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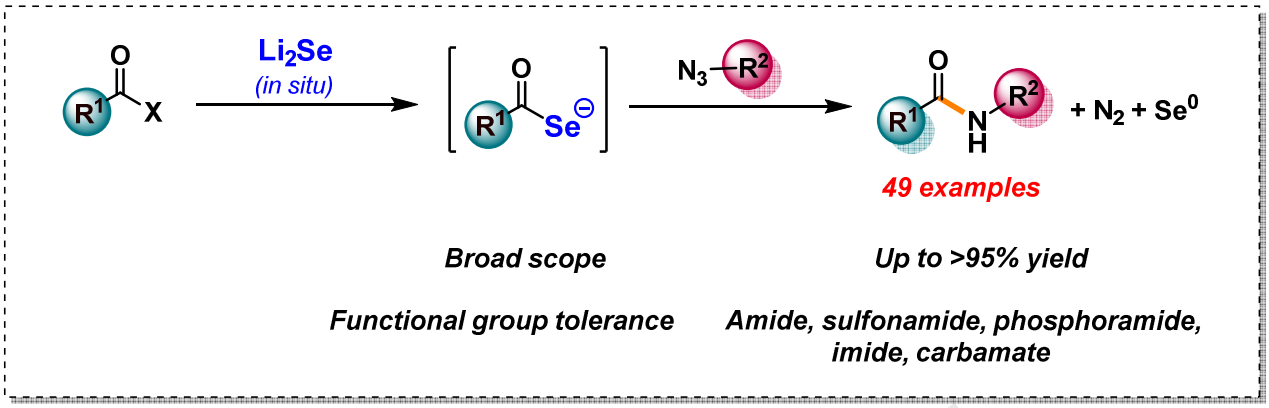
Graphical Abstract:



Traceless Selenocarboxylates for the One-Pot Synthesis of Amides and Derivatives

Luana Silva, Alisson R. Rosário, Bianca M. Machado and Diogo S. Lüdtke*

Instituto de Química, Universidade Federal do Rio Grande do Sul, UFRGS, Av. Bento Gonçalves 9500, 91501-970, Porto Alegre, RS, Brazil.

email: dsludtke@iq.ufrgs.br

Phone: +55 51 3308 9637

Abstract: We have recently reported a one-pot procedure for glycosyl amides synthesis using selenocarboxylate as traceless reagent. Herein, we present a further application of selenocarboxylate-azide reaction for amide bond formation on a broader range of substrates, including heterocyclic systems and fatty acid. This method proved to be highly efficient for the synthesis of primary and secondary amides, sulfonamides, imides, phosphoramide and also carbamate.

Keywords: amidation, selenium reagents, traceless

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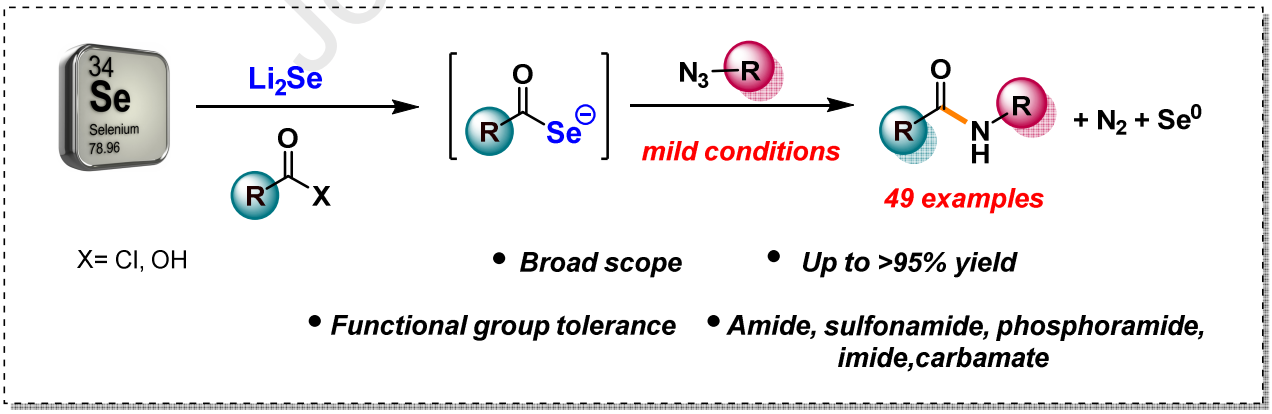


Introduction

The amide bond is a key linker found in biomolecules essential for maintenance of life, most notably at the backbones of all peptides and proteins.[1] Furthermore, this structural framework imparts significant biological importance, since it is present in many fine chemicals and drugs, being extensively applied in medicinal chemistry, (bio)polymers, agrochemicals, natural products and chemical intermediates (Figure 1).[2] Due to this reasons, the construction of amides is hugely important especially in the pharmaceutical industry, since amide bond-forming reactions are one of the most prevalent transformations carried out in medicinal chemistry, accounting for 16% of all reactions in this field.[3]

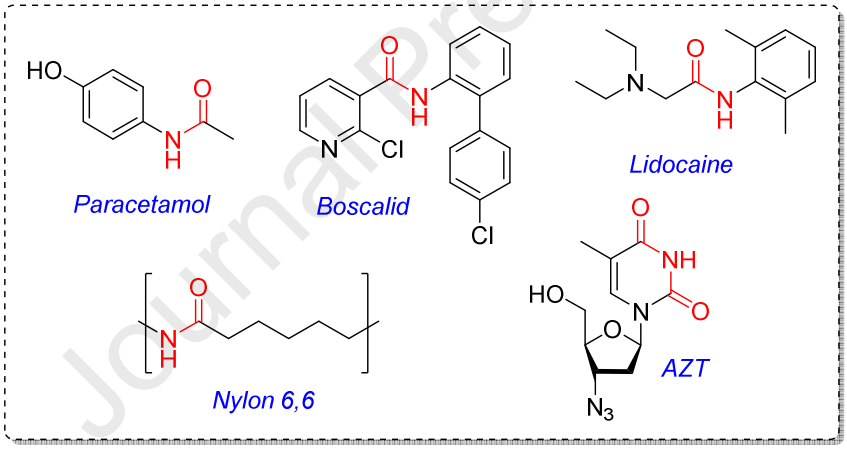


Figure 1. Important molecules containing secondary amide structures.

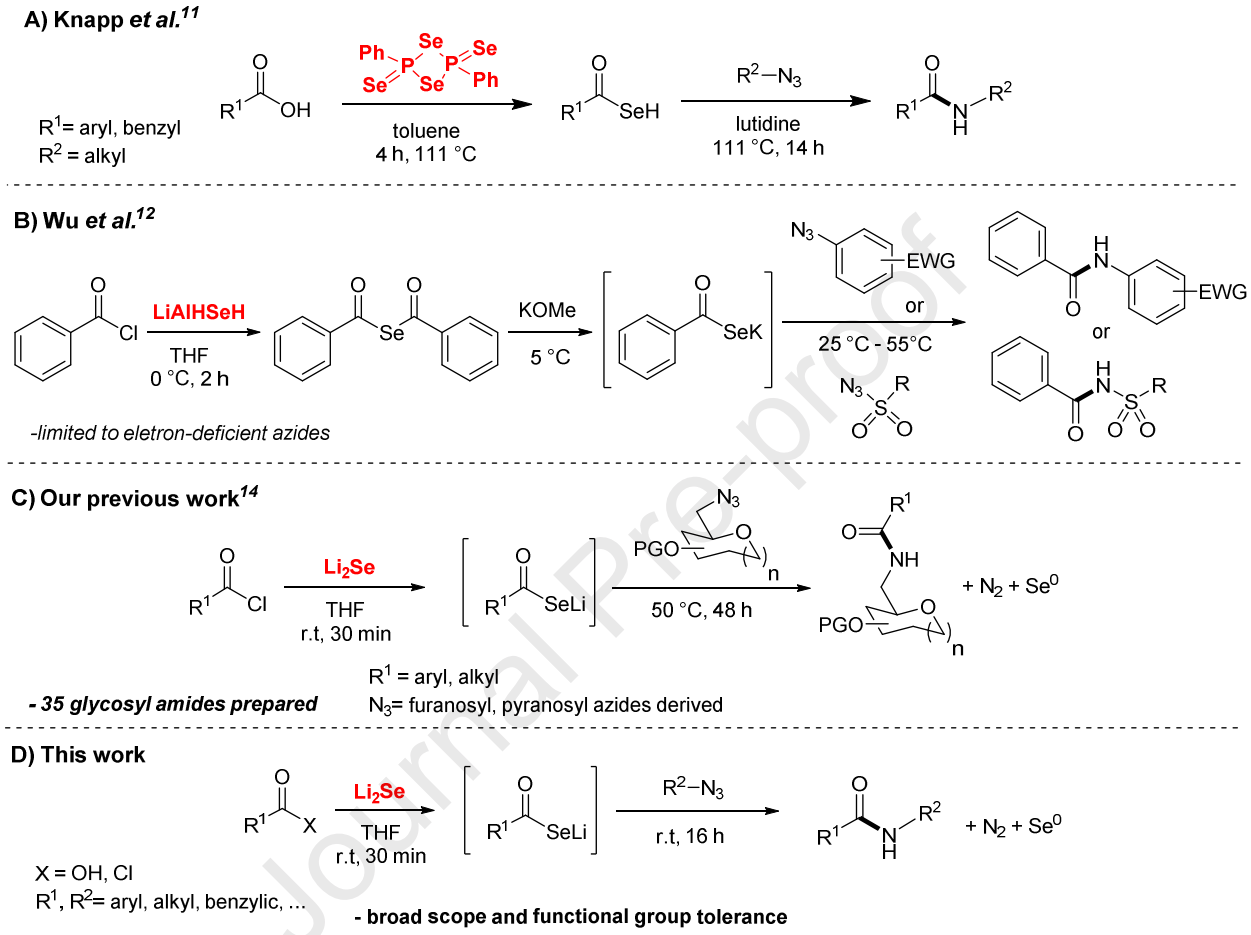
The most common methods for amide bond formation rely on the condensation between an activated carboxylic acid as the electrophile and a free amine as a nucleophile through the intermediacy of coupling reagents.[4] These methods have been successful for a variety of amides, but the coupling agents are often toxic and sometimes generate byproducts, which is not always easily separable from the amide. Moreover, in many cases free amines cannot be used due to either structural instability or the presence of

incompatible functional groups. As an alternative to conventional amide synthesis, highly innovative approaches have been recently reported[5], such as transamidation[6], α-ketoacid–hydroxylamine ligation[7], boronic acid-catalyzed amidation[8], reaction of Grignard reagents with isocyanates or N-carboxyanhydrides[9], and *umpolung* reactivity of α-bromo nitroalkanes[10]. Amongst the emergent methods, several strategies have used azides instead of amines as the substrate to form the desired amide bonds.[11] Organic azides have been an attractive nitrogen source since oxidative or basic conditions are not required, broad tolerance of chemicals, mild and green conditions applies since $N_{2(g)}$ is in general the by-product.[12] Among these, the Staudinger ligation[13], hydrative amide synthesis through alkyne–azide coupling[14], thioacid-azide ligation[15] and more recently selenocarboxylate-azide amidation[16, 17, 19] stand out. In particular, the reaction of selenocarboxylates with azides is a more reactive variation of the thioacid-azide ligation, since the selenide atom is larger and more easily polarizable - thus a better nucleophile than sulfur.[18]

In this context, we have reported an expedient methodology for the synthesis of glycosyl amides that successfully relied on the in situ generation of lithium selenocarboxylates from Se^0/$LiEt_3BH$ and activated carboxylic acid derivatives and subsequent reaction with sugar azides (Scheme 1). This protocol proved very convenient since it avoided the isolation and handling of reactive and sensitive selenium containing intermediates, providing to the selenocarboxylate the status of a traceless reagent.[19] Building up on the efficiency of this reaction, we have decided to investigate the applicability of our selenocarboxylate protocol to a broader range of substrates with different scaffolds. Therefore, herein we reported our results on the synthesis of a variety

of amides with structural diversity, including aryl, benzyl, alkyl, sulfonamide, phosphoramide, imide and carbamate.

