# 250. A Novel Three-Carbon Ring Expansion Sequence

## Synthesis of *Exaltone*® and (±)-Muscone [1])

by **Charles Fehr**

*Firmenich SA*, Research Laboratories, CH-1211 Geneva 8

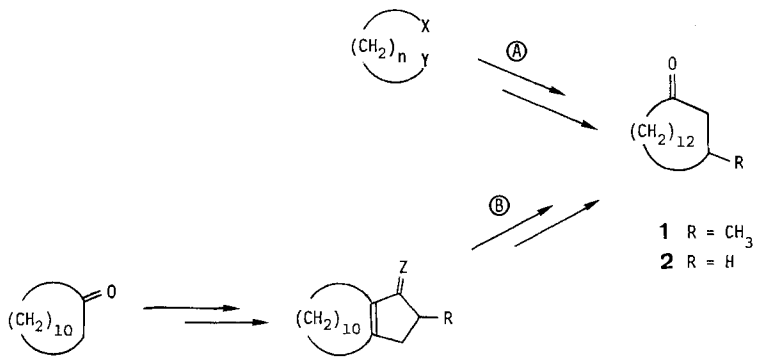
(23. VIII. 83)

*Summary*

Intramolecular *Grignard*-type reaction of the bromo lactones **3** and **8** affords the macrocycles **10, 11, 12** and **13, 14, 15,** respectively. More efficiently, **10** and **13** are obtained by intramolecular nucleophilic attack of the carbanions derived from the sulfonyl lactones **20** and **22** and *in situ* reduction of the intermediate sulfones **21** and **23.** The macrocylic hydroxy ketones **10** and **13** are converted into *Exaltone*® (**2**) and muscone (**1**), respectively.

Macrocyclic ketones such as muscone (**1**) and *Exaltone*® (**2**) have been obtained by two main synthetic approaches: cyclization of difunctionalized C-chain using high-dilution techniques (Ⓐ, *Scheme 1*) and cleavage of a bicyclic system (Ⓑ) [2]:

*Scheme 1*

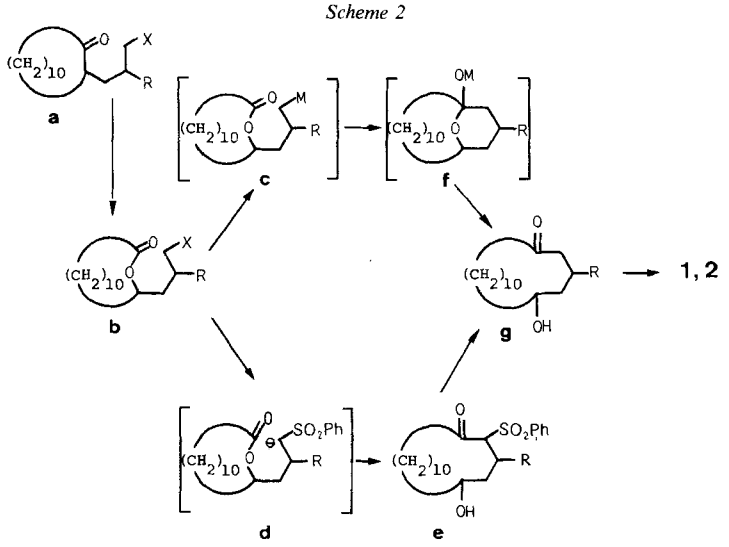



Approach Ⓑ, developed in *Firmenich* research laboratories [3], involves $C_3$-ring expansion sequences using cyclododecanone as the inexpensive starting material. Our strategy described herein uses an extension of this concept. Thus, regioselective *Baeyer-Villiger* reaction of an appropriately substituted cyclododecanone **a** affords a lactone **b**. Subse-

[1]) This work was presented at the Swiss Chemical Society Meeting in Berne, October 16, 1981. For a preliminary account, see [1].

quent intramolecular nucleophilic attack on the lactone carbonyl group by either an organometallic species **c** or a stabilized carbanion **d** allows 15-membered ring closure *via* a six-membered ring transition state, thus avoiding the use of high-dilution techniques [2] *(Scheme 2)*.

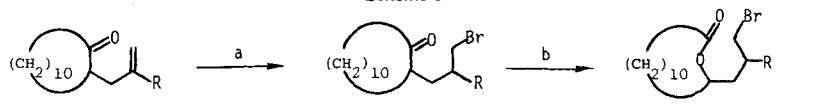
*Scheme 2*




To our knowledge the intramolecular *Grignard*-type reaction of a halo ester has not been reported [3], possibly because the resulting ketone may react further with a second substrate molecule. In our case we hoped that the pyranoid intermediate **f** would constitute a protected form of hydroxy ketone **g**.

