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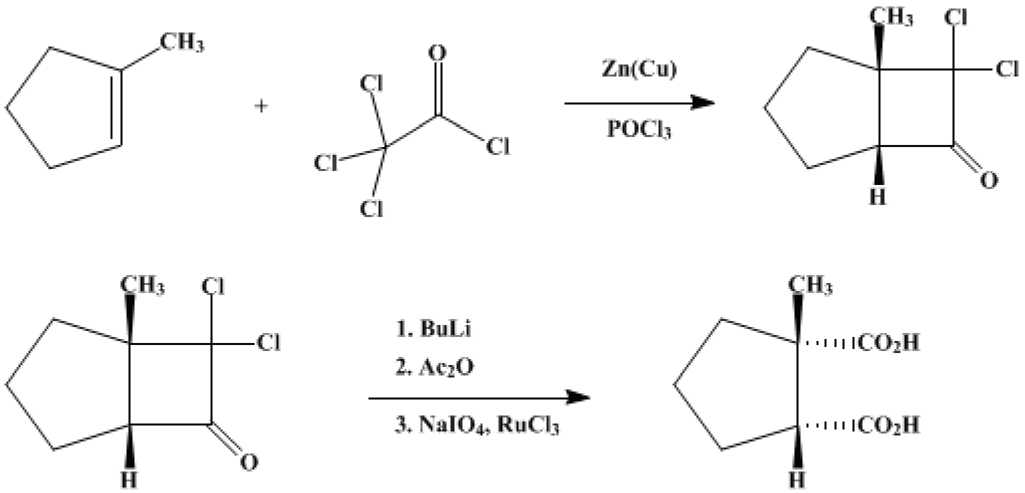
VICINAL DICARBOXYLATION OF AN ALKENE: *cis*-1-METHYLCYCLOPENTANE-1,2-DICARBOXYLIC ACID

[1,2-Cyclopentanedicarboxylic acid, 1-methyl-, *cis*-(±)-]



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1. Procedure

A. *7,7-Dichloro-1-methylbicyclo[3.2.0]heptan-6-one*. A 500-mL, two-necked, round-bottomed flask is equipped with a Teflon-covered magnetic stirring bar, a 250-mL pressure-equalizing addition funnel topped with a gas inlet, and a condenser connected to a Nujol-filled bubbler (Note 1). The system is flushed with nitrogen (Note 2). The flask is then charged with 10.0 g (ca. 150 mmol) of zinc–copper couple (Note 3), 200 mL of anhydrous ether (Note 4), and 10.5 mL (8.2 g, 100 mmol) of 1-methyl-1-cyclopentene (Note 5), and the addition funnel is filled with a solution of 13.4 mL (21.8 g, 120 mmol) of trichloroacetyl chloride (Note 5) and 11.2 mL (18.4 g, 120 mmol) of phosphorus oxychloride (Note 6) in 100 mL of anhydrous ether. Magnetic stirring is begun and the solution is added dropwise over 1 hr to the reaction flask at room temperature. After being stirred for an additional 14 hr, the reaction mixture is filtered under water pump pressure through 30 g of filter aid, which is then washed with 120 mL of ether. The filtrate is concentrated to ca. 100–120 mL, treated with 400 mL of hexane, and then briefly stirred to precipitate the zinc chloride. The supernatant solution is transferred to a separatory funnel and the viscous residue is washed with two 75-mL portions of 3 : 1 hexane–ether. The combined solution is washed successively with 200 mL of cold water, 200 mL of saturated aqueous sodium bicarbonate solution, and 2 × 50 mL of saturated aqueous sodium chloride solution, dried over anhydrous sodium sulfate, and concentrated to dryness by rotary evaporation at 25°C to give 17.0–17.8 g of a brown oil. Vacuum distillation of this material without fractionation provides 14.9–16.0 g (77–83%) of 7,7-dichloro-1-methylbicyclo[3.2.0]heptan-6-one as a clear, light-yellow oil, bp 38°C (0.2 mm), n_D^{20} 1.4970 (Note 7).