Scheme 1. Amide bond formation through Selenocarboxylate-azide reaction

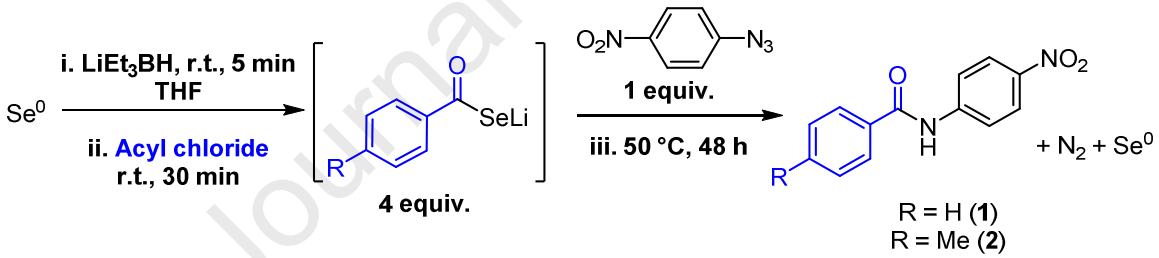


Results and Discussion

We started our studies from conditions previously employed for the amidation of glycosyl azides from selenocarboxylates.[19] Thus, the *in situ* generation of the reactive selenocarboxylate, took place with the reduction of elemental selenium with lithium triethylborohydride,[20] to generate a nucleophilic Se^{2-} species that then reacts with an activated carboxylic acid derivative (*e.g.* acyl chloride, activated carboxylic acid), generating *in situ* the desired selenocarboxylate. To validate our strategy of *one-pot* amide

synthesis from selenocarboxylates, we selected 4-nitrophenyl azide as the standard starting material, due to its well-known reactivity with selenocarboxylates in amide-bond forming reactions (Table 1).[17, 19] Under these conditions, the desired amide product **1** was obtained in excellent yield (entry 1). Additional attempts to improve even further the reaction conditions have been examined. Reducing the number of equivalents of the selenocarboxylate, unfortunately led to decreased isolated yields (entries 2-4). Lowering the temperature from 50 ^{o}C to room temperature didn't impact significantly the yield (entry 5). The reaction is also possible starting with toluyl instead of benzoyl chloride and gratifyingly, the reaction time was also reduced to 16 h (entries 6-7), leading to the amide **2** in excellent yield. Higher reaction temperature led to decomposition of the selenocarboxylate reagent (entry 8).

Table 1. Standard Conditions and deviations



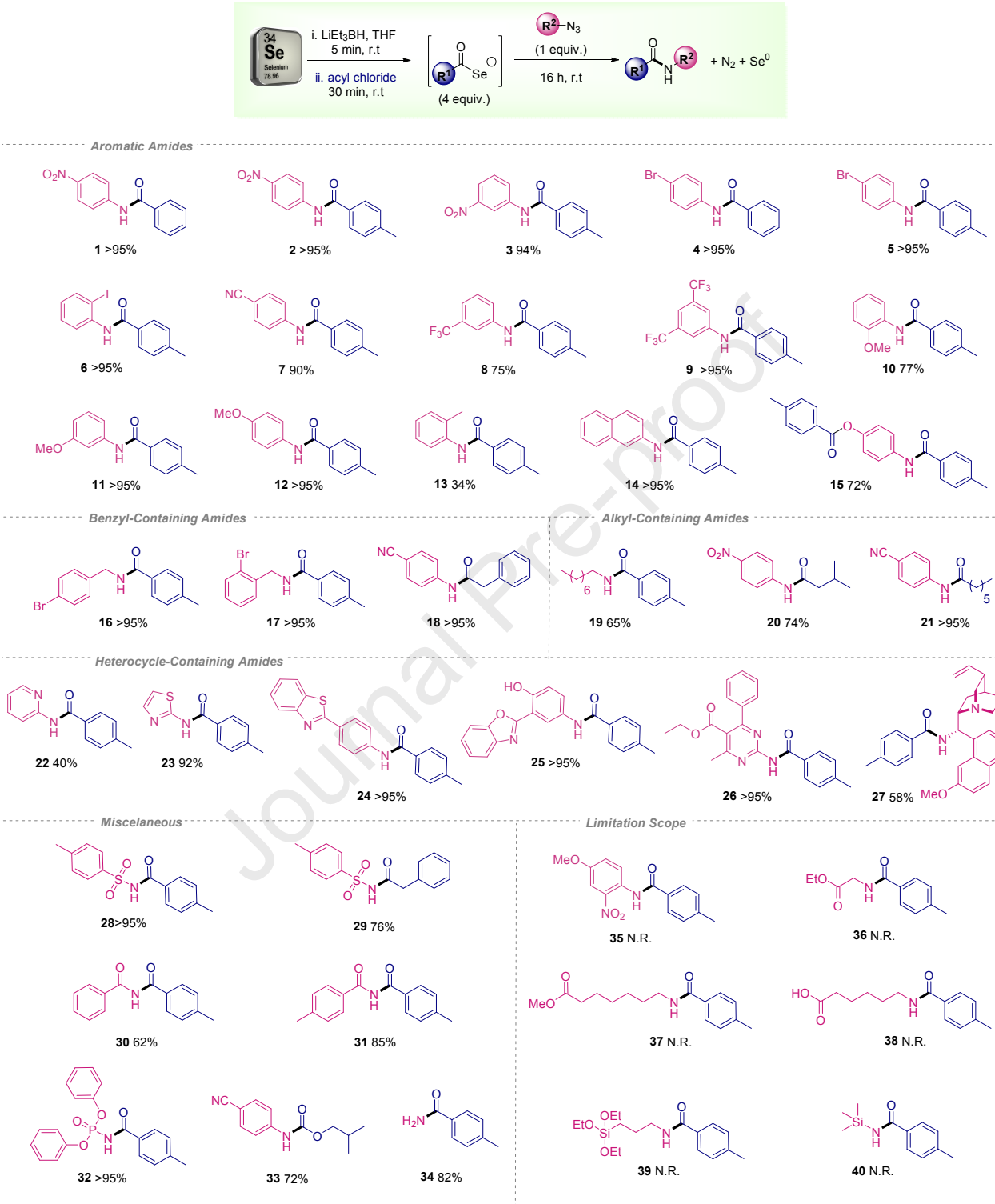
Entry	Deviation from standard condition	Yield (%)[a]
1	none	>95
2	1 equiv. of selenocarboxylate	75
3	0 ℃ instead of r.t./ 1 equiv. of selenocarboxylate	75
4	2 equiv. of selenocarboxylate	72
5	r.t. instead of 50 ℃	93
6	toluyl instead of benzoyl chloride/ r.t. instead of 50 ℃	**>95**
7	toluyl instead of benzoyl chloride /16 h instead of 48 h	**>95**
8	60 ℃ instead of 50 ℃	N.R.[b]

[a] Isolated yields. Reaction performed at room temperature in THF. N.R. = No reaction.
[b] Decomposition of selenocarboxylate

With the optimized reaction conditions in hands, the scope of this *one-pot* method was evaluated with a wide range of azides derivatives. In order to develop the methodology, expand the number of examples and evaluate possible steric and electronic effects, a variety of azides were subjected to amidation with selenocarboxylates in optimal reaction conditions. The evaluation of azides and acyl chlorides derivatives are presented in Scheme 2.

Under the standard conditions, a variety of aromatic azides bearing electron-withdrawing groups, in *ortho*, *meta* and *para* positions, such as nitro (-NO_2, **1**, **2**, **3** and **20**), cyano (-CN, **7**, **18**, **21** and **33**), bromine (-Br, **4** and **5**), iodine (-I, **6**), trifluoromethyl (-CF_3, **8** and **9**), reacted with selenocarboxylates to afford the corresponding amides in excellent yields. These results are consistent with our previous reports[19] wherein aromatic deficient-azides are highly reactive reaction partners with selenocarboxylates due the ability of stabilization the negative charge on nitrogen during the transition state, similarly as proposed for thiocarboxylates.[15c, d] For electron-rich aromatic azides, that are less reactive, (**10**-**14**), also good results were obtained. Even methoxy substituents have been well tolerated, gave good yields for the products bearing this strongly electron-donating group in *ortho*, *meta* and *para* positions. The electron-donating group methyl in *ortho* position, gave the amide **13** in a lower yield but with most of the starting azide recovered. Surprisingly, the azide bearing both nitro and methoxy substitute did not furnished the amide (**35**) with the starting material azide recovered. Sterically hindered aryl groups (**14**) also gave the desired amide in quantitative yield.

Scheme 2. Reaction scope from acyl chlorides derivatives.

