558. *Heterocyclic Analogues of Fluorene: Indeno(1′ : 2′-4 : 5)-thiazoles from 2-Bromoindan-1-one.*

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Reaction of 2-bromoindan-1-one (for which an improved method of preparation is reported) with thioformamide, thioacetamide, thiobenzamide, thiourea, and potassium thiocyanate gave indeno(1′ : 2′-4 : 5)thiazole and various 2-derivatives thereof.

Investigations have been described [1] in which, by means of azido-reactions, derivatives of fluorene yield phenanthridines. It is intended to apply this method of synthesis of a pyridine ring in a condensed ring system to compounds analogous to fluorene but in which one or both phenylene rings of the latter are replaced by heterocycles, and as a first stage several indenothiazoles (I) have been prepared by means of the Hantzsch thiazole synthesis.

Cinnamic acid was hydrogenated and then cyclised to indan-1-one, by modifications of known procedures. Reaction with bromine and potassium chlorate,[2] applied to indanone, gave 2-bromoindan-1-one more satisfactorily than Kipping's method [3] in which the ketone reacts with bromine in acetic acid.

Hantzsch's synthesis of thiazoles,[4] involving reaction of the thiol group of an *iso*-thioamide with the >CBr group of the bromo-ketone, applied to reaction of thioformamide,

[1] Arcus and Mesley, *J.*, 1953, 178; Arcus and Coombs, *J.*, 1954, 4319; Arcus and Lucken, *J.*, 1955, 1634; Arcus, Coombs, and Evans, *J.*, 1956, 1498; Arcus, Marks, and (in part) Coombs, *J.*, 1957, 4064; Arcus and Evans, *J.*, 1958, 789.

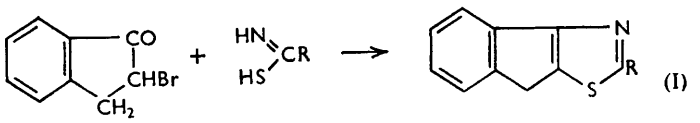
[2] Catch, Elliott, Hey, and Jones, *J.*, 1948, 272.

[3] Kipping, *J.*, 1894, **65**, 500.

[4] Literature summarised by Wiley, England, and Behr, " Organic Reactions," Vol. VI, Wiley and Sons, New York, 1951, pp. 367—409.

thioacetamide, and thiobenzamide with 2-bromoindan-1-one, yielded indeno(1′ : 2′-4 : 5)thiazole and its 2-methyl and 2-phenyl derivatives (I; R = H, Me, and Ph).

An attempt to prepare 2-methylindeno(1′ : 2′-4 : 5)oxazole by heating 2-bromoindan-1-one with acetamide gave 2 : 2-dibromoindan-1-one; acetamide is presumed to have acted as a halogen-carrier.



(I)

With thiourea 2-bromoindan-1-one gave 2-aminoindeno(1′ : 2′-4 : 5)thiazole.[5]

2-Bromoindan-1-one with potassium thiocyanate afforded 2-thiocyanatoindan-1-one. The presence of the thiocyanato-group therein was shown by the formation of thiocyanate ion on alkaline hydrolysis. On treatment with ethanolic hydrogen chloride, the thiocyanato-ketone rearranged to 2-hydroxyindeno(1′ : 2′-4 : 5)thiazole (I; R = OH). Analogous preparations of 2-hydroxythiazoles through α-thiocyanato-ketones have been recorded.[4]

Experimental

M. p.s are corrected. Ethanol refers to the 96% alcohol.

2-Bromoindan-1-one.—A suspension of cinnamic acid (200 g.) in ethanol (200 ml.) was stirred with Raney nickel (5 g.) in the presence of hydrogen (initial pressure 80 atm.); the temperature was raised during 1½ hr. to 55°; the pressure fell to the constant value 31 atm.; 633 g. of cinnamic acid thus yielded 437 g. of β-phenylpropionic acid,[6] b. p. 117·5—118°/0·35 mm., m. p. 46°.

