Tin-free Radical Cyanation of Alkyl Iodides and Alkyl Phenyl Tellurides

Sunggak Kim,* Hyun-Ji Song

Center for Molecular Design & Synthesis and Department of Chemistry, School of Molecular Science, Korea Advanced Institute of Science and Technology, Taejon 305-701, Korea
Fax +82(42)8698370; E-mail: skim@mail.kaist.ac.kr

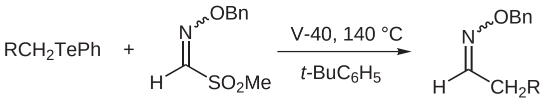
Received 7 June 2002

Abstract: As a result of much faster phenyl telluride group transfer relative to the corresponding iodine atom transfer, tin-free radical cyanation of alkyl phenyl tellurides has been achieved with *p*-toluenesufonyl cyanide and methyl allyl sulfone in the presence of V-40 as initiator.

Key words: radicals, tin-free, cyanation, alkyl phenyl tellurides, sulfones

Due to the toxicity and the purification problems of organotin reagents, tin-free radical reactions have received a great deal of recent attentions.[1] Among various approaches including the use of polymer-supported organotin compounds, organosilanes, and organophosphorous compounds,[2] an organosulfone-mediated method seems to be very attractive and has proved to be highly efficient for the carbon-carbon bond forming reactions such as allylation and vinylation.[3,4]

However, the reported methods did not work well with primary alkyl iodides and xanthates.[3,5] Recently, we also reported tin-free acylation approach using methanesulfonyl oxime ether, in which primary alkyl iodides and xanthates caused the same problem due to a small energy difference between a methyl radical and a primary alkyl radical.[5] We have found that a primary alkyl telluride is a useful precursor for the generation of the primary alkyl radical under tin-free conditions (Equation 1).[5]



Equation 1

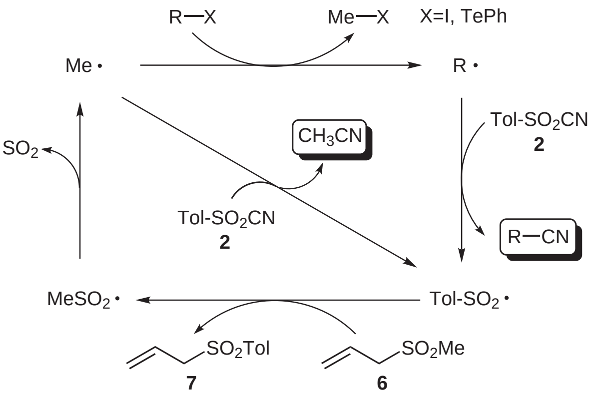
In connection with our recent interest in tin-free carbon-carbon bond forming reactions,[6] we have studied the feasibility of radical cyanation of alkyl iodides under tin-free conditions. Previously, decarboxylative cyanation of Barton's ester and addition of toluenesulfonyl cyanide onto the carbon-carbon double bonds have been reported.[7,8] However, radical cyanation of alkyl halides has not been studied previously. We initially studied tin-mediated radical cyanation of primary alkyl iodides with *p*-toluenesulfonyl cyanide (**2**). Reaction of 4-phenoxybutyl iodide (**1**) with **2** (1.2 equiv) and hexamethylditin (1.2 equiv) in benzene at 300 nm for 2 hours afforded the desired cyanide **3** in 89% yield (Equation 2). A similar result was also realized with **4** under the same conditions.[9]

$$\mathrm{R{-}I} \quad + \quad \mathrm{TolSO_2CN} \quad + \quad \mathrm{(Me_3Sn)_2} \xrightarrow[\mathrm{C_6H_6}]{\text{300 nm}} \mathrm{R{-}CN}$$

1:R=PhO$(CH_2)_4$ **2** **3** (89%)
4:R=EtOOC$(CH_2)_3$ **5** (88%)

Equation 2

Our approach for tin-free radical cyanation is outlined in Scheme 1 and methyl allyl sulfone (**6**) was employed as a source to generate a methyl radical for iodine atom transfer. We envisaged that the addition of a *p*-toluenesulfonyl radical onto **6** would produce a methanesulfonyl radical along with the formation of the *p*-tolyl allyl sulfone (**7**). Since thermal decomposition of the methanesulfonyl radical is relatively slow,[10] the addition of methanesulfonyl radical onto **6** and **7** can occur. However, both reactions can not cause any problems because the former is a degenerate process and the latter generates the *p*-toluenesulfonyl radical. Since the addition of the methyl radical onto **6** and **7** is relatively slow,[11] the methyl radical would undergo the iodine atom transfer from an alkyl iodide and/or direct addition onto **2** along with regeneration of the *p*-toluenesulfonyl radical for propagation of a radical chain reaction.