The bromo lactones **3** and **8** [4] were readily obtained from 2-allylcyclododecanone (**4**) [6] and 2-(2-methylallyl)cyclododecanone (**5**) [4a], respectively, by radical-initiated addition of HBr [7] and subsequent *Baeyer-Villiger* reaction [8]. *(Scheme 3)*.

*Scheme 3*




**4** R = H
**5** R = $CH_3$

**6** R = H (75%)
**7** R = $CH_3$ (54%)

**3** R = H (80%)
**8** R = $CH_3$ (78%)

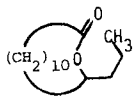
Reagents: a) HBr, *hv*, petroleum ether (PE)/20°; b) $CH_3CO_3H$ (7 equiv.), $BF_3 \cdot Et_2O$ (0.64 equiv.), $Cl_3CCH_3$/50°/5 days.

[2] A synthesis of muscopyridine using a *Beckmann* rearrangement is somewhat related to our approach [4a]. After completion of our work [1], this rearrangement was utilized in a synthesis of muscone [4b].

[3] For an unsuccessful attempt, see [5].

[4] Mixture of diastereomers.

The reaction of the lactone **3** (containing 1,2-dibromoethane as initiator) with Mg yielded 12-pentadecanolide (**9**) (39%) and the two desired cyclized products **10** (12%)



**9**

and **11** (10%) *(Scheme 4, Table)*. When the same reaction was performed in the presence of $BF_3$-etherate, only the reduced lactone **9** was obtained (75%), presumably *via* the intermediate alkyl radical [9] [10]. In the hope of favoring the cyclization, we examined metals with a higher electron potential than Mg [10]. Na in THF, although reacting more sluggishly with **3**, gave more cyclization than reduction; with Li in THF, only cyclization was observed *(Table)* [5]).

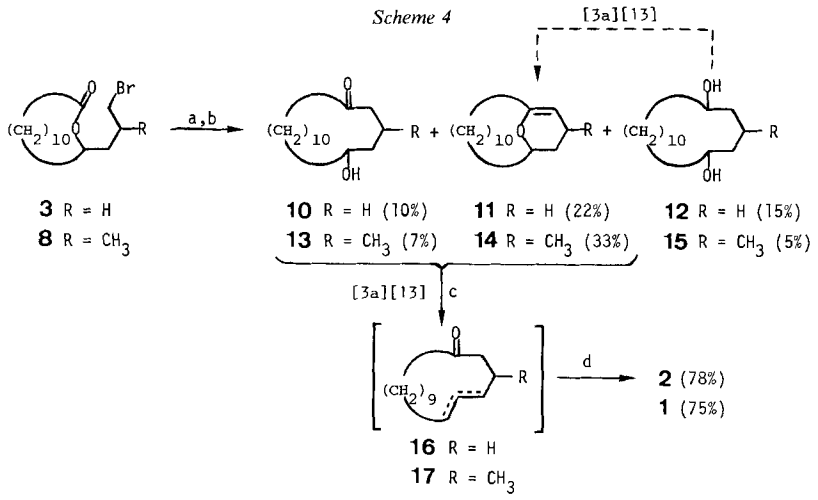
Table. *Cyclization of* **3**

| Reaction conditions[a]) | Yields of distilled products | | | | |
|---|---|---|---|---|---|
| | **10** | **11** | **12** | **9** | **3** |
| Mg/Br Br/$BF_3 \cdot Et_2O$/THF | – | – | – | 75% | 9% |
| Mg/Br Br/THF | 12% | 10% | – | 39% | – |
| Na/Br Br/THF | 2% | 21% | 2% | 6% | 10% |
| Li(1% Na)/Br Br/THF[b]) | 10% | 22% | 15% | – | 3% |

[a]) Other reaction conditions (Li/$Et_2O$; naphthyl-Li/$NH_3$ (liq.); *Rieke*-Mg [11]; *Rieke*-Zn [12]) gave predominantly decomposed or reduced products.

[b]) Li-dispersion and Li-wire gave similar results.

