

Dialkylamino-aminations with Dialkylformamides

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THE reported¹ failure to obtain 8-amino-6-methoxy-4-(4-diethylamino-1-methylbutylamine)quinoline by heating 4-diethylamino-3-methylbutylamine ("Noval diamine") with 8-amino-4-chloro-6-methoxyquinoline in the absence of solvent prompted us to repeat the reaction in refluxing dimethylformamide, in view of the remarkable rate enhancements shown when nucleophilic displacement reactions are conducted in this solvent.² The product (65%) was shown by analysis, n.m.r., and mass spectrometry to be 8-amino-4-dimethylamino-6-methoxyquinoline.

The use of dimethylformamide to replace active halogen atoms by dimethylamino-groups is well known (e.g. the chlorine atom in benzoyl chloride,³ in nitro-substituted chlorobenzenes,^{4,5} in 2-chlorobenzothiazole,⁶ and in 2-chlorobenzimidazole⁷), however, the extension of this application to the simple halogeno-pyridines and -quinolines to give alkyl-aminated heterocycles has not been reported.

The Table lists the yields of dialkylamino-substituted heterocycles obtained when the corresponding chloro-compound (1 g.) was refluxed in alkylformamide (15 ml.) for 12 hr. The products, contaminated with dimethylamine hydrochloride, are obtained as hydrochloride salts on removal of the excess of dimethylformamide under reduced pressure. Dissolution of the hydrochloride in sodium hydrogen carbonate solution, followed by ether extraction and distillation or recrystallisation gave the base. Thus the compounds are synthesised under anhydrous conditions without the use of elevated pressures required when dialkylamines are treated with the same halogeno-compounds.⁸ Further, the reaction shows that side reactions involving dimethylformamide may occur whenever this material is used as the solvent in displacement reactions which involve heterocycles containing reactive halogen atoms.

TABLE

Heterocyclic halide	Dialkylformamide	Product ^a	Yield	b.p.(°c/mm.) or (m.p.)	
8-Amino-4-chloro-6-methoxyquinoline	DMF	8-Amino-6-methoxy-4-dimethylaminoquinoline	65%	(65—66)	
2-Chloroquinoline	DMF	2-Dimethylaminoquinoline	76%	(70—71)	lit., ⁸ 70.5—71
2-Chloroquinoline	DEF ^b	2-Diethylaminoquinoline	77%	129—30/2.5	lit., ⁸ 154—155/4.0
4,7-Dichloroquinoline	DMF	7-Chloro-4-dimethylaminoquinoline	84%	128—129/0.35	
2-Chloro-5-nitropyridine	DMF	2-Dimethylamino-5-nitropyridine	94%	(153—154)	lit., ⁹ 154—155°

^a Satisfactory analyses were obtained for all new compounds;

^b DEF = diethylformamide.

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