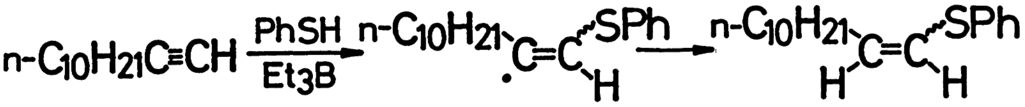
CHEMISTRY LETTERS, pp. 1647-1650, 1987.

Et_3B Induced Radical Addition of Thiols to Acetylenes

Yoshifumi ICHINOSE, Kuni WAKAMATSU, Kyoko NOZAKI, Jean-Luc BIRBAUM,
Koichiro OSHIMA,* and Kiitiro UTIMOTO
Department of Industrial Chemistry, Faculty of Engineering,
Kyoto University, Sakyo-ku, Kyoto 606

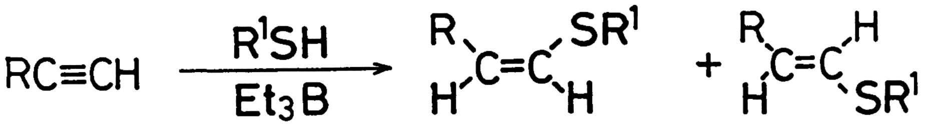
Thiols added easily to acetylenic compounds in the presence of Et_3B to give alkenyl sulfides in good yields. The reaction of acetylenes with 3-methyl-2-buten-1-thiol gave dihydrothiophene derivatives in one pot.

Free radical reactions have been used increasingly in recent years for the synthesis of organic molecules.$^{1)}$ Only little attention, however, has been paid to the methods for the primary generation of radicals. Photoinitiation and chemical initiation are general two methods and initiators such as dialkyl peroxides and azobisisobutyronitrile are widely and exclusively used in the latter case. Recently we have shown that Et_3B is an effective catalyst for the radical addition of triphenyltin hydride$^{2)}$ or triphenylgermyl hydride$^{3)}$ to acetylenes. Here we wish to report the further application of this new radical initiation method to the addition of thiols to acetylenes.$^{4)}$



A hexane solution of $Et_3B^{5)}$ (1.0 M, 1 M = 1 mol dm^{-3}, 1.0 ml, 1.0 mmol) was added to a solution of 1-dodecyne (0.17 g, 1.0 mmol) and benzenethiol (0.12 g, 1.1 mmol) in benzene (10 ml) at 25 °C under an argon atmosphere. The resulting mixture was stirred for 4 h at 25 °C. Workup$^{6)}$ (1 M NH_4Cl, AcOEt) followed by purification by silica gel column chromatography gave 1-phenylthio-1-dodecene (0.22 g, 81% yield) as a stereoisomeric mixture (Z/E = 40/60). Aliphatic thiols were less reactive than aromatic thiols.$^{7)}$ Thus, the reaction of phenylacetylene with n-BuSH or t-BuSH gave the corresponding styryl sulfide in 54% or 53% yield, respectively after stirring for prolonged reaction time (15 h) under the same reaction conditions. Fortunately, this problem was solved by the addition of methanol to the reaction mixture.$^{8)}$ For instance, treatment of a solution of phenylacetylene (1.0 mmol), n-BuSH (1.1 mmol), and MeOH (4.0 mmol)

Table 1. Et_3B Induced Addition of RSH to Acetylenes



Run	Acetylene R	Thiol R^1	Reaction time/h	Product Y/%$^{a)}$	 Z : E
1	n-$C_{10}H_{21}$	PhSH	4	81	40 : 60
2	Ph	PhSH	4	84	25 : 75
3	$HOCH_2$	PhSH	5	85	30 : 70
4	$HOCH_2CH_2$	PhSH	4	91	40 : 60
5	$THPOCH_2CH_2$	PhSH	4	70	40 : 60
6	Me_3Si	PhSH	15	80$^{b)}$	0 : 100
7	6-Dodecyne	PhSH	15	71	c)
8	n-$C_{10}H_{21}$	n-BuSH$^{d)}$	4	60	50 : 50
9	Ph	n-BuSH$^{d)}$	3	92	30 : 70
10	$HOCH_2CH_2$	n-BuSH$^{d)}$	4	70	50 : 50
11	n-$C_{10}H_{21}$	t-BuSH$^{d)}$	4	71	40 : 60
12	Ph	t-BuSH$^{d)}$	3	95	82 : 18
13	$HOCH_2CH_2$	t-BuSH$^{d)}$	4	89	60 : 40

