

# Alkylation of Esters. An Ester Enolate as a Possible Ambident Anion

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**Summary** Alkylation of methyl *O*-(tetrahydropyran-2-yl)-mandelate in dimethyl sulphoxide was shown to produce transesterification products at 80° whereas normal *C*-alkylation was observed at 25°.

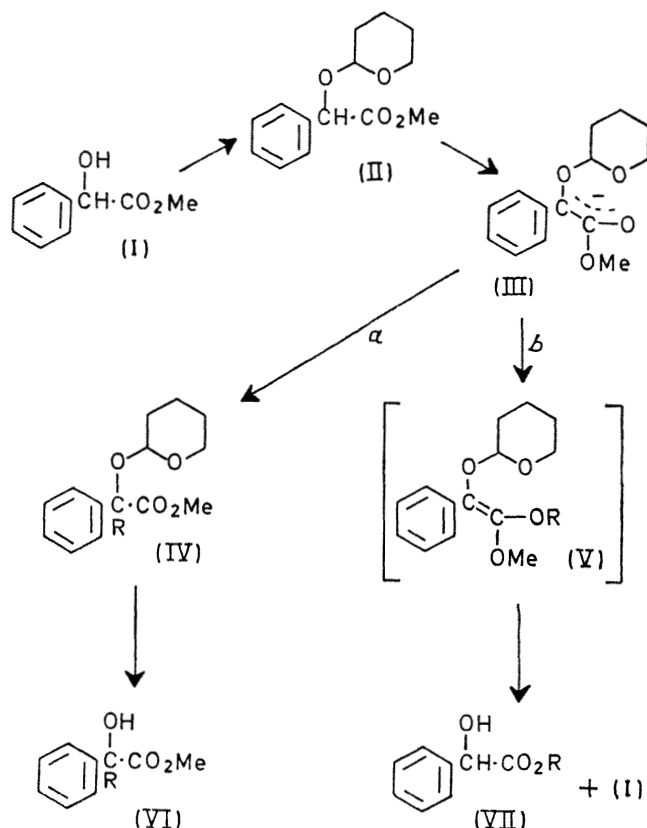
THE alkylation of esters under basic conditions has been extensively investigated as a method of preparation of substituted acetic acid esters.<sup>1</sup> We report the alkylation of methyl *O*-(tetrahydropyran-2-yl)mandelate (II) using alkyl halides and sodium hydride in dimethyl sulphoxide.<sup>2</sup> The products varied with the temperature at which the alkyl halide was introduced. Normal *C*-alkylation products (VI; R = PhCH<sub>2</sub>, Pr<sup>i</sup>, allyl, n-pentyl, or cyclopentyl) were formed at 25 °C (Scheme) but at 80°, transesterification products (VII; as above) were produced.

For example, in the synthesis of (VI; R = PhCH<sub>2</sub>), the ester (II) was added to a sodium methylsulphinyll carbanion solution at 25° and benzyl chloride was subsequently added at the same temperature. Acidic work-up and purification gave (VI; R = PhCH<sub>2</sub>). The ester was saponified and the acid was identified by comparison with an authentic sample of benzylphenylglycolic acid.<sup>3</sup>

An attempted repetition at 80° gave a solid identified as benzyl mandelate (VII; R = PhCH<sub>2</sub>) from spectral data. This was confirmed by comparison with an authentic sample.<sup>4</sup> No *C*-alkylation product (VI) was detected by g.l.c. at this temperature.

In experiments with allyl bromide, isopropyl bromide, n-pentyl iodide, or cyclopentyl bromide comparable products were obtained. The degree of product differentiation was not as great as with benzyl chloride, but analysis indicates that the transesterification products predominate by a wide margin at the higher temperature.

The normal *C*-alkylated products (VI) are produced by S<sub>N</sub>2 displacement of the halide by the negative carbon of the



enolate ion (III) (path *a*). We suggest that the transesterification products arise through *O*-alkylation of the intermediate enolate (path *b*) followed by decomposition of (V)

to (VII) or (I). In all cases the amount of recovered methyl mandelate (I) was low (g.l.c.), for which we have no explanation at present. The enolate (III) apparently acts as an ambident nucleophile which *C*-alkylates at lower temperatures and *O*-alkylates at higher temperatures.

The first products from oxygen alkylation of esters as the

result of nucleophilic displacement by ester enolate ions were characterized as ketene acetals.<sup>5</sup>

It is apparent that anions from certain esters might be ambident nucleophiles. Work is in progress to delineate the mechanism of transesterification and to determine the effect of temperature.

(Received, April 19th, 1971; Com. 582.)

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<sup>3</sup> J. Cast, T. S. Stevens, and J. Holmes, *J. Chem. Soc.*, 1960, 3521.

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<sup>5</sup> C. O. Parker, *J. Amer. Chem. Soc.*, 1956, **78**, 4944.