Intramolecular Photocyclization of 2-Acylphenyl Methacrylates: a Convenient Access to 4,5-Dihydro-1,4-epoxy-2-benzoxepin-3(1*H*)-ones (= Benzo[*c*]-6,8-dioxabicyclo[3.2.1]octan-7-ones

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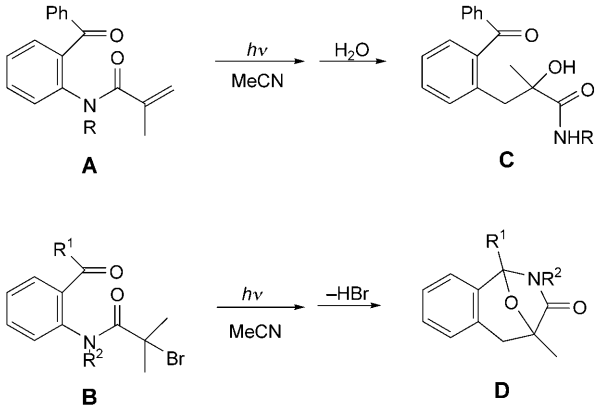
The photochemical reactions of 2-acylphenyl methacrylates (=2-acylphenyl 2-methylprop-2-enoates) **1** were investigated. Irradiation of 2-acylphenyl methacrylates **1a**–**d** in MeCN gave the tricyclic lactones **2a**–**d** in good yields, together with a small amount of O–C=O bond cleavage product, the 2-acylphenols **3a**–**d** (*Scheme 2*, *Table*). The formation of the tricyclic lactones **2** probably follows a mechanism involving a 1,7-diradical through ζ-H abstraction (1,8-H transfer) by the excited carbonyl O-atom (*Scheme 3*). Irradiation of 2-acylphenyl tiglate (=2-acylphenyl (2*E*)-2-methylbut-2-enoate) **1e** and 2-acylphenyl methacrylates **1g**–**i**, substituted by a MeO group (δ-H) at the 3,5-positions of the phenyl group, also gave the tricyclic lactones **2e** and **2g**–**i**, but in low yields. On the other hand, no H-abstraction products were observed on irridation of 2-(ethoxycarbonyl)phenyl methacrylate **1f**, of 2-acylphenyl methacrylate **1j** which is substituted by a Me group (γ-H) at the 3,5-positions of the phenyl group, and of **1k** with an OH group at the 3-position of the phenyl group.

1. Introduction. – Intramolecular H-abstraction reactions by the excited carbonyl group have been extensively investigated from synthetic and mechanistic viewpoints [1–3]. Generally, γ-H-atoms are abstracted most rapidly through six-membered cyclic transition states (1,5-H-transfer), as in the *Norrish*-Type-II reaction. This γ-H abstraction is greatly facilitated by favorable stereoelectronic or geometric requirements [2]. Abstraction from remote positions involving 1,6- and greater H-transfers is one of the most attractive subjects in the photochemistry of carbonyl groups [3–9], while these reactions are disfavored for medium and large cyclic transition states both statistically and energetically. Abstraction from such long-range positions has been observed in the photochemistry of imides [10], amino ketones [11], and S-containing glyoxylates [12] associated with electron-transfer character. In the course of our studies on the photochemistry of amide derivatives [13], we have reported that the long-range H-abstraction was observed in the photochemistry of *N*-(2-acylphenyl)prop-2-enamides and *N*-(2-acylphenyl)propanamides [13c,d]. For example, irradiation of *N*-(2-acylphenyl)-2-methylprop-2-enamides (**A**) [13c] and *N*-(2-acylphenyl)-2-bromo-2-methylpropanamides (**B**) [13d] afforded the open-chain amides **C** and the tricyclic lactams **D**, respectively, *via* ζ-H abstraction (1,8-H transfer) by the excited carbonyl O-atom through a nine-membered transition state (*Scheme 1*). We now report a new example of a ζ-H abstraction reaction in the photochemistry of 2-acylphenyl methacrylates **1**, whereby

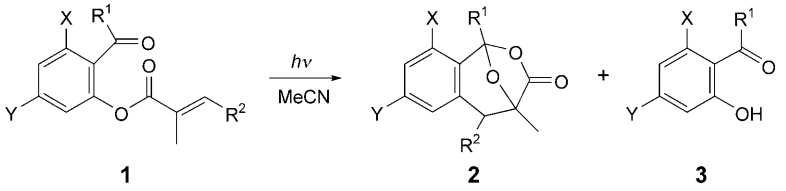
Scheme 1



cyclization, followed by rearrangement of the resulting 1,7-biradicals, leads to the formation of the unexpected tricyclic lactones **3**.

