179. *Recent Progress in the Chemistry of the Terpenes.*[*]

By J. L. SIMONSEN.

THREE years ago the Society had the privilege of hearing Professor Ruzicka deliver the third Pedler Lecture (J., 1932, 1582). In giving an account of the life and work of Wallach the lecturer outlined much of the earlier work in terpene chemistry and it is the purpose of the present paper to attempt to survey briefly the more important advances which have been made during the past five years in the study of the isoprene (*iso*pentane) derivatives of essential oils. It is perhaps not generally recognised that, though the relationship of the terpenes to isoprene was noted and commented upon by both Wallach and Semmler, it was first used systematically by Ruzicka as a means of determining structure.

Of the simpler members of the terpene group, namely, those containing ten carbon atoms, our knowledge is now so complete in its main essentials that there is little to record. To the old controversy regarding the homogeneity of geraniol and related compounds, reference is made later (p. 784). We owe to Read and his collaborators important advances in the stereochemistry of the menthols and carvomenthols, and by an interesting series of reactions Houben and Pfankuch (*inter al.*, *Annalen*, 1933, **501**, 219; **507**, 37) have converted *d*-camphor into *l*-camphor.

Two substances of great interest, a ketone and an aldehyde, have been described recently

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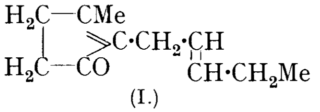
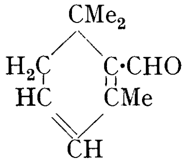
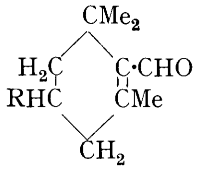
[*] A paper read at the opening of the discussion on this subject on March 21st, 1935.

and their constitutions determined. The ketone, jasmone, the odoriferous principle of oil of jasmine, has been shown independently by Treff and Werner (*Ber.*, 1933, **66**, *B*, 1521) and by Ruzicka and Pfeiffer (*Helv. Chim. Acta*, 1933, **16**, 1208) to be represented by (I). This ketone, which is not an isoprene derivative, contains a *cyclo*pentene ring and it is apparently the first occasion on which a substance containing this ring structure has been isolated from an essential oil. Its biochemical origin is obscure; it may possibly be formed from a 1 : 4-diketo-acid by intramolecular loss of water and elimination of carbon dioxide.

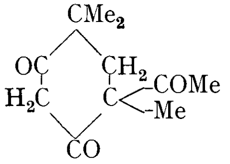
Of greater interest is the aldehyde, safranal, $C_{10}H_{14}O$, which Kuhn and Winterstein (*Ber.*, 1934, **67**, *B*, 344) separated in the form of its glycoside, pikrocrocin, from saffron. This aldehyde has been shown to be represented by (II), and the glycoside by (III). Its association in nature with the polyene dicarboxylic acid, crocetin, naturally suggests that it is the parent of this substance or alternatively, and from analogy more probably, one of its degradation products (compare Mayer, " Chemie der organischen Farbstoffe," II, p. 47).

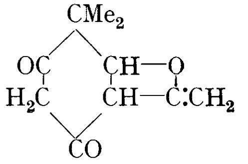

(I.)

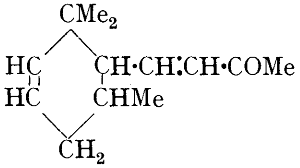

(II.)


(III.) (R = glucose.)

Safranal is obviously closely related to β-ionone, which Penfold and Philip (*J. Proc. Roy. Soc. W. Australia*, 1928, **14**, 1) have shown to be present in the essential oil from *Boronia megastigma*, and to the two diketones, angustione (IV) and dehydroangustione (IVa), separated by Penfold (*J. Proc. Roy. Soc. N.S. Wales*, 1924, **57**, 300) from the oil of *Backhousia angustifolia*, their structure being determined later (Gibson, Penfold, and Simonsen, J., 1930, 1184; Cahn, Gibson, Penfold, and Simonsen, J., 1931, 286). The occurrence in nature of these simple ionone derivatives is of importance, since irone, to which Tiemann and Krüger erroneously assigned formula (V), has now been shown by Ruzicka and his collaborators (*Helv. Chim. Acta*, 1933, **16**, 1143) to contain fourteen and not thirteen carbon atoms. The structure of this ketone, which possibly contains a *cyclo*heptane ring, has not been determined, but we cannot regret the mistake made by Tiemann and Krüger, since it led to the synthesis of α- and β-ionones, which have proved to be of such importance in the study of the structure of the carotinoids and of vitamin A.

