carbons by Ag(I) should be important. For example, recently reported ionization potentials for 1,[6] cubane,[7] and tricyclo[4.1.0.0^{2,7}]heptane[6] are 7.40, 8.74, and 8.15 eV, respectively. Hence, the reduction of silver ion to Ag^0 (IP 7.57 eV) should be energetically favorable with 1 but not with the latter two hydrocarbons. We note, however, that oxidation potentials in methanol, when they are measured, may not follow the same trend as gas-phase ionization potentials, and the above data must be regarded as merely indicative.

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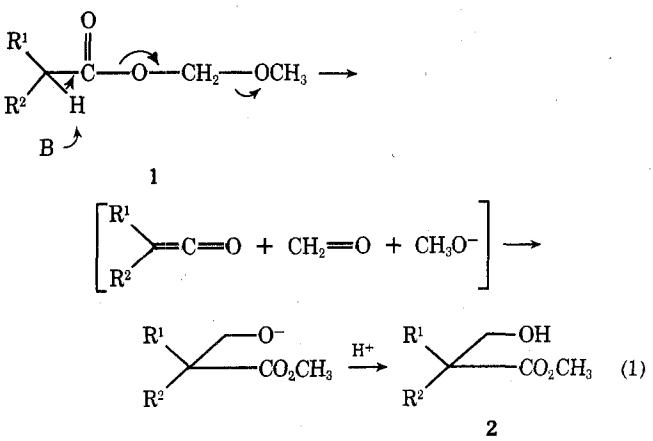
Fragmentation–Recombination of Methoxymethyl Ester Enolates. A Novel Method for Preparation of Hydracrylic and Glycidic Esters

Summary: Methoxymethyl ester enolates undergo fragmentation to ketenes, formaldehyde, and methoxide ion which recombine to give hydracrylic and glycidic esters in good yield.

Sir: A variety of ester enolates have been prepared by reaction of lithium *N*-dialkylamides with esters at low temperature.[1] Although solutions of these ester enolates were considered to be stable even at room temperature, an interesting opportunity for reaction exists with enolates generated from methoxymethyl esters, (eq 1). Thus, heterolytic

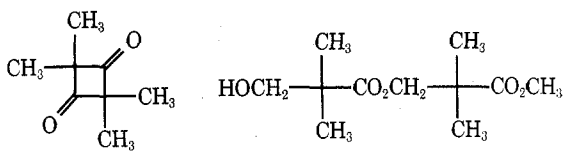


(1)

fragmentation[2] might be expected to occur as shown; in principle, recombination of the fragments should give the more stable hydracrylate ion. Herein, we report the realization of such a fragmentation–recombination and briefly discuss the mechanism and synthetic potential of the process.

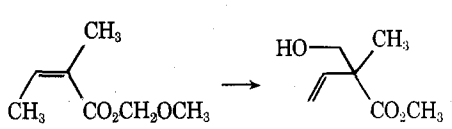
Methoxymethyl esters were conveniently prepared in excellent yield by reaction of sodium carboxylates (sodium hydride + carboxylic acid) with chloromethyl methyl ether in refluxing tetrahydrofuran (THF)–hexamethylphosphoric triamide (HMPA, 1 equiv).

Addition of a THF solution of the methoxymethyl ester derived from isobutyric acid (**1**, $R^1 = R^2 = CH_3$) to 1.1 equiv of lithium diisopropylamide (LDA) in THF at −78° followed by quenching with D_2O at −78° cleanly gave recovered 1 (50% D incorporation).[3] On the other hand, warming the solution of ester enolate to room temperature resulted in isolation of hydracrylate **2** ($R^1 = R^2 = CH_3$, 69% yield). Two minor reaction components were isolated and identified as dimethylketene dimer **3**[4] (~10%) and diester **4** (15%).[5] In similar fashion, except that HMPA was added to



3 **4**

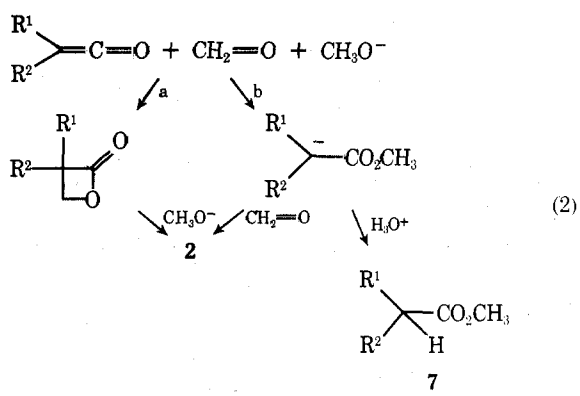
LDA before generation of the ester enolate,[6] the methoxymethyl ester derived from tiglic acid **5** gave the α-vinyl hydracrylate **6** in 61% isolated yield.



5 **6**

That a free alkoxide ion is involved in the process **1** → **2** was convincingly demonstrated by fragmentation–recombination of the ester enolate of **5** in the presence of ethoxymethyl ester enolate **1′** (OCH_3 replaced by OCH_2CH_3, $R^1 = R^2 = CH_3$); VPC comparison of the reaction components with previously isolated materials showed that four hydracrylic esters were present in about equal proportions and that these corresponded to the methyl and ethyl esters of **2** ($R^1 = R^2 = CH_3$) and **6**. Thus, intermediates derived from **1** and **5** must react indiscriminately with either methoxide or ethoxide generated in a fragmentation of the ester enolates (eq 1).[7]

At least two possible recombination paths to **2** have been considered (eq 2): a thermally allowed cycloaddition of ke-



(2)

7

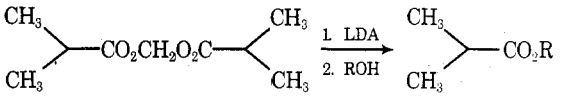
tene with formaldehyde and subsequent methoxide opening of the β-lactone (path a),[8] or ketene attack by methoxide to generate an ester enolate followed by trapping with formaldehyde (path b).

