336. *Some Reactions of Indan-4-ol.*

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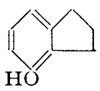
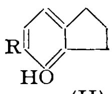
Indan-4-ol reacts in positions 5 and 7 when nitrated and when coupled with diazotised *p*-nitroaniline, and is oxidised by potassium persulphate to indane-4 : 7-diol. The Claisen rearrangement of 4-allyloxyindane gives the 5-allyl derivative, and the Fries rearrangement of 4-acetoxyindane gives a mixture of 5- and 7-acetylindan-4-ol. These hydroxy-ketones are oxidised by hydrogen peroxide in the presence of tetramethylammonium hydroxide and sodium hydroxide respectively to indane-4 : 5- and -4 : 7-diol. 4-Methoxyindane is brominated to 7-bromo-4-methoxyindane.

Indan-4-ol (I) was first prepared as an oil by Moschner in 1901 (*Ber.*, 1901, **34**, 1257) starting from indane and proceeding *via* indane-4-sulphonic acid (the main product is the 5-sulphonic acid); this synthesis has been improved by Arnold and Zaugg (*J. Amer. Chem. Soc.*, 1941, **63**, 1317). The compound was first obtained crystalline by Goth (*Ber.*, 1928, **61**, 1459), who prepared it from 4-nitroindane (available in 21% yield by low-temperature nitration of indane, Lindner and Bruhin, *Ber.*, 1927, **60**, 435) *via* the amine and diazonium salt, and this method was improved by Lindner, Schmitt, and Zaunbauer (*Monatsh.*, 1939, **72**, 216). Indan-4-ol was isolated from coal tar by Kruber and Schmieden (*Ber.*, 1939, **72**, 653). It is now produced from this source by Coalite and Chemical Products, Limited, of Bolsover, Derbyshire, and we thank Dr. H. F. Bondy for a generous gift of this phenol.

The only recorded substitution reaction of indan-4-ol appears to be its coupling in position 7 with diazotised sulphanilic acid (Arnold and Zaugg, *loc. cit.*), and we now describe a number of its simple reactions.



(I)



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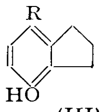

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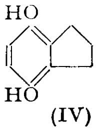

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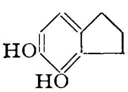

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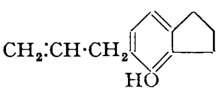

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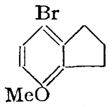

(VII)

Nitration of indan-4-ol (I) in glacial acetic acid gave a 41% yield of 5-nitroindan-4-ol (II; R = NO_2) and an 8% yield of the 7-nitro-compound (III; R = NO_2). Coupling with diazotised *p*-nitroaniline gave a high yield of 7-*p*-nitrophenylazoindan-4-ol (III; R = *p*-$NO_2{\cdot}C_6H_4{\cdot}N_2$) but under 1% of 5-*p*-nitrophenylazoindan-4-ol (II; R = *p*-$NO_2{\cdot}C_6H_4{\cdot}N_2$) isolated by chromatography on alumina; the orientation of these compounds was proved by reduction of the former to 7-aminoindan-4-ol and oxidation of this to the known indane-4 : 7-quinone. Formylation of (I) by the hexamine–acetic acid method (Duff and Bills, *J.*, 1932, 1987; 1934, 1305) gave the dialdehyde, 5 : 7-diformylindan-4-ol. The Elbs persulphate oxidation (see Baker and Brown, *J.*, 1948, 2303) applied to (I) yielded as the only product indane-4 : 7-diol (IV), characterised by formation of its diacetate and by oxidation with ferric chloride to indane-4 : 7-quinone. This quinone when submitted to Thiele acetylation yielded 4 : 5 : 7-triacetoxyindane. 4-Acetoxyindane, when treated with aluminium chloride, gave a mixture (in varying proportions according to the experimental conditions) of the steam-volatile 5-acetyl-indan-4-ol (II; R = CH_3·CO) and 7-acetylindan-4-ol (III; R = CH_3·CO); the latter was oxidised under the usual conditions by alkaline hydrogen peroxide (Dakin oxidation) to indane-4 : 7-diol (IV).

