Tin-free Radical Allylation of α-Acetoxy Alkyl Xanthates. Routes to Homoallyl Alcohols and α,β-Unsaturated Ketones

Jin Young Lee and Sunggak Kim*

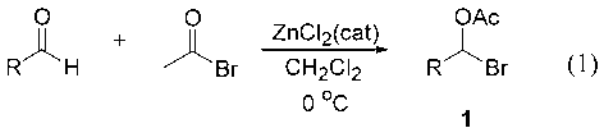
*Center for Molecular Design & Synthesis and Department of Chemistry, School of Molecular Science (BK-21), Korea Advanced Institute of Science and Technology, Daejeon 305-701, Korea. *E-mail: skim@kaist.ac.kr*

Received November 7, 2005

Key Words : Radical reaction, Allylation, Homoallyl alcohol, α,β-Unsaturated ketone

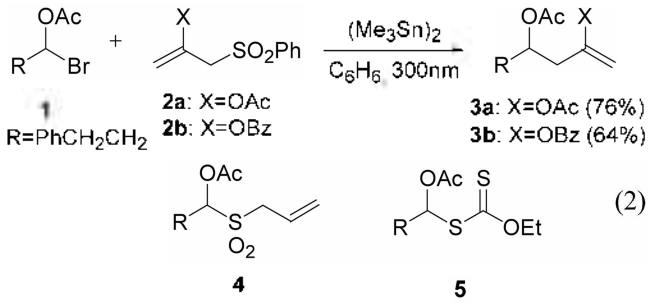
Radical allylations are most frequently used intermolecular radical carbon-carbon bond forming reactions and provide an easy access to introduce allyl groups into organic molecules under mild conditions.[1] Allylating agents normally utilize simple allyl and 2-substituted allyl stannanes[2] along with the corresponding sulfides[3] and sulfones.[4] Contrary to the radical allylations, radical-mediated aldol reactions have not been well developed due to the very high π-bond strength of C=O bonds. Thus, several indirect approaches for aldol-type products have been reported to date.[5-7] We studied the possibility of indirect radical-mediated aldol reactions using α-acetoxy alkyl radicals along with reagent equivalents of the α-ketone acceptor synthon. In this regard, 2-acetoxy and 2-benzoyloxy substituted allyl sulfones seemed to be promising for our purpose.[8] The combination of these new allylating agents together with the α-acetoxy alkyl radical precursors would provide α,β-unsaturated ketones after hydrolysis of the acetates and the following dehydration.

Among several α-alkoxy alkyl radical precursors, α-bromoalkyl acetate **1** seemed to be most attractive and promising to introduce an acetate group at the β-position of an alkenyl bond.[9] Previously, radical allylation of **1** with allyl stannane was known to give a homoallyl acetate.[10] Furthermore, chiral α-alkoxy alkyl radicals were generated from decarboxylation of α-alkoxy substituted Barton esters.[5] The α-bromoalkyl acetate **1** was readily prepared by the addition of acetyl bromide to an aldehyde in the presence of zinc chloride in methylene chloride at 0 °C (eq. 1).[11]



(1)

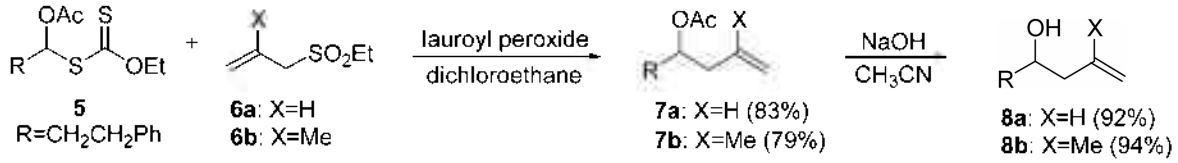
Since α-bromoacetates were unstable to aqueous workup, the crude α-bromoacetate **1** was used for the radical allylation reactions without purification. Irradiation of a solution of **1** and 2-acetoxyallyl phenyl sulfone (**2a**) in benzene at 300 nm for 9 h afforded the desired allylation product **3a** in 76% yield (eq. 2). A similar result was obtained with **2b**, yielding **3b** in 64% yield under the same condition.



