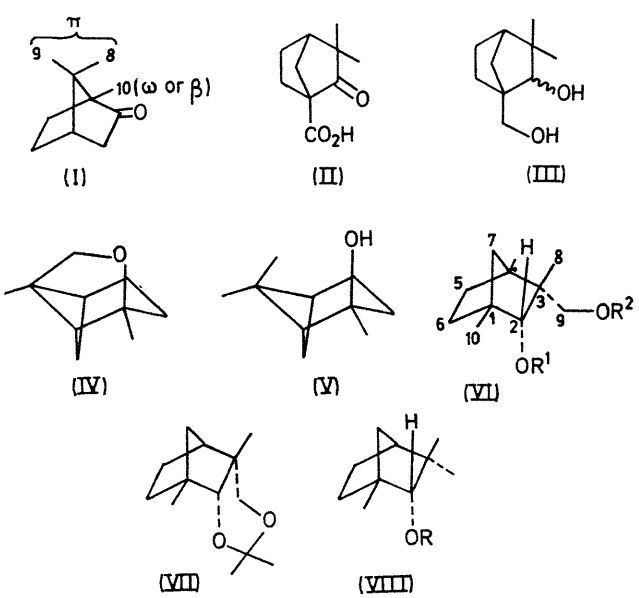
Synthesis of 9-Substituted Fenchane Derivatives

By N. BOSWORTH and P. D. MAGNUS*
(*Imperial College, London S.W.7*)

Summary 6,9-Dimethyl-7-oxatricyclo[4,3,0,$0^{3,9}$]nonane [readily prepared from (−)-β-pinene] provides convenient entry into 9-substituted fenchols, hitherto unknown derivatives.

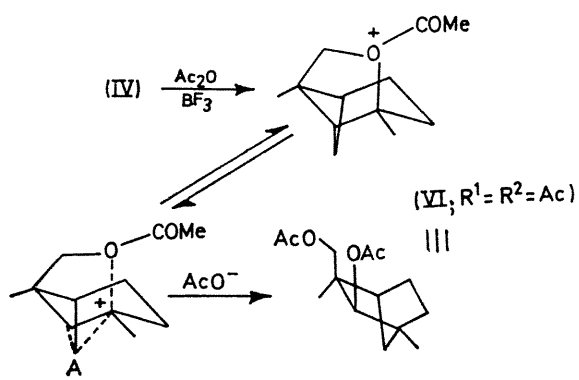
ESSENTIAL oil constituents based on the pinane skeleton represent an extensive series of compounds. The facility with which they are rearranged to other skeletal types has rendered them particularly useful as precursors of synthetic oils. The 10ω- or 10β, *cis*-8π- and *trans*-9π-substituted camphor derivatives (I) have been described[1a–f] but similar compounds in the fenchane series are virtually unknown. The only reported methyl substituted fenchane is Konovalov's "hydroxyfenchone"[2] established as 10-hydroxyfenchane.[3,4] The products (III) from reduction of camphenonic acid (II) were correlated with α- and β-fenchyl alcohol.[4]



6,9-Dimethyl-7-oxatricyclo[4,3,0,$0^{3,9}$]nonane[7,8] (IV) was prepared from (−)-β-pinene† *via* intramolecular (Br_2–HgO) oxidation of *trans*-pinanol (V)‡ following the procedure recently described.[7,8] Treatment of (IV) in acetonitrile at 20° with acetyl toluene-*p*-sulphonate[9] did not give the expected 9-substituted pinane but the 9-substituted fenchol (VI; $R^1 = SO_2{\cdot}C_6H_4Me$-*p*, R^2 = Ac) (80%), m.p. 156—158°, $[\alpha]_D^{25}$ + 54·0° (*c*, 1·9 in chloroform). Its structure was confirmed by its n.m.r. spectrum, τ 8·95 (3H, s), 8·99 (3H, s), 7·95 (3H, s), 7·55 (3H, s), 6·13 (2H, ABq, *J* 10 Hz), 5·48 (1H, bs), and 2·48 (4H, ABq *J* 8 Hz).§

