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Stereospecific and Nucleophilic Additions of 2- and 3-Thienylmethylene. Reactions of 2- and 3-Thienylmethylene with *cis*- and *trans*-Stilbene, Dimethyl Maleate, Dimethyl Fumarate, and Styrene Derivatives

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The addition reactions of 2-thienylmethylene with *cis*- and *tarns*-stilbene afforded stereospecific adducts, respectively, indicating that the multiplicity of the carbene is singlet. The nucleophilicity of the carbenes was elucidated by an investigation of the relative rate ratio of the reactions of the carbene with various styrenes. An analogous result was afforded by reactions of 3-thienylmethylene with the same olefins mentioned above.

Much attention has been paid to the chemistry of carbenes from the view point of their electronic natures and chemical reactivities.[1)] It is known that the reactivities of carbenes are influenced by substituents and especially by conjugation with olefinic groups.[1)] However, the number of papers concerning the chemistry of carbenes conjugated with heterocyclic moieties seem to be few.[1,2)]

Thiophene (**1**) is known to have an aromaticity due to the contribution of the ionic canonical formula (**1a**).[3)] The reactivities of 2-thienylmeythylene (**2**) and 3-thienylmethylene (**3**) are considered to reflect conjugation with a thiophene ring. While Shechter has documented the chemical behaviors of **2** and **3**,[2)] nothing is known concerning the addition reactions of these carbenes to olefins. As a part of our research on the reactivity of carbenes,[1)] we investigated the addition reactions of **2** and **3** with olefins. Here we wish to report the results of these reactions.

Results and Discussion

The reaction of sodium salt of 2-thiophenecarbaldehyde tosylhydrazone (**4**) and 4 molar equivalents of *trans*-stilbene (**6**) in anhydrous diglyme gave the adduct (**7**) in a 12.1% yield. The same reaction using *cis*-stilbene (**8**) afforded adducts **9** and **10** in 4.4 and 2.2% yields, respectively. The reaction of **4** with dimethyl fumarate (**11**) and dimethyl maleate (**12**) yielded the same adduct **13** in the yields of 41.3 and 36.7%, respectively. Similar reactions of **5** with **6** and **8** gave adducts **14**, **15**, and **16** in the yields of 14.9, 11.3, and 5.5%, respectively. The reactions of **5** with **11** and **12** afforded the same adduct **17** in 38.5 and 31.0% yields, respectively.

The structures of the adducts were deduced on the basis of their spectral properties and were confirmed by comparisons of these spectral properties with those of analogous compounds.[4)] The assignment of the structures of **9** and **10** are based on the chemical shifts of the cyclopropane proton H_b. Comparing the chemical shifts of the proton H_b of **9** and **10**, the chemical shift of the proton H_b of **9** should appear at lower field because of the paramagnetic anisotropic effect of the two phenyl groups located in the same side of the cyclopropane moiety as that of the proton H_b. The same consideration is applicable for **15** and **16**.

Reactions of the carbenes **2**, **3** with stilbenes **6**, **8** proceed in a stereospecific manner, indicating that the multiplicity of these carbenes are singlet.[1)] On the

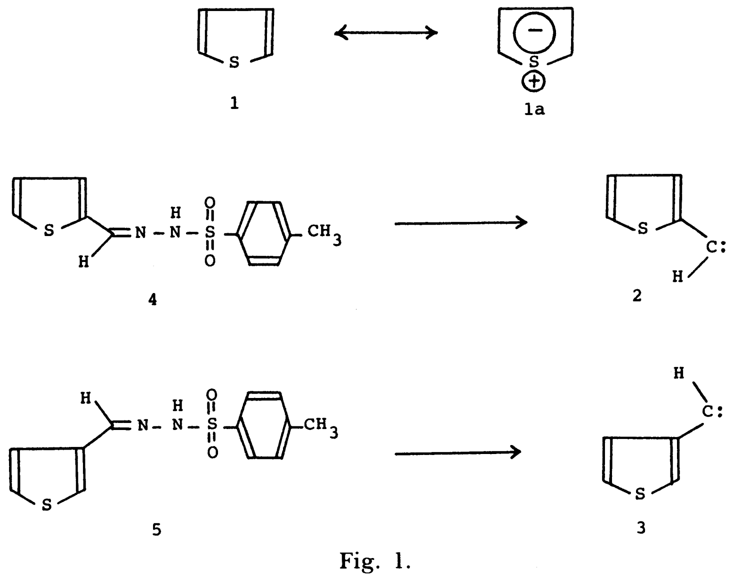

Fig. 1.

