



A Publication
of Reliable Methods
for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

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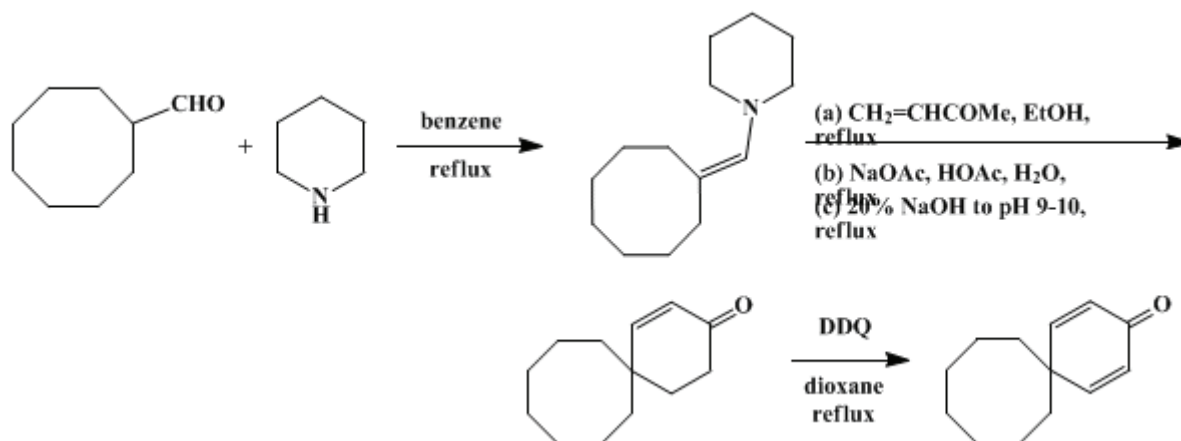
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

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SPIRO[5.7]TRIDECA-1,4-DIEN-3-ONE



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1. Procedure

Caution! The following reactions should be performed in an efficient hood to protect the experimentalist from noxious vapors (piperidine and methyl vinyl ketone).

A. *1-(Cyclooctylidene)methylpiperidine*. Cyclooctanecarboxaldehyde (12.5 g, 0.089 mol) (Note 1) and piperidine (8.35 g, 0.098 mol) are dissolved in 115 mL of toluene and placed in a 250-mL, one-necked flask equipped with a magnetic stirring bar and Dean-Stark water separator, on top of which is a condenser fitted with a nitrogen-inlet tube. The reaction mixture is placed under a nitrogen atmosphere, then brought to and maintained at reflux with stirring for 6 hr, at which time the theoretical amount of water (1.75 mL) has been collected. The reaction mixture is cooled and fractionally distilled under reduced pressure (Note 2); toluene and excess piperidine are removed at 40°C (0.5 mm), and the enamine product is distilled as a colorless liquid to yield 17.30 g (0.084 mol, 93.6%) of 1-(cyclooctylidene)methylpiperidine, bp 81–83°C (0.5 mm).

B. *Spiro[5.7]tridec-1-en-3-one*. A dry, 1-L, three-necked flask is equipped with a Teflon stirring bar, condenser, pressure-equalizing dropping funnel, and nitrogen-inlet tube. To this flask are introduced absolute ethanol (460 mL) (Note 3) and 1-(cyclooctylidene)methylpiperidine (17.3 g, 0.084 mol). After the solution has been stirred for 5 min, methyl vinyl ketone (6.44 g, 0.092 mol) (Note 4) is added dropwise over a period of 5 min. The solution is refluxed for 20 hr using a heating mantle. The mixture is cooled and anhydrous sodium acetate (15.0 g), acetic acid (25.5 mL), and water (46 mL) are added. The mixture is brought to and maintained at reflux for 8 hr. The heat is removed and the solution is cooled with ice water; aqueous sodium hydroxide (20% solution, approximately 65 mL) is added until pH 9–10 is attained. The solution is refluxed for another 15 hr; at the end of this period the reaction mixture is cooled. The reaction mixture (600 mL) is divided equally into two 2-L separatory funnels and each portion is diluted with 600 mL of ice-cold water. Each separatory funnel is extracted with ether (3 × 125 mL). The ether extract is washed successively with aqueous 5% hydrochloric acid (125 mL) and saturated brine (3 × 170 mL), dried over anhydrous magnesium sulfate, and filtered. The solvent is removed on a rotary evaporator and the product is distilled under vacuum (Note 5) as a colorless liquid to yield 7.05–7.75 g (44–49%) of spiro[5.7]tridec-1-en-3-one, bp 95–125°C (0.5 mm) (Note 6).

