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Concurrent Reductive Cleavage and Recombination of γ,δ-Alkylidenedioxy-α,β-unsaturated Esters Promoted by Organocuprates

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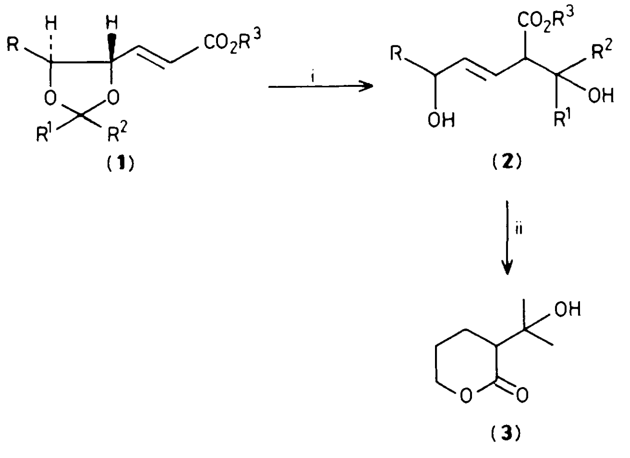
Treatment of γ,δ-alkylidenedioxy-α,β-unsaturated esters (**1**) with lithium dimethylcuprate furnishes β′,δ-dihydroxy-β,γ-unsaturated esters (**2**) in moderate to good yields by concurrent reductive cleavage to ketones (**5**) and enolates (**6**) and their aldolic recombination.

It has been reported that treatment of α,β-unsaturated esters bearing a reducible group on the γ-carbon with lithium dialkylcuprate often gives the corresponding β,γ-unsaturated esters by reductive cleavage of the γ-group[1,2] and migration of the double bond. We report here the reaction with the optically active α,β-unsaturated substrates[3] (**1**) bearing a γ,δ-alkylidenedioxy group which furnished the β′,δ-dihydroxy-β,γ-unsaturated esters† (**2**) in moderate to good yields in one stage. The results are summarized in Table 1.



a : R = H, $R^1 = R^2 = R^3 = Me$
b : R = H, $R^1 = R^2 = Me$, $R^3 = Et$
c : R = H, R^1, $R^2 = -(CH_2)_5-$, $R^3 = Me$
d : R = H, R^1, $R^2 = Me$, $R^3 = CH_2CH{=}CMe_2$
e : R = R^1 = H, R^2 = 3,4-methylenedioxyphenyl, $R^3 = Et$
f : R = *E*-$CH{=}CHCO_2Et$, $R^1 = R^2 = Me$, $R^3 = Et$
g : R = H, $R^1 = R^2 = Me$, $CO_2R^3 = CN$

Scheme 1. *Reagents and conditions:* i, Me_2CuLi, ether, −70 °C; ii, H_2, Pd–C, then pyridinium toluene-*p*-sulphonate, toluene, reflux.

Treatment of the substrates (**1**) with lithium dimethylcuprate (3 equiv.), prepared *in situ* from methyl-lithium and copper(I) iodide,[4] in tetrahydrofuran (THF) at −70 °C afforded the dihydroxy ester (**2**) almost instantaneously. Although some products showed optical activities, their optical purities were found to be negligible. Lithium di-n-butylcuprate[4] in place of lithium dimethylcuprate gave a similar result under the same conditions (entry 4). The same reaction occurred when the corresponding γ,δ-alkylidene-α,β-unsaturated cyanide (**1a**; CO_2R^3 replaced by CN) was used as substrate which afforded the β′,δ-dihydroxy-β,γ-unsaturated cyanide (**2a**; CO_2R^3 replaced by CN) in 42% yield as the sole product (entry 9). The configuration of the alkene bond of the products was determined to be *E* by ^{1}H n.m.r. spectroscopy which showed the alkene protons coupled each other with *J ca.* 15 Hz.‡ This was also supported by their inability to undergo lactone formation. As exemplified by (**2b**), δ-lactone (**3**) could only be formed after hydrogenation of the double bond.