*Scheme 4*



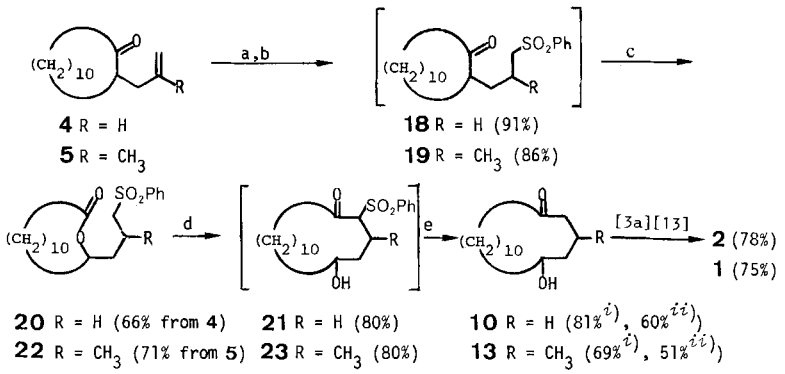

Reagents: a) Li, $Br(CH_2)_2Br$, THF/30°; b) dist. 170°/0.02 Torr; c) $H_3PO_4$, toluene/reflux/2 h; d) $H_2$/Pd–C (10%), EtOH.

[5]) Intermolecular *Barbier* reactions using an ester with an organic halide and Li in THF afford a tertiary alcohol [10]. For a review on *Barbier* reactions, see [14].

The cyclization products **10, 11** and **12** are known precursors for the synthesis of *Exaltone*® (**2**) [3a] [13]; accordingly our mixture of **10** and **11** was converted to **2** (78%). The Li-promoted cyclization was also applied to lactone **8** *(Scheme 4)*. The cyclized products **13, 14** and **15** were obtained in 45% yield, and **13** and **14** (40%) were transformed into (±)-muscone (**1**) (75%) [3a] [13].

We next examined the cyclization of the anion derived from sulfone **20** [16] and the subsequent reductive removal of the sulfonyl group [15b] [16] *(Scheme 5)*.

*Scheme 5*




Reagents: a) PhSH (1.2 equiv.), AIBN/80°/10–24 h; b) $CH_3CO_3H$ (2 equiv.), $Cl_3CCH_3$/30°; c) $CH_3CO_3H$ (6 equiv.); $BF_3 \cdot Et_2O$ (0.64 equiv.), $Cl_3CCH_3$/50°/5–10 days; d) LDA (2 equiv.), THF/–40°/5 min or *t*-BuOK (2 equiv.), toluene/20°/5 min or NaH (2 equiv.), DMSO/20°/5 min or NaH (2 equiv.), $H_2N(CH_2)_2$/20°/5 min or $NaNH_2$ (3 equiv.), $NH_3$, THF/–33°/20 min; e) Al (10 equiv.) (Hg), THF, $H_2O$/20°/15 h or Li (3 equiv.), $H_2N(CH_2)_2NH_2$, THF/20°/30 min or Na (3 equiv.), $NH_3$, THF/–33°/30 min[i]; d) + e) in one operation: $NaNH_2$ (3 equiv.), $NH_3$, THF/–33°/20 min, then Na (3 equiv.)/–33°/30 min[ii].

Radical-initiated addition of thiophenol to 2-allylcyclododecanone (**4**) furnished a thioether which, without purification, was oxidized with excess peracetic acid to the sulfone **18.** A regioselective *Baeyer-Villiger* reaction[6]) in the presence of $BF_3$-etherate at 50° for 5–10 days afforded the sulfonyl lactone **20.** Under basic conditions (see *Scheme 5*) the latter underwent ring closure to the sulfonyl ketone **21** (80%)[7]). For structural confirmation **21** was selectively reduced to the hydroxy ketone **10** with Al(Hg) [16a]. Compound **20** could also be converted to **10** in a one-pot procedure, using *N*-sodioethylenediamine in ethylenediamine for the cyclization, and Li for the reductive removal of the sulfone group [16b]. The most convenient method for preparing the hydroxy ketone **10** (60%) involved treatment of **20** with freshly prepared $NaNH_2$ in liquid $NH_3$/THF, and immediate reduction with Na, thus representing a preparatively valuable alternative to the direct bromo lactone → hydroxy ketone transformation *(vide infra)*. Subsequent dehydration and hydrogenation afforded *Exaltone*® (**2**) (78%) [3a] [13].

The same procedure was applied to the sulfonyl lactone **22**, obtained from 2-(2-methylallyl)cyclododecanone (**5**) (71%) *(Scheme 5)*. This furnished the macrocyclic

[6]) Regioselectivity ≥ 90%.

[7]) For an analogous intramolecular condensation of the sulfonyl ketones **18** and **19** see [17].

hydroxy ketone **13** (51%) which was dehydrated and hydrogenated to (±)-muscone (**1**) (75%) [3a] [13].

