Transmembrane anion transport promoted by thioamides

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Thioamide groups represent useful hydrogen-bonding motifs for the development of active transmembrane anion transporters. Using a 1,8-dithioamidocarbazole scaffold the superior performance of thioamides compared with the parent amides has been demonstrated.

Small molecules capable of performing protein functions represent attractive minimalistic models to study cellular processes and are appealing for potential biological applications.1-3 In recent years, small molecules capable of facilitating the selective permeation of anions through lipid bilayers have emerged as promising candidates for the development of anticancer and antimicrobial agents as well as therapeutics for the treatment of channelopathies caused by faulty anion transport, such as cystic fibrosis, Dent’s disease, and others.4-6

Transmembrane ion transport is a complex phenomenon influenced by a number of factors including binding energies and lipophilicity.7-9 Subtle changes in the molecular structure of anionophores often result in dramatic differences in their performance.10-12 Nevertheless, important insights into the design of this type of molecules have been obtained in recent years.13 Hydrogen bonding is the most frequently employed interaction in the design of synthetic anion transporters. Several hydrogen bond donors arranged in a convergent manner ensure effective binding between the transporter and the anion, thus forming a supramolecular complex capable of permeating the membrane. Ureas and thioureas are among the most successful anion binding motifs employed in this type of molecules.14,15 Thioureas usually outperform ureas as anion carriers because replacement of oxygen by sulfur improves the hydrogen bonding ability of the N-H groups, reduces tendency to self-assemble, and increases lipophilicity of the molecule. This strategy of using urea and thiourea derivatives has been extensively used to produce anionophores with increased activity.16 On the other hand, the potential of thioamides has remained largely unexplored despite a similar effect would be expected and amide groups are frequently employed in the construction of active anion receptors and transporters.17 In this paper, we explore the potential of the thioamide moiety in the development of active anionophores.

We have recently reported a family of 1,8-diamidocarbazoles as anion receptors and identified compound 4A as a highly active anion carrier (Fig. 1).18 We envisaged the
potential of this motif to prepare their thioamide derivatives and to explore their anion transport properties.

Thioamides 1T-5T as well as amido-thioamides 5AT and 6AT were synthesized from the corresponding 1,8-diamidocarbazoles by treatment with Lawesson’s reagent and fully characterized (Fig. 1, see ESI for details).

$^3$H NMR titrations of the thioamides with TBACl in DMSO-d$_6$ + 0.5% H$_2$O resulted in large downfield shifts of the carbazole NH protons ($\Delta \delta_{\text{max}}$ from 1.83 to 2.55 ppm, except for the most weakly bonding 1T, for which $\Delta \delta_{\text{max}}=0.94$ ppm was observed) as well as in much smaller downfield shifts of the thioamide NHs (0.42 < $\Delta \delta_{\text{max}}$ < 0.65 ppm, again with the exception of 1T, where $\Delta \delta_{\text{max}} = 0.89$ ppm). In case of the amido-thioamides 5AT and 6AT, the CSNH protons shifted slightly upfield upon chloride binding (by 0.13-0.18 ppm), mirroring the behaviour of CONH protons of their parent diamide receptors.19 All these observations suggest that the hydrogen bonds formed with the anion by the central carbazole NHs are much stronger than the bonds formed by the (thio)amide side arms.

This supposition was further corroborated by the X-ray crystal structure of the chloride complex of dithioamide 3T, in which the carbazole NH-Cl distance is much shorter (2.24 Å) than the two thioamide NH-Cl distances (2.581 Å and 2.830 Å), see figure 1. The inability of the thioamide arms to form shorter bonds with chloride might be related to the steric bulk of the sulfur atom, which enforces significant torsion of the thioamide arms with respect to the carbazole plane (44°-46°) as well as to geometric mismatch between the relatively wide binding cavity of the receptor and the relatively small chloride anion.

Qualitative analysis of the titration data revealed that the association constants with chloride turned out to be 2-3 times smaller for thioamides in comparison to their amide precursors (Table 1). This is in contrast to what might have been expected based on the much higher acidity of thioamides,20 but in line with some literature precedents.21,22 Very likely, the beneficial effect of enhanced hydrogen bond donating ability of the thioamide moieties23 is counterbalanced here by unfavourable conformational preferences of the thioamides.24

The anion transport properties of these compounds were investigated in POPC phospholipid vesicles using a chloride selective electrode.25 In these assays, the facilitated chloride efflux induced by aliquots of the compounds was monitored over time. All receptors were first screened at 2% carrier to POPC molar ratio and compounds eliciting more than 50% chloride efflux were further analysed at different concentrations. For these latter derivatives, the concentration-dependent chloride efflux activity was then fitted using the Hill equation to obtain the EC$_{50}$ parameters representing the amount of compound needed to induce 50% efflux of the encapsulated chloride. All the experiments were repeated at least three times using different batches of vesicles.

The positive effect of replacing the amide groups by the thioamide was evident with all 1,8-dithioamidocarbazoles outperforming their parent 1,8-diamidocarbazoles. The least active derivative was found to be the 1,8-dibenzothioamido derivative 1T. For this compound, no EC$_{50}$ could be calculated. The poor performance of transporters bearing aromatic substituents, such as 1T, is likely related to their much lower chloride affinity.18 Thioamides 2T-5T were found to be highly active in the chloride efflux assay with nitrate in the external solution, with EC$_{50}$ values in the submicromolar range. The most

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**Table 1.** Association constants $K_a$ for 1:1 complexes of compounds 1T-5T, 5AT and 6AT as well as their amide congeners (in brackets) with chloride (added as tetrabutylammonium salt) determined from $^3$H NMR titration experiments in DMSO-d$_6$ + 0.5% H$_2$O at 293 K and transport activities expressed as EC$_{50}$ (nM).

| Compound | $K_a$ (M$^{-1}$) | EC$_{50}$ (nM) NO$_3^-$/Cl$^-$ | EC$_{50}$ (% molar) NO$_3^-$/Cl$^-$ | EC$_{50}$ (nM) HCO$_3^-$/Cl$^-$ | EC$_{50}$ (% molar) HCO$_3^-$/Cl$^-$ |
|----------|----------------|-----------------|-----------------|-----------------|-----------------|
| 1T       | <10 (14)$^a$   | . . .           | . . .           | . . .           | . . .           |
| 2T       | 49 (104)$^a$   | 297             | 0.059           | 4290            | 0.858           |
| 3T       | 50 (109)$^a$   | 107             | 0.022           | 2910            | 0.582           |
| 4A       | 123$^a$        | 184             | 0.037           | . . .           | . . .           |
| 4T       | 46 (123)$^a$   | 66              | 0.013           | 385             | 0.077           |
| 5T       | 52 (159)$^a$   | 93              | 0.019           | 465             | 0.093           |
| 5AT      | 67 (159)$^a$   | 61              | 0.012           | 1719            | 0.344           |
| 6AT      | 23 (48)$^a$    | 353             | 0.071           | . . .           | . . .           |

$^a$ The association constants determined for parent bisamides were taken from ref. 18. $^b$ The compound did not display enough activity to calculate an EC$_{50}$ value.
active derivative was 4T, with a calculated EC₅₀ of 67 nM. The positive effect of replacing even a single amide group by thioamide is demonstrated in the case of compounds 5AT and 6AT. Compound 5AT displayed transport efficacy rivaling the best performers identified in this study. Compound 6AT is an active transporter derived from a non-chlorinated carbazole core, which was found unable to deliver any active carrier in our previous investigations.¹⁸

Experiments were also performed by suspending the vesicles in an external sulfate solution or an external mixture of sulfate and bicarbonate. These assays allow studying the impact of the anion composition of the external buffer on the observed chloride efflux. Bicarbonate is an anion of biological relevance and is significantly more hydrophilic than chloride and nitrate, thus more difficult to extract into the lipid bilayer. This was reflected in the higher calculated EC₅₀ values. Only thioamides 4T and 5T displayed EC₅₀ values in the submicromolar range under these conditions. No significant chloride efflux was detected in the presence of sulfate alone in the external milieu. This result supports an exchange mechanism accounting for the transport activity displayed by these compounds, where the higher hydrophilicity of the doubly charged sulfate renders the compounds inactive as a result of their inability to facilitate the transport of this anion. This result also rules out any unspecific transport or membrane destabilization effect promoted by these compounds. The ability of some of these compounds to exchange chloride and bicarbonate bodes well for their potential biological applications.

In summary, we have demonstrated the usefulness of thioamides in the development of highly active transmembrane anion transporters.²⁶ These compounds display enhanced activity compared to the parent amide derivatives. Taking into account the widespread use of amides as hydrogen-bonding motifs in successful anionophores it is expected that this strategy will allow the identification of new candidates with improved anion transport efficiency.

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**Conflicts of interest**
There are no conflicts to declare.

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1 General information

1.1 Materials

All solvents and reagents were commercially available and used as received unless otherwise stated. ACROS: Lawesson’s reagent 99%; Sigma-Aldrich: tetrabutylammonium chloride for ion pair chromatography, ≥99.0%; Euriso-top: DMSO-d$_6$ + 0.03%TMS v/v (>99.8% D).

TLC was carried out on Merck silica gel 60 F$_{254}$ plates. Preparative chromatography was done manually on Merck silica gel 60 (230 – 400 mesh) or with the aid of Teledyne ISCO CombiFlash instrument using RediSep normal-phase silica flash columns.

