Photoreactions of 2-Hydroxyindan-1-ones

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Irradiation of 2-hydroxyindan-1-ones generally results in α-cleavage, in which the intermediate may either recyclise or undergo intramolecular hydrogen transfer giving ring-opened ketoaldehydes; competition between these processes is sensitive to both substituent and solvent effects. When a 3-substituent is present which is a good leaving group, photolysis leads to isocoumarins and possible mechanistic paths for this last process are discussed.

DURING our early studies in the photocyclisation of 1-(*o*-alkylphenyl)propane-1,2-diones to 2-hydroxyindan-1-ones [1] we noted that some of the latter underwent further photolysis if light with $\lambda < 400$ nm were not excluded. Independently, Padwa and Au [2] have reported photochemical ring-opening reactions of 2-hydroxyindan-1-ones bearing a 2-phenyl or 2-ethoxycarbonyl substituent. Here we show from studies on several 2-hydroxyindanones how the photochemical behaviour is determined by the nature of the substituents, in particular those at the 3-position.

RESULTS AND DISCUSSION

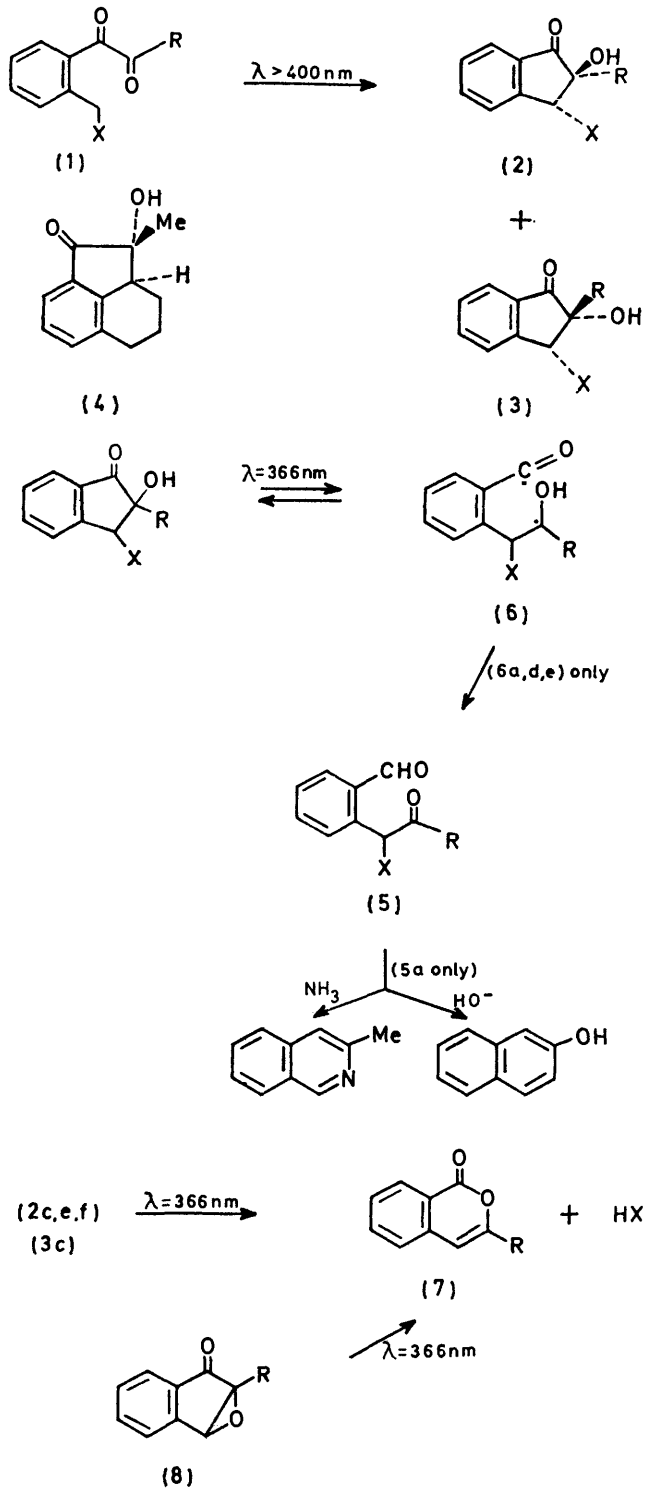
All the hydroxyindanones used were prepared by irradiation ($\lambda > 400$ nm) of an appropriately substituted 1,2-diketone (1) [1,3] in benzene solution. Those diketones bearing ester functions on the *o*-methyl group were obtained by radical bromination (*N*-bromosuccinimide) of *o*-methylbenzil followed by reaction of the product with the appropriate silver salt. In all cases the photocyclisation went in high yield (>85% as judged by ^{1}H n.m.r. spectra of crude reaction mixtures), giving hydroxyindanone mixtures of (2) and (3), in which the epimer (2) with the 2-hydroxy and the 3-H *cis* to each other predominated. When R = Me and X = Br substantial amounts (25%) of the *trans* epimer (3c) were also formed. The configurational assignments are based on the ^{1}H n.m.r. spectra, and the observation that (2c) and (2f) underwent rapid elimination in the presence of base to give the corresponding 2-methyl- and 2-phenyl-2,3-epoxyindan-1-ones whereas (3c) was stable under these conditions. Additional proof for the configurations of (2e) and (3e) was provided by the aqueous-base hydrolysis of (3e), formed in small quantities (*ca.* 10%) in the photocyclisation, to give 2,3c-dihydroxy-2-phenylindan-1-one.[4]

