N-HYDROXYAMIDE-CONTAINING HETEROCYCLES. PART 7.[1] PREPARATION AND PHOTOCHEMICAL BEHAVIOR OF 1-BENZYLOXY-2(1*H*)-PYRAZINONES

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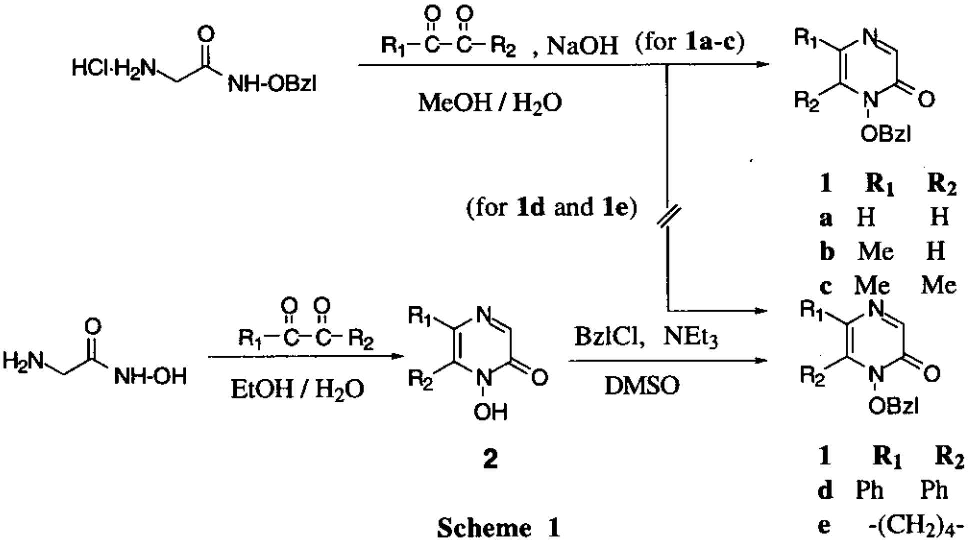
Abstract --- Synthesis of 1-benzyloxy-2(1*H*)-pyrazinones having substituents at C-5 and C-6 positions and their photochemical behavior have been studied. Upon irradiation 1-benzyloxy-2(1*H*)-pyrazinones underwent N-O bond cleavage in high quantum yields. The rearrangement of the benzyloxy group to C-3 position of the ring and [2+2] cycloaddition were also observed.

Recently we have investigated syntheses and reactions of *N*-hydroxyamide-containing diazine derivatives regarded as cyclic hydroxamic acids.[1-5] The diazine derivatives have been demonstrated to be quite useful as intermediates in organic synthesis[1,5] and as iron(III)-sequestering agents[2,4] by virtue of their low pKa values and high water solubilities. Reactivies of acyclic[6,7] and monoazine-type[7-10] hydroxamic acids in the ground and excited states have been well investigated. However, no paper concerning photochemical behavior of diazine-type hydroxamic acids has been reported. Photochemical reactions of heterocycles bearing 6π-electron system have been extensively studied.[11] The photochemical behavior of 2(1*H*)-pyrazinones is of interest because of their non aromatic 7π-electron system in the solutions. We report here on the synthesis of 1-benzyloxy-2(1*H*)-pyrazinones bearing substituents at C-5 and/or C-6 positions and the photochemical behavior of pyrazinones.

1-Benzyloxy-(**1a**) and -5,6-dimethyl-2(1*H*)-pyrazinone (**1c**) were prepared by the method previously reported (Scheme 1).[4] The formation of two structural isomers, 5-methyl- and 6-methyl-2(1*H*)-pyrazinones, was expected when *N*-(benzyloxy)glycinamide hydrochloride was treated with pyruvic aldehyde. However, only one isomer was formed. The ^{1}H nmr signal attributable to the methyl group of the isomer was observed at δ 2.15 ppm, and the chemical shift of the methyl group was very close to that of the 5-methyl group (δ 2.18 ppm) of **1c**. The chemical shift of the methyl group at C-6 position of the pyrazinone ring has been reported to be lower than that at C-5 position due to the anisotropic effect of the benzene ring at N-1 position,[4] and the signal of the 6-methyl group of **1c** was observed at δ 2.27 ppm. Therefore, the isomer was determined to be 1-benzyloxy-5-methyl-2(1*H*)-pyrazinone (**1b**). Cyclization of *N*-(benzyloxy)glycinamide hydrochloride with benzil may give **1d**. However, **1d** could not be obtained by the same manner as **1a-c** because the benzilic acid rearrangement occurred exclusively under the strong basic conditions. The preparation of **1d** could be achieved by the condensation of *N*-hydroxyglycinamide with benzil in 50% aqueous EtOH to 1-hydroxy-5,6-diphenyl-2(1*H*)-pyrazinone (**2**), and then *O*-benzylation of **2** with benzyl chloride. The cyclohexane-fused pyrazinone (**1e**) was also prepared by the similar manner for **1d**.

