Indane 3a,4-Oxide: Formation by Isomerisation of Indane 3a,7a-Oxide and Confirmation of Structure by an Alternative Synthesis

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Indane 3a,7a-oxide (1) is isomerised on heating to indane 3a,4-oxide (2). A number of attempts to prepare the latter from 3a,6-dihydroindanes were unsuccessful, but a preparation from 10-oxatricyclo[4.3.1.0^{1,6}]dec-3-ene provided confirmation of the assigned structure (2).

In general, benzene oxides exist in valency tautomeric equilibrium with their oxepin forms.¹ For indane 3a,7a-oxide (1) the oxepin form is sterically destabilised by the presence of the three-carbon bridge, and the compound is effectively constrained to be a benzene oxide. We find that on heating, either neat or in nonpolar solvents, indane 3a,7a-oxide is partly converted into an orange-coloured substance. This compound was difficult to obtain pure owing to its ready isomerisation to indan-4-ol, but its colour and spectroscopic data obtained by difference (see Table) suggest that it is an isomeric benzene oxide which is in equilibrium with a significant amount of an oxepin. In particular the n.m.r. solvent effect parallels that for benzene oxideoxepin itself,¹ where the more polar solvent (CDCl₃) leads to an increase in the proportion of benzene oxide in the equilibrium mixture.

Spectroscopic data for indane 3a,4-oxide ^a

λ _{sh} (EtOH)	305 nm
v _{max.} (film)	1 655, 1 570, 1 230, 1 070, 1 020, 840, 755 cm ⁻¹
$\tau(CCl_4)$	4.3 (2 H, m), 4.8 (2 H, m)
$\tau(CDCl_3)$	4.15 (2 H, m, H-6 and -7), 4.5 (1 H, br, H-5),
	5.07 (1 H, d, J 5 Hz, H-4)

^a Obtained by difference from mixtures with indane 3a,7a-oxide.

The indane 3a,4-oxide structure (2) derived by [1,5] signatropic shift ('oxygen walk') from (1) was postulated for the isomer, the corresponding oxepin being (3). Although (2) had been previously suggested ² as an intermediate involved in the solvolysis of (1), spectroscopic data had not been obtained, and we considered it desirable to confirm the proposed structure by an alternative preparation. Two different approaches were explored.

The first approach was based on the consideration that 3a,6-dihydroindane (4) should be selectively epoxidised at the trisubstituted double bond; bromination of the remaining double bond followed by dehydrobromination should then afford (2). Unfortunately we were unable



to devise a simple practicable route to the diene (4). All attempts oxidatively to decarboxylate the dicarboxylic acid (5), derived from the corresponding anhydride,³ gave either indane or indane-4,5-dicarboxylic anhydride. Equally, attempts to alkylate intramolecularly a radical anion derived from (6; X = Cl, I, OSO₂Me,

¹ E. Vogel and H. Günther, Angew. Chem. Internat. Edn., 1967, **6**, 385.

² G. J. Kasperek, P. Y. Bruice, T. C. Bruice, H. Yagi, and D. M. Jerina, *J. Amer. Chem. Soc.*, 1973, 95, 6041; T. C. Bruice and P. Y. Bruice, *Accounts Chem. Res.*, 1976, 9, 378.

³ V. F. Kucherov and E. P. Serebryakov, *Izvest. Akad. Nauk* S.S.S.R. Otdel. Khim. Nauk, 1960, 1057 (Chem. Abs., 1961, 55, 475h).

 $OSO_2C_6H_4Me-p$, or NEt₃) under Birch reduction conditions failed, and gave n-propylbenzene and/or 1,4dihydro-2-n-propylbenzene instead. Apparently efficient electron transfer with reduction of side chain functionality occurred either inter- or intra-molecularly to the exclusion of alkylation.* A variant on the latter approach involving an attempted preparation of the bicyclic acid (8) by reductive alkylation of the chloroacid (7) for which a more stable carbanionic intermediate might have been expected (cf. ref. 5 for intermolecular analogy) gave 1,4-dihydro-2-propylbenzoic acid via preferential side-chain reduction again. The chloro-acid (7) was prepared by treatment of the lactone (9) with hydrogen chloride-zinc chloride. Attempted preparation of the lactone (9) by pyrolysis of N-[3-(2carboxyphenyl)propyl]pyridinium chloride ⁶ gave a mixture of (9) and the isomeric lactone (10), the latter being presumably formed via acid catalysed eliminationaddition. This rearrangement was obviated by a modified preparation in which the zwitterionic 2-(3pyridinopropyl)benzoate was pyrolysed to give pure (9). On heating (9) with pyridinium chloride, isomerisation to the lactone (10) occurred.

