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CYCLOADDITION-ELIMINATION REACTIONS OF 4-METHYL-5-PHENYLIMINO-Δ^2-1,2,3,4-THIATRIAZOLINE WITH STRONG ELECTROPHILIC ISOTHIOCYANATES. MECHANISM OF THE ISOMERIZATION PROCESS

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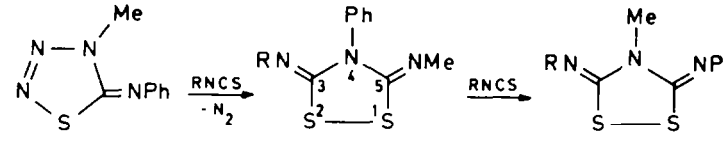
ABSTRACT. The 3,5-bis(substituted)imino-1,2,4-dithiazolidines (2), obtained from 4-alkyl-5-arylimino-1,2,3,4-thiatriazolines and isothiocyanates, rearrange to isomeric 3,5-bis(substituted)imino-1,2,4-dithiazolidines (3) by way of a cycloaddition-elimination reaction with the isothiocyanates. The previously suggested mechanism via a Dimroth rearrangement is now disproven by cross experiments.

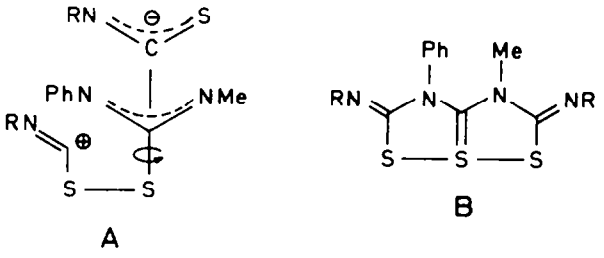
Some years ago we reported that 4-methyl-5-phenylimino-1,2,3,4-thiatriazoline (1) reacts as a masked 1,3-dipole with the C=S bond of carbonyl isothiocyanates to give 2a-c after elimination of nitrogen.[1,2] In the presence of an excess of isothiocyanate, 3a-c are obtained instead of 2a-c. Similar results were found during the present research for the reactions of 1 with picryl isothiocyanate (PiNCS) and tosyl isothiocyanate (TsNCS), yielding either 2d,e or 3d,e depending on the amount of isothiocyanate used.

What is the mechanism of the isomerization reaction 2 → 3 ? Earlier,[1,3] we assumed that the isothiocyanate complexes with the amidine moiety of 2 by cleavage of the heterocyclic C3-N4 bond to give intermediate A, which, after rotation around the C-S bond and elimination of isothiocyanate, recloses to 3.



1 2 3

	a	b	c	d	e
R	PhCO	p-ClC$_6$H$_4$CO	EtOCO	Picryl	Ts

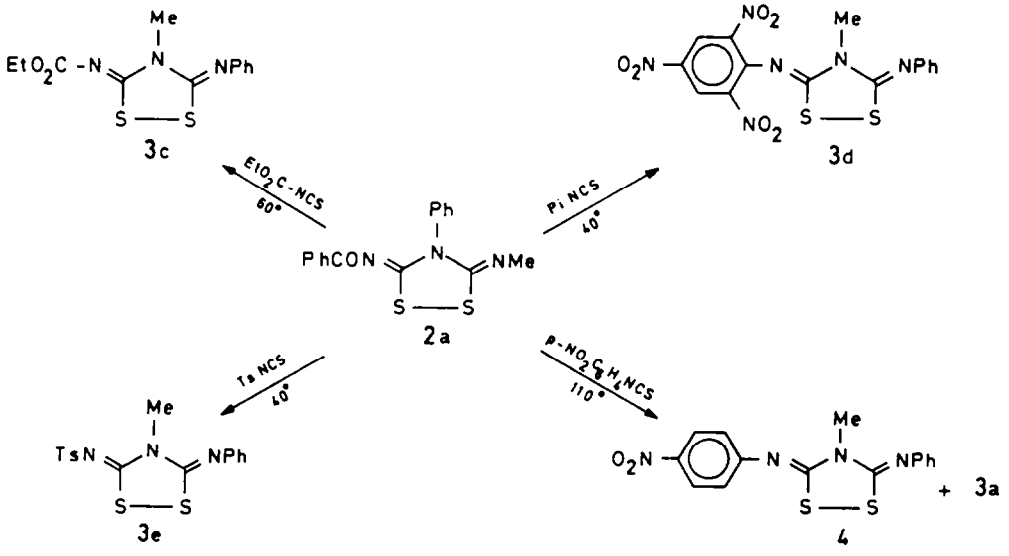


This picture, however, suffers from the disadvantage that the positive charge on the imine function would be destabilized by the electron-withdrawing R-substituent.

