Addition-Rearrangement Reactions of 5-Imino-Δ^3-1,2,4-thiadiazolines with Trichloroacetonitrile

Gerrit L'abbé*, Ernestine Albrecht and Suzanne Toppet

Department of Chemistry, University of Leuven,
Celestijnenlaan 200F, 3001 Leuven (Heverlee), Belgium

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The reactions of 2-alkyl-3-phenyl-Δ^3-1,2,4-thiadiazolin-5-imines **5a,b** with trichloroacetonitrile at room temperature yield rearranged products, which are shown by ^1H and ^{13}C nmr spectroscopy to exist in two tautomeric structures **6** and **7**.

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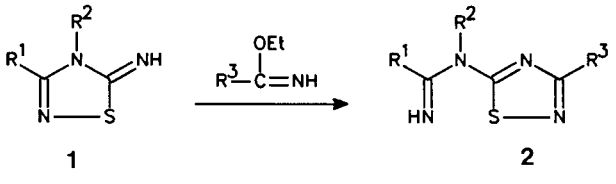
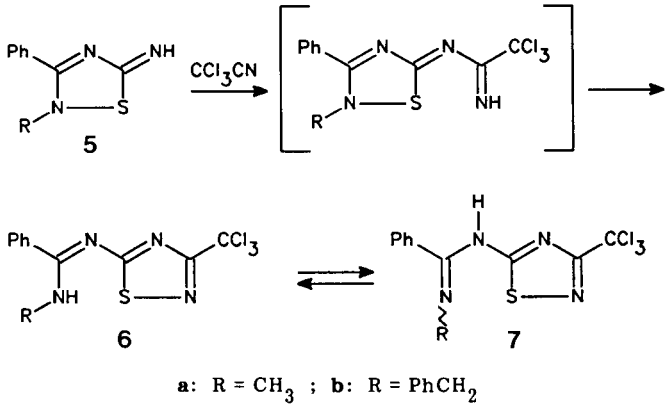
In 1979 Akiba *et al.* [1] reported the reactions of 5-imino-Δ^2-1,2,4-thiadiazolines **1** with imidates to give the rearranged products **2** as a result of bond-switching at hypervalent sulfur intermediates. Cyanamides gave similar results [2]. The Δ^3-isomers **4**, which are readily available from 5-amino-1,2,3,4-thiatriazole **3** and imidoyl chlorides [3], are also candidates for such reactions. Two examples with trichloroacetonitrile as electrophilic reagent are described below.

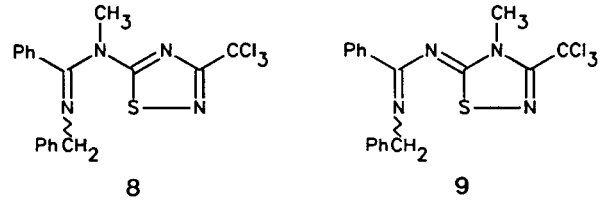


When **5a** was allowed to react at room temperature in trichloroacetonitrile, a rearranged product was isolated in 73% yield. The ^1H nmr spectrum of this product in deuterated dimethyl sulfoxide indicated the presence of the two tautomers **6a** and **7a** in a 60/40 ratio by integration of the methyl signals at δ 3.0 (d) and 3.2 (s). Compound **5b** reacted similarly with an excess of trichloroacetonitrile, and the resulting product was found to be a tautomeric mixture of **6b** and **7b** in dimethyl sulfoxide solution (ratio 1:2).

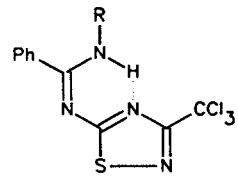


a: R = CH_3 ; **b**: R = $PhCH_2$

Whereas the tautomeric structure of **6** is evident from the doublet absorptions of the methyl and methylene R-protons in the ^1H nmr spectra, for **7** an alternative structure, having the amine hydrogen atom located at the N-4 atom of the thiadiazole ring, may be considered. In order to differentiate between these alternatives, we have compared the ^{13}C nmr data of our products with those of the methylated derivatives **8** and **9**; the results are shown in Table 1. The C-3 (δ 165), C-5 (δ 176) and exocyclic amidine carbon resonances (δ 154) of **7a,b** correspond to those of **8** and are quite different from those of **9**, thus indicating the position of the amine hydrogen atom in **7**.



