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Unusual α-hydroxyaldehyde with a cyclopentane framework from verbenol epoxide

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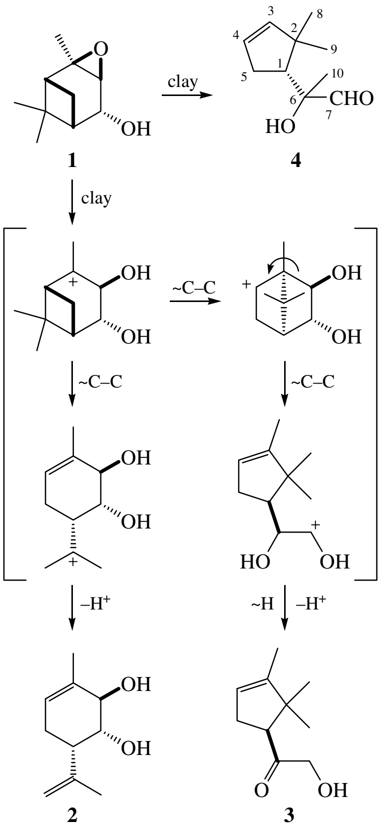
The isomerization of (–)-*cis*-verbenol epoxide in the presence of K10 clay forms optically active 2-(2,2-dimethylcyclopent-3-enyl)-2-hydroxypropanal as one of the products.

Interest in the chemistry of pinane terpenoids is due to the useful properties of these substances such as accessibility,[1] chemical lability, and generally high optical purity, which are of importance to asymmetric synthesis.[2–4] Recently,[5] we found that the storage of (–)-*cis*-verbenol epoxide **1** on natural montmorillonite askanite-bentonite clay unexpectedly formed *trans*-diol **2** with a *p*-menthane framework as the major product (47%). Hydroxyketone **3**, which had been obtained before as the major product of this reaction in the presence of ZnBr$_2$,[6] was isolated in minor quantities (5%) (Scheme 1). The possible mechanism leading to diol **2** involves the stage of an opening transformation of the cation with a pinane framework into a cation with a *p*-menthane framework; for compound **3**, the reaction probably follows the traditional route to compounds of the campholene aldehyde type. Diol **2** may be regarded as a unique, easily accessible and optically active precursor in asymmetric synthesis.

A larger scale synthesis of compound **2** was performed in the presence of synthetic montmorillonite K10 clay. In addition to products **2** and **3**, the reaction mixture contained one more compound with a cyclopentane framework, 2-(2,2-dimethylcyclopent-3-enyl)-2-hydroxypropanal **4**.†

In compound **4**, we can also observe a rather unusual arrangement of methyl groups. Formation of this compound cannot be explained by a traditional set of rearrangements of pinene epoxide and its derivatives into compounds with campholene or isocampholene frameworks.[1,5] Synthesis of a compound structurally related to α-hydroxyaldehyde **4** has been reported previously.[7] The behaviour of *cis*- and *trans*-δ-pinene epoxides **5a**,**b** in the presence of ZnBr$_2$ has been studied, and it was shown that the reaction afforded compounds **6a**,**b** related to compound **4** (Scheme 2). The mechanism suggested led to the formation of cation **7** at the key stage of the process.



