Deaminative Chlorination of Aminoheterocycles

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Abstract

Selective modification of heteroatom-containing aromatic structures is in high demand as it permits rapid evaluation of molecular complexity in advanced intermediates. Inspired by the remarkable selectivity of deaminases in Nature, herein we present a simple methodology that enables the NH₂ groups in aminoheterocycles to be conceived as masked modification handles; with the aid of a simple pyrylium reagent and a cheap chloride source, C(sp²)–NH₂ can be converted into C(sp²)–Cl bonds. The method is characterized by its remarkable substrate scope and wide functional group tolerance, allowing the modification of >20 different classes of heteroaromatic motifs (5- and 6-membered heterocycles), bearing numerous sensitive motifs. The facile conversion of NH₂ into Cl in a late-stage fashion enables practitioners to apply Sandmeyer- and Vilsmeier-type transforms without the burden of explosive and unsafe diazonium salts, stoichiometric transition metals, or highly oxidizing and unselective chlorinating agents.

Main text

Installation and removal of chemical functionalities in complex molecular settings with a high degree of precision still remains a challenging and highly coveted milestone for organic chemists, as it would permit facile decoration of any molecular entity at will.^{1,2} Nature is a clear example of this strategy and has mastered an intricate system of enzymatic biochemical processes to enable the selective modification of specific groups in large chemical systems. In this context, one of the remarkable examples is the conversion of cytidine to uridine via a deaminative process: aided by a Zn ion in the active site, such deaminases replace the NH₂ by a molecule of H₂O (Fig. 1A).^{3,4} From the chemical point of view, the

cleavage of a C(sp²)-N bond is energetically costly (BDE 102.6 ± 1.0 kcal•mol⁻¹) and amido groups are extremely poor leaving groups (NH₂⁻), with virtually no examples in the synthetic world.⁵ Yet, deaminases overcome these hurdles and enable the process to occur in remarkable efficiency at room temperature. Inspired by this selective deamination process, we hypothesized that a synthetic tool that enables the precise removal of C-NH₂ groups in various complex heterocyclic frameworks beyond nucleobases would be highly desirable. Aminoheterocycles are at the core of many biologically relevant compounds such as fungicides, herbicides, pharmaceutical compounds, natural products, vitamins, DNA, RNA, etc. (Fig. 1B).^{6,7,8} Hence, the conversion of the NH₂ group into a modular and versatile leaving group would be highly desirable. In this sense, we turned our attention to heteroaryl chlorides since they have occupied a preferential place in synthetic routes due to the myriad of robust methods available for their chemical modification.⁹

The classical Sandmeyer reaction remains the “textbook” reaction when the conversion of C(sp²)-NH₂ into C(sp²)-Cl is desired. Yet, it still relies on the diazonization of the amine followed by chlorination with CuCl (Fig. 1C, left).^{10,11} Such protocol has been useful in simple anilines and certain aminoheterocycles. However, the strongly oxidizing and acidic conditions to reveal the diazonium salt present a significant incompatibility when structures contain more sensitive functionalities. More importantly, the formation of nitrogen-rich heteroaryl diazonium salts result in highly energetic compounds, which raise severe concerns about their safe handling.^{12,13} Recently, awareness has also been raised by the use of aqueous nitrite solutions, which can lead to significant levels of carcinogenic *N*-nitrosamines.¹⁴ Altogether, these setbacks prohibited the translation of such strategy in complex settings and the perception of C(sp²)-NH₂ as late-stage functionalization handles was abandoned. With the aim of providing a robust protocol for C-Cl bond formation, we drew inspiration from the venerable Vilsmeier reaction (Fig. 1C, right). This powerful transformation has found notorious applications in organic synthesis; yet, the use of highly reactive and unselective POCl₃ relegates the Vilsmeier disconnection to the early stages of the synthesis, making it incompatible with late-stage modifications.^{15,16}

Herein, we present a method that merges the availability of starting materials offered by the Sandmeyer approach with the usefulness of the heteroaryl halides obtained when a Vilsmeier disconnection is desired. The method smoothly converts NH_2 groups from heteroaromatic compounds into Vilsmeier products by means of a simple and commercially available pyrylium reagent ($\text{Pyr}-\text{BF}_4$, **1**)¹⁷ and various chloride sources (Fig. 1D). The method is demonstrated to be applicable to >20 distinct types of heterocyclic motifs, including both 5- and 6-membered rings containing N, O and S. Importantly, the protocol is characterized by the broad functional group tolerance, thus permitting the formation of electrophilic $\text{C}(\text{sp}^2)\text{--Cl}$ bonds onto complex pharmaceuticals, agrochemicals and natural products in a late-stage fashion. To contextualize the functional group tolerance of the reported methodology, we benchmarked our system with the state-of-the-art Sandmeyer conditions, demonstrating that our protocol is truly enabling in providing the heteroaryl chloride.

Fig. 1. (A) Deaminases catalyze the conversion of cytidine to uridine by means of a mild and highly selective exchange of NH₂ for an OH. Enzyme picture from PDB ID: 6K63;¹⁸ (B) Compounds bearing the C(sp²)-NH₂ group are ubiquitous in Nature and are part of many biological compounds; (C) The Sandmeyer and Vilsmeier reactions: inspiration and limitations; (D) Chemoselective deaminative chlorination of aminoheterocycles using Pyry-BF₄ **1** is applicable to molecular systems bearing various heterocyclic frameworks.

Results

Our investigations started with an interesting behavior observed for the Zincke salt in solution. When 1-chloro-2,4-dinitrobenzene (**2**) is refluxed in the presence of pyridine (**3**), the Zincke salt precipitates in

quantitative yields (**4**) and is easily separated and purified by filtration (Fig. 2A).¹⁹ Yet, when **4** is dissolved in CH₃CN, partial formation of **2** and **3** was observed in a 1:1 ratio, suggesting a possible reversibility of the process. Increasing the temperature and diluting the solution led to almost quantitative recovery of the 1-chloro-2,4-dinitrobenzene (**2**) as well as pyridine (**3**). Despite the wealth of literature for the reaction of nucleophiles with the Zincke salt, the use of the chloride counter-ion as nucleophile to recover the parent aryl chloride **2** remained largely underexplored. A scrutiny of S_NAr reactions revealed that the role of chlorides is vastly relegated to their abilities as leaving group, with only a handful of examples where it is used as nucleophile.^{20,21} Inspired by these observations, we speculated that a similar behavior could be translated to other arylpyridinium chloride systems, namely the product of oxidative dimerization of pyridine (**6**).²² Indeed, when compound **6** is heated in MeCN at 80 °C under diluted conditions (0.1 M), almost complete conversion to 4-chloropyridine (**7**) was observed with concomitant formation of pyridinium hydrochloride (**8**). This result immediately suggested that this phenomenon is not restricted to activated aryl moieties but also extensive to heteroaromatic substrates. Our group has recently reported on the synthesis and properties of a simple pyrylium reagent (Pry-BF₄, **1**), and its capacity to engage certain azines in Zincke-type reactivity,^{23,24,25} although narrow in scope, the Pry-BF₄ displayed high chemoselectivity for amino groups. Then, we envisaged that a merger of the reactivity observed in Figure 2A in combination with the selectivity offered by Pry-BF₄ would provide an opportunity for a broad and chemoselective deaminative chlorination strategy. To test this hypothesis, we subjected oxazole **9** to pyridinium formation with Pry-BF₄ (**1**), which smoothly afforded pyridinium tetrafluoroborate **10** (Fig. 2B). At this point, various chloride sources were interrogated in order to effect an anion exchange and trigger the conversion of the C–N to a C–Cl bond (Fig. 2B, inset Table). When using an etherated HCl solution, complete chlorination was obtained at room temperature (Fig. 2B, entry 1, inset Table). The use of non-Brønsted acidic counterion such as MgCl₂ boded well and smoothly delivered **11** at 80 °C (entry 2, inset Table). Noteworthy, 2.0 equivalents of trimethylsilyl chloride (TMSCl) quantitatively furnished the desired oxazolyl chloride **11** under milder conditions (entry 3, inset Table). Anticipating potential issues when translating this methodology to complex molecules bearing acid sensitive functionalities, we tested a

chloride source bearing a non-coordinating cation. The use of 4.0 equivalents of $n\text{Bu}_4\text{NCl}$ displaced the pyridine and forged **11** in excellent yields (entry 4, inset Table). With the aim of providing facile and practical setups, a single-flask operation was established which enables the formation of the pyridinium salt and the subsequent *in situ* chlorination in high yields (Fig. 2C). This user-friendly protocol can be conducted under regular atmosphere with no special precautions required.

Fig. 2. (A) Unexpected findings on the reversible reactivity of the 1-arylpyridinium chlorides; (B) Development and implementation of a two-step deaminative chlorination of aminoheterocycles using various chloride sources and Pyry-BF₄; (C) Conditions for an open-flask one-pot deaminative chlorination.

Having established a protocol using various chloride sources, we turned our attention to explore the scope of the aminoheterocycle (Fig. 3). First of all, we engaged a panel of 4- and 2-aminopyridines (**7**, **12-20**). Tuning the temperature turned out to be crucial to achieve satisfactory yields and accommodate functionalities such as halides (**12**, **14**), aromatic rings (**16**, **17**), ester (**15**), morpholine (**18**), nitro (**19**) or cyano (**20**). Diazines, including pyrimidine (**21**, **22**) and pyridazine (**23**), were also smoothly converted to their chlorinated analogs in good yields. When our protocol was applied to herbicide chloridazone, high

yields of the dichlorinated pyridazone **24** were obtained. Even the tetralkylated and crowded acrisorcin could be converted in 9-chloroacridine (**25**) albeit in 36%. Importantly, fused polycyclic substrates present at the core of biologically relevant molecules such as adenine or remdesivir, were smoothly converted to their chlorinated analog in very good yields (**26** and **27**). Contrary to most strategies based on the Vilsmeier approach, our protocol boded well with 5-membered heteroaromatic amines. For example, fused triazolopyridine, a motif present in certain Na current inhibitors, smoothly afforded compound **28** in excellent yields.²⁶ Benzo-fused 5-membered rings bearing other heteroatoms, such as benzothiazoles and isobenzothiazoles, which include drugs such as riluzole, boded well with the protocol obtaining excellent yields of the chlorinated analogs (**29-31**). Simple 5-membered rings bearing sensitive functionalities such as ester or oximine were also well tolerated as exemplified by **11** and **32**. To further study the functional group tolerance, a variety of oxazole-based compounds bearing pendant functionalities were scrutinized. The presence of halogens (Cl, I, Br, F), pyridine, cinnamyl, cyano, methylsulfone or even aldehyde posed no difficulties for chlorination (**33-40**). Heterocycles bearing 3 heteroatoms prone to ring-opening such as thiadiazole and oxadiazole (**41**, **42**) were smoothly chlorinated in high yields. The presence of a free secondary alcohol in **43** required the use tBu_4NCl to avoid side-reactions through Mg-induced dehydration. Based on the remarkable functional group tolerance observed, we envisaged our protocol to be applicable to more complex and densely functionalized bioactive molecules. Gratifyingly, when the deaminative protocol was applied to hepatitis B pro-drug adefovir diethyl, analog **44** was obtained in 57% yield. The anti-inflammatory amlexanox was successfully chlorinated at the 2-position of the pyridine motif (**45**). Thiazole derivative from amoxapine and paroxetine behaved well and were smoothly converted to the corresponding chloride in high yields (**46**, **47**). Remarkably, chlorination of the pyrimidine moiety in BI665915 was obtained in 37% yield (**48**), tolerating the presence of the rather weak N–O bond of oxadiazole, among others. Insecticide fipronil bearing a cyano and a trifluoromethylsulfoxide embedded in a pyrazolyl ring posed no difficulties for chlorination (**49**). Despite the presence of a Michael acceptor and a piperidinyl moiety, chlorination of the pyrazolopyrimidine core of anti-cancer ibrutinib smoothly occurred in 87% yield (**50**). Finally, another anti-cancer such as

dabrafenib was also subjected to chlorination in a similar manner, obtaining 39% of **51**. To fully benchmark the usefulness of the protocol developed herein, some of the most critical examples were also tested under state-of-the-art Sandmeyer conditions. Whereas **24**, **30** and **32** could be obtained after Sandmeyer, the yields were comparably lower than when our protocol was applied. Although the Sandmeyer conditions were not optimized for each substrate and a general protocol was applied, no product was detected in any of the other 13 challenging substrates tested. Decomposition of the compounds leading to intractable mixtures was the general trend.

Fig. 3. Exemplification of the deaminative chlorination of aminoheterocycles. Unless otherwise stated, reactions were conducted in a one-step procedure as follows **[Pyry]**: aminoheterocycle (1 equiv.), **1** (1.5 equiv.), MgCl₂ (2.0–5.0 equiv.), CH₃CN (0.1 M), 50–120 °C, 16 h. **[Sandm]**: Sandmeyer conditions: aminoheterocycle (1 equiv.), NaONO (1.1 equiv.); HCl_{aq} 37% (0.2 M), 0 °C, 15 min; then, CuCl (1.3 equiv.), 25 °C, 3 h. [a] PMP = 4-methoxyphenyl; [b] two-steps procedure: pyridinium formation *then* chlorination; [c] CsCl (4 equiv.) instead of MgCl₂. [d] Me₄NCl (4 equiv.) instead of MgCl₂. [e] ⁿBu₄NCl (4 equiv.) instead of MgCl₂. n.d. = not detected.

Unlocking a late-stage deaminative chlorination strategy permits the incorporation of all the well-known reactions for aryl halides to be applied in a late-stage functionalization context (Fig. 4). For example, C(sp²)–C(sp²), C(sp²)–C(sp³) as well as C(sp²)–C(sp) cross-couplings can now be carried out in substrates where such reactivity was limited (Negishi **52**, Suzuki **53** and Sonogashira **54**). Nucleophilic aromatic substitution, one of the most robust and utilized reactions with aryl halides, is also within reach; aliphatic amines, both primary and secondary including duloxetine, can be incorporated in high yields through simple protocols (**55**, **56**). Secondary alcohols such as cholesterol can be easily decorated with a benzothiazole in good yield (**57**). Other nucleophiles, namely fluoride and azide, were also engaged and displaced the Cl atom leading to valuable products (**58**, **59**).

Fig. 4. Deaminative chlorination of drugs and heterocycles opens the door to late-stage functionalization of compounds at positions which were previously inaccessible.

Scalability of the protocol was demonstrated by the gram-scale reaction performed on **60** without erosion on the yield (**32**). The deaminative halogenation was also successfully extended to bromides. Both 5- and 6-membered rings afforded good yields of the desired aryl bromide **62** and **64**. Attempts to introduce fluorine atoms through a similar protocol using fluoride anion sources resulted in the isolation of the ring-opened compound, which was isolated as the hydrolyzed **65**.^{27,28} In the case of milder nucleophiles such as Cl or Br, the attack on the pyridinium might be reversible, and occur in both C2 and C4.²⁹ It is not until the *ipso* position is attacked that the process becomes irreversible and ultimately leads to the formation of pyridine and the aryl chloride.

Fig. 5. (A) Scalability of the process; (B) Deaminative bromination: Reaction conditions: aminoheterocycle (1 equiv.), **1** (1.5 equiv.) EtOH (1 mL) 50–80 °C, 16 h; then the solvent is removed and addition of Br source (4 equiv.), CD₃CN (1 mL), 50–80 °C, 16 h. (C) Ring-opening of the pyridinium intermediate using fluoride salts; (D) Tentative mechanism of the deaminative halogenation.

Conclusions

Inspired by natural deaminases, we herein report a synthetic tool that enables the conversion of C(sp²)–NH₂ groups into C(sp²)–Cl in high chemoselectivity under mild conditions. The use of the simple Pyry-BF₄ targets selectively the NH₂ attached to a heterocyclic motif and primes it for reactivity by converting it into a pyridinium intermediate, which further reacts with a chloride source. This protocol merges the potential of the venerable Vilsmeier reaction to decorate aromatic heterocycles, with the ubiquity of aminoheterocycles, resulting in a deaminative chlorination protocol that avoids the use of explosive intermediates or strongly oxidizing reagents. As a result, the high chemoselectivity permits the chlorination of >40 compounds containing a myriad of functional groups, embedded in >20 different aminoheterocycles including 5- and 6-membered rings. The method is easily scalable, without the need of air-extrusion and without problematic runaway exotherms. Deaminative bromination of the amino group has also been demonstrated with a similar efficiency. More importantly, this deaminative chlorination protocol was applicable to the late-stage chlorination of various drugs and agrochemicals, thus permitting

post-modification of complex structures beyond the realms of the Sandmeyer reaction. We believe this methodology provides practitioners with a new tool that will permit the scrutiny of new chemical space and ultimately accelerate the drug discovery process.

Data availability

The Supplementary Information contains all Experimental Procedures and analytical data (^1H , ^{19}F , ^{31}P , ^{13}C , ^{11}B NMR, HRMS and crystallographic data) for all new compounds. Crystallographic data for compound **43** (CCDC-2070324) can be downloaded free of charge from the Cambridge Crystallographic Data Center www.ccdc.cam.ac.uk.

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Author Contributions

C. G. optimized the process, designed the approach, performed the experiments, analyzed the experimental data, prepared the Supplementary Information and helped in the manuscript preparation. T. F. contributed to expand the applicability of the protocol to certain 5-membered rings. A. G. –P. contributed at the initial stages of the project and found conditions in the chlorination and bromination. J. C. conceived the idea, directed the investigations and prepared the manuscript.

Competing interests

No conflict to declare

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I. General considerations

Unless otherwise stated, all manipulations were performed using standard experimental techniques without any specific precautions. Anhydrous solvents were distilled from appropriate drying agents and were transferred under Argon: CH₃CN (MS), Dioxane (MS), EtOH (Mg, I₂), DMSO (MS).

All reagents were used as supplied. Pyrylium tetrafluoroborate **1** (CAS: 80279-50-1) was purchased from SigmaAldrich® or prepared according to the reported procedure.¹ Chemical *B1665915* was supplied by Boehringer Ingelheim.

Flash chromatography: Merck silica gel 60 (40-63 μm). MS (EI): Finnigan MAT 8200 (70 eV), ESI-MS: ESQ 3000 (Bruker). Accurate mass determinations: Bruker APEX III FT-MS (7 T magnet) or MAT 95 (Finnigan).

NMR spectra were recorded using a Bruker Avance VIII-300, Bruker Avance III HD 400 MHz spectrometer, Bruker Avance III 500MHz spectrometer equipped with a 5mm BBFO probe. ¹H NMR spectra were referenced to the residual protons of the deuterated solvent used. ¹³C {¹H} NMR spectra were referenced internally to the D-coupled ¹³C resonances of the NMR solvent. ¹⁹F NMR spectra were referenced externally to the ¹⁹F resonances of CFCl₃. ³¹P NMR spectra were referenced externally to the ³¹P resonances of H₃PO₄. Chemical shifts (δ) are given in ppm, relative to deuterated solvent residual peak, and coupling constants (*J*) provided in Hz.

Melting points were recorded on a Büchi® melting point apparatus, Model B-540 (Büchi, Switzerland) and are uncorrected.

II. Synthesis of starting materials

Procedure for cross-coupling reactions with heteroaryl chlorides

To a flame-dried schlenk flask under Ar are added Pd(PPh₃)₄ (225 mg, 0.195 mmol), arylboronic acid (4.675 mmol), 4-amino-2-chloropyridine (500 mg, 3.889 mmol), Na₂CO₃ 2M in water (5 mL, 10 mmol) and toluene (6.3 mL). The mixture is stirred 16 hours at 100 °C. The reaction is allowed to cool down to room temperature and is partitioned between water and EtOAc. The aqueous layer is extracted with EtOAc (3 x 30 mL). The combined organic layers are dried over Na₂SO₄, concentrated to dryness and purified on silica gel to afford the desired products **SM1** and **SM2**.

Synthesis of 2-phenylpyridin-4-amine (SM1)

White solid, 55 %

¹H NMR (300 MHz, CDCl₃) δ 8.32 (d, *J* = 5.6 Hz, 1H), 7.91 (m, 2H), 7.44 (m, 2H), 7.39 (m, 1H), 6.96 (dd, *J* = 2.3, 0.6 Hz, 1H), 6.50 (dd, *J* = 5.6, 2.3 Hz, 1H), 4.21 (bs, 2H).

Characterization data matched with a previously reported example.¹

Synthesis of 2-(4-methoxyphenyl)pyridin-4-amine (SM2)

Yellow solid, 62 %

¹H NMR (300 MHz, DMSO-*d*₆) δ 8.04 (d, *J* = 5.5 Hz, 1H), 7.86 (d, *J* = 8.3 Hz, 2H), 6.99 (d, *J* = 8.3 Hz, 2H), 6.92 (d, *J* = 2.2 Hz, 1H), 6.39 (dd, *J* = 5.5, 2.2 Hz, 1H), 5.97 (bs, 2H), 3.79 (s, 3H).

Characterization data matched with a previously reported example.¹

Procedure for the SNAr of 2-chloropyridin-4-amine (SM3)

To a microwave reactor are added 2-chloropyridin-4-amine (500 mg, 3.89 mmol) and morpholine (1.22 mL, 14 mmol). The mixture is heated at 200 °C for 15 min. The reaction is allowed to cool down to room temperature and is evaporated to dryness. The residue is then dissolved in saturated K₂CO₃ (40 mL). The aqueous phase is extracted 3 times with CH₂Cl₂ (3 x 40 mL). The combined organic layers are dried over Na₂SO₄ and concentrated to dryness afford **SM3** as a slightly yellow solid (635 mg, 91 %).

¹H NMR (400 MHz, CDCl₃) δ 7.88 (d, *J* = 5.6 Hz, 1H), 6.03 (dd, *J* = 5.6, 1.9 Hz, 1H), 5.84 (d, *J* = 1.9 Hz, 1H), 4.01 (bs, 2H), 3.81–3.78 (m, 4H), 3.43–3.41 (m, 4H).

Characterization data matched with a previously reported example.¹

General procedure for the amidation of ethyl 2-aminooxazole-4-carboxylate

To a flame-dried schlenk flask under Ar are added K_3PO_4 (0.3 equiv.), ethyl 2-aminooxazole-4-carboxylate (1 equiv.), amino alcohol (1 equiv.) and *i*PrOH (1 M). The mixture is stirred at 70 °C for 16 hours. The reaction is allowed to cool down to room temperature and is partitioned between water and EtOAc. The aqueous layer is extracted with EtOAc. The combined organic layers are dried over Na_2SO_4 , concentrated to dryness and purified on silica gel (gradient CH_2Cl_2 :MeOH) to afford the desired products **SM6** and **SM7**.²

Synthesis of (*R*)-2-amino-*N*-(2-hydroxy-1-phenylethyl)oxazole-4-carboxamide (**SM4**)

Off white solid (mp: 169.1 °C)

16.0 mmol scale, 2.2 g, 56 %

¹H NMR (300 MHz, MeOD) δ 7.72 (s, 1H), 7.39–7.22 (m, 6H), 5.11 (t, J = 6.0 Hz, 1H), 3.82 (dd, J = 6.1, 2.1 Hz, 2H).

Note: The signals for –NH₂ and –OH are not detected due to rapid exchange with MeOD.

¹³C NMR (75 MHz, MeOD) δ 163.5, 163.2, 141.0, 136.3, 135.8, 129.5, 128.5, 127.9, 66.1, 56.6.

HRMS (ESI) calculated $[M+Na]^+$ 270.084910, measured 270.084710.

