[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF NOTRE DAME]

Condensation of Aromatic Nitro Compounds with Acrylacetonitriles.[1,2] II. Some *p*-Substituted Nitrobenzenes

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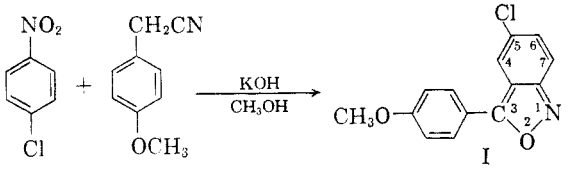
p-Nitrochlorobenzene and *p*-nitrobromobenzene react with some arylacetonitriles and potassium hydroxide in methanol to produce 3-aryl-5-haloanthranils and in pyridine to produce aryl(*p*-nitrophenyl)acetonitriles. *p*-Nitroanisole reacts with the arylacetonitriles and potassium hydroxide both in methanol and in pyridine to yield aryl(*p*-nitrophenyl)acetonitriles. *p*-Nitrotoluene under similar conditions in methanol undergoes self-condensation. Proof of structures is offered. The 3-aryl-5-haloanthranils may be transformed by known methods to 9-acridanones and acridines or to benzophenones. The aryl(*p*-nitrophenyl)acetonitriles may be oxidized to known benzophenones. A mechanism for the formation of the 3-aryl-5-haloanthranils is proposed.

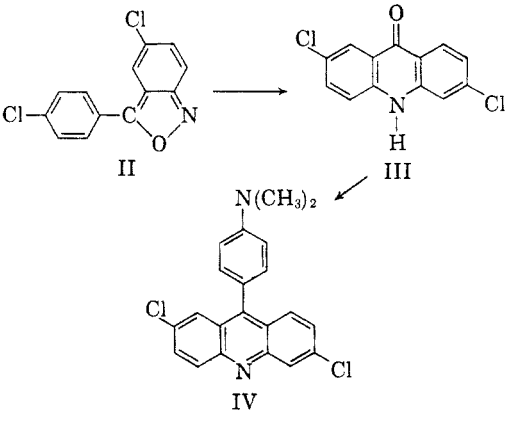
It has been reported[2] that nitrobenzene condenses with arylacetonitriles to produce arylcyanomethylene *p*-quinone oximes (4-arylcyanomethylene-2,5-cyclohexadiene-1-one oximes). We undertook the present investigation in order to determine whether *p*-substituted nitrobenzenes condense with arylacetonitriles to produce arylcyanomethylene *o*-quinone oximes (6-arylcyanomethylene-2,4-cyclohexadiene-1-one oximes).

When *p*-nitrochlorobenzene and *p*-methoxyphenylacetonitrile were allowed to react in methanolic potassium hydroxide solution, 3-(*p*-methoxyphenyl)-5-chloroanthranil (I) was obtained. This anthranil was previously prepared in a different manner by Guyot and Haller[3] and also by Simpson and Stephenson,[4] who likewise reported its reduction to 2-amino-5-chloro-4′-methoxybenzophenone. When our product was so reduced, the reported benzophenone was obtained.



I

The reaction of *p*-nitrochlorobenzene with *p*-chlorophenylacetonitrile in methanolic potassium hydroxide solution produced the known 3-*p*-chlorophenyl-5-chloroanthranil (II), which was rearranged according to the procedure of Tanasescu and Suciu[5] to 2,6-dichloro-9-acridanone (III). The reaction of this acridanone with dimethylaniline according to the method of the same authors produced 2,6-dichloro-9-(*p*-dimethylaminophenyl)-acridine (IV). In similar manner there was obtained



from *p*-nitrochlorobenzene and phenylacetonitrile the new 3-phenyl-5-chloroanthranil, the known 2-chloro-9-acridanone[6] and the known 2-chloro-9-(*p*-dimethylaminophenyl)acridine.[7]

Neresheimer and Ruppel[8] had previously reported the reaction of *p*-nitrochlorobenzene and phenylacetonitrile in the presence of potassium hydroxide and pyridine produces (*p*-nitrophenyl)-phenylacetonitrile. We repeated the reaction according to their directions and indeed obtained (*p*-nitrophenyl)phenylacetonitrile which we oxidized to the known *p*-nitrobenzophenone.[9] When *p*-chlorophenylacetonitrile and also *p*-methoxyphenylacetonitrile were used in place of phenylacetonitrile in the above reaction, we obtained the new (*p*-chlorophenyl)(*p*-nitrophenyl)acetonitrile and (*p*-methoxyphenyl)(*p*-nitrophenyl)acetonitrile, which were oxidized to the known 4-chloro-4′-nitrobenzophenone[10] and 4-methoxy-4′-nitrobenzophenone[11] respectively.