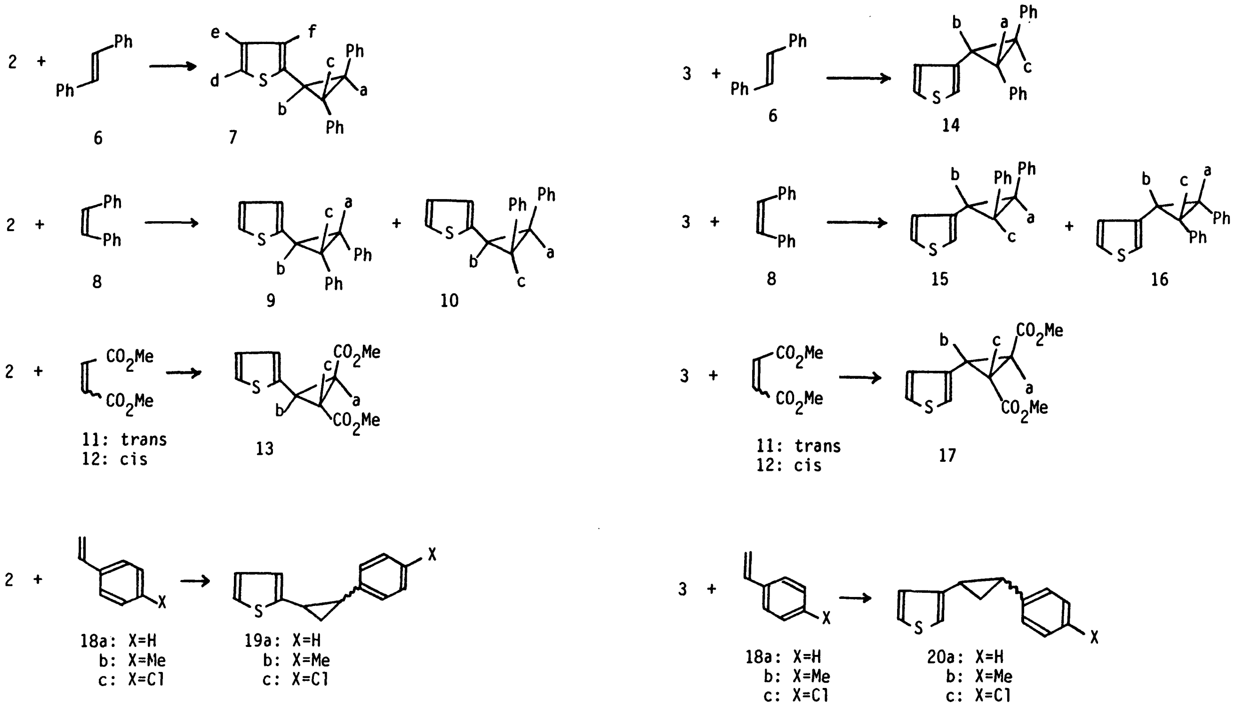

Fig. 2.

other hand, reactions of the carbenes **2**, **3** with the esters **11**, **12** do not seem to be stereospecific additions. It is known, however, that under the reaction conditions **12** isomerizes to **11**,[5] and that the reactivity of **11** to carbenes is higher than that of **12**.[6] Considering the above facts, the loss of stereospecificity of the present reactions is thought to be attributable to the isomerization of **12** to **11**.

There is a considerable difference in the product yields between reactions of the carbenes **2**, **3** with the stilbenes **6**, **8** and the esters **11**, **12**. Considering that the phenyl group of stilbenes is a very week electron-attracting group and, on the other hand, the ester group is a strong electron-attracting group, the above fact is thought to show the nucleophilicity of the carbenes.

