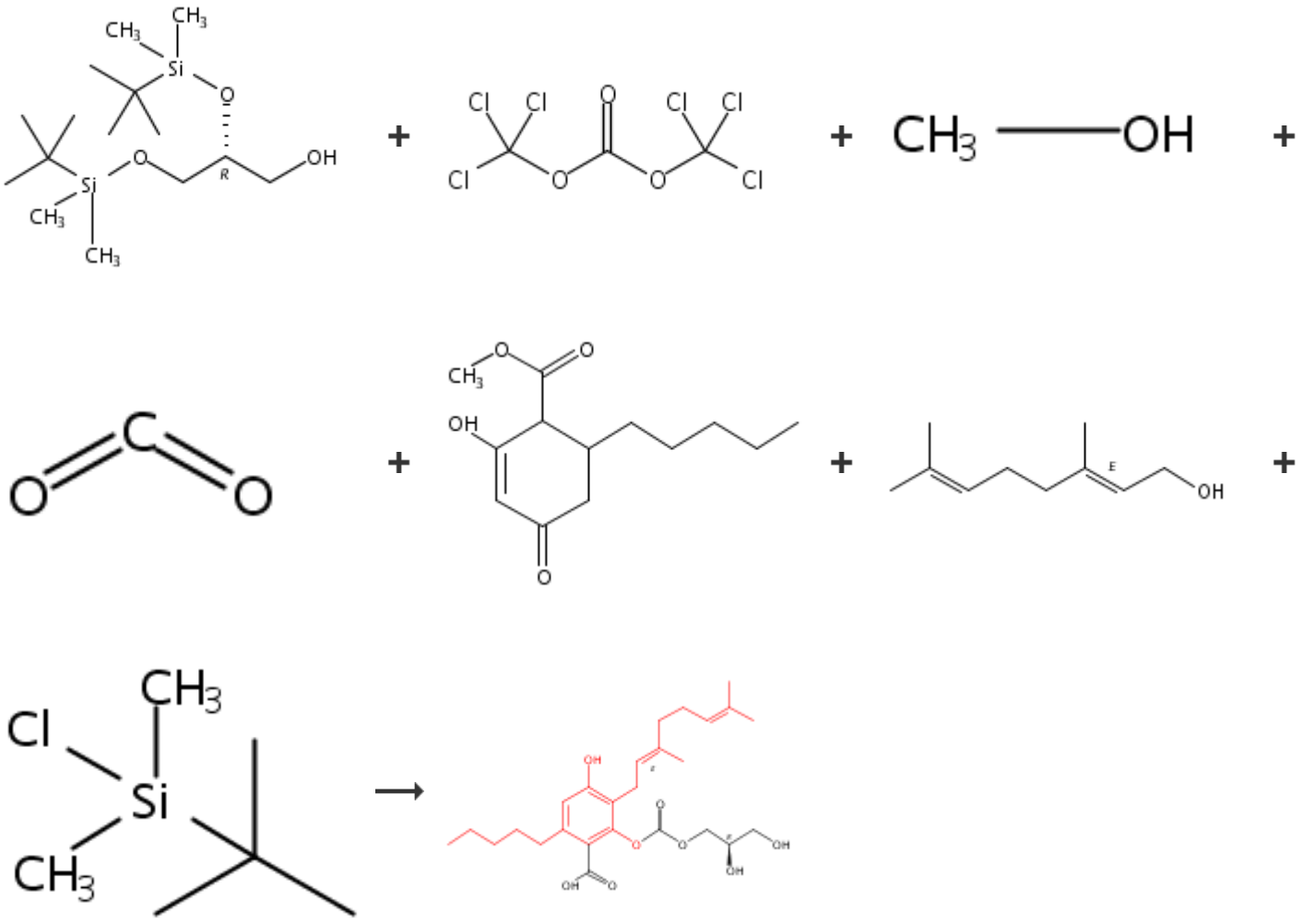
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

261. 9 Steps (Converging)



Overview

Steps/Stages

1.1 R:Et_3N, S:CH_2Cl_2, 3-5 h, 0°C

1.1 R:Mg, S:MeOH, rt
2.1 S:DMF, 140°C

1.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

2.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
3.1 S:DMF, 1 h, 120°C

3.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

4.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

4.2 R:NaCl, S:H_2O

5.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

6.1 R:Et_3N •3HF, S:CH_2Cl_2, -15°C; 65 h, 5°C

6.2 R:$NaHCO_3$, S:H_2O, S:AcOEt, 0°C

Notes

exothermic reaction, in the dark, conversion = 40%,alternative preparation shown, alternative preparation shown, regioselective, alternative preparation shown, Reactants: 7, Reagents: 9, Solvents: 6, Steps: 9, Stages: 12, Most stages in any one step: 2

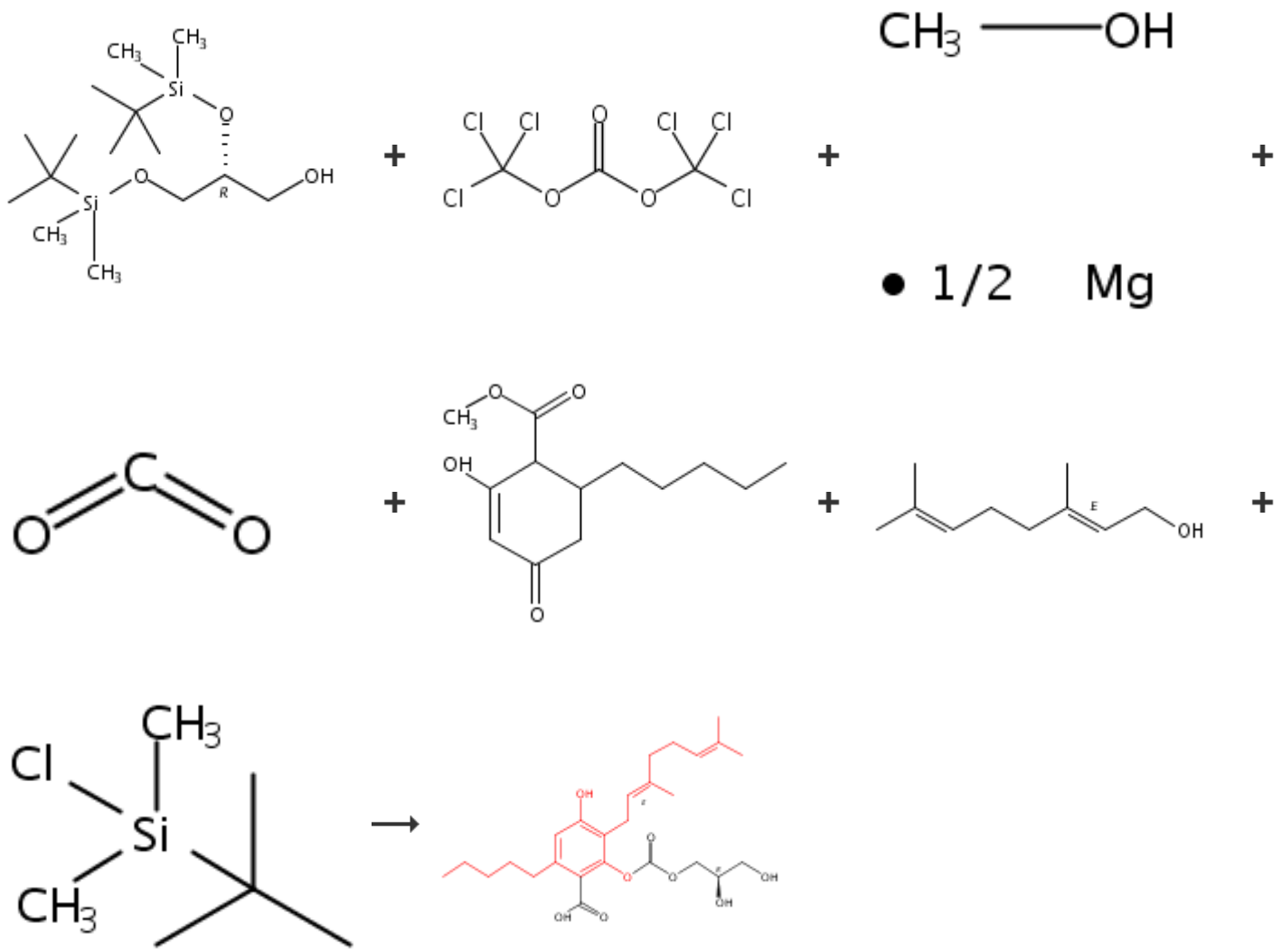
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

262. 8 Steps (Converging)



Overview

Steps/Stages **Notes**

1.1 R:Et_3N, S:CH_2Cl_2, 3-5 h, 0°C
1.1 S:DMF, 140°C

1.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

2.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
3.1 S:DMF, 1 h, 120°C

3.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

4.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

4.2 R:NaCl, S:H_2O

5.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

6.1 R:Et_3N •3HF, S:CH_2Cl_2, -15°C; 65 h, 5°C

6.2 R:$NaHCO_3$, S:H_2O, S:AcOEt, 0°C

exothermic reaction, in the dark, conversion = 40%,alternative preparation shown, alternative preparation shown, regioselective, alternative preparation shown, Reactants: 7, Reagents: 8, Solvents: 6, Steps: 8, Stages: 11, Most stages in any one step: 2

References

Biosynthesis of cannabinoid prodrugs

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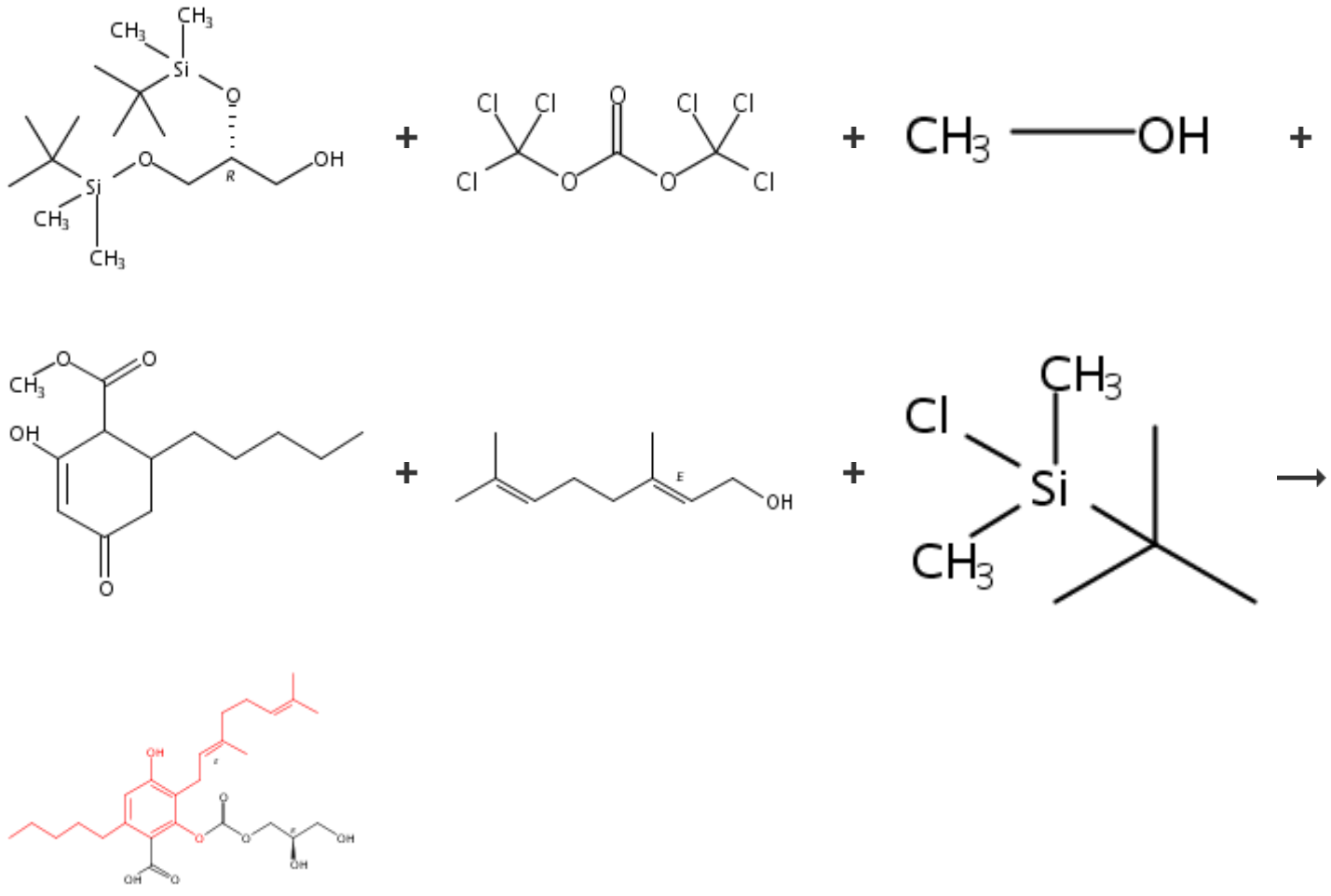
From PCT Int. Appl., 2017181118, 19 Oct 2017

263. 8 Steps (Converging)



Overview

Steps/Stages

Notes

1.1 R:Et_3N, S:CH_2Cl_2, 3-5 h, 0°C

1.1 R:Mg, S:MeOH, rt

1.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

2.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

3.1 S:H_2O, cooled; 50°C; 3 h, 50°C; 50°C → rt

3.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, rt, pH 2

4.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

4.2 R:NaCl, S:H_2O

5.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

6.1 R:Et_3N •3HF, S:CH_2Cl_2, -15°C; 65 h, 5°C

6.2 R:$NaHCO_3$, S:H_2O, S:AcOEt, 0°C

in the dark, conversion = 85%,alternative preparation shown,reaction in a sealed pressure vessel, alternative preparation shown, regioselective, alternative preparation shown, Reactants: 6, Reagents: 9, Solvents: 6, Steps: 8, Stages: 11, Most stages in any one step: 2

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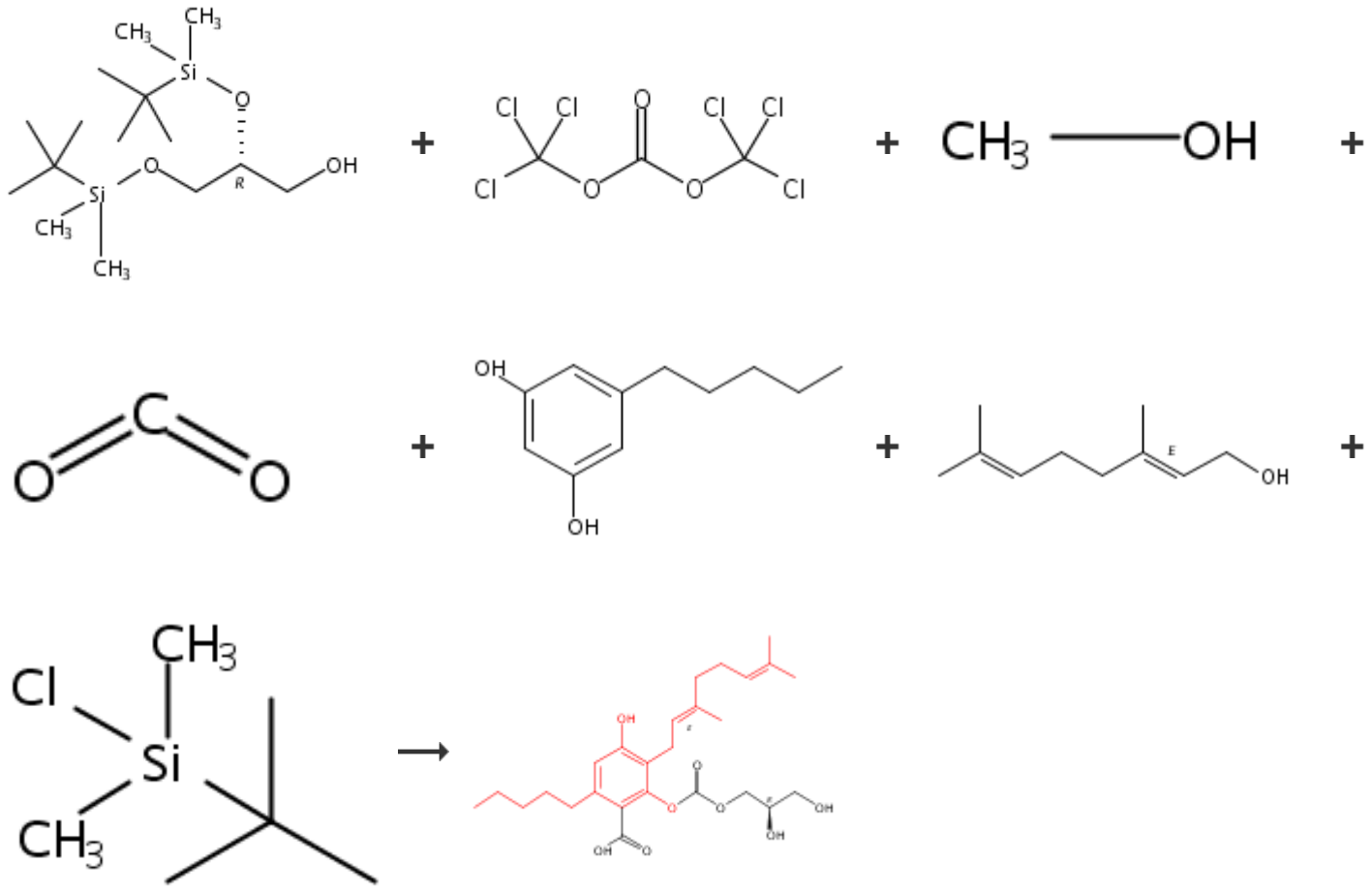
264. 8 Steps (Converging)



Overview

Steps/Stages

Notes

1.1 R:Et_3N, S:CH_2Cl_2, 3-5 h, 0°C

1.1 R:Mg, S:MeOH, rt
2.1 S:DMF, 140°C

1.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
2.1 S:DMF, 1 h, 120°C

2.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

3.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

3.2 R:NaCl, S:H_2O

4.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

5.1 R:Et_3N •3HF, S:CH_2Cl_2, -15°C; 65 h, 5°C

5.2 R:$NaHCO_3$, S:H_2O, S:AcOEt, 0°C

exothermic reaction, in the dark, conversion = 40%,alternative preparation shown, alternative preparation shown, regioselective, alternative preparation shown, Reactants: 7, Reagents: 8, Solvents: 6, Steps: 8, Stages: 11, Most stages in any one step: 2

References

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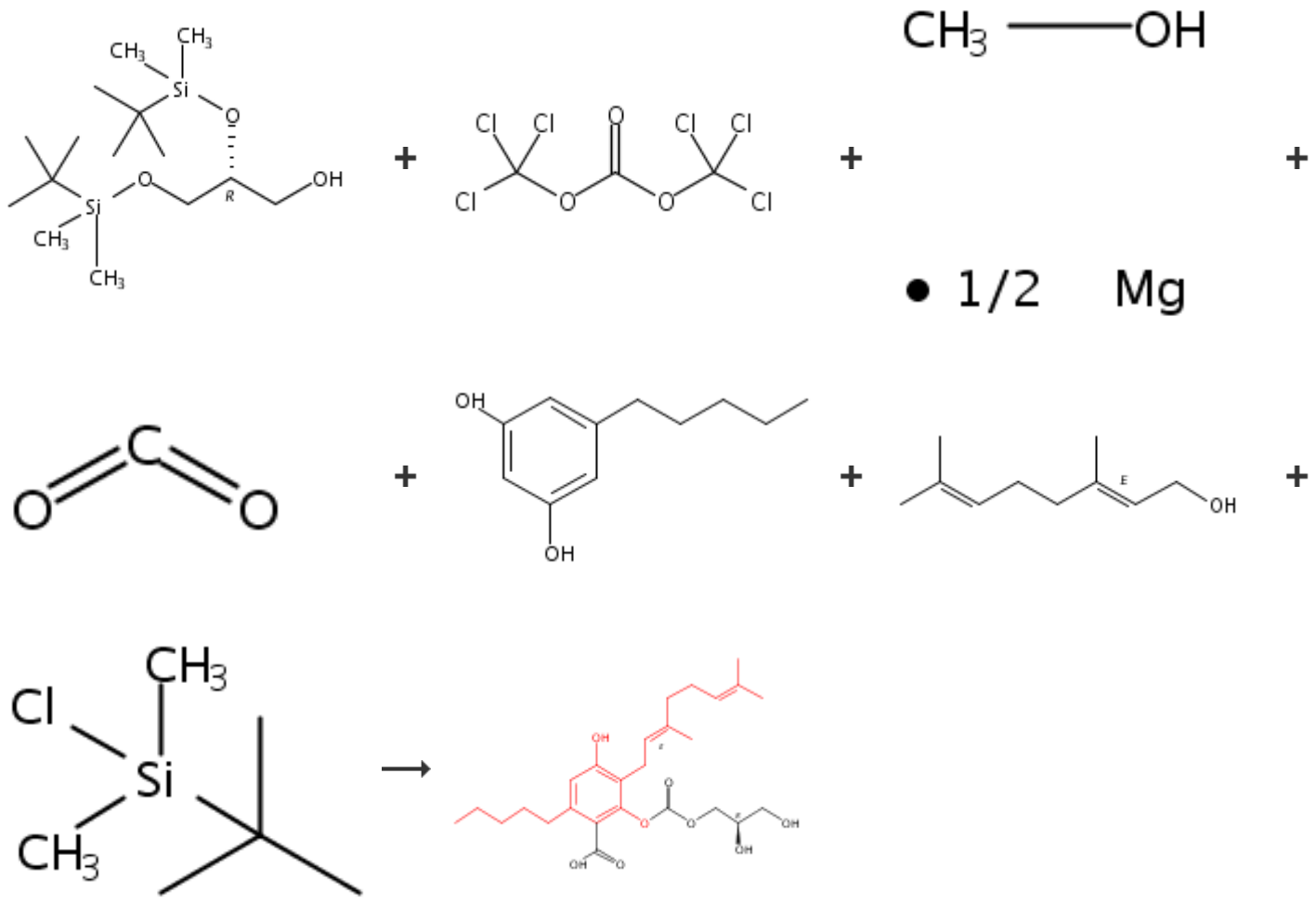
From PCT Int. Appl., 2017181118, 19 Oct 2017

265. 7 Steps (Converging)



Overview

Steps/Stages

1.1 R:Et_3N, S:CH_2Cl_2, 3-5 h, 0°C
1.1 S:DMF, 140°C

1.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
2.1 S:DMF, 1 h, 120°C

2.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

3.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

3.2 R:NaCl, S:H_2O

4.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

5.1 R:Et_3N •3HF, S:CH_2Cl_2, -15°C; 65 h, 5°C

5.2 R:$NaHCO_3$, S:H_2O, S:AcOEt, 0°C

Notes

exothermic reaction, in the dark, conversion = 40%,alternative preparation shown, alternative preparation shown, regioselective, alternative preparation shown, Reactants: 7, Reagents: 7, Solvents: 6, Steps: 7, Stages: 10, Most stages in any one step: 2

References

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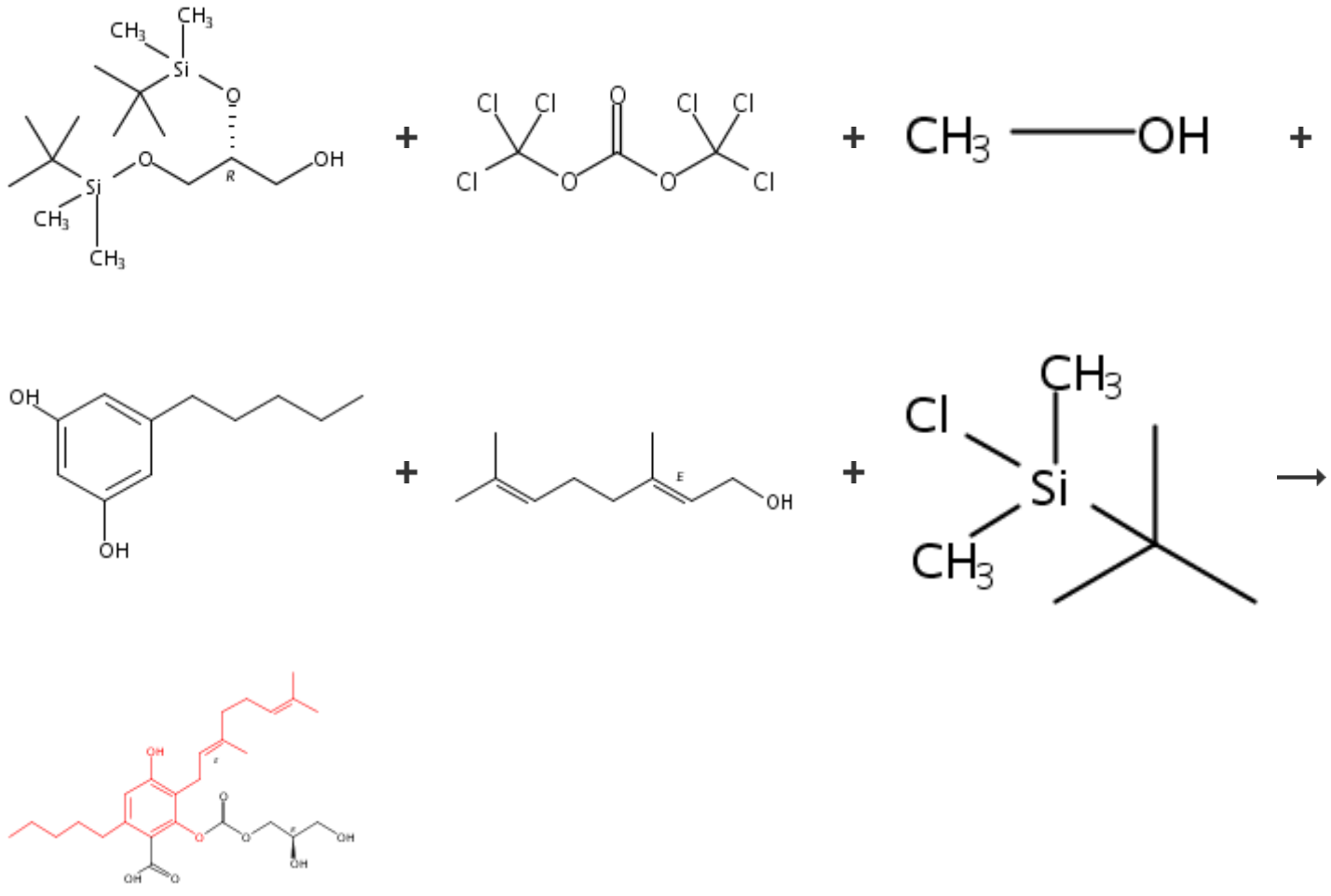
From PCT Int. Appl., 2017181118, 19 Oct 2017

266. 7 Steps (Converging)



Overview

Steps/Stages

Notes

1.1 R:Et_3N, S:CH_2Cl_2, 3-5 h, 0°C

1.1 R:Mg, S:MeOH, rt

1.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
2.1 S:H_2O, cooled; 50°C; 3 h, 50°C; 50°C → rt

2.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, rt, pH 2

3.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

3.2 R:NaCl, S:H_2O

4.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

5.1 R:Et_3N •3HF, S:CH_2Cl_2, -15°C; 65 h, 5°C

5.2 R:$NaHCO_3$, S:H_2O, S:AcOEt, 0°C

in the dark, conversion = 85%,alternative preparation shown,reaction in a sealed pressure vessel, alternative preparation shown, regioselective, alternative preparation shown, Reactants: 6, Reagents: 8, Solvents: 5, Steps: 7, Stages: 10, Most stages in any one step: 2

References

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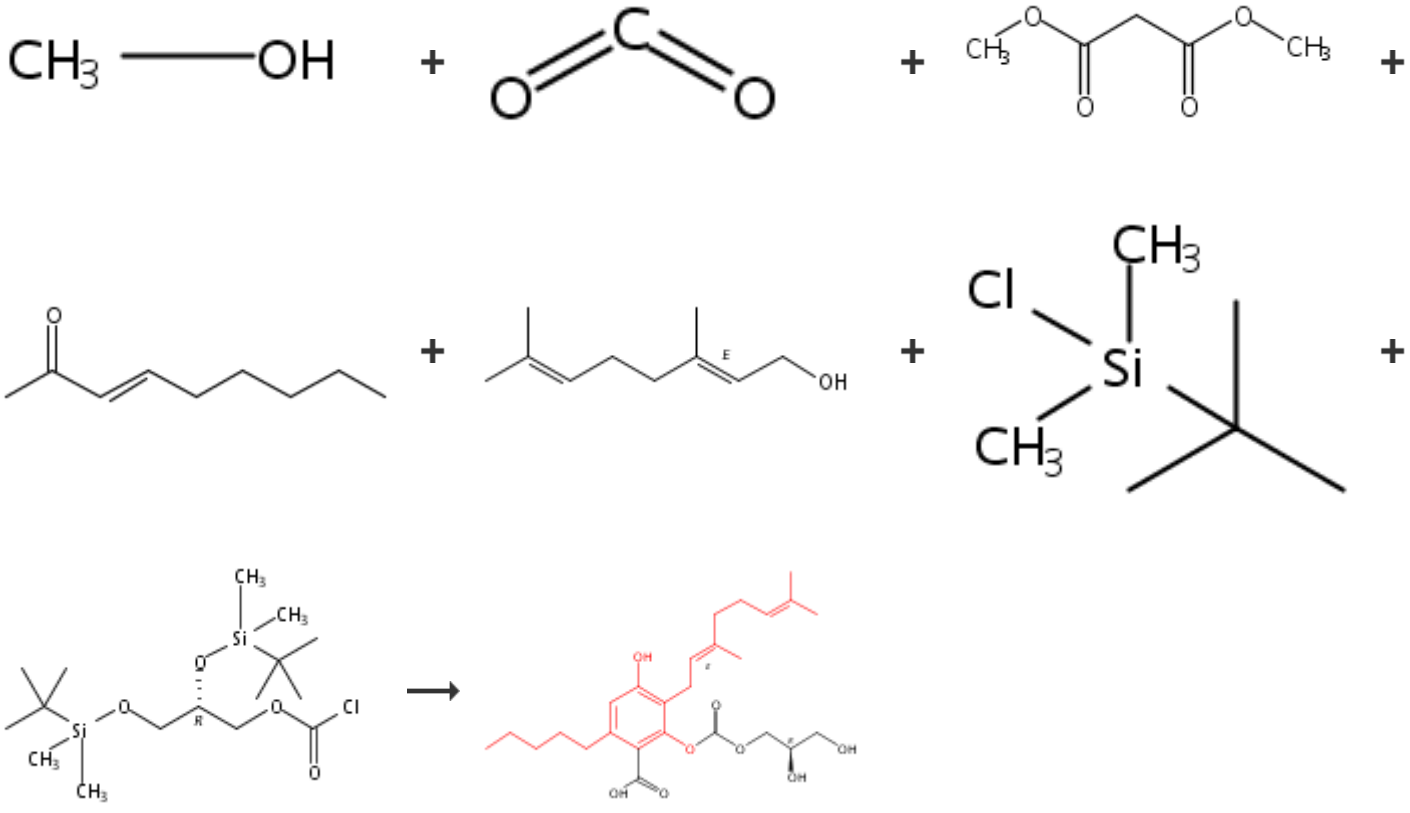
By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

267. 9 Steps (Converging)



Overview

Steps/Stages

Notes

1.1 R:Mg, S:MeOH, rt
2.1 S:DMF, 140°C

1.1 R:NaOMe, S:MeOH, rt; 3 h, reflux; reflux → rt

1.2 R:H_2O, rt

2.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

3.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
4.1 S:DMF, 1 h, 120°C

4.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

5.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

5.2 R:NaCl, S:H_2O

6.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

7.1 R:Et_3N •3HF, S:CH_2Cl_2, -15°C; 65 h, 5°C

7.2 R:$NaHCO_3$, S:H_2O, S:AcOEt, 0°C

exothermic reaction, in the dark, conversion = 40%,alternative preparation shown, alternative preparation shown, regioselective, alternative preparation shown, Reactants: 7, Reagents: 11, Solvents: 6, Steps: 9, Stages: 13, Most stages in any one step: 2

References

Biosynthesis of cannabinoid prodrugs

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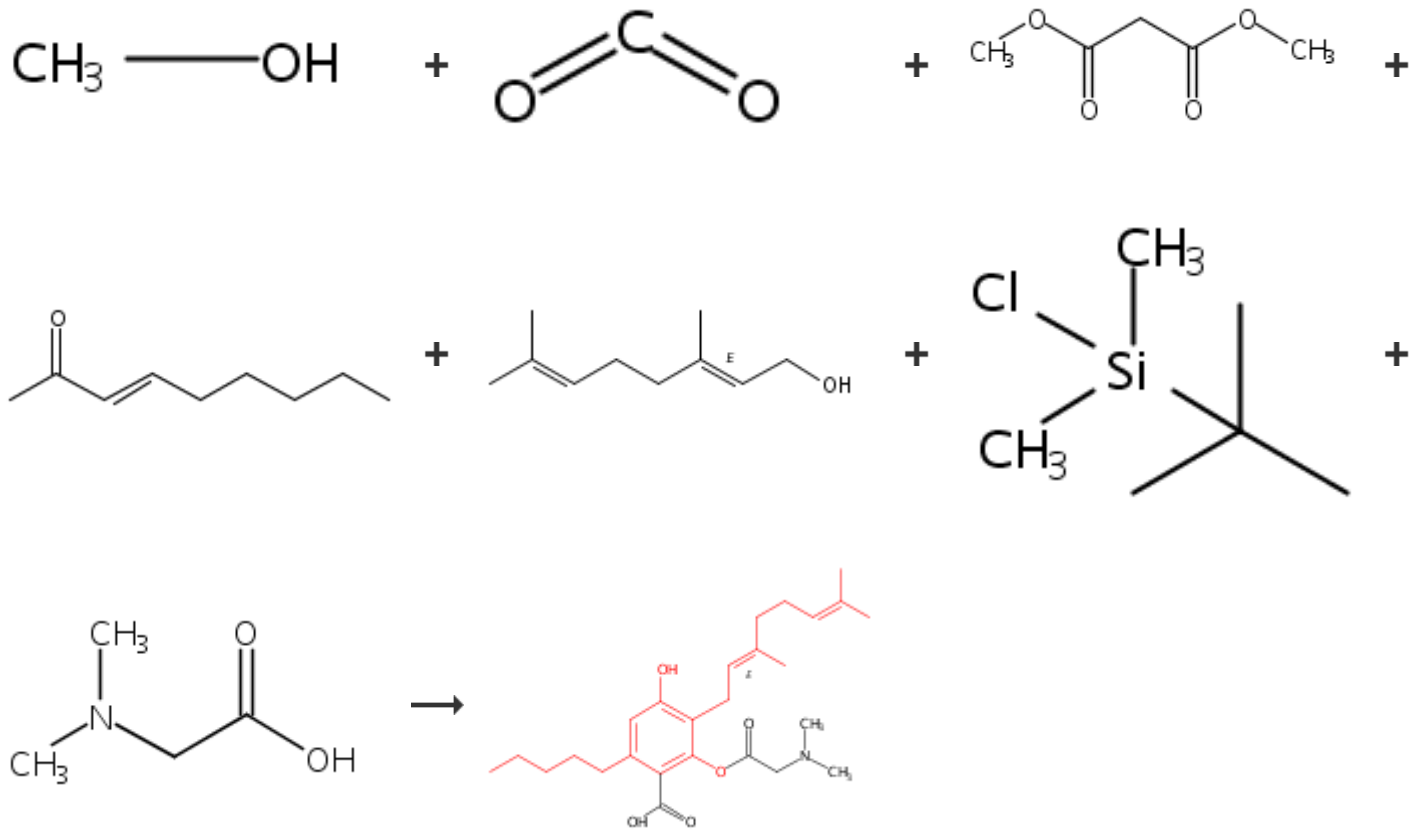
From PCT Int. Appl., 2017181118, 19 Oct 2017

268. 8 Steps (Converging)



Overview

Steps/Stages

Notes

1.1 R:Mg, S:MeOH, rt
2.1 S:DMF, 140°C

1.1 R:NaOMe, S:MeOH, rt; 3 h, reflux; reflux → rt

1.2 R:H_2O, rt

2.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

3.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
4.1 S:DMF, 1 h, 120°C

4.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

5.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

5.2 R:NaCl, S:H_2O

6.1 R:DCC, C:4-DMAP, S:CH_2Cl_2, rt; overnight, rt

6.2 R:$Bu_4N^+ \cdot F^-$, S:CH_2Cl_2, -15°C

exothermic reaction, in the dark, conversion = 40%,alternative preparation shown, alternative preparation shown, regioselective, alternative preparation shown,other reagent triethylamine trihydrofluoride may be used in stage 2, Reactants: 7, Reagents: 10, Catalysts: 1, Solvents: 5, Steps: 8, Stages: 12, Most stages in any one step: 2

References

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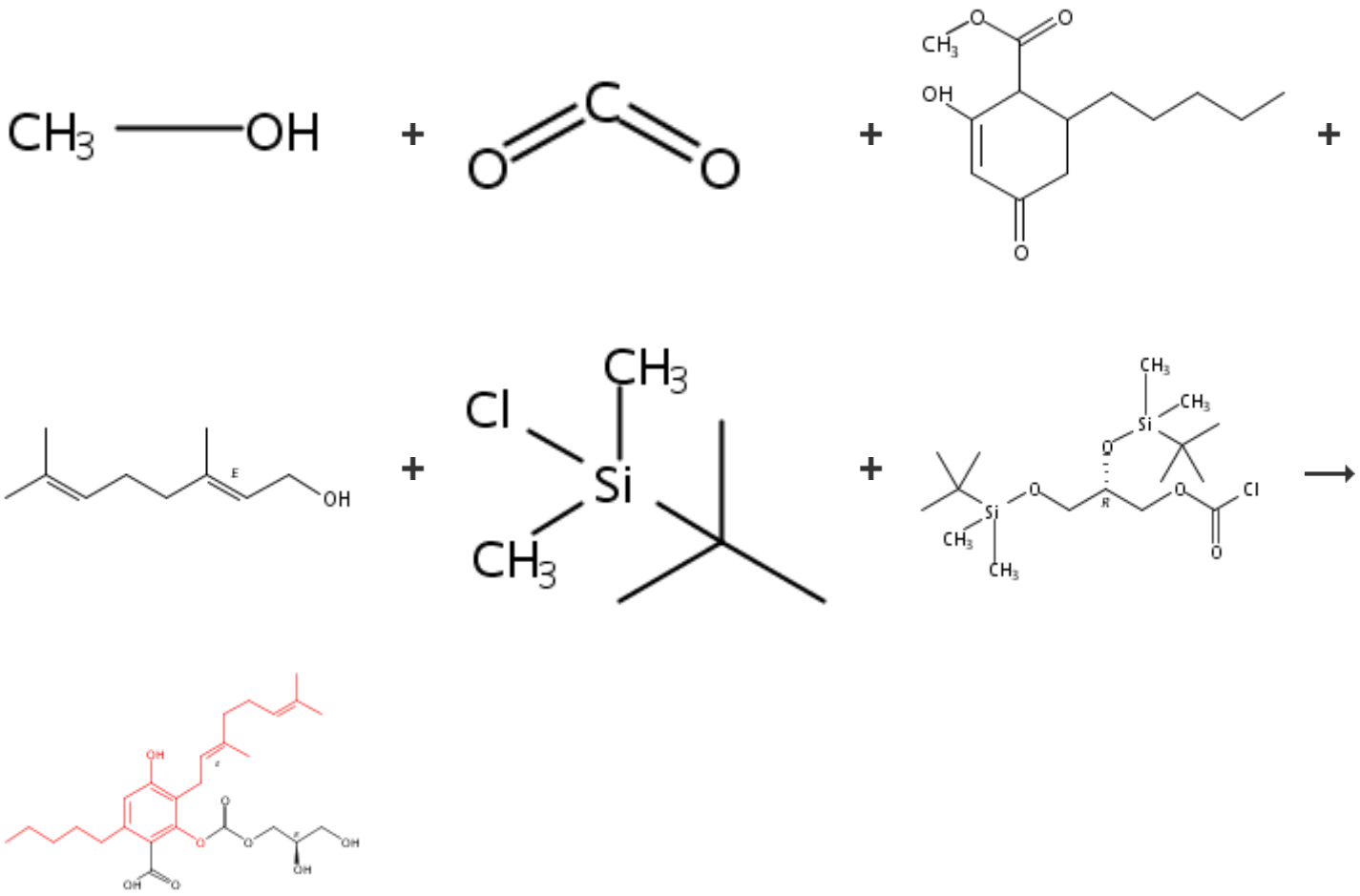
269. 8 Steps (Converging)



Overview

Steps/Stages

Notes

1.1 R:Mg, S:MeOH, rt
2.1 S:DMF, 140°C

1.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

2.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
3.1 S:DMF, 1 h, 120°C

3.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

4.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

4.2 R:NaCl, S:H_2O

5.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

6.1 R:Et_3N •3HF, S:CH_2Cl_2, -15°C; 65 h, 5°C

6.2 R:$NaHCO_3$, S:H_2O, S:AcOEt, 0°C

exothermic reaction, in the dark, conversion = 40%,alternative preparation shown, alternative preparation shown, regioselective, alternative preparation shown, Reactants: 6, Reagents: 9, Solvents: 6, Steps: 8, Stages: 11, Most stages in any one step: 2

References

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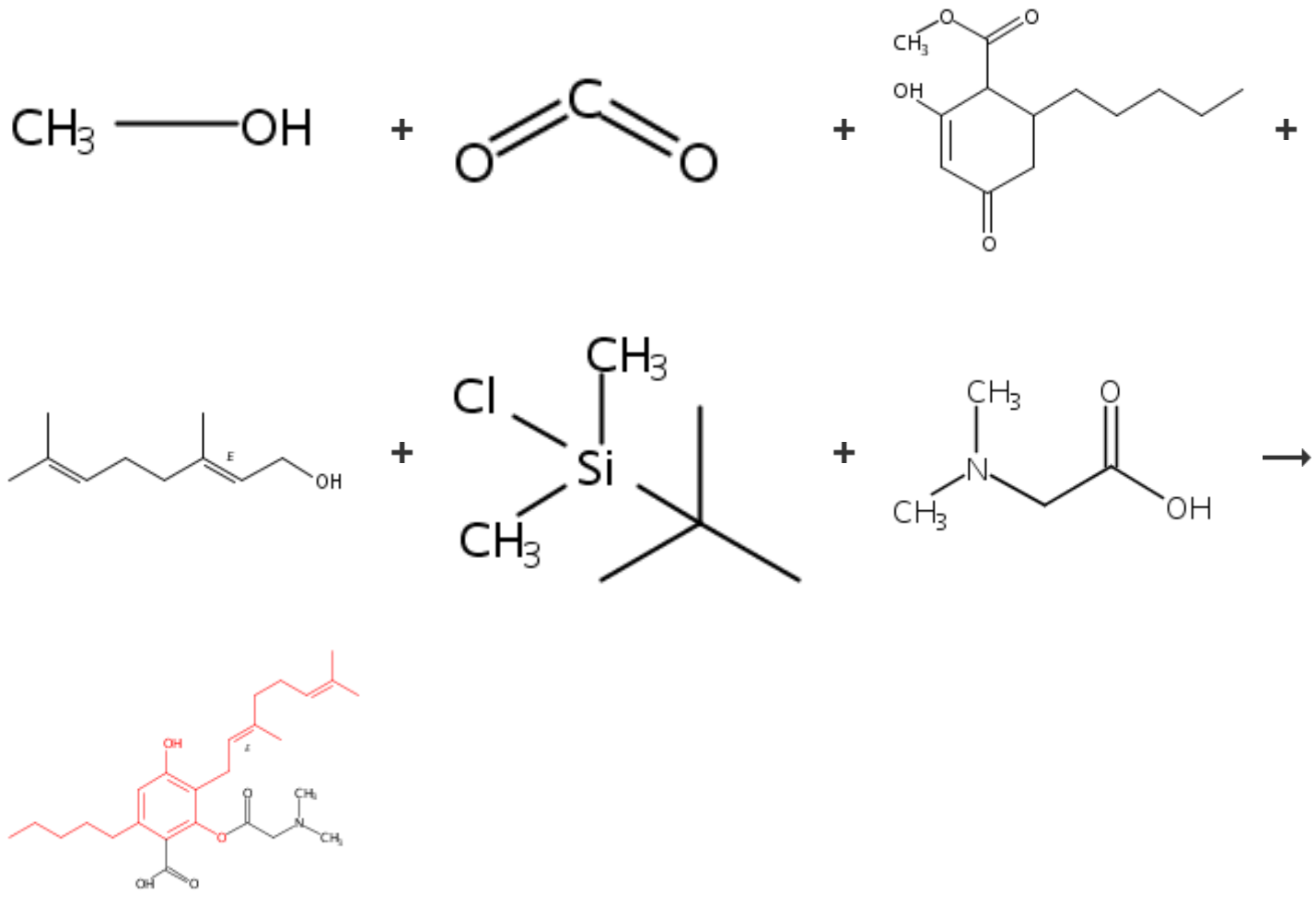
270. 7 Steps (Converging)



Overview

Steps/Stages

Notes

1.1 R:Mg, S:MeOH, rt
2.1 S:DMF, 140°C

1.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

2.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
3.1 S:DMF, 1 h, 120°C

3.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

4.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

4.2 R:NaCl, S:H_2O

5.1 R:DCC, C:4-DMAP, S:CH_2Cl_2, rt; overnight, rt

5.2 R:$Bu_4N^+ \cdot F^-$, S:CH_2Cl_2, -15°C

exothermic reaction, in the dark, conversion = 40%,alternative preparation shown, alternative preparation shown, regioselective, alternative preparation shown,other reagent triethylamine trihydrofluoride may be used in stage 2, Reactants: 6, Reagents: 8, Catalysts: 1, Solvents: 5, Steps: 7, Stages: 10, Most stages in any one step: 2

References

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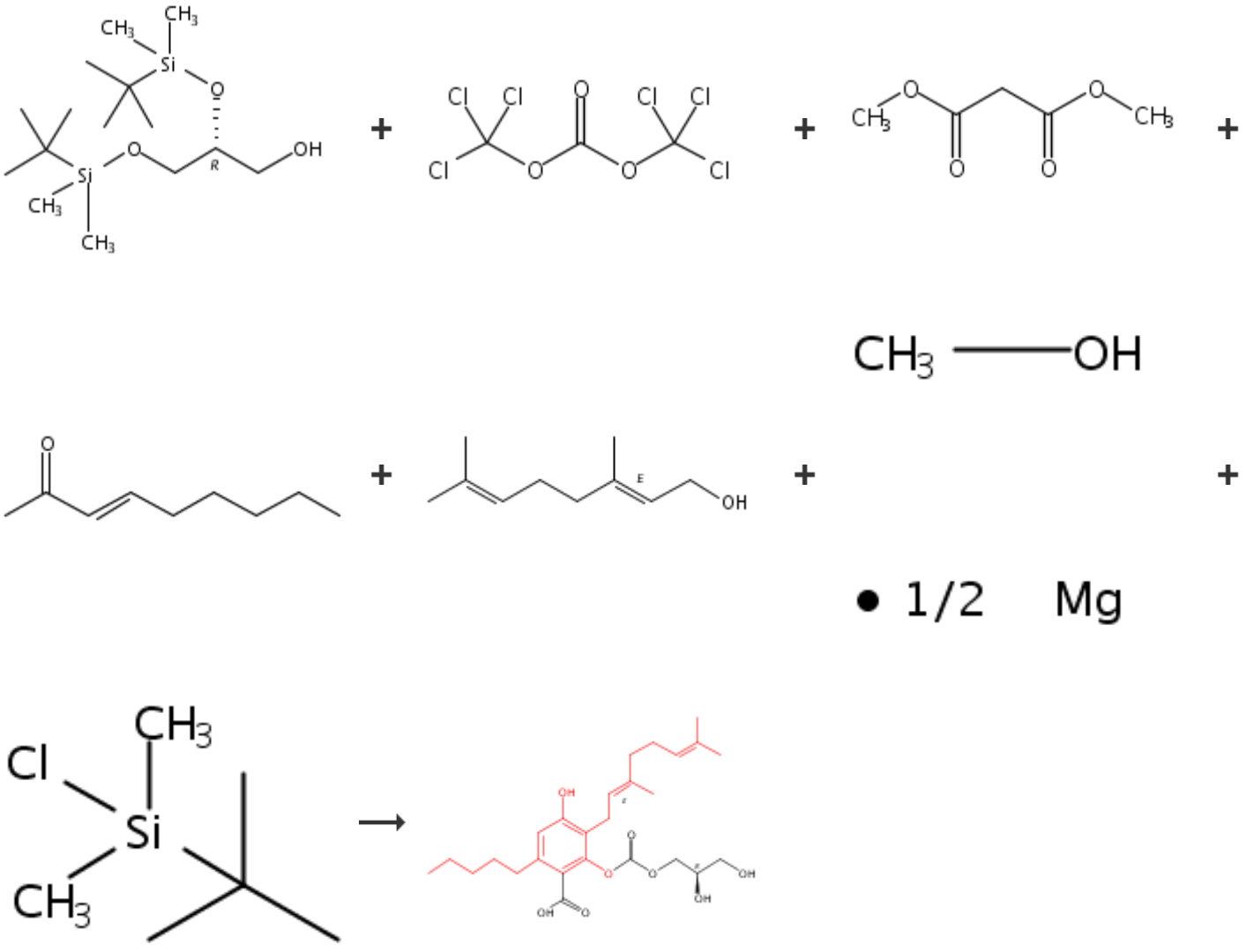
271. 8 Steps (Converging)



