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Synthesis of Thiazolo[4,3-a]isoindoles by Intramolecular Cycloaddition-Elimination Reactions of 4-Methyl-5-(substituted)imino-Δ^2-1,2,3,4-thiatriazolines

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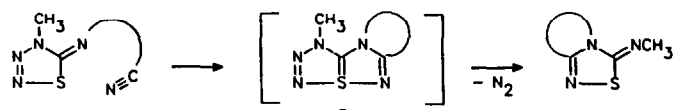
Abstract: Fused thiazolidine **11** and thiazoline derivatives **19a-c** are obtained by intramolecular cycloaddition-elimination reactions of appropriately substituted 5-iminothiatriazolines **10** and **18a-c**. The incorporation of a sidechain phenyl group excercises a favorable effect on cyclization since no reaction is observed with **25**. Comparable intermolecular reactions also fail to occur.

Recently we reported that 5-(cyano tethered)imino-Δ^2-1,2,3,4-thiatriazolines **1** thermolyze with loss of nitrogen to give fused 1,2,4-thiadiazole derivatives **3**.[1] These intramolecular cycloaddition-elimination reactions are assumed to proceed via thiapentalenoid intermediates **2** having a tetravalent sulfur atom.[2] In continuation of this research we have now extended this reaction principle to 5-imino-1,2,3,4-thiatriazolines bearing an olefin or acetylene group at the imine function. The results are discussed below.

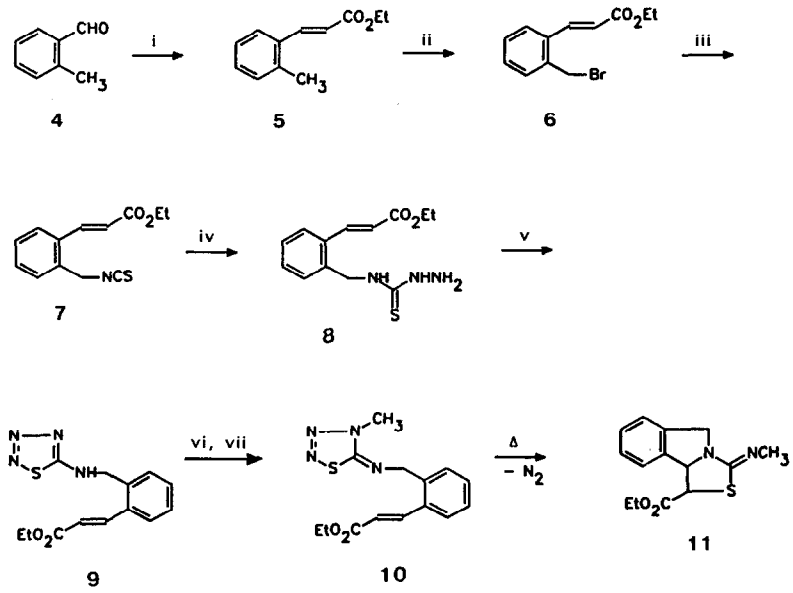


1 2 3

A convenient method for the synthesis of the functionalized thiatriazoline **10** starts from o-tolualdehyde **4** and proceeds through a series of transformations outlined in Scheme 1. Thus, the Wittig-Horner olefination of **4** with diethyl ethoxycarbonylmethylphosphonate in a two-phase liquid-solid system[3] furnished ethyl cinnamate **5** in high yield. This compound was brominated with N-bromosuccinimide following a known procedure[4] and then converted into the thiatriazole **9** by a classical method.[5] Methylation of **9** was performed with Meerwein's reagent and produced exclusively the N-4 methylated product **10**.[6] This compound was fully characterized by spectral methods (IR, ^{1}H NMR and ^{13}C NMR)

and microanalysis, but it deteriorated at room temperature on standing for a few weeks. On refluxing in chloroform for 3 days it thermolyzed with extrusion of nitrogen and formation of the thiazolo[4,3-a]isoindole **11**.

