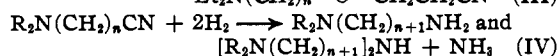
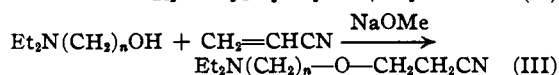
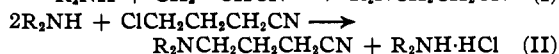


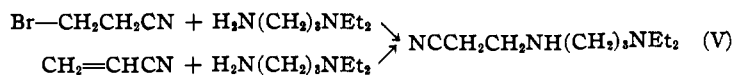
[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY AND PHYSICS OF THE PENNSYLVANIA STATE COLLEGE]

**Basically Substituted Aliphatic Nitriles and their Catalytic Reduction to Amines<sup>1</sup>**BY FRANK C. WHITMORE, HARRY S. MOSHER,<sup>2</sup> ROBERT R. ADAMS,<sup>3</sup> ROBERT B. TAYLOR, EARL C. CHAPIN,<sup>3</sup> CHARLES WEISEL AND WILLIAM YANKO<sup>3,4</sup>

In the course of our work on basically substituted heterocyclic compounds it became necessary to prepare a group of aliphatic substituted diamines. This paper is a report on the more successful of these experiments. Since it was necessary to produce rather large amounts of these compounds, the phthalimide synthesis which has been used most often for this purpose was judged unsuitable and it was finally decided to use the reduction of basically substituted nitriles to obtain these amines. The general procedures used are represented by the following equations, where R may be hydrogen, alkyl or bound in a heterocyclic ring system.

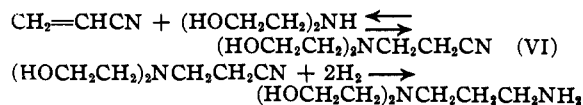


The basically substituted propionitriles are best obtained by the addition of ammonia, primary, or secondary amines to acrylonitrile.<sup>5</sup> Although this method has been used for the same purpose by Holcomb and Hamilton,<sup>6</sup> no studies of the reaction itself and the mechanism have been published. Structural proof of the products is furnished first by the non-identity of  $\alpha$ -diethylaminopropionitrile prepared by the cyanohydrin synthesis and the product obtained by the addition of diethylamine to acrylonitrile, and secondly by the identity of  $\gamma$ -diethylaminopropylamine prepared through the phthalimide synthesis<sup>7</sup> and the compound obtained by reducing the addition product from diethylamine and acrylonitrile. In addition to this,  $\beta$ -( $\gamma$ -diethylaminopropylamino)-propionitrile has been prepared by two separate methods as indicated below and the properties of the products and their picrates found to be identical.

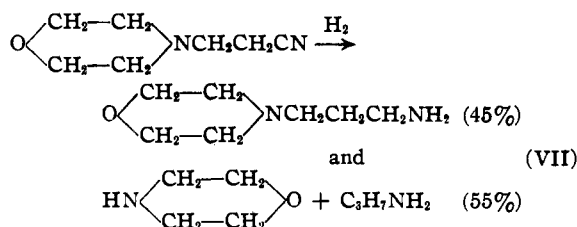


Thus the mechanism by which the addition takes place probably involves a typical 1,4-addition.

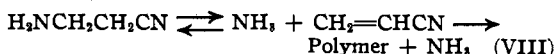
From the following experimental evidence it is apparent that the reaction is reversible. When the higher  $\beta$ -dialkylaminopropionitriles are heated near their boiling points for any length of time, they slowly decompose to give some of the dialkylamine. This is especially true in the case of diethanolamine, addition of which to acrylonitrile gives a viscous liquid from which is readily obtained the crystalline picrate of  $\beta$ -diethanolaminopropionitrile. Attempted distillation of this reaction product, however, gives back all of the diethanolamine used as starting material and leaves only a non-distillable polymer. If, however, the addition compound is reduced without distillation, a fair yield of  $\gamma$ -diethanolaminopropylamine, which can be distilled without decomposition, is obtained.



Secondly, when equal molar amounts of a secondary amine and acrylonitrile react, some of the unreacted starting materials are always recovered and the yield is never as high as when an excess of one of the starting materials is used. In addition to this, it was observed that when  $\beta$ -morpholinopropionitrile was reduced at an elevated temperature (190°) a 35% yield of morpholine was obtained.



Although this may be explained by hydrogenolysis, it can equally well be explained on the basis of a reversal of the morpholine-acrylonitrile- $\beta$ -morpholinopropionitrile equilibrium at the elevated temperature. Finally the spontaneous polymerization of  $\beta$ -aminopropionitrile on standing to give a polymer and ammonia can best be explained by assuming its disproportionation into acrylonitrile and ammonia followed by the polymerization of the acrylonitrile.



The ease with which the various amines react

(1) Presented before the Organic Division of The American Chemical Society at Detroit, April 12, 1943.

(2) The material herein presented is taken in part from a thesis submitted by Harry S. Mosher to The Pennsylvania State College in partial fulfillment of the requirements for the Ph.D. degree.

(3) Parke, Davis and Company Research Fellow 1942-43.

(4) Present address: Monsanto Chemical Company, Dayton, Ohio.

(5) (a) Hoffmann and Jacobi, U. S. Patents 1,992,615 and 2,017,537; (b) Roh and Wolff, German Patent 641,597.

(6) Holcomb and Hamilton, THIS JOURNAL, 64, 1309-1311 (1942).

(7) Shriner and Hickey, *ibid.*, 61, 888 (1939).

with acrylonitrile is interesting. Piperidine is the most reactive and the solution should be cooled during the addition; morpholine is next in activity, being only slightly less reactive than piperidine; diethylamine is the most reactive of the dialkylamines employed but its rate of addition is very much slower than that for either of the two above cyclic bases and no noticeable heat is evolved on mixing with acrylonitrile. The rate of addition of the remaining dialkylamines decreases progressively with the length and size of the alkyl groups and the formation of  $\beta$ -[di-(2-ethylhexylamino)]-propionitrile was only 77% complete after heating di-(2-ethylhexyl)-amine and acrylonitrile together for 360 hours at 100°. That the rate of addition is not a function of the basic strength of the addenda is shown by the relative reactivities of diethylamine, piperidine and morpholine (whose ionization constants are, respectively,  $1.2 \times 10^{-3}$ ,  $1.6 \times 10^{-3}$  and  $2.4 \times 10^{-5}$ )<sup>8</sup> but apparently is more dependent upon the size and shape of the entering molecule.

