Photolysis of 2-Amino-2′-azidobiphenyls: Formal Formation of Internally Trapped Didehydroazepines

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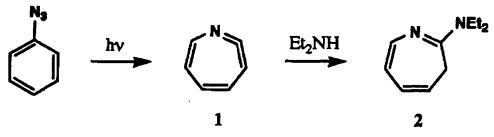
Synopsis. Photolysis of 2-amino-2′-azidobiphenyls in diethylamine gave 4,10-dihydroazepino[2,3-*b*]indoles (**7**), the structure of which corresponded to the didehydroazepines formally trapped with an internal amino group. However, the yields of **7** were considerably low, which was due to the significant intramolecular interaction of the photolytically generated nitrene with an amino group, to afford benzo[*c*]cinnoline as a final product.

In the photochemistry of aromatic azides, the intermediacy of didehydroazepines has been established. Didehydroazepine (**1**) from photolysis of phenyl azide was directly observed by means of IR in an Ar matrix at 8 K.[1] Further, Schuster and his co-workers showed the evidence for the intermediacy of didehydroazepines in the photochemistry of *p*-substituted phenyl azide in fluid solutions by the use of transient absorption techniques.[2] When the photolysis of phenyl azide was carried out in a nucleophilic solvent, such as diethylamine (DEA), **1** was trapped to give 2-diethylamino-3*H*-azepine (**2**) in a good yield (Scheme 1).[3] Though trapping of didehydroazepines with nucleophiles is a useful method for syntheses of 2-substituted azepines,[4] no attempt has been reported to trap didehydroazepines intramolecularly, which would lead to a new type of bicyclic azepines. We wish to report here the photochemistry of 2-amino-2′-azidobiphenyls, where 4,10-dihydroazepino[2,3-*b*]indoles, which appear to be the first example of internally trapped didehydroazepines, are produced, though a main reaction pathway is an ylide formation through the intramolecular interaction of nitrenes with an amino group, which gives benzo[*c*]cinnoline as a final product.

Photolysis (>300 nm) of 2-amino-2′-azidobiphenyl (**3a**)[5] in DEA yielded a complex mixture, from which four reaction products could be isolated after chromatographic separation. The product distribution is shown in Table 1. Benzo[*c*]cinnoline (**4**), which was obtained as a main product, 4-aminocarbazole (**5a**)[6] and 2,2′-diaminobiphenyl (**6a**) were identified by ^{1}H NMR and GC-MS comparison with authentic samples (Scheme 2). The last product was assigned to 4,10-dihydroazepino-[2,3-*b*]indole (**7a**), the ^{1}H NMR spectrum of which exhibited a set of signals due to the partial structure $-CH=CH-CH_2-CH=$.[7] The formation of **7a** would be rationalized in terms of the intramolecular trap of didehydroazepine with an amino group at the 2-position, followed by the proton migration. It should be noted that no azepines derived from the external trap of didehydroazepine with DEA could be detected.

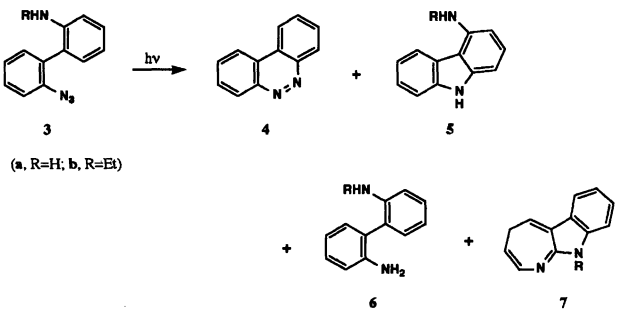


Scheme 1.

Table 1. Photoproduct Distributions of **3** in Various Solvents

Substrate	Solvent	Yield/%[a] 4	5	6	7
3a	DEA	26	6	4	5
3a	Cyclohexane[b]	20	3	17	0
3a	Methanol	23	12	18	0
3b	DEA	30	8	0	7
3b	Cyclohexane[b]	36	0	4	0
3b	Methanol	31	5	5	0

a) Yield by isolation. b) Containing 4% ether for solubility of substrates.



Scheme 2.

