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The Structure of Eremophilene, the Sesquiterpenic Hydrocarbon from Petasites genus[x].

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Examining the p.m.r. spectrum of eremophilene some years ago, we observed that the spectrum was not consistent with the formula I proposed (1), but lack of material precluded investigation at that time. A little later we had the occasion to obtain the hydrocarbon valencene (II), (2) whose infrared and p.m.r. spectra were so close to those of eremophilene that it was quite difficult to find the difference between them. Nevertheless, the spectra were not identical. The optical rotation was of opposite sign. From these facts it followed that the structural formula of eremophilene needed a revision and that there could be a close structural relationship with valencene. The recent synthesis of I by Piers and Keziere (4) confirms the incorrectness of this formula for eremophilene. We now wish to present evidence for a different structure for this substance.

We took advantage of an opportunity to get a larger amount of Petasites kablikianus Tausch and P. albus (L.) Gaertn. (3) and isolated a larger quantity of a mixture of hydrocarbons, which on chromatography on activated alumina followed by chromatography on silica gel impregnated with silver nitrate furnished eremophilene (96-98% purity by gas-liquid chromatography on a capillary column with Apiezon L as stationary phase using Perkin Elmer F-11 apparatus). This sample had constants:

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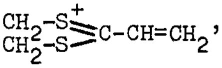
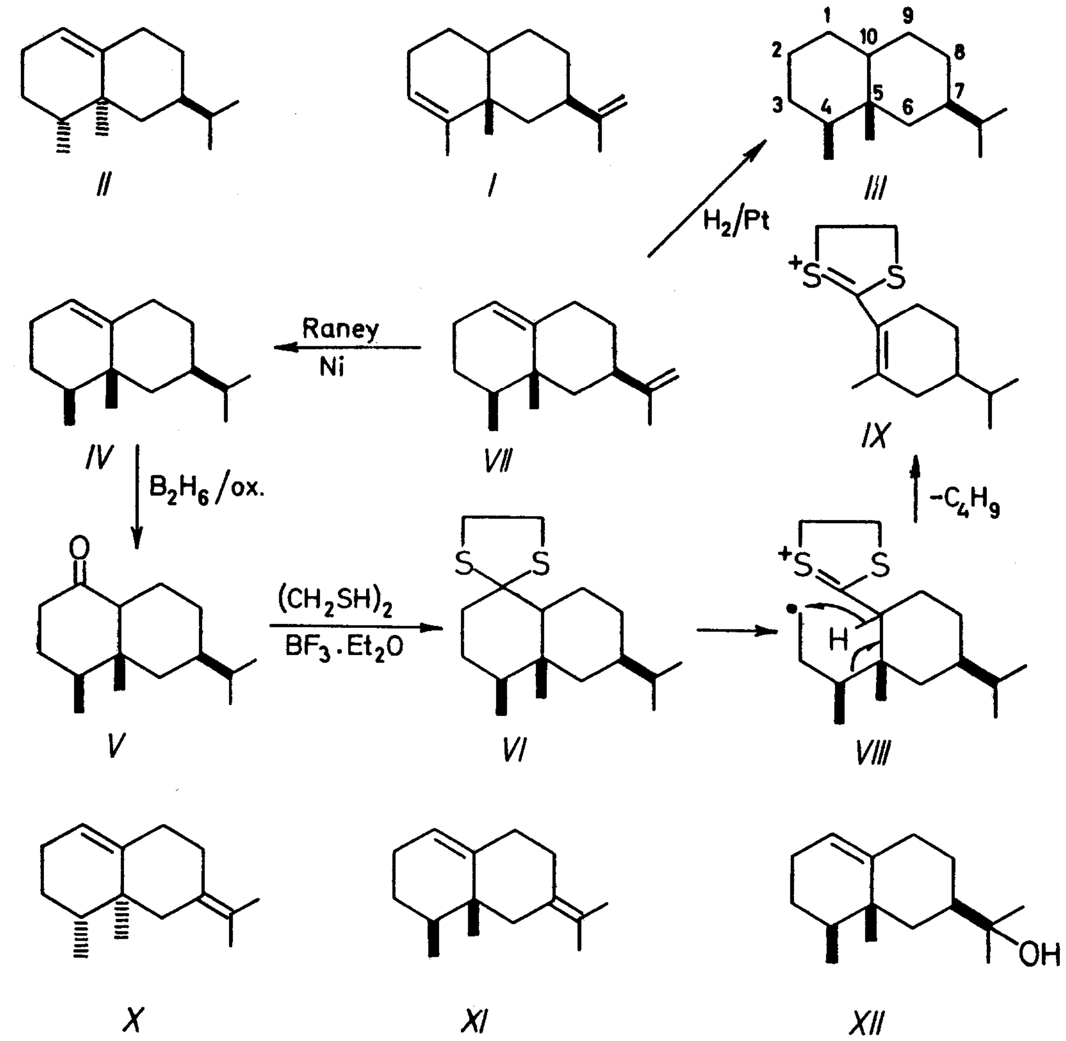
d_4^{24} 0.9341, n_D^{24} 1.5060, $[\alpha]_D^{24}$ -142.5° and exhibited in the p.m.r. spectrum signals of the following groups: $-C\underline{H}=C<$ (1H, a multiplet centered at 4.69τ), $C\underline{H}_2=C<$ (2H, 5.30τ, a broadened singlet), $H_2C=\overset{|}{C}-C\underline{H}_3$ (3H, a broad signal centered at 8.29τ), $\geqslant C-C\underline{H}_3$ (3H, 9.09τ, a singlet) and $>CH-C\underline{H}_3$ (a doublet centered at 9.14τ). Because the spectrum showed only one methyl group attached to a double bond and two upfield methyl groups, the invalidity of the formula I for eremophilene became clear. The second double bond of eremophilene was trisubstituted (one vinyl proton on it in the p.m.r. spectrum), and because the hydrocarbon furnished 7β-eremophilane (III) on hydrogenation over Pt catalyst and because the double bonds were not conjugated (UV), this double bond could be located in two positions on the eremophilane skeleton only: 9 or 1,10. In order to decide between these, we hydrogenated eremophilene on a deactivated Raney nickel catalyst and obtained a dihydroderivative IV which on treatment with B_2H_6 and subsequent oxidation according to Brown (5) gave a saturated ketone V. The last mentioned compound on treatment with $HSCH_2CH_2SH$ and $BF_3.Et_2O$ in acetic acid gave ethylene thioketal VI which in the mass spectrum showed a base peak due to the ion m/e = 131,



