

250. A Novel Three-Carbon Ring Expansion Sequence

Synthesis of *Exaltone*[®] and ($\pm$)-Muscone¹⁾

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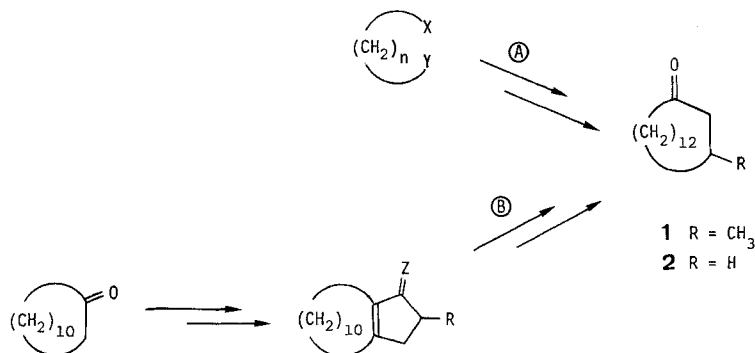
(23. VIII. 83)

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 macrocyclic 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

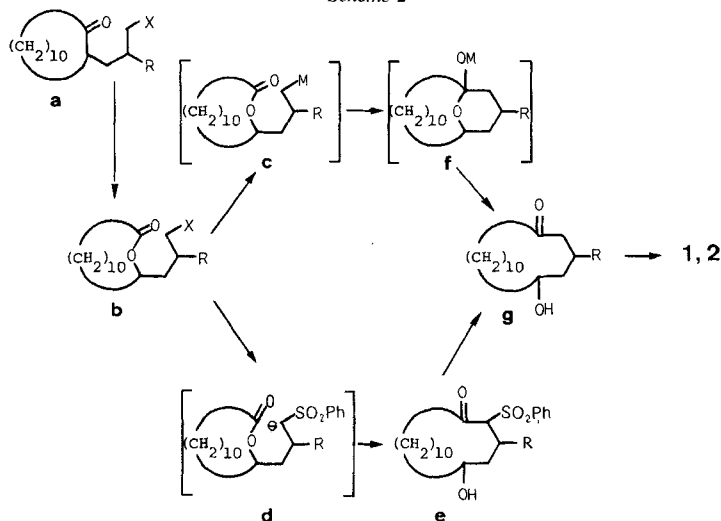


Approach Ⓑ, developed in *Firmenich* research laboratories [3], involves C₃-ring expansion sequences using cyclododecanone as the inexpensive starting material. Our strategy described herein uses an extension of this concept. Thus, regioselective *Baeyer-Villiger* reaction of an appropriately substituted 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).

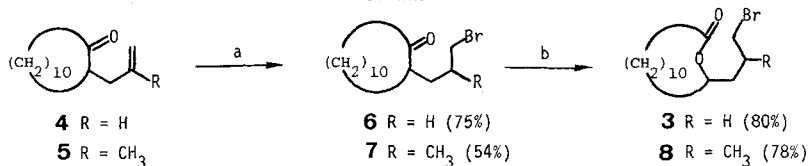
Scheme 2



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



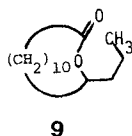
Reagents: a) HBr, *hν*, petroleum ether (PE)/20°; b) CH₃CO₃H (7 equiv.), BF₃·Et₂O (0.64 equiv.), Cl₃CCH₃/50°/5 days.