Synthesis of 2-amino-*N*-((1*R*,2*S*)-2-hydroxy-2,3-dihydro-1*H*-inden-1-yl)oxazole-4-carboxamide (**SM5**)

Beige solid (mp: 148.6 °C)

1.6 mmol scale, 191 mg, 46 %

¹H NMR (300 MHz, MeOD) δ 7.80 (s, 1H), 7.28–7.16 (m, 4H), 5.43 (d, J = 5.1 Hz, 1H), 4.60 (td, J = 5.1, 1.7 Hz, 1H), 3.18 (dd, J = 16.5, 5.1 Hz, 1H), 2.95 (dd, J = 16.5, 1.6 Hz, 1H).

Note: The signals for –NH₂, –NH, and –OH are not detected due to rapid exchange with MeOD.

¹³C NMR (75 MHz, MeOD) δ 163.9, 163.1, 142.2, 141.7, 136.3, 135.8, 129.0, 127.9, 126.2, 125.3, 74.0, 58.2, 40.8.

HRMS (ESI) calculated [M+H]⁺ 260.102966, measured 260.103220.

General procedure for the esterification of 2-amino-N-(2-hydroxyethyl)oxazole-4-carboxamide

To a round bottom flask are added the starting material (50.0 mg, 0.2 mmol), carboxylic acid (0.2 mmol), *N*-ethyl-*N'*-(dimethylaminopropyl)-carbodiimide hydrochloride (38.8 mg, 0.2 mmol), 4-(dimethylamino)-pyridine (29.6 mg, 0.24 mmol) and acetonitrile (1.5 mL). The reaction is stirred at rt for 16 hours. The reaction is partitioned between water and EtOAc. The aqueous layer is extracted with EtOAc (3 x 10 mL). The combined organic layers are dried over Na₂CO₃, concentrated to dryness and purified on silica gel (gradient CH₂Cl₂:MeOH) to afford the desired products **SM6** to **SM13**.

Synthesis of (*R*)-2-(2-aminooxazole-4-carboxamido)-2-phenylethyl (*E*)-3-(3-chlorophenyl)acrylate (**SM6**)

White solid (mp: 152.5 °C)

85 %

¹H NMR (300 MHz, CDCl₃) δ 7.70 (s, 1H), 7.58 (d, J = 16.0 Hz, 1H), 7.47 (m, 1H), 7.41–7.26 (m, 9H), 6.40 (d, J = 16.0 Hz, 1H), 5.51 (td, J = 7.6, 4.8 Hz, 1H), 4.84 (s, 2H), 4.59 (dd, J = 11.5, 7.1 Hz, 1H), 4.50 (dd, J = 11.5, 4.8 Hz, 1H).

¹³C NMR (75 MHz, CDCl₃) δ 166.6, 160.9, 159.5, 144.1, 138.3, 136.2, 135.5, 135.4, 135.1, 130.4, 130.3, 129.0, 128.2, 128.0, 126.9, 126.5, 119.0, 66.5, 52.1.

HRMS (ESI) calculated [M+Na]⁺ 434.087803, measured 434.087680.

Synthesis of (*R*)-2-(2-aminooxazole-4-carboxamido)-2-phenylethyl 2-bromobenzoate (SM7)

White solid (mp: 120.4 °C)

77 %

¹H NMR (300 MHz, CDCl₃) δ 7.72–7.67 (m, 2H), 7.62 (m, 1H), 7.48 (d, *J* = 8.7 Hz, 1H), 7.43–7.26 (m, 7H), 5.59 (ddd, *J* = 8.7, 6.7, 4.6 Hz, 1H), 4.87 (s, 2H), 4.72 (dd, *J* = 11.4, 6.7 Hz, 1H), 4.62 (dd, *J* = 11.5, 4.7 Hz, 1H).

¹³C NMR (75 MHz, CDCl₃) δ 166.2, 161.0, 159.9, 138.0, 135.3, 135.1, 134.3, 132.9, 131.7, 131.6, 128.9, 128.1, 127.2, 126.8, 121.7, 67.4, 51.8.

HRMS (ESI) calculated [M+Na]⁺ 452.021650, measured 452.021330.

Synthesis of (*R*)-2-(2-aminooxazole-4-carboxamido)-2-phenylethyl 3-cyanobenzoate (SM8)

White sticky solid (mp: 179.5 °C)

82 %

¹H NMR (300 MHz, DMSO-*d*₆) δ 8.43 (d, *J* = 9.0 Hz, 1H), 8.23 (t, *J* = 1.6 Hz, 1H), 8.14 (ddt, *J* = 14.8, 7.8, 1.4 Hz, 2H), 7.85 (s, 1H), 7.74 (t, *J* = 7.8 Hz, 1H), 7.50 (m, 2H), 7.37 (m, 2H), 7.30 (m, 1H), 6.83 (bs, 2H), 5.49 (td, *J* = 8.5, 5.4 Hz, 1H), 4.63 (m, 2H).

¹³C NMR (75 MHz, DMSO-*d*₆) δ 163.9, 160.9, 160.7, 139.1, 136.7, 135.2, 134.2, 133.4, 132.6, 130.7, 130.2, 128.4, 127.6, 127.1, 117.8, 112.1, 67.0, 51.0.

HRMS (ESI) calculated [M+Na]⁺ 399.106374, measured 399.106750.

Synthesis of (*R*)-2-(2-aminooxazole-4-carboxamido)-2-phenylethyl 2-iodobenzoate (SM9)

White solid (mp: 136.8 °C)

80 %

¹H NMR (300 MHz, MeOD) δ 7.96 (dd, J = 8.0, 1.1 Hz, 1H), 7.73 (s, 1H), 7.66 (dd, J = 7.8, 1.7 Hz, 1H), 7.47 (m, 2H), 7.42 – 7.35 (m, 3H), 7.32 (m, 1H), 7.17 (td, J = 7.7, 1.7 Hz, 1H), 5.55 (t, J = 6.5 Hz, 1H), 4.63 (d, J = 6.6 Hz, 2H).

Note: The signals for –NH₂ and –NH are not detected due to rapid exchange with MeOD.

¹³C NMR (75 MHz, MeOD) δ 168.0, 163.4, 163.2, 142.3, 139.6, 136.8, 136.2, 136.1, 133.9, 131.9, 129.8, 129.1, 129.1, 128.1, 94.3, 68.3, 53.4.

HRMS (ESI) calculated [M+Na]⁺ 500.007772, measured 500.007860.

Synthesis of (*R*)-2-(2-aminooxazole-4-carboxamido)-2-phenylethyl 4-formylbenzoate (SM10)

White solid (mp: 96.1 °C)

60 %

¹H NMR (300 MHz, DMSO-*d*₆) δ 10.10 (s, 1H), 8.41 (d, J = 9.0 Hz, 1H), 8.08 (d, J = 8.3 Hz, 2H), 8.03 (d, J = 8.5 Hz, 2H), 7.86 (s, 1H), 7.50 (m, 2H), 7.38 (m, 2H), 7.30 (m, 1H), 6.82 (bs, 2H), 5.48 (td, J = 8.6, 5.3 Hz, 1H), 4.70–4.57 (m, 2H).

¹³C NMR (75 MHz, DMSO-*d*₆) δ 192.8, 164.8, 160.9, 160.6, 139.2, 139.2, 135.1, 134.2, 134.2, 129.7, 129.6, 128.4, 127.5, 127.0, 66.9, 51.0.

HRMS (ESI) calculated [M+Na]⁺ 402.106040, measured 402.106620.

Synthesis of (*R*)-2-(2-aminooxazole-4-carboxamido)-2-phenylethyl 4-fluorobenzoate (SM11)

White solid (mp: 159.4 °C)

86 %

¹H NMR (300 MHz, MeOD) δ 8.00 (m, 2H), 7.73 (s, 1H), 7.47 (m, 2H), 7.37 (m, 2H), 7.31 (m, 1H), 7.15 (m, 2H), 5.54 (dd, *J* = 7.8, 5.4 Hz, 1H), 4.61 (m, 2H).

Note: The signals for –NH₂ and –NH are not detected due to rapid exchange with MeOD.

¹³C NMR (75 MHz, MeOD) δ 168.9, 165.6, 165.1 (d, ¹*J*(C,F) = 245 Hz), 163.2, 139.6, 136.1, 136.1, 133.4 (d, ³*J*(C,F) = 10 Hz), 129.8, 129.0, 128.0, 127.5 (d, ⁴*J*(C,F) = 3 Hz), 116.5 (d, ²*J*(C,F) = 22 Hz), 67.9, 53.5.

¹⁹F NMR (282 MHz, CDCl₃) δ -105.29 (s, 3F).

HRMS (ESI) calculated [M+Na]⁺ 392.101704, measured 392.102070.

Synthesis of (*R*)-2-(2-aminooxazole-4-carboxamido)-2-phenylethyl nicotinate (SM12)

Beige solid (mp: 100.6 °C)

68 %

¹H NMR (300 MHz, CDCl₃) δ 9.19 (d, *J* = 1.8 Hz, 1H), 8.76 (dd, *J* = 5.0, 1.7 Hz, 1H), 8.27 (m, 1H), 7.70 (m, 1H), 7.44–7.26 (m, 7H), 5.60 (m, 1H), 4.74 – 4.67 (m, 4H).

¹³C NMR (75 MHz, CDCl₃) δ 165.22 161.1, 159.9, 153.5, 151.0, 137.9, 137.3, 135.4, 135.1, 129.0, 128.3, 126.9, 125.8, 123.5, 67.2, 51.8.

HRMS (ESI) calculated [M+Na]⁺ 375.106374, measured 375.106510.

Synthesis of (*R*)-2-(2-aminooxazole-4-carboxamido)-2-phenylethyl 2-(4-(methylsulfonyl)phenyl)acetate (**SM13**)

White solid (mp: 186.0 °C)

64 %

¹H NMR (300 MHz, DMSO-*d*₆) δ 8.22 (d, *J* = 9.0 Hz, 1H), 7.86 (s, 1H), 7.81 (d, *J* = 8.1 Hz, 2H), 7.47 (d, *J* = 8.1 Hz, 2H), 7.39–7.25 (m, 6H), 6.84 (s, 2H), 5.28 (td, *J* = 8.5, 5.3 Hz, 1H), 4.45–4.32 (m, 2H), 3.81 (s, 2H), 3.18 (s, 3H).

¹³C NMR (75 MHz, DMSO-*d*₆) δ 170.3, 161.0, 160.5, 140.1, 139.3, 139.2, 135.2, 134.3, 130.4, 128.4, 127.5, 127.0, 126.9, 66.2, 51.0, 43.5, 39.9.

HRMS (ESI) calculated [M+Na]⁺ 466.104328, measured 466.103980.

Procedure for the methylation of *Amlexanox* (**SM14**)

To a 50 mL schlenk flask under normal atmosphere is added *Amlexanox* (201 mg, 0.67 mmol) in EtOAc and MeOH (10 and 4 mL respectively). The mixture is stirred at rt and (trimethylsilyl)-diazomethane (2M in Et₂O, 0.5 mL, 1 mmol) is added by syringe. The mixture is stirred 1 h at rt. The suspension is then filtered and washed with EtOH and Et₂O to afford **SM14** as a white solid (135 mg, 64 %).

¹H NMR (300 MHz, DMSO-*d*₆) δ 8.82 (s, 1H), 8.34 (bs, 1H), 8.06 (bs, 1H), 7.93 (d, *J* = 2.3 Hz, 1H), 7.74 (dd, *J* = 8.6, 2.4 Hz, 1H), 7.53 (d, *J* = 8.6 Hz, 1H), 3.89 (s, 3H), 3.06 (hept, *J* = 6.9 Hz, 1H), 1.26 (d, *J* = 6.9 Hz, 6H).

Characterization data matched with a previously reported example.³

Procedure for the amidation of 2-(2-aminothiazol-4-yl)acetic acid with *Amoxapine* (SM15)

To a round bottom flask are added 2-(2-aminothiazol-4-yl)acetic acid (69.6 mg, 0.44 mmol), *Amoxapine* (138.0 mg, 0.44 mmol), *N*-ethyl-*N'*-(dimethylaminopropyl)-carbodiimide hydrochloride (101.2 mg, 0.53 mmol), 4-(dimethylamino)-pyridine (80.6 mg, 0.66 mmol) and acetonitrile (2 mL). The reaction is stirred at rt for 16 hours. The reaction is partitioned between water and EtOAc. The aqueous layer is extracted with EtOAc (3 x 10 mL). The combined organic layers are dried over Na_2CO_3 , concentrated to dryness and purified on silica gel (gradient CH_2Cl_2 :MeOH) to afford the desired product **SM15** as a white solid (200 mg, quant.).

^1H NMR (300 MHz, CDCl_3) δ 7.40 (dd, J = 8.6, 2.6 Hz, 1H), 7.30 (d, J = 2.6 Hz, 1H), 7.18 (d, J = 8.7 Hz, 1H), 7.15–7.05 (m, 3H), 7.00 (m, 1H), 6.30 (s, 1H), 5.20 (bs, 2H), 3.83–3.60 (m, 6H), 3.55–3.41 (m, 4H).

^{13}C NMR (75 MHz, CDCl_3) δ 168.7, 167.9, 159.5, 158.8, 151.9, 145.6, 139.9, 132.9, 130.6, 129.0, 127.2, 126.0, 124.9, 124.8, 123.0, 120.3, 104.9, 46.0, 41.7, 37.5.

HRMS (ESI) calculated $[\text{M}+\text{H}]^+$ 454.109899, measured 454.110070.

Procedure for the amidation of 2-(2-aminothiazol-4-yl)acetic acid with *Paroxetine* (SM16)

To a round bottom flask are added 2-(2-aminothiazol-4-yl)acetic acid (52.7 mg, 0.33 mmol), *Paroxetine hydrochloride hemihydrate* (125.0 mg, 0.33 mmol), *N*-ethyl-*N'*-(dimethylaminopropyl)-carbodiimide hydrochloride (63.9 mg, 0.33 mmol), 4-(dimethylamino)-pyridine (89.6 mg, 0.73 mmol) and acetonitrile (2.5 mL). The reaction is stirred at rt for 16 hours. The reaction is partitioned between water and EtOAc. The aqueous layer is extracted with EtOAc (3 x 10 mL). The combined organic layers are dried over Na_2CO_3 , concentrated to dryness and purified on silica gel (gradient CH_2Cl_2 :MeOH) to afford the desired product **SM16** as a white solid (147 mg, 94%).

^1H NMR (300 MHz, CDCl_3) δ 7.08 (dd, J = 8.4, 5.3 Hz, 2H), 6.96 (m, 2H), 6.61 (dd, J = 8.4, 2.7 Hz, 1H), 6.34 (m, 1H), 6.26 (s, 1H), 6.12 (ddd, J = 8.3, 5.4, 2.5 Hz, 1H), 5.87 (d, J = 2.9 Hz, 2H), 5.68 (bs, 2H), 4.88 (m, 1H), 4.21 (m, 1H), 3.77–3.51 (m, 3H), 3.42 (td, J = 9.9, 6.1 Hz, 1H), 3.08 (m, 1H), 2.83–2.60 (m, 2H), 2.03–1.47 (m, 3H).

¹³C NMR (75 MHz, CDCl₃) δ 168.5–168.4 (m, 2C), 161.7 (dd, ¹J(C,F) = 245 Hz, *J* = 2 Hz), 154.3 (d, *J* = 18 Hz), 148.3 (d, *J* = 7 Hz), 145.8 (d, *J* = 2 Hz), 141.8 (d, *J* = 9 Hz), 138.8 (t, *J* = 3 Hz), 128.9 (t, ³J(C,F) = 7 Hz), 115.7 (dd, ²J(C,F) = 21 Hz, *J* = 5 Hz), 108.0 (d, *J* = 5 Hz), 105.7 (d, *J* = 9 Hz), 104.3 (d, *J* = 4 Hz), 101.2 (d, *J* = 6 Hz), 98.1 (d, *J* = 11 Hz), 68.7 (d, *J* = 1 Hz), 48.4 (d, *J* = 217 Hz), 45.5–41.9 (m, 3C), 37.8 (d, *J* = 6 Hz), 33.9 (d, *J* = 51 Hz).

¹⁹F NMR (282 MHz, CDCl₃) δ -115.94 (d, *J* = 27.0 Hz, 1F).

Note: The 2 conformations of piperidine led to a signal splitting in ¹H, ¹³C as well as ¹⁹F NMR.

HRMS (ESI) calculated [M+H]⁺470.154432, measured 470.154860.

Synthesis of methyl 2-(2-aminothiazol-4-yl)-2-(methoxyimino)acetate (**60**)

To a 18 mL screw-capped tube under normal atmosphere are added S-(benzo[d]thiazol-2-yl) 2-(2-aminothiazol-5-yl)-2-(methoxyimino)ethanethioate (144 mg, 0.41 mmol) and MeOH (5 mL). The resulting mixture is stirred 2 days at rt. The solvent was then removed. The crude solid is redissolved in EtOAc (5 mL) and extracted with 2M HCl (3 x 5 mL). The combined aqueous phases are neutralized with saturated NaHCO₃ and extracted with EtOAc (3 x 5 mL). The combined organic layers are dried over Na₂SO₄ and concentrated to dryness to afford **60** as a pale yellow solid (72 mg, 81 %).

¹H NMR (300 MHz, DMSO-*d*₆) δ 7.25 (bs, 2H), 6.93 (s, 1H), 3.87 (s, 3H), 3.80 (s, 3H).

Characterization data matched with a previously reported example.⁴

Procedure for the ethylation of adenine (**63**)

In a 250 mL round bottom flask are added adenine (2.26 g, 16.7 mmol), potassium carbonate (2.77 g, 20.0 mmol) and DMF (15 mL). The mixture is stirred at rt and iodoethane is added by syringe (1.61 mL, 20.0 mmol). The reaction is then heated at 50 °C overnight. The mixture is then cooled down to rt and diluted with water/brine (1:1, 50 mL). The aqueous layer is then extracted as many times as needed with EtOAc (20 mL each, extraction of the product monitored by TLC) and the combined organic layers are dried over Na₂SO₄. The crude is then concentrated to the minimum amount of solvent and Et₂O is then added. The precipitate is recovered

by filtration and washed with the minimum amount of Et₂O to afford **63** as a pale yellow solid (1.23 g, 45 %). The filtrate can be concentrated again to repeat this operation.

¹H NMR (300 MHz, DMSO-*d*₆) δ 8.14 (s, 1H), 8.13 (s, 1H), 7.14 (bs, 2H), 4.16 (q, *J* = 7.2 Hz, 2H), 1.40 (t, *J* = 7.3 Hz, 3H).

Characterization data matched with a previously reported example.⁵

III. Reactivity of pyridinium salts

Synthesis and reversibility experiments of the Zincke salt (**4**)

To a 18 mL screw-capped tube under normal atmosphere are added 1-chloro-2,4-dinitrobenzene **2** (413 mg, 2.04 mmol), pyridine **3** (177 mg, 2.24 mmol) and acetone (2 mL). The colorless mixture is gently stirred at 80 °C for 16 hours. After cooling down the reaction to rt, acetone (2 mL) is added to the mixture and the suspension is filtered and washed with acetone to afford **4** as a white solid (532 mg, 95 %).

¹H NMR (300 MHz, DMSO-*d*₆) δ 9.50 (d, *J* = 5.2 Hz, 2H), 9.12 (d, *J* = 2.5 Hz, 1H), 8.98 (m, 2H), 8.51 (d, *J* = 8.7 Hz, 1H), 8.46 (m, 2H).

Characterization data matched with a previously reported example.⁶

Reversibility experiments. All experiments are conducted in a 18 mL screw-capped tube under normal atmosphere filled with 0.5 mL of solvent. The corresponding starting materials **2+3** or **4** (either 0.05 or 0.5 mmol respectively for 0.1 or 1M) are dissolved at rt before heating the reaction 16 hours at 80 °C. Yields are determined by ¹H NMR with mesitylen (around 1 equiv., amount determined by mass) as internal standard.

Synthesis and reversibility experiments of 4-[pyridyl]pyridinium chloride hydrochloride (6)

To a 18 mL screw-capped tube under normal atmosphere are added pyridine **3** (500 mg, 6.32 mmol) and EtOAc (300 μL). The mixture is cooled down to 0 °C and SOCl₂ **5** (310 μL , 4.27 mmol) is added dropwise. The reaction is then allowed to reach rt and finally 80 °C for 4 hours. The reaction is cooled down to rt and EtOAc as well as remaining SOCl₂ as distilled off under high vacuum. The black crude oil is then dissolved in EtOH (2 mL) and vigorously stirred at 60 °C for 15 minutes. The mixture is cooled down to rt, filtered and washed with the minimum amount of EtOH and Et₂O (2x5 mL) to afford **6** product as a yellow powder (230 mg, 32 %).

¹H NMR (300 MHz, DMSO-*d*₆) δ 9.46 (d, *J* = 6.1 Hz, 2H), 9.01 (d, *J* = 5.9 Hz, 2H), 8.87 (t, *J* = 7.8 Hz, 1H), 8.38 (t, *J* = 7.1 Hz, 2H), 8.06 (m, 2H).

Characterization data matched with a previously reported example.^{7,8}

Reversibility experiment. In a 18 mL screw-capped tube under normal atmosphere are added starting material (11.5 mg, 0.05 mmol) and CD₃CN (0.5 mL). The reaction is stirred 16 hours at 80 °C. Yields are determined by ¹H NMR as the ratio between all components (everything was soluble).

Synthesis of ethoxycarbonyloxazole pyridinium tetrafluoroborate (**10**)

To a flame-dried schlenk under Ar are added **9** (78.1 mg, 0.5 mmol), pyridinium tetrafluoroborate **1** (84 mg, 0.5 mmol) in EtOH (5 mL). The flask is wrapped in aluminum foil and stirred 16 hours at 80 °C. The reaction is cooled down to rt and the precipitate is filtered and quickly washed with EtOAc (minimum amount to cover the solid) and Et₂O (2x5 mL) to afford **10** as an orange solid (143 mg, 93 %).

¹H NMR (300 MHz, DMSO-*d*₆) δ 9.72 (d, *J* = 6.2 Hz, 2H), 9.36 (s, 1H), 8.95 (t, *J* = 7.8 Hz, 1H), 8.36 (t, *J* = 7.1 Hz, 2H), 4.39 (q, *J* = 7.1 Hz, 2H), 1.34 (t, *J* = 7.1 Hz, 3H).

¹³C NMR (75 MHz, DMSO-*d*₆) δ 159.4, 151.8, 151.1, 146.9, 141.6, 133.8, 128.3, 61.5, 14.1.

¹⁹F NMR (282 MHz, DMSO-*d*₆) δ -148.40 (s, 4F).

HRMS (ESI) calculated [M-BF₄]⁺ 219.076417, measured 219.076560.

Optimization experiments. All experiments are conducted in a 18 mL screw-capped tube under normal atmosphere with **10** (15.3 mg, 0.05 mmol), chloride source and CH₃CN (0.5 mL). The reaction is stirred 16 hours at the corresponding temperature. Yields (product **11**) are determined by ¹H NMR with mesitylen (around 1 equiv., amount determined by mass) as internal standard.

