

Base-catalysed Reactions of 3-Benzylthioinden-1-ones

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Whereas 2-aryl-3-benzylthioinden-1-ones (Ia and b) are dealkylated by aqueous potassium hydroxide in dimethyl sulphoxide, the 2-unsubstituted analogue (Ic) undergoes self-condensation with formation of 3-benzylthio-8-phenylbenzofulvene; 2-alkyl-3-benzylthioinden-1-ones (Id and e) under similar conditions yield mixtures which include both the dealkylation product and the condensation product.

THIOETHERS react with nucleophiles in a variety of ways.¹ Examples have been reported of their cleavage by nucleophilic substitution at sulphur^{2,3} and at the α -carbon atom¹ and, with strong bases, by formation of an α -carbanion which rearranges to a thiol.⁴ In the case of 3-benzylthioinden-1-ones (I) we find that bases such as methanolic potassium hydroxide and morpholine react, as expected, at the β -carbon atom of the $\alpha\beta$ -unsaturated ketone with subsequent elimination of toluene- α -thiol. In contrast, however, reactions with potassium hydroxide in dimethyl sulphoxide occur at the benzylic position and result in debenzylation to 3-mercaptoinden-1-ones and/or formation of 8-phenylbenzofulvenes.

In extending earlier work on the preparation of 3-alkylsulphinylmethylinden-1-ones⁵ it was found that treatment of 3-methoxy-2-phenylinden-1-one (IIa) with sodium hydride in dimethyl sulphoxide yielded 2-phenylindane-1,3-dione. This result, which could be ascribed to demethylation by sodium methylsulphonylmethanide, prompted us to study a similar reaction with an alkyl thioether. The reaction with 3-benzylthio-2-phenylinden-1-one (Ia) gave as major product, although in low yield, 3-mercapto-2-phenylinden-1-one (IIIa), isolated as the sulphide (IVa) (*cf.* ref. 6). The dealkylation was improved by replacing sodium hydride by potassium hydroxide. Thus the indenone (Ia) in dimethyl sulphoxide on treatment with aqueous potassium hydroxide rapidly gave the mercapto-derivative (IIIa), isolated as the sulphide (IVa) in good yield. 3-Benzylthio-2-(1-naphthyl)inden-1-one (Ib) under the same conditions yielded mainly the thiol (IIIb), isolated as either the sulphide (IVb) or the methylthio-derivative (Vb). The latter was characterised as its S-oxide (VIb).

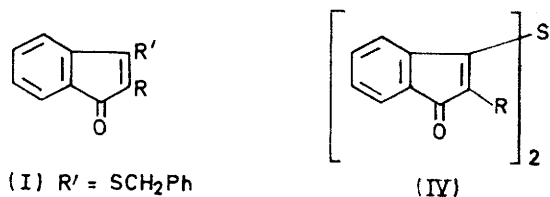
Unexpectedly, treatment of the 2-unsubstituted analogue (Ic) with potassium hydroxide in dimethyl sulphoxide yielded a compound which, on the basis of its analytical figures and i.r., n.m.r., and mass spectra, was tentatively identified as 3-benzylthio-8-phenylbenzofulvene (VIIc). In order to confirm this assignment, 3-benzylthioinden-1-one (Ic) was treated with benzylmagnesium chloride to yield both the 1,4-addition product (3-benzyl-3-benzylthioindan-1-one), and the 1,2-addition product [the carbinol (VIIIc)]. Dehydration of the latter afforded the benzofulvene (VIIc), identical with that obtained before.

¹ L. Brandsma and J. F. Arens, in 'The Chemistry of the Ether Linkage,' ed. S. Patai, Interscience, 1967, ch. 13.

² Y. Iskander and R. Tewfik, *J. Chem. Soc.*, 1961, 2393; Y. Iskander, Y. Riad, and R. Tewfik, *ibid.*, p. 2402.

³ M. Oki and W. Funakoshi, *Bull. Chem. Soc. Japan*, 1971, **44**, 832.

