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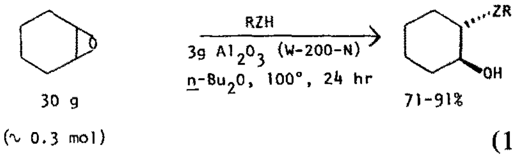
Alumina-Catalyzed Opening of Cyclohexene Oxide by Alcohols, Acetic Acid, and Aniline

Solid supports are essential for many industrial processes, especially those used in the petrochemical industry. Many different types of organic reactions are catalyzed efficiently and economically by diverse natural and synthetic solids; several reviews are available (*1*). We have reported recently that stoichiometric amounts of commercially available chromatographic γ-alumina promote heterogeneous opening of a wide range of epoxides by a variety of nucleophiles (e.g., alcohols, acetic acid, amines, mercaptans, selenols) under extraordinarily mild (25°C) and neutral conditions (*2*). We report here our discovery that *catalytic* amounts of Woelm alumina at 100°C cause stereospecific *trans*-opening of a representative olefin epoxide, cyclohexene oxide, by alcohols, acetic acid, and aniline.

As shown in Eq. (1) and Table 1, 3g of Woelm-200-neutral alumina (activity "super-1" on the Brockmann scale) (*3*) effects clean opening of 30 g of cyclohexene oxide by methanol, allyl alcohol, acetic acid, and aniline. 1,2-Glycol monoethers and monoesters and 1,2-amino-alcohols are valuable industrial intermediates. Alcoholysis has usually been achieved *homogeneously* by treating epoxides with alcohols and strong acids or strong bases, and homogeneous aminolysis of epoxides often requires vigorous reaction conditions and often leads to a mixture of products which are difficult to separate (*4*). In contrast, Eq. (1) represents a reproducible, convenient, simple, efficient, neutral, nonaqueous new procedure for preparation of multigram quantities of *trans*-1,2-glycol and *trans*-1,2-amino-alcohol derivatives. This alumina catalysis (i.e., catalytic conversion of 100 mmol of epoxide per 1 g of alumina) compares favorably with zeolite catalysts used for this type of process (*5*). Indeed these alumina-catalyzed epoxide openings have some distinct advantages over the zeolite reaction: (1) much higher conversion of epoxide to product and (2) ability to tolerate large (e.g., steroidal) (*2*) epoxides and large nucleophiles (e.g., aniline).



(1)

A typical procedure is given below.

W-200-N alumina (surface area ≈200 m^2/g) was obtained from ICN Pharmaceuticals (Cleveland, Ohio) or from Woelm (Eschwege, West Germany) and was used as received. Alumina freshly opened in a glove bag could be doped with RZH (e.g., allyl alcohol) and sealed in a glass vial; after 56 days, reaction of this stored alcohol-doped alumina with cyclohexene oxide gave results essentially the same as those reported in Table 1.

Cyclohexene oxide (Aldrich) was used as received. Di-*n*-butyl ether (Aldrich), allyl alcohol (Aldrich), methanol (Baker), acetic acid (Mallinckrodt), and aniline (Fisher) were distilled at atmospheric pressure prior to use.

A 500-ml, one-necked round bottom flask containing a 1-in. magnetic stirring bar was dried in a vacuum oven at 120°C for 1 hr. After being stoppered and cooled to room temperature, the flask was placed in a nitrogen-filled glove bag and was charged with 3.0 g of Woelm-200-neutral chromatographic alumina from a freshly opened container. Outside of the glove bag the flask was further charged with 70 ml of di-*n*-butyl ether, 97.1 g (1.04 mol) of aniline, and 20.5 g of (0.21 mol) cyclohexene oxide. After stoppering the flask, stirring was started

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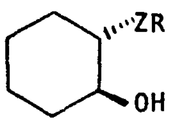
TABLE 1

Alumina-Catalyzed Opening of Cyclohexene Oxide by Various Nucleophiles RZH According to Eq. (1)

RZH	Product		
		Percentage yield (after distillation)	bp °C (mm Hg)
$CH_2{=}CHCH_2OH$	$OCH_2CH{=}CH_2$	70–78 (86)[b]	45.0–45.5 (0.2)[c]
CH_3OH[a]	OCH_3	87	90.5 (15)[d]
CH_3COOH	$OOCCH_3$	71	120 (15)[e]
$PhNH_2$	NHPh	85–91	mp 57.5–59[f]

[a] 65°C instead of 100°C reaction temperature for 24 hr.

[b] Yield using 6 g of alumina and 60 g of cyclohexene oxide.

[c] Lit bp 59°C (0.5 mm); Harding, J. S., and Owen, L. N., *J. Chem. Soc.* 1536 (1954).

[d] Lit bp 72.5–73.2°C (10 mm); Winstein, S., and Henderson, R. B., *J. Amer. Chem. Soc.* **65**, 2196 (1943).

[e] Lit bp 110–111°C (10 mm); Mamedov, S., and Nizker, I. L., *Zh. Obshch. Khim.* **33**, 841 (1963).

[f] Lit mp 58°C; Brunel, L., *Ann. Chim. Phys.* s8, **6**, 261 (1905); cf. Lewis, J. W., Myers, P. L., and Ormerod, J. A., *J. Chem. Soc. Perkin I* **20**, 2521 (1972), *cis*-2-anilinocyclohexanol, mp 72–74°C.

and the temperature raised by immersion of the lower half of the flask in an oil bath. The suspension was stirred rapidly and heated at 100°C for 24 hr, after which it was cooled to room temperature. Cooling was followed by addition of 100 ml of absolute methanol. After stirring for an additional 10 min, suction filtration through a sintered glass funnel containing a pad of celite gave a clear, light-yellow solution. Rotary evaporation of the methanol and most of the di-*n*-butyl ether followed by fractional distillation under reduced pressure (145°C, 0.4 mm) gave 36.7 g (91%) of *trans*-2-anilinocyclohexanol, mp 55–56.6°C, spectral properties of which were in excellent agreement with those of a sample previously prepared (2).

Recrystallization from 5% di-*n*-ethyl ether in pet. ether gave 34.9 g (85%) of the amino alcohol, mp 57–58°C.

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