



HAL
open science

Solvent free nucleophilic selenocyanation with [bmim][SeCN]. Direct access to perfluoroalkylselenide compounds

Arnaud De-Zordo Banliat, Kévin Grollier, Aurélie Damond, Thierry Billard, Guillaume Dagousset, Emmanuel Magnier, Bruce Pégot

► To cite this version:

Arnaud De-Zordo Banliat, Kévin Grollier, Aurélie Damond, Thierry Billard, Guillaume Dagousset, et al.. Solvent free nucleophilic selenocyanation with [bmim][SeCN]. Direct access to perfluoroalkylselenide compounds. *Tetrahedron*, 2021, 101, pp.132507. 10.1016/j.tet.2021.132507. hal-03834344

HAL Id: hal-03834344

<https://hal.science/hal-03834344v1>

Submitted on 29 Oct 2022

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

Solvent free nucleophilic selenocyanation with [bmim][SeCN]. Direct access to perfluoroalkylselenide compounds

Arnaud De-Zordo Banliat ^a, Kévin Grollier ^b, Aurélie Damond ^a, Thierry Billard ^{b, c},
Guillaume Dagousset ^a, Emmanuel Magnier ^{a, *}, Bruce Pégot ^{a, **}

^a Université Paris-Saclay, UVSQ, CNRS, UMR 8180, Institut Lavoisier de Versailles, 78035, Versailles Cedex, France

^b Institute of Chemistry and Biochemistry (ICBMS, UMR CNRS 5246), Univ Lyon, Université Lyon 1, CNRS, CPE, INSA, 43 Bd du 11 novembre 1918, 69622, Villeurbanne, France

^c CERMEP-In Vivo Imaging, 59 Bd Pinel, 69677, Lyon, France

A B S T R A C T

Available online-1-*n*-butyl-3-methylimidazolium selenocyanate ([bmim][SeCN]) proved to be a very efficient reagent for selenocyanation of alkyl halides. As part of an eco-friendly process, no organic solvents were used during the transformation and reaction times are reduced by using microwave as a heating source. The ionic liquid was carefully recycled in two different ways. Selenocyanate compounds were successfully transformed into trifluoromethylselenides in a one-pot two step procedure.

Keywords:

Selenocyanation
Ionic liquids
Nucleophilic substitution
Green chemistry
Microwaves

1. Introduction

Selenium (Se) is a necessary trace element. In the human body, it mainly exists in the form of selenocysteine and it has crucial antioxidant properties in humans when incorporated into selenoenzymes [1]. The increasing interest for organoselenium compounds stems from their potential biological activities [2]. Among them, organoselenocyanates, common in natural products, are highly interesting targets in the search for anticancer drugs [3]. They are useful synthetic intermediates that participate in a variety of reactions [4]. To get access to aliphatic selenocyanates, nucleophilic displacement of halides is the preponderant route. Commercially available potassium selenocyanates KSeCN is the reagent of choice for such transformation providing polar solvents like DMF or DMSO are used [5]. As an alternative to such solvents, other selenocyanate salts with better solubility were developed as an alternative source of potassium selenocyanate in less polar solvents (AgSeCN, (Me₄N)SeCN, CsSeCN, ...) [6]. Ionic liquids (ILs)

showed good solubilization performance and are important alternatives to non-ecofriendly solvents. These salts have been the subject of intense research as effective reaction solvents [7]. Recently, as part of our ongoing program to develop ecofriendly nucleophilic substitution processes, we have shown the potential of ILs both as reagent and solvent for nucleophilic substitution [8]. A few ILs with SeCN as anion have already been prepared (e.g. 1-ethyl-3-methylimidazolium selenocyanate [EMIM][SeCN]) and they are mainly used in materials for solar cells or redox-active electrolytes for hybrid electrochemical capacitors, but never as reagents for organic transformations [9].

Herein we report the first synthesis of the ionic liquid, [bmim][SeCN] as a new reagent for nucleophilic selenocyanation. The recyclability of this ionic liquid was carefully examined. Organic selenocyanates may be easily converted to other interesting functional groups and especially SeCF₃. Given the considerable interest in trifluoromethylselenide compounds [10] due to their promising anti-inflammatory and anticancer properties [11], we show here that it is possible to transform the selenocyanates obtained previously to perfluoroselenolated compounds. We also explore a two-step one-pot sequence to obtain trifluoromethylselenide compounds directly from halides.

* Corresponding author.

** Corresponding author.

E-mail address: emmanuel.magnier@uvsq.fr (E. Magnier).

2. Results and discussion

In order to access the [bmim][SeCN] reagent, a two-step procedure was developed (Scheme 1). Precursor [bmim][Cl] was first prepared via solvent-free *N*-alkylation under microwave irradiation according to a literature procedure, nevertheless it is also commercially available [12]. The second step, the anion exchange of azolium halides, was carried out with potassium selenocyanate. The anion metathesis was carried out in 1 h in water with a slight excess (1.1 equivalent) of KSeCN at room temperature. After workup, the selenolated IL was isolated with a high yield of 95% without further purification. The reaction could be conducted on large a scale (up to 25 g) with the same result.

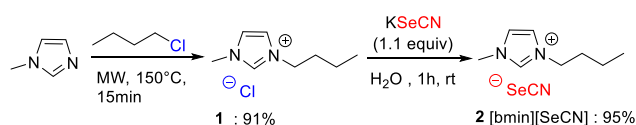
With this new IL reagent in hand, the nucleophilic selenocyanation of 1-bromo-3-phenylpropane was investigated as a model reaction (Table 1). During this study, no particular handling precautions were required. All the reactions described here were conducted under microwave irradiation. Since the dielectric properties of ionic liquids allow them to absorb microwave irradiation very efficiently, they are highly suitable for microwave assisted organic synthesis [13].

Selenocyanation occurred with a good yield of 66% in only 15 min, when 1-bromo-3-phenylpropane was stirred with 1 equivalent of [bmim][SeCN] at 110 °C (entry 1). Increasing the time had no influence on the yield, whereas decreasing the temperature resulted in a slight increase in the yield to 77% (entries 2 and 3). The use of a slight excess of IL (1.2 equiv.) gave complete conversion and the (3-selenocyanatopropyl)benzene was obtained with a good isolated yield, (93%, entry 3). The reaction has been conducted on a 6 mmol (1.2 g) scale with nearly the same yield and to afford 1.16 g of the desired product (entry 4). As a comparison, with conventional heating, a reaction time of 3 h was needed, with 1.5 equivalents of IL to obtain an equivalent yield (entry 5).

Encouraged by these results, we attempted the selenocyanation reaction without solvent on various substrates in order to evaluate the scope and limitations of [bmim][SeCN]. The previously optimized conditions (30 min at 90 °C under microwave irradiation) were successfully applied to a wide range of substrates (Scheme 2).

