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THE REACTION OF CARBOXYLIC ESTERS WITH BORON TRIBROMIDE A CONVENIENT METHOD FOR THE SYNTHESIS OF AMIDES AND TRANSESTERIFICATION

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The reaction of carboxylic esters with boron trihalide was extensively studied by W.Gerrard et.al. and the intermediary formation of ester-boron trihalide complex was suggested[1]. More recentry, P.S.Manchand showed that sterically hindered carboxylic esters can be converted by boron trichloride to the corresponding carboxylic acids[2].

In this paper, we wish to report the application of this reaction to the synthesis of amides and to transesterification.

Boron tribromide reacts smoothly with carboxylic esters under mild conditions, and the addition of amines to the reaction mixture of boron tribromide and carboxylic esters gave the amides in excellent yield.

The substitution of amines by alcohols in this reaction gave the corresponding esters (transesterification).

$$\text{R-COOR'} \xrightarrow[\text{HN(R'')}_2]{\text{BBr}_3} \text{R-CON(R'')}_2$$

$$\text{R-COOR'} \xrightarrow[\text{R''-OH}]{\text{BBr}_3} \text{R-COOR''}$$

A solution of an ester (0.01 mol) in CH_2Cl_2 or C_6H_6 was treated with BBr_3 (0.01~0.012 mol) dissolved in C_6H_6 and the solution was stirred at 20~40°. After 1~5 hrs, an amine or an alcohol (0.01 mol) was added and the mixture was stirred at 20~50° for 1~15 hrs. After removal of the solvent, water was added and the mixture was neutralized with aq $NaHCO_3$ sol and extracted with EtOAc. Evaporation of the solvent gave the amide or the ester corresponding to the starting ester.

This convenient method for the preparation of amides is particularly useful when the amines used are unstable, i.e., 7-aminocephalosporanic acid.

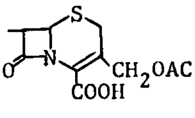
The results of reaction are illustrated in Table.

Table

ester	BBr_3 a)		amine or alcohol	conditions		product b)	(%)
	temp.	hr		temp.	hr		
$C_6H_5CH_2COOMe$	rt	5	$C_6H_5NH_2$	rt	3	$C_6H_5CH_2CONHC_6H_5$	81
MeCOOEt	40°	0.5	$C_6H_5NH_2$	rt	1	$C_6H_5NHCOMe$	61
MeCOOBu	40°	2	C_6H_5NHMe	rt	15	$C_6H_5N(Me)COMe$	35
$C_6H_5CH_2COOCH_2C_6H_5$	rt	1.5	$C_6H_5NH_2$	rt	4	$C_6H_5CH_2CONHC_6H_5$	74
$C_6H_5CH_2COOCH_2C_6H_5$	rt	1.5	NH_2CH_2COOH	rt	4	$C_6H_5CH_2CONHCH_2COOH$	62
$C_6H_5CH_2COOMe$	rt	5	7-ACA c)	rt	5	$C_6H_5CH_2CONH$-CA e)	67 d)
MeCOOMe	40°	1	7-ACA c)	rt	8	MeCONH-CA e)	44 d)
$C_6H_5CH_2COOCH_2C_6H_5$	rt	1.5	MeOH	rt	5	$C_6H_5CH_2COOMe$	83
MeCOOMe	40°	1	3Me,4ClC_6H_3OH	50°	5	3Me,4ClC_6H_3OCOMe	68

a) Commercially available BBr_3 (99%) was dissolved in anhydrous benzene. b) The known products were identified by the comparison of TLC and IR spectra with the authentic specimens, and the structural assignments of the new products were based primarily on IR and NMR date. c) 7-Aminocephalosporanic acid. d) Some amount of the starting material was recovered in each run. The yields of the amides are nearly quantitative, based on the reacted starting material.

e) -CA :



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