



A Publication
of Reliable Methods
for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

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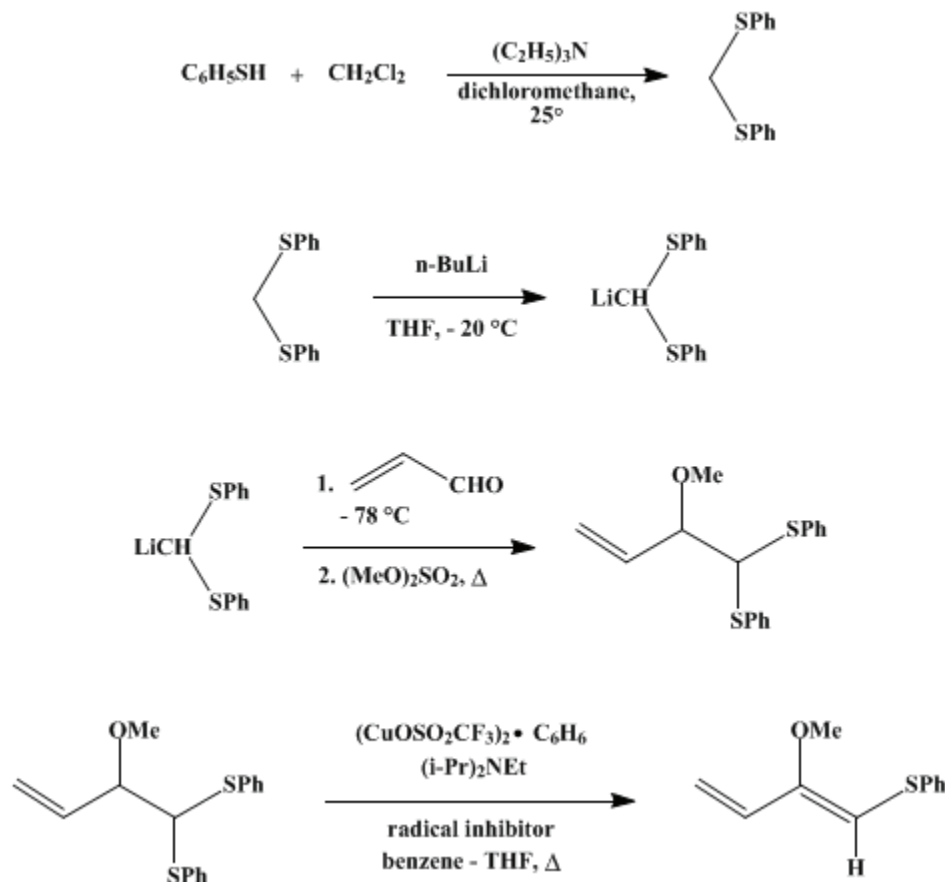
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

Organic Syntheses, Coll. Vol. 6, p.737 (1988); Vol. 59, p.202 (1979).

VINYL SULFIDES FROM THIOACETALS WITH COPPER(I) TRIFLUOROMETHANESULFONATE: (Z)-2-METHOXY-1-PHENYLTHIO-1,3-BUTADIENE

[Benzene, [(2-methoxy-1,3-butadienyl)thio]-, (Z)-]



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Checked by J. Bisaha and M. F. Semmelhack.

1. Procedure

Caution! Part A should be carried out in an efficient hood to minimize exposure to the foul-smelling thiophenol.

Benzene has been identified as a carcinogen; OSHA has issued emergency standards on its use. All procedures involving benzene should be carried out in a well-ventilated hood, and glove protection is required.