Primary alkylbromides were displaced with good yields to give rise to the desired molecules (4a-c, Scheme 2). Benzyl bromides were easily substituted by [bmim][SeCN] even on a multigram scale (4d). The functionalization of the aromatic part by fluorinated groups or fluorine atoms was not detrimental to the yields (4e-g). By adjusting the amount of reagent, a bis-substituted compound, known for their antioxidant properties, was easily obtained (4i) [14]. The reaction is slightly sensitive to steric hindrance, nevertheless the isolated yield remained correct (4q-r). This transformation was also compatible with various other functionalities, such as esters (4c, 4j), cyano (4l, 4o), imide (4n), and lactone (4m) groups. With non-activated fatty alkyl halides, good yields were obtained (4o-p).

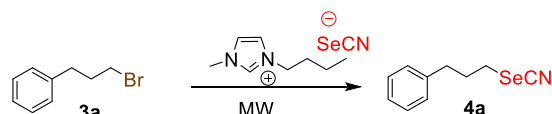
The recycling of the cationic core of our reagent was then carefully examined. After completion of the selenocyanation process, simple extraction of the crude mixture with diethyl ether afforded product 4e with excellent yield and purity (Scheme 3). After dissolution in water, the IL can be regenerated following the



Scheme 1. Synthesis of [bmim][SeCN] 2.

Table 1

Selenocyanation of 1-bromo-3-phenylpropane with [bmim][SeCN].



Entry	Time (min)	Temperature (°C)	[bmim][SeCN] (equiv.)	Yields (%) ^a
1	15	110	1	66
2	30	110	1	66
3	30	90	1	77
3	30	90	1.2	93
4 ^b	30	90	1.2	86
5 ^c	180	90	1.5	88

^a Isolated yields.

^b Reaction on 6 mmol, 1.2 g of 3a.

^c Reaction conducted under conventional heating.

same procedure as for its initial preparation (Path A). Regenerated IL was then re-engaged in the same reaction to give once again nearly the same yield. Alternatively, after the reaction and extraction, the cationic part could also be recovered by a simple anion exchange with LiNTf₂ to ensure total conversion to a unique and useful known IL [bmim][NTf₂] (Path B, yield up to 93%). This IL could be used later as a reaction media for other organic syntheses [7].

We then decided to transform some of the previously synthesized selenocyanates into trifluoromethylselenolated compounds using classical methodology (Ruppert-Prakash reagent TMSCF₃, TBAF) (Scheme 4). Pleasingly the reaction proceeded smoothly to give the desired compounds 5 in very good yields. This methodology was extended to the bromodifluoromethyl and pentafluoroethyl groups to give rise to molecule 6k and 7a with good yields.

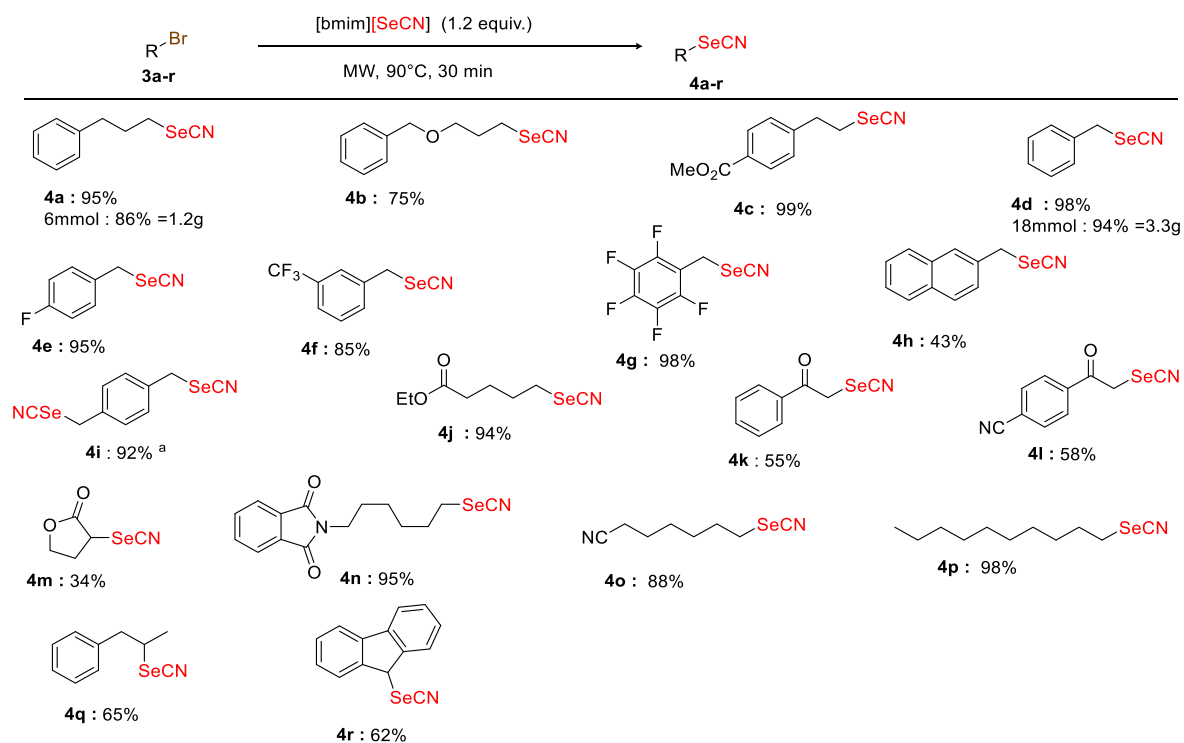
The final approach to get access to trifluoromethylselenolated compounds was to perform the transformation in a two-steps one-pot sequence reaction (Scheme 5). This procedure proved to be very efficient. Indeed, directly after the nucleophilic substitution, THF, Ruppert-Prakash reagent and TBAF were added according to the general procedure to give the desired product in good yield. The result was comparable to the two-step procedure (73% isolated yield for one-pot procedure vs 71% global yield for the two steps).

3. Conclusion

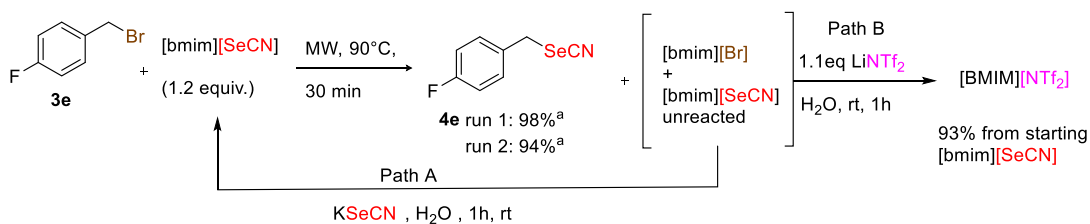
We have shown that 1-*n*-butyl-3-methylimidazolium selenocyanate [bmim][SeCN] is a practical and efficient reagent to perform soft nucleophilic substitution to give selenocyanate compounds. No solvent, special precautions, complex or hazardous additional reagents are necessary for this transformation. The ILs could be entirely recycled with two green and easy different pathways. Trifluoromethylselenolated compounds have been obtained from the selenocyanate derivatives with Ruppert-Prakash reagent, or directly via a two-step one-pot procedure from the corresponding halide. Further developments of this reagent and other applications are under study in our laboratory.

