

92. A Short Synthesis of (±)-Muscone

by Valentin Rautenstrauch*, Roger L. Snowden*, and Simon M. Linder

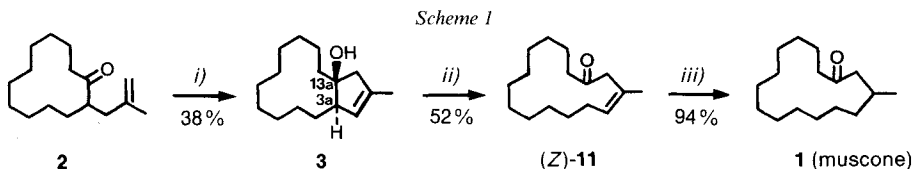
Firmenich SA, Laboratoires de Recherche, CH-1211 Genève 8

(26.III.90)

(±)-Muscone ((±)-**1**) has been synthesised in three steps from 2-(2'-methylprop-2'-enyl)cyclododecan-1-one (**2**). The synthesis involves two key transformations: a *Lewis*-acid-mediated intramolecular ene reaction (**2**→**3**) and the β -cleavage of the bicyclic potassium alkoxide **3a**' to the macrocyclic enone (*Z*)-**11**.

Introduction. – Muscone (**1**), a perfumistically important macrocyclic ketone, has attracted considerable synthetic interest over the past sixty years¹). An attractive approach is the three-C-atom ring-expansion concept developed in *Firmenich* research laboratories and which involves cleavage of a cyclopentacyclododecene system constructed from cyclododecanone [3]. We now present a short synthesis of (±)-**1** which represents an extension of this strategy.

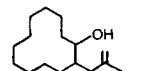
Results and Discussion. – The synthesis of **1** (*cf.* Scheme 1) starts by treatment of 2-(2'-methylprop-2'-enyl)cyclododecan-1-one (**2**) [4] with Me₂AlCl (1.3 mol-equiv.)²) in 1,2-dichloroethane/hexane at 70° during 8 h followed by an aqueous basic workup.

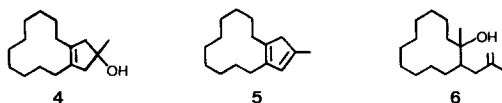


i) Me₂AlCl, 1,2-dichloroethane/hexane, 70°, then aq. NaOH soln. ii) KH, HMPA, 120°, then aq. NH₄Cl soln. iii) H₂, 5% Pd/C, cyclohexane.

¹) For a review of muscone syntheses prior to 1979–1980, see [1]; for more recent syntheses, see [2] [3 d, e].

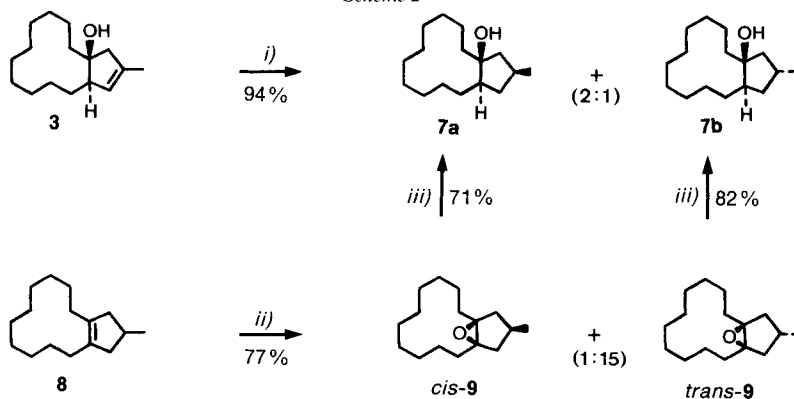
²) Other alkylaluminium halides gave inferior results. For example, Et₂AlCl afforded **3** in much lower yield (5–10%) producing substantial amounts (40–50%) of 2-(2'-methylprop-2'-enyl)cyclododecan-1-ol (i) (1.3:1 diastereoisomeric mixture) via reduction of **2**. Data of i. Major Isomer: colourless oil. B. p. (bulb-to-bulb dist.) 170–180°/0.02 Torr. *R_f* (cyclohexane/AcOEt 9:1) 0.30. IR (CDCl₃): 3450 (br.), 2910, 2860, 1450, 996, 892. ¹H-NMR (+D₂O): 1.05–1.60 (19 H); 1.72 (s, 3 H); 1.75 (m, 2 H); 1.94 (dd, *J* = 14.5, 6, 1 H); 2.23 (dd, *J* = 14.5, 8, 1 H); 3.80 (m, 1 H); 4.73 (s, 1 H); 4.78 (s, 1 H). MS: 238 (1, *M*⁺), 220 (7), 182 (44), 111 (26), 98 (47), 81 (37), 69 (67), 55 (86), 41 (100). Minor Isomer: white crystals. M. p. 89–90°. *R_f* (cyclohexane/AcOEt 9:1) 0.32. IR (CHCl₃): 3420 (br.), 2940, 2850, 1450, 896. ¹H-NMR (+D₂O): 1.20–1.60 (19 H); 1.74 (s, 3 H); 1.76 (m, 2 H); 1.93 (dd, *J* = 14.5, 10, 1 H); 2.29 (dd, *J* = 14.5, 4.5, 1 H); 3.80 (m, 1 H); 4.76 (s, 1 H); 4.78 (s, 1 H). MS: 238 (2, *M*⁺), 220 (20), 182 (10), 121 (16), 109 (17), 95 (32), 81 (36), 69 (63), 55 (89), 41 (100). The use of the stronger *Lewis* acids, MeAlCl₂ or EtAlCl₂, in CH₂Cl₂ at r. t., produced complex mixtures containing only small amounts (≤ 5%) of **3**.





