REARRANGEMENT OF 2,3-DIOXO-1,4-OXAZINES TO 4,5-DIOXOOXAZOLES IN THE REACTION WITH DIMETHYLSULFOXONIUM METHYLIDE [1)]

Jun TODA,[a] Masaharu SEKI,[a] Kazuko AMANO,[a] Taichi OYAMA,[a] Takehiro SANO,*,[a] Fumiyuki KIUCHI,[b] and Yoshisuke TSUDA[b]

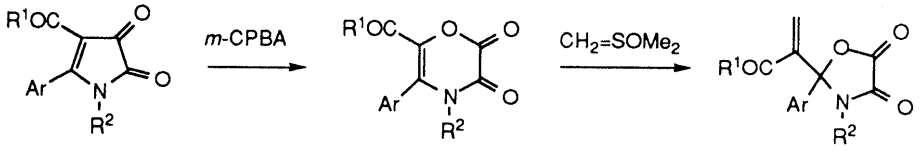
Showa College of Pharmaceutical Sciences,[a] 3-3365 Higashi-tamagawagakuen, Machida-shi, Tokyo 194, Japan and Faculty of Pharmaceutical Sciences, Kanazawa University,[b] 13-1 Takara-machi, Kanazawa 920, Japan

Reaction of 2,3-dioxo-2,3-dihydro-4*H*-1,4-oxazines **2a-e** with dimethylsulfoxonium methylide introduced an *exo*-methylene group with concomitant ring contraction to give 4,5-dioxo-2,3,4,5-tetrahydrooxazoles **3a-e** in moderate yields. Mechanism of this unusual reaction was discussed.

KEYWORDS 2,3-dioxo-2,3-dihydro-4*H*-1,4-oxazine; dimethylsulfoxonium methylide; 4,5-dioxo-2,3,4,5-tetrahydrooxazole; ring contraction; methylenation

Dimethylsulfoxonium methylide (DMSY) is known as a versatile nucleophilic reagent capable of reacting with a variety of unsaturated systems. Carbonyl compounds give oxiranes, and electron-deficient olefins yield cyclopropanes.[2)] Thus, it is of interest to examine the reaction of DMSY to 2,3-dioxo-2,3-dihydro-4*H*-1,4-oxazines (1,4-oxazinedione), since the compounds possess plural functionalities which are supposed to be reactive to DMSY. In this paper, we describe the reaction of DMSY with 5-aryl-2,3-dioxo-2,3-dihydro-4*H*-1,4-oxazines, which causes an unusual ring contraction with concomitant introduction of a methylene group, thus giving a new heterocycle, 4,5-dioxo-2,3,4,5-tetrahydrooxazole (oxazoledione). The reagent, DMSY, was generated either from trimethylsulfoxonium iodide (method A) or from trimethylsulfoxonium tetrafluoroborate (method B) by the action of sodium hydride in dimethyl sulfoxide (DMSO), and the substrates were prepared by Baeyer-Villiger oxidation of 1*H*-pyrrole-2,3-diones.[3)]

When 6-ethoxycarbonyl-5-phenyl-1,4-oxazinedione (**2a**) was treated with DMSY generated by method A at 60°C for 4 h, an oxazoledione **3a** was obtained in 31% yield. The reaction with DMSY generated by method B at room temperature for 17 h gave



1 2 3

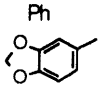
	R^1	Ar	R^2
a	OEt	Ph	Ph
b	OEt	Ph	Me
c	OEt	Ph	CH_2-CH=CH_2
d	Ph	Ph	Ph
e	OEt		Me

Chart 1

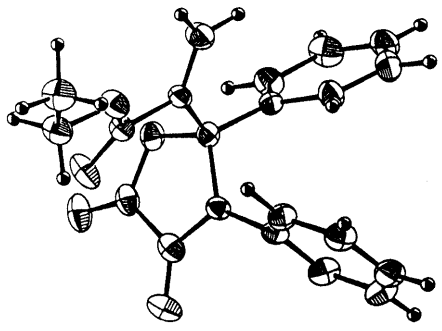


Fig. 1

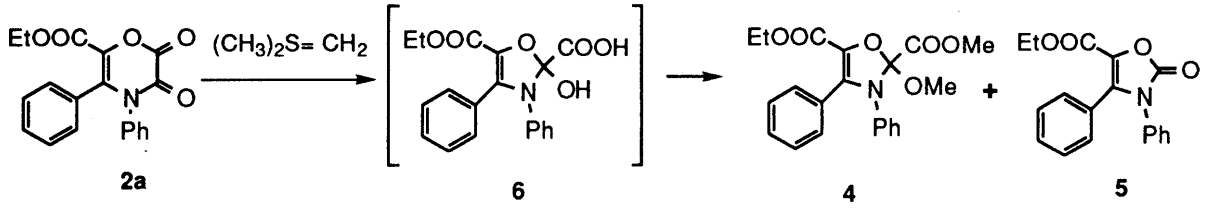
the same product in 17% yield. The structure of **3a** was elucidated by its spectral data[4] and finally confirmed by X-ray crystallographic analysis as shown in Fig.1.[5]

