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Photocyclization of *N*-Alkoxyalkylphthalimides with Favored δ-Hydrogen Abstraction: Syntheses of Oxazolo[4,3-*a*]isoindoles and Oxazolo[4,3-*a*]-isoindole-1-spiro-1′-cycloalkane Ring Systems[1)]

Yasuhiko Sato,*[a] Hideo Nakai,[a] Masao Wada,[a] Hiroshi Ogiwara,[a] Tomishige Mizoguchi,[a] Yoshihiro Migita,[b] Yasumaru Hatanaka[b] and Yuichi Kanaoka[b]

Organic Chemistry Research Laboratory, Tanabe Seiyaku Co., Ltd.,[a] 2-2-50, Kawagishi, Toda, Saitama 335, Japan and Faculty of Pharmaceutical Sciences, Hokkaido University,[b] Kitaku, Kita-12, Nishi-6, Sapporo 060, Japan

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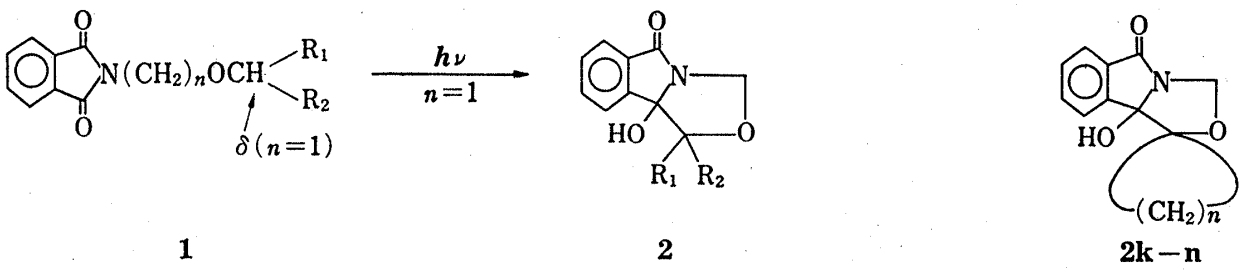
Photolysis of *N*-ω-alkoxyalkylphthalimides **1** gave the intramolecularly cyclized compounds, oxazolo[4,3-*a*]isoindoles **2a—g**, pyrrolo[2,1-*a*]isoindoles **6i—j**, oxazolo[4,3-*a*]-isoindole-1-spiro-1′-cycloalkanes **2k—n** and 3,4-dihydro-2-benzazepine-1,5(2*H*)-dione **3**, *via* δ-hydrogen abstraction and/or two-fold Norrish type II processes.

Keywords——*N*-ω-alkoxyalkylphthalimide; photolysis; δ-hydrogen abstraction; two-fold Norrish type II process; multicyclic spiro system

The photochemical behavior of cyclic imides is diverse and interesting,[2)] with reactions such as the Norrish type I and type II processes and oxetane formation. For example, the imide carbonyl of *N*-substituted phthalimides undergoes the Norrish type II photocyclization, leading to a variety of ring systems.[2)] In the earlier stage of this study, we briefly reported[3)] that, on irradiation, *N*-ω-alkoxyalkylphthalimides (**1**) undergo facile δ-hydrogen transfer to afford an oxazolo[4,3-*a*]isoindole system **2**. In addition, this finding was extensively applied for the photochemical synthesis of the corresponding 1-spiro ring system **2k—n**.[4)] In the present paper we wish to present a full account of the work described in these preliminary reports.



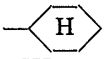
1 **2** **2k—n**

Chart 1

A series of *N*-ω-alkoxyalkylphthalimides (**1**) was prepared either from *N*-bromomethylphthalimide and alcohol or from *N*-carbethoxyphthalimide and alkoxy amine as described in the experimental section. The photolysis was performed with a 400 W high pressure mercury lamp in acetone (or acetonitrile) solution under a stream of argon, and the results are listed in Table I. The assignment of these structures was made on the basis of elemental analyses and spectral properties.

The N atom in the phthalimide system is regarded as the α-atom with respect to the imide carbonyl carbon. Generally in the typical Norrish type II processes γ-hydrogen transfer is the common reaction of the carbonyl system.[5,6)] As expected, however, photolysis of **1a** which lacks γ-hydrogen afforded **2a**, apparently as a result of δ-hydrogen transfer. Likewise,

TABLE I. Photocyclization of *N*-alkoxyalkylphthalimides **1a—j**

Substrate				Conditions[a]				Product[b] (yield %[c])			Recovery
				Weight		Concentration	Time	**2**	**6**	**3**	**1**
1	*n*	R_1	R_2	g	mmol	mM	(h)	(δ)	(δ)	(γ)	(yield %)
a	1	H	H	1.2	6.3	23.3	20.5[a]	12			63
b	1	H	CH_3	1.2	5.9	21.7	8.5	23			52
				5.0	24.4	48.8	0.5[b]	22[d]			50
c	1	H	Ph	1.1	4.0	16.1	3	60			18
d	1	H	CH_2CH_3	1.2	5.5	18.3	2	29 (t 23, c 6)			63
e	1	H		1.2	4.4	14.7	3	43			53
f	1	CH_3	CH_3	1.2	5.5	18.3	2	39			33
g	1	Ph	Ph	1.2	3.5	11.7	3	42			
h	2	H	H	4.2	20.6	29.4	8[a]			33	64
i	3	H	H	1.2	5.5	18.3	3		34 (t 10, c 24)		42
j	3	CHR_1R_2=H		1.2	5.9	22.5	7.5		10		53

a) The following high pressure mercury lamps were used; a=200 W, b=1 kW.
b) The following abbreviations are used; t=*trans*, c=*cis*.
c) Acetone was used as the irradiation solvent except for compounds **1d**, **1e**, **1f** and **1g** (in acetonitrile).
d) *tert*-Butanol was used as the irradiation solvent.

