



A Publication
of Reliable Methods
for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

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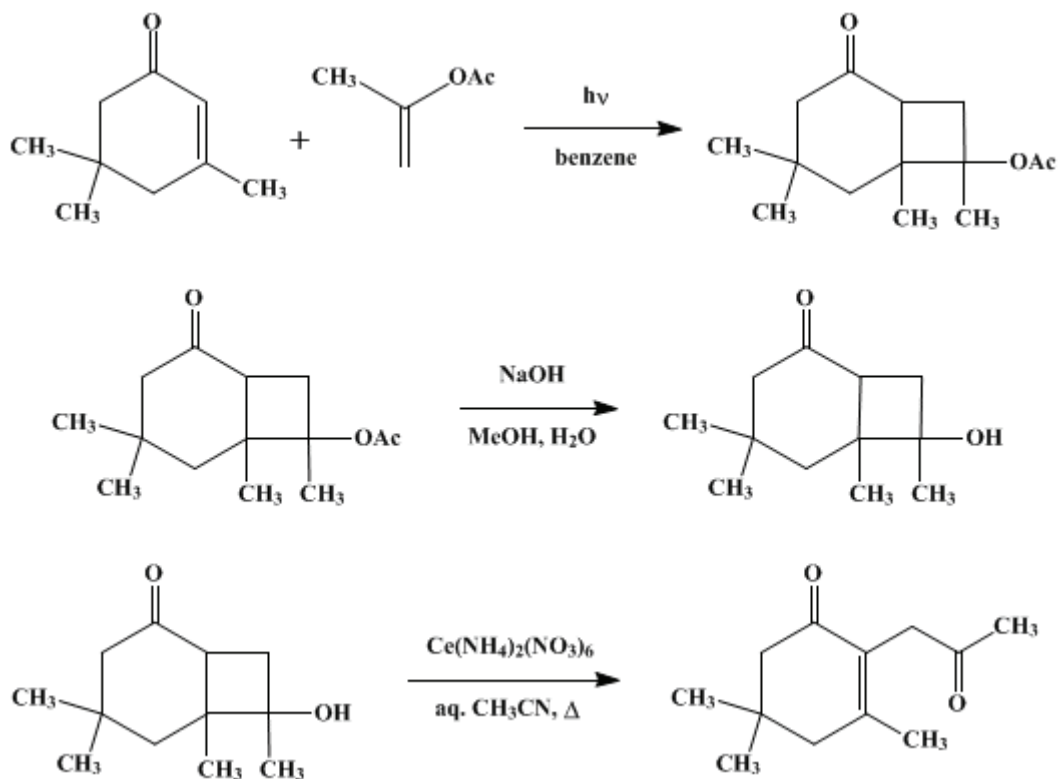
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

Organic Syntheses, Coll. Vol. 6, p.1024 (1988); Vol. 57, p.113 (1977).

3,5,5-TRIMETHYL-2-(2-OXOPROPYL)-2-CYCLOHEXEN-1-ONE

[2-Cyclohexen-1-one, 3,5,5-trimethyl-2-(2-oxopropyl)-]



Submitted by Z. Valenta¹ and H. J. Liu².

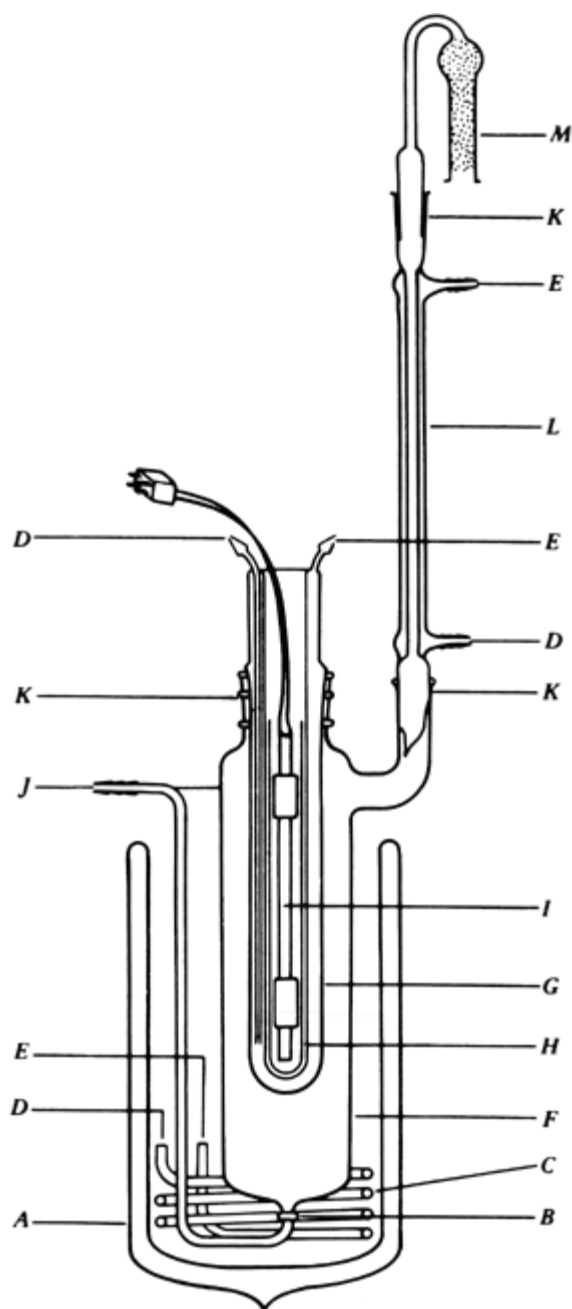
Checked by T. H. O'Neill, W. Thompson, D. H. Hawke, and R. E. Ireland.

