from ethanol afforded isomer V (least soluble) as white prisms, m.p. 162–164°.

Anal. Calcd. for $C_{13}H_{18}ClNO_3S$: C, 51.39; H, 5.97; N, 4.61; S, 10.55. Found: C, 50.86; H, 5.36; N, 4.18; S, 10.66.

From the mother liquors of the above recrystallizations there was isolated the more soluble isomer VI as a white granular powder, m.p. 125–126°.

Anal. Found: C, 51.70; H, 6.09; N, 4.50; S, 10.76.

Nuclear Acylation of Arylamines

B. STASKUN

Department of Chemistry, University of Witwatersrand, Johannesburg, South Africa

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Aromatic carboxylic acids react with arylamines in polyphosphoric acid solution at 180–200° to furnish aminobenzophenones in appreciable yield. Diphenylamine, triphenylamine, and 2-aminobiphenyl yield heterocyclic bases. Substituted benzanilides are converted to aminobenzophenones by the hot reagent. Mechanisms to account for the results are proposed.

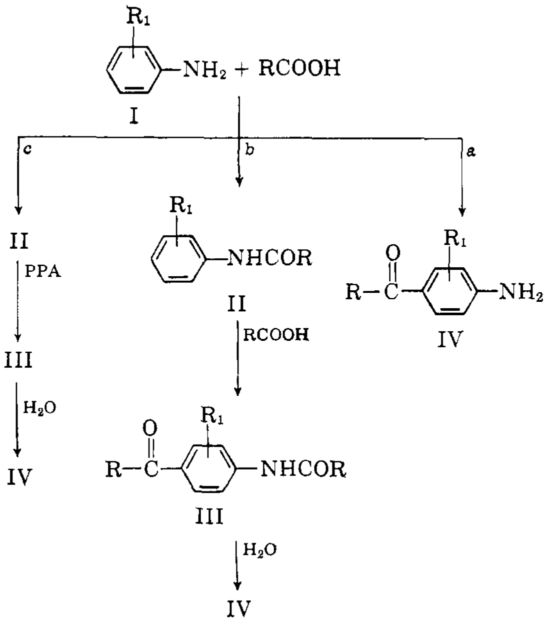
Whereas the intermolecular nuclear acylation reactions in polyphosphoric acid (PPA) of phenols, phenolic ethers, esters, and a variety of aromatic compounds have been extensively studied, little is known of a similar reaction of arylamines.[1–3] Only an occasional such amino ketone synthesis employing PPA has been reported.[4–6] The ring positions in the aromatic amines (I) are said to be unreactive towards carboxylic acids in the presence of PPA[4] and the usual product of reaction is an N-acylated arylamine (II).[7]

It has been found here that equimolar amounts of arylamine (I) and carboxylic acid condense to furnish aminobenzophenones (IV, R = aryl) in 5–55% yields (Table I) on heating with excess PPA at 180–200°. In some instances, 4-aminobenzophenone for example, the yield was improved (65–70%) by employing a molar excess of benzoic acid in the reaction with aniline. The unsubstituted and *ortho*-substituted arylamines gave 30–55% yields of amino ketones where the acyl group preferentially entered in the *para* position, but yields were lower (5–20%) for the *para*-substituted arylamines.[8]

The anilides (II) on treatment with carboxylic acid and excess PPA readily underwent nuclear acylation to N-acylaminobenzophenones (III). Moreover, heating benzanilide (0.01 mole) with either benzoic acid (0.01 or 0.02 mole) or benzoic anhydride[9] (0.01 mole) in PPA at 150° for 30 min. gave comparable yields (60–70%) of 4-aminobenzophenone.

The synthesis of IV directly from arylamine (I) and carboxylic acid is explicable by more than one reaction process: (a) a direct Friedel–Crafts type nuclear acylation of the arylamine to IV; (b) a similar reaction of anilide (II) derived in a preferential and preliminary step from the amine and carboxylic acid, to III; and (c) a PPA-catalyzed transformation of the initially formed II to III as discussed below. (See Scheme I.)

SCHEME I



It is suggested that the amino ketones (IV) listed in Table I, arose principally by routes b and c, and that nuclear acylation of the respective arylamines occurred, if at all, only to a minor extent.[10] The arylamines (I), unlike the relatively less basic anilides (II), would presumably be extensively and effectively protonated in PPA solution and consequently would resist nuclear acylation.[11] The availability in acid solution of an appreciable number of nonprotonated anilide (II) molecules, would allow for a rapid and facile reaction. Consistent with this view is the observation that benzoic anhydride (or benzoic acid) failed to acylate dimethylaniline in the presence of PPA, but the much weaker base triphenylamine reacted readily with benzoic acid to furnish what appears to be 9,10-diphenylacridinium hydroxide (V) in 20% yield. The carbinol (V) may

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(1) F. D. Popp and W. E. McEwen, *Chem. Rev.*, **58**, 377 (1958).

(2) F. Uhlig and H. R. Snyder, "Advances in Organic Chemistry: Methods and Results," Vol. 1, Interscience Publishers, Inc., New York, N. Y., 1960, p. 35.