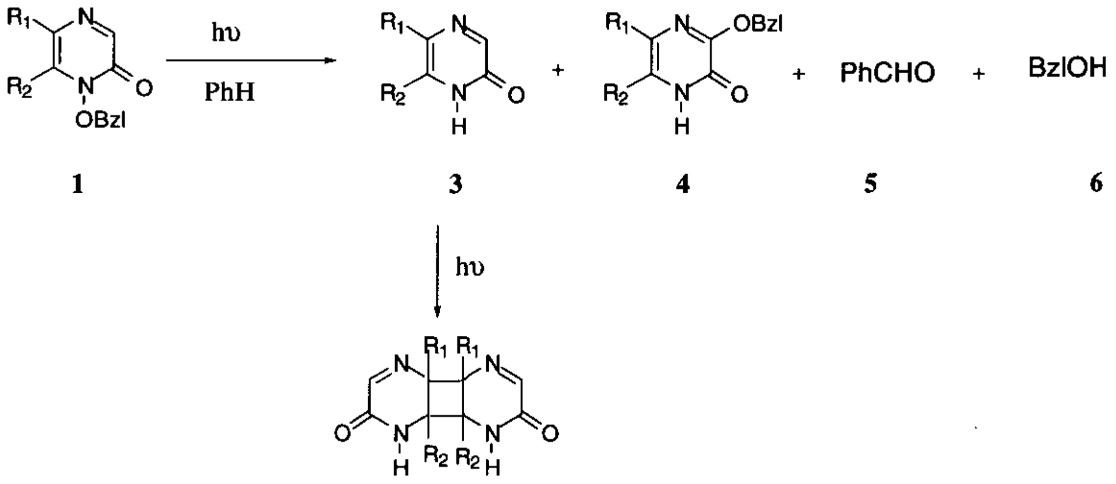


Scheme 1

Irradiation of a benzene solution of **1a** with a 450 W high-pressure mercury lamp through Pyrex filter under nitrogen for 1.5 h gave 2(1*H*)-pyrazinone (**3a**), benzaldehyde (**5**), and benzyl alcohol (**6**) in 53, 31, and 18% yields, respectively (Scheme 2 and Table 1). These compounds were identified with authentic samples.[12] Photolysis of **1b-e** under the same conditions gave **3b-e** and **5**. The photochemical behaviors of **1** are similar to those of 1-hydroxy-2(1*H*)-pyridinone.[10] In cases of **1c-e**, however, the rearrangement products (**4c-e**) were also isolated. In ^1H nmr spectra of **4c-e** the singlet of H-3 disappeared, and the benzylic methylene protons were observed at lower field than those of **1c-e** ($\Delta\delta$ 0.1-0.6 ppm). In the case of **1e**, cyclobutano[1,2-*e*:1,2-*e'*]dipyrazinone derivative (**7e**) was additionally obtained as the photoproduct though the yield was only 4%.

Table 1. Chemical and quantum yields

	1		Φ_{dis}			Yield / %		
	R_1	**R_2**		3	4	5	6	7
a	**H**	**H**	1.00	53	-	31	18	-
b	**Me**	**H**	0.71	48	-	24	-	-
c	**Me**	**Me**	0.95	50	5	26	-	-
d	**Ph**	**Ph**	0.90	61	10	25	-	-
e	**-(CH_2)$_4$-**		1.00	64	16	77	-	4



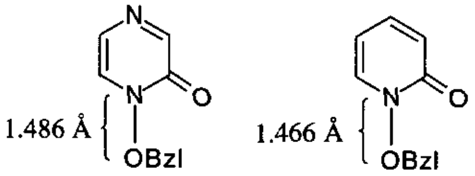
1 **3** **4** **5** **6**

7e

Scheme 2

Ir spectrum of **7e** showed the amide carbonyl stretching band at 1682 cm^{-1}, and its ^1H nmr spectrum showed a singlet at δ 7.75 ppm assignable to H-3, indicating that the pyrazinone ring remains in **7e**. The