2. Results and Discussion. – Irradiation of 2-acylphenyl methacrylates **1a**–**d** in MeCN with a high-pressure Hg lamp under Ar atmosphere (*Pyrex* filter, room temperature) gave tricyclic lactones, *i.e.*, 4,5-dihydro-1,4-epoxy-2-benzoxepin-3(1*H*)-ones (=benzo[*c*]-6,8-dioxobicyclo[3.2.1]octan-7-ones) **2a**–**d** in high yields (74–98%), along with a small amount of 2-acylphenols **3a**–**d**, produced by cleavage of the O–C(=O) bond (*Scheme 2*, *Table*). The tricyclic lactone **2a** was also obtained when **1a** was irradiated in benzene or MeOH, but in low yield. Irradiation of 2-benzoylphenyl tiglate (=2-benzoylphenyl (2*E*)-2-methylbut-2-enoate; **1e**) afforded the tricyclic lactone **2e**, and the possible isomeric lactone **2e′** (see below, *Scheme 3*) was not detected. Irradiation of 2-(ethoxycarbonyl)phenyl methacrylate **1f** gave no H-abstraction product. The formation of the tricyclic lactone **2a** was completely quenched by the addition of triplet quenchers such as 2,5-dimethylhexa-2,4-diene, cyclohexa-1,3-diene, and O_2, suggesting that this reaction proceeds *via* an n-π^* triplet state.

Scheme 2[a])



[a]) For R^1, R^2, X, and Y, see *Table*.

The structures of the photoproducts **2** described above were assigned on the basis of spectral and analytical evidence. In the case of the tricyclic lactone **2a**, assignment was further confirmed by an X-ray crystal structure analysis (*Fig.*).

Table 1. *Photochemical Reactions of the 2-Acylphenyl Methacrylates* **1** *in MeCN*

Entry	Starting material	Substituents				Isolated yield [%] of products	
		R^1	R^2	X	Y	**2**	**3**
1	**1a**	Ph	H	H	H	98	1
2[a])	**1a**	Ph	H	H	H	42	14
3[b])	**1a**	Ph	H	H	H	12	43
4	**1b**	Ph	H	H	MeO	84	12
5	**1c**	Me	H	H	H	70	1
6	**1d**	Et	H	H	H	74	5
7	**1e**	Ph	Me	H	H	14[c])	2
8	**1f**	EtO	H	H	H	–[d])	6
9	**1g**	Ph	H	MeO	MeO	trace	13
10	**1h**	Me	H	MeO	MeO	44	23
11	**1i**	Et	H	MeO	MeO	20	25
12	**1j**	Ph	H	Me	Me	–[d])	11
13	**1k**	Me	H	OH	H	–[d])	–[d])

[a]) Solvent: benzene. [b]) Solvent: MeOH. [c]) 2:1 Mixture of two diastereoisomers. [d]) Not detected.

