

3,3-Diethoxypropyl-lithium: A Masked Lithium Propanal Homoenoate

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3,3-Diethoxypropyl-lithium is prepared by lithiation of the corresponding chlorinated precursor with lithium naphthalenide at -78°C ; the reaction of this masked propanal homoenoate with different electrophilic reagents [H_2O , D_2O , $(\text{PhCH}_2)_2\text{S}_2$, $n\text{-C}_3\text{H}_7\text{CHO}$, PhCHO , $n\text{-C}_7\text{H}_{15}\text{CHO}$, PhCH=NPh] leads to the corresponding mono- and bi-functionalized compounds.

The chemistry of homoenoate derivatives has been subject of attention recently,¹ mainly in relation to the homoaldol reaction. Although some of these intermediates are stable species [(1), $\text{M} = \text{SnCl}_3$,^{2a} $\frac{1}{2}\text{Zn}^{2b}$ or ZnI ,^{2c} TiCl_3 ,^{2d}], the derivatives of the main group metals are very unstable species and decompose spontaneously after formation, yielding metallic cyclopropanolates (1').¹ A possible way to overcome this problem is the use of a 'defensive' strategy;^{1c} thus, intermediates (2) ($\text{M} = \text{MgBr}^3$) and (3) ($\text{Z} = \text{PhSO}_2$,^{1c} NO_2 ,^{4a} Ph_3P^+ ,^{4b} or $\text{Ph}_2\text{PO}^{4c}$) have been described.¹ However, the non-stabilized lithium derivative of type (2) ($\text{M} = \text{Li}$) is

unknown because 'it decomposed directly upon formation'.^{1b†} In this communication we describe the first preparation and

† While this manuscript was in preparation a paper was published⁵ which described the preparation of the intermediate (I) by reaction of the corresponding bromo derivative with *t*-butyl-lithium at -78°C .

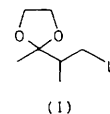
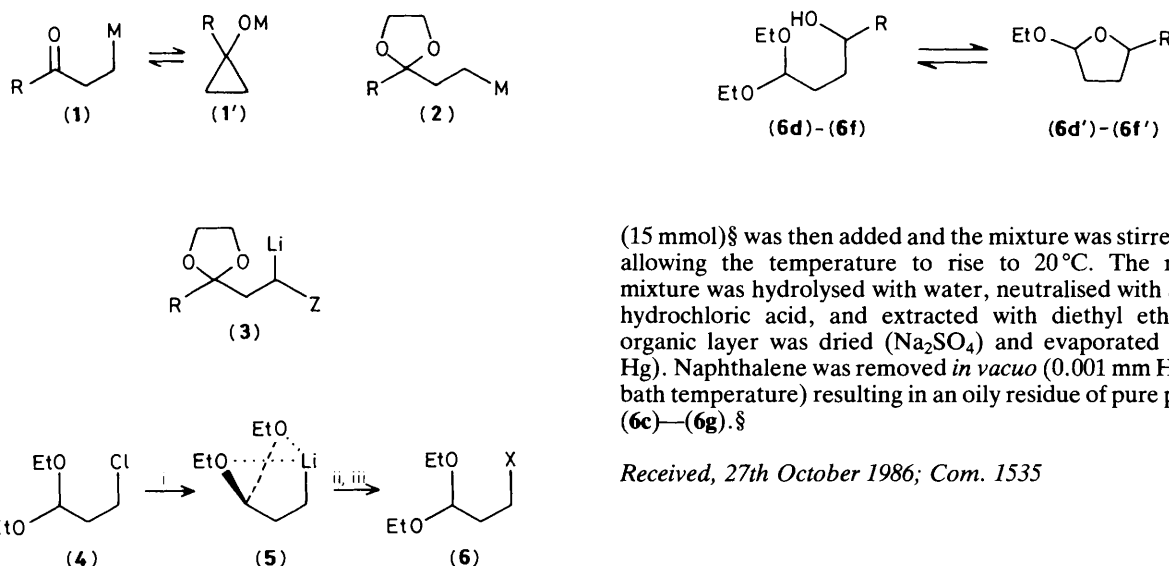


Table 1. Formation of 3,3-diethoxypropyl-lithium (5) and its reaction with electrophiles; preparation of compounds (6).