In order to confirm the nucleophilicity of the carbenes, substituent effects on the addition reactions were investigated with styrene derivatives **18a—c**. Reactions of **2** with **18** gave the corresponding addition products **19a—c** in yields of 33.2, 38.0, and 48.5%, respectively. Similar reactions of **3** with **18** also afforded adducts **20a—c** in yields of 34.4, 32.7, and 33.0%, respectively. The relative rate ratios of **2** to the substituted styrenes was measured with the addition reactions of **2** to a mixture of **18a** and **18b** and a mixture of **18a** and **18c**[7] and found to be **18b**:**18a**:**18c** is 0.8:1.0:1.3. The relative rate ratios of **3** to the styrenes was also measured in the same manner to be **18b**:**18a**:**18c** is 0.8:1.0:1.6. This result is considered to demonstrate the nucleophilicity of **2** and **3**.

The electronic natures of **2** and **3** are considered to be as shown in **21** and **23**, respectively. The carbenic carbons have two carbenic electrons in the sp^2 orbital and leave a vacant 2p orbital, which delocalizes to the π-orbital system of the thienyl group. Consequently, the carbenic carbon atom shares the negative charge on the ring part of the thienyl group while forming a nucleophilic singlet carbenes, as shown in **22** and **24**, respectively.

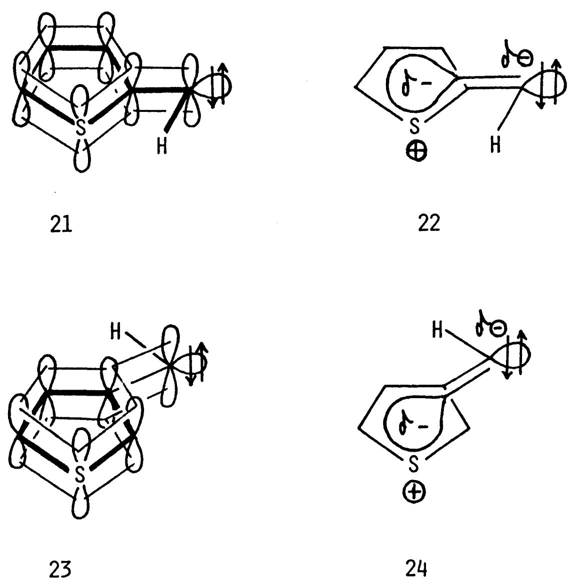

Fig. 3.

Experimental

Melting points were recorded on a Yanagimoto micro melting point apparatus and are uncorrected. NMR spectra were measured with a Varian XL 200 or Hitachi R-20B spectrometers with tetramethylsilane as an internal standard. IR sprectra were measured with a DS-701G spectrometer. Mass spectra were measured with a Hitachi M-52 or JMS-DX300 spectrometers. Wako gel C 200 and Wako gel B5F were used for column and thin-layer chromatogaphy, respectively. Diglyme was dried over Molecular Sieves 3A 1/16. In all reactions, quantitative amounts of nitrogen gas and sodium *p*-toluenesulfinate were generated.

Reaction of 2 with 6. To a solution of **4** (2.52 g, 9 mmol) in diglyme (40 ml) was added sodium hydride (230 mg, 9 mmol), and **6** (6.48 g, 36 mmol); the reaction mixture was heated at 105 °C for 10 min to evolve a quantitative amount of nitrogen gas. After separating of a quantitative amount of sodium *p*-toluenesulfinate by filtration, the filtrate was poured into water, extracted with ether, washed with water and dried over anhydrous sodium sulfate. After removing of the solvent on a rotary evaporator, the oily residue was chromatographed on silica gel to give crystals **7** (300 mg, 12.1%) by the use of pet ether-benzene 9 : 1. The crystals were recrystallized from cyclohexane to give pure **7**. **7**: Mp 51—52 °C. Found: C, 82.46; H, 5.79%. Calcd for $C_{19}H_{16}S$: C, 82.60; H, 5.80%. MS *m/z* (rel intensity) 276 (M^+, 100), 192 (55), 185 (36). IR (oil): 3030, 2950, 1600, 1497 cm^{-1}. ^1H NMR (C_6D_6) δ=2.66 (dd, H_a), 2.74 (ddd, H_b), 2.89 (dd, H_c), 6.58 (d, H_d), 6.67 (dd, H_e), 6.75 (dd, H_f). Coupling constants in Hz: J_{ab}=8, J_{ac}=6, J_{bc}=6, J_{bf}=1, J_{de}=3, J_{ef}=5.

