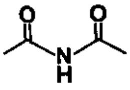
NORRISH TYPE II PHOTO-DEACYLATION OF SEMICYCLIC IMIDES

Akira Sera,*[a] Manabu Okada,[a] Akira Ohhata,[a]
Hiroaki Yamada,[a] Kuniaki Itoh,[a] and Yasuo Kubo[b]

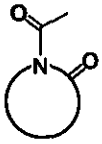
[a]Department of Chemistry, Faculty of Science,
Kobe University, Kobe 657, Japan
[b]Department of Chemistry, Faculty of Science,
Shimane University, Matue 690, Japan

Abstract-The photochemical deacylation of 1,4-diacyl-2,5-piperazinediones was found to proceed through the type II ketene eliminating process.

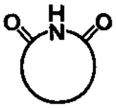
The photo-induced reactions of imides have been extensively investigated, and it has been shown that aliphatic imides undergo almost all types of photoreactions which are anticipated for corresponding carbonyl compounds.[1,2] Imides have been classified into three classes; acyclic imides (**1**), semicyclic imides (**2**), and cyclic imides (**3**).



(**1**)



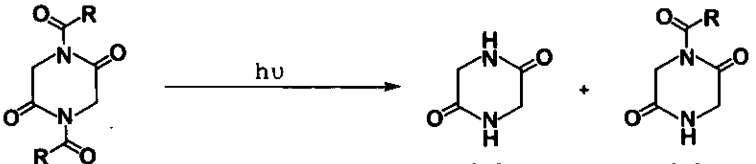
(**2**)



(**3**)

From the investigations of the photochemistry of aliphatic acyclic imides (**1**),[3,4] it has become clear that **1** efficiently undergoes the Norrish type II ketene elimination across the imide function.[3] On the other hand, aliphatic cyclic imides (**3**) appear to execute the Norrish type I cleavages of CO-C[4-6] and CO-N bonds,[7,8] preferentially. The Norrish type II cleavages of N-alkyl substituents of **3** have also been reported.[5,9] Less attention has been paid, however, to the photochemistry of semicyclic imides (**2**), but N-acylpyrrolidones were reported to be capable of undergoing competitive type I and II cleavage processes upon irradiation.[10] In the course of our investigation directed to synthesis of antibiotics possessing a piperazinedione ring, we examined the photolysis of 1,4-diacyl-2,5-piperazinediones (**4**), which possess two semicyclic imide functions.

Irradiation of 1,4-diacetyl-2,5-piperazinedione (**4a**) with a low pressure mercury arc lamp in ethanol afforded 1-acetyl-2,5-piperazinedione (**6a**, 6.9 %) and N,N'-diacetylglycylglycine ethyl ester (**8**, 2.4 %). The monodeacylated product (**6a**) might have arisen from ethanolysis of the acetyl group, or by the Norrish type I (α-cleavage of the exocyclic CO-N bond) and/or type II (ketene elimination caused by excitation of the endocyclic carbonyl group) processes. Since a reaction of **4a** in the dark only yielded the ethanolysis products; **8** (1.0 %) and N,N-diacetylglycylglycine ethyl ester (**9**, 3.1 %), it was suggested that the deacetylation product (**6a**) would be formed photochemically.



(5) (6)

(4)	R
a	Me
b	Pr
c	isoPr

The photolysis of **4a** in acetonitrile gave **6a** (8.1 %) as a sole product. Therefore it was deduced that no α-cleavage of the endocyclic CO-N bond occurred. To determine whether the deacetylation of **4a** proceeded by means of the exocyclic CO-N α-cleavage process or the ketene elimination process across the imide function, the photolysis was carried out in the presence of t-butylamine as a ketene trap. The photolysate was found to contain 2,5-piperazinedione (5, 7.2 %), **6a** (16.1 %), and N-acetyl-t-butylamine (**7a**, 10.6 %) which must be produced by trapping of ketene with the amine or direct aminolysis of the acetyl group by the amine. A control reaction in the dark also yielded **6a**, but the yield was pronouncedly decreased. Thus it was highly probable that the photodeacetylation of **4a** proceeds through the type II ketene elimination.

