Chem. Pharm. Bull. **41**(4) 752—754 (1993) Vol. 41, No. 4

Reactions of Carbene Conjugated with 1-Azaazulene Moiety: Additions of 3-(2-Chloro-1-azaazulenyl)methylene with *cis*- and *trans*-Stilbenes and *p*-Substituted Styrenes to Form 3-Cyclopropyl-1-azaazulenes

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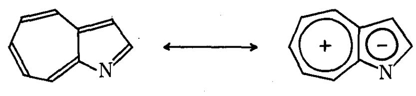
Received August 11, 1992

The addition reactions of 3-(2-chloro-1-azaazulenyl)methylene with *cis*- and *trans*-stilbenes proceeded in a stereospecific manner to afford the corresponding cyclopropane derivatives. The substitution effects on the relative rate ratio of the addition reactions of the carbene with styrenes having various substituents on the *p*-positions were measured to investigate the electronic nature of the carbene.

Keywords azaazulene; carbene; addition; cyclopropane; rate ratio

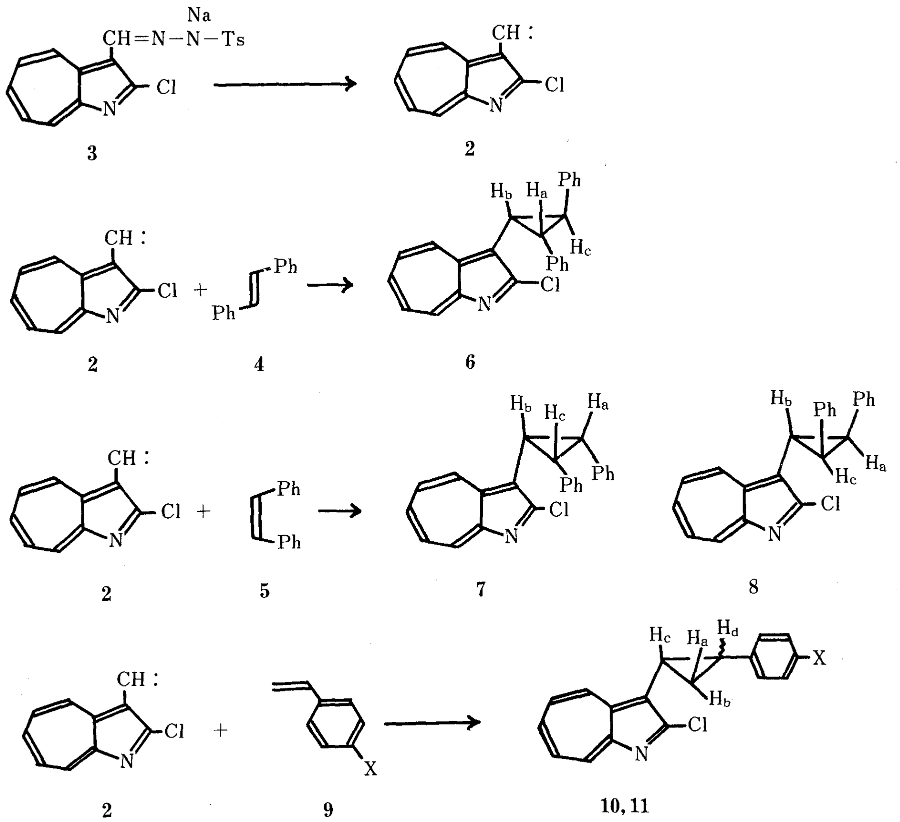
Much attention has been paid to the chemistry of carbenes not only from the viewpoint of their synthetic utility but also because of the interest in their electronic natures and chemical reactivities,[1)] which are influenced by substituents and especially by conjugation with olefinic groups.[1)] While the chemistry of carbenes conjugated with olefinic or aromatic groups or carbenes incorporated in conjugated cyclic frameworks has been researched extensively, relatively little is known about the chemistry of carbenes conjugated with hetero aromatic moieties.[1,2)]

The aromaticity of azaazulene is a result of the contribution of the ionic canonical formula (**1b**).[3)] The partial zwitterionic nature of **1** is expected to influence the reactivities of carbenes conjugated with **1**. As a part of our researches on the reactivities of carbenes,[2b,4)] we investigated the reactions of 3-(2-chloro-1-azaazulenyl)methylene (**2**)[2b)] with stilbenes and styrenes. The results are presented here.