Similarly, *N*-methyl **2b** and *N*-allyl **2c** derivatives as well as 5-methylenedioxyphenyl-4-methyl derivative **2e**, on the reactions with DMSY under similar conditions, gave the corresponding oxazolediones **3b**, **3c**, and **3e** in moderate yields. Interestingly, the 6-benzoyl derivative **2d** gave, on the reaction with DMSY, the oxazoledione **3d** with the intact 6-benzoyl group. The results are summarized in TABLE I. The relatively low yield of the product is probably attributable to the presence of plural electrophilic centers which decrease the site-selectivity of the reaction.

TABLE I. Reaction of 1,4-Oxazinediones **2a-e** with DMSY in DMSO

Oxazinedione **2** Substituents	Method	Conditions		Oxazoledione **3**	
		Temp (°C)	Time (h)	Yield (%)	mp (°C)
a	A	60	4	31	140-143
a	B	r.t.	18	17	
b	A	60	2	20	106-108
b	B	r.t.	20	37	
c	A	r.t.	48	21	gum
c	B	r.t.	48	50	
d	A	60	20	31	157-160
d	B	r.t.	18	26	
e	A	80	1	36	166-168

For comparison, we examined the reaction of **2a** with dimethylsulfonium methylide, which gave entirely different products **4** and **5** in yields of 22% and 15%, respectively. The structures of these products were elucidated by spectroscopic means, particularly by ^{13}C-NMR spectra.[6] The formation of **4** and **5** may be rationalized in terms of a base-catalyzed benzylic acid-type rearrangement of the diketone followed by methylation (by the ylide) or by decarbonylation of an intermediary α-hydroxy acid **6**.



2a **6** **4** **5**

Chart 2

For the above unexpected ring contraction reaction of oxazinediones induced by DMSY, two mechanisms (A and B) were taken into consideration. Mechanism A postulates a 1,3-dipolar cycloaddition of DMSY to an oxazinedione forming the intermediate **7**, which collapses by an electrocyclic reversion reaction to give the product **3**. Although this mechanism explains why DMSY behaves differently from dimethylsulfonium methylide on the same substrate, it seems to be unlikely, because there is no example of DMSY behaving as a 1,3-dipole.[2]

The other mechanism (mechanism B) includes non-concerted addition and elimination reactions of DMSY at C-6 of the oxazinedione. β-Elimination of the intermediary anion **8** followed by an allylic displacement of DMSO with a cyclization of the carboxylate anion **10** gives the oxazoledione **3**. An analogous mechanism was proposed for the reaction of a benzo-4-pyrone with DMSY to give a 2-vinyl-3-oxo-2,3-dihydrobenzo[*b*]furan.[7] However, charge distributions of **2a** calculated by the Nemesis program indicated that C-5 (+ 0.141) is more positive and, therefore, more electrophilic than C-6 (+ 0.041) is --- a fact that seems

to be contradictory to the above consideration that the ylide attacks C-6. This discrepancy was readily overcome by assuming that addition of the ylide reversibly occurs at either C-5 or C-6.[8)]