Similarly, treatment of (IV) with acetic anhydride–boron trifluoride–ether[10] gave (VI; $R^1 = R^2$ = Ac) (90%), m.p. 38—40°, $[\alpha]_D^{28.5}$ + 36·0° (*c*, 5·6 in chloroform).[10] The n.m.r. spectrum showed signals at τ 8·92 (3H, s), 8·95 (3H, s), 7·96 (3H, s), 7·98 (3H, s), 6·4 (2H, ABq *J* 6 Hz), and 5·45 (1H, d, *J* 1·5 Hz).

To establish the relative configuration of the two oxygen functions and the stereospecificity of the rearrangement, the following sequence of reactions was carried out. The diacetate (VI; $R^1 = R^2$ = Ac) was reduced with lithium aluminium hydride in ether to the diol (VI; $R^1 = R^2$ = H), m.p. 81°, $[\alpha]_D^{28.5}$ − 21·2° (*c*, 2·8 in chloroform). The *cis*-disposition of the two hydroxy-groups was readily demonstrated by treatment of (VI; $R^1 = R^2$ = H) with 2,2-dimethoxypropane–toluene-*p*-sulphonic acid to give (VII), m.p. 74—76° (characterised by mass spectroscopy), τ 8·90 (3H, s), 8·86 (3H, s), 8·75 (3H, s), 8·71 (3H, s), 6·9 (1H, s), and 6·65 (2H, ABq *J* 6 Hz). Reaction of (VI; $R^1 = R^2$ = H) with toluene-*p*-sulphonyl chloride in pyridine[11] gave the tosylate (VI; R^1 = H, $R^2 = SO_2{\cdot}C_6H_4Me$-*p*), m.p. 138—139°, $[\alpha]_D^{28.5}$ 0·3° (*c*, 0·66 in chloroform). Acetylation of (VI; R^1 = H, $R^2 = SO_2{\cdot}C_6H_4Me$-*p*) gave (VI; R^1 = Ac, $R^2 = SO_2{\cdot}C_6H_4Me$-*p*) as an unstable oil [*cf.* (VI; $R^1 = SO^2{\cdot}C_6H_4Me$-*p*, R^2 = Ac)]. Its instability to chromatographic isolation (silica gel) is readily explained by intramolecular displacement of the primary tosylate[12] by the 2-*endo*-acetate. Such as displacement is sterically impossible with (VI; $R^1 = SO_2{\cdot}C_6H_4Me$-*p*, R^2 = Ac).



SCHEME

Reduction of (VI; R^1 = H, $R^2 = SO_2{\cdot}C_6H_4Me$-*p*) with lithium aluminium hydride gave α-fenchol (VIII; R = H) as an impure oil, $[\alpha]_D^{24}$ + 14·5° (*c*, 0·32 in methanol), τ 9·13 (3H, s), 9·04 (3H, s), 8·98 (3H, s), and 6·74 (1H, d, *J* 1·3 Hz). The τ value for 2H and $J_{2,6}$ is in agreement with the published data.[13] Further characterisation of (VIII; R = H) as the *p*-nitrobenzoate (VIII; R = $CO{\cdot}C_6H_4{\cdot}NO_2$-*p*), m.p. 107° (lit.,[14,15] 108—109°), $[\alpha]_D^{24}$ + 17·9° (*c*, 0·66 in CS_2), confirmed the structure.

† We thank Fritzsche Dodge and Olcott (New York) for the gift of (−)-β-pinene, $[\alpha]_D$ −21·3° (neat). Formulae (IV)—(VIII) are represented in their absolute configuration which depends on the known correspondence of (−)-α-pinene to (−)-β-pinene. (See A. J. Birch, *Ann. Reports*, 1950, **47**, 191.)

‡ *trans*-Pinanol, m.p. 57—59°, $[\alpha]_D^{20}$ − 4·4° (ether),[5] was prepared by ozonolysis of (−)-β-pinene[6] and treatment of the resulting (+)-nopinone with methylmagnesium bromide.