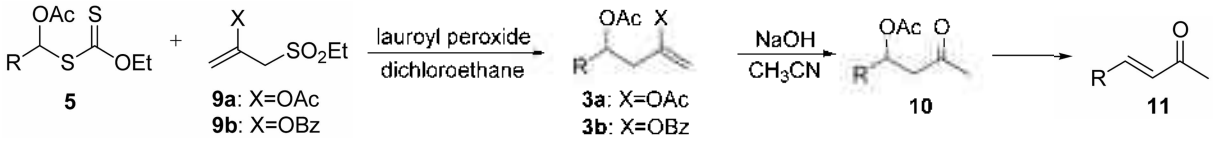
(2)

In order to achieve tin-free radical allylation,[12] we initially attempted to prepare allyl sulfone **4** by the reaction of **1** with sodium salt of allyl mercaptan and the subsequent oxidation to **4**.[13] However, when **1** was treated with sodium salt of allyl mercaptan in DMF at room temperature, the corresponding aldehyde was obtained, indicating that the allyl mercaptan anion reacted with the acetate group. Thus, our next attention was given to the xanthate precursor.[14] Treatment of **1** with potassium *O*-ethyl xanthate in acetone at room temperature to afford α-acetoxy xanthates **5** in good yields. The xanthates **5** were thermally and hydrolytically very stable. Furthermore, 2-acetoxy and 2-benzoyloxy allyl ethyl sulfone (**9a** and **9b**) were prepared by treatment of propargyl ethyl sulfone with acetic acid and benzoic acid, respectively.[8a]

We initially studied tin-free allylation using a xanthate precursor and an allyl ethyl sulfone acceptor (Scheme 1). Reaction of xanthate **5** with ethyl allyl sulfone **6a** using lauroyl peroxide as initiator in dichloroethane at 90 °C for 6 h afforded homoallyl acetate **7a** in 83% yield. Hydrolysis of **7a** with 0.1 N NaOH in acetonitrile for 9 h afforded **8a** in

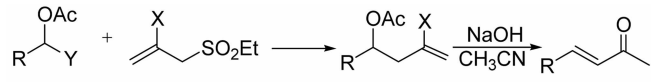


Scheme 1. Preparation of homoallylic alcohol **8** from **5** and **6**.



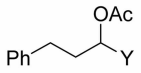
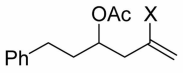
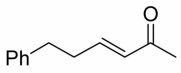
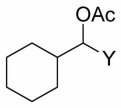
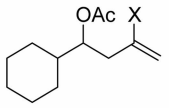
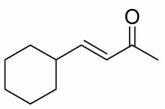
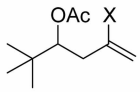
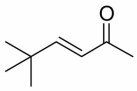
Scheme 2. Preparation of α,β-unsaturated ketone **11** from **5** and **9**.

Table 1. Tin-free Allylation of **5** with Allyl Sulfone **9** and Hydrolysis of **3** to **11**[a]



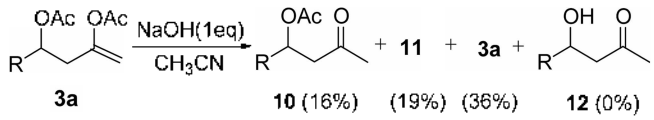
5 **9** **3** **11**

Y= SC(S)OEt **9a**: X=OAc **9b**: X=OBz

xanthate **5**	allylation product **3**	enone **11**
		
	X=OAc 74% X=OBz 71%	82% 87%
		
	X=OAc 72% X=OBz 69%	72% 85%
		
	X=OAc 66% X=OBz 68%	75% 86%

[a] 1 equiv of lauroyl peroxide in dichloroethane, 90 °C, 6 h

92% yield (Scheme 1). A similar result was obtained with **6b**. When the reaction was carried out with 2-acetoxy allyl ethyl sulfone (**9a**) under the same condition, the desired product **10a** was isolated in 74% yield (Scheme 2). Further experimental results are listed in Table 1 and illustrate the synthetic utility of the present approach. Secondary and tertiary alkyl substituted xanthates worked well, yielding β-acetoxy vinyl acetates and vinyl benzoates in good yields. Hydrolysis of enol acetate **3a** with 1 N NaOH (1 equiv) in acetonitrile at room temperature for 9 h gave a mixture of **10** and **11** along with the starting material **3a** (eq. 3). The use of an excess amount of NaOH (5 eq) gave α,β-unsaturated ketone **11** in 82% yield without yielding β-hydroxy ketone **12**.



3a **10** (16%) (19%) (36%) **12** (0%)

(3)

In conclusion, we have developed new tin-free radical allylation approaches to α,β-unsaturated ketones using α-acetoxy alkyl xanthates **5** as radical precursors and 2-acetoxy and 2-benzoyloxy allyl ethyl sulfone as radical acceptors.

Acknowledgment. We thank CMDS and BK21 project for financial support.