Product ^a	E ⁺	X	% Yield ^b	Selected spectral data	
				¹³ C n.m.r. (δ) ^c	Mass (m/z, %) ^d
(6a)	H ₂ O	H	80 ^e	8.6, 15.0 (CH ₃ CH ₂ C)	132 (M ⁺ , <1)
(6b)	D ₂ O	D	82 ^e	7.75 (t, J _{CD} 19.3 Hz, CH ₂ D)	133 (M ⁺ , <1)
(6c)	(PhCH ₂) ₂ S ₂	PhCH ₂ S	85 ^f	26.3, 33.3 (SCH ₂ CH ₂)	208 (M ⁺ - EtOH, 19)
(6d)	n-C ₃ H ₇ CHO	n-C ₃ H ₇ CHOH	54 ^f	29.4, 35.0, 73.2 (CH ₂ CH ₂ CHO)	158 (M ⁺ - EtOH, <1)
(6e)	PhCHO	PhCHOH	63 ^f	29.5, 37.1, 73.1 (CH ₂ CH ₂ CHO)	192 (M ⁺ - EtOH, 10)
(6f)	n-C ₇ H ₁₅ CHO	n-C ₇ H ₁₅ CHOH	56 ^f	29.4, 31.6, 70.5 (CH ₂ CH ₂ CHO)	214 (M ⁺ - EtOH, <1)
(6g)	PhCH=NPh	PhCHNPh	70 ^f	30.9, 33.5, 60.8 (CH ₂ CH ₂ CHN)	313 (M ⁺ , 7)

^a All compounds (6) gave satisfactory spectral data (i.r., ¹H and ¹³C n.m.r., and mass spectra). ^b Based on compound (4). Yields of isolated products have not been optimized. ^c CCl₄-D₂O capillary. Recorded using a Varian CFT-80 spectrometer. ^d 70 eV. Obtained using a Hewlett-Packard 5987 spectrometer. ^e This compound was condensed *in vacuo* (0.1 mm Hg) at 20 °C. ^f Oil.



Scheme 1. Reagents and conditions: i, Li⁺C₁₀H₈⁻, -78 °C; ii, E⁺ = H₂O, D₂O, (PhCH₂)₂S₂, n-C₃H₇CHO, PhCHO, n-C₇H₁₅CHO, PhCH=NPh; iii, HCl-H₂O.

application of the masked lithium homoenolate derived from propanal.

The reaction of 3-chloropropanal diethyl acetal (4) with lithium naphthalenide[‡] at -78 °C led to the corresponding 3,3-diethoxypropyl-lithium (5). The *in situ* treatment of this intermediate with different electrophilic reagents (water, deuterium oxide, dibenzyl disulphide, n-butanal, benzaldehyde, n-octanal, or benzylideneaniline) yielded the expected 3-substituted propanal diethyl acetal (6) (Scheme 1 and Table 1).

The products (6d)–(6f), derived from aldehydes, undergo intramolecular cyclization⁷ on standing at room temperature or on distillation⁸ *in vacuo*, affording a mixture of (6) and the cyclic acetal (6').

In a typical reaction, to a solution of 3-chloropropanal diethyl acetal (15 mmol) in tetrahydrofuran (30 ml) was added a solution of lithium naphthalenide in tetrahydrofuran (33 mmol) at -78 °C under argon and stirring was continued for 6 h at the same temperature. The corresponding electrophile

(15 mmol)[§] was then added and the mixture was stirred for 2 h allowing the temperature to rise to 20 °C. The resulting mixture was hydrolysed with water, neutralised with aqueous hydrochloric acid, and extracted with diethyl ether. The organic layer was dried (Na₂SO₄) and evaporated (15 mm Hg). Naphthalene was removed *in vacuo* (0.001 mm Hg; 60 °C bath temperature) resulting in an oily residue of pure products (6c)–(6g).[§]

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[§] When H₂O or D₂O was used as an electrophile a large excess (ca. 100 mmol) was added. In the final work up, the isolation of products (6a) and (6b) was carried out by condensation *in vacuo* (0.1 mm Hg). The purity of all compounds was checked by g.l.c. analysis (Varian Vista 6000 equipped with a Chromosorb G, 1.5% OV-101 column).

[‡] The metallation with lithium powder at low temperature failed.⁶