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.

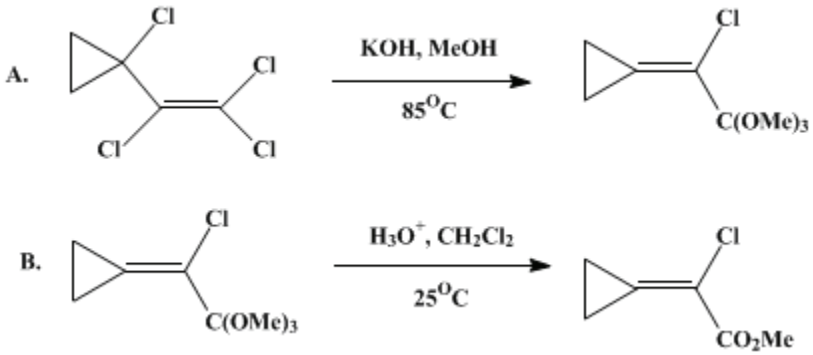
These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

DOI:10.15227/orgsyn.069.0148

Organic Syntheses, Coll. Vol. 8, p.373 (1993); Vol. 69, p.148 (1990).

METHYL 2-CHLORO-2-CYCLOPROPYLIDENACETATE

[Acetic acid, chlorocyclopropylidene-, methyl ester]



Submitted by Thomas Liese, Fereydoun Seyed-Mahdavi, and Armin de Meijere[1].
Checked by James S. Piecara and Bruce E. Smart.

1. Procedure

A. *Trimethyl 2-chloro-2-cyclopropylidenorthoacetate*. A 1-L, two-necked, round-bottomed flask equipped with a mechanical stirrer and a reflux condenser is charged with 40.0 g (0.19 mol) of 1-chloro-1-(trichloroethenyl)cyclopropane (Note 1), 120 g of potassium hydroxide, and 300 mL of methanol (Note 2). The mixture is stirred for 16–18 hr in an oil bath at 85°C. After the solution is cooled to room temperature, it is diluted with 1 L of ice water. The mixture is then transferred to a 3-L separatory funnel and extracted with three 200-mL portions of ether. The combined ether phases are washed with three 150-mL portions of saturated brine, dried over anhydrous magnesium sulfate, and filtered. The solvent is removed from the filtrate by distillation at atmospheric pressure, and the residue is distilled through a short-path column under water-aspirator vacuum to give 14.5–15.4 g (39–41%) of trimethyl 2-chloro-2-cyclopylidenorthoacetate bp 103–105°C (20 mm) (Note 3) and (Note 4).

B. *Methyl 2-chloro-2-cyclopropylidenacetate*. A 250-mL, one-necked, round-bottomed flask is charged with 60 mL of methylene chloride (Note 2), 3.5 g of a strongly acidic ion-exchange resin (Note 5), and 11.0 g (0.057 mol) of trimethyl 2-chloro-2-cyclopropylidenorthoacetate. The mixture is stirred for 12 hr at room temperature. The ion-exchange resin is removed by filtration and washed with three 10-mL portions of methylene chloride. The combined organic solutions are dried over anhydrous magnesium sulfate, filtered, and distilled at atmospheric pressure to remove the solvent. The residue is distilled through a short-path column under reduced pressure to give 6.2–6.7 g (74–80%) of methyl 2-chloro-2-cyclopropylidenacetate, bp 95–97°C (10 mm) (Note 6),(Note 7)(Note 8).