Irradiation of (2a) in benzene solution at 366 nm under N_2 gave a single product (ϕ *ca.* 0.15) provided conversion did not exceed 35%. The spectra of this were consistent with the keto-aldehyde structure (5) and it was converted to 2-naphthol and 3-methylisoquinoline by aqueous sodium hydroxide and ammonia respectively. Although this ring-opening reaction is similar to that reported for 2-hydroxy-2-phenylindan-1-one [2] in methanol solution we find that (2a) is apparently inert (see later) to irradiation in this solvent. It differs also in that when the hydroxy group in (2a) is exchanged for deuterium the deuterium appears in the aldehyde hydrogen of (5). In contrast the epimeric 2-hydroxy-2,3-dimethylindan-1-ones (2b, 3b) gave no ring-opened product of the type (5) but merely interconvert (ϕ *ca.* 0.2) on irradiation in benzene solution. This interconversion also occurs on irradiation in methanol solution but much less efficiently (ϕ *ca.* 0.02) in this solvent. Finally the related, but more rigid tetrahydroacenaphthenone derivative (4) was photochemically inert in both benzyl and methanol.

The reactions detailed above were photosensitised by added benzophenone but quenching by piperylene was observed only at high concentrations (≥0.1M). Thus it appears that the reactions may proceed from a short-lived triplet state but that some contribution from the n→π* singlet cannot be excluded. It is clear, however, that the products are those expected from initial Norrish type 1 cleavage giving (6), which may either recyclise to starting material (or its C-2 epimer) or undergo intramolecular H-transfer giving (5).[5,6] Since H-transfer from neither the hydroxy nor the benzylic proton can proceed *via* the favoured six-membered cyclic transition state, it is reasonable that the ability of either of these processes to compete with the recyclisation will be sensitive to substituent and solvent effects. On this basis the unreactivity of (2a) in methanol may be attributed to increased solvation of the hydroxy group in (6), which hinders the reorientation necessary for H-transfer. The contrasting behaviour of (2e) and (2d), [both of which give products of the type (5) on irradiation in benzene] compared with (2b) or (3b) is also understandable, since the phenyl substituent will stabilise the radical centre in (6), and thus increase its lifetime and the chance for the necessary H-transfer to occur.