An alternative and more attractive mechanism to be considered, is that 2 cycloadds with a second molecule of isothiocyanate to give the hypervalent sulfur intermediate B,[4,5] which would then give the thermodynamically most stable isomer 3 by elimination of the first isothiocyanate.

In order to test this possibility, we have carried out a series of cross experiments using isothiocyanates with different R-substituents; the results are shown in Scheme I. Thus, the electrophilic isothiocyanates are incorporated into the final products, indicating that 2a indeed reacts as a masked

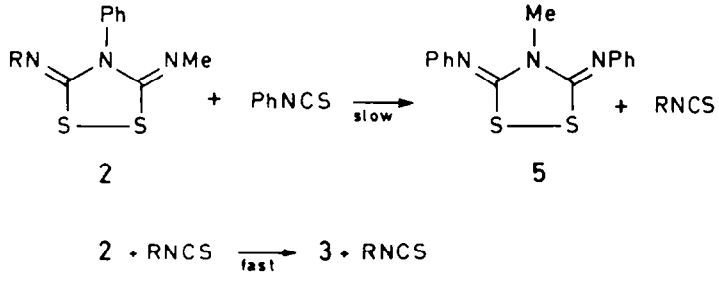
Scheme I



1,3-dipole with elimination of benzoyl isothiocyanate. The minor product 3a (8%), obtained with p-nitrophenyl isothiocyanate (see Scheme I), may result from the reaction of the eliminated benzoyl isothiocyanate with unreacted 2a. Compound 2d was similarly transformed into 3e by tosyl isothiocyanate at 40°.

Several isomerizations of 2 into 3 have been induced by less electrophilic isothiocyanates, such as phenyl isothiocyanate, without the isolation of crossover products. Examples are the reactions 2a → 3a, 2c → 3c,[1] and 2e → 3e which occur in refluxing toluene in the presence of phenyl isothiocyanate. A rationalization via intermediate A is untenable, since it does not explain why phenyl isothiocyanate would react differently from the other isothiocyanates with 2. We therefore propose Scheme II which includes a slow cycloaddition-elimination reaction of 2 with phenyl isothiocyanate at higher temperature to give the heterocycle 5 in addition to a highly reactive isothiocyanate (RNCS: R = PhCO, EtOCO, Ts). The latter would then be responsible for the fast isomerization of 2 into 3 (via B) without being consumed.

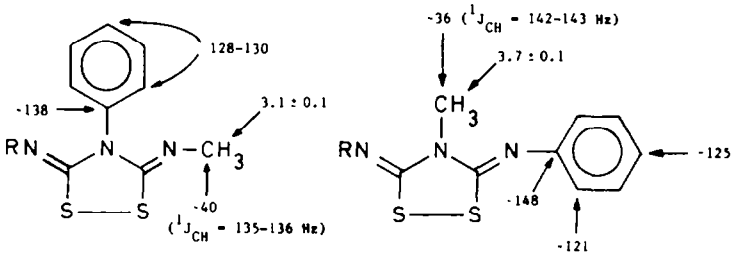
Scheme II



Support for this mechanism is found in the NMR spectrum when 2a (0.25 M) was heated with a fourfold excess of phenyl isothiocyanate in toluene (100°, 4 days). After replacement of toluene by deuteriochloroform, absorptions for 2a (δ 3.1, 19%) and 3a (δ 3.9, 77%) were observed in addition to a resonance peak at δ 3.6 (4%), corresponding exactly to the position expected for 5.[6] Addition of authentic 5 to the NMR tube increased the intensity of the peak already present at δ 3.6, thus leaving no doubt about the structure assignment.

