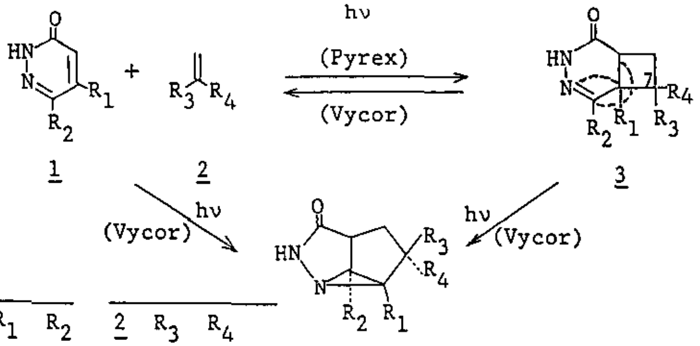
PHOTOCHEMISTRY OF CONJUGATED NITROGEN-CARBONYL SYSTEMS. V[1]: PHOTOISOMERIZATION OF 3,4-DIAZABICYCLO[4.2.0]OCT-4-EN-2-ONE SYSTEM

Eisuke Sato, Masato Hasebe,[2] and Yuichi Kanaoka*
Faculty of Pharmaceutical Sciences, Hokkaido University,
Sapporo 060, Japan

Abstract —— Irradiation through a Vycor filter of 3,4-diazabicyclo-[4.2.0]oct-4-en-2-ones (3) obtained by photoaddition of 3(2H)-pyridazinones (1) and olefin resulted in isomerization to give 2,3-diazatricyclo-[3.3.0.0^{2,8}]octa-4-ones (4).

In an extention of studies on conjugated nitrogen-carbonyl system,[1a] it was observed that irradiation of 5-methyl-3(2H)-pyridazinones in the presence of allyl alcohol gave 2,3-diazabicyclo[3.3.0.0^{2,8}]octa-4-ones (4) in addition to usual [2+2]cycloaddition products (3). In this paper we wish to report that the interesting tricyclic product (4) arises from the photoisomerization of the initially formed photoaddition products, 3,4-diazabicyclo[4.2.0]oct-4-en-2-ones (3). One of the authors had already reported a photochemical ring contraction of 3(2H)-pyridazinones.[3]



1 2 3 4

1	R$_1$	R$_2$
a	Me	H
b	H	Me

2	R$_3$	R$_4$
a	H	CH$_2$OH
b	Me	Me
c	H	OEt
d	H	CO$_2$Me

Chart 1

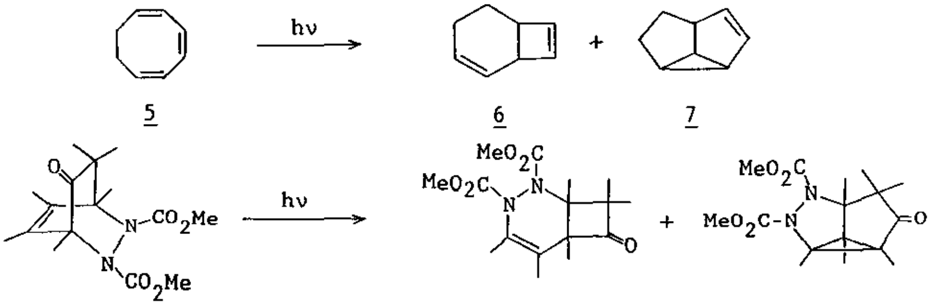
Table 1 Photoproducts Distribution

Pyridazinone (1.0 mmol)	Olefin (20 mmol)	Filter	Irradiation time (h)	Product (%)		
				3	4	1
1a	2a	Pyrex	5.0	91	0	
1a	2a	Vycor	1.5	0	42	
3aa	-	Vycor	1.0	-	45	
1b	2a	Pyrex	6.0	65	0	
3ba	-	Vycor	1.0	55	0	
1a	2b	Pyrex	12.0	76	0	
3ab	-	Vycor	1.5	-	0	22
1a	2c	Pyrex	2.0	87	0	
1a	2c	Vycor	3.0	0	33	
3ac	-	Vycor	1.0	-	31	19
1a	2d	Pyrex	6.0	77	0	
1a	2d	Vycor	3.0	0	24	
3ad	-	Vycor	1.0	-	28	11