a mixture of isomers **2b** (1: 1) was obtained from **1b**. Compound **1c** gave, after purification by preparative thin-layer chromatography (TLC), a single product **2c** in 60% yield. The formation of **2c** in a relatively good yield is undoubtedly due to the involvement of the more reactive benzyl-methylene in **1c**. A mixture obtained from **1d** was separated into two stereoisomers **2d**, *trans* and *cis*, which are due to the configuration of the ethyl with respect to the hydroxyl group. The assignment was confirmed on the basis of the nuclear magnetic resonance (NMR) spectra. The methyl part of the ethyl function in **2d** appeared as triplet peaks at δ 0.86 and 1.08 (in deuteriochloroform), for the *trans* isomer and *cis* isomer, respectively. Namely, the signal in the *trans* isomer of **2d** was shifted to a higher field than that of the corresponding *cis* isomer, due to the shielding effect of the phthalimide ring. In a similar manner, compounds **1e—g** gave the corresponding products in fairly good yields. Photolysis of compound **1h** having both γ- and ε-hydrogens gave 3,4-dihydro-2-benzazepine-1,5(2*H*)-dione **3**.[7] The formation of **3** can be explained on the basis of the general pattern of phthalimide photochemistry.[7] The primary product **4** of the Norrish type II cyclization (initiated by a γ-hydrogen abstraction) from **1h** has a newly formed carbonyl group which still has a γ-hydrogen that is ε in the original structure **1h**. Thus the second γ-hydrogen abstraction now follows, and the Norrish type II elimination, again by way of the biradical **5**, ultimately affords the benzazepinone lactam (**3**) accompanied by an olefin fragment (formaldehyde) (Chart 2). It is worth noting that the photolysis of **1i** having γ-, δ- and ζ-hydrogens also afforded predominantly the cyclized isomers **6i**, *trans* and *cis*, resulting from δ-hydrogen transfer in a moderate yield. Their structures were assigned in a manner similar to those described for **2d**. The chemical shift of the methoxy group in **6i**-*trans* (δ 2.91) appeared at a higher field than that of the corresponding **6i**-*cis* (δ 3.51). From **1j**, a low yield of **6j** was obtained as a result of δ-hydrogen transfer involving the methylene group adjacent to the hydroxy group. This reaction provides an example of intramolecular addition of an alcohol molecule to the phthalimide carbonyl.[8]

Normally γ-hydrogens of a ketone have much higher reactivity than δ-hydrogens. However, the δ-hydrogen of the δ-methoxy varelophenone (**7**) had reactivity comparable with that of the γ-hydrogen.[5] While the γ-C–H bonds of **7** were deactivated by the inductive

