

Yoshihisa Fukai, Tomoyuki Miyazawa, Mahiro Kojoh,
Tohru Takabatake and Minoru Hasegawa*

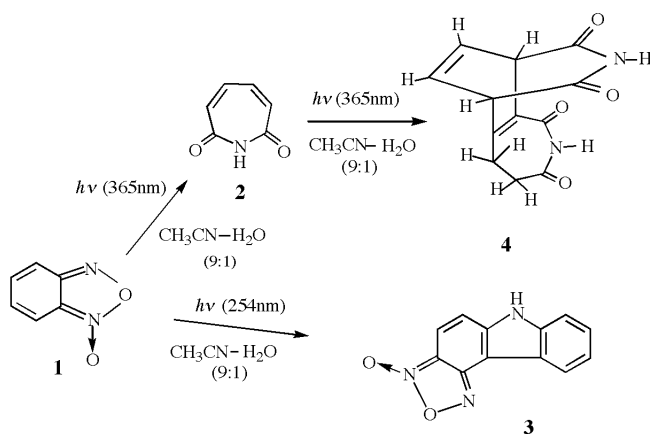
College of Pharmacy, Nihon University, 7-7-1 Narashinodai, Funabashi-shi, Chiba, 274-8555, Japan
Received June 22, 2000

Photolysis of 1*H*-azepine-2,7-dione **2** proceeded with alkali as in the photoreaction of *N*-alkylphthalimide to give 7-hydroxy-1*H*-azepine-2-one **13**.

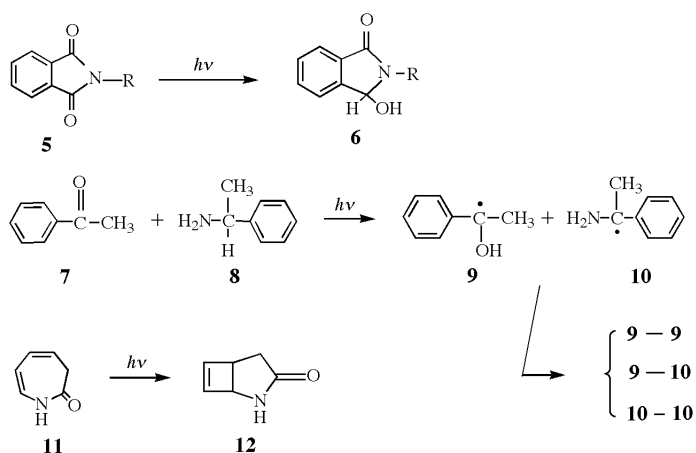
J. Heterocyclic Chem., **38**, 531 (2001).

As a part of benzofuroxan and benzofurazan chemistry, we have already reported the photoreaction of benzofuroxan **1** in acetonitrile containing a little water, under a high pressure mercury lamp, where it was found to give 1*H*-azepine-2,7-dione **2**, while under irradiation using a low pressure lamp, 6*H*-furazano[4,5-*c*]carbazole-3-oxide **3** and compound **2** were obtained[1], and then the photoproduct **2** produced photodimer **4** by irradiation in acetonitrile:water(9:1, v/v) using a high or low pressure mercury lamp[2] as depicted in Scheme I.

Scheme I



Scheme II



In this study, examination was made of the photolysis of product **2** in alkaline solution. The photoreaction of *N*-alkylphthalimide **5** proceeds in the presence of amines [3]. This reaction is quite similar to the photoreaction of carbonyl compounds with amines [4]. The photoreaction of 1*H*-azepine-2-one **11** yields cyclized **12** [5] as shown in Scheme II.

Prototropy was found in this study to possibly result from N-H to C=O bonds on compound **2** based on spectral behavior in uv spectra and nmr spectra following potassium hydroxide addition. In uv spectra, compound **2** in neutral solution exhibited two absorption bands with maxima near 208 and 282 nm, while the compound **2** solution with added alkali exhibited a different maximal absorption band near 234 nm. Moreover, it appeared that the absorption of the solution, which was neutralized with a corresponding amount of acid, agreed with that of the first neutral solution. In the nmr spectra, compound **2** exhibited two signals coupled together between H3 (= H6) [6.82 ppm] and H4 (= H5) [6.47 ppm], in neutral solution. However, in a solution with added alkali, compound **2** exhibited multiple signals near the absorption region of H4 (= H5) described above.