In another variation of the 3a,6-dihydroindane approach, the acid (11),[†] prepared by Birch reduction of indane-5-carboxylic acid, resisted all attempts at epoxidation and evasively regenerated the indane-5carboxylic acid.



The second approach to (2) which was tried started

from the known epoxide (12),⁸ and is summarised in the Scheme,[†] The n.m.r. spectrum of the mixture of diastereoisomeric dibromo-alcohols (14) indicated that no allylic rearrangement had occurred, and that all four stereoisomers of (14) were present. One of these, presumed to be (16), was isolated by chromatography and gave a compound considered to be (17) on treat-

been discussed by Grossel and Hayward.7

trans-Configuration assigned to (13) on the basis of expected inversion in the hydride reduction step.

ment with base. The crude dibromide mixture with sodium methoxide in ether gave the bromo-epoxide (17), 4-bromoindane (15), and indane 3a,4-oxide (2). The last-named material was spectroscopically identical with the orange compound which had been obtained by thermal isomerisation of indane 3a,7a-oxide. Assuming anti-elimination and diaxial ring closure to epoxide, it is



likely that (18) is the precursor of the indane oxide and (19) and (20) are progenitors of 4-bromoindane.

EXPERIMENTAL

¹H N.m.r. spectra were recorded with Perkin-Elmer R32 and R14 instruments operating at 90 and 100 MHz, respectively (Me₄Si as internal standard).

Thermal Isomerisation of Indane 3a,7a-Oxide.—A large number of experiments were carried out in an attempt to optimise conditions for formation of the orange coloured indane 3a,4-oxide. The chief difficulty was isomerisation to indan-4-ol which occurred capriciously after various time intervals, and particularly on heating the neat substrate.

Spectroscopic data given in the Table were obtained on material which had been heated in paraffin oil at 140 °C for 75 min, and then distilled (b.p. 28° at 0.3 mmHg). The product contained ca. 25% of indane 3a,4-oxide (by n.m.r.).

The best conversion (38%) was obtained after heating indane 3a,7a-oxide (200 mg) in toluene (1 ml) under reflux for 4 h, though attempts to repeat this experiment gave indan-4-ol.

Bicyclo [4.3.0] non-5-ene-2, 3-dicarboxylic Acid (5).--- A solution of bicyclo[4.3.0]non-5-ene-2,3-dicarboxylic anhydride ³ (27 g, 0.177 mol) and potassium hydroxide (2.2 equiv.) in methanol-water (9:1; 300 ml) was refluxed for 3 h. The cooled solution was added to water (500 ml) and acidified with hydrochloric acid. The product was extracted into ether and the combined ethereal solutions were washed with brine and dried $(MgSO_4)$. Evaporation gave a solid (28.5 g). Recrystallisation from acetone-light petroleum (1:2) gave crystals of the acid (5) (25.5 g, 87%), m.p. 170-171°

^{*} For reactions of radical anions of aromatic hydrocarbons with alkyl halides, etc., see ref. 4. † The five-bond homoallylic H,H coupling constant of (11) has

⁴ N. L. Holy, Chem. Rev., 1974, 74, 243.

⁵ H. van Bekkum, C. B. Van den Bosch, G. van Minnen-Pathuis, J. C. deMos, and Z. M. van Wijk, *Rec. Trav. chim.*, 1971, **90**, 137.

F. Krollpfeiffer and A. Muller, Ber., 1935, 68, 1169.

⁷ M. C. Grossel and R. C. Hayward, J.C.S. Perkin II, 1976, 851.

⁸ E. Giovannini and H. Wegmuller, Helv. Chim. Acta, 1958, 41, 933.