4. Experimental

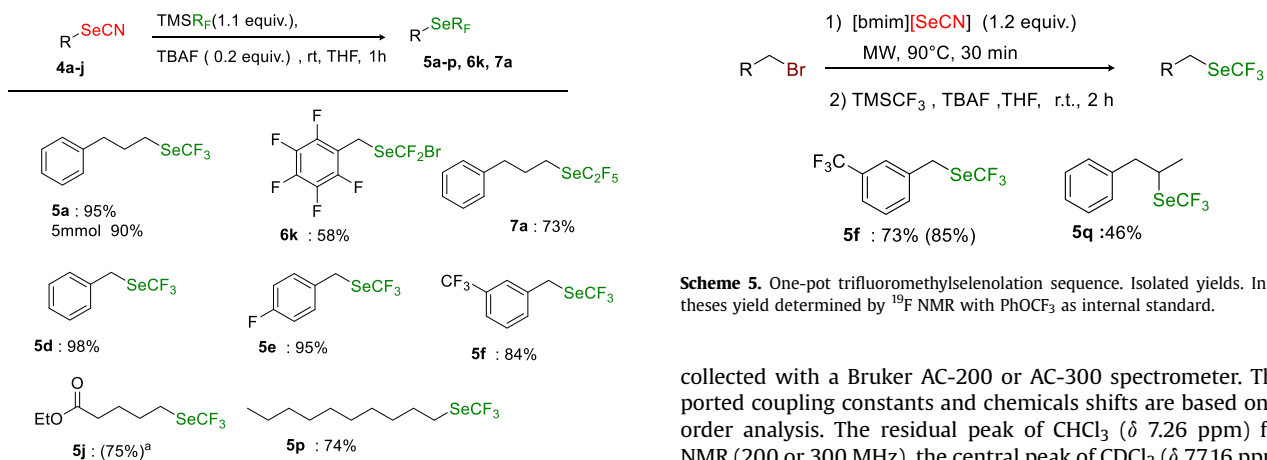
General. Chemicals were purchased from commercial sources unless otherwise stated in the Supporting Information. Reactions were monitored by ¹⁹F NMR spectroscopy. Yields refer to materials purified by preparative TLC chromatography. NMR spectra were



Scheme 2. Selenocyanation reaction on various substrates with [bmim][SeCN].^a with 2.2 equivalent of IL.



Scheme 3. Recycling of the IL.^a yield determined by ¹⁹F NMR with PhOCF₃ as internal standard.



Scheme 5. One-pot trifluoromethylselenolation sequence. Isolated yields. In parentheses yield determined by ¹⁹F NMR with PhOCF₃ as internal standard.

Scheme 4. Perfluoroalkylation of selenocyanide.^a In parentheses yield determined by ¹⁹F NMR with PhOCF₃ as internal standard.

collected with a Bruker AC-200 or AC-300 spectrometer. The reported coupling constants and chemical shifts are based on first-order analysis. The residual peak of CHCl₃ (δ 7.26 ppm) for ¹H NMR (200 or 300 MHz), the central peak of CDCl₃ (δ 77.16 ppm) for ¹³C NMR (75 or 50 MHz), and CFCl₃ (δ 0.00 ppm) for ¹⁹F NMR (188 MHz) were used as internal references. Multiplicities are indicated as follows: s (singlet), d (doublet), t (triplet), q (quartet), p (pintuplet), m (multiplet), br (broad), or a combination of these. All

coupling constants were reported in Hz. HRMS was performed with a XEVO-QTOF Mass Spectrometer in ESI(+) and ASAP(+) mode at the Institute Lavoisier of Versailles– University of Versailles Saint Quentin.

4.1. Synthesis of [bmim][SeCN] (2)

[bmim][Cl] (3.5 g, 0.02 mol) was dissolved in a minimum of water. In another flask KSeCN (1.1 eq, 3.168 g, 0.022 mol) was also dissolved in a minimum amount of water. Both solutions were mixed at room temperature for 1 h ensuring a complete anion exchange. At the end of the reaction the solution was extracted with CH₂Cl₂ (3 × 20ml) and dried over MgSO₄, and concentrated in vacuo to give the desired IL as a slightly viscous yellow liquid. Yield: 4.636 g, 95%; ¹H NMR (300 MHz, CDCl₃) δ 9.31 (s, 1H), 7.54 (s, 1H), 7.50 (s, 1H), 4.31 (t, J = 7.3 Hz, 2H), 4.09 (s, 3H), 1.91 (p, J = 7.4 Hz, 2H), 1.38 (h, J = 7.4 Hz, 2H), 0.95 (t, J = 7.3 Hz, 3H). ¹³C NMR (75 MHz, CDCl₃) δ = 136.52, 123.86, 122.45, 118.17, 50.11, 36.85, 32.05, 19.44, 13.42. ⁷⁷Se NMR (57 MHz, CDCl₃) δ –240.38.

4.2. Typical procedure for the selenolacyanation of alkyl halides

A microwave tube with a magnetic stirring bar was charged with a halide (1.0 equiv., 1 mmol) and [bmim][SeCN] (1.2 equiv., 1.2 mmol, 292 mg). After stirring the mixture was subjected to microwave irradiation at 90 °C for 30 min. The mixture was then cooled to room temperature, and the compound was extracted with diethyl ether (5 × 5 mL). Organic layers were combined and concentrated under reduced pressure. The product was purified by preparative thin layer chromatography (PTLC) on silica gel to give the desired product. On larger scales, the product was purified by chromatography on silica gel to afford 4.