§ The methylene signals occurred at τ 7·9—9·0 and only diagnostic signals are mentioned (similarly for all subsequent n.m.r. data).

The remarkably high yield in the rearrangement of (IV) to (VI; $R^1 = R^2 = Ac$) compared with the rearrangement of esters from *trans*-pinanol (V) to α-fenchyl esters,[5,15] suggests that the mechanism (see Scheme) operates *via* A as an ion pair.

9-Substituted fenchols should find use in the synthesis of natural and synthetic oils.

All new compounds gave satisfactory spectral and microanalytical data.

(*Received, April 1st*, 1971; *Com.* 480.)

[1] (a) J. L. Simonsen and L. N. Owen, 'The Terpenes,' Vol. II, 2nd edn., p. 386; (b) 'Rodd's Chemistry of Carbon Compounds,' ed. S. Coffey, Vol. II, 2nd edn., Part C, p. 207; (c) T. Hasselström, *J. Amer. Chem. Soc.*, 1931, **53**, 1097; (d) E. J. Corey, M. Ohno, S. W. Chow, and R. A. Scherrer, *J. Amer. Chem. Soc.*, 1959, **81**, 6305; (e) E. J. Corey, S. W. Chow, and R. A. Scherrer, *J. Amer. Chem. Soc.*, 1957, **79**, 5773; (f) F. Dallacker, K. Ulrichs, and M. Lipp, *Annalen*, 1963, **667**, 50.
[2] S. S. Nametkin and V. A. Chochrjakova, *J. Russ. Phys. Chem. Soc.*, 1915, **47**, 1611.
[3] G. Komppa and A. Klami, *Ber.*, 1935, **68B**, 2001.
[4] T. Kuusinen, *Ann. Acad. Sci. Fennicae, Ser. AII*, 1956, **69**, 55; (*Chem. Abs.*, 1957, **51**, 4317.)
[5] W. D. Burrows and R. H. Eastman, *J. Amer. Chem. Soc.*, 1959, **81**, 245.
[6] J. Meinwald and P. G. Gassman, *J. Amer. Chem. Soc.*, 1960, **82**, 5445.
[7] T. W. Gibson and W. F. Erman, *J. Amer. Chem. Soc.*, 1969, **91**, 4771.
[8] A. G. Hortmann and R. E. Youngstrom, *J. Org. Chem.*, 1969, **34**, 3392.
[9] M. H. Karger and Y. Mazur, *J. Amer. Chem. Soc.*, 1968, **90**, 3878.
[10] (a) C. R. Narayanan and K. N. Iyer, *J. Org. Chem.*, 1965, **30**, 1734; (b) R. D. Youssefyeh and Y. Mazur, *Tetrahedron Letters*, 1962, 1287.
[11] A. J. Aasen and C. C. J. Culvenor, *J. Org. Chem.*, 1969, **34**, 4143.
[12] (a) Pl. A. Plattner and W. Long, *Helv. Chim. Acta*, 1944, **27**, 1872; (b) D. K. Fukushima, N. S. Leeds, H. L. Bradlow, T. H. Kritchevsky, M. B. Stokem, and T. F. Gallagher, *J. Biol. Chem.*, 1955, **212**, 449; (c) D. Taub, R. D. Hoffsommer, and N. L. Wendler, *J. Amer. Chem. Soc.*, 1959, **81**, 3291.
[13] (a) J. I. Musher, *Mol. Phys.*, 1963, **6**, 93; (b) A. Coulombeau and A. Rassat, *Bull. Soc. chim. France*, 1965, 3338.
[14] J. Kenyon and H. E. M. Priston, *J. Chem. Soc.*, 1925, 1472.
[15] N. A. Abraham and M. Vilkas, (a) *Bull. Soc. chim. France*, 1960, 1450; (b) *Ann. Chim. (France)*, 1960, **5**, 961.