(Found: C, 62.6; H, 6.8. C₁₁H₁₄O₄ requires C, 62.8; H, 6.7%), $\tau[(CD_3)_2CO] - 0.5$ (2 H, br,s, CO_2H), 4.55 (1 H, m, =CH), 6.50 (2 H, m, CH·CO₂H), and 7.1-8.7 (9 H).

Attempted Decarboxylation of the Acid (5).-(a) The diacid (520 mg, 2.5 mmol), lead tetra-acetate (85%; 1.4 g, 1.05 mol), and pyridine (30 ml) were stirred at 70 °C for 1 h. After pouring into aqueous HCl (50%) isolation with ether gave a brown oil (200 mg). The i.r. and n.m.r. spectra indicated this was indane-4,5-dicarboxylic anhydride.

(b) 9 Oxygen was bubbled through anhydrous pyridine (12 ml) for 15 min. The diacid (1.05 g, 5 mmol) and lead tetra-acetate (85%; 3.85 g, 1.5 equiv.) were added and the flask was immersed in an oil-bath at 67 °C. After 10 min the mixture was cooled to 20 °C and poured into nitric acid (2m; 100 ml). Isolation with ether gave the anhydride (180 mg) as in method (a).

(c) 10 The diacid (1.05 g, 5 mmol), pyridine (720 mg, 2 equiv.), lead tetra-acetate (85%; 2.8 g, 1.1 equiv.), and anhydrous Me₂SO were mixed and stirred for 1 h. The solution rapidly became hot and effervesced. When it was cool, water (50 ml) was added and the product extracted into light petroleum. The combined organic solutions were washed successively with sodium hydroxide (2M), water, and HCl (2M), and dried (MgSO₄). Evaporation gave an oil (150 mg) shown by comparison (i.r. and n.m.r.) with authentic material to be indane.

(d) The diacid (1.05 g, 5 mmol), lead tetra-acetate (85%); 4.2 g, 1.7 equiv.), and anhydrous Me₂SO (10 ml) were stirred at 20 °C for 1 h. The mixture was worked up as before to give indane (165 mg).

Reductions of 3-Phenylpropyl Derivatives.-The 3-phenylpropyl derivative (0.025 mol) in anhydrous ether (15 ml) was added to a solution of lithium or sodium (2.2 equiv.) in liquid ammonia (100 ml) at -78 °C under nitrogen. After stirring for 2 h ethanol (5 ml) and ether (30 ml) were added and the mixture was stirred until the blue colour disappeared (ca. 5 min). The mixture was worked up to yield (80-90%) propylbenzene and 1,4-dihydro-2-propylbenzene (9:1), identified by comparison with authentic material.

The compounds reduced by this method were the iodide, methanesulphonate, and chloride. Reduction of the triethylammonium iodide by the above procedure using lithium (6 equiv.) produced only 1,4-dihydro-2-propylbenzene, b.p. 65° at 10 mmHg (Found: C, 88.2; H, 11.4. C₉H₁₄ requires C, 88.45; H, 11.55%), τ(CCl₄) 4.38 (2 H, s, =CH), 4.62 (1 H, s, =CH), 7.42 (4 H, H-1 and -4), 8.08 (2 H, t, CH₂·CH₂·CH₃), 8.57 (2 H, m, CH₂·CH₃), and 9.10 (3 H, t, CH₃).

8.9-Dihydro-6-oxabenzocyclohepten-5(7H)-one (9).—N-[3-(2-Carboxyphenyl)propyl]pyridinium chloride 6 (20 g, 0.072 mol) was dissolved in water (30 ml) and the pH adjusted to 7 with sodium hydroxide (2M). Evaporation gave a red oil that was dissolved in ethanol; the solution was filtered to remove inorganic salts and evaporated. The resulting solid was pyrolysed at 14 mmHg (flame). The products were removed by distillation as they formed. The crude distillate was dissolved in ether, washed with water, and dried (MgSO₄). Evaporation followed by distillation and crystallisation from light petroleum-ether (2:1) gave needles of the lactone (9) (7.48 g, 67%), m.p. 53.5-54.5°, b.p. 93-94° at 0.3 mmHg (lit.,¹¹ m.p. 53-55°, b.p. 55° at 0.01 mmHg) (Found: C, 74.0; H, 6.3. Calc. for C₁₀H₁₀O₂:

⁹ C. M. Cimarusti and J. Wolinsky, J. Amer. Chem. Soc., 1968,

90, 113. ¹⁰ N. B. Chapman, S. Sotheeswaran, and K. J. Toyne, *Chem.* Comm., 1965, 214.

