The Use of Anion-Exchange Resins in the Synthesis of Esters from Carboxylic Acids and Alkylating Agents

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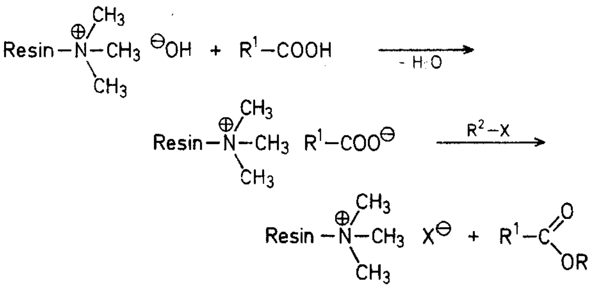
Anion-exchange resins are effective catalysts in many organic reactions as for instance, in aldol reactions[1], in malonic ester synthesis[2], and in the *C*-alkylation of phenols[3]; however, their use in the *O*-alkylation of carboxylate ions has, to our knowledge, not been reported.

Amberlite IRA-904, a macroreticular resin containing quaternary ammonium groups, was purchased as the chloride salt and converted to the $OH^{\ominus}$ form by washing with 1 *N* sodium hydroxide solution employing the usual column technique. The resin was rinsed with water, methanol, and ether; then, a solution of the carboxylic acid was percolated through the column to give the corresponding carboxylate resin. Esterification was usually achieved by a batch technique by stirring the resin thus obtained with an excess (4 mol equivalents) of alkylating agent in a suitable solvent.



The reaction product was isolated by simply filtering off the resin and removing the solvent by gentle distillation under reduced pressure.

Table. Carboxylic Acid Esters from Carboxylic Acids and Alkylating Agents in the Presence of Anion-Exchange Resin

R^1	R^2—X	Solvent	Reaction temperature	Reaction time [h]	Yield[a] [%]
C_6H_5	H_3C—J	hexane	r.t.	2	90
		water	r.t.	20	80
	i-C_3H_7—Br	hexane	50°	13	60
	t-C_4H_9—Br	hexane	50°	5	trace
	H_3C—OTos	hexane	r.t.	17	91[b]
	C_2H_5OOC—CH_2—Br	ether	r.t.	5	99[b]
	C_6H_5—CH_2—Cl	hexane	50°	6	73[c]
n-$C_{11}H_{23}$	H_3C—J	ether	r.t.	4	93
		ethanol	r.t.	4	90
	i-C_3H_7—Br	hexane	50°	6	52
	t-C_4H_9—Br	hexane	r.t.	200	trace
C_6H_5—CH=CH—	H_3C—J	hexane	r.t.	21	97[c]
	i-C_3H_7—Br	hexane	50°	14	59
c-C_6H_{11}	H_3C—J	ether	r.t.	16	76
	i-C_3H_7—Br	hexane	50°	14	28

[a] Yields are based on the amount of carboxylic acid bound to the resin.

[b] Crystalline product; m.p. in accordance with literature m.p. without recrystallization.

[c] Yield of ester determined by G.L.C.

The products were identified by their I.R.- and ^{1}H-N.M.R.-spectral data and by comparison of their G.L.C. retention times with those of authentic samples.

As expected, iodides were found to be better alkylating agents than bromides, whereas chlorides (except benzyl chloride) failed to react. Secondary halides gave reaction products only at 50°; from *t*-butyl bromide, only a trace of ester could be obtained.

An interesting feature of the reaction is that it proceeds in non-polar solvents as well as in water and ethanol. In the same solvents, the sodium carboxylates were not esterified by alkyl halides in the absence of catalysts. Thus, the resin seems to increase the nucleophilicity of the R—$COO^{\ominus}$ anion in a manner which is related to the principles of phase-transfer catalysis[4].

We observed that the exchanging power of the resin for carboxylic acids was about half its capacity and that only carboxylates bound to the resin were readily alkylated. Runs performed with catalytic amounts of resin did not give satisfactory results.

The column procedure, employed in some cases, was less satisfactory due to the much longer time required to obtain good yields. Regeneration of the resin was readily accomplished by washing with 1*N* sodium hydroxide solution.

O-Alkylation of Carboxylic Acids; General Procedure:

A solution of the carboxylic acid (10 mmol) in the solvent indicated in the Table is percolated through a column containing Amberlite IRA 904 resin ($OH^{\ominus}$ form) (Rohm&Haas Co.; 20 mequiv of dry resin). The resin is then placed in a flask, a solution of the alkylating agent (40 mmol) in the same solvent is added, and the mixture stirred under the conditions given in the Table. The resin is then filtered off and the filtrate slowly distilled under reduced pressure to remove the solvent and excess alkylating agent.

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