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%)



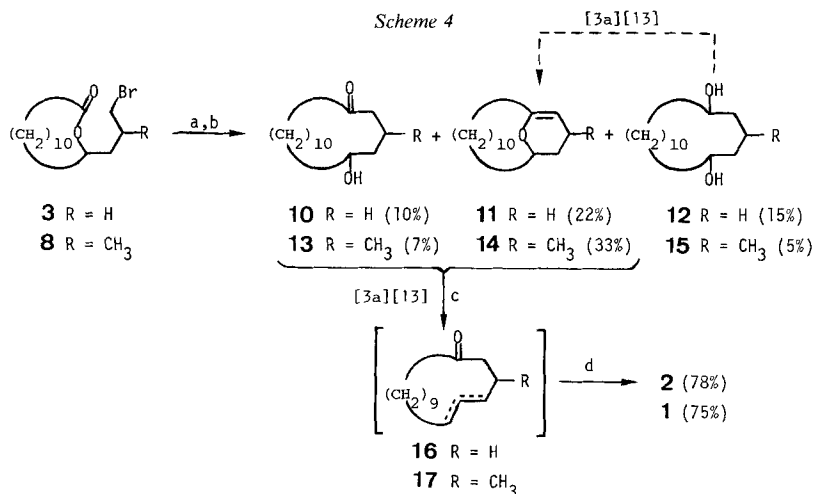
and **11** (10%) (Scheme 4, Table). When the same reaction was performed in the presence of BF_3 -etherate, only the reduced lactone **9** was obtained (75%), presumably via the intermediate alkyl radical [9] [10]. In the hope of favoring the cyclization, we examined metals with a higher electron potential 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/ $\overline{\text{Br}}$ Br/ $\text{BF}_3 \cdot \text{Et}_2\text{O}$ /THF	–	–	–	75%	9%
Mg/ $\overline{\text{Br}}$ Br/THF	12%	10%	–	39%	–
Na/ $\overline{\text{Br}}$ Br/THF	2%	21%	2%	6%	10%
Li (1% Na)/ $\overline{\text{Br}}$ 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.



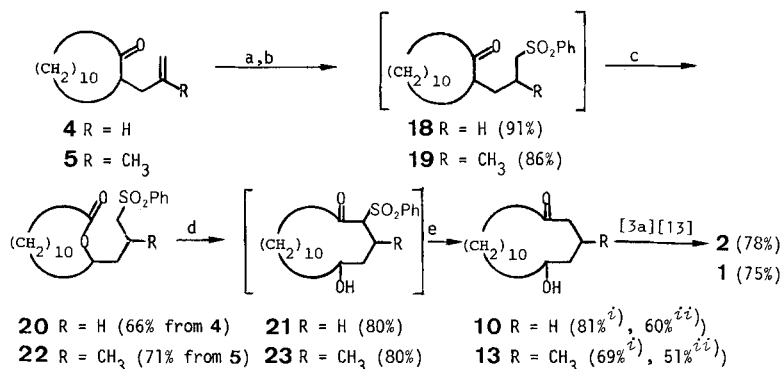
Reagents: a) Li, $\text{Br}(\text{CH}_2)_2\text{Br}$, THF/30°; b) dist. 170°/0.02 Torr; c) H_3PO_4 , toluene/reflux/2 h; d) H_2 /Pd–C (10%), EtOH.

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 ($\pm$)-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) CH₃CO₃H (2 equiv.), Cl₃CCH₃/30°; c) CH₃CO₃H (6 equiv.); BF₃·Et₂O (0.64 equiv.), Cl₃CCH₃/50°/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.), H₂N(CH₂)₂/20°/5 min or NaNH₂ (3 equiv.), NH₃, THF/–33°/20 min; e) Al (10 equiv.) (Hg), THF, H₂O/20°/15 h or Li (3 equiv.), H₂N(CH₂)₂NH₂, THF/20°/30 min or Na (3 equiv.), NH₃, THF/–33°/30 min^b; d) + e) in one operation: NaNH₂ (3 equiv.), NH₃, THF/–33°/20 min, then Na (3 equiv.)/–33°/30 minⁱⁱ.

