Organic Syntheses

A Publication
of Reliable Methods
for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

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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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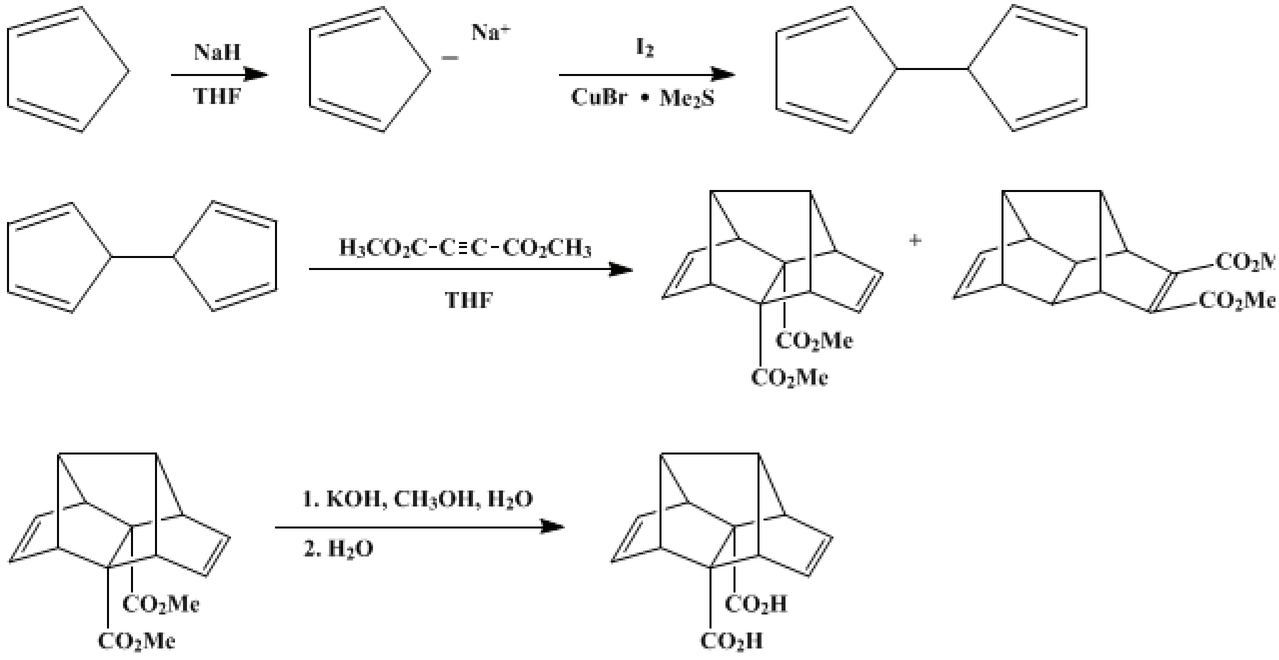
DOMINO DIELS–ALDER REACTION: 3,3a,3b,4,6a,7a-HEXAHYDRO-3,4,7-METHENO-7*H*-CYCLOPENTA[*a*]PENTALENE-7,8-DICARBOXYLIC ACID

[3,4,7-Metheno-7*H*-cyclopenta[*a*]pentalene-7,8-dicarboxylic acid, 3,3a,3b,4,6a,7a-hexahydro]



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1. Procedure

All apparatuses for Steps A and B should be dried overnight in an oven.

A. *9,10-Dihydrofulvalene.* A 5-L, three-necked, round-bottomed flask is fitted, while hot, with a Hirschberg stirrer, gas inlet, and stopper (Note 1). The assembled apparatus is flame-dried and allowed to cool to room temperature under a stream of dry, oxygen-free argon (Note 2). The stopper is replaced with a powder funnel and, under a sweep of positive argon, 100 g (4.17 mol) of dry sodium hydride (Note 3) is added followed by 2.0 L of dry tetrahydrofuran (Note 4). The powder funnel is replaced by a 500-mL, pressure-equalizing, jacketed addition funnel that is flushed with argon, then stoppered.

