  Bull. Chem. Soc. Jpn., 62, 211—218 (1989)

A Mechanistic Study on the Reaction of Iminothiadiazolines with Activated Acetylenes: Competitive Pathway through Hypervalent Sulfurane and Zwitterion

Yohsuke YAMAMOTO,† Tohru TSUCHIYA, Masahide OCHIUMI, Shin-ichi ARAI, Naoki INAMOTO,* and Kin-ya AKIBA*,†

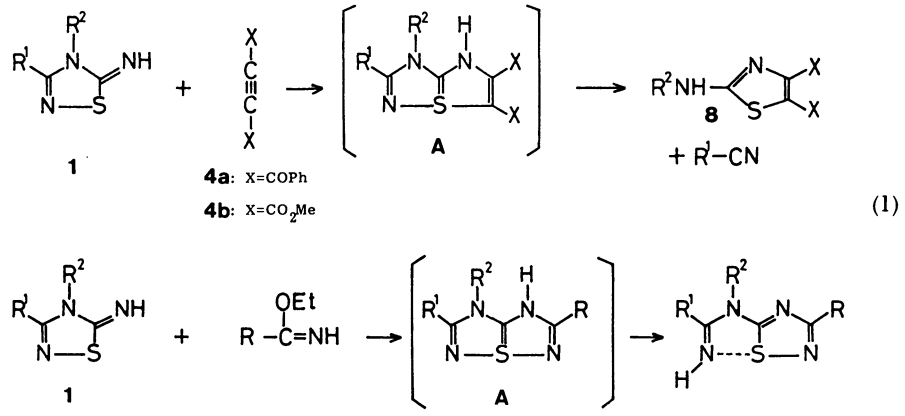
Department of Chemistry, Faculty of Science, The University of Tokyo, Hongo, Bunkyo-ku, Tokyo 113

(Received August 5, 1988)

The reaction of 3-aryl-5-benzoyl-2-imino-2,3-dihydro-1,3,4-thiadiazoles (**6**) with dimethyl acetylenedicarboxylate (**4b**) gave the corresponding thiazole (**8**) and benzoyl cyanide through sulfurane (**B**) by 1,3-dipolar cycloaddition and cis- (**9**) and trans-vinyl (**10**) compounds through zwitterion (**C**) by simple addition. Two types of addition reactions competed each other and the ratio of the two [*R*=**B**/**C**] depended solely on the solvent polarity (E_T). Dibenzoylacetylene behaved similarly. Several iminothiazolines and iminothiadiazolines reacted with activated acetylenes and the selectivity for the two types of addition reactions for each system was shown to be affected by quite subtle balance of electron-withdrawing ability of each heterocycle.

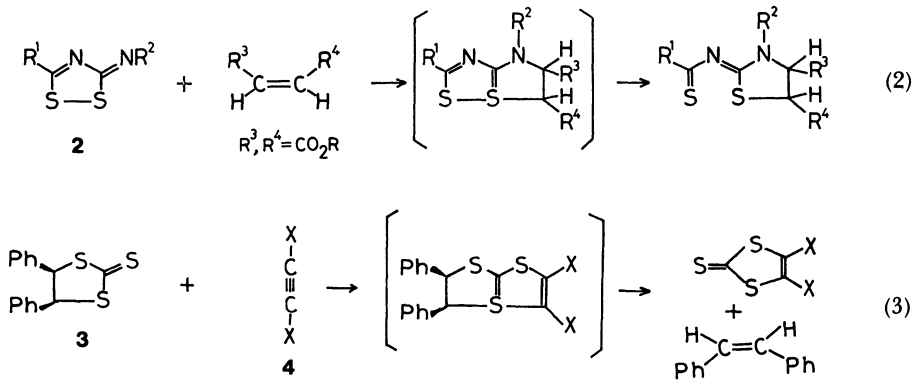
Many kinds of five-membered sulfur heterocycles have been used for cycloadditions as masked 1,3-dipoles. For example, aminothiatriazole,[1] dithiolanthiones,[2] dithiolethiones[3] and its aza-,[4] oxa-,[5] selena-[6] analogues have been reported to react with activated olefins, acetylenes, nitriles, and heterocumulenes. During our research on the role of hypervalent sulfur for ring-transformation,[7] we also reported the reaction of 5-imino-4,5-dihydro-1,2,4-thiadiazole (**1**) with activated acetylenes to give the corresponding 2-aminothiazole and nitrile and also that of the same compound with imidates to afford the corresponding adduct which has an aromatic 1,2,4-thiadiazole ring via hydrogen shift.[4g,7c] The characteristic feature of these reactions is that bond switching takes place at the central sulfur atom and the resulting products are adducts accompanied by ring-transformation or new heterocycles produced by elimination of small molecules from the adducts. Although almost all reactions are assumed to proceed through hypervalent sulfuranes, for example **A**, only a few mechanistic studies have been presented. Goerdeler reported the cycloaddition of 3-imino-3*H*-1,2,4-dithiazoles (**2**) with activated olefins,[4b] and found that fumarate and maleate reacted stereospecifically, which indicated that the reaction proceeded in a concerted manner. Another example is the reaction of cis- and trans-disubstituted dithiolanthiones (**3**) with activated acetylenes (**4**),[2a] and the former compound produced cis-olefin and vice versa (Scheme 2, Eqs. 2 and 3). The result also shows that any discrete polar or radical intermediate is not involved through the process.

