425. *Reactions of Organic Azides. Part IX.*[1] *Ring-expansions leading to 2-Phenyl-(?iso)quinolono- and -(?iso)quinolino-(4′,3′-4,5)thiazole and (?iso)Quinolono(3′,4′-2,3)thiophen. Attempted Rearrangements of Fluorenone Hydrazone.*

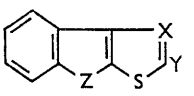
By C. L. Arcus and G. C. Barrett.

3′-Oxo-, 3′-hydroxy-, and 3′-benzylidene-2-phenylindeno(1′,2′-4,5)-thiazole, 3′-benzylideneindeno(1′,2′-4,5)thiazole, and 3′-oxo- and 3′-hydroxyindeno(2′,1′-2,3)thiophen have been subjected to the action of hydrazoic acid in the presence of a strong acid. The two ketones and the hydroxyindeno-thiazole underwent ring-expansion to the oxoquinolino-thiazole and -thiophen and the quinolino-thiazole respectively (or to the corresponding isoquinolines).

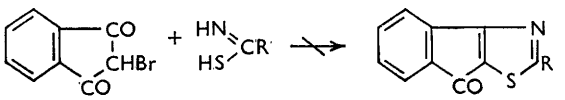
Fluorenone hydrazone was not converted into phenanthridone by reaction with polyphosphoric acid or by diazotisation.

The conversion of derivatives of fluorene into phenanthridines by azido-reactions has been described in earlier parts of this series. Application of these reactions to analogous compounds where a phenylene ring is replaced by a heterocycle is being investigated. A first stage, the synthesis of several indenothiazoles (I; X = N, Z = CH_2) has already been described.[2] The reactions which have been found to be effective for ring-expansion in the fluorene series are the Schmidt reaction of the 9-ketones,[3] interaction of the 9-hydroxy-compounds with hydrazoic acid and a strong acid,[4,5,6] and the action of these reagents on 9-benzylidenefluorene.[6] Accordingly, the preparation of analogous heterocyclic ketones, alcohols, and benzylidene derivatives was undertaken.

2-Phenylindeno(1′,2′-4,5)thiazole gave no ketone when heated with chromium trioxide and acetic acid, but at 220—240° with selenious acid it yielded 3′-oxo-2-phenylindeno-(1′,2′-4,5)thiazole, together with unchanged methylene compound and benzoic acid which must be derived from the 2-phenyl substituent by degradation of the thiazole ring. This ketone, on reduction with aluminium isopropoxide, gave 3′-hydroxy-2-phenylindeno-(1′,2′-4,5)thiazole.



(I)

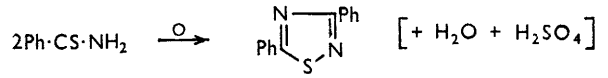


(II)

Preparation of the above ketone, and the unsubstituted compound, was attempted by application of the Hantzsch synthesis to 2-bromoindane-1,3-dione (II). This compound was prepared by reaction of the dione (i) in aqueous dioxan with bromine and potassium chlorate, a method found satisfactory for 2-bromoindan-1-one,[2] and (ii) with one mol. of bromine in carbon tetrachloride. Reaction of the bromo-dione with thioamides did not, however, yield the ketones; thioformamide was degraded to sulphur, and thiobenzamide gave, as its hydrobromide, 3,5-diphenyl-1,2,4-thiadiazole. This compound is known to

[1] Part VIII, Arcus and Evans, *J.*, 1958, 789.
[2] Arcus and Barrett, *J.*, 1958, 2740.
[3] Arcus, Coombs, and Evans, *J.*, 1956, 1498.
[4] Arcus and Mesley, *J.*, 1953, 178.
[5] Arcus and Lucken, *J.*, 1955, 1634.
[6] Arcus and Coombs, *J.*, 1954, 4319.

