

Disulfidation of Alkynes and Alkenes
with Gallium Trichloride

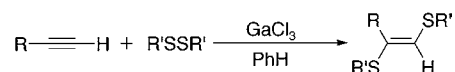
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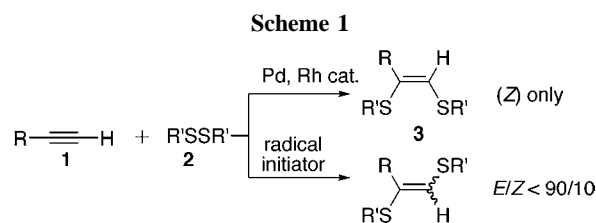
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ABSTRACT



Treatment of diphenyl disulfide and terminal alkynes with gallium trichloride afforded (*E*)-1,2-diphenylthio-1-alkenes selectively (*E/Z* > 20/1). Alkenes also underwent this reaction to form *trans* adducts.

Vinyl sulfides have synthetic utility in organic chemistry,¹ and stereoselective sulfidation of alkynes to obtain vinyl sulfides has been developed.² Stereoselective disulfidation of terminal alkynes was first reported by Sonoda et al., forming (*Z*)-1,2-dithio-1-alkenes under transition metal catalysis in 1991 (Scheme 1).³ Since then, much attention has been paid to transition-metal-catalyzed disulfidation.⁴ Although the radical process yielded *trans* adducts mainly, a mixture of *E/Z* isomers (*E/Z* < 90/10) was obtained except



(1) For example: (a) Ager, D. *J. Chem. Soc. Rev.* **1982**, *11*, 493. (b) Takeda, T.; Furukawa, H.; Fujimori, M.; Suzuki, K.; Fujiwara, T. *Bull. Chem. Soc. Jpn.* **1984**, *57*, 1863. (c) Grobel, B.-T. Seebach, D. *Synthesis* **1977**, 357. (d) Trost, B. M.; Lavoie, A. C. *J. Am. Chem. Soc.* **1983**, *105*, 5075. (e) Magnus, P.; Quagliato, D. *J. Org. Chem.* **1985**, *50*, 1621. (f) De Lucchi, O.; Pasquato, L. *Tetrahedron* **1988**, *44*, 6755. (g) Pettit, G. R.; van Tamelen, E. E. *Org. React.* **1962**, *12*, 356. (h) Boar, R. B.; Hawkins, D. W.; McGhie, J. F.; Barton, D. H. R. *J. Chem. Soc., Perkin Trans. 1* **1973**, 654. (i) Trost, B. M.; Ornstein, P. L. *Tetrahedron Lett.* **1981**, *22*, 3463. (j) Wenkert, E.; Ferreira, T. W. *J. Chem. Soc., Chem. Commun.* **1982**, 840. (k) Hojo, M.; Tanimoto, S. *J. Chem. Soc., Chem. Commun.* **1990**, 1284. (l) Hojo, M.; Harada, H.; Yoshizawa, J.; Hosomi, A. *J. Org. Chem.* **1993**, *58*, 6541.

(2) (a) Dabdoub, M. J.; Guerrero, P. G., Jr. *Tetrahedron Lett.* **2001**, *42*, 7167. (b) Watanabe, S.; Mori, E.; Nagai, H.; Iwama, T.; Kataoka, T. *J. Org. Chem.* **2000**, *65*, 8893. (c) Huang, X.; Xu, X.-H.; Zheng, W.-X. *Synth. Commun.* **1999**, 2399. (d) Ogawa, A.; Ikeda, T.; Kimura, K.; Hirao, T. *J. Am. Chem. Soc.* **1999**, *121*, 5108 and references therein.

(3) (a) Kuniyasu, H.; Ogawa, A.; Miyazaki, S.; Ryu, I.; Kambe, N.; Sonoda, N. *J. Am. Chem. Soc.* **1991**, *113*, 9796. Also see the followings for metal-catalyzed S–S bond cleavage. (b) Kuniyasu, H. In *Catalytic Heterofunctionalization*; Togni, A., Grutzmacher, H., Eds.; Wiley-VCH: Weinheim, 2001; p 271. (c) Kondo, T.; Mitsudo, T. *Chem. Rev.* **2000**, *100*, 3205. (d) Beleskaya, I.; Moberg, C. *Chem. Rev.* **1999**, *99*, 3435.

