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of Reliable Methods
for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

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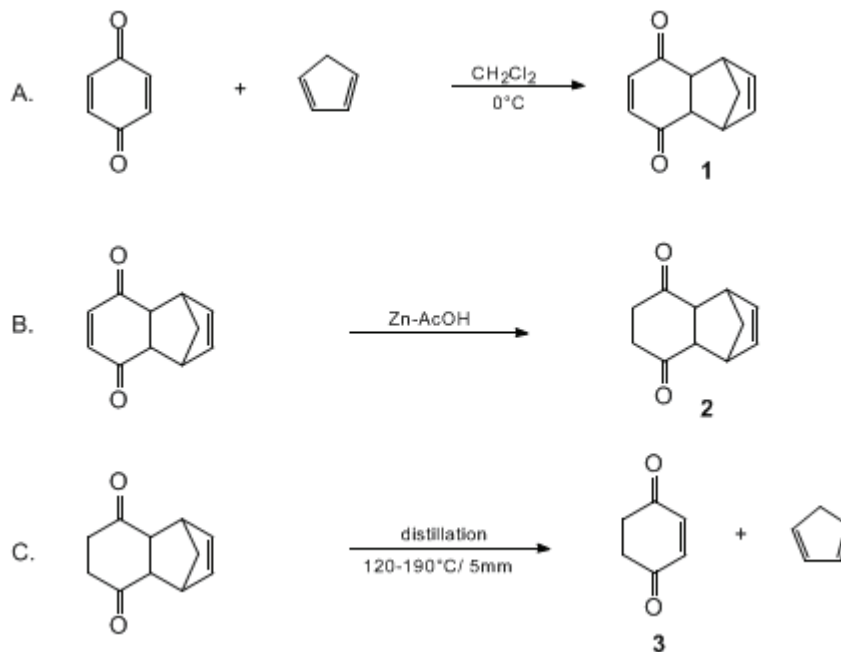
In some articles in *Organic Syntheses*, chemical-specific hazards are highlighted in red "Caution Notes" within a procedure. It is important to recognize that the absence of a caution note does not imply that no significant hazards are associated with the chemicals involved in that procedure. Prior 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.

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September 2014: The paragraphs above replace the section "Handling and Disposal of Hazardous Chemicals" in the originally published version of this article. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

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2-CYCLOHEXENE-1,4-DIONE



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1. Procedure

A. *endo-Tricyclo[6.2.1.0^{2,7}]undeca-4,9-diene-3,6-dione* **1**. A 1-L, three-necked, round-bottomed flask, equipped with a mechanical stirrer, 100-mL pressure-equalizing dropping funnel, and a thermometer, is charged with 108.1 g (1.0 mol) of 1,4-benzoquinone (Note 1) and 350 mL of dichloromethane (Note 2). The flask is cooled to 0°C with an ice bath. Via the addition funnel, 41.5 mL of cyclopentadiene (34.2 g, 0.52 mol) (Note 3) is added dropwise over a 45-min period with stirring at such a rate that the internal temperature remains below 8°C (Note 4). A second 41.5-mL portion (34.2 g, 0.52 mol) of cyclopentadiene is added in a similar way (Note 5). The resulting mixture is stirred for 1 hr in the ice bath, for 0.5 hr at room temperature, and then is transferred to a 1-L, pear-shaped flask by rinsing with a small amount of dichloromethane. Most of the solvent is removed by rotary evaporation under reduced pressure, and 200 mL of hexane is added to the residue. The flask is cooled in an ice bath for 0.5 hr. The pale yellow solids are collected by suction filtration, washed with three 30-mL portions of hexane, and air-dried to afford 150–155 g of the Diels-Alder adduct **1** (D-A adduct) of sufficient purity for use in the next step (Note 6). Concentration of the filtrate to about half the volume and cooling affords 12–15 g of a second crop of **1**. The combined yield of **1** is 164–169 g (94–97%).

B. *endo-Tricyclo[6.2.1.0^{2,7}]undec-9-ene-3,6-dione* **2**. A 3-L, three-necked, round-bottomed flask, equipped with a mechanical stirrer, thermometer, and heating mantle, is charged with 166 g (0.95 mol) of the crude D-A adduct **1** and 1.3 L of acetic acid (Note 7). Portionwise, 228.8 g (3.5 mol) of zinc dust (Note 8) is added to the mixture with stirring. The temperature rises to about 70°C over a 10-min period and then drops. The resulting mixture is then heated at 70–80°C for 1 hr, followed by addition of a further 32.7 g (0.5 mol) of zinc powder and continued heating and stirring for an additional 1.5 hr. After the mixture has cooled to room temperature, the gray solids are collected by suction filtration, and washed with 200 mL of acetic acid (Note 9). The dark yellowish filtrate is then concentrated by rotary evaporation under reduced pressure (Note 10), the residue diluted with 600 mL of water, and the resulting mixture extracted with three 300-mL portions of toluene (Note 11). The combined toluene extracts are washed with two 100-mL portions of water, 100 mL of aqueous 10% sodium hydroxide

solution, two 100-mL portions of brine, and dried over sodium sulfate, and filtered into a 500-mL round-bottomed flask. Removal of the solvent by rotary evaporation under reduced pressure yields 148–155 g of crude diketone **2**, sufficiently pure for further transformation, as a reddish liquid that solidifies on cooling (Note 12).

C. *2-Cyclohexene-1,4-dione* **3** (Note 13) and (Note 14). The 500-mL, round-bottomed flask containing ~150 g of crude diketone **2** from Part B is equipped with a magnetic stirring bar and fitted with a Claisen-type short path distillation head leading to a condenser and a 200-mL, round-bottomed receiver. Two cold traps are placed between the receiver and a vacuum pump. The first trap is cooled in a dry ice-ethanol bath and the second trap in liquid nitrogen (Note 15). The system is evacuated and the distillation pot is placed in an oil bath and heated rapidly to 140–180°C with magnetic stirring, whereupon diketone **2** distills fairly rapidly into the receiver to afford a mixture of diketone **2** and *2-cyclohexene-1,4-dione* **3**, bp 80–140°C (most at 130–140°C) at 4–7 mm (bath temperature 140–180°C), as a pale yellow oil (Note 16), (Note 17) and (Note 18).

The 200-mL, round-bottomed receiver, containing a mixture of diketone **2** and *2-cyclohexene-1,4-dione* **3**, is then fitted with a long path (25 cm) distillation head packed with Pyrex glass helices or chips, an air condenser (25 cm), and a 200-mL, two-necked, round-bottomed receiver with one neck connected to the vacuum pump via the traps described earlier. The distillation pot is placed in an oil bath, the system is evacuated, and the receiver is immersed in an ice bath. The bath is heated to 120°C and the mixture of diketone **2** and *2-cyclohexene-1,4-dione* **3** is redistilled at 4–8 mm while the bath temperature is gradually increased from 120°C to 190°C. Early in the distillation, the enedione **3**, which is already present, distills smoothly, then the rate of dissociation of **2** becomes rate-determining. The bath temperature is maintained at 180–190°C so as to keep the boiling point nearly constant (87°C/6 mm). Care is taken to assure that any enedione **3** that crystallizes in the condenser or receiver is quickly melted with an efficient heat gun to avoid occlusion of the distillation path (Note 19). A total of 73–80 g of crude yellow solid enedione **3** is obtained containing a small amount of diketone **2**.

The resulting crude solid enedione **3** is melted at 60–70°C in a water bath and 35 mL of carbon tetrachloride is added (Note 20). The mixture is cooled in an ice bath, 18 mL of hexane is added (Note 21), and the resulting mixture is gently stirred with a glass rod. After cooling for 20–30 min, the resulting pale yellow crystals are collected by suction filtration, washed with 20–30 mL of a cold mixture of carbon tetrachloride and hexane (1:1 v/v), and then with 40 mL of hexane. Brief air drying affords 65–71 g of almost pure enedione **3**, mp 54–54.5°C (Note 21) and (Note 22). Concentration of the filtrate to about 15 mL, addition of 8 mL of hexane, and cooling the mixture furnishes a further 1.5–2.5 g of **3**. In total, 67.0–72.5 g (61–66% from *1,4-benzoquinone*) of nearly pure **3** is obtained (Note 23), (Note 24) and (Note 25).

