

the course of the one-step reaction is identical with both oxidizing agents,¹²⁰ resulting in the acid $R-COOH$, because periodic acid is able to split the possible intermediate product $R-CO-CHO$, the same as it does any α -ketoaldehyde. α -Diketones are attacked only slowly to give, by the splitting of the $C-C$ chain, 2 moles of monocarboxylic acid.¹¹⁷ According to the work of Nicolet and Shinn¹²¹ α -hydroxylamines are also oxidized like the glycols. Since the α -amino acids react at least a thousand times more slowly than the α -hydroxy acids, formaldehyde and glyoxylic acid originate, for example, from serine, $CH_2(OH)-CH(NH_2)-COOH$, by division between the α and β - C -atoms. Diethanolamine, $CH_2(OH)-CH_2-NH-CH_2-CH_2OH$, decomposes in a fast reaction into 4 moles of formaldehyde and 1 mole of NH_3 . At first the division probably proceeds in one place forming CH_2O and $CH_2=N-CH_2OH$; this decomposes under hydrolysis into a second mole of CH_2O and $H_2N-CH_2-CH_2OH$, which is oxidized by periodic acid to $HN=CH_2$ and CH_2O , whereupon the imine finally decomposes into NH_3 and CH_2O . If the nitrogen atom in an α -hydroxyamine is tertiary, there is no oxidation, $(C_2H_5)_2N-CH_2-CH_2OH$ being stable.

In closing, periodic acid possesses a plain superiority for the oxidation of compounds which are soluble only in water and which are oxidized with difficulty. In these cases the earlier mentioned oxidation with lead tetraacetate in aqueous medium cannot be used. Thus the oxidative degradation of the starches, investigated by Jackson and Hudson¹²² and others,¹²³ is possible only with periodic acid.

¹²⁰ Raistrick and Smith, *Biochem. J.*, **29**, 606 (1935).

¹²¹ Nicolet and Shinn, *J. Am. Chem. Soc.*, **61**, 1615 (1939).

¹²² Jackson and Hudson, *J. Am. Chem. Soc.*, **59**, 2049 (1937).

¹²³ Caldwell and Hixon, *J. Biol. Chem.*, **123**, 595 (1933). Grangard, Michell, and Purves, *J. Am. Chem. Soc.*, **61**, 1290 (1939).

Dehydrogenation with Sulfur, Selenium, and Platinum Metals

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During the past twenty-five years, dehydrogenation has been established as a most useful aid in studying the constitution of organic natural products. The method achieved its first great success in polyterpene research, and since 1921 has been systematically used and developed in this field by Ruzicka.¹ It was well known at that time that the naphthalene hydrocarbons cadalene^{2,3} and eudalene³ could be obtained from some sesquiterpenes by dehydrogenation with sulfur. The same procedure applied to simple terpenes, such as limonene and terpinene, resulted in the formation of *p*-cymene,³ which had long been recognized as the parent aromatic hydrocarbon of these terpenes.

It had previously been proposed, first by Wallach⁴ and later by Semmler,⁵ that certain sesquiterpenes might be hydrogenated naphthalene derivatives. The dehydrogenation results obtained by Ruzicka confirmed this hypothesis in a manner surprisingly straightforward from the experimental standpoint. Further insight into the structure of the carbon residues of the sesquiterpenes in question was soon provided by the identification of cadalene, both by analysis and by synthesis, as 1,6-dimethyl-4-isopropyl-naphthalene,⁶ and eudalene as 1-methyl-7-isopropyl-naphthalene.⁷

The results obtained in the sesquiterpene series furnished the basis for further applications of dehydrogenation methods. The conversion of diterpenes, such as abietic acid, *d*-pimaric acid, and agathenedicarboxylic acid, into phenanthrene derivatives has helped to establish the constitution of these compounds. The same holds true for the chemistry of the triter-

¹ L. Ruzicka, *Fortschr. Chem., Physik physik. Chem.*, **19A**, No. 5 (1928), 57 pp. (*Constitution and Relationships in the Sesquiterpene Series*).

² L. Ruzicka and J. Meyer, *Helv. Chim. Acta*, **4**, 505 (1921).

³ L. Ruzicka, J. Meyer, and Mingazzini, *Helv. Chim. Acta*, **5**, 345 (1922).

⁴ Wallach, *Ann.*, **239**, 49 (1887).

⁵ Semmler and Becker, *Ber.*, **46B**, 1817 (1913). Semmler and Stenzel, *ibid.*, **47B**, 2557 (1914).

⁶ L. Ruzicka and Seidel, *Helv. Chim. Acta*, **5**, 369 (1922).

⁷ L. Ruzicka and Stoll, *Helv. Chim. Acta*, **5**, 923 (1922).

penes, some of which can be classified as hydrogenated picene derivatives, on the basis of dehydrogenation results.⁸

Successful applications of these methods have not, however, been confined solely to polyterpene chemistry. For example, the dehydrogenation of cholesterol and cholic acid has played an important part in determining the structure of the sterols. In 1932, the results of such experiments led Rosenheim and King,⁹ and Wieland and Dane¹⁰ to a new and now generally accepted formulation of the entire sterol chemistry. Dehydrogenation is largely responsible for the advances made during the last few years in the fields of the sterols and bile acids, the sex hormones, the D vitamins, the cardiac aglucons, and the carcinogenic hydrocarbons. The method has also been applied successfully to the investigation of other natural products such as alkaloids, and its field of usefulness is likely to be expanded still further in the future. Depending on the desired goal, emphasis may be placed on either the synthetic or the analytic aspect of these investigations. Although dehydrogenation reactions have been used to an increasing extent, during the last few years, in the synthesis of polycyclic aromatic compounds, their principal value is still in determining the constitution of organic natural products. This application will therefore be considered first.

The fundamentals of this work can be outlined as follows.¹ It is extremely difficult and time-consuming to establish the structure of the high molecular weight alicyclic compounds by the ordinary systematic methods of analysis. If these substances can be converted, in an unequivocal manner, into the parent aromatic compounds, then such questions as the relative positions of the rings and of the substituents can be answered comparatively easily, and a large number of possible isomers can be eliminated from consideration. Furthermore, the parent aromatic compounds exhibit typical properties, absorption spectra for example, and also are much more readily identified by synthesis than are the hydrogenated derivatives. In a familiar ring system it is much easier to determine the positions of the carbon-to-carbon double bonds and of the substituents, and to establish the stereochemical relationships.

I. SCOPE OF DEHYDROGENATION METHODS

Inasmuch as we are considering dehydrogenation essentially as an aid in determining the constitution of organic compounds, we can omit an exhaustive discussion of the theoretical basis for the formation of unsaturated and aromatic systems from more completely hydrogenated compounds. It

⁸ L. Ruzicka, *Angew. Chem.*, **51**, 5-11 (1938).

⁹ Rosenheim and King, *Chemistry and Industry*, **51**, 464-466, 954-956 (1932).

¹⁰ Wieland and Dane, *Z. physiol. Chem.*, **210**, 268-281 (1932). Wieland, Dane, and Martius, *ibid.*, **215**, 15-24 (1933).

also seems sufficient to confine the discussion of the products of dehydrogenation reactions almost exclusively to aromatic compounds, that is, derivatives of benzene and condensed benzene ring systems, and the completely dehydrogenated, so called aromatic, heterocyclic compounds with five- and six-membered rings, such as thiophene and pyridine.¹¹ The azulenes,¹² of which the nucleus is the *naphthalene type* combination of a five- and a seven-membered ring, form a supplement to these well known aromatic systems which is extremely interesting from the theoretical standpoint. In contrast to the azulene structure, isolated five- and seven-membered rings generally are not dehydrogenated even when, as in indane for example, they are combined with a benzene ring. Likewise, double bonds cannot be introduced into the longer aliphatic chains by the usual dehydrogenation methods, except in a few special cases. The behavior toward dehydrogenation reagents of these compounds which cannot be dehydrogenated will be briefly discussed for the individual case.

Oxidation processes, which on the basis of their probable reaction mechanisms were formerly classed as dehydrogenations, will not be discussed.

II. VARIOUS DEHYDROGENATION METHODS AND REAGENTS

Dehydrogenation reactions have been used intermittently for a long time. The exhaustive bromination method of von Baeyer and Villiger,¹³ which was used successfully in investigating the terpene series, and the dehydrogenative decomposition with manganese dioxide and sulfuric acid^{14,15} are two early methods which have practically no application at the present time.

Catalytic dehydrogenation in the vapor phase, especially with nickel catalysts, was introduced as a general method by Sabatier and Senderens¹⁶ at the beginning of this century. It was improved and systematically investigated by Zelinsky¹⁷ through the use of platinum metal catalysts. Since nickel requires very high reaction temperatures and therefore readily causes splitting out of carbon atoms and other side reactions, palladium and platinum catalysts are generally much better. There seems to be no fundamental difference between the action of palladium and that of platinum.

¹¹ Hückel, *Theoretische Grundlagen der organischen Chemie*, Akadem. Verlagsgesellschaft, Leipzig, 1931, Vol. I, 365 ff.

¹² Plattner and Pfau, *Helv. Chim. Acta*, **20**, 224-232 (1937).

¹³ von Baeyer and Villiger, *Ber.*, **32** B, 2429-2447 (1899).

¹⁴ See also L. Ruzicka, Schinz, and J. Meyer, *Helv. Chim. Acta*, **6**, 1077 (1923).

¹⁵ L. Ruzicka and Rudolph, *Helv. Chim. Acta*, **10**, 915-920 (1927).

¹⁶ Sabatier, *Catalytic Hydrogenation* (German), Akadem. Verlagsgesellschaft, Leipzig, 1914.

¹⁷ Zelinsky, *Ber.*, **44** B, 3121-3125 (1911).

Other platinum metals, such as ruthenium, rhodium, iridium, and osmium, have been tried by Zelinsky and Turova-Pollak.^{18,19}

The systematic use of sulfur as a dehydrogenation reagent dates back, as previously mentioned, to Ruzicka.¹⁻³ Even before that, Curie,²⁰ Kelbe,²¹ and Vesterberg²² had used sulfur in the dehydrogenation of rosin and the abietic acids derived from it, and had thereby obtained retene, but the general importance of this method was not realized at that time.¹

The use of selenium for dehydrogenation was introduced by Diels²³ and was quickly adopted, since selenium has a number of advantages over sulfur. On the other hand, the relatively high dehydrogenation temperatures necessitated by the use of selenium also involve various disadvantages.

In addition to these common reagents, various others have occasionally been used.²⁴ It is interesting to note that activated charcoal, which is often used as a carrier for the platinum metal catalysts, can cause dehydrogenation by itself.²⁵⁻²⁷ Under favorable conditions, even atmospheric oxygen,²⁸ selenium dioxide,²⁹ concentrated sulfuric acid,³⁰ etc., can effect dehydrogenation. The use of dialkyl sulfides instead of sulfur for dehydrogenation was proposed by Ritter and Sharpe.³¹ Chloranil was introduced as a mild dehydrogenation agent by Arnold and Collins,³² and has since been used by Barclay and Campbell³³ for the dehydrogenation of carbazole and its derivatives, and by Crawford and Nelson³⁴ for the preparation of 2,3-diphenylnaphthalene from the 3,4-dihydro compound. Other experiments with these reagents have not been successful, however; so their use in the degradation of natural products is open to question.

III. REACTION MECHANISMS

Little is actually known about the reaction mechanism of dehydrogenation. The problem is complicated by the fact that entirely normal dehy-

¹⁸ Zelinsky and Turova-Pollak, *Ber.*, **58 B**, 1298 (1925).

¹⁹ *Ber.*, **62 B**, 2865 (1929).

²⁰ P. Curie, *Chem. News*, **30**, 189 (1874).

²¹ Kelbe, *Ber.*, **11**, 2174 (1878).

²² Vesterberg, *Ber.*, **36 B**, 4200 (1903).

²³ See the summarized lecture, *Ber.*, **69 A**, 195 (1936).

²⁴ See, for example, H. Meyer, *Analyse und Konstitutionsermittlung organischer Chemie*, 6th ed., Springer, Berlin, 1938.

²⁵ Bahr, *Ber.*, **64 B**, 2258 (1931).

²⁶ Asahina and Nakanishi, *J. Pharm. Soc. Japan*, **48**, 1-20 (1928).

²⁷ Heisel and Dewein, German Patent, 701,514; cf. *Chem. Abstracts*, **35**, 8310 (1941).

²⁸ *E.g.*, Lewis, Ramadge, and R. Robinson, *J. Chem. Soc.*, **1935**, 1412-1414.

²⁹ Borgwardt and Schwenk, *J. Am. Chem. Soc.*, **56**, 1185-1187 (1934). See also Stein, *Angew. Chem.*, **54**, 146 (1941).

³⁰ *E.g.*, J. W. Cook and Hewett, *J. Chem. Soc.*, **1933**, 1098-1111.

³¹ Ritter and Sharpe, *J. Am. Chem. Soc.*, **59**, 2351-2352 (1937).

³² Arnold and Collins, *J. Am. Chem. Soc.*, **61**, 1407-1408 (1939).

³³ Barclay and Campbell, *J. Chem. Soc.*, **1945**, 530-533.

³⁴ Crawford and Nelson, *J. Am. Chem. Soc.*, **68**, 134-135 (1946).

drogenations, those in which no cleavage, formation, or rearrangement of carbon-to-carbon bonds occurs, are relatively rare. In most cases, indeed, the real dehydrogenation reaction is accompanied by partial thermal effects, such as cleavage of quaternary methyl groups. Attempts have been made to investigate the thermal decomposition and the dehydrogenation separately,^{35,36} but such a procedure, probably justly, has found no general application in the actual determination of constitution.

Catalytic dehydrogenations are probably based on fundamentally different reactions than are the dehydrogenations with sulfur and selenium. In the final effect, however, the dissimilarities in these three most common methods are not very important and seem to be due for the most part to the different reaction temperatures. Separate treatment of the three methods can therefore logically be omitted. However, the peculiarities of the individual reagents will be noted, where necessary, in the course of the detailed discussion.

Originally, dehydrogenation reactions were confined almost exclusively to hydrocarbons, but recently compounds containing functional groups, such as hydroxyl, have found increasing use as starting materials. In many cases the reaction products formed from these compounds are different from those obtained from the parent hydrocarbons; so much broader conclusions may be drawn from the dehydrogenation results. Also, it is often possible to preserve the functional groups during dehydrogenation, or at least to detect them in recognizable form in the final products. Keto groups, for example, can be converted into phenolic hydroxyl groups. Since the course of the dehydrogenation is often considerably influenced by the functional groups present, their behavior in dehydrogenation reactions will be dealt with first.