1a **1b**

Fig. 1



a : X=H, **b** : X=Cl
c : X=Me, **d** : X=OMe

Chart 1

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The sodium salt of 2-chloro-1-azaazulene-3-carbaldehyde tosylhydrazone (**3**) and 4 molar eq of *trans*-stilbene (**4**) were reacted at 110 °C for 10 min to give an adduct (**6**) in 25% yield. The same reaction using *cis*-stilbene (**5**) afforded two adducts (**7** and **8**) in 6 and 4% yields, respectively.

The structures of these adducts were deduced on the basis of their spectral properties and were confirmed by comparisons of these properties with those of analogous compounds.[5] The coupling constants between H_a and H_b (9.0 Hz) and H_a/H_b and H_c (6.0 Hz) of **6** are reasonable for the values between *cis*- and *trans*-cyclopropane protons, respectively. The assignment of the structures of **7** and **8** is based on the chemical shifts of the cyclopropane proton H_b. Comparing the chemical shifts of the protons H_b of **7** (2.96 ppm) and **8** (3.20 ppm), the chemical shift of the proton (H_b) of **8** should appear at lower field because of the anisotropic effect of the two phenyl groups located on the same side of the cyclopropane moiety as that of the proton H_b.[6] The observed coupling constants between H_b and H_a/H_c (6.0 Hz) of **8**, which are reasonable as the coupling constants between *trans*-cyclopropane protons, supported these structures.

The present results demonstrate that the reactions of **2** with stilbenes proceeded in a stereospecific manner showing the multiplicity of the carbene to be singlet. The next problem concerns the propensity of this carbene to behave electrophilically or nucleophilically. In order to clarify this problem, substitution effects on the addition reactions were investigated with styrene derivatives having various substituents at the *p*-position (**9a**—**d**).

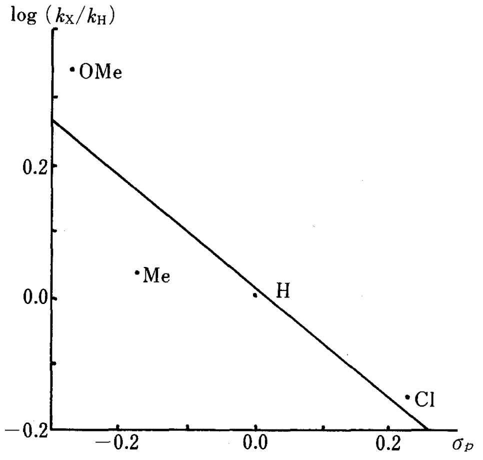

Fig. 2

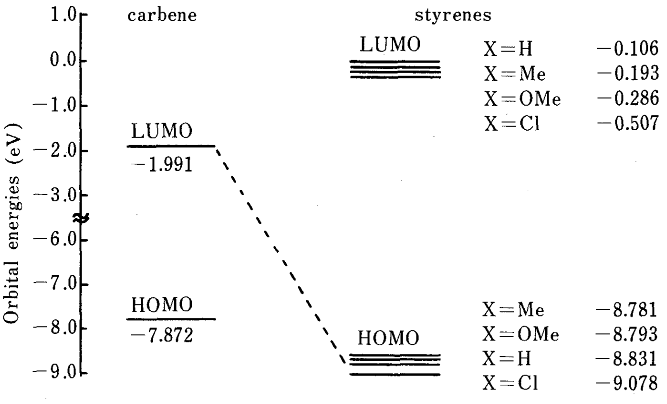

Fig. 3

Reactions of **2** with styrene (**9a**) gave *cis*- and *trans*-cyclopropane derivatives (**10a** and **11a**) in 15 and 7% yields, respectively. Similar reactions of **2** with *p*-chloro- (**9b**), *p*-methyl- (**9c**), and *p*-methoxystyrene (**9d**) gave the corresponding cyclopropane derivatives **10b** (13%), **11b** (9%), **10c** (15%), **11c** (7%), and **10d** (17%), **11d** (6%), respectively.