2. Notes

1. Reagent-grade *1,4-benzoquinone* was purchased from Wako Pure Chemical Industries, LTD and was used without additional purification.
2. Dichloromethane was distilled from phosphorus pentoxide.
3. Cyclopentadiene is prepared according to the procedure in *Org. Synth., Coll. Vol. VII 1990, 339*.
4. At higher temperatures, 1:2 adducts² between *1,4-benzoquinone* and cyclopentadiene are formed as by-products. Separation of the 1:1 adduct and 1:2 adducts is not easy on a large scale. If the material is contaminated by a small amount of the 1:2 adduct, it is best to carry the procedure on to the last step (see (Note 23)).
5. Cyclopentadiene was added in two portions to minimize dimerization during warming to room temperature. If a dropping funnel with cooling jacket is available, it is not necessary to divide the cyclopentadiene into two portions.
6. Recrystallization of a portion of the product from hexane-dichloromethane furnishes pure **1**, mp 78–79°C which exhibits the following spectral data: ¹H NMR (500 MHz, CDCl₃) δ: 1.39 (d, 1 H, J = 9), 1.51 (d, 1 H, J = 9), 3.19 (s(br), 2 H), 3.51 (s(br), 2 H), 6.03 (s(br), 2 H), 6.54 (s, 2 H); ¹³C (125 MHz, CDCl₃) δ: 48.31, 48.69, 48.74, 135.26, 142.02, 199.39; IR (CHCl₃) cm⁻¹: 3000, 2940, 2870, 1675, 1604, 1450, 1335, 1295, 12.75, 1230, 1120, 1105, 1050, 990, 960, 940, 910, 855.
7. Commercial reagent grade acetic acid was used as purchased.

8. Commercial reagent grade [zinc](#) dust was used immediately after opening.
9. The gray solids should be added to water as soon as possible after filtration and washing; otherwise, the solids become hot, probably because of air oxidation.
10. Do not distil to dryness.
11. [Diethyl ether](#) may be substituted for [toluene](#).
12. Crude diketone **2** may contain some [toluene](#). Chromatography of a portion of the material on silica gel furnishes pure diketone **2**, mp $\sim 22^\circ\text{C}$ which exhibits the following spectra data: ^1H NMR (500 MHz, CDCl_3) δ : 1.32 (d, 1 H, $J = 8$), 1.44 (d, 1 H, $J = 8$), 2.10–2.30 (m, 2 H), 2.50–2.60 (m, 2 H), 3.18 (s(br), 2 H), 3.42 (d, 2 H, $J = 1.8$), 6.14 (d, 2 H, $J = 1.8$); ^{13}C (125 MHz, CDCl_3) δ : 37.89, 47.38, 48.68, 51.77, 136.58, 209.48; IR (CHCl_3) cm^{-1} : 3000, 2940, 2865, 1710, 1415, 1330, 1250, 1220, 1150, 1100, 1050, 995, 895.
13. It is desirable that the following procedures be completed smoothly in one day to avoid possible isomerization of enedione **3** to hydroquinone. If two days are required, the distillate from the first distillation can be stored without change in a freezer in the dark.
14. All glassware used in these procedures should be free of acids or bases.
15. It is important that the first trap be of sufficient size to accommodate liberated [cyclopentadiene](#).
16. A silicone oil bath was used for the pyrolytic distillations.
17. The ratio of diketone **2** to enedione **3** varies with the precise conditions of distillation with **2** being the major product.
18. Rapid distillation serves to eliminate possible contamination of diketone **2** with trace amounts of acids or bases.
19. Toward the end of the pyrolytic distillation enedione **3** often crystallizes on the walls of the distillation head and condenser.
20. Spectrophotometric grade [carbon tetrachloride](#) was used without causing isomerization of enedione **3** to hydroquinone.
21. Enedione **3** crystallizes fairly rapidly; stirring controls the crystal size to some extent. Since enedione **3** sublimes easily, drying under reduced pressure is not appropriate.
22. Pure enedione **3** has the following spectral data: ^1H NMR (500 MHz, CDCl_3) δ : 2.84 (s, 4 H), 6.66 (s, 2 H); ^{13}C (125 MHz, CDCl_3) δ : 36.52, 141.05, 197.21; IR (CHCl_3) cm^{-1} : 3020, 2970, 2905, 1690, 1600, 1420, 1370, 1300, 1280, 1225, 1140, 1095, 1000, 985, 935, 845.
23. If D-A adduct **1** contains some 1:2 adducts as impurities, [1,4-benzoquinone](#) is formed by a retro-Diels-Alder reaction during the pyrolytic distillations. In this case, a dark yellow solid of [benzoquinone](#) can be seen on the walls of the air condenser, and the distillate has a deeper yellow color. Contamination with a small amount of [1,4-benzoquinone](#) apparently does not interfere with photochemical [2+2] cycloadditions of enedione **3** with alkenes and alkynes, an important application of **3**. Fractional distillation of the benzoquinone-contaminated **3** as described for the second distillation of **3** can remove the [benzoquinone](#) with some loss of enedione **3**. The [benzoquinone](#) deposits initially as a dark yellow solid on the walls of the distillation head and air condenser during early fractions.
24. Enedione **3** as a crystalline solid can be stored indefinitely below 0°C in a glass container in the dark.
25. Experiments starting from 1.5 mol of [1,4-benzoquinone](#) gave similar results.

