

CHLORODIDEUTERIOMETHYL-LITHIUM: A USEFUL REAGENT FOR

gem-DIDEUTERATED ORGANIC COMPOUNDS

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SUMMARY

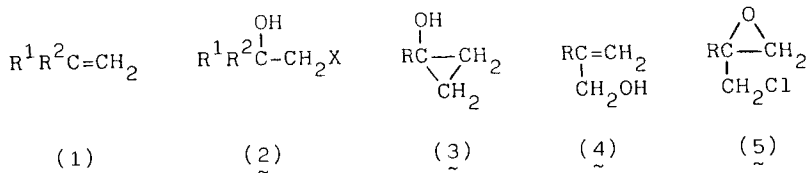
The reaction of ketones (**6**), at -78°C , with *in situ* generated chlorodideuteriomethyl-lithium followed by lithiation leads to the dianionic intermediate (**7**) which yields dideuterioalkenes (**8**) by warming or reacts with electrophiles such as dimethyl disulphide affording the compound (**9**); the same reaction sequence starting from benzoyl chloride leads to the cyclopropanol (**12**); when the intermediate in this last process (**11**) was warmed in absence or presence of lithium iodide the expected products (**13**) or (**14**) are respectively isolated.

Key Words: Chlorodideuteriomethyl-lithium, Deuterioalkenes, Deuterioalcohols, Deuterioepichlorohydrins.

INTRODUCTION

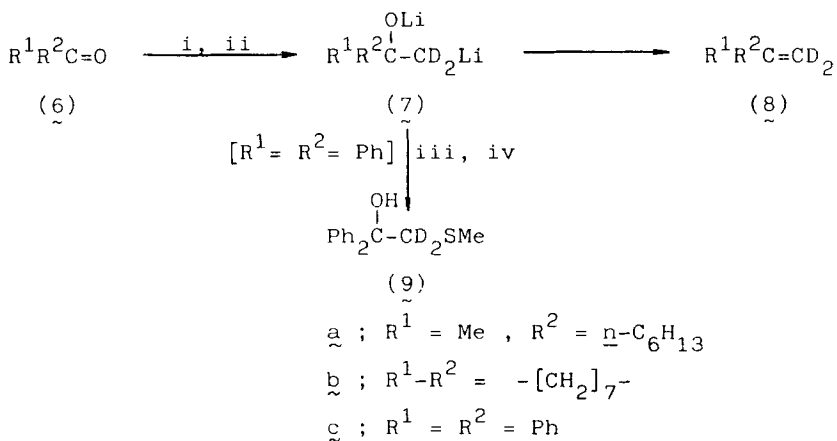
In recent papers we described the use of *in situ* generated chloromethyl-lithium for the synthesis of terminal and exocyclic olefins (**1**),^{1,2} functionalized alcohols (**2**),^{3,2} cyclopropanols (**3**),⁴ allylic alcohols (**4**),^{5,6} and epichlorohydrins (**5**)⁶ by reaction with carbonyl compounds or carboxylic acid chlorides.

Due to the interest of isotopically labeled compounds, we report here the results on the preparation of the corresponding *gem*-dideuterated systems by using chlorodideuteriomethyl-lithium as organometallic reagent and following the same methodology.



RESULTS AND DISCUSSIONS

The reaction of ketones (6) with chlorodideuteriomethyl-lithium (generated *in situ* by treatment of chlorodideuterio-iodomethane with methyl-lithium) at -78°C followed by lithiation with lithium powder at temperatures ranging between -78° and 20°C led to the expected olefins (8) arisen from β -elimination of the β -substituted organolithium intermediates (7). When the lithiation was performed at -78°C using lithium naphthalenide this dianion (7) was stable and reacted with dimethyl disulphide affording the compound (9). (Scheme 1 and Table).

