

Acid-catalysed Dimerisation of a 7-Hydroxyindene

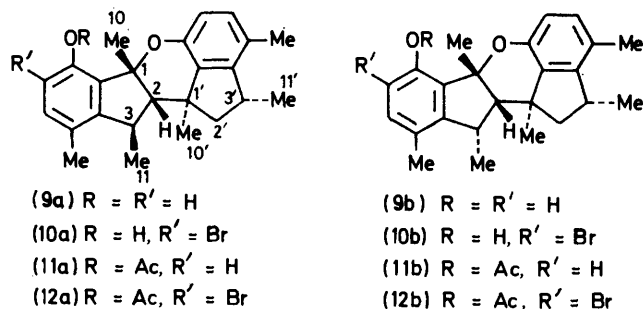
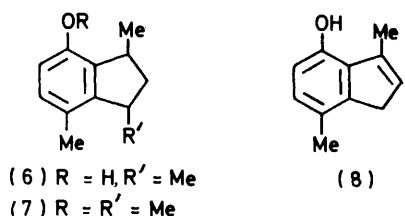
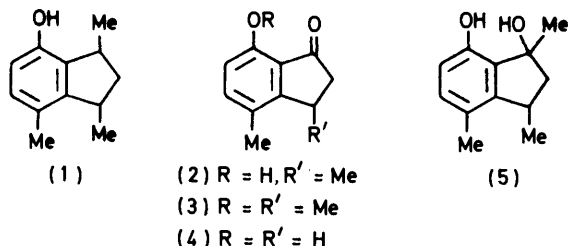
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Treatment of a 7-hydroxyindan-1-one (2) with methyl magnesium iodide gives the corresponding tertiary alcohol and two pentacyclic dimers, (9a) and (9b).

IN the course of studies on the functionalisation of alkyl groups by adjacent oxygen radicals,¹ we required a quantity of an indanol with *peri*-related phenolic hydroxy and aliphatic methyl groups. Compound (1) appeared accessible and we report its synthesis, and the structure and stereochemistry of two dimeric by-products.

RESULTS AND DISCUSSION

Addition of γ -butyrolactone and *p*-cresol to an aluminium chloride-sodium chloride melt^{2,3} gave the hydroxy-indanone (2) which was treated with methyl-



Only one enantiomer shown

magnesium iodide to give the expected diol (5) and a crystalline solid, subsequently shown to be a mixture of the epimeric hydroxy-ethers (9a) and (9b). The diol

(5) was not purified rigorously on account of the ease with which it underwent dehydration, but its spectral properties were consistent with this structure. On hydrogenation, it gave the trimethylindanol (6). The phenol (2) was also converted into its methyl ether (3); reaction of this compound with methylmagnesium iodide gave an unstable tertiary alcohol which was hydrogenated directly to the ether (7).

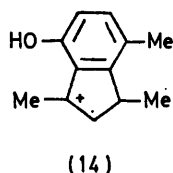
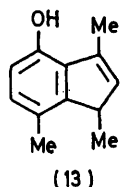
Initial work on the dimers was performed on the mixed isomers as they were inseparable by crystallisation and chromatography. Their structures were established as follows. The mixture analysed for $C_{24}H_{28}O_2$, had a mass-spectral molecular ion at m/e 348, and formed a mono-bromo derivative, a mono-acetate, and a bromo-acetate. The i.r. spectrum showed the presence of an ether linkage (ν_{max} 1260 and 1190 cm^{-1}) and an hydroxy (ν_{max} 3520 cm^{-1}). Careful fractional crystallisation gave one isomer of the bromo-acetate and this permitted interpretation of the 1H n.m.r. spectra of the mixed epimers. The n.m.r. spectra are entirely consistent with the assigned structure, the information being summarised in the Table. The spectra show one aliphatic methyl

1H N.m.r. spectra measured in CCl_4 ;
 chemical shifts expressed in δ relative to $SiMe_4$

Protons	Multiplicity	Compound							
		(9a)	(10a)	(11a)	(9b)	(10b)	(11b)	(12b)	
C-10'	s	0.72	0.72	0.69	0.92	0.92	0.89	0.89	
C-11	d	1.39	1.39	1.40	1.32	1.31	1.32	1.29	
C-11'	d	1.36	1.35	1.36	1.36	1.35	1.36	1.33	
C-10	s	1.67	1.66	1.62	1.59	1.60	1.55	1.54	
C-12	s	2.23	2.22	2.27	2.23	2.24	2.27	2.29	
C-12'	s	2.26	2.27	2.25	2.23	2.24	2.22	2.22	
C-3,3'	m	3.33	3.32	3.31	3.33	3.30	3.31	3.32	
C-7 OAc	s			2.31			2.31	2.31	
C-6 H	d	6.60		6.80	6.60		6.80		
C-6' H	d	6.60	6.69	6.80	6.60	6.71	6.80	6.55	
C-5 H	d	6.87	7.28	6.80	6.87	7.28	6.80	7.31	
C-5' H	d	6.87	6.94	6.80	6.87	6.95	6.80	6.82	