C, 74.1; H, 6.2%), m/e 162 $(M^+, 81\%)$, 132 (78), 131 (78), and 104 (100), τ (CCl₄) 2.40–2.95 (4 H, m, aryl), 5.97 (2 H, t, H-7), 7.19 (2 H, t, H-9), and 7.97 (2 H, quint, H-8).

(10).---The 3,4-Dihydro-3-methyl-2-oxanaphthalen-1-one lactone (9) (700 mg) and pyridinium chloride (500 mg, 1 equiv.) were heated under reflux for 30 min. When cool the product was dissolved in ether, washed with aqueous sodium carbonate, and dried (MgSO₄). Evaporation and distillation gave the lactone (10) (350 mg), b.p. 100° (bath) at 0.3 mmHg (Found: C, 74.4; H, 6.2. C₁₀H₁₀O₂ requires C, 74.1; H, 6.2%), τ (CCl₄) 2.05 (1 H, d, aryl), 2.50–2.95 (3 H, m, aryl), 5.40 (1 H, sext, J 7 Hz, H-3), 7.13 (2 H, d, J 7 Hz, H-4), and 8.55 (3 H, d, J 7 Hz, CH₃).

Heating the lactone (9) under reflux alone or in the presence of pyridine (1 equiv.) resulted in no change.

2-(3-Chloropropyl)benzoic Acid (7).-Dry HCl gas was passed through a mixture of the lactone (9) (3.0 g, 0.0185 mol), zinc chloride (1.0 g), and anhydrous nitrobenzene (125 ml) at 165° (bath) for 75 min. The cooled black solution was poured into water (200 ml) and the product was extracted into ether $(2 \times 150 \text{ ml})$. The combined organic solutions were washed with water and the acid was extracted into aqueous sodium carbonate. The resulting salt solution was washed with ether and acidified. Extraction with ether, drying (MgSO₄), and evaporation gave small crystals of 2-(3-chloropropyl)benzoic acid (2.3 g, 63%), m.p. 68.5-69.5° (Found: C, 60.6; H, 5.5; Cl, 17.7. C₁₀H₁₁ClO₂ requires C, 60.5; H, 5.5; Cl, 17.7%), τ(CDCl₃) -2.30 (1 H, br,s, CO₂H), 1.95 (1 H, m, aryl), 2.65 (3 H, m, aryl), 6.45 (2 H, t, CH₂Cl), 6.81 (2 H, t, ArCH₂), and 7.90 (2 H, quint, CH₂·CH₂Cl).

Reduction of 2-(3-Chloropropyl)benzoic Acid with Sodium in Liquid Ammonia.-2-(3-Chloropropyl)benzoic acid (950 mg, 0.0048 mol), ether (10 ml), and liquid ammonia (100 ml) were stirred at -33 °C under nitrogen during addition of sodium (small pieces; 440 mg, 4 equiv.). The mixture never became blue in colour. After stirring for 3 h the ammonia was allowed to evaporate. The residue was acidified (HCl; 2M) and extracted with ether. After washing with brine and ether solution was dried $(MgSO_4)$. Evaporation gave 1,4-dihydro-2-propylbenzoic acid (780 mg, 98%) as an oil, $\tau(CCl_4) - 1.85$ (1 H, s, CO_2H), 4.25 (2 H, AB system, H-5 and -6), 4.43 (1 H, br,s, H-3), 6.40 (1 H, m, CHCO₂), 7.30 (2 H, m, H-4), 8.0 (2 H, t, J 7 Hz, =C·CH₂·CH₂·CH₃), 8.55 (2 H, m, CH₂·CH₃), and 9.12 (3 H, t, J 8 Hz, CH₃).

Owing to its instability it was not possible to purify this compound any further although the oil was apparently pure by n.m.r. spectroscopy.