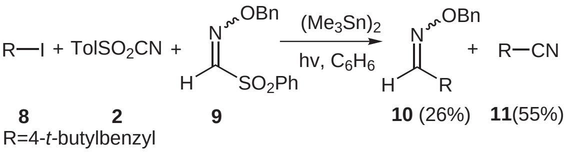


Scheme 1

To achieve tin-free cyanation of alkyl iodides, an efficient iodine atom transfer from the alkyl iodide to the methyl radical is the most important. Thus, we carried out a competition experiment to determine an approximate rate

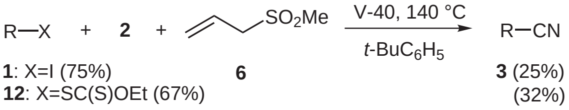
Synlett 2002, No. 12, Print: 02 12 2002.
Art Id.1437-2096,E;2002,0,12,2110,2112,ftx,en;U02502ST.pdf.
© Georg Thieme Verlag Stuttgart · New York
ISSN 0936-5214

constant for the addition of the alkyl radical onto **2**. When 4-*t*-butylbenzyl iodide (**8**) was treated with an equimolar mixture of **2** and **9** in the presence of hexamethylditin (1.0 equiv) in benzene at 300 nm for 3 h, a roughly 1:2 mixture of **10** and **11** was isolated, indicating that the approximate rate constant is in the order of 10^6 $M^{-1}s^{-1}$ as compared to our previous kinetic data with **9** and this addition was one of the most efficient intermolecular radical reactions (Equation 3).[12]



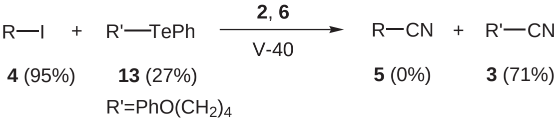
Equation 3

Radical cyanation of **1** with **2** (2.0 equiv) and V-40 [azobis(cyclohexanecarbonitrile)] (0.2 equiv) in *t*-butylbenzene at 140 °C for 12 h afforded the corresponding cyanide **3** in 25% yield along with the recovery of the starting iodide **1** (75%) (Equation 4), furthermore, it is noteworthy that **2** was completely consumed. Similarly, unsuccessful results were obtained with 4-phenoxybutyl xanthate **12**. In the cases of **1** and **12**, the direct addition became a major process because of a slow iodine atom transfer due to a small energy difference between the methyl and the primary alkyl radical.[5] Apparently, acetonitrile must be formed as a major product. With a solution of **2** and **6** in the presence of V-40 in *t*-butylbenzene at 140 °C for 6 h, acetonitrile was observed in GC along with the formation of **7** and the complete consumption of **2**. Since this fundamental problem associated with the fast direct addition of the methyl radical onto **2** could not be easily solved, we turned our attention to alkyl phenyl tellurides as radical precursors.



Equation 4

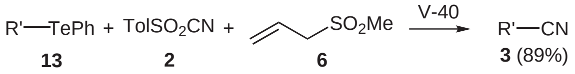
Since a phenyl telluride group transfer from a primary alkyl phenyl telluride to the methyl radical was much faster than the corresponding iodine atom transfer,[5] we examined the efficiency of the phenyl telluride transfer relative to the iodine atom transfer in radical cyanation. When a competition experiment was carried out with an equimolar mixture of **4** and **13**, **2** (1.5 equiv), **6** (1.5 equiv), and V-40 (0.2 equiv) in *t*-butylbenzene at 140 °C for 12 h, **3** was isolated in 71% yield along with the recovery of **4** (95%) and **13** (27%) without the formation of **5** (Equation 5). This result clearly indicates that the transfer of the phenyl telluride group from the primary alkyl phenyl telluride to the methyl radical was much faster than the direct addition of the methyl radical onto **2**. Thus, treatment of **13** with **2** (2.0 equiv), **6** (2.0 equiv), and V-40 (0.2 equiv) in *t*-butylbenzene at 140 °C for 12 h afforded **3** in 89% yield (Equation 6). Additional experimental results were obtained with primary and secondary alkyl phenyl tellurides under the same conditions (Table 1).[13]



$$\underset{\mathbf{4}\ (95\%)}{R\text{—}I} + \underset{\mathbf{13}\ (27\%)}{R'\text{—}TePh} \xrightarrow[\text{V-40}]{\mathbf{2},\,\mathbf{6}} \underset{\mathbf{5}\ (0\%)}{R\text{—}CN} + \underset{\mathbf{3}\ (71\%)}{R'\text{—}CN}$$