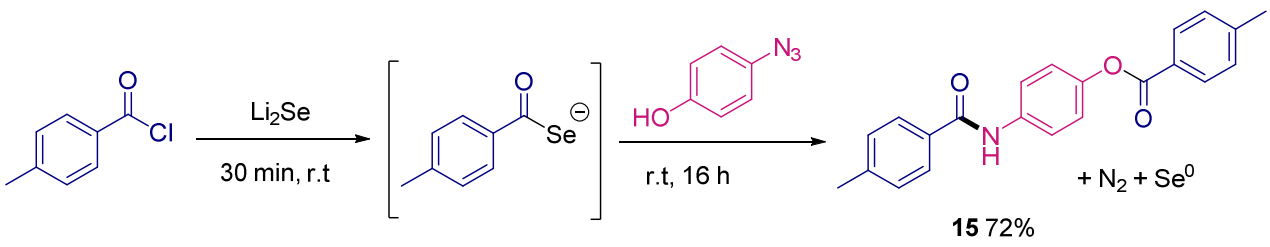


Amides substituted by heterocycles (**22**-**27**) such as pyridine (**22**), thiazole (**23**), benzothiazole (**24**), benzoxazole (**25**), pyrimidine (**26**) and quinine (**27**) could be accessed

from the corresponding azide. Moreover, amides functionalized with heterocycles are important from medicinal chemistry point-of-view, an amide bearing a pyrimidine moiety was prepared in quantitative yield (**26**). This heterocyclic compound, known as Biginelli adducts, presents a wide range of biological activity, such as antibacterial, antiviral, anti-inflammatory and especially anticancer, and also interesting photophysical properties.[21] Furthermore, benzazoles-derived amides, fluorescent molecules that belong to a class of compounds commonly used as fluorophores with potential applications as fluorescent probes and optical sensors, were also obtained (**24** and **25**) in excellent yields.[22] This amidation method was also applied to the modification of quinine, an alkaloid that has been extensively researched due to its potent antimalarial activity and role in catalysis.[23] The quinine moiety was successfully transferred from the starting azide to the final amide **27**.

Surprisingly, when *p*-phenol azide was submitted to amidation, a different product was obtained instead of the expected amide, with a free OH group. A second reaction took place at the hydroxyl and an amide functionalized with an ester was isolated in 72% yield (Scheme 3, **15**). Attempts to reduce the amount of the selenocarboxylate to achieve selectivity resulted in the same product, in lower yields.

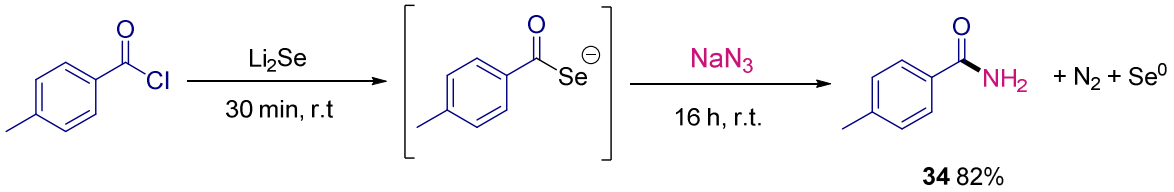
Scheme 3.



Apart from amides, other carbonyl derivatives were accessed from the corresponding azide, as sulfonamides (**28** and **29**), imides (**30** and **31**), phosphoramide (**32**) and carbamate (**33**). Worth to point out that the expansion of the methodology for the synthesis of this class of carbonyl compounds represents an important advance since several compounds bearing these functional group have pronounced pharmacological activities.[24] Benzylic azides were effective partners in reaction with selenocarboxylates, providing amides **16** and **17** in quantitative yields. These results are a positive aspect of our method, since previous reports from the literature indicate that aliphatic azides are not reactive substrates to react with selenocarboxylates to provide amides.[17] Alkyl azides were less efficient. An alkyl derivative was obtained in moderate yields (**19**). However, when alkyl azides containing carbonyl substituents were tested, the products were not obtained (**36**, **37** and **38**). Neither when azides containing organosilicon groups were used (**39** and **40**).

Furthermore, different commercial acyl chlorides were explored for generation of selenocarboxylate *in situ*, starting from elemental selenium. Besides aromatic (**1**-**17**, **19**, **22**-**28**, **30**-**32**, **34**), benzyl (**18** and **29**) and alkyl (**20** and **21**) selenocarboxylates have also been successfully employed in this amidation reaction. Additional functional group tolerance was observed for the use *iso*-butylchloroformate as the amidation substrate. When exposed to our reaction conditions, carbamate **33** was isolated in very good yield. Notably, the mildness of the reaction can be seen by the tolerance of a cyano group at the azide reactant, which remains untouched in the final product. Also worth to point out is the possibility of obtaining a primary amide simply by using sodium azide as ammonia equivalent (Scheme 4). The reaction with the selenocarboxylate occurred smoothly and, gratifyingly the desired primary amide was isolated yield of 82% yield (**34**, Scheme 4).

Scheme 4. Synthesis of a primary amide.



34 82%

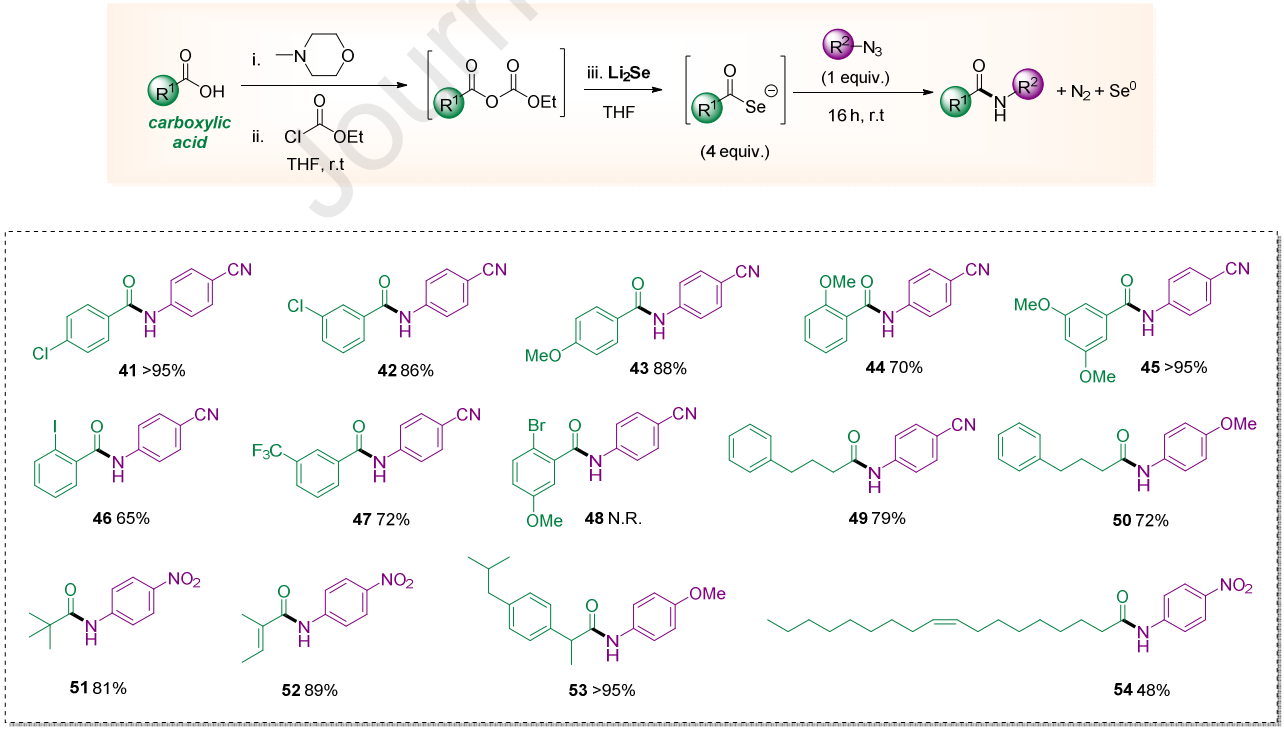
Next, to prove that the reaction is not limited to the use of acyl chlorides as the precursors for the selenocarboxylates, we have decided to explore the scope for the use of carboxylic acids as the source of selenocarboxylate, in a *one-pot* 4-step amidation reaction. Carboxylic acids are interesting starting material since less harmful that the acyl chlorides, are widely available, affordable, and present in a number of pharmaceuticals and medicinally relevant molecules.[25]

To evaluate the suitability of the use of carboxylic acids as the starting substrate, we selected the more reactive electron-deficient aromatic azides as the reaction partners. Therefore, the starting carboxylic acid material was first activated as a mixed anhydride[26] by reaction with *N*-methylmorpholine (NMM) and ethyl chloroformate. After full consumption of the carboxylic acid, reaction with freshly prepared Li_2Se took place, resulting in the corresponding selenocarboxylate, which can be used directly for the amidation reaction. Introduction of the azide to the reaction mixture resulted in evolution on N_2 and precipitation of elemental selenium indicating the completion of the reaction. The 4-step sequence occurs without isolation of any intermediates and only stable, easy-to-handle materials have been manipulated. All reactive intermediates are generated *in situ* and their handling avoided. In addition, by-products formed, Se and N_2, are harmless and removed by simple filtration. A variety of carboxylic acid were successfully employed in generation of selenocarboxylate furnishing amides bearing both aryl (Scheme 5, **41-47**) and alkyl (**49-54**) moieties. Functional group tolerance was also observed in aromatic

selenocarboxylates such as chloro (**41** and **42**), methoxy (**43-45**), iodine (**46**), trifluoromethyl (**47**), and only the carboxylic acid bearing both bromide and methoxy groups did not furnished the desired amide (**48**).

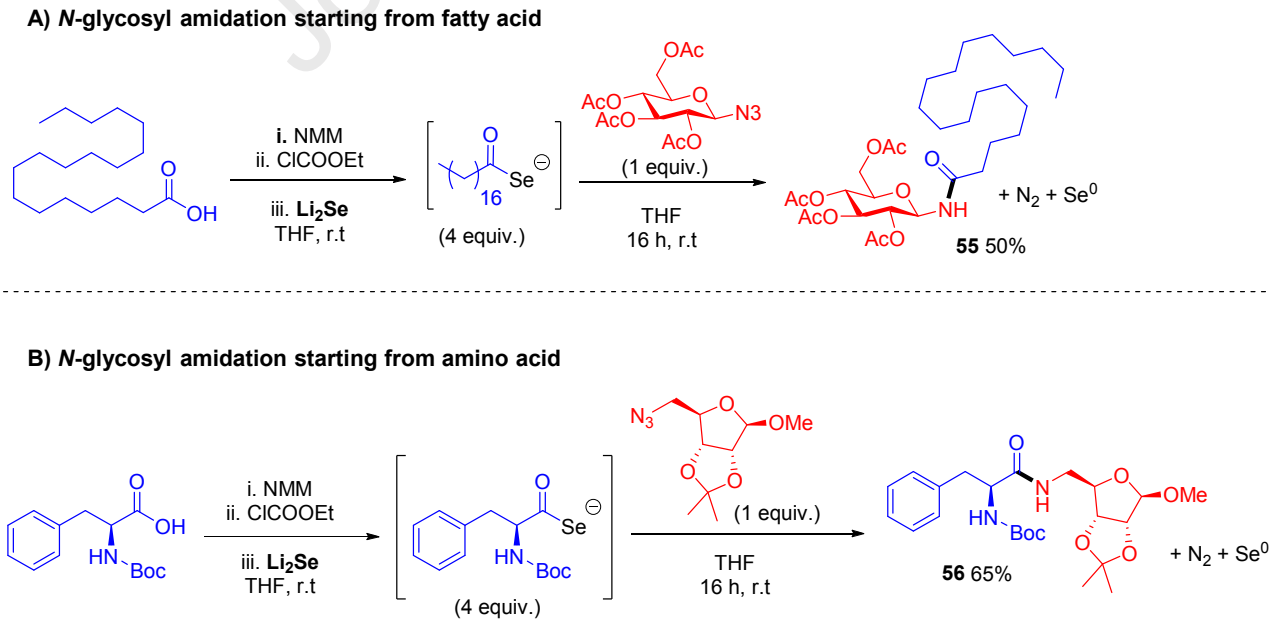
The reaction of the aliphatic selenocarboxylates (Scheme 5, **49**-**54**) gave comparable yields to aromatic selenocarboxylates. Amidation worked well when 4-phenylbutiric (**49** and **50**), sterically hindered pivalic (**51**), α,β-unsaturated tiglic (**52**), ibuprofen (**53**) and oleic acids have been used (**54**). Worth pointing out is the 4-step amidation was successfully applied to the modification of ibuprofen, which is a well-known anti-inflammatory drug,[27] to give an amide derivative in up to >95% yield. In addition, a fatty acid derivative from oleic acid was also obtained in a good 48% yield, which is a slight decrease compared to smaller alkyl substrates, likely due to solubility issues. These two examples highlight the potential utility of this method in medicinal chemistry.

