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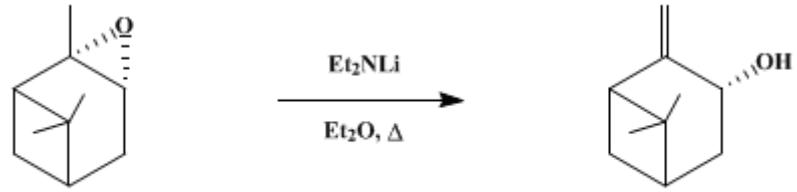
BASE-INDUCED REARRANGEMENT OF EPOXIDES TO ALLYLIC ALCOHOLS: *trans*-PINOCARVEOL

[Bicyclo[3.3.1]heptan-3-ol, 6,6-dimethyl-2-methylene-, (1α,3α,5α-]



α - pinene oxide — *trans* - pinocarveol

Submitted by J. K. Crandall[1] and L. C. Crawley.
Checked by Shoichiro Uyeo and Wataru Nagata.

1. Procedure

A dry, 300-ml., three-necked, round-bottomed flask is fitted with an effective reflux condenser, a 50-ml. pressure-equalizing dropping funnel, a rubber septum, a magnetic stirring bar, and a nitrogen inlet tube on the top of the condenser to maintain a static nitrogen atmosphere in the reaction vessel throughout the reaction. The flask is flushed with dry nitrogen, then charged with 2.40 g. (0.0329 mole) of diethylamine (Note 1) and 100 ml. of anhydrous diethyl ether (Note 2). The flask is immersed in an ice bath, the stirrer is started, and 25 ml. (0.035 mole) of 1.4 *M* *n*-butyllithium in hexane (Note 3) and (Note 4) is added carefully through the rubber septum with a syringe. After stirring for 10 minutes, the ice bath is removed and 5.00 g (0.0329 mole) of α-pinene oxide (Note 5) in 20 ml. of anhydrous ether is added dropwise over a 10-minute period. The resulting mixture is heated to reflux with stirring for 6 hours (Note 11). After the clear homogeneous mixture is cooled in an ice bath, it is stirred vigorously while 100 ml. of water is added. The ether phase is separated and washed successively with 100 ml. portions of 1 *N* hydrochloric acid, water, saturated aqueous sodium hydrogen carbonate, and water. The aqueous phase and each washing are extracted twice with 50 ml. portions of ether, and the ethereal extracts are combined and dried over anhydrous magnesium sulfate. Evaporation of the solvent on a rotary evaporator yields a light-yellow, oily residue which is distilled through a short-path distillation head, giving 4.50–4.75 g. (90–95%) of *trans*-pinocarveol as a colorless oil, b.p. 92–93° (8 mm.) n_D^{25} 1.4955 (Note 12) and (Note 13).

2. Notes

1. Commercial diethylamine, b.p. 55–58°, purchased from Fisher Scientific Company, was distilled from calcium hydride before use. The checkers used material purchased from Kanto Chemical Company, Inc. (Japan) and distilled it from sodium hydride.
2. The checkers used anhydrous ether, distilled from sodium hydride before use.
3. The *n*-butyllithium in hexane solution was purchased from Foote Mineral Company. The checkers obtained their material from Wako Pure Chemical Industries Ltd. (Japan) and titrated it with 0.80 *M* 2-butanol in xylene using 1,10-phenanthroline as indicator.[2] Care should be exercised in handling *n*-butyllithium solutions.
4. The submitters used about three molar equivalents of lithium diethylamide in about twice as much solvent. The checkers found that an amount of base slightly in excess of one molar equivalent was sufficient to convert the epoxide to exocyclic methylene alcohol of superior purity.
5. The submitters purchased α-pinene oxide from F.M.C. Corporation. However, since the compound is no longer available, the checkers prepared it from α-pinene as follows. A three-necked, round-bottomed flask fitted with a 50-ml. dropping funnel, a thermometer, and a magnetic stirring bar is charged with 22.0 g. (0.102 mole) of *m*-chloroperbenzoic acid (Note 6), 11.0 g. (0.131 mole) of sodium hydrogen carbonate, and 250 ml. of dichloromethane. The suspension is stirred with a powerful stirrer while being

cooled with an ice–salt bath. To this mixture is added dropwise a solution of 13.6 g. (0.010 mole) of α-pinene (Note 7) in 20 ml. of dichloromethane at a rate such that the inner temperature is kept between 5–10° (Note 8). During the addition, sodium *m*-chlorobenzoate begins to crystallize indicating that the reaction is proceeding. After completion of the addition, stirring is continued for 1 hour longer at the same temperature (Note 9). A solution of 5 g. of sodium sulfite in 50 ml. of water is added, and the mixture is stirred vigrously at room temperature for 30 minutes. Water (50 ml.) is added, and the dichloromethane phase is separated and washed with 100 ml. of 5% aqueous sodium carbonate. The two aqueous washings are extracted with 50 ml. of dichloromethane, and the organic solutions are combined and dried over anhydrous magnesium sulfate. Evaporation of the solvent on a rotary evaporator gives an oily residue that is distilled through a vacuum-jacketed column, yielding 12.5–12.8 g. (82–85%) of α-pinene oxide as a colorless oil, b.p. 89–90° (28 mm.) (Note 10).

