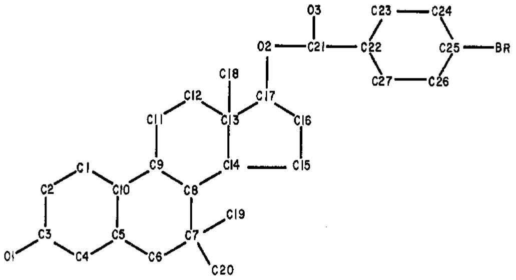


Figure 2.—Numbering.

After several cycles of refinement, w was set equal to the reciprocal of $\sigma^2(F_0^2)$ which was estimated during data reduction.

Because of the size (62 symmetry-independent atoms), the 259 refinable parameters were split into several matrices. All temperature factors were in one matrix together with the scale factor for F_0. Since a strong pseudosymmetric relation between the two molecules was noted, the coordinate matrix scheme was designed to put like parts of the molecules together in three different matrices. Anisotropic temperature factors for the bromine atoms were refined, but the data were judged not suitable for determination of anisotropic temperature factors on carbon and oxygen atoms or for determination of hydrogen atom coordinates. The addition of these parameters would have brought the total number of refinable parameters to 638, too many to determine with only 1176 observations. Refinement was terminated when all shifts were less than $^1/_4$ of corresponding standard deviations. The final value of the R index ($R = \Sigma||F_0| - |F_c||/\Sigma|F_0|$) was 0.111; the standard deviation of fit, $[(\Sigma w[|F_0|^2 - |F_c|^2]^2)]^{1/2}/(m - s)^{1/2}$, was 2.29

Final parameters are given in Table V for both symmetry independent molecules.[18] The numbering scheme is shown in Figure 2. Numbering follows the convention for steroids as far as possible; C(1) through C(18) have conventional numbering. The remainder of the atoms are numbered C(19)–C(27) and O(1)–O(3). Bond distances and angles are given in Tables II and III.

All calculations were carried out on IBM 360/30 and IBM 360/50 computers using the programs of the CRYM crystallographic system developed by one of the authors (D. J. D.). Atomic form factors are from "International Tables for X-Ray Crystallography.[19]"

Registry No.—**3,** 25380-93-2; **4,** 25380-94-3; **5,** 25380-95-4; **6,** 25380-96-5; **7,** 25380-97-6; **8,** 25380-98-7; **9,** 31020-45-8; **10,** 31025-03-3; **12,** 31025-04-4; **13,** 31025-05-5; **14,** 31025-06-6; **15,** 31025-07-7; **16,** 31025-08-8; **17,** 31025-09-9; **18,** 31025-10-2.

[18] Listings of observed and calculated structure factors will appear following these pages in the microfilm edition of this volume of the journal. Single copies may be obtained from the Reprint Department, ACS Publications, 1155 Sixteenth St., N.W., Washington, D. C. 20036, by referring to author, title of article, volume, and page number. Remit check or money order for $3.00 for photocopy or $2.00 for microfiche.

[19] "International Tables for X-Ray Crystallography," Vol. III, Kynoch Press, Birmingham, England, (1962), pp 202–205.

Synthesis of Racemic Muscone and Cyclopentadecanone (Exaltone) from 1,9-Cyclohexadecadiene

B. D. MOOKHERJEE,* R. W. TRENKLE, AND R. R. PATEL

Research and Development Department, International Flavors & Fragrances, Union Beach, New Jersey 07735

Received April 7, 1971

Muscone (**11**) and exaltone (**19**) have been synthesized from 1,9-cyclohexadecadiene (**1**). Unsaturated monoepoxide **2** upon treatment with butyllithium was converted into an α,β-unsaturated alcohol **3** and oxidized with chromic acid into the corresponding ketone **5**. This, upon treatment with methylmagnesium bromide in the presence of cuprous chloride, was converted into β-methylcyclohexadecenone (**6**) and then hydrogenated to β-methylcyclohexadecanone (**7**). The dibromide of **7** underwent a Favorski rearrangement to produce a mixture of 3-methyl and 15-methyl cyclopentadecene-1-carboxylate (7:3) which on treatment with hydrazoic acid was converted into muscone (**11**) and 2-methylcyclopentadecanone (**12**), respectively. In a similar way, 1-carboxymethyl-1-cyclopentadecene (**18**) obtained from dibromocyclohexadecanone was converted into exaltone (**19**). In another experiment, saturated epoxide **13** was rearranged to the allylic alcohol **15** and oxidized to the unsaturated ketone **16** which was then converted to **7**.

Muscone (**11**) [(−)-3-methylcyclopentadecanone] is the principal odorous constituent of musk pod obtained from the male deer *Moschus Moschiferus*. Owing to its rare occurrence in nature and its exotic and useful odor, many routes[1] have been developed for the synthesis of muscone. This paper reports a synthesis of (±)-muscone (**11**) and exaltone (**19**) from 1,9-cyclohexadecadiene (**1**).[2]

Addition of 1 mol of peracetic acid to diene **1** (three isomers, cis,cis, trans,trans, and cis,trans) yielded 69% of unsaturated monoepoxide **2** (four isomers, cis,cis, trans,trans, cis,trans, and trans,cis). All these isomers were separable on an analytical glc column. It should be noted that these unsaturated monoepoxides **2** and the corresponding saturated epoxides **13** possess weak musk odor.

