A portion of IV was dissolved in benzene under argon and stirred for 16 hr with 10 equiv of NH_4Cl. The mixture was filtered and the filtrate was evaporated to dryness at 0.5 mm to yield VII as shown by infrared analysis.

To a solution of 226 mg (0.92 mmole) of IV in 5 ml of benzene under argon was added 39 mg (0.92 mmole) of lithium chloride that had been previously dried over P_2O_5 in a vacuum. The reaction mixture was vigorously stirred for 2 hr at room temperature and then evaporated to dryness at 0.5 mm. The infrared and nmr spectra of the resulting white gummy solid were nearly identical with those of VIII.

Acknowledgments.—The authors are grateful to Drs. D. J. Peterson and C. D. Broaddus for helpful discussions and to Dr. R. G. Laughlin for kindly providing us with gaseous chloramine. The technical assistance of Mr. P. R. Handley is also appreciated.

Friedländer Syntheses with *o*-Aminoaryl Ketones. I. Acid-Catalyzed Condensations of *o*-Aminobenzophenone with Ketones[1]

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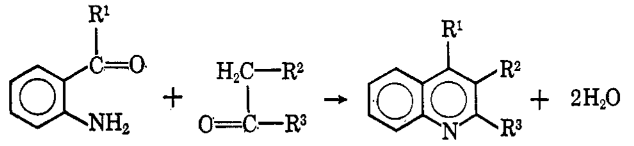
Received December 23, 1965

A study of the Friedländer reaction under conditions involving acid catalysis has shown that good yields of 4-phenylquinolines can be obtained in condensations of *o*-aminobenzophenone with ketones containing the grouping $-CH_2CO-$, many of which either fail to react or give unsatisfactory results when attempts are made to condense them with this *o*-aminoaryl ketone under classical Friedländer reaction conditions. Examples are given of reactions with a variety of aliphatic, aliphatic-aromatic, and alicyclic ketones, and the results of experiments carried out under different conditions are compared. Orientation in the condensation of *o*-aminobenzophenone with methyl ethyl ketone was found to be dependent on the type of catalyst used, acid catalysis leading predominantly to the formation of 2,3-dimethyl-4-phenylquinoline and base catalysis giving mostly 2-ethyl-4-phenylquinoline. Benzyl methyl ketone reacted exclusively at the α-methylene group in the presence of either acid or base, giving 2,4-diphenyl-3-methylquinoline as the only isolable product under both sets of conditions, although the yield was much higher in the acid-catalyzed reaction.

One of the most generally useful methods for preparing 2- and 3-substituted quinolines is the Friedländer synthesis,[2] in which *o*-aminobenzaldehyde (**1**, $R^1 = H$) is condensed with an aldehyde, ketone, or polyfunctional carbonyl compound having the grouping $-CH_2CO-$. Attempts to extend this method to the synthesis of 4-alkyl- and 4-arylquinolines from *o*-aminoaryl ketones (**1**, R^1 = alkyl or aryl), however, appear to have met with very limited success. Thus it has been reported that while *o*-aminobenzophenone behaves normally in Friedländer-type condensations with acetone[3] and acetophenone,[4] it fails to undergo analogous reactions with acetaldehyde,[3] cyclohexanone,[4] deoxybenzoin,[4] and β-keto esters.[5] These results have led some investigators to hypothesize that this aminoaryl ketone may be capable of undergoing Friedländer-type condensations only with ketones of the type $RCOCH_3$.[4]



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To test the validity of this conclusion and provide further information on the scope and limitations of the Friedländer synthesis, we have undertaken a systematic investigation of the reactions of *o*-aminoaryl ketones with various classes of carbonyl compounds under both classical and nonclassical conditions. The present paper describes the results obtained in a study of the condensation of *o*-aminobenzophenone with a number of representative monofunctional ketones of type **2**, selected to illustrate the influence of various alkyl and aryl substituents on the reactivity of the $-CH_2CO-$ group.

