(*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.

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

# The Amidomethylation of Aromatic Compounds[1a]

CHESTER L. PARRIS[1b] AND ROGER M. CHRISTENSON

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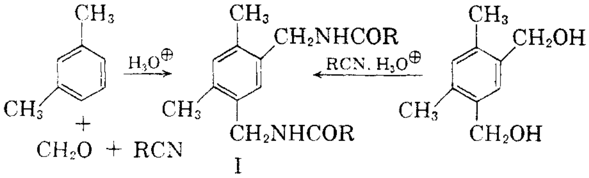
The joint condensation of aromatic compounds with formaldehyde and nitriles constitutes a new general method for the synthesis of *N*-aralkylamides and *N,N'*-bisaralkylamides. The scope and utility of the reaction are discussed.

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, $\beta$-chloropropionitrile, and benzonitrile, respectively, with 4,6-dimethyl-1,3-di(hydroxymethyl)benzene, according to the Parris and Christenson method.[2]



I

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.

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(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.

(2) C. L. Parris and R. M. Christenson, *J. Org. Chem.*, **25**, 331 (1960).

(3) J. Tscherniac, DRP **134,979** and **134,980**.

(4) A. Einhorn, *et al.*, DRP **157,355** and **158,088**; *Ann.*, **343**, 207 (1905); *Ann.*, **361**, 113 (1908).

(5) R. Schröter in Houben-Weyl, *Methoden der Organischen Chemie*, 4th Edition, Vol. II, Georg Thieme Verlag, Stuttgart, 1957 (pp. 795–805).

(6) H. Hellmann, *Angew. Chem.*, **69**, 463 (1957).

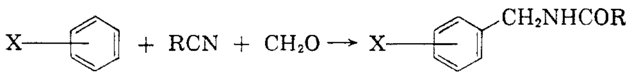
(7) R. O. Cinnéide, *Nature*, **175**, 47 (1955).

(8) C. D. Nenitzescu and I. Dinulsecu, *Rev. Chim. (Acad. rep. populaire Roumaine)*, **2**, 47 (1954).

(9) C. W. Shoppee, *J. Chem. Soc.*, 1225 (1931).

TABLE I

*N*-ARALKYLAMIDES FROM AROMATIC COMPOUNDS, NITRILES, AND FORMALDEHYDE



| Ring Substituents, X | R | Formula | Melting Point Found | Melting Point Lit. | Yield, % | | Analyses C | Analyses H | Analyses N |
|---|---|---|---|---|---|---|---|---|---|
| H | $CH_3$ | $C_9H_{11}NO$ | 62–63.5 | 64.5–66.5[a] | 50 | Calcd. | 72.45 | 7.43 | 9.39 |
| | | | | | | Found | 72.11 | 7.30 | 9.43 |
| | | | | | | | 72.03 | 7.50 | |
| 2-Methyl | $CH_3$ | $C_{10}H_{13}NO$ | 59–75 | 69[b] | 10 | Calcd. | 73.59 | 8.03 | 8.58 |
| | | | | 77.5–78[c] | | Found | 73.50 | 7.94 | 8.73 |
| | | | | | | | 73.55 | 8.07 | 8.63 |
| 4-Methyl | $CH_3$ | $C_{10}H_{13}NO$ | 112–113 | 111–112[a] | 36 | Calcd. | 73.59 | 8.03 | 8.58 |
| | | | | | | Found | 73.56 | 8.08 | 8.72 |
| | | | | | | | 73.59 | 7.86 | 8.53 |
| 4-Methyl | $CH_2{=}CH$ | $C_{11}H_{13}NO$ | 110–113.5 | | 89 | Calcd. | 75.40 | 7.48 | 8.00 |
| | | | | | | Found | 75.15 | 7.50 | 7.88 |
| | | | | | | | 75.35 | 7.34 | |
| 2,3(or 3,4-)-Dimethyl | $CH_3$ | $C_{11}H_{15}NO$ | 94–95 | | 54 | Calcd. | 74.54 | 8.53 | 7.90 |
| | | | | | | Found | 74.86 | 8.73 | 7.93 |
| | | | | | | | 75.11 | 8.54 | |
| 2,4-Dimethyl | $CH_3$ | $C_{11}H_{15}NO$ | 113–114 | 110.5–111.5[a] | 52 | Calcd. | 74.54 | 8.53 | 7.90 |
| | | | | | | Found | 74.62 | 8.31 | 8.25 |
| | | | | | | | 74.45 | 8.59 | |
| 2,4-Dimethyl | H | $C_{10}H_{13}NO$ | 122–124 | | 25 | Calcd. | | | 8.60 |
| | | | | | | Found | | | 8.54 |
| 2,5-Dimethyl | $CH_3$ | $C_{11}H_{15}NO$ | 91–92 | | | Calcd. | 74.54 | 8.53 | 7.90 |
| | | | | | | Found | 74.93 | 8.21 | 8.07 |
| | | | | | | | 74.83 | 8.13 | |
| 4-Ethyl | $CH_3$ | $C_{11}H_{15}NO$ | 79–81 | | 19 | Calcd. | 74.89 | 8.57 | 7.94 |
| | | | | | | Found | 74.93 | 8.84 | 8.13 |
| | | | | | | | 75.11 | 8.71 | |
| 4-Isopropyl | $CH_3$ | $C_{12}H_{17}NO$ | 66–67.5 | 65[d] | 75 | Calcd. | 75.35 | 8.96 | 7.32 |
| | | | | | | Found | 75.47 | 8.76 | 7.32 |
| | | | | | | | 75.38 | 8.89 | 7.16 |
| 4-Isopropyl | $CH_2{=}CH$ | $C_{13}H_{17}NO$ | 75–76.5 | | 53 | Calcd. | 76.81 | 8.43 | 6.86 |
| | | | | | | Found | 76.91 | 8.62 | 6.88 |
| | | | | | | | 77.19 | 8.47 | |
| 2,4,5-Trimethyl | $CH_3$ | $C_{12}H_{17}NO$ | 137–139 | 143.5[e] | 67 | Calcd. | 75.35 | 8.96 | 7.32 |
| | | | | | | Found | 76.07 | 9.02 | 7.30 |
| | | | | | | | 75.55 | 9.31 | |
| 4-Methoxy | $CH_3$ | $C_{10}H_{13}NO$ | 94–96 | 94.5–96[a] | 28.5 | Calcd. | 67.02 | 7.31 | 7.82 |
| | | | | | | Found | 67.42 | 7.13 | 8.03 |
| | | | | | | | 67.50 | 7.12 | |
| 4-Bromo | $CH_3$ | $C_9H_{10}BrNO$ | 118.5–120 | 113[f] | 37 | Calcd. | 47.38 | 4.42 | 6.14 |
| | | | | | | Found | 47.57 | 4.47 | 6.21 |
| | | | | | | | 47.83 | 4.33 | |

