Stereoselective Epoxidation of 3-*trans*-Benzylideneisoborneol

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2-Benzylidenecyclopentanol (**2**) can be epoxidized stereoselectively to furnish 2-*trans*-benzylidene-1β-hydroxycyclopentane β-oxide (**4**) with either *t*-butyl hydroperoxide in the presence of vanadium catalyst or *m*-chloroperoxybenzoic acid. Epoxidation of 3-*trans*-benzylideneisoborneol (**10**) with *t*-butyl hydroperoxide-vanadium catalyst furnishes stereoselectively 3-*trans*-benzylideneisoborneol *exo*-oxide (**11**) whereas epoxidation of alcohol **10** with *m*-chloroperoxybenzoic acid furnishes stereoselectively 3-*trans*-benzylideneisoborneol *endo*-oxide (**14**).

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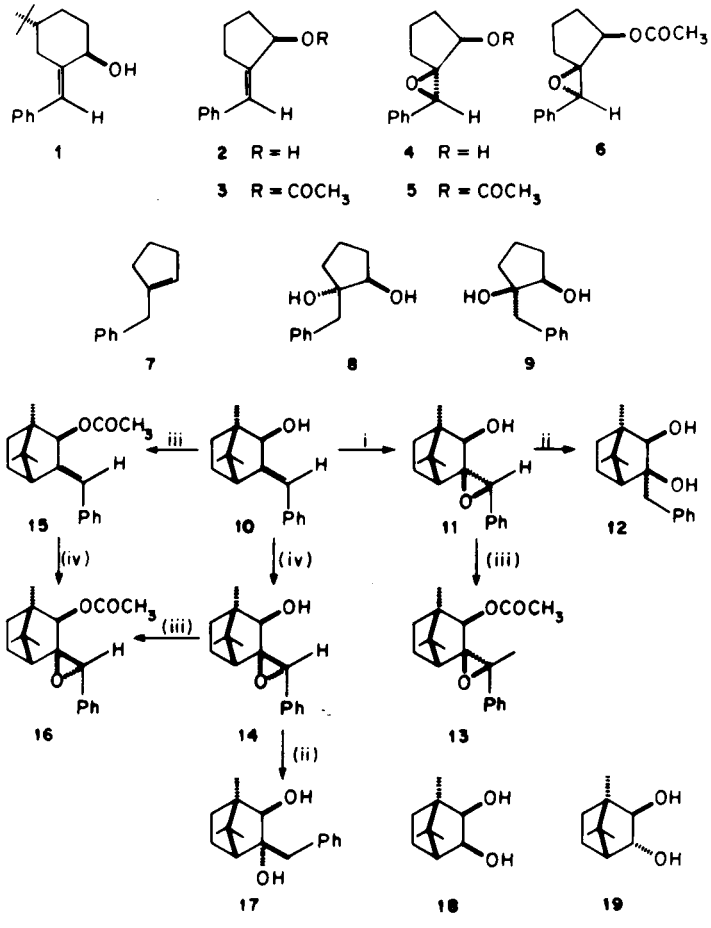
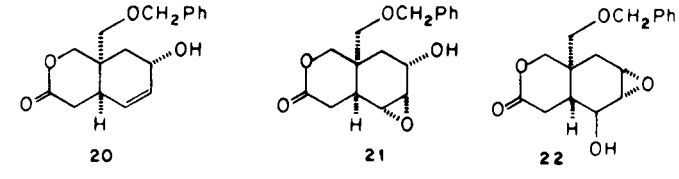
Several epoxy alcohols prepared through epoxidation of cyclic as well as acyclic allylic alcohols have proved useful in the synthesis of complex natural products [2-8]. Hydroxyl directed stereoselective *cis*-epoxidation of allylic cyclohexenols and allylic cyclopentenols having endocyclic double bonds can be carried out with either *t*-butyl hydroperoxide in the presence of a vanadium catalyst or a per-acid [9]. Our investigations [10,11] and also the investigations of Chautemps and Pierre [12] have shown that per-acid epoxidation of allylic alcohols having double bond exocyclic to cyclohexane ring, *e.g.* alcohol **1**, is not stereoselective if the hydroxyl is equatorial; even with *t*-butyl hydroperoxide-vanadium catalyst epoxidation of alcohol **1** and related compounds is not stereoselective [13]. Considering the importance of epoxy alcohols in organic synthesis and the occurrence of spiro oxiranes [14,15] as natural products we have studied the stereochemistry of epoxidation of allylic alcohols **2** and **10**. The results of this investigation are presented in this article.