Chromatographic purification afforded two major cyclisation products, alcohols **3** (m. p. 55–56°, 38%) and **4** (18%), together with minor amounts of cyclopentadiene **5**³⁾ (5%) and alcohol **6**⁴⁾ (2–3%)⁵⁾. Whereas **4–6** were readily identified from their spectra, the unsuitability of crystals of **3** and two derivatives⁶⁾ for X-ray structure analysis, coupled with the fact that NMR experiments were inconclusive, obliged us to determine the configuration of **3** by chemical correlation. Accordingly, catalytic hydrogenation of **3** gave alcohols **7a** and **7b** (2:1, 94%) which were also prepared from the bicyclic alkene **8** [2a] by epoxidation to *trans*- and *cis*-**9** (15:1, 77%) and reduction with LiAlH₄/AlCl₃ [5] (cf. Scheme 2). As it is established that hydride reduction of an epoxide favours nucle-

Scheme 2



i) H₂, 5% Pd/BaSO₄, MeOH. ii) mcpba, CH₂Cl₂, aq. NaHCO₃ soln. iii) LiAlH₄, AlCl₃, THF.

ophilic attack on the face opposite to the O-atom [6], it follows that the structures of **7a**, **7b**, and **3** are as shown⁷⁾.

An explanation for the formation of **3**⁸⁾ and **4** from **2** is presented in Scheme 3. It is proposed that the conformationally interconvertible *Lewis*-acid complexes of **2**, **I** and **I'**,

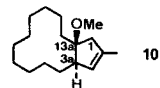
³⁾ A possible origin of **5** is from dehydration of either **3** or **4**.

⁴⁾ Tertiary alcohol **6**, the product of nucleophilic attack of an Al–Me group on **2**, was isolated as a single diastereoisomer whose configuration was not determined.

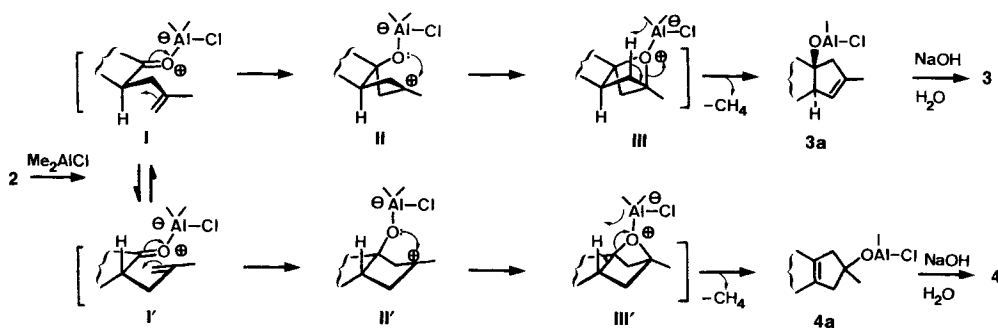
⁵⁾ Yields were calculated taking into account recovered **2** (ca. 35%, cf. *Exper. Part*).

⁶⁾ These two derivatives were the carbamates resulting from the reaction of **3** with either phenyl isocyanate or α -naphthyl isocyanate.

⁷⁾ Further evidence for the *trans*-fused bicyclic structure of **3** was obtained by ¹H-NMR nuclear Overhauser effect (NOE) experiments on the methyl ether **10** derived from **3** (cf. *Exper. Part*). Irradiation of the MeO group resulted in an enhancement of H(β)–C(1) and no enhancement of H–C(3a).



⁸⁾ The transformation of **2** to **3**, formally a 5-*endo*-trigonal closure [7], is the first reported example of an intramolecular *Type-III* ene reaction which leads to the isolation of a cyclopentenol [8]; for *Lewis*-acid-mediated intramolecular ene reactions using ketones as enophiles, see [9] and ref. cit. therein.