group and one methyl group attached to an oxygen-bearing carbon atom as singlets, two aliphatic methyl groups as doublets, and two aromatic methyl groups as singlets. The chemical shifts and multiplicities of the other protons are as expected. Conformational analysis and examination of the 1H n.m.r. spectra in the light of calculations,⁴ allowed us to assign structures (9a) and (9b) to the two dimers.⁵ The former structure was confirmed by an X-ray diffraction study performed in this Department;⁶ structure (9b) is indicated as correct by a comparison of the 1H n.m.r. spectra of the two epimers.

The comparative similarity of the two spectra demonstrates that the two isomers are of similar shape. A *trans*-fusion of rings B and c, or a *syn*-arrangement at C-2 and C-1' would produce a basket-shaped molecule, with the two aromatic rings lying over each other. Further, *trans*-fusion of a five- and a six-membered ring is less stable than *cis*-fusion. The two remaining chiral centres about which the molecules can differ are C-3 and C-3'. Examination of the pairs of n.m.r. spectra shows the biggest difference (0.2 p.p.m.) in chemical shift for the C-10' methyl group, with a smaller change (0.06–0.07 p.p.m.) for the C-10 and C-11 methyl groups. Other protons are little affected. Examination of models shows that isomerism about C-3' would be unlikely to produce the changes seen, as this centre is well removed from the main ring system. However, a change from the β - to the α -configuration about C-3 brings the C-11 and C-10' methyl groups very close together. This crowding can be avoided if rings B and c undergo a conformational change. This in turn will move the three methyl groups (C-10, C-10', C-11) with respect to the aromatic rings and thus affect their shielding. In (9a) the 10'-methyl is positioned more over the aromatic ring A than in (9b) and thus its signal appears at higher field. The 10- and 11-methyl groups move with respect to ring A, in this case the signals appearing further downfield in isomer (9a), which is consistent with a movement into the plane of this ring. The 11'-methyl group has a constant relationship to ring E in both isomers and is too far from ring A for the conformational changes here envisaged to affect its chemical shift. In each case, the examination of molecular models, and extrapolation of the published graphs⁴ connecting chemical shift with location of a proton relative to an aromatic ring, suggests that the chemical shifts observed in going from (9a), of established structure and stereochemistry, to (9b), are of the right order. The dimers are presumably formed by attack of a carbonium ion at C-1' (14) on an indene double bond (13); the cationic centre thus generated at C-1 then attacks the phenolic oxygen to complete the six-membered ring. An alternative mechanism, suggested by a referee,



would involve cyclo-addition of an *o*-quinone methide to an indene which, provided it obeys Alder's *endo* rule, would give a configuration at C-1' opposite to that established by the X-ray diffraction study.

In order to confirm and extend this work, an attempt was made to synthesise the dimer lacking methyl groups at C-3 and C-3'. To this end, *p*-tolyl acrylate was dropped onto a melt of aluminium chloride and

sodium chloride to give the indanone (4). Reaction of this ketone with methylmagnesium iodide gave the dimethylindene (8) but no evidence for the formation of a dimer.

EXPERIMENTAL

M.p.s were determined with a Reichert-Kofler hot-stage or an electrically heated copper block. I.r. spectra were measured with a Perkin-Elmer 237 spectrometer, and ¹H n.m.r. spectra with a Varian A60 spectrometer. Mass spectra were measured by Dr. J. S. Shannon, C.S.I.R.O., Australia, and microanalyses were performed by Professor A. D. Campbell, University of Otago, New Zealand.

2,3-Dihydro-3,4-dimethyl-7-hydroxyinden-1-one (2).—*p*-Cresol (22.4 g) and γ -butyrolactone (17.6 g) were added to a melt of aluminium chloride (200 g) and sodium chloride (20 g) at 140 °C. The mixture was stirred for 2 min at 200 °C and worked up to give the ketone (2) (28.0 g, 63%), b.p. 92–96 °C at 0.15 mmHg, m.p. 48.5–51.5 °C (from light petroleum) (lit.,² 54 °C).

