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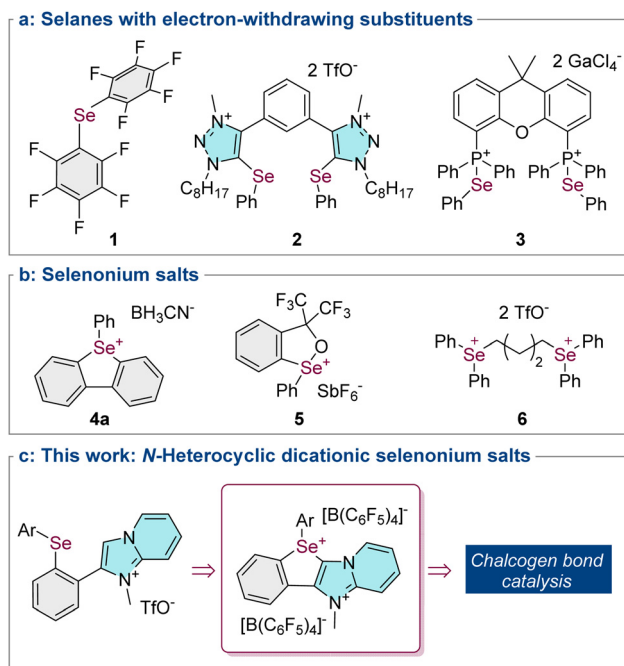
Imidazopyridine substituted cyclic selenonium(IV) salts as chalcogen bond catalysts†

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We present imidazopyridine-substituted dicationic selenonium(IV) salts as a new class of highly tuneable organoselenium catalysts. These monodentate chalcogen bond donors were prepared through a mild oxidation–cyclization protocol, incorporating cationic heterocycles to enhance the σ-hole on selenium. The selenonium salts demonstrate high catalytic activities in Povarov cyclizations and in activating gold complexes, highlighting their potential in advanced catalytic applications.

A chalcogen bond (ChB) describes an almost linear, non-covalent interaction between an electropositive region of a chalcogen atom and a Lewis base, which is shorter than the sum of their van der Waals radii.[1] Initially studied in crystal engineering,[2] ChB gained growing interest in several fields of chemistry.[3] ChB catalysis plays an important role in biological systems, such as selenium-containing proteins,[4] and is utilized in drug development.[5] In recent years, the application of ChB donors in organic synthesis led to improved catalyst designs[6] and a better understanding of the nature of the chalcogen bond.[7] Early works by Wirth investigated the stereoselective functionalization of styrene derivatives with chiral diselenides.[8] Matile and co-workers used perfluorinated aryl substituents in the neutral catalyst 1 to remove electron density from the selenium atom and enhancing the σ-hole (Scheme 1a).[9] Another conceptional approach that reduces the electron density is by implementing cationic substituents, such as N-alkyl N-heterocycles. Based on this approach, bidentate ChB catalysts containing benzimidazoliums[10] or triazoliums 2[11] were developed by Huber and co-workers, and were found to have applications in carbon–halogen bond activations and Povarov

Scheme 1 (a) Mono- and bidentate Se(II)-based ChB donors with electron withdrawing substituents. (b) Mono- and bidentate Se(IV)-based ChB donors. (c) Combination of concepts to generate dicationic imidazopyridinium-substituted selenonium salts.

cyclizations. Instead of heteroarenes, Wang and co-workers applied bidentate phosphonium chalcogenides with phenyl, alkyl, 1,1′-binaphthyl, or xanthene moieties as the backbone.[12] The latter led to catalyst 3, which was used as an activator in Rauhut–Currier-type condensation reactions.[13]

Instead of reducing the electron density by withdrawing ligands, cationic selenonium salts such as triarylselenonium 4a were investigated by Bolotin and co-workers and applied to selective reduction of imines using the counterion as a reducing agent (Scheme 1b).[14] Oxygen-bonded diarylselenonium salts of type 5 can activate styrenes in arylation reactions.[15]

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Bidentate selenonium salts **6** were also investigated, applying them as carbonyl activators in Diels–Alder reactions and electrophilic brominations.[16]

In this work, we present a new class of chalcogen bond (ChB) donors **11** by integrating cationic N-heterocycles and cationic Se(IV) species as key design principles (Scheme 1c). To further amplify the electron-withdrawing effect and enhance the σ-hole, we incorporated fluorinated aryl substituents into the molecular framework. The catalytic performance of these novel organocatalysts **11a** and **11b** was subsequently evaluated using established benchmark reactions to demonstrate their synthetic utility.

