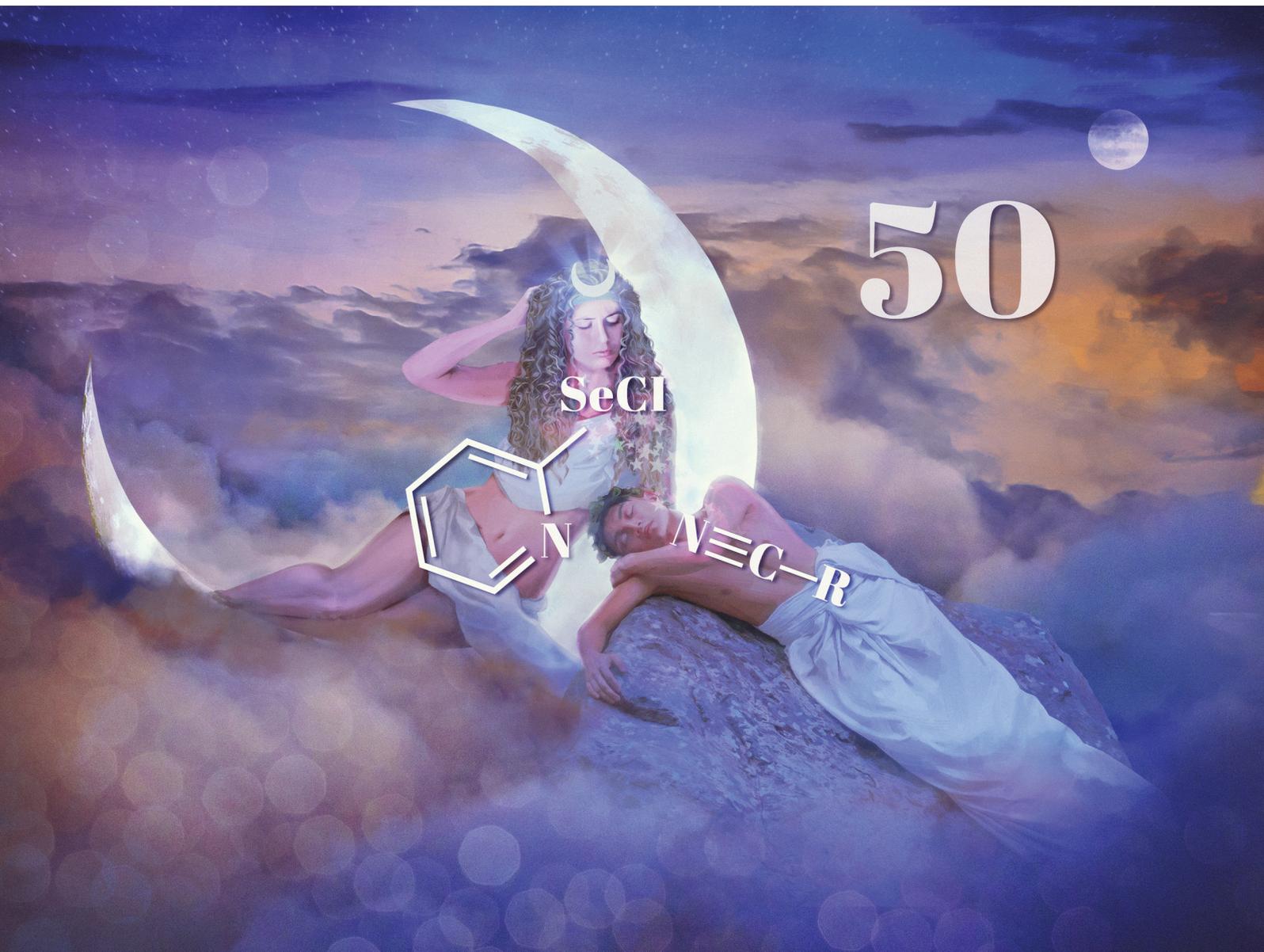


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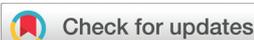
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Novel cationic 1,2,4-selenadiazoles: synthesis *via* addition of 2-pyridylselenenyl halides to unactivated nitriles, structures and four-center Se...N contacts†

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2-Pyridylselenenyl halides undergo facile coupling with a triple CN bond of unactivated nitriles. Unprecedented heterocyclization allowed the preparation of a novel class of cationic 1,2,4-selenadiazoles in remarkably high yields. Cationic 1,2,4-selenadiazoles form supramolecular dimers in the crystal *via* Se...N chalcogen bonding, which was studied theoretically.