Friedländer reactions are usually carried out either by refluxing an aqueous or alcoholic solution of the reactants in the presence of a base or by heating a mixture of the reactants at temperatures ranging from 150 to 220° in the absence of solvent and catalyst. Since preliminary experiments in this laboratory indicated that *o*-aminobenzophenone does indeed fail to condense with some simple ketones under these classical reaction conditions or, at best, gives poor yields of difficultly isolable products, other means of bringing about the desired condensation were investigated. It soon became evident that acids are particularly effective catalysts for this type of reaction[7] and that, under appropriate conditions, good yields of 4-phenylquinolines can be obtained in acid-catalyzed condensations of *o*-aminobenzophenone with ketones of type **2**, including cyclohexanone, deoxybenzoin, and

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[1] (a) This investigation was supported in part by Public Health Service Research Grant CY-2726(C3) from the National Cancer Institute of the National Institutes of Health. (b) Presented at the First Middle Atlantic Regional Meeting of the American Chemical Society, Philadelphia, Pa., Feb 1966.

[2] For a comprehensive review of the Friedländer synthesis, see R. C. Elderfield, "Heterocyclic Compounds," Vol. 4, R. C. Elderfield, Ed., John Wiley and Sons, Inc., New York, N. Y., 1950, pp 45–47, 209.

[3] R. Geigy and W. Koenigs, *Ber.*, **18**, 2400 (1885).

[4] W. Borsche and F. Sinn, *Ann.*, **538**, 283 (1939).

[5] Although quinoline derivatives are obtained in condensations of *o*-aminoaryl ketones with acetoacetic and benzoylacetic esters under appropriate conditions,[4,6] the products are 3-acylcarbostyrils (**3**, $R^2 = COCH_3$ or COC_6H_5, $R^3 = OH$) rather than the expected 3-quinolinecarboxylic esters (**3**, $R^2 = COOC_2H_5$, $R^3 = CH_3$ or C_6H_5). For a discussion of the unusual behavior of β-keto esters in these condensations, see E. A. Fehnel, J. A. Deyrup, and M. B. Davidson, *J. Org. Chem.*, **23**, 1996 (1958).

[6] R. Camps, *Ber.*, **32**, 3228 (1899).

[7] The only previously recorded examples of the use of acid catalysis in the Friedländer synthesis are to be found in the condensation of *o*-aminobenzaldehyde with 2-indanone in dilute hydrochloric acid [G. R. Clemo and D. G. I. Felton, *J. Chem. Soc.*, 1658 (1952)] and of *o*-aminoacetophenone (as the *hydrochloride*) with a number of cyclic ketones [G. Kempter, *et al.*, *Chem. Ber.*, **97**, 16 (1964); G. Kempter and S. Hirschberg, *ibid.*, **98**, 419 (1965)]. The work of Kempter and co-workers came to our attention only after most of the work described in the present paper had been completed.

TABLE I

ACID-CATALYZED CONDENSATIONS OF *o*-AMINOBENZOPHENONE WITH KETONES OF TYPE $R^2CH_2COR^3$

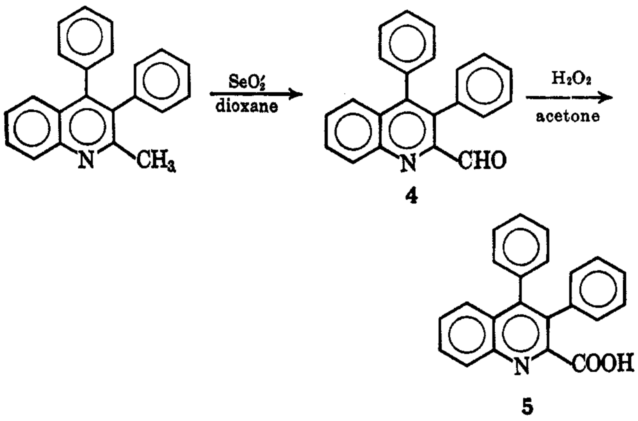
Ketone (2)	R^2	R^3	Method	Reaction time, hr	Product (3)	Yield,[a] %
Acetone	H	CH_3	A	6	4-Phenylquinaldine[b]	71
Methyl ethyl ketone	CH_3	CH_3	A	10	2,3-Dimethyl-4-phenylquinoline[c]	86
			B	1		0[d]
Acetophenone	H	C_6H_5	A	18	2,4-Diphenylquinoline[e]	67
			B	2		60
Propiophenone	CH_3	C_6H_5	A	24	2,4-Diphenyl-3-methylquinoline	66
Benzyl methyl ketone	C_6H_5	CH_3	A	2	3,4-Diphenylquinaldine	64
			B	1		56
Deoxybenzoin	C_6H_5	C_6H_5	A	3	2,3,4-Triphenylquinoline	59
			B	1		61
Dibenzyl ketone	C_6H_5	$C_6H_5CH_2$	A	4	2-Benzyl-3,4-diphenylquinoline	74
Cyclopentanone	$CH_2CH_2CH_2$		A	6	2,3-Dihydro-9-phenyl-1H-cyclopenta[*b*]-quinoline	81
			B	2		47[f]
Cyclohexanone	$CH_2CH_2CH_2CH_2$		A	4	1,2,3,4-Tetrahydro-9-phenylacridine	83
			B	1		68

[a] After one recrystallization; melting points of these products were not more than 2° below those given in the literature or in Table II for analytically pure samples. [b] Previously prepared by base-catalyzed condensation (ref 3); yield reported to be "nearly quantitative." [c] Accompanied by a trace of the isomer, 2-ethyl-4-phenylquinoline, which was isolated as the picrate. [d] Only unreacted *o*-aminobenzophenone (80% recovery) was isolated from the reaction mixture. [e] Previously prepared by base-catalyzed condensation (ref 4); yield 50% (isolated as the hydrochloride). [f] Isolated as the picrate.

other ketones which had previously been considered incapable of undergoing Friedländer-type reactions with this aminoaryl ketone.

The ketones whose acid-catalyzed condensations with *o*-aminobenzophenone were studied in the present investigation are listed in Table I. The condensations were effected either by refluxing acetic acid solutions of the reactants in the presence of small amounts of sulfuric acid (method A) or by heating mixtures of the reactants containing traces of hydrochloric acid in the absence of solvent at gradually increasing temperatures in the range 100–200° (method B). In general, method A appears to be the more satisfactory procedure, since it affords significantly higher yields in almost every case and can be applied equally well to low and high molecular weight ketones. Method B fails or gives poor results with the more volatile, low molecular weight ketones, presumably because loss of the low-boiling reactant occurs at the relatively high temperature required to complete the reaction.[8] On the basis of the results summarized in Table I, it seems reasonable to assume that under the nonclassical conditions of method A the reaction is entirely general for aliphatic, aliphatic-aromatic, and cyclic ketones which contain the grouping $-CH_2CO-$.

In Friedländer reactions with unsymmetrical ketones of the type CH_3COCH_2R, two different modes of cyclization should be theoretically possible, depending on whether the α-methyl or the α-methylene group undergoes condensation with the carbonyl group of the aminoaryl carbonyl component. To obtain information on the course of the reaction with such compounds, benzyl methyl ketone and methyl ethyl ketone were included in the present study. As might have been expected on the basis of the considerable difference in the relative reactivities of the two α-carbon atoms in benzyl methyl ketone, the product obtained in the acid-catalyzed condensation of this ketone with *o*-aminobenzophenone was 3,4-diphenylquinaldine (3, $R^1 = R^2 = C_6H_5$, $R^3 = CH_3$), *i.e.*, the isomer resulting from condensation at the α-methylene carbon. The structure of this product was established by stepwise oxidation *via* the aldehyde (4) to 3,4-diphenylquinaldic acid (5). The same isomer was obtained, though in very poor yield (5%), when the reaction was carried out under classical conditions in alcoholic alkali. No evidence of the formation of the other isomer (3, $R^1 = C_6H_5$, $R^2 = H$, $R^3 = C_6H_5CH_2$) was found in either the acid- or the base-catalyzed reaction.



In contrast to these results, methyl ethyl ketone was found to be capable of reacting at either α-carbon atom, the mode of cyclization being dependent on the type of catalyst used. Under the acidic conditions of method A, the predominant product (86%) was 2,3-dimethyl-4-phenylquinoline (3, $R^1 = C_6H_5$, $R^2 = R^3 = CH_3$). The formation of at least some of the alternative isomer, 2-ethyl-4-phenylquinoline (3, $R^1 = C_6H_5$, $R^2 = H$, $R^3 = C_2H_5$) was demonstrated by the isolation of a small amount of its picrate derivative from the mother liquor obtained in the recrystallization of the crude reaction product. When the condensation was carried out under classical conditions in the presence of base, a mixture of isomers was obtained which, after separation by way of the picrates, yielded 2-ethyl-4-phenylquinoline as the major product (71%) and 2,3-dimethyl-

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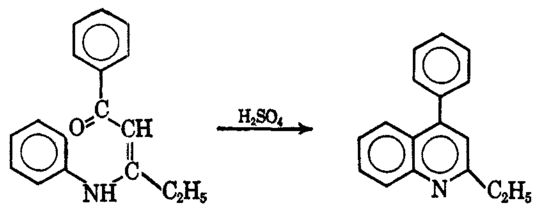
(8) This difficulty could probably be circumvented by carrying out the reaction in a sealed tube or autoclave, but method A is more convenient.

4-phenylquinoline as the minor product (11%). An unequivocal assignment of structures to these isomers was made possible by the independent synthesis of 2-ethyl-4-phenylquinoline from 3-anilino-1-phenyl-2-penten-1-one (6) by the Combes method and identification of this compound with the major product obtained in the base-catalyzed Friedländer reaction. The isomeric minor product in this reaction (*i.e.*, the major product in the acid-catalyzed reaction) must therefore have been the 2,3-dimethyl isomer. Direct confirmation of the structure thus assigned to the latter isomer was obtained by oxidizing it to 4-phenylquinaldine-3-carboxylic acid (7).



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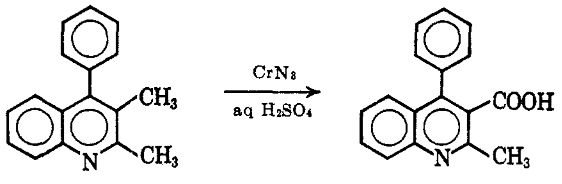

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The catalyst-dependent selectivity shown by methyl ethyl ketone in this reaction is reminiscent of the behavior of methyl alkyl ketones in aldol condensations and related reactions which involve electrophilic attack at "active methylene" groups. In such reactions it is usually observed that condensation occurs predominantly at the more highly substituted alpha position in the presence of acid and at the less highly substituted alpha position in the presence of base.[9] These results are consistent with the generally accepted view that electrophilic attack at the α-carbon of a carbonyl compound proceeds by way of an intermediate enol (in acid-catalyzed reactions) or enolate anion (in base-catalyzed reactions) and that, in the case of unsymmetrical ketones which can enolize in either of two directions, the relative stabilities of the isomeric enols or enolate anions will determine the relative susceptibilities of the α-carbon atoms to electrophilic attack. Although the detailed mechanism of the Friedländer synthesis is not known, an aldol-type condensation appears to be involved at some stage in the over-all reaction, either in or before the ring-closure step.[10] The results obtained with benzyl methyl ketone and methyl ethyl ketone in the present study suggest that the mode of cyclization is determined at this stage by the same factors that govern α-carbon selectivity in other aldol-type condensations with unsymmetrical aliphatic ketones.[11]

Experimental Section[12]

General Procedures for Acid-Catalyzed Friedländer Syntheses. Method A.—A solution of 0.01 mole of *o*-aminobenzophenone, 0.01 mole of ketone,[13] and 0.1 ml of concentrated sulfuric acid in 10 ml of glacial acetic acid was refluxed for the period of time given in Table I. The reaction mixture was then cooled and poured slowly with stirring into an ice-cold solution of 15 ml of concentrated ammonium hydroxide in 40 ml of water. The resultant suspension was allowed to stand in an ice bath until the initially oily precipitate had hardened, after which the crude product was collected, washed with water, and recrystallized from ethanol or aqueous ethanol. Picrate derivatives of the products were prepared in the usual way.[14]

Method B.—A mixture of equimolar amounts (2.5 to 10 mmoles) of the reactants was warmed on a steam bath until a homogeneous melt was obtained, after which 1 drop of 6 *N* hydrochloric acid was added and heating was continued for another 10 min. The mixture was then transferred to a metal bath at 150°[15] and the temperature was raised gradually to 200° over a 1- or 2-hr period (see Table I). The crude product thus obtained was dissolved in the minimum volume of hot ethanol or aqueous ethanol and allowed to crystallize.

The ketones used and the yields of products obtained in Friedländer syntheses carried out by the above procedures are listed in Table I. Melting points and analytical data for compounds not previously reported in the literature are given in Table II.

Base-Catalyzed Condensation of *o*-Aminobenzophenone with Methyl Ethyl Ketone.—A solution of 1.97 g (0.010 mole) of *o*-aminobenzophenone, 5.8 g (0.080 mole) of methyl ethyl ketone, and 4.7 ml of 67% aqueous potassium hydroxide in 16 ml of ethanol was refluxed for 10 hr and was then cooled and acidified with dilute (1:1) sulfuric acid. The ethanol was removed by distillation with steam, and the residue was cooled, diluted with enough water to give a clear solution, and extracted once with 20 ml of ether. The aqueous layer was made alkaline by the addition of aqueous sodium hydroxide and was extracted with two 15-ml portions of ether. The combined ether extracts were dried over anhydrous magnesium sulfate and evaporated on a steam bath to provide 2.15 g of syrupy residue, which gave two spots when subjected to thin-layer chromatographic analysis.[16]

A solution of 1.46 g of this syrup in 50 ml of ethanol was mixed with a hot solution of 3.0 g of picric acid in 50 ml of ethanol. After the mixture had cooled, the precipitate was collected and the mother liquor was set aside for use in recovery of the other isomer (see below). The picrate thus obtained was recrystallized from ethanol to give 2.32 g of yellow leaflets, mp 178–179°. A slurry of this product with 200 ml of 2% aqueous sodium hydroxide was extracted with three 50-ml portions of ether, and the combined extracts were washed with dilute sodium hydroxide and dried over anhydrous magnesium sulfate. Removal of the ether on a steam bath provided 1.13 g (71% over-all yield) of crude **2-ethyl-4-phenylquinoline** as a pale yellow syrup, which gave a single spot in tlc analysis and an infrared spectrum identical with that of the Combes reaction product described below. Distillation under reduced pressure afforded a colorless viscous oil, bp 161–162° (2 mm).

Anal. Calcd for $C_{17}H_{15}N$: C, 87.51; H, 6.48; N, 6.00. Found: C, 86.85; H, 6.03; N, 6.06.

The **picrate** of this product melted at 179–180° after recrystallization from ethanol and showed a marked melting-point depression when mixed with the picrate of 2,3-dimethyl-4-phenylquinoline.

Anal. Calcd for $C_{23}H_{18}N_4O_7$: C, 59.74; H, 3.92; N, 12.12. Found: C, 60.02; H, 4.20; N, 12.30.

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[9] See, for example, the discussion in H. O. House, "Modern Synthetic Reactions," W. A. Benjamin, Inc., New York, N. Y., 1965, pp 164–167, 221–223, 264–267, 278–280.

[10] For different viewpoints regarding possible mechanisms for the Friedländer reaction, *cf.* A. R. Katritsky and J. M. Lagowski, "Heterocyclic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1960, pp 39–40, and R. C. Elderfield, ref 2; no experimental evidence is cited to support either viewpoint.

[11] Surprisingly, however, the base-catalyzed condensation of methyl ethyl ketone with *o*-aminobenzaldehyde is reported to yield only 2,3-dimethylquinoline [J. Eliasberg and P. Friedländer, *Ber.*, **25**, 1752 (1892)]. This reaction merits further study.

[12] Microanalyses were performed by Clark Microanalytical Laboratory, Urbana, Ill.

[13] In the reactions with acetone and methyl ethyl ketone, an excess of the ketone (0.030 mole and 0.020 mole, respectively) was used.

[14] R. L. Shriner, R. C. Fuson, and D. Y. Curtin, "The Systematic Identification of Organic Compounds," 5th ed, John Wiley and Sons, Inc., New York, N. Y., 1964, p 263, method a.

[15] In the reactions with methyl ethyl ketone and cyclopentanone, heating in the metal bath was begun at 100°.

[16] Tlc analyses were carried out with silica gel (Camag DF-5) on glass plates in a solvent mixture consisting of benzene–methanol (97:3 v/v). Spots were detected by examination under ultraviolet radiation.

