



A Publication  
of Reliable Methods  
for the Preparation  
of Organic Compounds

## Working with Hazardous Chemicals

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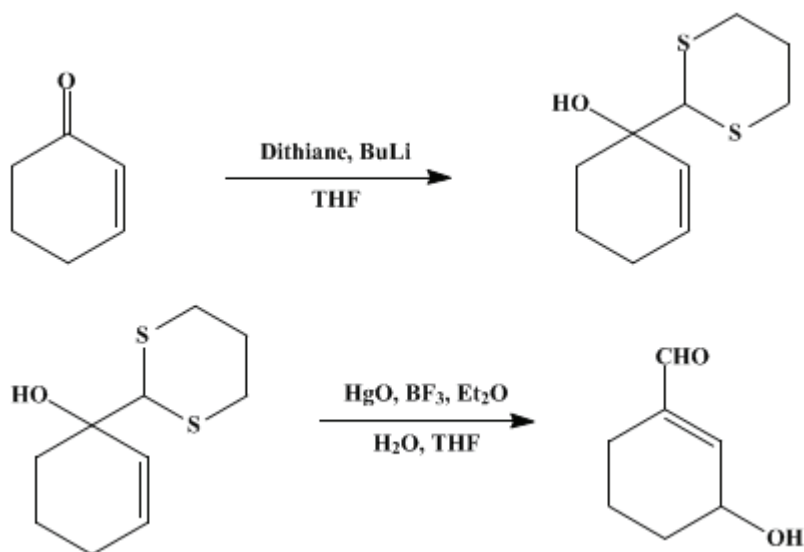
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*These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.*

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## 3-HYDROXY-1-CYCLOHEXENE-1-CARBOXALDEHYDE

### [1-Cyclohexene-1-carboxaldehyde, 3-hydroxy-]



Submitted by H. L. Rigby, M. Neveu, D. Pauley, B. C. Ranu, and T. Hudlicky<sup>1</sup>.  
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### 1. Procedure

A. *1-(1,3-Dithian-2-yl)-2-cyclohexen-1-ol* (2). To a suspension of 1,3-dithiane (Note 1) (12 g, 0.1 mol) in dry tetrahydrofuran (100 mL) (Note 2) at  $-78^{\circ}\text{C}$  is added butyllithium (40 mL, 2.5 M, 0.1 mol). The reaction is stirred for 2 hr. Initially the dithiane dissolves, followed by precipitation of the lithio salt. After 2 hr, 2-cyclohexen-1-one (9.6 g, 0.1 mol) (Note 3) in dry tetrahydrofuran (20 mL) is added dropwise. After about half of the cyclohexenone is added, the mixture becomes homogeneous. After the addition is complete, the reaction is stirred for an additional 30 min at  $-78^{\circ}\text{C}$  and then stored for 18 hr at  $0^{\circ}\text{C}$ . The solution is concentrated to one-fourth volume under reduced pressure. Water (100 mL) is added and the mixture is extracted with ether ( $3 \times 50$  mL). The extract is dried over sodium sulfate and evaporated to give an oil that is vacuum-distilled to give 14.0–14.7 g (65–68%) of the protected aldehyde 2, bp  $149\text{--}153^{\circ}\text{C}$  (0.8–1.0 mm) (Note 4).

B. *3-Hydroxy-1-cyclohexene-1-carboxaldehyde* (3). The hydroxy thioacetal 2 (5.5 g, 0.025 mol) in 25 mL of tetrahydrofuran is added dropwise to a mechanically stirred suspension of red mercuric oxide (11 g, 0.051 mol) (Note 5) and boron trifluoride etherate (7.2 g, 0.051 mol) (Note 6) in refluxing 15% aqueous tetrahydrofuran (50 mL). After the addition is complete, the mixture is stirred (Note 7) at reflux for an additional 2 hr. Another 5.5 g of red mercuric oxide is added and the reaction is stirred at reflux for 1 hr. The reaction is cooled to room temperature and ether (150 mL) is added, followed by 50 mL of brine. The mixture is filtered and the residue washed with ether ( $3 \times 50$  mL). The organic layer is separated and washed with saturated sodium bicarbonate solution ( $2 \times 50$  mL) and brine ( $1 \times 50$  mL). The organic layer is dried over sodium sulfate and the solvent evaporated to leave a residual oil. This oil is purified by medium-pressure liquid chromatography (silica gel, elution with 40% ethyl acetate in hexane) to give 1.5–1.6 g (47–50%) of the aldehyde 3, bp  $125^{\circ}\text{C}$  (0.075 mm) (Kugelrohr) (Note 8).

### 2. Notes

1. Dithiane was obtained from Aldrich Chemical Company, Inc. and was used without purification.
2. Tetrahydrofuran was distilled under nitrogen from potassium and benzophenone.
3. 2-Cyclohexen-1-one was obtained from Aldrich Chemical Company, Inc. and used as received.