(1) Research project supported in part by National Science Foundation grant, NSF-G10030.

(2) Previous paper, *J. Am. Chem. Soc.*, **82**, 2913 (1960).

(3) A. Guyot and A. Haller, *Bull. soc. chim. France*, [3] **31**, 530 (1904).

(4) J. Simpson and O. Stephenson, *J. Chem. Soc.*, 353 (1942).

(5) I. Tanasescu and M. Suciu, *Bull. soc. chim. France*, [5] **4**, 245 (1937).

(6) R. Goodall and W. Kermack, *J. Chem. Soc.*, 1164 (1936).

(7) I. Tanasescu and M. Macarovici, *Bull. soc. chim. France*, [4] **49**, 1295 (1931).

(8) H. Neresheimer and W. Ruppel, U. S. Patent **2,080,057** (1937).

(9) G. Schroeter, *Ber.*, **42**, 3356 (1909).

(10) J. Boeseken, *Rec. trav. chim.*, **23**, 107 (1904).

(11) K. Auwers, *Ber.*, **36**, 3899 (1903).

The reactions of *p*-nitrobromobenzene with phenylacetonitrile, *p*-chlorophenylacetonitrile, and *p*-methoxyphenylacetonitrile were found to be analogous to the reactions of *p*-nitrochlorobenzene with the same arylacetonitriles. When methanol was used as the solvent, the new 3-phenyl-5-bromoanthranil, 3-(*p*-chlorophenyl)-5-bromoanthranil, and 3-(*p*-methoxyphenyl)-5-bromoanthranil were obtained. The 3-phenyl-5-bromoanthranil was isomerized to the known 2-bromo-9-acridanone,[12] from which was prepared the known 2-bromo-9-(*p*-dimethylaminophenyl)acridine.[13] The 3-(*p*-chlorophenyl)-5-bromoanthranil was isomerized to the new 2-bromo-6-chloro-9-acridanone, from which was prepared the new 2-bromo-6-chloro-9-(*p*-dimethylaminophenyl)acridine. Attempts to rearrange the 3-(*p*-methoxyphenyl)-5-bromoanthranil and also the 3-(*p*-methoxyphenyl)-5-chloroanthranil (I) to the corresponding acridanones were unsuccessful. On the other hand, when pyridine was used in place of methanol in the above reactions, the same aryl-*p*-nitrophenylacetonitriles were obtained as were produced from *p*-nitrochlorobenzene.

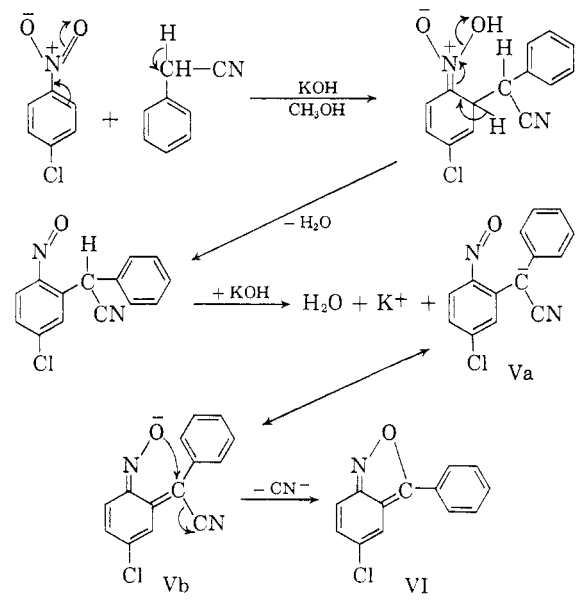
When *p*-nitroanisole was allowed to react with phenylacetonitrile, *p*-chlorophenylacetonitrile and *p*-methoxyphenylacetonitrile in both methanolic potassium hydroxide and in pyridine–potassium hydroxide, there was produced (*p*-nitrophenyl)-phenylacetonitrile, *p*-chlorophenyl-*p*-nitrophenylacetonitrile; and *p*-methoxyphenyl-*p*-nitrophenylacetonitrile respectively. We were unsuccessful in our attempts to isolate anthranils from the reactions conducted in methanol solution. It should also be pointed out that the reactions conducted in methanol solution gave poor yields of the diarylacetonitriles.