4.3. Synthesis of (3-selenocyanatopropyl)benzene (4a)

Yield: 213 mg, 95%; Eluent for PTLC: Et₂O/petroleum ether (2:8). ¹H NMR (300 MHz, CDCl₃) δ 7.30 (m, 5H), 3.07 (t, J = 7.3 Hz, 2H), 2.83 (t, J = 7.3 Hz, 2H), 2.29 (p, J = 7.3 Hz, 1H). ¹³C NMR (75 MHz, CDCl₃) δ 139.93, 128.72, 128.55, 126.50, 101.48, 34.95, 32.22, 28.73. ⁷⁷Se NMR (57 MHz, CDCl₃) δ 206.95. HRMS: TOF MS ASAP + calcd. for C₂₀H₂₃N₂Se₂ 451.0192; found 451.0187 [2 M + H]⁺ (δ = –1.1 ppm)

4.4. Synthesis of ((3-selenocyanatopropoxy)methyl)benzene (4b)

Yield: 191 mg, 75%; Eluent for PTLC: Et₂O/petroleum ether (2:8). ¹H NMR (300 MHz, CDCl₃) δ 7.54–7.08 (m, 5H), 3.60 (t, J = 5.5 Hz, 2H), 2.97 (t, J = 6.5 Hz, 1H), 2.25–2.12 (p, J = 5.9 Hz, 1H). ¹³C NMR (75 MHz, CDCl₃) δ 137.80, 128.54, 127.92, 127.86, 102.86, 73.24, 68.47, 30.35, 27.18. ⁷⁷Se NMR (57 MHz, CDCl₃) δ 202.00. HRMS: TOF MS ES + calcd. for C₁₁H₁₄NOSe 256.0241; found 256.0247 [M + H]⁺ (δ = 2.3 ppm)

4.5. Synthesis of methyl 4-(2-selenocyanatoethyl)benzoate (4c)

Yield: 192 mg, 98%; Eluent for PTLC: Et₂O/petroleum ether (2:8). ¹H NMR (300 MHz, CDCl₃) δ 7.54–7.08 (m, 4H), 4.27 (s, 2H). ¹³C NMR (75 MHz, CDCl₃) δ 135.58, 128.98, 128.89, 128.52, 102.11, 32.69. ⁷⁷Se NMR (57 MHz, CDCl₃) δ 346.90. HRMS: TOF MS ES + calcd. for C₁₁H₁₂NO₂Se 270.0033; found 270.0031 [M + H]⁺ (δ = –0.7 ppm)

4.6. Synthesis of (selenocyanatomethyl)benzene (4d)

Yield: 192 mg, 98%; Eluent for PTLC: Et₂O/petroleum ether (2:8). ¹H NMR (300 MHz, CDCl₃) δ 7.54–7.08 (m, 4H), 4.27 (s, 2H). ¹³C NMR

(75 MHz, CDCl₃) δ 135.58, 128.98, 128.89, 128.52, 102.11, 32.69. ⁷⁷Se NMR (57 MHz, CDCl₃) δ 346.90.

4.7. Synthesis of 1-fluoro-4-(selenocyanatomethyl)benzene (4e)

Yield: 203 mg, 95%; Eluent for the preparative TLC chromatography: Et₂O/petroleum ether (2:8). ¹H NMR (300 MHz, CDCl₃) δ 7.36–7.32 (m, 2H), 7.05 (t, J = 8.4 Hz, 2H), 4.26 (s, 2H). ¹³C NMR (75 MHz, CDCl₃) δ 162.76 (d, J = 248.5 Hz), 131.55 (d, J = 3.3 Hz), 130.87 (d, J = 8.4 Hz), 116.19 (d, J = 21.8 Hz), 101.87, 31.96. ¹⁹F NMR (188 MHz, CDCl₃) δ –112.87 (m, 1F) ⁷⁷Se NMR (57 MHz, CDCl₃) δ 293.15. HRMS: TOF MS ASAP + calcd. for C₁₆H₁₃N₂Se₂F₂ 430.9377; found 430.9388 [2 M + H]⁺ (δ = 2.6 ppm)

4.8. Synthesis of 1-(selenocyanatomethyl)-3-(trifluoromethyl)benzene (4f)

Yield: 224 mg, 85%; Eluent for PTLC: Et₂O/petroleum ether (2:8). ¹H NMR (300 MHz, CDCl₃) δ 7.62–7.48 (m, 4H), 4.30 (s, 2H). ¹³C NMR (75 MHz, CDCl₃) δ 136.81 (s), 132.36 (d, J = 0.8 Hz), 131.54 (q, J = 32.7 Hz), 125.72 (q, J = 3.8 Hz), 125.52 (q, J = 3.7 Hz), 123.70 (q, J = 272.3 Hz), 101.30 (s), 31.66 (s). ¹⁹F NMR (188 MHz, CDCl₃) δ –63.28 (s, 3F) ⁷⁷Se NMR (57 MHz, CDCl₃) δ 298.22. HRMS: TOF MS ASAP + calcd. for C₉H₇NF₃Se 265.9696; found 265.9688 [M + H]⁺ (δ = –3.0 ppm)

4.9. Synthesis of 1,2,3,4,5-pentafluoro-6-(selenocyanatomethyl)benzene (4g)

Yield: 281 mg, 98%; Eluent for PTLC: Et₂O/petroleum ether (2:8). ¹H NMR (300 MHz, CDCl₃) δ 4.28 (s, 2H). ¹³C NMR (75 MHz, CDCl₃) δ ¹³C NMR (75 MHz, CDCl₃) δ 146.85–146.49 (m), 143.52–143.16 (m), 140.11–139.19 (m), 136.32–135.84 (m), 110.59 (dt, J = 17.0, 4.1 Hz), 99.85, 17.34. ¹⁹F NMR (282 MHz, CDCl₃) δ –141.37 (dd, J = 21.0, 7.4 Hz), –152.53 (t, J = 20.8 Hz), –160.96 to –160.78 (qd, J = 10.3, 3.6 Hz). ⁷⁷Se NMR (57 MHz, CDCl₃) δ 304.83. HRMS: TOF MS ASAP + calcd. for C₈H₃NF₅Se 287.9351; found 287.9352 [M + H]⁺ (δ = 0.3 ppm)

4.10. Synthesis of 2-(selenocyanatomethyl)naphthalene (4h)

Yield: 105 mg, 43%; Eluent for PTLC: Et₂O/petroleum ether (2:8). ¹H NMR (300 MHz, CDCl₃) δ 7.91–7.77 (m, 4H), 7.64–7.39 (m, 3H), 4.48 (s, 2H). ¹³C NMR (75 MHz, CDCl₃) δ 133.24, 133.12, 132.67, 129.25, 128.25, 128.00, 127.82, 126.82, 126.79, 126.30, 101.88, 33.37. ⁷⁷Se NMR (57 MHz, CDCl₃) δ 280.27. HRMS: TOF MS ASAP + calcd. for C₂₄H₁₉N₂Se₂ 494.9879; found 494.9890 [2 M + H]⁺ (δ = 2.2 ppm)