Scheme 3. Proposed Mechanism for the Formation of **3** and **4** from **2**

undergo cyclisation to oxetanes **III** and **III'** via carbocations **II** and **II'**⁹⁾, respectively. Intramolecular proton abstraction by one of the Al–Me groups in **III/III'** then results in the formation of the aluminium alkoxides **3a** and **4a** with loss of CH₄. It is important to note that, for both **III** and **III'**, only one H-atom is ideally positioned for abstraction, and, assuming equal efficiencies for these H abstractions, the *trans/cis*-selectivity of the initial cyclisation step (**I/I'** → **II/II'**) is, thus, reflected in the ratio of **3** and **4**.

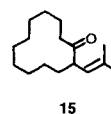
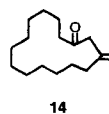
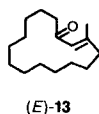
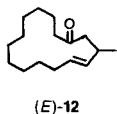
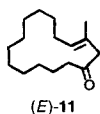
With **3** in hand, we were now ready to study the second step of the synthesis which involves β -cleavage¹⁰⁾ of the C(3a)–C(13a) bond and formation of the desired C₁₅ macrocyclic system¹¹⁾. Thus, treatment of **3** with KH (2.1 mol-equiv.) in hexamethylphosphoric triamide (HMPA) at r. t. followed by heating the resultant potassium alkoxide **3a'** at 120° during 2 h, afforded, after an aqueous workup, (*Z*)-**11**¹²⁾ (52%) and an 8:1 mixture **15/2** (22%). Two points are worthy of mention. Firstly, although there are two allylic C–C bonds, C(1)–C(13a) and C(3a)–C(13a), capable of undergoing β -cleavage, the major reaction pathway, as anticipated from model studies [13], involves cleavage of the latter, more substituted C–C bond; this is reflected in the 2.4:1 selectivity favouring (*Z*)-**11** over **15** and **2**. Secondly, the configuration of the C=C bond in **3** is retained in (*Z*)-**11**, a result which indicates that the transient allylic carbanion **IV** is rapidly quenched either intermolecularly, or intramolecularly via dienolate **V** (cf. Scheme 4).

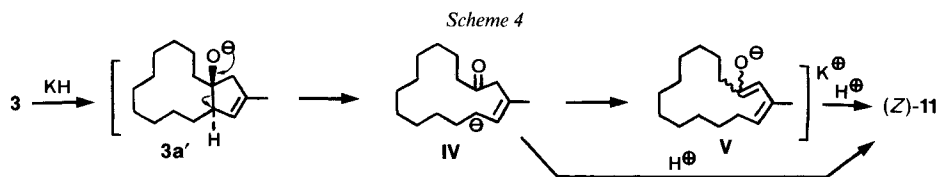
⁹⁾ For an example of a Lewis-acid-catalysed cyclisation of a δ,ϵ -enone to an oxetane, see [10].

¹⁰⁾ For other synthetic applications of the β -cleavage of homoallylic potassium alkoxides, see [11] and ref. cit. therein.

¹¹⁾ The possibility of converting **3** to **13** via a thermal *retro*-ene process was also briefly investigated. Thus, a solution of **3** in xylene was passed through a heated glass column using N₂ as the carrier gas; at 450° **3** was recovered unchanged, and, at 600°, a complex product mixture was formed in which **13** was not detected by ¹H-NMR analysis.

¹²⁾ Previously described by Karpf and Dreiding [12], (*Z*)-**11** was contaminated with small amounts ($\leq 5\%$) of enones (*E*)-**11**, (*E*)-**12**, (*E*)-**13**, and **14** (cf. Scheme 1) which were identified by ¹H-NMR spectroscopy (cf. *Exper. Part*) and originate by either protonation of **IV/V** or isomerisation of (*Z*)-**11** during the workup.





Finally, the synthesis was completed by catalytic hydrogenation of (Z)-11 which afforded **1** in 94% yield.

Experimental Part

General. See [13].

(3*a*RS,13*a*SR)-3*a*,4,5,6,7,8,9,10,11,12,13,13*a*-Dodecahydro-2-methyl-1*H*-cyclopentacyclododecen-13*a*-ol (**3**). A soln. of Me₂AlCl (1*M* soln. in hexane, Aldrich; 1100 ml) was added dropwise within 10 min to a stirred soln. of **2** [**4**] (20 g, 0.085 mol) in 1,2-dichloroethane (180 ml) at r. t. under N₂. The soln. was then heated at reflux (70°) during 8 h, cooled to r. t., poured into cold 1*N* aq. NaOH soln. (300 ml) with stirring, and extracted (Et₂O). The combined org. phase was washed with sat. aq. NaCl soln., dried (Na₂SO₄), and evaporated to afford a pale-yellow oil (20.6 g). CC (silica gel (540 g), cyclohexane/AcOEt 9:1) gave **3** as a white crystalline solid (4.9 g, 25%). M. p. 55–56° (petroleum ether). *R*_f (cyclohexane/AcOEt) 0.20. IR (CHCl₃): 3600, 3420 (br.), 2910, 2850, 1466, 1440, 1350, 990, 910, 862, 840. ¹H-NMR (+D₂O): 1.15–1.60 (18 H); 1.69 (*m*, 2 H); 1.74 (*s*, 3 H); 2.01 (*d*, *J* = 16, 1 H); 2.57 (*d*, *J* = 16, 1 H); 2.79 (br. *d*, *J* = 10, 1 H); 5.26 (br. *s*, 1 H). ¹³C-NMR: 137.3 (*s*); 126.4 (*d*); 84.4 (*s*); 49.0 (*t*); 46.2 (*d*); 32.9 (*t*); 26.5 (*t*); 26.3 (*t*); 24.9 (*t*); 23.1 (*t*); 22.4 (*t*); 22.3 (*t*); 22.2 (*t*); 21.8 (*t*); 21.3 (*t*); 17.1 (*q*). MS: 236 (69, *M*⁺), 221 (21), 123 (17), 109 (40), 95 (49), 81 (50), 67 (35), 55 (69), 41 (100).