In the case of certain heterocyclic and aromatic amines a catalyst was necessary. Thus methyl-aniline did not react with acrylonitrile in a sealed tube at 200° in the absence of a catalyst nor did any reaction take place between the two when refluxed in dioxane in the presence of benzyltrimethylammonium hydroxide. But in the presence of hydrated copper sulfate at 180° the desired  $\beta$ -(methylphenylamino)-propionitrile was produced. Likewise carbazole would not react without a catalyst but in the presence of benzyltrimethylammonium hydroxide, the reaction proceeded vigorously. Neither copper bronze, copper sulfate, small amounts of sulfuric acid, nor benzyltrimethylammonium hydroxide would catalyze the addition of tetrahydroquinoline to acrylonitrile but in acetic acid solution a good yield of the addition product was obtained.<sup>9</sup> All attempts to bring about a reaction between acrylonitrile and anisidine, 2-aminopyridine or urea were unsuccessful.

The special case of the addition of ammonia to acrylonitrile<sup>5</sup> is interesting because of the three possible products.

$$\text{H}_2\text{NCH}_2\text{CH}_2\text{CN} \quad \text{HN}(\text{CH}_2\text{CH}_2\text{CN})_2 \quad \text{N}(\text{CH}_2\text{CH}_2\text{CN})_3$$

When the reaction is carried out by shaking with aqueous ammonia, the secondary and tertiary amines predominate but when the reaction takes place in a seven molar excess of liquid ammonia at about 40°, a 22% yield of the primary amine and a 64% yield of the secondary amine result with very little of the completely substituted product. The data indicate that the addition of  $\beta$ -aminopropionitrile to acrylonitrile takes place approximately 20 times faster than the corresponding addition of ammonia. The reduction of a similar reaction mixture resulted in a 20% yield of trimethylenediamine.

(8) Ingram and Luder, *THIS JOURNAL*, **64**, 3043 (1942).

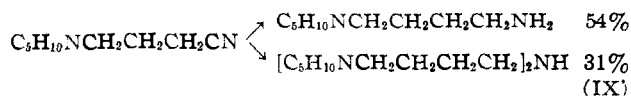
(9) The use of acetic acid as solvent for this reaction was made at the suggestion of Dr. I. B. Dickey of Eastman Kodak Company.

The group of amines which contain an ether linkage were obtained by the method of Bruson and Riener<sup>10</sup> by the action of acrylonitrile on a basically substituted alcohol such as diethylaminoethanol in the presence of sodium methoxide (Equation III). The yields with diethylaminoethanol and  $\gamma$ -diethylaminopropanol were 79.5 and 75.4%, respectively, while that for the secondary alcohol, 1-diethylamino-4-pentanol,<sup>11</sup> was 66%.

The  $\gamma$ -aminobutyronitriles were all obtained in excellent yields by the reaction of secondary amines with  $\gamma$ -chloro- or  $\gamma$ -bromo-butyronitriles according to the method employed by Utermohlen and Hamilton,<sup>12</sup> and Strukov.<sup>13</sup> Their yields were greatly improved by the use of a solvent.

The reduction of the nitriles to amines was usually accomplished with Raney nickel catalyst at temperatures of 90–130° and hydrogen pressures of 67 to 270 atmospheres. This was found to be superior to platinum at lower pressures or to reduction at higher temperatures. A typical example is the hydrogenation of  $\beta$ -morpholinopropionitrile, 4.8 moles of which was reduced without solvent in twenty minutes at 120° and 1400 lb. per sq. in. pressure to give a 60% yield of  $\gamma$ -morpholinopropylamine. The reduction of nitriles has been studied extensively<sup>14</sup> and is known to produce as a by-product the secondary amine as well as the primary amine (Equation IV) in which it seems quite certain that the mechanism involves the reaction of a part of the primary amine which has been produced, with the intermediate imine.<sup>15</sup> The formation of similar triamines has been reported by Mannich and Margotte,<sup>16</sup> in a patent by Münch and Schlichting,<sup>17</sup> by Winans and Adkins,<sup>15</sup> and Magidson<sup>18</sup> has also used such an amine in the synthesis of an acridine derivative.

These secondary amines were normally observed in each of our reductions when sufficiently large runs were made and constituted 5 to 32% yields. The  $\gamma$ -aminobutyronitriles gave uniformly higher yields of the secondary amines than the corresponding propionitriles; thus  $\gamma$ -piperidinobutyronitrile gave a 54% yield of the primary amine and a 31% yield of the secondary amine.



(10) Bruson and Riener, *THIS JOURNAL*, **65**, 23 (1943).

(11) Furnished through the courtesy of the Winthrop Chemical Company.

(12) Utermohlen and Hamilton, *THIS JOURNAL*, **63**, 156 (1941).

(13) Strukov, *Khim. Farm. Prom.*, 332 (1933); *C. A.*, **28**, 3714 (1934).

(14) Adkins, "Reactions of Hydrogen with Organic Compounds Over Chromium Oxide and Nickel Catalysts," University of Wisconsin Press, 1937.

(15) Winans and Adkins, *THIS JOURNAL*, **55**, 4167 (1933).

(16) Mannich and Margotte, *Ber.*, **68B**, 273–278 (1935).

(17) Münch and Schlichting, German Patent 561,156, Dec. 10, 1932.

while  $\beta$ -piperidinopropionitrile gave a 45% yield of primary amine and a 17% yield of the secondary amine under the same conditions. The reduction can be controlled and the yield of primary amine increased by carrying out the hydrogenation in the presence of ammonia,<sup>18</sup> thus reversing the reaction which produces the secondary amine. By this method the 45% yield of  $\gamma$ -piperidinopropylamine reported above was raised to 68.5%, the 54% yield of  $\gamma$ -diethylaminopropylamine raised to 72% and the 60% yield of  $\gamma$ -morpholinopropylamine raised to 70.6%. It was likewise found possible to increase the yield of secondary amine by performing the reduction of the nitrile in the presence of an excess of the primary amine. Thus when an equal molar mixture of  $\gamma$ -diethylaminopropylamine and  $\beta$ -diethylaminopropionitrile was reduced, a 28% yield of the di-( $\gamma$ -diethylaminopropyl)-amine was obtained in contrast to the 13% yield found when the hydrogenation was carried out in the normal manner or the 5% yield obtained when carried out in the presence of ammonia. It is apparent that this reduction may be controlled within limits to produce either a larger or smaller yield of primary or secondary amine depending upon which product is most desired. It is believed that the yields of the primary products can be increased in almost every case if hydrogen pressures of 250 to 300 atmospheres are employed and larger amounts of ammonia introduced. Tables I and II give the nitriles and amines which were prepared along with boiling points, indices, yields, melting points of the picrate derivatives and the observed and calculated neutralization equivalents. All of the propionitriles with the one exception noted were made from acrylonitrile, while all of the butyronitriles were prepared from  $\gamma$ -chlorobutyronitrile. The reductions were all carried out catalytically with approximately 10 g. of Raney nickel per mole of nitrile. All boiling points are within a one degree range and all melting points within a one-half degree range unless otherwise noted.

