A Stereoselective 1,3-Transposition Reaction of Allylic Alcohols[1)]

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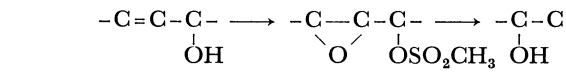
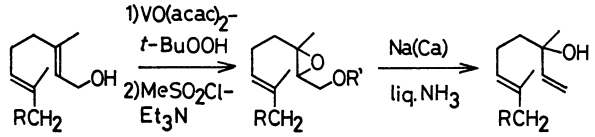
Reduction of glycidyl mesylate with dissolving metal produces allylic alcohol in fair to excellent yield. Combined with the highly stereoselective epoxidation of allylic alcohols with *t*-butyl hydroperoxide and oxobis(2,4-pentanedionato-*O*,*O*')vanadium(IV) as a catalyst, the sequence provides a new and efficient means for 1,3-transposition of allylic alcohols, by which geraniol is transformed into linalool, farnesol into nerolidol, and furthermore, (−)-*cis*-carveol into the (+) antipode and vice versa in a stereospecific way.

The recently discovered procedure for making 2,3-epoxy-1-alkanols by catalytic epoxidation of allylic alcohols[2)] has initiated an investigation into the possible utilization of the dissolving metal reduction of glycidyl mesylate (methanesulfonate) obtained therefrom as a possible way of 1,3-transposition of allylic alcohols.

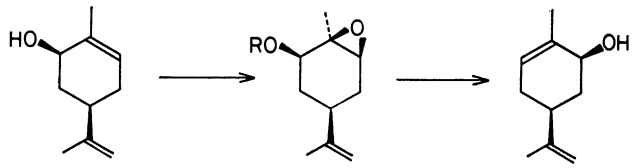


The epoxy alcohol **2** was treated with methanesulfonyl chloride and triethylamine in dichloromethane at −26 °C to give the mesylate **3**. Reduction of **3** with calcium metal in liquid ammonia-tetrahydrofuran furnished linalool (**4**) (88% yield). Some variations in the metal reagent have been studied: sodium, 87% yield; lithium, 50% yield. The use of methylamine, ethylamine, and hexamethylphosphoric triamide in place of liq. ammonia was tested without any success. Reduction with sodium-naphthalene in THF also effected the same transformation yielding linalool. This procedure gave the best result when a THF solution of the mesylate was added to a THF solution of the radical anion.[3,4)] Nerolidol (**8**)[5)] was similarly obtained by reaction of the mesylate **7** with sodium-metal in liq. ammonia-THF.



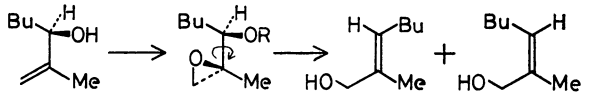
1 R=H **2** R=R'=H **4** R=H
3 R=H, R'=SO_2Me
5 R=Me_2C=$CHCH_2$ **6** R=Me_2C=$CHCH_2$, R'=H **8** R=Me_2C=$CHCH_2$
7 R=Me_2C=$CHCH_2$, R'=SO_2Me

Although the facility and directness of this procedure are appealing, even more important is the advantage that glycidols are prepared from allylic alcohols with high stereospecificity by the Sharpless reagent.[2)] For example, (−)-*cis*-carveol (**9**) was selectively oxidized to the *cis*-epoxy alcohol **10**. Treatment of the mesylate **11** with either Na–NH_3 or Na-naphthalene furnished (+)-*cis*-carveol (**12**) in good yield. The reverse transformation of **12** into **9** was smoothly carried out by employing the same sequence as described above. From the known specific rotation,[6)] each product was found to be no less than 90% optically pure.



9 **10** R=H, **11** R=Ms **12**

In order to examine the stereochemistry of the reduction of an open-chain glycidyl mesylate, (2*R**,3*S**)-glycidol **14**[2b)] was prepared and subjected to the transformation.



13 **14** R=H, **15** R=Ms **16**

Reduction of the mesylate **15** with dissolving calcium furnished an (*E*), (*Z*) mixture of allylic alcohols **16** in a ratio of ≈4: 1. Obviously, the oxirane ring opening is not in concert with the reductive cleavage of the mesylate moiety, but the indicated rotation around the C–C bond is allowed in the acyclic mesylate **15**.

Experimental

The optical rotations were measured using a Yanaco-OR-50 polarimeter. The infrared spectra were determined on a Shimadzu IR-27-G spectrometer; the mass spectra on a Hitachi RMU-6L mass machine; the glpc analyses on a Yanagimoto GCG-550F; and the NMR spectra on a JNM-PMX 60 or Varian EM-360 spectrometer. The chemical shifts are given in δ in ppm with TMS as the internal standard. Splitting patterns are designated as s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. The microanalyses were carried out by the staffs at the Elemental Analyses Center of Kyoto University. All experiments were carried out under an atmosphere of dry argon. Tetrahydrofuran was dried by distillation from sodium-benzophenone. During workup, drying of the organic solutions was performed over anhydrous sodium sulfate. Thin layer or preparative thick layer plates were made of E. Merck PF-254, and preparative column chromatography on silica gel E. Merck Art. 7734.

