and distilled in vacuum since it is a liquid. The yield, after two fractional distillations was 11.8 g. (57.6%) and the distillation temperature was 198–200° at 13 mm. pressure. The boiling point recorded in literature[4] is 270–276° at 80 mm. pressure.

Methyl β-(*p*-Biphenylamino)-crotonate (III).—A solution of 169 g. (1.0 mole) of *p*-aminobiphenyl and 131.5 g. (1.1 moles) of methyl acetoacetate in 375 ml. of chloroform, acidified with 4 drops of dilute hydrochloric acid, was refluxed under a heavier-than-water liquid separator until no more water collected. After cooling, the crystalline mass in the flask was diluted with 200 ml. of petroleum ether and the solid removed by filtration. The yield was 235.5 g. (88.5%) and the substance melted at 164–165.5°. Two grams of III was purified by recrystallization from ethyl alcohol. Pure III was obtained as white platelets which melted at 165–166.5°.

Anal. Calcd. for $C_{17}H_{17}NO_2$: N, 5.24. Found: N, 5.24.

6-Phenyl-4-hydroxyquinaldine (IV).—Diphenyl ether (130 ml.) was heated to boiling and 32.3 g. (0.12 mole) of crude III was added in one portion. The solution was boiled until no more methyl alcohol distilled. After the solution cooled to room temperature, it was diluted with 25–30 ml. of petroleum ether, filtered and the solid washed first with ethyl ether then with petroleum ether. The yield of IV was 23.5 g. (83%) and it melted at 315–316°. Recrystallization from isopropyl alcohol, with decolorizing charcoal, did not change the melting point.

Anal. Calcd. for $C_{16}H_{13}NO$: N, 5.95. Found: N, 5.96.

8-Phenyl-4-hydroxyquinaldine (V).—Methyl acetoacetate and *o*-aminobiphenyl were condensed in chloroform solution as in the preparation of III. The crude liquid methyl β-(*o*-biphenylamino)-crotonate could not be caused to solidify. In an attempt to remove the excess methyl acetoacetate, the liquid was heated in an oil-bath at 180–190° at a pressure of 13 mm. After cooling, the contents of the flask congealed. Recrystallization of the solid from dilute ethyl alcohol and from benzene gave 106 g. (45%) of V which melted at 207–209°. A mixed melting point with V which was produced by ring closure of a small amount of the above crude liquid *o*-biphenylaminocrotonate in boiling phenyl ether, showed no depression. The melting point for V recorded by Hughes and Lions[5] is 280°.

Anal. Calcd. for $C_{16}H_{13}NO$: N, 5.95. Found: N, 6.08.

6-Phenyl-4-methylcarbostyril (VI).—*p*-Phenylacetoacetanilide was prepared in an 85% yield from *p*-aminobiphenyl and diketene in benzene according to the general procedure described by Kaslow and Sommer.[9] The substance melted at 147–148.5°. Eighteen grams (0.07 mole) of *p*-phenylacetoacetanilide was added to 150 ml. of mineral oil at 275° and the heating continued for two minutes. After cooling, 100 ml. of petroleum ether was added, the solid removed by filtration and washed with ether. The yield of brown colored crude VI was 11.7 g. (70.5%) which melted at 187–196°. After recrystallization from ethyl alcohol and cellosolve, the substance melted at 213–214.5°.

Anal. Calcd. for $C_{16}H_{13}NO$: N, 5.95. Found: N, 5.72.

6-Phenyl-4-hydroxy-2-quinolinecarboxylic Acid (VII).—A mixture of 41 g. (0.2 mole) of *p*-aminobiphenyl hydrochloride and 43.5 g. (0.22 mole) of ethyl sodioethoxalylacetate in 250 ml. of absolute ethyl alcohol was stirred for 40 hours at room temperature with 60 g. of anhydrous sodium sulfate. The solution was diluted with 1.5 liters of water, the solid which separated was washed, dissolved in ether then shaken with 125 ml. of 10% hydrochloric acid. The ether layer was next washed with 2% sodium bicarbonate solution, and dried over sodium sulfate. After removal of the ether, the oily residue weighed 57 g. Five grams of the above oil was added in one portion to 40 ml. of boiling phenyl ether and after 5 minutes the solution allowed to cool. The solid was removed by filtration, washed with successive portions of ether and petroleum ether and dried. This procedure was repeated in 5-g. portions for the remainder of the crude ethyl β-carbethoxy-β-(*p*-biphenylamino)-crotonate. The yield of the light yellow crystalline 6-phenyl-4-hydroxy-2-carbethoxyquinoline (VIII) was 37 g. (63%). The substance melted at 226–227°; recrystallization did not raise the melting point. The ester (10 g., 0.034 mole) was refluxed with 75 ml. of 10% sodium hydroxide solution for one hour, filtered and then diluted with about 400 ml. of water and acidified with phosphoric acid. The yield of light cream-colored solid was 8.5 g. (94%). The substance melted at 261–261.5° with decomposition.

Anal. Calcd. for $C_{16}H_{11}NO_3$: N, 5.28. Found: N, 5.54.

