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FORMATION OF 1,1-DITHIODICARBOXYLIC ACID ESTERS FROM CYCLIC KETONES, CARBON DISULFIDE, AND LITHIUM METHOXIDE

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Methyl esters of 1,1-dithiodicarboxylic acids were formed by the reaction of cyclic ketones with lithium methoxide and carbon disulfide in tetrahydrofuran followed by the treatment with methyl iodide. The reaction proceeds *via* dithiocarboxylation and carbonyl carbon-carbon bond cleavage through an inverse Dieckmann-type reaction.

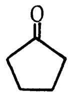
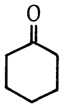
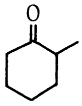
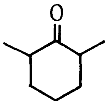
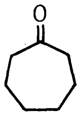
Carbonyl carbon-nitrogen bonds in amides[1)] and ureas[2)] are easily cleaved by the treatment with an strong base such as sodium hydride, butyllithium, or a Grignard reagent and carbon disulfide. However, the reaction of an aliphatic ketone with carbon disulfide under a basic condition usually affords the corresponding dithiocarboxylate or α-ketoketene dithioacetal,[3)] and products resulting from carbonyl carbon-carbon bond cleavage have not been reported. Corey obtained cyclic α-ketoketene dithioacetals in high yields from cyclic ketones by the treatment with carbon disulfide and a bulky base, lithium 4-methyl-2,6-di-*t*-butylphenoxide, followed by methylation.[4)] In contrast to the Corey's method, we use here a less bulky alkoxide, lithium methoxide, in tetrahydrofuran (THF) together with carbon disulfide to cause cleavage of the carbonyl carbon-carbon bonds of cyclic ketones after the usual dithiocarboxylation. This process is useful for a facile preparation of 1,1-dithiodicarboxylic acid esters.

Cyclopentanone (10 mmol), powder of lithium methoxide (10 mmol), and carbon disulfide (10 mmol) were stirred in anhydrous THF (10 ml) for 22 h at 45°C. The consumption of cyclopentanone and the appearance of methoxycarbonyl group (δ 3.65 ppm) were followed by NMR spectrum of the reaction mixture. After methyl iodide was added to the resultant solution followed by stirring for 3 h at room temperature, dimethyl 1,1-dithioadipate <u>5</u> (n=4) and dimethyl ketene dithioacetal <u>7</u> (n=4) were obtained in 51 and 24% yields, respectively, by column chromatography on silica gel. The product 5 was determined by elemental analysis, MS, IR, and NMR spectra,[5] and 7 was confirmed by comparisons of the spectral data with those of the authentic sample prepared by the Corey's method.

Yields of 1,1-dithiodicarboxylic acid esters from other cyclic ketones and lithium alkoxides are summarized in Table 1.

Cyclohexanone gave 5 in moderate yield as in the case of cyclopentanone. A monosubstituted ketone, 2-methylcyclohexanone, underwent cleavage of the carbonyl carbon-unsubstituted carbon bond to give the product, $MeOCOCHMe(CH_2)_4CS_2Me$, whose

Table 1. Reaction of cyclic ketones with lithium alkoxides and carbon disulfide[a]

