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Chemoselective Trifluoroethylation Reactions of Quinazolinones and Identification of Photostability

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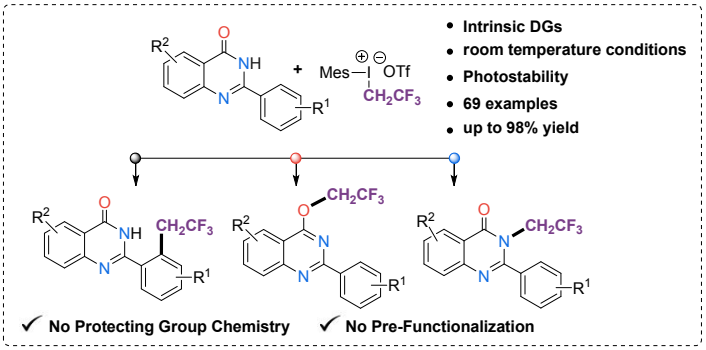
TOC Figure

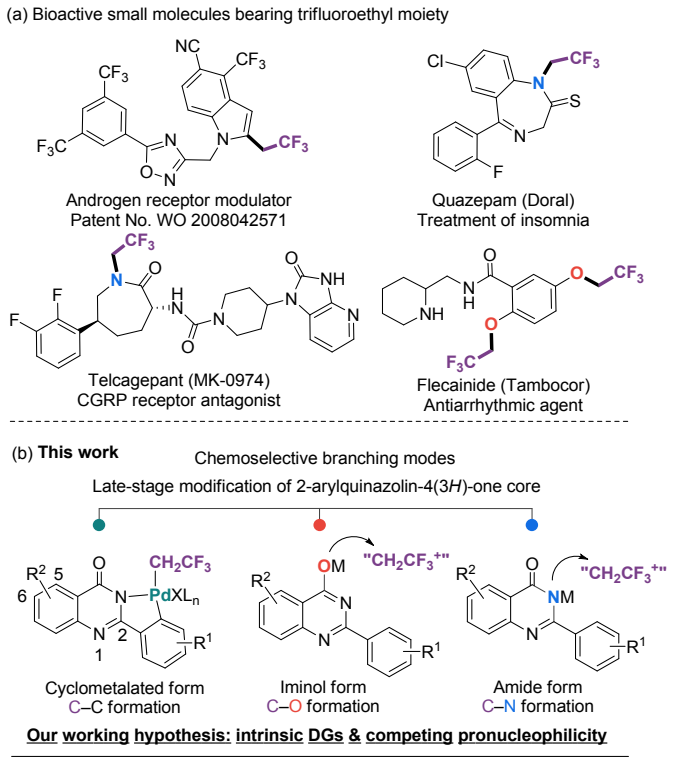


ABSTRACT: Herein, we report chemoselective trifluoroethylation routes of unmasked 2-arylquinazolin-4(3*H*)-ones using mesityl(2,2,2-trifluoroethyl)iodonium triflate at room temperature. Homologous *C*-, *O*-, and *N*-functionalized subclasses are accessed in a straightforward manner with a wide substrate scope. These chemoselective branching events are driven by Pd-catalyzed *ortho*-selective C–H activation at the pendant aryl ring and base-promoted reactivity modulation of the amide group, leveraging the intrinsic directing capability and competing pronucleophilicity of the quinazolin-4(3*H*)-one framework. Furthermore, outstanding photostability of the quinazolin-4(3*H*)-one family associated with nonradiative decay is presented.

INTRODUCTION

Chemoselective modifications of heterocycles constitute a central theme in synthetic methodology.[1] The incorporation of organofluorine entities profoundly affects the bioavailability, binding efficacy, and metabolic profiles of lead compounds.[2] In particular, the CH_2CF_3 moiety acts as an electron-withdrawing bioisostere of ethoxy or ethyl groups, and the illustrated examples of 2,2,2-trifluoroethylated small molecules having biological importance are shown in Scheme 1a.[2,3] Orthogonal reaction manifolds, protecting group-free operations, and late-stage functionalizations offer concise, complementary, and step economic routes to create molecular diversity and expand chemical space.[4] Given the difficulties in achieving chemoselective profiles and broad functional-group tolerance, the development of switchable trifluoroethylation methods to modify unactivated heterocycles remains a significant challenge.

Scheme 1. Triply Chemoselective Trifluoroethylation



The prevalence of quinazolinone alkaloids in natural products and pharmaceuticals makes their synthetic modifications appealing.[5] The unmasked and unactivated quinazolin-4(3*H*)-one framework possesses integral structural features with inherent directing group (DG) capability and amide-iminol tautomerism, posing both challenges and opportunities for late-stage trifluoroethylations (Scheme 1b).

Our strategy to modify quinazolin-4(3*H*)-one alkaloids has two notable features: (i) chemoselective activation of competing pronucleophilic sites to accomplish *C*-, *O*-, and *N*-trifluoroethylations and (ii) complete exclusion of protecting group chemistry and pre-functionalization.

Although indisputable synthetic advances in individual electrophilic trifluoroethylations have recently emerged,[6–8] *the switchable trifluoroethylations of heterocyclic scaffolds appear to be uncharted*. *The critical task in the efficient construction of molecular complexity is to establish orthogonal reaction manifolds, which obviate the need of multiple de novo operations.*[9] *Although a number of important chemoselective reactions are well-established,*[4c,4d] *the development of chemoselective reaction modes suitable for late-stage modification remains a challenging mission owing to cross-reactivity interference*.[9c] As a part of our continued studies on reactivity-controlled direct modifications using hypervalent iodine reagents,[10] herein we disclose trifluoroethylations of 2-arylquinazolin-4(3*H*)-ones (**1**) through reactivity discrimination (Scheme 1b): Pd-catalyzed direct site-selective C–H activation and base-promoted routes facilitate late-stage trifluoroethylations with a wide scope. In addition, the photostability of the parent and modified quinazolinone family is highlighted via steady-state and time-resolved spectroscopic analyses.

