Evidence for Intramolecular Ylide Formation in the Decay of a Singlet Aryl Nitrene

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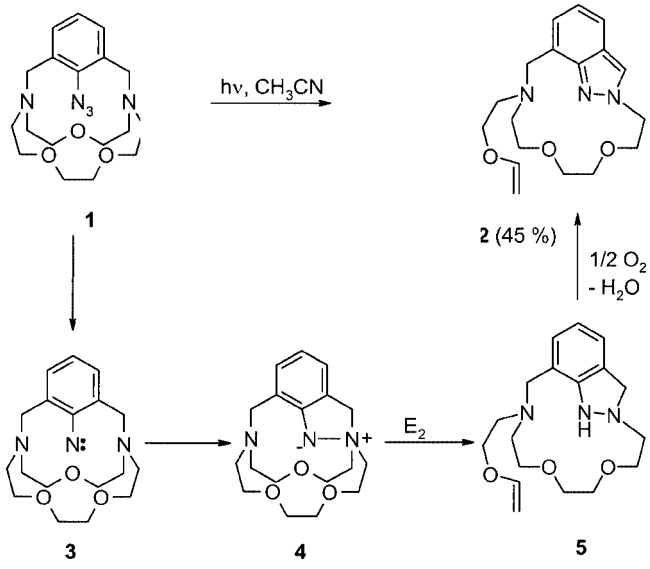
The photolysis of the azido-functionalized cryptand **1** yields the benzopyrazole **2**. The formation of **2** is rationalized to occur via the nitrene ammonium ylide **4**, which undergoes ring-opening by an intramolecular E2 elimination mechanism. The benzopyrazoline thus formed is then oxidized during aerobic workup.

Introduction

Ylide formation is a reaction frequently encountered in carbene chemistry. Among others, ylides may be formed in the reactions of (singlet) carbenes with pyridine,[1] carbonyl compounds,[2] thiocarbonyls,[3] and THF.[4] In aryl nitrene chemistry, ylide formation is much less common, although it is observed in the reactions of highly reactive fluorinated singlet aryl nitrenes.[5,6] Due to the open-shell character of singlet aryl nitrenes,[7–9] most singlet aryl nitrenes preferentially decay by intramolecular rearrangement or intersystem crossing to the triplet ground state, and show little preference for intermolecular reactions.[10–12] Intramolecular ylide formation has been observed in the case of certain azidophenyl-substituted pyrazole derivatives, where the ylides formed are highly stabilized aza-pentalene derivatives.[13]

In this contribution, we wish to report on the photochemistry of an azido-substituted cryptand **1**.



Scheme 1

Results and Discussion

Photolysis of **1** in acetonitrile solution yielded benzopyrazole **2** as the only isolable product in 45 % yield. The formation of **2** can be rationalized as proceeding via the singlet nitrene **3** and the ylide **4**. Ylide **4** undergoes intramolecular E2 elimination to yield benzopyrazoline **5**, which is oxidized to **2** during workup (Scheme 1).

Density functional theory was employed to calculate the barriers for key steps in the sequence shown in Scheme 1.[14] This approach is problematic for the ylide-forming reaction itself, as CASSCF theory would have to be used for a reliable description of singlet aryl nitrene **3**.[9a] DFT (UBPW91/cc-pVDZ) calculations on singlet aryl nitrenes have been reported.[9b] Using this method,[9c] we calculated the reaction enthalpy for (singlet) **3** → **4** as $\Delta H = -15.0$ kcal/mol. The formation of ylide **4** therefore should have a sufficiently large thermodynamic driving force. It should be noted, however, that at this point nothing can be said about the barrier of the ylide-forming reaction, and that this value for the reaction enthalpy should be considered preliminary.