[a] Ref. (2) and references cited therein. [b] H. Strassmann, *Ber.*, **21**, 576 (1888). [c] W. H. Carothers and G. A. Jones, *J. Am. Chem. Soc.*, **47**, 3051 (1935). [d] H. Goldschmidt and A. Gessner, *Ber.*, **20**, 2414 (1887). [e] R. Willstätter and H. Kubli, *Ber.*, **42**, 4151 (1909). [f] Ref. (9).

Amidomethylation of *p*-xylene gave mostly *N*,*N'*-diacetyl-2,5-dimethyl-1,4-di(aminomethyl)benzene together with *N*-(2,5-dimethylbenzyl)acetamide. Durene afforded *N*,*N'*-diacetyl-1,3,5,6-tetramethyl-1,4-di(aminomethyl)benzene.[2]

Amidomethylation of naphthalene gave a complex mixture of amides from which three products were isolated after acid hydrolysis. 1-Naphthalenemethylamine was obtained in 12% yield. The structure of this compound was established by the identity of its acetyl derivative[10] with the amide obtained by alkylation of acetonitrile with 1-naphthalenemethanol according to the procedure of Parris and Christenson.[2] The major product was a liquid diamine obtained in 25% yield, characterized by a diacetyl derivative melting at 262–263.5°. The diamide was identical with the product obtained by alkylation of acetonitrile with 1,4-di(hydroxymethyl)naphthalene.[2] The third product was a solid diamine obtained in 6% yield, m.p. 127–129°, characterized by a diacetyl derivative, m.p. 276–279°. This compound was thought to be the 1,5-isomer.

When the reaction of *m*-xylene, paraformaldehyde, and acetonitrile was carried out in mixtures of

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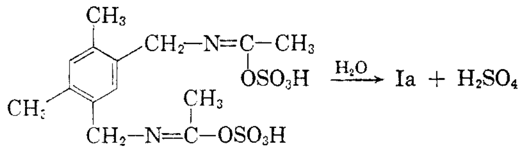
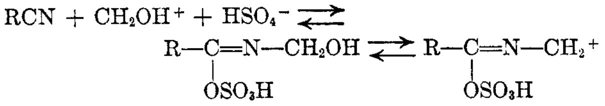
[10] J. von Braun, G. Blessing, and F. Zobel, *Ber.*, **56**, 1988 (1923).

acetic and sulfuric acid and the product was allowed to cool for at least one day, a voluminous precipitate was formed. This solid was stable and easily filterable, but had no definite melting point. Qualitative tests for both nitrogen and sulfur were positive. A slurry in water gave a strongly acidic supernatant liquid which gave a positive test for sulfate ions. Prolonged washing with water or neutralization with bases afforded a sulfur-free product which proved to be quite pure diamide Ia. Recrystallization from methanol or acetic acid also gave Ia. The sulfur and nitrogen content agreed well for the $N,N'$-bisaralkylamide sulfate (II).