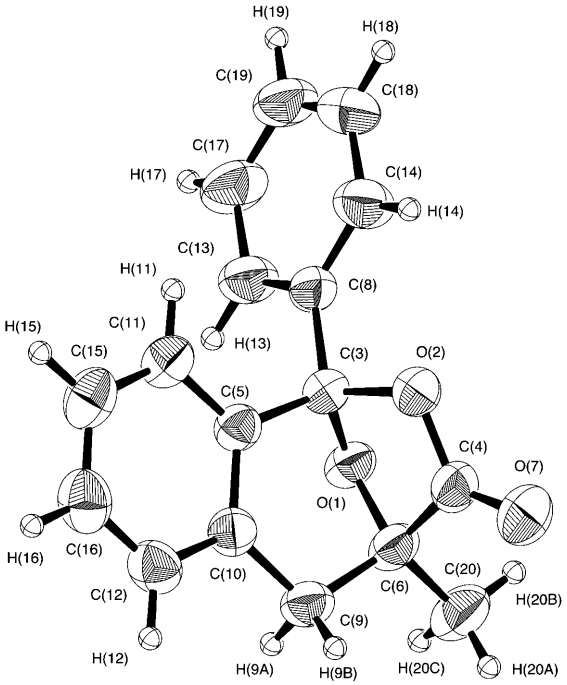
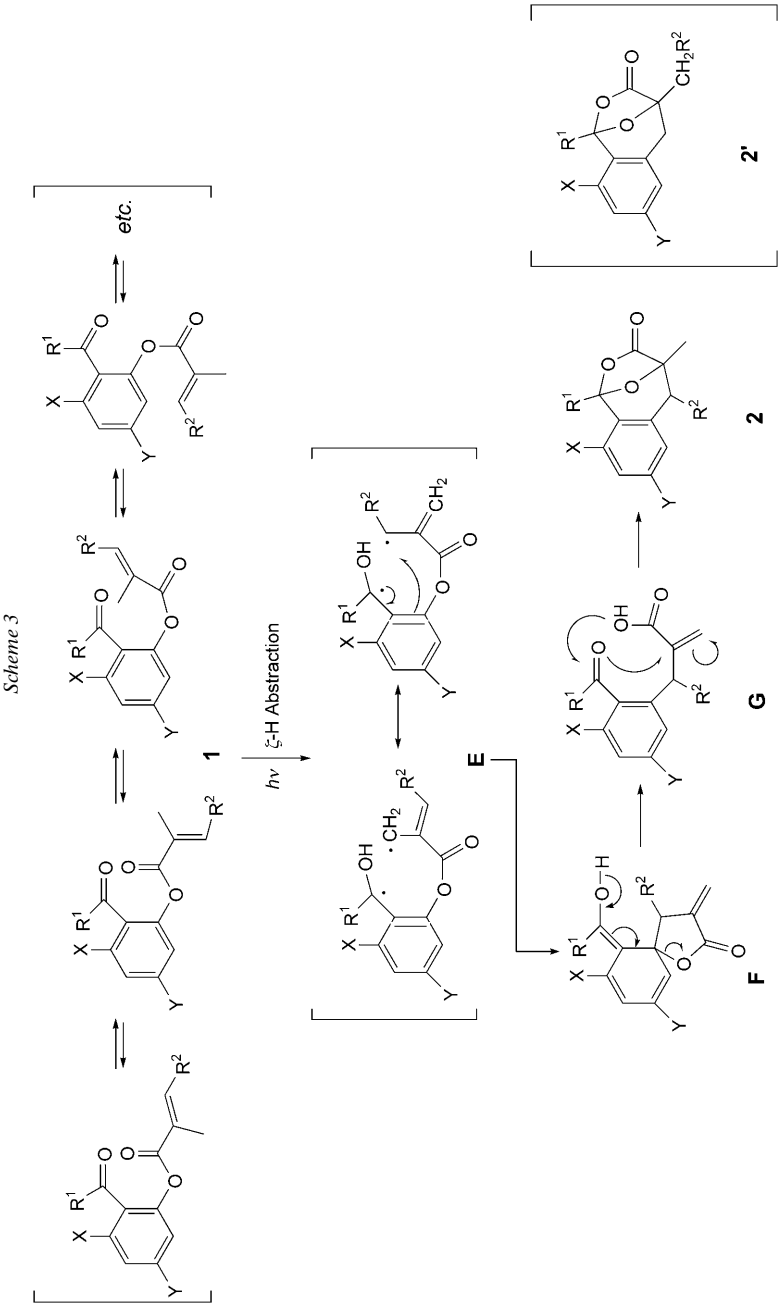


Figure. *X-Ray crystal structure of compound* **2a**. ORTEP view.

