

NEW METHODS FOR α -METHYLENATION OF γ -BUTYROLACTONES

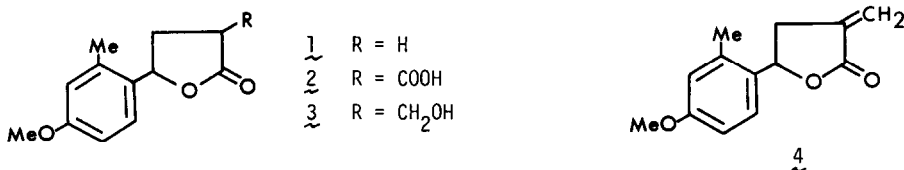
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In certain natural products, there is found the structural unit of the α -methylene- γ -butyrolactone grouping, which often reveals the biological activity.¹ In recent years, construction of this structural unit received attention, and a number of synthetic procedures for this group have been developed.² In the present paper, two methods of introducing the α -methylene function into the γ -lactone moiety under mild conditions are described; α -methylenation of the δ -lactone grouping was also effected.

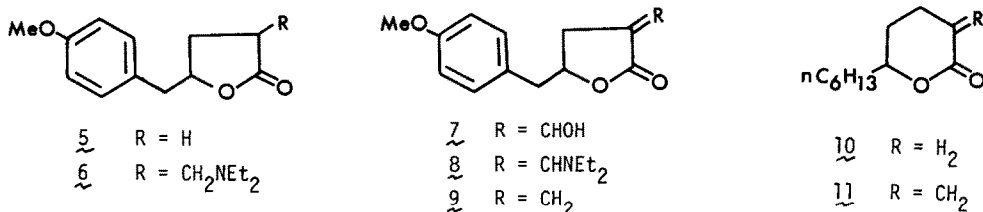
I. Carboxylation of the γ -butyrolactone (1)^{3,4,5} (liquid) with methyl methoxymagnesium carbonate^{2d,6} (20 molar equiv) in DMF (135°, 6 hr) afforded the acid (2),⁴ which, without purification, was reacted first with *N,N'*-carbonyldiimidazole⁷ (2 molar equiv) in DME (40°, 20 min) and then with $Zn(BH_4)_2$ (10 molar equiv) in DME (-20 — -30°, 40 min), giving the hydroxymethyl compound (3)^{3,4} [$>45\%$ from (1)]. Dehydration of (3) with $(PhO)_3PMe \cdot I$ ⁸ (4 molar equiv) in DMF (room temp, 20 hr) afforded the α -methylene- γ -butyrolactone (4),^{3,4} m.p. 41-44°, quantitatively. The overall isolated yield of (4) based on (1) was ca. 45%.



II. While the reaction scheme of the second method is essentially the same that reported by Harmon and Hutchinson^{2k} very recently, the reaction conditions were different and the overall yield of the α -methylenation of the δ -lactone grouping was better than the reported one.^{2k} The γ -butyrolactone (5)⁹ was treated with $HCOOMe$ (20 molar equiv) and NaH in ether (room temp, 12 hr) to afford the hydroxymethylene compound (7),⁴ which was directly converted

with Et_2NH (20 molar equiv) in benzene (50° , 1 hr) to the aminomethylene derivative (8)⁴ [$>95\%$ from (5)]. Catalytic hydrogenation (PtO_2/AcOH , room temp) of (8) gave the compound (6),¹⁰ which was heated in $\text{NaOAc} - \text{AcOH}$ (110° , 1 hr), affording the α -methylene- γ -butyrolactone (9)^{3,4} (liquid). The overall isolated yield of (9) based on (5) was $\sim 60\%$.

The same sequence of reactions as utilized in the γ -butyrolactone (5) were applied to the δ -lactone (10),¹¹ and the α -methylene- δ -lactone (11)^{3,4} (liquid) was obtained in 42% overall yield.



REFERENCES AND FOOTNOTES

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- The molecular formula of this compound was established by high resolution mass spectral data on the molecular ion.
- The structure of this compound was confirmed by the spectral data.
- This compound was prepared by sodium borohydride reduction of β -(4-methoxy-2-methylbenzoyl) propionic acid [R. D. Desai and M. A. Wali, *Proc. Indian Acad. Sci.*, **6A**, 144 (1937); *Chem. Abstr.*, **32**, 5095 (1938)] in EtOH.
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- As an alternative method of reducing the derivative (8) to (6), sodium borohydride in AcOH (room temp, 30 min) was employed and, in this case, the overall yield of (9) from (5) was somewhat lowered ($\sim 50\%$).
- Available from Tokyo Kasei Kogyo Co. Ltd. (Tokyo)