(3) J. Marthe and S. Munavalli, *Bull. soc. chim. France*, 2679 (1963).

(4) H. R. Snyder and C. T. Elston, *J. Am. Chem. Soc.*, **77**, 364 (1955).

(5) R. A. Abramovitch, D. H. Hey, and R. A. J. Long, *J. Chem. Soc.*, 1781 (1957).

(6) F. D. Popp, *J. Org. Chem.*, **27**, 2658 (1962).

(7) H. R. Snyder and C. T. Elston, *J. Am. Chem. Soc.*, **76**, 3039 (1954).

(8) A similar substitution pattern was observed by Dippy and Moss [*J. Chem. Soc.*, 2205 (1952)] when treating monobenzoyl anilides with benzoy chloride in the presence of zinc chloride.

(9) The nuclear acylation of II with benzoic anhydride and PPA was also reported by D. A. Denton and H. Suschitzky [*ibid.*, 4741 (1963)] before the present investigation was completed.

(10) Although aniline and benzoic acid are reported not to condense to benzanilide in PPA solution,[7] the anilide and also 4-benzaminobenzophenone were in fact isolated after reaction in about 20% yield (see Experimental). The N-acylation procedure of Snyder and Elston[7] may, in other instances as well, lead to a mixture of anilide (II) and N-acylated aminobenzophenone (III).

(11) The nature of the actual C-acylating agent is not known; a conjugate acid, $RCOOH_2^+$, or an oxocarbonium ion, RCO^+, derived from the carboxylic acid, RCOOH, merit consideration.

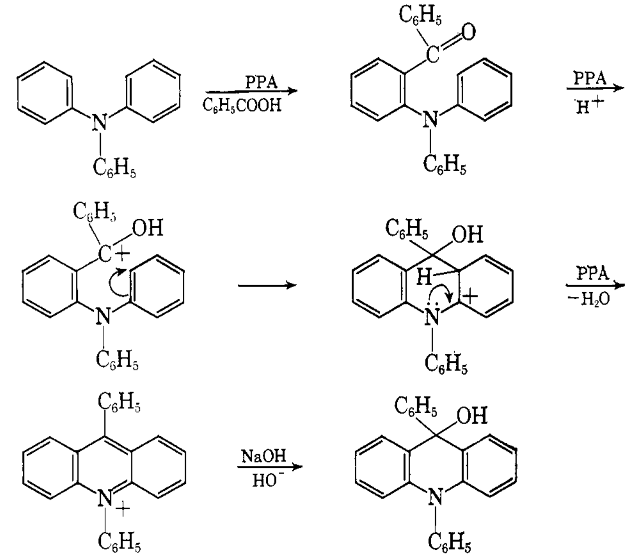
Table I

Arylamine	Acylating agent	Benzophenone derivative	Crude yield,[a] %	M.p., °C. Obsd.	M.p., °C. Lit.
Aniline	Benzamide	4-Amino-	40, 50[b]		
	Ethyl benzoate	4-Amino-	30–40		
	Benzonitrile	4-Amino-	30[c]	123–124	123[d]
	N-Benzoylmorpholine	4-Amino-	35[e]		
	N-Benzoyl-N-methylaniline[f]	4-Amino-	30		
	m-Chlorobenzoic acid[g]	4-Amino-3′-chloro-	30	154–155	. . .
	p-Toluic acid[h]	4-Amino-4′-methyl-	41	184–185	186–187[i]
	o-Fluorobenzoic acid	4-Amino-2′-fluoro-[j]	45[k]	130–131	. . .
	p-Fluorobenzoic acid	4-Amino-4′-fluoro-[l]	40[m]	129–130	. . .
p-Toluidine	*p*-Toluic acid	2-Amino-4′,5-dimethyl-[n]	10	94–95	. . .
p-Toluidine	Benzoic acid	2-Amino-5-methyl-[n]	20	66–67	62[d]; 66[o]
o-Toluidine	Benzoic acid	4-Amino-3-methyl-	50[k]	111–112	111[d]
p-Fluoroaniline	Benzoic acid	2-Amino-5-fluoro-[n]	5	117–118	118[d]
p-Chloroaniline	Benzoic acid	2-Amino-5-chloro-[n]	20[p]	100–101	97[d]; 100[q]
p-Bromoaniline	Benzoic acid	2-Amino-5-bromo-[n]	10	110–111	110[d]

[a] Recrystallizations from dilute ethanol. [b] Benzamide, 0.02 mole. [c] Reaction temperature raised from 100 to 190° over 20 min. and held at 190° for a further 45 min. [d] See ref. 23. [e] 180–190° for 50 min. [f] In the absence of aniline, the anilide yielded an acid-insoluble tar together with a small amount of unidentified ketonic material. [g] *m*-Chlorobenzoic acid, 0.03 mole, gave practically the same yield of amino ketone; the excess acid formed an immiscible layer on top of the PPA solution. [h] *p*-Toluic acid, 0.03 mole, gave a 54% yield of amino ketone. [i] H. P. Newton and P. H. Groggins, *Ind. Eng. Chem.*, **27**, 1397 (1935). [j] Pale yellow needles. Calcd. for $C_{13}H_{10}FNO$: N, 6.51. Found: N, 6.55. [k] 190° for 30 min. [l] Pale yellow needles. [m] 180–190° for 30 min. [n] Bright yellow needles. [o] F. D. Chattaway and W. H. Lewis, *J. Chem. Soc.*, 589 (1904). [p] A reaction temperature of 220–230°, or the use of 0.03 mole of benzoic acid at 200° led to comparable yields of amino ketone. [q] F. D. Chattaway, *J. Chem. Soc.*, 340 (1904).

