REACTIONS OF TOSYLHYDRAZONES OF 2-METHOXY-1-AZAAZULENE-3-CARBOXALDEHYDE AND AZULENE-1-CARBOXALDEHYDE WITH STYRENES AND STILBENES

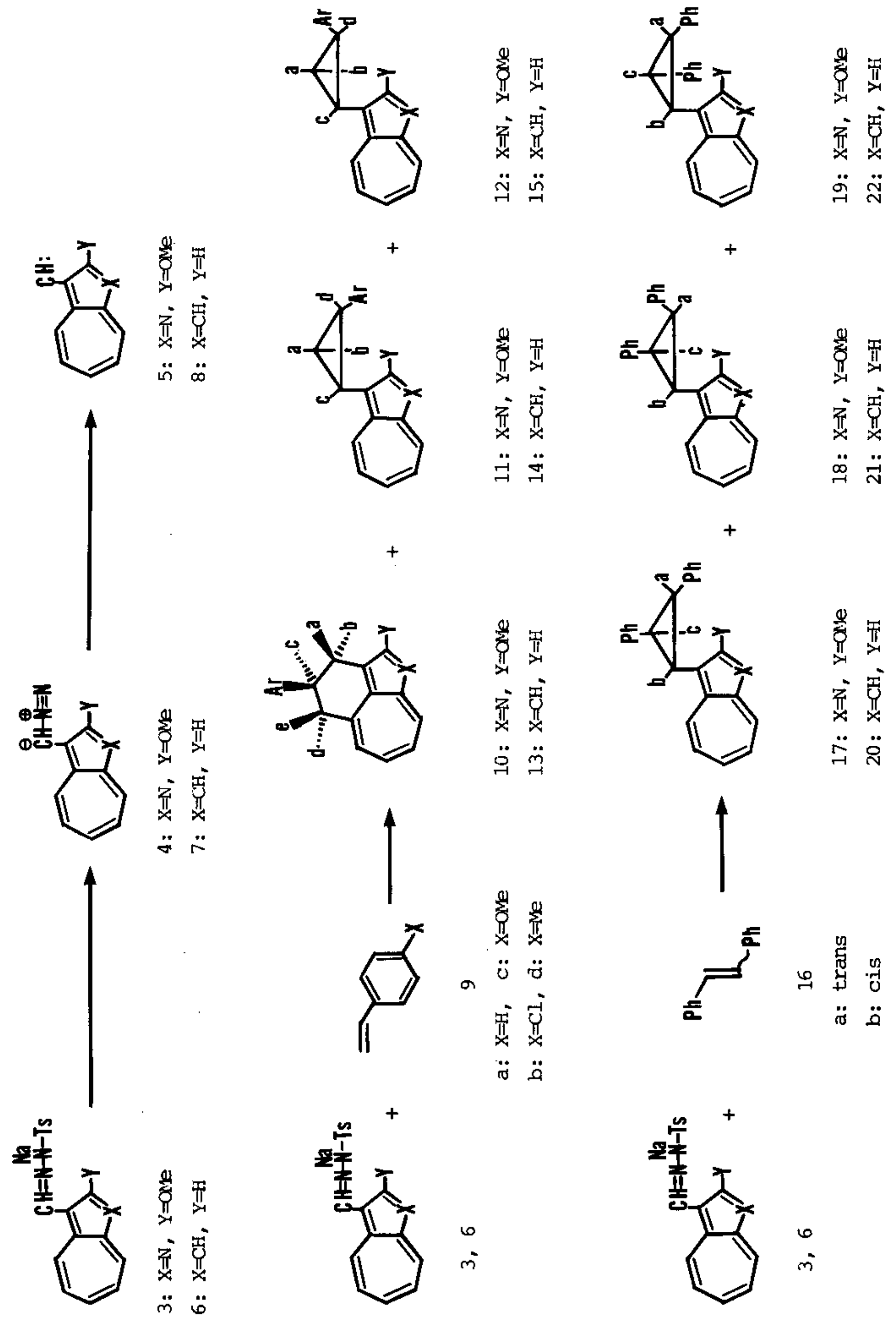
Katsuhiro Saito,* Hiroshi Fushihara, Kiichiro Tominaga, Kyoko Kumagai, Satoru Kondo, Kunihide Fujimori,+ Noritaka Abe,++ and Kensuke Takahashi

