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of Reliable Methods
for the Preparation
of Organic Compounds

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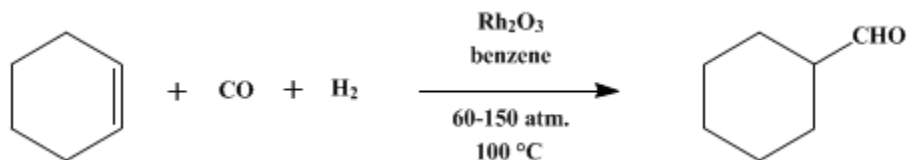
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

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ALDEHYDES FROM OLEFINS: CYCLOHEXANECARBOXALDEHYDE



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Checked by Mary M. Borecki, Joseph J. Mrowca, and Richard E. Benson.

1. Procedure

Caution! Benzene has been identified as a carcinogen; OSHA has issued emergency standards on its use. All procedures involving benzene should be carried out in a well-ventilated hood, and glove protection is required.

To a stainless-steel, 0.5-l. pressure vessel (Note 1) equipped with a 450-atm. manometer and a temperature recorder is added 0.2 g. (0.8 mmole) of rhodium(III) oxide (Note 2). The vessel is sealed and evacuated to 0.1 mm. pressure. A solution of 82 g. (1.0 mole) of cyclohexene (Note 3) in 140 ml. of anhydrous benzene is introduced by suction into the vessel. The vessel is placed in a heatable shaking device and pressured to 75 atm. with carbon monoxide; the total pressure is then increased to 150 atm. with hydrogen (Note 4). Shaking is begun and the vessel is heated to an internal temperature of 100° (Note 5). When the internal temperature reaches 100°, the pressure begins to fall. Whenever the pressure falls to 60 atm., rocking is stopped and the pressure is first increased to 105 atm. with carbon monoxide, then to 150 atm. with hydrogen. Rocking is started again, and the process is continued until no appreciable pressure decrease occurs. Approximately 2 hours is required, and the pressure decrease corresponds to the consumption of 2 moles of gas. The vessel is rapidly cooled to room temperature (Note 6) and the residual gas is carefully vented.

The vessel is opened, and the slightly yellow reaction mixture is transferred immediately to a 2-l., round-bottomed flask containing a freshly prepared solution of 200 g. of sodium hydrogen sulfite in 400 ml. of water. The flask is fitted with a stopper and is occasionally shaken at room temperature for a period of 3 hours (Note 7). The resulting precipitate is collected by suction filtration on a sintered-glass funnel and washed with 500 ml. of diethyl ether (Note 8). After drying in air, the bisulfite derivative is transferred to a 2-l. distillation flask containing 1 l. of 20% aqueous potassium carbonate. The resulting mixture is distilled, and the azeotropic mixture of water and aldehyde (b.p. 94–95°) is collected under nitrogen (Note 9).

The aldehyde is separated from the lower aqueous layer as a colorless liquid, dried over 10 g. of anhydrous sodium sulfate, filtered, and distilled under reduced pressure using a Claisen distillation apparatus, yielding 92–94 g. (82–84%) of cyclohexanecarboxaldehyde, b.p. 52–53° (18 mm.), n_D^{25} 1.4484 (Note 10), (Note 11). A purity of about 98% was established by GC analysis (Note 12); the product is suitable for synthetic use without further purification (Note 13).

2. Notes

1. The pressure vessel was tested to a pressure of 700 atm. at 300°.
2. The submitters used rhodium(III) oxide available from Fluka A G without further purification. The checkers obtained rhodium(III) oxide from Alfa Inorganics.
3. The cyclohexene was purified by distillation over sodium metal before use (n_D^{25} 1.4452). The submitters used the product available from Fluka A G, and the checkers used the product available from Aldrich Chemical Company, Inc.

