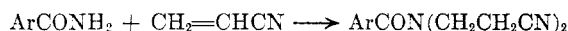


Cyanoethylation of Aromatic Amides¹

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Very little is known concerning the cyanoethylation of aromatic amides.² The one report indicates that benzamide is cyanoethylated to give *N*- β -cyanoethylbenzamide, m.p. 91–93°. In our laboratory eleven different aromatic amides (Table I) were cyanoethylated in the presence of an excess of acrylonitrile and the products uniformly contained two cyanoethyl groups on the amide nitrogen, as shown by the following equation:



This was proved by analysis and by the fact that

N,N-Di- β -cyanoethylnicotinamide. In a three-neck 300-ml. flask equipped with a reflux condenser, a mechanical stirrer, and a separatory funnel, were placed 0.2 mole (24.4 g.) of nicotinamide and 100 ml. of acrylonitrile. This mixture was stirred, and cooled by means of an external cooling bath. Then 2.0 ml. of 40% benzyl trimethylammonium hydroxide (Triton B) was added, dropwise, over a 15-min. period.

After all the base had been added, the cooling bath was removed, and the mixture was allowed to gradually warm. The nicotinamide dissolved with the liberation of heat, which was controlled by external cooling. A precipitate formed, and stirring and cooling were continued for 10 min., and then the reaction mixture was neutralized with glacial acetic acid. The excess acrylonitrile was removed under reduced pressure.

After all the excess acrylonitrile had been removed, the yellow precipitate (33 g.) was separated by filtration. The product was crystallized repeatedly from hot water.

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TABLE I
N,N-Di- β -CYANOETHYL AMIDES

Starting Amide	Empirical Formula	M.P., °C.	Yield, %	% Nitrogen	
				Calcd.	Found
Benzamide	C ₁₃ H ₁₃ N ₃ O	110	77	18.48	18.41
Nicotinamide	C ₁₂ H ₁₂ N ₄ O	104	70	24.54	24.59
Isonicotinamide	C ₁₂ H ₁₂ N ₄ O	108	67	24.54	24.46
<i>o</i> -Toluamide	C ₁₄ H ₁₆ N ₃ O	83	62	17.42	17.42
<i>p</i> -Toluamide	C ₁₄ H ₁₆ N ₃ O	87	65	17.42	17.29
2-Furamide	C ₁₁ H ₁₁ N ₃ O ₂	112	72	19.44	19.45
2-Naphthamide	C ₁₇ H ₁₆ N ₃ O	120	75	15.15	15.31
<i>o</i> -Chlorobenzamide	C ₁₃ H ₁₂ ClN ₃ O	83	70	16.06	16.28
3,4-Dichlorobenzamide	C ₁₃ H ₁₁ Cl ₂ N ₃ O	152	82	14.19	14.33
<i>o</i> -Iodobenzamide	C ₁₃ H ₁₂ IN ₃ O	99	66	11.92	12.17
<i>m</i> -Bromobenzamide	C ₁₃ H ₁₂ BrN ₃ O	83	62	13.73	13.73

the *N,N*-di- β -cyanoethylbenzamide was identical to that produced by the reaction of benzoyl chloride on HN(CH₂CH₂CN)₂.⁴

EXPERIMENTAL⁵

The synthetic method given below is essentially the same for all the aromatic amides, and is based on a method by Galat.⁶

(1) Taken from the M. S. thesis of Miss Romana Jonauskas.

(2) For leading reviews see (a) H. Bruson, *Org. Reactions*, Chapter 2 (1949) and (b) *The Chemistry of Acrylonitrile*, American Cyanamid Co. (1951), N. Y. 20, N. Y.

(3) I. G. Farbenind. A.G. Fr. Patent 877,120 (1942). When the reaction was run with essentially equimolar quantities of benzamide (2 moles) and acrylonitrile (2.26 moles) a 57% yield was obtained. No analytical figures were given. When the reaction was run between one mole of benzamide and 2.26 moles of acrylonitrile an oil was reported, and no physical constants nor analytical data were given.

(4) A. N. Kost, *Uchenye Zapiski Moskov. Gosudarst. Univ. im. M. V. Lomonosova*, No. 2, 141 (1947), *Chem. Abstr.*, 47, 9906 (1953). It is interesting to note that *N*- β -cyanoethylbenzamide was reported by Goldberg and Kelly, *J. Chem. Soc.*, 1369 (1947), to melt at 96–98°, when prepared by the reaction of benzoyl chloride and β -cyanoethylamine. It would appear that the compound reported in reference 3 was a mixture of mono- and dicyanoethylated products.

(5) Microanalyses by Micro-Tech Labs., Skokie, Ill.

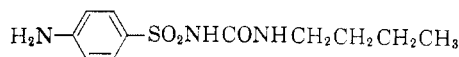
(6) A. Galat, *J. Am. Chem. Soc.*, 67, 1414 (1945).

Sulfonylureas and Related Compounds

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Attempts in this laboratory to prepare hypoglycemic compounds based upon the structure of *N*-sulfanilyl-*N'*-*n*-butylurea, also known as BZ-55 or Carbutamide, have led to a series of new and ac-



tive compounds. Marshall and Sigal¹ have reported upon the variations in the arylsulfonylureas. This note reports the preparation of some alkylsulfonylureas, and other varied compounds based upon the parent structure. The pharmacology² of these compounds will be reported elsewhere in the near future.

(1) F. J. Marshall and M. V. Sigal, Jr., *J. Org. Chem.*, 23, 927 (1958).

(2) The pharmacological testing was performed under the direction of Dr. M. Root.