DOI: 10.1002/ejoc.200901101

Green Synthesis of Vicinal Dithioethers and Alkenyl Thioethers from the Reaction of Alkynes and Thiols in Water

Zhuang Jin,[a] Bo Xu,[a] and Gerald B. Hammond*[a]

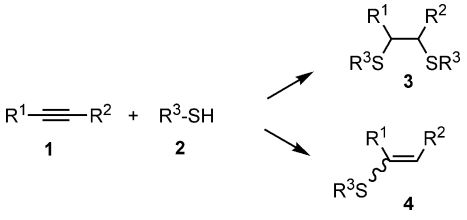
Keywords: Radicals / Green chemistry / Alkynes / Thiols / Hydrothiolation

The reaction of a wide range of alkynes with thiols to give vicinal dithioethers in water, under mild conditions, is reported. In addition, non-terminal propargyl alcohols react with aryl thiols in water to produce a highly regio- and stereoselective monohydrothiolation product, (*E*)-alkenyl thioether. Reaction mechanism and computational studies on the selectivity of the product are presented.

Introduction

Organosulfur compounds have become increasingly important as the role of sulfur is probed deeper in biological processes, new materials, and chemical synthesis.[1] As a result, the synthesis of organosulfur compounds has attracted much attention.[2] Specifically, vicinal dithioethers and alkenyl thioethers have been widely used as target or intermediates.[3–6] For example, vicinal dithioethers have been used as ligands for zirconium or titanium complexes for alkene polymerization[3–5] and hydroamination.[7]

Vicinal dithioethers can be made by nucleophilic substitutions,[3,4] or nucleophilic ring-opening reaction of thiolate.[5] Vicinal dithioethers can also be prepared from an alkene and a disulfide under acid or metal catalysis.[8] Hydroelementation is a versatile and atom-efficient method for installing heteroelements to unsaturated carbon–carbon bonds.[9] Therefore, one of the most straightforward methods to make vicinal dithioethers is the dihydrothiolation of an alkyne (Scheme 1). Under controlled conditions, monohydrothiolation of alkynes could yield alkenyl thioethers. There are reports on the preparation of vicinal dithioethers from alkynes and thiols in organic solvents[10] using various radical initiators, and/or heating or UV light. The use of water as solvent has also been reported by Oshima and co-workers, who isolated the vicinal dithioether as a side product, during their investigation of thiolyne radical reactions in water assisted by a water-soluble radical initiator.[11] In all these literature syntheses, there are detracting experimental limitations, including the use of metal catalysts, high temperatures or radical initiators, and organic solvent. The addition of thiols to alkenes has been used in the synthesis of dendrimers (so called "thiol-ene click" chemistry).[12] The spectrum of application of these dendrimers, ranging from medicine to nanoengineering[13] should spur the development of novel and efficient synthesis of macromolecules.[14] Herein, we wish to report an atom-economical and "green" synthesis of vicinal dithioethers from the reaction of alkyne and thiol without the use of metal catalysts or radical initiators, and using water as the sole solvent. Furthermore, this method can also be used for regio- and stereoselective monohydrothiolation of propargyl alcohols, which leads to an effective synthesis of alkenyl thioethers with exclusive (*E*)-selectivity.



Scheme 1. Synthesis of vicinal dithioethers and alkenyl thioethers from alkynes and thiols.

Results and Discussion

Effects of Solvents on Dihydrothiolation

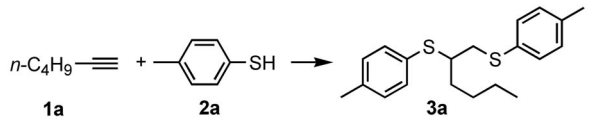
We used the reaction of 1-hexyne and 4-methylbenzenethiol as our model reaction (Table 1). While THF, MeOH, H_2O, individually or as a mixture, or non-solvent conditions gave good results, traditional organic solvents, such as CH_3CN, CH_2Cl_2 and toluene, were not satisfactory.

Considering both, chemical yields and the increasing environmental consciousness of the scientific community, we chose water as the ideal reaction media. It is surprising that water was found to be the best solvent for the reaction con-

[a] Department of Chemistry, University of Louisville, Louisville, Kentucky 40292, USA
E-mail: gb.hammond@louisville.edu

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/ejoc.200901101.

Table 1. Effect of solvents on dihydrothiolation of alkyne **1**.[a]



1a **2a** **3a**

Entry	Solvent	Yield[b] (%)
1	CH_3CN	31
2	CH_2Cl_2	24
3	toluene	34
4	THF	72
5	MeOH	65
6	H_2O:MeOH (4:1)	76
7	H_2O	80
8	no solvent	72

[a] 1 mmol alkyne, 2.4 mmol 4-methylbenzenthiol and 0.5 mL solvent, reacted for 24 h at room temp. [b] Determined by NMR, 0.4 mmol benzyl bromide as internal standard.

