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Polymer-bound "Dimethylaminopyridine" as a Catalyst for Facile Ester Synthesis

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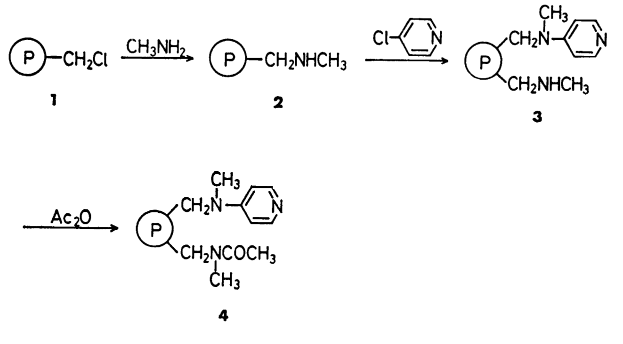
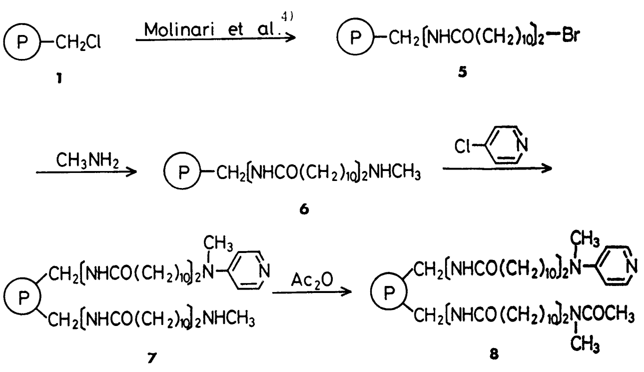
Synopsis. Polystyrene beads which covalently link a dimethylaminopyridine unit act as a catalyst for ester synthesis by the DCC method. The polystyrene beads are reusable and the synthetic method is very simplified.

The dicyclohexylcarbodiimide (DCC) method has been widely adopted for the synthesis of some sugar and amino acid derivatives. Recently, it was communicated that the method is applicable to the esterification of carboxylic acids in the presence of catalytic amounts of 4-dimethylaminopyridine (DMAP).[1,2] Klotz *et al.*[3] reported that the catalytic activity is due to both the increased electron-donating ability of the ring nitrogen and the augmented stability of the *N*-acylpyridinium species. Although this is an excellent, mild one-pot esterification method, there are two defects: (i) in the conventional DCC method in the amide synthesis the product is directly recovered by filtration owing to the precipitating nature of *N*,*N*′-dicyclohexylurea, whereas in the presence of DMAP one has to isolate the product ester from DMAP, and (ii) DMAP is relatively expensive. It occurred to us that two defects would be improved by immobilizing the DMAP unit in polymer beads. Here, we wish to report the method of the immobilization and the catalytic activity of the immobilized DMAP unit.

p-Chlormethylated polystyrene (**1**) (4% crosslinked, 4.0 mequiv Cl/g) was kindly supplied from Mitsubishi Kasei Co. Ltd. The polystyrene beads were treated according to the following reaction sequence. **1**→**2** : **1** was swelled in *N*,*N*-dimethylformamide and dry methylamine gas was introduced into the solution. The reaction was continued for 12 h at 60—70 °C. **2**→**3** : **2** was swelled in an ampule containing water and ethanol (3 : 1 in vol), and 4-chloropyridine and triethylamine (excess) were added. After sealing the ampule, the reaction mixture was heated at 150 °C for 4 d. **3**→**4** : **3** in dichloromethane was treated with acetic anhydride (excess). The reaction was continued for 3 h at room temperature. All the reactions were performed under efficient stirring. We also prepared the catalytic beads which have a spacer between the polymer surface and the DMAP unit. **5** was prepared according to the method of Molinari *et al.*[4] The reaction methods from **5** to **8** were similar to those from **1** to **4**. The DMAP contents determined by acid-base titration were: 1.6 mequiv DMAP/g for **4** and 0.60 mequiv DMAP/g for **8**.





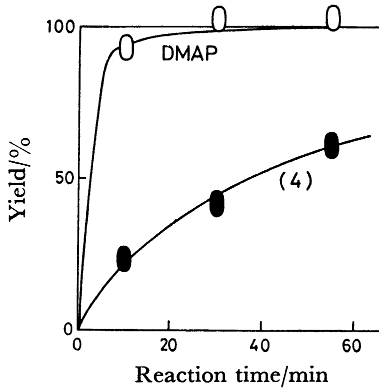


Fig. 1. Yield of methyl benzoate *vs.* reaction time. The yield was determined by GLC method (interanal standard, anisole). 20 °C, 10 ml of dichloromethane, 10 mmol of benzoic acid, 100 mmol of methanol, 12 mol of DCC, and 1.0 mmol of DMAP or DMAP unit in **4**.

