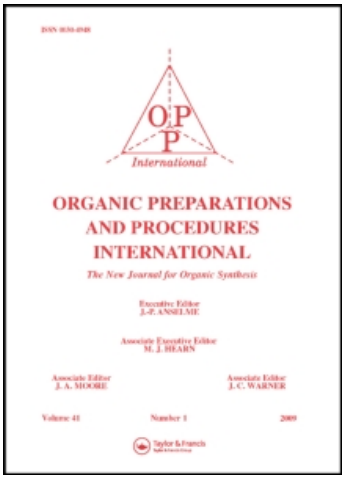

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SYNTHESIS OF 1,1-BIS(HYDROXYMETHYL)CYCLOPROPANES

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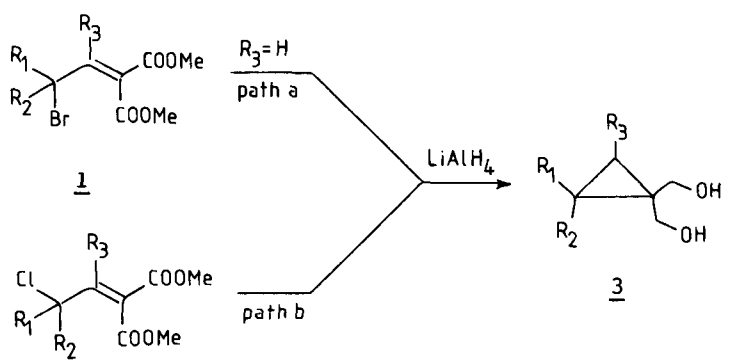
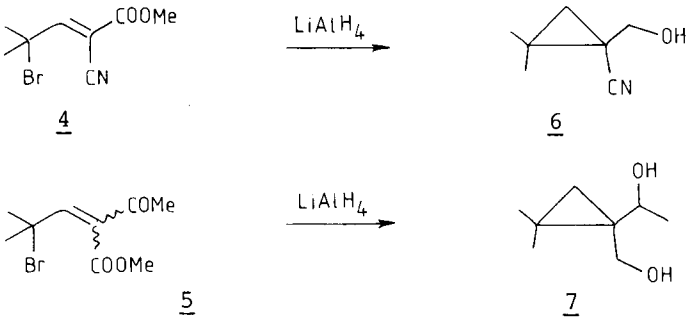
In our efforts to further the use of doubly activated allyl halides in the synthesis of small ring compounds,[1] we now report a facile synthesis of 1,1-bis(hydroxymethyl)cyclopropanes 3 by the reaction of halogenated alkylidene malonates 1, 2 with lithium aluminium hydride in ether.



Only few reports deal with the synthesis of hydroxymethylcyclopropanes. Primary cyclopropylcarbinols are obtained by reduction with lithium aluminium hydride of the corresponding cyclopropane esters.[2-4] Other methods involved diazo addition to allylic alcohols,[5] treatment of the dibromohydrin of pentaerythritol with zinc dust[6] and reduction of cyclic acylals with lithium aluminium hydride.[7]

Our method required 2-bromoalkylidene malonates 2 prepared by a Knoevenagel condensation of aliphatic aldehydes with dimethyl malonate, followed by bromination as previously described.[1-3] Treatment of these electrophilic allyl halides with an excess of lithium aluminium hydride in dry ether at 0° gave 1,1-bis(hydroxymethyl)cyclopropanes 3 in high yields. The same compounds were also obtained when 2-chloroalkylidene malonates, derived by condensation from α-chloroketones with dimethyl malonate in the presence of titanium tetrachloride and pyridine,[8] were treated with lithium aluminium hydride. 2-Methyl, 2-phenyl and 2,3-dimethyl derivatives 3 were readily synthesized by the latter method.

Under the same conditions the reaction of methyl 4-bromo-2-cyano-4-methyl-2-pentenoate 4 and methyl 2-acetyl-4-bromo-4-methyl-2-pentenoate 5 with lithium aluminium hydride gave 1-cyano-2,2-dimethyl-1-hydroxymethylcyclopropane 6 and 2,2-dimethyl-1-(1-hydroxyethyl)-1-hydroxymethylcyclopropane 7 respectively.



4 6

5 7

The reaction may involve a nucleophilic addition of an hydride anion at the double bond generating a carbanion stabilized by two electron withdrawing groups. Intramolecular nucleophilic substitution affords an intermediate cyclopropane

dicarboxylate. Further reduction of the ester functions gave the cyclopropanes 3.

