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Synthesis of Carbamoyl Fluorides Using a Difluorophosgene Surrogate Derived from Difluorocarbene and Pyridine *N*-Oxides

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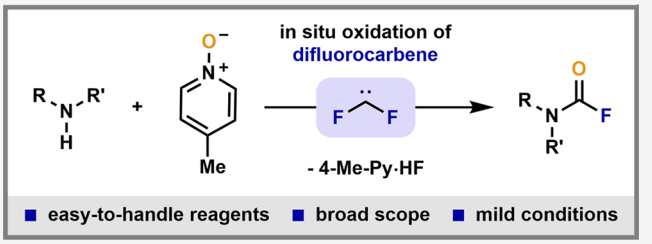
ABSTRACT: We report a method for the synthesis of carbamoyl fluorides from secondary amines using bench-stable, inexpensive, and readily accessible starting materials that, when combined, yield a surrogate for toxic difluorophosgene (COF_2) gas. In contrast to state-of-the-art methods for the synthesis of carbamoyl fluorides, our protocol does not require the use of pre-functionalized substrates, the preparation of light-, temperature-, and/or moisture-sensitive chemicals, or the application of explosive fluorinating reagents.



INTRODUCTION

Fluorinated molecules are desirable targets within the pharmaceutical and agrochemical industries owing to their enhanced medicinal properties when compared to non-fluorinated analogues.[1−3] While various fluoro-organic moieties have been distinctly classified as privileged motifs,[4] carbamoyl fluorides have been scarcely examined in this context. In the 1960s, Wilson investigated the mechanism of protease and esterase inhibition by carbamoyl halide electrophiles.[5] Their studies found that carbamoyl fluorides were more potent covalent inhibitors than the analogous chlorides despite the higher energy associated with cleaving strong C−F bonds.[6] In comparison to carbamoyl chlorides,[7] the use of carbamoyl fluorides in organic synthesis remains largely underdeveloped.[8,9] This observation could be related to the limitations associated with their synthesis and/or reduced electrophilicity. However, recent reports have demonstrated that carbamoyl fluorides are competent electrophiles in cross-coupling reactions, while also offering unique reactivity compared to their chlorinated counterparts.[10,11] Thus, developing more efficient methods for their preparation is an ongoing pursuit.[12−22]

Carbamoyl fluorides are commonly accessed from the carbamoyl chloride via halogen exchange with an inorganic metal fluoride salt, which is typically used in large excess.[10,13,14] Although this two-step protocol is robust, long reaction times are necessary and synthesis of the carbamoyl chloride starting materials requires the use of toxic (tri)phosgene.[23] It would be more convenient to obtain carbamoyl fluorides directly from secondary amines, but commercial sources of gaseous difluorophosgene (COF_2) are unavailable.[24−29] Most modern methods utilize reagents that liberate COF_2 in situ from a trifluoromethoxide anion (Scheme 1a).[30] For example, both trifluoromethyl triflate (TFMT, i) and $AgOCF_3$ (ii) have been shown to be excellent reservoirs for COF_2, enabling the facile preparation of carbamoyl fluorides under mild conditions.[15,17] Unfortunately, these reagents have some limitations in terms of storage and usage. TFMT is a volatile liquid (bp = 19 °C) that must be stored over P_2O_5 and used at low temperatures to avoid reagent loss, whereas $AgOCF_3$ is light-sensitive and must be stored as a solution in MeCN under an inert atmosphere. Previous methods for the synthesis of $AgOCF_3$ required the use of volatile TFMT,[31] but Schoenebeck and co-workers later developed a more convenient protocol using triphosgene and AgF.[17] Regardless, the use of stoichiometric silver salts can be prohibitively expensive. Recently, Toulgoat and Billard reported that an organic trifluoromethoxide salt (iii) derived from 2,4-dinitrotrifluoromethoxybenzene and DMAP can be used as an alternative COF_2 reservoir.[18] A number of COF_2-free methods have also been developed over the last few years. Tlili and co-workers described a deoxyfluorination strategy using CO_2 as a C1 synthon in combination with (diethylamino)sulfur trifluoride (DAST, iv) or a novel SF_5-based reagent (v) as a nucleophilic fluoride source (Scheme 1b).[19,20] Subsequently, Lim and co-workers showed that α-oximinoamides can undergo a fluorinative Beckmann rearrangement in the presence of DAST, providing a *de novo* approach to carbamoyl fluorides.[21] Although DAST is commercially available, its high cost and shock-sensitivity are important considerations.[32] In recent years, reactions involving difluorocarbene (DFC) synthons have become a prominent strategy for constructing fluorinated molecules.[33−35] Bolm and

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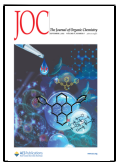

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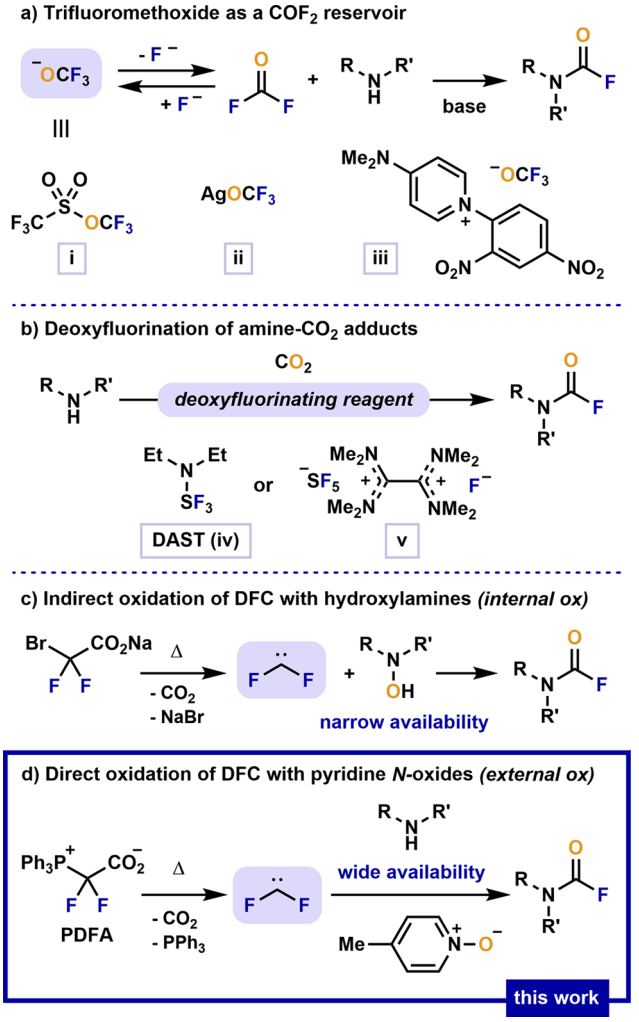
Scheme 1. Methods for the Synthesis of Carbamoyl Fluorides



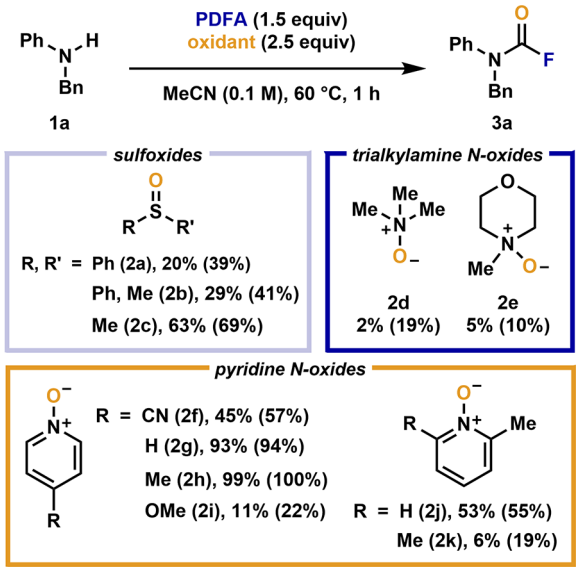
co-workers devised a unique method for carbamoyl fluoride synthesis using hydroxylamines as an internal oxidant for DFC, providing access to carbamoyl fluorides in yields ranging from 31 to 67% (Scheme 1c).[22] This method is limited by the narrow commercial availability of the hydroxylamines, thus requiring pre-functionalization (i.e., oxidation) of the amine starting materials—the conditions of which may also be incompatible with densely functionalized substrates.

To enable the synthesis of carbamoyl fluorides directly from secondary amines using DFC as a C1 source, we hypothesized that an appropriate external oxidant could be used instead.[36−38] Because secondary amines are more widely available than hydroxylamines, this strategy would allow a broader range of substrates to be applied. Herein, we disclose that pyridine *N*-oxides are an effective class of oxidants for this transformation in the presence of (triphenylphosphonio)-difluoroacetate (PDFA)[39,40] as the DFC source (Scheme 1d). Our protocol uses inexpensive starting materials that are bench-stable and easy to handle, providing practical advantages from prior reports that employ specialized reagents or explosive DAST. In addition to its operational simplicity, our method presents a broad substrate scope, enabling the synthesis of a diverse range of carbamoyl fluorides, such as those containing Lewis-basic heterocycles and electron-rich alkynes.

RESULTS AND DISCUSSION

Reaction Optimization. For our initial screening of oxidants, *N*-benzylaniline (**1a**) was selected as the model substrate and PDFA as the DFC source. We chose to optimize the reaction with PDFA because this reagent can be synthesized on scale using relatively inexpensive starting materials. Moreover, PDFA is a non-hygroscopic reagent that can be stored and weighed out on the benchtop. Xiao and co-workers recently reported a protocol for the trifluoromethoxylation of alkyl halides involving in situ generation of $AgCOF_3$ from a DFC source, diphenylsulfoxide, and AgF.[37] Thus, we expected that the simple removal of AgF in the reaction mixture would enable the synthesis of carbamoyl fluorides in the presence of a secondary amine. However, the use of diphenylsulfoxide (**2a**) as an oxidant provided carbamoyl fluoride **3a** in low yield (20%), thus warranting further reaction development (Scheme 2). A more electron-rich sulfoxide (**2b**)

Scheme 2. Screening of Oxidants[a]



[a]% Yield **3a** (% conversion **1a**) determined by ^{1}H NMR spectroscopy using 1,3,5-trimethoxybenzene as an internal standard.

only marginally improved the reactivity, whereas DMSO (**2c**) furnished the product in an improved 63% yield; however, incomplete conversion of **1a** was observed under these conditions. Switching to trialkylamine *N*-oxides proved to be ineffective, with both **2d** and **2e** providing trace amounts of product. We were motivated to explore pyridine *N*-oxides next because the oxidation event would generate an equivalent of pyridine—a common additive used in the synthesis of carbamoyl chlorides from triphosgene.

After screening several derivatives, 4-methylpyridine *N*-oxide (**2h**) emerged as the optimal oxidant providing **3a** in 99% yield, slightly outperforming the parent pyridine *N*-oxide (**2g**). The use of highly electron-deficient (**2f**) and electron-rich (**2i**) substrates both led to reduced yields, suggesting that the electronic components of the oxidant must be carefully balanced. Steric hindrance proximal to the *N*-oxide moiety in **2j** and **2k** also compromised the reactivity.

