Insoluble Resins with Mixed Carbonic-carboxylic Anhydride Functions. Preparation and Applications as Mild Selective Acylating Reagents

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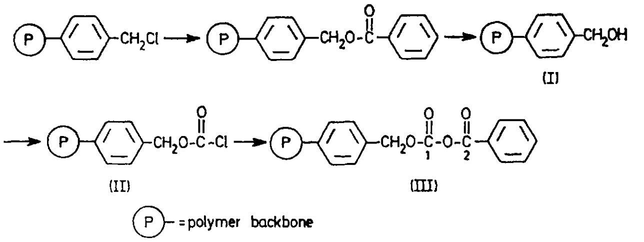
Summary Polystyrene resins bearing mixed carbonic-carboxylic anhydride functions have been synthesized and utilized to prepare amides and anhydrides from amines and carboxylic acids respectively, in high yields under mild conditions.

INSOLUBLE resins are useful reagents in organic synthesis because the excess reagent and other reaction products can be removed by simple filtration.[1] Thus the usual work-up and purification steps may be avoided. Here we report that polystyrene resins bearing highly reactive carbonic-carboxylic anhydride functions can be readily prepared and used to synthesise amides and anhydrides from amines and carboxylic acids respectively.



SCHEME 1

The reaction sequence leading to the polymeric carbonic-benzoic anhydride (III) is illustrated in Scheme 1. 'Pop-corn' polystyrene[2] (40—100 mesh) was chloromethylated by the usual procedure[3] (1·8 m equiv. g^{-1} polymer). The reaction with sodium benzoate in the presence of triethylamine followed by alkaline hydrolysis resulted in the formation of the carbinol (I) in a quantitative manner. Treatment with phosgene in benzene (12·5%) gave the chloroformate (II). The conversion to the mixed anhydride (III) was carried out by treatment with 20% excess benzoic acid and triethylamine in benzene at 0° for 20 min (i.r., doublet at 1740 and 1795 cm^{-1}; 1·3 m equiv. benzoic acid per gram).

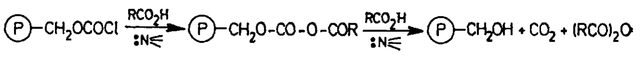
TABLE 1

Products from the reactions of (III) (25% excess) with nucleophiles in benzene[a]

Nucleophile	Reaction conditions	Products/%	
Aniline	25°, 4 h	benzanilide	75
		benzoic acid	20
Benzylamine ..	25°, 4 h	*N*-benzylbenzamide	80
		benzoic acid	15
n-Propylamine ..	25°, 2 h	*N*-n-propylbenzamide	95
n-Butylamine ..	25°, 2 h	*N*-n-butylbenzamide	95
Ethanol	80°, 6 h	ethyl benzoate	20

[a] 10·0 g of (III) in 75 ml benzene. Isolation of the products similar to the procedure in ref. 1; yields based on the nucleophile.

The products obtained by the treatment of (III) with various nucleophiles are shown in Table 1. The polymer is capable of benzoylating amines under mild conditions; the formation of benzoic acid during the reaction with aniline is a result of the competitive displacement at carbonyl-1 (III). The amount of benzoic acid decreased when benzylamine was used as the nucleophile and was negligible when primary aliphatic amines were used. Thus, after the addition of an aliphatic amine in benzene to a slight excess of



SCHEME 2

the polymeric reagent (III) the only product present in solution is the corresponding amide, since the excess reagent and the other reaction product (I) are completely insoluble. Alcohols, on the other hand, do not react with (III) under the same conditions.

TABLE 2

Polymer assisted synthesis of symmetrical anhydrides $(RCO)_2O$

Carboxylic acid	Yield/%
p-Chlorobenzoic acid	75
Benzoic acid	80
Cinnamic acid	90

The polymeric mixed anhydrides can also be utilized for the synthesis of symmetrical anhydrides by the treatment of the polymer (*e.g.* III) with an equimolar amount of a carboxylic acid and triethylamine in benzene at room temperature (Scheme 2). The yields of the anhydrides from three carboxylic acids range from good to excellent (Table 2). This polymer assisted synthesis, is better than the usual methods of synthesis of these anhydrides which require the prior conversion of the acid to acid chloride. The conditions employed are mild and the purity of the anhydrides was excellent as seen by m.pt.s. and n.m.r. spectra.

This investigation was supported by a Reasearch grant from the Kentucky Tobacco and Health Research Institute.

(*Received*, 16*th May* 1974; *Com.* 551.)

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