

The Indans Formed by Dimerization of Some Aromatic Terpenoids

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Abstract

Previous work upon the dimerization of carvacrol derivatives to form indans is corrected.

During attempts to synthesize compound (1), the diterpenoid occurring in *Callitris macleayana* heartwood,¹ we had occasion to reflux the *o*-quinol acetate (2) with ethanolic sulfuric acid. One product isolated from this reaction was the dihydroxy indan (3a), m.p. 179–180°.

The structure of compound (3a) was readily assigned from the 300-MHz ¹H n.m.r. spectrum. Three aromatic protons showed the expected coupling pattern (d; dd; d) for a 1,3,4-trisubstituted benzene ring. In addition, two sharp aromatic signals were apparent for a 1,2,4,5-tetrasubstituted ring, with one of these protons showing a small (0.5 Hz) coupling to a benzylic methyl group. An AB quartet (δ 2.13, 2.35; *J* 13 Hz) was ascribed to the C2 methylene group. The coupling constant suggests these protons are geminal, and the chemical shifts indicate that they are β to two aromatic rings. Two benzylic methyls (δ 2.19, 2.24), three further methyls (δ 1.02, 1.29 and 1.61) and two hydroxyl groups account for all the protons.

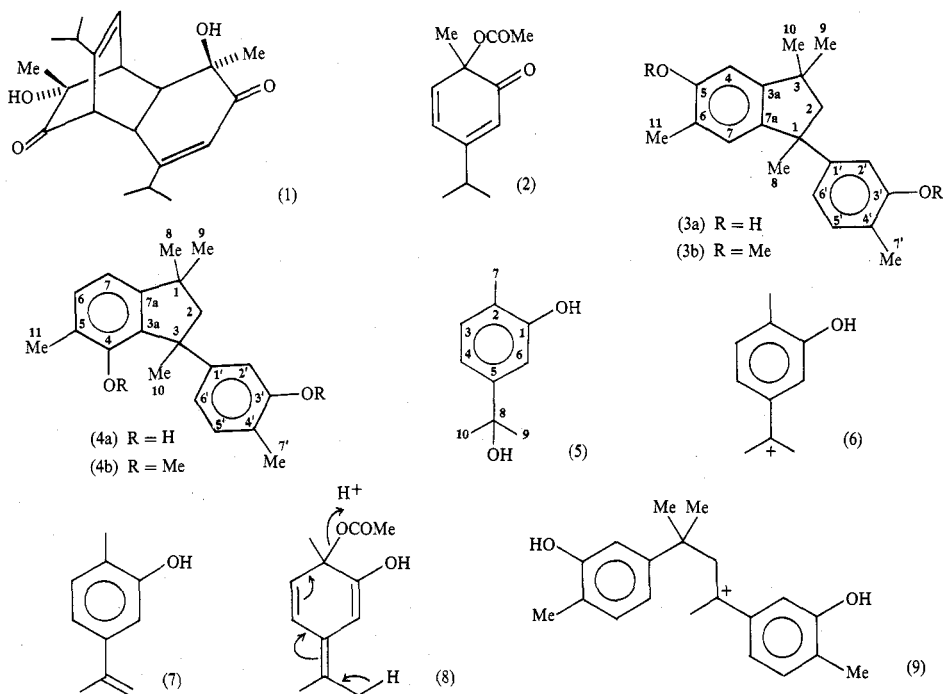
The indan (3a) appeared to be an unreported compound. However, the isomeric indan (4a) has been reported² to form when the tertiary alcohol (5) is kept in 'deuteriochloroform solution for a long time'. Comparison of the reported ¹H n.m.r. data and m.p. (170–171°) for compound (4a) with those now measured for compound (3a) indicated that they were likely to be the same, and that the Indian workers² had actually isolated compound (3a) rather than (4a). These workers² made reference to the dimethyl ether of an indan, which they claimed had structure (4b) (m.p. 104–105°) for which they quote a literature³ melting point (95–96°). However, the literature³ quoted, John and Krishna Rao, had claimed the structure (3b) rather than (4b) for the dimethyl ether, and had preferred this structure on the mechanistic grounds that the cyclization pathway leading to (4b) would be sterically unfavoured. The quality of the ¹H n.m.r. spectra presented in both these papers^{2,3} was not sufficient to assign structures unambiguously.

¹ Carman, R. M., Lambert, L. K., Owsia, S., and Van Dongen, J. M. A. M., unpublished data.

² Patwardhan, S. A., and Gupta, A. S., *Phytochemistry*, 1983, 22, 2080.