Attempts to oxidise 5-acetylindan-4-ol to indane-4 : 5-diol (V) by hydrogen peroxide in aqueous sodium hydroxide, as in the case of the isomer, did not succeed, probably owing to the very sparing solubility of the alkali salt of the *o*-hydroxy-ketone which may be largely covalent owing to co-ordination with the carbonyl oxygen atom. The difficulty was overcome by using as alkali tetramethylammonium hydroxide, whose salt with the hydroxy-ketone must be ionised, and which readily dissolves 5-acetylindan-4-ol; oxidation in presence of this base proceeded normally, giving indane-4 : 5-diol (V) isolated as its diacetate. Tetramethylammonium hydroxide, or similar quaternary bases such as benzyltrimethylammonium hydroxide, may find useful application in the Dakin oxidation or alkylation with alkyl sulphates of *o*-hydroxy-ketones which give sparingly soluble, possibly co-ordinated alkali salts with sodium and potassium hydroxide.

The Claisen thermal rearrangement of 4-allyloxyindane gave 5-allylindan-4-ol (VI), which shows the properties of a phenol with a free *para*-position.

Indan-4-ol is converted into 7-bromo-4-methoxyindane (VII) by methylation with methyl sulphate and alkali, and then bromination in acetic acid, the overall yield of pure compound being 81%. 4-Halogenoindanes (Barnes and Gordon, *J. Amer. Chem. Soc.*, 1949, **71**, 2644) and especially 7-bromo-4-methoxyindane (VII) (Barnes, Kraft, and Gordon, *J. Amer. Chem. Soc.*, 1949, **71**, 3523) are potentially important intermediates in syntheses of steroids in which rings A and B are built unambiguously on to the 4- and the 5-position of an indane which provides rings C and D. 7-Bromo-4-methoxyindane (VII) has previously been made from *p*-bromophenol and acrylonitrile by a six-step synthesis in an overall yield of 14·3% (Barnes, Kraft, and Gordon, *loc. cit.*).

In all these reactions indan-4-ol behaves as a normal *o*-substituted phenol, and this is in harmony with the preliminary results of Nowlan, Slavin, and Wheeler (*J.*, 1950, 340). The original hypothesis of Mills and Nixon (*J.*, 1930, 2510) predicted that the C–C bond common to the two rings in indanes should be single rather than double in character, and that in consequence bonds C_4–C_5 and C_6–C_7 should behave as single bonds. Considerable evidence, both practical (including the present work) and theoretical (see Springall, Hampson, May, and Spedding, *J.*, 1949, 1524; Berthier and Pullmann, *Bull. Soc. chim.*, 1950, **17**, 88) has, however, accumulated to show that this hypothesis is no longer tenable, and that the departure of the central C–C bond from the character of an ordinary aromatic link towards that of a single bond is extremely slight. The arrangement of the double bonds in formulæ (I)—(VII) of this paper is purely formal, and is not intended to imply that this is a preferred structure.

EXPERIMENTAL

M. p.s are uncorrected. Analyses are by Drs. Weiler and Strauss, Oxford, and Mr. W. M. Eno, Bristol.

5- *and* 7-*Nitroindan*-4-*ol*.—A solution of concentrated nitric acid (1 c.c.; *d* 1·42) in acetic acid (10 c.c.) was added to one of indan-4-ol (2 g.) in acetic acid (10 c.c.). After ½ hour at room temperature the mixture was steam-distilled, and the crystalline 5-*nitroindan*-4-*ol* (1·1 g.) which separated from the distillate was recrystallised from aqueous methanol and obtained as yellow needles, m. p. 56—57° (Found: C, 60·6; H, 5·3; N, 7·8. $C_9H_9O_3N$ requires C, 60·3; H, 5·1; N, 7·8%). This substance gives a red sodium salt, but no ferric chloride reaction.

The residual liquid from the steam-distillation was boiled with charcoal, filtered, and cooled, giving 7-*nitroindan*-4-*ol* (0·2 g.) which, after crystallisation from water, gave pale buff-coloured needles, m. p. 152—153° (Found: C, 60·6; H, 4·9; N, 7·7%). It gives a yellow sodium salt and a negative ferric chloride reaction.

