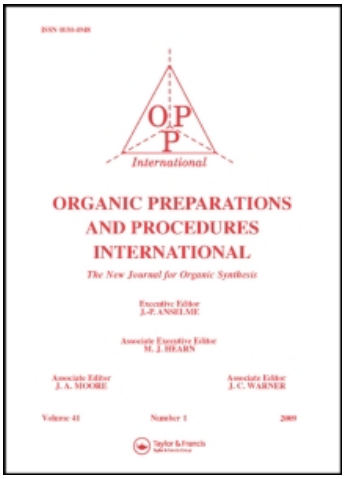

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AN EFFICIENT SYNTHESIS OF (±)-MUSCONE

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AN EFFICIENT SYNTHESIS OF (±)-MUSCONE

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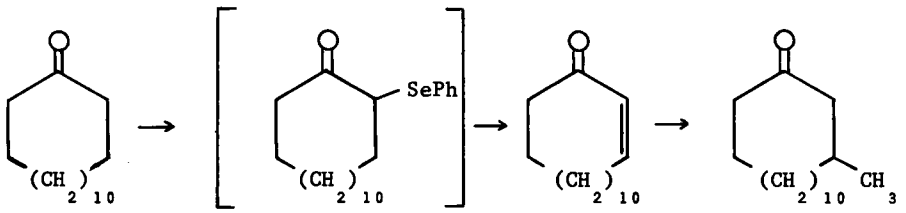
The necessity to effect a short synthesis of the commercially valuable musk and mammalian pheromone (±)-muscone (I)[1] from readily available starting materials has led to the development of an efficient preparation of this 15-membered cyclic ketone. Treatment of commercial exaltone[2]



II III IV I

(cyclopentadecanone, II) with lithium diisopropylamide at -78° followed by addition of benzeneselenyl bromide[3-5] to the enolate, gave α-phenylseleno cyclopentadecanone III. Oxidation of III with excess 30% H_2O_2 followed by selenoxide β-elimination[6-8] proceeded smoothly below 20° yielding the desired enone (IV)[9] as the major product. Treatment of crude IV with dimethylcopperlithium[10] in ether at -10° readily afforded (±)-muscone I. (±)-Muscone was obtained from exaltone in 79% yield. The synthesis described herein provides I in overall higher yield and in fewer steps than the two other syntheses reported.[11,12] Total syntheses of this ketone from other starting materials are also available.[13]

EXPERIMENTAL

The reactions were carried out under a dry nitrogen atmosphere. All glassware was oven dried, assembled hot and allowed to cool under a nitrogen stream. Syringes were flushed with dry nitrogen before use. Tetrahydrofuran (THF) was freshly distilled under nitrogen from $LiAlH_4$; diisopropylamine was distilled under nitrogen from CaH_2. Cuprous iodide was purified via Soxhlet extraction with THF and was subsequently dried under vacuum at 25° for 24 hr.

Vapour phase chromatography was performed on a Hewlett-Packard 7610A chromatograph using helium as a carrier gas on 6 mm OD, 2 mm ID 6-ft glass U-tube columns of 10% DEGS on Chromosorb WAW and 3% OV-1 on GAS-CHROM Q. Nuclear magnetic resonance spectra were recorded on a Varian A-60. Signals are reported downfield from tetramethylsilane in ppm(δ). Infrared spectra were recorded on a Perkin-Elmer model 257 grating spectrometer and are reported in cm^{-1}. Low resolution mass spectra were run on Finnigan 3200 Electron Impact GC-MS and 3300 Chemical Ionization GC-MS systems with 6000 computer data system; high resolution spectra were recorded on an AEI MS-902 mass spectrometer.

2-Cyclopentadecenone IV.- To a stirred solution of 54.2 mmol of lithium diisopropylamide at -78° (prepared from 7.60 ml diisopropylamine in 300 ml THF and 22.1 ml of 2.45 M n-BuLi in hexane) was added 10.1 g (45.1 mmol) of II in 100 ml THF, dropwise over 45 min. The solution was stirred for 10 min, then 54.2 mmol of benzeneselenyl bromide (prepared by addition of 1.39 ml of Br_2 to 8.45 g of diphenyldiselenide in 100 ml THF) was added rapidly dropwise. The solution was allowed to warm to 0° and 30 ml of H_2O and 8 ml acetic acid were added, followed by dropwise addition of 30 ml of 30% H_2O_2. After gas evolution had ceased (45 min), the solution was stirred an additional 45 min at room temp and then poured into a mixture of 600 ml of sat aq $NaHCO_3$ solution and 600 ml 1:1 ether:hexane. The organic layer was washed successively with H_2O, 0.1 N HCl, H_2O, brine, and dried (Na_2SO_4); the solvent was removed in vacuo, leaving 10.95 g of crude IV. Glpc analysis (3% OV-1 and 10% DEGS) showed one major peak (92%, IV) and one minor peak (8%, III). A sample of crude IV purified by column chromatography (florisil, or 20% $AgNO_3$-silica gel, hexane) and pure by glpc criteria exhibited the following spectral properties: Ir: ν_{max}^{film} 2910, 2835, 1692, 1665, 1622, 1453, 1438, 1338, 1270, 1200, and