A representative group of seven sulfanilamide derivatives was prepared from these aliphatic amines by shaking in acetone solution over a saturated potassium carbonate solution with acetylsulfanyl chloride. Because of the strongly basic character of the aliphatic amines, it was impossible to obtain the products by using pyridine or pyridine-acetone as solvents and only red, unworkable solutions resulted in these cases. These sulfanilamide derivatives are given in Table III along with melting points, yields, and the melting points of the acetyl derivatives. Compounds similar to these have been reported by Drozdov<sup>19</sup> and Walker.<sup>20</sup>

### Experimental

**Preparation of  $\beta$ -Aminopropionitriles.**—The addition of secondary amines to acrylonitrile has already been de-

(18) Schwoegler and Adkins, *THIS JOURNAL*, **61**, 3499 (1939).

(19) Drozdov and Starovskaya, *J. Gen. Chem.*, (U. S. S. R.) **9**, 1642-1646 (1939).

(20) Walker, *J. Chem. Soc.*, 686-692 (1940).

scribed in patents<sup>6</sup> and by Holcomb and Hamilton.<sup>6</sup> The general procedure used here is illustrated by the preparation of  $\beta$ -diethylaminopropionitrile. Fractionated acrylonitrile, b. p. 77.2° (732.4 mm.),  $n_D^{20}$  1.3911, 424 g. (8.0 moles) and diethylamine, 1000 g. (13.7 moles) were mixed and warmed at 50° for twenty-four hours and after standing at room temperature for two days, the excess diethylamine was removed at atmospheric pressure and the residue distilled through a modified Claisen flask to give 970 g. of material boiling from 119 to 120° at 70 mm. pressure;  $n_D^{20}$  1.4351 to 1.4353, yield 97%. Another run in which the reactants were mixed in mole to mole ratio, heated on the steam-bath for eight hours, and immediately distilled at atmospheric pressure (b. p. 196-198° at 737 mm.), resulted in a 74% yield. A third experiment in which 355 g. of diethylamine (5 moles) was added to 500 g. of commercial acrylonitrile (9.5 moles) with some cooling over a period of ten minutes and the reaction mixture refluxed for one-half hour, set in the refrigerator overnight and distilled, resulted in a 93% yield of  $\beta$ -diethylaminopropionitrile boiling between 104 and 106° at 35 mm. pressure. This product can be titrated to a sharp end-point with hydrochloric acid using methyl orange as the indicator; equivalent weight calculated, 126.2; found 126.1. It forms a picrate which is readily recrystallized from methanol-acetone mixture and melts sharply at 85°. In general it seems that a better yield results if the reaction is allowed to reach equilibrium at room temperature before the final distillation. For the same reason the product should be distilled more or less rapidly at a low temperature if possible. A slow, careful fractionation through an efficient fractionating column is a distinct disadvantage in the case of the higher dialkylamino derivatives since dissociation into the original reactants results.

**$\beta$ -[Di-( $\gamma$ -diethylaminopropyl)-amino]-propionitrile.**—In a 500-ml. flint glass bottle was mixed 26 g. (0.107 mole) of di-( $\gamma$ -diethylaminopropyl)-amine and 32 g. (0.6 mole) of acrylonitrile along with 0.1 g. of copper bronze. The flask was stoppered and heated at 100° for twenty-four hours, allowed to stand at room temperature for a like period, and distilled to give 24.6 g. (78% yield) of product, b. p. 145° (5 mm.),  $n_D^{20}$  1.3640.

**$\beta$ -( $\gamma$ -Diethylaminopropylamino)-propionitrile.**—This compound was made by two different methods; *i. e.*, by the addition of  $\gamma$ -diethylaminopropylamine to acrylonitrile in 79.4% yield and by the reaction of  $\beta$ -bromopropionitrile<sup>21</sup> with  $\gamma$ -diethylaminopropylamine in 76.4% yield by the same method as described for the preparation of  $\gamma$ -piperidinobutyronitrile.

**$\beta$ -( $\beta$ -Diethylaminoethoxy)-propionitrile.**—To a mixture of 220 g. (1.88 moles) of diethylaminoethanol and 2.3 g. of sodium methoxide in a 1-liter flask equipped with a thermometer, stirrer and dropping funnel was added 100 g. (189 moles) of acrylonitrile over a one-half hour period while the temperature was kept at 25°. The reaction mixture was stirred for a short while longer, allowed to stand overnight, 4.2 ml. of concd. sulfuric acid cautiously added, the solution filtered, and the filtrate distilled to give 260 g. (80% yield); b. p. 140-145° (25 mm.),  $n_D^{20}$  1.4430. With the secondary alcohol, 1-diethylamino-4-pentanol,<sup>11</sup> the reaction did not proceed as rapidly and a yield of only 66% was obtained.

**The Reaction of Ethylamine with Acrylonitrile.**—Acrylonitrile, 106 g. (2 moles), was added to a 70% aqueous solution of ethylamine, 200 g. (3 moles), over a period of two hours while the temperature was kept below 30°. The reaction mixture was stirred at room temperature for five hours and finally heated on the steam-bath for one hour. After the reaction mixture had stood overnight, the water was removed by adding 50 g. of anhydrous potassium carbonate and separating the aqueous layer. The product was purified by distillation to give 176.9 g., b. p. 92-95° (30 mm.),  $n_D^{20}$  1.4318-1.4322; yield 90.4% of  $\beta$ -ethyl-

(21) The  $\beta$ -bromopropionitrile used in this work was obtained in 95.2% yield by bubbling dry hydrogen bromide through acrylonitrile at room temperature according to the method of Moureu, *Chem. Zentr.*, **92**, I, 442 (1921).