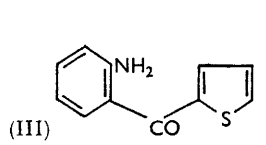
arise from thiobenzamide on reaction with iodine,[7] nitrous acid,[8] or thioperbenzamide;[9] essentially, therefore, by oxidation:



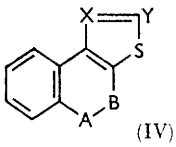
and it is inferred that 2-bromoindane-1,3-dione can act as an oxidising agent.

The 3′-benzylidene derivatives of indeno(1′,2′-4,5)thiazole and the 2-phenyl compound were prepared by condensation with benzaldehyde in the presence of potassium hydroxide.

Steinkopf and Gunther[10] prepared a thiophen analogue of fluorenone, 3′-oxoindeno-(2′,1′-2,3)thiophen (I; X = CH, Y = H, Z = CO), by treating the toluene-*p*-sulphonyl derivative of anthranilic acid with phosphorus pentachloride, aluminium chloride, and thiophen, and hydrolysing the product to the amino-ketone (III); the central ring was closed by diazotisation and heating. This process has been improved by the separate preparation, by means of thionyl chloride, of *N*-toluene-*p*-sulphonylanthraniloyl chloride, and by the use of stannic chloride in the condensation with thiophen. Reduction of this ketone gave 3′-hydroxyindeno(2′,1′-2,3)thiophen.



(III)



(IV)

Azido-reactions.—Schmidt reaction of 3′-oxo-2-phenylindeno(1′,2′-4,5)thiazole in sulphuric acid at 35—40° and of 3′-oxoindeno(2′,1′-2,3)thiophen in a mixture of trichloroacetic acid and sulphuric acid at 50—55° gave the products of ring-expansion, namely (IV; X = N, Y = Ph, A–B = NH–CO; and X = CH, Y = H, A–B = NH–CO) or their isoquinolono-isomers (where A–B = CO–NH).

Addition of 3′-hydroxy-2-phenylindeno(1′,2′-4,5)thiazole to a solution of hydrazoic acid in sulphuric acid and chloroform at 25° gave 2-phenyl(?iso)quinolino(4′,3′-4,5)thiazole (IV; X = N, Y = Ph, A–B = N=CH or CH=N). From a similar treatment of the hydroxyindenothiophen no quinolino-compound was obtained; nor was the azide formed by reaction with hydrazoic acid in trichloroacetic acid–chloroform, a method which converts 1,2-benzofluoren-9-ol into the azide.[11]

Treatment similar to that for the alcohols converts 9-benzylidenefluorene into 9-benzylphenanthridine,[6] but 3′-benzylideneindeno(1′,2′-4,5)thiazole and its 2-phenyl derivative did not react.

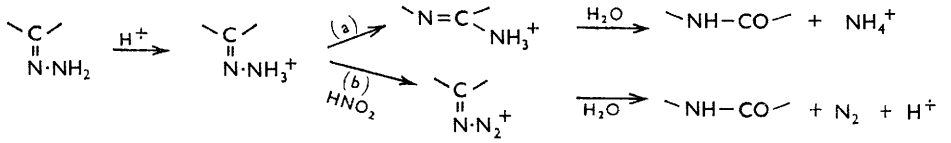
Nearly all the azido-reactions with 2- or 3-substituted fluorenols and fluorenones gave mixtures of 2- and 7- or 3- and 6-substituted phenanthridines and phenanthridones, though frequently the isomers were formed in very unequal amounts.[3,5] Each of the rearrangements above, however, gave only a single product. Also, Petrow[12] reports exclusive migration of the heterocyclic ring in the Schmidt reaction of 1,3-dimethyl-2-azafluorenone. Presumably, in these instances, the heterocyclic and homocyclic rings differ so widely in character that rearrangement proceeds almost entirely by migration of one type of ring. Comment on the relative migratory aptitudes of the phenylene and heterocyclic rings must await establishment of structures for the compounds from the azido-reactions. The products from degradation experiments have not yet enabled us