## Experimental Part

(with the valuable collaboration of *P. Wetter*)

*General Remarks.* Melting points (m. p.) are uncorrected. TLC was performed using *F 254* plates *(Merck)*; the spots were revealed using EtOH/anisaldehyde/$H_2SO_4$ 18 : 1 : 1. GC was carried out on a *Carlo Erba Fractovap 2350*. IR: *Perkin-Elmer A 21* or *Perkin Elmer 157 G* spectrometer (films or $CDCl_3$-solutions); band positions in $cm^{-1}$. $^1$H-NMR: *Varian A 60* (60 MHz, $CDCl_3$); chemical shifts in δ are reported in ppm relative to TMS as internal standard. MS: *Atlas CH$_4$* or *Varian MAT 112* (70 eV). Abbreviations: PE = petroleum ether (b. p. 80–100°), AIBN = α,α'-azoisobutyronitrile, LDA = lithium diisopropylamide.

*2-(3-Bromopropyl)cyclododecanone* (**6**). Dry HBr was bubbled through an irradiated (high-pressure Hg-lamp *(Philips/125 W)*) solution of 2-allylcyclododecanone (**4**) [6] (37.5 g, 0.169 mol) in PE (200 ml) in a *Pyrex* vessel at 20° for 20 min. $K_2CO_3$ (1 g) was added, the solvent evaporated and the residue (52 g) distilled (160–175°/0.1 Torr) to give crystalline **6** (40.2 g, 95% pure, 75%), m. p. 40°. IR (neat): 2950, 1705, 1470, 1255. $^1$H-NMR: 1.00–2.00 (*m*, 22 H); 2.35–2.70 (*m*, 3 H); 3.36 (*t*, $J \approx 6$, 2 H). MS: 304 and 302 (8, $M^+$), 223 (31), 180 (8), 178 (8), 167 (8), 139 (9), 111 (12), 98 (32), 83 (40), 69 (56), 55 (100), 41 (70).

*2-(3-Bromo-2-methylpropyl)cyclodecanone* (**7**)[4]). A solution of 2-(methylallyl)cyclododecanone (**5**) [4a] (10.0 g, 42.4 mmol) in PE (300 ml) was irradiated in the presence of HBr as above. Bulb-to-bulb distillation (160–180°/0.1 Torr) afforded **7** (24.5 g, 65% pure, 54%). A product of higher purity was obtained by redistillation[8]) (80%) or CC (silica gel) with cyclohexane (100%). IR (neat): 2920, 1705, 1470, 1430, 1380, 1250. $^1$H-NMR: 1.02 (*d*, $J \approx 6$, 3 H); 1.10–2.10 (*m*, 21 H); 2.40–2.80 (*m*, 3 H); 3.34 (*d*, $J \approx 5$, 2 H).

*15-Bromo-12-pentadecanolide* (**3**). $CH_3CO_3H$ (40%, 104 g, 0.55 mol) and $BF_3 \cdot Et_2O$ (9.20 ml, 10.4 g, 0.073 mol) were added to a stirred solution of **6** (36.4 g, 95% pure, 0.114 mol) in $Cl_3CCH_3$ (360 ml). The mixture was stirred at 50° for 10 days. At 2-day intervals additional 40% $CH_3CO_3H$ was added (4 × 10.4 g, 0.22 mol). The mixture was cooled to 20°, poured onto ice and neutralized to pH 8 with 10% aq. NaOH. The separated org. layer was washed with 10% aq. $NaHSO_3$ and with $H_2O$, dried ($Na_2SO_4$) and evaporated. Filtration of the crude product (42 g) through active charcoal and silica gel with cyclohexane afforded **3** (32.2 g, 90% pure, 80%). Under the same conditions, but using a total amount of 208 g of 40% $CH_3CO_3H$ (1.10 mol), the reaction was complete after 5 days. IR (neat): 2930, 1730, 1460, 1445, 1255, 1050. $^1$H-NMR: 1.10–2.20 (*m*, 22 H); 2.20–2.60 (*m*, 2 H); 340 (*t*, $J \approx 6$, 2 H); 4.94 (*m*, 1 H). MS: 300 and 302 (1, $M^+ - 18$), 238 (22), 197 (27), 168 (23), 125 (16), 111 (25), 98 (34), 83 (36), 69 (57), 55 (99), 43 (100).

*14-Methyl-15-bromo-12-pentadecanolide* (**8**)[4]). Using the same procedure as above, **7** (10.0 g, 80% pure, 25.2 mmol) gave **8** (7.2 g, 90% pure, 78%). IR (neat): 2950, 1730, 1460, 1250, 1060. $^1$H-NMR: 1.08 (2 *d*, $J \approx 6$, 3 H); 1.05–2.10 (*m*, 21 H); 2.10–2.60 (*m*, 2 H); 3.40 (*m*, 2 H); 4.98 (*m*, 1 H).