Reaction of 2 with 8. A mixture of **4** (2.52 g, 9 mmol), sodium hydride (230 mg, 9 mmol), and **8** (6.48 g, 36 mmol) in diglyme (40 ml) was reacted at 105 °C for 10 min. A column chromatographic separation of the reaction mixture gave an oil of 1 : 2 mixture of **9** and **10** (163 mg, **9**, 4.4%; **10**, 2.2%) by the use of pet. ether-benzene 9 : 1. Mixture of **9** and **10**: Found: *m/z* 276.0970. Calcd for $C_{19}H_{16}S$: M, 276.0967. MS *m/z* (rel intensity) 276 (M^+, 100), 192 (56), 185 (35). IR (oil): 3030, 2950, 1600, 1500 cm^{-1}. ^1H NMR (C_6D_6) δ=2.65 (bs, H_a, H_b, H_c of **10**), 2.75 (d, J=6 Hz, H_a, H_c of **9**), 3.01 (t, J=6 Hz, H_b of **9**), 6.4—7.4 (m).

Reaction of 2 with 11. A mixture of **4** (2.52 g, 9 mmol), sodium hydride (230 mg, 9 mmol), and **11** (5.18 g, 36 mmol) in diglyme (40 ml) was reacted at 140 °C for 30 min. Column chromatographic separation of the reaction mixture gave crystals **13** (893 mg, 41.3%) by the use of pet. ether-benzene 3 : 7. Recrystallization from ethyl acetate gave pure **13**. **13**: Mp 78—79 °C. Found: C, 54.80; H, 4.93%. Calcd for $C_{11}H_{12}O_4S$: C, 54.99; H, 5.03%. MS *m/z* (rel intensity) 240 (M^+, 65), 181 (95), 121 (100). IR (KBr): 3030, 2970, 1715, 1435 cm^{-1}. ^1H NMR (C_6D_6) δ=2.64 (dd, H_a), 2.85 (dd, H_b), 3.13 (dd, H_c), 6.96 (narrow m, 2H), 7.20 (narrow m, 1H). Coupling constants in Hz: J_{ab}=5, J_{ac}=10, J_{bc}=6.

Reaction of 2 with 12. A mixture of **4** (2.52 g, 9 mmol) sodium hydride (230 mg, 9 mmol), and **12** (5.18 g, 36 mmol) in diglyme (40 ml) was reacted at 140 °C for 30 min to give **13** (792 mg, 36.7%).

Reaction of 3 with 6. A mixture of **5** (2.52 g, 9 mmol), sodium hydride (230 mg, 9 mmol), and **6** (6.48 g, 36 mmol) in diglyme (40 ml) was reacted at 130 °C for 30 min. A column chromatogtraphic separation of the reaction mixture gave an oil **14** (370 mg, 14.9%) by the use of pet. ether-benzene 9 : 1. **14**: Found: *m/z* 276.0974. Calcd for $C_{19}H_{16}S$: M, 276.0972. MS *m/z* (rel intensity) 276 (M^+, 100), 192 (18), 185 (21). IR (oil): 3030, 2950, 1600 cm^{-1}. ^1H NMR (C_6H_6) δ=2.51 (m, H_a), 2.56 (m, H_b), 2.66 (m, H_c), 6.51 (narrow m, 2H), 6.73 (narrow m, 1H), 7.0—7.3 (m, 10H). Coupling constants in Hz: J_{ab}=8, J_{ac}=6, J_{bc}=6.