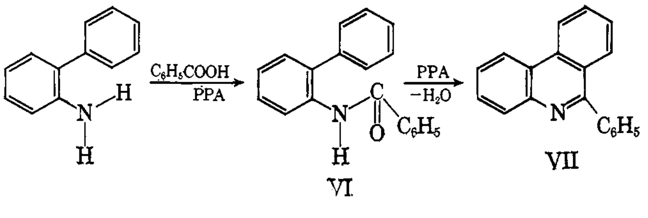
arise as described in Scheme II and the reaction is being further studied.

Scheme II



V

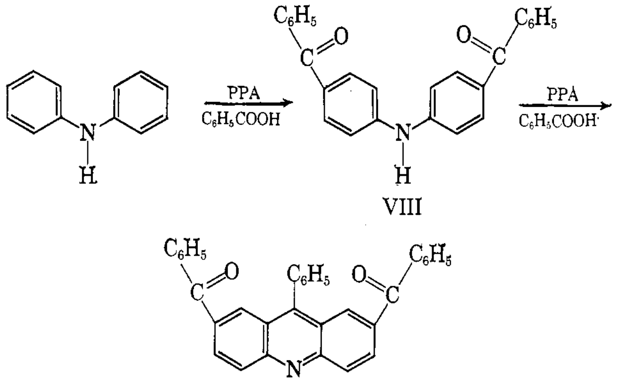
Under similar conditions, 2-aminobiphenyl and benzoic acid furnished 6-phenylphenanthridine (VII), providing evidence for the formation of 2-benzamidobiphenyl (VI) in an initial step. The latter, in a separate reaction, was quantitatively cyclodehydrated by PPA to the phenanthridine (VII).



VI

VII

The PPA treatment of diphenylamine and benzoic acid is reported[4,6] to give 9-phenylacridine and 4,4′-dibenzoyldiphenylamine (VIII). This has been confirmed using equimolar proportions of reactants; however, with an excess of benzoic acid, the main product was a new substance formulated as 2,7-dibenzoyl-9-phenylacridine (IX), together with some 9-phenylacridine. On treatment with benzoic acid and PPA, 4,4′-dibenzoyldiphenylamine (VIII), unlike 9-phenylacridine which did not react, was converted to IX in 80% yield and was evidently the latters precursor.



VIII

IX

Although generally believed[7,12,13] to possess considerable stability in PPA solution, the N-acylated arylamines (II) when heated with excess PPA at 180–200° were transformed into aminobenzophenones (IV) in 10–55% yield (Table II). A reaction of this type was first reported by Abramovitch, *et al.*,[5,14] and little is

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(12) F. D. Popp and W. E. McEwen, *Chem. Rev.*, **58**, 391 (1958).

(13) The possibility of anilides (II) undergoing degradation in PPA solution at elevated temperatures has been noted by Uhlig and Snyder.[2]

(14) The conversion of benzanilide into 4-aminobenzophenone with the aid of PPA has been recently effected by Denton and Suschitzky,[9] and by Staskun.[15]

(15) B. Staskun, *J. Org. Chem.*, **29**, 1153 (1964).

TABLE II

Anilide	Product	Crude yield,[a] %	M.p., °C. Obsd.	M.p., °C. Lit.
m-Chlorobenzanilide	4-Amino-3′-chlorobenzophenone[b]	48–52; 8[c]	154–155	. . .
p-Toluanilide	4-Amino-4′-methylbenzophenone	50–54; 32[c]	184–185	186–187[d]
Benz-*o*-toluidide	4-Amino-3-methylbenzophenone	43[e]	111–112	112[f]
Benz-*p*-toluidide	2-Amino-5-methylbenzophenone	10[e]	66–67	66[f]
Propionanilide	4-Aminopropiophenone	20[c]	139–140	140[g]
N,N-Dibenzoylaniline	4-Aminobenzophenone	66[h]	123–124	123[i]

[a] Recrystallizations from dilute ethanol. [b] Pale yellow needles. Calcd. for $C_{13}H_{10}ClNO$: N, 6.05. Found: N, 5.91. [c] 150° for 30 min. [d] See ref. *i*, Table I. [e] 190° for 30 min. [f] See ref. *o*, Table I. [g] C. G. Derick and J. H. Bormann, *J. Am. Chem. Soc.*, **35**, 1286 (1913). [h] 180° for 30 min. [i] See Ref. 23.

known of the mechanism except that it may be intermolecular.[5]

It is now proposed that the anilide (II) on treatment with an excess of PPA furnishes a carboxylic acid[16] which then acylates[11] unreacted anilide (and possibly, to a lesser extent, arylamine) yielding as the penultimate product of reaction, an N-acylated aminobenzophenone (III). This intermediate (and/or its phosphorylated derivative) is subsequently hydrolyzed to the amino ketone (IV).