When the substituent at the 3-position is the conjugate base of a strong acid, as in (2c), (2f), and (3c), the photolysis takes a different course. No products analogous to (5) were formed, and epimerisation at C-2 was largely, but not completely, suppressed. Instead, isocoumarins (7) were formed [ϕ *ca.* 0.1 for (2c) and (3c)] as the major product (70—80%) both in the presence or absence of added base. [The base used was 2,6-lutidine, since it is a relatively poor nucleophile owing to steric hindrance and is insufficiently basic to bring about elimination of (2e) and (2f) to epoxyindanones.] Unlike the earlier reaction the formation of isocoumarins does not appear to be sensitised by added benzophenone (which gives rise to other products) implying that the n→π* singlet is involved. Finally, while the 2,3-epoxyindan-1-ones (8) underwent the expected photorearrangement to iso-

coumarins [7-9] on irradiation under similar conditions they were not detected in these reactions of (2) or (3).



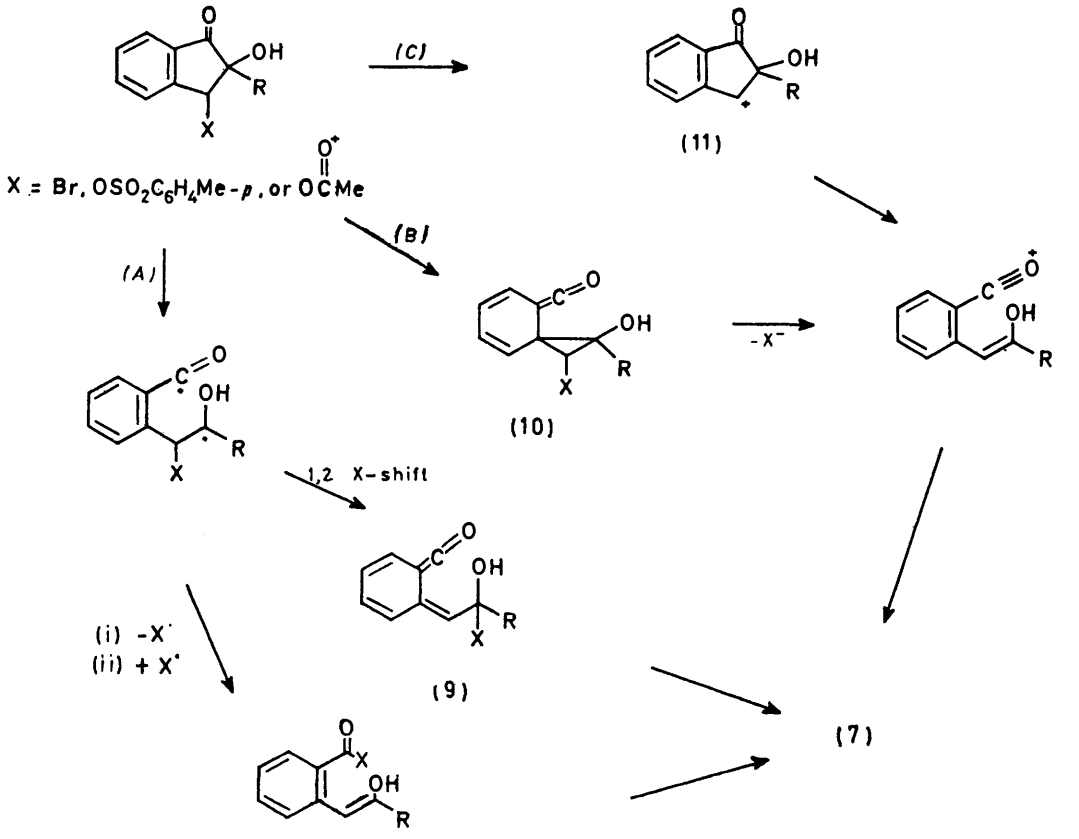
a; R = Me, X = H d; R = Ph, X = Me
b; R = Me, X = Me e; R = Ph, X = OAc
c; R = Me, X = Br f; R = Ph X = $OSO_2C_6H_4Me$-*p*

The behaviour of the acetate ester (2e) is interesting in that irradiation in benzene solution lead to traces (*ca.* 1%) only of (7), the major reaction (*ca.* 70%) leading to (5). However, the addition of trifluoroacetic acid to the photolysis medium gave substantially increased (7) production (15—20% at 1.5M) along with several other unidentified products. The acetate was unaffected in a similar dark reaction with added trifluoroacetic acid, nor was isocoumarin formed by subsequent additions of the acid after irradiation.