Overview

Steps/Stages

1.1 R:Et_3N, S:CH_2Cl_2, 3-5 h, 0°C

1.1 R:NaOMe, S:MeOH, rt; 3 h, reflux; reflux → rt

1.2 R:H_2O, rt

2.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

3.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
4.1 S:H_2O, cooled; 50°C; 3 h, 50°C; 50°C → rt

4.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, rt, pH 2

5.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

5.2 R:NaCl, S:H_2O

6.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

7.1 R:Et_3N •3HF, S:CH_2Cl_2, -15°C; 65 h, 5°C

7.2 R:$NaHCO_3$, S:H_2O, S:AcOEt, 0°C

Notes

in the dark, conversion = 85%,alternative preparation shown,reaction in a sealed pressure vessel, alternative preparation shown, regioselective, alternative preparation shown, Reactants: 7, Reagents: 10, Solvents: 6, Steps: 8, Stages: 12, Most stages in any one step: 2

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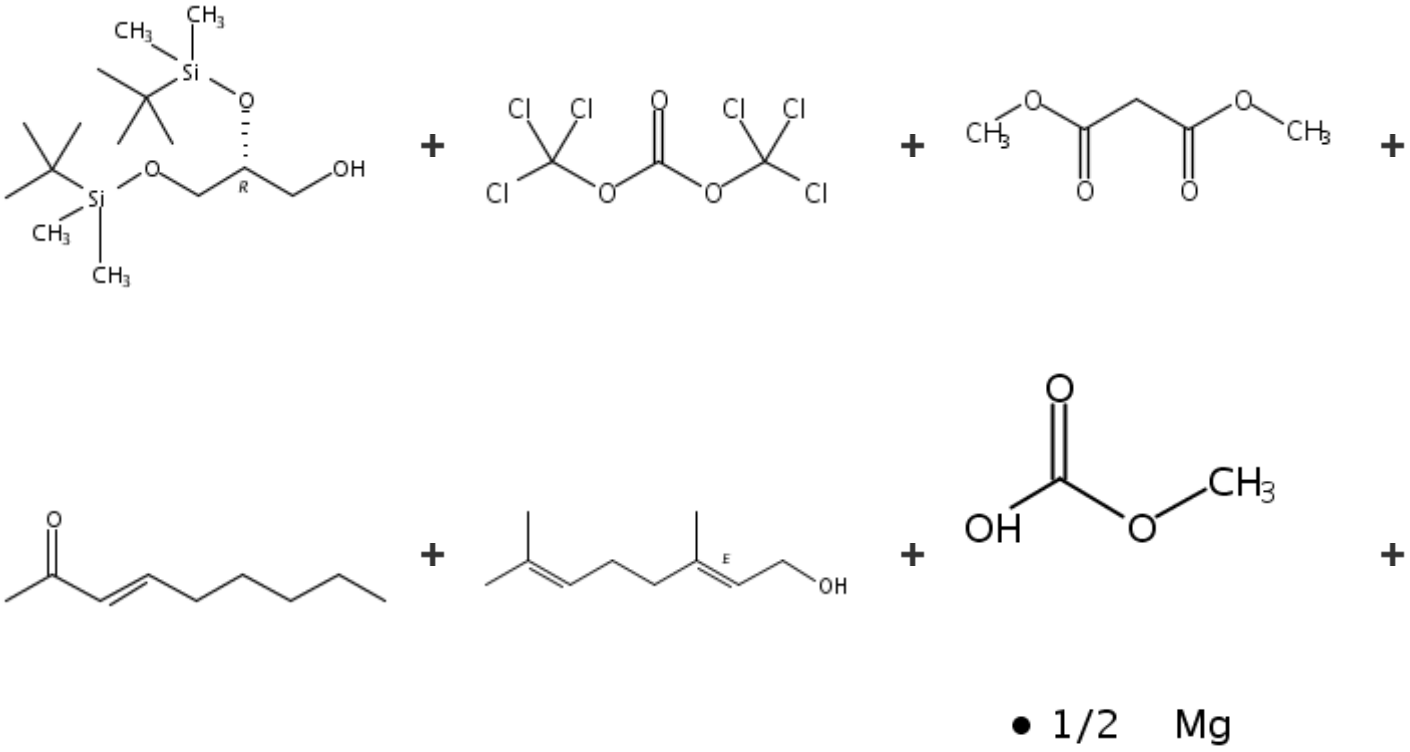
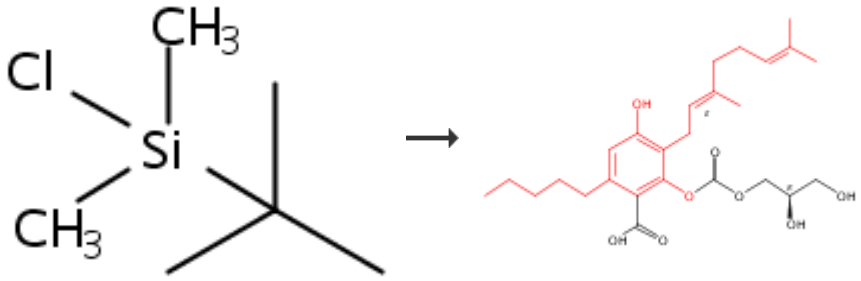
272. 8 Steps (Converging)





Overview

Steps/Stages

1.1 R:Et_3N, S:CH_2Cl_2, 3-5 h, 0°C

1.1 R:NaOMe, S:MeOH, rt; 3 h, reflux; reflux → rt

1.2 R:H_2O, rt

2.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

3.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
4.1 S:DMF, 1 h, 120°C

4.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

5.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

5.2 R:NaCl, S:H_2O

6.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

7.1 R:Et_3N •3HF, S:CH_2Cl_2, -15°C; 65 h, 5°C

7.2 R:$NaHCO_3$, S:H_2O, S:AcOEt, 0°C

Notes

in the dark, conversion = 40%,alternative preparation shown, alternative preparation shown, regioselective, alternative preparation shown, Reactants: 7, Reagents: 10, Solvents: 6, Steps: 8, Stages: 12, Most stages in any one step: 2

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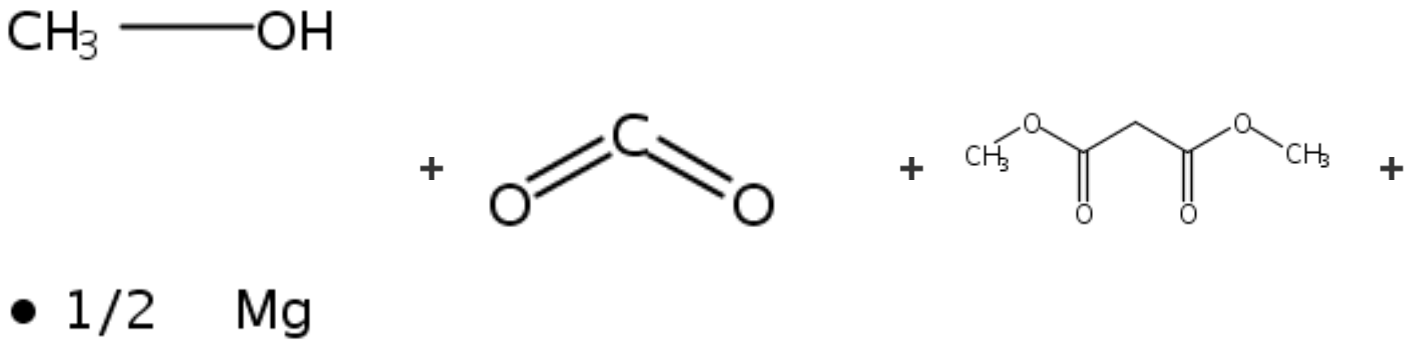
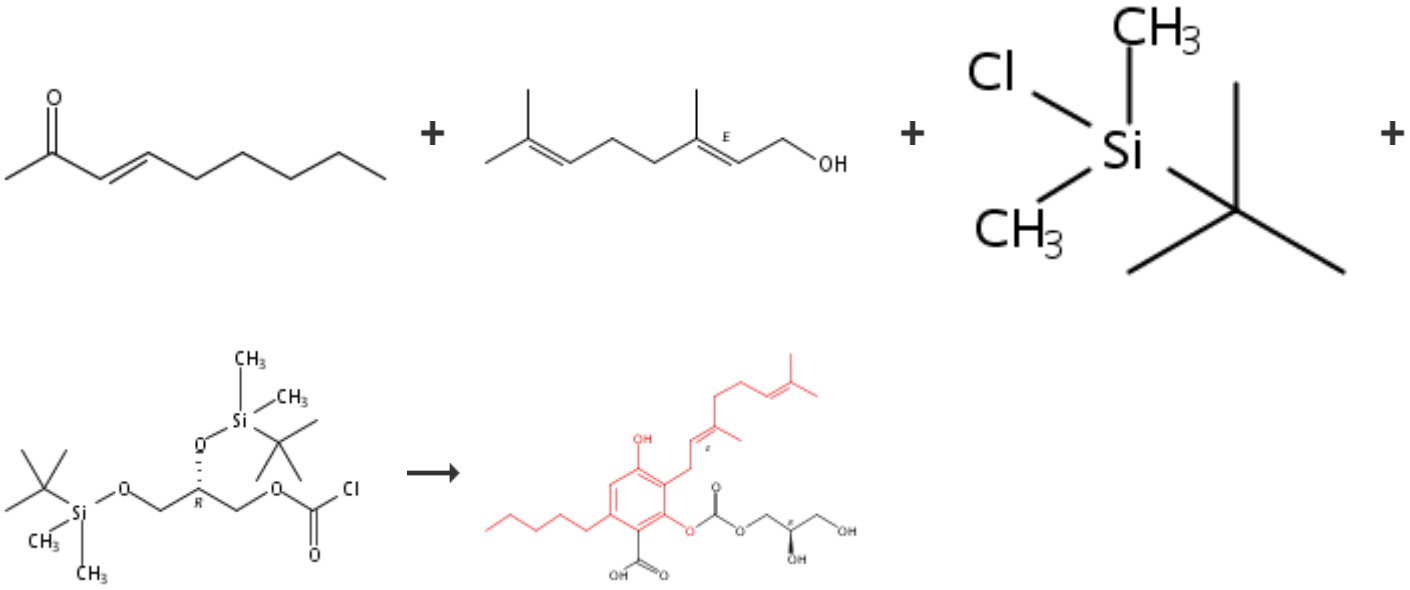
273. 8 Steps (Converging)



- 1/2 Mg



Overview

Steps/Stages

1.1 S:DMF, 140°C

1.1 R:NaOMe, S:MeOH, rt; 3 h, reflux; reflux → rt

1.2 R:H_2O, rt

2.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

3.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

4.1 S:DMF, 1 h, 120°C

4.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

5.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

5.2 R:NaCl, S:H_2O

6.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

7.1 R:Et_3N •3HF, S:CH_2Cl_2, -15°C; 65 h, 5°C

7.2 R:$NaHCO_3$, S:H_2O, S:AcOEt, 0°C

Notes

exothermic reaction, in the dark, conversion = 40%,alternative preparation shown, alternative preparation shown, regioselective, alternative preparation shown, Reactants: 7, Reagents: 10, Solvents: 6, Steps: 8, Stages: 12, Most stages in any one step: 2

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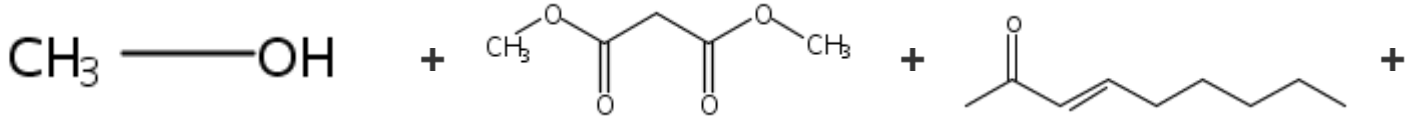
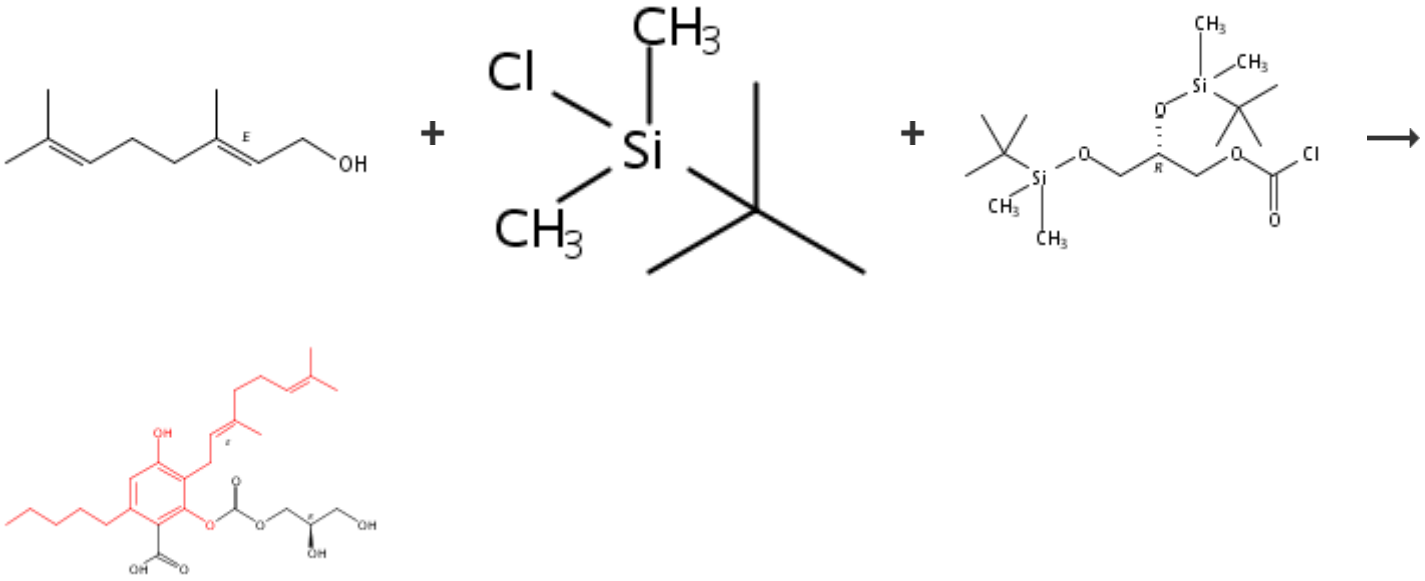
274. 8 Steps (Converging)





Overview

Steps/Stages

1.1 R:Mg, S:MeOH, rt

1.1 R:NaOMe, S:MeOH, rt; 3 h, reflux; reflux → rt

1.2 R:H_2O, rt

2.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

3.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

4.1 S:H_2O, cooled; 50°C; 3 h, 50°C; 50°C → rt

4.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, rt, pH 2

5.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

5.2 R:NaCl, S:H_2O

6.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

7.1 R:Et_3N •3HF, S:CH_2Cl_2, -15°C; 65 h, 5°C

7.2 R:$NaHCO_3$, S:H_2O, S:AcOEt, 0°C

Notes

in the dark, conversion = 85%,alternative preparation shown,reaction in a sealed pressure vessel, alternative preparation shown, regioselective, alternative preparation shown, Reactants: 6, Reagents: 11, Solvents: 6, Steps: 8, Stages: 12, Most stages in any one step: 2

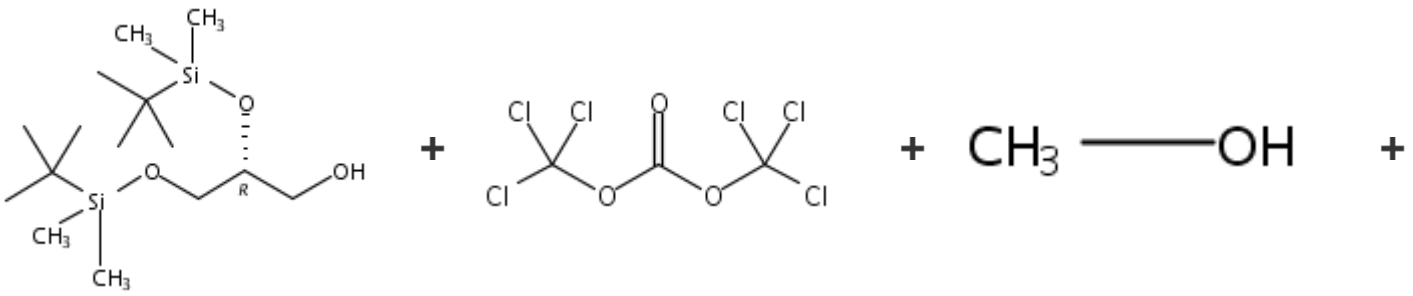
References

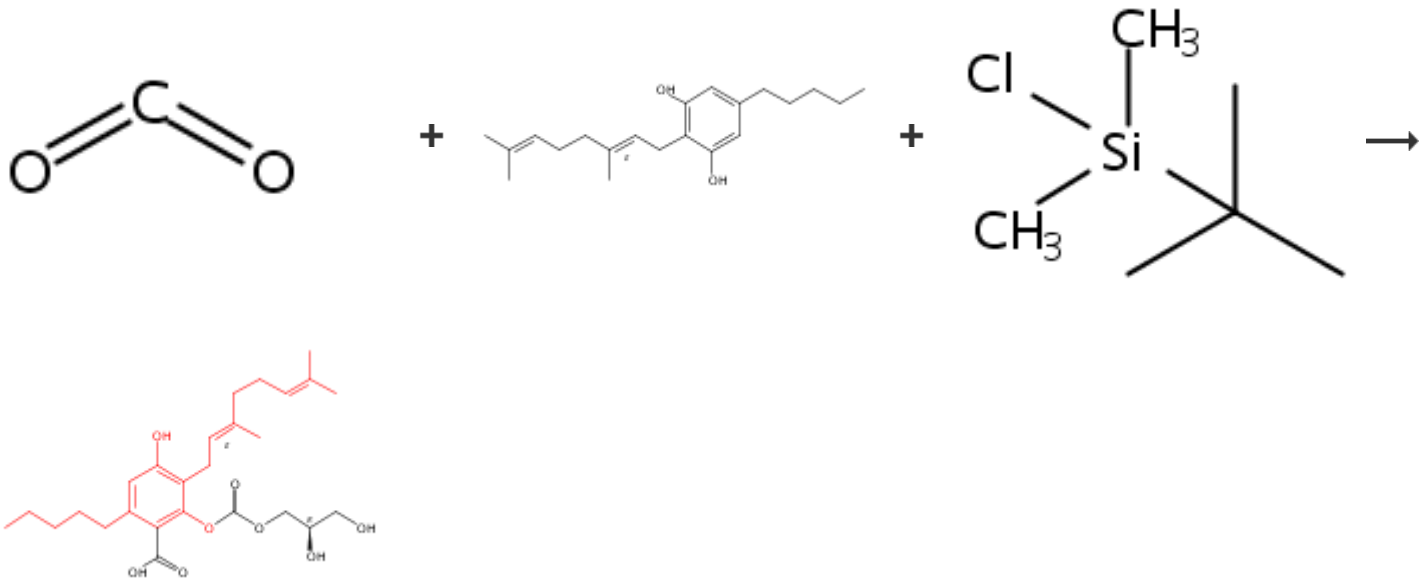
Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

275. 7 Steps (Converging)





Overview

Steps/Stages

1.1 R:Et_3N, S:CH_2Cl_2, 3-5 h, 0°C

1.1 R:Mg, S:MeOH, rt
2.1 S:DMF, 140°C
3.1 S:DMF, 1 h, 120°C

3.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

4.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

4.2 R:NaCl, S:H_2O

5.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

6.1 R:Et_3N •3HF, S:CH_2Cl_2, -15°C; 65 h, 5°C

6.2 R:$NaHCO_3$, S:H_2O, S:AcOEt, 0°C

Notes

exothermic reaction, conversion = 40%,alternative preparation shown, alternative preparation shown, regioselective, alternative preparation shown, Reactants: 6, Reagents: 7, Solvents: 6, Steps: 7, Stages: 10, Most stages in any one step: 2

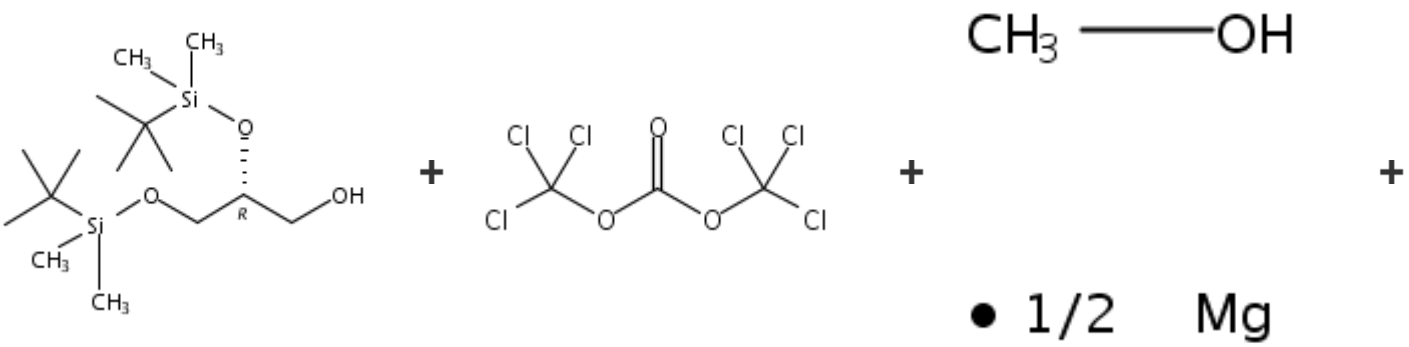
References

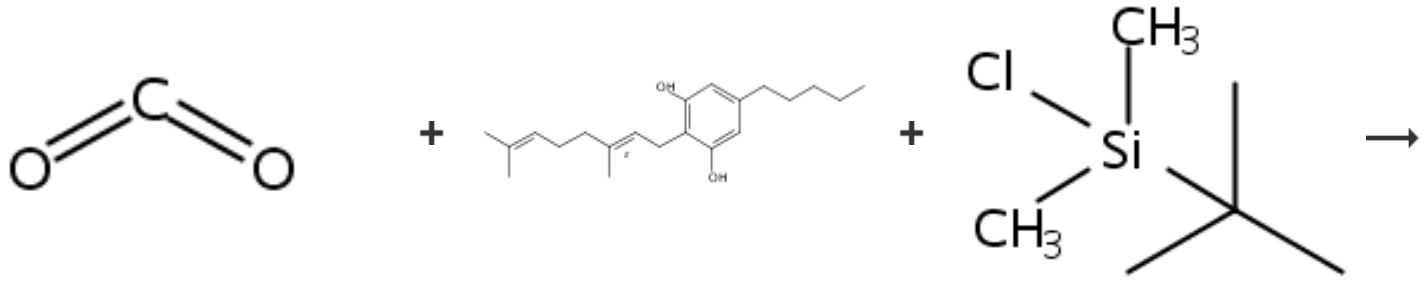
Biosynthesis of cannabinoid prodrugs

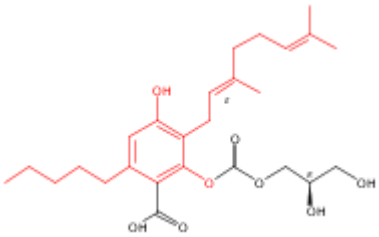
By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

276. 6 Steps (Converging)







Overview

Steps/Stages

1.1 R:Et_3N, S:CH_2Cl_2, 3-5 h, 0°C
1.1 S:DMF, 140°C
2.1 S:DMF, 1 h, 120°C

2.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

3.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

3.2 R:NaCl, S:H_2O

4.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

5.1 R:Et_3N •3HF, S:CH_2Cl_2, -15°C; 65 h, 5°C

5.2 R:$NaHCO_3$, S:H_2O, S:AcOEt, 0°C

Notes

exothermic reaction, conversion = 40%,alternative preparation shown, alternative preparation shown, regioselective, alternative preparation shown, Reactants: 6, Reagents: 6, Solvents: 6, Steps: 6, Stages: 9, Most stages in any one step: 2

References

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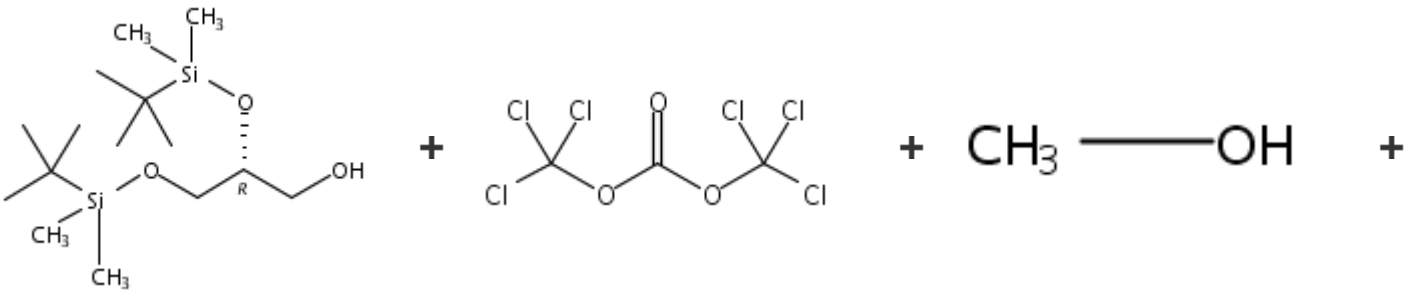
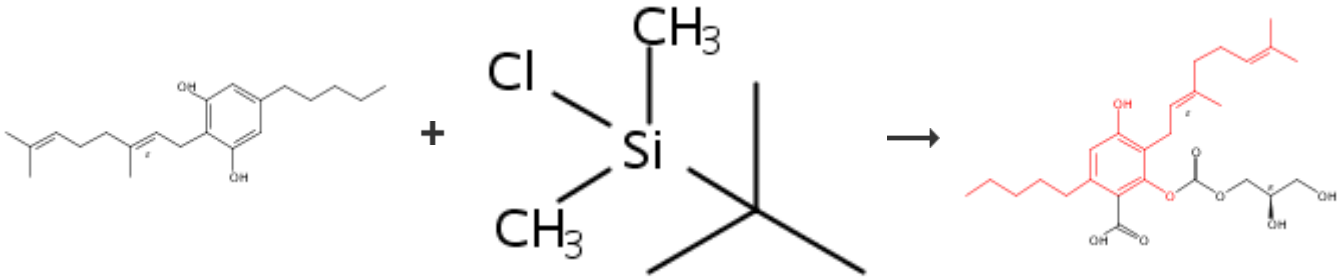
277. 6 Steps (Converging)





Overview

Steps/Stages

1.1 R:Et_3N, S:CH_2Cl_2, 3-5 h, 0°C

1.1 R:Mg, S:MeOH, rt

2.1 S:H_2O, cooled; 50°C; 3 h, 50°C; 50°C → rt

2.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, rt, pH 2

3.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

3.2 R:NaCl, S:H_2O

4.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

5.1 R:Et_3N •3HF, S:CH_2Cl_2, -15°C; 65 h, 5°C

5.2 R:$NaHCO_3$, S:H_2O, S:AcOEt, 0°C

Notes

conversion = 85%,alternative preparation shown,reaction in a sealed pressure vessel, alternative preparation shown, regioselective, alternative preparation shown, Reactants: 5, Reagents: 7, Solvents: 5, Steps: 6, Stages: 9, Most stages in any one step: 2

References

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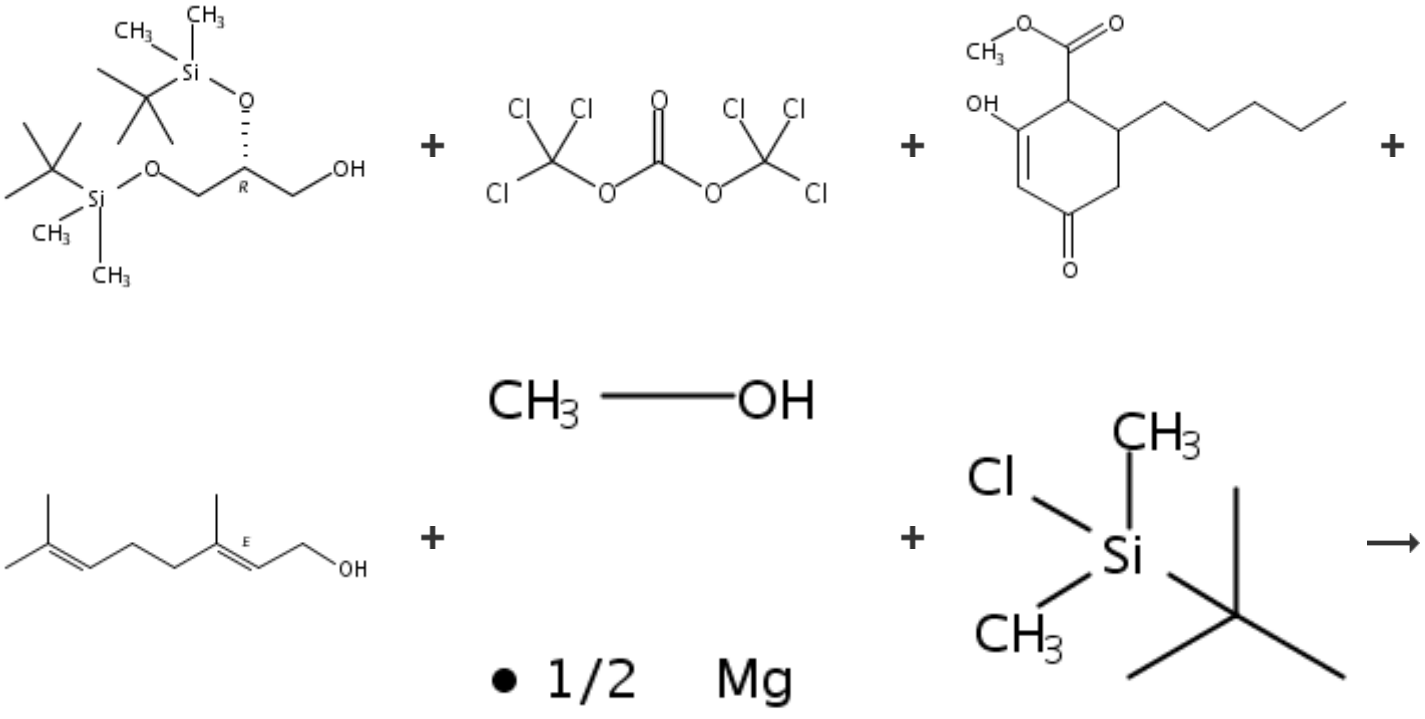
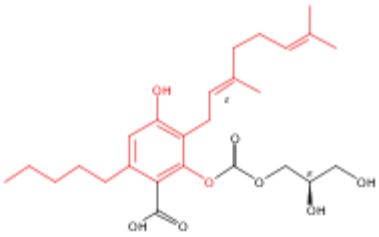
From PCT Int. Appl., 2017181118, 19 Oct 2017

278. 7 Steps (Converging)





Overview

Steps/Stages

1.1 R:Et_3N, S:CH_2Cl_2, 3-5 h, 0°C

1.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

2.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

3.1 S:H_2O, cooled; 50°C; 3 h, 50°C; 50°C → rt

3.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, rt, pH 2

4.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

4.2 R:NaCl, S:H_2O

5.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

6.1 R:Et_3N •3HF, S:CH_2Cl_2, -15°C; 65 h, 5°C

6.2 R:$NaHCO_3$, S:H_2O, S:AcOEt, 0°C

Notes

in the dark, conversion = 85%,alternative preparation shown,reaction in a sealed pressure vessel, alternative preparation shown, regioselective, alternative preparation shown, Reactants: 6, Reagents: 8, Solvents: 6, Steps: 7, Stages: 10, Most stages in any one step: 2

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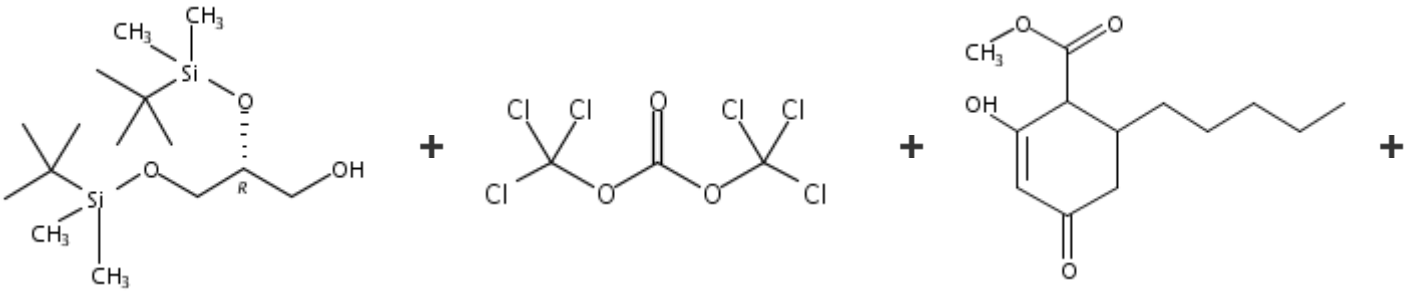

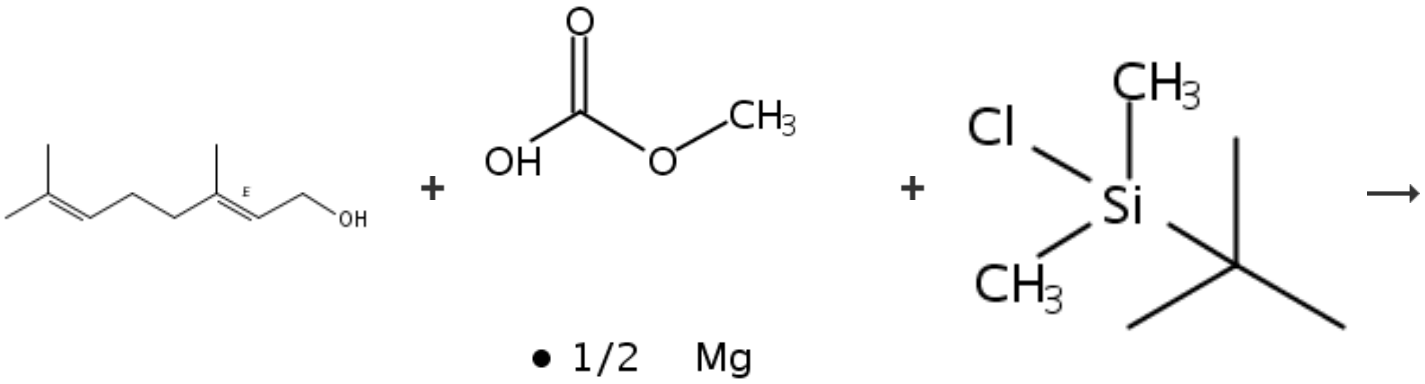

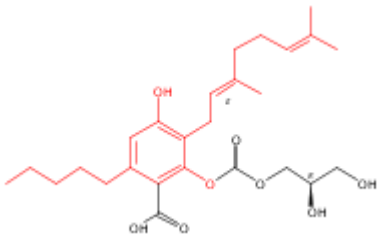

Overview

Steps/Stages

1.1 R:Et_3N, S:CH_2Cl_2, 3-5 h, 0°C

1.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

2.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
3.1 S:DMF, 1 h, 120°C

3.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

4.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

4.2 R:NaCl, S:H_2O

5.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

6.1 R:Et_3N •3HF, S:CH_2Cl_2, -15°C; 65 h, 5°C

6.2 R:$NaHCO_3$, S:H_2O, S:AcOEt, 0°C

Notes

in the dark, conversion = 40%,alternative preparation shown, alternative preparation shown, regioselective, alternative preparation shown, Reactants: 6, Reagents: 8, Solvents: 6, Steps: 7, Stages: 10, Most stages in any one step: 2

References

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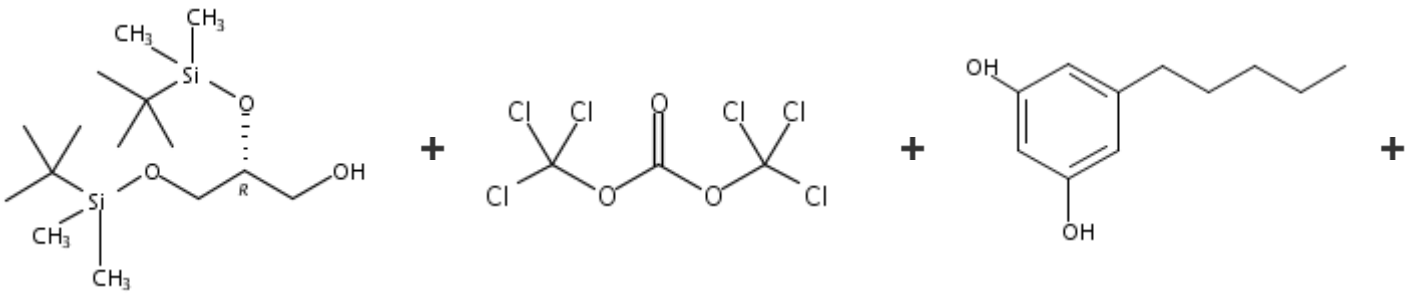
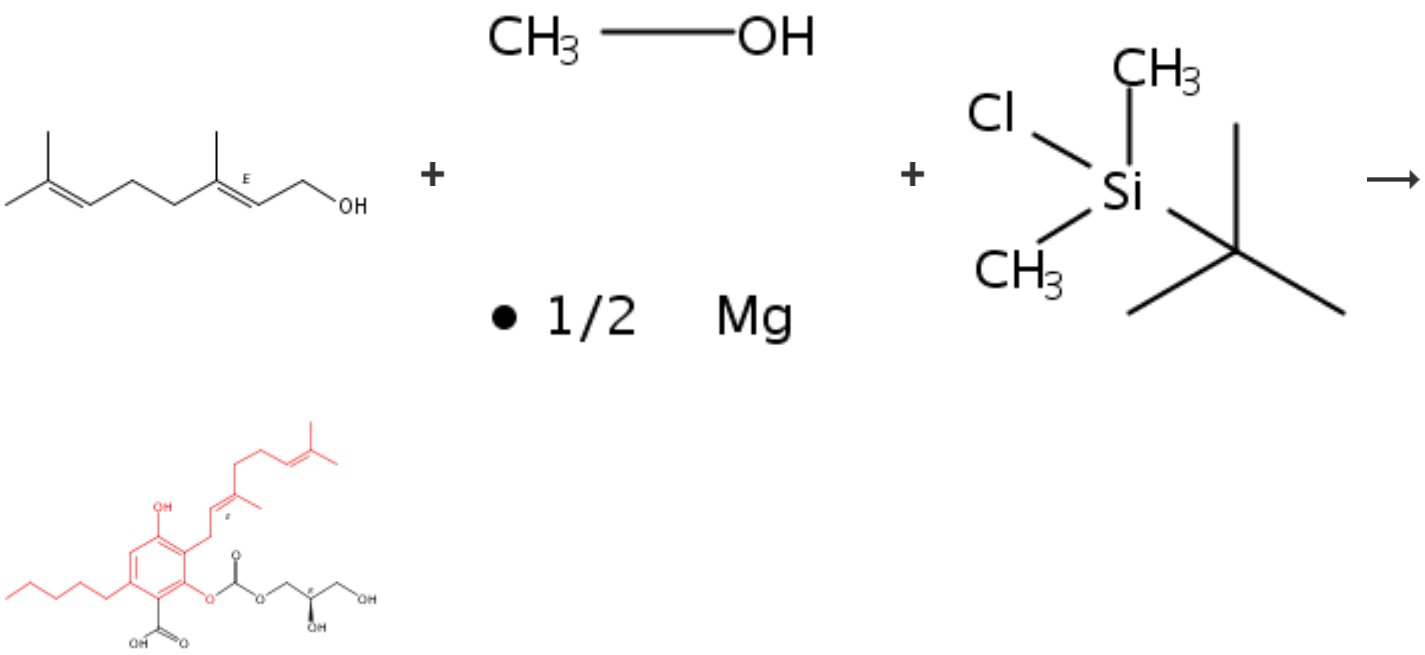
280. 6 Steps (Converging)





Overview

Steps/Stages

1.1 R:Et_3N, S:CH_2Cl_2, 3-5 h, 0°C

1.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
2.1 S:H_2O, cooled; 50°C; 3 h, 50°C; 50°C → rt

2.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, rt, pH 2

3.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

3.2 R:NaCl, S:H_2O

4.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

5.1 R:Et_3N •3HF, S:CH_2Cl_2, -15°C; 65 h, 5°C

5.2 R:$NaHCO_3$, S:H_2O, S:AcOEt, 0°C

Notes

in the dark, conversion = 85%,alternative preparation shown,reaction in a sealed pressure vessel, alternative preparation shown, regioselective, alternative preparation shown, Reactants: 6, Reagents: 7, Solvents: 5, Steps: 6, Stages: 9, Most stages in any one step: 2

References

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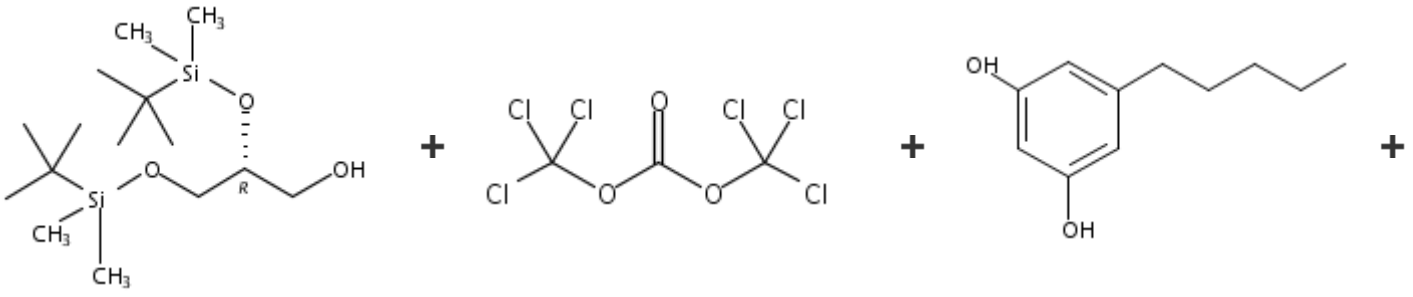
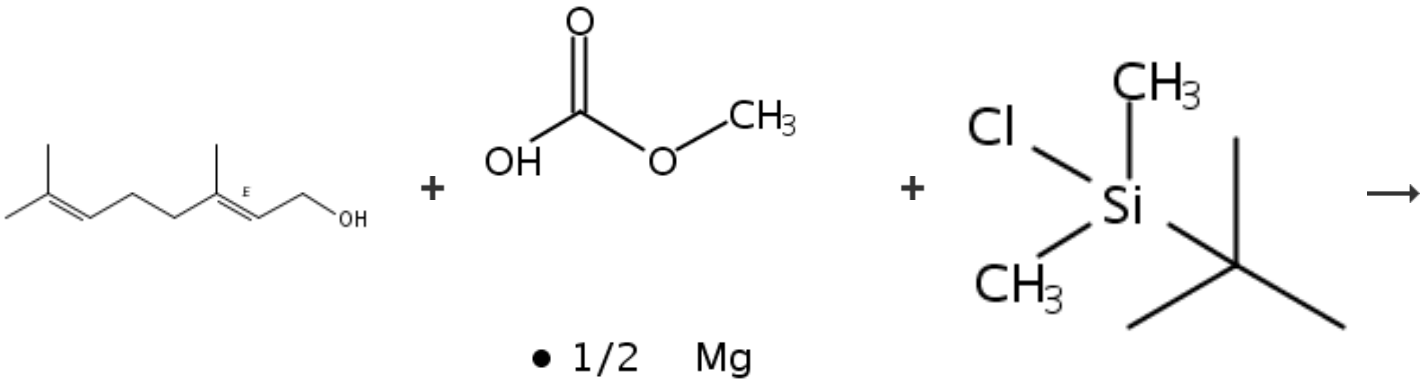
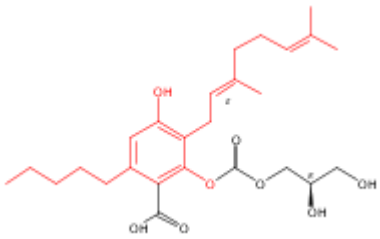
From PCT Int. Appl., 2017181118, 19 Oct 2017

281. 6 Steps (Converging)







Overview

Steps/Stages

1.1 R:Et_3N, S:CH_2Cl_2, 3-5 h, 0°C

1.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
2.1 S:DMF, 1 h, 120°C

2.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

3.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

3.2 R:NaCl, S:H_2O

4.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

5.1 R:Et_3N •3HF, S:CH_2Cl_2, -15°C; 65 h, 5°C

5.2 R:$NaHCO_3$, S:H_2O, S:AcOEt, 0°C

Notes

in the dark, conversion = 40%,alternative preparation shown, alternative preparation shown, regioselective, alternative preparation shown, Reactants: 6, Reagents: 7, Solvents: 6, Steps: 6, Stages: 9, Most stages in any one step: 2

