

**179. *Ancillary Mechanisms in the Hydrolysis and Esterification of Carboxylic Esters.***

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Ancillary mechanisms of hydrolysis (IV and VII, see text) and esterification (V and VI) are considered. Mechanisms (V) and (VI) are respectively related as the bimolecular and unimolecular forms of substitution, as also are mechanisms (IV) and (VII). It is shown that mechanisms (IV) and (VI) have some applicability. Mechanism (V), due to Kenner, was not detected.

THE preceding paper sets out what may be termed the standard mechanisms for hydrolysis and esterification, and in the case of hydrolysis there are two, one for the alkali-, and one for the acid-catalysed reaction.

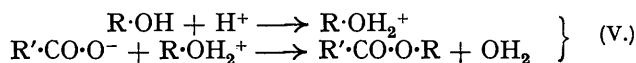
There is evidence of a third (comparatively unimportant) mechanism applying to hydrolysis of carboxylic esters in nearly neutral solution. It may be written



Since the first stage is a bimolecular substitution, this mechanism is characterised by the circumstance that, if R is asymmetric at the point of attachment, hydrolysis will be accompanied by an inversion of configuration.

The existence and characteristics of this form of hydrolysis were pointed out by Cowdrey, Hughes, Ingold, Masterman, and Scott (J., 1937, 1263) in a discussion of the hydrolysis of malolactonic acid; and what they wrote has since been confirmed in detail by Olson and Miller's very thorough investigation of the simpler case of  $\beta$ -butyrolactone (*J. Amer. Chem. Soc.*, 1938, 60, 2687). However, known results in the kinetics of the hydrolysis of esters generally make it clear that this mechanism will contribute very little to the rate of hydrolysis of ordinary esters under ordinary conditions, and it is probably significant that the only two esters for which (under carefully chosen conditions) it makes a dominating contribution to the rate are both relatively labile  $\beta$ -lactones.

Turning to esterification, a mechanism which is the inverse of (IV) has been suggested by Kenner for esterification of carboxylic acids (*Nature*, 1932, 130, 309):

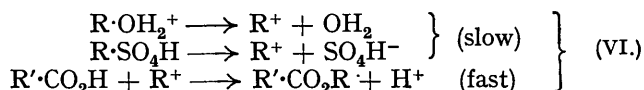


He also pointed out its most easily distinguished characteristic, *viz.*, that if R is asymmetric at the point of attachment, then the configuration of R should be inverted as a result of esterification.

Certainly this mechanism cannot be accepted with the implied degree of generality, because it does not fulfil the obvious requirements of the ordinary acid-catalysed reaction.\* However, further consideration may be given to esterification under special conditions, and analogy with the conditions under which mechanism (IV) has been realised suggests that mechanism (V) might reasonably be sought in esterification by the so-called "direct" method, *i.e.*, when the only acid present is the carboxylic acid which is being esterified; for then the esterification solution is as nearly neutral as it can be. The usual view is, of course, that "direct" esterification is the autocatalytic special case of the acid-catalysed reaction; and if this is true the configuration of an asymmetric R should be retained on esterification.

We have tested this matter, treating, however, only the ordinary ester  $\beta$ -*n*-octyl acetate, and nothing less typical, such as a lactone. By direct esterification of  $\beta$ -*n*-octyl alcohol with acetic acid we obtained an ester in which the configuration of the  $\beta$ -*n*-octyl radical is fully preserved. This result favours the usual view regarding esterification by the direct method, and excludes Kenner's mechanism. We think that this finding will hold for all ordinary carboxylic esters.

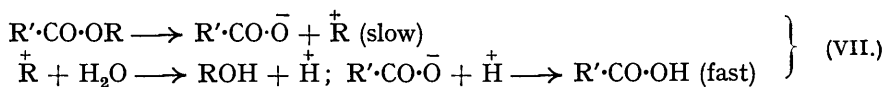
There is another possible subsidiary mechanism of esterification related to (V) as unimolecular substitution is to bimolecular substitution. It may be represented by



the first two lines illustrating alternative forms of the same type of process. This is evidently an acid-catalysed mechanism. Its stereochemical peculiarity is that an asymmetric R should become racemised (Cowdrey *et al.*, *loc. cit.*).

For reasons given in our papers on aliphatic substitution we expect this mechanism to become apparent (if it occurs at all) in the acid-catalysed esterification of aliphatic secondary alcohols, or, still more, of tertiary alcohols or aromatic alcohols of the  $\alpha$ -phenylethyl and benzhydrol types. As we were working with a secondary alcohol we took the opportunity to test for its occurrence by the stereochemical method. The results were positive. In contrast to the outcome of our esterification by the direct method, we found that when  $\beta$ -*n*-octyl alcohol and acetic acid form  $\beta$ -*n*-octyl acetate in the presence of sulphuric acid there is a small but definite racemisation of the  $\beta$ -*n*-octyl radical.

For completeness we also point to the possibility of unimolecular neutral hydrolysis (VII), which we might expect to realise, *e.g.*, in the tertiary esters of the very strongest carboxylic acids:



#### EXPERIMENTAL.

The only practical point which it is necessary to mention is that, since  $\beta$ -*n*-octyl acetate and  $\beta$ -*n*-octyl alcohol are not easily separated by distillation, a necessary stage in the purification of the crude acetate obtained by esterification is the removal of the alcohol by a chemical method. We used combination with phthalic anhydride, the acid phthalate being subsequently separated from the neutral acetate by means of ether and aqueous sodium hydrogen carbonate. Special experiments showed that the complete purification process does not cause any loss of optical activity in the ester.

The numerical data are given below. As we did not use optically pure  $\beta$ -*n*-octyl alcohol, the results are best exhibited by giving to the observed rotations of the ester a proportionate correction to correspond to optical purity in the original alcohol. This is done in the second

\* Making the safe assumption that  $\text{R}'\cdot\text{CO}_2^-$  would remove  $\text{H}^+$  from  $\text{R}\cdot\text{OH}_2^+$  much faster than it would remove  $\text{R}^+$ , we see that mechanism (V) would not be acid-catalysed.

column from the right. Actually the rotation thus obtained for the ester resulting from esterification by the "direct" method is slightly higher than that recorded by Pickard and Kenyon (J., 1914, 105, 830) for optically pure  $\beta$ -*n*-octyl acetate, and hence we have taken our rotation as representing complete retention of optical purity when calculating the figures in the last column on the right. Pickard and Kenyon's work shows quite clearly that when the alcohol and ester have the same sign of rotation they have corresponding configurations.

Expt. No.	Temp.	Time (hrs.)	Reagents (mols.)				$[\alpha]_D^{20^\circ}$ of ROH.	$[\alpha]_D^{20^\circ}$ of R'CO <sub>2</sub> R.		Optical purity (%).
			ROH.	R'CO <sub>2</sub> H.	H <sub>2</sub> SO <sub>4</sub> .	H <sub>2</sub> O.		Obs.	Corr.	
1	115°	15	1.0	10.8	0.00	0.00	+9.32°	+7.04°	+7.48°	+100
2	100	2.6	1.0	10.1	0.10	0.21	+8.61	+4.56	+5.29	+ 71
3	50	2.0	1.0	10.1	0.40	3.10	-5.91	-3.67	-6.15	+ 82

*Note :* All rotations are those of the pure liquids, without solvent.

*Analyses of Ester :* (Expt. 1) Found : C, 69.8; H, 11.4. (Expt. 3) Found : C, 70.0; H, 11.4. Calc. : C, 69.8; H, 11.6%.

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