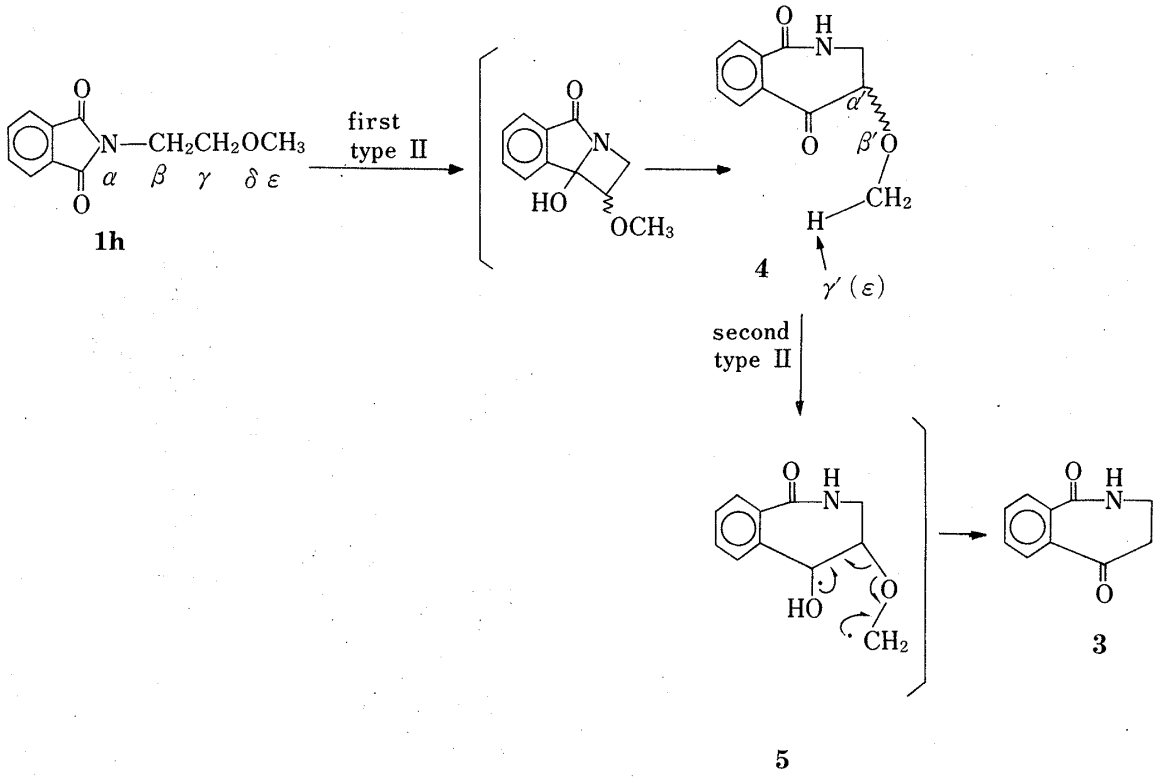


Chart 2

effect of the δ-methoxy group, the δ-C–H bonds of **7** are activated by the δ-methoxy group since an alkoxy group enhances the reactivity of the adjacent C–H bonds for triplet carbonyl by a factor of 5.[5] By contrast, photolysis of **1** ($n=3$) gave predominantly the δ-hydrogen-transferred product **6** as a result of the relatively favored δ-hydrogen abstraction, intrinsic to the phthalimide system, coupled with the activation due to the alkoxy group.[5] Such a consideration again points to the *N*-alkoxymethylphthalimides (**1**) ($n=1$) as canditate substrates for a possibly efficient photocyclization because these substrates **1** ($n=1$) have no γ-hydrogen but one δ-hydrogen that must be activated by the oxygen and two alkyl substituents.[5]

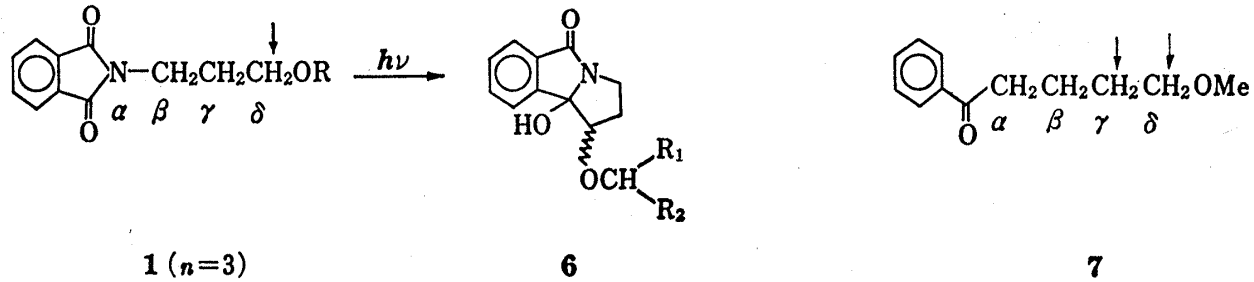


Chart 3

In the search for biologically active substances, syntheses of potentially active new compounds represent an important approach. These target new compounds could be either of an entirely novel class or of a group with certain structural characteristics. For example, the involvement of a quaternary carbon as a central atom is known to be essential in designing many synthetic narcotic analgesics.[8] Hydrogene abstraction from a tertiary carbon followed by C–C radical coupling is one of the attractive routes for the construction of a quaternary carbon. The above consideration, together with the rather good results of the photocyclization

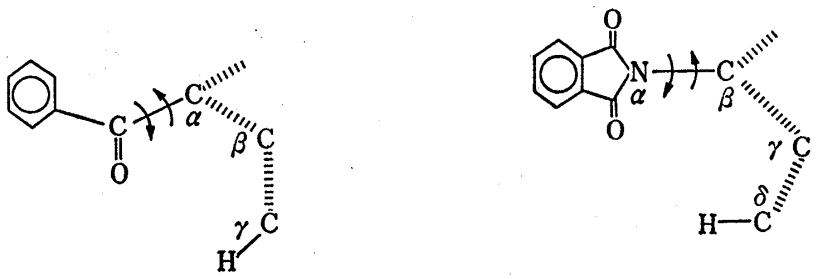
with compounds **1f—g**, immediately led us to examine whether a tertiary C–H of **1** (n=1) can participate or not in such a reaction to give, for example, spiro ring compounds which are otherwise difficult to access. As expected, the title compounds **2k—n** were smoothly obtained in moderate yields by photolysis of **1k—n**, respectively (Chart 1). Table II lists the results with varying spiro ring sizes (5—8 membered).

Table II. Syntheses of Oxazolo [4,3-*a*]isoindole-1-spiro-1′-cycloalkane **2k—n**

Substrate			Conditions				Product[a]	Recovery
			Weight	Concentration		Time	**2k—n**	**1**
1	n	R^1,R^2	g	mmol	mM	h	(yield %)	(yield %)
k	1	$-(CH_2)_4-$	1.2	4.9	16.3	2	38(28)	24(38)
l	1	$-(CH_2)_5-$	1.2	4.6	15.4	2	29(33)	23(38)
m	1	$-(CH_2)_6-$	1.2	4.2	14.6	2	49	43
n	1	$-(CH_2)_7-$	1.2	4.2	13.9	1	53	10

a) Acetonitrile was used as the irradiation solvent; the values in parenthesis are the yields obtained when acetone was used as the solvent.