*12-Pentadecanolide* (**9**). A solution of **3** (710 mg, 90% pure, 2.0 mmol), $Br(CH_2)_2Br$ (376 mg, 2.0 mmol) and $BF_3 \cdot Et_2O$ (284 mg, 2.0 mmol) in THF (1.5 ml) was added at 20° under Ar to a vigorously stirred suspension of Mg (140 mg, 5.8 mg-atom) in THF (0.5 ml). After 2 min the temp. rose to 66° and the reaction was complete after 10 min. Hydrolysis with sat. aq. $NH_4Cl$-solution, extraction ($Et_2O$) and bulb-to-bulb distillation at 120° (oven)/0.05 Torr afforded **9** (360 mg, 75%) as a colorless oil[9]). IR (neat): 2940, 1725, 1460, 1245. $^1$H-NMR: 0.90 (*m*, 3 H); 1.10–2.05 (*m*, 22 H); 2.35 (*m*, 2 H); 4.96 (*m*, 1 H). MS: 222 (15 $M^+ - 18$), 168 (29), 125 (28), 111 (39), 98 (50), 83 (47), 69 (63), 55 (100), 41 (92).

*Reaction of 15-Bromo-12-pentadecanolide* (**3**) *with Li. Preparation of* Exaltone® (**2**) via *Cyclopentadecenones* (**16**). A solution of **3** (710 mg, 90% pure, 2.0 mmol) and $Br(CH_2)_2Br$ (188 mg, 1.0 mmol) in THF (1.5 ml) was added at 20° under Ar to a vigorously stirred suspension of small Li-chips (containing 1% Na, 80 mg, 11.4 mmol) in THF (0.5 ml). The reaction was initiated by heating at 66° for 10 min. Hydrolysis, extraction and bulb-to-bulb distillation (160°/0.05 torr) afforded a mixture (225 mg, ≈ 50%) of **10**[10]) (10% by GC), **11**[10]) (22% by GC), **12**[10]) (15% by GC) and recovered **3** (3% by GC). Repetition of the above procedure (from 1.42 g of **3**, 90% pure, 4.0 mmol) followed by a fractional distillation at 140°/0.05 Torr gave **11** (241 mg, 95% pure, 26%) which was heated in toluene (10 ml) containing $H_3PO_4$ (85%, 1 drop) at reflux for 2 h using a *Dean Stark* apparatus. Extractive isolation ($ET_2O$/sat. aq. $NaHCO_3$-solution) afforded **16** (presumably as a mixture of isomers[10]),

[8]) The by-products were the result of *Markownikoff*-addition and decomposition of **7** during the distillation.

[9]) Lactone **9** was also prepared from **4** (80%) a) $H_2$/Pd–C; b) $CH_3CO_3H/BF_3 \cdot Et_2O/Cl_3CCH_3$/50°/5 days.

[10]) Identical to authentic samples [3a] [13].

201 mg, 86%), which was dissolved in EtOH (10 ml) and hydrogenated ($H_2$/Pd–C (10%), 50 mg) to give after filtration *(Celite)*, evaporation and bulb-to-bulb distillation (120°/0.05 Torr) **2** (190 mg, 91%), identical to an authentic sample [3c].

*Reaction of* **8** *with Li. Preparation of (±)-Muscone* (**1**). A solution of **8** (1.35 g, 90% pure, 3.66 mmol) and $Br(CH_2)_2Br$ (250 mg, 1.33 mmol) in THF (2 ml) was added at 20° under Ar to a vigorously stirred suspension of small Li-chips (containing 1% Na, 90 mg, 12.8 mmol) in THF (0.5 ml). After a few minutes the temp. rose to 40° and the reaction was complete within 20 min. Hydrolysis, extraction and bulb-to-bulb distillation (160°/0.05 Torr) afforded a mixture (405 mg, ≈45%) of **13**[10]) (7% by GC), **14**[10]) (33% by GC) and **15**[10]) (5% by GC). Using the same procedure as for **2**, the mixture (*ca.* 360 mg of **13** + **14**, ≈ 1.5 mmol) was converted to **1** (268 mg, 75%), identical to an authentic sample [3c].