Also isolated was unreacted **2** (7.1 g, *R*_f (cyclohexane/AcOEt 9:1) 0.55); 2,3,4,5,6,7,8,9,10,11,12,13-dodecahydro-2-methyl-1*H*-cyclopentacyclododecen-2-ol (**4**), colourless oil (2.3 g, 12%). B. p. (bulb-to-bulb distillation) 170–180°/0.02 Torr. *R*_f (cyclohexane/AcOEt 9:1) 0.13. IR (CHCl₃): 3600, 3450 (br.), 2910, 2850, 1442, 1350, 1220, 940, 800. ¹H-NMR (+D₂O): 1.12–1.52 (16 H); 1.40 (*s*, 3 H); 2.12 (*m*, 4 H); 2.38 (*AB*, *J* = 15, 4 H). ¹³C-NMR: 134.2 (*s*); 77.4 (*s*); 51.0 (*t*); 28.2 (*q*); 25.2 (*t*); 24.9 (*t*); 24.6 (*t*); 24.5 (*t*); 22.2 (*t*). MS: 236 (35, *M*⁺), 178 (35), 109 (19), 95 (21), 81 (22), 55 (31), 43 (100); 4,5,6,7,8,9,10,11,12,13-decahydro-2-methyl-1*H*-cyclopentacyclododecene (**5**) [14], colourless oil (0.6 g, 3%). B. p. (bulb-to-bulb distillation) 150–160°/0.04 Torr. *R*_f (cyclohexane/AcOEt 9:1) 0.80. IR (CHCl₃): 2940, 2860, 1470, 1446, 1380, 890. ¹H-NMR: 1.22 (4 H); 1.34 (8 H); 1.55 (4 H); 2.00 (*s*, 3 H); 2.25 (*t*, *J* = 7, 2 H); 2.32 (*t*, *J* = 7, 2 H); 2.78 (*s*, 2 H); 5.94 (br. *s*, 1 H). ¹³C-NMR: 141.5 (*s*); 139.8 (*s*); 138.3 (*s*); 129.5 (*d*); 46.3 (*t*); 27.9 (*t*); 26.5 (*t*); 24.6 (*t*); 24.5 (*t*); 23.7 (*t*); 22.4 (*t*); 22.3 (*t*); 16.2 (*q*). MS: 218 (18, *M*⁺) 119 (30), 105 (37), 94 (36), 91 (100), 71 (39); 1-methyl-2-(2'-methylprop-2'-enyl)cyclododecan-1-ol (**6**), colourless oil (0.4 g, 2%). B. p. (bulb-to-bulb distillation) 150–170°/0.2 Torr. *R*_f (cyclohexane/AcOEt 9:1) 0.19. IR (CHCl₃): 3630, 3460 (br.), 2950, 2890, 1460, 1432, 1360, 880. ¹H-NMR (+D₂O): 1.00–1.60 (19 H); 1.18 (*s*, 3 H); 1.71 (*m*, 2 H); 1.74 (*s*, 3 H); 1.93 (*dd*, *J* = 14.5, 5, 1 H); 2.36 (*dd*, *J* = 14.5, 6, 1 H); 4.74 (*s*, 1 H); 4.76 (*s*, 1 H). ¹³C-NMR: 146.2 (*s*); 111.1 (*t*); 76.0 (*s*); 40.0 (*t*); 39.3 (*t*); 38.4 (*d*); 26.9 (*t*); 26.6 (*q*); 26.3 (*t*); 25.5 (*t*); 23.9 (*t*); 23.2 (*t*); 23.0 (*t*); 22.8 (*q*); 22.4 (*t*); 21.1 (*t*). MS: 252 (0, *M*⁺), 125 (48), 97 (25), 83 (23), 69 (70), 43 (100).