The synthesis started with an *ortho*-N-heterocycle substituted diarylselane, **7**, wherein either phenyl (**7a**, R = Ph) or a strongly electron deficient 3,5-bis(trifluoromethyl)phenyl (**7b**, R = Ar^F) was used (Scheme 2a). Imidazopyridine was chosen as a heterocycle because we previously showed that it greatly enhances the reactivity of halogen bond donors.[17] Interestingly, the following oxidative–cyclization was achieved by implementing the Olofsson protocol for iodonium salt synthesis.[18] The use of *meta*-chloroperbenzoic acid (*m*CPBA) as the terminal oxidant in the presence of trifluoromethylsulfonic acid (TfOH) gave the mono-cationic selenonium salts **8a** and **8b** in high yields of 74% and 95%, respectively. To our knowledge, this established protocol was applied for the first time in the synthesis of cationic Se(IV) compounds. To enhance the σ-hole, *N*-methylated precursors **9a** and **9b** were oxidized *via* the same method, yielding dicationic catalysts **10a** and **10b** in 41% and 75% yields. Counterion exchange to non-coordinating $[B(C_6F_5)_4]^-$ provided ChB donors **11a** and **11b** in excellent yields. For comparison, the reference catalyst **4c** was also synthesized in good yield (Scheme 2b).

The molecular structure of catalyst **10a** was elucidated by single-crystal X-ray diffraction analysis (Scheme 2c). As expected, a shorter Se1–O1 distance of 2.80(2) Å (sum of van der Waals radii: 3.42 Å)[19] compared to the Se1–O5 distance of 3.02(8) Å was measured, indicating that the σ-hole on the opposite side of the heterocycle is more pronounced. Both σ-holes exhibit nearly linear Se···O interactions with the oxygen atoms of the respective triflate counterions. The phenyl substituent on the selenium atom adopts an orientation approximately perpendicular to the selenonium ring plane.

Next, the reactivity of these novel selenonium salts as ChB catalysts was investigated. As a model reaction, we investigated a Povarov cyclization between imine **13** and dihydrofuran (**14**), which was previously reported to be sustainable in Se- and Te-mediated ChB catalysis (Fig. 1).[11,20] Initial titration experiments with an equimolar mixture of catalyst **11a** and imine **13** revealed a downfield shift of the imine N=CH-proton from 8.42 ppm to 8.45 ppm, indicating a less shielded proton due to the coordination of the catalyst to the neighbouring nitrogen atom (see the ESI†). With this promising result, the cycloaddition reaction was carried out in the presence of 5 mol% of **11a** in 1,2-dichloroethane (DCE). Here, a high reactivity of the new catalysts **11** was observed, giving the product **15** in 55% (**11a**) and 62% (**11b**) yields after only 1 h (Fig. 1). The Ar^F-substituted
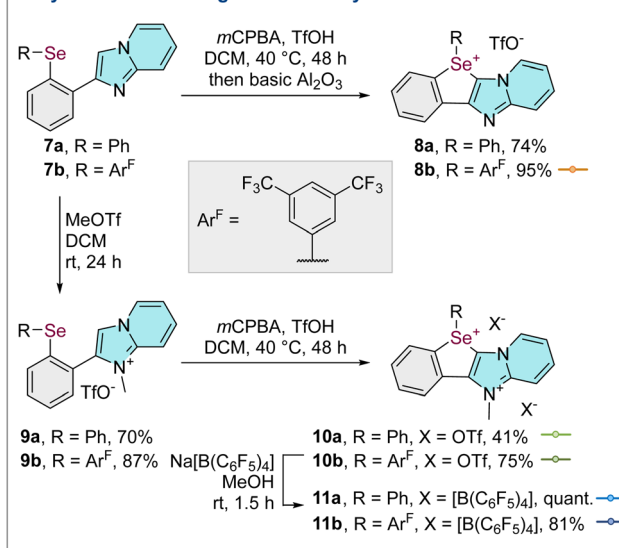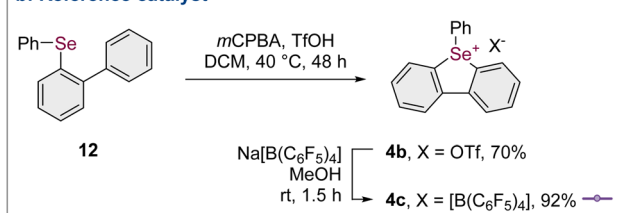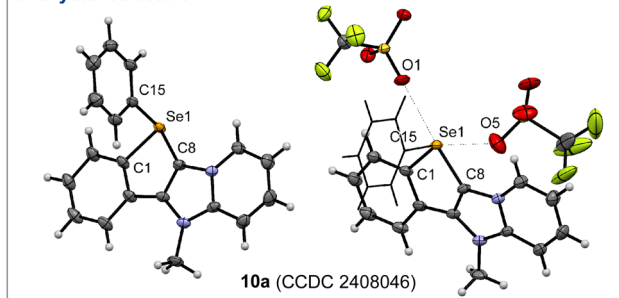