The photolysis of compound **2** was conducted in the presence of potassium hydroxide to produce the photoreduced compound 7-hydroxy-1*H*-azepine-2-one **13**. On using morpholine as alkali, the same result was obtained.

Assignment of product **13** was made based on its mass spectra, microanalyses, ir spectra, and nmr spectra using C-H COSY and H-H COSY experiments. In the ¹H nmr spectrum, four protons were observed resonating in the 5 – 7 ppm region, and a one proton around 4.2 ppm. The C-H COSY spectrum shows that these protons correlate with carbon resonances, in a manner consistent with an azepine-2-oxide structure. Based on correlations observed in the H-H COSY spectrum, the four protons resonating in the 5 - 7 ppm range are assigned to the ring system, thus verifying the structure of product **13** (Figure 1). The nmr signal of H-3 appears as a doublet of doublets, however in the H-H COSY only coupling with the ring proton H-4 is observed. Upon addition of D₂O the signal of H-3 changes from a doublet of doublets into a doublet. Also, in a spin-spin decoupling experiment, where the N-H proton resonance is irradiated, a doublet is observed for H-3.

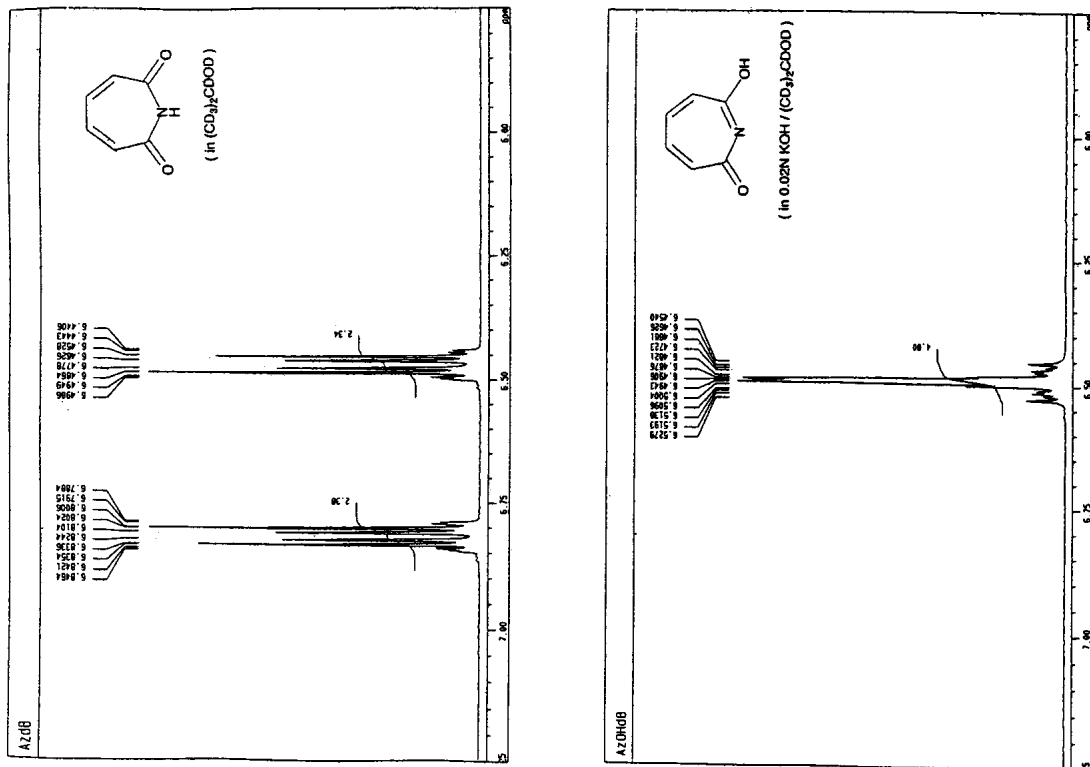


Figure 2. Nmr Spectra of Compound 2.

