199. *A New Synthesis of* NN′-*Diarylformamidines.*

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A new synthesis of *NN′*-diarylformamidines is described. The method enables the facile detection of formic acid in admixture with other monobasic aliphatic acids.

The chief methods described for the preparation of *NN′*-diarylformamidines are interaction of: (*a*) a primary aromatic amine with orthoformic ester (Claisen, *Annalen*, 1896, **287**, 366; v. Walther, *J. pr. Chem.*, 1886, **53**, 474); (*b*) an acid chloride with a mixture of a primary aromatic amine and the formanilide; (*c*) the complex 3HCl,2HCN (Gattermann, *Ber.*, 1883, **16**, 310) with primary aromatic amines (Dains, *Ber.*, 1902, **35**, 2496); (*d*) an arylamine with formic acid, heated under reflux with a catalyst such as boric acid plus iron filings (I.C.I., B.P. 353,138). The last is less well known.

The recent work of Lewis, Krupp, Tieckelmann, and Post (*J. Org. Chem.*, 1947, **12**, 303) throws considerable doubt upon the validity of procedure (*a*). These authors have shown that aniline and the three monochloroanilines react with orthoformic ester to produce compounds of the type $CH(NHR)_3$, and not amidines. Confusion between amidines and triarylaminomethanes has arisen owing to the close proximity of the melting points and nitrogen contents of the two series of compounds. The publication of Lewis *et al.* (*loc. cit.*) would thus appear to cast doubt upon the authenticity of other compounds prepared by method (*a*) and previously cited as formamidines. The values for the chlorine content of the compounds prepared by the present author indicate conclusively that they are amidine hydrochlorides and not mono- or di-hydrochlorides of the triarylaminomethanes.

The new method of preparation now to be described was discovered in the course of another investigation where it was necessary to detect small quantities of formic acid in admixture with other aliphatic monobasic acids, and is now published on account of its simplicity and the growing interest in *NN′*-diarylformamidines as synthetical intermediates (cf. Grothaus and Dains, *J. Amer. Chem. Soc.*, 1936, **58**, 1334; Meyer and Wagner, *J. Org. Chem.*, 1943, **8**, 239). The process can be used for the detection of formic acid as above because all other monobasic aliphatic acids, as well as dibasic aliphatic acids and the aromatic acids, react to form only the corresponding *N*-substituted amide.

According to the present method, *NN′*-diarylformamidines are prepared by refluxing an anhydrous mixture of a primary aromatic amine, its hydrochloride, and sodium formate. Reaction is complete in 10—15 minutes. The method, which has been applied to the preparation of several formamidine hydrochlorides, fails with benzidine and strongly negatively substituted bases such as the nitroanilines (cf. Dains, *loc. cit.*). Where other conditions are normally favourable, reaction proceeds slowly, if at all, in the absence of hydrogen chloride (cf. Hübner *et al.*, *Ber.*, 1877, **10**, 1720, 2165; Friedmann and Backeberg, *J.*, 1938, 469).

EXPERIMENTAL.

General Method for Preparation of NN′-*Diarylformamidines.*—Finely powdered anhydrous sodium formate is mixed with an equal weight of amine hydrochloride and five times the weight of amine. The mixture is heated under reflux for 15 minutes, although reaction is probably completed in 5 minutes. The cooled reaction mixture is acidified with 2N-hydrochloric acid (15 vols.), and the *NN′*-diarylformamidine hydrochloride separates as a crystalline mass. The product may be collected and recrystallised, in many cases from dilute hydrochloric acid, although this is not always possible, or it may be converted into the free base by any of the usual methods.

It will be noted that the efficacy of the method is largely dependent upon two requirements: (*a*) that the hydrochloride of the amidine should be much less soluble in dilute hydrochloric acid than the hydrochloride of the amine itself, and (*b*) that the m. p. of the amine should be low enough to allow it to function as the solvent for the reaction. Both these requirements are met by the majority of the common aromatic primary amines.

The yield of formamidine hydrochloride is at least 40% (as with aniline and *m*-xylidine), but often as high as 80—90% (as with *p*-toluidine); in general, the yields are nearer the higher limit than the lower one.

All m. p.s were determined in sealed tubes, but they are of doubtful value. They appear to be reproducible with difficulty, owing to dependence upon the rate of heating and the sublimation of several of the products.