TABLE I  
 BASICALLY SUBSTITUTED NITRILES

No.	Nitrile	Yield, %	Properties					Reduction <sup>a</sup> conditions			
			°C. B. p.	Mm.	<i>n</i> <sub>D</sub> <sup>20</sup>	Picrate M. p., °C.	Neut. eq. Calcd. Found	Moles	Temp., °C.	Press., atm.	
1	$\beta$ -Aminopropionitrile <sup>b</sup>	22 <sup>c</sup>	66-69	5	1.4396	178	70.0	70.3	5.0	90	120
2	Di-( $\beta$ -cyanoethyl)-amine <sup>b</sup>	64 <sup>c</sup>	165	4	1.4640	Oil	123.0	123.3			
3	$\beta$ -Diethylaminopropionitrile <sup>d</sup>	95	196	735	1.4356	85	126.2	126.1	6.3	100	83
									1.7	100	85
									4.0	130	85
4	$\beta$ -Ethylaminopropionitrile <sup>d</sup>	90.4	92	30	1.4318	163	98.1	98.1	1.3	115	107
5	Di-( $\beta$ -cyanoethyl)-ethylamine	60	200-202	30	1.4591	170			1.1	116	95
6	$\beta$ -Di- <i>n</i> -propylaminopropionitrile <sup>d</sup>	88	116	20	1.4381	111	154.2	154.3	0.7	95	3
7	$\beta$ -Di- <i>n</i> -butylaminopropionitrile <sup>d</sup>	91	141	20	1.4423	75	182.3	182.5	0.6	95	3
8	$\beta$ -Di- <i>n</i> -amylaminopropionitrile <sup>d</sup>	89	159-161	19	1.4457	Oil					
9	$\beta$ -Di- <i>n</i> -hexylaminopropionitrile <sup>d</sup>	85	145-146	2	1.4483	Oil					
10	$\beta$ -Piperidinopropionitrile	93	129-130	30	1.4697	160	138.2	138.3	1.3	110	117
									8.5	100	120
11	$\beta$ -Morpholinopropionitrile <sup>e</sup>	95	149	20	1.4710	139.5	140.2	140.1	4.8	130	95
									2.7	105	200
									4.0	190	90
12	$\gamma$ -Diethylaminobutyronitrile <sup>f</sup>	86	101-103	21	1.4351	69-70	140.2	140.1	2.3	105	150
13	$\gamma$ -Piperidinobutyronitrile <sup>f</sup>	87	127-129	25	1.4653	117	152.2	151.9	2.7	100	107
14	$\gamma$ -Morpholinobutyronitrile	70	148-150	25	1.4665	152-153	154.2	154.6	1.8	125	80
15	$\beta$ -Diethanolaminopropionitrile <sup>g</sup>					108-109			0.5	105	133
16	Di-( $\beta$ -cyanoethyl)-ethanolamine <sup>g</sup>					137-138					
17	Bis-( $\beta$ -cyanoethyl) ether <sup>h</sup>								0.9	100	240
18	$\beta$ -( $\gamma'$ -Diethylaminopropylamino)-propionitrile	79.4 <sup>m</sup> 76.4 <sup>n</sup>	163-165	25	1.4573	123	91.5	91.5	0.4	120	100
19	$\alpha$ -Diethylamino- $\gamma$ -[di-( $\beta'$ -cyanoethyl)-amino]-propane	8.8	233-235	25	1.4709	166-167	118.1	118.1			
20	$\beta$ -[Di-( $\gamma'$ -diethylaminopropyl)-amino]-propionitrile	70	153	3	1.4640	157-158			1.9	100	250
21	$\beta$ -( $\beta'$ -Morpholinoethylamino)-propionitrile	81.5	183	20	1.4817	176.5			1.5	118	250
22	$\beta$ -( $\gamma'$ -Morpholinopropylamino)-propionitrile	76	178-180	9	1.4819	148-149	98.6	98.1	1.5	105	215
23	$\beta$ -( $\beta'$ -Diethylaminoethoxy)-propionitrile	79.5	145	25	1.4430	75	170.2	169.0	1.5	105	74
24	$\beta$ -( $\gamma'$ -Diethylaminopropoxy)-propionitrile	75.4	148-150	25	1.4440	Oil	184.2	184.1	0.5	105	135
25	$\beta$ -( $\delta'$ -Diethylamino- $\alpha$ -methylbutoxy)-propionitrile	66	125-130	3	1.4456	Oil	211.3	209.3	0.9	103	80
26	$\gamma$ -(Methylphenylamino)-propionitrile	25	175-177	29		118			0.1	103	68
27	N-( $\beta$ -Cyanoethyl)-carbazole <sup>p</sup>	85.4	Solid, m. p. 155.5°						0.9	118	70
28	N-( $\beta$ -Cyanoethyl)-tetrahydroquinoline	75.5	192	10	1.5780	172			0.3	120	90

<sup>a</sup> Approximately 10 g. of Raney nickel catalyst used per mole of nitrile reduced. <sup>b</sup> See ref. 5a. <sup>c</sup> This yield represents only one of two products isolated in the reaction. <sup>d</sup> Mentioned in a paper presented by Dr. M. T. Leffler at the Medicinal Section of the American Chemical Society in Detroit, April 14, 1943. <sup>e</sup> See ref. 6. <sup>f</sup> This compound was only slightly water soluble and a satisfactory end-point could not be obtained by titration. <sup>g</sup> See Burckhalter, Jones, Holcomb and Sweet, THIS JOURNAL, 65, 2012 (1943). <sup>h</sup> Calcd. for C<sub>15</sub>H<sub>26</sub>N<sub>2</sub>: N, 14.0. Found: N, 13.7. <sup>i</sup> Calcd. for C<sub>16</sub>H<sub>24</sub>N<sub>2</sub>: N, 11.7. Found: N, 11.6. <sup>j</sup> See ref. 12. <sup>k</sup> This compound decomposes on distillation at 1 mm. press. into the starting amine and polymerized acrylonitrile. <sup>l</sup> See ref. 10. <sup>m</sup> Synthesized from acrylonitrile and  $\gamma$ -diethylaminopropylamine. <sup>n</sup> Synthesized from  $\beta$ -bromopropionitrile and  $\gamma$ -diethylaminopropylamine. <sup>o</sup> See the experimental for the conditions used in this reaction. <sup>p</sup> See ref. 5b. <sup>q</sup> Does not form a picrate derivative.

aminopropionitrile. Equivalent weight calculated: 98.15, found 98.15. When a 70% ethylamine solution, 130 g. (2 moles), was added to an excess of acrylonitrile, 250 g. (4.7 moles), and the warm mixture heated on the steam-bath for two hours and worked up as indicated above, a 60% yield (180.5 g.) of di-( $\beta$ -cyanoethyl)-ethylamine, b. p. 202-205° (30 mm.), *n*<sub>D</sub><sup>20</sup> 1.4585-1.4591 was obtained.

