Iron Catalysis

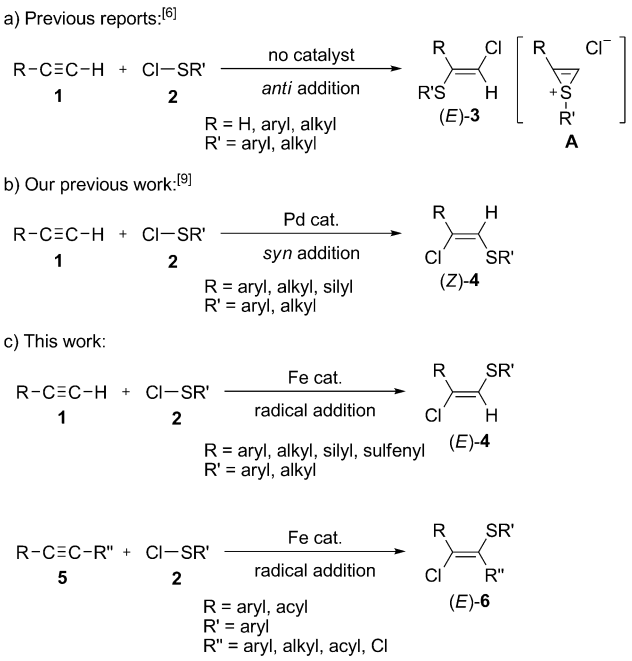
DOI: 10.1002/ange.201408121

Iron-Induced Regio- and Stereoselective Addition of Sulfenyl Chlorides to Alkynes by a Radical Pathway**

*Masayuki Iwasaki, Tomoya Fujii, Kiyohiko Nakajima, and Yasushi Nishihara**

Abstract: *The radical addition of the Cl–S σ-bond in sulfenyl chlorides to various C–C triple bonds has been achieved with excellent regio- and stereoselectivity in the presence of a catalytic amount of a common iron salt. The reaction is compatible with a variety of functional groups and can be scaled up to the gram-scale with no loss in yield. As well as terminal alkynes, internal alkynes underwent stereodefined chlorothiolation to provide tetrasubstituted alkynes. Preliminary mechanistic investigations revealed a plausible radical process involving a sulfur-centered radical intermediate via iron-mediated homolysis of the Cl–S bond. The resulting chlorothiolation adducts can be readily transformed to the structurally complex alkenyl sulfides by cross-coupling reactions. The present reaction can also be applied to the complementary synthesis of the potentially useful bis-sulfoxide ligands for transition-metal-catalyzed reactions.*

Addition of heteroatom–heteroatom bonds to carbon–carbon triple bonds has been considered to be one of the most powerful methods to install two heteroatoms efficiently in one step.[1] Among such reactions, the addition of organosulfur compounds to alkynes has been extensively studied[2] owing to the utility of the resulting alkenyl sulfides as bioactive compounds.[3] Although various addition reactions of S–E (E = B, Si, P, S, Se, Te, etc.) bonds to alkynes have been reported,[4,5] chlorothiolation across alkynes represents an attractive research topic in organic synthesis because the corresponding adducts can be converted into complex and diverse alkenyl sulfides by the transformation of the chloro moieties. Therefore, several efficient methods have been developed to synthesize 2-chloroalkenyl sulfides by chlorothiolation of alkynes through S–Cl bond cleavage of sulfenyl chlorides.[6,7] The reaction of terminal alkynes **1** with sulfenyl chloride **2** proceeds in an *anti* fashion to give adduct (*E*)-**3** as the sole product, probably via the thiirenium intermediate **A**[6c–e] (Scheme 1 A). However, conventional methods could not provide the other isomers (*Z*)-**3** and (*E*)/(*Z*)-**4**.[8] Moreover, when unsymmetrical internal alkynes were employed without any catalysts, the reaction gave a mixture of the regio- and stereoisomers.[6c–e] To overcome such significant drawbacks, we have investigated the transition-metal-catalyst-controlled regio- and stereoselective chlorothiolation of alkynes. Recently, we showed that a palladium catalyst could totally switch the reaction mode in the chlorothiolation of terminal alkynes, affording *syn* adducts (*Z*)-**4** with high regio- and stereoselectivity (Scheme 1 B).[9] Although (*E*)-**3** and (*Z*)-**4** had been prepared, the selective synthesis of (*E*)-**4** isomers has not been well-studied. This is because organosulfur compounds had been believed to be a catalyst poison[10] for the transition-metal catalysts that can control the selec-



Scheme 1. Chlorothiolation of alkynes.