The alcohol **2** was chosen for the study because of the ring size and the lack of severe steric interference for the approach of epoxidizing reagents. The alcohol **10** was chosen for study since it has a rigid ring structure and one of the geminal methyl groups can offer steric hindrance for hydroxylation from the side *cis* to the hydroxyl. The C-O bond in **2** as well as in **10** makes a dihedral angle of about 60° with the plane of the double bond and is hence favourably situated for directing *cis*-epoxidation with *m*-chloroperoxybenzoic acid or *t*-butyl hydroperoxide-vanadium catalyst [16]. Epoxidation of alcohol **2** with *t*-butyl hydroperoxide-vanadium catalyst was stereoselective (>99%) furnishing the *cis*-epoxy alcohol **4**. Acetylation of alcohol **4** furnished the acetate **5**. *m*-Chloroperbenzoic acid epoxidation of alcohol **2** was also stereoselective (>95%) furnishing the *cis*-epoxy alcohol **4**. Epoxidation of the acetate **3** with *m*-chloroperbenzoic acid furnished a 60:40 mixture of the acetates **5** and **6**. The oxirane singlet signals in the nmr spectra of the acetates **5** and **6** have been used for estimating the diastereomeric ratio of the epoxidation products prepared from the alcohol **2**. The *cis*-stereochemistry





has been assigned to the epoxy alcohol **4**, taking into consideration the dihedral angle of the C-O bond with respect to the plane of the double bond in the alcohol **2**. This assignment has been confirmed by carrying out the lithium-aluminium hydride reduction of the epoxy alcohol **4** and isolating the *cis*-diol **9** which was identical with an authentic sample. An authentic sample of diol **9** was prepared through *cis*-hydroxylation of the alkene **7** using iodine-silver acetate-aqueous acetic acid route. For comparison, an authentic sample of *trans*-diol **8** was also prepared from the alkene **7**.

Epoxidation of alcohol **10** with *t*-butyl hydroperoxide-vanadium catalyst [17] furnished stereoselectively (>99%) the *cis*-epoxy alcohol (**11**) which was acetylated to give the acetate **13**. *m*-Chloroperoxybenzoic acid epoxidation of alcohol **10** was stereoselective (>97%) furnishing the *trans*-epoxy alcohol **14** which was acetylated to give the acetate **16**. *m*-Chloroperoxybenzoic acid epoxidation of the acetate **15** furnished the acetate **16**. Inspection of models suggests that one of the geminal methyl groups of alcohol **10** offers steric hindrance to the approach of reagents from the side *cis*- to the hydroxyl. It is suggested that when epoxidation of alcohol **10** is carried out with *m*-chloroperoxybenzoic acid the steric hindrance is large enough to suppress the moderate assistance provided by allylic hydroxyl to *cis*-epoxidation and hence unassisted *trans*-epoxidation takes place. On the other hand during epoxidation of alcohol **10** with hydroperoxide-vanadium reagent the large assistance provided by allylic hydroxyl to *cis*-epoxidation is able to overcome the steric interference. It may be noted that the rate of epoxidation of allylic alcohols is more than 1000 times faster than the rate of epoxidation of corresponding alkenes when the epoxidizing reagent is hydroperoxide-vanadium catalyst [9,17]. The rate of epoxidation of an allylic alcohol is less than the rate of epoxidation of the corresponding alkene when the epoxidizing reagent is an organic per-acid [9]. Though the results of epoxidations of the alcohol **20** are not as dramatic as the results of the epoxidations of alcohol **10** observed during this study, it is of interest to note that the epoxidation of alcohol **20** took place exclusively from the side *cis* to hydroxyl when hydroperoxide-vanadium was employed for epoxidation [18]. On the other hand epoxidation of alcohol **20** with *m*-chloroperoxybenzoic acid furnished a 1:1 mixture of oxides **21** and **22** indicating that per-acid epoxidation takes place with same ease from the *cis* as well as *trans* side of the hydroxyl group [18]. Lithium aluminium hydride reduction of epoxy alcohol **11** furnished the *cis*-diol **12** whose ir spectrum (0.002 *M* solution in carbon tetrachloride) in the region 3700-3400 cm^{-1} was comparable with the ir spectrum of the *cis*-diol **18** (19). Lithium aluminium hydride reduction of epoxy alcohol **14** furnished the *trans*-diol **17** whose ir spectrum (0.002 *M* solution in carbon tetrachloride) in the region 3700-3400 cm^{-1} was comparable with the ir spectrum of the *trans*-diol **19** [19].

