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STEREOSELECTIVE PREPARATION OF γ-BUTYROLACTONE DERIVATIVES FROM γ-HYDROXY-α-NITRO-OLEFIN AND ACTIVE METHYLENE COMPOUNDS

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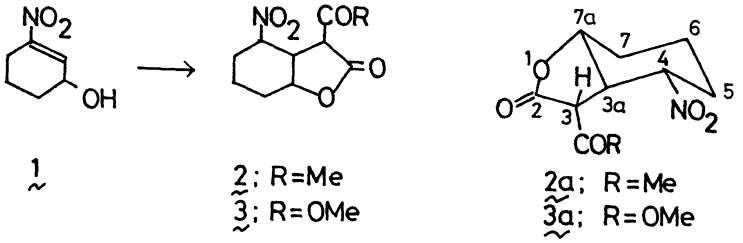
Stereoselective preparation of γ-butyrolactone derivatives from 5,5-dimethyl-3-nitrocyclohex-2-en-1-ol and active methylene compounds is described.

We have recently reported the synthesis of γ-hydroxy-α-nitro-olefins from α,β-unsaturated ketones,[1] which seem to be versatile in synthesis. In fact very recently Corey and Estreicher used 3-nitro-2-cyclohexenone, prepared by oxidation of 3-nitro-2-cyclohexen-1-ol (1),[1] as a unique dienophile in the Diels-Alder reaction.[2]

In this communication we wish to show this class of compounds versatile for highly stereoselective preparation of γ-butyrolactone derivatives.

Nucleophilic addition reactions to α-nitro olefins afford theoretically four isomers. Indeed a complex mixture was obtained by treatment of 1 with ethyl acetoacetate or dimethyl malonate in THF in the presence of 1M (=1 mol dm^{-3}) sodium hydroxide, from which only compound 2a (mp 140-141°C) or 3a (mp 124-125°C) could be isolated in 21 and 20% yield, respectively. The configurations of them were determined from the coupling constants; $J_{3a,3}=J_{3a,4}=J_{3a,7a}=10$, $J_{7a,7}=11$, $J_{7a,7'}=4.0$, $J_{4,5}=11$, and $J_{4,5'}=5.0$ Hz for 2a, $J_{3a,3}=12$, $J_{3a,4}=J_{3a,7a}=J_{4,5}=J_{7a,7}=10$, $J_{4,5'}=J_{7a,7'}=4.0$ Hz for 3a.

Under the same conditions, however, similar reaction of 5,5-dimethyl-3-nitrocyclohex-2-en-1-ol (4) could not be induced. If 4 could be converted into the ester 5 or 8, reactivity and stereoselectivity of a resulting carbanion should be increased due to the intramolecular γ-butyrolactone formation; i.e., the anion should approach to the nitro olefin moiety predominantly in the manner to make cis attachment of a five-membered ring to the six-membered one. Such an expectation was indeed realized.

