[CONTRIBUTION FROM THE VENABLE CHEMICAL LABORATORY OF THE UNIVERSITY OF NORTH CAROLINA]

Diamides from Carboxylic Acids and their Nitriles

BY RICHARD H. WILEY AND W. B. GUERRANT

The formation of diamides on heating together an acid and its nitrile was first observed by Gautier[1a] and subsequently extended[1b-h] to a variety of acid–nitrile combinations. These studies, although not defining optimum reaction conditions, established that yields of diamide are increased by the presence of negative substituents on the α-carbon atom. Trichloroacetic acid and nitrile gave a nearly quantitative yield and phenylacetic acid and its nitrile gave "good" yields of diamide. In the present study it has been shown that the phenylacetic acid–nitrile reaction is an equilibrium and that the yield is dependent upon reaction temperature and reaches a maximum of 45%. Also, it has been shown that the reaction of *p*-nitrophenylacetic acid with its nitrile to form the corresponding diamide, a new compound, takes place more rapidly than does the reaction of the unsubstituted phenylacetic type. Considerable decomposition accompanies the reaction of the nitro compounds.

$$RCO_2H + RCN \longrightarrow (RCO)_2NH$$

Experimental

Phenylacetic acid (Eastman Kodak Co.) was recrystallized from petroleum ether and vacuum dried over phosphorus pentoxide. Phenylacetonitrile (E. K. Co.) was redistilled from phosphorus pentoxide and a fraction b. p. 109–111° (4–6 mm.) collected. *p*-Nitrophenylacetic acid (E. K. Co.) was used and *p*-nitrophenylacetonitrile was prepared by nitration of phenylacetonitrile.[2]

The reaction between nitrile and acid was carried out by heating together equimolar amounts of acid and nitrile at the desired temperature. Since slightest exposure of the hot reaction mixture to air caused an immediate discoloration, all operations were conducted under oxygen-free nitrogen. The reaction mixture was sampled at time intervals and the composition of the phenylacetic acid-nitrile samples determined by one of the following methods.

A. The cooled, solidified sample (4–20 g.) was pulverized and thoroughly washed twice with 100 ml. of ether. The residue was dried and weighed as α,α'-diphenyldiacetamide, m. p. 189–191°, reported[1b] m. p. 192°. A typical sample gave the following analysis.

Anal. Calcd. for $C_{16}H_{15}NO_2$: N, 5.53. Found: N, 5.88.

The ether solution was titrated with standard potassium hydroxide to a phenolphthalein end-point and the acidity expressed as yield of phenylacetic acid. With three samples the aqueous alkaline extract of the ether solution was acidified to precipitate phenylacetic acid. A typical sample of acid gave the following analysis.

Anal. Calcd. for $C_8H_8O_2$: neut. equiv., 142. Found: neut. equiv., 136.

The yield of acid isolated in this way was 90% of the amount calculated from the titration. The ether extracts after washing with aqueous alkali were evaporated to dryness and the residue weighed as phenylacetonitrile. A typical sample of nitrile gave the following analysis.

Anal. Calcd. for C_8H_7N: sapon. equiv., 117. Found: sapon. equiv., 119.

The total yield of isolated products in the three fractions accounted for 86–89% of the starting materials. A prepared mixture of the three products was separated by this technique with 95.2% accuracy.

B. This procedure, similar to that used by Colby and Dodge,[1b] was considered less reliable because of possible alcoholysis or hydrolysis of the diamides noted by Konig[1c] with phthalonitrile. A sample of α,α'-diphenyldiacetamide, subjected to this separation procedure, was recovered in 87% yield. The sample was washed with 5% aqueous sodium carbonate, then with 95% ethanol at 0°, and finally recrystallized from 95% ethanol. Prolonged heating in dissolving the diamide was avoided. The yield of diamide was taken as the amount of dried, recrystallized solid.

The composition of the reaction mixture using *p*-nitrophenylacetic acid and its nitrile was determined by the following procedure.

C. The sample was extracted with ether in an Underwriter's extraction apparatus. The extracted residue was α,α'-di-(*p*-nitrophenyl)-diacetamide, m. p. 215–219° dec. Recrystallization from nitrobenzene gave a product m. p. 219–221° dec. in 95% recovery.

Anal. Cacld. for $C_{16}H_{13}N_3O_6$: C, 55.86; H, 3.82; N, 12.24. Found: C, 55.75; H, 3.81; N, 12.38.

The weight of extracted residue was taken as yield of diamide. The extracts were titrated for acidity, which, calculated as *p*-nitrophenylacetic acid, was taken as unreacted acid. The acid isolated was found to be essentially that calculated by titration. The unreacted nitrile was not separated from nitrobenzene solvent left in the neutral residue. The ether insoluble residue obtained in runs made for periods of time much beyond those reported in Fig. 3 was contaminated with a brown impurity which made the estimation of yield of diamide unreliable. Trituration with ether gave similar amounts of extract and was used in most separations in place of the extraction.

The reaction temperature, at first supposed to be of secondary importance, was controlled manually within ±5° for the series reported in Fig. 1. When it became apparent that narrow temperature limits were required, the reaction was carried out in a thermostatically controlled bath at ±2°. The series reported in Figs. 2 and 3 were made thus.

The conversion of α,α'-diphenyldiacetamide to an equilibrium mixture was demonstrated by heating 10 g. of diamide at 200°, for one hour to melt, and then at 190° for eight hours. Separation of the reaction mixture by procedure A gave 35.9% yield of recovered diamide, 29.4% of acid by titration, and 29.9% of nitrile as neutral residue. Both α,α'-diphenyldiacetamide and α,α'-di-(*p*-nitrophenyl)-diacetamide were converted to tars, from which no acid or nitrile was isolated, when heated at 180° for eight to fifteen hours in nitrobenzene.