In simple carbonyl compounds such as **8**, the C_α–C_β bond can assume various conformations as the C(carbonyl)-C_α bond rotates. In contrast, in phthalimides **9** the N_α–C_β bond is rigidly placed on the plane of the cyclic imide (Chart 4). Thus, in going from a carbonyl system to a phthalimide system, the "unprofitable rotamer distribution"[9] decreases and, consequently, the average distance between the carbonyl oxygen and the pertinent hydrogen for C_γ of simple ketones and C_δ of phthalimides would be nearly comparable. The relatively facile δ-hydrogen transfer in the phthalimide system, by way of seven-membered transition states, may be at least in part interpreted in terms of this favorable geometry for the Norrish type II process.[10] Irradiation of **1i** in the presence of *cis*-pentadiene showed no appreciable quenching of the photolysis. However, the problem of the multiplicity of the species involved remains undecided in view of the photochemistry of the closely related *N*-alkylphthalimides.[10]



8 **9**

Chart 4

Further quantitative studies of the imide photochemistry are under way.[11] So far none of the spiro compounds synthesized in this work has shown significant pharmacological activities. One of the purposes of our synthetic studies on cyclic imides[2] is the preparation of a variety of intermediate compounds with multifunctionalities. The next step will be, for example, pharmacological evaluations of new cyclic amine derivatives to be obtained by reduction of the amide moieties of the oxazoloisondole system **2**.

Experimental

All melting points were determined with a Yanagimoto capillary melting point apparatus (Model MP-1) and are uncorrected. Infrared (IR) spectra were recorded on a Hitachi IR-215 spectrophotometer. NMR

spectra were determined on JEOL ME 60 and FX 100 instruments in $CDCl_3$ (containing tetramethylsilane as an internal standard), unless otherwise specified. The chemical shifts are expressed in δ (ppm) values. Coupling constants (J) are given in Hz and the following abbreviations are used; s=singlet, d=doublet, t=triplet, q=quartet, m=multiplet, br=broad. Mass spectra (MS) were measured on a Hitachi RMS-4 mass spectrometer.

General Procedure for the Synthesis of 2-[(ω-Alkoxy)alkyl]isoindole-1,3(2*H*)-dione (=*N*-ω-Alkoxyalkylphthalimide) (1)——Method A:[12] A solution of 2-[(bromo)methyl]-isoindole-1,3(2*H*)-dione (=*N*-bromomethylphthalimide) (0.05 mol) and the alcohol (0.07 mol) in anhyd. dimethylformamide (20—30 ml) was heated at 90°C for 2 h. The mixture was poured into ice-water and extracted with chloroform. The extracts were washed and dried. The solution was concentrated to dryness *in vacuo* and the residue was subjected to silica gel column chromatography with benzene, followed by recrystallization.

2-[(Methoxy)methyl]-isoindole-1,3(2*H*)-dione (**1a**); mp 120—121°C (lit.,[12] mp 121°C).

2-[(Ethoxy)methyl]-isoindole-1,3(2*H*)-dione (**1b**); mp 80—83°C (lit.,[12] mp 83°C).

2-[(Benzyloxy)methyl]-isoindole-1,3(2*H*)-dione (**1c**); yield (92.0%), colorless prisms from isopropyl ether, mp 80—81°C. IR ν_{max}^{Nujol} cm^{-1}: 1765, 1710. *Anal.* Calcd for $C_{16}H_{13}NO_3$: C, 71.90; H, 4.90; N, 5.24. Found: C, 72.01; H, 4.93; N, 5.30.

2-[(*n*-Propyloxy)methyl]-isoindole-1,3(2*H*)-dione (**1d**); mp 52—53°C (lit.,[13] mp 53°C).

2-[(Cyclohexylmethyloxy)methyl]-isoindole-1,3(2*H*)-dione (**1e**); yield (95%), colorless prisms from hexane, mp 66—67°C. IR ν_{max}^{Nujol} cm^{-1}: 1765, 1710. *Anal.* Calcd for $C_{16}H_{19}NO_3$: C, 70.31; H, 7.01; N, 5.13. Found: C, 70.60; H, 7.04; N, 5.23.

2-[(Isopropyloxy)methyl]-isoindole-1,3(2*H*)-dione (**1f**); mp 98—99°C (lit.,[13] mp 93°C).

2-[(Diphenylmethyloxy)methyl]-isoindole-1,3(2*H*)-dione (**1g**); yield (38.8%), colorless needles from EtOAc–hexane, mp 112—113°C. IR ν_{max}^{Nujol} cm^{-1}: 1780, 1710. MS *m/e*: 343 (M^+). NMR: 5.19 (2H, s, NCH_2O), 5.62 (1H, s, OCH), 7.0—7.5 (10H, m, aromatic H), 7.5—7.9 (4H, m, aromatic H). *Anal. Calcd* for $C_{22}H_{17}NO_3$: C, 76.95; H, 4.99; N, 4.08. Found: C, 77.11; H, 5.20; N, 4.22.