II

The isolation of stable sulfur-containing intermediates was quite common throughout this work. Frequently the amide sulfates were quite insoluble and crystallized during the course of the reactions, presenting difficulties in agitation of the mixtures. It is interesting to note that Magat[11] isolated a sulfur-containing intermediate in the synthesis of $N,N'$-methylenebisamides by the acid-catalyzed reaction of formaldehyde with nitriles. It is reasonable to suggest that the electrophilic species both in Magat's reaction and in the present case is the amidomethyl sulfate carbonium ion (A).



$$\mathrm{RCN} + \mathrm{CH_2OH^+} + \mathrm{HSO_4^-} \rightleftarrows \mathrm{R{-}\underset{\substack{|\\ OSO_3H}}{C}{=}N{-}CH_2OH} \rightleftarrows \mathrm{R{-}\underset{\substack{|\\ OSO_3H}}{C}{=}N{-}CH_2^+}$$

(A)

The $N$-aralkylamides and $N,N'$-bisaralkylamides were hydrolyzed either by heating with aqueous alkali in an autoclave at 150° or by refluxing with concentrated hydrochloric acid in acetic acid. Thus, hydrolysis of Ia by the former method gave 4,6-dimethyl-1,3-di(aminomethyl)-benzene[12]; acid hydrolysis afforded the diamine as its dihydrochloride. In a few experiments some 2,4-dimethylbenzylamine was also isolated.

4,6-Dimethyldi(aminomethyl)benzene formed crystalline polysalts with adipic and sebacic acids which were converted to high-melting polyamides by melt polymerization. Reaction of 4,6-dimethyldi(aminomethyl)benzene with phosgene in boiling tetralin afforded 4,6-dimethyl-$m$-xylene-$\alpha,\alpha'$-diisocyanate.

## EXPERIMENTAL[13]

All aromatic hydrocarbons were obtained from the usual commercial sources and were of highest purity available. Hydrogen cyanide and acrylonitrile were products of the American Cyanamid Company. Acetonitrile was obtained from Union Carbide Chemical Company. All other nitriles were obtained from the Eastman Kodak Company. 1-Naphthalenemethanol, m.p. 58.5-61°, was prepared from 1-(bromomethyl)naphthalene[14] (lit., m.p. 63°,[14] 59.5-60°,[15] 59°[16]). 2-Naphthalenemethanol, m.p. 80.5-82.5°, was obtained by saponification of 2-naphthalenemethanol acetate which was prepared from 2-(bromomethyl)naphthalene by the method of Tarbell, Fukushima, and Dains[17] (lit., m.p. 80°,[18] 80-80.5°[19]). 1,4-Di(hydroxymethyl)naphthalene was prepared from 1-methylnaphthalene by the procedure of Lock and Schneider.[20b]

*Preparation of N,N'-diacetyl-1,3-di(aminomethyl)benzene* (Ia) *in phosphoric acid.* In a 5-l. three necked flask equipped with a Hershberg stirrer, condenser, and thermometer was placed 1500 ml. of 85% phosphoric acid, 360 g. (11 moles) of 91% paraformaldehyde, 530 g. (5.0 moles) of $m$-xylene, and 535 g. (13 moles) of acetonitrile. The mixture was heated with vigorous agitation to 65° whereupon a spontaneous reaction occurred. The temperature was held at 65-75° until the exothermic reaction was over, and then at 90° for an additional 4 hr. After cooling there remained a layer of 124-135 g. of unchanged xylene. The viscous acid layer was added in a slow stream with vigorous agitation to 8 l. of ice water containing 3 l. of ammonium hydroxide. The resulting suspension was stirred overnight, filtered, washed with dilute ammonium hydroxide, and dried at 75° in a convection oven for 24 hr. The yield of crude diamide, m.p. 225-235°, was 600-611 g. (61-66% based on xylene converted). After recrystallization from methanol the melting point of the analytical sample was raised to 245-246°. By mixture melting point determination and comparison of the infrared spectra the compound was proved to be identical with the diamide obtained by alkylation of acetonitrile with 4,6-dimethyl-1,3-di(hydroxymethyl)benzene.[2]

In similar manner, $N,N'$-diacrylyl-4,6-dimethyl-1,3-di(aminomethyl)benzene was obtained from acrylonitrile, m.p. about 250° with polymerization. The infrared spectrum was identical with the diacrylamide obtained by alkylation of acrylonitrile with 4,6-dimethyl-1,3-di(hydroxymethyl)benzene.[2]

*Preparation of* Ia *in acetic acid-sulfuric acid mixture.* A suspension of 264 g. (8.0 moles) of powdered 91% paraformaldehyde in 1750 ml. of glacial acetic acid and 450 ml. of concd. sulfuric acid was heated at 50° until the paraformaldehyde was dissolved. The clear solution was cooled to about 35° and then 328 g. (8.0 moles) of acetonitrile was added dropwise at 35-45°. Stirring was continued until the spontaneous reaction was completed, then 424 g. (4.0 mole)

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[11] E. E. Magat, B. F. Faris, S. E. Reith, and L. F. Salisbury, *J. Am. Chem. Soc.*, **73**, 1028 (1951).

[12] D. F. DeTar and C. J. De Pomme, U. S. Patent 2,640,080.

