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A CONVENIENT METHOD OF TRANSESTERIFICATION UNDER NEUTRAL CONDITIONS

S. Bittner*, Z. Barneis and S. Felix

Department of Chemistry and Research and Development Authority,

Ben-Gurion University of the Negev, Beer Sheva, Israel

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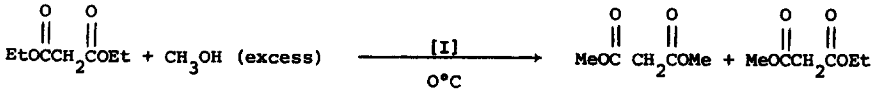
In continuation of our studies [1,2] on the chemical properties of the labile adduct (I), formed from triphenylphosphine and diethylazodicarboxylate, we reacted this quasi-1,3 salt with one equivalent of diethylmalonate in methanol at 0°C. Gas chromatographic follow up of the reaction showed disappearance of the ester peak within 1.5 hr and the appearance of two new peaks. The products were first suspected to be C-methylated derivatives of diethyl malonate [3], but comparison with an authentic sample showed that ester interchange had taken place, yielding predominantly the dimethyl ester (II), and minor quantities of the mixed ester (III).

[I]



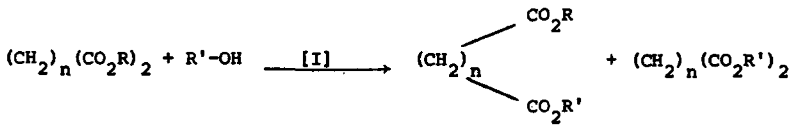
$$\mathrm{EtOC(=O)CH_2C(=O)OEt + CH_3OH\ (excess)} \xrightarrow[0^\circ C]{[I]} \mathrm{MeOC(=O)CH_2C(=O)OMe + MeOC(=O)CH_2C(=O)OEt}$$

[II] [III]

Common transesterifications proceed at high temperatures and with basic or acidic catalysts [4,5]. In some special cases, alcoholysis of an ester can be achieved under neutral conditions at steam-bath temperatures [5,6]. The interesting features of the present reaction are: a) rapid ester interchange under neutral and mild conditions (0°C) and b) a new type of phosphonium salt-catalysis which might find use in other types of reactions as well.

In order to explore the scope of the reaction and to gain some insight into its mechanism, transesterifications of a series of dicarboxylic esters using different alcohols were studied. The results are summarized in Table I:

TABLE I



$$(CH_2)_n(CO_2R)_2 + R'\text{-}OH \xrightarrow{[I]} (CH_2)_n(CO_2R)(CO_2R') + (CH_2)_n(CO_2R')_2$$

[A] [B]

				Yield %[2]	
n	R	R'	Time (hr)[1]	[A]	[B]
0	Et	Me	0.5	5	95
1	Et	Me	1.5	12	88
2	Et	Me	4	61	20[3]
2	Et	Me	24	7	92
3	Et	Me	24	45	6[3]
0	Me	Et	0.5	6	94
0	Me	Pr	0.5	15	76[3]
0	Me	iso-Pr	24	No reaction	
1	Me	Et	24	54	23[3]
2	Me	Et	24	32	5
1	Et	Pr	48	No reaction	
1	Pr	Me	1.5	7	93
1	Pr	Et	2	25[3]	-
2	Pr	Et	2	12[3]	-

1. The reaction mixture was prepared at 0°C under N_2 and allowed to warm to room temperature.
2. Calculated by GLC analysis.
3. The remainder is starting material.

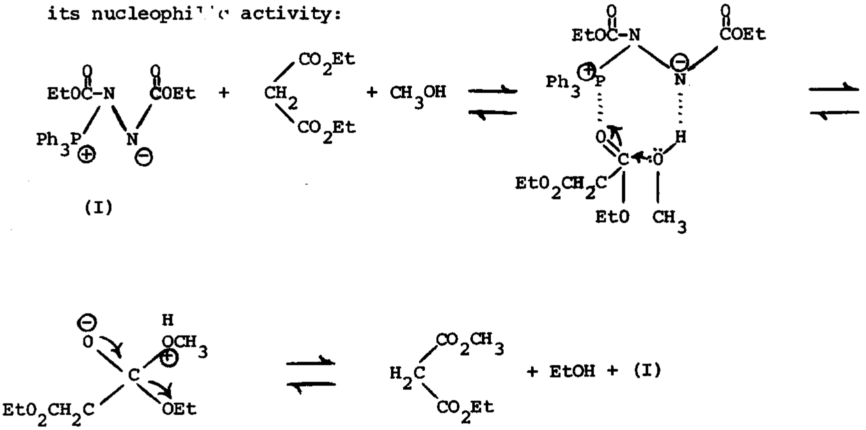
It can be seen that the ease of ester interchange is a function of the distance between the carboxylate groups. If n is the number of methylene groups, the rate of conversion follows the ordered n = 0 > 1 > 2 > 3. This result shows a profound inductive effect of the neighboring carbethoxy groups. This inductive effect can be seen also when examining the reactions of methyl esters with higher alcohols. Thus, dimethyloxalate reacts with ethanol, propanol and butanol (but not with iso-propanol or t-butanol), yielding the appropriate di-esters. Dimethyl malonate reacts only with ethanol; dimethyl succinate does not react.

It is also noteworthy that transesterification of higher esters to give methyl esters, proceeds rapidly and with high yield, whereas the reverse reaction proceeds slowly or not at all.

Monocarboxylic acid esters reacted somewhat more slowly under mild condtions. Methanolysis of higher esters took place but methyl esters did not react with higher alcohols.

As no transesterification takes place when only triphenylphosphine or diethylazodicarboxylate are used, it is certain that the adduct (I) formed from the two is the catalyst.

Common phosphonium ions do not show similar catalytic effects which proves that the internal structure of (I) is of crucial importance to its function as catalyst. This internal quasi-1,3 salt might react as a bifunctional catalyst, causing at the same time both carbonyl and alcohol activation. The phosphonium part of the adduct forms a transient interaction with the ester carbonyl oxygen atom, which causes electron withdrawal from the carbonyl carbon, increasing its electrophilic reactivity, thus enhancing reaction with donor oxygen of the solvent i.e., the R'OH molecule. Simultaneously the anionic position of the adduct forms a hydrogen bond with the alcohol increasing its nucleophilic activity:



All the steps would be expected to be reversible but as the reaction is carried out in excess alcohol, (used as solvent) the equilibrium favors ester interchange.

The present facile transesterification can be used to convert high molecular weight esters to more soluble and volatile esters and also provides a convenient method for the esterification of alcohols under very mild and neutral conditions.

Further studies are now under way to explore other reactions which might be catalyzed by adduct [I] and to gain better understanding about the connection between its structure and catalytic effects.

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