Treatment of **2** with 1 mol of butyllithium[3,4] afforded a mixture of α,β-unsaturated secondary alcohol **3** (50%) and cyclohexadecenone **4**. Attempts to convert **2** to **3** with other reagents, *viz.*, alumina[5] and aluminum isopropoxide,[6] were not successful. The allylic alcohol **3** thus formed was isolated by column chromatography and then oxidized to the corre-

[1] (a) K. Ziegler and K. Weber, *Justus Liebigs Ann. Chem.*, **521**, 164 (1934); (b) L. Ruzicka and M. Stoll, *Helv. Chim. Acta*, **17**, 1308 (1934); (c) H. Hunsdiecker, *Ber. Deut. Chem. Ges. B*, **75**, 1190, 1197 (1942); (d) M. Stoll and K. Commarmont, *Helv. Chim. Acta*, **31**, 554 (1948); (e) A. T. Blomquist and R. D. Spenser, *J. Amer. Chem. Soc.*, **69**, 472 (1947); **70**, (1948); (f) A. T. Blomquist, R. W. Holley, and R. D. Spenser, *ibid.*, **70**, 34 (1948); (g) M. Stoll and A. Rouve, *Helv. Chim. Acta*, **30**, 2019 (1947); (h) M. S. R. Nair, H. H. Mathur, and S. C. Bhattacharyya, *J. Chem. Soc.*, 4154 (1964); (i) V. R. Mamdapur, P. P. Pai, K. K. Chakravarti, U. G. Nayak, and S. C. Bhattacharyya, *Tetrahedron*, **20**, 2601 (1964); (j) G. Ohloff, J. Becker, and K. H. Schulte-Elte, *Helv. Chim. Acta*, **50**, 705 (1967); (k) A. Eschenmoser, D. Felix, and G. Ohloff *ibid.*, **50**, 708 (1967); (l) H. Nozaki, H. Yamamoto, and T. Mori, *Can. J. Chem.*, **47**, 1107 (1969); (m) E. Yoshii and S. Kimoto, *Chem. Pharm. Bull.*, **17**, 629 (1969).

[2] N. Calderon, E. A. Ofstead, and W. A. Judy, *J. Polym. Sci.*, **5**, 2209 (1967).

[3] H. Nozaki, T. Mori, and Noyori, *Tetrahedron*, **22**, 1207 (1966).

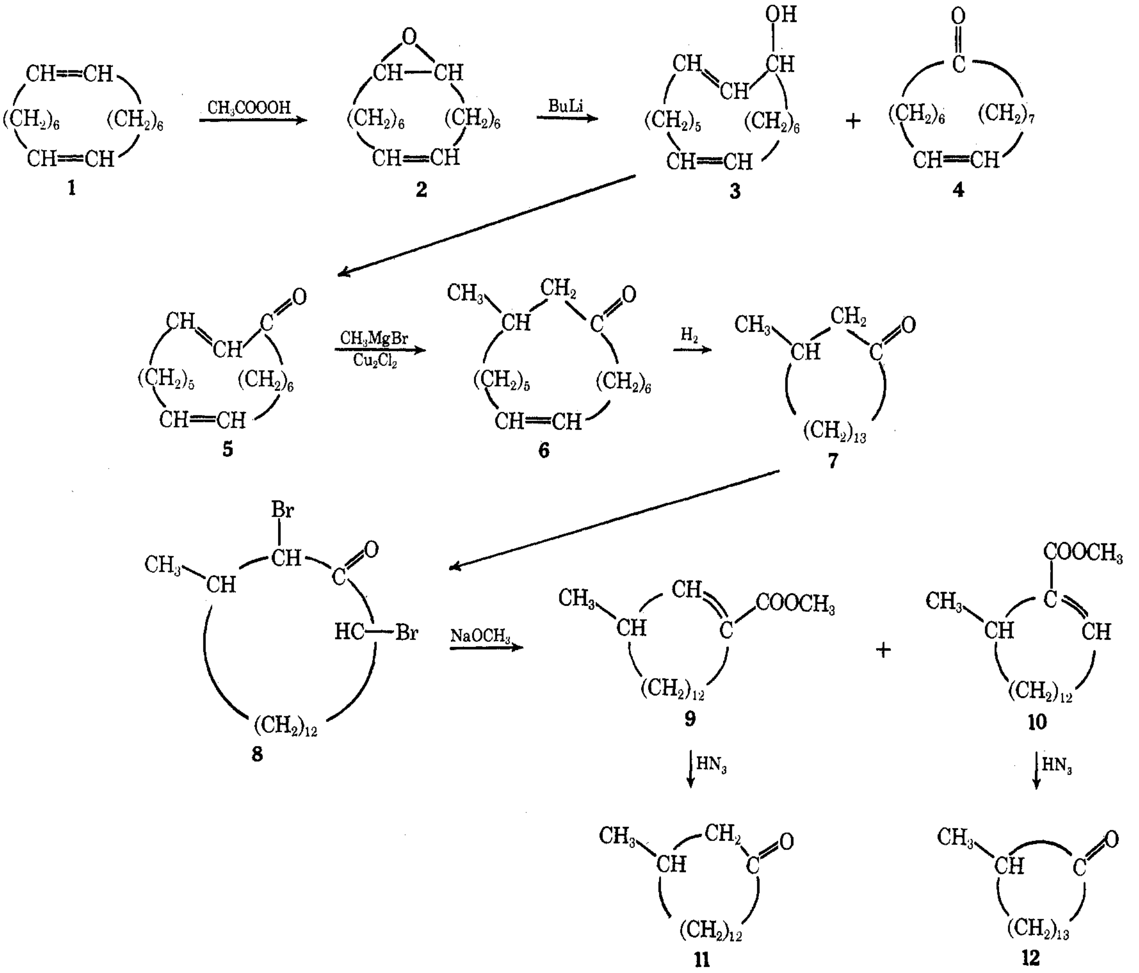
[4] K. H. Schulte-Elte and G. Ohloff, *Helv. Chim. Acta*, **51**, 494 (1968).

[5] V. S. Joshi, N. P. Damodaran, and Sukh Dev, *Tetrahedron*, **24**, 5817 (1968).

[6] E. H. Eschinasi, *Israel J. Chem.*, **6**, 713 (1968).