A. *Bis(phenylthio)methane*. A dry, 2-l., one-necked flask equipped with a magnetic stirring bar and a 250-ml., pressure-equalizing dropping funnel mounted with a combined inlet-outlet assembly for introducing argon (Note 1) is charged with 1.5 l. of distilled dichloromethane and 79.9 g. (110 ml., 0.791 mole) of triethylamine (Note 2), and purged with argon. The solution is stirred and cooled in an

ice bath as 87 g. (81 ml., 0.79 mole) of **thiophenol** (Note 3) is added over 20–30 minutes. The mixture is allowed to warm to 20° and stirred at this temperature for another 3 hours. **Triethylamine hydrochloride** is removed by filtration through a fritted-glass Büchner funnel, and the filtrate is washed with two 200-ml. portions of 10% aqueous **sodium hydroxide**, two 200-ml. portions of 2 *N* **hydrochloric acid**, and one 300-ml. portion of water. The **dichloromethane** solution is dried over anhydrous **magnesium sulfate** and evaporated under reduced pressure. Recrystallization of the residue from petroleum ether gives 51.2–59.6 g. (56–65%) of **bis(phenylthio)methane** as white crystals, m.p. 35–37° (Note 4).

B. **4,4-Bis(phenylthio)-3-methoxy-1-butene**. A 250-ml., two-necked, round-bottomed flask equipped with a magnetic stirring bar, a rubber septum, and a reflux condenser bearing an inlet-outlet assembly for argon (Note 1) is dried in an oven at 110° and cooled under a stream of **argon** passed through the septum with a syringe needle and vented through the argon bubbler. A solution of 5.00 g. (0.0215 mole) of **bis(phenylthio)methane** in 150 ml. of **tetrahydrofuran** (Note 5) is placed in the flask and cooled to –20° with a carbon tetrachloride–dry ice bath. A 15.8-ml. (0.0217 mole) aliquot from a 1.37 *M* solution of *n*-**butyllithium** in **hexane** (Note 6) is injected through the septum with a syringe. The resulting deep-yellow solution is stirred and cooled at –20° for 1 hour and then cooled to –78° with an acetone–dry ice bath. The color of the solution is discharged immediately when 1.4 g. (1.7 ml., 0.025 mole) of **acrolein** (Note 7) is added by syringe at –78°. Stirring and cooling are continued for 15 minutes, after which 2.90 g. (2.19 ml., 0.0230 mole) of **dimethyl sulfate** (Note 8) is added, and the cooling bath is removed. The solution is stirred at room temperature for 16 hours and heated at reflux for 2 hours. A 3-ml. portion of water is added to the cooled mixture, most of the **tetrahydrofuran** is removed by rotary evaporation, and the concentrate is partitioned between 30 ml. of water and 30 ml. of **diethyl ether**. The organic layer is washed three times with 10-ml. portions of concentrated **ammonia** and once with water. The ethereal solution is dried over anhydrous **magnesium sulfate** and evaporated under reduced pressure. Crystallization of the viscous yellow residue from 30 ml. of 95% **ethanol** at –20° gives 3.11–3.36 g. (48–52%) of **4,4-bis(phenylthio)-3-methoxy-1-butene** as a light-yellow solid, m.p. 45–48°, which is of adequate purity for use in the next step (Note 9).

C. **(Z)-2-Methoxy-1-phenylthio-1,3-butadiene**. A 250-ml., two-necked, round-bottomed flask equipped with a magnetic stirring bar, a rubber septum, and a reflux condenser bearing a combined inlet-outlet assembly for argon (Note 1) is flushed with **argon** and charged with 3.27 g. [0.00650 mole, 0.0126 g.-atom of copper(I)] of bis[copper(I) trifluoromethanesulfonate] benzene complex (Note 10), 0.036 g. (0.18 mmole) of **3-tert-butyl-4-hydroxy-5-methylphenyl sulfide** (Note 11), and 70 ml. of **benzene** (Note 12). With syringes 1.20 g. (0.00397 mole) of **4,4-bis(phenylthio)-3-methoxy-1-butene**, 1.33 g. (1.80 ml., 0.0103 mole) of *N,N*-diisopropylethylamine (Note 13), and 14 ml. of **tetrahydrofuran** (Note 5) are injected through the septum into the flask. The suspension is stirred and heated under reflux for 4.75 hours (Note 14), after which the starting thioacetal has completely reacted, as judged by TLC (Note 15). Water (2 ml.) is added to the cooled mixture, the insoluble material is removed by filtration through Celite, and the flask is rinsed with several portions of **ether**. A 40-ml. portion of water is added to the filtrate, the layers are separated, and the aqueous layer is extracted with three 25-ml. portions of **ether**. The organic solutions are combined, dried over anhydrous **magnesium sulfate**, and evaporated under reduced pressure. Bulb-to-bulb distillation of the residual brown oil (0.782 g.) in a Kugelrohr apparatus (Note 16) with an oven temperature of 85–95° (0.005 mm.) provides 0.421–0.486 g. (55–64%) of **(Z)-2-methoxy-1-phenylthio-1,3-butadiene** as a light-yellow oil (Note 17) and (Note 18).