³ John, T. K., and Krishna Rao, G. S., *Indian J. Chem. B*, 1976, 14, 805.

This work has now been repeated. Alcohol (5) after three weeks in deuteriochloroform provided two compounds (g.c. and t.l.c.) in the ratio 9:1. Chromatography allowed a separation. The major component was diol (3a). The minor isomer showed ^1H n.m.r. data consistent with structure (4a) with a large (J 7.6 Hz) coupling between the adjacent aromatic protons H 6 and H 7.



Methylation of the major isomer provided compound (3b), m.p. 111–112°, with n.m.r. characteristics very similar to those reported by John and Krishna Rao,³ although our melting point would suggest that both^{2,3} the earlier groups of workers were dealing with impure samples.

The ^{13}C n.m.r. spectra of isomers (3a) and (4a) are consistent with the assigned structures, although they do not allow a simple differentiation between the two isomers. A fully coupled ^{13}C n.m.r. spectrum of compound (3a) at 100.54 MHz provided the carbon atomic assignments listed in the Experimental section. C 2 (δ 59.29) was an aliphatic triplet of multiplets. C 1 (δ 49.97) and C 3 (δ 42.61) were differentiated on the basis of the much-larger substituent effect for a phenyl ring compared to a methyl group.⁴ C 4 (δ 108.73) was a sharp doublet with no observable

⁴ Wehrli, F. W., and Wirthlin, T., 'Interpretation of Carbon-13 N.M.R. Spectra' p. 37, 47 (Heyden: London 1978).

long-range coupling. C6 (δ 122.15) provided a quartet with coupling to the attached methyl protons, while C7 (δ 126.96) occurred as a doublet of quartets, with coupling to the same methyl protons. An unresolved multiplet at δ 140.90 was assigned to C7a. This shift is compatible with a value calculated by using published chemical shift substituent parameters.⁴ C2' (δ 113.58) occurred as a ddd with coupling to H2', H5' and H6'. C4' (δ 120.60) formed an apparent broadened quintet, with equal coupling to the three C4' methyl protons and to H6'. C5' (δ 130.49) was a doublet with additional long-range coupling to the three methyl protons and to H6'. C6' (δ 119.02) was a doublet with further long-range coupling to H2' and H5'. The oxygenated carbons C5 and C3' (δ 153.26 and 153.33) showed considerable overlap and could not be specifically assigned. Similarly, C3a and C1' (δ 150.97, 151.54) were not specifically assigned. The assignments to compounds (3b) and (4a) follow similar arguments.

The formation of indans (3a) and (4a) from either (2) or (5) can be readily rationalized. Mild acid-catalysed dehydration of the benzylic tertiary alcohol (5) provides both the carbocation (6) and the styrene (7). Deacetylation of compound (2), possibly in its enolic form (8) where aromatization will provide the driving force, also generates (6) and (7). Dimerization of cation (6) with the styrene (7) provides the new cation (9), which undergoes a Friedel-Crafts alkylation to form either (3a) or (4a), with (3a) likely to predominate for steric reasons.

Experimental

N.m.r. spectra were recorded upon Jeol JNM-PS 100 (¹H, 100 MHz), Bruker CXP-300 (¹H, 300 MHz) and Jeol JNM-GX 400 (¹H, 400 MHz; ¹³C, 100.54 MHz) spectrometers. All spectra were recorded in CDCl₃ containing internal tetramethylsilane. G.c.-m.s. data were obtained upon a Hewlett-Packard 5992 instrument with either a 25-m OVI or 25-m Carbowax 20M capillary column.

Indan (3a)

