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

José Barluenga,* Covadonga Rubiera, José R. Fernández, and Miguel Yus

Departamento de Química Organometálica, Facultad de Química, Universidad de Oviedo, 33071-Oviedo, Spain

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 homoenolate with different electrophilic reagents [H_2O, D_2O, $(PhCH_2)_2S_2$, n-C_3H_7CHO, PhCHO, n-$C_7H_{15}CHO$, PhCH=NPh] leads to the corresponding mono- and bi-functionalized compounds.

The chemistry of homoenolate derivatives has been subject of attention recently,[1] mainly in relation to the homoaldol reaction. Although some of these intermediates are stable species [(**1**), M = $SnCl_3$,[2a] $\frac{1}{2}$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**) (M = MgBr[3]) and (**3**) (Z = $PhSO_2$,[1c] NO_2,[4a] Ph_3P^+,[4b] or Ph_2PO[4c]) have been described.[1] However, the non-stabilized lithium derivative of type (**2**) (M = Li) is unknown because ‘it decomposed directly upon formation’.[1b]† In this communication we describe the first preparation and

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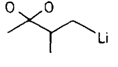
† While this manuscript was in preparation a paper was published[5] which described the preparation of the intermediate (I) by reaction of the corresponding bromo derivative with t-butyl-lithium at −78 °C.

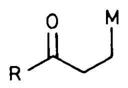


(I)

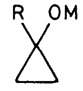
Table 1. Formation of 3,3-diethoxypropyl-lithium (**5**) and its reaction with electrophiles; preparation of compounds (**6**).

Product[a]	E^+	X	% Yield[b]	Selected spectral data ^{13}C n.m.r. (δ)[c]	 Mass (m/z, %)[d]
(**6a**)	H_2O	H	80[e]	8.6, 15.0 (CH_3CH_2C)	132 (M^+, <1)
(**6b**)	D_2O	D	82[e]	7.75 (t, J_{CD} 19.3 Hz, CH_2D)	133 (M^+, <1)
(**6c**)	$(PhCH_2)_2S_2$	$PhCH_2S$	85[f]	26.3, 33.3 (SCH_2CH_2)	208 (M^+ −EtOH, 19)
(**6d**)	$n-C_3H_7CHO$	$n-C_3H_7CHOH$	54[f]	29.4, 35.0, 73.2 (CH_2CH_2CHO)	158 (M^+ −EtOH, <1)
(**6e**)	PhCHO	PhCHOH	63[f]	29.5, 37.1, 73.1 (CH_2CH_2CHO)	192 (M^+ −EtOH, 10)
(**6f**)	$n-C_7H_{15}CHO$	$n-C_7H_{15}CHOH$	56[f]	29.4, 31.6, 70.5 (CH_2CH_2CHO)	214 (M^+ −EtOH, <1)
(**6g**)	PhCH=NPh	PhCHNHPh	70[f]	30.9, 33.5, 60.8 (CH_2CH_2CHN)	313 (M^+, 7)

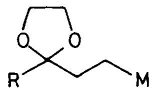
[a] All compounds (**6**) gave satisfactory spectral data (i.r., ^1H and ^{13}C n.m.r., and mass spectra). [b] Based on compound (**4**). Yields of isolated products have not been optimized. [c] CCl_4–D_2O capillary. Recorded using a Varian CFT-80 spectrometer. [d] 70 eV. Obtained using a Hewlett-Packard 5987 spectrometer. [e] This compound was condensed *in vacuo* (0.1 mm Hg) at 20 °C. [f] Oil.



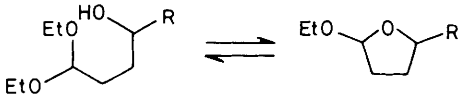
(**1**)



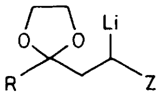
(**1′**)



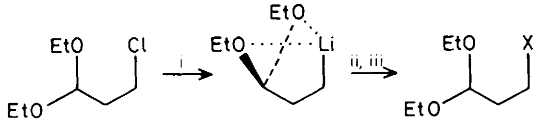
(**2**)



(**6d**)-(**6f**) (**6d′**)-(**6f′**)



(**3**)



(**4**) (**5**) (**6**)

Scheme 1. *Reagents and conditions:* i, $Li^+C_{10}H_8^-$, −78 °C; ii, E^+ = H_2O, D_2O, $(PhCH_2)_2S_2$, $n-C_3H_7CHO$, PhCHO, $n-C_7H_{15}CHO$, PhCH=NPh; iii, HCl–H_2O.

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 cyclization[7] on standing at room temperature or on distillation[8] *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 (Na_2SO_4) 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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‡ The metallation with lithium powder at low temperature failed.[6]

§ When H_2O or D_2O 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).