2. Notes

1. The inlet-outlet assembly is connected to both a source of argon and a bubbler which serves as exit for the inert gas. **Argon** is passed through the apparatus for 30 minutes, and the system is then kept under a slight positive pressure of inert gas by maintaining a slow flow of **argon** through the bubbler.
2. **Triethylamine** was purchased from Eastman Organic Chemicals and distilled from **calcium hydride** before use.
3. **Thiophenol** was purchased from Aldrich Chemical Company, Inc., and distilled, b.p. 75–77° (30 mm.), 168–169° (760 mm.).
4. The submitters obtained 59.6–64.1 g. (65–70%) of product, m.p. 36–37°, after recrystallization from **ethanol**. Reported melting points for **bis(phenylthio)methane** are 34–35°,² 38–40°,³ and 39.5–40.5°.⁴ The

¹H NMR spectrum (CCl₄) exhibits a two-proton singlet at δ 4.30 and a 10-proton multiplet at δ 7.10–7.56.

5. Tetrahydrofuran was distilled from lithium aluminum hydride by the submitters and collected in a flask containing molecular sieves. For a warning regarding this method of purifying tetrahydrofuran, see *Org. Synth., Coll. Vol. 5*, 976 (1973).

6. *n*-Butyllithium in hexane was purchased from Alfa Division, Ventron Corporation.

7. Acrolein was purchased by the submitters from Cationics, Division of Columbia Organic Chemicals Company, Inc. (Columbia, South Carolina) and distilled immediately before use, b.p. 51–53°.

8. Dimethyl sulfate was used as supplied by Eastman Organic Chemicals. The submitters obtained lower yields when methyl iodide was substituted for dimethyl sulfate.

9. The yield and melting point data given are those of the checkers. The purity of the products was estimated to be at least 98% from analysis of its ¹H NMR spectrum. The submitters report that the crude product crystallized on standing in a freezer and that one recrystallization from absolute ethanol afforded 3.6–4.1 g. (55–63%) of product, m.p. 49.5–51°. The ¹H NMR spectrum (CCl₄) exhibits the following absorptions, δ (multiplicity, coupling constant *J* in Hz., number of protons, assignment): 3.23 (s, 3H, OCH₃), 3.48–3.97 (m, 1H, CHOCH₃), 4.37 [d, *J* = 4.0, 1H, CH(SC₆H₅)₂], 5.03–5.43 (m, 2H, CH=CH₂), 5.67–6.13 (m, 1H, CH=CH₂), 6.90–7.57 (m, 10H, 2SC₆H₅).

10. Bis[copper(I) trifluoromethanesulfonate] benzene complex was prepared by a modification of a procedure reported by Salomon and Kochi⁵ as described in the following paragraph. The copper(I) oxide used was purchased from J. T. Baker Chemical Company, and trifluoromethanesulfonic anhydride was prepared by the procedure in *Org. Synth., Coll. Vol. 6*, 324 (1988). The submitters have found once-distilled anhydride to be satisfactory provided that the weight of phosphorus pentoxide used was approximately equal to the weight of sulfonic acid, and the reaction mixture was stirred vigorously. When twice-distilled anhydride was used in the procedure below, reaction times as long as 13 hours were required before decolorization occurred. The submitters suggest that the enhanced rates observed with once-distilled anhydride may be attributed to the presence of the sulfonic acid. Although trifluoromethanesulfonic anhydride is available from Aldrich Chemical Company, Inc., the commercial reagent has not been used in this procedure.