In order to investigate the photodecomposition process of **3a** and increase the yield of internally trapped didehydroazepines, the solvent effect on the product distributions was examined. Contrary to our expectations, photolysis of **3a** in cyclohexane, methanol, or acetonitrile gave no trace amounts of **7a**, where other three products, **4**, **5a**, and **6a** were isolated in comparable yields to the photolysis in DEA (Table 1). An addition of a base other than DEA, e.g., triethylamine, aniline, sodium methoxide in methanol, was of no effect on the formation of **7a**.[8,9] Thus, it seems that DEA, a nucleophile which can capture didehydroazepines most effectively, is necessary to produce **7a** in the photolysis of **3a**. These observations strongly suggested that **7a** was not formed by the intramolecular trap of didehydroazepine with an amino group, but by the external trap of dide-

hydroazepine with DEA, followed by the substitution of diethylamino group with an internal amino group.

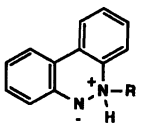
If benzo[*c*]cinnoline (**4**) was originated from the intramolecular NH-insertion of photolytically generated singlet nitrene, the alkylation of the amino group would reduce the formation of **4**, which would lead to an increase in the yield of **7**. Thus, we examined the photochemistry of an *N*-ethyl derivative **3b**. To our surprise, the main product obtained in the photolysis of **3b** in DEA was also **4**. The corresponding 4,10-dihydroazepino[2,3-*b*]indole **7b** was isolated in 7% yield, together with 4-(ethylamino)carbazole (**5b**, 8%). As in the case of **3a**, no internally trapped didehydroazepine **7b** was obtained in the photolysis in cyclohexane nor in methanol (Table 1). The facile formation of **4** in the photolysis of **3b**, as well as **3a**, implies that **4** is not derived from the direct NH-insertion reaction of the nitrene, but from the ylide **8** formed by an electrophilic attack of the nitrene on the nitrogen atom of the amino group (Scheme 3). The proton migration in **8** would give 5,6-dihydrobenzo[*c*]cinnoline derivatives, which could be readily oxidized to **4** by air.[10,11]

Finally, we have to refer to the thermal reactivity of **3a**. Thermolysis of **3a** in decalin at 132 °C gave **4** and **6a** in 54% and 28% yields, respectively. Neither **5a** and **7a** could be detected. The thermal lability of **3a** was comparable to that of 2-azidobiphenyl, indicating that the anchimeric substituent effect of the amino group for the elimination of nitrogen molecule in the azides **3a** was small.[12]

It is concluded that 4,10-dihydroazepino[2,3-*b*]indoles (**7**), a new type of azepines fused with a heterocyclic ring, were obtained in the photolysis of 2-amino-2′-azidobiphenyls (**3**). The internally trapped didehydroazepines **7** were, however, produced only in the presence of a nucleophile which could capture didehydroazepines effectively, e.g., DEA. Thus, the mechanism for the formation of **7** appears to be the external trap of didehydroazepine with DEA, followed by the replacement of diethylamino group by the internal amino function. Further, the yields of **7** were considerably low. This is due to the significant intramolecular interaction of the photolytically generated nitrene with an amino group, which results in the suppression of the ring-enlargement process to the didehydroazepine.

Experimental

General Methods. ^{1}H NMR spectra were recorded on a JEOL JNM-EX-270 spectrometer. The GC-MS spectra were recorded on a Shimadzu QP-1000 mass spectrometer with a GC column prepared from 5% Silicone OV-17 on Diasolid L (5.0 mm×1.0 m). The HPLC analyses were carried out on a JASCO 880-PU high-pressure liquid chromatograph with a JASCO Finepak C_{18}-T5 column. Gel permeation liquid chromatography (GPC) was carried out on a JASCO HLC-01 high-pressure liquid chromatograph equipped with a Shodex GPC H-2001 column. TLC was carried out on a Merck kieselgel 60 PF_{254}, and column chromatography was done on Fuji Davison silica gel BW-127ZH.



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Scheme 3.

