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STRUCTURE, STEREOCHEMISTRY AND ABSOLUTE CONFIGURATION OF AGAROL, A NEW SESQUITERPENE ALCOHOL FROM AGARWOOD OIL

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FROM the solvent-extracted essential oil of the fungus infected plant *Aquilaria agallocha, Roxb.*[1], the main characteristic constituent, an α,β-unsaturated monoethynoid eudalenic primary alcohol named agarol has been isolated in pure form by batch strip fractionation and column chromatography on alumina (grade II and IV). Its structure, stereochemistry and absolute configuration are reported in this communication.

Agarol [b.p. 117°/0.9 mm (inside temperature),[2] $[\alpha]_D^{23}$ -21.8° (C, 7.23), n_D^{29} 1.5052, d_4^{30} 0.9785; number of double bonds: 1 (Peracid - 1.06, catalytic hydrogenation - 1.02); M_D 67.81, Calc. for $C_{15}H_{25}OH$, 1 $|^{=}$67.79; no characteristic U.V. absorption, I.R. spectrum: 885 cm^{-1} ($>C=CH_2$), 3322 cm^{-1} (-OH); (Calc. for $C_{15}H_{26}O$: C, 81.02; H, 11.79. Found: C, 80.6; H, 11.4)] forms a monoacetate (Pyr. $-Ac_2O$)

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[1] Sadgopal and B. S. Varma, *Soap, Perf. & Cosmetics* 25, 169 (1952).

[2] Unless specified to the contrary, b.p. refers to bath temperature, $[\alpha]_D$ are for $CHCl_3$ solution; all products except solid derivatives were chromatographed over alumina; ultra-violet absorption spectra were determined on EtOH solution.

[b.p. 132°/0.3 mm, $[\alpha]_D^{23}$ -10° (C, 1.4); I.R.Spectrum: 1723 cm^{-1} (acetoxy group), 885 cm^{-1} ($>C = CH_2$); (Calc. for $C_{17}H_{28}O_2$: C, 77.22; H, 10.67. Found: C, 77.7; H, 10.9)] and gives a positive xanthate test (primary or secondary alcoholic group).

Primary α,β-unsaturated nature of the alcoholic group is revealed by its oxidation with CrO_3(HOAc) and MnO_2 ($CHCl_3$) to α,β-unsaturated aldehyde (Fehling's and Tollens' tests positive)- agaral (Calc. for $C_{15}H_{24}O$: C, 81.76; H, 10.98. Found: C, 80.5; H, 11.2); λ_{max} 243 and 320 mμ (ε 8480 and 72 respectively).

Methylenic nature ($>C=CH_2$) of the only double bond in agarol was revealed by, the formation of copious amount of formaldehyde during ozonolysis (dimedone derivative, m.p. and mixed m.p.), positive chromotropic acid test, strong absorption band at 885 cm^{-1} (both in agarol and its acetate) and the disappearance of the same in dihydroagarol.

Dehydrogenation of agarol with Se and Pd-C furnished eudalene (characterized through its spectrum and picrate, m.p. and mixed m.p. 90°). (Calc. for $C_{20}H_{19}O_7N_3$: C, 58.11; H, 4.63; N, 10.17. Found: C, 57.3; H, 4.68; N, 9.9) from which the partial expression (I) is arrived at for it.

The remaining carbon atom is presumably an angular methyl group (not geminal as shown by the absence of doublet in the region 1368 cm^{-1})[3], which assuming agarol obeys isoprene rule, can be located at C(10) in

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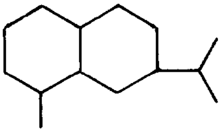
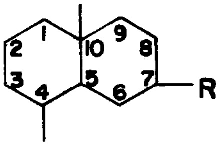
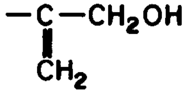
[3] A. R. H. Cole in Zechmeister's, *Progress in the Chemistry of Organic Natural Products* Vol. XIII, p. 44. Springer, Vienna (1956).

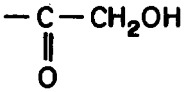


I



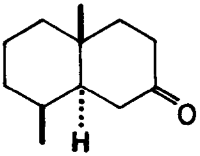
II, R = 

$-\underset{\underset{CH_2}{\|}}{C}-CH_2OH$

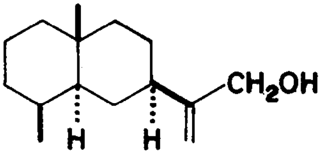
III, R = 

$-\underset{\underset{O}{\|}}{C}-CH_2OH$

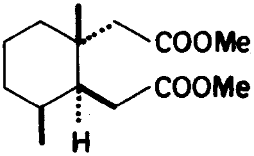
IV, R = O



V



VII



VI

which case the basic formula for agarol should be (II), this premise being further supported by degradation experiments described in the sequel. Numbering of carbon atoms is in accordance with Barton's formulation.[4]

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[4] D. H. R. Barton, P. de Mayo and M. Shafiq, *J. Chem. Soc.* 929 (1957); O. Motl, V. Herout and F. Sorm, *Coll. Czech. Chem. Comm.* **23**, 1293 (1958).