A dry, 1-l., two-necked, round-bottomed flask equipped with a magnetic stirring bar, a rubber septum, and a reflux condenser bearing a combined inlet-outlet assembly for argon (Note 1) is purged with argon and charged with 18.0 g. (0.126 mole) of copper(I) oxide and 600 ml. of degassed benzene (Note 12). With a syringe, 42.7 g. (25.5 ml., 0.151 mole) of trifluoromethanesulfonic anhydride is injected through the septum into the flask. The suspension is stirred and heated under reflux until nearly all of the red copper(I) oxide has dissolved. Although 3–5 hours is normally sufficient, reaction times as long as 19 hours were required on some occasions (see preceding paragraph). The hot suspension is filtered through a Büchner funnel in an argon-filled glove bag kept dry with a dish of phosphorus pentoxide. The filtrate is allowed to cool in the glove bag for 1 hour, after which the crop of fine white crystals is collected on a fritted-glass Büchner funnel. The funnel is tightly covered with aluminum foil and then placed in a vacuum desiccator containing anhydrous calcium sulfate and phosphorus pentoxide. The desiccator is removed from the glove bag, evacuated overnight, refilled with argon, and returned to the glove bag. The dry bis[copper(I) trifluoromethanesulfonate] benzene complex, 37.6–49.5 g. (60–79%), is transferred to vials in the glove bag. The product maintains its activity indefinitely when protected from moisture and air.

The procedure described above provides a sufficient quantity of bis[copper(I) trifluoromethanesulfonate] benzene complex for several reactions at the scale used in Part C. If bis[copper(I) trifluoromethanesulfonate] benzene complex for a single reaction is desired, the same procedure can be followed at the appropriate scale without the use of the glove bag. In this case, the decolorized solution is not filtered but instead cooled, and the product is crystallized in the reaction vessel. The supernatant benzene is decanted, and the crystals are washed in the flask with fresh benzene. The bis[copper(I) trifluoromethanesulfonate] benzene complex is then used without drying in the same flask.

11. 3-*tert*-Butyl-4-hydroxy-5-methylphenyl sulfide was purchased from Aldrich Chemical Company, Inc., and serves as a radical inhibitor, preventing the polymerization of the product. Lower yields of product were obtained when hydroquinone was used as the inhibitor.

12. Benzene was freshly distilled from calcium hydride and collected in a flask containing molecular sieves.

13. *N,N*-Diisopropylethylamine supplied by Aldrich Chemical Company, Inc., was distilled prior to use. The amine is added to prevent polymerization of the diene by acid generated during the reaction. If the product is not sensitive to acid, the amine may be omitted.

14. The temperature at which elimination of thiophenol occurs depends on the substituents on the sulfur-bearing carbon.⁶ Thioketals react rapidly at 25°. In some cases the elimination of thiophenol from the less reactive thioacetals may also be performed at 25°. However, in the present case the combined inductive effects of the vinyl and methoxy groups evidently destabilize the incipient carbonium ion and necessitate a higher temperature for the reaction.

15. TLC was carried out on plates coated with silica gel, using 1:10 (v/v) ether–hexane as developing solvent.

16. Kugelrohr distillation ovens manufactured by Büchi Glasapparatefabrik are available from Brinkmann Instruments, Inc., Westbury, New York.

17. The yields and boiling point range given are those reported by the checkers. When the checkers used starting thioacetal that had been purified by both column chromatography and recrystallization (m.p. 50–52°), the yield was 0.486 g. (64%). Using recrystallized thioacetal, m.p. 49.5–51°, the submitters obtained 0.532–0.646 g. (70–85%) of product.