IV. BEHAVIOR OF FUNCTIONAL GROUPS

As might be expected, *tertiary hydroxyl groups* are readily split off during dehydrogenation. In general, the products are identical with those obtained from the hydrocarbon, as is shown by the formation of eudalene from eudesmol by direct dehydrogenation with sulfur,³ and from 2-(hydroxyisopropyl)-8-methyl-1,2,3,4-tetrahydronaphthalene by dehydrogenation with selenium.³⁷ Catalytic dehydrogenation with palladium-charcoal readily removes tertiary hydroxyl groups attached directly to a saturated ring system.^{38,39}

³⁵ L. Ruzicka, Huyser, Pfeiffer, and Seidel, *Ann.*, **471**, 21 (1929).

³⁶ L. Ruzicka and van Veen, *Rec. trav. chim.*, **48**, 1018-1024 (1929).

³⁷ Chakravarti, *J. Indian Chem. Soc.*, **20**, 393-398 (1943).

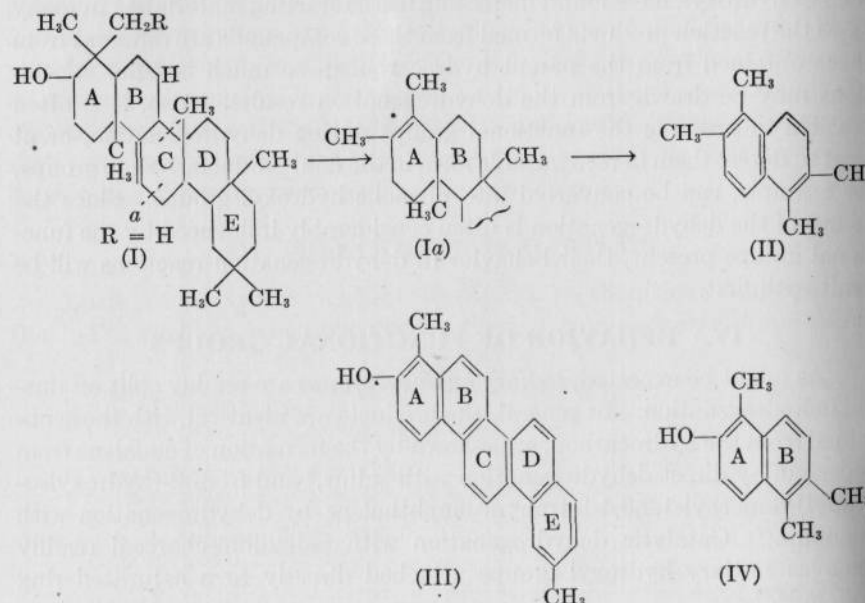
³⁸ Bachmann and Wilds, *J. Am. Chem. Soc.*, **60**, 624-627 (1938).

³⁹ W. S. Johnson, Goldman, and Schneider, *J. Am. Chem. Soc.*, **67**, 1357-1360 (1945).

Secondary hydroxyl groups are often split off in the form of water before the real dehydrogenation begins. To avoid the frothing which accompanies it, the removal of the water is best carried out carefully in the reaction vessel prior to the true dehydrogenation, as recommended by Ruzicka and co-workers in the selenium dehydrogenation of cholic acid. The composition of the products is not altered by this procedure.⁴⁰ At the relatively high temperatures of selenium dehydrogenations, secondary hydroxyl groups are usually eliminated, and the products are almost exclusively hydrocarbons. For example, cyclopentenophenanthrene derivatives are obtained by the selenium dehydrogenation of androstenediols.⁴¹ In the triterpene series such dehydrogenation products as 1,2,5,6-tetramethylnaphthalene (II) appear, the formation of which must be explained by retro-pinacolone rearrangement according to Formulas I, Ia, and II.^{42,43}

Surprisingly, the acetates of triterpene alcohols appear to behave differently, since in their dehydrogenation the retro-pinacolone rearrangement is strongly repressed.^{44,45}

Although in general hydrocarbons are the chief products of dehydro-



⁴⁰ L. Ruzicka, Goldberg, and Thomann, *Helv. Chim. Acta*, **16**, 813 (1933).

⁴¹ Butenandt and Surányi, *Ber.*, **75** B, 597-606 (1942).

⁴² L. Ruzicka, Goldberg, and K. Hofmann, *Helv. Chim. Acta*, **20**, 325-328 (1937).

⁴³ L. Ruzicka, Schellenberg, and Goldberg, *Helv. Chim. Acta*, **20**, 791-804 (1937).

⁴⁴ L. Ruzicka and Lambertson, *Helv. Chim. Acta*, **23**, 1338-1345 (1940).

⁴⁵ L. Ruzicka and Rosenkranz, *Helv. Chim. Acta*, **23**, 1311-1324 (1940).

genations carried out under such relatively vigorous conditions, it is also usually possible to detect certain amounts of oxygen-containing compounds, such as phenols. One of the most notable examples of this was the isolation of 1,8-dimethyl-2-hydroxypicene (III)^{42,43} from the dehydrogenation of amyrenes. The constitution of this product was established by the synthesis of the methyl ether.⁴⁶ By this reaction the relative positions of the 24 carbon atoms and the characteristic hydroxyl groups of the corresponding triterpenes were conclusively established. A trimethylnaphthol,^{47,48} which was later identified as hydroxygathalene (IV) (1,2,5-trimethyl-6-hydroxynaphthalene),^{49,50} and which is formed from the Rings A and B (Formula I) of the triterpene, was obtained as an additional phenolic dehydrogenation product from most of the triterpenes. Mention should also be made of the formation of 7-hydroxy-1-methylphenanthrene from the diterpene alcohol totarol,⁵¹ and of 9-phenanthrol from 9-hydroxyoctahydrophenanthrene.⁵² An example of a similar dehydrogenation carried out under very mild conditions is the conversion of neosterol (VI) into a naphthol derivative (VII).⁵³ Secondary hydroxyl groups protected by methylation may be unaffected even by selenium dehydrogenation.⁵⁴

Cyclic ketones are very readily converted to phenols by dehydrogenation. This reaction was thoroughly studied by Darzens and Lévy,⁵⁵ who obtained phenol from cyclohexanone, and α -naphthol from α -tetralone, by dehydrogenation with sulfur or selenium. Ruzicka⁵⁶ has investigated the dehydrogenation of *trans*- β -decalone and 3-methylcyclohexanone. Horning⁵⁷ obtained the corresponding phenols from some alkylcyclohexanones by refluxing with sulfur for 1 hour; the yields were 26 to 29%. According to Fieser, Hershberg, and Newman,⁵⁸ the corresponding hydroxybenzopyrene is obtained from the ketone (V) in about 20% yield by a short dehydrogenation with sulfur at low temperatures (220° to 230° C.); with selenium at 310° to 320° C., however, 1,2-benzopyrene is the main product, only traces of the hydroxyl derivatives being isolated.

A number of examples are known of the formation of phenols by the

⁴⁶ L. Ruzicka and K. Hofmann, *Helv. Chim. Acta*, **20**, 1155-1164 (1937).

⁴⁷ L. Ruzicka, Brüngger, Egli, Ehmann, Furter, and Hösli, *Helv. Chim. Acta*, **15**, 431-457 (1932).

⁴⁸ L. Ruzicka, Hösli, and K. Hofmann, *Helv. Chim. Acta*, **19**, 370-377 (1936).

⁴⁹ L. Ruzicka, K. Hofmann, and Frei, *Helv. Chim. Acta*, **19**, 386-392 (1936).

⁵⁰ L. Ruzicka, K. Hofmann, and Schellenberg, *Helv. Chim. Acta*, **19**, 1391-1402 (1936).

⁵¹ Short and Stromberg, *J. Chem. Soc.*, **1937**, 516-520.

⁵² J. W. Cook, Hewett, and Lawrence, *J. Chem. Soc.*, **1936**, 71-80.

⁵³ Honigsmann, *Ann.*, **511**, 292-301 (1934).

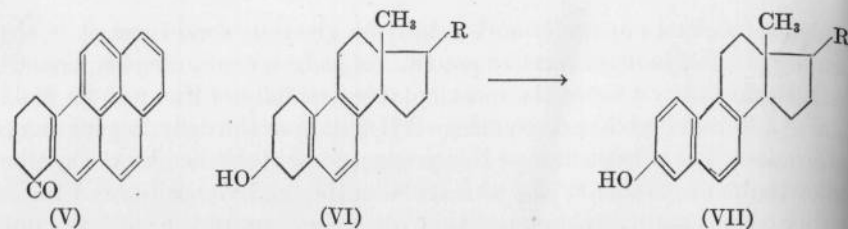
⁵⁴ L. Ruzicka, Rey, and Smith, *Helv. Chim. Acta*, **26**, 2057-2063 (1943).

⁵⁵ Darzens and Lévy, *Compt. rend.*, **194**, 181-183 (1932) and later articles.

⁵⁶ L. Ruzicka, *Helv. Chim. Acta*, **19**, 419-423 (1936).

⁵⁷ Horning, *J. Am. Chem. Soc.*, **67**, 1421-1422 (1945).

⁵⁸ L. F. Fieser, Hershberg, and Newman, *J. Am. Chem. Soc.*, **57**, 1509-1510 (1935).



catalytic dehydrogenation of cyclic ketones. 7-Methyl-1-naphthol is obtained from 7-methyl-1-tetralone with palladium,⁵⁹ thymol from piperitone with nickel⁶⁰ or palladium,⁶¹ and chrysenols from keto-hexahydrochrysenes also by the use of palladium.^{62,63}

Some dehydrogenations of this type have been investigated in detail by Linstead and Michaelis.⁶⁴ α -Tetralone, *ar*- and *ac*- β -tetralol, *trans*- α -decalone, *cis*- and *trans*- β -decalone, *cis*- and *trans*- β -decalol all give the corresponding naphthol in yields of 12 to 60%, along with varying amounts of naphthalene. The compounds which are already most nearly in the aromatic state can be dehydrogenated under milder conditions and give correspondingly more naphthol and less naphthalene. The investigation has also been extended to terpene ketones,⁶⁵ which can be converted to thymol and carvacrol in very good yields.

Extracyclic keto groups, on the other hand, are often unaffected by dehydrogenation under relatively mild conditions. According to Barbot,⁶⁶ for example, β -acetyltetralin can be converted by sulfur into methyl naphthyl ketone in 70% yield. It is interesting to note that anthraquinones are readily obtained by the dehydrogenation of hydrogenated anthraquinones especially with sulfur.⁶⁷ Johnson and co-workers⁶⁸ converted 3'-keto-3,4-dihydro-1,2-cyclopentenonaphthalene to 4,5-benzhydrindone-1 by dehydrogenation with sulfur for 1 hour at 220°C.

The catalytic dehydrogenation of some ketones derived from tetrahydronaphthalene has been investigated by Newman and co-workers,^{69,70} who dehydrogenated the following compounds with palladium-charcoal under fairly vigorous conditions: methyl 2-(5,6,7,8-tetrahydronaphthyl)

⁵⁹ L. Ruzicka and Mörgeli, *Helv. Chim. Acta*, **19**, 377-386 (1936).

⁶⁰ Treibs and Schmidt, *Ber.*, **60** B, 2335-2341 (1927).

⁶¹ Read, Watters, Robertson, and Hughesdon, *J. Chem. Soc.*, **1929**, 2068.

⁶² Wilds and Shunk, *J. Am. Chem. Soc.*, **65**, 469-475 (1943).

⁶³ Cook and Schoental, *J. Chem. Soc.*, **1945**, 288-293.

⁶⁴ Linstead and Michaelis, *J. Chem. Soc.*, **1940**, 1134-1139.

⁶⁵ Linstead, Michaelis, and Thomas, *J. Chem. Soc.*, **1940**, 1139-1147.

⁶⁶ Barbot, *Bull. soc. chim.*, **47**, 1314-1323 (1930).

⁶⁷ L. F. Fieser and Seligman, *J. Am. Chem. Soc.*, **56**, 2690-2696 (1934).

⁶⁸ W. S. Johnson, H. C. E. Johnson, and Petersen, *J. Am. Chem. Soc.*, **67**, 1360-1366 (1945).

⁶⁹ Newman and Zahm, *J. Am. Chem. Soc.*, **65**, 1097-1101 (1943).

⁷⁰ Newman and O'Leary, *J. Am. Chem. Soc.*, **68**, 258-261 (1946).

ketone; methyl β -(5,6,7,8-tetrahydro-2-naphthoyl)propionate; methyl 1-(1,2,3,4-tetrahydronaphthyl) ketone; 1-(1,2,3,4-tetrahydro)naphthyl-2-propanone; and 1-(1,2,3,4-tetrahydro-1-naphthyl)-3-butanone. The results indicate that the course of the reaction is greatly influenced by the position of the carbonyl group in the side chain and in relation to the hydrogenated structure. The carbonyl groups in the first two of the above compounds were reduced to methylene groups; the last three compounds exhibited no reduction of the carbonyl groups. Methyl 1-(1,2,3,4-tetrahydronaphthyl)ketone and 1-(1,2,3,4-tetrahydro-1-naphthyl)-3-butanone resisted dehydrogenation, most of the starting material being recovered unchanged. 1-(1,2,3,4-Tetrahydro)naphthyl-2-propanone was smoothly dehydrogenated to the naphthyl ketone in a yield of 84%.

From the fact that phenols are often obtained as products of the dehydrogenation of cyclic ketones, it is understandable that free and especially methylated *phenolic hydroxyl groups* are often unaffected by dehydrogenation. This is especially true of dehydrogenations with sulfur.⁷¹⁻⁷⁴ With selenium, the elimination of hydroxyl and methoxyl groups has been reported,^{72,75} as well as instances in which these groups were retained,⁷⁶⁻⁸⁰ which indicated that dehydrogenation temperatures above 300°C. promote the elimination. The examples given by Kon and Ruzicka,⁸¹ especially, confirm this.

In general, phenolic oxygen atoms are more likely to be eliminated during dehydrogenation at the higher reaction temperatures. At the present time there is no definite information about the effect of the position of the oxygen atoms on the ease of elimination.

Examples of dehydrogenations of compounds containing *primary hydroxyl groups* are not very numerous. By the dehydrogenation of abietinol (VIII),⁸² Ruzicka and Meyer⁸³ obtained retene (IX), which is also formed from abietic acid itself⁸³ and from methylabietene (X).⁸⁴ On the

⁷¹ L. F. Fieser and Holmes, *J. Am. Chem. Soc.*, **58**, 2319-2322 (1936).

⁷² Haberland, *Ber.*, **69** B, 1380-1386 (1936).

⁷³ Darzens and G. Lévy, *Compt. rend.*, **200**, 469-471 (1935).

⁷⁴ C. K. Chuang, Y.-L. Tien, and Y.-T. Huang, *Ber.*, **70** B, 858-863 (1937). Hill, Short, and Stromberg, *J. Chem. Soc.*, **1937**, 1619-1622.

⁷⁵ Chatterjee, *J. Indian Chem. Soc.*, **13**, 659 (1936).