C. *Spiro[5.7]trideca-1,4-dien-3-one*. Spiro[5.7]tridec-1-en-3-one (3.63 g, 0.0189 mol) and 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) (8.90 g, 0.0392 mol) (Note 7) are dissolved in 50 mL of dioxane (Note 8) in a 250-mL, one-necked flask equipped with a magnetic stirring bar and fitted with a condenser and drying tube. The reaction mixture is brought to and maintained at reflux with stirring for 6 hr. The mixture is cooled, filtered, and the dioxane removed in a rotary evaporator. The product is

taken up in ether (125 mL), and the ether layer is washed with aqueous sodium hydroxide (15%, 4 × 60 mL). The combined aqueous layers are further extracted with ether (3 × 60 mL). The ether layers are combined and washed with saturated sodium chloride (4 × 60 mL), dried over anhydrous magnesium sulfate and filtered. The solvent is removed on the rotary evaporator to afford a crude yellow liquid. To this crude product are added silica gel (6.25 g) (Note 9) and enough ether to cover the silica gel. The ether is removed with a rotary evaporator so as to absorb the crude product on the silica gel. This silica gel dry powder is poured onto a column (12 in. long × 1.0 in. diameter) containing silica gel (50 g) in hexane. The column is eluted with hexane (70 mL) and then with an increasing amount of ethyl acetate/hexane (Note 10). The desired fractions are combined (Note 11) and solvent is removed under vacuum to afford spiro[5.7]trideca-1,4-dien-3-one (2.65 g, 73.7%), (Note 12).

2. Notes

1. Cyclooctanecarboxaldehyde was obtained from Aldrich Chemical Company, Inc. and used without purification.
2. 1-(Cyclooctylidenemethyl)piperidine is typical of most enamines in that it discolors rapidly when exposed to air and therefore must be handled under an inert atmosphere, preferably nitrogen.
3. Absolute ethanol, distilled and stored over molecular sieves, was used.
4. Methyl vinyl ketone (bp 35–36°C at 140 mm) was obtained from Aldrich Chemical Company, Inc. and distilled immediately before use.
5. A heating mantle was used for this distillation. A forerun of 25–95°C (0.5 mm) was discarded. The exact boiling point of spiro[5.7]tridec-1-en-3-one is 86°C (0.1 mm).
6. The product has the following spectral properties: ¹H NMR (CCl₄) δ: 1.62 (s, 14 H), 1.85 (br d, 2 H), 2.25 (m, 2 H), 5.68 (d, 1 H, *J* = 10 Hz), 6.75 (d, 1 H, *J* = 10 Hz).
7. 2,3-Dichloro-5,6-dicyano-1,4-benzoquinone, supplied by Aldrich Chemical Company, Inc. was used without further purification.
8. Dioxane was refluxed over potassium hydroxide pellets, distilled, and stored over molecular sieves.
9. silica gel analytical reagent (60–200 mesh) was obtained from the J. T. Baker Chemical Co.
10. The silica gel column was eluted starting with hexane (70 mL), followed by 2% ethyl acetate–hexane (100 mL); 5% ethyl acetate–hexane (100 mL); 10% ethyl acetate–hexane (600 mL). The fractions were monitored with 20% ethyl acetate–hexane, using silica 7 GF plates (purchased from Analtech, Inc.), thickness 250 μm, 20 cm long × 5 cm wide. The plates were sprayed with 3% ceric sulfate and heated at 350°C to detect dienone and monoenone. Alternatively, silica gel 60 F-254 plates (purchased from EM Laboratories, Inc.), thickness 25 μm, 20 cm long × 5 cm wide may be used. Detection may be made with ultraviolet light. The ratio of 1 g of crude dienone to 15 g of silica gel is adequate for obtaining pure spiro[5.7]trideca-1,4-dien-3-one.
11. When 20% ethyl acetate/hexane is used, the monoenone, *R_f* 0.57, and the dienone, *R_f* 0.47 (Analtech Uniplat–Silica 7 GF), are obtained.
12. The product has the following spectral properties: ¹H NMR (CCl₄) δ: 1.65 (s, 14 H), 6.10 (d, 2 H), *J* = 10 Hz), 6.98 (d, 2 H, *J* = 10 Hz).