We were unsuccessful in our attempts to condense *p*-nitrotoluene with phenylacetonitrile. The material isolated from these attempts was apparently self-condensation products of *p*-nitrotoluene. Since other authors[14,15] have reported the self-condensation of *p*-nitrotoluene in alcoholic alkali solutions, we did not investigate this material further.

The yields of different products obtained from the reactions of the *p*-halonitrobenzenes with the arylacetonitriles and potassium hydroxide in methanol and pyridine demonstrate the fact that these reactions proceed by distinct paths in the two media. For example the reaction of *p*-nitrobromobenzene with phenylacetonitrile and potassium hydroxide produced 3-phenyl-5-bromoanthranil in 79% yield using methanol, and phenyl-*p*-nitrophenylacetonitrile in 76% yield using pyridine. While no completely satisfactory explanation is available for these distinct reaction paths, nevertheless, it may be said that pyridine is apparently more effective than methanol in aiding the removal of a halogen *para* to the nitro group in *p*-halonitrobenzenes. Likewise pyridine is apparently more effective than methanol in aiding the removal of the methoxy group from *p*-nitroanisole. No completely satisfactory explanation is available for the failure to obtain anthranils from the reactions of *p*-nitroanisole with the arylacetonitriles and potassium hydroxide in methanol. One might speculate that the resonance effect of the methoxy group is at least partially responsible.

It is pointed out that a large excess of potassium hydroxide was used in all the reactions of the *para*-substituted nitrobenzenes with the arylacetonitriles, both in pyridine and in methanol. A large excess was used with pyridine because the potassium hydroxide was present as a finely dispersed solid in that medium, apparently offering only its surface area for reaction. Previous investigators[8] likewise used large amounts of this reagent. A large excess was used with methanol because we found during the course of our former investigations[2] that such a practice gave better yields of condensation products.

The following mechanism is offered for the formation of the 3-aryl-5-haloanthranils. The initial steps follow the familiar lines proposed for the condensation of nitrobenzene with phenylacetonitrile,[2] differing only in that the phenylacetonitrile anion here attacks at a position *ortho* to the nitro group. Intermediate V may be considered as the potassium salt of a phenylcyanomethylene *o*-quinone oxime. However, a phenylcyanomethylene *o*-quinone oxime is not isolated because its potassium salt readily undergoes further reaction involving ring closure to a phenylanthranil.



(12) F. Ullmann, *Ann.*, **355**, 341 (1907).
(13) M. Polaczek, *Roczniki Chem.*, **16**, 76 (1936); *Chem. Abstr.*, 487 (1955).
(14) O. Fisher and E. Hepp, *Ber.*, **26**, 2231 (1893).
(15) A. G. Green, A. H. Davies, and R. S. Horsfall, *J. Chem. Soc.*, **91**, 2078 (1907).

It is suggested from this present investigation that phenylanthranils may also be formed in the condensations of nitrobenzene with arylacetonitriles. However, we were unsuccessful in our attempts to isolate anthranils in our former investigations.[2] Furthermore, we have subsequently obtained phenylcyanomethylene *p*-quinone oxime in as high as 92% yield from the reaction of nitrobenzene with phenylacetonitrile. It cannot be validly argued that the material isolated is actually a mixture of phenylcyanomethylene *p*-quinone oxime and 3-phenylanthranil because our method of isolation, particularly the treatment with boiling benzene,[2] is very conducive to removing large amounts of the anthranil. It may, therefore, be concluded that the *para* position in nitrobenzene is definitely the preferred position of attack.

It is pointed out that the formation of the 3-aryl-5-haloanthranils is reminiscent of the reaction of *o*-nitrotoluene in methanolic potassium hydroxide to produce anthranilic acid,[16] and the reaction of *o*-nitrophenylacetic acid with acetic anhydride to produce acetylanthranil,[17] wherein anthranils may be proposed as reaction intermediates.

EXPERIMENTAL[18,19]

Procedure A. (*a*) *3-Phenyl-5-chloroanthranil.* To a solution of 74 g. (1.1 moles) of potassium hydroxide (assay 85%) in 150 ml. of methanol were added with stirring and cooling in an ice bath 8.1 g. (0.069 mole) of phenylacetonitrile and a solution of 9.9 g. (0.063 mole) of *p*-nitrochlorobenzene in 100 ml. of methanol. The mixture was stirred for 4 hr. at 0–5°, and then 400 ml. of water was added with stirring. The precipitate was isolated by filtration, washed with water, and dried. There was obtained upon recrystallization from petroleum ether (b.p. 60–71°) pale yellow needles of 3-phenyl-5-chloroanthranil, m.p. 114–116°, 6.7 g. (46% yield), recrystallized a second time from petroleum ether, m.p. 115–117°.