References

1. For reviews, see: (a) Curran, D. P. *Synthesis* **1988**, 489. (b) Rosenstein, I. J. In *Radicals in Organic Synthesis*; Renaud, P.; Sibi, M. P., Eds.; Wiley-VCH: Weinheim, Germany, 2001; Vol. 1, p 50.
2. (a) Keck, G. E.; Enholm, E. J.; Yates, J. B.; Wiley, M. R. *Tetrahedron* **1985**, *41*, 4079. (b) Mizuno, K.; Ikeda, M.; Toda, S.; Otsuji, Y. *J. Am. Chem. Soc.* **1988**, *110*, 1288. (c) Miura, K.; Itoh, D.; Hondo, T.; Saito, H.; Ito, H.; Hosomi, A. *Tetrahedron Lett.* **1996**, *37*, 8539.
3. (a) Keck, G. E.; Byers, J. H. *J. Org. Chem.* **1985**, *50*, 5442. (b) Curran, D. P.; Yoo, B. *Tetrahedron Lett.* **1992**, *33*, 6931.
4. (a) Ueno, Y.; Aoki, S.; Okawara, M. *J. Chem. Soc., Chem. Commun.* **1980**, 683. (b) Smith, T. A. K.; Whitham, G. H. *Chem. Commun.* **1985**, 897. (c) Padwa, A.; Kline, D. N.; Murphree, S. S.; Yeske, P. E. *J. Org. Chem.* **1992**, *57*, 298. (d) Chatgilialoglu, C.; Alberti, A.; Ballestri, M.; Macciantelli, D. *Tetrahedron Lett.* **1996**, *37*, 6391.
5. (a) Garner, P.; Leslie, R.; Anderson, J. T. *J. Org. Chem.* **1996**, *61*, 6754. (b) Garner, P.; Anderson, J. T. *Org. Lett.* **1999**, *1*, 1057. (c) Garner, P.; Anderson, J. T.; Cox, P. B.; Klippenstein, S. J.; Leslie, R.; Scardovi, N. *J. Org. Chem.* **2002**, *67*, 6195.
6. (a) Lee, E.; Tae, J. S.; Lee, C.; Park, C. M. *Tetrahedron Lett.* **1993**, *34*, 4831. (b) Lee, E.; Yoo, S. K.; Choo, H.; Song, H. Y. *Tetrahedron Lett.* **1998**, *39*, 317.
7. (a) Sibi, M. P.; Zimmerman, J.; Rheault, T. *Angew. Chem. Int. Ed.* **2003**, *42*, 4521. (b) Sibi, M. P.; Patil, K. *Org. Lett.* **2005**, *7*, 1453.
8. (a) Appleyard, G. D.; Stirling, C. J. M. *J. Chem. Soc., Chem. Commun.* **1967**, 2686. (b) Ueno, Y.; Ohta, M.; Okawara, M. *J. Organomet. Chem.* **1980**, *197*, C1.
9. Chou, T. S.; Knochel, P. *J. Org. Chem.* **1990**, *55*, 4791.
10. Sun, S.; Curran, D. P. *Tetrahedron Lett.* **1991**, *32*, 6097.
11. (a) Neuenschwander, M.; Bigler, P.; Christen, K.; Iseli, R.; Kyburz, R.; Muhle, H. *Helv. Chim. Acta* **1978**, *61*, 2047. (b) Knochel, P.; Chou, T. S.; Jubert, C.; Rajagopal, D. *J. Org. Chem.* **1993**, *58*, 588.
12. For our previous reports on tin-free radical reactions, see (a) Kim, S.; Lim, C. J. *Angew. Chem. Int. Ed.* **2002**, *41*, 3265. (b) Kim, S.; Lim, C. J. *Bull. Korean Chem. Soc.* **2003**, *24*, 1219. (c) Kim, S.; Lee, S.; Lim, C. J. *Bull. Korean Chem. Soc.* **2004**, *25*, 1611. (d) Kim, S.; Kim, S.; Otsuka, N.; Ryu, I. *Angew. Chem.* **2005**, *117*, 6339.
13. (a) Quiclet-Sire, B.; Zard, S. Z. *J. Am. Chem. Soc.* **1996**, *118*, 1209. (b) Bertrand, F.; Quiclet-Sire, B.; Seguin, S.; Zard, S. Z. *J. Am. Chem. Soc.* **1997**, *119*, 7410.
14. Zard, S. Z. *Angew. Chem. Int. Ed.* **1997**, *36*, 672. (b) Forbes, J. E.; Zard, S. Z. *J. Am. Chem. Soc.* **1990**, *112*, 2034. (c) Sire, B.; Seguin, S.; Zard, S. Z. *Angew. Chem. Int. Ed.* **1998**, *37*, 2864.