[7] Hofmann and Gabriel, *Ber.*, 1892, **25**, 1578.
[8] Cronyn and Nakagawa, *J. Amer. Chem. Soc.*, 1952, **74**, 3693.
[9] Kitamura, *J. Pharm. Soc. Japan*, 1937, **57**, 809; *Chem. Abs.*, 1939, **33**, 1726.
[10] Steinkopf and Gunther, *Annalen*, 1936, **522**, 33.
[11] Arcus, Marks, and (in part) Coombs, *J.*, 1957, 4064.
[12] Petrow, *J.*, 1946, 200.

to distinguish quinoline from isoquinoline residues; syntheses of possible degradation products, for comparison with those obtained, are projected, whereby it is hoped that the structures above will be determined.

Under the conditions used in the azido-reactions of the ketone, alcohol, and benzylidene compounds of the indenothiazole series, the thiazole ring must almost certainly be protonated. Reaction with hydrazoic acid requires formation of a carbonium ion after protonation at the carbonyl, hydroxy-, or olefinic group, and such protonation will tend to be repressed by the presence in the molecule of a thiazolium ion. A possible explanation of the experimental finding that the benzylidene compounds do not react, whereas the oxo- and hydroxy-indenothiazoles undergo ring-expansion, is that repression is complete for the former, but not for the latter.

Fluorenone Hydrazone.—The rearrangement of the hydrazone derived from a cyclic ketone appeared to offer a method of ring-expansion, and no record has been found of its experimental investigation. Ring-expansion of fluorenone to phenanthridone, which is very stable, proceeds satisfactorily by the Beckmann and the Schmidt reaction. Accordingly, fluorenone hydrazone was (*a*) heated at 130° in polyphosphoric acid, which is known to be a good catalyst for the above reactions,[13] and (*b*) treated with nitrous acid, then added to hot dilute sulphuric acid. Supposed courses for rearrangement are as follows:



However, the product from conditions (*a*) was fluorenone azine, and from conditions (*b*) was a mixture of the azine and fluorenone.

Experimental

M. p.s are corrected.

Indeno-thiazoles and -thiophens.—A suspension of 2-phenylindeno(1′,2′-4,5)thiazole (5·0 g.) in a solution of selenium dioxide (10·0 g.) in water (12 ml.) was heated in a sealed tube at 220—240° for 2¾ hr. The solid product was collected, washed with water, and sublimed at 160°/0·1 mm. The most volatile crop was repeatedly re-sublimed; it then had equiv. 127 and m. p. 118°, not depressed by benzoic acid (equiv., 122). Subsequent crops were separated by fractional crystallisation from ethanol into the initial compound, and 3′-*oxo*-2-*phenylindeno*-(1′,2′-4,5)*thiazole*, which also constituted the final sublimation-crop. It (1·57 g.) formed orange needles, m. p. 174—175° (Found: C, 72·4; H, 3·3. $C_{16}H_9ONS$ requires C, 73·0; H, 3·45%).

This ketone (0·39 g.) was heated under reflux for 1½ hr. with a solution of aluminium isopropoxide (from aluminium, 0·2 g., and propan-2-ol, 10 ml.). The solution was poured into ice-cold 2N-sulphuric acid, and the precipitated solid collected, washed with water, and recrystallised from heptane. It yielded 3′-*hydroxy*-2-*phenylindeno*(1′,2′-4,5)*thiazole* (0·33 g.), pale yellow needles, m. p. 187° (Found: C, 71·95; H, 4·2. $C_{16}H_{11}ONS$ requires C, 72·45; H, 4·2%).