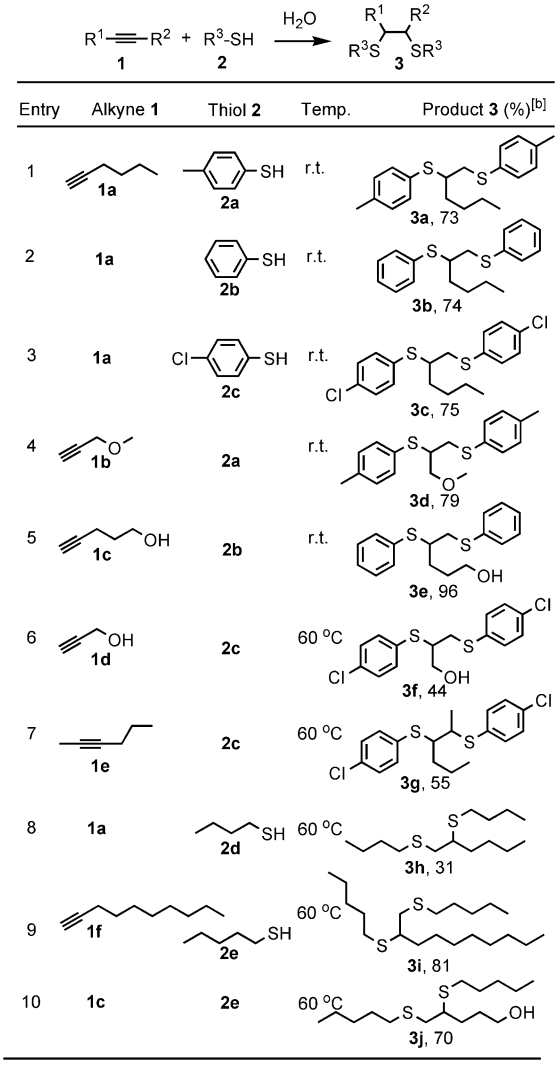
sidering that both starting material and product are virtually insoluble in water. According to Sharpless and coworkers,[15] reaction rates can be accelerated when insoluble reactants were stirred in aqueous suspension, denoted as "on water" conditions. Thus, this reaction could be considered as an "on water" reaction.

Scope of Aqueous Dihydrothiolation

With optimized conditions in hand, we examined the scope of this dihydrothiolation reaction; the results are summarized in Table 2. 1-Hexyne and aryl thiols reacted smoothly (Table 2, Entries 1, 2 and 3) and in good yields. The reaction of functionalized terminal alkynes, such as methyl propargyl ether and 4-pentyn-1-ol, with an aryl thiol also gave good to excellent yields (Entries 4 and 5). However, propargyl alcohol and 2-hexyne reacted with 4-chlorothiophenol to produce moderate yields of **3** (Entries 6 and 7). The low yield in Entry 8 is probably due to the volatility of the substrate, as higher molecular weight alkynes reacted effectively with aliphatic thiols under mild heating (Entries 9 and 10).

Unfortunately, under our conditions, phenylacetylene and other internal alkynes reacted with thiols to give only the monohydrothiolation product.[16] Upon further investigation, we found that aryl thiols are more reactive than aliphatic thiols; aryl chloride accelerates the dihydrothiolation, and weak electron-donating groups slow the reaction. The observed reaction rates follow this order: 4-chlorothiophenol > thiophenol > 4-methylbenzenthiol. Strong electron-withdrawing groups, such as nitro, methyl ester and carboxylic acid, on the *para* position of thiophenol hinder the reaction. This may be related to their ease of emulsification, as 4-nitrothiophenol, 4-mercaptobenzoic acid and methyl 4-mercaptobenzoate do not form an emulsion with alkynes, whereas the thiol in Table 2 readily formed an emulsion with alkyne in water upon stirring.

Table 2. Dihydrothiolation of alkyne **1**.[a]



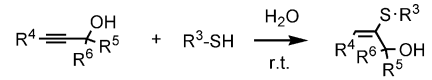
[a] 1 mmol alkyne, 2.4 mmol thiol and 0.5 mL water, reacted at indicated temperature for 24 h. [b] Isolated yields.

Our mechanistic studies hinted that the reaction probably proceeded through a radical mechanism, because no reaction occurred in the presence of galvinoxyl free radical (1.1 equiv. to thiol).[17] The possibility of a nucleophilic addition could be ruled out since nucleophilic dihydrothiolation of alkynes normally gives thioacetals.[18] Furthermore, small amounts of disulfide (less than 5% yield based on thiol), formed from the homocoupling of thiolate radical, were observed in the course of this study, which is consistent with the proposed radical mechanism. Furthermore, no hydration product was found in the reaction mixture. The radical initiator could be dioxygen in the air. The specific role of the solvent is not clear at this time, it seems water has some ability to stabilize the radical intermediate and therefore facilitates the radical-mediated reaction. A literature report[19] speculated that a hydrogen bond between thiol and water could enable a nucleophilic addition to the alkene.