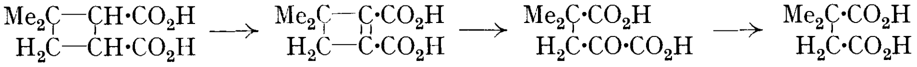

(IV.)


(IVa.)


(V.)

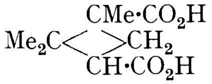
Considerable advances have been made in the field of sesquiterpene chemistry. In the years immediately following the classical experiments on the dehydrogenation of cadinene and selinene to cadalene and eudalene respectively, Ruzicka and his collaborators determined the structure of the more readily accessible sesquiterpenes and sesquiterpene alcohols. Once the relationship to either cadalene or eudalene has been established, the elucidation of the constitution of a sesquiterpene affords comparatively little difficulty. With dicyclic terpenes having a bridged ring or with tricyclic members of the series, the difficulties are very much greater and our knowledge is still very limited.

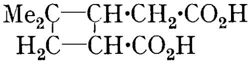
Some progress has been made recently with one noteworthy group, the so-called caryophyllenes, the hydrocarbons occurring in oil of cloves. The investigations of Semmler and of Deussen had shown by the preparation of a number of crystalline derivatives that there were in the sesquiterpene fraction of this oil at least three hydrocarbons, designated α-, β- and γ-caryophyllene respectively. The first of these is almost certainly identical with the hydrocarbon, humulene, first isolated by Chapman from hop oil. It probably differs completely in structure from the other two hydrocarbons, since it does not give a crystalline dihydrochloride or caryophyllenic alcohol on hydration. It was shown by Semmler in 1913 that caryophyllene (used here as a name for the mixture of hydrocarbons) on oxidation gave a liquid dibasic acid, caryophyllenic acid, which he suggested was methylnorpinic acid (VI). This acid has been shown (Evans, Ramage, and Simonsen, J., 1934, 1806; Ruzicka and Zimmermann, *Helv. Chim. Acta*, 1935, **18**, 219) to be a mixture of two crystalline acids, norcaryophyllenic acid, $C_8H_{12}O_4$, and caryophyllenic acid, $C_9H_{14}O_4$. By the reactions indicated in the scheme given below, norcaryophyllenic acid has been shown to be *d-cis*-3 : 3-dimethyl*cyclo*butane-1 : 2-dicarboxylic acid (VII); and caryophyllenic acid must be (VIII) or (IX), since it can be degraded to norcaryophyllenic acid (Ramage and Simonsen, this vol., p. 532).



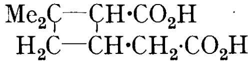
(VII.)

(VI.)

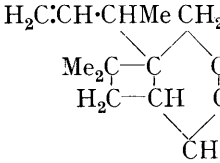




(VIII.)



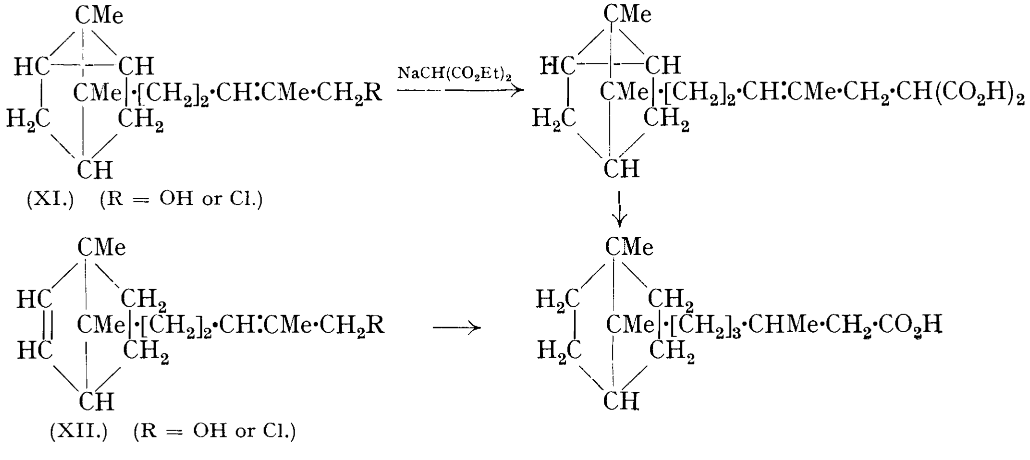
(IX.)



(X.)

