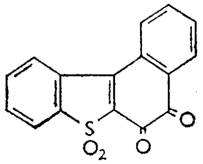
Heterocyclic Nitrogen Compounds. Part VI.[1] Preparation of 2,3-Dihydro-3-oxospiro{isoindole-1,3′-benzo[*b*]thiophen}-2′-carboxylic Acid *SS*-Dioxide by the Schmidt Reaction on Benzo[*b*]naphtho[1,2-*d*]thiophen-5,6-quinone *SS*-Dioxide

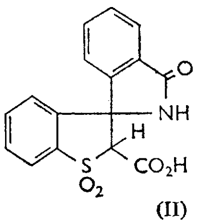
By **Helen J. Sare** and **Emily F. M. Stephenson**,* Organic Chemistry Department, University of Melbourne, Parkville, 3052, Victoria, Australia

The Schmidt reaction on benzo[*b*]naphtho[1,2-*d*]thiophen-5,6-quinone *SS*-dioxide (I) yields as a main product 2,3-dihydro-3-oxospiro{isoindole-1,3′-benzo[*b*]thiophen}-2′-carboxylic acid *SS*-dioxide (II). The product (IVa) of decarboxylatin of (II), has been converted by Raney nickel desulphurisation into 2,3-dihydro-3-methyl-3-phenylisoindol-1-one (Va). The *N*-methyl derivative of (IVa) has similarly been desulphurised to give 2,3-dihydro-2,3-dimethyl-3-phenylisoindol-1-one (Vc).

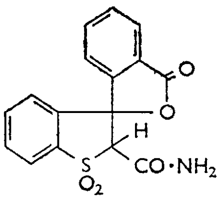
In the Schmidt reaction phenanthrenequinone is converted into phenanthridinone and 2′-carbamoylbiphenyl-2-carboxylic acid, the ratio of the products depending on the proportion of hydrazoic acid to quinone. A large excess of hydrazoic acid favours the formation of phenanthridinone.[2] With the unsymmetrical chrysenequinone and excess of hydrazoic acid Caronna [2] obtained benzo[*c*]phenanthridinone exclusively. Badger and Seidler [3] confirmed this and showed that with hydrazoic acid (1 mol.) 2-(*o*-carbamoylphenyl)-1-naphthoic acid and unchanged quinone were recovered. The isomeric benzo[*i*]phenanthridinone and 2-(*o*-carboxyphenyl)-1-naphthamide were not obtained. The Schmidt reaction on benzo[*b*]naphtho[1,2-*d*]thiophen-5,6-quinone *SS*-dioxide (I) has now been investigated to determine the effect of a strongly electron-attracting group (sulphone) close to the *ortho*-quinonoid carbonyl groups.



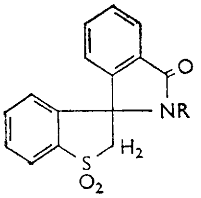
(I)



(II)

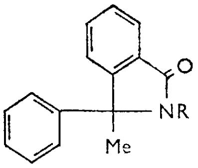


(III)



(IV)

a; R = H
b; R = Me
c; R = Ac



(V)

a; R = H
b; R = Ac
c; R = Me

In applying Smith's mechanism [4] for the Schmidt reaction with ketones to the quinone (I) it is necessary to consider both the ions (A) and (B) in turn. The initial protonation could occur at either carbonyl group, although it is considered that the ion (A) would predominate. When Smith's mechanism is applied to the ion (A) the sequence of reactions which can be formulated leads, after subsequent addition of water and loss

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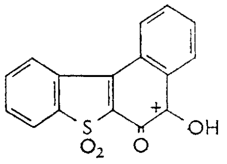
[1] Part V, E. F. M. Stephenson, *J. Chem. Soc.*, 1963, 1913.

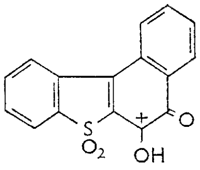
[2] G. Caronna, *Gazzetta*, 1941, **71**, 481 (*Chem. Abs.*, 1943, **37**, 118); *cf.* E. F. M. Stephenson, *J. Chem. Soc.*, 1949, 2620.

[3] G. M. Badger and J. H. Seidler, *J. Chem. Soc.*, 1954, 2329.

[4] (*a*) P. A. S. Smith, *J. Amer. Chem. Soc.*, 1948, **70**, 320; (*b*) P. A. S. Smith and P. J. Horwitz, *ibid.*, 1950, **72**, 3718; (*c*) P. A. S. Smith and B. Ashby, *ibid.*, 1950, **72**, 2503; (*d*) P. A. S. Smith and E. P. Antoniades, *Tetrahedron*, 1960, **9**, 210.

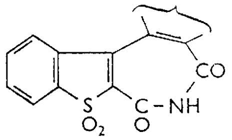


(A)

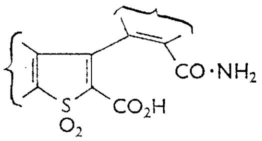


(B)

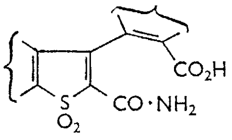
of a proton, to the intermediates (Q) and (P). With water (C) and (D) are formed from (Q), and (E) and (F) from (P).