Department of Applied Chemistry, Nagoya Institute of Technology, Gokiso-cho, Showa-ku, Nagoya 466, Japan
+ Department of Chemistry, Faculty of Science, Shinshu University, Asahi 3-1-1, Matsumoto 390, Japan
++ Department of Chemistry, Faculty of Science, Yamaguchi University, Yoshida 1677-1, Yamaguchi 753, Japan

Abstract —— The reactions of sodium salt of 2-methoxy-1-azaazulene-3-carboxaldehyde tosylhydrazone with styrenes gave 3,8-cyclohexeno-2-methoxy-1-azaazulenes and 3-cyclopropyl-2-methoxy-1-azaazulenes. The formers were afforded through the diazo compound generated from the tosylhydrazone and the latters were yielded *via* the carbene derived from the diazo compound. The reactions with stilbenes gave the corresponding cyclopropane derivatives. The similar reactions with sodium salt of azulene-1-carboxaldehyde tosylhydrazone gave the analogous result.

Sodium salts of tosylhydrazones are effective precursors of diazo compounds, which in turn generate the corresponding carbenes. Much attention has been paid to the chemistry of diazo compounds and carbenes regarding their synthetic utility and chemical reactivities.[1] The electronic natures of these species are influenced by conjugation with olefinic or aromatic moieties. Extensive research on these conjugated species has been carried out.[1] However, to our knowledge, the reports concerning the chemistry of these species conjugated with hetero aromatic moieties are rare.[1-3]

1 a: X=N, X=CH 2



3: X=N, Y=OMe
6: X=CH, Y=H

4: X=N, Y=OMe
7: X=CH, Y=H

5: X=N, Y=OMe
8: X=CH, Y=H

3, 6

9
a: X=H, c: X=OMe
b: X=Cl, d: X=Me

10: X=N, Y=OMe
13: X=CH, Y=H

11: X=N, Y=OMe
14: X=CH, Y=H

12: X=N, Y=OMe
15: X=CH, Y=H

3, 6

16
a: trans
b: cis

17: X=N, Y=OMe
20: X=CH, Y=H

18: X=N, Y=OMe
21: X=CH, Y=H

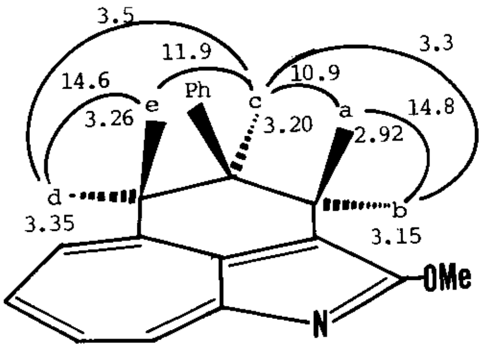
19: X=N, Y=OMe
22: X=CH, Y=H

1-Azaazulenes (1a), belong to condensed pyrrole derivatives, show peculiar reactivities as nonbenzenoid aromatic compounds. The aromaticity of azulenes is a result of a contribution of an ionic canonical formula (2).[4] It can be expected that these partially zwitterionic natures influence on the reactivities of carbenes and diazo compounds conjugated with azulenes. As a part of a study on the reactivities of carbenes and diazo compounds,[3b,5] we investigated the reactions of sodium salts of 2-methoxy-1-azaazulene-3-carboxaldehyde tosylhydrazone (3) and azulene-1-carboxaldehyde tosylhydrazone (6) with styrenes and stilbenes. The results are reported here.