When considering possible reaction mechanisms for the formation of isocoumarins certain points seem particularly relevant. Since the reaction proceeds efficiently when X = Br or $OSO_2C_6H_4Me$-*p* yet hardly at all when X = OAc, it seems that heterolytic cleavage of the C–X bond is important at some stage. In any event homolytic fission of a C–O bond is some 50 kJ mol^{-1} more endothermic than for a C–Br bond.[10] Nucleophilic intervention of the 2-hydroxy group in the expulsion of X^- is also excluded since, not only were epoxyindanones not detected, but the *cis* and *trans* isomers (2c) and (3c) underwent reaction with similar quantum efficiencies.

In the light of the above observations we shall limit consideration to the three pathways given in the Scheme since, for these, there are good precedents for the initial step in the photochemical behaviour of this or related systems. Path (*A*) is similar to the triplet ring opening above but does not, unless the migration of X forming (9) is concerted with ring opening, obviously explain why the singlet state only is involved. A more serious difficulty lies in accounting for the difference in behaviour of the tosylate ester (2f) and the acetate ester (2e) and the effect of added acid on the latter. Neither of these objections applies to path (*B*) where the first stage is similar to that reported in the photolysis of 5-hydroxycyclopent-2-en-1-one derivatives and in a 6-hydroxycyclohex-2-en-1-one derivative [11,12] although it has not so far been observed for indan-1-ones. Two substantial further assumptions are however necessary to accommodate all the observations on this route. The first requires that, when X is not a good leaving group, (10) reverts to starting material or its epimer and the second, necessary to account for the very similar behaviour of the epimeric bromides (2c) and (3c), is that when X^- is a good leaving group its loss from (10) is fast compared to the reversion irrespective of the configuration of X on the cyclopropane ring. Neither of these appear intrinsically unreasonable but there is at present no positive evidence to justify them.

Path (*C*) involves initial ionisation with loss of X^- which may occur from a ' hot ' ground state as has been observed in the photosolvolysis of certain benzylic halides [13] or possibly, from the n→π* singlet. Carbonium ions of the type (11) are almost certainly involved in the acid-catalysed rearrangement of 2-hydroxy-3-ethoxy-2,3-diphenylindan-1-one and several 2,3-epoxyindan-1-ones derivatives to isocoumarins.[8,9] However, it should be noted that neither the tosylate (2f) nor the



SCHEME

bromides (2c) and (3c) gave any trace of isocoumarins in refluxing acetic acid. Furthermore, the photochemical reaction of these compounds proceeded much less efficiently in acetonitrile solution than in the less polar benzene, which argues against such a mechanism.

The evidence currently available does not therefore enable us to make a definite choice between the three mechanistic pathways given above but we prefer (*B*). Further evidence on the seemingly analogous photorearrangement of a sulphate ester of 4,5-dihydroxy-2,5-dimethylcyclopent-2-en-1-one to an α-pyrone which has been reported recently [14] may be relevant in this connection.

EXPERIMENTAL

^{1}H N.m.r. spectra were obtained on a Varian HA 100 spectrometer in carbon tetrachloride solution (unless otherwise stated) with tetramethylsilane as internal standard. I.r. spectra were recorded on Nujol mulls (solids) or liquid films. Preparative t.l.c. separations were conducted on Merck Kieselgel in acetone–hexane. The photochemical synthesis of the hydroxyindanones by irradiation of 1,2-diketones used a Phillips 400-W medium-pressure Hg lamp cooled by a water jacket (Pyrex) with a filter solution (1 cm) of aqueous sodium nitrite (10%). For the photolysis of the hydroxyindanones, this filter solution was replaced by a filter (3 cm) of aqueous copper sulphate pentahydrate (10%).