TABLE I : Synthesis of 1,1-Bis(hydroxymethyl)cyclopropanes 3

Compound	R_1	R_2	R_3	Yield (%)	bp. (mmHg) mp. (°C)
3a	H	H	H	74	121°/13 lit.[8] 120°/12
3b	Me	H	H	58 (47)*	135°/18
3c	Et	H	H	61	132°/12
3d	Pr	H	H	44	84°/0.01
3e	iPr	H	H	78	79°/0.01
3f	H	H	C_6H_5	41*	130°/0.09
					68° lit.[9] 65-71°C
3g	Me	Me	H	71	135°/16
					59°
3h	Me	Et	H	81	47°
3i	Et	Et	H	80	70°
3j	cyclohexyl		H	83	80°
3k	Me	H	Me	38*	138°/12

* By path b

All compounds gave satisfactory microanalysis : C ± 0.15; H ± 0.08

EXPERIMENTAL

Infrared spectra were recorded on a Perkin-Elmer 257 spectrometer. NMR spectra were obtained with a Varian T-60 (CCl_4 solutions with TMS as the internal standard). Mass spectra were obtained with a A.E.I. MS 20 mass spectrometer coupled with a Pye Unicam gas chromatograph (1.5 m SE 30, 3%). Melting points were determined on a Kofler hot-stage. The starting materials 1 and 2 were prepared according to previously reported methods.[1,8]

1,1-Bis(hydroxymethyl)cyclopropanes (3). A solution of 0.02 mole allyl halide 1 or 2 in 25 ml of dry ether was added dropwise to a suspension of 0.05 mole lithium aluminium hydride in 25 ml of dry ether with stirring at 0°. After stirring for an additional 12 hrs, the reaction mixture was poured out into a mixture of 50 ml ether and 50 ml water. The organic layer was separated and the aqueous phase was extracted with ether (2x 100 ml). The combined ethereal extracts were dried and the solvent evaporated in vacuo. The crude cyclopropane was purified by vacuum distillation and/or recrystallization from carbon tetrachloride/hexane. The structure of the cyclopropanes 3 was fully determined by spectrometric methods. The spectrometric properties are examplified by the data of 3b and 3g. Full spectrometric data of compounds 3 are available upon request at the author's address.

2-Methyl-1,1-bis(hydroxymethyl)cyclopropane 3b.

NMR : 0.1-0.85(2H, m, CH_2); 1.05-1.30(4H, m, CH_3, CH); 3.38(2H, s, CH_2-O); 3.59(2H, q, J_{AB} = 13.8Hz, CH_2-O); 4.15(2H, s broad, OH)

Mass spectrum m/e : 116(M^+, 1); 99(2); 98(6); 97(5); 85(8); 83(19); 80(9); 79(11); 74(22); 73(24); 72(74); 71(14); 70(13); 69(32); 68(26); 67(29); 57(67); 56(97); 55(67); 54(19); 45(38); 43(59); 42(32); 41(100); 39(38).

2,2-Dimethyl-1,1-bis(hydroxymethyl)cyclopropane 3g.

NMR : 0.27(2H, s, CH_2); 1.18(6H, s, $(CH_3)_2$); 3.49(2H, d, J_{AB}= 11.0 Hz, CH_2-O); 3.87(2H, d, J_{AB}=11.0 Hz, CH_2-O); 4.40 (2H, s broad, OH).

Mass spectrum m/e : 97(5); 83(5); 82(8); 81(14); 79(15); 72(11); 69(10); 67(11); 59(100); 57(18); 56(20); 55(23); 54(6); 53(9); 43(36); 41(50); 39(22).

1-Cyano-2,2-dimethyl-1-hydroxymethylcyclopropane (6). Yield : 57%; bp. 117-120°/13 mm Hg. IR (neat) : 2240 cm^{-1} (CN). NMR : δ 0.85(1H, d, J_{AB} = 5.8Hz, $C\overset{H}{\underset{H}{<}}$); 1.05(1H, d, J_{AB} = 5.8Hz, $C\overset{H}{\underset{H}{<}}$); 1.25(3H, s, CH_3); 1.37(3H, s, CH_3); 3.35(1H, s broad, OH); 3.54 (1H, d, J_{AB} = 12.0Hz, CH_2-O); 3.86(1H, d, J_{AB} = 12.0Hz,CH_2-O). Mass spectrum m/e : 107(74); 106(37); 94(24); 92(67); 81(23); 80(68); 79(70); 68(29); 67(61); 66(24); 59(25); 56(24); 55(42); 54(33); 53(32); 43(29); 42(27); 41(100); 40(28); 39(63).

2,2-Dimethyl-1-(1-hydroxymethyl)-1-hydroxymethylcyclopropane (7). Yield : 78%; bp. 90-93°/0.05 mm Hg. NMR : δ 0.10(1H, d, J_{AB} = 4.4Hz, $C\overset{H}{\underset{H}{<}}$); 0.17(1H, d, J_{AB} = 4.4Hz, $C\overset{H}{\underset{H}{<}}$); 1.26(6H, s, CH_3); 1.30(3H, d, J = 6.1Hz, $C\underline{H}_3CH$); 3.22(1H, d, J_{AB} = 11.9Hz, CH_2-O); 3.60(1H, q, J = 6.1Hz, $CH_3C\underline{H}$); 4.15(1H, s broad, OH); 4.18(1H, d, J_{AB} = 11.9Hz, CH_2-O-). Mass spectrum m/e : 126(3); 93(15); 86(19); 81(10); 71(17); 70(14); 69(17); 68(52); 67(26); 59(100); 57(10); 56(11); 56(32); 55(32); 53(8); 45(12); 43(54); 41(29); 39(12).

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