We do not favor path a for two important reasons. First, in all cases of fragmentation–recombination of **1**, trace to significant amounts of untrapped methyl ester **7** were detected; most dramatically, with **1** ($R^1 = CH_3$; $R^2 = OCOC_6H_5$), only methyl ester **7** ($R^1 = CH_3$; R^2 =

Table I
Preparation of 10 from 1 and 7 (R^2 = Br)

No.	R^1	% isolated yield: Fragmentation–recombination of 1 (R^2 = Br)	% isolated yield: Methyl ester 7 (R^2 = Br) enolate trapping with formaldehyde
10a	CH_3	61	58
10b	CH_2CH_3	60	51
10c	$CH(CH_3)_2$	64	61

$OCOC_6H_5$) was isolated in 73% yield. Second, with methylene isobutyrate 8, mainly isobutyric acid (9a) was isolated on quenching the LDA reaction with water and similarly methyl isobutyrate (9b) with methanol. These data indi-



8

9a, R = H
b, R = CH_3

cate that nucleophilic attack of the ketene by methoxide precedes addition of formaldehyde (path b) and that, when the nucleophile generated in the fragmentation step is unreactive (isobutyrate), dimethyl ketene remains in solution to react with added water or methanol.

The viability of the second step in eq 2 (path b) was demonstrated by treatment of methyl ester lithium enolates (generated in the usual manner) with formaldehyde vapors and isolation of the corresponding hydracrylates 2 in yields comparable with those in the fragmentation–recombination process [2, $R^1 = R^2 = CH_3$, 60%; 6, 60% (see Table I)]. Although the condensation of formaldehyde with regiospecifically generated ketone[9] and lactone[10] enolates has recently been reported, the analogous reaction described here with ester enolates seems not to have been previously cited. In any event, trapping ester enolates with formaldehyde and fragmentation–recombination of alkoxymethyl ester enolates should prove useful for preparation of many α,α-disubstituted hydracrylates.[11,12]

We also have shown that these two methods are especially attractive for preparation of glycidic esters 10 derived from formaldehyde and α-bromo esters (Table I). Because the standard Darsens reaction of α-halo esters with formaldehyde gives glycidic esters in low yield,[13] we feel that the methodology described here clearly represents a valuable alternative for preparation of these important synthetic intermediates.[14]

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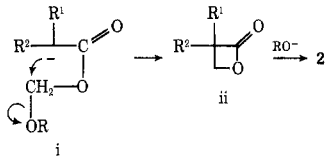
(7) Here, the operationally indistinguishable mechanism involving cyclization of ester enolate i to a β-lactone ii followed by methoxide opening of ii to give 2 was excluded by failure to detect β-lactones in reactions



i ii

of 1, consideration of the highly unfavorable transition state required for closure i → ii, and further suggestive experimental results (vide infra).
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(11) Preliminary experiments indicate that α-monosubstituted hydracrylates may not be attainable by the fragmentation–recombination method; indeed, reactions of LDA with α-monosubstituted methoxymethyl esters have resulted in complex mixtures of products.
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Cleavage of Esters by Superoxide[1]

Summary: The reaction of carboxylic esters with potassium superoxide in benzene in the presence of 18-crown-6 ether produces, upon aqueous work-up, the corresponding carboxylic acid and alcohol in good to excellent yields by a process which appears to involve an initial nucleophilic attack of O_2^- at the carbonyl carbon and by the subsequent formation of intermediate peroxo species.

Sir: The beneficial and deleterious effects of superoxide in biological systems have become increasingly evident in recent years.[2] However, until recently,[3,4,5] virtually nothing was known of the reactivity of superoxide with common biological substrates.[6] Ester and peptide bonds are ubiquitous functionalities in biological systems. Here we wish to report that esters, but *not* amides or nitriles, undergo a reaction with superoxide which results in the cleavage of the ester functionality. Aqueous work-up affords the corresponding carboxylic acid in generally high yield. A summary of the results obtained on treatment of various representative substrates is given in Table I.

$$RCO_2R' \xrightarrow[2.\ H_3O^+]{1.\ KO_2\text{-}18\text{-crown-}6,\ C_6H_6} RCO_2H + R'OH \quad (1)$$

In a typical experiment, a mixture of methyl octanoate (0.529 g, 3.34 mmol) and 18-crown-6 ether[7] (0.264 g, 1.00 mmol) dissolved in dry benzene (20 ml) was added to 0.710 g (10.0 mmol) of powdered potassium superoxide.[8] The resulting mixture was vigorously stirred for 24 h, then cautiously poured into 25 ml of water. The mixture was acidified with 6 M HCl and the organic layer separated. The remaining aqueous phase was extracted with an additional 25 ml of ether and the combined extracts dried ($MgSO_4$). GLC analysis indicated a 98% yield of *n*-octanoic acid.

The cleavage of carboxylate esters by superoxide seems applicable to a spectrum of esters including those of pri-