Scheme 1

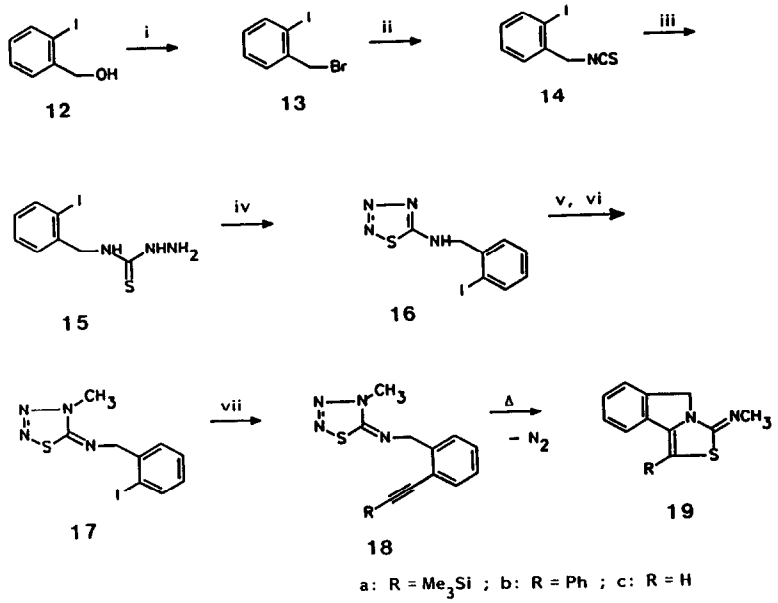


Reagents: i, $(EtO)_2P(O)CH_2CO_2Et/KOH$; ii, NBS; iii, KSCN; iv, N_2H_4; v,HNO_2; vi, $Me_3O^+BF_4^-$; vii, NaOH.

We next prepared the thiatriazolines **18a-c** having an acetylene function at the appropriate position for cyclization. o-Iodobenzyl alcohol **12** is a suitable starting material for this purpose and was transformed into the thiatriazolinimine **17** by conventional reactions (Scheme 2). The conversion of **17** into **18a,b** with terminal acetylenes in the presence of copper(I) iodide/bis(triphenylphosphine)palladium dichloride and triethylamine is based on Hagihara's publication[7] and proceeds smoothly and in high yield. Thermolysis of **18a,b** in refluxing benzene for 3 days provided the thiazolo[4,3-a]isoindoles **19a,b**. Also, the parent acetylene **18c**, prepared by desilylation of **18a**, furnished the fused isoindole **19c** upon heating in benzene.

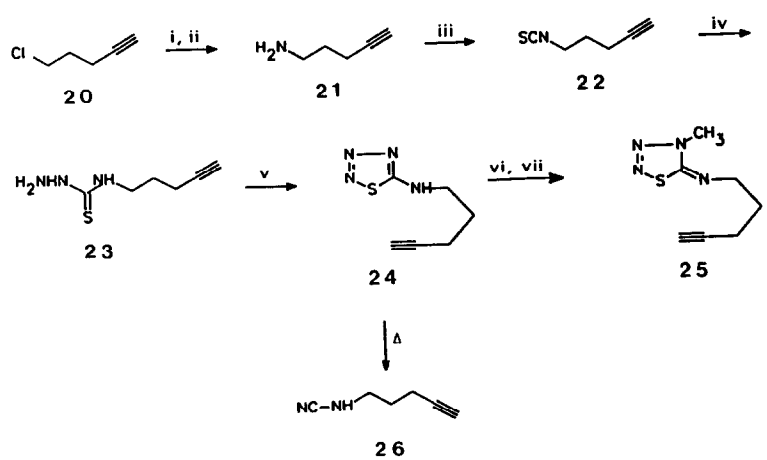
In the examples **10** and **18a-c** so far discussed the phenyl group facilitates the cycloaddition-elimination reaction by restricting the sidechain mobility and perhaps also by activating the multiple bond. In its absence, no such reaction was observed. Thus, thiatriazolinimine **25**, synthesized from 5-chloro-1-pentyne as shown in Scheme 3, proved to be thermally more stable than expected. It was recovered from an ethanol solution after heating overnight at 70°C, or from a toluene solution after refluxing for 4 hours.[8] In contrast, thiatriazole **24** is unstable at room temperature and was already partially decomposed into cyanamide **26** when the ^{13}C NMR spectrum was recorded in deuterated chloroform.

