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PHOTOCHEMISTRY OF 2,3-, 4,5-, AND 2,7-AZEPINOBENZODIOXINS: PHOTOCHEMICAL REARRANGEMENT OF 2,7-AZEPINOBENZODIOXIN TO 2,3- AND 4,5-AZEPINOBENZODIOXINS, AND FORMATION OF 2,3-DIHYDRODIBENZODIOXIN FROM 2,3- AND 4,5-AZEPINOBENZODIOXINS

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Abstract — Photoirradiation of a 2,7-azepinobenzodioxin with a low pressure mercury lamp afforded 2,3- and 4,5-azepinobenzodioxins, a 2,3-dihydrodibenzodioxin, and an azepine derivative. The analogous irradiation of a 2,3-azepinobenzodioxin gave a 2,3-dihydrodibenzodioxin. On the other hand, a 4,5-azepinobenzodioxin formed a dihydropyrrole derivative accompanied by a 2,3-dihydrodibenzodioxin. The effects of solvents and sensitizers were investigated.

Much amount of documents have been published on the reactivities of azepine derivatives from view point of pharmacological activities[1] and theoretical interest of a possibility of a 8π electrons antiaromaticity.[2] However, only a little is known about the chemistry of dihydroazepine derivatives. Not only as possible precursors of azepines, dihydroazepines have attracted attention of chemists as a cyclic conjugated enamines (2,3-azepinobenzodioxins), cyclic double enamines (4,5-azepinobenzodioxins) or possible bishomo heteroaromatic compounds (2,7-azepinobenzodioxins).[3]

The situation is same as photochemistries of heterocyclic systems. Contrary to the detailed studies on the photochemistry of azepines,[4] dihydroazepines have been researched only on a part of their photochemical reactivities.[5] The authors have researched on cycloaddition reactions of azepines and synthesized several types of new dihydroazepine systems containing several cage type compounds.[5] Our recent studies on photochemistries of some of these dihydroazepines revealed interesting photoreactions.[5]

As a series of our research on the reactivities of heterocyclic systems, we investigated photochemistry of azepinobenzodioxins (**3, 4,** and **5**) derived from a cycloaddition reaction of 1*H*-1-carboethoxyazepine (**1**) and *o*-chloranyl (**2**) (Figure 1).[5] Here, the results are discussed.

