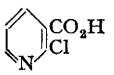
382. *Xanthones and Thioxanthones. Part IV. The Preparation and Properties of 9-Oxa-1-aza-anthrone and 9-Thia-1-aza-anthrone.*

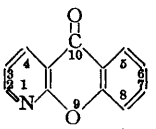
By Frederick G. Mann and (Mrs.) J. A. Reid.

The preparation of the intermediate 2-chloronicotinic acid and of 9-oxa-1-aza-anthrone has been improved, and the former has also been utilised for the preparation of 9-thia-1-aza-anthrone. The general properties and chemistry of these two anthrones have been studied, and the 8-carboxylic acid of the thia-aza-anthrone has been synthesised.

In Part III * a brief description was given of the condensation of 2-chloronicotinic acid (I) with sodium phenoxide, to give 2-phenoxynicotinic acid, which on treatment with phosphorus oxychloride underwent cyclisation to form 9-oxa-1-aza-anthrone (II). It was essential however to improve the preparation of the acid (I) before further work on these lines could be profitably undertaken. In the earlier work, 2-aminonicotinic acid was prepared from quinolinic imide : we now find it far better to start with quinolinic anhydride, which is converted by gaseous ammonia into 2-carbamylnicotinic acid (Fibel and Spoerri, *J. Amer. Chem. Soc.*, 1948, **70**, 3908), which in turn by the Hofmann reaction furnishes 2-aminonicotinic acid (Philips, *Annalen*, 1895, **288**, 253). Furthermore, modifications in the diazotisation of this acid have now greatly improved the yield of 2-hydroxynicotinic acid, the precursor of the chloro-acid (I). Our overall yield of the acid (I) from the anhydride is now 30%, whereas that from the imide was only 8%. We have moreover considerably improved the conversion of the acid (I) into the oxa-aza-anthrone (II), supplies of which in consequence are now reasonably readily available.



(I)



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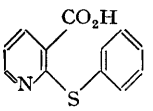

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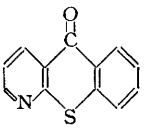


(IV)

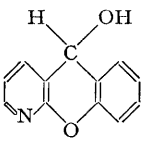
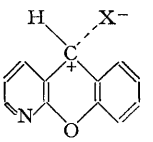
It is noteworthy that 2-chloronicotinic acid would not undergo condensation with the sodium derivative of thiophenol, similar to that with sodium phenoxide, considerable decomposition occurring when the two compounds were heated together. When however the acid was heated with free thiophenol under appropriate conditions, condensation occurred with the formation of 2-3′-carboxypyridyl phenyl sulphide (III) : this con-

* Part III, *J.*, 1951, 761.

densation apparently occurs only in acid media. The acid (III) when heated with phosphorus oxychloride underwent cyclisation to the hitherto unknown 9-thia-1-aza-anthrone (IV). It should be emphasised that success in the last two stages of this synthesis, as in the parallel stages in the synthesis of (II), is dependent on a very delicate control of the experimental conditions.

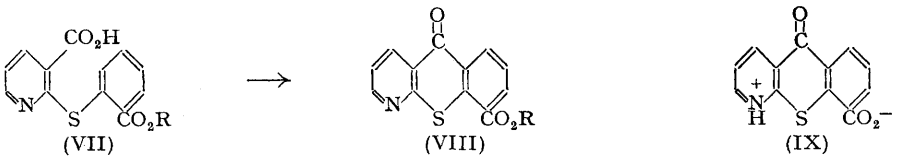
The chemical properties of both the oxa-aza-anthrone (II) and the thia-aza-anthrone (IV) have now been investigated. The basic properties of the thia-aza-anthrone (IV), although weak, are stronger than those of the oxa-analogue (II) : for example, a solution of the former in hydrochloric acid, when evaporated to dryness at room temperature, gave the hydrochloride of the thia-aza-anthrone, whereas a similar solution of the oxa-aza-anthrone when thus treated gave the oxa-aza-anthrone itself. Solutions of each anthrone in hydrochloric acid on treatment with chloroplatinic acid deposited chloroplatinates, but these salts, like the above hydrochloride, readily dissociated in water. The oxa-aza-anthrone however when heated with methyl toluene-*p*-sulphonate underwent quaternisation, and the product could readily be converted into the methiodide and the metho-picrate. The thia-aza-anthrone behaved similarly, but the constitution of the product is uncertain, since combination with the methyl group might occur at either the nitrogen or the sulphur atom. The general similarity between the metho-salts obtained from the two compounds indicated that in the thia-compound (IV), true quaternisation on the nitrogen atom had also occurred : but it must be emphasised that the sulphur atom in (IV) is not generally inactive, since hydrogen peroxide in acetic acid yielded the corresponding sulphone. Although in the quaternisation experiments the thia-aza-anthrone was heated with an excess of methyl toluene-*p*-sulphonate, no indication of the addition of two molecules of the latter was obtained : this was expected, because the positive pole arising from the union with the first molecule of the sulphonate, whether on the nitrogen or the sulphur, would almost certainly inactivate the neighbouring hetero-atom (cf. Mann and Watson, *J. Org. Chem.*, 1948, **13**, 502).