EXPERIMENTAL

General.

All melting points and boiling points are uncorrected. High dilution infrared spectra were recorded in carbon tetrachloride as solvent on Perkin-Elmer 221 spectrometer. Other infrared spectra were obtained in Nujol or as liquid film on Perkin-Elmer Infracord spectrometer-model 137B or 599B. The nmr spectra were taken on a Varian T-60 spectrometer using carbon tetrachloride as the solvent and tetramethylsilane as the internal standard. For determining the ratio of diastereomers formed during epoxidations spectroscopic studies were carried out on crude reaction products prior to purification. Elemental analyses were performed in the microanalytical division of this laboratory. Alcohol **2** and alcohol **10** employed for the present study are racemates, hence all the compounds prepared from them are racemates.

2-*trans*-Benzylidenecyclopentanol (**2**).

A solution of sodium borohydride (8.0 g) in water (25 ml) was added gradually to a solution of 2-benzylidenecyclopentanone (17.2 g, 0.1 mole) in ethanol (100 ml) kept cooled to 10°. The reaction mixture was stirred at 25° for 12 hours, diluted water and extracted with ether. The ether extract was dried over sodium sulfate and the solvent evaporated. Recrystallization of the residue from ethanol furnished (14.4 g, 83%) of alcohol **2**, mp 83°, lit [20] mp 83-83.5°; nmr (carbon tetrachloride): δ 4.33 (1H, m, *H*C-OH), 6.26 (1H, m, vinyl *H*), 7.00 (5H, s, Ar-*H*).

2-*trans*-Benzylidenecyclopentanyl Acetate (**3**).

Acetate **3** was prepared by acetylating the alcohol **2** with acetic anhydride in pyridine at 25° for 48 hours; ir (neat): 1750, 1500 and 1245 cm^{-1}.

Anal. Calcd. for $C_{14}H_{16}O_2$: C, 77.75; H, 7.46. Found: C, 77.94; H, 7.59.

2-*trans*-Benzylidene-1β-hydroxycyclopentane β-Oxide (**4**). Method a.

Vanadyl acetylacetonate (0.25 g, 0.9 mmole) was added to a solution of alcohol **2** (3.48 g, 0.02 mole) in dry benzene (25 ml) maintained at 25°. Subsequently *t*-butyl hydroperoxide (85% pure, 3.76 g, 0.04 mole) was added during 15 minutes. The reaction mixture was stirred at 25° for 3 hours. The benzene solution was washed with water (3 × 15 ml) and dried over sodium sulfate. Removal of solvent below 50° in vacuum furnished epoxy alcohol **4** (3.73 g, 98%). An analytical sample was obtained through chromatography on a column of grade II alumina; the column was eluted with benzene-petroleum ether (1:1) mixture; nmr (carbon tetrachloride): δ 2.36 (1H, s, exchanges with deuterium oxide, -O*H*), 4.03 (1H, s, oxirane *H*), 4.00 (1H, m, *H*C-OH), 7.20 (5H, s, Ar-*H*).

Anal. Calcd. for $C_{12}H_{14}O_2$: C, 75.76; H, 7.42. Found: C, 75.98; H, 7.54.

For determining the diastereomeric ratio of epoxidation product, the crude epoxidation product was acetylated with acetic anhydride and pyridine; the resulting acetylation product showed 1H singlet at δ 4.02 due to acetate **5** but no signal at δ 4.08 indicating the absence of acetate **6**.

Anal. Calcd. for $C_{14}H_{16}O_3$: C, 72.39; H, 6.94. Found: C, 72.63; H, 7.10.

Method b.

A mixture of the alcohol **2** (1.74 g, 0.01 mole), *m*-chloroperoxybenzoic acid (3.45 g, 0.02 mole) and chloroform (25 ml) was kept at 10° for 72 hours, washed with aqueous sodium carbonate, water and then dried. Removal of solvent furnished the epoxy alcohol **4** (1.83 g, 96%) identical (ir, nmr) with a sample prepared according to method a.

Epoxidation of 2-*trans*-Benzylidenecyclopentanyl Acetate (**3**).