Irradiation of 1a in the presence of allyl alcohol (2a) through a Pyrex filter gave the [2+2]cycloaddition product 3aa in a good yield. The 7-hydroxymethyl group of 3aa is assumed to be an exo-form from the analogy with the case of 3,4-diazabicyclo-5-methyl-7-exo-hydroxymethyl[4.2.0]oct-4-en-2-one obtained from 6-methyl-3(2H)-pyridazinone and allyl alcohol.[4] Interestingly, when the photolysis was conducted using Vycor filter, the only product isolated was the product (4aa), whose structure was assigned as shown in Chart 1 by spectral data. Mass spectrum of 4aa shows a molecular ion peak of 168, which is the same mass number with 3aa, suggesting photoisomerization. The nuclear magnetic resonance spectrum of 4aa shows the disappearance of vinyl proton signal which is observed in 3aa, and gives seven olefinic proton signals, implying the valence isomerization at C=N and cyclobutane ring, and the structure was finally confirmed by X-ray analysis as 2,3-diazatricyclo-7-hydroxymethyl-8-methyl$[3.3.0.0^{2,8}]$octan-4-one.[5] In order to confirm the assumption that the isolated photoproduct 4aa is formed by the secondary photoreaction of the initially formed 3aa, compound 3aa was then irradiated through a Vycor filter to afford 4aa as expected.

In order to see the role of 6-substituent of 3 on this photoisomerization, 3ba obtained from 6-methyl-3(2H)-pyridazinone (1b) and allyl alcohol (2a), was subjected to the photolysis. Irradiation of 3ba under the similar photolytic conditions with that for 3aa did not afford an expected isomerized product 4ba, but the starting material of 3ba was recovered (Table 1). Based on this result, 6-methyl group of 3 seems to be essential for the isomerization to 4.

As an extention of this photochemical valence isomerization, 7-disubstituted derivative 3ab obtained from 3(2H)-pyridazinone (1a) and isobutene (2b) was irradiated through a Vycor filter. Isomerized photoproduct 4ab was not obtained at all, but the reverse reaction took place affording 5-methyl-3(2H)-pyridazinone (1a). Presumably the dimethyl groups at C-7 position of 3ab stabilize the biradical intermediate which undergoes the elimination to 1a.[6] Thus, gem-disubstituted olefin is not desirable for the photoisomerization of 3 to 4. As further examination of the substituent effect, olefins with electron-donating or electron-withdrawing substituent were examined. The [2+2]cycloaddition products 3ac and 3ad thus prepared were subjected to the photolysis through a Vycor filter, to give the isomerized products (4) and 5-methyl-3(2H)-pyridazinone (1a) concomitantly formed by the reverse photoreaction, which is probably caused by the radical stabilization effect of alkoxy and methoxycarbonyl group.[7]



5 6 7

8 9 10

Chart 2

As shown in Chart 2, this photoisomerization of 3 to 4 is probably analogous, at least formally, to the formation of tricyclo[5.1.0.0^{4,8}]oct-2-ene (7) from 1,3,5-cyclooctatriene (5).[8] Although 7 is reported to be obtained directly from triene 5, it is also possible that photoproduct 7 is obtained from 6 by analogous secondary isomerization with 4 from 3. Formation of diazatricyclo[3.3.0.0^{4,6}]octan-7-ene (10), as an example of nitrogen-heterocyclic system, from diazabicyclo[2.2.2]octanone (8),[9] although the isomerization of 9 to 10 is also speculated to undergo via 8, in addition to the photochemical rearrangement of cyclohexadienones and related compounds such as lumisantonin from santonin,[10] would belong to the members of the same family. Although both radical process and concerted process are possible for these photolyses, substituent effects at C-7 suggest radical process for the reverse reaction of 3 to 1 and concerted process is favorable for the isomerization of 3 to 4 by the following reason. The stereostructure of 4 can be reasonably explained on the assumption that the photoisomerization of 3 to 4 proceeds via [σ2a + π2a]process, which requires antarafacial addition of C_1-C_6 bond to C=N, and inversion at C-6.[11]

The photo-process to the products from 3(2H)-pyridazinone (1) with olefins (2) was found to be energy dependent; that is, the product 3 was obtained through a Pyrex filter while the product 4 was obtained through a Vycor filter. Although photoisomerization of 3 to 4 competes with the reverse reaction due to the radical stabilizing substituent at C-7 position of 3, a valence isomerization to 4 is a general behavior for 3 with the 6-methyl group and the 7-monosubstituent. This reaction provides a specific synthetic entry to a strained ring system containing aziridine such as 4. Further application of this reaction and chemical properties of photoproducts of 4 are now under investigation.

EXPERIMENTAL

Melting points were determined with a Yamato MP-21 melting point apparatus and are uncorrected. Vacuum distillation was carried out using a Büchi Kugelrohr apparatus and boiling points are bath temperatures. Nuclear magnetic resonance (Nmr) spectra were taken on a JEOL JNM 100 FT-nmr spectrometer with tetramethylsilane (TMS) as an internal standard. Mass spectra (Ms) were obtained with a JMS-D 300 mass spectrometer. Infrared spectra (Ir) were recorded with JASCO IRA-1 infrared spectrometer. The light source was a Type UM-103B (Ushio) 100 W high-pressure mercury lamp.

