

Alternative Synthesis of 2-Hydroxy-3,5,5-trimethylcyclopent-2-en-1-one

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The 2-hydroxy-3,5,5-trimethylcyclopent-2-en-1-one (**1**) was synthesized in 42% yield by rearrangement of epoxy ketone **10** on treatment with $\text{BF}_3 \cdot \text{Et}_2\text{O}$ under anhydrous conditions. Intermediate **10** was available from the known enone **8**, either *via* direct epoxidation (60% H_2O_2 , NaOH, MeOH; yield 50%), or *via* reduction to the corresponding allylic alcohol **14** (LiAlH_4 , THF), followed by epoxidation ($[\text{VO}(\text{acac})_2]$, $t\text{BuOOH}$) and reoxidation under *Swern* conditions, in 37% total yield.

Introduction. – The title compound **1** was first isolated from the essential oil of *Backhousia angustifolia* in 1931 [1] and later identified in roasted coffee [2], as well as in the *Maillard* reaction of casein pancreatic hydrolyzate derived peptides with glucose [3]. Three syntheses have been published which are summarized in *Scheme 1*¹⁾. The first one consisted in the stoichiometric SeO_2 oxidation of 2,4,4-trimethylcyclopentanone (**2**) [5b–5d] giving **1** in 25% yield [5a].

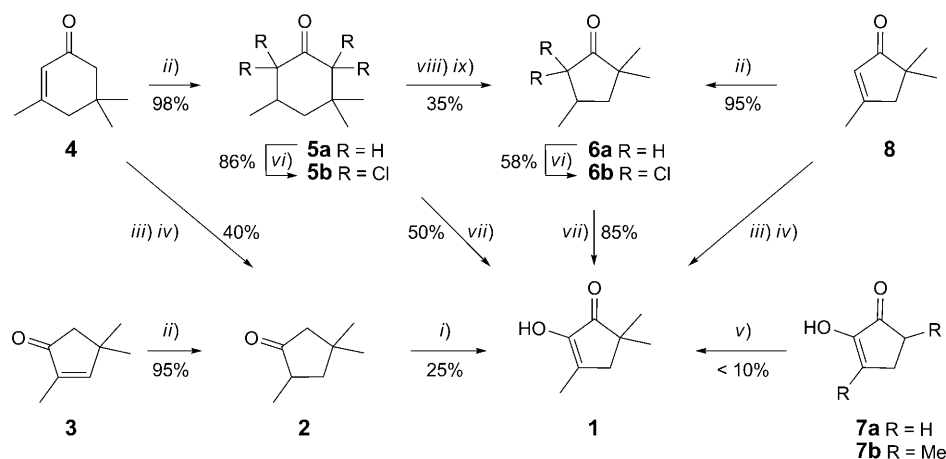
Intermediate **2**²⁾ is readily available, either *via* the corresponding enone **3** [6], by acidic cyclization of isobutyl methacrylate (=2-methylpropyl 2-methylprop-2-enoate) [7], followed by hydrogenation, or from isophorone **4**, *via* sequential $\text{BF}_3 \cdot \text{Et}_2\text{O}$ rearrangement and NaOH treatment of its corresponding epoxide [8]. Alternatively, hydrolytic NaOH treatment of either the tetrachlorocyclohexanone **5b**, with air oxidation, or dichlorocyclopentanone **6b**, afforded the desired compound **1** [9]. Finally, ingredient **1** was also unselectively obtained, as an inseparable mixture of mono- [10], di- [11], and trimethylated material, by alkylation of cyclotene **7a** *via* its ketimine derivative [12]. Nevertheless, none of these approaches is eligible for a viable industrial process for the safe production of a flavor, due to the toxicity of SeO_2 , Cl_2 , or trace amounts of halogenated materials in the last step. We thus decided to explore and present here an alternative approach, starting from cyclopentenone **8** [13], using classical scalable conditions.