4.11. Synthesis of 1,4-bis(selenocyanatomethyl)benzene (4i)

Yield: 0.5 mmol, 144 mg, 92%; Eluent for PTLC: Et₂O/petroleum ether (3:7). ¹H NMR (300 MHz, CDCl₃) δ 7.39 (s, 4H), 4.29 (s, 4H). ¹³C NMR (75 MHz, CDCl₃) δ 136.35, 129.40, 116.45, 101.80, 31.85. ⁷⁷Se NMR (57 MHz, CDCl₃) δ 302.29. HRMS: TOF MS ASAP + calcd. for C₁₀H₉N₂Se₂ 316.9096; found 316.9088 [M + H]⁺ (δ = –2.5 ppm)

4.12. Synthesis of ethyl 5-selenocyanatopentanoate (4j)

Yield: 219 mg, 92%; Eluent for PTLC: Et₂O/petroleum ether (4:6). ¹H NMR (300 MHz, CDCl₃) δ 4.12 (q, J = 7.1 Hz, 2H), 3.04 (t, J = 7.2 Hz, 2H), 2.34 (t, J = 7.1 Hz, 2H), 1.93 (p, J = 7.2 Hz, 2H), 1.76 (p, J = 7.2 Hz, 2H), 1.24 (t, J = 7.1 Hz, 3H). ¹³C NMR (75 MHz, CDCl₃) δ 172.98, 101.42, 60.59, 33.40, 30.28, 29.08, 24.35, 14.28. ⁷⁷Se NMR (57 MHz, CDCl₃) δ 209.28. HRMS: TOF MS ES + calcd. for

C₈H₁₄NO₂Se 236.0190; found 236.0181 [M+ H]⁺ ($\delta = -3.8$ ppm)

4.13. Synthesis of 1-phenyl-2-selenocyanatoethan-1-one (4k)

Yield: 123 mg, 55%; Eluent for PTLC: Et₂O/petroleum ether (2:8). ¹H NMR (300 MHz, CD₃CN) δ 8.02 (d, $J = 8.0$ Hz, 2H), 7.72 (t, $J = 7.0$ Hz, 1H), 7.58 (t, $J = 7.5$ Hz, 2H), 4.94 (s, 2H). ¹³C NMR (75 MHz, CD₃CN) δ 134.08, 133.88, 128.61, 128.38, 116.99, 101.65, 37.06. ⁷⁷Se NMR (57 MHz, CDCl₃) δ 160.57. HRMS: TOF MS ASAP + calcd. for C₉H₈NOSe 225.9771; found 225.9761 [M+ H]⁺ ($\delta = -4.4$ ppm)

4.14. Synthesis of 4-(2-selenocyanatoacetyl)benzotrile (4l)

Yield: 144 mg, 58%; Eluent for PTLC: Et₂O/petroleum ether (2:8). ¹H NMR (200 MHz, CDCl₃) δ 8.08 (d, $J = 8.4$ Hz, 1H), 7.85 (d, $J = 8.4$ Hz, 1H), 4.88 (s, 1H). ¹³C NMR (75 MHz, CDCl₃) δ 138.28, 133.83, 133.63, 130.12, 126.33, 102.57, 37.43. ⁷⁷Se NMR (57 MHz, CDCl₃) δ 172.96. HRMS: TOF MS ASAP + calcd. for C₁₀H₇N₂OSe 250.9724; found 250.9717 [M+H]⁺ ($\delta = -2.8$ ppm)

4.15. Synthesis of 3-selenocyanatodihydrofuran-2(3H)-one (4m)

Yield: 64 mg, 34%; Eluent for PTLC: Et₂O/petroleum ether (2:8). ¹H NMR (200 MHz, CDCl₃) δ 4.61–4.55 (m, 1H), 4.47–4.30 (m, 2H), 3.03–2.89 (m, 1H), 2.74–2.62 (m, 5H). ¹³C NMR (75 MHz, CDCl₃) δ 173.00, 99.33, 67.62, 37.39, 31.40. ⁷⁷Se NMR (57 MHz, CDCl₃) δ 315.46.

4.16. Synthesis of 2-(6-selenocyanatohexyl)isoindoline-1,3-dione (4n)

Yield: 0.5 mmol, 159.6 mg, 95%; Eluent for PTLC: Et₂O/petroleum ether (2:8). ¹H NMR (300 MHz, CDCl₃) δ 7.83–7.80 (m, 2H), 7.73–7.70 (m, 2H), 3.67 (t, $J = 7.0$ Hz, 2H), 3.04 (t, $J = 7.3$ Hz, 2H), 1.89 (p, $J = 6.9$ Hz, 1H), 1.69 (p, $J = 6.9$ Hz, 1H), 1.57–1.29 (m, 4H). ¹³C NMR (75 MHz, CDCl₃) δ 168.39, 133.96, 132.06, 123.18, 101.59, 37.66, 30.67, 29.46, 28.56, 28.33, 26.03. ⁷⁷Se NMR (57 MHz, CDCl₃) δ 208.19.

4.17. Synthesis of 7-selenocyanatoheptanenitrile (4o)

Yield: 190 mg, 88%; Eluent for PTLC: Et₂O/petroleum ether (5:5). ¹H NMR (300 MHz, CDCl₃) δ 3.04 (t, $J = 7.3$ Hz, 2H), 2.36 (t, $J = 6.9$ Hz, 2H), 1.93 (p, $J = 6.9$ Hz, 2H), 1.68 (p, $J = 6.9$ Hz, 2H), 1.60–1.44 (m, 4H). ¹³C NMR (75 MHz, CDCl₃) δ 119.63, 101.50, 30.59, 29.26, 28.29, 27.95, 25.17, 17.15. ⁷⁷Se NMR (57 MHz, CDCl₃) δ 208.96. HRMS: TOF MS ASAP + calcd. for C₈H₁₃N₂Se 217.0244; found 217.0235 [M+H]⁺ ($\delta = -4.1$ ppm)

4.18. Synthesis of 1-selenocyanatodecane (4p)

Yield: 209 mg, 98%; Eluent for PTLC: Et₂O/petroleum ether (2:8). ¹H NMR (300 MHz, CDCl₃) δ 3.09 (t, $J = 7.4$ Hz, 2H), 1.94 (p, $J = 7.3$ Hz, 2H), 1.53–1.40 (m, 2H), 1.31 (s, 12H), 0.92 (t, $J = 5.9$ Hz, 3H). ¹³C NMR (75 MHz, CDCl₃) δ 101.71, 32.00, 30.95, 29.83, 29.61, 29.52, 29.39, 29.27, 28.98, 22.80, 14.24. ⁷⁷Se NMR (57 MHz, CDCl₃) δ 206.25. HRMS: TOF MS ASAP + calcd. for C₁₁H₂₂NSe 248.0917; found 248.0915 [M+H]⁺ ($\delta = -0.8$ ppm)

4.19. Synthesis of (2-selenocyanatopropyl)benzene (4q)

Yield: 209 mg, 98%; Eluent for PTLC: Et₂O/petroleum ether (2:8). ¹H NMR (300 MHz, CDCl₃) δ 7.37–7.01 (m, 5H), 3.68 (h, $J = 7.1$ Hz,

