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(−)-Fenchone derived epoxy alcohols — preparation and configuration

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Abstract

Several chiral diastereoisomerically pure epoxy alcohols were prepared diastereoselectively in high yields after epoxidation of allyl and homoallyl alcohols containing the 1*R*-fenchone skeleton with $VO(acac)_2$/*t*-butyl hydroperoxide. The configurations of some of the new chiral compounds were determined by NMR methods. An interesting rearrangement reaction of an epoxy alcohol to an olefinic diol catalyzed by V^{5+} ions was observed.

1. Introduction

Recently, we have prepared chiral epoxy alcohols from allyl and homoallyl alcohols containing the 1*R*-camphor skeleton via epoxidation with the $VO(acac)_2$/*t*-butyl hydroperoxide (TBHP) system.[2] The approach was effective for the isolation of diastereoisomerically pure epoxy alcohols and it was possible to determine configuration of the newly formed stereogenic centers by NMR methods. Since chiral nonracemic functionalized epoxides exhibit a large potential for use in the asymmetric synthesis[3] we were interested in the preparation of similar compounds. With the synthesis of the chiral allyl and homoallyl alcohols **1**–**4** from 1*R*-(−)-fenchone[4] we had further convenient starting compounds for epoxidation experiments, which we would like to present here.

2. Results and discussion

The epoxidation of compounds **1**–**3** in CH_2Cl_2 solutions at room temperature with TBHP (3 M in octane) and $VO(acac)_2$ as catalysts (Scheme 1) provided epoxy alcohols **5**–**7** with high yields. It must be pointed out that the starting compounds **1** and **2** were mixtures of *endo*-OH:*exo*-OH isomers (92:8).

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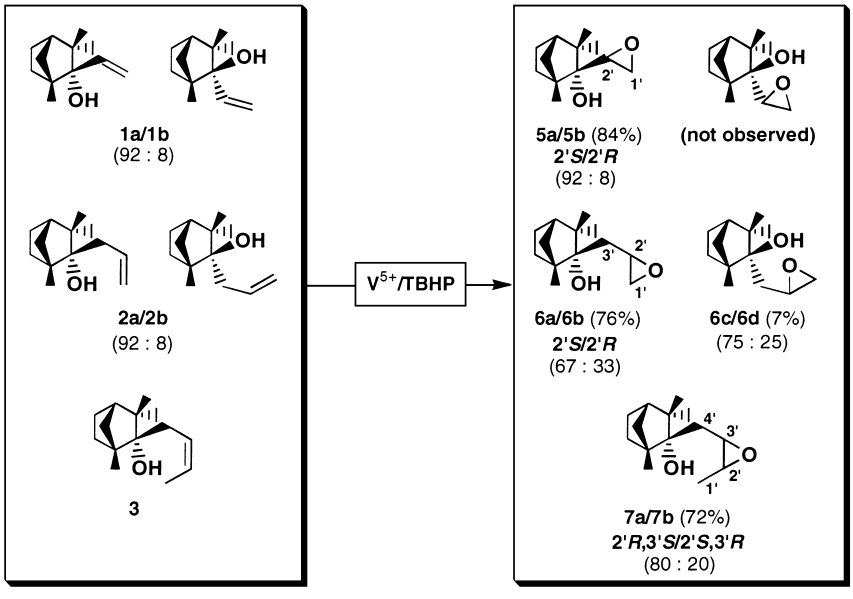
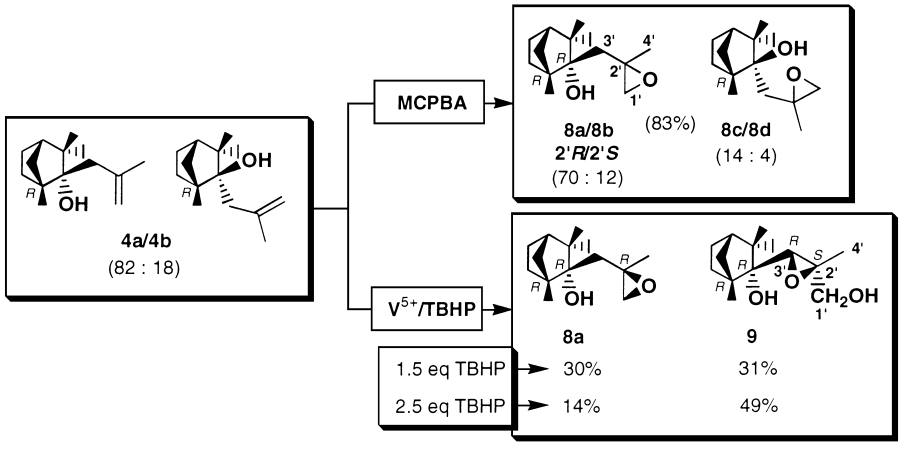
However, we could only observe the corresponding *exo*-OH-epoxy alcohols (**6c**/**d**) after the epoxidation of **2**. The diastereoselectivities of the epoxidation of **1** and **3** were good with a diastereoisomeric ratio of the corresponding products **5a**/**5b**=92:8 and **7a**/**7b**=80:20, contrary to the moderate diastereoselectivity observed for products **6a**/**b** (Scheme 1). The diastereoisomeric ratios of the epoxy alcohols **5**–**7** were determined by NMR spectroscopy of the crude products. In all cases we were able to isolate the individual diastereoisomers by flash chromatography.