SCHEME I

REARRANGEMENT OF UNSATURATED MONOEPOXIDE 2



sponding α,β-unsaturated ketone **5**[7] (69%). A 1,4 addition of methyl Grignard to **5** in the presence of cuprous chloride and ether[1d] went smoothly to produce 15-methyl-8-cyclohexadecen-1-one (**6**, 83%), which was purified by column chromatography and hydrogenated to 3-methylcyclohexadecanone (**7**).

Recently Garbisch[8] showed that cyclododecanone could be converted to cycloundecanone in good yield. We applied this method to cyclohexadecanone **17**. Bromination of **17** yielded dibromocyclohexadecanone, which on treatment with sodium methoxide underwent Favorskii rearrangement to the unsaturated ester **18**, which was converted to exaltone **19** in 78% yield by the Curtius reaction.

The same method was applied to **7**, bromination of which gave a quantitative yield of dibromo ketone **8**. When this dibromo ketone was treated with sodium methoxide for a short period of time, **9** and **10** were formed in the ratio of 7:3. These two esters were separated by careful column chromatography. On treatment with a mixture of sodium azide and sulfuric acid and then with steam, unsaturated esters **9** and **10** were smoothly converted to racemic muscone (**11**) and 2-methylcyclopentadecanone (**12**), respectively (Scheme I).

As an alternative method, the saturated epoxide **13** was also rearranged to allylic (trans)[9] alcohol **15**[10] (62%) and 1,3-cyclohexadecadiene (**14**, 4%) by means of lithium diethylamide.[11] Alcohol **15** was oxidized to the corresponding ketone **16** (70%) which was then converted to **7** (80%) by the methylmagnesium bromide–cuprous chloride method (Scheme II).

Experimental Section

Melting points were uncorrected. Glc analyses were performed on F & M 810 instrument using 5% Carbowax 20M and 5% silicone SE-30 coated on Anakrom ABS (80–100 mesh) packed in a stainless steel column (0.25 in. × 25 ft). The following spectrometers were used: ir, Beckman IR-5A and IR-4; nmr, Varian HA-100 (CCl_4, TMS as internal standard); mass spectra, CEC Model 21-110 and AEI-MS9 for high-resolution spectra. Mass spectral major fragmentation peaks were recorded in decreasing order of intensity. Deactivated silicic acid (5%) made by adding 5 ml of water to 95 g of silicic acid (Grace, 100–200 mesh) and alumina, neutral, (Fisher Scientific, 80–200 mesh) were used for column chromatography.

17-Oxobicyclo[14.1.0]heptadec-8-ene (2).—A solution of 40% peracetic acid (37.6 g, 0.18 mol) in methylene chloride (50 ml) was added dropwise to a stirred solution of 1,9-cyclohexadecadiene (**1**, 40 g, 0.18 mol) and sodium acetate (56 g) in methylene chloride (250 ml) at 0–5°. When the addition was completed,

---

[7] In another experiment ketone **5** was made in 9% yield by the autoxidation of **1**. Our attempts to make the α,β-unsaturated ketone **5** by either selenium dioxide or chromium trioxide oxidation of **1** were not very successful.

[8] E. W. Garbisch, Jr., and J. Wohllebe, *J. Org. Chem.*, **33**, 2157 (1968).

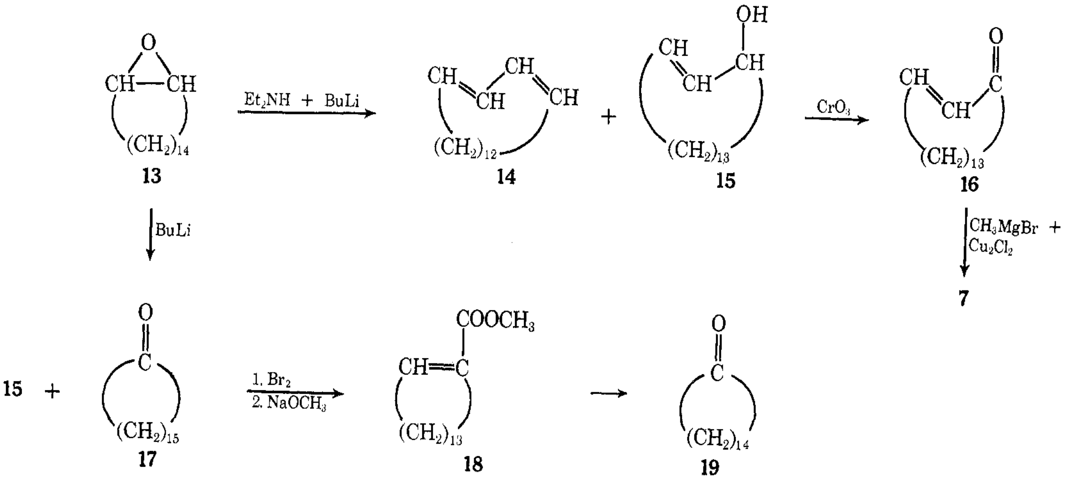
[9] During the rearrangement of epoxides **2** and **13** to allylic secondary alcohols **3** and **15** by alkyllithium, the new double bond thus formed on the ring was trans.

[10] When saturated epoxide **13** was treated with butyllithium, the yield of **15** and **17** was 19 and 54%, respectively.

[11] J. K. Crandall and L.-H. C. Lin, *J. Org. Chem.*, **33**, 2375 (1968).