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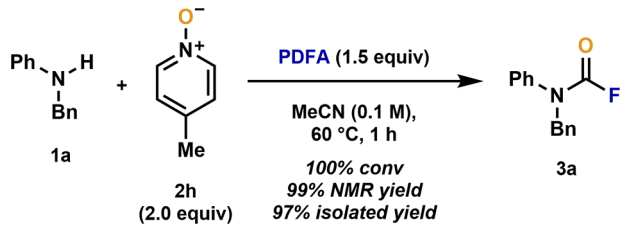
Having identified the oxidant of choice for this transformation, we then varied the relative amount of each component. The reactivity was unaffected when 2.0 equiv of **2h** was used instead of 2.5, which we later determined to be our optimized conditions (Table 1). In general, deviations

Table 1. Deviations from Standard Conditions



entry	conditions	conv. **1a**[a] (%)	yield **3a**[a] (%)
1	1.5 equiv **2h**	72	70
2	1.0 equiv PDFA	76	75
3	1.0 equiv **2h**, 1.0 equiv PDFA	67	65
4	TFDA with NaF (0.2 equiv) instead of PDFA	98	92
5	$BrCF_2CO_2K$ instead of PDFA	89	77
6	$ClCF_2CO_2Na$ instead of PDFA	2	trace
7	$TMSCF_3$ + NaI (0.2 equiv) instead of PDFA	5	trace
8	DMSO (solvent), without **2h**	100	99
9	40 °C	41	37

[a]Conversions and yields determined by ^{1}H NMR spectroscopy using 1,3,5-trimethoxybenzene as an internal standard. TFDA = trimethylsilyl 2,2-difluoro-2-(fluorosulfonyl)acetate (CAS 120801-75-4).

from a 2.0:1.5 stoichiometry between **2h** and PDFA led to diminished yields of the carbamoyl fluoride product (entries 1−3). The use of trimethylsilyl 2,2-difluoro-2-(fluorosulfonyl)-acetate (TFDA)[41] with catalytic NaF as an alternative DFC source provided **3a** in 92% yield (entry 4). However, we did not optimize further with TFDA due to the corrosive nature of this reagent combined with its high costs. Screening of other DFC sources revealed that potassium bromodifluoroacetate ($BrCF_2CO_2K$),[42] the precursor used to synthesize PDFA,[39] could also provide **3a** in acceptable yield (entry 5). While this protocol reduces the number of synthetic steps to access the DFC precursor, the hygroscopic nature of $BrCF_2CO_2K$ makes it more challenging to handle compared to PDFA, which is a free-flowing moisture-stable solid. Trace amounts of product were obtained with sodium chlorodifluoroacetate ($ClCF_2CO_2Na$) and $TMSCF_3$ with catalytic NaI (entries 6−7).[33]

In general, the reaction proceeds well in a range of solvents, with toluene, DCE, and THF providing comparable yields to MeCN (Table S4). When DMSO was used in solvent quantities, **2h** could be omitted entirely (entry 8). However, these conditions proved to be less general when applied to other secondary amines. The use of wet HPLC-grade MeCN led to lowered yields, which was expected due to the presence of electrophilic DFC and COF_2 species formed in solution (Table S4). Lastly, decreasing the temperature to 40 °C resulted in low conversion, likely due to the higher temperatures required for the thermolysis of PDFA (entry 9). Thus, we settled on the following conditions as our optimized system: amine (1.0 equiv), **2h** (2.0 equiv), and PDFA (1.5 equiv) in MeCN at 60 °C for 1 h, which gave full conversion of **1a** and provided **3a** in 99% yield by ^{1}H NMR (97% isolated).

Substrate Scope. With these ideal conditions in hand, we set out to explore the scope of the reaction (Scheme 3). Substrates featuring electron-donating substituents (**3b**, **3c**, **3g**) and halogen atoms (**3d**, **3e**, **3f**, **3h**) at either the para- or meta-positions of the aniline backbone performed well under the reaction conditions. Ortho-substitution with electron-donating substituents (**3i**, **3j**) was also tolerated. The application of *N*-benzylanilines featuring electron-withdrawing substituents, such as *p*-CN and *p*-NO_2, provided the desired carbamoyl fluoride products in 52 and 58%, respectively, by ^{1}H NMR (see the Supporting Information). Unfortunately, their isolation via chromatography proved challenging due to product decomposition. We believe that such carbamoyl fluorides are not hydrolytically stable due to the increased electrophilicity of the carbamoyl group. A 1-napthylamine derivative performed modestly (**3k**), although remote modifications to the benzyl ring (**3l**, **3m**, **3n**) did not negatively impact the yield. A number of simple secondary amines were also suitable substrates for this chemistry, providing products **3o**, **3p**, **3q**, and **3r**. Carbamoyl fluorides containing aromatic heterocycles, such as a furan (**3s**), thiophene (**3t**), pyridine (**3u**, **3v**), and an indole (**3w**) ring could also be accessed using our method in excellent to modest yields. Slightly longer reactions times were applied with **3u** to improve the yield. When Schoenbeck's conditions were applied to **1u** ($AgOCF_3$, DIPEA, MeCN, rt, 2 h), 41% conversion and 23% yield of **3u** was observed, thus exemplifying the challenging nature of this substrate.[17] Of note, an unprotected indole N−H bond was also tolerated, providing **3w** in an acceptable yield. We were able to obtain an X-ray crystal structure of **3w**, confirming functionalization of the benzylamine functionality over the indole nitrogen (see the Supporting Information). With this protocol, we could also access carbamoyl fluorides bearing medicinally relevant scaffolds, such as heterocycles **3x**, **3y**, and **3z**, cyclopropane **3aa**, and phenylalanine-derived **3ab**. The reactivity was unaffected in the presence of several unsaturated functional groups, such as alkenes (**3ac**, **3ad**) and alkynes (**3ae**, **3af**, **3ag**). Interestingly, *gem*-difluoro-cyclopropane[43] or -cyclopropene[44] byproducts were not observed under these conditions, likely due to the higher reaction temperatures required for these [2 + 1] cycloaddition reactions. Of note, alkene- and alkyne-tethered substrates **3ac**−**3ag** have vast potential in transition metal-catalyzed cross-coupling, where tandem migratory insertion processes can be used to build molecular complexity.[10] We have also tested this reaction on a 1 g scale with *N*-methylaniline (**1o**), which provided **3o** in 83% isolated yield.

Proposed Mechanism. Based on Xiao's seminal report,[37] our mechanistic hypothesis involves the in situ formation of COF_2 via the oxidation of DFC (Scheme 4). In this pathway, thermally induced decarboxylation of PDFA sets up an equilibrium between phosphonium ylide **A** and free DFC.[43] Subsequent trapping of DFC by **2h** forms zwitterionic species **B**, which liberates an equivalent of pyridine and COF_2 in the key oxidation step. Trapping of COF_2 by the secondary amine furnishes the carbamoyl fluoride. Because the byproduct of the oxidation is 4-Me-Py, no additional base is needed in this reaction to mop up the generated HF. The mechanism for the oxidation of DFC by sulfoxides was studied computationally by Xiao and co-workers.[37] To ascertain the presence of COF_2 under our reaction conditions, we ran a test reaction in the

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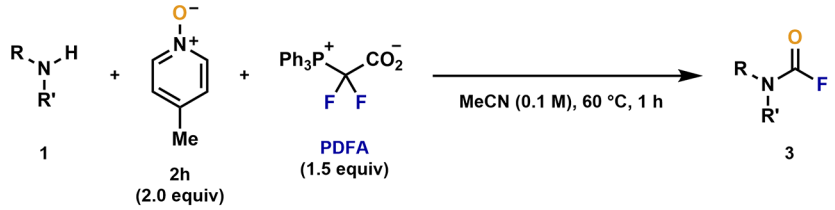
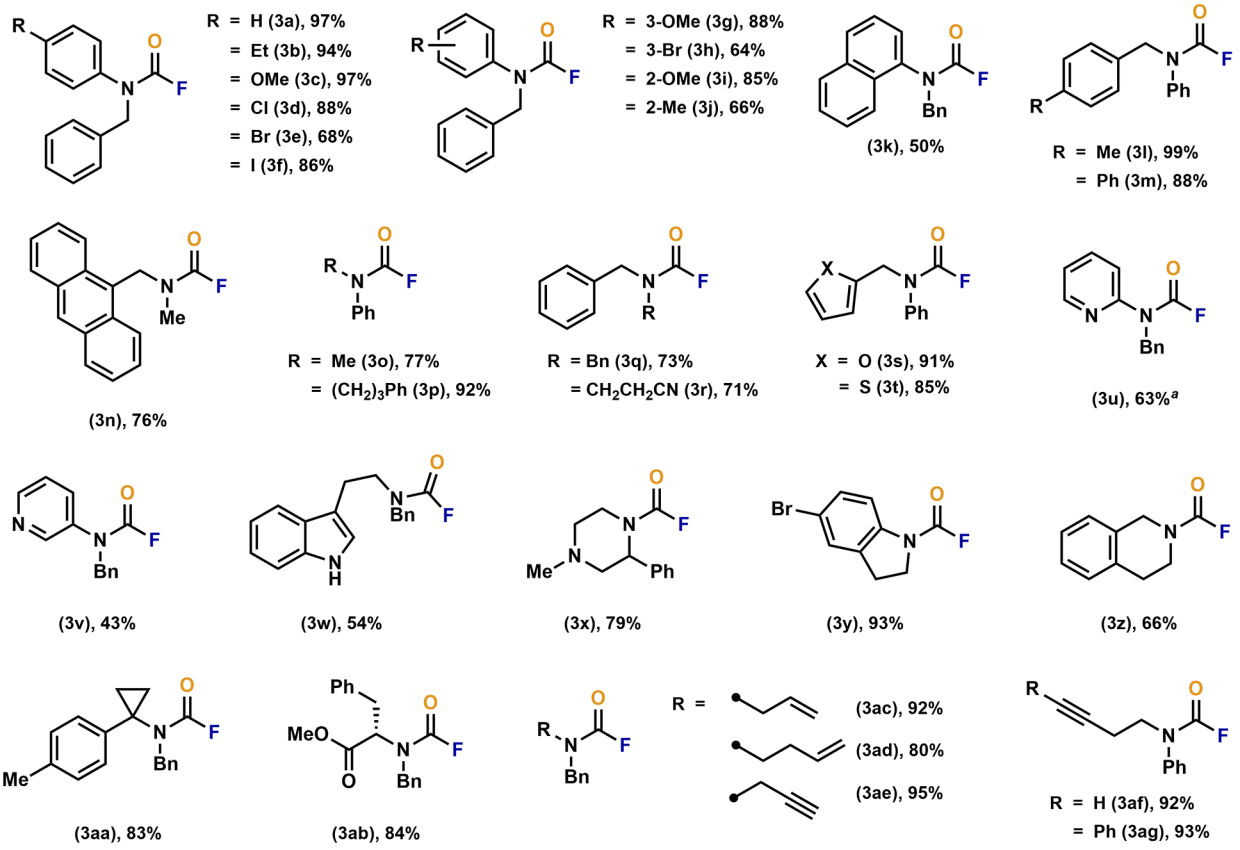
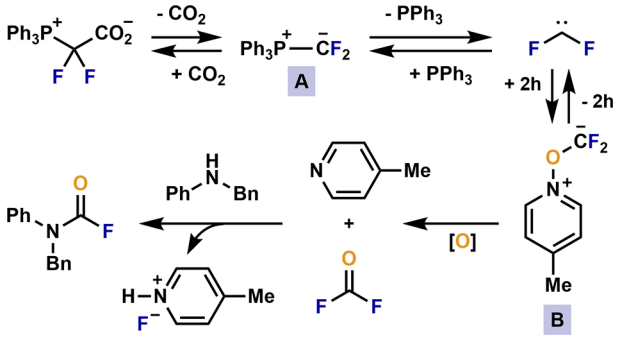
Scheme 3. Substrate Scope[a]



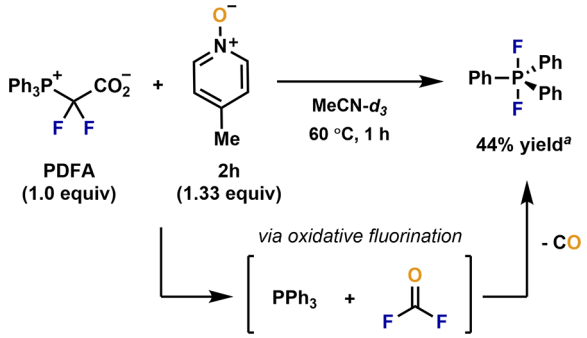


[a]Isolated yields are reported. [b]Reaction was run for 3

Scheme 4. Proposed Mechanism



Scheme 5. Reaction of PDFA with 2h[a]



[a]Yield determined by ^{1}H NMR spectroscopy using 1,3,5-trimethoxybenzene as the internal standard.