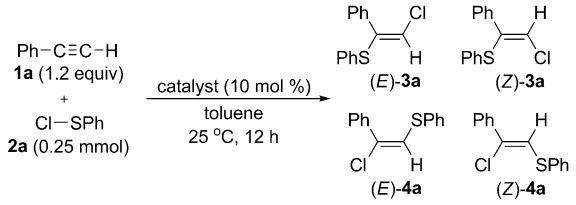
[*] Dr. M. Iwasaki, T. Fujii, Prof. Dr. Y. Nishihara
Division of Earth, Life, and Molecular Sciences
Graduate School of Natural Science and Technology
Okayama University, 3-1-1 Tsushimanaka, Kita-ku
Okayama 700-8530 (Japan)
E-mail: ynishiha@okayama-u.ac.jp
Prof. Dr. K. Nakajima
Department of Chemistry, Aichi University of Education
Igaya, Kariya 448-8542 (Japan)
Prof. Dr. Y. Nishihara
ACT-C Japan Science and Technology Agency
4-1-8 Honcho, Kawaguchi, Saitama 332-0012 (Japan)

[**] This work was partly supported by a Grant-in-Aid for Scientific Research (KAKENHI) (No. 26810060) from JSPS and the MEXT program for promoting the enhancement of research universities. The authors gratefully thank Prof. Dr. Yoshimi Sueishi and Misato Sue (Okayama University) for the ESR measurements and fruitful discussions, Megumi Kosaka and Motonari Kobayashi (Department of Instrumental Analysis, Advanced Science Research Center, Okayama University) for the measurements of elemental analyses, and the SC NMR Laboratory of Okayama University for the NMR measurements.

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/anie.201408121.

tivity of the addition reaction. As a result of their potential utility as synthetic intermediates,[11] a practical synthetic route to prepare (*E*)-**4** has been required for many years. During the course of our work, we found that cheap and abundant iron catalysts could absolutely control the selectivity of the reaction to yield (*E*)-**4** (Scheme 1 C). Notably, unsymmetrical internal alkyne **5** served as the substrate to furnish tetrasubstituted olefin (*E*)-**6** with perfect selectivity. Herein, we report the first complementary synthesis of 2-chloroalkenyl sulfides by a radical pathway by simply selecting the appropriate transition-metal catalyst.

To investigate the regio- and stereoselectivity of chlorothiolation using transition-metal catalysts, we first examined the reaction of phenylacetylene (**1a**) with benzenesulfenyl chloride (**2a**) in toluene at room temperature (Scheme 2).[12] In the absence of any catalyst, an *anti* chlorothiolation adduct



Scheme 2. Addition of benzenesulfenyl chloride (**2a**) to phenylacetylene (**1a**).

(*E*)-**3a** was solely formed in 38% yield, as reported previously.[6] In sharp contrast, in the presence of $Pd(tfa)_2$ (10 mol%; tfa = trifluoroacetate), the reaction provided (*Z*)-**4a** in 84% NMR yield with high regio- and stereoselectivity.[9] After extensive surveys of transition-metal catalysts,[12] we found that iron salts facilitate the novel *anti* chlorothiolation to yield (*E*)-**4a** preferentially over the other three regio- and stereoisomers. Indeed, the desired product (*E*)-**4a** was obtained in 36% yield when $FeCl_3$ was employed as the catalyst. $FeCl_2$ and $FeBr_2$ were shown to be the optimal catalysts, both of which could catalyze the selective addition of a Cl–S bond to give (*E*)-**4a** predominantly. Other iron(II) catalysts, such as $Fe(BF_4)_2{\cdot}7H_2O$, $FeSO_4{\cdot}7H_2O$ (melanterite), and $Fe(acac)_2$ (acac = acetylacetonato), were less effective, affording lower yields of (*E*)-**4a**. To our surprise, metallic iron also showed catalytic activity, producing regio- and stereoselective chlorothiolation. Further examination revealed that the reaction proceeded smoothly (83% yield) even in the presence of $FeCl_2$ (5 mol%), although the yield of (*E*)-**4a** was decreased to 54% when $FeCl_2$ (1 mol%) was employed.[13] Other ligands, such as PPh_3, DPPE (1,2-bis(diphenylphosphino)ethane), and TMEDA (*N*,*N*,*N*′,*N*′-tetramethylethylenediamine), used with the $FeCl_2$ catalyst gave lower yields of (*E*)-**4a**.[12] The choice of the reaction solvent was found to be crucial; nonpolar solvents (toluene, benzene, and chlorobenzene) can be utilized, but polar solvents (THF, DMF, and AcOEt) were ineffective.[12] Notably, the present reaction is scalable, and 1.9 g of (*E*)-**4a** was isolated in a comparable yield (77%) to that obtained when the reaction was performed on a 1.0 mmol scale (81%). The stereochemistry of (*E*)-**4a** was determined by comparison of the spectroscopic data for the known sulfone **7**, which was prepared by oxidation of (*E*)-**4a**. The precise configuration was unambiguously confirmed by single-crystal X-ray analysis of **7** (Figure 1).[14]

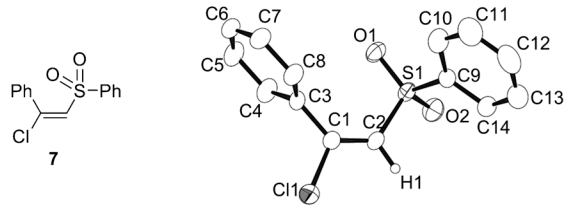
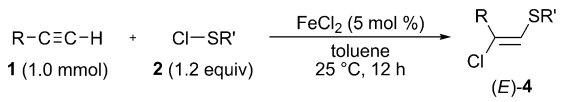


Figure 1. ORTEP Drawing of **7** with thermal ellipsoids set at 30% probability. Hydrogen atoms on the benzene rings are omitted for clarity.

