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REACTION OF 2-HYDRAZINO-1-AZAAZULENE WITH DIPHENYLNITRONE: UNEXPECTED FORMATION OF PHENYLIMINO-*p*-BENZOQUINON-*N*-OXIDE

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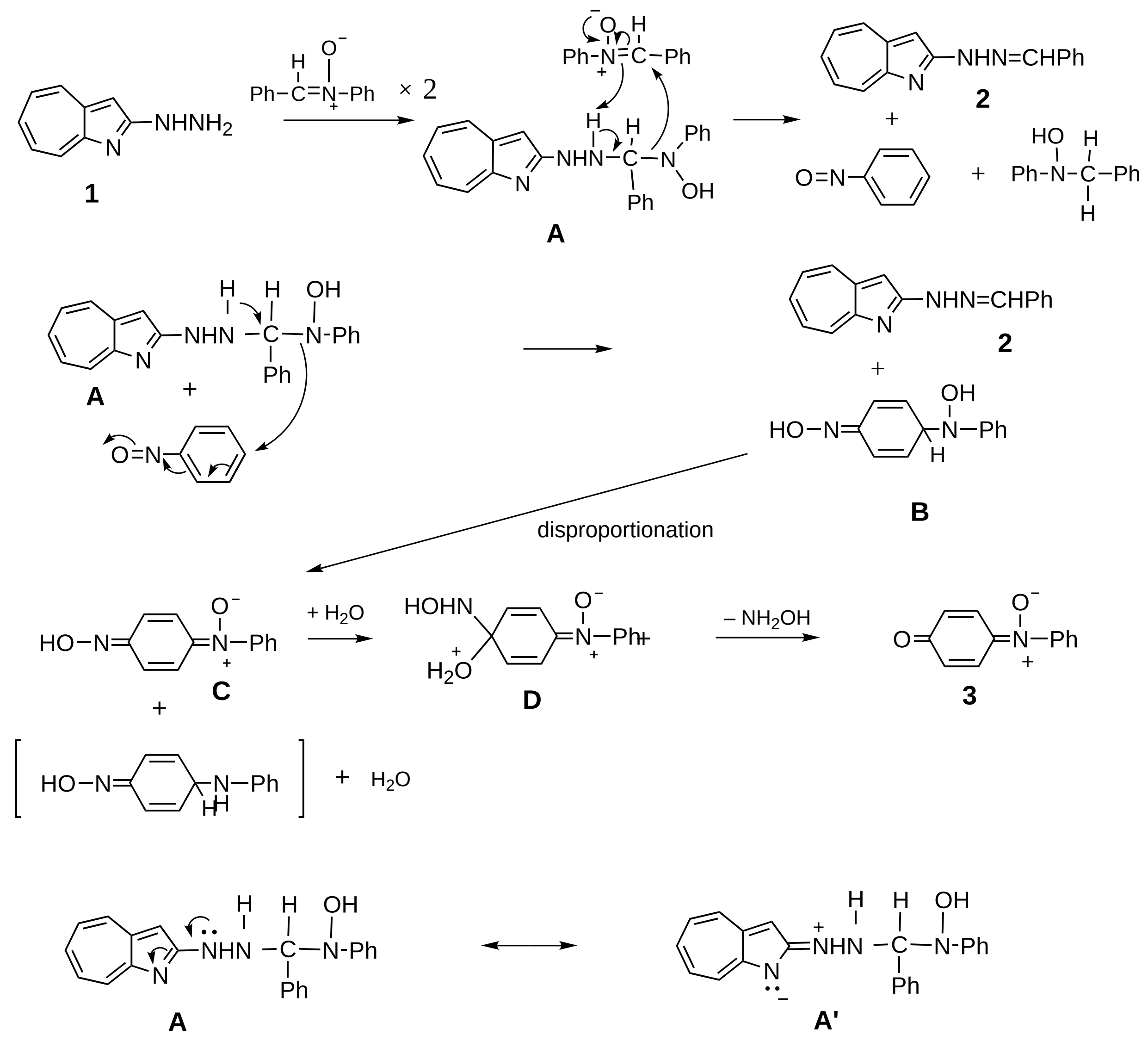
Abstract - Reaction of 2-hydrazino-1-azaazulene with diphenylnitrone gave benzaldehyde (1-azaazulen-2-yl)hydrazone (**2**) and phenylimino-*p*-benzoquinone-*N*-oxide (**3**). Reaction mechanism for the formation of **2** and **3** was discussed.