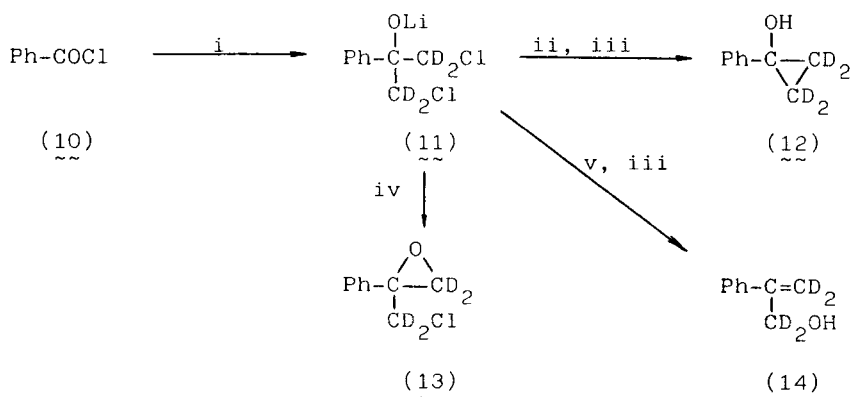


Scheme 1. Reagents and conditions: i, LiCD_2Cl , -78°C ; ii, Li, -78° to 20°C [for (8)] or $\text{Li}^+\text{C}_{10}\text{H}_8^-$, -78°C [for (9)]; iii, Me_2S_2 , -78° to 20°C ; iv, $\text{HCl-H}_2\text{O}$.

Table Preparation of compounds (8), (9), and (12)-(14)

Starting material	Product		
	no.	% Yield ^a	B.p. /°C (mm Hg) ^b
(6a)	(8a)	95	130-134 (760)
(6b)	(8b)	80	54-56 (0.1)
(6c)	(9)	95	85-88 (0.01)
(10)	(12)	80	103-105 (20)
(10)	(13)	90	56-60 (0.01)
(10)	(14)	85	57-61 (0.01)

^a Isolated yield based on the starting carbonyl compounds (6) or (10). ^b Distillation interval.



Scheme 2. Reagents and conditions: i, 2 LiCD₂Cl-LiBr, -78°C; ii, Li, -50°C; iii, HCl-H₂O; iv, -78° to 20°C; v, LiI, -78° to 20°C.

The possibility of obtaining isotopically labeled compounds of the type (3)-(5) was tested starting from benzoyl chloride (10). Thus, the reaction of this starting material with chlorodideuteriomethyl-lithium (1:2 molar ratio) in the presence of lithium bromide at -78°C yielded the intermediate (11), which by lithiation using lithium 1-dimethylamino-naphthalenide at -50°C yielded the corresponding cyclopropanol

(12). When the cooled solution of (11) was allowed to warm to room temperature in absence of lithium iodide the epichlorohydrin (13) was isolated as the sole reaction product. However in the presence of lithium iodide the same last warming afforded the allylic alcohol (14). (Scheme 2 and Table)

EXPERIMENTAL

The experimental techniques and spectroscopic instrumentation used in the course of this work were as described in ref. 2. All ^1H and ^{13}C N.m.r. spectra were recorded using a Bruker AC-300 instrument.

Chlorodideuterioiodomethane was prepared in ca.60% yield following the method described in the literature for Chloriodomethane⁷, b.p. 105-109°C at 760 mmHg, δ_{C} (neat) 3.4 (quintet J_{CD} 27.1 Hz); m/z 180 ($\text{M}^+ + 2$, 9%), 178 (M^+ , 33), 143 (19), 127 (100), 53 (13), 51 (31), and 35 (13).

Deuterioalkenes (8): General Procedure.- These products were prepared by the same method as for the corresponding undeuteriated compounds^{1,2} in a 2 mmol scale. 1,1-Dideuterio-2-methyl-1-octene (8a), ν_{max} (film) 1605 cm^{-1} (C=C); δ_{H} (CCl_4) 0.9 (3 H, t J 6 Hz, CH_3CH_2), 1.2-1.5 [8 H, m, (CH_2)₄CH₃], 1.7 (3 H, s, $\text{CH}_3\text{C}=\text{C}$), and 1.9 (2 H, t, J 7 Hz, $\text{CH}_2\text{C}=\text{C}$); δ_{C} (CCl_4) 14.0 (CH_3CH_2) 22.6, 23.5, 27.5, 29.0, 31.7, and 37.6 (5 x CH_2 and $\text{CH}_3\text{C}=\text{C}$), 109.4 (quintet J_{CD} 23.5 Hz, CD_2), and 144.8 ($\text{C}=\text{CD}_2$); m/z 128 (M^+ , 10%), 71 (28), 59 (24), 58 (100), 57 (16), 55 (16), 43 (15), 42 (11), and 41 (13). Dideuterio-methylenecyclooctane (8b), ν_{max} (film) 1645 cm^{-1} (C=C); δ_{H} (CCl_4) 1.5-2.0 (10 H, m, 5 x CH_2) and 2.0-2.5 (4 H, m, 2 x $\text{CH}_2\text{C}=\text{C}$); δ_{C} (CCl_4) 25.8, 26.7, 27.4, and 35.1 (7 x CH_2), 110.7 (quintet, J_{CD} 23.5 Hz, CD_2), and 151.0 ($\text{C}=\text{CD}_2$); m/z 126 (M^+ , 6%), 98 (100), 97 (37), 84 (32), 83 (90), 82 (27), 81 (98), 71 (32), 70 (33), 69 (35), 68 (39), 67 (66), 58 (30), 57 (27), 56 (19), 55 (29), 54 (35), 53 (13), 42 (17), 41 (33), and 39 (18).