1H), 3.13–2.93 (m, 1H), 1.62 (d, $J = 6.7$ Hz, 1H). ¹³C NMR (75 MHz, CDCl₃) δ 137.92, 129.13, 128.91, 127.46, 101.50, 44.90, 44.42, 22.88. ⁷⁷Se NMR (57 MHz, CDCl₃) δ 310.75. HRMS: TOF MS ASAP + calcd. for C₁₀H₁₂NSe 226.0135; found 226.0134 [M+H]⁺ ($\delta = -0.4$ ppm)

4.20. Synthesis of 9-selenocyanato-9H-fluorene (4r)

Yield: 209 mg, 98%; Eluent for PTLC: Et₂O/petroleum ether (2:8). ¹H NMR (300 MHz, CDCl₃) δ 7.76 (t, $J = 6.8$ Hz, 4H), 7.47 (t, $J = 7.4$ Hz, 2H), 7.38 (t, $J = 7.4$ Hz, 2H), 5.75 (s, 1H). ¹³C NMR (75 MHz, CDCl₃) δ 141.99, 140.38, 129.65, 128.27, 125.54, 120.79, 102.17, 45.66. ⁷⁷Se NMR (57 MHz, CDCl₃) δ 357.61. HRMS: TOF MS ASAP + calcd. for C₂₈H₁₉N₂Se₂ 542.9879; found 542.9890 [2 M + H]⁺ ($\delta = 2.0$ ppm)

4.21. Typical procedure for the perfluoroalkylation of selenocyanate compounds

To a dry round-bottom flask equipped with a magnetic stirrer were added selenocyanate (0.5 mmol, 1.0 equiv) and dry THF (0.5 mL). The flask was evacuated and refilled with argon three times, and TMSCF₃ (88 μ l, 0.6 mmol, 1.2 equiv) was added. The reaction mixture was cooled to 0 °C, and TBAF in 1 M THF (0.1 mL, 0.1 mmol, 0.2 equiv) was added dropwise. After 10 min at 0 °C, the reaction was allowed to warm to 23 °C and stirred for 2 h. The conversion was checked by ¹⁹F NMR with PhOCF₃ as internal standard. The reaction mixture was then partitioned between water and pentane, and the aqueous layer was extracted with pentane, dried over MgSO₄, filtered and concentrated to dryness (under moderate vacuum). The crude residue was purified by PTLC:

4.22. Synthesis of (3-phenylpropyl)(trifluoromethyl)selane (5a)

Yield: 0.5 mmol, 126.8 mg, 95%; Eluent for PTLC: Et₂O/petroleum ether (5:95). ¹H NMR (300 MHz, CDCl₃) δ 7.37–7.22 (m, 5H), 3.03 (t, $J = 7.2$ Hz, 2H), 2.79 (t, $J = 7.4$ Hz, 2H), 2.18 (t, $J = 7.4$ Hz, 2H). ¹³C NMR (75 MHz, CDCl₃) δ 140.64, 128.69, 128.61, 126.38, 122.79 (q, $J = 330.3$ Hz), 35.58, 31.92, 25.26. ¹⁹F NMR (188 MHz, CDCl₃) δ -34.51 (s, 3F). ⁷⁷Se NMR (57 MHz, CDCl₃) δ 443.20 (q, $J = 9.6$ Hz). HRMS: TOF MS ASAP + calcd. for C₁₀H₁₁F₃Se 267.9978; found 267.9974 [M +] ($\delta = -1.5$ ppm)

4.23. Synthesis of benzyl(trifluoromethyl)selane (5d)

¹H NMR (300 MHz, Chloroform-*d*) δ 7.37–7.27 (massif, 5H), 4.24 (s, 2H). ¹⁹F NMR (282 MHz, CDCl₃) δ -34.46 (s, 3F). Characterization data match that reported in the literature [15].

4.24. Synthesis of (4-fluorobenzyl)(trifluoromethyl)selane (5e)

¹H NMR (300 MHz, CDCl₃) δ 7.31 (m, 2H), 7.02 (m, 2H), 4.22 (s, 2H). ¹⁹F NMR (282 MHz, CDCl₃) δ -34.38 (s, 3F), -114.11 (m, 1H). Characterization data match that reported in the literature [15].

4.25. Synthesis of (trifluoromethyl)(3-(trifluoromethyl)benzyl)selane (5f)

Yield: 0.5 mmol, 129.4 mg, 95%; Eluent for PTLC: Et₂O/petroleum ether (5:95). ¹H NMR (300 MHz, CDCl₃) δ 7.61–7.45 (m, 4H), 4.28 (s, 2H). ¹³C NMR (75 MHz, CDCl₃) δ 137.48 (s), 132.35 (s), 131.31 (q, $J = 32.4$ Hz), 129.42 (s), 125.75 (q, $J = 3.7$ Hz), 124.65 (q, $J = 3.8$ Hz), 123.83 (q, $J = 272.4$ Hz), 122.61 (q, $J = 331.4$ Hz), 28.33 (q, $J = 1.6$ Hz). ¹⁹F NMR (188 MHz, CDCl₃) δ -34.81 (s, 3F), -63.28 (s, 3F). ⁷⁷Se NMR (57 MHz, CDCl₃) δ 514.50 (q, $J = 11.2$ Hz).

4.26. Synthesis of decyl(trifluoromethyl)selane (5p)

Yield: 0.5 mmol, 107.3 mg, 74%; Eluent for PTLC: Et₂O/petroleum ether (5:95). ¹H NMR (300 MHz, CDCl₃) δ 2.91 (t, *J* = 7.3 Hz, 2H), 1.72 (p, *J* = 7.2 Hz, 2H), 1.41–1.11 (m, 14H), 0.81 (t, *J* = 5.7 Hz, 3H). ¹³C NMR (75 MHz, CDCl₃) δ 122.89 (q, *J* = 330.3 Hz), 32.03, 30.39, 29.73, 29.66, 29.58, 29.43, 29.09, 26.03, 22.83, 14.25. ¹⁹F NMR (188 MHz, CDCl₃) δ –34.77 (s, 3F). ⁷⁷Se NMR (57 MHz, CDCl₃) δ 444.36 (q, *J* = 10.0 Hz). HRMS: TOF MS ASAP + calcd. for C₁₁H₂₁F₃Se 291.0761; found 291.0762 [M +.] (δ = 0.3 ppm)

4.27. Synthesis of (1-phenylpropan-2-yl)(trifluoromethyl)selane (5q)

Yield: 2.5 mmol, 307 mg, 46%; Eluent for column chromatography: Et₂O/petroleum ether (5:95). ¹H NMR (300 MHz, CDCl₃) δ 7.43–7.19 (m, 5H), 3.82 (s, *J* = 6.9 Hz, 1H), 3.23 (dd, *J* = 13.8, 5.7 Hz, 1H), 2.97 (dd, *J* = 13.7, 8.7 Hz, 1H), 1.56 (d, *J* = 6.9 Hz, 3H). ¹³C NMR (75 MHz, CDCl₃) δ 138.48, 129.29, 128.68, 127.06, 123.32 (q, *J* = 330.8 Hz), 77.58, 77.16, 76.74, 44.18, 40.24, 21.85. ¹⁹F NMR (188 MHz, CDCl₃) δ –32.72 (s, 3F). ⁷⁷Se NMR (57 MHz, CDCl₃) δ 543.36 (q, *J* = 10.6 Hz).