(4) (a) Arisawa, M.; Yamaguchi, M. *Org. Lett.* **2001**, *3*, 763. (b) Ogawa, A.; Kuniyasu, H.; Sonoda, N.; Hirao, T. *J. Org. Chem.* **1997**, *62*, 8361. (c) Gareau, Y.; Orellana, A. *Synlett* **1997**, 62, 8361. (d) Gareau, Y.; Tremblay, M.; Gauvreau, D.; Juteau, H. *Tetrahedron* **2001**, *57*, 5739.

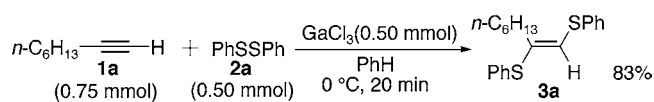
for some substrates.⁵ Highly stereoselective synthesis of (*E*)-1,2-dithio-1-alkenes is needed, complementary to transition-metal-catalyzed disulfidation of alkynes. Here we wish to report the highly selective disulfidation of terminal alkynes with disulfide in the presence of gallium trichloride to give (*E*)-1,2-dithio-1-alkenes (*E/Z* > 20/1).

Gallium trichloride (0.50 mmol, 1.0 M hexane solution, 0.50 mL) was added to a benzene solution (2 mL) of diphenyl disulfide (**2a**, 0.50 mmol, 109 mg) and 1-octyne (**1a**, 0.75 mmol, 83 mg) at 0 °C under argon. The solution turned brown. After the mixture was stirred for 20 min, extractive workup followed by silica gel column purification afforded (*E*)-1,2-di(phenylthio)-1-octene (**3a**, *E/Z* > 20/1) in 83% yield (Scheme 2).⁶ This compound was assigned by the ¹H

(5) (a) Heiba, E. I.; Dessau, R. M. *J. Org. Chem.* **1967**, *32*, 3837. (b) Benati, L.; Montevacchi, P. C.; Spagnolo, P. *J. Chem. Soc., Perkin Trans. 1* **1991**, 2103. (c) Benati, L.; Montevacchi, P. C.; Spagnolo, P. *J. Chem. Soc., Perkin Trans. 1* **1992**, 1659.

(6) Other Lewis acids such as BF₃·Et₂O, TiCl₄, InCl₃, Ga(OTf)₃, and GaF₃ were ineffective for this disulfidation. The use of GaI₃ yielded **3a** in 40% yield.

Scheme 2



NMR spectrum previously reported.⁷ Dichloromethane, 1,2-dichloroethane, and toluene were effective solvents for this reaction. The reaction resulted in complete recovery of the starting material in coordinating solvents such as tetrahydrofuran, diethyl ether, and DMF. An excess of 1-octyne did not influence the yield of **3a**. We obtained **3a** in 83% yield with the use of 3.0 equiv of 1-octyne.

Various alkynes were examined under the optimized reaction conditions (Table 1). Phenylacetylene gave (*E*)-1,2-

Table 1. GaCl₃-Mediated Reaction of Various Alkynes with Disulfide^a

entry	R	1	R'	2	3	yield (%)
1	<i>n</i> -Bu	1b	Ph	2a	3b	83
2	<i>i</i> -Pr	1c	Ph	2a	3c	58
3	<i>t</i> -Bu	1d	Ph	2a	3d	50
4	Ph	1e	Ph	2a	3e	87
5	<i>p</i> -CF ₃ C ₆ H ₄	1f	Ph	2a	3f	69
6	<i>p</i> -MeOC ₆ H ₄	1g	Ph	2a	3g	40
7	<i>n</i> -C ₆ H ₁₃	1a	Ph	2a	3a	83
8		1a	<i>p</i> -Tol	2b	3i	85
9		1a	<i>n</i> -Bu	2c	3j	49
10 ^c		1a		2c	3j	63
11		1a	<i>s</i> -Bu	2d	3k	20
12 ^c		1a		2d	3k	49
13	Ph	1e	<i>p</i> -Tol	2b	3l	84
14 ^c		1e	<i>n</i> -Bu	2c	3m	50