Reaction of Methylmagnesium Iodide with the Ketone (2).—The ketone (2) (4.6 g, 0.026 mol) in dry ether (20 ml) was added to methylmagnesium iodide (0.15 mol) to give a yellow solid which reacted to give a yellow solution. The mixture was heated under reflux for 1 h and the Grignard complex decomposed by the addition of 2M sulphuric acid and ice. The product was chromatographed on deactivated alumina (150 ml), the light petroleum-ether (19 : 1) eluate giving a mixture of the isomers of 7-hydroxy-1,3,4,1',3',4'-hexamethyl-1,7'-epoxy-2,1'-bi-indene (9a, b) (0.92 g, 20%) which was recrystallised from light petroleum to give blocks, m.p. 166–167 °C and needles, m.p. 166–169 °C (Found: M^+ , 348; C, 82.5; H, 8.1. Calc. for $C_{24}H_{28}O_2$: M , 348; C, 82.7; H, 8.1%), ν_{\max} (CCl₄) 3 520 (OH), 1 260 (ArO), and 1 190 cm⁻¹ (C-O); the ¹H n.m.r. spectrum is in the Table.

6-Bromo-7-hydroxy-1,1',3,3',4,4'-hexamethyl-1,7'-epoxy-2,1'-bi-indene.—The ether (9a, b) (0.25 g, 0.7 mmol) in dioxan (15 ml) and water (2.5 ml) was treated with bromine (0.7 mmol). Addition of water and extraction with ether yielded the 6-bromo-derivative (0.18 g, 60%) which was fractionally crystallised from light petroleum, the *bromo-phenol* (10a) crystallising first, m.p. 178–180 °C (Found: C, 67.5; H, 6.4; Br, 18.6. $C_{24}H_{27}O_2Br$ requires C, 67.4; H, 6.4; Br, 18.7%); ν_{\max} (CCl₄) 3 500 (OH), 1 260, 1 240 (Ar-O), and 1 180 cm⁻¹ (C-O).

7-Acetoxy-1,1',3,3',4,4'-hexamethyl-1,7'-epoxy-2,1'-bi-indene (11a, b).—The hydroxy-ether (9a, b) (0.25 g, 0.72 mmol) in acetic anhydride (5 ml) and pyridine (0.3 ml) containing sodium acetate (0.1 g) was heated at 100 °C for 24 h. Addition of water and extraction with ether gave the mono-acetate (11a, b) (0.19 g, 64%), m.p. 119–120 °C (from ethyl acetate) (Found: C, 79.7; H, 7.7. Calc. for $C_{26}H_{30}O_3$: C, 80.0; H, 7.7%); ν_{\max} (CCl₄) 1 780 (Ar-OAc), 1 260 (Ar-O), and 1 200 cm⁻¹ (C-O).

7-Acetoxy-6-bromo-1,1',3,3',4,4'-hexamethyl-1,7'-epoxy-2,1'-bi-indene (12b).—The *bromo-phenol* (10a, b) (0.343 g, 0.8 mmol) in acetic anhydride (5 ml) and pyridine (0.3 ml) containing sodium acetate (0.1 g) was heated at 100 °C for 48 h. Addition of water and extraction with ether gave a solid which was chromatographed on deactivated alumina. The light petroleum-ether (19 : 1) eluate yielded blocks of the *bromo-acetate* (12b) (0.1 g, 25%), m.p. 141–143 °C (from light petroleum) (Found: C, 66.5; H, 6.3; Br, 17.1.

$C_{26}H_{20}BrO_3$ requires C, 66.5; H, 6.2; Br, 17.0%; ν_{\max} (CCl_4) 1 790 (Ar-OAc), 1 260 (Ar-O), and 1 190 cm^{-1} (C-O).

2,3-Dihydro-1,3,4-trimethylindene-1,7-diol (5).—The ketone (2) (5 g, 0.028 mol) in dry ether (30 ml) was added to methylmagnesium iodide (0.1 mol) in ether (30 ml), as described above. Decomposition of the Grignard complex with ammonium chloride and ice yielded an oil which slowly solidified. The solid was shown by t.l.c. to contain the dimers (9a, b) and the diol (5) (1.5 g, 27%), m.p. 75–97 °C (from light petroleum); ν_{\max} ($CHCl_3$) 3 590 and 3 440 (OH), and 1 275 cm^{-1} (C-O), $\delta_H(CDCl_3)$, 1.22 (3 H, d, *J* 7 Hz, 3-Me), 1.65 (3 H, s, 1-Me), 2.17 (3 H, s, 4-Me), 6.56 (1 H, d, *J* 8 Hz, 6-H), and 6.91 (1 H, d, *J* 8 Hz, 5-H).

2,3-Dihydro-3,4-dimethyl-7-methoxyinden-1-one (3).—The phenol (2) (1 g, 5.8 mmol) in methanol (20 ml) was added to diazomethane (2.8 g, 67 mmol) in ether (30 ml). The solution was worked up after 8 d to give a red gum, which crystallised to give the methyl ether (3) (0.4 g, 37%) as needles, m.p. 77–77.5 °C (from light petroleum) (lit.,⁷ 77–78 °C) (Found: C, 76.0; H, 7.6. Calc. for $C_{12}H_{14}O_2$: C, 75.8; H, 7.4%); $\nu_{\max}(CCl_4)$ 1 720 (C=O), 1 290 (Ar-O), 1 050 (Me-O) cm^{-1} ; $\delta_H(CCl_4)$ 1.30 (3 H, d, *J* 7 Hz, 3-Me), 2.30 (3 H, s, 4-Me), 3.84 (3 H, s, OMe), 6.64 (1 H, d, *J* 8 Hz, 6-H), and 7.21 (1 H, d, *J* 8 Hz, 5-H).

