	Eqilibrium constants
$BrCl + H_2O \rightleftharpoons HOBr + H^+ + Cl^-$	2.95×10^{-5}
$HOBr \rightleftharpoons OBr^- + H^+$	2.00×10^{-9}
$HOBr + H^+ + Br^- \rightleftharpoons Br^2 + H_2O$	2.27×10^{8}
$Br_2 + Br^- \rightleftharpoons Br_3^-$	17

Scheme 2.

tions.[9] Hydrolysis reaction was accelerated by these bromine species which might act as a Lewis acid catalyst on the carbonyl group in the hydrolysis of PNPA.

However, in CTACl micellar solution the same reaction between N-chloro compound and ion yielded chlorine and various chlorine species, which were less reactive than bromine species[9]. The low reactivity of DCI in 16-OH micellar system was expected as the result. It may be due to the side reaction between the hydroxy group of 16-OH and DCI which might yield alkylhypochlorite. Its relative reactivity might be less than that of bromine species. This side reaction may even decrease the amount of active bromine species. In conclusion, the difference in reactivity of the catalytic hydrolysis of PNPA by DCI in various cationic micellar system was derived from the formation of different halogen species during the hydrolysis reactions. Similar studies of the effect of this halogen species on other organic reactions will be followed soon.

References

1. (a) R. A. Moss and S. Ganguli, *Tetrahedron Lett.*, **30**, 2071 (1989); (b) R. A. Mackay, F. R. Longo, B. L. Knier, and H. D. Durst, *J. Phy. Chem.*, **91**, 861 (1987); (c) F. M. Menger, L. H. Gan, E. Johnson, and D. H. Durst, *J. Amer. Chem. Soc.*, **109**, 2800 (1987); (d) R. A. Moss, K. Y. Kim, and S. Swarup, *ibid.*, **108**, 788 (1986); (e) F. M. Menger and L. G. Whitsell, *ibid.*, **107**, 707 (1985).
2. A. A. Frost and R. G. Pearson, "Kinetics and Mechanism", 2nd ed, Wiley, New York, 1961, pp. 166-169.
3. R. A. Moss, R. C. Nahas, S. Ramaswami, and W. J. Sanders, *Tetrahedron Lett.*, 3379 (1975).
4. The decomposition of p-nitrophenolate was also accelerated in CTABr micellar solution with the same amount of DCI. In separate experiments, when 2.5 eq of DCI was reacted with 72 mM of p-nitrophenolate in 4×10^{-3} M CTABr solution, only negligible amount of 2,6-dibromo-4-nitrophenol was able to be isolated.
5. J. J. Rook, *Environ, Sci. and Technol.*, **11**, 478 (1977).
6. M. Soulard, F. Block, and A. Hatterrer, *J. Chem. Soc. Dalton Trans.*, 2300 (1981).
7. Five seconds after DCI addition, the concentration of Br_3^- was measured by the absorbance at 264 nm, and the mole fraction of Br_3^- to the initial DCI concentration was calculated to be about 11%.
8. K. Kumar and D. W. Margerum *Inorg. Chem.*, **26**, 2706 (1987).
9. (a) E. A. Voudrias and M. Reinhard, *Environ. Sci. and Technol.*, **22**, 1049 (1988); (b) R. L. Jolly, "Water Chlorination Environmental Impact and Health Effects", Ann Arbor Sci., pp. 21-77 (1975); (c) J. F. Mills and J. A. Schneider, *Ind. End. Chem. Prod. Res. Dev.*, **12**, 160 (1973).