2-[(Cyclopentyloxy)methyl]-isoindole-1,3(2*H*)-dione (**1k**); yield (74.2%), colorless needles from hexane, mp 58—60°C. IR ν_{max}^{Nujol} cm^{-1}: 1780, 1730. MS *m/e*: 245 (M^+), 246 (M^++1). *Anal.* Calcd for $C_{14}H_{15}NO_3$: C, 68.55; H, 6.16; N, 5.71. Found: C, 68.70; H, 6.12; N, 5.90.

2-[(Cyclohexyloxy)methyl]-isoindole-1,3(2*H*)-dione (**1l**); mp 79—81°C (lit.[12] mp 81—83°C).

2-[(Cycloheptyloxy)methyl]-isoindole-1,3(2*H*)-dione (**1m**); yield (64.3%), colorless prisms from hexane, mp 49—50°C. IR ν_{max}^{Nujol} cm^{-1}: 1780, 1720. MS *m/e*: 273 (M^+), 274 (M^++1). *Anal.* Calcd for $C_{16}H_{19}NO_3$: C, 70.31; H, 7.01; N, 5.13. Found: C, 70.53; H, 6.98; N, 5.32.

2-[(Cyclooctyloxy)methyl]-isoindole-1,3(2*H*)-dione (**1n**); yield (66.8%), colorless prisms from hexane, mp 37—38°C. IR ν_{max}^{Nujol} cm^{-1}: 1780, 1730, 1710. MS *m/e*: 287 (M^+), 288 (M^++1). *Anal.* Calcd for $C_{17}H_{21}NO_3$: C, 71.05; H, 7.37; N, 4.87. Found: C, 71.22; H, 7.39; N, 4.99.

Method B:[14] 2-Carbethoxy-isoindole-1,3(2*H*)-dione (=*N*-carbethoxyphthalimide) (0.10 mol) was added to a solution of the alkoxy amine (0.11 mol) in chloroform (150 ml) at room temperature and the mixture was stirred for 1—2 h. The reaction mixture was washed with dil. hydrochloric acid and water. The chloroform layer was dried, the solution was concentrated to dryness *in vacuo* and the residue was purified by the described methods. (yield; 85—95%).

2-[(2-Methoxy)ethyl]-isoindole-1,3(2*H*)-dione (**1h**); mp 148—150°C (lit.,[15] mp 150°C).

2-[(3-Methoxy)propyl]-isoindole-1,3(2*H*)-dione (**1i**); mp 47—49°C (lit.,[16] mp 49°C).

2-[(3-Hydroxy)propyl]-isoindole-1,3(2*H*)-dione (**1j**); mp 74—75°C (lit.,[17] mp 75°C).

General Procedure for the Photolysis——A solution of **1** [1.1—5.0 g (3.5—24.4 mmol)] in acetone (11.7—48.8 mM) was irradiated with a 400 W high pressure mercury lamp under a stream of argon for 0.5—20.5 h at room temperature, unless otherwise specified. After removal of the solvent under reduced pressure, the residue was subjected to silica gel preparative TLC, followed by recrystallization of each fraction as appropriate. (Experimental details of the irradiation are given in Tables I, II).

3,9b-Dihydro-9b-hydroxyoxazolo[4,3-*a*]isoindol-5(1*H*)-one (2a)——Compounds **1a** (760 mg, 63.3%) and **2a** were obtained by preparative TLC with benzene–EtOAc (3:1). **2a** was recrystallized from EtOAc–hexane, colorless prisms of 144 mg (12.0%), mp 127—128°C. IR ν_{max}^{Nujol} cm^{-1}: 3325, 1680. MS *m/e*: 191 (M^+), 192 (M^++1). NMR: 3.61 and 4.01 (2H, each d, J=9.0 Hz, OCH_2), 4.25 (1H, m, OH), 4.58 and 5.06 (2H, each d, J=6.0 Hz, NCH_2), 7.48 (4H, m, aromatic H). *Anal.* Calcd for $C_{10}H_9NO_3$: C, 62.82; H, 4.75; N, 7.33. Found: 62.88; H, 4.74; N, 7.28.

3,9b-Dihydro-9b-hydroxy-1-methyloxazolo[4,3-*a*]isoindol-5(1*H*)-one (2b)——Compounds **1b** (620 mg, 51.6%) and **2b** were obtained by preparative TLC with benzene–EtOAc (1:1). **2b** was recrystallized from EtOAc–hexane, colorless needles of 370 mg (22.5%), mp 101—102°C. IR ν_{max}^{Nujol} cm^{-1}: 3325, 1680. MS *m/e*: 205 (M^+), 206 (M^++1). NMR: 0.80 and 1.40 (3H, each d, J=6.0 Hz, CH_3), 3.25—3.60 (0.5H, q-like, a part of CH), 4.05—5.30 (2.5H, m, NCH_2 and a part of CH), 5.20 (1H, m, OH), 7.30—7.90 (4H, m, aromatic H). *Anal.* Calcd for $C_{11}H_{11}NO_3$: C, 64.38; H, 5.40; N, 6.83. Found: C, 64.35; H, 5.38; N, 6.71. With *tert*-butanol as the solvent, compounds **1b** (2.49 g, 50%) and **2b** (1.09 g, 22%) were obtained from the residue.