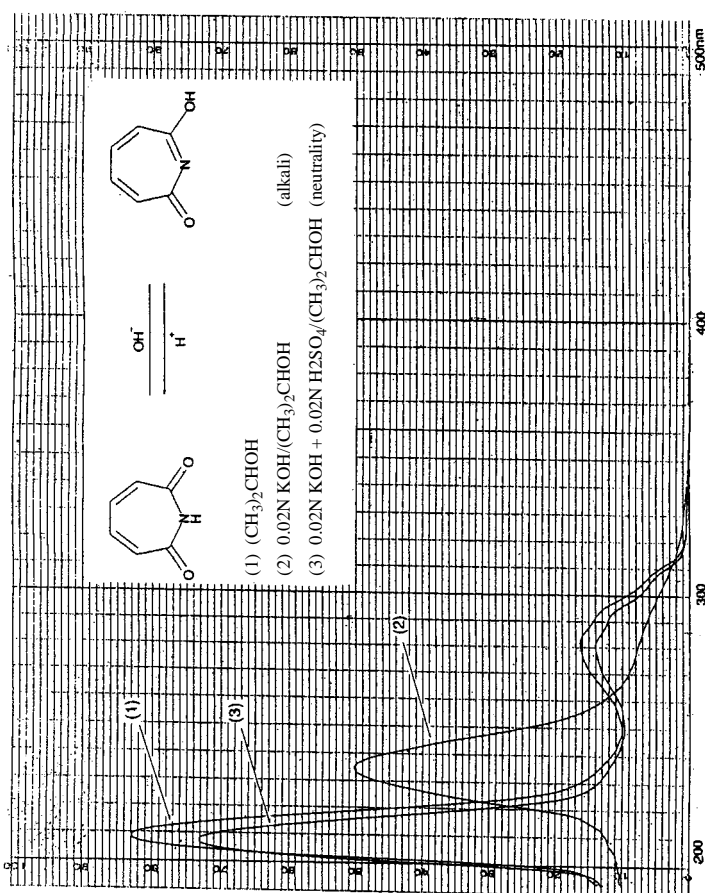


Figure 1. Uv Spectra of Compound 2.