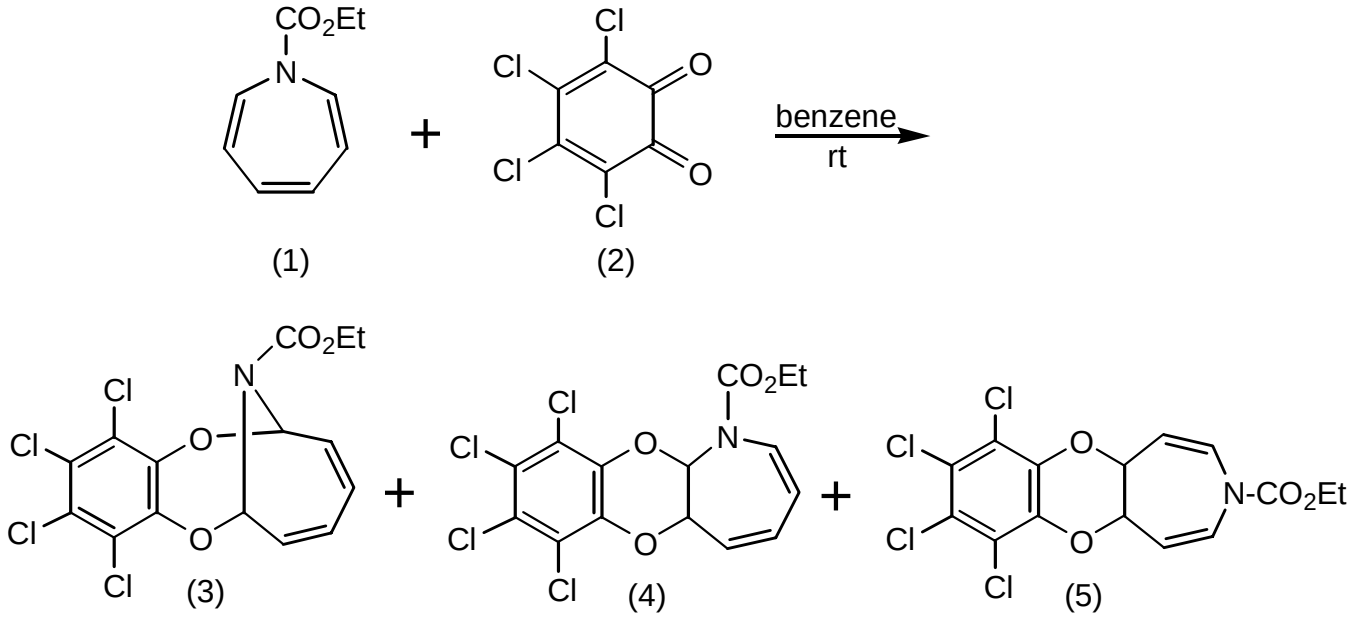

Figure 1

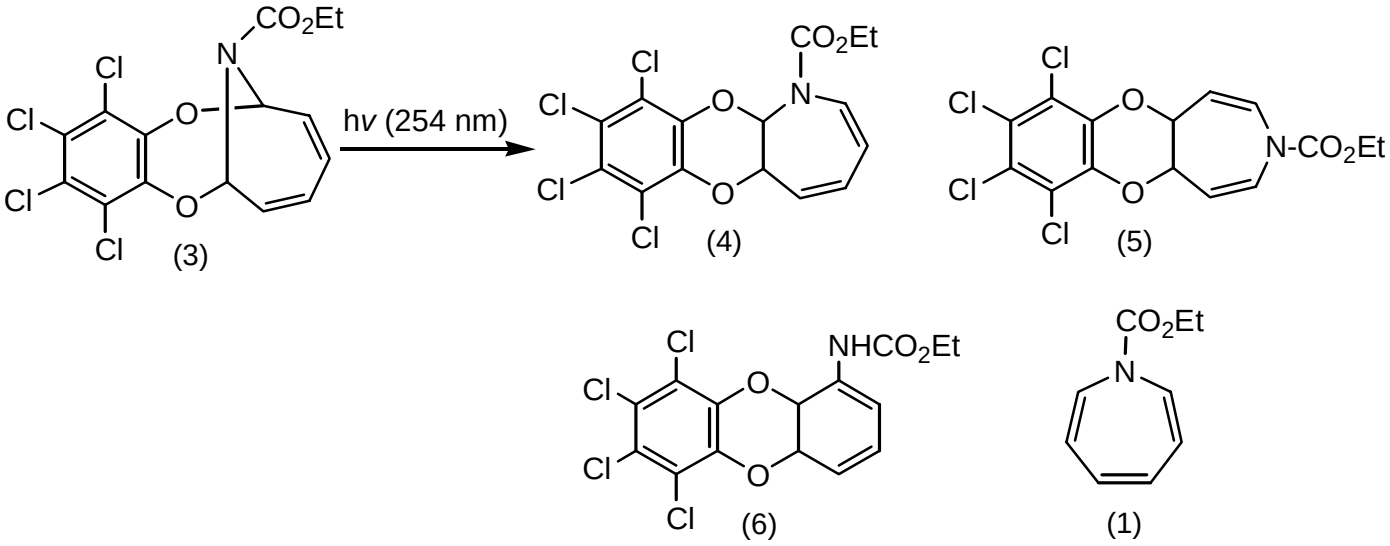

Figure 2

A solution of a 2,7-azepinobenzodioxin (**3**) in anhydrous acetonitrile was irradiated with a low pressure mercury lamp at room temperature under a nitrogen stream for 5 h (Figure 2). After evaporation of the solvent at 0 ^{o}C the residue was separated with thin layer chromatography on silica gel to give a 2,3-azepinobenzodioxin (**4**) and a 1,2-dihydrodibenzodioxin (**6**) in 17 and 56 % yields, respectively.

It was reported that **3** rearranged to **4** by heating at 90 ^{o}C in benzene for 4 h in yield of 63 %.[5] In order to deny the possible formation of **4** in the process of the solvent evaporation or separation the time dependence of the yield of **4** was monitored with an HPLC as shown in Figure 3. The photochemical initial formation of **4** and the following formation of **6** were clearly demonstrated in the figure.