1.2 Instruments and methods

Nuclear magnetic resonance (NMR) spectroscopy
The NMR spectra were recorded using Agilent NMR (1H: 400 MHz, 13C: 100 MHz) or Bruker AM-500 (1H: 500 MHz, 13C: 125 MHz) spectrometers at ambient temperature in DMSO-d$_6$. The chemical shifts, $\delta$, are reported in parts per million (ppm) and coupling constants, $J$, are given in hertz (Hz). The NMR spectra were referenced to the solvent residual signal ($^1$H: $\delta_{\text{DMSO}} = 2.50$ ppm, $\delta_{\text{chloroform}} = 7.26$ ppm, $^{13}$C: $\delta_{\text{DMSO}} = 39.50$ ppm). Data are reported as follows: chemical shift, multiplicity (s – singlet, bs – broad singlet, d – doublet, t – triplet, dd- doublet of doublets, dt – doublet of triplets, etc.), coupling constant and integration.

Mass spectrometry
The ESI-MS spectra were obtained using Mariner (ESI TOF) or API 365 (ESI 3Q) mass spectrometers with methanol as the spray solvent.

Elemental analysis
Elemental analysis was performed using a CHN analyzer Vario EL III.

Melting points determination
The melting points are uncorrected.

X-ray data collection and refinement
Good quality single-crystal of 3T-TBACl was selected for the X-ray diffraction experiment at $T = 100(2)$ K. Diffraction data were collected on the Agilent Technologies SuperNova Dual Source diffractometer with CuK$\alpha$ radiation ($\lambda = 1.54184$ Å) using CrysAlis RED software.$^3$ The analytical numeric absorption correction using a multifaceted crystal model based on expressions derived by R.C. Clark & J.S. Reid,$^2$ implemented in SCALE3 ABSPACK scaling algorithm, was applied.$^3$ The structural determination procedure was carried out using the SHELX package.$^4$ The structure was solved with direct methods and then successive least-square refinement was carried out based on the full-matrix least-squares method on $F^2$ using the SHELXL program.$^5$ All H-atoms linked to the N-atoms were located on a Fourier difference map and refined as riding with $U_{eq}(H) = 1.2U_{eq}(N)$. The N–N bond lengths were
restrained to 0.87 Å. Other H-atoms were positioned geometrically, with C–H equal to 0.93, 0.96 and 0.97 for the aromatic, methyl and methylene H-atoms, respectively, and constrained to ride on their parent atoms with \( U_{\text{iso}}(H) = xU_{\text{eq}}(C) \), where \( x = 1.2 \) for the aromatic and methylene H-atoms, and 1.5 for the methyl-H-atoms.

The CCDC 2027226 contains the supplementary crystallographic data for this paper. The data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/structures.

The data collection was accomplished at the Core Facility for Crystallographic and Biophysical research. The „Core facility for crystallographic and biophysical research to support the development of medicinal products” project is carried out within the TEAM-TECH Core Facility programme of the Foundation for Polish Science co-financed by the European Union under the European Regional Development Fund.
2 Synthetic procedures

Preparation of 1T

A 50 ml, 2-neck, round-bottomed flask was dried for 10 min with a stream of hot air (ca. 500°C) from heat-gun and cooled down to rt in a desiccator. Then the flask was charged with diamide 1A (238 mg, 0.502 mmol), Lawesson’s reagent (444 mg, 1.10 mmol) and a stir bar. Then the flask was equipped with a reflux condenser connected to a Schlenk line and its side neck was closed with a stopper. Air was removed by three pump/thaw cycles and then dry THF (30 ml) was added in a stream of argon through the side neck. The reaction mixture was intensively stirred and refluxed overnight. After this time the mixture was cooled down and 2.0 g of silica gel was added. Solvents were evaporated on a rotary evaporator and the solid residue was dried under high vacuum. Then the solid residue was suspended in hexane (40 ml) and put on top of a chromatographic column made of 110 g of silica suspended in CHCl₃. The column was eluted with CHCl₃ (ca. 500 ml), CHCl₃ : CH₃CO₂Et = 40 : 1 (ca. 500 ml) and CHCl₃ : CH₃CO₂Et = 30 : 1 until the desired product was completely washed out. Fractions containing pure product were combined and evaporated on a rotary evaporator yielding 293 mg (98.0%) of yellow solid.

M.p.: decomposition at 301°C

¹H NMR (500 MHz, DMSO-d₆) δDMSO: 11.69 (s, 2H, thioamide NHs), 11.23 (s, 1H, carbazole NH), 8.37 (bs, 2H, carbazole CH-4/5), 8.03 (d, J = 7.6 Hz, 4H, phenyl CH-orto), 7.77 (bs, 2H, carbazole CH-2/7), 7.56 (t, J = 7.3 Hz, 2H, phenyl CH-para), 7.48 (t, J = 7.5 Hz, 4H, phenyl CH-meta).

¹³C NMR (126 MHz, DMSO-d₆) δDMSO: 199.19, 141.09, 133.99, 131.30, 127.98, 125.66, 124.62, 124.46, 122.98, 119.23.

Elemental analysis: calcd. for C₂₆H₁₇Cl₂N₃S₂: C, 61.66; H, 3.38; N, 8.30; found: C, 61.56; H, 3.52; N, 8.27.

HR MS (TOF MS ES) m/z calcd. for C₂₆H₁₇Cl₂N₃S₂: 504.0163; found: 504.0168.
Figure S1. $^1$H NMR spectrum of 1T in DMSO-$d_6$.

Figure S2. $^{13}$C NMR spectrum of 1T in DMSO-$d_6$. 
Preparation of 2T

A 50 ml, 2-neck, round-bottomed flask was dried for 10 min with a stream of hot air (ca. 500°C) from heat-gun and cooled down to rt in a desiccator. Then the flask was charged with diamide 2A (96 mg, 0.25 mmol), Lawesson’s reagent (221 mg, 0.546 mmol) and a stir bar. Then the flask was equipped with a reflux condenser connected to a Schlenk line and its side neck was closed with a stopper. Air was removed by three pump/thaw cycles and then dry THF (35 ml) was added in a stream of argon through the side neck. The reaction mixture was intensively stirred and refluxed for 48 h. After this time the mixture was cooled down and 2.3 g of silica gel was added. Solvents were evaporated on a rotary evaporator and the solid residue was dried under high vacuum. Then the solid residue was suspended in hexane (40 ml) and put on top of a chromatographic column made of 100 g of silica suspended in CHCl₃. The column was eluted with CHCl₃ (ca. 250 ml), CHCl₃ : CH₃CO₂Et = 24 : 1 (ca. 250 ml), CHCl₃ : CH₃CO₂Et = 47 : 3 (ca. 250 ml), 23 : 2 (ca. 250 ml), 9 : 1 (ca. 250 ml), 22 : 3 (ca. 1000 ml) and 43 : 7 until the desired product was completely washed out. Fractions containing pure product were combined and evaporated on a rotary evaporator yielding 83 mg (79.7 %) of yellow solid.

M.p.: decomposition at 270°C;

¹H NMR (500 MHz, DMSO-d₆)  δDMSO: 11.53 (s, 2H, thioamide NH); 10.84 (s, 1H, carbazole NH); 8.31 (d, J = 2.0 Hz, 2H, carbazole CH); 7.75 (d, J = 2.0 Hz, 2H, carbazole CH); 2.88 (q, J = 7.5 Hz, 4H, methylene CH₂); 1.35 (t, J = 7.5 Hz, 6H, methyl CH₃).

¹³C NMR (126 MHz, DMSO-d₆)  δDMSO: 208.02, 133.48, 124.93, 124.47, 123.81, 122.99, 119.04, 38.84, 13.92.

Elemental analysis: calcd. for C₁₈H₁₇Cl₂N₃S₂: C, 52.68; H, 4.18; N, 10.24, found: C, 52.64; H, 4.35; N, 10.09.

HR MS (TOF MS ES) m/z calculated for C₁₈H₁₆Cl₂N₃S₂: 408.0163 found: 408.0161.
Figure S3. $^1$H NMR spectrum of 2T in DMSO-$d_6$.

Figure S4. $^{13}$C NMR spectrum of 2T in DMSO-$d_6$. 
Preparation of 3T

A 50 ml, 2-neck, round-bottomed flask was dried for 10 min with a stream of hot air (ca. 500°C) from heat-gun and cooled down to rt in a desiccator. Then the flask was charged with diamide 3A (102 mg, 0.251 mmol), Lawesson’s reagent (221 mg, 0.546 mmol) and a stir bar. Then the flask was equipped with a reflux condenser connected to a Schlenk line and its side neck was closed with a stopper. Air was removed by three pump/thaw cycles and then dry THF (20 ml) was added in a stream of argon through the side neck. The reaction mixture was intensively stirred and refluxed for 72 h. After this time the mixture was cooled down and 2.4 g of silica gel was added. Solvents were evaporated on a rotary evaporator and the solid residue was dried under high vacuum. Then the solid residue was suspended in hexane (40 ml) and put on top of a chromatographic column made of 100 g of silica suspended in CHCl₃. The column was eluted with CHCl₃ (ca. 500 ml), CHCl₃ : CH₃CO₂Et = 22 : 1 (ca. 250 ml), CHCl₃ : CH₃CO₂Et = 9 : 1 (ca. 250 ml) and CHCl₃ : CH₃CO₂Et = 4 : 1 until the desired product was completely washed out. Fractions containing pure product were combined and evaporated on a rotary evaporator yielding 85 mg (80.2%) of yellow solid.

