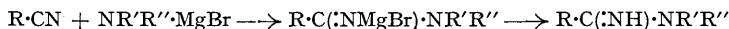


79. *Amidines. Part V. Preparation of Amidines from Cyanides and Substituted Aminomagnesium Halides.*

By R. P. HULLIN, J. MILLER, and W. F. SHORT.

Amidines are formed by decomposition of the complexes produced from alkyl or aryl cyanides and aminomagnesium halides, $\text{NRR}'\cdot\text{MgHal}$. When $\text{R} = \text{R}' = \text{H}$, the yields are very small, and no reaction occurs when $\text{R} = \text{R}' = \text{Ar}$. The reaction also fails with benzyl cyanide which is converted into a dimeride.

ODDO and CALDERARO (*Gazzetta*, 1923, **53**, 64) state that phenyl cyanide and aminomagnesium bromide combine in presence of ether to give an addition compound from which the cyanide is regenerated by the action of water. We find that, in anisole, phenyl cyanide and aminomagnesium iodide afford a small yield of benzamidine and that moderately good yields of substituted amidines may be obtained by the interaction between alkyl or aryl cyanides and diethylaminomagnesium bromide, benzylaminomagnesium bromide, methylanilinomagnesium bromide, or anilinomagnesium bromide in ethereal solution :



No amidine could be obtained from diphenylaminomagnesium bromide and either phenyl cyanide or *p*-cyanophenyl methyl sulphone even in anisole at 100°. Benzyl cyanide is largely converted into β -imino- α -cyano- $\alpha\gamma$ -diphenylpropane by either diethylaminomagnesium bromide or methylanilinomagnesium bromide and no amidine is formed. This dimeride was isolated by Rondou (*Bull. Soc. chim. Belg.*, 1922, **31**, 239) from the mixture obtained from benzyl cyanide and methylmagnesium bromide and is probably formed by addition of benzyl cyanide to its magnesium derivative :



Diethylcyanamide and diethylaminomagnesium bromide afford *s*-tetraethylguanidine in 58% yield.

EXPERIMENTAL.*

Benzamidine.—Ethylmagnesium iodide (from ethyl iodide, 31.2 g.; magnesium, 4.8 g.; and ether 60 c.c.) was added to a 0.4*N*-solution of ammonia in ether (500 c.c.). When the evolution of ethane had ceased, anisole (100 c.c.) was added, and the ether was removed from the suspension of aminomagnesium iodide by distillation. After addition of phenyl cyanide (20.6 g.), the mixture was stirred at room temperature for 48 hours and then poured into 5*N*-hydrochloric acid (100 c.c.) and ice (300 g.). The aqueous solution was extracted with ether, and phenyl cyanide (12 g.) was recovered from the united ethereal and anisole solutions. The acid solution was made alkaline with 5*N*-sodium hydroxide (200 c.c.), and the precipitated magnesium hydroxide was removed, washed with chloroform, and the solution added to a chloroform extract of the filtrate. The residue obtained by evaporating the chloroform solution afforded benzamidinium picrate (1.2 g.), m. p. and mixed m. p. 239—241°, with alcoholic picric acid.

N-Benzylbenzamidine.—A solution of benzylamine (21.4 g.) in ether (60 c.c.) was added to ethylmagnesium bromide (from ethyl bromide, 24.2 g.; magnesium, 4.8 g.; and ether, 90 c.c.) and, after boiling for 10 minutes, the mixture was cooled. An exothermic reaction occurred when a solution of phenyl cyanide (20.6 g.) in dry ether (60 c.c.) was added, and an oil separated. The mixture was stirred with ice and hydrochloric acid, and the benzylbenzamidine chloride, m. p. 227—229°, which separated was collected. Pyman (*J.*, 1923, **123**, 3373) records m. p. 227—229° (corr.). The filtrate was made alkaline, filtered from magnesium hydroxide, and extracted with chloroform. Distillation of the chloroform extract (14 g.) afforded benzylamine, b. p. 66—68°/1 mm. (4 g.), and a semi-solid residue of amidine (10 g. or 24%) which gave a picrate, m. p. 169—170° (Found: N, 15.85. Calc. for C₂₀H₁₇O₇N₅: N, 15.9%). Pyman (*loc. cit.*) states that *N*-benzylbenzamidine has m. p. 77—78° and affords a picrate, m. p. 169—170°.

*NN-Diethyl-*n*-valeramidine*.—A solution of diethylamine (14.6 g.) in dry ether (50 c.c.) was added with stirring to ethylmagnesium bromide (from ethyl bromide, 24.2 g.; magnesium 4.6 g.; and ether, 90 c.c.) and the mixture was boiled until no more ethane was evolved. A solution of *n*-butyl cyanide (16.6 g.) in ether (60 c.c.) was added, and the mixture was boiled for 30 mins., cooled, and poured with stirring into saturated ethereal hydrogen chloride (200 c.c.). Cold water was then added and the aqueous solution was removed, cooled in ice, and made alkaline with 5*N*-sodium hydroxide. The magnesium hydroxide was washed with chloroform and the filtrate was extracted with the same solvent. The chloroform solution afforded *NN*-diethyl-*n*-valeramidine, b. p. 60°/1 mm. (8 g. or 26%), which was characterised as the picrate, m. p. 93° (Found: N, 17.8. C₁₅H₂₃O₇N₅ requires N, 18.2%).