7- *and* 5-p-*Nitrophenylazoindan-4-ol.*—A solution of *p*-nitrobenzenediazonium chloride (1·1 mols.) was added slowly to an ice-cooled solution of indan-4-ol (1·0 mol.) in an excess of 15% aqueous sodium hydroxide, the mixture was then acidified, and the red solid was collected, washed, and dried (yield 90%). It was first crystallised several times from aqueous ethanol, and the two constituents were separated chromatographically on a column of alumina, with ethanol as solvent. Elution readily enabled the small amount of material contained in the more rapidly moving yellow band to be separated from the substance contained in the brown band. The yellow band gave a product in a yield of about 0·25% which, after sublimation, gave 5-p-*nitrophenylazoindan-4-ol* as small reddish-brown needles, m. p. 185° (Found: N, 15·0. $C_{15}H_{13}O_3N_3$ requires N, 14·8%). The brown band yielded a product which, after crystallisation from aqueous ethanol, and then aqueous dioxan gave 7-p-*nitrophenylazoindan-4-ol* as a red, crystalline powder, m. p. 189—190° (decomp.) (Found: C, 63·6; H, 4·7; N, 14·9. $C_{15}H_{13}O_3N_3$ requires C, 63·6; H, 4·6; N, 14·8%). Reduction of the latter azo-derivative at about 45° with sodium dithionite (hydrosulphite) in dilute alcoholic solution in presence of sodium carbonate and final addition of much water precipitated the amphoteric 7-aminoindan-4-ol (Arnold and Zaugg, *loc. cit.*), and oxidation of this with ferric chloride in dilute hydrochloric acid followed by steam-distillation under slightly diminished pressure gave the steam-volatile indane-4 : 7-quinone (see below).

5 : 7-*Diformylindan-4-ol.*—A mixture of indan-4-ol (2·0 g.) and hexamine (2 g.) in acetic acid (8 c.c.) was heated on a boiling-water bath for 6 hours. Concentrated hydrochloric acid (15 c.c.) and water (15 c.c.) were then added and heating continued for ½ hour, after which the mixture was steam-distilled. The crystalline product (0·5 g.) which separated from the distillate (1200 c.c.) was recrystallised twice from methyl alcohol and then sublimed *in vacuo* at 110—120°, giving 5 : 7-*diformylindan-4-ol* as small needles, m. p. 124—125° (Found: C, 69·8; H, 5·2. $C_{11}H_{10}O_3$ requires C, 69·5; H, 5·3%). Its alcoholic solution gives a deep reddish-purple colour with ferric chloride. No monoformyl compound, either volatile or involatile in steam, could be isolated, even when the reaction time was reduced to 2 hours.

Indane-4 : 7-diol (IV).—(a) *By the Elbs persulphate oxidation of indan-4-ol.* To a solution of indan-4-ol (3·0 g.; 1 mol.) in 2N-sodium hydroxide (55 c.c.; 5 mols.) was added during 4 hours an aqueous solution of potassium persulphate (5·7 g.; 1 mol.) saturated at room temperature. The temperature of the mixture was not allowed to rise above 20°, and after being left overnight it was saturated with carbon dioxide and extracted with ether to remove indan-4-ol (0·6 g.). The aqueous solution was now made strongly acid with hydrochloric acid, heated on the water-bath for ½ hour, saturated with sodium chloride, and extracted with ethyl acetate. The extract was washed with a little saturated aqueous sodium hydrogen carbonate, and then yielded the crude indane-4 : 7-diol (1·0 g.). It was purified by sublimation at 160—180° *in vacuo,* and then recrystallisation from ethyl methyl ketone–light petroleum (b. p. 60—80°), giving thin, irregular prisms, m. p. 183—184° (Found: C, 71·7; H, 6·7. Calc. for $C_9H_{10}O_2$: C, 72·0; H, 6·7%). Arnold and Zaugg (*loc. cit.*) give m. p. 184—185°. 4 : 7-*Diacetoxyindane*, prepared by boiling the dihydroxy-compound with acetic anhydride and a little pyridine for 3 hours and pouring into water, was crystallised several times from methanol and obtained in long needles, m. p. 143—144·5° (Found: C, 66·5; H, 6·0. $C_{13}H_{14}O_4$ requires C, 66·7; H, 6·0%).