2-Nitro-2′-phthalimidobiphenyl. A mixture of 1-iodo-2-phthalimidobenzene (200 mg, 0.57 mmol), 1-bromo-2-nitrobenzene (350 mg, 1.73 mmol) and copper powder (220 mg) was heated at 200 °C for 3 h. After cooling, the organic material was extracted with boiling $CHCl_3$. The solvent was removed under reduced pressure, and residue was developed on a silica-gel column with hexane–CH_2Cl_2 (1 : 2) to give 140 mg (71%) of 2-nitro-2′-phthalimidobiphenyl; orange granules; mp 214—217 °C; ^{1}H NMR ($CDCl_3$) δ=7.2—8.0 (12H, m); IR (KBr) 1720, 1535, 1370 cm^{-1}.

2-Amino-2′-azidobiphenyl (3a). To a solution of 2-nitro-2′-phthalimidobiphenyl (200 mg, 0.58 mmol) in 8 mL of acetone were added 0.8 mL of acetic acid and 0.8 mL of water, and then 400 mg of iron powder. The mixture was refluxed for 3 h. After filtration, the filtrate was concentrated under reduced pressure, and made basic with a saturated aqueous solution of Na_2CO_3. The organic material was extracted with CH_2Cl_2, and the extract was dried over Na_2SO_4. The solvent was removed to give 180 mg of crude 2-amino-2′-phthalimidobiphenyl. The amine was dissolved in 7 mL of dioxane, and 7 mL of 6 equiv H_2SO_4 was added to the solution. The mixture was cooled to 0 °C, and a solution of 44 mg (0.64 mmol) of $NaNO_2$ in 1.5 mL of water was added dropwise to the solution. The reaction mixture was stirred for 20 min at 0—5 °C, and added dropwise to solution of 1.5 g of NaN_3 in 6 mL of water with stirring at room temperature. The reaction mixture was stirred for 70 min. The organic material was extracted with CH_2Cl_2, and the extract was dried (Na_2SO_4). The solvent was removed to give 170 mg of 2-azido-2′-phthalimidobiphenyl. The crude azide was dissolved in 2 mL of methanol, and 0.2 mL of 80% hydrazine monohydrate was added to the solution. The mixture was stirred at room temperature for 1 h. To the reaction mixture 2 mL of a saturated aqueous solution of $NaHCO_3$ and 8 mL of water. The organic material was extracted with CH_2Cl_2, and the extract was dried over Na_2SO_4. The solvent was evaporated and the residue was separated by preparative TLC with hexane–CH_2Cl_2 (2 : 1) to give 87 mg (71%) of **3a** as colorless granules; mp 32—33 °C (lit,[5] oil); ^{1}H NMR ($CDCl_3$) δ=3.59 (1H, brs), 6.8—6.9 (2H, m), 7.04 (1H, d, J=7.6 Hz), 7.1—7.5 (5H, m); IR (NaCl) 3470, 3380, 2080, 1480, 1290, 750 cm^{-1}.

2-Azido-2′-(ethylamino)biphenyl (3b). To a solution of **3a** (140 mg, 0.67 mmol) in 4 mL of dry DMF was added ethyl iodide (0.18 ml, 2.2 mmol) and $NaHCO_3$ (185 mg, 2.2 mmol). The mixture was stirred overnight at 30 °C. To the reaction mixture 45 mL of a saturated aqueous $NaHCO_3$, and the organic material was extracted with CH_2Cl_2. The extract was washed with a saturated aqueous $NaHCO_3$, with water, and dried over Na_2SO_4. The solvent was removed, and the residue was separated by preparative TLC with hexane–CH_2Cl_2 (3 : 1) to afford 53 mg (34%) of **3b**, together with 7 mg of **3a**. **3b**: oil, ^{1}H NMR ($CDCl_3$)

δ=1.16 (3H, t, J=7.1 Hz), 3.16 (2H, q, J=7.1 Hz), 3.38 (2H, brs), 6.7—6.8 (2H, m), 7.00 (1H, d, J=7.6 Hz), 7.2—7.3 (4H, m), 7.4—7.5 (1H, m); IR (NaCl) 3420, 2970, 2110, 1290, 740 cm^{-1}.

