

Synthesis of (*R,S*)-Muscone

Short Communication

Hans G. Fliri, Dieter Scholz und Anton Stütz*

SANDOZ-Forschungsinstitut, Brunnerstraße 59
A-1235 Wien, Austria

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Construction of the carbon-skeleton of (*R,S*)-muscone was achieved by reacting methyllithium with the dianion of cyclopentadecanedione-1,3, itself accessible by hydration of cyclopentadecanediene-1,3.

(Keywords: Cyclopentadecanedione-1,3; Cyclopentadecanediene-1,3; (*R,S*)-Muscone, synthesis)

Synthese von (R,S)-Muscon (Kurze Mitteilung)

Die Konstruktion des Kohlenstoffgerüsts von (*R,S*)-Muscon gelingt durch Reaktion des Dianions von Cyclopentadecandion-1,3, das durch Hydratisierung von Cyclopentadecandiin mit Methyllithium erhältlich ist.

Recently one of us reported on the synthesis of macrocyclic 1,3-diketones and heterophanes¹. We now wish to demonstrate the potential of this method on a short synthesis of (*R,S*)-muscone² (**6**).

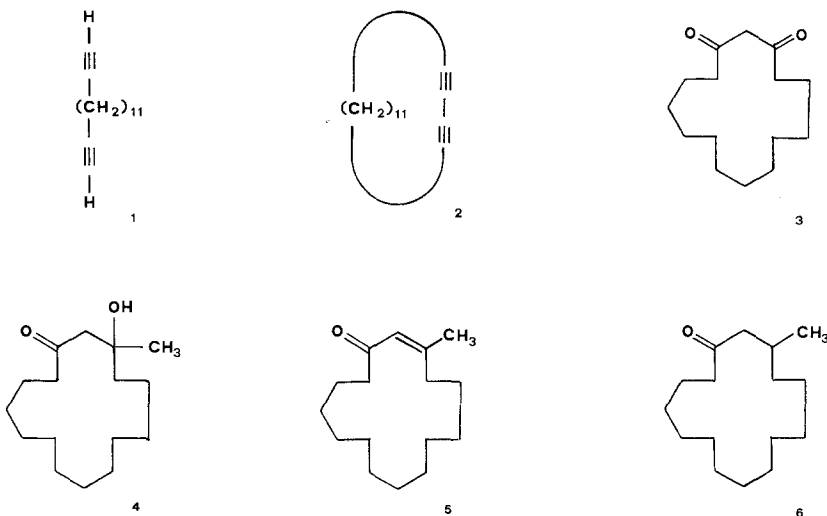
Acetylene was alkylated with 1,11-dibromoundecane³ (NaNH₂, NH₃) to give 1,14-pentadecanediene (**1**)⁴ in 95% yield. Oxidative cyclization (4.5 eq. cupric acetate in ether/benzene/pyridine 1 : 1 : 6 using a high dilution apparatus) afforded cyclopentadecanediene-1,3⁴ which was hydrated¹ yielding cyclopentadecanedione-1,3 (**3**)^{2a} (78%), mp 49–51°; IR (CHCl₃) 1685, 1600 cm⁻¹; NMR (CDCl₃) 1.20–1.80 ppm (20H), 2.2–2.4 ppm (4H), 5.55 ppm (1H); *m/e* 238.

Treatment of **3** in dry THF at 0° with 2 eq. NaH for 30 min, followed by 3 eq. methyllithium for 2 h yielded aldol **4** which without further

purification was dehydrated (*p*-TsOH, H₂O, dichloromethane, 25° 3h) to give enone **5** as a 1:4 mixture of *Z*- and *E*-isomers, $\lambda_{\max} = 235$ nm (hexane), $\epsilon = 12700$; IR (CHCl₃) 1615, 1600 cm⁻¹.

5 was converted to (*R,S*)-muscone **6** (63% from **3**) by catalytic hydrogenation^{2a} and shown to be identical with an authentic sample⁵ by GC⁶ and spectroscopic⁶ comparison.

The skilful technical assistance of Miss *W. Granitzer* is gratefully acknowledged.



References and Notes

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- ² For a review of syntheses of Muscone see *S. Abe, T. Eto, and Y. Tsujito*, *Cosmetics and Perfumery* **88**, 67 (1973). Recent syntheses of Muscone: a) *Y. Ito and T. Saegusa*, *J. Org. Chem.* **42**, 2326 (1977). b) *A. Fischli, Q. Branca, and J. Daly*, *Helv. Chim. Acta* **59**, 2443 (1976). c) *Q. Branca and A. Fischli*, *Helv. Chim. Acta* **59**, 925 (1976). d) *H. Taguchi, H. Yamamoto, and H. Nozaki*, *Tetrahedron Letters* **1976**, 2617. e) *G. Stork and T. L. Macdonald*, *J. Amer. Chem. Soc.* **97**, 1265 (1975). f) *T. Hiyama, T. Mishima, K. Kitatani, and H. Nozaki*, *Tetrahedron Letters* **1974**, 3297. g) *R. Baker, R. C. Cookson, and J. R. Vinson*, *Chem. Commun.* **1974**, 515. h) *R. Baker, B. N. Blackett, and R. C. Cookson*, *Chem. Commun.* **1972**, 802. i) *B. C. Mookherjee, R. R. Petel, and W. O. Ledig*, *J. Org. Chem.* **36**, 4142 (1971). j) *R. D. Mookherjee, R. N. Trenkle, and R. R. Petel*, *J. Org. Chem.* **36**, 3266 (1971). k) *D. Felix, J. Schreiber, G. Ohloff, and A. Eschenmoser*, *Helv. Chim. Acta* **54**, 2896 (1971). l) *K. Utimoto, M. Tanaka, M. Kitai, and H. Nozaki*, *Tetrahedron Letters* **1978**, 2301.

- ³ Purchased from FLUKA AG, Buchs.
- ⁴ *E. P. Zinkevich, I. K. Sarycheva, and N. A. Preobrazhenskii, Zh. Org. Khim. 2, 2021 (1966); CA 66, 75731 k.*
- ⁵ We are indebted to Dr. *W. Skorjanetz*, Firmenich SA, Geneva, for generously providing a sample of (*R,S*)-muscone.
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