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SYNTHESIS AND CYCLOADDITION REACTION OF 2a,4,5-TRIAZABENZ[*cd*]-AZULENE DERIVATIVES

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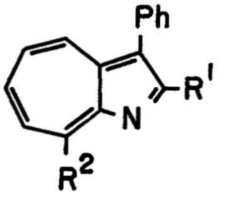
Abstract – 2a,4,5-Triazabenz[*cd*]azulene derivatives (2) were synthesized by the reaction of 8-hydrazino-3-phenyl-1-aza-azulenes (1) with triethyl orthoformate. 2-Chloro substituted compound (2b) was easily hydrolized on silica gel and gave (2-chloro-8-imino-3-phenyl-1-aza-1,8-dihydroazulen-1-yl)formaldehyde oxime. Reaction of 2a with dimethyl acetylenedicarboxylate gave dimethyl 1-phenyl-2a,5-diazabenz[*cd*]azulene-3,4-dicarboxylate and dimethyl (1-cyano-3-phenyl-1,8-dihydro-1-azaazulen-8-ylideneamino)maleate.

Some full conjugated peri-condensed azaazulenes[1-5] including cyclazine systems[6-12] have been investigated because of the interest concerning their physical and chemical properties. Regarding the research on cyclohepta[*ef*]-cycl[3.2.2]azine system, we carried out the synthesis of 2a,4,5-triazabenz[*cd*]-azulene derivatives (2a,b) and the reaction of 2a with dimethyl acetylenedicarboxylate (DMAD).

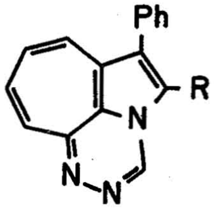
Heating of a mixture of 8-hydrazino-3-phenyl-1-azaazulene[13] (1a) and triethyl orthoformate in the presence of p-toluenesulfonic acid for 30 min gave 1-phenyl-2a,4,5-triazabenz[*cd*]azulene (2a) in 96% yield. The compound 2a was slightly unstable, and showed slight contamination after chromatographic separation and recrystallization. The ^{1}H NMR spectrum of 2a reveals signals at δ 5.56 (dd, J=11.0 and 7.3 Hz, H-7), 6.05 (dd, J=12.2 and 7.3 Hz, H-8), 6.16 (d, J=12.2 Hz, H-9), 6.45 (d, J=11.0 Hz, H-6), 7.06 (s, H-2), 7.25-7.50 (m, phenyl), and 8.02 (s, H-3). The signals of the seven-membered ring protons resonated at considerably high field and have large divergences of the coupling constants ($J_{6-7}\sim J_{7-8}$=3.7 Hz, $J_{7-8}\sim J_{8-9}$=4.9 Hz). The results indicate a high degree of bond alternation in the seven-membered ring as in the cases of 2a-aza-,[2] 2a,5-diaza-,[3] and 2,2a,4,5-tetraazabenz[cd]azulenes.[4]

When 1b was treated with triethyl orthoformate, 2b was obtained in only 9% yield and (2-chloro-8-imino-3-phenyl-1-aza-1,8-dihydroazulen-1-yl)formaldehyde oxime [3, MS m/z 297 (M$^+$)], which would be a hydrolized product of 2b, was obtained in 64% yield instead. Compound 2b was hydrolized on silica gel to give 3 in a good yield. In the IR spectrum of 3, characteristic absorptions assignable to an oxime are seen at 3190 (OH) 1650 cm^{-1} (C=N). Its ^{1}H NMR spectrum shows a signal of a sharp singlet at δ 8.29 (CH=N) and signals of two 1H broad singlets at δ 10.18 (NH) and 10.59 (OH).