A similar photolysis of 1,4-dibutyryl-2,5-piperazinedione (**4b**) afforded 5 (3.0 %) and **6b** (31.1 %). Careful inspection of the photolysate revealed the absence of 1-acetyl-4-butyryl-2,5-piperazinedione. This indicates the absence of the Norrish type II reaction along the butyryl group of **4b**, although the photolysis of N-butyrylpyrrolidone, a five-membered semicyclic imide, was reported to proceed through this type II reaction in some extent.[10] The photolysis of **4b** with added t-butylamine and the corresponding control reaction in the dark gave the results, from which one can deduce the cooperation of the Norrish type II ketene elimination and direct aminolysis. The results obtained from the photolysis of 1,4-di-isobutyryl-2,5-piperazinedione (**4c**) also sustained the ketene elimination mechanism. Despite the well known Norrish type II reactivity order that the tertiary hydrogen atom abstraction favors over the secondary hydrogen atom abstraction, **4c** did not show such high reactivity.

Table 1 Photolysis of 1,4-Diacyl-2,5-piperazinediones (**4**)

Starting compd.	Conditions[a]		Yields of products (%)[b]				
	Irradiation	Additive	**4**	**5**	**6**	**7**	Others
4a	$h\nu$[c]	-	83.0	-	6.9	-	**8**: 2.4
	dark[c]	-	85.8	-	d	-	**8**: 1.0 **9**: 3.1
	$h\nu$	-	79.0	-	8.1	-	
	$h\nu$	*t*-BuNH$_2$	67.0	7.2	16.1	10.6	
	dark	*t*-BuNH$_2$	87.0	-	8.0	-	
4b	$h\nu$	-	65.6	3.0	31.1	-	
	$h\nu$	*t*-BuNH$_2$	50.7	4.5	38.5	36.2	
	dark	*t*-BuNH$_2$	75.6	4.4	9.3	11.6	
4c	$h\nu$	-	62.7	8.9	24.1	-	
	$h\nu$	*t*-BuNH$_2$	59.7	9.1	25.8	21.2	
	dark	*t*-BuNH$_2$	78.0	6.0	15.2	19.3	

a) Photolyses were carried out in acetonitrile at 0 °C for 60 h.

b) Isolated yields. c) In ethanol. d) Trace.

Conformational factors are shown to be important to the photochemistry of imides.[2] However, calculated energy differences between a C=O/C=O trans conformation and a C=O/C=O cis conformation were found to be about 14 kcal/mol for **4b** as well as **4c**; the trans conformation being more stable. The reason of this unexpectedly low reactivity of **4c** is not rationalized yet. Molecular mechanics calculations also gave the atomic distances between the carbonyl oxygen atom and the hydrogen atom to be abstracted; that in **4a**, >3.0 Å; **4b**, 2.45 Å; **4c**, 2.28 Å; and N-acetylpyrrolidone, >3.0 Å. We assume that the shortened distances found in **4b** and **4c** account, in part, for the overwhelming preference of the ketene elimination process over the exocyclic N-CO α-cleavage and the type II elimination along the alkyl group (in the case **4b**).

EXPERIMENTAL

Infrared spectra were recorded on a JASCO IRA-3 spectrophotometer. ^{1}H and ^{13}C nmr spectra were recorded on a JEOL FX-90Q spectrometer. Chemical shifts are given in ppm downfield from internal tetramethylsilane. Mass spectra were recorded on an ESCO EMD-05 spectrometer. Melting points were determined on a Yanagimoto micro hot plate apparatus and are uncorrected. Molecular mechanics calculations were performed with Chem3D Plus (Cambridge Scientific Computing, Inc., Ver. 3.0) on Macintosh IIci (Information Processing Center of Shimane University).

1,4-Diacyl-2,5-piperazinediones (4). Acylation of 2,5-piperazinedione was carried out with an acyl anhydride in the usual manner to give **4**. **1,4-Diacetyl-2,5-piperazinedione (4a)**: mp 102-103 °C (benzene) (lit.,[11] mp 102 °C); ir (KBr) 1729 and 1700 cm^{-1}; ^{1}H nmr ($CDCl_3$) δ 2.59 (s, 6H) and 4.60 (s, 4H); ^{13}C nmr ($CDCl_3$) δ 26.6, 47.1, 165.9, and 170.7. **1,4-Dibutyryl-2,5-piperazinedione (4b)**: mp 103-104 °C (benzene); ir (KBr) 1722 and 1689 cm^{-1}; ^{1}H nmr ($CDCl_3$) δ 0.99 (t, 6H, J=4.4 Hz), 1.70 (m, 4H, J=4.4 Hz), 2.92 (t, 4H, J=4.4 Hz), and 4.59 (s, 4H); ^{13}C nmr ($CDCl_3$) δ 13.5, 17.7, 40.6, 47.4, 165.9, and 173.8. **1,4-Diisobutyryl-2,5-piperazinedione (4c)**: mp 89-91 °C (benzene); ir (KBr) 1744 and 1696 cm^{-1}; ^{1}H nmr ($CDCl_3$) δ 1.20 (d, 12H, J=6.8 Hz), 3.67 (m, 2H, J=6.8 Hz), and 4.57 (s, 4H); ^{13}C nmr ($CDCl_3$) δ 19.2, 35.9, 48.0, 165.8, and 178.6.

