Tetrahedron Letters No.8, pp. 677-681, 1967. Pergamon Press Ltd. Printed in Great Britain.

THE STRUCTURE OF VALERIANOL, A SESQUITERPENIC ALCOHOL OF EREMOPHILANE TYPE FROM VALERIANA OIL

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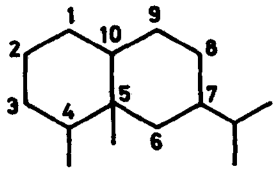
(Received 12 December 1966)

A. Stoll and his coworkers[1] described a sesquiterpenic alcohol valenol, $C_{15}H_{26}O$, of unknown structure (probably a mixture of alcohols[2] possessing guaiane skeleton) in roots of Valeriana officinalis L. Trying to isolate it from the essential oil we found another alcohol, $C_{15}H_{26}O$, n_D^{20} 1.5117, $[\alpha]_D^{20}$ +134° ($CHCl_3$), b. 120°/0.01 mm., characterized by means of its 3,5-dinitrobenzoyl derivative, m. 148°, which we named valerianol (4). It showed IR absorption at 1670 (double bond), 3440,3580 (hydroxy group) and a doublet at 1375 and 1385 cm^{-1} ($-C(CH_3)_2$). The PMR spectrum (HA 100, $CHCl_3$) confirmed the presence of the double bond (1H, 4.70τ, a broad signal) and the $-C(CH_3)_2$ grouping (6H, 8.85τ , a singlet) bearing probably the hydroxy group (1H, 7.58τ , confirmed by exchange with D_2O), and showed that another methyl group (3H, 9.08τ , a singlet) and a secondary methyl group (3H, a multiplet centered at 9.10τ) had to be present. On dehydrogenation with sulphur, valerianol yielded eudalene (1) whose picrate, m. 91-2°, did not show any depression of melting point on admixture with an authentic specimen.

In order to determine which of the two possible skeletons (i.e. eremophilane (2) and selinane (3); both giving eudalene on dehydrogenation) valerianol actually possesses, we prepared triol (5), $C_{15}H_{28}O_3$, m. 149-50°, $[\alpha]_D^{20}$ +32.6°



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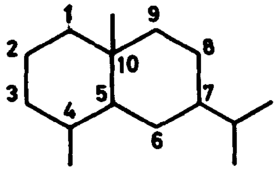

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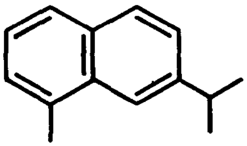