Scheme 2



Reagents: i, $SOBr_2$; ii, KSCN; iii, N_2H_4; iv, HNO_2; v, $Me_3O^+BF_4^-$; vi, NaOH; vii, $RC{\equiv}CH/(Ph_3P)_2PdCl_2/CuI/NEt_3$

Scheme 3



Reagents: i, potassium phthalimide; ii, N_2H_4; iii, $CSCl_2$; iv, N_2H_4; v, HNO_2; vi, $Me_3O^+BF_4^-$; vii, NaOH

For comparison with intermolecular reactions we have examined the reactivity of thiatriazoline **27** towards a fivefold excess of trimethylsilylacetylene and ethyl acrylate in deuterated chloroform at 50°C. When the reactions were followed by ^{1}H NMR spectroscopy during 1 week the methyl singlet of **27** at δ 3.95 disappeared slowly in favor of singlets at δ 2.6 and 3.5 of equal intensity, whereas the acetylene and acrylate resonances remained unaltered. The new peaks correspond exactly to the positions expected for the thiadiazolidine **28**. This was confirmed by adding authentic **28** to the NMR samples, thus increasing the intensities of the peaks already present at δ 2.6 and 3.5. Compound **28** is a known decomposition product of **27**.[9]

27 28

EXPERIMENTAL

5-[2-(Ethoxycarbonylvinyl)benzyl]amino-1,2,3,4-thiatriazole (9).

A solution of **4** (6 g, 50 mmol) and diethyl ethoxycarbonylmethylphosphonate (11.21 g, 50 mmol) in tetrahydrofuran (50 ml) was added to a stirred suspension of powdered KOH (5.61 g, 0.1 mol) in tetrahydrofuran (100 ml). After stirring for 30 min. the solvent was removed and the residue suspended in water (200 ml) and extracted twice with dichloromethane (200 ml). The combined extracts were washed with water (200 ml), dried ($MgSO_4$) and evaporated to give **5** as an oil in 89% yield (8.5 g).

This compound (8.5 g, 45 mmol) was reacted with N-bromosuccinimide (8.2 g, 46 mmol) and dibenzoyl peroxide (1 g) in refluxing carbon tetrachloride (200 ml) for 3-4 h. The cooled mixture was filtered and the filtrate was evaporated to give **6** as an oil which was used without further purification.

This compound was heated with potassium thiocyanate (8.9 g, 92 mmol) and sodium iodide (1 g) in dimethylformamide (60 ml) at 90°C for 7 h. The reaction mixture was poured into water (300 ml) and extracted twice with diethyl ether (300ml). The combined ether extracts were washed with water (300 ml), dried ($MgSO_4$) and chromatographed on silica gel with diethyl ether/light petroleum (1:1) as the eluent to give **7** in 44% overall yield (two steps from **5**, 4.85 g), mp 54-55°C (from EtOH at -16°C).

Aq. hydrazine (51%, 0.9 g), dissolved in ethanol (20 ml), was added dropwise to a stirred solution of **7** (4 g, 14 mmol) in ethanol (80 ml) at 0/-10°C. After 15 min. the resulting precipitate **8** was filtered off and washed with diethyl ether; yield 75% (3 g), mp 126-128°C.

To an ice-cooled suspension of this compound (2.9 g, 10 mmol) in a biphasic mixture of 10% hydrochloric acid (100 ml) and diethyl ether (150 ml) was added dropwise with stirring aq. sodium nitrite (2.53 g in 15 ml). When all the solids were dissolved, the two layers were separated and the aqueous phase was extracted with diethyl ether (100 ml). The combined organic fractions were washed successively with a saturated $NaHCO_3$ solution (150 ml) and water (150 ml), dried ($MgSO_4$) and evaporated to give **9** in 84% yield (2.53 g), mp with decomp. 101-103°C (from Et_2O/light petroleum); IR (KBr) 3200 (m, NH), 1715 cm^{-1} (s, CO); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.28 (t, 3 H, CH_3), 4.17 (q, 2 H, CH_2), 4.74 (d, 2 H, CH_2N), 6.35 and 7.93 (2 d, 2 H, CH=CH, J = 16 Hz), 7.35-7.65 (3 m, 4 aromatic H), 7.83 (br, 1 H, NH); ^{13}C NMR ($CDCl_3$) δ 14.2 and 60.8 (Et), 49.8 (CH_2N), 121.5 and 140.4 (C=CAr), 127.4, 129.1, 129.7, 130.3, 133.8 and 133.9 (aromatic C-atoms), 166.5 (CO), 178.2 (C-5). Anal. Calcd for $C_{13}H_{14}N_4O_2S$ (mol wt 290): C, 53.78; H, 4.86. Found: C, 53.61; H, 4.83.

5-[2-(Ethoxycarbonylvinyl)benzyl]imino-4-methyl-Δ^2-1,2,3,4-thiatriazoline (10).