The Reaction of Carbenes Formed by Decomposition of the Diazo Group in β- or γ-Position in 4-Alkylthioazetidin-2-one Derivatives

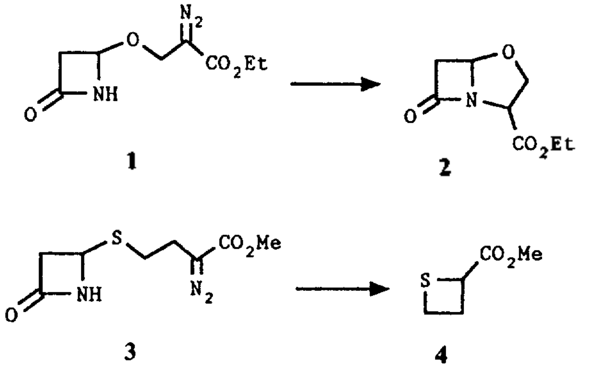
Jae Moon Yang, Han Cheol Wang, Youn Young Lee,* and Yang Mo Goo†

Department of Chemistry and †Department of Pharmacy,
Seoul National University, Seoul 151-742

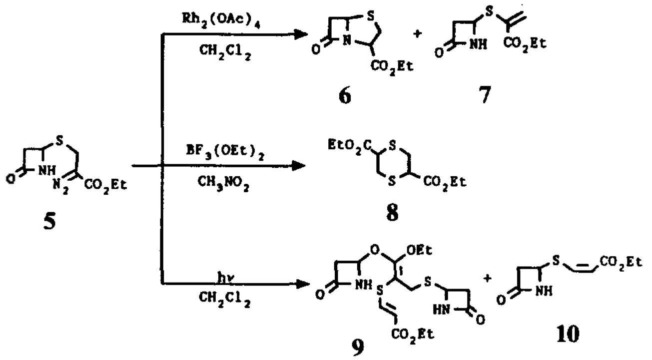
Received October 8, 1991

Oxonium,[1] ammonium[2] or sulfonium[3] ylide intermediates were presumed in carbene reactions and these intermediates should be very useful for the construction of organic compounds. Usually the empty orbital of carbenes interacts with the unshared electron pair of heteroatoms to form ylides. These reactive intermediates may abstract a nearby proton to induce sigmatropic rearrangements and may be transformed to stabilized products. The oxonium[1] and the ammonium[2] ylides were used for sigmatropic rearrangements and for the formation of carbapenems. The carbenes formed at the γ-position on the side chain at C-4 of azetidin-2-ones react easily with the nitrogen atoms of the β-lactam rings to give ammonium ylides which are converted to carbapenems through the rearrangement of the proton on the nitrogen atom.[2] Similarly the sulfur atom readily reacts with various carbenes to form sulfonium ylides.[4] The intermediates were adapted in the formation of new C-glycoside bonds.[3] The carbene-metal complexes, carbenoids, can be easily produced at low temperature when diazo compounds are reacted with metal powder or metal salts, and they are very selective in reactions.[5] During the course of our study on the synthesis of penem antibiotics, we have examined the reaction of carbenes formed by different ways and wish to report the result in this communication.

4-(2-Diazo-2-ethoxycarbonylethoxy)azetidin-2-one (**1**) was obtained from 4-acetoxyazetidin-2-one by reacting with 2-diazo-3-hydroxy propionate which was prepared from L-serine. 4-(2-Diazo-2-methoxycarbonylpropylthio)azetidin-2-one (**3**), and 4-(2-diazo-2-ethoxycarbonylethylthio)azetidin-2-one (**5**) were obtained by diazotization,[6] with isoamyl nitrite, of the amino compounds produced from 4-acetoxyazetidin-2-one by reaction with DL-homocysteine methyl ester hydrochloride[7] and L-cysteine ethyl ester hydrochloride, respectively.



Scheme 1.



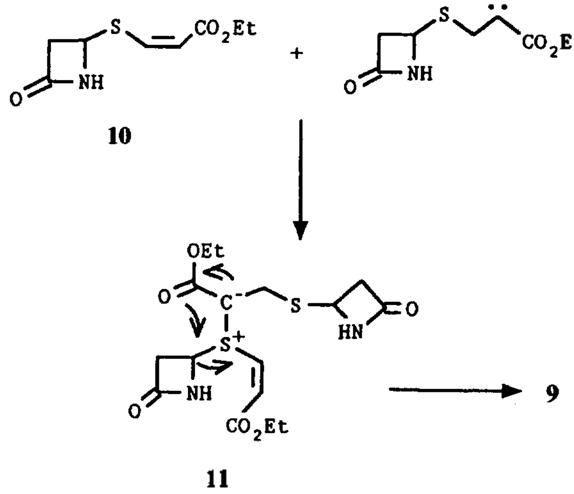
Scheme 2.

