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ON THE MULTIPLICITY OF CARBENES CONJUGATED WITH PYRROLE AND FURAN MOIETIES: MOLECULAR ORBITAL CALCULATION AND REACTION OF 2-(1-METHYL)-PYRROLYLMETHYLENE AND 2-FURYLMETHYLENE WITH CIS- AND TRANS-STILBENES

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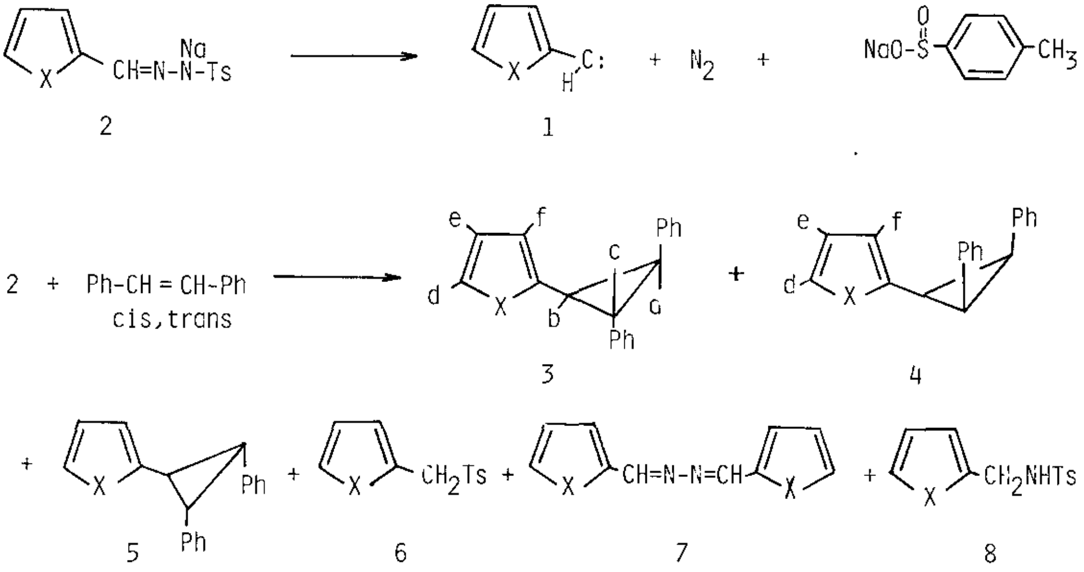
Abstract — The reaction of 2-(1-methyl)pyrrolylmethylene and 2-furylmethylene with cis- and trans-stilbenes proceeded in a stereospecific manner to give the corresponding cyclopropane derivatives to show that the multiplicities of these carbenes are singlet. The molecular orbital calculation showed that these carbenes are triplet in their ground state and nucleophilic both in singlet and triplet states.

The chemistry of carbenes has attracted much attention of chemists and many reports have been published on the reactivities and electronic natures including the multiplicities of carbenes.[1] It is known that the multiplicities of carbenes are influenced by conjugation with various unsaturated moieties.[2] While the chemistry of carbenes conjugating with olefins has been studied extensively, only a little has been studied on the reactivity of carbenes conjugating with heterocyclic moieties, except the researches of Shechter,[3] Maas,[4] and the present authors.[5] As a series of our study on the chemistry of carbenes, we investigated the reactions of 2-(1-methyl)pyrrolylmethylene (1a) and 2-furylmethylene (1b) with cis- and trans-stilbenes. Here the results are discussed.

Sodium salt of 1-methyl-2-pyrrolecarbaldehyde tosylhydrazone (2a) was heated in the presence of four molar equivalents of trans-stilbene in anhydrous diglyme at 110 °C for 10 min. Separation and purification of the reaction mixture with column and thin-layer chromatography afforded a cyclopropane derivative (3a) in



a:X=N-CH_3 b:X=O

6.7% yield, together with a p-toluenesulfonylmethane derivative (6a), a ketazine derivative (7a), and a tosylamine derivative (8a) in 3.5, 12.3, and 5.2% yields, respectively.

The similar reaction of 2a with cis-stilbene gave a 1:1 mixture of cyclopropane derivatives 4a and 5a in 2.1% yield, accompanied by 6a, 7a, and 8a in yields of 5.3, 7.6, and 4.1%, respectively. The analogous reaction of sodium salt of 2-furfural tosylhydrazone (2b) with trans-stilbene yielded a cyclopropane derivative (3b) and a ketazine derivative (7b) in 2.0 and 12.5% yields, resectively. The similar reaction of 2b with cis-stilbene afforded a 1:1 mixture of cyclopropane derivatives 4b and 5b in 4.5% yield.