The relative rate ratios of **2** to the substituted styrenes were measured using the addition reactions of **2** to 1 : 1 mixtures of **9a** and **9b**, **9a** and **9c**, and **9a** and **9d**[7] to compare the yields of the corresponding cyclopropane derivatives (**10** and **11**). The ratio of **9a** : **9b** : **9c** : **9d** was measured to be 1.0 : 0.7 : 1.1 : 2.2. The relation of the logarithm of the relative rate ratio ($\log k_X/k_H$) to Hammett's sigma values (σ_p) of the substituents gave a negative ρ-value (−1.84) suggesting a weak electrophilicity of **2**.[8]

The frontier orbital energies of **2** and the styrenes calculated by the modified neglect of diatomic overlap (MNDO) method[9] are shown in Fig. 3. The energy gaps between the LUMO of **2** and the HOMO of the styrenes are smaller than those of the opposite combinations, suggesting that the reactions are controlled by the orbital interactions between the LUMO of **2** and the HOMO of the styrenes.[10] The electrophilicity of **2** can be explained by the differences of the energy gap between these interacting orbitals, which is smaller in *p*-methoxystyrene (**9d**) and larger in *p*-chlorostyrene (**9b**). However, considering that the product yields of these reactions were not high, and the absolute value of the ρ-value was small, it is difficult to reach a definitive conclusion on the reactivities of this carbene at this stage.

Experimental

Melting points are uncorrected. NMR spectra were measured with a Varian XL 200 spectrometer with tetramethylsilane as an internal standard. IR and UV spectra were measured with JASCO FT/IR-5300 and Hitachi 220A spectrophotometers, respectively. Mass spectra were measured with a Hitachi M-2000S spectrometer. Only typical reactions are described below.

Reaction of 2 with 4 Sodium hydride (60% in oil, 40 mg, 1 mmol) and **4** (720 mg, 4 mmol) were added to a solution of 2-chloro-1-azaazulene-3-carbaldehyde tosylhydrazone[11] (360 mg, 1 mmol) in anhydrous diglyme (9 ml). The mixture was heated at 110 °C for 10 min. After filtration the filtrate was poured into water, extracted with ether. After evaporation of the solvent, the oily residue was subjected to thin-layer chromatography on silica gel using benzene–ether 9 : 11 as a developing solvent to give dark red crystals **6** (87 mg, 25%, *Rf* = 0.60), which were recrystallized from hexane.

6: mp 109—110 °C. HRMS *m/z*: 355.1108. Calcd for $C_{24}H_{18}ClN$ *m/z*: 355.1126. MS *m/z* (rel. intensity): 355 (M^+, 68), 320 (100). UV_{max}^{MeOH} nm ($\log\varepsilon$): 279 (4.55), 342 (sh, 3.42), 477 (3.01). IR (KBr): 3020, 1601 cm^{-1}. ^1H-NMR ($CDCl_3$) δ: 2.88 (dd, H_b, J=6.0, 9.0 Hz), 2.94 (dd, H_a, J=6.0, 9.0 Hz), 3.16 (dd, H_c, J=6.0, 6.0 Hz), 6.79 (m, 2H), 6.95 (m, 3H), 7.25—7.55 (m, 6H), 7.63 (dd, 1H, J=10.0, 10.0 Hz), 7.72 (dd, 1H, J=10.0, 10.0 Hz), 8.82 (d, 1H, J=10.0 Hz), 8.48 (d, 1H, J=10.0 Hz).

