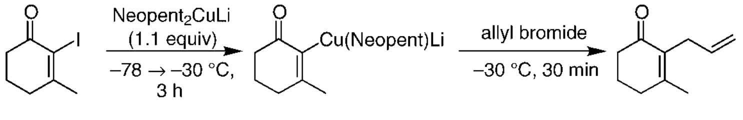

6 **7** **8**

Scheme 2. Iodine–copper exchange with 2-iodo-3-methyl-2-cyclohexenone.

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[5] Commercial neopentyl iodide was treated with *t*BuLi (2 equiv, Et_2O, −78 °C→RT, 1 h) to give neopentyllithium, which upon reaction with CuCN (0.5 equiv, 0 °C, 10 min) furnished the cuprate **1**. $PhMe_2CCH_2Cl$ (neophyl chloride) was converted into neophyllithium by reaction with lithium metal in dry hexane (heated overnight at reflux). The mixture was then transferred through a cannula into a 50-mL Schlenk tube, and the hexane was removed under vacuum. Dry diethyl ether was added and the mixture was centrifuged (2000 rpm, 30 min). Before use, the clear solution of neophyllithium thus obtained was titrated with menthol and *o*-phenantroline as indicator. Treatment with CuCN (0.5 equiv, room temperature, 10 min) gave the corresponding copper reagent **2**.

[6] Previously, we have shown that the neopentyl group does not readily participate in the formation of new C–C bonds: P. Jones, K. C. Reddy, P. Knochel, *Tetrahedron* **1998**, *54*, *1471*; see also: S. H. Bertz, M. Eriksson, G. Miao, J. P. Snyder, *J. Am. Chem. Soc.* **1996**, *118*, 10906.

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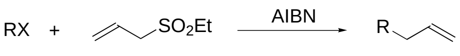
Tin-Free Radical-Mediated C–C-Bond Formations with Alkyl Allyl Sulfones as Radical Precursors**

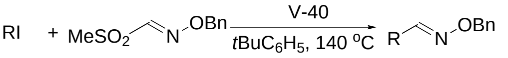
Sunggak Kim* and Chae Jo Lim

The synthetic importance of tin-free radical reactions has been well recognized in recent years.[1] Among several approaches, an organosulfone-mediated approach is very effective for allylation,[2] vinylation,[3] and azidation[4] [Eq. (1), AIBN = 2,2′-azobisisobutyronitrile]. However, the reported methods did not work well with primary alkyl iodides and xanthates owing to inefficient iodine-atom transfer and xanthate-group transfer, respectively. Recently, we also reported a tin-free acylation approach



X= I, xanthate (1)

using methanesulfonyl oxime ether, in which primary alkyl iodides and xanthates caused the same problem as a result of the small energy difference between the methyl radical and the primary alkyl radical [Eq. (2), V-40 = 1,1′-azobis(cyclohexane-1-carbonitrile)].[5]



(2)

As our extensive efforts to generate primary alkyl radicals from primary alkyl iodides and xanthates were unsuccessful, we have been interested in developing a new reliable method to generate primary alkyl radicals by using new types of radical precursors that do not require an atom- or a group-transfer step. In this regard, we have studied the possibility of using an alkyl allyl sulfone as a radical precursor. Alkyl allyl sulfones have been widely used as radical acceptors to transfer an allyl group to a radical precursor.[6] Although alkyl allyl sulfones have been used once as the radical precursor in an allylation reaction,[2a] primary alkyl allyl sulfones have not been examined. To the best of our knowledge, S-alkoxycarbonyl dithiocarbonates are the only generators of primary alkyl radicals from alcohols, but they cannot be applied to C–C-bond formations owing to the rapid formation of the corresponding xanthates.[7] We have found that alkyl allyl sulfones are highly efficient and reliable radical precursors for the generation of primary alkyl radicals under tin-free conditions and can be successfully applied to various C–C-bond-formation reactions.