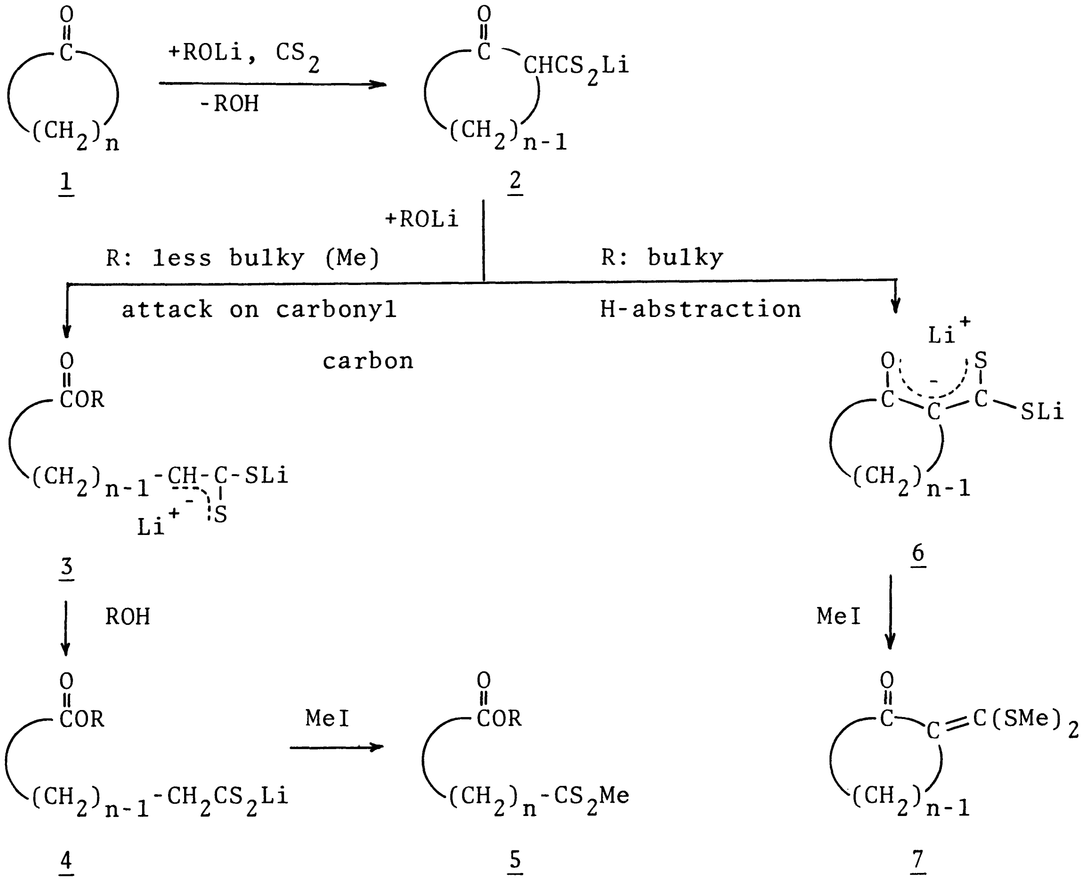
Cyclic ketone	ROLi	Product and yield (%)[b]	
		1,1-Dithiodicarboxylate[c]	Ketene dithioacetal[d]
	MeOLi	51, 68[e] (5; n=4, R=Me) 94-96/0.1[f]	24 (7; n=4)
	EtOLi	trace (5; n=4, R=Et)	23 (7; n=4)
	i-PrOLi	0	33 (7; n=4)
	MeOLi	46, 54[e] (5; n=5, R=Me) 113-116/0.4[f]	20 (7; n=5)
	MeOLi	39, 43[e] ($MeOCOCHMe(CH_2)_4$-CS_2Me) 109-111/0.3[f]	25 (7; n=4, 6-Me)
	MeOLi	0	47 (β-keto dithiocarboxylate)
	MeOLi	0	25 (7; n=6)

a) Cyclic ketone (10 mmol), lithium alkoxide (10 mmol), and carbon disulfide (10 mmol) were stirred in THF (10 ml) for 22 h at 45 °C and then the reaction mixture was treated with an excess amount of methyl iodide for 3 h at room temperature. b) Based on cyclic ketone. c) Isolated yields by column chromatography. d) The yields were determined by NMR spectra. e) Yield of 5 obtained by the reaction using 3 equivalent of methanol and isolated by distillation.[6] f) Bp (°C/mmHg).

structure was supported by NMR spectrum.[5)] From 2,6-dimethylcyclohexanone, large cyclic ketones,[7)] such as cycloheptanone and cyclododecanone, and camphor, 1,1-dithiodicarboxylic acid esters were not obtained. Acyclic ketones such as dipentyl ketone or propiophenone gave low yields (below 9%) of the products resulting from carbonyl carbon-carbon bond cleavage under the same conditions.