A mixture of 3 and 4 molar equivalent of styrene (9a) in anhydrous diglyme was heated at 110°C for 10 min to give a cyclohexene derivative (10a) in 18% yield and cyclopropane derivatives (11a) and (12a) in 4 and 3% yields, respectively. Similar reaction with *p*-chlorostyrene (9b) afforded 11b and 12b in 5 and 3% yields, respectively. The reaction with *p*-methoxystyrene (9c) gave 10c (26%), 11c (4%), and 12c (2%). The reactions with sodium salt of azulene-1-carboxaldehyde (6) gave the analogous results as above; Reactions of 6 with 9a–d gave 13a (11%), 14a (8%), and 15a (3%) from 9a, 13b (11%), 14b (4%), and 15b (3%) from 9b, 13c (9%), 14c (5%), and 15c (2%) from 9c, 13d (12%), 14d (15%), and 15d (2%) from 9d, respectively.

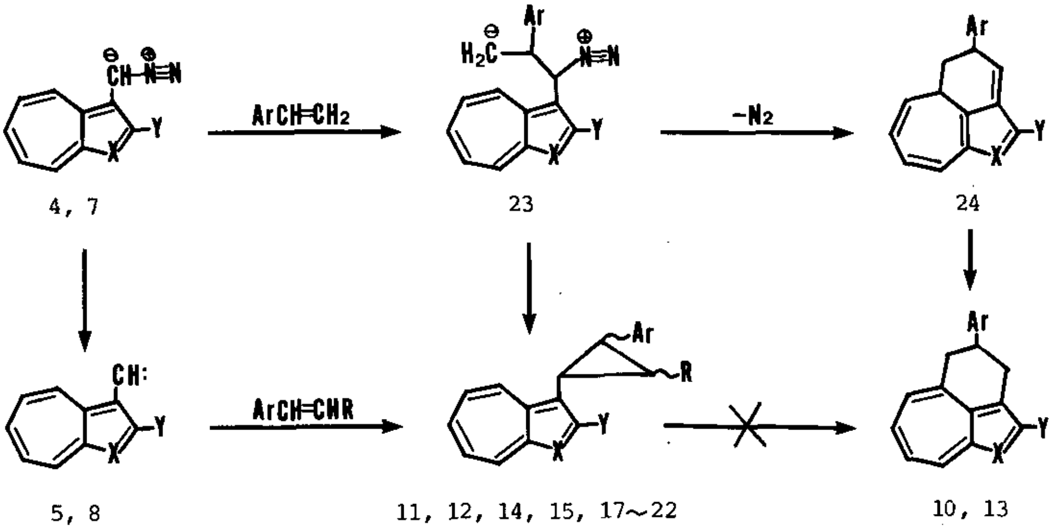
The reactions of 3 with stilbenes proceeded in a stereospecific manner, though the product yields were low. Thus, the reaction of 3 with *trans*-stilbene (16a) afforded a cyclopropane derivative (17) in 9% yield. The reaction of 3 with *cis*-stilbene (16b) gave two kinds of cyclopropane derivatives (18 and 19) in 1 and 2% yields, respectively. On the other hand, the reaction of 6 with 16a gave 20 in 5% yield. Three kinds of cyclopropane derivatives 20 (0.5%), 21 (1%), and 22 (2%) were afforded in the reaction of 6 with 16b.[6]

The structures of cyclopropane derivatives (11, 12, 14, and 15) were deduced on the basis of their spectral properties and were confirmed by comparisons of these spectral properties with those of the analogous compounds.[7] The coupling constant values (8.8 Hz) between H_c and H_d in 11 and 14 showed that these two protons are in *cis*-configuration. The high-field shift (ca. 6.8 ppm) of the signals of the phenyl groups in 11 and 14 can be explained by the anisotropic effects caused by the aromatic azulene systems which are located at the *cis*-positions to the phenyl groups. The structures of 17–22 were also deduced mainly on the basis of their nmr spectral properties. The coupling constant values between H_a and H_b (9.0 Hz) and H_a/H_b and H_c (6.0 Hz) of 17 and 20 are reasonable for the values between *cis*- and *trans*-cyclopropane protons, respectively. The assignments of the structures of 18, 19, 21, and 22 are based on the chemical shifts of the cyclopropane protons H_b. Compared with the chemical shifts of the protons H_b of 19 and 22 (all *cis*), the chemical shifts of the protons H_b of 18 and 21 appeared at lower fields because of the anisotropic ef-



