Cycloaddition-Elimination Reactions of 4-Methyl-5-phenylimino-Δ^2-1,2,3,4-thiatriazoline with Electrophilic Nitriles

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4-Methyl-5-phenyliminothiatriazoline **4** undergoes two consecutive cycloaddition-elimination reactions with ethyl cyanoformate and *p*-toluenesulfonyl cyanide in refluxing chloroform, and yields the 1,2,4-thiadiazolines **6a,b** *via* the isomers **5a,b**. In acetone as the solvent, the reactions occur at room temperature, due to the formation of the 1,2,4-oxathiazolidine **12** as the intermediate. When trichloroacetonitrile was used, only the decomposition products of **4**, namely **7** and **8** were obtained.

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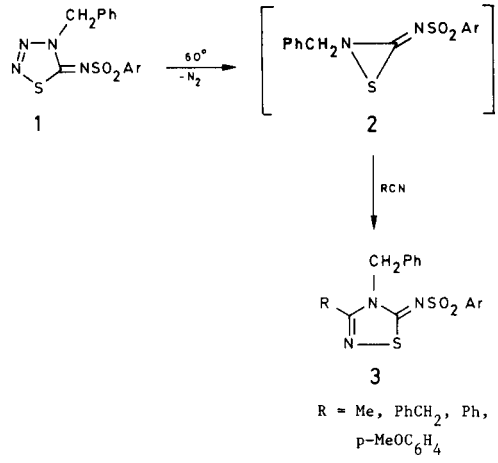
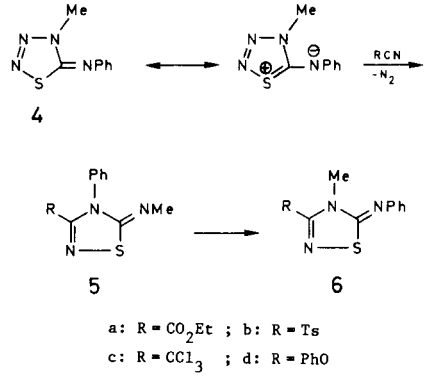
In previous work we have reported that 4-benzyl-5-sulfonyliminothiatriazolines **1** thermolyze in nitrile solution by first-order kinetics to yield 5-imino-1,2,4-thiadiazolines **3** [1]. These reactions were interpreted as proceeding via the elusive thiaziridinimines **2**, which are trapped by the nitriles acting as nucleophilic partners.



In contrast, 5-phenyliminothiatriazoline **4** reacts as a masked 1,3-dipole (see resonance structure) with electrophilic unsaturated systems [2], thus exhibiting a reactivity opposite to **1**. The results of our investigations with electrophilic nitriles are described in this paper.

Results and Discussion.

4-Methyl-5-phenyliminothiatriazoline **4** reacted with ethyl cyanoformate in refluxing chloroform with evolution of nitrogen and formation of the 1,2,4-thiadiazolines **5a** and **6a**. The reactions with one and three equivalents of nitrile were monitored by ^{1}H nmr spectroscopy by integration of the *N*-methyl singlets at δ 3.95 (**4a**), 2.97 (**5a**) and 3.75 (**6a**); the results are shown in Figures 1 and 2. Thus, **5a** was formed first and reached a maximum concentration of 48-49%, after which it decreased in intensity. Compound **6a** only appeared after an induction period, but constituted the major product at the end of the reaction.



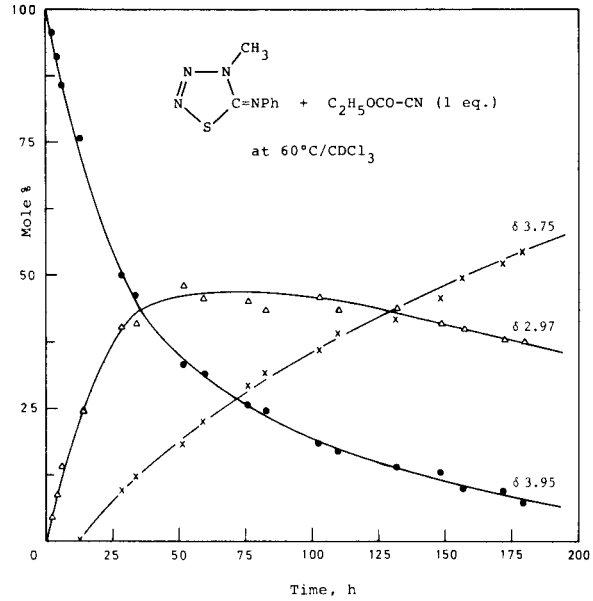


Figure 1. Reaction of **4** (0.5 *M*) with an equimolar amount of ethyl cyanoformate in deuteriochloroform at 60°. Relative concentrations of **4** (●), **5a** (△) and **6a** (x).