[13] All melting points and boiling points are uncorrected. The carbon and hydrogen analyses were by Galbraith Laboratories, Knoxville, Tenn. The Kjeldahl analyses were by Dr. James B. Lear and staff of these laboratories.

[14] R. H. F. Manske and A. E. Ledingham, *Can. J. Res.*, **17B**, 14 (1939).

[15] E. Bamberger and W. Lodter, *Ber.*, **21**, 256 (1888).

[16] E. Bourquelot and M. Bridel, *Compt. rend.*, **168**, 323 (1919).

[17] D. S. Tarbell, D. K. Fukushima, and H. Dains, *J. Am. Chem. Soc.*, **67**, 197 (1945).

[18] H. Rupe and F. Becherer, *Helv. Chim. Acta*, **6**, 880 (1923).

[19] E. Bamberger and O. Boekmann, *Ber.*, **20**, 1115 (1887).

[20] (a) G. Lock and E. Walter, *Ber.*, **75B**, 1158 (1942); (b) G. Lock and R. Schneider, *Ber.*, **84**, 636 (1951).

of *m*-xylene were added. The two-phase mixture was heated slowly to 65–75° whereupon a self-sustaining reaction occurred with formation of a clear yellow, homogeneous mixture. The temperature was raised to 85–90° for 5 hr. then cooled to about 50°. The slightly viscous product was treated with 250 ml. of water and the apparatus arranged for distillation at reduced pressure. The flask contents were heated on a steam bath with continued stirring while a vacuum of 20–25 mm. was applied to the system. A total of 1200-1700 ml. of aqueous acetic acid was thus distilled. The viscous residue was cooled, treated carefully with 1 l. of cold water, and then neutralized with an ice cold solution of 600 g. of sodium hydroxide in 1500 ml. of water. The resulting fine, sandy precipitate was filtered and washed with water until the washings were neutral. After drying at 75° the yield of crude diamide, m.p. 215–235°, was 757 g. (75%). Recrystallization raised the melting point to 246.5–248°. The infrared spectrum of this product was identical with Ia obtained by the phosphoric acid procedure.

The dichloroacetamide Id, prepared similarly, m.p. 231–232° (lit.,[8] m.p. 205°), did not depress the melting point of the product obtained by alkylation of chloroacetonitrile with 4,6-dimethyl-1,3-di(hydroxymethyl)benzene, m.p. 231–232°.[2]

*Anal.* Calcd. for $C_{14}H_{18}Cl_2N_2O_2$: C, 53.01; H, 5.72; N, 8.83; Cl, 22.35. Found: C, 53.21, 53.39; H, 5.51, 5.60; N, 8.83, 8.76; Cl, 22.21, 21.94.

The di-β-chloropropionamide Ie, m.p. 206° dec., did not depress the melting point of the diamide obtained by alkylation of β-chloropropionitrile with 4,6-dimethyl-1,3-di(hydroxymethyl)benzene, m.p. 206° dec.[2]

The dibenzamide, If, m.p. 262–263.5°, was identical with the diamide obtained by alkylation of benzonitrile with 4,6-dimethyl-1,3-di(hydroxymethyl)benzene, m.p. 263–264.5°.[2]

*Isolation of the disulfate of* Ia. To a suspension of 72.0 g. (2.2 moles) of 91% paraformaldehyde in a mixture of 1750 ml. of glacial acetic acid and 150 ml. of sulfuric acid was added 107.0 g. (2.4 moles) of acetonitrile at 30–70°. After the reaction was complete, 106.0 g. (1.0 mole) of *m*-xylene was added and the mixture heated at 90° for 6 hr. Upon cooling overnight there was formed a voluminous white solid which was collected on a sintered glass funnel, washed with fresh acetic acid, and then with ether. After air drying the yield was 384 g. (86.5%).

*Anal.* Calcd. for $C_{14}H_{20}N_2S_2O_8$: N, 6.85; S, 15.75. Found: 6.70; S, 14.62.

A 50-g. portion of the sulfate complex was stirred with 500 ml. of cold water. The suspension was made alkaline to phenolphthalein with sodium hydroxide, filtered, washed thoroughly with water, and dried at 70° to give 21 g. (75%) of Ia, m.p. 245–248°. Recrystallization from methanol raised the melting point to 247–249°. The product was shown by mixture melting point and its infrared spectrum to be Ia.

*Preparation of N-(2,4-dimethylbenzyl)acetamide.* A suspension of 75.0 g. (2.28 moles) of paraformaldehyde in 1050 ml. of acetic acid and 225 ml. of sulfuric acid was treated with 112.5 g. (2.8 moles) of acetonitrile at 30–70°, then 1594 g. (15 moles) of *m*-xylene were added. The mixture was heated for 4.5 hr. at 85–90°, then cooled. The clear organic phase was decanted and discarded. The lower orange acidic phase, which solidified upon cooling, was filtered. The residue was washed thoroughly with water until the washings were neutral. After air drying there was obtained 228 g. (52%) of crude amide, m.p. 95–115°, which was distilled. The product was a colorless oil, b.p. 190–195° (1 mm.), which solidified in the receiver, m.p. 110–112°. The distillate was recrystallized from a mixture of benzene and petroleum ether (b.p. 30–60°) to give white crystals, m.p. 113–114°. The melting point was not depressed by admixture with an authentic sample prepared by the method of Parris and Christenson.[2]