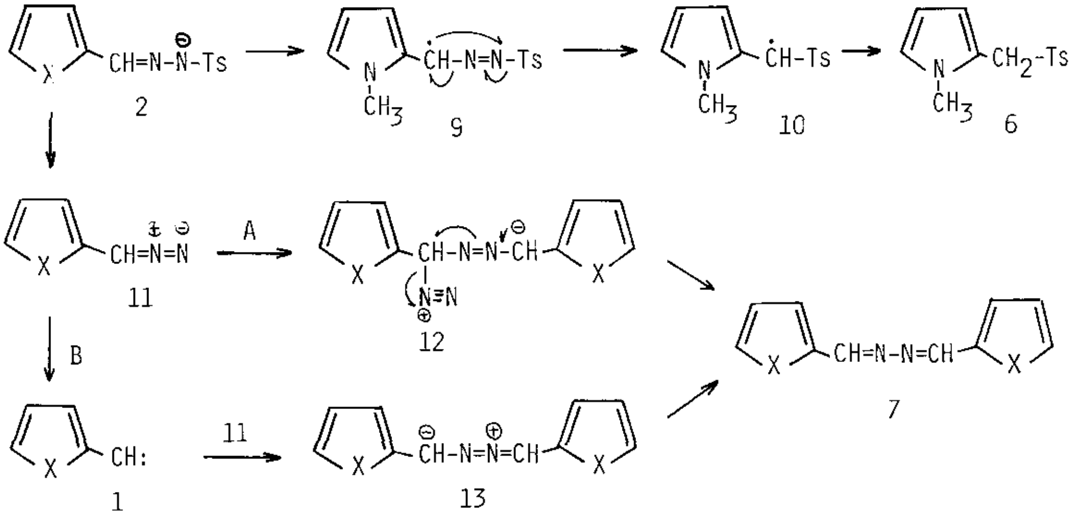
The structures of the cyclopropane derivatives were deduced on the basis of their spectral properties by comparisons with those of the analogous compounds.[6] The p-toluenesulfonylmethane derivative (6)[7] and the ketazines (7a, 7b) are literature known compounds.[5,7]

The structure of 8a was deduced on the basis of its spectral properties as follows. The triplet signal in the nmr spectrum at 4.98 ppm disappered when the spectrum was measured in a solvent containing D_2O, showing that this signal corresponds to a NH-proton. The nmr spectrum clearly demonstrated the existence of two 1-methylpyrrole moieties and a methylene group (d, 2H, 4.08 ppm) which is adjacent to the NH-proton. The signal at 1320 cm^{-1} in the ir spectrum shows that

8a is a sulfone derivative but not a sulfine derivative.[8] From the above facts, the molecular ion peak in the mass spectrum, and the molecular formula, the structure of 8a should be the one shown in the figure.[9]

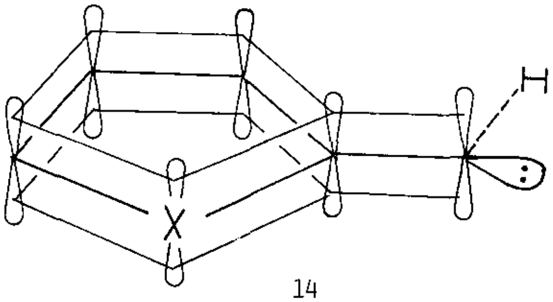
The formation process of the p-toluenesulfonylmethane derivative (6) is considered to be as follows according to the literatures.[5,7] One electron oxidation of the sodium salt (2a) generates a tosylhydrazyl radical intermediate (9).[10] The 1,3 N→C migration of the tosyl group eliminates nitrogen to form the radical intermediate (10). Hydrogen abstraction of 10 from the solvent affords 6.

