CHEMISTRY LETTERS, pp. 1437 - 1440, 1984.

A NEW SYNTHETIC ROUTE TO α-METHYLENE AND β-METHYLENE-γ-BUTYROLACTONES VIA HOMOLYTIC CARBOCYCLIZATION

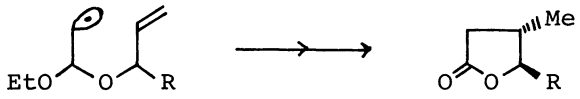
Osamu MORIYA,* Makoto OKAWARA,† and Yoshio UENO* †

Department of Chemistry, National Defence Academy, Hashirimizu, Yokosuka 239

†Research Laboratory of Resources Utilization, Tokyo Institute of Technology, Nagatsuta, Midori-ku, Yokohama 227

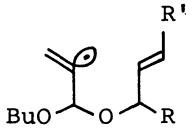
α-Methylene-γ-butyrolactones were prepared using butoxyallene via stereoselective homolytic carbocyclization of vinyl radicals. similarly, β-methylene analogues were also prepared.

Radical cyclization rapidly become an important method for the formation of various cyclic compounds under neutral conditions.[1] We have reported a highly stereoselective radical cyclization leading to γ-butyrolactones starting from bromoacetals.[2]



We have further investigated the scope of this type of reaction and found vinyl radical[3] cyclization is a useful approach for the preparation of α-methylene-γ-butyrolactones. The terpenes which have α-methylene-γ-lactone structual unit have been suggested to be an important class of compounds in natural products.[4]

The starting materials, bromoacetals (2) were easily prepared by the reaction of butoxyallene[5] with excess of allylic alcohols in the presence of N-bromosuccinimide (NBS) at −20 — 0 °C for 3 h. The vinyl radical (1) was successfully generated by the reaction of the bromoacetals (2) with tri-n-butyltin hydride as follows.



1

Thus to a solution of 2 and azobisisobutyronitrile (AIBN) (1 mol%) in dry benzene, was added dropwise an equivalent amount of tri-n-butyltin hydride in 30-60 min. After stirring for 5-7 h under reflux, distillation of the mixture gave the desired 2-butoxy-3-methylenetetrahydrofurans (3) (Table 1).

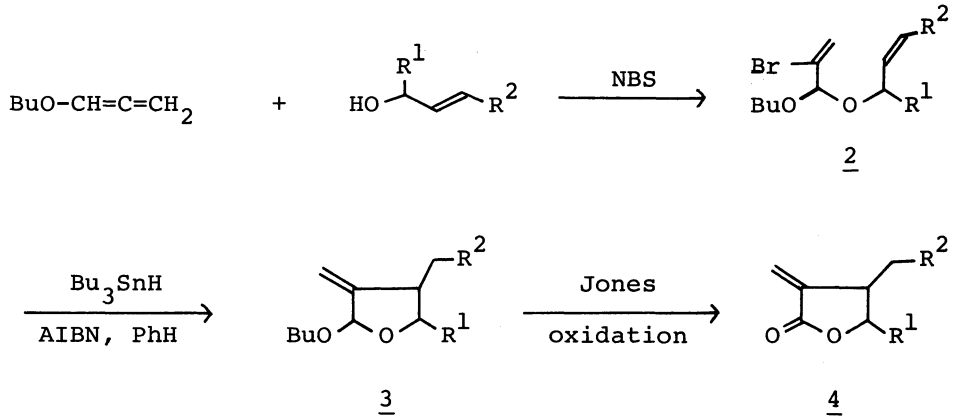


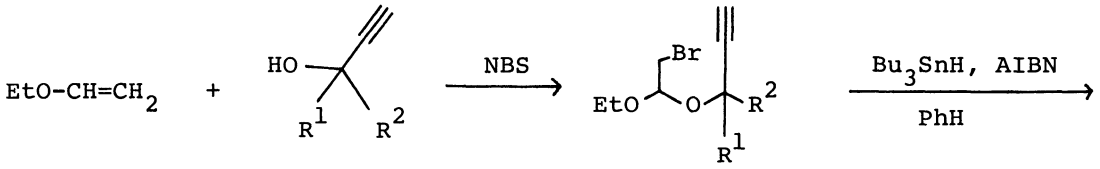
Table 1. Bromoacetals (2), Methylenetetrahydrofurans (3), and α-Methylene-γ-butyrolactones (4)[6)]

	R^1	R^2	Bromoacetals (2) Yield/%	Tetrahydrofurans (3) Yield/%	Lactones (4) Yield/%	Trans/Cis
a	H	H	74	62	65	
b	CH_3	H	68	65	64	93 / 7
c	$-(CH_2)_3-$		68	60	62	0 / 100

Although the starting material (2) has very susceptible hydrogen atoms, i.e., both allylic and acetal hydrogen atoms, any side products derived from the abstraction of such hydrogen atoms were not observed. Simple oxidation of cyclic acetals (3) with Jones reagent in acetone afforded the desired α-methylene-γ-butyrolactones (4) (Table 1). The stereochemistry of the resulting lactones (4) was estimated by comparison of the ^1H NMR data with those of reported values.[7, 8)] As summarized in the Table 1, in a monocyclic system (4b), trans-rich product was obtained in a high ratio (93/7).

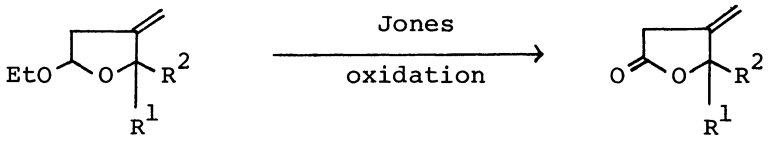
On the other hand, bicyclic system, i.e., 2c gave cis-fused lactone (4c) in a completely selective manner.

Only a simple modification of starting alcohols enables to prepare the regio-isomeric methylenelactones. Thus, propargylic alcohols reacted with vinyl ether to give bromoacetals (5) in a moderate yield. The compound (5) was similarly cyclized with tri-n-butyltin hydride to give 4-methylenetetrahydrofurans (6), which were easily converted to β-methylenelactones (7) with Jones reagent as formulated below.[9)]



5a 52%

5b 61%



6a 60% 7a 64%

6b 63% 7b 62%

[a: $R^1 = CH_3$, $R^2 = H$; b: R^1, $R^2 = -(CH_2)_5-$]

The characteristic points of the above process are the high stereo-selectivity observed in the case of α-methylene-γ-butyrolactones. In addition, both α-methylene and β-methylene-γ-butyrolactones were easily prepared by the suitable choice of the starting alcohols and olefinic ethers. Furthermore, asymmetric synthesis of the title compounds are also quite promising using chiral allylic alcohols, since the relative 1,2-asymmetric induction was observed in the case of lactones (4b and 4c).

References

1) a) G. Stork, R. Mook, Jr., S. A. Biller, and D. Rychnovsky, J. Am Chem. Soc., 105, 3720, 3741 (1983); b) N. N. Marinovic and H. Ramantan, Tetrahedron Lett., 24, 1871 (1983); c) M. Okabe and M. Tada, J. Org. Chem., 47, 5382 (1982); d) M. Okabe, M. Abe, and M. Tada, ibid., 47, 1775 (1982); e) H. Nagashima, H. Wakamatsu, K. Itoh, Y. Tomo, and J. Tsuji, Tetrahedron Lett., 24, 2395 (1983).

2) Y. Ueno, K. Chino, M. Watanabe, O. Moriya, and M. Okawara, J. Am. Chem. Soc., 104, 5564 (1982); Y. Ueno, O. Moriya, and M. Okawara, 2nd IUPAC Symposium on Organometallic Chemistry Directed toward Organic Synthesis, Abstr. P. 80, 1983, Dijon. See also Ref. 1a.

3) G. Stork and N. H. Baine, J. Am. Chem. Soc., 104, 2321 (1982).

4) For reviews, see S. Kano, S. Shibuya, and T. Ebata, Heterocycles, 14, 661 (1980); P. A. Grieco, Synthesis, 1975, 67.

5) R. Mantione, Bull. Soc. Chim. Fr., 1969, 4523.

6) 4b: ^{1}H NMR ($CDCl_3$) δ 1.25 (d, trans CH_3, 2.8H, J=6.6 Hz), 1.00 (d, cis CH_3, 0.2H, J=7.1 Hz), 1.15 (d, cis CH_3, 0.1H, J=7.1 Hz), 1.44 (d, trans CH_3, 2.9H, J=6.4 Hz), 2.69 (m, 1H), 4.11 (pentlet, 1H, J=6.4 Hz), 5.54 (d, 1H, J=2.7 Hz), 6.21 (d, 1H, J=3.2 Hz); ^{13}C NMR ($CDCl_3$) δ 13.84 (cis CH_3), 16.08 (trans CH_3), 16.33 (cis CH_3), 19.93 (trans CH_3), 41.91 (CH_3-$\underline{C}$H-C=CH_2), 81.34 (CH_3-$\underline{C}$H-O), 120.57 ($\underline{C}$=CH_2). 4c: ^{1}H NMR ($CDCl_3$) δ 1.48 (br, s, 8H), 3.19 (m, 1H), 4.54 (m, 1H), 5.43 (d, 1H, J=2.2 Hz), 6.19 (d, 1H, J=2.4 Hz); ^{13}C NMR ($CDCl_3$) δ 19.93, 20.57, 25.73, 28.32, 38.99, 76.37, 119.16, 139.44.

7) L. D. Martin and J. K. Still, J. Org. Chem., 47, 3630 (1982).

8) E. Campaigne and J. C. Beckman, Synthesis, 1978, 385.

9) 7a: bp 79 °C/10 mmHg (Kugelrohr), ^{1}H NMR ($CDCl_3$) δ 1.55 (d, 3H, J=6.0 Hz), 3.38 (dd, 2H, J=2.5 and 2.5 Hz), 5.20 (m, 3H). 7b: ^{1}H NMR ($CDCl_3$) δ 1.70 (br, 10H), 3.30 (m,2H), 5.05 (t, 2H, J=2.3 Hz).

(Received May 21, 1984)