Organic Syntheses

A Publication
of Reliable Methods
for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

The procedures in *Organic Syntheses* are intended for use only by persons with proper training in experimental organic chemistry. All hazardous materials should be handled using the standard procedures for work with chemicals described in references such as "Prudent Practices in the Laboratory" (The National Academies Press, Washington, D.C., 2011; the full text can be accessed free of charge at http://www.nap.edu/catalog.php?record_id=12654). All chemical waste should be disposed of in accordance with local regulations. For general guidelines for the management of chemical waste, see Chapter 8 of Prudent Practices.

In some articles in *Organic Syntheses*, chemical-specific hazards are highlighted in red "Caution Notes" within a procedure. It is important to recognize that the absence of a caution note does not imply that no significant hazards are associated with the chemicals involved in that procedure. Prior to performing a reaction, a thorough risk assessment should be carried out that includes a review of the potential hazards associated with each chemical and experimental operation on the scale that is planned for the procedure. Guidelines for carrying out a risk assessment and for analyzing the hazards associated with chemicals can be found in Chapter 4 of Prudent Practices.

The procedures described in *Organic Syntheses* are provided as published and are conducted at one's own risk. *Organic Syntheses, Inc.*, its Editors, and its Board of Directors do not warrant or guarantee the safety of individuals using these procedures and hereby disclaim any liability for any injuries or damages claimed to have resulted from or related in any way to the procedures herein.

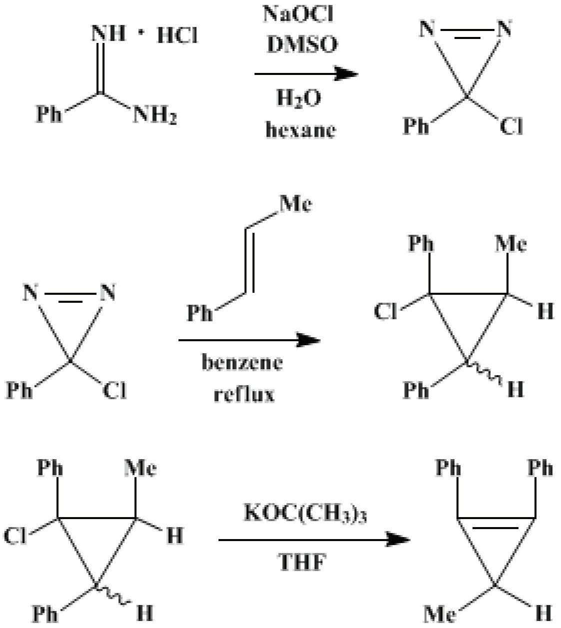
These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

DOI:10.15227/orgsyn.060.0053

Organic Syntheses, Coll. Vol. 7, p.203 (1990); Vol. 60, p.53 (1981).

PREPARATION OF CHLOROPHENYLDIAZIRINE AND THERMAL GENERATION OF CHLOROPHENYL CARBENE: 1,2-DIPHENYL-3-METHYLCYCLOPROPENE

[Benzene, 1,1'-(3-methyl-1-cyclopropene-1,2-diyl)-bis-]



Submitted by Albert Padwa, Mitchell J. Pulwer, and Thomas J. Blacklock[1].
Checked by M. F. Semmelhack and A. Zask.

1. Procedure

Caution! Phenylchlorodiazirine is highly explosive (Note 6). It should always be handled with adequate shielding and normal protective equipment such as face shield and leather gloves.

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 3-L, three-necked, round-bottomed flask equipped with a high-speed mechanical stirrer and a 250-mL pressure-equalized dropping funnel is charged with 22.5 g (0.143 mol) of benzamidine hydrochloride (Note 1), 37.5 g (0.62 mol) of sodium chloride, 300 mL of hexane, and 400 mL of dimethyl sulfoxide. The flask is cooled at 0°C in an ice–salt bath (Note 2), and a mixture containing 15.5 g (2.65 mol) of sodium chloride in 1.2 L of aqueous 5.25% sodium hypochlorite solution (Note 3) is added with vigorous stirring over a 15-min period using the dropping funnel. After the addition is complete, stirring is continued for 15 min. At this time the organic phase is separated and the aqueous phase is extracted three times with 75-mL portions of ether. The ethereal extracts are combined with the organic phase and the mixture is washed successively four times with 125-mL portions of water and once with a 125-mL portion of saturated aqueous sodium chloride. The mixture is dried over anhydrous magnesium sulfate and concentrated to a volume of approximately 75 mL at 25°C under aspirator vacuum. The mixture is filtered through a 3-cm × 14-cm column of silica gel (Note 4) and eluted with 200 mL of anhydrous benzene (Note 5) into a 1-L, single-necked, round-bottomed flask. Concentration under reduced pressure at room temperature to a volume of approximately 50 mL yields a yellow solution (Note 6). The flask is equipped with a magnetic stirrer, heating mantle, and reflux condenser protected from the atmosphere by a calcium chloride drying tube and then charged with 600 mL of anhydrous benzene (Note 5) and 7.49 g (0.0634 mol) of *trans*-β-methylstyrene.