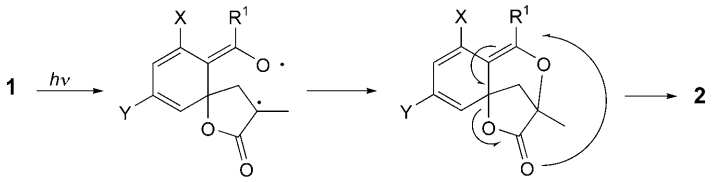
A plausible mechanism for the formation of the tricyclic lactones **2** is depicted in *Scheme 2*. ξ-H (Allylic-H) abstraction by the excited carbonyl O-atom *via* a nine-membered transition state would result in the 1,7-biradical **E**. Subsequent ring closure yields the spirolactone **F**, which may undergo ring opening to the oxo-carboxylic acid **G**, and then ring closure yields the tricyclic lactone **2**. The intramolecular *ortho* photocycliza-

Scheme 3



tion mechanism was reported in the photochemistry of 4-phenoxybut-1-enes [14]. A similar mechanistic sequence could also be considered, *i.e.*, *ipso*-cyclization of the olefinic C(β)-atom at the phenolic C-atom of the aromatic ring, followed by 1,6-cyclization of the formed biradical, and then 3,3-sigmatropic rearrangement yielding the final tricyclic products (*Scheme 4*)[1]). However, no cyclization product could be formed from 2-(ethoxycarbonyl)phenyl methacrylate **1f** as mentioned above, and irradiation of the parent phenyl methacrylate and 2-methoxyphenyl methacrylate resulted in the recovery of unchanged starting materials. Further, we recently proposed the analogous H-abstraction reaction of N-analogues, *i.e.*, of *N*-(2-acylphenyl)-2-methylprop-2-enamides [13c]. From these facts, we propose the long-range H-abstraction mechanism.

Scheme 4



Subsequently, to examine the intramolecular competition between δ-H (1,6-H transfer) and ζ-H abstraction (1,8-H transfer), and γ-H (1,5 H transfer) and ζ-H abstraction, we carried out the photoreaction of **1g**–**i** having MeO substituents (δ-hydrogen) at the *m*-positions of the phenyl group and **1j** having Me substituents (γ-hydrogen) at the *m*-positions of the phenyl group. Irradiation of **1g**–**i** in MeCN under the same conditions gave the tricyclic lactones **2g**–**i** (trace-44%), accompanied by the corresponding 2-acylphenols **3g**–**i** (13–25%), and benzofuran derivatives, which are expected to be produced *via* δ-H abstraction [2a][15], could not be observed. When **1j** was irradiated, no H-abstraction product was formed, only a small amount of the corresponding phenol **3j** was isolated. This is probably due to the lack of favorable stereoelectronic or geometric requirements [2]. Irradiation of 2-acyl-3-hydroxyphenyl methacrylate **1k** resulted in the recovery of unchanged starting material, probably due to intramolecular H-bonding between OH and the acetyl C=O of **1k**.

The H-abstraction reaction by the excited carbonyl O-atom is generally facilitated by favorable stereoelectronic and geometric requirements [2]. Long-range H-atom abstraction reactions are rare [3]. Our results herein establish the potential of long-range H-abstraction reactions in case of favorable conformation.

Experimental Part

General. Flash chromatography (FC): *Wakogel-C-300* silica gel. M.p.: *Yanaco-MP-J3* micro-melting point apparatus; uncorrected. B.p.: *Shibata-GTO-350-RD* glass-tube-oven distillation apparatus. IR Spectra: *Jasco-FT/IR-300* spectrophotometer; in cm^{-1}. ^1H- and ^{13}C-NMR Spectra: *Jeol-JNM-EX-270* (270 MHz) or *Varian-Gemini-200* (200 MHz) spectrometer; in $CDCl_3$, with Me_4Si as internal standard; δ in ppm, *J* in Hz.

Irradiation of 2-Acylphenyl Methacrylates **1**: *General Procedure.* A soln. of the **1** (1 mmol) in MeCN (70 ml), unless otherwise noted, was irradiated in a *Pyrex* tube with a high-pressure Hg lamp (*Halos EHP*

[1]) We thank a referee for suggesting this mechanism.

500 W; Eikosha) under Ar for 5–15 h at r.t. After removal of the solvent, the residue was subjected to FC (SiO_2, toluene/AcOEt 50:1 → 19:1) to give the photoproducts **2** and **3** (see *Table*). The structures of the 2-acylphenols **3** were confirmed by direct comparison of their spectral properties with those of commercially available materials.