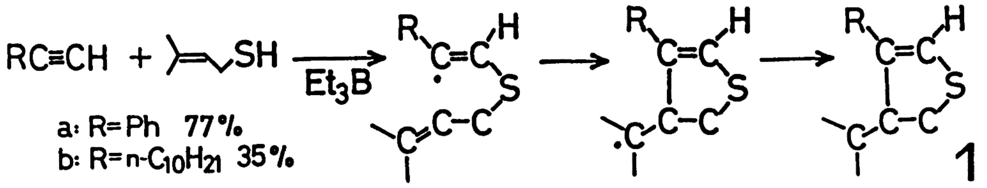
a) Isolated yields. b) Excess of trimethylsilylacetylene (5.0 mmol) was employed. The yield was based on PhSH. c) Stereoisomeric mixture (Z/E = 1/2 or 2/1) d) Acetylene (1.0 mmol), thiol (1.1 mmol), methanol (4.0 mmol), and Et_3B (1.0 mmol) were employed.

in benzene (10 ml) with Et_3B (1.0 mmol) gave 1-butylthio-2-phenylethene[9] in 92% yield after stirring for 3 h at 25 °C.

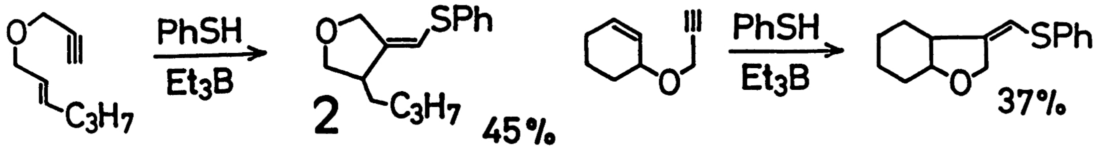
The representative results are summarized in Table 1. Thiyl group added to terminal acetylenic carbon regioselectively, but nonstereoselectively to give a mixture of (Z)- and (E)-alkenyl sulfides with an exception of the reaction of trimethylsilylacetylene which gave (E)-olefin exclusively. The Z/E ratios of double bonds were not affected by the solvents or reaction temperature. Dichloromethane and tetrahydrofuran were effective solvents as benzene or toluene, while the reaction did not take place in hexane. It is worth noting that this new method provided alkenyl sulfides in good yields without contamination by diaddition products. Generally, the alkenyl sulfides formed in the first addition step are more reactive than the starting alkynes and most thiol additions to alkynes are accompanied by at least partial diaddition.$^{4)}$

The new method is also effective for the addition of thiols to alkenes. Treatment of 1-dodecene, styrene, or 3-buten-1-ol with n-BuSH in the presence of Et_3B gave the corresponding butyl sulfide in 81%, 79%, or 83% yield, respectively. Alkenes and alkynes reacted with thiols at the comparable reaction rate.$^{10)}$

The reaction was successfully applied to the synthesis of dihydrothiophene derivatives from acetylenes and 3-methyl-2-buten-1-thiol.$^{11,12)}$



The thiyl radical also caused vinyl-radical cyclization of acetylenic olefins depicted below.$^{13-16)}$



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2) K. Nozaki, K. Oshima, and K. Utimoto, J. Am. Chem. Soc., 109, 2547 (1987).

3) Y. Ichinose, K. Nozaki, K. Wakamatsu, K. Oshima, and K. Utimoto, Tetrahedron Lett., in press.

4) Review for the free-radical addition of thiols to unsaturated compounds: K. Griesbaum, Angew. Chem., Int. Ed. Engl., 9, 273 (1970).

5) The reaction was not completed in the presence of a catalytic amount of Et_3B (10 mol%) after stirring for 15 h at 25 °C. We thank Toyo Stauffer Chemical Company for a gift of a hexane solution of Et_3B (1.0 M).

6) In the case of large scale reactions (>10 mmol), the reaction mixture was diluted with benzene and poured into ice-cooled 1 M NH_4Cl cautiously (exothermic) and extracted with AcOEt.

