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A FACILE SYNTHESIS OF 1,3-CYCLOALKADIONES

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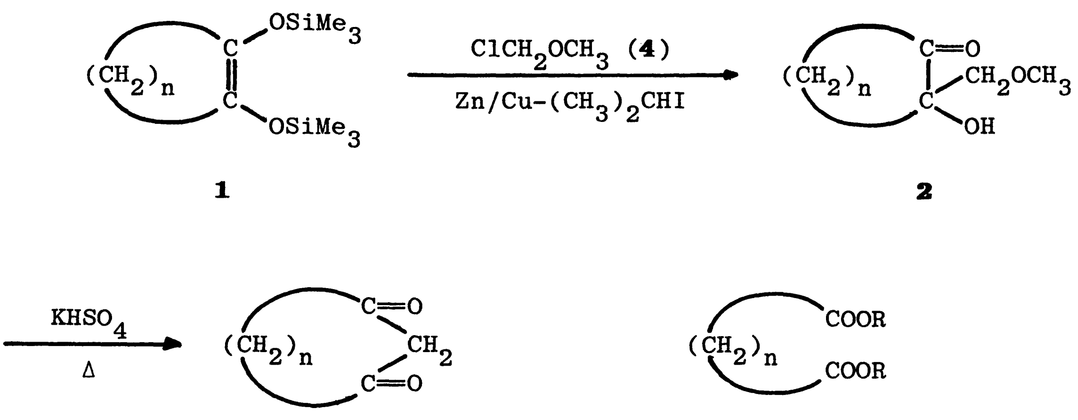
1,3-Cycloalkadiones were prepared by the reaction of 1,2-bis(trimethylsiloxy)cycloalkenes with chloromethyl methyl ether followed by treatment of the resulting 2-hydroxy-2-methoxymethyl cycloalkanones with potassium hydrogen sulfate. The first step of the reactions was effectively catalyzed by active zinc reagents prepared from zinc-copper and alkyl iodides.

Our previous studies on the chemical behavior of the active zinc reagents prepared from zinc-copper couple and alkyl iodides have shown that regioselective introduction of a methoxymethyl group to the α-position of a carbonyl group of ketones[1] can be promoted by the active zinc reagents. On the other hand, because of their high potentiality, 1,3-cycloalkadiones are undoubtedly the important targets in the study on organic synthesis.[2] In this study, we wish to report a novel synthesis of 1,3-cycloalkadiones **3** from 1,2-bis(trimethylsiloxy)cycloalkenes **1** through the reaction of **1** with chloromethyl methyl ether **4** in the presence of the active zinc reagents, followed by acid-catalyzed ring enlargement of the resulting 2-hydroxy-2-methoxymethylcycloalkanones **2**, as shown in the following equation.[3]



1 **2** **3** **5**

Since the 1,2-bis(trimethylsiloxy)cycloalkenes **1** are easily prepared from the corresponding α,ω-dicarboalkoxyalkanes **5**,[4] the present reaction seems to be equivalent to joining two carboalkoxyl group of **5** with the methylene group of **4**.

A typical procedure is as follows: To a solution of zinc-copper couple[5] prepared from 2.54 g (0.04 mol) of zinc dust and 0.40 g (0.004 mol) of cuprous chloride in methylene chloride was added 3.40 g (0.02 mol) of isopropyl iodide,[6] and the solution was refluxed for 30 min with stirring under an atmosphere of nitrogen. Then, to the solution was added 5.12 g (0.02 mol) of 1,2-bis(trimethylsiloxy)cyclohexene **1c** at 0 - 5 °C and subsequently a solution of 1.77 g (0.022 mol) of chloromethyl methyl ether **4** in 5 ml of methylene chloride at 0 - 2 °C in a dropwise manner with stirring. The mixture was stirred for 1 hr at 0 °C and for 2 hr at room temperature successively. Usual working up of the reaction mixture and fractional distillation gave 2-hydroxy-2-methoxymethylcyclohexanone **2c** in a 67% yield: bp 75 °C/3 mmHg; IR (neat) 3090, 1720, 1130 $\mathrm{cm^{-1}}$; NMR (CCl_4, ppm) δ 3.84, 3.75 (d, $J = 8.0$ Hz, 2H), 3.60 (br s, 1H), 3.39 (s, 3H), 2.62 - 1.80 (m, 8H); Anal. Calcd for $C_8H_{14}O_3$: C, 60.74; H, 8.92. Found: C, 60.91; H, 8.93.