Scheme 4. Reaction scope from carboxylic acid derivatives.



Next, the scope was further investigated in carbohydrate chemistry. The amidation method was successfully employed in *N*-glycosylation/modifying carbohydrates, using sugar-derived azides possessing a pyranosyl and furanosyl scaffold and carboxylic acids from biomolecules as starting materials for selenocarboxylate generation (Scheme 6). Amides derived from two different sugars have been studied. The glycosyl amide **55** was synthesized by reacting selenocarboxylate derived from fatty acid/estearic acid with and a glucosyl-derived azide in 50% yield. An amino acid derivative was also tested under the amidation conditions, and *N*-Boc-phenylalanine was used, followed by a ribose-derived azide as reaction partner, furnishing the expected amide **56** in 65% yield. Glycosyl amides are an important connection found in nature (e.g. glycopeptides, lipopolysaccharides), known for possessing a wide range of bioactivities and are important scaffolds on glycobiology studies.[28] These examples highlight the potential of the methodology in carbohydrate chemistry/ biomolecules amidation.

Scheme 5. Glycosyl amides synthesis by azide-selenocarboxylate amidation



Conclusions

In summary, a broad scope of 49 amides were prepared in up >95% yield for a wide range of substrates, in alkyl, aryl, and heterocyclic derivatives and displaying broad functional group tolerance at both reaction partners. Our one-pot procedure proved to be very efficient across a range of different acyl chlorides and carboxylic acids used as the selenocarboxylate precursors, including amino acid and fatty acid in mild reaction conditions. Selenocarboxylates were easily obtained *in situ* by reacting mixed anhydrides with Li_2Se, starting from elemental selenium and avoiding handling and isolating any intermediate, rendering to the selenocarboxylate the status of a traceless reagent. Generally, it weren't observed electronic and steric effects that exert much influence in reaction yield, once the amidation was successfully applied in a broad range of functional groups from both azides and selenocarboxylates reaction partners. However, a certain limitation was observed with the alkyl carbonyl compounds. In addition, selenocarboxylates formed from carboxylic acids presented slightly lower yields than from acyl chlorides. It is important to notice that selenocarboxylate-azide amidation were more effective when electron-deficient azides were employed but the improvement with less reactive azides, such as benzylic substrates, since other protocols in literature did not react at all to furnish amide with selenocarboxylate.

Experimental Section

General Information. ^{1}H, ^{13}C, ^{19}F, ^{31}P NMR spectra were recorded on a 400 MHz spectrometer (for ^{1}H NMR) at room temperature, using a 5-mm internal diameter probe in chloroform ($CDCl_3$), methanol (CD_3OD) or dimethyl sulfoxide (DMSO-d_6). ESI-QTOF-MS measurements were performed in the positive ion mode (*m/z* 50-2000 range). IR spectra

were obtained on an FTIR-ATR instrument. Melting points were measured optical microscope apparatus and are uncorrected. Optical rotation were obtained in polarimeter at 20 ^{o}C, unless otherwise noted. Flash column chromatography was performed using Silica Gel (230-400 mesh) following the methods described by Still[29] with the indicated solvent system. Thin layer chromatography (TLC) was performed using supported silica gel GF254, 0.25 mm thickness, and visualization of the compounds was accomplished with UV light (254 nm) or vanillin. Lithium triethylborohydride was used as a 1M THF commercial solution. Elemental selenium (-100 mesh) was dried in oven (80 ^{o}C) overnight prior to use. Applied azides are known compounds and were prepared according to literature procedures.[30]

General procedure for amidation using acyl chloride. Under an argon atmosphere, lithium triethylborohydride (2.0 mmol, 8 equiv.) was added over selenium powder (1.0 mmol, 4 equiv.) forming Li_2Se as a white solution. THF (3 mL) was added into the mixture and after 5 min stirring, the acyl chloride (1.0 mmol, 4 equiv.) was then added dropwise and the orange/yellow clear solution formed was stirred at room temperature for 30 min. After this time, the azide (0.25 mmol,1 equiv.) was added. The reaction was allowed to stir at room temperature for up to 16 h. After consumption of the starting azide, as shown by TLC or selenium powder precipitated, the reaction mixture was quenched with aqueous saturated NaCl (20 mL) and extracted with AcOEt (3x15 mL). The combined organic layers were dried with $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by flash column chromatography eluting with a mixture of hexane/ethyl acetate.

*N-(4-nitrophenyl)-benzamide (**1**)*

Yellow solid (0.060 g, >95%). CAS Registry Number 3393-96-2. R_f = 0.5 (30% ethyl acetate/n-hexane). ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) 10.83 (s, 1H), 8.28 (d, *J* = 9.3 Hz, 2H), 8.09 (d, *J* = 9.3 Hz, 2H), 8.00 (d, J = 7.1 Hz, 2H), 7.68 – 7.55 (m, 3H).^{13}C NMR (101 MHz, DMSO-d_6): δ (ppm) 166.7, 146.0, 142.9, 134.7, 132.6, 129.0, 128.4, 125.2, 120.2.

*4-methyl-N-(4-nitrophenyl)-benzamide (**2**)*

Yellow solid (0.063 g, >95%). CAS Registry Number 33667-88-8. R_f = 0.5 (30% ethyl acetate/n-hexane). ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) 10.71 (s, 1H), 8.25 (d, *J* = 9.3 Hz, 2H), 8.06 (d, *J* = 9.3 Hz, 2H), 7.90 (d, *J* = 8.0 Hz, 2H), 7.36 (d, *J* = 8.0 Hz, 2H), 2.39 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6): δ (ppm) 166.5, 146.1, 142.8, 131.8, 129.8, 129.5, 128.4, 125.2, 120.2, 21.5.

*4-methyl-N-(3-nitrophenyl)-benzamide (**3**)*

Yellow solid (0.060 g, 94%). m.p.: 118 – 120 ℃. R_f = 0.5 (30% ethyl acetate/n-hexane). ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) 10.61 (s, 1H), 8.82 (t, *J* = 2.2 Hz, 1H), 8.21 (ddd, *J* = 8.2, 2.2, 1.0 Hz, 1H), 7.96 (ddd, *J* = 8.2, 2.2, 1.0 Hz, 1H), 7.93 (d, *J* = 8.2 Hz, 2H), 7.65 (t, *J* = 8.2 Hz, 1H), 7.37 (d, *J* = 8.2 Hz, 2H), 2.40 (s, 3H).^{13}C NMR (101 MHz, DMSO-d_6): δ (ppm) 166.3, 148.3, 142.6, 140.9, 131.7, 130.4, 129.4, 128.2, 126.5, 118.4, 114.7, 21.52. IR (ν_{max}, cm^{-1}): 3378, 2960, 1665, 1528, 1353, 1260, 1018, 949, 743. HRMS (ESI+): *m/z*, calcd for $C_{14}H_{13}N_2O_3$ $[M+H]^+$ 257.0926, found 257.0926.

*N-(4-bromophenyl)-benzamide (**4**)*

White solid (0.135 g, >95%). CAS Registry Number 7702-38-7. R_f = 0.3 (10% ethyl acetate/n-hexane). ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) 10.38 (s, 1H), 7.96 (d, *J* = 7.4 Hz, 2H), 7.79 (d, *J* = 8.6 Hz, 2H), 7.63 – 7.47 (m, 5H). ^{13}C NMR (101 MHz, DMSO-d_6) δ (ppm) 166.1, 139.0, 135.2, 132.1, 131.9, 128.8, 128.1, 122.7, 115.8.

*4-methyl-N-(4-bromophenyl)-benzamide (**5**)*

White solid (0.069 g, 95%). CAS Registry Number 158525-82-7. R_f = 0.3 (10% ethyl acetate/n-hexane). ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) 10.27 (s, 1H), 7.87 (d, *J* = 8.2 Hz, 2H), 7.77 (d, *J* = 8.8 Hz, 2H), 7.52 (d, *J* = 8.8 Hz, 2H), 7.33 (d, *J* = 8.2 Hz, 2H), 2.38 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6): δ (ppm) 165.9, 142.2, 139.1, 132.2, 131.8, 129.4, 128.2, 122.6, 115.6, 21.5.

*N-(2-iodophenyl)-4-methyl-benzamide (**6**)*

White solid (0.150 g, >95%). CAS Registry Number 349089-26-5. R_f = 0.5 (30% ethyl acetate/n-hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.43 (dd, *J* = 8.0, 1.5 Hz, 1H), 8.26 (br, 1H), 7.85 (d, *J* = 8.0 Hz, 2H), 7.78 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.40 – 7.34 (m, 1H), 7.29 (d, *J* = 8.4 Hz, 2H), 6.85 (ddd, J = 8.0, 7.5, 1.5 Hz, 1H), 2.41 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) 165.1, 142.6, 138.6, 138.2, 131.5, 129.5, 129.2, 127.0, 125.8, 121.6, 90.2, 21.4.