Both **5a** and **6a** were isolated under appropriate conditions and easily distinguished by the chemical shifts of the methyl and phenyl substituents in the ^{1}H and ^{13}C nmr spectra (see Experimental) [2a]. The methyl $^1J_{CH}$ coupling

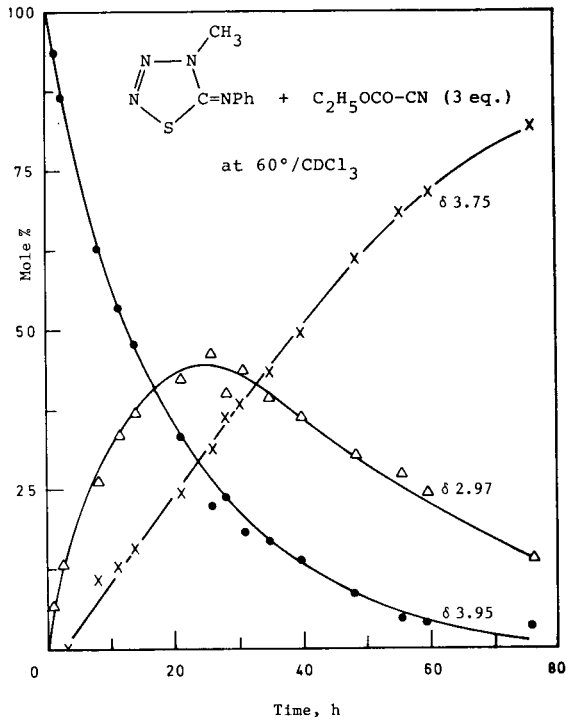
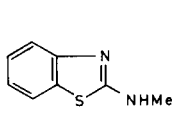


Figure 2. Reaction of **4** (0.5 *M*) with three equivalents of ethyl cyanoformate in deuteriochloroform at 60°. Relative concentations of **4** (●), **5a** (△) and **6a** (x).

constants (135 Hz for **5a** and 143 Hz for **6a**) also allow differentiation. Furthermore, the transformation of **4** into **6** is accompanied by a downfield shift of the C-5 carbon resonance (from δ 156 to 163, $\Delta\delta = 7$ ppm), similar to that observed in going from **1** to **3** [1a].

p-Toluenesulfonyl cyanide was more reactive towards **4** than was ethyl cyanoformate, and furnished **6b** as the only isolated product although no excess of reagent was used. The intermediate formation of **5b**, however, was inferred from the ^{1}H nmr spectra where a singlet was observed at δ 2.90 (10% after 1 hour), which disappeared as the reaction progressed.

No adduct was isolated from the reaction of **4** with trichloroacetonitrile. Upon heating in chloroform solution, 2-methylaminobenzothiazole **7** was formed as the major product together with a small amount of 2,4-dimethyl-3,5-diphenylimino-1,2,4-thiadiazolidine **8**; these are the decomposition products of **4** [3].



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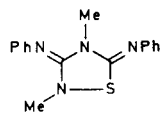

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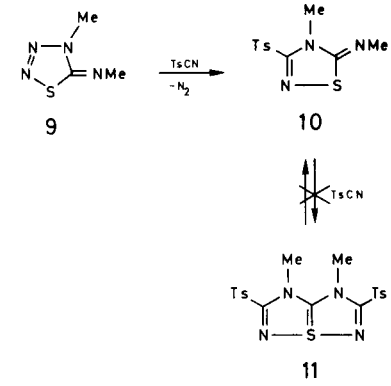
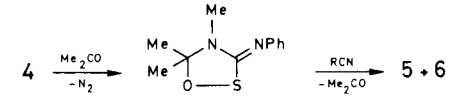
The isomerization of **5** into **6** is initiated by the presence of nitrile (see Figures 1 and 2) and may proceed via a thiapentalene intermediate [4]. Attempts to detect such a species by combining **10** with an excess of tosyl cyanide failed since no change was observed in the ^{1}H nmr spectrum. Compound **10** was obtained from **9** and tosyl cyanide and was expected to provide less crowded alkyl substituents for generating **11**.