(2*RS*,3*a*SR,13*a*RS)- and (2*RS*,3*a*RS,13*a*SR)-Tetradecahydro-2-methyl-1*H*-cyclopentacyclododecen-3*a*-ol (**7a** and **7b**). A soln. of **3** (0.2 g, 0.85 mmol) in MeOH (5 ml) containing 5% Pd/BaSO₄ (12 mg) was hydrogenated at r. t. After 5 h the mixture was filtered (*Hyflo*) and the filtrate concentrated. Bulb-to-bulb distillation (160–170°/0.02 Torr) afforded a 2:1 mixture **7a**/**7b** (0.19 g, 94%) which was separated by CC (silica gel (50 g), cyclohexane/AcOEt 4:1).

Data of **7a**. Colourless oil. *R*_f (cyclohexane/AcOEt 4:1) 0.40. IR: 3600, 3460 (br.), 2920, 2850, 1462, 1440, 1342, 984, 902, 842, 732. ¹H-NMR (+D₂O): 1.00–1.65 (22 H); 1.06 (*d*, *J* = 7, 3 H); 1.75–1.95 (2 H); 2.01 (*m*, 1 H); 2.13 (2*d*, *J* = 14, 11, 1 H). ¹³C-NMR: 83.6 (*s*); 45.9 (*t*); 42.3 (*d*); 40.0 (*t*); 35.1 (*t*); 31.3 (*d*); 26.5 (*t*); 26.2 (*t*); 25.2 (*t*); 24.0 (*t*); 22.4 (*t*); 22.1 (*t*); 22.1 (*q*); 20.5 (*t*). MS: 238 (8, *M*⁺), 223 (13), 125 (35), 111 (51), 98 (100), 84 (68), 69 (76), 55 (96).

Data of **7b**. Colourless oil. *R*_f (cyclohexane/AcOEt 4:1) 0.31. IR: 3440 (br.), 1462, 1440, 1342, 1250, 990, 842, 722. ¹H-NMR (+D₂O): 0.99 (*d*, *J* = 7, 3 H); 1.05–1.55 (20 H); 1.55–1.75 (4 H); 1.95 (*q*, *J* = 8, 1 H); 2.30 (*m*, 1 H).

¹³C-NMR: 84.4 (s), 46.3 (t), 39.2 (d), 36.9 (t), 34.1 (t), 29.3 (d), 26.5 (t), 26.2 (t), 25.1 (t), 24.9 (t), 22.4 (t), 22.2 (t), 22.2 (q), 22.1 (t), 21.9 (t), 20.5 (t). MS: 238 (6, *M*⁺), 223 (11), 125 (32), 111 (39), 98 (100), 84 (67), 69 (74), 55 (100).

3a,13a-Epoxytridecahydro-2-methyl-1H-cyclopentacyclododecene (9; trans/cis 15:1). *m*-Chloroperbenzoic acid (5.1 g, 0.016 mol) was added portionwise within 20 min to a stirred mixture of 2,3,4,5,6,7,8,9,10,11,12,13-dodecahydro-2-methyl-1H-cyclopentacyclododecene (**8**) [2a] (3.0 g, 0.014 mol) and NaHCO₃ (2.2 g, 0.026 mol) in CH₂Cl₂ (130 ml)/H₂O (55 ml) at r. t. After a further 5 min. at r. t., the mixture was poured into sat. aq. NaCl soln. (40 ml) and extracted (CH₂Cl₂). The combined org. phase was successively washed with 1N aq. NaOH, 10% aq. Na₂SO₃, 10% aq. NaCl soln., dried (Na₂SO₄), and evaporated: crude **9** (trans/cis 15:1, pale-yellow oil (3.1 g)) was separated by CC (silica gel (170 g), cyclohexane/AcOEt 19:1).

Data of trans-9. White crystalline solid (2.3 g, 72%). M. p. 56–57° (petroleum ether/Et₂O 1:1). *R*_f (cyclohexane/AcOEt 9:1) 0.56. IR (CHCl₃): 3000, 2940, 2860, 1464, 1442, 1430, 1342, 852, 699. ¹H-NMR: 0.97 (d, *J* = 7, 3 H); 1.15–1.65 (20 H); 1.70–1.95 (5 H). MS: 236 (10, *M*⁺), 221 (14), 137 (50), 109 (44), 95 (61), 81 (69), 678 (69), 55 (100).

Data of cis-9. White crystalline solid (0.15 g, 5%). M. p. 61–62° (petroleum ether). *R*_f (cyclohexane/AcOEt 9:1) 0.65. IR (CHCl₃): 2940, 1470, 1442, 1370, 1310, 858. ¹H-NMR: 0.99 (d, *J* = 7, 3 H); 1.15–1.65 (20 H); 1.79 (2 H); 2.06 (3 H). MS: 236 (10, *M*⁺), 221 (9), 137 (37), 111 (71), 98 (54), 81 (62), 67 (65), 55 (100).