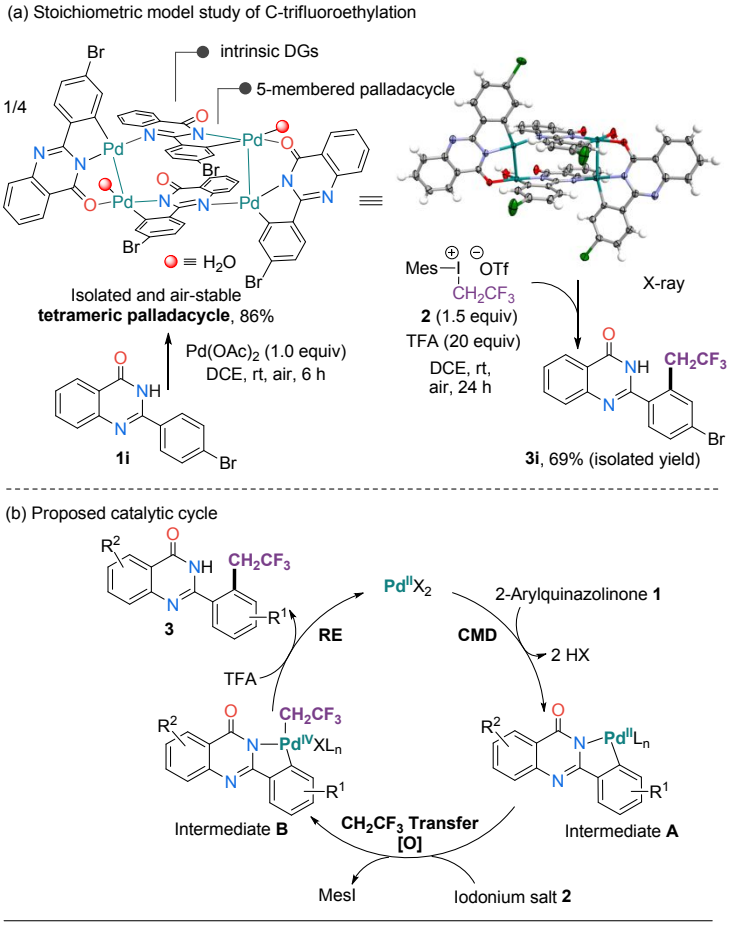
RESULTS AND DISCUSSION

We embarked on our *C*-trifluoroethylation approach through a stoichiometric model study, in which we synthesized and isolated the tetrameric palladacycle (Scheme 2a; see experimental section). Single crystal X-ray analysis of this complex corroborates that Lewis-basic heteroatoms within the quinazolin-4(3*H*)-one framework served as intrinsic DGs for C–H activation.[11] Among the various synthetic equivalents of a CH_2CF_3 synthon, mesityl(2,2,2-trifluoroethyl)iodonium triflate (**2**) introduced by the Novak group was selected due to its accessibility, bench stability, mildness, and versatile nucleofugality.[8,12] The tetrameric palladacycle and **2** in the presence of trifluoroacetic acid (TFA) provided the target product 2-(4-bromo-2-(2,2,2-trifluoroethyl)phenyl)quinazolin-4(3*H*)-one (**3i**) in 67% isolated yield (Scheme 2a).

Intrigued by this result, we tested the feasibility of catalytic *C*-trifluoroethylation using 2-(*p*-tolyl)quinazolin-4(3*H*)-one (**1a**), $Pd(OAc)_2$ and **2**. To our delight, the desired product 2-(4-methyl-2-(2,2,2-trifluoroethyl)phenyl)quinazolin-4(3*H*)-one (**3a**) was isolated in 91% yield under the standard conditions: 20 mol% $Pd(OAc)_2$ and 20 equiv TFA in 1,2-dichloroethane (DCE) at room temperature (rt) (see the Supporting Information, Section II, Table S1). On the basis of this experimental insight, we postulate that the catalytic cycle (Scheme 2b) is initiated by a concerted metalation deprotonation (CMD) pathway to give the putative intermediate **A**. The reaction conditions may favor the formation of a

monomeric palladacycle over a dimeric or tetrameric one. Iodonium salt **2** transfers the trifluoroethyl entity to generate a high-valent Pd(IV)–CH_2CF_3 intermediate **B**.[8] Finally, reductive elimination (RE) furnishes the respective product **3**, while releasing a Pd(II)-species.[12b,12c,12e] Alternatively, the two-electron oxidative CH_2CF_3 transfer and subsequent C–C bond forming RE may involve a dinuclear $Pd(III)_2$ intermediate, as both mononuclear Pd(IV)[13a,13b,13c] and dinuclear $Pd(III)_2$ complexes[13d,13e] have been observed in Pd-catalyzed C–H functionalization with hypervalent iodine reagents.

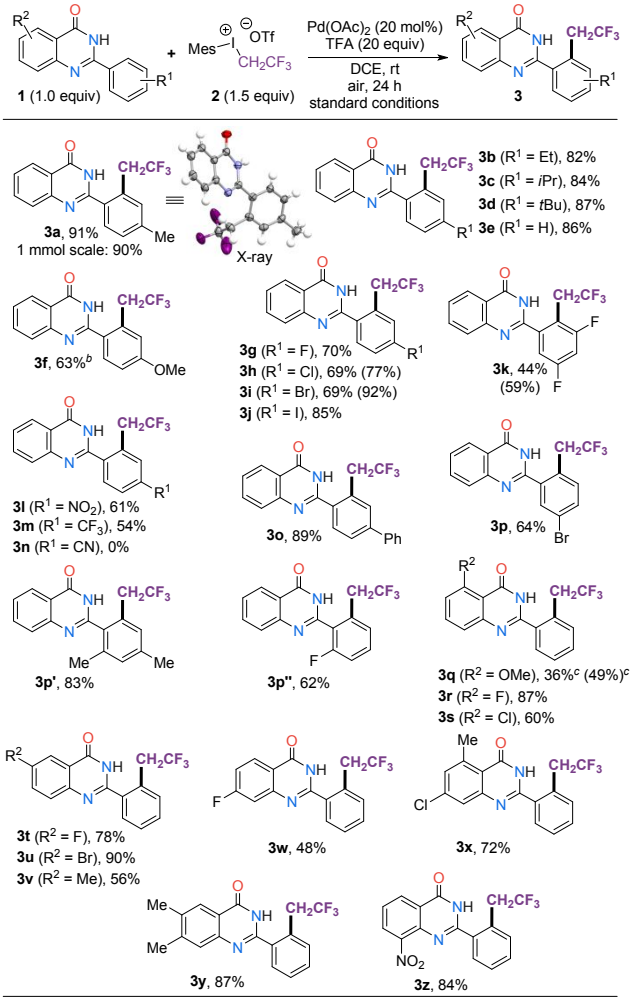
Scheme 2. *C*-Trifluoroethylation Approach



$X^- = AcO^-, CF_3CO_2^-$, or TfO^-.

We accordingly explored the generality of catalytic *C*-trifluoroethylation using structurally diverse substrates **1** (Scheme 3). Electron-rich substrates bearing alkyl substituents (Me, Et, *i*Pr, and *t*Bu) smoothly underwent the reaction to afford **3a**–**3d** in high yields. The structure of **3a** was unambiguously confirmed via single crystal X-ray analysis.[11] Even substrate 2-(4-methoxyphenyl)quinazolin-4(3*H*)-one (**1f**) was well tolerated; a reduced amount of TFA (10 equiv) was used to impede the concurrent ethereal cleavage. The *C*-trifluoroethylation was found to tolerate electron-deficient substituents such as halogens (**1g**–**1k, 1p**), nitro (**1l**), and trifluoromethyl (**1m**) groups in moderate-to-good yields. **3p** was obtained as the sole regioisomer, which may be attributed to steric hindrance between the bulky Br substituent and an adjacent ligand of the Pd complex that would arise if the other *ortho* position were to be metalated. Unfortunately, the nitrile bearing **1n** did not react. Conversely, compound **3o** bearing a biphenyl moiety was isolated in 89% yield. A substituent in one of the *ortho*-positions (*C*2′) of the pendant aryl ring was found to have no deleterious effect as revealed by the formation of **3p′** and **3p′′**. We also assessed the impact of R^2-substituents. Substrates bearing a halogen in different positions (**1r**–**1u, 1w**), a methoxy (**1q**), or a methyl (**1v**) group were tolerated to afford the respective *C*2′-products in moderate-to-good yields. The reaction of disubstituted substrates (**1x**, **1y**) gave their respective products in fair yields (72% and 87%, respectively). The NO_2-substituted **1z** underwent the reaction furnishing the *C*2′-product in 84% yield. The *C*2′-trifluoroethylation method appears to be selective for monofunctionalization, without formation of any bis(trifluoroethylated) product even in the presence of an excess amount of **2** (see the Supporting Information, Table S1).

