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REACTIONS OF ORGANOMAGNESIUM AND ORGANOLITHIUM COMPOUNDS WITH DIETHYL (2,3-EPOXYBUTYLIDENE)MALONATE. A SIMPLE SYNTHESIS OF CYCLOPROPANE CARBOXYLATES

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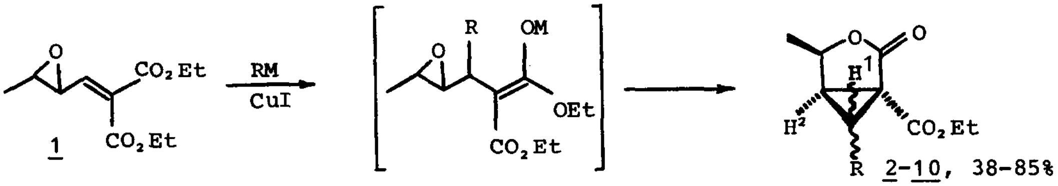
Summary: Reactions of diethyl (2,3-epoxybutylidene)malonate 1 with various magnesium and lithium organics afford lactones 2-10, each containing a cyclopropane fragment.

Different cyclopropanes containing functional groups can be effectively synthesized via the conjugated addition of nucleophiles to γ-halogen-α,β-unsaturated carbonyl substrates and the subsequent ring-closure of the resulting enolates (MIRC-reactions)[1-9]. Halogen derivatives of alkyl crotonates[1-5], diethyl alkylidenemalonates[6-8], or unsaturated acylphosphoranes[9] were successfully used in the reactions earlier. This communication is to show diethyl (2-alkenylidene)malonate monoepoxides to be potential substrates for the MIRC-reactions.

On treatment with either a Grignard reagent or a lithium organic compound in ether (-78 → 20°C, 3 h) in the presence of 5 mol % CuI, the epoxide 1 has been found[10] to lead to cyclopropane bearing lactones 2-10 (Table 1).



R= Me (2), Pr (3), CH_2=CH (4), Z-i-BuCH=CH (5), 1-cyclohexenyl (6), 1,3-butadien-2-yl (7), Ph (8), PrC≡C (9), PhC≡C (10); M= Li, MgCl, MgBr, MgI.

As it follows from the ^1H NMR spectral analysis, the substituent R and the lactone ring are preferably trans-positioned in 2-10. The values of H^1-H^2-coupling constants in the isomerically pure cyclopropanes 2, 5, 7, 8 are between 4.5 and 5.1 Hz, while those in compounds 4 and 10 are 4.5 and 8 Hz for the major and minor components.

According to the data given in Table 1, the maximum stereoselectivity is attained with cyclopropanes 2, 5, 7, 8 (minor isomers have not been registered by the ^1H and ^{13}C NMR spectroscopy), the ratio E/Z being otherwise varied within 60:40 - 92:8 with the rest.

Table 1. Reactions of Epoxide 1 with Mg and Li Organic Compounds.

Reagent	Product'	Yield,%^{a}	E/Z^b
MeMgI	2	65	>95:5
PrMgBr	3	85	60:40
CH_2=CHMgBr	4	70	76:24
Z-i-BuCH=CHLi	5	75	>95:5
(1-cyclohexenyl)Li	6	66	92:8
CH_2=CHC(MgCl)=CH_2	7	72	>95:5
PhMgBr	8	69	>95:5
PrC≡CLi	9	38	75:25
PhC≡CLi	10	66	82:18

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[a] the yields are given for isolated products;
[b] by the NMR spectral data.

A typical experimental procedure for the synthesis of lactones 2-10 is as follows. A solution of MeMgI (2.1 mmole) in ether (1 ml) was added to a solution of epoxide 1 (456 mg, 2 mmole) in ether (15 ml) with CuI (19 mg, 0.1 mmole) at -78°C under Ar. The reaction mixture was stirred for 15 min at -78°C, then heated to 20°C for 3 h, and hydrolyzed with 8% HCl (10 ml). A crude product was extracted with ether; the organic layer was dried with $MgSO_4$ and concentrated. The cyclopropane 2 was isolated as a colorless oil (257 mg, 65%) by column chromatography [silica gel (L 40/100), hexane/ether, 2:1].

m/e 198(M^+); ^{1}H NMR ($CDCl_3$)δ 1.35(3H, t, J= 7.2 Hz), 1.35(3H, d, J= 5 Hz), 1.38(3H, d, J= 5 Hz), 1.8(1H, dq, J_1=J_2= 5 Hz), 2.55(1H, dd, J_1=J_2= 5 Hz), 4.32(2H, q, J= 7.2 Hz), 4.8(1H, dq, J_1=J_2= 5 Hz);^{13}C NMR($CDCl_3$) δ 11.92q, 14.30q, 17.50q, 26.33d, 35.98d, 36.46s, 61.82t, 73.96d, 165.67s, 170.67s; IR(film): 1780, 1720 cm^{-1}.

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