2. Notes

1. 1-Chloro-1-(trichloroethenyl)cyclopropane was prepared from tetrachlorocyclopropene as described in *Org. Synth., Coll. Vol. VIII* **1993**, 124.
2. Methanol and methylene chloride were obtained from E. M. Science (Merck & Company, Inc.) and used without further purification.
3. The checkers obtained the same yields for 0.10-mol scale runs. The submitters report yields of 54–58%, however. The submitters report that the yields of 2-chloro-2-cyclopropylidenacetate are consistently better, when a larger excess of sodium methoxide (prepared by dissolving 20.1 g (0.87 mol) of sodium metal in 300 mL of dry methanol) is used. The reaction is monitored by thin layer chromatography; complete consumption of starting material may require up to 48 hr. The workup procedure was also modified. Instead of extracting with ether, the mixture is extracted with three 100-mL portions of methylene chloride. The combined methylene chloride extracts are washed with three 50-mL portions of saturated brine, dried over anhydrous magnesium sulfate, and filtered. The solution is

concentrated under slightly reduced pressure in a closed system (rotary evaporator) to a volume of 100 mL. In Step B this solution is treated with 10 g of a strongly acidic ion-exchange resin and the rest of the procedure is followed as described.
4. The submitters report bp 107–109°C (20 mm). The spectral properties of 2-chloro-2-cyclopropylidenorthoacetate are as follows: IR (neat) cm^{-1}: 2840 (OCH_3), 1780 (C=C); ^1H NMR ($CDCl_3$) δ: 1.27–1.80 (m, 4 H), 3.23 (s, 9 H).
5. The checkers used analytical-grade AG 50W-X8 resin, which is strongly acidic polystyrene-gel-type resin, supplied by Bio-Rad Laboratories. The submitters used the large-pore, strongly acidic ion-exchange resin Lewatit SPC 118, supplied by Bayer AG.
6. The submitters report obtaining 7.0–7.5 g (84–90%) of product, bp 60–63°C (3.7 mm), and note that 4.7–5.0 g of analytically pure material, mp 33–34°C, can be obtained by crystallization at −20°C from 10–15 mL of pentane and the remaining 2.3–2.5 g of product can be recovered from the mother liquor by chromatography on silica gel (60 g) using a 5 : 1 mixture of pentane/diethyl ether as the eluent.
7. The product obtained by the checkers is pure by NMR analysis and shows the following spectral properties: IR (neat) cm^{-1}: 3080 (cyclopropyl CH), 1720 (C=O); ^1H NMR ($CDCl_3$) δ: 1.42–1.52 (m, 2 H), 1.69–1.78 (m, 2 H), 3.84 (s, 3 H).
8. The submitters report that the product can be obtained in higher yields without isolation of the intermediate orthoester according to the following procedure. To a solution of sodium methoxide, freshly prepared by dissolving 14.0 g (0.61 mol) of sodium metal in 200 mL of dry methanol, at 65°C is added with stirring 30.0 g of 1-chloro-1-(trichloroethenyl)cyclopropane. The stirred mixture is refluxed (oil-bath temperature of 110°C) for 72 hr. After the solution is cooled to room temperature, 200 mL of ice water is added, and the mixture is extracted with three 200-mL portions of ether. The combined ether extracts are washed with three 50-mL portions of saturated brine, dried over anhydrous magnesium sulfate, and filtered. The solvent is removed from the filtrate by distillation at atmospheric pressure. The residue is dissolved in 100 mL of methylene chloride, 10 g of a strongly acidic ion-exchange resin is added (Note 5), and the mixture is stirred at room temperature for 48 hr. The resin is removed by filtration and is washed with three 10-mL portions of methylene chloride. The combined organic solutions are dried over anhydrous magnesium sulfate and filtered, and the solvent is removed from the filtrate by distillation at atmospheric pressure. The residual oil is taken up in 200 mL of pentane and the solution is refrigerated at 5°C. The precipitated crystals are collected by filtration to yield 11–13 g (51–60%) of 2-chloro-2-cyclopropylidenacetate. The checkers obtained a 50% yield of pure product, mp 40–41°C, when this procedure was repeated on about half the scale.