^{13}C nmr spectrum showed peaks at δ 30.5 (s), 30.6 (s), 128.1 (d), and 156.1 (s) ppm attributable to carbons of C-5 (or C-6), C-6 (or C-5), C-3 positions and the amide carbonyl carbon, respectively. When **3e** was irradiated in $CHCl_3$, **7e** was also obtained in 24% yield . Therefore, the formation of **7e** can be explained in terms of [2+2] cycloaddition of 2(1*H*)-pyrazinone (**3e**). Four configurations, *syn* and *anti*, head-to-head, and head-to-tail, are possible for **7e**. However, the configuration of **7e** could not be determined because of its unstability at room temperature. The quantum yields for disappearance of **1a-e** at 313 nm were determined by using a valerophenone actinometer, and were listed in Table 1. These results showed that the photoreactions of **1a-e** took place more efficiently than that of 1-benzyloxy-2(1*H*)-pyridinone (Φ_{dis} 0.27).[10] This can be attributable to weekness of the N-O bond owing to the π-electron deficient diazine ring system. The results of PM3[13] calculations also supported this assumption. From comparison of the optimized geometries between **1a** and 1-benzyloxy-2(1*H*)-pyridinone, N-O bond distances of **1a** (1.486 Å) was slightly longer than that of pyridinone (1.466 Å) as shown in Figure 1. The photoreactions of **1a-e** were not quenched with 2,5-dimethyl-2,4-hexadiene, indicating that the photoreactions proceeded *via* π, π^* singlet states. These results indicate that the rate of the N-O bond cleavage in the compound **1a-e** should be higher than that of the intersystem crossing.



1a

1-Benzyloxy-
2(1*H*)-pyridinone

Figure 1. The N-O bond distance estimated by PM3 calculation.

EXPERIMENTAL

Melting points were determined on a Mel-Temp apparatus in open capillaries and are uncorrected. Ir spectra were recorded on a JASCO A-100 infrared spectrophotometer and uv-vis spectra were measured with a JASCO Ubest V-550 spectrophotometer. ^{1}H and ^{13}C nmr spectra were obtained from $CDCl_3$ and DMSO-d_6 solutions on a 270 MHz JEOL GX-270 spectrometer. Chemical shifts are reported in ppm (δ) downfield from internal TMS. Mass spectra were taken on a JEOL DX-300. Thin layer chromatography (tlc) analyses were performed on silica gel 60 F-254 with a 0.2 mm layer thickness. Column chromatography was carried out with Merck Kieselgel 60 (230-400 mesh). Hplc was carried out on a JASCO 880-PU and a 875-UV equipped with a JASCO IT integrator by using a column packed with a Finepak SIL $C_{12}S$. Combustion analyses were performed on a YANACO MT-3 CHN corder. An Ushio 100 W or 450 W high-pressure mercury lamp was used as irradiation source. 1-Benzyloxy-(**1a**) and -5,6-dimethyl-2(1*H*)-pyrazinones (**1c**) were prepared according to the literature.[4]

1-Benzyloxy-5-methyl-2(1*H*)-pyrazinone (1b). The reaction of *N*-(benzyloxy)glycinamide hydrochloride (580 mg, 2.69 mmol) with pyruvic aldehyde (40% in H_2O: 623 mg, 3.46 mmol) by the similar procedure for **1a**[4] gave the product **1b**, 310 mg (53%): mp 111-113 °C; ^1H nmr ($CDCl_3$) δ 2.15 (3H, s), 5.30 (2H, s), 6.82 (1H, s), 7.40 (5H, m), and 8.25 (1H, s); Found: C, 65.13; H, 5.82; N, 12.52. Calcd for $C_{12}H_{12}N_2O_2 \cdot 0.3H_2O$: C, 65.02; H,5.72; N, 12.64.

1-Benzyloxy-5,6-diphenyl-2(1*H*)-pyrazinone (1d). To a solution of 1-hydroxy-5,6-diphenyl-2(1*H*)-pyrazinone (**2d**)[14] (1.1 g, 4.2 mmol) and NEt_3 (0.5 g, 5.0 mmol) in DMSO (5 ml) was added benzyl chloride (0.8 g, 6.5 mmol). After stirring for 24 h at room temperature, the resulting precipitate was collected by filtration, and washed with H_2O and then with Et_2O. Purification by column chromatography on silica gel with a $CHCl_3$-acetone-EtOH (100:20:4) mixture afforded the product **1d**, 1.4 g (98%): mp 160-162 °C; ^1H nmr ($CDCl_3$) δ 4.92 (2H, s), 7.18-7.45 (15H, m), and 8.43 (1H, s); Found: C, 76.04; H, 5.15; N, 7.29. Calcd for $C_{23}H_{18}N_2O_2 \cdot 0.5H_2O$: C, 76.02; H, 5.27; N, 7.71.