Flatow's method [14] for the preparation of 2-bromoindane-1,3-dione from ethyl 2-sodio-1,3-dioxoindane-2-carboxylate gave the crude compound in only 24% yield. More satisfactory preparations were as follows: (i) Bromine (3·0 g.) was added during 50 min. to a stirred suspension of potassium chlorate (0·70 g.) in a solution of indane-1,3-dione [15] (5·0 g.) in dioxan (12 ml.) and water (3 ml.) at 78—79°, the whole being illuminated by a 60-w lamp. The mixture was stirred for a further 40 min., then cooled and diluted with ether (50 ml.). The ethereal layer was washed with water, dried (Na_2SO_4), and evaporated; the product, on recrystallisation from heptane, gave 2-bromoindane-1,3-dione (2·55 g., 33%), m. p. 115—118°. (ii) Indane-1,3-dione (23·5 g.) was dissolved in warm carbon tetrachloride (300 ml.); the solution was cooled

[13] Horning and Stromberg, *J. Amer. Chem. Soc.*, 1952, **74**, 2680; Conley, *Chem. and Ind.*, 1958, 438.
[14] Flatow, *Ber.*, 1901, **34**, 2146.
[15] Kaufmann, *Ber.*, 1897, **30**, 385.

to room temperature (slight separation occurring) and bromine (7·8 g.) in carbon tetrachloride (20 ml.) was added during 2 hr. After distillation of the solvent, the product distilled at 132—138°/0·4 mm.; the 2-bromoindane-1,3-dione (13·6 g., 38%) solidified; it had m. p. 106—108°, and m. p. 113—114° after recrystallisation.

To 2-bromoindane-1,3-dione (2·00 g.) in ether (40 ml.), heated under reflux, a solution of thioformamide (0·55 g.) in ether (25 ml.) was added during 30 min. Heating was continued for 1 hr. and the whole kept for 2½ days. The solid product was ground with 0·5N-sodium hydroxide, ammonia being liberated; the yellow residue (0·22 g.) was sublimed *in vacuo*; it then had m. p. 119—119·5° (Found: S, 94·95%).

2-Bromoindane-1,3-dione (0·50 g.) in ether (25 ml.) was added during 30 min. to a solution, heated under reflux, of thiobenzamide (0·31 g.) in ether (10 ml.). Heating was continued for 15 min., and the whole cooled. The orange-yellow product which had separated was collected; it (0·32 g., m. p. 99—102°) was ground with 0·5N-sodium hydroxide; the filtrate contained bromide ion; the residue (0·21 g.) was sublimed *in vacuo*. It yielded 3,5-diphenyl-1,2,4-thiadiazole, pale yellow needles, m. p. 86·5—87° (Found: C, 70·45; H, 4·15; N, 11·6; S, 13·4. Calc. for $C_{14}H_{10}N_2S$: C, 70·6; H, 4·25; N, 11·75; S, 13·45%). Cronyn and Nakagawa [8] record m. p. 89—90°.

To a solution of indeno(1′,2′-4,5)thiazole (3·22 g.) and benzaldehyde (2·03 g.) in methanol (20 ml.) was added 15 ml. of a solution of potassium hydroxide (8 g.) in methanol (50 ml.). A dark oil slowly separated; after 60 hr. further methanol (10 ml.) was added, and the oil solidified. The solid (3·43 g.), on recrystallisation from methanol (charcoal), gave *3′-benzylideneindeno(1′,2′-4,5)thiazole*, yellow needles, m. p. 70° (Found: C, 77·65; H, 4·15; N, 5·6; S, 11·6. $C_{17}H_{11}NS$ requires C, 78·15; H, 4·25; N, 5·35; S, 12·25%).

2-Phenylindeno(1′,2′-4,5)thiazole (1·00 g.) and benzaldehyde (0·44 g.) in methanol (20 ml.), with 8 ml. of the above potassium hydroxide solution, gave in 20 min. a solid (1·24 g.) which, recrystallised from methanol (charcoal), gave *3′-benzylidene-2-phenylindeno(1′,2′-4,5)thiazole*, golden needles, m. p. 159·5—160° (Found: C, 81·85; H, 4·5; N, 4·25; S, 9·0. $C_{23}H_{15}NS$ requires C, 81·85; H, 4·5; N, 4·15; S, 9·5%).