The ¹H NMR spectrum (CCl₄) of the diene exhibits the following absorptions, δ (multiplicity, number of protons, assignment): 3.70 (s, 3H, OCH₃), 4.87–5.52 (m, 2H, CH=CH₂), 5.64 (s, 1H, CHSC₆H₅), 5.83–6.31 (m, 1H, CH=CH₂), 6.98–7.37 (m, 5H, SC₆H₅). TLC on silica gel with 3:2 (v/v) benzene–hexane as developing solvent showed a single spot. The single sharp peak for the methoxy group in the ¹H NMR spectrum and the absence of a spot at a high R_f value from TLC established that the product was not contaminated by its *E*-isomer. A mixture of the two isomers in which the *E*-isomer predominates can be prepared by heating a solution of the product in dichloromethane at reflux for 4 hours. The stereochemistry of the original product is assigned as *Z* on the basis of its high reactivity in Diels-Alder reactions and on the exclusive formation of an adduct with *cis* stereochemistry from reaction with methyl vinyl ketone.⁷ The *E*-isomer undergoes Diels-Alder reactions much more slowly.⁸

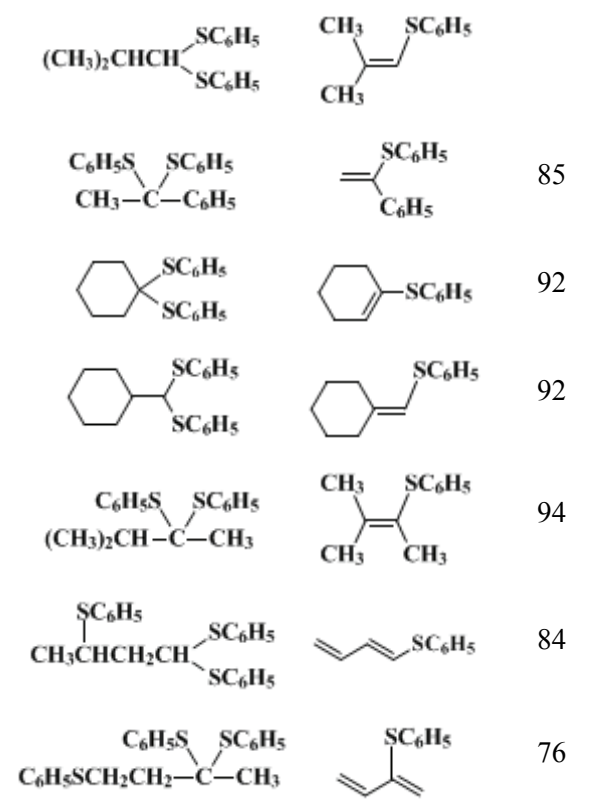
18. The product is stable for months when mixed with a small amount of the radical inhibitor, 3-*tert*-butyl-4-hydroxy-5-methylphenyl sulfide, and stored in a freezer. In the absence of the inhibitor, it isomerizes to a mixture of *E*- and *Z*-isomers over a period of some months.

3. Discussion

Part C of the present procedure illustrates a mild method for effecting the elimination of thiophenol from thioacetals and thioketals under essentially neutral conditions. The reaction of simple thioacetals and thioketals with bis[copper(I) trifluoromethanesulfonate] benzene complex in benzene-tetrahydrofuran at room temperature affords vinyl sulfides in high yield (Table I).^{6,7} The reaction presumably occurs by coordination of the thiophilic copper(I) reagent with sulfur, heterolysis to a phenylthio-stabilized carbonium ion with formation of the insoluble copper(I) thiophenoxide, and finally proton loss, giving the vinyl sulfide. Since trifluoromethanesulfonic acid is generated in stoichiometric quantity during the reaction, the medium becomes highly acidic. If the reactant or product is unstable to acid, as is the case in the present procedure, the pH can be kept neutral by adding *N,N*-diisopropylethylamine.