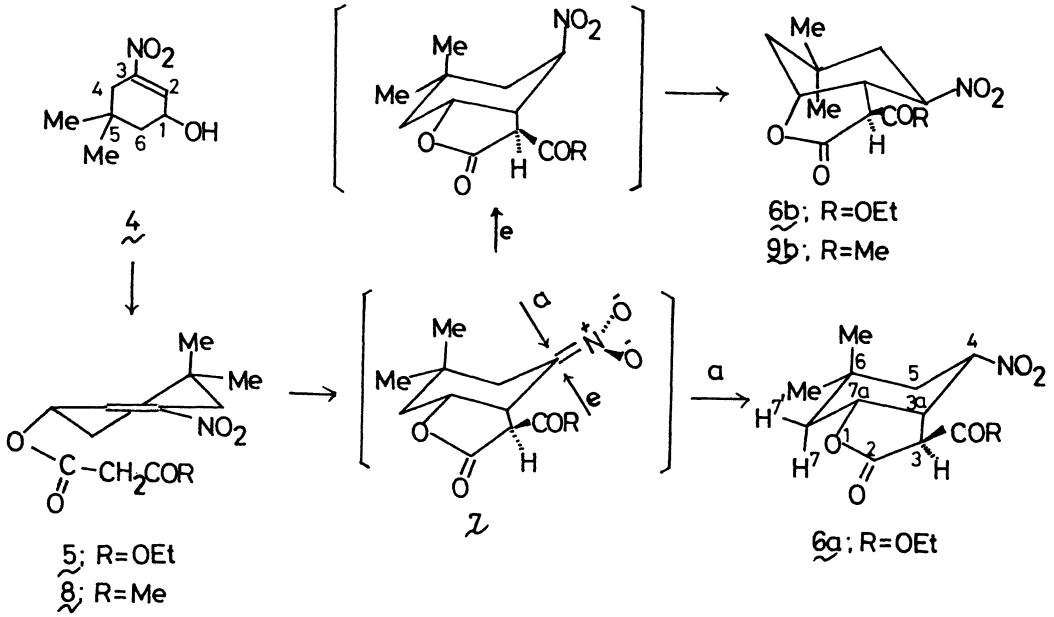


1

2; R=Me
3; R=OMe

2a; R=Me
3a; R=OMe

The ester 5 was prepared in 64% yield (not optimized) by treatment of 4 with a solution of monoethyl malonate and p-toluenesulfonyl chloride in pyridine. Under the mild conditions,[3] the ring closure occurred to give lactones 6a (mp 83.5-84.0°C, 55%) and 6b (mp 125-126°C, 27%), together with unchanged 5 (15%). By means of spin decoupling study of 6a and 6b as well as by comparison of ^{1}H-NMR data with their 4-deuterated derivatives, respectively, ring-proton signals could



be assigned and their structure was deduced as depicted in Scheme; $J_{3a,3} \leq 2.0$, $J_{3a,4}=5.0$, $J_{3a,7a}=3.5$, $J_{7a,7}=12$, and $J_{7a,7'}=7.0$ Hz for 6a, $J_{3,3a}=2.0$, $J_{3a,4}=10$, $J_{3a,7a}=5.5$, $J_{7a,7}=4.0$, and $J_{7a,7'}=3.0$ Hz for 6b. A carbanion should approach to the nitro olefin moiety from the axial side of the ring, because the substituent at C-1 of 5 occupies the sterically favorable quasi-equatorial position judging from ^{1}H-NMR spectroscopy ($J_{1,6}=10$ and $J_{1,6'}=6.0$ Hz). The intermediary nitronate should take a chair form 7 owing to stereoelectronic control.[4] If protonation occurred from the a-direction, compound 6a should be formed. On the other hand, the primary product formed by protonation from the e-direction should be converted into the more stable conformational isomer 6b, since the primary product was unstable for the 1,3-diaxial interaction between the nitro and methyl group at C-6.

Similar reaction of the ester 8, prepared from 4 by transesterification with ethyl acetoacetate, yielded 9b (mp 112-113°C) in 71% yield, whose configuration was determined by coupling constants; $J_{3a,3}=1.5$, $J_{3a,4}=11$, $J_{3a,7a}=5.5$, $J_{7a,7}=J_{7a,7'}=3.4$ Hz.

Although the stereochemistry of protonation to an intermediary nitronate is under investigation, it is noteworthy that the acetyl or ethoxycarbonyl group of the products exclusively occupies the sterically less crowded position.

References

1) T. Takamoto, Y. Ikeda, Y. Tachimori, A. Seta, and R. Sudoh, J. Chem. Soc., Chem. Commun., 1978, 350.
2) E. J. Corey and H. Estreicher, Tetrahedron Lett., 22, 603 (1981).
3) The reaction of 1 with dimethyl malonate required 1M sodium hydroxide for 3 d at room temperature, whereas reaction of 5 almost finished within 2 h at room temperature in the presence of 0.1M sodium hydroxide.
4) E. g., H. O. House, "Modern Synthetic Reactions," 2nd ed., W. A. Benjamin, Inc., California (1972), p 627.

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