

A NEW SYNTHESIS OF α -METHYLENE- γ -BUTYROLACTONES

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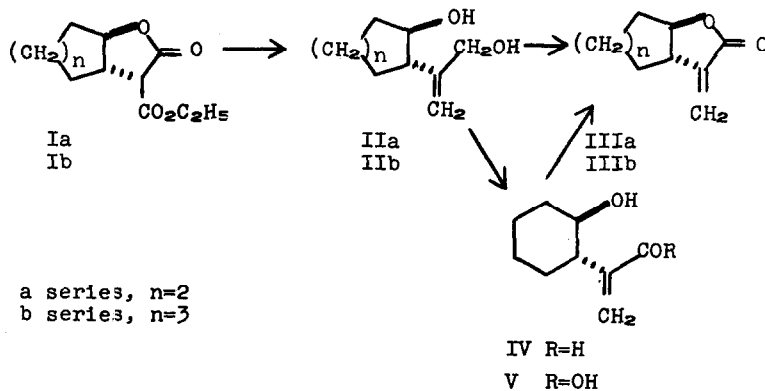
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The α -methylene- γ -butyrolactone grouping is a structural feature shared by various perhydroazulenic¹, perhydronaphthalenic², and medium-ring sesquiterpenes³ along with certain naturally-occurring antibiotics⁴. Our interest in the synthesis of these substances prompted a search for a convenient preparation of fused-ring α -methylene lactones such as IIIa⁵ and IIIb.

Our approach is based on the fact that, β -ketoesters, β -keto aldehydes and β -diketones are reduced, via their enolates, to allylic alcohols by lithium aluminum hydride⁶. Mechanistic considerations led us to believe that malonic ester derivatives such as I should undergo a similar reductive elimination⁷ to furnish diols such as II. Preliminary progress along these lines is highly promising and constitutes the subject of this report.

Condensation of diethyl sodiomalonate with cyclohexene oxide afforded lactone ester Ia⁹. Cycloheptene oxide gave the homologous lactone ester Ib⁹ [48% yield, b.p. 136-138°/0.5 mm.; $\lambda_{\text{max}}^{\text{film}}$ 5.61 μ (γ -lactone CO), 5.78 μ (ester CO); C, 63.7; H, 7.9]. The lactone ester Ia and Ib were converted to their enolates in ether-tetrahydrofuran or ether-dimethoxyethane with sodium hydride. The resulting slurries were reduced with excess lithium aluminum hydride and after four to twelve hours the methylene diols were purified by chromatography on silica (IIa, 40% yield, m.p. 66-67.5°; C, 69.1; H, 10.5; IIb, 46% yield, m.p. 58-58.5°; C, 70.5; H, 10.7).



Diol IIa was selectively oxidized with manganese dioxide¹⁰ to the hydroxy aldehyde IV [83% yield, b.p. 50-60° (bath temp.)/0.03 mm.; $\lambda_{\text{max}}^{\text{film}}$ 2.94 μ (OH), 3.70 μ (aldehyde CH), 5.91 μ (conj. CO), 6.17 μ (conj. C=C); C, 69.9; H, 9.2]. Further oxidation with silver oxide¹¹ afforded the hydroxy

acid V [94% yield, m.p. 84.5-85.5°; $\lambda_{\max}^{\text{CHCl}_3}$ 2.8-4.2 μ (bonded OH), 5.90 μ (conj. CO), 6.17 μ (conj. C=C); C, 63.6; H, 8.2] which was converted to the α -methylene lactone IIIa [60% yield, b.p. 70° (bath temp.)/0.10 mm.; $\lambda_{\max}^{\text{film}}$ 5.65 μ (γ -lactone CO), 5.99 μ (C=C); C, 71.0; H, 8.0] using dicyclohexylcarbodiimide in pyridine.¹²

Oxidation of diol IIb with manganese dioxide in benzene afforded lactone IIIb [87% yield, b.p. 60° (bath temp.)/0.03 mm.; $\lambda_{\max}^{\text{film}}$ 5.67 μ (γ -lactone CO), 6.0 μ (conj. C=C); C, 72.2; H, 8.5]. The contrasting formation of hydroxy aldehyde IV from diol IIa is a consequence of the strain associated with the required lactol precursor of lactone IIIa but not IIIb.¹³ Acyclic diols related to II are also readily oxidized to α -methylene lactones with manganese dioxide¹⁴. We anticipate a similar direct oxidation of cis-analogs of diol IIa to cis-fused α -methylene- γ -lactones related to IIIa.

Table I

Nuclear Magnetic Resonance of C=CH₂*

Compound	$\delta_{\text{TMS}}^{\text{CCl}_4}$ (ppm)	Multiplicity	J(cps)
IIa	5.01, 4.86	singlet	
IIb	5.03, 4.88	singlet	
IV	6.26, 6.01	singlet	
V	6.32, 5.65	singlet	
IIIa	5.91, 5.34	doublet	3
IIIb	6.18, 5.45	doublet	3

*A Varian A60 spectrometer was used.

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