B. *cis-1-Methylcyclopentane-1,2-dicarboxylic acid*. A 1-L, one-necked, round-bottomed flask (Note 1) equipped with a Teflon-covered magnetic stirring bar is flushed with nitrogen and then charged with 300 mL of dry tetrahydrofuran (Note 4) and 14.5 g (75 mmol) of 7,7-dichloro-1-methylbicyclo[3.2.0]heptan-6-one. The flask is capped with a septum and connected to a Nujol bubbler and to a nitrogen line by means of syringe needles (Note 2). To the stirred solution cooled in a dry ice–acetone bath is added by syringe over 5 min 33.2 mL (83 mmol) of a 2.50 *M* solution of butyllithium in hexane (Note 8). After being stirred for 15 min with continued cooling, the reaction mixture is treated with 14.2 mL (150 mmol) of acetic anhydride all at once (Note 9). The cooling bath is removed and the reaction mixture is allowed to warm to room temperature and then stirred for an additional 1 hr. Most of the solvent and excess acetic anhydride are directly removed with a rotary evaporator at 25°C under water pump pressure (Note 10). The resulting solid residue is further dried for 15–30 min at 4 mm and then dissolved in a mixture of 100 mL of acetonitrile, 100 mL of carbon tetrachloride, and 150 mL of distilled water. The mixture is cooled in an ice bath and, with efficient stirring, treated with 40.1 g (187 mmol) of sodium periodate and 346 mg (1.5 mmol) of ruthenium(III) chloride hydrate (Note 11). After 15 min, the cooling bath is removed (Note 12) and stirring is continued for 5 hr, whereupon the thick mixture is treated with 200 mL of 10% aqueous sodium hydroxide solution and then extracted in a separatory funnel with 500 mL of 1 : 1 ether–hexane (Note 13). The phases are separated and to the aqueous phase is added 900 mL of 2 : 1 ether–ethyl acetate followed by a 2 *N* aqueous hydrochloric acid solution until a pH of 2–3 is obtained (Note 14). After being vigorously agitated, the phases are separated and the organic phase is washed successively with solutions of 3% aqueous sodium thiosulfate (Note 15) and saturated aqueous sodium chloride. All aqueous phases are mixed and, at pH 2 to 3, extracted with 1 L of 3 : 2 ether–ethyl acetate, which is then washed as before. The ether–ethyl acetate solutions are combined and dried over anhydrous sodium sulfate and the solvents are removed by rotary evaporation to leave a light-yellow solid, mp 123–126°C. Trituration of this material with 1 : 1 ethyl acetate–petroleum ether (Note 16) gives 7.9–8.0 g (61–62%) of *cis*-1-methylcyclopentane-1,2-dicarboxylic acid as a white solid, mp 123–124.5°C (Notes 16-19).

2. Notes

1. All glassware was dried overnight in an oven at 115°C and allowed to cool in a desiccator.
2. A slight positive pressure of nitrogen is maintained throughout the reaction.
3. A literature procedure[2] for the preparation of the zinc–copper couple was followed except for the use of slightly more (28%) than the indicated amount of copper sulfate. The checkers found that the kind of zinc used is critical. Zinc dust, 325-mesh, from Aldrich Chemical Company, Inc. (catalog no. 20,998-8) gave 7,7-dichloro-1-methylbicyclo[3.2.0]heptan-6-one in 80–89% yield. Zinc metal (dust) from Fisher Scientific Company (Lot 8744394) gave the dichloro ketone in yields of 37–61% (five trials). The Fisher zinc was of unknown mesh, but was much more finely-divided than the Aldrich Chemical Company, Inc. zinc.
4. Ether and tetrahydrofuran were distilled from the sodium ketyl of benzophenone.
5. 1-Methyl-1-cyclopentene (96% pure) and trichloroacetyl chloride (99% pure) were purchased from the Aldrich Chemical Company, Inc. The trichloroacetyl chloride was distilled prior to use.
6. Phosphorus oxychloride (99% pure) was obtained from the Aldrich Chemical Company, Inc. and distilled from potassium carbonate prior to use.
7. This material was found to darken with time. Its spectral properties are the following: IR (film) cm^{-1}: 1805; ^1H NMR ($CDCl_3$, 80 MHz) δ: 1.57 (s, 3 H), 1.5–2.5 (m, 6 H), 3.50 (m, 1 H). These values are in accord with those reported in the literature.[3]
8. The solution of butyllithium in hexane was purchased from the Aldrich Chemical Company, Inc. and standardized with menthol and phenanthroline[4] before use.
9. Acetic anhydride was distilled prior to use.
10. A trap is used between the flask and the rotary evaporator as a precaution against possible bumping during the evaporation.
11. Sodium periodate was obtained from the Aldrich Chemical Company, Inc. and ruthenium(III) chloride hydrate (5–10% water) was purchased from Fluka. The more expensive periodic acid can replace sodium periodate; however, ruthenium(III) chloride appears to be somewhat more efficient than ruthenium(IV) oxide.
12. Should a noticeably exothermic reaction ensue, the cooling bath is replaced for a few minutes.
13. At this point the checkers filtered the mixture through a pad of 30 g of Celite to remove the green precipitate. This filtration reduces the problem of emulsions and clogging of the separatory funnel during subsequent extractions.
14. Iodine formation becomes substantial at lower pH.
15. Normally 50–100 mL of this solution is required.
16. This is done first with 20 mL and then with 8 mL. Product loss is minimized by storing the trituration flask overnight at −25°C prior to removal of the supernatant solution. On evaporation, the supernatant solution affords an oil containing the diacid and a small amount of the corresponding anhydride. Treatment of this oil with 10% aqueous NaOH at room temperature overnight and then