During our study on the scope of these reactions, we found some complexity of the product depending on the change of electronic nature of the starting iminothiadiazolines. Closely related 2-imino-2,3-dihydro-1,3,4-thiadiazoles **5** and **6a** reacted with dibenzoylacetylene (**4a**: X=PhCO) to give different types of compounds as main product, that is, **7a** (81%) and **8d** (98%), respectively (vide infra, Scheme 3, Eqs. 4 and 5). Hence, there is still to be elucidated on mechanism of the reaction of activated acetylenes

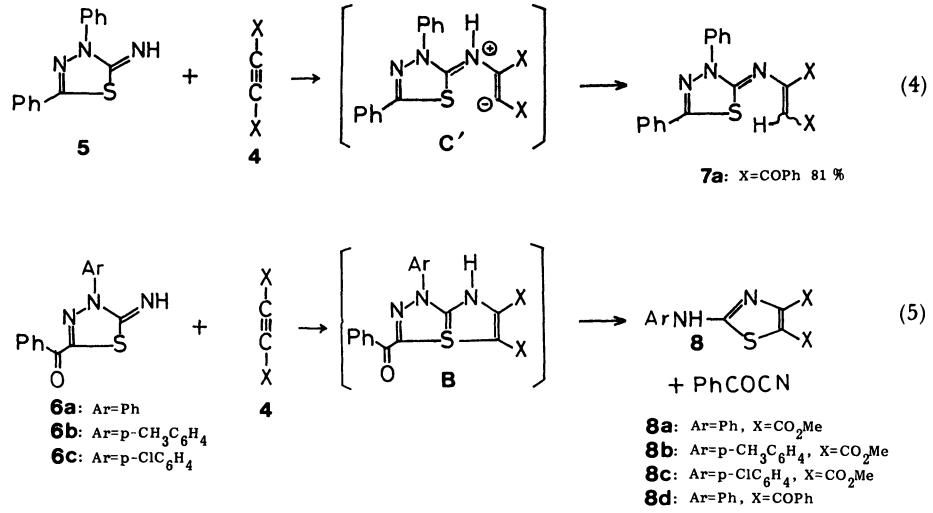


Scheme 1.

† Present address: Department of Chemistry, Faculty of Science, Hiroshima University, Higashisenda-machi, Naka-ku, Hiroshima 730.



Scheme 2.

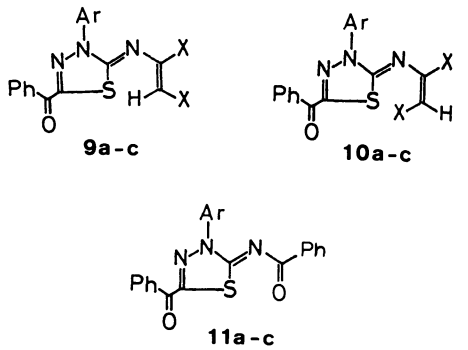


Scheme 3.

with those compounds. We examined the reaction of Eq. 5 in detail in comparison with Eq. 4 to obtain mechanistic insight of the reaction. It was concluded that the difference of the reaction course could be explained on the basis of competitive reactions which proceeded through two intermediates, sulfurane (**B**) and zwitterion (**C**).

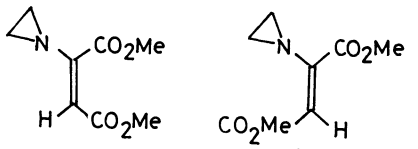
Results and Discussion

Products of the Reaction of 6 with 4b. The reaction of 3-aryl-5-benzoyl-2-imino-2,3-dihydro-1,3,4-thiadiazoles (**6**) with dimethyl acetylenedicarboxylate (**4b**) was carried out in a variety of solvents at 50 °C for several hours (Eq. 5). In all cases examined, the main product was the thiazole (**8**), which could be recrystallized from the reaction mixture. When the reaction was carried out in nonpolar solvents the yield of **8** always amounted to ca. 90%. In order to scrutinize the reaction the products were separated by dry column chromatography (SiO_2) using dichloromethane as an eluent. Besides the thiazole (**8**), three products **9**, **10**, **11**, and benzoyl cyanide were obtained. The structure of **11** was confirmed by comparison with authentic samples prepared from **6** and benzoyl



chloride. Structural assignment of **9** and **10** are based on the elemental analyses, ^1H NMR and mass spectra. ^1H NMR clearly shows that both products have an olefinic proton, and isomerization from **9** to **10** was observed by addition of a catalytic amount of chloroacetic acid. Therefore these are geometrical

isomers. By comparison of the ^{1}H NMR spectra of **9** and **10**, rather large difference was noticed between chemical shifts of olefinic protons (δ 5.5—5.7 and 6.2—6.4). As it is known that a greater deshielding of the vinyl proton occurs in fumarate ester than in maleate, the former compound with vinyl proton at higher field should be cis-vinyl **9** and the latter is trans-vinyl **10**.[8] By the same reason Dolfini[9] assigned structure of adduct (**12**) of aziridine with **4b** that **12** with a vinyl proton at higher field (δ 5.31) is **12a** and the another at lower field (δ 6.15) is **12b**. We were surprised to see that the thiazole (**8**), which is expected to result from sulfurane **B**, and vinyl compounds **9** and **10**, which should be produced through zwitterion **C**, were obtained together in aprotic solvents. Therefore we next examined the solvent and substituent effects on the reaction.



12a **12b**

Solvent and Substituent Effects on the Reaction of 6 with 4b. Reactions of **6b** with **4b** were carried out in eleven solvents to examine the solvent effect on the ratio of these products. A mixture of **4b** (1.2—1.4 mmol) and **6b** (0.99—1.01 mmol) in 50 ml of a dry solvent was heated at 50.0 °C for several hours. The reaction proceeded cleanly and four products were separated by chromatography. Total yield was almost quantitative (95—100%) and Table 1 shows the ratio of the four products. The formation of **11** is ascribed to the secondary reaction of **6b** with benzoyl cyanide which is produced together with **8** during the reaction. This was actually confirmed by a separate experiment.

Table 1. Solvent Effect on the Reaction of **6b** with **4b**[a]

Solvent	E_T	**8**	**9**	**10**	**11**	R[b]
PhH	34.5	86.4	2.1	0.9	10.6	28.8
CCl_4	32.5	90.6	3.3	0.1	6.0	26.6
THF	37.4	91.6	3.7	0.5	4.2	21.8
AcOEt	38.1	84.1	3.1	1.3	11.5	19.1
MeCOMe	42.2	72.8	6.3	1.6	19.2	9.2
Me_2SO	45.0	76.3	9.4	3.4	11.0	6.0
MeCN	46.0	73.9	14.7	1.5	9.9	4.6
t-BuOH	43.9	79.0	5.7	4.0	11.3	8.1
i-PrOH	48.6	71.9	5.3	12.4	10.4	4.1
EtOH	51.9	68.7	13.8	15.8	1.7	2.32
MeOH	55.5	41.8	38.5	18.9	0.8	0.73

a) Sum of the isolated yields of the four products were 95—100% and these values were normalized to correspond to the total yield of 100%. b) R=**8**/(**9**+**10**).