Anal. Calcd for $C_{12}H_{18}N_2O_4$: C, 56.68; H, 7.13; N, 11.02. Found: C, 56.77; H, 7.03; N, 11.03.

General photolysis procedure. A solution of 1,4-diacyl-2,5-piperazinedione (**4**, 3 mmol) in acetonitrile (or ethanol, 60 ml) was irradiated by using a 60 w low pressure mercury lamp (Eikosha, Halos EL-J-60) at 0 °C for 60 h. t-Butylamine (219 mg, 3 mmol) was added, if necessary. After the reaction, the solvent was evaporated off under reduced pressure to give a product mixture. Separation and purification of the products were achieved by silica gel column chromatography (eluent, AcOEt).

1-Acetyl-2,5-piperazinedione (6a): mp 187-187.5 °C (lit.,[12] mp 180 °C); ir (KBr) 3076, 1711, and 1689 cm^{-1}; ^1H nmr ($CDCl_3$) δ 2.60 (s, 3H), 4.13 (d, 2H, J=2.9 Hz), 4.41 (s, 2H), and 6.4 (br, 1H); ^{13}C nmr (DMSO-d_6) δ 17.3, 36.3, 37.0, 156.9, 158.8, and 161.9; ms (m/z) 156 (M^+), 128, 114, 71, and 43. **1-Butyryl-2,5-piperazinedione (6b):** mp 132 °C; ir (KBr) 3256, 1700, and 1655 cm^{-1}; ^1H nmr ($CDCl_3$) δ 0.98 (t, 3H, J=4.4 Hz), 1.70 (m, 2H, J=4.4 Hz), 2.94 (t, 2H, J=4.4 Hz), 4.10 (br, 2H), 4.39 (s, 2H), and 7.5 (br, 1H) ; ^{13}C nmr ($CDCl_3$) δ 13.7, 18.0, 41.0, 45.7, 47.0, 166.4, 167.4, and 174.7. Anal. Calcd for $C_8H_{12}N_2O_3$: C, 52.17; H, 6.57; N, 15.21. Found: C, 52.28; H, 6.72; N, 15.23. **1-Isobutyryl-2,5-piperazinedione (6c):** mp 142-144 °C; ir (KBr) 3000, 1718, 1689, and 1671 cm^{-1}; ^1H nmr ($CDCl_3$) δ 1.19 (d, 6H, J=6.8 Hz), 3.69 (m, 1H, J=6.8 Hz), 4.13 (d, 2H, J=2.6 Hz), 4.36 (s, 2H), and 7.59 (br, 1H); ^{13}C nmr ($CDCl_3$) δ 19.2, 36.0, 46.1, 47.1, 166.2, 167.8, and 179.5. Anal. Calcd for $C_8H_{12}N_2O_3$: C, 52.17; H, 6.57; N, 15.21. Found: C, 52.20; H, 6.56; N, 15.22.

N-Acetyl-t-butylamine (7a): mp 96-97 °C (lit.,[13] 97-98 °C); ir (KBr)

3292, 2968, and 1646 cm^{-1}; ^{1}H nmr (CDCl$_3$) δ 1.34 (s, 9H), 1.91 (s, 3H), and 6.0 (br, 1H); ^{13}C nmr (CDCl$_3$) δ 24.2, 28.6, 50.9, and 169.6. **N-Butyryl-*t*-butylamine (7b)**: mp 45.0-45.5 °C; ir (KBr) 3320, 2968, and 1650 cm^{-1}; ^{1}H nmr (CDCl$_3$) δ 0.93 (t, 3H, *J*=7.1 Hz), 1.35 (s, 9H), 1.67 (m, 2H), 2.08 (t, 2H, *J*=7.1 Hz), and 5.4 (br, 1H); ^{13}C nmr (CDCl$_3$) δ 13.3, 19.0, 28.5, 39.0, 50.6, and 172.4. *Anal*. Calcd for $C_8H_{17}NO$: C, 67.09; H, 11.96; N, 9.78. Found: C, 67.11; H, 11.94; N, 9.70. **N-Isobutyryl-*t*-butylamine (7c)**: mp 115-116 °C (lit.,[14] 118-120 °C); ir (KBr) 3316, 2972 and 1648 cm^{-1}; ^{1}H nmr (CDCl$_3$) δ 1.11 (d, 6H, *J*=6.8 Hz), 1.34 (s, 9H), 2.22 (m, 1H, *J*=6.8 Hz), and 5.2 (br, 1H); ^{13}C nmr (CDCl$_3$) δ 19.5, 28.7, 36.0, 50.6, and 176.3. *Anal*. Calcd for $C_8H_{17}NO$: C, 67.09; H, 11.96; N, 9.78. Found: C, 66.94; H, 11.91; N, 9.77.