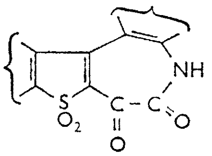
(Q)



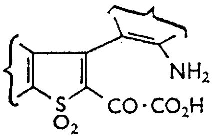
(C)



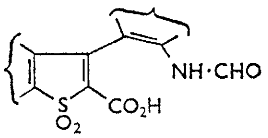
(D)



(P)

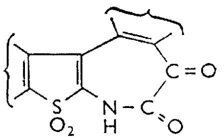


(E)

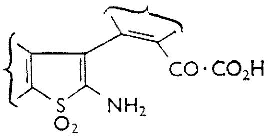


(F)

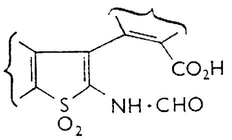
Application of Smith's mechanism to the ion (B) allows a similar formulation of mechanism leading to the intermediates (Q) and (R). With water (G) and (H) are formed from (R).



(R)

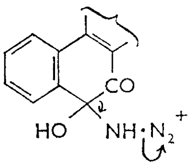


(G)

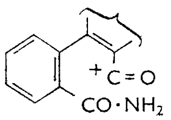


(H)

Badger and Seidler applied Smith's mechanism to *ortho*-quinones but to account for the formation of only one of the two possible isomeric products in their case they assumed that of the two possible intermediate isomeric ions only one (VI), was formed. Subsequent elimination of nitrogen and then fission of the carbon–carbon bond leads to the ion (VII). Addition of water to (VII) would lead to 2-(*o*-carbamoylphenyl)-1-naphthoic acid or reaction of (VII) with another 1 mol. of hydrazoic acid would give benzo[*c*]phenanthridinone.



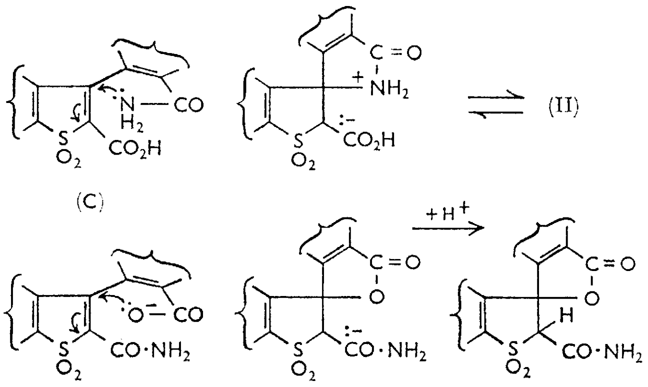
(VI)



(VII)

Application of the Badger–Seidler mechanism to the ion (A) leads (after final hydrolysis) to (C). Similarly, application of this mechanism to the ion (B) leads eventually to (D).

Mechanistic arguments thus lead to the possible products (C)—(H). The major product of the Schmidt reaction 2,3-dihydro-3-oxospiro{isoindole-1,3′-benzo[*b*]-thiophen}-2′-carboxylic acid *SS*-dioxide] (II), can readily arise from (C) by nucleophilic attack of the amide nitrogen at the 2,3-double bond of the sulphone ring. The minor product 3-oxospiro{benzo[*b*]thiophen-3,1′-isobenzofuran}-2-carboxamide *SS*-dioxide (III), can similarly arise from (D) by nucleophilic attack of the carboxylate anion.[5]



(D) (III)

No evidence was obtained for the presence of any of the compounds (E)—(H) (or simple transformation products thereof). However, this does not constitute evidence for the Badger–Seidler mechanism in preference to Smith's mechanism, since, as Smith and Antoniades [4d] have pointed out, steric and electronic factors may be so combined as to render alternative migrations of groups in the geometrically isomeric intermediate negligible.

The formation of the two products (II) and (III) is an immediate consequence of the activating effect of the sulphone group on the double bond of the five-membered ring of the compounds (C) and (D). In the absence of this activated bond the compounds (C) and (D) would either, (i) be isolated as such [2,3] or, (ii) be converted into the corresponding phenanthridinone types.[2,3] The sulphone group determines the predominant formation of the ion (A) in solution of the quinone (I) in conc. sulphuric acid and also the splitting of the intermediate (Q) to give a larger proportion of (C) than (D), and hence

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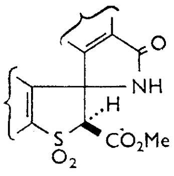
[5] B. Capon, *Quart. Rev.*, 1964, **18**, 45.

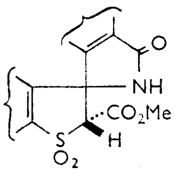
eventually determines (II) and not (III) as the major product.

The bulk of the crude product was soluble in cold sodium hydrogen carbonate solution. Acidification of this solution to pH 3 yielded the minor reaction product (III). The major product (II) was recovered by adjustment of the pH of the filtrate to 0·5. The molecular weight (mass spectrum) of (II) was 329 and analytical data gave the molecular formula $C_{16}H_{11}NO_5S$. The carboxylic acid (II) is decomposed when heated to 240° to give carbon dioxide and spiro{isoindole-1,3′-benzo[*b*]-thiophen}-3(2*H*)-one *SS*-dioxide (IVa). With boiling acetic anhydride (II) yielded the *N*-acetyl derivative (IVc) and hydrolysis of the latter gave (IVa). The acid (II) was also decarboxylated when heated under reflux with M-sodium hydroxide or with a slightly basic solution of hydrogen peroxide. Methylation of (II) with dimethyl sulphate and alkali gave the *N*-methyl derivative (IVb).