**The Reaction of Diethanolamine and Acrylonitrile.**— Freshly distilled diethanolamine (52.6 g., 0.5 mole) was mixed with acrylonitrile (160 g., 3 moles) and the heterogeneous mixture shaken until homogeneous. After this reaction mixture had stood at room temperature for eight hours, the excess acrylonitrile was removed under vacuum. The residue (77.5 g.) corresponded to an increase in weight

of 0.47 mole of acrylonitrile. A sample of the reaction product formed a picrate in alcohol which on recrystallization melted at 108-109°. The picrate of diethanolamine is completely soluble in alcohol but when crystallized from ether-alcohol mixture, melts at 108.8-109.0°. A mixture of these two picrates melted, however, at 94-97°. The addition product from the diethanolamine and acrylonitrile was reduced in 100 ml. of ethanol using Raney nickel catalyst and hydrogen at an average pressure of 133 atmospheres and a temperature of 105-110°. Separation by distillation was somewhat difficult because of the viscous nature of the product. Constant-index constant-boiling material 31.4 g., was obtained at 158° (2 mm.) and *n*<sub>D</sub><sup>20</sup> 1.4975 which had an equivalent weight of 84.1 as compared

TABLE II  
 REDUCTION PRODUCTS OF BASICALLY SUBSTITUTED NITRILES

No.	Reduction conditions Time, hr.	Solvent	Products	Yield, %	Properties					
					°C.	B. p. Mm.	$n_D^{20}$	Picrate M. p., °C.	Neut. eq. Calcd.	Found
1	4.0	B	Trimethylenediamine <sup>b</sup>	23 <sup>e</sup>	138	735	1.4600	178	35.0	36.1
3	0.5	A	$\gamma$ -Diethylaminopropylamine <sup>d</sup>	54 <sup>a</sup>	168	735	1.4355	194	65.0	65.3
			Di-( $\gamma$ -diethylaminopropyl)-amine	15 <sup>a</sup>	107	3	1.4541	153-154	81.3	81.0
	6.0	D	$\gamma$ -Diethylaminopropylamine	42 <sup>a</sup>						
			Di-( $\gamma$ -diethylaminopropyl)-amine	29 <sup>a</sup>						
0.8	C	$\gamma$ -Diethylaminopropylamine	72 <sup>a</sup>							
		Di-( $\gamma$ -diethylaminopropyl)-amine	5 <sup>a</sup>							
4	0.2	F	$\gamma$ -Ethylaminopropylamine	74	156	735	1.4441	193	51.1	51.6
5	0.5	D	Di-( $\gamma$ -aminopropyl)-ethylamine	16	135	20	1.4709	197-199	53.1	53.4
6	3.0	A	$\gamma$ -Di- <i>n</i> -propylaminopropylamine <sup>f</sup>	49	94	20	1.4435	181	79.1	80.0
7	3.0	A	$\gamma$ -Di- <i>n</i> -butylaminopropylamine <sup>g</sup>	32	121	20	1.4462	188	93.2	93.7
10	2.5	C	$\gamma$ -Piperidinopropylamine <sup>h</sup>	68.5	205	730	1.4750	209-210	71.1	71.2
			$\gamma$ -Piperidinopropylamine	56.4 <sup>i</sup>						
11	0.5	A	Di-( $\gamma$ -piperidinopropyl)-amine	10 <sup>i,a</sup>	153	2	1.4916	193	89.2	89.7
			$\gamma$ -Morpholinopropylamine <sup>h</sup>	60	219	733	1.4762	166	72.1	72.1
	1.5	H	$\gamma$ -Morpholinopropylamine	70.6						
			Di-( $\gamma$ -morpholinopropyl)-amine	10 <sup>a</sup>	185	5	1.4918	213-215	90.8	90.8
1.1	A	$\gamma$ -Morpholinopropylamine Morpholine	43.5 35							
12	4.5	A	$\delta$ -Diethylaminobutylamine <sup>j</sup>	51	85-88	18	1.4462	155-156	72.2	72.2
13	9.0	A	$\delta$ -Piperidinobutylamine <sup>j</sup>	53.8	118-120	25	1.4756	160.5	78.1	77.9
			Di-( $\delta$ -piperidinobutyl)-amine	32 <sup>a</sup>	220-225	25	1.4898	202-203	98.5	98.1
14	0.7	A	$\delta$ -Morpholinobutylamine	62 <sup>a</sup>	122	20	1.4760	148	79.1	79.3
			Di-( $\delta$ -morpholinobutyl)-amine	23.8	200-202	3	1.4900	136	99.8	100.4
15	1.5	F	$\gamma$ -Diethanolaminopropylamine	40 <sup>i</sup>	158	2	1.4975	157-158	81.1	81.2
17	1.0	F	Bis-( $\gamma$ -aminopropyl)-ether	29	113	32	1.4618	Oil	67.1	66.1
18	0.3	F	$\gamma$ -( $\gamma'$ -Diethylaminopropylamino)-propylamine	51	142-144	25	1.4630	197-198	62.4	62.3
			Di-[ $\gamma$ -( $\gamma'$ -diethylaminopropylamino)-propyl]-amine	31 <sup>a</sup>	253-260	25	1.4710	197	71.8	71.4
20	0.5	E	$\gamma$ -[Di-( $\gamma'$ -diethylaminopropyl)-amino]-propylamine	52	155-165	3	1.4662	162.5	75.1	75.2
21	1.0	H	$\gamma$ -( $\beta'$ -Morpholinoethylamino)-propylamine	57.5	120-123	2	1.4870	208	62.4	62.6
22	2.0	D	$\gamma$ -( $\gamma'$ -Morpholinopropylamino)-propylamine	45.2	137-140	1.5	1.4878	205	67.1	67.0
23	1.0	A	$\gamma$ -( $\beta'$ -Diethylaminoethoxy)-propylamine	56.7	118-122	25	1.4498	Oil	87.1	87.2
			Di-[ $\gamma$ -( $\beta'$ -diethylaminoethoxy)-propyl]-amine	23.8 <sup>a</sup>	175	3	1.4582	Oil	110.5	110.5
24	0.8	A	$\gamma$ -( $\gamma'$ -Diethylaminopropoxy)-propylamine	57.4	130-132	25	1.4500	Oil	94.1	93.6
			Di-[ $\gamma$ -( $\gamma'$ -diethylaminopropoxy)-propyl]-amine	28.2 <sup>a</sup>	182	3	1.4581	Oil	119.8	118.6
25	0.4	A	$\gamma$ -( $\delta'$ -Diethylamino- $\alpha$ -methylbutoxy)-propylamine	50.5	80-83	2	1.4492	88-89	108.1	107.8
			Di-[ $\gamma$ -( $\delta'$ -diethylamino- $\alpha$ -methylbutoxy)-propyl]-amine	23 <sup>a</sup>	210-215	3	1.4580	Oil	138.4	137.9
26	2.0	E	$\gamma$ -(Methylphenylamino)-propylamine	63	171-172	40		189		
27	2.0	G	N-( $\gamma$ -Aminopropyl)-carbazole	70.5	228	3	Solid	206-207		
28	0.7	H	N-( $\gamma$ -Aminopropylamino)-tetrahydroquinoline	82	132-135	3	1.5828			