Results and Discussion. – Alkylation of isobutyric acid **9a** with lithium diisopropylamide (LDA) and methallyl chloride (=3-chloro-2-methylprop-1-ene) afforded practically quantitatively the reported acid **9b** (95% yield) [14], which was cyclized with polyphosphoric acid into cyclopentenone **8**, with an improved yield of 83% [13f][15] (*Scheme 2*). Hydrogenation of enone **8** was already reported to afford

¹⁾ For the photolysis of **1**, see [4].

²⁾ ¹³C-NMR Data: 221.8 (s); 52.7 (t); 46.1 (t); 42.9 (d); 34.0 (s); 29.8 (q); 28.0 (q); 14.9 (q).

Scheme 1



i) SeO₂, EtOH, 78°. *ii*) H₂, Pd/C, EtOH. *iii*) 35% H₂O₂, NaOH, MeOH. *iv*) BF₃·Et₂O, then NaOH. *v*) PhNH₂, TsOH, then 2 equiv. of NaH, THF, MeI, then 15% HCl. *vi*) Cl₂, CCl₄, cat. DMF. *vii*) 3N NaOH, 100°. *viii*) HNO₃, NH₄VO₃. *ix*) Dist./Ba(OH)₂.

cyclopentanone **6a**³⁾ [16] in 95% yield [13b,c] (Scheme 1). We unsuccessfully attempted the oxidation of **6a** with either SeO₂/EtOH or the more practical 'BuOK/O₂ conditions [17]. We then came back to our initial strategy by epoxidizing the C=C bond (60% H₂O₂ solution, NaOH, MeOH), and could isolate the epoxy ketone **10**⁴⁾ in 50% yield⁵⁾ [19]. We also tried acidic *m*CPBA (3-chloroperbenzoic acid) conditions but, as expected, obtained the corresponding epoxy lactone **12** in a poor 12% yield⁶⁾.

To oxidize the α -position of enone **8**, we also treated it with two equiv. of BH₃·THF. Thus, after oxidative NaOH/H₂O₂ workup, we isolated diol **13** in 61% yield. Further oxidation (pyridinium chlorochromate (PCC), CH₂Cl₂) furnished a sample of **1** in 17% yield. The efficiency of this process could be improved by using *Swern* conditions (oxalyl chloride, CH₂Cl₂, DMSO, Et₃N, 25% yield) during the last step⁷⁾. This nonindustrial approach at least allowed us to obtain a sample of **1**, thus facilitating the

³⁾ MS Data: 126 (38, *M*⁺), 111 (27), 83 (50), 69 (48), 56 (100), 41 (48).

⁴⁾ Both **8** and **10** possess very similar *t*_R on both polar and apolar capillary GC columns, and UV/TLC or GC/IR analyses are recommended to follow the reaction.

⁵⁾ The known unsaturated lactone **11** was isolated as a by-product in 10% yield on using 30% H₂O₂ solution, beside **10** (30% yield). Phase-transfer conditions (30% H₂O₂ solution, Me₃BnNCl, CH₂Cl₂, H₂O, NaOH [10a]) were cleaner but also less efficient (35% yield), while (KF·Al₂O₃, 'BuOOH [18]) gave only 15% partial conversion.

⁶⁾ Alternative less industrial conditions, oxone [20] or F₂/H₂O/MeCN/CH₂Cl₂ [21], were not attempted.

⁷⁾ *Dess–Martin* conditions gave the worst result (8% of **1**), besides numerous linear derivatives of 2,2,4-trimethylpentanedial [22]; data of 2,2,4-trimethylpentanedial: ¹H-NMR: 9.57 (*d*, *J*=2, 1 H); 9.45 (*s*, 1 H); 2.42–2.35 (*m*, 1 H); 2.11 (*dd*, *J*=7, 14, 1 H); 1.44 (*dd*, *J*=5.5, 14, 1 H); 1.11 (*d*, *J*=7, 3 H); 1.09 (*s*, 3 H); 1.08 (*s*, 3 H). ¹³C-NMR: 205.3 (*d*); 203.8 (*d*); 45.7 (*s*); 42.8 (*d*); 37.2 (*t*); 22.2 (*q*); 21.7 (*q*); 15.6 (*q*). MS: 142 (1, *M*⁺), 113 (5), 95 (16), 72 (32), 58 (48), 43 (100), 41 (35). For an untested alternative aerobic oxidative technique, see [23].

