Photolysis and Thermolysis of 3-Azidonoradamantane. 'Anti-Bredt' Imines, 2-Aza-adamant-1-ene, and 4-Azaprotoadamant-3-ene[1]

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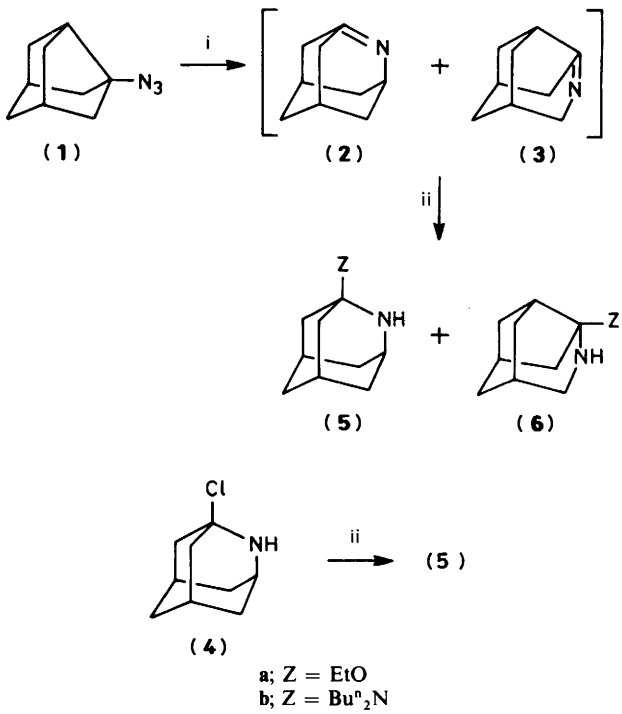
3-Azidoadamantane (**1**) when subjected to photolysis or thermolysis apparently forms the highly strained imines, 2-aza-adamant-1-ene (**2**), and 4-azaprotoadamant-3-ene (**3**). These reactive intermediates were trapped by ethanol or dibutylamine.

During the past few decades much effort has been devoted to the generation of highly strained bridgehead alkenes in bi- and tri-cyclic systems.[2] One of the most severely distorted molecules of this type is adamantene whose existence has been confirmed recently by direct spectroscopic evidence.[3] Following this line several groups turned their attention towards the synthesis of strained bridgehead systems containing hetero-atoms. Photorearrangement of bridgehead azides led to the formation of bridgehead imines[4] or their silicon analogues containing Si=N bonds.[5] In most cases the existence of these species has been postulated on the basis of indirect evidence involving characterization of the corresponding addition products. Recently three independent reports have shown that bridgehead imines do exist as chemically distinct entities. Matrix isolation experiments at 10—14 K in nitrogen or argon provided the i.r. and u.v. spectra of the unsaturated bridgehead intermediates.[6]

Since adamantene is one of the most interesting and intensively studied olefins in this category, we decided to prepare the aza analogue, 2-aza-adamant-1-ene (**2**) (2-azatricyclo[3.3.1.1^{3,7}]dec-1-ene, and investigate its chemical characteristics. The most promising route leading to compound (**2**) was photolysis of 3-azidonoradamantane (**1**) (3-azidotricyclo[3.3.1.0^{3,7}]nonane). The requisite precursor was prepared in 74% yield from 3-noradamantamine by the diaza transfer reaction. The preparation of this amine is presented in separate communications.[7-9] The photorearrangement of compound (**1**) may result in the formation of two strained imines (**2**) and (**3**). However, in related cases the reaction can occur regiospecifically. For instance, ring expansion in the case of 3-noradamantyl carbene, employed in the synthesis of adamantene, was regiospecific with no formation of the statistically more favourable protoadamantene.[10] Photolysis of compound (**1**) was performed in ethanol as the expected adduct, 1-ethoxy-2-aza-adamantane (**5a**) is a known compound accessible by ethanolysis of 1-chloro-2-aza-adamantane (**4**).[11] The reaction, conducted at room temperature, afforded 64% of two isomeric iminoethers, (**5a**) and 3-ethoxy-4-azaprotoadamantane (**6a**) (Scheme). The molar ratio of (**5a**) to (**6a**), determined by ^{13}C n.m.r. with a suppressed n.o.e. effect, was 1:1.10 which differs from the statistical 1:2 ratio. The non-statistical distribution of imine products was rationalized by Kyba and Abramovitch[12] on the basis of a preferred migratory orientation in the photochemically excited azide.