A suspension of **9** (1.7 g, 5.9 mmol) and one equivalent of trimethyloxonium tetrafluoroborate (0.87 g) in dry dichloromethane (50 ml) was stirred at 5°C for 48 h. The resulting solution was treated with aq. NaOH (10 g in 150 ml) and then extracted twice with dichloromethane (100 ml). The combined extracts were washed with water (200 ml), dried ($MgSO_4$) and evaporated. The residue was chromatographed on silica gel with diethyl ether/light petroleum (1:1) as the eluent to give **10** in 72% yield (1.3 g), mp 62-63°C (from ethanol/light petroleum); IR (KBr) 1710 (s, CO), 1640 (s, C=N); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.33 (t, 3 H, CH_3), 3.82 (s, 3 H, CH_3N), 4.26 (q, 2 H, CH_2), 4.36 (s, 2 H, CH_2N), 6.36 and 8.01 (2 d, 2 H, CH=CHAr, J = 16 Hz), 7.3-7.4 (dd + 2 td, 3 aromatic H), 7.59 (dd, 1 aromatic H); ^{13}C NMR ($CDCl_3$) δ 14.3, 60.1 and 60.4 (Et and CH_2N), 34.1 (CH_3N), 119.9 and 141.8 (C=CAr), 126.8, 127.9, 129.3, 129.9, 133.5 and 137.7 (aromatic C-atoms), 156.1 (C-5), 166.8 (CO). Anal. Calcd for $C_{14}H_{16}N_4O_2S$ (mol wt 304): C, 55.25; H, 5.29. Found: C, 55.09; H, 5.21.

1-Ethoxycarbonyl-5,9b-dihydro-3-methylimino-1*H*,3*H*-thiazolo[4,3-a]isoindole (11).

Compound **10** (1.2 g, 3.9 mmol) was dissolved in chloroform (40 ml) and heated at 65°C for 3 days. After evaporation of the solvent, the residual oil was chromatographed on silica gel with diethyl ether/light petroleum (3:1) as the eluent to give **11** in 71% yield (0.77 g), mp 102°C (from Et_2O at -16°C); IR (KBr) 1736 (s, CO), 1650 cm^{-1} (s, C=N); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.37 (t, 3 H, CH_3), 3.10 (s, 3 H, CH_3N), 4.30-4.40 (m, 2 H, CH_2O), 4.45 (d, 1 H, H-1), 4.60 and 4.90 (2 d, 2 H, CH_2), 5.60 (d, 1 H, H-9b), 7.2-7.4 (m + d, 4-aromatic H); ^{13}C NMR ($CDCl_3$) δ 14.1 and 62.3 (Et), 41.2 (CH_3N, $^1J_{CH}$ = 135 Hz), 52.6 (C-1, $^1J_{CH}$ = 146 Hz), 53.3 (C-5), 69.4 (C-9b, $^1J_{CH}$ = 151 Hz), 122.7, 123.0, 127.7, 128.6, 138.3 and 139.2 (aromatic C-atoms), 157.8 (C-3), 169.0 (CO); mass spectrum, m/z (%) 276 (3, $M^{+\cdot}$), 203 (100, $M^{+\cdot}$ - CO_2Et), 131 (19), 130 (34, $M^{+\cdot}$ - CO_2Et - MeNCS), 117 (23). Anal. Calcd for $C_{14}H_{16}N_2O_2S$ (mol wt 276): C, 60.85; H, 5.84. Found: C, 60.94; H, 5.71.

5-(2-Iodobenzyl)amino-1,2,3,4-thiatriazole (16).

To a suspension of **12** (10 g, 43 mmol) in chloroform (50 ml) was added dropwise one equivalent of thionyl bromide (8.9 g) dissolved in chloroform (20 ml). The resulting clear solution was refluxed for 3 h. After cooling, chloroform (100 ml) was added and the solution was washed successively with a saturated $NaHCO_3$ solution (100 ml) and water (100 ml), then dried ($MgSO_4$) and evaporated to give **13** in 95% yield (12.1 g), mp 55-56°C (from light petroleum).

This compound (12 g, 40 mmol) was heated with potassium thiocyanate (7.85 g, 80 mmol) and sodium iodide (0.5 g) in dimethylformamide (50 ml) at 95-100°C for 7 h. The reaction mixture was poured into water (200 ml) and extracted with diethyl ether (200 ml). The extract was washed twice with water (200 ml); dried ($MgSO_4$) and evaporated. The residue was chromatographed on silica gel using diethyl ether/light petroleum (1:3) as eluent to give two products: **14** as an oil in 62% yield (6.8 g) and o-iodobenzyl thiocyanate in 12% yield (1.35 g), mp 35-36°C (diethyl ether/light petroleum).