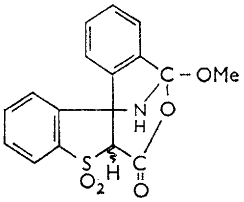
Esterification of the carboxylic acid (II) with methanol -sulphuric acid gave a product, m.p. 198—200°, which had the expected molecular weight, but analytical figures indicated that the specimen was not quite pure. For the normal methyl ester of (II) [(VIII) and (IX) represent geometrical isomerism of the methoxycarbonyl group in the spirane structure] four stereoisomers (two racemates) are possible. The same situation pertains for the compounds (II) and (III). That both racemates are present in the case of each of these products is inferred from the two signals (integral 1H) for the aliphatic hydrogen on the sulphur ring. Inability to separate these racemates by crystallisation suggests that in solution the equilibrium reaction of ring opening and closing is very rapid.* For the methyl ester of (II) some pseudo-ester may also be formed [isomer (X)]. The i.r. spectra of the products from various preparations showed only slight variations.



(VIII)



(IX)



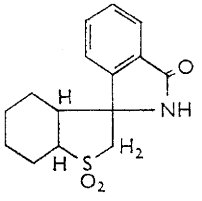
(X)

The same impure ester was obtained from (II) by the action of ethereal diazomethane. The silver salt of (II) gave analysis in close agreement with the theoretical value but when it was heated under reflux with methyl iodide the same slightly impure ester was obtained.

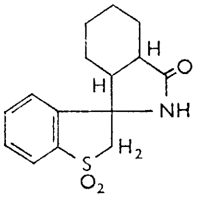
The product of decarboxylation (IVa) of the carboxylic acid (II) dissolved in boiling dilute sodium hydroxide solution and was recovered by acidification. When the alkaline solution was heated under reflux for a long time, no change occurred. The lactam (IVa) was also unaffected by hot 6M-hydrochloric acid and by nitrous acid. The results of further tests, mostly negative, with miscellaneous reagents are noted in the Experimental section.

Methylation of (IVa) with dimethyl sulphate and alkali gave the same *N*-methyl compound (IVb) as obtained by the action of this reagent on (II). In boiling acetic anhydride (IVa) gave the same *N*-acetyl compound (IVc) obtained by the action of this reagent on (II).

Both the lactam (IVa) and its *N*-methyl derivative (IVb) were desulphurised by heating under reflux with Raney nickel and ethanol. From (IVa) two crystalline products were separated. The more ethanol-soluble product was sulphur-free and has been shown to be 2,3-dihydro-3-methyl-3-phenylisoindol-1-one (Va). In boiling acetic anhydride this gave the *N*-acetyl derivative (Vb). The second product contains sulphur. Its analysis and molecular weight fitted the formula $C_{15}H_{17}NO_3S$, corresponding to the addition of six hydrogen atoms to the parent compound (IVa), and indicating the reduction of one of the benzene rings to form one of the cyclohexane derivatives (XI) and (XII). The u.v. absorption spectrum of the lactam (IVa) and this reduction product are very similar (Figure) to each other, and also to that of 2,3-dihydro-3-methyl-3-phenylisoindol-1-one (Va) (Figure); this suggests that the reduced compound has the structure (XI), in which the benzene ring of the benzo[*b*]thiophen *SS*-dioxide has been reduced. This conclusion is further supported by comparison of the spectrum of (XI) with that of 2,3-dihydrobenzo[*b*]thiophen *SS*-dioxide (Figure).



(XI)



(XII)

The action of Raney nickel in ethanol suspension on the *N*-methyl derivative (IVb) gave 2,3-dihydro-2,3-dimethyl-3-phenylisoindol-1-one (Vc), m.p. and i.r. spectrum identical with those of the compound obtained by Berti.[6,7]

The minor Schmidt reaction product (III) has a molecular weight of 329 (mass spectrum) and analysis fits the formula $C_{16}H_{11}NO_5S$. There is a marked difference between its u.v. spectrum and those of (II), (IVa), and (IVb). It melts with slow evolution of carbon dioxide. After the melt was maintained for some hours at 260° the lactam (IVa) was isolated in small yield. Decarboxylation of the product (III) readily occurred in boiling acetic anhydride to give the *N*-acetyl derivative (IVc). When (III) was heated under reflux in M-sodium

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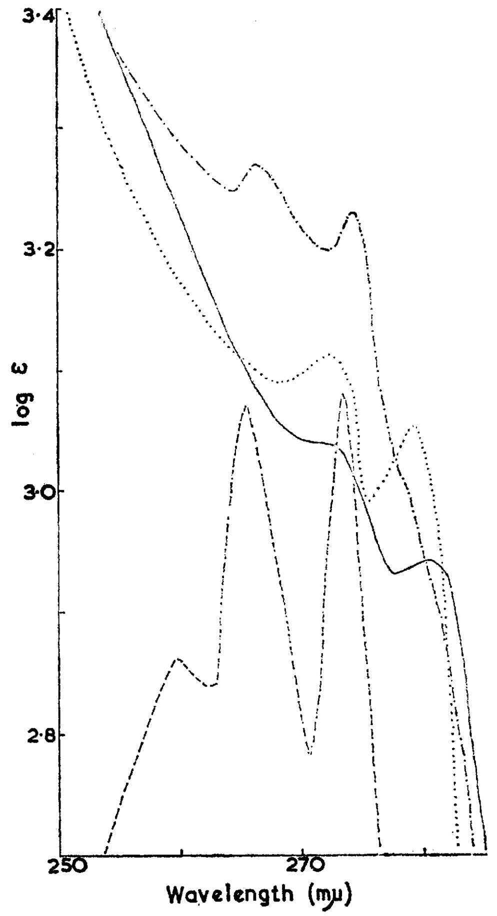
* We thank a referee for making these points.