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Transformation of Geraniol (1) into Linalool (4). To a mixture of epoxy alcohol **2** (340 mg, 2.0 mmol) prepared from geraniol (**1**) according to the procedure of Sharpless,[2a] and triethylamine (0.3 ml, 2.2 mmol) dissolved in dichloromethane (3 ml) a solution of mesyl chloride (252 mg, 2.2 mmol) in dichloromethane (3 ml) was added drop by drop at −26 °C. After stirring at this temperature for 1 h, the reaction mixture was quenched in ice-cold water. The organic phase was removed and the aqueous layer was extracted with ether. The combined organic solutions were washed with saturated brine, dried, and concentrated *in vacuo* to leave a crude oil, which was purified by preparative TLC (1:1 hexane–ether) to furnish epoxy mesylate **3** (436 mg, 96 % yield): TLC, R_f 0.50 (1: 1 hexane–ether, 2 developments); IR (neat), 1450 (m), 1340—1360 (s), 1240 (w), 1170 (s), and 940—980 cm^{-1} (s); NMR ($CDCl_3$), 1.34 (3H, s, CH_3–CO), 1.64 (3H, s, CH_3–C=), 1.71 (3H, s, CH_3–C=), 2.89—3.24 (1H, m, CH–O), 3.03 (3H, s, CH_3–S), 4.13 and 4.41 (2H, dd, J=11 and 5 Hz, CH_2–OS), and 5.07 (1H, bt, CH=).

To a mixture of the mesylate **3** (248 mg, 1.0 mmol), THF (1 ml), and redistilled ammonia (10 ml) freshly polished calcium metal was added in small pieces at −35 to −37 °C (cooling bath temperature) with vigorous stirring and as rapidly as the metal dissolved, until the blue color persisted. After another 10 min, ammonium chloride (1.00 g) was added carefully to discharge the blue color. The cooling bath was removed and the mixture was poured into ice-cold water. The product was extracted with ether, dried, and freed of the solvent. The residue was submitted to preparative TLC (1: 1 hexane–ether) to give linalool (**4**) (136 mg, 88 % yield) as a clear oil which was homogeneous by TLC. IR and NMR spectra were superimposable on those of authentic specimen.

Linalool (**4**) was also prepared from **3** using the sodium-naphthalene reagent as follows. A green solution of sodium-naphthalene (3.0 mmol) in THF (10 ml) was prepared in the usual manner.[7] To this a solution of the mesylate **3** (124 mg, 0.5 mmol) in THF (1 ml) was added drop by drop over a period of 10 min at room temperature. Stirring was continued for 10 min and the reaction was terminated by the addition of ammonium chloride (1.00 g). The resulting mixture was partitioned between ether and ice-cold water and the organic layer was washed with saturated brine, dried, and concentrated *in vacuo*. Preparative TLC purification (1: 1 hexane–ether) of the residue gave linalool (**4**) (64 mg, 83 % yield). NMR analysis indicated that the product was almost free from impurities.

Transformation of Farnesol (5) into Nerolidol (8). The epoxy alcohol **6**[8] was converted to the mesylate **7** in 97 % yield as described above: TLC, R_f 0.23 (1: 1 hexane–ether); IR (neat), 1450 (s), 1350 (s), 1250 (m), 1160—1180 (s), and 950—980 cm^{-1} (s); NMR ($CDCl_3$), 1.33 (3H, s, CH_3–CO), 2.85—3.20 (1H, m, CH–O), 2.99 (3H, s, CH_3–S), 4.10—4.35 (2H, dd, CH_2–OS), and 4.82—5.23 (2H, m, CH=).

Freshly cut sodium was added in small pieces to a mixture of the mesylate **7** (316 mg, 1.0 mmol), THF (1 ml), and redistilled ammonia (10 ml) at −37 °C (cooling bath temperature) until the blue color persisted. After stirring for another 10 min, the reaction mixture was worked up according to the above mentioned procedure. After drying and concentrating *in vacuo*, the remaining liquid was submitted to preparative TLC (1: 1 hexane–ether) to furnish nerolidol (**8**)[5] (194 mg, 87 % yield) as a clear oil. This material was identical in all respects with the reported one.[5]

Transformation of (−)-cis-Carveol (9) into the (+) Antipode (12). According to the previously reported procedure,[9] (−)-*cis*-carveol (**9**) (18.24 g, 80 % yield, $[\alpha]_D^{25}$ −26.4 (c=5.6, C_2H_5OH)) was prepared from (−)-carvone (22.50 g, $[\alpha]_D^{25}$ −58 (neat)) by reduction with lithium aluminum hydride (226 mg) in THF (150 ml) and purified by column chromatography (5: 1 hexane–ether) followed by distillation (106—107 °C/10 Torr). From the known specific rotation,[6] the product was estimated to contain 98 % of (−)-*cis*-carveol (**9**) and 2 % of the *trans* isomer. GLPC analysis (10 % PEG 20 Mesh, 120 °C, 0.2 kg/cm²) also showed the same isomer ratio.