4.28. Synthesis of (bromodifluoromethyl)((perfluorophenyl)methyl)selane (6k)

Yield: 0.5 mmol, 112.8 mg, 58%; Eluent for PTLC: Et₂O/petroleum ether (5:95). ¹H NMR (300 MHz, CDCl₃) δ 4.25 (s, 2H). ¹³C NMR (75 MHz, CDCl₃) δ 147.61–145.89 (m), 144.42–143.10 (m), 144.93–142.65 (m), 139.7–139.2 (m), 136.32–135.89 (m), 112.12–111.66 (m), 107.06 (t, *J* = 355.4 Hz), 17.1. ¹⁹F NMR (188 MHz, CDCl₃) δ –18.79 (s), –141.82 to –142.25 (m), –154.71 (t, *J* = 20.8 Hz), –161.78 to –162.06 (m). ⁷⁷Se NMR (57 MHz, CDCl₃) δ 673.5 (m). HRMS: TOF MS ASAP + calcd. for C₈H₂F₂SeBr 389.8393; found 389.8386 [M +.] (δ = –1.8 ppm)

4.29. Synthesis of (3-phenylpropyl)(pentafluoroethyl)selane (7a)

Yield: 0.5 mmol, 115.7, 73%; Eluent PTLC: Et₂O/petroleum ether (5:95). ¹H NMR (300 MHz, CDCl₃) δ 7.32–6.97 (m, 5H), 2.87 (t, *J* = 7.3 Hz, 2H), 2.61 (t, *J* = 7.5 Hz, 2H), 1.98 (p, *J* = 7.3 Hz, 2H). ¹³C NMR (75 MHz, CDCl₃) δ 140.58, 128.71, 128.60, 126.42, 119.02 (qt, *J* = 284.5, 35.0 Hz), 116.33 (tq, *J* = 302.2, 42.2 Hz) 35.60, 31.95, 24.55. ¹⁹F NMR (188 MHz, CDCl₃) δ –88.26 (m, 3F), –91.95 (m, 2F). ⁷⁷Se NMR (57 MHz, CDCl₃) δ 390.44 (m).

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

This work was supported by a grant from the French National Research Agency (ANR 18-CE07-0039-01). The authors are grateful to the French National Research Agency, the CNRS and the French Ministry of Research for financial support. The French Fluorine Network (GIS-FLUOR) is also acknowledged for its support. We warmly acknowledge Karen Wright for English improvement of the manuscript and François Metz (Rhodia-Solvay company) for the gift of LiNTf₂.