We also investigated the thermolysis of compound (**1**) at 200 °C. Although previous literature attempts entailing pyrolysis of bridgehead azides gave erratic results (*e.g.*, 1-azidonorbornane afforded only 30% of products, whereas 1-azidoadamantane failed to give any product), the thermal decomposition of compound (**1**) in a sealed glass tube in ethanol produced a mixture of compounds (**5a**) and (**6a**) in 50% yield. However, the molar ratio of (**5a**):(**6a**) changed to 1:1.44, closer to the statistical 1:2 ratio. In photolysis, an increase in temperature decreased the migratory selectivity of the adjacent σ bonds.[12]



Scheme. *Reagents:* i, *hν* or Δ*t*; ii, HZ

When this work was essentially completed, Sasaki and co-workers[4g] published in this general area. The photorearrangement of compound (**1**) in methanol led to the related iminoethers (**5**) and (**6**) (Z = MeO), produced in a similar ratio 1:1.17. The ^{13}C n.m.r. chemical shifts of the skeletal carbons are very close to those found for our compounds.

In all previous reports the intermediate imines have been trapped by alcohols or by [2 + 2] cycloaddition. We decided to employ a new trapping agent, an aliphatic amine. Both photolysis and thermolysis of compound (**1**) in di-n-butylamine gave high yields of the addition products, 1-dibutylamino-2-aza-adamantane (**5b**) and 3-dibutylamino-4-azaprotoadamantane (**6b**). Attempts to separate the mixture were unsuccessful.

The results demonstrate that, by the use of various trapping agents, bridgehead imines can be employed as useful intermediates in the synthesis of heterocyclic systems. Although bridgehead α-aminoethers are fairly well known, the literature on bridgehead *gem*-diamines appears to be sparse.[13]

The various products were characterized by elemental analysis, and their ^{1}H and ^{13}C n.m.r., i.r., and mass spectra. In

addition, authentic samples of compounds (**5a**) and (**5b**) were prepared by the solvolysis of 1-chloro-2-aza-adamantane (**4**) in ethanol and dibutylamine, respectively.

Experimental

I.r. spectra were obtained on a Nicolet MX-1 Fourier Transform (FT) instrument. ^{1}H N.m.r. spectra were recorded in p.p.m. at 60 MHz on a Varian EM 360L spectrometer, and ^{13}C n.m.r. spectra on a Varian CFT-20 or a Bruker 250 MHz multiple probe instrument ($CDCl_3$ as solvent and $SiMe_4$ as reference). Chemical ionization mass spectra were obtained using a Hewlett Packard 5895 system with methane as ionizing gas. Ether refers to diethyl ether.

3-*Noradamantamine*.—The procedure published previously[7] was modified by use of sodium hypochlorite solution (Clorox) as the chlorinating agent[14] for the conversion of 2-methyl-adamantan-2-ol into the corresponding hypochlorite.

A 2-l three-necked flask equipped with a mechanical stirrer and thermometer was charged with a 4% aqueous solution (1.1 l) of technical grade sodium hypochlorite (Clorox). To this solution, cooled in a salt–ice bath to −5 to 0 °C, a slurry of 2-methyladamantan-2-ol (27.0 g, 0.162 mol) in carbon tetrachloride (140 ml) was added followed by glacial acetic acid (28 ml). After the reaction mixture had been stirred at 0 °C for 3 h, the layers were separated. The aqueous one was extracted twice with 50-ml portions of CCl_4, the combined organic portion was washed once with saturated sodium hydrogen carbonate (150 ml) and the yellow organic solution was dried ($MgSO_4$), filtered, and used immediately in the next step.

The hypochlorite solution obtained in the preceding reaction was refluxed for 12 h. The solvent was evaporated to give yellow 3-chlorobicyclo[3.3.1]nonan-7-yl methyl ketone (33 g). The oil was distilled at 114—120 °C (0.6 mmHg) to give a colourless liquid (29.6 g, 91%) or was used in the next step without further purification.

The remaining steps were performed as reported in our previous communication to afford methyl tricyclo-[3.3.1.0^{3,7}]nonan-3-yl ketone (94%), noradamantane carboxylic acid (83%), and 3-noradamantamine (77%). m.p. 175 °C.

3-*Azidonoradamantane*.—*Procedure A*. 3-Noradamantamine (2.75 g, 20 mmol) was dissolved in anhydrous ether (50 ml). To the stirred solution, a 1.58M-solution of butyl-lithium (14 ml, 22 mmol) was added dropwise under nitrogen at 0 °C. The exothermic reaction produced a white precipitate. After the mixture had been stirred at room temperature for 2 h, toluene-*p*-sulphonyl azide (5 g, 25.4 mmol) in anhydrous ether (25 ml) was added dropwise. The reaction mixture was cooled to 15—20 °C, and then left for 24 h at room temperature.