Favoring this view were the following results. (a) Benzoic acid sublimed from the reaction mixtures of PPA and N-benzoylarylamines at 180–200°, showing the production of benzoic acid during the reaction.[17] (b) 4-Benzaminobenzophenone (III, R = C_6H_5; R_1 = H) was isolated from reaction mixtures of benzanilide and PPA; in the presence of benzoic acid, the reaction furnished an increased amount of 4-benzaminobenzophenone. (c) The PPA-catalyzed transformation of *p*-toluanilide in the presence of benz-*p*-toluidide (or N-benzoylmorpholine) led to 4-amino-4′-methylbenzophenone together with 4-aminobenzophenone. This is consistent with an intermolecular process. The above scheme can account for the optimum yields in the transformation being approximately 50%.[18]

The proportion of reagent employed influences the outcome of the reaction. Thus, benzanilide was converted into N,N′-diphenylbenzamidine (15%) and a negligible amount of amino ketone (IV) on treatment with an equal weight of PPA at 180°. With excess reagent (10:1) the amidine was not formed; the main (final) product was 4-aminobenzophenone. The amidine may result from condensation of either (a) benzanilide or (b) aniline, derived from PPA decomposition of the benzanilide, with unchanged benzanilide.

The instability of anilides (II) in hot, excess PPA has interesting consequences. For example: (a) benzophenone oxime was for the first time directly converted into 4-aminobenzophenone in 40% yield *via* the intermediate benzanilide formed by a Beckmann rearrangement[19]; (b) the PPA-catalyzed acylation of *p*-toluanilide with benzoic anhydride[9] (or benzoic acid) gave the expected 4-aminobenzophenone together with a significant proportion of 4-amino-4′-methylbenzophenone. The latter base resulted from a competitive acylation of the anilide by *p*-toluic acid produced *in situ*. 4-Amino-4′-methylbenzophenone contaminated with 4-aminobenzophenone was likewise obtained on warming together benzanilide and *p*-toluic acid in PPA.

Snyder's[20] modification of the Lossen reaction was further modified to yield (35%) 4-aminobenzophenone from hydroxylamine hydrochloride and excess benzoic acid.

Experimental[21]

4-Aminobenzophenone, by the Rearrangement of Benzanilide. Isolation Procedure A.—A mixture of benzanilide (2 g., 0.01 mole) and PPA (20 g., Riedel-de Haën) was heated with manual stirring at 200° for 30 min.,[22] during which period a small amount of benzoic acid sublimed from the dark red solution. The reaction mixture was diluted with water (about 8 ml.) and refluxed for about 30 min. (to hydrolyze 4-benzaminobenzophenone and/or the phosphate complex). Water (100 ml.) and 2 *N* hydrochloric acid (10 ml.) were added and the hot mixture was filtered from a small amount of acid-insoluble tar. Addition of concentrated ammonia to the filtrate (charcoal) precipitated the crude 4-aminobenzophenone (0.94 g., 47%, m.p. 112–120°). Purification of the base was effected by reprecipitation from dilute hydrochloric acid (charcoal) and subsequent recrystallization from dilute ethanol; colorless needles, m.p. 123–124° (lit., buff-colored needles, m.p. 123°[23]; pale yellow needles, m.p. 123–124°[9]). The product was identical (mixture melting point and infrared spectrum) with an authentic commercial sample. A reaction temperature of 180° (for 30 min. or for 1 hr.) led to 45–55% yields of 4-aminobenzophenone. At lower temperatures (for 30 min.) yields were decreased (125°, negligible; 140°, 10–13%; 150°, 25%). Denton and Suschitzky[9] obtained the amino ketone in 55% yield by heating benzanilide with PPA at 150–155° for 3 hr. Stirring benzanilide (1 g.) and PPA (10 g.) at 180° for 5 min. and pouring the reaction mixture into water afforded a product (0.62 g., m.p. 115–145°), shown by its infrared spectrum to be a mixture of benzanilide and 4-benzaminobenzophenone.

A number of other anilides (2 g.) were treated with PPA (20 g.) at 200° for 30 min. and the results are listed in Table II.

Benz-1-naphthalide, benz-2-naphthalide, *o*-chlorobenzanilide, *o*-toluanilide, benz-*p*-anisidide, and N-benzoyl-N-methylaniline each decomposed to furnish an acid-insoluble tar and a small quantity of ketonic material (2,4-dinitrophenylhydrazine test). 4-Aminobenzophenone was isolated (method A) in nearly theoretical yield after the PPA treatment of 4-benzaminobenzophenone.

