Cleavage of Amides with Methanolic Boron Trifluoride

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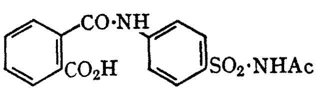
Summary Amides are cleaved by methanolic boron trifluoride to the volatile methyl esters, which are suitable for gas chromatography.

ATTEMPTED methylation of the carboxy-group of *o*-(*p*-*N*-acetylsulphamoylphenylcarbamoyl)benzoic acid (I) with refluxing methanolic boron trifluoride gave cleavage of the amide bond. Gas chromatography showed that dimethyl phthalate had been formed.

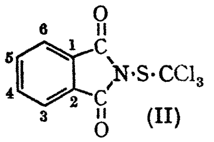
This presented a possible method of analysing amides, some of which are nonvolatile and unsuitable for gas chromatography, by converting the acid portion to the methyl ester, which could then be analysed by g.l.c.

Since refluxing methanolic boron trifluoride was found to be insufficiently vigorous to give good yields of the esters the reaction was carried out in sealed tubes at 105° and 130° for periods of 3 or 16 hr. (Table). The gas formed in these reactions was identified (i.r.[1]) as dimethyl ether. Although some alcohols are dehydrated to olefins by boron trifluoride under mild conditions[2] the dehydration of methanol to dimethyl ether has not been reported.

Quantitative conversion into the methyl esters was achieved for benzamide, benzanilide, 2,2-dichloropropionamide, and *N*-*p*-chlorophenyl-*N'*-dimethylurea (IV).

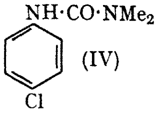


(I)

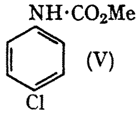


(II)

(III)1,2,3,6-tetrahydro-



(IV)



(V)

Percentage yields of methyl esters in the reactions at 130° for 16 hr. were lower than those at the shorter time. This shows that under these vigorous conditions the methyl esters themselves were decomposed.

Compound (IV) gave the ester (VI) in high yield which reacted further (VI) to give 4-chloroaniline. Reaction of urea with boron trifluoride and an alcohol has been said to give the carbonate ester;[3] dimethyl carbonate, however, was found to decompose under these conditions.

Ester products and yields

		% Yield			
		105°		130°	
Reactant	Ester product	3 hr.	16 hr.	3 hr.	16 hr.
(I)	Dimethyl phthalate	50	89	82	73
(II)	„ *	39	94	87	86
(III)	Dimethyl 1,2,3,6-tetrahydrophthalate*	52	65	57	35
	Methyl salicylate	23	65	60	69
(IV)	(V)	98	67	81	17
Benzamide . .	Methyl benzoate	102	99	96	86
Benzanilide . .	„ „	97	98	98	96
2,2-Dichloroproprionamide	Methyl 2,2-dichloropropionate	103	103	97	78

* Sulphur also formed.

Side-reactions prevented high yields of methyl salicylate from salicylanilide although no salicylanilide remained after 16 hr.

These results show that in some cases the reaction shows promise for the gas chromatographic analysis of amides.

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[1] Y. Mashiko and K. S. Pitzer, *J. Phys. Chem.*, 1958, **62**, 367.

[2] E. F. Mooney and M. A. Qaseen, *Chem. Comm.*, 1967, 230.

[3] F. J. Sowa, U.S.P. 2,834,799/58 (*Chem. Abs.*, 1958, **52**, 17118d).