$$\begin{matrix}CH_2-\overset{+}{S}\\ CH_2-S\end{matrix}\!\!>\!C-CH=CH_2$$

, which could be formed, if the double bond was located in the position 1,10 rather than in 9,10. If the double bond were in position 9,10, then this ion should contain the isopropyl group and should be found at mass 173 (2a). Therefore, eremophilene has the formula VII. In agreement with this is the large peak at m/e = 241 (M-57), which can be explained on the basis of presumed mechanism VI→VIII→IX.

The above findings are also in agreement with the fact that the hydrocarbon X obtained from valerianol (2a) has an identical infrared spectrum with the hydrocarbon XI, which was prepared by isomerisation of eremophilene with sulphuric acid in ethanol in low yield (and which is also one of the constituents of original hydrocarbon mixture from different Petasites species) and which was also obtained during the structure elucidation of eremoligenol (XII) (6).



The sign of the optical rotation is opposite, giving evidence of the enantiomeric nature of the compounds in question. The presence of eremoligenol in plants of Petasites ssp. suggests further that this compound could be the precursor of eremophilene as valerianol could be the precursor of valencene and related substances.

Practically all of the reactions mentioned in the earlier communication on eremophilene (1) can be satisfactorily explained on the basis of the newly proposed structure; the occasional impossibility to do this is due to the fact that sometimes the starting material used previously was not pure.

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