From Aniline and Benzoic Acid by Direct Condensation. Isolation Procedure B.—A mixture of aniline (0.93 g., 0.01 mole), benzoic acid (1.3 g., 0.01 mole), and PPA (20 g.) was heated with

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(16) The mode of the PPA-catalyzed decomposition of the anilide (II) to carboxylic acid remains a matter for conjecture and a number of schemes may be devised to account for the result. An example follows.

$$RCONHR \xrightarrow[H^+]{PPA} RC(OH)NHR^+ \rightleftharpoons RCONH_2R^+ \xrightarrow{\Delta}$$

$$RCO^+ \underset{}{\overset{PPA}{\rightleftharpoons}} RCOOH_2^+ \rightleftharpoons RCOOH + H^+$$

(17) Sublimation of benzoic acid from the hot PPA solution of N-methyl-2′-nitrobenzanilide has been observed.[5]

(18) 4-Benzaminobenzophenone on heating in PPA at 180° gave a sublimate of benzoic acid. The carboxylic acid formed by III similarly decomposing could react with arylamine derived from II, accounting for the yields of IV (from II) exceeding 50% on occasion.

(19) E. C. Horning, V. L. Stromberg, and H. A. Lloyd, *J. Am. Chem. Soc.*, **74**, 5153 (1952).

(20) H. R. Snyder, C. T. Elston, and D. B. Kellom, *ibid.*, **75**, 2014 (1953).

(21) All melting points are uncorrected. Infrared spectra were taken on a Perkin-Elmer Infracord Model 137 spectrophotometer (1-mg. sample in 300 mg. of potassium bromide) unless otherwise stated.

(22) Reaction for 1 hr. led to essentially the same result.

(23) J. F. J. Dippy and V. Moss, *J. Chem. Soc.*, 2205 (1952).

manual stirring at 200° for 30 min. and the crude 4-aminobenzophenone was isolated as above (1.1 g., 55%, m.p. 114–121°). Similar yields (50–55%) were obtained at 180° and were increased (65–70%) by using 0.02 mole of benzoic acid.

An alternative, although more tedious method (B) of obtaining the product involved isolation of an acid-insoluble (presumed) 4-benzaminobenzophenone–phosphate complex, and furnished the amino ketone in comparable yields. The PPA-reaction solution was treated with water (100 ml.) and concentrated hydrochloric acid (5 ml.) and warmed, when the orange color of the mixture was rapidly discharged. (This may indicate the hydrolysis of a colored Schiff-type base derived from self condensation of the amino ketone.) After cooling the mixture to room temperature, the acid-insoluble material (0.6 g.) was removed; the filtrate (charcoal) was made ammoniacal to deposit 4-aminobenzophenone (0.9 g., m.p. 114–121°). Hydrolysis of the acid- and alkali-insoluble, phosphorus-containing product was effected with 6–8 ml. of 66% (v./v.) sulfuric acid for 30 min. The hydrolysate was diluted with water, insoluble tar was removed, and the filtrate (which deposited the sparingly soluble amino ketone sulfate if allowed to cool) was made ammoniacal to give 4-aminobenzophenone (0.18 g., m.p. 90–110°, total yield 1.08 g., 54%).

Table I lists the results obtained on heating other amines (0.01 mole) and carboxylic acids (0.01 mole) in PPA (20–25 g.) at 200° for 30 min. 4-Aminobenzophenone was recovered unchanged (method A) after heating with benzoic acid in PPA at 180° for 30 min. Dimethylaniline likewise resisted nuclear acylation by benzoic anhydride or benzoic acid; negligible amino ketone resulted and the amine was recovered unchanged. N-Methylaniline yielded an acid-insoluble tar together with a small amount of an unidentified amino ketone. A number of carboxylic acids and arylamines were decomposed under the reaction conditions employed and included *o*-toluic acid, *p*-nitrobenzoic acid, the 1- and 2-naphthoic acids, the 2- and 4-methoxybenzoic acids, crotonic acid, cinnamic acid, *o*-nitroaniline, and 2-aminoanthracene. 2-Naphthoic acid and aniline furnished 4-(2′-naphthoyl)aniline in about 10% yield as pale yellow needles, m.p. 171–173°.

Anal. Calcd. for $C_{17}H_{13}NO$: N, 5.67. Found: N, 5.60.

Formation of Benzanilide and 4-Benzaminobenzophenone from Benzoic Acid and Aniline.—The amine (0.93 g., 0.01 mole), benzoic acid (1.3 g., 0.01 mole), and PPA (20 g.) were stirred and heated at 175° for 5 min. and the yellow-orange solution decomposed with water (100 ml.). The acid-insoluble crystalline precipitate was collected, successively treated with 1 *N* sodium hydroxide and 1 *N* hydrochloric acid, washed, and dried. The phosphorus-free product (0.4–0.5 g.) melted over a range and its infrared spectrum showed it to be a mixture of benzanilide and 4-benzaminobenzophenone. A separation of the anilides was effected by fractional recrystallization of the mixture from 50% ethanol in which the 4-benzaminobenzophenone was less soluble. The identity of each component was confirmed after separation and purification, by comparison (mixture melting point and infrared spectrum) with an authentic specimen. 4-Aminobenzophenone (2 g., 0.01 mole) when similarly treated with benzoic acid and PPA readily underwent N-acylation to the acid-insoluble 4-benzaminobenzophenone (1.9 g., 63% yield).