*Amidomethylation of N-(2,4-dimethylbenzyl)acetamide.* A suspension of 18.0 g. (0.6 mole) of paraformaldehyde in 440 ml. of acetic acid and 28 ml. of sulfuric acid was treated with 26.9 g. (0.65 mole) of acetonitrile in the usual way. Forty-four grams (0.25 mole) of *N*-(2,4-dimethylbenzyl)-acetamide was added and the temperature raised to 90° for 5 hr. After cooling and standing at room temperature for 1 week a white solid was deposited which was filtered and washed with water until the washings were neutral. There was obtained 28 g. (45%) of Ia, m.p. 247–248°.

*N,N'-Dipropionyl-4,6-dimethyl-1,3-di(aminomethyl)benzene* (Ic). A suspension of 27.2 g. (0.1 mole) of the diacrylamide Ib in 200 ml. of methanol was shaken with 0.5 g. of 5% palladized carbon catalyst at 20–60 p.s.i. and room temperature. The theoretical amount of hydrogen was rapidly absorbed. The product was boiled, filtered while hot through a Celite pad, and concentrated. Upon cooling there was obtained 23.3 g. (85%) of Ic, m.p. 216°. After two recrystallizations from methanol the melting point was 217.5–218°.

*Anal.* Calcd. for $C_{16}H_{24}N_2O_2$: C, 69.53; H, 8.75; N, 10.10. Found: C, 69.41, 69.48; H, 8.32, 8.47; N, 10.02, 10.25.

*Preparation of N,N'-diacetyl-2,5-dimethyl-1,4-di(aminomethyl)benzene and N-(2,5-dimethylbenzyl)acetamide.* A suspension of 144.0 g. (4.4 moles) of 91% paraformaldehyde in 1750 ml. of acetic acid and 360 ml. of sulfuric acid was treated with 214 g. (5.25 moles) of acetonitrile in the usual way. When the spontaneous reaction was complete 212 g. (2.0 moles) of *p*-xylene were added and the mixture heated at 90°. After about 3 hr. a white precipitate began to form and eventually the mixture could not be stirred. The solid was collected on a sintered glass funnel and washed thoroughly with petroleum ether (b.p. 30–60°). Both the residue and the filtrate were processed.

The solid was dried at 75° to give 600 g. (67.5%) of crude sulfate. This material was slurried with water, filtered, and washed thoroughly on the filter until the washings were neutral. After drying the yield of crude diamide was 282.5 g. (55% overall), m.p. 242–250°. The analytical sample, prepared by recrystallization from methanol, melted at 269°.

*Anal.* Calcd. for $C_{14}H_{20}N_2O_2$: C, 67.71; H, 8.12; N, 11.28. Found: C, 67.52, 67.53; H, 7.96, 7.73; N, 11.50.

The original filtrate was diluted with water, made basic with ammonium hydroxide, and extracted thoroughly with butanol. The extract was concentrated and the residue was distilled. The product consisted of 75 g. (21%) of colorless oil, b.p. 140–180° (0.1–0.3 mm.) which solidified in the receiver, m.p. 75–85°. The distillate was crystallized from a mixture of benzene and petroleum ether to give an analytical sample melting at 90–91°. The compound had the correct analysis for *N*-(2,5-dimethylbenzyl)acetamide (Table I).

*Preparation of N,N'-diacetyl-2,3,5,6-tetramethyl-1,4-di(aminomethyl)benzene.* A suspension of 72.0 g. (2.4 moles) of paraformaldehyde in 1750 ml. of acetic acid and 150 ml. of sulfuric acid was treated dropwise with 107.0 g. (2.6 moles) of acetonitrile at 30–70°. When the spontaneous reaction was complete 134 g. (1.0 mole) of durene were added and the temperature was raised to 85°. After 45 min. a voluminous precipitate began to appear. Heating was maintained for 5 hr. and, after cooling, the mixture was filtered on a sintered glass funnel, washed thoroughly with hexane, and dried *in vacuo.*

*Anal.* Calcd. for $C_{16}H_{24}N_2S_2O_8$: N, 6.42; S, 14.69; $H_2SO_4$, 45.0%. Found: N, 6.20, 6.22; S, 14.26; $H_2SO_4$ (by titration) 43.0%.

The product was washed thoroughly with water until the washings were neutral. After drying at 75°, the yield of white solid, not melting below 310°, was 198 g. (72%). An analytical sample was prepared by three recrystallizations from glacial acetic acid.

*Anal.* Calcd. for $C_{16}H_{24}N_2O_2$: C, 69.53; H, 8.75; N, 10.14. Found: C, 69.53, 69.36; H, 8.50, 8.58; N, 10.25.