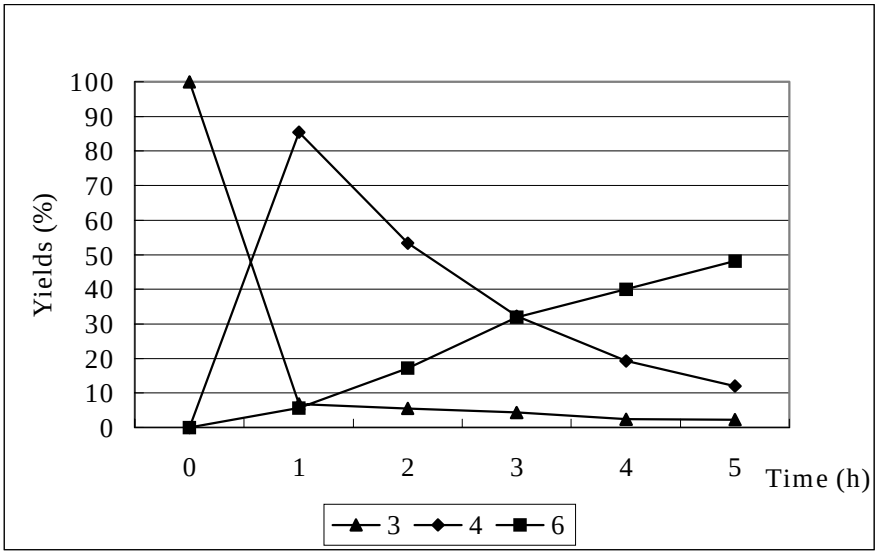

Figure 3. Time dependences in the photoirradiation of **3**

The short time irradiation of **3** under the same reaction conditions as above but for 30 min gave mainly **4** in 42 % yield accompanied by a trace amount of **6**. The results of the short time irradiation in various solvents were summarized in Table 1 together with dielectric constants of the solvents.

Table 1. Results of photoreaction of **3** with low pressure mercury lamp in various solvents※

Run	Solvent	Product yield (%)			
		4	**5**	**6**	**1**
1	MeCN	42	0	trace	0
2	EtOH	11	0	0	0
3	acetone	28	0	0	0
4	dioxane	22	13	0	trace
5	THF	14	0	0	14
6	AcOEt	19	14	0	0
7	benzene	23	17	0	0
8	monoglyme	30	0	0	0
9	toluene	17	14	0	0
10	Et_2O	13	14	0	7

※Every photoreaction was carried out for 30 min.

The best yield of **4** was achieved in acetonitrile solvent. In the reactions in ethanol or acetone, the yield of **4** was diminished. On the other hand, the third product, a 4,5-azepinobenzodioxin (**5**), was formed in some solvents. The solvents containing ether linkage except monoglyme afforded the azepine derivative (**1**) as the forth product, though the yields were small.

The influence of triplet sensitizers was examined as shown in Table 2. A marked improvement of the yield of **4** was observed in the use of acetophenone, which has 74 kcal/mol of triplet energy.

Table 2. Results of photoreaction of **3** with low pressure mercury lamp in the presence of sensitizers in MeCN

Sensititizer	Yield (%)	
	4	**5**
benzene※	23	17
acetone※	28	0
benzonitrile	22	12
acetophenone	72	0
9-cyanoanthracene	17	0
—	42	0

※Benzene and acetone were used as solvents.

The result demonstrated in Figure 3 suggests the formation of **6** in the photoreaction of **4**. An irradiation of anhydrous acetonitrile solution of **4** with a low pressure mercury lamp under the same reaction conditions as those of **3** afforded **6** in 56 % yield (Figure 4). The time dependence of the yield of **6** monitored with an HPLC was illustrated in Figure 5.