The reaction will be controlled by the steric effect of lithium alkoxide as shown in Scheme 1. Lithium dithiocarboxylate 2 initially formed from a ketone, lithium alkoxide, and carbon disulfide may be a common intermediate for the formation of 5 and 7. Less bulky methoxide can undergo nucleophilic attack on carbonyl carbon of 2 to cause cleavage of the carbonyl carbon-carbon bond and to form 3 which converts to 5 by methylation after protonation with methanol. This carbonyl carbon-carbon bond fission in cyclic ketones corresponds to an inverse Dieckmann-type reaction and its feasibility may be due to stabilization of the resultant carbanion by α-dithiocarboxylate. On the other hand, a bulky alkoxide does not attack on the

Scheme 1



carbonyl carbon but it abstracts the activated α-proton to afford 6 in which the carbanion is stabilized by the carbonyl group as described by Corey.$^{4)}$ Therefore, ethoxide predominantly and isopropoxide afforded only 7.

This reaction with a carbonyl carbon-carbon bond cleavage proceeded in THF, dioxane, and acetonitrile but not in methanol, diethyl ether, carbon disulfide, and benzene. Instead of lithium methoxide, sodium methoxide did not give 5.

More selective formation of 5 was not attained either by change in reaction temperature or the molar ratio of lithium methoxide to ketone. Although the presence of a large excess of methanol reduced the yield of 5, addition of a moderate amount of methanol prevented the formation of 7 (less than 10% yield) and improved the yield of 5 (Table 1).

References

1) I. Shahak and Y. Sasson, J. Am. Chem. Soc., 95, 3440 (1973).

2) S. Sakai, T. Fujinami, and T. Aizawa, Bull. Chem. Soc. Jpn., 50, 425 (1977).

3) For example, R. Gompper and H. Schaeffer, Chem. Ber., 100, 591 (1967); N. Fukuda, K. Arai, and T. Takeshima, Synthesis, 1980, 566.

4) E. J. Corey and R. H. K. Chen, Tetrahedron Lett., 1973, 3817.

5) All the dimethyl 1,1-dithiodicarboxylates gave satisfactory results in elemental analysis and M^+/e values. Spectral data are as follows. $CH_3OCO(CH_2)_4CS_2Me$: NMR ($CDCl_3$) δ 1.5-2.1 (m, 4H, CH_2CH_2), 2.32 (t, J=6.5 Hz, 2H, $C(O)CH_2$), 2.60 (s, 3H, SCH_3), 3.04 (t, J=7.4 Hz, $C(S)CH_2$), 3.65 ppm (s, 3H, OCH_3); IR ($CHCl_3$) 1730 ($\nu_{C=O}$), 1090 cm^{-1} ($\nu_{C=S}$). $CH_3OCO(CH_2)_5CS_2CH_3$: NMR ($CDCl_3$) δ 1.2-2.1 (m, 6H, $CH_2CH_2CH_2$), 2.34 (t, J=6.4 Hz, 2H, $C(O)CH_2$), 2.61 (s, 3H, SCH_3), 3.07 (t, J=7.4 Hz, 2H, $C(S)CH_2$), 3.65 ppm (s, 3H, OCH_3); IR ($CHCl_3$) 1730 ($\nu_{C=O}$), 1090 cm^{-1} ($\nu_{C=S}$). $CH_3OCOCH(CH_3)(CH_2)_4CS_2CH_3$: NMR ($CDCl_3$) δ 1.14 (d, J=7.1 Hz, 3H, CCH_3), 1.2-2.1 (m, 6H, $CH_2CH_2CH_2$), 2.4 (m, 1H, CH), 2.62 (s, 3H, SCH_3), 3.06 (t, J=7.4 Hz, 2H, $C(S)CH_2$), 3.67 ppm (s, 3H, OCH_3); IR ($CHCl_3$) 1720 ($\nu_{C=O}$), 1090 cm^{-1} ($\nu_{C=S}$).

6) After THF and methanol was evaporated, the reaction mixture was dissolved in chloroform and washed with water. The product 5 was obtained in high purity by distillation from the chloroform solution *in vacuo*.

7) A similar result on the influence of ring size was reported for alkaline cleavage of 2-acetylcycloalkanones; P. J. Hamric, Jr., C. F. Hauser, and C. R. Hauser, J. Org. Chem., 24, 583 (1959).

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