The chemistry of nitrone is extensively investigated because of its synthetically versatile use; an isoxazoline formation has been most worthy of remarks.[1] In the course of our investigation of azaazulene chemistry, we recently reported an interesting cyclization reaction where diphenylnitrone reacted with 2-alkylamino-1-azaazulenes and afforded novel pentacyclic heterocycles.[2] We also reported that 2-hydrazino-1-azaazulenes reacted with dimethyl acetylenedicarboxylate[3] and diphenylcyclopropenone[4] and gave some variety of cycloadducts and the hydrazones. From the expectation of the formation of new cycloadducts we expanded the investigation to the reaction of 2-hydrazino-1-azaazulenes with a nitrone. Some reports of phenylhydrazines with nitrones are appeared affording the corresponding hydrazones, but they were the reactions after hydrolysis of the nitrone.[5]

Reaction of 2-hydrazino-1-azaazulene (**1**) with diphenylnitrone in dry acetonitrile at rt for 3 days yielded benzaldehyde (1-azaazulen-2-yl)hydrazone (**2**) in 70% yield. When the reaction was performed under reflux for 3 days, a complex mixture was produced. From the mixture, two compounds, phenylimino-*p*-benzoquinone-*N*-oxide (**3**) (10.5% based on diphenylnitrone) and **2** (68%), were isolated. Compound (**2**) was deduced from the inspection of spectroscopic data as well as elemental analysis and independent synthesis; the reaction of **1** with benzaldehyde gave **2** in the 75% yield.



Scheme 1

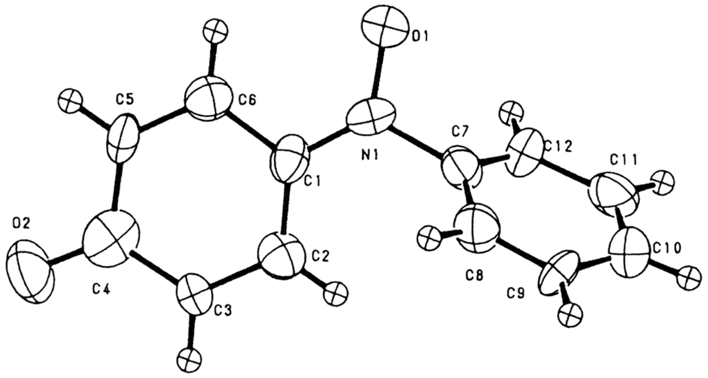


Figure 1. ORTEP drawing of **3** with thermal ellipsoid plot (50% probability)

O_1—N_1	1.29(1)	O_1—N_1—C_1—C_2	172(1)°
O_2—C_4	1.25(1)	O_1—N_1—C_1—C_6	−6(1)°
N_1—C_1	1.31(1)	O_1—N_1—C_7—C_{12}	−59(1)°
C_1—C_2	1.40(1)	O_1—N_1—C_7—C_8	119.1(9)°
C_1—C_6	1.44(1)	O_2—C_4—C_5—C_6	179(1)°
C_2—C_3	1.37(1)	C_1—N_1—C_7—C_8	−61(1)°
C_3—C_4	1.44(1)	C_2—C_1—N_1—C_7	−8(2)°
C_4—C_5	1.45(2)	C_2—C_1—C_6—C_5	1(2)°
C_5—C_6	1.34(1)	C_3—C_2—C_1—C_6	2(2)°