Next, we carried out the iron-induced chlorothiolation of various terminal alkynes **1** with benzenesulfenyl chloride (**2a**) to obtain the corresponding adducts (*E*)-**4**. Instead of **1a**, various arylethynes **1b**–**1e** which have an electron-donating methyl group and electron-withdrawing chloro, cyano, or trifluoromethyl groups reacted with **2a** to give the corresponding adducts (*E*)-**4b**–**4e** in good yield (Table 1, entries 1–

Table 1: Iron-induced chlorothiolation of terminal alkynes **1** with sulfenyl chlorides **2**.[a]



Entry	R	R′	Product	Yield [%][b]
1	Ph (**1a**)	Ph (**2a**)	(*E*)-**4a**	81
2	*p*-MeC_6H_4 (**1b**)	Ph (**2a**)	(*E*)-**4b**	76
3	*p*-ClC_6H_4 (**1c**)	Ph (**2a**)	(*E*)-**4c**	81
4	*p*-NCC_6H_4 (**1d**)	Ph (**2a**)	(*E*)-**4d**	66
5	*p*-$F_3CC_6H_4$ (**1e**)	Ph (**2a**)	(*E*)-**4e**	71
6[c]	2-Naphthyl (**1f**)	Ph (**2a**)	(*E*)-**4f**	71
7[c]	1-Naphthyl (**1g**)	Ph (**2a**)	(*E*)-**4g**	60[e]
8	*n*Hex (**1h**)	Ph (**2a**)	(*E*)-**4h**	70
9	$Cl(CH_2)_4$ (**1i**)	Ph (**2a**)	(*E*)-**4i**	59[e]
10[c]	$TsO(CH_2)_4$ (**1j**)	Ph (**2a**)	(*E*)-**4j**	60[f]
11	$PhthN(CH_2)_4$ (**1k**)	Ph (**2a**)	(*E*)-**4k**	46[e]
12	Me_3Si (**1l**)	Ph (**2a**)	(*E*)-**4l**	47
13	PhS (**1m**)	Ph (**2a**)	(*E*)-**4m**	34[g]
14	Ph (**1a**)	*p*-MeC_6H_4 (**2b**)	(*E*)-**4n**	88
15	Ph (**1a**)	*p*-$MeOC_6H_4$ (**2c**)	(*E*)-**4o**	81
16	Ph (**1a**)	*p*-BrC_6H_4 (**2d**)	(*E*)-**4p**	83
17	Ph (**1a**)	*p*-$F_3CC_6H_4$ (**2e**)	(*E*)-**4q**	58
18	Ph (**1a**)	*o*-MeC_6H_4 (**2f**)	(*E*)-**4r**	96
19	Ph (**1a**)	*o*-BrC_6H_4 (**2g**)	(*E*)-**4s**	86
20[d]	Ph (**1a**)	Me (**2h**)	(*E*)-**4t**	54

[a] Conditions: **1** (1.0 mmol), **2** (1.2 mmol), $FeCl_2$ (0.050 mmol), toluene (24 mL). [b] Yields of isolated product (*E*)-**4**, based on **1** after silica gel column chromatography. [c] The reaction was performed with $FeCl_2$ (10 mol%) for 24 h. [d] The reaction was performed with $FeCl_2$ (10 mol%). [e] Obtained as a mixture of stereoisomers in a 93:7 ratio. [f] Obtained as a mixture of stereoisomers in a 92:8 ratio. [g] Obtained as a mixture of stereoisomers in a 74:26 ratio. PhthN = phthalimidyl. TsO = tosyloxy, $CH_3C_6H_4SO_3$.

5). As well as 2-naphthylacetylene (**1f**) giving rise to (*E*)-**4f**, the reaction of the sterically congested 1-naphthylacetylene (**1g**) also afforded the desired product (*E*)-**4g** in 60% yield (entries 6 and 7). An aliphatic terminal alkyne such as 1-octyne (**1h**) reacted with **2a** under the same reaction conditions to furnish the corresponding product (*E*)-**4h** in 70% yield (entry 8). No isomerization of (*E*)-**4h** with **2a** was detected in the present reaction in the nonpolar solvent (toluene).[6f,g] Various functional groups were tolerated in the chlorothiolation of **1** with **2a**: chloro, tosyloxy, and phthalimide groups participated in the reaction to provide (*E*)-**4i**–**4k** without any loss of the functional moieties (entries 9–11). It is of note that both alkynylsilane **1l** and alkynyl sulfide **1m** derivatives also underwent chlorothiolation to give 1,1,2-trifunctionalized ethenes (*E*)-**4l** and (*E*)-**4m** (entries 12 and 13).