9 10 11

The reactions of **4** with nitriles are accelerated by using acetone as solvent. The latter is known to form adduct **12** [3], which is capable of undergoing cycloaddition-elimination reactions with electrophilic nitriles at room temperature. This proved to be the method of choice for isolating **5a** since it constituted the sole reaction end-product. In the case of tosyl cyanide, however, **5b** (δ 2.85) remained at low concentration because it was transformed continuously into **6b** (δ 3.80) as the reaction progressed. Finally, when **12** was treated with one equivalent of trichloroacetonitrile at room temperature, the ^{1}H nmr spectrum indicated the presence of much **8** along with a compound, presumably corresponding to structure **5c**, having a methyl chemical shift at δ 2.9 (10% after 3.5 days).



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In this context, it is interesting to note that Martin *et al.* [5] briefly reported on the reaction of **4** with phenyl cyanate to yield **6d**. The reaction, however, was carried out in acetone as solvent and is now interpreted as proceeding *via* **12**. We have repeated the experiment in deuteriochloroform and have observed the formation of the two isomers **5d** and **6d**; the results are summarized in Table 1.

Table 1

Reaction of **4** (0.5 *M*) with 3 Equivalents of Phenyl Cyanate in Deuteriochloroform at Room Temperature

Time (min)	**4** (%) δ 3.9	**5d** (%) δ 2.9	**6d** (%) δ 3.5
4	68	21	11
22	41	35	24
30	31	33	36
overnight	0	0	100

EXPERIMENTAL

The thiatriazolin-5-imines **4** (mp 68°) and **9** (oil) were prepared by the procedure of Toubro and Holm [6].

Reaction of **4** with Ethyl Cyanoformate.

A. In Chloroform.

A solution of **4** (1.5 g, 7.8 mmoles) and ethyl cyanoformate (2.3 g, 23.4 mmoles) in chloroform (40 ml) was refluxed for 4 days. The solvent was removed and the residue was crystallized from dry hexane.

3-Ethoxycarbonyl-4-methyl-5-phenylimino-1,2,4-thiadiazoline (**6a**).

This compound was obtained in 92% yield (1.89 g), mp 82°; ir (potassium bromide): 1735 (s, CO), 1625 cm^{-1} (s, C=N); ^1H nmr (250 MHz, deuteriochloroform): δ 1.40 (t, 3H, CH_3), 3.75 (s, 3H, N-CH_3), 4.45 (q, 2H, CH_2), 7.0-7.4 (two m, 5 aromatic H); ^{13}C nmr (deuteriochloroform): δ 13.9 and 63.1 (Et), 33.2 (NCH_3, $^1J_{CH}$ = 143.2 Hz), 120.6 (Ph C_o), 124.1 (Ph C_p), 129.6 (Ph C_m), 148.0 (C-3), 149.9 (Ph C_i), 156.9 (CO), 162.9 (C-5); ms: (%) m/z 263 (100, M^+), 135 (31, $PhNCS^+$), 132 (73, $MeN=C=NPh^+$), 91 (51, PhN^+), 77 (38, Ph^+).

Anal. Calcd. for $C_{12}H_{13}N_3O_2S$ (mol wt 263): C, 54.74; H, 4.98. Found: C, 54.64; H, 4.89.

B. In Acetone.

A solution of **4** (1 g, 5.2 mmoles) and ethyl cyanoformate (1.5 g, 15.6 mmoles) in acetone (10 ml) was stirred at room temperature for 30 hours. After evaporation of the solvent, the resulting oil was triturated with ether (10 ml) and 12 drops of n-hexane to give, after cooling, a precipitate of **5a**.

3-Ethoxycarbonyl-5-methylimino-4-phenyl-1,2,4-thiadiazoline (**5a**).

This compound was obtained in 37% yield (0.5 g), mp 88° (ether/*n*-hexane); ir (potassium bromide): 1744 (s, CO), 1658 cm^{-1} (s, C=N); ^1H nmr (250 MHz, deuteriochloroform): δ 1.15 (t, 3H, CH_3), 2.97 (s, 3H, N-CH_3), 4.20 (q, 2H, CH_2), 7.25-7.55 (two m, 5 aromatic H); ^{13}C nmr (deuteriochloroform): δ 13.6 and 62.7 (Et), 41.6 (NCH_3, $^1J_{CH}$ = 135 Hz), 127.5 (Ph C_o), 129.1 (Ph C_p), 129.4 (Ph C_m), 135.9 (Ph C_i), 148.9 (C-3), 156.7 (CO), 162.3 (C-5); ms: (%) m/z 263 (39, M^+), 262 (87), 132 (100, $MeN=C=NPh^+$), 117 (28, $PhNCN^+$), 104 (21, $PhNCH^+$), 77 (34, Ph^+).

Anal. Calcd. for $C_{12}H_{13}N_3O_2S$ (mol wt 263): C, 54.74; H, 4.98. Found: C, 54.79; H, 4.94.

Reaction of **4** with *p*-Toluenesulfonyl Cyanide.