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* reaction⁶⁾ in the presence of BF₃-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 NaNH₂ in liquid NH₃/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 ($\pm$)-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/H₂SO₄ 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 CDC1₃-solutions); band positions in cm⁻¹. ¹H-NMR: *Varian A 60* (60 MHz, CDC1₃); chemical shifts in δ are reported in ppm relative to TMS as internal standard. MS: *Atlas CH₄* 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. K₂CO₃ (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. ¹H-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)cyclododecanone (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 redistillation⁸) (80%) or CC (silica gel) with cyclohexane (100%). IR (neat): 2920, 1705, 1470, 1430, 1380, 1250. ¹H-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). CH₃CO₃H (40%, 104 g, 0.55 mol) and BF₃ · Et₂O (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 Cl₃CCH₃ (360 ml). The mixture was stirred at 50 ° for 10 days. At 2-day intervals additional 40% CH₃CO₃H 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. NaHSO₃ and with H₂O, dried (Na₂SO₄) 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% CH₃CO₃H (1.10 mol), the reaction was complete after 5 days. IR (neat): 2930, 1730, 1460, 1445, 1255, 1050. ¹H-NMR: 1.10–2.20 (*m*, 22 H); 2.20–2.60 (*m*, 2 H); 3.40 (*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. ¹H-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(CH₂)₂Br (376 mg, 2.0 mmol) and BF₃ · Et₂O (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. NH₄Cl-solution, extraction (Et₂O) and bulb-to-bulb distillation at 120 ° (oven)/0.05 Torr afforded **9** (360 mg, 75%) as a colorless oil⁹. IR (neat): 2940, 1725, 1460, 1245. ¹H-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(CH₂)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, $\approx$ 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 H₃PO₄ (85%, 1 drop) at reflux for 2 h using a *Dean Stark* apparatus. Extractive isolation (Et₂O/sat. aq. NaHCO₃-solution) afforded **16** (presumably as a mixture of isomers¹⁰),

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) H₂/Pd–C; b) CH₃CO₃H/BF₃ · Et₂O/Cl₃CCH₃/50 °/5 days.

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

201 mg, 86%), which was dissolved in EtOH (10 ml) and hydrogenated ($\text{H}_2/\text{Pd}-\text{C}$ (10%), 50 mg) to give after filtration (*Celite*), evaporation and bulb-to-bulb distillation ($120^\circ/0.05$ Torr) **2** (190 mg, 91%), identical to an authentic sample [3c].

Reaction of 8 with Li. Preparation of ($\pm$)-Muscone (1). A solution of **8** (1.35 g, 90% pure, 3.66 mmol) and $\text{Br}(\text{CH}_2)_2\text{Br}$ (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 ($160^\circ/0.05$ Torr) afforded a mixture (405 mg, $\approx 45\%$) 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% $\text{CH}_3\text{CO}_3\text{H}$ (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 ($\text{CH}_2\text{Cl}_2/\text{Et}_2\text{O}/\text{PE}$) 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. $97-102^\circ$. IR (CDCl_3): 2950, 1700, 1465, 1445, 1300, 1145, 1080, 790. $^1\text{H-NMR}$: 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. $98-103^\circ$. IR (CDCl_3): 2950, 1705, 1470, 1450, 1305, 1145, 1085. $^1\text{H-NMR}$: 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% $\text{CH}_3\text{CO}_3\text{H}$ (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 $\text{BF}_3 \cdot \text{Et}_2\text{O}$ (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. $^1\text{H-NMR}$: 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. $^1\text{H-NMR}$: 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 $\text{CH}_3\text{CO}_3\text{H}$ (40%, 417 g (365 ml), 2.50 mol), the mixture was concentrated to remove excess thiophenol (50° (bath)/8 Torr) and unreacted **4** ($155^\circ/0.2$ Torr).

For characterization the intermediate **21** was isolated (80%)¹²⁾ and crystallized from Et₂O, m.p.: 153–136°. IR (CDCl₃) 3630, 2960, 1720, 1450, 1310, 1150, 1080. ¹H-NMR: 1.10–2.50 (*m*, 23 H); 2.77 (*t'*, *J* ≈ 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 (CDCl₃): 3580, 2950, 1715, 1450, 1310, 1150. ¹H-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]).

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