Formation of *N*-bridgehead 1,2,5-thiadiazolium and selenadiazolium rings through an intramolecular cyclisation reaction†

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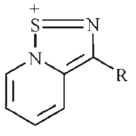
Treatment of *N*-lithiopyridylketimide derivatives Li[R(C = N)py] (R = Ph, py) with $\mathrm{ECl_2}$ (E = S, Se) affords the fused thiadiazolium and selenadiazolium salts $[\mathrm{RC_6H_4N_2E}]$Cl [1]Cl and [2]Cl containing a bridgehead N atom through intramolecular coordination.

Benzothiadiazole (**3**) and its derivatives have a diverse range of applications, including their biological activity as antiviral, antibacterial and antifungal agents[1] as well as components in organic light-emitting diodes (OLEDs)[2] and π-conjugated polymers.[3] Here we report a facile synthesis of the air-stable, cationic, fused thiadiazolylium rings $\mathbf{1}^+$ and their selenium analogues, $\mathbf{2}^+$ (R = Ph, py and 2-thiophenyl) through intramolecular attack at the chalcogen by the pendant pyridyl functional group. To our knowledge, derivatives in which the heteroatoms form part of a fused ring have not been explored, although recently Oakley and co-workers have reported[4] the *N*-alkylated benzochalcadiazolylium cations **4** (E = S, Se, Te).



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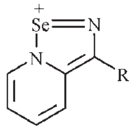

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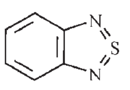

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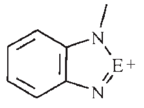

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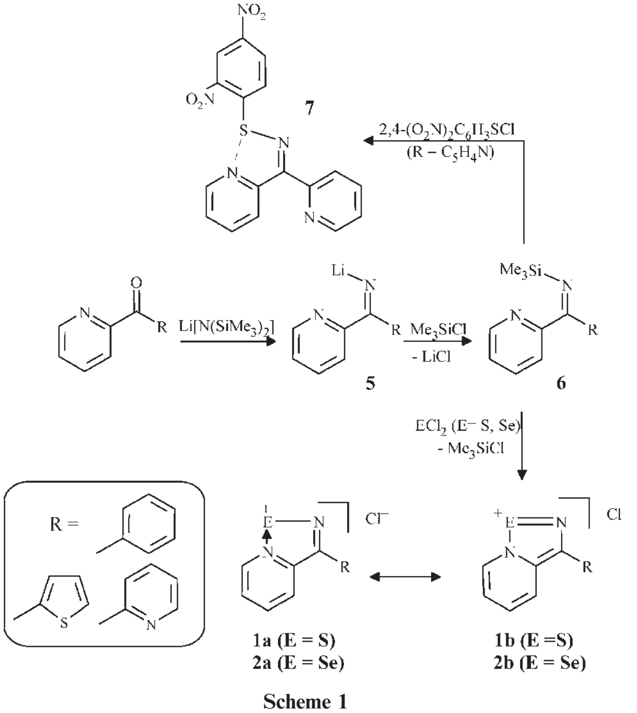
The key intermediate for the formation of [**1**]Cl is the *N*-lithioketimide **5** (Scheme 1). For [**1**]Cl (R = py) this was prepared *via* the reaction of dipyridyl ketone with $\mathrm{Li[N(SiMe_3)_2]}$ in toluene.[5] Treatment of **5** (R = py) with $\mathrm{Me_3SiCl}$ affords the *N*-silylketimide **6**. Condensation of **6** with $\mathrm{SCl_2}$ generates [**1**]Cl (R = py) in *ca.* 95% recovered yield.† This process could occur *via* (i) a condensation reaction at the ketimide nitrogen, followed by ring closure; (ii) prior coordination of S by the pyridyl-N followed by condensation; or (iii) a more concerted process involving simultaneous formation of both S–N bonds. Whilst Marder and co-workers have observed reactions of 2-pyridyl-alkynes with $\mathrm{R_2BH}$ to proceed *via* initial N-coordination,[6] the known adducts of $\mathrm{SCl_2}$ comprise Lewis-acid rather than Lewis-base derivatives.[7] We thus favour an initial condensation reaction followed by intramolecular coordination of the pendant pyridyl group to the electropositive S atom with loss of $\mathrm{Cl^-}$. In the presence of a poorer leaving group $[2,4\text{-}(\mathrm{O_2N})_2\mathrm{C_6H_3}]^-$ the acyclic compound **7** is isolated (54% recovered yield) (Scheme 1) which is formed by a similar condensation reaction and exhibits a weak intramolecular S···N contact.† A number of 4- or 5-membered hetero- and metallocycles have been prepared by similar intramolecular coordination reactions using pendant pyridyl or amine ligands.[8]