[6] G. Berti, P. Corti, and F. Mancini, *Ann. Chim.* (*Italy*), 1959, **49**, 1253 (*Chem. Abs.*, 1960, **54**, 17,402c).

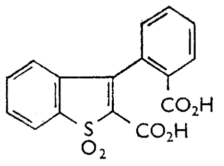
[7] G. Berti, *Gazzetta*, 1960, **90**, 559 (*Chem. Abs.*, 1961, **55**, 15,485b).

hydroxide ammonia was evolved readily, and a nitrogen-free carboxylic acid was formed, which has been assigned the tentative structure (XIII) on the basis of equivalent weight and evolution of carbon dioxide on melting.

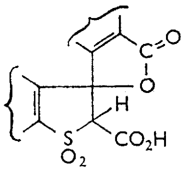


U.v. spectra of compounds (Va) (——), (XI) (· · · ·), and (IVa) (—·—), and of 2,3-dihydrobenzo[*b*]thiophen *SS*-dioxide (— — —)

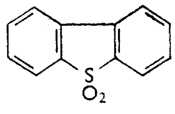
Alkaline hydrolysis of (III) with accompanying evolution of ammonia also indicates the structure (XIII). A referee has suggested that the dicarboxylic acid (XIII) would take up predominantly the structure (XIV).



(XIII)



(XIV)



(XV)

Spectral data (Experimental section) were considered not incompatible with these structures.

EXPERIMENTAL

Microanalyses were made by the Australian Microanalytical Service (Dr. K. W. Zimmermann and staff). U.v. spectra were measured for solutions in ethanol with an SP 700 Unicam instrument by Mrs. J. Troup except those of 2,3-dihydrobenzo[*b*]thiophen *SS*-dioxide and compounds (Vb and c), which were measured with a Cary 11 spectrophotometer by Mr. J. M. Edwards. I.r. spectra were determined for potassium chloride discs (unless otherwise stated) with a model 137 Perkin-Elmer Infracord by Mrs. J. Troup. N.m.r. spectra were determined with either a Varian H.R. 60 spectrometer by (the late) Mr. W. R. C. Stevenson or with a Varian A60 spectrometer by Mr. J. Little. The mass spectra were measured by direct insertion with an A.E.I. MS9 spectrometer by Dr. Q. N. Porter and Mr. A. Wedgwood (normal source temperatures up to 180°; ionising voltage 70 ev; ionising current at 100 μA).

M.p.s. marked with an asterisk were determined with a Kofler hot-stage apparatus and the remainder with an Electrothermal apparatus. Temperatures quoted for sublimations refer to the heating bath. Desulphurisations were carried out with W-4 grade Raney nickel.

I.r. spectra of the Schmidt reaction products and transformation products thereof were complex and assignment of a number of peaks was not attempted.

Mass spectra were obtained for the compounds (II), (III), (IVa, b, and c), (Va, b, and c), (XI), (XIII), and the methyl ester of (II). In all cases molecular weights were confirmed.

Benzo[b]*naphtho*[1,2-d]*thiophen*-5,6-*quinone* SS-*Dioxide* (I).—The procedure of Davies, Gamble, and Savige was modified.[8] Chromium trioxide (17·1 g.) in water (24 ml.) and glacial acetic acid (24 ml.) was added with shaking to a solution of 6a,11b-dihydrobenzo[*b*]naphtho[2,1-*d*]thiophen *SS*-dioxide (10·72 g.) in glacial acetic acid (320 ml.) at 55° during 12—15 min.; a small rise in temperature occurred. The mixture was kept at 60—65° for 15 min. (with shaking); addition of water (650 ml.) and storage for 4 hr. then yielded the quinone, which formed an orange crystalline powder (4·22 g.) after digestion with glacial acetic acid (65 ml.) at 100°; m.p. 331—335° (decomp.) (Found: C, 64·7; H, 3·15; O, 21·1; S, 10·7. Calc. for $C_{16}H_8O_4S$: C, 64·9; H, 2·7; O, 21·6; S, 10·8%), $\nu_{max.}$ 1704 (CO), 1667 (CO), 1300 (SO), and 1157 (SO) cm.$^{-1}$.

The quinone (I) was dissolved in concentrated sulphuric acid (*d* 1·84). After 1 hr. at 40—45° the solution was poured on crushed ice. The quinone was recovered in virtually quantitative yield. To detect any possible reaction of the sulphone groups with the hydrazoic acid–conc. sulphuric acid reagent, dibenzothiophen *SS*-dioxide (XV) was treated with hydrazoic acid–conc. sulphuric acid at 40—45° for 1 hr. The sulphone was recovered in virtually quantitative yield. It was assumed that the sulphone group of the quinone (I) would not react independently with the Schmidt reagent.

Schmidt Reaction on the Quinone (I).—Sodium azide (7·65 g.) was added to the quinone (I) (6·96 g.) in sulphuric acid (*d* 1·840; 94 ml.) during 15 min.; the internal temperature of the stirred mixture was maintained at 35—40°. The mixture was then kept at 40—45° for 0·5 hr. The sulphuric acid solution was decomposed with crushed ice (1200 ml.). After 1 hr. the precipitate (7·54 g.) was collected and stirred with 6·5% sodium hydrogen carbonate solution. After 5 min. a brown powdery precipitate (132 mg.) was removed, and the filtrate after acidification to pH 0·5 yielded a cream-coloured solid (6·82 g.). This was

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[8] W. Davies, N. W. Gamble, and W. E. Savige, *J. Chem. Soc.*, 1952, 4678.

stirred again with 6·5% sodium hydrogen carbonate solution, 3-*oxospiro{benzo*[b]*thiophen*-3,1′-*isobenzofuran}*-2-*carboxamide* SS-*dioxide* (III) (183 mg.) was filtered off, and more (III) (312 mg.) was obtained by acidification of the filtrate to pH 4. Acidification of the filtrate to pH 0·5 yielded 2,3-*dihydro*-3-*oxospiro{isoindole*-1,3′-*benzo*[b]*thiophen}*-2′-*carboxylic acid* SS-*dioxide* (II) (6·11 g.).

