

AN EFFICIENT AND CONVENIENT ROUTE TO SPIRO-FUSED γ -BUTYRO-
AND δ -VALEROLACTONES

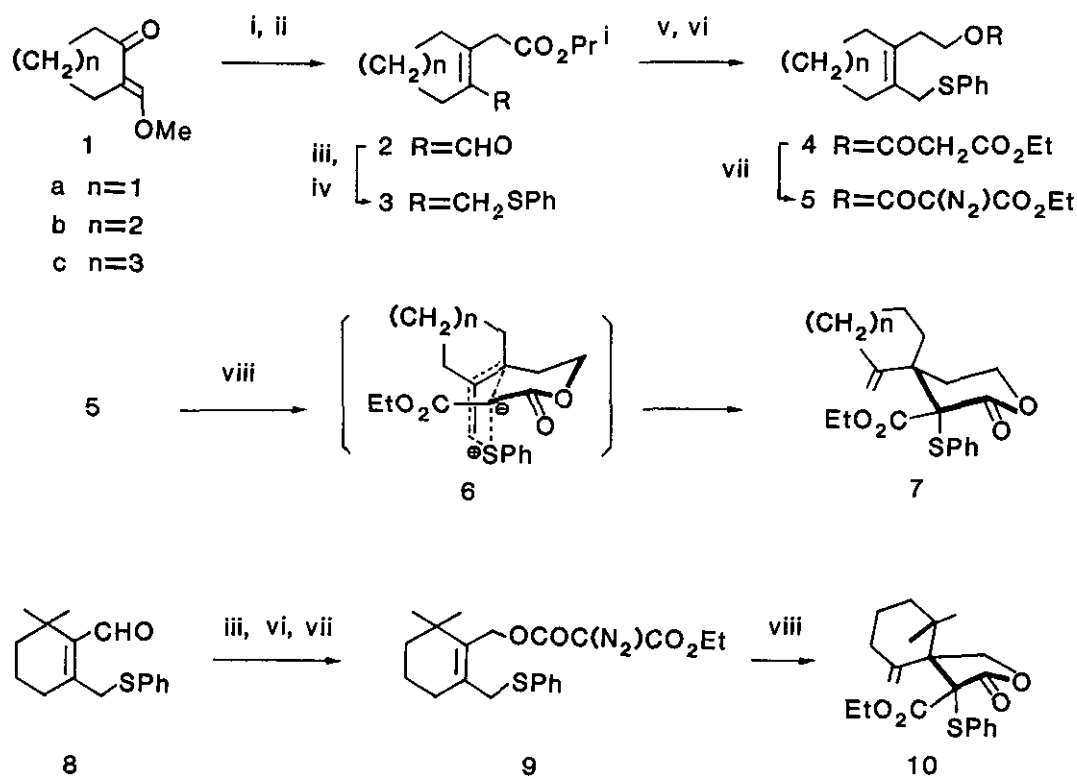
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Abstract — Treatment of the α -diazomalonates (**5a-c**) of 2-[(2-phenylthiomethyl)-1-cycloalkenyl]ethanols with rhodium acetate led to the [2,3] sigmatropic rearrangement of the cyclic allylsulfonium ylides (**6a-c**) to give the spiro-fused δ -valerolactones (**7a-c**) in excellent yields. Similarly, the spiro-fused γ -butyrolactone (**10**) was prepared starting with the α -diazomalonate (**9**) of [(2-phenylthiomethyl)-1-cyclohexenyl]methanol analog.

We have recently reported a highly efficient and stereoselective synthesis of contiguously substituted γ -butyro- and δ -valerolactones from a variety of acyclic α -diazomalonates by use of the [2,3] sigmatropic rearrangement via the eight- and nine-membered cyclic allylsulfonium ylides.^{1a,b}

In connection with utilization of this novel methodology toward the synthesis of spirocyclic compounds, the above findings prompted us to examine the rearrangement of the cyclic allylsulfonium ylides derived from 1,2-disubstituted cycloalkenes possessing diazomalonyl and phenylthiomethyl functions vicinally, giving spiro-fused lactones having the spirocyclic center at the β -position. We wish to describe herein that the [2,3] sigmatropic rearrangement generated from the α -diazomalonates (**5a-c**) of 2-[(2-phenylthiomethyl)-1-cycloalkenyl]ethanol and the analog (**9**) afforded excellent



i) $\text{LiCH}_2\text{CO}_2\text{Pr}^i$, THF, -78°C ; ii) pyridinium *p*-toluenesulfonate, MeOH, room temperature; iii) NaBH_4 , MeOH, -20°C ; iv) $(\text{PhS})_2$, Bu_3P , Py, room temperature; v) LiAlH_4 , Et_2O , 0°C ; vi) $\text{HO}_2\text{CCH}_2\text{CO}_2\text{Et}$, dicyclohexylcarbodiimide, 4-*N,N*-dimethylaminopyridine, CH_2Cl_2 , room temperature; vii) TsN_3 , Et_3N , MeCN; viii) $\text{Rh}_2(\text{OAc})_4$ (0.01 mole equiv.), PhH, reflux.

Scheme 1

yields of the spiro-fused δ - and γ -lactones, (**7a-c**) and (**10**), possessing an exocyclic methylene group adjacent to the spirocyclic center, respectively. Starting with the known 2-methoxymethylenecycloalkanones (**1a-c**),² preparation of the diazomalonates (**5a-c**) was performed by a sequence of conventional reactions as shown in Scheme 1: a) condensation of **1a-c** with the lithium enolate of isopropyl acetate followed by hydrolysis with formation

of the aldehydes (2a-c, 67-76%);³ b) sodium borohydride reduction of 2a-c and subsequent displacement⁴ of the resulting hydroxy group with thiophenyl group, giving the sulfides (3a-c, 50-58%); c) lithium aluminum hydride reduction of 3a-c, followed by esterification⁵ with malonic acid monoethyl ester, and d) diazotization⁶ of the resulting malonates (4a-c), providing the required diazomalones (5a-c, 73-85%).

Construction of the spirocyclic center was readily performed by use of our standard reaction conditions; treatment of 5a-c with catalytic amount of rhodium acetate in refluxing benzene resulted in the [2,3] sigmatropic rearrangement of the nine-membered cyclic sulfonium ylide intermediates (6) to produce the spiro-fused δ -valerolactones (7a-c)⁷ in excellent yields (92-93%). The stereochemistry of two substituents, the ethoxycarbonyl and phenylthio groups, in the lactone rings was surmised, as depicted, on the basis of the favorable conformation (6) of the transition state on the rearrangement.

This approach was then extended to the synthesis of a spiro-fused γ -lactone. The α -diazomalonate (9) prepared from the known aldehyde (8)⁸ in three steps was submitted to our rearrangement reaction conditions, providing the expected γ -butyrolactone (10) in 82% yield.⁷

This synthetic methodology would provide not only a convenient synthetic route to spiro-fused lactones, but also a promising access toward construction of the spiro-fused carbocyclic system. A further study toward natural product synthesis is now ongoing.

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Received, 20th June, 1991