References

Biosynthesis of cannabinoid prodrugs

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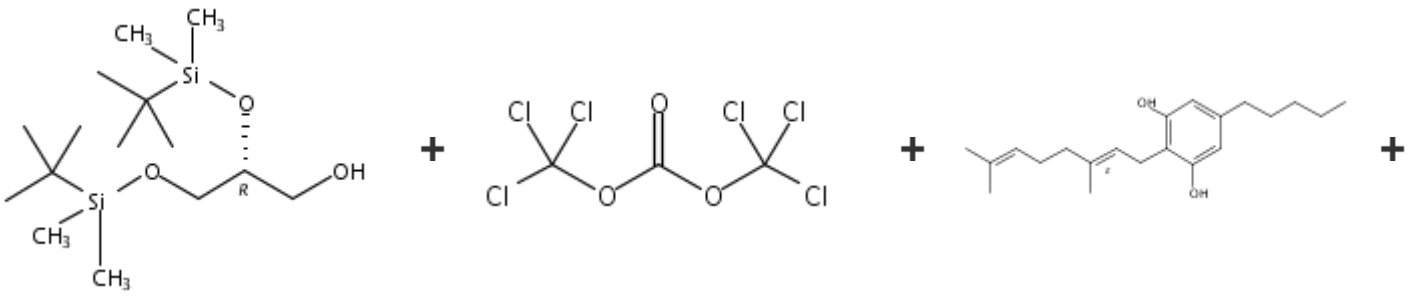
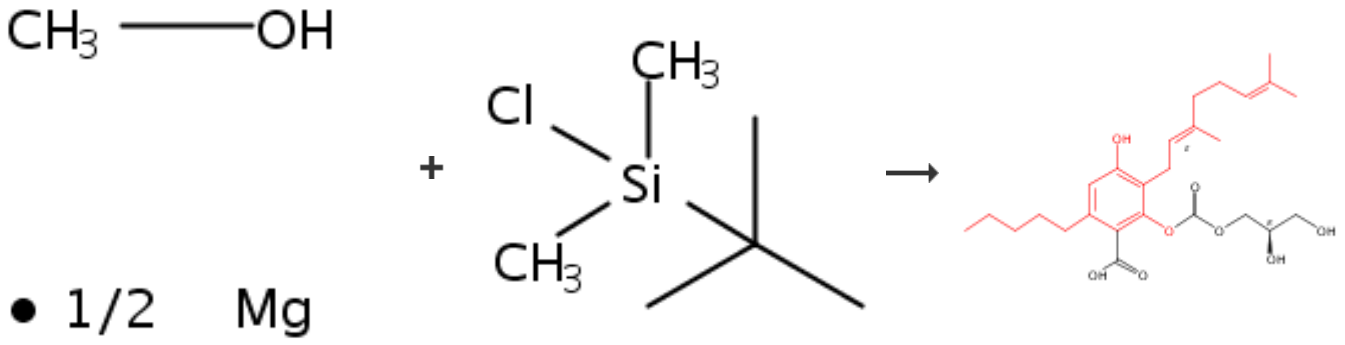
From PCT Int. Appl., 2017181118, 19 Oct 2017

282. 5 Steps (Converging)





Overview

Steps/Stages

1.1 R:Et_3N, S:CH_2Cl_2, 3-5 h, 0°C

1.1 S:H_2O, cooled; 50°C; 3 h, 50°C; 50°C → rt

1.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, rt, pH 2

2.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

2.2 R:NaCl, S:H_2O

3.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

4.1 R:Et_3N •3HF, S:CH_2Cl_2, -15°C; 65 h, 5°C

4.2 R:$NaHCO_3$, S:H_2O, S:AcOEt, 0°C

Notes

conversion = 85%,alternative preparation shown,reaction in a sealed pressure vessel, alternative preparation shown, regioselective, alternative preparation shown, Reactants: 5, Reagents: 6, Solvents: 5, Steps: 5, Stages: 8, Most stages in any one step: 2

References

Biosynthesis of cannabinoid prodrugs

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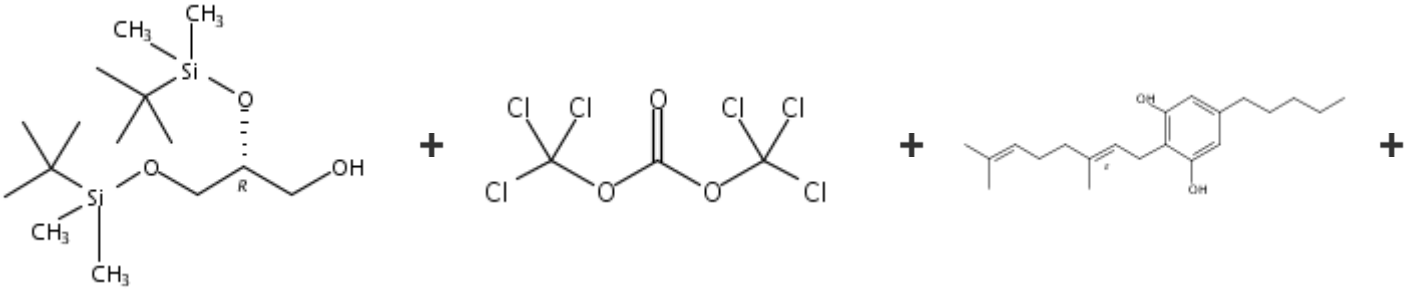
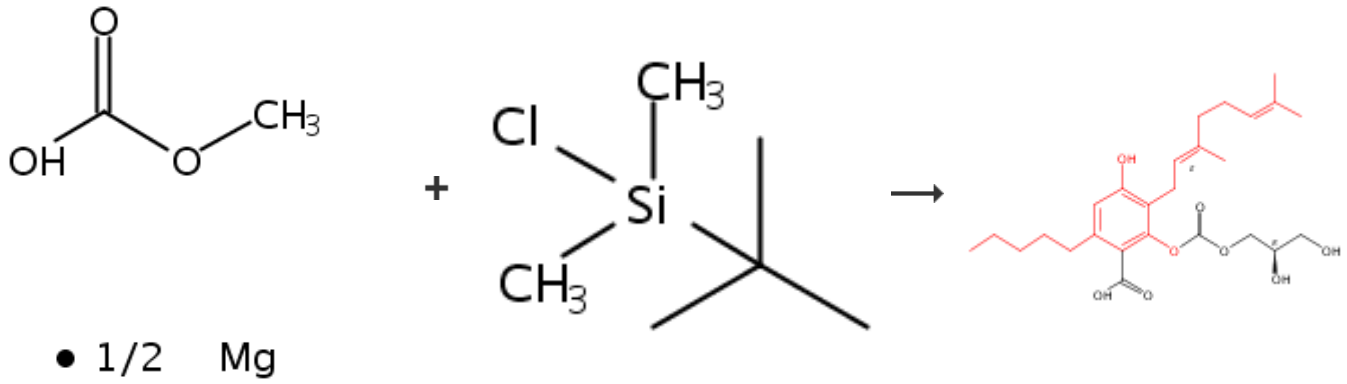
From PCT Int. Appl., 2017181118, 19 Oct 2017

283. 5 Steps (Converging)





- 1/2 Mg

Overview

Steps/Stages

1.1 R:Et_3N, S:CH_2Cl_2, 3-5 h, 0°C
1.1 S:DMF, 1 h, 120°C

1.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

2.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

2.2 R:NaCl, S:H_2O

3.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

4.1 R:Et_3N •3HF, S:CH_2Cl_2, -15°C; 65 h, 5°C

4.2 R:$NaHCO_3$, S:H_2O, S:AcOEt, 0°C

Notes

conversion = 40%,alternative preparation shown, alternative preparation shown, regioselective, alternative preparation shown, Reactants: 5, Reagents: 6, Solvents: 6, Steps: 5, Stages: 8, Most stages in any one step: 2

References

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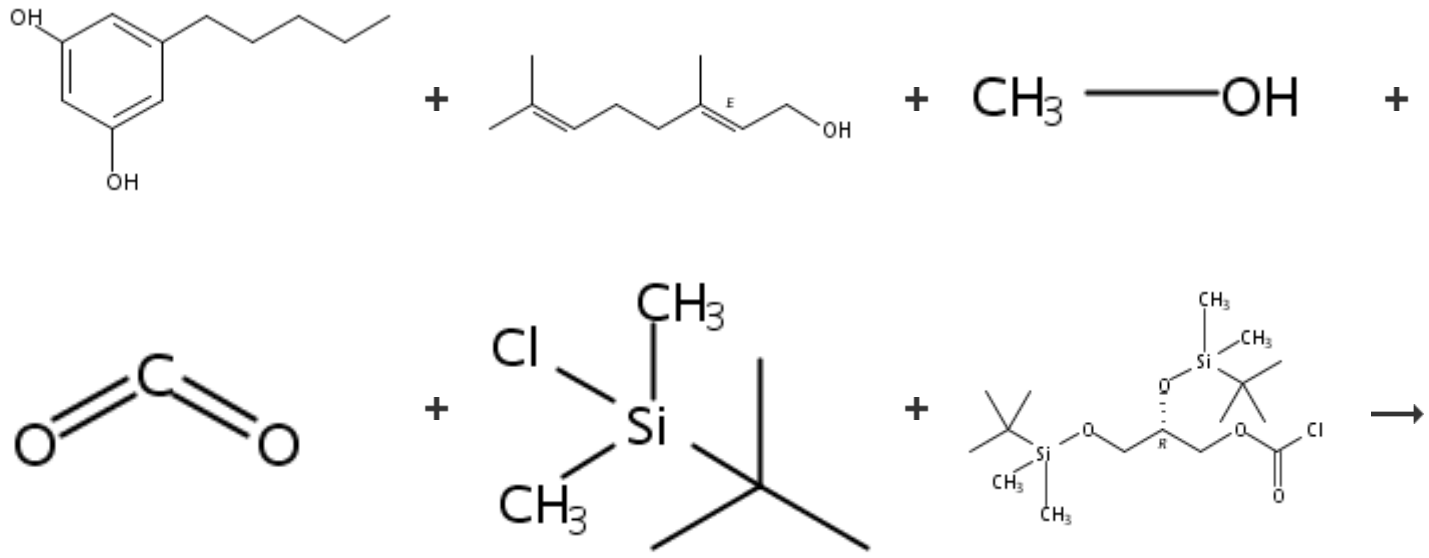
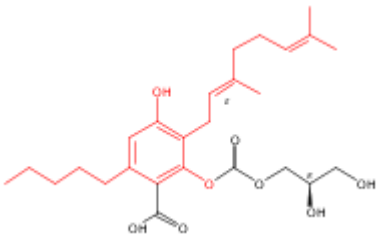
From PCT Int. Appl., 2017181118, 19 Oct 2017

284. 7 Steps (Converging)





Overview

Steps/Stages

1.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

1.1 R:Mg, S:MeOH, rt
2.1 S:DMF, 140°C
3.1 S:DMF, 1 h, 120°C

3.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

4.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

4.2 R:NaCl, S:H_2O

5.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

6.1 R:Et_3N •3HF, S:CH_2Cl_2, -15°C; 65 h, 5°C

6.2 R:$NaHCO_3$, S:H_2O, S:AcOEt, 0°C

Notes

in the dark, exothermic reaction, conversion = 40%,alternative preparation shown, alternative preparation shown, regioselective, alternative preparation shown, Reactants: 6, Reagents: 8, Solvents: 6, Steps: 7, Stages: 10, Most stages in any one step: 2

References

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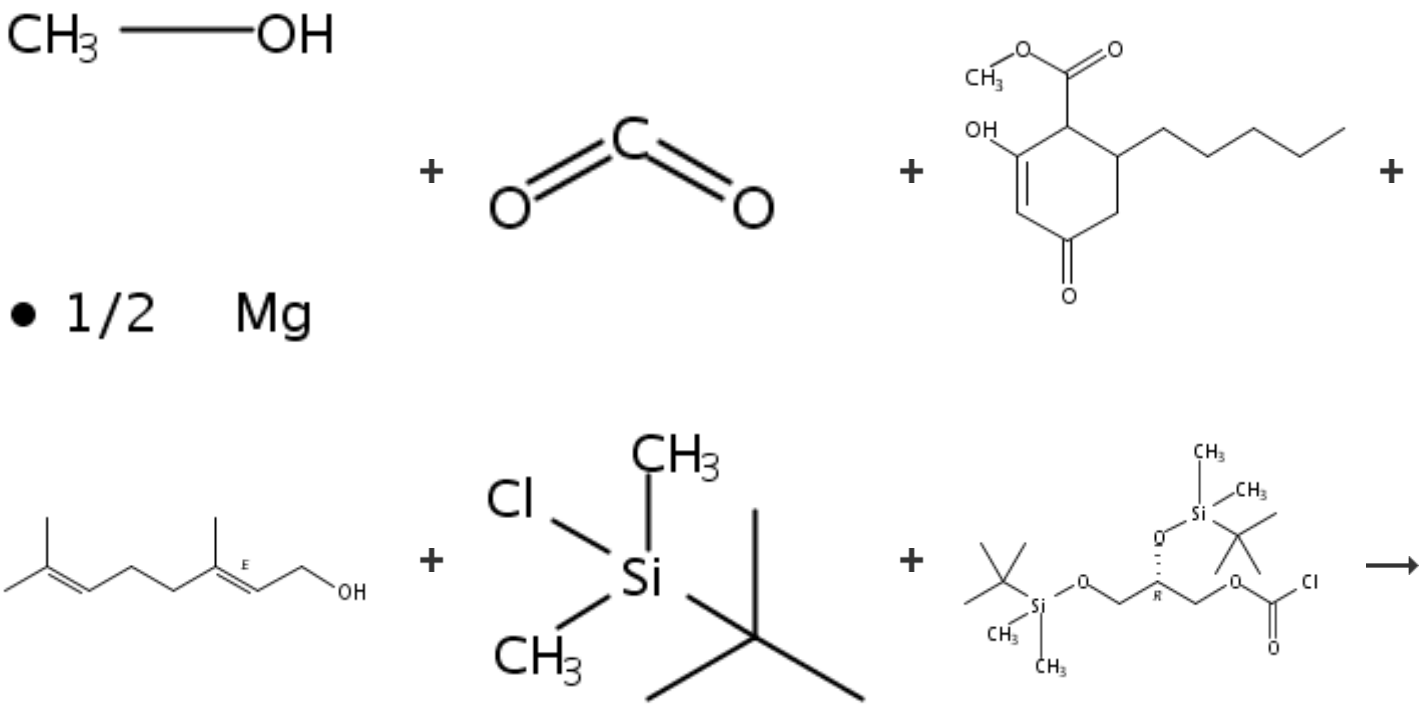
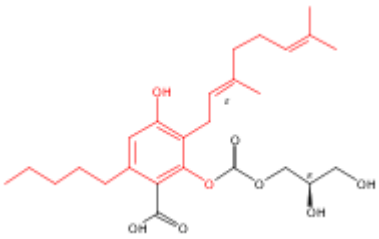
285. 7 Steps (Converging)





Overview

Steps/Stages

1.1 S:DMF, 140°C

1.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

2.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

3.1 S:DMF, 1 h, 120°C

3.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

4.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

4.2 R:NaCl, S:H_2O

5.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

6.1 R:Et_3N •3HF, S:CH_2Cl_2, -15°C; 65 h, 5°C

6.2 R:$NaHCO_3$, S:H_2O, S:AcOEt, 0°C

Notes

exothermic reaction, in the dark, conversion = 40%,alternative preparation shown, alternative preparation shown, regioselective, alternative preparation shown, Reactants: 6, Reagents: 8, Solvents: 6, Steps: 7, Stages: 10, Most stages in any one step: 2

References

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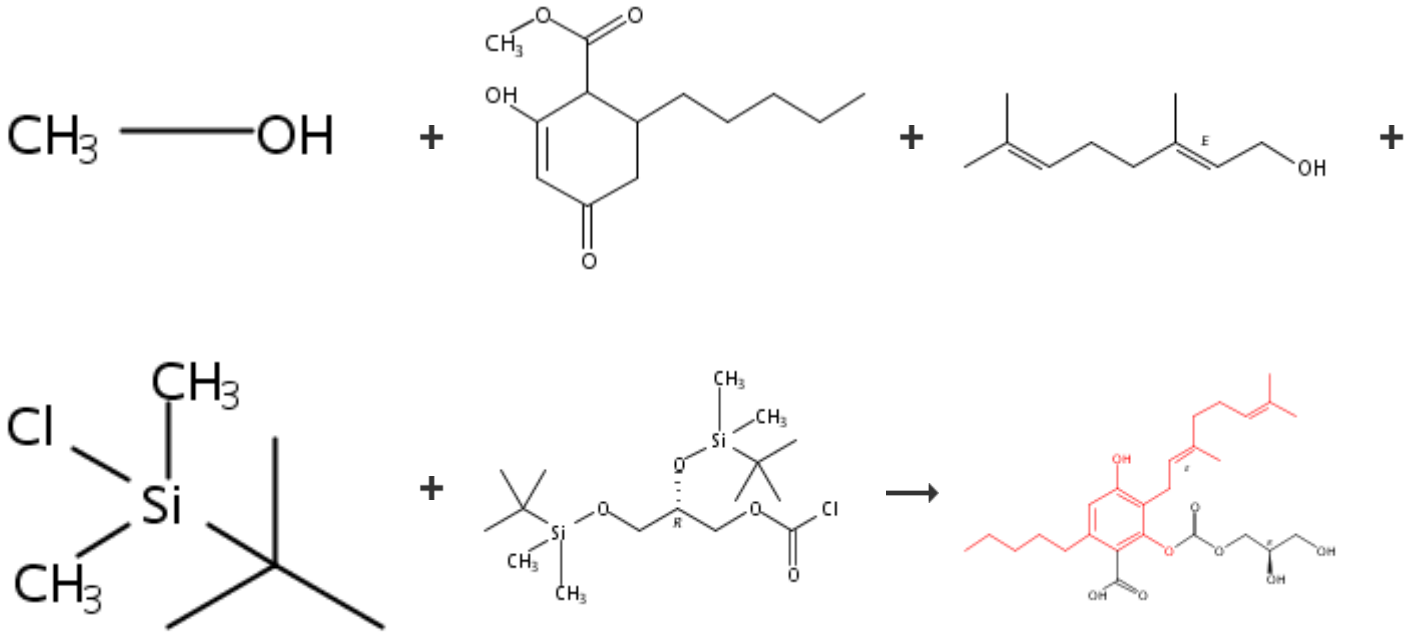
286. 7 Steps (Converging)



Overview

Steps/Stages

Notes

1.1 R:Mg, S:MeOH, rt

1.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

2.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

3.1 S:H_2O, cooled; 50°C; 3 h, 50°C; 50°C → rt

3.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, rt, pH 2

4.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

4.2 R:NaCl, S:H_2O

5.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

6.1 R:Et_3N •3HF, S:CH_2Cl_2, -15°C; 65 h, 5°C

6.2 R:$NaHCO_3$, S:H_2O, S:AcOEt, 0°C

in the dark, conversion = 85%,alternative preparation shown,reaction in a sealed pressure vessel, alternative preparation shown, regioselective, alternative preparation shown, Reactants: 5, Reagents: 9, Solvents: 6, Steps: 7, Stages: 10, Most stages in any one step: 2

References

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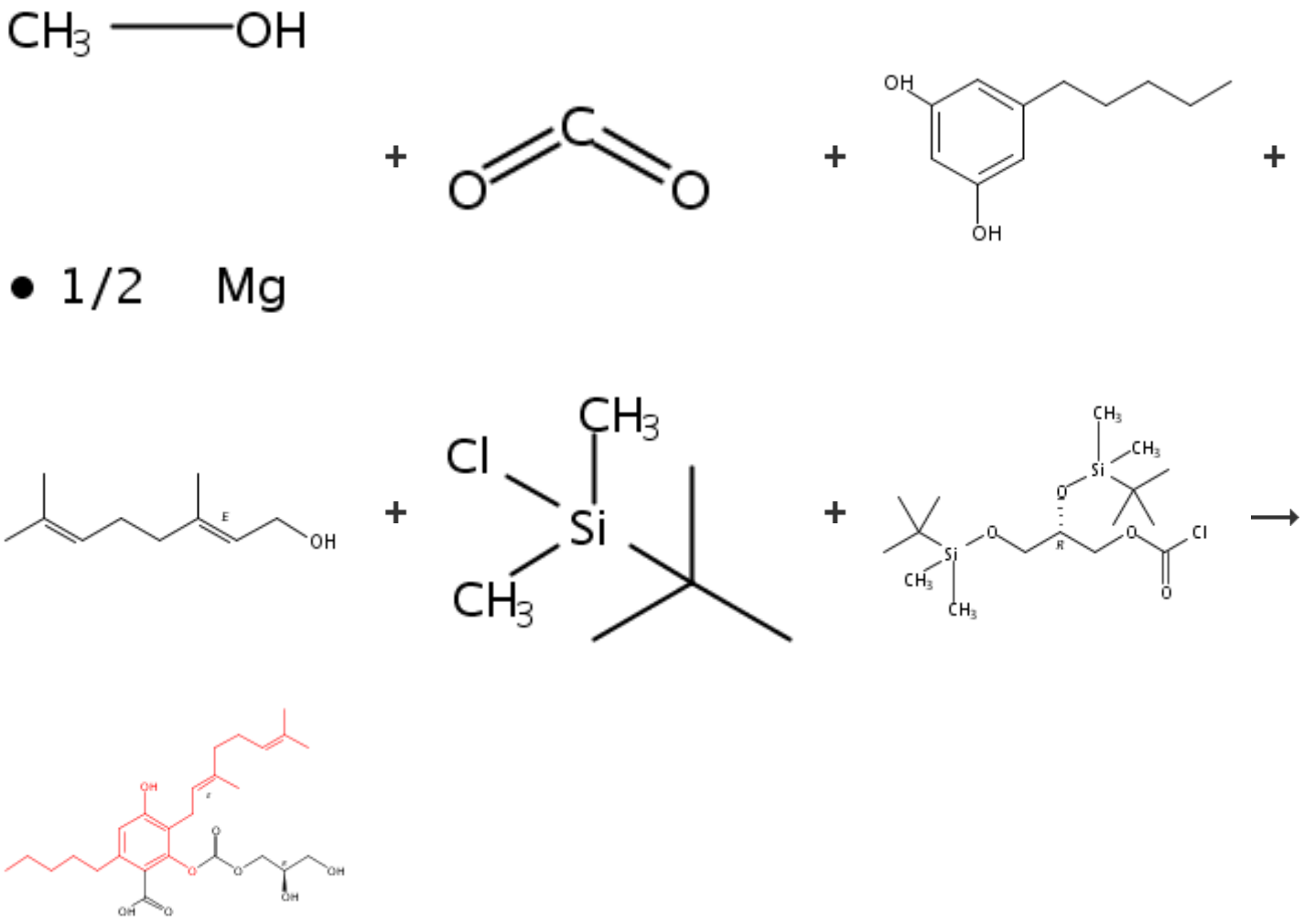
287. 6 Steps (Converging)



Overview

Steps/Stages

Notes

1.1 S:DMF, 140°C

1.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
2.1 S:DMF, 1 h, 120°C

2.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

3.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

3.2 R:NaCl, S:H_2O

4.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

5.1 R:Et_3N •3HF, S:CH_2Cl_2, -15°C; 65 h, 5°C

5.2 R:$NaHCO_3$, S:H_2O, S:AcOEt, 0°C

exothermic reaction, in the dark, conversion = 40%,alternative preparation shown, alternative preparation shown, regioselective, alternative preparation shown, Reactants: 6, Reagents: 7, Solvents: 6, Steps: 6, Stages: 9, Most stages in any one step: 2

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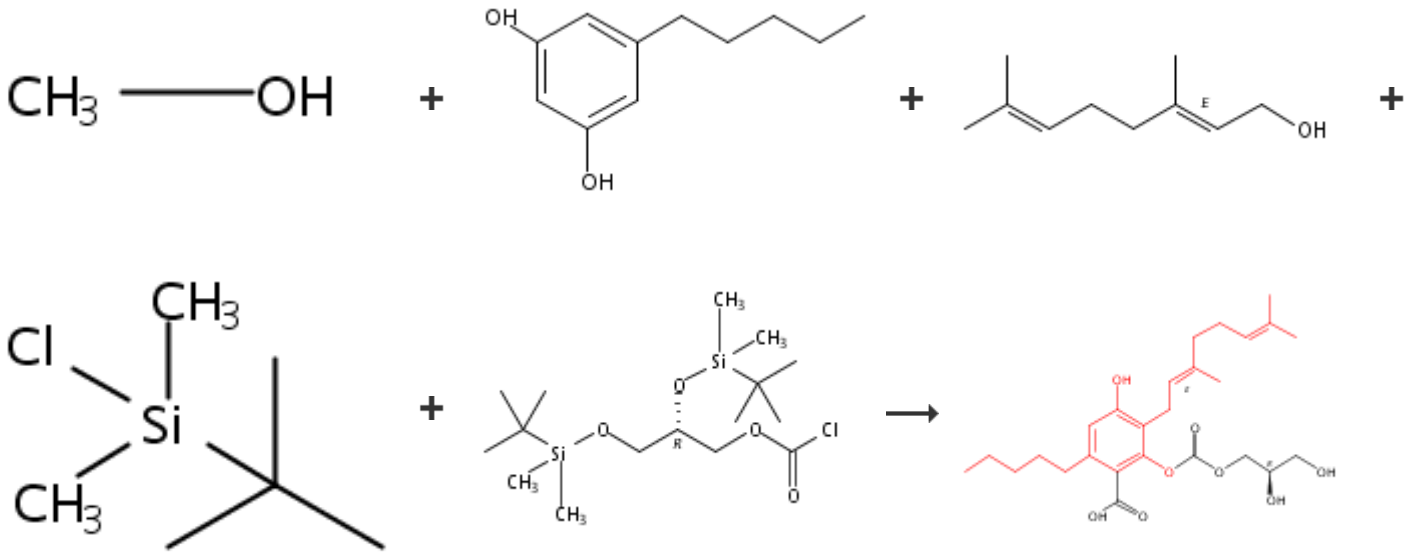
From PCT Int. Appl., 2017181118, 19 Oct 2017

288. 6 Steps (Converging)



Overview

Steps/Stages

1.1 R:Mg, S:MeOH, rt

1.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
2.1 S:H_2O, cooled; 50°C; 3 h, 50°C; 50°C → rt

2.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, rt, pH 2

3.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

3.2 R:NaCl, S:H_2O

4.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

5.1 R:Et_3N •3HF, S:CH_2Cl_2, -15°C; 65 h, 5°C

5.2 R:$NaHCO_3$, S:H_2O, S:AcOEt, 0°C

Notes

in the dark, conversion = 85%,alternative preparation shown,reaction in a sealed pressure vessel, alternative preparation shown, regioselective, alternative preparation shown, Reactants: 5, Reagents: 8, Solvents: 5, Steps: 6, Stages: 9, Most stages in any one step: 2

References

Biosynthesis of cannabinoid prodrugs

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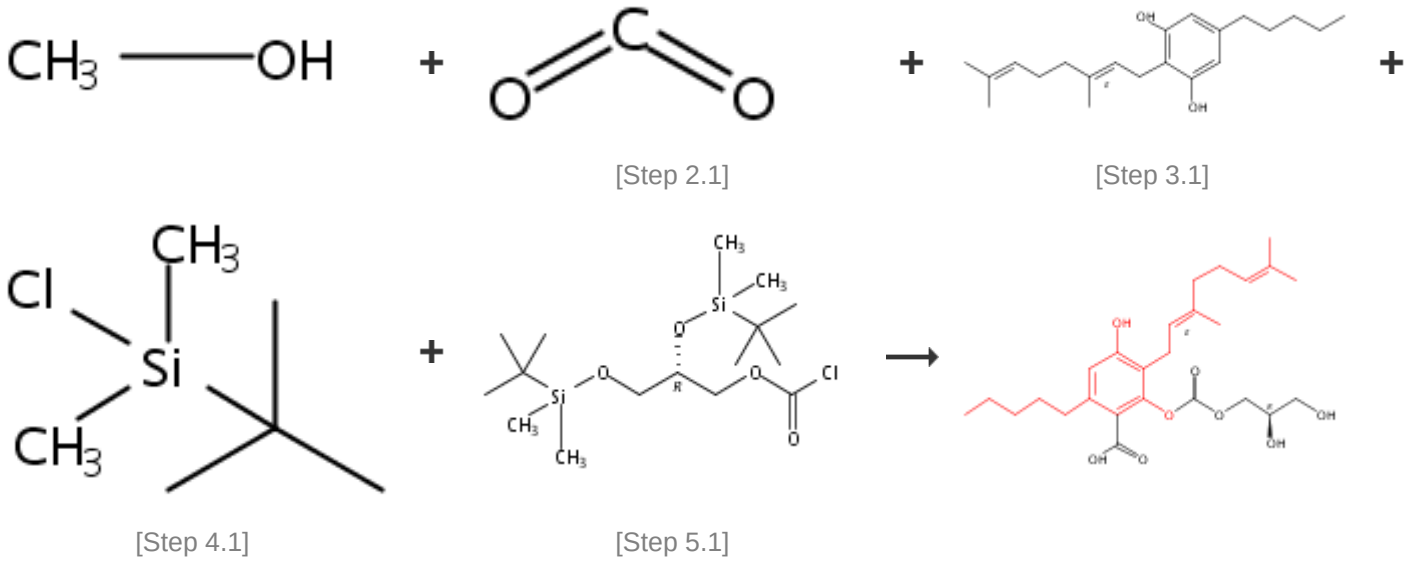
From PCT Int. Appl., 2017181118, 19 Oct 2017

289. 6 Steps



[Step 2.1] [Step 3.1]

[Step 4.1] [Step 5.1]

Overview

Steps/Stages

1.1 R:Mg, S:MeOH, rt
2.1 S:DMF, 140°C
3.1 S:DMF, 1 h, 120°C

3.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

4.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

4.2 R:NaCl, S:H_2O

5.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

6.1 R:Et_3N •3HF, S:CH_2Cl_2, -15°C; 65 h, 5°C

6.2 R:$NaHCO_3$, S:H_2O, S:AcOEt, 0°C

Notes

2) exothermic reaction, 3) conversion = 40%,alternative preparation shown, 4) alternative preparation shown, regioselective, 5) alternative preparation shown, Reactants: 5, Reagents: 7, Solvents: 6, Steps: 6, Stages: 9, Most stages in any one step: 2

References

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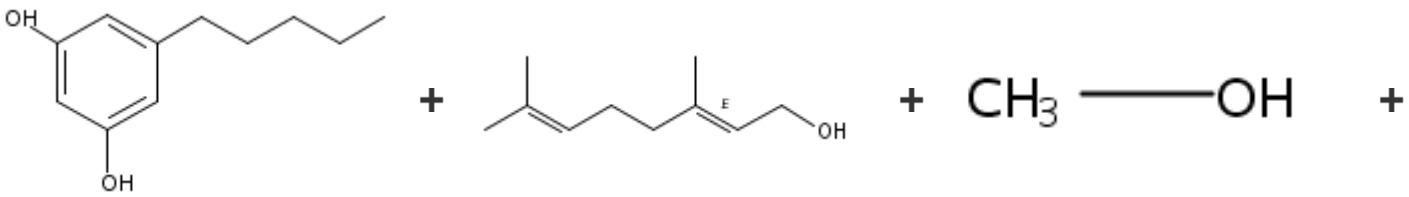
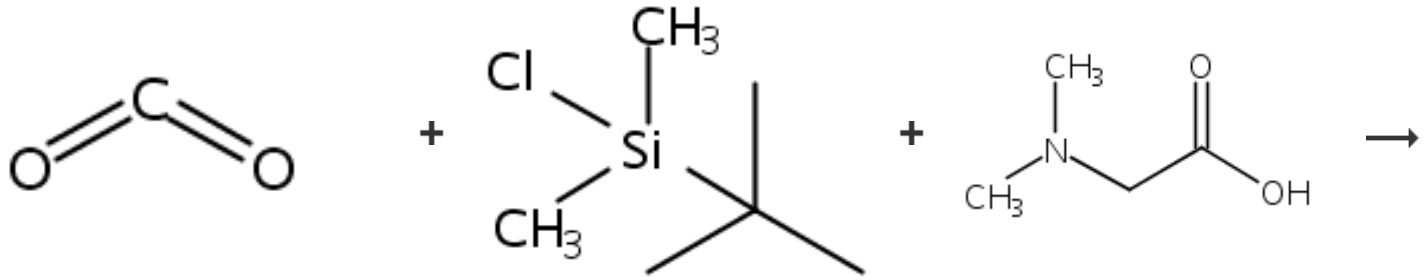
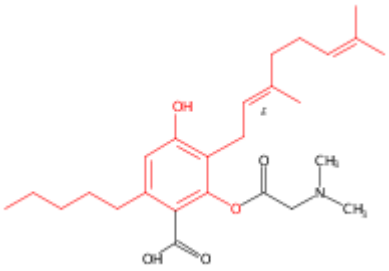
From PCT Int. Appl., 2017181118, 19 Oct 2017

290. 6 Steps (Converging)







Overview

Steps/Stages

1.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

1.1 R:Mg, S:MeOH, rt
2.1 S:DMF, 140°C
3.1 S:DMF, 1 h, 120°C

3.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

4.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

4.2 R:NaCl, S:H_2O

5.1 R:DCC, C:4-DMAP, S:CH_2Cl_2, rt; overnight, rt

5.2 R:$Bu_4N^+ \cdot F^-$, S:CH_2Cl_2, -15°C

Notes

in the dark, exothermic reaction, conversion = 40%,alternative preparation shown, alternative preparation shown, regioselective, alternative preparation shown,other reagent triethylamine trihydrofluoride may be used in stage 2, Reactants: 6, Reagents: 7, Catalysts: 1, Solvents: 5, Steps: 6, Stages: 9, Most stages in any one step: 2

References

Biosynthesis of cannabinoid prodrugs

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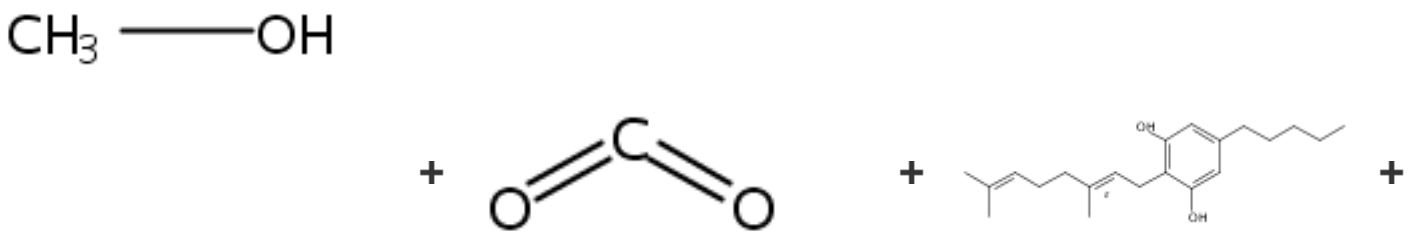
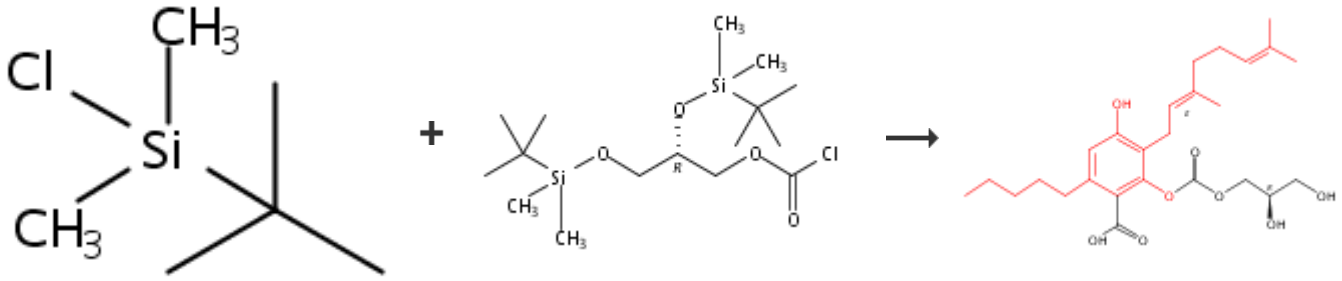
From PCT Int. Appl., 2017181118, 19 Oct 2017

291. 5 Steps



- 1/2 Mg

[Step 2.1]



[Step 3.1] [Step 4.1]

Overview

Steps/Stages

1.1 S:DMF, 140°C
2.1 S:DMF, 1 h, 120°C

2.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

3.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

3.2 R:NaCl, S:H_2O

4.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

5.1 R:Et_3N •3HF, S:CH_2Cl_2, -15°C; 65 h, 5°C

5.2 R:$NaHCO_3$, S:H_2O, S:AcOEt, 0°C

Notes

1) exothermic reaction, 2) conversion = 40%,alternative preparation shown, 3) alternative preparation shown, regioselective, 4) alternative preparation shown, Reactants: 5, Reagents: 6, Solvents: 6, Steps: 5, Stages: 8, Most stages in any one step: 2

References

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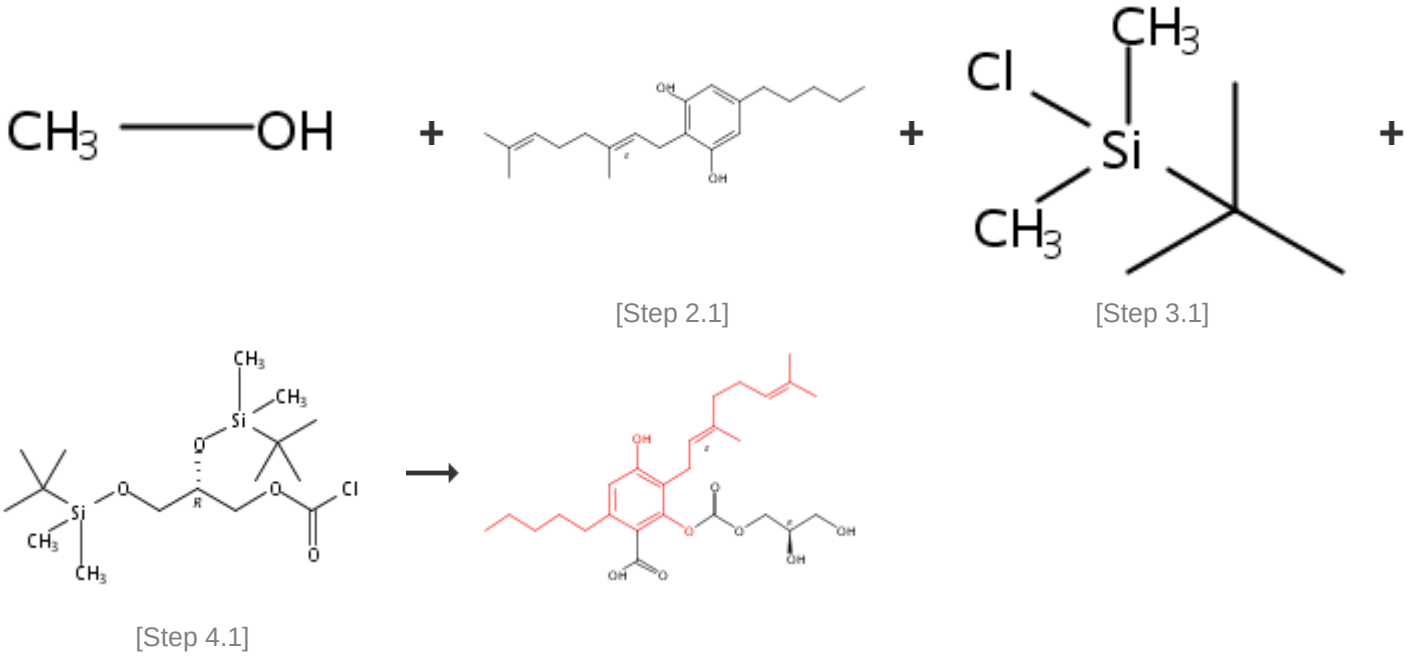
From PCT Int. Appl., 2017181118, 19 Oct 2017

292. 5 Steps



[Step 2.1] [Step 3.1] [Step 4.1]

Overview

Steps/Stages

Notes

1.1 R:Mg, S:MeOH, rt
2.1 S:H_2O, cooled; 50°C; 3 h, 50°C; 50°C → rt
2.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, rt, pH 2
3.1 R:1H-Imidazole, S:CH_2Cl_2, cooled
3.2 R:NaCl, S:H_2O
4.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt
5.1 R:Et_3N •3HF, S:CH_2Cl_2, -15°C; 65 h, 5°C
5.2 R:$NaHCO_3$, S:H_2O, S:AcOEt, 0°C

2) conversion = 85%,alternative preparation shown,reaction in a sealed pressure vessel, 3) alternative preparation shown, regioselective, 4) alternative preparation shown, Reactants: 4, Reagents: 7, Solvents: 5, Steps: 5, Stages: 8, Most stages in any one step: 2

References

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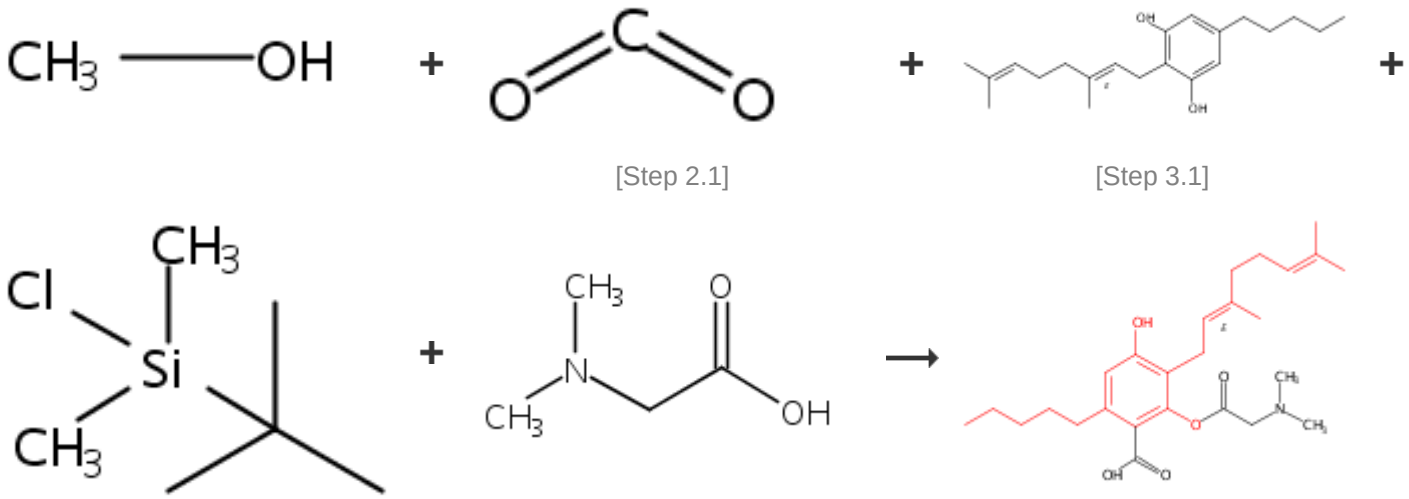
293. 5 Steps



[Step 2.1] [Step 3.1] [Step 4.1] [Step 5.1]

Overview

Steps/Stages

1.1 R:Mg, S:MeOH, rt
2.1 S:DMF, 140°C
3.1 S:DMF, 1 h, 120°C
3.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2
4.1 R:1H-Imidazole, S:CH_2Cl_2, cooled
4.2 R:NaCl, S:H_2O
5.1 R:DCC, C:4-DMAP, S:CH_2Cl_2, rt; overnight, rt
5.2 R:Bu_4N^+ •F^-, S:CH_2Cl_2, -15°C

Notes

2) exothermic reaction, 3) conversion = 40%,alternative preparation shown, 4) alternative preparation shown, regioselective, 5) alternative preparation shown,other reagent triethylamine trihydrofluoride may be used in stage 2, Reactants: 5, Reagents: 6, Catalysts: 1, Solvents: 5, Steps: 5, Stages: 8, Most stages in any one step: 2

References

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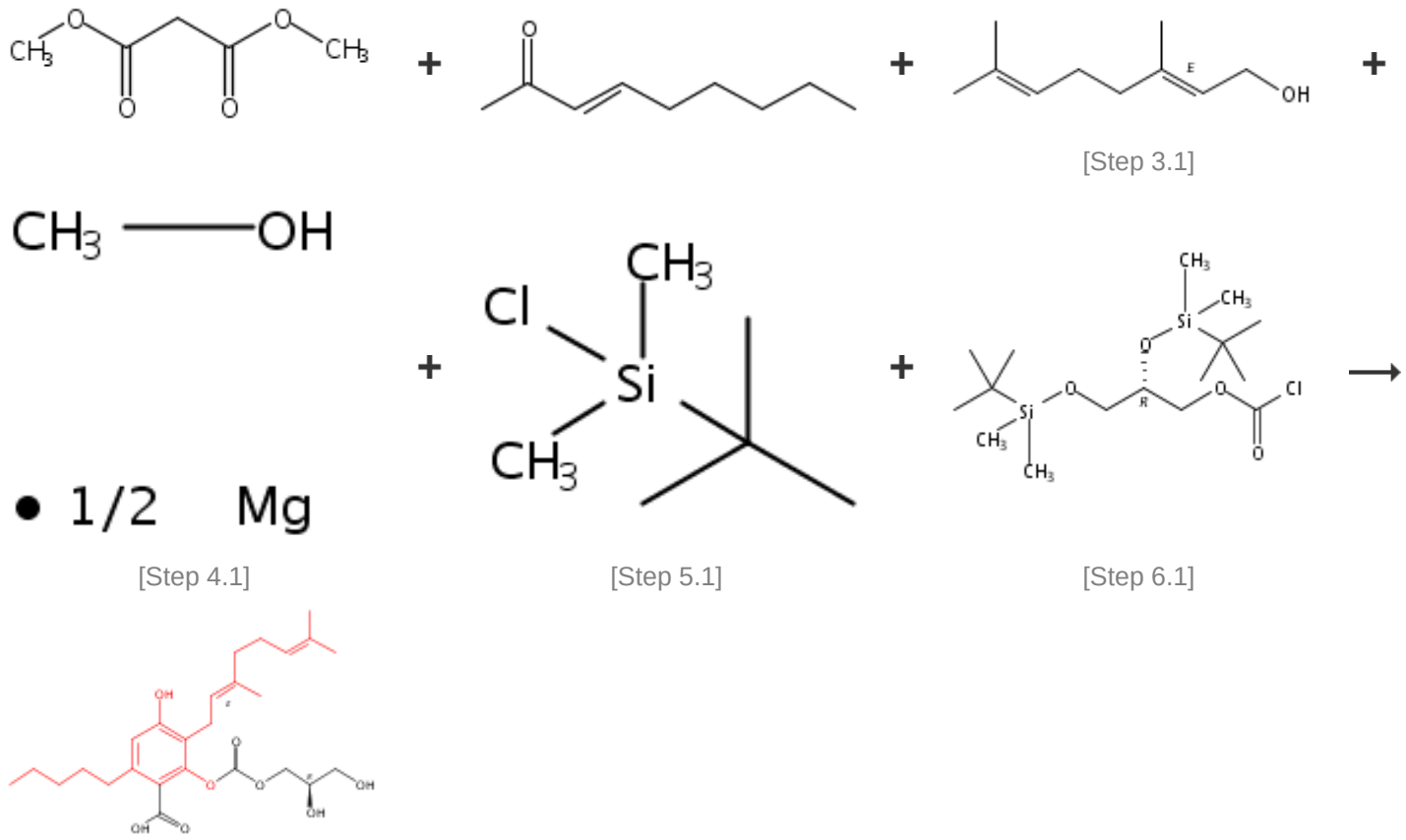
From PCT Int. Appl., 2017181118, 19 Oct 2017

294. 7 Steps



[Step 3.1]

[Step 4.1]

[Step 5.1]

[Step 6.1]

Overview

Steps/Stages

1.1 R:NaOMe, S:MeOH, rt; 3 h, reflux; reflux → rt

1.2 R:H_2O, rt

2.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

3.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

4.1 S:H_2O, cooled; 50°C; 3 h, 50°C; 50°C → rt

4.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, rt, pH 2

5.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

5.2 R:NaCl, S:H_2O

6.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

7.1 R:Et_3N •3HF, S:CH_2Cl_2, -15°C; 65 h, 5°C

7.2 R:$NaHCO_3$, S:H_2O, S:AcOEt, 0°C

Notes

3) in the dark, 4) conversion = 85%,alternative preparation shown,reaction in a sealed pressure vessel, 5) alternative preparation shown, regioselective, 6) alternative preparation shown, Reactants: 6, Reagents: 10, Solvents: 6, Steps: 7, Stages: 11, Most stages in any one step: 2

References

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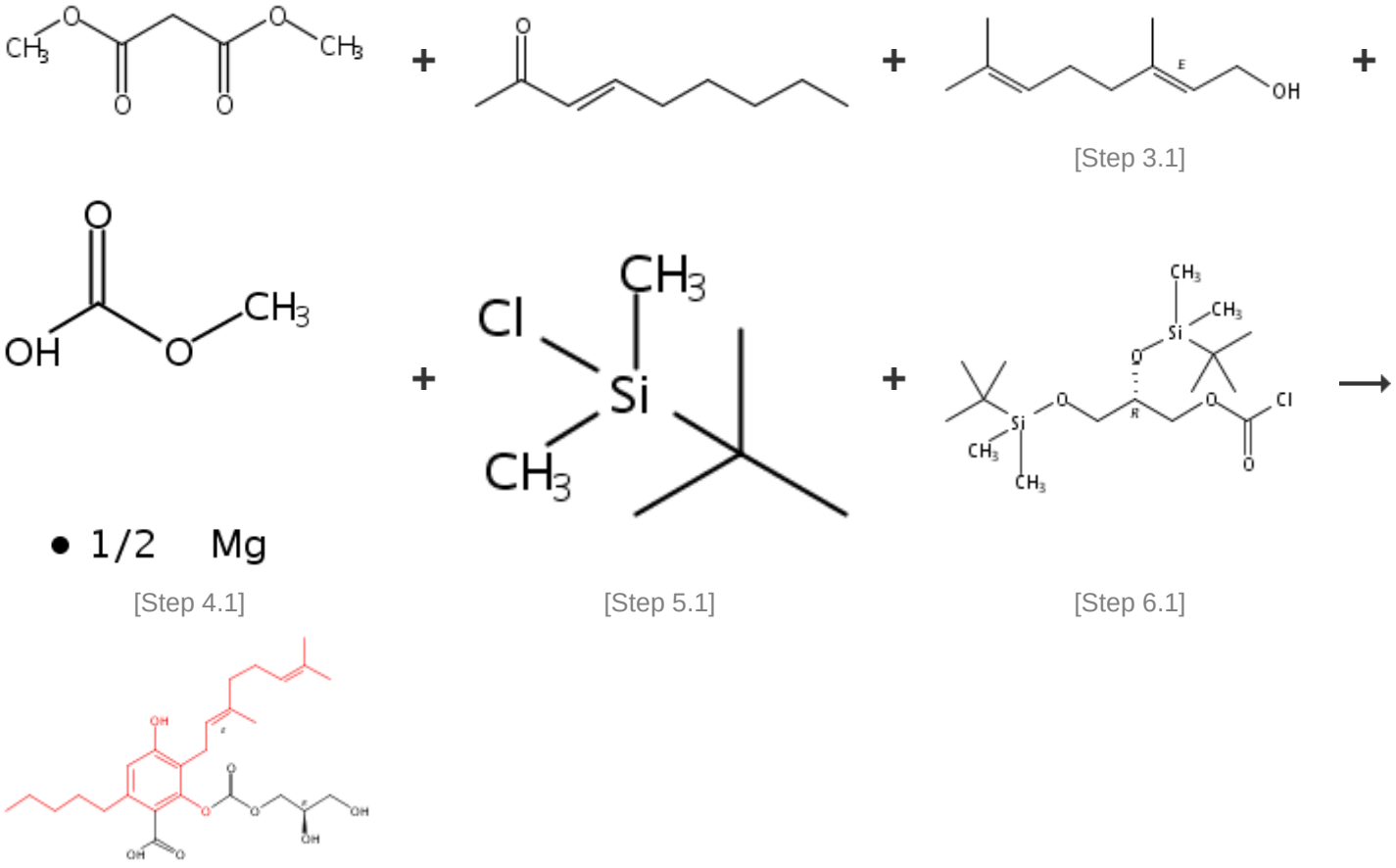
295. 7 Steps



Overview

Steps/Stages

1.1 R:NaOMe, S:MeOH, rt; 3 h, reflux; reflux → rt

1.2 R:H_2O, rt

2.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

3.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

4.1 S:DMF, 1 h, 120°C

4.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

5.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

5.2 R:NaCl, S:H_2O

6.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

7.1 R:Et_3N •3HF, S:CH_2Cl_2, -15°C; 65 h, 5°C

7.2 R:$NaHCO_3$, S:H_2O, S:AcOEt, 0°C

Notes

3) in the dark, 4) conversion = 40%,alternative preparation shown, 5) alternative preparation shown, regioselective, 6) alternative preparation shown, Reactants: 6, Reagents: 10, Solvents: 6, Steps: 7, Stages: 11, Most stages in any one step: 2

References

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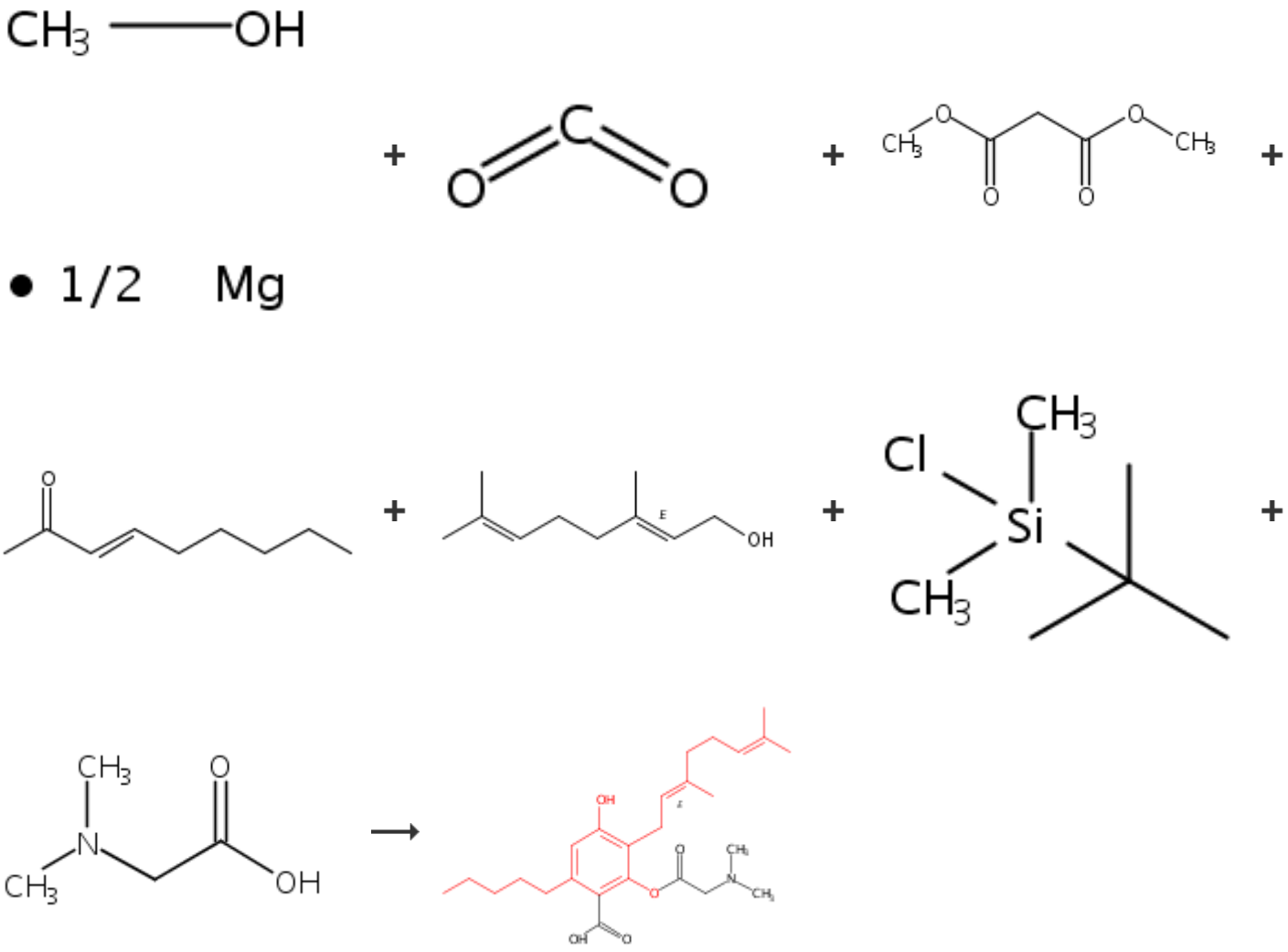
From PCT Int. Appl., 2017181118, 19 Oct 2017

296. 7 Steps (Converging)



Overview

Steps/Stages

1.1 S:DMF, 140°C

1.1 R:NaOMe, S:MeOH, rt; 3 h, reflux; reflux → rt

1.2 R:H_2O, rt

2.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

3.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

4.1 S:DMF, 1 h, 120°C

4.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

5.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

5.2 R:NaCl, S:H_2O

6.1 R:DCC, C:4-DMAP, S:CH_2Cl_2, rt; overnight, rt

6.2 R:$Bu_4N^+ \cdot F^-$, S:CH_2Cl_2, -15°C

Notes

exothermic reaction, in the dark, conversion = 40%,alternative preparation shown, alternative preparation shown, regioselective, alternative preparation shown,other reagent triethylamine trihydrofluoride may be used in stage 2, Reactants: 7, Reagents: 9, Catalysts: 1, Solvents: 5, Steps: 7, Stages: 11, Most stages in any one step: 2

References

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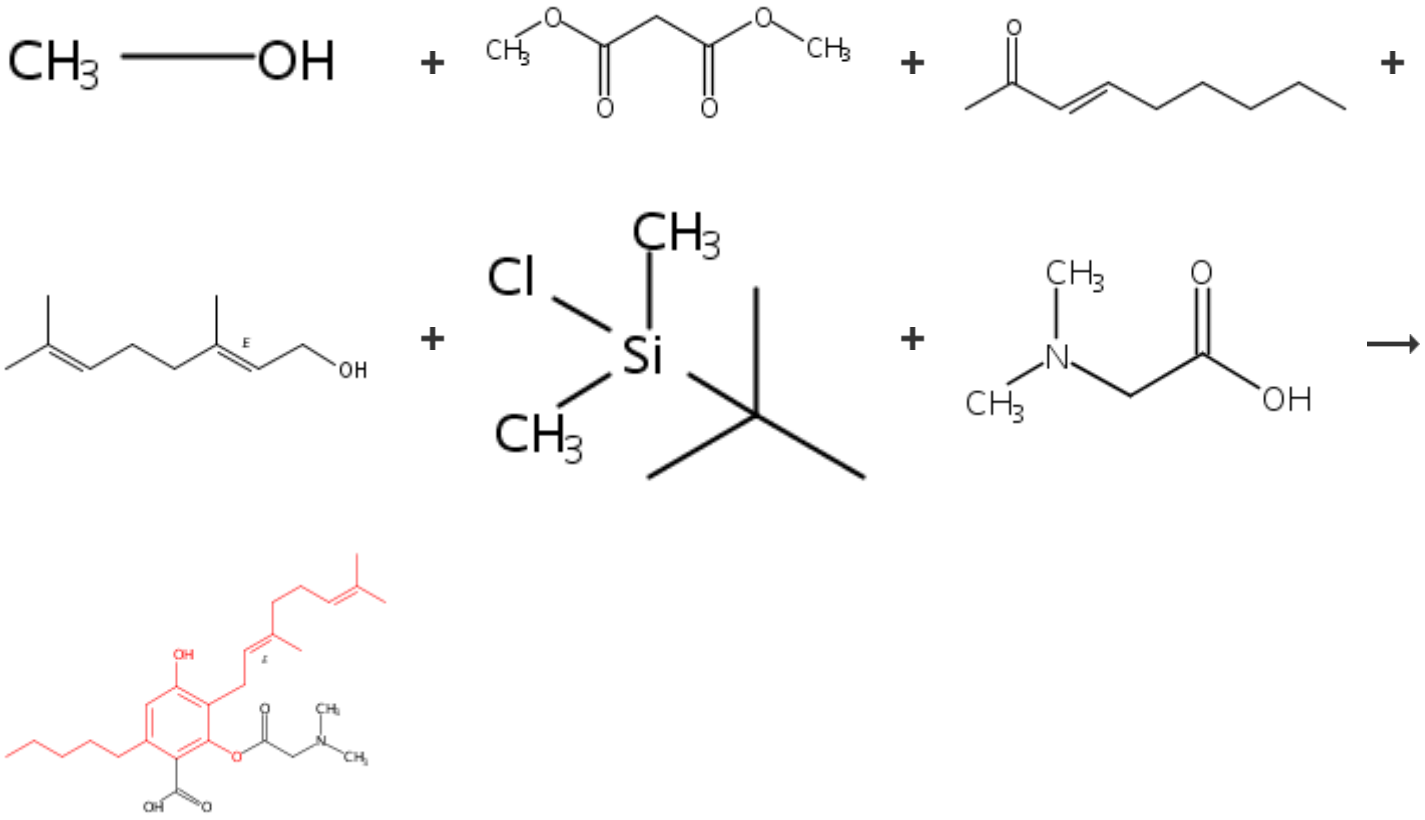
297. 7 Steps (Converging)



Overview

Steps/Stages

1.1 R:Mg, S:MeOH, rt

1.1 R:NaOMe, S:MeOH, rt; 3 h, reflux; reflux → rt

1.2 R:H_2O, rt

2.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

3.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

4.1 S:H_2O, cooled; 50°C; 3 h, 50°C; 50°C → rt

4.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, rt, pH 2

5.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

5.2 R:NaCl, S:H_2O

6.1 R:DCC, C:4-DMAP, S:CH_2Cl_2, rt; overnight, rt

6.2 R:$Bu_4N^+ \cdot F^-$, S:CH_2Cl_2, -15°C

Notes

in the dark, conversion = 85%,alternative preparation shown,reaction in a sealed pressure vessel, alternative preparation shown, regioselective, alternative preparation shown,other reagent triethylamine trihydrofluoride may be used in stage 2, Reactants: 6, Reagents: 10, Catalysts: 1, Solvents: 5, Steps: 7, Stages: 11, Most stages in any one step: 2

References

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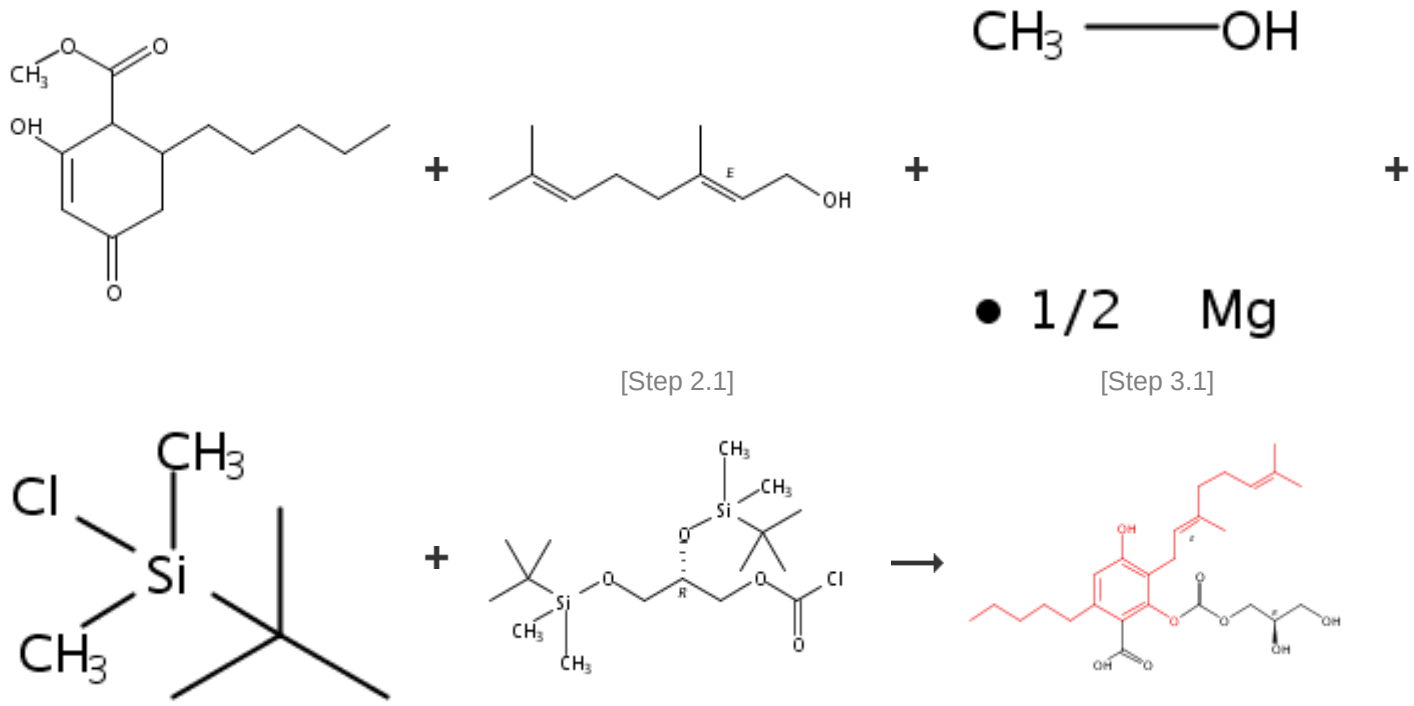
298. 6 Steps



Overview

Steps/Stages

1.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

2.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

3.1 S:H_2O, cooled; 50°C; 3 h, 50°C; 50°C → rt

3.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, rt, pH 2

4.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

4.2 R:NaCl, S:H_2O

5.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

6.1 R:Et_3N •3HF, S:CH_2Cl_2, -15°C; 65 h, 5°C

6.2 R:$NaHCO_3$, S:H_2O, S:AcOEt, 0°C

Notes

2) in the dark, 3) conversion = 85%,alternative preparation shown,reaction in a sealed pressure vessel, 4) alternative preparation shown, regioselective, 5) alternative preparation shown, Reactants: 5, Reagents: 8, Solvents: 6, Steps: 6, Stages: 9, Most stages in any one step: 2

References

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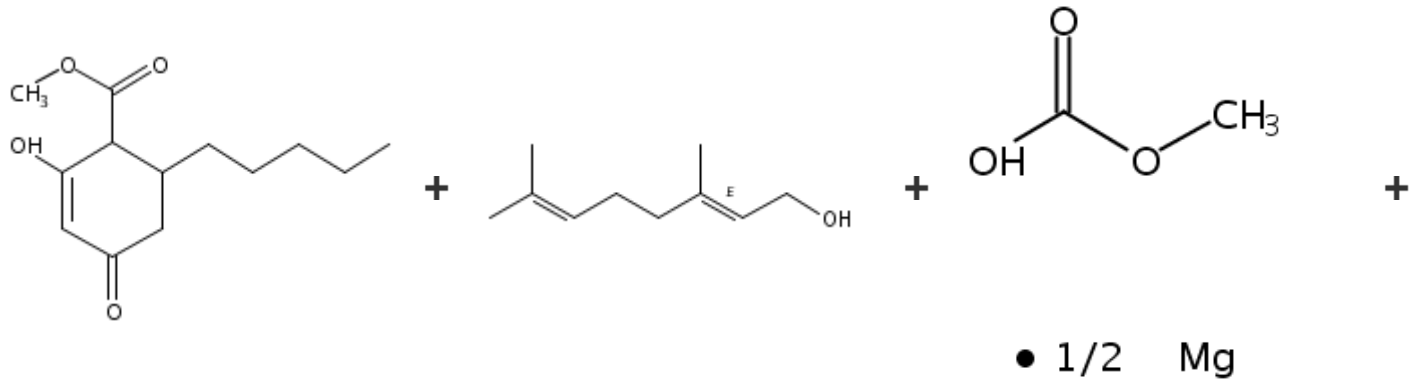
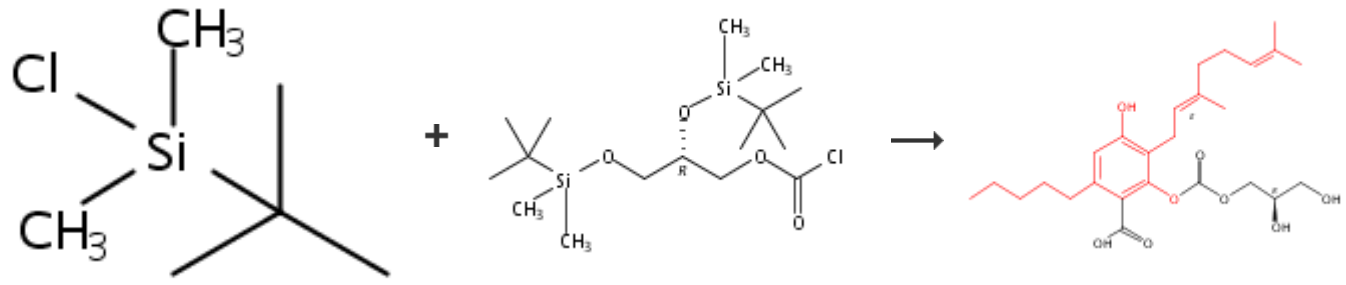
299. 6 Steps



[Step 2.1] [Step 3.1]



[Step 4.1] [Step 5.1]

Overview

Steps/Stages

1.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

2.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

3.1 S:DMF, 1 h, 120°C

3.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

4.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

4.2 R:NaCl, S:H_2O

5.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

6.1 R:Et_3N •3HF, S:CH_2Cl_2, -15°C; 65 h, 5°C

6.2 R:$NaHCO_3$, S:H_2O, S:AcOEt, 0°C

Notes

2) in the dark, 3) conversion = 40%,alternative preparation shown, 4) alternative preparation shown, regioselective, 5) alternative preparation shown, Reactants: 5, Reagents: 8, Solvents: 6, Steps: 6, Stages: 9, Most stages in any one step: 2

References

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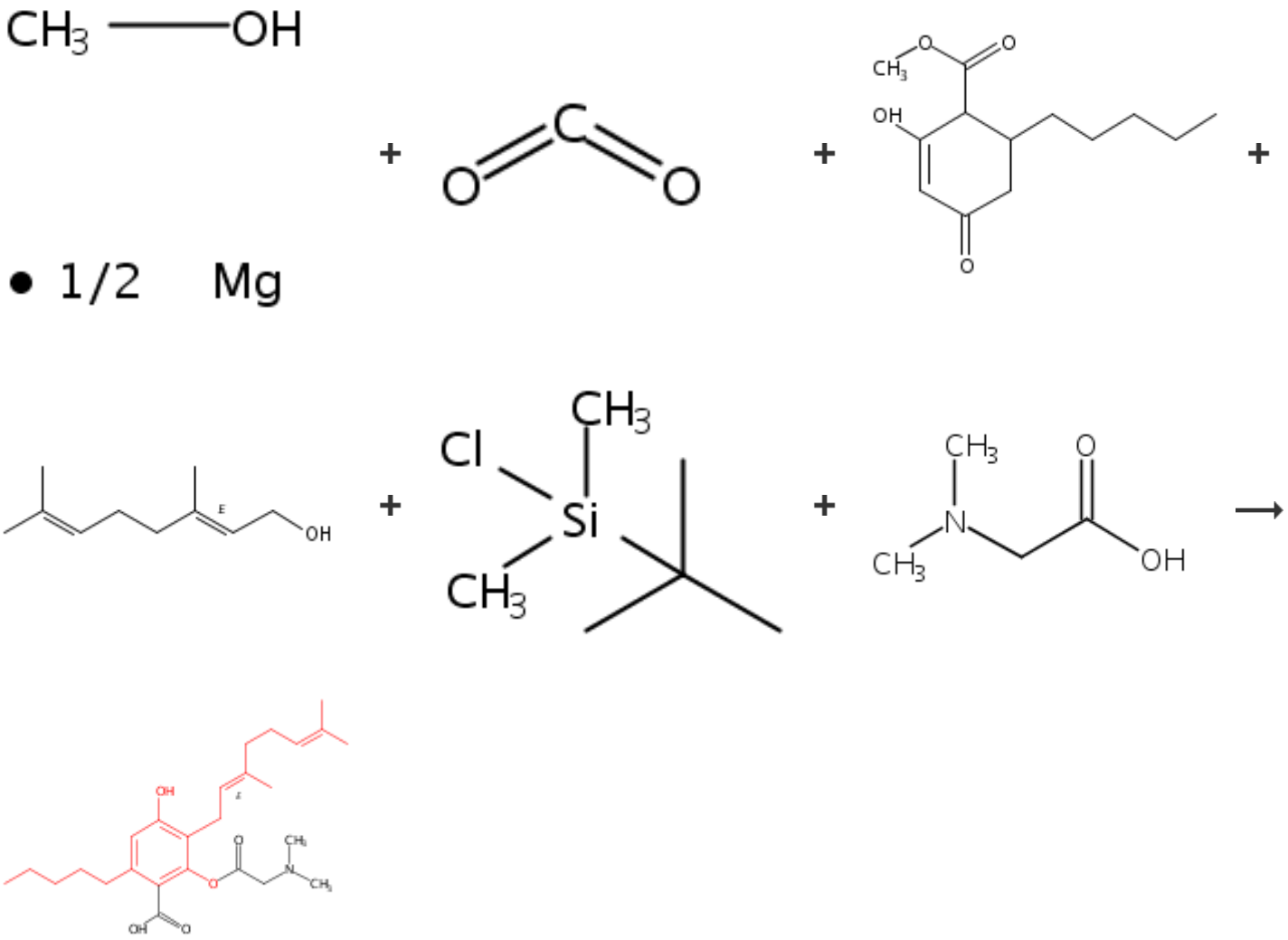
300. 6 Steps (Converging)



Overview

Steps/Stages

1.1 S:DMF, 140°C

1.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

2.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

3.1 S:DMF, 1 h, 120°C

3.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

4.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

4.2 R:NaCl, S:H_2O

5.1 R:DCC, C:4-DMAP, S:CH_2Cl_2, rt; overnight, rt

5.2 R:Bu_4N^+ •F^-, S:CH_2Cl_2, -15°C

Notes

exothermic reaction, in the dark, conversion = 40%,alternative preparation shown, alternative preparation shown, regioselective, alternative preparation shown,other reagent triethylamine trihydrofluoride may be used in stage 2, Reactants: 6, Reagents: 7, Catalysts: 1, Solvents: 5, Steps: 6, Stages: 9, Most stages in any one step: 2

References

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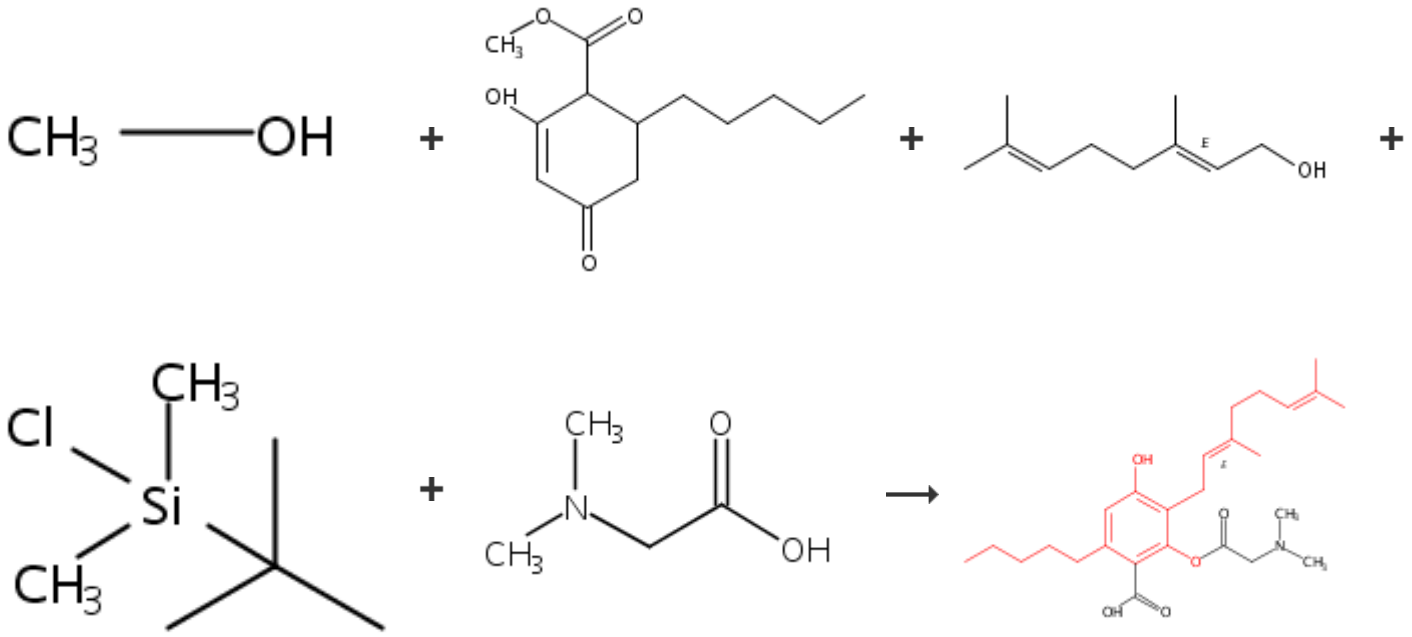
301. 6 Steps (Converging)



Overview

Steps/Stages

1.1 R:Mg, S:MeOH, rt

1.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

2.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

3.1 S:H_2O, cooled; 50°C; 3 h, 50°C; 50°C → rt

3.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, rt, pH 2

4.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

4.2 R:NaCl, S:H_2O

5.1 R:DCC, C:4-DMAP, S:CH_2Cl_2, rt; overnight, rt

5.2 R:$Bu_4N^+ \cdot F^-$, S:CH_2Cl_2, -15°C

Notes

in the dark, conversion = 85%,alternative preparation shown,reaction in a sealed pressure vessel, alternative preparation shown, regioselective, alternative preparation shown,other reagent triethylamine trihydrofluoride may be used in stage 2, Reactants: 5, Reagents: 8, Catalysts: 1, Solvents: 5, Steps: 6, Stages: 9, Most stages in any one step: 2

References

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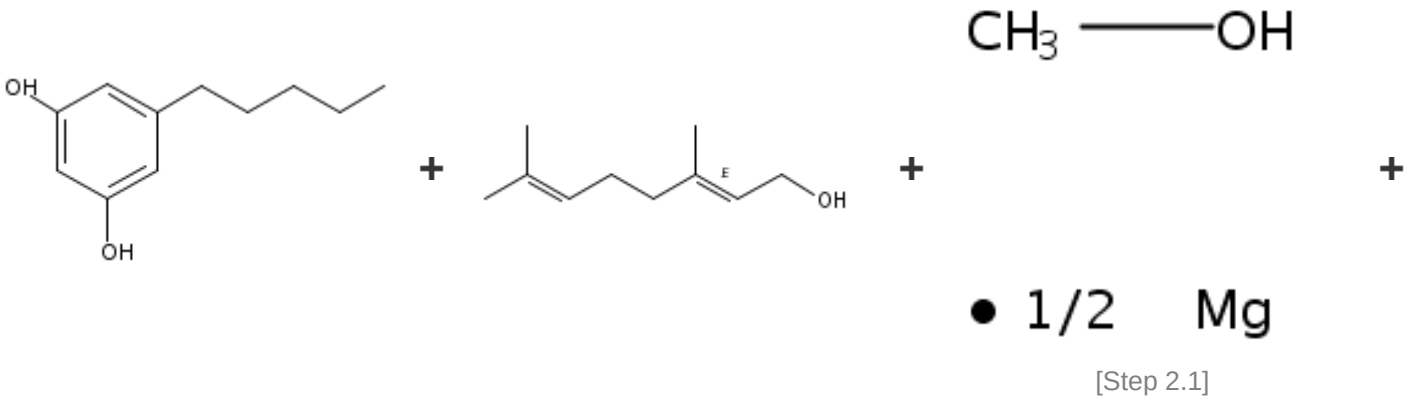
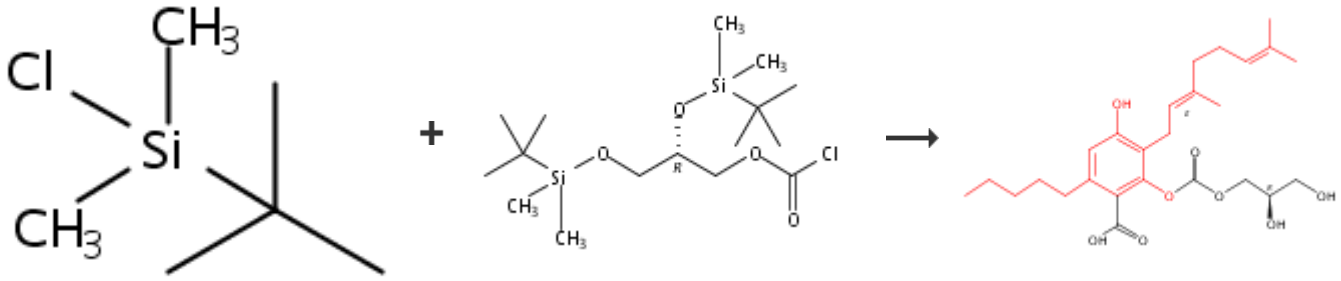
302. 5 Steps



[Step 2.1]



[Step 3.1] [Step 4.1]

Overview

Steps/Stages

1.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

2.1 S:H_2O, cooled; 50°C; 3 h, 50°C; 50°C → rt

2.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, rt, pH 2

3.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

3.2 R:NaCl, S:H_2O

4.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

5.1 R:Et_3N •3HF, S:CH_2Cl_2, -15°C; 65 h, 5°C

5.2 R:$NaHCO_3$, S:H_2O, S:AcOEt, 0°C

Notes

1) in the dark, 2) conversion = 85%,alternative preparation shown,reaction in a sealed pressure vessel, 3) alternative preparation shown, regioselective, 4) alternative preparation shown, Reactants: 5, Reagents: 7, Solvents: 5, Steps: 5, Stages: 8, Most stages in any one step: 2

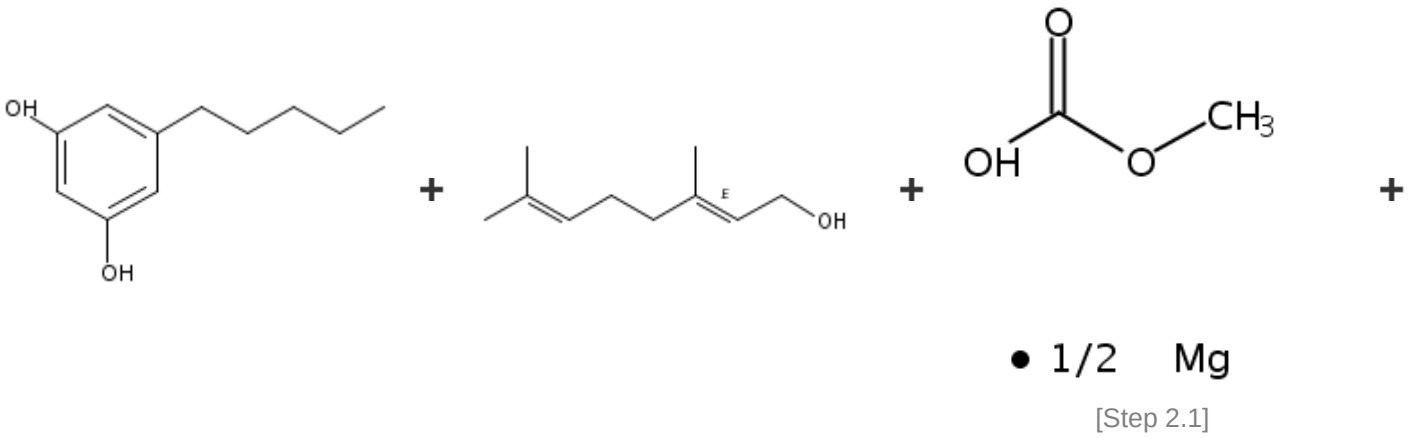
References

Biosynthesis of cannabinoid prodrugs

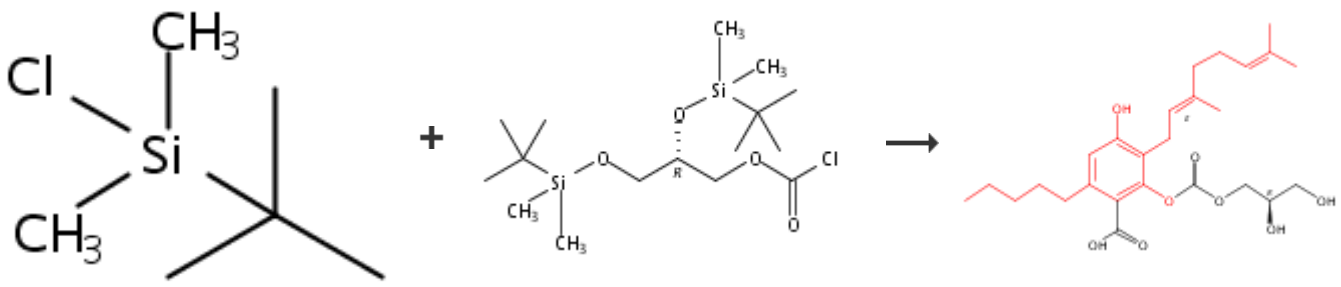
By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

303. 5 Steps



[Step 2.1]



[Step 3.1] [Step 4.1]

Overview

Steps/Stages

1.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
2.1 S:DMF, 1 h, 120°C

2.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

3.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

3.2 R:NaCl, S:H_2O

4.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

5.1 R:Et_3N •3HF, S:CH_2Cl_2, -15°C; 65 h, 5°C

5.2 R:$NaHCO_3$, S:H_2O, S:AcOEt, 0°C

Notes

1) in the dark, 2) conversion = 40%,alternative preparation shown, 3) alternative preparation shown, regioselective, 4) alternative preparation shown, Reactants: 5, Reagents: 7, Solvents: 6, Steps: 5, Stages: 8, Most stages in any one step: 2

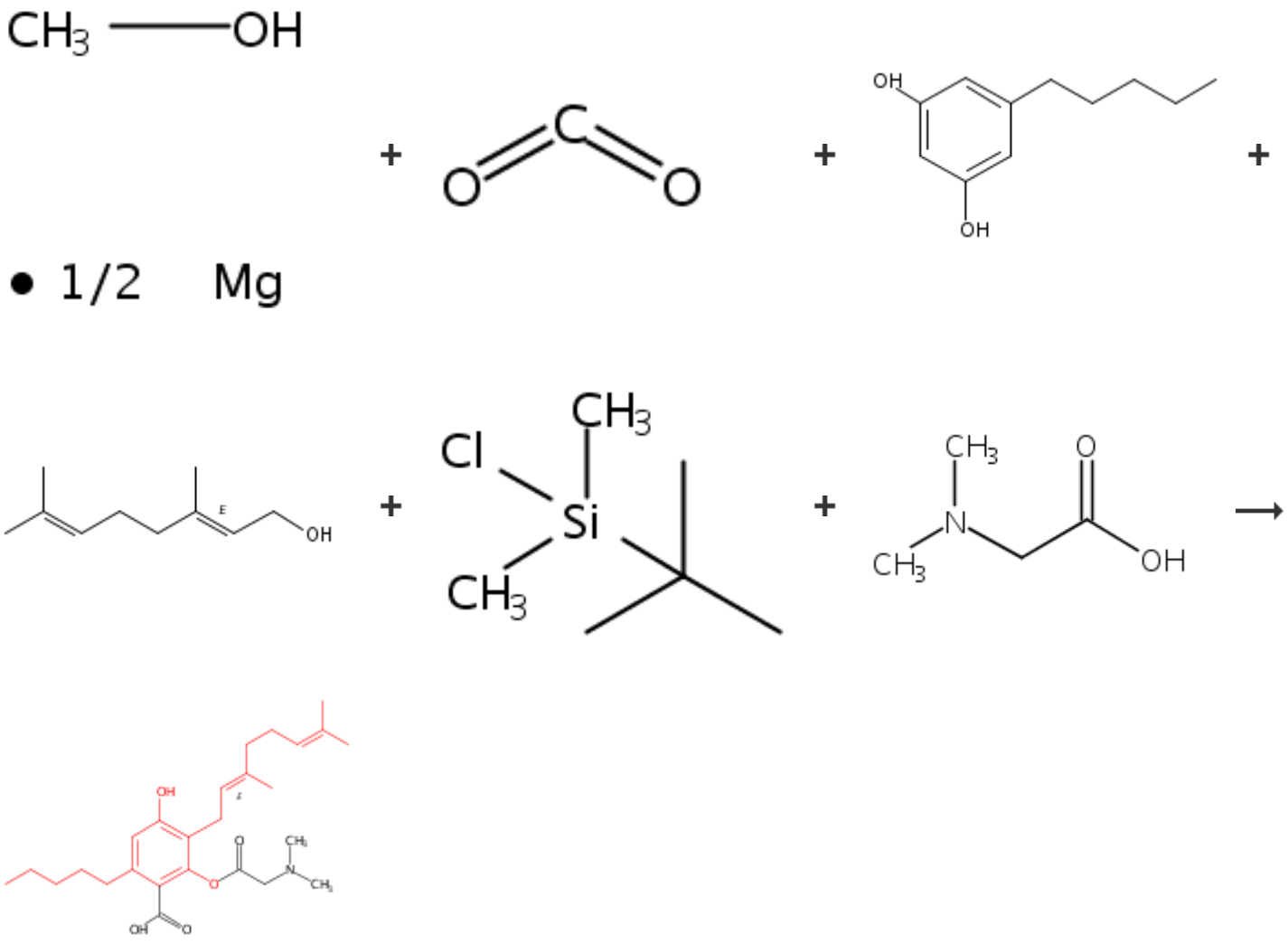
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

304. 5 Steps (Converging)



Overview

Steps/Stages

Notes

1.1 S:DMF, 140°C

1.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
2.1 S:DMF, 1 h, 120°C

2.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

3.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

3.2 R:NaCl, S:H_2O

4.1 R:DCC, C:4-DMAP, S:CH_2Cl_2, rt; overnight, rt

4.2 R:Bu_4N^+ •F^-, S:CH_2Cl_2, -15°C

exothermic reaction, in the dark, conversion = 40%,alternative preparation shown, alternative preparation shown, regioselective, alternative preparation shown,other reagent triethylamine trihydrofluoride may be used in stage 2, Reactants: 6, Reagents: 6, Catalysts: 1, Solvents: 5, Steps: 5, Stages: 8, Most stages in any one step: 2

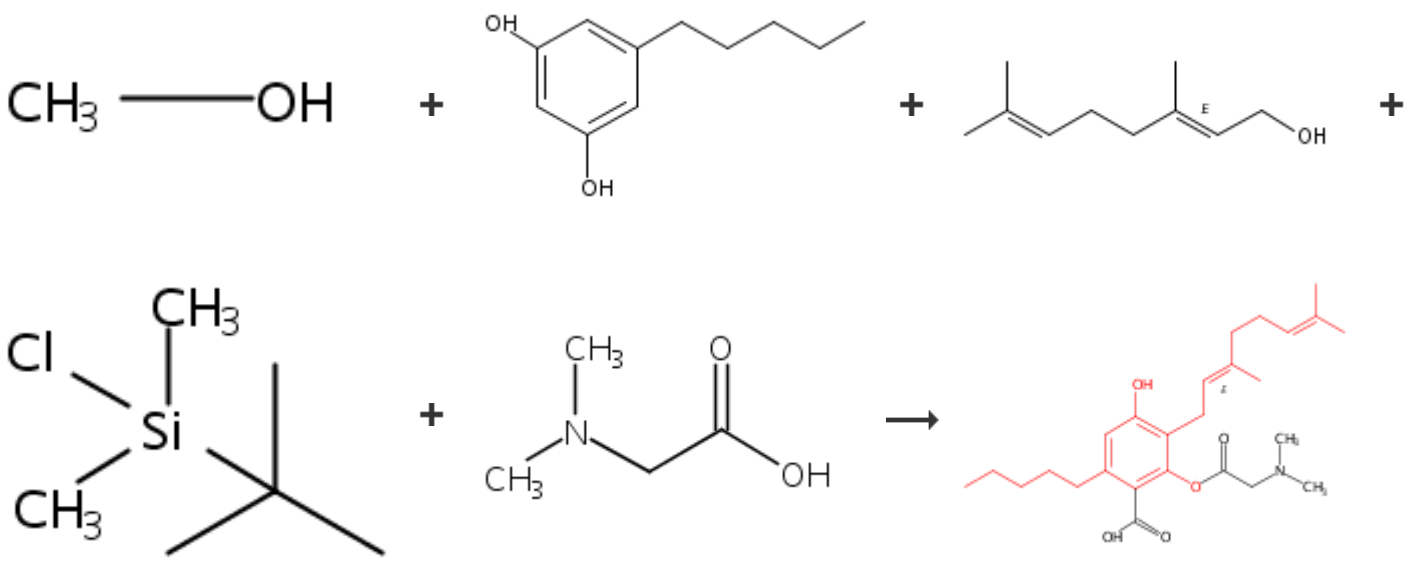
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

305. 5 Steps (Converging)



Overview

Steps/Stages

1.1 R:Mg, S:MeOH, rt

1.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
2.1 S:H_2O, cooled; 50°C; 3 h, 50°C; 50°C → rt

2.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, rt, pH 2

3.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

3.2 R:NaCl, S:H_2O

4.1 R:DCC, C:4-DMAP, S:CH_2Cl_2, rt; overnight, rt

4.2 R:Bu_4N^+ •F^-, S:CH_2Cl_2, -15°C

Notes

in the dark, conversion = 85%,alternative preparation shown,reaction in a sealed pressure vessel, alternative preparation shown, regioselective, alternative preparation shown,other reagent triethylamine trihydrofluoride may be used in stage 2, Reactants: 5, Reagents: 7, Catalysts: 1, Solvents: 4, Steps: 5, Stages: 8, Most stages in any one step: 2

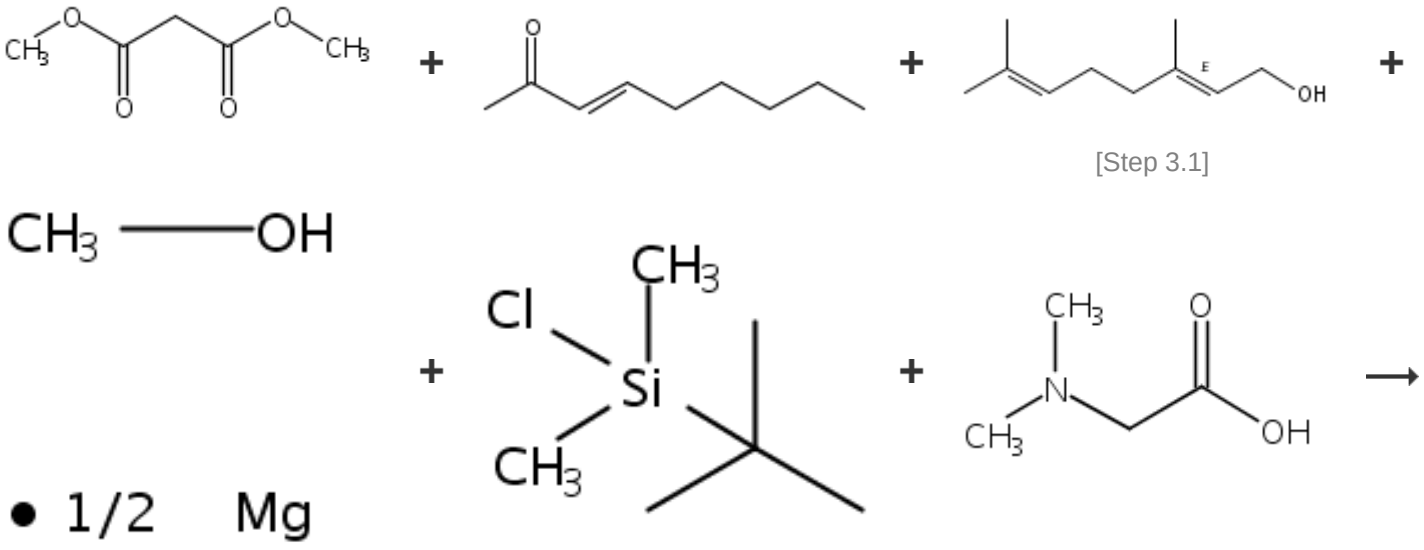
References

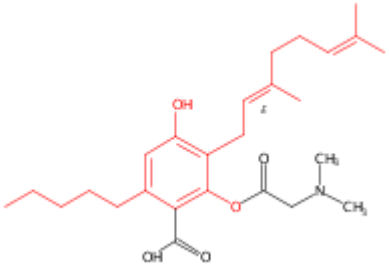
Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

306. 6 Steps





Overview

Steps/Stages

1.1 R:NaOMe, S:MeOH, rt; 3 h, reflux; reflux → rt

1.2 R:H_2O, rt

2.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

3.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

4.1 S:H_2O, cooled; 50°C; 3 h, 50°C; 50°C → rt

4.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, rt, pH 2

5.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

5.2 R:NaCl, S:H_2O

6.1 R:DCC, C:4-DMAP, S:CH_2Cl_2, rt; overnight, rt

6.2 R:$Bu_4N^+ \cdot F^-$, S:CH_2Cl_2, -15°C

Notes

3) in the dark, 4) conversion = 85%,alternative preparation shown,reaction in a sealed pressure vessel, 5) alternative preparation shown, regioselective, 6) alternative preparation shown,other reagent triethylamine trihydrofluoride may be used in stage 2, Reactants: 6, Reagents: 9, Catalysts: 1, Solvents: 5, Steps: 6, Stages: 10, Most stages in any one step: 2

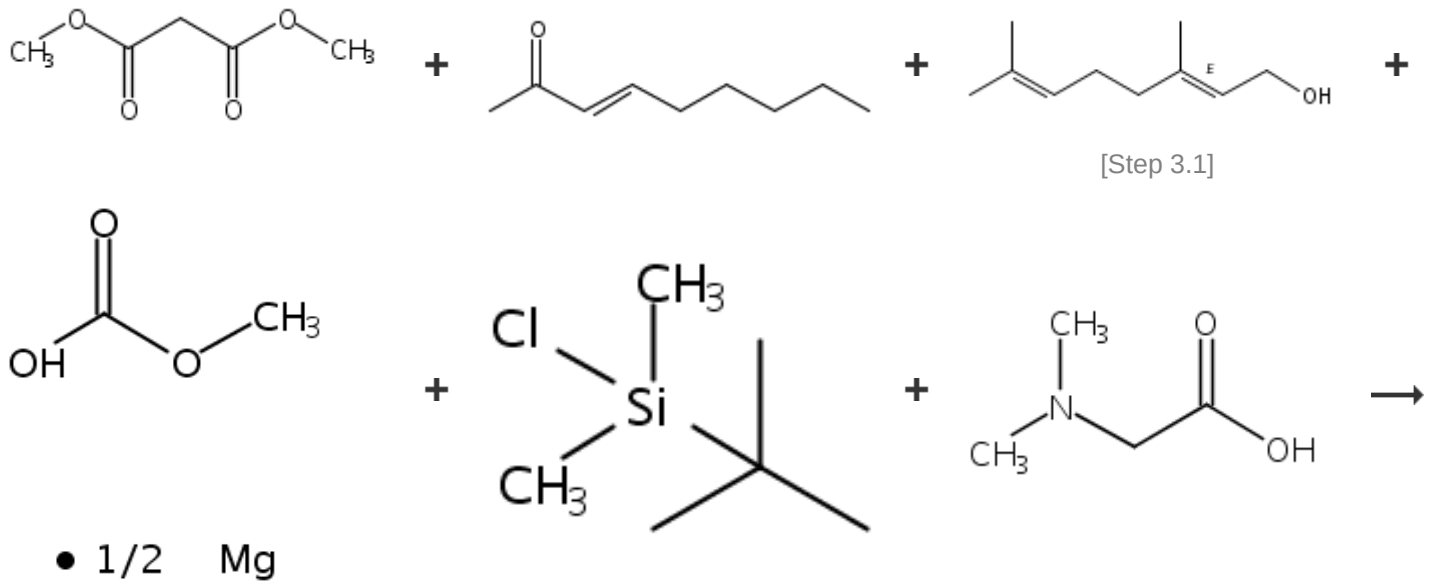
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

307. 6 Steps

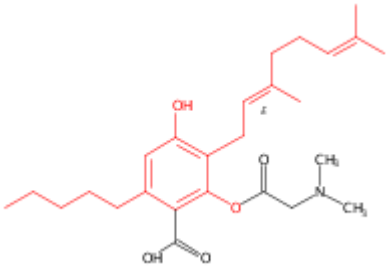


[Step 3.1]

[Step 4.1]

[Step 5.1]

[Step 6.1]



Overview

Steps/Stages

1.1 R:NaOMe, S:MeOH, rt; 3 h, reflux; reflux → rt

1.2 R:H_2O, rt

2.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

3.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

4.1 S:DMF, 1 h, 120°C

4.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

5.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

5.2 R:NaCl, S:H_2O

6.1 R:DCC, C:4-DMAP, S:CH_2Cl_2, rt; overnight, rt

6.2 R:Bu_4N^+ •F^-, S:CH_2Cl_2, -15°C

Notes

3) in the dark, 4) conversion = 40%,alternative preparation shown, 5) alternative preparation shown, regioselective, 6) alternative preparation shown,other reagent triethylamine trihydrofluoride may be used in stage 2, Reactants: 6, Reagents: 9, Catalysts: 1, Solvents: 5, Steps: 6, Stages: 10, Most stages in any one step: 2

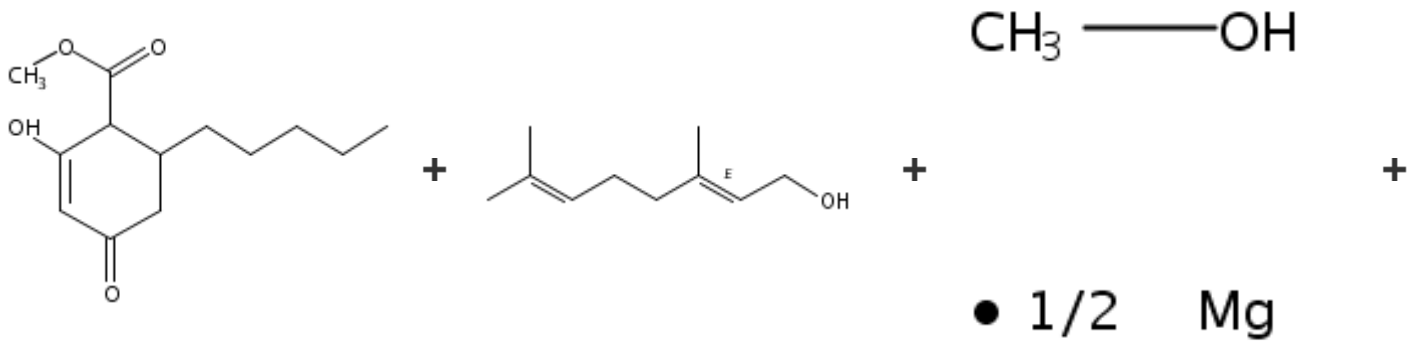
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

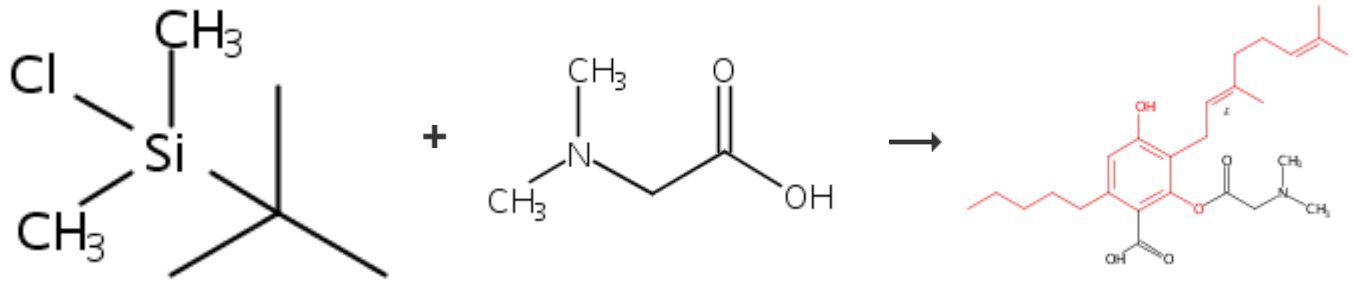
From PCT Int. Appl., 2017181118, 19 Oct 2017

308. 5 Steps



[Step 2.1]

[Step 3.1]



[Step 4.1]

[Step 5.1]

Overview

Steps/Stages

1.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

2.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

3.1 S:H_2O, cooled; 50°C; 3 h, 50°C; 50°C → rt

3.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, rt, pH 2

4.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

4.2 R:NaCl, S:H_2O

5.1 R:DCC, C:4-DMAP, S:CH_2Cl_2, rt; overnight, rt

5.2 R:Bu_4N^+ •F^-, S:CH_2Cl_2, -15°C

Notes

2) in the dark, 3) conversion = 85%,alternative preparation shown,reaction in a sealed pressure vessel, 4) alternative preparation shown, regioselective, 5) alternative preparation shown,other reagent triethylamine trihydrofluoride may be used in stage 2, Reactants: 5, Reagents: 7, Catalysts: 1, Solvents: 5, Steps: 5, Stages: 8, Most stages in any one step: 2

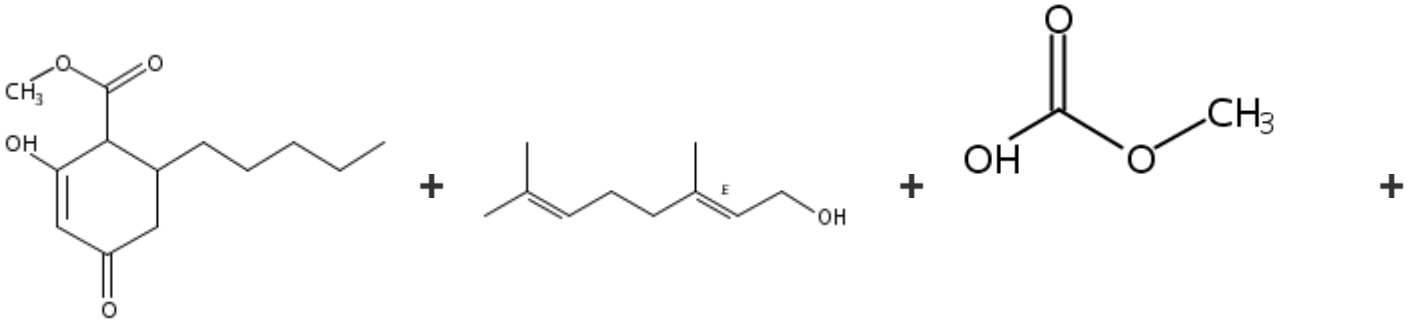
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

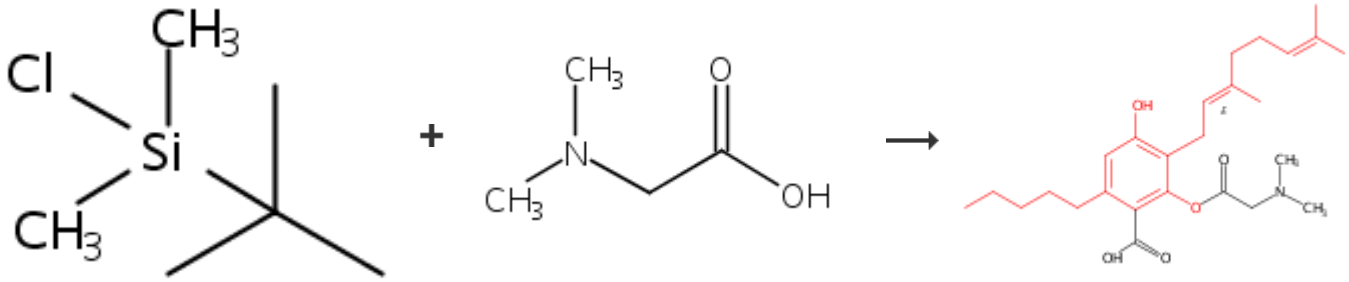
309. 5 Steps



• 1/2 Mg

[Step 2.1]

[Step 3.1]



[Step 4.1]

[Step 5.1]

Overview

Steps/Stages

1.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

2.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

3.1 S:DMF, 1 h, 120°C

3.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

4.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

4.2 R:NaCl, S:H_2O

5.1 R:DCC, C:4-DMAP, S:CH_2Cl_2, rt; overnight, rt

5.2 R:$Bu_4N^+ \cdot F^-$, S:CH_2Cl_2, -15°C

Notes

2) in the dark, 3) conversion = 40%,alternative preparation shown, 4) alternative preparation shown, regioselective, 5) alternative preparation shown,other reagent triethylamine trihydrofluoride may be used in stage 2, Reactants: 5, Reagents: 7, Catalysts: 1, Solvents: 5, Steps: 5, Stages: 8, Most stages in any one step: 2

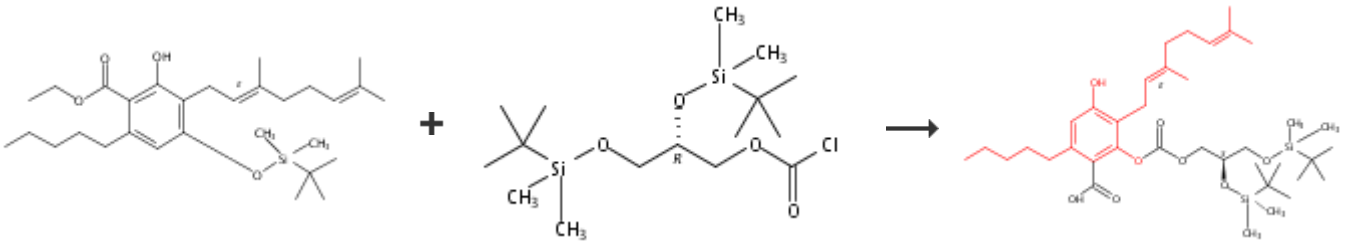
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

310. Single Step



Overview

Steps/Stages

1.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

Notes

alternative preparation shown, Reactants: 2, Reagents: 1, Solvents: 1, Steps: 1, Stages: 1, Most stages in any one step: 1

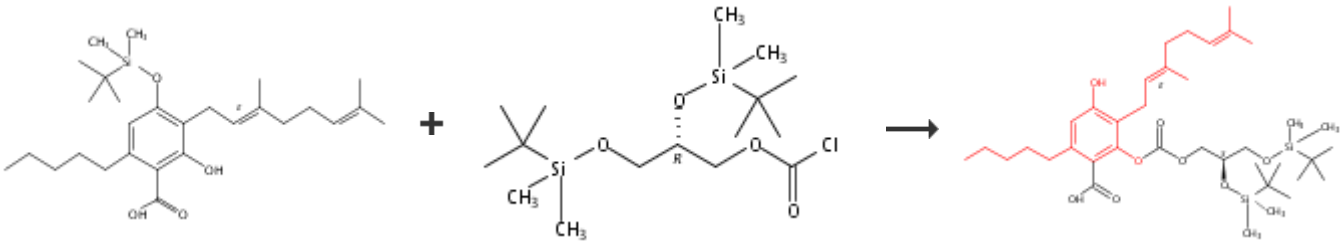
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

311. Single Step



Overview

Steps/Stages

1.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

Notes

alternative preparation shown, Reactants: 2, Reagents: 1, Solvents: 1, Steps: 1, Stages: 1, Most stages in any one step: 1

References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

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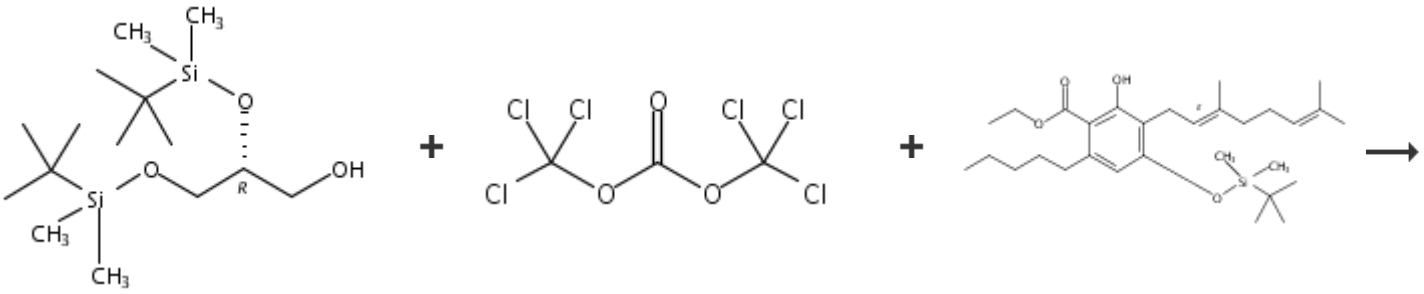
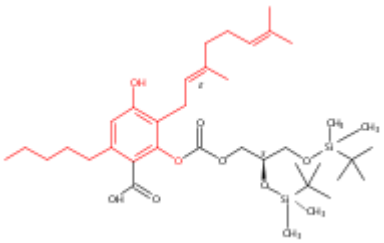
312. 2 Steps



[Step 2.1]



Overview

Steps/Stages

1.1 R:Et_3N, S:CH_2Cl_2, 3-5 h, 0°C

2.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

Notes

2) alternative preparation shown, Reactants: 3, Reagents: 1, Solvents: 1, Steps: 2, Stages: 2, Most stages in any one step: 1

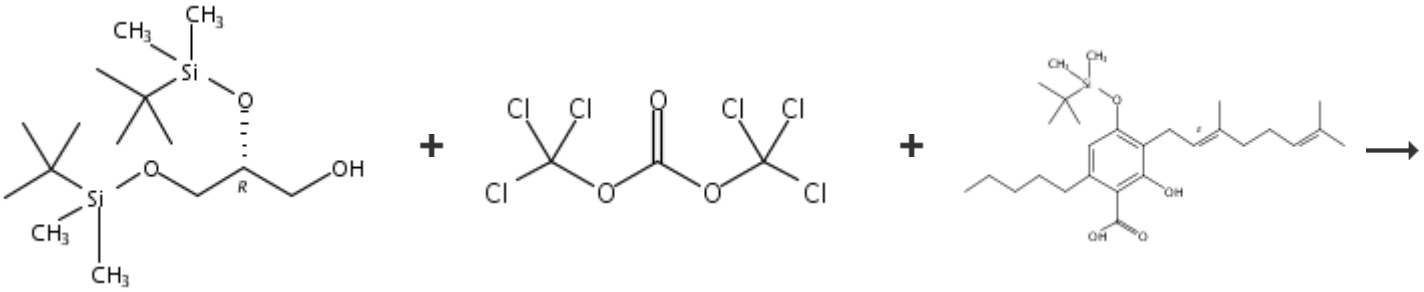
References

Biosynthesis of cannabinoid prodrugs

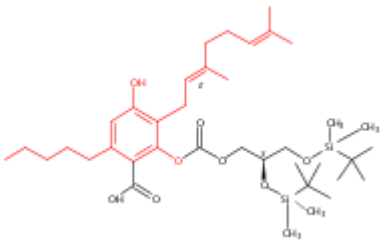
By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

313. 2 Steps



[Step 2.1]



Overview

Steps/Stages

1.1 R:Et_3N, S:CH_2Cl_2, 3-5 h, 0°C

2.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

Notes

2) alternative preparation shown, Reactants: 3, Reagents: 1, Solvents: 1, Steps: 2, Stages: 2, Most stages in any one step: 1

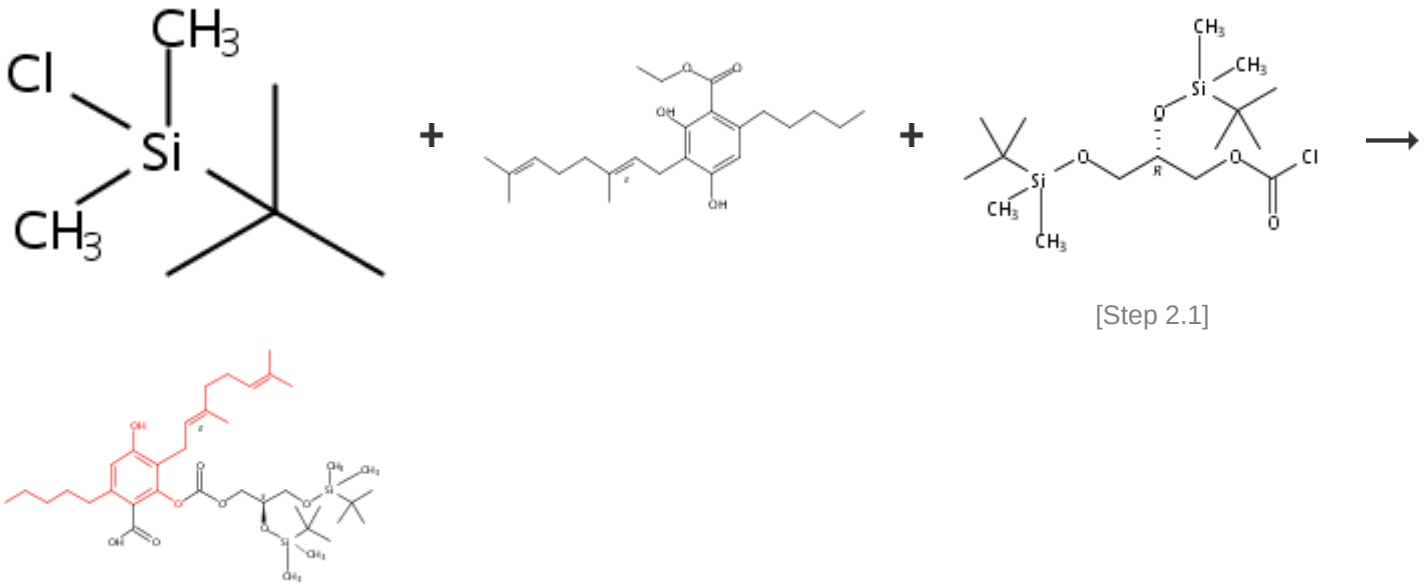
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

314. 2 Steps



[Step 2.1]

Overview

Steps/Stages

1.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

1.2 R:NaCl, S:H_2O

2.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

Notes

1) regioselective, 2) alternative preparation shown, Reactants: 3, Reagents: 3, Solvents: 2, Steps: 2, Stages: 3, Most stages in any one step: 2

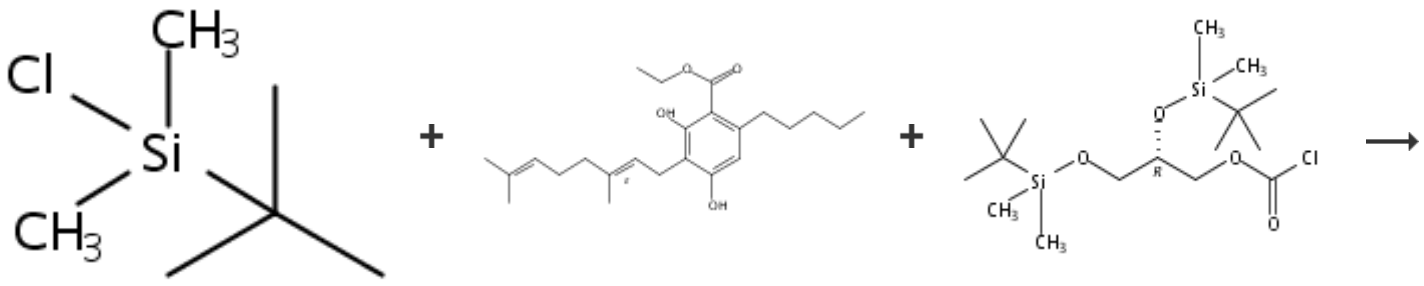
References

Biosynthesis of cannabinoid prodrugs

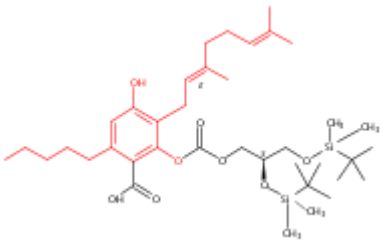
By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

315. 2 Steps



[Step 2.1]



Overview

Steps/Stages

1.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

1.2 R:NaCl, S:H_2O

1.3

2.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

Notes

1) unspecified reagent used for acidic hydrolysis in stage 3,alternative preparation shown, regioselective, 2) alternative preparation shown, Reactants: 3, Reagents: 3, Solvents: 2, Steps: 2, Stages: 4, Most stages in any one step: 3

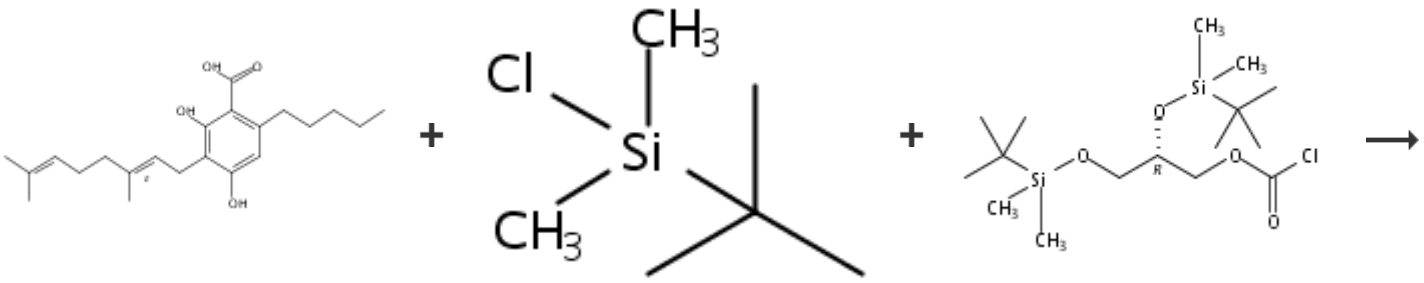
References

Biosynthesis of cannabinoid prodrugs

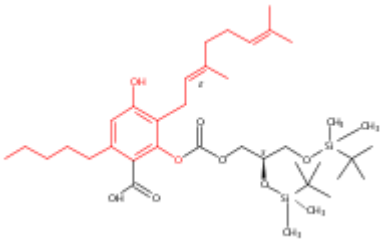
By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

316. 2 Steps



[Step 2.1]



Overview

Steps/Stages

Notes

1.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

1.2 R:NaCl, S:H_2O

2.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

1) alternative preparation shown, regioselective, 2) alternative preparation shown, Reactants: 3, Reagents: 3, Solvents: 2, Steps: 2, Stages: 3, Most stages in any one step: 2

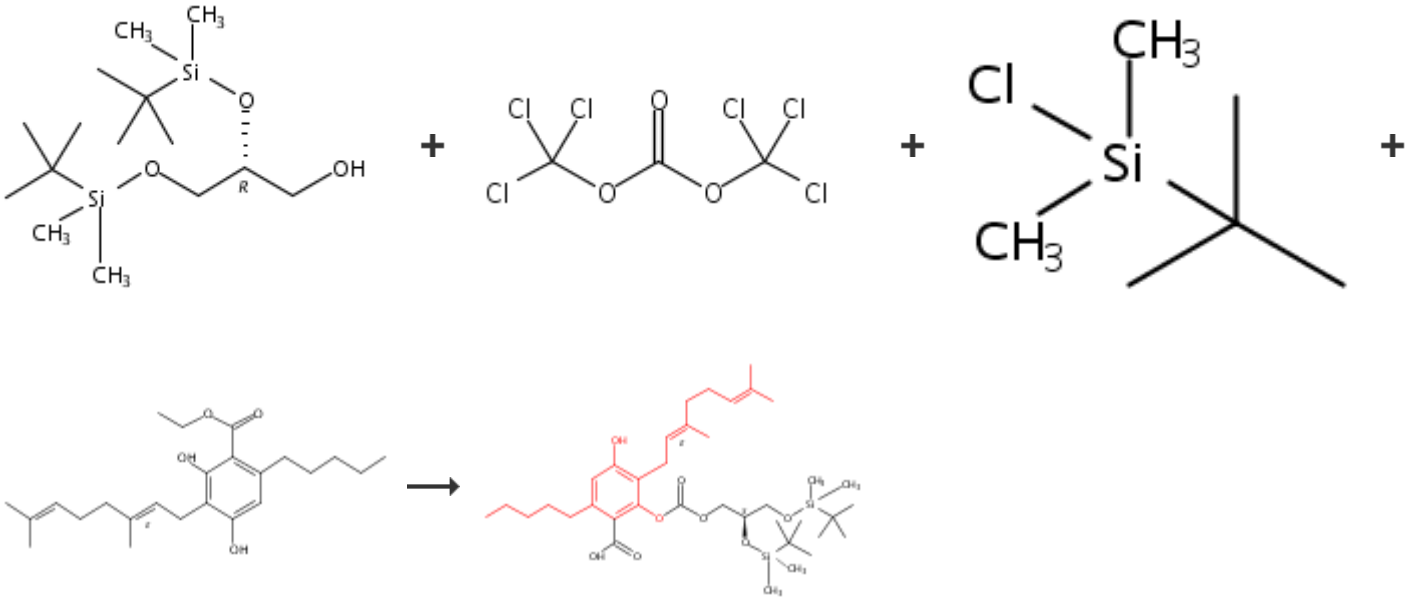
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

317. 3 Steps (Converging)



Overview

Steps/Stages

1.1 R:Et_3N, S:CH_2Cl_2, 3-5 h, 0°C

1.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

1.2 R:NaCl, S:H_2O

2.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

Notes

regioselective, alternative preparation shown, Reactants: 4, Reagents: 3, Solvents: 2, Steps: 3, Stages: 4, Most stages in any one step: 2

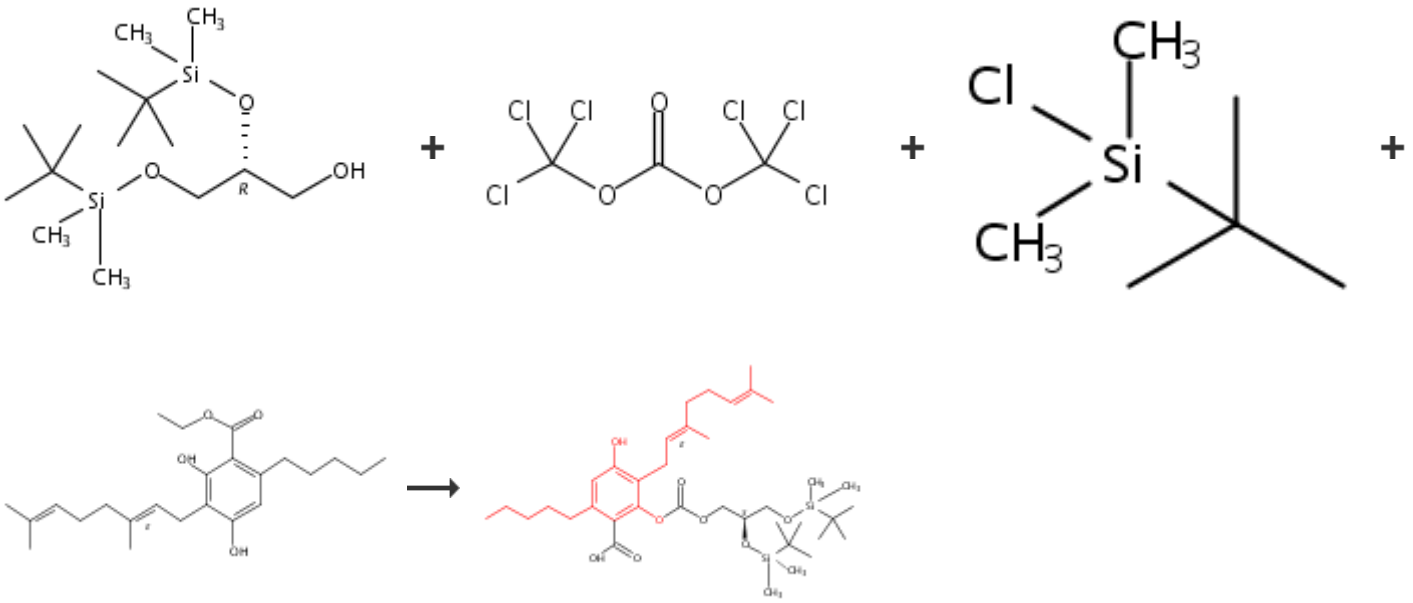
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

318. 3 Steps (Converging)



Overview

Steps/Stages

1.1 R:Et_3N, S:CH_2Cl_2, 3-5 h, 0°C

1.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

1.2 R:NaCl, S:H_2O

1.3

2.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

Notes

unspecified reagent used for acidic hydrolysis in stage 3,alternative preparation shown, regioselective, alternative preparation shown, Reactants: 4, Reagents: 3, Solvents: 2, Steps: 3, Stages: 5, Most stages in any one step: 3

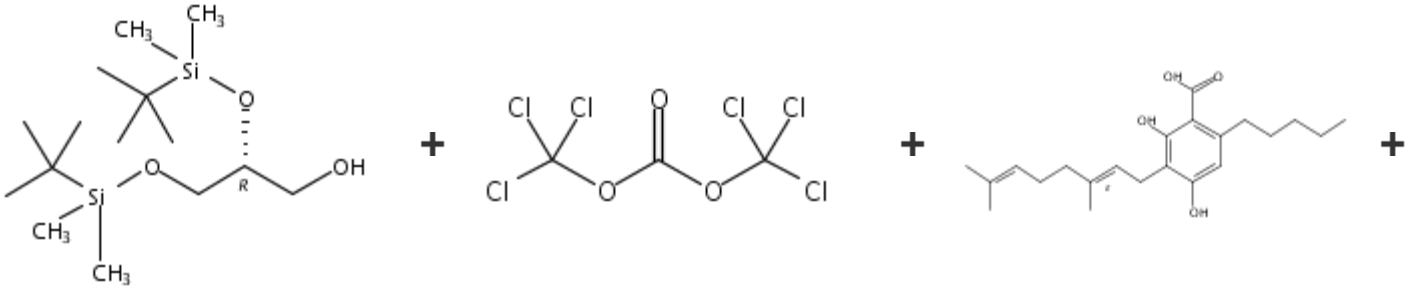
References

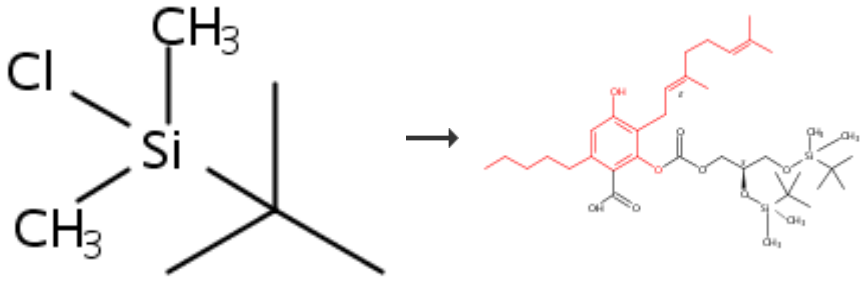
Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

319. 3 Steps (Converging)





Overview

Steps/Stages

1.1 R:Et_3N, S:CH_2Cl_2, 3-5 h, 0°C

1.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

1.2 R:NaCl, S:H_2O

2.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

Notes

alternative preparation shown, regioselective, alternative preparation shown, Reactants: 4, Reagents: 3, Solvents: 2, Steps: 3, Stages: 4, Most stages in any one step: 2

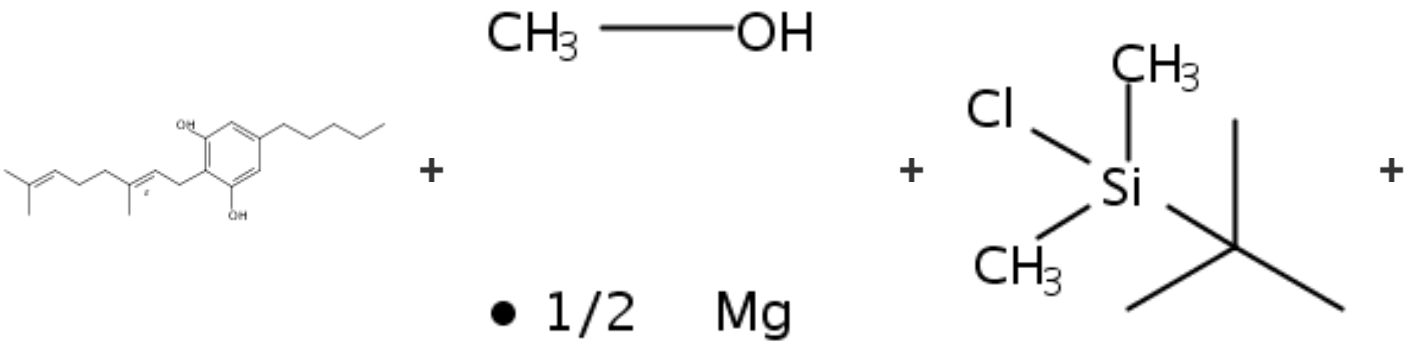
References

Biosynthesis of cannabinoid prodrugs

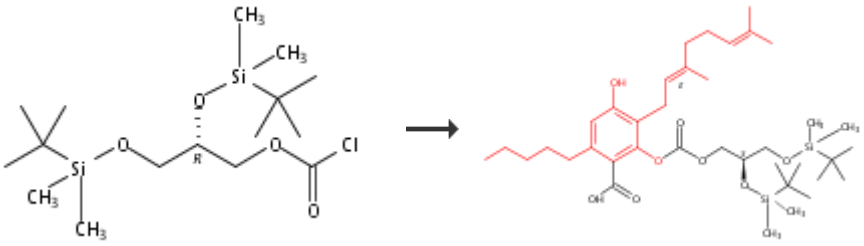
By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

320. 3 Steps



[Step 2.1]



[Step 3.1]

Overview

Steps/Stages

Notes

1.1 S:H_2O, cooled; 50°C; 3 h, 50°C; 50°C → rt

1.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, rt, pH 2

2.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

2.2 R:NaCl, S:H_2O

3.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

1) conversion = 85%,alternative preparation shown,reaction in a sealed pressure vessel, 2) alternative preparation shown, regioselective, 3) alternative preparation shown, Reactants: 4, Reagents: 4, Solvents: 4, Steps: 3, Stages: 5, Most stages in any one step: 2

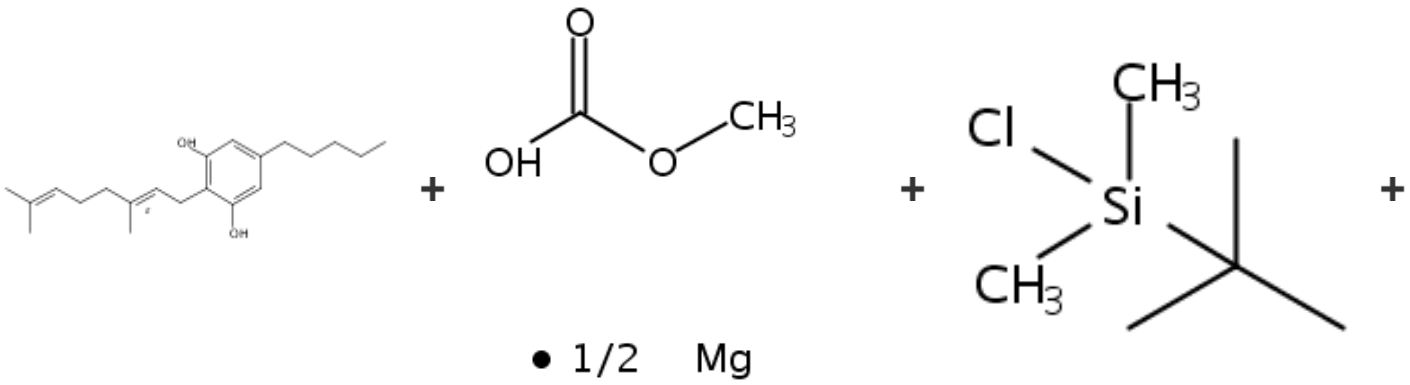
References

Biosynthesis of cannabinoid prodrugs

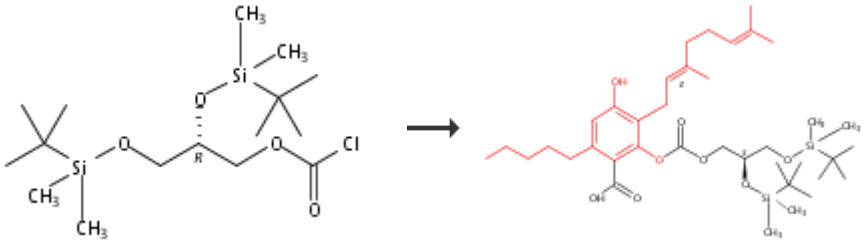
By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

321. 3 Steps



[Step 2.1]



[Step 3.1]

Overview

Steps/Stages

1.1 S:DMF, 1 h, 120°C

1.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

2.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

2.2 R:NaCl, S:H_2O

3.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

Notes

1) conversion = 40%,alternative preparation shown, 2) alternative preparation shown, regioselective, 3) alternative preparation shown, Reactants: 4, Reagents: 4, Solvents: 5, Steps: 3, Stages: 5, Most stages in any one step: 2

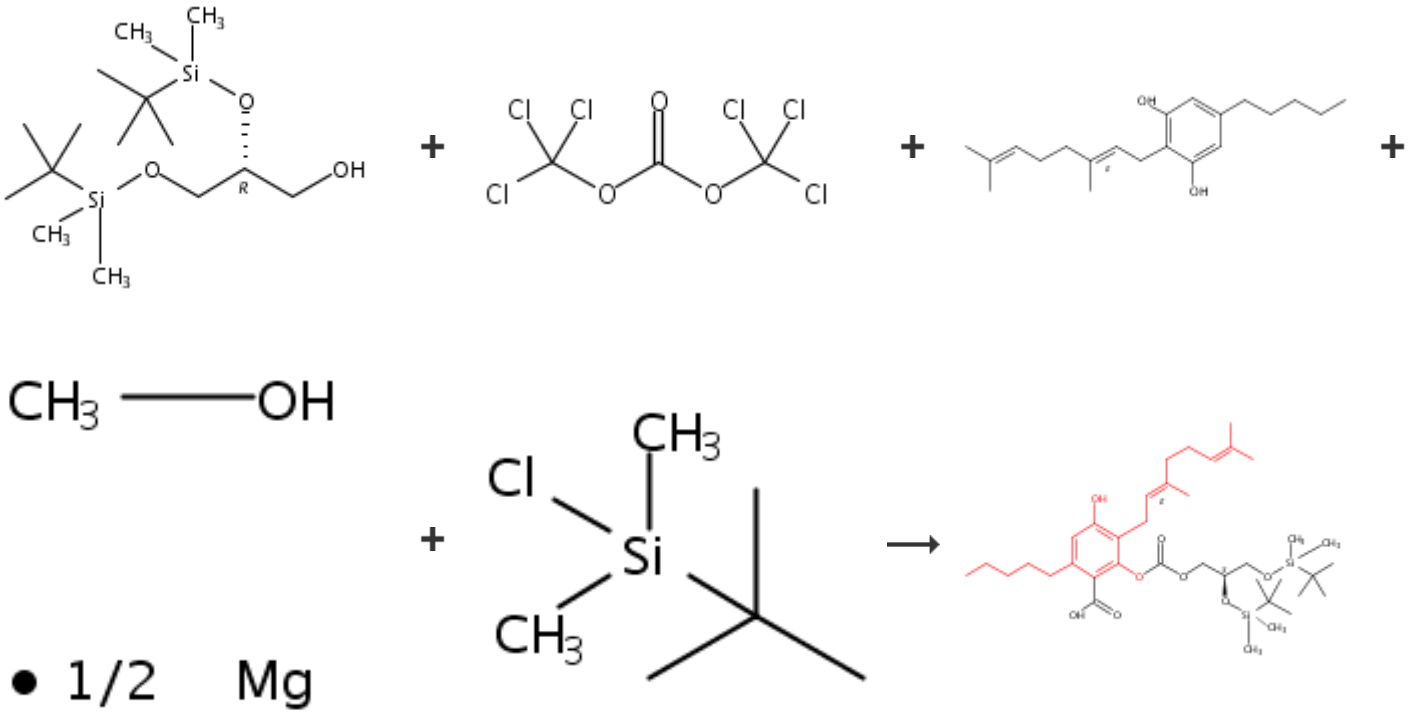
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

322. 4 Steps (Converging)



Overview

Steps/Stages

1.1 R:Et_3N, S:CH_2Cl_2, 3-5 h, 0°C

1.1 S:H_2O, cooled; 50°C; 3 h, 50°C; 50°C → rt

1.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, rt, pH 2

2.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

2.2 R:NaCl, S:H_2O

3.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

Notes

conversion = 85%,alternative preparation shown,reaction in a sealed pressure vessel, alternative preparation shown, regioselective, alternative preparation shown, Reactants: 5, Reagents: 4, Solvents: 4, Steps: 4, Stages: 6, Most stages in any one step: 2

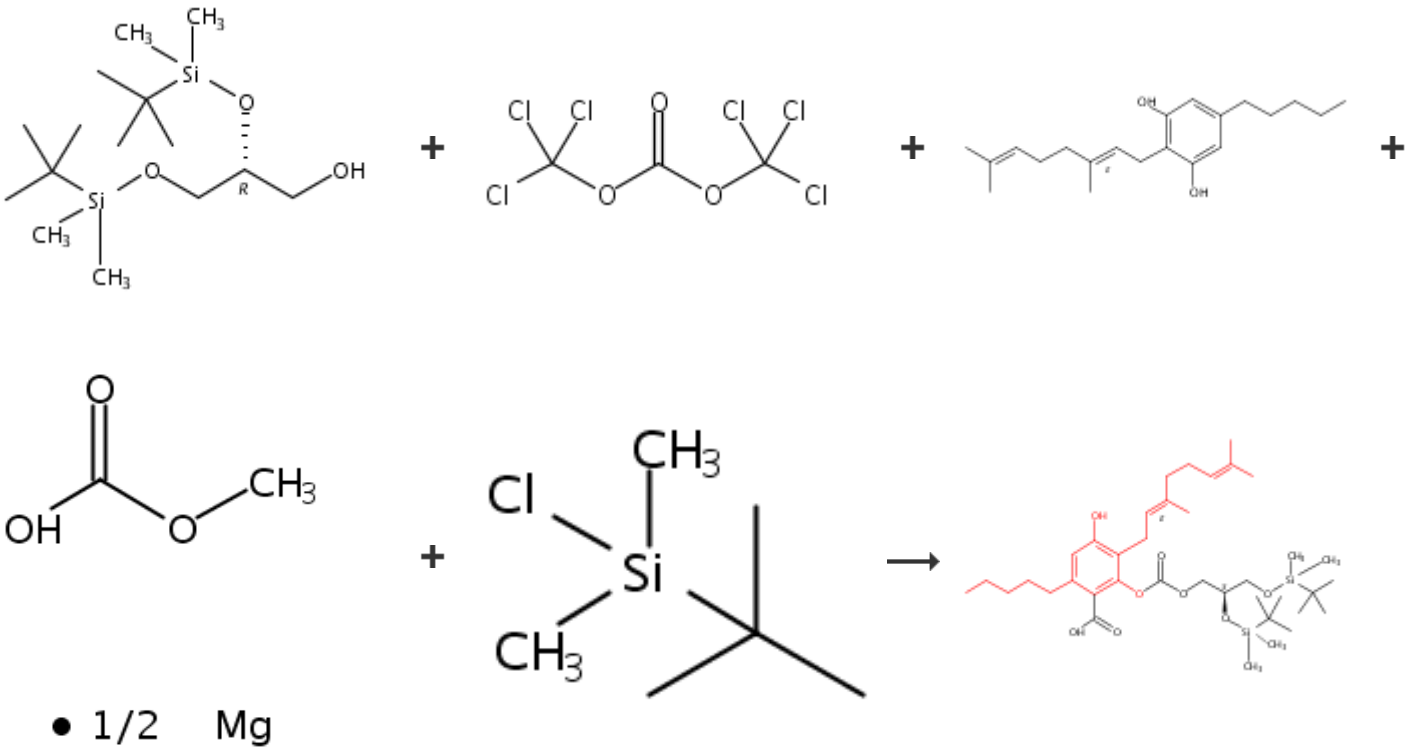
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

323. 4 Steps (Converging)



- 1/2 Mg

Overview

Steps/Stages

1.1 R:Et_3N, S:CH_2Cl_2, 3-5 h, 0°C
1.1 S:DMF, 1 h, 120°C

1.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

2.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

2.2 R:NaCl, S:H_2O

3.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

Notes

conversion = 40%,alternative preparation shown, alternative preparation shown, regioselective, alternative preparation shown, Reactants: 5, Reagents: 4, Solvents: 5, Steps: 4, Stages: 6, Most stages in any one step: 2

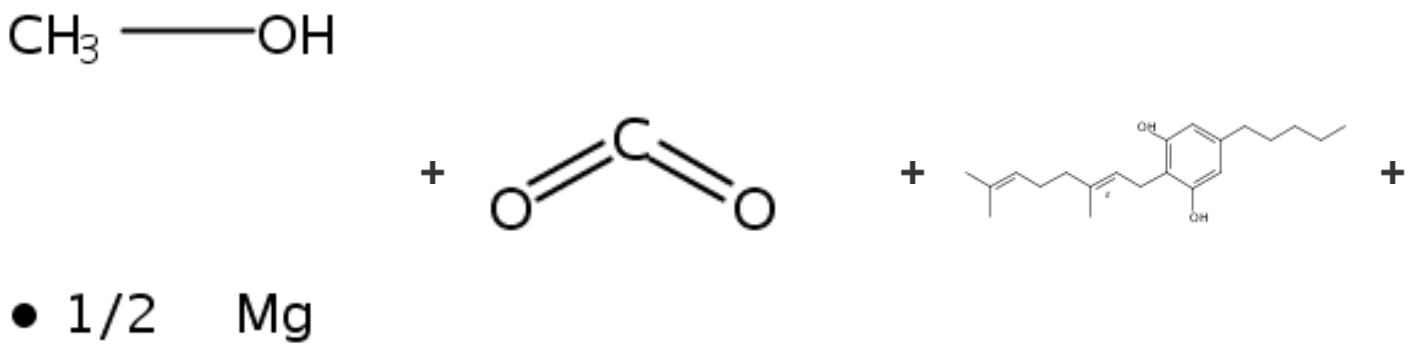
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

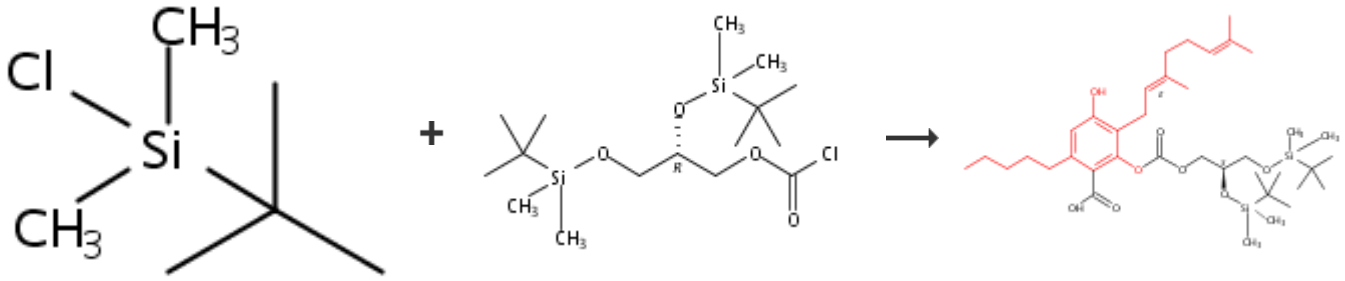
From PCT Int. Appl., 2017181118, 19 Oct 2017

324. 4 Steps



- 1/2 Mg

[Step 2.1]



[Step 3.1] [Step 4.1]

Overview

Steps/Stages

1.1 S:DMF, 140°C
2.1 S:DMF, 1 h, 120°C

2.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

3.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

3.2 R:NaCl, S:H_2O

4.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

Notes

1) exothermic reaction, 2) conversion = 40%,alternative preparation shown, 3) alternative preparation shown, regioselective, 4) alternative preparation shown, Reactants: 5, Reagents: 4, Solvents: 5, Steps: 4, Stages: 6, Most stages in any one step: 2

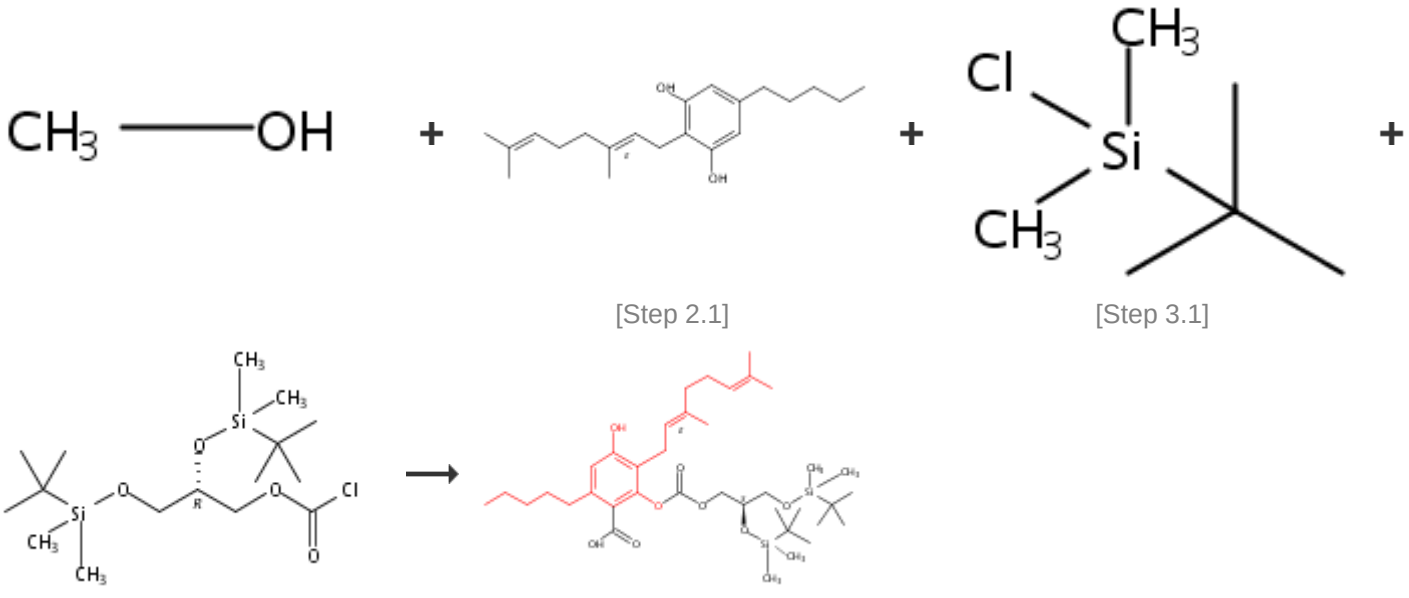
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

325. 4 Steps



[Step 2.1] [Step 3.1]

[Step 4.1]

Overview

Steps/Stages

Notes

1.1 R:Mg, S:MeOH, rt
2.1 S:H_2O, cooled; 50°C; 3 h, 50°C; 50°C → rt

2.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, rt, pH 2

3.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

3.2 R:NaCl, S:H_2O

4.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

2) conversion = 85%,alternative preparation shown,reaction in a sealed pressure vessel, 3) alternative preparation shown, regioselective, 4) alternative preparation shown, Reactants: 4, Reagents: 5, Solvents: 4, Steps: 4, Stages: 6, Most stages in any one step: 2

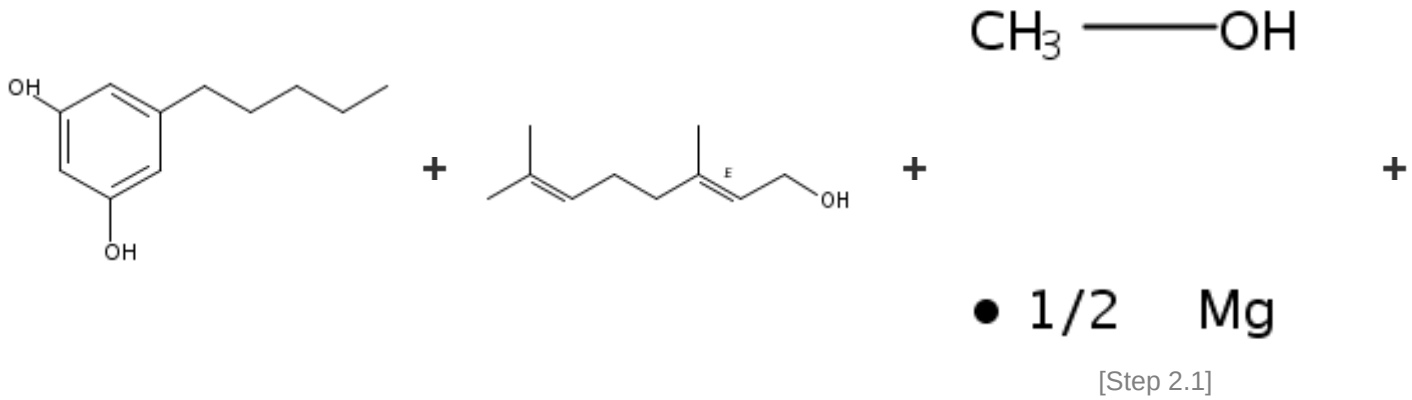
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

326. 4 Steps



[Step 2.1]

[Step 3.1]

[Step 4.1]

Overview

Steps/Stages

1.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
2.1 S:H_2O, cooled; 50°C; 3 h, 50°C; 50°C → rt

2.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, rt, pH 2

3.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

3.2 R:NaCl, S:H_2O

4.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

Notes

1) in the dark, 2) conversion = 85%,alternative preparation shown,reaction in a sealed pressure vessel, 3) alternative preparation shown, regioselective, 4) alternative preparation shown, Reactants: 5, Reagents: 5, Solvents: 4, Steps: 4, Stages: 6, Most stages in any one step: 2

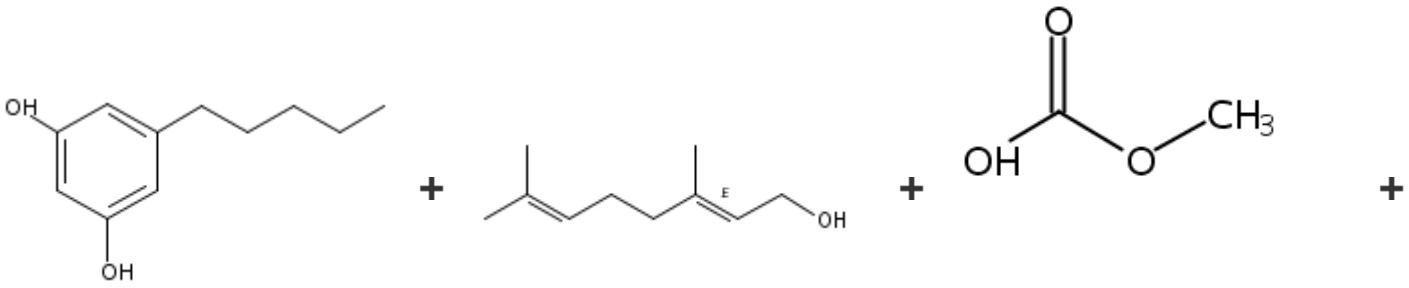
References

Biosynthesis of cannabinoid prodrugs

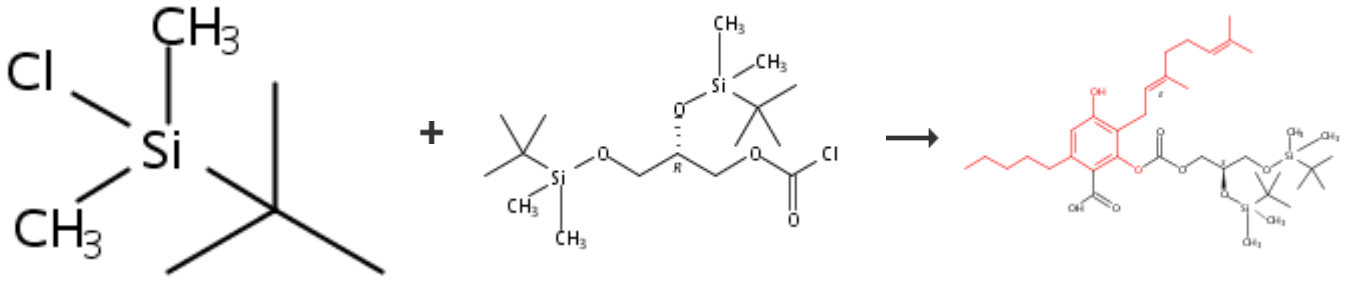
By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

327. 4 Steps



[Step 2.1]



[Step 3.1] [Step 4.1]

Overview

Steps/Stages

1.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
2.1 S:DMF, 1 h, 120°C

2.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

3.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

3.2 R:NaCl, S:H_2O

4.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

Notes

1) in the dark, 2) conversion = 40%,alternative preparation shown, 3) alternative preparation shown, regioselective, 4) alternative preparation shown, Reactants: 5, Reagents: 5, Solvents: 5, Steps: 4, Stages: 6, Most stages in any one step: 2

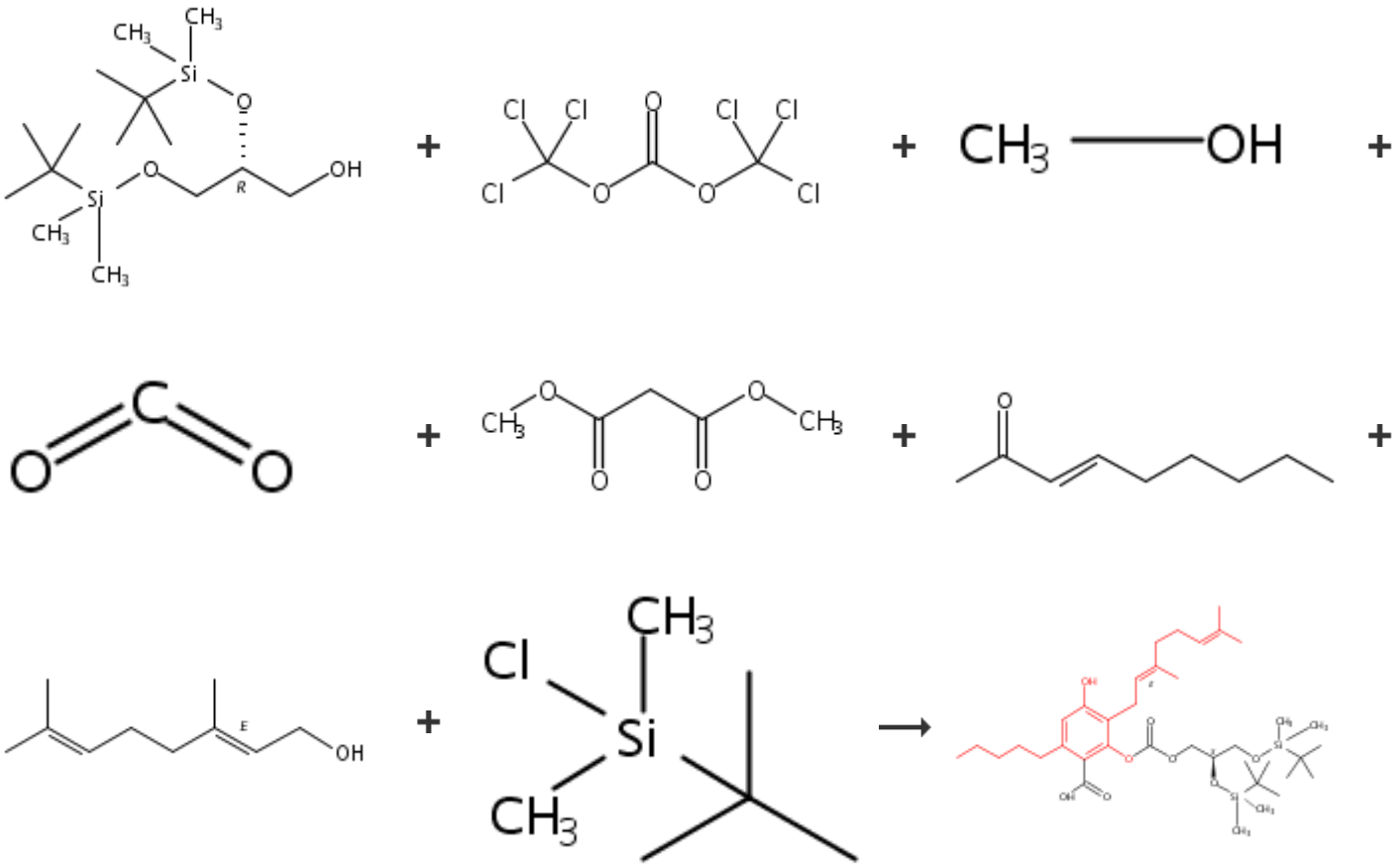
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

328. 9 Steps (Converging)



Overview

Steps/Stages

1.1 R:Et_3N, S:CH_2Cl_2, 3-5 h, 0°C

1.1 R:Mg, S:MeOH, rt
2.1 S:DMF, 140°C

1.1 R:NaOMe, S:MeOH, rt; 3 h, reflux; reflux → rt

1.2 R:H_2O, rt

2.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

3.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
4.1 S:DMF, 1 h, 120°C

4.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

5.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

5.2 R:NaCl, S:H_2O

6.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

Notes

exothermic reaction, in the dark, conversion = 40%,alternative preparation shown, alternative preparation shown, regioselective, alternative preparation shown, Reactants: 8, Reagents: 9, Solvents: 5, Steps: 9, Stages: 12, Most stages in any one step: 2

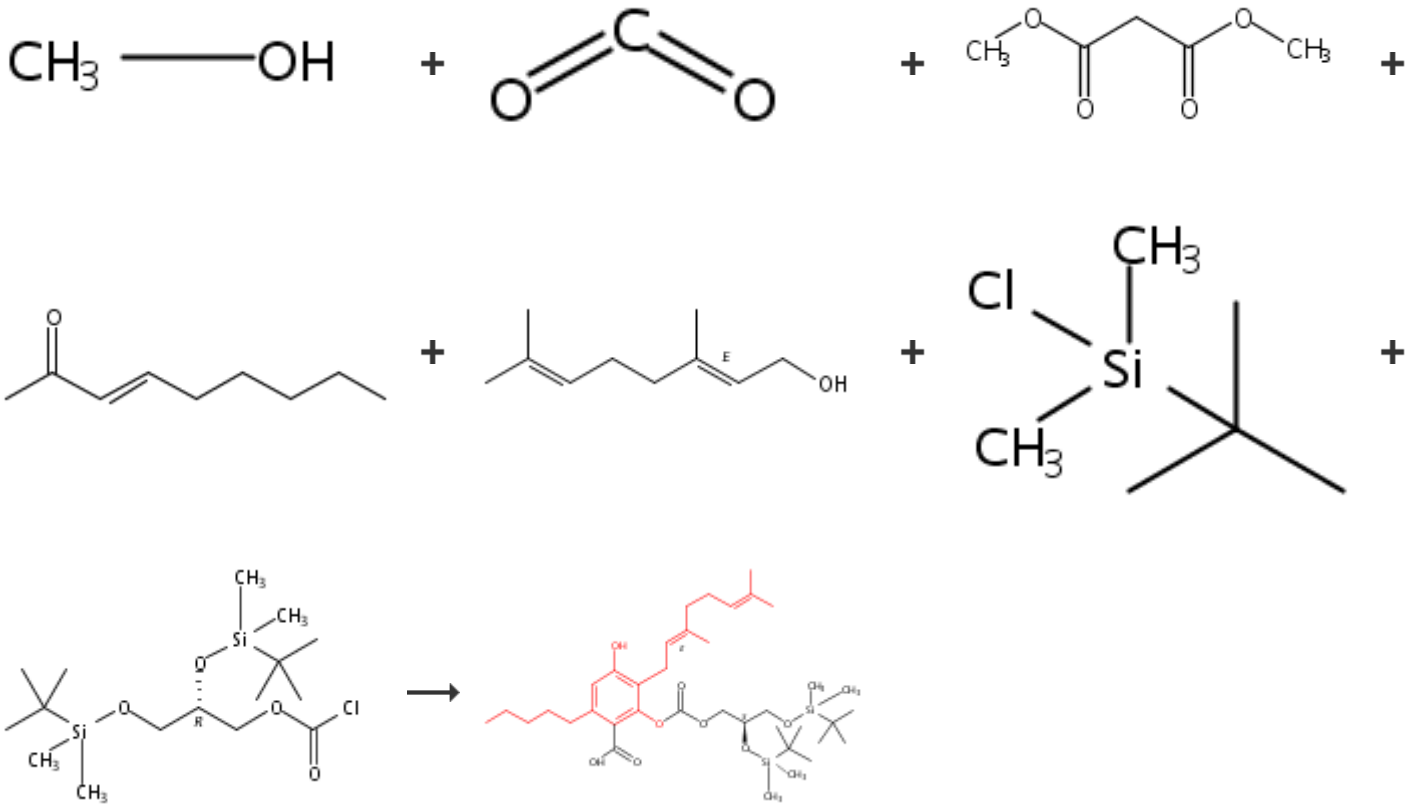
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

329. 8 Steps (Converging)



Overview

Steps/Stages

1.1 R:Mg, S:MeOH, rt
2.1 S:DMF, 140°C

1.1 R:NaOMe, S:MeOH, rt; 3 h, reflux; reflux → rt

1.2 R:H_2O, rt

2.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

3.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
4.1 S:DMF, 1 h, 120°C

4.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

5.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

5.2 R:NaCl, S:H_2O

6.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

Notes

exothermic reaction, in the dark, conversion = 40%,alternative preparation shown, alternative preparation shown, regioselective, alternative preparation shown, Reactants: 7, Reagents: 9, Solvents: 5, Steps: 8, Stages: 11, Most stages in any one step: 2

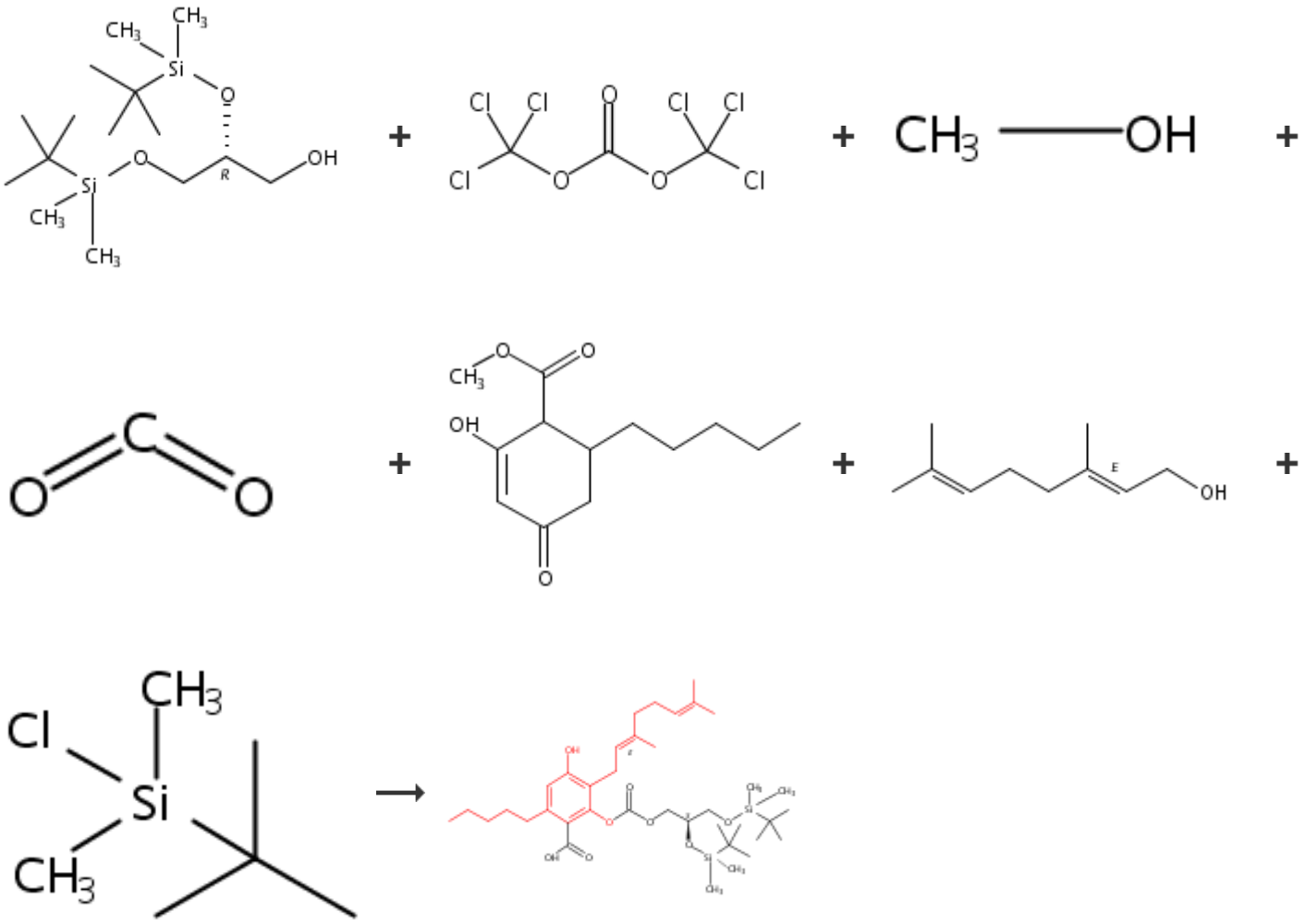
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

330. 8 Steps (Converging)



Overview

Steps/Stages

1.1 R:Et_3N, S:CH_2Cl_2, 3-5 h, 0°C

1.1 R:Mg, S:MeOH, rt
2.1 S:DMF, 140°C

1.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

2.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
3.1 S:DMF, 1 h, 120°C

3.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

4.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

4.2 R:NaCl, S:H_2O

5.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

Notes

exothermic reaction, in the dark, conversion = 40%,alternative preparation shown, alternative preparation shown, regioselective, alternative preparation shown, Reactants: 7, Reagents: 7, Solvents: 5, Steps: 8, Stages: 10, Most stages in any one step: 2

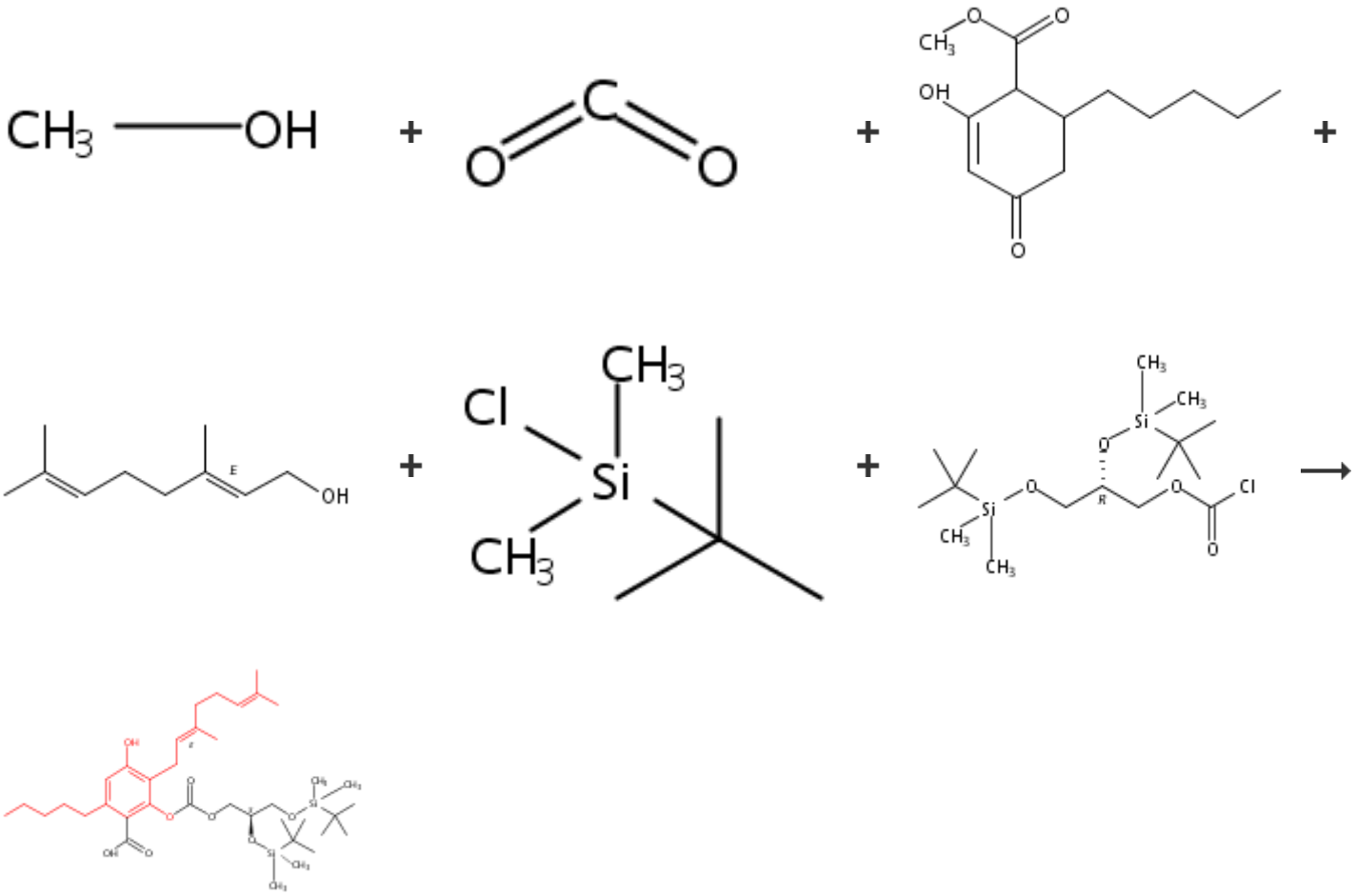
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

331. 7 Steps (Converging)



Overview

Steps/Stages

1.1 R:Mg, S:MeOH, rt
2.1 S:DMF, 140°C

1.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

2.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
3.1 S:DMF, 1 h, 120°C

3.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

4.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

4.2 R:NaCl, S:H_2O

5.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

Notes

exothermic reaction, in the dark, conversion = 40%,alternative preparation shown, alternative preparation shown, regioselective, alternative preparation shown, Reactants: 6, Reagents: 7, Solvents: 5, Steps: 7, Stages: 9, Most stages in any one step: 2

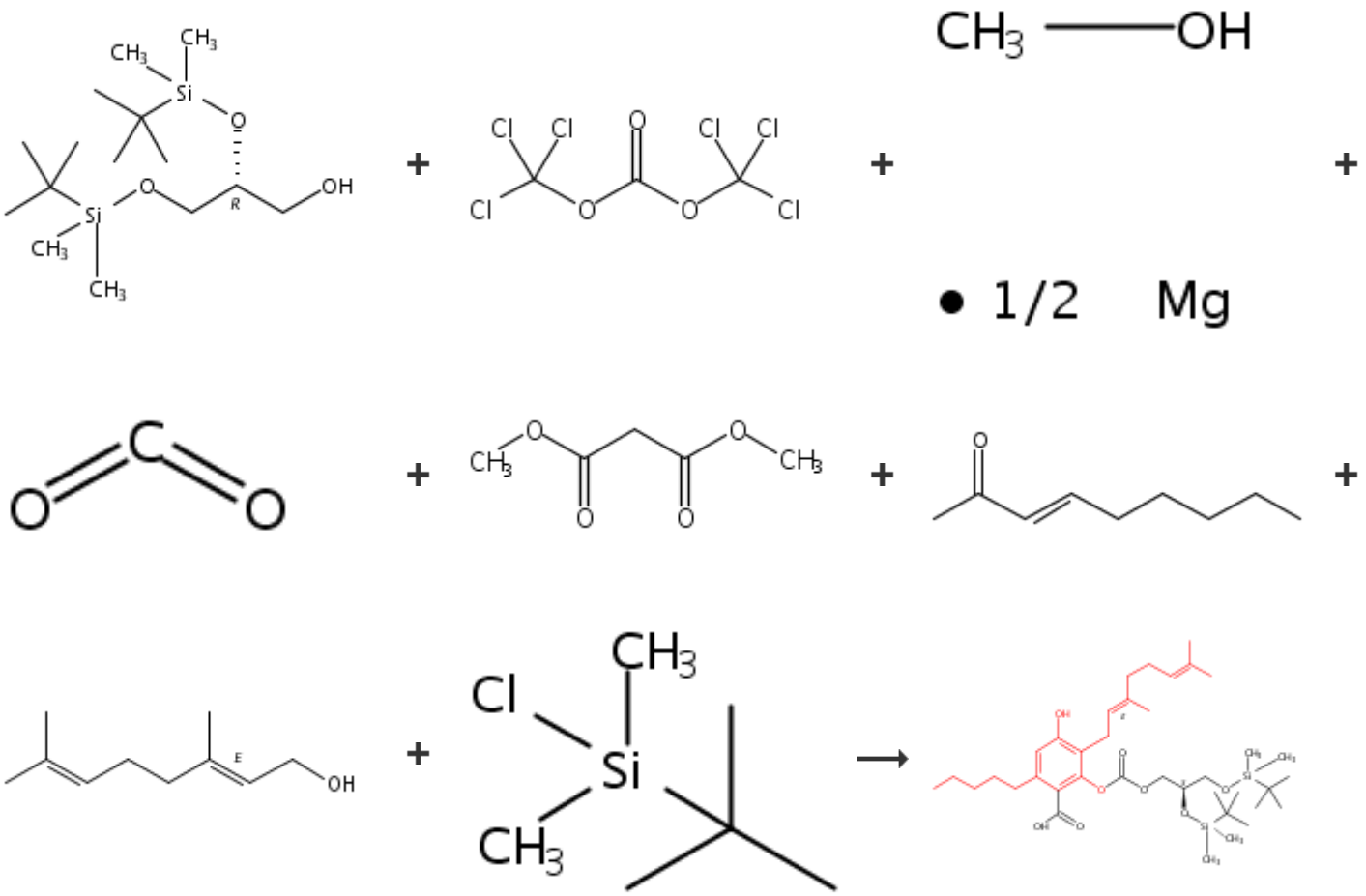
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

332. 8 Steps (Converging)



Overview

Steps/Stages

1.1 R:Et_3N, S:CH_2Cl_2, 3-5 h, 0°C
1.1 S:DMF, 140°C

1.1 R:NaOMe, S:MeOH, rt; 3 h, reflux; reflux → rt

1.2 R:H_2O, rt

2.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

3.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
4.1 S:DMF, 1 h, 120°C

4.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

5.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

5.2 R:NaCl, S:H_2O

6.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

Notes

exothermic reaction, in the dark, conversion = 40%,alternative preparation shown, alternative preparation shown, regioselective, alternative preparation shown, Reactants: 8, Reagents: 8, Solvents: 5, Steps: 8, Stages: 11, Most stages in any one step: 2

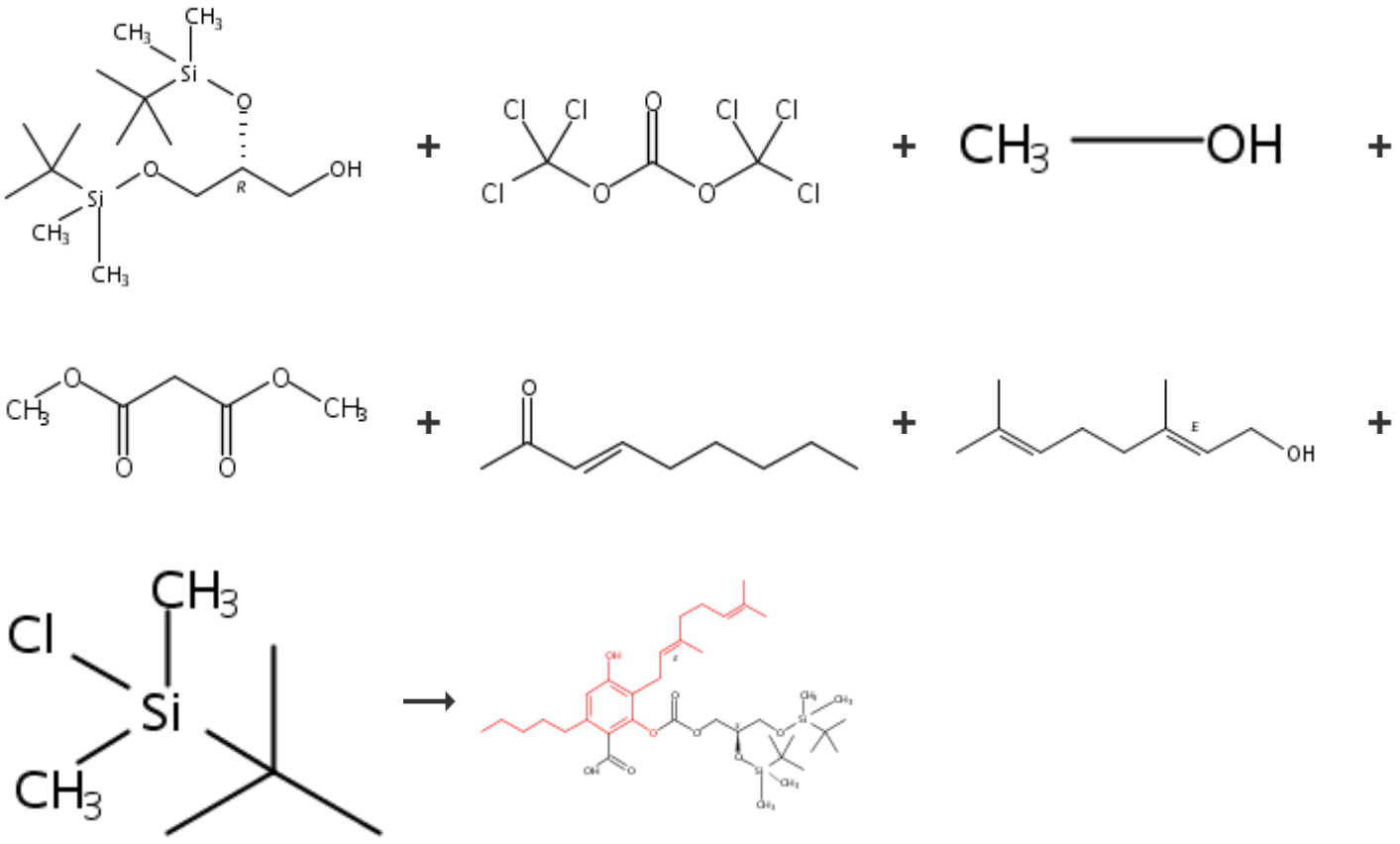
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

333. 8 Steps (Converging)



Overview

Steps/Stages

1.1 R:Et_3N, S:CH_2Cl_2, 3-5 h, 0°C

1.1 R:Mg, S:MeOH, rt

1.1 R:NaOMe, S:MeOH, rt; 3 h, reflux; reflux → rt

1.2 R:H_2O, rt

2.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

3.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

4.1 S:H_2O, cooled; 50°C; 3 h, 50°C; 50°C → rt

4.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, rt, pH 2

5.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

5.2 R:NaCl, S:H_2O

6.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

Notes

in the dark, conversion = 85%,alternative preparation shown,reaction in a sealed pressure vessel, alternative preparation shown, regioselective, alternative preparation shown, Reactants: 7, Reagents: 9, Solvents: 5, Steps: 8, Stages: 11, Most stages in any one step: 2

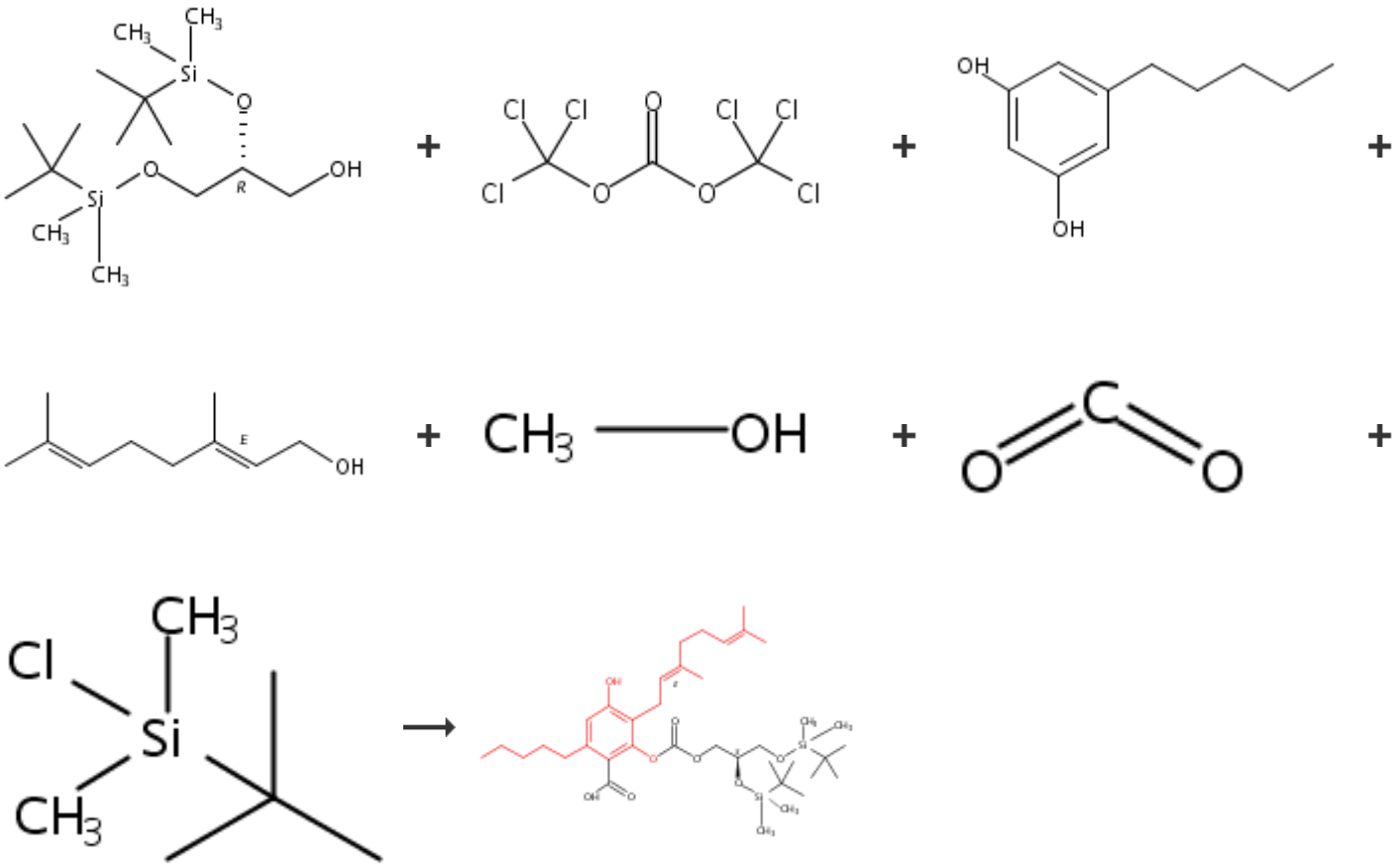
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

334. 7 Steps (Converging)



Overview

Steps/Stages

1.1 R:Et_3N, S:CH_2Cl_2, 3-5 h, 0°C

1.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

1.1 R:Mg, S:MeOH, rt
2.1 S:DMF, 140°C
3.1 S:DMF, 1 h, 120°C

3.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

4.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

4.2 R:NaCl, S:H_2O

5.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

Notes

in the dark, exothermic reaction, conversion = 40%,alternative preparation shown, alternative preparation shown, regioselective, alternative preparation shown, Reactants: 7, Reagents: 6, Solvents: 5, Steps: 7, Stages: 9, Most stages in any one step: 2

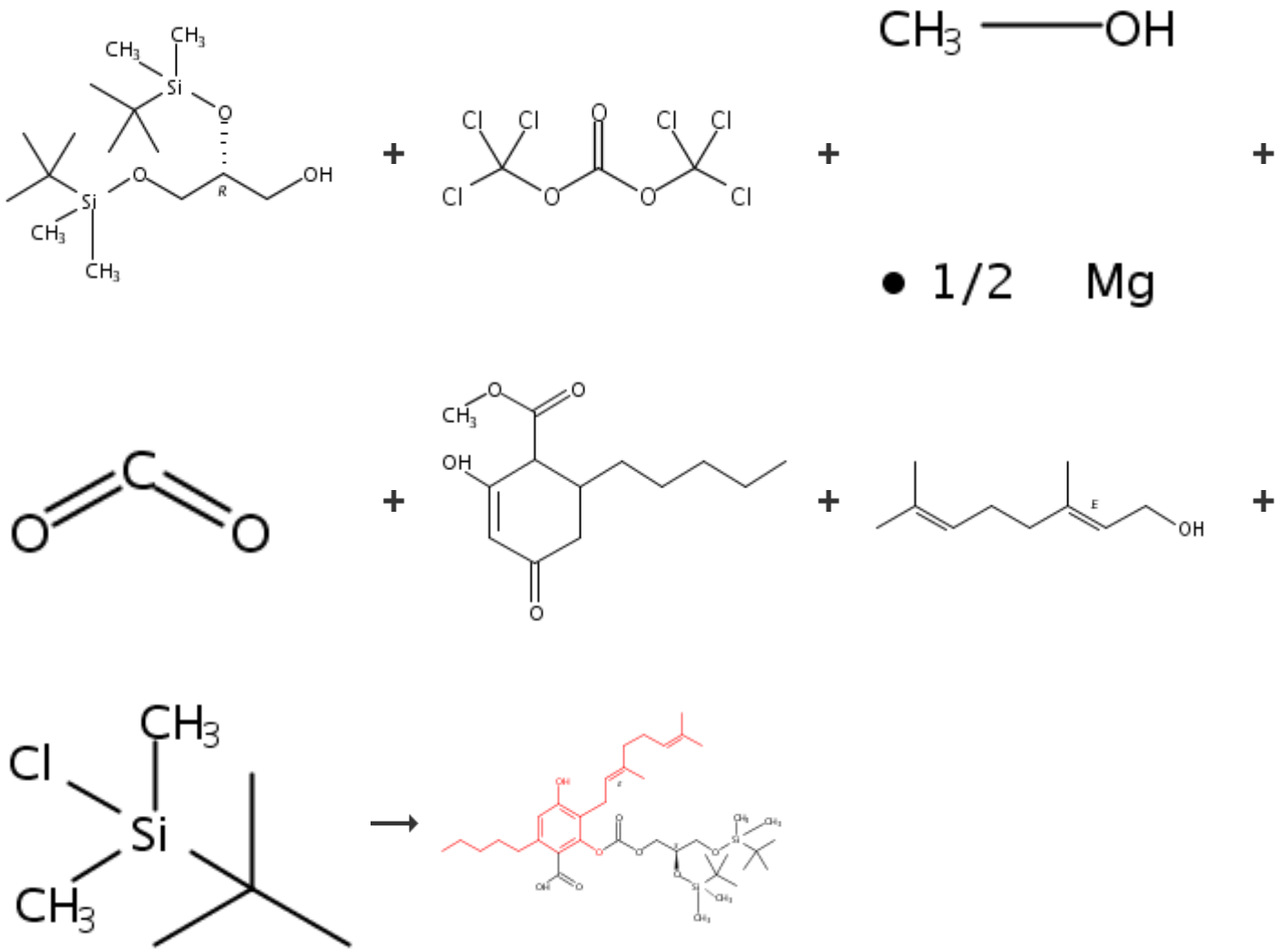
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

335. 7 Steps (Converging)



Overview

Steps/Stages

1.1 R:Et_3N, S:CH_2Cl_2, 3-5 h, 0°C
1.1 S:DMF, 140°C

1.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

2.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
3.1 S:DMF, 1 h, 120°C

3.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

4.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

4.2 R:NaCl, S:H_2O

5.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

Notes

exothermic reaction, in the dark, conversion = 40%,alternative preparation shown, alternative preparation shown, regioselective, alternative preparation shown, Reactants: 7, Reagents: 6, Solvents: 5, Steps: 7, Stages: 9, Most stages in any one step: 2

References

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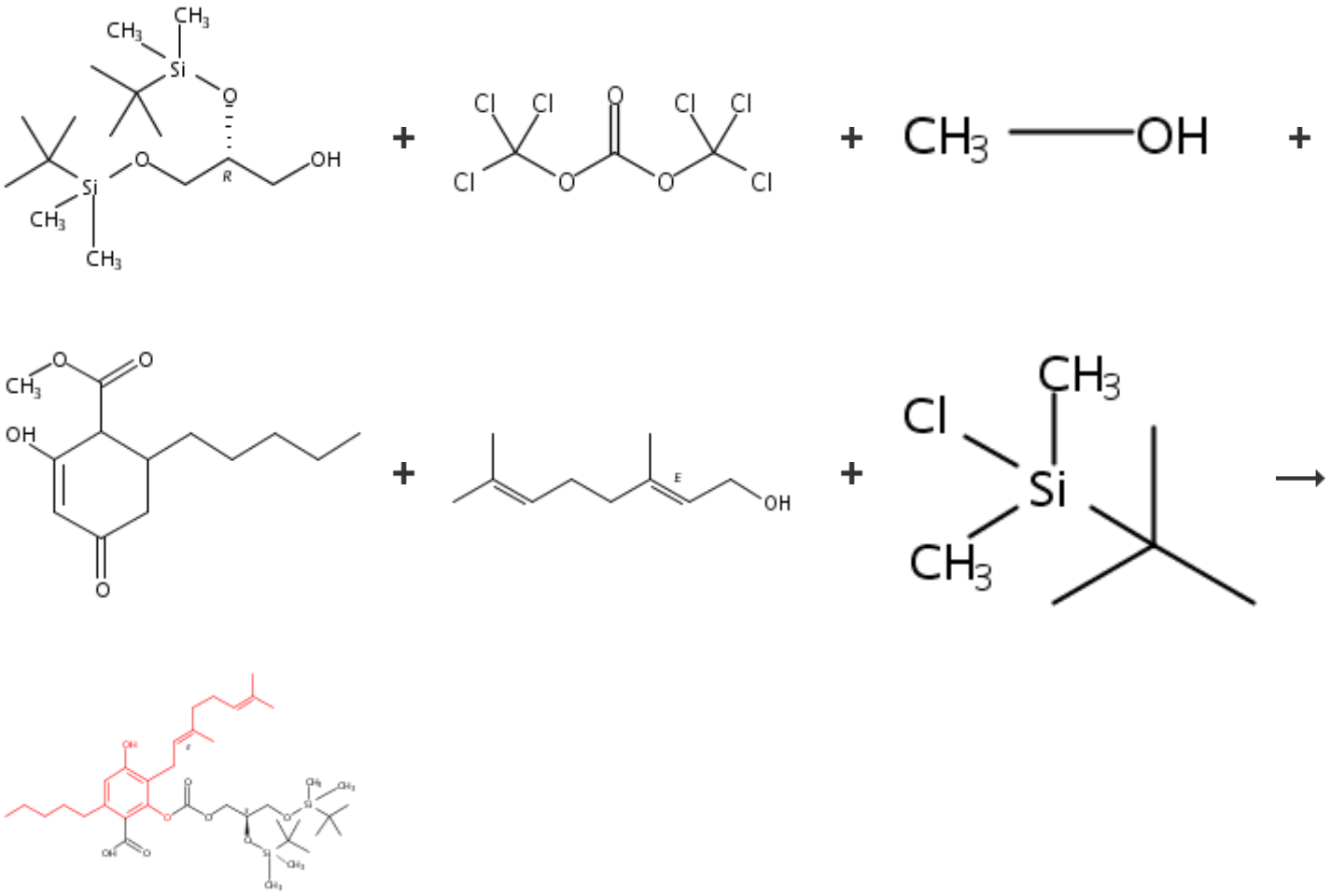
From PCT Int. Appl., 2017181118, 19 Oct 2017

336. 7 Steps (Converging)



Overview

Steps/Stages

1.1 R:Et_3N, S:CH_2Cl_2, 3-5 h, 0°C

1.1 R:Mg, S:MeOH, rt

1.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

2.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

3.1 S:H_2O, cooled; 50°C; 3 h, 50°C; 50°C → rt

3.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, rt, pH 2

4.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

4.2 R:NaCl, S:H_2O

5.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

Notes

in the dark, conversion = 85%,alternative preparation shown,reaction in a sealed pressure vessel, alternative preparation shown, regioselective, alternative preparation shown, Reactants: 6, Reagents: 7, Solvents: 5, Steps: 7, Stages: 9, Most stages in any one step: 2

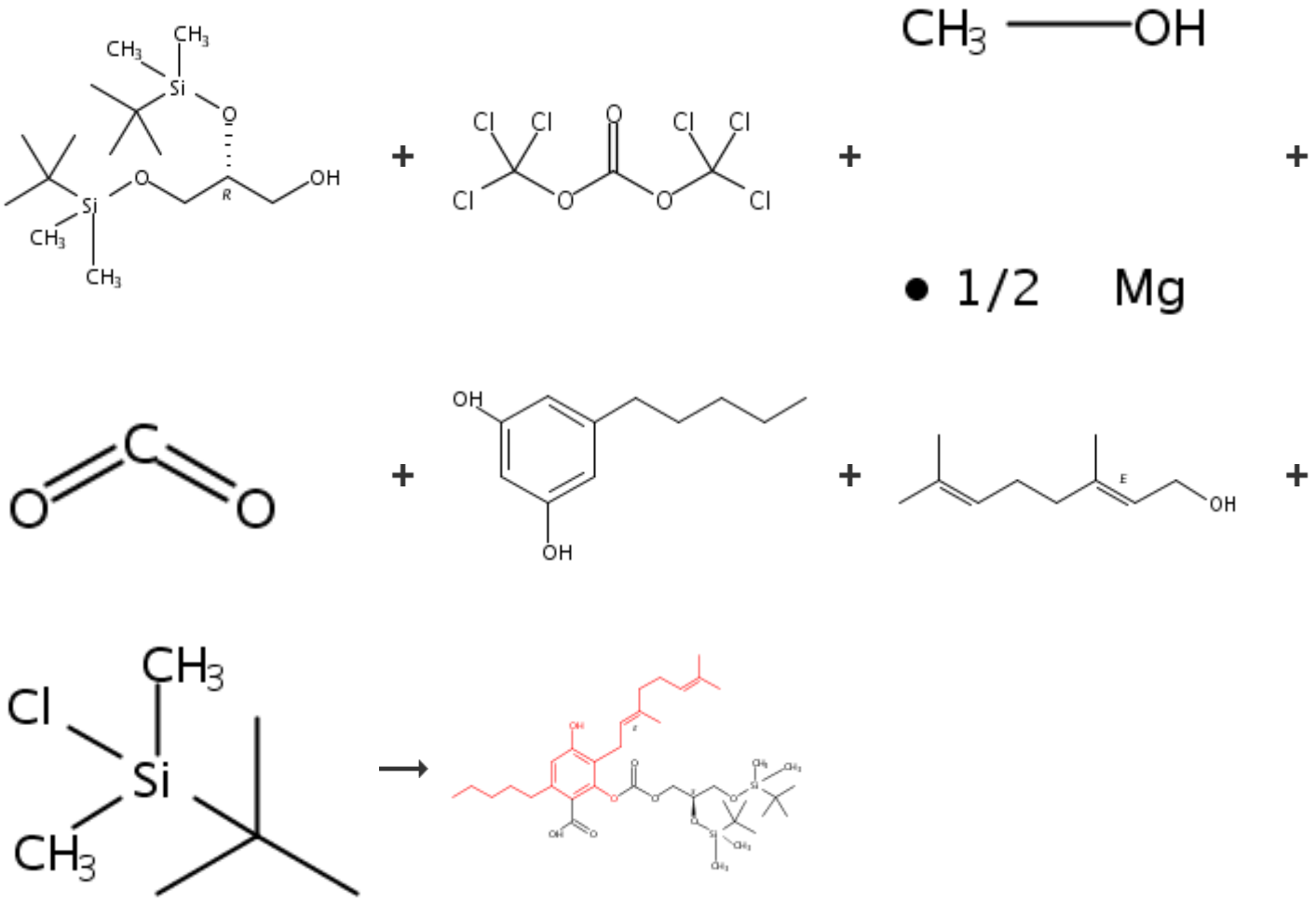
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

337. 6 Steps (Converging)



Overview

Steps/Stages

1.1 R:Et_3N, S:CH_2Cl_2, 3-5 h, 0°C
1.1 S:DMF, 140°C

1.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
2.1 S:DMF, 1 h, 120°C

2.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

3.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

3.2 R:NaCl, S:H_2O

4.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

Notes

exothermic reaction, in the dark, conversion = 40%,alternative preparation shown, alternative preparation shown, regioselective, alternative preparation shown, Reactants: 7, Reagents: 5, Solvents: 5, Steps: 6, Stages: 8, Most stages in any one step: 2

References

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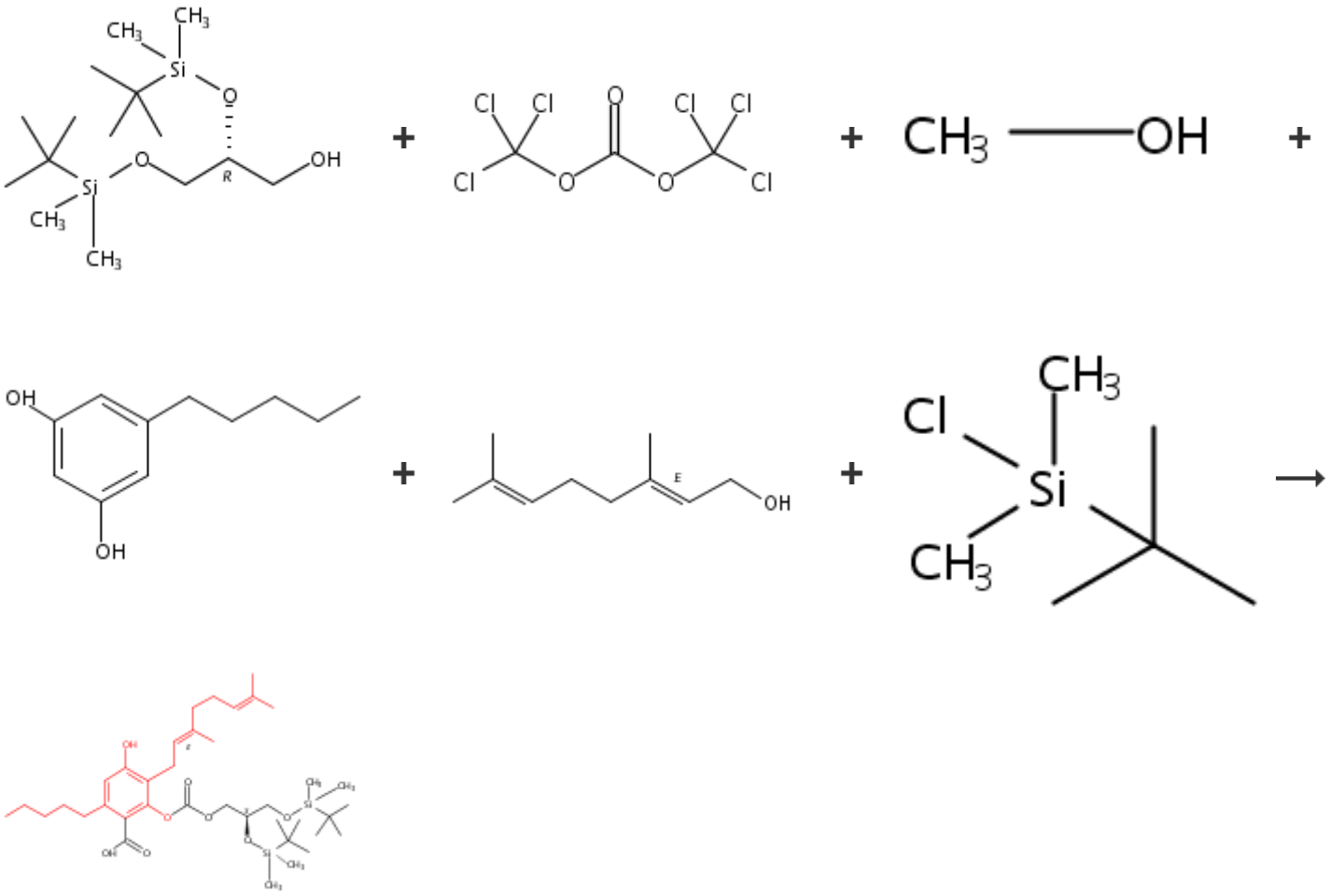
By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

338. 6 Steps (Converging)



Overview

Steps/Stages

1.1 R:Et_3N, S:CH_2Cl_2, 3-5 h, 0°C

1.1 R:Mg, S:MeOH, rt

1.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
2.1 S:H_2O, cooled; 50°C; 3 h, 50°C; 50°C → rt

2.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, rt, pH 2

3.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

3.2 R:NaCl, S:H_2O

4.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

Notes

in the dark, conversion = 85%,alternative preparation shown,reaction in a sealed pressure vessel, alternative preparation shown, regioselective, alternative preparation shown, Reactants: 6, Reagents: 6, Solvents: 4, Steps: 6, Stages: 8, Most stages in any one step: 2

References

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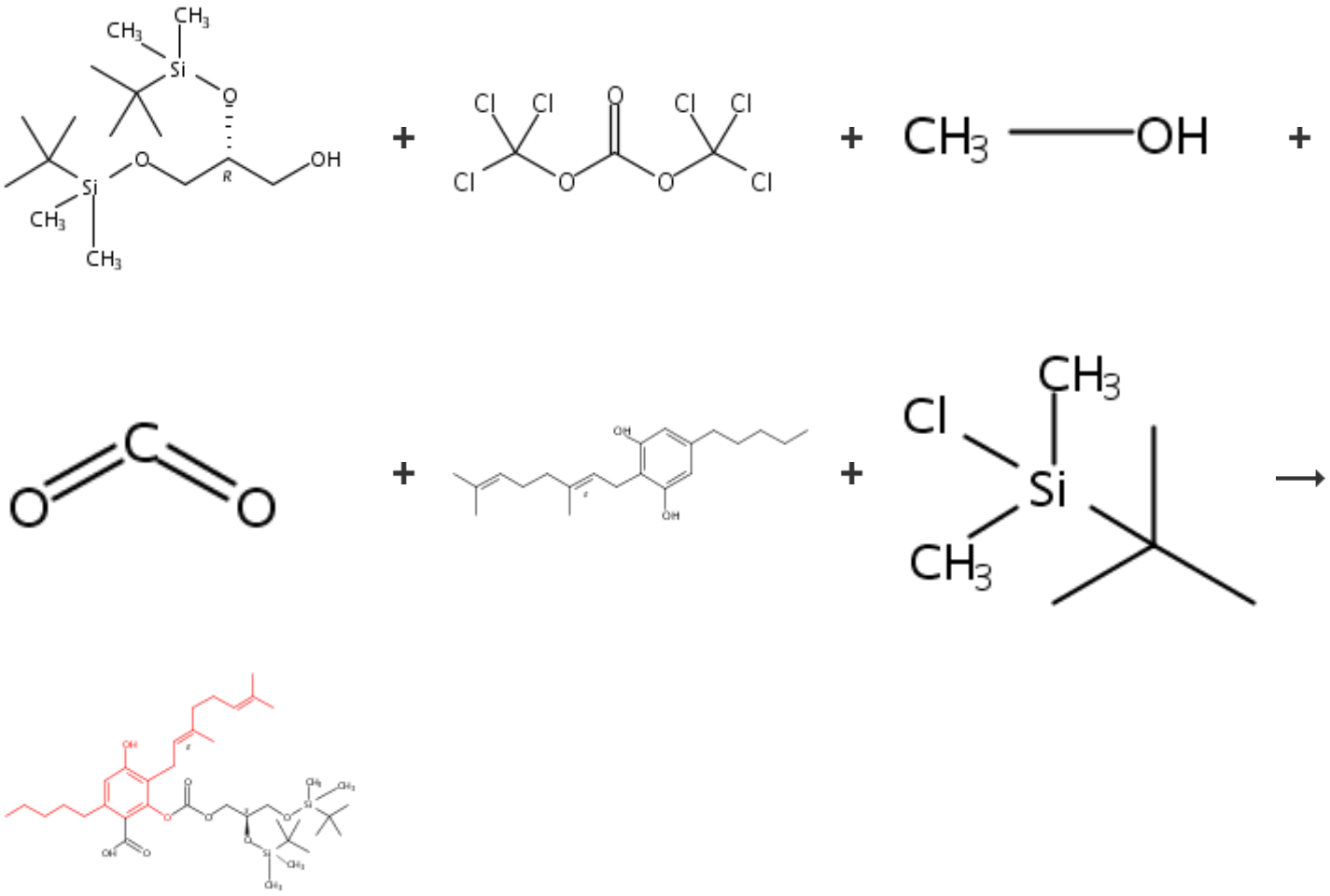
From PCT Int. Appl., 2017181118, 19 Oct 2017

339. 6 Steps (Converging)



Overview

Steps/Stages

1.1 R:Et_3N, S:CH_2Cl_2, 3-5 h, 0°C

1.1 R:Mg, S:MeOH, rt
2.1 S:DMF, 140°C
3.1 S:DMF, 1 h, 120°C

3.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

4.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

4.2 R:NaCl, S:H_2O

5.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

Notes

exothermic reaction, conversion = 40%,alternative preparation shown, alternative preparation shown, regioselective, alternative preparation shown, Reactants: 6, Reagents: 5, Solvents: 5, Steps: 6, Stages: 8, Most stages in any one step: 2

References

Biosynthesis of cannabinoid prodrugs

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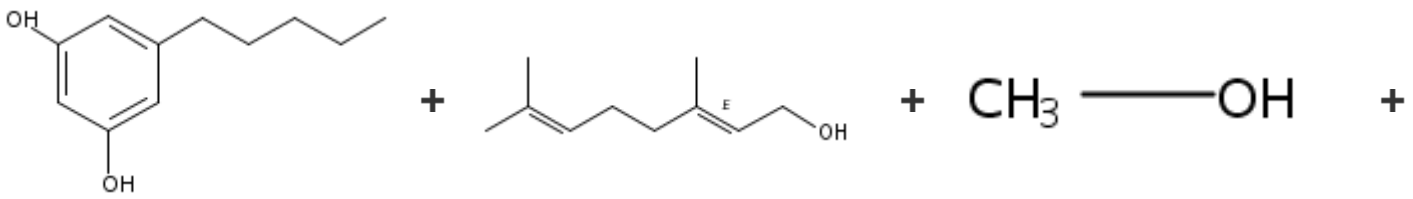
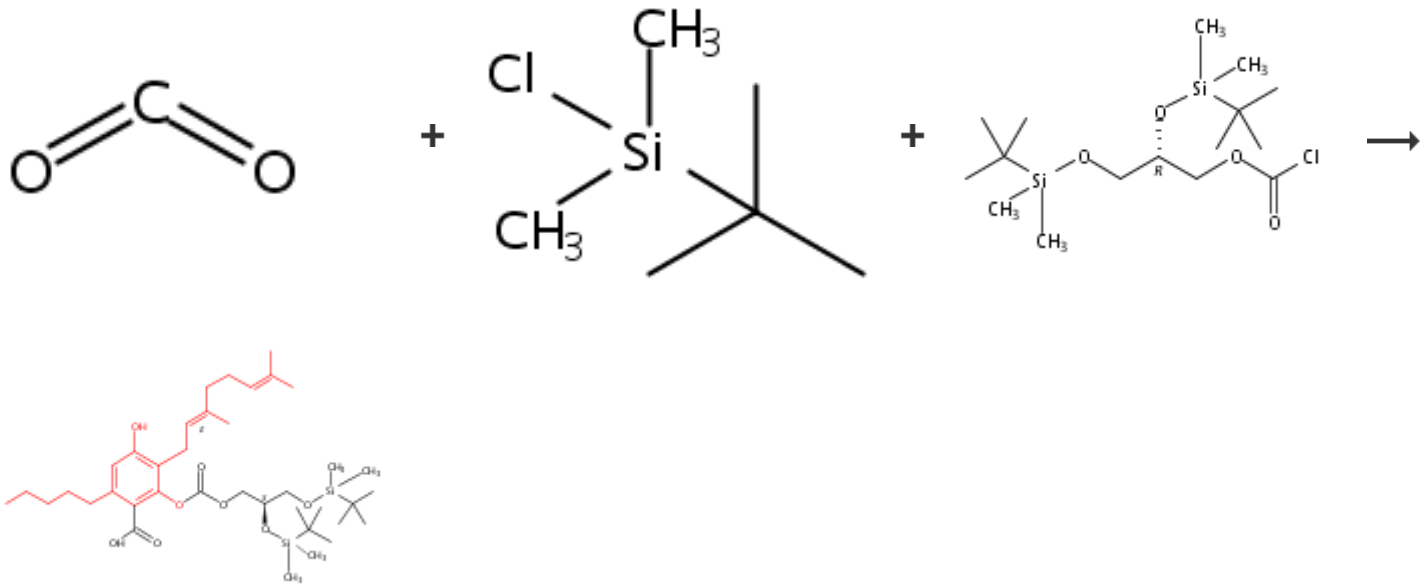
From PCT Int. Appl., 2017181118, 19 Oct 2017

340. 6 Steps (Converging)





Overview

Steps/Stages

1.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

1.1 R:Mg, S:MeOH, rt
2.1 S:DMF, 140°C
3.1 S:DMF, 1 h, 120°C

3.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

4.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

4.2 R:NaCl, S:H_2O

5.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

Notes

in the dark, exothermic reaction, conversion = 40%,alternative preparation shown, alternative preparation shown, regioselective, alternative preparation shown, Reactants: 6, Reagents: 6, Solvents: 5, Steps: 6, Stages: 8, Most stages in any one step: 2

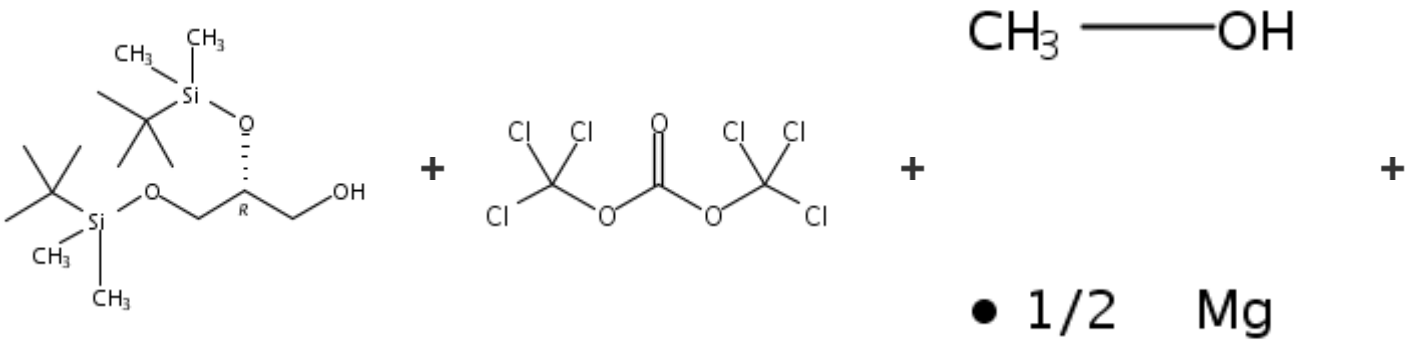
References

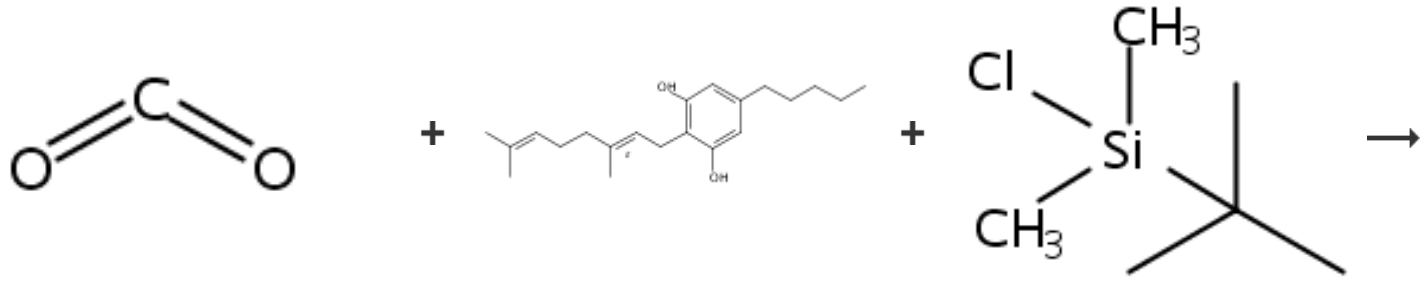
Biosynthesis of cannabinoid prodrugs

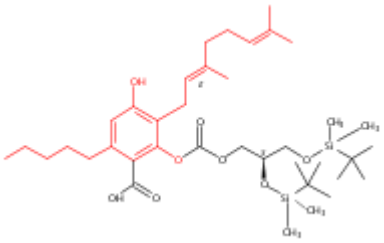
By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

341. 5 Steps (Converging)







Overview

Steps/Stages

1.1 R:Et_3N, S:CH_2Cl_2, 3-5 h, 0°C
1.1 S:DMF, 140°C
2.1 S:DMF, 1 h, 120°C

2.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

3.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

3.2 R:NaCl, S:H_2O

4.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

Notes

exothermic reaction, conversion = 40%,alternative preparation shown, alternative preparation shown, regioselective, alternative preparation shown, Reactants: 6, Reagents: 4, Solvents: 5, Steps: 5, Stages: 7, Most stages in any one step: 2

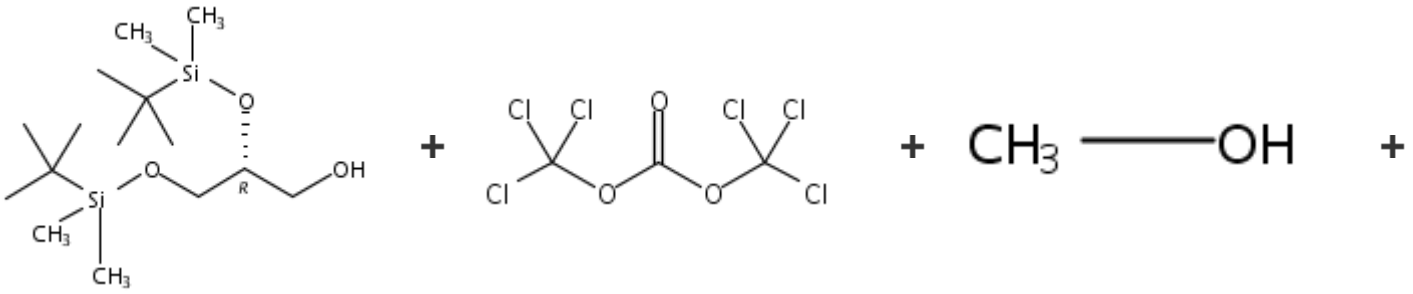
References

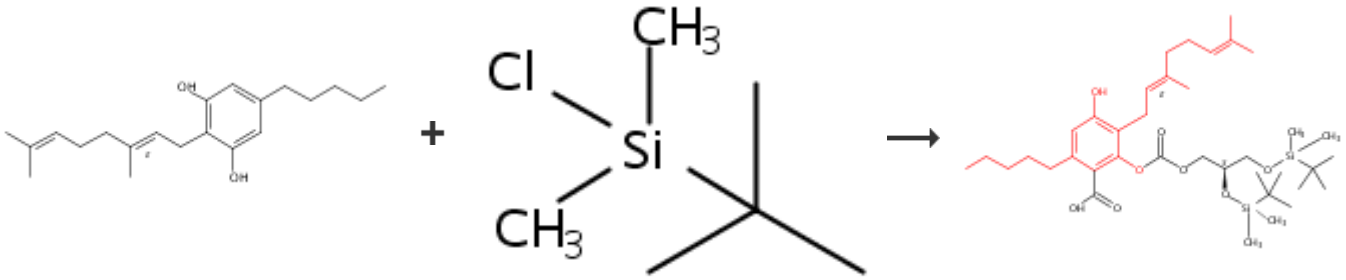
Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

342. 5 Steps (Converging)





Overview

Steps/Stages

1.1 R:Et_3N, S:CH_2Cl_2, 3-5 h, 0°C

1.1 R:Mg, S:MeOH, rt
2.1 S:H_2O, cooled; 50°C; 3 h, 50°C; 50°C → rt

2.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, rt, pH 2

3.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

3.2 R:NaCl, S:H_2O

4.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

Notes

conversion = 85%,alternative preparation shown,reaction in a sealed pressure vessel, alternative preparation shown, regioselective, alternative preparation shown, Reactants: 5, Reagents: 5, Solvents: 4, Steps: 5, Stages: 7, Most stages in any one step: 2

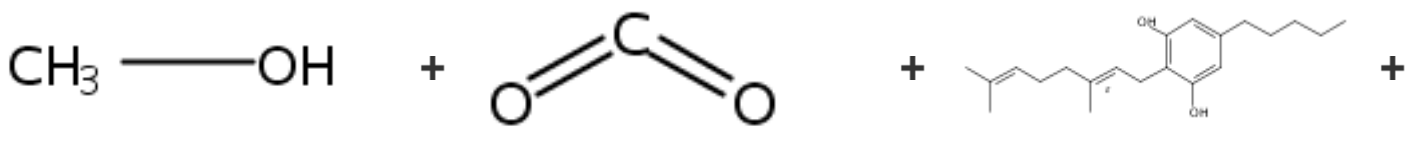
References

Biosynthesis of cannabinoid prodrugs

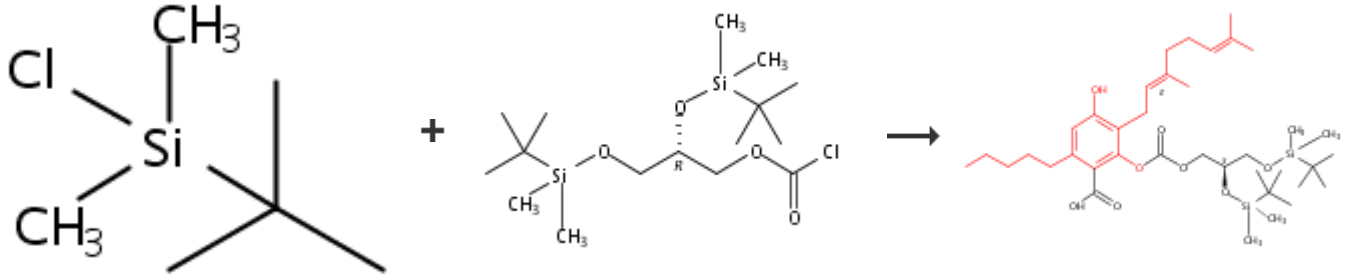
By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

343. 5 Steps



[Step 2.1] [Step 3.1]



[Step 4.1] [Step 5.1]

Overview

Steps/Stages

Notes

1.1 R:Mg, S:MeOH, rt
2.1 S:DMF, 140°C
3.1 S:DMF, 1 h, 120°C

3.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

4.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

4.2 R:NaCl, S:H_2O

5.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

2) exothermic reaction, 3) conversion = 40%,alternative preparation shown, 4) alternative preparation shown, regioselective, 5) alternative preparation shown, Reactants: 5, Reagents: 5, Solvents: 5, Steps: 5, Stages: 7, Most stages in any one step: 2

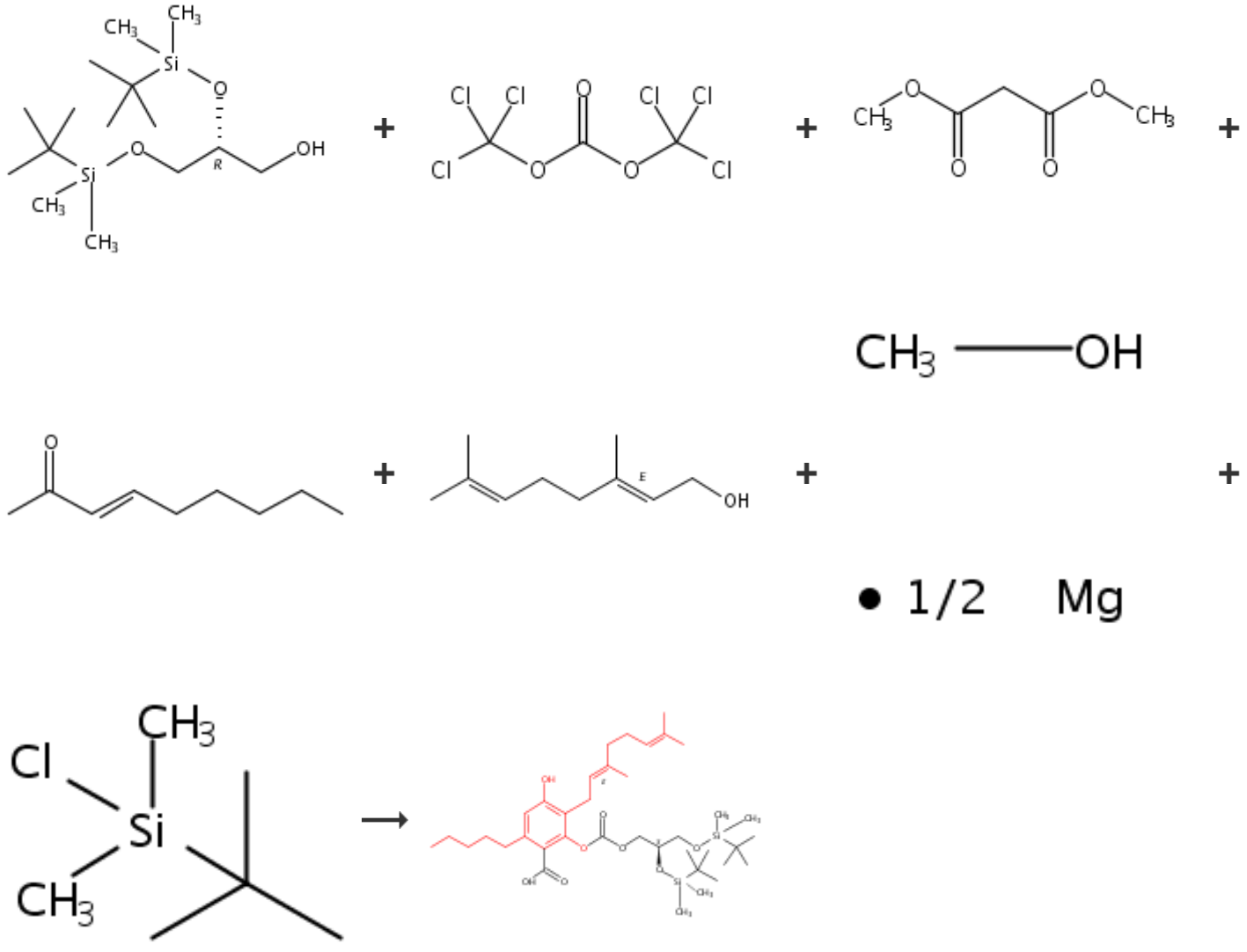
References

Biosynthesis of cannabinoid prodrugs

By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

344. 7 Steps (Converging)



Overview

Steps/Stages **Notes**

1.1 R:Et_3N, S:CH_2Cl_2, 3-5 h, 0°C

1.1 R:NaOMe, S:MeOH, rt; 3 h, reflux; reflux → rt

1.2 R:H_2O, rt

2.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

3.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
4.1 S:H_2O, cooled; 50°C; 3 h, 50°C; 50°C → rt

4.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, rt, pH 2

5.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

5.2 R:NaCl, S:H_2O

6.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

in the dark, conversion = 85%,alternative preparation shown,reaction in a sealed pressure vessel, alternative preparation shown, regioselective, alternative preparation shown, Reactants: 7, Reagents: 8, Solvents: 5, Steps: 7, Stages: 10, Most stages in any one step: 2

References

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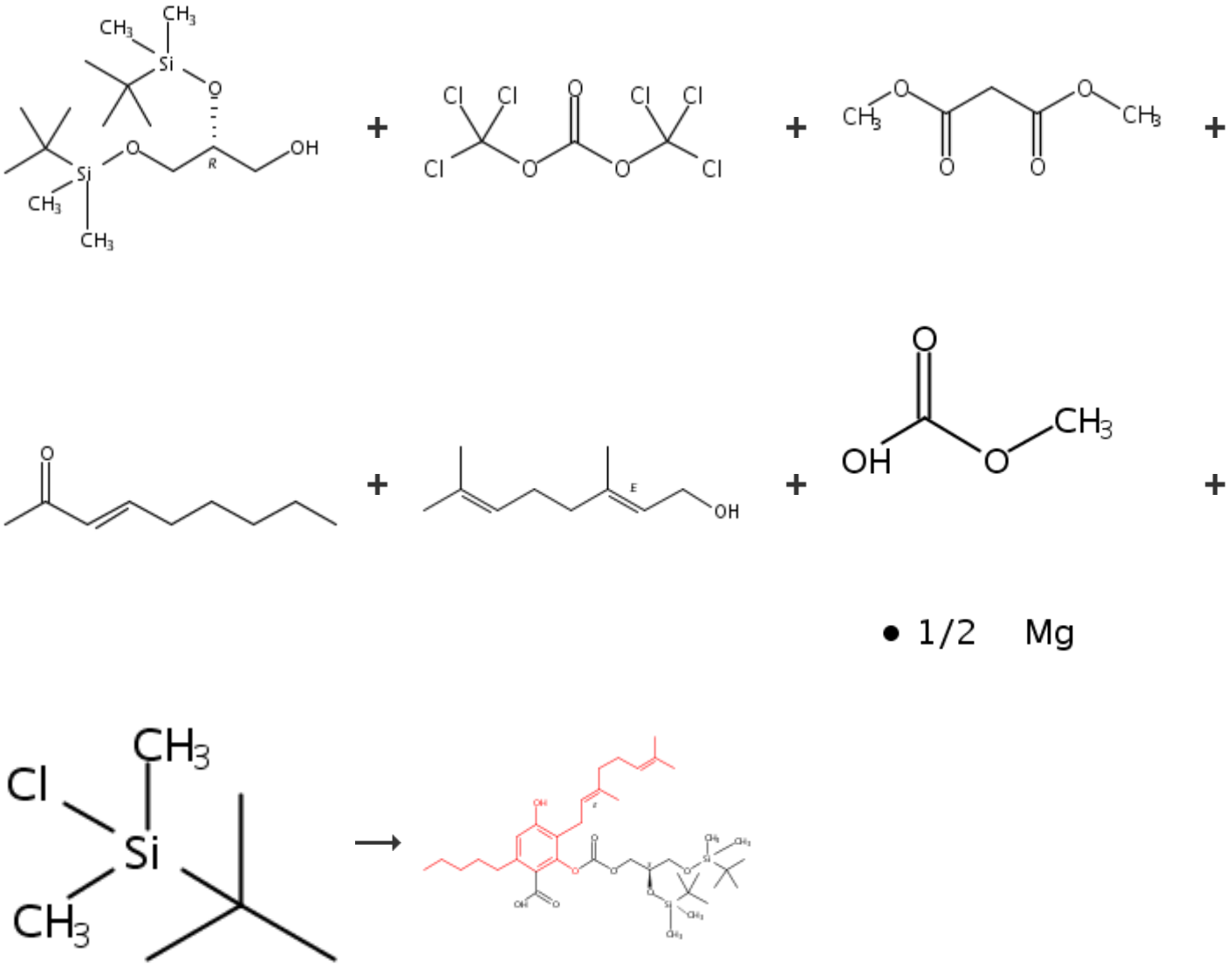
345. 7 Steps (Converging)



Overview

Steps/Stages

1.1 R:Et_3N, S:CH_2Cl_2, 3-5 h, 0°C

1.1 R:NaOMe, S:MeOH, rt; 3 h, reflux; reflux → rt

1.2 R:H_2O, rt

2.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

3.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
4.1 S:DMF, 1 h, 120°C

4.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

5.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

5.2 R:NaCl, S:H_2O

6.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

Notes

in the dark, conversion = 40%,alternative preparation shown, alternative preparation shown, regioselective, alternative preparation shown, Reactants: 7, Reagents: 8, Solvents: 5, Steps: 7, Stages: 10, Most stages in any one step: 2

References

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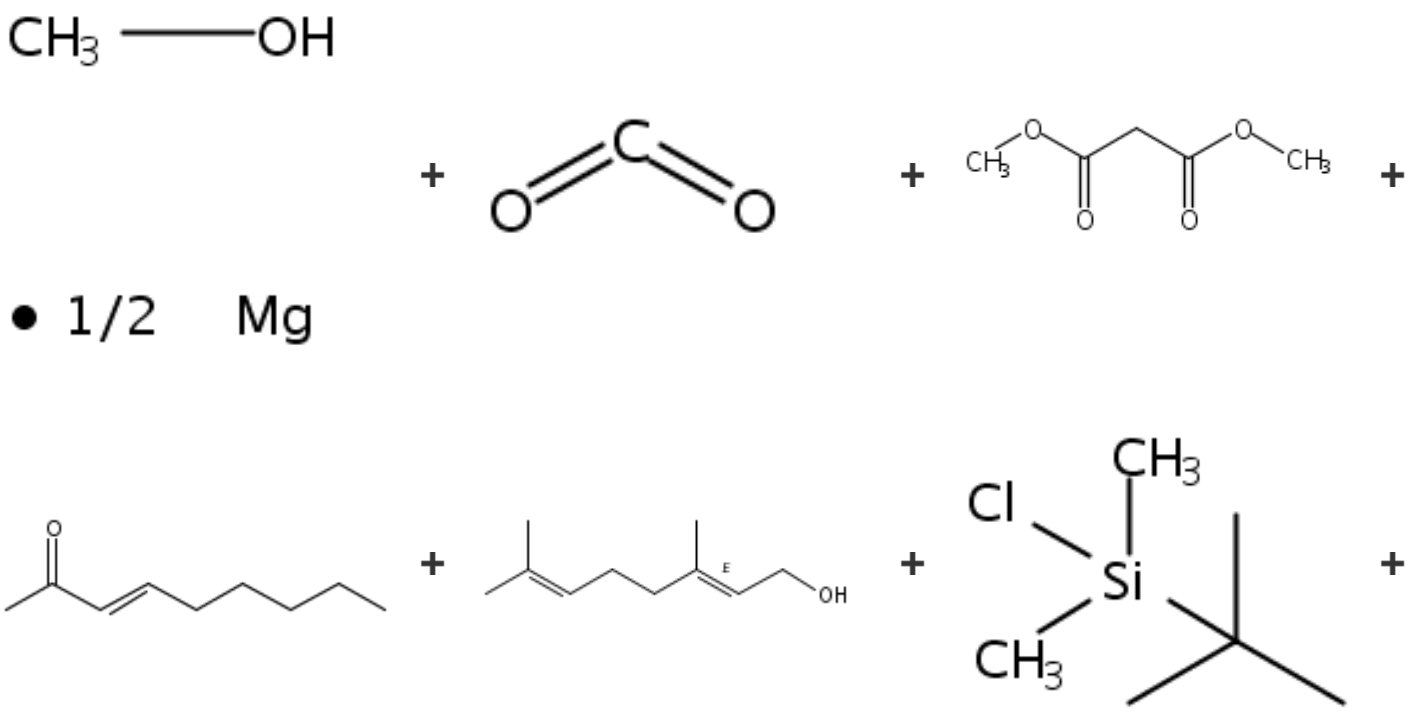
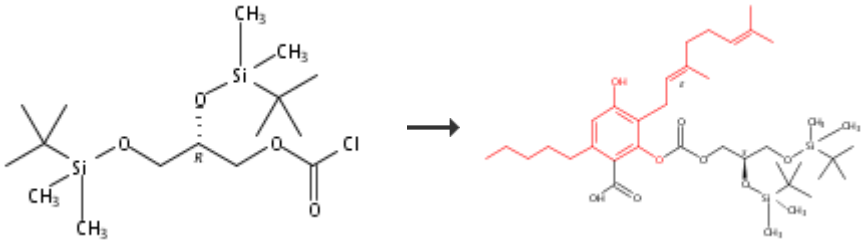
From PCT Int. Appl., 2017181118, 19 Oct 2017

346. 7 Steps (Converging)





Overview

Steps/Stages

1.1 S:DMF, 140°C

1.1 R:NaOMe, S:MeOH, rt; 3 h, reflux; reflux → rt

1.2 R:H_2O, rt

2.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

3.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

4.1 S:DMF, 1 h, 120°C

4.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

5.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

5.2 R:NaCl, S:H_2O

6.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

Notes

exothermic reaction, in the dark, conversion = 40%,alternative preparation shown, alternative preparation shown, regioselective, alternative preparation shown, Reactants: 7, Reagents: 8, Solvents: 5, Steps: 7, Stages: 10, Most stages in any one step: 2

References

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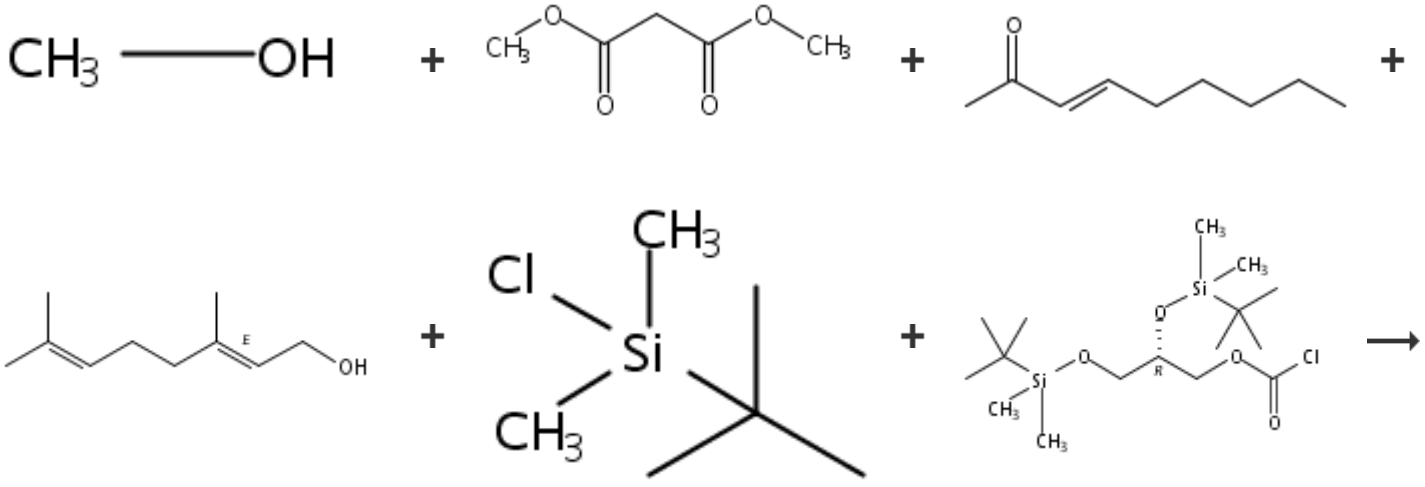
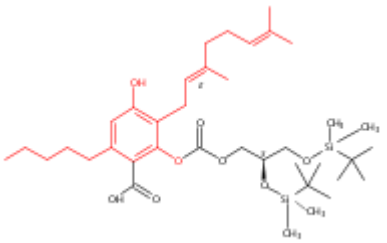
347. 7 Steps (Converging)