Scheme 3. Substrate Scope of the *C*-Trifluoroethylation[a]

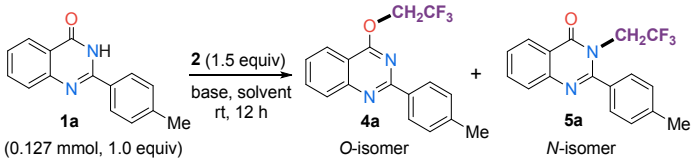


[a]Reaction conditions: **1** (1.0 equiv), **2** (1.5 equiv), $Pd(OAc)_2$ (20 mol%), TFA (20 equiv), DCE, rt, 24 h, isolated yields. [b]TFA (10 equiv). [c]TFA (5.0 equiv). Isolated yields based on the recovered starting materials are given in parentheses.

Next, we pursued switchable *O*- and *N*-trifluoroethylation modes of **1a** by leveraging the subtle differences in competing pronucleophilicity (Table 1). **1a** and **2** were subjected to metal-free and rt conditions. In the absence of base, the reaction preferentially occurred at the *O*-center to deliver **4a** in 49% yield (entry 1). Through base and solvent screening (entries 2–7; see also the Supporting Information, Section II), the optimized yield (93%) of **4a** was achieved using K_2CO_3 (1 equiv) in MeCN along with the minor *N*-isomer **5a**. Solid-phase reaction led to decrease in chemoselectivity, ~2.5:1 mixture of **4a** and **5a** in 92% yield (entry 8). The *N*-trifluoroethylated **5a** culminated in 89% yield, when 2.0 equiv of Li*O*tBu was used as a moderately strong base (entry 10). Dry toluene under an N_2 atmosphere was essential, because the isomeric ratio significantly changed under routine conditions (entries 9 and 10). The need for

inert conditions is likely due to the moisture-sensitivity of the base. A reduced amount of LiO*t*Bu (1.0 equiv) diminished the yield of **5a** (entry 11). LiMHDS (entry 12) also resulted in the preferential formation of *N*-isomer **5a** over *O*-isomer **4a**. This reactivity preference is presumably attributed to the amide-iminol tautomerism of the quinazolinone scaffold. Whereas mild bases lead to the putative iminol form, relatively stronger bases allow the direct lithiation at the *N*-center. However, pathways involving [2,3]-rearrangement of T-shaped O–I or N–I intermediates[14] or a 4-coordinate I(III)-intermediate[15] cannot be ruled out.

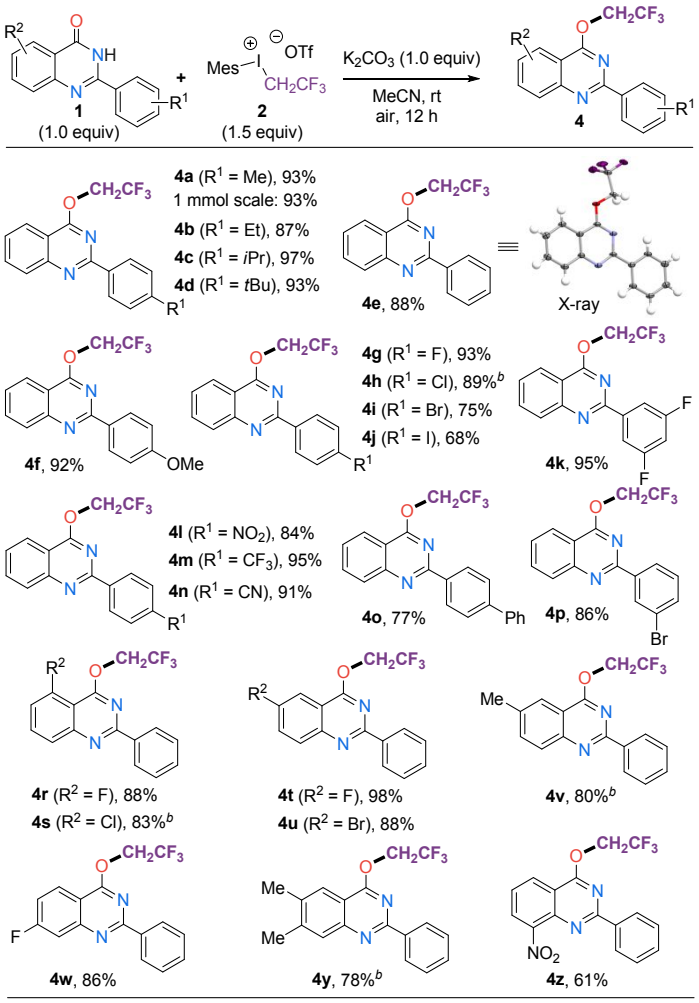
Table 1. Optimization of Reaction Conditions[a]



entry	base (equiv) and solvent conditions	yield (%)[b]	
		4a	**5a**
1	MeCN	49	trace
2	Na_2CO_3 (2.0), MeCN	81	trace
3	K_2CO_3 (2.0), MeCN	89	trace
4	Li_2CO_3 (2.0), MeCN	82	trace
5	K_2CO_3 (2.0), DCE	70	trace
6	K_2CO_3 (2.0), DCM	75	trace
7	**K_2CO_3 (1.0), MeCN**	**93**	**6**
8	K_2CO_3 (2.0), solvent-free[c]	66	26
9	LiO*t*Bu (2.0), toluene, air	41	49
10	**LiO*t*Bu (2.0), dry toluene, N_2**	**10**	**89**
11	LiO*t*Bu (1.0), dry toluene, N_2	22	69
12	LiMHDS (2.0), dry toluene, N_2	10	88

[a]Reaction conditions: **1a** (1.0 equiv), **2** (1.5 equiv), base, rt, 12 h. [b]Isolated yield. [c]Grinding with a mortar and pestle. DCM = dichloromethane, LiMHDS = lithium hexamethyldisilamide.

Scheme 4. Substrate Scope of the *O*-Trifluoroethylation[a]



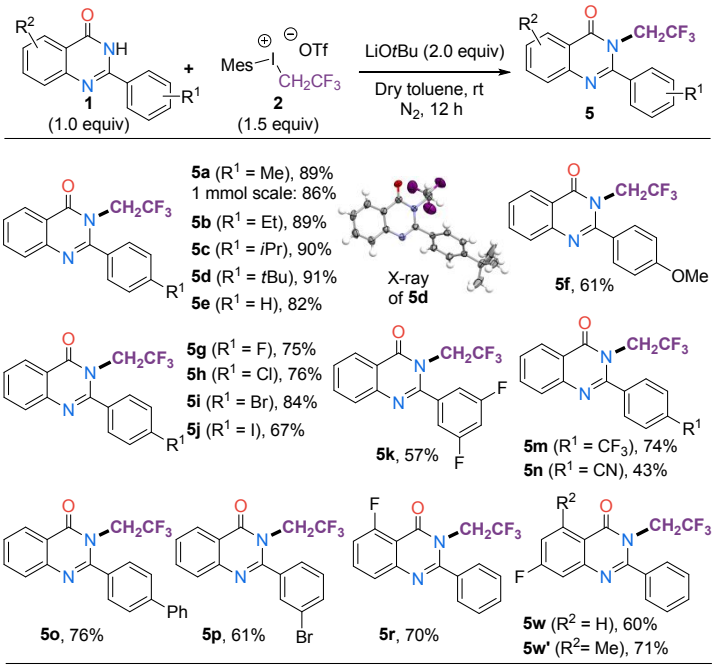
[a]Reaction conditions: 1 (1.0 equiv), **2** (1.5 equiv), K_2CO_3 (1.0 equiv), MeCN, rt, 12 h, isolated yields. [b]**1** (1.0 equiv), **2** (2.0 equiv), K_2CO_3 (1.5 equiv), MeCN, rt, 12 h, isolated yields.

