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Selective Esterification of Nonconjugated Carboxylic Acids in the Presence of Conjugated or Aromatic Carboxylic Acids Under Mild Conditions†

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Nonconjugated carboxylic acids are selectively esterified in good yields in the presence of conjugated or aromatic carboxylic acids by stirring over Amberlyst-15 in alcohol at room temperature.

Selective esterification of nonconjugated carboxyl groups in the presence of conjugated or aromatic carboxyl groups is an important reaction for the manipulation of functional groups in multistep organic synthesis.[1] In general nonconjugated carboxyl groups should be more reactive than conjugated ones in esterification reactions. However, a survey of the literature[2] reveals that such selective esterification of carboxylic acids has been carried out under reaction conditions or with carboxyl activating reagents which are not mild enough to be of general and wide applicability. Recently Spur and coworkers[3] have reported a methodology which is quite effective at room temperature but utilizes expensive reagents like 2,2-dimethoxypropane and chlorotrimethylsilane.

Here we report our observation that a saturated carboxylic acid can be selectively esterified at room temperature in the presence of a conjugated or aromatic carboxylic acid in good yield in the presence of macroreticular ion exchange resin Amberlyst-15 using methanol or ethanol as solvent. This result has been investigated through competition experiments in (i) a mixture of two different carboxylic acids (one nonconjugated and the other conjugated or aromatic), (ii) a molecule containing both a saturated and a conjugated or aromatic carboxylic acids groups. It has also been noted that an aromatic carboxylic acid is preferentially esterified over a conjugated carboxylic acid attached to an aromatic ring under these conditions. The procedure involves stirring of a 1 : 1 mixture of two different carboxylic acid compounds or a compound containing both functional groups in methanol or ethanol over Amberlyst-15 at room temperature and the progress of the reaction is monitored through TLC. The work up (after an appropriate interval of time) involves simply decantation of the solvent and evaporation followed by chemical separation of the residue. This methodology is quite inexpensive in view of the ready reuse of Amberlyst. The examples studied are given in Tables 1 and 2.

Experimental

General Procedure for the Selective Esterification of Cyclohexanecarboxylic Acid in the Presence of Benzoic Acid.—A solution of cyclohexanecarboxylic acid (0.01 mol) and benzoic acid (0.01 mol) in methanol (80 ml) containing Amberlyst-15 (50 g) was stirred at room temperature and the progress of reaction monitored by TLC. After 14 h, the solution was filtered and the Amberlyst washed with MeOH(3 × 30 ml). The combined solvent was evaporated and the residue was taken in CH_2Cl_2 (80 ml). The organic layer was washed with aqueous $NaHCO_3$ solution (20%, 30 × 60 ml), water (2 × 60 ml), brine (2 × 60 ml) and dried (Na_2SO_4). The solvent was removed completely to provide methyl cyclohexane carboxylate

Table 1 Selective esterification of a mixture of two carboxylic acids with methanol

Entry	Acid A + acid B	Time/h	Yield of ester[a] (%) A	B
1	Caproic acid (A) + benzoic acid (B)	13	82	0
2	Phenylacetic acid (A) + benzoic acid (B)	14	78	0
3	Citronellic acid (A) + geranic acid (B)	12	85	0
4	Cyclohexanecarboxylic acid (A) + benzoic acid (B)	14	81	0
5	Succinic acid (A) + maleic acid (B)	10	78	0
6	Caproic acid (A) + crotonic acid (B)	10	82	5
7	Cyclohexanecarboxylic acid (A) + 1-cyclohexenecarboxylic acid (B)	12	75	4
8	Benzoic acid (A) + cinnamic acid (B)	24	81	0

[a] Isolated yield.

Table 2 Competition esterification of dicarboxylic acids in methanol

Entry	Dicarboxylic acid	Time/h	Yield[a] (%) Non-conjugated monomethyl ester	Conjugated monomethyl ester	Dimethyl ester
1	Itaconic acid	12	94	0	0
2	2-(4-Hydroxycarbonyl phenyl)acetic acid	12	88	0	0
3	Prop-1-ene-1,3-dicarboxylic acid	12	76	0	5

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(1.15 g) in 81% yield identical with an authentic sample (IR, NMR, TLC).

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References

1 M. B. Smith, *Organic Synthesis,* McGraw-Hill, Inc., New York, 1994, p. 980.

2 S. Patai and Z. Rappoport, *Synthesis of Carboxylic Acids, Esters and their Derivatives*, John Wiley & Sons, Inc., New York, 1991, p. 145; R. N. Ram and I. Charles, *Tetrahedron*, 1997, **53**, 7335 and references therein; T. W. Greene and P. G. M. Wuts, *Protective Groups in Organic Synthesis*, John Wiley & Sons, Inc., New York, 2nd edn., 1991, p. 224; A. Banerjee, M. M. Adak, S. Das, S. Banerjee and S. Sengupta, *J. Ind. Chem. Soc*., 1987, **64**, 34; T. Ogawa, T. Hikasa, T. Ikegami, N. Ono and H. Suzuki, *J. Chem. Soc., Perkin Trans. 1*, 1994, **23**, 3473; E. C. Blossey, L. M. Turner and D. C. Neekers, *Tetrahedron Lett*., 1973, 1823.

3 A. Rodriguez, M. Nomen, B. W. Spur and J. J. Godfroid, *Tetrahedron Lett*., 1998, **39**, 8563.