General Procedure for the Photolysis —— A solution of 1[12] (110 mg, 1.0 mmol) with 2 (20 mmol), or 3 (1.0 mmol) in 250 ml of acetonitrile was irradiated for 1-12 h (Table 1) with a 100 W high-pressure mercury lamp through a filter (Table 1) under an argon atmosphere. The solvent and the excess olefin were removed under reduced pressure and the residue was separated by silica gel preparative layer chromatography (PLC, solvent ratio) (Kieselgel 60 PF_{254}, Merck, 20 x 20 cm), followed by recrystallization or distillation under reduced pressure. Spectral data are given in Table 2.

3,4-Diazabicyclo-6-methyl-7-hydroxymethyl-[4.2.0]-oct-4-en-2-one (3aa)

Recrystallization (without PLC) from AcOEt gave colorless prisms, 153 mg (91 %), mp 120-122 °C. Anal. Calcd for $C_8H_{12}N_2O_2$: C, 57.13; H, 7.19; N, 16.66. Found: C, 57.01; H, 7.04; N, 16.85.

2,3-Diazatricyclo-7-hydroxymethyl-8-methyl-[3.3.0.$0^{2,8}$]-octan-4-one (4aa)

PLC (AcOEt:EtOH = 20:1). Recrystallized from AcOEt, colorless prisms of 76 mg (45

Table 2 Spectral Data for the Products (3 and 4)

Product	Ir(Nujol) $\nu_{max}(cm^{-1})$	Ms, m/z	Nmr ($CDCl_3$) δ(ppm), J(Hz)
3aa	3330 1685 3180 1675 3080 1635	168(M^+) 150 110(base)	1.29 (3H, s), 2.22 (2H, t, J=7.9), 2.60 (1H, quint, J=7.9), 2.78 (1H, t, J=7.9), 3.59-3.77 (2H, m), 3.78 (1H, s, OH), 6.72 (1H, s), 9.69 (1H, s, NH),
4aa	3149 1690	169(M^++1) 168(M^+) 111 93(base)	1.26 (3H, s), 1.95 (1H, dd, J=10.6, 4.4), 2.18-2.32 (2H, m), 2.65 (1H, dd, J=5.9, 4.8), 3.14 (1H, d, J=4.8), 3.67-3.85 (2H, m), 3.78 (1H, s, OH), 8.31 (1H, s, NH).
3ba	3380 1655 1630	168(M^+) 150 110(base)	1.85 (3H, s), 2.31 (2H, t, J=7.0), 2.70 (1H, sixt, J=7.0), 2.95-3.05 (1H, m), 3.11 (1H, dd, J=9.5, 7.0), 3.54-3.70 (2H, m), 3.78 (1H, s, OH), 9.43 (1H, s, NH).
3ab	3220 1660 3080	167(M^++1) 166(M^+) 111(base)	1.13 (3H, s), 1.15 (6H, s), 2.10 (1H, d, J=9.3), 2.81 (1H, t, J=9.3), 6.76 (1H, s), 7.26 (1H, b, NH).
3ac	3230 1690 3090 1670 1630	183(M^++1) 182(M^+) 72(base)	1.20 (3H, t, J=7.0), 1.33 (3H, s), 2.56-2.78 (3H, m), 3.39 (2H, q, J=7.0), 4.15 (1H, dd, J=8.0, 6.2), 6.79 (1H, s), 8.57 (1H, s, NH).
4ac	3160 1690	183(M^++1) 182(M^+) 153 97(base)	1.22 (3H, t, J=7.0), 2.19 (1H, ddd, J=12.5, 8.3, 7.0), 2.53 (1H, dd, J=12.5, 5.7), 2.85 (1H, dd, J=7.0, 4.4), 3.24 (1H, d, J=4.4), 3.55 (2H, q, J=7.0), 3.93 (1H, dd, J=8.3, 5.7), 6.82 (1H, s, NH).
3ad	3200 1730 3090 1665 1635	196(M^+) 164 110(base)	1.28 (3H, s), 2.40-2.51 (1H, m), 2.85-2.97 (2H, m), 3.33-3.39 (1H, m), 3.75 (3H, s), 6.81 (1H, s), 8.43 (1H, s, NH).
4ad	3260 1720 1695	196(M^+) 139 79(base)	1.27 (3H, s), 2.21 (1H, dd, J=12, 6.2), 2.78-2.93 (2H, m), 3.13 (1H, dd, J=10, 5.9), 3.27 (1H, d, J=4.0), 3.78 (3H, s), 7.01 (1H, s, NH).

%) *from 3aa, 70 mg (42 %)* from 1a and 2a, mp 146-148 °C. Anal. Calcd for $C_8H_{12}N_2O_2$: C, 57.13; H, 7.19; N, 16.66. Found: C, 57.01; H, 7.06; N, 16.55.