Scheme 1

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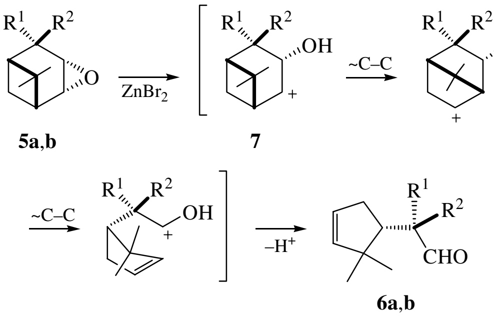
† A mixture of CH$_2$Cl$_2$ (150 ml) and (–)-*cis*-verbenol epoxide **1** {11.50 g, $[\alpha]_{580}^{20}$ –44 (*c* 12, CHCl$_3$)}, obtained from (–)-verbenone by oxidation with aqueous H$_2$O$_2$ and further reduction with LiAlH$_4$ according to published procedures,[5,9] was added with stirring to a suspension of K10 clay (30.0 g, Fluka), preliminarily calcinated for 3 h at 120 °C, in CH$_2$Cl$_2$ (200 ml). The reaction mixture was stirred for 1 h at room temperature. The catalyst was filtered off and washed with ethyl acetate, and the solvent was distilled off. The residue was separated by SiO$_2$ column chromatography (63–200 μ; Merck) using a 50–100% hexane solution of diethyl ether as an eluent. This gave 5.10 g (44%) of (1*R*,2*R*,6*S*)-3-methyl-6-(prop-1-en-2-yl)cyclohex-3-ene-1,2-diol **2** {$[\alpha]_D^{31}$ –49.1 (*c* 2.6, CHCl$_3$)}, 1.86 g (16%) of (*S*)-2-hydroxy-1-(2,2,3-trimethylcyclopent-3-enyl)-ethanone **3** {$[\alpha]_D^{31}$ –21.6 (*c* 2.1, CHCl$_3$)} and 1.13 g (10%) of compound **4**. The ^{1}H NMR spectra of compounds **2** and **3** coincided with the published spectra.[5]

For **4**: $[\alpha]_D^{31}$ –2.4 (*c* 2.3, CHCl$_3$). ^{1}H NMR (400 MHz, CDCl$_3$) δ: 0.85 (s, 3H, C^{9}H$_3$), 1.01 (s, 3H, C^{8}H$_3$), 1.25 (s, 3H, C^{10}H$_3$), 2.20 (dd, 1H, H^1, $J_{1,5'}$ 10 Hz, $J_{1,5}$ 8 Hz), 2.41 (dddd, 1H, H^5, $J_{5,5'}$ 16 Hz, $J_{5,1}$ 8 Hz, $J_{5,4}$ 3 Hz, $J_{5,3}$ 1.5 Hz), 2.62 (dddd, 1H, H$^{5'}$, $J_{5',5}$ 16 Hz, $J_{5',1}$ 10 Hz, $J_{5',3}$ 2.5 Hz, $J_{5',4}$ 2 Hz), 3.14 (br. s, 1H, OH), 5.30 (ddd, 1H, H^3, $J_{3,4}$ 6 Hz, $J_{3,5'}$ 2.5 Hz, $J_{3,5}$ 1.5 Hz), 5.54 (ddd, 1H, H^4, $J_{4,3}$ 6 Hz, $J_{4,5}$ 3 Hz, $J_{4,5'}$ 2 Hz), 9.64 (s, 1H, H^7). ^{13}C NMR, δ: 53.70 (d, C^1), 46.15 (s, C^2), 142.35 (d, C^3), 125.78 (d, C^4), 32.39 (t, C^5), 79.28 (s, C^6), 203.66 (d, C^7), 29.61 (q, C^8), 23.26 (q, C^9), 23.62 (q, C^{10}). The presence of a hydroxyl group at the C^6 atom is confirmed by the ^{13}C NMR spectrum recorded for a CDCl$_3$ solution of the substance with a D$_2$O addition, in which the high-field singlet at 79.28 ppm is shifted by 0.12 ppm due to the isotope effect. MS, *m*/*z*: 168.11479 [M$^+$]. Calc. for C$_{10}$H$_{16}$O$_2$: 168.11502.



a $R^1 = H$, $R^2 = Me$
b $R^1 = Me$, $R^2 = H$

Scheme 2

We can suggest three routes leading to cation **7** from verbenol epoxide **1** (Scheme 3). Route A includes the formation of neutral intermediate **8**, which undergoes epoxide ring cleavage after protonation to give cation **9** structurally similar to cation **7**. Processes of this kind, however, have been described only for highly basic media,[8] and they hardly take place in the presence of an acid catalyst such as K10 clay.