Nitriles are important building blocks that are widely employed both in the laboratory and industry.¹ Electrophilic or nucleophilic additions or asymmetric dipolar cycloaddition to the triple bond of nitriles often serves as an indispensable tool for the creation of various functionalities.^{1–4} However, the utilization of nitriles in organic synthesis is often hampered by their inert nature, which even allows the application of some of their congeners as media for the synthesis. Efficient electrophilic (or nucleophilic) activation of nitriles can be achieved upon their coordination to electron-poor, high-oxidation-state (or electron-rich, low-valent) metal centers.^{1,5,6}

Activation of nitriles by organometalloid compounds could be beneficial due to the fact that the activator of the CN triple bond is already present in the substrate, and the synthesis of organometalloid derivatives, which involves reactions with

nitriles, potentially could be performed in a catalyst-free fashion.

Organoselenium compounds are of considerable pharmacological importance.^{7,8} Therefore, the preparation of novel selenium-containing building blocks is of substantial interest. Recently, it has been demonstrated that 2-pyridylchalcogenyl halides react with alkenes or alkynes resulting in the formation of the corresponding five-membered heterocycles.^{9–12} Here we show that 2-pyridylselenenyl halides undergo facile coupling with unactivated nitriles, which allows the preparation of novel cationic 1,2,4-selenadiazoles in remarkably high yields. Novel heterocyclic compounds feature unusual attractive interactions *via* four-center Se...N chalcogen bonding in the crystal.

When a solution of 2-pyridylselenenyl chloride (**1**) in MeCN was stirred at room temperature for 3 h, a colorless precipitate of **3** was gradually formed. Isolation and analysis of the precipitate by NMR, mass spectrometry, and elemental analysis suggested the formation of an adduct of **1** with MeCN in 96% yield (Scheme 1).

A similar procedure was used to form bromide **4** starting from 2-pyridylselenenyl bromide (**2**) in 93% yield (Scheme 1). Aromatic nitriles were also reactive towards 2-pyridylselenenyl halides. The addition of *p*-bromobenzonitrile to **2** in DCM resulted in the formation of **5**, which was isolated in 92% yield (Scheme 1). Thus, the reaction proceeds smoothly for both aliphatic and aromatic nitriles.

Having established that 2-pyridylselenenyl halides easily react with nitriles, we were interested in whether their *in situ* gene-

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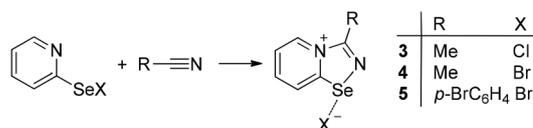
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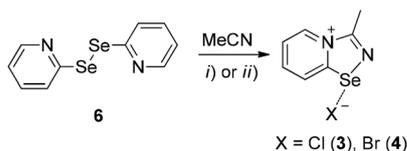
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Scheme 1 Synthesis of **3**–**5**.



Scheme 2 Synthesis of **3** and **4** from **6**. (i) SO_2Cl_2 and (ii) Br_2 .

ration and consequent addition to a CN triple bond were possible. Chlorination of diselenide **6** with sulfuryl chloride in acetonitrile afforded the desired cyclization product **3** in 88% yield (Scheme 2). Oxidation of **6** with Br_2 was also successful. However, bromide **4** was isolated in 84% yield (Scheme 2). Thus, a simple and convenient *in situ* procedure could be applied for the generation of cationic 1,2,4-selenadiazoles from 2,2'-dipyridyldiselenides.

3–5 were recrystallized from methanol to give single crystals, suitable for analysis by single crystal X-ray crystallography, which confirmed the formation of adducts and revealed that **3–5** were unprecedented [1,2,4]-selenadiazolo-[4,5-*a*]-pyridinium-4 halides (Fig. 1).