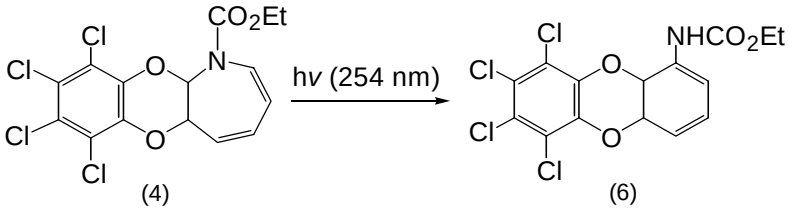

Figure 4

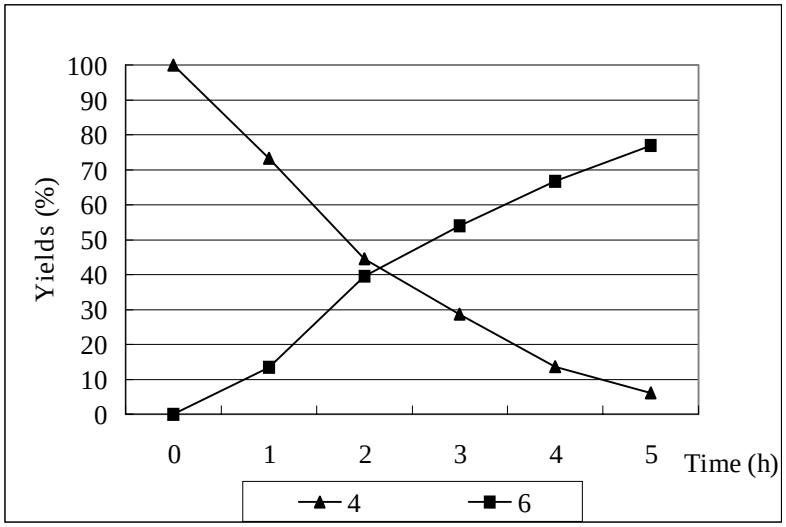

Figure 5. Time dependences in the photoirradiation of **4**

As same as the case of **3**, the solvents and triplet sensitizers affected the yield of **6** as summarized in Tables 3 and 4. An slight improvement of the yield was observed in benzene solvent, which can act as a triplet sensitizer. Almost all sensitizers examined in Table 4 except 9-cyanoanthracene increased the yield.

Table 3. Results of photoreaction of **4** with low pressure mercury lamp

Solvent	Yield (%)
MeCN	56
EtOH	56
THF	58
acetone	73
benzene	88

Table 4. Results of photoreaction of **4** with low pressure mercury lamp in the presence of sensitizers in MeCN

Sensitizer	Yield (%)
benzene※	88
acetone※	73
benzonitrile	88
acetophenone	74
9-cyanoanthracene	50
—	56

※Benzene and acetone were used as solvents.

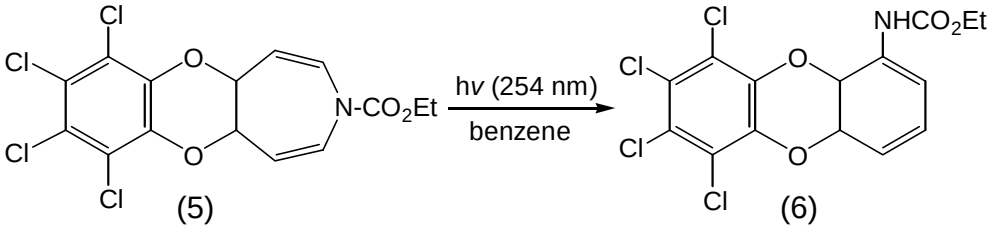

Figure 6

Photoreaction of **5** was influenced by the solvent used. Thus, the irradiation with the low pressure mercury lamp in acetonitrile, tetrahydrofuran, or ether failed to form any isolatable product except

resinous untreatable materials. The dihydrodibenzodioxin (**6**) was formed in 31 % in benzene solvent. The influences of the triplet sensitizers were summarized in Table 6.

Table 5. Results of photoreaction of **5** with low pressure mercury lamp

Solvent	Irradiation time (h)	Yield (%)
MeCN	5	0
EtOH	5	0
acetone	10	0
benzene	19	31

Table 6. Results of photoreaction of **5** with low pressure mercury lamp in the presence of sensitizers in MeCN

Sensitizer	Yield (%)
benzene※	31
acetone	0
benzonitril	0
acetophenone	15
—	0

※Benzene and acetone were used as solvents.

