Chlorodifluoromethane as a C1 Synthon in the Assembly of N-Containing Compounds

**HIGHLIGHTS**

- Quadruple cleavage of ClCF₂H to afford a C1 synthon
- The cleavage of two stable C(sp³)-F bonds in aliphatic gem-difluoroalkanes
- Enrich C1 chemistry, green chemistry, and fluorine chemistry
- Various N-containing compounds were afforded via different role of ClCF₂H

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Chlorodifluoromethane as a C1 Synthon in the Assembly of N-Containing Compounds

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SUMMARY
The development of C1 synthons to afford the products that add one extra carbon has become an important research theme in the past decade, and significant progress has been achieved with CO2, CO, HCOOH, and others as C1 units. Despite the great advance, the search for new C1 synthons that display unique reactivity, complement to the current C1 sources, and add more value to C1 chemistry is still desirable. Herein, we report a quadruple cleavage of chlorodifluoromethane to yield a C1 source, which was successfully employed in the construction of various N-containing compounds especially with pharmaceutical molecules under mild conditions. This strategy provides a useful method for late-stage modification of pharmaceutical compounds. Four bonds in ClCF2H were orderly cleaved under basic conditions in the absence of transition metals. Preliminary mechanistic studies revealed that (E)-N-phenylformimidoyl fluoride intermediate is involved in this process by in situ 1H NMR studies and control experiments.

INTRODUCTION
The C1 chemistry has emerged as an elegant strategy for efficient preparation of homologous compounds, which added one extra carbon in modern chemical transformations (Aresta et al., 2014; Sakakura et al., 2007; Huang et al., 2011; Yan et al., 2012; Natte et al., 2017; Wakade et al., 2017; Senadi et al., 2019). There are ample significance and a plethora of characteristics for C1 chemistry, for instance, carbon chain increasing (Aresta et al., 2014), construction of importance functional groups (carboxylic or carbonyl groups) (Huang et al., 2011; Cokoja et al., 2011), incorporation of two or more organic small molecules to yield important products (Oh and Hu, 2013), and modification of the pharmaceutical or natural products for value-added bulk (Liu et al., 2015; Ma et al., 2018a). Among all known C1 synthons, CO2, CO, and formic acid are the most famous ones, which have been widely used in various reaction processes, and many beautiful transformations have been developed with them, which further attracted more and more chemists devoted to this field (Aresta et al., 2014; Sakakura et al., 2007; Aresta et al., 2014; Huang et al., 2011; Cokoja et al., 2011; Oh and Hu, 2013; Sordakis et al., 2018; Gibson, 1969; Enthaler et al., 2010). Despite the significance and great advance of C1 chemistry, the search for C1 synthons that display unique reactivity, complement to the current C1 sources, and add more value to C1 chemistry is still highly desirable. Thus, direct introduction of one extra carbon from cheap and available materials under mild conditions to provide a cost-efficient, pragmatic, and valuable alternative avenue would be popular in the field of synthetic and pharmaceutical communities, which might have deep impact on industry as well.

Chlorodifluoromethane (ClCF2H) is well known as an inexpensive and abundant industrial raw material (Hudlicky and Pavlath, 1995) for the construction of various fluorinated compounds (Wang et al., 2014; Fier and Hartwig, 2012; Gu et al., 2014; Yu et al., 2017; Wu et al., 2019; Miao et al., 2018; Zhang et al., 2019), featuring thermodynamic stability and kinetic inertness as well as atomic economy as fluorine source. Therefore, efficient transformations of this easily accessible raw material to create valuable chemicals have deservedly gained great attention. The most common transformation of ClCF2H involves the formation of difluorocarbene (:CF2) by the cleavage of both C-Cl and C-H bonds (Figure 1Aa) (Feng et al., 2017), usually under basic conditions with heteroatom nucleophiles, rendering the corresponding difluoromethylated heteroatom compounds (Hine and Porter, 1957; Nawrot and Jonczyk, 2007). Pyrolysis of ClCF2H at high temperature or pressure leads to the important raw industrial material tetrafluoroethylene (Hudlicky and Pavlath, 1995; Sung et al., 2004). Very recently a reaction by palladium-catalyzed cross-coupling between aryloboronic acids and ClCF2H via a metal-difluorocarbene intermediate has been reported (Feng et al., 2017; Yu et al., 2019), representing the catalytic transformation of ClCF2H. Other conversion processes that do not involve difluorocarbene species were still difluoromethylation-related ones in which only one
C-Cl bond was broken through a difluoromethyl radical pathway (Figure 1A) (Xu et al., 2018). Trifluoromethyl anion (CF$_3$/C$_0$) is readily derived from the difluorocarbene species and external fluorine source via double cleavage of ClCF$_2$H (Figure 1Ac) (Zheng et al., 2015). Intriguingly and surprisingly, quadruple cleavage of ClCF$_2$H to provide versatile C$_1$ synthons, by breaking one C-Cl bond, two stable C-F bonds, and one C-H bond orderly in a single-vessel reaction (Figure 1B), has never been reported to date, probably mainly because of the high BDE of C(sp$^3$)-F bonds (the bond dissociation energy of a single C-F bond: 485 KJ/mol) (O’Hagan, 2008).

Herein, we report a quadruple cleavage of chlorodifluoromethane as a type of C$_1$ source to access valuable formimidamide derivatives that are widely employed as ligands or forming metal complexes as quasi-N-heterocyclic carbenes (NHCs) (Figure 1 (i) and (ii)) (Schroeder et al., 2009, 2010; Bitterlich et al., 2007; Boogaerts and Nolan, 2010; Ohishi et al., 2008; Hopkinson et al., 2014). Despite the importance of these compounds, their elegant syntheses are very rare. Therefore, expanding the toolbox of methods for their synthesis will enrich diversity of this kind of compounds. Amines are very common raw materials as well as crucial building blocks with rich chirality (France et al., 2014); we envision that formimidamides could be readily generated in a single-vessel synthesis from two amines with ClCF$_2$H as C$_1$ source due to the special reactivity of ClCF$_2$H. These processes represent a significant reaction modality for ClCF$_2$H, which might promote and enrich C$_1$ chemistry, organic fluorine chemistry (Gouverneur and Seppelt,
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2015), as well as green chemistry (Horváth, 2007). Meanwhile, ClCF₂H provides a unique and alternative approach for the current known C₁ sources: the control and comparison experiments with CO, CO₂, and formic acid as C₁ synthons were performed under our standard conditions as well as the reported procedures; notably, no desired formimidamides were ever formed or obtained under those reaction conditions. These results further underscore the uniqueness and peculiarity of ClCF₂H as a C₁ source (for further details, see also Schemes S1 and S2).

RESULTS AND DISCUSSION

Optimization of Reaction Conditions

Our design is based on our recent discovery in which ethyl bromodifluoroacetate (BrCF₂COOEt) (Ma et al., 2018b; Deng et al., 2019) could act as a C₁ source and formylating reagent with amines via quadruple cleavage under basic conditions (Ma et al., 2018a, 2018c, 2018d); we postulated that the quadruple cleavage of ClCF₂H could also be occurred under the similar sets since it is known that difluorocarbene could be readily accessible from ClCF₂H under basic conditions. Moreover, compared with BrCF₂COOEt, ClCF₂H is obviously much cheaper and more atomic economical. We commenced our hypothesis by using low-cost and widely available aniline (1a) and N-methyl aniline (2a) as model substrates. To our delight, the yield of 76% of the anticipated product 3a (Zhao et al., 2005) was obtained from the reaction of 1a with 2a under the ClCF₂H atmosphere without water (entry 1). More delightfully, the yield was significantly increased to 83%–92% with the increase of dosage of water (entries 2-3); notably, excess water caused deteriorated effect on the reaction, since some unknown by-products were observed when the amount of water was increased to 20–30 equivalents, and the yield of the desired product was dropped to 83% (entry 2 versus entry 3, and for further details, see also Table S2). Replacing KOH with either Cs₂CO₃ or K₂CO₃ as the base resulted in lower yields (entries 4-5). To our surprise, this transformation was completely suppressed with Na₂CO₃ and NaHCO₃ as the base (entries 6-7). The solvent was so crucial that no reaction occurred in other solvents, such as in THF and dioxane (entries 8-9) (for further details, see also Table S3). In addition, the yield of the desired product was slightly higher at the ambient temperature than at 50°C. In terms of reaction time, the longer time (36 h) led to the best result (entry 11).

Substrate Scope for Intermolecular Transformation

With the optimal reaction conditions in hand (entry 2 in Table 1), we explored the generality and limitation of this transformation (Figure 2). First, a variety of para-substituted amines with electron-donating groups (alkoxy, phenoxyl, alkyl, and N, N-dimethyl) (1b-1j), as well as electron-withdrawing groups, such as halogen (1k-1m) and nitro group (1n), delivered the desired formimidamide derivatives (3a-3n) in good to excellent yields under the standard conditions. We next examined 1,1′-biphenyl-4-amine (1o) under this reaction condition to provide the desired product 3o in 77% yield. Besides, a large-scale (10 mmol) reaction of the N-methyl aniline (2a) has been carried out to afford 3a in 62% yield (for further details, see also Scheme S3). Similar result could be obtained for meta-substituted (m-Br) aniline (1p). Using the disubstituted 3,4-dimethylaniline (1q) and trisubstituted 2,4,6-trimethylaniline (1r), the corresponding products (3q and 3r) could be obtained in good yields (83%–85%). 5,6,7,8-Tetrahydronaphthalen-1-amine (1s) and 9H-fluoren-2-amine (1t) were carried out under the standard conditions to provide the target molecules (3s and 3t) in 80% and 76% yields, respectively. The absolute molecular structure of product 3t was unambiguously confirmed by X-ray crystallography analysis (Figure 2, and for further details, see also Table S1 and Data S1) (CCDC: 1874971). The fused polycyclic amines 9,9-diphenyl-9H-fluoren-2-amine (1u) and naphthalen-1-amine (1v) were subjected under the optimized reaction conditions, rendering the expected products (3u-3v) in moderate yields (68%–77%). Heterocyclic compounds, such as benz[d]thiazol-2-amine (1w), were also amenable to this transformation, and the corresponding product was obtained in 62% yield. We then further investigated the scope of the N-substituted aniline derivatives with aniline (1a) under the viable reaction conditions. Delightedly, the corresponding products (3x-3z, 3aa-3ac) were obtained in good to excellent yields with good functional group tolerance. In addition, given the prevailing existence of amines in pharmaceutical molecules and natural products (Ma et al., 2018a; Brunet and Neibecker, 2001), we selected Benzocaine (1ad, local anesthetic), Amoxapine (2ae, antidepressant), 2-(piperazin-1-yl)-4-(tri-fluoromethyl)pyrimidine (2af, medical/material intermediates), and multi-functional Vildagliptin (2ag, inhibit glucagon/chiral reagent/medicinalintermediate) and exposed them under the standard conditions; the corresponding products were obtained in 59%, 76%, 61%, and 71% yields, respectively. Gratifyingly, the chiral molecule (S)-N-benzyl-1-phenylethan-1-amine (2ah) experienced the optimal reaction conditions to deliver (S,E)-N-benzyl-N’-phenyl-N-(1-phenylethyl)formimidamide (3ah) in 60% yield, which might be a potential chiral ligand to realize enantioselective-control reactions.
In addition, we found that aliphatic secondary amine is compatible under the standard conditions as well; in terms of the substrate dicyclohexylamine (4), the corresponding product 5 was acquired in 76% yield (Equation 1 in Figure 3A). It is worth mentioning that our strategy is highly regio-selective, for example, when \( \text{N}^1\text{-isopropyl-} \text{N}^3\text{-phenylbenzene-1,3-diamine (6) was investigated under viable reaction condition, only compound 7 was afforded with diphenylamine part intact (Equation 2). In addition, when the target 3a was hydrolyzing under 1 M HCl, the two original substrates (1a and 2a) as well as two formylated compounds 1a-1 and 2a-1 were obtained, respectively (Ma et al., 2018a) (for further details, see also Scheme S4), which infers that our strategy might be a potential method for drug delayed or sustainable release when two different pharmaceutical molecules are combined by one extra carbon with our strategy (Equation 3). We carried out, therefore, correlative experiment using Benzocaine (1ad) and Vildagliptin.

### Table 1. Representative Results for Optimization of the Formation of (E)-N-methyl-N',N'-diphenylformimidamide (3a)

| Entry | Base (3 Equiv) | H_2O (X Equiv) | Solvent (2 mL) | T (°C) | Yield (%)^a |
|-------|----------------|----------------|----------------|--------|-------------|
| 1     | KOH            | 0              | CH_3CN         | r.t.   | 76          |
| 2     | KOH            | 5              | CH_3CN         | r.t.   | 92 (88)^b   |
| 3     | KOH            | 30             | CH_3CN         | r.t.   | 83          |
| 4     | Cs_2CO_3       | 5              | CH_3CN         | r.t.   | 76          |
| 5     | K_2CO_3        | 5              | CH_3CN         | r.t.   | 79          |
| 6     | Na_2CO_3       | 5              | CH_3CN         | r.t.   | N.D.        |
| 7     | NaHCO_3        | 5              | CH_3CN         | r.t.   | N.D.        |
| 8     | KOH            | 5              | THF            | r.t.   | N.D.        |
| 9     | KOH            | 5              | Dioxane        | r.t.   | N.D.        |
| 10    | KOH            | 5              | CH_3CN         | 50     | 70          |
| 11^c,d| KOH            | 5              | CH_3CN         | r.t.   | 62 (79)^d   |
| 12^e  | KOH            | 5              | CH_3CN         | r.t.   | N.D.        |

Reaction condition: aniline (1a, 1.2 equiv. 0.12 mmol), N-methylaniline (2a, 0.1 mmol), the atmosphere of chlorodifluoromethane (CICF_2H) (cat. 0.3 mmol), base (3 equiv.), solvent (2 mL), for 36 h.

r.t., room temperature; N.D., not detected.

^aGC yields.
^bIsolated yields.
^cFor 12 h.
^dFor 24 h.
^eNo CICF_2H.
Figure 2. Synthesis of Formimidamide Derivatives

(A) Scope of the primary amines.