*2-[3-(Phenylsulfonyl)propyl]cyclododecanone* (**18**). A mixture of **4** (222.0 g, 1.0 mol), thiophenol (132.0 g (122 ml), 1.20 mol) and AIBN (3.0 g, 0.0183 mol) was heated for 10 h at 80°, while additional AIBN (6.0 g, 0.0366 mol) was added in small portions. A stirred and cooled (0°) solution of the resulting viscous yellow-red oil in $Cl_3CCH_3$ was treated with 40% $CH_3CO_3H$ (433 g (376 ml), 2.60 mol) at such a rate to maintain the temp. between 25 and 30°[11]). Aq. 10% $Na_2SO_3$-solution (until negative peroxide test) and aq. 10% NaOH (until pH 8–9) were added under ice cooling. Extraction ($CH_2Cl_2$) of the mixture, washing of the org. phases with $H_2O$ and brine, drying ($Na_2SO_4$) and removal of solvent gave a crystalline product which was recrystallized ($CH_2Cl_2$/$Et_2O$/PE) to afford **18** (332 g, 91%). (Distillation of the mother liquors (160° (bath)/0.02 Torr) gave 90% pure unreacted **4** (15.1 g, 6%)). M.p. 97–102°. IR ($CDCl_3$): 2950, 1700, 1465, 1445, 1300, 1145, 1080, 790. $^1$H-NMR: 1.00–2.00 (*m*, 22 H [max. 1.26]); 2.30–2.75 (*m*, 3 H); 2.90–3.25 (*m*, 2 H); 7.50–8.02 (*m*, 5 H). MS: 366 (3), 364 (30, $M^+$), 254 (8), 240 (15), 223 (12), 143 (32), 98 (41), 55 (100), 41 (59).

*2-[2-Methyl-3-(phenylsulfonyl)propyl]cyclododecanone* (**19**)[4]). Compound **5** (236.0 g, 1.0 mol) was added portionwise, during 8 h, to a mixture of thiophenol (132.0 g (122 ml), 1.20 mol) and AIBN (3.0 g, 0.0183 mol) at 80°. The mixture was heated for a further 16 h at 80°, while additional AIBN (10.0 g, 0.061 mol) was added in small portions, and was then treated in the same manner as described for **18**, to afford recrystallized **19** (325.0 g, 86%) and unreacted **5** (21.4 g, 90% pure, 8%). M.p. 98–103°. IR ($CDCl_3$): 2950, 1705, 1470, 1450, 1305, 1145, 1085. $^1$H-NMR: 0.90–2.20 (*m*, 24 H [max. 1.27]); 2.30–2.75 (*m*, 3 H); 3.00 (*d*, $J \approx 6$, 2 H); 7.50–8.02 (*m*, 5 H). MS: 380 (2), 378 (14, $M^+$), 267 (5), 255 (20), 237 (22), 143 (15), 98 (24), 95 (32), 83 (52), 81 (49), 77 (50), 69 (36), 67 (32), 55 (100), 43 (41), 41 (83).

*15-Phenylsulfonyl-12-pentadecanolide* (**20**). Reaction of **4** (22.0 g, 100 mmol) with thiophenol (13.2 g (12.2 ml), 120 mmol) and AIBN (0.90 g, 5.5 mmol) and subsequent concentration as above gave crude 2-[3-(phenylthio)-propyl]cyclododecanone (33.5 g, max. 90 mmol) which was dissolved in $Cl_3CCH_3$ (300 ml) and treated under ice-cooling and stirring with 40% $CH_3CO_3H$ (90.4 g (80 ml), 0.475 mol) at such a rate to maintain the reaction temp. between 30 and 40°. The resulting mixture containing **18** was treated with $BF_3 \cdot Et_2O$ (7.5 g (6.7 ml), 53.0 mmol) and stirred at 50° for 10 days. At 2-day intervals, additional peracetic acid (4 × 11.3 g (10 ml), 0.238 mol) was added. The mixture was cooled to 20°, poured on to ice and neutralized to pH 8 with aq. 10% NaOH. The separated org. layers were washed with aq. 10% $NaHSO_3$ and with $H_2O$, dried ($Na_2SO_4$) and evaporated. Filtration of the crude product (43 g) through silica gel (120 g) with PE/AcOEt 1:1 afforded **20** (27.7 g, 90% pure, 66%). IR ($CDCl_3$): 2920, 1720, 1450, 1300, 1240, 1140. $^1$H-NMR: *ca.* 1.10–2.00 (*m*, 22 H); 2.31 (*m*, 2 H); 3.15 (*m*, 2 H); 4.92 (*m*, 1 H); 7.50–8.02 (*m*, 5 H).