Scheme 2 Synthesis of selenonium salts and the crystal structure (ORTEP drawing with 50% probability) of **10a** with and without counterions. Selected bond lengths and angles: Se1–O1: 2.80(2) Å, Se1–O5: 3.02(8) Å, Se1–C8: 1.88(9) Å, O1–Se1–C8: 164.1(1)°, O5–Se1–C15: 168.8(9)°, O1–Se1–C15: 93.0(0)°, C1–Se1–C8–C15: 96.3(5)°.

derivative **11b** was slightly superior, showing a 14 times higher initial rate constant (k_{rel}) compared to the reference catalyst **4c**, while the k_{rel} value of the phenyl-substituted catalyst **11a** was 8 times higher. Both catalysts form *endo/exo* isomers **15a** and **15b** in about 70% total yield after 4 h. This isomer mixture was isolated in a yield of 57% (*endo* : *exo* = 46 : 54) using catalyst **11a** and 72% (*endo* : *exo* = 48 : 52) with **11b**. Higher turnovers might be hindered by coordination of the product to the catalyst or due to partial hydrolysis of imine **13**. The reference catalyst **4c** stopped after 14% product formation. No decomposition of the catalysts was detected during the reaction.

Addition of tetrabutylammonium chloride (TBACl) quenched catalysts **11a** and **11b**, resulting in complete inhibition of product
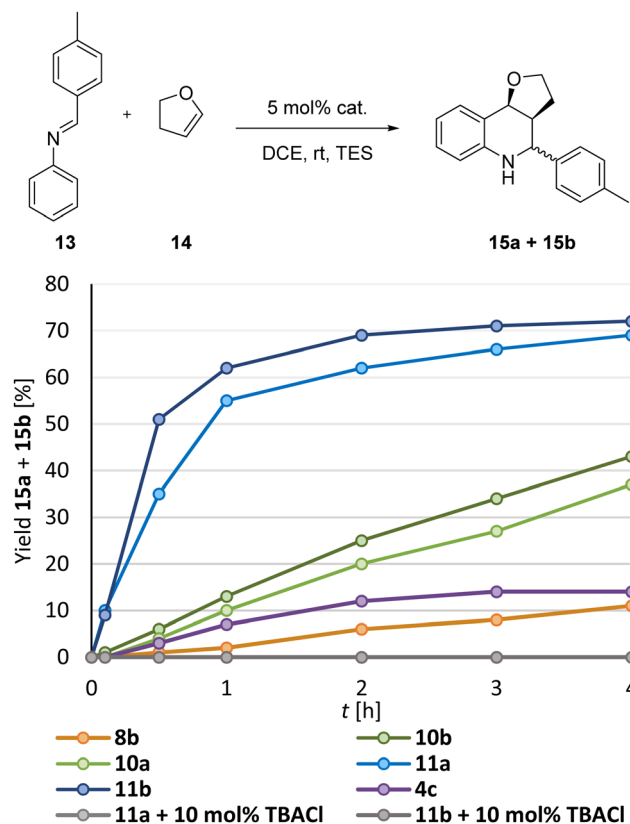
Fig. 1 ChB-activated Povarov cyclization reaction. Conditions: imine **13** (138 mM, 1.0 equiv.), 2,3-dihydrofuran (**14**, 2.0 equiv.) and the Se(ɪᴠ) catalyst (5 mol%) were stirred in DCE (0.4 mL) at room temperature and the conversion was determined with ^{1}H NMR using tetraethylsilane (TES, 0.25 equiv.) as an internal standard.
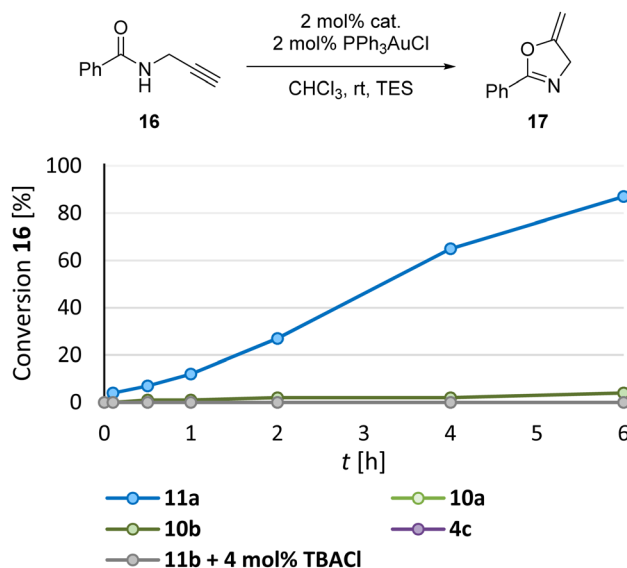