**M.p.:** decomposition at 282°C.

**¹H NMR** (500 MHz, DMSO-d₆) δDMSO: 11.56 (s, 2H, thioamide NH), 10.64 (s, 1H, carbazole NH), 8.31 (d, J = 1.9 Hz, 2H, carbazole CH), 7.71 (d, J = 2.0 Hz, 2H, carbazole CH), 2.85 (t, 4H, J = 6.0 Hz, CH₂C=S), 1.93 – 1.81 (m, 4H, CH₂), 1.02 (t, J = 7.4 Hz, 6H, CH₃).

**¹³C NMR** (126 MHz, DMSO-d₆) δDMSO: 206.45, 133.45, 124.90, 124.54, 123.78, 123.06, 119.12, 47.69, 22.61, 13.27.

**Elemental analysis:** calcd. for C₂₀H₂₁Cl₂N₃S₂: C, 54.79; H, 4.83; N, 9.58, found: C, 54.88; H, 5.06; N, 9.47.

**HR MS (TOF MS ES)** m/z calcd. for C₂₀H₂₁Cl₂N₃S₂: 438.44 found: 438.0472.
Figure S5. $^1$H NMR spectrum of 3T in DMSO-$d_6$.

Figure S6. $^{13}$C NMR spectrum of 3T in DMSO-$d_6$. 
Preparation of 4T

A 50 ml, 2-neck, round-bottomed flask was dried for 10 min with a stream of hot air (ca. 500°C) from heat-gun and cooled down to rt in a desiccator. Then the flask was charged with diamide 4A (108 mg, 0.25 mmol), Lawesson’s reagent (222 mg, 0.549 mmol) and a stir bar. Then the flask was equipped with a reflux condenser connected to a Schlenk line and its side neck was closed with a stopper. Air was removed by three pump/thaw cycles and then dry dichloroethane (20 ml) was added in a stream of argon through the side neck. The reaction mixture was intensively stirred and refluxed for 72 h. After this time the mixture was cooled down and 2 g of silica gel was added. Solvents were evaporated on a rotary evaporator and the solid residue was dried under high vacuum. Then the pre-loaded mixture was separated by chromatography on 40 g cartridge using CombiFlash instrument. The column was eluted with the flow rate of 8 mL/min with CHCl₃ (15 min), CHCl₃ : CH₃CO₂Et gradient from 0% to 5% over 15 min, CHCl₃ : CH₃CO₂Et = 19 : 1 (120 min). Fractions containing pure product were combined and evaporated on a rotary evaporator yielding 75 mg (64.7%) of yellow solid.

¹H NMR (500 MHz, DMSO-d₆) δDMSO: 11.57 (s, 2H, thioamide NH), 10.46 (s, 1H, carbazole NH), 8.33 (d, J = 1.5 Hz, 2H, carbazole CH-4), 7.66 (d, J = 1.5 Hz, 2H, carbazole CH-2), 2.75 (d, J = 7.2 Hz, 4H, CH₂), 2.40 – 2.25 (m, 2H, CH), 1.03 (d, J = 6.6 Hz, 12H, CH₃).

¹³C NMR (126 MHz, DMSO-d₆) δDMSO 205.56, 133.46, 124.89, 124.66, 123.79, 123.15, 119.22, 54.88, 39.50, 29.07, 21.96.

Elemental analysis: calcd. for C₂₂H₂₅Cl₂N₃S₂: C, 56.64; H, 5.40; N, 9.01, found: C, 56.75; H, 5.54; N, 8.94.

HR MS (TOF MS ES) m/z calcd. for C₂₂H₂₅Cl₂N₃S₂: 466.0789 found: 464.0786.
Figure S7. $^1$H NMR spectrum of 4T in DMSO-$d_6$.

Figure S8. $^{13}$C NMR spectrum of 4T in DMSO-$d_6$. 
Figure S9. $^1$H ROESY spectrum of 4T in DMSO-$d_6$. 
Preparation of 5T

A 50 ml, 2-neck, round-bottomed flask was dried for 10 min with a stream of hot air (ca. 500°C) from heat-gun and cooled down to rt in a desiccator. Then the flask was charged with diamide 5A (116 mg, 0.251 mmol), Lawesson’s reagent (222 mg, 0.549 mmol) and a stir bar. Then the flask was equipped with a reflux condenser connected to a Schlenk line and its side neck was closed with a stopper. Air was removed by three pump/thaw cycles and then dry dichloroethane (20 ml) was added in a stream of argon through the side neck. The reaction mixture was intensively stirred and refluxed for 72 h. After this time the mixture was cooled down and 2.0 g of silica gel was added. Solvents were evaporated on a rotary evaporator and the solid residue was dried under high vacuum. Then the solid residue was suspended in hexane (40 ml) and put on top of a chromatographic column made of 110 g of silica gel suspended in CHCl₃. The column was eluted with CHCl₃ (ca. 500 ml), CHCl₃ : EA = 25 : 1 (ca. 250 ml), 25 : 1 (ca. 250 ml), 22 : 1 (ca. 250 ml), 19 : 1 (ca. 250 ml) until the desired product was completely washed out. Fractions containing pure product were combined and evaporated on a rotary evaporator yielding 118 mg (95.1 %) of yellow solid.

M.p.: decomposition at 278°C.

¹H NMR (500 MHz, DMSO-d₆) δDMSO: 11.43 (s; 2H; thioamide NH); 10.30 (s; 1H; carbazole NH); 8.33 (d; J = 2.0 Hz; 2H; carbazole CH-4/5); 7.59 (d; J = 2.0 Hz; 2H; carbazole CH-2/7); 2.85 (s; 4H; methylene CH₂); 1.14 (s; 18H; t-butyl CH₃).

¹³C NMR (126 MHz, DMSO-d₆) δDMSO: 203.50, 133.43, 125.04, 124.75, 123.89, 123.17, 119.18, 59.12, 32.02, 29.77.

Elemental analysis: calcd. for C₂₄H₂₉Cl₂N₃S₂: C, 58.29; H, 5.91; N, 8.50, found: C, 58.37; H, 6.06; N, 8.25.

HR MS (TOF MS ES) m/z calcd. for C₂₄H₂₉Cl₂N₃S₂: 492.1102; found: 492.1113.
Figure S10. $^1$H NMR spectrum of 5T in DMSO-$d_6$.

Figure S11. $^{13}$C NMR spectrum of 5T in DMSO-$d_6$. 
A 50 ml, 2-neck, round-bottomed flask was dried for 10 min with a stream of hot air (ca. 500°C) from heat-gun and cooled down to rt in a desiccator. Then the flask was charged with diamide 5A (116 mg, 0.25 mmol), Lawesson’s reagent (101 mg, 0.25 mmol) and a stir bar. Then the flask was equipped with a reflux condenser connected to a Schlenk line and its side neck was closed with a stopper. Air was removed by three pump/thaw cycles and then dry dichloroethane (20 ml) was added in a stream of argon through the side neck. The reaction mixture was intensively stirred and refluxed for 72 h. After this time the mixture was cooled down and 2 g of silica gel was added. Solvents were evaporated on a rotary evaporator and the solid residue was dried under high vacuum. Then the pre-loaded mixture was separated by repeated chromatography on CombiFlash instrument. Preliminary separation was achieved on 40 g cartridge using flow rate of 8 mL / min and the following eluents CHCl₃ : CH₃CO₂Et = 19 : 1 (120 min), CHCl₃ : CH₃CO₂Et gradient from 5 to 10% over 15 min and finally CHCl₃ : CH₃CO₂Et = 9 : 1 (120 min). All fractions containing the desired monothioamide were combined and purified once again on two combined 12 g Gold cartridges using CHCl₃ : CH₃CO₂Et gradient from 0 to 5% over 240 min and CHCl₃ : CH₃CO₂Et 5% (60 min). Fractions containing pure product were combined and evaporated on a rotary evaporator yielding 20 mg (16.7 %) of yellow solid.

³¹H NMR (DMSO-d₆) δ (DMSO) : 11.55 (s, 1H, thioamides NH), 10.56 (s, 1H, carbazole NH), 10.00 (s, 1H, amide NH), 8.30 (d, J = 1.8 Hz, 1H, carbazole CH-5), 8.12 (d, J = 1.8 Hz, 1H, carbazole CH-4), 7.90 (d, J = 1.8 Hz, 1H, carbazole CH-2), 7.41 (d, J = 1.6 Hz, 1H, carbazole CH-7), 2.88 (s, 2H, CH₂C=S), 2.35 (s, 2H, CH₂C=O), 1.16 (s, 9H, t-Bu on the thioamide side), 1.08 (s, 9H, t-Bu on the amide side);

¹³C NMR (DMSO-d₆) δ (DMSO) : 203.85, 170.57, 157.57, 133.40, 129.89, 125.06, 124.64, 124.59, 124.24, 124.00, 123.73, 122.96, 119.26, 117.74, 115.92, 58.90, 49.20, 32.07, 30.89, 29.78, 29.59.

HR MS (TOF MS ES) : m/z calcd. for C₂₄H₂₉Cl₂N₃O₅S : 476.1330, found: 476.1331;

Elemental Analysis calcd. for C₂₄H₂₉Cl₂N₃O₅S: C, 60.24; H, 6.11; N, 8.78; found: C, 60.61; H, 6.39; N, 8.39.
Figure S12. $^1$H NMR spectrum of SAT in DMSO-$d_6$.

Figure S13. $^{13}$C NMR spectrum of SAT in DMSO-$d_6$. 
Figure S14. $^1$H ROESY spectrum of 5AT in DMSO-$d_6$.