7: HRMS *m/z*: 355.1135. Calcd for $C_{24}H_{18}ClN$ *m/z*: 355.1127. MS *m/z* (rel. intensity): 355 (M^+, 38), 320 (100). UV_{max}^{MeOH} nm ($\log\varepsilon$): 280 (4.68), 358 (sh, 3.63), 459 (3.31). IR (oil): 3030, 1601 cm^{-1}. ^1H-NMR ($CDCl_3$) δ: 2.96 (br s, 3H, H_a, H_b, H_c), 7.10—7.40 (m, 10H), 7.65 (dd, 1H, J=10.0, 10.0 Hz), 7.80 (dd, 1H, J=10.0, 10.0 Hz), 7.90 (dd, 1H, J=10.0, 10.0 Hz), 8.60 (d, 1H, J=10.9 Hz), 8.62 (d, 1H, J=10.0 Hz).

8: HRMS *m/z*: 355.1109. Calcd for $C_{24}H_{18}ClN$ *m/z*: 355.1126. MS *m/z* (rel. intensity): 355 (M^+, 42), 320 (100). UV_{max}^{MeOH} nm ($\log\varepsilon$): 279 (4.57), 355 (sh, 3.42), 478 (3.04). IR (oil): 3030, 1601 cm^{-1}. ^1H-NMR ($CDCl_3$)

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δ: 3.16 (d, 2H, $\mathrm{H_a}$, $\mathrm{H_c}$, J=6.0 Hz), 3.20 (t, $\mathrm{H_b}$, J=6.0 Hz), 6.90—7.10 (m, 11H), 7.60—7.90 (m, 3H), 8.55 (m, 1H).

10a: mp 120—121 °C. HRMS *m*/*z*: 279.0838. Calcd for $C_{18}H_{14}ClN$ *m*/*z*: 279.0814. MS *m*/*z* (rel. intensity): 279 (M^+, 60), 244 (100). $\mathrm{UV}_{\max}^{\mathrm{MeOH}}$ nm (log ε): 279 (4.82), 356 (3.46). IR (KBr): 3020, 1584 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.72 (ddd, $\mathrm{H_a}$, J=5.5, 5.5, 6.8 Hz), 1.79 (ddd, $\mathrm{H_b}$, J=5.5, 8.5, 8.5 Hz), 2.54 (ddd, $\mathrm{H_c}$, J=6.8, 8.5, 8.5 Hz), 2.65 (ddd, $\mathrm{H_d}$, J=5.5, 8.5, 8.5 Hz), 6.72 (m, 2H, Ph), 6.91 (m, 3H, Ph), 7.45 (dd, 1H, J=10.0, 10.0 Hz), 7.64 (dd, 1H, J=10.0, 1.0 Hz), 7.75 (dd, 1H, J=10.0, 10.0 Hz), 8.33 (d, 1H, J=10.0 Hz), 8.44 (d, 1H, J=10.0 Hz).

11a: HRMS *m*/*z*: 279.0841. Calcd for $C_{18}H_{14}ClN$ *m*/*z*: 279.0814. MS *m*/*z* (rel. intensity): 279 (M^+, 87), 256 (100). $\mathrm{UV}_{\max}^{\mathrm{MeOH}}$ nm (log ε): 279 (4.49), 335 (sh, 3.42), 478 (2.87). IR (oil): 3029, 1603 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.60 (m, 2H, $\mathrm{H_a}$, $\mathrm{H_b}$), 2.28 (m, $\mathrm{H_c}$), 2.34 (m, $\mathrm{H_d}$), 7.25—7.45 (m, 5H, Ph), 7.70 (dd, 1H, J=10.0, 10.0 Hz), 7.78 (dd, 1H, J=10.0, 10.0 Hz), 7.91 (dd, 1H, J=10.0, 10.0 Hz), 8.61 (d, 2H, J=10.0 Hz).