1-Benzyloxy-5,6,7,8-tetrahydro-2(1*H*)-quinoxalinone (1e). 1-Hydroxy-5,6,7,8-tetrahydro-2(1*H*)-quinoxalinone (**2e**) was prepared by the similar procedure for **2d** from *N*-(hydroxy)glycinamide and 1,2-cyclohexanedione. The crude product was recrystallized from a MeOH-Et_2O mixture. **2e**: 41%: mp 199-200 °C; ^1H nmr (DMSO-d_6) δ 1.75 (4H, m), 2.65 (2H, t, J=6 Hz), 2.75 (2H, t, J=6 Hz), and 7.88 (1H, s); Found: C, 56.99; H, 6.23; N, 16.28. Calcd for $C_8H_{10}N_2O_2 \cdot 0.1H_2O$: C, 57.20; H, 6.12; N, 16.67. The compound **1e** was prepared by the similar procedure for **1d** from compound **2e**. **1e**: 58%: mp 127-127.5 °C; ^1H-nmr ($CDCl_3$) δ 1.70 (4H, m), 2.60 (2H, t, J=6 Hz), 2.70 (2H, t, J=6 Hz), 5.30 (2H, s), 7.38-7.49 (5H, m), and 8.15 (1H, s); Found: C, 69.58; H, 6.13; N, 10.74. Calcd for $C_{15}H_{16}N_2O_2$:C, 69.80; H, 6.33; N, 10.85.

General Procedure for Photolysis of 1. A solution of **1a** (200 mg, 1.00 mmol) in benzene (30 ml) was irradiated with a 450 W high-pressure mercury lamp under nitrogen atmosphere for 1.5 h. After removal of the solvent, products were isolated by flash chromatography on silica gel with $CHCl_3$-acetone-EtOH (100:20:4) mixture as an eluent under nitrogen atmosphere. **3b**: mp 122-124 °C (lit.,[15] 126-128 °C).; **4c**: mp 212-215 °C; ^1H nmr ($CDCl_3$) δ 2.12 (3H, s), 2.21 (1H, s), 5.92 (2H, s), and 7.30-7.40 (5H, m). Found: C, 63.16; H, 6.10; N, 10.87. Calcd for $C_{15}H_{16}N_2O_2$:C, 62.89; H, 6.50; N, 11.28.; **3d**: mp 239-240 °C (lit.,[15]: 243-244 °C); **4d**: ^1H nmr ($CDCl_3$) δ 5.50 (2H, s), and 7.20-7.60 (15H, m). Found: C, 74.13; H, 5.42; N, 7.19. Calcd for $C_{23}H_{18}N_2O_2$:C, 74.63; H, 5.27; N, 7.25.; **3e**: mp 235-237 °C; ^1H nmr ($CDCl_3$) δ 1.78-1.88 (4H,m), 2.65-2.73 (4H, m), and 8.03 (1H, s); ^{13}C nmr ($CDCl_3$) δ 20.84, 22.04, 25.94, 28.26, 130.46, 135.00, 143.55, and 156.20. Found: C, 63.31; H, 6.65; N, 18.20. Calcd for $C_8H_{10}N_2O{\cdot}0.1H_2O$: C, 63.22; H, 6.76; N, 18.43.; **4e**: mp 235-237 °C; ^1H nmr ($CDCl_3$) δ 1.72-1.82 (4H, m), 2.48-2.58 (4H, m), 5.40 (2H, s), and 7.29-7.50 (5H, m). Found: C, 70.01; H, 6.30; N, 10.63. Calcd for $C_{15}H_{16}N_2O_2$: C, 69.80; H, 6.33; N, 10.85.; **7e**: mp 260-261 °C; ir (KBr) 1682 cm^{-1}; ^1H nmr (DMSO-d_6) δ 1.70-1.80 (4H, m), 2.53-2.60 (4H, m), and 7.75 (1H, s); ^{13}C-nmr (DMSO-d_6) δ 20.94, 22.11, 26.14, 28.40, 30.52, 30.60, 128.11, and 156.09; MS *m/z* 150 ($M^+/2$); Found: C, 72.99; H, 4.78; N, 13.83. Calcd for $C_{16}H_{20}N_4O_2$:C, 72.71; H,5.08; N, 14.13.

Quantum Yield Determination. The benzene solution of **1** (*ca.* 50 mM) containing a known concentration of eicosane (*ca.* 1 mM) as a caliburant, was placed in 15x150 mm Pyrex tube. The tube was degassed with three freeze-pump-thaw cycles and then sealed. Irradiation was performed on a "merry-go-round" apparatus with a 450 W high-pressure mercury lamp. A potassium chromate filter solution was used to isolate the 313 nm line. The conversions of **1** were within 10%. Analysis was performed on a Shimadzu GC-4B gas chromatograph equipped with a flame ionization detector using a 2 m column containing SE-30. Quantum yield was determined by using a valerophenone actinometer.

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