Organic Syntheses

A Publication
of Reliable Methods
for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

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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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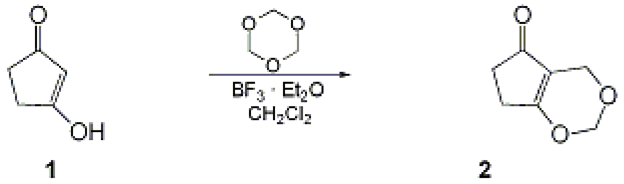
Organic Syntheses, Coll. Vol. 10, p.293 (2004); Vol. 75, p.189 (1998).

6,7-DIHYDROCYCLOPENTA-1,3-DIOXIN-5(4H)-ONE

[Cyclopenta-1,3-dioxin-5(4H)-one, 6,7-dihydro-]



Submitted by Kwunmin Chen, Christopher S. Brook, and Amos B. Smith, III[1] .
Checked by Aimee Reed and Louis S. Hegedus.

1. Procedure

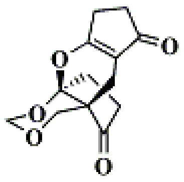
A 1-L, three-necked, round-bottomed flask equipped with a 2-cm magnetic stirring bar, rubber septum, 50-mL graduated addition funnel, and an argon inlet tube is charged with 10.0 g (0.1019 mol) of 1,3-cyclopentanedione (Note 1), 55.0 g (0.6106 mol) of 1,3,5-trioxane (Note 2), 5 g of activated, powered, 4 Å molecular sieves, and 500 mL of freshly distilled dichloromethane (Note 3). The resultant suspension is stirred at room temperature and 37.6 mL (0.3057 mol) of boron trifluoride etherate (Note 4) is added dropwise over 2 hr via the addition funnel (Note 5). After 48 hr, the reaction mixture is filtered through a pad of Celite and the yellow solid is washed twice with 100 mL of dichloromethane . The filtrate is poured into a 3-L separatory funnel containing 500 g of ice and 1 L of saturated sodium bicarbonate (Note 6). The aqueous phase is extracted with two 100-mL portions of dichloromethane , and the combined organic solutions are washed with 500 mL of brine , dried over magnesium sulfate , filtered, and concentrated under reduced pressure. Flash chromatography on 500 g of silica gel (Note 7) with hexane-acetone (3 : 1) as eluant (Note 8) gives 10.3 g (72% yield) of **2** as a white crystalline solid (Note 9) and (Note 10).

2. Notes

1. 1,3-Cyclopentanedione (ca. 97%) is purchased from Aldrich Chemical Company, Inc. , and used without purification.
2. 1,3,5-Trioxane (99+%) is purchased from Aldrich Chemical Company, Inc. , and used without purification.
3. Reagent-grade dichloromethane is distilled under argon from calcium hydride.
4. The submitters use the purified, redistilled grade of boron trifluoride etherate available from Aldrich Chemical Company, Inc.
5. Upon initial addition of boron trifluoride etherate, a slightly endothermic reaction takes place.
6. **CAUTION**: A large amount of carbon dioxide is generated in this extraction and appropriate care should be taken.
7. The crude residue is applied to the column head using a minimum of dichloromethane. The submitters use flash-grade (230-400 mesh) silica gel purchased from E. Merck and a column 10 cm in diameter. TLC values for **2** are R_f = 0.18 (hexane : acetone = 3 : 1) and for **3** (see (Note 10)) are R_f = 0.08 (hexane : acetone = 3 : 1), employing Whatman K6F silica gel TLC plates 60 Å. In a typical purification, collecting 200-mL fractions, **2** would elute in fractions 9-18 and **3** in fractions 20-30. The checkers found that immediate purification of the crude residue was necessary. Yields decreased dramatically with time between isolation and purification. Furthermore, the activity (related to the degree of dehydration) of the silica gel greatly affected yields. Only half the amount of silica mentioned above was used by the checkers to get the reported yields. When the full amount was used, the yield decreased to 40-50%.
8. Reagent-grade hexanes (Fisher Scientific Company) and HPLC-grade acetone (Baxter Diagnostics Inc.) were used without further purification.
9. The product can be recrystallized from hexane-ethyl acetate (5:1): mp 73-75°C; IR ($CHCl_3$) cm^{-1}:

3000 (m), 1690 (m), 1640 (s), 1430 (m), 1310 (m), 1180 (m), 1090 (br m), 910 (s), 890 (s) ; ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 2.36-2.38 (m, 2 H), 2.59-2.62 (m, 2 H), 4.44 (t, 2 H, J = 2.2), 5.20 (s, 2 H) ; ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 26.4, 32.6, 63.1, 92.7, 114.7, 181.9, 201.0 ; high resolution mass spectrum (CI, NH_3) m/z 140.0482 (M^+; calcd for $C_7H_8O_3$: 140.0473). Anal. Calcd for $C_7H_8O_3$: C, 60.00; H, 5.75. Found: C, 60.19; H, 5.82.