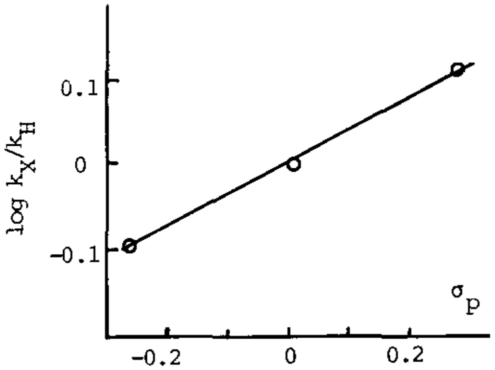
fects of the two phenyl groups both located in *cis*-configurations to the proton H_b. The observed coupling constant values between H_b and H_a/H_c (6.0 Hz) of 18 and 21, which are reasonable as the coupling constant values between the *trans*-cyclopropane protons, supported these structures.

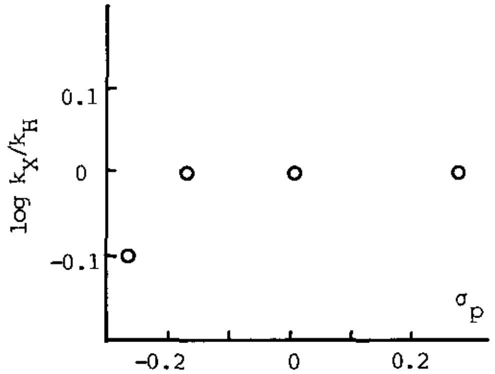
The structures of cyclohexene derivatives were deduced as follows. Ms spectra showed that these compounds had the same molecular formulae as those of the corresponding cyclopropane derivatives. An absence of the signals of the protons at 4-position of the azaazulene moieties and an existence of signals corresponding to five saturated protons in ^1H nmr spectra suggested the structures of cyclohexene derivatives. ^1H Nmr (400 MHz) spectra of 10a allowed a detailed analysis of the structure.[8] Two large coupling constant values J_{ab} (14.8 Hz) and J_{de} (14.6 Hz) suggest that these two pairs of protons (H_a-H_b and H_d-H_e) were geminal protons each other. The methin proton H_c had two relatively large coupling constant values, J_{ac} (10.9 Hz) and J_{ce} (11.9 Hz), which showed that these protons (H_a, H_c, and H_e) were vicinal protons, each other, with dihedral angles *ca.* 180°. The Dreiding Models of 10 and 13 demonstrated that the dihedral angles between H_a-H_c and H_c-H_e were all *ca.* 180°. It is known that the signals in ^1H nmr spectra of protons of a methyl group at 3-position of azulene moiety appeared at higher field than those at 4-position.[9] Thus, the higher chemical shifts of the signals of H_a (2.92 ppm) and H_b (3.15 ppm) compared to those of H_d (3.35 ppm) and H_e (3.26 ppm) showed that the structure and the assignment of the protons on the cyclohexene ring were determined to be as shown.



The reaction is considered to proceed as follows. The diazo compound (4 or 7) attacked the styrenes to give the ionic intermediates (23),[10] which then cyclized to form 24 releasing nitrogen gas. Hydrogen shift in 24 to form an aromatic system afforded the products (10, 13). The possible pathway leading to 10 and 13 from the corresponding cyclopropane derivatives (11, 12, 14, 15) was ruled out by the fact that the cyclopropane derivatives were recovered unchanged upon heating under the reaction conditions of the sodium salts (3, 6). Two paths can be proposed for the formation of cyclopropane derivatives. One through the carbenes(5, 8) and the other *via* the ionic intermediates (23). It is hard, at this stage, to select one form another. However, it can be said that the absence of stereospecificity in the reactions of 6 with stilbenes (16) showed that in these reactions, the singlet state of the carbene (8) is not involved. Contrary to this, the stereospecificity observed in the reactions of 3 with 16 may suggest that the reactions proceeded via the singlet state of 5. However, the poor material balance in these reactions can not allow to draw a conclusion.