Anal. Calcd. for $C_{13}H_8ClNO$: C, 67.98; H, 3.51; Cl, 15.44; N, 6.10. Found: C, 68.21; H, 3.73; Cl, 15.78; N, 6.55.

(*b*) *3-(p-Chlorophenyl)-5-chloroanthranil.* Following the procedure described above, 10.5 g. (0.069 mole) of *p*-chlorophenylacetonitrile and 9.9 g. (0.063 mole) of *p*-nitrochlorobenzene produced 7.6 g. (46% yield) of 3-(*p*-chlorophenyl)-5-chloroanthranil, m.p. 201–210°, recrystallized from chloroform, m.p. 214–215° (lit.[5] m.p. 202°).

Anal. Calcd. for $C_{13}H_7Cl_2NO$: C, 59.11; H, 2.67; N, 5.30. Found: C, 59.14; H, 2.74; N, 5.13.

(*c*) *3-(p-Methoxyphenyl)-5-chloroanthranil.* In similar manner, 10.3 g. (0.069 mole) of *p*-methoxyphenylacetonitrile and 9.9 g. of *p*-nitrochlorobenzene gave 8.1 g. (49% yield) of 3-(*p*-methoxyphenyl)-5-chloroanthranil, m.p. 138–143°, recrystallized from benzene, m.p. 143–145° (lit.[4] m.p. 143–145°).

(*d*) *3-Phenyl-5-bromoanthranil.* Likewise, 8.1 g. (0.069 mole) of phenylacetonitrile and 12.7 g. (0.063 mole) of *p*-nitrobromobenzene produced 13.7 g. (79% yield) of 3-phenyl-5-bromoanthranil, m.p. 105–110°, recrystallized from methanol, m.p. 116–118°.

Anal. Calcd. for $C_{13}H_8BrNO$: C, 56.96; H, 2.94; N, 5.11. Found:, C57.21; H, 3.25; N, 5.11.

(*e*) *3-(p-Chlorophenyl)-5-bromoanthranil.* Similarly, 10.5 g. (0.069 mole) of *p*-chlorophenylacetonitrile and 12.7 g. (0.063 mole) of *p*-nitrobromobenzene gave 9.28 g. (48% yield) of 3-(*p*-chlorophenyl)-5-bromoanthranil, m.p. 204–210°, recrystallized from ethyl acetate, m.p. 213–215°.

Anal. Calcd. for $C_{13}H_7BrClNO$: C, 50.60; H, 2.29; N, 4.54. Found: C, 50.72; H, 2.63; N, 4.68.

(*f*) *3-(p-Methoxyphenyl)-5-bromoanthranil.* In the usual way, 10.3 g. (0.069 mole) of *p*-methoxyphenylacetonitrile and 12.7 g. (0.063 mole) of *p*-nitrobromobenzene produced 13.3 g. (69% yield) of 3-*p*-methoxyphenyl-5-bromoanthranil, m.p. 126–130°, recrystallized from methanol, m.p. 134–135°.

Anal. Calcd. for $C_{14}H_{10}BrNO_2$: C, 55.28; H, 3.31; N, 4.61. Found: C, 55.03; H, 3.48; N, 4.67.

Procedure B. (*a*) *2-Chloro-9-acridanone* (*from 3-phenyl-5-chloroanthranil*). Using a modification of the procedure described by Tanasescu and Suciu,[5] 10 g. (0.15 mole) of sodium nitrite was added with stirring over a half-hour period to a solution of 2.0 g. (0.0087 mole) of 3-phenyl-5-chloroanthranil in 200 ml. of concd. sulfuric acid maintained at −10°. After the addition was completed, the mixture was allowed to warm to room temperature and to stand at room temperature for 17 hr. After pouring this mixture into 1 l. of water and crushed ice, the solid which precipitated was removed by filtration, was washed with water, and dried. There was obtained 1.8 g. (90% yield) of 2-chloro-9-acridanone, m.p. 390°, recrystallized from acetic acid, m.p. 394–396° (lit.[6] m.p. 398°).

(*b*) *2,6-Dichloro-9-acridanone* [*from 3-(p-chlorophenyl)-5-chloroanthranil*]. In a similar manner, 2.0 g. (0.0076 mole) of the indicated anthranil produced 1.9 g. (96% yield) of 2,6-dichloro-9-acridanone, m.p. about 420°, recrystallized from acetic acid, m.p. 422–424° (lit.[5] m.p. 416°).