absence of the amine to see if any COF_2-adducts could be identified by NMR spectroscopy. When PDFA and **2h** were mixed for 60 min at 60 °C in MeCN-d_3, the major product identified was difluorotriphenylphosphorane (F_2PPh_3) in 44% yield (Scheme 5).[45]

In the ^{31}P NMR spectrum, we also identified PPh_3 and trace amounts of triphenylphosphine oxide (O=PPh_3). The remaining mass balance can be allocated to unknown decomposition products. Only minor amounts of F_2PPh_3 are formed when heating only PDFA in MeCN-d_3; thus, pyridine *N*-oxides promote this side reaction. It has been reported in the literature that tertiary phosphines and trialkylphosphites can undergo oxidative fluorination in the presence of COF_2 to

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form related P(V) species upon decarbonylation.[46] We believe the formation of F_2PPh_3 under these conditions provides indirect evidence for the in situ formation of COF_2 from DFC and **2h**. NMR analysis of the standard reaction (amine + PFDA + **2h**) revealed that only small amounts of F_2PPh_3 are observed after 30 min (see the Supporting Information). This is likely due to the facile trapping of COF_2 with the amine, instead of with less nucleophilic PPh_3. It is also possible that O═PPh_3 can react with COF_2 to form the same product; however, we believe that this pathway is minor, as the reaction is run under a N_2 atmosphere and the formation of O═PPh_3 should be minimal.[45]

CONCLUSIONS

In conclusion, we have developed an efficient synthesis of carbamoyl fluorides that avoids use of light-, moisture-, temperature-, and/or shock-sensitive reagents. The reaction employs non-hygroscopic PDFA as a source of DFC and 4-methylpyridine *N*-oxide as a mild oxidant. The method was applied to a range of electronically diverse secondary amines, including those containing heterocycles and unsaturated functionalities. Overall, we anticipate that the operational simplicity of this method will help expand the chemistry of carbamoyl fluorides in both organic synthesis and chemical biology applications, as well as provide a new platform for generating unique fluorinated organic molecules.

EXPERIMENTAL SECTION

General Information. Commercial reagents were purchased from Acros-Organics, Alfa Aesar, Combi-Blocks, Fisher, Sigma-Aldrich, or TCI and used without further purification. Unless otherwise stated, all reactions were carried out under an inert atmosphere of nitrogen or argon using glassware that was oven- (175 °C) or flame-dried, whereas the work-up and isolation of the products were conducted on the benchtop using standard techniques. Solvents and solutions were transferred by a syringe or cannula. Anhydrous THF, toluene, DCM, and Et_2O were obtained from an MBraun MB-SPS 800 solvent drying system under a N_2 atmosphere and stored in a Strauss flask. The remaining anhydrous solvents were purchased directly from Sigma-Aldrich (sure-seal bottle). Amines **1a**, **1n**, **1o**, **1q**, **1r**, **1u**, **1x**, **1y**, and **1z**, as well as all oxidants **2**, are commercially available and were used without further purification. Reactions were monitored by thin layer chromatography (TLC) using SiliaPlate glass-backed silica gel plates (hard layer) with F254 indicator. Visualization was accomplished using 250 nm UV light, followed by immersion in $KMnO_4$ stain. Unless otherwise stated, flash chromatography was performed using SiliaFlash P60 40−63 μm (230−400 mesh) 60 Å irregular silica gel. NMR characterization data were collected at 296 K on a Bruker 700 MHz spectrometer, Bruker DRX 600 MHz spectrometer, Bruker ARX 400 MHz spectrometer, or Bruker ARX 300 MHz spectrometer. For samples in $CDCl_3$, ^{1}H NMR spectra were internally referenced to the residual solvent signal (7.26 ppm) or TMS (0 ppm) and ^{13}C NMR spectra were internally referenced to the residual solvent signal (77.16 ppm) and are reported as observed. Data for ^{1}H NMR are reported as follows: chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = double of doublets, dt = doublet of triplets, b = broad), coupling constant (Hz), and integration. Infrared (IR) spectra were recorded using Alpha-Platinum ATR Bruker, diamond crystal. High-resolution mass spectrometry (HRMS) spectra were recorded using Thermo Fisher Orbitrap Elite or JEOL AccuTOF Plus 4G mass spectrometers. NMR yields were obtained by analysis of the crude reaction mixtures by ^{1}H NMR spectroscopy using a 10 s relaxation delay and 1,3,5-trimethoxybenzene as the internal standard or by ^{19}F NMR spectroscopy using a 30 s relaxation delay and α,α,α-trifluorotoluene as the internal standard.

Synthesis and Characterization of Starting Materials. *General Procedure A.* The reductive amination procedure reported by Watson and co-workers was followed.[47] To a round-bottom flask equipped with a stir bar was added the primary amine (1.1 equiv) and aldehyde (1.0 equiv). 1,2-Dichloroethane was then added to achieve a concentration of 0.5 M with respect to the amine. Sodium triacetoxyborohydride (1.2 equiv) was added to the reaction in portions and was allowed to stir at room temperature until completion, as determined by thin-layer chromatography, and was quenched by the addition of saturated sodium bicarbonate solution. The reaction mixture was poured into a separatory funnel and extracted 3× with EtOAc. The organic layers were collected, washed with brine, and then dried over $MgSO_4$. The $MgSO_4$ was removed by filtration, and the filtrate was concentrated via rotary evaporation. The crude mixture was purified via flash column chromatography.

General Procedure B. The reductive amination procedure reported by Ghorai and co-workers was followed.[48] To an oven- or flame-dried round-bottomed flask equipped with a stir bar was added methanol (0.5 M with respect to the amine), followed by the primary amine (1.0 equiv) and aldehyde (1.5 equiv). The reaction was stirred at room temperature for 4 h and then cooled to 0 °C with an ice-water bath. The septum was removed, and sodium borohydride (2.0 equiv) was added in portions. The reaction was allowed to warm to room temperature and stirred for 4 h. The solvent was removed under reduced pressure and the residue was taken up in EtOAc. The solution was washed with water 3× and once with brine. The organic layer was dried over Na_2SO_4 and concentrated via rotary evaporation. The crude mixture was purified via flash column chromatography.

*N-Benzyl-4-ethylaniline (**1b**).* The title compound was synthesized with general procedure A using 4-ethylaniline (0.100 g, 0.83 mmol) and benzaldehyde (0.080 g, 0.75 mmol) and was isolated as an orange oil (0.114 g, 0.54 mmol, 65%) after purification by flash column chromatography: 2% EtOAc, 1% Et_3N in hexanes. The spectral data are consistent with literature values.[49]

*N-Benzyl-4-methoxyaniline (**1c**).* The title compound was synthesized with general procedure A using 4-methoxyaniline (0.100 g, 0.81 mmol) and benzaldehyde (0.078 g, 0.74 mmol) and was isolated as a yellow oil (0.110 g, 0.51 mmol, 63%) after purification by flash column chromatography: 2% EtOAc, 1% Et_3N in hexanes. The spectral data are consistent with literature values.[47]

*N-Benzyl-4-chloroaniline (**1d**).* The title compound was synthesized with general procedure A using 4-chloroaniline (0.100 g, 0.78 mmol) and benzaldehyde (0.075 g, 0.71 mmol) and was isolated as a yellow oil (0.106 g, 0.49 mmol, 62%) after purification by flash column chromatography: 2% EtOAc, 1% Et_3N in hexanes. The spectral data are consistent with literature values.[50]

*N-Benzyl-4-bromoaniline (**1e**).* The title compound was synthesized with general procedure A using 4-bromoaniline (0.100 g, 0.58 mmol) and benzaldehyde (0.056 g, 0.53 mmol) and was isolated as a yellow solid (0.107 g, 0.41 mmol, 71%) after purification by flash column chromatography: 2% EtOAc, 1% Et_3N, in hexanes. The spectral data are consistent with literature values.[51]

*N-Benzyl-4-iodoaniline (**1f**).* The title compound was synthesized with general procedure A using 4-iodoaniline (0.100 g, 0.46 mmol) and benzaldehyde (0.045 g, 0.42 mmol) and was isolated as a white solid (0.090 g, 0.29 mmol, 63%) after purification by flash column chromatography: 2% EtOAc, 1% Et_3N in hexanes. The spectral data are consistent with literature values.[52]

*N-Benzyl-3-methoxyaniline (**1g**).* The title compound was synthesized with general procedure A using 3-methoxyaniline (0.100 g, 0.81 mmol) and benzaldehyde (0.078 g, 0.74 mmol) and was isolated as a yellow oil (0.131 g, 0.62 mmol, 76%) after purification by flash column chromatography: 2% EtOAc, 1% Et_3N in hexanes. The spectral data are consistent with literature values.[53]

*N-Benzyl-3-bromoaniline (**1h**).* The title compound was synthesized with general procedure A using 3-bromoaniline (0.100 g, 0.58 mmol) and benzaldehyde (0.056 g, 0.53 mmol) and was isolated as a pale-yellow oil (0.101 g, 0.38 mmol, 66%) after purification by flash column chromatography: 2% EtOAc, 1% Et_3N in hexanes. The spectral data are consistent with literature values.[52]

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*N-Benzyl-2-methoxyaniline (**1i**).* The title compound was synthesized with general procedure B using 2-methoxyaniline (1.092 g, 8.87 mmol) and benzaldehyde (1.148 g, 10.82 mmol) and was isolated as an orange oil (1.490 g, 6.99 mmol, 79%) after purification by flash column chromatography: 5% EtOAc in hexanes. The spectral data are consistent with literature values.[53]

*N-Benzyl-2-methylaniline (**1j**).* The title compound was synthesized with general procedure A using 2-methylaniline (0.100 g, 0.93 mmol) and benzaldehyde (0.090 g, 0.85 mmol) and was isolated as a colorless oil (0.089 g, 0.45 mmol, 48%) after purification by flash column chromatography: 2% EtOAc, 1% Et_3N, in hexanes. The spectra data are consistent with literature values.[53]

*N-(1-Naphthyl)benzylamine (**1k**).* The title compound was synthesized with general procedure A using 1-naphthylamine (0.100 g, 0.81 mmol) and benzaldehyde (0.079 g, 0.74 mmol) and was isolated as a purple solid (0.110 g, 0.51 mmol, 63%) after purification by flash column chromatography: 2% EtOAc, 1% Et_3N in hexanes. The spectral data are consistent with literature values.[53]

*N-4-Methylbenzyl-aniline (**1l**).* The title compound was synthesized with general procedure A using aniline (0.100 g, 0.81 mmol) and 4-methylbenzaldehyde (0.078 g, 0.74 mmol) and was isolated as a yellow oil (0.1095 g, 0.51 mmol, 63%) after purification by flash column chromatography: 2% EtOAc in hexanes. The spectral data are consistent with literature values.[50]

*N-4-Phenylbenzyl-aniline (**1m**).* The title compound was synthesized with general procedure A using aniline (0.2 mL, 2.19 mmol) and 4-biphenylcarboxaldehyde (0.439 g, 2.41 mmol) and was isolated as a beige solid (0.301 g, 1.16 mmol, 53%) after purification by crystallization from ethanol. The spectral data are consistent with literature values.[54]

*N-3-Phenylpropyl-aniline (**1p**).* The title compound was synthesized with general procedure A using aniline (0.12 mL, 1.25 mmol) and hydrocinnamaldehyde (0.15 mL, 1.14 mmol) and was isolated as a colorless oil (0.172 g, 0.81 mmol, 71%) after purification by flash column chromatography: 1.5% EtOAc in hexanes. The spectral data are consistent with literature values.[47]

*N-Furfuryl-aniline (**1s**).* The title compound was synthesized with general procedure A using aniline (0.1 mL, 1.10 mmol) and furfural (0.11 mL, 1.3 mmol) and was isolated as a colorless oil (0.054 g, 0.31 mmol, 28%) after purification by flash column chromatography: 2% EtOAc in hexanes. The spectral data are consistent with literature values.[55]