A, No solvent. B, Liquid ammonia, 69 moles, used as solvent. C, The nitrile was saturated with ammonia at room temperature and approx. 15 atm. press. prior to hydrogenation. D, One mole equivalent of  $\gamma$ -diethylaminopropylamine used as solvent in the reduction. E, Approximately 150 ml. of sat. alc. ammonia solution used as solvent. The reduction was carried out in approx. 100 ml. of abs. alc. G, Reduced in 600 ml. of dioxane. H, Reduced in a solution of 40 ml. of liquid ammonia and 150 ml. of abs. alc. <sup>a</sup> This yield represents only one of two products isolated in the reduction. <sup>b</sup> See Fischer and Kock, *Ber.*, **17**, 1799 (1881). <sup>c</sup> This yield was obtained upon the reaction of a large excess of liquid ammonia with acrylonitrile and the reduction of the reaction mixture in liquid ammonia solvent. <sup>d</sup> See ref. 7. <sup>e</sup> See ref. 6. <sup>f</sup> This compound was only slightly soluble in water and a satisfactory end-point could not be obtained by titration. <sup>g</sup> See Burkhalter, Jones, Holcomb and Sweet, *This Journal*, **65**, 2012 (1943). <sup>h</sup> See ref. 24. <sup>i</sup> Combined yield on the addition and reduction. <sup>j</sup> See ref. 12. <sup>k</sup> Calcd. for the hydrobromide salt, C<sub>16</sub>H<sub>17</sub>N<sub>2</sub>Br, m. p. 120°: Br, 32.7. Found: Br, 32.8. <sup>l</sup> Calcd. for the hydrochloride salt, C<sub>16</sub>H<sub>17</sub>N<sub>2</sub>Cl, m. p. 273°: Cl, 13.6. Found: Cl, 13.6.

to the theoretical value of 81.1. It forms a picrate in alcohol which melts at 156.5-157.5° after recrystallization from acetone-ethyl acetate. When an attempt was made to distill the acrylonitrile diethanolamine addition product, a 67% recovery of material which was identified by its boiling point, picrate derivative, and equivalent weight as diethanolamine was obtained. The major portion of the remaining material was non-distillable residue.

**9-( $\gamma$ -Aminopropyl)-carbazole.**—An intimate mixture of 167 g. of carbazole<sup>22</sup> and 250 ml. of acrylonitrile was cooled

(22) Carbazole "95%" was furnished through the courtesy of Reilly Tar and Chemical Company.

in an ice-bath and then made to react by the addition of 2 cc. of 40% solution of benzyltrimethylammonium hydroxide to the well stirred mixture. Upon the addition of the catalyst a vigorous reaction ensued; the mixture warmed up and the pasty mass partially solidified. The mixture was heated on the steam-bath for one hour and upon cooling a mass of crystals separated from the solution. These were removed by filtration and added to a second crop of crystals obtained by concentrating the mother liquors. The yield was 188 g. (85.4%); m. p. 155.5°. Recrystallization from acetone did not raise the melting point. 9-( $\beta$ -Cianoethyl)-carbazole, 150 g., was reduced catalyti-

cally by dissolving in 600 ml. of warm dioxane, adding 20 g. of Raney nickel and shaking at 118° in the presence of 67 atmospheres pressure of hydrogen for one and one-half hours. The dioxane was removed from the reduction mixture by distillation at atmospheric pressure and the residue distilled to give 107 g. of 9-( $\gamma$ -aminopropylamino)-carbazole, b. p. 228–30° (3 mm.). The first fraction of this material melted at 47° and the last at 48°. The product forms a picrate, m. p. 206–207° after two crystallizations from alcohol, and a hydrochloride, m. p. 273° after recrystallization from 95% ethanol. *Anal.* Calcd. for  $C_{14}H_{17}N_2Cl$ : Cl, 13.59. Found: Cl, 13.62.

**The Reaction of Methylaniline and Acrylonitrile.**—When a mixture of 27 g. of acrylonitrile and 53 g. of methylaniline was sealed in a tube and heated at 180° for four hours and the reaction mixture distilled, all of the methylaniline was recovered unchanged. But when the identical reaction was performed in the presence of 1 g. of hydrated copper sulfate, only 18 g. of the methylaniline was recovered and 20 g. of  $\beta$ -(methylphenyl)-propionitrile, b. p. 175–7° (20 mm.), was obtained. This product is too water insoluble to titrate to a satisfactory end-point. It forms a well-defined picrate melting at 118°. When a mixture of 50 g. of methylaniline, 1 ml. of a 40% solution of benzyltrimethylammonium hydroxide and 100 ml. of dioxane was heated to 90–100° and 25 g. of acrylonitrile added dropwise over a period of one and one-half hours and the solution refluxed for an additional eight hours, no reaction took place and 47 g. of the methylaniline and 22 g. of the acrylonitrile were recovered unchanged.