Crystals of [**1**]Cl (R = py) could be grown from DMF or $\mathrm{MeOH/Et_2O}$ as colourless needles suitable for X-ray diffraction.‡ These reveal a planar, fused ring system (Fig. 1). The S(1)–N(2) distance (1.725(2) Å) falls at the longer end of conventional S–N single bond distances (1.69–1.72 Å)[7] whilst the S(1)–N(1) distance (1.627(2) Å) appears to have a little double-bond character (*cf.* $d_{\mathrm{S=N}}$ = 1.43–1.58 Å).[6] Similarly the C–C (1.447(3) Å) and C–N bonds (1.312(3) and 1.373(3) Å) in the five-membered ring appear intermediate between conventional single and double bonds, indicative of substantial π-delocalisation. This is consistent with significant contributions from the resonance forms **1a** and, to a lesser extent, **1b** (Scheme 1). The chloride anion exhibits a close contact to the electropositive S atom ($d_{\mathrm{S\cdots Cl}}$ = 3.012(2) Å, *cf.* sum of the van der Waals radii at 3.65 Å and $d_{\mathrm{S–Cl}}$ = 2.06 Å in $\mathrm{S_2Cl_2}$).[9]



Scheme 1

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† Electronic supplementary information (ESI) available: Experimental details for the preparation of [**1**]Cl (R = py), [**2**]Cl (R = Ph) and **7**; details of DFT calculations including NBO analysis for $\mathbf{1}^+$, $\mathbf{2}^+$, [**1**]Cl and [**2**]Cl; structural data for [**1**]Cl, [**2**]Cl and **7**: CCDC reference numbers 691668–691670. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/b809987a

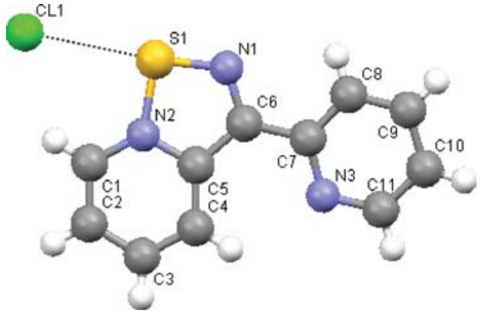

Fig. 1 Asymmetric unit of [**1**]Cl. Selected bond lengths (Å) and angles (°) are: N(1)C(6) 1.312(3), N(1)S(1) 1.627(2), S(1)N(2) 1.725(2), N(2)C(5) 1.373(3), C(5)C(6) 1.447(3), C(6)N(1)S(1) 113.8(2), N(1)S(1)N(2) 92.89(9), C(5)N(2)S(1) 110.4(1), N(2)C(5)C(6) 109.4(2), N(1)C(6)C(5) 113.6(2).

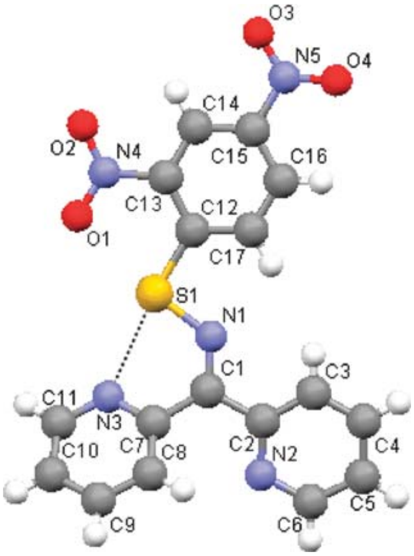

Fig. 2 Asymmetric unit of **7**. Selected bond lengths (Å) and angles (°) are: S(1)–N(1) 1.680(1), S(1)–C(12) 1.772(2), N(1)–C(1) 1.291(2), C(1)–C(7) 1.488(2), C(7)–N(3) 1.340(2), N(3)–S(1) 2.720(1), N(1)S(1)C(12) 96.48(7), C(1)N(1)S(1) 123.0(1), N(1)C(1)C(7) 124.7(2), N(3)C(7)C(1) 115.1(1), C(7)N(3)S(1) 91.3(1).

The acyclic derivative **7** (Fig. 2) exhibits‡ a longer N–S bond (1.680(1) Å) than $\mathbf{1}^+$ but is still a little shorter than a conventional S–N single bond (d_{S-N} = 1.69–1.72 Å). In comparison the intramolecular $S^{\delta+}\cdots N^{\delta-}$ contact ($d_{S\cdots N}$ = 2.720(1) Å) is substantially greater than an S–N single bond but shorter than the sum of the van der Waals radii (3.20 Å), consistent with an acyclic structure with a weak intramolecular S···N interaction.