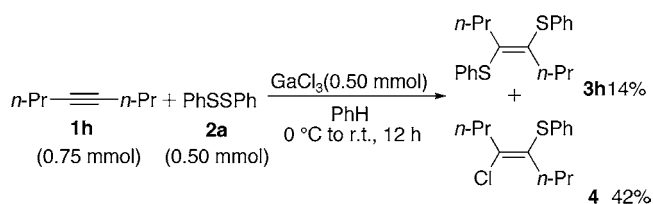
^a Disulfide (0.50 mmol), alkyne (0.75 mmol), GaCl₃(0.50 mmol), and PhH (2 mL) were employed. ^b A reaction mixture was allowed to warm to room temperature and stirred for 12 h. ^c 3.0 equiv of alkyne was used.

diphenylthio-1-phenylethene in 87% yield. The reactions of 3-methyl-1-butyne and 3,3-dimethyl-1-butyne with diphenyl disulfide afforded the corresponding di(phenylthio)alkenes in moderate yields. Coordinating functional groups such as hydroxy and carbonyl groups prevented the formation of the adduct. An internal alkyne, 4-octyne, gave (*E*)-4,5-di(phenylthio)-4-octene (**3h**) in low yield (14%), accompanied with an unexpected product, (*E*)-4-chloro-5-phenylthio-4-octene (**4**, 42%) (Scheme 3).

The addition of several disulfides to alkynes was also examined. Treatment of di(4-methylphenyl) disulfide with 1-octyne proceeded in good yield (entry 8). However, di(*n*-butyl) disulfide and di(*s*-butyl) disulfide gave rise to lower yields compared to diaryl disulfides (entries 9 and 11). Use

(7) Miyake, H.; Yamamura, K. *Bull. Chem. Soc. Jpn.* **1988**, *61*, 3752.


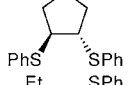

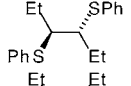

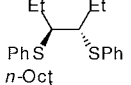

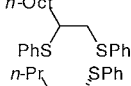

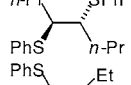

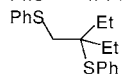
Scheme 3



of an excess of 1-octyne (3.0 equiv) improved the yield of 1,2-di(alkylthio)-1-octene (entries 10 and 12). The reaction of di(*tert*-butyl) disulfide afforded a complex mixture and di(*tert*-butylthio)alkene was not detected at all.

Table 2 summarizes the results of the addition of diphenyl disulfide to various alkenes in the presence of gallium

Table 2. Disulfidation of Various Alkenes with Gallium Trichloride^a

entry	alkene	Product	Yield (%)
1			87
2			93
3			88
4			65
5			71
6			74

^a Reaction conditions: PhSSPh (0.50 mmol), alkene (1.0 mmol), GaCl₃ (0.50 mmol), PhH (2 mL), 0 °C, 40 min.