Anal. Calcd. for $C_{13}H_7Cl_2NO$: C, 59.11; H, 2.67; N, 5.30. Found: C, 59.04; H, 2.95; N, 5.28.

(*c*) *2-Bromo-9-acridanone* (*from 3-phenyl-5-bromoanthranil*) Similarly, 2.0 g. (0.0073 mole) of the indicated anthranil gave 1.5 g. (72% yield) of 2-bromo-9-acridanone, m.p. about 375° dec., recrystallized from acetic acid, m.p. 382–385° (lit.[12] m.p. above 360°).

(*d*) *2-Bromo-6-chloro-9-acridanone* [*from 3-(p-chlorophenyl)-5-bromoanthranil*]. Isomerization of 1.8 g. (0.0058 mole) of the indicated anthranil in the usual way produced 1.6 g. (87% yield) of 2-bromo-6-chloro-9-acridanone, m.p. 414–416°, recrystallized from acetic acid, m.p. 416–418°.

Anal. Calcd. for $C_{13}H_7BrClNO$: C, 50.60; H, 2.20; N, 4.54. Found: C, 50.72; H, 2.63; N, 4.68.

Procedure C. (*a*) *2-Chloro-9-(p-dimethylaminophenyl)acridine.* Following the method of Tanasescu and Macarovici,[7] 0.67 g. (0.003 mole) of 2-chloro-9-acridanone and 1.0 g. of phosphorus oxychloride were added to 5.0 g. (0.04 mole) of dimethylaniline. The mixture was heated for 2 hr. on a hot water bath, cooled, diluted with 25 ml. of water and made basic to litmus with dilute sodium hydroxide. Unchanged dimethylaniline was removed by steam distillation, and the solid from the residue was isolated and dried. The yield of 2-chloro-9-(*p*-dimethylaminophenyl)acridine was 0.74 g. (74%), m.p. 236–238°, recrystallized from ethanol, m.p. 236–238° (lit.[7] m.p. 230–232°).

(*b*) *2,6-Dichloro-9-(p-dimethylaminophenyl)acridine.* In similar manner, 0.50 g. (0.003 mole) of 2,6-dichloro-9-acridanone and 5.0 g. (0.04 mole) of dimethylaniline gave 0.50 g. (72% yield) of 2,6-dichloro-9-(*p*-dimethylaminophenyl)acridine, m.p. 245–247° (lit.[20] m.p. 240–241°).

(*c*) *2-Bromo-9-(p-dimethylaminophenyl)acridine.* In like

(16) R. Scholl, *Monatsch.*, **34**, 1011 (1913); *Chem. Abstr.*, **7**, 3484 (1913).

(17) G. N. Walker, *J. Am. Chem. Soc.*, **77**, 6698 (1955).

(18) Analyses by Midwest Microlab, Incorporated, Indianapolis, Ind.

(19) All melting points are uncorrected.

(20) I. Tanasescu and M. Macarovici, *Bull. soc. chim. France*, [5] **4**, 240 (1937).

manner, 0.82 g. (0.003 mole) of 2-bromo-9-acridanone and 5.0 g. (0.04 mole) of dimethylaniline produced 1.0 g. (88% yield) of 2-bromo-9-(*p*-dimethylaminophenyl)acridine, m.p. 243–245° dec. (lit.[13] m.p. 239–240° dec.).

(*d*) *2-Bromo-6-chloro-9-(p-dimethylaminophenyl)acridine.* Similarly, 1.2 g. (0.0038 mole) of 2-bromo-6-chloro-9-acridanone and 5.0 g. (0.04 mole) of dimethylaniline gave 1.5 g. (95% yield) of 2-bromo-6-chloro-9-(*p*-dimethylaminophenyl)acridine, m.p. 227–235°, recrystallized from benzene–petroleum ether (b.p. 60–71°), m.p. 236–237°.

Anal. Calcd. for $C_{21}H_{16}BrClN_2$: C, 61.26; H, 3.92. Found: C, 61.69; H, 4.20.

Procedure D. 1. *(p-Nitrophenyl)phenylacetonitrile.* (*a*) *From p-nitrochlorobenzene and phenylacetonitrile in potassium hydroxide–pyridine.* Following the procedure described by Neresheimer and Ruppel,[8] a mixture of 20 g. (0.126 mole) of *p*-nitrochlorobenzene, 200 g. of pyridine and 84 g. of a paste, obtained by grinding equal weights of pyridine and potassium hydroxide in a ball-mill, was cooled to −5°. Phenylacetonitrile, 15 g. (0.13 mole) was added with stirring over 10 min. The mixture was stirred at about 0° for 10 hr., then 100 ml. of benzene was added with stirring and the mixture was filtered under suction. The solid material was washed with benzene and with ether. The solid was then placed in 1 l. of water with stirring, and upon the portionwise addition of 50 g. of acetic acid a new solid precipitated, which was isolated, washed with water, and dried. This product was (*p*-nitrophenyl)phenylacetonitrile, 21 g. (68% yield), m.p. 68–72°, recrystallized from ethanol, m.p. 70–72°.