**The Reaction of Tetrahydroquinoline with Acrylonitrile.**—The heating of a mixture of tetrahydroquinoline and acrylonitrile in the presence of a small amount of copper-bronze, copper sulfate, and sulfuric acid at 160° for four hours gave no appreciable reaction; 81% of the tetrahydroquinoline and 60% of the acrylonitrile were recovered. The remaining material was either very high boiling or a non-distillable residue. A basic catalyst was also found to be inadequate for bringing about the reaction. A mixture of 133 g. of tetrahydroquinoline, 100 ml. of acrylonitrile and 2 ml. of a 40% solution of benzyltrimethylammonium hydroxide was refluxed for ten hours, during which time the temperature of the boiling mixture rose from 88 to 120°. On cooling a polymer separated. The methanol extracts of this reaction mixture gave an 82% recovery of tetrahydroquinoline upon distillation. At the suggestion of Dr. J. B. Dickey, the reaction was carried out in acetic acid. A solution of 133 g. of tetrahydroquinoline and 100 g. of acetic acid was heated to 125° and 100 g. of acrylonitrile dropped in over a period of three hours. After the addition of the first mole, the temperature dropped to 108°. The mixture was heated at reflux for six hours. Neutralization of the reaction mixture with a saturated solution of potassium carbonate in the cold, extraction with 3, 100-ml. portions of chloroform, and distillation of the dried extracts gave 140.4 g. (75.5% yield) of *N*- $\beta$ -cyanoethyltetrahydroquinoline, b. p. 192° (10 mm.),  $n_D^{20}$  1.5780.<sup>23</sup>

**$\gamma$ -Aminobutyronitriles.**— $\gamma$ -Diethylaminobutyronitrile and  $\gamma$ -morpholinobutyronitrile have been prepared by Utermohlen and Hamilton<sup>12</sup> but in only fair yields. The following is an example of the general procedure used in the preparation of these compounds. In a 5-liter flask equipped with stirrer, condenser, and dropping funnel was placed a solution of 600 g. (7 moles) of piperidine in a mixture of 500 ml. of dry benzene and 100 ml. of chloroform. To the refluxing solution was added a total of 310 g. (3 moles) of  $\gamma$ -chlorobutyronitrile<sup>24</sup> over a one-half hour

(23) Dr. J. B. Dickey, private communication, has described a similar experiment using sulfuric acid as solvent and heating on the steam-bath for 65 hours which resulted in a 73% yield of *N*- $\beta$ -cyanoethyl-7-methyltetrahydroquinoline.

(24) This material was the crude  $\gamma$ -chlorobutyronitrile made in 70.4% yield according to a slight modification of the directions of Charles F. H. Allen, "Organic Syntheses," Collected Vol. I, second edition, 1941, p. 156. This product as obtained here is approximately 15%  $\gamma$ -bromobutyronitrile and 85%  $\gamma$ -chlorobutyronitrile. The yield is raised from the reported 40–47% to 68–70% by extract

period. The reaction mixture, after refluxing five hours was then allowed to stand overnight and the crystals of piperidine hydrochloride removed by filtration. These were washed with ether and the ether washings and the benzene-chloroform filtrate containing most of the  $\gamma$ -piperidinobutyronitrile were combined and distilled from a short Vigreux column until the temperature reached 108°. The residue was cooled and a second crop of piperidine hydrochloride collected and washed with ether. The total amount of piperidine hydrochloride was 350 g. or 96% of the theoretical amount. The filtrate and ether washings were combined, the ether removed by distillation and the residue vacuum distilled to obtain 393 g. (86.2% yield) of product, b. p. 129–131° (25 mm.),  $n_D^{20}$  1.4653. In the preparation of  $\gamma$ -diethylaminobutyronitrile,  $\gamma$ -bromobutyronitrile was substituted for the  $\gamma$ -chlorobutyronitrile; yield 86%.

**Reduction of the Nitriles.**—The reduction of basically substituted nitriles has been carried out using sodium and alcohol-toluene by Strukov<sup>13</sup> and Utermohlen and Hamilton,<sup>12</sup> and catalytically by Münch and Schlichting<sup>17</sup> using nickel on Kieselguhr and by Schwoegler and Adkins<sup>14</sup> using Raney nickel. After trying platinum oxide at low pressures and platinum oxide in the presence of acetic anhydride and discarding these methods, the method of Adkins was followed. The general procedure employed is illustrated by the preparation of  $\delta$ -piperidinobutylamine which follows.

**$\delta$ -Piperidinobutylamine.**—In a 1300-ml. capacity Adkins hydrogenation bomb was placed 390 g. of  $\gamma$ -piperidinobutyronitrile and 10 g. of Raney nickel catalyst under 109 atmospheres pressure of hydrogen. The bomb was heated to 100° and shaken for one and one-half hours after which time the absorption of hydrogen had ceased and was approximately 90% of the theoretical. A large amount of ammonia was evolved when the bomb was opened. The reduction mixture was transferred to a modified Claisen flask and distilled to give 215 g. (53.8% yield) of  $\delta$ -piperidinobutylamine; b. p. 120–122° (25 mm.),  $n_D^{20}$  1.4756 and 118.4 g. (31.2% yield) of di-( $\delta$ -piperidinobutyl)-amine; b. p. 195–200° (5 mm.),  $n_D^{20}$  1.4898. The total combined yield was 85%.

**$\gamma$ -Piperidinopropylamine and Di-( $\gamma$ -piperidinopropyl)-amine.**— $\beta$ -Piperidinopropionitrile was prepared by mixing 10 moles each of acrylonitrile and piperidine with cooling and allowing the mixture to stand overnight. This was used in the two subsequent experiments without purification.  $\gamma$ -Piperidinopropionitrile, 1180 g. (8.55 moles), was reduced at 120° and 109 atmospheres pressure in the presence of 60 g. of Raney nickel catalyst. The theoretical amount of hydrogen had been absorbed in thirty-five minutes; the product was fractionated through a 12-plate column to give 543 g. (45% over-all yield) of constant-boiling (203–204°), constant-index ( $n_D^{20}$  1.4750)  $\gamma$ -piperidinopropylamine<sup>25</sup> and 135.5 g. (19% over-all yield) of di-( $\gamma$ -piperidinopropyl)-amine; b. p. 205–207° (17 mm.),  $n_D^{20}$  1.4911–1.4917, picrate m. p. 190–192°. A 200-g. portion of the same crude  $\beta$ -piperidinopropionitrile as used above was reduced in the presence of 20 g. of Raney nickel catalyst after first saturating the nitrile with ammonia (at 8 atmospheres pressure). Hydrogen absorption had ceased after three hours at 1500 lb. per sq. in. pressure and 100° and was approximately 90% of the theoretical. The product was fractionated through a 12-plate column to give 137 g. (66.8% over-all yield) of  $\gamma$ -piperidinopropylamine.

**$\gamma$ -Morpholinopropylamine.**—A mixture of 150 ml. of absolute ethanol, 371 g. of  $\beta$ -morpholinopropionitrile, 50 cc. of liquid ammonia and 25 g. of Raney nickel was reduced by shaking in the presence of 200 to 280 atmospheres pressure of hydrogen at a temperature of 105°. The theoretical amount of hydrogen was absorbed in one and one-half hours. Distillation of the reduction mixture gave 270 g. (70.6% yield) of  $\gamma$ -morpholinopropylamine; b. p.

ing the reaction mixture with four portions of chloroform instead of one as recommended. The crude material is quite satisfactory for this reaction but may readily be separated into its components by fractionation through a 12-plate laboratory column.