*N-(4-cyanophenyl)-4-methyl-benzamide (**7**)*

White solid (0.062 g, 90%). m.p.: 211 – 213 ℃. R_f = 0.5 (10% ethyl acetate/n-hexane). ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) 10.54 (s, 1H), 8.00 (d, *J* = 9.0 Hz, 2H), 7.88 (d, *J* = 8.2 Hz, 2H), 7.80 (d, *J* = 9.0 Hz, 2H), 7.34 (d, *J* = 8.2 Hz, 2H), 2.38 (s, 3H). ^{13}C NMR (101

MHz, DMSO-d_6): δ (ppm) 166.4, 144.0, 142.6, 133.5, 131.9, 129.4, 128.3, 120.6, 119.5, 105.6, 21.5. IR (ν_{max}, cm^{-1}): 3378, 2980, 2170, 1734, 1374, 1233, 1038, 622. HRMS (ESI+): *m/z*, calcd for $C_{15}H_{13}N_2O$ $[M+H]^+$ 237.1028, found 237.1021.

*4-methyl-N-[3-(trifluoromethyl)phenyl]-benzamide (**8**)*

White solid (0.046 g, 75%). m.p.: 98 – 100 ℃. R_f = 0.4 (10% ethyl acetate/n-hexane). ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) 10.46 (s, 1H), 8.26 (s, 1H), 8.06 (d, *J* = 8.0 Hz, 1H), 7.91 (d, *J* = 8.0 Hz, 2H), 7.59 (t, J = 8.0 Hz, 1H), 7.44 (d, *J* = 8.0 Hz, 1H), 7.35 (d, *J* = 8.0 Hz, 2H), 2.39 (s, 3H).^{13}C NMR (101 MHz, DMSO-d_6): δ (ppm) 166.2, 142.4, 140.5, 132.0, 130.2, 129.8 (q, *J* = 31.3 Hz), 129.4, 128.2, 124.7 (q, *J* = 273.7 Hz), 124.1, 120.2 (q, *J* = 4.0 Hz), 116.7 (q, *J* = 4.0 Hz), 21.4. ^{19}F NMR (376 MHz, DMSO-*d*): δ (ppm) -61.3. IR (ν_{max}, cm^{-1}): 3297, 2932, 1654, 1540, 1448, 1327, 1128, 801, 702. HRMS (ESI+): *m/z*, calcd for $C_{15}H_{13}F_3NO$ $[M+H]^+$ 280.0949, 280.0946.

*N-[3,5-bis(trifluoromethyl)phenyl]-4-methyl- benzamide (**9**)*

White solid (0.064 g, >95%). CAS Registry Number 424812-38-4. R_f = 0.3 (10% ethyl acetate/n-hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.09 (s, 3H), 7.70 (d, *J* = 8.0 Hz, 2H), 7.55 (s, 1H), 7.22 (d, *J* = 8.0 Hz, 2H), 2.36 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) 165.9, 143.3, 139.4, 132.3 (q, *J* = 34.3 Hz), 130.8, 129.6, 127.0, 123.0 (q, *J* = 272.7 Hz), 119.7 (m), 117.6 (m), 21.5. ^{19}F NMR (376 MHz, $CDCl_3$): δ (ppm) -63.0.

*N-(2-methoxyphenyl)-4-methyl-benzamide (**10**)*

White solid (0.047 g, 77%). CAS Registry Number 122589-84-8. R_f = 0.5 (30% ethyl acetate/n-hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.53 (dd, *J* = 7.6, 1.6 Hz, 2H),

7.78 (d, *J* = 8.2 Hz, 2H), 7.27 (d, *J* = 8.2 Hz, 2H), 7.03 (dtd, *J* = 22.0, 7.6, 1.6 Hz, 2H), 6.89 (dd, *J* = 7.6, 1.6 Hz, 1H), 3.89 (s, 3H), 2.40 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) 165.1, 148.0, 142.0, 132.3, 129.3, 127.8, 126.9, 123.6, 121.0, 119.6, 109.8, 55.7, 21.3.

*N-(3-methoxyphenyl)-4-methyl-benzamide (**11**)*

White solid (0.133 g, >95%). CAS Registry Number 101078-45-9. R_f = 0.5 (30% ethyl acetate/n-hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.25 (br, 1H), 7.72 (d, *J* = 8.2 Hz, 2H), 7.42 (t, *J* = 2.5 Hz, 1H), 7.22 – 7.09 (m, 4H), 6.66 (ddd, *J* = 8.2, 2.5, 1.0 Hz, 1H), 3.74 (s, 3H), 2.36 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) 165.9, 159.9, 142.1, 139.2, 131.8, 129.4, 129.1, 127.0, 112.4, 110.2, 105.7, 55.1, 21.3.

*N-(4-methoxyphenyl)-4-methyl-benzamide (**12**)*

White solid (0.075 g, >95%). CAS Registry Number 33667-91-3. R_f = 0.5 (30% ethyl acetate/n-hexane). ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) 10.05 (br, 1H), 7.88 (d, *J* = 8.0 Hz, 2H), 7.70 (d, *J* = 9.0 Hz, 2H), 7.32 (d, *J* = 8.0 Hz, 2H), 6.93 (d, *J* = 9.0 Hz, 2H), 3.75 (s, 3H), 2.38 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6): δ (ppm) 165.3, 155.9, 141.7, 132.8, 132.6, 129.3, 128.0, 122.4, 114.1, 55.6, 21.4.

*N-(2-methylphenyl)-4-methyl-benzamide (**13**)*

White solid. (0,020 g, 34%). CAS Registry Number 55577-26-9. R_f = 0.7 (30% ethyl acetate/n-hexane). ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) 9.78 (s, 1H), 7.89 (d, *J* = 8.2 Hz, 2H), 7.33 (d, *J* = 8.2 Hz, 2H), 7.34 – 7.12 (m, 4H), 2.38 (s, 3H), 2.23 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6): δ (ppm) 165.5, 141.9, 136.9, 134.1, 132.1, 130.7, 129.3, 128.1, 127.1, 126.4, 126.3, 21.4, 18.3.

*4-methyl-N-2-naphthalenyl-benzamide (**14**)*

White solid (0.090 g, >95%). CAS Registry Number 84647-12-1. R_f = 0.7 (30% ethyl acetate/n-hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.30 (d, *J* = 2.0 Hz, 1H), 8.19 (br, 1H), 7.76 (dd, *J* = 16.0, 8.0 Hz, 5H), 7.58 (dd, *J* = 8.5, 2.0 Hz, 1H), 7.46 – 7.35 (m, 2H), 7.22 (d, *J* = 8.5 Hz, 2H), 2.38 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) 165.9, 142.3, 135.4, 133.7, 131.9, 130.6, 129.3, 128.6, 127.6, 127.4, 127.0, 126.4, 124.9, 120.2, 117.0, 21.4.

*4-methyl-4-[(4-methylbenzoyl)amino]phenyl ester benzoic acid (**15**)*

White solid (0.049 g, 56%). R_f = 0.6 (30% ethyl acetate/n-hexane). ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) 10.26 (s, 1H), 8.02 (d, *J* = 8.1 Hz, 2H), 7.88 (d, *J* = 8.1 Hz, 2H), 7.83 (d, *J* = 9.0 Hz, 2H), 7.41 (d, *J* = 8.0 Hz, 2H), 7.34 (d, *J* = 8.0 Hz, 2H), 7.24 (d, *J* = 9.0 Hz, 2H), 2.42 (s, 3H), 2.38 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6): δ (ppm) 146.7, 144.9, 142.1, 137.4, 132.4, 130.3, 130.0, 129.4, 128.1, 126.7, 122.4, 121.7, 21.7, 21.5.

*N-[(4-bromophenyl)methyl]-4-methyl-benzamide (**16**)*

White solid (0.076 g, >95%). m.p.: 151 – 153 ℃. R_f = 0.6 (30% ethyl acetate/n-hexane). ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) 8.99 (t, *J* = 6.0 Hz, 1H), 7.79 (d, *J* = 8.2 Hz, 2H), 7.51 (d, *J* = 8.2 Hz, 2H), 7.3 – 7.25 (m, 4H), 4.43 (d, *J* = 6.0 Hz, 2H), 2.35 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6): δ (ppm) 166.5, 141.6, 139.7, 131.8, 131.5, 129.9, 129.4, 129.3, 127.7, 120.1, 42.4, 21.4. IR (ν_{max}, cm^{-1}): 3297, 2932, 2848, 1639, 1547, 1479, 1303,

1258, 1068, 992, 801, 664. HRMS (ESI+): *m/z*, calcd for $C_{15}H_{15}BrNO$ $[M+H]^+$ 304.0337, found 304.0339.

*N-[(2-bromophenyl)methyl]-4-methyl-benzamide (**17**)*

White solid (0.080 g, >95%). CAS Registry Number 1306052-87-8. R_f = 0.6 (30% ethyl acetate/n-hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.68 (d, *J* = 8.0 Hz, 2H), 7.52 (d, *J* = 7.5 Hz, 1H), 7.37 (d, *J* = 7.5 Hz, 1H), 7.26 – 7.07 (m, 4H), 6.98 (br, 1H), 4.63 (d, *J* = 6.0 Hz, 2H), 2.36 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) 167.3, 141.8, 137.2, 132.6, 131.2, 130.0, 129.0, 128.9, 127.5, 126.9, 123.5, 44.0, 21.3.

*N-(4-cyanophenyl)-benzeneacetamide (**18**)*

White solid (0.062 g, >95%). CAS Registry Number 89246-38-8. R_f = 0.4 (30% ethyl acetate/n-hexane). ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) 10.62 (s, 1H), 7.81 (d, *J* = 9.0 Hz, 2H), 7.76 (d, *J* = 9.0 Hz, 2H), 7.38 – 7.22 (m, 5H), 3.72 (s, 2H). ^{13}C NMR (101 MHz, DMSO-d_6): δ (ppm) 170.4, 143.8, 135.8, 133.7, 129.6, 128.8, 127.1, 119.58, 119.51, 105.4, 43.8.

*4-methyl-N-octyl-benzamide (**19**)*

Colorless oil (0.040 g, 65%). CAS Registry Number 203627-10-5. R_f = 0.8 (30% ethyl acetate/n-hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.67 (d, *J* = 8.2 Hz, 2H), 7.20 (d, *J* = 8.2 Hz, 2H), 6.44 (br, 1H), 3.41 (q, *J* = 7.0 Hz, 2H), 2.37 (s, 3H), 1.63 – 1.53 (m, *J* = 14.8, 7.4 Hz, 2H), 1.46 – 1.07 (m, 10H), 0.87 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) 167.6, 141.6, 131.7, 129.0, 126.8, 40.0, 31.7, 29.5, 29.2, 29.1, 26.9, 22.5, 21.3, 14.0.

*3-methyl-N-(4-nitrophenyl)-butanamide (**20**)*

Yellow solid (0.041 g, 74%). CAS Registry Number 151860-14-9. R_f = 0.5 (30% ethyl acetate/n-hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.19 (d, *J* = 9.2 Hz, 2H), 8.12 (br, 1H), 7.76 (d, *J* = 9.2 Hz, 2H), 2.31 (d, *J* = 6.6 Hz, 2H), 2.29 – 2.17 (m, 1H), 1.03 (s, 3H), 1.01 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) 171.6, 144.0, 143.2, 124.9, 119.0, 46.8, 26.1, 22.3.