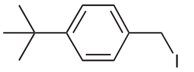
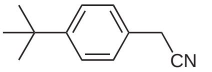
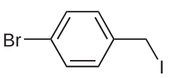
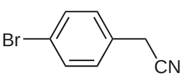
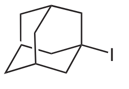
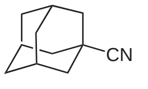
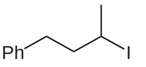
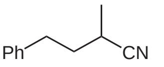
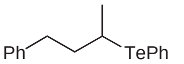
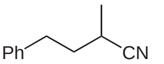
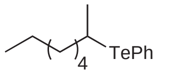
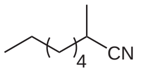
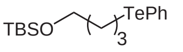
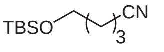
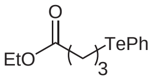
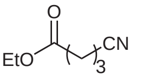
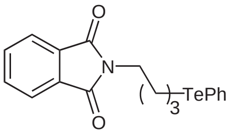
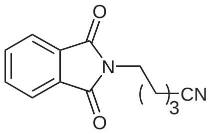
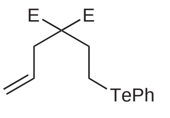
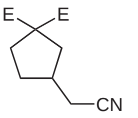
R'=PhO(CH$_2$)$_4$

Equation 5



Equation 6

Table 1 Tin-free Radical Cyanation of RI and RTePh

Substrate	Product	Yield[a]
		94%
		95%
		55% (30%)
		53% (42%)
		90%
		93%
		71%[b]
		86%
		77%
		66%[c]

[a] The numbers in parentheses indicates the recovered iodides. Reaction time was 8 h for benzyl iodides and secondary alkyl tellurides, and 12 h for secondary alkyl iodides and primary alkyl tellurides.

[b] TBS = *t*-butyldimethylsilyl.

[c] E = COOEt

Tin-free radical cyanation did not work well with primary, secondary, and tertiary alkyl iodides because the direct addition process involving the methyl radical addition to

2 was much faster than the iodine atom transfer process. However, benzylic iodides worked well due to the fast iodine atom transfer. For alkyl tellurides, primary and secondary alkyl phenyl tellurides underwent clean radical cyanation under tin-free conditions. Also, a tandem radical reaction involving cyclization and cyanation sequence could be performed.

Acknowledgment

This research was supported by the Center for Molecular Design and Synthesis (CMDS) and BK 21 project.

References

(1) Baguley, P. A.; Walton, J. C. *Angew. Chem. Int. Ed.* **1998**, *37*, 3072.

(2) (a) Gerigke, U.; Gerlach, M.; Neumann, W. P.; Vieler, R.; Weintritt, V. *Synthesis* **1990**, 448. (b) Gerlach, M.; Jordens, F.; Kuhn, H.; Neumann, W. P.; Peterseim, M. *J. Org. Chem.* **1991**, *56*, 5971. (c) Dumartin, G.; Ruel, G.; Kharboutli, J.; Delmond, B.; Connil, M.-F.; Jousseaume, B.; Pereyre, M. *Synlett* **1994**, 952. (d) Chatgilialoglu, C.; Griller, D.; Lesage, M. *J. Org. Chem.* **1988**, *53*, 3641. (e) Giese, B.; Kopping, B.; Chatgilialoglu, C. *Tetrahedron Lett.* **1989**, *30*, 681. (f) Ballestri, M.; Chatgilialoglu, C. *J. Org. Chem.* **1991**, *56*, 678. (g) Chatgilialoglu, C. *Acc. Chem. Res.* **1992**, *25*, 188. (h) Chatgilialoglu, C. *Chem. Rev.* **1995**, *95*, 1229. (i) Brumwell, J. E.; Simpkins, N. S.; Terrett, N. K. *Tetrahedron Lett.* **1993**, *34*, 1215.

(3) (a) Quiclet-Sire, B.; Zard, S. Z. *J. Am. Chem. Soc.* **1996**, *118*, 1209. (b) Guyader, F. L.; Quiclet-Sire, B.; Seguin, S.; Zard, S. Z. *J. Am. Chem. Soc.* **1997**, *119*, 7410. (c) Zard, S. Z. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 672.

