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REVISION OF THE STRUCTURE ASSIGNED TO A MONOTERPENE ISOLATED FROM *PIQUERIA TRINERVIA*[1]

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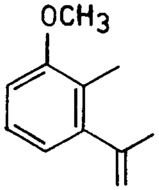
Summary: Unambiguous synthesis of 2-methyl-3-isopropenylanisole (1) and 2-isopropenyl-3-methylanisole (4) has led to revision, from (1) to (4), of the structure assigned to a monoterpene phenol ether isolated from *Piqueria trinervia*.

From *Piqueria trinervia* Cav. Bohlmann and Suwita[2] isolated a monoterpene phenol ether for which structure (1) was proposed mainly on the basis of its ^{1}H-NMR spectrum and its co-occurrence with a carquejol derivative (2), to which phenol ether (1) is presumed to be related biogenetically. However, in carquejol (3) the vicinal disposition of the hydroxy and isopropenyl groups has been well established[3]. Therefore from the presumed biogenetic relationship of the newly isolated phenol ether (1) with carquejols, one could not rule out structure (4) for the natural product, especially in view of the close resemblance of (4) to carquejol (3) itself. Further, sole reliance on ^{1}H-NMR would not unequivocally distinguish between the two structures (1) and (4). In order to solve this problem, we undertook an unambiguous synthesis of both the isopropenyl phenol ethers (1) and (4).



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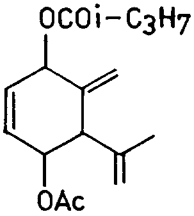

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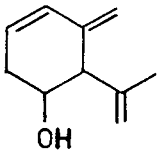

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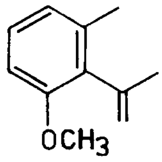

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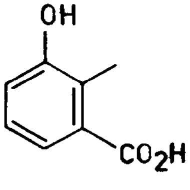

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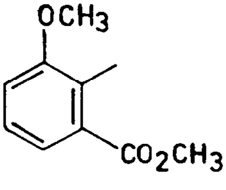

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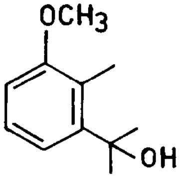

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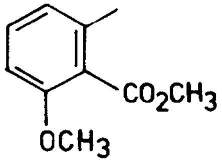

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2-Methyl-3-hydroxybenzoic acid[4] (5), prepared from 3-aminonaphthalene-1,5-disulphonic acid is the starting material for the synthesis of 2-methyl-3-isopropenylanisole (1). The methoxy ester[5] (6) derived from (5) was reacted with excess methylmagnesium iodide and the resulting carbinol[5] (7) was dehydrated (24h) at room temperature in benzene medium with pre-dried *p*-toluenesulphonic acid (10%, by weight) to afford after preparative TLC analytically pure 2-methyl-3-isopropenylanisole[6a] (1). Subjecting the methoxy ester[7,8] (8) to a repetition of the sequence of reactions carried out on the isomeric methoxy ester (6) gave after preparative TLC analytically pure 2-isopropenyl-3-methylanisole[6b] (4). Comparison of IR and ^{1}H-NMR spectra of the two anisoles (1 and 4) with those[9] of the monoterpene phenol ether isolated from the natural source showed complete identity (superimposable IR and tally of chemical shifts and splitting patterns of proton signals) of the natural product with 2-isopropenyl-3-methylanisole (4) and not with (1) as assigned.[2]

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References and notes

1. Studies in Terpenoids: Part LIII. For Part LII, see T.P. Velusamy and G.S. Krishna Rao, communicated.
2. F. Bohlmann and A. Suwita, *Phytochemistry*, 17, 560 (1978).
3. Y.R. Naves, *Bull. Soc. Chim. France* 1871 (1959); A.F. Thomas, *Helv. Chim. Acta*, 50, 963 (1967); G. Snatzke, A.F. Thomas and G. Ohloff, *Helv. Chim. Acta*, 52, 1253 (1969).
4. L.F. Fieser and W.C. Lothrop, *J. Am. Chem. Soc.*, 58, 752 (1936); R.E. Dean, A. Midgley, E.N. White and D. McNeil, *J. Chem. Soc.* 2773 (1961).
5. M.S. Carpenter and W.M. Easter, *J. Org. Chem.*, 20, 401 (1955).
6. (a) 2-Methyl-3-isopropenylanisole (1) (Found: C, 81.12; H, 9.14. $C_{11}H_{14}O$ requires C, 81.44; H, 8.70%) exhibited: IR(CCl$_4$) ν_{max} 1642, 1600, 1585, 1260, 1085 and 908 cm^{-1}; δ (CDCl$_3$) 2.02 (3H, q, *J* 0.5 Hz, vinylic-CH$_3$), 2.17 (3H, s, Ar-CH$_3$), 3.83 (3H, s, OCH$_3$), 4.82 (1H, q, *J* 1 Hz, E-vinylic-H), 5.17 (1H, pent, *J* 1 Hz, Z-vinylic-H), 6.75 (2H, m, H$_4$ and H$_6$) and 7.12 (1H, t, *J* 8 Hz, H$_5$).
   (b) 2-Isopropenyl-3-methylanisole (4) (Found: C, 81.32; H, 8.53. $C_{11}H_{14}O$ requires C, 81.44; H, 8.70%) exhibited: IR(CCl$_4$) ν_{max} 1647, 1608, 1585, 1260, 1100 and 906 cm^{-1}; δ (CCl$_4$) 1.93 (3H, d, *J* 1 Hz, vinylic-CH$_3$), 2.20 (3H, s, Ar-CH$_3$), 3.73 (3H, s, OCH$_3$), 4.67 (1H, m, *J* 1 Hz, E-vinylic-H), 5.13 (1H, m, Z-vinylic-H), 6.53 (1H, dd, *J* 8 and 2 Hz, H$_6$), 6.67 (1H, dd, *J* 8 and 2 Hz, H$_4$) and 6.96 (1H, t, *J* 8 Hz, H$_5$).
7. D. Peltier, *Bull. Soc. Sci. Bretagne* 31, 7 (1956); *Chem. Abst.* 52, 9017f (1958).
8. The methoxy ester (8) was obtained by pyrolysis of the Diels-Alder adduct formed *in situ* from 1,4-dihydroanisole and methyl tetrolate (C.C.Kanakam and G.S.R.Subba Rao, unpublished). We thank Mr. C.C.Kanakam, Indian Institute of Science, Bangalore for a sample of the ester (8).
9. We are grateful to Professor F. Bohlmann, Berlin, West Germany for the IR and ^{1}H-NMR spectra of the terpenic phenol ether isolated[2] from *Piqueria trinervia*.

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