Reaction of 3 with 8. A mixture of **5** (2.52 g, 9 mmol), sodium hydride (230 mg, 9 mmol), and **8** (6.48 g, 36 mmol) in diglyme (40 ml) was reacted at 120 °C for 20 min. A column chromatographic separation of the reaction mixture gave an oil **15** (282 mg, 11.3%) and an oil **16** (137 mg, 5.5%) by the use of pet. ether-benzene 9 : 1 and 8 : 2, respectively. **15**: Found: *m/z* 276.0943. Calcd for $C_{19}H_{16}S$: M, 276.0973. MS *m/z* (rel intensity) 276 (M^+, 100), 192 (19), 185 (24). IR (oil): 3030, 2950, 1600, 1495 cm^{-1}. ^1H NMR (C_6H_6) δ=2.57 (d, J=6 Hz, H_a, H_b), 2.78 (t, J=6 Hz, H_c), 6.74 (narrow m, 1H), 6.81 (narrow m, 1H), 6.9—7.2 (m, 11H). **16**: Found: *m/z* 276.0952. Calcd for $C_{19}H_{16}S$: M, 276.0973. MS *m/z* (rel intensity) 276 (M^+, 100), 243 (14), 185 (24). IR (oil): 3030, 2950, 1600, 1497 cm^{-1}. ^1H NMR (C_6D_6) δ=2.54 (s, 3H, H_a, H_b, H_c), 6.64 (m, 3H), 7.0, (m, 10H).

Reaction of 3 with 11. A mixture of **5** (2.80 g, 10 mmol), sodium hydride (250 mg, 10 mmol), and **11** (5.76 g, 40 mmol) in diglyme (40 ml) was reacted at 130 °C for 30 min. A column chromatographic separation of the reaction mixture gave crystals **17** (924 mg, 38.5%) by the use of pet. ether-benzene 2 : 8. Recrystallization from cyclohexane gave pure **17**. **17**: Mp 72—73 °C. Found: C, 54.75; H, 4.99%. Calcd for $C_{11}H_{12}O_4S$: C, 54.99; H, 5.03%. MS *m/z* (rel intensity) 240 (M^+, 52). 181 (100), 122 (91). IR (KBr): 3110, 3020, 2960, 1723 cm^{-1}. ^1H NMR ($CDCl_3$) δ=2.59 (m, H_a), 2.79 (m, H_b), 2.98 (m, H_c), 3.56 (s, 3H), 3.76 (s, 3H), 7.02 (m, 1H), 7.14 (m, 1H), 7.25 (m, 1H).

Reaction of 3 with 12. A mixture of **5** (2.80 g, 10 mmol), sodium hydride (250 mg, 10 mmol), and **12** (5.76 g, 40 mmol) in diglyme (40 ml) was reacted at 130 °C for 30 min to give **17** (744 mg, 31.0%).

Reaction of 2 with 18a. A mixture of **4** (2.52 g, 9 mmol), sodium hydride (230 mg, 9 mmol) and **18a** (3.75 g, 36 mmol) in diglyme (30 ml) was reacted at 105 °C for 10 min. A thin-layer chromatographic separation of the reaction mixture using pet. ether-benzene 4 : 1 as a developing solvent gave an oil **19a** (590 mg, 33.2 %, R_f=0.61).

19a: Found: C, 77.96; H, 5.97%. Calcd for $C_{13}H_{12}S$: C, 77.98; H, 6.04%. *m/z* (rel intensity) 200 (M^+, 100), 185 (13), 167 (14). IR (oil): 3100, 3050, 1600, 1500 cm^{-1}. ^1H NMR ($CDCl_3$) δ=1.36 (m, 2H), 2.28 (m, 2H), 6.5—7.5 (m, 8H).

Reaction of 2 with 18b. A mixture of **4** (2.52 g, 9 mmol), sodium hydride (230 mg, 9 mmol), and **18b** (4.25 g, 36 mmol) in diglyme (30 ml) was reacted at 105 °C for 10 min. A thin-layer chromatographic separation of the reaction mixture using pet. ether-ether 9 : 1 as a developing solvent gave **19b** (617 mg, 40.7%, R_f=0.60).

19b: Found: *m/z* 214.0826. Calcd for $C_{14}H_{14}S$: M, 214.0826. MS *m/z* (rel intensity): 214 (M^+, 100), 199 (43), 150 (30). IR (oil): 3100, 3030, 2930, 1520 cm^{-1}. ^1H NMR ($CDCl_3$) δ=1.26 (m, 2H), 2.23 (m, 2H), 2.24 (s, 3H), 6.5—7.2 (m, 7H).