Figure S15. $^1$H COSY spectrum of 5AT in DMSO-$d_6$. 
Preparation of 6AT

Monothioamide 6AT has been obtained as a side product from the synthesis of 6T. After purification by column chromatography 83 mg (40.3%) of 6AT was obtained.

**M.p.:** decomposition above 282°C.

**1H NMR** (500 MHz, DMSO-d$_6$) $\delta_{\text{DMSO}}$: 11.47 (s; 1H; thioamide NH); 10.06 (s; 1H; carbazole NH); 9.95 (s; 1H; amide NH); 8.08 (d, $J = 7.5$ Hz, 1H; CH-5 on the thioamide side); 7.65 (d, $J = 7.7$ Hz, 1H; CH-4 on the amide side); 7.61 (dd; $J_1 = 7.8, J_2 = 1.0$ Hz; 1H; CH-2 on the amide side); 7.44 (d, $J = 7.7$, 1H; CH-7 on the thioamide side); 7.22 (t; $J = 7.7$ Hz; 1H; CH-6 on the thioamide side); 7.17 (t; $J = 7.8$ Hz; 1H; CH-3 on the amide side); 2.87 (s; 2H; methylene CH$_2$ from the thioamide arm); 2.34 (s; 2H; methylene CH$_2$ from the amide arm); 1.17 (s; 9H; t-butyl CH$_3$ from the thioamide arm); 1.10 (s; 9H; t-butyl from the amide arm).

**13C NMR** (126 MHz, DMSO-d$_6$) $\delta_{\text{DMSO}}$: 202.76, 170.19, 134.29, 131.48, 124.60, 124.47, 124.10, 123.61, 119.43, 119.07, 119.05, 118.28, 116.28, 58.89, 49.13, 31.91, 30.84, 29.85, 29.68.

**Elemental analysis:** calcd. for C$_{24}$H$_{31}$N$_3$OS: C, 70.38; H, 7.63; N, 10.26; found: C, 70.07; H, 7.61; N, 10.05.

**HR MS (TOF MS ES)** m/z calcd. for C$_{24}$H$_{30}$N$_3$OS: 408.2110 found: 408.2112.
Figure S17. $^{13}$C NMR spectrum of 6AT in DMSO-$d_6$.

Figure S18. $^1$H ROESY spectrum of 6AT in DMSO-$d_6$. 
3 Binding studies

3.1 Materials

Tetrabutylammonium chloride was obtained from Sigma-Aldrich and was used as received.

DMSO-d₆ (99.8% isotopic purity, containing less than 0.02% water) was obtained from Eurisotop in septum-sealed vials.

DMSO-d₆/H₂O mixtures were obtained using distilled H₂O and their concentrations are expressed as weight-weight percentage.

3.2 General procedure for ¹H NMR titrations

All the reagents were weighted separately on a Mettler Toledo Excellence XA105DU analytical balance (readability 0.01 mg) in screw-capped vials sealed with Teflon-covered septa. All the solvent/solution manipulations were done using gas-tight Hamilton glass syringes. Titrants were prepared by dissolving appropriate salts in the solution of the receptor in order to avoid dilution of the receptor during titration. Titrations were performed in screw-capped NMR tubes sealed with Teflon-covered septa, by adding aliquots of the titrant solution to the receptor solution and recording ¹H NMR spectra after each addition. The NMR spectra were measured on Agilent 400 MHz spectrometer.

Typical ¹H NMR titration procedure. To a solution of host (600 μl, typically 0.005 M or 0.01 M) in a septum-sealed screw-cap NMR tube appropriate aliquots of titrant (typically 15 times more concentrated than the host solution, dissolved in the solution of host to avoid dilution) were added with a 25 μl gas-tight microsyringe. Association constants were calculated from changes in chemical shifts of most affected protons of the ligands, as indicated in each case below.

3.3 Data fitting

The ¹H NMR titration data were fitted with BindFit software. Association constants β₁:₁ and chemical shifts of 1:1 complexes were set as free parameters for fitting, whereas chemical shifts of free ligands were constrained to be equal to experimentally measured values. Association constants derived from independent experiments were averaged using arithmetic mean.
3.4 $^1$H NMR titration of 0.005 M solution of receptor 1T in DMSO-d$_6$/0.5% H$_2$O with 0.15 M solution of TBA$^+\text{Cl}^-$ (dissolved in the solution of receptor 1T).

Titration of 1T with TBACl produced very weak changes in the $^1$H NMR chemical shifts of all protons. The changes for protons a and b were the most pronounced and were therefore simultaneously fitted to the 1:1 model using BindFit software.

Scheme 1. Chloride binding to 1T. Chemical shifts of the indicated protons were used for fitting.

Figure S19. $^1$H NMR titration of 1T (0.005 M) with TBACl. The marked peaks were used for fitting.
Raw data:

| Added volume of titrant solution [µL] | Equivalents of TBA’Cl’ | Chemical Shift [ppm] |  |
|-------------------------------------|------------------------|----------------------|---|
|                                     |                        | NH$_{\text{thioamide}}$ | NH$_{\text{carbazole}}$ |
| 0.0                                 | 0.00                   | 11.6801              | 11.2081          |
| 4.0                                 | 0.20                   | 11.6847              | 11.2131          |
| 8.0                                 | 0.39                   | 11.6892              | 11.2175          |
| 12.0                                | 0.59                   | 11.6934              | 11.2225          |
| 16.5                                | 0.80                   | 11.6983              | 11.2278          |
| 20.5                                | 0.99                   | 11.7024              | 11.2320          |
| 25.0                                | 1.20                   | 11.7071              | 11.2370          |
| 31.5                                | 1.50                   | 11.7136              | 11.2438          |
| 43.0                                | 2.01                   | 11.7244              | 11.2553          |
| 54.5                                | 2.50                   | 11.7348              | 11.2663          |
| 66.5                                | 2.99                   | 11.7448              | 11.2769          |
| 79.0                                | 3.49                   | 11.7548              | 11.2874          |
| 92.0                                | 3.99                   | 11.7646              | 11.2978          |
| 120.0                               | 5.00                   | 11.7837              | 11.3177          |
| 150.0                               | 6.00                   | 11.8019              | 11.3365          |
| 218.0                               | 8.00                   | 11.8358              | 11.3715          |
| 300.0                               | 10.0                   | 11.8673              | 11.4030          |

Figure S20. Data points and fitting curves for $^1$H NMR titration of 1T (0.005 M in DMSO-d$_6$/0.5% H$_2$O) with TBACl.

a) Binding constant $K$ derived from simultaneous fitting of 1:1 model to the two selected protons using BindFit:

$$K = 5.42 \text{ M}^{-1} \pm 0.19 \text{ M}^{-1}$$
b) Chemical shifts derived from simultaneous fitting of 1:1 model to the two selected protons using BindFit:

|                      | NH$_{\text{thioamide}}$ | NH$_{\text{carbazole}}$ |
|----------------------|--------------------------|--------------------------|
| Receptor 1T [ppm]    | 11.6801                  | 11.2081                  |
| 1T × TBA$^+$Cl$^-$ [ppm] | 12.5695                  | 12.1433                  |

c) Binding constant K derived from independent experiment repeated according to the same methodology:

\[ K = 4.64 \text{ M}^{-1} \pm 0.17 \text{ M}^{-1} \]

d) Binding constant averaged from the two experiments:

\[ K = 5.03 \text{ M}^{-1}, \text{ reported as } < 10 \text{ M}^{-1} \]
3.5  "H NMR titration of 0.005 M solution of receptor 2T in DMSO-d_6/0.5% H_2O with 0.15 M solution of TBA\('Cl\)' (dissolved in the solution of receptor 2T).

Titration of 2T with TBACl produced the most significant changes in the "H NMR chemical shifts of the carbazole NH and the thioamide NHs. The data sets for these two signals were therefore simultaneously fitted to the 1:1 model using Bindfit software.

Scheme 2. Chloride binding to 2T.

Figure S21. "H NMR titration of 2T (0.005 M) with TBACl.
### Raw data

| Added volume of titrant solution [µL] | Equivalents of TBA'Cl | Chemical Shift [ppm] |
|--------------------------------------|-----------------------|----------------------|
|                                      |                       | NH$_\text{thioamide}$ | NH$_\text{carbazole}$ |
| 0.0                                  | 0.00                  | 11.5302              | 10.8343              |
| 4.0                                  | 0.20                  | 11.5546              | 10.9044              |
| 8.0                                  | 0.39                  | 11.5772              | 10.9692              |
| 12.0                                 | 0.59                  | 11.5977              | 11.0285              |
| 16.5                                 | 0.80                  | 11.6194              | 11.091               |
| 20.5                                 | 0.99                  | 11.6374              | 11.1425              |
| 25.0                                 | 1.20                  | 11.6562              | 11.1966              |
| 31.5                                 | 1.50                  | 11.6814              | 11.2685              |
| 43.0                                 | 2.01                  | 11.7198              | 11.3779              |
| 54.5                                 | 2.50                  | 11.7524              | 11.4699              |
| 66.5                                 | 2.99                  | 11.7811              | 11.5511              |
| 79.0                                 | 3.49                  | 11.8068              | 11.6226              |
| 92.0                                 | 3.99                  | 11.8299              | 11.6855              |
| 120.0                                | 5.00                  | 11.8695              | 11.7949              |
| 150.0                                | 6.00                  | 11.9021              | 11.8818              |
| 218.0                                | 8.00                  | 11.9529              | 12.0124              |
| 300.0                                | 10.0                  | 11.9914              | 12.1053              |

Figure S22. Data points and fitting curves for $^1$H NMR titration of 2T (0.005 M in DMSO-d$_6$/0.5% H$_2$O) with TBACl.
a) Binding constant $K$ derived from simultaneous fitting of 1:1 model to the two selected protons using BindFit:

$$K = 49.2 \pm 0.4 \text{ M}^{-1}$$

b) Chemical shifts derived from simultaneous fitting of 1:1 model to the two selected protons using BindFit:

|              | $\text{NH}_{\text{thioamide}}$ | $\text{NH}_{\text{carbazole}}$ |
|--------------|---------------------------------|---------------------------------|
| Receptor $2T$ [ppm] | 11.5302                         | 10.8343                         |
| $2T \times \text{TBA}^+\text{Cl}^-$ [ppm] | 12.1806                         | 12.6656                         |

c) Binding constant $K$ derived from independent experiment repeated according to the same methodology:

concentration of host: 0.005M

$$K = 49.0 \pm 0.4 \text{ M}^{-1}$$

d) Binding constant averaged from the two experiments:

$$K = 49.1 \text{ M}^{-1}$$
3.6 $^1$H NMR titration of 0.005 M solution of receptor 3T in DMSO-d$_6$/0.5% H$_2$O with 0.15 M solution of TBA$^+$Cl$^-$ (dissolved in the solution of receptor 3T).