The structure of **6** was deduced on the basis of its spectral properties and confirmed by a good coincidence of these properties with those of the analogous compounds.[6] The molecular ion peak of **6** (411.0) in the mass spectrum was same as the molecular weight of **4** suggesting **6** to be a skeletal isomer of **4**. The IR spectrum showed two peaks at 1707 and 3435 cm^{-1} due to C=O and NH groups, respectively. The ^{1}H NMR spectrum demonstrated the existence of four continued protons. The number of peaks of saturated and unsaturated carbon atoms in the ^{13}C NMR spectrum were consistent with the structure of **6**.

The reactions of **3** are considered to proceed as follows. A 1,5-oxygen shift followed by suitable double bond migrations generates the product (**4**), which then forms the another product (**6**) *via* a ring contraction reaction (Figure 7). The formation path of **5** is not clear now, but tentatively, the following route is suggestible as shown in Figure 8. A 1,3-nitrogen shift can form an intermediate (**8**), which

further undergoes the second 1,3-nitrogen migration to form an aziridine intermediate (**9**). An opening of the aziridine ring in **9** forms the final product (**5**).

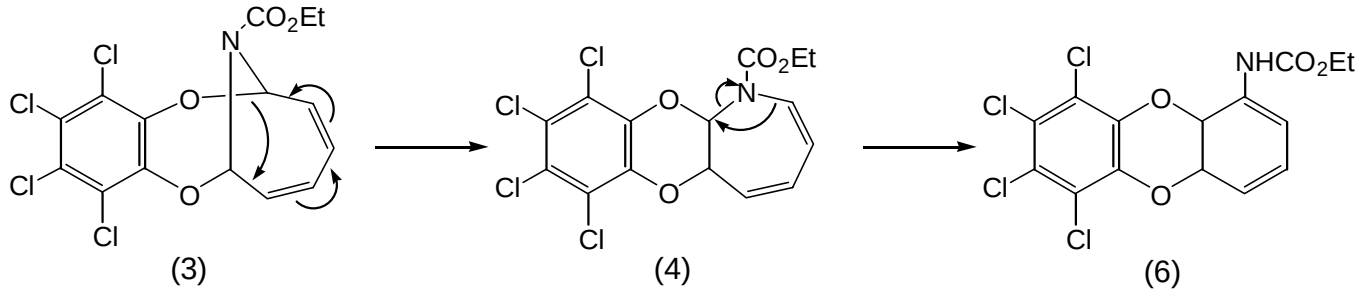

Figure 7

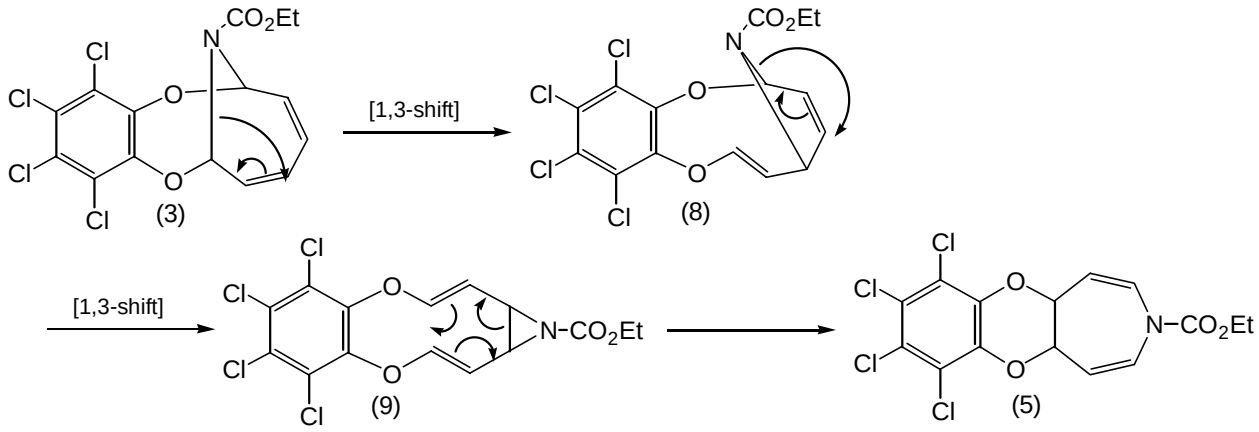

Figure 8

The reaction paths of **5** are thought to be as follows (Figure 9). A di-π-methane rearrangement in **5** forms **11** *via* a diradical intermediate (**10**),[7] then **11** was converted to **6**.