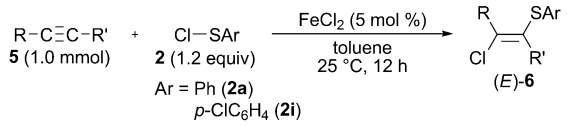
With the optimized conditions in hand, a wide range of arenesulfenyl chlorides **2** were found to be employable in the chlorothiolation of **1a** (Table 1). The reaction was compatible with electron-rich (methyl and methoxy) and electron-deficient (bromo and trifluoromethyl) groups in the *para* position of benzenesulfenyl chlorides **2b**–**2e** (entries 14–17). The substituents in the *ortho* position did not affect the product yields and (*E*)-**4r** and (*E*)-**4s** were obtained in 96% and 86% yields, respectively (entries 18 and 19).

Our attempts to use alkyl-substituted sulfenyl chlorides for the present iron-promoted chlorothiolation of alkynes **1** were unsuccessful because such sulfenyl chlorides were too unstable to isolate and readily decomposed to generate disulfides. We thus examined the one-pot reaction involving the preparation of sulfenyl chloride and the subsequent chlorothiolation of a terminal alkyne (entry 20). Dimethyl disulfide was treated with sulfuryl chloride in situ to form methanesulfenyl chloride (**2h**).[15] Phenylacetylene (**1a**) and a catalytic amount of $FeCl_2$ were subsequently added to the reaction mixture, and the desired adduct (*E*)-**4t** was obtained in 54% yield with high regio- and stereoselectivity.

To our delight, iron-induced chlorothiolation of unsymmetrical internal alkynes **5** also proceeded with excellent regio- and stereoselectivity, whereas the reaction gave a mixture of isomers without $FeCl_2$ (Table 2). When 1-phenyl-1-propyne (**5a**) was employed, the selective reaction with **2a** and *p*-chlorobenzenesulfenyl chloride (**2i**) proceeded exclusively to afford (*E*)-**6a** and (*E*)-**6b** as the single products in 94% and 88% yields, respectively (entries 1 and 2).[16] Additionally, other 1-alkyl-2-arylethynes, such as 1-phenyl-1-hexyne (**5b**) and 1-phenyl-3-methyl-1-butyne (**5c**), provided (*E*)-**6c** and (*E*)-**6d** with the chlorine atom located at the benzylic position (entries 3 and 4). Furthermore, phenylpropiolate **5d**, ynone **5e**, and alkynyl chloride **5f** also underwent regio- and stereoselective chlorothiolation to give the desired adducts (*E*)-**6e**–**6g** in moderate to high yields (entries 5–7). It should be noted that ethyl 2-heptynolate (**5g**) can also be used as the substrate, furnishing (*E*)-**6h** substituted with a chlorine in the α-position of an ester group (entry 8).[17]

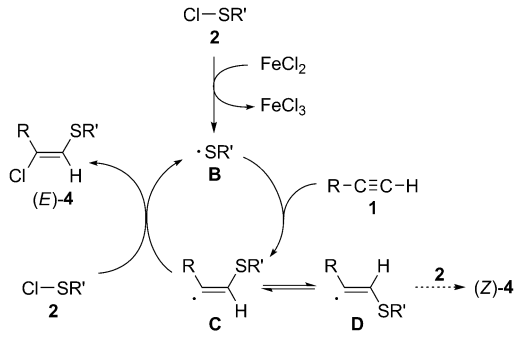
The present chlorothiolation was found to proceed through a radical process by ESR analysis.[12,18] We thus propose a radical mechanism for the present chlorothiolation

Table 2: Iron-induced chlorothiolation of internal alkynes **5** with sulfenyl chlorides **2**.[a]



Entry	R	R′	5	2	Product	Yield [%][b]
1	Ph	Me	**5a**	**2a**	(*E*)-**6a**	94
2	Ph	Me	**5a**	**2i**	(*E*)-**6b**	88
3	Ph	*n*Bu	**5b**	**2a**	(*E*)-**6c**	91
4	Ph	*i*Pr	**5c**	**2a**	(*E*)-**6d**[d]	73
5[c]	Ph	CO_2Et	**5d**	**2a**	(*E*)-**6e**	97
6	Ph	COMe	**5e**	**2a**	(*E*)-**6f**	53
7	Ph	Cl	**5f**	**2a**	(*E*)-**6g**	47
8[c]	CO_2Et	*n*Bu	**5g**	**2a**	(*E*)-**6h**	30

[a] Conditions: **1** (1.0 mmol), **2** (1.2 mmol), $FeCl_2$ (0.050 mmol), toluene (24 mL). [b] Yields of isolated product (*E*)-**6**, based on **5** after silica gel column chromatography. [c] The reaction was performed with $FeCl_2$ (15 mol%) and Cl-SPh (3.6 equiv). [d] (*Z*)-**6d** was formed in 24% yield.