TABLE II

NEW SUBSTITUTED QUINOLINES AND THEIR PICRATE DERIVATIVES

Compound	Mp, °C	Formula	Calcd, % C	Calcd, % H	Calcd, % N	Found, % C	Found, % H	Found, % N
2,3-Dimethyl-4-phenylquinoline	119–120	$C_{17}H_{15}N$	87.51	6.48	6.00	87.13	6.46	5.96
Picrate	183–184	$C_{23}H_{18}N_4O_7$	59.74	3.92	12.12	59.95	4.02	12.16
2,4-Diphenyl-3-methylquinoline	145–146	$C_{22}H_{17}N$	89.45	5.80	4.74	89.51	5.56	4.79
Picrate	176–177	$C_{28}H_{20}N_4O_7$	64.11	3.84	10.68	64.07	3.62	10.75
3,4-Diphenylquinaldine	174–175	$C_{22}H_{17}N$	89.45	5.80	4.74	89.73	5.86	4.80
Picrate	234–235 dec	$C_{28}H_{20}N_4O_7$	64.11	3.84	10.68	64.12	3.75	10.61
2,3,4-Triphenylquinoline	198–199	$C_{27}H_{19}N$	90.73	5.36	3.92	90.73	5.10	3.95
Picrate[a]	154–155	$C_{39}H_{25}N_7O_{14}$	57.43	3.09	12.02	57.41	3.08	11.89
2-Benzyl-3,4-diphenylquinoline	136–137	$C_{28}H_{21}N$	90.53	5.70	3.77	90.23	5.68	3.94
Picrate	181–182 dec	$C_{34}H_{24}N_4O_7$	67.99	4.03	9.33	67.93	4.10	9.19
2,3-Dihydro-9-phenyl-1H-cyclopenta[*b*]-quinoline	134–135	$C_{18}H_{15}N$	88.13	6.16	5.71	87.71	5.71	5.93
Picrate	192–193 dec	$C_{24}H_{18}N_4O_7$	60.76	3.82	11.81	61.10	3.85	11.85
1,2,3,4-Tetrahydro-9-phenylacridine	142–143	$C_{19}H_{17}N$	87.99	6.61	5.40	87.48	6.31	5.54
Picrate	193–194 dec	$C_{25}H_{20}N_4O_7$	61.47	4.13	11.47	61.75	4.09	11.22

[a] The analytical data for this derivative show it to be the dipicrate, $C_{27}H_{19}N \cdot 2C_6H_3N_3O_7$.

The mother liquor from the above picrate precipitation procedure was evaporated to dryness on a steam bath, and the crystalline residue was treated with aqueous sodium hydroxide and ether as described above. Evaporation of the ether solution provided 0.17 g (11% over-all yield) of crude 2,3-dimethyl-4-phenylquinoline as straw-colored crystals melting at 107–114°. Recrystallization from ligroin (bp 65–75°) gave colorless microcrystalline powder, mp 119–120°, which showed no melting-point depression when mixed with the product obtained in the acid-catalyzed condensation of *o*-aminobenzophenone with methyl ethyl ketone.

Synthesis of 2-Ethyl-4-phenylquinoline *via* the Combes Method.—A solution of 1.17 g of 3-anilino-1-phenyl-2-penten-1-one[17] in 6.0 ml of concentrated sulfuric acid was heated on a steam bath for 3 hr and was then cooled and poured onto 12 g of cracked ice. The resultant solution was made alkaline by the addition of 20 ml of concentrated ammonium hydroxide and was extracted with three 10-ml portions of ether. The combined extracts were washed with water, dried over anhydrous magnesium sulfate, and evaporated on a steam bath to give 0.65 g (60%) of 2-ethyl-4-phenylquinoline as an almost colorless syrup. The picrate derivative of this product melted at 178–180° after one recrystallization from ethanol and showed no melting-point depression when mixed with the picrate prepared from the major product of the base-catalyzed condensation of *o*-aminobenzophenone with methyl ethyl ketone.

Oxidation of 2,3-Dimethyl-4-phenylquinoline with Chromic Acid.[18]—A mixture of 1.00 g of 2,3-dimethyl-4-phenylquinoline, 0.86 g of chromium trioxide, and 10 ml of 30% sulfuric acid was heated on a steam bath for 30 hr. The reaction mixture was then cooled, filtered, and made alkaline by the addition of 20 ml of 5 *M* ammonium hydroxide. The mixture was again filtered, and the filtrate was concentrated to a small volume on a steam bath. The residue was acidified with acetic acid and the resultant precipitate was collected, washed with water, and dried to give 0.074 g of gray powder, mp 260–263° dec. Recrystallization from ethanol provided a colorless microcrystalline powder which melted at 265–267° dec and showed no melting-point depression when mixed with an authentic sample of 4-phenyl-3-quinaldinecarboxylic acid.[19]