All bicyclic systems **3–5** are planar (Table S4[†]). Selenium atoms adopt a T-shaped geometry (N–Se–C angles are $87.16(6)^\circ$ (**3**), $87.29(10)^\circ$ (**4**) and $87.31(17)^\circ$ (**5**)) with weakly binding halide anions. The Se–N and Se–C bond distances (Table S4[†]) are within the typical range for the corresponding single bond values, while N=C bonds are unambiguously double (Table S4[†]).

Interestingly, **3–5** all form supramolecular dimers *via* Se...N chalcogen bonding in the crystal (2.986(1) Å (**3**), 2.941(2) Å (**4**) and 3.008(4) Å (**5**), Fig. 2). Similar, but still rare, four-center Te...N contacts were observed earlier for benzotellurodiazolium cations.¹³

In order to approximately quantify Se...N energies from a theoretical point of view, we carried out DFT calculations at the $\omega\text{B97XD}/6\text{-}31\text{+G}^*$ level of theory and performed the topological analysis of the electron density distribution within the framework of Bader's theory (QTAIM analysis)¹⁴ for model

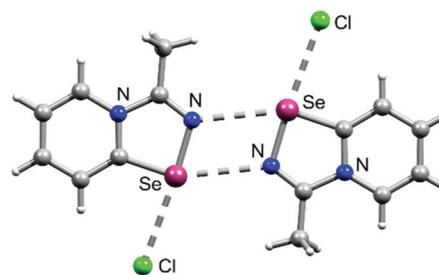


Fig. 2 Ball-and-stick representation of the crystal structure of **3**, demonstrating attractive Se...N interactions. Grey and light-grey spheres represent carbon and hydrogen, respectively.

associates (Cartesian atomic coordinates for these model associates are shown in the ESI, Table S1[†]). The results of the QTAIM analysis are presented in Table S2;[†] the contour line diagrams of the Laplacian of the electron density distribution $\nabla^2\rho(r)$, bond paths, and selected zero-flux surfaces, visualization of the electron localization function (ELF) and reduced density gradient (RDG) analyses for Se...N noncovalent interactions in **3–5** are shown in Fig. 3, S1, and S2,[†] respectively.

The noncovalent interaction analysis as a scatter graph of RDG *vs.* real space function $\text{sign}(\lambda_2)\rho$, namely the product of the sign of λ_2 (second largest eigenvalue of the Hessian matrix of the electron density) and ρ (electron density) (NCI plot¹⁵) for model associates, and visualization of intermolecular contacts in 3D using the NCI analysis technique are shown in Fig. S3.[†]

The QTAIM analysis demonstrated the presence of appropriate bond critical points (3, –1) for Se...N contacts in model associates (Table S1[†]). The low magnitude of the electron density (0.014–0.016 a.u.), positive values of the Laplacian of the electron density (0.044–0.050 a.u.), very close to zero positive energy density in these bond critical points (3, –1), and estimated strengths for appropriate short contacts ($2.5\text{--}3.1\text{ kcal mol}^{-1}$) are typical for chalcogen bonds in similar chemical systems.¹⁶ The balance between the Lagrangian kinetic energy $G(r)$ and potential energy density $V(r)$ at the bond critical points (3, –1) corresponding to Se...N contacts in model associates reveals that a covalent contribution is absent in these chalcogen bonds.¹⁷ The Laplacian of the electron density is typically decomposed into the sum of contributions along the three principal axes of maximal variation, giving the three eigenvalues of the Hessian matrix (λ_1 , λ_2 and λ_3), and the sign of λ_2 can be utilized to distinguish weak bonding (attractive, $\lambda_2 < 0$) interactions from nonbonding ones (repulsive, $\lambda_2 > 0$).^{15,18} Thus, Se...N noncovalent interactions in **3–5** are attractive (Table S2[†]).

In conclusion, we have discovered that 2-pyridylselenyl halides easily undergo addition to the CN triple bond of nitriles. An unprecedented process allowed the preparation of novel cationic 1,2,4-selenadiazoles in remarkably high yields. Moreover, we demonstrated that 2-pyridylselenyl halides could be conveniently generated *in situ* by oxidation of 2,2'-dipyridyldiselenides and further reacted with nitriles to give the desired products in high yields.