Following the success in establishing the *O*- and *N*-functionalization sets, we evaluated the versatility of *O*-trifluoroethylation on various substrates **1** (Scheme 4). A marginal effect of the electronic properties of R^1-substituents within the 2-phenyl ring was observed, yielding the *O*-products in moderate-to-high yields. Electron-deficient NO_2 (**1l**), CF_3 (**1m**), and CN (**1n**) substituents were well-tolerated and exhibited good yields. R^2-bearing substrates (**1r**–**1w, 1y**) were shown to provide the *O*-products in good-to-high yields. The NO_2-substituted substrate **1z** afforded its corresponding *O*-product in 61% yield. Subsequently, we evaluated the substrate scope of the alternative *N*-trifluoroethylation (Scheme 5). The reactions were performed under inert conditions. A wide range of substituents were compatible with standard conditions.

Electron-rich substrates afforded the corresponding *N*-isomers (**5a**–**5f**, **5o**) more efficiently and in higher yields than those of the electron-deficient species (**5g**–**5k**, **5m**, **5n**, **5p**, **5r**, **5w**, **5w'**), due to the strong nucleophilic character.

In place of the iodonium salt **2**, we further evaluated the feasibility of 1,1,1-trifluoro-2-iodoethane (CF_3CH_2I) in base-promoted *O*- and *N*-trifluoroethylations. Quinazolinone **1g** (0.125 mmol) was treated with CF_3CH_2I (1.5 equiv) and K_2CO_3 (1.0 equiv) in MeCN (1.5 mL) under ambient conditions. However, even after 20 h, no *O*-trifluoroethylated product (**4g**) was detected giving the remaining starting material. Similarly, when we treated **1g** (0.083 mmol) with CF_3CH_2I (1.5 equiv) in presence of LiO*t*Bu (2.0 equiv) in dry toluene (1.5 mL), no *N*-trifluoroethylation occured. These results indicate that the switchable reaction modes are not solely controlled by basicity, but also governed by the suitable electrophilic character of the trifluoroethylating reagent. The stronger electrophilicity of hypervalent iodine(III) reagent **2** over CF_3CH_2I allowed more effective and readily tunable reaction modes.

Scheme 5. Substrate Scope of the *N*-Trifluoroethylation[a]



[a]Reaction conditions: **1** (1.0 equiv), **2** (1.5 equiv), LiO*t*Bu (2.0 equiv) , dry toluene, rt, 12 h, isolated yields.

Regarding the identity of the products, single crystal X-ray analyses of **4e** and **5d** unambiguously confirmed their molecular structures.[11] In addition, the CH_2CF_3 signals of the *O*- and *N*-isomers in their respective ^{19}F NMR spectra (377 MHz, $CDCl_3$) revealed distinct chemical shift signatures at about -73 and -68 ppm, respectively. As revealed by the ^{1}H and ^{13}C NMR spectra, the CH_2CF_3 signals of the *O*-isomers appeared downfield-shifted compared to those of the *N*-isomers due to the stronger inductive character.

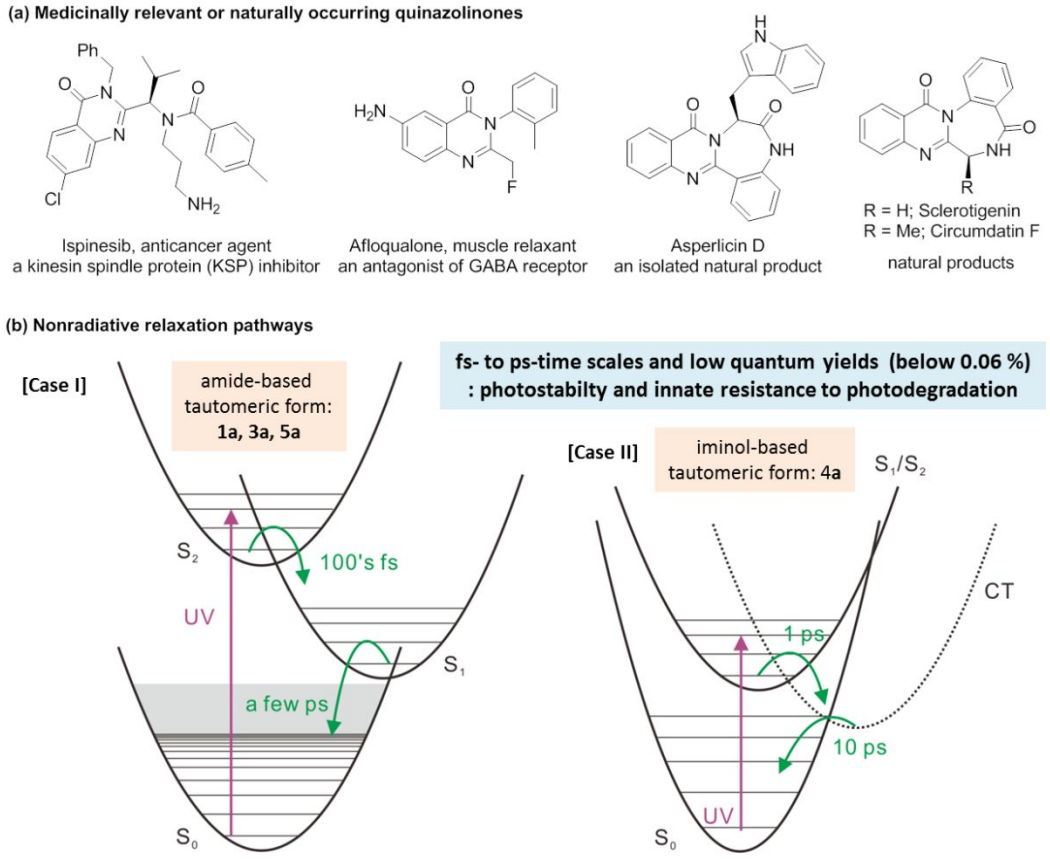


Figure 1. Photophysical studies of quinazolinones. a) Biologically important quinazolinones and b) their photophysics with schematic energy diagrams.