Fig. 2 Chalcogen bond mediated activation of an Au catalyst for a 5-*exo-dig* cyclization reaction towards oxazoline **17**. Conditions: propargylic amide **16** (80.0 mM, 1.0 equiv.), AuClPPh₃ (2 mol%) and the Se(ɪᴠ) catalyst (2 mol%) were stirred in CHCl₃ (1 mL) at room temperature and the conversion was determined with ^{1}H NMR using TES (0.25 equiv.) as an internal standard.

formation, which confirms these selenonium salts as active ChB catalysts. Catalysts **10a** and **10b** exhibited reduced activity (about 40% product formation after 4 h) due to competing coordination of triflate counterions to the selenium σ-hole. Monocationic catalyst **8b** demonstrated significantly lower reactivity (11% after 4 h), comparable to the reference catalyst **4c**, highlighting the critical role of *N*-methylation in enhancing the catalytic performance. In all reactions, nearly equal *endo* : *exo* ratios of products **15a** and **15b** were observed.

The selenonium salts **11** clearly outperformed the bidentate Se(ɪɪ)-based ChB catalyst **2**, which was previously tested in Povarov reactions. Moreover, the catalysts **11a** and **11b** showed only slightly lower conversions in NMR experiments compared to the more active Te analogue of **2**. Interestingly, the better performance of triflate salts compared to their $[B(C_6F_5)_4]$ analogues described by Huber and co-workers was not observed for compounds **10** and **11**.[11] Our catalysts were also less reactive than the tris(3,5-bis(trifluoromethyl)phenyl)telluronium salts presented by Mamane and co-workers, which achieved an NMR yield of 97% after 5 h.[20] Bidentate iodine(ɪ)-based halogen bond catalysts were also superior to **11a** and **11b**, particularly in terms of shorter reaction times.[21]

Along with the activation of organic molecules, the ChB catalysts were also investigated in the Au–Cl bond activation of an Au catalyst, which initiates a 5-*exo-dig* cyclization of propargylic amide **16** to oxazoline **17** (Fig. 2).[22] Here, the triflate salts **10a** and **10b**, as well as the reference catalyst **4c** showed only negligible reactivity. The phenyl-substituted catalyst **11a** led to 87% conversion after 6 h. Unfortunately, we observed decomposition of the Ar^F analog **11b** in this reaction, indicating this highly electron-poor catalyst to be incompatible with the Au complex. Again, blocking of the σ-holes by the addition of a chloride anion led to no conversion of **16**, proving that the activation is likely driven by an Au–Cl···Se coordination. The reaction profile indicates an induction period, likely caused by the slow formation of the active Au catalyst. Consequently, the initial turnover of the substrate is low and is accelerated as more active Au-catalyst is formed. Slow formation of the active Au-catalyst might result from the free NH function of the starting material **16**, which undergoes a competitive coordination to the σ-hole of the selenonium salt. This coordination is rather weak, while the activation of the Au catalyst *via* chloride abstraction is binding the halogen irreversibly to the selenonium salt. A similar observation can be made with iodine-based catalysts. While the higher activity of most of those organocatalysts leads to no observable induction period, weaker halogen bond donors show a similar reaction profile to the ChB donor **11a**.[17]

In conclusion, we have successfully developed a new class of monodentate selenonium(ɪᴠ)-based chalcogen bond donors through a mild one-pot oxidation–cyclization protocol. Our findings demonstrate that *N*-methylation of the imidazopyridine heterocycle is crucial for achieving enhanced catalytic activity. The resulting selenonium salts exhibit excellent catalytic performance in Povarov cyclizations, showing efficacies

comparable to established tellurium-based ChB donors. However, highly electron-deficient selenonium salts displayed limited compatibility with gold complexes, indicating substrate-dependent reactivity constraints. This straightforward synthetic methodology provides a versatile platform for the rational design and optimization of next-generation chalcogen bond donors with precisely tuned electronic properties.

Conflicts of interest

There are no conflicts of interest to declare.

Data availability

The data supporting this article have been included as part of the ESI.† Crystallographic data for **10a** have been deposited at the CCDC database under 2408046.

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