A mixture (0.5 g.) of benzanilide and 4-benzaminobenzophenone was likewise obtained on stirring together the aniline and benzoic acid in PPA at 150° for 15 min.

Action of Benzoic Anhydride on *p*-Toluanilide.—The anilide (2.1 g., 0.01 mole), anhydride (2.3 g., 0.01 mole), and PPA (30 g.) were heated with manual stirring at 150° for 30 min. and the crude aminoketone (1.4 g., m.p. 120–140°) was isolated by method A. When reprecipitated from dilute hydrochloric acid (charcoal), the product (1.1 g.) had m.p. 128–137°. A recrystallization from dilute ethanol (charcoal) furnished colorless needles, m.p. 124–136°. Each of the above three samples was shown by its infrared spectrum to be a mixture of 4-aminobenzophenone and (smaller amounts) 4-amino-4′-methylbenzophenone. In the absence of the anhydride, *p*-toluanilide under similar conditions was converted to 4-amino-4′-methylbenzophenone in appreciable yield ($\sim$30%).

Benzanilide (2 g., 0.01 mole) when similarly treated with benzoic anhydride (2.3 g., 0.01 mole) gave a 60–70% yield of 4-aminobenzophenone. Substitution of benzoic acid (0.02 or 0.01 mole) for the anhydride in this reaction furnished the amino ketone in comparable yields.

Acylation of benzanilide (2 g., 0.01 mole) with *p*-toluic acid (2.8 g., 0.02 mole) in PPA (30 g.) at 150° for 30 min. yielded a base (1.38 g., m.p. 160–175°) shown by its infrared spectrum to be a mixture of 4-amino-4′-methylbenzophenone and (a smaller amount of) 4-aminobenzophenone. Repeated recrystallizations from dilute ethanol furnished a sample of pure (infrared spectrum) 4-amino-4′-methylbenzophenone, m.p. 184–185°. Utilization of 0.01 mole *p*-toluic acid in the reaction gave practically the same yield of amino ketone mixture.

Acylation of Triphenylamine.—The amine (1.2 g., 0.005 mole), benzoic acid (0.6 g., 0.005 mole), and PPA (20 g.) were stirred and heated at 160–165° for 30 min. and the dark green mixture was treated with dilute hydrochloric acid. After removal of the acid-insoluble gum, which dissolved in glacial acetic acid to give an intensely dark green-colored solution, the yellow, fluorescent filtrate was made alkaline to yield a pale yellow solid. The base was reprecipitated from its cold, dilute hydrochloric acid solution (charcoal) with dilute sodium hydroxide, washed, and oven-dried at 50° (0.35 g., 20% yield). (If the drying was prolonged, the substance darkened in color and appeared to decompose.) Some difficulty was experienced in purifying the product, and after two recrystallizations from ligroin (100–120°) it was obtained as colorless crystals, m.p. 142–152°. 9,10-Diphenylacridinium hydroxide (V), prepared from phenylmagnesium bromide and N-phenylacridone, is reported to melt at 178°.[24]

Anal. Calcd. for $C_{25}H_{19}NO$: N, 4.01. Found: N, 4.08.

The infrared spectrum (KBr disk, Perkin-Elmer Model 221 spectrophotometer) differed from that of 9-phenylacridine, and exhibited a strong hydroxyl peak at 3540 cm.$^{-1}$, NH stretching being absent. Absorption occurred also at 3060 (w, CH stretching), 1650 (w), 1590 (s), 1490 (m), 1470 (s), 1440 (s), 1330 (s), 1265 (m), 1150 (m), 1010 (m), 880 (m), 745 (s), and 690 (s) cm.$^{-1}$. The base was readily soluble in concentrated sulfuric acid, in dilute mineral acids, and in dilute acetic acid. The respective yellow solutions exhibited a striking green fluorescence similar to that of 9-phenylacridine. Yellow crystals separated on warming the compound with a dilute sulfuric acid solution of 2,4-dinitrophenylhydrazine; a similar precipitate was given by acridine and by 9-phenylacridine.

9-Phenylacridine and 4,4′-Dibenzoyldiphenylamine (VIII). A.—N-Benzoyldiphenylamine (2 g.) and PPA (20 g.) were stirred together at 140° for 30 min.; some benzoic acid sublimed from the opaque, deep red solution. Treatment with 2 *N* hydrochloric acid (100 ml.) precipitated the dark green, acid-insoluble, crude 4,4′-dibenzoyldiphenylamine. This was removed and the filtrate (charcoal) was made ammoniacal to yield 9-phenylacridine (0.13 g., $\sim$10%, m.p. 174–181°); colorless needles from dilute ethanol (charcoal), m.p. 184–185° (lit.[6] 184–185°). Recrystallization of the green, acid-insoluble solid from glacial acetic acid (charcoal) furnished glistening, greenish plates ($\sim$0 5 g.), m.p. 241–242° (lit.[4] 243–244°); infrared peaks were identical with those reported by Snyder and Elston[4] for dibenzoyldiphenylamine.