The activation enthalpy for the intramolecular E2 elimination of **4**, yielding **5**, was calculated at the B3LYP/6–31G(d) level of theory as $\Delta H^{\#} = 13.8$ kcal/mol, with $\Delta H = -43.4$ kcal/mol. At the same level of theory, the activation enthalpy for the alternative E2 elimination, leading to **6**, was predicted to be significantly higher, at $\Delta H^{\#} = 17.9$ kcal/mol ($\Delta H = -13.4$ kcal/mol). Other reactions of **4** were

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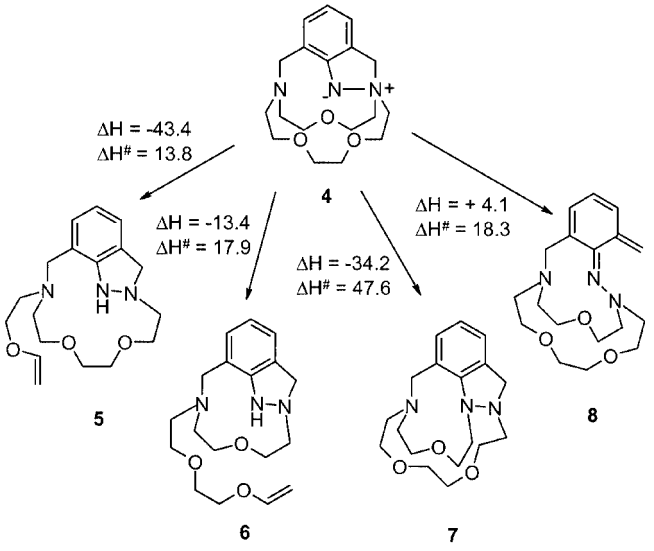
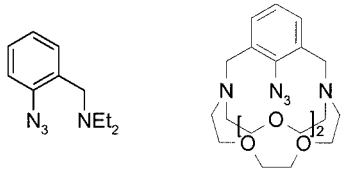
calculated to be impeded by higher activation enthalpies (Scheme 2). Thus, the Aza-Stevens rearrangement leading to **7** was predicted to have $\Delta H^{\#}$ = 47.6 kcal/mol (ΔH = −34.2 kcal/mol) and the activation enthalpy for the ring-opening to provide the quinone methide hydrazone **8** was calculated as $\Delta H^{\#}$ = 18.3 kcal/mol (ΔH = +4.1 kcal/mol).



Scheme 2. B3LYP/6-31G(d), all enthalpies in kcal/mol

In conclusion, evidence has been presented for the intermediacy of an intramolecular nitrene-ammonium ylide. In agreement with experimental findings, calculations predict preferential decay by an E2 elimination mechanism, in which the nitrogen atom formerly belonging to the nitrene acts as a base. This observation is surprising because neither studies on the photochemistry of 2-(diethylaminomethyl)azidobenzene **9**,[15] nor on the photochemistry of the related cryptand **10**[16] gave any evidence for intramolecular ylide formation. Further studies on the photochemistry of **1** and on intramolecular ylide-forming reactions of ortho-substituted derivatives of singlet phenyl nitrene are currently underway.