*4,5-Dihydro-4-methyl-1-phenyl-1,4-epoxy-2-benzoxepin-3(1*H*)-one* (**2a**): M.p. 141–142°. IR (KBr): 1795. ^{1}H-NMR: 1.73 (*s*, 3 H); 3.13 (*d*, *J* = 17.5, 1 H); 3.28 (*d*, *J* = 17.5, 1 H); 6.70 (*d*, *J* = 7.9, 1 H); 7.06 (*t*, *J* = 7.6, 1 H); 7.18 (*d*, *J* = 7.3, 1 H); 7.24–7.34 (*m*, 1 H); 7.54–7.58 (*m*, 3 H); 7.62–7.66 (*m*, 2 H). ^{13}C-NMR: 21.2; 35.4; 79.7; 108.6; 126.1; 126.3; 126,4; 128.4; 128.9; 129.6; 131.7; 134.7; 136.4; 175.0. Anal. calc. for $C_{17}H_{14}O_3$: C 76.67, H 5.30; found: C 76.37, H 5.32.

*4,5-Dihydro-4-methyl-1-phenyl-7-methoxy-1,4-epoxy-2-benzoxepin-3(1*H*)-7-one* (**2b**): M.p. 130–131°. IR (KBr): 1794. ^{1}H-NMR: 1.71 (*s*, 3 H); 3.09 (*d*, *J* = 17.4, 1 H); 3.27 (*d*, *J* = 17.4, 1 H); 3.77 (*s*, 3 H); 6.58–6.72 (*m*, 2 H); 7.36 (*s*, 1 H); 7.46–7.52 (*m*, 3 H); 7.60–7.66 (*m*, 2 H). ^{13}C-NMR: 20.6; 35.3; 54.7; 79.0; 108.2; 110.9; 113.7; 125.7; 127.0; 127.8; 129.0; 132.9; 134.4; 159.9; 174.7. Anal. calc. for $C_{18}H_{16}O_3$: C 72.96, H 5.44; found: C 73.16, H 5.44.

*4.5-Dihydro-1,4-dimethyl-1,4-epoxy-2-benzoxein-3(1*H*)-7-one* (**2c**): M.p. 67–68°. IR (KBr): 1783. ^{1}H-NMR: 1.67 (*s*, 3 H); 2.05 (*s*, 3 H); 3.01 (*d*, *J* = 17.5, 1 H); 3.13 (*d*, *J* = 17.5, 1 H); 7.12–7.36 (*m*, 4 H). ^{13}C-NMR: 20.1; 21.2; 35.3; 79.4; 107.4; 123.2; 126.6: 129.1; 129.7; 131.4; 135.4; 175.5. Anal. calc. for $C_{12}H_{12}O_3$: C 70.57, H 5.96; found: C 70.67, H 5.97.

*1-Ethyl-4,5-dihydro-4-methyl-1,4-epoxy-2-benzoxepin-3(1*H*)-one* (**2d**): M.p. 62–63°. IR (KBr): 1790. ^{1}H-NMR: 1.13 (*t*, *J* = 7.4, 3 H); 1.67 (*s*, 3H); 2.35–2.49 (*m*, 2 H): 3.00 (*d*, *J* = 17.4, 1 H); 3.14 (*d*, *J* = 17.4, 1 H); 7.12–7.36 (*m*, 4 H). ^{13}C-NMR: 6.1; 20.6; 24.9; 35.1; 78.7; 108.5; 122.9; 126.2; 127.9; 129.2; 131.6; 134.3; 175.3. Anal. calc. for $C_{13}H_{14}O_3$: C 71.54, H 6.47; found: C 71.30, H 6.47.