The reaction mixture is then heated at reflux for 3.5 hr and allowed to cool to 25°C. The benzene is removed at 25°C on a rotary evaporator to afford a dark-brown oil. This was diluted with 50 mL of ether, filtered through a 3-cm × 14-cm column of silica gel (Note 4), and eluted with an additional 175 mL of ether. Removal of the ether under reduced pressure yields ca. 21 g of an oily orange solid that consists of a mixture of diastereomeric 1-chloro-1,2-diphenyl-3-methylcyclopropanes (Note 7).

The crude mixture is transferred to a 1-L, one-necked flask equipped with a magnetic stirrer and a calcium chloride drying tube. To the flask is added 450 mL of anhydrous tetrahydrofuran (Note 8), and the mixture is cooled to −78°C in a dry ice–acetone bath. The drying tube is removed for a brief period, and 28.5 g (0.25 mol) of potassium *tert*-butoxide (Note 9) is quickly added in one portion using a powder funnel. The reaction is stirred for 1 hr at −78°C, warmed to 0°C, stirred for 3 hr, and then allowed to warm to room temperature and stirred for 12 hr. At the end of this time 60 mL of water is added slowly to the reaction mixture. The reaction mixture is concentrated on a rotary evaporator at 25°C to a volume of ca. 150 mL. The mixture is taken up in 160 mL of ether and washed successively with six 60-mL portions of water and one 60-mL portion of saturated aqueous sodium chloride. The ether layer is dried over anhydrous magnesium sulfate, and the solvent is removed under reduced pressure at room temperature. The resulting dark-brown oil is chromatographed through a 4-cm × 41-cm column of silica gel (Note 10) with eluting with hexane. Removal of the solvent under reduced pressure at 25°C affords 10.5–11.5 g (80–88%) of 1,2-diphenyl-3-methylcyclopropene as a pale yellow oil (Note 11).

2. Notes

1. Commercial benzamidine hydrochloride may be used without further purification.
2. Dimethylsulfoxide solidifies on the walls of the container but quickly dissolves on addition of the sodium hypochlorite solution.
3. Any commercial laundry bleach containing 5.25% by weight sodium hypochlorite is suitable.
4. Silica gel of 60–200-mesh was used (35 g).
5. Reagent-grade benzene was distilled from calcium hydride. The first 10% of the distillate was discarded.
6. Alternatively, to isolate the pure phenylchlorodiazirine, distillation through a 3-cm Vigreux column at 25°C (0.1 mm) affords 21.0–23.2 g (48–53%) of a pale-yellow oil; IR (cm^{-1}): 3067, 2967, 1706, 1567, 1490, 1437, 1332, 1258, 1200, 1081, 1013, 1001, 905, 758, 692. Foaming may occur during distillation as the residual solvent is removed under high vacuum. A water bath is employed to heat the distillation pot, and at no time should the pot temperature be allowed to rise above 35°C. The distillation receiving flask should be immersed in a cold bath at −60°C to avoid loss of phenylchlorodiazirine. Phenylchlorodiazirine is reputedly highly explosive and can be detonated by shock and/or elevated temperature.[2] The authors have encountered one such explosion due to a malfunctioning water bath thermostat that allowed the pot temperature to rise to 80°C. At this point the distillation mixture detonated. *In the pure form, phenylchlorodiazirine is considerately more shock-sensitive than nitroglycerine*.[3] Diluted with cyclohexane or benzene, it is not shock-sensitive.
7. The ^{1}H NMR spectrum shows the intermediate chlorocyclopropane to consist of a mixture of two stereoisomers in a 2 : 3 ratio resulting from the nonregio-specific addition of phenylchlorocarbene to *trans*-β-methylstyrene. Crystallization from hexane produced the major isomer as long white needles, mp 98–99°C, which was identified as (*S*)-1-chloro-(*S,S*)-1,2-diphenyl-(*R*)-3-methylcyclopropane; ^{1}H NMR (CDCl$_3$, 100 MHz) δ: 1.6 (d, 3 H, J = 6.0 Hz), 2.02 (dq, 1 H, J = 7.5 Hz and J = 6.0 Hz), 2.44 (d, 1 H, J = 7.5 Hz), and 6.6–7.2 (m, 10 H); IR (KBr) cm^{-1}: 3012, 2941, 2899, 2857, 1603, 1580, 1493, 1445, 1383, 1081, 1042, 987, 909, 853, 758, 751, 694. Successive crystallizations to remove the major isomer produced the minor component as a colorless oil identified as (S)-1-chloro-(*S,R*)-1,2-diphenyl-(*S*)-3-methylcyclopropane; ^{1}H NMR (CDCl$_3$, 100 MHz) δ: 0.96 (d, 3 H, J = 6.0 Hz), 2.02 (dq, 1 H, J = 7.5 Hz and J = 6.0 Hz), 2.44 (d, 1 H, J = 7.5 Hz), and 7.2–7.6 (*m*, 10 H); IR (neat, cm^{-1}): 3021, 2941, 2924, 1603, 1493, 1449, 1170, 1079, 1044, 1033, 913, 855, 758, 692.
8. Reagent-grade tetrahydrofuran was distilled from lithium aluminum hydride prior to use.
9. Commercial-grade potassium *tert*-butoxide (available from MSA Research Corporation, Evans City, PA 16033) was used without further purification.
10. Silica gel (200 g, 60–200 mesh) was used as the adsorbent. The eluant was monitored by thin-layer