NN-Diethylbenzamidine.—This amidine, b. p. 95°/2 mm., was prepared in 58% yield in the same way from phenyl cyanide and diethylaminomagnesium bromide in dry ether. The picrate, m. p. 161°, did not depress the m. p. of an authentic specimen prepared by Mr. P. Oxley by a different method.

*N-Phenyl-*N*-methylbenzamidine*.—Methylanilinomagnesium iodide was prepared by adding methylaniline (21.4 g.) in ether (60 c.c.) to an ethereal solution of ethylmagnesium iodide (1 mol.) and boiling for 15 mins. to complete the reaction. A solution of phenyl cyanide (20.6 g.) in ether (60 c.c.) was then added slowly, with subsequent stirring at room temperature for 2 hrs. The complex was decomposed in the usual way, and the amidine collected in chloroform and crystallised from light petroleum. The *N*-phenyl-*N*-methylbenzamidine (11.5 g. or 25%) so obtained had m. p. 85° (Found: N, 13.2. Calc. for C₁₄H₁₄N₂: N, 13.3%) in agreement with v. Pechmann (*Ber.*, 1897, **30**, 1782). The picrate had m. p. 186—188° (Found: N, 15.7. Calc. for C₂₀H₁₇O₇N₅: N, 15.9%); v. Pechmann (*loc. cit.*) records m. p. 184°.

*N-Phenyl-*p*-methoxybenzamidine*.—A solution of *p*-methoxyphenyl cyanide (13.5 g.) in ether (150 c.c.) was slowly added at room temperature to anilinomagnesium bromide, prepared in the usual way from ethyl bromide (10.9 g.), magnesium (2.3 g.), aniline (9.3 g.), and ether (90 c.c.). After being stirred

* See also B.P. Appln. 23,412/11.9.1945.

for 2 hrs., the mixture was added to 5*N*-hydrochloric acid (50 c.c.) and ice (150 g.), and the solid was crystallised from acetone-alcohol, giving *N*-phenyl-*p*-methoxybenzamidinium chloride, m. p. 224—225° (Found: N, 10.7. $C_{14}H_{16}O_2N_2Cl$ requires N, 10.7%). The yield was 25%, and 8.4 g. of the cyanide were recovered from the ethereal solution. *N*-Phenyl-*p*-methoxybenzamidine, liberated from the chloride by cold aqueous sodium hydroxide, crystallised from isopropanol in plates, m. p. 147—149° (Found: N, 12.6. $C_{14}H_{14}O_2N_2$ requires N, 12.4%).

s-Tetraethylguanidine.—Diethylaminomagnesium bromide was prepared from diethylamine (10.3 g.) in the usual way, a solution of diethylcyanamide (9.8 g.; McKee, *Amer. Chem. J.*, 1906, **36**, 210) in ether (100 c.c.) was added with cooling, and stirring was continued for $\frac{3}{4}$ hr. The mixture of ether and thin oil was decomposed with ice and concentrated hydrochloric acid (20 c.c.), and the aqueous layer was extracted with ether and made alkaline to Titan-yellow with 5*N*-sodium hydroxide. Magnesium hydroxide was removed and the filtrate shaken with chloroform (2 × 100 c.c.) which extracted *s*-tetraethylguanidine, b. p. 71°/2 mm. (10 g., 58%). Lecher and Demmler (*Z. physiol. Chem.*, 1927, **167**, 175) state that *s*-tetraethylguanidine has b. p. 83.5°/10 mm. The picrate, m. p. 85°, was prepared from the base and alcoholic picric acid (Found: N, 20.8. $C_{16}H_{24}O_7N_6$ requires N, 21.0%). Lecher and Demmler (*loc. cit.*) obtained an oily picrate.

β -Imino- α -cyano- $\alpha\gamma$ -diphenylpropane.—Methylanilinomagnesium bromide and benzyl cyanide (1 mol.) were brought into reaction in ether and the product was decomposed with cold dilute acid in the usual way. The ethereal solution contained unchanged benzyl cyanide, b. p. 62°/2 mm. (13%), and a viscous oil, b. p. 206°/1 mm. (81%), which set to a resin on cooling (Found: N, 11.8. Calc. for C_8H_7N : N, 11.9%). The b. p. of this product agrees with that of the dimeride of benzyl cyanide obtained by Meyer (*J. pr. Chem.*, 1895, **52**, 114; 1908, **78**, 497) and shown by Atkinson and Thorpe (*J.*, 1906, **89**, 1934) and Lees and Thorpe (*J.*, 1907, **91**, 1287) to be β -imino- α -cyano- $\alpha\gamma$ -diphenylpropane. Rondou (*loc. cit.*) obtained this dimeride in solid form, m. p. 114.5—115°. Similarly, benzyl cyanide and diethylaminomagnesium bromide afforded 75% of the dimeride and 21% of recovered cyanide.

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

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