The reactions of the 2-alkyl-3-benzylthioinden-1-ones (Id and e) with potassium hydroxide in dimethyl sulphoxide gave mixtures which contained both the 3-mercaptoindenone (Id or e) and the benzofulvene (VIIc)



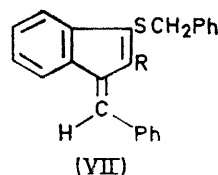
(I) R' = SCH₂Ph

(II) R' = OMe

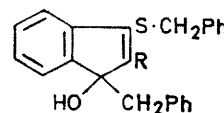
(III) R' = SH

(V) R' = SMe

(VI) R' = SOMe



(VII)



(VIII)

a; R = Ph
b; R = 1-naphthyl
c; R = H
d; R = CH₂Ph
e; R = Me

or e). The structures (VIIId and e) were confirmed by independent syntheses. The thiol (IIIId) was isolated as its sulphide (IVd), also obtained by independent synthesis. The thiol (IIIe) was isolated as its methyl ether and characterised as its S-oxide (VIe).

Products from 3-benzylthioinden-1-ones with potassium hydroxide in dimethyl sulphoxide

3-Benzylthioinden-1-one (I)	Composition of product (%)		
	(III)	(VII)	Unchanged (I)
(Ia)	87	0	
(Ib)	48	0	
(Ic)	0	66	20
(Id)	39	8	
(Ie)	30	32	6

The yields (Table) show the influence of the 2-substituent on the formation of the benzofulvenes.

The mechanism of the formation of the benzofulvenes

⁴ C. R. Hauser, S. W. Kantor, and W. R. Braser, *J. Amer. Chem. Soc.*, 1953, **75**, 2660.

⁵ K. Buggle and D. O'Sullivan, *J.C.S. Perkin I*, 1975, 572.

⁶ K. Buggle, D. O'Sullivan, and W. D. Ryan, *Chem. and Ind.*, 1974, 164.

is not clear; however, the failure to isolate a major debenzylated fragment from the reaction may be due to the instability of such a product.

EXPERIMENTAL

¹H N.m.r. spectra were recorded with a Perkin-Elmer R12 60 MHz spectrometer for solutions in [²H]chloroform with tetramethylsilane as internal standard. I.r. spectra were obtained with a Perkin-Elmer IR700 spectrometer for potassium bromide discs. Preparative layer chromatography (p.l.c.) was carried out with Merck Kieselgel 60 PF₂₄₂₊₃₆₆.

Reaction of 3-Benzylthio-2-phenylinden-1-one (Ia) with Methanolic Potassium Hydroxide.—Potassium hydroxide (180 mg) was added to a methanolic solution of 3-benzylthio-2-phenylinden-1-one (Ia) (135 mg) and the mixture was stirred for 18 h. The solvent was evaporated off and the residue taken up in chloroform. The solution was washed with aqueous sodium carbonate. The alkaline washings on acidification afforded 2-phenylindane-1,3-dione (20 mg), m.p. and mixed m.p. 147—148°. The chloroform solution was dried and evaporated. P.l.c. of the residue gave dibenzyl disulphide (44 mg), m.p. and mixed m.p. 70—71°, 3-methoxy-2-phenylinden-1-one (43 mg), m.p. and mixed m.p. 72—73°, and oils (13 and 20 mg) which were not identified.

Reaction of 3-Benzylthio-2-phenylinden-1-one (Ia) with Morpholine (cf. ref. 7). 3-Benzylthio-2-phenylinden-1-one (100 mg) was dissolved in morpholine. Removal of the morpholine *in vacuo* at 70 °C and p.l.c. of the residue gave 3-morpholino-2-phenylinden-1-one (87 mg, 90%), m.p. 138—139° (lit.,⁷ 137—139°).