TABLE I
VINYL SULFIDES FROM THIOACETALS AND
THIOKETALS WITH COPPER(I)
TRIFLUOROMETHANESULFONATE

Thioacetal or Thioketal	Vinyl Sulfide	Yield (%)
$\text{CH}_3\text{CH}_2\text{CH}(\text{SC}_6\text{H}_5)_2$	$\text{CH}_3\text{CH}=\text{CHSC}_6\text{H}_5$	91



The reaction of crotonaldehyde and methyl vinyl ketone with thiophenol in the presence of anhydrous hydrogen chloride effects conjugate addition of thiophenol as well as acetal formation. The resulting β -phenylthio thioacetals are converted to 1-phenylthio- and 2-phenylthio-1,3-butadiene, respectively, upon reaction with 2 equivalents of copper(I) trifluoromethanesulfonate (Table I).⁷ The copper(I)-induced heterolysis of carbon–sulfur bonds has also been used to effect pinacol-type rearrangements of bis(phenylthio)methyl carbinols.⁹ Thus, the addition of bis(phenylthio)methyl lithium to ketones and aldehydes followed by copper(I)-induced rearrangement results in a one-carbon ring expansion or chain-insertion transformation, giving α -phenylthio ketones. Monothioketals of 1,4-diketones are cyclized to 2,5-disubstituted furans by the action of copper(I) trifluoromethanesulfonate.^{6,10}

The most common procedure previously employed to effect the elimination of thiols from thioacetals has been heating in the presence of a protic acid.^{11,12} For example, propionaldehyde diethyl thioacetal is converted to 1-ethylthio-1-propene on heating at 175° in the presence of phosphoric acid.¹¹ The relatively high temperature and acidic conditions of such procedures are, however, distinct disadvantages of this method. Another approach consists of oxidation of a thioacetal to the mono *S*-oxide and thermal elimination of a sulfenic acid at 140–150°.¹³

Vinyl sulfides have found numerous synthetic applications. Vinyl sulfides unsubstituted in the 1-position are metallated readily, and the resulting 1-phenylthio- or 1-alkylthiovinyl lithium reagents have been utilized for nucleophilic acylation and other applications.^{14,15} The phenylthio-substituted 1,3-butadienes serve as interesting functionalized dienes in Diels-Alder reaction.^{7,16,17} For example, (*Z*)-2-methoxy-1-phenylthio-1,3-butadiene and methyl vinyl ketone afford an adduct with the normally inaccessible "meta" relationship between the methoxy and acetyl substituents.⁷ The isomeric 2-methoxy-3-phenylthio- and 1-methoxy-4-phenylthio-1,3-butadienes have been prepared recently by thermal ring opening of the appropriate cyclobutenes.¹⁷

When methacrolein is substituted for acrolein in the present procedure, (*Z*)-2-methoxy-3-methyl-1-phenylthio-1,3-butadiene is produced in good yield.¹⁸ However, when a β -alkyl group is present on the enal, a rearranged product, a 4-alkyl-1-methoxy-2-phenylthio-1,3-butadiene, is produced as a pair of