Reduction of sodium 2-(3-chloropropyl)benzoate under the same conditions also produced 1,4-dihydro-2-propylbenzoic acid.

cis-3a, 6-Dihydroindane-6-carboxylic Acid (11).-Indane-5-carboxylic acid 12 (5.6 g, 0.035 mol) in ether (100 ml) was added to liquid ammonia (500 ml) at -33 °C under nitrogen. Lithium (small pieces; 1.0 g, 4 equiv.) was added and the resulting dark blue solution stirred for 4 h at -33 °C. Ammonium chloride (10 g) was cautiously added and the ammonia allowed to evaporate. The residue was dissolved in water (200 ml) and acidified (concentrated HCl), and the product was extracted into ether. The ethereal solutions were washed with water, dried $(MgSO_4)$, and evaporated.

¹¹ A. Rieche and H. Gross, Chem. Ber., 1962, 95, 91.

¹² R. T. Arnold, K. Murai, and R. M. Dodson, J. Amer. Chem. Soc., 1950, 72, 4193.

The crude product was recrystallised twice from light petroleum to give needles of the *dihydro-acid* (4.75 g, 85%), m.p. 69.5—70.5° (Found: C, 73.2; H, 7.4. C₁₀H₁₂O₂ requires C, 73.1; H, 7.4%), *m/e* 164 (M^+ , 27%), 119 (81), 117 (17), 92 (14), 91 (100), and 65 (11), τ (CDCl₃) – 1.90 (1 H, br,s, CO₂H), 4.03 (2 H, AB system, H-4 and -5), 4.35 (1 H, br,s, H-7), 6.24 (1 H, d further split, $J_{6,3a}$ 11.8 Hz, H-6), 7.30 (1 H, m, H-3a), 7.63 (2 H, m, H-1), 7.95 (1 H, m), 8.25 (2 H, m), and 8.74 (1 H, sext), ¹³C n.m.r. δ 180.0 (CO₂H, s), 145.4 (C-7a, s), 130.3 (d), 122.4 (d), 111.9 (d), 43.2 (C-6 or C-3a, d), 40.5 (C-3a or C-6, d), 31.9 (t), 29.5 (t), and 22.9 (t).

Reactions of cis-3a, 6-Dihydroindane-6-carboxylic Acid with Peroxy-acids.—The dihydro-acid (840 mg, 0.005 mol), sodium acetate (3.0 g), peracetic acid (40%; 1.9 ml, 2 equiv.), and methylene chloride (20 ml) were stirred at 20 °C for 14 h. Ether was then added and the solution washed with brine and dried (MgSO₄). Evaporation gave indane-5-carboxylic acid (600 mg), identified by comparison with a sample previously obtained.

Reaction of the dihydro-acid with *m*-chloroperbenzoic acid (2 equiv.) in methylene chloride also produced indane-5-carboxylic acid.

trans-1-Hydroxybicyclo[4.3.0]non-3-ene (13) -10-Oxatricvclo[4.3.1.0^{1,6}]dec-3-ene⁸ (34 g, 0.25 mol) in anhydrous tetrahydrofuran (THF) (100 ml) was added dropwise to a stirred suspension of lithium aluminium hydride (10 g, 1.05 equiv.) in THF (300 ml) under nitrogen. The resulting mixture was refluxed for 3 h and cooled to 0 °C. Water (150 ml) was carefully added followed by sulphuric acid (2_M; 1 000 ml). The organic phase was separated and the aqueous phase was washed with ether. The combined ethereal solutions were washed with water and dried $(MgSO_4)$. Evaporation gave a liquid that was purified by column chromatography (100 g silica gel M60) using light petroleum-ether (2:1) as eluant. Distillation gave trans-1-hydroxybicyclo[4.3.0]non-3-ene (26.7 g, 77%), b.p. 45-46° at 0.07 mmHg (Found: C, 78.2; H, 10.15. C9H14O requires C, 78.2; H, 10.2%), m/e 138 $(M^+, 2\%)$, 120 (100), 105 (23), 92 (65), 91 (91), 84 (50), and 79 (32), $\tau(CCl_4)$ 4.40 (2 H, AB system, =CH), 7.8-8.6 (11 H), and 8.60 (1 H, br,s, OH, D₂O exch.), ^{13}C n.m.r. $\delta(\text{CDCl}_3)$ 127.3 (d, C-3 or C-4), 125.0 (d, C-4 or C-3), 96.2 (s, C-1), 43.2 (d, C-6), 38.7 (t, C-2 or C-5), 37.9 (t, C-5 or C-2), 28.3 (t), 27.4 (t), and 20.8 (t).