The mixture was washed with water, the aqueous phase was extracted with ether, and then the organic portion was dried and evaporated. The remaining oil was passed through silica gel with n-hexane as the eluant. The desired azide appears in the first fraction. The hexane solution was vacuum distilled to give a colourless liquid (**1**) (1.45 g, 45%), b.p. 89—92 °C (12 mmHg), *m/z* (C.I.; CH_4) 164 (*M* + 1, 8.7), 136 (*M* + 1 − N_2, 100), and 121 (noradamantyl, C_9H_{13}, 76). The spectrum also contained ions corresponding to secondary products: *m/z* 284 (6.7), and 256 (37.7); $\nu_{max.}$(neat) 2 930, 2 870, 2 095 (N_3), 1 460, 1 347, 1 255, 1 114, and 992 cm^{-1}; δ_H($CDCl_3$) 1.3—3.8 (br m), 1.7, 1.95, and 2.35; δ_C($CDCl_3$) 34.4 (C-9, t), 37.6 (C-1, -5, d), 43.2 (C-7, d), 43.7 (C-6, -8, t), 48.2 (C-2, -4, -5), and 72.2 p.p.m. (C-3, -5) (Found: C, 66.2; H, 8.0; N, 25.75. Calc. for $C_9H_{13}N_3$: C, 66.26; H, 8.03; N, 25.75%).

Procedure B. An alternative method[4g] with tetrahydrofuran as solvent and sodium hydride as the deprotonating base gave distilled product (**1**) (74%). 3-Noradamantamine (6.86 g, 0.05 mol), sodium hydride (2.5 g, 0.052 mol; 50% suspension in paraffin oil washed with dry hexane prior to the reaction), and toluene-*p*-sulphonyl azide (10.4 g, 0.053 mol) were stirred magnetically in dry tetrahydrofuran (70 ml) for 46 h. The mixture was diluted with water (250 ml) and then extracted three times with hexane. The hexane layer was dried and vacuum distilled to yield compound (**1**) (6.04 g, 74%), b.p. 57 °C (0.6 mmHg) or 48 °C (0.05 mmHg).

Photolysis of Compound (**1**) *in Ethanol*.—A solution of compound (**1**) (380 mg, 233 mmol) in anhydrous ethanol (20 ml) was irradiated at 2 537 Å in a Rayonet photochemical reactor in a quartz vessel cooled externally with water and kept under nitrogen. After 11 h the solvent was evaporated to give a yellow oil (490 mg) which was vacuum distilled to afford a colourless liquid (270 mg), b.p. 92—95 °C (3 mmHg) (Found: C, 72.6; H, 10.7; N, 7.6. $C_{11}H_{19}NO$ requires C, 72.88; H, 10.56; N, 7.73%). T.l.c. showed the presence of two products (**5a**) and (**6a**) which were separated by preparative t.l.c. on silica gel with EtOAc–hexane (1 : 3) as eluant.

1-*Ethoxy-2-aza-adamantane* (**5a**), $\nu_{max.}$(neat) 3 420, 2 979, 2 925, 2 849, 1 425, 1 315, 1 151, 1 138, 1 120, 1 109, 1 092, 1 059, 1 038, and 844 cm^{-1}; δ_H($CDCl_3$) 1.05 (t, *J* 7 Hz, CH_3), 1.3—2.6 m (maxima at δ 1.4, 1.65, 1.9, and 2.2), 3.25 (1 H, s), and 3.65 (q, *J* 7 Hz, CH_2); δ_C($CDCl_3$) 16.3 (q, CH_3), 30.0 (C-5, -7, d), 36.1 (C-6, t), 36.5 (C-4, -10, t), 41.6 (C-8, -9, t), 50.2 (C-3, d), 55.0 (CH_2, t), and 82.5 p.p.m. (C-1, s); *m/z* (%) (C.I.; CH_4) 182 (65.4, *M* + 1), 181 (29.5), 180 (24.5), and 136 (100, *M* − EtO).

Synthesis of an Authentic Sample of (**5a**).—This compound was prepared directly from compound (**4**) according to the published procedure.[11] All spectral characteristics were identical with those of the compound isolated from the photolysis of (**1**).