Chloride source (equiv.)	Temperature (°C)	Yield of 11 (%)
MgCl ₂ (2)	120	>95
MgCl ₂ (2)	80	>95
MgCl ₂ (2)	25	50
MgCl ₂ (1)	80	>95
MgCl ₂ (0.5)	120	60
<i>n</i> Bu ₄ NCl (1)	80	27
<i>n</i> Bu ₄ NCl (2)	80	41
<i>n</i> Bu ₄ NCl (4)	80	47
<i>n</i> Bu ₄ NCl (4)	120	87
HCl in Et ₂ O (1)	25	90
HCl in Et ₂ O (2)	25	>95
TMSCl (1)	50	70
TMSCl (2)	50	>95

IV. Chlorination reactions and products characterization

General procedure for the chlorination of amino heteroaromatic compounds

Unless otherwise specified: a 18 mL screw-capped tube under normal atmosphere is charged with pyrylium tetrafluoroborate **1** (1.5 equiv.) and MgCl_2 (2.0 equiv.). The starting material (1.0 equiv.) is then added and directly followed by CH_3CN (0.1 M). The resulting mixture is then stirred 5 minutes at room temperature and then 16 hours at 120 °C. The reaction is allowed to cool down to room temperature.

NMR yields: Mesitylen (around 1 equiv., amount determined by mass) is added to the reaction. A sample of the reaction is transferred into a NMR tube and $\text{DMSO}-d_6$ (300 μL) is added.

Purification: The crude mixture is partitioned between water and EtOAc. The aqueous layer is extracted with EtOAc (3 x 10 mL). The combined organic layers are dried over Na_2SO_4 , concentrated to dryness and purified on silica gel to afford the desired product.

General procedure for the Sandemeyer reaction of amino heteroaromatic compounds

The starting heteroaromatic amine (0.1 mmol) is dissolved in concentrated HCl 37 % (0.5 mL) at 0 °C. A solution of NaONO 0.11M (1 mL, 0.11 mmol) is added dropwise to the solution. The mixture is stirred 15 minutes at 0 °C. Then, CuCl (12.9 mg, 0.13 mmol) is added and the mixture is stirred 3 hours at rt. The mixture is warmed up at 60 °C until the end of the bubbling (N_2). The reaction is carefully quenched with saturated NaHCO_3 and extracted with CH_2Cl_2 (3x5 mL). The combined organic layers are dried over Na_2SO_4 and concentrated to dryness. Mesitylen (around 1 equiv., amount determined by mass) is added to the crude. A sample of the reaction is transferred into a NMR tube with CDCl_3 to determine the dosed yield.

Synthesis of 4-chloropyridine (**7**)

The reaction was performed at 100 °C instead of 120 °C.

^1H NMR – in situ (300 MHz, $\text{DMSO}-d_6$) δ 8.86 (d, $J = 6.9$ Hz, 2H), 8.13 – 8.02 (m, 2H)*.

*Note: Overlap with pyridine

Confirmed with the commercially available product [7379-35-3].

Synthesis of ethyl 2-chlorooxazole-4-carboxylate (11)

No column was required for this compound; characterized after the work up. Slightly yellow liquid

$^1\text{H NMR}$ (300 MHz, CDCl_3) δ 8.17 (s, 1H), 4.37 (q, $J = 7.2$ Hz, 2H), 1.36 (t, $J = 7.1$ Hz, 3H).

$^{13}\text{C NMR}$ (75 MHz, CDCl_3) δ 160.1, 148.3, 145.5, 135.2, 61.8, 14.3.

HRMS (EI) calculated $[\text{M}]^+$ 175.003072, measured 175.003070.

Characterization data matched with supplier data [460081-18-9].

Synthesis of 4-chloro-3-fluoropyridine (12)

The reaction was performed at 100 °C instead of 120 °C.

$^1\text{H NMR}$ – in situ (300 MHz, $\text{DMSO}-d_6$) δ 8.71 (d, $J = 1.6$ Hz, 1H), 8.46 (t, $J = 6.4$ Hz, 1H)*, 7.73 (t, $J = 5.9$ Hz, 1H).

**Note: Overlap with impurities*

Confirmed with the commercially available product [2546-56-7].

Synthesis of 4-chloro-2-methylpyridine (13)

The reaction was performed at 100 °C instead of 120 °C.

$^1\text{H NMR}$ – in situ (300 MHz, $\text{DMSO}-d_6$) δ 8.70 (d, $J = 6.4$ Hz, 1H), 8.16 – 8.03 (m, 1H)*, 7.95 (d, $J = 6.5$ Hz, 1H), 2.77 (s, 3H).

**Note: Overlap with pyridine*

HRMS (EI) calculated $[\text{M}]^+$ 128.026152, measured 128.026220.

Synthesis of 2,4-dichloropyridine (14)

The reaction was performed at 100 °C instead of 120 °C.

¹H NMR – in situ (300 MHz, DMSO-*d*₆) δ 8.39 (d, *J* = 5.4 Hz, 1H), 7.69 (d, *J* = 1.8 Hz, 1H), 7.52 (dd, *J* = 5.4, 1.8 Hz, 1H).

HRMS (ESI) calculated [M+H]⁺ 147.971530, measured 147.971520.

Synthesis of methyl 4-chloropicolinate (15)

The reaction was performed at 80 °C instead of 120 °C.

¹H NMR – in situ (300 MHz, DMSO-*d*₆) δ 8.70 (d, *J* = 5.2 Hz, 1H), 8.11 (d, *J* = 2.1 Hz, 1H), 7.77 (dd, *J* = 5.3, 2.1 Hz, 1H), 3.94 (s, 3H).

Characterization data matched with a previously reported example.⁹

Synthesis of 4-chloro-2-phenylpyridine (16)

Colorless oil (volatile)

¹H NMR (300 MHz, CDCl₃) δ 8.59 (dd, *J* = 5.3, 0.6 Hz, 1H), 7.99–7.95 (m, 2H), 7.74 (dd, *J* = 1.9, 0.6 Hz, 1H), 7.52–7.341 (m, 2H), 7.25 (d, *J* = 4.9 Hz, 1H).

Characterization data matched with a previously reported example.¹⁰

Synthesis of 4-chloro-2-(4-methoxyphenyl)pyridine (17)

Colorless oil

$^1\text{H NMR}$ (300 MHz, CDCl_3) δ 8.54 (dd, $J = 5.3, 0.6$ Hz, 1H), 7.96–7.91 (m, 2H), 7.67 (dd, $J = 1.9, 0.6$ Hz, 1H), 7.18 (dd, $J = 5.3, 1.9$ Hz, 1H), 7.02–6.97 (m, 2H), 3.87 (s, 3H).

Characterization data matched with a previously reported example.¹¹

Synthesis of 4-(4-chloropyridin-2-yl)morpholine (18)

The reaction was performed at 140 °C instead of 120 °C.

$^1\text{H NMR}$ – in situ (300 MHz, $\text{DMSO}-d_6$) δ 8.06 (d, $J = 6.4$ Hz, 1H), 7.42 (s, 1H), 6.98 (d, $J = 6.4$ Hz, 1H), 3.80–3.70 (m, 8H).

Characterization data matched with a previously reported example.¹²

Synthesis of 2-chloro-5-nitropyridine (19)

$^1\text{H NMR}$ – in situ (300 MHz, $\text{DMSO}-d_6$) δ 9.23 (d, $J = 2.9$ Hz, 1H), 8.60 (m, 1H)*, 7.77 (d, $J = 8.8$ Hz, 1H).

*Note: Overlap with pyridine

Characterization data matched with a previously reported example.¹³

Synthesis of 6-chloronicotinonitrile (20)

The reaction was performed at 140 °C instead of 120 °C.

¹H NMR – in situ (300 MHz, DMSO-*d*₆) δ 8.86 (m, 1H)*, 8.30 (dd, *J* = 8.4, 2.4 Hz, 1H), 7.73 (d, *J* = 8.4 Hz, 1H).

**Note: Overlap with pyridine*

HRMS (ESI) calculated [M+H]⁺ 139.005770, measured 139.005750.

Synthesis of 2,4-dichloropyrimidine (21)

5 equivalents of MgCl₂ were used.

¹H NMR – in situ (300 MHz, DMSO-*d*₆) δ 8.75 (d, *J* = 5.3 Hz, 1H), 7.77 (d, *J* = 5.3 Hz, 1H).

HRMS (EI) calculated [M]⁺ 147.958954, measured 147.959150.

Synthesis of 4-chloro-2-phenylpyrimidine (22)

Colorless liquid

¹H NMR (300 MHz, CDCl₃) δ 8.67 (d, *J* = 5.2 Hz, 1H), 8.46–8.43 (m, 2H), 7.53–4.41 (m, 3H), 7.23 (d, *J* = 5.3 Hz, 1H).

¹³C NMR (75 MHz, CDCl₃) δ 165.8, 161.7, 158.4, 136.3, 131.7, 128.8, 128.7, 119.5.

HRMS (EI) calculated [M]⁺ 190.029225, measured 190.029520.

Synthesis of 3,6-dichloropyridazine (23)

4 equivalents of CsCl were used instead of MgCl₂.

¹H NMR – in situ (300 MHz, DMSO-*d*₆) δ 8.01 (s, 2H).

HRMS (ESI) calculated [M+H]⁺ 148.966778, measured 148.966910.

Synthesis of 4,5-dichloro-2-phenylpyridazin-3(2H)-one (24)

Yellow solid

¹H NMR (300 MHz, CDCl₃) δ 7.92 (s, 1H), 7.57 (d, *J* = 7.2 Hz, 2H), 7.52 – 7.40 (m, 3H).

¹³C NMR (75 MHz, CDCl₃) δ 156.3, 141.0, 136.5, 136.2, 135.4, 129.0, 129.0, 125.3.

HRMS (ESI) calculated [M+Na]⁺ 262.974938, measured 262.975020.

Synthesis of 9-chloroacridine (25)

¹H NMR – in situ (300 MHz, DMSO-*d*₆) δ 8.85 (d, *J* = 8.7 Hz, 2H), 8.09 (d, *J* = 8.0 Hz, 2H)*, 7.99 (t, *J* = 7.7 Hz, 2H), 7.57 (t, *J* = 7.7 Hz, 2H).

*Note: Overlap with pyridine

Confirmed with the commercially available product [1207-69-8].

Synthesis of 6-chloro-9-ethyl-9H-purine (26)

A 18 mL screw-capped tube under normal atmosphere is charged with pyrylium tetrafluoroborate **1** (25.2 mg, 0.15 mmol), aminoheterocycle **63** (16.3 mg, 0.1 mmol) and EtOH (2 mL). The resulting mixture is then stirred 5 minutes at room temperature and then 16 hours at 80 °C (covered with aluminium foil). The reaction is allowed to cool down to room temperature and the solvent is removed under high vacuum. The crude mixture is then dissolved in CH₃CN (2 mL) and MgCl₂ (19.0 mg, 0.2 mmol) is added. The resulting mixture is then stirred 5 minutes at room temperature and then 16 hours at 120 °C. The reaction is allowed to cool down to room temperature and concentrated to dryness. The crude mixture can be purified on a silica pad and washed several times with CH₂Cl₂ to afford the desired product as a colorless liquid (11 mg, 60 %).

¹H NMR (300 MHz, CDCl₃) δ 8.74 (s, 1H), 8.14 (s, 1H), 4.36 (q, *J* = 7.3 Hz, 2H), 1.58 (t, *J* = 7.3 Hz, 3H).

¹³C NMR (75 MHz, CDCl₃) δ 152.0, 151.2, 144.8, 134.7, 131.9, 39.7, 15.4.

HRMS (ESI) calculated [M+H]⁺ 183.043198, measured 183.043180.

Synthesis of 4-chloropyrrolo[2,1-*f*][1,2,4]triazine (27)

A 18 mL screw-capped tube under normal atmosphere is charged with pyrylium tetrafluoroborate **1** (25.2 mg, 0.15 mmol), aminoheterocycle (13.4 mg, 0.1 mmol) and EtOH (2 mL). The resulting mixture is then stirred 5 minutes at room temperature and then 16 hours at 80 °C (covered with aluminium foil). The reaction is allowed to cool down to room temperature and Me₄NCl (43.8 mg, 0.4 mmol) is added. The resulting mixture is then stirred 5 minutes at room temperature and then 16 hours at 80 °C. After cooling down the reaction to room temperature, the yield is determined by NMR. Attempts to purify the compound were unsuccessful and led to decompositions.

¹H NMR – in situ (300 MHz, DMSO-*d*₆) δ 7.76 (d, *J* = 2.0 Hz, 1H), 7.52 (d, *J* = 2.6 Hz, 1H), 6.86 (dd, *J* = 4.4, 1.6 Hz, 1H), 6.50 (t, *J* = 3.5 Hz, 1H).

HRMS (EI) calculated [M]⁺ 153.008824, measured 153.008950.

Synthesis of 3-chloro-[1,2,4]triazolo[4,3-a]pyridine (28)

Colorless liquid

¹H NMR (300 MHz, CDCl₃) δ 8.00 (dt, *J* = 7.0, 1.2 Hz, 1H), 7.75 (dt, *J* = 9.3, 1.1 Hz, 1H), 7.33 (ddd, *J* = 9.4, 6.6, 1.2 Hz, 1H), 6.97 (td, *J* = 6.8, 1.0 Hz, 1H).

¹³C NMR (75 MHz, CDCl₃) δ 150.7, 132.9, 127.8, 121.9, 116.8, 114.8.

HRMS (EI) calculated [M]⁺ 153.008824, measured 153.009070.

Synthesis of 2-chlorobenzo[d]thiazole (29)

Colorless liquid (volatile)

¹H NMR (300 MHz, CDCl₃) δ 7.95 (ddd, *J* = 8.1, 1.4, 0.6 Hz, 1H), 7.78 (ddd, *J* = 7.8, 1.4, 0.6 Hz, 1H), 7.49 (td, *J* = 7.7, 1.4 Hz, 1H), 7.41 (ddd, *J* = 7.8, 7.3, 1.3 Hz, 1H).

Confirmed with the commercially available product [615-20-3].

Synthesis of 2-chloro-6-(trifluoromethoxy)benzo[d]thiazole (30)

Colorless liquid (volatile)

¹H NMR (300 MHz, CDCl₃) δ 7.96 (dd, *J* = 8.9, 0.5 Hz, 1H), 7.66 (ddd, *J* = 2.5, 1.0, 0.5 Hz, 1H), 7.37 (ddq, *J* = 8.8, 2.5, 0.9 Hz, 1H).

¹³C NMR (75 MHz, CDCl₃) δ 154.3, 149.7, 147.0 (q, ³*J*(C,F) = 1.7 Hz), 137.0, 124.0, 120.8 (q, ⁴*J*(C,F) = 0.67 Hz), 120.6 (q, ¹*J*(C,F) = 258.0 Hz), 113.9 (q, ⁴*J*(C,F) = 1.3 Hz).

¹⁹F NMR (282 MHz, CDCl₃) δ -58.06 (s, 3F).

HRMS (EI) calculated [M]⁺ 252.957050, measured 252.957470.

Synthesis of 3-chloro-5-nitrobenzo[d]isothiazole (31)

Yellow solid

¹H NMR (300 MHz, CDCl₃) δ 8.71 (d, *J* = 2.3 Hz, 1H), 8.24 (dd, *J* = 9.7, 2.3 Hz, 1H), 7.86 (d, *J* = 9.7 Hz, 1H).

¹³C NMR (75 MHz, CDCl₃) δ 161.5, 155.9, 145.5, 130.9, 123.9, 123.0, 118.0.

HRMS (ESI) calculated [M+H]⁺ 214.967653, measured 214.967750.

Synthesis of methyl (*E*)-2-(2-chlorothiazol-4-yl)-2-(methoxyimino)acetate and methyl (*Z*)-2-(2-chlorothiazol-4-yl)-2-(methoxyimino)acetate (32a and 32b)

Colorless liquids

Gram scale experiment: A similar procedure was applied: To a 100 mL pressure schlenk under normal atmosphere were added pyrylium tetrafluoroborate **1** (1.170 g, 6.97 mmol), MgCl₂ (0.884 g, 9.29 mmol) and **60** (1.000 g, 4.65 mmol) in CH₃CN (50 mL). The resulting mixture is then stirred 5 minutes at room temperature and then 2 days at 120 °C (conversion monitored by crude ¹H NMR). The reaction is allowed to cool down to room temperature. The crude mixture is partitioned between water and EtOAc. The aqueous layer is extracted with EtOAc (3 x 100 mL). The combined organic layers are dried over Na₂SO₄, concentrated to dryness and purified on silica gel (hexanes:EtOAc, 70/30) to afford the mixed desired products **32 a** as pale yellow oil (0.895 mg, 82%)..

A) ¹H NMR (300 MHz, CDCl₃) δ 7.50 (s, 1H), 4.04 (s, 3H), 3.94 (s, 3H).

A) ¹³C NMR (75 MHz, CDCl₃) δ 162.7, 153.2, 145.2, 145.2, 120.3, 63.6, 52.9.

B) ¹H NMR (300 MHz, CDCl₃) δ 8.03 (s, 1H), 4.13 (s, 3H), 3.93 (s, 3H).

B) ¹³C NMR (75 MHz, CDCl₃) δ 163.3, 151.2, 143.1, 141.4, 127.8, 64.2, 53.3.

HRMS (ESI) calculated [M+Na]⁺ 256.975812 measured 256.975680.

Synthesis of (*R*)-2-(2-chlorooxazole-4-carboxamido)-2-phenylethyl (*E*)-3-(3-chlorophenyl)acrylate (39)

Beige solid (mp: 152.4 °C)

¹H NMR (300 MHz, CDCl₃) δ 8.15 (s, 1H), 7.61 (d, *J* = 16.0 Hz, 1H), 7.49 (d, *J* = 2.0 Hz, 1H), 7.45-7.28 (m, 9H), 6.42 (d, *J* = 16.0 Hz, 1H), 5.52 (ddd, *J* = 8.5, 6.9, 4.9 Hz, 1H), 4.62-4.50 (m, 2H).

¹³C NMR (75 MHz, CDCl₃) δ 166.4, 158.9, 147.2, 144.2, 143.3, 137.8, 137.6, 136.1, 135.1, 130.4, 130.2, 129.1, 128.3, 128.0, 126.9, 126.5, 118.9, 66.3, 52.3.

HRMS (ESI) calculated [M+Na]⁺ 453.037932, measured 453.038660.

Synthesis of (*R*)-2-(2-chlorooxazole-4-carboxamido)-2-phenylethyl 2-bromobenzoate (34)

Off-white foam (mp: 151.2 °C)

¹H NMR (300 MHz, CDCl₃) δ 8.15 (s, 1H), 7.72 (m, 1H), 7.65 (m, 1H), 7.56 (d, *J* = 8.6 Hz, 1H), 7.44-7.28 (m, 7H), 5.60 (m, 1H), 4.754.63 (m, 2H).

¹³C NMR (75 MHz, CDCl₃) δ 166.2, 158.9, 147.2, 143.3, 137.9, 137.6, 134.5, 133.0, 131.9, 131.8, 129.1, 128.3, 127.4, 127.0, 121.9, 67.4, 52.1.

HRMS (ESI) calculated [M+Na]⁺ 470.971780, measured 470.972260.

Synthesis of (*R*)-2-(2-chlorooxazole-4-carboxamido)-2-phenylethyl 3-cyanobenzoate (35)

Beige solid (mp: 101.2 °C)

¹H NMR (300 MHz, CDCl₃) δ 8.25 (s, 1H), 8.20 (d, *J* = 7.9 Hz, 1H), 8.15 (s, 1H), 7.83 (d, *J* = 7.8 Hz, 1H), 7.56 (t, *J* = 7.8 Hz, 1H), 7.44-7.31 (m, 6H), 5.61 (dt, *J* = 8.5, 6.3 Hz, 1H), 4.72-4.64 (m, 2H).

¹³C NMR (75 MHz, CDCl₃) δ 164.5, 159.0, 147.3, 143.3, 137.5, 137.3, 136.3, 133.9, 133.5, 131.1, 129.7, 129.3, 128.7, 126.9, 117.9, 113.2, 67.3, 52.2.

HRMS (ESI) calculated [M+Na]⁺ 418.056503, measured 418.056640.

Synthesis of (*R*)-2-(2-chlorooxazole-4-carboxamido)-2-phenylethyl 2-iodobenzoate (36)

Off-white foam (mp: 118.3 °C)

¹H NMR (300 MHz, CDCl₃) 8.14 (s, 1H), 7.97 (dd, *J* = 7.9, 1.2 Hz, 1H), 7.71 (dd, *J* = 7.8, 1.7 Hz, 1H), 7.54 (d, *J* = 8.6 Hz, 1H), 7.44-7.29 (m, 6H), 7.14 (td, *J* = 7.7, 1.7 Hz, 1H), 5.61 (ddd, *J* = 8.6, 6.7, 4.7 Hz, 1H), 4.76-4.62 (m, 2H).

¹³C NMR (75 MHz, CDCl₃) δ 166.4, 158.9, 147.2, 143.3, 141.4, 137.8, 137.6, 134.9, 133.0, 131.5, 129.1, 128.4, 128.1, 127.0, 94.2, 67.3, 52.2.

HRMS (ESI) calculated [M+Na]⁺ 518.957902, measured 518.957980.

Synthesis of (*R*)-2-(2-chlorooxazole-4-carboxamido)-2-phenylethyl 4-formylbenzoate (37)

Slightly yellow solid (mp: 143.4 °C)

¹H NMR (300 MHz, CDCl₃) δ 10.09 (s, 1H), 8.15-8.12 (m, 3H), 7.93 (d, *J* = 8.1 Hz, 2H), 7.45-7.32 (m, 6H), 5.62 (dt, *J* = 8.6, 6.2 Hz, 1H), 4.75-4.64 (m, 2H).

¹³C NMR (75 MHz, CDCl₃) δ 191.6, 165.5, 159.0, 147.3, 143.3, 139.5, 137.5, 137.5, 134.7, 130.5, 129.7, 129.2, 128.6, 126.9, 67.1, 52.2.

HRMS (ESI) calculated [M+Na]⁺ 421.056169, measured 421.056580.

Synthesis of (*R*)-2-(2-chlorooxazole-4-carboxamido)-2-phenylethyl 4-fluorobenzoate (38)

White solid (mp: 176.8 °C)

¹H NMR (300 MHz, CDCl₃) δ 8.14 (s, 1H), 8.00 (m, 2H), 7.44-7.30 (tt, *J* = 13.5, 6.4 Hz, 6H), 7.09 (t, *J* = 8.6 Hz, 2H), 5.59 (ddd, *J* = 8.6, 7.1, 5.3 Hz, 1H), 4.70-4.59 (m, 2H).

¹³C NMR (75 MHz, CDCl₃) δ 166.1 (d, ¹*J*(C,F) = 255 Hz), 165.5, 159.0, 147.2, 143.2, 137.8, 137.6, 132.4 (d, ³*J*(C,F) = 9 Hz), 129.2, 128.5, 126.9, 126.0 (d, ⁴*J*(C,F) = 3 Hz), 115.8 (d, ²*J*(C,F) = 22 Hz), 66.8, 52.3.

¹⁹F NMR (282 MHz, CDCl₃) δ -105.10 (s, 3F).

HRMS (ESI) calculated [M+Na]⁺ 411.051833, measured 411.052650.

Synthesis of (*R*)-2-(2-chlorooxazole-4-carboxamido)-2-phenylethyl nicotinate (39)

Brown solid (mp: 152.4 °C)

¹H NMR (300 MHz, CDCl₃) δ 9.16 (s, 1H), 8.76 (d, *J* = 4.6 Hz, 1H), 8.24 (d, *J* = 8.0 Hz, 1H), 8.14 (s, 1H), 7.44-7.30 (m, 7H), 5.61 (q, *J* = 6.8 Hz, 1H), 4.69 (d, *J* = 6.2 Hz, 2H).

¹³C NMR (75 MHz, CDCl₃) δ 165.2, 159.0, 153.8, 151.1, 147.3, 143.3, 137.5, 137.5, 137.3, 129.2, 128.6, 126.9, 125.8, 123.5, 67.0, 52.2.