*4,5-Dihydro-4,5-dimethyl-1-phenyl-1,4-epoxy-2-benzoxepin-3(1*H*)-one* (**2e**; 2:1 diastereoisomer mixture): B.p. 185–187°/3 Torr. IR (film): 1797. ^{1}H-NMR: 1.46 (*d*, *J* = 7.3, 2 H); 1.47 (*d*, *J* = 7.3, 1 H); 1.63 (*s*, 1 H); 1.71 (*s*, 2 H); 3.05 (*q*, *J* = 7.3, $^1/_3$ H); 3.42 (*q*, *J* = 7.3, $^2/_3$ H); 6.66 (*d*, *J* = 7.9, 1 H); 6.99–7.06 (*m*, 1 H); 7.22–7.35 (*m*, 2 H); 7.46–7.50 (*m*, 3 H), 7.59–7.67 (*m*, 2 H). ^{13}C-NMR (nonarom. signals): 15.3; 17.8; 19.0; 19.9; 36.9; 39.5; 82.0; 82.6; 108.2; 108.9; 173.1; 175.9. MS: 280 (M^+).

*4,5-Dihydro-7,9-dimethoxy-1,4-dimethyl-1,4-epoxy-2-benzoxepin-3(1*H*)-one* (**2h**): M.p. 32–33°. IR(KBr): 1790. ^{1}H-NMR: 1.63 (*s*, 3 H); 2.14 (*s*, 3 H); 2.91 (*d*, *J* = 17.3, 1 H); 3.08 (*d*, *J* = 17.3, 1 H); 3.78 (*s*, 3 H); 3.79 (*s*, 3 H); 6.23 (*d*, *J* = 2.3, 1 H); 6.29 (*d*, *J* = 2.3, 1 H). ^{13}C-NMR: 21.3; 24.1; 36.2; 55.3; 55.4; 78.8; 97.3; 105.2; 108.1; 116.9; 157.7; 160.9; 176.0. Anal. calc. for $C_{14}H_{16}O_5$: C 63.38, H 6.01; found: C 63.62, H 6. 01.

*1-Ethyl-4,5-dihydro-7,9-dimethoxy-4-methyl-1,4-epoxy-2-benzoxepin-3(1*H*)-one* (**2i**): M.p. 43–44°. IR (KBr): 1787. ^{1}H-NMR: 1.03 (*t*, *J* = 7.3, 3 H); 1.62 (*s*, 3 H); 2.31–2.42 (*m*, 1 H); 2.69–2.79 (*m*, 1 H); 2.90 (*d*, *J* = 17.3, 1 H); 3.10 (*d*, *J* = 17.3, 1 H): 3.77 (*s*, 3 H); 3.79 (*s*, 3 H); 6.24 (*d*, *J* = 2.3, 1 H); 6.29 (*d*, *J* = 2.3, 1 H). MS: 278 (M^+).

X-Ray Crystal-Structure Determination[2]). A crystal of **2a** was grown from CH_2Cl_2/hexane. The intensity data were collected on a *Mac-Science-MXC-18* diffractometer, with graphite-monochromated CuK_α radiation ($\lambda = 1.54178$ Å), in the ω-2θ scan mode ($2\theta < 69.99°$). Out of 2844 total reflections, 2204 reflections with intensities greater than $3\sigma(I)$ were used. No absorption correction was made. The structure was solved by direct methods with the maXus program. Least-square refinements were performed, including anisotropic thermal parameters for non-H-atoms and isotropic refinement of H-atoms located in difference *Fourier* synthesis.

Crystal data for **2a**: $C_{18}H_{14}O_3$; *M* 266.296; *V* = 1353.4 (10) Å, *Z* = 4, $D_x = 1.307$ Mg cm^{-3}; monoclinic, space group $P2_{1/c}$, *a* = 10.295 (3) Å, *b* = 8.355 (3) Å, *c* = 17.400 (10) Å, $\alpha = 90.00°$, $\beta = 115.27°$, $\gamma = 90.00°$; *R* = 0.071, *Rw2* = 0.066.

REFERENCES

[1] P. J. Wagner, *Acc. Chem. Res.* **1971**, *4*, 168; *Acc. Chem. Res.* **1983**, *16*, 461; *Acc. Chem. Res.* **1989**, *22*, 83; P. J. Wagner, in 'CRC Handbook of Organic Photochemistry and Photobiology', Eds. W. M. Horspool and P.-S. Song, CRC Press Inc., New York, 1995, p. 449.

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[2]) CCDC-269753 contains the supplementary crystallographic data for this paper. These data can be obtained free charge from the *Cambridge Crystallographic Data Centre via* (www.ccdc.cam.ac.uk/data_request/cif).

