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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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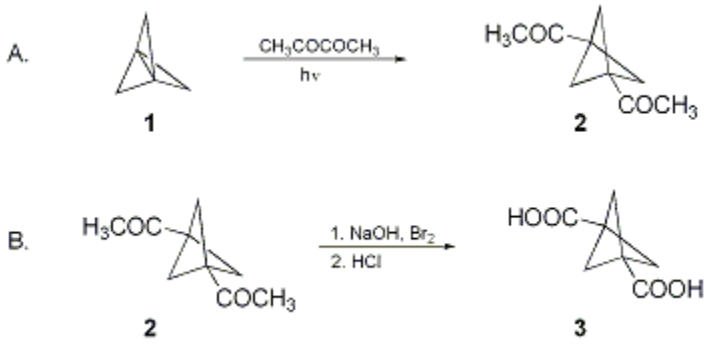
PHOTOCHEMICAL SYNTHESIS OF BICYCLO[1.1.1]PENTANE-1,3-DICARBOXYLIC ACID



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1. Procedure

A. 1,3-Diacetylbicyclo[1.1.1]pentane **(2)**. [1.1.1]Propellane is generated from 50 g (0.167 mol) of 1,1-dibromo-2,2-bis(chloromethyl)cyclopropane (Note 1) in pentane (Note 2) according to the procedure of Lynch and Dailey.[3] To the solution of [1.1.1]propellane, **1** (Note 3), is added 15 mL of freshly distilled 2,3-butanedione and the mixture is irradiated with a 450 W medium pressure UV lamp (Ace Glass Co, catalog no. 7825-34) at −10 ± 5°C for 8 hr (Note 4). Solvents are evaporated on a rotary evaporator. The resulting crystalline material is washed three times with cold 2:1 pentane:diethyl ether to give 16.95 g of 1,3-diacetylbicyclo[1.1.1]pentane **(2)** (Note 5). Another 1 g of the diketone is obtained upon concentration and crystallization of the pentane/diethyl ether rinses. Thus the total yield of **2** is 17.95 g [70% from 1,1-dibromo-2,2-bis(chloromethyl)cyclopropane], mp 67.5-69°C (lit.[4] mp, 67-69°C) (Note 6).

B. Bicyclo[1.1.1]pentane-1,3-dicarboxylic acid **(3)**. A 1-L, three-necked, round-bottomed flask, equipped with a mechanical stirrer, addition funnel, and thermometer is charged with a solution of 43.3 g (1.08 mol) of sodium hydroxide in 315 mL of water and 25.5 mL (79.1 g, 0.495 mol) of bromine . The mixture is cooled to 0°C. A solution of the diketone (10 g, 0.066 mol) obtained in Part A in 36 mL of dioxane is added dropwise at such a rate that the temperature does not exceed 3°C (Note 7). After the addition is finished, the reaction mixture is stirred for 1 hr at 0°C, then overnight at room temperature. Sodium bisulfite (1.8 g) is added and the solution is extracted with chloroform (3 × 50 mL). Subsequently, 36 mL of concd hydrochloric acid is added to the aqueous layer. After the acidified solution is cooled to room temperature, the mixture is continuously extracted with diethyl ether for 50 hr (Note 8) in an extraction apparatus. Evaporation of ether from the extract yields 9.68 g (94.5% from diketone **2**) of pure diacid **3**, mp 302-305°C, with decomposition [lit.[4] mp, 305°C (d)] (Note 9).

2. Notes

1. 1,1-Dibromo-2,2-bis(chloromethyl)cyclopropane was purchased from the Aldrich Chemical Company, Inc. It can be synthesized from 3-chloro-2-chloromethyl-1-propene, available from the Aldrich Chemical Company, Inc. , by phase-transfer dibromocyclopropanation.[3,5,6]
2. Pentane (98% grade) was obtained from Acros Organics and used without further purification.
3. The solution of [1.1.1]propellane should be warmed to −20-15°C to avoid crystallization of the 2,3-butanedione (which may not redissolve during the course of the irradiation).
4. It is recommended that the NMR spectrum of the reaction mixture be measured before discontinuing the irradiation. As long as any signal of [1.1.1]propellane (δ 2.0 ppm) is present, the irradiation should be continued.
5. The pentane-ether washes remove a yellow color from the crude product.

6. Spectral data were as follows: ^{1}H NMR δ: 2.14 (s, 6 H), 2.24 (s, 6 H) ; ^{13}C NMR δ: 26.6, 43.3, 52.0, 205.6 ; IR (KBr) cm^{-1}: 1699 . MS 152 (1, M^{+}), 137 (11), 109 (43), 95 (10), 43 (100), 39 (25) ; HRMS for $C_9H_{12}O_2$ calcd 152.0837, found 152.0835 . Anal. Calcd for $C_9H_{12}O_2$: C, 71.02; H, 7.95. Found: C, 71.01; H, 7.97.
7. Cooling of the reaction flask with an ice-salt or circulating bath held at −10°C helps to speed up the addition process.
8. Most of the product is extracted in the first 10 hr.
9. Spectral data were as follows: ^{13}C NMR (acetone d_6) δ: 38.1, 53.0, 170.6 ; IR (KBr) cm^{-1}: 3017, 1698 . Anal. Calcd for $C_9H_8O_4$: C, 53.85; H, 5.16. Found: C, 53.43; H, 5.30.

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

The procedure described above is an improved version of the one published by Kaszynski and Michl.[4] [1.1.1]Propellane is a recently reviewed[7] useful precursor for the synthesis of bicyclo[1.1.1] pentanes by radical addition across the central bond, followed by further transformations of the bridgehead substituents.[4,8] Under suitable conditions, one can obtain mixtures of [n]staffanes [oligomeric bicyclo[1.1.1]pentanes], which have been isolated in rapidly decreasing yields up to n = 5.[5,8] A review of their chemistry has appeared.[9]

References and Notes

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

Bicyclo[1.1.1]pentane-1,3-dicarboxylic acid (9); (56842-95-6)

1,3-Diacetylbicyclo[1.1.1]pentane:
Ethanone, 1,1'-(bicyclo[1.1.1]pentane-1,3-diyl)bis- (12); (115913-30-9)

[1.1.1]Propellane:
Tricyclo[1.1.1.$0^{1,3}$]pentane (9); (35634-10-7)

1,1-Dibromo-2,2-bis(chloromethyl)cyclopropane:
Cyclopropane, 1,1-dibromo-2,2-bis(chloromethyl)- (11); (98577-44-7)

2,3-Butanedione (9); (431-03-8)

Bromine (8,9); (7726-95-6)

3-Chloro-2-(chloromethyl)-1-propene:
1-Propene, 3-chloro-2-(chloromethyl)- (8,9); (1871-57-4)