Synthesis of *N,N'*-Linked Isothiazolium Salts *via* Intramolecular Cyclocondensation of Hydrazonium Salts*

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Interaction of β-thiocyanatovinyl aldehydes with *N*-amino heterocycles leads to formation of α,β-unsaturated hydrazonium salts dependent on the functional surroundings. The latter can undergo further intramolecular cyclocondensation giving rise to N,N'-linked isothiazolium salts as the final product. The isolated hydrazonium salts, not undergoing ring formation, have *s-trans* conformation of the azadiene system.

Key words: β-Thiocyanatovinyl Aldehydes, *N*-Amino Heterocycles, Hydrazonium Salts, Isothiazolium Salts

Introduction

β-Thiocyanatovinyl aldehydes **1** are known as versatile C_3S synthons. For instance, they are used for transformation of *N*-nucleophiles (*e. g.* ammonia) into isothiazoles [1] and of substituted anilines into isothiazolium salts [2].

Several cases of interaction of compounds **1a, b** with substituted hydrazines $RNHNH_2$ are known [3 – 6]. The reaction course strongly depends both on the substituent R in the hydrazine derivative, and on the thiocyanatovinyl aldehyde structure. Thiocyanates **1a, b** easily react with semicarbazides (R = $CONH_2$) and thiosemicarbazides (R = $CSNH_2$), yielding stable semicarbazones **2** and thiosemicarbazones **3** which exhibit high antiviral activity [3]. However, ring closure with participation of the thiocyanato group does not occur (Fig. 1).

On the other hand, the reaction of **1a, b** with arylhydrazines, benzhydrazides and benzenesulfonylhydrazides, depending on the substituents, can furnish hydrazones **4 – 6**, 1,2,3-thiadiazinium salts **7** [4], or iminium salts **8a, b** [5 – 7] as products of cyclocondensation of heteroaromatic *N*-imino compounds.

All amino compounds employed in foregoing reactions are acyclic hydrazines, while similar reactions with heterocyclic *N*-amino nucleophiles have not been yet investigated. At the same time implementation of this methodology to such substrates could essentially extend the capability of this process and also enhance the synthetic potential of the chemistry of thiocyanatovinyl aldehydes in creation of new N,N'-connected bis(azaheterocycles), many of which have gained significant importance in view of their pharmacological activity [8].

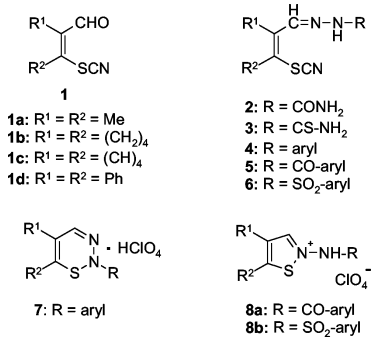

Fig. 1.

Herein we report on a new study of the interaction of β-thiocyanatovinyl aldehydes **1** with cyclic *N*-amino compounds and an approach to an N,N'-linked isothiazolium structure *via* intramolecular cyclocondensation.

Results and Discussion

The four alicyclic and aliphatic β-thiocyanatovinyl aldehydes **1a – d** were used in this research (Fig. 1).

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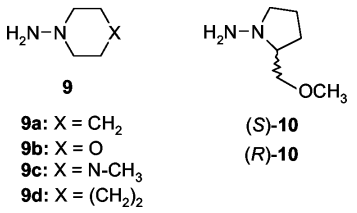
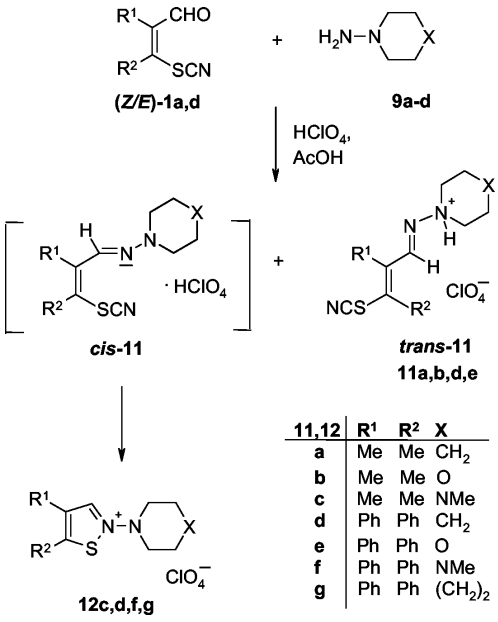


Fig. 2. *N*-Amino heterocycles.



11,12	R¹	R²	X
a	Me	Me	CH_2
b	Me	Me	O
c	Me	Me	NMe
d	Ph	Ph	CH_2
e	Ph	Ph	O
f	Ph	Ph	NMe
g	Ph	Ph	$(CH_2)_2$

Scheme 1. The reaction of acyclic β-thiocyanatovinyl aldehydes with *N*-amino heterocycles.

The synthesis of **1a, b, d** was performed by a known method from corresponding ketones [9], while 2-thiocyanatobenzaldehyde was prepared *via* a two-step procedure from 2-aminobenzaldehyde [10].