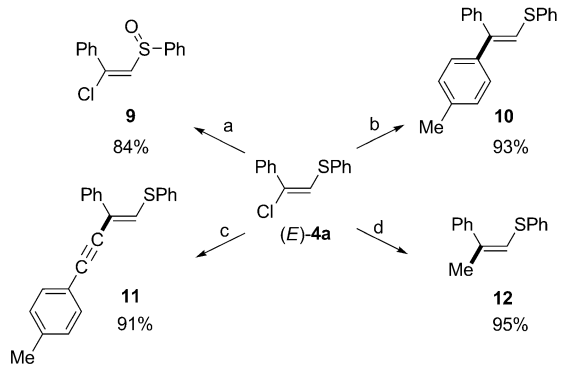
Scheme 3. Proposed chlorothiolation reaction mechanism by a radical pathway.

of terminal alkyne **1** with sulfenyl chloride **2**, as shown in Scheme 3. As the first step toward the generation of the radical species (initiation step), iron-mediated homolysis of the S–Cl bond of **2** may take place to give the corresponding sulfenyl radical **B**.[19] Then, sulfur-centered radical **B** adds to the less sterically hindered terminal carbon of **1** to form the alkenyl radical **C**. This step may control the excellent regioselectivity of the reaction. Finally, the radical S_H2 substitution of **C** with **2** affords the product (*E*)-**4** and regenerates the sulfenyl radical **B** to complete the radical chain.[20] The high *E*-selectivity of the reaction can be rationalized as follows. The alkenyl radical **D** may be as abundant as **C** at equilibrium.[21] However, sulfenyl chloride **2** may approach the intermediary alkenyl radical **C** more readily than **D** to avoid a steric repulsion from the sulfenyl group.[22]

With respect to the regioselectivity in the chlorothiolation of internal alkynes **5**, the stability of the generated alkenyl radical **C** has to be considered, as well as a steric congestion of the substituents on alkynes **5**.[23] As the benzylic radical is highly stabilized by its delocalization into the benzene ring,[24] (*E*)-**6a**–**6g** were obtained with perfect regioselectivity. The

formation of (*E*)-**6h** can be explained by the stability order of the alkenyl radical intermediates with the substituents (CO_2Et > alkyl). On the other hand, its stereoselectivity can be explained by a mechanism that involves the addition of an SR' radical to develop a singly occupied sp^2-hybridized orbital on the side opposite to the SR′ group, which is followed by a rapid chlorine transfer thanks to a weak Cl–S bond.[22,25] As another possible pathway, the reaction could proceed via cationic intermediates,[26] but no Lewis acid except $FeCl_2$ promoted selective chlorothiolation.[12]

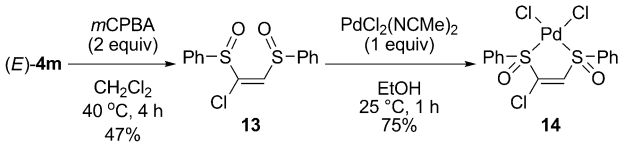
To demonstrate the synthetic utility of the chlorothiolation adducts obtained by the present method, we undertook a series of reactions using the representative product (*E*)-**4a** (Scheme 4). Mono-oxidation of (*E*)-**4a** with equimolar



Scheme 4. Transformations of (*E*)-**4a**. a) *m*CPBA (1 equiv), CH_2Cl_2, 40 °C, 4 h. b) *p*-$MeC_6H_4B(OH)_2$ (2 equiv), $Pd(OAc)_2$ (5 mol%), XPhos (10 mol%), K_2CO_3 (2 equiv), toluene, 110 °C, 12 h. c) *p*-MeC_6H_4CCH (2 equiv), $PdCl_2(NCPh)_2$ (10 mol%), CuI (10 mol%), piperidine, 25 °C, 3 h. d) MeMgBr (2 equiv), $Pd(dba)_2$ (5 mol%), P*t*Bu_3 (10 mol%), THF, 50 °C, 4 h. XPhos = 2-dicyclohexylphosphino-2′,4′,6′-triisopropylbiphenyl. dba = dibenzylideneacetone.

