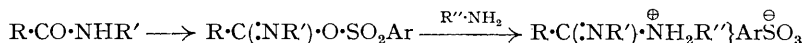


328. Amidines. Part X. Preparation of Amidines from Substituted Amides, a Sulphonyl Chloride, and an Amine.

By P. OXLEY, D. A. PEAK, and W. F. SHORT.

Amidines are prepared by the reaction of amines with imidosulphonates, produced *in situ*, from *N*-monosubstituted amides and sulphonyl chlorides in presence of pyridine.

AMIDINES are obtained in good yield by carrying out the Beckmann rearrangement of ketoxime sulphonates in presence of ammonia or an amine, so that the intermediate imidosulphonate undergoes immediate ammonolysis (Part IX; this vol., p. 1514). If no ammonia or amine is present, the imidosulphonate undergoes further change with production of a sulphonic anhydride and an acylamidine, this transformation being retarded by pyridine. Since *N*-substituted amides are alkylated on nitrogen or on oxygen according to the experimental conditions (Lander, *J.*, 1903, **83**, 766; Grunfeld, *Bull. Soc. chim.*, 1936, **3**, 668), and there is evidence that imido-esters may be formed as intermediates in the production of diacylamines, $(R \cdot CO)_2NR'$, by the acylation of amides (Mumm, Hesse, and Volquartz, *Ber.*, 1915, **48**, 379; cf. Brunner, *Monatsh.*, 1915, **36**, 509), it seemed possible that *N*-substituted imidosulphonates would be formed by the action of sulphonyl chlorides on these amides and could be preserved in presence of pyridine long enough to yield amidines on subsequent addition of amines:



We now report the preparation of a number of *NN'*-disubstituted and -trisubstituted amidines from anilides and other *N*-monosubstituted amides, including 2-ketohexamethyleneimine, by dissolving them in pyridine and adding successively a sulphonyl chloride and an amine. Attempts to prepare *N*-phenylbenzamidine from benzamide, benzenesulphonyl chloride, and aniline were unsuccessful since the imidosulphonate decomposed even at -10° and the sole products were phenyl cyanide and phenylammonium benzenesulphonate.

EXPERIMENTAL.*

NN'-Diphenylformamidine.—Benzenesulphonyl chloride (18 g.; 1.1 mols.) was slowly added at -10° to a solution of formanilide (11.1 g.) in dry pyridine (25 c.c.; 3.4 mols.) and, after a further 40 minutes' stirring at -10° , aniline (10 g.; 1.2 mols.) was gradually added. The cooling bath was removed and when the mixture had warmed to room temperature it was heated on the steam-bath for $\frac{1}{2}$ hour. The semi-solid product was diluted with benzene (50 c.c.) and cooled, and the crystals were filtered off and washed with benzene, giving *NN'*-diphenylformamidinium chloride, m. p. $250-252^\circ$ (18.5 g., 86.5%). Recrystallisation from water (charcoal) afforded colourless prisms of the pure chloride, m. p. $252-254^\circ$ (decomp.). Nef (*Annalen*, 1892, **270**, 297) records m. p. 255° . The amidine salt must be cautiously crystallised from water, otherwise complete hydrolysis occurs. The free base, liberated by means of ammonia, had m. p. 135° . Nef (*loc. cit.*) gives 138° as the m. p. of *NN'*-diphenylformamidine; Dains (*Ber.*, 1902, **35**, 2498) gives 143° .

NN'-Diphenylacetamidine.—A suspension of acetanilide (15 g.) in alcohol-free chloroform (50 c.c.) was added to a solution of benzenesulphonyl chloride (19.6 g.; 1 mol.) in pyridine (15 c.c.; 1.7 mols.) and alcohol-free chloroform (30 c.c.). The temperature rose from 20° to 27° and, after being stirred at room temperature for 3 hours, the red solution was added during 45 minutes at $22-25^\circ$ to a mixture of aniline (10.5 g.; 1.0 mol.), pyridine (5 c.c.; 0.6 mol.), and chloroform (10 c.c.). The resulting solution was washed with aqueous sodium carbonate, dried ($MgSO_4$), evaporated to dryness in a vacuum, and the residue dissolved in cold alcohol (25 c.c.). The crystals which separated on adding water (25 c.c.) were collected, washed with aqueous alcohol (1 : 1), and dried, giving 15.2 g. of crude amidine, m. p. $115-123^\circ$. When the filtrate was acidified with dilute hydrochloric acid, acetanilide (2.5 g.) was recovered, and addition of ammonia to the acid filtrate gave a further precipitate of amidine, bringing the total yield to 69.5%. Recrystallisation from aqueous alcohol raised the m. p. of the amidine to $130-131^\circ$ (see Part IX, *loc. cit.*) and the picrate had m. p. $168-169^\circ$. Von Pechmann (*Ber.*, 1897, **30**, 2792, 2879) records m. p. 169° for the picrate, and Oxley and Short (*J.*, 1947, 384) give m. p. 171° .