In order to investigate the substituent effects the relative rate ratios of the reactions to the substituted styrenes were measured using the reactions of the tosylhydrazones to 1:1 mixtures of 9a and 9b, 9a and 9c, and 9a and 9d[11] to compare the yields of the corresponding cyclopropane derivatives (11, 12, 14, and 15). The ratio of 9a : 9b : 9c was measured to be 1.0 : 1.3 : 0.8 for 3. On the other hand the ratio of 9a : 9b : 9c : 9d was measured to be 1.0 : 1.0 : 1.0 : 0.8 for 6. Thus the relation of the logalisms of the relative rate ratios (log k_X/k_H) against Hammett's sigma values (σ_p) of the substitiuents gave ρ-values, 0.44 for 3 and ca. 0 for 6.[11] Considering that the product yields of these reactions were not so high and the absolute value of the ρ-values were small, it is hard to say more than that these reactive species are weak nucleophiles.





EXPERIMENTAL

Nmr spectra were measured with a Varian XL 200 spectrometer with tetramethylsilane as an internal standard. Uv spectra were measured with a Hitachi 220A spectrophotometer. Ms spectra were measured with a Hitachi M-2000S spectrometer. Sodium hydride coated by mineral oil in 60% was used.

A typical reaction procedure is described here. *Reaction of 3 with 9a.* A mixture of 2-methoxy-1-azaazulene-3-carboxaldehyde tosylhydrazone (360 mg, 1 mmol), sodium hydride 60% in oil, 40 mg, 1 mmol), and 9a (720 mg, 4 mmol) in anhydrous diglyme (9 ml) was heated at 110°C for 10 min. After filtration, the filtrate was poured into water, extracted with ether, washed with water and dried over anhydrous sodium sulfate. After filtration the solvent was evaporated to give an oily residue, which was subjected to thin-layer chromatography on silica gel using benzene-ether 9:11 as a developing solvent to give dark red oils of 10a (50 mg, 18%, R_f=0.40), 12a (9 mg, 3%, R_f=0.50), and 11a (11 mg, 4%, R_f=0.54).

