Synthesis of Optically Active, Cyclic α-Hydroxy Ketones and 1,2-Diketones from Verbenone Epoxide

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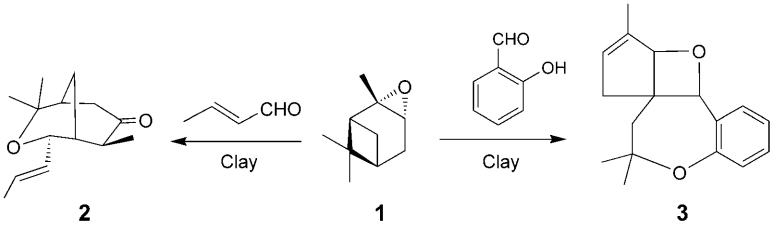
The reactivity of verbenone epoxide (**5**), a terpenoid from the pinane series, towards different aliphatic and aromatic aldehydes in the presence of natural montmorillonite (askanite–bentonite) clay has been studied. A series of mechanistically different transformations afforded a number of new, optically active, polyfunctional compounds (**7**, **8**, **10**–**14**, **16**). These products are potentially interesting synthons in asymmetric synthesis.

Introduction. – Oxygen-containing monoterpenes from the pinane series are commercially available compounds of high optical purity, and may serve as precursors of biologically active compounds [1] and intermediates in asymmetric synthesis [2]. In acidic media, they generally easily undergo numerous transformations, affording complex mixtures of products [3]. As shown previously, the natural montmorillonite clay askanite–bentonite and its synthetic analog *K-10* can be used as catalysts for the transformation of pinane terpenoids, which facilitates the synthetic procedure and improves the ecological aspects of such chemical processes. Moreover, the use of clays also occasionally allows the selective synthesis of complex products. For example, the reaction of α-pinene epoxide (**1**) with aliphatic or aromatic aldehydes gave the new polyheterocyclic compounds **2** and **3** [4] (*Scheme 1*).

Scheme 1

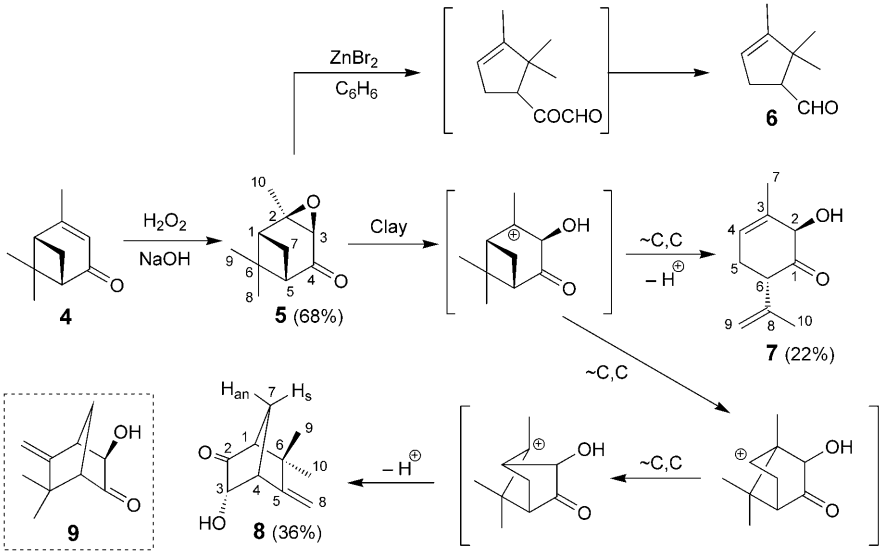


Verbenone (**4**) is an interesting and important pinane terpenoid showing pheromone activity in bark beetle [5]. In the presence of acid catalysts, including clays, verbenone rearranges into compounds with *para*- and *ortho*-menthane frameworks, giving rise to multi-component mixtures of products that are hardly separable [6]. Our previ-

ous investigations [4] have indicated that, in the presence of clays, the epoxidation of the C=C bond of α- and β-pinenes gives rise to unusual products. Therefore, in the present work, we wanted to investigate the properties of verbenone epoxide (**5**) as a synthon.

Results and Discussion. – Verbenone epoxide (**5**) was synthesized by oxidation of **4** with H_2O_2 according to a general procedure [7] in 68% yield (*Scheme 2*). When **5** was exposed to *Lewis* acids such as $ZnBr_2$ in benzene, 2,2,3-trimethylcyclopent-3-en-1-carbaldehyde (**6**) was obtained as the major product in 30% yield [8]. However, when **5** was stored over askanite–bentonite clay at room temperature, the α-hydroxy ketones **7** and **8** with a *para*-menthane and a camphane framework, respectively, were isolated; the previously reported aldehyde **6** was not formed in this reaction.

Scheme 2



To rationalize the formation of **8**, we suggest a sequence of rearrangements not observed previously for oxygen-containing pinenes (*Scheme 2*). A similar rearrangement takes place only for α- and β-pinenes proper, giving rise to the corresponding camphenes in racemic forms. In our case, however, we obtained an *optically active* compound of apparently very high optical purity[1]). Curiously, this reaction forms an *endo*-isomer as the sole product; therefore, the mechanism that leads to the hydroxy ketone **8** should inevitably include a formal epimerization at C(3). This epimerization probably occurs during the course of the carbon-skeleton rearrangement from the pinane to the camphene framework, and is presumably determined by the adsorption of the starting epoxide **5** on the askanite–bentonite clay. The *exo*-isomer of compound **8**, *i.e.*, **9**, has

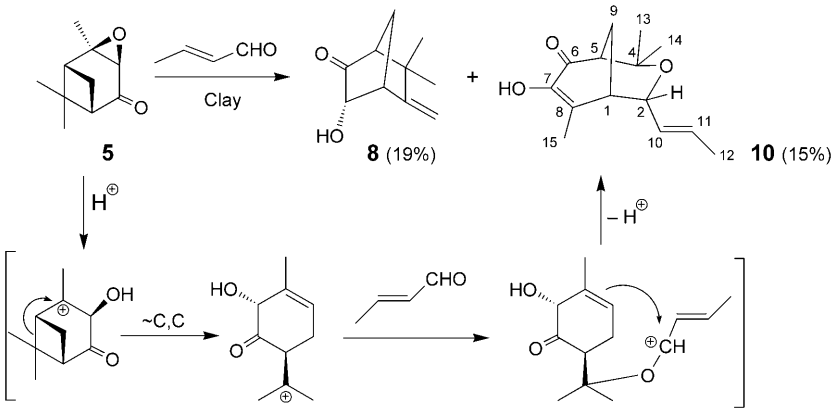
[1]) In the ^{1}H-NMR spectrum of **8** recorded in the presence of [Eu(tfc)$_3$] (chiral shift reagent), basically all signals were shifted without being separated, indicating a very high degree of stereoselectivity.

been obtained before in a multi-step synthesis of the monoterpenoid analog of *cis*-sativenediol, starting from camphor [9]. Clearly, our route from verbenone to the α-hydroxy ketone with a camphane framework is much more facile and short.

Acid-catalyzed transformations of oxygen-containing pinane terpenoids generally suffer from moderate yields. This disadvantage is compensated by the accessibility and relatively low cost of the starting terpenoids and reagents. Since isomerization of verbenone epoxide (**5**) gave the optically active compounds **7** and **8** in 22 and 36% yield, respectively, this route to optically active α-hydroxy ketones from the camphane and *para*-menthane series can be regarded as preparative. The products **7** and **8** are new compounds, and may be used as synthons in asymmetric synthesis.

In contrast to verbenone (**4**), verbenone epoxide (**5**) also underwent intermolecular cyclization after reaction with aromatic and aliphatic aldehydes in the presence of askanite–bentonite clay. Thus, reaction of **5** with crotonaldehyde (=(*E*)-but-2-enal) in the presence of the clay afforded, besides the isomerization product **8**, the heterocyclic '1,2-diketone' **10** (*Scheme 3*). This compound was isolated in its enol form, which turned out to be stable even upon heating to 40°. In *Scheme 3*, a hypothetical mechanism for this reaction is presented. Product **10** is an analog of ketone **2** previously obtained from α-pinene epoxide [4a] (see *Scheme 1*). The mechanism includes protonation and cleavage of the epoxide ring, skeletal rearrangement into a cation with a *para*-menthane framework, and further reaction of the cation with crotonaldehyde. Interestingly, although **10** has several O-atoms, carbocyclization is preferred to heterocyclization in the last step.

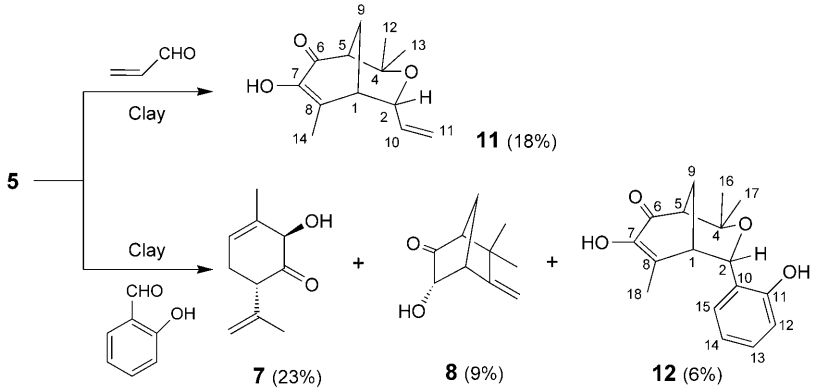
Scheme 3



When crotonaldehyde was replaced with acrolein (=prop-2-ene), compound **11** was formed from **5** as the sole product (*Scheme 4*). Here, no isomerization products similar to **8** were found.

On passing from aliphatic aldehydes to aromatic ones such as salicylaldehyde (=2-hydroxybenzaldehyde), the key process was isomerization of **5** to the hydroxy ketones **7** (23%) and **8** (9%). Here, the product of the intermolecular reaction, compound **12**, was isolated only in 6% yield (*Scheme 4*). Note that all previously studied reactions between pinane, carane, and *para*-menthane terpenoids with salicylaldehyde gave

Scheme 4

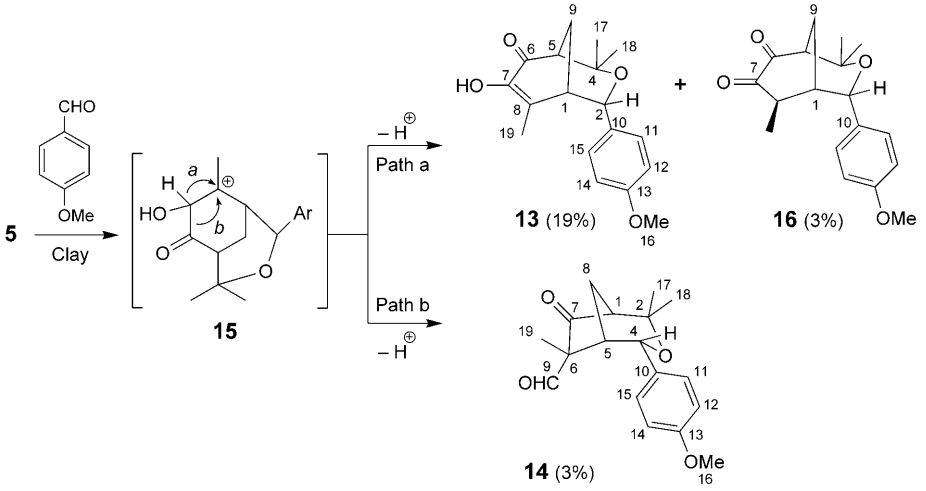


rise to the products of a double heterocyclization involving the phenol group of salicylaldehyde [10]. In the case of verbenone epoxide, however, this group remained intact.

When salicylaldehyde was replaced with 4-methoxybenzaldehyde, the reaction with **5** followed a different route (*Scheme 5*). Compound **13** was the major product in the presence of clay, but, in addition, we also isolated the oxo aldehyde **14**, apparently resulting from an unexpected ring contraction of the intermediate carbocation **15**. As a matter of fact, such a ring contraction has not been observed before in similar reactions in which bicyclic ethers are formed from terpenoids and aldehydes [4a][10]. Finally, we also isolated the tautomer of **13**, *i.e.*, the 1,2-diketone **16**. Notably, **13** and **16** did not undergo interconversion, even upon heating to 40°. Again, no isomerization products of **5** were found.

A comparison of the products obtained in the reaction of verbenone epoxide (**5**) with different aliphatic and aromatic aldehydes in the presence of clay shows that

Scheme 5



even minor changes in the structure of the aldehyde give rise to substantial changes in the distribution of the intra- or intermolecularly formed products. We had reached a similar conclusion in our previous work concerning the clay-catalyzed reactions between myrcene and aldehydes [11].

All compounds synthesized from **5** are described herein for the first time. Their structures were identified by ^{1}H-NMR and ^{13}C-NMR spectroscopy (see *Table* in the *Exper. Part*), and by mass spectrometry. In the ^{1}H-NMR spectrum of **8**, the vicinal coupling constant between the H–C(4) and H–C(3) indicated that the latter was in *exo*-position, with the OH group being in *endo*-position. In compounds **10**–**13** and **16**, the J(2,1) value was 2.5 Hz in all cases, indicating that H–C(2) was in the same relative position. The absence of an *W*-type coupling between H–C(2) and CH_2(9) (methylene bridge) suggested that the latter was β-oriented in these compounds. For all bicyclic ethers (compounds **10**–**13** and **16**), except aldehyde **14**, quantum-mechanical calculations showed that the six-membered heterocyclic ring was in a boat-like conformation; hence, the bulky substituent was in pseudo-equatorial position. The bicyclic aldehyde **14** was drawn in a chair conformation (*Scheme* 5) in accordance with quantum-mechanical calculations. The ^{13}C-NMR data of compounds **5**, **7**, **8**, **10**–**14**, and **16** are summarized in the *Table* (see *Exper. Part*).

In summary, we have found a ready access to a series of new, highly functionalized, cyclic α-hydroxy ketones, 1,2-diketones, and α-oxo aldehydes from the reaction of verbenone epoxide (**5**) with different aldehydes in the presence of the montmorillonite clay askanite–bentonite. All of the new compounds were optically active, and may be regarded as valuable synthons in asymmetric synthesis.

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Experimental Part

1. *General.* As catalyst, we used askanite–bentonite clay obtained (according to *Specs TU-113-12-86-82*) by acidic activation of bentonite clay from the Askan group of deposits; a synthetic analog of this clay is *K10*. The clay was calcinated at 110° for 3 h immediately before use. Compound purities were determined by GLC on a *Model 3700* instrument with a quartz capillary column (15 m × 0.22 mm), *VC-30* phase, flame-ionization detector, and He (1 atm) as carrier gas. Column chromatography (CC) was performed on silica gel (70–230 mesh; *Merck*). Optical rotations: *Polamat A* spectrometer, in $CHCl_3$ soln. ^{1}H- and ^{13}C-NMR Spectra: *Bruker AM-400* apparatus at 400.13 (^{1}H) and 100.61 MHz (^{13}C) in CCl_4/$CDCl_3$ 1:1 (*v*/*v*); chemical shifts δ in ppm rel. to residual $CHCl_3$ [δ(H) 7.24, δ(C) 76.90 ppm], J in Hz. The structures of the compounds were elucidated by analyzing the geminal, vicinal, and long-range ^{1}H-NMR spin-spin coupling constants in ^{1}H,^{1}H double-resonance spectra, and by considering the ^{13}C-NMR spectra using proton off-resonance saturation, including ^{13}C,^{1}H-type 2D-COSY (^1J(C,H) = 135 Hz) and ^{13}C,^{1}H-type 1D-LRJMD (J(C,H) = 10 Hz) spectra. For ^{13}C-NMR spectra, see *Table*. HR-MS: *Finnigan MAT-8200* instrument; in *m*/*z*.

2. *Preparation of Verbenone Epoxide* (= *(1*R,*2*R,*4*R,*6S)-2,7,7-Trimethyl-3-oxatricyclo[4.1.1.0^{2,4}]-octan-5-one*; **5**). To a soln. of (–)-verbenone (10 g; *Acros*) in MeOH (100 ml) was added 30% aq. H_2O_2 (20 ml), and the mixture was cooled to 12°. Then, 6M aq. NaOH (5 ml) was added, and the mixture was stirred for 2 h at 12–15°. The reaction was monitored by GLC. After completion of the reaction, H_2O (100 ml) was added, and the mixture was extracted with Et_2O (3 × 80 ml). The org. layer was washed neutral with H_2O, dried ($MgSO_4$), and evaporated to afford **5** (7.55 g, 68%). $[\alpha]_{580}^{20} = -137$ (c = 3.5, $CHCl_3$).

Table. *^{13}C-NMR Data of Selected Compounds.* At 100.6 MHz in $CCl_4/CDCl_3$ 1:1; chemical shifts δ in ppm. Arbitrary atom numbering.

Position	**5**	**7**	**8**	**10**	**11**	**12**	**13**	**14**	**16**
1	45.71 (*d*)	209.60 (*s*)	60.19 (*d*)	42.09 (*d*)	41.91 (*d*)	43.55 (*d*)	43.71 (*d*)	55.43 (*d*)	43.10 (*d*)
2	59.49 (*s*)	72.42 (*d*)	214.19 (*s*)	72.28 (*d*)	72.40 (*d*)	76.22 (*d*)	72.21 (*d*)	76.44 (*s*)	74.94 (*d*)
3	58.72 (*d*)	136.25 (*s*)	75.00 (*d*)						
4	205.11 (*s*)	120.89 (*d*)	49.86 (*d*)	71.68 (*s*)	71.77 (*s*)	73.92 (*s*)	72.09 (*s*)	74.46 (*d*)	74.05 (*s*)
5	56.28 (*d*)	30.15 (*t*)	154.27 (*s*)	48.48 (*d*)	48.53 (*d*)	48.35 (*d*)	48.53 (*d*)	50.84 (*d*)	55.98 (*d*)
6	49.55 (*s*)	52.96 (*d*)	42.21 (*s*)	195.15 (*s*)	195.18 (*s*)	194.31 (*s*)	195.44 (*s*)	61.93 (*s*)	202.69 (*s*)
7	21.63 (*t*)	18.66 (*q*)	30.00 (*t*)	145.54 (*s*)	145.59 (*s*)	145.69 (*s*)	145.54 (*s*)	214.71 (*s*)	200.12 (*s*)
8	26.45 (*q*)	141.43 (*s*)	107.52 (*t*)	128.46 (*s*)	128.36 (*s*)	129.37 (*s*)	129.17 (*s*)	29.97 (*t*)	44.37 (*d*)
9	21.51 (*q*)	112.88 (*t*)	28.66 (*q*)	31.59 (*t*)	31.67 (*t*)	31.68 (*t*)	31.88 (*t*)	197.10 (*d*)	25.10 (*t*)
10	20.80 (*q*)	21.81 (*q*)	26.17 (*q*)	130.91 (*d*)	137.65 (*d*)	123.11 (*s*)	133.11 (*s*)	132.10 (*s*)	131.70 (*s*)
11				126.37 (*d*)	115.23 (*t*)	155.93 (*s*)	126.58 (*d*)	125.96 (*d*)	126.74 (*d*)
12				17.65 (*q*)	28.49 (*q*)	117.27 (*d*)	113.42 (*d*)	113.70 (*d*)	113.81 (*d*)
13				28.52 (*q*)	22.71 (*q*)	126.87 (*d*)	158.76 (*s*)	158.82 (*s*)	158.90 (*s*)
14				22.73 (*q*)	18.30 (*q*)	119.44 (*d*)	113.42 (*d*)	113.70 (*d*)	113.81 (*d*)
15				18.22 (*q*)		128.95 (*d*)	126.58 (*d*)	125.96 (*d*)	126.74 (*d*)
16						28.47 (*q*)	54.97 (*q*)	54.97 (*q*)	55.06 (*q*)
17						22.39 (*q*)	28.60 (*q*)	27.69 (*q*)	28.57 (*q*)
18						17.01 (*q*)	22.66 (*q*)	23.09 (*q*)	22.68 (*q*)
19							17.39 (*q*)	18.15 (*q*)	15.76 (*q*)

^{1}H-NMR: 0.96 (*s*, Me(9)); 1.37 (*s*, Me(8)); 1.44 (*s*, Me(10)); 2.01 (*d*, *J*(7an,7s) = 10, H_{an}–C(7)); 2.20 (*ddd*, *J* = 10, *J*(7*s*,1) = *J*(7*s*,5) = 5.5, H_s–C (7)); 2.24 (*dd*, *J*(1,7s) = *J* (1,5) = 5.5, H–C(1)); 2.34 (*ddd*, *J*(5,1) = *J*(5,7*s*) = 5.5, *J*(5,3) = 1.7, H–C(5)); 3.05 (*d*, *J*(3,5) = 1.7, H–C(3)). ^{13}C-NMR: see *Table.*

3. *Isomerization of* **5** (see *Scheme 2*). A soln. of **5** (0.400 g) in CH_2Cl_2 (5 ml) was added at 20° to a suspension of the clay (2.5 g) in CH_2Cl_2 (20 ml). The mixture was stirred for 1 h. Then, Et_2O (5 ml) was added, the catalyst was filtered off, and the solvent was evaporated. The mixture was purified by CC (SiO_2; hexane/Et_2O 100:0 → 50:50) to afford **7** (0.088 g, 22%) and **8** (0.143 g, 36%).

*Data of (2*R*,6*S*)-2-Hydroxy-3-methyl-6-(1-methylethenyl)cyclohex-3-en-1-one* (**7**). $[\alpha]_{580}^{20} = -128.3$ (*c* = 14, $CHCl_3$). ^{1}H-NMR: 1.72 (br. *s*, Me(10)); 1.77 (*tdd*, *J*(7,5) = 2, *J*(7,4) = 1.5, *J*(7,2) = 1.2, Me(7)); 2.48–2.62 (*m*, CH_2(5)); 3.11–3.15 (*m*, H–C(6)); 3.28 (br. *s*, OH); 4.52 (*dddq*, *J*(2,4) = *J*(2,5) = 2.5, *J*(2,5′) = 1.5, *J*(2,7) = 1.2, H–C(2)); 4.95 (*m*, H–C(9)); 4.96 (*m*, H′–C(9)); 5.52 (*tdq*, *J*(4,5) = 4, *J*(4,2) = 2.5, *J*(4,7) = 1.5, H–C (4)). ^{13}C-NMR: see *Table.* HR-MS: 166.0972 (M^+, $C_{10}H_{14}O_2^+$; calc. 166.0994).

*Data of (1*S*,3*S*,4*S*)-3-Hydroxy-6,6-dimethyl-5-methylidenebicyclo[2.2.1]heptan-2-one* (**8**). $[\alpha]_{580}^{20} = -66.9$ (*c* = 32, $CHCl_3$). ^{1}H-NMR: 0.98 (*s*, Me(10)); 1.13 (*s*, Me(9)); 1.60 (br. *d*, *J*(7an,7s) = 11.5, H_{an}–C(7)); 2.03 (*ddd*, *J*(7s,7an) = 11.5, *J*(7s,4) = 2.5, *J*(7s,1) = 1, H_s–C(7)); 2.24 (br. *s*, H–C(1)); 3.09 (*dddd*, *J*(4,3-*exo*) = 5, *J*(4,7s) = 2.5, *J*(4,7an) = 1.5, *J*(4,1) = 1, H–C(4)); 3.50 (br. *s*, OH); 3.81 (*dd*, *J*(3-*exo*,4) = 5, *J*(3-*exo*,1) = 1.5, H_{exo}–C(3)); 4.94 (*s*, H–C(8)); 5.04 (br. *s*, H′–C(8)). ^{13}C-NMR: see *Table.* HR-MS: 166.0992 (M^+, $C_{10}H_{14}O_2^+$; calc. 166.0994).

4. *Reaction of* **5** *with Crotonaldehyde* (see *Scheme 3*). A soln. of crotonaldehyde (0.500 g) in CH_2Cl_2 (5 ml) was added to a suspension of the clay (2.5 g) in CH_2Cl_2 (15 ml), and **5** (0.500 g) in CH_2Cl_2 (5 ml) was added at 20°. The mixture was stirred at r.t. for 40 min. Then, Et_2O (5 ml) was added. The catalyst was filtered off, and the solvent was evaporated. The residue was purified by CC (SiO_2; hexane/Et_2O 100:0 → 50:50) to afford **8** (0.097 g, 19%) and **10** (0.100 g, 15%).

*Data of (1*R*,2*R*,5*S*)-7-Hydroxy-4,4,8-trimethyl-2-[(*E*)-prop-1-en-1-yl]-3-oxabicyclo[3.3.1]non-7-en-6-one* (**10**). $[\alpha]_{580}^{20} = -108.4$ (*c* = 20.3, $CHCl_3$). ^{1}H-NMR: 1.11 (*s*, Me(13)); 1.33 (*s*, Me(14)); 1.65 (*ddd*, *J*(12,11) = 6.5, *J*(12,10) = 1.5, *J*(12,2) = 1, Me(12)); 1.83 (*s*, Me(15)); 2.10 (*td*, *J*(5,9) = 3, *J*(5,1) = 1, H–C(5)); 2.19 (*td*, *J*(1,9) = 3, *J*(1,2) = 2.5, H–C(1)); 2.28 (*ddd*, *J*(9,9′) = 13, *J*(9,1) = *J*(9,5) = 3, H–C(9)); 2.33 (*ddd*, *J*(9′,9) = 13, *J*(9′,1) = *J*(9′,5) = 3, H′–C(9)); 4.32 (*dddd*, *J*(2,10) = 6.5, *J*(2,1) = 2.5,

J(2,11) = 1.2, *J*(2,5) = 1, H–C(2)); 5.32 (*ddq*, *J*(10,11) = 15, *J*(10,2) = 6.5, *J*(10,12) = 1.5, H–C(10)); 5.63 (*dqd*, *J*(11,10) = 15, *J*(11,12) = 6.5, *J*(11,2) = 1.2, H–C(11)); 6.02 (br. *s*, OH). ^{13}C-NMR: see *Table*. HR-MS: 236.1404 (M^+, $C_{14}H_{20}O_3^+$; calc. 236.1412).

5. *Reaction of* **5** *with Acrolein* (see *Scheme 4*). A soln. of acrolein (0.400 g) in CH_2Cl_2 (5 ml) was added to a suspension of the clay (2 g) in CH_2Cl_2 (15 ml). Then, **5** (0.300 g) in CH_2Cl_2 (5 ml) was added at 20°, and the mixture was stirred for 40 min at r.t. Then, Et_2O (5 ml) was added, the catalyst was filtered off, and the solvent was evaporated. The residue was purified by CC (SiO_2; hexane/Et_2O 100 : 0 → 50 : 50) to afford **11** (0.074 g, 18%).