References

- (a) X. Zhang, Chem. Eur J. 25 (2019) 2649–2650; (b) L.V. Papp, A. Holmgren, K.K. Khanna, Antioxidants Redox Signal. 12 (2010) 793–795; (c) H.J. Reich, R.J. Hondal, ACS Chem. Biol. 11 (2016) 821–841 (4) D. R. Ellis, D. E. Salt, Current Opinion in Plant Biology 6 (2003) 273-279.
- (a) T. Wirth, Organoselenium Chemistry: Synthesis and Reactions, Wiley-VCH, Weinheim, 2011; (b) S.-H. Juang, C.-C. Lung, P.-C. Hsu, K.-S. Hsu, Y.-C. Li, P.-C. Hong, H.-S. Shiah, C.-C. Kuo, C.-W. Huang, Y.-C. Wang, L. Huang, T.S. Chen, S.-F. Chen, K.-C. Fu, C.-L. Hsu, M.-J. Lin, C.-J. Chang, C.L. Ashendel, T.C.K. Chan, K.-M. Chou, J.-Y. Chang, Mol. Cancer Therapeut. 6 (2007) 193–202; (c) H.-S. Shiah, W.-S. Lee, S.-H. Juang, P.-C. Hong, C.-C. Lung, C.-J. Chang, K.-M. Chou, J.-Y. Chang, Biochem. Pharmacol. 73 (2007) 610–619; (d) E.A. Wilhelm, C.R. Jesse, C.F. Bortolatto, C.W. Nogueira, L. Savegnago, Brain Res. Bull. 79 (2009) 281–287; (e) E.A. Wilhelm, C.R. Jesse, S.S. Roman, C.W. Nogueira, L. Savegnago, Exp. Mol. Pathol. 87 (2009) 20–26; (f) S.W. May, L. Wang, M.M. Gill-Wozniczak, R.F. Browner, A.A. Ogonowski, J.B. Smith, S.H. Pollock, J. Pharmacol. Exp. Therapeut. 283 (1997) 470; (g) S.W. May, Expet Opin. Invest. Drugs 11 (2002) 1261–1269; (h) E.A. Wilhelm, C.R. Jesse, C.F. Bortolatto, C.W. Nogueira, L. Savegnago, Pharmacol. Biochem. Behav. 93 (2009) 419–425; (i) T. Gobel, L. Gsell, O.F. Huter, P. Maiefisch, R. Naef, A.C.O. Sullivan, T. Pittnera, T. Rapold, G. Seifert, M. Sern, H. Szczepanski, D.J. Wadsworth, Pestic. Sci. 55 (1999) 355–357.
- (a) D. Plano, D.N. Karelia, M.K. Pandey, J.E. Spallholz, S. Amin, A.K. Sharma, J. Med. Chem. 59 (2016) 1946–1959; (b) S. Singha Roy, P. Ghosh, U. Hossain, Sk, P. Chakraborty, J. Biswas, S. Mandal, A. Bhattacharjee, S. Bhattacharya, Bioorg. Med. Chem. Lett 20 (2010) 6951–6955; (c) W. Ali, M. Álvarez-Pérez, M.A. Marc, N. Salardón-Jiménez, J. Handzlik, E. Domínguez-Álvarez, Curr Pharmacol Rep 4 (2018) 468–481; (d) M. Soriano-García, Curr. Med. Chem. 11 (2004) 1657–1669.
- (a) A. Tshohimitsu, Organic Selenocyanates, Tellurocyanates and Related Compounds Patai's Chemistry of Functional Groups, Wiley & Sons, Ltd, 2013; (b) E. Bulka, Cyanates and Their Thio Derivatives (1977) Part2 Volume2, John Wiley & Sons, Ltd, 1977, pp. 887–922; (c) A.A. Heredia, Synlett 25 (2014) 748–749; (d) C. Paulmier, Selenium Reagents and Intermediates in Organic Synthesis, Pergamon, Oxford, 1986, p. 27.
- (a) L.A. Jacob, B. Matos, C. Mostafa, J. Rodriguez, J.K. Tillotson, Molecules 9 (2004) 622–626; (b) W. Kern, K. Hummel, Polymer 37 (1996) 2055–2059; (c) A. Krief, W. Dumont, C. Delmotte, Angew. Chem. Int. Ed. 39 (2000) 1669–1672; (d) G.A. Krafft, P.T. Meinke, J. Am. Chem. Soc. 108 (1986) 1314–1315; (e) A.A. Heredia, A.B. Peññory, RSC Adv. 5 (2015) 105699–105706; (f) E.H. Riague, J.-C. Guillemin, Organometallics 21 (2002) 68–73; (g) Sk U. Hossain, S. Sengupta, S. Bhattacharya, Bioorg. Med. Chem. 13 (2005) 5750–5758; (h) T. Manna, A. Rana, A.K. Misra, Tetrahedron 95 (2021) 132358.
- (a) F. Cataldo, Polyhedron 19 (2000) 681–688; (b) J. Songstad, L.J. Stangeland, J. Bjerrum, P.H. Nielsen, S.E. Rasmussen, E. Sunde, N.A. Sørensen, Acta Chem. Scand. 24 (1970) 804–808; (c) Q.-M. Wang, G.-C. Guo, T.C.W. Mak, Polyhedron 20 (2001) 2683–2687; (d) P.T. Meinke, G.A. Krafft, A. Guram, J. Org. Chem. 53 (1988) 3632–3634; (e) L. Du, L. Yao, M. Ge, Eur. J. Inorg. Chem. (2007) 4514–4519; (f) L. Birckenbach, K. Kellermann, Chem. Ber. 58 (1925) 786–794; (g) T.M. Klapötke, B. Krumm, P. Mayer, H. Piotrowski, I. Schwab, M. Vogt, Eur. J. Inorg. Chem. 9 (2002) 2701–2709.
- (a) R.D. Rogers, K.R. Seddon, Ionic liquids industrial applications to green chemistry, ACS (Am. Chem. Soc.) Symp. Ser. (2001) 818; (b) P. Wasserscheid, T. Welton, Ionic Liquids in Synthesis, second ed., Wiley-VCH, Weinheim, 2008; (c) R.D. Rogers, K.R. Seddon, Ionic Liquids as Green Solvents. Progress and Prospects, Oxford University, USA, Washington, 2003.
- (a) S. Bouvet, B. Pégot, J. Marrot, E. Magnier, Tetrahedron Lett. 55 (2014) 826–829; (b) E. Anselmi, C. Simon, J. Marrot, P. Bernardelli, L. Schio, B. Pégot, E. Magnier, Eur. J. Org. Chem. (2017) 6319–6326.
- (a) P. Wang, S.M. Zakeeruddin, J.-E. Moser, R. Humphry-Baker, M. Grätzel, J. Am. Chem. Soc. 126 (2004) 7164–7165; (b) P. Wang, S.M. Zakeeruddin, J.-E. Moser, R. Humphry-Baker, M. Grätzel, J. Am. Chem. Soc. 126 (2004) 7164–7165; (c) C.-T. Li, C.-P. Lee, C.-T. Lee, S.-R. Li, S.-S. Sun, K.-C. Ho, ChemSusChem 8 (2015) 1244–1253; (d) Y.-F. Lin, C.-T. Li, C.-P. Lee, Y.-A. Leu, Y. Ezhumalai, R. Vittal, M.-C. Chen, J.-J. Lin, K.-C. Ho, ACS Appl. Mater. Interfaces 8 (2016) 15267–15278; (e) K. Fic, B. Gorska, P. Bujewska, F. Béguin, E. Frackowiak, Electrochim. Acta 314 (2019) 1–8.
- (a) X.-H. Yang, D. Chang, R. Zhao, L. Shi, Asian J. Org. Chem. 10 (2021) 61–73; (b) F. Toulgoat, F. Liger, T. Billard, Chemistry of OCF₃, SCF₃, and SeCF₃

- functional groups, in: K. Szabó, N. Selander (Eds.), *Organofluorine Chemistry: Synthesis, Modeling, and Applications*, Wiley-VCH, Weinheim, Germany, 2021, pp. 49–97;
- (c) T. Billard, F. Toulgoat, When fluorine meets selenium, in: D. Cahard, J.A. Ma (Eds.), *Emerging Fluorinated Motifs: Synthesis, Properties and Applications*, Wiley, Weinheim, Germany, 2020, pp. 691–721;
- (d) Y. Wang, Z. Ye, H. Zhang, Z. Yuan, *Adv. Synth. Catal.* 363 (2021) 1835–1854;
- (e) A. Tlili, E. Ismalaj, Q. Glenadel, C. Ghiazza, T. Billard, *Chem. Eur J.* 24 (2018) 3659–3670.
- [11] (a) X. He, M. Zhong, S. Li, X. Li, Y. Li, Z. Li, Y. Gao, F. Ding, D. Wen, Y. Lei, Y. Zhang, *Eur. J. Med. Chem.* 208 (2020) 112864;
- (b) X. He, Y. Nie, M. Zhong, S. Li, X. Li, Y. Guo, Z. Liu, Y. Gao, F. Ding, D. Wen, Y. Zhang, *Eur. J. Med. Chem.* 218 (2021) 113384.
- [12] Aupoix, A.; Pégot, B.; Vo-Thanh, G. *Tetrahedron* 66, 2010 1352.
- [13] G. Chapter 3 Vo-Thanh, B. Pégot, A. Aupoix, in: J.P. Bazureau, M. Draye (Eds.), *Solvent-free Microwave-Assisted Preparation of Ionic Liquids. Applications for Organic Synthesis in Ultrasound and Microwave: Recent Advances in Organic Chemistry*, Transworld Research Network, Kerala (India), 2011.
- [14] D. Plano, Y. Baquedano, E. Ibáñez, I. Jiménez, J.A. Palop, J.E. Spallholz, C. Sanmartín, *Molecules* 15 (2010) 7292–7312.
- [15] (a) Q. Glenadel, E. Ismalaj, T. Billard, *J. Org. Chem.* 81 (2016) 8268–8275;
- (b) C. Ghiazza, L. Khrouz, T. Billard, C. Monnereau, A. Tlili, *Eur. J. Org. Chem.* 2020 (2020) 1559–1566.