3. Discussion

This procedure is applicable to a number of substituted 1-chloro-1-(trichloroethenyl)cyclopropanes,[2] and in general gives good yields of methyl 2-chloro-2-cyclopropylidenacetates.[3] These are highly reactive Michael acceptors that react rapidly with nucleophiles to give 1'-substituted-2-chloro-2-cyclopropylacetates. The parent 2-chloro-2-cyclopropylidenacetate is a particularly useful building block in organic synthesis since it adds to cyclic dienolates to give complex skeletons in high yields.[4,5] In addition, it is a reactive dienophile[5,6] and can be further modified to 2-arylthio-substituted derivatives as well as to the parent methyl 2-cyclopropylidenacetate in high yields.[7] The corresponding ethyl 2-cyclopropylidenacetate has been prepared in poor yield by a Wittig–Horner–Emmons olefination of cyclopropanone hemiacetal magnesium salt (8%),[8] and more recently in vastly improved yield (87%) by the benzoic-acid-catalyzed Wittig olefination.[9]

This preparation is referenced from:

- Org. Syn. Coll. Vol. 8, 124

References and Notes

1. Institut für Organische Chemie der Universität Hamburg, Martin-Luther-King-Platz 6, D-2000 Hamburg 13, Federal Republic of Germany. Present address: Institut für Organische Chemie der Georg-August-Universität, Tammannstrassse 2, D-3400 Göttingen, Federal Republic of

Germany.
2. Weber, W.; de Meijere, A. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 138; Weber, W.; de Meijere, A. *Chem. Ber.* **1985**, *118*, 2450; Liese, T.; Splettstösser, G.; de Meijere, A. *Tetrahedron Lett.* **1982**, *23*, 3341.
3. Liese, T.; Splettstösser, G.; de Meijere, A. *Angew. Chem. Suppl.* **1982**, *1715*; Liese, T.; Splettstösser, G.; de Meijere, A. *Angew. Chem., Intn. Ed. Engl.* **1982**, *21*, 790; Liese, T.; Teichmann, S.; de Meijere, A. *Synthesis* **1988**, 25.
4. Spitzner, D.; Engler, A.; Liese, T.; Splettstösser, G.; de Meijere, A. *Angew. Chem. Suppl.* **1982**, 1722; Spitzner, D.; Engler, A.; Liese, T.; Splettstösser, G.; de Meijere, A. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 791.
5. Spitzner, D.; Engler, A.; Wagner, P.; de Meijere, A.; Bengtson, G.; Simon, A.; Peters, K.; Peters E.-M. *Tetrahedron* **1987**, *43*, 3213; de Meijere, A., Teichmann, S.; Yu, D.; Kopf, J.; Oly, M.; von Thiemen, N. *Tetrahedron* **1989**, *45*, 2957.
6. Primke, H.; de Meijere, A. unpublished results; cf. de Meijere, A. *Chem. Ber.* **1987**, *23*, 865; de Meijere, A., Wessijohann, L. *Synlett.* **1990**, 20.
7. Seyed-Mahdavi, F.; Teichmann, S.; de Meijere, A. *Tetrahedron Lett.* **1986**, *27*, 6185.
8. Salaün, J.; Bennani, F.; Compain, J.-C.; Fadel, A.; Ollivier, J. *J. Org. Chem.* **1980**, *45*, 4129.
9. Spitzner, D.; Swoboda, H. *Tetrahedron Lett.* **1986**, *27*, 1281.

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

silica gel

brine

trimethyl 2-chloro-2-cyclopylidenorthoacetate

cyclopropanone hemiacetal magnesium salt

methanol (67-56-1)

ether,
diethyl ether (60-29-7)

sodium methoxide (124-41-4)

potassium hydroxide (1310-58-3)

sodium (13966-32-0)

Pentane (109-66-0)

methylene chloride (75-09-2)

magnesium sulfate (7487-88-9)

tetrachlorocyclopropene

1-CHLORO-1-(TRICHLOROETHENYL)CYCLOPROPANE (82979-27-9)

Methyl 2-chloro-2-cyclopropylidenacetate,
Acetic acid, chlorocyclopropylidene-, methyl ester (82979-45-1)

Trimethyl 2-chloro-2-cyclopropylidenorthoacetate (82979-34-8)

methyl 2-cyclopropylidenacetate

ethyl 2-cyclopropylidenacetate