NN′-Diphenylformamidine hydrochloride was obtained in colourless needles, m. p. 251° (decomp.), from dilute aqueous hydrochloric acid, or in platelets, m. p. 251° (decomp.), from ethyl acetate containing a trace of hydrogen chloride [Found: N, 12·1; Cl, 15·2. Calc. for $C_{13}H_{12}N_2,HCl$: N, 12·1; Cl, 15·3%. Calc. for $CH(NHPh)_3,HCl$: N, 12·9; Cl, 10·8%. Calc. for $CH(NHPh)_3,2HCl$: N, 11·3; Cl, 19·3%]. Nef (*Annalen*, 1892, **270**, 297) records m. p. 255° for $C_{13}H_{12}N_2,HCl,3H_2O$, and Friedmann and Backeberg (*loc. cit.*), using method (*b*), record m. p. 259°.

NN′-*Di*-(o-*tolyl*)*formamidine hydrochloride* was obtained in colourless needles, m. p. 205° (decomp.), after crystallisation from dilute aqueous hydrochloric acid (Found: N, 10·2; Cl, 13·5. $C_{15}H_{16}N_2,HCl$ requires N, 10·8; Cl, 13·5%). The *m*-tolyl salt crystallised in colourless needles, m. p. 214° (decomp.), from dilute aqueous hydrochloric acid (Found: N, 10·5; Cl, 13·80%). Von Niementowski (*Ber.*, 1887, **20**, 1893) records m. p. 214° (decomp.) for a specimen prepared by prolonged boiling of the formyl derivative of *m*-toluidine.

NN′-*Di*-(p-*tolyl*)*formamidine hydrochloride* crystallises in colourless needles, m. p. 228—230° (decomp.), from a large volume of very dilute aqueous hydrochloric acid (Found: N, 10·1; Cl, 12·5%). Senier (*Ber.*, 1885, **18**, 2296) records the preparation of this compound but no m. p. or analysis.

NN′-Di-(*m*-xylyl)formamidine hydrochloride crystallises in colourless needles, m. p. 236° with decomposition and sublimation, from dilute aqueous hydrochloric acid (Found: N, 9·4; Cl, 11·9. Calc. for $C_{17}H_{20}N_2,HCl$: N, 9·7; Cl, 12·3%). Dains (*loc. cit.*), using method (*c*), records m. p. 243° (decomp.).

NN′-*Di*-(o-*chlorophenyl*)*formamidine hydrochloride* crystallises in large, colourless, square-ended prisms, subliming at about 250°, from dilute aqueous hydrochloric acid (Found: N, 9·0; Cl, 36·4. $C_{13}H_{10}N_2Cl_2,HCl$ requires N, 9·3; Cl, 35·5%). The m-*chlorophenyl* salt was obtained in buff-coloured needles, m. p. 298° (decomp.), insoluble in very dilute hydrochloric acid and purified by extraction with hot dilute hydrochloric acid (Found: N, 9·1; Cl, 34·0%).

NN′-Di-(ψ-cumyl)formamidine hydrochloride crystallised in colourless needles, m. p. 236° (decomp.), from aqueous hydrochloric acid. Dains (*loc. cit.*), using method (*c*), records m. p. 236° (decomp.) (Found: N, 9·1; Cl, 10·9. Calc. for $C_{19}H_{24}N_2,HCl$: N, 8·9; Cl, 11·2%).

Detection of Formic Acid in Admixture with Other Aliphatic Monobasic Acids.—Prepared from the acids, the well-powdered sodium salts (1 part) are mixed with aniline hydrochloride (5 parts) and freshly distilled aniline (10 parts) and heated under refluxed for 15 minutes. After cooling, the darkened solution is acidified with 2N-hydrochloric acid (100 parts). *NN′*-Diphenylformamidine hydrochloride crystallises out immediately or on cooling, and after standing for 5 minutes is removed by filtration, and washed with a very small quantity of 2N-hydrochloric acid. The product may be further purified by recrystallisation from dilute aqueous hydrochloric acid.

The anilides of higher aliphatic acids may separate out from the filtrate on standing, but more usually have to be removed by ether extraction, followed by purification in the normal way.

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