1. Procedure

Caution! 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. *7-Acetoxy-4,4,6,7-tetramethylbicyclo[4.2.0]octan-2-one*. The apparatus used for the photocycloaddition reaction is shown in Figure 1. In the reaction vessel is placed a solution of 34.5 g. (0.250 mole) of 3,5,5-trimethyl-2-cyclohexen-1-one (isophorone) (Note 1) and 500 g. (5.00 moles) (Note 2) of 1-propen-2-yl acetate (Note 3) in 625 ml. of benzene. A constant and moderate flow of argon (Note 4) is maintained, agitating the solution throughout the reaction period. The trap is filled with 2-propanol and dry ice (Note 5). The solution is irradiated with a 450-watt, Hanovia high-pressure, quartz, mercury vapor lamp, using a Pyrex filter, for 96 hours (Note 6). Concentration of the resulting solution under reduced pressure (water aspirator) gives 65–80 g. of crude *7-acetoxy-4,4,6,7-tetramethylbicyclo[4.2.0]octan-2-one* (Note 7).

Figure 1. A, Dewar flask; B, sintered-glass filter; C, metal cooling coil; D, water inlet; E, water outlet; F, reaction vessel; G, quartz immersion well; H, Pyrex filter; I, lamp; J, nitrogen gas inlet; K, ground glass joint; L, condenser; M, calcium chloride drying tube.



B. *7-Hydroxy-4,4,6,7-tetramethylbicyclo[4.2.0]octan-2-one*. The preceding crude photo-adduct is dissolved in 250 ml. of **methanol** and transferred to a 1-l., three-necked, round-bottomed flask fitted with overhead stirrer with Teflon blade, addition funnel, and argon inlet. The solution is cooled with an ice bath, and 500 ml. of 4 M aqueous **sodium hydroxide** is added, with stirring, over a period of 20 minutes. Upon completion of the addition, the ice bath is removed, and stirring is continued for 16 hours. The brown solution is extracted with four 500-ml. portions of **chloroform**. The organic extract is washed with saturated **sodium chloride** solution, dried over **magnesium sulfate**, filtered, and concentrated under reduced pressure. Distillation of the residue through a 6-cm. Vigreux column affords, after a small forerun, 23.0–27.9 g. (47–57%) of *7-hydroxy-4,4,6,7-tetramethylbicyclo[4.2.0]octan-2-one* (Note 8), collected at 92–101° (0.2 mm.).

C. *3,5,5-Trimethyl-2-(2-oxopropyl)-2-cyclohexen-1-one*. A 2-l., three-necked, round-bottomed flask, fitted with an overhead stirrer with Teflon blade, a Fries condenser, and a stopper, is charged with a solution of 9.8 g. (0.050 mole) of *7-hydroxy-4,4,6,7-tetramethylbicyclo[4.2.0]octan-2-one* in 600 ml. of

50% (by volume) aqueous **acetonitrile**, and 82 g. (0.15 mole) (**Note 9**) of **ceric ammonium nitrate** (**Note 10**) is added in one portion with stirring. Immediately after completion of the addition, the flask is immersed in an oil bath preheated to 170°. Refluxing occurs in about 10 minutes and is continued for 5 minutes. During this period the color of the solution changes from light brown to pale yellow. At the end of this time the reaction mixture is immediately poured onto crushed ice and extracted with four 600-ml. portions of **chloroform**. The combined extracts are washed with saturated **sodium hydrogen carbonate** and saturated **sodium chloride**, dried over **magnesium sulfate**, and filtered. The solvent is removed under reduced pressure, and the residue distilled, using a short-path distillation apparatus. All material boiling at 70–100° (0.25 mm.) is collected. Fractionation of the yellow oil through a 6-cm. Vigreux column gives 4.68–4.71 g. (48–50%) of **3,5,5-trimethyl-2-(2-oxopropyl)-2-cyclohexene-1-one**, b.p. 81–85° (0.4 mm.) (**Note 11**).