References and Notes

1. Department of Chemistry, University of Pittsburgh, Pittsburgh, Pennsylvania 15260.
 2. L. Field and C. H. Banks, *J. Org. Chem.*, **40**, 2774 (1975).
 3. A. W. Harriott and D. Picker, *Synthesis*, 447 (1975).
 4. E. J. Corey and D. Seebach, *J. Org. Chem.*, **31**, 4097 (1966).
 5. R. G. Salomon and J. K. Kochi, *J. Am. Chem. Soc.*, **95**, 1889, 3300 (1973).
 6. T. Cohen, G. Herman, J. R. Falck, and A. J. Mura, Jr., *J. Org. Chem.*, **40**, 812 (1975).
 7. T. Cohen, A. J. Mura, Jr., D. W. Shull, E. R. Fogel, R. J. Ruffner, and J. R. Falck, *J. Org. Chem.*, **41**, 3218 (1976).
 8. T. Cohen and D. W. Shull, unpublished results.
 9. T. Cohen, D. Kuhn, and J. R. Falck, *J. Am. Chem. Soc.*, **97**, 4749 (1975).
 10. A. J. Mura, Jr., Ph.D. Thesis, University of Pittsburgh, 1976.
 11. H. J. Boonstra, L. Brandsma, A. W. Weigman, and J. F. Arens, *Recl. Trav. Chim. Pays-Bas*, **78**, 252 (1959);
 12. L. Brandsma, P. Vermeer, J. G. A. Kooijman, H. Boelens, and J. T. M. Maessen, *Recl. Trav. Chim. Pays-Bas*, **91**, 729 (1972).
 13. A. Deljac, Z. Stefanac, and K. Balenovic, *Tetrahedron*, Suppl. **8**, 33 (1966).
 14. For a review see B.-T. Gröbel and D. Seebach, *Synthesis*, 357 (1977).
 15. K. Oshima, K. Shimoji, H. Takahashi, H. Yamamoto, and H. Nozaki, *J. Am. Chem. Soc.*, **95**, 2694 (1973); I. Vlattas, L. D. Vecchia, and A. O. Lee, *J. Am. Chem. Soc.*, **98**, 2008 (1976); B. Harirchian and P. Magnus, *J. Chem. Soc. Chem. Commun.*, 522 (1977); R. R. Schmidt and B. Schmid, *Tetrahedron Lett.*, 3583 (1977).
 16. D. A. Evans, C. A. Bryan, and C. L. Sims, *J. Am. Chem. Soc.*, **94**, 2891 (1972).
 17. B. M. Trost and A. J. Bridges, *J. Am. Chem. Soc.*, **98**, 5017 (1976); B. M. Trost, S. A. Godleski, and J. Ippen, *J. Org. Chem.*, **43**, 4559 (1978).
 18. T. Cohen and Z. Kosarych, *Tetrahedron Lett.*, **21**, 3955 (1980).
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Appendix

Chemical Abstracts Nomenclature (Collective Index Number); (Registry Number)

petroleum ether

bis[copper(I) trifluoromethanesulfonate] benzene

benzene-tetrahydrofuran

2-methoxy-3-phenylthio- and 1-methoxy-4-phenylthio-1,3-butadienes

ethanol (64-17-5)

hydrogen chloride,
hydrochloric acid (7647-01-0)

ammonia (7664-41-7)

Benzene (71-43-2)

ether,
diethyl ether (60-29-7)

sodium hydroxide (1310-73-2)

Acrolein (107-02-8)

hydroquinone (123-31-9)

sulfur (7704-34-9)

dimethyl sulfate (77-78-1)

copper(I) oxide

phosphoric acid (7664-38-2)

Methyl iodide (74-88-4)

Triethylamine hydrochloride (554-68-7)

dichloromethane (75-09-2)

Thiophenol (108-98-5)

magnesium sulfate (7487-88-9)

n-butyllithium (109-72-8)

Tetrahydrofuran (109-99-9)

lithium aluminum hydride (16853-85-3)

hexane (110-54-3)

crotonaldehyde (123-73-9)

methyl vinyl ketone (78-94-4)

triethylamine (121-44-8)

methacrolein (78-85-3)

argon (7440-37-1)

calcium hydride (7789-78-8)

trifluoromethanesulfonic acid (1493-13-6)

copper(I) thiophenoxide (34012-88-9)

Trifluoromethanesulfonic anhydride (358-23-6)

N,N-diisopropylethylamine (7087-68-5)

COPPER(I) TRIFLUOROMETHANESULFONATE

Bis(phenylthio)methane (3561-67-9)

4,4-Bis(phenylthio)-3-methoxy-1-butene (60466-65-1)

vinyl sulfide (627-51-0)

bis(phenylthio)methyl lithium

propionaldehyde diethyl thioacetal

1-ethylthio-1-propene

phosphorus pentoxide (1314-56-3)

(Z)-2-Methoxy-1-phenylthio-1,3-butadiene,
Benzene, [(2-methoxy-1,3-butadienyl)thio]-, (Z)- (60466-66-2)

3-tert-butyl-4-hydroxy-5-methylphenyl sulfide (96-66-2)

(Z)-2-methoxy-3-methyl-1-phenylthio-1,3-butadiene