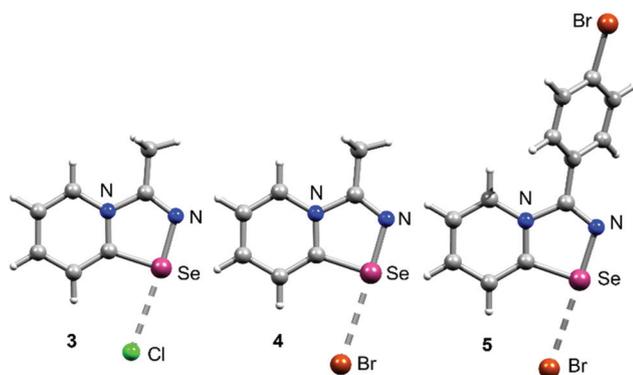


Fig. 1 Ball-and-stick representations of the crystal structures of **3–5**. Grey and light-grey spheres represent carbon and hydrogen, respectively.

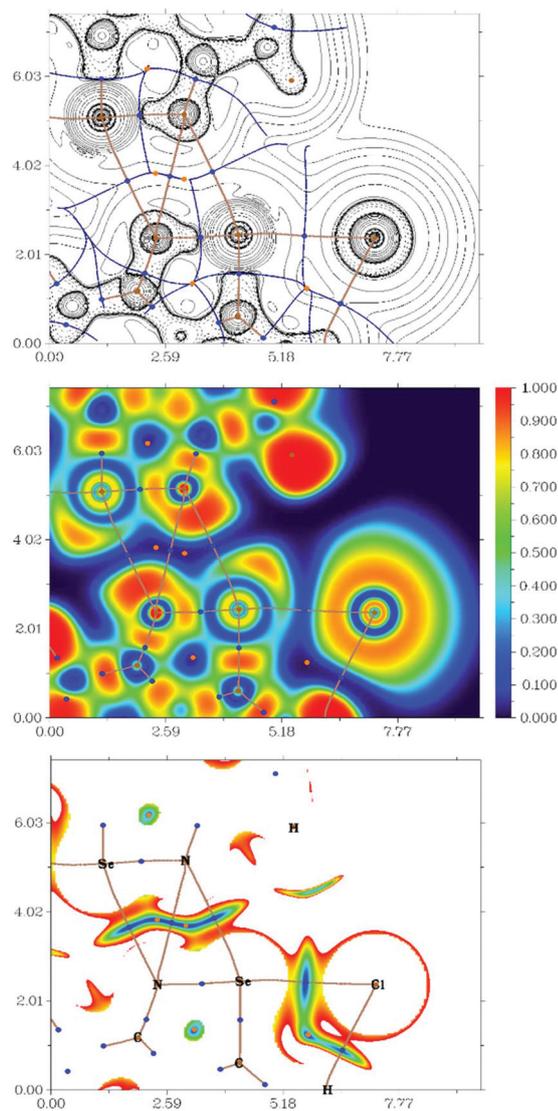


Fig. 3 Contour line diagram of the Laplacian of the electron density distribution $\nabla^2\rho(r)$, bond paths, and selected zero-flux surfaces (top panel), visualization of the electron localization function (ELF, center panel) and reduced density gradient (RDG, bottom panel) analyses for Se...N interactions in **3**. Bond critical points (3, -1) are shown in blue, nuclear critical points (3, -3) in pale brown, and ring critical points (3, +1) in orange, bond paths are shown as pale brown lines, length units – Å, and the color scale for the ELF and RDG maps are presented in a.u.

Novel cationic 1,2,4-selenadiazoles form supramolecular dimers in the crystal *via* Se...N chalcogen bonding. Unusual non-covalent interactions were studied theoretically, which showed that the estimated strength of these weak contacts vary from 2.5 to 3.1 kcal mol⁻¹. Further studies on the novel addition of 2-pyridylselenyl halides to nitriles as well as unprecedented 1,2,4-selenadiazoles are underway and will be reported in due course.

Conflicts of interest

There are no conflicts to declare.

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