As the *N*-amino heterocycles for our investigation several commercially available compounds of type **9** were selected, as well as the enantiomerically pure compounds (*S*)- and (*R*)-2-(methoxymethyl)-1-pyrrolidinamine (SAMP, RAMP) (**10**) (Fig. 2).

The interaction of thiocyanatovinyl aldehydes **1a – d** with *N*-amino heterocycles **9a-d, 10** was carried out in glacial acetic acid in presence of perchloric acid for the salt formation.

The reaction of acyclic aldehydes (*Z/E*)-**1a,d** with *N*-amino compounds **9a – d** produced hydrazonium salts *trans*-**11** or iminium salts **12** (Scheme 1). Formation of the compounds depends on the substituent X in the *N*-amino compound **9**. In case of reaction with **9a, b** (X = CH_2, O) hydrazonium salts *trans*-**11a, b, d, e** were obtained in moderate yields (38 – 63%), while the reaction with **9c,d** (X = N-Me, $(CH_2)_2$) through intramolecular cyclocondensation of not isolable azadienes *cis*-**11** furnished isothiazolium salts **12c,f,g** which were separated in good yields (60 – 98%). Only for the reaction of **9a** with **1d**, a mixture of isothiazolium salt **12d** with **11d** was obtained.

The structure of novel compounds **11a, b, d, e** was established by means of NMR spectra, mass spectrometry studies, and confirmed by IR, UV spectra and elemental analysis. Typical signals of these compounds are found in the ^{1}H NMR spectra at $\delta = 7.50 – 8.70$ ppm (CH) and 5.30 – 7.60 ppm (NH), in the ^{13}C NMR spectra at 130 – 150 ppm (CH) and 108 – 111 ppm (SCN). The typical absorption bonds in the IR spectra were observed at 2150 – 2170 cm^{-1} (SCN), 1100 – 1120 cm^{-1} (ClO_4).

The molecular structure of one of the adducts, 1-(2-methyl-3-thiocyanato-but-2-enylidenamino)-piperidinium perchlorate (**11a**), has been determined by X-ray crystallography (Fig. 3). It was shown that the perchlorate anion is connected to the hydrazonium cation by a strong hydrogen bond with the following parameters: N(1)-H(1N) 0.88(3) Å; N(1)-O(2) 2.855(2) Å; O(2)-H(1N) 1.98(3) Å; N(1)-H(1N)-O(2) 173(2)°.

According to X-ray structure determination, the torsion angle of C(1)-C(2)-C(3)-N(2) is 178.5(2)° and therefore the obtained hydrazonium salts **11** have *s-trans* conformation. This fact let us to suggest that the ability for cyclocondensation depends on the configuration of the hydrazonium salt isomer formed. Apparently, the *trans*-isomer of **11** is stable, while the *cis*-isomer undergoes an intramolecular cyclization with formation of compound **12** (Scheme 1).

Typical of isothiazolium salts **12c, d, f, g** is the infrared absorption of the perchlorate anion at 1090 – 1100 cm^{-1}. In the ^{1}H NMR spectra of **12** the signal of 3-H appears at $\delta = 9.30 – 10.00$ ppm, and the ^{13}C NMR chemical shifts of C-3 (156 – 159 ppm), C-4 (130 – 133 ppm) and C-5 (164 – 168 ppm) are characteristic.

In order to obtain the isothiazolium salts and avoid the isolation of hydrazonium salts from the reaction mixture, we investigated β-thiocyanatovinyl aldehydes of cyclic structure **1b, c**, having a fixed configuration around the double C=C bond (Scheme 2).

As expected, compound **1b** ($R^1 = R^2 = (CH_2)_4$) interacts with *N*-amino heterocycles **9a – c** with

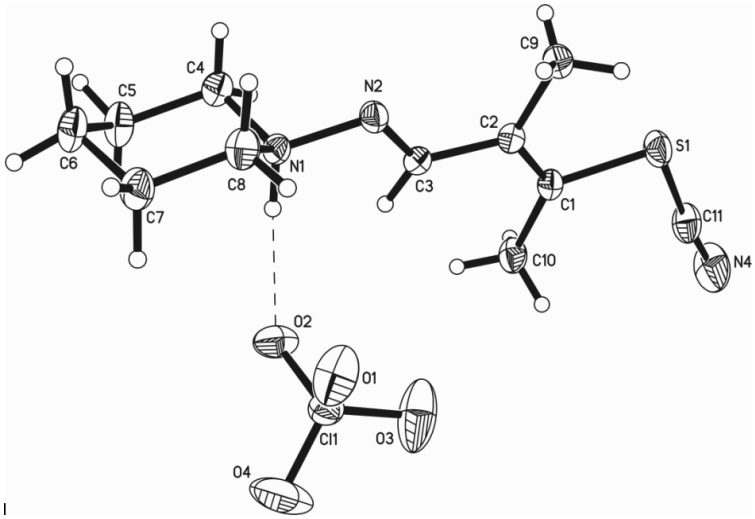


Fig. 3. Molecular structure of **11a**.