3,9b-Dihydro-9b-hydroxy-1-phenyloxazolo[4,3-*a*]isoindol-5(1*H*)-one (2c)——Compounds **1c** (198 mg, 18.4%) and **2c** were obtained by preparative TLC with EtOAc–chloroform (1:1). **2c** was recrystallized

from EtOAc–hexane, colorless prisms of 649 mg (60%), mp 149—150°C. IR ν_{max}^{Nujol} cm^{-1}: 3280, 1690. MS *m/e*: 267 (M$^+$), 268 (M$^+$+1). NMR: 4.01 (1H, s, OH), 4.72 and 5.50 (2H, each d, J=6.0 Hz, NCH$_2$), 5.17 (1H, s, CHPh), 6.70—7.70 (9H, m, aromatic H). *Anal.* Calcd for $C_{16}H_{13}NO_3$: C, 71.90; H, 4.90; N, 5.24. Found: C, 72.21; H, 4.85; N, 5.36.

3,9b-Dihydro-1-ethyl-9b-hydroxyoxazolo[4,3-*a*]isoindol-5(1*H*)-one (*trans* and *cis*) (2d)——With acetonitrile as the solvent, compounds **1d** (720 mg, 62.5%) and **2d** (*trans* and *cis*) were obtained by preparative TLC with benzene–EtOAc (3: 1). **2d** (*trans*) was recrystallized from EtOAc–hexane, colorless prisms of 280 mg (23.3%), mp 125—128°C. IR ν_{max}^{Nujol} cm^{-1}: 3300, 1695. MS *m/e*: 219 (M$^+$), 220 (M$^+$+1). NMR (100 MHz): 0.86 (3H, t, J=5.0 Hz, CH$_3$), 1.62 (2H, m, CH$_2$), 3.12 (1H, s, OH), 4.06 (1H, m, CH), 4.66 and 5.35 (2H, each d, J=6.0 Hz, NCH$_2$), 7.40—8.00 (4H, m, aromatic H). *Anal.* Calcd for $C_{12}H_{13}NO_3 \cdot 1/2H_2O$: C, 63.14; H, 6.18; N, 6.14. Found: C, 63.29; H, 5.84; N, 6.17. Moreover, from the mother liquor, 70 mg (6%) of **2d** (*cis*) was obtained as colorless prisms, mp 114—115°C. IR ν_{max}^{Nujol} cm^{-1}: 3300, 1695. MS *m/e*: 219 (M$^+$), 220 (M$^+$+1). NMR (100 MHz): 1.08 (3H, t, J=6.0 Hz, CH$_3$), 1.90 (2H, q, J=6.0 Hz, CH$_2$), 3.19 (1H, s, OH), 3.37 (1H, m, CH), 4.98 and 5.16 (2H, each d, J=5.0 Hz, NCH$_2$), 7.40—7.84 (4H, m, aromatic H). *Anal.* Calcd for $C_{12}H_{13}NO_3$: C, 65.74; H, 5.98; N, 6.39. Found: 65.25; H, 5.93; N, 6.45.

1-Cyclohexyl-3,9b-dihydro-9b-hydroxyoxazolo[4,3-*a*]isoindol-5(1*H*)-one (2e)——With acetonitrile as the solvent, compounds **1e** (630 mg, 52.5%) and **2e** were obtained by preparative TLC with benzene–EtOAc (3: 1). **2e** was recrystallized from EtOAc–hexane, colorless needles of 520 mg (43.3%), mp 166—168°C. IR ν_{max}^{Nujol} cm^{-1}: 3290, 1690. MS *m/e*: 273 (M$^+$), 274 (M$^+$+1). NMR: 0.80—2.90 (11H, m, cyclohexyl H), 3.17 (1H, d, J=7.5 Hz, CH), 4.77 and 5.25 (2H, each d, J=4.5 Hz, NCH$_2$), 6.25 (1H, br s, OH), 7.60 (4H, m, aromatic H). *Anal.* Calcd for $C_{16}H_{19}NO_3$: C, 70.31; H, 7.01; N, 5.13. Found: C, 70.24; H, 7.11; N, 5.15.

3,9b-Dihydro-1,1-dimethyl-9b-hydroxyoxazolo[4,3-*a*]isoindol-5(1*H*)-one (2f)——With acetonitrile as the solvent, compounds **1f** (393 mg, 32.8%) and **2f** were obtained by preparative TLC with benzene–EtOAc (4: 1). **2f** was recrystallized from EtOAc–hexane, colorless feathers of 484 mg (39.3%), mp 123—124°C. IR ν_{max}^{Nujol} cm^{-1}: 3220, 1683. MS *m/e*: 219 (M$^+$), 220 (M$^+$+1). NMR: 0.68 and 1.54 (6H, each s, CH$_3$×2), 3.35 (1H, br s, OH), 4.90 and 5.05 (2H, each d, J=5.0 Hz, NCH$_2$), 7.35—7.80 (4H, m, aromatic H). *Anal.* Calcd for $C_{12}H_{13}NO_3$: C, 65.74; H, 5.98; N, 6.39. Found: C, 65.96; H, 6.16; N, 6.32.