*m*CPBA (*m*-chloroperoxybenzoic acid) afforded the corresponding sulfoxide **9** in 84% yield.[6f] Arylation of (*E*)-**4a** by Suzuki–Miyaura coupling with *p*-tolylboronic acid gave **10** with complete stereoselectivity.[27] Sonogashira–Hagihara coupling of (*E*)-**4a** with *p*-tolylacetylene provided conjugated enyne **11** in 91% yield.[28] Moreover, palladium-catalyzed Kumada–Tamao–Corriu alkylation of (*E*)-**4a** with methylmagnesium bromide produced **12** in 95% yield.[29]

Selective chlorothiolation was also applied to the synthesis of potentially valuable bis-sulfoxide ligands for transition-metal catalysts (Scheme 5).[12,30] Oxidation of (*E*)-**4m** proceeded diastereoselectively to provide the corresponding bis-sulfoxide derivative **13** substituted with a transformative chloro group.[12] Complexation of a palladium



Scheme 5. Synthesis of bis-sulfoxide ligand **13** and palladium complex **14**.

salt with **13** afforded the benchtop-stable palladium complex **14**,[31] which could be a potent catalyst precursor similar to White's catalyst.[32,33]

In summary, we have developed the first radical addition of sulfenyl chlorides to alkynes by employing an iron catalyst, which afforded (*E*)-2-chloroalkenyl sulfides with excellent regio- and stereoselectivity. The present method provides a synthesis for chlorothiolation adducts that could not be prepared by earlier procedures. Several mechanistic studies revealed that the reaction involves radical intermediates. The synthetic utility of the present chlorothiolation was also demonstrated by cross-coupling reactions (arylation, alkynylation, and alkylation) of the adducts. The scalable catalytic reaction proceeded with high functional group compatibility under mild conditions, which should contribute to the practical syntheses of bioactive complex alkenyl sulfides.

Received: August 9, 2014
Revised: September 25, 2014
Published online: October 15, 2014

Keywords: alkynes · chlorothiolation · iron · radical reactions · synthetic methods

[1] a) I. Beletskaya, C. Moberg, *Chem. Rev.* **1999**, *99*, 3435–3461; b) L.-B. Han, M. Tanaka, *Chem. Commun.* **1999**, 395–402; c) I. Beletskaya, C. Moberg, *Chem. Rev.* **2006**, *106*, 2320–2354.

[2] I. P. Beletskaya, V. P. Ananikov, *Chem. Rev.* **2011**, *111*, 1596–1636.

[3] For examples, see: a) E. Marcantoni, M. Massaccesi, M. Petrini, G. Bartoli, M. C. Bellucci, M. Bosco, L. Sambri, *J. Org. Chem.* **2000**, *65*, 4553–4559; b) H. S. Sader, D. M. Johnson, R. N. Jones, *Antimicrob. Agents Chemother.* **2004**, *48*, 53–62.

[4] For addition of S–B bonds, see: a) T. Ishiyama, K. Nishijima, N. Miyaura, A. Suzuki, *J. Am. Chem. Soc.* **1993**, *115*, 7219–7225; For addition of S–S bonds, see: b) H. Kuniyasu, A. Ogawa, S. Miyazaki, I. Ryu, N. Kambe, N. Sonoda, *J. Am. Chem. Soc.* **1991**, *113*, 9796–9803; c) Y. Gareau, A. Orellana, *Synlett* **1997**, 803–804; d) M. Arisawa, M. Yamaguchi, *Org. Lett.* **2001**, *3*, 763–764; e) Y. Gareau, M. Tremblay, D. Gauvreau, H. Juteau, *Tetrahedron* **2001**, *57*, 5739–5750; f) V. P. Ananikov, M. A. Kabeshov, I. P. Beletskaya, G. G. Aleksandrov, I. L. Eremenko, *J. Organomet. Chem.* **2003**, *687*, 451–461; g) M. Arisawa, Y. Kozuki, M. Yamaguchi, *J. Org. Chem.* **2003**, *68*, 8964–8967; h) V. P. Ananikov, K. A. Gayduk, I. P. Beletskaya, V. N. Khrustalev, M. Y. Antipin, *Chem. Eur. J.* **2008**, *14*, 2420–2434; i) V. P. Ananikov, K. A. Gayduk, N. V. Orlov, I. P. Beletskaya, V. N. Khrustalev, M. Y. Antipin, *Chem. Eur. J.* **2010**, *16*, 2063–2071; For addition of S–Si bonds, see: j) L.-B. Han, M. Tanaka, *J. Am. Chem. Soc.* **1998**, *120*, 8249–8250; For addition of S–P bonds, see: k) L.-B. Han, M. Tanaka, *Chem. Lett.* **1999**, 863–864; l) N. Hoshi, T. Kashiwabara, M. Tanaka, *Tetrahedron Lett.* **2012**, *53*, 2078–2081.