*N-(o- and p-Methylbenzyl)acetamide.* A suspension of 165 g. (5.8 moles) of paraformaldehyde in 1050 ml. of acetic acid and 450 ml. of sulfuric acid was treated with 226 g. (5.5

moles) of acetonitrile at 30–70°. When the exothermic reaction was treated with 226 g. (5.5 moles) of acetonitrile at 30–70°. When the exothermic reaction was over, 460 g. (5.0 moles) of toluene was added and the mixture was heated for 4 hr. at 90°. The cooled mixture was poured into 10 l. of cold water and extracted thoroughly with fresh toluene. The extract was washed, concentrated, and distilled to give 433 g. (53%) of mixed isomers, b.p. 130° (0.05 mm.), m.p. 65–100°. The material was redistilled and a middle fraction was collected for analysis.

*Anal.* Calcd. for $C_{10}H_{13}NO$: C, 73.59; H, 8.03; N, 8.58. Found: C, 73.67, 73.28; H, 7.84, 8.07; N, 8.84.

A crude undistilled mixture of isomers prepared as above was dissolved in a hot mixture of acetone and petroleum ether (b.p. 30–60°). Upon cooling a yellow oil separated which partially solidified upon standing. The solid was filtered and pressed tightly on the funnel to remove adhering oil droplets. Both the solid residue and oily filtrate were processed.

The solid was recrystallized from a mixture of benzene and petroleum ether (b.p. 30–60°) to give colorless needles of *N*-(*p*-methylbenzyl)acetamide, m.p. 110–112°. The analytical sample, prepared by two additional recrystallizations from benzene, melted at 112–113° (Table I).

The oily filtrate was distilled to give 82.5 g. of colorless oil, b.p. 132–135° (0.05 mm.), which solidified in the receiver, m.p. 44–68°. Three recrystallizations raised the melting range to 59–75° but the *N*-(*o*-methylbenzyl)-acetamide could not be purified further (Table I).

*N-Acetyl-1-naphthalenemethylamine.* To 100 ml. of acetonitrile at 5° was added dropwise with stirring 7.5 ml. of concd. sulfuric acid. After 0.5 hr., 15.8 g. (0.1 mole) of 1-naphthalenemethanol was added in small portions at 5°, then allowed to warm slowly to room temperature. Polymer which precipitated during the reaction was removed mechanically. After 5 days the product was diluted with water and extracted thoroughly with ethyl acetate. The extract was washed, dried and concentrated. The residue was distilled to give 6.0 g. of yellow oil, b.p. 150–215° (0.1 mm.) which solidified in the receiver. The distillate was recrystallized twice from a mixture of benzene and petroleum ether (b.p. 30–60°) and twice more from a mixture of ethyl acetate and petroleum ether to give white crystals, m.p. 127–128.5° (lit.,[10] m.p. 134°).

*Anal.* Calcd. for $C_{13}H_{13}NO$: C, 78.37; H, 6.58; N, 7.03. Found: C, 78.47, 78.54; H, 6.52, 6.76; N, 7.09, 7.09.

*N-Acetyl-2-naphthalenemethylamine.* By the same procedure employed for the 1-isomer above, there was obtained from 2-naphthalenemethanol a colorless oil, b.p. 169–200° (0.1 mm.), m.p. 113–119° after recrystallization from benzene and petroleum ether (b.p. 30–60°). After repeated recrystallization from a mixture of ethyl acetate and petroleum ether the analytical sample melted at 125–125.5° (lit.,[25] m.p. 126°). A mixture with the 1-isomer showed a melting point depression of 35°.

*Anal.* Calcd. for $C_{13}H_{13}NO$: C, 78.37; H, 6.58; N, 7.03. Found: C, 78.90, 78.73; H, 6.56, 6.38; N, 7.18, 7.20.

*N,N'-Diacetyl-1,4-di(aminomethyl)naphthalene.* To a solution of 3.8 ml. of sulfuric acid in 25 ml. of acetonitrile was added 4.7 g. (0.025 mole) of 1,4-di(hydroxymethyl)naphthalene with shaking and cooling at 5°. After having stood overnight, the mixture had separated into two phases. It was diluted with water, made basic with ammonium hydroxide and extracted thoroughly with ethyl acetate. The organic phase was filtered to give a 0.5 g. of residue, m.p. 261–262.5°, after recrystallization from methanol. Concentration of the organic phase yielded a gummy residue which, after repeated recrystallization from methanol, gave an additional yield of diamide, m.p. 260–262.5°. The total yield was 2.5 g. (37%).

*Anal.* Calcd. for $C_{16}H_{18}N_2O_2$: C, 71.09; H, 6.71; N, 10.37. Found: C, 70.42, 70.53; H, 7.18, 7.07; N, 10.26.

*Amidomethylation of naphthalene.* To a solution of 180.0 g. of paraformaldehyde in 1740 ml. of acetic acid and 450 ml. of sulfuric acid was added 270 g. (6.6 moles) of acetonitrile dropwise at 30–50° in the usual way. After cooling slightly 384 g. (3.0 moles) of naphthalene were added and the temperature was maintained at 70° until the mixture was homogeneous. The temperature was then held at 90° for 5 hr. longer and cooled. The apparatus was arranged for distillation *in vacuo* and about 1200 ml. of acetic acid was distilled at 20 mm. pressure. The viscous residue was treated with 1 l. of water and then neutralized with ammonium hydroxide.

