γ-Substituted Butyrolactones from Acrolein and Carbonyl Compounds

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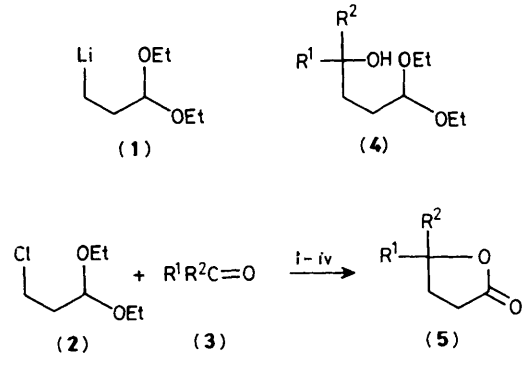
The lithiation of 3-chloropropanal diethyl acetal (easily prepared from acrolein) at −78 °C with lithium naphthalenide followed by reaction with various carbonyl compounds, and final oxidation with *m*-chloroperbenzoic acid leads to γ-substituted butyrolactones.

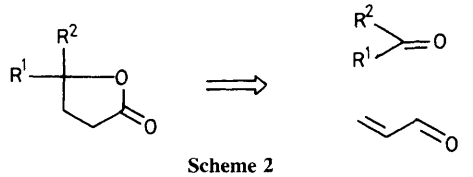
γ-Butyrolactones are an important class of compounds not only because they are present in many natural products,[1] but also because they may be easily transformed into the corresponding butenolides.[2] In the case of the γ-substituted derivatives, the reported methods generally use either sophisticated reagents or several reactions steps.[3] Recently[4] we reported the first preparation of a masked lithium homoenolate (**1**) and a preliminary account of its reactivity toward electrophilic reagents. Here we report use of the reaction of the intermediate (**1**) with carbonyl compounds followed by *in situ* oxidation for the preparation of γ-substituted butyrolactones in a tandem process.

When a tetrahydrofuran (THF) solution of the intermediate (**1**) [obtained by lithiation of 3-chloropropanal diethyl acetal (**2**)† with lithium naphthalenide at −78 °C][4] is treated with various carbonyl compounds (**3**), the expected acetals (**4**) are obtained after hydrolysis. *In situ* oxidation of the acetals (**4**) using *m*-chloroperbenzoic acid affords the butyrolactones (**5**)‡ (Scheme 1 and Table 1).



Scheme 1.‡ *Reagents and conditions:* i, $Li^+C_{10}H_8$, −78 °C; ii, $R^1R^2C{=}O$ (**3**), −78 to 20 °C overnight; iii, NH_4Cl; iv, $3\text{-}ClC_6H_4CO_3H\text{–}BF_3{\cdot}OEt_2$.

In conclusion, the methodology reported here represents a



Scheme 2

† Compound (**2**) is easily prepared by addition of hydrogen chloride to acrolein in anhydrous ethanol. It is also commercially available in technical grade (Aldrich).

‡ *Typical procedure:* to a solution of the chloroacetal (**2**) (15 mmol) in THF (20 ml) was added a THF solution of lithium naphthalenide (32 mmol) at −78 °C under argon, and stirring was continued for 3 h at the same temperature. To the resulting suspension was added the carbonyl compound (**3**) and the mixture was allowed to warm to room temperature overnight. Then it was hydrolysed with aqueous ammonium chloride and extracted with diethyl ether, and the organic layer washed with water and dried with sodium sulphate. The solvents were evaporated, napthalene was removed *in vacuo* (0.001 mmHg; 60 °C bath temperature), and the residue was dissolved in dichloromethane (40 ml). To the resulting solution was added *m*-chloroperbenzoic acid (17 mmol) and boron trifluoride–diethyl ether (3 mmol). After stirring overnight, the resulting suspension was hydrolysed with water, neutralized with sodium hydrogen carbonate, and extracted with ether. The organic layer was washed with water and dried with sodium sulphate. The solvents were evaporated (15 mmHg) and the residue distilled under reduced pressure to afford the products (**5**).

Table 1. γ-Substituted butyrolactones (**5**) from (**2**) and carbonyl compounds (**3**).

Carbonyl compound (**3**)					Selected data		
R^1	R^2	Product (**5**)[a]	% Yield[b]	B.p./°C (*P*/mmHg)	$\nu_{(C=O)}$	$\delta_{(C=O)}$	*m/z* (%)
H	Et	(**5a**)	44	50—52 (10^{-1})	1765	175.6	128 (<1, M^+)
H	Pr^i	(**5b**)	52	57—60 (10^{-1})	1765	175.2	142 (<1, M^+)
H	Ph	(**5c**)	51	96—98 (10^{-1})	1765	176.1	162 (100, M^+)
H	PhCH=CH	(**5d**)	62	62—63 (10^{-4})	1770	177.0	188 (97, M^+)
Me	Ph	(**5e**)	59	55—57 (10^{-4})	1760	176.0	154 (18, M^+)
$-(CH_2)_5-$		(**5f**)	53	44—46 (10^{-4})	1760	176.0	182 (2, M^+)
$-(CH_2)_7-$		(**5g**)	66	60—62 (10^{-4})	1770	176.5	176 (12, M^+)

[a] All compounds (**5**) gave satisfactory i.r., ^1H and ^{13}C n.m.r., and mass spectra. [b] Yield of isolated products, based on the starting compound (**2**).

reasonable route to butyrolactones starting from acrolein† and carbonyl compounds (**3**) (Scheme 2).

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