2-*Ethylbenzil*.—To a solution of benzylmagnesium chloride (*ca.* 0.1 mol) in ether (100 ml) was added *o*-ethylbenzonitrile (6.5 g) [15] and the mixture refluxed for 5 h. After the usual work-up the crude ketone so obtained was oxidised with selenium dioxide (6.0 g) in aqueous acetic acid (20 ml) [16] to give the product, m.p. 54—55 °C (from hexane) (Found: C, 80.9; H, 6.0. $C_{16}H_{14}O_2$ requires C, 80.7; H, 5.9%).

2-*Hydroxymethylbenzil* p-*Toluenesulphonate* (1f).—A mixture of 2-methylbenzil [17] (1.1 g), *N*-bromosuccinimide (0.9 g), and benzoyl peroxide (15 mg) in dry carbon tetrachloride (13 ml) was refluxed for 2h, after which time t.l.c. indicated the formation of 80—85% of the monobromo-derivative. The precipitated succinimide was filtered off, the filtrate washed with water (20 ml), and then the organic extract dried and the solvent removed *in vacuo* at room temperature. To the residual oil (1.4 g) was added a solution of silver *p*-toluenesulphonate (2.0 g) in dry acetonitrile (12 ml) and the mixture set aside for 24 h at 20 °C. After the addition of benzene (50 ml) the precipitated silver salts were removed by filtration, and the filtrate washed with 5% sodium hydrogencarbonate solution (20 ml), and then water (20 ml). Removal of the solvent at 20 °C *in vacuo* gave a gum which was taken up in dry ether and set aside for 24 h at 0 °C, during which time the product (1.12 g) crystallised as yellow plates. After recrystallisation from benzene–ether it had m.p. 81—82 °C (decomp.), δ 8.0—7.2 (13 H, m), 5.65 (2 H, s), and 2.45 (3 H, s) (Found: C, 67.0; H, 4.55. $C_{22}H_{18}O_5S$ requires C, 67.0; H, 4.55%).

2-*Hydroxymethylbenzil Acetate* (1e).—This was prepared in a similar manner to the above tosylate from 2-methylbenzil (1.1 g) but addition of glacial acetic acid (5 ml) was necessary to dissolve the silver acetate (1.5 g) in acetonitrile (7 ml). After work-up as before and recrystallisation

from ether–hexane the product (0.92 g) was obtained as pale yellow needles, m.p. 72—73 °C; $\nu_{max.}$ 1 735, 1 680, and 1 662 cm^{-1}; δ 9.0—7.2 (9 H, m), 5.5 (2 H, s), and 2.02 (3 H, s) (Found: C, 72.1; H, 5.05. $C_{17}H_{14}O_4$ requires C, 72.3; H, 5.0%).

3-*Bromo*-2t-*hydroxy*-2-*methylindan*-1-*one* (2c).—A solution of freshly prepared 1-(*o*-bromomethylphenyl)propane-1,2-dione (1.0 g) (but not purified by chromatography [3]) in dry benzene (50 ml) was purged with nitrogen and irradiated until reaction was complete. Removal of the solvent, followed by crystallisation of the residue from carbon tetrachloride, gave the product (0.42 g), m.p. 126—127 °C, after a further recrystallisation; $\nu_{max.}$ 3 415 and 1 715 cm^{-1}; δ($CDCl_3$) 7.8—7.3 (4 H, m), 5.6 (1 H, s), 3.0 (1 H, br s, exchangeable), and 1.5 (3 H, s) (Found: C, 49.7; H, 3.9; Br, 33.4. $C_{10}H_9BrO_2$ requires C, 49.8; H, 3.6; Br, 33.2%).

3-*Bromo*-2c-*hydroxy*-2-*methylindan*-1-*one* (3c).—This was obtained from the mother liquor of the previous irradiation after preparative t.l.c. (0.23 g), m.p. 79—80 °C (from carbon tetrachloride); $\nu_{max.}$ 3 420 and 1 712 cm^{-1}; δ($CDCl_3$) 7.9—7.4 (4 H, m), 5.34 (1 H, s), 3.4 (1 H, br s, exchangeable), and 1.42 (3 H, s) (Found: C, 49.4; H, 3.8; Br, 33.3. $C_{10}H_9BrO_2$ requires C, 49.8; H, 3.6; Br, 33.2%). From the t.l.c. plates was isolated a further quantity (0.17 g) of (2c).