⁷⁶ Short, Stromberg, and Wiles, *J. Chem. Soc.*, **1936**, 319-322.

⁷⁷ Hill, Short, and Higginbottom, *J. Chem. Soc.*, **1936**, 317-319.

⁷⁸ Haworth and Sheldrick, *J. Chem. Soc.*, **1934**, 864-867.

⁷⁹ L. Ruzicka and H. Waldmann, *Helv. Chim. Acta*, **15**, 907-914 (1932).

⁸⁰ Butenandt, Weidlich, and Thompson, *Ber.*, **66** B, 601 (1933).

⁸¹ Kon and F. C. J. Ruzicka, *J. Chem. Soc.*, **1936**, 187-192.

⁸² Formula of abietic acid according to L. Ruzicka and Sternbach, *Helv. Chim. Acta*, **21**, 565-583 (1938).

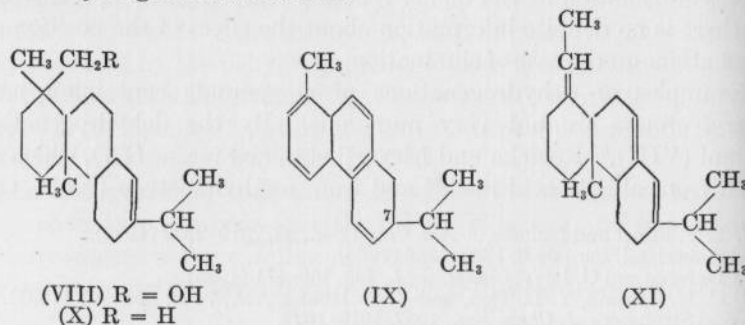
⁸³ L. Ruzicka and J. Meyer, *Helv. Chim. Acta*, **5**, 581 (1922).

⁸⁴ L. Ruzicka, Waldmann, P. J. Meyer, and Hösli, *Helv. Chim. Acta*, **16**, 169-181 (1933). The methylabietene (X) was obtained from abietinol through the corresponding aldehyde and reduction of the semicarbazone by the Wolff-Kishner method.

other hand, if water is first split out of abietinol, the main product is a homoretene,⁸³ which has been identified as 1-ethyl-7-isopropylphenanthrene.^{85,86} Similar relationships have also been observed in the dehydrogenation of *d*-pimaric acid.⁸⁵⁻⁸⁷ Therefore, during the elimination of water from abietinol (VIII), a retopinacoline rearrangement takes place, which results in the formation of XI; this rearrangement does not occur during the direct dehydrogenation. Also, retopinacoline rearrangement to an ethyl derivative does not seem to result from the dehydrogenation of hederagenin (I, R = OH).⁸⁸ Derivatives which would correspond to homoretene and to homopimanthrene (1-ethyl-7-methylphenanthrene) cannot be isolated for this reason.⁸⁹

In connection with the dehydrogenation of hederagenin, it is interesting to note that there seems to be no migration of one of the geminal methyl groups, which in other cases results in the formation of 1,2,5,6-tetramethylnaphthalene,^{42,43} indicating that this product is not formed when one of the geminal methyl groups carries an oxygen atom. This is true of the dehydrogenation of the corresponding aldehyde, gypsogenin,^{88,90} as well as of hederagenin itself.

Newman and co-workers^{69,70} investigated the behavior of some primary alcohols in connection with their study of the catalytic dehydrogenation of substituted tetrahydronaphthalenes. As in the case of the ketones, the reaction of the primary hydroxyl group appears to depend on its position relative to the hydrogenated structure.



A great many compounds containing free and also esterified carboxyl groups have been dehydrogenated. The formation of retene from abietic

⁸⁵ L. Ruzicka, de Graaff, and Müller, *Helv. Chim. Acta*, **15**, 1300-1303 (1932).

⁸⁶ Haworth, *J. Chem. Soc.*, **1932**, 2717-2720.

⁸⁷ L. Ruzicka and Balas, *Helv. Chim. Acta*, **7**, 875 (1924).

⁸⁸ For the constitution of hederagenin and gypsogenin, see L. Ruzicka and Giacomello, *Helv. Chim. Acta*, **20**, 299-309 (1937).

⁸⁹ L. Ruzicka, Hösl, and Ehmann, *Helv. Chim. Acta*, **17**, 442-455 (1934).

⁹⁰ L. Ruzicka, Brüngger, Egli, Ehmann, and Goldberg, *Helv. Chim. Acta*, **15**, 1496-1506 (1932).

acid by dehydrogenation with sulfur, which was one of the first dehydrogenation reactions to be thoroughly investigated, shows that decarboxylation can readily occur under these conditions. Experience in a number of analogous cases indicates that a carboxyl group on a quaternary carbon atom is readily split off, even when it is esterified.^{75,87} This is confirmed not only by the behavior of natural products but also by the results of synthetic work.^{91,92}

Secondary and primary carboxyl groups, on the other hand, are very likely to be retained during dehydrogenation. Probably the first application of this tendency was made by Darzens and Lévy⁹³ in the preparation of 1-methyl-7-isopropyl-3-naphthoic acid from the corresponding 1,2,3,4-tetrahydro compound by dehydrogenation with sulfur at 230° to 240°C. 4-Methyl- α -naphthoic acid, however, could not be prepared in this way, since carbon dioxide was always split out during dehydrogenation.⁹⁴ The procedure was later extended to phenanthrenecarboxylic acids⁹⁵ and in recent years has frequently been applied to preparative work. Examples of its application are found in the work of Darzens and Lévy,⁹⁶⁻⁹⁸ of Fieser and Hersberg,^{71,99,100} of Cohen and co-workers,¹⁰¹⁻¹⁰³ and of Newman.¹⁰⁴ The dehydrogenation with palladium-charcoal of esters of some tetrahydronaphthylcarboxylic acids was studied by Newman and co-workers.^{69,70} Even under the fairly vigorous conditions employed, smooth conversion to the corresponding naphthyl derivative resulted. The same procedure was applied by Johnson and co-workers⁶⁸ in the preparation of β -1-naphthylpropionic acid and 1-naphthylsuccinic acid from the 3,4-dihydro compounds. In general, sulfur, palladium, and platinum are better than selenium for such dehydrogenations, since selenium readily causes decarboxylation, probably because of the higher dehydrogenation temperatures.

It is not surprising that side reactions often accompany the dehydrogenation of carboxylic acids and their functional derivatives. Thus it has been observed that free carboxylic acids are formed from esters, and anhydrides from dicarboxylic acids.^{56,105}

⁹¹ Bardhan and Sen-Gupta, *J. Chem. Soc.*, **1932**, 2520.

⁹² J. W. Cook, Haslewood, and A. M. Robinson, *J. Chem. Soc.*, **1935**, 667-671.

⁹³ Darzens and A. Lévy, *Compt. rend.*, **194**, 2056 (1932).

⁹⁴ Darzens and A. Lévy, *Compt. rend.*, **199**, 1131-1133 (1934).

⁹⁵ Darzens and A. Lévy, *Compt. rend.*, **200**, 2187-2189 (1935).

⁹⁶ Darzens and A. Lévy, *Compt. rend.*, **201**, 902-904 (1935).

⁹⁷ Darzens and A. Lévy, *Compt. rend.*, **202**, 427-428 (1936).

⁹⁸ Darzens and A. Lévy, *Compt. rend.*, **203**, 669-671 (1936).

⁹⁹ L. F. Fieser and Hersberg, *J. Am. Chem. Soc.*, **57**, 1508-1509 (1935).

¹⁰⁰ L. F. Fieser and Hersberg, *J. Am. Chem. Soc.*, **57**, 1851-1854 (1935).

¹⁰¹ Cohen, *Nature*, **136**, 869-870 (1935).

¹⁰² Cohen, Cook, and Hewett, *J. Chem. Soc.*, **1936**, 52-53.

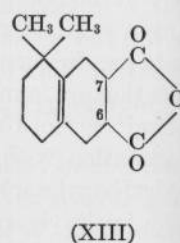
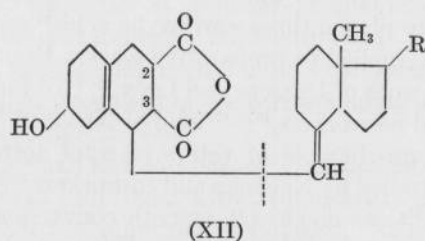
¹⁰³ Cohen and Warren, *J. Chem. Soc.*, **1937**, 1315-1320.

¹⁰⁴ Newman, *J. Org. Chem.*, **9**, 518-528 (1944).

¹⁰⁵ Cartwright and Haworth, *J. Chem. Soc.*, **1944**, 535-537.

An interesting discovery is that carboxyl groups can be reduced to methyl groups in the course of their dehydrogenation, though this type of reaction seems so far to have been observed only in dehydrogenations with selenium. For example, Windaus and Thiele¹⁰⁶ obtained 2,3-dimethylnaphthalene from dihydro-vitamin D₂-maleic anhydride (XII).

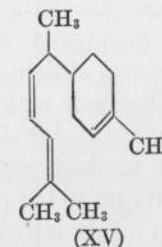
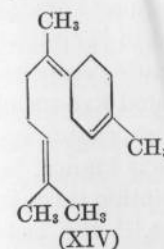
According to Thiele and Trautmann,¹⁰⁷ 2,3-dimethylnaphthalene is also obtained from 2,3-naphthalic anhydride by treatment with selenium in the presence of *p*-cyclohexylphenol as a hydrogen donor. A somewhat similar reaction occurred with 1,8-naphthalic anhydride; one of the carboxyl groups was converted into a methyl group, while the other was eliminated, α -methylnaphthalene being formed. Ruzicka⁵⁶ has also reported a case of the same kind in which 1,6,7-trimethylnaphthalene was formed from the anhydride XIII with selenium at 350°C.



In connection with these discussions on functional groups, the influence of *double bonds* already present in the molecule upon the result of the dehydrogenation must still be considered. As a rule, dehydrogenation goes more readily and in better yield, the more nearly the starting material is to being in the aromatic condition; that is, the more double bonds it already contains. In this respect the position of the double bonds can play an important part. For example, terpinene is converted to cymene in about 50% yield by dehydrogenation with sulfur, while the isomeric limonene gives a yield of only 15% under the same conditions.³

Not only do the position and number of the double bonds in the starting material generally have considerable influence on the yield of dehydrogenation products, but in some cases they can even determine the constitution of the products. It is known, for example, that the isomeric monocyclic sesquiterpenes bisabolene (XIV) and zingiberene (XV) behave differently on dehydrogenation in that the bicyclic compound, cadalene, results from zingiberene with sulfur,^{3,108} while bisabolene, both with sulfur and

with selenium, gives only benzenoid hydrocarbons (probably methylisooctylbenzene).¹⁰⁹



This is explainable by the different cyclization tendencies of these isomeric sesquiterpenes, and it may be assumed that in the case of zingiberene the cyclization precedes the dehydrogenation. In similar fashion it is also possible to explain the behavior of (bicyclic) agathenedicarboxylic acid (XXVIII),^{110,111} which on dehydrogenation gives phenanthrene derivatives in addition to naphthalene derivatives.

Since, other things being equal, the ease of dehydrogenation is dependent on the number of double bonds already present in the molecule, perhydro compounds can be expected to dehydrogenate only with extreme difficulty. With the more volatile of these compounds, the boiling temperature under atmospheric pressure is not sufficient to effect dehydrogenation, and reaction in the vapor phase over a catalyst or in a sealed tube must be resorted to. These facts probably account for many of the contradictory statements found in the literature about the ease of dehydrogenation of such compounds.

V. HYDROGENATION EFFECTS

It is often impossible to determine whether the disappearance of the extracyclic double bond in such dehydrogenations as that of limonene to cymene is due to migration in the nucleus or to hydrogenation. The latter hypothesis is supported by the fact that similar hydrogenations have been proved in other cases. For example, indenes are converted to the corresponding indanes in the presence of selenium in a sealed tube at 350°C.¹¹² The hydrogenation of double bonds has been observed in the triterpene series,⁸⁹ contrary to normal hydrogenation procedure; the saturated hydrocarbon C₂₉H₅₀ was obtained from oleanolic acid, and β -amyrene was partly converted into amyrene.⁴³ In a similar manner, Dorée and Petrov ob-

¹⁰⁶ Windaus and Thiele, *Ann.*, **521**, 160-175 (1936).

¹⁰⁷ Thiele and Trautmann, *Ber.*, **68 B**, 2245-2247 (1935).

¹⁰⁸ L. Ruzicka and van Veen, *Ann.*, **468**, 143-162 (1929).

¹⁰⁹ L. Ruzicka and van Veen, *Ann.*, **468**, 133-143 (1929).

¹¹⁰ L. Ruzicka and Hosking, *Helv. Chim. Acta*, **14**, 203 (1931).

¹¹¹ L. Ruzicka and Hosking, *Helv. Chim. Acta*, **13**, 1402 (1930).

¹¹² L. Ruzicka and Peyer, *Helv. Chim. Acta*, **18**, 676-684 (1935).

tained cholestane from cholesterolene,¹¹³ and cholestanone from cholesterol in 30 to 40% yields,¹¹⁴ by heating with selenium at 250°C. In general, therefore, it can be expected that side chains and similar parts of molecules, such as attached five-membered rings, will be obtained in completely saturated form in the products of dehydrogenation. Aromatic compounds with unsaturated side chains or with attached, unsaturated five-membered rings, such as indene or acenaphthalene type combinations, cannot be expected as dehydrogenation products and have not, so far as is known, been detected with any certainty up to the present. This assumption is confirmed by the dehydrogenation of hexahydroindane to indane,¹¹⁵ the isolation of γ -methylcyclopentenophenanthrene and methylcholanthrene, and also a number of experiments on compounds containing allyl side chains¹¹⁶⁻¹¹⁹ and on a series of unsaturated fatty acids.¹²⁰

Hydrogenation effects can appear even in double bonds which are part of a six-membered ring in which dehydrogenation to a parent aromatic compound should be possible. An example of this is the formation of α -naphthylcyclohexane from α -naphthylcyclohexene, reported by Cook and Lawrence.¹²¹ Such reactions are especially frequent in catalytic dehydrogenation, which often involves disproportionation rather than the complete removal of hydrogen.

VI. NORMAL DEHYDROGENATION

Normal dehydrogenations, those in which no cleavage, rearrangement, or formation of a carbon-to-carbon bond occurs, in general proceed readily and in good yield with all three of the common dehydrogenation methods, so that these processes can often be used in preparative work. The developments of the past few years have brought the catalytic method into considerable favor for the dehydrogenation of those compounds which contain no quaternary carbon atoms.