A mixture of the acetate **3** (2.16 g, 0.01 mole), *m*-chloroperoxybenzoic acid (3.45 g, 0.02 mole) and chloroform (25 ml) was kept at 25° for 72 hours, washed with aqueous sodium carbonate, water and then dried. Removal of solvent furnished a 60:40 mixture of acetates **5** and **6**; nmr (carbon tetrachloride): δ 2.02 (3H, s, -OCOC*H*$_3$), 4.02 (0.60H, s, oxirane *H* of 5), 4.08 (0.40H, s, oxirane *H* of 6), 4.87 (0.40H, m, -C*H*OAc of 6), 5.08 (0.60H, -C*H*OAc of 5), 7.15 (5H, s, Ar-*H*).

Anal. Calcd. for $C_{14}H_{16}O_3$: C, 72.39; H, 6.94. Found: C, 72.06; H, 6.83.

Benzylcyclopent-1-ene (**7**).

Dehydration of 1-benzylcyclopentanol by heating with a mixture of phosphorus oxychloride and pyridine [21,10] furnished in 80% yield the alkene **7** having nmr spectrum identical with that of an authentic sample reported in literature [22].

trans-1-Benzylcyclopentane-1,2-diol (**8**).

The alkene **7** was reacted with peroxyformic acid and subsequently hydrolysed with alkali according to a standard procedure [10] to furnish the diol **8**. An analytical sample was obtained through chromatography on a column of grade II alumina; the column was eluted with benzene; nmr (carbon tetrachloride): δ 2.75 (1H, d, J = 13 Hz, Ar-CH_2-), 2.89 (1H, d, J = 13 Hz, Ar-CH_2-), 3.63 (1H, m, *H*C-OH), 7.10 (5H, s, Ar-*H*).

Anal. Calcd. for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39. Found: C, 74.99; H, 8.35.

cis-1-Benzylcyclopentane-1,2-diol (**9**).

The alkene **7** was reacted with iodine, silver acetate and wet acetic acid [23] to furnish the diol **9**. an analytical sample was obtained through chromatography on a column of grade II alumina; the column was eluted with benzene; nmr (carbon tetrachloride): δ 2.65 (2H, s, Ar-CH_2-), 3.0 (2H, exchanges with deuterium oxide, -O*H*), 3.57 (1H, m, *H*C-OH), 6.97 (5H, s, Ar-*H*).

Anal. Calcd. for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39. Found: C, 74.73; H, 8.34.

3-*trans*-Benzylideneisoborneol (**10**).

Racemic *trans*-benzylidene-3-camphor was reduced with sodium borohydride in aqueous ethanol at 25° for 24 hours. Recrystallization of the reduction product from petroleum ether (bp 60-80°) furnished in 70% yield the alcohol **10**, mp 84°; nmr (carbon tetrachloride): δ 0.86 (3H, s, CH_3-), 0.96 (6H, s, CH_3-), 2.76 (1H, m, CH_2-C*H*-), 3.86 (1H, s, *H*C-OH), 6.46 (1H, s, C=C*H*-), 7.20 (5H, s, Ar-*H*).

Anal. Calcd. for $C_{17}H_{22}O$: C, 84.25; H, 9.15. Found: C, 84.01; H, 9.03.

3-*trans*-Benzylideneisoborneol *exo*-Oxide (**11**).

Epoxidation of the alcohol **10** with *t*-butyl hydroperoxide-vanadyl acetylacetonate in the manner described for the preparation of **4** furnished in quantitative yield the oxirane **11**. A sample recrystallized from petroleum ether showed mp 130°; nmr (carbon tetrachloride): δ 0.80 (3H, s, CH_3-), 0.97 (3H, s, CH_3), 1.15 (3H, s, CH_3-), 1.98 (1H, exchanges with deuterium oxide -O*H*), 3.50 (1H, s, *H*C-OH), 3.98 (1H, s, 2H of oxirane), 7.26 (5H, s, Ar-*H*).

Anal. Calcd. for $C_{17}H_{22}O_2$: C, 79.03; H, 8.58. Found: C, 79.11; H, 8.60.

3-*endo*-Benzyl-1,7,7-trimethylbicyclo[2.2.1]heptane-2-*exo*-3-*exo*-diol (**12**).

A solution of epoxy alcohol **11** (0.077 g, 0.3 mmole) in ether (10 ml) was added with stirring to a suspension of lithium aluminium hydride (0.08 g) in ether (10 ml) at 0°. After adding benzene (10 ml) the reaction mixture was heated under reflux for 20 hours, cooled to 0° and the excess lithium aluminium hydride was decomposed by careful addition of water. The reaction mixture was stirred with a saturated solution of sodium potassium tartrate (20 ml). The organic layer was separated, washed with water, dried and the solvent evaporated to furnish 0.067 g (86%) of **12**, mp 114°; nmr (carbon tetrachloride): δ 0.90 (9H, s, CH_3-), 3.06 (2H, s, Ar-CH_2-), 3.43 (1H, s, *H*C-OH), 7.13 (5H, s, Ar-H).