(4) (a) Xiang, J.; Fuchs, P. L. *J. Am. Chem. Soc.* **1996**, *118*, 11986. (b) Bertrand, F.; Quielet-Sire, B.; Zard, S. Z. *Angew. Chem. Int. Ed.* **1999**, *38*, 1943.

(5) Kim, S.; Song, H.-J.; Choi, T.-L.; Yoon, J.-Y. *Angew. Chem. Int. Ed.* **2001**, *40*, 2524.

(6) (a) Kim, S.; Lim, C. J.; Song, S.-E.; Kang, H.-Y. *Synlett* **2001**, 688. (b) Kim, S.; Kim, N.; Chung, W.-J.; Cho, C. H. *Synlett* **2001**, 937. (c) Kim, S.; Lim, C. J.; Song, S.-E.; Kang, H.-Y. *Chem. Commun.* **2001**, 1410.

(7) (a) Barton, D. H. R.; Jaszberenyi, J. Cs.; Theodorakis, E. A. *Tetrahedron Lett.* **1991**, *32*, 3321. (b) Barton, D. H. R.; Jaszberenyi, J. Cs.; Theodorakis, E. A. *Tetrahedron* **1992**, *48*, 2613.

(8) Fang, J.-M.; Chen, M.-Y. *Tetrahedron Lett.* **1987**, *28*, 2853.

(9) Typical procedure for Equation 2: The degassed solution of ethyl 4-iodobutyrate (**4**, 48 mg, 0.20 mmol), *p*-toluenesulfonyl cyanide (**2**, 46 mg, 0.24 mmol) and hexamethylditin (79 mg, 0.24 mmol) in benzene (1 mL) was irradiated under 300 nm UV lamp at room temperature for 2 h. The solvent was evaporated under reduced pressure and the residue was chromatographed on a silica gel column (*n*-hexane/ethyl acetate = 1:5) to yield ethyl 4-cyanobutyrate (**5**, 25 mg, 0.18 mmol, 88% yield). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.21 (t, J = 7.1 Hz, 3 H), 1.87–1.97 (m, 2 H), 2.38–2.44 (m, 4 H), 4.09 (q, J = 7.1 Hz, 2 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.0, 16.4, 20.6, 32.3, 60.6, 118.9, 171.8; IR (NaCl) 2994, 2950, 2880, 2365, 2344, 2252, 1734, 1458, 1378, 1222, 1198, 1028 cm^{-1}.

(10) (a) Horowitz, A.; Rajbenbach, L. A. *J. Am. Chem. Soc.* **1975**, *97*, 10. (b) Chatgilialoglu, C. In *The Chemistry of Sulfones and Sulfoxides*; Patai, S.; Rappoport, Z.; Stirling, C. J. M., Eds.; Wiley: Chichester, **1988**, 1089–1113. (c) Bertrand, M. *Org. Prep. Proc. Int.* **1994**, *26*, 257.

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

(12) Kim, S.; Lee, I. Y. *Tetrahedron Lett.* **1998**, *39*, 1587.

(13) Typical procedure for Equation 6: The degassed solution of 4-phenoxybutyl phenyl telluride (**13**, 65 mg, 0.18 mmol), *p*-toluenesulfonyl cyanide (**2**, 70 mg, 0.37 mmol), methyl allyl sulfone (**6**, 44 mg, 0.37 mmol) and V-40 (9 mg, 0.037 mmol) in *t*-butylbenzene (1 mL) was stirred at 140 °C under N_2 for 12 h. The solvent was evaporated under reduced pressure and the residue was chromatographed on a silica gel column (*n*-hexane/ethyl acetate = 1:10) to yield 5-phenoxy pentanenitrile (29 mg, 0.16 mmol, 89% yield). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.85–1.95 (m, 4 H), 2.41–2.45 (t, J = 6.7 Hz, 2 H), 3.98–4.00 (t, J = 5.7 Hz, 2 H), 6.85–6.92 (d, J = 5.6 Hz, 2 H), 6.93–6.95 (t, J = 7.3 Hz, 1 H), 7.23–7.28 (m, 2 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 16.6, 22.0, 27.8, 66.0, 113.9, 119.0, 120.4, 129.0, 158.2; IR (NaCl) 2946, 2877, 2362, 2343, 2247, 1600, 1498, 1245 cm^{-1}.