The acid (II), after repeated dissolution in 6·5% sodium hydrogen carbonate solution and precipitation with acid (as before) formed a colourless, micro-crystalline powder, m.p. 174—175° (with vigorous gas evolution) (Found: C, 58·0; H, 3·3; N, 4·2; O, 24·4; S, 9·5. $C_{16}H_{11}NO_5S$ requires C, 58·4; H, 3·35; N, 4·25; O, 24·3; S, 9·7%), $\lambda_{max.}$ 260sh, 269, and 275 mμ (log ε 3·30, 3·31, and 3·28), $\lambda_{min.}$ 265 and 273 mμ (log ε 3·26 and 3·23), $\nu_{max.}$ 1745 (CO), 1715 (CO), 1667 (CO), 1639 (CO), 1318 (SO), 1186 (SO), and 3322 (NH) cm.$^{-1}$, τ (CF_3CO_2H) 4·20 and 4·67 (combined integral 1H), as expected for a methine group α to a strongly electron-attracting group such as sulphone, and τ 0·94 (sharp, 1H), tentatively assigned to the secondary amide proton.

The amide (III), after further separation from (II) as described above, formed a cream-coloured micro-crystalline powder, m.p. 234—235° (with slow gas evolution) (Found: C, 57·5; H, 3·5; N, 4·4; O, 24·2; S, 9·45%), $\lambda_{max.}$ 220sh, 270sh, 276, 284, and 314 mμ (log ε 4·11, 3·48, 3·52, 3·50, and 3·45), $\lambda_{min.}$ 266, 280, and 298 mμ (log ε 3·46, 3·50, and 3·40), $\nu_{max.}$ 3460 (NH), 3344 (NH), 1779 (CO), 1704 (CO), 1312 (SO), and 1190 (SO) cm.$^{-1}$. The two sharp N–H stretching vibration modes of medium intensity at 3460 and 3344 cm.$^{-1}$ indicate a primary amide. There was no evidence of an O–H stretching band, which is further indication of the absence of the carboxy-group. N.m.r. spectrum (Me_2SO): τ 4·80, 4·98, and 5·83 (non-aromatic protons, peak height of the last approximately equal to the sum of the peak heights of the other two; the last two peaks possibly due to the methine proton α to the sulphone). The n.m.r. spectrum of a solution in pyridine suggests that the γ-lactone ring of (III) is opened in the presence of base to give the corresponding -amic acid: τ *ca.* −0·90 to −0·87 (CO_2H) and *ca.* 1·00 to 1·17 ($CONH_2$) (relative intensities 1 : 2) (tentative assignments). This interpretation was supported by the i.r. spectrum (pyridine): the peak at 1779 cm.$^{-1}$ ascribed to γ-lactone C=O stretching was greatly reduced in intensity and the amide C=O stretching peak at 1704 cm.$^{-1}$ was reduced to a shoulder of a broad peak at 1680—1690 cm.$^{-1}$. The compound recovered from pyridine solution showed the normal i.r. spectrum of (III). All other peaks in the n.m.r. spectrum of (III) in pyridine were assigned to aromatic protons.

2-*Acetylspiro{isoindole*-1,3′-*benzo*[b]*thiophen}*-3(2H)-*one* SS-*Dioxide* (IVc).—(a) *From the Schmidt reaction product* (II). The acid (II) (200 mg.) dissolved readily in boiling acetic anhydride (2·5 ml.). After 5 hr. ethanol was added to the clear solution and the solvents were removed. The residue (165 mg.), after digestion with boiling ethanol (5 ml.), was sublimed at 170—180°/0·03 mm. The *acetyl derivative* (IVc) formed white crystals, m.p. 291·5—292·5° (Found: C, 62·4; H, 4·1; N, 4·05; O, 19·2; S, 9·9. $C_{17}H_{13}NO_4S$ requires C, 62·4; H, 4·0; N, 4·3; O, 19·6; S, 9·7%), $\nu_{max.}$ 1742 (CO), 1686 (CO), 1299 (SO), and 1152 (SO) cm.$^{-1}$. The absence of the N–H stretching vibration and the presence of two C=O stretch bands at 1742 and 1686 cm.$^{-1}$ were taken as evidence for (IVc) being an *N*-acetyl, rather than an *O*-acetyl compound. The large difference between the two C=O stretching frequencies suggests that splitting of one C=O stretching vibration, as in (IVa), is unlikely. N.m.r. spectrum: (thionyl chloride) τ 7·39 (NAc) and 5·43, 5·66, 6·29, and 6·52 (ABq, *J* 13·8 c./sec., CH_2). The compound was recovered unchanged from the thionyl chloride solution.