6. *m*-Chloroperbenzoic acid was obtained from F.M.C. Corporation. It was shown to be 80% pure by titration.

7. Technical grade α-pinene, purchased from Wako Pure Chemical Industries Ltd. (Japan), was used without purification.

8. A more efficient cooling system, such as an acetone–dry ice bath, is necessary to shorten the addition time in large-scale preparations.

9. Completion of the reaction may be checked by GC.

10. GC of this product using a 1-m. column containing 5% KF-54 on Chromosorb W at 100° gave a single peak. The material gave the following $_1$H NMR spectrum ($CDCl_3$): δ 0.95, 1.30, and 1.33 (3 s, 9H, 3CH_3), 1.53–2.20 (m, 6H, 2CH_2 and 2C*H*), 3.03 (m, 1H, C*H*OC). The boiling point is reported to be 70–71° (12 mm.).[3]

11. Completion of the reaction may be checked by GC analysis. Refluxing for prolonged periods can give saturated ketone as an impurity if excess base is used.

12. The reported[4] value is n_D^{20} 1.4993.

13. The spectral properties are: IR (neat) cm.$^{-1}$ 3360 ms (OH), 1644 vw (C=C), 893 ms (C=CH_2); $_1$H NMR ($CDCl_3$): δ 0.65 and 1.28 (2 s, 6H, 2CH_3), 1.63–2.55 (m, 6H, 2CH_2 and 2C*H*), 4.42 (d, *J* = 7 Hz., 1H, C*H*OH), 4.82 and 5.00 (2 m, 2H, C=CH_2). Purity of the product is greater than 98% as determined by GC using a Carbowax 20 M on 60–80 Chromosorb W column or a 1-m. column containing 5% KF-54 on Chromosorb W at 100°.

3. Discussion

Pinocarveol has been prepared by the autoxidation of α-pinene,[5] by the oxidation of β-pinene with lead tetrăcetate,[6] and by isomerization of α-pinene oxide with diisobutylaluminum,[7] lithium aluminum hydride,[8] activated alumina,[9] potassium *tert*-butoxide in dimethyl sulfoxide,[10] and lithium diethylamide.[11] The present method is preferred for the preparation of pinocarveol, since the others give mixtures of products. It also illustrates a general method for converting 1-methylcycloalkene oxides into the corresponding exocyclic methylene alcohols.[11] The reaction is easy to perform, and the yields are generally high.

In general, the strong base isomerization of epoxides to allylic alcohols constitutes a useful synthetic reaction. Since the rearrangement is a highly specific process, it should be of value in organic synthesis. For example, there is a very high propensity for Hofmanntype eliminations to yield the least substituted double bond from unsymmetrically substituted epoxides.[12] There is also a large conformational effect arising from the operation of a syn-elimination mechanism which leads to specificity in conformational eliminations of cyclic epoxides.

This preparation is referenced from:

- Org. Syn. Coll. Vol. 6, 946

References and Notes

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

alumina

trans-Pinocarveol

Bicyclo[3.3.1]heptan-3-ol, 6,6-dimethyl-2-methylene-, (1α,3α,5α-

Pinocarveol

hydrochloric acid (7647-01-0)

ether,
diethyl ether (60-29-7)

sodium sulfite (7757-83-7)

sodium hydrogen carbonate (144-55-8)

sodium carbonate (497-19-8)

nitrogen (7727-37-9)

xylene (106-42-3)

diethylamine (109-89-7)

dichloromethane (75-09-2)

magnesium sulfate (7487-88-9)

butyllithium,
n-butyllithium (109-72-8)

lithium aluminum hydride (16853-85-3)

sodium hydride (7646-69-7)

hexane (110-54-3)

dimethyl sulfoxide (67-68-5)

lithium diethylamide

calcium hydride (7789-78-8)

2-Butanol (78-92-2)

1,10-phenanthroline (66-71-7)

methylene alcohol (463-57-0)

α-pinene oxide (72936-74-4)

diisobutylaluminum (1191-15-7)

α-pinene (7785-70-8)

β-pinene (18172-67-3)

m-Chloroperbenzoic acid (937-14-4)

potassium tert-butoxide (865-47-4)

sodium m-chlorobenzoate

lead tetracetate (546-67-8)