Two paths can be considered for the formation of the ketazines (7a, 7b). Dimerization of the diazo compound (11), which is generated by decomposition of 2, gives an ionic intermediate (12) (Path A). Elimination of nitrogen from 12 can give the ketazines. Another path (Path B) contains a reaction of the carbene (1) with 11 to form directly the canonical formula (13) of 7.[5]



The above results show that the reactions of 1 with cis-stilbene afforded the cis-cyclopropane derivatives while the reaction with trans-stilbene gave the trans-cyclopropane derivatives. Thus the product analysis clearly demonstrated that the cyclopropane formation reactions proceeded in a stereospecific manner indicating that the mutilicities of 1a and 1b are both singlet.[2]

Considering that pyrroles and furans are well known to have an aromaticity because of a contribution of 6π -electron aromatic structures,[11] it seems reasonable to think the electronic structure of 1 to be as follows. The carbene carbon is in a sp^2-hybridization bearing two electrons in its sp^2-orbital. The vacant 2p-orbital of the carbenic carbon conjugates with the heterocyclic π-system. Thus the electronic structures of 1a and 1b are considered to be a singlet state conjugated with 6π-electron aromatic heterocycles as shown in 14.[5]



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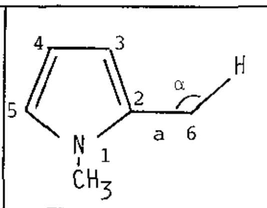
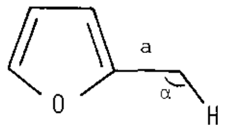
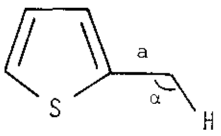
In order to further clarify the electronic natures of the carbenes, molecular orbital calculation was carried out by MNDO method on 1a, 1b and 2-thienylmethylene. The results are summerized in the Table and the Figure. The heats of formation of triplet states are smaller than those of singlet states, showing that the ground state of these carbenes are triplet.

						
multiplicity	S	T	S	T	S	T
heat of formation (kcal/mol)	119.4	104.8	81.2	63.7	118.8	99.9
a (A)	1.39	1.34	1.40	1.34	1.38	1.32
α	123.8°	160.8°	123.2°	165.2°	127.4°	170.3°
π-electron density on carbene carbon	0.238	1.066	0.193	1.012	0.215	0.966
dihedral angle* (C_3-C_2-C_6-H)	0.0	0.0	180.0	180.0	180.0	180.0
charge on carbene carbon	-0.123	-0.230	-0.039	-0.169	-0.069	-0.128

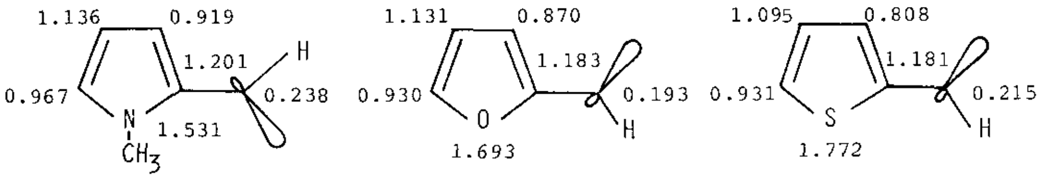
• There exist two planar conformers of the carbenes (dihedral angle=0° or 180°). The data for the more stable ones are shown in the Table.

Previously, Trozzolo et al. reported that arylcarbenes undergo stereospecific addition reactions in spite of their ground states triplet.[13] This phenomena was explained by the higher reactivities of the singlet carbenes comparing to the triplet carbenes. The same explanation is applicable to the present case.

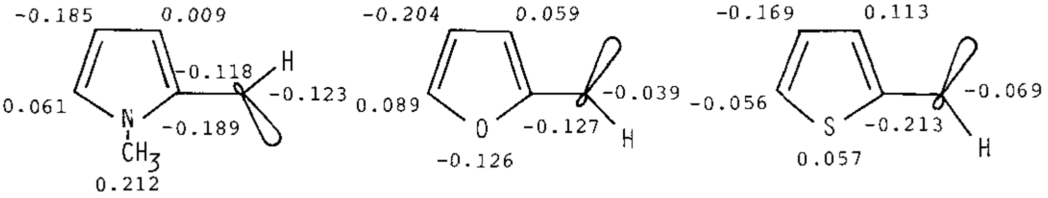
The bonds "a" are longer in the singlet states rather than in the triplet states, suggesting the existence of stronger conjugations between the heterocyclic ring p-systems and the carbene-carbons in triplet states.

The net atomic charges on carbene carbons are negative either in singlet or in triplet states showing that these carbenes have nucleophilic natures, which have been demonstraited by our previous report.[5]

π-ELECTRON DENSITY (SINGLET STATE)



NET ATOMIC CHARGE (SINGLET STATE)



EXPERIMENTAL

Nmr spectra were measured with a Varian XL 200 or a Hitachi R-20B spectrometer with tetramethylsilane as an internal standard. Uv and ir spectra were measured with a Hitachi 220A and a JASCO A-102 spectrometers, respectively. Mass spectra were measured with a Hitachi M-52 or a JMX-DX300 spectrometer. Wako gel C 200 and Wako gel B5F were used for column and thin-layer chromatography, respectively. Diglyme was dried over molecular sieves 3A 1/16.