Anal. Calcd. for $C_{14}H_{10}N_2O_2$: C, 70.58; H, 4.23; N, 11.76. Found: C, 70.50; H, 4.32; N, 11.79.

(*b*) *From p-nitrobromobenzene and phenylacetonitrile in potassium hydroxide–pyridine.* In a similar manner, 13 g. (0.064 mole) of *p*-nitrobromobenzene and 7.5 g. (0.065 mole) of phenylacetonitrile produced 12 g. (76% yield) of (*p*-nitrophenyl)phenylacetonitrile, m.p. 68–70°, recrystallized from methanol, m.p. 70–72°, which was not depressed on mixing with the sample previously described.

(*c*) *From p-nitroanisole and phenylacetonitrile in potassium hydroxide–pyridine.* In like manner, 10 g. (0.66 mole) of *p*-nitroanisole and 15 g. (0.13 mole) of phenylacetonitrile gave 7.0 g. (45% yield) of (*p*-nitrophenyl)phenylacetonitrile, m.p. 66–70°, recrystallized from methanol, m.p. 70–72°, not depressed on mixing with above sample.

(*d*) *From p-nitroanisole and phenylacetonitrile in methanolic–potassium hydroxide (according to Procedure A).* Following the method previously described, 9.6 g. (0.063 mole) of *p*-nitroanisole and 8.1 g. (0.069 mole) of phenylacetonitrile produced 2.3 g. (15% yield) of (*p*-nitrophenyl-phenylacetonitrile, m.p. 69–72°, recrystallized from methanol, m.p. 71–72°, not depressed on mixing with a sample described above.

2. *(p-Chlorophenyl)-(p-nitrophenyl)-acetonitrile.* (*a*) *From p-nitrochlorobenzene and p-chlorophenylacetonitrile in potassium hydroxide–pyridine.* Following the method formerly described, 10 g. (0.63 mole) of *p*-nitrochlorobenzene and 9.7 g. (0.064 mole) of *p*-chlorophenylacetonitrile produced 15 g. (86% yield) of *p*-chlorophenyl-*p*-nitrophenylacetonitrile, m.p. 108–112°, recrystallized from ethanol, m.p. 110–112°.

Anal. Calcd. for $C_{14}H_9ClN_2O_2$: C, 61.66; H, 3.33. Found: C, 61.57; H, 3.47.

(*b*) *From p-nitrobromobenzene and p-chlorophenylacetonitrile in potassium hydroxide–pyridine.* Likewise, 13 g. (0.064 mole) of *p*-nitrobromobenzene and 9.7 g. (0.064 mole) of *p*-chlorophenylacetonitrile gave 15 g. (87% yield) of *p*-bromophenyl-*p*-nitrophenylacetonitrile, m.p. 105–109°, recrystallized from methanol, m.p. 109–111°, not depressed on mixing with above sample.

(*c*) *From p-nitroanisole and p-chlorophenylacetonitrile in potassium hydroxide–pyridine.* In similar manner, 9.6 g (0.063 mole) of *p*-nitroanisole and 10.5 g. (0.069 mole) of *p*-chlorophenylacetonitrile produced 9.8 g. (55% yield) of *p*-chlorophenyl-*p*-nitrophenylacetonitrile, m.p. 105–109°, recrystallized from ethanol, m.p. 109–111°, not depressed on mixing with a sample described above.

(*d*) *From p-nitroanisole and p-chlorophenylacetonitrile in methanolic–potassium hydroxide (according to Procedure A).* Following the method formerly described, 9.6 g. (0.063 mole) of *p*-nitroanisole and 10.5 g. (0.069 mole) of *p*-chlorophenylacetonitrile gave 3.2 g. (18% yield), m.p. 106–111°, recrystallized from ethanol, m.p. 110–112°, not depressed on mixing with a sample described above.