SCHEME II

REARRANGEMENT OF SATURATED EPOXIDE 13



the solution was stirred for an additional 3 hr at 0–5° and then allowed to reach room temperature. Water (200 ml) was added and the two phases separated. The aqueous layer was extracted with methylene chloride. The combined organic extracts were washed with saturated sodium chloride solution and dried (Na_2SO_4). Removal of the solvent yielded 42 g of crude material which was chromatographed on deactivated silicic acid (500 g)–20% ether in hexane (2 l.) eluted 30 g (yield 69%) of epoxide **2**. Glc analysis showed four peaks. The mass spectrum of the mixture of these four isomers **2** showed a molecular ion peak at *m/e* 236 and other major peaks at *m/e* 55, 67, 41, 81, 95; ir (neat) (mixture of four isomers) 3.41, 3.5, 6.9, 7.25, 7.3, 9.9, 10.35, 13.5, 14.0 μ; nmr (mixture of four isomers) δ 1.35 (m with a s at 1.35, internal methylene), 2.0 (b, 4 H, $CH_2C{=}CCH_2$), 2.5 (m, 1 H, epoxy CH), 2.7 (m, 1 H, epoxy CH), 5.3 (m, 2 H, $CH{=}CH$).

Anal. Calcd for $C_{16}H_{28}O$: *m/e* 236.2140. Found: *m/e* 236.2137.

Reaction of Monoepoxide 2 with Butyllithium.—A solution of **2** (23.6 g, 0.1 mol) in hexane (100 ml) was added dropwise over a 1.5-hr period to a stirred solution of 15% butyllithium (80 ml, 0.13 mol) in hexane at 0° under nitrogen. After the addition was complete, the mixture was stirred for an additional 0.5 hr at 0°. The temperature was then slowly raised to 65°, and the mixture refluxed for 3 hr. The reaction mixture was cooled to 5° and water (30 ml) was added. The organic layer was separated, washed with water, dried (Na_2SO_4), and on removal of solvent yielded 24 g of crude product which was chromatographed on silicic acid (300 g)–10% ether in hexane eluted an 11.1-g mixture of unreacted epoxide **2** (minor amount) and cyclohexadecenone **4**[12] (major product); 20–40% ether in hexane eluted 12 g (yield 50.8%) of alcohol **3**. Glc of **3** showed two peaks. The mass spectrum of 2-*trans*-9-*trans*-cyclohexadecadien-1-ol (**3**) showed a peak at *m/e* 218 (M − 18) and other major peaks at *m/e* 41, 67, 79, 39, 80, 81; ir (neat) 3.0 (strong, OH), 3.5, 6.05 6.99, 7.45, 7.7, 9.8 ($C{=}CCHOH$), 10.35 (strong, trans $CH{=}CH$), 14.0 μ (broad, medium). The mass spectrum of 2-*trans*-9-*cis*-cyclohexadecadien-1-ol (**3**) showed a peak at *m/e* 218 (M − 18) and other major peaks at *m/e* 41, 67, 79, 80, 39, 81; ir (neat) 3.0 (strong, OH), 3.5, 6.1, 7.0, 7.5, 7.8, 9.45, 9.85 ($C{=}CCHOH$), 10.4 (medium, *trans* $CH{=}CH$), 14.1 μ (broad, strong); nmr (mixture of *cis*- and *trans*-**3**) δ 1.33 (m with a s at 1.33, internal methylene), 2.0 (b, 6 H, $CH_2C{=}C$), 3.94 (b, 1 H, CHO), 5.3 (m, 4 H, $CH{=}CH$).

Anal. Calcd for $C_{16}H_{28}O$: *m/e* 236.2140. Found: *m/e* 236.2151.

Chromium Trioxide Oxidation of 3.—A solution of chromium trioxide (10 g) in concentrated sulfuric acid (11 ml) and water (50 ml) was cautiously added to a stirred solution of **3** (12 g) in acetone (300 ml) at 0° until an orange-yellow color persisted. The solution was stirred for an additional 3 hr at 0° and allowed to reach room temperature. Half of the acetone (150 ml) was removed under reduced pressure without heat. Water (200 ml) was added and then extracted with methylene chloride. The methylene chloride extract was washed with saturated sodium chloride, dried (Na_2SO_4), and on removal of solvent produced an oil (10 g) which was chromatographed on silicic acid (120 g)–5–15% ether in hexane eluted 8.3 g (yield 69.1%) of ketone **5** whose glc (Carbowax 20M) showed two peaks. The mass spectrum of 2-*trans*-9-*trans*-cyclohexadecadien-1-one (**5**) showed molecular ion peak at *m/e* 234 and other major peaks at *m/e* 41, 67, 55, 81; ir (neat) 3.35 (very weak), 3.45, 3.55, 5.88, and 5.95 (sh) of 6.02 ($C{=}CC{=}O$), 6.19, 6.99, 7.35, 7.45, 7.8, 8.0, 8.12, 8.3, 10.35 (strong, trans $CH{=}CH$), 13.9 μ (broad, weak). The mass spectrum of 2-*trans*-9-*cis*-cyclohexadecadien-1-one (**5**) showed molecular ion peak at *m/e* 234 and other major peaks at *m/e* 41, 67, 55, 81; ir (neat) 3.35 (weak), 3.45, 3.54, 5.89 (weak, sh), 5.95 and 6.04 (almost equal intensity, $C{=}CC{=}O$), 6.2, 6.9, 7.49, 7.8, 8.0, 8.3, 9.0 (broad, weak), 9.79, 10.25 (medium, trans $CH{=}CH$), 14.0 μ (broad, cis $CH{=}CH$); nmr (mixture of *cis*- and *trans*-**5**) δ 2.0 (b, 4 H, $CH_2C{=}CCH_2$), 2.39 (m, 4 H, $CH_2C{=}CCOCH_2$), 5.24 (m, 2 H, $CH{=}CH$), 5.88–6.14 and 6.50–6.85 (m, 2 H, $CH{=}CHC{=}O$).

Anal. Calcd for $C_{16}H_{26}O$: *m/e* 234.1983. Found: *m/e* 234.1976.

