Tetrahedron Letters,Vol.27,No.12,pp 1355-1358,1986 0040-4039/86 $3.00 + .00
Printed in Great Britain

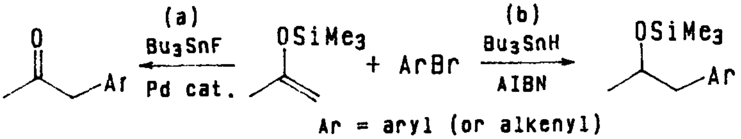
A RADICAL CYCLIZATION BETWEEN ENOL SILYL ETHERS AND ARYL OR ALKENYL BROMIDE MOIETIES

Hirokazu Urabe and Isao Kuwajima*
Department of Chemistry, Tokyo Institute of Technology, Meguro,
Tokyo 152, Japan

Summary: Enol silyl ethers bearing aryl or alkenyl bromide moieties at their appropriate positions undergo radical cyclization in the presence of Bu_3SnH and AIBN to yield the corresponding 5- and 6-membered cycloalkanols in good yields.

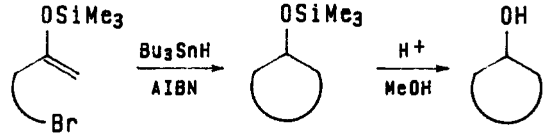
Enol silyl ethers are recognized as versatile building blocks in organic synthesis, and their reactivity as well as synthetic utilities have been well investigated.[1] Most of their reactions are based on their highly polarized ionic behaviors which have allowed a selective carbon chain homologation or an introduction of various functional groups. Another important feature is a use for [4 + 2] cycloaddition reaction where enol silyl ethers act as either dienes or dienophiles. However, their behavior as well as synthetic utility in radical reactions are not elucidated until now.[2]

We recently described arylation[3a] and alkenylation[3b] of enol silyl ethers with aryl and alkenyl bromides (Eq 1, path a). Extension of this study led us to examine a methodology to connect aryl or alkenyl groups with enol ether moieties via a radical intermediate (Eq 1, path b).



(1)

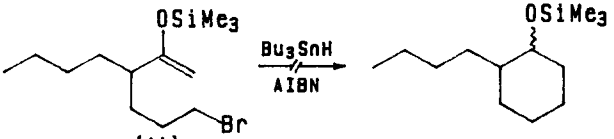
Although an intermolecular addition of an aryl radical onto 2-(trimethylsiloxy)-1-hexene failed under standard conditions[4,5] (C_6H_5Br, Bu_3SnH, a catalytic amount of azobisisobutyronitrile (AIBN) in benzene), an intramolecular version of this addition reaction compensated the low reactivity of enol ethers toward radical species to effect this transformation cleanly.[6,7] As shown in Table 1, the cyclization products were isolated as alcohols after desilylation under acidic conditions.



(2)

A representative procedure is as follows (Table 1, run 7). A 0.03 *M* benzene solution of **1g** (1 equiv), Bu$_3$SnH (1.1 equiv), and AIBN (0.05 equiv) was heated to reflux under nitrogen for 6 h.^{7a,b} After removal of the solvent, the residue was successively treated with dilute HCl in methanol and aqueous NaOH solution. Extractive workup with ether followed by separation with silica gel column chromatography afforded **2g** in 72% yield. Methylindene (ca. 10%), which resulted from dehydration of the regioisomer, and 4-phenyl-2-butanone (ca. 10%) were also isolated as by-products.

On an attempt for 5-membered cyclization, the enol silyl ether of bromide **1a** afforded no cyclization product but the debrominated one exclusively (run 1). The unfavorable endo mode cyclization may account for the failure of this substrate.^{8} The five-membered cyclization to the exo direction took place cleanly to give the expected product in good yield (run 2)^{8} Six-membered ring annulation proceeded equally well, but a structural factor is crucial on these cases. Enol ethers of methyl *prim*-alkyl ketones of unhindered aryl or alkenyl bromides afforded the corresponding cyclohexanols in good yields (runs 3, 5, and 7). The enol silyl ether of methyl *sec*-alkyl ketones **1h** also undergoes cyclization, but the presence of an alkyl group closely situated to the reaction site usually prevents an efficient trap of the alkenyl radical with the enol ether. For instance, an introduction of an allylic methyl group *cis* to the bromine atom reduced the product yield (run 4). Further, efficacy for cyclization again decreased in the cases of enol ethers other than those of methyl ketones. Irrespective of such limitations, results in the Table clearly revealed that appropriately designed substrates nicely undergo this cyclization. In contrast to the aryl or alkenyl radicals, alkyl radicals usually did not react with enol silyl ethers (Eq 3).