970 cm^{-1}; nmr (CCl_4): δ 1.10-2.06 [m, 20H, $-(CH_2)_n-$], 2.09-2.57 (m, 4H, $-CH_2COC=CCH_2$), 5.95-7.02 (m, 2H, $-HC=CHCO-$); ms: m/e 222 $(M)^+$, 81 (base), 164, 109, 97, 96, 95, 68, 67, 55, 41; chemical ionization ms (CH_4): m/e 223 $(M+1)^+$, 251 (M+29), 263 (M+41).

(±)-Muscone I.- A solution of IV (10.9 g, 49.1 mmol, used as obtained, vide supra) in ether (150 ml) was added dropwise to a slurry of dimethylcopperlithium [prepared by dropwise addition of 143.5 ml (223.9 mmol) of 1.56 M MeLi in ether to a stirred suspension of 21.78 g (114.4 mmol) of purified CuI in 350 ml anh ether at 0°]. The mixture was stirred for 40 min at -10°, then poured into 1 l. sat NH_4Cl solution. Enough aq NH_4OH was added to dissolve the salts. The ethereal layer was washed with 20% aq NH_4OH, H_2O, brine, and dried (Na_2SO_4). The solvent was removed in vacuo, leaving 10.78 g of crude ketone I as a yellow oil. Column chromatography (florisil, hexane) afforded 8.97 g of (±)-muscone I (95% pure by glpc). A glpc pure sample of I exhibited the following spectral properties: Ir: ν_{max}^{film} 2915, 2842, 1713, 1458, 1404, 1361, 1268, 1118, 1075, 1046, 1008, and 704 cm^{-1}; nmr (CCl_4): δ 0.92 (d, J = 6 Hz, 3H, CH_3-CH), 1.1-1.8 [m, 23H, $-(CH_2)_n-$, and CH_3CH-], 2.1-2.5 (m, 4H, $-CH_2COCH_2-$); ms: m/e 238 $(M)^+$, 55 (base), 223, 220, 209, 180, 125, 85, 71, 69, 43, 41; chemical ionization ms (CH_4): m/e 239 $(M+1)^+$, 267 (M+29), 279 (M+41). The spectral data were superimposable with those of an authentic sample of (±)-muscone I.[14]

Anal. Calcd for $C_{16}H_{30}O$: m/e 238.2296. Found: m/e 238.2294. The overall yield of I from II was 79%.

REFERENCES

1. H. Walbaum, J. prakt. Chem., 73, 408 (1906); L. Ruzicka, Helv. Chim. Acta, 9, 715 (1926).

2. Exaltone (97% pure via glpc) was obtained from Aldrich Chem. Co.

3. H. J. Reich, I. L. Reich and J. M. Renga, J. Am. Chem. Soc., 97, 5434 (1975); H. J. Reich, I. L. Reich and J. M. Renga, ibid, 95, 5813 (1973).

4. K. B. Sharpless, R. F. Lauer and A. Y. Teranishi, ibid., 95, 6137 (1973).

5. When the lithium enolate of II was treated with diphenyldiselenide either in the presence or absence of HMPA, only 15-20% of enone IV was obtained.

6. K. B. Sharpless, M. W. Young and R. F. Lauer, Tetrahedron Lett., 1959 (1973).

7. D. N. Jones, D. Mundy and R. D. Whitehouse, Chem. Commun., 86 (1970).

8. K. B. Sharpless and R. F. Lauer, J. Am. Chem. Soc., 95, 2697 (1973).

9. Reaction of an ethyl acetate solution of exaltone II with PhSeCl at room temperature (see ref. 4) and oxidation with 30% H_2O_2 gave nearly a 60% yield of enone IV. The yield was determined by glpc relative to n-hexadecane as an internal standard.

10. H. O. House, W. L. Respess and G. L. Whitesides, J. Org. Chem., 31, 3128 (1966).

11. L. Ruzicka and M. Stoll, Helv. Chim. Acta, 17, 1308 (1934).

12. B. D. Mookherjee, R. R. Patel and W. O. Ledig, J. Org. Chem., 36, 4124 (1971).

13. G. Stork and T. L. Macdonald, J. Am. Chem. Soc., 97, 1264 (1975), and references therein.

14. The authors wish to thank Dr. W. I. Taylor of International Flavors and Fragrances for an authentic sample of (±)-muscone, R. Petcavich, N. Pelick and D. Mahadevan for their assistance, Ms. S. Peters and Ms. C. Corin for preparation of this note and D. Hindenlang and Dr. R. Minard for the mass spectral data.

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