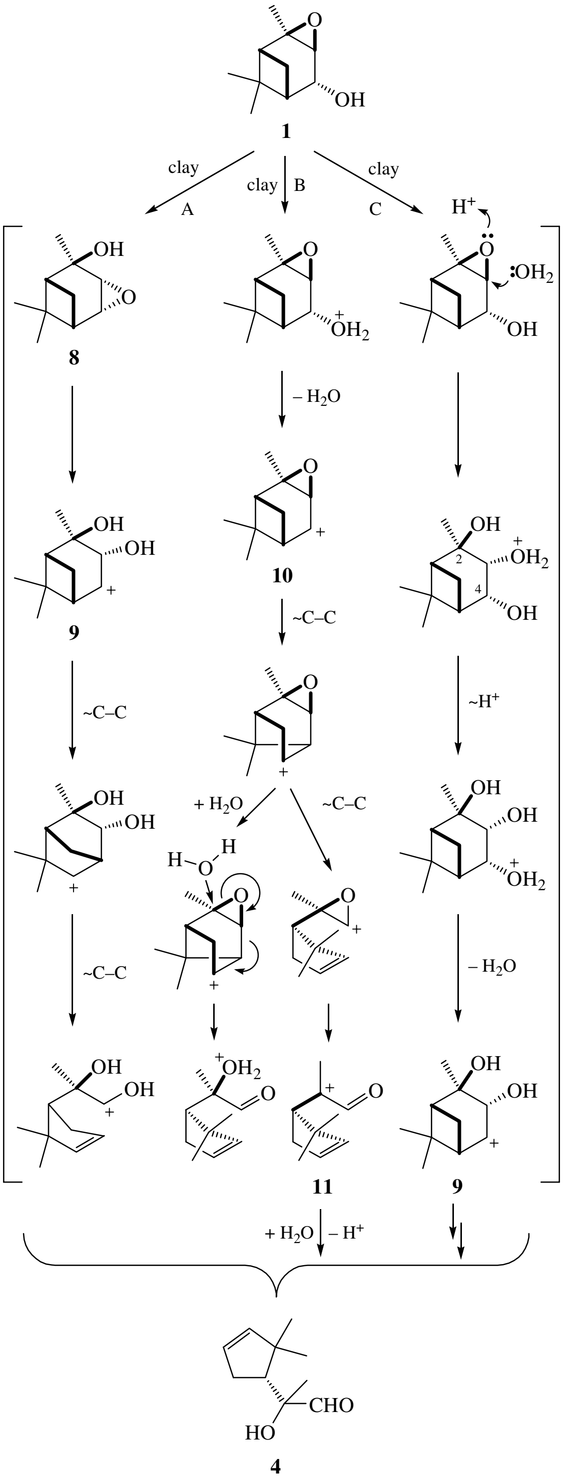
Route B suggests initial protonation of the hydroxyl group and elimination of the water molecule, leading to cation **10**. Further rearrangements of cation **10** can yield compound **4**. For route B to be feasible we have to assume that the reaction does not start with cleavage of the protonated epoxide ring as it normally does when epoxides are kept in acid media. Furthermore, we assume that, before epoxide ring cleavage, the intermediate cation has enough time to undergo a number of skeletal rearrangements. We have not found any examples of such a very unusual behaviour in the literature.

The optical purity of verbenone $\{[\alpha]^{20}_{580}$ –179.5 (*c* 21.5, $CHCl_3$)$\}$[9] employed for the synthesis of (–)-*cis*-verbenol epoxide **1** is ~60% {lit.,[10] $[\alpha]^{22}_{D}$ –264 (*c* 3, $CHCl_3$) for verbenone with 90% optical purity}. We determined the optical purity of compound **4** by recording its ^{1}H NMR spectrum with the chiral shift reagent Eu(hfc)$_3$. The optical purity of hydroxyaldehyde **4** was 60%; that is, the reaction is stereospecific. This also agrees with the ^{1}H and ^{13}C NMR spectra, which contain no signals of the diastereomers of **4**.

In view of the high stereoselectivity of the reaction that leads to compound **4**, one can assume that carbocation **11** is not produced in a pure form if the reaction follows mechanism B. Otherwise, the addition of the water molecule to the α-position relative to the aldehyde group would be accompanied by the formation of two diastereomers. Therefore, it seems most likely that the water molecule interacts with the cation containing an epoxy group.