Titration of 3T with TBACl produced the most significant changes in the $^1$H NMR chemical shifts of the carbazole NH and the thioamide NHs. The data for these two signals were simultaneously fitted to the 1:1 model using Bindfit software.

Scheme 3. Chloride binding to 3T.

Figure S23. $^1$H NMR titration of 3T (0.005 M) with TBACl.
### Raw data

| Added volume of titrant solution [µL] | Equivalents of TBA'Cl⁻ | Chemical Shift [ppm] |  |
|--------------------------------------|------------------------|----------------------|----|
|                                      |                        | NH₃(thioamide)        | NH₃(carbazole)   |
| 0.0                                  | 0.00                   | 11.5663              | 10.6433          |
| 4.0                                  | 0.20                   | 11.5879              | 10.7170          |
| 8.0                                  | 0.39                   | 11.6088              | 10.7876          |
| 12.0                                 | 0.59                   | 11.6280              | 10.8523          |
| 16.5                                 | 0.80                   | 11.6479              | 10.9193          |
| 20.5                                 | 0.99                   | 11.6640              | 10.9738          |
| 25.0                                 | 1.20                   | 11.6816              | 11.0329          |
| 31.5                                 | 1.50                   | 11.7048              | 11.1107          |
| 43.0                                 | 2.01                   | 11.7401              | 11.2288          |
| 54.5                                 | 2.50                   | 11.7704              | 11.3292          |
| 66.5                                 | 2.99                   | 11.7973              | 11.4174          |
| 79.0                                 | 3.49                   | 11.8210              | 11.4956          |
| 92.0                                 | 3.99                   | 11.8425              | 11.5649          |
| 120.0                                | 5.00                   | 11.8796              | 11.6839          |
| 150.0                                | 6.00                   | 11.9100              | 11.7785          |
| 218.0                                | 8.00                   | 11.9573              | 11.9211          |
| 300.0                                | 10.0                   | 11.9933              | 12.0224          |

Figure S24. Data points and fitting curves for ³H NMR titration of 3T (0.005 M in DMSO-d₆/0.5% H₂O) with TBACl.
a) Binding constant $K$ derived from simultaneous fitting of 1:1 model to the two selected protons using BindFit:

$$K = 48.3 \pm 0.4 \text{ M}^{-1}$$

b) Chemical shifts derived from simultaneous fitting of 1:1 model to the two selected protons using BindFit:

\[
\begin{array}{|c|c|c|}
\hline
& \text{NH}_{\text{thioamide}} & \text{NH}_{\text{carbazole}} \\
\hline
\text{Receptor 3T [ppm]} & 11.5663 & 10.6433 \\
\text{3T × TBA⁺Cl⁻ [ppm]} & 12.1715 & 12.6425 \\
\hline
\end{array}
\]

c) Binding constant $K$ derived from independent experiment repeated according to the same methodology:

concentration of host: 0.005M

$$K = 50.9 \pm 0.3 \text{ M}^{-1}$$

d) Binding constant averaged from the two experiments:

$$K = 49.6 \text{ M}^{-1}$$
3.7 $^1$H NMR titration of 0.01 M solution of receptor 4T in DMSO-d$_6$/0.5% H$_2$O with 0.15 M solution of TBA$^+$Cl$^-$ (dissolved in the solution of receptor 4T).

Titration of 4T with TBACl produced the most significant changes in the $^1$H NMR chemical shifts of the carbazole NH, thioamide NHs and carbazole CH-2 protons. However, due to severe broadening, the carbazole NH signal was not suitable for binding constant determination. Therefore, the data for the thioamide NH and carbazole CH-2 were supplemented by chemical shifts of methylene protons c and all three simultaneously fitted to the 1:1 model using Bindfit software.

Scheme S4. Chloride binding to 4T.

Figure S25. $^1$H NMR titration of 4T (0.01 M) with TBACl.
Raw data

| Added volume of titrant solution [µL] | Equivalents of TBA’Cl⁻ | Chemical Shift [ppm] |
|--------------------------------------|------------------------|----------------------|
|                                      |                        | NH(thioamide) | CH-2  | CH(CH₃)₂ |
| 0.00                                 | 0.00                   | 11.5783       | 7.6544 | 2.7449   |
| 8.00                                 | 0.20                   | 11.6137       | 7.6942 | 2.7572   |
| 16.25                                | 0.40                   | 11.6447       | 7.7303 | 2.7683   |
| 25.00                                | 0.60                   | 11.6731       | 7.7642 | 2.7791   |
| 33.75                                | 0.80                   | 11.6972       | 7.7932 | 2.7880   |
| 42.75                                | 1.00                   | 11.7190       | 7.8196 | 2.7964   |
| 52.25                                | 1.20                   | 11.7405       | 7.8446 | 2.8041   |
| 67.25                                | 1.51                   | 11.7697       | 7.8781 | 2.8148   |
| 92.25                                | 2.00                   | 11.8080       | 7.9229 | 2.8290   |
| 120.50                               | 2.50                   | 11.8437       | 7.9609 | 2.8413   |
| 150.50                               | 3.01                   | 11.8700       | 7.9913 | 2.8511   |
| 183.00                               | 3.51                   | 11.8923       | 8.0164 | 2.8592   |
| 218.75                               | 4.01                   | 11.9132       | 8.0379 | 2.8663   |
| 300.50                               | 5.01                   | 11.9456       | 8.0715 | 2.8774   |
| 400.50                               | 6.00                   | 11.9805       | 8.0968 | 2.8860   |
| 575.50                               | 7.34                   | 12.0084       | 8.1211 | 2.8945   |

Figure S26. Data points and fitting curves for ³H NMR titration of 4T (0.01 M in DMSO-d₆/0.5% H₂O) with TBACl.
Figure S27. Data points and fitting curves for $^1$H NMR titration of 4T (0.01 M in DMSO-d$_6$/0.5% H$_2$O) with TBACl.

a) Binding constant $K$ derived from simultaneous fitting of 1:1 model to the three selected protons using BindFit:

$$K = 47.1 \pm 1.21 \text{ M}^{-1}$$

b) Chemical shifts derived from simultaneous fitting of 1:1 model to the three selected protons using BindFit:

|             | NH$_{\text{thioamide}}$ | CH-2  | CH(CH$_3$)$_2$ |
|-------------|-------------------------|-------|---------------|
| Receptor 4T [ppm] | 11.5783                | 7.6543| 2.7449        |
| 4T $\times$ TBA$^+$Cl [ppm] | 12.1296               | 8.2786| 2.9425        |

c) Binding constant $K$ derived from independent experiment repeated according to the same methodology:

concentration of host: 0.01 M

$$K = 44.1 \pm 0.5 \text{ M}^{-1}$$

d) Binding constant averaged from the two experiments:

$$K = 45.6 \text{ M}^{-1}$$
3.8 $^1$H NMR titration of 0.005 M solution of receptor 5T in DMSO-d$_6$/0.5% H$_2$O with 0.15 M solution of TBA$^+Cl^-$ (dissolved in the solution of receptor 5T).

Titration of 5T with TBACl produced significant changes in the $^1$H NMR chemical shifts of the carbazole NH and the thioamide NHs. The data for these two signals were simultaneously fitted to the 1:1 model using BindFit software.

Scheme 5. Chloride binding to 5T.