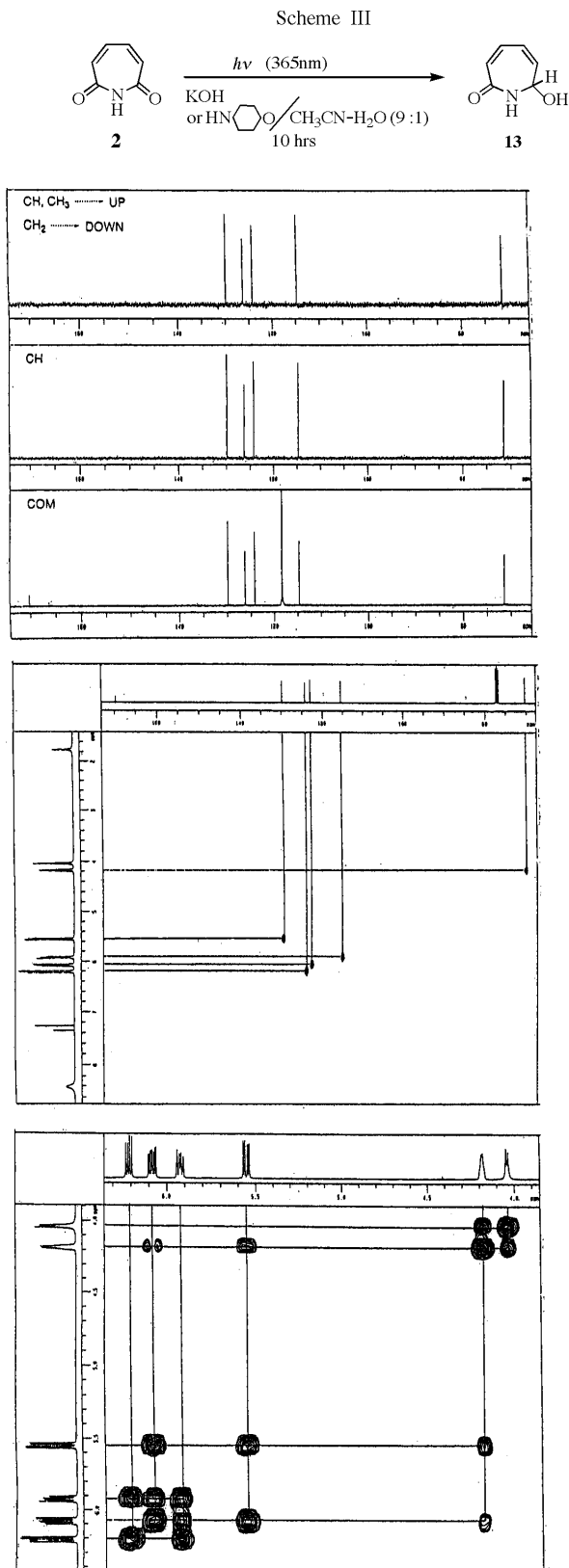


Figure 3. Nmr Spectra of Compound **13** (a) ¹³C-nmr spectra; (b) Nmr Spectra using C-H-COSY; (c) Nmr spectra using H-H COSY.

These experiments show that H-3 is coupled with the proton of N-H bond.

The photoreduction of compound **2** by morpholine may proceed in overall reactions similar to that of the photoreduction of *N*-alkylimide by amines [3]. Next examination

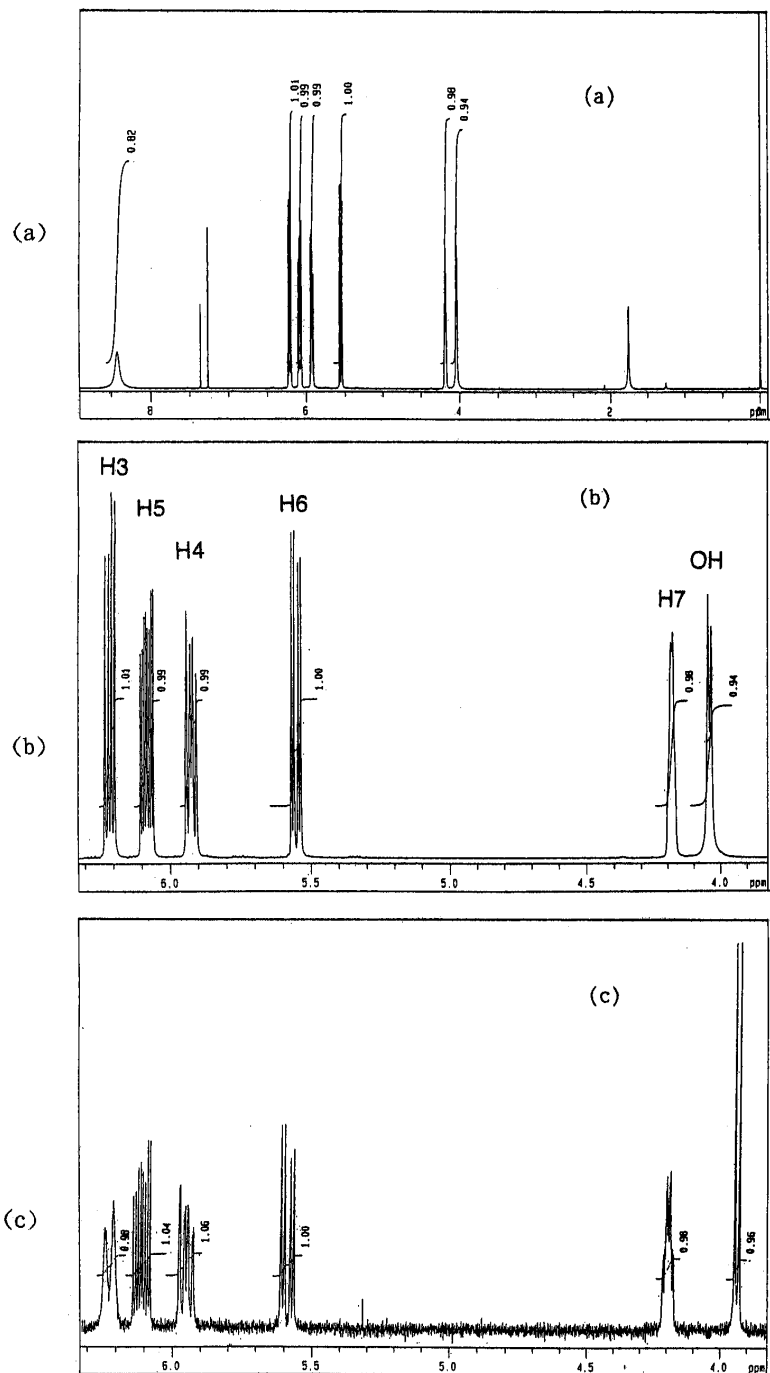
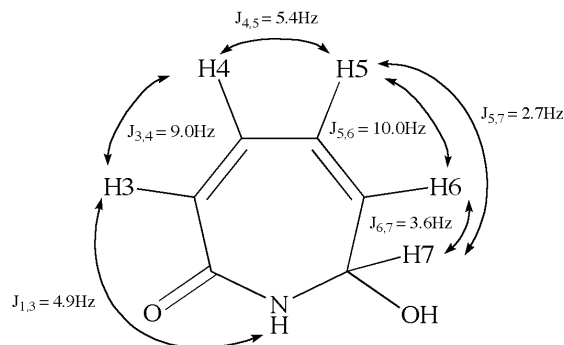