Initially, we focused on radical cyanation,[8] and began our study with a primary alkyl iodide and methanesulfonyl cyanide.[9] The reaction of 4-phenoxybutyl iodide with methanesulfonyl cyanide (2 equiv) and V-40 (0.2 equiv) in *tert*-butylbenzene at 140 °C for 5 h afforded 4-phenoxybutyl cyanide in only 21% yield together with recovered 4-phenoxybutyl iodide (77%). Notably, methanesulfonyl cyanide was completely consumed, with acetonitrile as the major product [Eq. (3)].[10] However, allyl sulfone **1** was an effective

$$\underset{R=PhO(CH_2)_4}{RI} + MeSO_2CN \xrightarrow[tBuC_6H_5,\ 140\ ^{\circ}C]{V\text{-}40} \underset{21\%}{RCN} + CH_3CN \qquad (3)$$

precursor for radical cyanation, and our approach is outlined in Scheme 1. We envisaged that the addition of a *p*-toluenesulfonyl radical to **1** would produce an alkyl sulfonyl radical as well as *p*-tolyl allyl sulfone **4**. Although the alkyl sulfonyl

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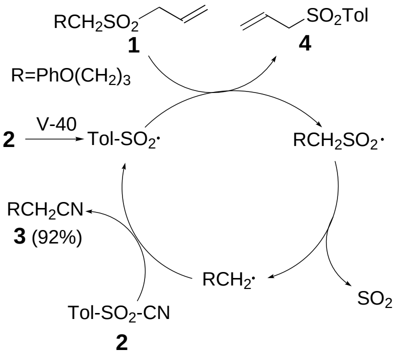
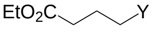
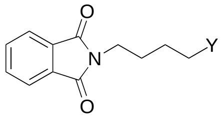
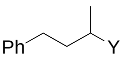
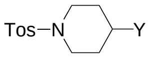
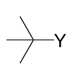
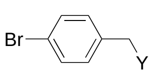


Scheme 1. Pathway for radical cyanation of an alkyl allyl sulfone with *p*-toluenesulfonyl cyanide.

radical could add to **1** and **4**, the former is a degenerate process, and the latter produces the *p*-toluenesulfonyl radical. Thus, neither of the reactions interferes with the desired process. As the addition of an alkyl radical to **4** and **1** is relatively slow,[11] the alkyl radical that is generated from the thermal decomposition of the alkyl sulfonyl radical, should preferentially add to *p*-toluenesulfonyl cyanide (**2**) and regenerate the *p*-toluenesulfonyl radical for propagation of the radical chain reaction.

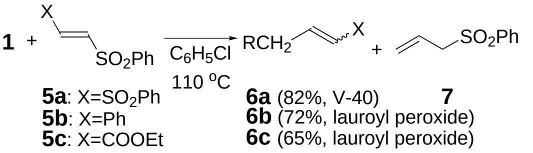
The reaction of **1** with **2** (1.5 equiv) in the presence of V-40 initiator (0.2 equiv) in chlorobenzene at 110°C for 6 h proceeded cleanly, yielding **3** in 92 % yield. The high-yielding formation of **3** indicates that the primary alkyl radical is generated cleanly under tin-free conditions (Scheme 1).[12] As shown in Table 1, the present method worked well with primary and secondary alkyl allyl sulfones as well as with a benzyl allyl sulfone.

Table 1. Tin-free cyanation, vinylation and allylation.[a]

Alkyl allyl sulfone (**1**) RY (Y = $SO_2CH_2CH{=}CH_2$)	Yields [%][b]		
	3[c]	**6a**[d]	**9a**[e]
	93	88	84
	96	94	85
	98	96	90
	98	98	88
		98	98
	98	97	97

[a] The reaction was carried out with V-40 in chlorobenzene at 110°C for 4–6 h. [b] Yield of isolated products. [c] **3**: Obtained from the reaction of **1** and **2**. [d] (*E*)-**6a**: Obtained from the reaction of **1** and (*Z*)-**5a**. [e] **9a**: Obtained from the reaction of **1** and **8a**.

The present approach can be further applied to radical vinylation and allylation reactions. For radical vinylations,[3,13] we found that (*E*)- and (*Z*)-1,2-bis(phenylsulfonyl)ethylene (**5a**)[14] are excellent radical acceptors and transfer a vinyl sulfonyl group to an alkyl group.[15] Treatment of **1** with **5a** and V-40 in chlorobenzene at 110°C for 6 h afforded **6a** in 82 % yield [Eq. (4)].[16] Apparently, the addition of the primary alkyl radical derived from **1** to activated vinyl sulfone **5a** is much faster than the addition to unactivated allyl sulfone **1** and **7**. When (*Z*)-1,2-bis(phenylsulfonyl)ethylene was used, various alkyl allyl sulfones worked equally well, yielding (*E*)-1-phenylsulfonyl alkenes as a major product in high yields (Table 1).[16]

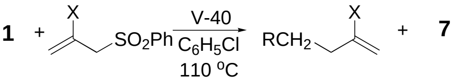


(4)