6-Phenyl-4-hydroxyquinoline (IX).—Sixty-five milliliters of phenyl ether was heated to boiling and 7.5 g. (0.028 mole) of VIII was added in 0.2–0.4 g. portions over a period of 5–10 minutes and the heating continued for an additional 5–10 minutes. After cooling, the crude IX was removed by filtration and washed with successive portions of diethyl ether and petroleum ether. The crude IX was recrystallized from ethyl alcohol giving 3.9 g. of light gray colored needles which melted at 279–281°.

Anal. Calcd. for $C_{15}H_{11}NO$: N, 6.33. Found: N, 6.35.

8-Phenyl-4-hydroxy-2-quinolinecarboxylic Acid (X).—This substance was prepared from *o*-aminobiphenyl and ethyl sodioöxaloacetate by exactly the same procedure as was employed for VII. The yield of the intermediate ester, 8-phenyl-4-hydroxy-2-carbethoxyquinoline (XI), was 29 g. (49%) from 0.2 mole of *o*-aminobiphenyl. XI melted at 154.5–156°. Saponification of XI (8 g.) was carried out as in the case of VIII but on acidification with phosphoric acid, the precipitated acid contained a large amount of the sodium salt. Acidification of the hot solution gave pure X as a voluminous white solid. The yield was 5.2 g. (71.5%). X melted at 236–238° with decomposition.

Anal. Calcd. for $C_{16}H_{11}NO_3$: N, 5.28. Found: N, 5.53.

8-Phenyl-4-hydroxyquinoline (XII).—Decarboxylation of XI was carried out in the same manner as for VIII; 4.8 g. of XI gave 2.4 g. (60%) of pure XII after recrystallization from aqueous ethyl alcohol. The substance melted at 203.5–204°.

Anal. Calcd. for $C_{15}H_{11}NO$: N, 6.33. Found: N, 6.10.

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[9] C. E. Kaslow and N. B. Sommer, THIS JOURNAL, **68**, 644 (1946).

Totally Synthetic Lumiestrone

BY WILLIAM S. JOHNSON AND LELAND J. CHINN

In our total synthesis of estrone[1] three of the seven possible racemic stereoisomers of estrone were also produced. For reasons which were implied[1] (and are now stated below) we suggested that one of these isomers, estrone "g," m.p. 240°, represented the *dl* modification of lumiestrone. More recently Anner and Miescher[2] dismissed this hypothesis, and presented the counter proposal that their estrone "f" (m.p. 190°), which is clearly different from our "g," was indeed *dl*-lumiestrone. The arguments which they presented in support of this thesis are, in our opinion, inconclusive. The low reactivity of the carbonyl group toward Girard reagent would not be expected to be unique for lumiestrone. Moreover, there is no assurance that those reactions to produce estrone "f" from "keto ester B" and those leading to lumidoisynolic acid (from the same keto ester) take the same stereochemical course. Even if this is the case, however, the fact that only single substances were isolated in each series cannot be taken to mean that they were the exclusive products formed.

In the preparation of estrone "g" the β form of the benzylidene derivative I was methylated with potassium *t*-butoxide and methyl iodide. This treatment gave two products, β^1 and β^2, which by analogy to the established structure of the methyla-

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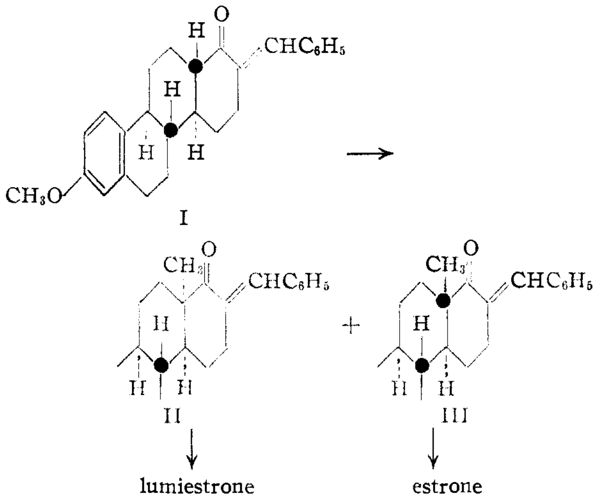
[1] W. S. Johnson, D. K. Banerjee, W. P. Schneider and C. D. Gutsche, THIS JOURNAL, **72**, 1426 (1950).

[2] G. Anner and K. Miescher, *Helv. Chim. Acta*, **33**, 1379 (1950).



tion products of benzylidenedecalone,[3] were undoubtedly the stereoisomers II and III epimeric about the carbon holding the methyl group. One of these isomers (β^2) was converted to estrone by reactions already described[1] and is therefore represented by formula III which corresponds to the most probable configuration for the natural product. The β^1 epimer (formula II) yielded estrone "g" which differs from natural estrone only in the configuration at C_{13} and therefore represents unequivocally that stereoisomeric form which was postulated by Butenandt and co-workers[4] for lumiestrone. We have now compared the infrared spectra of *dl*-estrone "g" methyl ether and lumiestrone methyl ether,[4] m.p. 130–130.6°, $[\alpha]^{32}\mathrm{D}$ $-27°$ in chloroform, and have found them to be identical.[5] These results clearly demonstrate that our estrone "g" instead of Anner and Miescher's estrone "f" is lumiestrone. Moreover, the identity of lumiestrone with synthetic material known to be epimeric with estrone at C_{13}, establishes the configuration postulated by Butenandt for this stereoisomer, and proves that the photoisomerization of estrone involves inversion only at C_{13}.