4. The purity of the gases used was greater than 99%.
5. During the course of the reaction the temperature was maintained at $100^{\circ} \pm 2^{\circ}$.
6. This procedure avoids secondary reactions of the aldehydes, which lead to high-boiling products. It is particularly advisable when linear aliphatic aldehydes are synthesized using cobalt catalysts.³
7. The formation of the bisulfite derivative is an exothermic reaction; the flask is cooled with a bath of cold water for the first 10–15 minutes.
8. It is impossible to obtain a completely white precipitate by this procedure.
9. In order to avoid oxidation of the product the submitters recommend use of a nitrogen atmosphere for all manipulations involving cyclohexanecarboxaldehyde.
10. Literature⁴ values for cyclohexanecarboxaldehyde: b.p. $78.5\text{--}80^{\circ}$ (57 mm.), n_D^{25} 1.4485.
11. Cyclohexanecarboxaldehyde is stable at room temperature under nitrogen; the submitters noted no appreciable variation in the refractive index after 30 days.
12. The submitters state that GC analysis was made using a 2-m. column packed with polypropylene glycol (LB-550-X available from Perkin-Elmer) on Chromosorb. The retention time at 140° is 5.2 minutes at a flow rate of 30 ml./minute of nitrogen. The 2,4-dinitrophenylhydrazone derivative⁴ melts at $173\text{--}174^{\circ}$, and the semicarbazone derivative⁵ melts at $172\text{--}173^{\circ}$.
13. In addition to rhodium(III) oxide, cobalt(II) acetylacetonate or dicobalt octacarbonyl has been used by the submitters as catalyst precursors for the hydroformylation of cyclohexene. The results are given in Table I.

TABLE I
HYDROFORMYLATION OF CYCLOHEXENE WITH COBALT CATALYSTS^a

Catalyst Precursor (mole/l.)	Solvent ^b	Reaction Temperature	Reaction Time (hours)	Yield ^c (%)
[Bis(acetylacetonate) cobalt(II)] (0.08)	Benzene	$150^{\circ d}$	1.5	70
[Bis(acetylacetonate) ^e cobalt(II)] (0.08)	Heptane	110°	12	74
Dicobalt octacarbonyl ^f (0.006)	Benzene	120°	8	80

^a 4.15 mole/l. of cyclohexene; CO:H₂ = 1:1; 150 atm. initial pressure.

^b 140 ml.

^c The aldehyde was isolated from the reaction mixture through its bisulfite derivative as described in the procedure.

^d Induction time, 40–60 minutes.

^e This catalyst precursor (5 g.) in 140 ml. of heptane was heated in the autoclave at 160° with a mixture of CO:H₂ (1:1) at 150 atm. for 2 hours. The vessel was cooled, the gas released, 1 mole of cyclohexene was charged, and the reaction was carried out according to the usual procedure.

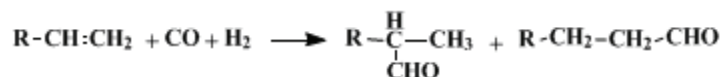
^f The submitters used product available from Fluka A G that was dried under reduced pressure after recrystallization from heptane at -70° .

3. Discussion

This preparation is an illustration of the hydroformylation of olefins (oxo synthesis). The reaction occurs in the presence of soluble catalytic complexes of Group VIII metals. Although the metal originally used by Roelen⁶ and still largely used in industry for the production of aliphatic aldehydes and alcohols⁷ is cobalt, the most active and selective catalysts are rhodium-containing compounds. The catalytic activity of the other Group VIII metals is, in general, much poorer. Although the hydroformylation of unsaturated substrates is a very general reaction,^{7,8} some important limitations associated with the olefin structure may lead to the formation of isomeric aldehydes. In addition, especially in the presence of cobalt catalysts, further reactions of synthesized aldehydes may occur under hydroformylation conditions.