2-*Hydroxy*-3t-*methyl*-2-*phenylindan*-1-*one* (2d).—From (1d) (0.5 g) similarly there was obtained (2d) (0.39 g), m.p. 125—126 °C (from carbon tetrachloride–hexane); δ 7.9—7.1 (9 H, m), 3.6 (1 H, q, *J* 7 Hz), 3.2 (H, s, exchangeable), and 1.02 (3 H, d, *J* 7 Hz) (Found: C, 80.7; H, 6.2. $C_{16}H_{14}O_2$ requires C, 80.7; H, 5.9%).

N.m.r. of the residue from the crystallisation showed that it consisted largely of the epimer (3d) in which the methyl protons appeared as a doublet at δ 1.3 (*J* 7 Hz). It was not isolated.

2,3t-*Dihydroxy*-2-*phenylindan*-1-*one* 3-*Acetate* (2e).—From (1e) (0.4 g) irradiated similarly there was obtained the product (2e) (240 mg), m.p. 139—140 °C (from benzene–hexane; δ($CDCl_3$) 7.9—7.2 (9 H, m), 6.25 (1 H, s), 3.90 (1 H br s, exchangeable), and 1.8 (3 H, s) (Found: C, 72.1; H, 5.05. $C_{17}H_{14}O_4$ requires C, 72.3; H, 5.0%).

From the mother liquors, preparative t.l.c. yielded a further quantity (38 mg) of (2e) and in addition another product (37 mg), which, after saponification with sodium hydroxide in aqueous methanol, gave 2,3*c*-dihydroxy-2-phenylindan-1-one, m.p. 121—123 °C (lit., 122—123 °C), *i.e.* (3e).

2,3t-*Dihydroxy*-2-*phenylindan*-1-*one* 3-p-*Toluenesulphonate* (2f).—A similar irradiation of (1f) (600 mg) in benzene (50 ml) gave, after evaporation of the solvent and crystallisation of the residue from benzene–ether the product (2f) (470 mg), m.p. 157—158 °C (decomp.); δ($CDCl_3$) 7.9—6.8 (13 H, m), 6.15 (1 H, s), 3.1 (1 H, s, exchangeable), and 2.4 (3 H, s) (Found: C, 67.6; H, 4.7. $C_{22}H_{18}O_5S$ requires C, 67.0; H, 4.55%).

2,3-*Epoxy*-2-*methylindan*-1-*one*.—To a solution of (2c) (220 mg) in acetonitrile (5 ml) was added 1,5-diazabicyclo-[4.3.0]non-5-ene (150 mg), whereupon an immediate reaction occurred with separation of a viscous gum. After the addition of water (20 ml) the solution was brought to pH 7.0, extracted with ether (2 × 20 ml), and the combined extracts dried. The residue after removal of the solvent gave, on bulb-to-bulb distillation, the product (83 mg), b.p. 64—66 °C (at 0.06 mmHg); $\nu_{max.}$ 1 715 cm^{-1}; δ 7.7—7.2 (4 H, m), 4.15 (1 H, s), and 1.68 (3 H, s) (Found: C, 74.95; H, 5.2. $C_{10}H_8O_2$ requires C, 75.0; H, 5.0%).

2,3-*Epoxy*-2-*phenylindan*-1-*one*.—Following a similar procedure with (2f) (200 mg), recrystallisation from ether–hexane afforded the product (86 mg) as colourless needles, m.p. 77—78 °C; $\nu_{max.}$ 1 720 cm^{-1}; δ 7.8—7.3 (9 H, m) and 4.38 (1 H, s) (Found: C, 81.0; H, 4.7. $C_{15}H_{10}O_2$ requires C, 81.1; H, 4.5%).

Photolysis of (2a).—A solution of (2a) (300 mg) in benzene (50 ml) was irradiated under N_2 to *ca.* 30% conversion. After evaporation of the solvent the residue was subjected to preparative t.l.c. under N_2 to give the product as a viscous oil (81 mg); $\nu_{max.}$ 1 710 and 1 692 cm^{-1}; δ 10.01 (1 H, s), 7.6—7.1 (4 H, m), 4.05 (2 H, s), and 2.25 (3 H, s), along with recovered (2a) (174 mg). When the benzene solution was shaken with D_2O prior to irradiation the absorption at δ 10.01 was absent from the product.