HRMS (ESI) calculated [M+Na]⁺ 394.056503, measured 394.056660.

Synthesis of (*R*)-2-(2-chlorooxazole-4-carboxamido)-2-phenylethyl 2-(4-(methylsulfonyl)phenyl)acetate (40)

White solid (mp: 116.9 °C)

¹H NMR (300 MHz, CDCl₃) δ 8.16 (s, 1H), 7.85 (d, *J* = 8.3 Hz, 2H), 7.40 (d, *J* = 8.1 Hz, 2H), 7.37-7.20 (m, 6H), 5.45 (dt, *J* = 8.7, 6.1 Hz, 1H), 4.46 (d, *J* = 6.1 Hz, 2H), 3.71 (s, 2H), 3.03 (s, 3H).

¹³C NMR (75 MHz, CDCl₃) δ 170.2, 158.9, 147.3, 143.3, 139.9, 139.6, 137.4, 137.4, 130.5, 129.1, 128.5, 127.8, 126.8, 66.7, 52.0, 44.7, 41.1.

HRMS (ESI) calculated [M+Na]⁺ 485.054457, measured 485.055210.

Synthesis of 2-chloro-5-methyl-1,3,4-thiadiazole (41)

¹H NMR – in situ (300 MHz, DMSO-*d*₆) δ 2.72 (s, 3H).

HRMS (EI) calculated [M]⁺ 133.969998, measured 133.970270.

Synthesis of 2-chloro-5-phenyl-1,3,4-oxadiazole (42)

Attempts to purify the compound were unsuccessful and led to decompositions.

¹H NMR – in situ (300 MHz, DMSO-*d*₆) δ 8.13-7.82 (m, 2H), 7.78-7.45 (m, 3H).

Note: The signals from the product are overlapping with the pyridine. However, the dosed yield remains consistent with both components.

HRMS (EI) calculated [M]⁺ 180.008490, measured 180.008840.

Synthesis of 2-chloro-*N*-((1*R*,2*S*)-2-hydroxy-2,3-dihydro-1*H*-inden-1-yl)oxazole-4-carboxamide (43)

A 18 mL screw-capped tube under normal atmosphere is charged with pyrylium tetrafluoroborate **1** (25.2 mg, 0.15 mmol), SM5 (25.9 mg, 0.01 mmol) and EtOH (2 mL). The resulting mixture is then stirred 5 minutes at room temperature and then 16 hours at 50 °C (covered with aluminum foil). The reaction is allowed to cool down to room temperature and the solvent is removed under high vacuum. The crude mixture is then dissolved in CH₃CN (2 mL) and *n*Bu₄NCl (111.2 mg, 0.4 mmol) is added. The resulting mixture is then stirred 5 minutes at room temperature and then 16 hours at 50 °C. The reaction is allowed to cool down to room temperature and directly purified on silica gel (hexanes:EtOAc, 50:50) to afford the desired product as a colorless oil (16 mg, 57 %).

¹H NMR (300 MHz, CDCl₃) δ 8.21 (s, 1H), 7.42 (d, *J* = 7.4 Hz, 1H), 7.36-7.20 (m, 4H), 5.52 (dd, *J* = 8.6, 5.1 Hz, 1H), 4.73 (s, 1H), 3.23 (dd, *J* = 16.4, 5.3 Hz, 1H), 3.00 (d, *J* = 16.5 Hz, 1H), 2.21 (s, 1H).

¹³C NMR (75 MHz, CDCl₃) δ 160.1, 160.0, 143.3, 140.1, 140.1, 137.7, 128.7, 127.5, 125.6, 124.9, 73.9, 57.5, 39.9.

HRMS (ESI) calculated [M+Na]⁺ 301.035039, measured 301.034780.

Synthesis of diethyl ((2-(6-chloro-9H-purin-9-yl)ethoxy)methyl)phosphonate (44)

A schlenk under Ar is charged with pyrylium tetrafluoroborate **1** (25.2 mg, 0.15 mmol), *diethyl-Adefovir* (32.9 mg, 0.01 mmol) and EtOH (2 mL). The resulting mixture is then stirred 5 minutes at room temperature and then 16 hours at 80 °C (covered with aluminum foil). The reaction is allowed to cool down to room temperature and the solvent is removed under high vacuum. The crude mixture is then dissolved in CH₃CN (2 mL) and *n*Bu₄NCl (111.2 mg, 0.4 mmol) is added. The resulting mixture is then stirred 5 minutes at room temperature and then 16 hours at 80 °C. The reaction is allowed to cool down to room temperature and directly purified on silica gel (CH₂Cl₂:MeOH, 100:0 to 90:10) to afford the desired product as an orange oil (20 mg, 57 %).

*Note: trace amounts of *n*Bu₄N⁺ can sometimes be detected after the column. The resulting mixture can be dissolved in Et₂O, sonicated (orange solution + black solids) and filtered through celite without any loss.*

¹H NMR (300 MHz, CDCl₃) δ 8.71 (s, 1H), 8.27 (s, 1H), 4.49 (t, *J* = 4.9 Hz, 2H), 4.11–4.02 (m, 4H), 3.96 (t, *J* = 5.0 Hz, 2H), 3.76 (d, *J* = 8.1 Hz, 2H), 1.29–1.23 (m, 6H).

¹³C NMR (75 MHz, CDCl₃) δ 151.9, 152.0, 151.1, 146.3, 131.6, 70.9 (d, ³*J*(C,F) = 10 Hz), 65.5 (d, ¹*J*(C,F) = 167 Hz), 62.6 (d, ²*J*(C,F) = 7 Hz), 44.1, 16.6 (d, ³*J*(C,F) = 6 Hz).

³¹P NMR (243 MHz, CDCl₃) δ 20.21 (s, 1P).

HRMS (ESI) calculated [M+Na]⁺ 371.064641, measured 371.064630.

Synthesis of methyl 2-chloro-7-isopropyl-5-oxo-5H-chromeno[2,3-b]pyridine-3-carboxylate (**45**)

A schlenk under Ar is charged with pyrylium tetrafluoroborate **1** (25.2 mg, 0.15 mmol), **SM16** (31.2 mg, 0.01 mmol) and EtOH (2 mL). The resulting mixture is then stirred 5 minutes at room temperature and then 16 hours at 80 °C (covered with aluminum foil). The reaction is allowed to cool down to room temperature and the solvent is removed under high vacuum. The crude mixture is then dissolved in CH₃CN (2 mL) and *n*Bu₄NCl (111.2 mg, 0.4 mmol) is added. The resulting mixture is then stirred 5 minutes at room temperature and then 16 hours at 80 °C. The reaction is allowed to cool down to room temperature and directly purified on silica gel (hexanes:EtOAc, 80:20) to afford the desired product as a white solid (17 mg, 51 %).

¹H NMR (300 MHz, CDCl₃) δ 9.19 (s, 1H), 8.14 (d, *J* = 2.3 Hz, 1H), 7.70 (dd, *J* = 8.7, 2.3 Hz, 1H), 7.55 (d, *J* = 8.6 Hz, 1H), 4.01 (s, 3H), 3.07 (hept, *J* = 6.9 Hz, 1H), 1.33 (d, *J* = 7.0 Hz, 6H).

¹³C NMR (75 MHz, CDCl₃) δ 176.4, 163.6, 160.0, 154.5, 153.9, 146.9, 142.5, 135.4, 123.8, 121.5, 118.7, 115.0, 53.2, 33.9, 24.0.

HRMS (EI) calculated [M]⁺ 331.060587, measured 331.060640.

Synthesis of 1-(4-(2-chlorodibenzo[*b,f*][1,4]oxazepin-11-yl)piperazin-1-yl)-2-(2-chlorothiazol-4-yl)ethan-1-one (46)

The reaction was performed at 80 °C instead of 120 °C. Yellow sticky oil

¹H NMR (300 MHz, CDCl₃) δ 7.40 (dd, *J* = 8.6, 2.6 Hz, 1H), 7.31 (d, *J* = 2.5 Hz, 1H), 7.19 (d, *J* = 8.6 Hz, 1H), 7.17-7.06 (m, 4H), 7.01 (m, 1H), 3.86 (s, 2H), 3.82-3.68 (m, 4H), 3.65-3.34 (m, 4H).

¹³C NMR (75 MHz, CDCl₃) δ 167.7, 159.3, 158.5, 151.7, 151.4, 148.7, 139.7, 132.8, 130.4, 128.8, 127.1, 125.8, 125.0, 124.7, 122.8, 120.1, 118.0, 47.4, 47.4, 45.9, 41.6, 36.7.

HRMS (ESI) calculated [M+H]⁺ 473.060028, measured 473.059970.

Synthesis of 1-((3*S*,4*R*)-3-((benzo[*d*][1,3]dioxol-5-yloxy)methyl)-4-(4-fluorophenyl)piperidin-1-yl)-2-(2-chlorothiazol-4-yl)ethan-1-one (47)

The reaction was performed at 80 °C instead of 120 °C. Yellow sticky oil

¹H NMR (600 MHz, DMSO-*d*₆) δ 7.48 (dd, *J* = 3.4, 0.9 Hz, 1H), 7.27 (ddd, *J* = 10.2, 8.7, 6.2 Hz, 2H), 7.12 (td, *J* = 8.8, 2.1 Hz, 2H), 6.72 (dd, *J* = 8.5, 1.7 Hz, 1H), 6.46 (dd, *J* = 10.1, 2.5 Hz, 1H), 6.17 (dd, *J* = 8.5, 2.5 Hz, 1H), 5.92 (bs, 2H), 4.68 (m, 1H), 4.13 (m, 1H), 3.89 (m, 2H), 3.51 (m, 2H), 3.11 (m, 1H), 2.78 (dtd, *J* = 16.0, 11.7, 3.9 Hz, 1H), 2.62 (m, 1H), 1.98 (dtt, *J* = 11.1, 7.5, 3.5 Hz, 1H), 1.74 (dq, *J* = 13.3, 2.9 Hz, 1H), 1.61 (dq, *J* = 45.7, 12.6, 4.3 Hz, 1H).

¹³C NMR (151 MHz, DMSO-*d*₆) δ 166.9 (d, *J* = 13 Hz), 160.9 (d, ¹*J*(C,F) = 242 Hz), 153.9, 153.8, 149.5 (m), 147.8, 141.2, 139.6, 129.1 (dd, ³*J*(C,F) = 8 Hz, *J* = 3 Hz), 119.7 (d, *J* = 3 Hz), 115.2 (d, ²*J*(C,F) = 21 Hz), 107.9 (d, *J* = 7 Hz), 105.6 (d, *J* = 13 Hz), 101.0, 97.8 (d, *J* = 10 Hz), 68.7 (d, *J* = 75 Hz), 47.4 (d, *J* = 414 Hz), 43.9 (d, *J* = 232 Hz), 42.5 (d, *J* = 186 Hz), 41.4 (d, *J* = 106 Hz), 36.0 (d, *J* = 26 Hz), 33.6 (d, *J* = 109 Hz).

¹⁹F NMR (282 MHz, DMSO-*d*₆) δ -116.45 (d, *J* = 3.8 Hz, 1F).

Note: The 2 conformations of piperidine led to a signal splitting in ¹H, ¹³C as well as ¹⁹F NMR.

HRMS (ESI) calculated [M+Na]⁺ 511.086506, measured 511.086620.

Synthesis of (*R*)-2-(5-(3-(1-(4-(2-chloropyrimidin-5-yl)phenyl)-1-cyclopropylethyl)-1,2,4-oxadiazol-5-yl)-1H-pyrazol-1-yl)-*N,N*-dimethylacetamide (48)

A schlenk under Ar is charged with pyrylium tetrafluoroborate **1** (3.4 mg, 0.02 mmol) and MgCl_2 (4.9 mg, 0.05 mmol). *B*/665915 (4.7 mg, 0.01 mmol) is then added and directly followed by CH_3CN (1 mL). The resulting mixture is then stirred 5 minutes at room temperature and then 16 hours at 120 °C. The reaction is allowed to cool down to room temperature and is concentrated to dryness. The resulting solids were dissolved in the minimum amount of CH_2Cl_2 and purified by preparative TLC (CH_2Cl_2 :MeOH, 90:10) to afford the desired product (1.8 mg, 37 %).

^1H NMR (600 MHz, $\text{DMSO}-d_6$) δ 8.55 (s, 2H), 8.49 (d, $J = 0.8$ Hz, 1H), 8.06 (d, $J = 0.7$ Hz, 1H), 7.56 (d, $J = 8.5$ Hz, 2H), 7.38 (d, $J = 8.6$ Hz, 2H), 5.21 (s, 2H), 3.03 (s, 3H), 2.85 (s, 3H), 1.66 (m, 1H), 1.48 (s, 3H), 0.64 (m, 1H), 0.49 (m, 1H), 0.43 (m, 1H), 0.34 (m, 1H).

^{13}C NMR (151 MHz, $\text{DMSO}-d_6$) δ 175.6, 172.3, 170.3, 165.8, 155.8, 143.8, 138.5, 134.0, 133.5, 127.3, 125.2, 121.7, 106.6, 53.6, 53.25, 2.0, 1.0.

Note: Due to the amount of material recovered as well as the presence of several peaks in the aliphatic area, 4 carbons cannot be precisely attributed.

HRMS (ESI) calculated $[\text{M}+\text{H}]^+$ 478.175274, measured 478.174910.

Synthesis of 5-chloro-1-(2,6-dichloro-4-(trifluoromethyl)phenyl)-4-((trifluoromethyl)sulfinyl)-1H-pyrazole-3-carbonitrile (49)

5 equivalents of MgCl_2 were used. Yellow solid

^1H NMR (300 MHz, CDCl_3) δ 7.84 (bs, 2H).

^{13}C NMR (75 MHz, CDCl_3) δ 136.1 (d, $J = 3$ Hz)*, 135.9 (q, $^2J(\text{C},\text{F}) = 35$ Hz), 134.7, 134.2 (bs), 128.0, 126.47 (qd, $^3J(\text{C},\text{F}) = 4$ Hz, $J = 1$ Hz)*, 125.2 (q, $^1J(\text{C},\text{F}) = 336$ Hz), 121.9 (q, $^1J(\text{C},\text{F}) = 274$ Hz), 118.5, 109.3.

**Note: A potential steric hindrance impedes a free rotation between the 2 aromatic rings. Therefore, a signal splitting is detected for those signals.*

¹⁹F NMR (282 MHz, CDCl₃) δ -63.38 (s, 3F), -72.54 (s, 3F).

HRMS (ESI) calculated [M+Na]⁺ 477.878058, measured 477.877890.

Synthesis of (R)-1-(3-(4-chloro-3-(4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidin-1-yl)prop-2-en-1-one (50)

A schlenk under Ar is charged with pyrylium tetrafluoroborate (25.2 mg, 0.15 mmol), *Ibrutinib* (44.0 mg, 0.01 mmol) and EtOH (2 mL). The resulting mixture is then stirred 5 minutes at room temperature and then 16 hours at 50 °C (covered with aluminum foil). The reaction is allowed to cool down to room temperature and the solvent is removed under high vacuum. The crude mixture is then dissolved in CH₃CN (4 mL) and *n*Bu₄NCl (111.2 mg, 0.4 mmol) is added. The resulting mixture is then stirred 5 minutes at room temperature and then 16 hours at 50 °C. The reaction is allowed to cool down to room temperature and directly purified on silica gel (hexanes:EtOAc, 20:80) to afford the desired product as a yellow oil (40 mg, 87 %).

¹H NMR (300 MHz, CDCl₃) δ 8.75 (s, 1H), 7.74 (d, *J* = 8.7 Hz, 2H), 7.38 (t, *J* = 7.7 Hz, 2H), 7.20 – 6.98 (m, 5H), 6.58 (dt, *J* = 25.2, 13.6 Hz, 1H), 6.30 (d, *J* = 16.1 Hz, 1H), 5.69 (t, *J* = 14.4 Hz, 1H), 4.98 (bs, 1H), 4.74 (dd, *J* = 80.5, 10.4 Hz, 1H), 4.13 (dd, *J* = 52.9, 13.3 Hz, 1H), 3.61 (dt, *J* = 111.9, 11.9 Hz, 1H), 3.08 (dt, *J* = 92.2, 14.0 Hz, 1H), 2.41 (m, 1H), 2.28 (m, 1H), 2.03 (m, 1H), 1.77 (m, 1H).

¹³C NMR (75 MHz, CDCl₃) δ 165.8, 158.8, 156.6, 154.4, 154.1, 144.9, 131.7, 130.0, 128.4, 127.6, 125.9, 125.7, 124.0, 119.7, 118.2, 111.4, 54.3 (0.5 C), 53.2 (0.5 C), 50.1 (0.5 C), 46.1 (0.5 C), 46.0 (0.5 C), 42.3 (0.5 C), 30.3 (0.5 C), 30.1 (0.5 C), 25.3 (0.5 C), 24.0 (0.5 C).

Note: The 2 conformations of piperidine led to a signal splitting in both ¹H and ¹³C NMR.

HRMS (ESI) calculated [M+H]⁺ 460.153476, measured 460.153380.

Synthesis of *N*-(3-(2-(tert-butyl)-5-(2-chloropyrimidin-4-yl)thiazol-4-yl)-2-fluorophenyl)-2,6-difluorobenzenesulfonamide (51)

A schlenk under Ar is charged with pyrylium tetrafluoroborate (4.0 mg, 0.02 mmol) and MgCl_2 (9.5 mg, 0.10 mmol). *Dabrafenib* (4.7 mg, 0.01 mmol) is then added and directly followed by CH_3CN (1 mL). The resulting mixture is then stirred 5 minutes at room temperature and then 16 hours at 120 °C. The reaction is allowed to cool down to room temperature and filtered through celite with EtOAc. The resulting mixture is concentrated to the minimum and purified by preparative TLC (hexanes:EtOAc, 50:50) to afford the desired product (1.9 mg, 39 %).

^1H NMR (300 MHz, CDCl_3) δ 8.30 (d, J = 5.3 Hz, 1H), 7.75 (m, 1H), 7.51 (m, 1H), 7.34 (ddd, J = 8.1, 6.4, 1.7 Hz, 1H), 7.26 (s, 1H), * 7.21 (d, J = 6.6 Hz, 1H), 6.99 (t, J = 8.8 Hz, 2H), 6.74 (dd, J = 5.4, 1.1 Hz, 1H), 1.48 (s, 9H).

*Note: Overlap with CHCl_3 .

^{13}C NMR (151 MHz, $\text{DMSO}-d_6$) δ 183.3, 160.6, 160.5, 159.8, 158.2, 130.5, 129.6, 128.9, 128.2, 125.3, 124.2 (d, $^3J(\text{C},\text{F})$ = 9 Hz), 115.1, 112.6 (d, $^2J(\text{C},\text{F})$ = 24 Hz), 37.9, 30.2.

Note: 4 quaternary carbons cannot be detected due to the low amount as well as the C-F couplings.

^{19}F NMR (282 MHz, CDCl_3) δ -106.85 (d, J = 3.7 Hz, 2F), -129.95 (bs, 1F).

HRMS (ESI) calculated $[\text{M}+\text{H}]^+$ 539.058459, measured 539.058050.

V. Post-functionalization

Negishi coupling of **30**

To a flame-dried schlenk under Ar are added **30** (11 mg, 0.043 mmol), Pd(PPh₃)₄ (5 mg, 0.004 mmol) and THF (1 mL). The mixture is stirred at room temperature is Bn-ZnBr 0.5 M in THF (130 μ L, 0.065 mmol) is added by syringe. The reaction is then stirred 2 hours at 70 $^\circ$ C. After cooling down, water is added to the reaction (5 mL) and the aqueous phase is extracted with Et₂O (3x5 mL), dried over Na₂SO₄ and purified on silica gel (*n*-pentane:Et₂O, 100:0 to 90:10) to afford **52** as a colourless oil (12 mg, 89 %).

¹H NMR (300 MHz, CDCl₃) δ 7.99 (d, *J* = 8.9 Hz, 1H), 7.65 (m, 1H), 7.37 – 7.27 (m, 6H), 4.44 (s, 2H).

¹³C NMR (75 MHz, CDCl₃) δ 172.7, 151.9, 146.4 (q, ³*J*(C,F) = 2 Hz), 136.9, 136.6, 129.3, 129.1, 127.7, 123.7, 120.7 (q, ¹*J*(C,F) = 258 Hz), 120.1, 114.3, 40.8.

¹⁹F NMR (282 MHz, CDCl₃) δ -58.06 (s, 3F).

HRMS (EI) calculated [M]⁺ 309.042972, measured 309.043220.

Suzuki coupling of **44**

To a flame-dried schlenk under Ar are added **44** (9 mg, 0.026 mmol), K₂CO₃ (7 mg, 0.052 mmol), Pd(PPh₃)₄ (5 mg, 0.004 mmol), 2-thiopheneboronic acid (5 mg, 0.039 mmol) and Toluene (1.5 mL). The mixture is stirred at 120 $^\circ$ C for 16 hours. After cooling down, water is added to the reaction (5 mL) and the aqueous phase is extracted with EtOAc (3x5 mL), dried over Na₂SO₄ and purified on silica gel (CH₂Cl₂:MeOH, 100:0 to 95:5) to afford **53** as an orange oil (8 mg, 78 %).

¹H NMR (600 MHz, CDCl₃) δ 8.87 (s, 1H), 8.68 (dd, *J* = 3.8, 1.2 Hz, 1H), 8.24 (s, 1H), 7.61 (dd, *J* = 5.0, 1.2 Hz, 1H), 7.26 (m, 1H), 4.50 (dd, *J* = 5.4, 4.6 Hz, 2H), 4.11 – 4.06 (m, 4H), 3.98 (dd, *J* = 5.3, 4.6 Hz, 2H), 3.78 (d, *J* = 8.2 Hz, 2H), 1.28 (2t overlap, *J* = 7.1, 0.4 Hz, 6H).

¹³C NMR (151 MHz, CDCl₃) δ 152.5, 152.0, 150.2, 145.5, 140.1, 132.8, 130.9, 128.9, 128.9, 71.1 (d, ³*J*(C,P) = 10 Hz), 65.5 (d, ¹*J*(C,P) = 167 Hz), 62.6 (d, ²*J*(C,P) = 7 Hz), 43.6, 16.6 (d, ³*J*(C,P) = 6 Hz).

³¹P NMR (243 MHz, CDCl₃) δ 20.31 (s, 1P).

HRMS (ESI) calculated [M+Na]⁺ 419.091336, measured 419.091270.

Sonogashira coupling of **11**

To a flame-dried schlenk under Ar are added **11** (35.1 mg, 0.2 mmol), Pd(PPh₃)₄ (11.6 mg, 0.01 mmol), CuI (3.8 mg, 0.02 mmol), phenylacetylene (44 μ L, 0.4 mmol), trimethylamine (56 μ L, 0.4 mmol) and DMF (1.5 mL). The mixture is stirred at 80 $^\circ$ C for 16 hours. After cooling down, aqueous solution of saturated NaHCO₃ is added to the reaction (5 mL) and the aqueous phase is extracted with EtOAc (3x5 mL), dried over Na₂SO₄ and purified on silica gel (*n*-pentane:Et₂O, 70:30) to afford **54** as a brown solid (27 mg, 56 %).

¹H NMR (300 MHz, CDCl₃) δ 8.24 (s, 1H), 7.60 (m, 2H), 7.49–7.36 (m, 3H), 4.42 (q, *J* = 7.1 Hz, 2H), 1.40 (t, *J* = 7.1 Hz, 3H).