2,5-Dibromo-trans-1-hydroxybicyclo[4.3.0]non-3-ene (14). trans-1-Hydroxybicyclo[4.3.0]non-3-ene (10.4 g, 0.075 mol), N-bromosuccinimide (NBS) (26.8 g, 2 equiv.), dibenzoyl peroxide (100 mg), and carbon tetrachloride (250 ml) were mixed and quickly brought to reflux. The reaction became exothermic after about 5 min. The mixture was cooled to 20 °C when all the NBS, which remains on the bottom of the flask, had been converted into succinimide, which rises to the surface. The mixture was filtered, washed successively with aqueous sodium carbonate and brine, and dried (MgSO₄). Evaporation gave the dibromo-compounds (quantitative yield), τ (CCl₄) 3.9—4.5 (2 H, four m, =CH), 5.0—5.6 (2 H, CHBr), 7.45 (1 H, OH, D₂O exch.), and 7.5—8.5 (7 H). The n.m.r. spectrum indicated that the four possible isomers were present.

T.l.c. of the crude mixture of dibromides showed only two spots ($R_{\rm F}$ 0.5 and 0.25). Column chromatography [silica gel M60–120; light petroleum–ether (2:1) as eluant] of the mixture (3.07 g) gave a fraction corresponding to the first t.l.c. spot ($R_{\rm F}$ 0.5), which was shown by n.m.r. spectroscopy to be a mixture (1.3 g) of three of the dibromides (three multiplets in the olefinic region). The fraction corresponding to the second t.l.c. spot ($R_{\rm F}$ 0.25) was tentatively assigned the structure (1SR,2SR,5RS,6RS)-2,5-dibromo-1-hydroxybicyclo[4.3.0]non-3-ene (16) (440 mg, 14%), τ (CDCl₃) 4.08 (2 H, m, =CH), 5.32 (1 H, d, $J_{5.6}$ 10 Hz, H-5), 5.48 (1 H, d, $J_{2.3}$ 4 Hz, H-2), and 7.3—8.6 (8 H, m).

The dibromide (16) (440 mg) and sodium methoxide (4 equiv.) in ether (20 ml) were stirred at 20 °C for 1 h. Workup as before gave an epoxide that was tentatively assigned the structure (1SR,3RS,6RS,7RS)-6-bromo-2-oxatricyclo-[5.3.0.0^{1,3}]dec-4-ene (17) (220 mg), τ (CDCl₃) 4.02 (2 H, m, =CH), 5.57 (1 H, d, $J_{5.6}$ 10 Hz, H-6), 6.54 (1 H, m, H-3), and 7.6—9.3 (7 H, m).

Indane 3a,4-Oxide (2) and 4-Bromoindane (15).—The crude mixture of dibromides (3.07 g, 0.01 mol) in ether (10 ml) was added in one portion to a stirred suspension of sodium methoxide (3 equiv.) in ether (30 ml). After 15 min the mixture was poured into sodium hydroxide (2M; 100 ml) and extracted with ether. The combined ethereal solutions were washed with brine, dried (Na₂CO₃), and evaporated to give an orange liquid. Distillation afforded a mixture of indane 3a,4-oxide (30%) and 4-bromoindane.

The spectroscopic data for indane 3a,4-oxide agreed with those obtained previously (cf. Table); τ (CCl₄) 4.22 (2 H, m), 4.77 (2 H, br,s), and 7.6—8.2 (6 H, m), τ (CDCl₃) 4.0 (2 H, m), 4.30 (1 H, br,m), 4.96 (1 H, d, J 5 Hz), and 7.4—8.2 (6 H, m), $\nu_{max.}$ (film) 1 655, 1 570, 1 230, 1 070, 840, and 755 cm⁻¹.

Column chromatography gave 4-bromoindane, τ (CCl₄) 8.7—7.3 (3 H, ABC system, aryl), 7.02 (2 H, t, J 7 Hz), 7.10 (2 H, t, J 7 Hz), and 7.95 (2 H, quint, J 7 Hz).

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