Reaction of 2a with trans-Stilbene. To a solution of 1-methyl-2-pyrrolecarbaldehyde tosylhydrazone (2.77 g, 10 mmol) in anhydrous diglyme (40 ml) was added sodium hydride (50% in mineral oil, 0.53 g, 11 mmol). After evolution of hydrogen gas had ceased, trans-stilbene (7.20 g, 40 mmol) was added and the mixture was heated at 110°C for 10 min. After a removal of sodium p-toluenesulfinate by filtration, the filtrate was poured into water, extracted with ether, washed with water and brine, and dried over anhydrous sodium sulfate. After filtration, the solvent was removed on a rotary evaporator to give a mixture of an oil and crystals. After the crystals of the recovered trans-stilbene (4.83g) were filtered off, the filtrate was chromatographed on silica gel column to give an oil 3a (183 mg, 6.7%) by n-hexane-benzene (3:2) and an oily mixture (700 mg) by benzene-ether (7:3), which was then chromatographed on silica gel thin-layer plate using benzene-ether (4:1) as a developing solvent to give an oil 6[5,7] (87 mg, 3.5%, R_f=0.76), crystals 7[5,7] (264 mg, 12.3%, R_f=0.94), and an oil 8 (136 mg, 5.2%, R_f=0.62).

3a: Hrms: 273.1506. Calcd for $C_{20}H_{19}N$: 273.1517. Mass m/z (rel intensity): 273 (M^+, 100), 195 (44), 169 (28). Ir (oil): 3050, 2820, 1600, 1500 cm^{-1}. ^{1}HNmr ($CDCl_3$) δ ppm: 2.56 (dd, H_a), 2.63 (dd, H_b), 2.83 (dd, H_c), 3.21 (s, 3H), 5.98 (d, 2H, H_d, H_f), 6.38 (dd, H_e), 6.92-7.34 (narrow m, 10H, Ph). Coupling constants in Hz: J_{ab}=8.0, J_{ac}=J_{bc}=6.0, J_{de}=J_{ef}=2.7.

8: Hrms: 264.0939. Calcd for $C_{13}H_{16}N_2O_2S$: 264.0931. Mass m/z (rel intensity): 264 (M^+, 43), 263 (100), 183 (25), 171 (16), 154 (35). Ir (oil): 3400, 3030, 1980, 1490, 1320 cm^{-1}. ^{1}HNmr ($CDCl_3$) δ ppm: 2.45 (s, 3H), 3.57 (s, 3H), 4.08 (d, 2H, J=6.0 Hz), 4.98 (t, 1H, J=6.0 Hz, NH), 6.02 (narrow m, 1H), 6.64 (narrow m, 1H), 7.73 (d, 2H, J=8.0 Hz), 7.94 (d, 2H, J=8.0 Hz).

Reaction of 2a with cis-Stilbene. A mixture of 1-methyl-2-pyrrolecarbaldehyde tosylhydrazone (2.77 g, 10 mmol), sodium hydride (50% in mineral oil, 0.53 g, 11 mmol), and cis-stilbene (7.20 g, 40 mmol) in anhydrous diglyme (40 ml) was heated as usual at 110°C for 10 min. After the same treatment as above, the reaction mixture was distilled under a reduced pressure to remove the recovered cis-stilbene (6.98 g, 0.2 Torr, 80°C), and the residual oil was chromatographed on silica gel thin-layer plate using benzene-ether (1:1) as a developing solvent to give an oil of a 1:1 mixture of 4a and 5a (58 mg, 2.1%, R_f=0.81), 6 (132 mg, 5.3%, R_f=0.26), crystals 7 (162 mg, 7.6%, R_f=0.57), and 8 (107 mg, 4.1%, R_f=0.19). The molar ratio of 4a and 5a was deduced using the intensities of the signals of the methyl groups in the nmr spectrum.

Mixture of 4a and 5a: Hrms: 273.1522. Calcd for $C_{20}H_{19}N$: 273.1518. Mass m/z (rel intensity): 273 (M^+, 43), 209 (30), 195 (100), 169 (52). Ir (oil): 3040, 1600, 1500, 1450 cm^{-1}. ^{1}HNmr ($CDCl_3$) δ ppm: 2.60-2.95 (narrow m, 6H), 3.27 (s, 3H), 3.64 (s, 3H), 5.80 (d,H_d), 5.89 (dd, H_e), 6.00 (d, H_d), 6.12 (dd, H_e), 6.46 (dd, H_f), 6.64 (dd, H_f), 6.90-7.35 (narrow m, 20H).