Developing the work of Sabatier¹²² on the dehydrogenation of cyclohexane to benzene by the use of finely divided nickel, Zelinsky¹⁷ observed that the platinum metals catalyze this reaction at considerably lower temperatures. Since under these mild reaction conditions some other hydro-

¹¹³ Dorée and Petrov, *J. Chem. Soc.*, 1934, 1129-1130.

¹¹⁴ Dorée and Petrov, *J. Chem. Soc.*, 1935, 1391-1393.

¹¹⁵ Zelinsky and Titz, *Ber.*, 62 B, 2869-2873 (1929).

¹¹⁶ Levina and Trakhtenberg, *J. Gen. Chem. (U. S. S. R.)*, 6, 764-773 (1936).

¹¹⁷ Levina and Tzurikov, *J. Gen. Chem. (U. S. S. R.)*, 4, 1250-1257 (1934).

¹¹⁸ Cohen, J. W. Cook, and Hewett, *J. Chem. Soc.*, 1935, 1633-1637.

¹¹⁹ J. W. Cook and Haslewood, *J. Chem. Soc.*, 1935, 767-770.

¹²⁰ Yokoyama and Kotake, *Bull. Chem. Soc. Japan*, 10, 138 (1935); also in *J. Chem. Soc. Japan*, 56, 336-337 (1935).

¹²¹ J. W. Cook and Lawrence, *J. Chem. Soc.*, 1936, 1431-1434.

¹²² Sabatier, *Ber.*, 44, 1984 (1911).

carbons, such as cyclopentane derivatives, are not attacked, hydrocarbon mixtures can be separated by selective dehydrogenation.¹²³ This method was applied to the investigation of the "naphthenes" of petroleum^{124,125} and to the determination of cyclopentanes in paraffin hydrocarbons.¹²⁶

A large number of substituted cyclohexanes, hydrogenated naphthalenes and phenanthrenes, and hydrogenated derivatives of higher condensed aromatic systems can be readily dehydrogenated to their parent aromatic compounds. Examples are the dehydrogenation of menthane,¹²⁷ hexahydrozingiberene,¹⁰⁸ decalin,^{125,128,129} 2-benzyldecalin,¹³⁰ hydrindane,¹¹⁵ hexahydrofluorene,¹³⁰ and octahydroanthracene.¹³¹ With the higher boiling compounds dehydrogenation in the vapor phase, which is somewhat inconvenient from the standpoint of the apparatus involved, can be replaced by simple heating under reflux in the presence of the catalyst. However, care must always be taken that the dehydrogenation mixture really attains the required temperature, which in certain cases can be as high as 350°C.

The behavior of tetralin, octalin, decalin, octahydroanthracene, and octahydrophenanthrene toward platinum and palladium catalysts has been very thoroughly investigated by Linstead and co-workers.^{64,129,132} According to their results, tetralin is rapidly dehydrogenated in the liquid phase even at a temperature of 185°C. when vigorous boiling is insured, by the application of a slight vacuum for example; decalin, on the other hand, requires a temperature of about 300°C. Octalin undergoes disproportionation to tetralin and decalin before dehydrogenation. The catalytic dehydrogenation of limonene proceeds in a similar manner⁶⁵; it is disproportionated to menthane and cymene by heating in the presence of the catalyst, even at 140°C. Complete dehydrogenation occurs only at about 305°C. The same is true of cadinene.

Even though, because of their simplicity and cleanliness, the catalytic methods really give the best results for such dehydrogenations, sulfur and selenium have also frequently been used. In general, both of these reagents give good results for the dehydrogenation of partially unsaturated compounds, as is apparent from the work of Ruzicka, Haworth, Cook, and others. Perhydro compounds, however, resist dehydrogenation by these chemical methods, even at temperatures above 350°C. The fact that

¹²³ Zelinsky, *Ber.*, 45, 3678-3682 (1912).

¹²⁴ Zelinsky, *Ber.*, 56, 1718-1723 (1923).

¹²⁵ Kaffer, *Ber.*, 57 B, 1261 (1924).

¹²⁶ Turova-Pollak, Zelinsky, and Gasan-Zade, *Compt. rend. acad. sci. U. R. S. S.*, 32, 551-554 (1941).

¹²⁷ Zelinsky, *Ber.*, 56, 787-788 (1923).

¹²⁸ Zelinsky, *Ber.*, 56, 1723-1724 (1923).

¹²⁹ Linstead, Millidge, Thomas, and Walpole, *J. Chem. Soc.*, 1937, 1146-1157.

¹³⁰ J. W. Cook and Hewett, *J. Chem. Soc.*, 1936, 62-71.

¹³¹ Maillard, *Compt. rend.*, 200, 1856-1858 (1935).

¹³² Linstead and Thomas, *J. Chem. Soc.* 1940, 1127-1134.

tetrahydrocadinene, in contrast to cadinene itself, is not dehydrogenated by sulfur at 200° to 260°C. was established very early.³ It is interesting to note, however, that the perhydroazulenes can be dehydrogenated by sulfur and selenium.¹³³ *trans*-Decalin is only slightly attacked by selenium in the sealed tube at 350°C.,¹³⁴ and 2-methyldecalin at 320° to 350°C gives only a very small yield of dehydrogenation product.¹³⁵ This extraordinary resistance of perhydrogenated compounds to the chemical methods of dehydrogenation is probably related to the mechanism of the reactions.

VII. DEHYDROGENATION ACCOMPANIED BY CHANGE IN CARBON SKELETON

The behavior of *quaternary methyl groups* during dehydrogenation has been studied in detail, and is of decided interest, since a large number of natural products contain groups of this type. The fact that certain methyl groups can be eliminated by dehydrogenation was definitely established for the first time by Ruzicka and co-workers,^{3,6,7} who noted that sulfur dehydrogenation of the sesquiterpenes of the eudasmol series yielded eudalene. To explain this, it was pointed out that the position occupied in the original hydrogenated ring system by the methyl group does not exist in the corresponding aromatic structure. The methyl group is therefore split out, since it is a hindrance to the dehydrogenation. This assumption has subsequently been proved valid. The important point in this connection is that the quaternary group is almost always completely eliminated from the molecule, only in a few definite cases migrating to a neighboring carbon atom. This rule has been derived from the dehydrogenation results of a large number of natural products, particularly the sterols. Because of its importance, this regularity of behavior has also been thoroughly investigated with synthetic compounds. Ionene, for example, which contains two geminal methyl groups, gives 1,6-dimethylnaphthalene on dehydrogenation with sulfur or selenium.^{15,136} Similar results have been obtained from a number of other experiments, particularly those by Cook^{92,121,137,138} and Linstead.^{139,140}

The work of Zelinsky¹⁴¹⁻¹⁴³ gave some support to the original supposi-

¹³³ L. Ruzicka and Haagen-Smit, *Helv. Chim. Acta*, **14**, 1104-1122 (1931).

¹³⁴ L. Ruzicka and Seidel, *Helv. Chim. Acta*, **19**, 424-433 (1936).

¹³⁵ Barret, A. H. Cook, and Linstead, *J. Chem. Soc.*, **1935**, 1065-1069.

¹³⁶ Clemo and Dickenson, *J. Chem. Soc.*, **1935**, 735-738.

¹³⁷ J. W. Cook and Girard, *Nature*, **133**, 377-378 (1934).

¹³⁸ Bachmann, J. W. Cook, Hewett, and Iball, *J. Chem. Soc.*, **1936**, 54-61.

¹³⁹ Hibbit and Linstead, *J. Chem. Soc.*, **1936**, 470-476.

¹⁴⁰ Errington and Linstead, *J. Chem. Soc.*, **1938**, 666-672.

¹⁴¹ Zelinsky and Shuikin, *Ber.*, **62 B**, 2180-2186 (1929).

¹⁴² Zelinsky, *Ber.*, **56**, 1716-1718 (1923).

¹⁴³ Zelinsky, Packendorff, and Khokhlova, *Ber.*, **68 B**, 98-101 (1935).

tion that catalytic dehydrogenation is completely inhibited by the presence of quaternary methyl groups. More recent data do not confirm this opinion, but catalytic dehydrogenation does differ fairly markedly from the chemical methods in this respect.

Ruzicka and Waldmann¹⁴⁴ pointed out some time ago that retene is formed in excellent yield (85%) from both abietic acid and fichtelite¹⁴⁵ with palladium-charcoal. In both cases the gases evolved contain large amounts of methane. These results indicate that quaternary groups are no intrinsic hindrance to catalytic dehydrogenation.

The influence of quaternary groups on catalytic dehydrogenation was recently carefully studied by Linstead and co-workers.^{65,129,132} Octalins without quaternary methyl groups are rapidly disproportionated at the boiling point to tetralin and decalin, following which the tetralin is further dehydrogenated; the dehydrogenation of the completely saturated decalin, however, proceeds very slowly under these conditions. In the case of octalins substituted in the 9 position, the disproportionation is hindered; so these compounds are dehydrogenated only at higher temperatures, as high as those required for even the completely saturated decalins to react with a practical velocity (about 330°C.). No real difference seems to exist, however, between the dehydrogenation temperatures of decalins with or without quaternary methyl groups; the dehydrogenation of 9-methyldecalin proceeds somewhat more slowly and in somewhat poorer yield than does that of the unsubstituted compound.¹²⁹

It is of interest to note, however, that both decalin and 9-methyldecalin are dehydrogenated at lower temperature by the catalytic methods than by the use of selenium.

Selinene, which also contains a quaternary methyl group, is converted about one-third to eudalene, in addition to tetrahydroselinene, at a temperature as low as 205°C., but in a relatively slow reaction.⁶⁵ This is probably the first reported example of the splitting out of an angular methyl group by catalytic dehydrogenation at so low a temperature.

In contrast to the catalytic methods, the temperatures necessary for dehydrogenation by sulfur and selenium are increased only slightly by the presence of quaternary methyl groups. For example, ionene,¹⁵ the sesquiterpenes of the eudasmol group,³ and similar compounds have been dehydrogenated with sulfur at temperatures not greatly in excess of those required for the dehydrogenation of the cadalene derivatives.³ The yields of aromatic hydrocarbons were, to be sure, considerably lower in most cases, about 10% with ionene and eudasmol in contrast to 50 to 60% with

¹⁴⁴ L. Ruzicka and H. Waldmann, *Helv. Chim. Acta*, **16**, 842 (1933).

¹⁴⁵ L. Ruzicka and E. Waldmann, *Helv. Chim. Acta*, **18**, 611-612 (1935).

cadinene. Similar yields have also been obtained by dehydrogenation with selenium.¹⁴⁶ Perhydro compounds, however, usually differ from these partially unsaturated compounds; they are dehydrogenated with selenium only at temperatures above 350°C., whether they contain quaternary methyl groups or not. For example, cholestane,¹³⁰ perhydro-vitamin D₂,¹³⁰ and other completely saturated compounds^{136,147,148} are dehydrogenated only incompletely or not at all with selenium at temperatures up to 350°C. The failure of 1,1-dimethyltetralin to dehydrogenate with sulfur, and of 2,2-dimethyl- or 2,2-diethyltetralin with selenium,^{149,150} by heating under atmospheric pressure, can probably be attributed to the low boiling points of these compounds, since 2,2-dimethyltetrahydrophenanthrene readily gives 2-methylphenanthrene by reaction with selenium at 300° to 340°C.; also the dehydrogenation of the above tetralins can be readily accomplished at a temperature as low as 320°C. in the sealed tube.^{149,151} According to Barker and Clemo,¹⁵² 2-methylphenanthrene is obtained from 2-methyl-2-ethyl-1,2,3,4-tetrahydrophenanthrene by heating with selenium at 280° to 300°C. for 24 hours.

In the researches mentioned above,^{129,132} Linstead and co-workers made several fundamental new observations on the behavior of quaternary methyl groups during catalytic dehydrogenation. By the action of the majority of the platinum and palladium catalysts investigated, the angular methyl group of 9-methyldecalin is almost completely eliminated to form naphthalene, but small amounts of α -methylnaphthalene are always formed as a by-product. This migration seems to occur especially with platinum and palladium catalysts precipitated on asbestos. Attempts to investigate the mechanism of these reactions by means of experiments on dimethylated decalins and octalins have not yet yielded conclusive results.¹³² A similar migration also occurs in traces during the dehydrogenation of 1,1-dimethylnaphthalene, which gives some 1,2-dimethylnaphthalene in addition to 1-methylnaphthalene.

Aside from those cases which can be interpreted as retropinacoline rearrangements (see p. 26), this migration is probably the first definitely established exception to the rule that quaternary methyl groups are always completely eliminated. If it were possible to generalize the conditions necessary for migration, a means would be provided of fixing the position of

¹⁴⁶ Diels and Karstens, *Ber.*, **60** B, 2323-2325 (1927).

¹⁴⁷ C. K. Chuang, Y.-L. Tien, and C. M. Ma, *Ber.*, **69** B, 1494-1505 (1936).

¹⁴⁸ Clemo and Haworth, *J. Chem. Soc.*, 1930, 2579.

¹⁴⁹ Sen-Gupta, *Science and Culture*, **2**, 589 (1937); *Chem. Zentr.*, 1937, II, 2165.

¹⁵⁰ Clemo and Dickenson, *J. Chem. Soc.*, 1937, 255-257. Bogert, Davidson, and Apfelbaum, *J. Am. Chem. Soc.*, **56**, 959 (1934).

¹⁵¹ Sen-Gupta, *J. prakt. Chem.*, **151**, 82-96 (1938).

¹⁵² Barker and Clemo, *J. Chem. Soc.*, 1940, 1277-1279.

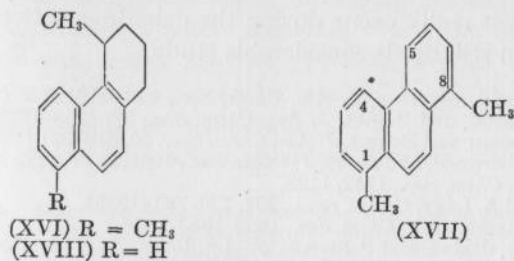
quaternary groups, with the help of specific catalysts which promote migration. Linstead and co-workers have reported on a similar but fruitless research on selinene.⁶⁵

The fact that no groups but quaternary methyl groups are split out or migrate during dehydrogenation is of absolutely fundamental importance in applying the method to the determination of constitution. This principle has been confirmed by experiment in the great majority of cases. Certain exceptions recorded in the literature are discussed below.

MIGRATION OF SIDE CHAINS. Mayer and Schiffner¹⁵³ have pointed out that α -alkylnaphthalenes are converted into β -alkylnaphthalenes in the presence of silica gel at about 420°C. In the case of α -phenylnaphthalene this migration occurs even at 350°C. Such rearrangements, which are independent of true dehydrogenation processes, might possibly be promoted by the material of the reaction vessel or by the catalyst carrier, effects which have occasionally been noticed during dehydrogenation. According to the results published so far, an α - β migration in naphthalene derivatives evidently does not occur during selenium dehydrogenation at temperatures below 350°C. Since for structural reasons this type of migration can take place only in one direction, it would be very worth while to have accurate data on the thermal stability of alkyl derivatives of phenanthrene, chrysene, picene, and the other aromatic hydrocarbons which commonly form the nuclei of dehydrogenation products.