Figure 4. Nmr Spectra of Compound **13** (a) Spectra in all region. 8.22 ppm (N-H), 3.95 ppm (O-H): deuterium oxide-exchangeable; (b) Spectra in region of 3.9~6.3 ppm; (c) Spin-spin decoupling experiment by irradiating a peak of N-H proton absorption (8.22 ppm).

Figure 5. Structure of Compound **13**

was made of the photolysis of compound **1**, the parent material in this reaction. Compound **1** was irradiated in acetonitrile containing a little water with a high pressure mercury lamp for 30 hours, followed by photolysis of the reaction solution with a little morpholine or potassium hydroxide added for 10 hours, and compound **13** described above was obtained. Compound **13** underwent conversion to compound **2** on exposure to air in a desiccator over a period of three months.

Photolysis of 1*H*-Azepine-2,7-dione(**2**) with Morpholine.

A solution of 100 mg (8 mmoles) of compound **2** and 0.3 ml of morpholine dissolved in 300 ml of acetonitrile:water (9:1,v/v) was irradiated using a 400-W high pressure mercury lamp with a Pyrex filter at room temperature. After irradiation 10 hours, unreacted **2** (1.4 mg, 1.4%) and product **13** (3.9 mg, 3.8%) were separated by column chromatography and identified.