3-*Ethoxy*-4-*azaprotoadamantane* (**6a**), $\nu_{max.}$(neat) 3 570, 2 938, 2 925, 2 866, 1 461, 1 442, 1 330, 1 217, 1 114, 1 104, 1 090, 1 062, 921, and 733 cm^{-1}; δ_H($CDCl_3$) 1.2 (t, *J* 7 Hz, CH_3), 1.3—2.4m (maxima at δ 1.5, 1.65, and 2.0), 3.0 (1 H, s), and 3.65 (q, *J* 7 Hz, CH_2); δ_C($CDCl_3$) 16.3, 28.0, 32.5, 34.8, 38.4, 39.2, 42.0, 42.5, 48.4, 57.6, and 96.5 p.p.m.; *m/z* (%) (C.I.; CH_4) 182 (*M* + 1), 181, 180, and 136 (100, *M* − EtO).

Thermolysis of Compound (**1**) *in Ethanol*.—Compound (**1**) (400 mg, 2.45 mmol) in ethanol (10 ml) was heated in a sealed glass tube for 12 h at 200 °C. After the tube had been cooled to room temperature, the solution was evaporated to give a light-coloured oil (540 mg) which was vacuum distilled, b.p. 78—82 °C/1 Torr, to give a colourless mixture (220 mg) of products (**5a**) and (**6a**). The quantitative analysis was obtained from the crude mixture prior to distillation.

Photolysis of Compound (**1**) *in Dibutylamine*.—The azide (**1**) (510 mg, 3.1 mmol) was dissolved in dry dibutylamine (30 ml). The solution was irradiated at 2 537 Å in a Rayonet photochemical reactor in the same manner as for EtOH. After 20 h the solvent was evaporated under reduced pressure to give a yellow oil (0.65 g) which was distilled (pot temperature 130—135 °C/0.6 mmHg) in a Kugelrohr apparatus to give a mixture of products (**5b**) and (**6b**) (0.53 g, 65%). Attempts to separate the mixture by g.c. (Hewlett-Packard fused silica capillary column, 25 m, I.D. 0.31 mm; film thickness, 0.52 μm; stationary phase: crosslinked 5% phenyl methyl silicone) and t.l.c. failed (Found: C, 77.4; H, 12.4; N, 10.7. $C_{17}H_{32}N_2$ requires C, 77.21; H, 12.20; N, 10.60%), *m/z* (%) (C.I.; CH_4) 266 (*M* + 2, 19), 265 (*M* + 1, 100), 264 (*M*, 89), 263 (54.5), 221 (26), and 136 (17.5).

Synthesis of Authentic Compound (**5b**).—This compound was obtained independently by heating compound (**4**) (1.0 g, 5.8 mmol) with dibutylamine (10 ml) in a sealed glass tube at 200 °C for 9 h. On cooling, dibutylamine hydrochloride crystallized. The mixture was washed with 10% aqueous NaOH. The organic layer was separated and dried ($MgSO_4$). Vacuum distillation at 123—125 °C (0.4 mmHg) gave compound (**5b**) (0.9 g, 58.4%); $\nu_{max.}$(neat) 3 300w, 1 467, 1 445, 1 420, 1 375, 1 317, 1 213, 1 097, 1 090, 1 047, 1 021, 832, and 812 cm $^{-1}$; *m/z* (%) (C.I.; CH_4) 266 (*M* + 2, 17), 265 (*M* + 1, 95), 264 (*M*, 100), and 221 (29); $\delta_C(CDCl_3)$ 14.3, 20.7, 29.3, 33.9, 36.6, 37.0, 39.8, 47.8, 49.1, and 69.0 p.p.m.

3-*Dibutylamino*-4-*azaprotoadamantane* (**6b**), δ_C [the figures resulted from subtraction of the resonance lines for (**5b**) from the spectral data for the mixture] 14.2 (CH_3, Bu), 20.7 (CH_2, Bu), 27.8, 34.0 (CH_2, Bu), 34.8, 38.9, 40.4, 42.1, 47.8, 49.9, 52.0, and 84.0 p.p.m.

Thermolysis of Compound (**1**) *in Dibutylamine*.—The azide (**1**) (520 mg, 3.2 mmol) was heated for 2 h in a sealed glass tube with dry dibutylamine (10 ml) at 200 °C. Excess of dibutylamine was removed under vacuum; the remaining oil was distilled (Kugelrohr), pot temperature 200—210 °C (12 mmHg), to give a mixture of compounds (**5b**) and (**6b**) (0.44 g, 52%).

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