Chemical reaction scheme showing the synthesis of various bicyclic compounds from 9a and 9b.

Starting materials: 9a (R = H) and 9b (R = methallyl).

Reaction conditions and yields:

- 9a $\xrightarrow{i)$ 9b (95% yield)
- 9a $\xrightarrow{ii)$ 8 (83% yield)
- 8 $\xrightarrow{iii)$ 11 (10% yield)
- 8 $\xrightarrow{v)$ 13 (61% yield)
- 8 $\xrightarrow{vii)$ 14 (88% yield)
- 8 $\xrightarrow{iv)$ 12 (12% yield)
- 13 $\xrightarrow{vi)$ 1 (25% yield)
- 14 $\xrightarrow{viii)$ 15 (62% yield)
- 14 $\xrightarrow{xii)$ 10 (50% yield)
- 15 $\xrightarrow{ix)$ 16 (21% yield)
- 15 $\xrightarrow{vi)$ 10 (67% yield)
- 10 $\xrightarrow{x)$ 17 (15% yield)
- 10 $\xrightarrow{xi)$ 1 (42% yield)

Chemical structures of the products are shown, including bicyclic ketones, alcohols, and lactones.

analysis of alternative processes. Since enone **8** seemed sensitive to oxidative conditions, and prone to *Bayer–Villiger* reaction, we also decided to reduce it (LiAlH₄, THF, 88% yield) to the corresponding allyl alcohol **14**. At this stage, we could readily and stereoselectively epoxidize the C=C bond (tBuOOH, [VO(acac)₂], 62% yield, [24]) to the *cis*-epoxy alcohol **15**⁸). This compound is also very sensitive and was readily transformed into triol **16** by a simple washing with 15% aqueous HCl solution during an extraction. *Swern* oxidation of **15** (oxalyl chloride, DMSO, Et₃N, 67% yield) afforded the desired epoxy ketone **10**. Following a known procedure, used for a monomethylated isomer [9], we attempted to isomerize **10** with 0.2% H₂SO₄ solution, but isolated instead of **1** the crystalline dihydroxy ketone **17** in 15% yield. Formally, a further dehydration at a more acidic pH should result in the target molecule [25], but

8) Due to the geometry of the five-membered ring, and even with the NOESY experiments in hand, we were unable to fully ascertain the relative *cis* or *trans* configuration of both OH groups in structures of **13**, **16**, and **17**, based on undisputable arguments. Simulated ¹H-NMR and IR spectra suggest the following relative configurations: *rel*-(1*RS*,2*SR*,5*SR*)-**13**; *rel*-(1*RS*,2*RS*,3*RS*)-**16**; *rel*-(4*RS*,5*SR*)-**17**; but in view of the absence of chirality in the final compound **1**, further derivatizations or X-ray structure analyses were not undertaken.

we preferred instead to directly isomerize epoxide **10** by treatment with $\text{BF}_3 \cdot \text{Et}_2\text{O}$ under anhydrous conditions. Thus, we readily obtained the desired crystalline flavor ingredient **1** in 42% yield⁹⁾. Although this alternative approach is longer and globally less efficient than the direct epoxidation of enone **8**, this reduction/oxidation route could eventually be shortened by a direct access to the allyl alcohol **14**¹⁰⁾.

Conclusion. – We could obtain pure **1** by rearrangement of epoxy ketone **10** with $\text{BF}_3 \cdot \text{Et}_2\text{O}$ under anhydrous conditions (42% yield⁹⁾). This latter intermediate is available from the reported enone **8**, either by direct 60% $\text{H}_2\text{O}_2/\text{NaOH}$ epoxidation (50% yield¹¹⁾ or, less efficiently (37% yield), via $[\text{VO}(\text{acac})_2]/\text{BuOOH}$ epoxidation of the corresponding allyl alcohol **14**, prior to reoxidation under *Swern* conditions. Another two-step transformation of **8**, involving a hydroboration/*Swern* oxidation sequence, is less industrial (15% global yield).