Both the oxa- and the thia-aza-anthrone were reduced to the corresponding anthranols (as V) when treated in ethanolic solution with mercury and sodium (cf. Oehlschlaeger and MacGregor, *J. Amer. Chem. Soc.*, 1950, **72**, 5332). When the oxa-aza-anthranol (V) was treated with acids, the composition of the products showed that salt formation had occurred, not by neutralisation at the tertiary nitrogen atom, but by the molecule's acting as a true xanthhydrol, *i.e.*, the salts were of composition (VI; X = acid radical). The cation in such salts will clearly be a resonance hybrid having more canonical forms than the unsubstituted xanthhydrylium cation, since the positive charge in (VI) can be carried by carbon atoms 2, 4, 5, 7, or 10 or by the oxygen or nitrogen atom (cf. Mann and Turnbull, *J.*, 1951, 757).

(V)   (VI)

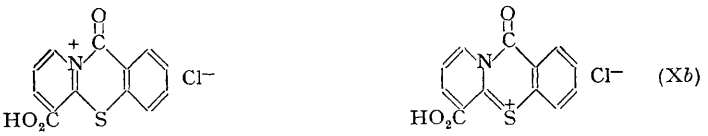
We have synthesised 9-thia-1-aza-anthrone-8-carboxylic acid (VIII; R = H) as one of a series of substituted derivatives of (IV) which we are preparing for therapeutic examination. The acid (I) condensed with thiosalicylic acid under special conditions to give 2-carboxyphenyl 2-3′-carboxypyridyl sulphide (VII; R = H), but all attempts to cyclise this acid to the required anthrone (VIII; R = H) failed. The constitution of this acid was not in doubt however, since treatment of it with phosphorus oxychloride followed by methanol gave a dimethyl ester which was identical with that obtained by the condensation of methyl chloronicotinate with methyl thiosalicylate. Moreover, the chloro-acid (I) also condensed with methyl thiosalicylate to give 2-carbomethoxyphenyl 2-3′-carboxypyridyl sulphide (VII; R = Me), m. p. 167—168°, and the latter on gentle hydrolysis furnished the same acid (VII ; R = H). The methyl ester (VII; R = Me) when boiled with phosphorus oxychloride underwent cyclisation to methyl 9-thia-1-aza-anthrone-8-carboxylate (VIII; R = Me), m. p. 194—195°, which on hydrolysis gave the free acid (VIII; R = H),

m. p. 348—349°. The remarkably high m. p. of this acid indicated that it probably exists as the zwitter-ion (IX).



(VII) (VIII) (IX)

The above condensation of the chloronicotinic acid (I) with methyl thiosalicylate, in addition to furnishing the colourless ester (VII; R = Me), gave as a by-product a bright yellow compound $C_{13}H_8O_3NClS$. When treated with sulphuric acid this evolved hydrogen chloride, and when heated with water readily gave the colourless acid (VII; R = H), although the corresponding methyl ester (VII; R = Me) was virtually unaffected by water or even very dilute hydrochloric acid under these conditions. The yellow compound was converted by cold methanol into the methyl ester (VII; R = Me) and conversely the latter when heated with methyl thiosalicylate or diphenyl ether in the presence of hydrogen chloride regenerated the yellow product.



These properties afford considerable evidence that the yellow compound is 1-carboxy-9-thia-4*a*-aza-anthronium chloride, a compound in which the cation will have the two canonical forms shown in (X*a* and *b*) and hence would almost certainly be coloured. This novel structure, if correct, must clearly involve a very reactive N–C linkage in the central ring, since this bond is so readily broken by water and methanol (with loss of hydrogen chloride) to form the acid and the methyl ester (VII; R = H and Me respectively). In this respect it is comparable to the similar group in an *N*-acylpyridinium salt.

The compounds (II) and (IV) and certain of their derivatives are being tested as possible drugs for treatment of schistosomiasis and of amoebic infections; initial tests carried out by Mr. O. D. Standen at the Wellcome Laboratories of Tropical Medicine indicate that (II) and (IV) have no significant effect on schistosomiasis infections.

Experimental

The following preparation of 2-chloronicotinic acid embodies various improvements on published methods.

2-*Carbamylnicotinic Acid.*—A solution of quinolinic anhydride (27 g.) in ethyl methyl ketone (370 c.c.) was treated with an excess of gaseous ammonia (Fibel and Spoerri, *loc. cit.*). The copious white precipitate was collected; the bulk of it was soluble in water and complete dissolution was obtained by adding a small quantity of ammonia solution. 2-Carbamylnicotinic acid (17 g.), m. p. 172° (decomp.), was precipitated by acidification of the solution with sulphur dioxide.

2-*Aminonicotinic Acid.*—The foregoing acid (18 g.) was added with stirring to a solution at 0° of bromine (7·65 c.c.) and sodium hydroxide (32 g.) in water (350 c.c.). The solution thus obtained was stirred at 0° for 5 minutes, at room temperature for 10 minutes, and at 70—75° for 1 hour. The cooled solution was neutralised with concentrated hydrochloric acid and then acidified to pH 5·0 with acetic acid. The mixture was stirred at 0° for 1 hour; the solid was then collected and when once crystallised from water gave 2-aminonicotinic acid (11 g.), m. p. 297° (decomp.).

2-*Hydroxynicotinic Acid.*—2-Aminonicotinic acid (10 g.) was diazotised essentially according to Mann and Turnbull (*loc. cit.*) but the yield was considerably increased by using 7·5 g. of sodium nitrite. 2-Hydroxynicotinic acid (10 g.), m. p. 253—255° (decomp.) (inserted at 230°), was obtained.

2-*Chloronicotinic Acid.*—This was prepared from 2-hydroxynicotinic acid according to Fibel and Spoerri (*loc. cit.*).

9-*Oxa*-1-*aza-anthrone* (II).—A mixture of 2-phenoxynicotinic acid (0·7 g.) and phosphorus oxychloride (14 c.c.) was heated under reflux at 130—140° for 90 minutes and then cooled and diluted with light petroleum (b. p. 40—60°) (50 c.c.). The crude anthrone separated as a brown oil which when triturated in turn with light petroleum (2 × 25 c.c.) and with dilute sodium carbonate solution formed a pale brown solid (0·6 g.), m. p. 178°, which was collected, washed with water, dried, and sublimed under reduced pressure. The pale yellow sublimate (0·57 g.), m. p. 181—182°, when recrystallised from ethanol, gave the pure anthrone (II) as needles, m. p. 182—183°. It gave a pale yellow solution in concentrated sulphuric acid. Its solution in concentrated hydrochloric acid on dilution with water, or on evaporation to dryness *in vacuo* at room temperature, deposited the free base (Found : N, 7·0. Calc. for $C_{12}H_7O_2N$: N, 7·1%). But when an ethereal solution of the base was treated with hydrogen chloride a white solid separated which rapidly decomposed on exposure to moist air. A solution of the anthrone in 20% hydrochloric acid when added to a solution of chloroplatinic acid deposited a yellow chloroplatinate, which however when treated with water readily regenerated the anthrone.

A mixture of the anthrone (II) and methyl toluene-*p*-sulphonate (10 parts by wt.) was heated at 150—160° for 2 hours and then at 170° for 2 hours. After cooling, the mixture was extracted thrice with ether; the oily undissolved residue was taken up in ethanol and treated with ethanolic sodium iodide. After 30 minutes at room temperature, the precipitated *methiodide* was collected and recrystallised from methanol, forming golden-yellow needles, m. p. 206° (decomp.) (after cooling it remelted at 182—183°) (Found : C, 46·3; H, 3·15. $C_{13}H_{10}O_2NI$ requires C, 46·05; H, 2·95%).

The above ethanolic solution of the methotoluene-*p*-sulphonate when treated with ethanolic sodium picrate deposited the *methopicrate*, which from methanol formed pale yellow crystals, m. p. 197—198° (Found : C, 51·6; H, 2·65. $C_{19}H_{12}O_9N_4$ requires C, 51·8; H, 2·75%).

9-*Oxa*-1-*aza-anthran*-10-*ol* (V).—Sodium (0·12 g.) was added to a mixture of the anthrone (II) (0·2 g.), ethanol (3 c.c.), and mercury (10 g.) during 15 minutes with vigorous shaking, the temperature being kept at *ca.* 40°. After a further 15 minutes' shaking, the ethanolic solution was separated and the amalgam washed with hot ethanol. The combined ethanolic solutions were filtered, concentrated to 2 c.c., and diluted with water (10 c.c.), The anthranol was collected and recrystallised successively from benzene and water, to give white crystals, m. p. 149·5—150° (decomp.) (inserted at 140°) (Found : C, 72·6; H, 4·7. $C_{12}H_9O_2N$ requires C, 72·35; H, 4·55%). It gave a yellow colour with concentrated sulphuric acid. A hot aqueous solution was added to a solution of chloroplatinic acid; the *chloroplatinate dihydrate* separated as a yellow solid (Found : C, 35·85; H, 2·7; Pt, 24·15. $C_{24}H_{16}O_2N_2Cl_6Pt,2H_2O$ requires C, 35·6; H, 2·5; Pt, 24·15%), which when dried at 100°/0·1 mm. gave the anhydrous *salt* (Found : C, 37·3; H, 2·5; Pt, 25·4. $C_{24}H_{16}O_2N_2Cl_6Pt$ requires C, 37·3 ; H, 2·1 ; Pt, 25·4%).

2-3′-*Carboxypyridyl Phenyl Sulphide* (III).—A mixture of 2-chloronicotinic acid (1·57 g.) and thiophenol (2 c.c.) was heated at 140° until it effervesced and a clear solution was obtained; heating was then continued at 185—190° for 1 hour. The mixture, which solidified on cooling, was dissolved in sodium hydrogen carbonate solution and then extracted with ether. The aqueous layer, when acidified with glacial acetic acid, deposited the *sulphide* (1·58 g.), m. p. 170—171°, which was collected after 1 hour and recrystallised from carbon tetrachloride, forming colourless plates, m. p. 171—171·5° (Found : C, 62·65; H, 3·65; N, 6·2. $C_{12}H_9O_2NS$ requires C, 62·3; H, 3·9; N, 6·05%).

9-*Thia*-1-*aza-anthrone* (IV).—A mixture of the sulphide (III) (1 g.) and phosphorus oxychloride (20 c.c.) was heated under reflux at 130—140° for 2 hours. The dark red-brown solution, from which a small amount of oil had separated, was cooled and treated with light petroleum (b. p. 40—60°) as in the preparation of 9-oxa-1-aza-anthrone. The pale brown solid (0·6 g.), m. p. 227—229°, was sublimed at 180°/2 mm., and the 9-*thia*-1-*aza-anthrone* thus obtained was then recrystallised from ethanol, forming white needles, m. p. 234° (Found : C, 67·55; H, 3·45; N, 6·65. $C_{12}H_7ONS$ requires C, 67·6; H, 3·3; N, 6·5%). The anthrone gave a yellow solution both in concentrated hydrochloric acid and in sulphuric acid. A solution in hydrochloric acid was evaporated to dryness *in vacuo* at room temperature : the *hydrochloride* separated as long pale yellow needles (Found : N, 5·45. $C_{12}H_7ONS,HCl$ requires N, 5·6%), which when treated with water deposited the thia-aza-anthrone. A solution of the anthrone in 20% hydrochloric acid when added to chloroplatinic acid gave a yellow precipitate which was similarly unstable to water.