On ozonolysis agarol, apart from formaldehyde affords hydroxyacetone (iodoform test, Feigl's periodate test, green coloured acyloino-oxime type copper complex[5] from its oxime, presumably formed through isopropylidene - isopropenyl transformation) and two other key compounds: Ketol (III) [b.p. 170°/0.5 mm, (Calc. for $C_{14}H_{24}O_2$: C, 74.95; H, 10.78. Found: C, 74.53; H, 10.50); I.R. spectrum: 1723 cm^{-1} ($>C = O$ group in aliphatic chain), 3367 cm^{-1} (-OH), 1672 cm^{-1} (hydrogen bridge due to hydroxy-carbonyl interaction);[6] semicarbazone, m.p. 229° (Calc. for $C_{15}H_{27}O_2N_3$: C, 64.02; H, 9.67. Found: C, 63.45; H, 9.51)] and ketone (IV) [b.p. 125°/0.6 mm, n_D^{23} 1.4989; λ_{max} 290 mμ (ϵ , 30), band at 1702 cm^{-1} (keto group attached to six membered ring),[7] (Calc. for $C_{12}H_{20}O$: C, 79.94; H, 11.18. Found: C, 78.72; H, 11.10)] identical with the ketone of known absolute configuration[8] (V) obtained from eudesmol (stereochemically correlated with the steroids);[9] identity being further established by comparative infra-red study, $[\alpha]_D^{24}$ + 22° (C, 0.3 in HOAc), m.p. and mixed 221° of the semicarbazone[10] (Calc. for

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[5] F. J. Welcher, *Organic Analytical Reagents* Vol. III, p. 237. Van Nostrand, New York (1949).

[6] R. N. Jones, P. Humphries, F. Herling and K. Dobriner, *J. Amer. Chem. Soc.* **74**, 2820 (1952).

[7] C. Djerassi, E. Farkas, A. J. Lemin, J. C. Collins and F. Walls, *J. Amer. Chem. Soc.* **76**, 2969 (1954).

[8] W. Klyne, *J. Chem. Soc.* 3072 (1953).

[9] B. Riniker, J. Kalvoda, D. Arigoni, A. Fürst, O. Jeger, A. M. Gold and R. B. Woodward, *J. Amer. Chem. Soc.* **76**, 313 (1954).

[10] L. Ruzicka, P. A. Plattner and A. Fürst, *Helv. Chim. Acta* **25**, 1364 (1942). We are indebted to Professor Ruzicka for providing us this specimen.

$C_{13}H_{23}ON_3$: C, 65.78; H, 9.77. Found: C, 66.54; H, 9.7). Its configuration was further confirmed by the preparation of dimethyl ester (VI) [b.p. 160°/2.4 x 10^{-2} mm, $[\alpha]_D^{23}$ + 5.9° (C, 1.86 in acetone); (Calc. for $C_{14}H_{24}O_4$: C, 65.59; H, 9.44. Found: C, 64.9; H, 9.0)] via the dicarboxylic acid obtained through oxidation with $KMnO_4$.

Absolute configuration of the side chain attachment at C(7) was established from the identity of dihydroagarol [b.p. 110-115°/0.5 mm, $[\alpha]_D^{25}$ + 16.6° (C, 2.7 in EtOH); (Calc. for $C_{15}H_{28}O$: C, 80.29; H, 12.58. Found: C, 80.33; H, 12.70)] with tetrahydrocostol.[11] Further proof in support of this assignment was provided by the preparation of selinane [b.p. 152°/10 mm, n_D^{23} 1.4946; (Calc. for $C_{15}H_{28}$: C, 86.46; H, 13.54. Found: C, 86.10; H, 12.80)] from dihydroagarol via its bromide and subsequent reduction with LiH-$LiAlH_4$ in tetrahydrofuran.[12] The absolute configuration of agarol is thus represented by (VII).

Additional evidence for the presence of allylic moiety in agarol and costol was provided by their metal amine reduction[13] to dihydroselinene (Calc. for $C_{15}H_{26}$: C, 87.30; H, 12.70. Found: C, 86.52; H, 12.14) and selinene [b.p. 130°/7 mm, n_D^{25} 1.4983, $[\alpha]_D^{26}$ + 22.04° (C, 2.54); (Calc. for $C_{15}H_{24}$: C, 88.16; H, 11.84. Found: C, 87.5; H, 11.2)] respectively.

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[11] V. Benešová, V. Sýkora, V. Herout and F. Sorm, Chem. & Ind. 363 (1958). Refer also T. Ukita and S. Nakazawa, Pharm. Bull. (Soc. Japan) **2**, 239 (1954).

[12] J. E. Johnson, R. H. Blizzard and H. W. Carhart, J. Amer. Chem. Soc. **70**, 3664 (1948).

[13] For pertinent references see A. J. Birch and H. Smith, Quart. Rev. **12**, 17 (1958).