



A Publication
of Reliable Methods
for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

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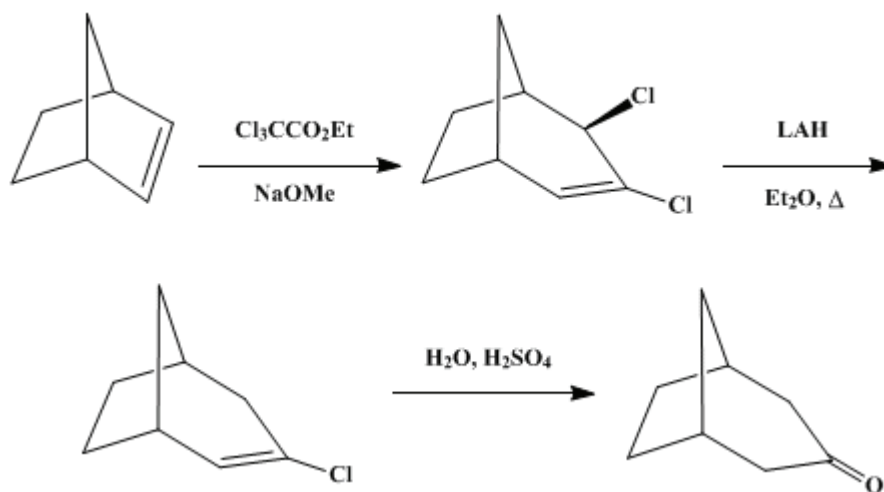
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

Organic Syntheses, Coll. Vol. 6, p.142 (1988); Vol. 51, p.60 (1971).

BICYCLO[3.2.1]OCTAN-3-ONE

[Bicyclo[3.2.1]octan-3-one]



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1. Procedure

A. *exo-3,4-Dichlorobicyclo[3.2.1]oct-2-ene*. A 1-l., four-necked, round bottomed flask is fitted with an efficient stirrer, a thermometer, a reflux condenser protected by a calcium chloride tube, and a 500-ml., stoppered, pressure-equalizing addition funnel. After the addition of a solution of 52.5 g. (0.558 mole) of *norbornene* (Note 1) in 400 ml. of petroleum ether (Note 2), b.p. 45–60° to the flask, 112 g. (2.06 moles) of *sodium methoxide* (Note 3) is added, and stirring is begun. The flask is immersed in an ice-salt mixture (Note 4) before 349 g. (1.82 moles) of *ethyl trichloroacetate* (Note 5) is placed in the addition funnel and allowed to drip slowly into the stirred mixture at a rate such that the temperature does not rise above 0° (Note 6). The addition requires about 4 hours, and the originally white reaction mixture becomes increasingly yellow in color. The mixture is stirred at a temperature below 0° for 4 hours (Note 6) before the temperature is allowed to rise gradually to room temperature overnight. The reaction mixture is poured onto 500 g. of crushed ice in 300 ml. of water. After the ice has melted, the organic layer is separated, and the aqueous layer is shaken with four 200-ml. portions of *diethyl ether*. The aqueous layer is neutralized with 10% *hydrochloric acid* and shaken again with two 200-ml. portions of *ether*. The original organic layer and the *ether* extractions are combined, washed with 300 ml. of a saturated solution of *sodium chloride*, dried for 6 hours over 20 g. of anhydrous *magnesium sulfate*, filtered, and concentrated to about 200 ml. by distillation. The resulting product is distilled through a 20-cm. Vigreux column, giving 72.5–87.0 g. (74–88%) of *exo-3,4-dichlorobicyclo[3.2.1]oct-2-ene* as a colorless liquid, b.p. 72–73° (0.9 mm.), n_D^{25} 1.5333 (Note 7) and (Note 8).