*N-Phenyl-thiphenemethylamine (**1t**).* The title compound was synthesized with general procedure B using aniline (0.1 mL, 1.10 mmol) and thiophenecarboxaldehyde (0.1 mL, 1.1 mmol) and was isolated as a colorless oil (0.117 g, 0.62 mmol, 56%) after purification by flash column chromatography: 2% EtOAc in hexanes. The spectral data are consistent with literature values.[55]

*N-3-Pyridyl-benzylamine (**1v**).* The title compound was synthesized with general procedure A using 3-aminopyridine (0.114 g, 1.21 mmol) and benzaldehyde (0.11 mL, 1.1 mmol) and was isolated as a yellow oil (0.075 g, 0.41 mmol, 37%) after purification by flash column chromatography: 40% EtOAc in hexanes. The spectral data are consistent with literature values.[56]

*N-Benzyl Tryptamine (**1w**).* The title compound was synthesized with general procedure B using tryptamine (0.500 g, 3.12 mmol) and benzaldehyde (0.32 mL, 3.12 mmol) and was isolated as a red oil (0.524 g, 2.09 mmol, 67%) after purification by flash column chromatography: 10% MeOH in EtOAc. The spectral data are consistent with literature values.[57]

*N-Benzyl-1-(p-tolyl)cyclopropanamine (**1aa**).* Following a literature procedure by Bertus and co-workers,[58] $Ti(^iOPr)_4$ (1.63 mL, 5.5 mmol, 1.1 equiv) was added to a cooled (−78 °C) solution of *p*-tolunitrile (586 mg, 5.0 mmol, 1.0 equiv) in Et_2O (25 mL) under nitrogen. Ethylmagnesium bromide (3.7 mL, 3 M in Et_2O, 2.2 equiv) was added dropwise, stirred for 10 min at −78 °C, and subsequently warmed to room temperature. After 1 h, $BF_3{\cdot}OEt_2$ (1.23 mL, 10.0 mmol, 2.0 equiv) was added dropwise. After stirring for an additional 1 h, 1 M HCl (15 mL) was added dropwise (vigorous bubbling occurred) and the reaction was diluted with Et_2O (ca. 60 mL). NaOH (10% aq, 50 mL) was then added leading to the formation of a blue precipitate. The mixture was extracted with Et_2O, and the combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (5% MeOH in DCM) and visualized by TLC (staining with ninhydrin) to provide **1ab′** as a light-yellow oil (0.354 g, 2.42 mmol, 48%). The spectra data are consistent with literature values.[58] Following a literature procedure by Cramer and co-workers,[59] to a solution of **1ab′** (259 mg, 1.76 mmol, 1.0 equiv) in THF (7.0 mL) was added benzaldehyde (179 μL, 1.76 mmol, 1.0 equiv) and $Ti(iOPr)_4$ (0.6 mL, 1.9 mmol, 1.1 equiv). The reaction was stirred at room temperature for 15 h under nitrogen. Absolute EtOH (205 mL, 20 equiv) and $NaBH_4$ (133 mg, 3.51 mmol, 2.0 equiv) was added in one portion. After stirring for 5 h, the reaction was cooled to 0 °C, quenched with 6 M HCl (ca. 6 mL) and stirred for 30 min. The reaction was warmed to room temperature, stirred for 30 min, and then basified with NaOH (10% aq, ca. 10 mL). The reaction mixture was extracted 3× with DCM and the combined organics were washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (0 → 3% MeOH in DCM) to provide **1ab** as a light-yellow oil (288 mg, 1.21 mmol, 69%). ^1H NMR (300 MHz, $CDCl_3$): δ 7.33−7.26 (m, 6H), 7.25−7.14 (m, 3H), 3.70 (s, 2H), 2.37 (s, 3H), 1.93 (br s, ^1H), 1.02 (m, 2H), 0.93 (m, 2H). ^{13}C {^1H} NMR (76 MHz, $CDCl_3$): δ 140.7, 140.3, 135.8, 128.9, 128.2, 128.1, 127.5, 126.6, 50.6, 42.2, 20.9, 15.3. HRMS (ESI) *m*/*z*: $[M + H]^+$ $C_{17}H_{20}N$ calcd for 238.1590; found, 238.1577.

*N-Benzyl-phenylalanine Methyl Ester (**1ab**).* The title compound was synthesized according to general procedure B using L-phenylalanine methyl ester hydrochloride (0.237 g, 1.10 mmol) and benzaldehyde (0.17 mL, 1.65 mmol) with the addition of triethylamine (0.153 mL, 1.10 mmol, 1.0 equiv). The title compound was isolated as a colorless oil (0.150 g, 0.56 mmol, 56%) after purification by flash column chromatography (3 → 5% EtOAc in hexanes). The spectral data are consistent with literature values.[48]

*N-Benzyl-allylamine (**1ac**).* Benzyl bromide (1.19 mL, 10 mmol) was added slowly to allylamine (4.49 mL, 60 mmol) neat at room temperature and the reaction was stirred for 16 h. The reaction was quenched with 1 M NaOH and extracted 3× with Et_2O. The combined organic layers were dried over $MgSO_4$ and concentrated via rotary evaporation. The pale-yellow liquid (1.403 g, 9.5 mmol, 95%) was isolated after purification by filtration through silica gel (EtOAc). The spectral data are consistent with literature values.[60]

*N-3-Butenyl-benzylamine (**1ad**).* To a solution of benzylamine (1.37 mL, 12.5 mmol) and 4-bromo-1-butene (0.25 mL, 2.5 mmol) in EtOH (5 mL) was added NaI (0.037 g, 0.25 mmol). The mixture was refluxed for 4 h before quenching with 1 M NaOH and removing the organic solvent under reduced pressure. The remaining solution was extracted 3× with Et_2O. The combined organic layers were dried over $MgSO_4$ and concentrated via rotary evaporation. The pale-yellow liquid (0.249 g, 1.55 mmol, 62%) was isolated after purification by flash column chromatography: 10 → 20% EtOAc in hexanes. The spectral data are consistent with literature values.[61]

*N-Benzyl-propargylamine (**1ae**).* Propargyl bromide (0.1 mL, 1.1 mmol) was slowly added to benzylamine (0.72 mL, 6.6 mmol) neat at room temperature and the reaction was stirred for 16 h. The reaction was quenched with 1 M NaOH and extracted 3× with Et_2O. The combined organic layers were dried over $MgSO_4$ and concentrated via rotary evaporation. The colorless oil (0.106 g, 0.73 mmol, 66%) was isolated after purification by flash column chromatography: 25% EtOAc in hexanes. The spectral data are consistent with literature values.[62]

*N-But-3-ynylaniline (**1af**).* The title compound was synthesized by stirring aniline (0.44 mL, 4.86 mmol), but-3-ynyl 4-methylbenzenesulfonate (0.727 g, 3.24 mmol), potassium iodide (0.057 g, 0.32 mmol), and K_2CO_3 (1.344 g, 9.72 mmol) in DMF at 90 °C for 16 h. The reaction was diluted with water and extracted 3× with Et_2O. The combined organic layers were dried over $MgSO_4$ and concentrated via rotary evaporation. A colorless oil (0.181 g, 1.24 mmol, 38%) was isolated after purification by flash column chromatography: 2%

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EtOAc in hexanes. The spectral data are consistent with literature values.[63]

*N-(4-Phenylbut-3-ynyl)aniline (**1ag**).* The title compound was synthesized by stirring aniline (0.27 mL, 2.97 mmol), 4-phenylbut-3-ynyl 4-methylbenzenesulfonate (0.594 g, 1.98 mmol), potassium iodide (0.035 g, 0.2 mmol), and K_2CO_3 (0.821 g, 5.94 mmol) in DMF at 90 °C for 16 h. The reaction was diluted with water and extracted 3× with Et_2O. The combined organic layers were dried over $MgSO_4$ and were concentrated via rotary evaporation. A colorless oil (0.133 g, 0.60 mmol, 30%) was isolated after purification by flash column chromatography: 2% EtOAc in hexanes. The spectral data are consistent with literature values.[63]

Synthesis and Characterization of Products. *General Procedure for Carbamoyl Fluoride Synthesis from Secondary Amines.* Representative procedure for a 0.2 mmol scale reaction: to 1-dram vial was added a stir bar, amine **1** (0.20 mmol, 1.0 equiv), PDFA (0.107 g, 0.30 mmol, 1.5 equiv), and 4-methylpyridine *N*-oxide (**2h**) (0.044 g, 0.40 mmol, 2.0 equiv). The vial was fitted with a septum cap then evacuated and backfilled 3× with nitrogen. To the vial was added MeCN (2.0 mL) and the septum cap was rapidly removed and replaced with a Teflon-lined screw cap before submerging the vial in a pre-heated 60 °C oil bath. The reaction was stirred at this temperature for 1 h. After completion of the reaction, the vial was removed from the oil bath and the reaction transferred directly to a round-bottomed flask. The crude material was dry loaded on silica gel and was purified by column chromatography to yield the carbamoyl fluoride. If amine is an oil or liquid, the following procedure was followed: to screw-cap vial was added a stir bar, PDFA (0.107 g, 0.30 mmol, 1.5 equiv), and 4-methylpyridine *N*-oxide (**2h**) (0.044 g, 0.40 mmol, 2.0 equiv). The vial was fitted with a septum cap then evacuated and backfilled 3× with nitrogen. To the vial was added 1 mL of a 0.1 M solution of amine 1 in MeCN, and the septum cap was rapidly removed and replaced with a Teflon-lined screw cap before submerging the vial in a pre-heated 60 °C oil bath. The reaction was stirred at this temperature for 1 h. After completion of the reaction, the vial was removed from the oil bath and the reaction transferred directly to a round-bottomed flask. The crude material was dry loaded on silica gel and was purified by column chromatography to yield the carbamoyl fluoride.

Safety Precautions: the reactions are conducted in a sealed system and gaseous byproducts are formed (e.g., CO_2 and COF_2). The reaction vessels should be cooled to room temperature before opening the vial cap. Although we expect the concentration of COF_2 to be low at any given point under our conditions, all reactions and workup procedures should be conducted in a well-ventilated fumehood.

Note: in line with previous reports, carbamoyl fluorides demonstrate restricted rotation about the N–C_{acyl} bond, giving rise to rotamers in solution.[10,19] Distinct resonances for the two rotamers are observed in the NMR spectra for unsymmetrically substituted carbamoyl fluorides (R′ ≠ R), although not all peaks may be fully resolved. The chemical shifts for both rotamers are listed as they appear in the ^{13}C NMR data. In instances where the signals for the two rotamers overlap in the ^{13}C NMR spectrum, a "2C" notation is provided in the chemical shift listing.[21]

*N-Benzyl-N-phenyl-carbamoyl Fluoride (**3a**).* The title compound was synthesized using **1a** (0.073 g, 0.40 mmol) and isolated as a colorless oil, or a white solid upon standing (0.089 g, 0.39 mmol 97%, mp 36–37 °C), after purification by flash column chromatography: 1% EtOAc in hexanes. Scale up: the title compound was synthesized in an oven-dried 100 mL Schlenk tube instead of a vial using *N*-benzylaniline (**1a**) for 2 h (0.500 g, 2.73 mmol) and isolated as a colorless oil, or a white solid upon standing (0.597 g, 2.59 mmol, 95%), flash column chromatography: 1% EtOAc in hexanes. ^1H NMR (700 MHz, $CDCl_3$): δ 7.38–7.27 (m, 6H), 7.25–7.20 (m, 2.5H), 7.06 (d, *J* = 7.3 Hz, 1.5H), 4.83 (s, 2H). ^{13}C {^1H} NMR (176 MHz, $CDCl_3$): δ 146.8 (d, *J* = 287.9 Hz), 146.6 (d, *J* = 292.2 Hz), 140.5, 139.2, 135.9, 135.6, 129.3 (2C), 128.8, 128.6, 128.5, 128.1, 127.6, 127.5, 126.9, 125.9, 55.6, 55.0 (2C for minor rotamer overlapping with peaks in the region from 129.3 to 125.9 ppm). ^{19}F NMR (659 MHz, $CDCl_3$, rotamers): δ −14.63 (s, 1F), −17.06 (s, 0.32F). HRMS (DART) *m*/*z*: $[M + H]^+$ calcd for $C_{14}H_{13}FNO$, 230.0976; found, 230.0968. IR (ATR, neat, cm^{-1}) 2934, 1784, 1594, 1491, 1215, 731, 692.