Table 1. ^1H Nmr Spectral Data

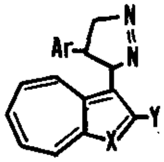
	Chemical Shifts (in $CDCl_3$) δ ppm														Coupling Constants in Hz					
	H_a	H_b	H_c	H_d	OMe (3H)	Phenyl Ring	Azulene Ring							J_{ab}	J_{ac}	J_{ad}	J_{bc}	J_{bd}	J_{cd}
11a	1.50	1.78	2.30	2.70	4.05	6.70-6.94 (m,5H)	7.20-7.55 (m,3H)	7.90-8.20 (m,2H)						multiplet					
b	1.50-1.80		2.40	2.50	4.05	6.73-6.94 (m,4H)	7.25-7.60 (m,3H)	8.00-8.20 (m,2H)						multiplet					
c	1.50-1.70		2.20-2.50		3.63 4.08	6.52-6.75 (m,4H)	7.20-7.55 (m,3H)	7.90-8.20 (m,2H)						multiplet					
12a	1.48	1.72	2.20	2.43	4.31	7.10-7.60 (m,8H)	8.05-8.28 (m,2H)							4.7	5.6	8.8	8.8	5.7	5.7
b	1.44	1.72	2.15	2.40	4.30	7.19-7.33 (m,4H)	7.27-7.60 (m,3H)	8.07-8.22 (m,2H)						4.7	5.7	8.8	8.8	5.8	5.9
c	1.41	1.65	2.12	2.39	3.84 4.31	6.90-7.20 (m,4H)	7.30-7.55 (m,3H)	8.06-8.26 (m,2H)						4.6	5.7	8.8	8.8	5.9	5.9
							7-H	5-H	3-H	2-H	6-H	4-H	8-H						
14a	1.55	1.68	2.62	2.84		6.84-7.00 (m,5H)	7.02	7.06	7.14		7.51	8.16	8.44	5.0	6.6	6.6	8.8	8.8	8.8
b	1.50	1.69	2.55	2.85		6.80-6.95 (m,4H)	7.02	7.09	7.16	7.36	7.52	8.17	8.40	4.8	6.6	6.6	8.8	8.8	8.8
c	1.45	1.64	2.56	2.79	3.64	6.55-6.84 (m,4H)	7.01	7.06	7.13	7.29	7.51	8.16	8.45	5.2	6.6	6.6	8.8	8.8	8.8
d	1.50	1.67	2.59	2.82	2.17 (Me,3H)	6.42 (s,4H)	7.03	7.08	7.16	7.35	7.52	8.18	8.47	5.0	6.6	6.6	8.8	8.8	8.8
15a	1.57	1.61	2.24	2.61		7.15-7.40 (m,5H)	7.08	7.08	7.35	7.56	7.69	8.28	8.44	multiplet					
b	1.56	1.61	2.20	2.57		7.17-7.32 (m,4H)	7.10	7.10	7.35	7.57	7.67	8.28	8.40	multiplet					
c	1.50	1.56	2.20	2.53	3.51	6.90-7.18 (m,4H)	7.05	7.06	7.34	7.54	7.67	8.28	8.44	multiplet					
d	1.54	1.58	2.21	2.58	2.37 (Me,3H)	7.17 (s,4H)	7.08	7.08	7.35	7.56	7.69	8.28	8.45	multiplet					
														J_{ab}	J_{ac}	J_{bc}			
17	2.74	2.85	3.11		4.30	6.82-7.60 (m,13H)	7.92-8.30 (m,2H,4-H,8-H)							9.0	6.0	6.0			
18	2.88-3.12 (m,3H)				4.16	6.80-7.80 (m,13H)	8.10-8.20 (m,2H,4-H,8-H)							multiplet					
19	2.84 (2H)		3.12		4.33	6.90-7.60 (m,13H)	8.10-8.30 (m,2H,4-H,8-H)							multiplet					
20	2.95 (2H)		3.21			6.95-7.45 (m,12H)			7.20	7.39	7.55	8.22	8.45	multiplet					
21	2.95	8.28	2.95			6.95-7.30 (m,12H)			7.40	7.87	7.59	8.32	8.55	6.0		6.0			
22	3.13	3.39	3.13			6.95-7.30 (m,12H)			7.40	7.87	7.52	8.20	8.48	9.0		9.0			
	H_a	H_b	H_c	H_d H_e															
10a	2.78-3.44 (m,5H)				4.28	7.04-7.48 (m,8H)	8.02-8.18 (m,1H)												
c	2.78-3.36 (m,5H)				3.82 4.28	7.13-7.46 (m,7H)	8.06-8.15 (m,1H)												
13a	3.35 (m,5H)					7.25-7.43 (m,6H)	6.93	6.99		7.48	7.67	8.26							
b	3.34 (m,5H)					7.03-7.37 (m,4H)	6.94	7.00	7.36	7.56	7.67	8.27							
c	3.28 (m,5H)				3.80	6.92-7.28 (m,4H)	6.90	6.92	7.34	7.45	7.65	8.24							
d	3.30 (m,5H)				2.37 (Me,3H)	7.20-7.28 (m,4H)	6.92	6.98	7.34	7.46	7.66	8.25							