(b) *From the Schmidt reaction product* (III). The amide (III) (212 mg.) dissolved readily in boiling acetic anhydride (2·5 ml.), but a solid precipitate soon separated and then disappeared after 1 hr. under reflux. After 5 hr. ethanol (5 ml.) was added to the clear solution, the solvents were removed, and purification was completed as in (a). The product (165 mg.) had m.p. 290—291° and its identity with (IVc) was shown by mixed m.p., i.r. spectrum, and analysis (Found: C, 62·8; H, 4·1; N, 4·15; O, 19·5; S, 9·55%).

(c) *From the decarboxylated product* (IVa). The decarboxylated product (IVa) (200 mg.) dissolved readily in boiling acetic anhydride; no precipitate formed during 5 hr. under reflux. The solution was worked up as described in (a). The product (180 mg.) had m.p. 291—292°. Mixed m.p., i.r. spectrum, and analysis proved its identity with the product from (a) (Found: C, 62·5; H, 4·1; N, 4·4; O, 19·7; S, 9·75%).

Spiro{isoindole-1,3′-*benzo*[b]*thiophen}*-3(2H)-*one* SS-*Dioxide* (IVa).—(a) *From the major Schmidt reaction product* (II). (i) *Thermal decarboxylation of* (II). The product (II) (2·0 g.) was heated to 240° during 20 min. and the temperature was kept at 240° during a further 20 min. Sublimation of the residue at 200°/0·05 mm. yielded the *decarboxlation product* (IVa) (1·6 g.). After digestion with boiling ethanol (5 ml.) and sublimation at 180°/0·04 mm., (IVa) formed colourless crystals, m.p.* 226—227° (Found: C, 63·0; H, 4·0; N, 4·7; O, 17·2; S, 11·1. $C_{15}H_{11}NO_3S$ requires C, 63·2; H, 3·85; N, 4·9; O, 16·8; S, 11·2%), $\lambda_{max.}$ 267 and 275 mμ (log ε 3·27 and 3·23), $\lambda_{min.}$ 265 and 273 mμ (log ε 3·25 and 3·20), $\nu_{max.}$ 3425 (NH), 1715 (CO), 1692 (CO), 1307 (SO), and 1166 (SO) cm.$^{-1}$; the two C=O stretching frequency bands are 23 cm.$^{-1}$ apart in both the potassium chloride disc and the Nujol mull spectra. The N–H stretching band at 3425 cm.$^{-1}$ indicates a free NH. N.m.r. spectrum: (thionyl chloride) τ 6·11 (s, CH_2); compound recovered unchanged from solution.

(ii) *Action of hydrogen peroxide on* (II). A mixture of (II) (150 mg.), hydrogen peroxide (30%; 5 ml.), and water (10 ml.) was made slightly alkaline with potassium hydroxide solution (10%; 0·8 ml.) and heated to boiling; vigorous gas evolution occurred. The mixture was then heated under reflux for 2·5 hr. (only intermittent heating was required). After acidification, the precipitate (79 mg.) was collected, digested with boiling methanol (0·5 ml.), and sublimed at 200°/0·01 mm. to yield (IVa), m.p. 228·5—229·5°, identical (mixed m.p. and i.r. spectrum) with the product from (i).

(iii) *Action of sodium hydroxide on* (II). A solution of (II) (500 mg.) in M-sodium hydroxide (30 ml.) was heated under reflux for 5 hr. and then set aside overnight. The precipitate (233 mg.) had m.p. 230—232°. Acidification of the filtrate yielded more precipitate (142 mg.), m.p. 224—226°. Both fractions were identical (mixed m.p. and i.r. spectrum) with (IVa).

(b) *From the minor Schmidt reaction product* (III). The minor product (III) (200 mg.) was heated to 260° during 20 hr.; very slow gas evolution occurred. The crude product (82 mg.) was collected by sublimation, and after crystallisation from ethanol and fractional sublimation, yielded white crystals (5 mg.), m.p. 229—230°, identical (mixed m.p. and i.r. spectrum) with (IVa).

(c) *From the* N-*acetyl derivative* (IVc). The *N*-acetyl derivative (IVc) (950 mg.) and 4M-hydrochloric acid (130 ml.) were heated under reflux for 15 hr. The precipitate was digested with boiling ethanol (5 ml.) and sublimed at 190—200°/0·03 mm. to give colourless crystals (617 mg.), m.p.* 226—228°, identical (mixed m.p., i.r. spectrum, and analysis) with (IVa) (Found: C, 63·4; H, 3·9; N, 4·55; O, 17·0; S, 11·4%).

Compound (IVa) was unchanged when heated with conc. sulphuric acid for 1 hr. at 45—50°. It did not react with benzoyl chloride or with arenesulphonyl chlorides under Schotten–Baumann conditions, nor with the usual carbonyl reagents. Attempts to prepare a benzylidene derivative were not successful. It did not react with a boiling solution of bromine in acetic acid, nor with phosphorus pentachloride. The compound was resistant to alkali and was unchanged after fusion with a mixture (1 : 1) of sodium and potassium hydroxide at 200°. Fusion with this mixture above 240° caused a complete change, but no pure product was isolated. Reductive alkaline attack on (IVa) also caused decomposition, as did oxidation with alkaline permanganate, but no pure product was isolated. When the compound in methanol was treated with a large excess of ethereal diazomethane only pure (IVa) was recovered.