Experimental Section

Synthesis of Cryptand 1: A solution of 1-azido-2,6-bis(bromomethyl)benzene (1.12 g, 3.7 mmol) in acetonitrile (50 mL) was added dropwise to a vigorously stirred mixture of diaza[15]crown-5 (0.8 g, 3.7 mmol) and K_2CO_3 (4.5 g) in refluxing acetonitrile (600 mL) over a period of 2 h. The mixture was refluxed for 16 h. After evaporation of the solvent under reduced pressure, the residue was dissolved in CH_2Cl_2 and dried over $MgSO_4$. Purification by column chromatography (SiO_2, cyclohexane/Et_2NH 95:5) and recrystallization from pentane afforded **1** as a colorless solid (0.32 g, 24 %). M.p. 105 °C. ^{1}H NMR (400 MHz, CD_2Cl_2): δ = 2.27−2.31 (m, 4 H), 2.56−2.68 (m, 2 H), 2.96−3.00 (m, 2 H), 3.08−3.14 (m, 2 H), 3.23−3.29 (m, 4 H), 3.36 (d, J = 13.08 Hz, 2 H, benzylic CH_2), 3.55−3.60 (m, 2 H), 3.62−3.67 (m, 2 H), 3.74−3.79 (m, 2 H), 4.07 (d, J = 13.08 Hz, 2 H, benzylic CH_2), 6.85−7.02 (m, 3 H, ArH) ppm. ^{13}C NMR: (100.6 MHz, CD_2Cl_2) δ = 54.84, 58.17, 58.53 (benzylic CH_2), 70.25, 71.58, 71.71, 122.71, 130.09, 135.99, 141.82 ppm. IR (KBr): ṽ = 2940 (s), 2839 (s), 2797 (s), 2113 (vs), 1438 (m), 1351 (m), 1308 (m), 1142 (m), 1124 (s), 1057 (m), 920 (m), 830 (m), 763 (m) cm^{-1}. MS (EI): *m/z* (%) = 361 (8) $[M]^+$, 333 (20) $[M - N_2]^+$, 318 (22), 302 (58), 276 (10), 260 (15), 245 (15), 216 (18), 189 (25), 173 (39), 159 (42), 145 (60), 132 (79), 118 (30), 100 (25), 91 (35), 86 (22), 77 (18), 70 (21), 65 (15), 56 (100), 42 (58), 28 (60). $C_{18}H_{27}N_5O_3$ (361.4): calcd. C 59.88, H 7.54, N 19.39; found C 59.80, H 8.01, N 19.18.

Photolysis of 1: Cryptand **1** (50 mg, 0.14 mmol) was dissolved in CH_3CN (30 mL, HPLC grade) and put into a quartz tube which was covered by a septum. After purging the solution with Ar for 30 min, the sample was irradiated for 45 min with 320 nm radiation (Hg low-pressure lamp). After evaporation of the solvent, the residue was dissolved in CH_2Cl_2 and purified by column chromatography (SiO_2, TBME/Et_2NH, 100:5), to afford **2** as a colorless solid (20 mg, 45 %). M.p. 89 °C. ^{1}H NMR: (400 MHz, CD_2Cl_2) δ = 2.68 (t, 2 H), 2.97 (t, 2 H), 3.45−3.47 (m, 2 H), 3.57−3.59 (m, 2 H), 3.63 (t, 2 H), 3.87 (t, 2 H), 3.98 (dd, 1 H, J = 2, 7.04 Hz), 4.07 (t, 2 H), 4.19 (dd, 1 H, J = 2, 14.56 Hz), 4.20 (s, 2 H), 4.57 (m, 2 H), 6.50 (dd, 1 H, J = 7.04, 14.56 Hz), 7.01 (dd, 1 H), 7.12 (dd, 1 H, J = < 1, 6.5 Hz), 7.54 (dd, 1 H, J = 1, 8.5 Hz), 7.88 (s, 1 H). ^{13}C NMR (100.6 MHz, CD_2Cl_2) δ = 55.15, 52.81, 53.70, 53.96, 66.38, 67.13, 68.61, 69.14, 69.78, 86.43, 119.35, 121.58, 121.93, 122.89, 126.44, 126.94, 149.20, 151.86 ppm. IR (KBr): ṽ = 3118 (w), 2946 (s), 2862 (s), 1620 (m), 1529 (m), 1468 (m), 1390 (m), 1370 (m), 1321 (m), 1262 (m), 1201 (s), 1135 (s), 995 (m), 964 (m), 869 (m), 813 (m), 754 (m) cm^{-1}. MS (EI): *m/z* (%): 331 (5) $[M]^+$, 303 (40) $[M - C_2H_4]^+$, 288 (40) $[M - CH_2CHO]^+$, 274 (50) $[M - CH_2CHOCH_2]^+$, 219 (100), 202 (5), 186 (5), 173 (10), 157 (22), 144 (5), 131 (35), 112 (40), 90 (10), 70 (5), 56 (18). $C_{18}H_{25}N_3O_3$ (331.4): calcd. C 65.19, H 7.60, N 12.73; found C 64.90, H 7.58, N 12.70.

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