Anal. Calcd. for $C_{17}H_{24}O_2$: C, 78.42; H, 9.29. Found: C, 78.22; H, 9.00.

3-*trans*-Benzylideneisobornyl Acetate *exo*-Oxide (**13**).

Acetate **13** was prepared by acetylating the alcohol **11** with acetic anhydride in pyridine at 25° for 48 hours. A sample recrystallized from petroleum ether showed mp 106°; nmr (carbon tetrachloride): δ 0.83 (3H, s, CH_3-), 0.93 (3H, s, CH_3-), 1.18 (3H, s, CH_3-), 2.03 (3H, s, -OCOCH_3), 3.98 (1H, s, 2H of oxirane), 4.63 (1H, s, *H*C-OAc), 7.03 (5H, s, Ar-*H*).

Anal. Calcd. for $C_{19}H_{24}O_3$: C, 75.97; H, 8.05. Found: C, 76.13; H, 8.19.

3-*trans*-Benzylideneisoborneol *endo*-Oxide (**14**).

Epoxidation of alcohol **10** with *m*-chloroperoxybenzoic acid, in the manner described for the preparation of **4**, furnished the oxirane **14**. A sample recrystallized from petroleum ether showed mp 124°; nmr (carbon tetrachloride): δ 0.70 (3H, s, -CH_3), 0.90 (6H, s, CH_3-), 3.40 (1H, s, *H*-C-OH), 4.30 (1H, s, 2H of oxirane), 7.20 (5H, s, Ar-*H*).

Anal. Calcd. for $C_{17}H_{22}O_2$: C, 79.03; H, 8.58. Found: C, 78.83; H, 8.68.

3-*trans*-Benzylideneisobornyl Acetate (**15**).

Acetate **15** was prepared by acetylating the alcohol **10** with acetic anhydride and pyridine. An analytical sample was obtained through chromatography; nmr (carbon tetrachloride): δ 0.86 (6H, s, CH_3-), 0.93 (3H, s, CH_3-), 2.03 (3H, s, -OCOCH_3), 2.73 (1H, m, -C*H*-CH_2), 5.20 (1H, s, *H*-C-OAc), 6.26 (1H, s, vinyl *H*), 7.13 (5H, s, Ar-*H*).

Anal. Calcd. for $C_{19}H_{24}O_2$: C, 80.24; H, 8.51. Found: C, 80.43; H, 8.64.

3-*trans*-Benzylideneisobornyl Acetate *endo*-Oxide (**16**). Method a.

Acetylation of alcohol **14** with acetic anhydride and pyridine furnished the acetate **16**. A sample recrystallized from petroleum ether showed mp 119°; nmr (carbon tetrachloride): δ 0.70 (3H, s, CH_3-), 0.80 (3H, s, CH_3-), 0.88 (3H, s, CH_3-), 2.03 (3H, s-OCOCH_3), 4.00 (1H, s, 2H of oxirane), 4.63 (1H, s, *H*C-OAc), 7.00 (5H, s, Ar-*H*).

Anal. Calcd. for $C_{19}H_{24}O_3$: C, 75.97; H, 8.05. Found: C, 76.29; H, 8.14.

Method b.

Epoxidation of the acetate **15** with *m*-chloroperoxybenzoic acid furnished the oxirane **16** which did not contain even a detectable (~1%) amount of the oxirane **13**. The oxirane **16** thus prepared was identical (mp, mmp, nmr) with a sample prepared acccording to method a.

3-*exo*-Benzyl-1,7,7-trimethylbicyclo[2.2.1]heptane-3-*endo*-2-*exo*-diol (**17**).

Alcohol **14** was reduced with lithium aluminium hydride in the manner described for the preparation of **12** to furnish the diol **17**, mp 68°; nmr (carbon tetrachloride): δ 0.81 (3H, s, CH_3-), 0.86 (3H, s, CH_3-), 1.11 (3H, s, CH_3-), 2.80 (2H, s, Ar-CH_2-), 3.23 (1H, s, *H*C-OH), 7.10 (5H, s, Ar-*H*).

Anal. Calcd. for $C_{17}H_{24}O_2$: C, 78.42; H, 9.29. Found: C, 78.12; H, 9.02.

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