B. *3-Chlorobicyclo[3.2.1]oct-2-ene*. A 2-l., three-necked, round-bottomed flask equipped with a stirrer, a reflux condenser protected by a calcium chloride tube, and a 500-ml., stoppered, pressure-equalizing addition funnel is charged with 350 ml. of dry *ether* and 15 g. (0.40 mole) of powdered *lithium aluminum hydride* (Note 9). The flask is placed in a mixture of ice and water, and 1050 ml. of dry *tetrahydrofuran* (Note 10) is added. Stirring is begun, and a solution of 39.5 g. (0.224 mole) of *exo-3,4-dichlorobicyclo[3.2.1]oct-2-ene* in 50 ml. of dry *tetrahydrofuran* (Note 10) is added dropwise from the addition funnel over a 30-minute period. After the addition is complete, the reaction mixture is heated under gentle reflux for 18 hours. The mixture is cooled to 0°, and the remaining *lithium aluminum hydride* is decomposed by the careful addition of wet *ether*, followed by the cautious dropwise addition of 10 ml. of water. The resulting mixture is poured onto 500 g. of crushed ice in 200

ml. of water. After the ice has melted, the organic layer is separated, and the aqueous layer is acidified to a pH of 5–6 with 10% hydrochloric acid, dissolving the lithium and aluminum salts present (Note 11). The aqueous solution is shaken five times with 200-ml. portions of ether. The organic layers are combined, washed with 200 ml. of a saturated solution of sodium chloride, and dried overnight over 20 g. of anhydrous magnesium sulfate. The ether and tetrahydrofuran are removed by distillation at atmospheric pressure, and the product is distilled through a 20-cm. Vigreux column, yielding 23.5–23.9 g. (74–75%) of 3-chlorobicyclo[3.2.1]oct-2-ene as a colorless oil, b.p. 76–77° (21 mm.), n_D^{20} 1.5072 (Note 12).

C. *Bicyclo[3.2.1]octan-3-one*. A magnetic stirring bar is placed in a 300-ml., round-bottomed flask and 100 ml. of concentrated sulfuric acid (Note 13) is added. Stirring is begun, the flask is cooled in an ice bath, and 9.0 g. (0.63 mole) of 3-chlorobicyclo[3.2.1]oct-2-ene is added in one portion. The mixture is stirred, allowed to warm slowly over 4 hours to room temperature, then stirred overnight. The resulting solution is poured onto 200 g. of ice with stirring. After the ice has melted, the mixture is shaken with three 100-ml. portions of ether. The ether layers are combined, washed once with 50 ml. of water, and dried over 10 g. of magnesium sulfate. The ether is removed by careful distillation, and the crude product is sublimed at a bath temperature of 70° (15 mm.) directly onto a cold finger inserted into the flask. The crude product is twice sublimed, yielding 5.9–6.3 g. (75–81%) of bicyclo[3.2.1]octan-3-one, m.p. 137°, 98% pure by analysis (Note 14), (Note 15), and (Note 16).

2. Notes

1. Norbornene can be prepared by the Diels-Alder reaction of ethylene with dicyclopentadiene, as described in *Org. Synth., Coll. Vol. 4*, 738 (1963). It can be purchased from Matheson, Coleman and Bell or the Aldrich Chemical Company, Inc.
2. The petroleum ether used must be olefin-free.
3. The submitters used sodium methoxide available from Schuchardt, Ainmillerstrasse 25, 8-Munich 13, Germany. The checkers used product available from Matheson, Coleman and Bell.
4. An amount sufficient to fill a 5-l. container is recommended.
5. It is used as purchased from either Schuchardt or Eastman Organic Chemicals. It appears that when equimolar amounts of carbene precursor and olefin are used, the adduct is obtained in only 25% yield.⁴
6. Efficient stirring and maintenance of a low temperature are required if high yields are to be obtained.
7. For the final distillation the pressure is regulated with a manostat.
8. The IR spectrum (neat) shows absorption at 1645, 1450, 1305, 1223, 1052, 974, 959, 866, 796, and 750 cm^{-1} . The ^1H NMR spectrum (CCl_4) shows absorption at δ 4.1 (d, $J \sim 3$ Hz.), and 6.08 (d, $J \sim 4$ Hz) attributable to the vinyl and allyl protons, respectively.
9. This was purchased from Metal Hydrides, Inc., and is also obtainable from Schuchardt.
10. The checkers used reagent grade tetrahydrofuran (available from Fisher Scientific Company) from a freshly opened bottle. The submitters used tetrahydrofuran purified as described in the literature.⁵ [See *Org. Synth., Coll. Vol. 5*, 976 (1973) for a warning regarding the purification of tetrahydrofuran.]
11. A small amount of insoluble material may remain at this point. If it interferes with the extraction procedure it may be removed by filtration.
12. The IR spectrum (neat) shows absorption at 1635, 1440, 1038, 952, 841, 833, and 685 cm^{-1} . The ^1H NMR spectrum (CCl_4) shows three major peaks between δ 2.0–2.8 and a doublet at 5.91 ($J \sim$ Hz., 1H, CH)
13. Sulfuric acid of specific gravity 1.84 is used.
14. The IR spectrum (Nujol) has an intense band at 1710 cm^{-1} . The ^1H NMR spectrum (CDCl_3) has a broad peak at δ 1.7 (6H), a sharp peak at 2.35 (4H) and a broad peak at 2.55 (2H).
15. The GC data were obtained using 3 m. \times 7 mm. column packed with nonacid-washed Chromosorb 45/60 W containing 15% 200M Apiezon silicone oil as the immobile phase.
16. The oxime has m.p. 96°. The ketone can be further purified *via* the semicarbazone derivative, which can be purified by crystallization and subsequently hydrolyzed by dilute hydrochloric acid.