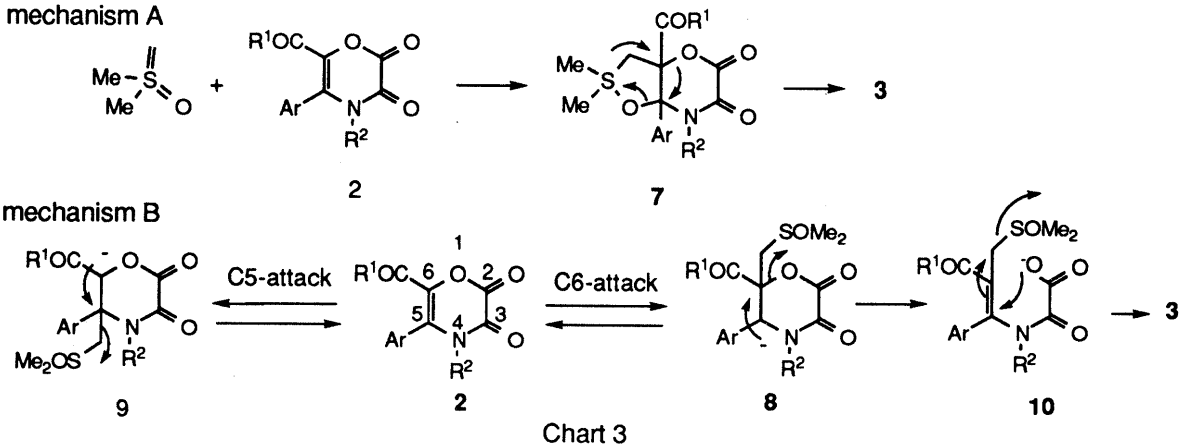


Chart 3

REFERENCES AND NOTES

1) Part LVIII of Dioxopyrrolines: Part LVII. T. Sano, K. Amano, M. Seki, H. Hirota, J. Toda, F. Kiuchi, Y. Tsuda, *Heterocycles*, **37**, 523 (1994).

2) C. R. Johnson, "Comprehensive Organic Chemistry," Vol. 3, ed. by D. H. R. Barton and W. D. Ollis, Pergamon Press, Oxford, 1979, pp. 247-260; Yu. G. Gololobov, A. N. Nesmeyanov, V. P. Lysenko, I. E. Boldeskul, *Tetrahedron*, **43**, 2609 (1987).

3) See Part LVII. **2e**: colorless prisms, mp 157-160°C.

4) **3a**: IR (KBr): 1820, 1748, 1710, 1490, 1400 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.31 (3H, t, *J*=7 Hz, $OCH_2C\underline{H}_3$), 4.30 (2H, q, *J*=7 Hz, $OC\underline{H}_2CH_3$), 5.80, 6.78 (each 1H, s, $=C\underline{H}_2$), 7.08-7.43 (10H, m, ArH). ^{13}C-NMR ($CDCl_3$) δ: 13.9 (q), 62.4 (t), 95.2 (s), 126.4 (dx2), 127.1 (dx2), 128.6 (dx2), 129.0 (d), 129.6 (dx2), 130.3 (d), 133.7 (s), 134.6 (s), 136.1 (s), 137.1 (t), 153.1 (s), 158.0 (s), 164.2 (s). HRMS (*m/z*): Calcd for $C_{20}H_{17}NO_5$ (M^+): 351.1116, Found: 351.1117. The structures of **3b-e** were established by the spectral analogy with those of **3a**.

5) Crystal data of **3a**: Monoclinic. Space group $P2_1/n$. *a* =9.470 (2), *b* =19.066 (4), *c* =9.977 (4) Å. β=102.06 (2)°. V=1761.7 (8) $Å^3$. Z value=4. D_C=1.325 g/cm^3. *R* =0.026.

6) **4**: mp118-120°C. IR (KBr): 1742, 1721 cm^{-1}. ^{13}C-NMR ($CDCl_3$) δ: 13.9 (q), 52.7 (q), 60.4 (q), 62.3 (t), 126.0 (dx2), 127.1 (d), 128.2 (dx2), 128.8 (dx2), 129.7 (d), 129.9 (dx2), 132.3 (s), 136.3 (s), 137.3 (s), 145.1 (s), 160.6 (s), 163.1 (sx2). UV: 268 (ε =14800) nm. LRMS (*m/z*): 383 (M^+). **5**: mp 125-126°C. IR (KBr): 1777, 1719, 1599, 1497 cm^{-1}. ^{13}C-NMR ($CDCl_3$) δ: 14.1 (q), 61.3 (t), 125.0 (s), 127.6 (dx2), 128.1 (dx2), 128.5 (d), 129.3 (dx2), 130.2, (dx2), 130.24 (d+s), 132.9 (s), 136.3 (s), 152.3 (s), 157.6 (s). LRMS (*m/z*): 309 (M^+).

7) G. A. Caplin, W. D. Ollis, I. O. Sutherland, *J. Chem. Soc., Chem. Commun.*, 575 (1967); *idem*, *J. Chem. Soc. (C)*, 2302 (1968); L. Crombie, P. W. Freeman, D. A. Whiting, *J. Chem. Soc. Perkin Trans. I*, 1277 (1973).

8) Regioselective formation of cyclopropane on reaction of α,β-unsaturated ketone with DMSY is attributable to the reversibility of the intermediate anion initially formed by attack of the ylide to electrophilic centers. [cf. C.R. Johnson, C. W. Schroeck, J. R. Shanklin, *J. Am. Chem. Soc.*, **95**, 7418 (1973)].

(Received January 12, 1994; accepted February 5, 1994)