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Convenient Selective Monoesterification of α, ω-Dicarboxylic Acids Catalyzed by Ion-Exchange Resins

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Abstract: Symmetric dicarboxylic acids, ranging from pentanedioic acid to tetradecanedioic acid, gave selectively the corresponding monoesters in high yields in the transesterification catalyzed by strongly acidic ion-exchange resins in ester/octane mixtures.

Investigation of the preparation of monoesters of alkanedicarboxylic acids is important when the corresponding cyclic anhydrides are not readily available. Dicarboxylic acids have been reported to be selectively monoprotected in the reaction with diazomethane[1] or dimethyl sulfate[2] to form monomethyl esters in the presence of alumina. Methods to obtain monoesters of malonic acid derivatives via cyclic compounds have also been developed.[3] Enzymatic methods to give monoesters have been thoroughly reviewed.[4] Selective esterification reaction of diacids by alkyl halides under phase-transfer catalysis has also been reported.[5] Selective monoacylation of diols has been studied more intensively.[4,6-10] We have reported that symmetric diols are selectively monoprotected by monoacylation in an ester/alkane solvent mixture[7] or monotetrahydropyranyl ether formation in a dihydropyran/alkane solvent[8] in reactions catalyzed by metallic sulfates supported on silica gel. Moreover, we have also found that diols are selectively monoacylated in an ester/alkane[9] and monotetrahydropyranylated in a dihydropyran/hydrocarbon[10] in reactions catalyzed by strongly acidic ion-exchange resins. The last two studies suggested that similar selectivities can be observed in the reactions catalyzed by ion-exchange resins containing water when the solubility in water decreases successively from starting materials to final products. These results prompted us to study the selective monoesterification of symmetric dicarboxylic acids by transesterification catalyzed by sulfonic acid-type ion-exchange resins. Esterification of carboxylic acids with alcohols catalyzed by ion-exchange resins is well known.[11]

$$\mathrm{HO_2C\text{-}R^1\text{-}CO_2H} \xrightarrow[\mathrm{R^2CO_2R^3/Alkane}]{\text{Ion-exchange resin}} \mathrm{R^3O_2C\text{-}R^1\text{-}CO_2H} \;+\; [\mathrm{R^3O_2C\text{-}R^1\text{-}CO_2R^3}]$$

Figure 1 shows an example of the dependence of the product yield upon the reaction period. Hexanedioic acid (1 mmol) and Dowex 50W-X2 (50-100 mesh) (1.0 g) were stirred in butyl formate/octane (1:1, 10 ml) at 70 °C. The reaction was monitored by GC. The yield of the dibutyl ester increased only slowly, even when the increase of the yield of the monobutyl ester became gradual after the initial steep rise. The yield of the monoester reached 91% when the yield of the diester reached 5%, and yields of both esters did not change rapidly even after the yield of the monoester reached the maximum. This result shows that the reaction rate of the monoester is much lower than that of the dicarboxylic acid and that the rate of the monoester did not rise very much even after most of the dicarboxylic acid had been consumed.

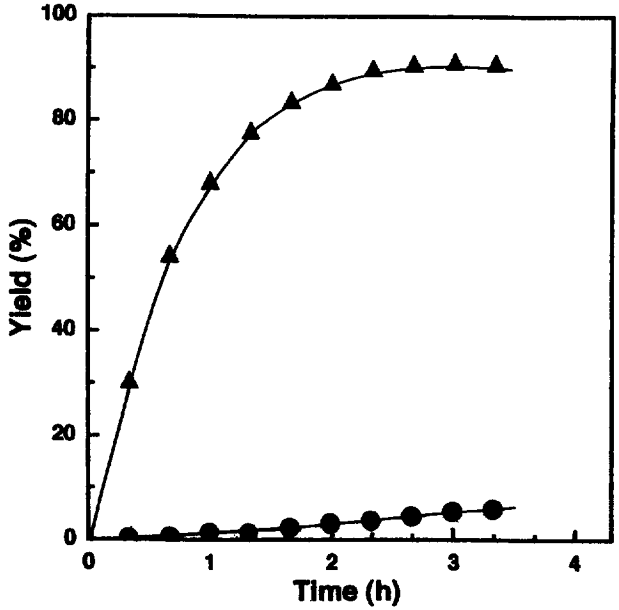

Figure 1. Yields vs. reaction time. Hexanedioic acid (1 mmol) and Dowex 50W-X2 (50-100 mesh) (1.0 g) were stirred at 70 °C in HCO_2Bu/octane (1:1, 10 ml): the monoester (▲) and the diester (●).

Table 1 shows that all the dicarboxylic acids that were examined ranging from pentanedioic acid to tetradecanedioic acid gave the corresponding monobutyl esters in acceptable yields (about 90%) and selectivities in transesterification catalyzed by the strongly acidic ion-exchange resin in butyl formate/octane mixtures. The use of propyl formate in place of butyl formate produced the corresponding propyl esters in the reaction of hexanedioic acid (entry 4). By these results the general applicability and practical utility of this method were confirmed. The use of butyl acetate instead of butyl formate reduced the reaction rate in the reaction of pentanedioic acid (entry 2). The amount of the catalyst is important. In order to realize the high selectivity we need to use about ten times the amount of the ion-exchange resin that was used in the selective acylation of diols by transesterification.[9] The reason for the large amount of the catalyst needed in the selective monoesterification of dicarboxylic acid is not clear yet. A particular ester/octane solvent ratio that gives the highest selectivity exists in the reaction of each dicarboxylic acid, although the dependence of the selectivity on the solvent composition is slight. Generally, the larger the hydrocarbon part of dicarboxylic acids becomes, the smaller the ester ratio of the most suitable solvents.

