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Enantiopure vicinally trisubstituted all-*cis*-bis(hydroxymethyl)-cyclopentenols and their derivatives

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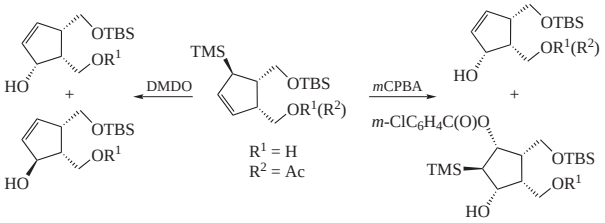
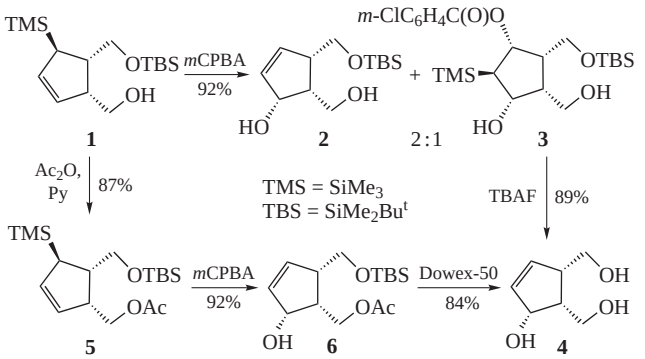
Oxidations of {(1*R*,4*R*,5*S*)-2-[*tert*-butyl(dimethyl)silyloxymethyl]-4-(trimethylsilyl)cyclopent-2-en-1-yl}methanol with *m*-chloroperoxybenzoic acid (*m*CPBA) and dimethyldioxirane were studied. In the case of *m*CPBA, an allylicic alcohol expected according to the protodesilylation mechanism and an anomalous product of 1,2-migration of the Me_3Si group were obtained. The latter was formed due to the coordination and directing effects of the free OH group.



The uniqueness of the chemistry of allylsilanes provides good opportunities for their application in rational synthesis.[1,2] This work was aimed at the investigation of features and stereochemistry in the model epoxidation–fragmentation of cyclopentane allylsilane **1**[3] and its derivatives using *m*-chloroperoxybenzoic acid (*m*CPBA) and dimethyldioxirane (DMDO) as the oxidants. Note that the epoxidation of allylsilanes gives labile epoxy silanes, which would undergo the acid-catalyzed Peterson-type fragmentation leading to allylic alcohols *via* a transfer of double bond according to the *anti*-$S_{E'}$ mechanism.[4]

In our case, the epoxidation of alcohol **1** under the standard conditions for *m*CPBA afforded a 2:1 mixture of two products of the oxirane ring opening, namely, allylic alcohol **2** and trimethylsilyl-containing ester **3** (Scheme 1).† The latter was converted into triol **4** by a treatment with Bu_4NF. Under the same conditions, the epoxidation of acetate **5** resulted in the selective formation of allylic alcohol **6** only.



Scheme 1

Stereochemical assignments for compounds **2** and **3** were based on the 2D-data of ^1H NMR spectra. In case of **2**, strong NOE interactions were observed for *cis*-protons at C^1/C^5 (5.9 Hz) and C^1/C^2 (6.7 Hz) (Figure 1). The mutual position and stereochemistry of the substituents in compound **3** were in agreement with the reported data[5] and were confirmed by the presence of characteristic HMBC and NOE interactions. Thus, the proton at C^5 was interacting both with the protons at C^4 (3.4 Hz) and at C^1 (7.9 Hz) and with the carbon atoms. Subsequently, the proton at C^1 exhibited NOE with protons at C^2 (7.1 Hz) and C^3 (0.9 Hz)

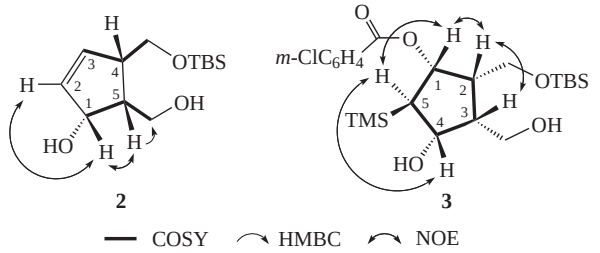


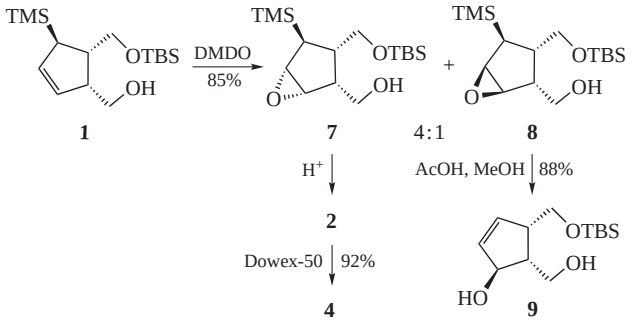
Figure 1 Selected NOE, HMBC and COSY data for compounds **2** and **3**.