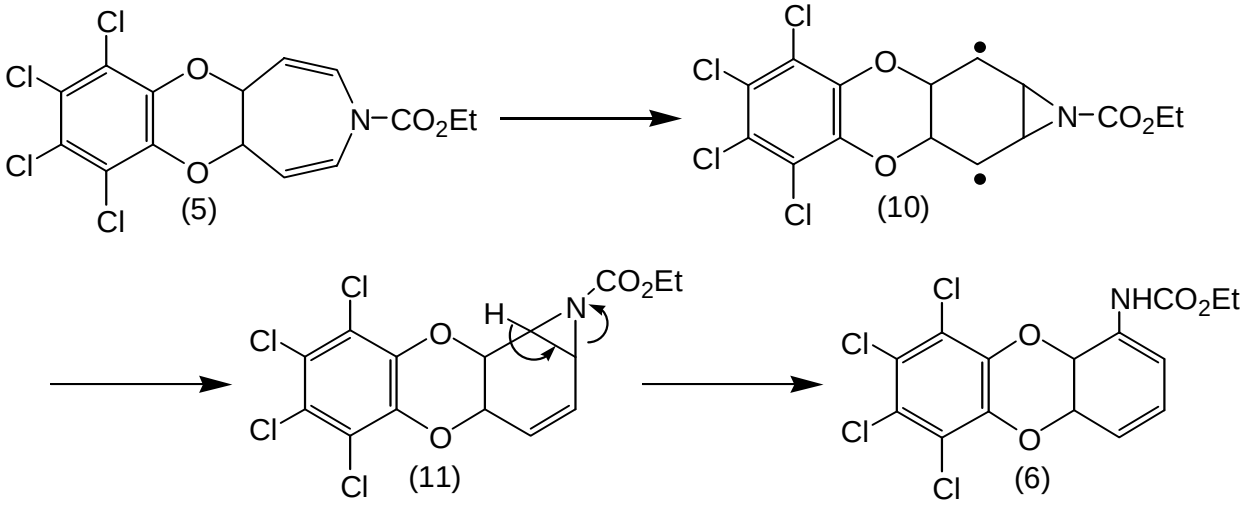

Figure 9

EXPERIMENTAL

Photoreactions were carried out with six low pressure mercury lamps (National GL-15) in a quartz pear shaped round bottomed flask under a nitrogen stream at room temperature in a dried solvent. YAMAMURA A-303 (S-5 120A ODS) was used for a column of HPLC. Wakogel C200 and B5F were used for column and thin-layer chromatography, respectively. NMR and MS spectra were measured with Varian GEMINI 2000/300 and Hitachi 220A spectrometers, respectively. IR spectra were measured with a JASCO FT/IR-5300 spectrophotometer.

Typical reactions are mentioned bellow.

*Photoreaction of **3** in MeCN*. A solution of a 2,7- azepinobenzo-dioxin (**3**) (108 mg, 0.25 mmol) in dry MeCN (40 mL) was irradiated for 30 min. After evaporation of the solvent on a rotary evaporator, the residue was chromatographed with hexane-ethyl acetate (4:1) to give colorless crystals (**4**) (46 mg, 42 %).

*Photoreaction of **3** in the presence of acetophenone*. A solution of a 2,7- azepinobenzo-dioxin (**3**) (209 mg, 0.5 mmol) and acetophenone (83 mg, 0.8 mmol) in dry MeCN (40 mL) was irradiated for 30 min. After evaporation of the solvent on a rotary evaporator, the residue was chromatographed with hexane-ethyl acetate (85:15) to give colorless crystals (**4**) (150 mg, 72 %).

*Photoreaction of **4** in benzene*. A solution of a 2,3- azepinobenzo-dioxin (**4**) (207 mg, 0.5 mmol) in dry benzene (40 mL) was irradiated for 5 h. After evaporation of the solvent on a rotary evaporator, the residue was chromatographed with hexane-ethyl acetate (4:1) to give colorless crystals (**4**) (60 mg, 29 %) and colorless crystals (**6**) (130 mg, 88 %).