Regio- and Stereo-Selective Monohydrothiolation of Non-Terminal Propargyl Alcohols

While investigating dihydrothiolation conditions for non-terminal propargyl alcohols (e.g. **1g**), we found, to our surprise, that only the monohydrothiolation product was obtained, and this reaction proceeded in a regio- and stereoselective manner. The thiol only attacked the carbon next to the alcohol and only the (*E*)-isomer was isolated. The reaction scope is shown in Table 3. But-2-yn-1-ol and 4-chlorothiophenol gave a moderate yield of product with high stereoselectivity (Entry 1). Similarly, **1h** reacted with three different thiophenols in moderate to high yields with high (*E*)-selectivity (Entries 2–4). Entry 5 also showed satisfactory yield and stereoselectivity. Reaction of secondary alcohols (**1j** and **1k**) with thiophenols gave satisfactory yields and excellent stereoselectivity (Entries 6–9), while tertiary propargyl alcohol **1l** gave very high stereoselectivity (100% *E*), albeit in low yield (Entry 10). Reaction of **1m** and 4-chlorothiophenol **2c** was also highly stereoselective (Entry 11). In Entries 12 and 13, we investigated substrates having a phenyl group; both of them, without exception, reacted with aryl thiols to give products with very high stereoselectivity. During this study, we also found that alkyl thiols are not effective under these conditions, and terminal alkynes, such as propargyl alcohol, overreacted with thiophenol to give dihydrothiolation products (Table 2). Regio- and stereoselective monohydrothiolation was observed only with non-terminal propargyl alcohols, even with excess thiol in water. While the monohydrothiolation of non-terminal propargyl alcohol with thiol has been studied before,[20–22] our mild reaction conditions showed distinctive regio- and stereoselectivity for a wider range of substrates. A case in point is the base mediated nucleophilic addition of thiol to propargyl alcohol (Scheme 2, top) that yields the *trans* adduct product, *Z*-alkenyl thioether[20] or a mixture of (*Z*)- and (*E*)-alkenyl thioethers.[21] And, addition of a thiol, using a radical initiator, usually affords a mixture of (*Z*)-(predominant) and (*E*)-alkenyl thioethers (Scheme 2, bottom).[22]

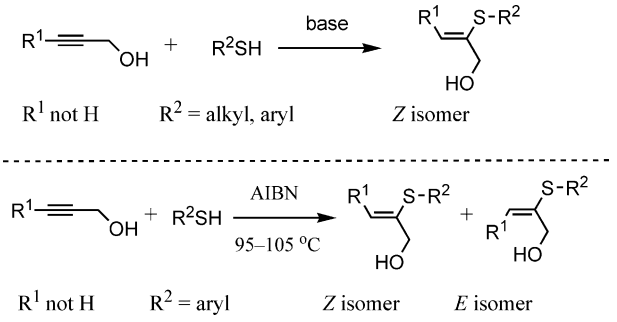
Table 3. Regio and stereoselective monohydrothiolation of propargyl alcohols.[a]



1 2 4

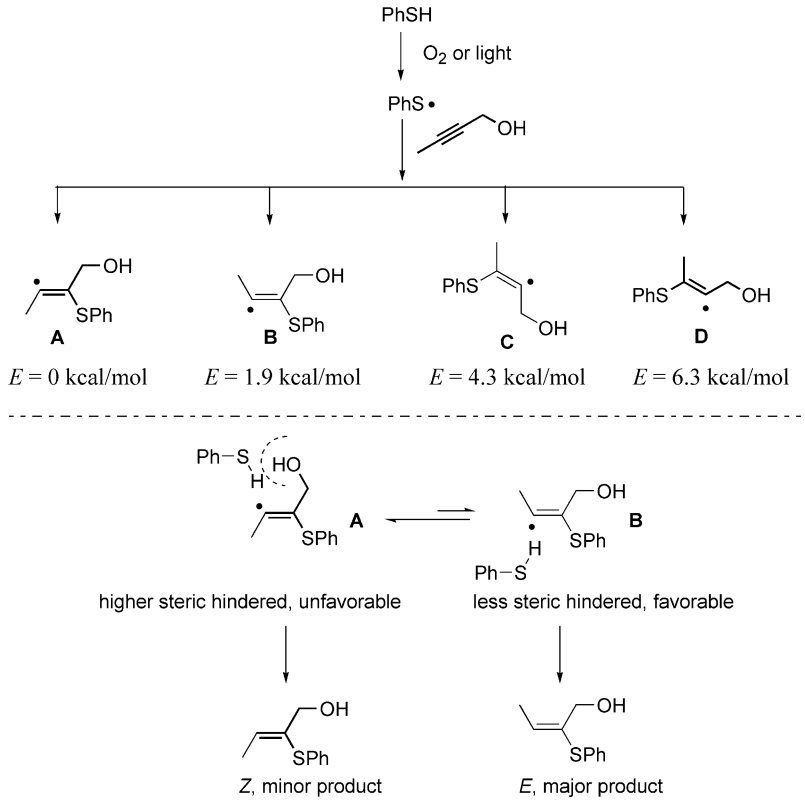
Entry	Alkyne 1	Thiol 2	Product 4	Yield [b]
1	1g	2c	4a	53 (*E*:*Z* = 9:1)
2	1h	2c	4b	76 (*E*:*Z* = 9:1)
3	1h	2b	4c	66 (*E*:*Z* = 12.5:1)
4	1h	2a	4d	58 (*E*:*Z* = 12.5:1)
5	1i	2b	4e	77 (*E*:*Z* = 12.5:1)
6	1j	2c	4f	64 (*E*:*Z* = 17:1)
7	1j	2b	4g	63 (*E*:*Z* = 17:1)
8	1k	2c	4h	78 (*E*:*Z* = 17:1)
9	1k	2a	4i	70 (*E*:*Z* = 20:1)
10	1l	2b	4j	17 (*E*:*Z* = 100:0)
11	1m	2c	4k	65 (*E*:*Z* = 100:0)
12	1n	2a	4l	42 (*E*:*Z* = 100:0)
13	1o	2b	4m	44 (*E*:*Z* = 50:1)

[a] 1 mmol alkyne, 1.2 mmmol thiol and 0.25 mL water reacted for 12 h at room temp. [b] Isolated yield, *E* and *Z* were determined by NOESY studies.