6-Acetoxy-3-isopropyl-6-methylcyclohexa-2,4-dienone (2) (4.0 g) was refluxed (50 h) in ethanol (100 ml) containing ethanolic sulfuric acid (5%, 10 ml). The solution was cooled, diluted with water and extracted with dichloromethane. Chromatography of the product over silica (ether/hexane, 6 : 1) provided 1-(3'-hydroxy-4'-methylphenyl)-1,3,3,6-tetramethylindan-5-ol* (3a) (0.5 g), m.p. 179–180° (from hexane) [lit.² 170–171° for the compound (?) assigned a different structure] (Found: C, 80.9; H, 8.3. C₂₀H₂₄O₂ requires C, 81.0; H, 8.2%). U.v. (ethanol) 283.5 nm (ϵ 607). ¹H n.m.r. (300 MHz) δ 1.02, 1.29, two s, 3,3-Me₂; 1.61, s, 1-Me; 2.13, 2.35, ABq, *J* 13 Hz, 2×H₂; 2.19, br s, 4'-Me; 2.24, br s, 6-Me; 4.61, 4.70, two br s, 2×OH; 6.57, d, H₂'; 6.59, s, H₄; 6.70, dd, H₆'; 6.84, q, H₇; 6.99, dq, H₅'; with *J*_{7,6-Me} 0.5, *J*_{2',6'} 1.8, *J*_{5',6'} 7.8 and *J*_{5',4'-Me} 0.5 Hz. ¹³C n.m.r. (100.54 MHz) δ 15.25, 16.03, two q, C₁₁ and C₇'; 30.37, 30.66, 31.01, three q, C₈, C₉ and C₁₀; 42.61, s, C₃; 49.97, s, C₁; 59.29, t, C₂; 108.73, d, C₄; 113.58, ddd, C₂'; 119.02, ddd, C₆'; 120.60, quintet, C₄'; 122.15, q, C₆; 126.96, dq, C₇; 130.49, dq, C₅'; 140.90, s, C_{7a}; 150.97, 151.54, two s, C_{3a} and C₁'; 153.26, 153.33, two s, C₅ and C₃'; with ¹*J*_{C₂H₂} 128.9, ¹*J*_{C₄H₄} 154.0, ²*J*_{C₆H₁₁} 5.3, ¹*J*_{C₇H₇} 154.0, ³*J*_{C₇H₁₁} 5.0, ¹*J*_{C₁₁H₁₁} 126.8, ³*J*_{C₁₁H₇} 5.1, ¹*J*_{C₂'H₂'} 154.1, ³*J*_{C₂'H₆'} 6.8, ²*J*_{C₄'H₇'} = ³*J*_{C₄'H₆'} 6.0, ¹*J*_{C₅'H₅'} 154.3, ²*J*_{C₅'H₆'} 2.1, ³*J*_{C₅'H₇'} 4.8, ¹*J*_{C₆'H₆'} 156.0, ²*J*_{C₆'H₅'} 2.3, ³*J*_{C₆'H₂'} 6.9, ¹*J*_{C₇'H₇'} 126.8, ³*J*_{C₇'H₅'} 5.1 Hz. *m/z*: 297 (M+1, 7%), 296 (M, 28), 295 (2), 283 (3), 282 (21), 281 (M-Me, 100), 280 (2), 266 (2), 265 (3), 251 (3), 189 (6), 174 (3), 173 (13), 165 (6), 159 (3), 158 (4), 135 (3), 133 (5), 121 (5).

* The extra numbering of carbon atoms 8–11 in structures (3) and (4) is included for convenience.

Indan (4a)

Compound (5) was synthesized by addition of methylmagnesium iodide to 3-hydroxy-4-methylacetophenone. Compound (5) had m.p. 105–107° (benzene/hexane) (lit.² 103–105°). ¹H n.m.r. (100 MHz) δ 1.51, s, 2×Me; 2.20, s, 2-Me; 2.36, s, OH; 6.37, d, H₆; 6.81, dd, H₄; 7.05, d, H₃; 7.10, s, OH; with $J_{3,4}$ 8 and $J_{4,6}$ 2 Hz. ¹³C n.m.r. (100.54 MHz) δ 15.41, q, C₇; 31.36, q, C₉ and C₁₀; 73.18, s, C₈; 111.58, d, C₆; 116.15, d, C₄; 122.84, s, C₂; 130.71, d, C₃; 148.04, s, C₅; 154.09, s, C₁; with $^3J_{C_1,H_3}$ 3.4, $^3J_{C_1,H_7}$ 4.7 $^1J_{C_3,H_3}$ 155.1, $^2J_{C_3,H_4}$ 1.7, $^3J_{C_3,H_7}$ 4.6, $^2J_{C_4,H_3}$ 1.7, $^1J_{C_4,H_4}$ 157.2, $^3J_{C_4,H_6}$ 6.4, $^1J_{C_6,H_6}$ 155.7, $^3J_{C_6,H_4}$ 6.7, $^3J_{C_7,H_3}$ 5.2, $^4J_{C_4,H_4}$ 1.2, $^1J_{C_7,H_7}$ 127.1, $^2J_{C_8,H_9} = ^2J_{C_8,H_{10}}$ 3.7, $^1J_{C_9,H_9} = ^1J_{C_{10},H_{10}}$ 126.5 Hz. *m/z*: 166 (M, 12%), 151 (17), 148 (32), 133 (17), 108 (14), 107 (10), 105 (10), 77 (14), 51 (10), 43 (100), 39 (13).