Reaction of 3-Methoxy-2-phenylinden-1-one (IIa) with Sodium Hydride in Dimethyl Sulphoxide.—Sodium hydride (120 mg; 60% dispersion) was added to dimethyl sulphoxide (10 ml) and the slurry was heated to *ca.* 60° until dissolution was complete. The solution was cooled to room temperature and added to a solution of 3-methoxy-2-phenylinden-1-one (IIa) (270 mg) in dimethyl sulphoxide (5 ml). The mixture was stirred for 40 min, taken up in chloroform, and acidified with dilute hydrochloric acid (10%). The chloroform extract was washed with water and extracted with saturated aqueous sodium carbonate. Acidification of the alkaline layer afforded 2-phenylindane-1,3-dione (67 mg, 26.4%). The organic layer on p.l.c. afforded starting material (101 mg, 34%) and a crystalline product (47 mg) which was not identified. When 3-methoxy-2-phenylinden-1-one (236 mg) in dimethyl sulphoxide was treated with aqueous potassium hydroxide (1 ml; 16%) for 4 min and the mixture worked up as above, 2-phenylindane-1,3-dione was obtained in 73.6% yield.

Reaction of 3-Benzylthio-2-phenylinden-1-one (Ia) with Sodium Hydride in Dimethyl Sulphoxide.—Sodium hydride (176 mg; 60% dispersion) was added to a solution of 3-benzylthio-2-phenylinden-1-one (200 mg) in dimethyl sulphoxide (25 ml) under nitrogen and the mixture was stirred until the starting material had reacted completely (*ca.* 2 h as judged by t.l.c.). Chloroform was added and the mixture was acidified with dilute hydrochloric acid and then washed with water. The organic layer was dried and concentrated and the residue on p.l.c. gave bis-(1-oxo-2-phenylinden-3-yl) sulphide (23 mg, 17%), m.p. and mixed m.p. 207—208°, and numerous other products which were not identified.

Reactions of 3-Benzylthioinden-1-ones (Ia—e) with Potassium Hydroxide in Dimethyl Sulphoxide.—Aqueous potassium hydroxide was added to a stirred solution of the indenone in dimethyl sulphoxide. After 1—5 min the mixture was taken up in chloroform and acidified with 10% hydrochloric acid. The chloroform extract was washed with water, dried (Na₂SO₄), and concentrated. The residue was chromatographed directly or treated with ethereal diazomethane and then chromatographed.

(a) 3-Benzylthio-2-phenylinden-1-one (Ia) (272 mg) in dimethyl sulphoxide (5 ml) treated with aqueous potassium hydroxide (180 mg in 1.3 ml) for 5 min yielded bis-(1-oxo-2-phenylinden-3-yl) sulphide (IVa) (158 mg, 86.3%), m.p. and mixed m.p. 208°.

(b) 3-Benzylthio-2-(1-naphthyl)inden-1-one (Ib) (426 mg) treated with aqueous potassium hydroxide (240 mg in 2 ml) gave bis-[2-(1-naphthyl)-1-oxoinden-3-yl] sulphide (IVb) (52 mg, 48%), m.p. and mixed m.p.⁶ 244—245°. The experiment was repeated and the crude thiol (IIIb) was treated with ethereal diazomethane. The solvent was evaporated off and the residue, on chromatography, gave 3-methylthio-2-(1-naphthyl)inden-1-one (Vb) as a red oil (185 mg, 54%), τ 2.6 (16 H, m) and 8.36 (3 H, s), which was characterised as the S-oxide.

(c) 3-Benzylthioinden-1-one (Ic) (538 mg) in dimethyl sulphoxide (10 ml), treated with aqueous potassium hydroxide (350 mg in 1.5 ml) for 2 min, yielded 3-benzylthio-8-phenylbenzofulvene (VIIc) (227 mg; 66%), m.p. and mixed m.p. 119.5—120° (from methanol), and unchanged indenone (Ia) (108 mg).

(d) 2-Benzyl-3-benzylthioinden-1-one (Id) (220 mg) in dimethyl sulphoxide (8 ml), treated with aqueous potassium hydroxide (90 mg in 3 ml) for 2 min, gave 2-benzyl-3-benzylthio-8-phenylbenzofulvene (VIIId) (9 mg, 8%), m.p. and mixed m.p. 115—116° (from methanol), and bis-(2-benzyl-1-oxoinden-3-yl) sulphide (61 mg, 39.2%), m.p. and mixed m.p. 136—137° (from methanol).