Dropwise addition of 1.58 g (0.01 mol) of **2c** to a catalytic amount (0.2 - 0.3 g) of potassium hydrogen sulfate at 170 - 180 °C under reduced pressure (20 - 25 mmHg) gave 0.95 g (Y = 75%) of 1,3-cycloheptadione **3c**, which was identical with an authentic sample[7] in spectroscopic and gas chromatographic analyses.

A variety of 1,3-cycloalkadiones **3a–e** was obtained from the corresponding 1,2-bis(trimethylsiloxy)cycloalkenes **1a–e** by using similar procedures. The yields are shown in Table 1.[8]

Table 1. Synthesis of 1,3-Cycloalkadiones **3**.

	1	**2**		**3**	
	n	Yield (%)a)	Bp (°C/mmHg)	Yield (%)a)	Bp (°C/mmHg)
a	2	51	92/10	52	151b) (lit.[9] 151 - 152)b)
b	3	59	99/10	61	105b) (lit.[10] 105 - 106)b)
c	4	67	75/3	75	122/10 (lit.[7] 84 - 85/1)
d	5	48	80/3	51	95/3 (lit.[2c] 110 - 112/8)
e	6	47	84/3	50	99/3 (lit.[2c] 122/10)

a) Isolated yield.
b) Mp (°C).

On the basis of the simple procedure, generality and moderate yields, the present method is reasonably promising in the synthesis of 1,3-cycloalkadiones.

References and Notes

1) T. Shono, I. Nishiguchi, T. Komamura, and M. Sasaki, *J. Am. Chem. Soc.*, **101**, 984 (1979).

2) Recent papers on synthesis of 1,3-cycloalkadiones:

   a) Y. Ito, S. Fujii, and T. Saegusa, *J. Org. Chem.*, **41**, 2073 (1976); *ibid.*, **42**, 2326 (1977).

   b) E. Nakamura and I. Kuwajima, *J. Am. Chem. Soc.*, **99**, 961 (1977).

   c) K. Schank and B. Eistert, *Chem. Ber.*, **99**, 1414 (1966), and others cited therein.

3) Ring enlargement of 1,2-bis(trimethylsiloxy)-1-cyclobutene to 2,2-dialkyl-1,3-cyclopentadiones has been reported.[2b] The application of this method to synthesis of nonsubstituted cyclic 1,3-diones may be difficult.

4) J. J. Bloomfield, D. C. Owsley, and J. M. Nelke, "Organic Reactions", John Wiley & Sons, Inc., New York (1976), Vol. 23, Chap. 2, P. 259.

5) R. J. Rawson and I. T. Harrison, *J. Org. Chem.*, **35**, 2057 (1970).

6) Substitution of isopropyl iodide with methyl iodide or methylene iodide resulted in decrease in the yield of **2b**. Employment of zinc chloride or iodide instead of the active zinc reagents gave only a trace amount of **2b** and much tarry material.

7) M. W. Cronyu and J. E. Goodrich, *J. Am. Chem. Soc.*, **74**, 3331 (1952).

8) All the products showed satisfactory spectral data for assigned structures.

9) T. Waller, *J. Am. Chem. Soc.*, **74**, 4978 (1952).

10) T. Merling, *Liebigs Ann. Chem.*, **278**, 28 (1894).

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