15-Methyl-8-cyclohexadecen-1-one (**6**).—A solution of **5** (5.5 g, 0.023 mol) in anhydrous ether (40 ml) was added slowly over 1.5 hr to a stirred mixture of cuprous chloride (0.15 g) and methylmagnesium bromide (10 ml, 0.03 mol) in anhydrous ether (40 ml) at 10°. Stirring was continued for an additional 1 hr at 10°. Cold 10% hydrochloric acid (25 ml) was added. The ether layer was separated, washed first with a 10% sodium bicarbonate solution and then with water, and dried (Na_2SO_4). Evaporation of solvent yielded 5.7 g of an oil which was chromatographed on silicic acid (50 g)–5–20% ether in hexane eluted 4.9 g (yield 83.4%) of **6** whose glc (Carbowax 20M) showed two peaks. The mass spectrum of 15-methyl-8-*trans*-cyclohexadecen-1-one (**6**) showed molecular ion peak at *m/e* 250 and other major peaks 41, 55, 67, 69, 27, 81; ir (neat) 3.45, 3.55, 5.89 ($C{=}O$), 6.9, 6.95, 7.13, 7.35, 7.8, 9.0, 9.7, 10.35 (strong, trans $CH{=}CH$), 14.0 μ (weak). The mass spectrum of 15-methyl-8-*cis*-cyclohexadecen-1-one (**6**) showed molecular ion peak at *m/e* 250 and other major peaks at *m/e* 41, 55, 67, 69, 81, 27; ir (neat) 3.35 (weak and broad), 3.45, 3.52, 5.89 ($C{=}O$), 6.9, 6.95 (sh), 7.12, 7.35, 7.85, 9.0, 9.7, 14.0 μ (strong, broad); nmr (mixture of *cis*- and *trans*-**6**) 0.9 (q, 3 H, CH_3CH), 1.98–2.30 (m, 7 H, $CHCH_2COCH_2CH_2$), 5.3 (m, 2 H, $CH{=}CH$).

Anal. Calcd for $C_{17}H_{30}O$: *m/e* 250.2296. Found: *m/e* 250.2271.

3-Methylcyclohexadecanone (**7**).—A solution of **6** (10 g) in methanol (200 ml) was hydrogenated under normal temperature and pressure using 10% palladium on carbon (1.5 g) as a catalyst. After usual work-up 10 g of 3-methylcyclohexadecanone (**7**) was obtained. Glc of **7** gave one peak whose mass spectrum showed a molecular ion peak at *m/e* 252 and other major peaks at 41, 55, 43, 42, 69, 85; ir (neat) 3.41, 3.5, 5.83 ($C{=}O$), 6.85, 7.09, 7.3, 7.8, 8.7, 8.9, 9.15, 9.6, 14.0 μ (broad); nmr δ 0.92 (d, J = 6 Hz, 3 H, CH_3CH), 1.1–2.0 (m, 25 H, with s at 1.31), 2.0–2.4 (m, 4 H, CH_2COCH_2).

---

[12] L. G. Wideman, *J. Org. Chem.*, **33**, 4541 (1968).

Anal. Calcd for $C_{17}H_{32}O$: *m/e* 252.2453. Found: *m/e* 252.2450.

3-Methyl-2,16-dibromocyclohexadecanone (8).—Bromine (19.2 g, 0.12 mol) was added dropwise to a solution of 7 (15 g, 0.059 mol) in a mixture of anhydrous benzene (200 ml) and anhydrous ether (20 ml) at 25° over a period of 0.5 hr. The hydrogen bromide thus liberated was removed by connecting the reaction flask to the house vacuum (20 mm) and simultaneously heating the flask to 50°. This operation was continued until the solution of the flask was neutral to litmus paper. This solution was then ready for next step. The mass spectrum of **8** showed molecular ion peaks at *m/e* 408 (M^+) and 410 (M + 2) and other major peaks at *m/e* 112, 55, 41, 69, 98, 249; ir (neat) 3.45, 3.51, 5.81 (C=O), 6.9, 7.29, 7.45, 7.9, 9.0, 9.7 μ; nmr δ 1.07 (d, J = 6.5 Hz, 3 H, CH_3CH), 4.3 (d, J = 6.5 Hz, 1 H, CHBr), 4.5 (t, 1 H, CHBr).

Anal. Calcd for $C_{17}H_{30}OBr_2$: *m/e* 408.0664. Found: *m/e* 408.0657.

3-Methyl 1-Cyclopentadecene-1-carboxylate (9) and 15-Methyl 1-Cyclopentadecene-1-carboxylate (10).—To the reaction flask containing the dibromide **8** from the previous experiment, sodium methoxide (7.6 g, 0.14 mol) was added over a period of 1 hr. Since the reaction was exothermic, the temperature was maintained at 25–30° by an ice bath. The mixture was stirred for an additional 0.5 hr at room temperature and then cooled to 5°. Cold water (200 ml) was added, the organic layer was separated, washed with 5% hydrochloric acid and 50% sodium chloride solution, and dried (Na_2SO_4), and on removal of solvent produced 19 g of crude oil product. Glc (Carbowax 20M) showed two peaks due to **9** (70%) and **10** (30%) which were isolated.

The mass spectrum of **9** showed molecular ion peak at *m/e* 280 and other major peaks at *m/e* 55, 41, 67, 95; ir (neat) 3.45, 3.52, 5.85 ($C=CCOOCH_3$), 6.12, 6.9, and 6.99 (equal intensity), 7.3, 7.45, 7.55, 7.8, 7.9, 8.15 (sh), 8.25, 8.3, 8.6, 8.9, 9.1, 9.35, 9.55, 9.65, 10.0, 11.2 (broad, weak), 14.0 μ (broad, weak); nmr δ 0.93 (d, J = 7 Hz, 3 H, CH_3CH), 3.68 (s, 3 H, $COOCH_3$), 5.46 (d, 1 H, C=CH).