The *methiodide* was prepared precisely as the oxa-analogue, and crystallised from methanol as orange needles, m. p. 234° (previous darkening) (Found : C, 44·1; H, 2·7. $C_{13}H_{10}ONIS$ requires C, 43·95; H, 2·85%).

The *methopicrate*, prepared as the analogous oxa-compound, separated from methanol as yellow crystals, m. p. 216—217° (Found: C, 50·3; H, 3·0; N, 12·2. $C_{19}H_{12}O_8N_4S$ requires C, 49·8; H, 2·65; N, 12·2%).

9-*Thia*-1-*aza-anthrone* 9 : 9-*Dioxide*.—A suspension of 9-thia-1-aza-anthrone (0·1 g.) in glacial acetic acid (2 c.c.) and 30% hydrogen peroxide (0·4 c.c.) was set aside at 40° for 48 hours; after 8 hours and after a further 20 hours more hydrogen peroxide (2 × 0·1 c.c.) was added. The mixture was then cooled and the *sulphone*, m. p. 258—259°, collected; it separated from ethanol as white needles, m. p. 263—263·5° (Found: C, 59·0; H, 3·05; N, 5·8. $C_{12}H_7O_3NS$ requires C, 58·75; H, 2·9; N, 5·7%). This compound is considered to be the sulphone and not the isomeric amine-oxide sulphoxide because: (i) Although a tertiary aliphatic amine can usually be converted into an amine oxide by hydrogen peroxide, the tertiary nitrogen atom in an "aromatic" ring usually requires peracetic, perbenzoic, or perphthalic acid for a similar oxidation (cf. Meisenheimer, *Ber.*, 1926, **59**, 1848; Mamalis and Petrow, *J.*, 1950, 703). (ii) The N→O link has marked polar properties, and consequently tertiary amine oxides unite readily with acids, *e.g.*, with hydrogen chloride to give a hydroxychloride: sulphoxides have similar (although less marked) properties, and often combine, *e.g.*, with nitric acid to give compounds of type $[R_2S(OH)]NO_3$; our compound however was unchanged when treated with hydrochloric acid or with picric acid. (iii) The fact that the thia-aza-anthrone (IV) will not combine with 2 mols. of methyl toluene-*p*-sulphonate is strong evidence that the nitrogen and the sulphur atom cannot both increase their normal valency state. It is probable therefore that the initial action of the hydrogen peroxide is to convert the sulphide into a sulphoxide group, a process which deactivates the nitrogen while allowing further oxidation to a sulphone to occur.

Spectroscopic confirmation of these conclusions has been obtained by Dr. N. Sheppard, who has kindly provided the following report. "The most reliable method of distinguishing between the sulphone and the isomeric amine oxide sulphoxide by infra-red spectroscopic means is to examine the spectra for the absorption bands of sulphone or sulphoxide groups. Sulphones with normal aliphatic or aromatic groups usually have strong absorption bands in the regions of 1340—1295 and 1160—1120 cm.$^{-1}$, whereas sulphoxides exhibit a single strong absorption band between 1060 and 1030 cm.$^{-1}$ (Barnard, Fabian, and Koch, *J.*, 1949, 2442). Tertiary amine oxide groups do not seem to have been so reliably characterised by infra-red means.

"The spectrum of the substance was investigated in the region 1500—1000 cm.$^{-1}$ as a mull in "Nujol," with a Hilger D209 double-beam infra-red spectrometer. Apart from the "Nujol" absorption band near 1460 cm.$^{-1}$, the two strongest bands in the spectrum occurred at 1315 and 1165 cm.$^{-1}$. The former falls well in the region to be expected for sulphone groups and the latter is just outside the region characteristic of simpler molecules containing this group. No absorption band of appreciable strength occurred in the usual sulphoxide region from 1060 to 1030 cm.$^{-1}$, the nearest absorption being a band of medium strength at 1067 cm.$^{-1}$ which was several times weaker than either of the above two absorption bands. This spectroscopic evidence thus strongly favours the formulation of the compound as a sulphone rather than a sulphoxide."