Scheme 2. Nucleophilic and radical additions of thiol to propargyl alcohols.

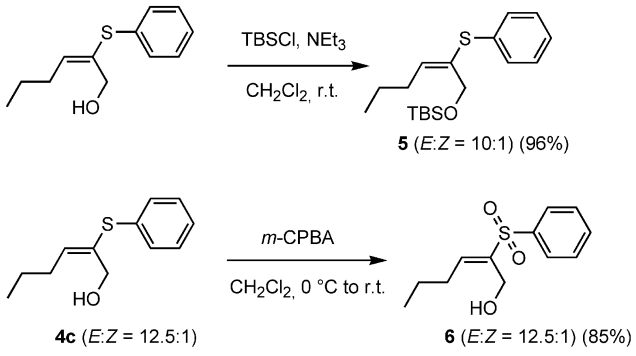
The reason for the high regio- and stereoselectivity of **4** can be explained by the relative stability of vinyl radical intermediates (Scheme 3, top). The vinyl radical intermediates **C** and **D** are higher in energy than **A** and **B** [Gaussian 03, UB3LYP/6-311+G(d)]. This can explain why the thiol always attacks the carbon next to hydroxymethyl group. The stereoselectivity outcome of **4** can be explained by steric effects and the isomerization of vinyl radical **A** to **B**. It is widely accepted that a hydrogen donor can approach from the less hindered side of the vinyl radical.[23] The bulkiness of hydroxymethyl group in radical **A** may hinder



Scheme 3. Regioselectivity and stereoselectivity considerations.

the approach of the hydrogen donor (thiol) to form a (*Z*)-isomer (Scheme 3, bottom). However, the thiol can easily approach the less hindered side of the vinyl radical **B** to produce the (*E*)-isomer. As a result, radical **A** may slowly isomerize to radical **B**. This is consistent with the fact that the bulkier the hydroxyalkyl, the higher the stereoselectivity observed (Table 3). And, the mild conditions (room temperature/water as solvent) minimized the isomerization of the final product. This is in contrast with literature reports in which isomerization may occur at high temperature (Scheme 2, bottom).[22]

Alkenyl thioesters have already demonstrated their utility.[24] Compound **4** can be used in further transformations; for example, the free hydroxy group in **4** can be protected to give **5**, and **4** can be easily oxidized to sulfone **6** with *m*CPBA (Scheme 4). Both **5** and **6** have been used in nickel-catalyzed cross-coupling reactions with Grignard reagents[25] or organozinc reagents[26] to give functionalized allylic alcohols, which are important intermediates in total synthesis[27] and methodology.[28]



Scheme 4. Synthetic transformations of **4**.

Conclusions

We have found that a wide range of alkynes react with excess thiols to give vicinal dithioethers under mild condition using only water as solvent, without radical initiator or UV light sources. Alternatively, non-terminal propargyl alcohols reacted with phenyl thiols in water to produce (*E*)-alkenyl thioethers in highly regio- and stereoselective fashion. Considering the mild conditions of our reaction, it could have great potential in the preparation of highly branched dendrimers, and as linkers incorporating fluorescence tags in biological applications.

Experimental Section

General: Substrates **1m** and **1o** were prepared using a literature method.[29] Other substrates and reagents were commercially obtained from Alfa or Adrich, and were used without further purification. Structures were identified by NMR spectra, assisted by elemental analysis or/and IR spectra. ^{1}H and ^{13}C NMR spectra were recorded at 500 and 125 MHz, respectively, using $CDCl_3$ as solvent. The chemical shifts were reported in δ (ppm) value relative to $CDCl_3$ (δ =7.26 ppm for ^{1}HNMR and 77.0 for ^{13}C NMR), and multiplicities are indicated by s (for singlet), d (doublet), dd (double

doublet), m (multiplet), and br (broad). Coupling constant, *J*, was reported in Hz.

General Procedure for Dihydrothiolation of Alkynes: Alkyne (1 mmol), thiol (2.4 mmol), and water (0.5 mL) were added to a reaction flask containing a stir bar, and the resulting mixture was sealed and stirred for 24 h at the indicated temperature. Then the mixture was extracted by CH_2Cl_2 (10 mL × 3), dried with Na_2SO_4, filtered, and concentrated in vacuo to finish crude residue, which was subjected to silica gel column chromatography using gradient elution from pure hexane to a mixture of hexane/ethyl acetate (10:1) to get final pure product **3**.