2-*Methylspiro*{*isoindole*-1,3′-*benzo*[b]*thiophen*}-3(2H)-*one* SS-*Dioxide* (IVb).—(a) *From* (II). Dimethyl sulphate (7 ml.) was added to a solution of (II) (658 mg.) in 1·25M-sodium hydroxide (60 ml.). The mixture was shaken for 4 hr. and then heated on a boiling water bath for 2 hr. The precipitate was filtered from the now acid filtrate and digested with hot M-sodium hydroxide (40 ml.). Recrystallisation from methanol yielded the *decarboxylation product* (IVb) (368 mg.), m.p. 220·5—221·5°, $\lambda_{max.}$ 244sh, 266infl, 273, and 279infl mμ (log ε 3·75, 3·52, 3·36, and 3·05), $\lambda_{min.}$ 272 mμ (log ε 3·36), $\nu_{max.}$ 1692 (CO), 1307 (SO), and 1152 (SO) cm.$^{-1}$. Lack of absorption due to N–H stretching and the presence of a strong C=O peak showed that *N*-methylation had occurred. N.m.r. spectrum: (deuteriochloroform) τ 7·08 (NMe) and 6·13 (CH_2).

(b) *From the decarboxylated derivative* (IVa). Compound (IVa) (500 mg.) was dissolved in boiling 2·5M-sodium hydroxide solution (13·4 ml.), water (28 ml.) was added, and then dimethyl sulphate (3 ml.) was added gradually while the temperature was maintained at 30°. The mixture was shaken for 2 hr. and then heated under reflux for 2 hr. The precipitate (459 mg.) was digested with boiling M-sodium hydroxide solution (20 ml.), recrystallised from methanol, and sublimed at 180°/0·05 mm. to yield the *N*-methyl derivative (IVb), m.p.* 218·5—219·5°, identical (mixed m.p., i.r. spectrum, and analysis) with the product from (a) (Found: C, 64·3; H, 4·55; N, 4·2; O, 16·3; S, 10·8. $C_{16}H_{13}NO_3S$ requires C, 64·2; H, 4·35; N, 4·7; O, 16·1; S, 10·7%).

Esterification of the major Schmidt reaction product (II).—(*a*) A mixture of (II) (700 mg.), absolute methanol (12 ml.), and conc. sulphuric acid (0·06 ml.) was heated under reflux at 60° for 8 hr. and then boiled for 4 hr., and methanol (8 ml.) was distilled off. After decomposition of the residue with crushed ice (20 ml.) a cream precipitate (654 mg.) was collected, stirred with 6·5% sodium hydrogen carbonate solution for 5 min., then crystallised from methanol and sublimed at 180°/0·01 mm. to give *methyl* 2,3-*dihydro*-3-*oxospiro*{*isoindole*-1,3′-*benzo*[b]*thiophen*}-2′-*carboxylate* SS-*dioxide* (Found: C, 59·1; H, 3·85; N, 3·45; O, 23·9; S, 9·25. $C_{17}H_{13}NO_5S$ requires C, 59·5; H, 3·8; N, 4·1; O, 23·3; S, 9·35%), $\lambda_{max.}$ 202, 267, 275, and 317 mμ (log ε 4·86, 3·36, 3·36, and 3·08), $\lambda_{min.}$ 265, 272, and 292 mμ (log ε 3·31, 3·31, and 3·00), $\nu_{max.}$ 3165 (NH), 1739 (CO), 1701 (CO), 1321 (SO), and 1186 (SO) cm.$^{-1}$, τ (deuteriochloroform) 6·07, 6·12, and 6·24 (total 3H), 5·26 (*ca.* 1H), and aromatic signals.

(*b*) Compound (II) (575 mg.) was shaken with a large excess of ethereal diazomethane and then stored for 3 days at room temperature. The residual ether was evaporated off in the cold. The yellow sticky residue was stirred with 6·5% sodium hydrogen carbonate solution, then recrystallised from methanol. The m.p. was not sharp. The i.r. spectrum closely resembled that of the product from (*a*).

(c) A mixture of the dry *silver salt* of (II) (114 mg.) and methyl iodide (2 ml.) was boiled for 3 hr. and the methyl iodide was then evaporated off. The residue was extracted with boiling methanol (25 ml.) and the insoluble material was filtered off and discarded. After evaporation of the methanol the residue was stirred with 6·5% sodium hydrogen carbonate solution, then crystallised from methanol and then benzene to yield a white crystalline solid, m.p. 220—222° (decomp.). The i.r. spectrum closely resembled that of the product from (*a*). {Found [for the silver salt of (II)]: Ag, 24·9. $C_{16}H_{10}NO_5SAg$ requires Ag, 24·8%}.

3-(o-*Carboxyphenyl*)*benzo*[b]*thiophen*-2-*carboxylic Acid* SS-*Dioxide* (XIII).—The minor Schmidt reaction product (III) (50 mg.) was heated under reflux with M-sodium hydroxide (3 ml.) for 3 hr. Evolution of ammonia was observed after a few min. The solution was acidified to pH 1; the precipitate (42 mg.) had m.p. 141° (decomp.). After dissolution in 6·5% sodium hydrogen carbonate and removal of insoluble material by filtration, acidification of the filtrate yielded the *di-acid*, m.p. 137—138° (decomp.), which was shown to be free of nitrogen. A sharp end point was obtained on titration with alkali (calc. equiv. weight 191); $\nu_{max.}$ 1751 (CO), 1316 (SO), and 1183 (SO) cm.$^{-1}$; the Nujol mull spectrum also showed one C=O stretching band at *ca.* 1752 cm.$^{-1}$.