Hydride Reduction of cis-9 and trans-9. A soln. of *cis*-**9** (70 mg, 0.3 mmol) in THF (0.5 ml) was added to a stirred mixture of powdered anh. AlCl₃ (10 mg, 0.07 mmol) and LiAlH₄ (8 mg, 0.21 mmol) in THF (2 ml) at r. t. under N₂. The mixture was refluxed during 6 h, cooled to 0° and H₂O (0.5 ml) added dropwise. Filtration (*Hyflo*), evaporation, and CC (silica gel (10 g), cyclohexane/AcOEt 4:1) afforded **7a** (50 mg, 71%), identical in all respects with an authentic sample (*vide supra*). Using the same experimental procedure, *trans*-**9** (1 g, 4.2 mmol), with anh. AlCl₃ (0.13 g, 1 mmol), LiAlH₄ (0.11 g, 2.9 mmol) in THF (10 ml), was converted to **7b** (0.82 g, 82%), identical in all respects with an authentic sample (*vide supra*).

(*3aRS,13aSR*)-**3a,4,5,6,7,8,9,10,11,12,13,13a-Dodecahydro-13a-methoxy-2-methyl-1H-cyclopentacyclododecene (10).** A soln. of **3** (0.1 g, 0.42 mmol) in THF (2 ml) was added dropwise to a stirred slurry of NaH (80% dispersion in oil (*Fluka*); 20 mg, 0.67 mmol) in THF (2 ml) at r. t. under N₂. The mixture was refluxed during 1 h, cooled to r. t., and MeI (0.36 g, 2.6 mmol) added. The mixture was then refluxed during 40 h, cooled, poured into cold H₂O, and extracted (Et₂O). The combined org. phase was washed with sat. aq. NaCl soln., dried (Na₂SO₄), and evaporated to afford a pale-yellow oil (0.11 g). Purification by CC (silica gel (10 g), cyclohexane/AcOEt 4:1) furnished **10** as a colourless oil (55 mg, 52%). B. p. (bulb-to-bulb distillation) 150–160°/0.02 Torr. *R*_f (cyclohexane/AcOEt 9:1) 0.57. IR (CHCl₃): 2940, 2850, 1464, 1440, 1072, 812. ¹H-NMR: 1.15–1.80 (20 H); 1.72 (s, 3 H); 2.28 (AB, *J* = 18, 2 H); 2.82 (br. d, *J* = 10, 1 H); 3.17 (s, 3 H); 5.30 (br. s, 1 H). ¹³C-NMR: 136.2 (s); 127.1 (t); 88.3 (s); 50.6 (q); 47.3 (d); 42.8 (t); 31.3 (t); 26.6 (t); 26.1 (t); 25.0 (t); 23.4 (t); 23.0 (t); 22.6 (2 t); 22.2 (t); 21.9 (t); 16.7 (q). MS: 250 (20, *M*⁺), 218 (17), 123 (79), 107 (58), 94 (100), 79 (38), 55 (40).

(*Z*)-**3-Methylcyclopentadec-3-en-1-one ((Z)-11)** [11]. A soln. of **3** (2.9 g, 0.012 mol) in HMPA (25 ml) was added dropwise within 15 min to a stirred slurry of KH (*pract.*; ca. 35% dispersion in oil (*Aldrich*), 3 g, 0.026 mol) in HMPA (35 ml) at r. t. under N₂. This mixture was stirred for 4 h at r. t., heated at 120° during 2 h, cooled (10°), poured cautiously into cold sat. aq. NH₄Cl soln., (200 ml) and extracted (Et₂O). The combined org. phase was washed with sat. aq. NaCl soln., dried (Na₂SO₄), evaporated, and the residual oil purified by CC (silica gel (360 g), cyclohexane/AcOEt 19:1) to afford (*Z*)-**11** as a colourless oil (1.6 g, purity: ca. 95%; 52% yield). B. p. (bulb-to-bulb distillation) 140–150°/0.02 Torr. *R*_f (cyclohexane/AcOEt 9:1) 0.58. IR (CHCl₃): 2920, 2850, 1716, 1440, 1350, 970, 904. ¹H-NMR: 1.20–1.45 (16 H); 1.66 (m, 2 H); 1.71 (s, 3 H); 1.97 (m, 2 H); 2.43 (t, *J* = 7, 2 H); 3.15 (s, 2 H); 5.41 (br. t, *J* = 7, 1 H). ¹³C-NMR: 129.2 (d); 47.2 (t); 40.4 (t); 27.7 (t); 27.5 (t); 27.2 (t); 26.2 (t); 25.8 (t); 25.6 (t); 25.3 (t); 24.2 (q); 23.0 (t). MS: 236 (67, *M*⁺), 221 (12), 109 (22), 95 (31), 81 (36), 67 (41), 55 (62), 41 (100). Contaminants (ca. 5%) were identified by ¹H-NMR spectroscopy: (*E*)-**3-methylcyclopentadec-3-en-1-one ((E)-11)** [11] (2.14 (s, 3 H); 3.02 (s, 2 H); 5.34 (m, 1 H)), (*E*)-**3-methylcyclopentadec-4-en-1-one ((E)-12)** [14] (1.03 (d, *J* = 7, 3 H); 5.34 (m, 2 H)), (*E*)-**3-methylcyclopentadec-2-en-1-one ((E)-13)** [11] (6.15 (br. s, 1 H)), and **3-methylidenecyclopentadecan-1-one (14)** [15] (3.13 (s, 2 H); 4.89 (s, 1 H); 4.97 (s, 1 H)).