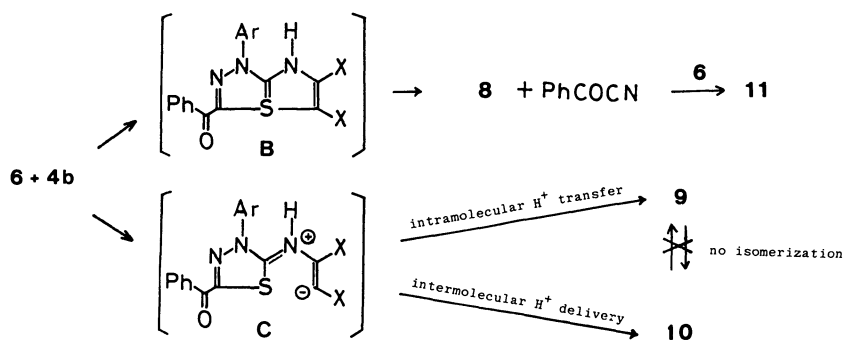
Important informations can be extracted from Table 1: (i) The yield of the main product **8** decreases and that of total vinyl compounds (**9**+**10**) increases according to the increase of polarity of solvents (E_T),[10] i.e., R ([**8**/(**9**+**10**)])[11] decreases according to the increase of E_T, (ii) vinyl compounds are produced even in nonpolar aprotic solvents and cis-vinyl (**9**) is the major one in all the aprotic solvents, (iii) ratio of cis-vinyl (**9**) to trans-vinyl (**10**) is dependent on the kind of alcohols used.

When log R was plotted against the parameter E_T, good linear relationship was observed (corr. coeff. 0.980) for all of the solvents (Fig. 1). This means that the ratio of **8** to total vinyl compounds (**9**+**10**) is determined solely by the polarity of the solvent irrespective of the participation of alcoholic protons in the formation of **9** and **10**. These can be explained by competitive reactios (Scheme 4), that is, the vinyl compounds and the thiazole are formed through different intermediates, i.e., nonpolar sulfurane (**B**) and polar one, zwitterion (**C**), the ratio of which is determined by the solvent polarity.

Table 2. Substituent Effect on the Reaction of **6** with **4b** in Methanol[a]

Ar	**8**	**9**	**10**	**11**	R[b]
p-MeC_6H_4	41.8	38.5	18.9	0.8	0.61
C_6H_5	45.3	35.6	18.9	0.2	0.83
p-ClC_6H_4	48.8	26.5	23.4	1.3	0.98

a) Sum of the isolated yields of the four products were 95—100% and these values were normalized to correspond to the total yield of 100%. b) R=**8**/(**9**+**10**).



Scheme 4.

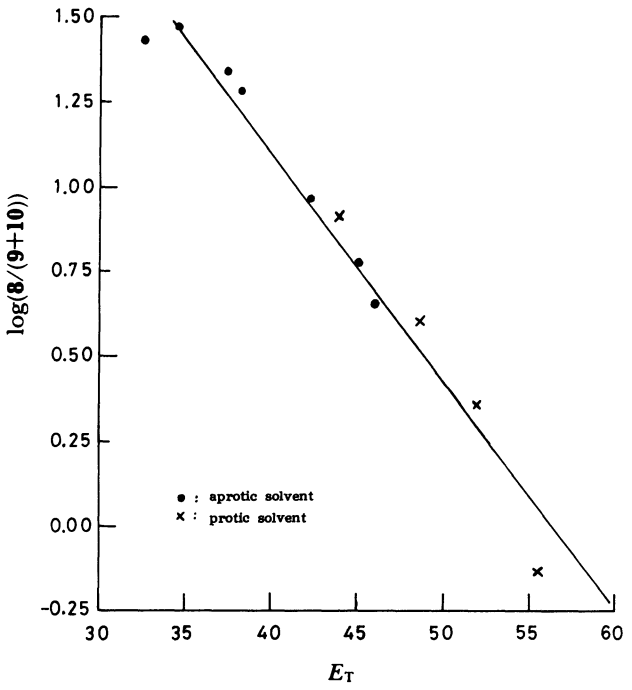


Fig. 1. Relationship between product distribution and solvent polarity E_T.

Substituent effect of the aryl group was examined in methanol as a solvent and results are shown in Table 2. These indicate that the ratio R increased according to the increase of the electron-withdrawing ability of substituent Ar. It is reasonable that formation of sulfurane (**B**) is favored and stability of zwitterion (**C**) is disfavored by increasing electron-withdrawing ability of Ar.

The cis-trans ratio of vinyl compounds (**9** and **10**) remained constant under the reaction conditions and workup procedure. The cis-trans ratio of vinyl compounds in methanol was examined at appropriate intervals by ^{1}H NMR and no change of the ratio was observed at 20, 25, 45, 70, and 138 h. In addition the isomerization during workup was carefully checked by subjecting the isolated vinyl compounds again to chromatography and no change of the ratio was confirmed. Therefore, it is concluded that the ratio of the vinyl compounds (**9** and **10**) was actually determined by the reaction. Such a ratio of vinyls is consistent with that of aziridine with **4b**.[9,12] It was reported that cis adduct **12a** formed via intramolecular path was exceedingly formed in aprotic solvent and trans adduct was predominant in methanol because intermolecular protonation by the solvent became favored. Also in our result, cis-vinyl **9** was invariably preferred to trans-vinyl **10** in aprotic solvents, which probably results from intramolecular prototropy. Ratios of **9** to **10** in protic solvents were quite different from those in aprotic ones, for example, the dramatic difference exists between acetonitrile (**9**/**10**=14.6/1.5) and 2-propanol (5.3/12.4) which have similar polarity (E_T). The ratios in alcohols seem to depend on bulkiness of alkyl groups and to acidity of alcohols. The result indicates that alcohols participate to form vinyl compounds (**9** and **10**) from **C**.