This problem came up especially in connection with the rearrangements observed during the dehydrogenation of various phenanthrene derivatives.¹⁵⁴ For example, from the hydrocarbon XVI with selenium there were obtained mainly 1,8-dimethylphenanthrene (XVII) and only a small amount of the expected 1,5 isomer. In other cases, also, a migration of methyl groups from the 4 or 5 position to the 1 or 8 position, respectively, has occurred.

Neither 4- nor 1-methylphenanthrene could be isolated from the products of dehydrogenation of XVIII. In contrast to all these results, how-

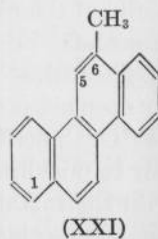
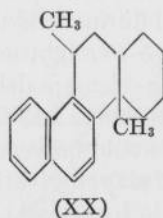
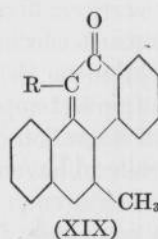


¹⁵³ Mayer and Schiffner, *Ber.*, **67** B, 67-69 (1934).

¹⁵⁴ Haworth, Mavin, and Sheldrick, *J. Chem. Soc.*, 1934, 454-461.

ever, Bachmann and Edgerton¹⁵⁵ were able to obtain 4-methylphenanthrene from XVIII by a very smooth reaction with palladium-charcoal at 300° to 320°C.; other phenanthrenes substituted in the 4 position are also readily prepared by dehydrogenation. Similar contradictions appear in the preparation of 1,4-dimethylphenanthrene^{91,156,157} and of 4-methylphenanthrene,^{77,158-160} in which, according to the method employed, different products are obtained.

Unexpected results have also been obtained in the chrysene series at various times. Thus, in the dehydrogenation of the ketone XIX (R = CH₃) and of the ketone XIX (R = H) with selenium, chrysene was the main product, along with small amounts of a monomethylchrysene.¹⁶¹ Fieser and co-workers¹⁶² obtained 6-methylchrysene in low yield from XX with selenium, instead of the expected 5 isomer.



However, Newman¹⁶³⁻¹⁶⁵ was able to prepare methylchrysene by a different method, which also employed a dehydrogenation as the final step. This, however, was achieved with sulfur at the comparatively low temperature of 250°C. Attempts have been made to explain the anomalous results as due to steric hindrance. The work on this phase of the question will not be discussed in any detail, but it may be mentioned that even 4,5-dimethylchrysene can be obtained as a reaction product by careful dehydrogenation with sulfur, without any indication of rearrangement or splitting off of methyl groups, although the yield is poor.¹⁶⁶ It is still very questionable, therefore, whether the rearrangements which have been noticed in monomethyl derivatives really occur during the dehydrogenation. This entire complex question still needs considerable study.

¹⁵⁵ Bachmann and Edgerton, *J. Am. Chem. Soc.*, **62**, 2219-2223 (1940).

¹⁵⁶ Akin, Stamatoff, and Bogert, *J. Am. Chem. Soc.*, **59**, 1268-1272 (1937).

¹⁵⁷ Papa, Perlmann, and Bogert, *J. Am. Chem. Soc.*, **60**, 319-321 (1938).

¹⁵⁸ Radcliffe, Sherwood, and Short, *J. Chem. Soc.*, 1931, 2293-2297.

¹⁵⁹ Haworth, *J. Chem. Soc.*, 1932, 1125.

¹⁶⁰ Darzens and A. Lévy, *Compt. rend.*, **201**, 730-733 (1935).

¹⁶¹ Jones and Ramadge, *J. Chem. Soc.*, 1938, 1853-1858.

¹⁶² L. F. Fieser, Joshel, and Seligman, *J. Am. Chem. Soc.*, **61**, 2134-2139 (1939).

¹⁶³ Newman, *J. Am. Chem. Soc.*, **62**, 870-874 (1940).

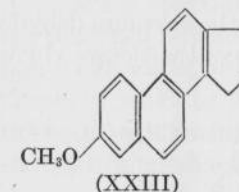
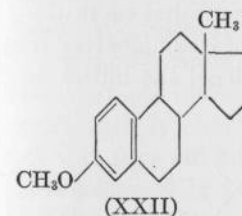
¹⁶⁴ See also L. F. Fieser and Joshel, *J. Am. Chem. Soc.*, **62**, 1211-1214 (1940).

¹⁶⁵ See also Bachmann and Edgerton, *J. Am. Chem. Soc.*, **62**, 2550-2553 (1940).

¹⁶⁶ Newman, *J. Am. Chem. Soc.*, **62**, 2295-2300 (1940).

Other rearrangements of methyl groups, such as that observed in the decomposition of alantolactone,¹⁶⁷ probably result from the thermal effects which precede and are independent of the dehydrogenation.

These isolated cases, for which the mechanism is still not completely understood, are quite different from migrations of alkyl groups which have the character of a retopinacoline rearrangement and which have already been mentioned (p. 26) in connection with the discussion of the behavior of secondary hydroxyl groups. The same type of rearrangement of quaternary methyl groups also occurs when other adjacent groups, such as long side chains, are eliminated. The best known and most accurately investigated example of this is the formation of γ -methylcyclopentenophenanthrene by the dehydrogenation of the sterols. In this case, certainly, the isooctyl side chain in first split off (an example of the thermal decomposition, independent of the dehydrogenation, which was observed some time ago¹⁶⁸), after which the methyl group in position 13 migrates to position 17 and thereby makes possible the dehydrogenation of Ring C.¹⁶⁹⁻¹⁷² This reaction mechanism is also supported by the fact that the compound XXII is converted into XXIII by dehydrogenation with selenium, with the elimination (not migration!) of the methyl group.¹³⁷ (See also the dehydrogenation of 8-methylhexahydroindane to indane.¹⁴⁰)



ELIMINATION OF SIDE CHAINS. There appear to be no well established examples of the elimination of non-quaternary methyl groups. A somewhat similar reaction, the simultaneous elimination of two geminal methyl groups, may have occurred in traces during the dehydrogenation of 1,1-dimethyltetralin with very active catalysts,¹³² but the behavior of longer non-quaternary side chains has not yet been worked out. It is very probable that long side chains can be retained in the molecule by careful dehydrogenation at moderate temperatures.

A number of dehydrogenation products have been reported which con-

¹⁶⁷ L. Ruzicka, Pieth, Reichstein, and Ehmann, *Helv. Chim. Acta*, **16**, 268 (1933).

¹⁶⁸ Fischer and Treibs, *Ann.*, **446**, 241 (1925).

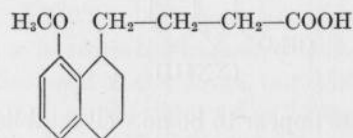
¹⁶⁹ J. W. Cook, *Chemistry and Industry*, **54**, 176 (1935).

¹⁷⁰ Bergmann, *Chemistry and Industry*, **54**, 175-176 (1935).

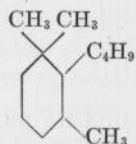
¹⁷¹ Rosenheim and King, *Chemistry and Industry*, **52**, 299-301 (1933).

¹⁷² Cohen, J. W. Cook, and Hewett, *J. Chem. Soc.*, 1935, 445-455.

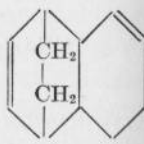
tain isopropyl, *n*-propyl, *t*-butyl,⁶⁶ and even heavier side chains.¹³⁰ For example, β -phenylethynaphthalene can be prepared from β -phenylethylocatalin.¹⁷³ On the other hand, there are numerous cases of the cleavage of such side chains, particularly at the relatively high temperatures of selenium dehydrogenation. This is the case, for example, in the dehydrogenation of the maleic anhydride adduct of vitamin D₂ (XII), which forms 2,3-dimethylnaphthalene with selenium, and β -naphthoic acid and naphthalene with palladium-charcoal; the side chain with Rings C and D is therefore completely eliminated.¹⁰⁶ The splitting off of butyric acid from XXIV with the formation of α -naphthol has also been reported.¹⁷⁴ A similar observation was made by Bergmann.¹⁷⁵ However, with selenium at 390° to 400°C., 1,1,3-trimethyl-2-*n*-butylcyclohexane (XXV) gives a mixture of *m*-xylene and 1,3-dimethyl-2-*n*-butylbenzene.¹³⁴ The reaction involves in part, therefore, the complete elimination of the butyl side chain, without a simultaneous migration of the quaternary methyl groups resulting. Dehydrogenation of the dimeric cyclohexadiene (XXVI) gives naphthalene.¹⁷⁶ In this case the thermal splitting off of ethylene is to be expected on the basis of other experiments; similar results were obtained with various derivatives of bicyclo[2.2.2]octane.¹⁷⁷ The splitting off of isopropyl groups, probably in the form of isopropylene, has also been observed.^{51,65} It has been suggested¹⁷⁸ that the presence of 1,6-dimethylnaphthalene in the product obtained from the selenium dehydrogenation of isozingiberene may be due to the cleavage of the isopropyl group of cadalene, the initial product of the reaction.



(XXIV)



(XXV)



(XXVI)

In all of the above examples, existing side chains are completely split out. In other cases, dehydrogenation reactions have been interpreted as taking place with only a partial elimination of the side chain, so that a methyl group is left behind. According to this, the formation of agathalene (XXVII) from agathenedicarboxylic acid (XXVIII) would be explained by fission at *a*¹¹⁰; and thus the methyl group in the 5 position of the agathalene

¹⁷³ J. W. Cook and Hewett, *J. Chem. Soc.*, 1934, 365-377.

¹⁷⁴ L. F. Fieser and Hershberg, *J. Am. Chem. Soc.*, 58, 2382-2385 (1936).

¹⁷⁵ Bergmann, *J. Am. Chem. Soc.*, 60, 1798-1799 (1938).

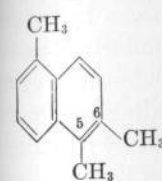
¹⁷⁶ F. Hofmann, *Chem.-Ztg.*, 57, 5-6 (1933).

¹⁷⁷ Kasansky and Plate, *Ber.*, 68 B, 1259-1264 (1935).

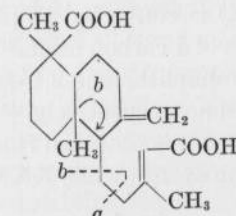
¹⁷⁸ Seidel, Müller, and Schinz, *Helv. Chim. Acta*, 27, 738-747 (1944).

molecule would be indicated as the place of attachment of the C₆ side chain. Except in the case of sclareol,^{179,180} a similar reaction mechanism has been adopted to explain the formation of the various methylated naphthalenes by the dehydrogenation of the pentacyclic triterpenes, in which case the breaking apart of the molecule at Ring C can be formally compared with the splitting off of side chains. (See Formula I, fission according to *a*; for corresponding formulations see the literature.^{43,47,49,181})

In a number of instances, however, the results can be explained just as well by assuming complete splitting out of the longer side chain or of the corresponding rings, with simultaneous migration of a neighboring quaternary methyl group (*e.g.*, scheme *b*, Formula XXVIII). This reaction is known from sterol chemistry (see the preceding section).



(XXVII)



(XXVIII)

Cleavage *a* with elimination of methyl group

Cleavage *b* with migration of methyl group

Since type experiments on synthetic materials containing long side chains are almost non-existent at the present time, it is impossible to decide which of these two mechanisms best describes the reaction, whether the side chains are preferentially eliminated completely or with the retention of a methyl group. It is possible that both processes can proceed simultaneously. A more accurate knowledge of this reaction mechanism would be valuable in interpreting the results of the dehydrogenation of many natural products. It would then perhaps be possible to obtain criteria for the presence of quaternary methyl groups, just as the formation of γ -methylclopentenophenanthrene points to the presence of a quaternary methyl group on C₁₃.

EXPANSION OF RINGS. Many of the familiar ring expansions can be formulated in a manner formally analogous to the migration of alkyl groups. The dehydrogenation results obtained with spiro compounds, especially, frequently have the nature of retropinacoline rearrangements. This applies, for example, to the formation of naphthalene from cyclopentanespirocyclohexanone.¹⁸² Of course, the dehydrogenation of hydrocarbons, such as

¹⁷⁹ L. Ruzicka and Janot, *Helv. Chim. Acta*, 14, 645 (1931).

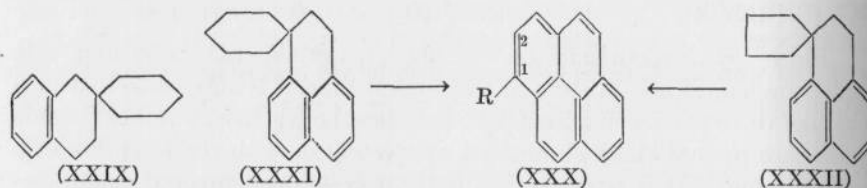
¹⁸⁰ L. Ruzicka, Engel, and Fischer, *Helv. Chim. Acta*, 21, 364-370 (1938).

¹⁸¹ L. Ruzicka, Furter, Pieth, and Schellenberg, *Helv. Chim. Acta*, 20, 1564-1570 (1937).

¹⁸² Clemo and Ormston, *J. Chem. Soc.*, 1933, 352-353.

cyclopentanespirocyclohexane, cannot be formulated as retropinacoline rearrangement, but in some cases it is possible that a rearrangement of this type has occurred during the preparation of the hydrocarbon. The dehydrogenation of spiro compounds has been thoroughly treated by Chatterjee and co-workers,¹⁸³⁻¹⁸⁵ in connection with synthetic work. According to Sen-Gupta, a small amount of anthracene is formed, in addition to a large quantity of phenanthrene, by the dehydrogenation of 1,2,3,4-tetrahydronaphthalene-3,1'-spirocyclopentane with selenium at 300° to 350°C.¹⁸⁶ This indicates that the reaction involves cleavage of a quaternary bond and ring closure of the resulting side chain.¹⁸⁷ This reaction takes place at a remarkably low temperature.

Sen-Gupta has reported also that 1,2,3,4-tetrahydronaphthalene-2,1'-spirocyclohexane (XXIX) is converted to phenanthrene by selenium dehydrogenation, with the loss of 1 carbon atom.^{188,189} Similarly, 7-methyl- and 7-ethyl-1,2,3,4-tetrahydronaphthalene-2,1'-spirocyclohexane give 3-methyl- and 3-ethylphenanthrene, respectively.¹⁸⁹ According to Cook and Hewett,¹⁷³ pyrene (XXX, R = H) is obtained from XXXI by a similar reaction, with the loss of 2 carbon atoms, while XXXII gives 1-methylpyrene (XXX, R = CH₃).



