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HYDROXYTOTAROL

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A HYDROXY totarol has been reported to be a minor constituent of Podocarpus totara.[2] Through the courtesy of Dr. B.R. Thomas we received a small sample of the product of the original isolation and have been able to inspect its chemical constitution. It is a colorless crystalline $C_{20}H_{30}O_2$ compound (Found: C, 79.1; H, 10.1. Calc.: C, 79.4; H, 10.0), m.p. 230-231°, $[\alpha]_D^{26}$ + 29° (ethanol), whose ultraviolet spectrum $\lambda_{max}^{95\%EtOH}$ 279 mμ (ε 1990) is identical with that of totarol (Ia)[3,4] and whose infrared spectra in both chloroform solution and Nujol exhibit all bands (in several instances, of different intensity) revealed by the spectra of totarol (Ia) as well as peaks at 2.99(m), 9.80(s), 9.89(s) and 10.87(m)μ, characteristic of a carbinol group. Early chromic acid oxidation experiments led to an aldehyde,[5] indicative of the presence of a primary alcohol function in the natural product. The exceedingly low yields encountered in our degradation experiments and the

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[1] Public Health Service Predoctoral Research Fellow, 1960-1961.

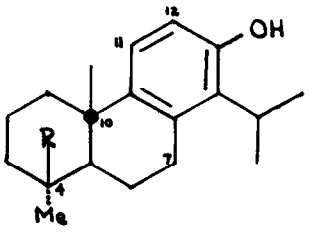
[2] C.W. Brandt and B.R. Thomas, Nature,Lond. 170, 1018 (1952).

[3] J.D.S. Goulden in W.F. Short and H. Wang, J.Chem.Soc. 2979 (1951).

[4] Dr. J.C. Dacre (University of Otago, Dunedin, New Zealand) kindly supplied us with a sample of totarol acetate.

[5] J.W. Chamberlin, unpublished observations.

availability of only a small quantity of material precluded a structure analysis by chemical means. As a consequence a proton magnetic resonance study of hydroxytotarol and various model compounds was undertaken.[6]

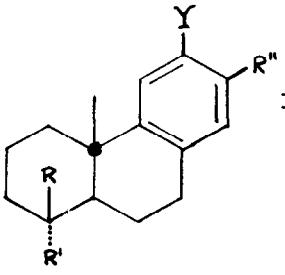


Ia, R=Me
b, R=CH_2OH

The p.m.r. spectrum of totarol (Ia) exhibits an AB quartet centered at 6.70δ (J=8.9 c.p.s.) due to the C-11 and 12 aromatic hydrogens, a low broad 4.35δ phenolic proton peak, five peaks of the expected septet for the isopropyl methine hydrogen centered at 3.07δ (J=7.2 c.p.s.), a complex multiplet at 2.78δ due to the C-7 methylene hydrogens, a doublet centered at 1.29δ (J=7.2 c.p.s.) characteristic of the isopropyl methyl groups, a 1.12δ C-10 methyl peak and two peaks, 0.94 and 0.92δ, due to the C-4 gem-dimethyl function. The spectrum of hydroxytotarol differs substantially from that of totarol (Ia) only by the replacement of the gem-dimethyl peaks by a 1.04δ methyl peak and an AB quartet centered at 3.66δ (J=10.9 c.p.s.) due to the methylene hydrogens of a hydroxymethyl group. Its isopropyl methyl groups show up as a doublet centered at 1.32δ (J=7.2 c.p.s.) and its C-10 methyl function as a 1.16δ peak. These data and the correspondence of the chemical shift of the angular methyl group in totarol (Ia) and hydroxy-

[6] Assignment of the chemical shifts of methyl groups is based on a larger study of the n.m.r. spectra of various diterpenic compounds to be published in the near future.

totarol with that of dehydroabietol (IIa),[7] 1.18δ, and O-methylpodocarpol (IIb),[8] 1.16δ, prove that hydroxytotarol possesses a C-4 hydroxymethyl function.