(e) 2-Methyl-3-benzylthioinden-1-one (Ie) (420 mg) in dimethyl sulphoxide (15 ml) on treatment with aqueous potassium hydroxide (200 mg in 2 ml) for 1 min yielded an orange-red oil which was treated with ethereal diazomethane. Evaporation, and p.l.c. of the residue afforded 3-benzylthio-2-methyl-8-phenylbenzofulvene (85 mg), m.p. and mixed m.p. 56.5° (from methanol); 3-methylthio-2-methylinden-1-one as a red oil (91 mg, 30.3%), τ 2.49 (4 H, m), 7.34 (3 H, s), and 8.02 (3 H, s), characterised as its S-oxide, and unchanged indenone (Ie) (24 mg).

3-Benzylthio-8-phenylbenzofulvene (VIIc).—Ethereal benzylmagnesium chloride was added dropwise to a stirred solution of 3-benzylthioinden-1-one (Ic) (468 mg) in ether (50 ml). When the initial orange colour had faded, water (100 ml) was added. The organic layer was washed with dilute hydrochloric acid, water, and saturated sodium chloride solution and dried. Evaporation and p.l.c. (chloroform) of the residue afforded three products: 3-benzylthio-8-phenylbenzofulvene (VIIc) (15 mg, 2.4%), m.p. 120—121° (from methanol-chloroform) (Found: C, 84.6; H, 5.5; S, 9.7. C₂₃H₁₈S requires C, 84.6; H, 5.6; S, 9.8%); ν_{\max} 1 600 cm⁻¹; τ 2.42 (14 H, m), 3.14 (1 H, s), and 5.69 (2 H, s); 3-benzyl-3-benzylthioindan-1-one (185 mg, 29%), m.p. 97.5—98° [from light petroleum (b.p. 60—80°)] (Found: C, 80.7; H, 5.8. C₂₃H₂₀OS requires C, 80.2; H, 5.9%); ν_{\max} 1 715 cm⁻¹; τ 2.64 (14 H, m), 6.5 (2 H, ABq),

⁷ V. A. Usov and J. Freimanis, *Latv. P.S.R. Zinat. Akad. Vestis, Kim. Ser.*, 1969, 616 (*Chem. Abs.*, 1970, 72, 66679w).

6.63 (2 H, ABq), and 7.0 (2 H, ABq); and 1-benzyl-3-benzylthioinden-1-ol (VIIIc), as an oil (322 mg, 48.7%); τ 2.66 (14 H, m), 4.15 (1 H, s), 5.91 (2 H, s), 6.93 (2 H, q, *J* 13.1 Hz), and 7.92 (1 H, s). Heating compound (VIIIc) to 60 °C in dilute hydrochloric acid yielded the benzofulvene (VIIc) (199 mg, 65%).

2-Benzyl-3-benzylthio-8-phenylbenzofulvene (VIId).—2-Benzyl-3-benzylthioinden-1-one (Id) (200 mg), when treated with benzylmagnesium chloride as described for 3-benzylthioinden-1-one, yielded as major product 1,2-dibenzyl-3-benzylthioinden-1-ol (VIIIId) (80 mg, 32.3%) as an oil; τ 2.93 (19 H, m), 6.3 (2 H, q, *J* 17.4 Hz), 6.305 (2 H, s), 7.35 (2 H, q, *J* 13.2 Hz), and 8.6 (1 H, s). A solution of the carbinol (VIIIId) in chloroform (5 ml) was treated with concentrated hydrochloric acid (10 ml) and the mixture was heated at 80 °C for 15 min, cooled, and extracted with chloroform. The extract was dried and concentrated. P.l.c. (petroleum-chloroform, 3 : 1) of the residue afforded 2-benzyl-3-benzylthio-8-phenylbenzofulvene (20 mg, 26.1%), 115.5–116.5° (from methanol) (Found: C, 86.8; H, 6.0 S, 7.6. $C_{30}H_{24}S$ requires C, 86.5; H, 5.8; S, 7.7%); ν_{max} 1 600 cm^{-1} .