Figure S28. $^1$H NMR titration of 5T (0.005 M) with TBACl. The marked peaks were used for fitting.
Raw data

| Added volume of titrant solution [µL] | Equivalents of TBA'Cl⁻ | Chemical Shift [ppm] |
|-----------------------------|-----------------------|---------------------|
|                             |                       | NH₃(thioamide) | NH₃(carbazole) |
| 0.0                         | 0.00                  | 11.4281       | 10.2759       |
| 4.0                         | 0.20                  | 11.4444       | 10.3712       |
| 8.0                         | 0.39                  | 11.4596       | 10.4595       |
| 12.0                        | 0.59                  | 11.4733       | 10.5400       |
| 16.5                        | 0.80                  | 11.4880       | 10.6251       |
| 20.5                        | 0.99                  | 11.4999       | 10.6945       |
| 25.0                        | 1.20                  | 11.5121       | 10.7683       |
| 31.5                        | 1.50                  | 11.5292       | 10.8641       |
| 43.0                        | 2.01                  | 11.5544       | 11.0091       |
| 54.5                        | 2.50                  | 11.5758       | 11.1313       |
| 66.5                        | 2.99                  | 11.5946       | 11.2381       |
| 79.0                        | 3.49                  | 11.6114       | 11.3326       |
| 92.0                        | 3.99                  | 11.6264       | 11.4164       |
| 120.0                       | 5.00                  | 11.6525       | 11.5583       |
| 150.0                       | 6.00                  | 11.6729       | 11.6729       |
| 218.0                       | 8.00                  | 11.7064       | 11.8379       |
| 300.0                       | 10.0                  | 11.7315       | 11.9557       |

Figure S29. Data points and fitting curve for ¹H NMR titration of 5T (0.005 M in DMSO-d₆/0.5% H₂O) with TBACl.
a) Binding constant $K$ derived from simultaneous fitting of 1:1 model to the two selected protons using BindFit:

$$K = 52.9 \pm 0.3 \text{ M}^{-1}$$

b) Chemical shifts derived from simultaneous fitting of 1:1 model to the two selected protons using BindFit:

|                | $\text{NH}_{(\text{thioamide})}$ | $\text{NH}_{(\text{carbazole})}$ |
|----------------|----------------------------------|----------------------------------|
| Receptor 5T [ppm]       | 11.4281                          | 10.2759                          |
| $5T \times \text{TBA}^+\text{Cl}^-$ [ppm] | 11.8446                          | 12.6446                          |

c) Binding constant $K$ derived from independent experiment repeated according to the same methodology:

concentration of host: 0.005M

$$K = 51.6 \pm 0.3 \text{ M}^{-1}$$

d) Binding constant averaged from the two experiments:

$$K = 52.3 \text{ M}^{-1}$$
3.9 $^1$H NMR titration of 0.005 M solution of receptor 5AT in DMSO-d$_6$/0.5% H$_2$O with 0.15 M solution of TBA$^+$Cl$^-$ (dissolved in the solution of receptor 5AT).

Titration of 5AT with TBACl produced significant changes (>0.3ppm) in the $^1$H NMR chemical shifts of 4 protons: carbazole NH, amide NH, carbazole CH-2 and carbazole CH-7. Remarkably, the thioamide proton NH shifted upfield, unlike in d(thioamides), and to a relatively weak extent. Nevertheless, all three NH protons directly involved in the binding event were used for binding constant determination and simultaneously fitted to the 1:1 model using BindFit software.

Scheme 6. Chloride binding to 5AT.

Figure S30. $^1$H NMR titration of 5AT (0.005 M) with TBACl.
Raw data

| Added volume of titrant solution [µL] | Equivalents of TBA'Cl⁻ | Chemical Shift [ppm] |  |
|--------------------------------------|------------------------|----------------------|--|
|                                      |                        | NH₃(thioamide)        | NH₃(carbazole) | NH₃(amide) |  |
| 0.0                                  | 0.00                   | 11.5609              | 10.5538        | 10.0039    |  |
| 4.0                                  | 0.20                   | 11.5519              | 10.6757        | 10.0311    |  |
| 8.0                                  | 0.39                   | 11.5436              | 10.7876        | 10.0559    |  |
| 12.25                                | 0.60                   | 11.5352              | 10.8981        | 10.0804    |  |
| 16.5                                 | 0.80                   | 11.5282              | 10.9974        | 10.1025    |  |
| 20.75                                | 1.00                   | 11.5216              | 11.0885        | 10.1226    |  |
| 25.0                                 | 1.20                   | 11.5154              | 11.1723        | 10.1415    |  |
| 31.5                                 | 1.50                   | 11.5073              | 11.2882        | 10.1672    |  |
| 42.75                                | 2.00                   | 11.4948              | 11.4566        | 10.2048    |  |
| 54.5                                 | 2.50                   | 11.4845              | 11.6021        | 10.2369    |  |
| 67.25                                | 3.02                   | 11.4759              | 11.7293        | 10.2656    |  |
| 79.25                                | 3.50                   | 11.4686              | 11.8292        | 10.2877    |  |
| 92.25                                | 4.00                   | 11.4626              | 11.9197        | 10.3082    |  |
| 120.0                                | 5.00                   | 11.4526              | 12.0696        | 10.3417    |  |
| 150.0                                | 6.00                   | 11.4454              | 12.1866        | 10.3682    |  |
| 218.25                               | 8.00                   | 11.4361              | 12.3546        | 10.4069    |  |
| 300.0                                | 10.00                  | 11.4312              | 12.4694        | 10.4342    |  |
Figure S31. Data points and fitting curves for $^1$H NMR titration of SAT (0.005 M in DMSO-d$_6$/0.5% H$_2$O) with TBACl.

a) Binding constant $K$ derived from simultaneous fitting of 1:1 model to the two selected protons using BindFit:

$$K = 68.3 \pm 0.2 \text{ M}^{-1}$$

b) Chemical shifts derived from simultaneous fitting of 1:1 model to the two selected protons using BindFit:

|                | $\text{NH}_{\text{thioamide}}$ | $\text{NH}_{\text{carbazole}}$ | $\text{NH}_{\text{amide}}$ |
|----------------|-------------------------------|---------------------------------|-----------------------------|
| Receptor SAT [ppm] | 11.5609                       | 10.5538                         | 10.0039                     |
| SAT $\times$ TBA$^+$Cl [ppm] | 11.3821                       | 13.0784                         | 10.5674                     |
c) Binding constant $K$ derived from independent experiment repeated according to the same methodology:

concentration of host: 0.005M

$$K = 65.7 \pm 0.3 \text{ M}^{-1}$$

d) Binding constant averaged from the two experiments:

$$K = 67.0 \text{ M}^{-1}$$
3.10 $^3$H NMR titration of 0.005 M solution of receptor 6AT in DMSO-d$_6$/0.5% H$_2$O with 0.15 M solution of TBA$^+$Cl$^-$ (dissolved in the solution of receptor 6AT).

Titration of 6AT with TBACl produced significant changes (>0.3ppm) in the $^1$H NMR chemical shifts of only 1 NH proton and 2 CH protons: carbazole NH, CH-2 and CH-7. Remarkably, the thioamide proton NH shifted slightly upfield, like in the mono(thioamide) 5AT and unlike in di(thioamides). Nevertheless, all three NH protons directly involved in the binding event were used for binding constant determination and to this end simultaneously fitted to the 1:1 model using BindFit software.

Scheme 7. Chloride binding to 6AT.

Figure S32. $^1$H NMR titration of 6AT (0.005 M) with TBACl. The marked peaks were used for fitting.
### Raw data

| Added volume of titrant solution [µL] | Equivalents of TBA'Cl⁻ | Chemical Shift [ppm] |  |
|--------------------------------------|-------------------------|----------------------|---|
| 0.0                                  | 0.00                    | 11.4639              | 10.0393 | 9.9441 |
| 4.0                                  | 0.20                    | 11.4609              | 10.0910 | 9.9510 |
| 8.0                                  | 0.39                    | 11.4585              | 10.1398 | 9.9578 |
| 12.0                                 | 0.59                    | 11.4561              | 10.1859 | 9.9640 |
| 16.5                                 | 0.80                    | 11.4534              | 10.2355 | 9.9707 |
| 20.5                                 | 0.99                    | 11.4512              | 10.2781 | 9.9761 |
| 25.0                                 | 1.20                    | 11.4489              | 10.3232 | 9.9826 |
| 31.5                                 | 1.50                    | 11.4455              | 10.3839 | 9.9908 |
| 43.0                                 | 2.01                    | 11.4403              | 10.4821 | 10.0042 |
| 54.5                                 | 2.50                    | 11.4358              | 10.5705 | 10.0160 |
| 66.5                                 | 2.99                    | 11.4314              | 10.6526 | 10.0271 |
| 79.0                                 | 3.49                    | 11.4277              | 10.7290 | 10.0375 |
| 92.0                                 | 3.99                    | 11.424               | 10.7995 | 10.0470 |
| 120.0                                | 5.00                    | 11.4174              | 10.9285 | 10.0644 |
| 150.0                                | 6.00                    | 11.4119              | 11.0391 | 10.0794 |
| 218.0                                | 8.00                    | 11.4032              | 11.2228 | 10.1045 |
| 300.0                                | 10.0                    | 11.3966              | 11.3681 | 10.1244 |
Figure S33. Data points and fitting curve for $^1$H NMR titration of 6AT (0.005 M in DMSO-d$_6$/0.5% H$_2$O) with TBACl.

a) Binding constant $K$ derived from simultaneous fitting of 1:1 model to the two selected protons using BindFit:

$$K = 23.1 \pm 0.1 \text{ M}^{-1}$$

b) Chemical shifts derived from simultaneous fitting of 1:1 model to the two selected protons using BindFit:

| Receptor 6AT [ppm] | NH$_{(thioamide)}$ | NH$_{(carbazole)}$ | NH$_{(amide)}$ |
|--------------------|--------------------|--------------------|----------------|
| 11.4639            | 10.0393            | 9.9441             |
| 6AT × TBA′Cl [ppm] | 11.3320            | 12.5856            | 10.2891        |

c) Binding constant $K$ derived from independent experiment repeated according to the same methodology:
concentration of host: 0.005M

\[ K = 23.4 \pm 0.04 \text{ M}^{-1} \]

d) Binding constant averaged from the two experiments:

\[ K = 23.3 \text{ M}^{-1} \]
4 Transmembrane anion transport experiments

4.1 Preparation of phospholipid vesicles

A chloroform solution of 1-palmitoyl-2-oleoyl-sn-glycero-3-phosphocholine (POPC) (20 mg/mL) (Sigma Aldrich) was evaporated to dryness using a rotary evaporator and the resulting film was dried under high vacuum for, at least, two hours. A sodium chloride aqueous solution (489 mM and 5 mM phosphate buffer, pH 7.2, or 451 mM and 20 mM phosphate buffer, pH 7.2) was added to rehydrate the lipid film. The resulting suspension was vortexed and subjected to nine freeze-thaw cycles; subsequently, it was extruded through a polycarbonate membrane (200 nm) employing a LiposoFast basic extruder (Avestin, Inc.). The resulting unilamellar vesicles were dialysed against a sodium nitrate (489 mM and 5 mM phosphate buffer, pH 7.2) or a sodium sulphate (150 mM and 20 mM phosphate buffer, pH 7.2) aqueous solutions, to remove unencapsulated chloride.

