An Approach towards the Synthesis of 4-Phenyl-5-arylimino-Δ^2-1,2,3,4-thiatriazolines

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4-Phenyl-5-arylimino-Δ^2-1,2,3,4-thiatriazolines are presumably formed by reacting 5-arylaminothiatriazoles with benzyne at 50°, but decompose *in situ* to benzothiazole derivatives by way of the two pathways (a) and (b) shown in Scheme 4.

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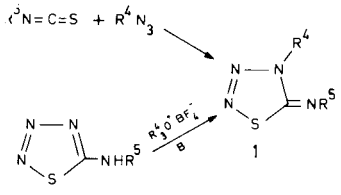
4,5-Disubstituted 5-iminothiatriazolines **1** are of interest from both the synthetic and the mechanistic viewpoints. They react with unsaturated molecules either by a cycloaddition-elimination or an elimination-cycloaddition pathway, giving access to a multitude of other *S,N*-heterocycles [1]. Their synthetic potential is limited by the availability of the starting materials since only two methods are known for their preparation. These are: (i) 1,3-dipolar cycloadditions of alkyl azides with sulfonyl isothiocyanates [2], and (ii) alkylation of alkyl-, aryl- and sulfonylaminothiatriazoles with diazomethane [3] or , even better, with trialkyloxonium tetrafluoroborates (Scheme 1) [4]. Thus, the two methods furnish thiatriazolinimines with an alkyl group at the 4-position.

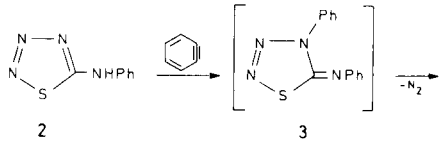
Scheme 1

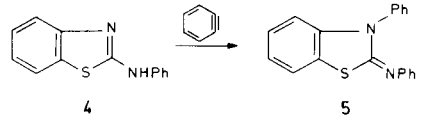


We have now studied the preparation of the title compounds in order to compare their reactivity with that of the 4-alkyl analogues. The direct combination of aryl azides with isothiocyanates cannot be used due to lack of reactivity. Therefore, we have devised another approach which consists of reacting arylaminothiatriazoles with benzyne, generated from benzenediazonium-2-carboxylate [5].

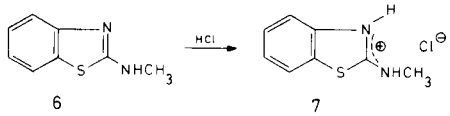
When an excess of the benzyne precursor was added in portions to a chloroform solution of anilinothiatriazole **2** at *ca* 50°, two products were isolated and identified as the known 2-anilinobenzothiazole **4** (23%) [6] and the unknown 3-phenyl-2-phenyliminobenzothiazoline **5** (50%) on the basis of spectral data.

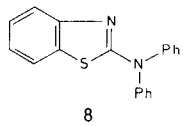
Scheme 2





Characterization of the major product **5** was essentially based on the ^{13}C nmr spectrum which discloses the presence of two different phenyl substituents (Table 1). Indeed, the resonances at δ 151-152 (C_i), 121-122 (C_o) and 123-124 (C_p) are diagnostic for a phenylimino substituent, whereas those at δ 136-138 (C_i) and 128-129 (C_o and C_p) are typical of a phenyl group attached to a ring-nitrogen atom [7]. Furthermore, the chemical shifts observed for C-2, C-3a, C-4 and C-7a in going from **4** to **5** are consistent with the removal of an endocyclic C=N double bond [8]. This is also illustrated with our model compound **6** which manifests similar shifts for C-3a, C-4 and C-7a upon protonation (see Table 1). On the basis of these arguments we exclude the alternative structure **8**.





Structure **5** is further confirmed by the mass spectrum which shows a base peak at m/z 302 for the molecular ion, in addition to significant fragment peaks for M-H (m/z 301, 99.6%) and M-H-PhNC (m/z 198, 27.4%). The latter fragment is also found in the mass spectrum of **4**, but with a much lower intensity (4.2%) since it requires a phenyl migration before the elimination of HCN [9]. Scheme 3 summarizes the most pertinent fragmentations of **5**.

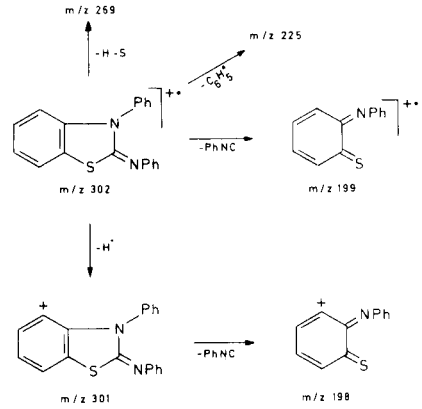
Mechanistically, we believe that the reaction of anilinothiatriazole **2** with benzyne produces 4-phenyl-5-phenylimino-1,2,3,4-thiatriazoline **3** as an elusive intermediate which is responsible for the formation of **4** and its further