The stirred sodium hydride suspension is cooled by an external ice–water bath and the jacket of the addition funnel is cooled in a dry ice–isopropyl alcohol bath. Into the addition funnel is introduced 275 g (4.16 mol) of neat, freshly distilled cyclopentadiene (Note 5). The cyclopentadiene is added rapidly, dropwise over 30–40 min to the stirred slurry *(Caution: Avoid excess foaming.)* (Note 6). After the addition is complete, the cooling bath is removed and the solution is stirred for 1 hr at room temperature.

The jacketed addition funnel is removed and 1.5 g of cuprous bromide–dimethyl sulfide complex (Note 7) is added through a powder funnel. A 500-mL, pressure-equalizing addition funnel (long-tipped) is attached to the flask and flushed with argon. As the anion solution is cooled in a dry ice–isopropyl alcohol bath, a solution of 530 g (2.08 mol) of sublimed iodine in 500 mL of anhydrous tetrahydrofuran is placed in the addition funnel. This solution is added dropwise to the cooled slurry over approximately 90 min (Note 8). The solution is stirred for about 15 min at low temperature.

B. *Diels–Alder reaction.* A 500-mL, pressure-equalizing addition funnel containing 330 g (2.32 mol) of dimethyl acetylenedicarboxylate (Note 9) is placed in the flask and the ester is added rapidly dropwise over 10 min. The solution is stirred for 30 min, the cooling bath is removed, and stirring is maintained for 4 hr (Note 10).

The reaction solution is filtered through a Celite pad (ca. 5 cm thick on a 32-cm Büchner funnel), and the solid is washed repeatedly with tetrahydrofuran (1.5 L). The combined filtrates are concentrated under reduced pressure at a temperature not above 30°C. To the concentrate is added 1.5 L of ether. The solution is stirred for 15 min, again filtered through Celite, and concentrated at 30°C (Note 11).

C. *Hydrolysis.* Into a three-necked, 5-L, round-bottomed flask equipped with mechanical stirrer, thermometer, and 500-mL addition funnel with gas inlet is placed the above concentrate and 2 L of methanol. The solution is cooled to −5 to 0°C by means of an ice–salt bath. A precooled (0°C) solution containing 220 g of 87.5% potassium hydroxide in 400 mL of water is added dropwise at such a rate as to keep the reaction temperature below 10°C. The reaction mixture is stirred for an additional 2 hr at 0° C and for 1 hr at room temperature prior to the addition of 100 mL of glacial acetic acid. Solid sodium carbonate is added to bring the pH to 8 and the solution is filtered through Celite. Concentration off the filtrate at 35°C and reduced pressure affords about 1 L of a dark liquid. The liquid is diluted with 2 L of water and extracted with petroleum ether (6 × 600 mL). The combined extracts are washed with aqueous sodium thiosulfate solution (800 mL) and dried (magnesium sulfate). Concentration at 30°C affords a clear red liquid (occasionally a yellow solid) which is almost pure internal diester (Note 12).

The diester is dissolved in 130 mL of methanol, placed in a 1-L, one-necked flask equipped with a magnetic stirring bar and reflux condenser, and treated with a solution containing 35 g of potassium hydroxide in 130 mL of water. The mixture is stirred at reflux temperature for 1 hr. Methanol is removed under reduced pressure and 250 mL of water is added. Heating is continued for another 5 hr. After the solution is cooled, 5 g of activated charcoal is added and the mixture is stirred for 8 hr at room temperature. Filtration through Celite is followed by cooling of the stirred filtrate in an ice bath with acidification to pH 1 (dropwise addition of concentrated hydrochloric acid). The tan solid is isolated by filtration and dried under vacuum at room temperature. On the average, the yield is 52–55 g (10–11%) but can vary from 42 to 68 g (8–13% yield) (Note 13).