Photolysis of 3a and 3b. A solution (25 mL) of the azide (ca. 30 mg) was placed in a Pyrex tube, purged with N_2 for 10 min, and irradiated for 45 min with a 300-W high-pressure mercury lamp at room temperature. After evaporation of the solvent, the residue was separated by GPC with chloroform eluent to give four products, together with the unchanged starting material (4—15%). The yield of products shown in Table 1 was determined by isolation on the basis of the reacted material. Benzo[*c*]cinnoline (**4**), 4-aminocarbazole (**5a**),[6] and 2,2′-diaminobiphenyl (**6a**) were identified by ^{1}H NMR and GC-MS comparison with authentic samples. 4,10-Dihydroazepino[2,3-*b*]indole (**7a**): oil; ^{1}H NMR ($CDCl_3$) δ=2.63 (2H, dd, J=5.0, 6.4 Hz), 5.17 (1H, td, J=6.4, 8.9 Hz), 6.93 (1H, t, J=5.0 Hz), 7.18 (1H, d, J=8.9 Hz), 7.20 (1H, t, J=7.9 Hz), 7.31 (1H, t, J=7.9 Hz), 7.39 (1H, d, J=7.9 Hz), 7.75 (1H, d, J=7.9 Hz), 8.51 (1H, brs). HRMS Found: m/z 182.0849 (M^+). Calcd for $C_{12}H_{10}N_2$: M^+, 182.0844. 4-(Ethylamino)carbazole (**5b**): oil; ^{1}H NMR ($CDCl_3$) δ=1.45 (3H, t, J=7.1 Hz), 3.42 (2H, q, J=7.1 Hz), 4.42 (1H, brs), 6.49 (1H, d, J=7.6 Hz), 6.86 (1H, d, J=7.9 Hz), 7.2—7.5 (4H, m), 7.94 (1H, d, J=7.6 Hz), 8.06 (1H, brs). 10-Ethyl-4,10-dihydroazepino[2,3-*b*]indole (**7b**): oil, ^{1}H NMR ($CDCl_3$) δ=1.39 (3H, t, J=7.3 Hz), 2.57 (2H, dd, J=5.0, 6.5 Hz), 4.36 (2H, q, J=7.3 Hz), 5.15 (1H, td, J=6.5, 8.9 Hz), 6.95 (1H, t, J=5.0 Hz), 7.2—7.4 (4H, m), 7.77 (1H, d, J=7.9 Hz). HRMS Found: 210.1163 (M^+). Calcd for $C_{14}H_{14}N_2$: M^+, 210.1157.

Thermolysis of 3a. The azide (ca. 2 mg) and an internal standard (biphenyl, 1.3 mg) were dissolved in 1 mL of decalin, and the solution was transferred into glass capillaries and then sealed. The solution was heated in boiling chlorobenzene (132 °C). The decrease of **3a** was monitored by HPLC with methanol–water (3:1) elution. The first-order kinetic analysis gave a rate constant of 3.30×10^{-5} s^{-1}. The yield of the products **4** and **6a** was determined to be 54% and 28%, respectively, by HPLC and GC on the basis of the reacted material. Thermolysis of 2-azidobiphenyl was carried out under the same conditions, where the first-order rate constant was obtained as 2.69×10^{-5} s^{-1} at 132 °C.

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7) 3,10-Dihydroazepino[2,3-*b*]indole as a possible structure for **7a** would be ruled out owing to the absence of a ^{1}H NMR signal assigned to –CH=N–, which is expected to appear at around δ=7.8.

8) Only when **3a** was irradiated in methanol in the presence of a large amount of sodium methoxide (1.0 mol dm^{-3}), trace amounts of **7a** (<2% yield) was detected by ^{1}H NMR of the photoreaction mixture.

9) No specific interaction between the azide and DEA was detected in the UV absorption spectrum. In addition, no practical change in the product distribution was observed when the azide was irradiated in DEA with longer wavelength light (>350 nm).

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11) The detailed mechanism of elimination of the ethyl group has not been elucidated yet. Attempts to detect ethylene and ethane by GC (Porapak Q, 2 m) in the irradiation of **3b** in methanol were unsuccessful at the present stage. It would be a possible mechanism that α-position of the ethyl group in 5-ethyl-5,6-dihydrobenzo[*c*]cinnoline was oxygenated by air to give a hydroperoxide, which was cleaved to **4** and acetaldehyde.

12) It has been reported that neighboring-group participation causes an acceleration of the thermal decomposition of azido group: L. K. Dyall and J. E. Kemp, *J. Chem. Soc. B*, **1968**, 976.