Anal. Calcd for $C_{18}H_{32}O_2$: *m/e* 280.2402. Found: 280.2411.

The mass spectrum of **10** showed a molecular ion peak at *m/e* 280 and other major peaks at *m/e* 41, 55, 81, 67, 95; ir (neat) 3.45, 3.52, 5.85 ($C=CCOOCH_3$), 6.12, 6.9, and 7.0 (equal intensity), 7.25, 7.45, 7.6, 8.1 (sh), 8.25, 8.4, 8.65, 9.0, 9.55, 12.35, 12.75, 13.15, 14.0 μ; nmr δ 1.04 (d, J = 6 Hz, 3 H, CH_3CH), 2.34 (m, 3 H, $CH_2C=CCH$), 3.7 (s, 3 H, $COOCH_3$), 5.6 (t, 1 H, CH=C).

Anal. Calcd for $C_{18}H_{32}O_2$: *m/e* 280.2402. Found: *m/e* 280.2408.

Mixture of Muscone (11) and 2-Methylcyclopentadecanone (12).—Without further purification the above obtained crude oil (19 g) containing **9** and **10** (7:3) was added to slowly stirred concentrated sulfuric acid (42 ml) at 0°. After stirring for several minutes, chloroform (50 ml) was added and the temperature of the mixture was raised to 40°. Sodium azide (6.2 g, 0.095 mol) was added to the reaction mixture in small portions over a period of 30 min while maintaining the temperature between 35 and 40°. Stirring was continued for 5 min at 40° followed by cooling the reaction mixture to below 5° and then pouring it into wet ice (200 g). Then the whole mixture was steam distilled at a temperature of 100–200° (steam temperature) to obtain approximately 4 l. of distillate. The distillate was saturated with solid sodium chloride and extracted with ether. The ether extract was washed with saturated sodium chloride solution, dried (Na_2SO_4), and on evaporation of solvent yielded 12 g of crude ketone which was chromatographed on silicic acid (200 g)–0–10% ether in hexane yielded 11.1 g (yield 78.7% on the basis of **7**) of liquid containing the mixture of muscone (**11**) and 2-methylcyclopentadecanone (**12**). All our attempts to separate muscone (**11**) from 2-methylcyclopentadecanone (**12**) either by column chromatography or by glc were unsuccessful. The mass spectrum of the mixture of **11** and **12** showed a molecular ion peak at *m/e* 238; ir (neat) 5.85 μ (C=O); nmr (mixture of **11** and **12**) δ 0.9 (d, J = 6 Hz, $CH_3CHCH_2C=O$), 0.98 (d, J = 6 Hz, $CH_3CHC=O$), 1.3 (s, internal methylene H), 2–2.5 (m).

Anal. (mixture of **11** and **12**). Calcd for $C_{16}H_{30}O$: *m/e* 238.2296. Found: *m/e* 238.2293.

Separation of 9 and 10 by Column Chromatography.—A mixture of **9** (70%) and **10** (30%) (8.7 g) was first chromatographed on silicic acid (185 g). Ether (3%) in hexane eluted a fraction (fraction 1, 4.5 g) enriched with **9** (80%); 5–50% ether in hexane eluted another fraction (fraction 2, 3.1 g) which contained **9** and **10** (1:1). By repeated chromatography (five times) of fraction 1 and 2 separately on neutral alumina (activity II, 150–350 g), pure **9** (1.8 g) and a fraction (0.3 g) containing 93% **10** and 7% **9** were obtained.

Muscone (11).—Pure **9** (2 g, 0.007 mol), obtained by the repeated column chromatography, was slowly added to concentrated sulfuric acid (5.2 g) at 5° over 15 min. After this addition chloroform (20 ml) was added to the reaction mixture and warmed to 40°. At this temperature sodium azide (0.6 g, 0.0095 mol) was added in small portions. The mixture was stirred for 15 min at 40°, cooled to 5°, and poured into wet ice (50 g). The whole mixture was then transferred into a microsteam distillation apparatus and steam distilled (pot temperature 160° and head temperature 140°) to obtain approximately 500 ml of distillate. The distillate was saturated with solid sodium chloride and extracted with ether. The ether extract was dried (Na_2SO_4) and on removal of solvent yielded 1.2 g of crude oil which was chromatographed on silicic acid (80 g)–2% ether in hexane (500 ml) eluted 1 g (yield 58.8%) of pure muscone (**11**). Glc (both Carbowax 20M and silicone SE-30) of **11** gave one peak whose mass spectrum showed molecular ion peak at *m/e* 238 and other major peaks at *m/e* 55, 41, 43, 85, 69, 71; ir (neat) 3.42, 3.5, 5.85 (C=O), 6.85, 7.1, 7.3, 7.85, 8.4, 8.7, 8.9, 9.5, 14.0 μ (broad); nmr δ 0.92 (d, J = 6 Hz, 3 H, CH_3CH), 1.1–2.0 (m, 23 H, with s at 1.30), 2.1–2.4 (m, 4 H, CH_2COCH_2). (All these spectral data were superimposable with those of natural muscone.)

Anal. Calcd for $C_{16}H_{30}O$: *m/e* 238.2296. Found: *m/e* 238.2298.