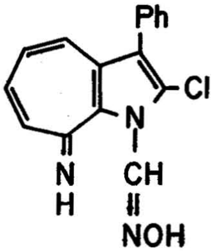
The reaction of 2a with DMAD in hot acetonitrile for 2 h gave dimethyl 1-phenyl-2a,5-diazabenz[cd]azulene-3,4-dicarboxylate (4) (4%), dimethyl (1-cyano-3-phenyl-1,8-dihydro-1-azaazulen-8-ylideneamino)maleate (5) (5%), and some undefined compounds. When the reaction was carried out in hot xylene, the compound 5 was isolated in a 19% yield. In the mass spectrum of 4, a molecular peak is



1a: R^1 = H, R^2=NHNH$_2$
1b: R^1 =Cl, R^2=NHNH$_2$



2a: R = H
2b: R = Cl



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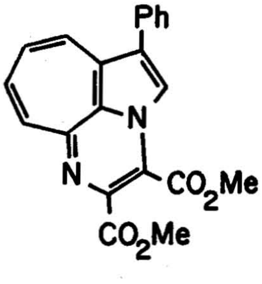

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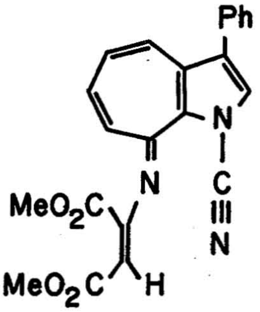
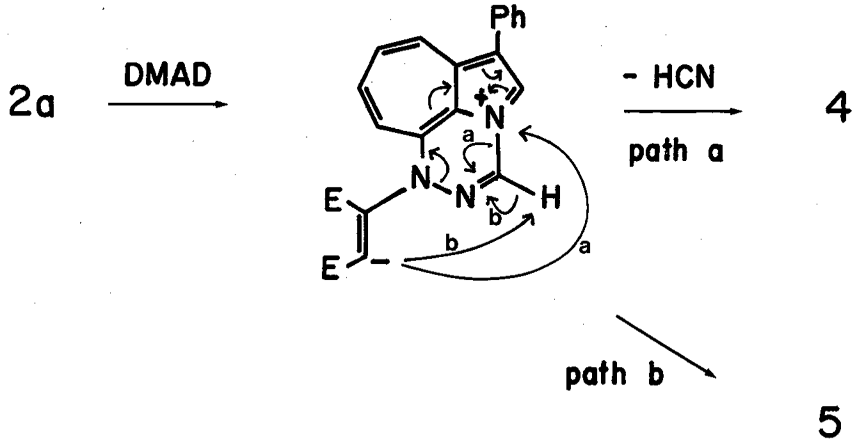


5

observed at m/z 360. The ^{1}H NMR spectrum of 4 shows two methyl ester singlets at δ 3.86 and 3.89, and a 1H singlet assignable to H-2 at δ 8.16, which would be deshielded by the ester group at C-3, together with seven-membered ring protons and phenyl protons. Its IR spectrum shows ester carbonyl absorptions at 1750 and 1700 cm^{-1}. The same compound was obtained on the reaction of 8-amino-3-phenyl-1-azaazulene with DMAD.[14] The ^{1}H NMR spectrum of 5 shows signals at δ 3.68 (s, OMe), 3.91 (s, OMe), 6.91 (s, H-vinyl), 7.00 (dd, J=10.4 and 8.9 Hz, H-6), 7.27 (s, H-2), 7.34 (dd, J=12.2 and 8.9 Hz, H-5), 7.39-7.51 (m, phenyl), 7.72 (d, J=12.2 Hz, H-4), and 7.89 (d, J=10.4 Hz, H-7). In its IR spectrum, CN absorption is seen at 2170 cm^{-1}. These results accord with the structures. While 2a,5-diazabenz[cd]azulene reacted with DMAD to give azacyclohepta[ef]-cycl[3.2.2]azine,[3] 2a,4,5-triazabenz[cd]azulene gave no corresponding cyclazine but another type of products 4 and 5 instead. This would be caused by the presence of a reactive azine moiety in the latter molecule. A plausible mechanism is shown in the Scheme 1.