4. The submitters report bp 157°C (1 mm). The spectral properties of **2** are as follows: IR (neat)  $\text{cm}^{-1}$ : 3450 (br), 3030, 2940, 2900 (sh), 2830, 1645 (w), 1425, 1280, 1185, 1085, 985;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz)  $\delta$ : 1.57–2.08 (m, 8 H), 2.40 (s, 1 H), 2.74–2.90 (m, 4 H), 4.17 (s, 1 H), 5.68 (d, 1 H,  $J = 10.05$ ), 5.85–5.91 (m, 1 H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 20 MHz)  $\delta$ : 18.53, 24.98, 25.75, 30.35, 30.54, 33.03, 59.54, 71.75, 129.43, 132.18; MS:  $\text{M}^+$  198, 120, 119 (base), 97, 91 (no  $\text{M}^+$  peak).

5. Mercuric oxide (red) was purchased from Aldrich Chemical Company, Inc. and used without purification.

6. Boron trifluoride etherate was distilled from calcium hydride at aspirator pressure.

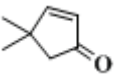
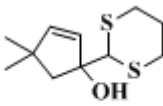
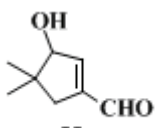
7. Mechanical stirring was found to be essential, and in some cases addition of sea sand to the reaction mixture reduced clogging of the reagents and led to higher yields.

8. The submitters report bp 70°C ( $10^{-4}$  mm). The spectral properties of **3** are as follows: IR (neat)  $\text{cm}^{-1}$ : 3400 (br), 2950, 2870, 2720, 1675, 1435, 1305, 1180, 1135, 1070, 1045, 995, 965, 925;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz)  $\delta$ : 1.47–1.54 (m, 2 H), 1.71–1.79 (m, 1 H), 1.90–1.98 (m, 1 H), 2.06 (s, 2 H), 3.49 (br s, 1 H), 4.37 (br s, 1 H), 6.63 (s, 1 H), 9.34 (s, 1 H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz)  $\delta$ : 18.54, 20.94, 31.35, 65.84, 77.43, 141.63, 150.88, 194.49; MS:  $\text{M}^+$  97 (base), 79, 69, 55, 41.

### 3. Discussion

Preparation of a compound such as **3** is useful where extensive functionalization of a cyclic enone is required. In addition to **3**, 4,4-dimethyl-3-hydroxy-1-cyclopentene-1-carboxaldehyde was prepared using the same procedure from 4,4-dimethyl-2-cyclopenten-1-one.<sup>2</sup> Table I gives yields and physical properties for this compound, which has been used as a starting material in the syntheses of coriolin and pentalenic acid.<sup>3,4</sup>

TABLE I  
PREPARATION OF 4,4-DIMETHYL-3-HYDROXY-1-CYCLOPENTENE-1-CARBOXALDEHYDE

Enone	Dithiane	Hydroxy Aldehyde
	 79% bp 130–132°C, 0.05 mm	 55%
	79% bp 130–132°C, 0.05 mm	55%

### References and Notes

1. Department of Chemistry, Virginia Polytechnic Institute and State University, Blacksburg, VA 24061.
2. Magnus, P. D.; Nobbs, M. S. *Synth. Commun.* **1980**, *10*, 273.
3. Hudlicky, T.; Kwart, L. D.; Tiedje, M. H.; Ranu, B. C.; Short, R. P.; Frazier, J. O.; Rigby, H. L. *Synthesis* **1986**, 716.
4. Hudlicky, T.; Sinai-Zingde, G.; Natchus, M. G.; Ranu, B. C.; Papadopolous, P. *Tetrahedron* **1987**, *43*, 5685.

**(Registry Number)**

brine

red mercuric oxide

Mercuric oxide (red)

coriolin

Hydroxy Aldehyde

ethyl acetate (141-78-6)

ether (60-29-7)

sodium bicarbonate (144-55-8)

sodium sulfate (7757-82-6)

nitrogen (7727-37-9)

Benzophenone (119-61-9)

potassium (7440-09-7)

butyllithium (109-72-8)

Tetrahydrofuran (109-99-9)

hexane (110-54-3)

boron trifluoride etherate (109-63-7)

dithiane (505-20-4)

calcium hydride (7789-78-8)

2-cyclohexen-1-one,  
cyclohexenone (930-68-7)

1,3-Dithiane (505-23-7)

4,4-Dimethyl-2-cyclopenten-1-one (22748-16-9)

3-Hydroxy-1-cyclohexene-1-carboxaldehyde,  
1-Cyclohexene-1-carboxaldehyde, 3-hydroxy- (67252-14-6)

1-(1,3-Dithian-2-yl)-2-cyclohexen-1-ol (53178-46-4)

4,4-dimethyl-3-hydroxy-1-cyclopentene-1-carboxaldehyde

## pentalenic acid

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