10b: mp 131—132 °C. HRMS *m*/*z*: 313.0425. Calcd for $C_{18}H_{13}Cl_2N$ *m*/*z*: 313.0424. MS *m*/*z* (rel. intensity): 313 (M^+, 52), 278 (100). $\mathrm{UV}_{\max}^{\mathrm{MeOH}}$ nm (log ε): 278 (4.80), 356 (3.46), 475 (3.08). IR (KBr): 3017, 1584 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.69 (ddd, $\mathrm{H_a}$, J=5.7, 6.0, 6.0 Hz), 1.80 (ddd, $\mathrm{H_b}$, J=5.7, 8.4, 8.4 Hz), 2.55 (ddd, $\mathrm{H_c}$, J=6.0, 8.4, 8.4 Hz), 2.62 (ddd, $\mathrm{H_d}$, J=6.0, 8.4, 8.4 Hz), 6.65 (d, 2H, Ph, J=8.0 Hz), 6.89 (d, 2H, Ph, J=8.0 Hz), 7.51 (dd, 1H, J=10.0, 10.0 Hz), 7.68 (dd, 1H, J=10.0 Hz), 7.80 (dd, 1H, J=10.0, 10.0 Hz), 8.36 (d, 1H, J=10.0 Hz), 8.47 (d, 1H, J=10.0 Hz).

11b: HRMS *m*/*z*: 313.0418. Calcd for $C_{18}H_{13}Cl_2N$ *m*/*z*: 313.0424. MS *m*/*z* (rel. intensity): 313 (M^+, 53), 278 (100). $\mathrm{UV}_{\max}^{\mathrm{MeOH}}$ nm (log ε): 277 (4.60), 353 (sh, 3.34), 475 (2.96). IR (oil): 3020, 1582 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.56 (ddd, $\mathrm{H_a}$, J=4.6, 6.4, 8.2 Hz), 1.61 (ddd, $\mathrm{H_b}$, J=4.6, 6.4, 8.6 Hz), 2.24 (ddd, $\mathrm{H_c}$, J=4.6, 6.4, 8.6 Hz), 2.33 (ddd, $\mathrm{H_d}$, J=4.6, 6.4, 8.2 Hz), 7.26 (d, 2H, Ph, J=8.0 Hz), 7.36 (d, 2H, Ph, J=8.0 Hz), 7.70 (dd, 1H, J=10.0, 10.0 Hz), 7.78 (dd, 1H, J=10.0, 10.0 Hz), 7.91 (dd, 1H, J=10.0, 10.0 Hz), 8.58 (d, 2H, J=10.0 Hz).

10c: mp 132—133 °C. HRMS *m*/*z*: 293.0959. Calcd for $C_{19}H_{16}ClN$ *m*/*z*: 293.0970. MS *m*/*z* (rel. intensity): 293 (M^+, 38), 258 (100). $\mathrm{UV}_{\max}^{\mathrm{MeOH}}$ nm (log ε): 278 (4.79), 355 (3.65). IR (KBr): 3030, 1516 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.69 (ddd, $\mathrm{H_a}$, J=5.8, 6.5, 7.2 Hz), 1.76 (ddd, $\mathrm{H_b}$, J=5.8, 8.4, 8.7 Hz), 2.50 (ddd, $\mathrm{H_c}$, J=7.2, 8.4, 8.7 Hz), 2.61 (ddd, $\mathrm{H_d}$, J=6.5, 8.4, 8.4 Hz), 2.08 (s, 3H, Me), 6.62 (d, 2H, Ph, J=8.0 Hz), 6.73 (d, 2H, Ph, J=8.0 Hz), 7.48 (dd, 1H, J=10.0, 10.0 Hz), 7.64 (dd, 1H, J=10.0, 10.0 Hz), 7.75 (dd, 1H, J=10.0, 10.0 Hz), 8.38 (d, 1H, J=10.0 Hz), 8.45 (d, 1H, J=10.0 Hz).

