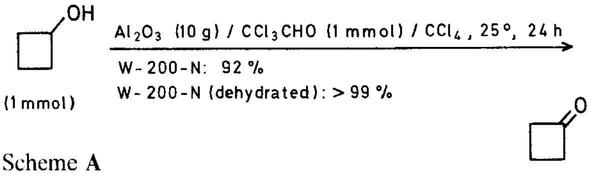
Organic Reactions at Alumina Surfaces. Mild, Selective, and High-Yield Oxidation of Cyclobutanol to Cyclobutanone[1]

Gary H. Posner*, Marc J. Chapdelaine

Department of Chemistry, The Johns Hopkins University, Baltimore, Maryland 21218, U.S.A.

Oxidation of strained cycloalkanols is often accompanied by fragmentation of the carbon skeleton. Cyclobutanols in particular are difficult to convert cleanly into the corresponding cyclobutanones[2]. One-electron oxidants such as chromium and cerium compounds cause cyclobutanol ring cleavage, and this characteristic fragmentation process has been used to distinguish between one- and two-electron oxidants; two-electron oxidizing agents generally produce no ring opened products[3].

Ruthenium tetroxide converts cyclobutanols into cyclobutanones, but this vigorous oxidizing agent reacts also with alkenes (cleavage to ketones, aldehydes, and acids), with arenes (oxidation to dicarboxylic acids), and with ethers (oxidation to esters)[2c,4]. Likewise, 1-chlorobenzotriazole effects cyclobutanol to cyclobutanone oxidation, but this oxidant poses the danger of spontaneous ignition and it forms adducts with alkenes[5]. We report here that trichloroacetaldehyde (chloral) on activated. Woelm, neutral chromatographic alumina at room temperature converts cyclobutanol cleanly and reproducibly into cyclobutanone in >99% yield (Scheme **A**) and that alkenes, arenes, ethers, and amines are stable under these conditions. The cyclobutanol oxidation in Scheme **A** was performed on 0.25 g scale; we have done larger scale (e.g., 6 g) carbonyl reduction and alcohol oxidation reactions of other systems on activated alumina[1], and therefore we envision no problem in oxidizing larger quantities of cyclobutanol[6]. As a control, cyclobutanol was oxidized by chloral on activated alumina also in the presence of 1-tetradecene, which was recovered in 99% yield. Using benzaldehyde or cinnamaldehyde in place of chloral, cyclobutanone was formed in 58% or 99% yield. Using 10 g of *unactivated* Woelm-200 neutral alumina directly from the commercial can and 1 mmol each of cyclobutanol and chloral, we obtained 92% conversion to cyclobutanone (<1% recovered cyclobutanol). Attempted Oppenauer oxidation[7] of cyclobutanol using acetone and aluminum isopropoxide in refluxing benzene gave very poor results.



Scheme **A**

This report extends our recent results using chloral on dried alumina for selective heterogeneous oxidation of various secondary alcohols, including 1-phenylethanol (an arene) and 2-norbornen-5-ol (an alkene), under conditions which allow survival of cyclohexyl methyl ether and of *N*,*N*-dimethylbenzylamine[8]. We have found that chloral/alumina also effectively oxidizes cyclopentanol into cyclopentanone. Alumina-promoted oxidation of cyclobutanol without any fragmentation indicates that chloral acts as a hydride acceptor and thus as a two-electron oxidant[2]. The mildness, functional group selectivity, high yield, and convenient product isolation make chloral on alumina a promising new reagent for oxidation of strained cycloalkanols even in the presence of many other types of sensitive functional groups.