Considering the biological importance of quinazolinone alkaloids (Figure 1a),[5] the chemoselective incorporation of trifluoroethyl moiety can profoundly affect their pharmaceutical aspects by modifying the lipophilicity, chemical and metabolic stabilities.[2,3] Over the last few decades, the importance of photochemical inertness of bio-active molecules, pharmaceutical drugs, and biomaterials has been recognized, which is closely linked to their efficacy and/or safety.[16] For example, the DNA bases reveal an exceptionally high photostability under photoexcitation conditions. This largely allows organisms in

Nature to avoid photo-triggered mutagenesis.[17] In addition, securing the photostability of pharmaceutical drugs is important to avoid adverse effects (e.g., production of phototoxic metabolites) or reduced shelf-life associated with photodegradation (Figure 1b).[16,17] Yet, in the context of the photophysical/photochemical properties of parent and modified quinazolinone alkaloids, their ultrashort excited-state lifetimes and high photostability have not been disclosed.

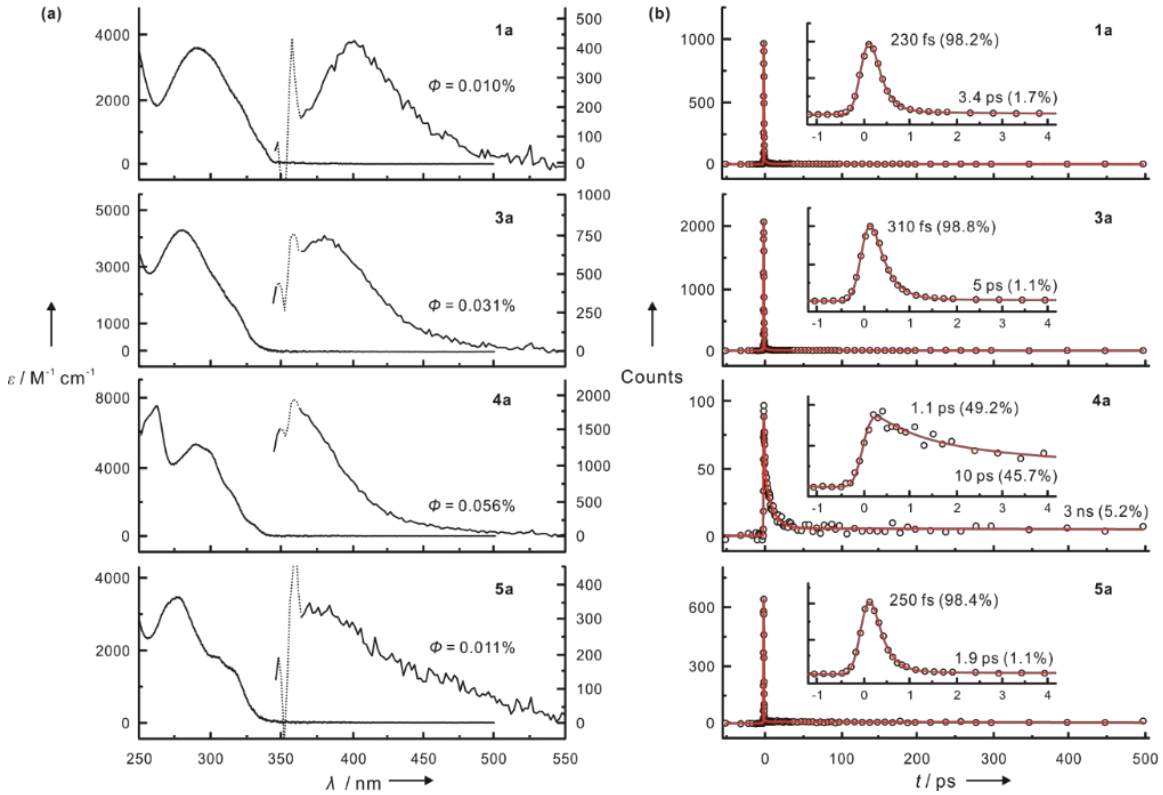


Figure 2. Representative photophysics in MeCN. a) Steady-state electronic absorption and emission spectra. b) fs-Resolved fluorescence measured at 380 nm. The compounds are given in each panel. Excitation wavelength was set at 320 nm to induce the lowest electronic transition. Fluorescence quantum yields and lifetime constants are also given in each corresponding panel. Dotted lines in the panel (a) correspond to the wavelength region of Raman scatter from MeCN after subtracting the signals from the solvent.

In this regard, we investigated the photophysics of compounds **1a**, **3a**, **4a**, and **5a** by measuring static electronic spectra as well as femtosecond (fs)-resolved fluorescence kinetic profiles in a series of solvents (the spectra in Figure 2 were recorded in MeCN; see also the Supporting Information, Section III, Figures S1–S3 recorded in $CHCl_3$, n-hexane, and MeOH, respectively). The compounds were found to barely

emit with the quantum yields of 0.6–3.1 × 10^{-4}. This originated from the ultrashort lifetimes of the excited states on the timescales of mainly several hundreds fs. The ultrashort-lived nature of the excited states of the parent quinazolinone and trifluoroethylated structural subclasses indicates an exceptionally high photostability. It is noteworthy that this characteristic feature is comparable to the nucleobases, whose excited states with ring puckering can be mixed/crossed and connected to the ground state by the occurrence of conical intersections; this mediates facile internal conversion on comparable timescales.[17] For **1a** and **3a**, the prototropic tautomers can coexist. This may cause the observation of multiple lifetime components. However, this is not the case here based on the fact that the lifetimes and their fractions for both **1a** and **3a** match well those of **5a**, which constitutes only the amide tautomer (Table S4). It follows that the main tautomer of **1a** and **3a** at rt is the amide form, showing ultrafast relaxation via the conical intersections among multiple electronic states as in the case of **5a** (Figure 1b, case I).

Interestingly, the excited-state lifetime of iminol-based/*O*-trifluoroethylated **4a** is significantly elongated to several tens of picosecond (ps) timescale with a slight increase in the quantum yield (Figure S1, chloroform). The longer lifetime by *O*-substitution has been previously reported by Ashwood *et al.* through the time-resolved study of *O*-methylguanine.[17e] The raised energy barrier of iminol-based *O*-substitution is attributed to the retarded vibrational relaxation. Accordingly, in the less viscous n-hexane, the decay was observed to accelerate with the time constant of 14 ps. In MeOH and MeCN, the contribution of this slow component to the relaxation of photoexcited **4a** becomes significantly smaller compared to new faster components having the time constants of 1 and 10 ps (Figure 2 and Figure S3; see also Table S4). The emergence of the new components can be understood if we consider the role of the charge-transferred (CT) state as a mediating state for efficient relaxation to the ground state in this system. In the polar solvents, this CT state can be stabilized such that the conical intersection to the CT state becomes accessible, *e.g.*, in 1 ps, and finally relaxes to the ground state in 10 ps (Figure 1b, case II).

CONCLUSION

In summary, we have developed chemoselective trifluoroethylation methods to afford *C*-, *O*-, and *N*-functionalized quinazolinone subclasses at room temperature. The inherent directing capability and competing pronucleophilicity of the unmasked and unactivated quinazolin-4(3*H*)-one framework were leveraged with a Pd catalyst or bases in the presence of mesityl(2,2,2-trifluoroethyl)iodonium triflate. Based on a stoichiometric model study with an isolated tetrameric palladacycle, the Pd-catalyzed site-

selective direct C–H trifluoroethylation was established. The switchable *N*- and *O*-reactivity modes were accomplished through the base-promoted reactions, and the synthetically suitable electrophilic character of the iodonium salt over CF_3CH_2I was disclosed. In addition, the inherent high photostability of parent and modified quinazolinones was inferred from the ultrashort fluorescence lifetimes and low quantum yields. We envision that the chromophoric scaffold of the quinazolinone family will be beneficial for the design of pharmaceutics for which photodegradation needs to be minimized.