We are indebted to Dr. *Jean-Yves de Saint Laumer* for calculations of the coupling constants in theoretical ^1H -NMR analyses (CDCl_3) of **13** and **16**¹²⁾.

Experimental Part

General. See [26]. All the chiral compounds presented here were obtained as racemates.

2-Hydroxy-3,5,5-trimethylcyclopent-2-en-1-one (1). $\text{BF}_3 \cdot \text{Et}_2\text{O}$ (1.6 g, 11 mmol) was added dropwise to a soln. of epoxy ketone **10** (15.5 g, 110 mmol) in CH_2Cl_2 (200 ml). After 2 h at 20° , the mixture was diluted with CH_2Cl_2 (100 ml) and washed with sat. aq. NaHCO_3 soln. to neutrality. The org. phase was dried (Na_2SO_4) and concentrated and the residue bulb-to-bulb distilled: pure **1** (42%). White crystals. M.p. (pentane) $84.5\text{--}85.5^\circ$. B.p. $77^\circ/6$ mbar. IR: 3501, 3421, 3329, 2968, 2928, 2869, 1756, 1695, 1651, 1460, 1404, 1358, 1299, 1234, 1197, 1177, 1147, 1087, 1055, 1028, 959, 932, 839, 781, 704, 658. ^1H -NMR: 2.30 (*q*, $J=1.5$, 2 H); 2.00 (*t*, $J=1.5$, 3 H); 1.30 (*s*, 6 H); 1.28 (*s*, OH). ^{13}C -NMR: 208.3 (*s*); 146.4 (*s*); 142.4 (*s*); 44.8 (*t*); 41.2 (*s*); 25.1 (*2q*); 14.2 (*q*). MS: 140 (100, M^{+}), 125 (85), 107 (22), 97 (26), 85 (15), 79 (18), 69 (23), 56 (20), 43 (22), 41 (27).

3,5,5-Trimethylcyclopent-2-en-1-one (8). A mixture of enone **9b** (17.8 g, 125 mmol) and polyphosphoric acid (85 g) was heated to 140° for 4 h. Ice (100 g) was added to the cold mixture which was then stirred for 1 h. The aq. phase was extracted with Et_2O (5×80 ml), the org. phase washed to neutrality with sat. aq. NaHCO_3 soln. and then H_2O , dried (Na_2SO_4), and concentrated, and the residue distilled: pure **8** (83%). B.p. $67^\circ/8.5$ to $62^\circ/7.4$ mbar. IR: 2960, 2926, 2867, 1701, 1624, 1432, 1378, 1323, 1302, 1224, 1128, 1099, 848, 720, 616. ^1H -NMR: 5.85 (*s*, 1 H); 2.44 (*s*, 2 H); 2.11 (*s*, 3 H); 1.11 (*s*, 6 H). ^{13}C -NMR: 214.6 (*s*); 175.5 (*s*); 128.0 (*d*); 49.7 (*t*); 44.6 (*s*); 25.0 (*2q*); 19.4 (*q*). MS: 124 (30, M^{+}), 109 (100), 81 (28), 79 (15), 53 (8), 41 (9), 39 (12).

2,2,4-Trimethylpent-4-enoic Acid (9b). Obtained in 95% yield according to [14] and [13f]. B.p. $80^\circ/8$ mbar. IR: 3076, 2972, 2931, 1696, 1474, 1448, 1407, 1366, 1311, 1279, 1221, 1163, 1137, 942, 893, 867, 825,

⁹⁾ Compound **1** is also very sensitive to purification conditions. For example, a column chromatography (SiO_2) with the eluent AcOEt should be avoided due to partial transesterification to the corresponding 2,4,4-trimethyl-5-oxocyclopent-1-en-1-yl acetate. MS: 182 (0, M^{+}), 140 (96), 125 (74), 112 (23), 107 (13), 97 (22), 85 (27), 69 (19), 56 (38), 43 (100), 41 (39).

¹⁰⁾ Thus, for example, the intramolecular oxo-ene reaction of 2,2,4-trimethylpent-4-enal was already reported to form the endocyclic homoallyl alcohol, an analogue of **14** [13a].

¹¹⁾ This shorter access will be further optimized.

¹²⁾ **13**: $^3J=4.8$ vs. 8.5 Hz between *trans*-positioned H-C(1) and H-C(5) for *cis*- vs. *trans*-positioned OH-C(1) and OH-C(2), resp. **16**: $^3J=5.2$ vs. 7.6 Hz between *trans*-positioned OH-C(1) and OH-C(2) for *cis*- vs. *trans*-positioned OH-C(3) and OH-C(2), resp.

788. $^1\text{H-NMR}$: 12.0 (s, OH); 4.84 (s, 1 H); 4.71 (s, 1 H); 2.34 (s, 2 H); 1.72 (s, 3 H); 1.21 (s, 6 H). $^{13}\text{C-NMR}$: 185.2 (s); 142.2 (s); 114.5 (t); 48.2 (t); 42.0 (s); 25.4 (2q); 23.6 (q). MS: 142 (10, M^{++}), 127 (16), 97 (100), 81 (14), 70 (15), 55 (52), 41 (23).

3,3,5-Trimethyl-6-oxabicyclo[3.1.0]hexan-2-one (10). DMSO (1.2 g, 15 mmol) was added dropwise at -70° to a soln. of $(\text{COCl})_2$ (981 mg, 7.7 mmol) in CH_2Cl_2 (14 ml). A soln. of alcohol **15** (1.0 g, 7 mmol) in CH_2Cl_2 (7 ml) was added dropwise, followed, after 0.25 h, by Et_3N (3.55 g, 35 mmol). The temp. was then slowly increased to 20° during 1 h, Et_2O (30 ml) was added, and the org. phase was washed to neutrality with aq. sat. NH_4Cl soln., dried, and concentrated. Bulb-to-bulb distillation afforded pure ketone **10** (67%). B.p. $71^\circ/0.7$ mbar. IR: 2967, 2930, 2869, 1741, 1470, 1450, 1410, 1382, 1360, 1268, 1226, 1144, 1126, 1060, 918, 865, 809, 774, 710, 682, 613. $^1\text{H-NMR}$: 3.24 (s, 1 H); 2.20 (d, $J = 14.7$, 1 H); 1.84 (d, $J = 14.7$, 1 H); 1.56 (s, 3 H); 1.13 (s, 3 H); 1.06 (s, 3 H). $^{13}\text{C-NMR}$: 214.7 (s); 64.0 (s); 62.2 (d); 43.4 (t); 43.2 (s); 27.6 (q); 25.9 (q); 18.2 (q). MS: 140 (95, M^{++}), 125 (9), 109 (18), 97 (65), 83 (75), 70 (100), 55 (68), 43 (72), 41 (80), 39 (45).

4,4,6-Trimethyl-3,7-dioxabicyclo[4.1.0]heptan-2-one (12). A soln. of enone **8** (300 mg, 2.4 mmol) in CH_2Cl_2 (5 ml) was added at 0° to a soln. of 70% *m*CPBA (600 mg, 2.4 mmol) in CH_2Cl_2 (5 ml). After 18 h at 20° , the mixture was diluted with CH_2Cl_2 and extracted with sat. aq. NaHCO_3 soln. The org. phase was washed to neutrality with H_2O , dried (Na_2SO_4), and concentrated and the residue purified by CC (SiO_2 ; Et_2O): pure **12** (12%). B.p. $75^\circ/0.15$ mbar. IR: 2980, 2934, 1725, 1445, 1419, 1386, 1372, 1362, 1303, 1281, 1198, 1133, 1075, 1018, 997, 984, 908, 855, 834, 808, 761, 735, 686. $^1\text{H-NMR}$: 3.36 (s, 1 H); 2.20 (d, $J = 15$, 1 H); 2.10 (d, $J = 15$, 1 H); 1.55 (s, 3 H); 1.48 (s, 3 H); 1.39 (s, 3 H). $^{13}\text{C-NMR}$: 168.6 (s); 81.3 (s); 60.1 (s); 53.8 (d); 38.8 (t); 31.7 (q); 29.6 (q); 21.0 (q). MS: 156 (1, M^{++}); 100 (20), 97 (63), 83 (14), 69 (43), 55 (26), 43 (100), 41 (46).