*Photoreaction of **4** in the presence of benzonitrile*. A solution of a 2,3- azepinobenzo-dioxin (**4**) (206 mg, 0.5 mmol) and benzonitrile (54 mg, 0.5 mmol) in dry MeCN (40 mL) was irradiated for 5 h. After evaporation of the solvent on a rotary evaporator, the residue was chromatographed with hexane-ethyl acetate (4:1) to give colorless crystals (**4**) (13 mg, 7 %) and colorless crystals (**6**) (169 mg, 88 %).

*Photoreaction of **5** in benzene*. A solution of a 4,5- azepinobenzo-dioxin (**5**) (206 mg, 0.5 mmol) in dry benzene (40 mL) was irradiated for 19 h. After evaporation of the solvent on a rotary evaporator, the residue was chromatographed with hexane-ethyl acetate (4:1) to give colorless crystals (**5**) (32 mg, 16 %) and colorless crystals (**6**) (53 mg, 31 %).

*Photoreaction of **5** in the presence of acetophenone*. A solution of a 4,5- azepinobenzo-dioxin (**5**) (208 mg, 0.5 mmol) and acetophenone (61 mg, 0.5 mmol) in dry MeCN (40 mL) was irradiated for 10 h. After evaporation of the solvent on a rotary evaporator, the residue was chromatographed with hexane-ethyl acetate (4:1) to give colorless crystals (**5**) (26 mg, 13 %) and colorless crystals (**6**) (27 mg, 15 %).

3: Colorless crystals. mp 175-176^{o}C. MS m/z (rel intensity): 411 (M^{+}, 9), 165 (100), 92 (82). IR (KBr): 3030, 2980, 1720 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ: 1.29 (t, 3 H, J = 7.0 Hz), 4.20 (d, 2 H, J = 7.0 Hz), 6.04 (br s,

4 H), 6.83 (d, 2 H, *J* = 4.5 Hz). Anal. Calcd for $C_{15}H_{11}Cl_4NO_4$: C, 43.82, H, 2.70, N, 3.41. Found: C, 43.55, H, 2.67, N, 3.27.

4: Colorless crystals. mp 200-202°C. MS m/z (rel intensity): 411 (M^+, 8), 165 (100), 152 (48), 92 (84). IR (KBr): 3030, 2980, 1730 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 1.36 (t, 3 H, *J* = 7.0 Hz), 4.31 (q, 2 H, *J* = 7.0 Hz), 5.11 (narrow m, 1 H), 5.28 (dd, 1 H, *J* = 8.6, 7.5 Hz), 5.39 (dd, 1 H, *J* = 11.9, 2.1 Hz), 5.91 (ddd, 1 H, *J* = 11.9, 7.5, 2.1 Hz), 6.63 (narrow m, 1 H), 6.87 (d, 1 H, *J* = 8.6 Hz). Anal. Calcd for $C_{15}H_{11}NO_4Cl_4$: C, 43.82, H, 2.70, N, 3.41. Found: C, 43.93, H, 2.62, N, 3.31.

5: Colorless crystals. mp 165-166°C. MS m/z (rel intensity): 411 (M^+, 1), 165 (31), 152 (98), 80 (100). IR (KBr): 3030, 2980, 1735 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 1.36 (t, 3 H, *J* = 7.0 Hz), 4.30 (q, 2 H, *J* = 7.0 Hz), 4.97 (br s, 4 H), 7.06 (d, 2 H, *J* = 9.0 Hz). Anal. Calcd for $C_{15}H_{11}NO_4Cl_4$: C, 43.82, H, 2.70, N, 3.41. Found: C, 43.78, H, 2.54, N, 3.40.

6: Colorless crystals. mp 156-157°C. HRMS m/z 410.9425 Calcd for $C_{15}H_{11}Cl_4NO_4$: 410.9413. MS m/z (rel intensity): 411 (M^+, 79), 338 (35), 165 (29), 139 (100), 92 (58), 67 (65). IR (KBr): 3435, 2980, 1707, 1089 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 1.34 (t, 3 H, *J* = 7.1 Hz), 3.95 (s, 1 H), 4.29 (q, 2 H, *J* = 7.1 Hz), 4.94 (d, 2 H, *J* = 5.2 Hz), 5.88 (d, 1 H, *J* = 5.2, 2.2 Hz), 5.96 (br s, NH), 6.35 (d, 1 H, *J* = 2.2 Hz). ^{13}C NMR ($CDCl_3$) δ=14.55, 47.88, 48.94, 59.85, 62.41, 73.52, 82.20, 119.94, 120.56, 125.06, 137.37, 138.07, 138.71, 142.50, 153.80.