Base-Catalyzed Condensation of *o*-Aminobenzophenone with Benzyl Methyl Ketone.—A solution of 5.91 g (0.030 mole) of *o*-aminobenzophenone and 4.02 g (0.030 mole) of benzyl methyl ketone in 100 ml of 5% ethanolic potassium hydroxide was refluxed for 24 hr and was then steam-distilled until all the ethanol had been removed. The residue was extracted with three 50-ml portions of ether, and the combined extracts were washed with water and dried over anhydrous magnesium sulfate. After removal of the ether on a steam bath, the oily residue was digested with 100 ml of boiling petroleum ether (bp 30–60°) and the hot hydrocarbon layer was separated from undissolved material by decantation. On cooling in an ice bath, the petroleum ether extract deposited 1.80 g of yellow powder, mp *ca.* 95–135°, which provided 0.46 g (5%) of colorless microcrystalline powder, mp 172–173°, after repeated recrystallization from aqueous ethanol. This product showed no melting-point depression when mixed with 3,4-diphenylquinaldine prepared by acid-catalyzed condensation of *o*-aminobenzophenone with benzyl methyl ketone. The infrared spectra of the products obtained in the acid- and base-catalyzed reactions were identical and were easily distinguishable from the spectrum of the isomer, 2-benzyl-4-phenylquinoline.[20]

Oxidation of 3,4-Diphenylquinaldine with Selenium Dioxide.—A mixture of 2.15 g (7.3 mmoles) of the product from the acid-catalyzed condensation of *o*-aminobenzophenone with benzyl methyl ketone, 0.82 g (7.4 mmoles) of freshly resublimed selenium dioxide, 7 ml of purified dioxane,[21] and 0.7 ml of water was refluxed for 1 hr, and the hot reaction mixture was then filtered to remove the precipitated selenium. The filtrate was diluted with 50 ml of water and allowed to stand for several hours, after which the resultant precipitate was collected, washed with water, dried at 100°, and finally recrystallized from cyclohexane to give 1.27 g (56%) of yellow microcrystalline powder, mp 141–143°. Further recrystallization from cyclohexane provided analytically pure **3,4-diphenylquinaldaldehyde**, mp 142–143°, $\lambda_{\max}^{\text{Nujol}}$ 5.89 μ (C=O).

Anal. Calcd for $C_{22}H_{15}NO$: C, 85.41; H, 4.89; N, 4.53. Found: C, 85.32; H, 4.95; N, 4.52.

Oxidation of 3,4-Diphenylquinaldaldehyde with Hydrogen Peroxide.—A solution of 1.28 g of 3,4-diphenylquinaldaldehyde and 4.0 ml of 30% hydrogen peroxide in 45 ml of acetone was refluxed for 2 hr and was then concentrated by distillation to about half its original volume. The residue was diluted with 75 ml of water and allowed to stand for 1 hr, after which the resultant precipitate was collected, washed with water, and dried at 100° to yield 1.21 g (90%) of **3,4-diphenylquinaldic acid** as an almost colorless powder melting at 180–182° dec. Recrystallization from benzene raised the melting point to 182–183° dec.

Anal. Calcd for $C_{22}H_{15}NO_2$: C, 81.21; H, 4.65; N, 4.31. Found: C, 81.97; H, 4.99; N, 4.31.

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[17] A. B. E. Lovett and E. Roberts, *J. Chem. Soc.*, 1975 (1928).

[18] *Cf.* the analogous oxidation of 2,3-dimethylquinoline to 3-quinaldinecarboxylic acid [G. Rohde, *Ber.*, **22**, 267 (1889)].

[19] The synthesis and characterization of 4-phenyl-3-quinaldinecarboxylic acid will be described in the next paper in this series.

[20] 2-Benzyl-4-phenylquinoline (mp 77–78.5°) has been prepared by the Wolff–Kishner reduction of 2-benzoyl-4-phenylquinoline. The synthesis and characterization of these compounds will be described in a forthcoming paper in this series.

[21] L. F. Fieser, "Experiments in Organic Chemistry," 3rd ed, D. C. Heath and Co., Boston, Mass., 1955, p 285, method a.