3. Discussion

Studies by the submitters have indicated that the procedure reported here is the preferred method for

the preparation of bicyclo[3.2.1]octan-3-one. It employs readily available, inexpensive reagents, and the overall yield is good. In addition, the method can be used for the synthesis of the relatively inaccessible, higher homologues of bicyclo[2.2.2]oct-2-ene, as well as for derivatives of norbornene. Bicyclo[3.2.2]nonan-3-one and 1-methylbicyclo[3.2.1]octan-3-one have been prepared by a similar route⁶ in 60% and 47% yields, respectively (based on adduct). However, the preferred procedure for the formation of the dichlorocarbene adduct of bicyclo[2.2.2]oct-2-ene is that of Seyferth, using phenyltrichloromethylmercury. Even in this case the overall yield is moderate (37%).

The present procedure is a refinement of existing methods,^{6,7,8,9} an adaption of the method of Parham and Schweizer¹⁰ that furnishes the carbene adduct in higher yield than other methods. The submitters' studies indicate that the procedure of Doering,¹¹ involving the interaction of chloroform with potassium *tert*-butoxide, is unsatisfactory since traces of *tert*-butyl alcohol present react with the rearranged adduct during the reduction step. In addition, the yields of adduct are poor (4–15%).⁴ The method of Wagner,¹² utilizing the pyrolysis of sodium trichloroacetate, is easy to perform, but the yields of initial adduct are poor (13%). That of Seyferth,¹³ involving the pyrolysis of phenyltrichloromethylmercury, gives the adduct in 45% yield. However, the higher cost and additional steps entailed in the preparation of the reagent, together with the hazards associated with mercury, detract from its use.

Other preparations leading to bicyclo[3.2.1]octan-3-one include the oxidation of the mixture of alcohols obtained by the action of nitrous acid on 2-aminomethylnorbornane,¹⁴ the chromic acid oxidation of bicyclo[3.2.1]octane,¹⁵ and the oxidative hydroboration of bicyclo[3.2.1]oct-2-ene.¹⁶ These reactions lack preparative utility, and all have a common disadvantage of being accompanied by isomer formation.

References and Notes

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Appendix

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

petroleum ether

sulfuric acid (7664-93-9)

hydrochloric acid (7647-01-0)

ether,
diethyl ether (60-29-7)

chloroform (67-66-3)

sodium chloride (7647-14-5)

nitrous acid (7782-77-6)

mercury (7439-97-6)

sodium methoxide (124-41-4)

chromic acid (7738-94-5)

ethylene (9002-88-4)

carbene (2465-56-7)

magnesium sulfate (7487-88-9)

Tetrahydrofuran (109-99-9)

lithium aluminum hydride (16853-85-3)

dicyclopentadiene (77-73-6)

tert-butyl alcohol (75-65-0)

ethyl trichloroacetate (515-84-4)

Norbornene

dichlorocarbene

sodium trichloroacetate (650-51-1)

phenyltrichloromethylmercury (3294-57-3)

Bicyclo[3.2.1]octan-3-one (14252-05-2)

3-Chlorobicyclo[3.2.1]oct-2-ene (35242-17-2)

bicyclo[2.2.2]oct-2-ene

1-methylbicyclo[3.2.1]octan-3-one

2-aminomethylnorbornane

bicyclo[3.2.1]octane (6221-55-2)

bicyclo[3.2.1]oct-2-ene

potassium tert-butoxide (865-47-4)

exo-3,4-dichlorobicyclo[3.2.1]oct-2-ene (2394-47-0)

Bicyclo[3.2.2]nonan-3-one