Also isolated was a 5:1 mixture 2-(2'-methylprop-1'-enyl)cyclododecan-1-one (**15**)/**2** as a colourless oil (0.64 g, 22%). B. p. (bulb-to-bulb distillation) 160–170°/0.02 Torr.

Data of 15. *R*_f (cyclohexane/AcOEt 9:1) 0.67. ¹H-NMR: 1.15–1.45 (16 H); 1.67 (s, 3 H); 1.71 (s, 3 H); 1.89 (m, 2 H); 2.45 (m, 2 H); 3.51 (m, 1 H); 5.06 (d, *J* = 9, 1 H). MS: 236 (28, *M*⁺), 109 (32), 95 (95), 82 (100), 67 (99), 55 (62).

3-Methylcyclopentadecan-1-one (= (±)-Muscone; 1). A soln. of (*Z*)-**11** (0.1 g, purity: ca. 95% (*vide supra*); 0.4 mmol) in cyclohexane (5 ml) containing 10% Pd/C (5 mg) was hydrogenated during 16 h at r. t. Filtration

(*Hyflo*), concentration, and distillation *i.v.* afforded **1** as a colourless oil (95 mg, 94%), identical to an authentic sample [2a].

Data of 1. B. p. (bulb-to-bulb distillation) 140–150°/0.02 Torr. R_f (cyclohexane/AcOEt 9:1) 0.58. IR: 2950, 2870, 1720, 1468, 1418, 1378, 1282, 1140, 1060, 720. $^1\text{H-NMR}$: 0.94 (*d*, $J = 7, 3$ H); 1.10–1.50 (20 H); 1.50–1.75 (2 H); 2.05 (*m*, 1 H); 2.18 (*dd*, $J = 14.5, 6, 1$ H); 2.41 (*t*, $J = 7, 2$ H); 2.42 (*dd*, $J = 14.5, 7, 1$ H). MS: 238 (4, M^+), 223 (2), 125 (28), 97 (41), 85 (83), 69 (64), 55 (100), 41 (77).