3.(*p-Methoxyphenyl)-(p-nitrophenyl)-acetonitrile.* (*a*) *From p-nitrochlorobenzene and p-methoxyphenylacetonitrile in potassium hydroxide–pyridine.* In the usual manner, 10 g. (0.063 mole) of *p*-nitrochlorobenzene and 9.4 g. (0.064 mole) of *p*-methoxyphenylacetonitrile produced 11 g. (65% yield) of *p*-methoxyphenyl-*p*-nitrophenylacetonitrile, m.p. 60–65°, recrystallized from methanol, m.p. 69–71°.

Anal. Calcd. for $C_{15}H_{12}N_2O_3$: C, 67.15; H, 4.51; N, 10.44. Found: C, 66.83; H, 4.64; N, 10.02.

(*b*) *From p-nitrobromobenzene and p-methoxyphenylacetonitrile in potassium hydroxide–pyridine.* In similar manner, 13 g. (0.064 mole) of *p*-nitrobromobenzene and 9.4 g. (0.064 mole) of *p*-methoxyphenylacetonitrile produced 11 g. (65% yield) of *p*-methoxyphenyl-*p*-nitrophenylacetonitrile, m.p. 61-65°, recrystallized from methanol, m.p. 71–72°, not depressed on mixing with a previously described sample.

(*c*) *From p-nitroanisole and p-methoxyphenylacetonitrile in potassium hydroxide–pyridine.* Likewise, 10 g. (0.066 mole) of *p*-nitroanisole and 19 g. (0.13 mole) of *p*-methoxyphenylacetonitrile yielded 6.1 g. (34%) of *p*-methoxyphenyl-*p*-nitrophenylacetonitrile, m.p. 63–67°, recrystallized from methanol, m.p. 71–72°, not depressed on mixing with a previously described sample.

(*d*) *From p-nitroanisole and p-methoxyphenylacetonitrile in methanolic–potassium hydroxide (according to Procedure A).* Following the method formerly described, 10 g. (0.066 mole) of *p*-nitroanisole and 9.6 g. (0.066 mole) of *p*-methoxyphenylacetonitrile gave 1.6 g. (9% yield) of *p*-methoxyphenyl-*p*-nitrophenylacetonitrile, m.p. 64–67°, recrystallized from methanol, m.p. 70–71°, not depressed on mixing with a sample previously described.

Procedure E. (*a*) *2-Amino-5-chloro-4′-methoxybenzophenone [from 3-(p-methoxyphenyl)-5-chloroanthranil].* Following the procedure of Simpson and Stephenson,[4] a solution of 2.0 g. (0.0077 mole) of 3-(*p*-methoxyphenyl)-5-chloroanthranil in 20 ml. of acetic acid was heated on a hot water bath, and 3.0 g. (0.064 mole) of iron filings was added over 2.5 hr., during which 6.5 ml. of water was also added. The mixture was then cooled, diluted with 100 ml. of water and was extracted with three 50-ml. portions of ether. The filtered extract was washed with dilute sodium carbonate solution, with water, and was dried over magnesium sulfate. Upon removal of the ether by distillation, there was obtained 1.7 g. (82% yield) of 2-amino-5-chloro-4′-methoxybenzophenone, recrystallized from methanol, m.p. 101–102° (lit.[4] m.p. 100–101°).

(*b*) *p-Nitrobenzophenone[from (p-nitrophenyl)phenylacetonitrile].* Following the directions of Neresheimer and Ruppel,[8] 0.37 g. (0.0015 mole) of (*p*-nitrophenyl)phenylacetonitrile, 1.0 g. (0.01 mole) of chromium trioxide and 50 ml. acetic acid were refluxed for 1 hr. The solution was cooled and then poured into 300 ml. of cold water. The resulting precipitate was isolated, washed with water, and dried. The yield of *p*-nitrobenzophenone thus obtained was 0.26 g. (76%), m.p. 137–139° (lit.[9] m.p. 138°), not depressed on mixing with a sample previously reported.[2]

(*c*) *4-Chloro-4′-nitrobenzophenone [from (p-chlorophenyl)(p-nitrophenyl)acetonitrile].* Following the method just described, 0.41 g. (0.0015 mole) of (*p*-chlorophenyl)(*p*-nitrophenyl)acetonitrile and 1.0 g. (0.01 mole) of chromium trioxide gave 0.21 g. (54% yield) of 4-chloro-4′-nitrobenzophenone, m.p. 98–100° (lit.[10] m.p. 98°), not depressed on mixing with a sample previously reported.[3]

(*d*) *4-Methoxy-4'-nitrobenzophenone* [*from* (*p-methoxyphenyl*)(*p-nitrophenyl*)*acetonitrile*]. In like manner, 0.40 g. (0.0015 mole) of *p*-methoxyphenyl-*p*-nitrophenylacetonitrile and 1.0 g. (0.01 mole) of chromium trioxide produced 0.16 g. (42% yield) of 4-methoxy-4'-nitrobenzophenone, m.p. 122–123° (lit.[11] m.p. 121°).