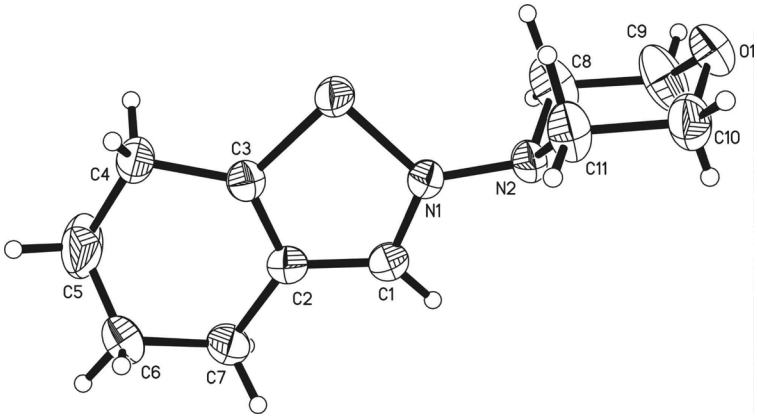
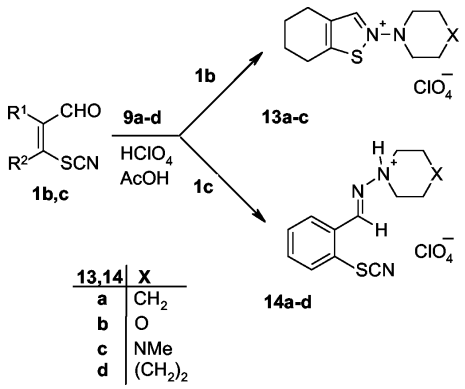


Fig. 4. Molecular structure of **13b**. The perchlorate anion (not shown) is disordered and maintains no hydrogen bonds to the cation.

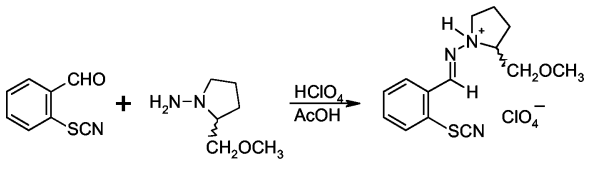


Scheme 2. The reaction of cyclic β-thiocyanatovinyl aldehydes with *N*-amino heterocycles.

formation of isothiazolium salts **13a – c** as cyclocondensation products. Attempts to isolate salt **13d** or the corresponding hydrazonium salt failed.

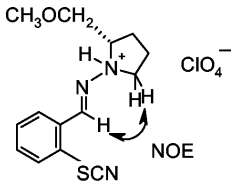
The main spectroscopic characteristics of **13a – c** are similar to those of **12c, d, f, g** described above. The structure of the isothiazolium salt **13b** was proved by X-ray crystal structure analysis (Fig. 4). The isothiazolium ring is connected with the morpholine ring by an N(1)-N(2) single bond (1.414(2) Å).

Surprisingly, analogous reactions of **9a – d** with **1c** ($R^1 = R^2 = (CH)_4$) did not give the expected isothiazolium salts. However, in all cases hydrazonium salts **14a – d** were obtained (Scheme 2). Probably, the inability of compounds **14** to cyclize in this case is due to the influence of the benzo ring and the reduced electrophilic character of the thiocyanato group. Additional experiments with optically active hydrazine derivatives SAMP and RAMP gave the same results and hydrazonium salts **(*S*)-**



1c (*S*)-**10** (*R*)-**10** (*S*)-**15** (*R*)-**15**

Scheme 3. Pathway of optically active hydrazonium salts using SAMP and RAMP.



(*S*)-**15**

Fig. 5. HOESY experiments for **(*S*)-15**.

15 and **(*R*)-15** were obtained as the sole products (Scheme 3).

The analytical characteristics of novel compounds **14, 15** are close to those of **11**, however signals of NH group in the ^{1}H NMR spectra are shifted to the weak field and found at $\delta = 9.60 - 11.10$ ppm, while in the ^{13}C NMR spectra the typical signals are at 129 – 135 (CH) and 112 – 114 ppm (SCN).

Studies of compounds **15** using a NOESY experiment have shown a clear interaction between the imine hydrogen atom and the diastereotopic hydrogen atoms of the CH_2 group at the heterocyclic ring (Fig. 5). Therefore, hydrazonium salts **15** as well as compounds **11** have the *E* configuration around the C=N double bond.

In conclusion, a number of N,N'-linked isothiazolium salts **12, 13** were synthesized by reaction of alicyclic thiocyanates with *N*-amino heterocycles. Interaction of compounds **1** with **9**, **10** apparently occurs in a similar manner as with their acyclic counterparts and on the first stage gives rise to hydrazonium salts. However, ability for the further intramolecular cyclocondensation depends on substituents in both molecules of the initial compounds and gives rise to isothiazolium salts only with favorable configuration for cyclization of the intermediate hydrazonium salts like *cis* configuration of the C(1)-C(2) double bond and *s-cis* conformation of the azadiene.

Experimental Section

General. M. p.: Boetius micro-melting-point apparatus; corrected. Elemental analysis: Heraeus CHNO Rapid Analyser. UV/vis spectra: Beckman DU650; λ_{max} in nm ($\log\varepsilon$). IR spectra: Genesis FTIR Unicam Analytical System (ATI Mattson); KBr pellets; values in cm^{-1}. ^{1}H (300 MHz) and ^{13}C (75 MHz) spectra: Varian Gemini-300 spectrometer; δ in ppm rel. to Me_4Si as internal standard, *J* in Hz. MS: Quadrupole-MS VG 12-250; 70 eV.

General procedure. To a magnetically stirred solution of 1 mmol β-thiocyanatovinyl aldehyde **1** in 2 ml of glacial acetic acid under argon atmosphere was added dropwise 1 mmol of *N*-amino compound **9**, **10**. The reaction mixture was stirred for 15 min and 0.4 ml of perchloric acid was added. After stirring for 1 h, the reaction mixture was diluted with 20 ml of diethyl ether (water in the case of reactions with **1d**) and the precipitate was filtered and recrystallized from ethanol.

1-[(E,2E)-2-Methyl-3-thiocyanato-2-butenylidenamino] piperidinium perchlorate (**11a**)

Yield: 53%, white crystals, m. p. 173 – 175 °C. – IR (KBr): $\nu = 2156$ (SCN), 1111 (ClO_4) cm^{-1}. – UV/vis (ethanol): λ_{max} ($\lg\varepsilon$) = 303 nm (4.00). – ^{1}H NMR (300 MHz, [D]$_6$-DMSO): $\delta = 1.60$ (m, 2H, CH_2), 1.79 (m, 4H, $2CH_2$), 1.97 (s, 3H, CH_3), 2.46 (s, 3H, CH_3), 3.34 (m, 4H, $2CH_2$), 7.27 (s, 1H, NH), 8.47 (s, 1H, CH). – ^{13}C NMR (75 MHz, [D]$_6$-DMSO): $\delta = 156.6$ (C=C), 151.9 (C=C), 132.2 (CH), 109.5 (SCN), 54.5 (2 CH_2), 23.0 ($2CH_2$), 21.5 (CH_2), 19.6 (CH_3), 14.6 (CH_3). – $C_{11}H_{18}N_3O_4SCl$ (323.79): calcd. C 40.80, H 5.60, N 12.98, S 9.90; found C 40.70, H 5.81, N 12.90, S 10.11. – ESI-MS: $m/z = 224$ ([M-ClO_4]$^+$).

4-[(E,2E)-2-Methyl-3-thiocyanato-2-butenylidenamino] morpholin-4-ium perchlorate (**11b**)

Yield: 54%, white solid, m. p. 165 – 167 °C. – IR (KBr): $\nu = 2167$ (SCN), 1111 (ClO_4) cm^{-1}. – UV/vis (ethanol): λ_{max} ($\lg\varepsilon$) = 296 nm (4.05). – ^{1}H NMR (300 MHz, [D]$_6$-DMSO): $\delta = 1.99$ (s, 3H, CH_3), 2.35 (s, 3H, CH_3), 3.13 (m, 4H, $2CH_2$), 3.75 (m, 4H, $2CH_2$), 7.40 (s, 1H, NH), 7.73 (s, 1H, CH). – ^{13}C NMR (75 MHz, [D]$_6$-DMSO): $\delta = 136.4$ (C=C), 135.6 (CH), 121.0 (C=C), 110.5 (SCN), 65.4 ($2CH_2$), 51.8 ($2CH_2$), 19.4 (CH_3), 15.6 (CH_3). – $C_{10}H_{16}N_3O_5SCl$ (325.77): calcd. C 36.87, H 4.92, N 12.90, S 9.83; found C 36.81, H 5.01, N 12.83, S 10.45. – ESI-MS: $m/z = 226$ ([M-ClO_4]$^+$).

1-[(E,2E)-2,3-Diphenyl-3-thiocyanato-propenylidenamino] piperidinium perchlorate (**11d**)

Yield: 38%, brown solid, m. p. 148 – 150 °C. – IR (KBr): $\nu = 2154$ (SCN), 1108 (ClO_4) cm^{-1}. – UV/vis (ethanol): λ_{max} ($\lg\varepsilon$) = 204 nm (4.21), 318 nm (4.07). – ^{1}H NMR (300 MHz, [D]$_6$-DMSO): $\delta = 1.64$ (m, 2H, CH_2), 1.89 (m, 4H, $2CH_2$), 3.49 (m, 4H, $2CH_2$), 7.49 – 7.66 (m, 11H, 2Ph, NH), 8.63 (s, 1H, CH). – ^{13}C NMR (75 MHz, [D]$_6$-DMSO):

δ = 165.8 (C=C), 148.5 (CH), 137.0 (C=C), 134.7 (arom. C), 134.1 (arom. C), 131.8 (arom. CH), 131.1 (2 arom. CH), 130.6 (2 arom. CH), 130.3 (arom. CH), 130.0 (2 arom. CH), 129.8 (2 arom. CH), 108.3 (SCN), 57.9 ($2CH_2$), 22.9 ($2CH_2$), 21.3 (CH_2). – $C_{21}H_{22}N_3O_4SCl$ (447.94): calcd. C 56.31, H 4.95, N 9.38, S 7.16; found C 56.40, H 5.01, N 9.29, S 7.17. – ESI-MS: m/z = 348 ([M-ClO_4]$^+$).

1-[(E,2E)-2,3-Diphenyl-3-thiocyanato-propenylidenamino] morpholin-4-ium perchlorate (**11e**)

Yield: 63%, brown solid, m. p. 85 – 87 °C. – IR (KBr): ν = 2153 (SCN), 1105 (ClO_4) cm^{-1}. – UV/vis (ethanol): λ_{max} (lg ε) = 210 nm (4.30), 310 nm (4.06). – ^{1}H NMR (300 MHz, [D]$_6$-DMSO): δ = 2.74 (m, 4H, $2CH_2$), 3.56 (m, 4H, $2CH_2$), 7.23 – 7.54 (m, 11H, 2Ph, NH), 7.50 (s, 1H, CH). – ^{13}C NMR (75 MHz, [D]$_6$-DMSO): δ = 142.9, 136.9, 135.5, 133.8 (arom. CH), 130.0 (arom. CH), 129.5 (arom. CH), 129.4 (2 arom. CH), 129.1 (2 arom. CH), 128.4 (2 arom. CH), 128.3 (arom. CH), 126.0 (C=C), 110.1 (SCN), 65.3 ($2CH_2$), 50.7 ($2CH_2$). – $C_{20}H_{20}N_3O_5SCl$ (449.92): calcd. C 53.39, H 4.48, N 9.34, S 7.13; found C 53.18, H 4.59, N 9.35, S 7.10. – ESI-MS: m/z = 350 ([M-ClO_4]$^+$).

4,5-Dimethyl-2-(4-methylpiperazin-1-yl)isothiazolium perchlorate (**12c**)

Yield: 98%, white solid, m. p. 199 – 201 °C. – IR (KBr): ν = 1090 (ClO_4) cm^{-1}. – UV/vis (ethanol): λ_{max} (lg ε) = 223 nm (3.48), 277 nm (3.34). – ^{1}H NMR (300 MHz, [D]$_6$-DMSO): δ = 2.76 (s, 3H, CH_3), 2.73 (s, 3H, CH_3), 2.94 (s, 3H, CH_3), 3.69 (m, 4H, $2CH_2$), 3.80 (m, 4H, $2CH_2$), 9.34 (s, 1H, H-3). – ^{13}C NMR (75 MHz, [D]$_6$-DMSO): δ = 164.9 (C-5), 156.7 (C-3), 130.0 (C-4), 54.0 ($2CH_2$), 52.2 ($2CH_2$), 41.7 (CH_3), 13.3 (CH_3), 10.7 (CH_3). – $C_{10}H_{18}N_3O_4SCl$ (311.78): calcd. C 38.52, H 5.82, N 13.48, S 10.28; found C 38.49, H 5.68, N 13.49, S 10.33. – ESI-MS: m/z = 212 ([M-ClO_4]$^+$).

2-(4-Methylpiperazin-1-yl)-4,5-diphenylisothiazolium perchlorate (**12f**)

Yield: 59%, brown solid, m. p. 214 – 216 °C. – IR (KBr): ν = 1096 (ClO_4) cm^{-1}. – UV/vis (ethanol): λ_{max} (lg ε) = 206.0 nm (4.02), 218 nm (3.95), 288 nm (3.56). – ^{1}H NMR (300 MHz, [D]$_6$-DMSO): δ = 3.05 (s, 3H, CH_3), 3.96 (m, 4H, $2CH_2$), 4.09 (m, 4H, $2CH_2$), 7.45 – 7.62 (m, 7H, 6 arom. H, CH), 7.69 (m, 2H, 2 arom. H), 7.83 (2 arom. H), 9.92 (s, 1H, H-3). – ^{13}C NMR (75 MHz, [D]$_6$-DMSO): δ = 167.6 (C-5), 156.8 (C-3), 132.3 (C-4), 133.5 – 124.1 (12 arom. C), 54.0 ($2CH_2$), 52.1 ($2CH_2$), 42.2 (CH_3). – $C_{20}H_{22}N_3O_4SCl$ (435.93): calcd. C 55.10, H 5.09, N 9.64, S 7.44; found C 54.85, H 4.99, N 9.56, S 7.30. – ESI-MS: m/z = 336 ([M-ClO_4]$^+$).

2-(Azepan-1-yl)-4,5-diphenylisothiazolium perchlorate (**12g**)

Yield: 91%, brown solid, m. p. 91 – 93 °C. – IR (KBr): ν = 1095 (ClO_4) cm^{-1}. – UV/vis (ethanol): λ_{max} (lg ε) = 203 nm (4.05), 208 nm (4.08), 320 nm (3.52). – ^{1}H NMR (300 MHz, [D]$_6$-DMSO): δ = 1.75 (m, 4H, $2CH_2$), 1.93 (m, 4H, $2CH_2$), 3.72 (m, 4H, $2CH_2$), 7.11-7.62 (m, 10H, 2Ph), 9.35 (s, 1H, 3-H). – ^{13}C NMR (75 MHz, [D]$_6$-DMSO): δ = 165.9 (C-5), 159.7 (C-3), 133.6 – 129.1 (12 arom. C), 131.7 (C-4), 63.3 ($2CH_2$), 27.8 ($2CH_2$), 27.7 ($2CH_2$). – $C_{20}H_{22}N_3O_4SCl$ (434.93): calcd. C 57.99, H 5.33, N 6.44, S 7.37; found C 58.17, H 5.38, N 6.38, S 7.50. – ESI-MS: m/z = 335 ([M-ClO_4]$^+$).