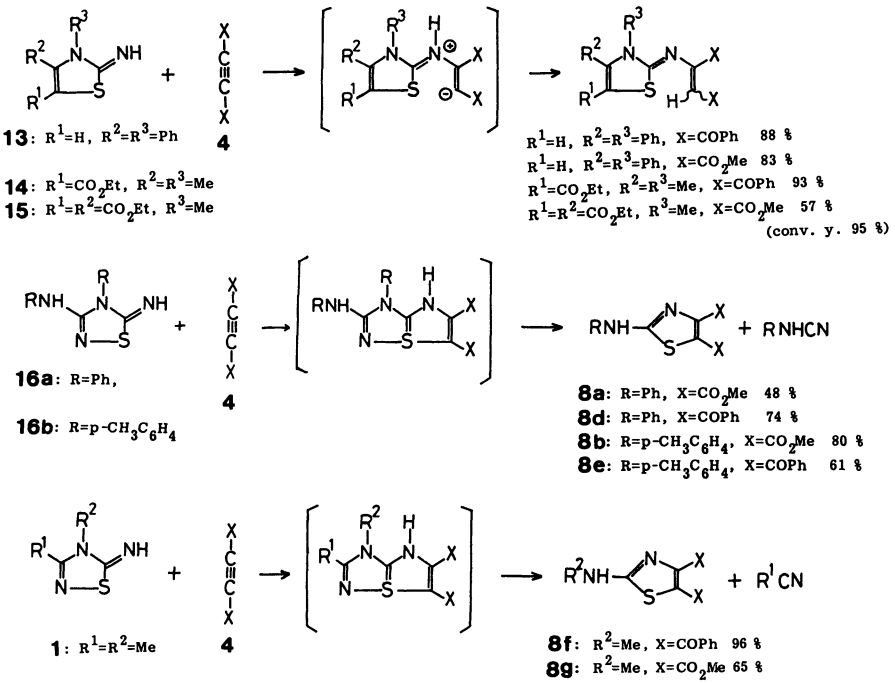
Reaction of Closely Related Thiazolines and Thiadiazolines with Activated Acetylenes. Now it is interesting to compare the results with closely related systems. We examined six types of compounds, **1**, **5**, **13**—**16** in addition to **6**. All these compounds reacted smoothly with activated acetylenes **4a** and **4b** at room temperature or at 50 °C within several hours. Results are summarized in Scheme 5. Reaction course was not affected by using either **4a** or **4b**.

In thiazolines (**13**—**15**), any ring-transformed thiazole was not obtained but only simple adduct was formed in high yield even in nonpolar aprotic solvents. On the other hand, 1,2,4-thiadiazolines, **1** and **16a** (Hector's base) reacted with dibenzoyl acetylene to give only ring-transformed thiazole in 96 and 74% yields and the same kind of results was obtained with dimethyl acetylenedicarboxylate. It is noteworthy here that the reaction of 1,3,4-thiadiazoline **6** with **4a** gave the ring-transformed thiazole as a main product (vide supra), but only simple adduct **7a** was obtained from **4a** and **5**, in which the benzoyl group at 2 position was substituted by a phenyl group (Scheme 3, Eqs. 4 and 5).

All these results can be interpreted by competitive reactions similarly to Scheme 4. That is, relative stability of the intermediate sulfurane **D** and zwitterion **E** determines the reaction course. It is well-known that the hypervalent bond, i.e., three-center four-electron bond, is stabilized by electronegative groups at apical positions.[13] In sulfurane **D** the hypervalent bond corresponds to 1, 6a, 6 bond, so that the groups at 1 and 6 positions are most important in order to form the sulfurane by 1,3-dipolar cycloaddition. In 1,2,4-thiadiazolines **1** and **16** (Hector's base) sulfurane **D** was formed due to the presence of an electronegative nitrogen atom at position-M. In three thiazolines, **13**—**15**, less electronegative carbon than nitrogen should come to position-M, thus not sulfurane (**D**) but zwitterion (**E**) was generated as an intermediate. In 1,3,4-thiadiazolines the nitrogen at position-L has electron-withdrawing effect but the effect is not so much as the nitrogen at position-M in 1,2,4-thiadiazolines. Thus the group at position-M became important in 1,3,4-thiadiazolines. The benzoyl group attached at position-M was electronegative enough to let **6** participate in cycloaddition to generate sulfurane **D** but the phenyl group was not enough so and **5** gave vinyl compounds via zwitterion **E**.

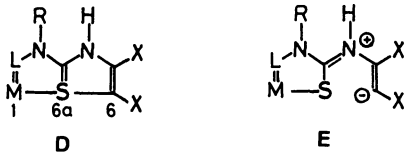
Conclusion

The reaction of iminothiadiazolines and 2-imino-4-



Scheme 5.

thiazolines with activated acetylenes can be understood by competitive reactions, invoking the formation of sulfurane **D** by concerted 1,3-dipolar cycloaddition and that of zwitterion **E** by simple addition. Selectivity between the two reactions stands on quite subtle balance of electron-withdrawing ability of the heterocycles. It is not yet clear whether sulfurane **D** can open to zwitterion **E** or **E** can close to **D** during the reaction, however, the presence of the two intermediates was verified for the present case, i.e., **6**+**4a**.