2. Notes

1. **Isophorone** obtained from M C and B Manufacturing Chemists was freshly distilled, b.p. 73° (4.5 mm.).
2. To minimize the formation of cyclohexenone dimer and achieve a cleaner photo-adduct, it is essential to use a large excess of olefin.³
3. **1-Propen-2-yl acetate** was supplied by Aldrich Chemical Company, Inc.
4. Submitters used **nitrogen** purified by passing it through a set of gas wash bottles containing Fieser's solution,⁴ concentrated **sulfuric acid**, **sodium hydroxide**, and **calcium chloride**.
5. The submitters filled the Dewar flask with ice and water. After 2 hours the ice had melted and water was left in the flask for cooling.
6. The progress of the reaction was monitored by injecting, after each 24-hour period, an aliquot into a GC and checking the peak corresponding to **isophorone**. Alternatively, TLC (E. Merck 0.25-mm. silica gel plates developed with **ethyl acetate**) can be used.
7. This crude product is contaminated mainly by polymeric compounds. An attempted distillation of this material was unsuccessful; partial decomposition occurred at 110–125° (0.3 mm.). If it is desirable, purification can be achieved by extensive silica gel column chromatography with 5% **ether** in **benzene**.
8. The product is a mixture of at least two diastereomers as indicated by its ¹H NMR spectrum (CCl₄), showing eight singlets at δ 0.9–1.22, for a total of twelve methyl protons. Its IR spectrum (neat) exhibits absorption bands at 3440 and 1695 cm.⁻¹ A molecular ion peak at 196.1447 (calcd. for C₁₂H₂₀O₂:196.1463) is displayed in its mass spectrum.
9. Use of less of the reagent resulted in partial recovery of the starting material.
10. **Ceric ammonium nitrate** was supplied by Fisher Scientific Company.
11. IR (neat) cm.⁻¹: 1720, 1670, 1645; ¹H NMR (CDCl₃), δ : 1.03, 1.87, 2.13, 2.20, 2.25, 3.43 (all singlets); mass spectrum *m/e* 194.1299 (M⁺).

3. Discussion

Recently, the application of photocycloaddition reactions to organic synthesis has been gaining importance.^{5,6} The procedure described is illustrative of a general method,³ based on a photocycloaddition reaction, for the introduction of an activated alkyl group specifically to the α -carbon atom of an α,β -unsaturated cyclohexenone. Especially significant is the fact that the method is also applicable to α,β -unsaturated cyclohexenones which do not possess enolizable γ -hydrogen atoms and to which normal alkylation reactions⁷ cannot be applied. A closely related procedure involving the photocycloaddition of **vinyl acetate** to 2-cyclohexenones (in which enolization toward the 6-position is forbidden) followed by bromination and fragmentation of the adduct has been reported.^{3,8} It has also been observed⁹ that photoadducts of cycloalkenones and **vinylene carbonate** undergo fragmentation upon alkali treatment, giving 2-(2-oxoethyl)-2-cycloalken-1-ones.

References and Notes

1. Department of Chemistry, University of New Brunswick, Fredericton, N.B., Canada E3B 6E2.
2. Department of Chemistry, University of Alberta, Edmonton, Alberta, Canada T6G 2G2.

3. N. R. Hunter, G. A. MacAlpine, H. J. Liu, and Z. Valenta, *Can. J. Chem.*, **48**, 1436 (1970).
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 5. References cited in Ref. ³.
 6. For reviews, P. E. Eaton, *Acc. Chem. Res.*, **1**, 50 (1968); P. de Mayo, *Acc. Chem. Res.*, **4**, 41 (1971); P. G. Bauslaugh, *Synthesis*, 287 (1970).
 7. H. O. House, "Modern Synthetic Reactions," 2nd ed, W. A. Benjamin, Menlo Park, Calif., Chap. 9.
 8. H.-J. Liu, Z. Valenta, J. S. Wilson, and T. T. J. Yu, *Can. J. Chem.*, **47**, 509 (1969).
 9. P. T. Ho, S. F. Lee, D. Chang, and K. Wiesner, *Experientia*, **27**, 1377 (1971).
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Appendix
Chemical Abstracts Nomenclature (Collective Index Number);
(Registry Number)

cyclohexenone dimer

calcium chloride (10043-52-4)

Benzene (71-43-2)

ethyl acetate (141-78-6)

methanol (67-56-1)

ether (60-29-7)

acetonitrile (75-05-8)

sodium hydroxide (1310-73-2)

chloroform (67-66-3)

sodium hydrogen carbonate (144-55-8)

sodium chloride (7647-14-5)

nitrogen (7727-37-9)

2-propanol (67-63-0)

magnesium sulfate (7487-88-9)

1-propen-2-yl acetate (108-22-5)

vinyl acetate (108-05-4)

argon (7440-37-1)

isophorone,
3,5,5-trimethyl-2-cyclohexen-1-one

ceric ammonium nitrate

3,5,5-Trimethyl-2-(2-oxopropyl)-2-cyclohexen-1-one,
2-Cyclohexen-1-one, 3,5,5-trimethyl-2-(2-oxopropyl)-,
3,5,5-trimethyl-2-(2-oxopropyl)-2-cyclohexene-1-one (61879-73-0)

7-Acetoxy-4,4,6,7-tetramethylbicyclo[4.2.0]octan-2-one (66016-89-5)

7-Hydroxy-4,4,6,7-tetramethylbicyclo[4.2.0]octan-2-one (61879-76-3)

sulfuric acid, sodium hydroxide

vinylene carbonate