With regard to the structure of the olefins, tetrasubstituted olefins do not undergo hydroformylation

under typical reaction conditions, and olefinic substrates containing functional groups sometimes give poor yields and unexpected products.^{7,8} If there is no plane of symmetry in the substrate across the double bond, at least two isomeric aldehydes are obtained.⁹ Although methods for shifting the isomeric composition of the products have been proposed,^{12,13,14} complete control of the isomeric composition has not been achieved despite the fact that the reaction mechanism is fairly well understood.¹⁵ In addition, if the structure of the olefin is such that a double-bond shift is possible, isomers other than the two shown below can be formed.¹⁰ Further reactions of the synthesized aldehydes may occur, especially when cobalt catalysts are used, leading to alcohols, aldol condensation products or acetal derivatives. Some of the secondary reactions can be avoided by carrying out the hydroformylation in the presence of orthoformic acid esters¹⁶ or of other reagents protecting the aldehyde group.¹⁷ However, care must be taken when ortho esters are used, since hydroformylation of ortho esters may occur and yield aldehydes or acetals.¹⁸



Although cobalt catalysts are the best known and the most commonly used, in recent years rhodium has been preferred for laboratory syntheses because of its higher activity and selectivity. As catalyst precursors Rh_2O_3 ,¹¹ $\text{Rh}_4(\text{CO})_{12}$,¹⁹ or $\text{HRh}(\text{CO})(\text{PPh}_3)_3$ ¹³ are commonly used. Rhodium complexes supported on polymers have also been used.¹⁴ For typical organic syntheses the easily accessible Rh_2O_3 seems preferable, even if higher temperature and pressures are required to carry out the olefin hydroformylation. Using $\text{HRh}(\text{CO})(\text{PPh}_3)_3$, olefin hydroformylation at room temperature and pressure is possible.¹³ Carrying out the reaction in the presence of (-)DIOP [(4*R*,5*R*)-2,2-dimethyl-4,5-bis(5-dibenzophosphol-5-ylmethyl)-1,3-dioxolane], produced optically active aldehydes from monosubstituted ethylenes, as well as from 1,1- and 1,2-disubstituted ethylenes.²⁰

The hydroformylation of cyclohexene has been extensively investigated.^{13,14,16,21,22,23} The present procedure is an adaptation of the rhodium-catalyzed hydroformylation of 2-butene.¹¹

Other methods for the preparation of cyclohexanecarboxaldehyde include the catalytic hydrogenation of 3-cyclohexene-1-carboxaldehyde, available from the Diels–Alder reaction of butadiene and acrolein,²⁴ the reduction of cyclohexanecarbonyl chloride by lithium tri-*tert*-butoxyaluminum hydride,²⁵ the reduction of *N,N*-dimethylcyclohexanecarboxamide with lithium diethoxyaluminum hydride,²⁶ and the oxidation of the methane sulfonate of cyclohexylmethanol with dimethyl sulfoxide.²⁷ The hydrolysis, with simultaneous decarboxylation and rearrangement, of glycidic esters derived from cyclohexanone gives cyclohexanecarboxaldehyde.^{4,28}

References and Notes

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

cobalt(II) acetylacetonate

Bis(acetylacetonate) cobalt(II)

Bis(acetylacetonate)^e cobalt(II)

(-)DIOP [(4R,5R)-2,2-dimethyl-4,5-bis(5-dibenzophosphol-5-ylmethyl)-1,3-dioxolane]

methane sulfonate of cyclohexylmethanol

potassium carbonate (584-08-7)

Benzene (71-43-2)

diethyl ether (60-29-7)

hydrogen (1333-74-0)

carbon monoxide (630-08-0)

Acrolein (107-02-8)

Cyclohexanone (108-94-1)

Cyclohexene (110-83-8)

sodium sulfate (7757-82-6)

nitrogen (7727-37-9)

sodium hydrogen sulfite (7631-90-5)

sodium (13966-32-0)

butadiene (106-99-0)

heptane (142-82-5)

cobalt (7440-48-4)

dimethyl sulfoxide (67-68-5)

N,N-Dimethylcyclohexanecarboxamide (17566-51-7)

Cyclohexanecarboxaldehyde (2043-61-0)

cyclohexanecarbonyl chloride (2719-27-9)

rhodium (7440-16-6)

rhodium(III) oxide (12036-35-0)

2-butene

3-cyclohexene-1-carboxaldehyde

lithium diethoxyaluminum hydride

lithium tri-tert-butoxyaluminum hydride