Solution ^{1}H NMR studies on [**1**]Cl (R = py) reveal two distinct pyridyl-ring environments. Whilst the overlapping multiplets in $\mathbf{1}^+$ can be assigned by ^{1}H COSY to two chemically distinct pyridyl rings, the hindered rotation about the ketimine bond does not directly distinguish between cyclic and acyclic forms of [**1**]Cl (R = py) in solution. However, the low field ^{1}H NMR chemical shift (δ = +10.05) in $\mathbf{1}^+$ (R = py) is comparable to other *ortho*-^{1}H resonances in pyridinium salts[10] and supports the retention of the ring-closed form in solution. This peak is notably shifted to higher field in acyclic derivatives such as **7** (δ = +8.97, +8.66), as well as in the dipyridyl ketone precursor itself (δ = +9.03).

An NBO analysis of $\mathbf{1}^+$ (R = H) based on DFT (B3LYP/DZVP) studies[11] is consistent with the dominant resonance form **1a** (Scheme 1) in which the S atom bears the greatest positive charge (+0.87 e^-). Inclusion of the Cl$^-$ counterion in the calculations leads to a short S···Cl contact (2.69 Å) and a modest lengthening of the N–S bonds by 0.037–0.054 Å with the pyridyl-N–S bond showing a greater sensitivity to the presence of the Cl$^-$ anion (see ESI†), *cf*. [**2**]Cl (see later).

Work by Oakley *et al*. has recently shown that one electron reduction of *N*-alkylated benzothiadiazolyium salts generates stable free radicals through addition of one electron to the LUMO of $\mathbf{1}^+$ (Fig. 3).[4] In the current system reduction may lead to ring-opening through addition of an electron into the LUMO (Fig. 3) which is antibonding with respect to N–S. However, *in situ* EPR studies utilising a range of reducing agents and solvents have so far failed to detect the radical $\mathbf{1}^{\bullet}$.

The isoelectronic Se analogues can be prepared in a similar fashion.† Whilst we have not been able to crystallise [**2**]Cl (R = py), the phenyl-derivative [**2**]Cl (R = Ph) proved readily accessible from phenyl,pyridyl-ketone using $SeCl_2$ (generated *in situ* from Se and SO_2Cl_2).[12] Crystals of [**2**]Cl (R = Ph) were grown from DMF as colourless plates suitable for X-ray diffraction.‡

The X-ray structure of [**2**]Cl (R = Ph) reveals a planar, fused ring system (Fig. 4) with one molecule in the asymmetric unit. Whilst the Se(1)–N(1) distance (1.819(4) Å) appears firmly within this reported range for Se–N single bonds (1.81–1.85 Å),[13] the Se(1)–N(2) distance (2.013(4) Å) is substantially longer. This longer bond may arise as a result of significantly stronger E–Cl covalency (E = S, Se) in $\mathbf{2}^+$ (*cf*. more ionic nature of S···Cl in $\mathbf{1}^+$). Indeed the Se–Cl distance in [**2**]Cl (2.530(1) Å) is typical of other reported Se–Cl bond distances (d_{Se-Cl} = 2.23–2.85 Å).[14]

The Cl atom adopts a position close to the C/N/Se ring plane, *trans* to N(2), and is likely to result in a strong inter-dependence of the Se–N and Se–Cl bond lengths. A natural bond orbital (NBO) analysis based on DFT calculations (B3LYP/DZVP) on the isolated cation $\mathbf{2}^+$ (R = H) reveals that the resonance form **2a** contributes most significantly to the total structure with a formal positive charge of +0.95 e^- on the Se centre. Inclusion of the Cl$^-$ counter-ion *trans* to the pyridyl-N in the DFT calculations leads to pronounced changes in the heterocyclic geometry of $\mathbf{2}^+$ with significantly more electron density transferred from anion to cation in $\mathbf{2}^+$ (NBO charge on Cl = −0.37 e^-) than in $\mathbf{1}^+$ (NBO charge on Cl = −0.71 e^-). This charge-transfer process leads to a more marked increase in Se–N bond lengths (+0.046 and +0.483 Å). Geometry

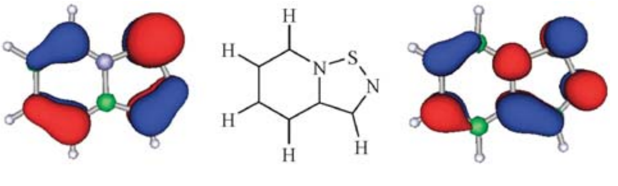

Fig. 3 HOMO (left) and LUMO (right) of $\mathbf{1}^+$ (R = H) (centre) based on geometry-optimised DFT B3LYP/6-31G* calculations.