2,3-Dihydro-7-methoxy-1,3,7-trimethylindene (7).—Methylmagnesium iodide (0.01 mol) was added slowly to the ketone (3) (1 g, 0.0053 mol) in ether (10 ml) and benzene (3 ml). The mixture was heated under reflux for 30 min and set aside overnight. Decomposition with ammonium chloride and ice, and extraction with ether, gave an oil showing two products on t.l.c. The oil was hydrogenated in ethyl acetate (50 ml) over 5% palladium-charcoal (0.1 g) for 1.5 h. Removal of solvent and chromatography on alumina gave the ether (7) (0.63 g, 65%) as needles, m.p. 48.5–49 °C (from ethanol-water) (Found: C, 82.3; H, 9.4; O, 8.5. $C_{13}H_{18}O$ requires C, 82.1; H, 9.5; O, 8.4%); $\nu_{\max}(CCl_4)$ 1 265 (Ar-O) and 1 075 (Me-O) cm^{-1} ; $\delta_H(CCl_4)$ 1.27 (3 H, d, *J* 7 Hz, 1-Me), 1.28 (3 H, d, 7 Hz, 3-Me), 2.21 (3 H, s, 7-Me), 3.74 (3 H, s, OMe), 6.50 (1 H, d, *J* 8 Hz, 5-H), and 6.88 (1 H, d, *J* 8 Hz, 6-H).

2,3-Dihydro-1,3,7-trimethylinden-4-ol (1).—The indandiol (5) (0.7 g, 3.6 mmol) in ethyl acetate (30 ml) was hydrogen-

ated over 5% palladium-charcoal (0.1 g) during 1 h. Removal of solvent and catalyst gave the indanol (1) (0.6 g, 93%) as blocks, m.p. 83.5–84 °C (from light petroleum) (Found: C, 82.0; H, 9.3. $C_{12}H_{16}O$ requires C, 81.8; H, 9.15%); $\nu_{\max}(CHCl_3)$ 3 590 and 3 400 (OH), and 1 190 cm^{-1} (C-O); $\delta_H(CCl_4)$ 1.32 (3 H, d, *J* 7 Hz, 1-Me), 1.37 (3 H, d, *J* 7 Hz, 3-Me), 2.24 (3 H, s, 7-Me), 6.55 (1 H, d, *J* 8 Hz, 5-H), and 6.90 (1 H, d, *J* 8 Hz, 6-H).

3,7-Dimethylinden-4-ol (8).—*p*-Tolyl acrylate (18.0 g, 0.11 mol) was dropped onto a melt (140 °C) of aluminium chloride (400 g, 3.0 mol) and sodium chloride (100 g, 1.7 mol). The black solid that formed on cooling was decomposed with ice and hydrochloric acid to give the ketone (4) (1.9 g, 10%), m.p. 100–108 °C (lit.,² 110 °C); $\nu_{\max}(CCl_4)$ 3 350 (OH) and 1 690 cm^{-1} (C=O); $\delta_H(CCl_4)$ 2.19 (3 H, s, 4-Me), 2.75 (4 H, m, 2-H₂ and 3-H₂), 6.69 (2 H, d, *J* 8 Hz, 6-H), and 7.20 (2 H, d, *J* 8 Hz, 5-H). The ketone (4) (0.8 g, 5.4 mmol) in ether (25 ml) and benzene (1 ml) was added to methylmagnesium iodide (28 mmol) in ether (25 ml). The mixture was heated under reflux for 3 h, set aside overnight, and the complex decomposed with 2M-sulphuric acid. Ether extraction and chromatography on alumina gave the hydroxy-indene (8) (0.629 g, 79%) as needles (from light petroleum), m.p. 101.5–102 °C (Found: C, 82.5; H, 7.65; O, 10.2. $C_{11}H_{12}O_2$ requires C, 82.5; H, 7.55; O, 10.0%); $\nu_{\max}(CCl_4)$ 3 620 (OH) and 1 280 cm^{-1} (Ar-O); $\delta_H(CCl_4)$ 2.20 (3 H, s, 4-Me), 2.31 (3 H, m, 1-Me), 3.07 (2 H, m, 3-H₂), 5.94 (1 H, m, 2-H), 6.40 (1 H, d, *J* 8 Hz, 6-H), and 6.74 (1 H, d, *J* 8 Hz, 5-H).

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