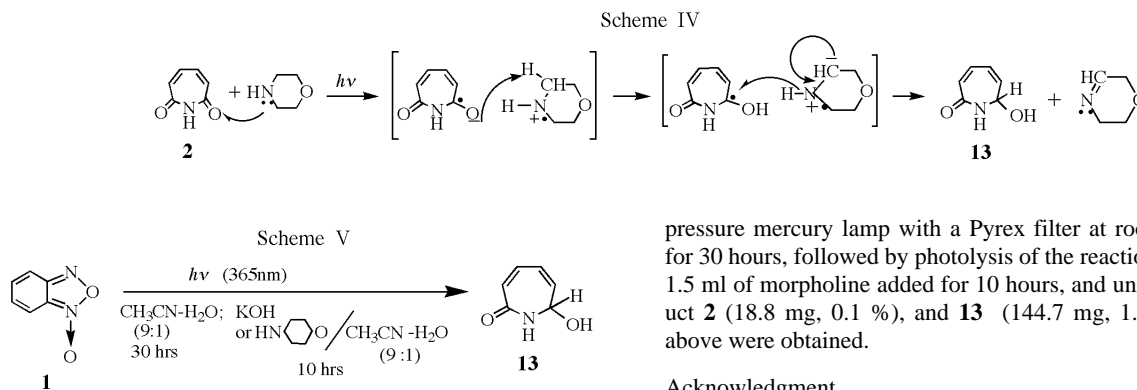
7-Hydroxy-1*H*-azepine-2-oxo-7-ol (**13**).

This compound was obtained as colorless crystals (hexane:ethylacetate (7:3,v/v)), mp 112~113 °C; ir (potassium bromide): ν 1684 (N-C=O), 3216, 3470 (OH, NH) cm^{-1} ; ^1H nmr (acetonitrile- d_3): δ 2.21 (s, 1H, OH, deuterium oxide-exchangeable); 4.05~4.06 (t, 1H, C(OH)-H), 5.44 (q, 1H, C=C-CH=CH-C<), 5.68 (q, 1H, C=C-CH=CH-C<), 6.08 (m, 1H, O=C-CH=CH-), 6.23 (d, 1H, O=C-CH=), 8.03 (s, 1H, NH, deuterium oxide-exchangeable); ^{13}C nmr (acetonitrile- d_3): δ 70.0 (C(OH)-H), 114.0, 123.5, 125.6, 129.2 (C-H), 169.0 (C=O); hrms: (m/z) 125.0476. Calcd. for $\text{C}_6\text{H}_7\text{NO}_2$: M, 125.0476.

Anal. Calcd. for $\text{C}_6\text{H}_7\text{NO}_2$: C, 57.59; H, 5.64; N, 11.19. Found: C, 57.68; H, 5.57; N, 11.33.

Photolysis of Benzofuroxan (**1**) with Morpholine.

A solution of 10.0 g of compound **1** dissolved in 1500 ml of acetonitrile:water (9:1,v/v) was irradiated using a 400-W high



pressure mercury lamp with a Pyrex filter at room temperature for 30 hours, followed by photolysis of the reaction solution with 1.5 ml of morpholine added for 10 hours, and unreacted **1**, product **2** (18.8 mg, 0.1%), and **13** (144.7 mg, 1.2%) described above were obtained.

Acknowledgment.

The authors thank Ph.D. Yasuteru Urano, University of Tokyo, for fruitful discussion.

EXPERIMENTAL

Compound **2** was prepared as previously described [1]. The photoreactions were carried out with Nikko Sekiei Works photochemical reactor. Melting points were determined with a Yanagimoto micromelting point apparatus and are uncorrected. The ir spectra were recorded on a Jasco IR-810 spectrometer. The ^1H and ^{13}C nmr spectra were recorded on a JNM-GSX 400 FT NMR instrument with TMS as the internal standard. The mass spectra were recorded on a Hitachi M-2000 spectrometer with an electron beam energy of 70 eV. Microanalyses were performed at the microanalytical laboratory of the Center for Instrumental Analysis in College of Pharmacy, Nihon University.

REFERENCES AND NOTES

- [1] M. Hasegawa and T. Takabatake, *J. Heterocyclic Chem.*, **28**, 1079 (1991).
- [2] T. Takabatake and M. Hasegawa, *J. Heterocyclic Chem.*, **31**, 215 (1994).
- [3] Y. Kanaoka, *J. Synth. Org. Chem., Japan*, **33**, 949 (1975).
- [4] S. G. Cohen, A. Parola, and G. H. Parsons, *Chem. Rev.*, **73** 141 (1973).
- [5] E. Vogel, R. Erb, G. Lenz, and A. A. Bothner, *Liebigs Ann. Chem.*, **682**, 1 (1965).