NN'-Diphenylbenzamidine.—There was no reaction below 50° when benzenesulphonyl chloride (9 g.; 1 mol.) was added to a solution of benzanilide (9.85 g.) in dry pyridine (12 c.c.; 3 mols.). The

* See also B.P. 577,478.

mixture was heated on the steam-bath for 90 minutes, and aniline (9 g.; 1.9 mols.) was then added to the hot solution and the mixture heated on the steam-bath for a further 90 minutes. The crystals which separated on cooling were washed with a little pyridine and consisted of *NN'*-diphenylbenzamidinium chloride, m. p. 300° (8.3 g., 54%). Sach and Bry (*Ber.*, 1901, **34**, 118) record m. p. 286° (decomp.) and Busch and Falco (*ibid.*, 1910, **43**, 2557) give m. p. 299° (decomp.). The free base had m. p. 146.5—147°, undepressed on admixture with an authentic specimen (Part I, *J.*, 1946, 147). Addition of water to the filtrate afforded recovered benzanilide, m. p. and mixed m. p. 160—163° (3.8 g., 39%), and an oil, which was probably the pyridine salt of benzenesulphonanilide, since this anilide, m. p. and mixed m. p. 107—108° (4.5 g., 39%), was obtained when it was shaken with dilute hydrochloric acid.

N-Phenyl-N'-methylbenzamidine.—Toluene-*p*-sulphonyl chloride (9.6 g.; 1 mol.) was added to a solution of benzamide (6.8 g.) in dry pyridine (10 c.c.; 2.5 mols.), and, after this had been heated on the steam-bath for 2 hours, aniline (5 g.; 1.1 mols.) was added, after cooling slightly. The mixture was then heated on the steam-bath for a further 1½ hours, cooled, diluted with alcohol (50 c.c.), and filtered from an insoluble gum containing a few crystals. The filtrate was made alkaline with 5*N*-sodium hydroxide to liberate the crude amidine, m. p. 133—134° (6.35 g., 60%), which was collected and recrystallised from 50% aqueous alcohol, giving *N-phenyl-N'-methylbenzamidine*, m. p. 134.4—134.8°. Pyma (*J.*, 1923, **123**, 3366) records m. p. 135° (corr.).

N-Methyl-N'-n-amybenzamidine.—Benzamide (13.6 g.), pyridine (10 c.c.), benzene (50 c.c.) toluene-*p*-sulphonyl chloride (19.2 g.; 1 mol.), and *n*-amylamine (8.7 g.; 1 mol.) were brought into reaction as described in the last example, and the cold reaction product was poured into aqueous sodium hydroxide at 0°. The oil was collected (5.6 g.) and distilled under diminished pressure, and the fraction (5 g.), b. p. 125—128°/1.5 mm., was triturated with benzene-light petroleum and filtered. The solid consisted of unchanged benzamide (3 g.), and the evaporated filtrate afforded a picrate, m. p. 108—109°, which with alkali gave *N-methyl-N'-n-amybenzamidine* (2 g., 9.7%), m. p. 40°. There was no depression in m. p. when the amidine and its picrate were mixed with authentic specimens prepared as described in Part III (*J.*, 1947, 384).

2-Anilohexamethyleneimine.—The temperature rose to 28° when benzenesulphonyl chloride (9 g., 1 mol.) was added to a stirred solution of 2-ketohexamethyleneimine (5.7 g.) in dry pyridine (5 c.c.; 1.2 mols.) and benzene (20 c.c.). After the mixture had been stirred for another hour, addition of aniline (5 g.; 1.1 mols.) raised the temperature to 53°. The red solution was cooled and stirred at room temperature for 1½ hours during which an oil separated. The product was diluted with water (25 c.c.) and the aqueous layer was separated and made alkaline with sodium hydroxide solution. The 2-anilohexamethyleneimine, m. p. 95—100° (4 g., 42%), was collected and recrystallised from benzene, giving the pure compound, m. p. and mixed m. p. 105° (Part IX, *loc. cit.*).

NNN'-Trimethylacetamidine (Experiment by DR. P. T. CHARLTON).—Benzenesulphonyl chloride (17.65 g.; 1 mol.) was added during 15 minutes at 4° to a solution of acetomethylamide (7.3 g.) in a mixture of dry chloroform (80 c.c.) and pyridine (10 g.). The solution was stirred for 6 hours and a solution of dimethylamine (4.1 g.; 1 mol.) in chloroform was then added, stirring was continued for 12 hours, and the mixture was boiled under reflux for 2 hours. The dark solution was extracted with excess of dilute aqueous sodium hydroxide and the alkaline solution was extracted with chloroform. Evaporation of the chloroform solution afforded benzenesulphondimethylamide (7%), m. p. and mixed m. p. 47—48° (Found: N, 7.6. Calc. for C₈H₁₁O₂NS: N, 7.6%). The alkaline solution was acidified with hydrochloric acid, evaporated to dryness under diminished pressure, and the residue extracted with ethanol. The alcohol was removed and the residue recrystallised from acetone to give *NNN'-trimethylacetamidinium benzenesulphonate* as hygroscopic plates, m. p. 117—118° (Found: N, 10.7; S, 12.3. C₁₁H₁₈O₃N₃S requires N, 10.85; S, 12.4%); yield, 8.5%. The *picrate*, prepared from the benzenesulphonate and saturated aqueous lithium picrate, separated from ethanol in yellow prisms, m. p. 96° (Found: N, 21.25. C₁₁H₁₅O₇N₅ requires N, 21.3%).

RESEARCH LABORATORIES, MESSRS. BOOTS PURE DRUG CO. LTD.,
NOTTINGHAM.

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