Figure 1 shows the plots of the yield of methyl benzoate *versus* reaction time. The reaction conditions are recorded in the caption for Fig. 1. The homogeneous reaction catalyzed by DMAP was completed within 10 min, and the conversion was almost quantitative.[5] On the other hand, the reaction catalyzed by **4** was relatively slow, the half-life being about 30 min. After one day, the precipitate (*N*,*N*′-dicyclohexylurea) and **4** were removed by filtration and the filtrate was analyzed by GLC. The dichloromethane solution contained only methyl benzoate and methanol, so that the concentration *in vacuo* readily gave "pure" methyl benzoate. The yield of methyl benzoate was 65%, but unreacted benzoic acid was not detected in the filtrate. The loss may be caused by the adsorption to the polystyrene

Table 1. Yield of esters[a)]

Catalyst	Acid	Alcohol	Yield (%) after		
			1 h	3 h	1 d
DMAP	$C_6H_5CO_2H$	MeOH	100[d)]		
4	$C_6H_5CO_2H$	MeOH	61	59	65
4 reused	$C_6H_5CO_2H$	MeOH		65	
4[b)]	$C_6H_5CO_2H$	MeOH		51[e)]	
8	$C_6H_5CO_2H$	MeOH		41	53
4	$C_6H_5CO_2H$	*t*-BuOH		0	0
4	$CH_2(CO_2H)_2$	MeOH		84	98
4	$CH_5CH{=}CHCO_2H$	MeOH		61	
4[c)]	CH_3CO_2H	$C_6H_5CH_2OH$		40	47

a) The reaction solution (10 ml of dichloromethane) contains 1.0 mmol of catalyst, 10 mmol of acid, 100 mmol of alcohol, and 12 mmol of DCC. The yields were calculated on the basis of acid. b) 20 mmol of DCC were added. c) The reaction solution (10 ml of dichloromethane) contains 1.0 mmol of catalyst, 20 mmol of acetic acid, 10 mmol of benzyl alcohol, and 20 mmol of DCC. The yield was calculated on the basis of benzyl alcohol. d) 30 min. e) 4 h.

beads. The same reaction was carried out with **8**, but the yield was not improved significantly (yield 53%). After washing the recovered **4** by hot *N*,*N*-dimethylformamide, it was reused for the synthesis of methyl benzoate. The yield after 3 h was 53%. The result indicates that **4** is reusable without losing the catalytic activity.

The yields of other esters are summarized in Table 1. As mentioned above, starting carboxylic acids were not found in the filtrate. Table 1 shows that the yields in the present two phase system are somewhat lower than those in the homogeneous system.[2)] In particular, the yield of *t*-butyl benzoate was extremely low. Also in the homogeneous system catalyzed by DMAP,[2)] the low yield (40%) resulted for this ester due to the steric hindrance. The steric term may be further amplified in the solid catalyst system. On the contrary, dimethyl malonate was produced quantitatively. We cannot explain readily the difference in the yield between methyl benzoate and dimethyl malonate. One possible explanation is that benzoic acid which is more apolar than malonic acid is adsorbed to the resin surface in a non-productive manner in preference to malonic acid.

In conclusion, the catalytic activity of the DMAP unit bound to polystyrene beads is somewhat lower than that of DMAP in the homogeneous system. However, there are two merits in the immobilized DMAP catalysis: (i) the product esters are directly recovered by filtration, and (ii) the catalytic resin is reusable by simply washing with *N*,*N*-dimethylformamide.

References

1) A. Hassner and V. Alexanian, *Tetrahedron Lett.*, **1978**, 4475.

2) B. Neises and W. Steglich, *Angew. Chem. Int. Ed. Engl.*, **17**, 522 (1978).

3) M. A. Hierl, E. P. Gamson, and I. M. Klotz, *J. Am. Chem. Soc.*, **101**, 6020 (1979).

4) H. Molinari, F. Montanari, S. Quici, and P. Tundo, *J. Am. Chem. Soc.*, **101**, 3920 (1979).

5) The homogeneous system in the absence of DMAP gave methyl benzoate in 1.1% yield (after 1 d).