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

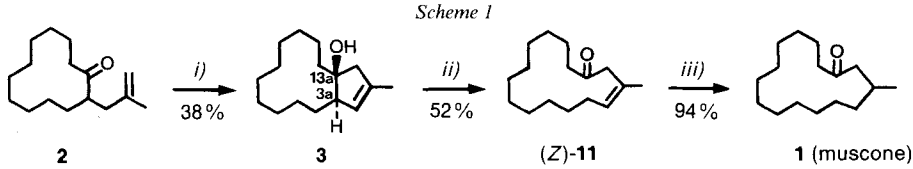
(26.III.90)

(±)-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 years[1]). 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 Me_2AlCl (1.3 mol-equiv.)[2]) in 1,2-dichloroethane/hexane at 70° during 8 h followed by an aqueous basic workup.

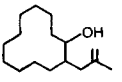
Scheme 1



i) Me_2AlCl, 1,2-dichloroethane/hexane, 70°, then aq. NaOH soln. *ii*) KH, HMPA, 120°, then aq. NH_4Cl soln. *iii*) H_2, 5% Pd/C, cyclohexane.

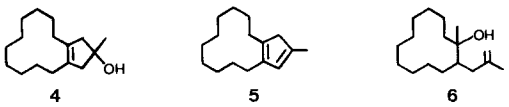
[1]) For a review of muscone syntheses prior to 1979–1980, see [1]; for more recent syntheses, see [2] [3d, e].

[2]) Other alkylaluminium halides gave inferior results. For example, Et_2AlCl 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($CDCl_3$): 3450 (br.), 2910, 2860, 1450, 996, 892. ^{1}H-NMR (+D_2O): 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).



i

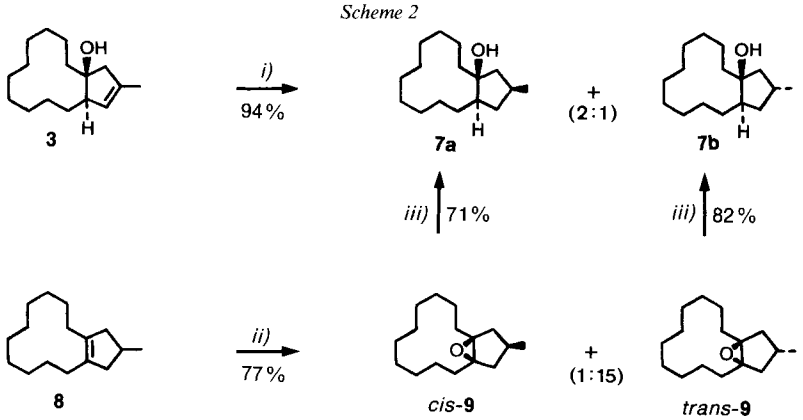
Minor Isomer: white crystals. M.p. 89–90°. R_f (cyclohexane/AcOEt 9:1) 0.32. IR ($CHCl_3$): 3420 (br.), 2940, 2850, 1450, 896. ^{1}H-NMR (+D_2O): 1.20–1.60 (19 H); 1.74 (*s*, 3 H); 1.76 (*m*, 2 H); 1.93 (*dd*, *J* = 14.5, 10, 1 H); 2.29 (*dd*, *J* = 14.5, 4.5, 1 H); 3.80 (*m*, 1 H); 4.76 (*s*, 1 H); 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, $MeAlCl_2$ or $EtAlCl_2$, in CH_2Cl_2 at r.t., produced complex mixtures containing only small amounts ($\leq$ 5%) of **3**.



4 5 6

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 derivatives[6]) 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 $LiAlH_4/AlCl_3$ [5] (*cf. Scheme 2*). As it is established that hydride reduction of an epoxide favours nucle-

Scheme 2



i) H_2, 5% $Pd/BaSO_4$, MeOH. *ii*) mcpba, CH_2Cl_2, aq. $NaHCO_3$ soln. *iii*) $LiAlH_4$, $AlCl_3$, THF.