N-Toluene-*p*-sulphonylanthranilic acid [16] (58 g.) and thionyl chloride (60 ml.) were heated under reflux for 1½ hr.; excess of reagent was then distilled off, finally under reduced pressure. The product (59 g.) was recrystallised from carbon tetrachloride (charcoal), yielding *N*-toluene-*p*-sulphonylanthraniloyl chloride, prisms, m. p. 126·5—127·5°. Schroeter and Eisleb [17] record m. p. 128—129°.

Anhydrous stannic chloride (41 g.), dissolved in carbon disulphide (50 ml.), was added during 1 hr. to a stirred suspension of *N*-toluene-*p*-sulphonylanthraniloyl chloride (48 g.) in thiophen (24 g.) and carbon disulphide (100 ml.) at 30°; stirring was continued for 2 hr. The carbon disulphide solution was decanted, and the residual tar repeatedly extracted with mixtures of ether and dilute hydrochloric acid. The carbon disulphide solution was washed with dilute hydrochloric acid and added to the ethereal extracts. The organic solution was shaken with 0·5N-sodium hydroxide (1 l.), and the aqueous alkaline layer was separated, washed with ether, diluted to 2·5 l., and acidified with hydrochloric acid. This precipitated *o*-(toluene-*p*-sulphonamido)phenyl 2-thienyl ketone (46 g.), m. p. 118—121°; a portion recrystallised from ethanol formed pale yellow needles, m. p. 124·5—125·5°. Steinkopf and Gunther [10] record m. p. 125°.

These authors' methods were used to convert the sulphonamido-ketone into the amino-ketone hydrochloride, and thence into 3′-oxoindeno(2′,1′-2,3)thiophen, which formed pale yellow needles, m. p. 107—109° (Steinkopf and Gunther [10] record m. p. 109—110°).

Reduction of this compound (3·36 g.) with aluminium isopropoxide (from aluminium, 1·35 g., and propan-2-ol, 40 ml.), as for the hydroxythiazole, gave *3′-hydroxyindeno(2′,1′-2,3)-thiophen*. After recrystallisation from ethanol it (2·56 g.) had m. p. 116°; further recrystallisation from heptane gave plates, m. p. 110·5°, which depressed the m. p. of the ketone; when kept at 80°/0·1 mm. they became non-crystalline and had m. p. 116° (Found: C, 69·4; H, 4·3. $C_{11}H_8OS$ requires C, 70·15; H, 4·3%).

Azido-reactions.—(*a*) Sodium azide (1·00 g.) was added during 50 min. to a stirred solution of 3′-oxo-2-phenylindeno(1′,2′-4,5)thiazole (1·58 g.) in 98% sulphuric acid (16 ml.) at 35—40°. The mixture was stirred at 40° for a further 2 hr., then poured into ice-water. After 2 hr., the

[16] Scheifele and DeTar, *Org. Synth.*, 1952, **32**, 8.
[17] Schroeter and Eisleb, *Annalen*, 1909, **367**, 111.

solid which had been precipitated was filtered off, ground with 2N-sodium hydroxide, washed, and dried. On sublimation, one fraction separated at 120°/0·1 mm., and a second at 180—200°/0·1 mm. The latter was washed with methylene chloride; from the washings and the first fraction there was recovered the initial ketone (0·55 g.). The washed second fraction (0·82 g.), m. p. 375°, gave on recrystallisation from nitrobenzene *2-phenyl(?iso)quinolono-(4′,3′-4,5)thiazole*, yellow needles, m. p. 376° (uncorr.) (Found: C, 68·95; H, 3·7; N, 9·85. $C_{16}H_{10}ON_2S$ requires C, 69·05; H, 3·7; N, 10·05%).