1,2-Bis(*p*-tolylsulfanyl)hexane (3a): 241 mg, 73%, Colorless oil. $C_{20}H_{26}S_2$ (330.2): calcd. C 72.67, H 7.93; found C 72.80, H 8.25. IR (neat): $\tilde{\nu}$ = 2955, 2925, 1491 and 804 cm^{-1}. ^1H NMR (500 Hz. $CDCl_3$): δ = 0.93 (t, ^3J = 7.0 Hz, 3 H, CH_3), 1.29–1.39 (m, 2 H, $CH_2CH_2CH_3$), 1.43–1.46 (m, 1 H, SCHC*H*HCH$_2$), 1.53–1.59 (m, 2 H, $CH_2CH_2CH_2$), 1.95–1.98 (m, 1 H, SCHCH*H*CH$_2$), 2.34 (s, 3 H, CH_3), 2.36 (s, 3 H, CH_3), 2.86 (dd, ^3J = 10, ^2J = 13.25 Hz, 1 H, SCHC*H*HS), 3.05–3.10 (m, 1 H, SC*H*CH$_2$S), 3.23 (dd, ^3J = 4.0, ^2J = 13.75 Hz, 1 H, SCHCH*H*S), 7.04 (d, ^3J = 8.0 Hz, 2 H, PhH), 7.09 (d, ^3J = 7.5 Hz, 2 H, PhH), 7.13 (d, ^3J = 7.5 Hz, 2 H, PhH), 7.25 (d, ^3J = 8.0 Hz, 2 H, PhH) ppm. ^{13}C NMR ($CDCl_3$, 125 Hz): δ = 14.29, 21.31, 21.41, 22.79, 29.22, 32.44, 40.11, 48.80, 129.92, 129.94, 130.52, 130.68, 132.45, 133.39, 136.51, 137.60 ppm.

General Procedure for Monohydrothiolation of Non-Terminal Propargyl Alcohols: Alkyne (1 mmol), thiol (1.2 mmol), and 0.25 mL water were added to a reaction flask containing a stir bar, and the resulting mixture was sealed and stirred for 12 h at room temp. Final product **4** is purified from the mixture by silica gel column chromatography using gradient elution from pure hexane to mixture of hexane/ ethyl acetate (10:1).

(*E*)-2-(4-Chlorophenylsulfanyl)but-2-en-1-ol (4a): 113 mg, 53%, Colorless oil. $C_{10}H_{11}ClOS$ (214.0): calcd. C 56.00, H 5.12; found C 55.94, H 5.16. IR (neat): $\tilde{\nu}$ = 3355, 2912, 2854, 1474, 1388, 1079, 1011 and 816 cm^{-1}. ^1H NMR ($CDCl_3$, 500 Hz): δ = 1.94 (d, ^3J = 7.0 Hz, 3 H, CH_3), 4.10 (s, 2 H, CH_2OH), 6.38 (q, ^3J = 6.5 Hz, 1 H, *H*C=CS), 7.20–7.27 (m, 4 H, PhH) ppm. ^{13}C NMR ($CDCl_3$, 125 Hz): δ = 15.31, 65.99, 129.11, 130.04, 132.09, 132.96, 134.02, 135.91 ppm.

Acknowledgments

We are grateful to the US National Science Foundation (NSF) for financial support (CHE-0809683).

[1] a) R. J. W. Cremlyn, *An introduction to organosulfur chemistry*, Wiley, Chichester, New York, **1996**; b) G. H. Whitham, *Organosulfur chemistry*, Oxford University Press, Oxford, New York, **1995**.

[2] a) T. Kondo, T. Mitsudo, *Chem. Rev.* **2000**, *100*, 3205–3220; b) C. Cao, L. R. Fraser, J. A. Love, *J. Am. Chem. Soc.* **2005**, *127*, 17614–17615; c) A. Ogawa, T. Ikeda, K. Kimura, T. Hirao, *J. Am. Chem. Soc.* **1999**, *121*, 5108–5114; d) C. J. Weiss, S. D. Wobser, T. J. Marks, *J. Am. Chem. Soc.* **2009**, *131*, 2062–2063; e) J. Yang, A. Sabarre, L. R. Fraser, B. O. Patrick, J. A. Love, *J. Org. Chem.* **2009**, *74*, 182–187; f) S. Shoai, P. Bichler, B. Kang, H. L. Buckley, J. A. Love, *Organometallics* **2007**, *26*, 5778–5781; g) L. R. Fraser, J. Bird, Q. Wu, C. Cao, B. O. Patrick, J. A. Love, *Organometallics* **2007**, *26*, 5602–5611; h) R. Sridhar, K. Surendra, N. S. Karishnaveni, B. Srinivas, K. R. Rao, *Synlett* **2006**, 3495–3497; i) D. A. Malyshev, N. M. Scott, N. Marion, E. D. Stevens, V. P. Ananikov, I. P. Beletskaya, S. P. Nolan, *Organometallics* **2006**, *25*, 4462–4470; j) V. P. Ananikov, D. A. Malyshev, I. P. Beletskaya, G. G. Aleksandrov, I. L. Eremenko, *Adv. Synth. Catal.* **2005**, *347*, 1993–2001.

[3] A. Ishii, T. Toda, N. Nakata, T. Matsuo, *J. Am. Chem. Soc*. 10.1021/ja903369q.