REFERENCES

- [1] B. D. Mookherjee, R. A. Wilson, in 'Fragrance Chemistry', Ed. E. T. Theimer, Academic Press, New York, 1982, p. 433.
- [2] S. Hacin, R. Pardo, M. Santelli, *Tetrahedron Lett.* **1979**, 4553; J. Tsuji, T. Yamada, M. Kaito, T. Mandai, *Bull. Chem. Soc. Jpn.* **1980**, 53, 1417; Q. Y. Yao, X. Chen, Z. Y. Gao, W. Z. Zhao, *Hua Hsueh Hsueh Pao* **1980**, 38, 596 (CA: **1980**, 94, 208 417 q); B. M. Trost, J. E. Vincent, *J. Am. Chem. Soc.* **1980**, 102, 5680; G. Catoni, C. Galli, L. Mandolini, *J. Org. Chem.* **1980**, 45, 1906; S. R. Wilson, R. N. Misra, G. M. Georgiadis, *ibid.* **1980**, 45, 2460; L. A. Paquette, W. E. Fristad, D. S. Dime, T. R. Bailey, *ibid.* **1980**, 45, 3017; J. Tsuji, T. Yamada, I. Shimizu, *ibid.* **1980**, 45, 5209; T. Takahishi, T. Nagashima, J. Tsuji, *Tetrahedron Lett.* **1981**, 22, 1359; T. Yoshida, S. Saito, *Yukagaku* **1982**, 31, 353; R. K. Brunner, H. J. Borschberg, *Helv. Chim. Acta* **1983**, 66, 2608; P. A. Wender, D. A. Holt, S. M. Sieburth, *J. Am. Chem. Soc.* **1983**, 105, 3348; S. Sakane, K. Maruoka, H. Yamamoto, *Tetrahedron Lett.* **1983**, 24, 943; T. Mandai, T. Yanagi, K. Araki, Y. Morisaki, M. Kawada, J. Otera, *J. Am. Chem. Soc.* **1984**, 106, 3670; H. Sakurai, Y. Eriyama, Y. Kamiyama, Y. Nakadaira, *J. Organomet. Chem.* **1984**, 264, 229; Y. Morizawa, H. Oda, K. Oshima, H. Nozaki, *Tetrahedron Lett.* **1984**, 25, 1163; G. Mehta, K. S. Rao, *ibid.* **1984**, 25, 1839; M. Asuoka, M. Abe, H. Takei, *Bull. Chem. Soc. Jpn.* **1985**, 58, 2145; S. Taechachoonhakit, P. Ratananukul, *Chem. Lett.* **1986**, 911; K. A. Nelson, E. A. Mash, *J. Org. Chem.* **1986**, 51, 2721; A. Abad, M. Arno, J. R. Pedro, E. Seoane, *An. Quim., Ser. C* **1987**, 83, 263 (CA: **1987**, 109, 110 145 c); S. Bienz, M. Hesse, *Helv. Chim. Acta* **1987**, 70, 2146; S. Ohta, S. Hayakawa, Y. Tamai, T. Yuasa, M. Okamoto, *Heterocycles* **1987**, 26, 1401; D. Terunuma, M. Motegi, M. Tsuda, T. Sawada, H. Nozawa, H. Nohira, *J. Org. Chem.* **1987**, 52, 1630; R. W. Thies, K. P. Darawala, *ibid.* **1987**, 52, 3798; H. Suginome, S. Yamada, *Tetrahedron Lett.* **1987**, 28, 3963; S. Bienz, M. Hesse, *Helv. Chim. Acta* **1988**, 71, 1704; Y. Wang, G. Wang, Y. Liu, *Yiyao Gongye* **1988**, 19, 291 (CA: **1988**, 110, 38 806 v); N. A. Porter, B. Lacher, V. H. T. Chang, D. R. Magnin, *J. Am. Chem. Soc.* **1989**, 111, 8309; J. P. Deprés, B. Navarro, A. E. Greene, *Tetrahedron* **1989**, 45, 2989; Z. F. Xie, K. Sakai, *J. Org. Chem.* **1990**, 55, 820.
- [3] a) G. Ohloff, J. Becker, K. H. Schulte-Elte, *Helv. Chim. Acta* **1967**, 50, 705; J. Becker, K. H. Schulte-Elte, G. Ohloff, to *Firmenich SA*, 1971, Swiss Pat. 513 791; 1973, US Pat. 3 778 483 (CA: **1972**, 76, 99 222 c); b) A. Eschenmoser, D. Felix, G. Ohloff, *Helv. Chim. Acta* **1967**, 50, 708; D. Felix, J. Schreiber, G. Ohloff, A. Eschenmoser, *ibid.* **1971**, 54, 2896; c) C. Fehr, G. Ohloff, G. Büchi, *ibid.* **1979**, 62, 2655; d) C. Fehr, *ibid.* **1983**, 66, 2512; *ibid.* **1983**, 66, 2519; e) L. L. Limacher, F. D. Delay, N. Bédert, P. Tissot, *ibid.* **1989**, 72, 1383.
- [4] R. Dubs, R. Stüssi, *J. Chem. Soc., Chem. Commun.* **1976**, 1021.
- [5] K. N. Gurudutt, B. Ravindranath, *Synthesis* **1983**, 888.
- [6] M. N. Rerick, in 'Reduction', Ed. R. L. Augustine, Marcel Dekker, New York, 1968, p. 1–94.
- [7] J. E. Baldwin, R. C. Thomas, L. I. Kruse, L. Silberman, *J. Org. Chem.* **1977**, 42, 3846.
- [8] Reviews: a) H. M. R. Hoffmann, *Angew. Chem. Int. Ed.* **1969**, 8, 556; b) W. Oppolzer, V. Sniekus, *ibid.* **1978**, 17, 476; c) B. B. Snider, *Acc. Chem. Res.* **1980**, 13, 426.
- [9] A. C. Jackson, B. E. Goldman, B. B. Snider, *J. Org. Chem.* **1984**, 49, 3988.
- [10] E. Demole, P. Enggist, C. Borer, *Helv. Chim. Acta* **1971**, 54, 1845.
- [11] R. L. Snowden, R. Brauchli, P. Sonnay, *Helv. Chim. Acta* **1989**, 72, 570.
- [12] M. Karpf, A. S. Dreiding, *Helv. Chim. Acta* **1975**, 58, 2409.
- [13] R. L. Snowden, S. M. Linder, B. L. Muller, K. H. Schulte-Elte, *Helv. Chim. Acta* **1987**, 70, 1858.
- [14] M. Baumann, to *BASF AG*, 1980, Germ. Pat. 2916 418 (CA: **1981**, 94, 156 417 t).
- [15] A. Fischli, Q. Branca, J. Daly, *Helv. Chim. Acta* **1976**, 59, 2443.
- [16] *Nippon Mining Co. Ltd.*, 1984, Jap. Pat. 59 157 047 (CA: **1985**, 102, 78 437 s).