EXPERIMENTAL SECTION

Instrumentation and Chemicals. All reagents were purchased from standard suppliers (Sigma-Aldrich, Alfa Aesar, or TCI) and were used without further purification. Flash column chromatography was performed using Merck silica gel 60 (mesh 230-400). Analytic thin layer chromatography (TLC) was performed on Merck Silica Gel F254 plates (0.25 mm). ^{1}H, broadband proton-decoupled ^{13}C, and ^{19}F NMR spectra were recorded on a Bruker Avance III HD 400 MHz instrument. The chemical shift values are reported in parts per million (ppm) with respect to residual solvent signals. ^{19}F NMR chemical shift values are calibrated to α,α,α-trifluorotoluene (δ = -62.61 ppm, $CDCl_3$).[18] Data are given as follows: chemical shift in ppm (δ), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, brs = broad singlet, m = multiplet), coupling constant (*J*, Hz), and integration. High-resolution mass spectra (HRMS) were performed on a Thermo Scientific Q Exactive Plus Hybrid Quadrupole-Orbitrap mass spectrometer or on a JEOL AccuTOF LC-Plus 4G+ DART coupled to a DART-SVP ion source (Ionsense Inc.). FTIR spectra in attenuated total reflectance (ATR) mode were recorded on a Shimadzu IRTracer-100 and reported in wave number (cm^{-1}). Melting points of the compounds were measured by using a digital melting point apparatus (KRUSS, Germany). Experimental details of for steady-state and time-resolved spectroscopic methods can be found in the Supporting Information (Section III). Crystal structures of **tetrameric palladacycle**, **3a**, **5d**, and **4e** were solved by the direct method and refined by full-matrix least-squares calculations using the SHELXTL program package (Supporting Information, Section IV). Thermal ellipsoid plots were drawn at the 50% probability level.

Materials. *Preparation of mesityl(2,2,2-trifluoroethyl)iodonium trifluoromethanesulfonate* ***2***: Iodonium salt **2** was prepared according to the previously reported literature procedure.

(Step 1)[19] To a reaction mixture of trifluoroacetic anhydride (TFAA, 18 mL, 130 mmol) and trifluoroacetic acid (TFA, 155 μL, 2.0 mmol, 10 mol%) was added H_2O_2 (2.0 mL, 50 wt. % aq. solution, 35 mmol) in a dropwise manner at 0 °C. After stirring for 5 min, CF_3CH_2I (2.0 mL, 20 mmol) was added.

Thereafter, the reaction mixture was warmed to rt. After 20 h, it was concentrated in vacuo and the residue was recrystallized to furnish the intermediate, (2,2,2-trifluoroethyl)-λ^3-iodanediyl bis(2,2,2-trifluoroacetate) (3.5 g, 8.0 mmol, 40% yield). It was directly used for the next step.

(Step 2)[8a] To the intermediate in DCM (15 mL) were added mesitylene (1.7 mL, 12 mmol) and triflic acid (TfOH, 0.71 mL, 8.0 mmol, in a dropwise manner) at 0 °C. After 24 h at 0 °C, the reaction mixture was concentrated in vacuo. A white precipitate was formed by the addition of Et_2O (30 mL). The target product **2** was obtained through filtration, rinsing (Et_2O), and then recrystallization (Et_2O/conc. MeOH). White solid (2.9 g, 6.1 mmol, 76% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 6.89 (s, 2H), 4.71 (q, *J* = 8 Hz, 2H), 2.43 (s, 6H), 2.24 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 141.9, 137.4, 128.0, 118.5 (q, *J* = 318 Hz), 104.3, 68.7 (q, *J* = 39 Hz), 29.6, 20.7.

*Preparation of 2-arylquinazolin-4(3H)-ones (**1**)[5]:*

R^1-substituted 2-arylquinazoline-4(3*H*)-ones (**1**) were prepared based on the previously reported literature procedure using anthranilamide and corresponding benzaldehyde derivatives.[5c] Anthranilamide (1.0 equiv) and benzaldehyde derivative (1.2 equiv) were dissolved in DMSO. Then, the reaction mixture was stirred at 100 °C. After completion of the reaction, the mixture was cooled to rt. The precipitate was formed by addition of water, and collected by filtration. Recrystallization in ethanol afforded the target compound **1**. *** 1a**,[5c] **1b**,[5g] **1c**,[5g] **1d**,[5g] **1e**,[5c] **1f**,[5c] **1g**,[5h] **1h**,[5c] **1i**,[5g] **1j**,[5i] **1k**,[5j] **1l**,[5k] **1m**,[5l] **1n**,[5g] **1o**,[5m] **1p**,[5m] **1p'**,[5q] and **1p''**[5g] were previously reported in the literature.

R^2-substituted 2-arylquinazoline-4(3*H*)-ones (**1**) were prepared based on the previously reported literature procedure using 2-halobenzoic acids and benzamidine hydrochloride.[5e] Into a two-neck round-bottom flask were added substituted 2-halobenzoic acid (1.0 equiv) and benzamidine hydrochloride (1.5 equiv) in DMF. The reaction flask was evacuated, back-filled with nitrogen several times, and then vigorously stirred for 10 min. Cs_2CO_3 (2.0 equiv) was added to the reaction mixture. After 15 min, CuI (20 mol%) was subsequently added and stirred at rt for 12 h under a nitrogen atmosphere. After completion of the reaction, the reaction mixture was filtered. The solvent residue was concentrated in vacuo, and the residue was purified by flash column chromatography to yield the target compound **1**. *** 1q**,[5n] **1r**,[5o] **1s**,[5p] **1t**,[5p] **1u**,[5p] **1v**,[5p] **1w**,[5o] **1x**,[10b] **1y**,[10b] **1z**,[10b] and **1w'**[10b] were previously reported in the literature.

Data of Starting Materials (all the compounds **1** were previously reported. Thus ^{1}H NMR data are provided)

*2-(p-Tolyl)quinazolin-4(3H)-one (**1a**)*.[5c] White solid (2.39 g, 74%); ^{1}H NMR (400 MHz, DMSO-d_6) δ = 12.46 (s, 1H), 8.15 (d, J = 8 Hz, 1H), 8.10 (d, J = 8 Hz, 1H), 7.83 (t, J = 8 Hz, 1H), 7.73 (d, J = 8 Hz, 1H), 7.51 (t, J = 8 Hz, 1H), 7.36 (d, J = 8 Hz, 2H), 2.39 (s, 3H).

*2-(4-Ethylphenyl)quinazolin-4(3H)-one (**1b**)*.[5g] White solid (421 mg, 56%); ^{1}H NMR (400 MHz, DMSO-d_6) δ = 12.47 (s, 1H), 8.16 – 8.11 (m, 3H), 7.83 (t, J = 8 Hz, 1H), 7.73 (d, J = 8 Hz, 1H), 7.51 (t, J = 8 Hz, 1H), 7.39 (d, J = 8 Hz, 2H), 2.69 (q, J = 8 Hz, 2H), 1.22 (t, J = 8 Hz, 3H).