Cyclobutanone from Cyclobutanol:

Woelm W-200 neutral alumina (ICN Pharmaceuticals, Inc., Cleveland, Ohio) is heated in a quartz vessel at 400° and 0.06 torr for 24 h. About 10 g of the dehydrated alumina is transferred inside a nitrogen-filled glove bag to an oven-dried, tared 25 ml round bottom flask containing a magnetic stirring bar. The flask is stoppered and removed from the glove bag. Carbon tetrachloride (~10 ml) containing cyclobutanol (82 mg, 1.13 mmol) is added. After stirring for 0.5 h at 25°, freshly distilled trichloroacetaldehyde (166 mg, 1.13 ml) in carbon tetrachloride (1 ml) is added and stirring is continued for 24 h at 25°. The reaction is quenched by addition of methanol (5 ml) and stirring for 15 min. Vacuum filtration through Celite and washing the alumina with methanol (35 ml) gives >99% cyclobutanone and <1% cyclobutanol as determined by vapor phase chromatography (10′ × 0.125″ in 5% SE-30 Chromosorb G 100/140) with decane as a calibrated internal standard and as identified by comparison with known samples.

In a larger scale experiment using cyclobutanol (0.25 g, 3.5 mmol), addition of the product mixture solution to a freshly prepared 2,4-dinitrophenylhydrazine solution gives the crude 2,4-dinitrophenylhydrazone. Recrystallization affords the 2,4-dinitrophenylhydrazone of cyclobutanone with identical spectral and physical properties to those of an authentic sample: yield: 0.69 g (79%); m.p. 144°; Lit.[9] m.p. 143–145°.

^{1}H-N.M.R. ($CDCl_3$): $\delta = 10.7$ (broad, 1 H, NH); 9.1 (d, 1 H); 8.45–7.65 (m, 2 H); 3.35–2.9 (m, 4 H, $-\underline{CH_2}-C{=}N$); 2.5–2.0 ppm (m, 2 H).

Hydrolysis of 2,4-dinitrophenylhydrazones into the corresponding ketones can be achieved in several different ways[10].

Acknowledgment is made to the NIH (CA-16068) for financial support and to Professor K. B. Wiberg (Yale University) for pointing out to us the difficulty of cyclobutanol oxidation.

Received: February 7, 1977
(Revised form: April 5, 1977)

---

[1] For use of 2-propanol on alumina for selective carbonyl reductions, see G. H. Posner, A. W. Runquist, M. J. Chapdelaine, *J. Org. Chem.* **42**, 1202 (1977).

[2] (a) J. M. Conia, J. Gore, *Bull. Soc. Chim. Fr.* **1963**, 726.
(b) K. B. Wiberg, Ed., *Oxidation in Organic Chemistry*, Part A; Academic Press, New York, New York, 1965.
(c) W. S. Trahanovsky, Ed., *Oxidation in Organic Chemistry*, Part B; Academic Press, New York, New York, 1973, Ch. 4.

[3] (a) M. Rahman, J. Rocek, *J. Am. Chem. Soc.* **93**, 5455, 5462 (1971) and references therein.
(b) J. Rocek, D. E. Aylward, *J. Am. Chem. Soc.* **97**, 5452 (1975).
(c) K. B. Wiberg, S. K. Mukherjee, *J. Am. Chem. Soc.* **96**, 6647 (1974) and references therein.
(d) For lead(IV) acetate oxidation of cyclobutanol, see M. L. Mihailović, Ž. Čerović, V. Andrejević, R. Matić, D. Jeremić, *Tetrahedron* **24**, 4947 (1968).

[4] J. A. Caputo, R. Fuchs, *Tetrahedron Lett.* **1967**, 4729.

[5] (a) J. B. Sieja, *J. Chem. Eng. Data*, **17**, 108 (1972).
(b) C. W. Rees, R. C. Storr, *J. Chem. Soc. [C]* **1969**, 1478.

[6] Larger scale oxidations were not done because cyclobutanol is so expensive ($ 31/g from Aldrich Chemical Co.).

[7] C. Djerassi, *Org. React* **6**, 207 (1951).

[8] G. H. Posner, R. B. Perfetti, A. W. Runquist, *Tetrahedron Lett.* **1976**, 3499.

[9] F. Hasan, J. Rocek, *J. Am. Chem. Soc.* **96**, 534 (1974).

[10] See: I. T. Harrison, S. Harrison, *Compendium of Organic Synthetic Methods*, Wiley-Interscience, New York, New York, 1971, p. 456.