When diazo compound **1** was treated with rhodium acetate,[2a] 1-oxacarbapenam **2** was obtained in good yield.[8] However, when the diazo compound **3** was treated with rhodium acetate, no β-lactam compound was detected; methyl thietane-2-carboxylate (**4**) was obtained as the major product, which was probably derived from the thietanium ylide.[9]

Attempt to construct a penam ring through decomposition of the diazo group of compound **5** gave the desired product, ethyl 7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylate (**6**) in a very low yield (4%); the major product was 4-(1-ethoxycarbonylethenylthio)azetidin-2-one (**7**, yield: 35%).[8] The major product was probably derived either from the thiiranium ylide[10] or from the rhodium complex[11] formed by the reaction of rhodium on the diazonium group. Reactivity of the sulfur atom on the carbene seems to be higher than that of the nitrogen atom of the β-lactam ring. To increase the relative ratio of the penam, **6** to the undesired product, **7**, we examined the reaction of the carbene formed with boron trifluoride-ethyl ether complex. However, no desired product was obtained at all; instead only diethyl 1,4-dithiane-2,5-dicarboxylate (**8**) was obtained in 5% yield. The carbene formed by decomposition[12] of the diazo compound (**5**) by boron trifluoride-ethyl ether complex seemed to preferentially react with S intermolecularly; the intramolecular reaction seems to be blocked due to the steric hindrance. The third attempt to improve the formation of penam through the carbene reaction was peerformed by irradiation with UV (Hanovia lamp, 450 W) at -10°C. In this reaction ethyl 6-ethoxy-5-[(2-oxoazetidin-4-yl)thiomethyl]-6-[(2-oxoazetidin-4-yl)oxy]-4-thia-2,5-hexadienecarboxylate (**9**) and 4-(*cis*-2-ethoxycarbonylethenylthioazetidin-2-one (**10**) were obtained in yields of 16% and 24%, respectively.

Compound **9** shows characteristic signals at δ 1.29 (t, 3H, J=7.1 Hz, Me), 1.34 (t, 3H, J=7.1 Hz, Me), 2.91-3.55 (m, 6H, β-lactam -$COCH_2$-, SCH_2-), 4.05-4.42 (crude quintet, 4H, enol, two O-CH_2), 4.83 (dd, 1H, J=5.0 and 2.6 Hz, β-lactam N-CH-S), 5.06 (dd, 1H, J=4.9 and 2.4 Hz, β-lactam N-CH-O), 5.84 (d, 1H, J=15 Hz, C=CH), 6.95 (bm, 1H, NH), 7.18 (bm, 1H, NH), and 7.66 ppm (d, 1H, J=15 Hz, C=CH) in its NMR spectrum, and bands at 3320, 1760, 1590, 1270, and 1170 cm^{-1} in its IR spectrum.

Photodecomposition of a diazo group is known to give both a ground singlet, which should be equivalent to a carbonium ion, and an excited singlet carbenes,[5] which should be equivalent to a linear *sp* hybrid. Thus, irradiation of UV on diazo compound **5** should induce very quick formation of both the excited singlet and the ground singlet state carbenes. The former is quickly transformed stereospecifically to *cis*-ethoxycarbonylethenylthioazetidin-2-one derivative (**10**) and the latter would react slowly with the sulfur atom of **10** intermolecularly followed with rearrangement[13] eventually to give compound **9**. Thus, product **9** should be formed by the route given in Scheme 3.



Scheme 3.

Acknowledgement. The financial support for this work by Korea Science Engineering Foundation is greatly appreciated.