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

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'**,

---

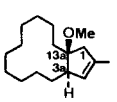
[3]) A possible origin of **5** is from dehydration of either **3** or **4**.

[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.

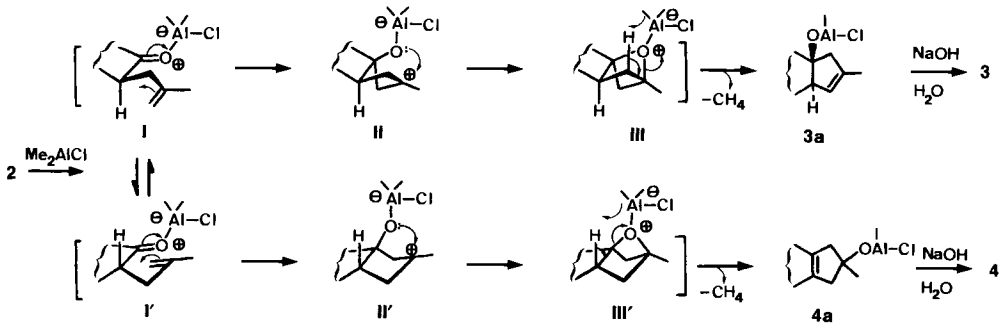
[7]) Further evidence for the *trans*-fused bicyclic structure of **3** was obtained by ^{1}H-NMR nuclear *Overhauser* effect (NOE) experiments on the methyl ether **10** derived from **3** (*cf. Exper. Part*). Irradiation of the MeO group resulted in an enhancement of H(β)–C(1) and no enhancement of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



10

[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 CH_4. 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-cleavage[10]) of the C(3a)–C(13a) bond and formation of the desired C_{15} macrocyclic system[11]). 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*).

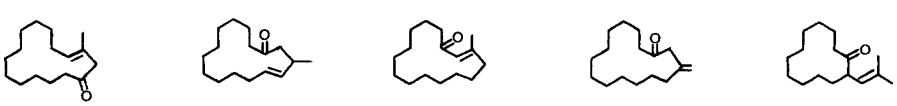
---

[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.

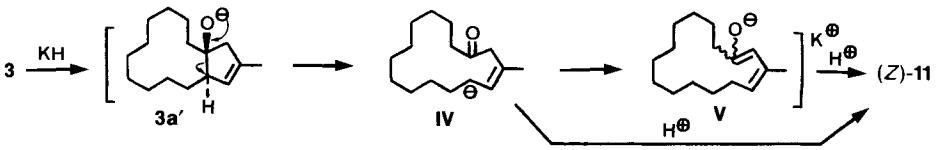
[11]) The possibility of converting **3** to **13** *via* a thermal *retro*-ene process was also briefly investigated. Thus, a solution of **3** in xylene was passed through a heated glass column using N_2 as the carrier gas; at 450° **3** was recovered unchanged, and, at 600°, a complex product mixture was formed in which **13** was not detected by ^{1}H-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 ^{1}H-NMR spectroscopy (*cf. Exper. Part*) and originate by either protonation of **IV**/V or isomerisation of (*Z*)-**11** during the workup.



(*E*)-**11** (*E*)-**12** (*E*)-**13** **14** **15**

Scheme 4



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

Experimental Part

General. See [13].