Aq. hydrazine (51%, 1.9 g) was added dropwise to a stirred solution of **14** (6.5 g, 24 mmol) in ethanol (100 ml) at -20°C. After 15 min. the precipitate **15** was collected in 77% yield (5.7 g), mp 132-133°C.

To an ice-cooled suspension of this compound (5.5 g, 18 mmol) in 10% hydrochloric acid (150 ml) was added dropwise with stirring aq. sodium nitrite (1.24 g, 18 mmol in 20 ml). The mixture was stirred for 30 min., then the precipitate was filtered off, washed with water, dissolved in dichloromethane and dried ($MgSO_4$). After removal of the solvent, **16** was obtained in 89% yield (5.1 g), mp with decomp. 106-108°C (from CH_2Cl_2/hexane); IR (KBr) 3175 (m, NH); ^{1}H NMR (400 MHz, DMSO-d_6) δ 4.66 (d, 2 H, CH_2), 7.0- 8.0 (2 m + d, 4 aromatic H), 9.25 (br, 1 H, NH); ^{13}C NMR (DMSO-d_6) δ 54.3 (br, CH_2N), 99.3, 128.5, 129.1, 129.7, 138.8 and 139.2 (aromatic C-atoms), 176.7 (C-5). Anal. Calcd for $C_8H_7IN_4S$ (mol wt 318): C, 30.20; H, 2.22. Found: C, 30.17; H, 2.23.

5-(2-Iodobenzyl)imino-4-methyl-Δ^2-1,2,3,4-thiatriazoline (17).

A suspension of **16** (4.3 g, 13.5 mmol) and one equiv. of trimethyloxonium tetrafluoroborate (2.0 g) in dry dichloromethane (150 ml) was stirred at 5°C for 2 days. The resulting mixture was treated with aq. NaOH (30 g in 300 ml) for 15 min. The organic layer was collected, washed twice with water (200 ml), dried ($MgSO_4$) and evaporated. The residue was chromatographed on silica gel using diethyl ether/light petroleum (1:1) as eluent to give **17** in 87% yield (3.90 g), mp 62-64°C (from light petroleum); IR (KBr) 1646 cm^{-1} (s, C=N); ^1H NMR (400 MHz, $CDCl_3$) δ 3.88 (s, 3 H, CH_3N), 4.22 (s, 2 H, CH_2), 6.9-7.9 (2 td + 2 dd, 4 aromatic H); ^{13}C NMR ($CDCl_3$) δ 34.2 (CH_3N, $^1J_{CH}$ = 143 Hz), 67.0 (CH_2, $^1J_{CH}$ = 135 Hz), 98.9, 128.3, 128.9, 129.0, 139.2 and 141.0 (aromatic C-atoms), 156.5 (C-5). Anal. Calcd for $C_9H_9IN_4S$ (mol wt 332) : C, 32.54; H, 2.73. Found C, 32.67; H, 2.65.

4-Methyl -5-[2-(trimethylsilylethynyl)benzyl]imino-Δ^2-1,2,3,4-thiatriazoline (18a).

To a solution of **17** (2.5 g, 7.5 mmol) in triethylamine (30 ml) was added trimethylsilylacetylene (0.89 g, 9 mmol), bis(triphenylphosphine)palladium dichloride (140 mg, 0.2 mmol) and copper(I) iodide (10 mg, 0.1 mmol), and the reaction mixture was stirred under nitrogen at room temperature for 4 h. The precipitate was filtered off and the filtrate was evaporated. The resulting oil was chromatographed on silica gel using diethyl ether/light petroleum (1:1) as eluent to give **18a** as an oil in 97% yield (2.2 g). Crystallization from light petroleum at -78°C furnished pale orange needles in 77% yield (1.75 g), mp 65-67°C; IR (KBr) 2153 (m, C≡C), 1636 cm^{-1} (s, C=N); ^1H NMR (400 MHz, $CDCl_3$) δ 0.28 (s, 9 H, Me_3Si), 3.88 (s, 3 H, CH_3N), 4.42 (s, 2 H, CH_2), 7.2-7.5 (2 td + dd, 4 aromatic H); ^{13}C NMR ($CDCl_3$) δ 0.0 (Me_3Si), 34.1 (CH_3N, $^1J_{CH}$ = 142.5 Hz), 61.0 (CH_2, $^1J_{CH}$ = 135 Hz), 99.6 and 102.8 (C≡C), 121.8, 126.8, 127.3, 128.7, 132.2 and 141.1 (aromatic C-atoms), 156.4 (C-5). Anal. Calcd for $C_{14}H_{18}N_4SSi$ (mol wt 302.5): C, 55.59; H, 6.00. Found: C, 55.34; H, 5.89.