Anal. Calcd. for $C_{26}H_{19}NO_2$: N, 3.71. Found: N, 3.63.

The substance formed a red 2,4-dinitrophenylhydrazone, was not affected by hot, 50% sulfuric acid, and dissolved sparingly in hot ethanol.

B.—Comparable yields of the above two products resulted on reacting diphenylamine (1.3 g.) with benzoic acid (0.9 g.) in PPA (20 g.) under similar conditions.

2,7-Dibenzoyl-9-phenylacridine (IX). A.—Treatment of diphenylamine (1 g., 0.006 mole) with an excess (2.5 g., 0.02 mole) of benzoic acid in PPA (20 g.) at 180° for 30 min. yielded the acid-soluble 9-phenylacridine [0.27 g., 20%, m.p. 165–177°; colorless needles from dilute ethanol (charcoal), m.p. 184–185°], together with a canary yellow, acid-insoluble solid (1.7 g.). Recrystallization of the latter from glacial acetic acid (charcoal) gave tiny, glistening yellow needles ($\sim$0.9 g.), m.p. 211–212°.

Anal. Calcd. for $C_{33}H_{21}NO_2$: N, 3.02. Found: N, 3.04.

The substance, whose infrared spectrum showed no NH absorption, and which formed an orange 2,4-dinitrophenylhydrazone, was insoluble in hot, dilute hydrochloric acid and sparingly soluble in hot ethanol. Its yellow, glacial acetic acid solution showed a marked green fluorescence. The "very impure mixture," m.p. 130–235°, obtained by Snyder and Elston[4] in a similar reaction, probably consisted of 4,4′-dibenzoyldiphenylamine together with 2,7-dibenzoyl-9-phenylacridine.

B.—Addition of water to the mixture of 4,4′-dibenzoyldiphenylamine (0.3 g.), benzoic acid (0.2 g.), and PPA (3 g.) which

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[24] L. H. Cone, *J. Am. Chem. Soc.*, **36**, 2104 (1914).

had been stirred at 170° for 30 min. precipitated a bright yellow acid-insoluble solid (0.28 g., m.p. 175–200°). Recrystallization from glacial acetic acid gave yellow needles, m.p. 211–212°, identical (mixture melting point) with the sample prepared in A. 9-Phenylacridine (0.3 g.) when similarly treated with benzoic acid and PPA was recovered unchanged.

6-Phenylphenanthridine (VII). A.—A mixture of 2-benzamidobiphenyl (1 g., m.p. 89–90°, lit.[25] 84–86°) and PPA (10 g.) was stirred at 170° for 30 min. during which period effervescence occurred. The dark orange solution, which exhibited a violet fluorescence, was diluted with water and freed from negligible acid-insoluble impurities. The filtrate contained no ketonic material and on adding ammonia deposited a gum which gradually solidified (0.9 g., 96%, m.p. 102–107°). Recrystallization from ethanol (charcoal) furnished glistening, tiny, colorless crystals, m.p. 106–107° (lit.[26] 105–107°), giving, no precipitate with 2,4-dinitrophenylhydrazine.

Anal. Calcd. for $C_{19}H_{13}N$: N, 5.49. Found: N, 5.28.

The substance dissolved readily in dilute mineral acids and the pale green solutions on dilution exhibited a notable violet fluorescence.

B.—After reaction of 2-aminobiphenyl (1 g., 0.006 mole), benzoic acid (0.7 g., 0.006 mole), and PPA (15 g.) at 180° for 30 min., the dark red solution was treated with water and a small amount of acid-insoluble impurity was removed. The filtrate gave an orange precipitate with 2,4-dinitrophenylhydrazine, and on adding ammonia yielded a gum which gradually solidified. The crude 6-phenylphenanthridine (1.23 g., m.p. 85–96°) was contaminated with ketonic material (most likely 2-benzoyl-6-phenylphenanthridine) and, after several recrystallizations from ethanol, furnished colorless crystals (~0.5 g.), m.p. 106–107°, free of ketone impurity, and identical (mixture melting point) with the base prepared in A. Use of excess of benzoic acid (2.2 g., 0.018 mole) in the reaction gave substantially the same result.

Beckmann Rearrangement of Benzophenone Oxime to 4-Aminobenzophenone.—A mixture of the oxime (1 g.) and PPA (20 g.) was heated with manual stirring at 120–130° for 30 min.[19] and then at 180° for a further 30 min. Isolation by method A furnished crude 4-aminobenzophenone (0.4 g., 40%, m.p. 112–120°). The recrystallized material was identical (mixture melting point and infrared spectrum) with authentic amino ketone.