Discussion

Phenylacetic Acid–Nitrile Reaction.—The data for two series of runs are given in Figs. 1 and 2. The data obtained at 225 and 250° (Fig. 1) show that the reaction produces about 25% of diamide within one to three hours and then on

---

[1] (a) Gautier, *Compt. rend.*, **67**, 1255 (1868); *Ann.*, **150**, 187 (1869); (b) Colby and Dodge, *Am. Chem. J.*, **13**, 1 (1891); (c) Konig, *J. prakt. Chem.*, [2] **69**, 1 (1904); (d) Miller, THIS JOURNAL, **16**, 433 (1894); (e) Seldner, *Am. Chem. J.*, **17**, 532 (1895); (f) Mathews, THIS JOURNAL, **20**, 648 (1898); (g) Hoogewerff and Van Dorp, *Rec. trav. chim.*, **11**, 91 (1892); (h) Liebermann, *Ber.*, **19**, 2281 (1886).

[2] Robertson, "Organic Syntheses," Coll. Vol. I, 2nd ed., John Wiley and Sons, Inc., New York, N. Y., 1941, p. 396.

prolonged heating the yield of diamide drops off presumably due to decomposition since there is considerable discoloration and tar formation. At 200°, the yield of diamide levels off at about 30% and there is no extensive discoloration and tar formation. At 175° (Fig. 1) and at 180 and 190° (Fig. 2) a constant yield of diamide is established at 35–46%. These data indicate the existence of an equilibrium reaction which was established by converting the melted diamide by heating at 190° for nine hours to a mixture similar in composition to that obtained from the nitrile–acid reaction at this temperature.

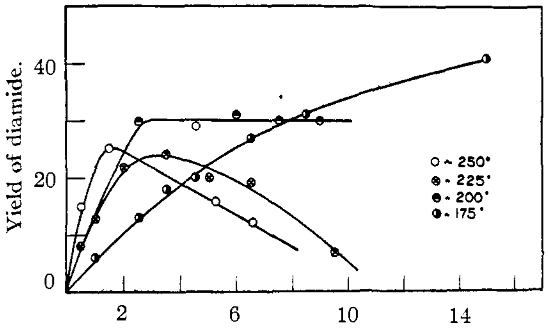

Fig. 1.—Yield of α,α'-diphenyldiacetamide at different temperatures; separation by procedure B.

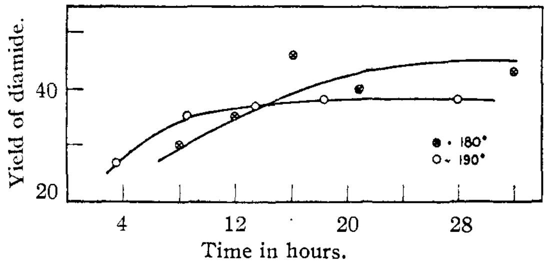

Fig. 2.—Yield of α,α'-diphenyldiacetamide at 180–190°; separation by procedure A.

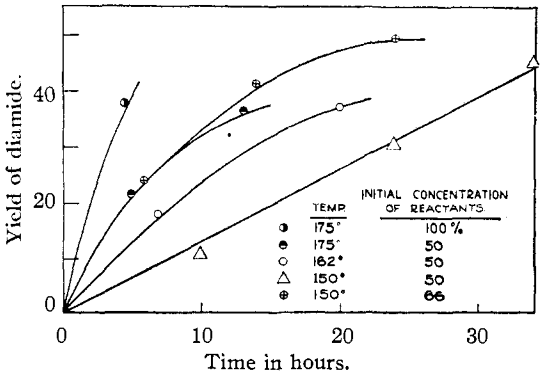

Fig. 3.—Yield of α,α'-di-(p-nitrophenyl)-diacetamide at different temperatures and concentrations.

p-Nitrophenylacetic Acid–Nitrile Reaction.—The data for this series of runs are given in Fig. 3. Extensive decomposition takes place when the reaction is run at 160° or over. At 175° the reaction mixture solidifies after four hours with formation of 38% yield of diamide. A weight of nitrobenzene equal to or one-half that of the combined weight of nitrile and acid was added to the reaction mixture to give 50 and 66% concentration of total reactants and to keep the reaction mixture liquid in the other run. At the 50% concentration, the reaction rate increases as the temperature is raised from 150 to 175° but decomposition becomes extensive. At 66% concentration yields of 50 and 45% diamide are obtained at twenty-four and thirty-six hours, respectively. Under the conditions tried the maximum yield of diamide was 50% obtained at 66% concentration and 150° for twenty-four hours. The presence of an α-p-nitrophenyl group increases the rate of reaction. High yields are not formed presumably because of side reactions caused by the oxidizing action of the nitro groups.

Summary

The reaction between phenylacetic acid and phenylacetonitrile gives an equilibrium mixture containing 35–46% α,α'-diphenyldiacetamide at 180–190°.

The reaction between p-nitrophenylacetic acid and p-nitrophenylacetonitrile gives a 38% yield of α,α'-di-(p-nitrophenyl)-diacetamide in four hours at 175°. With nitrobenzene as a solvent 50% of the diamide is formed at 150° in twenty-four hours.

CHAPEL HILL, N. C. RECEIVED JUNE 28, 1948