(b) *By oxidation of 7-acetylindan-4-ol with hydrogen peroxide.* 7-Acetylindan-4-ol (1·5 g.; 1 mol.; see below) was dissolved in 0·1N-aqueous sodium hydroxide (10 c.c.), and 3% hydrogen peroxide (13 c.c.; 1·25 mols.) added at room temperature. A slow rise in temperature of 14° took place, and after 2 hours a little sodium dithionite (hydrosulphite) was added and the solution was acidified with dilute sulphuric acid, saturated with sodium chloride, and extracted with ethyl acetate. The extract was shaken with saturated aqueous sodium hydrogen carbonate, dried, and evaporated, leaving a crude product (0·8 g.) which was purified as above, giving finally indane-4 : 7-diol (IV), m. p. and mixed m. p. 182—184°.

Indane-4 : 7-quinone.—Indane-4 : 7-diol (1 g.), suspended in water (50 c.c.) and covered with a layer of benzene (50 c.c.), was treated slowly, whilst being shaken, with a solution of ferric chloride (2 g.; anhyd.) in water (20 c.c.) and a few drops of concentrated hydrochloric acid. The mixture was shaken for a further ½ hour, the benzene layer separated, and the aqueous layer extracted several times with benzene. The united benzene solutions yielded a dark red product (0·8 g.) which, after sublimation, was obtained as golden-yellow prisms (0·55 g.), m. p. 42—43°. Arnold and Zaugg (*loc. cit.*) record m. p. 41—42°.

4 : 5 : 7-*Triacetoxyindane.*—Indane-4 : 7-quinone (0·5 g.) was dissolved in acetic anhydride (4 c.c.), and concentrated sulphuric acid (1 drop) added. The mixture was boiled for ¾ hour, poured into water, and extracted with ether, and the extract washed with aqueous sodium hydrogen

carbonate, then with 1% aqueous sodium hydroxide, dried, and distilled. After several crystallisations from benzene–light petroleum (b. p. 60—80°) 4 : 5 : 7-*triacetoxyindane* was obtained in small prisms, m. p. 92—93° (Found : C, 61·4; H, 5·4. $C_{15}H_{16}O_6$ requires C, 61·6; H, 5·5%).

4-*Acetoxyindane*.—A solution of indan-4-ol (4·5 g.; 1 mol.) in one of sodium hydroxide (2·0 g.; 1·1 mols.) in water (15 c.c.) containing crushed ice was vigorously shaken after the addition of acetic anhydride (4·2 c.c.; 1·3 mols.), and the solid product collected, washed, and dried (yield 5·6 g.). A portion, after crystallisation from aqueous methanol, was obtained as prisms, m. p. 31—32° (Lindner, Schmitt, and Zaunbauer, *Monatsh.*, 1939, **72**, 216, give m. p. 30—32°).

5- *and* 7-*Acetylindan*-4-*ol*.—4-Acetoxyindane (5·0 g.; 1 mol.) was melted, anhydrous aluminium chloride (5·6 g.; 1·2 mols.) added, and the mixture heated on the steam-bath for 5 hours, and submitted to steam-distillation after addition of dilute hydrochloric acid. The solid 5-*acetylindan*-4-*ol* in the distillate (1200 c.c.) was collected (yield : 3·0 g., 60%) and recrystallised from aqueous ethanol, being obtained in small plates, m. p. 47° (Found : C, 74·7; H, 6·8. $C_{11}H_{12}O_2$ requires C, 75·0; H, 6·9%). It forms a yellow, very sparingly soluble sodium salt, and its alcoholic solution gives a strong, purple ferric chloride reaction. The residue from the steam-distillation was cooled, the solid collected (1·6 g., 32%), recrystallised from methanol, and finally sublimed (at 170—180°/30 mm.), giving 7-*acetylindan*-4-*ol* as prismatic needles, m. p. 185° (Found : C, 75·3; H, 7·1%). It gives a weak yellow colour with ferric chloride in ethanol solution.

The yields of 5- and of 7-acetylindan-4-ol when the Fries reaction was carried out at 140—150° (3 hours) were 57 and 20% respectively, and when nitrobenzene was used as solvent at room temperature (48 hours) the yields were 22 and 48% respectively.