Selective Bond Lengths (Å) and Torsional Angles

The structure of **3** was confirmed by X-Ray structure analysis by direct method and an ORTEP drawing is shown in Figure 1.[6] Compound **3** was first synthesized by Wieland and Roth,[7] and attracted attentions; several investigations were reported about the synthesis, physical properties and reactions.[8—11] The X-Ray structure analytical investigation of **3** itself has not been successful so far, only the report insufficient analysis of (*p*-methoxyphenyl)imino-*p*-benzoquinone-*N*-oxide was seen.[12]

Reaction of **1** with α-(*p*-methoxyphenyl)-*N*-phenylnitrone gave similar result as for **1**, and **3** (12%) and *p*-methoxybenzaldehyde (1-azaazulen-2-yl)hydrazone (**4**) (67%) were obtained.

A plausible mechanism is shown in the Scheme 1. The hydrazine (**1**) reacts with diphenylnitrone to give an adduct (**A**). Reaction of intermediate (**A**) with a second molar of diphenylnitrone causes cleavage of **A** and would give benzaldehyde (1-azaazulen-2-yl)hydrazone (**2**) and nitrosobenzene. The nitrosobenzene then reacts with **A** to give rise to **2** and the hydroxylamine (**B**). It is known that hydroxylamine underwent disproportionation and gave nitrone and amine,[7,13] *e.g.*, *N*-ethyl-*N*-phenylhydroxylamine gave α-methyl-*N*-phenylnitrone and *N*-ethylaniline.[13] Moreover, it is known that the reaction of nitrosobenzene with *p*-benzoquinone gave dinitrone derivative.[14] Therefore it is considered that dispropotionation of **B** would give *p*-diiminoqinon-*N*-oxide (**C**). Addition of water to **C** gives **D**, and successive elimination of hydroxyamine furnishes **3**. Similar treatment of phenylhydrazine with diphenylnitrone did not give **3**. Therefore the results suggest a participation of 1-azaazulene moiety. Large electron-withdrawing character of the 1-azaazulene ring as shown in the resonance form **A'** would facilitate the reaction of **A** with nitrosobenzene.

EXPERIMENTAL

Melting points are uncorrected. ^{1}H NMR spectra (250 MHz) were recorded on a Hitachi R-250H spectrometer using deuteriochloroform as a solvent with tetramethylsilane as an internal standard; *J* values are recorded in Hz. Electronic spectra were taken with a Hitachi 220A spectrophotometer using ethanol as a solvent. IR spectra were recorded for KBr pellets on a Hitachi 270-50 infrared spectrophotometer. Kieselgel 60 was used for column chromatography.

Reaction of 2-hydrazino-1-azaazulene with diphenylnitrone

a) A solution of 2-hydrazino-1-azaazulene (**1**) (0.159 g, 1.00 mmol) and diphenylnitrone (0.591 g, 3.00 mmol) in dry acetonitrile (40 mL) was stirred at rt for 3 days and evaporated. The residue was chromatographed with chloroform to give benzaldehyde (1-azaazulen-2-yl)hydrazone (**2**) (0.174 g, 70%). Compound (**2**): orange prisms (from ethyl acetate), mp 223—224 ℃; δ_H 7.10—7.30 (1H, br), 7.25—7.55 (7H, m), 7.71 (2H, d, *J* 7.0), and 7.80—8.20 (3H, m); ν_{max} / cm$_{-1}$ 1616 (C=N); λ_{max} nm (log ε) 252

(4.38), 288 (4.25), 340 (4.39), 410 (4.24), and 450 (4.13); *m/z* (rel. intensity) 248 (M^+ +1, 24), 171 (81), 144 (90), and 90 (100); *Anal.* Calcd for $C_{16}H_{13}N_3$: C, 77.71; H, 5.30; N, 16.99. Found: C, 77.57; H, 5.34; N, 16.98.