Table 2. Hrms and Uv Spectral Data

	Hrms m/z			λ_{max} nm (log ε)					
	Obsd	Calcd for							
11a	275.1292	$C_{19}H_{17}NO$	275.1309	229.2(4.44)	283.7(4.75)	303.2(sh,4.30)	345.0(3.72)	360.2(3.77)	
b	309.0902	$C_{19}H_{16}NOCl$	309.0919	224.3(4.32)	280.0(4.52)	303.5(sh,4.15)	346.2(3.51)	360.9(3.62)	
c	305.1440	$C_{20}H_{19}NO_2$	305.1414	228.9(4.36)	278.0(4.76)	304.6(sh,4.24)	345.8(3.66)	360.0(3.72)	
12a	275.1331	$C_{19}H_{17}NO$	275.1310	228.5(4.42)	279.7(4.69)	303.8(sh,4.22)	345.8(3.69)	359.7(3.70)	
b	309.0891	$C_{19}H_{16}NOCl$	309.0919	226.6(4.27)	279.8(4.51)	303.4(sh,4.17)	345.8(3.48)	360.5(3.68)	
c	305.1440	$C_{20}H_{19}NO_2$	305.1414	227.4(4.29)	278.5(4.52)	300.9(sh,4.18)	345.9(3.59)	360.6(3.70)	
14a	244.1249	$C_{19}H_{16}$	244.1250	239.8(4.47)	283.6(4.72)	336.0(sh,3.63)	351.7(3.75)	362.6(3.59)	369.6(3.67)
b	278.0877	$C_{19}H_{15}Cl$	278.0861	239.2(4.43)	284.8(4.73)	337.7(sh,3.67)	351.3(3.80)	362.0(3.67)	369.6(3.74)
c	274.1360	$C_{20}H_{18}O$	274.1356	230.7(4.53)	285.4(4.87)	337.9(sh,3.75)	352.4(3.90)	362.2(3.70)	370.4(3.81)
d	258.1386	$C_{20}H_{18}$	258.1407	240.5(4.36)	283.6(4.63)	336.0(sh,3.53)	352.0(3.62)	363.3(3.45)	370.6(3.54)
15a	244.1251	$C_{19}H_{16}$	244.1251	239.3(4.26)	284.9(4.55)	337.6(sh,3.51)	351.3(3.64)	362.2(3.51)	369.4(3.59)
b	278.0880	$C_{19}H_{15}Cl$	278.0861	238.8(4.69)	285.2(4.74)	337.8(sh,3.85)	354.8(4.01)	361.5(3.85)	368.5(3.96)
c	274.1341	$C_{20}H_{18}O$	274.1356	239.2(4.42)	284.4(4.69)	339.4(sh,3.60)	352.1(3.72)	362.6(3.59)	369.4(3.60)
d	258.1410	$C_{20}H_{18}$	258.1408	240.2(4.41)	284.4(4.67)	337.8(sh,3.60)	351.6(3.73)	362.1(3.61)	369.7(3.68)
17	351.1643	$C_{25}H_{21}NO$	351.1622	222.6(4.29)	282.3(4.69)	301.5(4.13)	345.4(3.52)	360.0(3.68)	
18	351.1609	$C_{25}H_{21}NO$	351.1622	229.4(4.36)	282.4(4.72)	305.7(4.25)	345.7(3.68)	360.8(3.72)	
19	351.1639	$C_{25}H_{21}NO$	351.1622	226.4(4.37)	281.6(4.70)	299.3(4.20)	345.4(3.59)	360.4(3.70)	
20	320.1568	$C_{25}H_{20}$	320.1564	237.6(4.08)	282.9(4.36)	301.1(sh,3.88)	346.7(3.42)	362.5(3.26)	
21,22	320.1568	$C_{25}H_{20}$	320.1564	238.6(4.36)	285.6(4.63)	337.6(sh,3.56)	350.8(3.69)	364.0(3.54)	368.3(3.62)
10a	275.1321	$C_{19}H_{17}NO$	275.1310	236.4(4.34)	276.5(4.75)	306.7(sh,4.00)	345.7(3.64)	358.9(3.85)	
c	305.1417	$C_{20}H_{19}NO_2$	305.1414	232.5(4.14)	277.9(4.42)	304.5(sh,3.88)	345.8(3.57)	358.7(3.72)	
13a	244.1250	$C_{19}H_{16}$	244.1250	243.5(4.19)	281.6(4.45)	287.0(4.67)	301.7(3.81)	347.7(3.51)	361.2(3.38)
b	278.0857	$C_{19}H_{15}Cl$	278.1861	243.3(4.46)	281.8(4.68)	287.2(4.71)	302.0(4.03)	348.0(3.77)	361.4(3.65)
c	274.1359	$C_{20}H_{18}O$	274.1356	243.6(4.51)	281.6(4.73)	286.5(4.72)	301.6(4.06)	348.0(3.80)	361.4(3.68)
d	258.1399	$C_{20}H_{18}$	258.1407	243.1(4.47)	281.9(4.70)	287.0(4.72)	302.1(4.11)	347.9(3.81)	361.3(3.70)