2-Methylcyclopentadecanone (12).—Cyclopentadecene carboxylate **10** (0.15 g containing 7% **9**, obtained by column chromatography) was added to concentrated sulfuric acid (1 ml) at 5°. The mixture turned dark. Chloroform (3 ml) was added and warmed to 40°. Sodium azide (0.1 g) was added over 15 min and stirred for an additional 15 min at 40°. Then the reaction mixture was cooled to 5°, poured into wet ice (15 g), and steam distilled (pot temperature 210° and head temperature 160°) to obtain 300 ml of distillate which was saturated with solid sodium chloride and extracted with ether. The ether extract was dried (Na_2SO_4) and on removal of solvent yielded 0.1 g (yield 78.7%) of 2-methylcyclopentadecanone (**12**). Glc of **12** gave one peak whose mass spectrum showed molecular ion peak at *m/e* 238 and other major peaks at *m/e* 55, 41, 72, 43, 69; ir (neat) 3.45, 3.51, 5.85 (C=O), 6.85, 6.89 (sh), 7.1, 7.2 (sh), 7.25, 7.4, 7.8, 8.35, 8.65, 8.85, 9.35, 9.5, 9.8, 14.0 μ (broad); nmr δ 1.0 (d, J = 6 Hz, 3 H, CH_3CH), 1.1–2.2 (m, 24 H, with s at 1.32), 2.32 (m, 3 H, $CHCOCH_2$).

Anal. Calcd for $C_{16}H_{30}O$: *m/e* 238.2296. Found: *m/e* 238.2295.

Cyclopentadecanone (Exaltone, 19).—Bromine (10.24 g, 0.064 mol) was added dropwise to a solution of cyclohexadecanone **17** (8.2 g, 0.032 mol) in anhydrous ether (45 ml) at 5°. The reaction mixture was poured over ice water (45 g), benzene (25 ml) was then added, and the organic layer was separated. The aqueous layer was extracted with benzene. The combined benzene extract was washed with saturated solution of sodium bicarbonate and a saturated solution of sodium chloride until neutral, dried ($MgSO_4$), and on removal of solvent yielded 12.8 g (yield 96.2%) of crude dibromide. Without further purification and characterization the solution of crude dibromide (12.5 g) in anhydrous benzene (10 ml) was slowly added to the suspension of sodium methoxide (5.68 g, 0.105 mol) in anhydrous benzene (50 ml) over 20 min at 25–30°. Stirring was followed for an additional 15 min at 25°. The reaction mixture was poured into ice–water (50 g) and the organic layer was separated. The aqueous layer was extracted with benzene. The combined benzene extract was washed first with 5% hydrochloric acid solution and then with a saturated solution of sodium chloride, dried ($MgSO_4$), and on removal of solvent yielded 12.1 g of crude 1-carboxymethyl-1-cyclopentadecene (**18**). Pure material was isolated by glc (Carbowax 20M). The mass spectrum of **18** showed molecular ion peak at *m/e* 266 and other major peaks at *m/e* 41, 55, 81, 67, 95; ir (neat) 3.45, 3.54, 5.85 ($C=CCOOCH_3$), 6.15, 6.9 (sh), 7.0, 7.3, 7.45, 7.6, 8.15 (sh), 8.25 (sh), 8.4, 8.7, 9.8, 12.35 (broad), 13.55, 14.1 μ.

Anal. Calcd for $C_{17}H_{30}O_2$: *m/e* 266.2245. Found: *m/e* 266.2247.

Without further purification the unsaturated ester **18** (11.24 g, 0.04 mol) was added to concentrated sulfuric acid (25 ml) at

0° under nitrogen. After the addition was completed, chloroform (25 ml) was added and the temperature was raised to 35°. Sodium azide (3.12 g, 0.048 mol) was added in small portions at 35-40° over 20 min, and the mixture was stirred for additional 15 min. The reaction mixture was cooled to 25° and poured into ice-water (100 g), after which the whole mixture was steam distilled to obtain 3 l. of distillate. The distillate was saturated with solid sodium chloride and extracted with ether. The extract was washed with saturated sodium chloride solution, dried, and upon evaporation of solvent yielded 6.7 g yellow solid which was crystallized from petroleum ether (bp 30-60°) to obtain 6 g (yield 77.8%) of exaltone (**19**), mp 61-62°. Ir and mass spectrum were superimposable with those spectra of the authentic sample.

17-Oxobicyclo[14.1.0]heptadecane (13).—A solution of monoepoxide **2** (5 g) in methanol (100 ml) was hydrogenated under normal temperature and pressure using 10% palladium on carbon (1.5 g) as a catalyst. After usual work-up 5 g of solid saturated epoxide **13** (mp 33-35°) was obtained. Glc (Carbowax 20M) showed two peaks. The mass spectrum of the mixture of two isomers showed molecular ion peak at *m/e* 238 and other major peaks at *m/e* 55, 41, 82, 69, 67, 95; ir (neat) (mixture of two isomers) 3.42, 3.5, 6.87, 7.25, 7.3, 7.8, 7.95, 8.95, 9.4, 10.9, 11.25, 11.9, 12.9, 13.5, 14.0 μ (after 7.95 μ all bands were weak); nmr δ 1.35 (m with a s at 1.35, internal methylene), 2.46 (m, 1 H, epoxy CH), 2.7 (b, 1 H, epoxy CH).