4-Methyl-5-[2-(phenylethynyl)benzyl]imino-Δ^2-1,2,3,4-thiatriazoline (18b).

To a solution of **17** (1.5 g, 4.5 mmol) in triethylamine (20 ml) was added phenylacetylene (0.55 g), bis(triphenylphosphine)palladium dichloride (100 mg) and copper(I) iodide (10 mg), and the reaction mixture was stirred under nitrogen at room temperature for 4 h. The precipitate was filtered off and the filtrate was evaporated. The resulting oil was chromatographed on silica gel using diethyl ether/light petroleum (1:3) as eluent to give **18b** as an oil which was crystallized from hexane at -78°C; yield 78% (1.07 g), mp 46-47°C; IR (KBr) 1637 cm^{-1} (s, C=N); ^1H NMR (250 MHz, $CDCl_3$) δ 3.83 (s, 3 H, CH_3N), 4.49 (s, 2 H, CH_2), 7.2-7.6 (2 m, 9 aromatic H); ^{13}C NMR ($CDCl_3$) δ 34.0 (CH_3N), 61.0 (CH_2), 87.2 and 94.4 (C≡C), 122.0, 123.1, 126.9, 127.6, 128.3, 128.5, 131.4, 132.0 and 140.5 (aromatic C-atoms), 156.2 (C-5). Anal. Calcd for $C_{17}H_{14}N_4S$ (mol wt 306): C, 66.65; H, 4.61. Found: C, 66.64; H, 4.69.

5-[2-(Ethynyl)benzyl]imino-4-methyl-Δ^2-1,2,3,4-thiatriazoline (18c).

To a solution of **18a** (0.9 g, 3 mmol) in dichloromethane-methanol (8 ml, 1:1) aq. KOH (4 N, 5 ml) was added dropwise and the whole was stirred at room temperature for 12 h. The precipitate was filtered off (0.25 g) and the organic layer was separated and cooled at -20°C to give a second crop of product **18c** (0.28 g); total yield 75%. This product was subjected to column chromatography on silica gel with diethyl ether/light petroleum (1:1) as the eluent, and then crystallized from diethyl ether to give crystals which melted at 65-72°C; IR (KBr) 3264 (s, ≡CH), 2103 (vw, C≡C), 1641 cm^{-1} (s, C=N); ^1H NMR (400 MHz, $CDCl_3$) δ 3.33 (s, 1 H, C≡CH), 3.88 (s, 3 H, CH_3N), 4.42 (s, 2 H, CH_2), 7.2-7.5 (2 td + 2 dd, 4 aromatic H); ^{13}C NMR ($CDCl_3$) δ 34.1 (CH_3N, $^1J_{CH}$ = 142.5 Hz), 60.7 (CH_2, $^1J_{CH}$ = 134.9 Hz), 81.4 and 82.2 (C≡CH, $^1J_{CH}$ = 251.5 Hz), 120.7, 126.8, 127.5, 129.0, 132.7 and 141.3 (aromatic C-atoms), 156.4 (C-5); Anal. Calcd for $M^{+\cdot}$: 230.0626. Found: 230.0629. Note: This compound deteriorates on standing at room temperature.

3-Methylimino-1-trimethylsilyl-3*H*,5*H*-thiazolo[4,3-a]isoindole (19a).

A solution of **18a** (0.8 g, 2.6 mmol) in benzene (30 ml) was refluxed for 3 days. After cooling to room temperature, picric acid (0.63 g, 2.75 mmol) was added and the mixture was stirred for 1 h. Diethyl ether (50 ml) was added and the precipitated picrate of **19a** was filtered off in 73% yield (0.96 g), mp 202-206°C (from toluene).

This compound (0.7 g, 1.4 mmol) was taken up in dichloromethane (100 ml) and washed successively with aq. NaOH (20 g in 200 ml) and water (100 ml), dried ($MgSO_4$) and evaporated to give **19a** in 83% yield (0.32 g), mp 135-140°C; IR (KBr) 1636 cm^{-1} (s, C=N); ^1H NMR (400 MHz, $CDCl_3$) δ 0.40 (s, 9 H, Me_3Si), 3.07 (s, 3 H, CH_3N), 4.76 (s, 2 H, CH_2), 7.35-7.65 (2 td + 2 dd, 4 aromatic H); ^{13}C NMR ($CDCl_3$) δ -0.2 (Me_3Si), 40.9 (CH_3N, $^1J_{CH}$ = 134 Hz), 48.3 (CH_2, $^1J_{CH}$ = 145 Hz, $^3J_{CH}$ = 3.5 Hz), 99.4 (C-1), 121.7, 124.3, 127.9, 128.3, 131.0 and 142.3 (aromatic C-atoms), 146.8 (C-9b), 157.5 (C-3). Anal. Calcd for $C_{14}H_{18}N_2SSi$ (mol wt 274.5): C, 61.23; H, 6.61. Found: C, 61.07; H, 6.67.