A solution of *t*-butyl hydroperoxide (600 mg, 6.0 mmol) in benzene (8 ml) was added drop by drop to a mixture of (−)-*cis*-carveol (**9**) (608 mg, 4.0 mmol) and oxobis(2,4-pentanedionato-*O*,*O*′)vanadium(IV) (16 mg, 0.06 mmol) dissolved in benzene (8 ml) at 0 °C. After stirring at 50 °C for 4.5 h, the reaction mixture was cooled to room temperature and poured into saturated sodium sulfite. The product was extracted with ether, washed with water, dried, and freed of the solvent. The residue was submitted to column chromatography (5: 1 hexane–ether) to give epoxy alcohol **10** (420 mg, 64 % yield) as a pale yellow oil:[10] TLC, R_f 0.18 (1: 1 hexane–ether); IR (neat), 3400—3500 (s), 1370 (m), 1065 (m), 890 (s), and 860 cm^{-1} (m); NMR ($CDCl_3$), 1.25 (3H, s, CH_3–CO), 1.60 (3H, s, CH_3–C=), 3.10—3.25 (2H, m, CH–O), and 4.95 (2H, s, CH_2=). GLPC analysis (5 % PEG 20 Mesh, 140 °C, 0.2 kg/cm²) showed that the product was >94 % chemically pure.

Treatment of **10** with mesyl chloride–triethylamine as described above afforded the epoxy mesylate **11** in 87 % yield: TLC, R_f 0.15 (1: 1 hexane–ether); IR (neat), 1450 (m), 1350 (s), 1170 (s), 960 (s), and 890 cm^{-1} (s); NMR ($CDCl_3$), 1.34 (3H, s, CH_3–CO), 1.60 (3H, s, CH_3–C=), 3.10 (3H, s, CH_3–S), 3.50—4.55 (2H, m, CH–O), and 4.98 (2H, s, CH_2=).

Dissolving sodium reaction with the epoxy mesylate **11** (246 mg, 1.0 mmol) furnished 57 % yield of (+)-*cis*-carveol (**12**)[11] (87 mg) as a clear oil: $[\alpha]_D^{25}$ +35.9 (c=4.3, C_2H_5OH), >92 % optically pure. IR, NMR, and mass spectra were identical with those of the authentic sample.

The sodium-naphthalene reagent also effected the same reductive cleavage to give **12** in 54 % yield.

Transformation of (+)-cis-Carveol (12) into the (−) Antipode (9). The same sequence described above afforded (−)-*cis*-carveol (**9**) $[\alpha]_D^{25}$ −23.0 (c=5.6, C_2H_5OH) (98 % optically pure) from **12** $[\alpha]_D^{25}$ +35.9 (c=5.6, C_2H_5OH) (95 % optically pure).

Preparation of (E)-2-Methyl-2-hepten-1-ol (16). The epoxy alcohol **14**[2b] was converted to the mesylate **15** in 95 % yield: bp 110 °C (bath temp, 1 Torr); TLC, R_f 0.28 (1: 1 hexane–ether); IR (neat), 1450 (s), 1360 (m), 1230—1240 (w), 1100 (m), and 970 cm^{-1} (s); NMR ($CDCl_3$), 1.21 (3H, s, CH_3–CO), 2.96 (2H, dd, CH_2–O), 3.03 (3H, s, CH_3–S), and 4.32 (1H, t, CH–O). Found: C, 48.8; H, 8.2 %. Calcd for $C_9H_{18}O_4S$: C, 48.6; H, 8.2 %.

The epoxy mesylate **15** (222 mg, 1.0 mmol) was treated with calcium metal in liq NH_3–THF as described above to give the alcohol **16** (74 mg, 58 % yield) as a clear oil: bp 120 °C (bath temp, 25 Torr); TLC, R_f 0.35 (1: 1 hexane–ether); IR (neat), 3300—3360 (s), 1470 (m), 1380 (m), and 1005 cm^{-1} (s); NMR (CCl_4), 1.75 (3H, s, CH_3–C=), 4.12 (2H, s, CH_2–O), and 5.29 (1H, bt, CH=); MS (m/e), 128 (M^+).

Found: C, 74.7; H, 12.7 %. Calcd for $C_8H_{16}O$: C, 74.9; H, 12.6 %.

GLPC analysis (20 % PEG 20 Mesh, 130 °C, 0.4 kg/cm²) of the product showed two peaks in the ratio of 81: 19. The major peak, having the longer retention time, was ascribed to the (*E*) isomer by comparison with the previously reported results.[12]

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