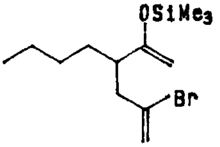
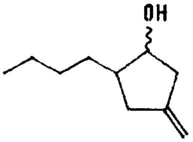
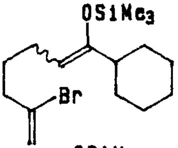
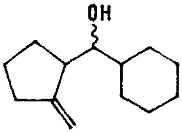
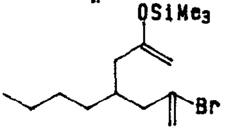
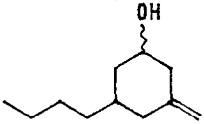
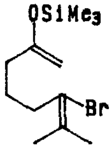
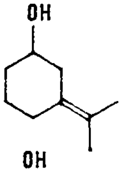
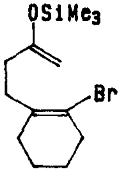
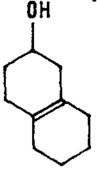
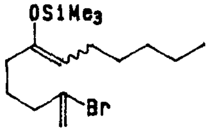
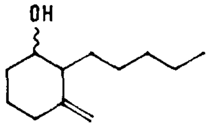
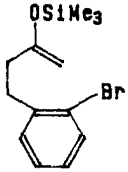
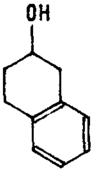
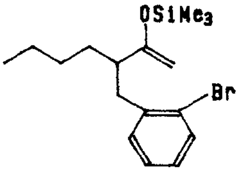
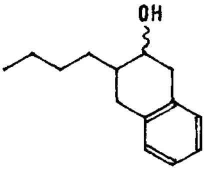


(**1i**)

(3)

In conclusion, the results described above have clearly disclosed not only a new aspect on the reactivity of enol silyl ethers toward alkenyl and aryl radicals but also synthetic utility of the radical cyclization. We are currently investigating further application of this methodology.

Table 1. Radical Cyclization of Enol Silyl Ethers.[a]

Run	Enol Silyl Ether (1)		Product (2)	Yield (Ratio)
1.		(a)		<trace
2.		(b)[b]		85% (1:1)
3.		(c)		72%
4.		(d)		29%
5.		(e)		54%
6.		(f)		27%
7.		(g)		72%
8.		(h)		74% (1:1)

[a] 1→2: Bu$_3$SnH (1.1 eq), AIBN (1.1 eq), 0.03--0.035 M benzene solution, reflux, 6 hr; HCl-MeOH. [b] Prepared with LDA and Me$_3$SiCl.

References and Notes

(1) (a) E. W. Colvin, "Silicon in Organic Synthesis"; Butterworths: London, 1981; pp 198-287. (b) W. P. Weber, "Silicon Reagents for Organic Synthesis"; Springer-Verlag: Berlin, 1983; pp 206-272. (c) P. Brownbridge, Synthesis, 1, 85 (1983).

(2) Review on C-C bond formation with radicals: B. Giese, Angew. Chem. Int. Ed. Engl., **22**, 753 (1983).

(3) (a) I. Kuwajima and H. Urabe, J. Am. Chem. Soc., **104**, 6831 (1982). (b) H. Urabe and I. Kuwajima, Abstr. III IUPAC Symp. Organomet. Chem. Directed toward Org. Synth., 67 (1985).

(4) S. D. Burke, W. F. Fobare, and D. M. Armistead, J. Org. Chem., **47**, 3348 (1982).

(5) This result has exhibited a good contrast to the success of intermolecular trap of alkyl radicals with electron deficient olefins (e.g., acrylic acid derivatives) (ref 4). Discussion on reactivities of radicals: I. Fleming, "Frontier Orbitals and Organic Chemical Reactions"; John Wiley and Sons: London, 1976; pp 182-207.

(6) Intramolecular addition of an alkyl radical to alkyl vinyl ether with a reversed regioselectivity was recently reported: M. Ladlow and G. Pattenden, Tetrahedron Lett., **25**, 4317 (1984). However, this result may not be conflicting with our case, since the direction of radical addition is known to be dependent on structures of substrates.

(7) Recent examples for radical cyclizations: (a) G. Stork and N. H. Baine, Ibid., **104**, 2321 (1982). (b) G. Stork and R. Mook, Jr. Ibid., **105**, 3720 (1983). (c) G. Stork, R. Mook, Jr., S. A. Biller, and S. D. Rychnovsky, Ibid., **105**, 3741 (1983). (d) G. Stork and M. Kahn, Ibid., **107**, 500 (1985). (e) Y. Ueno, K. Chino, M. Watanabe, O. Moriya, and M. Okawara, J. Am. Chem. Soc., **104**, 5564 (1982). (f) D. J. Hart and K. Kanai, J. Am. Chem. Soc., **105**, 1255 (1983). (g) D. J. Hart and H.-C. Huang, Tetrahedron Lett., **26**, 3749 (1985). (h) S. Danishefsky, S. Chackalamannil, and B. J. Uang, J. Org. Chem., **47**, 2231 (1982). (i) A. L. J. Beckwith, D. M. O'Shea, and D. H. Roberts, J. Chem. Soc., Chem. Commun., 1445 (1983). (j) E. J. Corey and S. G. Pyne, Tetrahedron Lett., **24**, 2821 (1983). (k) D. P. Curran and D. M. Rakiewicz, J. Am. Chem. Soc., **107**, 1448 (1985), and references cited therein.

(8) J. E. Baldwin, J. Chem. Soc., Chem. Commun., 734 (1976). Review: A. L. J. Beckwith, Tetrahedron, **37**, 3073 (1981).

(Received in Japan 24 December 1985)