References

1. M. C. Pirrung and J. A. Werner, *J. Am. Chem. Soc.*, **108**, 6060 (1986).
2. (a) R. W. Ratcliffe, T. N. Salzmann, and B. G. Christensen, *Tetrahedron Lett.*, **21**, 31 (1980); T. N. Salzmann, R. W. Ratcliffe, and B. G. Christensen, *J. Am. Chem. Soc.* **21**, 6161 (1980); P. J. Reider and E. J. J. Grabowski, *Tetrahedron Lett.*, **23**, 2293 (1982); T. N. Salzmann, R. W. Ratcliffe, and B. G. Christensen, *Tetrahedron Lett.*, **21**, 1193 (1980); (b) M. A. Williams and M. J. Miller, *Tetrahedron Lett.*, **31**, 1807 (1990).
3. T. Kametani, K. Kawamura, and T. Honda, *J. Am. Chem. Soc.* **109**, 3010 (1987).
4. B. M. Trost, *J. Am. Chem. Soc.*, **88**, 1587 (1966).
5. T. L. Gilchrist and C. W. Rees, "Carbenes, nitrenes, and aryenes", Applecton-Century-Crofts, N.Y. 1969.
6. N. Takemura, T. Mizoguchi, K. Koga, and S. Yamada, *Tetrahedron*, **31**, 227 (1975).
7. M. Beck and H. Wagner, *CA*, **63**, 14980
8. 7-Oxo-4-thia-1-azabicyclo[3,2,0]heptane-2-carboxylic acid S,S-dioxide was produced from 4-(2-diazo-2-ethoxycarbonylthio)azetidin-2-one S,S-dioxide by a carben insertion reaction in high yield in a patent: U.S. Patent 4,241,050.
9. K. Kondo and I. Ojima, *Bull. Chem. Soc. Jpn.*, **48**, 1490 (1975).
10. I. Ojima and K. Kondo, *Bull. Chem. Soc. Jpn.*, **46**, 1539 (1973).
11. A. J. Anciaux, A. J. Hubert, A.F. Noels, N. Petiniot, and P. Teyssie, *J. Org. Chem.* **45**, 695 (1980).

12. (a) A. B. Smith III. and R. K. Dieter, *Tetrahedron*, **37**, 2407 (1981); (b) D. E. McClure, P. K. Lumma, B. H. Arison, J. H. Jones, and J. J. Baldwin, *J. Org. Chem.*, **48**, 2675 (1983).
13. T. Kametani, N. Kanaya, T. Mochizuki, and T. Honda, *Tetrahedron Lett.*, **24**, 221 (1983).

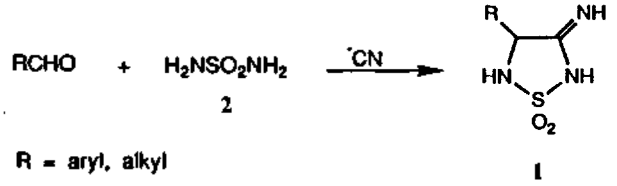
Reactivity and Synthesis of 1,2,5-Thiadiazolidine 1,1-Dioxides: Synthesis of 4-Aryl-3-imino-1,2,5-thiadiazolidine 1,1-Dioxides

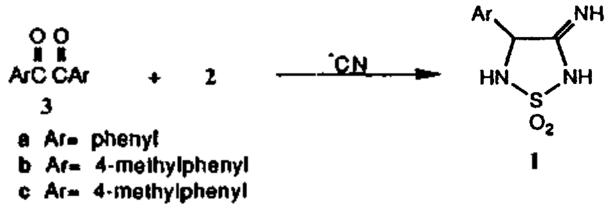
Chai-Ho Lee*, Sun-Yong Jin, Chong-Yul Lee[†], and
Bong Young Chung[‡]

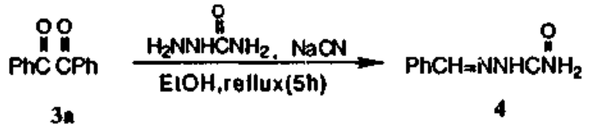
Department of Chemistry, Won Kwang University,
Iri 570-749
[†]*Central Research Institute, Chong Kuen Dang, Seoul 152-070*
[‡]*Department of Chemistry, Korea University,*
Seoul 136-701