10. Further elution furnishes a small amount (0.57 g, 2% yield) of crystalline propellane **3**: mp 178-180° C; IR ($CHCl_3$) cm^{-1}: 3000 (m), 1760 (s), 1700 (m), 1650 (s), 1450 (s), 1400 (s), 1195 (m), 1165 (m), 970 (m) ; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.95-2.06 (m, 3 H), 2.33-2.38 (m, 1 H), 2.42-2.74 (m, 6 H), 3.28 (d, 1 H, J = 11.7), 4.21 (d, 1 H, J = 11.7), 4.80 (d, 1 H, J = 6.4), 4.82 (d, 1 H, J = 6.6) ; ^{13}C NMR (125 MHz, $CDCl_3$) δ: 20.4, 25.9, 30.7, 33.3, 44.7, 64.7, 87.7, 106.8, 111.0, 180.7, 202.1, 210.2 ; high resolution mass spectrum (CI, NH_3) m/z 250.0841 (M^+; calcd for $C_{13}H_{14}O_5$: 250.0836). Structure **3** is confirmed by single-crystal X-ray analysis.



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Waste Disposal Information

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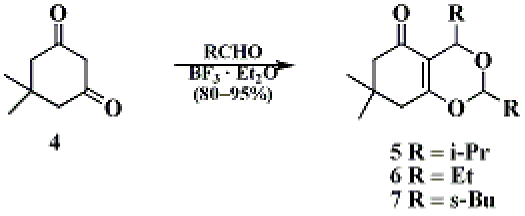
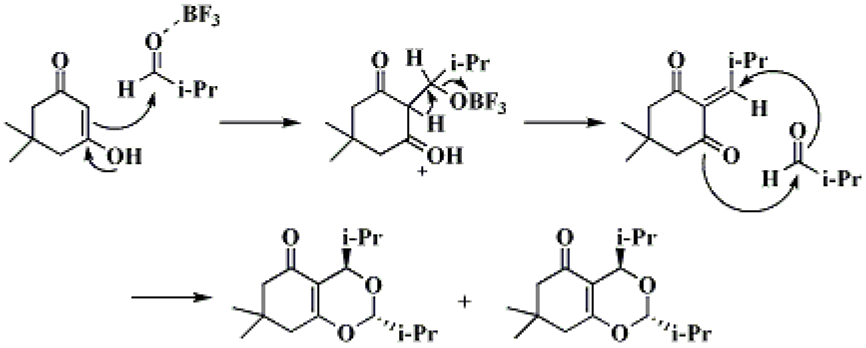
All toxic materials were disposed of in accordance with "Prudent Practices in the Laboratory"; National Academy Press; Washington, DC, 1995.

3. Discussion

1,3-Dioxin vinylogous esters derived from cyclic 1,3-diketones (e.g., **4**) are valuable building blocks for the construction of natural and unnatural carbocyclic products.[2] In connection with a synthesis of plant-growth regulators, Crow and co-workers reported the preparation of substituted 1,3-dioxins **5-7** in 1982.[3] To account for their formation, Crow proposed a Prins mechanism whereby the enol of the 1,3-diketone adds to the BF_3-aldehyde complex (Scheme 1).[4] Incorporation of a second equivalent of aldehyde and cyclization then yields the dioxin. Use of a slight excess of aldehyde (ca. 2.5-3.0 equiv) was recommended.[3]



Scheme 1



A systematic investigation[5] demonstrated that this reaction could be successfully generalized by employing a larger excess of 1,3,5-trioxane (or paraformaldehyde) and increasing the $BF_3 \cdot Et_2O$ to 1,3,5-trioxane ratio. Presumably the latter results in more rapid breakdown of 1,3,5-trioxane to formaldehyde and/or its BF_3 complex, analogous to the sulfuric acid-induced depolymerization of paraformaldehyde.[6] Best results were obtained by using 6 equiv of 1,3,5-trioxane and 3 equiv of $BF_3 \cdot Et_2O$.[5]

The synthetic usefulness of dioxin vinylogous esters as β-keto vinyl cation equivalents was demonstrated by a variety of reductive and alkylative 1,3-carbonyl transpositions.[5,7] Regioselective alkylation and hydroxylation at the α'-position (and, in some cases, at the γ-position)[8,9] further extend the usefulness of 1,3-dioxin vinylogous ester templates in organic synthesis.

References and Notes

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

6,7-Dihydrocyclopenta-1,3-dioxin-5(4H)-one:
Cyclopenta-1,3-dioxin-5(4H)-one, 6,7-dihydro- (11); (102306-78-5)

1,3-Cyclopentanedione (8,9); (3859-41-4)

1,3,5-Trioxane (8,9); (110-88-3)

4 Å Molecular sieves: Zeolites, 4 Å (10); (70955-01-0)

Boron trifluoride etherate:
Ethyl ether, compd. with boron fluoride (BF_3) (1:1) (8);
Ethane, 1,1'-oxybis-, compd. with trifluoroborane (1:1) (9); (109-63-7)