Scheme I

EXPERIMENTAL

Melting points were uncorrected. ^{1}H NMR spectra were taken on a Hitachi R-250H (250 MHz) spectrometers using deuteriochloroform as a solvent (TMS as an internal standard), unless otherwise stated. IR spectra were recorded for Nujol mulls with a Hitachi 270-50 infrared spectrophotometer.

*Syntheses of **2**.* A mixture of **1a** (0.471 g), p-toluenesulfonic acid (0.040 g), and triethyl orthoformate (10 ml) was heated at 140 ℃ for 30 min. The mixture was evaporated and the residue was chromatographed on silica gel rapidly. Elution with ethanol gave **2a** as violet crystals (0.470 g, 96%), which was crystallized from n-hexane-dichloromethane to give violet needles (0.353 g, 72%), mp 200-201 ℃ (Found: m/z 245.0955. $C_{16}H_{11}N_3$ requires 245.0952); ^{1}H NMR δ =5.56 (dd, J=11.0 and 7.3 Hz, H-7), 6.05 (dd, J=12.2 and 7.3 Hz, H-8), 6.16 (d, J=12.2 Hz, H-9), 6.45 (d, J=11.0 Hz, H-6), 7.06 (s, H-2), 7.25-7.50 (m, phenyl), and 8.02 (s, H-3); IR 750 and 695 cm^{-1} (phenyl).

Similarly, a solution of **1b** (0.542 g), p-toluenesulfonic acid (0.040 g), and triethyl orthoformate (10 ml) in dry xylene (20 ml) was heated for 20 min at 140 ℃, and worked up. Chromatography of the residue with chloroform gave **3** (0.367 g, 64%) and **2b** (0.048 g, 9%), successively. [**3**: orange needles (from benzene-dichloromethane), mp 167-168 ℃ (Found: C, 64.48; H, 3.92; N, 13.27; M$^+$, 297. $C_{16}H_{12}ClN_3O$ requires C, 64.54; H, 4.06; N, 14.11; M, 297); ^{1}H NMR δ (DMSO-d_6)=7.17 (t, J=9.7 Hz, H-5) 7.35-7.60 (m, H-4 and phenyl), 7.76 (t, J=9.7 Hz, H-6), 7.98 (d, J=9.7 Hz, H-7), 8.29 (s, CH=N), 10.18 (bs, exch., NH), and 10.59 (bs, exch., OH); IR 3190 (broad, OH), 3100-2800 (broad, NH), 1650 and 1630 (C=N), and 695 cm^{-1} (phenyl). **2b**: violet prisms (from dichloromethane-n-hexane), mp 212-213 ℃ (Found: m/z 279.0547. $C_{16}H_{10}N_3{}^{35}Cl$ requires 279.0563); ^{1}H NMR δ =5.60 (dd, J=11.6 and 7.9 Hz, H-7), 6.10 (dd, J=12.2 and 7.9 Hz, H-8), 6.25 (d, J=12.2 Hz, H-9), 6.33 (d, J=11.6 Hz, H-6), 7.25-7.55 (m, phenyl), and 8.10 (s, H-3); IR 690 cm^{-1} (phenyl)].

*Hydrolysis of **2b**.* A mixture of **2b** (0.020 g) and silica gel (0.70 g) in chloroform (10 ml) was left to stand at room temperature for 3 d, then filtered. Silica gel was washed with ethanol. Evaporation of the combined solution gave **3** (18 mg, 85%).