*N-Benzyl-N-(4-ethylphenyl)carbamoyl Fluoride (**3b**).* The title compound was synthesized using **1b** (0.085 g, 0.40 mmol) and isolated as an orange oil (0.098 g, 0.38 mmol, 94%) after purification by flash column chromatography: 2% EtOAc in hexanes. ^1H NMR (700 MHz, $CDCl_3$): δ 7.36–7.28 (m, 3H), 7.25–7.19 (m, 2.3H), 7.18–7.11 (m, 2.3H), 6.96 (d, *J* = 8.0 Hz, 1.4H), 4.81 ppm (s, 2H), 2.63 (q, *J* = 7.6 Hz, 2H), 1.22 ppm (t, *J* = 7.6 Hz, 3H). ^{13}C {^1H} NMR (176 MHz, $CDCl_3$): δ 147.0 (d, *J* = 287.5 Hz), 146.8 (d, *J* = 291.5 Hz), 144.2, 143.7, 138.1, 136.8, 136.0, 135.8, 128.7 (2C), 128.64, 128.56, 128.5, 128.13, 128.09, 127.5, 126.6, 125.8, 55.6, 55.1, 28.3 (2C), 15.23, 15.17. ^{19}F NMR (282 MHz, $CDCl_3$): δ −15.85 (s, 1F), −18.32 (s, 0.31F). HRMS (DART) *m*/*z*: $[M + NH_4]^+$ calcd for 275.1554; found, 275.1557. IR (ATR, $CDCl_3$, cm^{-1}) 3034, 2966, 2933, 2874, 1779, 1513, 1391, 1265, 1028, 839, 748, 702, 632, 570.

*N-Benzyl-N-(4-methoxyphenyl)carbamoyl Fluoride (**3c**).* The title compound was synthesized using **1c** (0.085 g, 0.40 mmol) and isolated as a pale orange-yellow oil (0.101 g, 0.39 mmol, 97%) after purification by flash column chromatography: 2% EtOAc in hexanes. ^1H NMR (700 MHz, $CDCl_3$): δ 7.35–7.28 (m, 3H), 7.24–7.22 (m, 2H), 7.10 (d, *J* = 8.8 Hz, 0.5H), 6.94 (d, *J* = 8.8 Hz, 1.5H), 6.85 (d, *J* = 8.9 Hz, 0.5H), 6.82 (d, *J* = 8.9 Hz, 1.5H), 4.77 (s, 2H), 3.78 (s, 3H). ^{13}C {^1H} NMR (176 MHz, $CDCl_3$): δ 159.1, 158.8, 147.2 (d, *J* = 287.0 Hz), 147.1 (d, *J* = 291.2 Hz), 136.0, 135.8, 133.2, 132.0, 128.9, 128.8, 128.7, 128.23, 128.18, 128.16, 127.9, 127.6, 114.6, 114.5, 55.9 (2C), 55.5 (2C). ^{19}F NMR (282 MHz, $CDCl_3$): δ −15.93 (s, 1F), −19.22 (s, 0.30F). HRMS (DART) *m*/*z*: $[M + H]^+$ calcd for $C_{15}H_{15}FNO_2$, 260.1081; found, 260.1078. IR (ATR, $CDCl_3$, cm^{-1}) 1786, 1513, 1250, 1034, 836, 696, 631, 628, 592, 571.

*N-Benzyl-N-(4-chlorophenyl)carbamoyl Fluoride (**3d**).* The title compound was synthesized by using **1d** (0.087 g, 0.40 mmol) and isolated as a colorless oil (0.092 g, 0.35 mmol, 88%) after purification by flash column chromatography: 2% EtOAc in hexanes. ^1H NMR (300 MHz, $CDCl_3$): δ 7.33–7.28 (m, 5H), 7.25–7.16 (m, 2.5H), 6.99 (d, *J* = 8.4 Hz, 1.5H), 4.81 (s, 2H). ^{13}C {^1H} NMR (176 MHz, $CDCl_3$): δ 146.6 (d, *J* = 288.4 Hz, 2C), 139.0, 137.7, 135.6, 135.4, 134.1, 133.4, 129.7, 129.1, 128.9, 128.7 (2C), 128.4 (2C), 127.6, 127.5, 55.7, 55.1 (1C overlapping with another peak in the region from 129.7 to 128.4). ^{19}F NMR (282 MHz, $CDCl_3$): δ −14.25 (s, 1F), −16.99 (s, 0.35F). HRMS (ESI) *m*/*z*: $[M + Na]^+$ calcd for $C_{14}H_{11}ClFNNaO$, 286.0405; found, 286.0404. IR (ATR, $CDCl_3$, cm^{-1}) 3090, 3065, 3034, 2927, 2853, 1781, 1492, 1386, 1261, 1091, 1011, 834, 746, 718, 698, 627, 569, 506.

*N-Benzyl-N-(4-bromophenyl)carbamoyl Fluoride (**3e**).* The title compound was synthesized by using **1e** (0.105 g, 0.40 mmol) and isolated as a pale-yellow oil (0.084 g, 0.27 mmol, 68%) after purification by flash column chromatography: 2% EtOAc in hexanes. ^1H NMR (700 MHz, $CDCl_3$): δ 7.48–7.45 (m, 2H), 7.35–7.32 (m, 3H), 7.26–7.20 (m, 2H), 7.13 (d, *J* = 8.1 Hz, 0.5H), 6.92 (d, *J* = 8.1 Hz, 1.5H), 4.81 (s, 2H). ^{13}C {^1H} NMR (75 MHz, $CDCl_3$): δ 146.5 (d, *J* = 288.3 Hz, 2C), 139.5, 138.2, 135.6, 135.4, 132.7 (2C), 129.0, 128.9, 128.7, 128.6, 128.41, 128.36, 127.7, 127.6, 122.1, 121.4, 55.6, 55.0. ^{19}F NMR (282 MHz, $CDCl_3$): δ −15.16 (s, 1 F), −17.80 (s, 0.35 F). HRMS (ESI) *m*/*z*: $[M + H]^+$ calcd for $C_{14}H_{12}BrFNO$, 308.0081; found, 308.0079. IR (ATR, $CDCl_3$, cm^{-1}) 1786, 1491, 1264, 832, 697, 627, 570.

*N-Benzyl-N-(4-iodophenyl)carbamoyl Fluoride (**3f**).* The title compound was synthesized using **1f** (0.124 g, 0.40 mmol) and isolated as a colorless oil (0.122 g, 0.34 mmol, 86%) after purification by flash column chromatography: 2% EtOAc in hexanes. ^1H NMR (300 MHz, $CDCl_3$): δ 7.66 (d, 7.3 Hz, 2H), 7.31 (m, 3H), 7.25–7.17 (m, 2H), 7.00 (d, 7.9 Hz, 0.5H), 6.80 (d, 8.1 Hz, 1.5H), 4.81 (s, 2H). ^{13}C {^1H} NMR (176 MHz, $CDCl_3$): δ 146.5 (d, *J* = 288.5 Hz, 2C),

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140.3, 139.0, 138.7 (2C), 135.7, 135.4, 129.1, 128.9 (2C), 128.7, 128.43, 128.39, 127.9, 127.6, 93.5, 92.7, 55.6, 55.0. ^{19}F NMR (282 MHz, $CDCl_3$): δ −15.09 (s, 1F), −17.50 (s, 0.36F). HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{14}H_{12}FINO$, 355.9942; found, 355.9939. IR (ATR, $CDCl_3$, cm^{-1}) 3063, 3006, 2924, 2852, 1783, 1486, 1452, 1284, 1220, 1008, 734, 570.

*N-Benzyl-N-(3-methoxyphenyl)carbamoyl Fluoride (**3g**).* The title compound was synthesized by using **1g** (0.085 g, 0.40 mmol) and isolated as a pale orange-yellow oil (0.091 g, 0.35 mmol, 88%) after purification by flash column chromatography: 2% EtOAc in hexanes. ^{1}H NMR (700 MHz, $CDCl_3$): δ 7.37−7.24 (m, 6H), 6.92−6.80 (m, 1.5H), 6.71 ppm (d, J = 7.8 Hz, 0.75H), 6.63 ppm (s, 0.75H), 4.87 ppm (s, 2H), 3.77 (s, 3H). ^{13}C {^{1}H} NMR (176 MHz, $CDCl_3$): δ 160.23, 160.17, 146.9 (d, J = 288.0 Hz), 146.7 (d, J = 291.0 Hz), 141.6, 140.3, 136.1, 135.8, 130.14, 130.08, 128.9, 128.75, 128.67, 128.21, 128.17, 127.7, 119.2, 118.2, 113.8, 113.4, 112.9, 112.1, 55.6, 55.4 (2C), 55.2. ^{19}F NMR (282 MHz, $CDCl_3$): δ −15.40 (s, 1F), −17.59 (s, 0.32F). HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{15}H_{15}FNO_2$, 260.1081; found, 260.1082. IR (ATR, $CDCl_3$, cm^{-1}) 1781, 1604, 1493, 1394, 696.

*N-Benzyl-N-(3-bromophenyl)carbamoyl Fluoride (**3h**).* The title compound was synthesized by using **1h** (0.105 g, 0.40 mmol) and isolated as a pale-yellow oil (0.080 g, 0.26 mmol, 64%) after purification by flash column chromatography: 2% EtOAc in hexanes. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.44 (d, J = 7.7 Hz, 1.25H), 7.39−7.29 (m, 3H), 7.28−7.14 (m, 4H), 6.98 ppm (d, J = 7.7 Hz, 0.75H), 4.82 (s, 2H). ^{13}C {^{1}H} NMR (176 MHz, $CDCl_3$): δ 146.5 (d, J = 290.0 Hz, 2C), 141.7, 140.5, 135.6, 135.3, 131.4, 130.9, 130.7, 130.2, 129.2, 129.1, 128.9, 128.8, 128.6, 128.4, 127.5, 127.4, 125.9, 124.8, 122.7 (2C), 55.7, 55.1. ^{19}F NMR (282 MHz, $CDCl_3$): δ −14.83 (s, 1F), −17.30 (s, 0.35F). HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{14}H_{12}BrFNO$, 308.0081; found, 308.0081. IR (ATR, $CDCl_3$, cm^{-1}) 1784, 1574, 1478, 1389, 785, 693.

*N-Benzyl-N-(2-methoxyphenyl)carbamoyl Fluoride (**3i**).* The title compound was synthesized by using **1i** (0.043 g, 0.20 mmol) and isolated as a colorless oil (0.044 g, 0.17 mmol, 85%) after purification by flash column chromatography: 5% EtOAc in hexanes. ^{1}H NMR (400 MHz, $CDCl_3$) δ7.37−7.18 (m, 6H), 7.04−6.79 (m, 3H), 4.99 (bd, J = 13.2 Hz, 0.8H), 4.71 (s, 0.4H), 4.50 (bd, J = 13.2 Hz, 0.8H), 3.81 (bd, 1.7 Hz, 0.5H), 3.76 (bd, 1.8 Hz, 2.5H). ^{13}C {^{1}H} NMR (176 MHz, $CDCl_3$): δ 154.8 (2C), 147.6 (d, J = 287.2 Hz), 146.8 (d, J = 291.3 Hz), 136.1, 136.0, 129.8, 129.8, 129.3, 129.0 (2C), 128.6, 128.4, 128.01, 127.99, 127.7, 120.8, 120.6, 112.3, 111.9, 55.7, 55.6, 54.9, 54.7 (2C overlapping with peaks in the region from 129.8 to 127.7 ppm). ^{19}F NMR (659 MHz, $CDCl_3$): δ −16.69 (s, 1F), −20.00 (s, 0.16F). HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{15}H_{14}FNNaO_2$, 282.0901; found, 282.0885. IR (ATR, $CDCl_3$, cm^{-1}) 3065, 3032, 2932, 1783, 1501, 1393, 1266, 1250, 747, 697.