Reaction of 2b with trans-Stilbene. A mixture of furfural tosylhydrazone (2.64 g, 10 mmol), sodium hydride (50% in mineral oil, 0.53 g, 11 mmol), and trans-stilbene (7.20 g, 40 mmol) in anhydrous diglyme (40 ml) was heated at 90°C for 15 min. After the same treatment as above, crystals of the recovered trans-stilbene (4.29 g) were removed by filtration. The filtrate was chromatograhed on silica gel column to give crystals 3b (51 mg, 2.0%) by n-hexane-benzene (7:3) and crystals 7b (235 mg, 12.5%) by benzene-ether (7:3).

3b: mp 69-70°C. Hrms: 260.1201. Calcd for $C_{19}H_{16}O$: 260.1201. Mass m/z (rel intensity): 260 (M^+, 17), 230 (37), 214 (100), 191 (34). Ir (KBr): 3155, 3050, 1600, 1500 cm^{-1}. ^{1}HNmr ($CDCl_3$) δ ppm: 2.75 (d, 2H, H_a, H_b), 2.92 (dd, H_c), 5.83 (d, H_d), 6.17 (dd, H_e), 7.14-7.36 (narrow m. 11H). Coupling constants in Hz: J_{ab}=6.2, J_{ac}=J_{bc}=5.5, J_{de}=3.4, J_{ef}=2.0.

Reaction of 2b with cis-Stilbene. A mixture of furfural tosylhydrazone (2.86 g, 10 mmol), sodium hydride (50% in mineral oil, 0.53 g, 11 mmol), and cis-stilbene (14.4 g, 80 mmol) was heated at 120°C for 30 min. After filtration the recovered cis-stilbene was removed by distillation under a reduced pressure (11.64 g, 0.2 Torr, 80°C). The residue was chromatographed on silica gel thin-layer plate using n-hexane-ethyl acetate (9:1) as a developing solvent to give an oil of a 1:1 mixture of 4b and 5b (118 mg, 4.5%, R_f=0.83). The molar ratio of 4b and 5b was calculated using the intensities of the signals of the furan moieties in the nmr sectrum.

Mixture of 4b and 5b: Hrms: 260.1235. Calcd for $C_{19}H_{16}O$: 260.1201. Ms m/z (rel intensity): 260 (M^+, 100), 230 (46), 214 (40), 191 (34). Ir (oil): 3040, 1600, 1500, 1450 cm^{-1}. ^{1}HNmr ($CDCl_3$) δ ppm: 2.73-2.92 (narrow m, 6H), 5.59 (d, H_d), 6.12 (dd, H_e), 6.16 (d, H_d), 6.34 (dd, H_e), 6.60 (s, H_f), 6.90-7.40 (narrow m, 21H). Coupling constants in Hz: J_{de}=2.9, J_{ef}=2.4.

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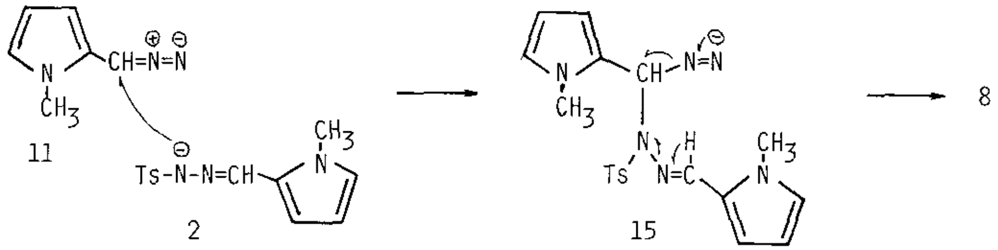
9. The formation process of 8 is not clear now but we tentatively suggest the following path. A nucleophilic attack of the anion nitrogen of 2a to the imino carbon atom of the diazo compound 12 gives an intermediate 15, which then cleaves to form 8.



10. The fact that 6 has never been formed in the absence of stilbene seems to show that the oxidation was carried out by stilbene.
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12. For all molecules a geometry optimization was performed with the imposed restrictions of planarity for the heterocyclic and carbene π-systems. The half-electron method was used for triplets. Calculations were carried out at the Computer Center of the Institute for Molecular Science, using MOPAC program (J. J. P. Stewart, *Q. C. P. E. Bull.*, 1983, **3**, 43).
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