*Reaction of **2a** with DMAD.* a) A solution of **2a** (0.245 g) and DMAD (0.310 g) in acetonitrile (50 ml) was heated under reflux for 2 h. The solvent was evaporated and the residue was chromatographed. Elution with benzene-chloroform (1:1) gave **4** (0.015 g, 4%), which was crystallized from cyclohexane-dichloromethane to give violet scales, mp 156-158 ℃ (Found: C, 69.85; H, 4.43; N, 7.86; M$^+$, 360. $C_{21}H_{16}N_2O_4$ requires C, 69.99; H, 4.48; N, 7.77%; M, 360); ^{1}H NMR δ =3.86 (s, OMe), 3.89 (s, OMe), 5.58-5.70 (m, H-7), 6.10-6.20 (m, H-8 and 9), 6.70 (d, J=11.0 Hz, H-6), 7.30-7.50 (m, phenyl), and 8.16 (s, H-2); IR 1750, 1700 (C=O), 720, and 695 cm^{-1} (phenyl). Further elution gave 5 (0.021 g, 5%), which was crystallized from cyclohexane-dichloromethane to give yellow needles, mp 175-176 ℃ (Found: C, 68.22; H, 4.32; N 10.48; M$^+$, 387. $C_{22}H_{17}N_3O_4$ requires C, 68.21; H, 4.42; N, 10.85%; M, 387); ^{1}H NMR δ =3.68 (s, OMe), 3.91 (s, OMe), 6.91 (s, H-vinyl), 7.00 (dd, J=10.4 and 8.9 Hz, H-6), 7.27 (s, H-2), 7.34 (dd, J=12.2 and 8.9 Hz, H-5), 7.39-7.51 (m, phenyl), 7.72 (d, J=12.2 Hz, H-4), and 7.89 (d, J=10.4 Hz, H-7); IR 2170 (CN), 1740, 1730 (C=O), 1655 (C=N), and 710 cm^{-1} (phenyl).

b) A solution of 2a (0.245 g) and DMAD (0.284 g) in dry xylene (30 ml) was heated under reflux for 1 h and worked up as above. Elution with chloroform gave 4 (trace) and 5 (0.075 g, 19%), successively.

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REFERENCES

1. T. Nishiwaki and N. Abe, Heterocycles, 1981, 15, 547.
2. T. Nishiwaki, N. Abe, K. Ishida, and K. Miura, Bull. Chem. Soc. Jpn., 1978, 51, 1573.
3. N. Abe, Heterocycles, 1987, 26, 59.
4. K. Imafuku, M. Sumio, and H. Matsumura, J. Heterocyclic Chem., 1980, 17, 1057.
5. A. Hallberg and A. R. Martin, J. Heterocyclic Chem., 1981, 18, 1255; A. Hallberg, T. Dahlgren, A. Martin, and K. Christiansen, ibid., 1983, 20, 37.
6. W. Flitsch and U. Kramer, Adv. Heterocyclic Chem., 1978, 22, 321.
7. D. Leaver, Pure Appl. Chem., 1986, 58, 143.
8. W. Flisch, A. Gurke, and B. Muter, Chem. Ber., 1975, 108, 2969; W. Flitsch and Mukidjamn, ibid., 1979, 112, 3577.
9. W. Flitsch and E. R. Gesing, Tetrahedron Lett., 1979, 3405; idem, Chem. Ber., 1983, 116, 1174.

10. M. A. Jessep and D. Leaver, *J. Chem. Soc., Perkin Trans. 1*, **1980**, 1324; V. Batroff, W. Flitsch, D. Leaver, and D. Skinner, *Chem. Ber.*, 1984, **117**, 1649.

11. N. Abe, T. Nishiwaki, H. Yamamoto, and, N. Kunishige, *Bull. Chem. Soc. Jpn.*, 1983, **56**, 3703.

12. M. Noguchi, Y. Tamai, and S. Kajigaeshi, *Abstructs of the 53 Annual Meeting of the Chemical Society of Japan*, Nagoya, **1986** 1F15.

13. K. Yamane, K. Fujimori, J.-K. Sin, and T. Nozoe, *Bull. Chem. Soc. Jpn.*, 1977, **50**, 1184.

14. Reaction of 8-amino-3-phenyl-1-azaazulene with DMAD in hot acetonitrile gave **4** in a 9% yield. N. Abe, to be published.

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