*N-Benzyl-N-(o-tolyl)carbamoyl Fluoride (**3j**).* The title compound was synthesized by using **1j** (0.079 g, 0.40 mmol) and isolated as a colorless oil (0.064 g, 0.26 mmol, 66%) after purification by flash column chromatography: 2% EtOAc in hexanes. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.39−7.31 (m, 3H), 7.30−7.14 (m, 5H), 7.03 (d, J = 7.7 Hz, 0.2H), 6.92 (d, J = 7.9 Hz, 0.8H), 4.94 (d, J = 14.2 Hz, ^{1}H), 4.61 (d, J = 14.2 Hz, ^{1}H), 2.11 (s, 0.6H), 2.08 (s, 2.4H). ^{13}C {^{1}H} NMR (176 MHz, $CDCl_3$): δ 147.1 (d, J = 286.6 Hz), 146.1 (d, J = 291.7 Hz), 138.7, 137.8, 135.8, 135.7, 135.52, 135.47, 131.5, 131.3, 129.4, 128.9, 128.83, 128.76, 128.74, 128.70, 128.42, 128.40, 128.0, 127.8, 127.1, 127.0, 55.40, 55.37, 17.44, 17.36. ^{19}F NMR (282 MHz, $CDCl_3$): δ −16.49 (s, 1F), −20.66 (s, 0.25F). HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{15}H_{15}FNO$, 244.1132; found, 244.1129. IR (ATR, $CDCl_3$, cm^{-1}) 3065, 3033, 2928, 2857, 1779, 1493, 1455, 1393, 1258, 1082, 1006, 749, 716, 698, 637, 575, 455.

*N-Benzyl-N-(1-naphthyl)carbamoyl Fluoride (**3k**).* The title compound was synthesized by using **1k** (0.093 g, 0.40 mmol) and isolated as a colorless oil (0.056 g, 0.20 mmol, 50%) after purification by flash column chromatography: 2% EtOAc in hexanes. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.98−7.77 (m, 3H), 7.63−7.54 (m, 2H), 7.45−7.20 (m, 6H), 7.17 (d, J = 7.3 Hz, 0.15H), 7.04 (d, J = 7.3 Hz, 0.85H), 5.33 (d, J = 14.3 Hz, 0.85H), 5.24 (d, J = 14.9 Hz, 0.15H), 4.53 (d, J = 14.9 Hz, 0.15H), 4.52 (d, J = 14.3 Hz, 0.85H). ^{13}C {^{1}H} NMR (176 MHz, $CDCl_3$): δ 147.6 (d, J = 287.6 Hz), 146.9 (d, J = 292.4 Hz), 136.1, 135.88, 135.85, 135.1, 134.8, 134.6, 129.7, 129.4 (2C), 129.3, 129.2, 128.9, 128.8, 128.73, 128.71 (2C), 128.43, 128.40, 127.5, 127.4, 126.75, 126.70, 126.3, 126.2, 125.5, 125.3, 121.9 (2C), 55.67, 55.65. ^{19}F NMR (282 MHz, $CDCl_3$): δ −14.73 (s, 1F), −19.50 (s, 0.2F). HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{18}H_{14}FNNaO$, 302.0952; found, 302.0950. IR (ATR, $CDCl_3$, cm^{-1}) 3063, 3034, 2929, 2854, 1778, 1597, 1404, 1383, 1272, 1250, 1040, 901, 803, 775, 749, 701, 632, 538, 429.

*N-Phenyl-N-(p-tolylmethyl)carbamoyl Fluoride (**3l**).* The title compound was synthesized by using **1l** (0.039 g, 0.20 mmol) and isolated as a colorless oil (0.048 g, 0.20 mmol, >99%) after purification by flash column chromatography: 1 → 2% EtOAc in hexanes. ^{1}H NMR (700 MHz, $CDCl_3$): δ 7.38−7.31 (m, 2H), 7.31−7.27 (m, 1H), 7.23 (bd, J = 7.4 Hz, 0.5H), 7.16−7.08 (m, 4H), 7.05 (d, J = 7.6 Hz, 1.5H), 4.79 (s, 2H), 2.33 (s, 3H). ^{13}C {^{1}H} NMR (176 MHz, $CDCl_3$): δ 147.0 (d, J = 287.7 Hz), 146.9 (d, J = 292.0 Hz), 140.6, 139.4, 138.0 (2C), 133.0, 132.8, 129.6, 129.4 (2C), 128.7, 128.2 (2C), 127.72, 127.66, 127.1, 126.2, 55.5, 55.0, 21.3 (2C). ^{19}F NMR (377 MHz, $CDCl_3$): δ −14.57 (s, 1F), −17.23 (s, 0.33F). HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{15}H_{15}NOF$, 244.1132; found, 244.1129. IR (ATR, neat, cm^{-1}) 3026, 1779, 1391, 695.

*N-Phenyl-N-[(4-phenylphenyl)methyl]carbamoyl Fluoride (**3m**).* The title compound was synthesized by using **1m** (0.052 g, 0.20 mmol) and isolated as a white solid (0.054 g, 0.18 mmol, 88%, mp 53−54 °C) after purification by flash column chromatography: 2% EtOAc in hexanes. ^{1}H NMR (700 MHz, $CDCl_3$): δ 7.58 (d, J = 7.3 Hz, 2.5H), 7.55 (d, J = 8.0 Hz, 1.5H), 7.44 (t, J = 7.6 Hz, 2H), 7.40−7.34 (m, 3H), 7.33−7.27 (m, 3.5H), 7.11 (d, J = 7.6 Hz, 1.5H), 4.87 (s, 2H). ^{13}C {^{1}H} NMR (176 MHz, $CDCl_3$): δ 147.0 (d, J = 288.0 Hz), 146.8 (d, J = 291.5 Hz), 141.1 (2C), 140.62, 140.55, 140.5, 139.4, 135.0, 134.8, 129.5, 129.1, 128.9, 128.2, 128.1, 127.8, 127.63, 127.59, 127.5, 127.1, 127.0, 126.1, 55.4, 54.9 (4C for minor rotamer overlapping with peaks in the region from 129.1 to 126.1 ppm). ^{19}F NMR (659 MHz, $CDCl_3$): δ −14.53 (s, 1F), −16.90 (s, 0.3F). HRMS (ESI) m/z: calcd for $C_{20}H_{17}NOF$ $[M + H]^+$, 306.1289; found, 306.1291. IR (ATR, neat, cm^{-1}) 2988, 1779, 1391, 745, 694.

*N-(9-Anthrylmethyl)-N-methyl-carbamoyl Fluoride (**3n**).* The title compound was synthesized by using 9-(methylaminomethyl)-anthracene (**1n**) (0.089 g, 0.40 mmol) and isolated as a yellow solid (0.082 g, 0.31 mmol, 76%, mp 141−143 °C) after purification by flash column chromatography: 2% EtOAc in hexanes. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.53 (s, 1H), 8.31 (d, J = 8.8 Hz, 1.5H), 8.23 (d, J = 8.8 Hz, 0.5H), 8.07 (d, J = 8.4 Hz, 2H), 7.61 (t, J = 7.7 Hz, 2H), 7.52 (t, J = 7.4 Hz), 5.57 (s, 1.5H), 5.53 (s, 0.5H), 2.59 (s, 2.25H), 2.57 (s, 0.75H). ^{13}C {^{1}H} NMR (176 MHz, $CDCl_3$): δ 148.1 (d, J = 287.8 Hz), 147.5 (d, J = 286.2 Hz), 131.4 (2C), 131.3, 131.2, 129.6, 129.5, 129.4, 129.2, 127.3, 127.2, 125.4, 125.3 (2C), 124.5, 123.6, 123.1, 44.3 (d, J = 1.4 Hz), 43.8 (d, J = 4.8 Hz), 32.9 (d, J = 1.5 Hz), 32.1 (d, J = 4.1 Hz). ^{19}F NMR (282 MHz, $CDCl_3$): δ −22.16 (s, 1F), −22.40 (s, 0.3F). HRMS (ESI) m/z: calcd for $[M + H]^+$ $C_{17}H_{15}FNO$, 268.1132; found, 268.1135. IR (ATR, $CDCl_3$, cm^{-1}) 3050, 2952, 2922, 2852, 1772, 1446, 1394, 1246, 1105, 990, 894, 845, 792, 772, 730, 701, 592, 583, 516.

*N-Methyl-N-phenyl-carbamoyl Fluoride (**3o**).* The title compound was synthesized by using *N*-methylaniline (**1o**) (0.021 g, 0.20 mmol) and isolated as a colorless oil (0.024 g, 0.16 mmol, 77%) after purification by flash column chromatography: 5% EtOAc in hexanes. The spectral data are consistent with literature values.[18] Scale up: the title compound was synthesized in an oven-dried 100 mL Schlenk flask instead of a vial (side arm was opened to vent gas build up every 30 min) using **1r** for 2 h (1.000 g, 9.33 mmol) and isolated as a colorless oil (1.198 g, 7.44 mmol, 83%), flash column chromatography: 1% EtOAc in hexanes.

*N-Phenyl-N-(3-phenylpropyl)carbamoyl Fluoride (**3p**).* The title compound was synthesized by using **1p** (0.042 g, 0.20 mmol) and isolated as a colorless oil (0.048 g, 0.18 mmol, 92%) after purification by flash column chromatography: 3% EtOAc in hexanes. ^{1}H NMR (700 MHz, $CDCl_3$): δ 7.45−7.40 (m, 2H), 7.38−7.33 (m, 1H),

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7.32−7.25 (m, 2.5H), 7.20 (d, J = 7.6 Hz, 2.5H), 7.13 (d, J = 7.3 Hz, 2H), 3.74 (t, J = 7.5 Hz, 1.5H), 3.71 (t = 7.2 Hz, 0.5H), 2.68−2.63 (m, 2H), 1.94 (p, J = 7.6 Hz, 2H). ^{13}C {^{1}H} NMR (176 MHz, $CDCl_3$): δ 147.0 (d, J = 290.7 Hz), 146.5 (d, J = 287.6 Hz), 141.0, 140.7, 140.3, 139.3, 129.6 (2C), 128.62, 128.57, 128.4, 128.3, 128.2, 127.8, 126.9, 126.3 (2C), 126.2, 51.4, 50.9, 32.9, 32.8, 30.2, 29.2. ^{19}F NMR (659 MHz, $CDCl_3$): δ −13.72 (s, 1F), −18.75 (s, 0.25F). HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{16}H_{17}NOF$, 258.1289; found, 258.1285. IR (ATR, neat, cm^{-1}) 2941, 1779, 1495, 1396, 1265, 746, 695.

*N,N-Dibenzylcarbamoyl Fluoride (**3q**).* The title compound was synthesized by using dibenzylamine (**1q**) (0.079 g, 0.40 mmol) and isolated as a colorless oil (0.071 g, 0.29 mmol, 73%) after purification by flash column chromatography: 2% EtOAc in hexanes. The spectral data are consistent with literature values.[19]

*N-Benzyl-N-(2-cyanoethyl)carbamoyl Fluoride (**3r**).* The title compound was synthesized by using 3-(benzylamino)propionitrile (**1r**) (0.064 g, 0.40 mmol) and isolated as an orange oil (0.046 g, 0.28 mmol, 71%) after purification by flash column chromatography: 20% EtOAc in hexanes. The spectral data are consistent with literature values.[22]

*N-(2-Furylmethyl)-N-phenyl-carbamoyl Fluoride (**3s**).* The title compound was synthesized by using **1s** (0.035 g, 0.20 mmol) and isolated as a colorless oil (0.040 g, 0.18 mmol, 91%) after purification by flash column chromatography: 3% EtOAc in hexanes. ^{1}H NMR (700 MHz, $CDCl_3$): δ 7.42−7.35 (m, 3H), 7.33 (t = 7.5 Hz, 1H), 7.28 (d, J = 7.7 Hz, 0.5H), 7.13 (d, J = 7.7 Hz, 1.5H), 6.33 (br s, 0.25H), 6.31 (t, J = 2.2 Hz, 0.75H), 6.25 (d, J = 3.0 Hz, 0.75H), 6.23 (bd, J = 3.0 Hz), 4.80 (s, 1.5H), 4.77 (s, 0.5H). ^{13}C {^{1}H} NMR (176 MHz, $CDCl_3$): δ 149.3, 149.0, 146.7 (d, J = 292.6 Hz), 146.5 (d, J = 288.7 Hz), 143.0, 142.9 (d, J = 2.6 Hz), 140.4, 139.2, 129.52, 129.49, 128.4, 128.0, 126.9, 126.2, 110.6 (2C), 110.0, 109.4, 48.3, 48.1. ^{19}F NMR (659 MHz, $CDCl_3$): δ −14.13 (s, 1F), −17.07 (s, 0.3F). HRMS (ESI) m/z: calcd for $C_{12}H_{11}NO_2F$, $[M + H]^+$ 220.0768; found, 220.0770. IR (ATR, neat, cm^{-1}) 2988, 1781, 1597, 1494, 743, 694, 595.