The determination of the structure of norcaryophyllenic acid has provided a valuable key, but since the caryophyllene hydrocarbons cannot be separated from one another, the final elucidation of the structures of the individual hydrocarbons must depend upon the degradation of crystalline derivatives. Preliminary experiments with the blue nitrosite derived from β-caryophyllene suggest that the parent hydrocarbon is represented by (X), according to which it would be derived from cadalene.

Attention has been directed recently to the chemistry of the santalols, since Penfold (*J. Proc. Roy. Soc. New South Wales*, 1928, **52**, 60; 1932, **66**, 240) has isolated from the wood oil of *Santalum lanceolatum* a new santalol containing three ethylenic linkages (Bradfield, Penfold, and Simonsen). As is well known, Semmler showed α-santalol to be the tricyclic alcohol (XI; R = OH), and β-santalol has now been found to be (XII; R = OH) (Bradfield, Penfold, and Simonsen, this vol., p. 309). This constitution was proved by the reactions outlined in the scheme :



(XI.) (R = OH or Cl.)

(XII.) (R = OH or Cl.)

The contemporaneous experiments of Ruzicka and Thomann (*Helv. Chim. Acta*, 1935, **18**,

355) suggest the presence of a third alcohol of the camphene type in sandalwood oil.* It is not without interest to note that, whereas α-santalol, as was pointed out by Ruzicka, is derived from eudalene, β-santalol may be regarded as a derivative of cadalene.

During the course of this investigation an observation of more general interest and importance was made. There has been much discussion as to the correct formulation of such simple terpene derivatives as geraniol, citral, etc., namely, as to whether they should be represented as having an *iso*propenyl or an *iso*propylidene group at the end of the chain. The majority of substances about which this discussion has ranged have been oils and the view most generally held has been that they were inseparable mixtures of substances containing these two groups. Kuhn and Roth (*Ber.*, 1932, **65**, *B*, 1258) have estimated quantitatively the acetone formed in the oxidation of a number of substances containing the *iso*propylidene group and have found it to vary from 60—90% of the theoretical value. They studied in particular the crystalline acid, dehydrogeranic acid (XIII or XIV), and here, in agreement with earlier observations (Cahn, Penfold, and Simonsen, J., 1931, **3134**),

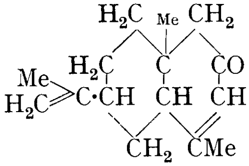
(XIII.) $Me_2C{:}CH{\cdot}CH{:}CH{\cdot}CH{:}CMe{\cdot}CO_2H$ $H_2C{:}CMe{\cdot}CH_2{\cdot}CH{:}CH{\cdot}CH{:}CMe{\cdot}CO_2H$ (XIV.)

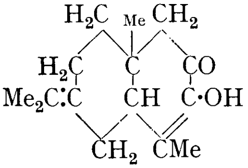
both acetone and formaldehyde were obtained, the yield of acetone being only 60% of the theoretical value. Kuhn and Roth concluded that the acid was homogeneous and represented by (XIII), but the oxidation proceeded abnormally. A more satisfactory explanation has been provided by recent observations on the oxidation of α-santalylmalonic acid. When this acid, which is crystalline and readily purified, is oxidised with ozone, it yields practically quantitatively tri*cyclo*ekasantalal (or the corresponding acid) (XVI). On the other hand, in alkaline solution oxidation with potassium permanganate yields the keto-acid (XVII). The only adequate explanation appears to be that α-santalylmalonic acid exists in the tautomeric forms (XV) and (XV*a*).

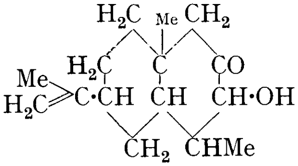
$$\begin{tikzcd}
\text{(XV.)}\ C_{11}H_{17}{\cdot}CH{:}CMe{\cdot}CH_2{\cdot}CH(CO_2H)_2 \arrow[r, shift left] \arrow[d, "O_3"] & C_{11}H_{17}{\cdot}CH_2{\cdot}C({:}CH_2){\cdot}CH_2{\cdot}CH(CO_2H)_2\ \text{(XV}a\text{.)} \arrow[l, shift left] \arrow[d, "KMnO_4"] \\
\text{(XVI.)}\ C_{11}H_{17}{\cdot}CHO & C_{11}H_{17}{\cdot}CH_2{\cdot}CO{\cdot}CH_2{\cdot}CH(CO_2H)_2\ \text{(XVII.)}
\end{tikzcd}$$

These represent the *iso*propenyl and the *iso*propylidene form of the acid and tautomerism of this nature provides an adequate explanation of Kuhn and Roth's results with dehydrogeranic acid. It seems very probable that a similar tautomerism occurs also in the cases of geraniol, citral, etc.