Catalytic dehydrogenation, also, can convert spiro compounds into fully condensed aromatic ring systems. Levitz and Bogert¹⁹⁰ obtained 9-methylphenanthrene from 4-methyl-1,2,3,4-tetrahydronaphthalene-1,1'-spirocyclopentane by heating with palladium-charcoal at 330° to 340°C. for 5 hours. Marvel and Brooks¹⁹¹ converted spirodecane and 3-methylspirodecane to naphthalene and 1-methylnaphthalene, respectively, with either palladium- or platinum-charcoal at a temperature of 325°C. Surprisingly, selenium at 330° to 350°C. did not dehydrogenate these spiranes, the starting material being recovered unchanged.

¹⁸³ Chatterjee, *J. Indian Chem. Soc.*, **14**, 259-263 (1937).

¹⁸⁴ Chatterjee, *J. Indian Chem. Soc.*, **13**, 536-541 (1936).

¹⁸⁵ Chatterjee, *J. Indian Chem. Soc.*, **13**, 588-592 (1936).

¹⁸⁶ Sen-Gupta, *J. Indian Chem. Soc.*, **11**, 389-394 (1934).

¹⁸⁷ See L. Ruzicka and Waldmann, *Helv. Chim. Acta*, **16**, 843, note 2 (1933).

¹⁸⁸ S. C. Sen-Gupta, *Science and Culture*, **3**, 57 (1937).

¹⁸⁹ S. C. Sen-Gupta, *J. Indian Chem. Soc.*, **19**, 467-472 (1942).

¹⁹⁰ Levitz and Bogert, *J. Org. Chem.*, **8**, 253-255 (1943).

¹⁹¹ Marvel and Brooks, *J. Am. Chem. Soc.*, **63**, 2630-2632 (1941).

Other work has been reported, however, in which spiranes have not undergone rearrangement and consequently have not been aromatized by dehydrogenation.^{91,92,118,192,193} No definite rules can be derived from the data published so far. Spiro compounds appear to be unaffected, particularly, by careful catalytic dehydrogenation¹⁴¹ and thus can be separated from isomers which are more readily attacked.

The ring enlargement to chrysene which results during the dehydrogenation of the sterols has been of great importance in determining the constitution of these compounds. This enlargement was first noticed by Diels and co-workers^{194,195} during the dehydrogenation of cholesterol with palladium-charcoal and of cholic acid with selenium.¹⁹⁶ Exhaustive experiments showed that this type of ring enlargement occurred only at temperatures above 400°C.^{197,198} Inasmuch as γ -methylcyclopentenophenanthrene¹⁹⁷ could not be definitely detected in the product when chrysene was present, it is probably safe to assume that the chrysene is formed from the γ -methylcyclopentenophenanthrene as a result of the high dehydrogenation temperature. Although it has not yet been possible to duplicate this reaction experimentally, somewhat similar experiments by Ruzicka and Peyer¹¹² have nevertheless led to interesting results. α -Methylindane gives a good yield of naphthalene, both with selenium and with palladium-charcoal, at about 450°C. Naphthalene is also formed from β -methyl-, from α - and β -ethyl-, and even from isooctylindane under these conditions. This investigation has shown that the dehydrogenation temperatures should not be permitted to go much above 350°C. if these secondary reactions are not desired. In general, such reactions could not be detected at temperatures below 350°C.¹⁹⁹

CONTRACTION OF RINGS. At temperatures of about 400°C., cycloheptane and cyclooctane derivatives undergo contraction of the ring. The conditions necessary for this reaction have been thoroughly investigated by experiments on type materials, especially by Ruzicka and Seidel.¹³⁴ Cycloheptane was converted to toluene by treatment with selenium at 440°C., and cyclooctane to *p*-xylene at 390° to 410°C. Alkyl derivatives of these hydrocarbons and cyclopentadecane were also studied. A uniform reaction scheme could not be set up; however, the cycloheptane ring is aromatized with selenium even under conditions not much more vigorous than those

¹⁹² Bogert, *Science*, **84**, 44-45 (1936).

¹⁹³ Perlmann, Davidson, and Bogert, *J. Org. Chem.*, **1**, 300-304 (1936).

¹⁹⁴ Diels and Gädke, *Ber.*, **58 B**, 1231 (1925).

¹⁹⁵ Diels and Gädke, *Ber.*, **60 B**, 140-147 (1927).

¹⁹⁶ Diels and Karstens, *Ann.*, **478**, 129 (1930).

¹⁹⁷ L. Ruzicka, Thomann, Brandenburg, Furter, and Goldberg, *Helv. Chim. Acta*, **17**, 200-221 (1934).

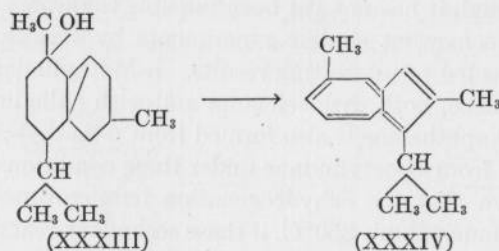
¹⁹⁸ L. Ruzicka and Goldberg, *Helv. Chim. Acta*, **20**, 1245-1253 (1937).

¹⁹⁹ See, however, Nenitzescu and Cioranescu, *Ber.*, **69 B**, 1040-1041 (1936).

necessary for the conversion of decalin to naphthalene. Ruzicka and Seidel¹³⁴ also briefly discuss earlier experiments by Zelinsky and co-workers.¹²³

The catalytic dehydrogenation and isomerization of methylcycloheptane with platinized carbon at 305° to 310°C. is reported by Turóva-Pollak and Rappoport.²⁰⁰ In six passes over the catalyst, a 94% yield is obtained of an aromatic product consisting mainly of *p*-xylene, with traces of the meta isomer.

CLEAVAGE OF RINGS. In addition to ring enlargements and ring contractions, the cleavage of rings and the formation of new rings are also frequently observed during dehydrogenation. The cleavage of three-membered rings in polycyclic systems occurs very readily when the dehydrogenation to aromatic products is made possible by that means. One example of this which has been known for a long time is the formation of cadalene from the tricyclic sesquiterpene copaene,²⁰¹ which is readily converted even by treatment with hydrochloric acid into the bicyclic cadinene dihydrochloride.



More recently, the analogous formation of azulenes from tricyclic sesquiterpenes has been observed. Komppa²⁰² found that both cadalene and an azulene result from ledol or ledene on dehydrogenation. This reaction has been formulated, as shown in Formulas XXXIII and XXXIV, by Komppa and Nyman.²⁰³

According to Radcliffe and Short,²⁰⁴ the formation of guaiazulene from aromadendrene may proceed in an analogous manner. It is surprising that in these cases the ring disintegration which produces azulenes appears to take preference over the equally possible formation of naphthalenes. The primary process in these reactions is probably the thermal cleavage of a ring structure, resulting in the formation of unsaturated derivatives. If

²⁰⁰ Turóva-Pollak and Rappoport, *J. Gen. Chem. (U. S. S. R.)*, **13**, 353-357 (1943).

²⁰¹ Henderson, McNab, and Robertson, *J. Chem. Soc.*, **1926**, 3077.

²⁰² Komppa, *Kgl. Norske Videnskab. Selskabs, Skrifter*, **1933**, No. 1, 16 pp.; *Chem. Abstracts*, **28**, 4724 (1934).

²⁰³ Komppa and Nyman, *Compt. rend. trav. lab. Carlsberg, Sér. chim.*, **22**, 272-274 (1938); *Chem. Abstracts*, **32**, 6234 (1938).

²⁰⁴ Radcliffe and Short, *J. Chem. Soc.*, **1938**, 1200-1203.

these have a suitable structure, they are then dehydrogenated. Aside from the cases just mentioned, however, such phenomena are very rare in dehydrogenations with sulfur and selenium. The tricyclic sesquiterpenes, for example, in general give either none at all or only traces of aromatic dehydrogenation products.^{1,205}

The use of catalytic dehydrogenation, on the other hand, enabled Zelinsky and co-workers to conduct a thorough investigation into the behavior of various ring systems. Their first experiments show that five membered rings are not attacked by metallic catalysts. Certain exceptions, such as cyclohexylmethylcyclopentane²⁰⁶ and dicyclopentyl,²⁰⁷ which yield diphenyl and naphthalene, respectively, could be ascribed to the fact that the hydrogenated hydrocarbons are well suited to become the carbon skeleton of the dehydrogenation product.^{207,208} Catalytic dehydrogenation therefore gives consistent results and has been very valuable in explaining the rearrangements which take place during the preparation of the hydrogenated compounds.

In the course of such investigations, the dehydrogenation of a number of members of a series of bicyclic systems, such as bicyclo[1.2.2]heptanes,²⁰⁹ bicyclo[2.2.2]octanes,^{176,177} bicyclo[0.3.3]octanes,²¹⁰ and bicyclo[1.3.3]nonanes,¹³⁰ has been studied. Of these compounds, the bicyclo[2.2.2]octanes are dehydrogenated relatively easily, since they can decompose into a cyclohexane and an ethylene derivative in accordance with a familiar reaction.^{211,212}

Elagina and Zelinsky²¹³ dehydrogenated 2,3-benzobicyclo[3.3.1]-2-nonene over platinized charcoal at 300°C. With a moderately active catalyst, diphenylmethane is the main product; with a more active platinized charcoal, increasing amounts of fluorene are found in the product.

The catalytic dehydrogenation of bicyclic terpenes of the carane, pinane, and thujane types has also been investigated.^{65,214-216} In some cases *p*-cymene was obtained. In others, breaking up of one of the rings occurred, with the formation of cyclopentane derivatives which resisted further dehydrogenation.

²⁰⁵ L. Ruzicka and Stoll, *Helv. Chim. Acta*, **6**, 846 (1923).

²⁰⁶ Zelinsky, *Ber.*, **58 B**, 2755-2763 (1925).

²⁰⁷ Zelinsky, Titz, and Fataiev, *Ber.*, **59 B**, 2580 (1926).

²⁰⁸ Zelinsky and Titz, *Ber.*, **64 B**, 183-188 (1931).

²⁰⁹ Zelinsky, Kasansky, and Plate, *Ber.*, **66 B**, 1415 (1933).

²¹⁰ Barrett and Linstead, *J. Chem. Soc.*, **1936**, 611-616.

²¹¹ Diels, Alder, and Stein, *Ber.*, **62 B**, 2337-2372 (1929).

²¹² Alder and Rickert, *Ann.*, **524**, 180-189 (1936); *Ber.*, **70 B**, 1354-1363, 1364-1369 (1937).

²¹³ Elagina and Zelinsky, *Compt. rend. acad. sci. U. R. S. S.*, **30**, 726-727 (1941).

²¹⁴ Zelinsky and Levina, *Ann.*, **476**, 60-70 (1929).

²¹⁵ Zelinsky and Kasansky, *Ber.*, **60 B**, 1096-1100 (1927).

²¹⁶ Zelinsky, *Ber.*, **58 B**, 864-869 (1925).

The passivity of cyclopentane derivatives^{210,217,218} has been quite generally confirmed, but further research has shown that they are not completely resistant. Cyclopentane itself, for example, is hydrogenated to *n*-pentane in a hydrogen atmosphere over platinized charcoal even at 300°C.;²⁰⁹ other compounds behave similarly.²¹⁹⁻²²²

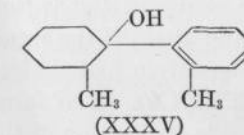
Under certain conditions, these aliphatic compounds can be again cyclicized to cyclohexane derivatives, which in turn can be dehydrogenated.²²³ This reaction mechanism is supported by the fact that under similar conditions aliphatic compounds also yield small amounts of aromatic dehydrogenation products. For example, *p*-xylene is formed from diisobutyl, and *m*-cymene from diisooamyl.^{223,224}

These observations detract little from the diagnostic value of catalytic dehydrogenation, however, since there is a marked difference between normal dehydrogenations and the phenomena described above, especially in the yields.

FORMATION OF NEW RINGS. The formation of new rings by the dehydrogenation reactions mentioned above is not unique. In addition to the conversion of the monocyclic zingiberene into a naphthalene derivative, numerous ring closures have been observed in dehydrogenations by both the chemical and the catalytic methods. Examples of these are the formation of fluorene from dicyclohexylmethane,^{213,225,226} from diphenylmethane,^{213,225,226} and from benzophenone, the formation of phenanthrene from cyclohexylcycloheptylmethane,²²⁷ from diphenylethane,^{116,225} and from stilbene.^{116,225} This last reaction, according to Dewar and Read,²²⁸ can be accomplished only with a palladium-charcoal catalyst prepared by Zelinsky's procedure; other platinum- and palladium-charcoals produce no cyclization. Berger obtained phenanthrene from di-*o*-tolyl with sulfur, at temperatures as low as 250°C.²²⁹; selenium did not cause ring formation. On the other hand, it has been reported elsewhere⁷⁶ that by the use of 2 moles of sulfur at 180° to 250°C. the compound XXXV is converted smoothly to di-*o*-tolyl, which gives phenanthrene only by distilling in the

- ²¹⁷ Zelinsky, Mikhlin, and Eventova, *Ber.*, **66 B**, 1422 (1933).
²¹⁸ Denisenko, *Ber.*, **69 B**, 2183-2187 (1936).
²¹⁹ Zelinsky, Kasansky, and Plate, *Ber.*, **68 B**, 1869-1872 (1935).
²²⁰ Zelinsky and Shuikin, *Compt. rend. acad. sci. U. R. S. S.*, **3**, 255-257 (1934).
²²¹ Denisenko, *Ber.*, **69 B**, 1668-1670 (1936).
²²² Zelinsky and Shakhnazarova, *Bull. acad. sci. U. R. S. S., Classe sci. math. nat., Sér. chim.*, **1936**, 571-574; *Chem. Abstracts*, **31**, 6621 (1937).
²²³ Kasansky and Plate, *Ber.*, **69 B**, 1862-1869 (1936).
²²⁴ Kasansky and Plate, *J. Gen. Chem. (U. S. S. R.)*, **9**, 496-502 (1939).
²²⁵ Zelinsky, Titz, and Gaverdovskaia, *Ber.*, **59 B**, 2590 (1926).
²²⁶ See also Zelinsky and Gaverdovskaia, *Ber.*, **61 B**, 1049-1053 (1928).
²²⁷ Elagina and Zelinsky, *Compt. rend. acad. sci. U. R. S. S.*, **30**, 728-731 (1941).
²²⁸ Dewar and Read, *J. Soc. Chem. Ind.*, **55**, 347-349T (1936).
²²⁹ Berger, *J. prakt. Chem.*, **133**, 331 (1932).

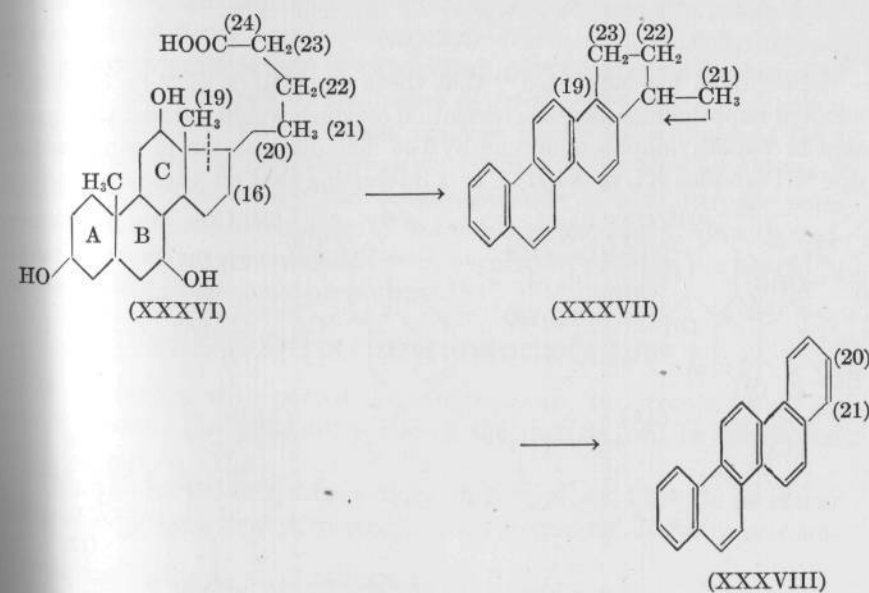
presence of sulfur. In further contrast to these results, Orchin obtained 4-methylfluorene from di-*o*-tolyl²³⁰ and fluorene from 2-methyldiphenyl²³¹



by dehydrogenation with palladium-charcoal at 450°C. Naphthalene has been obtained from 1,2-diethyl-1-cyclohexene by the use of selenium under very vigorous conditions, heating in a sealed tube at 410° to 420°C.¹¹² Such side reactions can probably be prevented, however, by careful procedure.

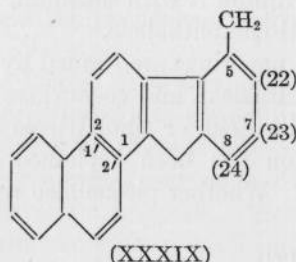
Of a somewhat different type is the ring closure which took place during the dehydrogenation of vitamin A with selenium,²³² and which resulted in the formation of 1,6-dimethylnaphthalene.

In a similar manner, new rings are formed by the dehydrogenation of sterols and gallic acids. Ruzicka and co-workers obtained picene by the dehydrogenation of cholic acid or cholatrienic acid with selenium at 360°C.^{40,233} This reaction has been explained according to Formulas XXXVI to XXXVIII.¹⁹⁷ Whether picene also results from the dehydro-

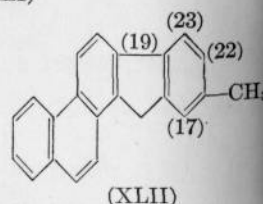
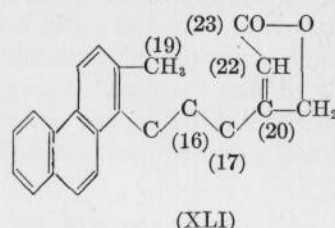
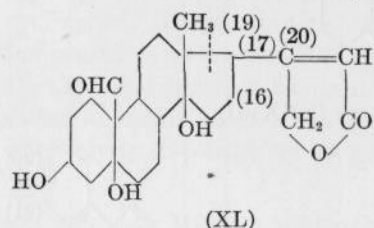


- ²³⁰ Orchin and Woolfolk, *J. Am. Chem. Soc.*, **67**, 122-124 (1945).
²³¹ Orchin, *J. Am. Chem. Soc.*, **67**, 499 (1945).
²³² Heilbron, Morton, and Webster, *Biochem. J.*, **26**, 1194 (1932).
²³³ L. Ruzicka and Thomann, *Helv. Chim. Acta*, **16**, 216 (1933).

genation of cholesterol and other sterols has apparently not been established. On the other hand, a different type of cyclization was discovered in connection with both cholic acid and the various sterols. According to Bachmann, Cook, Hewett, and Iball,¹³⁸ the product obtained from cholic acid by this type of dehydrogenation had the constitution of a 5-methyl-2',1'-naphtho-1,2-fluorene (XXXIX). The formation of this product is possibly explained by the simple cyclization of the side chain with the carbon atom in position 16 in the sterol skeleton. The hydrocarbons obtained by the analogous dehydrogenation of cholesterol, ergosterol, and the phytosterols,^{198,234} which should have a substituent in the 8 position on the basis of this reaction mechanism, do not possess the expected constitution,¹³⁸ although from their absorption spectra¹⁹⁷ they probably contain the naphthofluorene nucleus.



Bergmann has suggested²³⁵ that these compounds may be 5,7-disubstituted naphthofluorenes, the formation of which would parallel the formation of 7-methylnaphthofluorene by the dehydrogenation of strophanthidin²³⁶ (Formulas XL to XLII). It is interesting that all these cyclizations



²³⁴ Diels, Gädke, and Körding, *Ann.*, **459**, 1 (1927).

²³⁵ Bergmann, *J. Am. Chem. Soc.*, **60**, 2306-2307 (1938).

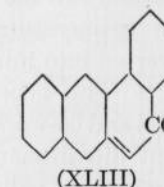
²³⁶ Elderfield and Jacobs, *J. Biol. Chem.*, **107**, 143-154 (1934).

take place at lower temperatures than does the well known formation of chrysene.

The type of cyclization which results from the dehydrogenation of the monocyclic sesquiterpene alcohols with selenium or sulfur, and which leads to eudalene,²³⁷ is still not entirely explained.

OTHER REARRANGEMENTS. In conclusion, brief mention should be made of several isolated and so far unexplained rearrangements which have been observed in various dehydrogenation reactions.

Examples of these are the formation of phenanthrene (with sulfur) from a hydrocarbon which is considered to be 1-cyclopentylindane,²³⁸ and the formation of chrysene from the compound XLIII (with platinum black at 300° to 320°C.).²³⁹ In both cases accurate data are lacking.



Also, it is still unexplained why the homogeneous sesquiterpene alcohol guaial yields a different azulene when selenium is used for the dehydrogenation than when sulfur is used.¹³³ This result may be due to a displacement of an alkyl group caused by the higher reaction temperature of selenium dehydrogenation.²⁴⁰ Two different azulenes may also be obtained from ledol by similarly varying the reaction conditions.²⁴¹ The formation of naphthalene derivatives by the dehydrogenation of sesquiterpene compounds with an azulene structure²⁴² has not been thoroughly investigated. Similar rearrangements occur, however, even when azulenes are heated in the absence of dehydrogenation reagents.²⁴⁰

VIII. PARTIAL DEHYDROGENATION

In connection with partial dehydrogenations, two points which especially concern the preparative use of the method will be mentioned briefly.

Although partial dehydrogenations, in general, are likely to be rather undesirable for analytical purposes, they are frequently useful in prepara-

²³⁷ L. Ruzicka and van Veen, *Ann.*, **476**, 70-112 (1929).

²³⁸ R. Robinson, *J. Chem. Soc.*, **1936**, 80.

²³⁹ J. W. Cook and Lawrence, *J. Chem. Soc.*, **1937**, 817-827.

²⁴⁰ Unpublished researches of the author.

²⁴¹ Nyman and Mikander, *Suomen Kemistilehti*, **14 B**, 3-4 (1941); *Chem. Abstracts*, **35**, 4755 (1941).

²⁴² Pfau and Plattner, *Helv. Chim. Acta*, **23**, 768-792 (1940).

tive work. Sulfur, used in proportionately smaller amount, or perhaps the catalytic method, is probably preferable to selenium for this work.

Von Braun and Irmisch²⁴³ were able to obtain octahydrochrysene from dodecahydrochrysene by the use of 2 atoms of sulfur. Dimeric cyclohexadiene can be converted into a tetralin with a methylene bridge.²⁴⁴ Several examples of partial dehydrogenation are to be found in the work of Cook and co-workers.^{118,173,244} One of the best examples of this type of reaction is the partial dehydrogenation of neoergosterol, carried out by Honigmann⁵³ (Formulas VI and VII).

IX. DISPROPORTIONATION

The so called disproportionations are of particular importance, especially in catalytic dehydrogenation. In the presence of platinum metal catalysts, even at relatively low temperatures, unsaturated compounds, such as cyclohexadiene, are converted into mixtures of aromatic and completely saturated hydrocarbons.²⁴⁵ This type of reaction seems to have been first observed by Knoevenagel and co-workers.²⁴⁶

Wieland²⁴⁷ later showed that dihydronaphthalene is converted into naphthalene and tetralin in the presence of palladium black, with the evolution of heat. These reactions are completely understandable from the standpoint of the thermodynamic relationships, as Böeseken,²⁴⁸ for example, has shown. A most thorough study of these disproportionations has been made by Zelinsky and by Linstead and co-workers. In the course of their investigations they surveyed cyclohexene,²⁴⁵ various methylcyclohexenes,²⁴⁹ terpenes, such as limonene^{65,250} and α -pinene,^{65,216} and also compounds with unsaturated side chains.^{116,117} The work of Linstead especially^{64,65,129,132} shows that disproportionations play an extremely important role in catalytic dehydrogenation.

In this connection it is interesting to note that the dehydrogenation tendency of tetralin can be utilized for the hydrogenation of a variety of unsaturated compounds,²⁵¹⁻²⁵³ corresponding to a disproportionation reaction between dissimilar molecules. Benzene has also been used as a hydrogen acceptor in catalytic dehydrogenation.²⁵⁴

²⁴³ von Braun and Irmisch, *Ber.*, **65** B, 883 (1932).

²⁴⁴ J. W. Cook and Haslewood, *J. Chem. Soc.*, 1934, 428-433.

²⁴⁵ Zelinsky and Pavlov, *Ber.*, **66** B, 1420 (1933).

²⁴⁶ Knoevenagel and Heckel, *Ber.*, **36**, 2816-2822 (1903); Knoevenagel and Fuchs, *ibid.*, 2848-2857; Knoevenagel and Bergdolt, *ibid.*, 2857-2861.

²⁴⁷ Wieland, *Ber.*, **45**, 484 (1912).

²⁴⁸ Böeseken, *Rec. trav. chim.*, **37**, 255 (1918).

²⁴⁹ Zelinsky, *Ber.*, **57** B, 2055 (1924).

²⁵⁰ Zelinsky, *Ber.*, **57** B, 2058-2059 (1924).

²⁵¹ Akabori and Suzuki, *Proc. Imp. Acad. Tokyo*, **5**, 255-256 (1929).

²⁵² See also Kindler and Peschke, *Ann.*, **501**, 191 (1933).

²⁵³ Orchin, *J. Am. Chem. Soc.*, **66**, 535-538 (1944).

²⁵⁴ Adkins, Richards, and Davis, *J. Am. Chem. Soc.*, **63**, 1320-1325 (1941).

Similar dismutations¹²¹ can take place during chemical dehydrogenation and have been discussed in the section on hydrogenation effects. For this reason, it is understandable that completely saturated compounds are often obtained in addition to the aromatic dehydrogenation products. As a matter of fact, the removal of the calculated amount of hydrogen is seldom achieved in catalytic dehydrogenation. However, the yields of aromatic products obtained by disproportionation are usually sufficient to identify the *dehydrogenation products*, even with reactions in the sealed tube, where hydrogenation is certain to occur to a considerable extent.

An interesting example of disproportionation is the isomerization of 2,6-dibenzalcylohexanone to 2,6-dibenzylphenol by palladium-charcoal at 235° to 245°C.²⁵⁵

X. HETEROCYCLIC COMPOUNDS

So far, the discussion has been confined almost exclusively to the dehydrogenation of isocyclic compounds. Recently, the various methods of dehydrogenation, particularly the catalytic methods, have also been applied successfully to heterocyclic compounds, of which those containing nitrogen have been fairly thoroughly investigated. The behavior of piperidine in reactions over platinum and palladium catalysts has been described in detail.²⁵⁶ Pyrrolidine^{257,258} and its derivatives²⁵⁹⁻²⁶¹ can be readily dehydrogenated to pyrroles. In like manner, nicotine is rapidly converted into nicotyrine.^{262,263} Sulfur has also been used for this last dehydrogenation, although the yields are very unsatisfactory.²⁶⁴ Decahydroquinoline^{265,266} and decahydroisoquinoline^{267,268} are dehydrogenated very readily. In this connection it is interesting to note that 5,6,7,8-tetrahydroquinoline can be obtained²⁶⁵ by the partial dehydrogenation of decahydroquinoline, indicating that the ring containing the nitrogen atom exhibits the greater dehydrogenation tendency. This procedure is very valuable from the preparative standpoint, since only 1,2,3,4-tetrahydroquinoline can be obtained by the hydrogenation of quinoline. 2-Alkylimidazolines are de-

²⁵⁵ Horning, *J. Org. Chem.*, **10**, 263-266 (1945).

²⁵⁶ Zelinsky and Borisov, *Ber.*, **57** B, 150 (1924).

²⁵⁷ Zelinsky and Yur'ev, *Ber.*, **64** B, 101 (1931).

²⁵⁸ Wibaut, Molster, Kauffmann, and Lenssen, *Rec. trav. chim.*, **49**, 1127-1130 (1930).

²⁵⁹ Zelinsky and Yur'ev, *Ber.*, **62** B, 2589-2590 (1929).

²⁶⁰ Ehrenstein, *Ber.*, **64** B, 1137 (1931).

²⁶¹ Yur'ev and Shen'yan, *J. Gen. Chem. (U. S. S. R.)*, **4**, 1258-1261 (1934).

²⁶² Wibaut and Overhoff, *Rec. trav. chim.*, **47**, 935-939 (1928).

²⁶³ Frank, Holley, and Wikholm, *J. Am. Chem. Soc.*, **64**, 2835-2838 (1942).

²⁶⁴ Morton and Horvitz, *J. Am. Chem. Soc.*, **57**, 1860-1861 (1935).

²⁶⁵ Ehrenstein and Bunge, *Ber.*, **67** B, 1715-1729 (1934).

²⁶⁶ Yur'ev and Mironenko, *Sci. Repts. Moscow State Univ.*, 1936, No. 6, 277-279; *Chem. Zentr.*, 1937, II, 2356.

²⁶⁷ Späth and Polger, *Monatsh.*, **51**, 190-204 (1929).