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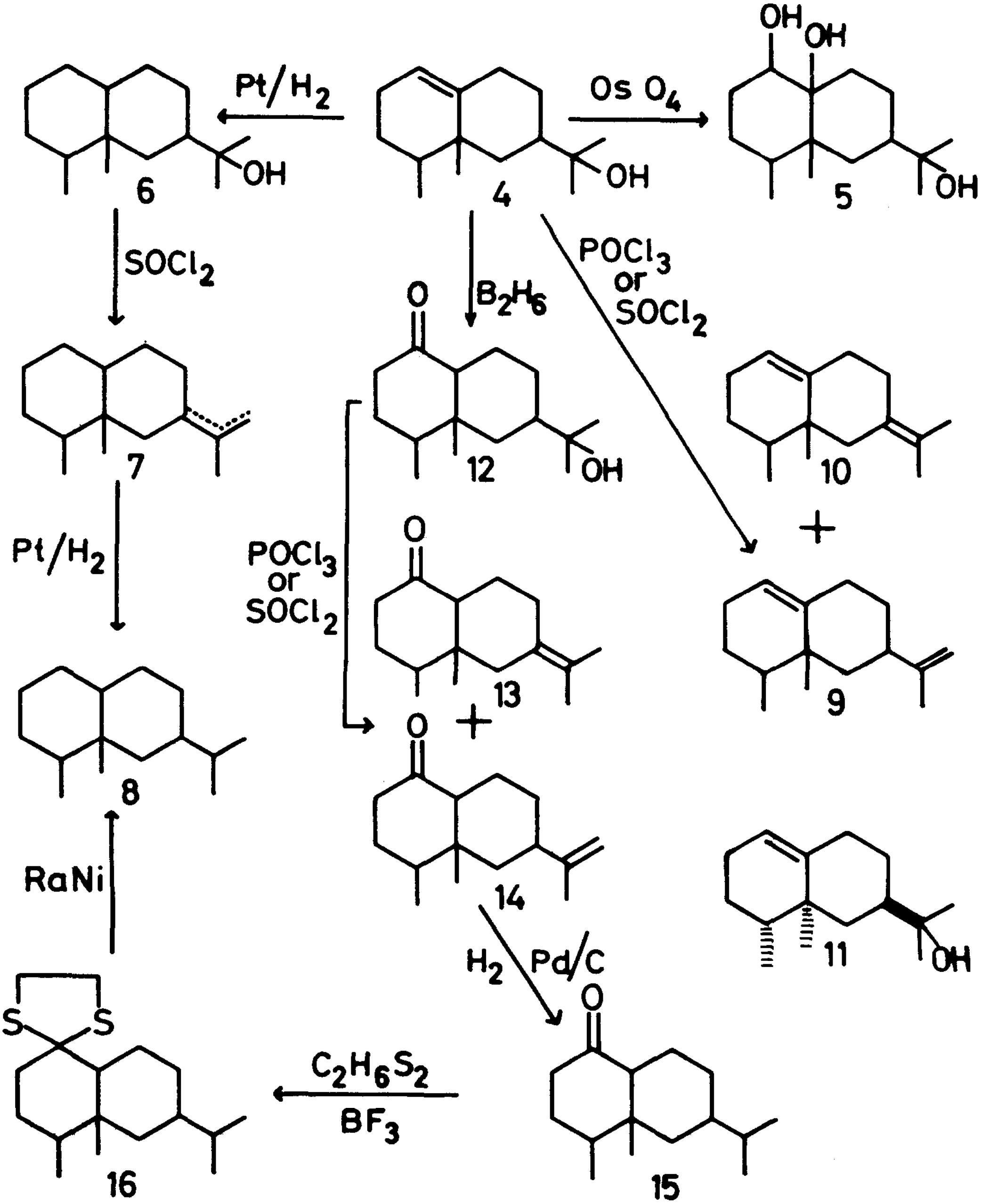
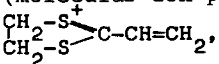
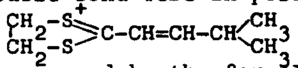
($CHCl_3$) on treatment the native alcohol with OsO_4 and pyridine in ether. The PMR spectrum of the former contains again signals of the $>C(CH_3)_2$ grouping (6H, 8.83τ, a singlet), $\geqslant CCH_3$ group (3H, 9.13τ, a singlet), $>CHCH_3$ (3H, a doublet, J = 7 c/s, centered at 9.23τ), and three OH groups (confirmed by exchange with D_2O). Furthermore, the presence of a broad unresolved multiplet of a proton in the grouping $C\underline{H}OH$ (1H, centered at 6.47τ) which after exchange with D_2O gives a triplet (J = 8.5 c/s) confirms that the molecule contains the group $-CH_2CHOH$, the fact excluding the possible location of the double bond in the position 5,6 of selinane skeleton (3). Because the dehydration of valerianol with $POCl_3$ or $SOCl_2$, or pyrolysis of its 3,5-dinitrobenzoate, afforded no conjugated diene which had to be formed if the double bond were located in the positions 6,7 or 7,8 on the selinane skeleton, we could exclude the skeleton (3) definitely (on the same basis, the original double bond could not to be located in the positions 6,7 or 7,8 on the eremophilane skeleton). The above findings were supported by the formation of dihydrovalerianol, $C_{15}H_{28}O$ (6), in a good yield on hydrogenation on Pt catalyst thus showing that no hydrogenolysis occured, which would be probable, if valerianol were an allylic alcohol. Therefore, the double bond could be located in the positions 9,10 or 1,10 on eremophilane skeleton (2), only.

We confirmed further the position of tertiary hydroxy group (tentatively located on isopropyl group on the basis of spectroscopic evidence) by the following chemical means: valerianol did not oxidize on treatment with chromic acid according to Jones[3] and on dehydration with $POCl_3$ or $SOCl_2$ gives a mixture of two hydrocarbons. The first one (75%), $C_{15}H_{24}$ (9), d_4^{20} 0.9339, n_D^{20} 1.5073, $[\alpha]_D^{20}$+141° (neat), contained trisubstituted double bond (805,1643 cm^{-1}) and an exomethylene double bond (886,1668,3090 cm^{-1}) and exhibited PMR signals of the following groups: $CH_2=$ (2H, 5.35τ, a broadened singlet), $-CH=C<$ (1H, a multiplet centered at 4.70τ), $H_2C=\overset{|}{C}-C\underline{H}_3$ (3H, a broad signal centered at 8.30τ), $\geqslant CCH_3$ (3H, 9.04τ, a singlet) and $>CHC\underline{H}_3$ (3H, a doublet centered at 9.05τ). The other hydrocarbon (25%), $C_{15}H_{24}$ (10), d_4^{20} 0.9378, n_D^{20} 1.5135, $[\alpha]_D^{20}$+167;5° (neat), contained the trisubstituted double bond (805,1645 cm^{-1}; 1H, a broadened signal at 4.70τ), $>C=C<^{CH_3}_{CH_3}$ (6H, 8.30τ, a singlet), $>CHC\underline{H}_3$ (3H, a doublet centered at 9.10τ) and $\geqslant CCH_3$ (3H, 9.20τ, a singlet). Thus we located hydroxy group unambiguously on the isopropyl group, as can be seen in formula 4.