11c: HRMS *m*/*z*: 293.0958. Calcd for $C_{19}H_{16}ClN$ *m*/*z*: 293.0969. MS *m*/*z* (rel. intensity): 293 (M^+, 40), 258 (100). $\mathrm{UV}_{\max}^{\mathrm{MeOH}}$ nm (log ε): 279 (4.46), 353 (sh, 3.31), 478 (2.98). IR (oil): 3030, 1584 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.57 (m, 2H, $\mathrm{H_a}$, $\mathrm{H_b}$), 2.24 (ddd, $\mathrm{H_c}$, J=5.0, 7.6, 7.6 Hz), 2.32 (ddd, $\mathrm{H_d}$, J=5.0, 7.6, 7.6 Hz), 2.37 (s, 3H, Me), 7.22 (m, 4H, Ph), 7.67 (dd, 1H, J=10.0, 10.0 Hz), 7.75 (dd, 1H, J=10.0, 10.0 Hz), 7.88 (dd, 1H, J=10.0, 10.0 Hz), 8.55 (d, 1H, J=10.0 Hz), 8.58 (d, 1H, J=10.0 Hz).

10d: mp 99—100 °C. HRMS *m*/*z*: 309.0931. Calcd for $C_{19}H_{16}ClNO$ *m*/*z*: 309.0919. MS *m*/*z* (rel. intensity): 309 (M^+, 35), 274 (100). $\mathrm{UV}_{\max}^{\mathrm{MeOH}}$ nm (log ε): 277 (4.51), 355 (3.30), 481 (2.96). IR (KBr): 3030, 1612 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.66 (m, $\mathrm{H_a}$), 1.73 (m, $\mathrm{H_b}$), 2.46 (m, $\mathrm{H_c}$), 2.59 (m, $\mathrm{H_d}$), 3.56 (s, 3H, Me), 6.45 (d, 2H, Ph, J=8.7 Hz), 6.65 (d, 2H, Ph, J=8.7 Hz), 7.46 (dd, 1H, J=10.0, 10.0 Hz), 7.62 (dd, 1H, J=10.0, 10.0 Hz), 7.73 (dd, 1H, J=10.0, 10.0 Hz), 8.35 (d, 1H, J=10.0 Hz), 8.42 (d, 1H, J=10.0 Hz).

11d: HRMS *m*/*z*: 309.0926. Calcd for $C_{19}H_{16}ClNO$ *m*/*z*: 309.0919. MS *m*/*z* (rel. intensity): 309 (M^+, 32), 274 (100). $\mathrm{UV}_{\max}^{\mathrm{MeOH}}$ nm (log ε): 278 (4.52), 355 (sh, 3.30), 479 (2.95). IR (oil): 3030, 1581 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.36 (m, 2H, $\mathrm{H_a}$, $\mathrm{H_b}$), 2.19 (ddd, $\mathrm{H_c}$, J=5.1, 7.3, 7.3 Hz), 3.16 (ddd, $\mathrm{H_d}$, J=5.1, 7.3, 7.3 Hz), 3.83 (s, 3H, Me), 6.94 (d, 2H, Ph, J=8.7 Hz), 7.38 (d, 2H, Ph, J=8.7 Hz), 7.66 (dd, 1H, J=10.0, 10.0 Hz), 7.73 (dd, 1H, J=10.0, 10.0 Hz), 7.86 (dd, 1H, J=10.0, 10.0 Hz), 8.54 (d, 1H, J=10.0 Hz), 8.59 (d, 1H, J=10.0 Hz).