¹³C NMR (75 MHz, CDCl₃) δ 160.7, 147.4, 144.3, 134.7, 132.4, 130.5, 128.8, 120.2, 92.7, 76.3, 61.6, 14.4.

HRMS (EI) calculated [M]⁺ 241.073344, measured 241.073490.

SNAr of **50** with cyclohexylamine

To a flame-dried schlenk under Ar are added **50** (13 mg, 0.028 mmol) and cyclohexylamine (20 μ L, 0.175 mmol) in CDCl₃ (1 mL). The mixture is cooled down to 0 $^\circ$ C and DIPEA (30 μ L, 0.172 mmol) is slowly added. The mixture is stirred from 0 $^\circ$ C to rt during 16 hours (conversion checked by NMR). The product is then directly purified on silica gel (CH₂Cl₂:MeOH, 100:0 to 95:5) to afford **55** as a white film (11 mg, 74 %).

¹H NMR (600 MHz, CDCl₃) δ 8.44 (s, 1H), 7.60 (d, *J* = 8.1 Hz, 2H), 7.40 (m, 2H), 7.20–7.16 (m, 3H), 7.08 (m, 2H), 6.58 (m, 1H), 6.28 (t, *J* = 17.8 Hz, 1H), 5.68 (dd, *J* = 38.3, 10.7 Hz, 1H), 5.52 (bs, 1H), 4.86–4.57 (m, 2H), 4.27–4.01 (m, 2H), 3.58 (dt, *J* = 209.9, 11.5 Hz, 1H), 3.04 (m, 1H), 2.35 (m, 1H), 2.25 (m, 1H), 2.01–1.98 (m, 3H), 1.73 (m, 1H), 1.64–1.60 (m, 3H), 1.51–1.45 (m, 2H), 1.23–1.19 (m, 3H).

SNAr of **29** with cholesterol

To a 18 mL screw-capped tube under normal atmosphere are added **29** (33.9 mg, 0.2 mmol), cholesterol 92.5 % (100.3 mg, 0.24 mmol) and DMF (2 mL). The mixture is cooled down to 0 °C and NaH (5.8 mg, 0.24 mmol) is added. The mixture is stirred 5 minutes at 0 °C and is then allowed to reach room temperature for 16 hours. The reaction is then carefully quenched with water. The aqueous phase is then extracted with EtOAc (3x10 mL), dried over Na₂SO₄ and purified on silica gel (hexanes:EtOAc, 95:5) to afford **57** as a colorless sticky oil (81 mg, 78 %).

¹H NMR (300 MHz, CDCl₃) δ 7.67-7.61 (m, 2H), 7.34 (m, 1H), 7.20 (td, *J* = 7.7, 1.2 Hz, 1H), 5.45 (dt, *J* = 5.6, 1.9 Hz, 1H), 5.02 (tt, *J* = 11.4, 4.8 Hz, 1H), 2.67 (ddd, *J* = 13.0, 5.1, 2.3 Hz, 1H), 2.50 (td, *J* = 12.7, 12.2, 2.7 Hz, 1H), 2.18 (m, 1H), 2.06-1.89 (m, 3H), 1.88-1.69 (m, 2H), 1.65 – 0.96 (m, 23H)*, 0.93 (d, *J* = 6.5 Hz, 3H), 0.89 (d, *J* = 1.3 Hz, 3H), 0.86 (d, *J* = 1.3 Hz, 3H), 0.70 (s, 3H).

*Note: This integral should represent 23 H but actually represents 26 H due to complex overlaps between the signals as well as residual grease and water.

¹³C NMR (75 MHz, CDCl₃) δ 172.4, 149.8, 139.6, 131.9, 126.0, 123.4, 123.3, 121.3, 120.8, 82.0, 56.9, 56.3, 50.3, 42.5, 39.9, 39.7, 38.3, 37.1, 36.8, 36.4, 36.0, 32.1, 32.0, 28.4, 28.2, 28.0, 24.5, 24.0, 23.0, 22.7, 21.3, 19.5, 18.9, 12.0.

HRMS (ESI) calculated [M+Na]⁺ 542.342705, measured 542.342660.

Azidation of **24**

To a 18 mL screw-capped tube under normal atmosphere are added **24** (12 mg, 0.05 mmol) and sodium azide (5.5 mg, 0.085 mmol) in THF/water (0.4 mL, 3/1 v/v). The reaction is stirred 19 hours at 65 °C. The mixture is then cooled down to rt and quenched with water (5 mL). The aqueous layer is then extracted with EtOAc (3x5 mL) and the combined organic layers are dried over Na₂SO₄ and concentrated to dryness to obtained **58** as a white solid (12 mg, quant.).

¹H NMR (300 MHz, CDCl₃) δ 7.74 (s, 1H), 7.56 (m, 2H), 7.51 – 7.38 (m, 3H).

HRMS (ESI) calculated $[M+Na]^+$ 270.015306, measured 270.015370.

Characterization data matched with a previously reported example.¹⁴

Fluorination of 45

To a flame-dried schlenk under Ar are added **45** (13 mg, 0.039 mmol) and THF (1 mL). The mixture is cooled down to 0 °C and TBAF 1 M in THF (80 μ L, 0.080 mmol) is slowly added. The mixture is stirred 1.5 hours at 0 °C and 30 minutes at room temperature. The reaction is then quenched with water (1 mL) and extracted with EtOAc (3x5 mL) and the combined organic layers are dried over Na₂SO₄ and purified on silica gel (hexanes:EtOAc, 8:2) to afford **59** as a white solid (7.5 mg, 61 %).

Note: the purification is easier once full conversion is reached.

¹H NMR (300 MHz, CDCl₃) δ 9.38 (d, ⁴J(H,F) = 9.0 Hz, 1H), 8.16 (d, *J* = 2.3 Hz, 1H), 7.70 (dd, *J* = 8.6, 2.3 Hz, 1H), 7.55 (d, *J* = 8.7 Hz, 1H), 4.01 (s, 3H), 3.08 (hept, *J* = 6.9 Hz, 1H), 1.33 (d, *J* = 6.9 Hz, 7H).

¹³C NMR (151 MHz, CDCl₃) δ 176.0, 162.9 (d, ¹J(C,F) = 263 Hz), 162.3 (d, ³J(C,F) = 8 Hz), 161.0 (d, ³J(C,F) = 18 Hz), 153.9, 147.0, 146.0 (d, ³J(C,F) = 4 Hz), 135.2, 123.9, 121.4, 118.6, 114.9 (d, ⁴J(C,F) = 4 Hz), 111.7 (d, ²J(C,F) = 24 Hz), 53.1, 33.9, 24.0.

¹⁹F NMR (282 MHz, CDCl₃) δ -51.44 (s, 3F).

HRMS (EI) calculated $[M]^+$ 315.090137, measured 315.090100.

VI. Deaminative brominations

Synthesis of 2-bromo-6-(trifluoromethoxy)benzo[d]thiazole (**62**)

To a 18 mL screw-capped tube under normal atmosphere are added *Riluzole* **61** (23.4 mg, 0.1 mmol) and pyrylium tetrafluoroborate **1** (25.2 mg, 0.15 mmol) in EtOH (1 mL). The resulting mixture is then stirred 5 minutes at room temperature and then 16 hours at 80 °C (covered with aluminum foil). The reaction is allowed to cool down to room temperature and the solvent is removed under high vacuum. The crude mixture is then dissolved in CD₃CN (1 mL) and LiBr (34.7 mg, 0.4 mmol) is added. The resulting mixture is then stirred 5 minutes at room temperature and then 16 hours at 80 °C. The reaction is allowed to cool down to room temperature. The crude mixture is partitioned between water and Et₂O. The aqueous layer is extracted with Et₂O (3 x 10 mL). The combined organic layers are dried over Na₂SO₄,

concentrated to dryness and purified on silica gel (*n*-pentane:Et₂O, 100:0 to 80:20) to afford the desired product **62** as an off white solid (28 mg, 94%).

¹H NMR (300 MHz, CDCl₃) δ 7.99 (d, *J* = 8.9 Hz, 1H), 7.68 (dt, *J* = 2.1, 1.1 Hz, 1H), 7.35 (m, 1H).

¹³C NMR (75 MHz, CDCl₃) δ 151.0, 147.0 (q, ³*J*(C,F) = 2 Hz), 139.9, 138.3, 123.9, 120.7, 120.6 (q, ¹*J*(C,F) = 258 Hz), 113.6.

¹⁹F NMR (282 MHz, CDCl₃) δ -58.05 (s, 3F).

HRMS (EI) calculated [M]⁺ 296.906547, measured 296.906890.

Characterization data matched with a previously reported example.

Synthesis of 6-bromo-9-ethyl-9H-purine (**64**)

A 18 mL screw-capped tube under normal atmosphere is charged with pyrylium tetrafluoroborate **1** (12.6 mg, 0.075 mmol), aminoheterocycle **63** (8.2 mg, 0.05 mmol) and EtOH (1 mL). The resulting mixture is then stirred 5 minutes at room temperature and then 16 hours at 80 °C (covered with aluminium foil). The reaction is allowed to cool down to room temperature and the solvent is removed under high vacuum. The crude mixture is then dissolved in CH₃CN (1 mL) and MgBr₂ (18.4 mg, 0.1 mmol) is added. The resulting mixture is then stirred 5 minutes at room temperature and then 16 hours at 120 °C. The reaction is allowed to cool down to room temperature and concentrated to dryness. The crude mixture can be purified on a silica pad and washed several times with CH₂Cl₂ to afford the desired product **64** as a colorless liquid (12 mg, 53 %).

¹H NMR (300 MHz, CDCl₃) δ 8.71 (s, 1H), 8.16 (s, 1H), 4.36 (q, *J* = 7.3 Hz, 2H), 1.59 (t, *J* = 7.3 Hz, 3H).

¹³C NMR (75 MHz, CDCl₃) δ 152.0, 150.6, 144.7, 143.3, 134.4, 39.8, 15.5.

HRMS (EI) calculated [M]⁺ 225.984870, measured 225.984890.

VII. Ring-opening at the 2-position with fluorides

Synthesis of ethyl 2-(((1E,3E)-5-oxopenta-1,3-dien-1-yl)amino)oxazole-4-carboxylate (**65**)

To a 18 mL screw-capped tube under Ar atmosphere are added ethoxycarbonyloxazole pyridinium tetrafluoroborate **10** (10 mg, 0.033 mmol) in CD_3CN (0.5 mL). TBAF 1M in THF (0.131 mL, 0.131 mmol) is added. The reaction turned immediately deep green. After 1 hour, the reaction is carefully quenched with water (2 mL) and extracted with EtOAc (3x5 mL). The combined organic layers are dried over Na_2SO_4 and concentrated to dryness. The redish crude oil is dissolved in the minimum amount of CH_2Cl_2 and purified on preparative TLC (hexanes:EtOAc, 50:50) to afford **65** as a dark red oil (3 mg, 39 %).

^1H NMR (500 MHz, CD_3CN) δ 9.44 (d, $J = 8.1$ Hz, 1H), 8.67 (bs, 1H), 7.99 (s, 1H), 7.35–7.28 (m, 2H), 6.24 (ddd, $J = 13.6, 11.4, 0.6$ Hz, 1H), 6.01 (ddt, $J = 15.0, 8.1, 0.7$ Hz, 1H), 4.28 (q, $J = 7.1$ Hz, 2H), 1.31 (t, $J = 7.1$ Hz, 3H).*

*Note: This integral should represent 3 H but actually represents 4 H due to the small amount of product as well as the presence of grease.

^{13}C NMR (126 MHz, CD_3CN) δ 193.9, 162.0, 157.0, 153.7, 140.5, 137.8, 134.0, 128.0, 109.2, 61.7, 14.5.

HRMS (ESI) calculated $[\text{M}+\text{Na}]^+$ 259.068926, measured 259.068840.

VIII. Crystallographic data for compound **43**

CCDC: 2070324

Table 1. Crystal data and structure refinement.

Identification code	13594	
Empirical formula	C ₁₃ H ₁₁ Cl N ₂ O ₃	
Color	colourless	
Formula weight	278.69 g.mol ⁻¹	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	ORTHORHOMBIC	
Space group	P2₁2₁2, (no. 18)	
Unit cell dimensions	a = 13.361(2) Å	α = 90°.
	b = 18.177(3) Å	β = 90°.
	c = 5.0728(3) Å	γ = 90°.
Volume	1232.0(3) Å ³	
Z	4	
Density (calculated)	1.503 mg.m ⁻³	
Absorption coefficient	0.315 mm ⁻¹	
F(000)	576 e	
Crystal size	0.30 x 0.06 x 0.04 mm ³	
θ range for data collection	2.711 to 33.097°.	
Index ranges	-20 ≤ h ≤ 20, -27 ≤ k ≤ 27, -7 ≤ l ≤ 7	
Reflections collected	24317	
Independent reflections	4671 [R _{int} = 0.0464]	
Reflections with I > 2σ(I)	4069	
Completeness to θ = 25.242°	99.8 %	
Absorption correction	Gaussian	
Max. and min. transmission	0.99 and 0.95	
Refinement method	Full-matrix least-squares on F ²	
Data / restraints / parameters	4671 / 0 / 188	
Goodness-of-fit on F ²	1.069	
Final R indices [I > 2σ(I)]	R ₁ = 0.0364	wR ² = 0.0772
R indices (all data)	R ₁ = 0.0478	wR ² = 0.0818
Absolute structure parameter	-0.02(3)	
Largest diff. peak and hole	0.3 and -0.4 e · Å ⁻³	

Table 2. Bond lengths [Å] and angles [°].

Cl(1)-C(4)	1.6882(18)	O(1)-C(1)	1.239(2)
O(2)-C(3)	1.371(2)	O(2)-C(4)	1.352(2)
O(3)-H(3)	0.79(3)	O(3)-C(6)	1.420(2)
N(1)-H(1)	0.84(3)	N(1)-C(1)	1.336(2)
N(1)-C(5)	1.451(2)	N(2)-C(2)	1.402(2)
N(2)-C(4)	1.286(2)	C(1)-C(2)	1.479(2)
C(2)-C(3)	1.350(2)	C(5)-H(5)	0.95(2)
C(5)-C(6)	1.563(2)	C(5)-C(13)	1.517(2)
C(6)-H(6)	0.95(3)	C(6)-C(7)	1.546(2)
C(7)-C(8)	1.509(2)	C(8)-C(9)	1.393(3)
C(8)-C(13)	1.396(2)	C(9)-C(10)	1.394(3)
C(10)-C(11)	1.389(3)	C(11)-C(12)	1.396(3)
C(12)-C(13)	1.382(2)		
C(4)-O(2)-C(3)	103.46(14)	C(6)-O(3)-H(3)	107(2)
C(1)-N(1)-H(1)	117.0(17)	C(1)-N(1)-C(5)	122.24(16)
C(5)-N(1)-H(1)	120.5(17)	C(4)-N(2)-C(2)	102.73(15)
O(1)-C(1)-N(1)	124.37(16)	O(1)-C(1)-C(2)	119.72(16)
N(1)-C(1)-C(2)	115.89(15)	N(2)-C(2)-C(1)	123.75(15)
C(3)-C(2)-N(2)	109.56(15)	C(3)-C(2)-C(1)	126.65(16)
C(2)-C(3)-O(2)	107.93(15)	O(2)-C(4)-Cl(1)	115.76(13)
N(2)-C(4)-Cl(1)	127.89(15)	N(2)-C(4)-O(2)	116.32(16)
N(1)-C(5)-H(5)	109.8(13)	N(1)-C(5)-C(6)	115.44(14)
N(1)-C(5)-C(13)	112.54(15)	C(6)-C(5)-H(5)	109.0(13)
C(13)-C(5)-H(5)	107.0(13)	C(13)-C(5)-C(6)	102.56(14)
O(3)-C(6)-C(5)	112.06(14)	O(3)-C(6)-H(6)	106.0(15)
O(3)-C(6)-C(7)	111.65(16)	C(5)-C(6)-H(6)	112.8(15)
C(7)-C(6)-C(5)	102.85(14)	C(7)-C(6)-H(6)	111.6(15)
C(8)-C(7)-C(6)	103.25(14)	C(9)-C(8)-C(7)	129.96(16)
C(9)-C(8)-C(13)	119.85(16)	C(13)-C(8)-C(7)	110.19(15)
C(8)-C(9)-C(10)	118.51(16)	C(11)-C(10)-C(9)	121.36(17)
C(10)-C(11)-C(12)	120.00(17)	C(13)-C(12)-C(11)	118.71(17)
C(8)-C(13)-C(5)	109.81(15)	C(12)-C(13)-C(5)	128.63(16)
C(12)-C(13)-C(8)	121.56(16)		

IX. References

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SM4

SM4

Mass to be matched (m/z): 270.084710 Charge: 1

Mass Tolerance: ± 0.005000

Restriction of atom numbers:

C	H	N	O	Na
1-100	1-100	1-3	max 10	1-1

Number of calculated Formulas: 3

Formula	Diff.(ppm)	theor. m/z
C12 H13 N3 O3 Na1	0.74	270.084910
C9 H15 N2 O6 Na1	-9.18	270.082231
C17 H13 N1 O1 Na1	15.64	270.088933

Datum 22.09.2020

Analyse: 149430c-00

Sigel: GHC-AA-030-01

COP: Dr. Clement Ghiazza

Messung: HRMS

Methode: ESIPos

Lösungsmittel: CH3OH

Spektrometer: Exactive

Auswerter: Kampen (2242)

Suggestion:

C12H13N3O3 MW 247

characteristical ion

270 = [247 + Na]⁺

Mass to be matched (m/z): 260.103220 Charge: 1

Mass Tolerance: ± 0.005000

Restriction of atom numbers:

C H N O
1-100 1-100 1-5 1-10

Number of calculated Formulas: 4

Formula	Diff.(ppm)	theor. m/z
C13 H14 N3 O3	-0.98	260.102966
C10 H16 N2 O6	-11.27	260.100287
C18 H14 N1 O1	14.49	260.106989
C8 H14 N5 O5	-16.44	260.098944

Datum: 1.10.2020

Analyse: 149625c-00

Sigel: GHC-AA-042-01

COP: Dr. Clement Ghiazza

Method: HR-MS

Ionis. : ESIPos

solvent : CH₂Cl₂ + CH₃OH

Spectrometer: Exactive

Auswerter: Marcus, Tel:2243

suggestion:

C₁₃H₁₃N₃O₃ MW: 259

Characteristic Ions:

260 = [259 + H]

Mass to be matched (m/z): 434.087680 Charge: 1

Mass Tolerance: ± 0.005000

Restriction of atom numbers:

C	H	Cl	N	O	Na
1-100	1-100	1-1	1-3	max 10	1-1

Number of calculated Formulas: 3

Formula	Diff. (ppm)	theor. m/z
C21 H18 Cl1 N3 O4 Na1	0.28	434.087803
C18 H20 Cl1 N2 O7 Na1	-5.89	434.085125
C26 H18 Cl1 N1 O2 Na1	9.55	434.091826

Datum 5.10.2020

Analyse: 149709c-00

Sigel: GHC-AA-044-01

COP: Dr. Clement Ghiazza

Messung: HRMS

Methode: ESIPos

Lösungsmittel: CH₂Cl₂+CH₃OH

Spektrometer: Exactive

Auswerter: Kampen (2242)

Suggestion:

C₂₁H₁₈Cl₁N₃O₄ MW 411

characteristical ion

434 = [411 + Na]⁺

Mass to be matched (m/z): 452.021330 Charge: 1

Mass Tolerance: ± 0.005000

Restriction of atom numbers:

C H N O Br Na
1-110 1-100 1-3 1-4 1-1 1-1
Number of calculated Formulas: 2

Formula	Diff. (ppm)	theor. m/z
C19 H16 N3 O4 Br1 Na1	0.71	452.021650
C24 H16 N1 O2 Br1 Na1	9.61	452.025673

09.10.2020

File: 149797b-00

Analyse: GHC-AA-059-01

COP: Dr. Clement Ghiazza

Messung: HRMS ESIPos

Lösemittel: CH3OH

Spektrometer: Exactive

Auswerter: Kohler (2243)

Suggestion:

C19H16N3O4Br1 Mw 429

Characteristicial ions:

452 = [429 + Na]+

Mass to be matched (m/z): 399.106750 Charge: 1

Mass Tolerance: ± 0.005000

Restriction of atom numbers:

C	H	N	O	Na
1-100	1-100	2-4	max 10	1-1

Number of calculated Formulas: 3

Formula	Diff.(ppm)	theor. m/z
C20 H16 N4 O4 Na1	-0.94	399.106374
C17 H18 N3 O7 Na1	-7.65	399.103695
C25 H16 N2 O2 Na1	9.14	399.110396

Datum 6.10.2020

Analyse: 149718b-00

Sigel: GHC-AA-049-01

COP: Dr. Clement Ghiazza

Messung: HRMS

Methode: ESIPos

Lösungsmittel: CH3OH

Spektrometer: Exactive

Auswerter: Kampen (2242)

Suggestion:

C20H16N4O4 MW 376

characteristical ion

399 = [376 + Na]⁺

Mass to be matched (m/z): 500.007860 Charge: 1

Mass Tolerance: ± 0.005000

Restriction of atom numbers:

C	H	I	N	O	Na
1-100	1-100	max 1	max 5	max 5	1-1

Number of calculated Formulas: 9

Formula	Diff.(ppm)	theor. m/z
C19 H16 I1 N3 O4 Na1	-0.18	500.007772
C34 H5 O4 Na1	0.29	500.008004
C32 H3 N3 O3 Na1	-2.40	500.006660
C21 H18 I1 O5 Na1	2.51	500.009116
C35 H1 N4 Na1	2.96	500.009339
C22 H14 I1 N4 O1 Na1	5.18	500.010451
C37 H3 N1 O1 Na1	5.65	500.010683
C24 H16 I1 N1 O2 Na1	7.87	500.011795
C28 H14 I1 Na1	-9.24	500.003241

Datum	5.10.2020
Analyse:	149697b-00

Sigel:	GHC-AA-043-01
COP:	Dr. Clement Ghiazza

Messung:	HRMS
Methode:	ESIpos
Lösungsmittel:	CH3OH
Spektrometer:	Exactive

Auswerter:	Kampen (2242)
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Assumed suggestion based on the reaction of previous samples: C19H16I1N3O4 MW 477

characteristical ion

500 = [477 + Na]⁺

Mass to be matched (m/z): 402.106620 Charge: 1

Mass Tolerance: ± 0.005000

Restriction of atom numbers:

C H N O Na

1-100 1-100 1-5 1-10 1-1

Number of calculated Formulas: 5

Formula	Diff.(ppm)	theor. m/z
C20 H17 N3 O5 Na1	-1.44	402.106040
C23 H15 N4 O2 Na1	5.22	402.108719
C17 H19 N2 O8 Na1	-8.10	402.103361
C25 H17 N1 O3 Na1	8.56	402.110063
C15 H17 N5 O7 Na1	-11.45	402.102018

Datum: 15.10.2020

Analyse: 149875c-00

Sigel: GHC-AA-063-01

COP: Dr. Clement Ghiazza

Method: HR-MS

Ionis. : ESIPos

solvent : CH3OH

Spectrometer: Exactive

Auswerter: Marcus, Tel:2243

suggestion:

C20H17N3O5 MW: 379

402 = [379 + Na]

Mass to be matched (m/z): 392.102070 Charge: 1

Mass Tolerance: ± 0.050000

Restriction of atom numbers:

C H N O Na F

1-100 1-100 1-3 1-4 1-1 1-1

Number of calculated Formulas: 13

Formula	Diff.(ppm)	theor. m/z
C19 H16 N3 O4 Na1 F1	-0.93	392.101704
C24 H16 N1 O2 Na1 F1	9.33	392.105726
C23 H14 N2 O2 Na1 F1	-22.75	392.093150
C20 H18 N2 O4 Na1 F1	31.14	392.114280
C23 H16 N3 O1 Na1 F1	37.97	392.116959
C22 H12 N3 O2 Na1 F1	-54.82	392.080574
C21 H20 N1 O4 Na1 F1	63.21	392.126856
C24 H18 N2 O1 Na1 F1	70.05	392.129535
C23 H12 N1 O3 Na1 F1	-83.47	392.069341
C20 H20 N3 O3 Na1 F1	91.86	392.138088
C25 H20 N1 O1 Na1 F1	102.12	392.142111
C22 H10 N2 O3 Na1 F1	-115.54	392.056765
C21 H22 N2 O3 Na1 F1	123.93	392.150665

2.10.2020

File: 149636c-00

Analysis: GHC-AA-040-01

COP: Dr. Clement Ghiazza

Messung: HR-MS
 Ionisierung: ESIpos
 Lösungsmittel: CH₂Cl₂ + CH₃OH
 Spektrometer: Exactive
 ELNA: 27611

Auswerter: Haupt (2243)

Suggestion:
 C19H16N3O4F1 MW: 369

 Characteristic ions:
 392 = [369 + Na]+

SM12

SM12

Mass to be matched (m/z): 375.106510 Charge: 1

Mass Tolerance: ± 0.005000

Restriction of atom numbers:

C H N O Na

1-100 1-100 1-5 1-10 1-1

Number of calculated Formulas: 5

Formula	Diff.(ppm)	theor. m/z
C18 H16 N4 O4 Na1	-0.36	375.106374
C20 H18 N1 O5 Na1	3.22	375.107718
C21 H14 N5 O1 Na1	6.78	375.109052
C15 H18 N3 O7 Na1	-7.50	375.103695
C23 H16 N2 O2 Na1	10.36	375.110396

Datum: 15.10.2020

Analyse: 149876c-00

Sigel: GHC-AA-064-01

COP: Dr. Clement Ghiazza

Method: HR-MS

Ionis. : ESIPos

solvent : CH3OH

Spectrometer: Exactive

Auswerter: Marcus, Tel:2243

suggestion:

C18H16N4O4 MW: 352

Characteristic Ions:

375 = [352 + Na]

Mass to be matched (m/z): 466.103980 Charge: 1

Mass Tolerance: ± 0.005000

Restriction of atom numbers:

C H N O S Na
1-110 1-100 1-3 1-6 1-1 1-1
Number of calculated Formulas: 2

Formula	Diff.(ppm)	theor. m/z
C21 H21 N3 O6 S1 Na1	0.75	466.104328
C26 H21 N1 O4 S1 Na1	9.38	466.108350

09.10.2020

File: 149779b-00

Analyse: GHC-AA-053-01

COP: Dr. Clement Ghiazza

Messung: HRMS ESIPos

Lösemittel: CH3OH

Spektrometer: Exactive

Auswerter: Kohler (2243)

Suggestion:

C21H21N3O6S1 MW 443

Characteristicial ions:

466 = [443 + Na]⁺

SM14

Mass to be matched (m/z): 454.110070 Charge: 1

Mass Tolerance: ± 0.005000

Restriction of atom numbers:

C H N O S Cl
1-100 1-100 1-5 1-10 1-1 1-1

Number of calculated Formulas: 5

Formula	Diff. (ppm)	theor. m/z
C22 H21 N5 O2 S1 Cl1	-0.38	454.109899
C24 H23 N2 O3 S1 Cl1	2.58	454.111243
C21 H25 N1 O6 S1 Cl1	-3.32	454.108564
C19 H23 N4 O5 S1 Cl1	-6.28	454.107220
C12 H27 N4 O10 S1 Cl1	6.66	454.113096

Datum: 29.10.2020

Analyse: 150158c-00

Sigel: GHC-GA-406-01

COP: Dr. Clement Ghiazza

Method: HR-MS

Ionis. : ESIPos

solvent : CH₂Cl₂ + CH₃OH

Spectrometer: Exactive

Auswerter: Marcus, Tel:2243

suggestion:

C₂₂H₂₀N₅O₂S₁Cl₁ MW: 453

Characteristic Ions:

454 = [453 + H]

SM16

-115.89
-115.99

1.00

140 120 100 80 60 40 20 0 -20 -40 -60 -80 -100 -120 -140 -160 -180 -200 -220 -240 -260 -280 -300 -320 -340
f1 (ppm)

100000
90000
80000
70000
60000
50000
40000
30000
20000
10000
0

Mass to be matched (m/z): 470.154860 Charge: 1

Mass Tolerance: ± 0.005000

Restriction of atom numbers:

C H N O S F
1-100 1-100 1-3 1-10 1-1 1-1

Number of calculated Formulas: 3

Formula	Diff. (ppm)	theor. m/z
C24 H25 N3 O4 S1 F1	-0.91	470.154432
C21 H27 N2 O7 S1 F1	-6.61	470.151753
C29 H25 N1 O2 S1 F1	7.65	470.158455

Datum: 25.02.2021

Analyse: 151917b-00

Sigel: GHC-GA-615-01

COP: Dr. Clement Ghiazza

Method: HR-MS

Ionis. : ESIPos

solvent : CH₂Cl₂ + CH₃OH

Spectrometer: Exactive

Auswerter: Marcus, Tel:2243

suggestion:

C₂₄H₂₄N₃O₄S₁F₁ MW: 469

Characteristic Ions:

470 = [469 + H]

60

63

10

Mass to be matched (m/z): 219.076560 Charge: 1

Mass Tolerance: ± 0.050000

Restriction of atom numbers:

C H N O
1-100 1-100 1-2 1-3

Number of calculated Formulas: 7

Formula	Diff. (ppm)	theor. m/z
C11 H11 N2 O3	-0.65	219.076417
C15 H9 N1 O1	-39.69	219.067864
C12 H13 N1 O3	56.75	219.088994
C14 H7 N2 O1	-97.10	219.055287
C12 H15 N2 O2	165.43	219.112802
C14 H5 N1 O2	-205.78	219.031479
C13 H17 N1 O2	222.84	219.125379

7.12.2020

File: 150859b-00

Analysis: GHC-GA-431-01

COP: Dr. Clement Ghiazza

Messung: HR-MS
Ionisierung: ESipos
Lösungsmittel: CH₂Cl₂
Spektrometer: Exactive
ELNA: 28796

Auswerter: Haupt (2243)

Suggestion:

[C11H11N2O3]+[BF4]- MW: 306

Characteristic ions:

219 = [306 - BF₄]+

Mass to be matched (m/z): 175.003070 Charge: 1

Mass Tolerance: ± 0.050000

Restriction of atom numbers:

C H N O Cl

1-100 1-100 1-2 1-3 1-2

Number of calculated Formulas: 12

Formula	Diff. (ppm)	theor. m/z
C6 H6 N1 O3 Cl1	0.01	175.003072
C3 H9 N2 O2 Cl2	2.79	175.003558
C5 H4 N2 O3 Cl1	-71.85	174.990495
C4 H11 N1 O2 Cl2	74.66	175.016135
C9 H2 N1 O1 Cl1	-120.73	174.981942
C3 H7 N1 O3 Cl2	-133.26	174.979750
C6 H8 N2 O2 Cl1	136.06	175.026880
C2 H5 N2 O3 Cl2	-205.12	174.967173
C7 H10 N1 O2 Cl1	207.92	175.039456
C4 H13 N2 O1 Cl2	210.70	175.039943
C6 H3 N1 O1 Cl2	-254.00	174.958620
C5 H15 N1 O1 Cl2	282.57	175.052520

8.07.2020

File: 147978b-00.raw

Analyse: GHC-GA-190-01

COP: Dr. Clement Ghiazza

Messung: GC-MS
Ionisierung: GC-EI
Spektrometer: Q Exactive GC Orbitrap
Säule: MS 75 ZB-5HT 30+5
Länge: 30+5
Temp.: 35-10-285-5
GC-Nr.: -
ELNA-Nr.: 25987

Auswerter: Haupt (2243)

Suggestion:

C6H6N1O3Cl1 MW:175

Mass to be matched (m/z): 128.026220 Charge: 1

Mass Tolerance: ± 0.005000

Restriction of atom numbers:

C H Cl N
1-100 1-100 1-1 1-3

Number of calculated Formulas: 1

Formula	Diff.(ppm)	theor. m/z
C6 H7 Cl1 N1	-0.53	128.026152

Datum 20.07.2020

Analyse: 148239c-00

Sigel: GOA-GA-386-01

COP: Dr. Gomez, Alejandro

Messung: HRMS

Methode: ESIPos

Lösungsmittel: CH3CN

Spektrometer: Exactive

Auswerter: Kampen (2242)

Suggestion:

C6H6Cl1N1 MW 127

characteristical ion

128 = [127 + H]⁺

Mass to be matched (m/z): 147.971520 Charge: 1

Mass Tolerance: ± 0.005000
Restriction of atom numbers:

C H N Cl
1-110 1-100 1-3 1-2

Number of calculated Formulas: 1

Formula	Diff.(ppm)	theor. m/z
C5 H4 N1 Cl2	0.06	147.971530

15.06.2020

File: 147522b-00

Analyse: GOA-GA-332-01

COP: Dr. Gomez, Alejandro

Messung: HRMS ESIPos

Lösemittel: CH3OH

Spektrometer: Exactive

Auswerter: Kohler (2243)

Suggestion:

C5H3N1Cl2 MW 147

Characteristicial ions:

148 = [147 + H]⁺

Mass to be matched (m/z): 191.037120 Charge: 1

Mass Tolerance: ± 0.005000
Restriction of atom numbers:

C H N Cl
1-110 1-100 1-3 1-2

Number of calculated Formulas: 1

Formula	Diff.(ppm)	theor. m/z
C10 H8 N2 Cl1	-0.36	191.037050

Suggestion:

[C10H8N2Cl1]⁺ [BF4]⁻ MW 278

Characteristicial ions:

191 = [278 - BF4]⁺

No.	MW.	Comment
1	171	Your proposed structure is possible. Heteroatoms: 1 Cl Ref.-spectrum: U22331:148235a-00 GOA-GA-395-01

20.07.2020
File: 148235a-00.raw
Analyse: GOA-GA-395-01
COP: Dr. Gomez, Alejandro

Messung: GC-MS
Ionisierung: GC-EI
Spektrometer: ISQ Series
Säule: MS 84 TG-5 SILMS
Länge: 30
Temp.: 35-5-285-5
GC-Nr.: -
ELNA-Nr.: 26231

Auswerter: Haupt (2243)

U22331 27% MW:171/171.58 C7H6Cl1N1O2 148235a-00 GOA-GA-395-01

36	0.17	60	1.09	87	1.56	108	0.05	138	0.01
37	0.85	61	2.05	88	0.30	109	0.05	139	0.08
38	1.33	62	2.31	89	0.06	110	0.15	140	10.08
39	0.92	63	1.04	90	0.14	111	0.70	141	27.46
41	0.05	64	1.25	91	0.07	112	50.38	142	5.18
42	0.45	65	2.82	92	1.73	113	100.00	143	8.78
43	0.03	66	0.55	93	0.18	114	21.55	144	0.62
44	0.03	67	0.13	94	0.12	115	32.10	145	0.04
45	0.09	68	0.02	95	0.02	116	1.89	153	0.01
46	0.01	69	0.03	96	0.07	117	0.06	155	0.01
48	0.12	70	0.01	97	0.03	121	0.01	156	0.03
50	12.18	71	0.14	98	0.04	122	0.01	158	0.01
51	4.19	72	0.37	99	0.25	126	0.15	167	0.02
52	0.50	73	0.92	100	0.24	127	0.29	170	0.04
53	0.55	74	0.76	101	0.16	128	0.08	171	3.38
54	0.16	75	5.72	102	0.12	129	0.08	172	0.29
55	0.06	76	33.76	103	0.06	130	0.01	173	1.08
56	0.15	77	6.89	104	0.06	131	0.02	174	0.07
57	0.07	78	10.24	105	0.52	133	0.68		
58	0.05	81	0.02	106	0.01	134	0.82		
59	4.24	85	4.49	107	0.01	135	0.05		

U22331 27% MW:171/171.58 C7H6Cl1N1O2 148235a-00 GOA-GA-395-01

16

34	0.43	59	0.74	82	0.81	107	0.94	130	0.80	157	3.84	182	0.40
36	0.28	60	0.71	85	6.13	108	0.15	131	1.31	159	0.36	183	3.99
37	1.38	61	1.09	86	2.64	110	0.16	132	2.01	161	0.31	184	0.54
38	0.82	62	1.78	87	2.40	111	0.57	133	0.40	162	0.49	185	1.07
39	3.90	63	1.52	89	0.23	112	22.48	136	1.98	163	0.35	186	0.05
41	2.50	64	3.95	90	0.86	113	100.00	137	0.82	164	0.16	187	0.14
42	2.24	65	1.57	91	1.04	114	15.21	138	0.50	165	0.70	192	0.11
43	1.42	66	1.10	92	1.79	115	30.85	139	5.05	166	0.83	195	0.82
44	4.75	67	1.24	93	0.01	116	3.57	140	14.18	167	62.70	196	1.91
45	0.05	68	1.06	95	0.21	117	0.36	141	52.16	168	10.16	197	29.94
46	0.23	69	1.38	96	0.68	118	2.11	142	9.81	169	23.89	198	36.09
48	2.67	70	0.13	97	0.28	119	0.79	143	17.78	170	7.59	199	12.14
50	6.46	72	0.22	98	0.44	121	0.50	144	0.89	171	1.64	200	13.16
51	3.77	73	1.16	99	1.38	122	0.50	145	0.72	172	1.02	201	0.86
52	2.08	74	0.08	100	0.23	123	0.17	149	0.32	173	0.27	202	0.11
53	1.50	75	1.63	101	0.86	124	0.01	150	0.40	174	0.23		
54	2.46	76	20.18	102	0.95	125	0.33	152	1.61	176	0.34		
55	2.21	77	3.17	103	0.73	126	1.63	153	26.34	178	0.37		
56	3.37	78	28.82	104	0.76	127	3.28	154	5.01	179	4.70		
57	3.11	79	3.07	105	1.45	128	1.73	155	16.39	180	0.37		
58	1.83	80	0.77	106	2.45	129	1.35	156	2.56	181	2.30		

U22277 14% MW:198/198.65 C₉H₁₁ClN₂O 148066a-00 GHC-GA-167-01

U22337 17% MW:158/158.54 C5H3Cl1N2O2 148237a-00 GOA-GA-389-01

34	0.03	55	0.32	78	0.58	99	0.51	127	0.08	157	0.27
35	0.49	56	0.03	79	0.21	100	29.79	128	4.32	158	69.85
36	1.16	59	0.16	80	0.13	101	1.79	129	0.31	159	4.41
37	5.41	60	2.70	81	0.05	102	9.47	130	1.34	160	22.59
38	5.89	61	2.81	82	0.01	103	0.63	131	0.08	161	1.37
39	2.54	62	5.56	83	0.32	104	0.05	133	0.04	162	0.12
40	0.55	63	4.04	84	3.01	105	0.04	134	0.06		
41	0.20	64	4.69	85	49.41	108	0.01	135	0.01		
42	0.08	65	0.99	86	4.60	109	0.13	137	0.03		
43	0.06	66	0.51	87	15.96	110	0.26	138	0.08		
44	0.21	67	0.21	88	1.23	111	1.00	139	0.01		
45	0.07	68	0.06	89	0.11	112	100.00	140	0.05		
46	1.98	69	0.03	90	0.08	113	6.22	141	1.23		
47	2.05	70	0.01	91	0.05	114	31.62	142	1.35		
48	1.39	71	0.29	92	0.42	115	1.78	143	0.49		
49	9.20	72	1.11	93	0.55	116	0.05	144	0.45		
50	40.60	73	7.39	94	0.11	119	0.01	145	0.03		
51	17.05	74	2.30	95	0.21	122	0.01	146	0.01		
52	4.50	75	13.50	96	0.05	123	0.08	153	0.01		
53	0.42	76	63.17	97	0.09	125	0.01	154	0.01		
54	0.11	77	8.29	98	0.24	126	0.03	156	0.02		

U22337 17% MW:158/158.54 C5H3Cl1N2O2 148237a-00 GOA-GA-389-01

Mass to be matched (m/z): 139.005770 Charge: 1

Mass Tolerance: ± 0.005000

Restriction of atom numbers:

C H N Cl
1-110 1-100 1-3 1-2

Number of calculated Formulas: 1

Formula	Diff.(ppm)	theor. m/z
C6 H4 N2 Cl1	-0.14	139.005750

15.06.2020

File: 147526b-00

Analyse: GOA-GA-337-01

COP: Dr. Gomez, Alejandro

Messung: HRMS ESipos

Lösemittel: CH3OH

Spektrometer: Exactive

Auswerter: Kohler (2243)

Suggestion:

C6H3N2Cl1 MW 138

Characteristicial ions:

139 = [138 + H]⁺

Mass to be matched (m/z): 182.071430 Charge: 1

Mass Tolerance: ± 0.005000

Restriction of atom numbers:

C H N Cl
1-110 1-100 1-3 1-2

Number of calculated Formulas: 1

Formula	Diff.(ppm)	theor. m/z
Cl10 H13 N1 Cl1	9.18	182.073102

Suggestion:

[Cl10H13N1Cl1]⁺ [BF4]⁻ MW 269

Characteristicial ions:

182 = [269 - BF4]⁺

33	0.02	60	2.76	96	0.12	153	0.31
34	1.44	61	0.71	105	7.54		
35	0.03	62	4.09	106	0.87		
36	0.04	63	0.22	111	0.02		
37	0.09	64	0.88	113	100.00		
38	0.20	65	0.03	114	4.70		
39	0.20	73	0.29	115	30.17		
40	0.09	74	0.13	116	1.44		
41	0.11	75	0.02	117	0.12		
42	0.25	76	0.08	119	0.03		
43	1.06	77	1.97	120	3.22		
44	0.85	78	0.32	121	0.11		
45	0.38	79	0.54	122	0.24		
46	0.11	82	0.04	125	0.00		
47	1.14	84	0.18	131	0.01		
48	0.14	85	0.77	147	0.02		
49	3.89	86	25.19	148	77.49		
50	0.36	87	2.53	149	3.59		
51	0.14	88	8.70	150	46.88		
52	1.00	89	0.66	151	2.18		
53	0.17	95	3.99	152	7.86		

Mass to be matched (m/z): 147.959150 Charge: 1

Mass Tolerance: ± 0.005000

Restriction of atom numbers:

C H N Cl

1-110 1-100 1-2 2-2

Number of calculated Formulas: 1

Formula	Diff.(ppm)	theor. m/z
C4 H2 N2 Cl2	-1.33	147.958954

18.01.2021

File: 151244a-00.raw

Analyse: GHC-GA-535-01

COP: Dr. Clement Ghiazza

Messung:	GC-MS
Ionisierung:	GC EI
Spektrometer:	QExactiveGC
Säule:	MS 50 RTX1+VS
Länge:	30+7
Temp.:	35-10-285-5
GC-Nr.:	-
MS-Nr.:	29197

Auswerter: Margold (2242)

Mass to be matched (m/z): 190.029520 Charge: 1

Mass Tolerance: ± 0.050000

Restriction of atom numbers:

C H N Cl
1-100 1-100 1-2 1-2

Number of calculated Formulas: 4

Formula	Diff.(ppm)	theor. m/z
C10 H7 N2 C11	-1.55	190.029225
C8 H10 N1 C12	-58.10	190.018480
C11 H9 N1 C11	64.63	190.041802
C7 H8 N2 C12	-124.28	190.005903

2.10.2020

File: 149660b-00.raw

Analyse: GHC-GA-361-01

COP: Dr. Clement Ghiazza

Messung: GC-MS
Ionisierung: GC-EI
Spektrometer: Q Exactive GC Orbitrap
Säule: MS 50 TX1+VS
Länge: 30+7
Temp.: 35-10-285-5
GC-Nr.: -
ELNA-Nr.: 27638

Auswerter: Haupt (2243)

Suggestion:
C10H7N2C11 MW: 190

Mass to be matched (m/z): 148.966910 Charge: 1

Mass Tolerance: ± 0.020000

Restriction of atom numbers:

C H N Cl
1-100 1-100 1-5 2-2

Number of calculated Formulas: 3

Formula	Diff.(ppm)	theor. m/z
C4 H3 N2 Cl2	-0.88	148.966778
C5 H5 N1 Cl2	83.54	148.979354
C3 H1 N3 Cl2	-85.31	148.954202

Datum: 3.08.2020

Analyse: 148468c-00

Sigel: GHC-GA-251-01

COP: Dr. Clement Ghiazza

Method: HR-MS

Ionis. : ESIPos

solvent : CH₂Cl₂ + CH₃OH

Spectrometer: Exactive

Auswerter: Marcus, Tel:2243

suggestion:

C₄H₂N₂Cl₂ MW: 148

Characteristic Ions:

149 = [148 + H]

24

24

Mass to be matched (m/z): 262.975020 Charge: 1

Mass Tolerance: ± 0.050000

Restriction of atom numbers:

C H N O Na Cl

1-100 1-100 1-2 1-3 1-1 1-2

Number of calculated Formulas: 11

Formula	Diff.(ppm)	theor. m/z
C10 H6 N2 O1 Na1 Cl2	-0.31	262.974938
C13 H3 N1 O2 Na1 Cl1	-2.17	262.974451
C11 H8 N1 O1 Na1 Cl2	47.51	262.987514
C12 H1 N2 O2 Na1 Cl1	-49.99	262.961875
C7 H10 N2 O3 Na1 Cl2	80.04	262.996068
C13 H5 N2 O1 Na1 Cl1	88.37	262.998260
C10 H4 N1 O2 Na1 Cl2	-90.85	262.951129
C8 H12 N1 O3 Na1 Cl2	127.86	263.008644
C14 H7 N1 O1 Na1 Cl1	136.19	263.010836
C9 H2 N2 O2 Na1 Cl2	-138.67	262.938552
C10 H9 N2 O3 Na1 Cl1	168.72	263.019389

18.08.2020

File: 148735f-00

Analysis: GHC-GA-210-01

COP: Dr. Clement Ghiazza

Messung: HR-MS
Ionisierung: ESIpos
Lösungsmittel: CH₂Cl₂ + CH₃OH
Spektrometer: Exactive
ELNA: 26714

Auswerter: Haupt (2243)

Suggestion:
C₁₀H₆N₂O₁Cl₂ MW: 240
Characteristic ions:
263 = [240 + Na⁺]

Mass to be matched (m/z): 183.043180 Charge: 1

Mass Tolerance: ± 0.005000

Restriction of atom numbers:

C H Cl N
1-100 1-100 1-1 2-4

Number of calculated Formulas: 1

Formula	Diff.(ppm)	theor. m/z
C7 H8 Cl1 N4	0.10	183.043198

Datum 24.07.2020

Analyse: 148346c-00

Sigel: GHS-GA-224-01

LIS: Dr. Gosh, Santanu

Messung: HRMS

Methode: ESIPos

Lösungsmittel: CH₂Cl₂+CH₃OH

Spektrometer: Exactive

Auswerter: Kampen (2242)

Suggestion:

C₇H₇Cl₁N₄ MW 182

characteristical ion

183 = [182 + H]⁺

OE1052 51% MW:153/153.57 C₆H₄ClN₃

36	0.01	64	4.17	91	10.44	136	0.15
37	0.51	65	0.87	92	7.12	152	0.06
38	0.48	66	0.86	93	0.38	153	100.00
39	0.45	67	0.02	96	0.15	154	7.30
40	0.10	71	0.04	97	0.93	155	30.85
41	0.10	72	1.18	98	0.60	156	2.21
44	0.38	73	0.23	99	1.43	157	0.04
45	0.01	74	0.49	100	0.37		
47	0.09	75	0.18	101	0.42		
48	0.12	76	0.21	102	0.06		
49	0.15	79	0.12	104	0.04		
50	0.16	81	0.93	112	0.04		
52	0.09	82	1.79	117	0.11		
54	0.06	83	0.05	118	8.13		
55	0.02	84	0.02	119	0.54		
56	0.01	85	0.04	124	0.01		
59	0.01	86	0.10	125	0.40		
60	0.03	87	0.09	126	2.97		
61	0.44	88	0.06	127	0.29		
62	1.06	89	0.05	128	0.91		
63	2.68	90	0.25	129	0.04		

OE1052 51% MW:153/153.57 C₆H₄ClN₃

Mass to be matched (m/z): 153.008950 Charge: 1

Mass Tolerance: ±0.005000

Restriction of atom numbers:

C H N Cl
1-110 1-100 1-3 1-1

Number of calculated Formulas: 1

Formula	Diff.(ppm)	theor. m/z
C ₆ H ₄ N ₃ Cl ₁	-0.82	153.008824

9.10.2020

File: 149786a-00.raw

Analyse: GHC-GA-372-01

COP: Dr. Clement Ghiazza

Messung:	GC-MS
Ionisierung:	GC-EI
Spektrometer:	QExactiveGC
Säule:	MS 50 TX1+VS
Länge:	30+7
Temp.:	35-10-285-5
GC-Nr.:	-

Auswerter: Margold

28

28

Mass to be matched (m/z): 153.009070 Charge: 1

Mass Tolerance: ± 0.005000

Restriction of atom numbers:

C H N Cl
1-110 1-100 1-3 1-2

Number of calculated Formulas: 2

Formula	Diff.(ppm)	theor. m/z
C6 H4 N3 Cl1	-1.61	153.008824
C5 H9 N1 Cl2	10.36	153.010655

7.10.2020

File: 149750a-00.raw

Analyse: GHC-GA-370-01

COP: Dr. Clement Ghiazza

Messung: GC-MS
Ionisierung: GC-EI
Spektrometer: QExactiveGC
Säule: MS 50 TX1+VS
Länge: 30+7
Temp.: 35-10-285-5
GC-Nr.: -

Auswerter: Margold

29

Mass to be matched (m/z): 252.957470 Charge: 1

Mass Tolerance: ± 0.005000

Restriction of atom numbers:

C	H	N	O	S	Cl	F
1-100	1-100	1-5	1-10	1-1	1-1	3-3

Number of calculated Formulas: 2

Formula	Diff. (ppm)	theor. m/z
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C8 H3 N1 O1 S1 Cl1 F3	-1.66	252.957050
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C3 H3 N3 O3 S1 Cl1 F3	-17.56	252.953027
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Datum: 6.08.2020

Analyse: 148532c-00

Sigel: GHC-GA-262-01

COP: Dr. Clement Ghiazza

Method: HR-MS

Ionis. : GC-EI

Spectrometer: Q-Exactive

Auswerter: Marcus, Tel:2243

suggestion:

C8H3N1O1S1Cl1F3 MW: 253

31

31

Mass to be matched (m/z): 214.967750 Charge: 1

Mass Tolerance: ± 0.005000

Restriction of atom numbers:

C H N O S Cl
1-100 1-100 1-5 1-10 1-1 1-1

Number of calculated Formulas: 4

Formula	Diff.(ppm)	theor. m/z
C7 H4 N2 O2 S1 Cl1	-0.45	214.967653
C5 H2 N5 O1 S1 Cl1	-6.70	214.966309
C4 H6 N1 O5 S1 Cl1	-12.91	214.964974
C2 H4 N4 O4 S1 Cl1	-19.16	214.963631

Datum: 24.07.2020

Analyse: 148347c-00

Sigel: GHC-GA-192-01

COP: Dr. Clement Ghiazza

Method: HR-MS

Ionis. : ESIPos

solvent : CH₂Cl₂ + CH₃OH

Spectrometer: Exactive

Auswerter: Marcus, Tel:2243

suggestion:

C₇H₃N₂O₂S₁Cl₁ MW: 214

Characteristic Ions:

215 = [214 + H]

32a, major

32a, major

32b, *minor*

32b, minor

Mass to be matched (m/z): 256.975680 Charge: 1

Mass Tolerance: ± 0.020000

Restriction of atom numbers:

C	H	N	O	S	Cl	Na
1-100	1-100	1-5	1-3	1-1	1-1	1-1

Number of calculated Formulas: 6

Formula	Diff.(ppm)	theor. m/z
C7 H7 N2 O3 S1 Cl1 Na1	0.51	256.975812
C5 H5 N5 O2 S1 Cl1 Na1	-4.72	256.974468
C11 H5 N1 O1 S1 Cl1 Na1	-32.77	256.967258
C6 H7 N4 O2 S1 Cl1 Na1	44.22	256.987044
C6 H5 N3 O3 S1 Cl1 Na1	-48.43	256.963236
C8 H9 N1 O3 S1 Cl1 Na1	49.45	256.988388

Datum: 22.07.2020

Analyse: 148260c-00

Sigel: GHC-GA-209-02

COP: Dr. Clement Ghiazza

Method: HR-MS

Ionis. : ESIPos

solvent : CH₂Cl₂ + CH₃OH

Spectrometer: Exactive

Auswerter: Marcus, Tel:2243

suggestion:

C₇H₇N₂O₃S₁Cl₁ MW: 234

Characteristic Ions:

257 = [234 + Na]

Mass to be matched (m/z): 453.038660 Charge: 1

Mass Tolerance: ± 0.005000

Restriction of atom numbers:

C H N O Cl Na
1-100 1-100 1-5 1-10 2-2 1-1

Number of calculated Formulas: 6

Formula	Diff. (ppm)	theor. m/z
C21 H16 N2 O4 Cl2 Na1	-1.61	453.037932
C24 H14 N3 O1 Cl2 Na1	4.31	453.040611
C19 H14 N5 O3 Cl2 Na1	-4.57	453.036589
C18 H18 N1 O7 Cl2 Na1	-7.52	453.035253
C12 H18 N5 O8 Cl2 Na1	8.40	453.042464
C16 H16 N4 O6 Cl2 Na1	-10.49	453.033910

Datum: 15.10.2020

Analyse: 149874c-00

Sigel: GHC-AA-058-01

COP: Dr. Clement Ghiazza

Method: HR-MS

Ionis. : ESIPos

solvent : CH3OH

Spectrometer: Exactive

Auswerter: Marcus, Tel:2243

suggestion:

C21H16N2O4Cl2 MW: 430

Characteristic Ions:

453 = [430 + Na]

Mass to be matched (m/z): 470.972260 Charge: 1

Mass Tolerance: ± 0.005000

Restriction of atom numbers:

C	H	N	O	Br	Cl	Na
1-100	1-100	1-5	1-10	1-1	1-1	1-1

Number of calculated Formulas: 6

Formula	Diff. (ppm)	theor. m/z
C19 H14 N2 O4 Br1 Cl1 Na1	-1.02	470.971780
C17 H12 N5 O3 Br1 Cl1 Na1	-3.87	470.970436
C22 H12 N3 O1 Br1 Cl1 Na1	4.67	470.974458
C16 H16 N1 O7 Br1 Cl1 Na1	-6.71	470.969101
C10 H16 N5 O8 Br1 Cl1 Na1	8.60	470.976311
C14 H14 N4 O6 Br1 Cl1 Na1	-9.56	470.967757

Datum: 15.10.2020

Analyse: 149897d-00

Sigel: GHC-AA-061-01

COP: Dr. Clement Ghiazza

Method: HR-MS

Ionis. : ESIPos

solvent : CH3OH

Spectrometer: Exactive

Auswerter: Marcus, Tel:2243

suggestion:

C19H14N2O4Br1Cl1 MW: 448

Characteristic Ions:

471 = [448 + Na]

Mass to be matched (m/z): 418.056640 Charge: 1

Mass Tolerance: ± 0.005000

Restriction of atom numbers:

C H N O Cl Na
1-110 1-100 1-3 1-4 1-2 1-1
Number of calculated Formulas: 4

Formula	Diff. (ppm)	theor. m/z
C20 H14 N3 O4 Cl1 Na1	-0.33	418.056503
C19 H19 N1 O4 Cl2 Na1	4.05	418.058334
C25 H14 N1 O2 Cl1 Na1	9.29	418.060526
C22 H17 N2 O1 Cl2 Na1	10.46	418.061013

13.10.2020

File: 149822c-00

Analyse: GHC-AA-056-01

COP: Dr. Clement Ghiazza

Messung: HRMS ESIPos

Lösemittel: CH3OH

Spektrometer: Exactive

Auswerter: Kohler (2243)

Suggestion:

C20h14N3O4Cl1 MW 395

Characteristicial ions:

418 = [395 + Na]⁺

Mass to be matched (m/z): 518.957980 Charge: 1

Mass Tolerance: ± 0.005000

Restriction of atom numbers:

C	H	N	O	Cl	I	Na
1-100	1-100	1-5	1-10	1-1	1-1	1-1

Number of calculated Formulas: 6

Formula	Diff.(ppm)	theor. m/z
C19 H14 N2 O4 Cl1 I1 Na1	-0.15	518.957902
C17 H12 N5 O3 Cl1 I1 Na1	-2.74	518.956558
C22 H12 N3 O1 Cl1 I1 Na1	5.01	518.960581
C16 H16 N1 O7 Cl1 I1 Na1	-5.31	518.955223
C14 H14 N4 O6 Cl1 I1 Na1	-7.90	518.953879
C10 H16 N5 O8 Cl1 I1 Na1	8.58	518.962433

Datum: 30.10.2020

Analyse: 150172c-00

Sigel: GHC-AA-051-01

COP: Dr. Clement Ghiazza

Method: HR-MS

Ionis. : ESipos

solvent : CH3OH

Spectrometer: Exactive

Auswerter: Marcus, Tel:2243

suggestion:

C19H14N2O4I1Cl1 MW: 496

Characteristic Ions:

519 = [496 + Na]

Mass to be matched (m/z): 421.056580 Charge: 1

Mass Tolerance: ± 0.005000

Restriction of atom numbers:

C	H	N	O	Cl	Na
1-100	1-100	1-5	1-10	1-1	1-1

Number of calculated Formulas: 6

Formula	Diff. (ppm)	theor. m/z
C20 H15 N2 O5 Cl1 Na1	-0.98	421.056169
C18 H13 N5 O4 Cl1 Na1	-4.17	421.054826
C23 H13 N3 O2 Cl1 Na1	5.39	421.058848
C17 H17 N1 O8 Cl1 Na1	-7.34	421.053491
C11 H17 N5 O9 Cl1 Na1	9.79	421.060700
C15 H15 N4 O7 Cl1 Na1	-10.53	421.052147

Datum: 15.10.2020

Analyse: 149877c-00

Sigel: GHC-AA-065-01

COP: Dr. Clement Ghiazza

Method: HR-MS

Ionis. : ESIPos

solvent : CH3OH

Spectrometer: Exactive

Auswerter: Marcus, Tel:2243

suggestion:

C20H15N2O5Cl1 MW: 398

Characteristic Ions:

421 = [398 + Na]

Mass to be matched (m/z): 411.052650 Charge: 1

Mass Tolerance: ± 0.005000

Restriction of atom numbers:

C	H	N	O	Cl	F	Na
1-100	1-100	1-5	1-10	1-1	1-1	1-1

Number of calculated Formulas: 6

Formula	Diff.(ppm)	theor. m/z
C19 H14 N2 O4 Cl1 F1 Na1	-1.99	411.051833
C22 H12 N3 O1 Cl1 F1 Na1	4.53	411.054512
C17 H12 N5 O3 Cl1 F1 Na1	-5.26	411.050489
C16 H16 N1 O7 Cl1 F1 Na1	-8.50	411.049154
C10 H16 N5 O8 Cl1 F1 Na1	9.04	411.056364
C14 H14 N4 O6 Cl1 F1 Na1	-11.77	411.047810

Datum: 15.10.2020

Analyse: 149871c-00

Sigel: GHC-AA-048-01

COP: Dr. Clement Ghiazza

Method: HR-MS

Ionis. : ESIPos

solvent : CH3OH

Spectrometer: Exactive

Auswerter: Marcus, Tel:2243

suggestion:

c19H14N2O4Cl1F1 MW: 388

Characteristic Ions:

411 = [388 + Na]

Mass to be matched (m/z): 394.056660 Charge: 1

Mass Tolerance: ± 0.005000

Restriction of atom numbers:

C H N O Cl Na
1-100 1-100 1-5 1-10 1-1 1-1

Number of calculated Formulas: 5

Formula	Diff. (ppm)	theor. m/z
C18 H14 N3 O4 Cl1 Na1	-0.40	394.056503
C21 H12 N4 O1 Cl1 Na1	6.40	394.059182
C15 H16 N2 O7 Cl1 Na1	-7.20	394.053824
C23 H14 N1 O2 Cl1 Na1	9.81	394.060526
C13 H14 N5 O6 Cl1 Na1	-10.61	394.052481

Datum: 15.10.2020

Analyse: 149898c-00

Sigel: GHC-AA-066-01

COP: Dr. Clement Ghiazza

Method: HR-MS

Ionis. : ESIPos

solvent : CH3OH

Spectrometer: Exactive

Auswerter: Marcus, Tel:2243

suggestion:

C18H14N3O4Cl1 MW: 371

Characteristic Ions:

394 = [371 + Na]

Mass to be matched (m/z): 485.055210 Charge: 1

Mass Tolerance: ± 0.005000

Restriction of atom numbers:

C	H	N	O	S	Cl	Na
1-100	1-100	1-5	1-10	1-1	1-1	1-1

Number of calculated Formulas: 6

Formula	Diff. (ppm)	theor. m/z
C21 H19 N2 O6 S1 Cl1 Na1	-1.55	485.054457
C24 H17 N3 O3 S1 Cl1 Na1	3.97	485.057135
C19 H17 N5 O5 S1 Cl1 Na1	-4.32	485.053113
C18 H21 N1 O9 S1 Cl1 Na1	-7.08	485.051778
C12 H21 N5 O10 S1 Cl1 Na1	7.79	485.058988
C16 H19 N4 O8 S1 Cl1 Na1	-9.85	485.050434

Datum: 15.10.2020

Analyse: 149873c-00

Sigel: GHC-AA-057-01

COP: Dr. Clement Ghiazza

Method: HR-MS

Ionis. : ESIPos

solvent : CH3OH

Spectrometer: Exactive

Auswerter: Marcus, Tel:2243

suggestion:

C21H19N2O6S1Cl1 MW: 462

Characteristic Ions:

485 = [462 + Na]

Mass to be matched (m/z): 133.970270 Charge: 1

Mass Tolerance: ± 0.050000

Restriction of atom numbers:

C H N Cl S
1-100 1-100 1-2 1-2 1-1

Number of calculated Formulas: 3

Formula	Diff. (ppm)	theor. m/z
C3 H3 N2 Cl1 S1	-2.03	133.969998
C1 H6 N1 Cl2 S1	-82.24	133.959252
C4 H5 N1 Cl1 S1	91.84	133.982574

Suggestion:
C3H3N2Cl1S1 MW: 134

8.07.2020

File: 147977c-00.raw

Analyse: GHC-GA-191-01

COP: Dr. Clement Ghiazza

Messung: GC-MS
Ionisierung: GC-EI
Spektrometer: Q Exactive GC Orbitrap
Säule: MS 75 ZB-5HT 30+5
Länge: 30+5
Temp.: 35-10-285-5
GC-Nr.: -
ELNA-Nr.: 25986

Auswerter: Haupt (2243)

No.	MW.	Comment
1	180	Your proposed structure is possible Heteroatoms: Cl1
2	222	Ref.-Spektr. Nr. OU1563: Compare NJ232760:1,3,4-Oxadiazole, 2,5-diphenyl- Overlapping with MW:242, Unknown structure, Heteroatoms: Cl1

6.10.2020

File: 149714a-00.raw

Analyse: GHC-GA-366-01

COP: Dr. Clement Ghiazza

Messung: GC-MS
 Ionisierung: GC-EI
 Spektrometer: QExactiveGC
 Säule: MS 50 TX1+VS
 Länge: 30+7
 Temp.: 35-10-285-5
 GC-Nr.: -

Auswerter: Margold

OU1563 19% MW:180/180.59 C8H5Cl1N2O1									
34	0.06	61	0.68	87	1.32	116	0.08	149	0.03
35	0.06	62	2.30	88	0.58	117	16.56	150	0.03
36	0.03	63	8.35	89	46.00	118	1.41	157	0.03
37	0.15	64	0.63	90	4.18	119	0.06	169	0.03
38	0.29	65	1.02	91	0.26	121	0.04	180	89.25
39	1.04	66	0.28	92	0.03	123	0.17	181	7.94
40	0.10	67	0.03	93	0.03	124	100.00	182	28.41
41	0.06	69	0.03	94	0.03	125	7.30	183	2.29
42	0.03	70	0.10	95	1.30	126	30.94	184	0.04
43	0.03	73	0.43	96	0.06	127	2.22		
44	0.20	74	1.57	97	0.06	128	0.08		
46	0.06	75	2.01	99	0.12	129	0.03		
47	0.38	76	7.41	100	0.12	130	0.15		
48	0.06	77	74.93	102	0.37	135	0.03		
49	0.34	78	4.74	103	19.45	138	0.06		
50	4.68	79	0.07	104	1.48	139	0.04		
51	1.75	80	0.06	105	14.46	144	0.06		
52	0.18	83	0.03	106	1.07	145	38.12		
54	0.03	84	0.05	109	0.03	146	3.53		
56	0.03	85	0.46	110	0.06	147	0.08		
60	0.07	86	1.13	112	0.03	148	0.03		

OU1563 19% MW:180/180.59 C8H5Cl1N2O1

2

33	0.01	57	0.03	87	0.19	117	0.09	152	0.15	191	0.06	222	59.98
34	0.03	58	0.01	88	0.14	118	0.08	153	0.01	192	0.01	223	9.30
35	0.02	59	0.02	89	3.38	119	0.13	157	0.01	193	0.34	224	0.61
36	0.04	60	0.01	90	0.75	121	0.01	162	0.09	194	0.10	232	0.01
37	0.07	61	0.12	91	0.31	124	0.01	163	1.41	196	0.00	237	0.00
38	0.12	62	0.43	92	0.04	125	0.10	164	4.03	200	0.00	238	0.00
39	0.34	63	1.87	95	0.88	126	0.08	165	100.00	201	0.00	240	0.01
40	0.04	64	0.30	99	0.11	127	0.08	166	25.92	202	0.02	241	1.34
44	2.75	65	0.05	100	0.07	128	0.07	167	4.09	204	0.00	242	2.67
45	0.03	66	0.10	101	0.02	129	1.15	168	0.25	205	0.36	243	0.79
46	0.03	72	0.00	102	0.26	130	0.27	170	0.00	206	0.12	244	0.86
47	0.01	73	0.08	103	11.72	131	0.09	172	0.00	207	5.67	245	0.12
48	0.01	74	0.78	104	18.75	133	0.07	174	0.00	208	0.93	249	0.00
49	0.06	75	1.04	105	36.93	135	0.27	175	0.01	209	0.20	250	0.01
50	2.34	76	5.36	106	2.76	137	0.02	176	0.11	213	0.00		
51	1.38	77	37.99	107	0.16	138	0.06	177	0.13	214	0.01		
52	0.14	78	2.82	111	0.72	139	0.80	178	0.35	215	0.09		
53	0.05	79	0.07	113	0.10	140	0.09	179	0.14	216	0.00		
54	0.02	82	0.00	114	0.02	141	0.01	180	2.82	217	0.01		
55	0.01	85	0.05	115	0.50	143	0.01	181	0.63	218	0.00		
56	0.01	86	0.22	116	0.05	151	0.15	182	0.04	221	0.10		

R4: 1268(23:25) m(1264-1275) 149714a-00! -m(1227-1291) 14361 27% 149714a-00 * GHC-GA-366-01

Mass to be matched (m/z): 180.008840 Charge: 1

Mass Tolerance: ± 0.005000

Restriction of atom numbers:

C H N O Cl

1-110 1-100 1-2 1-5 1-1

Number of calculated Formulas: 2

Formula	Diff.(ppm)	theor. m/z
C8 H5 N2 O1 Cl1	-1.94	180.008490
C5 H7 N1 O4 Cl1	-16.82	180.005812

6.10.2020

File: 149714a-00.raw

Analyse: GHC-GA-366-01

COP: Dr. Clement Ghiazza

Messung: GC-MS
 Ionisierung: GC-EI
 Spektrometer: QExactiveGC
 Säule: MS 50 TX1+VS
 Länge: 30+7
 Temp.: 35-10-285-5
 GC-Nr.: -

Auswerter: Margold

Mass to be matched (m/z): 301.034780 Charge: 1

Mass Tolerance: ± 0.005000

Restriction of atom numbers:

C	H	Cl	N	O	Na
1-100	1-100	1-1	max 2	max 10	1-1

Number of calculated Formulas: 3

Formula	Diff. (ppm)	theor. m/z
C13 H11 Cl1 N2 O3 Na1	0.86	301.035039
C10 H13 Cl1 N1 O6 Na1	-8.04	301.032361
C18 H11 Cl1 O1 Na1	14.22	301.039062

Datum 19.10.2020

Analyse: 149943c-00

Sigel: GHC-AA-069-01

COP: Dr. Clement Ghiazza

Messung: HRMS

Methode: ESIPos

Lösungsmittel: CH3OH

Spektrometer: Exactive

Auswerter: Kampen (2242)

Suggestion:

C13H11Cl1N2O3 MW 278

characteristical ion

301 = [278 + Na]⁺

44

44

Mass to be matched (m/z): 371.064630 Charge: 1

Mass Tolerance: ± 0.005000

Restriction of atom numbers:

C	H	N	O	Cl	P	Na
1-100	1-100	1-5	1-10	1-1	1-1	1-1

Number of calculated Formulas: 5

Formula	Diff. (ppm)	theor. m/z
C12 H18 N4 O4 Cl1 P1 Na1	0.03	371.064641
C14 H20 N1 O5 Cl1 P1 Na1	3.65	371.065985
C9 H20 N3 O7 Cl1 P1 Na1	-7.19	371.061963
C15 H16 N5 O1 Cl1 P1 Na1	7.25	371.067320
C17 H18 N2 O2 Cl1 P1 Na1	10.87	371.068664

Datum: 16.10.2020

Analyse: 149929b-00

Sigel: GHC-GA-380-01

COP: Dr. Clement Ghiazza

Method: HR-MS

Ionis. : ESIPos

solvent : CH₂Cl₂ + CH₃OH

Spectrometer: Exactive

Auswerter: Marcus, Tel:2243

suggestion:

C12H18N4O4Cl1P1 MW: 348

Characteristic Ions:

371 = [348 + Na]

Mass to be matched (m/z): 331.060640 Charge: 1

Mass Tolerance: ± 0.005000

Restriction of atom numbers:

C H N O Cl
1-100 1-100 1-5 1-10 1-1

Number of calculated Formulas: 5

Formula	Diff.(ppm)	theor. m/z
C17 H14 N1 O4 Cl1	-0.16	331.060587
C15 H12 N4 O3 Cl1	-4.22	331.059243
C20 H12 N2 O1 Cl1	7.93	331.063265
C12 H14 N3 O6 Cl1	-12.31	331.056564
C8 H16 N4 O8 Cl1	13.53	331.065118