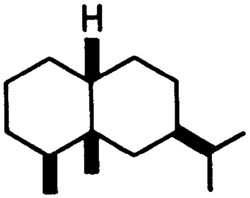
In order to decide between the two possible positions of a double bond (9,10 or 1,10) on the eremophilane skeleton, we treated valerianol with B_2H_6 and after subsequent oxidation according to Brown[4] we obtained a ketoalcohol (12), m. 88-9°, $[\alpha]_D^{20}$+40.5° ($CHCl_3$), which showed IR absorption bands at 1697 (C=O), 1450 ($C\underline{H}_2CO$)

and 3460, 3600 cm^{-1} (-OH). Compound 12 does not isomerize on refluxing in 5% solution KOH in methanol and its dehydration with $POCl_3$ or $SOCl_2$ gives two unsaturated ketones 13 and 14. On hydrogenation over Pd/C in methanol, 14 gave satura-



ted ketone 15, which on treatment with $HSCH_2CH_2SH$ and $BF_3.Et_2O$ in acetic acid gave ethylene thioketal (16). In the mass spectrum of the last mentioned compound (molecular ion peak m/e = 298) the base peak was 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 position 1,10. If the double bond were in position 9,10, then as base peak had to be expected an ion  $\begin{matrix}CH_2-\overset{+}{S}\\ CH_2-S\end{matrix}\!>C-CH=CH-CH\!<\begin{matrix}CH_3\\ CH_3\end{matrix}$ m/e = 173 (see Ref.[5]). Therefore, valerianol has to be expressed by the formula 4.

The fact that naturally occurring hydrocarbon valencene[7,8] is identical[9] (according to IR and mass spectra, and physical constants) with hydrocarbon 9 obtained from valerianol proves unequivocally the absolute stereochemistry of valerianol as 11. In this connection it is of interest that 7 on hydrogenation over Pt catalyst in acetic acid gave a mixture of two saturated hydrocarbons (8), $C_{15}H_{28}$, differing in the stereochemistry of the isopropyl group. When ethylene thioketal 16 is refluxed with Raney nickel in dioxane, only one hydrocarbon 8, n_D^{20} 1.4870, $[\alpha]_D^{20}$ +43.7° ($CHCl_3$) is formed, identical with one of the above mixture. According to GVC analysis, neither of both hydrocarbons is identical with eremophilanes 17, 18, 19 described earlier[10]. The complete analysis of the ORD curve of ketoalcohol (12) exhibiting negative Cotton effect (a = -26.64) similar to that showed[11] by 10-methyl-trans-decalone-1 (20) (a = -32) in terms of the octant rule of other sterical combinations than those derived from 17, 18, 19, confirmed the previous statement[10], i.e. the stereochemistry 21 of the above ketoalcohol.



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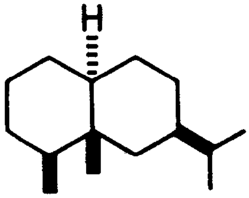

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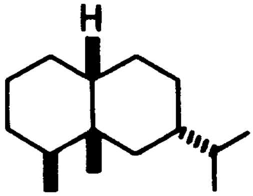

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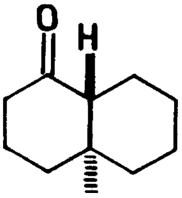

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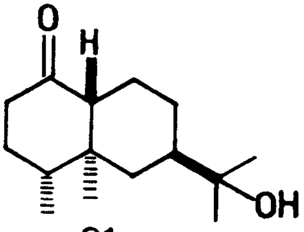

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Valerianol is therefore another member of the family of compounds with unusual eremophilane skeleton (i.e. nootkatone, valencene and nootkatene[10]).

Acknowledgement. The authors thank Dr. Z. Samek for measurements of PMR spectra on a Varian HA 100 instrument, Drs. J. Smolíková and G. Severini-Ricca for IR spectra, Dr. L. Dolejš for the mass spectrum and Dr. I. Frič for ORD measurements. Further the authors thank to Dr. M.K. Veldhuis, Agricultural Research Service, US Department of Agriculture, Winter Haven, Florida, for the kind comparison of IR spectra.

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