Experimental

IR spectra were recorded on a Hitachi EPI-G2 spectrometer. ^{1}H NMR spectra were determined with a Hitachi R-24B or a Hitachi R-20B spectrometer. UV spectra were measured with a EPS-G3 spectrometer. Mass spectra were obtained with a Hitachi RMU-6 and JEOL D-300 spectrometer. All melting points are uncorrected. All solvents employed in the reaction were purified as follows; methanol and ethanol were distilled from magnesium alkoxide. 2-Propanol, *t*-butyl alcohol, and benzene were distilled from sodium. Carbon tetrachloride and ethyl acetate were distilled from phosphorus pentaoxide and redistilled from anhydrous potassium carbonate. Acetone was treated with potassium permanganate and redistilled from potassium carbonate. Tetrahydrofuran was distilled from sodium/benzophenone. Dimethyl sulfoxide was distilled over calcium hydride. Acetonitrile was spectral grade stored over 4-A Molecular Sieves. Dibenzoyl acetylene (**4a**)[14] and dimethyl acetylenedicarboxylate (**4b**)[15] were prepared by the reported procedure.

5-Benzoyl-2-imino-3-phenyl-2,3-dihydro-1,3,4-thiadiazole (6a) was prepared from phenacyl thiocyanate and benzenediazonium chloride in ethanol–water–tetrahydrofuran solution at pH 4.[16]

6a: Yield 50%; mp 94—96 °C (lit, 89—90 °C);[16] UV (CH_2Cl_2) λ_{max} 265 (log ε=4.28), 375 nm (4.15); IR (KBr) 3310, 1640, 1600 cm^{-1}.

5-Benzoyl-2-imino-3-*p*-tolyl-2,3-dihydro-1,3,4-thiadiazole (6b). Yield 60%; mp 123—124 °C (lit, 112 °C);[16] UV (CH_2Cl_2) λ_{max} 265 (log ε=4.24), 377 nm (4.09); IR (KBr) 3250, 1640, 1600 cm^{-1}.

5-Benzoyl-2-imino-3-(*p*-chlorophenyl)-2,3-dihydro-1,3,4-thiadiazole (6c). Yield 60%; mp 139.5—141 °C (lit, 127 °C);[16] IR (KBr) 3300, 1640, 1600 cm^{-1}.

Reactions of 6 and 4b. General Procedure: A solution of **4b** (1.2—1.4 mmol) and **6** (0.99—1.01 mmol) in 50 ml of dry solvent was heated at 50 °C for several hours. After disappearance of **6** was checked by TLC, the solvent was evaporated. The reaction mixture was subjected to dry column chromatography (SiO_2) with chloroform as an eluent. This column was divided into four fractions, each of which was composed of **8**, **9**, **10** an **11**.

4,5-Bis(methoxycarbonyl)-2-(phenylamino)thiazole (8a). Mp 115—116 °C; IR (KBr) 3150, 3125, 1745, 1720, 1590 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=3.70 (s, 3H), 3.80 (s, 3H), 7.2—7.5 (m, 5H), 9.5 (brs, 1H); MS, *m/z* (relative intensity) 292 (M^+, 100), 232 (72). Calcd for $C_{13}H_{12}N_2O_4S$: C, 53.43; H, 4.14; N, 9.59%. Found: C, 53.37; H, 3.98; N, 9.33%.

4,5-Bis(methoxycarbonyl)-2-(*p*-tolylamino)thiazole (8b). Mp 173.5—175.5 °C; IR (KBr) 3200, 3150, 1730, 1690,

1600 cm^{-1}; ^1H NMR ($CDCl_3$) δ=2.40 (s, 3H), 3.80 (s, 3H), 3.85 (s, 3H), 7.1—7.4 (m, 4H), 8.85 (brs, 1H); MS, *m/z* (relative intensity) 306 (M^+, 100), 246 (87). Calcd for $C_{14}H_{14}N_2O_4S$: C, 54.90; H, 4.61; N, 9.15%. Found: C, 54.96; H, 4.61; N, 9.24%.

4,5-Bis(methoxycarbonyl)-2-(*p*-chlorophenylamino)thiazole (8c). Mp 191—192 °C; IR (KBr) 3220, 3170, 1730, 1690, 1600 cm^{-1}. Calcd for $C_{13}H_{11}N_2O_4SCl$: C, 47.79; H, 3.39; N, 8.51; S, 9.81; Cl, 10.85%. Found: C, 47.79; H, 3.53; N, 8.31; S, 9.97; Cl, 10.68%.

5-Benzoyl-3-phenyl-2-[[(*E*)-1,2-bis(methoxycarbonyl)vinyl]-imino]-2,3-dihydro-1,3,4-thiadiazole (9a). Mp 121.5—122.5 °C; UV (CH_2Cl_2) λ_{max} 272 (log ε=4.17), 318 (4.24), 381 nm (4.10); ^1H NMR ($CDCl_3$) δ=3.69 (s, 3H), 3.80 (s, 3H), 5.56 (s, 1H), 7.2—8.4 (m, 10H); MS, *m/z* (relative intensity) 423 (M^+, 4), 105 (100). Calcd for $C_{21}H_{17}N_3O_5S$: C, 59.57; H, 4.05; N, 9.93%. Found: C, 59.59; H, 3.91; N, 10.21%.

Compound 9b. Mp 123.5—124.5 °C; UV (CH_2Cl_2) λ_{max} 270 (log ε=4.21), 319 (4.16), 386 nm (4.09); ^1H NMR ($CDCl_3$) δ=2.35 (s, 3H), 3.70 (s, 3H), 3.85 (s, 3H), 5.65 (s, 1H), 7.1—8.4 (m, 9H); MS, *m/z* (relative intensity) 437 (M^+, 4), 105 (100). Calcd for $C_{22}H_{19}N_3O_5S$: C, 60.40; H, 4.38%. Found: C, 60.32; H, 4.37%.

Compound 9c. Mp 121.0—122.5 °C; ^1H NMR ($CDCl_3$) δ=3.75 (s, 3H), 3.90 (s, 3H), 5.70 (s, 1H), 7.2—8.4 (m, 9H). Calcd for $C_{21}H_{16}N_3O_5SCl$: C, 55.09; H, 3.52; N, 9.18%. Found: C, 54.51; H, 3.33; N, 8.90%.

5-Benzoyl-3-phenyl-2-[[(*Z*)-1,2-bis(methoxycarbonyl)vinyl]-imino]-2,3-dihydro-1,3,4-thiadiazole (10a). Mp 131.5—132.5 °C; UV (CH_2Cl_2) λ_{max} 272 (log ε=4.33), 380 nm (4.06); ^1H NMR ($CDCl_3$) δ=3.67 (s, 3H), 3.76 (s, 3H), 6.23 (s, 1H), 7.2—8.4 (m, 10H); MS, *m/z* (relative intensity) 423 (M^+, 18), 105 (100). Calcd for $C_{21}H_{17}N_3O_5S$: C, 59.57; H, 4.05; N, 9.93%. Found: C, 59.72; H, 4.07; N, 9.66%.

Compound 10b. Mp 148.5—149.5 °C; UV (CH_2Cl_2) λ_{max} 272 (log ε=4.34), 383 nm (4.03); ^1H NMR ($CDCl_3$) δ=2.40 (s, 3H), 3.71 (s, 3H), 3.80 (s, 3H), 6.35 (s, 1H),7.1—8.5 (m, 9H); MS, *m/z* (relative intensity) 437 (M^+, 5), 105 (100). Calcd for $C_{22}H_{19}N_3O_5S$: C, 60.40; H, 4.38; N, 9.61%. Found: C, 60.41; H, 4.11; N, 9.35%.

Compound 10c. Mp 161—162 °C; ^1H NMR ($CDCl_3$) δ=3.70 (s, 3H), 3.80 (s, 3H), 6.35 (s, 1H), 7.2—8.4 (m, 9H). Calcd for $C_{21}H_{16}N_3O_5SCl$: C, 55.09; H, 3.52; N, 9.18%. Found: C, 55.66; H, 3.70; N, 9.43%.

5-Benzoyl-2-benzoylimino-3-phenyl-2,3-dihydro-1,3,4-thiadiazole (11a) was prepared by the reaction of **6a** with benzoyl chloride in quantitative yield. Mp 202.5—204 °C. Calcd for $C_{22}H_{15}N_3O_5S$: C, 68.56; H, 3.92; N, 10.91%. Found: C, 68.56; H, 3.77; N, 10.79%.

Compound 11b. Mp 233.0—233.5 °C. Calcd for $C_{23}H_{17}N_3O_5S$: C, 69.15; H, 4.29; N, 10.52%. Found: C, 69.69; H, 4.18; N, 10.62%.

Compound 11c. Mp 216—217.5 °C. Calcd for $C_{22}H_{14}N_3O_2SCl$: C, 62.93; H, 3.36; N, 10.01%. Found: C, 62.91; H, 3.24; N, 9.92%.

Reaction of 6a with 4a. In 30 ml of THF **6a** (435 mg, 1.55 mmol) was mixed with **4a** (467 mg, 1.99 mmol). After stirring for 4 h at room temperature, the reaction mixture was recrystallized from benzene to give 4,5-dibenzoyl-2-(phenylamino)thiazole (**8d**) in 98% yield. Mp 173.5—175 °C; IR (KBr) 3200, 3150, 1680, 1620 cm^{-1}; ^1H NMR ($CDCl_3$) δ=7.0—7.9 (m, 15H), 8.75 (brs, 1H); MS, *m/z* (relative intensity) 384 (M^+, 100), 279 (29). Calcd for $C_{23}H_{16}N_2O_2S$: C, 71.87; H, 4.20; N, 7.29%. Found: C, 71.60; H, 3.95; N, 7.04%.

2-Imino-3,5-diphenyl-2,3-dihydro-1,3,4-thiadiazole (5) was prepared from a reported method.[17] Mp 99.5—101 °C (lit, 97 °C).[17]

Reaction of 5 with 4a. In 5 ml of THF **5** (33 mg, 0.13 mmol) was mixed with **4a** (113 mg, 0.48 mmol) at room temperature and heated at 50 °C for 2 h. The reaction mixture was submitted to TLC (SiO_2) with chloroform to give 52 mg (81%) of simple addition product. Mp 141—142.5 °C; IR (KBr) 1680, 1640 cm^{-1}; ^1H NMR ($CDCl_3$) δ=7.0 (s, 1H), 7.4—8.6 (m, 20H); MS, *m/z* (relative intensity) 487 (M^+, 10), 382 (71), 105 (100). Calcd for $C_{30}H_{31}N_3O_2S$: C, 73.90; H, 4.34; N, 8.62; S, 6.58%. Found: C, 73.92; H, 4.30; N, 8.32; S, 6.50%.

5-Imino-4-phenyl-3-phenylamino-4,5-dihydro-1,2,4-thiadiazole (16a). Hector's bases were prepared from the corresponding arylthioureas by oxidation with acidic hydrogen peroxide.[18] Yield 54%; mp 181—182 °C (lit, 181 °C).[18]

Compound 16b. Yield 47%; Mp 126—127 °C (lit, 127 °C).[18]

Reaction of 16a and 4b. To a stirred solution of **16a** (1.34 g, 5.01 mmol) in 100 ml of chloroform, **4b** (0.93 g, 6.6 mmol) in 20 ml of chloroform was added dropwise during 7 h at room temperature. After being stirred for 3 h, the reaction mixture was subjected to dry column chromatography (alumina) to give **8a** in 48% yield.

Reaction of 16a with 4a. To a solution of **16a** (1.34 g, 5.01 mmol) in 100 ml of chloroform, **4a** (1.53 g, 6.5 mmol) was added portionwise. After the mixture was stood for 1 h, the solvent was evaporated. The residual oil was crystallized from benzene-hexane to give 4,5-dibenzoyl-2-(phenylamino) thiazole (**8d**) in 74% yield.

4,5-Dibenzoyl-2-(*p*-methylphenylamino)thiadiazole (8e). Yield 61%; mp 203—204 °C; IR (KBr) 3200, 3150, 1680, 1620 cm^{-1}; ^1H NMR ($CDCl_3$) δ=2.3 (s, 3H), 7.0—7.8 (m, 14H), 8.7 (brs, 1H); MS, *m/z* (relative intensity) 398 (M^+, 97), 293 (23).

3,4-Dimethyl-5-imino-4,5-dihydro-1,2,4-thiadiazole (1) was prepared from a similar method described in the literature.[19] Mp 64—69 °C (lit, 66 °C);[19] IR (KBr) 3200, 1595, 1580 cm^{-1}; ^1H NMR ($CDCl_3$) δ=2.25 (s, 3H), 3.28 (s, 3H), 5.85 (brs, 1H).

Reaction of 1 with 4a. The solution of **4a** (1.07 g, 4.58 mmol) in 5 ml of THF was added dropwise to a solution of **1** (495 mg, 3.83 mmol) in 10 ml of THF. After stirring overnight at room temperature, the reaction mixture was crystallized from ethanol to give 4,5-dibenzoyl-2-(methylamino)thiazole (**8f**) in 96% yield. Mp 197—198.5 °C; IR (KBr) 3200, 1680, 1620 cm^{-1}. ^1H NMR ($CDCl_3$) δ=2.87 (bd, *J*=6 Hz, 3H), 7.2—7.8 (m, 10H), 8.4 (brm, 1H). Calcd for $C_{18}H_{14}N_2O_2S$: C, 67.06; H, 4.38; N, 8.69; S, 9.95%. Found: C, 67.10; H, 4.22; N, 8.68; S, 9.94%.

Reaction of 1 with 4b. To a solution of **1** (126 mg, 0.98 mmol) in 5 ml of hexane **4b** (142 mg, 1.00 mmol) was added dropwise at 0 °C. The reaction occurred exothermally to form precipitates. After 1 h, the solvent was evaporated and the residue was submitted to TLC (SiO_2, ether). 4,5-Bis(methoxycarbonyl)-2-(methylamino)-thiazole (**8 g**) was obtained in 65% yield. Mp 156.5—158 °C

(recrystallized from benzene–hexane); IR (KBr) 3200, 3100, 1730, 1620 cm^{-1}; ^1H NMR ($CDCl_3$) δ=2.97 (d, J=6 Hz, 3H), 3.84 (s, 3H), 3.95 (s, 3H), 8.27 (bs, 1H); MS, m/z (relative intensity) 230 (M^+, 100), 199 (81), 172 (28). Calcd for $C_8H_{10}N_2O_4S$: C, 41.73; H, 4.38; N, 12.17; S, 13.93%. Found C, 41.62; H, 4.65; N, 12.05; S, 14.09%.

2-Imino-3,4-diphenyl-4-thiazoline (13) was prepared from a similar method described in the literature.[20] Mp 112—113 °C (lit, 111 °C).[20]

Reaction of 13 with 4a. To a solution of **13** (1.27 g, 5.05 mmol) in 50 ml of chloroform, **4a** (1.52 g, 6.51 mmol) was added portionwise at room temperature. After the mixture was stood overnight, the solvent was evaporated. The residual oil was crystallized from ethanol to give 3,4-diphenyl-2-[(1,2-dibenzoylvinyl)imino]-4-thiazoline in 88% yield. Mp 183.5—185.5 °C; IR (KBr) 1670, 1640 cm^{-1}; ^1H NMR ($CDCl_3$) δ=6.4 (s, 1H), 6.9 (s, 1H), 6.8—8.1 (m, 20H); MS, m/z (relative intensity) 486 (M^+, 14), 381 (65), 279 (100).

Reaction of 13 with 4b. To a stirred solution of **13** (1.26 g, 5.01 mmol) in 50 ml of chloroform, **4b** (933 mg, 6.57 mmol) in 50 ml of chloroform was added portionwise After the mixture was stood overnight, the solvent was evaporated. The residue was crystallized from ethanol to give 3,4-diphenyl-2-[[1,2-bis(methoxycarbonyl)vinyl]imino]-4-thiazoline in 83% yield. Mp 162—163 °C; IR (KBr) 1740, 1710, 1685 cm^{-1}; ^1H NMR ($CDCl_3$) δ=3.7 (s, 3H), 3.8 (s, 3H), 5.7 (s, 1H), 6.5 (s, 1H), 7.1—7.6 (m, 10H); MS, m/z (relative intensity) 394 (M^+, 78), 335 (94), 303 (100). Calcd for $C_{21}H_{18}N_2O_4S$: C, 63.95; H, 4.60; N, 7.10%. Found: C, 64.15; H, 4.67; N, 7.13%.

5-Ethoxycarbonyl-3,4-dimethyl-2-imino-4-thiazoline (14) was prepared by methylation of 2-amino-5-ethoxycarbonyl-4-methylthiazole[21] with trimethyloxonium tetrafluoroborate in 32% yield. Mp 76—77 °C; ^1H NMR ($CDCl_3$) δ= 1.30 (t, J=6 Hz, 3H), 2.50 (s, 3H), 3.30 (s, 3H), 4.20 (q, J=6 Hz, 2H), 6.85 (brs, 1H); High resolution MS, Calcd for $C_8H_{12}N_2O_2S$: 200.0617. Found: m/z 200.0496.

4,5-Bis(ethoxycarbonyl)-2-imino-3-methyl-4-thiazoline (15) was prepared by methylation of 2-amino-4,5-bis(ethoxycarbonyl)thiazole[22] with trimethyloxonium tetrafluoroborate in 35% yield. Oil; ^1H NMR ($CDCl_3$) δ=1.30 (t, J= 6 Hz, 3H), 1.40 (t, J=6 Hz, 3H), 3.30 (s, 3H), 4.20 (q, J= 6 Hz, 2H), 4.40 (q, J=6 Hz, 2H), 7.0—7.5 (brs, 1H); High resolution MS, Calcd for $C_{10}H_{14}N_2O_4S$: M, 258.0673. Found: m/z 258.0632.

Reaction of 14 with 4a. A mixture of **14** (418 mg, 2.09 mmol) and **4a** (554 mg, 2.37 mmol) in 25 ml of benzene was heated at 50 °C for one day. The reaction mixture was chromatographed (dry column chromatography, SiO_2) with dichlorometane as an eluent to give a vinyl compound in 93% yield. ^1H NMR ($CDCl_3$) δ=1.40 (t, J=6 Hz, 3H), 2.60 (s, 3H), 3.45 (s, 3H), 4.30 (q, J=6 Hz, 2H), 7.00 (s, 1H), 7.2—8.1 (m, 10H).

Reaction of 15 with 4b. A mixture of **15** (340 mg, 1.32 mmol) and **4b** (218 mg, 1.53 mmol) in 40 ml of methanol was heated at 50 °C for 5 h. About 1:1 mixture of vinyl compounds were obtained after chromatographic separation in 57% yield (And 40% of **15** was recovered). To the $CDCl_3$ solution was added chloroacetic acid, resulting in isomerization and the ratio of the compounds changed to 5:1. cis-vinyl: ^1H NMR ($CDCl_3$) δ=1.30 (t, J=7 Hz, 3H), 3.44 (s, 3H), 3.70 (s, 3H), 3.88 (s, 3H), 4.0—4.5 (m, 4H), 5.60 (s, 1H). trans-vinyl: ^1H NMR ($CDCl_3$) δ=1.41 (t, J=7 Hz, 3H), 3.44 (s, 3H), 3.70 (s, 3H), 3.81 (s, 3H), 4.1—4.6 (m, 4H), 6.29 (s, 1H).

References

1) a) G. L'abbé, *Tetrahedron*, **24**, 3537 (1982) and references therein; b) R. J. S. Beer and I. Hart, *J. Chem. Soc., Chem. Commun.*, **1977**, 143.

2) a) D. B. J. Easton, D. Leaver, and T. J. Rawlings, *J. Chem. Soc., Perkin Trans. 1*, **1972**, 41; b) B. R. O'Connor and F. N. Jones, *J. Org. Chem.*, **35**, 2002 (1970).

3) a) H. Behringer and R. Wiedenmann, *Tetrahedron Lett.*, **1965**, 3705; b) H. Behringer, D. Bender, J. Falkenberg, and R. Wiedenmann, *Chem. Ber.*, **101**, 1428 (1968).

4) a) G. Lang and J. Vialle, *Bull. Soc. Chim. Fr.*, **1967**, 2865; b) J. Goerdeler and H. W. Linden, *Tetrahedron Lett.*, **1975**, 3387; c) J. E. Oliver and R. T. Brown, *J. Org. Chem.*, **39**, 2228 (1978); d) K-y. Akiba, M. Ochiumi, T. Tsuchiya, and N. Inamoto, *Tetrahedron Lett.*, **1975**, 459; e) K-y. Akiba, T. Tsuchiya, and N. Inamoto, *ibid.*, **1976**, 1877; f) K-y. Akiba, T. Tsuchiya, N. Inamoto, K. Yamada, H. Tanaka, and H. Kawazura, *ibid.*, **1976**, 3819; g) K-y. Akiba, T. Tsuchiya, M. Ochiumi, and N. Inamoto, *ibid.*, **1975**, 455; h) M. S. Chauhan, M. E. Hassan, and D. M. McKinnon, *Can. J. Chem.*, **52**, 1738 (1974); i) A. Cuthbertson and C. Glidewell, *J. Mol. Struct.*, **90**, 227 (1982).

5) M. Baudy and A. Robert, *J. Chem. Soc., Chem. Commun.*, **1976**, 912.

6) M. V. Lakshmikantham and M. P. Cava, *J. Org. Chem.*, **41**, 879 (1976).

7) a) K-y. Akiba, K. Kashiwagi, Y. Ohyama, Y. Yamamoto, and K. Ohkata, *J. Am. Chem. Soc.*, **107**, 2721 (1985); b) Y. Yamamoto and K-y. Akiba, *ibid.*, **106**, 2713 (1984); c) K-y. Akiba, A. Noda, and K. Ohkata, *Phosphorus and Sulfur*, **16**, 111 (1983); d) K-y. Akiba, T. Kobayashi, and S. Arai, *J. Am. Chem. Soc.*, **101**, 5857 (1979); e) K-y. Akiba, S. Arai, T. Tsuchiya, Y. Yamamoto, and F. Iwasaki, *Angew. Chem., Int. Ed. Engl.*, **18**, 166 (1979).

8) The prefix cis and trans was based on the mode of addition, not on the configuration of the compound.

9) J. E. Dolfini, *J. Org. Chem.*, **30**, 1298 (1965).

10) K. Dimroth, C. Reichardt, T. Siepmann, and F. Bohlmann, *Justus Liebigs Ann. Chem.*, **661**, 1 (1963).

11) As previously noted **11b** was the secondary product and the ratio of thiazole to vinyls (**8b**/(**9b**+**10b**)) is meaningful.

12) R. Huisgen, B. Giese, and H. Huber, *Tetrahedron Lett.*, **1967**, 1883.

13) J. I. Musher, *Angew. Chem., Int. Ed. Engl.*, **8**, 54 (1969); J. C. Martin, *Science*, **221**, 509 (1983) and references cited therein.

14) R. E. Lutz and W. R. Smithey, *J. Org. Chem.*, **16**, 51 (1955).

15) E. H. Huntress, T. E. Lesslie, and J. Bornstein, *Org. Synth.*, Coll. Vol. 4, 329 (1963).

16) S. Shawali and O. Abdelhamid, *Tetrahedron Lett.*, **1975**, 163.

17) R. Fusco and C. Musante, *Gazz. Chim. Ital.*, **68**, 147 (1938).

18) D. S. Hector, *Ber.*, **22**, 1176 (1889); **23**, 357 (1890).

19) J. Goerdeler and W. Roth, *Chem. Ber.*, **96**, 534 (1963).
20) H. Bayer and G. Ruhlig, *Chem. Ber.*, **89**, 107 (1956).
21) R. M. Dodson and L. C. King, *J. Am. Chem. Soc.*, **67**, 2242 (1945).
22) L. H. Conover and D. S. Tarbell, *J. Am. Chem. Soc.*, **72**, 5221 (1950).