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(3) W. S. Johnson, THIS JOURNAL, **65**, 1317 (1943).

(4) A. Butenandt, A. Wolff and P. Karlson, *Ber.*, **74**, 1308 (1941); A. Butenandt, *et al.*, *ibid.*, **75**, 1931 (1942); **77**, 392 (1944).

(5) We are indebted to Dr. R. N. Jones of the National Research Council, Canada, for determining the spectra.

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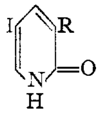
Thiation with Phosphorus Pentasulfide in Pyridine Solution

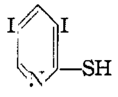
BY ERWIN KLINGSBERG[1] AND DOMENICK PAPA

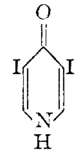
The conversion of pyridones to thiopyridones by means of phosphorus pentasulfide has hitherto been effected by fusion[2] or by heating in a liquid medium, such as benzene[3] or toluene,[4] with limited solvent power for one or both reactants. These reactions, however, have apparently been limited to comparatively low-melting pyridones. Rath[5] treated 5-iodo-2-pyridone (I) with phosphorus pentasulfide and obtained not the corresponding iodothiopyridones, but 2-thiopyridone, the iodine having been lost in the conversion.

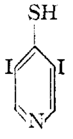
In the present investigation, initial experiments with 3,5-diiodo-2-pyridone (II) were unsuccessful, the diiodopyridone being recovered unchanged after prolonged reflux in benzene with phosphorus pentasulfide. Fusion of the two reactants at various temperatures resulted only in intractable reaction mixtures.

It appeared necessary to find a solvent which would permit the conversion reaction to proceed in solution. Pyridine proved excellent for the purpose, having ample solvent power for the reactants, a suitable boiling temperature; and, by its miscibility in water, providing a simple method of isolation. On heating a mixture of 3,5-diiodo-2-pyridone, phosphorus pentasulfide and pyridine for 1.5 hours and pouring the reaction solution into approximately twice its volume of water, an excellent yield of 3,5-diiodo-2-thiopyridone (III) separated in substantially pure form. The phosphorus-containing by-products remained in the aqueous pyridine. Similarly, 3,5-diiodo-4-pyridone (IV) was converted to the thiopyridone (V) in quantitative yield. This method facilitates the conversion of the high-melting pyridones to the corresponding mercaptans in one step, in contrast to the former two-step procedure of converting the pyridone to the active chlorine derivative and subsequent metathesis with hydrosulfide.[6]


I, R = H
II, R = I


III


IV


V

The great versatility of pyridine as an organic solvent suggests its use in a variety of thiations with phosphorus pentasulfide, and in a single exploratory experiment, benzanilide was converted to thiobenzanilide in 73% yield.

Experimental

3,5-Diiodo-2-thiopyridone (III).—A solution of 70 g. (0.202 mole) of 3,5-diiodo-2-pyridone and 50 g. (0.225 mole) of phosphorus pentasulfide in 300 ml. of pyridine was refluxed for 1.5 hours and poured into 500 ml. of hot water. Cold water tends to give a gummy product, probably due to incomplete solution of the phosphorus by-products. The slurry was cooled and filtered. On recrystallization from dilute pyridine, there was obtained 65 g. of product (89% of theory), m.p. 200–203°. A second recrystallization gave 52 g. (70%) of product, m.p. 206–206.5°.

Anal. Calcd. for $C_5H_3NI_2S$: C, 16.54; H, 0.83; N, 3.86. Found: C, 16.08; H, 1.09; N, 3.85.

Dohrn and Diedrich[6] prepared this compound from 2-chloro-3,5-diiodopyridine and reported m.p. 181°, but no analysis.

3,5-Diiodo-4-thiopyridone (V).—3,5-Diiodo-4-pyridone (140 g., 0.404 mole) and phosphorus pentasulfide (110 g., 0.495 mole) were refluxed in 550 ml. of pyridine for 2 to 2.5 hours and the solution then poured into 800 ml. of hot water. On cooling, filtering, washing and drying, there

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(1) American Cyanamid Company, Calco Chemical Division, Bound Brook, New Jersey.

(2) King and Ware, *J. Chem. Soc.*, 873 (1939).

(3) Arndt and Kalischek, *Ber.*, **63**, 587 (1930).

(4) Arndt, *ibid.*, **65**, 92 (1932).

(5) Rath, *Ann.*, **487**, 105 (1931).

(6) Dohrn and Diedrich, *ibid.*, **494**, 284 (1932).