2,2-Dideuterio-2-methylthio-1,1-diphenylethanol (9).- This compound was prepared by the same method as for the corresponding undeuteriated compound^{2,3} in a 2 mmol scale, ν_{max} (film) 3250 (OH), 3020, 1600, and 1490 cm^{-1} (Ph); δ_{H} (CDCl_3) 1.7 (3 H, s, CH_3), 3.6 (1 H, s, OH), and 6.8-7.3 (10 H, m, Ph); δ_{C} (CDCl_3) 16.8 (CH_3), 47.3 (quintet J_{CD} 22.1 Hz CD_2), 76.7 (CO), 125.6, 126.5, 127.6, and 145.2 (Ph); m/z 227 ($\text{M}^+ - \text{H}_2\text{O}$, 2%), 184 (31), 183 (100), 105 (93), and 77 (36).

2,2,3,3-Tetradeuterio-1-phenylcyclopropanol (12).- This product was prepared by the same method as for the corresponding undeuteriated compound⁴ in a 2 mmol scale, $\nu_{\max.}$ (CCl₄) 3380 (OH), 3060, 1600, and 1500 cm⁻¹ (Ph); δ_{H} (CDCl₃) 3.5 (1 H, s, OH) and 7.0-7.8 (5 H, m, Ph); δ_{C} (CDCl₃) 16.7 (quintet J_{CD} 24.2 Hz, 2 x CD₂), 55.7 (CO), 124.2, 126.0, 128.0, and 144.2 (Ph); m/z 138 (M⁺, 28%), 137 (100), 106 (14), 105 (95), 93 (11), 80 (13), 78 (25), 77 (71), 58 (23), and 51 (19).

2-(Chlorodideuteriomethyl)-3,3-dideuterio-2-phenyloxirane (13).- This compound was prepared by the same method as for the corresponding undeuteriated compound⁶ in a 2 mmol scale, $\nu_{\max.}$ (film) 3060, 1610, and 1490 cm⁻¹ (Ph); δ_{H} (CDCl₃) 7.2-7.4 (5 H, m, Ph); δ_{C} (CDCl₃) 47.0 (quintet J_{CD} 23.1 Hz, CD₂Cl), 54.3 (quintet J_{CD} 26.9 Hz, CD₂O), 58.7 (CO), 125.9, 128.0, 128.1, and 136.4 (Ph); m/z 174 (M⁺ + 2, 5%), 172 (M⁺, 15), 171 (26), 137 (18), 107 (49), 106 (18), 105 (100), 93 (45), 79 (16), 78 (15), 77 (14), and 51 (12).

1,1,2,2-Tetradeuterio-2-phenylprop-2-en-1-ol (14).- This compound was prepared by the same method as for the corresponding undeuteriated compound^{5,6} in a 2 mmol scale, $\nu_{\max.}$ (film) 3360 (OH), 3070, 1630, and 1500 cm⁻¹ (Ph); δ_{H} (CDCl₃) 2.6 (1 H, s, OH) and 7.1-7.4 (5 H, m, Ph); δ_{C} (CDCl₃) 63.7 (quintet J_{CD} 21.4 Hz, CD₂O), 111.7 (quintet J_{CD} 24.6 Hz, CD₂=C), 125.8, 127.6, 128.2, and 138.4 (Ph), and 146.8 (C=CD₂); m/z 138 (M⁺, 61%), 137 (27), 118 (12), 108 (43), 106 (17), 105 (100), 95 (18), 94 (50), 93 (20), 92 (24), 80 (24), 79 (50), 78 (43), 77 (24), 52 (14), and 51 (28).

Acknowledgements

We wish to acknowledge Dr. Pablo Bernad, Servicio de Espectrometría de Masas, Universidad de Oviedo for mass spectra determinations.

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