When the ^1H nmr spectrum of the benzyl derivative was recorded in deuterated chloroform solution at $-40°$, it showed the presence of the hydrogen-bonded isomer **10b** (43%) in addition to **6b** (25%) and **7b** (32%). Upon raising the temperature to 0°, the benzyl methylene doublets of the rotamers **6b** (δ 4.81) and **10b** (δ 4.65) coalesced, and complete coalescence of all the benzyl methylene protons, including that of **7b** at δ 4.77, occurred at 60°.



a: R = CH_3 ; **b**: R = $PhCH_2$

The structure of **10b** was ascertained, *inter alia*, by the NH resonance at low field which remained almost unaffected by raising the temperature from $-40°$ (δ 11.0) to 0°

Table 1

^{13}C NMR Chemical Shifts of the Heterocycles

Compound	Solvent	C-3	C-5	Exocyclic N-C=N	Other absorptions [a]
6a		166.8 [b]	190.7	166.4 [b]	29.0 (CH_3), 91.1 (CCl_3)
⇌	DMSO-d_6				
7a		164.8	175.8	153.6	35.8 (CH_3), 92.0 (CCl_3)
6b		166.8	190.8	166.0	45.0 (CH_2), 91.0 (CCL_3)
⇌	DMSO-d_6				
7b		164.9	175.9	153.9	53.0 (CH_2), 91.9 (CCl_3)
8	$CDCl_3$	164.7	176.9	156.6	37.2 (CH_3), 54.1 (CH_2), 92.2 (CCl_3)
9	$CDCl_3$	148.9	170.6	162.2	35.4 (CH_3), 53.3 (CH_2), 89.2 (CCl_3)

[a] The phenyl C-absorptions are at the expected positions and are omitted. [b] The reverse assignment is possible.

Table 2

^{13}C NMR Chemical Shifts of the Equilibrium Mixture **6b** ⇌ **7b** ⇌ **10b** in Deuteriochloroform at -40°

Compound	C-3	C-5	Exocyclic N-C=N	Other absorptions
6b	167.0	191.0	165.0	46.6 (CH_2), 130.6 and 135.9 (C_i of Ph and $PhCH_2$)
7b	163.6	175.4	151.8	53.75 (CH_2), 129.4 and 139.3 (C_i of Ph and $PhCH_2$)
10b	166.2	190.5	165.3	49.75 (CH_2), 133.0 and 136.2 (C_i of Ph and $PhCH_2$)

(δ 10.95). During this process the NH protons of **6b** (δ 6.45) and **7b** (δ 9.3) shifted upfield by *ca* 0.4 ppm. In the ^{13}C nmr spectrum the resonances of **10b** are comparable with those of **6b**, indicating similar structures (see Table 2) [4].

In view of these results we have also checked the methyl derivative in deuteriochloroform at −40° and have observed three NH signals corresponding to **6a** (δ 6.48, 36%), **7a** (δ 8.99, 16%) and **10a** (δ 10.44, 48%). A fourfold dilution of this solution resulted in an upfield shift of the NH signals of **6a** (δ 6.48 → 5.98) and **7a** (δ 8.99 → 8.74), whereas that of **10a** remained unchanged at δ 10.44 as expected for an intramolecular hydrogen bond.

EXPERIMENTAL

2-Methyl-3-phenyl-Δ^3-1,2,4-thiadiazolin-5-imine (**5a**).

N-Methylbenzimidoyl chloride (7.5 g, 50 mmoles) was added to a solution of **3** (5 g, 50 mmoles) in dry acetonitrile (100 ml) at −78°. The reaction mixture was allowed to come to room temperature and the precipitated hydrochloride salt of **5a** was filtered off in 91% yield (10.2 g), mp 134-136° (acetonitrile); ^1H nmr (400 MHz, dimethyl sulfoxide-d_6): δ 3.75 (s, 3H, CH_3), 7.6-7.9 (two m, 5H, Ph), 10.0-10.2 (two s, 2H, NH_2); ^{13}C nmr (dimethyl sulfoxide): δ 35.6 (CH_3, $^1J_{CH}$ = 144 Hz), 126.6, 128.8, 129.6 and 132.2 (Ph C-atoms), 166.5 (C-3), 177.8 (C-5).

Anal. Calcd. for $C_9H_{10}ClN_3S \cdot ½ H_2O$ (mol wt 236.5): C, 45.67; H, 4.65. Found: C, 45.93; H, 4.62.

Note: Before use in the reaction with trichloroacetonitrile, this salt was treated with sodium hydrogen carbonate in water and the precipitated **5a** was filtered off, washed with water, acetone and ether, and dried.

2-Benzyl-3-phenyl-Δ^3-1,2,4-thiadiazolin-5-imine (**5b**).

N-Benzylbenzimidoyl chloride (11.25 g, 50 mmoles) was added dropwise to a solution of **3** (5 g, 50 mmoles) in dry acetonitrile (100 ml) at −78°. The reaction mixture was allowed to come to room temperature, and after nitrogen evolution ceased the mixture was evaporated to give the hydrochloride of **5b** in 95% yield (14.2 g), mp 155-157° (chloroform/hexane 1:2); ^1H nmr (250 MHz, dimethyl sulfoxide-d_6): δ 5.3 (s, 2H, CH_3), 7.2-7.8 (four m, 10H, two Ph), 10.25 (br, 2H, NH_2); ^{13}C nmr (dimethyl sulfoxide-d_6): δ 51.7 (CH_2), 126.9-134.7 (eight aromatic C-atoms), 167.2 (C-3), 178.4 (C-5).