REFERENCES

1. A. Mizuno, M. Miya, T. Kamei, M. Shibata, T. Tatsuoka, K. Nakanishi, C. Takiguchi, T. Hidaka, A. Yamaki, and N. Inomata, *Chem. Pharm. Bull.*, 2000, **48**, 1129; J. Tatsugi, K. Ikuma, and Y. Izawa, *Tetrahedron Lett.*, 1995, **36**, 8611; H. Muramatsu, S. Hiroyuki, N. Iwasaki, M. Kakiuchi, T. Ohashi, H. Kato, and Y. Ito, *Yakugaku Zasshi*, 1994, **114**, 54.
2. K. Saito, H. Kojima, T. Okudaira, and K. Takahashi, *Bull. Chem. Soc. Jpn.*, 1983, **56**, 175; M. G. Barlow, S. Culshaw, R. N. Haszeldine, and W. D. Morton, *J. Chem. Soc., Perkin Trans. 1*, **1982**, 2105; T. Kumagai, A. Tokida, K. Kidoura, O. Seshimoto, and T. Mukai, *Tetrahedron Lett.*, 1982, **23**, 873.
3. T. Ikemoto, T. Ito, S. Miura, and K. Tomimatsu, *PCT Int. Appl.*, **2001**, 86; A. S. Glover and J. Warkentin, *J. Org. Chem.*, 1993, **58**, 2115; V. N. Pshenichnyi, O. F. Lakhvich, E. V. Borisov, N. V. Khripach, and V. A. Khripach, *Zh. Org. Khim.*, 1991, **27**, 928; M. Labelle and D. Gravel, *Can. J. Chem.*, 1985, **63**, 1884.
4. T. Tomita, H. Ishiguro, and K. Saito, *Heterocycles*, 1999, **51**, 141; G. Mass, B. Manz, T. Mayer, and U. Werz, *Tetrahedron*, 1999, **55**, 1309; K. Marx and W. Eberbach, *Tetrahedron*, 1997, **53**, 14687; S. Klötgen, R. Fröhlich, and E. Würthwein, *Tetrahedron*, 1996, **52**, 14801; M. Uchida and M. Irie, *J. Am.*

Chem. Soc., 1993, **115**, 6442; T. Tsuchiya, H. Arai, H. Hasegawa, and H. Igeta, *Tetrahedron Lett.*, **1974**, 4103; L. A. Paquette and D. E. Kuhla, *J. Org. Chem.*, 1969, **34**, 2885.

5. K. Saito and Y. Emoto, *Heterocycles*, 2001, **54**, 567; T. Tomita, H. Ishiguro, and K. Saito, *Heterocycles*, 1999, **51**, 141; K. Saito, T. Mukai, and S. Iida, *Bull. Chem. Soc. Jpn*., 1986, **59**, 2485.
6. M. D. Ennis and N. B. Ghazal, *Tetrahedron Lett.*, 1992, **33**, 6287; C. F. Neville, M. F. Grundon, V. N. Ramachandran, and J. Reisch, *J. Chem. Soc., Perkin Trans. 1*, **1991**, 259; R. M. Bowman and M. F. Grundon, *J. Chem. Soc. C*, **1967**, 2368.
7. R. Altundas, A. Dastan, S. N. Unaldi, K. Guven, O. Uzun, T. M. Balci, *Eur. J. Org. Chem.*, 2002, **3**, 526; M. J. Ortiz, A. R. Agarrabetia, S. Aparico-Lara, and D. Armesto, *Tetrahedron Lett.*, 1999, **40**, 1759; O. Muraoka, G. Tanabe, E. Yamamoto, M. Ono, T. Minematsu, and T. Kimura, *J. Chem. Soc., Perkin Trans. 1*, **1997**, 2879; D. Armesto, M. G. Gallego, W. M. Horspool, and A. R. Agarrabeitia, *Tetrahedron*, 1995, **51**, 9223.