According to mechanism C, the reaction starts with cleavage of the epoxy group involving a water molecule. This stage is possibly followed by protonation of the hydroxyl group at the 4-position and elimination of the water molecule, leading to the formation of cation **9**. Further transformations of this carbocation can follow route A. The most serious disadvantages of this version are the following: (1) this kind of epoxide cleavage into *trans*-diols in the presence of clay has never been observed previously;[5,9,11,12] (2) the reasons for protonation of the hydroxyl group in the intermediate triol are vague; it is not clear why the water molecule should be further eliminated in the 4-position, and why it should lead to the formation of a secondary rather than tertiary carbocation, as would be expected in protonation of the hydroxyl group at the 2-position.

Despite of its singularity, route B seems to be more probable.



Scheme 3

Thus, when investigating the isomerization of (–)-*cis*-verbenol epoxide **1** in the presence of K10 clay, we found that this reaction gives new unusual α-hydroxyaldehyde **4** with a cyclopentane framework. To explain the formation of this compound, we have to invoke mechanisms not typical of these compounds. The reaction routes as unusual as these may be explained by specific adsorption of compound **1** on montmorillonite clay.

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References

1 W. F. Erman, *Chemistry of the Monoterpenes, Part A*, Marcel Dekker Inc., New York, 1985, p. 213.

2 K. P. Volcho, L. N. Rogoza, N. F. Salakhutdinov, A. G. Tolstikov and G. A. Tolstikov, *Preparativnaya khimiya terpenoidov, Chast' 1. Bitsiklicheskie monoterpenoidy* (*The Preparative Chemistry of Terpenes. Part 1. Bicyclic Monoterpenes*), *Izdatel'stvo SO RAN*, 2006 (in Russian).

3 X. Sala, A. M. Rodriguez, M. Rodriguez, I. Romero, T. Parella, A. von Zelewsky, A. Llobet and J. Benet-Buchholz, *J. Org. Chem.*, 2006, **71**, 9283.
4 T. M. Khomenko, O. V. Salomatina, S. Yu. Kurbakova, I. V. Il'ina, K. P. Volcho, N. I. Komarova, D. V. Korchagina, N. F. Salakhutdinov and A. G. Tolstikov, *Zh. Org. Khim.*, 2006, **42**, 1666 (*Russ. J. Org. Chem.*, 2006, **42**, 1653).
5 I. V. Il'ina, K. P. Volcho, D. V. Korchagina, V. A. Barkhash and N. F. Salakhutdinov, *Helv. Chim. Acta*, 2007, **90**, 353.
6 H. Amri, M. M. El Gaied and M. M'Hirsi, *J. Soc. Chim. Tunis*, 1983, **10**, 25.
7 Y. Bessiere-Chrentien and J.-P. Bras, *Compt. Rend. Acad. Sc., C: Sc. Chim.*, 1970, **271**, 200.
8 L. I. Kas'yan, I. N. Tarabara and A. O. Kas'yan, *Zh. Org. Khim.*, 2004, **40**, 1279 (*Russ. J. Org. Chem.*, 2004, **40**, 1227).
9 I. V. Il'ina, K. P. Volcho, D. V. Korchagina, V. A. Barkhash and N. F. Salakhutdinov, *Helv. Chim. Acta*, 2006, **89**, 507.
10 M. A. Cooper, J. R. Salmon, D. Whittaker and U. Scheidegger, *J. Chem. Soc. (B)*, 1967, 1259.
11 I. V. Il'ina, D. V. Korchagina, N. F. Salakhutdinov and V. A. Barkhash, *Zh. Org. Khim.*, 2000, **36**, 1483 (*Russ. J. Org. Chem.*, 2000, **36**, 1446).
12 K. P. Volcho, L. E. Tatarova, D. V. Korchagina, N. F. Salakhutdinov and V. A. Barkhash, *Zh. Org. Khim.*, 2000, **36**, 41 (*Russ. J. Org. Chem.*, 2000, **36**, 32).

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