Scheme 1.



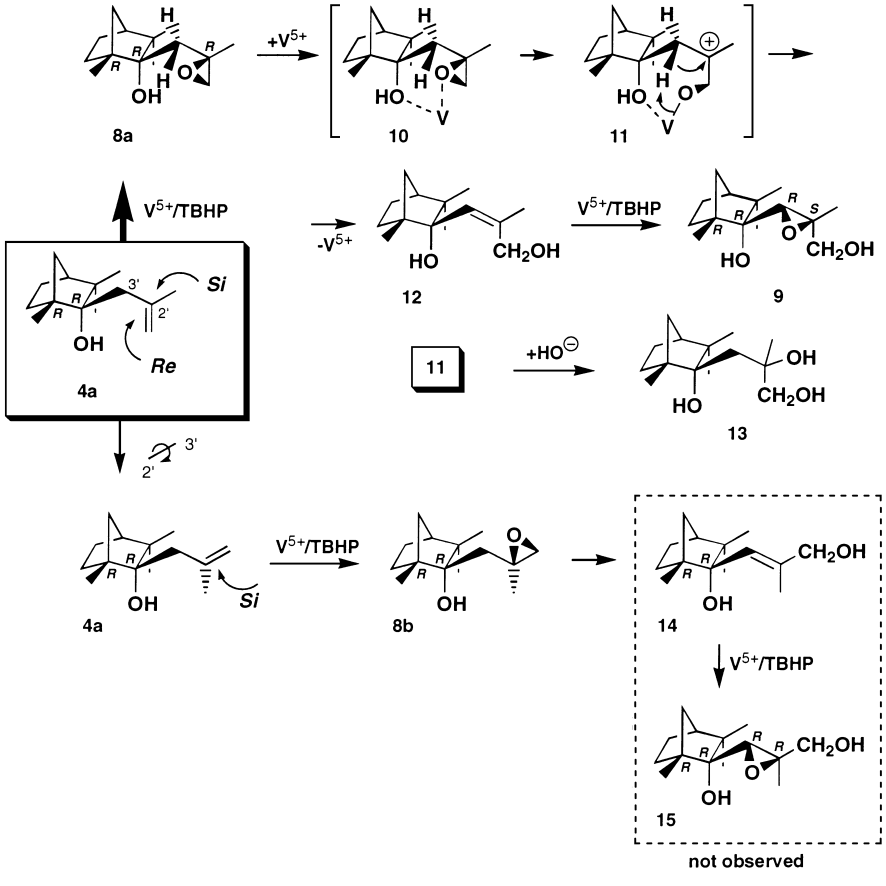
Scheme 2.

Reaction of homoallyl alcohol **4** during the epoxidation process was quite different and somewhat surprising in respect of the V^{5+}/TBHP procedure (Scheme 2). We were able to get a high yield and good diastereoselectivity when using, as an epoxidation agent, *m*-chloroperbenzoic acid (MCPBA). In this case, starting from homoallyl alcohol **4** (*endo*-OH:*exo*-OH mixture **4a**/**4b**=82:12)[4] all four diastereoisomers were obtained in a ratio **8a**/**8b**/**8c**/**8d**=70:12:14:4. However, none of the isomers could

be isolated in diastereoisomeric pure form. Only the major diastereoisomer **8a** was isolated relatively pure by flash chromatography (**8a**/**8d**=94:6) in 61% yield.

Applying the V^{5+}/TBHP procedure (in standard protocol, 1.5 equiv. TBHP, see Experimental) we isolated the main expected epoxidation product **8a** in only 30% yield; however, as a single diastereoisomer only, and with the same amount as epoxy diol **9**. A mixed fraction of the diastereoisomers **8b**/**8c** (11% yield, **8b**/**8c**=31:69 by NMR) was also obtained, but isomer **8d** could not be detected. Interestingly, when using a larger amount of TBHP (2.5 equiv.) the yield of **9** increased to 49% at the expense of **8a**, which decreased to 14%. With 3.5 equiv. TBHP we only isolated epoxy diol **9** within a 24 h reaction time.