3,3,5-Trimethylcyclopentane-1,2-diol (13). A soln. of $\text{BH}_3 \cdot \text{THF}$ complex (1.0M in THF; 32 ml, 32 mmol) was added dropwise at 0° to a soln. of enone **8** (2.0 g, 16 mmol) in THF (20 ml). After 1.5 h, a 15% aq. NaOH soln. (4 ml) was added, followed at 0° by 35% H_2O_2 soln. (2.0 ml). The mixture was diluted with Et_2O (30 ml) and washed to neutrality with H_2O . The org. phase was dried (Na_2SO_4) and concentrated and the residue purified by CC (SiO_2 ; cyclohexane/ Et_2O 95:5 $\rightarrow$ 5:95): pure **13** (61%). This material crystallized from cyclohexane. M.p. $74-77^\circ$. IR: 3223, 2969, 2954, 2925, 2892, 2863, 1457, 1346, 1286, 1117, 1068, 1016, 999, 911, 843, 790, 715. $^1\text{H-NMR}$: 3.72 (br. s, 2 OH); 3.46 (d, $J = 4.3$, 2 H); 1.80–1.70 (m, 2 H); 1.20–1.10 (m, 1 H); 1.05 (d, $J = 7$, 3 H); 1.04 (s, 3 H); 0.93 (s, 3 H). $^{13}\text{C-NMR}$: 85.7 (d); 83.8 (d); 44.3 (t); 36.7 (s); 34.4 (d); 29.6 (q); 24.9 (q); 18.7 (q). MS: 144 (8, M^{++}), 126 (16), 111 (69), 88 (28), 83 (54), 71 (100), 69 (76), 57 (70), 43 (56), 41 (70).

3,5,5-Trimethylcyclopent-2-en-1-ol (14). A soln. of enone **8** (6.7 g, 53 mmol) in Et_2O (10 ml) was added dropwise at 0° to a suspension of LiAlH_4 (1.0 g, 27 mmol) in Et_2O (230 ml). After 2 h at 20° , H_2O (1 ml), 15% NaOH soln. (1 ml), and H_2O (10 ml) were successively added. The mixture was filtered and the filtrate dried (MgSO_4) and concentrated. Bulb-to-bulb distillation afforded pure **14** (88%). B.p. $68^\circ/9.0$ mbar. IR: 3337, 3045, 2953, 2911, 2866, 2839, 1658, 1466, 1440, 1378, 1363, 1322, 1195, 1154, 1038, 1020, 992, 942, 885, 865, 825, 671. $^1\text{H-NMR}$: 5.38 (s, 1 H); 4.13 (s, 1 H); 2.22 (d, $J = 16.2$, 1 H); 1.94 (d, $J = 16.2$, 1 H); 1.73 (s, 3 H); 1.26 (br. s, OH); 1.05 (s, 3 H); 1.04 (s, 3 H). $^{13}\text{C-NMR}$: 145.0 (s); 126.4 (d); 85.2 (d); 50.4 (t); 42.2 (s); 28.7 (q); 22.8 (q); 17.1 (q). MS: 126 (8, M^{++}), 111 (100), 108 (30), 93 (99), 91 (55), 77 (43), 55 (20), 43 (20), 41 (18), 39 (20).

3,3,5-Trimethyl-6-oxabicyclo[3.1.0]hexan-2-ol (15). At 20° , 70% aq. $t\text{-BuOOH}$ soln. (9.0 g, 70 mmol) was added dropwise to a soln. of alcohol **14** (5.9 g, 47 mmol) and $[\text{VO}(\text{acac})_2]$ (186 mg, 0.7 mmol) in toluene (80 ml). After 2 h at 20° , the mixture was diluted with Et_2O (120 ml) and extracted with sat. aq. NaHCO_3 soln. and H_2O to neutrality. The org. phase was dried (Na_2SO_4) and concentrated and the residue bulb-to-bulb distilled: pure **15** (62%). B.p. $78^\circ/4.8$ mbar. IR: 3423, 2954, 2929, 2868, 1469, 1448, 1426, 1383, 1362, 1309, 1221, 1169, 1150, 1088, 1051, 1029, 1000, 984, 965, 922, 882, 868, 832, 804, 693, 662. $^1\text{H-NMR}$: 3.83 (s, 1 H); 3.38 (s, 1 H); 2.03 (br. s, OH); 1.89 (d, $J = 14.4$, 1 H); 1.59 (d, $J = 14.4$, 1 H); 1.40 (s, 3 H); 1.03 (s, 3 H); 1.00 (s, 3 H). $^{13}\text{C-NMR}$: 80.7 (d); 67.3 (d); 62.9 (s); 45.8 (t); 39.2 (s); 30.1 (q); 24.7 (q); 18.4 (q). MS: 142 (11, M^{++}), 127 (10), 109 (33), 85 (100), 72 (33), 57 (41), 55 (35), 43 (65), 41 (38).

1,4,4-Trimethylcyclopentane-1,2,3-triol (16). A soln. of epoxy alcohol **15** (4.1 g, 29 mmol) in Et_2O (50 ml) was washed with 15% aq. HCl soln. (3×30 ml) and then with sat. aq. NH_4Cl soln. to neutrality. The org. phase was dried (MgSO_4) and concentrated and the residue bulb-to-bulb distilled: **16** (21%).

B.p. 73°/1.3 mbar. IR: 3395, 2961, 2933, 2870, 1700, 1656, 1469, 1448, 1407, 1378, 1366, 1306, 1259, 1224, 1202, 1140, 1093, 1028, 1011, 990, 948, 894, 854, 781, 698, 657. ¹H-NMR: 4.26 (*d*, *J* = 4.4, 1 H); 4.09 (*d*, *J* = 4.4, 1 H); 2.76 (br. *s*, 3 H); 2.11 (*s*, 2 H); 1.64 (*s*, 3 H); 1.21 (*s*, 3 H); 1.02 (*s*, 3 H). ¹³C-NMR: 82.9 (*d*); 80.3 (*d*); 74.4 (*s*); 55.0 (*t*); 39.6 (*s*); 29.9 (*q*); 27.4 (*q*); 25.3 (*q*). MS: 160 (1, *M*⁺), 142 (7), 109 (9), 83 (11), 72 (100), 57 (17), 43 (14).

4,5-Dihydroxy-2,2,4-trimethylcyclopentanone (**17**). A mixture of epoxy ketone **10** (200 mg, 1.4 mmol) in 0.2% H₂SO₄ soln. (0.9 ml) was heated to reflux for 1 h. The mixture was diluted with H₂O (10 ml) and extracted with CH₂Cl₂ (3 × 10 ml). The org. phase was dried (Na₂SO₄) and concentrated and the residue purified by CC (SiO₂; cyclohexane/Et₂O 95:5): pure **17** (15%). White crystals. IR: 3358, 3270, 2974, 2963, 2931, 2866, 2843, 1742, 1464, 1448, 1389, 1378, 1359, 1315, 1302, 1231, 1182, 1144, 1102, 1058, 1033, 1001, 952, 945, 892, 827, 795, 678. ¹H-NMR: 4.53 (*s*, 1 H); 3.53 (br. *s*, OH); 3.26 (br. *s*, OH); 2.11 (*d*, *J* = 13.5, 1 H); 2.00 (*d*, *J* = 13.5, 1 H); 1.22 (*s*, 3 H); 1.19 (*s*, 3 H); 1.13 (*s*, 3 H). ¹³C-NMR: 219.2 (*s*); 82.6 (*d*); 75.3 (*s*); 48.3 (*t*); 42.0 (*s*); 28.8 (*q*); 25.4 (*q*); 22.4 (*q*). MS: 158 (21, *M*⁺), 140 (48), 125 (35), 101 (100), 88 (42), 74 (42), 55 (32), 43 (60), 41 (30).

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