[4] A. Cohen, A. Yeori, I. Goldberg, M. Kol, *Inorg. Chem.* **2007**, *46*, 8114–8116.

[5] a) K. Beckerle, R. Manivannan, B. Lian, G. M. Meppelder, G. Raabe, T. P. Spaniol, H. Ebeling, F. Pelascini, R. Mülhaupt, J. Okuda, *Angew. Chem. Int. Ed.* **2007**, *46*, 4790–4793; b) G. M. Meppelder, K. Beckerle, R. Manivannan, B. Lian, G. Raabe, T. P. Spaniol, J. Okuda, *Chem. Asian J.* **2008**, *3*, 1312–1323; c) B. T. Gall, F. Pelascini, H. Ebeling, K. Beckerle, J. Okuda, R. Mülhaupt, *Macromolecules* **2008**, *41*, 1627–1633; d) B. Lian, K. Beckerle, T. P. Spaniol, J. Okuda, *Angew. Chem. Int. Ed.* **2007**, *46*, 8507–8510; e) C. Capacchione, R. Manivannan, M. Barone, K. Beckerle, R. Centore, L. Oliva, A. Proto, A. Tuzi, T. P. Spaniol, J. Okuda, *Organometallics* **2005**, *24*, 2971–2982; f) C. Capacchione, A. Proto, H. Ebeling, R. Mülhaupt, K. Möller, T. P. Spaniol, J. Okuda, *J. Am. Chem. Soc.* **2003**, *125*, 4964–4965.

[6] S. Poulain, S. Julien, E. Dunach, *Tetrahedron Lett.* **2005**, *46*, 7077–7079.

[7] K. Marcseková, C. Loos, F. Rominger, S. Doye, *Synlett* **2007**, 2564–2568.

[8] a) M. C. Caserio, C. L. Fisher, J. K. Kim, *J. Org. Chem.* **1985**, *50*, 4390–4393; b) T. Kitamura, J. Matsuyuki, H. Taniguchi, *J. Chem. Soc. Perkin Trans. 1* **1991**, *1*, 1607–1608; c) T. Kondo, S. Uenoyama, K. Fujita, T. Mitsudo, *J. Am. Chem. Soc.* **1999**, *121*, 482–483; d) S. Usugi, H. Yorimitsu, H. Shinokubo, K. Oshima, *Org. Lett.* **2004**, *6*, 601–603; e) T. Nishimura, T. Yoshinaka, S. Uemura, *Bull. Chem. Soc. Jpn.* **2005**, *78*, 1138–1141; f) N. Yamagiwa, Y. Suto, Y. Torisawa, *Bioorg. Med. Chem. Lett.* **2007**, *17*, 6197–6201.

[9] a) J. F. Hartwig, *Nature* **2008**, *455*, 314–322; b) F. Alonso, I. P. Beletskaya, M. Yus, *Chem. Rev.* **2004**, *104*, 3079–3160; c) S. B. Amin, T. J. Marks, *Angew. Chem. Int. Ed.* **2008**, *47*, 2006–2025; d) G. A. Molander, J. A. C. Romero, *Chem. Rev.* **2002**, *102*, 2161–2185.

[10] Selected references for radical initiator and/or heating/UV light/X-rays assisted dihydrothiolation of alkynes in organic solvents: a) E. A. Il'yasov, G. G. Galust'yan, *Chem. Heterocycl. Compd.* **1999**, *35*, 1187–1189; b) E. I. Troyansky, R. F. Ismagilov, Y. A. Strelenko, V. V. Samoshin, D. V. Demchuk, G. I. Nikishin, S. V. Lindeman, V. V. Khrustalyov, Y. T. Struchkov, *Tetrahedron Lett.* **1995**, *36*, 2293–2294; c) D. V. Demchuk, M. I. Lazareza, S. V. Lindeman, V. N. Khrustalyov, Y. T. Struchkov, R. F. Ismagilov, E. I. Troyansky, G. I. Nikishin, *Synthesis* **1995**, 307–311; d) E. I. Troyansky, R. F. Ismagilov, E. N. Korneeva, M. S. Pogosynan, G. I. Nikishin, *Mendeleev Commun.* **1995**, *5*, 18–20; e) E. I. Troyansky, M. I. Lazareza, D. V. Demchuk, V. V. Samoshin, Y. A. Strelenko, G. I. Nikishin, *Synlett* **1992**, 233–234; f) G. I. Nikishin, E. I. Troyansky, D. V. Demchuk, *Phosphorus Sulfur Silicon Relat. Elements* **1991**, *59*, 239–242; g) D. V. Demchuk, A. I. Lutsenko, E. I. Troyansky, G. I. Nikishin, *Izv. Akad. Nauk SSSR, Ser. Khim.* **1990**, 2801–2810; h) E. I. Troyansky, D. V. Demchuk, V. V. Samoshin, Y. A. Strelenko, G. I. Nikishin, *Izv. Akad. Nauk SSSR, Ser. Khim.* **1990**, 2663–2664; i) E. I. Troyansky, Y. A. Strelenko, D. V. Demchuk, A. I. Lutsenko, G. I. Nikishin, *Izv. Akad. Nauk SSSR, Ser. Khim.* **1990**, 1191–1192; j) D. V. Demchuk, E. I. Troyansky, G. I. Nikishin, *Izv. Akad. Nauk SSSR, Ser. Khim.* **1989**, 1443–1444; k) K. Yamagishi, T. Tanaka, T. Hoshino, *Bull. Chem. Soc. Jpn.* **1957**, *30*, 455–458; l) A. T. Blomquist, J. Wolinsky, *J. Org. Chem.* **1958**, *23*, 551–554; m) F. W. Stacey, J. F. Harris, *J. Am. Chem. Soc.* **1963**, *85*, 963–965.