NOTRE DAME, IND.

[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF THE PAINT DIVISION OF THE PITTSBURGH PLATE GLASS CO.]

The Amidomethylation of Aromatic Compounds[1a]

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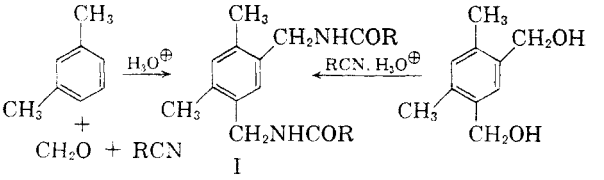
The joint condensation of aromatic compounds with formaldehyde and nitriles constitutes a new general method for the synthesis of *N*-aralkylamides and *N,N'*-bisaralkylamides. The scope and utility of the reaction are discussed.

When *m*-xylene was heated at 70–90° with an excess of paraformaldehyde and acetonitrile in phosphoric acid, or in a mixture of acetic and sulfuric acids, there was obtained *N,N'*-diacetyl-4,6-dimethyl-1,3-di(aminomethyl)benzene (Ia) in yields of 60–70%. The structure of Ia was established by its identity with the diamide obtained by alkylation of acetonitrile with 4,6-dimethyl-1,3-di(hydroxymethyl)-benzene according to the method of Parris and Christenson.[2] When the reaction was carried out with an excess of *m*-xylene the product was *N*-(2,4-dimethylbenzyl)acetamide.[2] Reaction of the monoamide with formaldehyde and acetonitrile gave the diamide Ia. This reaction of aromatic compounds with formaldehyde polymers and nitriles is a general one and has been found useful for the preparation of a large number of *N*-aralkylamides and *N,N'*-bisaralkylamides, frequently in high yields.

Methods for substitution of an aromatic nucleus by an amidomethyl group are known in the literature. German patents issued to Tscherniac[3] in 1901 disclosed the condensation of *N*-hydroxymethylphthalimide with *o*-nitrotoluene and other substituted aromatic compounds to give *N*-aralkylphthalimides. About the same time a large number of methylol derivatives of primary amides were synthesized by Einhorn[4] and condensed with a variety of aromatic compounds, especially substituted phenols, under acidic conditions. Further extensions of the Tscherniac-Einhorn method have been summarized in reviews.[5,6] The reaction of *N*-hydroxymethylamides with aromatic hydrocarbons has been the subject of recent papers by Cinnéide[7] and Nenitzescu and Dinulsecu.[8] However, the simple joint condensation described in this paper has not previously been reported.

The new method of amidomethylation was readily extended to other nitriles. The reaction of *m*-xylene and formaldehyde with acrylonitrile gave a good yield of *N,N'*-diacrylyl-4,6-dimethyl-1,3-di(aminomethyl)benzene[2] (Ib) from which the dipropionamide Ic was obtained by catalytic hydrogenation. The diamides Id, Ie, and If were prepared similarly. The three latter compounds were identical with the diamides prepared by alkylation of chloroacetonitrile, β-chloropropionitrile, and benzonitrile, respectively, with 4,6-dimethyl-1,3-di(hydroxymethyl)benzene, according to the Parris and Christenson method.[2]



Ia. R = CH_3
b. R = CH_2=CH
c. R = C_3H_7
Id. R = $ClCH_2$
e. R = $ClCH_2CH_2$
f. R = C_6H_5

In mixtures of acetic acid and sulfuric acid all of the lower aromatic hydrocarbons reacted in similar fashion. *N*-Aralkylacetamides were obtained from the reaction of acetonitrile and formaldehyde with benzene, toluene, ethylbenzene, *o*-xylene, cumene, pseudocumene, and anisole. The product of the amidomethylation of toluene was predominantly *N*-(*p*-methylbenzyl)acetamide together with a lesser amount of difficultly purified *ortho* isomer. Amidomethylation of bromobenzene required the use of concentrated sulfuric acid to give *N*-(*p*-bromobenzyl)acetamide.[9] The properties of these and other related amides are summarized in Table I.

(1) (a) Portion of a paper presented before the Meeting-in-Miniature of the Central Pennsylvania Section, American Chemical Society, March 15, 1958, Pennsylvania State University, State College, Pa. (b) Present address: Pennsalt Chemical Corp., Box 4388, Phila. 18, Pa.

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