chromatography with collection of only the first eluted component.

11. Distillation of 1,2-diphenyl-3-methylcyclopropene should not be attempted, as much decomposition occurs. The product is characterized by ^{1}H NMR ($CDCl_3$, 100 MHz) δ: 1.36 (d, 3 H, $J = 5.0$ Hz), 2.18 (q, 1 H, $J = 5.0$ Hz), and 7.1–7.8 (m, 10 H); IR (neat) cm^{-1}: 3049, 3012, 2907, 1815, 1603, 1490, 1370, 1348, 1087, 1073, 1030, 990, 755, 738, 685. 1,2-Diphenyl-3-methylcyclopropene decomposes slowly at 25°C.

3. Discussion

The formation of aryl-substituted cyclopropenes by the addition of phenylchlorocarbene to olefins followed by dehydrohalogenation is a general reaction. The reagent phenylchlorodiazirine decomposes readily to produce phenylchlorocarbene in high yield.[4,5,6,7] Phenylchlorocarbene adds to many olefins to give halocyclopropanes, which can easily eliminate hydrogen chloride on treatment with base. The reaction of phenylchlorodiazirine with acetylenes produces cyclopropenyl chlorides, which can readily be converted to the corresponding biscyclopropenyl ethers on treatment with aqueous alcohol.[4,8,9] 1,2-Diphenyl-3-methylcyclopropene has been used to prepare a wide assortment of 1,2-diphenyl-3,3-disubstituted cyclopropenes.[10,11]

References and Notes

1. Chemistry Department, Emory University, Atlanta, GA 30322.
2. Graham, W. H. *J. Am. Chem. Soc.* **1965**, *87*, 4396–4397.
3. DeBoer, C. D. *J. Chem. Soc., Chem. Commun.* **1972**, 377–378.
4. Padwa, A.; Eastman, D. *J. Org. Chem.* **1969**, *34*, 2728–2732.
5. Frey, H. M.; Stevens, I. D. R. *J. Chem. Soc.* **1965**, 1700–1706.
6. Mitch, R. A. *J. Am. Chem. Soc.* **1965**, *87*, 758–761.
7. Moss, R. A. *Tetrahedron Lett.* **1967**, 4905–4909.
8. Breslow, R.; Chang, H. W. *J. Am. Chem. Soc.* **1961**, *83*, 2367–2375.
9. Farnum, D. G.; Burr, M. *J. Am. Chem. Soc.* **1960**, *82*, 2651.
10. Johnson, R. W.; Widlanski, T.; Breslow, R. *Tetrahedron Lett.* **1976**, 4685–4686.
11. Padwa, A.; Blacklock, T. J.; Getman, D.; Hatanaka, N.; Loza, R. *J. Org. Chem.* **1978**, *43*, 1481–1492.

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

1-chloro-1,2-diphenyl-3-methylcyclopropanes

1,2-diphenyl-3,3-disubstituted cyclopropenes

hydrogen chloride (7647-01-0)

Benzene (71-43-2)

ether (60-29-7)

Benzamidine hydrochloride (1670-14-0)

sodium chloride (7647-14-5)

cyclohexane (110-82-7)

sodium hypochlorite (7681-52-9)

magnesium sulfate (7487-88-9)

Tetrahydrofuran (109-99-9)

lithium aluminum hydride (16853-85-3)

hexane (110-54-3)

dimethyl sulfoxide,
dimethylsulfoxide (67-68-5)

calcium hydride (7789-78-8)

phenylchlorocarbene

Chlorophenyldiazirine

CHLOROPHENYL CARBENE

1,2-Diphenyl-3-methylcyclopropene,
Benzene, 1,1'-(3-methyl-1-cyclopropene-1,2-diyl)-bis- (51425-87-7)

Phenylchlorodiazirine

nitroglycerine

chlorocyclopropane

potassium tert-butoxide (865-47-4)

trans-β-methylstyrene (873-66-5)

(S)-1-chloro-(S,S)-1,2-diphenyl-(R)-3-methylcyclopropane

(S)-1-chloro-(S,R)-1,2-diphenyl-(S)-3-methylcyclopropane