[5] For reviews of radical additions of dichalcogenides, see: a) A. Ogawa, *J. Synth. Org. Chem. Jpn.* **1995**, *53*, 869–880; b) A. Ogawa, T. Hirao, *Rev. Heteroat. Chem.* **1998**, *18*, 1–10; c) P. Renurd, *Top. Curr. Chem.* **2000**, *208*, 81–112; For reviews of radical additions of S–P bonds, see: d) H. Yorimitsu, *Beilstein J. Org. Chem.* **2013**, *9*, 1269–1277; e) U. Wille, *Chem. Rev.* **2013**, *113*, 813–853; f) S. Kawaguchi, A. Ogawa, *Synlett* **2013**, 2199–2215.

[6] For selected examples, see: a) R. C. Fuson, C. C. Price, R. A. Bauman, O. H. Bullitt, Jr., W. R. Hatchard, E. W. Maynert, *J. Org. Chem.* **1946**, *11*, 469 – 474; b) W. E. Truce, H. E. Hill, M. M. Boudakian, *J. Am. Chem. Soc.* **1956**, *78*, 2760 – 2762; c) V. Caló, G. Scorrano, G. Modena, *J. Org. Chem.* **1969**, *34*, 2020 – 2022; d) G. H. Schmid, A. Modro, D. G. Garratt, K. Yates, *Can. J. Chem.* **1976**, *54*, 3045 – 3049; e) G. H. Schmid, A. Modro, F. Lenz, D. G. Garratt, K. Yates, *J. Org. Chem.* **1976**, *41*, 2331 – 2336; f) G. Capozzi, C. Caristi, V. Lucchini, G. Modena, *J. Chem. Soc. Perkin Trans. 1* **1982**, 2197 – 2201; g) G. Capozzi, G. Romeo, V. Lucchini, G. Modena, *J. Chem. Soc. Perkin Trans. 1* **1983**, 831 – 835; h) L. Zhong, P. R. Savoie, A. S. Filatov, J. T. Welch, *Angew. Chem. Int. Ed.* **2014**, *53*, 526 – 529; *Angew. Chem.* **2014**, *126*, 536 – 539; For the related bromothiolation reaction, see: i) L. Benati, P. C. Montevecchi, P. Spagnolo, *Tetrahedron* **1993**, *49*, 5365 – 5376.

[7] Addition reactions of sulfonyl halides to alkynes are well-known, see: a) W. E. Truce, G. C. Wolf, *J. Org. Chem.* **1971**, *36*, 1727 – 1732; b) Y. Amiel, *J. Org. Chem.* **1971**, *36*, 3691 – 3696; c) Y. Amiel, *J. Org. Chem.* **1971**, *36*, 3697 – 3702; d) Y. Amiel, *Tetrahedron Lett.* **1971**, *12*, 661 – 663; e) Y. Amiel, *J. Org. Chem.* **1974**, *39*, 3867 – 3870; f) X. Liu, X. Duan, Z. Pan, Y. Han, Y. Liang, *Synlett* **2005**, 1752 – 1754; g) X. Zeng, L. Ilies, E. Nakamura, *Org. Lett.* **2012**, *14*, 954 – 956; h) C. Chen, J. Su, X. Tong, *Chem. Eur. J.* **2013**, *19*, 5014 – 5018; i) X. Li, X. Shi, M. Fang, X. Xu, *J. Org. Chem.* **2013**, *78*, 9499 – 9504.

[8] *E*/*Z* isomerization of (*E*)-**3** to (*Z*)-**3** was reported in the presence of an excess amount of sulfenyl chloride **2**, see: Refs. [6f] and [6g].

[9] M. Iwasaki, T, Fujii, A. Yamamoto, K. Nakajima, Y. Nishihara, *Chem. Asian J.* **2014**, *9*, 58 – 62.

[10] a) L. L. Hegedus, R. W. McCabe, *Catalyst Poisoning*, Marcel Dekker, New York, **1984**; b) A. T. Hutton in *Comprehensive Coordination Chemistry*, *Vol. 5* (Eds.: G. Wilkinson, R. D. Gillard, J. A. McCleverty), Pergamon, Oxford, **1984**.

[11] For example, a series of (*E*)-**4** could be utilized for the short-step synthesis of thienamycin derivatives, see: a) B. Jiang, H. Tian, Z.-G. Huang, M. Xu, *Org. Lett.* **2008**, *10*, 2737 – 2740; b) M. J. Bodner, R. M. Phelan, C. A. Townsend, *Org. Lett.* **2009**, *11*, 3606 – 3609.

[12] See the Supporting Information for details.

[13] As iron-induced chlorothiolation may involve a radical process, a free-radical-mediated reaction was conducted. In fact, the reaction with $ZnEt_2$ in air gave (*E*)-**4a** in 17% yield although neither BEt_3 in air nor AIBN (azobisisobutyronitrile) systems facilitated a radical addition. Besides, the reaction under photo-irradiation with a high-pressure mercury quartz lamp (400 W) gave a complex mixture of products.

[14] CCDC-1018081 (**7**) and 1018083 (**13**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

[15] Y. Hou, I. A. Abu-Yousef, D. N. Harpp, *Tetrahedron Lett.* **2000**, *41*, 7809 – 7812.