2. Notes

1. A paste made from a 1 : 1 mixture of mineral oil and silicone grease is used to lubricate the stirrer.
2. Prepurified argon (Linde) can be used with no further treatment.
3. Dry sodium hydride is available from Aldrich Chemical Company, Inc., as a fine powder. In multiple runs, it is most convenient to weigh the bulk reagent into 100-g (one reaction) lots. Extreme care should be used in handling this moisture-sensitive, flammable solid.
4. Tetrahydrofuran is distilled from calcium hydride and then from sodium–benzophenone immediately prior to use.
5. This amount of cyclopentadiene can be prepared in 2–3 hr using any of a variety of procedures.[3,4,5]
6. The checkers transferred cyclopentadiene by using a stainless-steel cannula from a cooled (dry ice–methanol), 500-mL, round-bottomed flask to the reaction vessel.
7. The complex was purchased from Aldrich Chemical Company, Inc.
8. A bright emerald-green color (usually) develops as the addition proceeds. If the iodine is impure, a brown color develops with no decrease in yield.
9. While dimethyl acetylenedicarboxylate is available commercially, it is easily prepared by the procedure of Huntress et al.[6] Care should be taken with this compound as it is a severe lachrymator and vesicant.
10. A tan to white precipitate of sodium iodide forms and a gentle exotherm is observed.
11. This concentrate (a dark red oil) may be stored in a refrigerator if time does not permit further work.
12. While the Diels–Alder reaction affords a wide variety of products, all of the esters formed hydrolyze faster than the desired internal adduct. The above hydrolysis removes all byproducts through base extraction. The internal diester has spectral properties as follows: ^{1}H NMR ($CDCl_3$) δ: 2.50 (tt, 2 H, *J* = 2.0, 4.3), 3.30 (dd, 4 H, *J* = 2.0, 4.3), 3.59 (s, 6 H), 6.07 (t, 4 H, *J* = 2.0); ^{13}C NMR ($CDCl_3$) δ: 51.5,

58.8, 64.6, 69.5, 132.7, 172.7.

13. Spectral properties of the diacid are as follows: ^{1}H NMR (d_6-DMSO) δ: 2.36 (tt, 2 H, J = 1.5, 4.1), 3.21 (dd, 4 H, J = 1.5, 4.1), 5.95 (t, 4 H, J = 1.7).

3. Discussion

The present procedure is a modification of the method previously reported.[7] [8] While the overall yield is similar, the method described here is simpler in that it avoids a cumbersome transfer of the sodium cyclopentadienide solution.

The first step leading to 9,10-dihydrofulvalene is adapted from the earlier work of Matzner.[9] The utility of this thermally labile hydrocarbon ranges from its ability to engage in multiple [4+2] cycloadditions[7,8,10] to its capacity for bonding to a pair of metal atoms.[11] [12] [13] [14] [15]

The product diacid has served as starting material for the synthesis of tetracyclo[7.2.1.0^{4,11}.0^{6,10}]dodeca-2,7-diene-5,12-dione,[16] [17] C_{16}-hexaquinacene,[18] [19] [20] [21] (C_s)-C_{17}-heptaquinane derivatives,[22] [23] the parent dodecahedrane molecule,[24] [25] [26] and a number of substituted dodecahedranes.[27] [28] [29] [30] [31] [32] [33] [34]

References and Notes

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

petroleum ether

9,10-Dihydrofulvalene

activated charcoal

C_{16}-hexaquinacene

(C_s)-C_{17}-heptaquinane

dodecahedrane

Dry Ice

hydrochloric acid (7647-01-0)

acetic acid (64-19-7)

methanol (67-56-1)

ether (60-29-7)

sodium carbonate (497-19-8)

oxygen (7782-44-7)

sodium thiosulfate (7772-98-7)

iodine (7553-56-2)

potassium hydroxide (1310-58-3)

Benzophenone (119-61-9)

sodium (13966-32-0)

sodium iodide (7681-82-5)

magnesium sulfate (7487-88-9)

Tetrahydrofuran (109-99-9)

sodium hydride (7646-69-7)

CYCLOPENTADIENE (542-92-7)

argon (7440-37-1)

Dimethyl acetylenedicarboxylate (762-42-5)

calcium hydride (7789-78-8)

sodium cyclopentadienide (4984-82-1)

3,3a,3b,4,6a,7a-Hexahydro-3,4,7-metheno-7H-cyclopenta[a]pentalene-7,8-dicarboxylic acid, 3,4,7-Metheno-7H-cyclopenta[a]pentalene-7,8-dicarboxylic acid, 3,3a,3b,4,6a,7a-hexahydro (61206-25-5)