2-(Piperidin-1-yl)-4,5,6,7-tetrahydro-1,2-benzisothiazolium perchlorate (**13a**)

Yield: 54%, yellow solid, m. p. 135 – 137 °C. – IR (KBr): ν = 1093 (ClO_4) cm^{-1}. – UV/vis (ethanol): λ_{max} (lg ε) = 229 nm (3.64). – ^{1}H NMR (300 MHz, [D]$_6$-DMSO): δ = 1.55 (m, 2H, CH_2), 1.76 – 1.87 (m, 8H, $4CH_2$), 2.71 (m, 2H, CH_2), 3.08 (m, 2H, CH_2), 3.23 (m, 4H, $2CH_2$), 9.31 (s, 1H, 3-H). – ^{13}C NMR (75 MHz, [D]$_6$-DMSO): δ = 165.7 (C-7a), 156.1 (C-3), 131.2 (C-3a), 59.9 ($2CH_2$), 26.1 ($2CH_2$), 26.0, 23.0, 22.6, 22.0 (C-4,5,6,7), 21.3 ($2CH_2$). – $C_{12}H_{19}N_2O_4SCl$ (322.81): calcd. C 44.65, H 5.93, N 8.68, S 9.93; found C 45.00, H 6.04, N 8.79, S 10.06. – ESI-MS: m/z = 223 ([M-ClO_4]$^+$).

2-(Morpholin-4-yl)-4,5,6,7-tetrahydro-1,2-benzisothiazolium perchlorate (**13b**)

Yield: 77%, white crystals, m. p. 191 – 193 °C. – IR (KBr): ν = 1086 (ClO_4) cm^{-1}. – UV/vis (ethanol): λ_{max} (lg ε) = 223 nm (4.02). – ^{1}H NMR (300 MHz, [D]$_6$-DMSO): δ = 1.83 (m, 4H, $2CH_2$), 2.73 (m, 2H, CH_2), 3.07 (m, 2H, CH_2), 3.32 (m, 4H, $2CH_2$), 3.85 (m, 4H, $2CH_2$), 9.38 (s, 1H, 3-H). – ^{13}C NMR (75 MHz, [D]$_6$-DMSO): δ = 166.0 (C-7a), 156.3 (C-3), 131.5 (C-3a), 66.5 ($2CH_2$), 58.7 ($2CH_2$), 26.1, 23.0, 21.9, 21.3 (C-4,5,6,7). – $C_{11}H_{17}N_2O_5SCl$ (324.78): calcd. C 40.68, H 5.28, N 8.62, S 9.87; found C 40.29, H 5.21, N 8.71, S 9.95. – ESI-MS: m/z = 225 ([M-ClO_4]$^+$).

2-(4-Methyl-piperazin-1-yl)-4,5,6,7-tetrahydro-1,2-benzisothiazolium perchlorate (**13c**)

Yield: 93%, yellow crystals, m. p. 190 – 192 °C. – IR (KBr): ν = 1095 (ClO_4) cm^{-1}. – UV/vis (ethanol): λ_{max} (lg ε) = 227.0 nm (3.25), 279 nm (3.08). – ^{1}H NMR (300 MHz, [D]$_6$-DMSO): δ = 1.83 (m, 4H, $2CH_2$), 2.74 (s, 2H, CH_2), 2.94 (s, 3H, CH_3), 3.08 (s, 2H, CH_2), 3.42 (m, 4H, 2 CH_2), 3.68 (m, 4H, 2 CH_2), 9.34 (s, 1H, 3-H). – ^{13}C NMR (75 MHz, [D]$_6$-DMSO): δ = 165.9 (C-7a), 156.0 (C-3), 131.1 (C-3a), 54.1 ($2CH_2$), 52.2 ($2CH_2$), 41.8

(CH_3), 25.5, 22.4, 21.2, 22.5 (C-4,5,6,7). – $C_{12}H_{20}N_3O_4SCl$ (337.82): calcd. C 42.67, H 5.93, N 12.44, S 9.48; found C 42.30, H 5.98, N 12.31, S 9.62. – ESI-MS: $m/z = 238$ ($[M\text{-}ClO_4]^+$).

1-[(E)-1-(2-Thiocyanato-benzylidene)amino]piperidinium perchlorate (**14a**)

Yield: 59%, yellow solid, m. p. 134 – 136 °C. – IR (KBr): $\nu = 2156$ (SCN), 1114 (ClO_4) cm^{-1}. – UV/vis (ethanol): λ_{max} ($\lg\varepsilon$) = 206 nm (3.65), 246 nm (3.77), 307 nm (3.83). – ^{1}H NMR (300 MHz, [D]$_6$-DMSO): $\delta = 1.50$ (m, 2H, CH_2), 1.66 (m, 4H, 2 CH_2), 3.20 (m, 4H, 2CH_2), 7.42 (m, 2H, 2 arom. H), 7.60 (m, 1H, arom. H), 7.68 (m, 1H, arom. H), 7.96 (s, 1H, CH), 10.84 (s, 1H, NH). – ^{13}C NMR (75 MHz, [D]$_6$-DMSO): $\delta = 138.0$ (C=C), 133.1 (CH), 130.8, 129.3, 128.3, 128.2 (4 arom. CH), 123.5 (C=C), 112.8 (SCN), 52.0 (2CH_2), 23.9 (2CH_2), 22.9 (CH_2). – $C_{13}H_{16}N_3O_4SCl$ (345.80): calcd. C 45.15, H 4.63, N 12.16, S 9.26; found C 44.91, H 4.93, N 11.85, S 9.44. – ESI-MS: $m/z = 246$ ($[M\text{-}ClO_4]^+$).

4-[(E)-(2-Thiocyanato-benzylidene)amino]morpholin-4-ium perchlorate (**14b**)

Yield: 76%, yellow solid, m. p. 135 – 137 °C. – IR (KBr): $\nu = 2158$ (SCN), 1120 (ClO_4) cm^{-1}. – UV/vis (ethanol): λ_{max} ($\lg\varepsilon$) = 209 nm (3.91), 244 nm (4.10), 302 nm (4.15). – ^{1}H NMR (300 MHz, [D]$_6$-DMSO): $\delta = 3.11$ (m, 4H, 2CH_2), 3.73 (m, 4H, 2CH_2), 7.39 (m, 2H, 2 arom. H), 7.55 (m, 1H, arom. H), 7.65 (m, 1H, arom. H), 7.81 (s, 1H, CH), 11.09 (s,1H, NH). – ^{13}C NMR (75 MHz, [D]$_6$-DMSO): $\delta = 134.4$ (CH), 133.3 (C=C), 130.5, 128.8, 128.1, 128.0 (4 arom. CH), 123.0 (C=C), 112.9 (SCN), 65.4 (2CH_2), 51.2 (2CH_2). – $C_{12}H_{14}N_3O_5SCl$ (347.78): calcd. C 41.44, H 4.03, N 12.09, S 9.21; found C 41.12, H 4.29, N 11.84, S 9.56. – ESI-MS: $m/z = 248$ ($[M\text{-}ClO_4]^+$).

4-Methyl-1-[(E)-(2-thiocyanato-benzylidene)amino]-piperazin-1-ium perchlorate (**14c**)

Yield: 91%, yellow solid, m. p. 152 – 154 °C. – IR (KBr): $\nu = 2148$ (SCN), 1122 (ClO_4) cm^{-1}. – UV/vis (ethanol): λ_{max} ($\lg\varepsilon$) = 239 nm (4.19), nm 297 (4.16). – ^{1}H NMR (300 MHz, [D]$_6$-DMSO): $\delta = 2.86$ (s, 3H, CH_3), 3.05 (m, 4H, 2CH_2), 3.55 (m, 4H, 2CH_2), 7.46 (m, 2H, 2 arom. H), 7.60 (m, 1H, arom. H), 7.69 (m, 1H, arom. H), 7.93 (s, 1H, CH), 9.59 (s, 1H, NH). – ^{13}C NMR (75 MHz, [D]$_6$-DMSO): $\delta = 137.1$ (C=C), 132.8 (CH), 130.8, 129.2, 128.1, 128.0 (4 arom. CH), 123.3 (C=C), 112.6 (SCN), 51.1 (2CH_2), 47.4 (2CH_2), 41.9 (CH_3). – $C_{13}H_{17}N_4O_4SCl$ (361.82): calcd. C 43.15, H 4.74, N 15.48, S 8.86; found C 43.10, H 4.71, N 15.55, S 8.92. – ESI-MS: $m/z = 362$ ($[M\text{-}ClO_4]^+$).

Table 1. Crystal data and structure refinment for **11a** and **13b**.

	11a	**13b**
Empirical formula	$C_{11}H_{18}ClN_3O_4S$	$C_{11}H_{17}ClN_2O_5S$
Formula weight	323.79	324.78
Temperature [K]	223(2)	213(2)
Crystal system	monoclinic	orthorhombic
Space group	$P2(1)/n$	*Pbca*
a [Å]	9.851(2)	13.506 (7)
b [Å]	8.214(2)	10.497(1)
c [Å]	19.208(4)	20.172(2)
α [°]	90	90
β [°]	102.11(3)	90
γ [°]	90	90
Volume [Å^3]	1519.6(5)	2859.8(4)
Z	4	8
Density [Mg/m^3]	1.415	1.509
Absorption coeff. [mm^{-1}]	0.404	0.433
Crystal size [mm]	$0.1\times0.1\times0.1$	$0.4\times0.2\times0.2$
θ range for data collect. [°]	2.57 – 28.00	2.52 – 28.07
Index ranges	$-12 \le h \le 12$	$-17 \le h \le 17$
	$-10 \le k \le 10$	$-12 \le k \le 12$
	$-18 \le l \le 25$	$-26 \le l \le 26$
Reflections collected	9825	19603
Independent reflections	3605	3289
	[$R_{int} = 0.0227$]	[$R_{int} = 0.0320$]
Max./min. transmission	0.9607/0.9607	0.9184/0.8458
Data/parameters	3605/254	3289/243
Goodness-of-Fit on F^2	0.635	1.193
Final R indices [$I > 2\sigma(I)$]	$R_1 = 0.0445$	$R_1 = 0.0377$
	$wR_2 = 0.1453$	$wR_2 = 0.1113$
R Indices (all data)	$R_1 = 0.0572$	$R_1 = 0.0499$
	$wR_2 = 0.1578$	$wR_2 = 0.1161$
Lgst diff. Peak/hole [e Å^{-3}]	0.603/−0.432	1.493/−0.359