*Data of (1*R,*2*R,*5*S*)-2-Ethenyl-7-hydroxy-4,4,8-trimethyl-3-oxabicyclo[3.3.1]non-7-en-6-one* (**11**). $[\alpha]_{580}^{20} = -77.0$ (*c* = 20, $CHCl_3$). ^{1}H-NMR: 1.14 (*s*, Me(12)); 1.35 (*s*, Me(13)); 1.84 (*s*, Me(14)); 2.14 (*td*, *J*(5,9) = 3, *J*(5,1) = 1.2, H–C(5)); 2.26 (*tdd*, *J*(1,9) = 3, *J*(1,2) = 2.5, *J*(1,5) = 1.2, H–C(1)); 2.31 (*ddd*, *J*(9,9′) = 13, *J*(9,1) = 3, *J*(9,5) = 3, H–C(9)); 2.36 (*ddd*, *J*(9′,9) = 13, *J*(9′,1) = 3, *J*(9′,5) = 3, H′–C(9)); 4.39 (*ddt*, *J*(2,10) = 6, *J*(2,1) = 2.5, *J*(2,11) = 1.5, H–C(2)); 5.07 (*ddd*, *J*(11-*cis*,10) = 10.5, *J*(11-*cis*, 11-*trans*) = 1.8, *J*(11-*cis*,2) = 1.5, H_{cis}–C(11)); 5.23 (*ddd*, *J*(11-*trans*,10) = 17, *J*(11-*trans*,11-*cis*) = 1.8, *J*(11-*trans*,2) = 1.5, H_{trans}–C (11)); 5.71 (*ddd*, *J*(10,11-*trans*) = 17, *J*(10,11-*cis*) = 10.5, *J*(10,2) = 6, H–C(10)); 6.02 (br. *s*, OH). ^{13}C-NMR: see *Table*. HR-MS: 222.1256 (M^+, $C_{13}H_{18}O_3^+$; calc. 222.1256).

6. *Reaction of* **5** *with Salicylaldehyde* (see *Scheme 4*). A soln. of salicylaldehyde (0.400 g) in CH_2Cl_2 (5 ml) was added to a suspension of the clay (2 g) in CH_2Cl_2 (10 ml). Then, **5** (0.400 g) in CH_2Cl_2 (5 ml) was added at 20°, and the mixture was stirred for 1 h at r.t. Then, Et_2O (5 ml) was added, the catalyst was filtered off, the solvent was evaporated, and the residue was purified by CC (SiO_2; hexane/Et_2O 100 : 0 → 0 : 100) to afford **7** (0.091 g, 23%), **8** (0.034 g, 9%), and **12** (0.040 g, 6%).

*Data of (1*R,*2*S,*5*S*)-7-Hydroxy-2-(2-hydroxyphenyl)-4,4,8-trimethyl-3-oxabicyclo[3.3.1]non-7-en-6-one* (**12**). $[\alpha]_{580}^{20} = -192.7$ (*c* = 6.7, $CHCl_3$). ^{1}H-NMR: 1.31 (*s*, Me(16)); 1.35 (*s*, Me(18)); 1.49 (*s*, Me(17)); 2.27 (*td*, *J*(5,9) = 3, *J*(5,1) = 1.2, H–C(5)); 2.44–2.47 (*m*, CH_2(9)); 2.51–2.55 (*m*, H–C(1)); 5.21 (*d*, *J*(2,1) = 2.5, H–C(2)); 6.02 (*s*, 7-OH); 6.73 (*dd*, *J*(12,13) = 8.5, *J*(12,14) = 1.2, H–C(12)); 6.77 (*td*, *J* = 7.5, *J*(14,12) = 1.2, H–C(14)); 6.94 (*dd*, *J*(15,14) = 7.5, *J*(15,13) = 1.5, H–C(15)); 7.09 (*ddd*, *J* = 8.5, *J*(13,14) = 7.5, *J*(13,15) = 1.5, H–C(13)); 7.91 (br. *s*, 11-OH). ^{13}C-NMR: see *Table*. HR-MS: 288.1355 (M^+, $C_{17}H_{20}O_4^+$; calc. 288.1362).