5a: X=SO2Ph
5b: X=Ph
5c: X=COOEt
6a (82%, V-40)
6b (72%, lauroyl peroxide)
6c (65%, lauroyl peroxide)
7

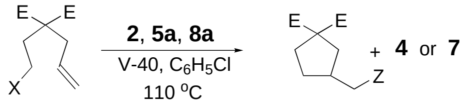
However, the reaction of **1** with **5b** under similar conditions gave the desired alkene **6b** in 21 % yield. A similar result was also obtained with **5c** (18 %). However, when the reactions were performed with lauroyl peroxide as initiator, much better results were obtained with **5b** and **5c**, showing the generality of vinylations.

We next studied radical allylations with several C2-substituted allyl sulfones [Eq. (5)]. Radical reaction of **1** with **8a** (1.5 equiv) in chlorobenzene in the presence of V-40 (0.2 equiv) for 6 h afforded 2-phenylsulfonyl alkene **9a** in 85 % yield. Additional experimental results with **8a** clearly demonstrate the synthetic efficiency of the present method (Table 1). When allylations were carried out with other functionalized allyl sulfones (**8b**, **8c**, **8d**) under similar conditions, the corresponding allylated products were isolated in high yields without the formation of **9e**, which results from the concomitant addition of the alkyl radical to **1** and **7**. Finally, when tandem radical reactions involving cyclization and C–C-bond formation were briefly studied with **10**, the reactions worked well, yielding **11** in high yield [Eq. (6)].



(5)

8a: X=SO2Ph
8b: X=Br
8c: X=CN
8d: X=COOEt
9a (85%)
9b (74%)
9c (74%)
9d (70%)
9e: X=H



(6)

10
X= SO2CH2CH=CH2
E= COOEt
11a: Z=CN (92%)
11b: Z=(*E*)-CH=CHSO2Ph (92%)
11c: Z=CH2C(SO2Ph)=CH2 (82%)

In conclusion, we have found that primary alkyl allyl sulfones are one of the most useful and reliable sources of primary alkyl radicals under tin-free conditions and developed highly efficient tin-free radical-mediated cyanation, vinylation, and allylation reactions, which we believe have great synthetic potential.

Experimental Section

Typical procedure: A solution of **1** (0.2 mmol), **2** (0.3 mmol), and V-40 (0.04 mmol) in chlorobenzene (1 mL) was degassed with nitrogen for 10 min and the solution was then heated at 110 °C under nitrogen for 6 h. The solvent was evaporated under reduced pressure and the residue was separated by silica-gel column chromatography (Et_2OAc/n-hexane 1:3) to give **3**. ^1H NMR ($CDCl_3$, 400 MHz): $\delta = 1.85$–1.95 (m, 4H), 2.43 (t, $J = 7.0$ Hz, 2H), 4.00 (t, $J = 5.6$ Hz, 2H), 6.86–6.96 (m, 3H), 7.24–7.29 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): $\delta = 17.0$, 22.5, 28.2, 66.5, 114.4, 119.5, 120.9, 129.5, 158.6; IR (polymer): $\tilde{\nu} = 2927$, 1601, 1586, 1497, 1474, 1247, 757, 693 cm^{-1}; HRMS [M^+] calcd for $C_{11}H_{13}NO$: 175.0997, found: 175.0997.

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[10] The reaction of methanesulfonyl cyanide in the presence of V-40 (0.1 equiv) in *tert*-butylbenzene at 140 °C for 5 h gave acetonitrile.

[11] According to our competition experiment between allyl phenyl sulfone and allyltributyltin, the addition of a primary alkyl radical to allyltributyltin is approximately five times faster than that to allyl phenyl sulfone; the rate constant for the former reaction is known to be in the range of 10^4–$10^5 M^{-1} s^{-1}$ at 50–80 °C:D. P. Curran, P. A. van Elburg, B. Giese, S. Giles, *Tetrahedron Lett.* **1990**, *31*, 2861–2864.

[12] Decomposition of primary alkyl sulfonyl radicals into primary alkyl radicals and SO_2 requires heating at around 100 °C. When secondary and tertiary alkyl allyl sulfones are employed, the reaction temperature can be lowered to some extent and AIBN can be used as initiator.

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[16] **6a** (*E*/*Z* 12:1): (*E*)-1-phenylsulfonyl alkene (**6**) was obtained as the major product and the *E*/*Z* ratios can be found in the Supporting Information.