1-[(E)-(2-Thiocyanato-benzylidene)amino]azepanium perchlorate (**14d**)

Yield: 84%, yellow solid, m. p. 145 – 147 °C. – IR (KBr): $\nu = 2156$ (SCN), 1122 (ClO_4) cm^{-1}. – UV/vis (ethanol): λ_{max} ($\lg\varepsilon$) = 207 nm (3.91), 232 nm (3.82), 320 nm (4.20). – ^{1}H NMR (300 MHz, [D]$_6$-DMSO): $\delta = 1.50$ (m, 4H, 2CH_2), 1.71 (m, 4H, 2 CH_2), 3.48 (m, 4H, 2CH_2), 7.28 – 7.37 (m, 3H, 2 arom. H, CH), 7.47 (d, 1H, $J = 7.8$ Hz, arom. H), 7.63 (d, 1H, $J = 7.8$ Hz, arom. H), 10.52 (s, 1H, NH). – ^{13}C NMR (75 MHz, [D]$_6$-DMSO): $\delta = 135.8$ (C=C), 129.4 (CH), 128.6 (2 arom. CH), 127.5 (arom. CH), 125.5 (arom. CH), 121.7 (C=C), 113.7 (SCN), 53.5 (2CH_2), 28.4 (2CH_2), 27.3 (2CH_2). – $C_{14}H_{18}N_3O_4SCl$ (360.01): C 46.73, H 5.01, N 11.68, S 8.90; found C 46.49, H 5.16, N 11.53, S 9.24. – ESI-MS: $m/z = 260$ ($[M\text{-}ClO_4]^+$).

2-Methoxymethyl-1-[(E)-(2-thiocyanato-benzylidene) amino]pyrrolidinium perchlorate (**(S)-15**, **(R)-15**)

Yield: 83% **(S)-15**, 80% **(R)-15**, yellow solid, m. p. 126 – 128 °C. – IR (KBr): $\nu = 2156$ (SCN), 1110 (ClO_4) cm^{-1}. – UV/vis (ethanol): λ_{max} ($\lg\varepsilon$) = 205 nm (3.94), 233 nm (4.03), 314 nm (4.24). – ^{1}H NMR (300 MHz, [D]$_6$-DMSO):

$\delta = 1.73/1.90$ (m, H^A, H^B, 3-H_2), 1.92/1.94 (m, H^A, H^B, 4-H_2), 3.03/3.33 (m, H^A, H^B, 5-H_2), 3.25 (s, 3H, CH_3), 3.45/3.55 (m, H^A, H^B, CH_2-OCH_3), 3.65 (m, 1H, 2-H), 7.31 (m, 3H, 2 arom. H, CH), 7.49 (d, 1H, $J = 8.1$ Hz, arom. H), 7.61 (d, 1H, $J = 8.1$ Hz, arom. H), 10.58 (s, 1H, NH). – ^{13}C NMR (75 MHz, [D]$_6$-DMSO): $\delta = 135.1$ (C=C), 130.1 (CH), 129.8 (arom. CH), 128.7 (2 arom. CH), 128.1 (arom. CH), 121.8 (C=C), 113.4 (SCN), 74.1 (CH_2-OCH_3), 63.1 (CH-2), 59.2 (CH_3), 49.1 (CH_2-5), 27.2 (CH_2-3), 22.4 (CH_2-4). – $C_{14}H_{18}N_3O_5SCl$ (376.01): calcd. C 44.74, H 4.79, N 11.19, S 8.52; found C 44.71, H 5.03, N 11.12, S 9.09. – ESI-MS: $m/z = 276$ ([M-ClO_4]$^+$).

X-ray crystal structure analysis

Crystals of **11a** and **13b** were obtained from ethanol. The intensities were measured on an IPDS1 diffractometer (Fa. STOE). The relevant crystallographic data are listed in the Table. The structures were solved by direct methods, and refinement was performed with SHELX-97 [11]. The details of the structure analyses have been deposited at the Cambridge Crystallographic Data Centre, CCDC-293085 for **11a** and -293084 for **13b**. The copies of the data can be obtained, free of charge, from CCDC, 12 Union Road, Cambridge, CB2 1EZ UK (fax: +44-1233-336033; E-mail: deposite@ccdc.cam.ac.uk, internet: //www.ccdc.cam.ac.uk).

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