Difference in Photochemical Behavior In 3,6- and 2,5-Di-*tert*-butyl-3*H*-azepine: The First Photochemical Bond Formation Between 2- and 6-Position of 3*H*-Azepine Ring

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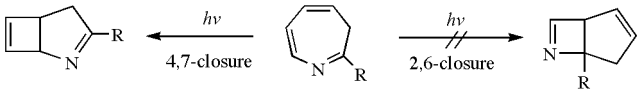
Received March 28, 2002

Different photochemical behavior between 3,6- and 2,5-di-*t*-butyl-3*H*-azepine was observed. The former gave wavelength dependent products 3,5-di-*t*-butylpyridine on irradiation through Pyrex filter *via* photolysis and 4,7-di-*t*-butyl-2-azabicyclo[3.2.0]hepta-2,6-diene on irradiation through quartz filter *via* photoisomerization. Meanwhile, 2,5-di-*t*-butyl derivative gave exclusively a labile 2,5-di-*t*-butyl-6-azabicyclo-[3.2.0]hepta-2,6-diene on irradiation through Pyrex filter *via* hitherto unknown photoisomerization mode of the bond formation between 2- and 6-position of the ring.

J. Heterocyclic Chem., **39**, 1337(2002).

One of the typical behavior of cycloheptatriene (CHT) on photo-irradiation is the photoelectrocyclic isomerization giving strained bicyclo[3.2.0]heptadiene ring system. Similarly, photochemical behavior of 3*H*-azepine has been described by the exclusive formation of 2-azabicyclo[3.2.0]hepta-2,6-diene system *via* bond formation between 4- and 7-position of the ring (4,7-closure) based on the irradiation of 2-alkyloxy- and 2-dialkylamino-3*H*-azepine derivatives, which were considered to be stabilized azatriene system by iminoether or amidine conjugation [1]. Strangely enough, the other possible bond formation between 2- and 6-position (2,6-closure) giving 6-azabicyclo[3.2.0]hepta-2,6-diene system has never been observed (Scheme 1). Although, unsubstituted 3*H*-azepine has been found to be a labile substance, [2] we developed di-*t*-butyl-3*H*-azepines as another stable class of 3*H*-azepines, which are not stable due to conjugative stabilization, but rather due to steric protection by the bulky *t*-butyl substituents [3]. Therefore, their behavior upon irradiation can be expected to be different than that previously reported.

Scheme 1

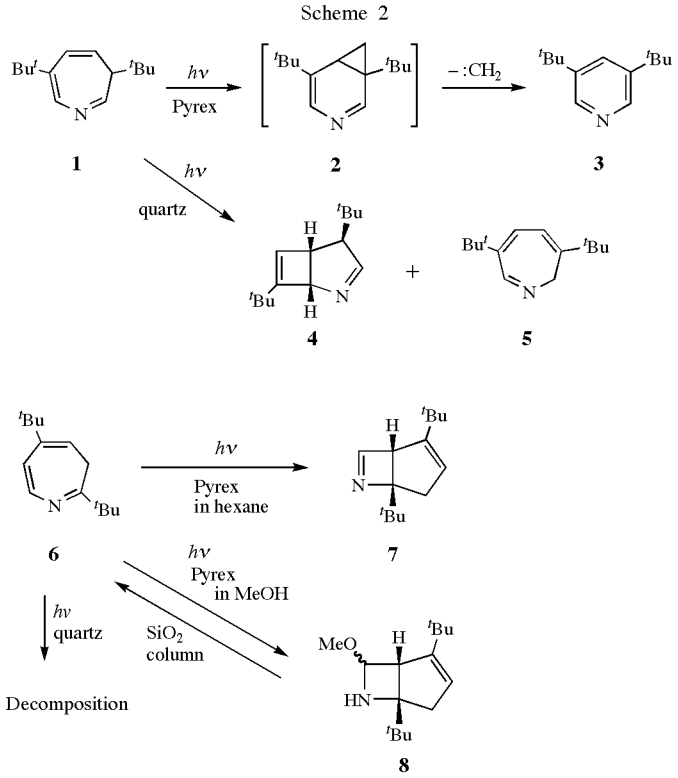


R = OMe or *N,N*-dialkylamino

Photoirradiation [4] of 3,6-di-*t*-butyl-3*H*-azepine (**1**, 68 mg, 0.33 mmol) in hexane (110 ml) at room temperature through a Pyrex filter for 24 h gave 3,5-di-*t*-butylpyridine (**3**) in 8% yield with 48% recovery of **1**, however no photoisomer was found in the reaction mixture. A similar photochemical ring contraction reaction of 2-methoxy-3*H*-azepine derivative has been reported [5]. The reaction may be explained through the initial formation of azanorcaradiene intermediate **2** followed by the subsequent elimination of methylene. On irradiation through quartz filter of a hexane (100 ml) solution of **1** (98 mg, 0.48 mmol) for 3 h, photoisomers 4,7-di-*t*-butyl-2-azabicyclo[3.2.0]hepta-2,6-diene (**4**) *via* 4,7-closure and 3,6-di-*t*-butyl-2*H*-azepine (**5**) *via* photochemically allowed 1,7-hydrogen shift [6] were obtained in 26% and 12% yield, respectively, with 43% recovery of **1**. The structures **3** [7], **4** [8], and **5** [3] obtained here were confirmed by respective comparison with reported data. The regioselectivity of the photoelectrocyclization for **1** was found to be similar to other previously reported 3*H*-azepines [1].