IIa, R=Me,R'=CH_2OH,R"=i-Pro,Y=H
b, R=CH_2OH,R'=Me,R"=H,Y=OMe
c, R=R'=Me,R"=H,Y=OMe
d, R=Me,R'=CH_2OAc,R"=i-Pro,Y=H
e, R=CH_2OAc,R'=Me,R"=H,Y=OMe

The stereochemistry of the hydroxymethyl group was resolved by the observation that an axial group shows its quartet ca. 0.4 p.p.m. downfield of that of an equatorial group. Thus, the axial systems O-methylpodocarpol (IIb) and vouacapenol (IIIa)[9,10] reveal their quartets at 3.69δ (J=11.3 c.p.s.) and 3.60δ (J=10.9 c.p.s.), respectively, while the equatorial compounds dehydroabietol (IIa) and vinhaticol (IIIb)[9,10] show four peaks centered at 3.28δ (J=10.4 c.p.s.) and 3.25δ (J=10.2 c.p.s.), respectively. On this basis hydroxytotarol possesses an axial hydroxymethyl group. Finally, the close relationship of the spectra (in position and shape of the peaks) of two sets of two similar compounds each, totarol (Ia) and hydroxytotarol vs. O-methylpodocarpane (IIc) and O-methylpodocarpol (IIb), as contrasted with the spectral differences encountered between A/B trans and cis ring

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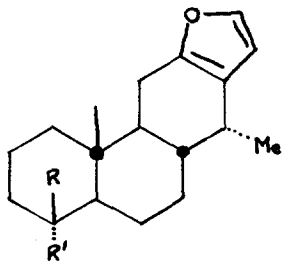
[7] L.F. Fieser and W.P. Campbell, J.Amer.Chem.Soc. 61, 2528 (1939).

[8] W.P. Campbell and D. Todd, J.Amer.Chem.Soc. 64, 928 (1942).

[9] F.E. King, D.H. Godson and T.J. King, J.Chem.Soc. 1117 (1955).

[10] Drs. F.E. King and T.J. King kindly supplied us with samples of vouacapenic and vinhaticoic acids.

systems,[6] speaks strongly in favor of a trans ring juncture in hydroxytotarol.[11] As a consequence structure Ib can be assigned to this natural product.



IIIa, R=CH_2OH, R'=Me
b, R=Me, R'=CH_2OH

It is noteworthy that the n.m.r. analysis of primary alcohols readily obtainable by the reduction of naturally occurring carboxylic acids may serve as a supplement to present methods of determination of the stereochemistry of the carboxy group in resin acids and similar substances.[12] Unfortunately it is limited to compounds possessing no other hydrogens which would yield signals in the hydroxymethyl region. Thus for example, it is hard to uncover the crucial quartet in a spectrum of iresin (IV)[13,14] from among the signals of the C-11 hydrogens and, to a less extent, those of the C-3 hydrogen. In some cases it may prove useful to inspect the spectra of the carbinol acetates in view of an appreciable downfield shift[15] of

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[11] For the stereochemistry of totarol (Ia) cf. J.A. Barltrop and N.A.J. Rogers, J.Chem.Soc. 2566 (1958) and Y.L. Chow and H. Erdtman, Acta Chem.Scand. 14, 1852 (1960).

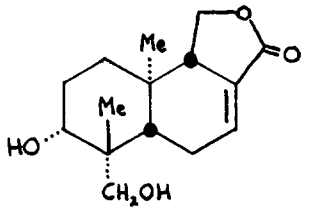
[12] Cf. E. Wenkert and B.G. Jackson, J.Amer.Chem.Soc. 80, 217 (1958).

[13] C. Djerassi and S. Burstein, Tetrahedron 7, 37 (1959).

[14] Professor C. Djerassi kindly supplied us with a sample of this compound.

[15] Cf. L.M. Jackman, Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry p. 55. Pergamon Press, London (1959).

their methylene quartets, e.g.: dehydroabietyl acetate (IId)——3.84δ (J=10.5 c.p.s.); O-methylpodocarpyl acetate (IIe)——4.16δ (J=11.3 c.p.s.).[16]



IV

[16] All spectra were obtained with ca. 25% deuterochloroform solutions on a Varian Model HR60 spectrometer at 60 mc/sec with tetramethylsilane acting as internal standard. Position of the major peaks was determined by the audiofrequency side band technique, that of minor peaks by linear interpolation.