We have suggested the interpretation presented in Scheme 3 as the explanation for the formation of compound **9**. In accordance with the cyclic transition state,[5] the hydroxy-directed vanadyl-promoted epoxidation should preferably proceed in a conformation of **4a** in which the *Re*-face of the double bond and the hydroxy group are close to each other. Additionally, epoxy alcohol **8a** which formed the V^{5+} ion could coordinate with both oxygen atoms (structure **10** in Scheme 3), which leads, via a carbonium ion **11** and rearrangement, to allylic diol **12**. Similar observations have been published by Sharpless.[6] Thereafter, compound **12** smoothly epoxidizes under the reaction conditions (V^{5+} and excess of TBHP) forming epoxy diol **9**.



Scheme 3.

The formation mode of **9** was supported by experimentation — addition of V^{5+} (prepared separately from $VO(acac)_2$ and TBHP in 1:1 ratio) to pure epoxy alcohol **8a** in CH_2Cl_2 mainly provided compound **12**, which was isolated by flash chromatography. Interestingly, we also isolated a small amount of triol

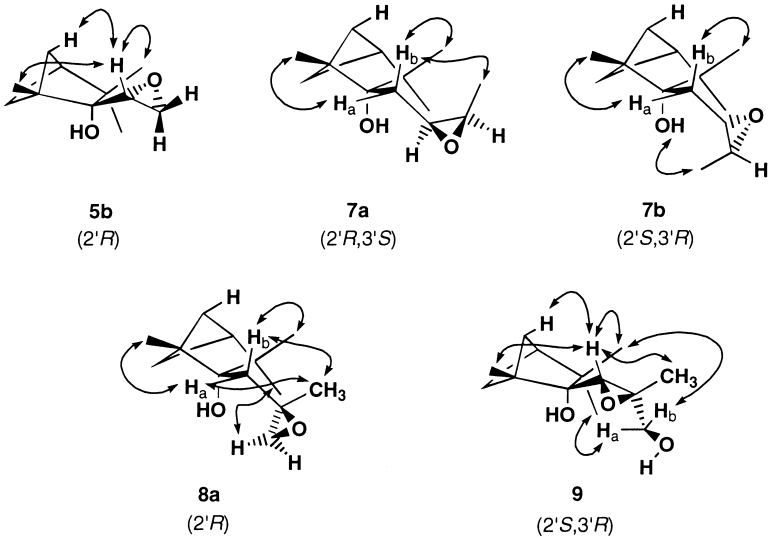
13, which could be formed from the intermediate **11** compound. Epoxidation of **4a** from the *Si*-side was less favoured; most probably because of a steric hindrance between the two methyl groups of the fenchone skeleton and the methyl group of the methyl–allyl moiety in the conformation in which the *Si*-face of the double bond was on the side of the hydroxy group (Scheme 3). Furthermore, we did not observe formation of products **14** and **15** (Scheme 3) indicating that the minor isomer **8b** was not able to undergo V^{5+} promoted rearrangement.

Determination of the configuration for the newly-formed chiral epoxide C-atoms for the individual diastereoisomers with *endo*-positioned hydroxy group was achieved (Table 1). Evidence based on the determined NOE enhancements, taking into account the observed differences between the chemical shifts and coupling constants of the diastereoisomers, is summarized in Scheme 4.

Table 1
^{13}C NMR chemical shifts for compounds **5**–**9** and **12**, **13** in $CDCl_3$

C-atom No.*	5a	5b	6a	6b	7a	7b	8a	8b	9	12	13
1	52.66	50.89	52.50	52.58	52.57	52.57	53.26	52.77	53.94	53.38	50.79
2	76.64	n.o.**	81.65	80.92	81.72	81.03	81.06	82.73	78.31	83.56	89.91
3	42.97	43.95	44.07	44.34	44.02	44.19	43.21	44.28	43.10	44.78	42.57
4	48.60	48.82	50.06	49.47	50.05	49.53	50.19	49.87	48.73	48.49	48.80
5	25.41	25.39	25.04	25.07	25.10	25.01	25.59	25.57	25.12	25.50	26.28
6	29.25	29.69	29.84	29.99	29.82	30.04	29.02	29.24	29.18	28.99	31.38
7	40.59	40.85	40.81	41.04	40.77	40.96	40.12	40.65	40.56	40.44	39.88
8	25.41	26.75	28.29	27.66	28.22	27.60	27.90	28.83	26.30	29.36	29.02
9	22.04	22.46	22.29	22.05	22.28	22.25	22.40	21.42	21.77	22.37	23.15
10	16.23	17.07	17.63	18.23	17.56	18.00	18.03	18.19	15.87	16.88	18.84
1'	43.30	44.43	48.34	48.26	13.10	13.33	54.92	55.68	62.69	63.49	69.95
2'	53.43	55.14	50.95	50.10	53.19	53.32	58.89	57.52	62.82	134.33	76.96
3'	-	-	38.36	38.65	55.34	54.26	36.99	37.34	67.40	131.24	26.97
4'	-	-	-	-	32.63	33.39	25.12	24.87	20.31	24.38	23.73

*assignments are based on heteronuclear CH-correlation experiments(HSQC)[7]; for the numbering of the C-atoms see Schemes 1 and 2.
**not observed due to overlapping with the signals of the $CDCl_3$.