[11] Water soluble radical initiator assisted dihydrothiolation in water: a) H. Yorimitsu, K. Wakabayashi, H. Shinokubo, K. Oshima, *Tetrahedron Lett.* **1999**, *40*, 519–522; b) H. Yorimitsu, K. Wakabayashi, H. Shinokubo, K. Oshima, *Bull. Chem. Soc. Jpn.* **2001**, *74*, 1963–1970.

[12] a) K. L. Killops, L. M. Campos, C. J. Hawker, *J. Am. Chem. Soc.* **2008**, *130*, 5062–5064; b) J. W. Chan, B. Yu, C. E. Hoyle, A. B. Lowe, *Chem. Commun.* **2008**, 4959–4961.

[13] a) S. M. Grayson, J. M. J. Fréchet, *Chem. Rev.* **2001**, *101*, 3819–3868; b) B. Helms, E. W. Meijer, *Science* **2006**, *313*, 929–930; c) A. Almutairi, S. J. Guillaudeu, M. Y. Berezin, S. Achilefu, J. M. J. Fréchet, *J. Am. Chem. Soc.* **2008**, *130*, 444–445.

[14] C. R. Becer, R. Hoogenboom, U. S. Schubert, *Angew. Chem. Int. Ed.* **2009**, *48*, 4900–4908.

[15] a) S. Narayan, J. Muldoon, M. G. Finn, V. V. Fokin, H. C. Kolb, K. B. Sharpless, *Angew. Chem. Int. Ed.* **2005**, *44*, 3275–3279; b) V. V. Fokin, K. B. Sharpless, *Angew. Chem. Int. Ed.* **2001**, *40*, 3455–3457.

[16] Phenylacetylene reacted with thiol to form linear vinyl sulfide; other internal alkyne reacted with thiol to form small amounts of monohydrothiolation products. This is congruent with the reference: a) T. Kondo, S. Uenoyama, K. Fujita, T. Mitsudo, *J. Am. Chem. Soc.* **1999**, *121*, 482–483; b) J. S. Yadav, B. V. S. Reddy, A. Raju, K. Ravindar, G. Baishya, *Chem. Lett.* **2007**, *36*, 1474–1475.

[17] Radical quencher does not always prove radical mechanism: P. Ionita, *Chem. Pap.* **2005**, *59*, 11–16.

[18] Selected reference for nucleophilic dithidrothiolation of alkynes to give thioacetals: a) B. C. Ranu, S. Banerjee, R. Jana, *Tetrahedron* **2007**, *63*, 776–782; b) L. L. Santos, V. R. Ruiz, M. J. Sabater, A. Corma, *Tetrahedron* **2008**, *64*, 7902–7909; c) C. Xu, J. K. Bartley, D. I. Enache, D. W. Knight, M. Lunn, M. Lok, G. J. Hutchings, *Tetrahedron Lett.* **2008**, *49*, 2454–2456; d) H. F. Sneddon, A. V. D. Heuvel, A. K. H. Hirsch, R. A. Booth, D. M. Shaw, M. J. Gaunt, S. V. Ley, *J. Org. Chem.* **2006**, *71*, 2715–2725; e) B. C. Ranu, S. Bhar, R. Chakraborti, *J. Org. Chem.* **1992**, *57*, 7349–7352.

[19] B. C. Ranu, T. Mandal, *Synlett* **2007**, 925–928.

[20] Selected references for nucleophilic monohydrothiolation to form (*Z*)-alkenyl sulfide: a) A. Kondoh, K. Takami, H. Yorimitsu, K. Oshima, *J. Org. Chem.* **2005**, *70*, 6468–6473; b) M. S. Waters, K. Snelgrove, P. Maligres, *Org. Synth.* **2003**, *80*, 190–194; c) L. V. Andriyankova, S. A. Zhivet'ev, A. G. Mal'kina, P. N. Kudryakova, E. I. Kositsyna, L. N. Il'icheva, I. A. Ushakov, A. V. Afonin, B. A. Trofimov, *Russ. J. Org. Chem.* **2002**, *38*, 1681–1685; d) *US Pat*. 6 239 280, **2001**; e) M. S. Waters, J. A. Cowen, J. C. McWilliams, P. E. Maligres, D. Askin, *Tetrahedron Lett.* **2000**, *41*, 141–144; f) M. Koreeda, Y. Wang, *J. Org. Chem.* **1997**, *62*, 446–447; g) *US Pat*. 5 453 500, **1995**; h) D. E. Bierer, J. M. Dener, L. G. Dubenko, R. E. Gerber, J. Litvak, S. Peterli, P. Peterli-Roth, T. V. Truong, G. Mao, B. E. Bauer, *J. Med. Chem.* **1995**, *38*, 2628–2648; i) M. Koreeda, W. Yang, *J. Am. Chem. Soc.* **1994**, *116*, 10793–10794; j) M. Koreeda, W. Yang, *Synlett* **1994**, 201–203.