Compound (5) (100 mg) was stored in (D)chloroform (1 ml, 26 days at ambient temperature). The solvent was removed, and chromatography (silica; dichloromethane) afforded firstly 3-(3'-hydroxy-4'-methylphenyl)-1,1,3,5-tetramethylindan-4-ol (4a) (6 mg), m.p. 104–106° (from hexane) [lit.² 170–171° for the compound now shown to have structure (3a)]. The compound was pure by g.c. ¹H n.m.r. (400 MHz) δ 1.27, 1.35, two s, 1,1-Me₂; 1.74, s, 3-Me; 2.16, 2.22, two br s, 5-Me and 4'-Me; 2.16, 2.27, ABq, J 13.4 Hz, 2×H₂; 4.34, 4.73, two br s, 2×OH; 6.70, d, H₂'; 6.71, d, H₇; 6.84, dd, H₆'; 7.07, dq, H₆, 7.08, dq, H₅'; with $J_{6,7}$ 7.6, $J_{6,11}$ 0.5, $J_{2',6'}$ 1.7, $J_{5',6'}$ 7.8, $J_{5',7'}$ 0.5 Hz. ¹³C n.m.r. (100.54 MHz) δ 15.32, 15.36, two q, C₁₁ and C₇'; 26.90, q, C₁₀; 31.43, 31.53, two q, C₈ and C₉; 43.31, s, C₁; 49.59, s, C₃; 60.93, t, C₂; 113.11, 114.48, two d, C₇ and C₂'; 118.35, d, C₆'; 122.14, 123.02, two s, C₅ and C₄'; 130.80, 131.47, two d, C₆ and C₅'; 134.14, s, C_{3a}; 148.10, 150.02, two s, C_{7a} and C₁'; 151.59, 154.16, two s, C₄ and C₃'. *m/z*: 297 (M+1, 9%), 296 (M, 43), 282 (24), 281 (M-Me, 100), 279 (3), 189 (9), 188 (6), 174 (7), 173 (53), 159 (4), 158 (6), 149 (10), 135 (4), 133 (4), 121 (9).

Further analysis gave the *indan* (3a) (60 mg), identical (¹H and ¹³C n.m.r. spectra) with the compound described above.

Dimethoxy Indan (3b)

Dimethyl sulfate (1 ml) was added to a mixture of *indan* (3a) (150 mg) and potassium carbonate (540 mg) in acetone (10 ml). The mixture was refluxed (15 h), cooled, filtered and the solvent removed. The residue in ether was washed (aqueous ammonia; saturated sodium chloride) and dried (sodium sulfate) to afford 5-methoxy-1-(3'-methoxy-4'-methylphenyl)-1,3,3,6-tetramethylindan (3b) (110 mg), m.p. 111–112° (from hexane) (lit.³ 95–96°) (Found: C, 81.5; H, 8.8. Calc. for C₂₂H₂₈O₂: C, 81.4; H, 8.7%). ¹H n.m.r. (400 MHz) δ 1.06, 1.33, two s, 3,3-Me₂; 1.64, s, 1-Me; 2.16, 2.21, two br s, 6-Me and 4'-Me; 2.17, 2.39, ABq, J 13.0 Hz, 2×H₂; 3.73, 3.82, two s, 2×OMe; 6.63, s, H₄; 6.65, dd, H₆'; 6.70, d, H₂'; 6.88, q, H₇; 6.97, dq, H₅'; with $J_{7,6-Me}$ 0.5; $J_{2',6'}$ 1.7; $J_{5',6'}$ 7.7 and $J_{5',4'-Me}$ 0.5 Hz. ¹³C n.m.r. (100.54 MHz) δ 15.70, 16.49, two q, C₁₁ and C₇'; 30.54, 30.78, 31.16, three q, C₈, C₉ and C₁₀; 42.91, s, C₃; 50.30, s, C₁; 55.23, 55.37, two q, 2×OMe; 59.80, t, C₂; 103.80, d, C₄; 108.99, d, C₂'; 118.67, d, C₆'; 123.54, s, C₄'; 125.09, s, C₆; 126.68, d, C₇; 129.93, d, C₅'; 140.21, s, C_{7a}; 150.53, 150.69, two s, C_{3a} and C₁'; 157.37, 157.49, two s, C₅ and C₃'. *m/z*: 325 (M+1, 5%), 324 (M, 22), 310 (23), 309 (M-Me, 100), 203 (7), 188 (5), 187 (31), 173 (5), 172 (10), 157 (5), 147 (11), 135 (7), 134 (8), 132 (6), 129 (5), 128 (5), 111 (5).