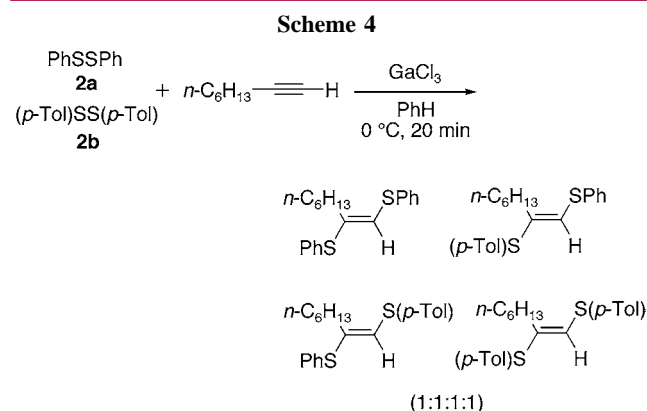
trichloride.⁸ Treatment of cyclopentene with diphenyl disulfide and gallium trichloride afforded *trans*-1,2-di(phenylthio)cyclopentane **6a** in good yield. Exclusive formation of the *trans* isomer was deduced by the examination of the ¹H NMR spectrum previously reported.⁹ (*E*)-3-Hexene gave *meso*-form **6b** and (*Z*)-3-hexene gave *dl*-form **6c**, which indicates the stereospecificity of the reaction. Mono- and disubstituted alkenes **5d–5f** were suitable to yield the corresponding adducts **6d–6f**. An attempt to react diphenyl disulfide with tri- and tetrasubstituted alkenes failed to give the di(phenylthio)alkanes.

Treatment of a 1:1 mixture of diphenyl disulfide and di-(4-methylphenyl) disulfide with 1-octyne in the presence of

(8) BF₃-catalyzed *trans* addition of disulfides to alkenes was reported. However, disulfidation of alkynes gave a mixture of *E/Z* isomers in low yield. See: Caserio, M. C.; Fisher, C. L.; Kim, J. K. *J. Org. Chem.* **1985**, *50*, 4390.

(9) Kitamura, T.; Matsuyuki, J.; Taniguchi, H. *J. Chem. Soc., Perkin Trans. 1* **1991**, 1607.

gallium trichloride gave a statistical mixture of four adducts (1:1:1:1) (Scheme 4). Moreover, an addition of gallium

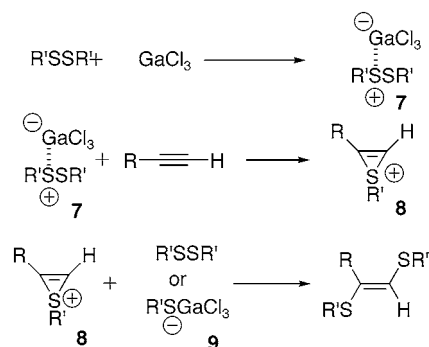


trichloride to a 1:1 mixture of diphenyl disulfide and di(4-methylphenyl) disulfide in the absence of alkyne provided an equilibrium mixture of disulfides (4-methylphenyl phenyl disulfide, diphenyl disulfide, and di(4-methylphenyl) disulfide) in the ratio of 2:1:1 within 30 min at 0 °C.¹⁰ This exchange reaction also proceeded with a catalytic amount of gallium trichloride (5 mol%).

We assume the reaction mechanism as shown in Scheme 5.⁷ Gallium trichloride coordinates with disulfide to form thiosulfonium-like species **7**. This species **7** reacts with alkyne to generate a thiirenium ion **8**.¹¹ Nucleophilic attack of **8** yields *trans* adduct.

(10) (a) Arisawa, M.; Yamaguchi, M. *J. Am. Chem. Soc.* **2003**, *125*, 6624. Disulfide-thiol exchange reaction was reported. See: (b) Dalman, G.; McDermid, J.; Gorin, G. *J. Org. Chem.* **1964**, *29*, 1480. (c) Eldjarn, L.; Pihl, A. *J. Am. Chem. Soc.* **1957**, *79*, 4589.

Scheme 5



In conclusion, we have developed highly stereoselective *trans* addition of disulfides to alkynes selectively. This method will be a useful synthetic tool for the formation of (*E*)-dithioalkenes, complementary to transition-metal-catalyzed *cis* addition of disulfides.

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Supporting Information Available: Experimental procedures and compound data. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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(11) The reaction of thiirenium ion with diphenyl disulfide to afford (*E*)-1,2-diphenylthio-alkene selectively in low yield was reported. See: (a) Benati, L.; Montecchi, P. *C. Gazz. Chim. Ital.* **1991**, *121*, 387. (b) Benati, L.; Montecchi, P. *C. Gazz. Chim. Ital.* **1989**, *119*, 609.