Measurements of Relative Rate Ratios of the Reactions of 2 with 9a—d 2-Chloro-1-azaazulene-3-carbaldehyde tosylhydrazone sodium salt was reacted with a 1 : 1 mixture of **9a** and **9b** as usual. The summations of the integrations of the signals of the cyclopropane protons of **10a** and **11a** and those of **10b** and **11b** in the ^{1}H-NMR spectra showed the ratio of the summation of **10a** and **11a** and that of **10b** and **11b**, which indicates the relative rate ratio of **2** to **9b**, to be 0.7, based on the value of 1.0 for the reaction of **2** with **9a**.[6] The same procedure as above using 1 : 1 mixtures of **9a** and **9c**, and **9a** and **9d** gave the relative rate ratio of the reaction of **2** with **9a** and **9c**, and with **9a** and **9d** as 1.1 and 2.2, respectively.

References and Notes

1) W. M. Jones and C. L. Ennis, *J. Am. Chem. Soc.*, **91**, 6391 (1969); M. Oda, Y. Ito, and Y. Kitahara, *Tetrahedron Lett.*, **1975**, 2587; S. J. Chang, B. K. R. Shankar, and H. Shechter, *J. Org. Chem.*, **47**, 4226 (1982); K. Saito and H. Ishihara, *Bull. Chem. Soc. Jpn.*, **59**, 1095 (1986).

2) *a*) G. Mass and C. Hummel, *Chem. Ber.*, **113**, 3679 (1980); *b*) K. Saito, H. Ishihara, T. Murase, Y. Horie, and E. Maekawa, *Bull. Chem. Soc. Jpn.*, **60**, 4317 (1987); K. Saito, T. Sato, H. Ishihara, and K. Takahashi, *ibid.*, **62**, 1925 (1989).

3) Y. Kurita and M. Kubo, *J. Am. Chem. Soc.*, **79**, 5460 (1957).

4) K. Saito and H. Ishihara, *Bull. Chem. Soc. Jpn.*, **60**, 4447 (1987); K. Saito and K. Takahashi, *Chem. Lett.*, **1989**, 925; K. Saito, T. Watanabe, and K. Takahashi, *ibid.*, **1989**, 2099.

5) M. Jones, Jr. and E. W. Petrillo, *Tetrahedron Lett.*, **1969**, 3953; C. J. Rostek and W. M. Jones, *ibid.*, **1969**, 3957; T. Toda, K. Saito, and T. Mukai, *Bull. Chem. Soc. Jpn.*, **52**, 151 (1979).

6) G. J. Karabatsos, G. C. Sonnichsen, N. Hsi, and J. Fenoglio, *J. Am. Chem. Soc.*, **89**, 5067 (1967).

7) L. W. Christensen, E. E. Waali, and W. M. Jones, *J. Am. Chem. Soc.*, **94**, 2118 (1972).

8) H. C. Brown and Y. Okamoto, *J. Am. Chem. Soc.*, **79**, 1915 (1957).

9) The authors are indebted to the Computer Center of the Institute for Molecular Science for molecular orbital calculations using the MOPAC program (J. J. P. Stewart, *Q. C. P. E. Bull.*, **3**, 43 (1983)).

10) R. B. Woodward and R. Hoffmann, *Angew. Chem. Int. Ed. Engl.*, **8**, 781 (1969).

11) 2-Chloro-1-azaazulene-3-carbaldehyde tosylhydrazone was synthesized in 85% yield from 2-chloro-1-azaazulene-3-carbaldehyde and tosyl hydrazide according to the usual method. mp 181—182 °C. $\mathrm{UV}_{\max}^{\mathrm{EtOH}}$ nm (log ε): 301.9 (4.42), 310.8 (4.47), 370.0 (3.79). ^{1}H-NMR (acetone-d_6) δ: 2.39 (s, 3H, Me), 2.95 (br s, 1H, NH), 7.47 (d, 2H, Ph, J=7.0 Hz), 8.00 (d, 2H, Ph, J=7.0 Hz), 8.10—8.35 (m, 3H), 8.42 (s, 1H), 8.69 (dd, 1H, J=8, 1 Hz), 9.50 (dd, 1H, J=8, 1 Hz).

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