Reaction of 2 with 18c. A mixture of **4** (2.52 g, 9 mmol), sodium hydride (230 mg, 9 mmol), and **18c** (4.99 g, 36 mmol) in diglyme (30 ml) was reacted at 105 °C for 10 min. A thin-layer chromatographic separation of the reaction mixture using cyclohexane-ethyl acetate 4 : 1 as a developing solvent gave an oil **19c** (802 mg, 38.1%, R_f=0.60).

19c: Found: *m/z* 234.0251. Calcd for $C_{13}H_{11}SCl$: M, 234.0270. MS *m/z* (rel intensity) 236 (M^+, 45), 234 (M^+, 100), 199 (55), 191 (41). IR (oil): 3080, 2920, 1493 cm^{-1}. ^1H NMR ($CDCl_3$) δ=1.30 (m, 2H), 2.18 (m, 2H), 6.4—7.3 (m, 7H).

Relative Rate Ratios of the Reaction of 2 to 18a—c.

Tosylhydrazone (**4**) was reacted with a 1 : 1 mixture of **18a** and **18b** as usual. The integrations of the signals of the cyclopropane carbons of **19a** and **19b** in ^{13}C NMR spectra show that the ratio of **19a** and **19b**, which indicates the relative rate ratios of **2** to **18a** and **18b** to be 1.0 and 0.8, respectively.[7] The same procedure as above using a 1 : 1 mixture of **18a** and **18c** gave the relative rate ratio of the reaction of **2** to **18a** and **18c** to be 1.0 and 1.3, respectively.

Reaction of 3 with 18a. A mixture of **5** (2.52 g, 9 mmol), sodium hydride (230 mg, 9 mmol), and **18a** (3.75 g, 36 mmol) in diglyme (30 ml) was reacted at 140 °C for 30 min. A thin-layer chromatographic separation of the reaction mixture using pet. ether-benzene 4 : 1 as a developing solvent gave **20a** (618 mg, 34.4%, R_f=0.50).

20a: Found: *m/z* 200.0667. Calcd for $C_{13}H_{12}S$: M, 200.0660. MS *m/z* (rel intensity): 200 (M^+, 100), 185 (25), 167 (25). IR (oil): 3030, 2930, 1603, 1500 cm^{-1} ^{1}H NMR ($CDCl_3$) δ=1.34 (m, 2H), 2.20 (m, 2H), 6.5—7.4 (m, 8H).

Reaction of 3 with 18b. A mixture of **5** (2.52 g, 9 mmol), sodium hydride (230 mg, 9 mmol), and **18b** (4.25 g, 36 mol), in diglyme (30 ml) was reacted at 140 °C for 60 min. A thin-layer chromatographic separation of the reaction mixture using pet. ether-benzene 4 : 1 as a developing solvent gave **20b** (630 mg, 32.7%, R_f=0.57).

20b: Found: *m/z* 214.0798. Calcd for $C_{14}H_{14}S$: M, 214.0817. MS *m/z* (rel intensity) 214 (M^+, 100), 200 (37), 181 (9). IR (oil): 3010, 2920, 1518 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ=1.28 (m, 2H), 2.20 (m, 2H), 2.29 (s, 3H), 6.6—7.2 (m, 7H).

Reaction of 3 with 18c. A mixture of **5** (2.52 g, 9 mol), sodium hydride (230 mg, 9 mmol), and **18c** (4.25 g, 36 mmol) in diglyme (30 ml) was reacted at 140 °C for 60 min. A thin-layer chromatographic separation of the reaction mixture using pet. ether-benzene 4 : 1 as a developing solvent gave **20c** (697 mg, 33.0%, R_f=0.57).

20c: Found: *m/z* 234.0268. Calcd for $C_{13}H_{11}SCl$: M, 214.0270. MS *m/z* (rel intensity) 234 (M^+, 100), 199 (44), 183 (12). IR (oil): 3080, 2920, 1492 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ=1.30 (m, 2H), 2.31 (m, 2H), 6.5—7.2 (m, 7H).

Relative Rate Ratios of the Reaction of 3 to 18a—c. Tosylhydrazone (**5**) was reacted with 1 : 1 mixtures of **18a** and **18b** or **18a** and **18c** as usual. The ratios of products **20a**, **20b**, and **20c** were measured by the same method as that employed in the case of reactions of **4** to be 1.0, 0.8, and 1.6, respectively.

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