4.2 ISE transport experiments

Unilamellar vesicles (average diameter: 200 nm) made of POPC and containing a sodium chloride aqueous solution (489 mM and 5 mM phosphate buffer, pH 7.2, for chloride/nitrate exchange assays, or 451 mM and 20 mM phosphate buffer, pH 7.2, for chloride/bicarbonate exchange assays) were suspended in a sodium nitrate (489 mM and 5 mM phosphate buffer, pH 7.2) or a sodium sulphate (150 mM and 20 mM phosphate buffer, pH 7.2) aqueous solution, respectively, the final lipid concentration being 0.5 mM and the final volume 5 mL. A solution of the carrier in DMSO, usually 5 µL to avoid the influence of the organic solvent during the experiments, was added, and the chloride released was monitored employing a chloride-selective electrode (HACH 9652C). Once the experiment was finished, a surfactant (Triton-X, 10% dispersion in water, 20 µL) was added to lyse the vesicles and release all the encapsulated chloride. This value was taken as 100% release and used as such. For the chloride/bicarbonate exchange assays, a sodium bicarbonate aqueous solution was added to the vesicles suspended in the sodium sulphate one (150 mM and 20 mM phosphate buffer, pH 7.2), the final bicarbonate concentration during the experiment being 40 mM. The chloride efflux was monitored for another five minutes, until the vesicles were lysed with the surfactant.
4.3 Study of the Cl⁻/NO₃⁻ exchange

Figure S34. Chloride efflux promoted by 2T at different concentrations (2% - 0.02% carrier to POPC molar ratio, 10 - 0.1 µM) in unilamellar POPC vesicles. Vesicles loaded with 489 mM NaCl were buffered at pH 7.2 with 5 mM phosphate and dispersed in 489 mM NaNO₃ buffered at pH 7.2. Each trace represents the average of at least three trials.

![Graph showing chloride efflux over time for different concentrations of 2T.](image)

Figure S355. Normalised chloride efflux at 300 s plotted against the concentration of compound 2T. Data have been plotted with Hill equation fitting curve (continuous line).

![Table showing Hill equation parameters.](image)
Figure S36. Chloride efflux promoted by 3T at different concentrations (2% - 0.01% carrier to POPC molar ratio, 10 - 0.05 µM) in unilamellar POPC vesicles. Vesicles loaded with 489 mM NaCl were buffered at pH 7.2 with 5 mM phosphate and dispersed in 489 mM NaNO₃ buffered at pH 7.2. Each trace represents the average of at least three trials.

Figure S37. Normalised chloride efflux at 300 s plotted against the concentration of compound 3T. Data have been plotted with Hill equation (continuous line).
Figure S38. Chloride efflux promoted by 4T at different concentrations (1% - 0.005% carrier to POPC molar ratio, 5 - 0.025 µM) in unilamellar POPC vesicles. Vesicles loaded with 489 mM NaCl were buffered at pH 7.2 with 5 mM phosphate and dispersed in 489 mM NaNO₃ buffered at pH 7.2. Each trace represents the average of at least three trials.

Figure S39. Normalised chloride efflux at 300 s plotted against the concentration of compound 4T. Data have been plotted with Hill equation (continuous line).
Figure S40. Chloride efflux promoted by 5T at different concentrations (2% - 0.01% carrier to POPC molar ratio, 10 - 0.05 µM) in unilamellar POPC vesicles. Vesicles loaded with 489 mM NaCl were buffered at pH 7.2 with 5 mM phosphate and dispersed in 489 mM NaNO₃ buffered at pH 7.2. Each trace represents the average of at least three trials.

Figure S41. Normalised chloride efflux at 300 s plotted against the concentration of compound 5T. Data have been plotted with Hill equation (continuous line).
Figure S42. Chloride efflux promoted by \textit{5AT} at different concentrations (3% - 0.002% carrier to POPC molar ratio, 15 - 0.05 µM) in unilamellar POPC vesicles. Vesicles loaded with 489 mM NaCl were buffered at pH 7.2 with 5 mM phosphate and dispersed in 489 mM NaNO\textsubscript{3} buffered at pH 7.2. Each trace represents the average of at least three trials.

Figure S43. Normalised chloride efflux at 300 s plotted against the concentration of compound \textit{5AT}. Data have been plotted with Hill equation (continuous line).
Figure S44. Chloride efflux promoted by 6AT at different concentrations (2% - 0.01% carrier to POPC molar ratio, 10 - 0.05 µM) in unilamellar POPC vesicles. Vesicles loaded with 489 mM NaCl were buffered at pH 7.2 with 5 mM phosphate and dispersed in 489 mM NaNO₃ buffered at pH 7.2. Each trace represents the average of at least three trials.

Figure S45. Normalised chloride efflux at 300 s plotted against the concentration of compound 6AT. Data have been plotted with Hill equation (continuous line).
4.4 Study of the Cl⁻/HCO₃⁻ exchange

Figure S46. Chloride efflux promoted by 2T at different concentrations (2% - 0.05% carrier to POPC molar ratio, 10 - 0.25 µM) in unilamellar POPC vesicles. Vesicles, which contained NaCl (451 mM NaCl and 20 mM phosphate buffer, pH 7.2), were immersed in Na₂SO₄ (150 mM Na₂SO₄, 40 mM HCO₃⁻ and 20 mM phosphate buffer, pH 7.2). Each trace represents an average of at least three different experiments.

Figure S47. Normalised chloride efflux at 300 s plotted against the concentration of compound 2T. Data have been plotted with Hill equation (continuous line).
Figure S48. Chloride efflux promoted by 3T at different concentrations (4% - 0.05% carrier to POPC molar ratio, 20 - 0.25 µM) in unilamellar POPC vesicles. Vesicles, which contained NaCl (451 mM NaCl and 20 mM phosphate buffer, pH 7.2), were immersed in Na₂SO₄ (150 mM Na₂SO₄, 40 mM HCO₃⁻ and 20 mM phosphate buffer, pH 7.2). Each trace represents an average of at least three different experiments.

Figure S49. Normalised chloride efflux at 300 s plotted against the concentration of compound 3T. Data have been plotted with Hill equation (continuous line).
Figure S50. Chloride efflux promoted by 4T at different concentrations (2% - 0.03% carrier to POPC molar ratio, 10 - 0.15 µM) in unilamellar POPC vesicles. Vesicles, which contained NaCl (451 mM NaCl and 20 mM phosphate buffer, pH 7.2), were immersed in Na$_2$SO$_4$ (150 mM Na$_2$SO$_4$, 40 mM HCO$_3$– and 20 mM phosphate buffer, pH 7.2). Each trace represents an average of at least three different experiments.

Figure S51. Normalised chloride efflux at 300 s plotted against the concentration of compound 4T. Data have been plotted with Hill equation (continuous line).
Figure S5.2. Chloride efflux promoted by 5T at different concentrations (2% - 0.02% carrier to POPC molar ratio, 10 - 0.1 µM) in unilamellar POPC vesicles. Vesicles, which contained NaCl (451 mM NaCl and 20 mM phosphate buffer, pH 7.2), were immersed in Na₂SO₄ (150 mM Na₂SO₄, 40 mM HCO₃⁻ and 20 mM phosphate buffer, pH 7.2). Each trace represents an average of at least three different experiments.

Figure S5.3. Normalised chloride efflux at 300 s plotted against the concentration of compound 5T. Data have been plotted with Hill equation (continuous line).
Figure S5. Chloride efflux promoted by 5AT at different concentrations (2% - 0.1% carrier to POPC molar ratio, 10 - 0.5 µM) in unilamellar POPC vesicles. Vesicles, which contained NaCl (451 mM NaCl and 20 mM phosphate buffer, pH 7.2), were immersed in Na$_2$SO$_4$ (150 mM Na$_2$SO$_4$, 40 mM HCO$_3^-$ and 20 mM phosphate buffer, pH 7.2). Each trace represents an average of at least three different experiments.

