Reaction of Di(bromomagnesio)alkanes with Lactones

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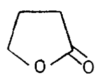
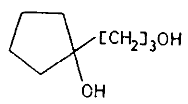
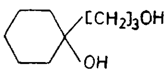
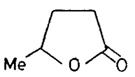
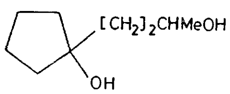
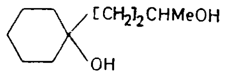
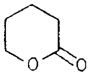
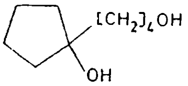
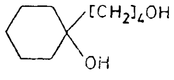
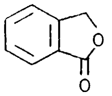
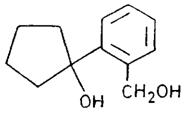
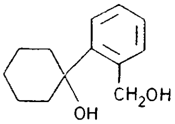
Summary The action of the di(bromomagnesio)alkanes $BrMg[CH_2]_4MgBr$ and $BrMg[CH_2]_5MgBr$ on γ- and δ-lactones leads, after cyclopentyl and cyclohexyl annelation, to the formation of 1-(3-hydroxyalkyl)- and 1-(4-hydroxyalkyl)-cycloalkanols.

ALTHOUGH the reaction between di(bromomagnesio)alkanes and esters was investigated some time ago,[1] the corresponding reaction with lactones has not been studied. We now report preliminary results of a study of the reaction of di(bromomagnesio)alkanes with lactones. The reaction with butane-1,4-diyl- and pentane-1,5-diyl-dimagnesium dibromide occurs by addition of the two nucleophilic centres of the dimagnesium on the carbonyl of the lactone. Consequently, cyclopentane and cyclohexane rings are formed leading to the synthesis of 1-(ω-hydroxyalkyl)cycloalkanols; for example, 1-(3-hydroxyalkyl)cyclalkanols are obtained from γ-lactones and 1-(4-hydroxyalkyl)cycloalkanols from δ-lactones. Furthermore, this method can be extended to aromatic lactones such as phthalide and provides a new synthesis of *o*-(1-hydroxycyclopentyl)- and *o*-(1-hydroxycyclohexyl)-benzyl alcohol.

Alternative preparations[2–8] of these compounds involve several steps and the overall yields are lower. The diols synthesized in this work are shown in the Table. In a typical preparation, the lactone (0·06 mol) in anhydrous tetrahydrofuran (THF) (50 ml) was added with vigorous stirring under nitrogen to the di(bromomagnesio)alkane (0·06 mol) in anhydrous THF (150 ml). The mixture was left overnight under nitrogen. After hydrolysis with saturated aqueous ammonium chloride and work-up in the usual manner, the diols were isolated by fractional distilla-

TABLE

Lactone	Product with $BrMg[CH_2]_4MgBr$	Product with $BrMg[CH_2]_5MgBr$
	 (1) 88%[a]	 (5) 89%[b]
	 (2) 71%	 (6) 72%
	 (3) 76%[c]	 (7) 78%[d]
	 (4) 63%	 (8) 67%[e]

[a] Ref. 2. [b] Refs. 2—5. [c] Ref. 6. [d] Ref. 7. [e] Ref. 8.

tion [(**1**)—(**3**); (**5**)—(**7**)] or by chromatography through silica gel, with ether–pentane (1 : 1) as eluant [(**4**), (**8**)]. The diols were characterized by i.r. and ^{1}H n.m.r. spectroscopy, and also by elemental analysis for the new compounds (**2**), (**4**), and (**6**).†

(*Received, 27th March* 1979; *Com.* 314.)

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† Compound (**2**): b.p. 104—106 °C at 0·3 mmHg; m.p. 88—89 °C (from Et_2O–n-pentane), ν_{max} (OH) 3305 cm^{-1}, δ ($CDCl_3$; Me_4Si) 1·22 (d, *J* 6 Hz, Me), 1·44—1·91 (m, 6 × CH_2), 2·11—2·44 (br s, 2 × OH), and 3·86 (m, C*H*Me); (**4**): m.p. 50—51 °C (from Et_2O–n-pentane), i.r. and n.m.r. data comparable to those for (**2**); (**6**): b.p. 100—103 °C at 0·1 mmHg, i.r. and n.m.r. data comparable to those for (**2**).

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