*14-Methyl-15-phenylsulfonyl-12-pentadecanolide* (**22**)[4]). Using the same procedure as for **20**, addition of thiophenol (8.7 g (8.04 ml), 79.0 mmol) to **5** (15.6 g, 66.0 mmol) in the presence of AIBN (600 mg, 3.66 mmol) at 80° for 24 h afforded crude 2-[2-methyl-3-(phenylthio)propyl]cyclododecanone (20.4 g, 59.0 mmol) which was directly converted to **22** (20.1 g, 90% pure, 78%). IR (neat): 2930, 1720, 1445, 1300, 1245, 1085. $^1$H-NMR: 1.05–1.90 (*m*, 24 H); 2.25 (*m*, 2 H); 2.80–3.40 (*m*, 2 H); 4.96 (*m*, 1 H); 7.50–8.03 (*m*, 5 H). MS: 394 (0.2 $M^+$), 376 (6), 366 (6), 253 (15), 168 (24), 143 (15), 125 (18), 111 (26), 98 (55), 83 (42), 69 (61), 55 (93), 43 (100).

*5-Hydroxycyclopentadecanone* (**10**) *and its Conversion to* Exaltone® (= *Cyclopentadecanone)* (**2**). A solution of **20** (6.30 g, 90% pure, 14.9 mmol) in THF (100 ml) was added dropwise (during 20 min) to a stirred suspension of $NaNH_2$ (46.8 mmol) in liq. $NH_3$ [18] (600 ml). The yellow-red mixture was stirred for 20 min and treated with Na-chips (1.08 g, 46.8 mmol). After 30 min, a dark blue coloration indicated the end of the reduction. The suspension was quenched by dropwise addition of aq. sat. NaCl-solution (200 ml). Extraction (AcOEt), washing of the org. layer with aq. sat. NaCl-solution, drying ($Na_2SO_4$) and evaporation afforded crude **10** (4.0 g), which was chromatographed (silica gel) with cyclohexane/AcOEt 4:1 to give pure **10** (2.15 g, 60%) [3a] [13].

---

[11]) Alternative procedure: prior to the treatment with $CH_3CO_3H$ (40%, 417 g (365 ml), 2.50 mol), the mixture was concentrated to remove excess thiophenol (50° (bath)/8 Torr) and unreacted **4** (155°/0.2 Torr).

For characterization the intermediate **21** was isolated (80%)[12]) and crystallized from $Et_2O$, m.p.: 153–136°. IR ($CDCl_3$) 3630, 2960, 1720, 1450, 1310, 1150, 1080. $^1$H-NMR: 1.10–2.50 (*m*, 23 H); 2.77 (*t*, $J \approx 6$, 2 H); 3.40 (*m*, 1 H); 4.22 (*m*, 1 H); 7.45–7.94 (*m*, 5 H). MS: 380 (1, $M^+$), 362 (16), 239 (33), 221 (30), 169 (23), 141 (41), 125 (27), 109 (20), 95 (39), 77 (100), 55 (96), 41 (88). Reduction of purified **21** as above and chromatography (silica gel) with cyclohexane/AcOEt 4:1 afforded pure **10** (81%) which was converted to **2** (78%) (see above and [3a] [13]).

*5-Hydroxy-3-methylcyclopentadecanone* (**13**)[4]) *and its Conversion to* (±)*-muscone* (= *3-Methylcyclopentanone*, **1**). Using the same procedure as for **10**, **22** (13.1 g, 90% pure, 30.0 mmol) was converted to **13** (3.88 g, 51%) [3a] [13].

For characterization **23** was isolated (80%) and chromatographed (silica gel) with cyclohexane/AcOEt 4:1. IR ($CDCl_3$): 3580, 2950, 1715, 1450, 1310, 1150. $^1$H-NMR: 0.90–1.90 (*m*, 21 H); 2.10–2.60 (*m*, 4 H); 3.02 (*m*, 2 H); 3.60 (*m*, 1 H); 7.47–8.10 (*m*, 5 H). Reduction of **23** afforded pure **13** (69%) which was converted to **1** (75%) (see above and [3a] [13]).

## REFERENCES


[1] *C. Fehr (Firmenich SA)*, Ger. Offen. 3,214,546 (18.11.1982); CH Appl. 81/2593 (21.4.1981); Chem. Abstr. *98* 125913e (1983).

[2] *B. D. Mookherjee & R. A. Wilson* in 'Fragrance Chemistry', ed. E. T. Theimer Academic Press, New York, 1982, p. 433; *P. A. Wender, D. A. Holt & S. M. Sieburth*, J. Am. Chem. Soc. *105*, 3348 (1983) and references cited therein.