β-Phenylpropionic acid (20 g.), heated with polyphosphoric acid [200 g.; prepared from equal weights of phosphoric oxide and phosphoric acid (65% P_2O_5)] at 80° for 80 min., yielded indan-1-one (15·4 g.), b. p. 120—122°/15 mm., m. p. 38°. The use of polyphosphoric acid is described by Koo;[7] the procedure outlined above gave the highest yields: smaller yields were obtained by (*a*) use of commercial "tetraphosphoric acid"; (*b*) use of half the quantity of polyphosphoric acid; (*c*) as the last but with further phosphoric oxide in suspension.

To a stirred suspension of potassium chlorate (7·7 g.) in a solution of indan-1-one (50 g.) in dioxan (50 ml.) and water (20 ml.) at 77—80°, bromine (12 ml.) was added during 50 min.; the flask was illuminated by a 60-w lamp. The product was twice extracted with ether; the extract was washed with water, dried (Na_2SO_4), and on evaporation yielded crude bromoindanone (78—82 g.). Repeated recrystallisation from light petroleum (b. p. 60—80°) gave 2-bromoindan-1-one, m. p. 38·5—40°. A mixture of indan-1-one and 2-bromoindan-1-one liquefied. Separation of the bromo-ketone by distillation is much more economical: the crude product (79·8 g.) gave 2-bromoindan-1-one (57·4 g.), b. p. 110—112°/0·4 mm., f. p. 37·2°.

Indeno(1′ : 2′-4 : 5)thiazoles.—An ethereal solution of thioformamide was prepared according to Willstätter and Wirth.[8] The concentration was determined as follows: a portion of the solution (10 ml.) was pipetted into N-sodium hydroxide (50 ml.), and the whole was heated under reflux for 1 hr.; the ether was then distilled, and the remaining solution heated under reflux for a further hour; the resultant sodium sulphide was converted[9] into barium sulphate.

To a solution of 2-bromoindan-1-one (10·0 g.) in ether (50 ml.) heated under reflux, thioformamide (3·1 g.) in ether (70 ml.) was added during 40 min.; the whole was further heated for 1 hr., during which the hydrobromide separated as a red oil, which solidified in 3 days (9·8 g.). It (9·3 g.) was ground with excess of cold N-sodium hydroxide. (Other hydrobromides, below,

[5] King and Hlavacek, *J. Amer. Chem. Soc.*, 1950, **72**, 3722.
[6] Adkins and Billica, *ibid.*, 1948, **70**, 695.
[7] Koo, *ibid.*, 1953, **75**, 1891.
[8] Willstätter and Wirth, *Ber.*, 1909, **42**, 1911.
[9] Allen and Bishop, "Scott's Standard Methods of Chemical Analysis," Vol. I, 5th Edition, van Nostrand, New York, 1939, p. 910.

were similarly converted into the bases.) The crude base was extracted with warm N-hydrochloric acid and the extract, on being made alkaline, gave a pink powder (4·0 g.), m. p. 65·5—66·5°, which sublimed at 80—100°/10 mm. to yield *indeno*(1′ : 2′-4 : 5)*thiazole*, colourless needles, m. p. 66·5—67° (Found: C, 69·25; H, 4·25; N, 7·8; S, 18·1. $C_{10}H_7NS$ requires C, 69·35; H, 4·05; N, 8·1; S, 18·5%).

Thioacetamide (3·6 g.) in ethanol (20 ml.) was added during 20 min. to a solution, heated under reflux, of 2-bromoindan-1-one (10·0 g.) in ethanol (20 ml.); heating was maintained for 40 min. On cooling, the hydrobromide (3·72 g.) separated, and was converted into the base (1·60 g.), m. p. 82—83°. The hydrobromide crystallised from ethanol as needles, m. p. 266—267·5° (decomp.). The base was twice distilled and yielded 2-*methylindeno*(1′ : 2′-4 : 5)*thiazole*, b. p. 120—122°/0·6 mm., prisms, m. p. 91·5—92° (Found: C, 70·7; H, 4·6; N, 7·55; S, 17·5. $C_{11}H_9NS$ requires C, 70·55; H, 4·85; N, 7·5; S, 17·1%).