Reaction of Saturated Epoxide 13 with Lithium Diethylamide.—To an ice-cold solution of diethylamine (8 g, 0.1 mol) in anhydrous ether (3.50 ml), 15% commercial butyllithium in hexane (62.5 ml, 0.1 mol) was added under a nitrogen atmosphere. After 10 min, a solution of **13** (10 g, 0.042 mol) in anhydrous ether (50 ml) was added, stirred for 1 hr at room temperature, and then refluxed for 51 hr. The reaction mixture was cooled and poured into ice-cold water, and the organic layer was separated. The aqueous layer was saturated with solid sodium chloride and extracted with ether, and the combined organic layers were washed with 50% sodium chloride solution and dried (Na_2SO_4). Evaporation of solvent yielded 9.4 g of material which was chromatographed on silicic acid (130 g)-hexane eluted 0.5 g (yield 5.4%) of 1,3-cyclohexadecadiene **14**; 10% ether in hexane eluted 6.2 g of mixture of epoxide **13** and 2-*trans*-cyclohexadecen-1-ol (**15**); 50% ether in hexane eluted another 2.6 g of pure alcohol **15**. The mixture of **13** and **15** (6.2 g) was rechromatographed on silicic acid (150 g)-5% ether in hexane eluted 2.5 g (25%) of epoxide **13**; and 10% ether in hexane eluted 3.6 g of alcohol **15**. The total amount of **15** thus obtained was 6.2 g (yield 62%). Glc of **15** showed one peak whose mass spectrum showed molecular ion at *m/e* 238 and other major peaks at *m/e* 41, 55, 57, 83, 43, 70; ir (neat) 3.0 (OH), 3.5, 6.02, 6.9, 6.95 (sh), 7.1, 7.3, 7.45, 7.75, 8.5, 8.7, 8.95, 9.4, 9.85 (C=CCHOH), 10.1, 10.35 (strong, trans CH=CH), 11.9, 12.7, 13.8 μ (broad); nmr δ 2.08 (b, 2 H, CH_2C=C), 2.88 (s, 1 H, OH), 3.96 (b, 1 H, CHO), 5.4 (m, 2 H, CH=CH).

Anal. Calcd for $C_{16}H_{30}O$: *m/e* 238.2296. Found: *m/e* 238.2300.

The mass spectrum of **14** showed a molecular ion peak at *m/e* 220 and other major peaks at *m/e* 80, 41, 67, 81, 82, 68; ir (neat) 3.35 (very weak), 3.45, 3.51, 5.95 and 6.05 (very weak), 6.9, 7.3, 7.45, 7.75, 8.15, 9.3, 10.15, and 10.35 (strong, broad, trans CH=CH), 13.9 μ (weak, broad); nmr δ 1.35 (strong s, internal methylene H), 2.11 (diffused q, 4 H, CH_2C=CC=C-CH), 5.26-6.5 (m, 4 H, CH=CHCH=CH).

Anal. Calcd for $C_{16}H_{28}$: *m/e* 220.2190. Found: *m/e* 220.2189.

Reaction of Saturated Epoxide 13 with Butyllithium.—Epoxide **13** (28 g) was treated with 15% butyllithium (75 ml) exactly as in the case of **2**. After usual work-up and column chromatography obtained were 15.2 g (yield 54.2%) of **17** (mp 58-60°, undepressed with the authentic sample) and 5.3 g (yield 18.9%) of **15**.

2-Cyclohexadecen-1-one (16).—Alcohol **15** (6 g) was oxidized with a solution of chromium trioxide in the same way as in the case of compound **3**. After usual work-up and column chromatography, there was obtained 4.2 g (yield 70%) of ketone **16**. The mass spectrum showed the molecular ion peak at *m/e* 236 and other major peaks *m/e* 55, 41, 81, 96; ir (neat) 3.35, 3.45, 3.52, 5.88 and 5.94, sh of 6.02 (C=CCO), 6.2, 6.9, 6.98, 7.29, 7.35, 7.45, 7.89, 8.3, 8.75, 8.95, 10.25 (strong, trans CH=CH), 11.3, 13.95 μ; nmr δ 1.28 (strong s, internal methylene H), 1.6 (broad m), 2.4 (m, 4 H, CH_2C=$CCOCH_2$), 5.94-6.10 (d, 1 H) and 6.50-6.80 (m, 1 H, CH=CHC=O).

Anal. Calcd for $C_{16}H_{28}O$: *m/e* 236.2140. Found: *m/e* 236.2135.

3-Methylcyclohexadecanone (7).—The ethereal (80 ml) solution of **16** (4 g) was treated with methylmagnesium bromide (7.2 ml) in the presence of cuprous chloride (0.11 g) exactly as in the case of **5**. After usual work-up and column chromatography obtained was 3.5 g (yield 80%) of **7**.

Autoxidation of 1,9-Cyclohexadecadiene (1).—Air was passed through a test tube containing 1,9-cyclohexadecadiene **1** (5 g) at 60-65°. After every 24 hr the oxidation was followed by glc. After 114 hr of passing air, an appreciable amount of oxygenated products was formed. The material became viscous and weighed 6.8 g. Glc (Carbowax 20M) of this autoxidized material indicated the formation of four isomeric monoepoxides (four peaks, 13%), whose ir and mass spectra were superimposable with the spectra of the four epoxides **2** formed by the epoxidation of 1,9-cyclohexadecadiene **1**, and two α,β-unsaturated ketones (two peaks, 9%), whose ir and mass spectra were superimposable with the spectra of the two ketones **5** obtained by the chromium trioxide oxidation of alcohol **4**.

Registry No.—*cis,cis*-**2**, 31446-71-6; *trans,trans*-**2**, 31446-72-7; *cis,trans*-**2**, 31489-81-3; *trans,cis*-**2**, 31446-73-8; *trans,trans*-**3**, 31489-82-4; *trans,cis*-**3**, 31446-74-9; *trans,trans*-**5**, 31446-75-0; *trans,cis*-**5**, 31446-76-1; *trans*-**6**, 31446-77-2; *cis*-**6**, 31446-78-3; **7**, 31446-79-4; **8**, 31446-80-7; **9**, 31446-81-8; **10**, 31446-82-9; **11**, 956-82-1; **12**, 22460-48-6; *cis*-**13**, 31446-85-2; *trans*-**13**, 31446-86-3; **14**, 31489-83-5; **15**, 31446-87-4; **16**, 31446-88-5; **17**, 2550-52-9; **18**, 31446-90-9; **19**, 502-72-7.

Acknowledgment.—The authors express their gratitude to Dr. W. I. Taylor. Without his constant encouragement, this paper would probably not have been written. The authors also wish to thank Mr. H. A. Bondarovich for doing all high-resolution mass spectrometric analyses.