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SYNTHESIS OF dl-MUSCONE

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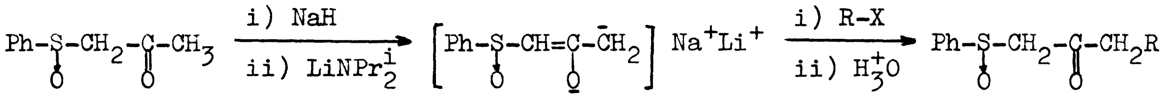
dl-Muscone was prepared in a good yield by cyclization of β-keto ω-halo sulfoxide (**3**), followed by thermolysis and methylation.

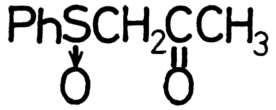
The dianions of β-keto sulfoxides have recently been applied to synthesis of some ketones by I. Kuwajima et al. and P. Grieco et al.¹⁾



$$\mathrm{Ph\text{-}\underset{\underset{O}{\downarrow}}{S}\text{-}CH_2\text{-}\underset{\underset{O}{\|}}{C}\text{-}CH_3} \xrightarrow[\text{ii) LiNPr}^{i}_{2}]{\text{i) NaH}} \left[\mathrm{Ph\text{-}\underset{\underset{O}{\downarrow}}{S}\text{-}CH{=}\underset{\underset{\underline{O}}{|}}{C}\text{-}\bar{C}H_2}\right] \mathrm{Na^+Li^+} \xrightarrow[\text{ii) } \mathrm{H_3^+O}]{\text{i) R-X}} \mathrm{Ph\text{-}\underset{\underset{O}{\downarrow}}{S}\text{-}CH_2\text{-}\underset{\underset{O}{\|}}{C}\text{-}CH_2R}$$

In this communication, a new type of dianion of β-keto sulfoxide (**4**) which is available for a synthesis of macrocyclic ketone (**5**) will be described.

The reaction of α-phenylsulfinylacetone (**1**) with sodium hydride and then with 12-bromododecyl iodide (**2**)²⁾ in dimethylformamide at room temperature for 10 hours provided 3-phenylsulfinyl-15-bromopentadecan-2-one (**3**) in a 60% yield. The structure of diastereomeric mixture of **3** was characterized from the following spectral data; ir (neat) 2900, 2840, 1705 (C=O), 1050 (S→O) cm^{-1}; nmr ($CDCl_3$) δ 2.00 and 2.06 (3H, s, $-COCH_3$), 3.37 (2H, t, $-CH_2Br$), 3.66 and 3.78 (1H, t, -SO-CH-CO-). The β-keto ω-bromo sulfoxide (**3**) was treated with 2 equiv of lithium diisopropylamide in tetrahydrofuran³⁾ at 0°C for 2 hours to give 2-phenylsulfinylcyclopentadecanone (**5**) in a 70% yield; ir (neat) 2900, 2840, 1705 (C=O), 1040 (S→O) cm^{-1}; nmr ($CDCl_3$) δ 2.40 (2H, m, $-CH_2CO-$), 3.63 and 3.74 (1H, t -SO-CH-CO-). 2-Cyclopentadecenone (**6**) was obtained in a quantitative yield by the thermolysis of β-keto sulfoxide (**5**) in dry benzene at 80°C for 1.5 hour.⁴⁾ The spectral data of **6** were as follows, ir (neat) 2920, 2840, 1690 (C=O), 1665 (C=O), 1625 (C=C), 1460, 980 cm^{-1}; nmr ($CDCl_3$) δ 2.22 (2H, m, $-CH_2CO-$), 2.42 (2H, dt, $-CH_2$-C=C-CO-), 6.12 (1H, d, -C=CH-CO-), 6.75 (1H, dt, -CH=C-CO-). The α,β-unsaturated ketone (**6**) was converted by the treatment with excess dimethylcopper lithium⁵⁾ in ether at 0°C for 6 hours to dl-muscone in a 90% yield.

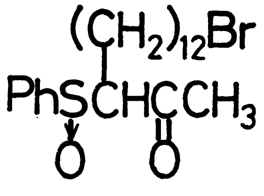


$\mathrm{Ph}\underset{\underset{O}{\downarrow}}{S}\mathrm{CH_2}\underset{\underset{O}{\|}}{C}\mathrm{CH_3}$

1

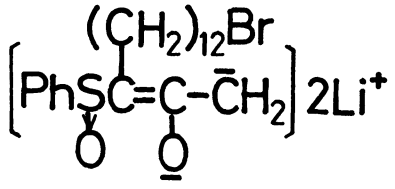
$\mathrm{Br(CH_2)_{12}I}$

2



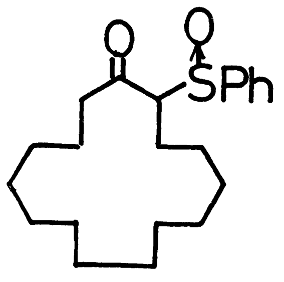
$\mathrm{Ph}\underset{\underset{O}{\downarrow}}{S}\overset{(\mathrm{CH_2})_{12}\mathrm{Br}}{\overset{|}{C}}\mathrm{H}\underset{\underset{O}{\|}}{C}\mathrm{CH_3}$

3



$\left[\mathrm{Ph}\underset{\underset{O}{\downarrow}}{S}\overset{(\mathrm{CH_2})_{12}\mathrm{Br}}{\overset{|}{C}}=\underset{\underset{\underline{O}}{|}}{C}-\bar{C}\mathrm{H_2}\right]2\mathrm{Li}^+$

4



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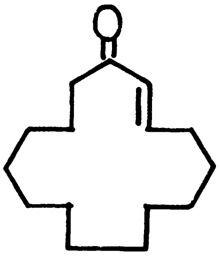
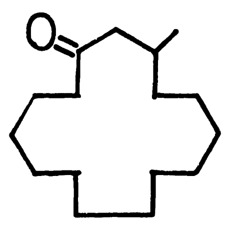


6



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References and Notes

1) I. Kuwajima and H. Iwasawa, Tetrahedron Lett., 107 (1974); P. A. Grieco and C. S. Pogonowski, J. Org. Chem., 39, 732 (1974).

2) 12-Bromododecyl iodide (2) was prepared by a treatment of 1,12-dibromododecane with equimolar of sodium iodide in refluxing ethanol in a 70% yield; nmr ($\mathrm{CDCl_3}$) δ 3.17 (2H, t, $\mathrm{-CH_2I}$), 3.37 (2H, t, $\mathrm{-CH_2Br}$).

3) Dry tetrahydrofuran was used ca. 1 ml per 1 mg of 3.

4) For synthetic applications of thermolysis of sulfoxides, see J. Nokami, N. Kunieda, and M. Kinoshita, Tetrahedron Lett., 2841 (1975); and the references cited therein.

5) E. J. Corey and G. H. Posner, J. Am. Chem. Soc., 89, 3911 (1967).

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