*2-(4-Isopropylphenyl)quinazolin-4(3H)-one (**1c**)*.[5g] White solid (343 mg, 61%); ^{1}H NMR (400 MHz, DMSO-d_6) δ = 12.47 (s, 1H), 8.16 – 8.11 (m, 3 H), 7.83 (t, J = 8 Hz, 1H), 7.73 (d, J = 8 Hz, 1H), 7.51 (t, J = 8 Hz, 1H), 7.42 (d, J = 8 Hz, 2H), 3.00 (sept, J = 8 Hz, 1H), 1.24 (d, J = 8 Hz, 6H).

*2-(4-(tert-Butyl)phenyl)quinazolin-4(3H)-one (**1d**)*.[5g] White solid (411 mg, 70%); ^{1}H NMR (400 MHz, DMSO-d_6) δ = 12.48 (s, 1H), 8.16 – 8.12 (m, 3H), 7.83 (t, J = 8 Hz, 1H), 7.73 (d, J = 8 Hz, 1H), 7.56 (d, J = 8 Hz, 2H), 7.51 (t, J = 8 Hz, 1H), 1.32 (s, 9H).

*2-Phenylquinazolin-4(3H)-one (**1e**)*.[5c] White solid (576 mg, 48%); ^{1}H NMR (400 MHz, DMSO-d_6) δ = 12.55 (s, 1H), 8.20 – 8.15 (m, 3H), 7.87 – 7.83 (m, 1H), 7.75 (d, J = 8 Hz, 1H), 7.60 – 7.51 (m, 4H).

*2-(4-Methoxyphenyl)quinazolin-4(3H)-one (**1f**)*.[5c] White solid (289 mg, 52%); ^{1}H NMR (400 MHz, DMSO-d_6) δ = 12.41 (s, 1H), 8.19 (d, J = 8 Hz, 2H), 8.13 (d, J = 8 Hz, 1H), 7.81 (t, J = 8 Hz, 1H), 7.70 (d, J = 8 Hz, 1H), 7.48 (t, J = 8 Hz, 1H), 7.09 (d, J = 8 Hz, 2H), 3.85 (s, 3H).

*2-(4-Fluorophenyl)quinazolin-4(3H)-one (**1g**)*.[5h] White solid (388 mg, 44%); ^{1}H NMR (400 MHz, DMSO-d_6) δ = 12.57 (s, 1H), 8.27 – 8.23 (m, 2H), 8.15 (d, J = 8 Hz, 1H), 7.84 (t, J = 8 Hz, 1H), 7.74 (d, J = 8 Hz, 1H), 7.52 (t, J = 8 Hz, 1H), 7.40 (t, J = 8 Hz, 2H).

*2-(4-Chlorophenyl)quinazolin-4(3H)-one (**1h**)*.[5c] White solid (430 mg, 38%); ^{1}H NMR (400 MHz, DMSO-d_6) δ = 12.75 (s, 1H), 8.34 (d, J = 8 Hz, 2H), 8.17 (d, J = 8 Hz, 1H), 8.04 (d, J = 8 Hz, 2H), 7.87 (t, J = 8 Hz, 1H), 7.78 (d, J = 8 Hz, 1H), 7.57 (t, J = 8 Hz, 1H).

*2-(4-Bromophenyl)quinazolin-4(3H)-one (**1i**)*.[5g] White solid (521 mg, 53%); ^{1}H NMR (400 MHz, DMSO-d_6) δ = 12.61 (s, 1H), 8.17 – 8.11 (m, 3H), 7.85 (t, J = 8 Hz, 1H), 7.78 – 7.73 (m, 3H), 7.54 (t, 1H).

*2-(4-Iodophenyl)quinazolin-4(3H)-one (**1j**)*.[5i] White solid (676 mg, 68%); ^{1}H NMR (400 MHz, DMSO-d_6) δ = 12.59 (s, 1H), 8.15 (d, J = 8 Hz, 1H), 7.98 – 7.92 (m, 4H), 7.84 (t, J = 8 Hz, 1H), 7.74 (d, J = 8 Hz, 1H), 7.53 (t, J = 8 Hz, 1H).

*2-(3,5-Difluorophenyl)quinazolin-4(3H)-one (**1k**)*.[5j] White solid (209 mg, 37%); ^{1}H NMR (400 MHz, DMSO-d_6) δ = 12.65 (s, 1H), 8.17 (d, *J* = 8 Hz, 1H), 7.96 – 7.85 (m, 3H), 7.78 (d, *J* = 8 Hz, 1H), 7.59 – 7.51 (m, 2H).

*2-(4-Nitrophenyl)quinazolin-4(3H)-one (**1l**)*.[5k] Yellow solid (281 mg, 19%); ^{1}H NMR (400 MHz, DMSO-d_6) δ = 12.83 (s, 1H), 8.43 – 8.37 (m, 4H), 8.19 (d, *J* = 8 Hz, 1H), 7.88 (t, *J* = 8 Hz, 1H), 7.80 (d, *J* = 8 Hz, 1H), 7.58 (t, *J* = 8 Hz, 1H).

*2-(4-(Trifluoromethyl)phenyl)quinazolin-4(3H)-one (**1m**)*.[5l] White solid (372 mg, 49%); ^{1}H NMR (400 MHz, DMSO-d_6) δ = 12.75 (s, 1H), 8.37 (d, *J* = 8 Hz, 2H), 8.18 (d, *J* = 8 Hz, 1H), 7.93 (d, *J* = 8 Hz, 2H), 7.87 (t, *J* = 8 Hz, 1H), 7.78 (d, *J* = 8 Hz, 1H), 7.57 (t, *J* = 8 Hz, 1H).

*4-(4-Oxo-3,4-dihydroquinazolin-2-yl)benzonitrile (**1n**)*.[5g] White solid (348 mg, 40%); ^{1}H NMR (400 MHz, DMSO-d_6) δ = 12.61 (s, 1H), 8.21 (d, *J* = 8 Hz, 2H), 8.16 (d, *J* = 8 Hz, 1H), 7.85 (t, *J* = 8 Hz, 1H), 7.75 (d, *J* = 8 Hz, 1H), 7.63 (d, *J* = 8 Hz, 2H), 7.54 (t, *J* = 8 Hz, 1H).

*2-([1,1'-Biphenyl]-4-yl)quinazolin-4(3H)-one (**1o**)*.[5m] White solid (526 mg, 49%); ^{1}H NMR (400 MHz, DMSO-d_6) δ = 12.59 (s, 1H), 8.31 (d, *J* = 8 Hz, 2H), 8.17 (d, *J* = 8 Hz, 1H), 7.88 – 7.83 (m, 3H), 7.79 – 7.75 (m, 3H), 7.55 – 7.50 (m, 3H), 7.43 (t, *J* = 8 Hz, 1H).

*2-(3-Bromophenyl)quinazolin-4(3H)-one (**1p**)*.[5m] White solid (1.15 g, 52%); ^{1}H NMR (400 MHz, DMSO-d_6) δ = 12.62 (s, 1H), 8.38 (s, 1H), 8.20 – 8.15 (m, 2H), 7.86 – 7.80 (m, 1H), 7.79 – 7.76 (m, 2H), 7.57 – 7.50 (m, 2H).