*N-(4-cyanophenyl)-heptanamide (**21**)*

White solid (0.059 g, >95%). m.p.: 69 - 71 ℃. R_f = 0.6 (30% ethyl acetate/n-hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.38 (s, 1H), 7.73 (d, *J* = 8.7 Hz, 2H), 7.58 (d, *J* = 8.7 Hz, 2H), 2.41 (t, *J* = 8.0 Hz, 2H), 1.71 (quint, *J* = 8.0 Hz, 2H), 1.40 – 1.24 (m, 6H), 0.87 (t, *J* = 6.5 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) 172.5, 142.4, 133.0, 119.5, 118.9, 106.2, 37.5, 31.3, 28.7, 25.3, 22.3, 13.8. IR (ν_{max}, cm^{-1}): 3239, 3169, 3101, 3039, 2925, 2857, 2222, 1664, 1587, 1527, 1404, 831, 541. HRMS (ESI+): *m/z*, calcd for $C_{14}H_{19}N_2O$ $[M+H]^+$ 231.1497, found 231.1483.

4-methyl-N-*2-pyridinyl-benzamide (**22**)*

White solid (0.050 g, 40%). R_f = 0.4 (30% ethyl acetate/n-hexane). RMN ^{1}H (400 MHz, $CDCl_3$): δ (ppm) 8.43 (dt, *J* = 8.4 Hz, 1H), 8.26 (br, 1H), 7.85 (d, *J* = 8.3 Hz; 2 H), 7.78 (dd, *J* = 8.4 Hz, 1.44 Hz; 1H), 7.37 (ddd, *J* = 7.0, 1.1 Hz, 1H); 7,31-7,29 (m, 2H); 6,85 (td, *J* = 7,8 Hz e 1,7 Hz; 1H); 2,41 (s, 3H). RMN ^{13}C (101 MHz, $CDCl_3$): δ (ppm) 171,3; 148,5; 144,4; 131,9; 130,1; 129,1; 126,6; 125,4; 116,6; 115,9; 21,7.

*4-methyl-N-2-thiazolyl-benzamide (**23**)*

White solid (0.050 g, 92%). CAS Registry Number 150175-93-2. R_f = 0.4 (30% ethyl acetate/n-hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.99 (d, *J* = 8.0 Hz, 2H), 7.31 (d, *J* = 8.0 Hz, 2H), 7.18 (d, *J* = 3.7 Hz, 1H), 6.95 (d, *J* = 3.7 Hz, 1H), 2.45 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) 165.6, 160.6, 143.4, 136.6, 130.0, 129.4, 128.1, 113.3, 21.6.

*N-[4-(2-benzothiazolyl)phenyl]-4-methyl-benzamide (**24**)*

Yellow solid (0.087 g, >95%). m.p.: 252 – 253 ℃. R_f = 0.5 (30% ethyl acetate/n-hexane). ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) 10.48 (s, 1H), 8.16 – 8.07 (m, 3H), 8.06 – 7.99 (m, 3H), 7.91 (d, *J* = 8.2 Hz, 2H), 7.57 – 7.50 (m, 1H), 7.48 – 7.41 (m, 1H), 7.36 (d, J = 8.2 Hz, 2H), 2.40 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6): δ (ppm) 167.5, 166.1, 154.1, 142.7, 142.4, 134.8, 132.2, 129.4, 128.3, 128.3, 128.3, 127.0, 125.7, 123.0, 122.7, 120.8, 21.5. IR (ν_{max}, cm^{-1}): 3372, 3009, 2919, 2854, 1652, 1586, 1520, 1479, 1405, 1306, 961, 821, 747, 713, 614. HRMS (ESI+): *m/z*, calcd for $C_{21}H_{17}N_2OS$ $[M+H]^+$ 345.1062, found 345.1062.

*N-[3-(2-benzoxazolyl)-4-hydroxyphenyl]-4-methyl-benzamide (**25**)*

White solid (0.121 g, >95%). m.p.: 260 – 262 ℃. R_f = 0.3 (30% ethyl acetate/n-hexane).^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) 11.04 (s, 1H), 10.28 (s, 1H), 8.64 (d, *J* = 2.6 Hz, 1H), 7.91 (d, *J* = 8.0 Hz, 2H), 7.90 – 7.83 (m, 3H), 7.52 – 7.43 (m, 2H), 7.35 (d, *J* = 8.0 Hz, 2H), 7.13 (d, *J* = 8.9 Hz, 1H), 2.39 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6): δ (ppm) 165.6, 162.7, 154.4, 149.3, 142.1, 140.0, 132.3, 129.4, 128.1, 127.1, 126.4, 125.8, 119.7, 119.1, 117.7, 111.5, 110.2, 21.5. IR (ν_{max}, cm^{-1}): 3363, 3031, 2910, 2858, 1653, 1585,

1479, 1404, 1314, 960, 839, 741, 613. HRMS (ESI+): *m/z*, calcd for $C_{21}H_{17}N_2O_3$ $[M+H]^+$ 345.1239, found 345.1214.

*2-(4-methylbenzamido)-4-methyl-6-phenyl ethyl ester-5-pyrimidinecarboxylic acid (**26**)*

White solid (0.090 g, >95%). m.p.: 180 - 182 ℃. R_f = 0.4 (30% ethyl acetate/n-hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.67 (s, 1H), 7.84 (d, *J* = 8.0 Hz, 2H), 7.74 – 7.58 (m, 2H), 7.50 – 7.42 (m, 3H), 7.29 (d, *J* = 8.0 Hz, 2H), 4.18 (q, *J* = 7.2 Hz, 2H), 2.65 (s, 3H), 2.43 (s, 3H), 1.05 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) 167.6, 167.3, 165.1, 164.7, 156.7, 142.9, 137.3, 131.1, 130.0, 129.2, 128.3, 128.1, 127.4, 121.1, 61.6, 22.6, 21.3, 13.4. IR (v_{max}, cm^{-1}): 3295, 2985, 1732, 1695, 1582, 1489, 1422, 1257, 1092, 746, 700. HRMS (ESI+): *m/z*, calcd for $C_{22}H_{21}N_3O_3$ $[M+H]^+$ 376.1661, found 376.1666.

*N-[(8α,9S)-6'-methoxycinchonan-9-yl]-4-methyl-benzamide (9CI) (**27**)*

White solid (0.1664 g, 58%). $[\alpha]_D^{20}$= - 36.0 ° (c 1.000, MeOH). m.p.: 79 – 81 ℃. R_f = 0.3 (90% ethyl acetate/10% methanol). ^{1}H NMR (400 MHz, CD_3OD): δ (ppm) 8.69 (d, *J* = 4.8 Hz, 1H), 7.95 (d, *J* = 9.2 Hz, 1H), 7.88 (d, *J* = 2.6 Hz, 1H), 7.73 (d, *J* = 8.5 Hz, 2H), 7.71 (d, *J* = 4.8 Hz, 1H), 7.41 (dd, *J* = 9.2, 2.6 Hz, 1H), 7.16 (d, *J* = 8.5 Hz, 2H), 6.13 (br, 1H, *CH*, 5.94 (ddd, *J* = 17.4, 10.4, 7.3 Hz, 1H), 5.15 (d, *J* = 17.2 Hz, 1H), 5.10 (d, *J* = 10.4 Hz, 1H). 4.11 – 4.03 (m, 1H), 4.01 (s, 3H), 3.81 – 3.65 (m, 1H), 3.42 (dd, *J* = 13.5, 10.3 Hz, 1H), 3.10 (ddd, *J* = 13.5, 5.5, 2.1 Hz, 1H), 3.06 – 2.96 (m, 1H), 2.58 – 2.47 (m, 1H), 2.29 (s, 3H), 1.88 – 1.73 (m, 4H), 0.99 (dd, *J* = 13.5, 6.3 Hz, 1H).^{13}C NMR (75 MHz, CD_3OD): δ (ppm) 169.6, 159.9, 148.2, 145.6, 145.1, 143.5, 141.0, 131.9, 131.4, 129.97, 129.93, 128.6, 123.7, 121.3, 116.0, 103.1, 60.0, 56..4, 55.9, 51.1, 42.5, 39.5, 28.4, 27.0, 26.9, 21.4. IR (v_{max}, cm^{-1}): 3292, 3074, 2932, 2864, 2100, 1735, 1641, 1617, 1503, 1474, 1365,

1321, 1237, 1040, 1025, 921, 829. HRMS (ESI+): *m/z*, calcd for $C_{28}H_{32}N_3O_2$ $[M+H]^+$ 442.2495, found 442, 2495.

*4-methyl-N-[(4-methylphenyl)sulfonyl]-benzamide (**28**)*

White solid (0.110 g, >95%). CAS Registry Number 120336-96-1. R_f = 0.4 (30% ethyl acetate/n-hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 9.52 (br, 1H), 8.04 (d, *J* = 8.3 Hz, 2H), 7.72 (d, *J* = 8.3 Hz, 2H), 7.33 (d, *J* = 8.0 Hz, 2H), 7.19 (d, *J* = 8.0 Hz, 2H), 2.42 (s, 3H), 2.35 (s, 3H).^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) 164.4, 145.0, 144.2, 135.5, 129.5, 129.4, 128.5, 128.2, 127.9, 21.6, 21.5.

*N-[(4-methylphenyl)sulfonyl]-benzeneacetamide (**29**)*

White solid (0.055 g, 76%). CAS Registry Number 1788-13-2. R_f = 0.4 (30% ethyl acetate/n-hexane). ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) 7.79 (d, *J* = 8.2 Hz, 2H), 7.39 (d, *J* = 8.2 Hz, 2H), 7.30 – 7.19 (m, 3H), 7.18 – 7.13 (m, 2H), 3.54 (s, 1H), 2.38 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6): δ (ppm) 169.8, 144.7, 136.8, 134.4, 129.9, 129.7, 128.8, 128.0, 127.3, 42.9, 21.5.

*N-benzoyl-4-methyl-benzamide (**30**)*

White solid (0.037 g, 62%). CAS Registry Number 58010-65-4. R_f = 0.4 (30% ethyl acetate/n-hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 9.18 (br, 1H), 7.85 (dd, *J* = 8.4, 1.3 Hz, 2H), 7.76 (d, *J* = 8.2 Hz, 2H), 7.57 (tt, *J* = 7.5, 1.3 Hz, 1H), 7.46 (t, *J* = 7.5 Hz, 2H), 7.26 (d, *J* = 8.4 Hz, 2H), 2.40 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) 166.6, 166.3, 143.8, 133.3, 132.8, 130.3, 129.4, 128.6, 128.0, 127.9, 21.5.