Received October 15, 1991

In recent years, an increasing number of articles describing the synthesis, properties, and biological activities of 1,2,5-thiadiazolidine 1,1-dioxides which contain the sulfamide moiety has appeared[1]. Previously, Lee and Kohn have reported a general method for the synthesis of 3-imino-1,2,5-thiadiazolidine 1,1-dioxides **1** from aldehydes, sodium cyanide and sulfamide (**2**) by modifying the Strecker synthesis of hydantoins[3]. The compounds **1** have been known to possess anticonvlusant effect[4].



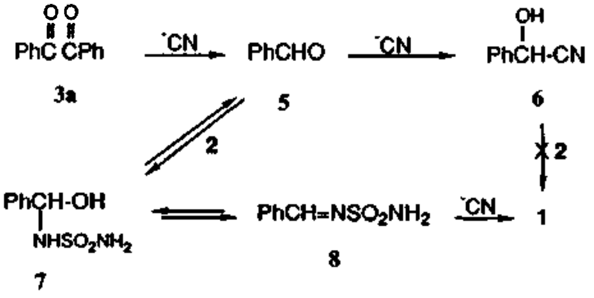




In this paper, we wish to describe a new route for the preparation of **1** from benzil derivatives **3** instead of aldehydes, which were originally used in the Lee-Kohn procedure. Table 1 summarizes the experimental results. Showen reported in 1971 that the cyanide-mediated cleavage of benzil (**3a**) furnished benzaldehyde along with benzoic acid[5]. When we repeated this experiment in the presence of semicarbazide hydrochloride benzaldehyde semicarbazone was obtained in 75% yield. Treatment of benzil (**3a**) with sodium cyanide and sulfamide also produced 4-phenyl compound **1a** in 51% yield.

Table 1. Synthesis of **1** from Benzil Derivatives **3**

Products		mp. (℃)^2	Isolated
No.	Ar		yields (%)
1a	phenyl	272-273	51
1b	4-methylphenyl	252-254	50
1c	4-methoxyphenyl	247-248	62



Scheme 1

A typical experimental procedure for the synthesis of **1** from benzil derivatives is as follows: An ethanolic solution (20 ml) of 4-methylbenzil (240 mg, 10 mmol), sulfamide (290 mg, 300 mmol), and sodium cyanide (54 mg, 11 mmol) was heated at reflux for 5 h and then cooled to room temperature. The mixture was acidified to pH 2.0 and then allowed to stand at 0-5℃ for 24 h. The resulting crystalline material was collected by filtration and dried *in vacuo* to give 115 mg (50%) of **1b**: mp. 252-254℃ (dec); IR (KBr) 3450, 1645, 1355, 1120 cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ 2.35 (s, 3H), 5.20 (d, 1H, J=6.0 Hz), 7.00-7.30 (m, 4H), 7.34 (s, 1H, exchangeable with D_2O), 7.50 (s, 1H, J=6.0 Hz, exchangeable with D_2O), 8.10 (s, 1H, exchangeable with D_2O).

The probable mechanism of this reaction is depicted in Scheme 1. When N-benzylidenesulfamide (**8**)[6], which was prepared by the reaction of N,N'-dibenzilidene-sulfamide with aniline, was reacted with sodium cyanide, the compound **1a** was obtained in 15% yield. However reaction of mandelonitrile (**6**) with sulfamide under the same reaction conditions did not produce compound **1**. This fact suggests that the mechanism should be **3a**→**5**→**7**→**8**→**1**. Although this procedure permitted the preparation of aryl derivatives **3** from benzil derivatives **4**, reaction of aliphatic diones such as 1,2-cyclohexanedione proved to be unsuccessful. Further application of this procedure to various aromatic heterocyclic diones and reactivity studies of the resulting products **1** are in progress.

Acknowledgement. This paper supported by NON DIRECTED RESEARCH FUND, Korea Research Foundation, 1990.