3,4-Diazabicyclo-5-methyl-7-hydroxymethyl-[4.2.0]-oct-4-en-2-one (3ba)

PLC (AcOEt:EtOH = 20:1). Recrystallization from AcOEt gave colorless prisms, 110 mg (65 %), mp 113-114 °C. Anal. Calcd for $C_8H_{12}N_2O_2$: C, 57.13; H, 7.19; N, 16.66. Found: C, 57.15; H, 7.06; N, 16.72.

3,4-Diazabicyclo-6,7,7-trimethyl-[4.2.0]-oct-4-en-2-one (3ab)

PLC (AcOEt). Recrystallization from ethyl ether-n-hexane, colorless prisms of 126 mg (76 %), mp 106-107 °C. Anal. Calcd for $C_9H_{14}N_2O_2$: C, 65.03; H, 8.49; N, 16.85. Found: C, 64.99; H, 8.33; N, 16.63.

3,4-Diazabicyclo-6-methyl-7-ethoxy-[4.2.0]-oct-4-en-2-one (3ac)

PLC (CH_2Cl_2:AcOEt = 1:1). Distillation in vacuo gave a colorless oil, 158 mg (87 %), bp 170 °C/0.2 mmHg. Anal. Calcd for $C_9H_{14}N_2O_2$: C, 59.32; H, 7.74; N, 15.37. Found: C, 59.13; H, 7.89; N, 15.10.

2,3-Diazatricyclo-7-ethoxy-8-methyl-[3.3.0.$0^{2,8}$]-octan-4-one (4ac)

PLC (CH_2Cl_2:AcOEt = 1:1). Recrystallization from ethyl ether-n-hexane gave colorless needles of 56 mg (31 %) from 3ac, 60 mg (33 %) from 1a and 2c, mp 103-105 °C. Anal. Calcd for $C_9H_{14}N_2O_2$: C, 59.32; H, 7.74; N, 15.37. Found: C, 59.32; H, 7.84; N, 15.42.

3,4-Diazabicyclo-6-methyl-7-methoxymethyl-[4.2.0]-oct-4-en-2-one (3ad)

PLC (CH_2Cl_2:AcOEt = 2:1). Recrystallized from ethyl ether-n-hexane, colorless needles, 151 mg (77 %), mp 93-95 °C. Anal. Calcd for $C_9H_{12}N_2O_3$: C, 55.09; H, 6.17; N, 14.28. Found: C, 55.07; H, 6.22; N, 14.30.

2,3-Diazatricyclo-7-methoxycarbonyl-8-methyl-[3.3.0.$0^{2,8}$]-octan-4-one (4ad)

PLC (CH_2Cl_2:AcOEt = 1:1). Recrystallization from ethyl acetate-n-hexane gave colorless prisms of 54 mg (28 %) from 3ad, 47 mg (24 %) from 1a and 2d, mp 112-114 °C. Anal. Calcd for $C_9H_{12}N_2O_3$: C, 55.09; H, 6.17; N, 14.28. Found: C, 55.09; H, 6.18; N, 14.28.

REFERENCES AND NOTES

1) a) Part IV: E. Sato, Y. Ikeda, and Y. Kanaoka, Heterocycles, 1987, 26, 1611;
   b) Photoinduced Reactions 103. Part 102: H. Takechi, M. Machida, and Y. Kanaoka, submitted.
2) Present address: School of Pharmacy, Hokuriku University, Kanazawa 920, Japan.
3) T. Tsuchiya, M. Hasebe, H, Arai, and H. Igeta, Chem. Pharm. Bull., 1974, 22, 2276.
4) I. L. Karle, Acta Cryst., 1982, B38, 1019.
5) Idem, ibid., 1982, B32, 1022.
6) W. A. Pryor, "Free Radicals," McGraw Hill, Inc., 1966, p. 207.
7) P. J. Wagner and A. E. Kemppainen, J. Am. Chem. Soc., 1972, 94, 7495.
8) O. L. Chapman, G. W. Borden, R. W. King, and B. Winkler, J. Am. Chem. Soc., 1964, 86, 2660.
9) H. Hart, R. K. Murray,Jr. and G. D. Appleyard, Tetrahedron Lett., 1969, 4785.
10) P. J. Kropp, Org. Photochem., 1967, 1. 1.
11) R. B. Woodward and R. Hoffmann, "The Conservation of Orbital Symmetry," Academic Press Inc., 1970, p. 90.
12) a) M. Ogata and H. Kano, Chem. Pharm. Bull., 1963, 11, 35; b) W. G. Overend and L. F. Wiggins, J. Chem. Soc., 1947, 239.

Received, 22nd February, 1988