# The Mechanism of Ester Acidolysis

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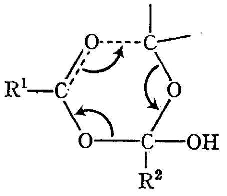
ACYL-OXYGEN cleavage of the ester function has been reported during the acidolysis of acetyltestosterone. The fact that acetyltestosterone did not change its configuration during reaction with [$^{14}$C]acetic acid in the presence of HCl was taken as evidence for acyl-oxygen cleavage.[1] We question the validity of this conclusion since retention of configuration is known to occur in $S_Ni$ reactions.[2] If the mechanism of acidolysis involves formation of a tetrahedral intermediate, as commonly occurs in nucleophilic reactions of carboxylic acids,[3] a transition state (I) may be written that accounts for retention of configuration. However, this mechanism predicts that alkyl-oxygen cleavage takes place. A tetrahedral intermediate has previously been postulated for the acidolysis of esters,[4] but the mode of cleavage of the ester function has not been reported.


(I)

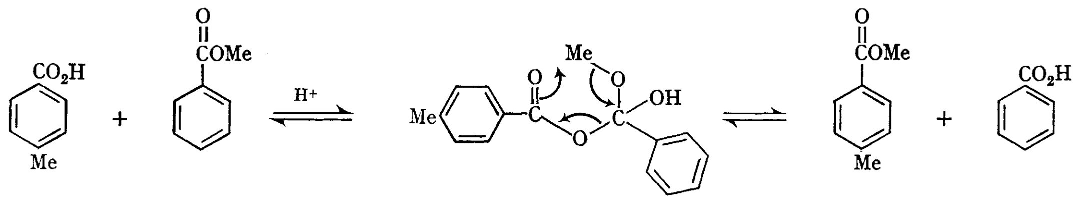
The data in the Table summarizes results of mass spectrometric analysis of *p*-toluic acid, $^{18}$O-labelled *p*-toluic acid, methyl *p*-toluate, and $^{18}$O-labelled methyl *p*-toluate, prepared from the labelled acid. The analysis involved the ratio of the ($m + 1$) and ($m + 2$) peaks of the parent ions.

*Comparison of mass* (m + 1) *and* (m + 2) *peaks from* $^{18}$O *acid and ester with* $^{16}$O *acid and ester peaks.*

| Compound | ($m + 1 : m + 2$) | $^{16}$O : $^{18}$O |
|---|---|---|
| $^{16}$O acid[a] | 6·44 | > 2·16 |
| $^{18}$O acid[b] | 2·98 | |
| $^{16}$O ester[c] | 5·50 | > 2·06 |
| $^{18}$O ester[d] | 2·67 | |

[a] Obtained from Distillation Products Industries, recrystallized from hexane–methylene chloride. [b] Prepared from *p*-toluoyl chloride and $^{18}$O (1·6%) enriched $H_2O$. [c] Prepared from MeOH–$H_2SO_4$ treatment of *p*-toluic acid. [d] Prepared from $^{18}$O containing acid and diazomethane.

When methyl benzoate (5·0 g.) was allowed to react with $^{18}$O-labelled *p*-toluic acid (1·0 g.) at 170° in the presence of concentrated $H_2SO_4$ (0·1 g.) for 30 min., methyl *p*-toluate was isolated from the reaction mixture (about 50% conversion). The ratio of the mass ($m + 1$): ($m + 2$) peaks was 2·58, in close agreement with the value of 2·67 (Table) found for the ester prepared with diazomethane. Our results are most consistent with the following mechanism.



If acyl-oxygen cleavage were to occur during the reaction of methyl benzoate with $^{18}$O-labelled *p*-toluic acid, the ($m + 1$): ($m + 2$) ratio for the resulting methyl *p*-toluate would be expected to fall halfway between the values for the $^{16}$O ester and the $^{18}$O ester (prepared by reaction of the labelled acid with diazomethane) (Table). On the other hand if alkyl-oxygen cleavage occurs [transition state (I)] this ratio should be very close to that of the [$^{18}$O]ester prepared with diazomethane.

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[3] M. L. Bender, *Chem. Rev.*, 1960, **60**, 53.

[4] E. Cherbuliez and M. Fuld, *Helv. Chim. Acta*, 1952, **35**, 1282.