Anal. Calcd. for $C_{15}H_{14}ClN_3S \cdot ¼ H_2O$ (mol wt 308): C, 58.44; H, 4.71. Found: H, 58.55; H, 4.68.

Note: Before use in the reaction with trichloroacetonitrile, an aqueous suspension of this salt was treated with sodium hydrogen carbonate, and **5b** was filtered off and washed with water, acetone/ether (1:1) and ether.

5-(3-Methyl-2-phenylamidino)-3-trichloromethyl-1,2,4-thiadiazole (**6a** ⇌ **7a**).

A solution of **5a** (0.5 g, 2.6 mmoles) in trichloroacetonitrile (5 ml) was stirred overnight at room temperature. The precipitate was filtered off (440 mg) and the filtrate was evaporated and triturated with chloroform/diethyl ether (1:2) to give another crop of product (200 mg), total yield 73%, mp 129° (diethyl ether/hexane 1:1); ir (potassium bromide): 3390 cm^{-1} (m, NH); ^1H nmr (400 MHz, dimethyl sulfoxide-d_6): **6a**: δ 3.0 (d, CH_3), 7.4-7.6 (m, Ph), 9.1 (br, NH); **7a**: δ 3.2 (s, CH_3), 7.4-7.6 (m, Ph), 12.6 (s, NH); ^{13}C nmr:

see Table 1.

Anal. Calcd. for $C_{11}H_9Cl_3N_4S$ (mol wt 335.5): C, 39.34; H, 2.68. Found: C, 39.38; H, 2.72.

5-(3-Benzyl-2-phenylamidino)-3-trichloromethyl-1,2,4-thiadiazole (**6b** ⇌ **7b**).

A solution of **5b** (0.5 g, 1.87 mmoles) in trichloroacetonitrile (5 ml) was stirred overnight at room temperature. The reaction mixture was subjected to column chromatography on silica gel with dichloromethane as the eluent. The resulting yellow oil was triturated with hexane to give a solid product in 64% yield (490 mg), mp 98-100° (diethyl ether/hexane 1:1); ir (potassium bromide): 3210 cm^{-1} (w, NH); ^1H nmr (400 MHz, dimethyl sulfoxide-d_6): **6b**: δ 4.75 (d, CH_2), 7.2-7.7 (m, two Ph), 9.6 (br, NH); **7b**: δ 4.65 (s, CH_2), 7.2-7.7 (m, two Ph), 12.7 (s, NH); ^{13}C nmr: see Table 1.

Anal. Calcd. for $C_{17}H_{13}Cl_3N_4S$ (mol wt 411.5): C, 49.57; H, 3.16. Found: C, 49.58; H, 3.23.

Methylation of 5-(3-Benzyl-2-phenylamidino)-3-trichloromethyl-1,2,4-thiadiazole.

A mixture of **6b**/**7b** (0.5 g, 1.2 mmoles) and three equivalents of trimethyloxonium tetrafluoroborate (540 mg) in dichloromethane (15 ml) was stirred at room temperature for 6 days. The solvent was evaporated and the residue was treated with aqueous sodium hydrogen carbonate. After extraction with chloroform the organic extracts were washed with water, dried over magnesium sulfate and evaporated. The ^1H nmr analysis showed the presence of **8** (10%) and **9** (60%) in addition to 30% of unreacted starting material. This mixture was subjected to column chromatography on silica gel with hexane/diethyl ether (25:10) as the eluent to give **8** (50 mg) and **9** (300 mg) as oils.

The spectral data of **8** are ^1H nmr (400 MHz, deuteriochloroform): δ 3.4 (s, 3H, CH_3), 4.5 (s, 2H, CH_2), 7.1-7.25 and 7.50-7.55 (two m, 10H, two Ph); ^{13}C nmr: see Table 1.

The spectral data of **9** are ^1H nmr (400 MHz, deuteriochloroform): δ 4.05 (s, 3H, CH_3), 4.9 (s, 2H, CH_2), 7.2-7.6 (four m, 10H, two Ph); ^{13}C nmr: see Table 1.

Note: Although clean spectra could be obtained for **8** and **9**, these compounds deteriorated upon standing.

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REFERENCES AND NOTES

[1] K. Akiba, S. Arai, T. Tsuchiya, Y. Yamamoto and F. Iwasaki, *Angew. Chem., Int. Ed. Engl.*, **18**, 166 (1979).

[2] K. Akiba, T. Tsuchiya and N. Inamoto, *Chem. Letters*, 723 (1976).

[3] G. L'abbé, G. Verhelst and G. Vermeulen, *Angew. Chem., Int. Ed. Engl.*, **16**, 403 (1977); G. L'abbé and G. Vermeulen, *Bull. Soc. Chim. Belg.*, **90**, 89 (1981).

[4] A single crystal X-ray analysis showed that the hydrogen-bonded structure **10b** is also present in the solid state; J. Feneau-Dupont and J. P. Declercq, unpublished results.