Oxidation of 5-*Acetylindan*-4-*ol with Hydrogen Peroxide in Presence of Tetramethylammonium Hydroxide*. 4 : 5-*Diacetoxyindane*.—5-Acetylindan-4-ol (1·5 g.; 1 mol.) was dissolved in a 10% aqueous solution of tetramethylammonium hydroxide (20 c.c.; 2·5 mols.) at room temperature, and a 6% aqueous solution of hydrogen peroxide (6·5 c.c.; 1·25 mols.) added in an atmosphere of nitrogen. A spontaneous rise in temperature to 40° occurred during 10 minutes; after ½ hour the mixture was warmed again to 40°, and after a further 20 minutes a little sodium dithionite (hydrosulphite) was added to the cooled solution, which was then acidified with dilute sulphuric acid and extracted thoroughly with ether–ethyl acetate. The extracts were shaken with 2% aqueous sodium hydroxide, the alkaline layer was acidified and again extracted as before, and the extracts were distilled, leaving a semi-solid product (0·4 g.). This was boiled with acetic anhydride (2 c.c.) and a trace of sulphuric acid for 1 hour, then shaken with water, and the dark oil heated (at 80—100°/20 mm.), giving a sublimate (45 mg.), m. p. 72—74°. Crystallisation from aqueous ethanol and final sublimation gave 4 : 5-*diacetoxyindane* as prisms, m. p. 79—80° (Found : C, 66·3; H, 6·0. $C_{13}H_{14}O_4$ requires C, 66·7; H, 6·0%).

4-*Allyloxyindane*.—A mixture of indan-4-ol (2 g.), allyl iodide (2·7 g.), ethyl methyl ketone (35 c.c.), and anhydrous potassium carbonate (2·4 g.) was boiled for 24 hours, then poured into water, and the oily *product* isolated and distilled, giving a pale yellow liquid (2·1 g.), b. p. 122—125°/14 mm. (Found, in material twice distilled : C, 82·6; H, 8·2. $C_{12}H_{14}O$ requires C, 82·7; H, 8·1%).

5-*Allylindan*-4-*ol* (VI).—4-Allyloxyindane (3·6 g.) was heated in an oil-bath at 220° for 2 hours, and the product dissolved in ether and repeatedly extracted with small quantities of 2N-sodium hydroxide. The united alkaline extracts were acidified and yielded to ether an oil, b. p. 101—102°/0·7—0·8 mm. (2·1 g.) (Found, in material redistilled at 0·2 mm.: C, 82·6; H, 8·0. $C_{12}H_{14}O$ requires C, 82·7; H, 8·1%). This 5-*allylindan*-4-*ol* dissolves only slightly in dilute aqueous sodium hydroxide, and gives virtually no colour with ferric chloride in alcoholic solution. It gives a blue indophenol reaction with *p*-aminodimethylaniline and alkaline hypochlorite, and a purplish-blue colour with alkaline 2 : 6-dichloroquinonechloroimide (see Gibbs, *J. Biol. Chem.*, 1927, **72**, 649), reactions indicative of a phenol with a free *para*-position. When heated with α-naphthyl *iso*cyanate and a trace of triethylamine it gave the related α-naphthylurethane, which was crystallised from light petroleum; it is probably dimorphic and melted at 70—80° depending on the rate of heating, and after cooling and reheating it then melted at 126—128°.

7-*Bromo*-4-*methoxyindane* (VII).—Indan-4-ol (10 g.), dissolved in a little dilute sodium hydroxide, was shaken vigorously during the portionwise addition of sodium hydroxide (20 g.) in water (75 c.c.) and methyl sulphate (30 g.), the temperature being kept at about 50°. After 2 hours' heating on the water-bath, the mixture was diluted, and then yielded to ether 4-methoxyindane as an oil (10·2 g.). To this crude product in glacial acetic acid (20 c.c.) was added dropwise, whilst cooling in water, a solution of bromine (11·1 g.; 1 mol.) in acetic acid (20 c.c.), and the mixture was then vigorously shaken with water (100 c.c.). The oil rapidly crystallised, and was collected, washed, and dried (yield 15·5 g.; m. p. 60—63°). Recrystallisation from light petroleum (b. p. 40—60°) gave 4 crops (totalling 13·8 g.; 81% from indan-4-ol), m. p. 66° (Barnes, Kraft, and Gordon, *loc. cit.*, give m. p. 66—66·5°).

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