[2] a) P. J. Wagner, B.-S. Park, in 'Organic Photochemistry', Ed. A. Padwa, Marcel Dekker, New York, 1991, Vol. 11, p 227; b) P. J. Wagner, P. Klan, in 'CRC Handbook of Organic Photochemistry and Photobiology', 2nd edn., Eds. W. M. Horspool and F. Lenci, CRC Press Inc., Boca Raton, 2004, p. 52-1.
[3] G. L. Descotes, in 'CRC Handbook of Organic Photochemistry and Photobiology', Eds. W. M. Horspool and P.-S. Song, CRC Press Inc., New York, 1995, p. 501; T. Nishio, *Koukagaku* [Photochemistry] **2003**, *34*, 2.
[4] H. A. J. Carless, S. Mwesigye-Kibense, *J. Chem. Soc.*, *Chem. Commun.* **1987**, 1673.
[5] G. Adam, A. Preiss, P. D. Hung, *Tetrahedron* **1987**, *43*, 5815.
[6] F. Cottet, L. Cottier, G. Descotes, *Can. J. Chem*. **1990**, *68*, 1251.
[7] G. A. Kraus, Y. Wu, *J. Am. Chem. Soc*. **1992**, *114*, 8705.
[8] G. A. Kraus, W. Zhang, Y. Wu, *Chem. Commun*. **1996**, 1439.
[9] K. Mizuno, S. Konishi, Y. Yoshimi, A. Sugimoto, *Chem. Commun*. **1998**, 1659.
[10] Y. Kanaoka, *Acc. Chem. Res.* **1978**, *11*, 407; P. H. Mazzocchi, in 'Organic Photochemistry', Ed. A. Padwa, Marcel Dekker, New York, 1981, p. 421; J. D. Coyle, in 'Synthetic Organic Photochemistry', Ed. W. M. Horspool, Plenum Press, New York, 1984, p. 259; H. Mauder, A. G. Griesbeck, in 'CRC Handbook of Organic Photochemistry and Photobiology', Eds. W. M. Horspool and P.-S. Song, CRC Press Inc., New York, 1995, p. 513.
[11] T. Hasegawa, T. Ogawa, K. Miyata, A. Karakizawa, M. Komiyama, K. Nishizawa, M. Yoshioka, *J. Chem. Soc., Perkin Trans. 1* **1990**, 901; T. Hasegawa, Y. Yamazaki, M. Yoshioka, *Trends Photochem. Photobiol.* **1997**, *4*, 27.
[12] S. Hu, D. C. Neckers, *Tetrahedron* **1997**, *53*, 7165; *J. Org. Chem.* **1997**, *62*, 7827.
[13] a) T. Nishio, H. Asai, T. Miyazaki, *Helv. Chim. Acta* **2000**, *83*, 1475; b) T. Nishio, K. Iseki, N. Araki, T. Miyazaki, *Helv. Chim. Acta* **2005**, *88*, 35; c) T. Nishio, M. Tabata, H. Koyama, M. Sakamoto, *Helv. Chim. Acta* **2005**, *88*, 78; d) T. Nishio, H. Koyama, D. Sasaki, M. Sakamoto, *Helv. Chim. Acta* **2005**, *88*, 996.
[14] A. Gilbert, in 'CRC Handbook of Organic Photochemistry and Photobiology', 2nd edn., Eds. W. M. Horspool and F. Lenci, CRC Press Inc., Boca Raton, 2004, p. 41-1; S. Y. Al-Qaradawi, K. B. Cosstick, A. Gilbert, *J. Chem. Soc.*, *Perkin Trans. 1*, **1992**, 1145; P. J. Wagner, R. P. Smart, *Tetrahedron Lett*. **1995**, *29*, 5135.
[15] P. J. Wagner, in 'CRC Handbook of Organic Photochemistry and Photobiology', 2nd edn., Eds. W. M. Horspool and F. Lenci, CRC Press Inc., Boca Raton, 2004, p. 58-1; E. M. Sharshira, T. Horaguch, *J. Heterocycl. Chem*. **1997**, *34*, 1837 and ref. cit. therein; R. Singh, M. P. S. Ishar, *Tetrahedron* **2002**, *58*, 7595 and ref. cit. therein.

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