3,9b-Dihydro-1,1-diphenyl-9b-hydroxyoxazolo[4,3-*a*]isoindol-5(1*H*)-one (2g)——Acetonitrile was used as the solvent. The residue was recrystallized from acetone, colorless prisms of 498 mg (41.5%), mp 248—249°C. IR ν_{max}^{Nujol} cm^{-1}: 3320, 1695. MS *m/e*: 343 (M$^+$), 344 (M$^+$+1). NMR (DMSO-d_6): 5.17 and 5.63 (2H, each d, J=5.0 Hz, NCH$_2$), 6.95—8.20 (14H, m, aromatic H). *Anal.* Calcd for $C_{22}H_{17}NO_3$: C, 76.95; H, 4.99; N, 4.08. Found: C, 77.23; H, 5.09; N, 4.33.

3,4-Dihydro-2-benzazepine-1,5(2*H*)-dione (3) (Photolysis of 1h)——Compound **1h** (2.30 g, 63.8%), an unknown compound (40 mg, 1.1%) and **3** were obtained by preparative TLC with EtOAc. **3** was recrystallized from EtOAc, colorless prisms of 1.17 g (32.5%), mp 159—161°C. IR ν_{max}^{Nujol} cm^{-1}: 1680, 1660. MS *m/e*: 175 (M$^+$). NMR: 2.90—3.08 (2H, m, COCH$_2$), 3.14—3.70 (2H, m, NCH$_2$), 7.50—8.10 (4H, m, aromatic H), 8.10—8.50 (1H, m, NH). *Anal.* Calcd for $C_{10}H_9NO_2$: C, 68.56; H, 5.18; N, 8.00. Found: C, 68.68; H, 5.33; N, 7.99. The physico-chemical properties of this compound were identical with those of an authentic sample.[7]

9b-Hydroxy-1-methoxy-1,2,3,9b-tetrahydropyrrolo[2,1-*a*]isoindol-5-one (*trans* and *cis*) (6i)——Compounds **1i** (501 mg, 41.6%) and **6i** (*trans* and *cis*) were obtained by preparative TLC with EtOAc–cyclohexane (2: 1). **6i** (*trans*) was recrystallized from isopropyl ether, colorless prisms of 120 mg (10.0%), mp 119—121°C. IR ν_{max}^{Nujol} cm^{-1}: 3325, 1690. MS *m/e*: 219 (M$^+$), 220 (M$^+$+1). NMR: 2.20—2.75 (2H, m, CH$_2$), 2.91 (3H, s, OCH$_3$), 3.20—3.87 (3H, m, NCH$_2$ and CH), 4.67 (1H, br s, OH), 7.30—7.60 (4H, m, aromatic H). *Anal.* Calcd for $C_{12}H_{13}NO_3$: C, 65.74; H, 5.98; N, 6.39. Found: C, 65.80; H, 5.91; N, 6.31. **6i** (*cis*) was recrystallized from EtOAc, colorless prisms of 290 mg (24.1%), mp 176—178°C. IR ν_{max}^{Nujol} cm^{-1}: 3225, 1680. MS *m/e*: 219 (M$^+$), 220 (M$^+$+1). NMR: 2.20—2.80 (2H, m, CH$_2$), 3.51 (3H, s, OCH$_3$), 3.40—3.80 (3H, m, NCH$_2$ and CH), 3.95 (1H, br s, OH), 7.25—7.80 (4H, m, aromatic H). *Anal.* Calcd for $C_{12}H_{13}NO_3$: C, 65.74; H, 5.98; N, 6.39. Found: C, 65.78; H, 5.98; N, 6.51.

1,9b-Dihydroxy-1,2,3,9b-tetrahydropyrrolo[2,1-*a*]isoindol-5-one (6j)——Compounds **1j** (643 mg, 52.7%) and **6j** were obtained by preparative TLC with benzene–EtOAc (1: 1). **6j** was recrystallized from EtOAc, colorless prisms of 119 mg (9.8%), mp 176—178°C. IR ν_{max}^{Nujol} cm^{-1}: 3400, 3240, 1650. MS *m/e*: 205 (M$^+$). NMR (DMSO-d_6): 2.20—2.60 (2H, m, CH$_2$), 3.20—3.75 (3H, m, NCH$_2$ and CH), 4.00—5.40 (2H, br, OH×2), 7.50—7.80 (4H, m, aromatic H). *Anal.* Calcd for $C_{11}H_{11}NO_3$: C, 64.38; H, 5.40; N, 6.83. Found: C, 64.30; H, 5.39; N, 6.56.

