

A SIMPLE AND FACILE SYNTHESIS OF d,l-MUSCONE

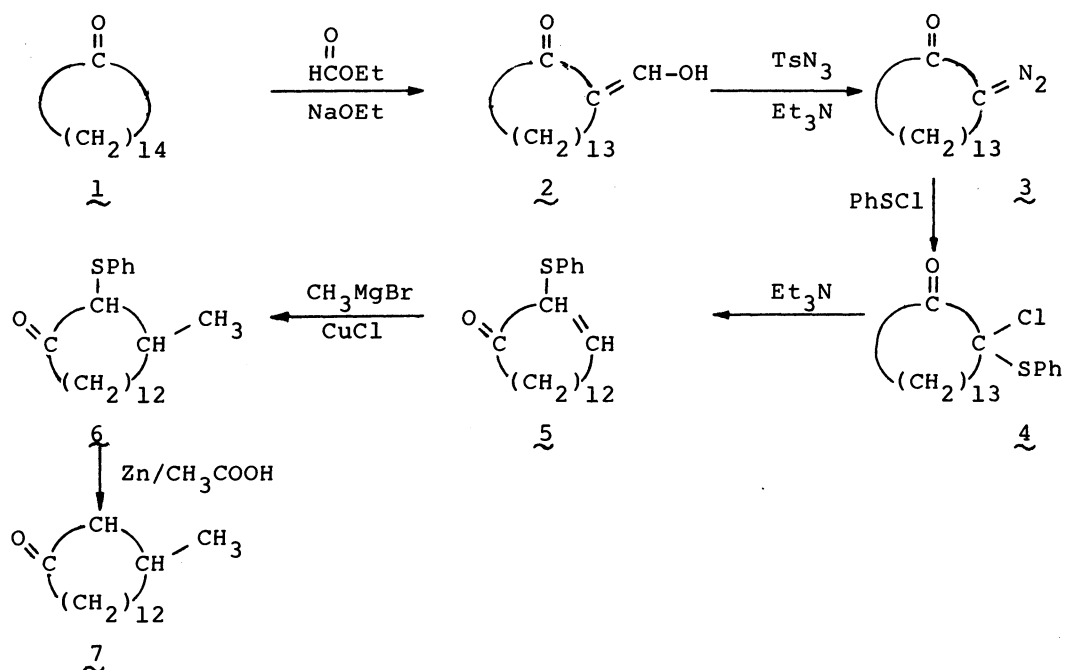
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An efficient method for the synthesis of d,l-muscone has been developed.

The necessity to effect a short synthesis of the valuable musk and mammalian pheromone d,l-muscone¹⁾ from readily available starting materials has led to the development of an efficient preparation of this 15-membered cyclic ketone. In connection to our previous work,²⁾ we now wish to report here on a new route for the synthesis of d,l-muscone, with which we have now achieved quite a short and efficient route to the target molecule. Our synthetic strategy is based upon the preparation of α -(phenylthio)cycloalkenones, followed by introduction of the methyl group by the Michael addition of CH_3MgBr and subsequent reductive desulphurization (Scheme 1).

Treatment of commercial exaltone (1) with ethyl formate and sodium ethoxide in dry ether provided an 85% yield of the 2-(hydroxymethylene)cyclopentadecanone (2) which was then converted to 2-diazocyclopentadecanone (3) by the action of p-toluenesulphonyl azide and triethylamine. The crude product was purified by column chromatography (silica gel, hexane-dichloromethane 1/1) to give 3 in 60% yield. The reaction of 3 with benzenesulphenyl chloride in dry ether at room temperature for 3 h gave 2-chloro-2-(phenylthio)cyclopentadecanone (4) in nearly quantitative yield. Addition of triethylamine to a stirred solution of 4 in dry ether resulted in elimination of HCl and 2-(phenylthio)-2-cyclopentadecenone (5) was isolated after chromatography with a short column (silica gel, hexane-dichloromethane 1/2) in 70% yield. The Michael addition of methylmagnesium bromide to 5 in ether in the presence of copper(I) chloride smoothly gave (6) in 65% yield. Desulphurization of 6 with zinc in refluxing acetic acid furnished 85% yield of d,l-muscone (7).^{3,4)} Spectral properties of the synthetic d,l-muscone were identical in all respects with those of an authentic sample.



Scheme 1.

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References

- 1) d,l-Muscone is a naturally occurring 15-membered cyclic ketone with musk odor. It is the principal constituent (1%) of musk pod obtained from the male deer *Moschus moschiferus*.
- 2) M.A. McKervery and P. Ratananukul, *Tetrahedron Lett.*, **23**, 2509 (1982); M.A. McKervery and P. Ratananukul, *ibid.*, **24**, 117 (1983).
- 3) Satisfactory spectroscopic data were obtained for each reaction product using a chromatographically purified sample.
- 4) For reviews on the synthesis of d,l-muscone see: S. Sakane, K. Maruoka and H. Yamamoto, *Tetrahedron Lett.*, **24**, 943 (1983); L.A. Paquette, G.L. Wells, K.A. Horn, and T.H. Yan, *ibid.*, **23**, 263 (1982); T. Takahashi, T. Nagashima, and J. Tsuji, *ibid.*, **22**, 1359 (1981); B.M. Trost and J.E. Vincent, *J. Am. Chem. Soc.*, **102**, 5680 (1980); J. Tsuji, T. Yamada, and I. Shimizu, *J. Org. Chem.*, **45**, 5209 (1980); L.A. Paquette, W.E. Frietad, D.S. Deine, and T.R. Bailey, *ibid.*, **45**, 3017 (1980).

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