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CATHODIC ESTERIFICATION OF CARBOXYLIC ACIDS

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A cathodic method for the esterification of carboxylic acids under mild conditions was found. The esterification proceeded smoothly at room temperature by the reaction of alkylating reagents with quaternary ammonium carboxylates formed in a cathode chamber.

The esterification of carboxylic acids is an important and well-established reaction in organic synthesis. Reasonably, simple methods for the esterification under mild conditions should be required in many cases. One of the "simple" methods may be to react metal salts of carboxylic acids with alkylating reagents but this is generally "not mild" because of the high temperatures required.[1] In a previous paper,[2] one(M.M.B.) of the authors reported that quaternary ammonium salts of carboxylic acids reacted with alkyl halides to give the corresponding esters in high yields. In this method, the esterification reaction itself could proceed smoothly at room temperature, in other words, under "mild" conditions, but the preparation of either quaternary ammonium hydroxides or their carboxylates was not very "simple". Afterward, some other methods which seemed to be mild were proposed but they were not simple because of the use of special and expensive reagents such as 1,8-diazabicyclo[5.4.0]undec-7-ene,[3,4] 1-ethyl-2-fluoropyridinium tetrafluoroborate,[5] and alkyl chloroformates.[6]

In this paper, we wish to report a convenient method for preparing quaternary ammonium salts of carboxylic acids by cathodic reaction and the successive one-pot esterification in a cathode chamber.

$$RCOOH \xrightarrow[Et_4N^{+-}OTs/DMF]{e\ -1/2H_2} RCOO^{-+}NEt_4 \xrightarrow[(X:\ Halo,\ OTs)]{R'X} RCOOR' + X^{-+}NEt_4$$

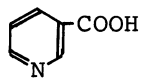
Shono et al. have reported another excellent cathodic esterification using a base electrogenerated from 2-pyrrolidone.[7] Our method is simpler without use of any electrogenerated bases.[8]

General procedures for electrolysis and esterification were as follows: A divided H-type cell and platinum electrodes were used. The catholyte was 40 cm^3 of 0.5 mol dm^{-3} Et_4NOTs/DMF containing carboxylic acids(10 mmol). The electrolysis was carried out by passing 1.0 - 1.2 F(1 F=9648 C)mol^{-1} of charge at room temperature under a galvanostatic condition(cathodic current density, 1.7 A dm^{-2}). Method A: Alkylating reagents(11 mmol of alkyl halides or tosylates) had been added to the catholyte before the electrolytic current was turned on. After the electrolysis, the catholyte was allowed to stand for 1 h at room temperature. Method B: Similar to Method A except that the alkylating reagents were added to the catholyte after the current had been turned off. In the both methods, the catholyte was poured into water and then extracted with dichloromethane. The extract was analyzed by gas chromatography using a 2 m PEG 20M column at 100 - 200 °C.

As shown in Table 1, the yield of butyl acetate formed in Method A was greatly affected by kind of butyl halide used as alkylating reagents. The less electrophilic chloride gave a lower yield than the bromide. Although the iodide should be more electrophilic than the bromide, the former gave a lower yield. This fact is rationalized as due to a less negative reduction potential of the iodide than the bromide; it was confirmed that considerable amounts of the iodide were simultaneously reduced to the corresponding hydrocarbon. Butyl tosylate was also available for the esterification, but it did not give a higher yield than the bromide. Although a fairly good yield could be obtained when the bromide was used, Method A[8] did not seem to be satisfactory from an aspect of synthetic chemistry.

In order to prevent the simultaneous reduction of alkylating reagents, they were added to the catholyte after completion of the electrolysis in Method B. In the esterification of acetic acid with butyl halides by this method, the most electrophilic iodide and the least chloride gave the highest and lowest yields, respectively. Method B also resulted in high or reasonable yields in the esterification of other simple acids such as propionic and benzoic acids.

Table 1. Cathodic Esterification of Carboxylic Acids

RCOOH	R'X	Method[a]	Charge passed / F mol^{-1}	Yield of RCOOR' / %
MeCOOH	BuCl	A	1.2	24
MeCOOH	BuBr	A	1.2	60
MeCOOH	BuI	A	1.2	25
MeCOOH	BuOTs	A	1.1	48
MeCOOH	BuCl	B	1.1	27
MeCOOH	BuBr	B	1.1	68
MeCOOH	BuI	B	1.1	96
PrCOOH	EtI	B	1.1	96
PrCOOH	EtOTs	A	1.1	70
PhCOOH	MeI	B	1.1	80
PhCOOH	EtI	B	1.1	83
PhCOOH	MeOTs	A	1.1	75
$HOOC(CH_2)_4COOH$	MeI	B	1.0	24[b]
$HOOC(CH_2)_4COOH$[c]	MeI	B	2.2	80[b]
PhCH(OH)COOH	EtI	B	1.1	90
$ClCH_2COOH$	MeI	B	1.1	42[d]
MeCH=CHCOOH	MeI	B	1.0	77
HC≡CCOOH	MeI	B	1.0	58
	MeI	B	1.1	70

a) See the text. b) Dimethyl adipate. c) Five milimoles of adipic acid was used. d) Analyzed after removal of DMF by washing repeatedly with water.

The esterification was successfully extended to somewhat complicated acids. It is noticeable that adipic acid gave not the monoester but the diester, though only 1.0 F mol^{-1} of charge was passed. When stoichiometric amounts of charge and methyl iodide for the formation of the diester were used, the yield of the diester reached to 80%. An α-hydroxy acid(mandelic acid) was also esterified in a high yield. Acids with electroreducible groups such as chloro, active olefinic, acetylenic and pyridyl groups could be esterified without the

simultaneous reduction of their electroreducible groups.

This cathodic esterification should be affected by a number of experimental factors and conditions such as solvent, cathode and diaphragm materials, cathodic current density and potential under galvanostatic and potentiostatic conditions, respectively, amount of charge passed, kind and amounts of starting acids and alkylating reagents, reaction time and so on. Any optimization for this esterification has not been done. A more detailed investigation is in progress.

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8) According to private information from T. Shono, his group has also confirmed that the cathodic esterification by Method A can proceed without any electrogenerated bases. However, they have not attempted Method B.

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