*N-Phenyl-N-(2-thienylmethyl)carbamoyl Fluoride (**3t**).* The title compound was synthesized by using **1t** (0.038 g, 0.20 mmol) and isolated as a yellow solid (0.040 g, 0.17 mmol, 85%, mp 43−44 °C) after purification by flash column chromatography: 1 → 2% EtOAc in hexanes. ^{1}H NMR (700 MHz, $CDCl_3$): δ 7.41−7.31 (m, 3H), 7.26 (m, 1.5H), 7.12 (d, J = 7.6 Hz, 1.5H), 6.96−6.92 (m, 1H), 6.96−6.94 (m, 0.2H), 6.93−6.91 (m, 0.8H), 6.91−6.90 (m, 1H), 4.97 (br s, 2H). ^{13}C {^{1}H} NMR (176 MHz, $CDCl_3$): δ 146.6 (d, J = 289.0 Hz), 146.4 (d, J = 292.6 Hz), 140.1, 139.0, 138.1, 137.4, 129.61, 129.56, 128.5, 128.1 (2C), 127.4, 127.1 (2C), 126.9, 126.5, 126.4, 126.2, 50.3, 50.1. ^{19}F NMR (659 MHz, $CDCl_3$): δ −14.61 (s, 1F), −16.99 (s, 0.25F). HRMS (ESI) m/z: calcd for $C_{12}H_{11}NOFS$ $[M + H]^+$, 236.0540; found, 236.0538. IR (ATR, neat, cm^{-1}) 2988, 1777, 1597, 1493, 1394, 693.

*N-Benzyl-N-(2-pyridyl)carbamoyl Fluoride (**3u**).* The title compound was synthesized by using 2-benzylaminopyridine (**1u**) (0.074 g, 0.40 mmol) and isolated as a yellow oil (0.041 g, 0.18 mmol, 45%) after purification by flash column chromatography: 10% EtOAc in hexanes. When the reaction time was increased to 3 h, the yield was found to increase significantly (0.058 g, 0.25 mmol, 63%). ^{1}H NMR (700 MHz, $CDCl_3$): δ 8.44 (d, J = 4.8 Hz, 1H), 7.74−7.64 (m, 1.2H), 7.61−7.37 (m, 0.5H), 7.35−7.19 (m, 5.3H), 7.14 (dd, J = 8.1 Hz, 4.9 Hz, 1H), 5.22 (s, 2H). ^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$): δ 151.9, 148.3, 146.1 (d, J = 292.6 Hz), 138.1, 136.6, 128.6 (2C), 127.7, 121.6, 119.1, 51.0. ^{19}F NMR (282 MHz, $CDCl_3$): δ −7.71 (br s, 1F), −15.21 (br s, 0.81F). HRMS (DART) m/z: $[M + H]^+$ calcd for $C_{13}H_{12}FN_2O$, 231.0928; found, 231.0922. IR (ATR, $CDCl_3$, cm^{-1}) 1789, 1590, 1472, 1435, 1392, 1305, 1274, 1223, 779, 697.

*N-Benzyl-N-(3-pyridyl)carbamoyl Fluoride (**3v**).* The title compound was synthesized by using **1v** (0.037 g, 0.20 mmol) and isolated as a yellow oil (0.020 g, 0.09 mmol, 43%) after purification by flash column chromatography: 40% EtOAc in hexanes. Unlike with structurally similar **3u**, increased reaction time does not provide an increase in the yield of **3v**. ^{1}H NMR (700 MHz, $CDCl_3$) 8.57−8.50 (m, 1.25H), 8.38 (br s, 0.75H), 7.57 (bd, J = 6.6 Hz, 0.25H), 7.38−7.26 (m, 4.75H), 7.25−7.18 (m, 2H), 4.87 and 4.85 (overlapping singlets, 2H total). ^{13}C {^{1}H} NMR (176 MHz, $CDCl_3$): δ 149.3, 148.7, 148.4, 147.4, 146.5 (d, 289.5 Hz, 2C), 137.2, 135.9, 135.2, 135.0, 134.6, 133.7, 129.2, 129.1, 128.7, 128.64, 128.57, 127.6, 124.0, 123.9, 55.7, 55.1. ^{19}F NMR (659 MHz, $CDCl_3$): δ −13.85 (s, 1F), −16.79 (s, 0.30F). HRMS (DART) m/z: $[M + H]^+$ calcd for $C_{13}H_{12}N_2OF$, 231.0928; found, 231.0937. IR (ATR, neat, cm^{-1}) 3064, 2987, 1779, 1391, 1266, 695.

*N-Benzyl-N-[2-(1H-indol-3-yl)ethyl]carbamoyl Fluoride (**3w**).* The title compound was synthesized by using **1w** (0.202 g, 0.81 mmol) and isolated as an orange-yellow solid (0.128 g, 0.44 mmol, 54%, mp 72−74 °C) after purification by flash column chromatography: 20% EtOAc in hexanes. Single crystals suitable for X-ray crystallography were grown via slow evaporation of a saturated solution of **3w** in 1:1 diethyl ether/hexanes. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.04 (br s, 1H), 7.54 (d, J = 7.8 Hz, 0.5H), 7.48 (d, J = 7.8 Hz, 0.5H), 7.40−7.29 (m, 4H), 7.26−7.10 (m, 4H), 7.02 (d, J = 2.2 Hz, 0.5H), 6.98 (d, J = 2.2 Hz, 0.5H), 4.39 (s, 1.1H), 4.32 (s, 0.9H), 3.55 (t, J = 7.6 Hz, 0.9H), 3.47 (t, J = 7.6, 1.1H), 3.07 (t, J = 7.6 Hz, 0.9H), 2.99 (t, J = 7.6 Hz, 1.1H). ^{13}C {^{1}H} NMR (176 MHz, $CDCl_3$): δ 148.7 (d, J = 287.46 Hz), 147.7 (d, J = 288.78 Hz), 136.43, 136.41, 136.0, 135.9, 129.02, 128.97, 128.32, 128.25, 128.2, 127.7, 127.3, 127.1, 122.4, 122.32 (2C), 122.30, 119.71, 119.67, 118.6, 118.5, 112.2, 112.0, 111.5, 111.4, 52.3, 51.8 (d, J = 2.61 Hz), 48.7, 47.7, 24.7, 23.2. ^{19}F NMR (659 MHz, $CDCl_3$): δ −21.50 (s, 0.86F), −21.95 (s, 1F). HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{18}H_{17}FN_2NaO$, 319.1217; found, 319.1194. IR (ATR, neat, cm^{-1}) 3356, 3083, 2924, 2858, 1757, 1422, 741, 556.

*4-Methyl-2-phenyl-piperazine-1-carbonyl Fluoride (**3x**).* The title compound was synthesized by using 1-methyl-3-phenylpiperazine (**1x**) (0.035 g, 0.20 mmol) and isolated as a colorless oil (0.034 g, 0.16 mmol, 79%) after purification by flash column chromatography: 10 → 30% EtOAc in hexanes. ^{1}H NMR (700 MHz, $CDCl_3$): δ 7.61−7.54 (bm, 1H), 7.49 (br s, 1H), 7.36 (t, J = 7.4 Hz, 2H), 7.29 (t, J = 7.3 Hz, 1H), 5.21 (br s, 0.5H), 5.07 (br s, 0.5H), 3.86 (bd, J = 10.9 Hz, 0.5H), 3.73 (br, J = 11.8 Hz, 0.5H), 3.33 (bd, J = 10.9 Hz, 1H), 3.21 (dt, J = 12.8, 3.2 Hz, 1H), 2.81 (br s, 1H), 2.49 (dd, J = 12.0, 3.6 Hz, 1H), 2.32 (s, 3H), 2.21−2.12 (m, 1H). ^{13}C {^{1}H} NMR (176 MHz, $CDCl_3$): δ 147.1 (d, J = 286.9 Hz), 146.9 (d, J = 282.9 Hz), 138.5 (2C), 128.8, 128.7, 128.0, 127.8 (2C), 127.4, 57.3, 56.8, 55.0, 54.8 (2C), 54.4, 46.3 (2C), 41.5, 41.3. ^{19}F NMR (659 MHz, $CDCl_3$): δ −23.69 (s, 0.9F), −24.16 (s, 1F). HRMS (DART) m/z: $[M + H]^+$ calcd for $C_{12}H_{16}N_2OF$, 223.1241; found, 223.1236. IR (ATR, neat, cm^{-1}) 2796, 1777, 1401, 693.

*5-Bromoindoline-1-carbonyl Fluoride (**3y**).* The title compound was synthesized by using 5-bromoindoline (**1y**) (0.079 g, 0.40 mmol) and isolated as a white solid (0.091 g, 0.37 mmol, 93%, mp 115−117 °C) after purification by flash column chromatography: 5% EtOAc in hexanes. ^{1}H NMR (700 MHz, $CDCl_3$): δ 7.63 (dd, J = 8.4, 1.4 Hz, 0.75H), 7.38−7.29 (m, 2H), 7.16 (dd, J = 9.2, 4.1 Hz, 0.25H), 4.16−4.05 (m, 2H), 3.19 (t, J = 8.60 Hz, 2H). ^{13}C {^{1}H} NMR (176 MHz, $CDCl_3$): δ 143.7 (d, J = 294.8 Hz), 143.0 (d, J = 289.8 Hz), 139.6, 138.9 (d, J = 5.1 Hz), 133.9, 133.5 (d, J = 4.5 Hz), 130.9 (d, J = 2.3 Hz), 130.8, 128.6, 128.1, 117.2, 117.1, 116.42, 116.35, 48.5, 47.9, 27.2, 27.1. ^{19}F NMR (282 MHz, $CDCl_3$): δ −5.74 (s, 1F), −13.48 (s, 0.3F). HRMS (ESI) m/z: $[M]^+$ calcd for C_9H_7BrFNO, 242.9690; found, 242.9684. IR (ATR, $CDCl_3$, cm^{-1}) 2924, 2861, 1780, 1513, 1426, 1396, 1338, 953.

*3,4-Dihydro-1H-isoquinoline-2-carbonyl Fluoride (**3z**).* The title compound was synthesized using 1,2,3,4-tetrahydroisoquinoline (**1z**) (0.025 mL, 0.20 mmol) and isolated as a colorless oil (0.024 g, 0.13 mmol, 66%) after purification by flash column chromatography: 5% EtOAc in hexanes. The spectral data are consistent with literature values.[19]

*N-Benzyl-N-[1-(p-tolyl)cyclopropyl]carbamoyl Fluoride (**3aa**).* The title compound was synthesized by using **1aa** (0.048 g, 0.20 mmol) and isolated as a colorless oil (0.047 g, 0.17 mmol, 83%) after purification by flash column chromatography: 5% EtOAc in hexanes. ^{1}H NMR (700 MHz, $CDCl_3$): δ 7.30 (t, J = 7.3 Hz, 2H), 7.28−7.25

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(m, 1H), 7.24−7.21 (m, 2H), 7.13 (d, J = 7.9 Hz, 2H), 7.11 (d, J = 7.5 Hz, 0.75H), 7.04 (d, J = 8.1 Hz, 1.25H), 4.63 (s, 1.25H), 4.57 (s, 0.75H), 2.34 (s, 3H), 1.38−1.33 (m, 2H), 1.23−1.19 (m, 2H). ^{13}C {^{1}H} NMR (176 MHz, $CDCl_3$): δ 149.5 (d, J = 293.7 Hz), 147.8 (d, J = 292.7 Hz), 137.8, 137.28, 137.27, 137.11, 137.07, 136.9, 129.4, 129.3, 128.72, 128.68, 127.62, 127.56, 127.3, 126.8, 126.6, 125.3, 53.3, 52.7, 44.1, 43.3, 21.0, 20.9, 17.8, 16.7. ^{19}F NMR (659 MHz, $CDCl_3$): δ −13.21 (s, 0.6H), −13.92 (s, 1F). HRMS (DART) m/z: [M + NH_4]$^+$ calcd for $C_{18}H_{22}N_2OF$, 301.1711; found, 301.1712. IR (ATR, neat, cm^{-1}) 2988, 1778, 1392, 697.