† *Compounds* **2** *and* **3**. A solution of 75% *m*CPBA (0.29 g, 1.28 mmol) in CH_2Cl_2 (20 ml) was added to a solution of compound **1** (0.20 g, 0.64 mmol) in CH_2Cl_2 (15 ml) at 0 °C. After being stirred at 0 °C for 15 min, the solution was heated to room temperature and stirred for 2 h (TLC control, light petroleum–ethyl acetate, 1:1). Saturated solution of $Na_2S_2O_3$ (5 ml) was added, and the mixture was stirred for 1 h. The organic layer was separated and washed with 5% aqueous solution of $NaHCO_3$ (15 ml). The aqueous layer was extracted with CH_2Cl_2 (3×15 ml), the combined organic extracts were dried over $MgSO_4$ and evaporated under reduced pressure. Purification of the products by column chromatography (light petroleum–ethyl acetate, 1:1) afforded compounds **2** and **3**.

*(1*R*,4*S*,5*R*)-4-[*tert*-Butyl(dimethyl)silyloxymethyl]-5-(hydroxymethyl)-cyclopent-2-en-1-ol* **2**. Yield 0.11 g (63%), transparent viscous oil, R_f = 0.6 (light petroleum–ethyl acetate, 1:1), $[\alpha]_D^{20}$ –39.5 (*c* 0.9, CH_2Cl_2). ^1H NMR (500 MHz, $CDCl_3$) δ: 6.11 (dt, 1H, C^2H, *J* 1.7, 5.7 Hz), 5.48 (dd, 1H, C^3H, *J* 2.3, 5.8 Hz), 4.54–4.62 (br. s, 1H, C^1H), 4.02 (dd, 1H, $CH_\alpha H_\beta OH$, *J* 8.3, 11.1 Hz), 3.85 (dd, 1H, $CH_\alpha H_\beta OH$, *J* 7.2, 11.3 Hz), 3.69 (dd, 1H, $CH_\alpha H_\beta OSi$, *J* 2.3, 10.5 Hz), 3.64 (dd, 1H, $CH_\alpha H_\beta OSi$, *J* 3.1, 10.5 Hz), 3.03–3.10 (br. s, 1H, OH), 2.81–2.86 (m, 1H, C^4H), 2.48 (quintet, 1H, C^5H, *J* 7.0 Hz), 2.25–2.40 (br. s, 1H, OH), 0.93 (s, 9H, Bu^t), 0.06 (s, 6H, Me_2Si). ^{13}C NMR (125.76 MHz, $CDCl_3$) δ: 135.58 (C^3), 135.22 (C^2), 74.85 (C^1), 60.68 (CH_2OSi), 60.12 (CH_2OH), 47.10 (C^5), 37.63 (C^4), 25.94 (Me_3C), 18.48 (Me_3C), –5.53 (Me_2Si). IR (ν/cm^{-1}): 3386, 2955, 2930, 1472, 1256, 1029, 838, 779. MS (ACPI), *m*/*z*: 259 $[M+H]^+$. Found (%): C, 60.16; H, 9.96. Calc. for $C_{13}H_{26}O_3Si$ (%): C, 60.34; H, 10.05.

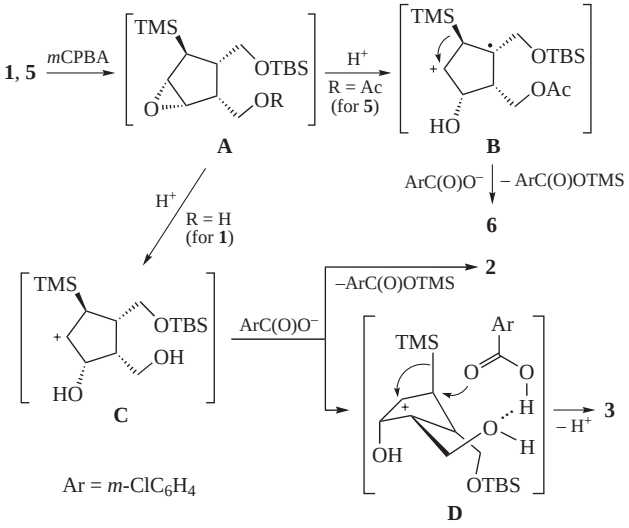
and HMBC interaction with carbon atoms C^4, in the carbonyl and protected alcohol groups. Similarly, the proton at C^4 manifested NOE with the proton at C^3 (5.8 Hz) and the HMBC interaction with the carbon atoms C^1 and C^3. The presence of signals corresponding to the proton interactions at C^1/C^5, C^1/C^2, C^4/C^5, and C^4/C^3 in COSY spectra also confirmed the proposed structure. The removal of the protective groups in compound **3** led to triol **4**. The unexpected easiness of this transformation also supports the proposed *trans*-position of the leaving groups (silyl and acyl), which is confirmed by the reported close precedents, in particular, by fragmentation of epoxides of allylsilanes.[1] The same triol was obtained *via* the **1** → **5** → **6** → **4** sequence, which indicated the correct orientation of the hydroxyl group in structure **3**.

On using DMDO (generated *in situ* from Oxone®), a 4:1 mixture of epoxides **7** and **8** (TLC control) was formed (Scheme 2). Isomer **7** was subsequently converted into allylic alcohol **2** during the working up and isolation while isomer **8** was isolated unchanged. The obtained compounds were readily separated by chromatography. The treatment of compound **8** with a AcOH/MeOH mixture gave diol **9** epimeric to **2**. The removal of TBS protecting group converted compound **2** into triol **4**.



Scheme 2

The possible ways of formation of alcohols **2**, **3**, and **6** in epoxidation reactions of **1** and **5** with *m*CPBA are worthy of note. The major difference was the selective formation of allylic alcohol **6** from homoallylic acetate **5**. In this case, no product of 1,2-migration of the TMS group was formed. These differences explain the step-by-step routes of transformations of **1** and **5** shown in Scheme 3. The electron-rich double bond in allylsilane **1** is active towards *m*CPBA, the resulting epoxide **A** was subsequently smoothly converted into α-carbocations **B** and **C** (the stabilizing β-effect[6] of the TMS group should also promote their



Scheme 3

generation). In case of acetate **5**, transformation of species **B** proceeds in a standard way to give product **6**. In case of alcohol **1**, the corresponding crbocation **C** partially undergoes the similar protodesilylation with the formation of diol **2**. Simultaneously, the free hydroxyl group in **C** is coordinated with $ArCO_2H$ by H-bonding and involved $ArCO_2H$ into a 'push–pull' type transition state **D** with the synchronous 1,2-migration of the silyl group (*cf.* ref. 7).

In conclusion, this study revealed new synthetically promising orthogonally functionalized cyclopentene alcohol **6**, diols **2** and **9**, and triol **4**. The initial step of epoxidation is sterically controlled by the TMS group, which is directing the oxidant attack from the spatially less hindered α-part of allylsilane **1**.

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Online Supplementary Materials

Supplementary data associated with this article can be found in the online version at doi: 10.1016/j.mencom.2018.09.033.

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*(1*R,*2*S,*3*R,*4*S,*5*R*)-2-[*tert*-Butyl(dimethyl)silyloxymethyl]-4-hydroxy-3-(hydroxymethyl)-5-(trimethylsilyl)cyclopentyl 3-chlorobenzoate* **3**. Yield 0.09 g (29%), transparent viscous oil, R_f = 0.4 (light petroleum–ethyl acetate, 1:1), $[\alpha]_D^{20}$ +8.0 (*c* 0.77, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.40, 7.56, 7.90, 7.99 (4H, Ph), 5.23 (dd, 1H, C^1H, *J* 7.1, 8.0 Hz), 4.18 (dd, 1H, C^4H, *J* 3.4, 5.8 Hz), 4.00 (dd, 1H, $CH_\alpha H_\beta OH$, *J* 7.8, 11.3 Hz), 3.90 (dd, 1H, $CH_\alpha H_\beta OH$, *J* 5.8, 11.3 Hz), 3.77 (dd, 1H, $CH_\alpha H_\beta OSi$, *J* 4.7, 11.0 Hz), 3.67 (dd, 1H, $CH_\alpha H_\beta OSi$, *J* 3.6, 11.0 Hz), 2.56 (dddd, 1H, C^2H, *J* 3.6, 4.7, 6.4, 7.3 Hz), 2.20 (m, 1H, C^3H), 1.48 (dd, 1H, C^5H, *J* 3.4, 8.2 Hz), 0.88 (s, 9H, Bu^t), 0.02 (s, 6H, Me_2Si), 0.01 (s, 9H, Me_3Si). ^{13}C NMR (125.76 MHz, $CDCl_3$) δ: 164.96 (C=O), 127.70, 129.60, 129.81, 131.58, 133.24, 134.66 (Ph), 77.84 (C^1), 73.67 (C^4), 60.37 (CH_2OH), 59.34 (CH_2OSi), 47.02 (C^3), 44.67 (C^2), 42.02 (C^5), 25.78 (Me_3C), 18.23 (Me_3C), –3.06 (Me_3Si), –5.69 (Me_2Si). IR (ν/cm^{-1}): 3347, 2954, 2929, 1721, 1291, 1255, 837, 749. MS (ACPI), *m*/*z*: 488 $[M+H]^+$. Found (%): C, 56.55; H, 7.87. Calc. for $C_{23}H_{39}O_5Si_2$ (%): C, 56.67; H, 8.00.