Solutions of thiobenzamide [10] (m. p. 119·5°; 3·3 g.) and 2-bromoindan-1-one (5·0 g.) in ethanol (respectively 15 and 10 ml.) were mixed, and heated under reflux for 45 min. On cooling there separated the hydrobromide (5·0 g.), yellow needles, m. p. 240—242° (decomp.), from which was obtained the base (3·7 g.), m. p. 100—100·5°. Neither recrystallisation nor sublimation effected complete purification; however, distillation (bath-temp. 200—235°) of the base (1·0 g.) gave as the main fraction (b. p. 164—170°/0·1 mm.) 2-*phenylindeno*(1′ : 2′-4 : 5)-*thiazole* (0·4 g.), prisms, m. p. 101·5—102° (Found: C, 77·75; H, 4·4; N, 5·5; S, 12·45. $C_{16}H_{11}NS$ requires C, 77·1; H, 4·45; N, 5·6; S, 12·85%).

A mixture of 2-bromoindan-1-one (3·0 g.) and acetamide (0·84 g.) was fused on a steam-bath; a red colour developed; ethanol (10 ml.) was then added, and heating discontinued. After 4 hr. there separated, on shaking, from the solution which had become pale yellow, a product (0·58 g.), m. p. 120—123·5°, recrystallisation of which from ethanol yielded 2 : 2-dibromoindan-1-one, prisms, m. p. 132—133·5° (Found: C, 37·2; H, 2·45; Br, 55·2. Calc. for $C_9H_6OBr_2$: C, 37·3; H, 2·1; Br, 55·1%). Kipping [3] records m. p. 132°.

To a solution of thiourea (1·07 g.) in ethanol (5 ml.) heated under reflux, 2-bromoindan-1-one (3·00 g.) in ethanol (15 ml.) was added during 1½ hr.; heating was continued for ¼ hr. The pink hydrobromide separated on cooling and, after recrystallisation from ethanol, had m. p. 260—262° (decomp.). It (4·0 g.) was converted into the base (2·5 g.), m. p. 199—203° (decomp.), which on treatment with charcoal yielded 2-aminoindeno(1′ : 2′-4 : 5)thiazole, pale violet needles, m. p. 210—211° (decomp.) (Found: C, 63·75; H, 4·2; N, 15·15; S, 16·95. Calc. for $C_{10}H_8N_2S$: C, 63·75; H, 4·3; N, 14·9; S, 17·0%). King and Hlavacek [5] record m. p. 213—214° (decomp.).

To a solution of potassium thiocyanate (1·38 g.) in ethanol (10 ml.) was added 2-bromoindan-1-one (3·0 g.) in ethanol (10 ml.), and the whole was heated under reflux for 5 min. Precipitated potassium bromide was filtered off, and from the filtrate and ethanolic washings there separated on cooling 2-*thiocyanatoindan*-1-*one* (2·4 g.), prisms (from ethanol), m. p. 91·5—92° (Found: C, 62·6; H, 3·6; N, 7·25; S, 16·1. $C_{10}H_7ONS$ requires C, 63·45; H, 3·75; N, 7·4; S, 16·95%). A portion (0·2 g.) was heated under reflux for 30 min. with potassium hydroxide (0·2 g.) in ethanol (5 ml.); the whole was cooled and filtered; acetic acid in slight excess was added to the filtrate, which was then evaporated *in vacuo*; the residue was extracted with aqueous ethanol (1 : 1), and the filtered extract gave positive tests for thiocyanate ion.

Hydrogen chloride, dried by sulphuric acid, was passed for 2 hr. through a boiling solution of 2-thiocyanatoindan-1-one (1·0 g.) in ethanol (20 ml.). From the green fluorescent solution there separated on concentration a product (0·58 g.), m. p. 210—220° (decomp.), which on recrystallisation from ethanol (charcoal) yielded 2-*hydroxyindeno*(1′ : 2′-4 : 5)*thiazole*, prisms, m. p. 228—229° (decomp.) (Found: C, 63·35; H, 3·6; N, 7·3; S, 17·1%).

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[10] Fairfull, Lowe, and Peak, *J.*, 1952, 742.