(3aRS,13aSR)-3a,4,5,6,7,8,9,10,11,12,13,13a-Dodecahydro-2-methyl-1H-cyclopentacyclododecen-13a-ol (**3**). A soln. of Me_2AlCl (1M 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 N_2. The soln. was then heated at reflux (70°) during 8 h, cooled to r.t., poured into cold 1N aq. NaOH soln. (300 ml) with stirring, and extracted (Et_2O). The combined org. phase was washed with sat. aq. NaCl soln., dried (Na_2SO_4), and evaporated to afforded 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 ($CHCl_3$): 3600, 3420 (br.), 2910, 2850, 1466, 1440, 1350, 990, 910, 862, 840. ^{1}H-NMR (+D_2O): 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). ^{13}C-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-1H-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 ($CHCl_3$): 3600, 3450 (br.), 2910, 2850, 1442, 1350, 1220, 940, 800. ^{1}H-NMR (+D_2O): 1.12–1.52 (16 H); 1.40 (*s*, 3 H); 2.12 (*m*, 4 H); 2.38 (*AB*, *J* = 15, 4 H). ^{13}C-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-1H-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 ($CHCl_3$): 2940, 2860, 1470, 1446, 1380, 890. ^{1}H-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). ^{13}C-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 ($CHCl_3$): 3630, 3460 (br.), 2950, 2890, 1460, 1432, 1360, 880. ^{1}H-NMR (+D_2O): 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). ^{13}C-NMR: 146.2 (*s*); 111.1 (*t*); 76.0 (*s*); 40.0 (*t*); 39.3 (*t*); 38.4 (*d*); 26.9 (*t*); 26.7 (*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).

(2RS,3aSR,13aRS)- and (2RS,3aRS,13aSR)-Tetradecahydro-2-methyl-1H-cyclopentacyclododecen-3a-ol (**7a** and **7b**). A soln. of **3** (0.2 g, 0.85 mmol) in MeOH (5 ml) containing 5% Pd/$BaSO_4$ (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. ^{1}H-NMR (+D_2O): 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). ^{13}C-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. ^{1}H-NMR (+D_2O): 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).

^{13}C-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-Epoxytetradecahydro-2-methyl-1*H-*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-1*H-*cyclopentacyclododecene* (**8**) [2a] (3.0 g, 0.014 mol) and $NaHCO_3$ (2.2 g, 0.026 mol) in CH_2Cl_2 (130 ml)/H_2O (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 (CH_2Cl_2). The combined org. phase was successively washed with 1N aq. NaOH, 10% aq. Na_2SO_3, 10% aq. NaCl soln., dried (Na_2SO_4), 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/Et_2O 1:1). R_f (cyclohexane/AcOEt 9:1) 0.56. IR ($CHCl_3$): 3000, 2940, 2860, 1464, 1442, 1430, 1342, 852, 699. ^{1}H-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 ($CHCl_3$): 2940, 1470, 1442, 1370, 1310, 858. ^{1}H-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. $AlCl_3$ (10 mg, 0.07 mmol) and $LiAlH_4$ (8 mg, 0.21 mmol) in THF (2 ml) at r.t. under N_2. The mixture was refluxed during 6 h, cooled to 0° and H_2O (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. $AlCl_3$ (0.13 g, 1 mmol), $LiAlH_4$ (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*).

*(3a*RS,*13a*SR*)-3a,4,5,6,7,8,9,10,11,12,13,13a-Dodecahydro-13a-methoxy-2-methyl-1*H-*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 N_2. 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 H_2O, and extracted (Et_2O). The combined org. phase was washed with sat. aq. NaCl soln., dried (Na_2SO_4), 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 ($CHCl_3$): 2940, 2850, 1464, 1440, 1072, 812. ^{1}H-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). ^{13}C-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 N_2. This mixture was stirred for 4 h at r.t., heated at 120° during 2 h, cooled (10°), poured cautiously into cold sat. aq. NH_4Cl soln., (200 ml) and extracted (Et_2O). The combined org. phase was washed with sat. aq. NaCl soln., dried (Na_2SO_4), 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 ($CHCl_3$): 2920, 2850, 1716, 1440, 1350, 970, 904. ^{1}H-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). ^{13}C-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 ^{1}H-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. ^{1}H-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 (2 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}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. Hacini, 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,* 208417q); 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. Ratananukel, *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,* 110145c); 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,* 38806v); 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. 513791; 1973, US Pat. 3778483 (*CA:* **1972,** *76,* 99222c); 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. 2916418 (*CA:* **1981,** *94,* 156417t).

[15] A. Fischli, Q. Branca, J. Daly, *Helv. Chim. Acta* **1976,** *59,* 2443.

[16] *Nippon Mining Co. Ltd.,* 1984, Jap. Pat. 59157047 (*CA:* **1985,** *102,* 78437s).