7) Aliphatic thiols have been reported to be less reactive than aromatic thiols in the addition to alkenes. M. S. Kharasch, W. Nudenberg, and G. J. Mantell,

J. Org. Chem., 16, 524 (1951).

8) The addition of methanol increased the reaction rate and yields of the products. The reason for these effects is not clear. We are tempted to assume that methanol may facilitate the generation of radicals from Et$_3$B as molecular oxygen. A. Suzuki, S. Nozawa, M. Itoh, H. C. Brown, G. W. Kabalka, and G. W. Holland, J. Am. Chem. Soc., 92, 3503 (1970); H. C. Brown and M. M. Midland, Angew. Chem., Int. Ed. Engl., 11, 692 (1972).

9) 1-Butylthio-2-phenylethene (Z/E = 30/70): Bp 100 °C (bath temp, 2.0 Torr, 1.0 Torr = 133.322 Pa); IR (neat) 2926, 2868, 1597, 1492, 1444, 937, 771, 736, 690 cm^{-1}; NMR (CDCl$_3$, 200 MHz) δ 0.98 (t, J = 5.0 Hz, 3H), 1.30-1.75 (m, 4H), 2.80 (t, J = 7.0 Hz, 0.6H), 2.82 (t, J = 7.0 Hz, 1.4H), 6.30 (d, J = 11.0 Hz, 0.3H), 5.50 (d, J = 11.0 Hz, 0.3H), 6.52 (d, J = 16.0 Hz, 0.7H), 6.80 (d, J = 16.0 Hz, 0.7H). Found: C, 74.86; H, 8.58%. Calcd for $C_{12}H_{16}S$: C, 74.94; H, 8.39%.

10) Heiba and Dessau have reported that the propene reacts about 1.2 times rapidly as the propyne for CH_3SH addition by irradiation. E. J. Heiba and R. M. Dessau, J. Org. Chem., 32, 3837 (1967).

11) **1a**: Bp 110 °C (bath temp, 2.0 Torr); IR (neat) 2926, 2894, 2866, 1597, 1585, 1492, 1462, 1442, 1386, 1368, 827, 809, 748, 692 cm^{-1}; NMR (CDCl$_3$, 200 MHz) δ 0.84 (d, J = 6.9 Hz, 3H), 0.96 (d, J = 6.9 Hz, 3H), 2.10 (m, 1h), 3.30 (dd, J = 4.0, 10.5 Hz, 1H), 3.52 (dd, J = 10.5, 10.5 Hz, 1H), 3.62 (dddd, J = 1.3, 4.0, 4.0, 10.5 Hz, 1H), 6.41 (d, J = 1.3 Hz, 1H), 7.25-7.35 (m, 5H). Found: C, 76.46; H, 7.98%. Calcd for $C_{13}H_{16}S$: C, 76.42; H, 7.89%.

12) The reaction of phenylacetylene with 2-propen-1-thiol instead of 3-methyl-2-buten-1-thiol resulted in the formation of 4-methyl-3-phenyl-4,5-dihydrothiophene in 25% yield along with (Z)- and (E)-allyl styryl sulfide (25%) and unidentified complex mixtures.

13) Very recently this type cyclization reaction has been reported. C. A. Broka and D. E. C. Reichert, Tetrahedron Lett., 28, 1503 (1987).

14) **2**: Bp 130 °C (bath temp, 2.0 Torr); IR (neat) 2954, 2926, 2852, 1583, 1479, 1466, 1439, 1088, 1025, 930, 738, 689 cm^{-1}; NMR (CDCl$_3$, 200 MHz) δ 0.91 (t, J = 6.5 Hz, 3H), 1.20-1.80 (m, 6H), 2.80 (m, 1H), 3.57 (dd, J = 6.6, 8.4 Hz, 1H), 4.08 (dd, J = 6.8, 8.4 Hz, 1H), 4.42 (d, J = 2.5 Hz, 1H), 4.44 (d, J = 2.5 Hz, 1H), 6.05 (dd, J = 2.4, 4.3 Hz, 1H), 7.19-7.32 (m, 5H). Found: C, 72.78; H, 8.21%. Calcd for $C_{15}H_{20}OS$: C, 72.54; H, 8.12%.

15) Et$_3$B induced addition of PhSeH to acetylenes was not so effective as the addition of thiols. The reaction of PhSeH with phenylacetylene gave the corresponding alkenyl selenide in 73% yield as a stereoisomeric mixture (Z/E = 92/8) after stirring for 3 h at 25 °C, whereas the reaction of PhSeH with 1-hexyne gave the desired alkenyl selenide in only 9% yield.

16) Financial support by the Ministry of Education, Science, and Culture, Japanese Government (Grant-in-Aid for Special Project Research No. 61211016) is acknowledged.

(Received June 1, 1987)