CHEMISTRY LETTERS, pp. 813-814, 1982.

NOVEL CONVERSION OF A KETONE DIMETHYL DITHIOACETAL S,S-DIOXIDE TO THE CORRESPONDING KETONE AND ITS APPLICATION TO SYNTHESIS OF ACYCLIC AND CYCLIC KETONES

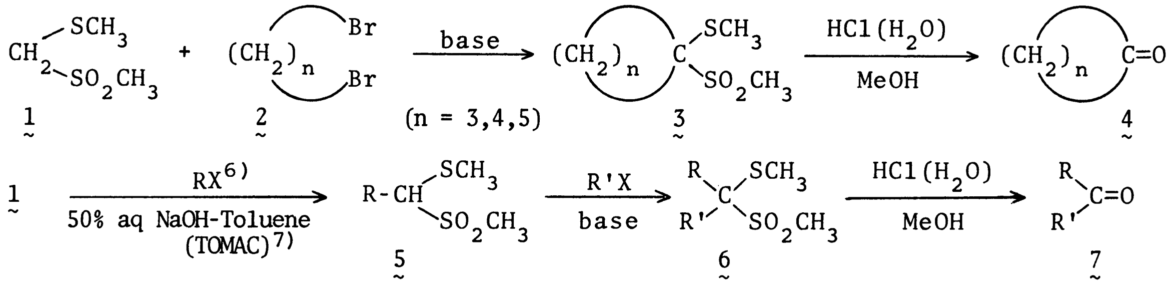
Katsuyuki OGURA,*† Michiyo SUZUKI, Jun-ichi WATANABE,† Mitsuo
YAMASHITA, Hirotada IIDA,† and Gen-ichi TSUCHIHASHI*1)
Sagami Chemical Research Center, Nishi-Ohnuma 4-4-1, Sagamihara, Kanagawa 229 and
†Department of Synthetic Chemistry, Faculty of Engineering, Chiba University,
Yayoicho 1-33, Chiba 260

A ketone dimethyl dithioacetal S,S-dioxide was easily hydrolyzed with hydrochloric acid in refluxing methanol and this transformation was applied to a new method for making acyclic and cyclic ketones by the use of formaldehyde dimethyl dithioacetal S,S-dioxide.

Dithioacetal and its oxide functional groups are well known as useful protective groups of ketones and aldehydes, and many kinds of reaction have been developed to deprotection of these groups.2) However, hydrolysis of dithioacetal S,S-dioxides leading to the corresponding carbonyl groups was unknown in literatures. We surveyed its reaction conditions and this hydrolysis has appeared to be achieved by treatment with hydrochloric acid in refluxing methanol.

For the acid hydrolysis of cyclohexanone dimethyl dithioacetal S,S-dioxide, several reagents were examined, and $TiCl_4$, $AlCl_3$, H_2SO_4, and HCl were found to be effective.3) From standpoints of convenient procedure, reaction rate, and yield, the use of conc hydrochloric acid is recommended.4) Thus, the S,S-dioxide (209 mg: 1.00 mmol) was dissolved in methanol (5 ml) and, after addition of conc hydrochloric acid (0.5 ml), the resulting mixture was refluxed for 3 h. GLC and TLC analyses showed complete consumption of the starting material and formation of cyclohexanone, the yield of which was determined by derivation into the 2,4-dinitrophenylhydrazone derivative (259 mg: 93% yield).

By combination of this hydrolysis with dialkylation of formaldehyde dimethyl dithioacetal S,S-dioxide (1),5) we have also established a new method for production of cyclic and acyclic ketones using 1, as shown in the following scheme.



The results are summarized in Tables 1 and 2. Thus, formaldehyde dimethyl dithioacetal S,S-dioxide (1) has been proven to be a useful reagent for synthesis of cyclic and acyclic ketones.