N,N'-Diacetylglycylglycine ethyl ester (8): mp 83-84 °C; ir (KBr) 1728, 1708, 1644, and 1552 cm^{-1}; ^{1}H nmr (CDCl$_3$) δ 1.30 (t, 3H, *J*=7.1 Hz), 2.07 (s, 3H), 2.39 (s, 3H), 4.24 (q, 2H, *J*=7.1 Hz), 4.43 (d, 2H, *J*=3.4 Hz), 4.45 (s, 2H), and 6.6 (br, 1H); ^{13}C nmr (CDCl$_3$) δ 14.1, 23.0, 25.6, 45.6, 45.8, 62.0, 168.2, 170.3, 172.1, and 172.2. *Anal*. Calcd for $C_{10}H_{16}N_2O_5$: C, 49.18; H, 6.56; N, 11.48. Found: C, 49.18; H, 6.67; N, 11.54. **N,N-Diacetylglycylglycine ethyl ester (9)**: mp 96-97 °C; ir (KBr) 3304, 1756, 1704, and 1656 cm^{-1}; ^{1}H nmr (CDCl$_3$) δ 1.29 (t, 3H, *J*=7.1 Hz), 2.44 (s, 6H), 4.03 (q, 2H, *J*=5.7 Hz), 4.20 (d, 2H, *J*=7.1 Hz), 4.41 (s, 2H), and 6.6 (br, 1H); ^{13}C nmr (CDCl$_3$) δ 14.2, 26.2, 41.5, 48.0, 61.7, 168.0, 169.5, and 173.3. *Anal*. Calcd for $C_{10}H_{16}N_2O_5$: C, 49.18; H, 6.56; N, 11.48. Found: C, 49.26; H, 6.54; N, 11.39.

ACKNOWLEDGMENT

We are indebted to Miss M. Nishinaka for ms determination and microanalysis.

REFERENCES

1. Y. Kanaoka, Acc. Chem. Res., 1978, **11**, 407.
2. P. H. Mazzocci, "Organic Photochemistry", Vol. 5, ed. by A. Padwa, Marcel Dekker, New York, **1981**, p. 421.
3. P. H. Mazzocci, C. W. Jameson, T. Nishiyama, and A. DeCamp, Tetrahedron Lett., 1980, **21**, 989.
4. G. Scharf and B. Fuchs, J. Chem. Soc., Chem. Commun., **1975**, 244.
5. Y. Kanaoka, H. Okajima, and Y. Hatanaka, Heterocycles, 1977, **8**, 339 ; J. Org. Chem., 1979, **44**, 1749.
6. K. Maruyama, T. Ishitoku, and Y. Kubo, J. Am. Chem. Soc., 1979, **101**, 3670; Chem. Lett., **1980**, 265.
7. J. A. Schutyser and F. C. De Schryver, Tetrahedron, 1976, **32**, 251.
8. H. Nakai, Y. Sato, T. Mizoguchi, M. Yamazaki, and Y. Kanaoka, Heterocycles, 1977, **8**, 345.
9. Y. Kanaoka and Y. Hatanaka, J. Org. Chem., 1976, **41**, 400.
10. M. Machida, H. Takechi, A. Sakushima, and Y. Kanaoka, Heterocycles, 1981, **15**, 479.
11. L. N. Akimova and Z. V. Kirjuchina, Z. Obs. Khim., 1957, **27**, 1917 (Chem. Abstr., 1958, **52**, 6183d).
12. R. G. Petrowa, L. N. Akimova, and N. I. Gavrilov, Z. Obs. Khim., 1954, **24**, 2230 (Chem. Abstr., 1956, **50**, 359g).
13. J. J. Ritter and P. P. Minieri, J. Am. Chem. Soc., 1948, **70**, 4045.
14. W. D. Emmons, J. Am. Chem. Soc., 1957, **79**, 5739.

Received, 26th October, 1992