1-Ethoxyvinyl Carboxylates as 1,4-Dipolar Reagents. Conversion of Aldehydes into β-Hydroxy-esters

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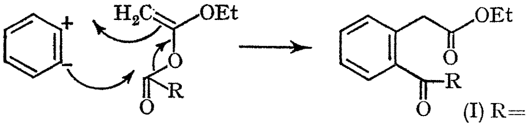
Summary Reactions of aromatic and aliphatic aldehydes with ethoxyvinyl esters lead to β-acyloxy-esters.

WE recently reported[1] that the reaction of benzyne and 1-ethoxyvinyl acetate yielded ethyl *o*-acetylphenylacetate (I) along with a product of cycloaddition. It was suggested that (I) is formed through an ionic process in which the alkoxyvinyl ester acts as a 1,4-dipolar reagent. We have now found that other polar species such as aliphatic and aromatic aldehydes (II)† may react in a similar fashion with alkoxyvinyl esters (III), providing a novel and mild method for the preparation of β-acyloxy-esters. Formation of β-hydroxy-esters by hydrolysis of the latter thus makes available an alternative method for carrying out the Reformatsky synthesis. This reaction is pictured below as a 1,4-addition, and the cases studied are summarized in the Table.‡



(I) R=Me

As indicated, the aldehydes employed were substituted either by electron-attracting or electron-releasing groups, while the vinyl ester was either acetate, chloroacetate, or

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† Ketones do not appear to take part in this reaction.

‡ All compounds reported show infrared and n.m.r. spectra consistent with the assigned structures. Satisfactory elemental analyses were obtained for all products previously unreported.

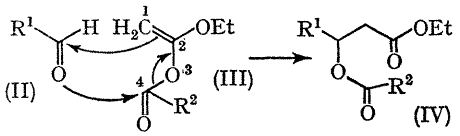
trichloroacetate. With aldehydes bearing electron-withdrawing substituents such as *p*-nitrobenzaldehyde, the yields were generally superior if 1-ethoxyvinyl acetate rather than a chloroacetate was used. Thus, employing (IIIa) with *p*-nitrobenzladehyde, and on heating the reactants under nitrogen at 110° for two days, formation of (IVa) took place in 70% yield. With *m*-methoxybenzaldehyde (IIc), the product (IVc) was formed in only 11% yield, while *p*-methoxybenzaldehyde was unreactive. On the other hand, it was possible to obtain good yields of products from aldehydes bearing electron-donating substituents by adding zinc halides (0·5 equiv.) to the reaction medium. Under these conditions, the yield of (IVg) from *p*-methoxybenzaldehyde (IIg) was 62%. In the case of the aliphatic aldehydes such as heptaldehyde (IId) and isobutyraldehyde (IIe), optimum conditions involved the use of 1-ethoxyvinyl trichloroacetate as the ester component, yielding products (IVd) (60%)§ and (IVe) (40%).

TABLE

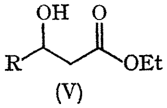
(II) a; $R^1 = p\text{-}NO_2C_6H_4$
b; $R^1 = p\text{-}ClC_6H_4$
c; $R^1 = m\text{-}MeOC_6H_4$
d; $R^1 = n\text{-}C_6H_{13}$
e; $R^1 = Pr^i$
f; $R^1 = Ph$
g; $R^1 = p\text{-}MeOC_6H_4$

(III) a; $R^2 = Me$
b; $R^2 = CH_2Cl$
c; $R^2 = CCl_3$

(IV) a; $R^2 = p\text{-}NO_2C_6H_4$, $R^2 = Me$
b; $R^1 = p\text{-}ClC_6H_4$, $R^2 = Me$
c; $R^1 = m\text{-}MeOC_6H_4$, $R^2 = Me$
d; $R^1 = n\text{-}C_6H_{13}$, $R^2 = CCl_3$
e; $R^1 = Pr^i$, $R^2 = CCl_3$
f; $R^1 = Ph$, $R^2 = CH_2Cl$
g; $R^1 = p\text{-}MeOC_6H_4$, $R^2 = Me$

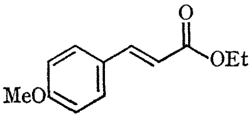


Hydrolysis of the products (IV) to the corresponding alcohols takes place under mild, basic conditions (0·18 N-KOH at room temperature in ethanol for 15 min.) and occurs most readily when the diesters (IV) contain chlorinated acyl groups. For example, (IVd) and (IVf) were transformed in high yields to the 3-hydroxy-esters (Va) (85%) and (Vb) (90%). On the other hand, (IVg) was converted nearly quantitatively into ethyl *p*-methoxycinnamate (VI). The methods described above, employing neutral or mildly acidic conditions for the reaction between aldehyde (II) and ester (III) thus constitute a new way of carrying out the Reformatsky reaction, traditionally run under basic conditions.[2]



(V)

(a) $R = n\text{-}C_6H_{13}$
(b) $R = Ph$



(VI)

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§ When zinc chloride is used as a catalyst, an appreciable yield of ethyl 3-chlorononanate is also obtained.

[1] H. H. Wasserman and J. Solodar, *J. Amer. Chem. Soc.*, 1965, **87**, 4002.

[2] Ethoxyacetylene has been condensed with aldehydes (and other carbonyl compounds) using boron trifluoride as a catalyst to yield αβ-unsaturated esters. H. Vieregge, H. M. Schmidt, J. Renema, H. J. T. Bos, and J. R. Arens, *Rec. Trav. chim.*, 1966, **85**, 929. See also D. H. R. Barton, G. Hewitt, and P. G. Sammes, *J. Chem. Soc.* (*C*), 1969, **16**, for related condensations of 1,1-bisdialkylaminoethenes with aromatic aldehydes to give cinnamoyl amides.