[3] a) *G. Ohloff, J. Becker & K. H. Schulte-Elte*, Helv. Chim. Acta *50*, 705 (1967); *J. Becker, K. H. Schulte-Elte & G. Ohloff* (Firmenich et Cie), US Pat. 3,778,483 (11. 12. 1973); Swiss Pat. 513,791 (30. 11. 1971); Chem. Abstr. 76, 99222c (1972); b) *A. Eschenmoser, D. Felix & G. Ohloff*, Helv. Chim. Acta *50*, 708 (1967); *D. Felix, J. Schreiber, G. Ohloff & A. Eschenmoser*, ibid. *54*, 2896 (1971); c) *C. Fehr, G. Ohloff & G. Büchi*, ibid. *62*, 2655 (1979).

[4] a) *R. Dubs & R. Stüssi*, J. Chem. Soc., Chem. Commun *1976*, 1021; b) *S. Sakane, K. Maruoka & H. Yamamoto*,Tetrahedron Lett. *1983*, 943.

[5] *Y. Leroux*, Bull. Soc. Chim. Fr. *1968*, 359.

[6] *H. C. Araújo & J. R. Mahajan*, Synthesis *1978*, 228.

[7] a) *H. O. House, C. C. Yau & D. van Derveer*, J. Org. Chem. *44*, 3031 (1979); b) *F. W. Stacey & J. F. Harris, Jr.*, Org. React. *13*, 150 (1963).

[8] *B. D. Mookherjee, R. W. Trenkle & R. R. Patel*, J. Org. Chem. *37*, 3846 (1972); *R. Kaiser & D. Lamparsky*, Helv. Chim. Acta *61*, 2671 (1978).

[9] *J. J. Barber & G. M. Whitesides*, J. Am. Chem. Soc. *102*, 239 (1980) and references cited therein; *L. M. Lawrence & G. M. Whitesides*, ibid. *102*, 2493 (1980).

[10] *P. J. Pearce, D. H. Richards & N. F. Scilly*, J. Chem. Soc., Perkin Trans. 1 *1972*, 1655.

[11] *R. D. Rieke & S. E. Bales*, J. Chem. Soc., Chem. Commun. *1973*, 879.

[12] *R. D. Rieke, S. J. Uhm & P. M. Hudnall*, J. Chem. Soc., Chem. Commun. *1973*, 269

[13] *K. H. Schulte-Elte, A. Hauser & G. Ohloff*, Helv. Chim. Acta *62*, 2673 (1979); *K. H. Schulte-Elte, J. Becker & W. Schenk* (Firmenich SA), Ger. Offen. 3,034,040 (2. 4. 1981); US Pat. 4,335,262 (15. 6. 1982); Chem. Abstr. *95*, 97 190 j (1981).

[14] *C. Blomberg & F. A. Hartog*, Synthesis *1977*, 18.

[15] a) Review on sulfone chemistry: *P. D. Magnus*, Tetrahedron *33*, 2019 (1977); intra- and intermolecular condensations of esters with sulfones: *W. E. Truce & R. H. Knospe*, J. Am. Chem. Soc. *77*, 5063 (1955); *W. E. Truce, W. W. Bannister & R.H. Knospe*, J. Org. Chem. *27*, 2821 (1962); *D. Heissler & J.-J. Riehl*, Tetrahedron Lett. *1980*, 4707; intramolecular cyclization of a lactam sulfone: *Y. Ohtsuka & T. Oishi*, ibid. *1979*, 4487; intramolecular cyclization of a sulfone carbonate: *V. Reutrakul, P. Tuchinda & K. Kusamran*, Chem. Lett. *1979*, 1055; b) *K. Kondo & D. Tunemoto*, Tetrahedron Lett. *1975*, 1397; *C. H. Heathcock, C. T. White, J. J. Morrison & D. van Derveer*, J. Org. Chem. 46, 1296 (1981); *T. Yoshida & S. Saito*, Bull. Chem. Soc. Jpn. *55*, 3047 (1982).

[16] a) *E. J. Corey & M. Chaykovsky*, J. Am. Chem. Soc. *86*, 1639 (1964); *D. A. Chass, D. Buddhasukh & P. D. Magnus*, J. Org. Chem. *43*, 1750 (1978); b) *M. Julia & D. Uguen*, Bull. Soc. Chim. Fr. *1976*, 513.

[17] *C. Fehr*, Helv. Chim. Acta *66*, 2519 (1983).

[18] *L. Brandsma*, 'Preparative Acetylenic Chemistry', Elsevier, Amsterdam–London–New York, 1971, p. 19.


[12]) Same yield using NaH/DMSO or LDA (2 equiv.) in THF at −40°.