All new products were fully characterized by spectral methods (see Experimental). A distinction between the endocyclic and exocyclic positions of the methyl and phenyl substituents was made on the basis of ^{1}H and ^{13}C NMR criteria discussed previously,[1] and summarized in Scheme III.

Scheme III



EXPERIMENTAL

All the compounds are numbered as shown on structure 2. 4-Methyl-5-phenylimino-1,2,3,4-thiatriazoline (1) and 3-benzoylimino-5-methylimino-4-phenyl-1,2,4-dithiazolidine (2a) were prepared following the procedures of the literature.[1,7]

5-Methylimino-3-picrylimino-4-phenyl-1,2,4-dithiazolidine (2d).

Equimolar amounts (7.4 mmol) of 1 (1.42 g) and picryl isothiocyanate[8] (2 g) were stirred in 15 ml of dry chloroform at 60°C for 1 hour. After removing the solvend in vacuo, the residue was crystallized (without heating) from chloroform-ether to give 2d in 89% yield (2.86 g), mp 174°C; IR (KBr) 1630 and 1600 cm^{-1} (s); ^1H NMR (250 MHz, $CDCl_3$) δ 3.2 (s, 3H, CH_3), 7.2-7.6 (two m, 5H, Ph), 9.0 (s, 2H, picryl); ^{13}C NMR ($CDCl_3$) δ 39.4 (CH_3, $^1J_{CH}$ = 136.5 Hz), 124.7, 141.0, 142.1 and 142.3 (picryl C-atoms), 128.8, 129.8, 129.9 and 137.4 (Ph C-atoms), 150.3 (C-5, $^3J_{CH}$ = 10.1 Hz), 158.7 (C-3).

Anal. Calcd for $C_{15}H_{10}N_6O_2S_2$ (mol wt 434): C, 41.47; H, 2.30. Found: C, 41.47; H, 2.29.

5-Methylimino-4-phenyl-3-tosylimino-1,2,4-dithiazolidine (2e).

To a solution of 1 (1 g, 5.2 mmol) in 10 ml of dry dichloromethane was added one equivalent of tosyl isothiocyanate[9] (1.108 g) and the whole was stirred at room temperature for 45 minutes. Compound 2e crystallized out in 79.3% (1.555 g), mp 219°C; IR (KBr) 1645 (s), 1500 cm^{-1} (s); ^1H NMR (250 MHz, DMSO-d_6) δ 2.4 (s, 3H, CH_3Ar), 3.0 (s, 3H, CH_3N), 7.2-7.65 (three m, 9H, aryl); ^{13}C NMR (DMSO-d_6) δ 20.9 (CH_3Ar), 39.1 (CH_3N, $^1J_{CH}$ = 136.1 Hz), 125.9, 128.3, 128.9, 129.3, 129.6, 137.6, 138.1 and 143.4 (aryl C-atoms), 151.9 (C-5), 167.9 (C-3).

Anal. Calcd for $C_{16}H_{15}S_3O_2N_3$ (mol wt 377): C, 50.92; H, 3.97. Found: C, 50.84; H, 3.93.

3-Ethoxycarbonyl-4-methyl-5-phenylimino-1,2,4-dithiazolidine (3c).

A solution of 2a (200 mg, 0.61 mmol) and three equivalents of ethoxycarbonyl isothiocyanate (240 mg) in 2.5 ml of chloroform was heated at 60°C for 6 hours. The reaction mixture was subjected to preparative tlc on silica gel with n-hexane-ether as the eluate to give 3c in 22% yield (40 mg), mp 100°C. The spectral data were identical with those reported.[1]

4-Methyl-3-picrylimino-5-phenylimino-1,2,4-dithiazolidine (3d).

Equimolar amounts (0.35 mmol) of 2d (150 mg) and picryl isothiocyanate (94 mg) were heated in 2 ml of dry chloroform at 60°C. The reaction was subjected to preparative tlc with dichloromethane as the eluate, giving 3d in 43% yield (65 mg), mp 248°C; IR (KBr) 1625 and 1610 cm^{-1} (s); ^1H NMR (250 MHz, $CDCl_3$) δ 3.65 (s, 3H, CH_3), 7.0-7.5 (three m, 5H, Ph), 9.0 (s, 2H, picryl); ^{13}C NMR ($CDCl_3$) δ 35.6 (CH_3, $^1J_{CH}$ = 143.5 Hz), 120.7, 125.7, 129.8 and 147.5 (Ph C-atoms), 124.6, 141.3, 142.0 and 142.6 (picryl C-atoms), 151.9 (C-5), 159.1 (C-3).

