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# Enantioselective preparation of (2*R*,3*R*)-(+)- and (2*S*,3*S*)-(−)-2,3-epoxy-2-methylbutanoic acids and some derivatives

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**Abstract**

(2*R*,3*R*)-(+)- and (2*S*,3*S*)-(−)-2,3-epoxy-2-methylbutanoic acids (epoxyangelic acids) were prepared from (*Z*)-2-methyl-2-butenoic acid using the Sharpless asymmetric epoxidation method in combination with the use of (−)- and (+)-menthol as chiral auxiliaries. Both substances, obtained in high enantiomeric excess, were characterized by spectroscopic and optical activity data. Their absolute configuration was determined by correlation with (*R*)-(+)-2-methyl-1,2-butanediol. © 1998 Elsevier Science Ltd. All rights reserved.

## 1. Introduction

A literature survey revealed that there are more than 170 natural products which contain either (2*R*,3*R*)- or (2*S*,3*S*)-2,3-epoxy-2-methylbutanoic acid residues as part of their structures. Most of these substances are sesquiterpene lactones such as germacranolides (approximately 70), guaianolides (nearly 25) and eudesmanolides (almost 25). Even some kaurenes, coumarins, furanoeremophilanes, alkaloids and longipinene derivatives have been found to contain this kind of ester group. The absolute configuration of the epoxyangelate moiety has been elucidated only in a few cases by X-ray diffraction analysis. However, the problem still remains unsolved for at least 150 of these substances, in spite of the fact that some of them have relevant biological activity as tumor inhibitors,[1,2] antibiotics,[3] antipyretics[4] or antiinflammatory agents.[5]

The present paper describes the enantioselective preparation of both (2*R*,3*R*)- and (2*S*,3*S*)-2,3-epoxy-2-methylbutanoic acids [(+)- and (−)-epoxyangelic acids] by means of the Sharpless asymmetric epoxidation method[6,7] combined with the use of (−)- and (+)-menthol as chiral auxiliaries. These results, together with our previous report[8] on the obtention of (2*R*,3*S*)- and (2*S*,3*R*)-2,3-epoxy-2-methylbutanoic

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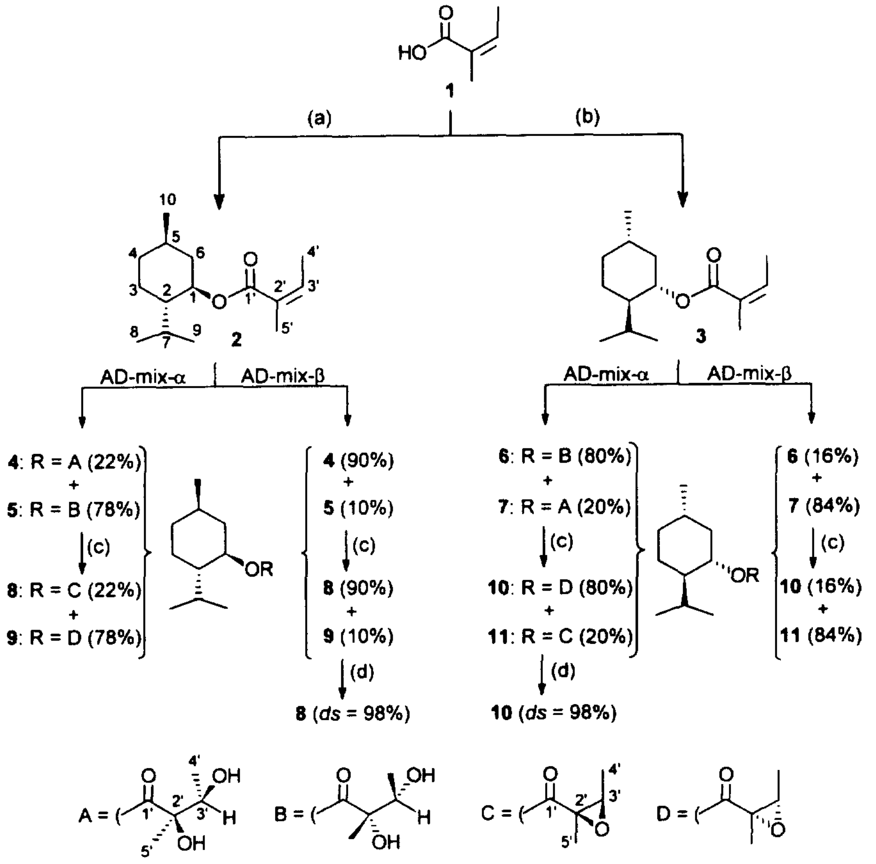
acids [(−)- and (+)-epoxytiglic acids], provide preparation procedures to obtain the four stereoisomers of 2,3-epoxy-2-methylbutanoic acid in high enantiomeric excess.

## 2. Results and discussion

The synthesis of (2*R*,3*R*)-(+)- and (2*S*,3*S*)-(−)-2,3-epoxy-2-methylbutanoic acids **14** and **15** was carried out starting from (*Z*)-2-methyl-2-butenoic acid (angelic acid) **1** as shown in Schemes 1 and 2. Angelic acid **1** was esterified with (1*R*,2*S*,5*R*)-(−)-menthol to give ester **2**[9] which was treated with AD-mix-β and AD-mix-α reagents[6] to provide diolesters **4** and **5**, respectively. AD-mix-β and AD-mix-α are reagents for asymmetric dihydroxylation which contain potassium osmate, potassium ferricyanide, potassium carbonate and the chiral ligands dihydroquinidine 1,4-phthalazinediyl diether or dihydroquinine 1,4-phthalazinediyl diether, correspondingly. Although the ligands are diastereoisomeric entities, they essentially induce opposite stereoselectivities.[6]



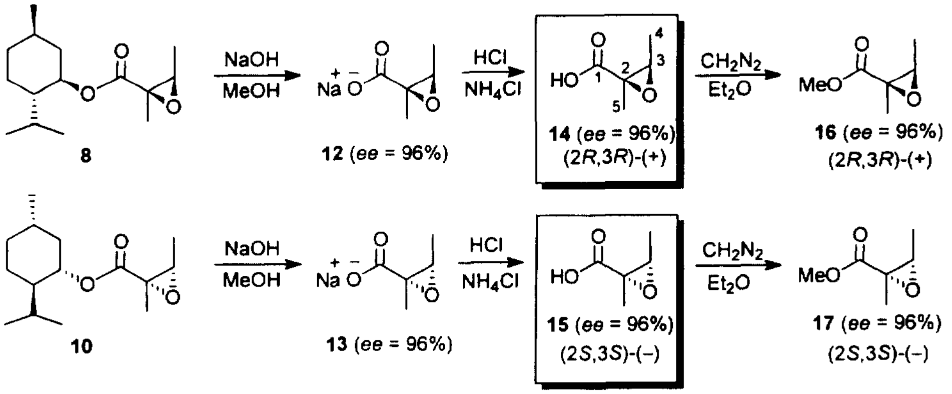
(a) 1. KOH/MeOH; 2. $(ClCO)_2$; 3. (1*R*,2*S*,5*R*)-(−)-menthol;

(b) 1. KOH/MeOH; 2. $(ClCO)_2$; 3. (1*S*,2*R*,5*S*)-(+)-menthol;

(c) 1. $MeC(OMe)_3$; 2. AcBr; 3. $K_2CO_3$/MeOH; (d) flash chromatography.

Scheme 1.

When using AD-mix-β for the treatment of **2**, a 90% diastereoselectivity (*ds*) towards ester **4** was achieved, while when AD-mix-α was employed, only 78% diastereoselectivity towards ester **5** was



Scheme 2.

obtained. These values were ascertained from the $^1$H-NMR spectra of the reaction products measured at 300 MHz in CDCl$_3$. The mixtures of compounds **4** and **5** were converted into epoxyangelate esters **8** and **9**, respectively, by known procedures,[7] which preserved the chiral centers and also the diastereoselectivity values. Compound **8** was obtained with a diastereoselectivity of 98% after flash chromatography[10] of the diastereomeric mixture formed by **8** and **9** in a 9:1 ratio by elution with hexane:EtOAc (100:7). The improvement in diastereoselectivity was carefully monitored by $^1$H-NMR. Compound **8** was subjected to alkaline hydrolysis with NaOH in MeOH, leading to the respective sodium salt **12** and (−)-menthol. The sodium salt **12** was neutralized with HCl in aqueous NH$_4$Cl solution to give the corresponding (2*R*,3*R*)-(+)-2,3-epoxy-2-methylbutanoic acid **14** as shown in Scheme 2.

Attempts to obtain ester **9** in high diastereomeric excess (*d.e.*), and thus prepare (2*S*,3*S*)-(−)-2,3-epoxy-2-methylbutanoic acid **15**, were unsuccessful. Even chromatographies of the mixture enriched up to 78% of **9** gave unsatisfactory results. Presumably, the fact that ester **9** is not the first eluate of the column hinders its purification. To overcome this difficulty, we decided to prepare the enantiomer of compound **8**, that is to say ester **10**. This substance (**10**) will emerge from the column as the first eluate, thus allowing its obtention in high diastereomeric excess as was the case for **8**. Esterification of angelic acid **1** with (1*S*,2*R*,5*S*)-(+)-menthol yielded ester **3** which was also treated with AD-mix-β and AD-mix-α reagents[6] affording diolesters **6** and **7**. When AD-mix-α was employed, an 80% diastereoselectivity (*ds*) towards ester **6** was obtained, and when AD-mix-β was used, an 84% diastereoselectivity towards ester **7** was obtained, as was observed in the $^1$H-NMR spectra of the crude reaction products. The mixture formed by **6** and **7** in an 8:2 ratio was converted to epoxyangelates **10** and **11** (see Scheme 1). As expected, flash chromatography of this mixture afforded compound **10** with 98% diastereoselectivity. This value was also obtained by $^1$H-NMR measurements. Ester **10** was hydrolyzed with NaOH in MeOH affording the sodium salt **13** and (+)-menthol. Finally, the sodium salt **13** was neutralized to give the corresponding (2*S*,3*S*)-(−)-2,3-epoxy-2-methylbutanoic acid **15**.

In the reactions of (−)- and (+)-menthyl angelate esters (**2** and **3**) with AD-mix-β and AD-mix-α, the (−)- and (+)-menthol moieties make small contributions to stereodifferentiation because there was only a modest change in the diastereoselectivities, as can be seen in Scheme 1 for **5** (78%) *versus* **4** (90%) and **6** (80%) *versus* **7** (84%). Furthermore, epoxidation of **2** with *m*-chloroperbenzoic acid gave a mixture of **8** and **9** in a *ca* 1:1 ratio. However, the use of (−)- and (+)-menthol was well appreciated when measuring diastereoselectivities by $^1$H-NMR as well as for the chromatographic purification of **8** and **10**.

The absolute configuration of the compounds depicted in Schemes 1 and 2 was determined by chemical correlation of ester **8** with (*R*)-(+)-2-methyl-1,2-butanediol[11] as follows. Treatment of **8** (*ds*=90%) with LiAlH$_4$ in THF gave (*R*)-(+)-2-methyl-1,2-butanediol with $[\alpha]_D^{25}$=+7, *c* 1.30 in CHCl$_3$, *ee*=80% (lit.[11]

$[\alpha]_D^{20}$=+8.7, *c* 1.35 in $CHCl_3$, *ee*=94%). This correlation is possible because the hydride, besides reduction of the ester group to the alcohol, attacks at C-3′ while C-2′ retains its configuration. On the other hand, epoxyacids **14** and **15** were treated with diazomethane to give the corresponding methyl esters **16** with $[\alpha]_D^{25}$=+19, *c* 1.10 in $CHCl_3$ and **17** with $[\alpha]_D^{25}$=−19, *c* 1.30 in $CHCl_3$. Methyl ester **16** has already been described in the literature[12] with $[\alpha]_D^{25}$=+21, neat. Assignments of the $^1H$- and $^{13}C$-NMR spectra for all compounds were confirmed by COSY and HETCOR experiments.

According to the results shown in this work, the following sequence can be proposed for the absolute configuration assignment of the epoxyangelic acid moiety present in natural products:

(i) hydrolysis of the ester group in those compounds where the absolute configuration of the epoxyangelate moiety is unknown;
(ii) esterification of the resulting alcohol with both enantiomers of the epoxyangelic acid, prepared as described herein; and
(iii) comparison of the $^1H$-NMR spectra of both semi-synthetic samples with that of the original natural product.

## 3. Experimental

$^1H$, $^{13}C$, COSY-$^1H/^1H$, and HETCOR-NMR spectra: Varian XL-300 GS. $^1H$ measured at 300 MHz, $^{13}C$ at 75.4 MHz, TMS as internal standard, solvent $CDCl_3$, unless otherwise stated. IR spectra: Perkin–Elmer 16F PC FT-IR spectrophotometer. Mass spectra: Hewlett–Packard 5989-A, 70 and 20 eV. Specific rotations: Perkin–Elmer 241 polarimeter. Column chromatography (CC): Merck silica gel, particle size: 0.040–0.063 mm (230–400 mesh ASTM). Angelic acid **1**, was prepared from tiglic acid following published procedures.[13] Tiglic acid, (−)- and (+)-menthol were commercially available (Aldrich).

### 3.1. *(−)-Menthyl angelate 2*

Angelic acid **1**[13] (8.0 g) was treated with KOH (4.5 g) in MeOH (25 ml) on an ice–water bath. The solvent was removed with an $N_2$ stream and acetone was added to precipitate the salt which was filtered, washed and dried on a vacuum oven. The resulting potassium angelate was treated with oxalyl chloride (10 ml) in $Et_2O$ (70 ml) to give angeloyl chloride[14] which was immediately added to a solution of (−)-menthol (9.3 g) in $CH_2Cl_2$ (30 ml). The mixture was stirred at room temp. for 48 h. The solvent was evaporated under vacuum and the residue was chromatographed on a silica gel column eluting with hexane:$CH_2Cl_2$ (2:1, v/v) to afford **2** (13.8 g, 73%). Spectroscopic data were in agreement to those reported.[9]

### 3.2. *(+)-Menthyl angelate 3*

Prepared as described for compound **2**, but using angelic acid **1**[13] (5.0 g) and (+)-menthol (5.8 g) to afford **3** (8.9 g, 75%) as a colorless oil. $[\alpha]_D^{25}$=+83 (*c*=1.22, $CHCl_3$). Spectroscopic data were identical to those of compound **2**.

### 3.3. (−)-Menthyl (2′R,3′R)-2′,3′-dihydroxy-2′-methylbutanoate 4

Compound **2** (4.0 g) was treated with AD-mix-β[6] yielding compound **4** as a colorless oil (4.22 g, 92%). The product was obtained with a *d.e.* of 90% showing $[\alpha]_D^{25}=-66$ ($c$=2.58, $CHCl_3$). IR ($CHCl_3$) $\nu_{max}$: 3572, 3524, 3044, 2960, 1716, 1456, 1376, 1254, 1178, 954, 914 cm$^{-1}$. $^1$H-NMR δ: 4.74 (d/t, $J$=4.4/10.9 Hz, H-1), 1.47 (m, H-2), 1.70 (m, H-3eq), 1.71 (m, H-4), 1.50 (m, H-5), 2.01 (m, H-6eq), 1.01 (m, H-6ax), 1.88 (d/sep, $J$=2.7/9.8 Hz, H-7), 0.75 (d, $J$=7.0 Hz, Me-8,9), 0.91 (d, $J$=6.9 Hz, Me-8,9), 0.92 (d, $J$=6.5 Hz, Me-10), 3.81 (d/q, $J$=8.8/6.4 Hz, H-3′), 1.14 (d, $J$=6.4 Hz, Me-4′), 1.43 (s, Me-5′), 2.26 (d, $J$=8.8 Hz, OH at C-2′), 3.45 (s, OH at C-3′) ppm. $^{13}$C-NMR δ: 76.65 (C-1), 46.86 (C-2), 22.98 (C-3), 34.12 (C-4), 31.41 (C-5), 40.58 (C-6), 26.01 (C-7), 15.73 (C-8,9), 20.82 (C-8,9), 21.94 (C-10), 175.29 (C-1′), 77.09 (C-2), 71.85 (C-3′), 17.76 (C-4′), 22.46 (C-5′) ppm.

### 3.4. (−)-Menthyl (2′S,3′S)-2′3′-dihydroxy-2′-methylbutanoate 5

Ester **2** (4.0 g) was treated with AD-mix-α[6] yielding **5** as a colorless oil (4.15 g 91%). The product was obtained with a *d.e.* of 78% showing $[\alpha]_D^{25}=-74$ ($c$=2.75, $CHCl_3$). IR ($CHCl_3$) $\nu_{max}$: 3666, 3522, 3042, 2992, 1710, 1456, 1378, 1280, 1130, 1090, 958, 914 cm$^{-1}$. $^1$H-NMR δ: 4.77 (d/t, $J$=4.4/10.9 Hz, H-1), 1.46 (m, H-2), 1.71 (m, H-3eq), 1.70 (m, H-4), 1.50 (m, H-5), 2.01 (m, H-6eq), 1.01 (*m*, H-6ax), 1.87 (d/sep, $J$=2.6/9.8 Hz, H-7), 0.76 (d, $J$=6.9 Hz, Me-8,9), 0.91 (d, $J$=7.1 Hz, Me-8,9), 0.92 (d, $J$=6.6 Hz, Me-10), 3.82 (d/q, $J$=8.5/6.4 Hz, H-3′), 1.16 (d, $J$=6.4 Hz, Me-4′), 1.44 (s, Me-5′), 2.33 (d, $J$=8.5 Hz, OH at C-2′), 3.54 (s, OH at C-3′) ppm. $^{13}$C-NMR δ: 76.53 (C-1), 47.01 (C-2), 23.13 (C-3), 34.14 (C-4), 31.43 (C-5), 40.55 (C-6), 26.14 (C-7), 15.90 (C-8,9), 20.80 (C-8,9), 21.95 (C-10), 175.19 (C-1′), 76.98 (C-2), 72.03 (C-3′), 17.66 (C-4′), 22.45 (C-5′) ppm.

### 3.5. (+)-Menthyl (2′S,3′S)-2′,3′-dihydroxy-2′-methylbutanoate 6

Compound **3** (4.0 g) was treated with AD-mix-α[6] giving ester **6** as a colorless oil (4.02 g, 88%). The product was obtained with a *d.e.* of 80% showing $[\alpha]_D^{25}=+64$ ($c$=2.45, $CHCl_3$) and spectroscopic data identical to those of ester **4**.

### 3.6. (+)-Menthyl (2′R,3′R)-2′,3′-dihydroxy-2′-methylbutanoate 7

Compound **3** (0.50 g) was treated with AD-mix-β[6] to yield ester **7** as a colorless oil (0.51 g, 90%). The product was obtained with a *d.e.* of 84% showing $[\alpha]_D^{25}=+69$ ($c$=2.55, $CHCl_3$) and spectroscopic data identical to those of ester **5**.

### 3.7. (−)-Menthyl (2′R,3′R)-2′,3′-epoxy-2-methylbutanoate 8

Ester **4** (4.0 g) with a *d.e.* of 90% was converted to **8** by known procedures.[7] The product was obtained as a colorless oil (2.20 g, 59%) with the same *d.e.* as the starting material. Flash chromatography using hexane:EtOAc (100:7, v/v) as eluent yielded compound **8** with a *d.e.* of 98%. This sample showed $[\alpha]_D^{20}=-39$ ($c$=2.90, $CHCl_3$). IR ($CHCl_3$) $\nu_{max}$: 3040, 1730, 1452, 1270, 1152, 1084, 980 cm$^{-1}$. EIMS m/z (%): $[M+1]^+$ 255 (1), 155 (1), 139 (31), 138 (57), 123 (18), 116 (94), 95 (43), 83 (100), 81 (45), 72 (10), 71 (19), 69 (42), 57 (32), 43 (89), 41 (46). $^1$H-NMR δ: 4.80 (d/t, $J$=4.4/10.9 Hz, H-1), 1.50 (m, H-2), 1.62 (m, H-3eq), 1.71 (m, H-4), 1.46 (m, H-5), 1.98 (m, H-6eq), 1.03 (m, H-6ax), 1.87 (d/sep, $J$=2.7/7.0 Hz, H-7), 0.75 (d, $J$=7.0 Hz, Me-8,9), 0.91 (d, $J$=7.0 Hz, Me-8,9), 0.90 (d, $J$=7.1 Hz, Me-10), 3.04 (q, *J*=5.5 Hz, H-3′), 1.32 (d, *J*=5.5 Hz, Me-4′), 1.55 (s, Me-5′) ppm. $^{13}$C-NMR δ: 75.52 (C-1), 46.85 (C-2), 23.41 (C-3), 34.19 (C-4), 31.43 (C-5), 40.89 (C-6), 26.27 (C-7), 16.20 (C-8.9), 20.63 (C-8,9), 21.96 (C-10), 169.48 (C-1′), 59.86 (C-2), 59.76 (C-3′), 13.80 (C-4′), 19.29 (C-5′) ppm.

### 3.8. *(−)-Menthyl (2′S,3′S)-2′,3′-epoxy-2-methylbutanoate **9***

Ester **5** (4.0 g) with a *d.e.* of 78% was converted to epoxyester **9** by known procedures.[7] The product was obtained as a colorless oil (2.31 g, 62%) with a *d.e.* of 78% showing $[\alpha]_D^{25}=-59$ (*c*=1.40, $CHCl_3$). IR ($CHCl_3$) $\nu_{max}$: 3040, 2924, 1734, 1454, 1268, 1170, 778 cm$^{-1}$. EIMS m/z (%): $[M+1]^+$ 255 (1), 138 (36), 116 (54), 95 (29), 83 (84), 95 (29), 57 (33), 55 (63), 43 (100), 41 (54). $^1$H-NMR δ: 4.76 (d/t, *J*=4.4/10.8 Hz, H-1), 1.50 (m, H-2), 1.67 (m, H-3eq), 1.70 (m, H-4), 1.46 (m, H-5), 1.98 (m, H-6eq), 1.01 (m, H-6ax), 1.92 (d/sep, *J*=2.9/7.5 Hz, H-7), 0.76 (d, *J*=6.8 Hz, Me-8,9), 0.92 (d, *J*=7.0 Hz, Me-8,9), 0.91 (d, *J*=6.4 Hz, Me-10), 3.03 (q, *J*=5.4 Hz, H-3′), 1.32 (d, *J*=5.4 Hz, Me-4′), 1.56 (s, Me-5′) ppm. $^{13}$C-NMR δ: 75.61 (C-1), 46.88 (C-2), 23.10 (C-3), 34.19 (C-4), 31.40 (C-5), 40.85 (C-6), 26.14 (C-7), 15.92 (C-8,9), 20.94 (C-8,9), 21.98 (C-10), 169.40 (C-1′), 59.66 (C-2), 59.77 (C-3′), 13.81 (C-4′), 19.31 (C-5′) ppm.

### 3.9. *(+)-Menthyl (2′S,3′S)-2′,3′-epoxy-2-methylbutanoate **10***

Ester **6** (4.0 g) with a *d.e.* of 80% was converted to epoxyester **10** by known procedures.[7] The product was obtained as a colorless oil (2.26 g, 61%) with a *d.e.* of 80%. Flash chromatography using hexane:EtOAc (100:7, v/v) as the eluent yielded **10** with a *d.e.* of 98% showing $[\alpha]_D^{25}=+40$ (*c*=1.29, $CHCl_3$). Spectroscopic data were identical to those of **8**.

### 3.10. *(+)-Menthyl (2′R,3′R)-2′,3′-epoxy-2-methylbutanoate **11***

Ester **7** (4.0 g) with a *d.e.* of 84% was converted to epoxyester **11** by known procedures.[7] The product was obtained as a colorless oil (2.31 g, 62%) with a *d.e.* of 84% showing $[\alpha]_D^{25}=+62$ (*c*=1.20, $CHCl_3$). Spectroscopic data were identical to those of **9**.

### 3.11. *Sodium (2R,3R)-(+)-2,3-epoxy-2-methylbutanoate **12***

A solution of **8** with a *d.e.* of 98% (657 mg) in MeOH (11 ml) was stirred with NaOH (103 mg) for 12 h at room temperature. The solvent was removed with an $N_2$ stream and acetone (10 ml) was added to precipitate the sodium salt. The suspension was filtered and washed with acetone (10 ml) to provide **12** (263 mg, 74%). $[\alpha]_D^{25}=+62$ (*c*=1.0, $H_2O$). IR (KBr) $\nu_{max}$: 1615, 1450, 1078, 843, 790 cm$^{-1}$. $^1$H-NMR ($D_2O$, HDO centered at 4.63 ppm) δ: 2.99 (q, *J*=5.5 Hz, H-3), 1.08 (d, *J*=5.5 Hz, Me-4), 1.33 (s, Me-5) ppm. $^{13}$C-NMR ($D_2O$, 1,4-dioxane as internal standard centered at 66.40 ppm) δ: 177.00 (C-1), 64.07 (C-2), 60.46 (C-3), 13.69 (Me-4), 18.92 (Me-5) ppm. The chiral auxiliary, (−)-menthol, was recovered after evaporation of the solvent.

### 3.12. *Sodium (2S,3S)-(−)-2,3-epoxy-2-methylbutanoate **13***

A solution of **10** with a *d.e.* of 98% (550 mg) in MeOH (8 ml) was stirred with NaOH (96 mg) and treated as described for the obtention of **12** to yield compound **13** (207 mg, 70%). $[\alpha]_D^{25}=-62$ (*c*=1.0, $H_2O$). Spectral data were identical to those of **12**.

### *3.13. (2R,3R)-(+)-2,3-Epoxy-2-methylbutanoic acid* **14**

A solution of sodium salt **12** (100 mg) in a saturated solution of $NH_4Cl$ (5 ml) was cooled on an ice–water bath, neutralized with HCl 0.5 N and extracted with EtOAc (20 ml). The organic layer was dried with $Na_2SO_4$ and evaporated at room temperature to yield **14** as a colorless oil (27 mg, 32%). $[\alpha]_D^{25}$=+30 (*c*=1.8, $CHCl_3$). IR ($CHCl_3$) $\nu_{max}$: 3672, 3494, 1736, 1380, 1268, 1102 $cm^{-1}$. EIMS m/z (%): $[M+1]^+$ 117 (7), 99 (4), 88 (11), 72 (57), 71 (21), 45 (100), 43 (98), 41 (18). $^1$H-NMR δ: 3.16 (q, *J*=5.5 Hz, H-3), 1.40 (d, *J*=5.5 Hz, Me-4), 1.61 (s, Me-5), 5.00 (br s, COOH) ppm; $^{13}$C-NMR δ: 172.65 (C-1), 60.39 (C-2), 60.94 (C-3), 13.66 (C-4), 18.45 (C-5) ppm.

### *3.14. (2S,3S)-(−)-2,3-Epoxy-2-methylbutanoic acid* **15**

A solution of sodium salt **13** (100 mg) in a saturated solution of $NH_4Cl$ (5 ml) was treated as described for the obtention of **14** affording compound **15** as a colorless oil (25 mg, 30%). $[\alpha]_D^{25}$=−29 (*c*=1.4, $CHCl_3$). Spectral data were identical to those of **14**.

### *3.15. Methyl (2R,3R)-(+)-2,3-epoxy-2-methylbutanoate* **16**

Epoxyacid **14** (135 mg) was treated with an ethereal solution of diazomethane[15] (20 ml) at room temperature. After evaporation of the solvent, methyl ester **16** (24 mg, 16%) was obtained as a colorless oil. $[\alpha]_D^{25}$=+19 (*c*=1.1, $CHCl_3$). IR ($CHCl_3$) $\nu_{max}$: 3040, 1720, 1460, 1380, 1265, 1160 $cm^{-1}$. EIMS m/z (%): $[M+1]^+$ 131 (1), 115 (1), 99 (1), 83 (2), 71 (10), 59 (93), 55 (8), 43 (100). $^1$H-NMR δ: 3.06 (q, *J*=5.4 Hz, H-3), 1.33 (d, *J*=5.4 Hz, Me-4), 1.57 (s, Me-5), 3.78 (s, MeO) ppm. $^{13}$C-NMR δ: 170.48 (C-1), 59.77 (C-2), 59.95 (C-3), 13.62 (C-4), 19.14 (C-5), 52.25 (MeO) ppm.

### *3.16. Methyl (2S,3S)-(−)-2,3-epoxy-2-methylbutanoate* **17**

Epoxyacid **15** (80 mg) was treated as described for **16** to yield methyl ester **17** (13 mg, 14%) as a colorless oil. $[\alpha]_D^{25}$=−19 (*c*=1.3, $CHCl_3$). Spectroscopic data were identical to those of **16**.

### *3.17. (2R)-(+)-2-Methyl-1,2-butanediol*

A solution of **8** with a *d.e.* of 90% (250 mg) in THF (8 ml) was treated with $LiAlH_4$ (150 mg) at 0°C. The mixture was stirred under reflux for 4 h, cooled to 0°C, treated with EtOAc, MeOH and $H_2O$, filtered and extracted with EtOAc. The organic layer was washed with $H_2O$, dried with $Na_2SO_4$ and evaporated. The product was chromatographed on silica gel. Elution with $CH_2Cl_2$:EtOAc (1:1) yielded the title compound (72 mg, 71%). $[\alpha]_D^{25}$=+7 (*c* 1.30, $CHCl_3$). Spectroscopic data were identical to those reported.[11]

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