Table 1
^{13}C NMR Data of the Benzothiazoles

Compound	Solvent	C-2	C-3a	C-4	C-5	C-6	C-7	C-7a	Aryl at 2-position [a]				Aryl at 3-position			
									C_i	C_o	C_m	C_p	C_i	C_o	C_m	C_p
4	$(CD_3)_2SO$	161.5	152.1	119.2	125.8	122.2	120.9	129.9	140.6	117.7	128.9	122.0				
5	CD_3CN	157.6	141.9	111.1	127.2	123.1	123.2	122.7	152.2	121.9	130.4	124.4	137.9	129.6	130.8	129.6
	$CDCl_3$	156.9	141.1	110.3	126.0	122	122	122.3	151.4	121.4	129.3	123.6	136.7	128.5	129.9	128.5
6	$(CD_3)_2SO$	166.8	152.6	117.9	125.4	120.7	120.8	130.3								
7	$(CD_3)_2SO$	167.4	139.8	114.4	127.2	122.8	123.9	124.2								
10	$(CD_3)_2SO$	160.9	150.1	118.9	127.0	131.6	120.9	130.1	140.8	117.7	129.0	121.9				
11	$(CD_3)_2SO$	161.7	152.1	119.0	125.8	122.0	120.9	129.9	138.2	118.0	129.3	131.0				
12	$CDCl_3$	156.9	139.0	110.0	126.7	131.6	122.3	122.25	151.5	121.5	129.3	123.5	137.1	128.5	129.8	128.5
13	$CDCl_3$	156.7	141.3	110.2	125.9	122.0	122.0	122.35	149.0	121.2	129.9	133.0	137.0	128.6	129.9	128.4

[a] C_i, C_o, C_m and C_p denote positions with respect to the amine (or imine) nitrogen.

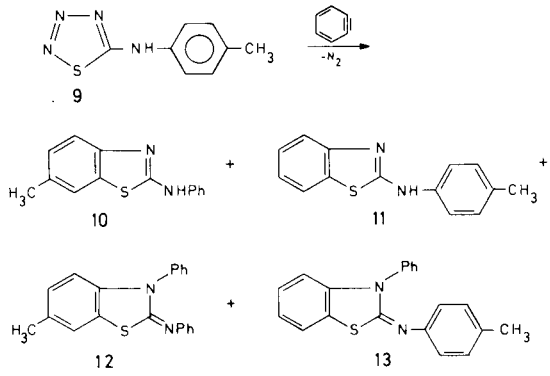
Scheme 3



phenylation to **5** (Scheme 2). Two pathways can be envisaged for the thermal decomposition of **3** as shown in Scheme 4. According to path (a), a thiaziridinimine is formed first and undergoes an electrocyclization-aromatization process similar to phenyl-substituted thiiranimines [10]. Path (b) involves an intramolecular cycloaddition-elimination reaction, comparable with the decomposition of acylaminothiatriazoles [10].

A distinction between the two pathways can be made easily by introducing a *p*-methyl substituent at the phenyl

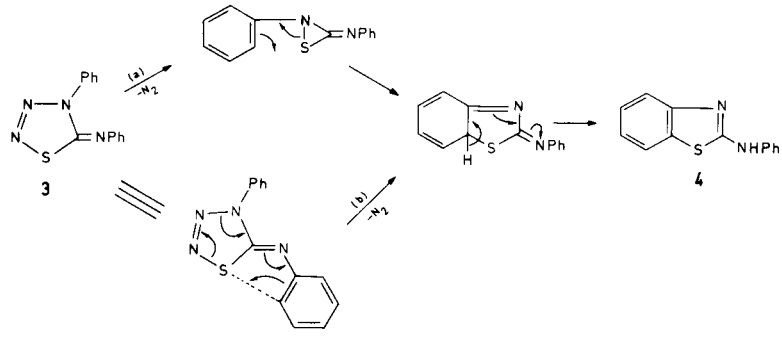
Scheme 5



ring of **2**. This substituent would end up in **4** either at the anilino group if the path is (a) or at the benzothiazole C-6 position if it is (b).

The reaction of **9** with an excess of benzyne furnished the known benzothiazoles **10** (15%) [11] and **11** (9.4%) [12], and a mixture of the two isomeric bis-adducts **12** and **13** in a 2:1 ratio (37%) which could not be separated chromatographically. They were unambiguously characterized by ^{13}C nmr spectroscopy using the nmr criteria discussed above and taking into account the methyl substituent effect (Table 1). Thus, compared with **4** and **5**, compounds

Scheme 4



10-13 differ only significantly at the resonance positions of the *ipso*- and *para*-C atoms with respect to the methyl substituent.

From these results we conclude that 4-phenyl-5-arylimino-1,2,3,4-thiatriazolines decompose by the two pathways (a) and (b) (Scheme 4) in a ratio of about 1:2.