3-Methylimino-1-phenyl-3*H*,5*H*-thiazolo[4,3-a]isoindole (19b).

A solution of **18b** (0.8 g, 2.6 mmol) in benzene (30 ml) was refluxed for 3 days. After cooling to room temperature, picric acid (0.66 g, 1.1 equiv.) was added and the mixture was stirred for 1 h. The precipitated picrate of **19b** was filtered off and washed with diethyl ether; yield 76.5% (1.01 g), mp 243-246°C.

This compound (0.7 g, 1.4 mmol) was taken up in dichloromethane (100 ml) and washed successively with aq. NaOH (20 g in 200 ml) and water (100 ml), dried ($MgSO_4$) and evaporated to give **19b** in 95% yield (0.37 g), mp 184-186°C; IR (KBr) 1636 cm^{-1} (s, C=N); ^1H NMR (400 MHz, $CDCl_3$) δ 3.09 (s, 3 H, CH_3N), 4.80 (s, 2 H, CH_2), 7.2-7.7 (t + 2 m + 2 d, 9 aromatic H); ^{13}C NMR ($CDCl_3$) δ 40.9 (CH_3N, $^1J_{CH}$ = 134 Hz), 48.6 (CH_2, $^1J_{CH}$ = 145 Hz, $^3J_{CH}$ = 3 Hz), 106.5 (C-1), 121.3, 124.1, 127.7, 127.8, 128.3, 128.7, 128.8, 129.9, 132.3 and 142.0 (aromatic C-atoms), 136.2 (C-9b), 155.1 (C-3, $^3J_{CH}$ = 9 Hz). Anal. Calcd for $C_{17}H_{14}N_2S$ (mol wt 278): C, 73.35; H, 5.07. Found: C, 73.22; H, 5.13.

3-Methylimino-3*H*,5*H*-thiazolo[4,3-a]isoindole (19c).

A solution of **18c** (0.8 g, 3.5 mmol) in benzene (30 ml) was refluxed for 3 days. After cooling to room temperature, one equiv. of picric acid (1.36 g) was added and the mixture was stirred for 1 h. The precipitated picrate of **19c** was filtered off and washed with diethyl ether; yield 69% (1.1 g), mp 218-221°C.

This compound (0.5 g, 1.16 mmol) was taken up in dichloromethane (100 ml) and washed successively with aq. NaOH (2 x 10 g in 100 ml) and water (2 x 100 ml), dried ($MgSO_4$) and evaporated to give **19c** in 98% yield (0.23 g); IR (KBr) 1635 cm^{-1} (s br, C=N); ^1H NMR (400 MHz, $CDCl_3$) δ 3.05 (s, 3 H, CH_3N), 4.78 (s, 2 H, CH_2), 6.09 (s, 1 H, H-1), 7.35-7.55 (3 m, 4 aromatic H); ^{13}C NMR ($CDCl_3$) δ 40.8 (CH_3N, $^1J_{CH}$ = 134.5 Hz), 48.7 (CH_2, $^1J_{CH}$ = 145 Hz), 87.0 (C-1, $^1J_{CH}$ = 194.6 Hz), 120.6, 124.1, 128.0, 128.6, 129.8 and 142.0 (aromatic C-atoms), 141.5 (quintet, C-9b), 156.2 (C-3). Anal. Calcd for $M^{+\cdot}$: 202.0565. Found: 202.0572. Anal. Calcd for the picrate $C_{17}H_{13}N_5O_7S$ (mol wt 431.4): C, 47.33; H, 3.04. Found: C, 47.57; H, 3.21.

5-(Pent-4-ynyl)amino-1,2,3,4-thiatriazole (24).

A solution of **20** (11 g, 107 mmol), potassium phthalimide (20.4 g, 110 mmol) and potassium iodide (17.8 g, 107 mmol) in dimethylformamide (50 ml) was heated at 100°C for 6 h. The reaction mixture was poured into water (500 ml) and the precipitated phthalimide derivative was filtered off and crystallized from ethanol; yield 69% (15.7 g), mp 87-89°C.