(B) Scope of the secondary amines.

(C) Scope of R groups.

(D) Scope of the pharmaceutical molecules.

Reaction Condition 1: the primary amine (1, 0.12 mmol), the secondary amine (2, 0.1 mmol), KOH (3 equiv), H$_2$O (5 equiv), CH$_3$CN (2 mL), rt for 36 h under CF$_3$H atmosphere, isolated yield. $^a$ 2a 10 mmol.
(2ag) as the substrates under standard reaction condition 1; to our delight, the corresponding product 3ai was obtained in 70% yield (Equation 4). More interestingly, a highly chemoselective process was disclosed with two primary amines, in which N,N′-diphenylformimidamide and N-(difluoromethyl)-N,N′-diphenylformimidamide were obtained, respectively, by careful control of reaction conditions. Bases and additives played key roles on these two successful transformations: with K2CO3 as base, phenol and water as
additives (see condition 2 in Figure 3 and for further details, see also Table S4), N,N'-diphenylformimidamides (8 and 9) were obtained in moderate yields; with Cs₂CO₃ as the base and S₈ as additive (see condition 3 in Figure 3, and for further details, see also Table S5) (Zheng et al., 2017), N-(difluoromethyl)-N,N'-diphenylformimidamides (10–15) were acquired in good yields. In the latter transformation, CICF₂H played a dual role as both C₁ source and difluorocarbene source (Figure 3C).

Substrate Scope for Intramolecular Transformation

The success of the above-mentioned intermolecular transformation prompted us to exploit the intramolecular transformations, since the latter one always leads to cyclic compounds that are the essential skeletons in pharmaceutical and natural products (Sasaki et al., 2006; Kubo et al., 1993). Gratifyingly, when N'-methylbenzene-1,2-diamine (16) was subjected to the standard conditions for intermolecular transformation, benzimidazole 17 was obtained in 90% yield, which could be readily converted into 2-bromo-benzimidazole 18 in the presence of NBS. Then, after a series of transformation, Telmisartan, a potent angiotensin II receptor antagonist used in the treatment of essential hypertension, will be afforded (Figure 4A) (Martin et al., 2015). In addition, the transformation could be easily scaled up to 70 times from 16 to 17 without loss of the efficiency (for details, see also Scheme S6). Encouraged by this promising result, we next focused on the exploration of the formation of benzo[d]oxazoles and 1H-benzo[d]imidazoles compounds via intramolecular pattern, since it is well known that benzo[d]oxazoles and 1H-benzo[d]imidazoles are prevalent molecular scaffolds in various bioactive natural products, agrochemicals, and pharmaceuticals. After many attempts, an optimized condition was obtained (for further details, see also Tables S6 and S7). These transformations demonstrated a good functional group tolerance (Figure 4B). Different substituent groups on the benzene ring, including alkyl (19a, 19b), halo groups (19c, 19d), were all compatible, rendering the corresponding products (20a–20d) in moderate to good yield (68%–81%). Surprisingly, no desired products were detected when 2-amino-4-nitrophenol (19e) and 2-amino-5-nitrophenol (19f) underwent the same conditions, instead, the selective difluoromethylation of hydroxyl group occurred (20e and 20f). Good yields were achieved on various benzene-1,2-diamine compounds under the standard Reaction Condition 5 with K₂CO₃ as base in CH₂CN (2 mL) and H₂O (0.5 mL) at 100 °C for 16 h (Figure 4C). Remarkably, the products of difluoromethylation of benzimidazoles (21–29) were acquired in moderate yields via the slight adjustment of reaction condition (see reaction condition 6 for details); once again, CICF₂H played a dual role as both C₁ source and difluorocarbene source in this transformation (Figure 4D).

Mechanism Investigation

To gain more insights into the mechanism of the aforementioned transformations, some control experiments were performed. Initially, isotope labeling experiments were conducted, 84% (3a) and 78% (20g) of D atoms were incorporated into the final products correspondingly for intermolecular and intramolecular versions, and N-H of benzimidazole was replaced by N-D completely (Figures 5A and 5B). These results suggested that the hydrogen atom attached on the extra introduced carbon (from ClCF₂H) was originated of D atoms were incorporated into the final products correspondingly for intermolecular and intramolecular versions, and N-H of benzimidazole was replaced by N-D completely (Figures 5A and 5B). These results suggested that the hydrogen atom attached on the extra introduced carbon (from ClCF₂H) was originated from H₂O in this process possibly (for further details, see alsoScheme S8). The trace amount of the desired product 3a was observed when benzimidazole was added into the reaction system as a difluorocarbene scavenger; instead, 1-(difluoromethyl)-1H-benzo[d]imidazole was detected by GC-MS (Figure 5C). When N-methyl-N-phenylformamide (30) or isocyanobenzene (31) was subjected to the earlier standard reaction conditions with amines, the corresponding target products 3a and 3b were not obtained (Figure 5D), indicating that the compounds 30 and 31 are not intermediates for this transformation, which is in sharp contrast to our previous reports in which isocyanides are the key intermediates for those transformations with BrCF₂COOEt (Ma et al., 2018c, 2018d). To thoroughly understand the reaction sequence, two more control experiments were carried out, in which the primary amine and the secondary amine were added to the reaction mixture stepwise instead of one-pot to check which one is the first amine species interacting with CICF₂H. It turned out that primary amine might react with CICF₂H before the secondary one since 47% of the desired product was obtained in the primary-secondary amine sequence, whereas no desired product was detected with the secondary-primary amine sequence (Figures 5E and 5F). Finally, we carried out comparison experiments for CO₂, CO and HCOOH as C₁ source with amines, the corresponding target products were not obtained (Figure 5G), which further highlighted the uniqueness of CICF₂H as the C₁ source in these transformations.

Proposed Mechanism

To thoroughly figure out the possible reactive intermediate, we carried out in situ ¹H NMR studies between 4-ethoxyaniline (1c) and CICF₂H (Figure 6A). Since isocyanides have been ruled out to be the possible
Figure 4. The Synthetic Route of the Telmisartan and the Intramolecular Reaction Scope

(A) Telmisartan synthesis with our strategy.
(B) Scope of benzoxazoles.
(C) Scope of benzimidazoles.
(D) Scope of N-difluoromethyl benzimidazoles.

* The scale of the original material 16 is 0.1 mmol; ** The scale of the original material 16 is 7 mmol. (a) 1-Methylbenzimidazole (17) (5 mmol) and N-bromosuccinimide (3 equiv) in 25 mL of THF were heated under reflux for 1 h. Condition 4: The amine (0.2 mmol), K₂CO₃ (3 equiv), H₂O (5 equiv.), CH₃CN (2 mL), 50 °C for 12 h under the atmosphere of CICF₃H, isolated yield; Condition 5: The amine (0.2 mmol), K₂CO₃ (3 equiv), H₂O (0.5 mL), CH₃CN (2 mL), 100 °C for 16 h under the atmosphere of CICF₃H, isolated yield. Condition 6: The amine (0.1 mmol), K₂CO₃ (5 equiv), H₂O (30 μL), CH₃CN (2 mL), 110 °C for 48 h under the atmosphere of CICF₃H.
intermediates for this transformation, we envision that a type of intermediate \( \text{3c} \) might be formed in this transformation. To our delight, in situ \(^1\)H NMR studies indeed indicated the formation of \((\text{E})-N-(4\text{-ethoxyphenyl})\text{formimidoyl fluoride (3c)}\), which was increased continually at the first 6 h, whereafter it started to decline probably owing to its volatile property and the existence of various nucleophiles in the reaction system, such as \( \text{H}_2\text{O} \) and amines. The intermediate \( \text{3c} \) was totally consumed after 18 h or during the process of striping the solvent (for further details, see also Schemes S9–S11). To validate its presence, various nucleophiles (phenols, alcohols, amines, and carboxylic acids) were added into the system after 2 h, and the corresponding desired products were detected in GC-MS (Equation 1 in Figure 6B, and for further details, Scheme S12). In addition, one more control experiment was carried out with a \( \text{CICF}_2\text{H} \) balloon for 5 h;
Figure 6. *In situ* $^1$H NMR, the Capture of Reaction Intermediates and the Proposed Mechanism

(A) *In situ* $^1$H NMR studies.

(B) The capture of reaction intermediates.

(C) The plausible reaction mechanism.
the product 32, isocyanide 33, and N-(4-ethoxyphenyl)formamide (34) were obtained in 15%, 27%, and 38% yields, respectively (Equation 2 in Figure 6B), suggesting that the intermediate is a chemically active compound, which will further decompose into isocyanide by one more C-F bond cleavage easily. We have carried out the control experiments in the presence of radical scavengers; the reactions proceeded smoothly at room temperature to afford desired products in moderate yields. Those results suggest that the single electron transfer (SET) pathway could not be involved in this transformation (for further details, see also Scheme S13). On the basis of the above-mentioned results, a proposed mechanism for the reaction of ClCF₂H as a C₁ source is depicted in Figure 6C. The base coordinates with ClCF₂H to generate difluorocarbene first. Then the primary amine traps the in situ generated difluorocarbene affording intermediate I, which is very sensitive under basic conditions to lead to monofluoroimine species via the cleavage of one C-F bond; subsequent inter- or intramolecular nucleophilic attack on the imine species (II and III) eventually delivers products 3, 5, 7, and 20 by SN₂Ar substitution (path a) or nucleophilic addition (path b) (Ma et al., 2018a). As either R² or R³ is H, the product could embark on capturing one more in situ generated difluorocarbene unceasingly to render the products (10–15). The products 21–29 were obtained in one-pot synthesis when compound 20 (X = NH) meets with excess ClCF₂H in basic conditions as a difluorocarbene scavenger.

Conclusion
In summary, we have disclosed a C₁ source generated from chlorodifluoromethane (ClCF₂H). This method allows the synthesis of a broad range of the formimidamides and benzo[d]oxazoles, benzo[d]imidazole derivatives via intermolecular and intramolecular reactions with good efficiency as well as high regio- and chemoselectivity under mild reaction condition. To our knowledge, this is the first example that ClCF₂H proceeds quadruple cleavage to act as a C₁ synthon and the valuable products were fabricated from readily available starting materials under transition-metal-free conditions. This process might enrich C₁ chemistry, green chemistry, and fluorine chemistry as well as might partially solve the problem of the disposition of ODS. Preliminary mechanistic studies revealed that (E)-N-phenylformimidoyl fluoride intermediate is involved in this process, which is a distinct intermediate from BrCF₂COOEt case. Further studies toward the detailed mechanism and transformations and applications as well as exploration on more intriguing methodologies with this unusual C₁ source are under way in our laboratory.

Limitation of the Study
Primary aliphatic amines showed poor or no reactivity toward this reaction system. In addition, reactive intermediate (e.g., 3c') was not isolated owing to its high reactivity.

METHODS
All methods can be found in the accompanying Transparent Methods supplemental file.

DATA AND CODE AVAILABILITY
The structures of 3t reported in this article have been deposited in the Cambridge Crystallographic Data Centre under accession numbers CCDC: 1874971.

SUPPLEMENTAL INFORMATION
Supplemental Information can be found online at https://doi.org/10.1016/j.isci.2019.07.005.

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AUTHOR CONTRIBUTIONS
X.M. and J.S. performed the experiments and developed the reactions. X.Z. checked the manuscript and came up with suggestions for this transformation. Q.S. designed and directed the project and wrote the manuscript with the feedback of X.M.
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Supplemental Information

Chlorodifluoromethane as a C1 Synthon in the Assembly of N-Containing Compounds
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Supplementary Figures

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Figure S2. $^{13}$C NMR spectrum of 3a, related to Figure 2
Figure S3. $^1$H NMR spectrum of 3b, related to Figure 2

Figure S4. $^{13}$C NMR spectrum of 3b, related to Figure 2
Figure S5. $^1$H NMR spectrum of 3c, related to Figure 2

Figure S6. $^{13}$C NMR spectrum of 3c, related to Figure 2
**Figure S7.** $^1$H NMR spectrum of 3d, related to Figure 2

**Figure S8.** $^{13}$C NMR spectrum of 3d, related to Figure 2
Figure S9. $^1$H NMR spectrum of 3e, related to Figure 2

Figure S10. $^{13}$C NMR spectrum of 3e, related to Figure 2
Figure S11. $^1$H NMR spectrum of 3f, related to Figure 2

Figure S12. $^{13}$C NMR spectrum of 3f, related to Figure 2
Figure S13. $^1$H NMR spectrum of 3g, related to Figure 2

Figure S14. $^{13}$C NMR spectrum of 3g, related to Figure 2
Figure S15. $^1$H NMR spectrum of 3h, related to Figure 2

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Figure S17. $^1$H NMR spectrum of 3i, related to Figure 2

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Figure S76. $^{13}$C NMR spectrum of 8, related to Figure 3
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Figure S152. $^1$H NMR spectrum of 33, related to Figure 6
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Figure S154. $^1$H NMR spectrum of 34, related to Figure 6
Figure S155. $^{13}$C NMR spectrum of 34, related to Figure 6
Supplemental Item Legends

Table S1: Crystal data and structure refinement, related to Figure 2
Table S2. The effect of H₂O for this process, related to Table 1
Table S3. The effect of base and solvent for this reaction, related to Table 1
Table S4. The optimization experiment conditions of 8, related to Figure 3C.
Table S5. The optimization experiment conditions of 10, related to Figure 3D.
Table S6. The optimization experiment conditions of 20a, related to Figure 4B.
Table S7. The optimization experiment conditions of 20g, related to Figure 4C.
Transparent Methods

General Methods for Experiments

All chemicals were purchased from Adamas Reagent, Energy chemical company, Bide Pharmatech Ltd and Shang Fluoro company (ClCF₂H). Unless otherwise stated, all experiments were conducted in a sealed tube under ClCF₂H atmosphere. Reactions were monitored by TLC or GC-MS analysis. Flash column chromatography was performed over silica gel (200-300 mesh).

¹H-NMR and ¹³C-NMR spectra were recorded in CDCl₃ and DMSO-d₆ on a Bruker Avance III 500 MHz NMR spectrometer (500 MHz ¹H, 125 MHz ¹³C (CPD), 470 MHz ⁹F (CPD)) at room temperature. Chemical shifts were reported in ppm on the scale relative to CDCl₃ (δ = 7.26 for ¹H-NMR, δ = 77.00 for ¹³C-NMR) as an internal reference. Coupling constants (J) were reported in Hertz (Hz).

General Procedure for the Transformations of CO₂, CO and HCOOH as C₁ sources.

![Reaction Conditions Diagram](image)

**Reaction Condition 1**: the amine (1a, 0.12 mmol), N-methyl amine (2a, 0.1 mmol), KOH (3 equiv), H₂O (5 equiv), CH₃CN (2 mL), (HCOOH 3 equiv) rt for 36 h under CO₂/CO atmosphere.

**Reaction condition 2**: the amine (1a, 0.12 mmol), N-methyl amine (2a, 0.1 mmol), K₂CO₃ (3 equiv), phenol (10 mol%), H₂O (5 equiv), CH₃CN (2 mL), (HCOOH 3 equiv) 80 °C for 12 h under CO₂/CO atmosphere.

**Reaction condition 3**: the amine (1a, 0.12 mmol), N-methyl amine (2a, 0.1 mmol), Cs₂CO₃ (3 equiv), S₈ (5 mol%), CH₃CN (5 mL), (HCOOH 3 equiv) 80 °C for 26 h under CO₂/CO atmosphere.

**Reaction Condition 4**: the amine (1a, 0.12 mmol), N-methyl amine (2a, 0.1 mmol), K₂CO₃ (3 equiv), H₂O (5 equiv.), CH₃CN (2 mL), (HCOOH 3 equiv) 50 °C for 12 h under CO₂/CO atmosphere.

**Reaction Condition 5**: the amine (1a, 0.12 mmol), N-methyl amine (2a, 0.1 mmol), K₂CO₃ (3 equiv), H₂O (0.5
Reaction Condition 6: the amine (1a, 0.12 mmol), N-methyl amine (2a, 0.1 mmol), K$_2$CO$_3$ (5 equiv), H$_2$O (30 mL), CH$_3$CN (2 mL), (HCOOH 3 equiv) 110 °C for 48 h under CO$_2$/CO atmosphere.

Scheme S1. The transformations of CO$_2$, CO and HCOOH as C1 sources, related to Figure 1

No desired product 3a was obtained when we carried out many experiments by using CO$_2$, CO and HCOOH as C1 synthons under reaction conditions 1/2/3/4/5/6.

Scheme S2. The transformation for CO$_2$ and CO as C1 sources under transition metals, related to Figure 1

In addition, various transformations for using CO$_2$ and CO as C1 sources in presence of transition metals (TM = Pd, Rh, Ni, Zn, Al) were also carried out according to the reported literature procedures (Tlii et al., 2015; Huang et al., 2011), unfortunately, no desired product 3a was detected.

General Procedure for Large-scale Reaction of the N-methyl Aniline (2a).

Large-scale reaction of the N-methyl aniline

In a dried Schlenk round flask (1500 mL) were placed amine 1a (12 mmol, 1.2 equiv, 1.1 g), N-methyl amine 2a (10 mmol, 1 equiv, 1.07 g) and KOH (30 mmol, 3 equiv, 1.7 g). Then the flask was filled with ClCF$_2$H. Whereafter the solvent was added into Schlenk tube by injector. The resulting mixture was stirred at room temperature for 4 days. Upon completion of the reaction, the solvent was evaporated under reduced pressure and the residue was purified by flash column chromatograph (silica gel, Petroleum ether : Ethyl acetate = 50:1, v/v) to give the desired product 3a (62%, 1.31 g).
General Procedure for the Experiment for the Decomposition of Target Product.

![Chemical structure]

**Scheme S4. The experiment for the decomposition of target product, related to Figure 3B**

**The Decomposition of Target Product 3a**

To a mixture of \((E)-N\text{-}methyl\text{-}N,N'\text{-}diphenyl\text{-}formimidamide\) 3a (0.2 mmol) in MeOH (2 mL), 1 M HCl was added to the seal tube. The resulting mixture was stirred at 80 °C for 3 h. Upon completion of the reaction, the compounds 1a, 2a, 1a-1 and 2a-1 were detected via TLC and GC-MS.

**General Procedure for the synthesis of 3, 8-9 and 10-15.**

![Chemical structure]

**Scheme S5. General process for the synthesis of 3, 8-9 and 10-15, related to Figure 2, Figure 3C and Figure 3D.**

**Preparations of target product 3**

In a dried Schlenk tube were placed the primary amines 1 (0.12 mmol, 1.2 equiv), the secondary aniline 2 (0.1 mmol), KOH (0.3 mmol, 3 equiv) and H₂O (0.5 mmol, 5 equiv). Then the tube was vacuumized for removing the air. Subsequently, chlorodifluoromethane and CH₃CN (2 mL) were added into the mixtures via an injector. The resulting mixture was stirred at room temperature for 36 h. Upon completion of the reaction, the solvent was evaporated under reduced pressure and the residue was purified by flash column chromatography (silica gel, Petroleum ether : Ethyl acetate = 80:1, v/v) to give the desired product (3).

**Preparations of target product 8 and 9**

In a dried Schlenk tube were placed the anilines 1 (0.2 mmol, 1.2 equiv), K₂CO₃ (0.6 mmol, 3 equiv), phenol (0.02 mmol, 10 mol%) and H₂O (1 mmol, 5 equiv), Then the tube was vacuumized for removing the air. Subsequently, chlorodifluoromethane and CH₃CN (2 mL) were added into the mixtures via an injector. The resulting mixtures
was stirred at 80 °C for 12 h. Upon completion of the reaction, the solvent was evaporated under reduced pressure and the residue was purified by flash column chromatography (silica gel, Petroleum ether : Ethyl acetate = 50:1, v/v) to give the desired product (8-9).

Preparations of target product 10-15
In a dried Schlenk tube were placed the aniline 1 (0.2 mmol), Cs₂CO₃ (0.6 mmol, 3 equiv), S₈ (0.02 mmol, 10 mol%) and H₂O (1 mmol, 5 equiv), Then the tube was vacuumized for removing the air. Subsequently, chlorodifluoromethane and CH₃CN (5 mL) is added into the mixtures via an injector. The resulting mixture was stirred at 80 °C for 26 h. Upon completion of the reaction, the solvent was evaporated under reduced pressure and the residue was purified by flash column chromatography (silica gel, Petroleum ether : Ethyl acetate = 100:1, v/v) to give the desired product (10-15).

General Procedure for the Large-scale Synthesis of 18

Preparations of target product 17
In a dried Schlenk tube were placed N¹-methylbenzene-1,2-diamine 16 (7 mmol), KOH (21 mmol, 3 equiv) and H₂O (35 mmol, 5 equiv), Then the tube was vacuumized for removing the air. Subsequently, chlorodifluoromethane and solvent is added into the mixtures via an injector. The resulting mixture was stirred at room temperature for 48 h. Upon completion of the reaction, the solvent was evaporated under reduced pressure and the residue was purified by flash column chromatography (silica gel, Petroleum ether : Ethyl acetate = 10:1, v/v) to give the desired product 17 in 78% yield.

Preparations of target product 18
Methylbenzimidazole (17) (5 mmol) and N-bromosuccinimide (15 mmol) in 30 mL of THF were heated under reflux for 1 h. The solvent was removed by a rotary evaporator, and the residue was recrystallized from EtOAc to afford 18 in 90% yield as a white solid.
General process for the synthesis of 20 and 21-29.

Preparations of target products 20a-20d, 20e' and 20f'
In a dried Schlenk tube were placed 2-aminophenol compounds (19a-19f) (0.2 mmol), K$_2$CO$_3$ (0.6 mmol, 3 equiv) and H$_2$O (1 mmol, 5equiv). Then the tube was vacuumized for removing the air. Subsequently, chlorodifluoromethane and CH$_3$CN (2 mL) is added into the mixtures via an injector. The resulting mixture was stirred at 50 °C for 12 h. Upon completion of the reaction, the solvent was evaporated under reduced pressure and the residue was purified by flash column chromatography (silica gel, Petroleum ether : Ethyl acetate = 100:1, v/v) to give the desired product.

Preparations of target products 20g-20o
In a dried Schlenk tube were placed benzene-1,2-diamine compounds (0.2 mmol), K$_2$CO$_3$ (0.6 mmol, 3 equiv) and H$_2$O (0.5 mL). Then the tube was vacuumized for removing the air. Subsequently, chlorodifluoromethane and CH$_3$CN (2 mL) is added into the mixtures via an injector. The resulting mixture was stirred at 100 °C for 16 h. Upon completion of the reaction, the solvent was evaporated under reduced pressure and the residue was purified by flash column chromatography (silica gel, Petroleum ether : Ethyl acetate = 10:1, v/v) to give the desired product.

Preparations of target products 21-29
In a dried Schlenk tube were placed benzene-1,2-diamine compounds (0.1 mmol), K$_2$CO$_3$ (0.5 mmol, 5 equiv) and H$_2$O (0.5 mL). Then the tube was vacuumized for removing the air. Subsequently, chlorodifluoromethane and CH$_3$CN (2 mL) is added into the mixtures via an injector. The resulting mixture was stirred at 100 °C for 48 h. Upon completion of the reaction, the solvent was evaporated under reduced pressure and the residue was purified by flash column chromatography (silica gel, Petroleum ether : Ethyl acetate = 50:1, v/v) to give the desired product 21-29.
The experiment for H-scrambling of the target product 3a

\[
\begin{align*}
\text{3a, 2 mmol} & \quad \text{KOH (3 equiv)} \\
& \quad \text{D}_2\text{O (5 equiv)} \\
& \quad \text{CH}_3\text{CN (2 mL)} \\
& \quad \text{RT, 24 h} \\
\rightarrow & \quad \text{H/D > 99%}
\end{align*}
\]

Scheme S8. The experiment for H-scrambling of the target product 3a, related to Figure 5a-5b

We carried out a H-scrambling experiment by exposing the product 3a to the standard condition in the presence of D\textsubscript{2}O. No corresponding deuterium-labeling product 3a-D was detected (Scheme S8).

In-situ \textsuperscript{1}H NMR of 3c’

\[
\begin{align*}
\text{EtO} & \quad \text{NH}_2 \\
\text{1c, 0.1 mmol} & \quad \text{KOH (3 equiv)} \\
& \quad \text{CD}_3\text{CN (2 mL)} \\
\rightarrow & \quad \text{EtO} \\
\text{3c’} & \quad \text{N} \\
& \quad \text{F}
\end{align*}
\]

Scheme S9. In-situ \textsuperscript{1}H NMR of 3c’, related to Figure 6A.

General Procedure for In-situ \textsuperscript{1}H NMR of 3c’

There still is plentiful ClCF\textsubscript{2}H dissolved in solvent (CD\textsubscript{3}CN) in the first couple of hours, which caused a problem to detect compound 3c’ by NMR analysis (Scheme S9-S11). In order to see \textsuperscript{1}H peak of compound 3c’ more clearly, we carried out an experiment for about 1 hour and stripped the excess ClCF\textsubscript{2}H at low temperature, the
resulting mixture was analyzed by in situ NMR. The below figure has shown the change of possible reactive intermediate at different time.

Scheme S10. In-situ $^1$H NMR of 3c’, related to Figure 6A.

Scheme S11. The change of possible reactive intermediate at different time, related to Figure 6A.
The experiments for capturing of reaction intermediate 3c’

\[
\begin{align*}
\text{Scheme S12. Various nucleophiles for capturing 3c’, related to Figure 6B.}
\end{align*}
\]

**General Procedure for various nucleophiles for capturing 3c’**

In order to validate the presence of the compound 3c’, various nucleophiles, such as phenols, 1,1,2,3,3,3-hexafluoropropan-1-ol, benzoic acid, hexanoic acid and diphenylmethanol were added into the system after 2 h (entries 1-5), the corresponding desired products were detected by GC-MS (MW: 241, 329, 269, 263 and 331). In addition, we conducted the tests of HRMS (ESI, m/z). Delightedly, we detected corresponding m/z of various anticipated products (Scheme S12).
The experiments for capturing of radical

\[
\text{1a} + \text{2a} + \text{ClF}_2\text{H} \xrightarrow{\text{KOH (3 equiv) H}_2\text{O (5 equiv) Radical Scavengers (2.5 equiv) \text{CH}_3\text{CN (2 mL) \text{r.t. 36 h}}}} \text{3a}
\]

| Entry | Radical Scavengers          | Yield of 3a (iso.) |
|-------|------------------------------|--------------------|
| 1     | TEMPO                        | 79%                |
| 2     | BHT                          | 57%                |
| 3     | ethene-1,1-diyl dibenzene    | 85%                |
| 4     | (1-cyclopropylviny)benzene   | 82%                |

Scheme S13. The experiments for capturing of radical, related to Figure 6C.

We have carried out the control experiments in presence of radical scavengers (TEMPO, BHT, ethene-1,1-diyl dibenzene and (1-cyclopropylviny)benzene), the reactions proceeded smoothly at room temperature to afford desired products in moderate yields. Those results suggest the SET pathway could not be involved in this transformation.

Characterization data for products

\((E)-N\text{-methyl-}N,N'\text{-diphenylformimidamide (3a) (CAS number: 32189-59-6)}\)

The reaction was performed following the general procedure. The residue was purified by flash column chromatography (silica gel, Petroleum ether: AcOEt = 80:1, v/v) to give the product as a yellow oil (19 mg, 88%).\(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 8.11 (s, 1H), 7.41 – 7.35 (m, 2H), 7.34 – 7.29 (m, 2H), 7.20 – 7.12 (m, 3H), 7.11 – 7.00 (m, 3H), 3.52 (s, 3H).

\(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\) 151.5, 151.2, 145.1, 129.5, 129.1, 124.1, 123.4, 121.3, 119.9, 34.1.

\((E)-N'\text{-}(4\text{-methoxyphenyl})-N\text{-methyl-}N\text{-phenylformimidamide (3b)}\)

The reaction was performed following the general
procedure. The residue was purified by flash column chromatography (silica gel, Petroleum ether: AcOEt = 80:1, v/v) to give the product as a yellow oil (20 mg, 82%).$^1^H$ NMR (500 MHz, CDCl$_3$) $\delta$ 8.09 (s, 1H), 7.37 (dd, $J = 8.6$, 7.4 Hz, 2H), 7.18 – 7.11 (m, 3H), 7.01 – 6.96 (m, 2H), 6.86 (d, $J = 8.9$ Hz, 2H), 3.80 (s, 3H), 3.50 (s, 3H). $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 156.1, 150.7, 145.2, 144.8, 129.5, 123.9, 121.9, 119.7, 114.4, 55.5, 34.0. HRMS (ESI, m/z) calcd for C$_{15}$H$_{10}$N$_2$O$^{[M+H]^+}$: 241.1335; found: 241.1337

(E)-N'-{(4-ethoxyphenyl)}-N-methyl-N-phenylformimidamide (3c)

The reaction was performed following the general procedure. The residue was purified by flash column chromatography (silica gel, Petroleum ether: AcOEt = 80:1, v/v) to give the product as a yellow oil (22 mg, 85%).$^1^H$ NMR (500 MHz, CDCl$_3$) $\delta$ 8.09 (s, 1H), 7.37 (dd, $J = 8.4$, 7.5 Hz, 2H), 7.20 – 7.10 (m, 3H), 7.02 – 6.94 (m, 2H), 6.91 – 6.81 (m, 2H), 4.01 (q, $J = 7.0$ Hz, 2H), 3.50 (s, 3H), 1.41 (t, $J = 7.0$ Hz, 3H). $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 155.5, 150.6, 145.2, 144.6, 129.5, 123.99, 121.9, 119.7, 115.1, 63.7, 34.1, 15.0. HRMS (ESI, m/z) calcd for C$_{16}$H$_{11}$N$_2$O$^{[M+H]^+}$: 255.1492; found: 255.1491.

(E)-N-methyl-N'-{(4-phenoxyphenyl)}-N-phenylformimidamide (3d)

The reaction was performed following the general procedure. The residue was purified by flash column chromatography (silica gel, Petroleum ether: AcOEt = 80:1, v/v) to give the product as a yellow oil (24 mg, 81%).$^1^H$ NMR (500 MHz, CDCl$_3$) $\delta$ 8.11 (s, 1H), 7.41 – 7.35 (m, 2H), 7.34 – 7.28 (m, 2H), 7.19 – 7.13 (m, 3H), 7.09 – 6.96 (m, 7H), 3.52 (s, 3H). $^{13}$C NMR (125MHz, CDCl$_3$) $\delta$ 158.22 (s), 1529, 151.0, 147.4, 145.1, 129.6, 124.2, 122.6, 122.2, 120.3, 119.9, 118.0, 34.1. HRMS (ESI, m/z) calcd for C$_{20}$H$_{19}$N$_2$O$^{[M+H]^+}$: 303.1492; found: 303.1491.

(E)-N-methyl-N'-(4-(methylthio)phenyl)-N-phenylformimidamide (3e)

The reaction was performed following the general procedure. The residue was purified by flash column chromatography (silica gel, Petroleum ether: AcOEt = 80:1, v/v) to give the product as a yellow oil (21 mg, 83%).$^1^H$ NMR (500 MHz, CDCl$_3$) $\delta$ 8.08 (s, 1H), 7.38 (dd, $J = 8.6$, 7.4 Hz, 2H), 7.26 – 7.22 (m, 2H), 7.19 – 7.12 (m, 3H), 7.03 – 6.95 (m, 2H), 3.51 (s, 3H), 2.47 (s, 3H). $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 151.0, 149.3, 145.0, 132.1, 129.5, 128.8, 124.3, 121.8, 120.0, 34.2, 17.2.
HRMS (ESI, m/z) cale for C$_{15}$H$_{17}$N$_2$[M+H]$^+$: 257.1107; found: 257.1109.

**(E)-N-methyl-N-phenyl-N'-p-tolylformimidamide (3f)**

The reaction was performed following the general procedure. The residue was purified by flash column chromatography (silica gel, Petroleum ether: AcOEt = 80:1, v/v) to give the product as a yellow oil (19 mg, 86%). $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 8.10 (s, 1H), 7.42 – 7.33 (m, 2H), 7.20 – 7.06 (m, 5H), 7.00 – 6.90 (m, 2H), 3.51 (s, 3H), 2.33 (s, 3H). $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 150.9, 149.0 145.2, 132.8, 129.7, 129.5, 124.0, 121.0, 119.8, 34.1, 20.9.

HRMS (ESI, m/z) cale for C$_{15}$H$_{17}$N$_2$[M+H]$^+$: 225.1386; found: 225.1388.

**(E)-N'-4-ethylphenyl-N-methyl-N-phenylformimidamide (3g)**

The reaction was performed following the general procedure. The residue was purified by flash column chromatography (silica gel, Petroleum ether: AcOEt = 80:1, v/v) to give the product as a yellow oil (20 mg, 83%). $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 8.11 (s, 1H), 7.41 – 7.30 (m, 2H), 7.20 – 7.08 (m, 5H), 7.03 – 6.92 (m, 2H), 3.51 (s, 3H), 2.63 (q, $J$ = 7.6 Hz, 2H), 1.24 (t, $J$ = 7.6 Hz, 3H). $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 150.9, 149.1, 145.2, 139.3, 129.5, 128.5, 124.0, 121.1, 119.8, 34.1, 28.3, 15.8.

HRMS (ESI, m/z) cale for C$_{16}$H$_{19}$N$_2$[M+H]$^+$: 239.1543; found: 239.1543.

**(E)-N'-4-(tert-buty1)phenyl-N-methyl-N-phenylformimidamide (3h)**

The reaction was performed following the general procedure. The residue was purified by flash column chromatography (silica gel, Petroleum ether: AcOEt = 80:1, v/v) to give the product as a yellow oil (21 mg, 79%). $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 8.12 (s, 1H), 7.41 – 7.29 (m, 4H), 7.20 – 7.09 (m, 3H), 7.03 – 6.91 (m, 2H), 3.51 (s, 3H), 1.33 (s, 9H). $^{13}$C NMR (125MHz, CDCl$_3$) $\delta$ 150.9, 148.8, 146.2, 145.2, 129.5, 126.0, 123.9, 120.7, 119.7, 34.3 34.0, 31.5.

HRMS (ESI, m/z) cale for C$_{18}$H$_{23}$N$_2$[M+H]$^+$: 267.1856; found: 267.1853.

**(E)-N'-4-isopropylphenyl-N-methyl-N-phenylformimidamide (3i)**

The reaction was performed following the general procedure. The residue was purified by flash column chromatography (silica gel, Petroleum ether: AcOEt = 80:1, v/v) to give the product as a yellow oil (22 mg, 86%). $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 8.11 (s, 1H), 7.41 – 7.32 (m, 2H), 7.19 – 7.10 (m, 5H), 7.01 – 6.93 (m, 2H), 3.51 (s, 3H), 2.89 (dt, $J$
= 13.8, 6.9 Hz, 1H), 1.25 (d, J = 6.9 Hz, 6H). $^{13}$C NMR (125 MHz, CDCl$_3$) δ 150.9, 149.2, 145.2, 143.9, 129.4, 127.0, 123.9, 121.0, 119.7, 34.0, 33.5, 24.2.

HRMS (ESI, m/z) calcd for C$_7$H$_2$N$_2$[M+H]$^+$: 253.1699; found: 253.1701.

**(E)-N’-(4-(dimethylamino)phenyl)-N-methyl-N-phenylformimidamide (3j)**

The reaction was performed following the general procedure. The residue was purified by flash column chromatography (silica gel, Petroleum ether: AcOEt = 80:1, v/v) to give the product as a yellow oil (19 mg, 77%). $^1$H NMR (500 MHz, CDCl$_3$) δ 8.12 (s, 1H), 7.39 – 7.31 (m, 2H), 7.18 – 7.07 (m, 3H), 7.02 – 6.94 (m, 2H), 6.79 – 6.64 (m, 2H), 3.50 (s, 3H), 2.92 (s, 6H). $^{13}$C NMR (125 MHz, CDCl$_3$) δ 150.9, 148.8, 146.2, 145.2, 129.5, 126.0, 123.9, 120.7, 119.7, 34.3, 34.0, 31.5.

HRMS (ESI, m/z) calcd for C$_{14}$H$_{20}$N$_3$[M+H]$^+$: 254.1652; found: 254.1655.

**(E)-N’-(4-fluorophenyl)-N-methyl-N-phenylformimidamide (3k)**

The reaction was performed following the general procedure. The residue was purified by flash column chromatography (silica gel, Petroleum ether: AcOEt = 80:1, v/v) to give the product as a yellow oil (17 mg, 75%). $^1$H NMR (500 MHz, CDCl$_3$) δ 8.05 (s, 1H), 7.46 – 7.31 (m, 2H), 7.15 (dd, J = 10.9, 4.2 Hz, 3H), 7.06 – 6.87 (m, 4H), 3.50 (s, 3H). $^{13}$C NMR (125 MHz, CDCl$_3$) δ 160.6, 158.6, 151.2, 147.6, 145.1, 129.5, 124.2, 122.2, 120.0, 115.7, 115.5, 34.2.

HRMS (ESI, m/z) calcd for C$_{14}$H$_{13}$F$_3$N$_2$[M+H]$^+$: 229.1136; found: 229.1137.

**(E)-N’-(4-chlorophenyl)-N-methyl-N-phenylformimidamide (3l)**

The reaction was performed following the general procedure. The residue was purified by flash column chromatography (silica gel, Petroleum ether: AcOEt = 80:1, v/v) to give the product as a yellow oil (19 mg, 77 %). $^1$H NMR (500 MHz, CDCl$_3$) δ 8.05 (s, 1H), 7.44 – 7.34 (m, 2H), 7.29 – 7.22 (m, 2H), 7.20 – 7.10 (m, 3H), 7.04 – 6.91 (m, 2H), 3.50 (s, 3H). $^{13}$C NMR (125 MHz, CDCl$_3$) δ 151.3, 150.1, 145.0, 129.5, 129.1, 128.5, 124.4, 122.5, 120.1, 34.3.

HRMS (ESI, m/z) calcd for C$_{14}$H$_{14}$ClN$_2$[M+H]$^+$: 245.0840; found:245.0838.

**(E)-N’-(4-bromophenyl)-N-methyl-N-phenylformimidamide (3m)**

The reaction was performed following the general procedure. The residue was purified by flash column chromatography (silica gel, Petroleum ether: AcOEt = 80:1, v/v) to give the product as a yellow oil (21 mg,
\[ \text{1H NMR (500 MHz, CDCl}_3\] \delta 8.06 (s, 1H), 7.44 - 7.35 (m, 4H), 7.21 - 7.14 (m, 3H), 6.98 - 6.88 (m, 2H), 3.51 (s, 3H). \text{13C NMR (125 MHz, CDCl}_3\] \delta 151.3, 150.6, 144.9, 132.0, 129.5, 124.5, 123.0, 120.1 116.2, 34.3.

HRMS (ESI, m/z) calcd for C_{14}H_{14}BrN_2[M+H]^+: 289.0335; found: 289.0336.

\textbf{(E)-N-methyl-N’-(4-nitrophenyl)-N-phenylformimidamide (3n)}

The reaction was performed following the general procedure. The residue was purified by flash column chromatography (silica gel, Petroleum ether: AcOEt = 80:1, v/v) to give the product as a yellow oil (15 mg, 58%).\text{1H NMR (500 MHz, CDCl}_3\] \delta 8.22 - 8.13 (m, 2H), 8.10 (s, 1H), 7.46 - 7.37 (m, 2H), 7.22 (dd, \( J = 17.7, 7.7 \text{ Hz}, 3H)\), 7.13 - 7.05 (m, 2H), 3.55 (s, 3H).\text{13C NMR (125 MHz, CDCl}_3\] \delta 152.1, 144.4, 143.5, 129.7, 125.3, 121.4, 120.7, 34.7.

HRMS (ESI, m/z) calcd for C_{14}H_{14}N_2O_2[M+H]^+: 256.1081; found: 256.1079.

\textbf{(E)-N’-([1,1’-biphenyl]-4-yl)-N-methyl-N-phenylformimidamide (3o)}

The reaction was performed following the general procedure. The residue was purified by flash column chromatography (silica gel, Petroleum ether: AcOEt = 80:1, v/v) to give the product as a yellow oil (22 mg, 77%).\text{1H NMR (500 MHz, CDCl}_3\] \delta 8.17 (s, 1H), 7.61 (dd, \( J = 7.3, 1.0 \text{ Hz}, 2H)\), 7.57 (dt, \( J = 9.0, 1.8 \text{ Hz}, 2H)\), 7.41 (dt, \( J = 19.8, 7.7 \text{ Hz}, 4H)\), 7.32 (td, \( J = 7.5, 1.1 \text{ Hz}, 1H)\), 7.22 - 7.10 (m, 5H), 3.55 (s, \( J = 0.7 \text{ Hz}, 3H)\).

\text{13C NMR (125 MHz, CDCl}_3\] \delta 151.1, 150.8, 145.1, 141.0, 136.2, 129.5, 128.7, 127.8, 126.7, 124.2, 121.6, 120.0, 34.2.

HRMS (ESI, m/z) calcd for C_{20}H_{19}N_2[M+H]^+: 289.1543; found: 289.1544.

\textbf{(E)-N’-(3-bromophenyl)-N-methyl-N-phenylformimidamide (3p)}

The reaction was performed following the general procedure. The residue was purified by flash column chromatography (silica gel, Petroleum ether: AcOEt = 80:1, v/v) to give the product as a yellow oil (21 mg, 71%).\text{1H NMR (500 MHz, CDCl}_3\] \delta 8.05 (s, 1H), 7.43 - 7.34 (m, 2H), 7.23 - 7.11 (m, 6H), 7.03 - 6.92 (m, 1H), 3.50 (s, 3H).\text{13C NMR (125 MHz, CDCl}_3\] \delta 153.0, 151.5, 144.8, 130.3, 129.5, 126.1, 124.6, 124.1, 1227, 120.3, 34.3.

HRMS (ESI, m/z) calcd for C_{14}H_{12}BrN_2[M+H]^+: 289.0335; found: 289.0333.

\textbf{(E)-N’-(3,4-dimethylphenyl)-N-methyl-N-phenylformimidamide (3q)}

The reaction was performed following the general procedure. The residue was purified by flash column chromatography (silica gel, Petroleum ether: AcOEt = 80:1, v/v) to give the product as a yellow oil (20
mg, 83%).

\(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 8.11 (s, 1H), 7.37 (dd, \(J = 8.6, 7.4\) Hz, 2H), 7.19 – 7.10 (m, 3H), 7.07 (d, \(J = 7.9\) Hz, 1H), 6.86 (d, \(J = 2.0\) Hz, 1H), 6.80 (dd, \(J = 7.9, 2.3\) Hz, 1H), 3.51 (s, 3H), 2.25 (d, \(J = 8.3\) Hz, 6H).

\(^13\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\) 150.8, 149.3, 145.2, 137.2, 131.5, 130.3, 129.4, 123.9, 122.6, 119.8, 118.3, 34.0, 19.9, 19.1.

HRMS (ESI, m/z) calcd for C\(_{16}H_{18}N_2\)[M+H\(^+\)]: 239.1543; found: 239.1546.

(E)-N'-mesityl-N-methyl-N-phenylformimidamide (3r)

The reaction was performed following the general procedure. The residue was purified by flash column chromatography (silica gel, Petroleum ether: AcOEt = 80:1, v/v) to give the product as a yellow oil (22 mg, 85%).

\(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 7.84 (s, 1H), 7.35 (dd, \(J = 8.6, 7.5\) Hz, 2H), 7.16 – 7.04 (m, 3H), 6.92 – 6.81 (m, 2H), 3.54 (s, 3H), 2.26 (s, 3H), 2.16 (s, 6H).

\(^13\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\) 151.2, 146.9, 145.1, 131.7, 129.4, 129.0, 128.6, 123.5, 119.2, 33.6, 20.7, 18.7.

HRMS (ESI, m/z) calcd for C\(_{17}H_{21}N_2\)[M+H\(^+\)]: 253.1699; found: 253.1704.

(E)-N-methyl-N-phenyl-N'-(5,6,7,8-tetrahydronaphthalen-1-yl)formimidamide (3s)

The reaction was performed following the general procedure. The residue was purified by flash column chromatography (silica gel, Petroleum ether: AcOEt = 80:1, v/v) to give the product as a yellow oil (21 mg, 80%).

\(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 8.03 (s, 1H), 7.42 – 7.32 (m, 2H), 7.20 – 7.09 (m, 3H), 7.05 (t, \(J = 7.6\) Hz, 1H), 6.84 (d, \(J = 7.6\) Hz, 1H), 6.64 (d, \(J = 7.6\) Hz, 1H), 3.52 (s, 3H), 2.79 (dt, \(J = 12.7, 6.2\) Hz, 4H), 1.86 – 1.74 (m, 4H).

\(^13\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\) 150.0, 149.5, 145.2, 137.9, 130.7, 129.4, 125.7, 124.4, 123.6, 119.3, 116.0, 33.7, 29.9, 25.4, 23.4, 23.2.

HRMS (ESI, m/z) calcd for C\(_{18}H_{21}N_2\)[M+H\(^+\)]: 265.1699; found:265.1702.

N-methyl-N-phenylformimidamide (3t)

The reaction was performed following the general procedure. The residue was purified by flash column chromatography (silica gel, Petroleum ether: AcOEt = 80:1, v/v) to give the product as a yellow oil (23 mg, 76%).

\(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 8.20 (s, 1H), 7.73 (t, \(J = 7.1\) Hz, 2H), 7.52 (d, \(J = 7.4\) Hz, 1H), 7.45 – 7.33 (m, 3H), 7.26 (dd, \(J = 11.1, 3.7\) Hz, 2H), 7.22 – 7.13 (m, 3H), 7.09 (dd, \(J = 8.0, 1.9\) Hz, 1H), 3.89 (s, 2H), 3.56 (s, 3H).

\(^13\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\) 151, 150.6, 1452, 144.6, 143.0, 141.9, 137.3, 129.5, 126.7, 125.8 124.9, 124.1, 120.3, 120.0, 119.3, 117.8, 37.0, 34.2

HRMS (ESI, m/z) calcd for C\(_{21}H_{19}N_2\)[M+H\(^+\)]: 299.1543; found: 299.1547.
(E)-N’-(9H-fluoren-2-yl)-(E)-N’-(9,9-diphenyl-9H-fluoren-2-yl)-N-methyl-N-phenylformimidamide (3u)

The reaction was performed following the general procedure. The residue was purified by flash column chromatography (silica gel, Petroleum ether: AcOEt = 80:1, v/v) to give the product as a yellow oil (31 mg, 68%). 1H NMR (500 MHz, CDCl3) δ 8.09 (s, 1H), 7.73 (dd, J = 7.8, 4.5 Hz, 2H), 7.38 (ddd, J = 14.9, 7.4, 6.1 Hz, 4H), 7.30 – 7.11 (m, 16H), 7.06 (dd, J = 8.0, 1.9 Hz, 1H), 3.52 (s, 3H).13C NMR (125 MHz, CDCl3) δ 151.9, 151.1, 150.9, 146.1, 145.1, 140.3, 135.7, 129.8, 128.2, 127.4, 126.8, 126.5, 126.1, 124.2, 120.7, 120.4, 120.0, 119.5, 65.5, 34.5.

HRMS (ESI, m/z) calcd for C21H10N2[M+H]+: 299.1543; found: 299.1541.

(E)-N-methyl-N’-(E)-N-methyl-N’-(naphthalen-1-yl)-N-phenylformimidamide (3v)

The reaction was performed following the general procedure. The residue was purified by flash column chromatography (silica gel, Petroleum ether: AcOEt = 80:1, v/v) to give the product as a yellow oil (20 mg, 77%).1H NMR (500 MHz, CDCl3) δ 8.24 (s, 1H), 7.78 (dd, J = 18.2, 8.3 Hz, 3H), 7.46 – 7.29 (m, 6H), 7.24 – 7.10 (m, 3H), 3.58 (s, 3H).13C NMR (125 MHz, CDCl3) δ 151.4, 149.3, 145.1, 134.6, 130.7, 129.5, 128.78, 127.6 127.11, 126.1, 124.2, 123.0, 116.4, 34.3.

HRMS (ESI, m/z) calcd for C18H16N2[M+H]+: 261.1386; found: 261.1383.

(E)-N’-(benzo[d]thiazol-2-yl)-N-methyl-N-phenylformimidamide (3w)

The reaction was performed following the general procedure. The residue was purified by flash column chromatography (silica gel, Petroleum ether: AcOEt = 80:1, v/v) to give the product as a yellow oil (17 mg, 62%).1H NMR (500 MHz, CDCl3) δ 8.80 (s, 1H), 7.73 (dd, J = 22.2, 8.0 Hz, 2H), 7.43 (t, J = 7.9 Hz, 2H), 7.39 – 7.35 (m, 1H), 7.28 (dd, J = 8.6, 0.8 Hz, 3H), 7.22 (t, J = 7.6 Hz, 1H), 3.59 (s, 3H).13C NMR (125 MHz, CDCl3) δ 172.9, 155.2, 151.9, 143.9, 133.7, 129.7, 126.2, 125.9, 123.3, 121.5 121.4, 121.2, 35.3.

HRMS (ESI, m/z) calcd for C15H15N3S[M+H]+: 268.0903; found: 268.0902.

(E)-N-methyl-N’-phenyl-N-(p-tolyl)formimidamide (3x)

The reaction was performed following the general procedure. The residue was purified by flash
column chromatography (silica gel, Petroleum ether: AcOEt = 80:1, v/v) to give the product as a yellow oil (19 mg, 85%).\textsuperscript{1}H NMR (500 MHz, CDCl\textsubscript{3}) \(\delta\) 8.05 (s, 1H), 7.31 (t, \(J = 7.8\) Hz, 2H), 7.18 (d, \(J = 8.2\) Hz, 2H), 7.13 – 6.95 (m, 5H), 3.49 (s, 3H), 2.35 (s, 3H).\textsuperscript{13}C NMR (125 MHz, CDCl\textsubscript{3}) \(\delta\) 151.6, 152.8, 143.7, 129.4, 129.1, 123.6, 121.2, 120.9, 34.2.
HRMS (ESI, m/z) calcd for C\textsubscript{15}H\textsubscript{17}N\textsubscript{2}[M+H]\textsuperscript{+}: 225.1386; found: 225.1390.

\textbf{(E)}-\textit{N-}(4-chlorophenyl)-\textit{N-methyl-}\textsuperscript{N'}-phenylformimidamide (3y)

[Image of molecule with labels]
The reaction was performed following the general procedure. The residue was purified by flash column chromatography (silica gel, Petroleum ether: AcOEt = 80:1, v/v) to give the product as a yellow oil (20 mg, 83%).\textsuperscript{1}H NMR (500 MHz, CDCl\textsubscript{3}) \(\delta\) 8.04 (s, 1H), 7.35 – 7.28 (m, 4H), 7.11 – 7.06 (m, 3H), 7.06 – 7.00 (m, 2H), 3.49 (s, 3H).\textsuperscript{13}C NMR (125 MHz, CDCl\textsubscript{3}) \(\delta\) 151.2, 150.6, 143.7, 129.4, 129.1, 123.6, 121.2, 120.9, 34.2.
HRMS (ESI, m/z) calcd for C\textsubscript{15}H\textsubscript{17}ClN\textsubscript{2}[M+H]\textsuperscript{+}: 245.0840; found: 245.0836.

\textbf{(E)}-\textit{N-methyl-}\textsuperscript{N'}-phenyl-\textit{N-(o-tolyl)}formimidamide (3z)

[Image of molecule with labels]
The reaction was performed following the general procedure. The residue was purified by flash column chromatography (silica gel, Petroleum ether: AcOEt = 80:1, v/v) to give the product as a yellow oil (15 mg, 68%).\textsuperscript{1}H NMR (500 MHz, CDCl\textsubscript{3}) \(\delta\) 7.73 (s, 1H), 7.32 – 7.24 (m, 5H), 7.17 (dd, \(J = 6.8, 2.1\) Hz, 1H), 7.06 (t, \(J = 8.0\) Hz, 3H), 3.39 (s, 3H), 2.35 (s, 3H).\textsuperscript{13}C NMR (125 MHz, CDCl\textsubscript{3}) \(\delta\) 152.8, 151.6, 134.8, 131.5, 129.0, 127.3, 127.0, 123.0, 121.3, 31.5, 18.2.
HRMS (ESI, m/z) calcd for C\textsubscript{15}H\textsubscript{17}ClN\textsubscript{2}[M+H]\textsuperscript{+}: 225.1386; found: 25.1389.

\textbf{(E)}-\textit{N-ethyl-}\textsuperscript{N'}-\textit{diphenylformimidamide (3aa)}

[Image of molecule with labels]
The reaction was performed following the general procedure. The residue was purified by flash column chromatography (silica gel, Petroleum ether: AcOEt = 80:1, v/v) to give the product as a yellow oil (18 mg, 82%).\textsuperscript{1}H NMR (500 MHz, CDCl\textsubscript{3}) \(\delta\) 7.98 (s, 1H), 7.41 – 7.34 (m, 2H), 7.33 – 7.27 (m, 2H), 7.20 – 7.13 (m, 3H), 7.10 – 7.00 (m, 3H), 4.09 (q, \(J = 7.1\) Hz, 2H), 1.31 (d, \(J = 7.1\) Hz, 3H).\textsuperscript{13}C NMR (125MHz, CDCl\textsubscript{3}) \(\delta\) 151.7, 150.5, 144.0, 129.5, 129.1, 124.4, 123.2, 121.3, 120.9, 41.9, 12.8.
HRMS (ESI, m/z) calcd for C\textsubscript{15}H\textsubscript{17}ClN\textsubscript{2}[M+H]\textsuperscript{+}: 225.1386; found:225.1390.

\textbf{(E)}-\textit{N-ethyl-}\textsuperscript{N'}-phenyl-\textit{N-(p-tolyl)}formimidamide (3ab)

[Image of molecule with labels]
The reaction was performed following the general procedure. The residue was purified by flash column chromatography (silica gel, Petroleum ether: AcOEt = 80:1, v/v) to give the product as a yellow oil (19 mg,
80%). $^1$H NMR (500 MHz, CDCl$_3$) δ 7.92 (s, 1H), 7.29 (dd, $J = 8.1, 7.5$ Hz, 2H), 7.17 (d, $J = 8.1$ Hz, 2H), 7.09 – 7.00 (m, 5H), 4.05 (q, $J = 7.1$ Hz, 2H), 2.35 (s, 3H), 1.30 – 1.28 (m, 3H). $^{13}$C NMR (125 MHz, CDCl$_3$) δ 151.9, 150.7, 141.6, 134.3, 130.0, 129.0, 123.0, 121.6, 121.3, 42.0, 20.8, 12.8.

HRMS (ESI, m/z) caleed for C$_{16}$H$_{18}$N$_2$[M+H]$^+$: 239.1543; found: 239.1542.

**$^{(E)}$-N-butyl-$N,N'$-diphenylformimidamide (3ac)**

The reaction was performed following the general procedure. The residue was purified by flash column chromatography (silica gel, Petroleum ether: AcOEt = 80:1, v/v) to give the product as a yellow oil (19 mg, 76%). $^1$H NMR (500 MHz, CDCl$_3$) δ 7.99 (s, 1H), 7.40 – 7.34 (m, 2H), 7.29 (t, $J = 7.8$ Hz, 2H), 7.16 (dd, $J = 12.0$, 7.6 Hz, 3H), 7.10 – 6.99 (m, 3H), 4.13 – 3.93 (m, 2H), 1.70 (tt, $J = 7.7$, 6.7 Hz, 2H), 1.44 – 1.35 (m, 2H), 0.94 (t, $J = 7.4$ Hz, 3H). $^{13}$C NMR (125 MHz, CDCl$_3$) δ 155.3, 151.8, 150.9, 144.3, 129.4, 129.0, 124.9, 123.1, 121.3, 46.5, 29.5, 20.2, 13.9.

HRMS (ESI, m/z) caleed for C$_{16}$H$_{18}$N$_2$[M+H]$^+$: 239.1543; found: 239.1544.

**Ethyl ($^{(E)}$)-4-(((methyl(phenyl)amino)methylene)amino)benzoate (3ad)**

The reaction was performed following the general procedure. The residue was purified by flash column chromatography (silica gel, Petroleum ether: AcOEt = 80:1, v/v) to give the product as a yellow oil (17 mg, 59%). $^1$H NMR (500 MHz, CDCl$_3$) δ 8.13 (s, 1H), 8.07 – 7.98 (m, 2H), 7.47 – 7.36 (m, 2H), 7.21 (dd, $J = 7.7$, 4.8 Hz, 3H), 7.12 – 7.00 (m, 2H), 4.38 (q, $J = 7.1$ Hz, 2H), 3.55 (s, 3H), 1.41 (t, $J = 7.1$ Hz, 3H). $^{13}$C NMR (125 MHz, CDCl$_3$) δ 166.7, 155.7, 151.6, 144.8, 130.9, 129.6, 125.2, 124.7, 121.1, 120.4, 60.7, 34.4, 14.4.

HRMS (ESI, m/z) caleed for C$_{17}$H$_{18}$N$_2$O$_2$[M+H]$^+$: 283.1441; found: 283.1442.

**$^{(E)}$-1-(4-(2-chlorodibenzo[b,f][1,4]oxazepin-11-yl)piperazin-1-yl)-N-p
genylmethanimine (3ae)**

The reaction was performed following the general procedure. The residue was purified by flash column chromatography (silica gel, Petroleum ether: AcOEt = 80:1, v/v) to give the product as a yellow oil 32 mg, 76%). $^1$H NMR (500 MHz, CDCl$_3$) δ 7.59 (s, 1H), 7.42 (dd, $J = 8.7$, 2.6 Hz, 1H), 7.36 (d, $J = 2.6$ Hz, 1H), 7.32 – 7.27 (m, 2H), 7.23 – 7.16 (m, 2H), 7.12 (ddd, $J = 13.6$, 5.3, 3.7 Hz, 2H), 7.08 – 6.97 (m, 4H), 3.59 (s, 8H). $^{13}$C NMR (125 MHz, CDCl$_3$) δ
HRMS (ESI, m/z) calcd for C_{24}H_{21}ClN_{4}O[M+H]^+: 417.1477; found: 417.1479.

**(E)-N-phenyl-1-(4-(4-(trifluoromethyl)pyrimidin-2-yl)piperazin-1-yl)methanimine (3af)**

The reaction was performed following the general procedure. The residue was purified by flash column chromatography (silica gel, Petroleum ether: AcOEt = 80:1, v/v) to give the product as a yellow oil (20.5 mg, 61%).^1^H NMR (500 MHz, CDCl₃) δ 8.53 (d, J = 4.8 Hz, 1H), 7.61 (s, 1H), 7.28 (t, J = 7.8 Hz, 2H), 7.04 (t, J = 7.3 Hz, 1H), 6.99 (d, J = 7.4 Hz, 2H), 6.82 (d, J = 4.8 Hz, 1H), 3.99 – 3.94 (m, 4H), 3.60 (s, 4H).^1^C NMR (125 MHz, CDCl₃) δ 161.4, 160.3, 156.8, 156.5, 156.2, 155.9, 152.3, 151.4, 129.1, 123.0, 121.1, 119.9, 119.4, 118.9, 105.2, 43.6.

HRMS (ESI, m/z) calcd for C_{16}H_{16}F_{3}N_{5}[M+H]^+: 336.1431; found: 336.1430.

**(E)-N-(2-((S)-2-cyanopyrrolidin-1-yl)-2-oxoethyl)-N'-(1R,3R,5R,7S)-3-hydroxyadamantan-1-yl)-N'-phenylformimidamide compound with

11-methane and methane (1:1:2) (3ag)**

The reaction was performed following the general procedure. The residue was purified by flash column chromatography (silica gel, Petroleum ether: AcOEt = 10:1, v/v) to give the product as a yellow oil (29 mg, 71%).^1^H NMR (500 MHz, CDCl₃) δ 7.92 (s, 1H), 7.25 (dd, J = 14.9, 7.3 Hz, 2H), 7.01 (dt, J = 14.7, 7.4 Hz, 1H), 6.87 (dd, J = 16.8, 7.5 Hz, 2H), 5.69 – 4.72 (m, 1H), 4.34 (dd, J = 28.7, 15.6 Hz, 1H), 4.07 (t, J = 14.5 Hz, 1H), 3.82 – 3.47 (m, 2H), 2.41 – 1.81 (m, 15H), 1.71 (s, 4H).^1^C NMR (125 MHz, CDCl₃) δ 169.5, 168.9, 152.0, 151.6, 149.7, 149.6, 129.1, 129.0, 122.8, 122.6, 121.3, 121.2, 119.4, 118.6, 69.5, 69.4, 59.2, 58.8, 49.9, 49.7, 47.5, 46.8, 46.6, 46.2, 45.0, 44.4, 43.8, 41.1, 41.1, 34.6, 32.3, 30.7, 29.9, 29.7, 25.4, 23.2.

**(S,E)-N-benzyl-N'phenyl-N-(1-phenylethyl)formimidamide (3ah)**

The reaction was performed following the general procedure. The residue was purified by flash column chromatography (silica gel, Petroleum ether: AcOEt = 80:1, v/v) to give the product as a yellow oil (19 mg, 60%).^1^H NMR (500 MHz, CDCl₃) δ 7.97 (s, 1H), 7.57 – 7.15 (m, 12H), 7.05 (ddd, J = 9.5, 5.2, 1.0 Hz, 7.15 – 6.75 (m, 2H), 6.63 (t, J = 7.3 Hz, 2H), 6.47 (t, J = 7.3 Hz, 2H).
4.90 (s, 1H), 4.51 (d, J = 65.1 Hz, 2H), 1.59 (d, J = 7.1 Hz, 3H). \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\) 152.3, 151.9, 141.6, 138.4, 129.1, 128.7, 128.6, 128.3, 127.7, 127.1, 126.90 – 125.52 (m), 122.7, 121.4, 58.3, 48.5, 20.6.

HRMS (ESI, m/z) caleld for C\(_{22}\)H\(_{22}\)N\(_2\)[M+H]\(^+\): 315.1856; found: 315.1858.

\((E)-N,N\text{-dicyclohexyl-}N'\text{-phenylformimidamide (5)}\)

The reaction was performed following the general procedure. The residue was purified by flash column chromatography (silica gel, Petroleum ether: AcOEt = 80:1, v/v) to give the product as a yellow oil (22 mg, 76%). \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 7.70 (s, 1H), 7.28 (dd, \(J = 10.8, 4.8\) Hz, 2H), 7.02 – 6.93 (m, 3H), 1.77 (dd, \(J = 69.6, 11.6\) Hz, 11H), 1.58 – 1.31 (m, 9H), 1.19 – 1.10 (m, 2H), 0.89 (dt, \(J = 12.6, 6.5\) Hz, 1H). \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\) 153.3, 150.6, 128.9, 122.0, 121.3, 29.7, 25.6.

HRMS (ESI, m/z) caleld for C\(_{19}\)H\(_{19}\)N\(_2\)[M+H]\(^+\): 285.2325; found: 285.2321.

\((Z)-N\text{-isopropyl-}N'\text{-phenyl-}N\text{-}(3-(phenylamino)phenyl)formimidamid}\)

The reaction was performed following the general procedure. The residue was purified by flash column chromatography (silica gel, Petroleum ether: AcOEt = 80:1, v/v) to give the product as a yellow oil (18 mg, 54%). \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 7.35 – 7.28 (m, 4H), 7.13 – 6.99 (m, 10H), 5.84 (s, 1H), 1.28 (d, \(J = 6.8\) Hz, 7H). \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\) 153.0, 152.1, 142.6, 142.4, 133.9, 129.8, 129.5, 129.0, 123.5, 122.6, 121.6, 121.3, 118.4, 117.4, 114.8, 23.1, 21.1.

\(4\text{-}((E\text{-}((2\text{-}((S\text{-}2\text{-}cyanopyrrolidin-1-yl)-2\text{-}oxoethyl)((1r,3R,5R,7S)-3-hydroxyadamantan-1-yl)amino)methylene)amino)benzoate (3ai)}\)

The reaction was performed following the general procedure. The residue was purified by flash column chromatography (silica gel, Petroleum ether: AcOEt = 20:1, v/v) to give the product as a yellow oil (33.5 mg, 70%). \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 7.92 (s, 1H), 7.88 (dd, \(J = 8.4, 4.6\) Hz, 2H), 6.84 (dd, \(J = 16.5, 8.5\) Hz, 2H), 5.48 – 4.63 (m, 1H), 4.38 – 4.18 (m, 3H), 4.15 – 3.93 (m, 2H), 3.78 – 3.66 (m, 2H), 3.62 – 3.34 (m, 1H), 2.59 (d, \(J = 138.4\) Hz, 1H), 2.37 – 2.07 (m, 7H), 2.03 – 1.98 (m, 1H), 1.98 – 1.80 (m, 6H), 1.67 (s, 4H), 1.56 – 1.47 (m, 2H), 1.33 (t, \(J = 7.1\) Hz, 3H), 1.24 – 1.12 (m, 1H). \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\) 171.2, 171.1, 168.9, 168.4,
166.8, 166.7, 156.3, 155.9, 150.1, 150.0, 130.9, 130.8, 124.3, 121.0, 120.9, 119.1, 118.5, 74.6, 69.3, 69.2, 67.1, 60.6, 60.5, 60.4, 59.6, 59.2, 56.7, 49.7, 49.5, 47.4, 46.8, 46.6, 46.2, 45.0, 44.5, 43.6, 41.0, 41.0, 34.6, 34.5, 32.3, 30.6, 29.9, 25.4, 23.2, 21.1, 21.0, 16.2, 14.4, 14.2.

(E)-N,N’-diphenylformimidamide (8)

The reaction was performed following the general procedure. The residue was purified by flash column chromatography (silica gel, Petroleum ether: AcOEt = 50:1, v/v) to give the product as a yellow oil (11 mg, 53%). ¹H NMR (500 MHz, CDCl₃) δ 8.20 (s, 1H), 7.31 (t, J = 7.8 Hz, 4H), 7.24 – 6.64 (m, 6H). ¹³C NMR (125 MHz, CDCl₃) δ 129.4, 123.4, 118.9.

HRMS (ESI, m/z) calcd for C₁₃H₁₄N₂[M+H]⁺: 197.1073; found: 197.1076.

(E)-N,N’-di-p-tolylformimidamide (9)

The reaction was performed following the general procedure. The residue was purified by flash column chromatography (silica gel, Petroleum ether: AcOEt = 50:1, v/v) to give the product as a yellow oil (11 mg, 48%). ¹H NMR (500 MHz, CDCl₃) δ 8.17 (s, 1H), 7.11 (d, J = 8.1 Hz, 4H), 6.94 (d, J = 8.0 Hz, 4H), 2.33 (s, 6H). ¹³C NMR (125 MHz, CDCl₃) δ 149.3, 132.8, 129.9, 119.5, 118.9, 29.7, 20.7.

HRMS (ESI, m/z) calcd for C₁₅H₁₆N₂[M+H]⁺: 225.1386; found: 225.1389.

(E)-N-(difluoromethyl)-N,N’-diphenylformimidamide (10)

The reaction was performed following the general procedure. The residue was purified by flash column chromatography (silica gel, Petroleum ether: AcOEt = 100:1, v/v) to give the product as a yellow oil (17 mg, 67%). ¹H NMR (500 MHz, CDCl₃) δ 7.84 (t, J = 2.8 Hz, 1H), 7.57 (t, J = 52.5 Hz, 1H), 7.45 (dd, J = 6.9, 1.6 Hz, 2H), 7.42 – 7.37 (m, 3H), 7.32 (dd, J = 10.7, 5.0 Hz, 2H), 7.14 (t, J = 7.4 Hz, 1H), 7.06 – 7.00 (m, 2H). ¹³C NMR (125 MHz, CDCl₃) δ 149.4, 149.1, 136.4, 129.5, 129.2, 128.2, 127.4, 124.6, 121.1 110.2 (s, J=243.75Hz). ¹⁹F NMR (470 MHz, CDCl₃) δ -97.8, -102.8.

HRMS (ESI, m/z) calcd for C₁₄H₁₂F₂N₂[M+H]⁺: 247.1041; found: 247.1042.

(E)-N-(difluoromethyl)-N,N’-di-p-tolylformimidamide (11)

The reaction was performed following the general procedure. The residue was purified by flash column chromatography (silica gel, Petroleum ether: AcOEt = 100:1, v/v) to give the product as a yellow oil (17 mg, 61%). ¹H NMR (500 MHz, CDCl₃) δ 7.82 (t, J =
2.8 Hz, 1H), 7.55 (dd, J = 67.5, 54.9 Hz, 1H), 7.17 – 7.11 (m, 2H), 6.94 (d, J = 8.2 Hz, 2H), 2.42 (s, 3H), 2.35 (s, 3H).\(^{13}\text{C}\) NMR \((125\text{ MHz, CDCl}_3)\) \(\delta\) 149.0, 147.0, 138.2, 134.1, 133.7, 130.1, 129.7, 127.5, 120.9, 110.2 (s, J = 237.5 Hz), 21.1, 20.8.\(^{19}\text{F}\) NMR \((470\text{ MHz, CDCl}_3)\) \(\delta\) -97.8, -103.0. HRMS (ESI, m/z) caledd for \(\text{C}_{16}\text{H}_{13}\text{F}_2\text{N}_2\text{[M+H]}^+:275.1354\); found: 275.1356.

\((E)-\text{N-(difluoromethyl)-N',N'-bis(4-ethylphenyl)formimidamid})) (12)

The reaction was performed following the general procedure. The residue was purified by flash column chromatography (silica gel, Petroleum ether: AcOEt = 100:1, v/v) to give the product as a yellow oil (18 mg, 59%).\(^1\text{H}\) NMR \((500\text{ MHz, CDCl}_3)\) \(\delta\) 7.81 (t, \(J = 2.8\text{ Hz, 1H})\), 7.53 (t, \(J = 61.2\text{ Hz, 1H})\), 7.27 (s, 4H), 7.14 (d, \(J = 8.4\text{ Hz, 2H})\), 6.98 – 6.91 (m, 2H), 2.69 (q, \(J = 7.6\text{ Hz, 2H})\), 2.63 (q, \(J = 7.6\text{ Hz, 2H})\), 1.26 (s, 3H), 1.23 (t, \(J = 7.6\text{ Hz, 3H})\).\(^{13}\text{C}\) NMR \((125\text{ MHz, CDCl}_3)\) \(\delta\) 149.0, 147.1, 144.4, 140.6, 133.9, 128.9, 128.5, 127.5, 121.0, 110.2 (s, \(J = 242.5\text{Hz})\), 28.5, 28.3, 15.7, 15.4. \(^{19}\text{F}\) NMR \((470\text{ MHz, CDCl}_3)\) \(\delta\) -98.5, -103.0. HRMS (ESI, m/z) caledd for \(\text{C}_{18}\text{H}_{21}\text{F}_2\text{N}_2\text{[M+H]}^+:303.1667\); found: 303.1668.

\((E)-\text{N-(difluoromethyl)-N',N'-bis(4-isopropylphenyl)formimidamid})) (13)

The reaction was performed following the general procedure. The residue was purified by flash column chromatography (silica gel, Petroleum ether: AcOEt = 100:1, v/v) to give the product as a yellow oil (21 mg, 62%).\(^1\text{H}\) NMR \((500\text{ MHz, CDCl}_3)\) \(\delta\) 7.81 (t, \(J = 2.8\text{ Hz, 1H})\), 7.55 (t, \(J = 61.2\text{ Hz, 1H})\), 7.28 (s, 4H), 7.20 – 7.13 (m, 2H), 7.00 – 6.90 (m, 2H), 2.92 (ddt, \(J = 30.5, 13.8, 6.9\text{ Hz, 2H})\), 1.28 (s, 3H), 1.26 (s, 3H), 1.24 (s, 3H), 1.23 (s, 3H).\(^{13}\text{C}\) NMR \((125\text{ MHz, CDCl}_3)\) \(\delta\) 149.0, 147.2, 145.2, 134.0, 127.4, 127.1, 120.9, 110.2 (s, \(J = 247.5\text{Hz})\), 33.8, 33.6, 24.1, 23.9. \(^{19}\text{F}\) NMR \((470\text{ MHz, CDCl}_3)\) \(\delta\) -98.0, -103.0. HRMS (ESI, m/z) caledd for \(\text{C}_{20}\text{H}_{23}\text{F}_2\text{N}_2\text{[M+H]}^+:331.1980\); found: 331.1986.

\((E)-\text{N',N'-bis(4-\text{(tert-butyl)phenyl})-N-(difluoromethyl)formimidamid})) (14)

The reaction was performed following the general procedure. The residue was purified by flash column chromatography (silica gel, Petroleum ether: AcOEt = 100:1, v/v) to give the product as a yellow oil (23 mg, 65%). \(^1\text{H}\) NMR \((500\text{ MHz, CDCl}_3)\) \(\delta\) 7.85 (t, \(J = 2.8\text{ Hz, 1H})\), 7.59 (t, \(J = 55.2\text{ Hz, 1H})\).
Hz, 1H), 7.48 – 7.44 (m, 2H), 7.44 – 7.28 (m, 5H), 7.03 – 6.94 (m, 2H), 1.37 (s, 9H), 1.34 (s, 9H). $^{13}$C NMR (125 MHz, CDCl$_3$) δ 151.2, 149.1, 147.5, 146.8, 133.7, 126.9, 126.4, 126.0, 120.7, 110.2 (t, $J = 242.5$ Hz), 34.7, 34.4, 31.38, 31.1. $^{19}$F NMR (470 MHz, CDCl$_3$) δ -98.1, -102.9.

$^{(E)}$-$N,N'$-bis(4-bromophenyl)-$N$-(difluoromethyl)formimidamide (15)

The reaction was performed following the general procedure. The residue was purified by flash column chromatography (silica gel, Petroleum ether: AcOEt = 10:1, v/v) to give the product as a yellow oil (23 mg, 57%). $^1$H NMR (500 MHz, CDCl$_3$) δ 7.78 (t, $J = 2.4$ Hz, 1H), 7.66 (t, $J = 38.0$ Hz, 1H), 7.59 – 7.56 (m, 2H), 7.43 – 7.40 (m, 2H), 7.26 – 7.23 (m, 2H), 6.91 – 6.84 (m, 2H). $^{13}$C NMR (125 MHz, CDCl$_3$) δ 148.6, 135.0, 132.8, 132.2, 129.1, 122.8, 117.9 (t, $J = 571.3$ Hz), 100.0. $^{19}$F NMR (470 MHz, CDCl$_3$) δ -99.5, -102.9.

1-methyl-1H-benzo[d]imidazole (17) (CAS number:1632-83-3)

The reaction was performed following the general procedure. The residue was purified by flash column chromatography (silica gel, Petroleum ether: AcOEt = 10:1, v/v) to give the product as a yellow oil (12mg, 90%). $^1$H NMR (500 MHz, CDCl$_3$) δ 7.86 (s, 1H), 7.81 (dd, $J = 7.1$, 1.2 Hz, 1H), 7.39 (dd, $J = 7.0$, 1.1 Hz, 1H), 7.35 – 7.26 (m, 2H), 3.84 (s, 3H).$^{13}$C NMR (125 MHz, CDCl$_3$) δ 143.7, 143.5, 122.94 (s), 122.1, 120.3, 109.3, 31.0.

6-methylbenzo[d]oxazole (20a) (CAS number:10531-80-3)

The reaction was performed following the general procedure. The residue was purified by flash column chromatography (silica gel, Petroleum ether: AcOEt = 100:1, v/v) to give the product as a colourless oil (21 mg,81%).$^1$H NMR (500 MHz, CDCl$_3$) δ 8.03 (s, 1H), 7.65 (d, $J = 8.1$ Hz, 1H), 7.39 (s, 1H), 7.18 (dd, $J = 8.1$, 0.7 Hz, 1H), 2.50 (s, 3H).$^{13}$C NMR (125 MHz, CDCl$_3$) δ 152.1, 150.3, 137.8, 136.1, 125.9, 119.9, 111.1, 21.8.

5-methylbenzo[d]oxazole (20b) (CAS number:10531-78-9)

The reaction was performed following the general procedure. The residue was purified by flash column chromatography (silica gel, Petroleum ether: AcOEt = 100:1, v/v) to give the product as a colourless oil (21 mg,77%).$^1$H NMR (500 MHz, CDCl$_3$) δ 8.07 (s, 1H), 8.07 (s, 1H), 7.40 (d, $J = 8.2$ Hz, 1H), 7.40 (d, $J = 8.2$ Hz, 1H), 7.27 (t, $J = 7.8$ Hz, 1H), 7.27 (t, $J = 7.8$ Hz, 1H), 7.16 (d, $J = 7.5$ Hz, 1H), 7.16 (d, $J = 7.5$ Hz, 1H), 2.64 (s, 3H), 2.64 (s, 3H).$^{13}$C NMR (125 MHz, CDCl$_3$) δ 151.8, 149.7, 139.2, 131.0, 125.3, 125.1, 108.2, 16.5.
5-chlorobenzo[d]oxazole (20c) (CAS number: 17200-29-2)

The reaction was performed following the general procedure. The residue was purified by flash column chromatography (silica gel, Petroleum ether: AcOEt = 100:1, v/v) to give the product as a colourless oil (22 mg, 70%). $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 8.11 (s, 1H), 7.77 (d, $J = 2.0$ Hz, 1H), 7.51 (d, $J = 8.7$ Hz, 1H), 7.36 (dd, $J = 8.7$, 2.0 Hz, 1H). $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 153.7, 148.5, 141.1, 130.2, 126.1, 120.6, 111.8.

5-bromobenzo[d]oxazole (20d) (CAS number: 132244-31-6)

The reaction was performed following the general procedure. The residue was purified by flash column chromatography (silica gel, Petroleum ether: AcOEt = 100:1, v/v) to give the product as a colourless oil (25 mg, 68%). $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 8.09 (s, 1H), 7.93 (d, $J = 1.7$ Hz, 1H), 7.49 (dt, $J = 20.0$, 5.2 Hz, 2H). $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 153.5, 149.0, 141.6, 128.8, 123.7, 117.4, 112.3.

2-(difluoromethoxy)-5-nitroaniline (20e’)

The reaction was performed following the general procedure. The residue was purified by flash column chromatography (silica gel, Petroleum ether: AcOEt = 100:1, v/v) to give the product as a colourless oil (36 mg, 89%). $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.63 (d, $J = 2.7$ Hz, 1H), 7.59 (dd, $J = 8.8$, 2.7 Hz, 1H), 7.12 (d, $J = 8.8$ Hz, 1H), 6.58 (t, $J = 72.8$ Hz, 1H), 4.20 (s, 2H). $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 145.7, 142.3, 139.0, 117.8 (s, $J = 261.25$ Hz), 113.5, 110.6. $^{19}$F NMR (470 MHz, CDCl$_3$) $\delta$ -81.0.

2-(difluoromethoxy)-4-nitroaniline (20f’)

The reaction was performed following the general procedure. The residue was purified by flash column chromatography (silica gel, Petroleum ether: AcOEt = 100:1, v/v) to give the product as a colourless oil (34 mg, 84%). $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 8.03 – 7.90 (m, 2H), 6.76 (d, $J = 8.8$ Hz, 1H), 6.57 (t, $J = 72.9$ Hz, 1H), 4.66 (s, 2H). $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 145.1, 138.2, 136.0, 118.1, 116.1, 116.0 (s, $J = 262.5$ Hz) 114.0. $^{19}$F NMR (470 MHz, CDCl$_3$) $\delta$ -80.8.

Benzo[d]oxazole (20g) (CAS number: 51-17-2)

The reaction was performed following the general procedure. The residue was purified by flash column chromatography (silica gel, Petroleum ether: AcOEt = 10:1, v/v) to give the product as a white solid (20 mg, 86%). $^1$H NMR (500 MHz,
6-methylbenzo[d]oxazole (20h) (CAS number: 4887-83-6)

The reaction was performed following the general procedure. The residue was purified by flash column chromatography (silica gel, Petroleum ether: AcOEt = 10:1, v/v) to give the product as a white solid (24 mg, 92%). $^1$H NMR (500 MHz, DMSO) $\delta$ 12.47 (s, 1H), 8.18 (s, 1H), 7.39 (d, $J = 7.6$ Hz, 1H), 7.07 (t, $J = 7.6$ Hz, 1H), 6.98 (d, $J = 7.2$ Hz, 1H), 2.52 (s, 3H). $^{13}$C NMR (125 MHz, DMSO) $\delta$ 141.77 (s), 122.16 (s), 17.24 (s).

5-fluoro-1H-benzo[d]imidazole (20i) (CAS number: 1977-72-6)

The reaction was performed following the general procedure. The residue was purified by flash column chromatography (silica gel, Petroleum ether: AcOEt = 10:1, v/v) to give the product as a white solid (21 mg, 78%). $^1$H NMR (500 MHz, DMSO) $\delta$ 12.56 (s, 1H), 8.25 (s, 1H), 7.58 (dd, $J = 8.4$, 4.9 Hz, 1H), 7.42 – 7.36 (m, 1H), 7.07 – 7.01 (m, 1H). $^{13}$C NMR (125 MHz, DMSO) $\delta$ 159.9, 158.0, 143.8, 110.5.

7-chloro-1H-benzo[d]imidazole (20j) (CAS number: 16931-35-4)

The reaction was performed following the general procedure. The residue was purified by flash column chromatography (silica gel, Petroleum ether: AcOEt = 10:1, v/v) to give the product as a white solid (26 mg, 86%). $^1$H NMR (500 MHz, DMSO) $\delta$ 12.80 (s, 1H), 8.32 (s, 1H), 7.53 (s, 1H), 7.30 – 7.17 (m, 2H). $^{13}$C NMR (125 MHz, DMSO) $\delta$ 143.3, 123.5, 121.6, 111.4.

5-bromo-1H-benzo[d]imidazole (20k) (CAS number: 4887-88-1)

The reaction was performed following the general procedure. The residue was purified by flash column chromatography (silica gel, Petroleum ether: AcOEt = 10:1, v/v) to give the product as a white solid (29 mg, 75%). $^1$H NMR (500 MHz, DMSO) $\delta$ 12.63 (s, 1H), 8.26 (s, 1H), 7.79 (s, 1H), 7.55 (s, 1H), 7.32 (d, $J = 8.2$ Hz, 1H). $^{13}$C NMR (125 MHz, DMSO) $\delta$ 143.8, 100.0.

6-nitro-1H-benzo[d]imidazole (20l) (CAS number: 94-52-0)

The reaction was performed following the general procedure. The residue was purified by flash column chromatography (silica gel, Petroleum ether: AcOEt = 10:1, v/v) to give the product as a yellow solid (14 mg, 42%). $^1$H NMR (500 MHz, DMSO) $\delta$ 8.63 – 8.41 (m, 2H), 8.17 – 7.97 (m, 1H), 7.75 (ddd, $J = 8.4$, 7.5, 1.8 Hz,
1H). $^{13}$C NMR (126 MHz, DMSO) δ 147.17 (d, $J = 9.3$ Hz), 143.09 (s), 118.00 (d, $J = 9.4$ Hz), 115.29 (s), 113.18 (s).

5-5,6-dimethyl-1H-benzo[d]imidazole (20m) (CAS number: 582-60-5)

The reaction was performed following the general procedure. The residue was purified by flash column chromatography (silica gel, Petroleum ether: AcOEt = 10:1, v/v) to give the product as a white solid (23mg, 79%). $^1$H NMR (500 MHz, DMSO) δ 8.05 (s, 1H), 7.34 (s, 2H), 2.29 (s, 6H). $^{13}$C NMR (125 MHz, DMSO) δ 141.4, 130.5, 115.8, 20.4.

5,6-difluoro-1H-benzo[d]imidazole (20n) (CAS number: 78581-99-4)

The reaction was performed following the general procedure. The residue was purified by flash column chromatography (silica gel, Petroleum ether: AcOEt = 10:1, v/v) to give the product as a white solid (24mg, 77%). $^1$H NMR (500 MHz, DMSO) δ 12.65 (s, 1H), 8.28 (s, 1H), 7.64 (d, $J = 22.7$ Hz, 2H). $^{13}$C NMR (125 MHz, DMSO) δ 144.5.

5,6-dichloro-1H-benzo[d]imidazole (20o) (CAS number: 6478-73-5)

The reaction was performed following the general procedure. The residue was purified by flash column chromatography (silica gel, Petroleum ether: AcOEt = 10:1, v/v) to give the product as a white solid (28mg, 75%). $^1$H NMR (500 MHz, DMSO) δ 12.75 (s, 1H), 8.35 (s, 1H), 7.88 (s, 2H). $^{13}$C NMR (125 MHz, DMSO) δ 145.2

1-(difluoromethyl)-1H-benzo[d]imidazole (21)

The reaction was performed following the general procedure. The residue was purified by flash column chromatography (silica gel, Petroleum ether: AcOEt = 10:1, v/v) to give the product as a white solid (11.4 mg, 61%). $^1$H NMR (500 MHz, CDCl$_3$) δ 8.12 (s, 1H), 7.93 – 7.76 (m, 1H), 7.61 (dd, $J = 5.4$, 3.6 Hz, 1H), 7.37 (ddd, $J = 85.8$, 55.8, 43.2 Hz, 3H). $^{13}$C NMR (125 MHz, CDCl$_3$) δ 143.9, 139.1, 130.6, 124.8, 124.2, 121.0, 111.1, 109.0 (t, $J = 248.8$ Hz) $^{19}$F NMR (470 MHz, CPD, CDCl$_3$) δ -93.7.

1-(difluoromethyl)-5(6)-methyl-1H-benzo[d]imidazole (22)

The reaction was performed following the general procedure. The residue was purified by flash column chromatography (silica gel, Petroleum ether: AcOEt = 10:1, v/v) to give the product as a white solid (11 mg, 58%). $^1$H NMR (500 MHz, CDCl$_3$) δ 8.05 (d, $J = 11.4$ Hz, 1H), 7.71 (d, $J = 8.3$ Hz, 1H), 7.62 (s, 1H), 7.48 (d, $J = 8.3$ Hz, 1H), 7.41 (d, $J = 4.1$ Hz, 1H), 7.29 (s, 1H), 7.20 (d, $J = 11.8$, 4.5 Hz, 1H), 7.17 (s, 1H), 2.50 (d, $J = 8.8$ Hz, 3H). $^{13}$C NMR (125 MHz, CDCl$_3$) δ 144.2, 142.0,
139.1, 138.6, 135.6, 134.1, 130.7, 128.5, 126.2, 125.7, 120.7, 120.4, 110.98 (d, J = 5.5 Hz), 110.56 (s), 108.97 (s), 106.99 (s), 21.79 (s), 21.51 (s).\(^1\)F NMR (470 MHz, CDCl\(_3\)) \(\delta\) -93.6, -93.7.

1-(difluoromethyl)-4,7-dimethyl-1\(H\)-benzo[d]imidazole (23)

The reaction was performed following the general procedure. The residue was purified by flash column chromatography (silica gel, Petroleum ether: AcOEt = 10:1, v/v) to give the product as a white solid (11 mg, 63%).\(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 8.13 (d, \(J = 27.9\) Hz, 1H), 7.69 (d, \(J = 8.1\) Hz, 1H), 7.61 (s, 1H), 7.49 (s, 1H), 7.45 – 7.38 (m, 1H), 7.37 (s, 1H), 7.33 – 7.26 (m, 1H), 7.18 (t, \(J = 6.0\) Hz, 1H), 2.66 (d, \(J = 18.6\) Hz, 3H).\(^13\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\) 143.2, 139.7, 138.1, 131.1, 130.3, 124.7, 124.5, 124.1, 121.6, 118.7, 110.9, 109.0, 108.4, 19.2, 16.6.\(^1\)F NMR (471 MHz, CDCl\(_3\)) \(\delta\) -87.3, -93.8.

1-(difluoromethyl)-5(6)-fluoro-1\(H\)-benzo[d]imidazole (24)

The reaction was performed following the general procedure. The residue was purified by flash column chromatography (silica gel, Petroleum ether: AcOEt = 10:1, v/v) to give the product as a white solid (10 mg, 53%).\(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 8.11 (d, \(J = 20.5\) Hz, 1H), 7.78 (dd, \(J = 8.9, 4.7\) Hz, 1H), 7.56 (dd, \(J = 8.9, 4.5\) Hz, 1H), 7.52 (dd, \(J = 8.9, 2.4\) Hz, 1H), 7.41 (d, \(J = 9.8\) Hz, 1H), 7.35 – 7.27 (m, 1H), 7.15 (m, \(J = 13.5, 9.1, 2.2\) Hz, 1H).\(^13\)C NMR (125 MHz, CDCl\(_3\)) 161.5 (d, \(J = 46.3\) Hz), 159.5 (d, \(J = 37.5\) Hz), 140.5, 139.5, 122.8 (d, \(J = 10.0\) Hz), 112.9 (d, \(J = 47.5\) Hz), 112.6 (t, \(J = 113.8\) Hz), 98.4 (d, \(J = 28.8\) Hz).\(^1\)F NMR (470 MHz, CDCl\(_3\)) \(\delta\) -93.7, -94.0, -115.6, -118.0.

5(6)-chloro-1-(difluoromethyl)-1\(H\)-benzo[d]imidazole (25)

The reaction was performed following the general procedure. The residue was purified by flash column chromatography (silica gel, Petroleum ether: AcOEt = 10:1, v/v) to give the product as a white solid (12 mg, 58%).\(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 8.14 (s, 1H), 7.85 (d, \(J = 1.8\) Hz, 1H), 7.56 (d, \(J = 8.7\) Hz, 1H), 7.45 (s, 1H), 7.40 (dd, \(J = 8.6, 1.9\) Hz, 1H), 7.33 (s, 1H), 7.21 (s, 1H).\(^13\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\) 144.8, 140.2, 129.9, 129.1, 125.4, 120.9, 112.0, 108.8 (\(J = 248.75\) Hz).\(^1\)F NMR (470 MHz, CDCl\(_3\)) \(\delta\) -93.8.

5(6)-bromo-1-(difluoromethyl)-1\(H\)-benzo[d]imidazole (26)

The reaction was performed following the general procedure. The residue was purified by flash column chromatography (silica gel, Petroleum ether: AcOEt = 10:1, v/v) to give the product as a white solid (15 mg, 60%).\(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 8.09 (d, \(J = 7.1\) Hz, 1H), 7.97 (d, \(J = 0.6\) Hz, 1H), 7.77 (s, 1H), 7.68 (d, \(J = 8.6\) Hz, 1H), 7.52 – 7.45 (m, 2H), 7.43 (d, \(J = 6.2\) Hz, 1H),
7.31 (d, J = 6.1 Hz, 1H), 7.19 (d, J = 6.1 Hz, 1H). $^{13}$C NMR (125 MHz, CDCl$_3$) δ 145.2, 142.9, 140.1, 139.6, 131.4, 129.4, 128.0, 127.7, 123.9, 122.2, 118.2, 117.3, 114.4, 112.4, 108.9 (t, J = 250.0 Hz), 108.8 (t, J = 250.0 Hz). $^{19}$F NMR (470 MHz, CDCl$_3$) δ -93.8.

1-(difluoromethyl)-5,6-dimethyl-1H-benzo[d]imidazole (27)

The reaction was performed following the general procedure. The residue was purified by flash column chromatography (silica gel, Petroleum ether: AcOEt = 10:1, v/v) to give the product as a white solid (13 mg, 69%). $^1$H NMR (500 MHz, CDCl$_3$) δ 7.99 (s, 4H), 7.99 (s, 4H), 7.59 (s, 4H), 7.59 (s, 4H), 7.38 (s, 1H), 7.38 (d, J = 5.7 Hz, 5H), 7.37 (s, 4H), 7.26 (s, 2H), 7.26 (d, J = 2.0 Hz, 3H), 7.14 (s, 1H), 7.14 (s, 1H), 2.38 (d, J = 8.9 Hz, 25H), 2.38 (d, J = 8.9 Hz, 25H). $^{13}$C NMR (125 MHz, CDCl$_3$) δ 142.5, 138.3, 134.2, 133.2, 129.0, 120.9, 111.24, 109.00 (t, J = 247.5 Hz), 20.5, 20.3.$^{19}$F NMR (470 MHz, CDCl$_3$) δ -93.6.

1-(difluoromethyl)-5,6-difluoro-1H-benzo[d]imidazole (28)

The reaction was performed following the general procedure. The residue was purified by flash column chromatography (silica gel, Petroleum ether: AcOEt = 10:1, v/v) to give the product as a white solid (10 mg, 51%). $^1$H NMR (500 MHz, CDCl$_3$) δ 8.11 (s, 1H), 7.62 (dd, J = 10.0, 7.2 Hz, 1H), 7.44 (dd, J = 9.3, 6.8 Hz, 1H), 7.41 (s, 1H), 7.29 (s, 1H), 7.17 (s, 1H). $^{13}$C NMR (126 MHz, CDCl$_3$) δ 150.15 (d, J = 15.5 Hz), 149.80 (d, J = 14.8 Hz), 148.19 (d, J = 15.5 Hz), 147.86 (d, J = 15.0 Hz), 140.44 (s), 139.35 (d, J = 9.0 Hz), 125.7, 108.8, 108.7 (t, J = 228.8 Hz), 108.5, 106.8, 100.0, 99.8.$^{19}$F NMR (470 MHz, CDCl$_3$) δ -94.0, -137.9, -138.0, -140.3, -140.3.

5,6-dichloro-1-(difluoromethyl)-1H-benzo[d]imidazole (29)

The reaction was performed following the general procedure. The residue was purified by flash column chromatography (silica gel, Petroleum ether: AcOEt = 10:1, v/v) to give the product as a white solid (13 mg, 55%). $^1$H NMR (500 MHz, CDCl$_3$) δ 8.11 (s, 1H), 7.95 (s, 1H), 7.75 (s, 1H), 7.40 (s, 1H), 7.28 (s, 1H), 7.16 (s, 1H). $^{13}$C NMR (125 MHz, CDCl$_3$) δ 143.2, 140.7, 129.3, 128.8, 122.3, 112.9, 110.7 (t, J = 228.8 Hz). $^{19}$F NMR (470 MHz, CDCl$_3$) δ -93.9.

$^{(E)}$-N,N'-bis(4-ethoxyphenyl)formimidamide (32)

The reaction was performed following the general procedure. The residue was purified by flash column chromatography (silica gel, Petroleum ether: AcOEt = 10:1, v/v) to give the product as a white solid (8.5 mg, 15%). $^1$H NMR (500 MHz, CDCl$_3$) δ 8.02 (s, 1H), 6.97 (d, J = 8.6 Hz, 4H), 6.89 – 6.81 (m, 4H), 4.01
(q, \( J = 7.0 \) Hz, 4H), 1.40 (t, \( J = 7.0 \) Hz, 6H). \( ^{13} \)C NMR (125 MHz, CDCl\(_3\)) \( \delta \) 155.4, 120.2, 115.3, 63.8, 14.9.

1-ethoxy-4-isocyanobenzene (33)

The reaction was performed following the general procedure. The residue was purified by flash column chromatography (silica gel, Petroleum ether: AcOEt = 10:1, v/v) to give the product as a colourless oil (8 mg, 27%). \( ^{1} \)H NMR (500 MHz, CDCl\(_3\)) \( \delta \) 7.29 (d, \( J = 8.9 \) Hz, 2H), 6.87 – 6.82 (m, 2H), 4.03 (q, \( J = 7.0 \) Hz, 2H), 1.42 (t, \( J = 7.0 \) Hz, 3H). \( ^{13} \)C NMR (125 MHz, CDCl\(_3\)) \( \delta \) 162.3, 159.3, 127.8, 115.0, 63.9, 14.7.

N-(4-ethoxyphenyl)formamide (34)

The reaction was performed following the general procedure. The residue was purified by flash column chromatography (silica gel, Petroleum ether: AcOEt = 10:1, v/v) to give the product as a colourless oil (8 mg, 27%). \( ^{1} \)H NMR (500 MHz, CDCl\(_3\)) \( \delta \) 8.50 (d, \( J = 11.5 \) Hz, 0.49 H), 8.31 (d, \( J = 1.8 \) Hz, 0.49 H), 8.09 (s, 0.46 H), 7.47 – 7.35 (m, 1.42 H), 7.06 – 6.96 (m, 1H), 6.90 – 6.81 (m, 2H), 4.00 (qd, \( J = 7.0 \), 4.3 Hz, 2H), 1.40 (q, \( J = 6.9 \) Hz, 3H). \( ^{13} \)C NMR (125 MHz, CDCl\(_3\)) \( \delta \) 163.1, 158.9, 157.0, 156.1, 129.8, 129.4, 121.8, 121.7, 115.5, 114.8, 63.8, 63.7, 14.8, 148.

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