*4-methyl-N-(4-methylbenzoyl)-benzamide (**31**)*

White solid (0.054 g, 85%). m.p.: 108 - 110 ℃. R_f = 0.5 (30% ethyl acetate/n-hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 9.13 (s, 1H), 7.75 (d, *J* = 8.0 Hz, 4H), 7.26 (d, *J* = 8.0 Hz, 4H), 2.40 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) 166.2, 143.8, 130.5, 129.4, 127.9, 21.6. IR (ν_{max}, cm^{-1}): 3249, 2913, 1720, 1612, 1474, 1230, 1115, 824, 733. HRMS (ESI+): *m/z*, calcd for $C_{16}H_{16}NO_2$ $[M+H]^+$ 254.1181, found 254.1179.

*N-(4-methylbenzoyl)-diphenyl ester phosphoramidic acid (**32**)*

White crystal solid (0.180 g, >95%). CAS Registry Number 1376827-57-4. R_f = 0.3 (30% ethyl acetate/n-hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 9.77 (d, J_{P-H} = 10.0 Hz, 1H), 7.87 (d, *J* = 8.3 Hz, 2H), 7.26 – 7.17 (m, 8H), 7.17 – 7.08 (m, 4H), 2.36 (s, 3H).^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) 167.4 (d, *J* = 3.5 Hz), 150.0 (d, *J* = 6.7 Hz), 143.5, 129.57, 129.56, 129.0, 125.40 (d, *J* = 1.4 Hz), 128.46, 120.43 (d, *J* = 4.8 Hz), 21.4. Decoupled ^{31}P NMR (162 MHz, $CDCl_3$): δ (ppm) -9.02. Coupled ^{31}P NMR (162 MHz, $CDCl_3$): δ (ppm) -9.03 (d, J_{P-H} = 10.0 Hz).

*N-(4-cyanophenyl)-2-methylpropyl ester carbamic acid (**33**)*

White solid (0.040 g, 72%). m.p.: 110 - 112 ℃. R_f = 0.8 (30% ethyl acetate/n-hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.58 (d, *J* = 9.0 Hz, 2H), 7.55 (d, *J* = 9.0 Hz, 2H), 7.36 – 7.21 (m, 1H), 3.97 (d, *J* = 6.7 Hz, 2H), 2.04 – 1.92 (m, 1H), 0.96 (d, *J* = 6.7 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) 153.1, 142.4, 133.2, 118.9, 118.1, 105.7, 71.7, 27.7, 18.8. IR (ν_{max}, cm^{-1}): 3343, 2954, 2924, 2870, 2222, 1726, 1589, 1519, 1214, 1054, 818, 543. HRMS (ESI+): *m/z*, calcd for $C_{12}H_{15}N_2O_2$ $[M+H]^+$ 219.1134, found 219.1138.

*4-methyl-benzamide (**34**)*

White solid (0.028 g, 82%). CAS Registry Number 619-55-6. R_f = 0.2 (30% ethyl acetate/n-hexane). ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) 7.90 (br, 1H), 7.79 (d, *J* = 8.0 Hz, 2H), 7.27 (br, 1H), 7.25 (d, *J* = 8.0 Hz, 2H), 2.35 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6): δ (ppm) 168.2, 141.5, 131.9, 129.2, 127.9, 21.4.

General procedure for amidation using carboxylic acids. Under argon atmosphere, to a solution of the carboxylic acid (1.0 mmol, 4 equiv.) in THF (3 mL) was added *N*-methylmorpholine (1.0 mmol, 4 equiv.). After stirring for 5 minutes at room temperature, ethyl chloroformate (1.0 mmol, 4 equiv.) was added and stirring was prolonged for additional 15 minutes. Then, freshly prepared Li_2Se (as previous procedure) (1 mmol, 4 equiv.) was quickly added into the obtained mixed anhydride solution using a syringe. After additional 15 min of stirring, the azide (0.25 mmol, 1 equiv.) was added over the selenocarboxylate solution. The reaction was carried out at room temperature. The reaction was allowed to stir at room temperature for up to 16 h. After consumption of the starting azide, as shown by TLC or selenium powder precipitated, the reaction mixture was quenched with HCl 10% (3x20 mL), washed with aqueous saturated NaCl (20 mL) and extracted with AcOEt (3x15 mL). The combined organic layers were dried with $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by flash column chromatography eluting with a mixture of hexane/ethyl acetate (90:10).

*4-chloro-N-(4-cyanophenyl)-benzamide (**41**)*

White solid (0.065 g, >95%). m.p.: 120 - 123 ℃. R_f = 0.5 (30% ethyl acetate/n-hexane). ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) 10.71 (s, 1H), 8.02 (d, *J* = 2.0 Hz, 2H), 7.99 (d, *J* =

2.0 Hz, 2H), 7.83 (d, *J* = 8.7 Hz, 2H), 7.64 (d, *J* = 8.7 Hz, 2H).^{13}C NMR (101 MHz, DMSO-*d*$_6$): δ (ppm) 165.5, 143.8, 137.4, 133.6, 133.5, 130.3, 129.0, 120.7, 119.5, 106.0. IR (ν_{max}, cm^{-1}): 3247, 2916, 2855, 2211, 1651, 1590, 1505, 1406, 1322, 1260, 991, 831, 731, 539. HRMS (ESI+): *m/z*, calcd for $C_{14}H_{10}ClN_2O$ $[M+H]^+$ 257.0482, found 257,0481; calcd for $C_{14}H_9ClN_2ONa$ $[M+Na]^+$ 279.0301, found 279.0296.

*3-chloro-N-(2-cyanophenyl)-benzamide (**42**)*

White solid (0.055 g, 86%). m.p.: 143 - 145 ℃. R_f = 0.6 (30% ethyl acetate/n-hexane). ^{1}H NMR (400 MHz, DMSO-*d*$_6$): δ (ppm) 10.73 (s, 1H), 8.02 (t, *J* = 2.0 Hz, 1H), 7.99 (d, *J* = 8.9 Hz, 2H), 7.94 – 7.91 (m, 1H), 7.84 (d, *J* = 8.9 Hz, 2H), 7.70 (ddd, *J* = 8.0, 2.0, 1.0 Hz, 1H), 7.60 (t, *J* = 8.0 Hz, 1H). ^{13}C NMR (101 MHz, DMSO-*d*$_6$): δ (ppm) 165.1, 143.6, 136.8, 133.7, 133.6, 132.3, 130.9, 128.0, 127.1, 120.7, 119.4, 106.1. IR (ν_{max}, cm^{-1}): 3321, 3083, 2845, 2222, 1684, 1599, 1523, 1407, 1300, 1253, 839, 716, 546. HRMS (ESI+): *m/z*, calcd for $C_{14}H_{10}ClN_2O$ $[M+H]^+$ 257.0482, found 257.0480.

*N-(4-cyanophenyl)-4-methoxy-benzamide (**43**)*

White solid (0.055 g, 88%). CAS Registry Number 134925-97-6. R_f = 0.3 (30% ethyl acetate/n-hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.27 (s, 1H), 7.84 (d, *J* = 8.7 Hz, 2H), 7.80 (d, *J* = 8.7 Hz, 2H), 7.60 (d, *J* = 8.7 Hz, 2H), 6.95 (d, *J* = 8.7 Hz, 2H), 3.87 (s, 3H).^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) 165.5, 162.8, 142.3, 133.1, 129.1, 126.0, 119.8, 118.9, 114.0, 106.8, 55.4.

*N-(4-cyanophenyl)-2-methoxy-benzamide (**44**)*

White solid (0.045 g, 70%). CAS Registry Number 361464-65-5. R_f = 0.4 (30% ethyl acetate/n-hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 10.05 (br, 1H), 8.25 (dd, *J* = 8.0, 2.0 Hz, 1H), 7.80 (d, *J* = 8.8 Hz, 2H), 7.61 (d, *J* = 8.8 Hz, 2H), 7.53 (ddd, *J* = 8.4, 7.3, 2.0 Hz, 1H), 7.17 – 7.11 (m, 1H), 7.05 (d, *J* = 8.4 Hz, 1H), 4.07 (s, 3H).^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) 163.4, 157.1, 142.3, 133.8, 133.1, 132.4, 121.7, 120.8, 120.0, 118.9, 111.5, 106.6, 56.28.

N-(4-cyanophenyl)-3,5-dimethoxy-benzamide (**45**)

White solid (0.075 g, >95%). m.p.: 116 – 118 ℃. R_f = 0.5 (30% ethyl acetate/n-hexane). ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) 10.56 (s, 1H), 7.99 (d, *J* = 8.8 Hz, 2H), 7.83 (d, *J* = 8.8 Hz, 2H), 7.11 (d, *J* = 2.3 Hz, 2H), 6.76 (t, *J* = 2.3 Hz, 1H), 3.84 (s, 6H). ^{13}C NMR (101 MHz, DMSO-d_6): δ (ppm) 166.1, 160.9, 143.8, 136.8, 133.5, 120.7, 119.5, 106.3, 105.9, 104.1, 56.03. IR (ν_{max}, cm^{-1}): 3318, 2939, 2832, 2219, 1642, 1590, 1513, 1346, 1203, 1150, 1043, 831, 664, 551. HRMS (ESI+): *m/z*, calcd for $C_{16}H_{15}N_2O_3$ $[M+H]^+$ 283.1083, found 283.1079.

*N-(4-cyanophenyl)-2-iodo-benzamide (**46**)*

Light yellow solid (0.057 g, 65%). CAS Registry Number 81654-64-0. R_f = 0.4 (30% ethyl acetate/n-hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.94 (br, 1H), 7.91 (d, *J* = 8.0 Hz, 1H), 7.76 (d, *J* = 8.5 Hz, 2H), 7.64 (d, *J* = 8.5 Hz, 2H), 7.50 (dd, *J* = 7.5, 1.6 Hz, 1H), 7.44 (td, *J* = 7.5, 1.0 Hz, 1H), 7.17 (td, *J* = 7.5, 1.6 Hz, 1H).^{13}C NMR (101 MHz, DMSO): δ (ppm) 168.6, 143.6, 142.9, 139.5, 133.8, 131.8, 128.7, 128.6, 120.1, 119.5, 106.0, 94.0.

*N-(4-cyanophenyl)-3-(trifluoromethyl)-benzamide (**47**)*

White solid (0.052 g, 72%). m.p.: 120 - 122 ℃. R_f = 0.5 (30% ethyl acetate/n-hexane). ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) 10.98 (br, 1H), 8.30 – 8.24 (m, 2H), 7.98 (d, *J* = 8.9 Hz, 2H), 7.95 (d, *J* = 7.8 Hz, 1H), 7.80 (d, *J* = 8.9 Hz, 2H), 7.76 (t, *J* = 7.8 Hz, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ (ppm) 165.2, 143.65, 135.75, 133.64, 132.53, 130.30, 129.73 (q, *J* = 32.1 Hz), 129.04 (q, *J* = 3.7 Hz), 124.94 (q, *J* = 3.9 Hz), 124.4 (q, J = 273.8 Hz), 120.9, 119.5, 106.22. ^{19}F NMR (376 MHz, DMSO-d_6): δ (ppm) -61.2. IR (ν_{max}, cm^{-1}): 3366, 3335, 2929, 2851, 2231, 1686, 1594, 1525, 1418, 1326, 1249, 1165, 1111, 1065, 812, 682, 544. HRMS (ESI+): *m/z*, calcd for $C_{15}H_9F_3N_2ONa$ $[M+Na]^+$ 313.0565, found 315.0565.