7. *Reaction of* **5** *with 4-Methoxybenzaldehyde* (see *Scheme 5*). A soln. of 4-methoxybenzaldehyde (0.500 g) in CH_2Cl_2 (5 ml) was added to a suspension of the clay (2.5 g) in CH_2Cl_2 (10 ml). Then, **5** (0.500 g) in CH_2Cl_2 (5 ml) was added at 20°, and the mixture was stirred for 1 h at r.t. Then, Et_2O (5 ml) was added, the catalyst was filtered off, and the solvent was evaporated. The residue was purified by CC (SiO_2; hexane/Et_2O 100 : 0 → 0 : 100) to afford **13** (0.104 g, 19%) and a 1 : 1 mixture of **14** and **16** (0.030 g, 6% based on ^{1}H-NMR), which was further separated into pure **14** and **16** by repeated CC (conditions as above).

*Data of (1*R,*2*S,*5*S*)-7-Hydroxy-2-(4-methoxyphenyl)-4,4,8-trimethyl-3-oxabicyclo[3.3.1]non-7-en-6-one* (**13**). $[\alpha]_{580}^{20} = -108.0$ (*c* = 8, $CHCl_3$). ^{1}H-NMR: 1.11 (*s*, Me(19)); 1.25 (*s*, Me(17)); 1.42 (*s*, Me(18)); 2.21 (*td*, *J*(5,9) = 3, *J*(5,1) = 1.2, H–C(5)); 2.38–2.42 (*m*, H–C(1)); 2.39–2.44 (*m*, H–C(9)); 2.46 (*ddd*, *J*(9′,9) = 13, *J*(9′,1) = 4, *J*(9′,5) = 3, H′–C(9)); 3.76 (*s*, MeO); 4.97 (*d*, *J*(2,1) = 2.5, H–C(2)); 6.07 (br. *s*, OH); 6.78 (*d*, *J* = 8.5, H–C(12), H–C(14)); 7.15 (*d*, *J* = 8.5, H–C(11), H–C(15)). ^{13}C-NMR: see *Table*. HR-MS: 302.1519 (M^+, $C_{18}H_{22}O_4^+$; calc. 302.1518).

*Data of (1*S,*4*R,*5*R,*6*R*)-4-(4-Methoxyphenyl)-2,2,6-trimethyl-7-oxo-3-oxabicyclo[3.2.1]octane-6-carbaldehyde* (**14**). $[\alpha]_{580}^{20} = -27.8$ (*c* = 3.0, $CHCl_3$). ^{1}H-NMR: 1.20 (*s*, Me(19)); 1.44, 1.45 (2*s*, Me(17), Me(18)); 2.25–2.32 (*m*, H–C(1), H–C (8)); 2.47–2.53 (*m*, H′–C(8)); 2.85–2.89 (*m*, H–C(5)); 3.76 (*s*, MeO); 5.10 (br. *s*, H–C(4)); 6.76 (*d*, *J* = 8.5, H–C(12), H–C(14)); 7.13 (*d*, *J* = 8.5, H–C(11), H–C(15)); 9.23 (*s*, CHO). ^{13}C-NMR: see *Table*. HR-MS: 302.1525 (M^+, $C_{18}H_{22}O_4^+$; calc. 302.1518).

*Data of (1*R,*2*S,*5*S,*8*R*)-2-(4-Methoxyphenyl)-4,4,8-trimethyl-3-oxabicyclo[3.3.1]nonane-6,7-dione* (**16**). $[\alpha]_{580}^{20} = -111.3$ (*c* = 1.0, $CHCl_3$). ^{1}H-NMR: 1.01 (*d*, *J*(19,8) = 7, Me(19)); 1.23 (*s*, Me(17)); 1.44 (*s*, Me(18)); 1.95–1.99 (*m*, H–C(1)); 2.44 (*ddd*, *J* (9,9′) = 14, *J*(9,1) = 3, *J*(9,5) = 3, H–C(9)); 2.54 (*dddd*, *J*(9′,9) = 14, *J*(9′,1) = 3, *J*(9′,5) = 3, *J*(9′,8) = 2.5, H′–C(9)); 2.57 (*td*, *J*(5,9) = 3, *J*(5,1) = 1.2, H–C(5)); 2.71 (*qdd*, *J*(8,19) = 7, *J*(8,9′) = 2.5, *J*(8,1) = 2, H–C(8)); 3.79 (*s*, MeO); 5.04 (*d*, *J*(2,1) = 2.5, H–C(2)); 6.85 (*d*, *J* = 8.5, H–C(12), H–C(14)); 7.12 (*d*, *J* = 8.5, H–C(11), H–C(15)). ^{13}C-NMR: see *Table*. HR-MS: 302.1549 (M^+, $C_{18}H_{22}O_4^+$; calc. 302.1518).

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