3. Discussion

This procedure illustrates a general method for preparing a wide range of spirocyclohexenones and hence spirocyclohexadienones. A number of intramolecular and intermolecular reactions are known to give spirodienones; however, these methods have limited synthetic application.² This procedure is superior³ to that developed by Bordwell and Wellman⁴ for side reactions such as aldol condensation of the aldehyde and polymerization of methyl vinyl ketone are avoided. These spirodienones are useful intermediates in the synthesis of paracyclophanes.^{5,6}

Cyclopentanecarboxaldehyde (47%), cyclohexanecarboxaldehyde (41%), 1,2,5,6-tetrahydrobenzaldehyde (43%), cycloheptanecarboxaldehyde (41%), cyclooctanecarboxaldehyde (42%), cycloundecanecarboxaldehyde (36%), 5-norbornene-2-carboxaldehyde (32%), adamantanecarboxaldehyde (20%), and 1,2,3,4-tetrahydro-1-naphthylaldehyde (40%) gave corresponding spiroenones.⁷ Spiroenones obtained from cyclohexanecarboxaldehyde, cycloheptanecarboxaldehyde and cyclooctanecarboxaldehyde were converted to the corresponding dienones using the dichlorodicyanobenzoquinone (DDQ). The yields for all three dienones are in the

range of 56 to 58%.

References and Notes

1. Department of Chemistry, Princeton University, Princeton, NJ 08544.
 2. Krapcho, A. P. *Synthesis* **1974**, 383.
 3. Kane, V. V. *Synth. Commun.* **1976**, 6, 237.
 4. Bordwell, F. G.; Wellman, K. M. *J. Org. Chem.* **1963**, 28, 1347, 2544.
 5. Wolf, A. D.; Kane, V. V.; Levin, R. H.; Jones, Jr., M. *J. Am. Chem. Soc.* **1973**, 95, 1680.
 6. Kane, V. V.; Wolf, A. D.; Jones, Jr., M. *J. Am. Chem. Soc.* **1974**, 96, 2643.
 7. Yields are for the overall conversion.
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Appendix Chemical Abstracts Nomenclature (Collective Index Number); (Registry Number)

silica gel

brine

ethanol (64-17-5)

hydrochloric acid (7647-01-0)

acetic acid (64-19-7)

ethyl acetate (141-78-6)

ether (60-29-7)

sodium acetate (127-09-3)

sodium hydroxide (1310-73-2)

sodium chloride (7647-14-5)

nitrogen (7727-37-9)

potassium hydroxide (1310-58-3)

toluene (108-88-3)

piperidine (110-89-4)

magnesium sulfate (7487-88-9)

dioxane (5703-46-8)

hexane (110-54-3)

methyl vinyl ketone (78-94-4)

ceric sulfate (13590-82-4)

2,3-dichloro-5,6-dicyano-1,4-benzoquinone,
dichlorodicyanobenzoquinone

Cyclohexanecarboxaldehyde (2043-61-0)

Cyclopentanecarboxaldehyde (872-53-7)

1,2,5,6-tetrahydrobenzaldehyde

Spiro[5.7]trideca-1,4-dien-3-one (41138-71-0)

Cyclooctanecarboxaldehyde (6688-11-5)

1-(Cyclooctylidenemethyl)piperidine (65226-88-2)

Spiro[5.7]tridec-1-en-3-one (60033-39-8)

cycloheptanecarboxaldehyde

cycloundecanecarboxaldehyde

5-norbornene-2-carboxaldehyde

adamantanecarboxaldehyde

1,2,3,4-tetrahydro-1-naphthylaldehyde