(25) Blicke, Parke and Jenner, *THIS JOURNAL*, **62**, 3316 (1940).

129–132° (40 mm.),  $n_D^{20}$  1.4763–1.4769. A higher boiling product, b. p. 185° (5 mm.),  $n_D^{20}$  1.4923–1.4924, proved to be di-( $\gamma$ -morpholinopropyl)-amine; yield 36 g. (10%).

**$\gamma$ -Diethylaminopropylamine.**—In a similar manner 4 moles of  $\beta$ -diethylaminopropionitrile which had been saturated with ammonia at 7 atmospheres pressure (by attaching an ammonia tank to one of the leads of the bomb and shaking it for one-half hour) was reduced to give a 72% yield of  $\gamma$ -diethylaminopropylamine; b. p. 167.5–167.7° (735 mm.),  $n_D^{20}$  1.4419,  $d_4^{20}$  0.8254, picrate m. p. 193.5–194.0°, phenylurea derivative m. p. 66–67°, and phenylthiourea derivative m. p. 116.5–117.0°. The mixed melting point of this last substance with the phenylthiourea derivative obtained from  $\gamma$ -diethylaminopropylamine made by the phthalimide synthesis according to Shriner and Hickey<sup>1</sup> was 116.0–116.5°. Molecular refraction calculated, 41.89; observed, 41.71. The higher boiling fraction, 150–155° (15 mm.), 25 g. (5% yield), is di-( $\gamma$ -diethylaminopropyl)-amine,  $n_D^{20}$  1.4541; equivalent weight calculated, 81.3; found, 81.0; picrate m. p. 153.4°.

**$N^1$ -( $\gamma$ -Morpholinopropyl)-sulfanilamide.**—To a solution of 28.2 g. (0.2 mole) of  $\gamma$ -morpholinopropylamine in 150 cc. of acetone which was contained in a separatory funnel over a solution of 33 g. of potassium carbonate dissolved in 30 cc. of water was added a total of 50 g. (0.21 mole) of *p*-acetylaminobenzenesulfonyl chloride with intermittent shaking over a period of one and one-half hours. Upon completion of the addition, a white crystalline solid separated which was filtered and washed three times with 50-cc. portions of water to remove potassium carbonate and potassium chloride. The filtrate was concentrated to 100 ml. and on cooling a second crop was collected. These crystals were dried and recrystallized from acetone–water mixture to give 62.5 g. of product which melted sharply at 97°; yield 91.5%. The acetyl derivative was hydrolyzed by heating on the steam-bath with 20% hydrochloric acid for three and one-half hours. The cold hydrolysis mixture was carefully neutralized to the equivalence point with sodium hydroxide and cooled in the refrigerator overnight. The crystallized cake was recrystallized from an acetone–water mixture to give a total of 39.8 g. of  $N^1$ -( $\gamma$ -morpholinopropyl)-sulfanilamide, m. p. 47–50°. On recrystallizing from acetone–ether an anhydrous crystalline product, 33.4 g., was obtained which melted at 94.5–95°; yield 70%.

TABLE III  
SULFANILAMIDE DERIVATIVES

$N^1$ -Sulfanilamide	M. p., °C.	Yield, %	Acetyl derivative, m. p., °C.
$\gamma$ -Diethylaminopropyl-	109–110	20	<sup>a</sup>
$\gamma$ -Dipropylaminopropyl-	98–98.5	57	<sup>a</sup>
$\gamma$ -Dibutylaminopropyl- (as hydrochloride)	110–115	53.5	<sup>a</sup>
$\gamma$ -Piperidinopropyl-	105.5–106	63.5	109–111
$\gamma$ -Morpholinopropyl-	94.5–95	79	97–98
Di-( $\gamma$ -diethylaminopropyl)- (as hydrochloride)	195–197	66.5	83–85
Di-( $\gamma$ -piperidinopropyl)-	74–76	71	<sup>a</sup>

<sup>a</sup> The acetyl derivatives were obtained only as thick viscous sirups which would not crystallize and were so hydrolyzed without purification.

### Summary

The reaction of acrylonitrile with ammonia, primary amines, secondary amines, and amino alcohols and the reduction of the resultant beta-substituted propionitriles to the very useful  $\gamma$ -aminopropylamines has been studied. Twenty of these compounds are described.

$\gamma$ -Aminobutyronitriles have been prepared from  $\gamma$ -chlorobutyronitrile and reduced to the corresponding  $\delta$ -aminobutylamines.

The reduction of these basically substituted nitriles not only gives the primary amines but also basically substituted secondary amines in yields of 5 to 30%. Eleven new compounds of this type were isolated.

The procedures described offer a convenient and general method for the synthesis of  $\gamma$ - and  $\delta$ -basically substituted alkylamines in good yields.

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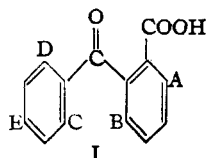
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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE OHIO STATE UNIVERSITY]

## Normal and Pseudo Esters of 2-Benzoylbenzoic Acid Types. II

BY MELVIN S. NEWMAN AND BRADLEY T. LORD<sup>1</sup>

A study of the acid catalyzed esterification of substituted 2-benzoylbenzoic acids was undertaken in order to find out more about the structural features which determine whether normal or pseudo esters will form. In a previous publication<sup>2</sup> we outlined a program for the preparation of all of the substituted 2-benzoylbenzoic acids having one or more methyl groups at positions A, B, C, and D of I.



(1) The material in this paper was taken from the Thesis of B. T. L., presented to the Ohio State University in partial fulfillment of the requirements for the Ph.D. degree, August, 1943.

(2) Newman and McCleary, *This Journal*, **63**, 1537 (1941).

We have modified our program to include methyl groups at E because the compounds containing groups at C and/or D are easier to make if they also have a group at E. The presence of a group at E would not be expected to affect any results greatly.

Furthermore, by having groups at E, the preparation of the required compounds becomes more instructive because it is possible to compare the behavior of substituted phthalic anhydrides in the Friedel–Crafts and Grignard condensations. For example, it is possible to compare the behavior of 3-methylphthalic anhydride with benzene in the Friedel–Crafts reaction and with phenylmagnesium bromide since a mixture of the same keto-acids is obtained in each case.<sup>3</sup> It is not possible to compare these reactions using toluene and *o*-tolylmagnesium bromide because toluene

(3) Newman and McCleary, *ibid.*, **63**, 1542 (1941).