Table 1. Synthesis of Cyclic Ketones (4) Using 1

2	2 → 3		3 → 4	
	Conditions[a]	Yield	Conditions[b]	Yield
$n = 3$	A [room temp. 22 h]	78%	C [100 °C 20 h]	85%
$n = 4$	B [60 °C 96 h]	71%	D [reflux 3 h]	94%
$n = 5$	B [60 °C 64 h]	68%	D [reflux 3 h]	93%
$n = 6$	B [60 °C 72 h]	none[c]	------------	

[a] A: The lithio derivative (2 mol-equiv), formed from 1 and n-BuLi, was reacted with 2 (1 mol-equiv) in THF; B: A solution containing 1 and 2 in an equimolar ratio in toluene was stirred together with 50% aq NaOH in the presence of TOMAC7) (0.02 mol-equiv). [b] C: A solution of 3 (1 mmol) and conc hydrochloric acid (0.5 ml) in dioxane (5 ml) was heated in a sealed tube. D: A solution of 3 (1 mmol) and conc hydrochloric acid (0.5 ml) in MeOH (5 ml) was heated. [c] 1,8-Bis(methylsulfonyl)-1,8-bis(methylthio)octane and 7-bromo-1-methylsulfonyl-1-methylthioheptane were formed in 26% and 49% yields, respectively, based on the unrecovered 1.

Table 2. Synthesis of Acyclic Ketones (7) Using 1

5 6)	R'X	5 → 6		6 → 7	
		Conditions[a]	Yield	Conditions[b]	Yield
R = n-$C_{12}H_{25}$	CH_3I	A [room temp.(rt) 48 h → 60 °C 2 h]	81%	[reflux 2 h]	95%
		B [-78 °C 10 min → 0 °C 30 min → rt 1 h]	88%	--------	
	n-$C_{12}H_{25}Br$	B [-78 °C 15 min → 0 °C 35 min → rt 17 h]	--[c]	[reflux 2 h]	53% (67%)[d]
	$PhCH_2Br$	B [-78 °C 15 min → 0 °C 30 min → rt 16 h]	--[c]	[reflux 1.5 h]	85% (93%)[d]
R = $PhCH_2$	CH_3I	A [rt 90.5 h → 60 °C 3 h]	81%	[reflux 2 h]	86%
R = CH_3	n-$C_{12}H_{25}Br$	B [-78 °C 10 min → 0 °C 30 min → rt 1 h]	81%	--------	
	$PhCH_2Br$	B [0 °C 20 min → rt 16 h]	77%	--------	

[a] A: 1 and CH_3I (1.4 mol-equiv) were stirred in the presence of NaH (1.3 equiv) in DMF; B: The lithio derivative (1 mol-equiv) produced from 3 and n-BuLi was reacted with an alkyl halide. [b] A solution containing 6 (1.0 mmol) and conc hydrochloric acid (0.5 ml) in MeOH (5 ml) was heated. [c] 6 was not isolated because of its unstableness and the crude mixture was directly subjected to the following acid hydrolysis. [d] The overall yield from 5. The value in parenthesis indicates the yield based on unrecovered 5.

Acknowledgment: The present work was supported by the Grant-in-Aid for Scientific Research (No. 56470070) provided by the Ministry of Education, Science and Culture.

References

1) Present Address: Faculty of Science and Technology, Keio University, Hiyoshi 3-14-1, Yokohama 223.
2) T. W. Greene, "Protective Groups in Organic Synthesis", John Wiley & Sons, pp 129–140 (1981); R. Kuhn and F. A. Neugebauer, *Chem. Ber.*, 94, 2629 (1961)
3) CuCl, $CuCl_2$, and $SnCl_4$ were ineffective.
4) When the present hydrolytic reaction was applied to tridecanal dimethyl dithioacetal S,S-dioxide, formation of tridecanal was observed, but aldol condensation occurred simultaneously to make the yield of tridecanal extremely low.
5) K. Ogura, M. Suzuki, and G. Tsuchihashi, *Bull. Chem. Soc. Jpn.*, 53, 1414 (1980).
6) K. Ogura, J. Watanabe, and H. Iida, *Tetrahedron Lett.*, 22, 4499 (1981).
7) Trioctylmethylammonium chloride (TOMAC) was used as a phase-transfer catalyst.

(Received April 12, 1982)