EXPERIMENTAL

5-Anilinothiatriazole (**2**, mp 148-150°) and 5-(*p*-toluidino)thiatriazole (**9**, mp 137-139°) were prepared following the procedure of Vorbrüggen and Krolikiewicz [13]. The ^1H and ^{13}C nmr spectra were recorded on a Bruker WM (FT) spectrometer at 250 and 62.9 MHz respectively. The chemical shifts are reported in ppm relative to TMS as an internal reference. The ^{13}C resonances were assigned by selective decoupling and C,H 2D correlation for **5**.

Reaction of Anilinothiatriazole with Benzyne.

To a solution of anilinothiatriazole **2** (1.48 g, 8.33 mmoles) in chloroform (130 ml) at 47-50° was added in portions and with stirring a chloroform slurry of benzenediazonium-2-carboxylate (prepared from 3.42 g = 25 mmoles of anthranilic acid as reported [5]). Nitrogen evolution occurred during 15 minutes. After removal of the solvent, the residue was chromatographed on silica gel with chloroform as the eluent.

2-Anilinobenzothiazole (**4**).

This compound was obtained in 38% yield (0.71 g) and crystallized from chloroform-cyclohexane in colourless needles, yield 23% (0.43 g), mp 158-161° (lit [6] 157-159°); ^1H nmr (dimethyl sulfoxide-d_6): δ 7.62 (dd, H-4), 7.32 (td, H-5), 7.15 (td, H-6), 7.80 (dd, H-7), 10.5 (NH), 7.81, 7.36 and 7.02 (dd, t and tt for *ortho, meta* and *para* phenylamino hydrogens).

3-Phenyl-2-phenyliminobenzothiazoline (**5**).

This compound was obtained as an oil in 50% yield (1.26 g). After further chromatographic purification of the side fractions and crystallization from ether, colourless needles were obtained in 34% yield (0.86 g), mp 90-92.5°; ir (potassium bromide): 1732 (m), 1624 cm^{-1} (s); ^1H nmr (acetonitrile-d_3): 6.6 (dd, H-4), 7.14 (td, H-5), 7.04 (td, H-6), 7.4 (dd, H-7), 6.95, 7.32 and 7.07 (dd, t and tt for *ortho, meta* and *para*-phenylimino hydrogens), 7.5, 7.6 and 7.5 (m, t and m for *ortho, meta* and *para*-phenyl hydrogens).

Anal. Calcd. for $C_{19}H_{14}N_2S$ (mol wt 302.4): C, 75.47; H, 4.67. Found: C, 75.21; H, 4.78.

Reaction of *p*-Toluidinothiatriazole with Benzyne.

To a solution of *p*-toluidinothiatriazole **9** (1.046 g, 5.44 mmoles) in chloroform (90 ml) at 47-50° was added in portions and with stirring a chloroform slurry of benzenediazonium-2-carboxylate (prepared from 2.28 g = 16.7 mmoles of anthranilic acid [5]). Nitrogen evolution occurred during 20 minutes. After removal of the solvent, the reaction mixture was chromatographed on silica gel with chloroform as the eluent.

2-Anilino-6-methylbenzothiazole (**10**) and 2-*p*-Toluidinobenzothiazole (**11**).

These compounds were obtained as a mixture in 24% yield (0.314 g) and further separated by fractional crystallization from chloroform-cyclohexane. Compound **10** was isolated in 15% yield (0.191 g) and recrystallized twice from chloroform-hexane in colourless needles which sublime at 156°, mp 164-166° (lit [11] 164°); ir (potassium bromide): 1626 (s), 1579 (s), 1498 cm^{-1} (m); ^1H nmr (dimethyl sulfoxide-d_6): δ 7.50 (d, H-4), 7.14 (dd, H-5), 7.6 (d, H-7), 10.4 (NH), 7.8, 7.36 and 7.02 (dd, t and tt for *ortho, meta* and *para*-phenylamino hydrogens), 2.4 (s, CH_3).

Compound **11** was isolated in 6.3% yield (0.082 g) as colourless needles, mp 176-179° (lit [12] 178-180°); ir (potassium bromide): 1625 (s), 1573 (s), 1515 cm^{-1} (m); ^1H nmr (dimethyl sulfoxide-d_6): δ 7.59 (dd, H-4), 7.32 (td, H-5), 7.14 (td, H-6), 7.79 (dd, H-7), 10.4 (NH), 7.68 and 7.18 (two d, *ortho* and *meta* toluidino hydrogens), 2.3 (s, CH_3).

6-Methyl-3-phenyl-2-phenyliminobenzothiazoline (**12**) and 3-Phenyl-2-(*p*-tolyl)iminobenzothiazoline (**13**).

These compounds were obtained as an oily mixture in a 2:1 ratio in 37% yield (0.63 g); ir (neat): 1728 (w), 1627 cm^{-1} (s); ^1H nmr (deuteriochloroform): δ 2.23 and 2.26 (two s, ratio 2:1, CH_3), 6.5-7.5 (m, aromatic H).

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