This compound (15.7 g, 74 mmol) and aq. hydrazine (51%, 10 g) were dissolved in ethanol (250 ml) and stirred overnight at room temperature. Then, water (50 ml) was added and the whole was acidified to pH 3.5. The precipitate was removed and the filtrate was concentrated, cooled to 0°C and treated with aq. NaOH (10 N, 50 ml). The solution was extracted twice with dichloromethane (150 ml) and the combined organic layers were dried ($MgSO_4$) and evaporated to give **21** as an oil in 69% yield (4.2 g).

To a cooled solution of this compound (4.2 g, 50.5 mmol) and two equiv. of triethylamine (10.2 g) in dichloromethane (130 ml) was added dropwise one equiv. of thiophosgene (5.81 g), dissolved in dichloromethane (20 ml), while keeping the temperature below -10°C. After stirring at room temperature for 18 h, the solvent was removed and the residue was extracted twice with diethyl ether (150 ml). The combined ether extracts were washed with water (2 x 200 ml), dried ($MgSO_4$) and evaporated to give **22** in 84% yield (5.31 g).

A solution of this compound (5.31 g, 42 mmol) and aq. hydrazine (50%, 5.4 g) in ethanol (50 ml) was stirred at -20°C for 10 min., and then allowed to crystallize overnight at this temperature, giving **23** in 51% yield (3.43 g), mp 89-91°C.

To an ice-cooled solution of this compound (3.4 g, 22 mmol) in 10% hydrochloric acid (30 ml) was added dropwise with stirring aq. sodium nitrite (1.46 g, 22 mmol in 10 ml). The precipitate was filtered off, dried in vacuo at room temperature, and crystallized from dichloromethane/light petroleum at -16°C to give **24** in 74% yield (2.69 g), mp with decomp. 83-85°C; IR (KBr) 3350 and 3260 cm^{-1} (s, NH and ≡CH); ^1H NMR (90 MHz, $CDCl_3$) δ 1.8-2.45 (2 m, 5 H, CH_2CH_2 and ≡CH), 3.4 (q, 2 H, CH_2N), 8.27 (br, 1 H, NH); ^{13}C NMR ($CDCl_3$) δ 15.8, 27.1 and 48.3 (C-C-C-N), 69.9 and 82.4 (HC≡C), 179.3 (C-5). Anal. Calcd for $C_6H_8N_4S$ (mol wt 168): C, 42.84; H, 4.79. Found: C, 42.62; H, 4.62.

Note: The ^{13}C NMR spectrum also showed resonances of **26** and complete conversion in this compound was achieved at 60°C within a few hours: δ 15.4, 27.9 and 44.9 (C-C-C-N), 69.7 and 82.4 (HC≡C), 116.0 (C≡N).

4-Methyl-5-(pent-4-ynyl)imino-Δ^2-1,2,3,4-thiatriazoline (25).

A suspension of **24** (2.5 g, 14.9 mmol) and 1 equiv. of trimethyloxonium tetrafluoroborate (2.2 g) in dry dichloromethane (100 ml) was stirred at 5°C for 24 h. After slow addition of aq. NaOH (20 g in 200 ml), the whole was extracted twice with dichloromethane (150 ml). The combined extracts were washed with water (2 x 200 ml), dried ($MgSO_4$), and evaporated to give **25** as a yellow-orange oil in 90% yield (2.44 g); IR (neat) 3300 (s, ≡CH), 2120 (w, C≡C), 1650 cm^{-1} (br s, C=N); ^1H NMR (250 MHz, $CDCl_3$) δ 1.89 (quint., 2 H, C-CH_2-C), 1.98 (t, 2 H, ≡CH), 2.31 (td, 2 H, CH_2-C≡), 3.12 (t, 2 H, CH_2N), 3.79 (s, 3 H , CH_3N); ^{13}C NMR ($CDCl_3$) δ 16.0, 29.3 and 58.3 (C-C-C-N), 33.8 (CH_3N), 68.6 and 83.7 (HC≡C), 155.3 (C-5).

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8. A referee suggested that the reactions **10**→**11** and **18**→**19** may involve homolytic cleavage of the S-N bond, followed by loss of nitrogen and reaction of the stabilized radical (S=C-N·) with the alkene or alkyne. If this is the case, **25** would not survive the thermal conditions used but decompose to a carbodiimide or derivative which is nog observed. We therefore believe that the sidechain functions in **10** and **18** assist in the decomposition of the thiatriazole ring, a process best rationalized through a thiapentlene-like intermediate or transition state.
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