Meanwhile, the direct irradiation of 2,5-di-*t*-butyl-3*H*-azepine (**6**) in hexane resulted in a complete decomposition of **6**. Even the *in situ* observation, during irradiation of cyclohexane-d_{12} solution of **6** by means of NMR spectroscopy, no clear products were observed. On the other hand, when a sealed NMR tube containing a cyclohexane-d_{12} (0.7 ml) solution of **6** (13 mg, 63 μmol) was irradiated through a Pyrex filter at room temperature, peaks attributed **6** decreased concurrent with the increase of a new peak set attributed to 2,5-di-*t*-butyl-6-azabicyclo[3.2.0]hepta-2,6-diene (**7**) [9]. After 2.5 h, the relative ratio **6**:**7** reached to 22:78 on the basis of peak area of C7–H (δ 7.29, 1H) for **6** and a proton at δ 8.16 for **7**. Unfortunately, isolation of **7** was unsuccessful owing to its instability. In the ^{1}H NMR, **7** exhibits two olefinic protons at δ 5.35 and 8.16, two methylene protons with geminal coupling constant of 18.0 Hz at δ 2.22 and 2.53, a bridge head proton at δ 3.64, and two *t*-butyl singlet signals at δ 0.92 and 1.05. The ^{13}C NMR spectrum also is instrumental in the elucidation of the 2-azabicyclo[3.2.0]hepta-2,6-diene ring structure. Characteristic signals observed at δ_C 182.1 (d) and δ_H 8.16 (d, J = 3.6 Hz, 1H) can be assigned to imine-carbon and adjacent imine-proton of azetine ring, respectively. Observed shifts are inconsistent with the reported chemical shifts for the imine moiety of 1-azetine whose shifts are δ_C 187.0, δ_H 8.22 [10]. Thus

Scheme 2



observed 2,6-closure reaction was further confirmed by the formation of methanol addition product **8**. Irradiation of **6** (101 mg, 0.49 mmol) in methanol (100 ml) through Pyrex filter for 3 h resulted in 80% conversion from starting azepine **6** to **8** by monitoring with ^{1}H NMR. Chromatographic work up for purification of **8** reproduced **6** again *via* elimination of methanol in 70% yield.

Electronic spectra of **1** and **6** are shown in Figure 1 along with that of cycloheptatriene. Although, no remarkable difference in electronic spectra between **1** and **6** is observed, their behavior upon irradiation is found to be entirely different each. Interestingly, it is found that the regioselectivity for photoelectrocyclization is not exclusively caused by the steric hindrance of a product. This is clear because the more sterically hindered cyclization occurred to give **7**, while the sterically favorable product formed from **1**. To clarify the difference in photochemical behavior, further details in the photochemistry of 3*H*-azepines are underway.

Acknowledgment.

We thank the SC-NMR Laboratory of Okayama University for ^{13}C and ^{1}H NMR spectral measurements.

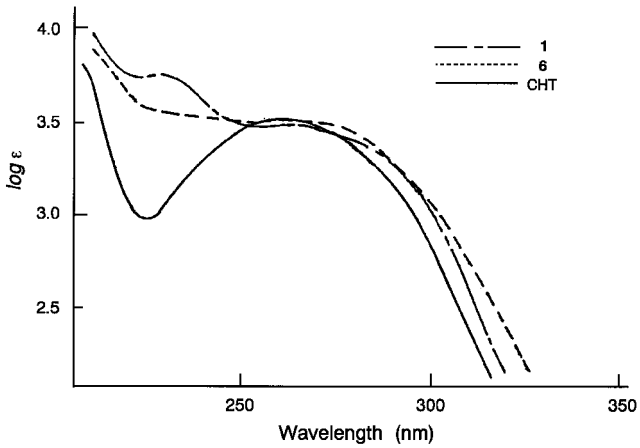


Figure 1. Electronic spectra for 3,6-di-*t*-butyl-3*H*-azepine (**1**), 2,5-di-*t*-butyl-3*H*-azepine (**6**) and cycloheptatriene (CHT) in ethanol.

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[9] Compound **7**; ^{1}H NMR (300 MHz, cyclohexane-d_{12}): δ 0.92 (s, 9H), 1.05 (s, 9H), 2.22 (ddd, *J* = 18.0, 2.4, and 1.5 Hz, 1H), 2.53 (dd, *J* = 18.0 and 2.4 Hz, 1H), 3.64 (dd, *J* = 3.6 and 1.5 Hz, 1H), 5.35 (t, *J* = 2.4 Hz, 1H), 8.16 (d, *J* = 3.6 Hz, 1H); ^{13}C NMR (67 MHz, cyclohexane-d_{12}): δ 24.9 (q), 29.6 (q), 33.6 (s), 34.0 (s), 35.0 (t), 54.2 (d), 86.3 (s), 123.7 (d), 150.8 (s), 182.1 (d); MS (GCMS) m/z 205 (M^+, 0.4%), 190 (12), 163 (28), 107 (62), 57 (100).

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Compound **8**; ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.87 (s, 9H), 1.06 (s, 9H), 1.99 (br s, 1H), 2.12 (ddd, *J* = 17.7, 2.4, and 1.7 Hz, 1H), 2.78 (dd, *J* = 17.7 and 2.4 Hz, 1H), 3.11 (dd, *J* = 2.4 and 1.7 Hz, 1H), 3.23 (s, 3H), 4.35 (d, *J* = 2.4 Hz, 1H), 5.44 (t, *J* = 2.4 Hz, 1H).