3,9b-Dihydro-9b-hydroxy-5-oxo-oxazolo[4,3-*a*]isoindole-1-spiro-1′-cyclopentane (2k)——Compounds **1k** (450 mg, 37.5%) and **2k** were obtained by preparative TLC with benzene–EtOAc (4: 1). **2k** was recrystallized from EtOAc–hexane, colorless scales of 330 mg (27.5%), mp 135—137°C. IR ν_{max}^{Nujol} cm^{-1}: 3220, 1690. MS *m/e*: 245 (M$^+$), 246 (M$^+$+1). NMR: 0.70—2.40 (8H, m, CH$_2$×4), 3.94 (1H, br s, OH), 4.88 and 4.96 (2H, each d, J=5.0 Hz, NCH$_2$), 7.40—7.80 (4H, m, aromatic H). *Anal.* Calcd for $C_{14}H_{15}NO_3$: C, 68.55; H,; 6.16 N, 5.17. Found: C, 68.18; H, 6.17; N, 5.17. With acetonitrile as the solvent, compounds **1k** (280 mg, 24.0%) and **2k** (450 mg, 37.5%) were obtained.

3,9b-Dihydro-9b-hydroxy-5-oxo-oxazolo[4,3-*a*]isoindole-1-spiro-1′-cyclohexane (2l)——Compounds **1l** (460 mg, 38.3%) and **2l** were obtained by preparative TLC with benzene–EtOAc (4: 1). **2l** was recrystallized

from EtOAc–hexane, colorless needles of 390 mg (32.5%), mp 185—186°C. IR ν_{max}^{Nujol} cm^{-1}: 3230, 1695. MS *m/e*: 259 (M^+), 260 (M^++1). NMR: 0.50—2.50 (10H, m, $CH_2\times5$), 4.88 and 5.03 (2H, each d, J=5.0 Hz, NCH_2), 6.20—6.60 (1H, m, OH), 7.35—7.80 (4H, m, aromatic H). *Anal.* Calcd for $C_{15}H_{17}NO_3$: C, 69.48; H, 6.61; N, 5.40. Found: C, 69.54; H, 6.79; N, 5.31. With acetonitrile as the solvent, compounds **1l** (276 mg, 23.0%) and **2l** (339 mg, 28.5%) were obtained.

3,9b-Dihydro-9b-hydroxy-5-oxo-oxazolo[4,3-*a*]isoindole-1-spiro-1′-cycloheptane (2m)——With acetonitrile as the solvent, compounds **1m** (510 mg, 42.5%) and **2m** were obtained by preparative TLC with benzene–EtOAc (4: 1). **2m** was recrystallized from EtOAc–hexane, colorless needles of 590 mg (49.2%), mp 131—132°C. IR ν_{max}^{Nujol} cm^{-1}: 3250, 1695. MS *m/e*: 273 (M^+), 274 (M^++1). NMR: 0.60—2.40 (12H, m, $CH_2\times6$), 3.70 (1H, br s, OH), 4.87 and 4.95 (2H, each d, J=5.0 Hz, NCH_2), 7.20—7.70 (4H, m, aromatic H). *Anal.* Calcd for $C_{16}H_{19}NO_3$: C, 70.31; H, 7.01; N, 5.13. Found: C, 70.11; H, 7.24; N, 5.09.

3,9b-Dihydro-9b-hydroxy-5-oxo-oxazolo[4,3-*a*]isoindole-1-spiro-1′-cyclooctane (2n)——With acetonitrile as the solvent, compounds **1n** (121 mg, 10.0%) and **2n** were obtained by preparative TLC with benzene–EtOAc (4: 1). **2n** was recrystallized from EtOAc–hexane, a colorless powder of 630 mg (52.5%), mp 130—131°C. IR ν_{max}^{Nujol} cm^{-1}: 3225, 1690. MS *m/e*: 287 (M^+), 288 (M^++1). NMR: 0.80—2.30 (14H, m, $CH_2\times7$), 3.80—4.30 (1H, m, OH), 4.77 and 4.91 (2H, each d, J=5.0 Hz, NCH_2), 7.30—7.80 (4H, m, aromatic H) *Anal.* Calcd for $C_{17}H_{21}NO_3$: C, 71.05; H, 7.37; N, 4.87. Found: C, 70.92; H, 7.54; N, 4.85.

The Photolysis of Compound 1i in the Presence of *cis*-1,3-Pentadiene——(A): A solution of 438 mg (20.0 mmol) of **1i** in acetonitrile (250 ml) was irradiated with a 400 W high pressure mercury lamp at room temperature for 1.0 h in an atmosphere of argon. The residue obtained on removal of the solvent *in vacuo* was purified by silica gel preparative TLC with EtOAc to give 220 mg (50.2%) of unreacted **1i** 50 mg (11.2%) of **6i** (*trans*) and 90 mg (22.5%) of **6i** (*cis*).

(B): A solution of 438 mg (20.0 mmol) of **1i** and *cis*-1,3-pentadiene (68 mg, 10.0 mmol) in acetonitrile (250 ml) was processed in a manner similar to that described above. **1i** 259 mg (59.3%), **6i** (*trans*) 63 mg (14.3%) and **6i** (*cis*) 75 mg (17.1%) were obtained.

(C): A solution of 438 mg (20.0 mmol) of **1i** and *cis*-1,3-pentadiene (136 mg, 20.0 mmol) in aceotnitrile (250 ml) was prosessed in a manner similar to that described above. **1i** 280 mg (63.9%), **6i** (*trans*) 59 mg (13.7%) and **6i** (*cis*) 70 mg (15.9%) were obtained.

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