*Methyl (2S)-2-[Benzyl(fluorocarbonyl)amino]-3-phenyl-propanoate (**3ab**).* The title compound was synthesized by using **1ab** (0.054 g, 0.20 mmol) and isolated as a colorless oil [0.053 g, 0.17 mmol, 84%, $[\alpha]_D^{19}$ +82 (c 0.34, acetone)] after purification by flash column chromatography: 3−5% EtOAc in hexanes. ^{1}H NMR (700 MHz, $CDCl_3$): δ 7.34−7.25 (m, 6H), 7.16−7.14 (m, 1H), 7.13 (d, J = 7.0 Hz, 1H), 7.10 (d, J = 7.0 Hz), 7.08−7.06 (m, 1H), 4.52 (d, J = 15.1 Hz, 0.4H), 4.41 (d, J = 15.6 Hz, 0.6H), 4.23 (dd, J = 10.1, 5.5 Hz, 0.6H), 4.11 (dd, J = 9.9, 5.6 Hz, 0.4H), 3.91 (d, J = 15.7 Hz, 0.6H), 3.88 (d, J = 15.1 Hz, 0.4H), 3.67 (s, 1.8H), 3.65 (s, 1.2H), 3.39 (dt, J = 14.7, 5.5 Hz, 1H), 3.30 (d, J = 10.1 Hz, 0.4H), 3.28 (d, J = 10.2 Hz, 0.2H), 3.10−3.05 (m, 0.4H). ^{13}C {^{1}H} NMR (176 MHz $CDCl_3$): δ 169.7, 169.6, 148.0 (d, J = 291.2 Hz), 147.1 (d, J = 292.3 Hz), 136.9, 136.6, 134.8, 129.17, 129.15, 129.0, 128.9, 128.73, 128.70, 128.3, 128.2, 127.3, 127.1, 62.1 (d, J = 5.8 Hz), 61.6 (d, J = 6.4 Hz), 53.4 (d, J = 6.4 Hz, 2C), 52.8 (d, J = 4.1 Hz), 52.7 (d, J = 4.9 Hz), 36.6 (2C), 34.8 (2C) (2C for −OCH3 overlapping with peaks for both rotamers in region from 52.8 to 52.7 ppm). ^{19}F NMR (659 MHz, $CDCl_3$): δ −15.23 (s, 0.9F), −18.06 (s, 1F). HRMS (ESI) m/z: [M + Na]$^+$ calcd for $C_{18}H_{18}FNNaO_3$, 338.1163; found, 338.1166. IR (ATR, neat, cm^{-1}) 2971, 1782, 1741, 1219, 748, 697.

*N-Allyl-N-benzyl-carbamoyl Fluoride (**3ac**).* The title compound was synthesized by using **1ac** (0.029 g, 0.20 mmol) and isolated as a colorless oil (0.036 g, 0.19 mmol, 92%) after purification by flash column chromatography: 1% EtOAc in hexanes. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40−7.27 (m, 4H), 7.24 (m, 1H), 5.84−5.68 (m, 1H), 5.28−5.16 (m, 2H), 4.48 (s, 1H), 4.42 (s, 1H), 3.86 (d, J = 6.0 Hz, 1H), 3.77 (d, J = 5.7 Hz, 1H). ^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$): δ 148.3 (d, J = 288.3 Hz), 147.6 (d, J = 288.4 Hz), 135.70, 135.65, 131.7, 131.4, 129.04, 128.96, 128.4, 128.3, 128.2, 127.8, 119.3, 118.5, 51.0, 50.1 (d, J = 3.2 Hz), 49.9, 49.0 (d, J = 3.2 Hz). ^{19}F NMR (659 MHz, $CDCl_3$): δ −22.12 (s, 0.9F), −22.66 (s, 1F). HRMS (DART) m/z: [M + H]$^+$ calcd for $C_{11}H_{13}NOF$, 194.0976; found, 194.0976. IR (ATR, neat, cm^{-1}) 3067, 1777, 1415, 1225, 698.

*N-Benzyl-N-but-3-enyl-carbamoyl Fluoride (**3ad**).* The title compound was synthesized by using **1ad** (0.032 g, 0.20 mmol) and isolated as a colorless oil (0.033 g, 0.16 mmol, 80%) after purification by flash column chromatography: 3% EtOAc in hexanes. ^{1}H NMR (700 MHz, $CDCl_3$): δ 7.39−7.35 (m, 2H), 7.34−7.31 (m, 1H), 7.30 (d, J = 7.2 Hz, 1H), 7.24 (d, J = 7.4 Hz, 1H), 5.77−5.68 (m, 1H), 5.10−5.05 (m, 2H), 4.49 (s, 1H), 4.44 (s, 1H), 3.32 (t, J = 7.3 Hz, 1H), 3.24 (t, J = 7.3 Hz, 1H), 2.34 (dt, J = 7.2, 7.2, 1H), 2.27 (dt, J = 7.2, 7.2, 1H). ^{13}C {1H} NMR (176 MHz, $CDCl_3$): δ 148.5 (d, J = 287.5 Hz), 147.6 (d, J = 288.3 Hz), 135.88, 135.86, 134.3, 134.0, 129.1, 129.0, 128.25, 128.22, 127.6 (2C), 118.0, 117.7, 51.8, 51.3, 47.4, 46.4, 32.7, 31.6. ^{19}F NMR (659 MHz, $CDCl_3$): δ −21.56(s, 0.9F), −22.04 (s, 1F). HRMS (ESI) m/z: calcd for $C_{12}H_{15}NOF$ [M + H]$^+$, 208.1132; found, 208.1134. IR (ATR, neat, cm^{-1}) 3067, 2981, 1778, 1419, 698.

*N-Benzyl-N-prop-2-ynyl-carbamoyl Fluoride (**3ae**).* The title compound was synthesized by using 1ae (0.029 g, 0.20 mmol) and isolated as a pale-yellow oil (0.036 g, 0.19 mmol, 95%) after purification by flash column chromatography: 3% EtOAc in hexanes. 1H NMR (700 MHz, $CDCl_3$): δ 7.39−7.28 (m, 4H), 7.27−7.21 (m, 1H), 4.59 (s, 1H), 4.56 (s, 1H), 4.02 (s, 1H), 3.91 (s, 1H), 2.32 (s, 1H). ^{13}C {1H} NMR (176 MHz, $CDCl_3$): δ 147.25 (d, J = 290.0 Hz), 147.18 (d, J = 288.6 Hz), 134.84, 134.82, 129.13, 129.06, 128.6, 128.5, 128.1 (2C), 76.93, 76.88, 74.0 (d, J = 2.5 Hz), 73.7 (d, J = 2.5 Hz), 50.7 (2C), 50.0 (d, J = 2.6 Hz, 2C), 36.7, 35.9. ^{19}F NMR (659 MHz, $CDCl_3$): δ −21.62 (s, 1F), −22.38 (s 1F). HRMS (ESI) m/z: [M + H]$^+$ calcd for $C_{11}H_{11}NOF$, 192.0819; found, 192.0818. IR (ATR, neat, cm^{-1}) 3290, 3034, 1779, 1416, 1223, 697.

*N-But-3-ynyl-N-phenyl-carbamoyl Fluoride (**3af**).* The title compound was synthesized by using **1af** (0.029 g, 0.20 mmol) and isolated as a colorless oil (0.035 g, 0.18 mmol, 92%), flash column chromatography: 3% EtOAc in hexanes. ^{1}H NMR (700 MHz, $CDCl_3$): δ 7.45−7.40 (m, 2H), 7.38−7.33 (m, 1.5 H), 7.28−7.25 (m, 1.5 H), 3.85 (t, J = 7.08 Hz, 2H, overlapping with signal at 3.84 ppm), 3.84 (t, J = 7.19 Hz, overlapping with signal at 3.85 ppm), 2.49 (td, J = 7.05, 2.54 Hz, 1.5 H), 2.45 (td, J = 6.93, 2.20 Hz, 0.5 H), 2.06 (t, J = 2.79 Hz, 0.25 H), 2.02 (t, J = 2.52 Hz, 0.75 H) ^{13}C {^{1}H} NMR (176 MHz, $CDCl_3$): δ 146.6 (d, J = 291.4 Hz), 146.3 (d, J = 288.5), 139.4, 138.7, 129.6, 129.5, 128.3, 128.1, 126.9, 126.5, 80.0, 79.6, 71.1, 70.6 (d, J = 3.5 Hz), 50.0 (t*, J = 6.1 Hz, 2C), 49.4 (bt*, 2C), 18.4, 17.4. Note: *t = apparent triplet, likely two overlapping doublets for the two rotamers. ^{19}F NMR (659 MHz, $CDCl_3$): δ −13.59 (s, 1F), −18.62 (s, 0.25F). HRMS (ESI) m/z: calcd for $C_{11}H_{11}NOF$[M + H]$^+$, 192.0819; found, 192.0817. IR (ATR, neat, cm^{-1}) 3295, 3063, 1779, 1496, 1396, 1270, 694.

*N-Phenyl-N-(4-phenylbut-3-ynyl)carbamoyl Fluoride (**3ag**).* The title compound was synthesized by using **1ag** (0.044 g, 0.20 mmol) and isolated as a colorless oil (0.049 g, 0.18 mmol, 93%) after purification by flash column chromatography: 2% EtOAc in hexanes. ^{1}H NMR (700 MHz, $CDCl_3$): δ 7.46−7.33 (m, 5H), 7.32−7.24 (m, 5H), 3.96−3.91 (m, 2H), 2.74 (t, J = 6.7 Hz, 1.5H), 2.69 (t, J = 6.4 Hz, 0.5H). ^{13}C {^{1}H} NMR (176 MHz, $CDCl_3$): δ 146.9 (d, J = 291.4 Hz), 146.5 (d, J = 288.5 Hz), 139.8, 139.2, 131.7 (2C), 129.71, 129.65, 128.4 (2C), 128.23, 128.17, 128.1, 127.1, 126.7, 123.3, 123.1, 85.8, 85.2, 83.3, 82.8, 50.5 (2C), 49.9 (2C), 19.7, 18.6 (1C for minor rotamer overlapping with peaks in the region from 129.7 to 128.1 ppm). ^{19}F NMR (659 MHz, $CDCl_3$): δ −13.56 (s, 1F), −18.51 (s, 0.25F). HRMS (ESI) m/z: [M + H]$^+$ calcd for $C_{17}H_{15}NOF$, 268.1132; found, 268.1130. IR (ATR, neat, cm^{-1}) 3063, 1780, 1491, 1395, 1271, 753, 690.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.2c01017.

Reaction optimization tables; experimental procedures for the synthesis of DFC precursors; copies of ^{1}H, ^{13}C, and ^{19}F NMR spectra for all new compounds; and single crystal X-ray crystallography data for **3w** (CCDC 2169660) (PDF)

Accession Codes

CCDC 2169660 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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Author Contributions

C.M.L. and D.C. conceptualized the project and wrote the manuscript. D.C., T.R.T., and G.A.C. carried out the experimental work. C.M.L. directed the research.

Notes

The authors declare no competing financial interest.

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