In these reactions, neither the addition products nor the conjugated aldol products were obtained. Moreover, the cyclization product (**9**), indicating the intervention of a radical intermediate,[5] could not be detected when (**1**) was used as

Table 1. Reaction of γ,δ-alkylidenedioxy-α,β-unsaturated esters with lithium dimethylcuprate.

Entry	Substrate	β′, δ-Dihydroxy ester (%)[a]
1	(**1a**)	(**2a**) (61)
2	(**1b**)	(**2b**) (76)
3	(**1c**)	(**2c**) (94)
4	(**1c**) ($Bu^n{}_2CuLi$)	(**2c**) 79)
5	(**1c**) + acetone	(**2c**) (51) + (**2a**) 35
6	(**1d**)	(**2d**) (80)
7	(**1e**)	(no reaction)
8	(**1f**)	(**2f**) (27)
9	(**1g**)	(**2g**) (42)

[a] Isolated yield after silica gel column chromatography.

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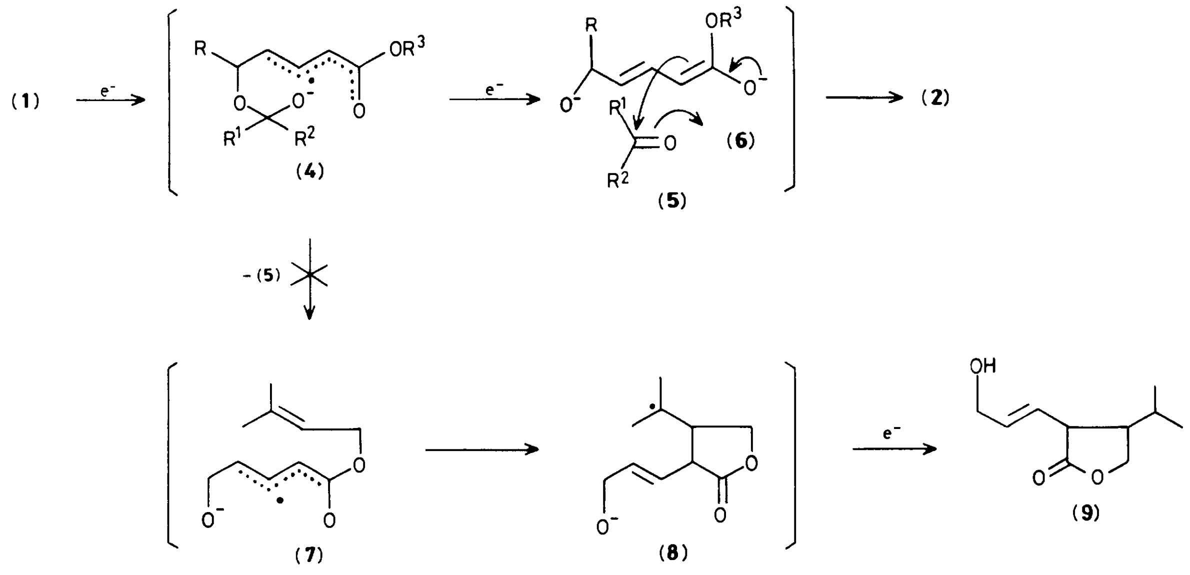
† All new compounds gave satisfactory spectral, microanalytical, and/or high-resolution mass data.

‡ Determined by 500 MHz ^{1}H n.m.r. spectroscopy.



Scheme 2

substrate. Compound (**1**) formed the cleavage–recombination product (**2**), exclusively, in good yield (entry 6). When acetone (1 equiv.) was mixed with the substrate (**1**), a mixture (*ca.* 2:1) of (**2c**) and the cross -coupling product (**2a**) was formed in good total yield under the same treatment (entry 5). These results indicate that the reaction proceeds by reductive cleavage of the γ-oxygen bond accompanied by migration of the double bond forming both ketone (**5**) and conjugated enolate (**6**) followed by aldolic recombination of these species selectively at the α-position of the enolate[6] to furnish the β,γ-unsaturated diol (**2**) (Scheme 2).

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