3-Benzylthio-2-methyl-8-phenylbenzofulvene (VIIe).—3-Benzylthio-2-methylinden-1-one (Ie) (256 mg), when treated with benzylmagnesium chloride as described for 3-benzylthioinden-1-one, yielded 1-benzyl-3-benzylthio-2-methylinden-1-ol (VIIIE) (62 mg, 17.9%) as an oil; τ 2.73 (14 H, m), 6.33 (2 H, s), 7.123 (2 H, q, *J* 13.4 Hz), and 8.21 (s, 3 H). A solution of compound (VIIIE) (62 mg) in chloroform was heated with concentrated hydrochloric acid (5 ml) at 80 °C for 15 min. The organic layer was separated, dried, and concentrated. P.l.c. (chloroform) yielded as major product 3-benzylthio-2-methyl-8-phenylbenzofulvene (VIIe) (35 mg, 59.4%), m.p. 56.5° (Found: C, 84.8; H, 6.0; S, 9.4. $C_{24}H_{20}S$ requires C, 84.7; H, 5.9; S, 9.4%); τ 2.42 (14 H, m), 5.47 (2 H, s), and 8.24 (3 H, s).

Bis-(2-benzyl-1-oxoinden-3-yl) Sulphide (IVd).—Hydrogen sulphide was passed through a solution of 2-benzyl-3-morpholinoinden-1-one (240 mg) in methanol (3 ml) for 5 min. Concentrated sulphuric acid (2 drops) was added and

passage of hydrogen sulphide was continued until the starting material had completely reacted (t.l.c.). Upon cooling to 0 °C the mixture deposited a brown oil, the i.r. spectrum of which showed ν_{max} 2 550 cm^{-1} (SH). The oil was dissolved in ether and treated with ethereal diazomethane. When evolution of nitrogen had ceased the solvent was removed and the residual oil was combined with the residue from the methanolic mother liquor and chromatographed (chloroform) to give 2-benzyl-3-methylthioinden-1-one as a red oil (42 mg); τ 2.6 (9 H, m), 6.11 (2 H, s), and 7.38 (3 H, s), characterised as the *S*-oxide (VIId), and the sulphide (IVd) (61 mg) (Found: C, 81.2; H, 4.4; S, 6.7. $C_{22}H_{22}O_2S$ requires C, 81.7; H, 4.7; S, 6.8%); ν_{max} 1 710 cm^{-1} ; τ 2.698 (18 H m), and 6.22 (4 H, s).

Oxidation of 3-Methylthioindenones (Vb, d, and e).—Hydrogen peroxide (30%) was added to a solution of the 3-methylthioinden-1-one in acetic acid and the mixture was either stirred at room temperature or heated at 80 °C until the starting material had reacted (t.l.c.). The former procedure gave better yields (ca. 60%). A solution of the mixture in chloroform was washed with saturated aqueous sodium carbonate, water, and saturated sodium chloride, dried (Na_2SO_4), and evaporated and the residue was chromatographed (chloroform). 3-Methylthio-2-(1-naphthyl)inden-1-one (Vb) yielded the *S*-oxide (VIb), m.p. 149–150° (from ether) (Found: C, 75.4; H, 4.3; S, 10.1. $C_{20}H_{14}SO_2$ requires C, 75.5; H, 4.4; S, 10.05%); ν_{max} 1 710 and 1 065 cm^{-1} . 2-Benzyl-3-methylthioinden-1-one (Vd) gave the *S*-oxide (VIId), m.p. 97–98° (from ether) (Found: C, 72.05; H, 4.8; S, 11.35. $C_{17}H_{14}SO_2$ requires C, 72.3; H, 5.0; S, 11.3%); ν_{max} 1 710 and 1 065 cm^{-1} . 2-Methyl-3-methylthioinden-1-one (Ve) gave the *S*-oxide (VIe), m.p. 103.5–104.5° (from ether) (Found: C, 64.2; H, 4.9; S, 15.3. $C_{11}H_{10}SO_2$ requires C, 64.1; H, 4.9; S, 15.5%); ν_{max} 1 710 and 1 060 cm^{-1} ; τ 2.45 (4 H, m), 6.95 (3 H, s), and 7.93 (3 H, s).

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