The product was a heavy gummy solid which was isolated by decantation of the liquid. The gum was washed briefly with water then refluxed for 24 hr. with a mixture of 1250 ml. of acetic acid and an equal volume of concd. hydrochloric acid. The mixture was concentrated by distillation at reduced pressure. The residue was neutralized with sodium hydroxide and a small amount of polymer which precipitated was removed mechanically. The *p*H was then adjusted to 11 with additional alkali and the resulting oil was extracted with butanol. After removal of the solvent distillation of the residue gave 285.2 g. of an oil, b.p. 138–190° (0.2 mm.), which partially crystallized upon refrigeration for 24 hr. The product was filtered and pressed on the filter with a rubber dam to remove adhering oil droplets. Both filtrate (A) and residue (B) were processed.

The viscous yellow-green filtrate (A) was distilled through a Vigreux column:

*Fraction* 1, b.p. 97–109° (0.1 mm.), consisted of 55.5 g. of colorless oil. A center fraction of the material obtained upon redistillation boiled at 92° (0.1 mm.).

*Anal.* Calcd. for $C_{11}H_{11}N$: C, 84.00; H, 7.06; N, 8.91. Found: C, 83.46, 83.67; H, 7.09, 7.08; N, 8.92.

The hydrochloride was prepared in the usual way and recrystallized from acetic acid, m.p. 253.5–255°.

*Anal.* Calcd. for $C_{11}H_{12}ClN$: C, 68.21; H, 6.25; N, 7.23. Found: C, 68.20, 68.28; H, 6.26, 5.93; N, 7.26.

The acetyl derivative, prepared by treatment of the amine with acetyl chloride in pyridine solution, melted at 127.5–128.5°. A mixture with the *N*-acetyl-1-naphthalenemethylamine prepared from 1-naphthalenemethanol showed no depression in melting point.

*Anal.* Calcd. for $C_{13}H_{13}NO$: C, 78.37; H, 6.58; N, 7.03. Found: C, 78.58, 78.21; H, 6.79, 6.72; N, 7.08.

*Fraction* 2, b.p. 158–165° (0.3 mm.), consisted of 124.5 g. of slightly viscous yellow-green oil. A center fraction of redistilled material boiled at 147° (0.2 mm.). Upon exposure to air a bluish fluorescence was developed.

*Anal.* Calcd. for $C_{12}H_{14}N_2$: C, 77.38; H, 7.56; N, 15.04. Found: C, 77.09, 76.97; H, 7.81; N, 14.84, 14.78.

The dihydrochloride did not melt below 300° after repeated recrystallization from aqueous acetic acid, then from a mixture of benzene and methanol.

*Anal.* Calcd. for $C_{12}H_{16}Cl_2N_2$: C, 55.61; H, 6.22; N, 10.81. Found: C, 55.96, 55.87; H, 6.46, 6.24; N, 10.60.

The diacetyl derivative prepared from acetyl chloride in pyridine melted at 261–263°. A mixture melting point with the diacetamide prepared from 1,4-di(hydroxymethyl)-naphthalene (*vide supra*) showed no depression.

*Anal.* Calcd. for $C_{16}H_{18}N_2O_2$: C, 71.09; H, 6.71; N, 10.37. Found: C, 71.03, 71.31; H, 6.74, 6.60; N, 10.15.

The solid residue (B) (31 g.) melted at 115–125° after washing with a little fresh benzene and petroleum ether. The analytical sample melted at 128–129.5° after two recrystallizations from benzene.

*Anal.* Calcd. for $C_{12}H_{14}N_2$: C, 77.38; H, 7.56; N, 15.04. Found: C, 77.17, 76.94; H, 7.80, 7.63; N, 14.81.

The dihydrochloride melted above 300° after repeated recrystallization from aqueous acetic acid.

*Anal.* Calcd. for $C_{12}H_{16}Cl_2N_2$: C, 55.61; H, 6.22; N, 10.81. Found: C, 55.83, 55.57; H, 6.18, 5.95; N, 10.99.

The diacetyl derivative, prepared from acetyl chloride in pyridine, melted at 276–279°.

*Anal.* Calcd. for $C_{16}H_{18}N_2O_2$: C, 71.09; H, 6.71; N, 10.37 Found: C, 71.57, 71.17; H, 6.67, 6.87; N, 10.31.

*Alkaline hydrolysis of N,N'-diacetyl-1,3-di(aminomethyl)-benzene.* A one-gallon stainless steel autoclave, charged with 496 g. (2.0 moles) of the diamide Ia and a solution of 240 g. (6.0 moles) of sodium hydroxide in 1800 ml. of water was heated for 16 hr. at 175°. The cooled autoclave contents were extracted with butanol and the extract was concentrated. The residue was heated to about 125° and then vacuum from a rotatory oil pump was applied. The hot diamine was distilled rapidly into the receiver where it crystallized. The product was melted under nitrogen and poured into a Pyrex tray. The cooled solid, m.p. 120–127°, was further purified by recrystallization from methanol, m.p. 126–127°.