*N-(4-cyanophenyl)-benzenebutanamide (**49**)*

White solid (0.052g, 79%). m.p.: 80 – 82 ℃. R_f = 0.5 (30% ethyl acetate/n-hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.79 (s, 1H), 7.66 (d, *J* = 9.0 Hz, 2H), 7.56 (d, *J* = 9.0 Hz, 2H), 7.28 (t, *J* = 7.5 Hz, 2H), 7.22 – 7.14 (m, 3H), 2.70 (t, *J* = 7.5 Hz, 2H), 2.38 (t, *J* = 7.5 Hz, 2H), 2.06 (quint, *J* = 7.5 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) 171.5, 142.1, 140.9, 133.1, 128.4, 126.0, 119.4, 118.8, 106.6, 36.6, 34.9, 26.5. IR (ν_{max}, cm^{-1}): 3482, 3359, 3243, 3028, 2928, 2220, 1596, 1511, 1412, 1303, 1173, 834, 695, 542. HRMS (ESI+): *m/z*, calcd for $C_{17}H_{17}N_2O$ $[M+H]^+$ 264.1263, found 264.1279.

*N-(4-methoxyphenyl)-benzenebutanamide (**50**)*

Pale yellow solid (0.048 g, 72%). m.p.: 98 - 100 ℃ . R_f = 0.5 (30% ethyl acetate/n-hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.42 – 7.34 (m, 3H), 7.27 (t, *J* = 7.5 Hz, 2H), 7.18 (t, *J* = 7.5 Hz, 3H), 6.82 (d, *J* = 8.0 Hz, 2H), 3.76 (s, 3H), 2.67 (t, *J* = 7.5 Hz, 2H), 2.30 (t, *J* = 7.5 Hz, 2H), 2.03 (quint, *J* = 7.5 Hz, 2H).^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) 170.9,

156.2, 141.3, 130.9, 128.4, 128.3, 125.9, 121.7, 114.0, 55.4, 36.5, 35.0, 26.9. IR (ν_{max}, cm^{-1}): 3280, 3027, 2936, 2859, 1643, 1520, 1230, 1031, 817, 694. HRMS (ESI+): *m/z*, calcd for $C_{17}H_{20}NO_2$ $[M+H]^+$ 270.1494, found 270.1474.

*2,2-dimethyl-N-(4-nitrophenyl)-propanamide (**51**)*

Pale yellow solid (0.045 g, 81%). CAS Registry Number 56619-95-5. R_f = 0.8 (30% ethyl acetate/n-hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.19 (d, *J* = 8.8 Hz, 2H), 7.84 (br, 1H), 7.76 (d, *J* = 8.8 Hz, 2H), 1.35 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) 177.1, 144.0, 143.2, 124.8, 119.2, 39.9, 27.3.

2-methyl-N-*(4-nitrophenyl)-(*E*)-(9CI)-2-butenamide (**52**)*

Orange solid (0.049 g, 89%). m.p.: 91 - 93 ℃. R_f = 0.6 (30% ethyl acetate/n-hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.19 (d, *J* = 9.2 Hz, 2H), 8.06 (br, 1H), 7.77 (d, *J* = 9.2 Hz, 2H), 6.59 (qq, *J* = 6.9, 1.2 Hz, 1H), 1.95 – 1.94 (m, 3H), 1.83 (dq, *J* = 6.9, 1.2 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) 167.8, 144.2, 143.1, 133.0, 132.3, 124.9, 119.2, 14.1, 12.3. IR (ν_{max}, cm^{-1}): 3387, 2921, 1689, 1590, 1536, 1482, 1314, 1245, 1108, 847, 740. HRMS (ESI+): *m/z*, calcd for $C_{11}H_{13}N_2O_3$ $[M+H]^+$ 221.0926, found 221.0924.

*N-(4-methoxyphenyl)-α-methyl-4-(2-methylpropyl)-benzeneacetamide (**53**)*

White solid (0.082 g, >95%). m.p.: 101 - 103 ℃. R_f = 0.6 (20% ethyl acetate/n-hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.31 (d, *J* = 9.0 Hz, 2H), 7.25 (d, *J* = 8.0 Hz, 2H), 7.14 (d, *J* = 8.0 Hz, 3H), 6.79 (d, *J* = 9.0 Hz, 2H), 3.75 (s, 3H), 3.67 (q, *J* = 7.2 Hz, 1H), 2.46 (d, *J* = 7.2 Hz, 1H), 1.92 – 1.79 (m, 1H), 1.57 (d, *J* = 7.2 Hz, 3H), 0.90 (d, *J* = 6.6 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) 172.4, 156.2, 140.9, 138.1, 131.0, 129.7, 127.3, 121.5,

113.9, 55.3, 47.4, 44.9, 30.1, 22.3, 18.5. IR (ν_{max}, cm^{-1}): 3306, 2950, 1661, 1514, 1399, 1244, 819. HRMS (ESI+): *m/z*, calcd for $C_{20}H_{26}NO_2$ $[M+H]^+$ 312.1964, found 312.1960; calcd for $C_{20}H_{25}NO_2Na$ $[M+Na]^+$ 334.1783, found 334.1779.

*N-(4-nitrophenyl)-(9Z)- 9-octadecenamide (**54**)*

Colorless oil (0.048 g, 48%). R_f = 0.7 (30% ethyl acetate/n-hexane). ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.19 (d, *J* = 9.0 Hz, 2H), 7.96 (s, 1H), 7.74 (d, *J* = 9.0 Hz, 2H), 5.39 – 5.28 (m, 2H), 2.42 (t, *J* = 7.5 Hz, 2H), 2.07 – 1.97 (m, 4H), 1.77 – 1.69 (m, 2H), 1.35 – 1.22 (m, 20H), 0.87 (t, *J* = 6.4 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) 172.0, 144.0, 143.2, 130.0, 129.5, 125.0, 118.9, 37.7, 31.8, 29.7, 29.6, 29.4, 29.2, 29.2, 29.1, 29.0, 27.1, 27.0, 25.2, 22.6, 14.0. IR (ν_{max}, cm^{-1}): 3341, 2917, 2855, 1693, 1551, 1505, 1331, 1104, 846. HRMS (ESI+): *m/z*, calcd for $C_{24}H_{39}N_2O_3$ $[M+H]^+$ 403.2961, found 403.2960.

*N-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-5-octadecanamide (**55**)*

Yellow solid (0.142 g, 50%). $[\alpha]_D^{20}$ = + 2.2 (c 1.000, CH_2Cl_2). m.p.: 90 - 92 ℃. R_f = 0.5 (30% ethyl acetate/n-hexane). ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 6.38 (d, *J* = 9.7 Hz, 1H), 5.32 (t, *J* = 9.7 Hz, 1H), 5.28 (t, *J* = 9.7 Hz, 1H), 5.06 (t, *J* = 9.7 Hz, 1H), 4.93 (t, *J* = 9.7 Hz, 1H), 4.32 (dd, *J* = 12.5, 4.2 Hz, 1H), 4.08 (dd, *J* = 12.5, 2.1 Hz, 1H), 3.84 (ddd, *J* = 9.7, 4.2, 2.1 Hz, 1H), 2.25 – 2.13 (m, 2H), 2.08 (s, 3H), 2.04 (s, 3H), 2.03 (s, 3H), 2.02 (s, 3H), 1.70 – 1.52 (m, 2H), 1.33 – 1.18 (m, 28H), 0.88 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 173.5, 170.7, 170.4, 169.7, 169.4, 77.9, 73.3, 72.6, 70.5, 68.0, 61.5, 36.4, 31.7, 29.5, 29.5, 29.5, 29.4, 29.3, 29.2, 29.1, 28.9, 25.0, 22.5, 20.5, 20.47, 20.41,

20.40, 13.9. IR (ν_{max}, cm^{-1}): 3307, 2915, 2849, 1747, 1673, 1535, 1369, 1221, 1038. HRMS (ESI+): *m/z*, calcld for $C_{32}H_{56}NO_{10}$ $[M+H]^+$ 614.3918, found 614.3904.

*N-(1-Methyl-5-deoxy-2,3-O-isopropylidene-β-D-ribofuranoside)-5-[(1S)-2-(ethylamino)-2-oxo-1-(phenylmethyl)ethyl]-1,1-dimethylethyl ester (9CI) carbamic acid (**56**)*

White solid (0.070 g, 65%). $[\alpha]_D^{20}$ = - 17.60 (c 1.000, CH_2Cl_2). m.p.: 152 - 154 ℃. R_f = 0.6 (30% ethyl acetate/n-hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.34 – 7.17 (m, 5H), 6.79 (br, 1H), 5.10 – 4.99 (m, 1H), 4.89 (s, 1H), 4.39 – 4.23 (m, 3H), 3.50 (ddd, *J* = 14.0, 6.9, 5.6 Hz, 1H), 3.29 (s, 3H), 3.28 – 3.18 (m, *J* = 14.0 Hz, 1H), 3.14 – 3.00 (m, *J* = 6.6 Hz, 2H), 1.44 (s, 3H), 1.40 (s, 9H), 1.27 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) 171.3, 155.1, 136.7, 129.2, 128.5, 126.8, 112.2, 109.7, 85.7, 85.3, 81.8, 80.0, 56.0, 55.10, 42.00, 38.4, 28.1, 26.3, 24.9 IR (ν_{max}, cm^{-1}): 3348, 3281, 2981, 2934, 1710, 1636, 1528, 1247, 1172, 1080, 870, 701. HRMS (ESI+): *m/z*, calcd for $C_{23}H_{34}N_2O_7Na$ $[M+H]^+$ 473.2259, found 473.2264.

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Supporting Information:

Copies of ^{1}H, ^{13}C, ^{19}F, ^{31}P NMR spectra for all compounds.

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Highlights

- one-pot procedure for the synthesis of a broad range of amides, enabled by the reaction of selenocarboxylates with organic azides.
- Over 45 amides were prepared in up to >95% yield using alkyl, aryl, and heterocyclic derivatives and displaying broad functional group tolerance at both reaction partners.
- Selenocarboxylates were easily obtained in situ, avoiding handling and isolating any intermediate, rendering to the selenocarboxylate the status of a traceless reagent

Declaration of interests

☒ 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.

☐The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: