A Synthetic Route to Allenylidene Tetrahydrofurans

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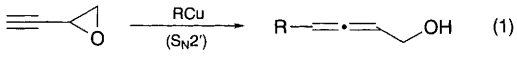
Radical mediated carbocyclization of bromoalkynyloxiranes **4** affords allenylidenetetrahydrofurans **5** *via* a new α-hydroxyallene-terminated cyclization.

α-Allenyl alcohols are versatile building blocks in synthesis; they have therefore been widely used in organic chemistry,[1] and reports of their preparation are of continuing recent interest.[2] Moreover, many useful biologically active molecules contain the α-hydroxy allenyl skeleton.[1] The tetrahydrofuran ring is also present in a number of biologically significant natural products.[3] For these reasons, we were interested in the synthesis of compounds bearing both the tetrahydrofuran and the α-hydroxyallenyl moieties.

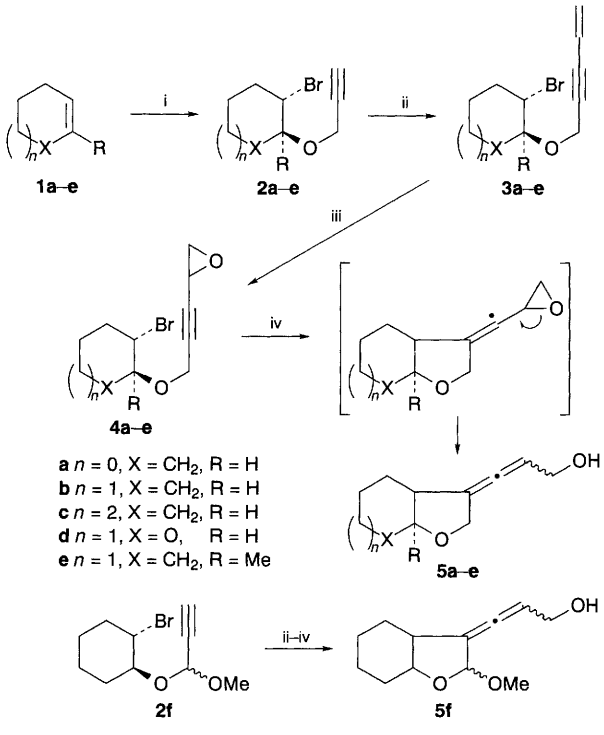
In this communication we report a new methodology that provides, through a radical carbocyclization, convenient access to compounds **5** from readily available bromoalkynyloxiranes **4**.

The cyclization of hex-5-ynyl radicals and tandem radical cyclizations have formed the basis for a wide variety of synthetic methods during recent years.[4] Whereas alkynyloxiranes are known to undergo S_N2' displacements into α-allenylcarbinols [eqn. (1)],[5] to the best of our knowledge, only

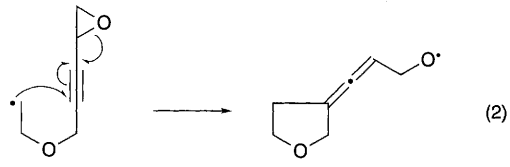


(1)

one report deals with the reactivity of such compounds in radical processes.[6] In this particular case, an oxygen-induced free radical reaction of organoboranes was involved and resulted in the formation of α-allenyl alcohols. Although this route to allenes did not receive further synthetic application, we decided to test the feasibility of the carbocyclization shown in eqn. (2).



Scheme 1 *Reagents and conditions*: i, NBS, prop-2-ynyl alcohol;[8] ii, $(Ph_3P)_2PdCl_2$, CuI, vinyl bromide (54–89%); iii, MCPBA (60–87%); iv, Bu_3SnH, AIBN, benzene, *hν*, 4 h (25–30%)


(2)

Suitable model bromoalkynyloxiranes **4a–f** were easily prepared through coupling[7] of β-bromoprop-2-ynyl ethers **2a–f**[8] with vinyl bromide, followed by epoxidation of the resulting enynes **3a–f** with *m*-chloroperbenzoic acid (Scheme 1).

Intramolecular carbocyclization of oxiranes **4** (0.2 mol dm^{-3} in benzene), promoted by tri-*n*-butyltin hydride (Bu_3SnH, 1.1 equiv., *hν*, 20 °C, 4 h) through a new α-hydroxyallene-terminated cyclization afforded allenylidene tetrahydrofurans **5a–f** (25–30%).†‡

These findings show that the addition of a radical to alkynyloxiranes leads, as for their vinyl analogues,[9] to a homolytic ring scission of the epoxide. Under these conditions, an allylic alkoxyl radical is generated, according to the previously reported Bu_3SnH reduction of α,β-epoxy-*O*-thiocarbonylimidazolide derivatives of alcohols.[10] The reaction proceeds selectively, according to the 5-*exo* mode,[11] through vinyl radical **A** to provide allenylidene tetrahydrofurans **5a–d**. As expected from ring-fusion rules,[12] **5a,b**, **d–f** were obtained only as two *cis*-ring fused diastereoisomers [*cis*-(*R**) : *cis*-(*S**) = 1 : 1], while **5c**§ was formed as a mixture of four diastereoisomers [*cis*-(*R**) : *cis*-(*S**) : *trans*-(*R**) : *trans*-(*S**) = 8 : 7 : 1 : 1]. A similar sequence of events transformed propynyl acetal **2f**[8] into the alkoxy allenylidene tetrahydrofuran **5f**, a potential precursor through oxidation, of allenic lactone derivatives,[13] a somewhat rare class of compounds.

In conclusion, the radical mediated carbocyclization of bromoalkynyloxiranes constitutes a new procedure for the synthesis of hitherto unknown allenylidene tetrahydrofurans. Moreover, the formation of the α-allenyl alcohol moiety through this intramolecular radical process is without literature analogy. Finally, the versatile functionalizations of α-allenyl alcohols[1] should make these structures suitable intermediates for the preparation of spiro heterocycles.

Received, 16th December 1994; Com. 4/07677J

Footnotes

† Satisfactory analytical and spectral data were obtained for all compounds.

‡ Removal of organotin residues according to known procedures[4a] was inefficient and required two successive chromatography columns (SiO_2).

§ **5c** HRMS calc. for $C_{12}H_{18}O_2$ (M^+) *m/z* 194.1307, found 194.131. IR ν/cm^{-1} 3400, 2925, 1973 and 1057. NMR ($CDCl_3$), major *cis* diastereoisomer: ^1H (400 MHz) δ 5.46 (m, 1H), 4.42 (ddd, 1H, *J* = 11.2, 2.8, 1.3 Hz), 4.27 (ddd, 1H, *J* = 11.2, 4.2, 1.1 Hz), 4.09 (m, 3H), 2.92 (m, 1H), 1.98 (m, 1H) and 1.8–1.5 (m, 9H); ^{13}C (100.61 MHz) δ 193.5, 110.5, 96.4, 83.7, 68.7, 60.8, 47.5, 31.7, 31.4, 28.7, 26.8 and 24.0.

References

1 *The Chemistry of Ketenes, Allenes and Related Compounds*, ed. S. Patai, Wiley, New York, 1980; *The Chemistry of the Allenes*, ed. S. R. Landor,

Academic, London, 1982; G. M. Coppola and H. F. Schuster, *Allenes in Organic Chemistry*, Wiley, New York, 1984.
2 K. Belyk, M. J. Rozema and P. Knochel, *J. Org. Chem.*, 1992, **57**, 4070; C. Darcel, C. Bruneau and P. H. Dixneuf, *J. Chem. Soc., Chem. Commun.*, 1994, 1845; C. Darcel, S. Bartsch, C. Bruneau and P. H. Dixneuf, *Synlett*, 1994, 457.
3 M. H. D. Postema, *Tetrahedron*, 1992, **48**, 8545; W. Westle, *Polyethers Antibiotics: Naturally Occuring Acid Ionophores*, Marcel Dekker, New York, 1982, vol. 1 and 2.
4 (*a*) W. B. Motherwell and D. Crich, *Free Radical Chain Reactions in Organic Synthesis*, Academic, New York, 1992; (*b*) M. Regitz and B. Giese, *C-Radikale, Houben-Weyl, Methoden der organischen Chemie*, Georg Thieme Verlag, Stuttgart, 1989; (*c*) M. Ramaiah, *Tetrahedron*, 1987, **43**, 3541; (*d*) D. P. Curran, *Synthesis*, 1988, 417; 789; (*e*) B. Giese, *Radicals in Organic Synthesis: Formation of Carbon–Carbon Bonds*, Pergamon, Oxford, 1986.
5 P. R. Ortiz de Montellano, *J. Chem. Soc., Chem. Commun.*, 1973, 709; A. C. Oehlschlager and E. Czyzewska, *Tetrahedron Lett.*, 1983, **24**, 5587; A. Alexakis, I. Marek, P. Mangeney and J. F. Normant, *Tetrahedron*, 1991, **47**, 1677; J. A. Marshall and K. G. Pinney, *J. Org. Chem.*, 1993, **58**, 7180.
6 A. Suzuki, N. Miyaura and M. Itoh, *Synthesis*, 1973, 305.
7 K. Sonogashiro, Y. Tohda and N. Hagihara, *Tetrahedron Lett.*, 1975, 4467.
8 J. P. Dulcère, M. N. Mihoubi and J. Rodriguez, *J. Org. Chem.*, 1993, **58**, 5709.
9 E. L. Stogryn and M. H. Gianni, *Tetrahedron Lett.*, 1970, 3025; S. Kim, S. Lee and J. S. Koh, *J. Am. Chem. Soc.*, 1991, **113**, 5106.
10 D. H. R. Barton, R. S. H. Motherwell and W. B. Motherwell, *J. Chem. Soc., Perkin Trans. 1*, 1981, 2363.
11 A. L. Beckwith and C. H. Schiesser, *Tetrahedron*, 1985, **41**, 3925.
12 S. Wolff and W. C. Agosta, *J. Chem. Res.*, (*S*), 1991, 78; D. L. Clive, D. R. Cheshire and L. Set, *J. Chem. Soc., Chem. Commun.*, 1987, 353.
13 F. Fotiadu, A. Archavlis and G. Buono, *Tetrahedron Lett.*, 1990, **31**, 4859; M. E. Jung and C. N. Zimmermann, *J. Am. Chem. Soc.*, 1991, **113**, 7813.