b) A solution of 2-hydrazino-1-azaazulene (**1**) (0.477 g, 3.00 mmol) and diphenylnitrone (1.773 g, 9.00 mmol) in dry acetonitrile (60 mL) was refluxted for 3 days and evaporated. Chromatography of the residue with chloroform gave phenylimino-*p*-benzoquinone-*N*-oxide (**3**) (0.188 g, 10.5%) and **2** (0.504 g, 68%), successively. Compound (**3**): orange needles (from hexane–dichloromethane), mp 140—142 ℃ (lit.,[2] 140 ℃); δ_H 6.26 (1H, dd, *J* 10.4 and 1.8), 6.67 (1H, dd, *J* 10.4 and 1.8), 7.19 (1H, dd, *J* 10.3 and 3.1), 7.45—7.60 (5H, m), and 8.05 (1H, dd, *J* 10.4 and 3.1); ν_{max} / cm^{-1} 1622 (C=O); λ_{max} nm (log ε) 261 (2.35), and 387 (3.03); *m/z* (rel. intensity) 200 (M^+ +1, 15), 199 (M^+, 15), and 92 (100); *Anal*. Calcd for $C_{12}H_9NO_2$: C, 72.35; H, 4.55; N, 7.03. Found: C, 72.09; H, 4.64; N, 7.05.

Synthesis of benzaldehyde (1-azaazulen-2-yl)hydrazone (2)

A solution of **1** (3.98 g, 25.0 mmol) and benzaldehyde (2.65 g, 25.7 mmol) in ethanol (100 mL) was refluxed for 1 h and evaporated. The residue was chromatographed with chloroform to give **2** (4.66 g, 75%).

Reaction of 2-hydrazino-1-azaazulene with α-(*p*-methoxyphenyl)-*N*-phenylnitrone

A solution of 2-hydrazino-1-azaazulene (**1**) (0.477 g, 3.00 mmol) and α-(*p*-methoxyphenyl)-*N*-phenylnitrone (1.704 g, 7.50 mmol) in acetonitrile (50 mL) was refluxted for 3 days and evaporated. The residue was chromatographed with chloroform to give *p*-methoxybenzaldehyde (1-azaazulen-2-yl)hydrazone (**4**) (0.540 g, 67%) and phenylimino-*p*-benzoquinone-*N*-oxide (**3**) (0.180 g, 12%).

Compound (**4**): orange prisms (from ethyl acetate—hexane), mp 192—194 ℃; δ_H 3.86 (3H, s), 6.94 (2H, d, *J* 8.7), 7.10—7.20 (1H, br), 7.30—7.42 (1H, br), 7.42—7.55 (1H, br), 7.68 (2H, d, *J* 8.7), 7.85—8.05 (2H, br m); ν_{max} / cm^{-1} 2830 (OCH_3) and 1614 (C=N); λ_{max} nm (log ε) 258 (4.33), 266 (4.42), 296 (4.37), 343 (447), 417 (4.36), and 452 (4.27); *Anal.* Calcd for $C_{17}H_{15}N_3O$: C, 73.63; H, 5.45; N, 15.15. Found: C, 73.72; H, 5.38; N, 15.33.

X-Ray structure determinations

Crystal data for 3: brown prism, $C_{12}H_9NO_2$, *M*=199.21, monoclinic, space group $P2_1/a$, *a*=7.510(3), *b*=12.6355(9), *c*=10.302(2) Å, β=101.08(2)°, *V*=959.4(4) $Å^3$, *Z*=4, D_{calcd}=1.379 g/cm^3, crystal dimensions 0.24 x 0.88 x 1.00 mm. Data were measured on a Rigaku AFC 5S radiation diffractometer with graphite-monochromated Mo-Kα radiation. A total 2476 reflections (2309 unique) were collected using the $\omega-2\theta$ scan technique to a maximum 2θ value of 55.0 °. The structure was solved by direct methods and refined by a full-matrix least-squares method using TEXAN structure analysis software, [15] using 150 variables and 709 observed reflections ($I > 3\sigma(I)$). The non-hydrogen atoms were refined anisotropically. The weighting scheme $\omega = 4Fo^2/\sigma^2(Fo^2)$ gave satisfactory agreement analyses. The final R and Rw values were 0.093 and 0.115. The maximum peak and the minimum peak in final difference map were 0.48 $e^-/Å^3$ and –0.40 $e^-/Å^3$.

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