A solution of **4** (1.5 g, 7.8 mmoles) and tosyl cyanide (1.4 g, 7.8 mmoles) in dry chloroform (40 ml) was refluxed for 1 day. After removal of the solvent, the residue was crystallized from ether.

4-Methyl-5-phenylimino-3-(p-toluenesulfonyl)-1,2,4-thiadiazoline (**6b**).

This compound was obtained in 38% yield (1.0 g), mp 112° (ether); ir (potassium bromide): 1620 and 1585 cm^{-1} (s); ^1H nmr (250 MHz, deuteriochloroform): δ 2.5 (s, 3H, CH_3), 3.80 (s, 3H, N-CH_3), 6.9-8.0 (m, 9 aromatic H); ^{13}C nmr (deuteriochloroform): δ 21.9 (CH_3), 32.3 (NCH_3, $^1J_{CH}$ = 142.5 Hz), 120.5 (Ph C_o), 124.4 (Ph C_p), 129.7, 129.9, 130.0 (Ph C_m and Tol CH), 132.9 (Tol C_p), 146.9 (Tol C_i), 149.4 (Ph C_i), 154.9 (C-3), 161.8 (C-5); ms: (%) m/z 345 (100, M^+), 135 (45, $PhNCS^+$), 132 (50, $MeN=C=NPh^+$), 91 (44, $C_7H_7^+$), 77 (31, Ph^+).

Anal. Calcd. for $C_{16}H_{15}N_3O_2S_2$ (mol wt 345): C, 55.64; H, 4.38. Found: C, 55.56; H, 4.27.

Reaction of **4** with Trichloroacetonitrile.

A solution of **4** (1.5 g, 7.8 mmoles) and trichloroacetonitrile (1.1 g, 7.8 mmoles) in dry chloroform (40 ml) was refluxed for 7 days. The solvent was removed and the residue was crystallized from dry ether.

2-Methylaminobenzothiazole (**7**) was obtained in 48% yield (0.61 g), mp 136° (lit [7] 140°). This compound was identical in all respects with an authentic sample. **Note**: When the reaction was carried out in deuteriochloroform for 66 hours, the ^1H nmr spectrum showed the presence of unreacted **4** (δ 3.9, 4%), **7** (δ 3.09, 82%) and **8** (δ 2.75 and 3.45, 14%).

Reaction of **9** with *p*-Toluenesulfonyl Cyanide.

A solution of **9** (1.0 g, 7.9 mmoles) and tosyl cyanide (1.5 g, 8.3 mmoles) in chloroform (40 ml) was refluxed for 4 hours. The solvent was removed, the residue was dissolved in dry *n*-hexane, filtered and the filtrate allowed to crystallize.

4-Methyl-5-methylimino-3-(p-toluenesulfonyl)-1,2,4-thiadiazoline (**10**).

This compound was obtained in 78% yield (1.7 g), mp 119° (ether); ir (potassium bromide): 1665 cm^{-1} (s); ^1H nmr (250 MHz, deuteriochloroform): δ 2.5 (s, 3H, CH_3), 3.0 (s, 3H, $=NCH_3$), 3.65 (s, 3H, N-CH_3), 7.4 and 7.9 (two d, 4 aromatic H); ^{13}C nmr (deuteriochloroform): δ 21.8 (CH_3), 31.7 (NCH_3, $^1J_{CH}$ = 142.5 Hz), 40.9 ($=NCH_3$, $^1J_{CH}$ = 135 Hz), 129.8, 129.9 (Tol CH), 132.9 (Tol C_p), 146.8 (Tol C_i), 155.5 (C-3), 161.9 (C-5); ms: (%) m/z 283 (100, M^+), 139 (29, $TolSO^+$), 128 (59, M^+-Tos), 105 (32), 91 (49, $C_7H_7^+$), 87 (55), 73 (15, $MeNCS^+$), 65 (22).

Anal. Calcd. for $C_{11}H_{13}N_3O_2S_2$ (mol wt 283): C, 46.64; H, 4.63. Found: C, 46.69; H, 4.57.

Kinetics.

The nmr tubes containing **4** (0.5 *M*) and one or three mole-equivalents of ethyl cyanoformate in deuteriochloroform were placed in a thermostat at 60° (±0.1°). At several time intervals the nmr tubes were cooled to 0° and analyzed by ^1H nmr spectroscopy (90 MHz). The concentrations of the products were followed by integration of the *N*-methyl singlets in the spectra (δ 3.95 for **4**, δ 2.97 for **5a** and δ 3.75 for **6a**) and the results are plotted in Figures 1 and 2.

Acknowledgement.

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