4-Aminobenzophenone by a Modified Lossen Reaction.—Hydroxylamine hydrochloride (0.8 g., 0.012 mole) and PPA (20 g.) were stirred together at 100–130° for 30 min. or until the frothing had subsided. Excess benzoic acid (2.5 g., 0.02 mole) was added to the solution and the temperature was gradually raised from 130 to 150° over 20 min. and then kept at 180° for a further 30 min. to yield crude amino ketone (0.71 g., 35%, based on benzoic acid). Snyder, *et al.*,[20] employed approximately equimolar proportions of the two reactants in a similar reaction, and obtained aniline. Use of benzophenone (1.8 g., 0.01 mole) in place of the benzoic acid led to 4-aminobenzophenone in 35% yield, *via* a Beckmann rearrangement of the intermediate benzophenone oxime formed *in situ*. Reaction of the benzophenone with a 2 mole excess of hydroxylamine hydrochloride in PPA at 160–165° was reported by Snyder, *et al.*,[20] to furnish aniline in 66% yield.

Conversion of Benzanilide to N,N′-Diphenylbenzamidine.—The orange solution at benzanilide (2 g.) and PPA (2 g.) resulting from reaction at 180° for 30 min. was treated with dilute hydrochloric acid and the acid-insoluble material was removed. Addition of ammonia to the filtrate (charcoal) deposited crude N,N′-diphenylbenzamidine (0.3 g., 15%, m.p. 133–141°, no precipitate with 2,4-dinitrophenylhydrazine). Recrystallization from dilute ethanol (charcoal) furnished colorless, woolly needles, m.p. 145–146°, identical (mixture melting point and infrared spectrum) with an authentic specimen. The acid-insoluble material was found to consist of benzanilide and 4-benzaminobenzophenone (infrared spectrum). The use of 4 g. of PPA in the reaction led to an increased proportion of 4-benzaminobenzophenone in the acid-insoluble mixture; the acid filtrate contained some 4-aminobenzophenone and negligible amidine.

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[25] E. Wenkert and B. F. Barnett, *J. Am. Chem. Soc.*, **82**, 4671 (1960).

[26] H. W. Moore and H. R. Snyder, *J. Org. Chem.*, **28**, 535 (1963).

The Oxidative Cyclization of 2,5-Dihydroxyphenylalkylamines to 5-Hydroxyindoles and 6-Hydroxyquinolines[1]

JAMES A. MOORE AND EUGENE C. CAPALDI

Department of Chemistry, University of Delaware, Newark, Delaware 19711

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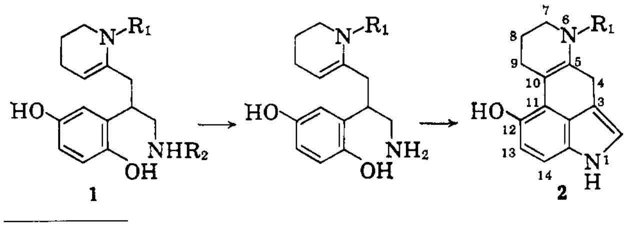
2-(2,5-Dihydroxyphenyl)-3-(1-methyl-2-piperidyl)propylamine (11) was prepared and cyclized to the 5-hydroxy-3-(2-piperidylmethyl)indole **12**. The attempted mercuric acetate oxidation of derivatives of **11** to the enamine was unsuccessful. Ferricyanide oxidation of γ-(2,5-dihydroxyphenyl)propylamine (**15**) gave a mixture of 6-hydroxyquinoline and 6-hydroxy-1,2,3,4-tetrahydroquinoline. The reversible redox system of these quinolines is discussed.

In an earlier paper[2] we reported the synthesis of 6-hydroxy-1,3,4,5-tetrahydrobenz[*cd*]indole as a preliminary stage in developing a total synthetic approach to ergoline derivatives containing a 12-hydroxyl group. Since this report, interest in 12-hydroxyergolines has been heightened by the finding that lysergic acid diethylamide and propanolamide are hydroxylated *in vivo* at the 12-position.[3] The introduction of a hydroxyl group at this site in lysergic acid amides by chemical oxidation has very recently been described.[4] We now present the results of further work on the projected synthesis of 12-hydroxyergoline and some related experiments.

The over-all synthetic plan envisioned the preparation of a 2,5-dihydroxyphenethylpiperidene **1** and closure of both rings C and B by oxidation and accompanying nucleophilic attack on the quinoid ring A by the enamine and primary amino groups, respectively. The enamine cyclization step was projected on the findings of Henbest and co-workers[5]; the application of the Harley-Mason cyclization to a benz[*cd*]-



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[2] J. A. Moore and M. Rahm, *J. Org. Chem.*, **26**, 1109 (1961).

[3] M. B. Slaytor and S. E. Wright, *J. Med. Chem.*, **5**, 483 (1962).

[4] P. A. Stadler, *Oesterr. Chemiker-Ztg.*, **64**, H.10, 298 (1963); we are grateful to Dr. A. Hofmann, Basel, for informing us of this work.

[5] D. Buckley, H. B. Henbest, and P. Slade, *J. Chem. Soc.*, 4891 (1957).