Anal. Calcd for $C_{15}H_{10}N_6O_6S_2$ (mol wt 434): C, 41.47; H, 2.30. Found: C, 41.61; H, 2.27.

This compound was also obtained by reacting 2a (200 mg, 0.61 mmol) with picryl isothiocyanate (329 mg, 1.22 mmol) in 2.5 ml of dry dichloromethane at 40°C for 3 days. The precipitate was filtered off and crystallized from ethanol-acetonitrile to give 3d in 31% yield (82 mg).

4-Methyl-5-phenylimino-3-tosylimino-1,2,4-dithiazolidine (3e).

A solution of 2e (200 mg, 0.53 mmol) and tosyl isothiocyanate (339 mg, 1.59 mmol) in 2 ml of dry dichloromethane was stirred at 40°C for 4 hours. Upon addition of n-hexane, 3e crystallized out in 81% yield (162 mg), mp 164°C; IR (KBr) 1650 (s), 1515 cm^{-1} (s); ^1H NMR (90 MHz, $CDCl_3$) δ 2.50 (s, 3H, CH_3Ar), 3.60 (s, 3H, CH_3N), 6.9-8.1 (three m, 9 aromatic H); ^{13}C NMR ($CDCl_3$) δ 21.6 (CH_3Ar), 36.6 (CH_3N, $^1J_{CH}$ = 143 Hz), 125.5 and 148.2 (C_p and C_i Ph), 137.6 and 144.0 (C_i and C_p Ts), 120.4, 126.9, 129.6 and 129.7 (aromatic CH), 152.7 (C-5), 166.2 (C-3).

Anal. Calcd for $C_{16}H_{15}N_3O_2S_3$ (mol wt 377): C, 50.92; H, 3.97. Found: C, 50.90; H, 3.90.

This compound was also obtained by reacting 2a (200 mg, 0.61 mmol) with tosyl isothiocyanate (39.1 mg, 1.83 mmol) in 2.5 ml of dry dichloromethane at 40°C for 5 hours. After addition of ether and cooling, 3e crystallized out in 71% yield (163 mg).

This compound was also obtained by heating 2e (200 mg, 0.53 mmol) with phenyl isothiocyanate (286 mg, 2.12 mmol) in 2.5 ml of toluene at 100°C for 4 days. After addition of n-hexane, 3e crystallized out in 70.5% yield (141 mg).

This compound was also obtained by heating 2d (150 mg, 0.35 mmol) with tosyl isothiocyanate (221 mg, 1.04 mmol) in 2 ml of dry dichloromethane at 40°C for 4 hours. Preparative tlc on silica gel with dichloromethane as the eluate furnished 3e in 58% yield (75 mg).

4-Methyl-3-(p-nitrophenyl)imino-5-phenylimino-1,2,4-dithiazolidine (4).

A solution of 2a (0.5 g, 1.53 mmol) and p-nitrophenyl isothiocyanate (1.38 g, 5 equiv.) in 10 ml of dry toluene was stirred at 100°C for 4 days. The reaction mixture was subjected to column chromatography on silica gel with dichloromethane as the eluent to give 3a (8.5%) and 4 in 59% yield (310 mg), mp 115°C; IR (KBr) 1620 cm^{-1} (s); ^1H NMR (250 MHz, $CDCl_3$) δ 3.65 (s, 3H, CH_3), 6.9-7.4 (four m, 7 aromatic H), 8.2 (d, 2 aromatic H); ^{13}C NMR ($CDCl_3$) δ 35.4 (CH_3, $^1J_{CH}$ = 142.8 Hz), 121.9, 125.4, 144.6 and 154.4 ($p\text{-}NO_2C_6H_4$), 121.0,

125.2, 129.6 and 148.3 (Ph C-atoms), 153.2 and 154.8 (C-3 and/or C-5).

Anal. Calcd for $C_{15}H_{12}N_4O_2S_2$ (mol wt 344): C, 52.33; H, 3.49. Found: C, 52.40; H, 3.52.

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