Datum: 7.08.2020

Analyse: 148567c-00

Sigel: GHC-GA-272-01

COP: Dr. Clement Ghiazza

Method: HR-MS

Ionis. : GC-EI

Spectrometer: Q-Exactive

Auswerter: Marcus, Tel:2243

suggestion:

C17H14N1O4Cl1

MW: 331

Mass to be matched (m/z): 473.059970 Charge: 1

Mass Tolerance: ± 0.005000

Restriction of atom numbers:

C H N O S Cl
1-100 1-100 1-5 1-10 1-1 2-2

Number of calculated Formulas: 4

Formula	Diff. (ppm)	theor. m/z
C22 H19 N4 O2 S1 Cl2	0.12	473.060028
C24 H21 N1 O3 S1 Cl2	2.96	473.061372
C19 H21 N3 O5 S1 Cl2	-5.54	473.057350
C12 H25 N3 O10 S1 Cl2	6.88	473.063225

Datum: 30.10.2020

Analyse: 150219c-00

Siegel: GHC-GA-410-01

COP: Dr. Clement Ghiazza

Method: HR-MS

Ionis. : ESIPos

solvent : CH3OH

Spectrometer: Exactive

Auswerter: Marcus, Tel:2243

suggestion:

C22H18N4O2S1Cl2 MW: 472

Characteristic Ions:

473 = [472 + H]

Mass to be matched (m/z): 511.086620 Charge: 1

Mass Tolerance: ± 0.005000

Restriction of atom numbers:

C	H	Cl	F	N	O	S	Na
1-100	1-100	1-1	1-1	max 2	max 5	1-1	1-1

Number of calculated Formulas: 2

Formula	Diff.(ppm)	theor. m/z
C24 H22 Cl1 F1 N2 O4 S1 Na1	-0.22	511.086506
C29 H22 Cl1 F1 O2 S1 Na1	7.65	511.090528

Datum 2.03.2021

Analyse: 152006b-00

Sigel: GHC-GA-618-01

COP: Dr. Clement Ghiazza

Messung: HRMS

Methode: ESIPos

Lösungsmittel: CH2Cl2+CH3OH

Spektrometer: Exactive

Auswerter: Kampen (2242)

Suggestion:

C24H22Cl1F1N2O4S1 MW 488

characteristical ion

511 = [488 + Na]⁺

Mass to be matched (m/z): 478.174910 Charge: 1

Mass Tolerance: ± 0.050000

Restriction of atom numbers:

C H N O Cl
1-100 1-100 7-7 1-3 1-2

Number of calculated Formulas: 6

Formula	Diff. (ppm)	theor. m/z
C24 H25 N7 O2 Cl1	0.76	478.175274
C22 H30 N7 O1 Cl2	28.08	478.188337
C21 H26 N7 O2 Cl2	-48.01	478.151952
C19 H34 N7 O3 Cl2	72.27	478.209467
C23 H21 N7 O3 Cl1	-75.33	478.138889
C25 H29 N7 O1 Cl1	76.85	478.211659

12.11.2020

File: 150394c-00

Analysis: GHC-GA-419-01

COP: Dr. Clement Ghiazza

Messung: HR-MS
Ionisierung: ESIpos
Lösungsmittel: CH₂Cl₂ + CH₃OH
Spektrometer: Exactive
ELNA: 28360

Auswerter: Haupt (2243)

Suggestion:
C₂₄H₂₄Cl₁N₇O₂ MW: 477

Characteristic ions:
478 = [477 + H]⁺

Mass to be matched (m/z): 477.877890 Charge: 1

Mass Tolerance: ± 0.005000

Restriction of atom numbers:

C	H	Cl	F	N	O	S	Na
1-100	1-100	3-3	6-6	1-3	max 5	1-1	1-1

Number of calculated Formulas: 2

Formula	Diff.(ppm)	theor. m/z
C12 H2 Cl3 F6 N3 O1 S1 Na1	0.35	477.878058
C9 H4 Cl3 F6 N2 O4 S1 Na1	-5.25	477.875379

Datum	31.07.2020
Analyse:	148457b-00.raw

Sigel:	GHC-GA-243-01
COP:	Dr. Clement Ghiazza

Messung:	HRMS
Methode:	ESIpos
Lösungsmittel:	CH ₂ Cl ₂ +CH ₃ OH
Spektrometer:	LTQ FT

Auswerter:	Kampen (2242)
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Suggestion:

C₁₂H₂Cl₃F₆N₃O₁S₁ MW 455

characteristical ion

478 = [455 + Na]⁺

Mass to be matched (m/z): 460.153380 Charge: 1

Mass Tolerance: ± 0.005000

Restriction of atom numbers:

C H Cl N O
1-100 1-100 1-1 1-5 max 5

Number of calculated Formulas: 4

Formula	Diff.(ppm)	theor. m/z
C25 H23 Cl1 N5 O2	0.21	460.153476
C27 H25 Cl1 N2 O3	3.13	460.154821
C22 H25 Cl1 N4 O5	-5.61	460.150798
C30 H23 Cl1 N3	8.95	460.157499

Datum 11.08.2020

Analyse: 148633b-00

Sigel: GHC-GA-268-01

COP: Dr. Clement Ghiazza

Messung: HRMS

Methode: ESIPos

Lösungsmittel: CH₂Cl₂+CH₃OH

Spektrometer: Exactive

Auswerter: Kampen (2242)

Suggestion:

C₂₅H₂₂Cl₁N₅O₂ MW 459

characteristical ion

460 = [459 + H]⁺

Mass to be matched (m/z): 539.058050 Charge: 1

Mass Tolerance: ± 0.005000

Restriction of atom numbers:

C	H	Cl	F	N	O	S
1-100	1-100	1-1	3-3	2-4	max 5	2-2

Number of calculated Formulas: 3

Formula	Diff.(ppm)	theor. m/z
C23 H19 Cl1 F3 N4 O2 S2	0.76	539.058459
C20 H21 Cl1 F3 N3 O5 S2	-4.21	539.055780
C28 H19 Cl1 F3 N2 S2	8.22	539.062481

Datum 4.03.2021

Analyse: 152063b-00

Sigel: GHC-GA-629-01

COP: Dr. Clement Ghiazza

Messung: HRMS

Methode: ESIPos

Lösungsmittel: CH₂Cl₂+CH₃OH

Spektrometer: Exactive

Auswerter: Kampen (2242)

Suggestion:

C₂₃H₁₈Cl₁F₃N₄O₂S₂ MW 538

characteristical ion

539 = [538 + H]⁺

52

No.	MW.	Comment
1	309	Your proposed structure is possible Ref.-Spektr. Nr. OU1617:

6.11.2020
File: 150300a-00.raw
Analyse: GHC-GA-426-01
COP: Dr. Clement Ghiazza

Messung: GC-MS
Ionisierung: GC-EI
Spektrometer: QExactiveGC
Säule: MS 50 RTX1+VS
Länge: 30+7
Temp.: 35-10-285-5
GC-Nr.: -
MS-Nr.: 28258

Auswerter: Margold (2242)

OU1671 33% MW:309/309.28 C15H10F3N1O1S1

39	0.76	80	0.14	106	0.13	134	0.80	169	0.08	206	0.10	241	1.30
41	0.09	81	0.37	107	0.31	135	0.30	171	0.25	207	0.07	242	0.56
44	1.86	82	0.27	108	0.50	136	0.20	173	0.07	208	0.16	249	0.15
45	0.77	83	0.27	109	0.41	139	0.70	177	0.36	209	0.56	252	2.32
50	0.45	84	0.11	110	0.19	140	0.41	178	1.07	210	6.15	253	0.30
51	0.15	85	0.19	111	0.23	141	0.21	179	0.67	211	4.12	254	0.09
57	0.07	87	0.10	112	0.96	146	0.49	180	0.94	212	3.97	264	0.34
62	0.38	88	0.13	113	0.10	148	0.15	181	0.13	213	0.72	275	0.07
63	1.55	89	3.81	114	0.12	150	0.21	183	0.31	214	0.20	276	0.09
64	0.17	90	1.08	115	0.32	151	0.43	184	1.38	221	0.15	277	0.15
65	5.48	91	19.83	116	1.48	152	1.03	185	0.47	222	1.52	281	0.38
66	0.23	92	1.41	117	0.19	153	0.40	186	0.15	223	7.98	282	0.13
69	4.82	93	0.78	120	0.21	154	1.21	187	0.07	224	2.44	283	0.32
70	0.29	94	0.41	121	2.75	155	0.23	188	0.15	225	0.46	294	0.17
71	0.08	95	2.00	122	0.62	160	0.17	190	0.36	226	0.07	306	0.08
74	0.25	96	0.30	123	1.33	162	0.11	191	0.25	230	0.16	307	7.84
75	0.25	97	0.07	125	0.27	164	0.35	192	0.09	232	1.20	308	100.00
76	0.36	102	0.44	126	0.14	165	0.21	195	0.25	233	0.20	309	50.05
77	1.23	103	0.71	127	0.16	166	0.60	196	0.17	238	1.05	310	12.97
78	0.23	104	0.10	128	0.29	167	1.00	197	0.28	239	2.93	311	2.93
79	0.11	105	0.38	133	0.20	168	0.71	205	0.33	240	5.85	312	0.34

OU1671 33% MW:309/309.28 C15H10F3N1O1S1

lim: 0.07%

Mass to be matched (m/z): 309.043220 Charge: 1

Mass Tolerance: ± 0.005000

Restriction of atom numbers:

C	H	N	O	S	F
1-110	1-100	1-1	1-3	1-1	1-3

Number of calculated Formulas: 1

Formula	Diff.(ppm)	theor. m/z
C15 H10 N1 O1 S1 F3	-0.80	309.042972

6.11.2020

File: 150300a-00.raw

Analyse: GHC-GA-426-01

COP: Dr. Clement Ghiazza

Messung:	GC-MS
Ionisierung:	GC-EI
Spektrometer:	QExactiveGC
Säule:	MS 50 RTX1+VS
Länge:	30+7
Temp.:	35-10-285-5
GC-Nr.:	-
MS-Nr.:	28258

Auswerter: Margold (2242)

53

8.87
8.68
8.68
8.67
— 8.24
7.62
7.62
7.61
7.61
7.27
7.26
7.26
7.25

4.51
4.51
4.50
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4.11
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4.06
3.99
3.98
3.98
3.97
3.79
3.78
1.29
1.29
1.28
1.28
1.27
1.27

1.00
1.00
1.00
1.00
1.89

2.24
4.34
2.06
2.03

6.08

12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0

f1 (ppm)

53

Mass to be matched (m/z): 419.091270 Charge: 1

Mass Tolerance: ± 0.005000

Restriction of atom numbers:

C	H	N	O	P	S	Na
1-100	1-100	2-4	max 10	1-1	1-1	1-1

Number of calculated Formulas: 3

Formula	Diff.(ppm)	theor. m/z
C16 H21 N4 O4 P1 S1 Na1	0.16	419.091336
C13 H23 N3 O7 P1 S1 Na1	-6.24	419.088657
C21 H21 N2 O2 P1 S1 Na1	9.76	419.095358

Datum 23.10.2020

Analyse: 150104b-00

Sigel: GHC-GA-395-01

COP: Dr. Clement Ghiazza

Messung: HRMS

Methode: ESIPos

Lösungsmittel: CH₂Cl₂+CH₃OH

Spektrometer: Exactive

Auswerter: Kampen (2242)

Suggestion:

C₁₆H₂₁N₄O₄P₁S₁ MW 396

characteristical ion

419 = [396 + Na]⁺

54

54

Mass to be matched (m/z): 241.073490 Charge: 1

Mass Tolerance: ± 0.050000

Restriction of atom numbers:

C H N O
1-100 1-100 1-2 1-5

Number of calculated Formulas: 11

Formula	Diff. (ppm)	theor. m/z
C14 H11 N1 O3	-0.61	241.073344
C10 H13 N2 O5	34.88	241.081898
C13 H9 N2 O3	-52.77	241.060768
C11 H15 N1 O5	87.04	241.094474
C17 H7 N1 O1	-88.26	241.052214
C14 H13 N2 O2	98.15	241.097153
C16 H5 N2 O1	-140.42	241.039637
C15 H15 N1 O2	150.32	241.109729
C13 H7 N1 O4	-151.54	241.036959
C11 H17 N2 O4	185.80	241.118282
C12 H5 N2 O4	-203.70	241.024382

25.01.2021

File: 151335b-00

Analyse: GHC-GA-552-01

COP: Dr. Clement Ghiazza

Messung: (HRMS)
Ionisierung: EI
Spektrometer: Q Exactive GC Orbitrap
Säule: MS50 RTX-1+VS
Länge: 30+7
Temp.: 35-10-285-5
GC-Nr.:
ELNA-Nr.: 29288

Auswerter: Haupt (2243)

Suggestion:

C14H11N1O3 MW: 241

Mass to be matched (m/z): 523.281660 Charge: 1

Mass Tolerance: ± 0.005000

Restriction of atom numbers:

C H N O
1-100 1-100 4-6 max 10

Number of calculated Formulas: 4

Formula	Diff.(ppm)	theor. m/z
C31 H35 N6 O2	-0.12	523.281597
C28 H37 N5 O5	-5.24	523.278919
C21 H41 N5 O10	5.99	523.284793
C36 H35 N4	7.57	523.285620

Datum 19.11.2020

Analyse: 150555c-00

Sigel: GHC-GA-453-01

COP: Dr. Clement Ghiazza

Messung: HRMS

Methode: ESIPos

Lösungsmittel: CH₂Cl₂+CH₃OH

Spektrometer: Exactive

Auswerter: Kampen (2242)

Suggestion:

C₃₁H₃₄N₆O₂ MW 522

characteristical ion

523 = [522 + H]⁺

Mass to be matched (m/z): 476.109480 Charge: 1

Mass Tolerance: ± 0.005000

Restriction of atom numbers:

C	H	N	O	S
1-100	1-100	1-3	max 5	2-2

Number of calculated Formulas: 2

Formula	Diff.(ppm)	theor. m/z
C25 H22 N3 O3 S2	0.49	476.109711
C30 H22 N1 O1 S2	8.93	476.113734

Datum 3.11.2020

Analyse: 150251b-00

Sigel: GHC-GA-417-01

COP: Dr. Clement Ghiazza

Messung: HRMS

Methode: ESIPos

Lösungsmittel: CH₂Cl₂+CH₃OH

Spektrometer: Exactive

Auswerter: Kampen (2242)

Suggestion:

C₂₅H₂₂N₃O₃S₂ MW 475

characteristical ion

476 = [475 + H]⁺

Mass to be matched (m/z): 542.342660 Charge: 1

Mass Tolerance: ± 0.005000

Restriction of atom numbers:

C	H	N	O	S	Na
1-100	1-100	1-3	max 5	1-1	1-1

Number of calculated Formulas: 2

Formula	Diff.(ppm)	theor. m/z
C34 H49 N1 O1 S1 Na1	0.08	542.342705
C29 H49 N3 O3 S1 Na1	-7.33	542.338683

Datum	19.11.2020
Analyse:	150538c-00.RAW

Sigel:	GHC-GA-454-01
COP:	Dr. Clement Ghiazza

Messung:	HRMS
Methode:	ESIpos
Lösungsmittel:	CH ₂ Cl ₂ +CH ₃ OH
Spektrometer:	Exactive

Auswerter:	Kampen (2242)
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Suggestion:

C₃₄H₄₉N₁O₁S₁ MW 519

characteristical ion

542 = [519 + Na]⁺

58

Mass to be matched (m/z): 270.015390 Charge: 1

Mass Tolerance: ± 0.005000

Restriction of atom numbers:

C	H	Cl	N	O	Na
1-100	1-100	1-1	1-5	max 105	1-1

Number of calculated Formulas: 4

Formula	Diff.(ppm)	theor. m/z
C10 H6 Cl1 N5 O1 Na1	-0.31	270.015306
C12 H8 Cl1 N2 O2 Na1	4.66	270.016649
C9 H10 Cl1 N1 O5 Na1	-5.26	270.013971
C7 H8 Cl1 N4 O4 Na1	-10.23	270.012627

Datum	23.10.2020
Analyse:	150103b-00

Sigel:	GHC-AA-089-01
COP: Dr. Clement Ghiazza	

Messung:	HRMS
Methode:	ESIpos
Lösungsmittel:	CH ₂ Cl ₂ +CH ₃ OH
Spektrometer:	Exactive

Auswerter:	Kampen (2242)
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Suggestion:

C₁₀H₆Cl₁N₅O₁ MW 247

characteristical ion

270 = [247 + Na]⁺

59

Mass to be matched (m/z): 315.090100 Charge: 1

Mass Tolerance: ± 0.050000

Restriction of atom numbers:

C H N O F
1-100 1-100 1-2 1-4 1-1

Number of calculated Formulas: 8

Formula	Diff. (ppm)	theor. m/z
C17 H14 N1 O4 F1	0.12	315.090137
C20 H12 N2 O1 F1	8.62	315.092816
C16 H12 N2 O4 F1	-39.79	315.077561
C21 H14 N1 O1 F1	48.53	315.105392
C20 H10 N1 O2 F1	-66.94	315.069007
C17 H16 N2 O3 F1	75.68	315.113946
C19 H8 N2 O2 F1	-106.86	315.056431
C18 H18 N1 O3 F1	115.59	315.126522

11.11.2020

File: 150390d-00

Analyse: GHC-GA-435-01

COP: Dr. Clement Ghiazza

Messung: (HRMS)
Ionisierung: EI
Spektrometer: Q Exactive GC Orbitrap
Säule: MS50 RTX-1+VS
Länge: 30+7
Temp.: 35-10-285-5
GC-Nr.:
ELNA-Nr.: 28353

Auswerter: Haupt (2243)

Suggestion:
C17H14N1O4F1 MW: 315

62

62

62

No. MW. Comment
 1 297 Spectrum correlates with your
 expected structure
 Ref.-spectrum: OU2077:

HRMS see below

17.03.2021

File: 152336a-00.raw

Analyse: GHC-GA-645-01

COP: Dr. Clement Ghiazza

Messung: GC-MS

Ionisierung: GC-EI

Spektrometer: Q Exactive GC Orbitrap

Säule: MS 81 ZB1ms

Länge: 30

Temp.: 35-15-300-3

GC-Nr.: -

ELNA-Nr.: 30257

Auswerter: Vetere (2243)

OU2077 14% MW:297/298.05 C8H3Br1F3N1O1S1

34	0.47	63	2.83	84	0.37	108	7.98	133	10.19	175	0.21	231	4.84
37	0.13	64	0.53	85	1.24	109	0.63	134	1.06	190	0.55	232	2.93
38	0.15	65	0.10	86	0.26	111	0.12	135	0.42	192	0.08	233	0.41
39	0.19	66	0.44	87	0.60	113	0.08	140	0.68	198	0.22	240	4.31
41	0.23	67	0.28	88	1.97	115	0.20	141	0.09	200	56.13	241	0.28
42	0.11	68	0.41	89	0.24	117	0.44	146	1.08	201	3.87	242	4.09
43	0.15	69	27.39	91	0.63	118	0.35	147	0.16	202	53.72	243	0.27
44	1.84	70	4.51	92	0.38	119	1.16	148	1.11	203	3.55	244	0.16
45	0.95	71	1.16	93	5.09	120	4.72	149	3.14	204	2.31	278	0.12
49	0.09	72	0.19	94	10.83	121	33.99	150	0.33	205	0.12	280	0.13
50	0.31	73	0.20	95	10.08	122	3.05	151	3.32	207	0.09	297	100.00
51	0.21	74	0.65	96	0.93	123	8.35	152	4.13	211	0.10	298	8.60
53	0.29	75	0.72	97	0.52	124	0.49	153	0.35	212	0.77	299	97.44
54	0.07	76	1.11	98	0.14	125	3.38	154	0.15	213	0.12	300	7.60
55	0.33	77	0.76	99	0.21	126	1.26	156	0.16	214	0.72	301	3.69
56	0.19	78	0.07	100	0.16	127	0.15	158	0.09	218	0.86	302	0.33
57	1.30	79	0.72	103	0.10	128	0.26	163	0.15	219	0.18		
58	0.14	80	0.35	104	0.26	129	0.24	170	0.48	227	0.07		
60	0.07	81	2.98	105	1.22	130	0.26	171	0.17	228	68.77		
61	0.91	82	2.12	106	1.83	131	0.27	173	0.20	229	5.44		
62	1.72	83	0.60	107	1.12	132	1.41	174	0.95	230	64.55		

OU2077 14% MW:297/298.05 C8H3Br1F3N1O1S1

lim: 0.07%

Mass to be matched (m/z): 296.906890 Charge: 1

Mass Tolerance: ± 0.001000

Restriction of atom numbers:

C	H	N	O	Br	S	F
				max 3	1-1	max 1

Number of calculated Formulas: 5

Characteristic ions (singly charged):
297 = [M]⁺suggested composition of M:
C₈H₃BrF₃NOS

Formula	Diff. (ppm)	theor. m/z
C ₈ H ₃ N ₁ O ₁ Br ₁ S ₁ F ₃	-1.15	296.906547
C ₃ H ₂ N ₄ O ₁ Br ₁ S ₁ F ₄	-1.83	296.906346
C ₆ N ₇ O ₁ Br ₁ S ₁	-1.98	296.906303
C ₈ H ₂ N ₄ O ₂ Br ₁ S ₁	2.55	296.907648
C ₅ H ₄ N ₁ O ₂ Br ₁ S ₁ F ₄	2.70	296.907691

367(8:00) 51806 12% 152336a-00 * GHC-GA-645-01/GC-MS/GC-EI/QExactiveGC/MS 81 ZB1ms/30/35-1

Mass to be matched (m/z): 225.984890 Charge: 1

Mass Tolerance: ± 0.050000

Restriction of atom numbers:

C H N Br
1-100 1-100 1-4 1-1

Number of calculated Formulas: 4

Formula	Diff.(ppm)	theor. m/z
C7 H7 N4 Br1	-0.09	225.984870
C8 H9 N3 Br1	55.56	225.997446
C9 H11 N2 Br1	111.21	226.010023
C10 H13 N1 Br1	166.86	226.022599

22.03.2021

File: 152395b-00.raw

Analyse: GHC-GA-653-01

COP: Dr. Clement Ghiazza

Messung: GC-MS
Ionisierung: GC-EI
Spektrometer: Q Exactive GC Orbitrap
Säule: MS 81 ZB1ms
Länge: 30
Temp.: 35-15-300-3
GC-Nr.: -
ELNA-Nr.: 30330

Auswerter: Haupt (2243)

Suggestion:
C7H7N4Br1 MW: 226

Mass to be matched (m/z): 259.068840 Charge: 1

Mass Tolerance: ± 0.005000

Restriction of atom numbers:

C H N O Na
1-110 1-100 1-3 1-5 1-1

Number of calculated Formulas: 2

Formula	Diff. (ppm)	theor. m/z
C11 H12 N2 O4 Na1	0.33	259.068926
C14 H10 N3 O1 Na1	10.67	259.071605

03.12.2020

File: 150769c-00

Analyse: GHC-GA-464-03

COP: Dr. Clement Ghiazza

Messung: HRMS ESIPos

Lösemittel: CH₂Cl₂+CH₃OH

Spektrometer: Exactive

Auswerter: Kohler (2243)

Suggestion:

C₁₁H₁₂N₂O₄ MW 236

Characteristic ions:

259 = [236 + Na]⁺