²⁶⁸ Späth, Berger, and Kuntara, *Ber.*, **63** B, 134 (1930).

hydrogenated to the corresponding imidazoles by various metallic catalysts including platinum and palladium.²⁶⁹

In other cases the breaking up of rings, ring closures, and rearrangements result.^{225,270} Prelog and co-workers^{271,272} have reported a rearrangement which occurs in the dehydrogenation of 3-acetylpyridine derivatives with selenium at 300°C. The corresponding 2,3-dimethylpyridine is obtained instead of the expected 3-ethylpyridine. The same author has also investigated the dehydrogenation of some azabicycloparaffins with selenium or palladium-charcoal at 350°C.²⁷³ 1-Azabicyclo[2.2.1]heptane gave γ -picoline, 1-azabicyclo[2.2.2]octane gave 4-ethylpyridine, and 1-azabicyclo[2.2.0]decane yielded a small amount of quinoline.

Späth and co-workers have applied catalytic dehydrogenation with great success to their researches on alkaloids.²⁷⁴

A number of experiments on heterocyclic substances containing oxygen and sulfur have also been published. Dihydrocoumarins can be dehydrogenated to coumarins,²⁷⁵ hydrofuranes to furanes, and tetrahydrothiophene to thiophene.^{276,277}

XI. SECONDARY REACTIONS

In the foregoing discussion, in general only those examples of dehydrogenation reactions which yielded aromatic dehydrogenation products have been considered. Various interferences can also take place, especially by the action of sulfur on organic compounds, and in many cases result in a greatly lowered yield of the normal dehydrogenation products. A compilation of the older literature on this subject is found in the frequently cited treatise by Ruzicka.²⁷⁸ A product containing sulfur has been isolated from the dehydrogenation of elemol,²³⁷ to mention one of the more recent observations. Fieser has reported a similar experience.²⁷⁹ Since the presence of these by-products does not greatly increase the difficulty of working up the aromatic hydrocarbon, however, the scope of the dehydrogenation is not greatly changed.

Selenium is less readily introduced into organic molecules,²³ which probably accounts for the general applicability of this reagent.

²⁶⁹ Gränacher and J. Meyer, German Patent, 703,899, Feb. 13, 1941; *Chem. Abstracts*, **36**, 1045 (1942).

²⁷⁰ Ehrenstein and Marggraff, *Ber.*, **67** B, 486-491 (1934).

²⁷¹ Prelog, Komzak, and Moor, *Helv. Chim. Acta*, **25**, 1654-1664 (1942).

²⁷² Prelog, Moor, and Führer, *Helv. Chim. Acta*, **26**, 846-848 (1943).

²⁷³ Prelog and Balenovic, *Ber.*, **74** B, 1508-1510 (1941).

²⁷⁴ See the summary by Späth and Galinovsky, *Ber.*, **69** B, 2059-2061 (1936).

²⁷⁵ Späth and Galinovsky, *Ber.*, **70** B, 235-238 (1937).

²⁷⁶ Yur'ev and Borisov, *J. Gen. Chem. (U. S. S. R.)*, **7**, 138 (1937).

²⁷⁷ Yur'ev and Borisov, *Ber.*, **69** B, 1395-1398 (1936).

²⁷⁸ See p. 12 of Ruzicka's report (footnote 1).

²⁷⁹ L. F. Fieser, *J. Am. Chem. Soc.*, **55**, 4977-4984 (1933).

XII. DEHYDROGENATION TECHNIQUES

1. Sulfur

The original procedure described by Ruzicka and co-workers^{1,3} is still employed, as a rule, for dehydrogenations with sulfur. The exact, calculated amount of sulfur is always used; an excess should be avoided because of the danger of secondary reactions. The evolution of hydrogen sulfide usually begins at about 180°C. and is complete in a few hours. Rapid temperature increase at the start of the reaction should be avoided, since there is danger of frothing over, especially with large runs. Toward the end of the reaction, the temperature may, if necessary, be raised to approximately 260°C., although prolonged heating at higher temperatures in the presence of unchanged sulfur should be avoided. A temperature of 200° to 220°C. can be regarded as normal. In many cases it has proved useful to carry out the dehydrogenation under a slight vacuum.²⁸⁰

The first step in the working up of the reaction mixture is almost always a direct vacuum distillation of all the volatile material. The distillate usually contains some sulfur. It is not advisable, however, to attempt to remove sulfur by distillation over sodium, since part of the aromatic hydrocarbon is also destroyed by this procedure. Usually after a second distillation, the separate fractions are sufficiently pure for preparing the picrate or trinitrobenzene derivative, or for other means of identification.

2. Selenium

The material to be dehydrogenated is heated with the calculated amount of amorphous or crystalline powdered selenium¹⁴⁶ in a flask with a sealed-on reflux condenser. The use of an excess of selenium is not generally detrimental. The evolution of hydrogen selenide begins at about 250° to 280°C., and can readily be followed by the progressive coloration in a tower of bleaching powder. The temperature, which should always be closely controlled by use of a metal bath, is slowly raised as necessary. Temperatures up to 350°C. can be considered safe. Experience has shown that much above this limit, various rearrangements may be expected. In general, dehydrogenations with selenium appear to proceed much more slowly than those with sulfur, and often very long reaction times are employed (20 to 100 hours). It must be remembered, however, that too long heating at high temperature may cause unnecessary decomposition of the reaction products. For example, according to Nagel and Körnchen,²⁸¹ 12 hours of heating at 280° to 305°C. are the best conditions for

²⁸⁰ Melville, *J. Am. Chem. Soc.*, **55**, 2462-2465 (1933).

²⁸¹ Nagel and Körnchen, *Chem. Umschau Fette, Öle, Wachse, Harze*, **39**, 1 (1932).

the preparation of retene from rosin oil. In many other cases, still shorter reaction times suffice.

For working with fairly volatile materials or with very small amounts, dehydrogenation with selenium in the sealed tube has proved very satisfactory.^{56,112,134} After the reaction is complete, the mixture is usually extracted with ether or benzene, and the residue from the evaporation of the extracts is then fractionated and further worked up.

3. Catalytic Methods

Experience has shown that the method of preparation of dehydrogenation catalysts greatly influences their activity and in many cases also their effect on the organic compounds. Zelinsky and co-workers,^{18,256,282,283} in particular, have made a systematic study of this subject. On the basis of their results, the use of palladium-charcoal has come into considerable favor. Precise directions for the preparation of dehydrogenation catalysts have been given by Zelinsky and Turova-Pollak,¹⁸ Diels and Gädke,¹⁹⁴ and Packendorff and Leder-Packendorff,²⁸⁴ among others. Recently, Linstead and co-workers compared the activities of catalysts prepared in different ways, under conditions which are readily adaptable to practical requirements.^{129,132} They arrived at the following conclusions.

1. Very active catalysts result from the method of Willstätter and Waldschmidt-Leitz,²⁸⁵ but somewhat higher activity and better reproducibility are obtained if the metal is precipitated in slightly higher dilution.
2. Platinum and palladium catalysts prepared under the same conditions have very similar activity. Palladium seems to be somewhat more inclined to cause side reactions.
3. The activity of both these metals is very dependent on the nature of the carrier and decreases in the following order: metal on activated charcoal > metal on asbestos > metal as "black."
4. The course of the dehydrogenation of substances with quaternary, cyclic carbon atoms is strongly influenced by the catalyst carrier, but not by the choice of the metal.

Apparatus for catalytic dehydrogenation in the vapor phase has been described at various times.^{24,286,287} In the determination of constitution, however, the use of relatively simple apparatus is preferable, and dehydrogenation in the liquid phase has been tried by simply heating the com-

²⁸² Zelinsky, *Ber.*, **59** B, 156-162 (1926).

²⁸³ Zelinsky and Pavlov, *Ber.*, **56** B, 1250 (1923).

²⁸⁴ Packendorff and Leder-Packendorff, *Ber.*, **67** B, 1388-1391 (1934).

²⁸⁵ Willstätter and Waldschmidt-Leitz, *Ber.*, **54**, 123 (1921).

²⁸⁶ See, for example, L. Ruzicka and Stoll, *Helv. Chim. Acta*, **7**, 84 (1924).

²⁸⁷ Levitz and Bogert, *J. Am. Chem. Soc.*, **64**, 1719-1720 (1942).

ound in the presence of the catalyst.^{194,288} Since in general the main requirement is only that the temperature necessary for dehydrogenation be attained, this simple procedure can give good results for all substances that boil at 300°C. or higher under atmospheric pressure. It is of practical importance that a number of the more volatile compounds, such as terpenes and sesquiterpenes, can also be treated in this manner, because at their boiling point they are dehydrogenated or disproportionated to aromatic compounds.⁶⁵ These disproportionations can be carried out with good results in the sealed tube, a procedure which is especially recommended for very small amounts of material.

The temperature and duration of catalytic dehydrogenation naturally vary within wide limits. As a matter of information, tetralin has been smoothly dehydrogenated at temperatures as low as 180°C., but decalin and 9-methyldecalin only at 300° to 350°C.^{129,132} At temperatures much in excess of 350°C., many secondary reactions may be expected.

For dehydrogenations in the liquid phase, palladium-charcoal in the amount of 10 to 50% of the weight of the material is commonly used; the catalyst in turn usually contains 10 to 30% of the metal. Because of the relatively high price of the platinum metals, it is important that they can be regenerated from the spent catalyst and used again without detriment. According to Linstead,¹³² the method of Baldeschwiler and Mikeska²⁸⁹ gives good results for the recovery of platinum, and that of Keiser and Breed²⁹⁰ for palladium.

4. Solvents

Occasionally, dehydrogenations with sulfur and selenium, especially those used for preparations, have been carried out in the presence of solvents such as naphthalene,⁵⁵ quinoline,^{291,292} and acetanilide.²⁹³ A series of other solvents was investigated by Morton and Horvitz²⁶⁴ in connection with the dehydrogenation of nicotine with sulfur. The use of solvents is likely to be more advantageous in catalytic dehydrogenations, however. The yields of phenols from alcohols and ketones, especially, can be significantly increased by the use of mesitylene or *p*-cymene as a diluent.⁶⁴ A thorough investigation has been made of the influence of various solvents on the dehydrogenation of 1- and 4-keto-1,2,3,4-tetrahydrophenanthrene to

²⁸⁸ See L. Ruzicka and Waldmann, *Helv. Chim. Acta*, **18**, 611-612 (1935); Waldmann, Dissertation, Eidgenössische Technische Hochschule, Zurich, 1935.

²⁸⁹ Baldeschwiler and Mikeska, *J. Am. Chem. Soc.*, **57**, 977-978 (1935).

²⁹⁰ Keiser and Breed, *Am. Chem. J.*, **16**, 20 (1894).

²⁹¹ Winterstein, Vetter, and Schön, *Ber.*, **68** B, 1079-1085 (1935).

²⁹² L. F. Fieser, M. Fieser, and Hershberg, *J. Am. Chem. Soc.*, **58**, 1463-1468 (1936).

²⁹³ Diels and Stephan, *Ann.*, **527**, 279-290 (1937).

1- and 4-phenanthrol, respectively,^{64,294} and of a number of isomeric keto-hexahydrochrysenes to the corresponding chrysenols.^{62,63}

5. Development and Identification of Dehydrogenation Products

Since complex mixtures of various reaction products may usually be expected from dehydrogenation, as is always the case for example with the triterpenes, a very careful fractional distillation is recommended as the first step. The individual fractions are then freed of phenols if necessary, and finally purified further by recrystallization of the picrate or trinitrobenzene derivative. Even an approximately quantitative separation of these mixtures is a lengthy and difficult procedure. The preparation of picrates, which can readily be decomposed by sodium hydroxide or ammonia, was originally the principal means of isolating the individual dehydrogenation products, but more recently the trinitrobenzene derivatives have also been frequently employed. In general, these appear to be rather less soluble and somewhat more stable than the picrates, and can equally well be resolved chromatographically on aluminum oxide. This last method for the resolution and regeneration of the free hydrocarbons is also recommended for the picrates, because of its neatness and simplicity.¹² If the picrates cannot be obtained directly from the fractionated dehydrogenation products by treatment with alcoholic picric acid solution, Ruzicka¹ recommends that the alcohol be allowed to evaporate in a porcelain dish. In the residual oil, the traces of picrates, which almost without exception crystallize in small needles, are then readily distinguishable from the nearly colorless plates of crystalline picric acid. The needles can be freed from adhering oil on a clay plate.

The positive identification of even known dehydrogenation products is sometimes difficult. For example, the work of Ruzicka and co-workers^{50,295} has shown that the picrates and trinitrobenzene derivatives of the different trimethylnaphthalenes give only very slight, if any, depression in the mixed melting point. Whenever their preparation is possible, therefore, the styphnates and trinitrotoluene derivatives, or oxidation products of the hydrocarbons, such as quinones, may be used as an additional help in identification.

Absorption spectra have been of the greatest importance in furnishing information on the nature of the ring system of high molecular weight dehydrogenation products.

XIII. CONCLUSION

The value of dehydrogenation methods for determining constitution has frequently been questioned. The results have often been regarded as

²⁹⁴ Mosettig and Duvall, *J. Am. Chem. Soc.*, **59**, 367-369 (1937).

²⁹⁵ L. Ruzicka and Ehmann, *Helv. Chim. Acta*, **15**, 140-162 (1932).

unreliable, particularly because of the numerous changes which may occur in the carbon skeleton. However, these rearrangements, in the main, conform to definite reactions which may be regularly formulated. Frequently, moreover, the results of the dehydrogenation itself have proved on more careful study to be valid, and the rearrangements to be merely a result of the synthetic methods used. In addition, these secondary reactions can often be avoided by careful manipulation, such as more accurate control of temperature. In view of this, an important task for the future will be detailed reinvestigation of the early results obtained on natural products, possibly by means of type experiments. The dehydrogenation conditions, especially the temperature, are doubtless most important in weighing the reliability of the results, and accurate knowledge of their influence can help to avoid false conclusions.

Dehydrogenation is very useful as a quick source of information on the general nature of alicyclic compounds. The relationship of the cardiac aglucons to the sterols, for example, was established for the first time by means of dehydrogenation. Also, the question of whether the various saponogens belong to the sterol or to the triterpene series can be readily decided on the basis of dehydrogenation results.^{296,297}

The role which dehydrogenation, along with the isoprene hypothesis and the analytical methods, has played in the study of the polyterpenes, particularly the pentacyclic triterpenes, was recognized several years ago by Ruzicka.⁸ Although there are still a number of questions, which perhaps can be answered only by systematic analysis, dehydrogenation nevertheless first made possible a fuller understanding of this difficult field. The great importance of dehydrogenation in other fields, also, is generally recognized today, and indeed there are few methods which can compete with it in the determination of the carbon nuclei of complex natural products.

²⁹⁶ L. Ruzicka and van Veen, *Z. physiol. Chem.*, **184**, 69-82 (1929).

²⁹⁷ Schulze, *Z. physiol. Chem.*, **238**, 35-53 (1936).