Figure S5. Normalised chloride efflux at 300 s plotted against the concentration of compound 5AT. Data have been plotted with Hill equation (continuous line).
4.5 Study of the Cl⁻/SO₄²⁻ exchange

Figure S56. Chloride efflux promoted by 5T, 3T, 2T and 6AT (10 µM, 2 % mol carrier to lipid concentration) in unilamellar POPC vesicles. Vesicles loaded with 451 mM NaCl buffered at pH 7.2 with 20 mM phosphate dispersed in 150 mM Na₂SO₄ buffered at pH 7.2. Each trace represents the average of at least three trials.
Table S1. Transport activities expressed as EC₅₀ (nM) and Hill parameter for compounds (1A-6AT).

| Compound | EC₅₀ (nM) NO₃⁻/Cl⁻ | Hill parameter, n NO₃⁻/Cl⁻ | EC₅₀ (nM) HCO₃⁻/Cl⁻ | Hill parameter, n HCO₃⁻/Cl⁻ | Lipophilicity (logP)⁹ |
|----------|----------------------|----------------------------|----------------------|----------------------------|-----------------------|
| 1A       | - ⁷      | - ⁷          | - ⁷          | - ⁷          | 5.74                  |
| 1T       | - ⁷      | - ⁷          | - ⁷          | - ⁷          | 6.25                  |
| 2A       | - ⁷      | - ⁷          | - ⁷          | - ⁷          | 3.98                  |
| 2T       | 297      | 0.93         | 4290        | 0.74         | 5.13                  |
| 3A       | 107      | 1.14         | 2910        | 0.59         | 5.67                  |
| 3T       | 184      | 0.725        | 385         | 0.92         | 5.86                  |
| 4A       | 66       | 1.37         | 385         | 0.92         | 5.08                  |
| 4T       | 61       | 0.99         | 1719        | 0.90         | 5.98                  |
| 5A       | 93       | 1.35         | 465         | 0.67         | 6.44                  |
| 5AT      | 353      | 0.88         | -           | -            | 5.48                  |
| 6AT      |          |              |             |              |                       |

⁹ Determined using ALOGPS 2.1 software. ⁷ The compound was not active enough to calculate EC₅₀ value. ⁸ Values from reference.
5 X-ray measurements

5.1 General procedure for crystallizations

X-ray quality single crystals of 3T·TBACl were grown by slow diffusion of pentane into a solution of 3T and TBACl (slight excess) in 1,2-dichloroethane.

5.2 X-ray structure

Table S2. Crystal data and structure refinement for 3T·TBACl

| Identification code | 3T·TBACl |
|---------------------|----------|
| Empirical formula   | C_{36}H_{57}Cl_{3}N_{4}S_{2} |
| Formula weight      | 716.32   |
| Temperature/K       | 100(2)   |
| Crystal system      | monoclinic |
| Space group         | P2_1/c   |
| a/Å                 | 12.06169(12) |
| b/Å                 | 15.09891(15) |
| c/Å                 | 21.2481(2)  |
| α/°                 | 90        |
| β/°                 | 99.4856(10) |
| γ/°                 | 90        |
| Volume/Å³           | 3816.77(7) |
| Z                   | 4         |
| ρ calc g/cm³        | 1.247     |
| μ/Å⁻¹               | 3.419     |
| F(000)              | 1536.0    |
| Crystal size/mm³    | 0.36 x 0.23 x 0.08 |
| Radiation           | CuKα (λ = 1.54184) |
| 2θ range for data collection/° | 7.216 to 134.156 |
| Index ranges        | -14 ≤ h ≤ 14, -18 ≤ k ≤ 18, -25 ≤ l ≤ 25 |
| Reflections collected | 51923    |
| Independent reflections | 6805 [R_{int} = 0.0359, R_{sigma} = 0.0173] |
| Data/restraints/parameters | 6805/3/421 |
| Goodness-of-fit on F² | 1.063   |
| Final R indexes [I>2σ (I)] | R₁ = 0.0419, wR₂ = 0.1179 |
| Final R indexes [all data] | R₁ = 0.0457, wR₂ = 0.1228 |
| Largest diff. peak/hole / e Å⁻³ | 1.39/-0.57 |

Table S3. Bond lengths for 3T·TBACl

| Atom | Atom | Length/Å | Atom | Atom | Length/Å |
|------|------|----------|------|------|----------|
| C(1) | C(2) | 1.404(3) | C(15)| C(16)| 1.519(4) |
| C(1) | C(6) | 1.411(3) | C(17)| C(18)| 1.521(3) |
| C(1) | N(1) | 1.374(3) | C(17)| N(3) | 1.345(3) |
| C(2) | C(3) | 1.385(3) | C(17)| S(2) | 1.648(2) |
| C(2) | N(2) | 1.420(3) | C(18)| C(19)| 1.518(3) |
| C(3) | C(4) | 1.403(3) | C(19)| C(20)| 1.526(4) |
| C(4) | C(5) | 1.384(3) | C(21)| C(22)| 1.522(3) |
| C(4) | C(1) | 1.7472(19)| C(21)| N(33)| 1.520(2) |
| C(5) | C(6) | 1.400(3) | C(22)| C(23)| 1.532(3) |
| C(6) | C(7) | 1.452(3) | C(23)| C(24)| 1.522(3) |
| C(7) | C(8) | 1.391(3) | C(25)| C(26)| 1.521(3) |
| C(7) | C(12)| 1.410(3) | C(25)| N(33)| 1.520(3) |
Table S4. Values of valence angles for 3T×TBACI

| Atom | Atom | Atom | Angle/° | Atom | Atom | Atom | Angle/° |
|------|------|------|---------|------|------|------|---------|
| C(2) | C(1) | C(6) | 121.86(18) | N(2) | C(13) | S(1) | 124.83(16) |
| N(1) | C(1) | C(2) | 127.65(18) | C(15) | C(14) | C(13) | 114.7(2) |
| N(1) | C(1) | C(6) | 110.48(17) | C(16) | C(15) | C(14) | 112.5(2) |
| C(1) | C(2) | N(2) | 117.97(17) | C(18) | C(17) | S(2) | 124.58(16) |
| C(3) | C(2) | C(1) | 118.09(18) | N(3) | C(17) | C(18) | 111.36(18) |
| C(3) | C(2) | N(2) | 123.90(18) | N(3) | C(17) | S(2) | 124.03(17) |
| C(2) | C(3) | C(4) | 119.23(18) | C(19) | C(18) | C(17) | 118.73(19) |
| C(3) | C(4) | C(1) | 117.34(15) | C(18) | C(19) | C(20) | 114.5(2) |
| C(5) | C(4) | C(3) | 123.95(18) | C(1) | N(1) | C(12) | 107.57(17) |
| C(5) | C(4) | C(1) | 118.68(15) | C(13) | N(2) | C(2) | 127.71(17) |
| C(4) | C(5) | C(6) | 116.79(18) | C(17) | N(3) | C(11) | 129.68(18) |
| C(1) | C(6) | C(7) | 105.75(17) | N(33) | C(21) | C(22) | 114.34(16) |
| C(5) | C(6) | C(1) | 120.08(18) | C(21) | C(22) | C(23) | 111.62(17) |
| C(5) | C(6) | C(7) | 134.17(19) | C(24) | C(23) | C(22) | 111.52(19) |
| C(8) | C(7) | C(6) | 134.05(19) | N(33) | C(25) | C(26) | 116.14(17) |
| C(8) | C(7) | C(12) | 120.04(18) | C(25) | C(26) | C(27) | 109.1(2) |
| C(12) | C(7) | C(6) | 105.90(18) | C(28) | C(27) | C(26) | 114.5(3) |
| C(9) | C(8) | C(7) | 116.94(19) | N(33) | C(29) | C(30) | 115.63(16) |
| C(8) | C(9) | C(10) | 123.6(2) | C(29) | C(30) | C(31) | 109.07(17) |
| C(8) | C(9) | C(2) | 118.32(17) | C(32) | C(31) | C(30) | 111.7(2) |
| C(10) | C(9) | C(2) | 118.03(16) | C(34) | C(33) | N(33) | 116.58(16) |
| C(11) | C(10) | C(9) | 119.45(18) | C(33) | C(34) | C(35) | 109.01(16) |
| C(10) | C(11) | C(12) | 117.83(19) | C(36) | C(35) | C(34) | 111.69(17) |
| C(10) | C(11) | N(3) | 124.79(18) | C(21) | N(33) | C(29) | 106.61(14) |
| C(12) | C(11) | N(3) | 117.14(18) | C(21) | N(33) | C(33) | 111.28(15) |
| C(11) | C(12) | C(7) | 122.10(19) | C(25) | N(33) | C(21) | 111.41(15) |
| N(1) | C(12) | C(7) | 110.26(17) | C(25) | N(33) | C(29) | 111.54(15) |
| N(1) | C(12) | C(11) | 127.64(19) | C(25) | N(33) | C(33) | 105.77(15) |
| C(14) | C(13) | S(1) | 121.83(16) | C(29) | N(33) | C(33) | 110.30(15) |
| N(2) | C(13) | C(14) | 113.34(18) | | | | |

Table S5. Values of torsion angles for 3T×TBACI

| A | B | C | D | Angle/° | A | B | C | D | Angle/° |
|---|---|---|---|-------|---|---|---|---|-------|
| C(1) | C(2) | C(3) | C(4) | 0.7(3) | C(17) | C(18) | C(19) | C(20) | 76.3(3) |
| C(1) | C(2) | N(2) | C(13) | -136.6(2) | C(18) | C(17) | N(3) | C(11) | 174.52(19) |
| C(1) | C(6) | C(7) | C(8) | -178.7(2) | C(1) | C(4) | C(5) | C(6) | 178.21(14) |
| C(1) | C(6) | C(7) | C(12) | 0.1(2) | C(2) | C(9) | C(10) | C(11) | 178.94(15) |
| C(2) | C(1) | C(6) | C(5) | 0.3(3) | N(1) | C(1) | C(2) | C(3) | -179.27(18) |
| C(2) | C(1) | C(6) | C(7) | 179.72(17) | N(1) | C(1) | C(2) | N(2) | 2.9(3) |
| C(2) | C(1) | N(1) | C(12) | -178.99(18) | N(1) | C(1) | C(6) | C(5) | 179.10(17) |
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