2,3-*Dihydro*-3-*methyl*-3-*phenylisoindol*-1-*one* (Va) *and* 3a′,4′,5′,6′,7′,7a′-*Hexahydrospiro*{*isoindole*-1,3′-*benzo*[b]-*thiophenol*}-3(2H)-*one* (XI).—A mixture of the decarboxylated compound (IVa) (1·74 g.), Raney nickel (ethanol) suspension (24 g.), and ethanol (180 ml.) was heated under reflux for 16 hr.; the Raney nickel was then removed by centrifugation and washed with ethanol (20 × 150 ml.). The ethanol was distilled from the combined extracts. The residue was recrystallised from ethanol (75 ml.) to yield a white crystalline solid (x) (754 mg.), m.p. 265—268·5°. The filtrate (y) was retained. The precipitate (x) after crystallisation from ethanol and sublimation at 200°/0·1 mm. yielded the *hexahydro-compound* (XI), m.p. 271·5—272·5° (Found: C, 61·7; H, 5·8; N, 4·6; O, 16·8; S, 11·0. $C_{15}H_{17}NO_3S$ requires C, 61·9; H, 5·85; N, 4·8; O, 16·5; S, 11·0%), $\lambda_{max.}$ 223sh, 273 and 280 mμ (log ε 4·08, 3·11, and 3·05), $\lambda_{min.}$ 269 and 276 mμ (log ε 3·09 and 2·99), $\nu_{max.}$ 3185 (NH), 1695 (CO), 1307 (SO), and 1121 (SO) cm.$^{-1}$. The N–H absorption at 3185 cm.$^{-1}$ indicated hydrogen bonding. Two peaks of medium intensity at 2933 cm.$^{-1}$ and 2857 cm.$^{-1}$ were assigned to CH_2 stretching vibrations. N.m.r. spectrum (thionyl chloride): τ 6·07, 6·30, 6·55, and 6·78 (ABq, *J* 13·8 c./sec., CH_2) and 7·4—9·2 (complex, cyclohexane). The filtrate (y) was diluted with water (225 ml.) and after storage for 24 hr. yielded a white sulphur-free precipitate (365 mg.). After repeated crystallisation from water and sublimation at 145°/0·4 mm. the precipitate yielded the *isoindolone* (Va), m.p. 209—211° (Found: C, 79·9; H, 6·65; N, 6·4. $C_{15}H_{13}NO$ requires C, 80·7; H, 5·85; N, 6·3%), $\lambda_{max.}$ 272sh and 281 mμ (log ε 3·04 and 2·94), $\lambda_{min.}$ 278 mμ (log ε 2·93), $\nu_{max.}$ 1678 (CO) and 3195 (H-bonded NH) cm.$^{-1}$. There is no sulphone absorption for (Va) or the other isoindolones. The n.m.r. spectra of the isoindolones (Va, b, and c) showed *C*-methyl signals at τ 8·05, 7·85, and 8·13, respectively. The respective peaks for the *N*-acetyl and *N*-methyl protons of (Vb) and (Vc) were at τ 7·38 and 7·18. The aromatic regions of the spectra of the Schmidt reaction products and the transformation products thereof were complex, especially those of the sulphone compounds, where two ABCD systems were present. The protons deshielded to the greatest extent are believed to be those at the 4 and 7′ carbon atoms β to the sulphone and carbonyl groups respectively. The 3-phenyl peaks of the phthalimidines (Vb and c) occurred at τ 2·80 and 2·77, respectively and between τ 2·68 and 2·72 for the slightly impure 2,3-dihydro-3-methyl-3-phenylisoindol-1-one (Va).

N-*Acetyl*-2,3-*dihydro*-3-*methyl*-3-*phenylisoindol*-1-*one* (Vb) was formed in boiling acetic anhydride (5 hr.), m.p. 102—104° (from aqueous methanol), $\lambda_{max.}$ 236, 282, and 287sh mμ (log ε 4·06, 3·26, and 3·24), $\lambda_{min.}$ 274 mμ (log ε 3·21) $\nu_{max.}$ 1724 (CO) and 1689 (CO) cm.$^{-1}$.

2,3-*Dihydro*-2,3-*dimethyl*-3-*phenylisoindol*-1-*one* (Vc).—A mixture of the *N*-methyl derivative (IVb) (1·4 g.), Raney nickel suspension (16 g.), and ethanol (120 ml.) was heated under reflux for 16 hr. The Raney nickel was removed by centrifugation and washed with ethanol (20 × 150 ml.). The ethanol was distilled from the combined extracts. The residue was recrystallised from ethanol (28 ml.) to yield white crystals (488 mg.). Addition of an equal volume of water to the filtrate yielded more precipitate (73 mg.). The filtrate (z) was retained. The combined precipitates after crystallisation from ethanol and vacuum sublimation were shown by mixed m.p. and i.r. spectrum to be unchanged (IVb). Further dilution of the filtrate (z) with water yielded a sulphur-free crystalline precipitate (341 mg.), m.p. 107—111°. Further crystallisation from aqueous ethanol yielded 2,3-dihydro-2,3-dimethyl-3-phenylisoindol-1-one (Vc), m.p. 109·5—112° (lit.,[6] 113—115°), $\lambda_{max.}$ 246, 272infl and 281 mμ (log ε 3·78, 3·41, and 3·26), $\lambda_{min.}$ 240 and 279 mμ (log ε 3·77 and 3·26). The i.r. spectrum was identical with that of the compound obtained by Berti:[6,7] $\nu_{max.}$ 1684 (CO) cm.$^{-1}$.

We thank Dr. T. J. Batterham for assistance in interpreting the n.m.r. spectra.

[6/136 *Received, 2nd February*, 1966]