(*b*) Sodium azide (3·58 g.) and sulphuric acid (18 ml.) were added during 1 hr. in alternate portions to a stirred solution of 3′-oxoindeno(2′,1′-2,3)thiophen (4·93 g.) in trichloroacetic acid (55 g.) at 50—55°; stirring was continued for 1½ hr., and the whole was then poured into water (500 ml.). A tar separated and solidified; on sublimation at 160°/0·1 mm. it gave a product (2·59 g.), m. p. 260—265°, which on recrystallisation from nitrobenzene yielded *(?iso)quinolono-(3′,4′-2,3)thiophen*, pale yellow prisms, m. p. 281° (Found: C, 66·25; H, 3·75; N, 6·8; S, 15·5. $C_{11}H_7ONS$ requires C, 65·65; H, 3·5; N, 6·95; S, 15·95%).

(*c*) Sulphuric acid (1·0 ml.) was added during 10 min. to a stirred suspension of sodium azide (0·20 g.) in chloroform (6 ml.) at 0°. The temperature was raised to 25°, and 3′-hydroxy-2-phenylindeno(1′,2′-4,5)thiazole (0·30 g.) was added during 1 hr. The whole was stirred for a further hour, then poured on ice. Next day the solid which had separated was filtered off; on being shaken with N-sodium hydroxide and ether it dissolved; the product (0·20 g.) from the ethereal layer had, after recrystallisation from benzene, m. p. 146—146·5°. To the filtrate further chloroform (10 ml.) was added, the whole was shaken, and the chloroform layer separated; it yielded 0·11 g. of the product above. Further recrystallisation yielded *2-phenyl-(?iso)quinolino(4′,3′-4,5)thiazole* (0·25 g.), prisms, m. p. 147° (Found: C, 73·35; H, 3·85; N, 10·65; S, 12·6. $C_{16}H_{10}N_2S$ requires C, 73·25; H, 3·85; N, 10·7; S, 12·25%).

Treatment, as in (*c*), of 3′-hydroxyindeno(2′,1′-2,3)thiophen gave a black product, and no base. Reaction with sodium azide, trichloroacetic acid, and chloroform, as for 1,2-benzofluoren-9-ol,[11] gave a dark powder, m. p. ≮320°, which did not contain nitrogen.

3′-Benzylideneindeno(1′,2′-4,5)thiazole was recovered after treatment as in (*c*). Sodium azide was added to a solution of this compound in sulphuric acid at 65—70°; no ether-soluble product was obtained, sulphonation having apparently occurred.

3′-Benzylidene-2-phenylindeno(1′,2′-4,5)thiazole was recovered after treatment with sodium azide, sulphuric acid, and chloroform at 50°.

Fluorenone Hydrazone.—This compound [4] (4·0 g.) was stirred into polyphosphoric acid (P_2O_5 83%; 40 g.) at 130°. The mixture was so kept for 10 min., then poured into water. The precipitate, on recrystallisation from toluene, formed violet-red needles, m. p. 272—273° (Curtius and Kof [18] record m. p. 265° for fluorenone azine).

To a stirred suspension of fluorenone hydrazone (4·0 g.) in N-hydrochloric acid (55 ml.) at 0°, was added sodium nitrite (1·45 g.) in water (5 ml.). Frothing occurred; after 10 min. at 0° the resultant suspension was poured into boiling 2N-sulphuric acid (60 ml.), and the whole was boiled for 10 min. After cooling, the solid product was collected and crystallised from pyridine. It yielded fluorenone azine (0·95 g.), m. p. 272°, and the mother-liquor, after dilution with 5 volumes of hot water and filtration, deposited fluorenone (1·33 g.), m. p. 79—80°, not depressed by the authentic compound.

We thank the Department of Scientific and Industrial Research for a maintenance grant (to G. C. B.) and Imperial Chemical Industries Limited for participation in a grant.

BATTERSEA COLLEGE OF TECHNOLOGY, LONDON, S.W.11. [*Received, December 3rd*, 1959.]

[18] Curtius and Kof, *J. prakt. Chem.*, 1912, **86**, 130.