[21] Reference for nucleophilic monohydrothiolation to form mixture of (*Z*)- and (*E*)-alkenyl sulfide: a) B. V. Trzhtsinskaya, N. D. Abramova, L. F. Teterina, L. V. Andriyankova, A. V. Afonin, *Izv. Akad. Nauk SSSR, Ser. Khim.* **1989**, 416–419; b) Y. M. Skvortsov, A. G. Mal'kina, E. I. Moshchevitina, V. B. Modonov, B. A. Trofimov, *Sulfur Lett.* **1989**, *9*, 141–148.

[22] References for radical monohydrothiolation to form mixture of (*Z*)- (predominant) and (*E*)-alkenyl sulfide: a) G. Galambos, P. Csókási, C. Szántay, C. Szántay, *Liebigs Ann./Recueil* **1997**, 1969–1978; b) G. Galambos, P. Csókási, C. Szántay, G. Gzira, C. Szántay, *Heterocycles* **1994**, *38*, 1459–1464.

[23] K. Miura, K. Oshima, K. Utimoto, *Bull. Chem. Soc. Jpn.* **1993**, *66*, 2356.

[24] S. R. Dubbaka, P. Vogel, *Angew. Chem. Int. Ed.* **2005**, *44*, 7674–7684; and references there in.

[25] a) E. Wenkert, T. W. Ferreira, E. L. Michelotti, *J. Chem. Soc., Chem. Commun.* **1979**, 637–638; b) E. Wenkert, M. E. Shepard, A. T. Mcphail, *J. Chem. Soc., Chem. Commun.* **1986**, 1390–1391; c) E. Wenkert, D. Chianelli, *J. Chem. Soc., Chem. Commun.* **1991**, 627–628; d) E. Wenkert, J. B. Fernandes, E. L. Michelotti, C. S. Swinndell, *Synthesis* **1983**, 701–703; e) E. Wenkert, E. L. Michelotti, C. S. Swinndell, *J. Am. Chem. Soc.* **1979**, *101*, 2246–2247; f) F. Rebière, O. Riant, L. Ricard, H. B. Kagan, *Angew. Chem.* **1993**, *105*, 644–646; *Angew. Chem. Int. Ed. Engl.* **1993**, *32*, 568–570; g) A. Sabarre, J. Love, *Org. Lett.* **2008**, *10*, 3941–3944.

[26] S. Ma, H. Ren, Q. Wei, *J. Am. Chem. Soc.* **2003**, *125*, 4817–4830.

[27] Selected references for allylic alcohol as intermediate in total synthesis of natural products or medicine: a) J. A. Hadfield, K. Gaukroger, N. Hirst, A. P. Weston, N. J. Lawrence, A. T. McGown, *Eur. J. Med. Chem.* **2005**, *40*, 529–541; b) C. Spino, C. Gobdout, *J. Am. Chem. Soc.* **2003**, *125*, 12106–12107; c) M. Haidoune, I. Raynaud, N. O'Connor, P. Richomme, R. Mornet, M. Laloue, *J. Agric. Food Chem.* **1998**, *46*, 1577–1582; d) E. Pinard, M. Gaudry, F. Hénot, A. Thellend, *Tetrahedron Lett.* **1998**, *39*, 2739–2742; e) H. Miyauchi, T. Nakamura, N. Ohashi, *Bull. Chem. Soc. Jpn.* **1996**, *69*, 2625–2632; f) *US Pat*., 5 399 708, **1995**.

[28] Selected references for allylic alcohol as substrate for methodology: a) L. Mantilli, D. Gérard, S. Torche, C. Besnard, C. Mazet, *Angew. Chem. Int. Ed.* **2009**, *48*, 5143–5147; b) Z. Bourhani, A. V. Malkov, *Synlett* **2006**, *20*, 3525–3528; c) A. V. Malkov, Z. Bourhani, P. Kocovsky, *Org. Biomol. Chem.* **2005**, *3*, 3194–3200; d) A. Lattanzi, S. Piccirillo, A. Scettri, *Eur. J. Org. Chem.* **2005**, 1669–1674; e) W. Zhang, A. Basak, Y. Kosugi, Y. Hoshino, H. Yamamoto, *Angew. Chem. Int. Ed.* **2005**, *44*, 4389–4391; f) W. Adam, P. L. Alsters, R. Neumann, C. R. Saha-Möller, D. Seebach, A. K. Beck, R. Zhang, *J. Org. Chem.* **2003**, *68*, 8222–8231; g) W. Adam, A. K. Beck, A. Pichota, C. R. Saha-Möller, D. Seebach, N. Vogl, R. Zhang, *Tetrahedron: Asymmetry* **2003**, *14*, 1355–1361.

[29] L. Brandsma, *Preparative Acetylenic Chemistry*, Elsevier, Amsterdam, The Netherlands, **1988**.

Received: September 25, 2009
Published Online: November 17, 2009