9-*Thia*-1-*aza-anthran*-10-*ol* (*as* V).—The reduction of 9-thia-1-aza-anthrone was performed similarly to that of 9-oxa-1-aza-anthrone except that 4 times the quantities of sodium, mercury, and ethanol were used, the reaction mixture being finally boiled under reflux for 10 minutes. The *anthranol* was crystallised in turn from benzene and water, forming a white solid, m. p. 147—148° (decomp.) (inserted at 130°) (Found: C, 66·8; H, 3·95. $C_{12}H_9ONS$ requires C, 66·95; H, 4·2%). It gave an orange-red colour with concentrated sulphuric acid.

2-*Carboxyphenyl* 2-3′-*Carboxypyridyl Sulphide* (VII; R = H).—(*a*) Chloronicotinic acid (0·7 g.) and thiosalicylic acid (0·7 g.) were intimately mixed in a 150-c.c. conical flask which was then plunged into a bath at 170—175° for 6 minutes. The mixture effervesced and formed a bright yellow hard solid which was then dissolved in sodium hydrogen carbonate solution. Acidification of the solution with hydrochloric acid deposited the *sulphide* (1 g.), m. p. 186—187°, which after 5 hours at room temperature was collected and recrystallised from water, forming colourless crystals, m. p. 192—193° (this m. p. was very dependent on particle size and traces of water) (Found: C, 56·65; H, 3·25; N, 5·1. $C_{13}H_9O_4NS$ requires C, 56·7; H, 3·3; N, 5·1%).

(*b*) The methyl ester (VII; R = Me) (see below) was hydrolysed by boiling 0·5N-sodium carbonate for 30 minutes. The solution, on acidification with hydrochloric acid, gave the sulphide (VII; R = H), m. p. 191° (unchanged when mixed with the above specimen).

Attempted Ring Closure of the Sulphide (VII; R = H).—The sulphide (0·1 g.) and phosphorus oxychloride (3 c.c.) were boiled under reflux for 5 hours. The cold product was diluted

with light petroleum (b. p. 60—80°), and the dark oil which separated was then boiled under reflux with methanol (7 c.c.) for 30 minutes. The solution was concentrated to small bulk and poured into water. 2-Carbomethoxyphenyl 2-3′-carbomethoxypyridyl sulphide separated as an oil which slowly solidified and formed colourless crystals, m. p. 76—77° (unchanged when mixed with the specimen obtained as below) from light petroleum (b. p. 60—80°).

Methyl 2-Chloronicotinate.—A solution of 2-chloronicotinic acid (0·5 g.) in methanol (5 c.c.) was treated with ethereal diazomethane until there was a faint permanent yellow colour. The ether was removed and the oily residue distilled. The distillate solidified and was recrystallised twice from petroleum (b. p. 45—50°), to give *methyl 2-chloronicotinate*, m. p. 23° (Found: C, 49·3; H, 3·65; N, 8·0. $C_7H_6O_2NCl$ requires C, 49·0; H, 3·5; N, 8·15%).

2-Carbomethoxyphenyl 2-3′-Carbomethoxypyridyl Sulphide.—A solution of methyl 2-chloronicotinate (0·1 g.) and methyl thiosalicylate (0·2 c.c.) was heated at 170° for 1 hour. The product was extracted with hot light petroleum (b. p. 60—80°) (25 c.c.). The extract, on cooling, deposited an oil which tended to solidify. The petroleum was decanted and the semi-solid residue was dissolved in methanol. Addition of water precipitated an oil which slowly solidified as needles, m. p. 75—77°. The crystals were collected, washed with water, and recrystallised twice from light petroleum, to give the *sulphide* as colourless crystals, m. p. 77—78° (Found: C, 59·3; H, 4·4; N, 4·35. $C_{15}H_{13}O_4NS$ requires C, 59·4; H, 4·3; N, 4·6%).

2-Carbomethoxyphenyl 2-3′-Carboxypyridyl Sulphide (VII; R = Me).—A mixture of 2-chloronicotinic acid (0·5 g.) and methyl thiosalicylate (1 c.c.), when heated at 170°, rapidly formed a clear solution, hydrogen chloride being evolved; a yellow solid gradually separated. After 30 minutes at 170° the sludge was boiled with benzene (5 c.c.); the bright yellow solid which remained undissolved was collected and again extracted with hot benzene (2 × 5 c.c.). The combined benzene extracts, on concentration, gave the *sulphide* (VII; R = Me) (0·5 g.), m. p. 159—164°, which formed heavy crystals, m. p. 167—168° (decomp.), from benzene (Found: C, 58·05; H, 4·1; N, 4·85. $C_{14}H_{11}O_4NS$ requires C, 58·1; H, 3·85; N, 4·85%). The sulphide, after it had been boiled with water for an hour, had m. p. 160—164°, and after it had been boiled with 0·1% hydrochloric acid (1 molecular proportion) for 2 hours had m. p. 158°.

9-Thia-1-aza-anthrone-8-carboxylic Acid (VIII; R = H).—A mixture of the sulphide (VII; R = Me) (0·2 g.) and phosphorus oxychloride (6 c.c.) was heated under reflux at 145—155° for 2 hours. *Methyl 9-thia-1-aza-anthrone-8-carboxylate* (VIII; R = Me) (0·1 g.), m. p. 189—190° (softening at 183°), was extracted from the reaction mixture by a procedure similar to that used for 9-oxa-1-aza-anthrone, and when sublimed and then recrystallised from methanol gave white needles, m. p. 194—195° (Found: C, 61·9; H, 3·35; N, 5·25. $C_{14}H_9O_3NS$ requires C, 62·0; H, 3·35; N, 5·15%). This ester (0·05 g.) was boiled under reflux with 0·2N-sodium hydroxide (2·5 c.c.) for 2 hours, and the hot solution was acidified with acetic acid and cooled. *9-Thia-1-aza-anthrone-8-carboxylic acid* which separated was recrystallised from ethanol, forming white crystals, m. p. 348—349° (decomp.) (Found: C, 60·5; H, 2·95; N, 5·4. $C_{13}H_7O_3NS$ requires C, 60·7; H, 2·75; N, 5·45%). It was insoluble in water and in benzene.

1-Carboxy-9-thia-4a-aza-anthronium Chloride (X*a–b*).—The bright yellow solid, obtained as a by-product in the preparation of 2-carbomethoxyphenyl 2-3-carboxypyridyl sulphide (VII; R = Me), was purified by extraction with hot dry acetone; its composition was that of *1-carboxy-9-thia-4a-aza-anthronium chloride* (Found: C, 53·4; H, 3·0; N, 5·2; Cl, 12·1. $C_{13}H_8O_3NClS$ requires C, 53·0; H, 2·75; N, 4·75; Cl, 12·05%). The compound was insoluble in benzene, acetone, *cyclo*hexanone, *cyclo*hexanol, chloroform, toluene, light petroleum, dioxan, or dimethylformamide. The compound reacted with concentrated sulphuric acid with evolution of hydrogen chloride, to form a yellow solution which became colourless on dilution with water. When boiled with water it rapidly gave a colourless solution which on cooling deposited 2-carboxyphenyl 2-3′-carboxypyridyl sulphide (VII; R = H) (Found: C, 56·8; H, 4·2; N, 8·2%), m. p. 190—191°, unchanged when mixed with the sulphide obtained either by direct interaction of chloronicotinic acid with thiosalicylic acid or by hydrolysis of the monomethyl ester. Treatment with cold methanol overnight gave 2-carbomethoxyphenyl 2-3′-carboxypyridyl sulphide (VII; R = Me), m. p. 164—167°, unchanged by admixture with the authentic material. The yellow salt was also obtained by treating the methyl ester (VII; R = Me) in either diphenyl ether or methyl thiosalicylate with hydrogen chloride at 170°.

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