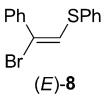
[16] The configurations of (*E*)-**6a** and (*E*)-**6b** were in agreement with previous reports, see: a) N. Taniguchi, *Tetrahedron* **2009**, *65*, 2782 – 2790; b) See Ref. [6d].

[17] See the Supporting Information for the structural determination of (*E*)-**6h**.

[18] The addition of TEMPO (2,2,6,6-tetramethylpiperidine 1-oxyl) to the reaction of **1a** with **2a** totally suppressed the formation of product (*E*)-**4a**, instead giving (*E*)-**3a** in 10% yield. Garvinoxyl also suppressed the reaction, dramatically decreasing the yield of (*E*)-**4a** to 20%. See the Supporting Information for details.

[19] a) A. G. Larsen, A. H. Holm, M. Roberson, K. Daasbjerg, *J. Am. Chem. Soc.* **2001**, *123*, 1723 – 1729; b) C. Ji, M. Ahmida, M. Chahma, A. Houmam, *J. Am. Chem. Soc.* **2006**, *128*, 15423 – 15431.

[20] The reaction of **1a** with **2a** with a stoichiometric amount of $FeBr_2$ gave (*E*)-**4a** in 22% yield, whereas the bromothiolated product (*E*)-**8** was not detected at all, which clearly indicates that the chlorine atom in the product is derived from sulfenyl chloride. This is also supported by the fact that a catalytic reaction with $FeBr_2$ did not provide (*E*)-**8** (Table S1, entry 5).



(*E*)-**8**

[21] R. W. Fessenden, R. H. Schuler, *J. Chem. Phys.* **1963**, *39*, 2147 – 2195.

[22] D. P. Curran, N. A. Porter, B. Giese, *Stereochemistry of Radical Reactions*, VCH Publishers, New York, **1995**, chap. 6.3.

[23] O. Ito, M. D. C. M. Fleming, *J. Chem. Soc. Perkin Trans. 2* **1989**, 689 – 693.

[24] L. A. Singer, J. Chen, *Tetrahedron Lett.* **1969**, *10*, 4849 – 4854.

[25] In the reactions of $CBrCl_3$ with a vinyl radical, the inversion of the radical competes with bromine atom transfer, see: O. Simamura, K. Tokumaru, H. Yui, *Tetrahedron Lett.* **1966**, *7*, 5141 – 5144. The vinyl radical inversion is very fast, but this *anti* addition is followed by a rapid chlorine transfer.

[26] Lewis acid-catalyzed addition reactions of allyl halides, acyl chlorides, and benzyl halides to alkynes have been reported, see: a) A. Miller, M. Moore, *Tetrahedron Lett.* **1980**, *21*, 577 – 580; b) H. Zhou, C. Zeng, L. Ren, W. Liao, X. Huang, *Synlett* **2006**, 3504 – 3506; c) G. R. Cook, R. Hayashi, *Org. Lett.* **2006**, *8*, 1045 – 1048; d) Z. Liu, J. Wang, Y. Zhao, B. Zhou, *Adv. Synth. Catal.* **2009**, *351*, 371 – 374.

[27] R. Martin, S. L. Buchwald, *Acc. Chem. Res.* **2008**, *41*, 1461 – 1473.

[28] M. Alami, B. Crousse, F. Ferri, *J. Organomet. Chem.* **2001**, *624*, 114 – 123.

[29] J. Shi, E. Negishi, *J. Organomet. Chem.* **2003**, *687*, 518 – 524.

[30] M. Mellah, A. Voituriez, E. Schulz, *Chem. Rev.* **2007**, *107*, 5133 – 5209.

[31] C. Pettinari, M. Pellei, G. Cavicchio, M. Crucianelli, W. Panzeri, M. Colapietro, A. Cassetta, *Organometallics* **1999**, *18*, 555 – 563.

[32] For recent examples, see: a) D. J. Covell, M. C. White, *Tetrahedron* **2013**, *69*, 7771 – 7778; b) J. H. Delcamp, P. E. Gorminsky, M. C. White, *J. Am. Chem. Soc.* **2013**, *135*, 8460 – 8463; c) I. I. Strambeanu, M. C. White, *J. Am. Chem. Soc.* **2013**, *135*, 12032 – 12037; d) J. H. Howell, W. Lei, A. J. Young, M. C. White, *J. Am. Chem. Soc.* **2014**, *136*, 5750 – 5754; e) T. J. Osberger, M. C. White, *J. Am. Chem. Soc.* **2014**, *136*, 11176.

[33] With the prepared palladium/bis-sulfoxide catalyst **14** in hand, allylic C–H amidation of 1-decene with methyl *N*-tosylcarbamate was performed, but the yield was not satisfactory (10%), though regio- and stereoselectivity of the amidation product was excellent. See the Supporting Information for details.