Scheme 4.

The NOEs for **5a**,**5b** showed, in both isomers, spatial connectivity of the H-2′ proton with H-10, H-7_{syn} and H-8. Therefore, in the predominant conformation for both isomers the H-2′ proton lies between the H-8 and H-10 methyl groups. Consequently, the observed deshielding of 0.15 ppm for H-8 and H-$1'_{trans}$ in **5b**, when compared with **5a**, indicated 2′*R* configuration for the former, because of the proximity of both the epoxy and hydroxy oxygen atoms, respectively.

The NOEs for **6**, **7** and **8** showed a disposition of the methylene group nearest to the bicyclic skeleton so that one proton (H_a) was close to H-10 and the other (H_b) close to the H-8 methyl group. The pairs of the diastereoisomers **6a**/**7a** and **6b**/**7b** had very similar spectral patterns. Comparable differences are observed between the chemical shifts of H_a/H_b in both isomers — larger for **6a**/**7a** and smaller for **6b**/**7b**. The vicinal coupling constants for H_a and H_b in both pairs (**6a**/**7a** and **6b**/**7b**) were in fact equal, indicating no predominant conformation for these diastereoisomers. Thus, unambiguous assignment of the configurations for **6** and **7** was not possible. We tentatively assigned **7a** as 2′*R*,3′*S* and **7b** as 2′*S*,3′*R* using the following NOE observations: proximity of the H-1′ methyl group to H-$4'_b$ in **7a** and to the OH-group in **7b**, respectively. Due to the close similarities of **6a**/**7a** and **6b**/**7b** in chemical shifts and coupling constants we correspondingly assigned **6a** as the 2′*S* and **6b** as the 2′*R* diastereoisomer. The observed NOEs for compound **8a** allowed unambiguous configuration determination: the H-4′ methyl protons were equally close to H_a and H_b, whereas the H-$1'_{trans}$, *trans* located to this methyl group, showed NOE to H-9.

In the rearranged product **9** the H-3′ proton was situated analogously to **5**. The H-4′ methyl protons lay in *cis* position to H-3′, whereas the two diastereotopic H-1′ were close to the H-8 and H-9 methyl groups, respectively.

In the isomer with *exo*-positioned OH-group (**6c**/**d** and **8c**/**d**) no determination of the configuration of the newly formed chiral centers has been done. However, they could be easily discriminated from their *exo*-OH partners using the characteristic H-6_{endo} proton shifts and/or the C-8/C-9 differences in the ^{13}C chemical shifts.

In conclusion, we have effectively prepared new chiral epoxy alcohols with defined absolute configuration, which are of practical interest for further synthetic use.

3. Experimental

3.1. General methods and starting materials

All reactions were carried out under argon atmosphere to avoid moisture from the air. The solvents were dried and distilled. Thin layer chromatography (TLC): aluminium sheets precoated with silica gel 60 F_{254} (Merck). Column chromatography: at normal pressure, silica gel 60 (0.040–0.063 nm, Merck).

$[\alpha]_D^{20}$: Perkin–Elmer 241 polarimeter. Mass spectra (MS): Finnigan MAT 90 or Finnigan SSQ 700; fragmentation in *m/z* with relative intensities (%) in parentheses. NMR spectra: Bruker Avance DRX-250 (^1H at 250.1 MHz; ^{13}C at 62.9 MHz; TMS as internal standard); samples for the NOE difference experiments were prepared by blowing argon through the $CDCl_3$ solution, the individual lines in the multiplet were irradiated for 0.05 s maintaining the whole irradiation time for 4 s, the irradiation power was adjusted to suppress approximately 80% of the multiplet intensity. Elemental analyses were performed by the Microanalytical Service Laboratory of the Institute of Organic Chemistry, Bulgarian Academy of Sciences.

The following starting materials (commercially available or prepared according to the literature) were used: alcohols **1**–**4**,[4] vanadium(IV) oxide-bis(2,4-pentadionate) ($VO(acac)_2$) (Fluka AG), *t*-butyl

hydroperoxide (TBHP) 3 M solution in octane (Fluka AG), *m*-chloroperbenzoic acid (MCPBA) 55% (Fluka).

3.2. General procedure for V^{5+}-catalyzed epoxidation of alcohols **1**–**4**

To a ca. 0.1 M solution of the corresponding alcohol **1**–**4** in anhydrous CH_2Cl_2 was added 1–2% of $VO(acac)_2$ and 1.5–2.5 equiv. of TBHP (anhydrous 3 M solution in octane) at ice-bath temperature. The mixture was then stirred at room temperature. The reaction was monitored by TLC. After completion of the reaction the mixture was washed with sat. NaCl soln, dried (Na_2SO_4) and concentrated under reduced pressure. The crude product (containing TBHP) was purified by column chromatography.

3.3. (1R,2R)-2-exo-(1′,2′-Epoxyethyl)-1,3,3-trimethylbicyclo[2.2.1]heptan-2-ol **5**

Following the general procedure, 0.50 g (2.80 mmol) of **1** in 30 ml CH_2Cl_2, 0.01 g (0.04 mmol) $VO(acac)_2$ and 1.4 ml (4.20 mmol) 3 M TBHP were combined and stirred for 24 h. After workup 0.52 g of crude **5** (1*R*,2*R*,2′*S*-**5a**/1*R*,2*R*,2′*R*-**5b**=92:8 by NMR) were chromatographed (∅ 17 mm, h=520 mm, 46 g silica gel, hexane:Et_2O=15:1) to give 0.01 g unconverted **1**, 0.33 g (78%) **5a** (colorless solid) and 0.03 g (7%) **5b** (colorless solid). The total yield of **5** was 0.36 g (85%) in respect of the reacted **1**.

MS (CI: NH_3) *m/z* (%)=214 ($[M+18]^+$,100), 197 ($[M+1]^+$,13), 179 ($[(M-H_2O)+1]^+$, 28). Anal. calcd for $C_{12}H_{20}O_2$ (196.3): C, 73.43; H, 10.27; O, 16.30; found: C, 73.56; H, 10.37.

Data for (1*R*,2*R*,2′*S*)-**5a**: mp 75°C. $[\alpha]_D^{20}$=−26.3 (*c* 1.05, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 K): δ=0.91 (s, 3H, 9-H), 0.96–1.08 (m, 1H, 6-H_{exo}), 1.01 (s, 3H, 8-H), 1.05 (s, 3H, 10-H), 1.20–1.25 (m, 1H, 7-H_{anti}), 1.36–1.50 (m, 1H, 5-H_{exo}), 1.66–1.79 (m, 3H, 4-H, 5-H_{endo}, 7-H_{syn}), 1.87 (s, 1H, OH), 1.87–2.09 (m, 1H, 6-H_{endo}), 2.69 (dd, 1H, 1′-H_{trans}, J=5.3, 3.1 Hz), 2.73 (dd, 1H, 1′-H_{cis}, J=5.3, 4.2 Hz), 3.10 (dd, 1H, 2′H, J=4.2, 3.1 Hz).

Data for (1*R*,2*R*,2′*R*)-**5b**: mp 56°C. $[\alpha]_D^{20}$=−7.7 (*c* 1.05, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 K): δ=0.93 (s, 3H, 9-H), 1.03 (s, 3H, 10-H), 0.96–1.08 (m, 1H, 6-H_{exo}), 1.16 (s, 3H, 8-H), 1.15–1.22 (m, 1H, 7-H_{anti}), 1.38–1.53 (m, 1H, 5-H_{exo}), 1.54 (s, 1H, OH), 1.68–1.79 (m, 3H, 4-H, 5-H_{endo}, 7-H_{syn}), 1.95–2.06 (m, 1H, 6-H_{endo}), 2.67 (dd, 1H, 1′-H_{cis}, J=5.2, 4.0 Hz), 2.84 (dd, 1H, 1′-H_{trans}, J=5.2, 2.9 Hz), 3.15 (dd, 1H, 2′-H, J=4.0, 2.9 Hz).

3.4. (1R,2R)-2-exo-(1′,2′-Epoxypropyl)-1,3,3-trimethylbicyclo[2.2.1]heptan-2-ol **6**

Following the general procedure, 0.50 g (2.60 mmol) of **2** in 26 ml CH_2Cl_2, 0.01 g (0.04 mmol) $VO(acac)_2$ and 1.3 ml (3.90 mmol) 3 M TBHP were combined and stirred for 42 h. After workup 0.54 g of crude **6** (diastereoisomeric ratio 1*R*,2*R*,2′*S*-**6a**/1*R*,2*R*,2′*R*-**6b**=67:33 by NMR) was chromatographed (∅ 17 mm, h=520 mm, 46 g silica gel, hexane:Et_2O=8:1) to give 0.07 g unconverted **2**, 0.24 g (51%) **6a** (colorless solid), 0.04 g mixed fraction (7%; **6c**/**6d**=75:25) and 0.12 g (25%) **6b** (colorless solid). The total yield of **6a** and **6b** was 0.36 g (76%) in respect of the reacted **2**.

MS (EI) *m/z* (%)=210 (M^+, 2), 195 (0.4), 180 (0.1), 153 (8), 125 (27), 123 (21), 109 (15), 85 (44), 81 (100), 69 (55). Anal. calcd for $C_{13}H_{22}O_2$ (210.3): C, 74.24; H, 10.54; O, 15.25; found: C, 74.25; H, 10.52.

Data for (1*R*,2*R*,2′*S*)-**6a**: mp 36°C. $[\alpha]_D^{20}$=−24.6 (*c* 2.15, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 K): δ=0.99 (s, 3H, 10-H), 1.04 (s, 3H, 9-H), 1.13 (s, 3H, 8-H), 0.93–1.13 (m, 2H, 6-H_{exo}, 7-H_{anti}), 1.37–1.60 (m, 2H, 5-H_{exo}, 7-H_{syn}), 1.53 (dd, 1H, 3′-Ha, J=14.7, 6.8 Hz), 1.60–1.73 (m, 2H, 4-H, 5-H_{endo}), 1.93–2.08 (m,

1H, 6-H_{endo}), 2.04 (dd, 1H, 3′-H_b, J=14.7, 4.1 Hz), 2.41 (s, 1H, OH), 2.50 (dd, 1H, 1′-H_{trans}, J=4.9, 2.8 Hz), 2.82 (dd, 1H, 1′-H_{cis}, J=4.9, 4.2 Hz), 3.23 (m, 1H, 2′-H).

Data for (1*R*,2*R*,2′*R*)-**6b**: mp 53°C. $[\alpha]_D^{20}$=−7.5 (*c* 2.15, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 K): δ=0.97 (s, 3H, 9-H), 1.07 (s, 6H, 8-H, 10-H), 0.85–1.15 (m, 2H, 6-H_{exo}, 7-H_{anti}), 1.37–1.51 (m, 1H, 5-H_{exo}), 1.57–1.63 (m, 1H, 7-H_{syn}), 1.65–1.77 (m, 2H, 4-H, 5-H_{endo}), 1.76 (dd, 1H, 3′-H_b, J=15.0, 5.4 Hz), 1.85 (dd, 1H, 3′-Ha, J=15.0, 4.8 Hz), 2.51 (dd, 1H, 1′-H_{trans}, J=5.0, 2.8 Hz), 2.81 (dd, 1H, 1′-H_{cis}, J=5.0, 4.2 Hz), 3.19 (m, 1H, 2′-H).

3.5. (1R,2R)-2-exo-(2′,3′-Epoxybutyl)-1,3,3-trimethylbicyclo[2.2.1]heptan-2-ol **7**

Following the general procedure, 0.300 g (1.40 mmol) of **3** in 14 ml CH_2Cl_2, 0.006 g (0.02 mmol) $VO(acac)_2$ and 0.72 ml (2.20 mmol) 3 M TBHP were combined and stirred for 48 h. After workup 0.320 g of crude **7** (1*R*,2*R*,1′*R*,2′*S*-**7a**/1*R*,2*R*,1′*S*,2′*R*-**7b**=80:20 by NMR) were chromatographed (Ø 13 mm, h=430 mm, 25 g silica gel, hexane:Et_2O=10:1) to give 0.030 g unconverted **3**, 0.165 g (57%) **7a** and 0.043 g (15%) **7b**. The total yield of **7** was 0.208 g (72%) in respect of the reacted **3**.

MS (CI:NH_3) *m/z* (%)=242 ($[M+18]^+$, 89), 224 ($[(M-H_2O)+18]^+$, 85), 207 ($[(M-H_2O)+1]^+$, 100). Anal. calcd for $C_{14}H_{24}O_2$ (224.3): C, 74.95; H, 10.78; O, 14.26; found: C, 74.38; H, 10.67.

Data for (1*R*,2*R*,2′*R*,3′*S*)-**7a**: $[\alpha]_D^{20}$=−9.3 (*c* 1.78, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 K) δ=0.89–1.00 (m, 1H, 6-H_{exo}), 1.01 (s, 6H, 9-H, 10-H), 1.12 (s, 3H, 8-H), 1.05–1.10 (m, 1H, 7-H_{anti}), 1.29 (dd, 3H,1′-H, J=5.5, 0.6 Hz), 1.30–1.44 (m, 1H, 5-H_{exo}), 1.52–1.74 (m, 3H, 4-H, 7-H_{syn}, 5-H_{endo}), 1.56 (dd, 1H, 4′-H_a, J=14.8, 6.5 Hz), 1.92 (dd, 1H, 4′-Hb, J=14.8, 4.5 Hz), 1.93–2.05 (m, 1H, 6-H_{endo}), 2.48 (s, 1H, OH), 3.09 (qdd, 1H, 2′-H, J=5.5, 4.5, 0.5 Hz), 3.27 (dtd, 1H, 3′-H, J=6.5, 4.5, 0.6 Hz).

Data for (1*R*,2*R*,2′*S*,3′*R*)-**7b**: $[\alpha]_D^{20}$=−14.3 (*c* 1.78, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 K): δ=0.99 (s, 3H, 9-H), 0.99–1.07 (m, 1H, 6-H_{exo}), 1.05 (s, 3H, 10-H), 1.11 (s, 3H, 8-H), 1.131–1.15 (m, 1H, 7-H_{anti}), 1.27 (d, 3H, 1′-H, J=5.5 Hz), 1.33–1.51 (m, 1H, 5-H_{exo}), 1.57–1.77 (m, 4H, 7-H_{syn}, 4-H, 5-H_{endo}, OH), 1.66 (dd, 1H, 4′-H_b, J=15.2, 5.0 Hz), 1.85 (dd, 1H, 4′-H_a, J=15.2, 4.7 Hz), 1.88–1.99 (m, 1H, 6-H_{endo}), 3.08 (qd, 1H, 2′-H, J=5.5, 4.5 Hz), 3.21 (q, 1H, 3′-H, J=4.7 Hz).

3.6. (1R,2R)-2-exo-(2′-Methyl-1′,2′-epoxypropyl)-1,3,3-trimethylbicyclo[2.2.1]heptan-2-ol **8**

3.6.1. Epoxidation with t-butyl hydroperoxide

Following the general procedure, 0.50 g (2.40 mmol) of **4** in 24 ml CH_2Cl_2, 0.01 g (0.04 mmol) $VO(acac)_2$ and 1.2 ml (3.60 mmol) 3 M TBHP were combined and stirred for 6 days. After workup the crude product was chromatographed (Ø 17 mm, h=490 mm, 44 g silica gel, hexane:Et_2O=8:1–500 ml, hexane:Et_2O=5:1–150 ml, hexane:Et_2O=4:1–125 ml, hexane:Et_2O=3:1–1000 ml) to give 0.07 g unconverted **4**, 0.14 g (30%) **8a** (oil), 0.05 g (11%; **8b**/**8c**=31:69) and 0.15 g (31%) **9**. Yields were calculated in respect of the reacted **4**.

Data for (1*R*,2*R*,2′*R*)-**8a**: MS (EI) *m/z* (%)=224 (M^+, 0.9), 193 (1.4), 153 (3.7), 123 (12), 99 (18), 81 (100), 69 (41), 53 (16). Anal. calcd for $C_{14}H_{24}O_2$ (224.3): C, 74.95; H, 10.78; O, 14.24, found: C, 74.84; H, 10.57. $[\alpha]_D^{20}$=−34.39 (*c* 2.28, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 K): δ=0.86–1.10 (m, 2H, 6-H_{exo}, 7-H_{anti}), 0.99 (s, 3H, 9-H), 1.00 (s, 3H, 8-H), 1.02 (s, 3H, 10-H), 1.22–1.43 (m, 1H, 5-H_{exo}), 1.40 (s, 3H, 4′-H), 1.45–1.52 (m, 1H, 7-H_{syn}), 1.58–1.75 (m, 2H, 4-H, 5-H_{endo}), 1.93 (d, 1H, 3′-H_b, J=15.9 Hz), 1.99–2.08 (m, 1H, 6-H_{endo}), 2.13 (d, 1H, 3′-H_a, J=15.9 Hz), 2.67 (d, 1H, 1′-H_{cis}, J=4.4 Hz), 2.96 (s, 1H, OH), 3.28 (d, 1H, 1′-H_{trans}, J=4.4 Hz).

3.6.2. Epoxidation with m*-chloroperbenzoic acid*

To a solution of 0.500 g (2.4 mmol) **4** in 24 ml CH_2Cl_2 was added 1.500 g (4.8 mmol) MCPBA at 0°C. The mixture was stirred at 0°C for 3 h, then treated with 30% aqueous solution of NaOH and the mixture was extracted with Et_2O. The organic layer was washed with water and then with brine, dried (Na_2SO_4) and concentrated. The crude product **8** (0.517 g) was chromatographed (Ø 17 mm, h=490 mm, 44 g silica gel, hexane:Et_2O=10:1) to give 0.330 g (61%; **8a**/**8d**=94:6), 0.018 g (35; **8a**/**8b**=20:80), 0.055 g (10%; **8b**/**8c**=65:35) and 0.044 g (8%; **8b**/**8c**=5:95). The total yield of **8** was 0.445 g (82%).

*3.7. (1*R*,2*R*,2′*S*,3′*R*)-2*-exo-*(1′-Hydroxy-2′-methyl-2′,3′-epoxypropyl)-1,3,3-trimethylbicyclo[2.2.1]-heptan-2-ol (**9**)*

Following the general procedure, 0.50 g (2.40 mmol) of **4** in 24 ml CH_2Cl_2, 0.01 g (0.04 mmol) $VO(acac)_2$ and 2.0 ml (6.00 mmol) 3 M TBHP were combined and stirred for 6 days. After workup the crude product was chromatographed (Ø 17 mm, h=490 mm, 44 g silica gel, hexane:Et_2O=8:1–500 ml, hexane:Et_2O=5:1–150 ml, hexane:Et_2O=4:1–125 ml, hexane:Et_2O=3:1–1000 ml) to give 0.06 g unconverted **4**, 0.07 g (14%) **8a**, 0.05 g (10%; **8b**/**8c**=11:89) and 0.25 g (49%) **9** (colorless solid) in respect of the reacted **4**.

Data for **9**: MS (EI) *m/z* (%)=240 (M^+, 0.5), 209 (3), 123 (16), 81 (100), 69 (25). Anal. calcd for $C_{14}H_{24}O_3$ (240.3): C, 69.98; H, 10.07; O, 19.97; found: C, 69.95; H, 10.14. Mp 85°C. $[\alpha]_D^{20}$=−9.4 (*c* 1.76, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 K): δ=0.91 (s, 3H, 9-H), 0.91–1.08 (m, 1H, 6-H_{exo}). 0.95 (s, 3H, 8-H), 1.05 (s, 3H, 10-H), 1.20–1.25 (m, 1H, 7-H_{anti}), 1.28–1.52 (m, 1H, 5-H_{exo}), 1.44 (s, 3H, 4′-H), 1.64–1.80 (m, 3H, 7-H_{syn}, 4-H, 5-H_{endo}), 1.96–2.17 (m, 1H, 6-H_{endo}), 2.13 (s, OH), 2.88 (s, 1H, 3′-H), 3.76 (d, 1H, 1′-H_b, J=12.3 Hz), 4.14 (d, 1H, 1′-H_a, J=12.3 Hz).

*3.8. (1*R*,2*R*)-2*-exo-*(1′-Hydroxy-2′-methyl-prop-2′-en-3′-yl)-1,3,3-trimethylbicyclo[2.2.1]heptan-2-ol* ***12***

A solution of 0.150 g (0.670 mmol) of **7a** in 6 ml CH_2Cl_2 was added to a V^{5+}-solution [prepared separately from 0.004 g (0.016 mmol) $VO(acac)_2$ and 0.005 ml (0.015 mmol) 3 M TBHP in CH_2Cl_2] at 0°C. The mixture was then stirred at room temperature for 3 days. After workup according to the general procedure, the crude product (0.143 g) was chromatographed (Ø 12 mm, h=550 mm, 20 g silica gel, hexane:Et_2O=10:1) to give 0.017 g **13**, 0.017 g mixed fraction and 0.040 g (27%) **12** (colorless solid).

Data for **12**: mp 55°C. MS (CI:NH_3) *m/z* (%)=242 ($[M+18]^+$, 38), 224.3 ($[(M-H_2O)+18]^+$, 12), 207.3 ($[(M-H_2O)+1]^+$, 100). Anal. calcd for $C_{14}H_{24}O_2$: C, 74.95; H, 10.78; O, 14.26; found: C, 74.77; H, 10.88. $[\alpha]_D^{20}$=−57.81 (*c* 2.01, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 K): δ=0.86 (s, 3H, 8-H), 0.98 (s, 6H, 9-H, 10-H), 1.02–1.19 (m, 2H, 6-H_{exo}, 7-H_{anti}), 1.36–1.49 (m, 1H, 5-H_{exo}), 1.61–1.77 (m, 3H, 4-H, 7-H_{syn}, 5-H_{endo}), 1.81 (d, 3H, 4′-H, J=1.4 Hz), 1.79–1.90 (m, 1H, 6-H_{endo}), 2.94 (s, 1H, OH), 4.01 and 4.23 (AB-system, 2H, 1′-H, J=12.5 Hz), 5.34 (s, 1H, 3′-H).

Data for **13**: (2-*exo*-(1′-hydroxy-2′-hydroxy-2′-methyl)-1,3,3-trimethylbicyclo[2.2.1]heptan-2-ol) ^{1}H NMR ($CDCl_3$, 300 K): δ=1.01 (s, 3H, 9-H), 1.06 (s, 3H, 8-H), 0.98-1.08 (m, 2H, 7-H_{anti}, 6-H_{exo}), 1.19 (s, 3H, 10-H), 1.28-1.47 (m, 2H, 7-H_{syn}, 5-H_{exo}), 1.41 (s, 3H, 4′-H), 1.62–1.80 (m, 3H, 4-H, 5-H_{endo}, 6-H_{endo}), 2.04 (s, OH), 2.15 and 2.33 (AB-system, 2H, 3′-H, J=11.9 Hz), 3.43 (dd, 1H, 1′-H_b, J=11.1, 7.1 Hz), 3.69 (dd, 1H, 1′-H_a, J=11.1, 2.7 Hz).

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