Table 1. Selective monoesterification of HO_2C-R^1-CO_2H with $R^2CO_2R^3$ catalyzed by ion-exchange resin[a].

Entry	R^1	Ester			Temp.	Time	Yield (%)	
		R^2	R^3	%	(°C)	(min)	Monoester	Diester
1	$(CH_2)_3$	H	Bu	50	70	180	95	5
2	$(CH_2)_3$	Me	Bu	50	70	440	92	5
3	$(CH_2)_4$	H	Bu	50	70	160	91	5
4	$(CH_2)_4$	H	Pr	50	70	160	85	6
5	$(CH_2)_6$	H	Bu	20	100	100	92	5
6[b]	$(CH_2)_8$	H	Bu	10	100	260	93	4
7[b]	$(CH_2)_{12}$	H	Bu	10	100	750	89	6

[a]Dicarboxylic acid (1.0 mmol) and Dowex 50W-X2 (50-100 mesh) (1.0 g) were heated in an ester/octane mixture (10 ml). [b]Amount of the solvent was 20 ml.

We presume that the selectivity arises from the factors enumerated below. (1) Most of the sulfonic acid-type ion-exchange resins usually contain 50-80% water (suppliers' catalogs). Therefore, a strongly acidic water layer seems to be formed in the resins. (2) A partition equilibrium between the aqueous layer and the aprotic ester/octane layer would be set up, and dicarboxylic acids have higher partition coefficients for water than the product monoesters. (3) Esterification of carboxylic acids takes place in the aqueous layer and/or at the interface between the aqueous and the nonaqueous liquid layers. (4) The formed monoesters move out of the aqueous layer into the aprotic layer and remain there without reacting further. Similar factors were also deduced in the selective acylation[9] and etherification[10] of diols.

Almost all the sulfonic-type ion-exchange resins of wet types showed nearly the same monoester selectivity as Dowex 50W, while the resins for non-aqueous application, for example, Amberlyst 15 (dry), Amberlyst XN-1010, and Nafion NR-50, showed much lower selectivity. This result also shows that a certain amount of water in the resins is essential for the high selectivity. As the use of solid reagents has the advantage of facile set-up and work-up, this method of selective esterification is quite simple and practical.

References

1 H. Ogawa, T. Chihara and K. Taya, *J. Am. Chem. Soc.*, **107,** 1365-1369 (1985); H. Ogawa, T. Chihara, S. Teratani, and K. Taya, 1337-1338 (1986); H. Ogawa, N. Hiraga, T. Chihara, S. Teratani and Taya, *Bull. Chem. Soc. Jpn.*, **61,** 2383-2386 (1988); T. Chihara, *J. Chem. Soc., Chem. Commun.*, 1215-1216 (1980).

2 H. Ogawa, Y. Ichimura, T. Chihara, S. Teratani and K. Taya, *Bull. Chem. Soc. Jpn.*, **59,** 2481-2483 (1986).

3 B. Rigo, D. Fasseur, P. Cauliez and D. Couturier, *Tetrahedron Lett.*, **30**, 3073-3076 (1989); K. Matoba and T. Yamazaki, *Chem. Pharm. Bull.* **31**, 2955-2956 (1983); H. Junek, E. Ziegler, U. Herzog and H. Kroboth, *Synthesis*, 332-334 (1976).

4 H. J. Gais, in "Enzyme Catalysis in Organic Synthesis," ed. by K. Dares, and H. Walkman, Weinheim, Weinheim (1995), Section B, Chap. 1 p 178-226; L.-M. Zhu and M. C. Tedford, *Tetrahedron,* **48**, 6587-6611 (1990). A. M. Klibanov, *Acc. Chem. Res.*, **23**, 114-120 (1990); See also E. Ozaki, T. Uragaki, K. Sakasita, and A. Sakimac, *Chem. Lett.*, 539-540 (1995) and the references cited therein.

5 J. Zerda, G. Barak, and Y. Sasson, *Tetrahedron*, 1533-1536 (1989).

6 W. F. Balley, L. M. J. Zarcone and A. D. Rivera, *J. Org. Chem.*, **60**, 2532-2536 (1994) and references cited therein.

7 T. Nishiguchi, K. Kawamine, and T. Ohtsuka, *J. Org. Chem.*, **57,** 312-316 (1992); T. Nishiguchi, and H. Taya, *J. Am. Chem. Soc.*, **111,** 9102-9103 (1989).

8 T. Nishiguchi, K. Kawamine, and T. Ohtsuka, *J. Chem. Soc., Perkin Trans. 1,* 153-156 (1992).

9 T. Nishiguchi, S. Fujisaki, Y. Ishii, Y. Yano and A. Nishida, *J. Org. Chem.*, **59,** 1191-1195 (1994).

10 T. Nishiguchi, M. Kuroda, M. Saitoh, A. Nishida and S. Fujisaki, *J. Chem. Soc., Chem. Commun.,* 2491-2492 (1995).

11 M. Petrini, R. Ballini, E. Marcantoni, and G. Rossini, *Syn. Commun.*, **18**, 847-853 (1988); G. F. Vesley and V. Stenberg, *J. Org. Chem.*, **36**, 2548-2550 (1971); M. B. Bochner, G. M. Gerber, W. R. Vieth, and A. J. Rodger, *Ind. Eng. Chem., Fundamentals,* **4**, 314-317 (1965); F. Andreas, *Chem. Tech. (Berlin)*, **11**, 24-28 (1959); J. Mill and R. W. C. Crimmin, *Biochem. Biophys. Acta,* **23**, 432-434 (1957); C. L. Levesque and A. M. Craig, *Ind. Eng. Chem.*, **40**, 96-99 (1948); S. Sussman, *Ind. Eng. Chem.*, **38**, 1228-1230 (1946).

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