processing the solution as before yields an additional 0.4 g (3%) of the diacid, mp 126–127°C.
17. The submitters report a crude yield of 11.5 g (89%) and a recrystallized yield of 9.0 g (70%), mp 128–129°C.
18. Melting points of 123–129°C have been reported for this compound.[5]; [6]; [7]; [8]; [9] Its spectral properties are the following: IR (Nujol) cm^{-1}: 2720, 2630, 1690; ^{1}H NMR ($CDCl_3$, 80 MHz) δ: 1.44 (s, 3 H), 1.5–2.5 (m, 6 H), 2.72 (pseudo-t, 1 H, $J = 8$), 10.8 (br s, 2 H).
19. Gas-chromatographic analysis (10%, Carbowax 20 M on 80–100 mesh Chromosorb W, 2.5 × 2 mm, column temperature 180°C, injection temperature 230°C, flow rate 10 mL/min, retention time 10 min) of the corresponding dimethyl ester, formed with ethereal diazomethane, indicated a purity of greater than 99%.

3. Discussion

This procedure serves to illustrate a relatively inexpensive, two-pot, stereoselective method for effecting vicinal dicarboxylation of alkenes that is more generally applicable and higher-yielding than the palladium-catalyzed carbonylation reaction and other more circuitous procedures.[10] Part A of this procedure is a slight modification of the dichloroketene–olefin cycloaddition method previously described by Krepski and Hassner.[2] Part B makes use of Sharpless and co-workers' ruthenium(III) chloride-catalyzed oxidation process[11] for the cleavage of the β-chloro enol acetate, which is formed on trapping the β-chloro enolate intermediate with acetic anhydride. A slightly different, nonoptimized version of this procedure has been used[10,12] for the vicinal dicarboxylation of 1-decene, *cis*- and *trans*-2-butene, 2-methyl-2-butene, 2,3-dimethyl-2-butene, 1-methyl-1-cyclohexene, 1,6-dimethyl-1-cyclohexene, and 5α-cholest-2-ene with overall yields of 52–83%.

cis-1-Methylcyclopentane-1,2-dicarboxylic acid has been previously prepared by a variety of methods: by oxidative cleavage (HNO_3) of cyclobutanone[5] and cyclopentanone[6] precursors, through saponification and oxidation ($KMnO_4$) of a γ-butyrolactone intermediate,[7] and by anhydride formation and then hydrolysis starting from mixtures of the *cis*- and *trans*-diacids (obtained in about five steps).[8,9] Compared with these methods, the cycloaddition–cleavage procedure is much more efficient and practical. It requires only readily available reagents and easily affords, without any chromatographic separations, a product of high purity.

References and Notes

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Appendix
Chemical Abstracts Nomenclature (Collective Index Number);

(Registry Number)

petroleum ether

sodium ketyl of benzophenone

copper couple

1,2-Cyclopentanedicarboxylic acid, 1-methyl-, cis-(±)-

potassium carbonate (584-08-7)

hydrochloric acid (7647-01-0)

ethyl acetate (141-78-6)

ether (60-29-7)

acetic anhydride (108-24-7)

acetonitrile (75-05-8)

sodium hydroxide,
NaOH (1310-73-2)

sodium bicarbonate (144-55-8)

sodium chloride (7647-14-5)

sodium sulfate (7757-82-6)

carbon tetrachloride (56-23-5)

sodium thiosulfate (7772-98-7)

nitrogen (7727-37-9)

copper sulfate (7758-98-7)

iodine (7553-56-2)

Phosphorus Oxychloride (21295-50-1)

zinc,
Zinc metal (dust) (7440-66-6)

palladium (7440-05-3)

zinc chloride (7646-85-7)

Cyclopentanone (120-92-3)

γ-butyrolactone (96-48-0)

menthol (15356-60-2)

2,3-dimethyl-2-butene (563-79-1)

2-methyl-2-butene (513-35-9)

butyllithium (109-72-8)

Tetrahydrofuran (109-99-9)

hexane (110-54-3)

periodic acid

1-methyl-1-cyclohexene

ruthenium(III) chloride (14898-67-0)

phenanthroline

Cyclobutanone (1191-95-3)

trichloroacetyl chloride (76-02-8)

Sodium periodate (7790-28-5)

cis- and trans-2-butene

1-decene (872-05-9)

1-methyl-1-cyclopentene

7,7-Dichloro-1-methylbicyclo[3.2.0]heptan-6-one (51284-43-6)

ruthenium(III) chloride hydrate (13815-94-6)

ruthenium(IV) oxide

1,6-dimethyl-1-cyclohexene

5α-cholest-2-ene

cis-1-Methylcyclopentane-1,2-dicarboxylic acid (70433-31-7)