Overview

Steps/Stages

1.1 R:Mg, S:MeOH, rt

1.1 R:NaOMe, S:MeOH, rt; 3 h, reflux; reflux → rt

1.2 R:H_2O, rt

2.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

3.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

4.1 S:H_2O, cooled; 50°C; 3 h, 50°C; 50°C → rt

4.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, rt, pH 2

5.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

5.2 R:NaCl, S:H_2O

6.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

Notes

in the dark, conversion = 85%,alternative preparation shown,reaction in a sealed pressure vessel, alternative preparation shown, regioselective, alternative preparation shown, Reactants: 6, Reagents: 9, Solvents: 5, Steps: 7, Stages: 10, Most stages in any one step: 2

References

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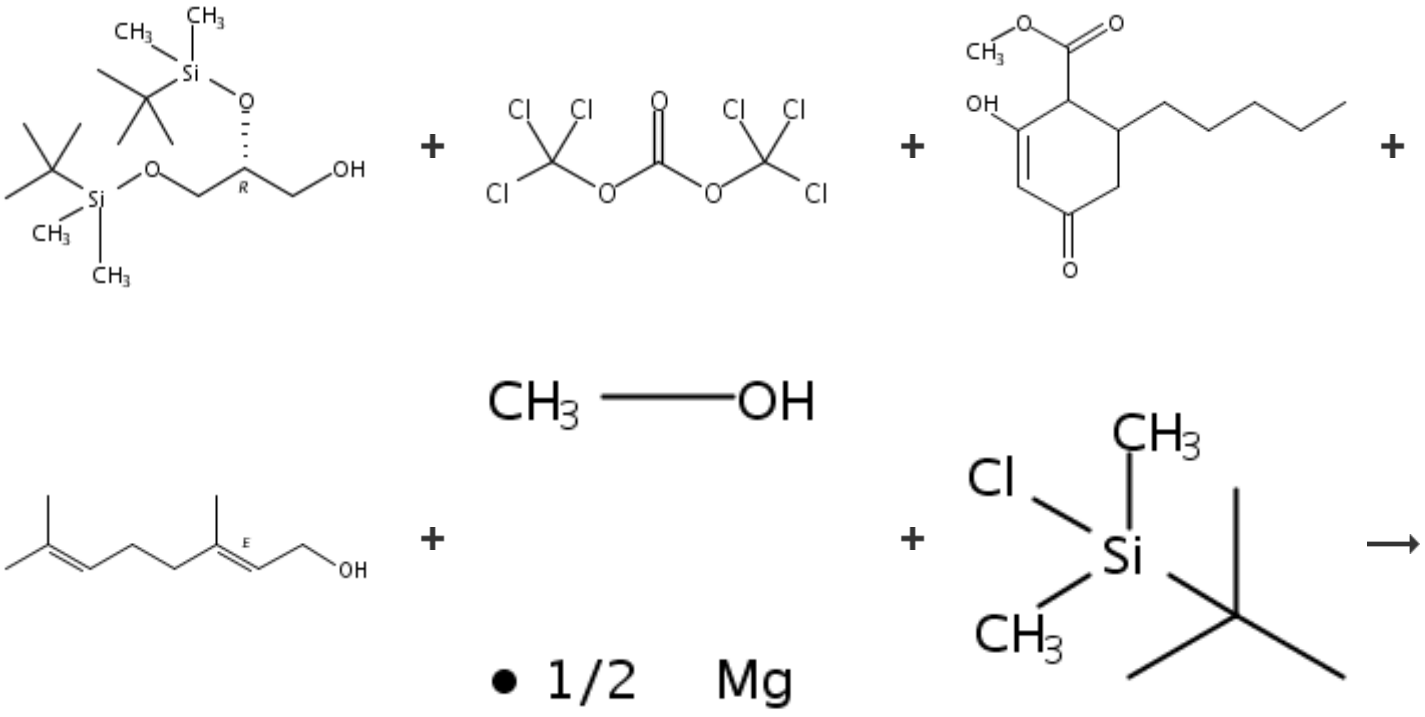
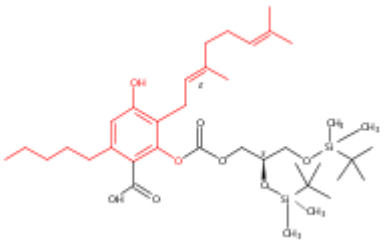
From PCT Int. Appl., 2017181118, 19 Oct 2017

348. 6 Steps (Converging)





Overview

Steps/Stages

1.1 R:Et_3N, S:CH_2Cl_2, 3-5 h, 0°C

1.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

2.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

3.1 S:H_2O, cooled; 50°C; 3 h, 50°C; 50°C → rt

3.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, rt, pH 2

4.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

4.2 R:NaCl, S:H_2O

5.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

Notes

in the dark, conversion = 85%,alternative preparation shown,reaction in a sealed pressure vessel, alternative preparation shown, regioselective, alternative preparation shown, Reactants: 6, Reagents: 6, Solvents: 5, Steps: 6, Stages: 8, Most stages in any one step: 2

References

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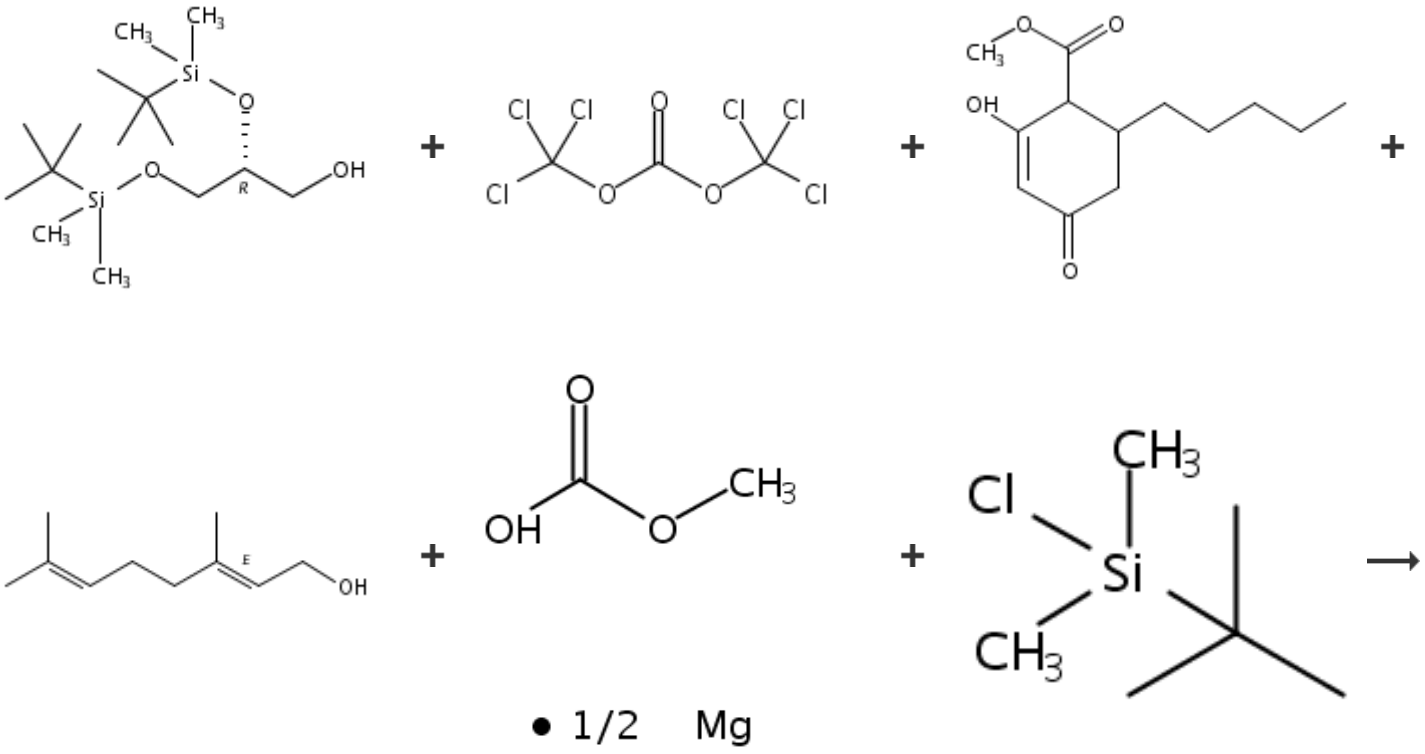
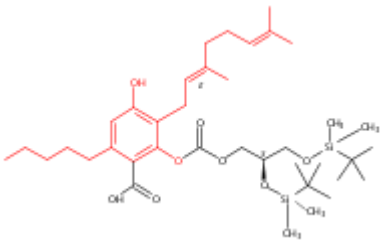
By Peet, Ricard C. and Kavarana, Malcolm J.

From PCT Int. Appl., 2017181118, 19 Oct 2017

349. 6 Steps (Converging)





Overview

Steps/Stages

1.1 R:Et_3N, S:CH_2Cl_2, 3-5 h, 0°C

1.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

2.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

3.1 S:DMF, 1 h, 120°C

3.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

4.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

4.2 R:NaCl, S:H_2O

5.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

Notes

in the dark, conversion = 40%,alternative preparation shown, alternative preparation shown, regioselective, alternative preparation shown, Reactants: 6, Reagents: 6, Solvents: 5, Steps: 6, Stages: 8, Most stages in any one step: 2

References

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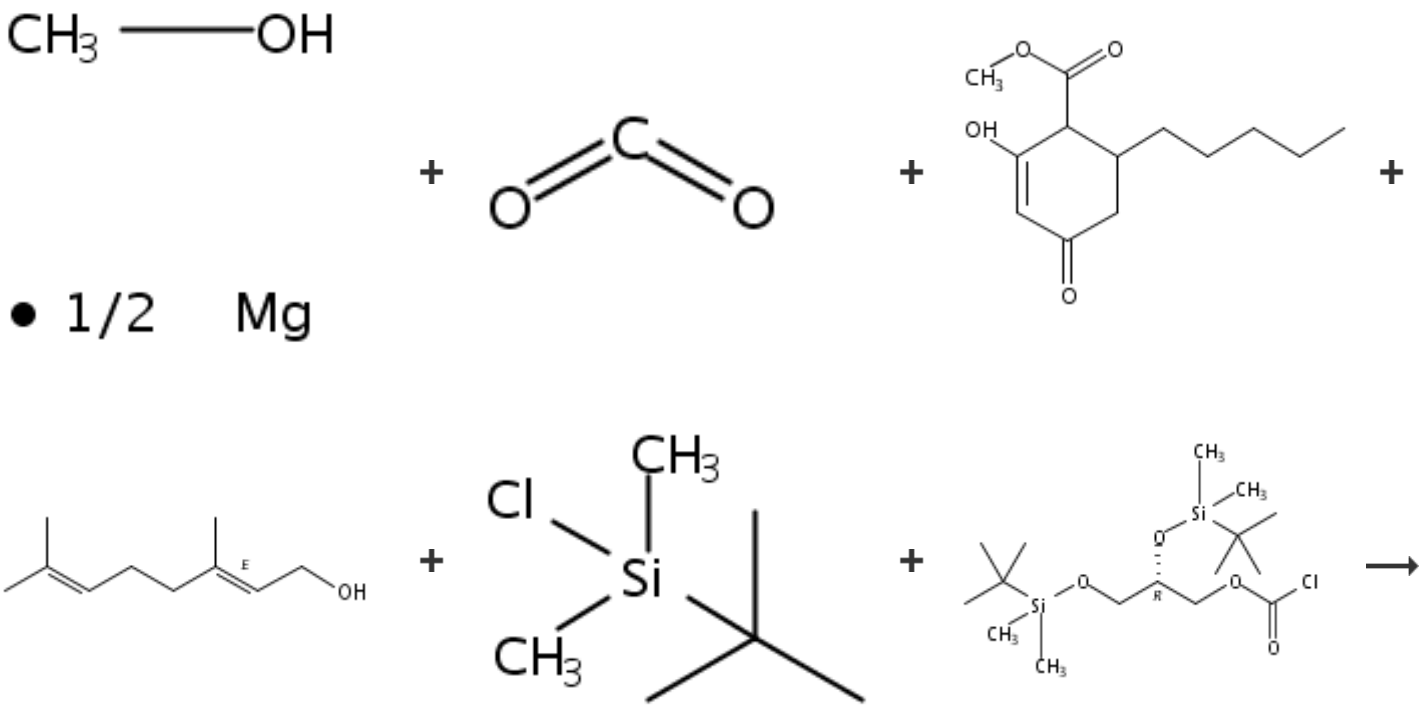
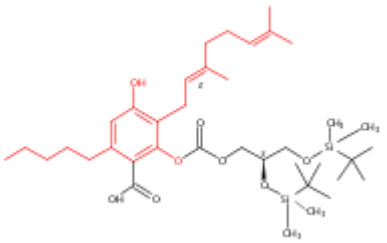
From PCT Int. Appl., 2017181118, 19 Oct 2017

350. 6 Steps (Converging)





Overview

Steps/Stages

1.1 S:DMF, 140°C

1.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

2.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

3.1 S:DMF, 1 h, 120°C

3.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

4.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

4.2 R:NaCl, S:H_2O

5.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

Notes

exothermic reaction, in the dark, conversion = 40%,alternative preparation shown, alternative preparation shown, regioselective, alternative preparation shown, Reactants: 6, Reagents: 6, Solvents: 5, Steps: 6, Stages: 8, Most stages in any one step: 2

References

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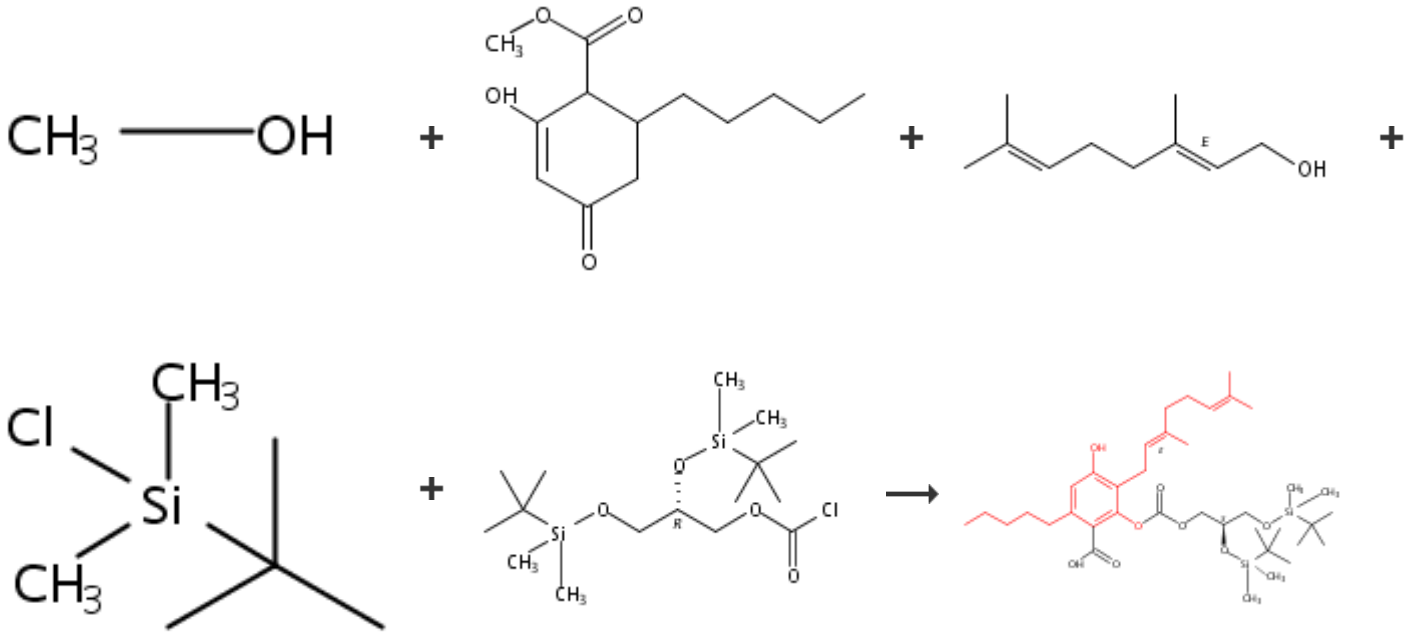
351. 6 Steps (Converging)



Overview

Steps/Stages

Notes

1.1 R:Mg, S:MeOH, rt

1.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

2.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

3.1 S:H_2O, cooled; 50°C; 3 h, 50°C; 50°C → rt

3.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, rt, pH 2

4.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

4.2 R:NaCl, S:H_2O

5.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

in the dark, conversion = 85%,alternative preparation shown,reaction in a sealed pressure vessel, alternative preparation shown, regioselective, alternative preparation shown, Reactants: 5, Reagents: 7, Solvents: 5, Steps: 6, Stages: 8, Most stages in any one step: 2

References

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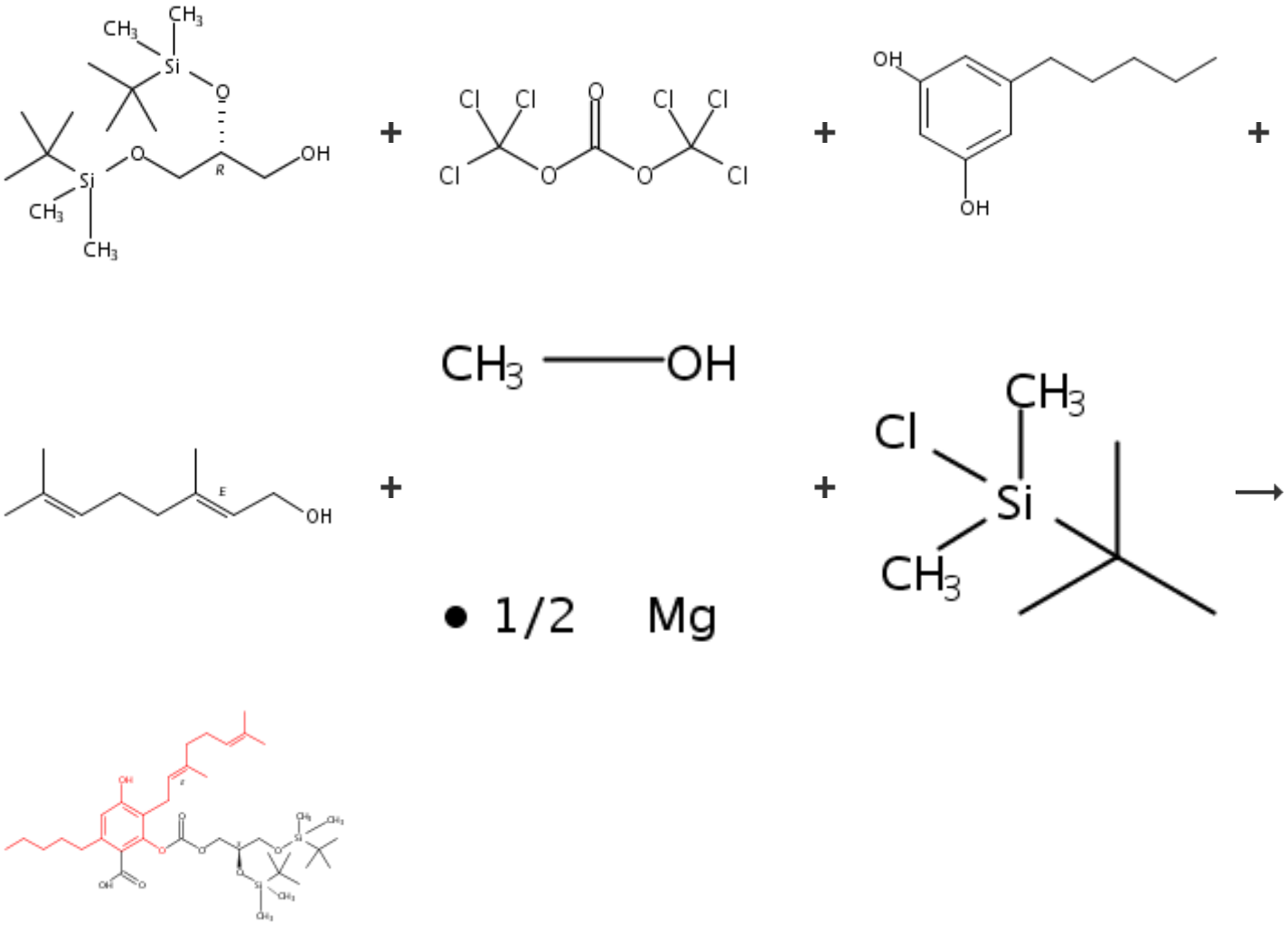
From PCT Int. Appl., 2017181118, 19 Oct 2017

352. 5 Steps (Converging)



Overview

Steps/Stages

Notes

1.1 R:Et_3N, S:CH_2Cl_2, 3-5 h, 0°C

1.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
2.1 S:H_2O, cooled; 50°C; 3 h, 50°C; 50°C → rt

2.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, rt, pH 2

3.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

3.2 R:NaCl, S:H_2O

4.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

in the dark, conversion = 85%,alternative preparation shown,reaction in a sealed pressure vessel, alternative preparation shown, regioselective, alternative preparation shown, Reactants: 6, Reagents: 5, Solvents: 4, Steps: 5, Stages: 7, Most stages in any one step: 2

References

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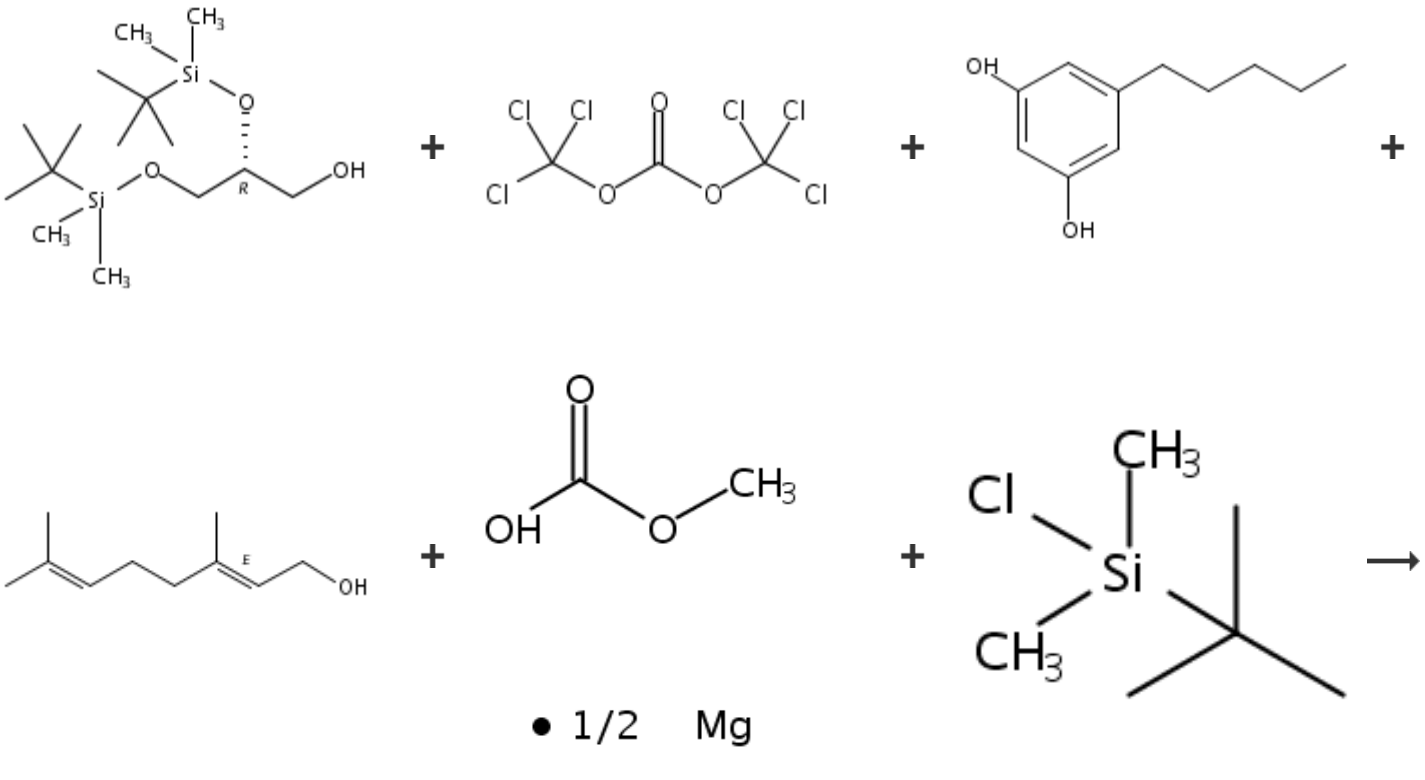
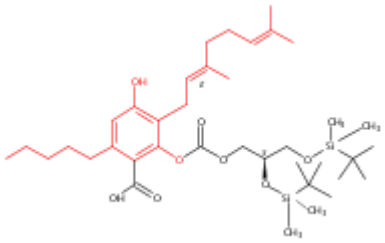
From PCT Int. Appl., 2017181118, 19 Oct 2017

353. 5 Steps (Converging)





Overview

Steps/Stages

Notes

1.1 R:Et_3N, S:CH_2Cl_2, 3-5 h, 0°C

1.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
2.1 S:DMF, 1 h, 120°C

2.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

3.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

3.2 R:NaCl, S:H_2O

4.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

in the dark, conversion = 40%,alternative preparation shown, alternative preparation shown, regioselective, alternative preparation shown, Reactants: 6, Reagents: 5, Solvents: 5, Steps: 5, Stages: 7, Most stages in any one step: 2

References

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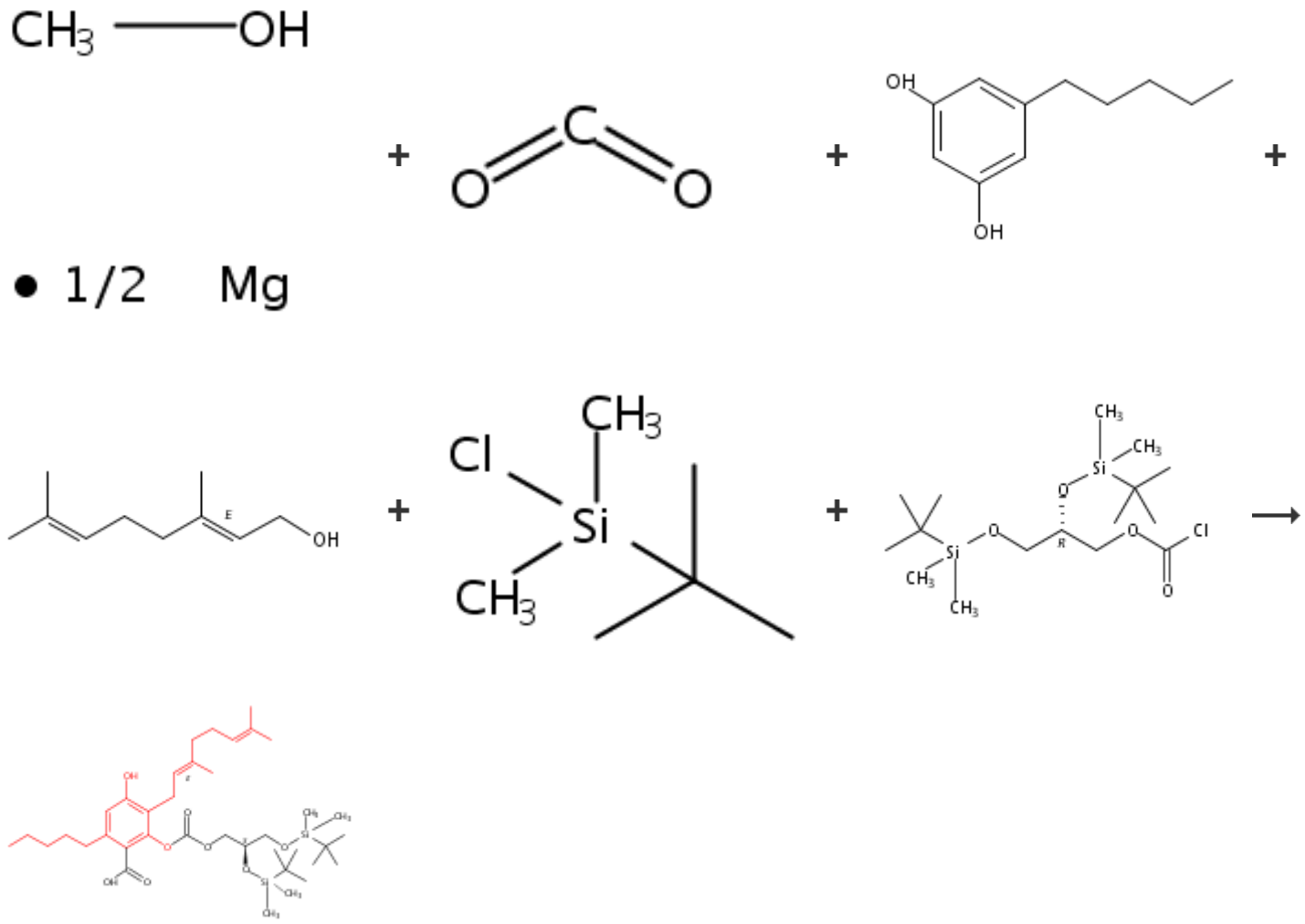
354. 5 Steps (Converging)



Overview

Steps/Stages

Notes

1.1 S:DMF, 140°C

1.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
2.1 S:DMF, 1 h, 120°C

2.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

3.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

3.2 R:NaCl, S:H_2O

4.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

exothermic reaction, in the dark, conversion = 40%,alternative preparation shown, alternative preparation shown, regioselective, alternative preparation shown, Reactants: 6, Reagents: 5, Solvents: 5, Steps: 5, Stages: 7, Most stages in any one step: 2

References

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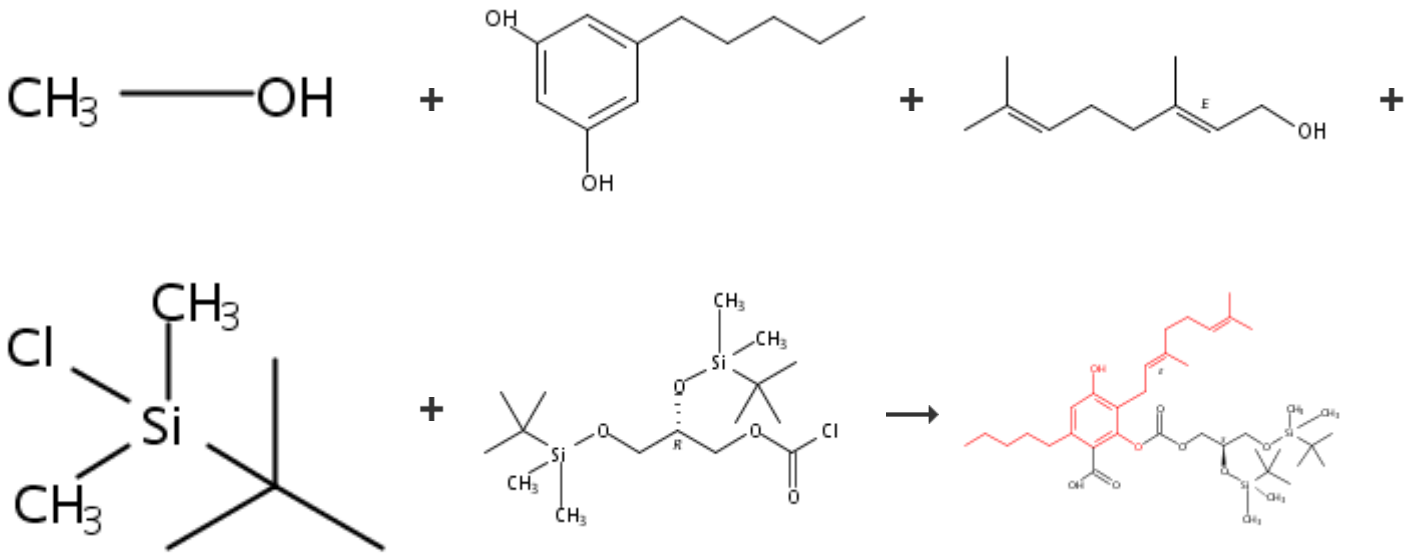
From PCT Int. Appl., 2017181118, 19 Oct 2017

355. 5 Steps (Converging)



Overview

Steps/Stages

1.1 R:Mg, S:MeOH, rt

1.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt
2.1 S:H_2O, cooled; 50°C; 3 h, 50°C; 50°C → rt

2.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, rt, pH 2

3.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

3.2 R:NaCl, S:H_2O

4.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

Notes

in the dark, conversion = 85%,alternative preparation shown,reaction in a sealed pressure vessel, alternative preparation shown, regioselective, alternative preparation shown, Reactants: 5, Reagents: 6, Solvents: 4, Steps: 5, Stages: 7, Most stages in any one step: 2

References

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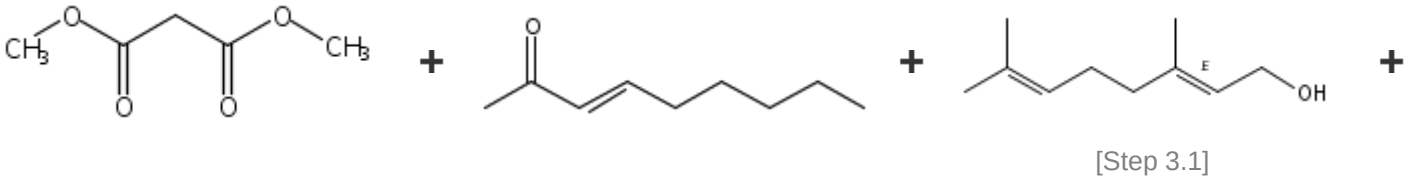
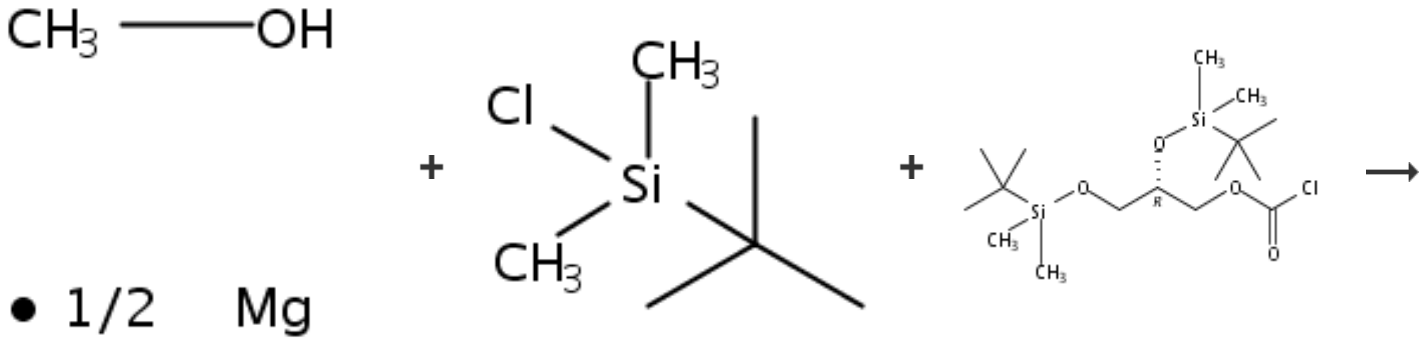
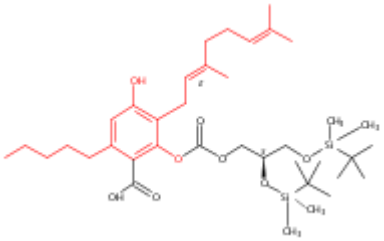
356. 6 Steps



[Step 3.1]



[Step 4.1] [Step 5.1] [Step 6.1]



Overview

Steps/Stages

1.1 R:NaOMe, S:MeOH, rt; 3 h, reflux; reflux → rt

1.2 R:H_2O, rt

2.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

3.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

4.1 S:H_2O, cooled; 50°C; 3 h, 50°C; 50°C → rt

4.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, rt, pH 2

5.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

5.2 R:NaCl, S:H_2O

6.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

Notes

3) in the dark, 4) conversion = 85%,alternative preparation shown,reaction in a sealed pressure vessel, 5) alternative preparation shown, regioselective, 6) alternative preparation shown, Reactants: 6, Reagents: 8, Solvents: 5, Steps: 6, Stages: 9, Most stages in any one step: 2

References

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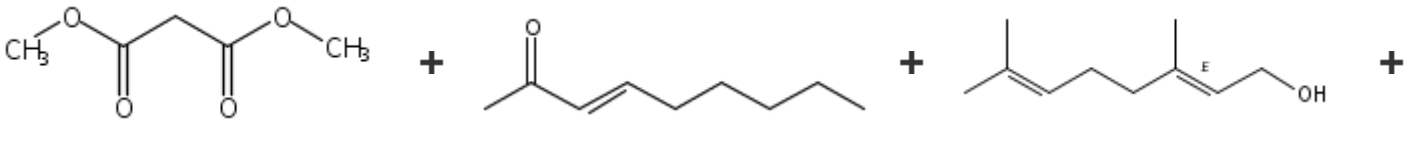
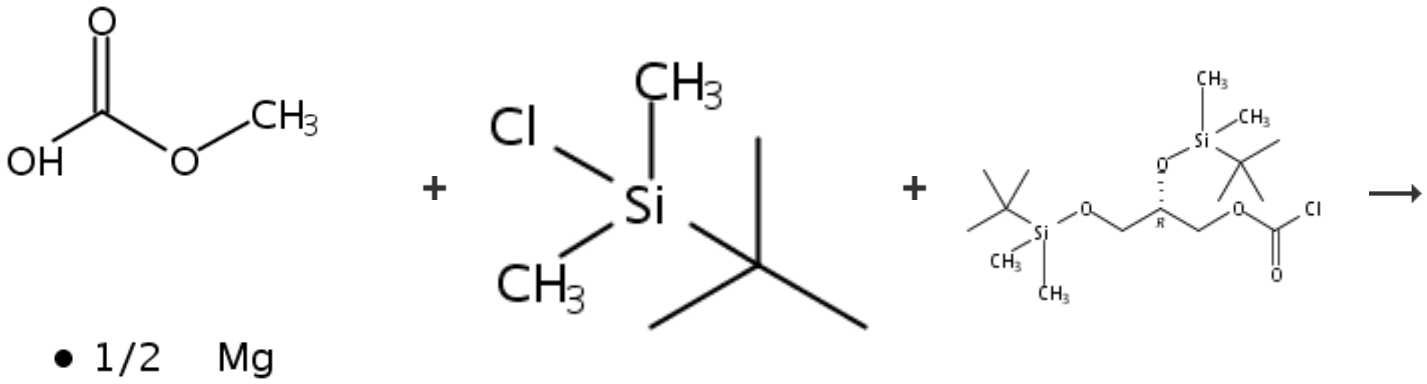
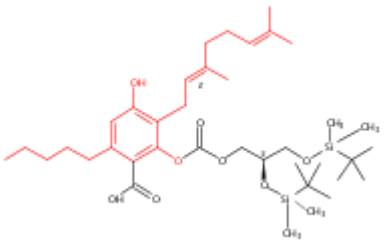
357. 6 Steps



[Step 3.1]



[Step 4.1] [Step 5.1] [Step 6.1]



Overview

Steps/Stages

1.1 R:NaOMe, S:MeOH, rt; 3 h, reflux; reflux → rt

1.2 R:H_2O, rt

2.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

3.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

4.1 S:DMF, 1 h, 120°C

4.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

5.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

5.2 R:NaCl, S:H_2O

6.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

Notes

3) in the dark, 4) conversion = 40%,alternative preparation shown, 5) alternative preparation shown, regioselective, 6) alternative preparation shown, Reactants: 6, Reagents: 8, Solvents: 5, Steps: 6, Stages: 9, Most stages in any one step: 2

References

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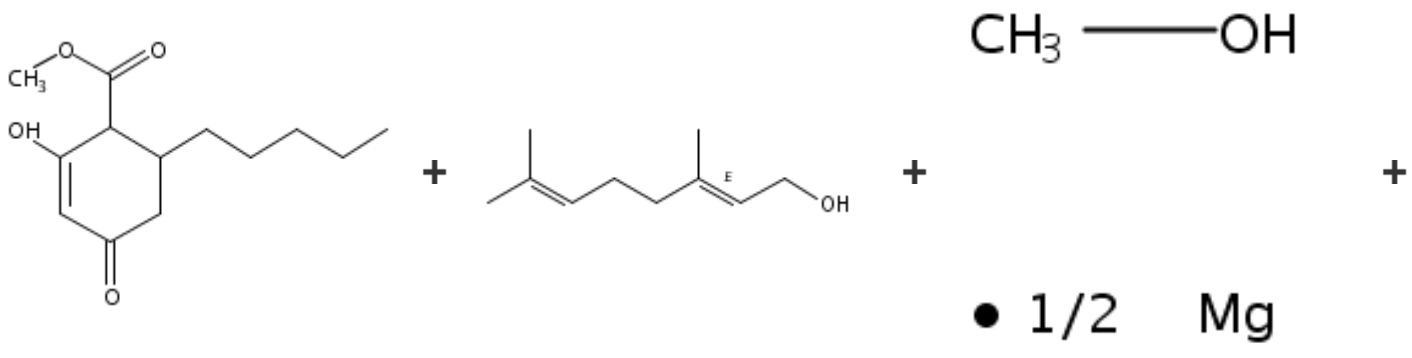
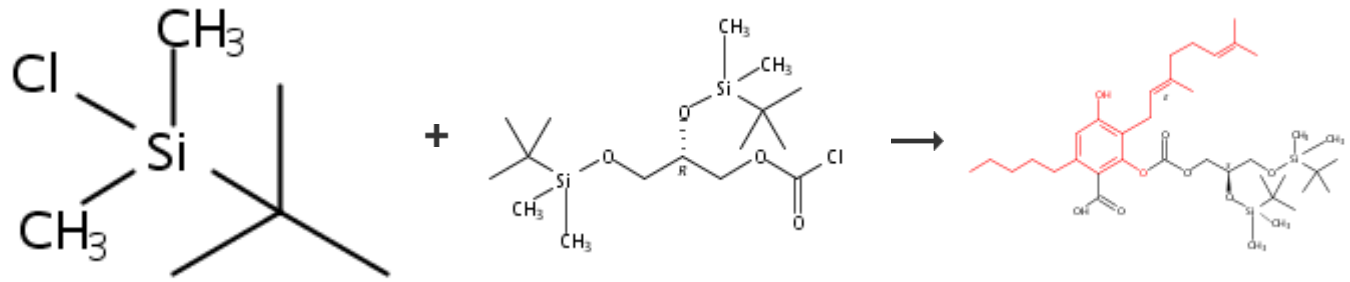
358. 5 Steps



[Step 2.1] [Step 3.1]



[Step 4.1] [Step 5.1]

Overview

Steps/Stages

1.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

2.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

3.1 S:H_2O, cooled; 50°C; 3 h, 50°C; 50°C → rt

3.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, rt, pH 2

4.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

4.2 R:NaCl, S:H_2O

5.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

Notes

2) in the dark, 3) conversion = 85%,alternative preparation shown,reaction in a sealed pressure vessel, 4) alternative preparation shown, regioselective, 5) alternative preparation shown, Reactants: 5, Reagents: 6, Solvents: 5, Steps: 5, Stages: 7, Most stages in any one step: 2

References

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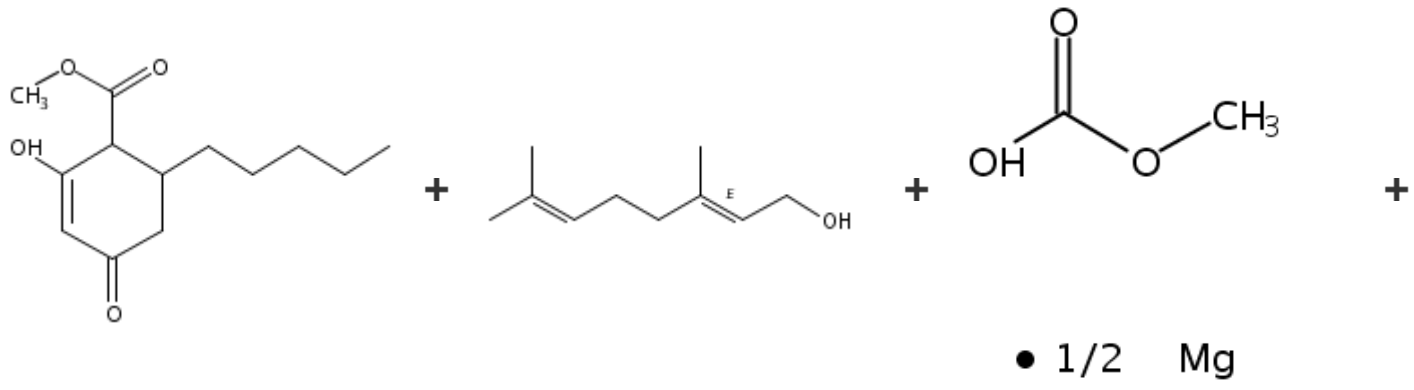
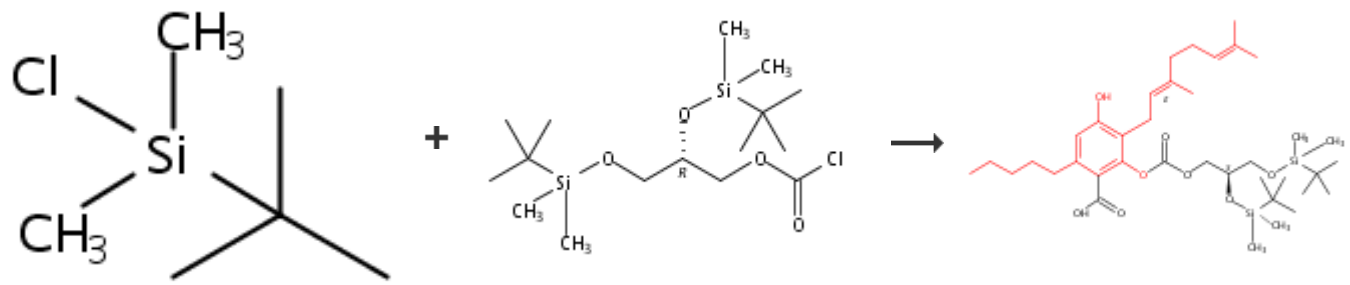
359. 5 Steps



[Step 2.1] [Step 3.1]



[Step 4.1] [Step 5.1]

Overview

Steps/Stages

1.1 R:Br_2, S:DMF, rt; 90 min, rt → 80°C; 80°C → 160°C; 10 h, 160°C

2.1 R:*p*-$MeC_6H_4SO_3H$, S:$CHCl_3$, 12 h, rt

3.1 S:DMF, 1 h, 120°C

3.2 R:HCl, S:MeOH, S:H_2O, S:$CHCl_3$, pH 2

4.1 R:1H-Imidazole, S:CH_2Cl_2, cooled

4.2 R:NaCl, S:H_2O

5.1 R:Et_3N, S:CH_2Cl_2, 0°C; rt

Notes

2) in the dark, 3) conversion = 40%,alternative preparation shown, 4) alternative preparation shown, regioselective, 5) alternative preparation shown, Reactants: 5, Reagents: 6, Solvents: 5, Steps: 5, Stages: 7, Most stages in any one step: 2

References

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