The isolation of sesquiterpene ketones has opened up a new and interesting field of research. Although only a few members of this group have been described, there is little doubt that many of the sesquiterpene alcohols recorded in the literature will be found to be ketones. Two years ago the wood oil from *Eremophila Mitchelli* was shown to contain three closely related ketones, eremophilone (XVIII), hydroxyeremophilone (XIX), and


(XVIII.)


(XIX.)


(XX.)

hydroxydihydroeremophilone (XX) (Bradfield, Penfold, and Simonsen, J., 1933, **2744**). Their relationship to selinene and eudesmol was commented upon at the time. Shortly afterwards, St. Pfau and Plattner (*Helv. Chim. Acta*, 1934, **17**, 129) described two ketones, α-atlantone (XXI) and β-atlantone (XXII), occurring in cedar wood oil. Their presence

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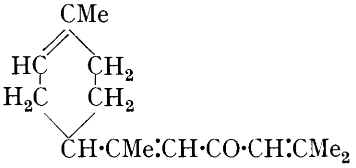
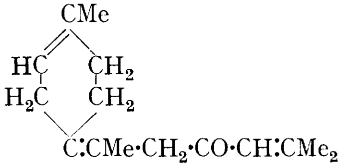
* The rotatory powers recorded by Ruzicka and Thomann for their α- and β-santalols indicate that their alcohols were impure. An alternative explanation to the one suggested above (occurrence of a third hydrocarbon) is that the conversion of α-santalylacetic acid into dihydro-β-santalylacetic acid is accompanied by a Wagner rearrangement.

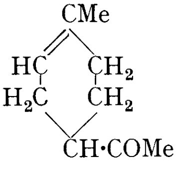
in this oil had been overlooked previously, since α-atlantone is hydrolysed readily by alkali to 4-methyl-Δ^3-tetrahydroacetophenone (XXIII), which was erroneously considered to be a constituent of the oil.



(XXI.)

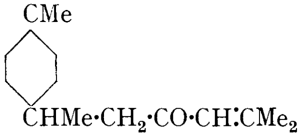


(XXII.)

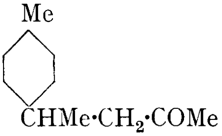


(XXIII.)

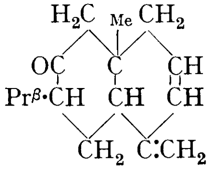
Closely related to these two ketones, but of an aromatic type, is the ketone turmerone present in admixture with sesquiterpenic ketones in the oil obtained from the tubers of *Curcuma longa*; this has been shown by Rupe, Clar, St. Pfau, and Plattner (*Helv. Chim. Acta*, 1934, **17**, 372) to be represented by (XXIV). Turmerone on treatment with alkali yields curcumone (XXV), which has been prepared synthetically.



(XXIV.)



(XXV.)



(XXVI.)

Recently B. Sanjiva Rao has isolated from the oil present in the tubers of *Cyperus rotundus* a sesquiterpene ketone, cyperone, which, like eremophilone, is a derivative of eudalene. This ketone has most probably the structure (XXVI) (Bradfield, Sanjiva Rao, and Simonsen).

Two outstanding problems in terpene chemistry remain to be solved. First, what is the mechanism of the formation of terpenes in plants and, secondly, what part do they play in the plant metabolism? With regard to the former problem, an admirable outline has been given by Robinson ("The Molecular Architecture of some Plant Products," IX Congreso Internacional de Quimica pura y aplicada, Madrid, 1934). It is simple on paper to derive any terpene from geraniol or α-pinene, but there seems to be little justification for such a procedure. It is not possible in the present state of our knowledge to go further than to regard, for example, α-pinene as the parent of myrtenal or verbenone. In the majority of theories the assumption is made that the more complex terpenes are built up from the simpler. Analogy would suggest that this assumption is incorrect. There seems to be little doubt that starch is the progenitor of the simpler saccharides, and the proteins of the alkaloids; it is more probable, therefore, that the simpler terpenes originate with the degradation of the polyterpenes. Our knowledge of the chemistry of these is still too limited for the elaboration of any definite scheme, but the occurrence of pikrocrocin in saffron supports the view advanced. Of the part the terpenes play in plant metabolism we are still ignorant, although some interesting investigations have been made recently in this connexion (Suchorukoda and Drushinina, *Sci. Mem. Univ. Saratov*, 1933, **10**, No. 2, 81; Nilov, *Plant Inst. U.S.S.R.*, 1933, *A*, No. 7, 3).

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