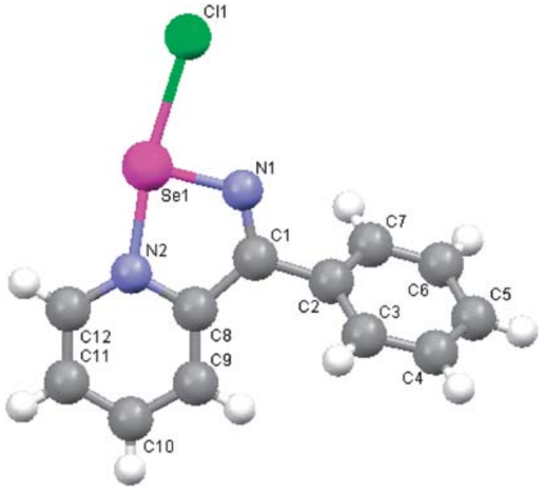

Fig. 4 Asymmetric unit of [**2**]Cl. Selected bond lengths (Å) and angles (°) are Se(1)–N(1) 1.819(4), Se(1)–N(2) 2.013(4), Se(1)–Cl(1) 2.530(1), N(1)–C(1) 1.290(6), C(1)–C(8) 1.461(7), C(8)–N(2) 1.357(6), N(1)Se(1)N(2) 84.0(2), N(1)Se(1)Cl(1) 87.4(1), N(2)Se(1)Cl(1) 170.9(1), C(1)N(1)Se(1) 115.2(3), N(1)C(1)C(8) 119.3(5), N(2)C(8)C(1) 110.3(4), C(8)N(2)Se(1) 111.2(3).

optimisation yields a formal Se–Cl bond (2.294 Å) and a long trans Se–N contact (2.396 Å, see ESI for full details†), consistent with a considerable contribution from an acyclic structure analogous to **7**. Nevertheless, solution ^{77}Se NMR studies (singlet, δ = +952.2 *vs.* Me_2Se) indicate a single species in solution and the well-resolved ^{1}H spectra with low field resonance for the *ortho*-H (δ = +9.96) indicate that [**2**]Cl (R = Ph) also retains its closed conformation in solution.

This synthetic methodology offers access to a new family of *N*-bridgehead thiadiazolylium and selenadiazolylium rings through intramolecular *N*-coordination. It would seem broadly applicable to modification and primarily limited by the availability of 2-pyridylketone derivatives. To date we have successfully prepared derivatives bearing phenyl, pyridyl and thiophenyl substituents. However, the methodology should offer the ability to incorporate a wider range of substituents on both the fused ring and pendant arms as well as incorporation of alternative heteroatoms. Further studies of the structure, bonding and reactivity of this novel structural motif are in progress.

Notes and references

‡ *Crystal data for* [**1**]Cl, **7** and [**2**]Cl were collected on a Nonius Kappa 4 CCD at 180(2) K with Mo Kα radiation (λ = 0.71073 Å).

[**1**]Cl [$C_{11}H_8N_3S$]Cl·H_2O *FW* 267.73, monoclinic, $C2/c$, a = 24.1059(6), b = 4.9368(2), c = 20.7418(6) Å, β = 111.024(2)°. Z = 8, ρ_c = 1.544 Mg m^{-3}, V = 2304.07(13) Å^3. Full-matrix least-squares refinement on 2635 independent reflections (10 420 reflections measured with R_{int} = 0.0507) yielded R_1 = 0.0388 ($I > 2\sigma(I)$), wR_2 = 0.0884 (all data). Residual electron density within +0.30/−0.26 e^-.

[**2**]Cl [$C_{12}H_9N_2Se$]Cl *FW* 295.62, tetragonal, space group $P4_32_12$, $a = b$ = 8.27180(10), c = 33.0787(7) Å, Z = 8, ρ_c = 1.735 Mg m^{-3}, V = 2263.33(6) Å^3. Full-matrix least-squares refinement on 2314 independent reflections (11 060 reflections measured with R_{int} = 0.0552) yielded R_1 = 0.0412 ($I > 2\sigma(I)$), wR_2 = 0.0812 (all data). Residual electron density within +0.87/−0.45 e^-. The Flack parameter [0.019(19)] was indicative of the correct absolute structure.

7 $C_{17}H_{11}N_5O_4S$ *FW* 381.37, monoclinic, $C2/c$, a = 18.4166(3), b = 6.4849(1), c = 27.9654(6) Å, β = 100.4673(7)°. Z = 8, ρ_c = 1.543 Mg m^{-3}, V = 3284.32(10) Å^3. Full-matrix least-squares refinement on 3728 independent reflections (14 171 reflections measured with R_{int} = 0.0561) yielded R_1 = 0.0406 ($I > 2\sigma(I)$), wR_2 = 0.0967 (all data). Residual electron density within +0.20/−0.35 e^-.

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