*Acid hydrolysis of diamide* Ia. A mixture of 744.0 g. (3.0 mole) of crude diamide Ia in a mixture of 1 l. of glacial acetic acid and 1 l. of concd. hydrochloric acid was refluxed for 24 hr. The excess acids were distilled at reduced pressure until the residue became a thick gummy mass. The residue was stirred vigorously with 1200 ml. of 25% sodium hydroxide and 1 l. of toluene. The resulting mixture consisted of a solid phase and two liquid layers. The lower aqueous layer was rejected and the organic product was filtered. Both residue and filtrate were processed.

The residue was washed with toluene and hexane, then recrystallized from methanol to give 163 g. of 4,6-dimethyl-1,3-di(aminomethyl)benzene, m.p. 124–126°. Recrystallization from benzene gave an analytical sample melting at 125–126.5° (lit.,[12] m.p. 124–125°).

*Anal.* Calcd. for $C_{10}H_{16}N_2$: C, 73.12; H, 9.82; N, 17.06. Found: C, 72.92, 73.03; H, 9.69, 9.70; N, 17.17, 17.08.

The monohydrochloride, prepared from a little hydrogen chloride in methanol and benzene, melted at 213–213.5° dec.

*Anal.* Calcd. for $C_{10}H_{17}ClN_2$: C, 59.84; H, 8.54; N, 13.96. Found: C, 59.88, 59.92; H, 8.13, 8.44; N, 13.83.

The dihydrochloride prepared from excess methanolic hydrogen chloride in benzene melted at 274.5–276.5° dec.

*Anal.* Calcd. for $C_{10}H_{18}Cl_2N_2$: N, 11.81. Found: N, 11.64.

The polysebacate prepared in methanol melted at 152–153°.

*Anal.* Calcd. for $C_{20}H_{34}N_2O_4$: C, 65.54; H, 9.35; N, 7.65. Found: C, 65.28, 65.36; H, 9.14, 9.07; N, 7.68.

The toluene phase was dried, concentrated, and distilled. There was obtained 43 g. of 2,4-dimethylbenzylamine, b.p. 86–90° (10 mm.), 105–115° (20 mm.). The hydrochloride prepared in the usual way melted at 231–233°.

*Anal.* Calcd. for $C_9H_{14}ClN$: N, 8.20; Cl, 20.75. Found: N, 8.07; Cl, 20.30.

*N-(2,4-Dimethylbenzyl)formamide.* A mixture of 6.8 g. (0.05 mole) of 2,4-dimethylbenzylamine, 20 g. (0.40 mole) of 90% formic acid and 100 ml. of toluene was refluxed while the theoretical amount of water was removed *via* a Dean-Stark trap. On chilling the residue there was obtained 7.5 g. (91%) of product, m.p. 120–121.5°. After two recrystallizations from benzene the analytical sample melted at 122–124°, and did not depress the melting point of the monoamide prepared from *m*-xylene, formaldehyde, and hydrogen cyanide (Table I).

*Anal.* Calcd. for $C_{10}H_{13}NO$: N, 8.60. Found: N, 8.62.

*Melt polymerization of 4,6-dimethyl-1,3-di(aminomethyl)-benzene sebacate.* Two grams of the salt were heated in a sealed evacuated Carius tube for 2 hr. at a temperature of 190–200°. The tube was cooled, opened and then heated for 2 hr. at 295–310° and 0.1 mm. The polymer formed a clear, slightly greenish melt. Upon cooling an opaque white solid was obtained, m.p. 258–260°.

*4,6-Dimethyl-m-xylene-α,α'-diisocyanate.* In a 1-l. three necked flask equipped with a Hershberg stirrer, reflux condenser, and gas inlet tube was placed 59.3 g. (0.25 mole) of 4,6-dimethyl-1,3-di(aminomethyl)benzene dihydrochloride and 1650 ml. of dry tetralin. The mixture was heated at 200–205° and treated with a stream of chlorine-free phosgene. After 7 hr. evolution of hydrogen chloride had ceased and the mixture was purged with a stream of inert gas. The dark solution was cooled, filtered through Celite, and concentrated. The residue was distilled to give 36–38 g. (69–70%) of a colorless oil, b.p. 171–173° (8 mm.), $n_D^{24}$ 1.5407.

*Anal.* Calcd. for $C_{12}H_{12}N_2O_2$: C, 66.65; H, 5.60. Found: C, 66.84, 67.02; H, 5.68, 5.74.

A small portion of the diisocyanate was treated with excess methanol. An exothermic reaction occurred and a crystalline mass was formed. After one recrystallization from methanol the 4,6-dimethyl-1,3-di(carbomethoxyaminomethyl)benzene melted at 173–174°.

*Anal.* Calcd. for $C_{14}H_{20}N_2O_4$: C, 59.98; H, 7.19; N, 10.00. Found: C, 60.69, 60.65; H, 7.28, 7.45; N, 9.85.

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