REFERENCES

1. W. Kirms, "Carbene Chemistry", Academic Press, 1964; G. L. Cross, *Top. Stereochem.*, 1968, 3, 193; T. T. Coburn and W. M. Jones, *J. Am. Chem. Soc.*, 1974, 96, 5218; M. Oda, Y. Ito, and Y. Kitahara, *Tetrahedron Lett.*, 1975, 2587; K. Saito, Y. Omura, and T. Mukai, *Chem. Lett.*, 1980, 349; S, J. Chang, B. K. R. Shankar, and H. Shechter, *J. Org. Chem.* 1982, 47, 4226; R. H. Paker and W. M. Jones, *Tetrahedron Lett.*, 1984, 25, 1245; K. Saito, Y. Omura, and T. Mukai, *Bull. Chem. Soc. Jpn.*, 1985, 58, 1663; K. Saito and H. Ishihara, *ibid.*, 1985, 58, 2664; *idem, ibid.*, 1986, 59, 1095.
2. R. V. Hoffman and H. Shechter, *J. Am. Chem. Soc.*, 1971, 93, 5940; R. V. Hoffman, G. G. Orphanides, and H. Shechter, *ibid.*, 1978, 100, 7927; R. V. Hoffman and H. Shechter, *ibid.*, 1978, 100, 7934.
3. Maas has reported on insertion reactions of carbenes conjugated with pyrrole, furan, or pyridine moieties.[3a] We have published on addition reactions of carbenes conjugated with thiophene and pyrrole moieties and clarified that they reacted as singlet carbenes with nucleophilic natures.[3b] a) G. Maas and C. Hummel, *Chem. Ber.*, 1980, 113, 3679. b) K. Saito, T. Sato, H. Ishihara, and K. Takahashi, *Bull. Chem. Soc. Jpn.*, 1989, 62, 1925; K. Saito, H. Fushihara, T. Sato, H. Ishihara, and K. Takahashi, *Heterocycles,* 1989, 29, 1537; K. Saito, T. Ushida, H. Fushihara, Y. Yamashita, S. Tanaka, and K. Takahashi, *ibid.*, 1990, 31, 115.
4. Y. Kurita and M. Kubo, *J. Am. Chem. Soc.*, 1957, 79, 5460.
5. K. Saito, Y. Omura, and T. Mukai, *Chem. Lett.*, 1980, 349; *idem, Bull. Chem. Soc. Jpn.*, 1985, 58, 1663; K. Saito and H. Ishihara, *ibid.*, 1985, 58, 2664; *idem, ibid.*, 1986, 59, 1095; K. Saito, *ibid.*, 1987, 60, 2105; K. Saito and H. Ishihara, *ibid.*, 1987, 60, 4447; K. Saito and K. Takahashi, *Chem. Lett.,* 1989, 925; K. Saito, T. Watanabe, and K. Takahashi, *ibid.*, 1989, 2099.
6. The decomposition of sodium salt of 2-formylazulene tosylhydrazone failed to form corresponding diazo compound or carbene, probably because of the unstability of the tosylhydrazone itself.
7. G. L. Cross, R. A. Moss, and J. J. Coyle, *J. Am. Chem. Soc.*, 1962, 84, 4985; 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.*, 1979, 52, 151.
8. The authors are indebted to the Institute for Molecular Science for measurement of 400 MHz ^{1}H nmr spectra.
9. J. R. Llinas, D. Roard, M. Derbesy, and E. J. Vincent, *Can. J. Chem.*, 1975, 53, 2911.
10. It is possible to consider that the reaction proceeded *via* a thermal 1,3-dipolar cycloaddition to give the pyrazoline derivatives (A), which then opened the ring to form the ionic intermediates (23).



A

11. L. W. Christensen, E. E. Waali, and W. M. Jones, *J. Am. Chem. Soc.*, 1972, 94, 2118; H. S. Tirakornpannarai and E. E. Waali, *Tetrahedron Lett.*, 1986, 27, 3701.

Received, 21st December, 1992