A sample of the product (40 mg) in methanolic sodium hydroxide (5 ml, 0.5M) was refluxed for 15 min, then cooled and diluted with water (10 ml). The mixture was extracted with dichloromethane (10 ml), and the aqueous extract concentrated to *ca.* 4 ml and then acidified to pH 6, whereupon extraction with ether gave 2-naphthol (22 mg).

A further sample (35 mg) was taken up in methanolic ammonia (5 ml), set aside for 12 h at room temperature, and the solvent then removed. The residue was taken up in 2% hydrochloric acid (5 ml), the mixture extracted with ether (5 ml), and the aqueous extract heated with aqueous sodium picrate (2%) to give 3-methylisoquinoline picrate (29 mg), m.p. 197—199 °C (lit.,[18] 197—198 °C).

General Irradiation Procedures.—Solutions of the hydroxyindanones (0.03M) in dry benzene under N_2 were irradiated to 10—30% conversion (other than those which were photochemically unreactive). The reaction mixtures were examined by ^1H n.m.r. and h.p.l.c. (Waters ALC 202 chromatograph) to obtain crude yields followed by isolation of the major photoproducts by preparative t.l.c. Yields quoted are based on starting material consumed.

Compound (2c) evolved hydrogen bromide during photolysis giving, as the major product, 3-methylisocoumarin (74% crude, 50% isolated), identical with an authentic sample from 2-acetonylbenzoic acid; no isomerisation to (3c) was found. A separate experiment with added 2,6-lutidine (0.06M) present during irradiation gave, apart from the gradual crystallisation of the base hydrobromide, a similar result. Compound (3c) behaved similarly on irradiation, giving 3-methylisocoumarin (71% crude, 58% isolated) but in this case a small amount (*ca.* 8%) of isomerisation to (2c) was observed.

The photolysate from (2d) consisted of a mixture of the epimer (3d) along with (5d), both in yields of *ca.* 40%. The latter had $\nu_{max.}$ 1 690 cm^{-1}; δ 10.65 (1 H, s), 7.65—7.0 (9 H, m), 6.10 (1 H, q, *J* 6 Hz), and 1.45 (3 H, d, *J* 6 Hz).

From (2e) there was obtained an oil (70% crude, 55% isolated) which did not crystallise and oxidised on standing, but whose spectra show it to be (5e); $\nu_{max.}$ 1 745 and 1 695 cm^{-1}; δ 10.05 (1 H, s), 8.0—7.1 (10 H, m), and 2.1 (3 H, s). Oxidation of a sample (45 mg) with chromic acid in aqueous acetic acid gave benzil-2-carboxylic acid, m.p. 139—141 °C (lit.,[19] 140—141 °C). Also isolated from this photolysis was a small amount (*ca.* 1%) of 3-phenylisocoumarin.[19]

In a separate experiment (2e) was irradiated in benzene with added trifluoroacetic acid. Under these conditions several unidentified products were formed, but the amount of 3-phenylisocoumarin increased with increasing acid concentration (*ca.* 20% in 1.5M acid).

From (2f), *p*-toluenesulphonic acid separated during

photolysis and 3-phenylisocoumarin (82% crude, 70% isolated) was formed.

Quantum Yields.—These are approximate and were determined on degassed solutions using benzophenone in toluene ($\phi = 0.45$ [20]) as actinometer, since this obviates the need of a second filter to remove the visible lines from the Hg lamp. Owing to the relatively low extinction coefficients of the hydroxyindanones at 366 nm, concentrations of 0.1—0.2M were necessary. Reactions were carried to conversions $\leqslant 5\%$, and no correction for product absorption was attempted.

Photosensitisation and Quenching Studies.—These were carried out in the presence of either benzophenone (0.15M) where it absorbed >95% of the incident light or of added piperylene. Reactions were followed as described above.

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