Waste Disposal Information

All toxic materials were disposed of in accordance with "Prudent Practices in the Laboratory"; National Academy Press; Washington, DC, 1995.

3. Discussion

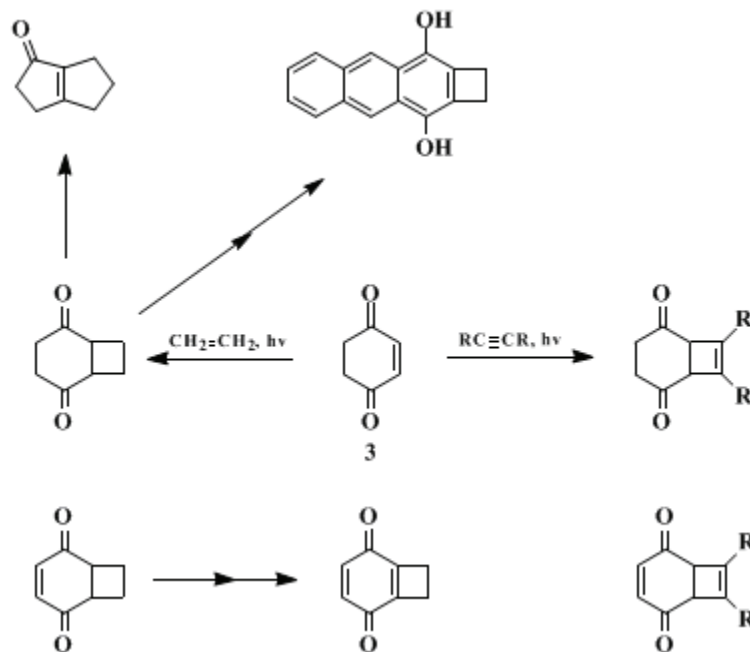
[2-Cyclohexene-1,4-dione](#) **3** was first synthesized by careful acid hydrolysis of its monoacetal.³ Because of the high sensitivity of **3** to acids and bases, this method is not suitable for large-scale preparations. The present method is essentially identical to that reported by Chapman, et al.,⁴ with modifications for large-scale and minimal solvent use. Alkyl substituted 2-cyclohexene-1,4-diones can be prepared similarly.⁴

The 1,4-benzoquinone-cyclopentadiene Diels-Alder adduct **2** is well known.⁵ The procedure described here is adapted for large-scale preparation. For the [zinc](#) reduction, aqueous [acetic acid](#) has

also been used.⁴ The present procedure allows recovery of most of the acetic acid. The entire procedure can be completed in 3–4 days.

The most useful application of **3** is its use in photochemical [2+2] cycloadditions with alkenes and alkynes at the carbon-carbon double bond to afford bicyclo[4.2.0]octane-2,5-diones and bicyclo[4.2.0]oct-7-ene-2,5-diones in good to excellent yield.⁶ Since selenium dioxide oxidation of the resulting adducts furnishes the corresponding 3-ene-2,5-diones, diketone **3** can be regarded as a 1,4-benzoquinone equivalent leading to [2+2] cycloadducts at the carbon-carbon double bond.

Some typical applications are shown below.^{6,7}



References and Notes

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Appendix

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

endo-Tricyclo[6.2.1.0^{2,7}]undeca-4,9-diene-3,6-dione

brine

1,4-benzoquinone-cyclopentadiene

acetic acid (64-19-7)

diethyl ether (60-29-7)

sodium hydroxide (1310-73-2)

sodium sulfate (7757-82-6)

carbon tetrachloride (56-23-5)

nitrogen (7727-37-9)

selenium dioxide (7446-08-4)

toluene (108-88-3)

zinc,
zinc powder (7440-66-6)

1,4-benzoquinone,
benzoquinone (106-51-4)

dichloromethane (75-09-2)

hexane (110-54-3)

CYCLOPENTADIENE (542-92-7)

phosphorus pentoxide (1314-56-3)

2-Cyclohexene-1,4-dione (4505-38-8)

endo-Tricyclo[6.2.1.0^{2,7}]undec-9-ene-3,6-dione (21428-54-6)