*2-(2,4-Dimethylphenyl)quinazolin-4(3H)-one (**1p'**)*.[5q] White solid (1.4 g, 76%); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 9.85 (s, 1H), 8.29 (d, *J* = 8 Hz, 1H), 7.80 – 7.78 (m, 2H), 7.53 – 7.47 (m, 1H), 7.45 (s, 1H), 7.15 (d, *J* = 8 Hz, 2H), 2.51 (s, 3H), 2.40 (s, 3H).

*2-(2-Fluorophenyl)quinazolin-4(3H)-one (**1p''**)*.[5g] White solid (1.1 g, 62%); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 10.01 (s, 1H), 8.36 (t, *J* = 8 Hz, 1H), 8.30 (d, *J* = 8 Hz, 1H), 7.82 – 7.77 (m, 2H), 7.56 – 7.49 (m, 2H), 7.36 (t, *J* = 8 Hz, 1H), 7.24 – 7.21 (m, 1H).

*5-Methoxy-2-phenylquinazolin-4(3H)-one (**1q**)*.[5n] White solid (201 mg, 5%); ^{1}H NMR (400 MHz, DMSO-d_6) δ = 12.20 (s, 1H), 8.17 (d, *J* = 8 Hz, 2H), 7.71 (t, *J* = 8 Hz, 1H), 7.58 – 7.51 (m, 3H), 7.26 (d, *J* = 8 Hz, 1H), 7.02 (d, *J* = 8 Hz, 1H), 3.89 (s, 3H).

*5-Fluoro-2-phenylquinazolin-4(3H)-one (**1r**)*.[5o] White solid (430 mg, 24%); ^{1}H NMR (400 MHz, DMSO-d_6) δ = 12.55 (s, 1H), 8.19 – 8.16 (m, 2H), 7.83 – 7.78 (m, 1H), 7.61 – 7.53 (m, 4H), 7.28 – 7.23 (m, 1H).

*5-Chloro-2-phenylquinazolin-4(3H)-one (**1s**)*.[5p] White solid (282 mg, 16%); ^{1}H NMR (400 MHz, DMSO-d_6) δ = 12.55 (s, 1H), 8.19 – 8.16 (m, 2H), 7.77 – 7.67 (m, 1H), 7.61 – 7.59 (m, 1H), 7.57 – 7.51 (m, 4H).

*6-Fluoro-2-phenylquinazolin-4(3H)-one (**1t**)*.[5p] White solid (1.24 g, 71%); ^{1}H NMR (400 MHz, DMSO-d_6) δ = 12.67 (s, 1H), 8.17 (d, J = 8 Hz, 2H), 7.85 – 7.81 (m, 2H), 7.76 – 7.71 (m, 1H), 7.60 – 7.53(m, 3H).

*6-Bromo-2-phenylquinazolin-4(3H)-one (**1u**)*.[5p] White solid (528 mg, 43%); ^{1}H NMR (400 MHz, DMSO-d_6) δ = 12.73 (s, 1H), 8.23 (s, 1H), 8.19 – 8.16 (m, 2H), 7.99 (d, J = 8 Hz, 1H), 7.70 (d, J = 8 Hz, 1H), 7.61 – 7.54 (m, 3H).

*6-Methyl-2-phenylquinazolin-4(3H)-one (**1v**)*.[5p] White solid (976 mg, 30%); ^{1}H NMR (400 MHz, DMSO-d_6) δ = 12.46 (s, 1H), 8.17 (d, J = 8 Hz, 2H), 7.96 (s, 1H), 7.66 (d, J = 8 Hz, 2H), 7.58 – 7.52 (m, 3H), 2.46 (s, 3H).

*7-Fluoro-2-phenylquinazolin-4(3H)-one (**1w**)*.[5o] White solid (780 mg, 44%); ^{1}H NMR (400 MHz, DMSO-d_6) δ = 12.62 (s, 1H), 8.21 – 8.15 (m, 3H), 7.61 – 7.47 (m, 4H), 7.38 – 7.33 (m, 1H).

*7-Chloro-5-methyl-2-phenylquinazolin-4(3H)-one (**1x**)*.[10b] White solid (933 mg, 57%); ^{1}H NMR (400 MHz, DMSO-d_6) δ = 12.45 (s, 1H), 8.18 – 8.15 (m, 2H), 7.61 – 7.53 (m, 4H), 7.36 (s, 1H), 2.80 (s, 3H).

*6,7-Dimethyl-2-phenylquinazolin-4(3H)-one (**1y**)*.[10b] White solid (582 mg, 32%); ^{1}H NMR (400 MHz, DMSO-d_6) δ = 12.37 (s, 1H), 8.16 (d, J = 8 Hz, 2H), 7.91 (s, 1H), 7.58 – 7.52 (m, 4H), 2.39 (s, 3H), 2.37 (s, 3H).

*8-Nitro-2-phenylquinazolin-4(3H)-one (**1z**)*.[10b] Yellowish solid (228 mg, 12%); ^{1}H NMR (400 MHz, DMSO-d_6) δ = 12.95 (s, 1H), 8.38 (d, J = 8 Hz, 1H), 8.31 (d, J = 8 Hz, 1H), 8.16 (d, J = 8 Hz, 2H), 7.67 – 7.55 (m, 4H).

*7-Fuoro-5-methyl-2-phenylquinazolin-4(3H)-one (**1w'**)*.[10b] White solid (844 mg, 53%); ^{1}H NMR (400 MHz, DMSO-d_6) δ = 12.39 (s, 1H), 8.16 (d, J = 8 Hz, 2H), 7.60 – 7.52 (m, 3H), 7.29 (d, J = 8 Hz, 1H), 7.16 (d, J = 8 Hz, 1H), 2.81 (s, 3H).

Stoichiometric Model Study of *C*-Trifluoroethylation.

Synthesis of the tetrameric palladacycle and its C-trifluoroethylation: An oven-dried 10 mL round-bottom flask was charged with 2-(4-bromophenyl)quinazolin-4(3*H*)-one **1i** (86 mg, 0.29 mmol) and $Pd(OAc)_2$ (64 mg, 0.29 mmol, 1.0 equiv). This mixture was dissolved in 1,2-dichloroethane (DCE, 5 mL), and stirred at rt for 6 h. Then the mixture was filtered, and the residue was washed with hexane to give the

desired **tetrameric palladacycle** as a yellow solid (103 mg, 0.062 mmol (0.25 mmol: tetrameric form), 86%). ^{1}H NMR (400 MHz, DMSO-d_6) δ = 8.09 (d, J = 8 Hz, 1H), 7.86 – 7.79 (m, 3H), 7.71 (s, 1H), 7.49 (d, J = 8 Hz, 2H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ = 164.8, 134.3, 134.2, 133.8, 133.7, 133.6, 128.7, 128.6, 128.2, 126.3, 126.2, 125.8, 123.2, 120.4; ATR-FTIR (cm^{-1}): 1682, 1651, 1579, 1471, 1381, 1195, 1159, 1080. Single crystals were obtained from hexane/acetone through the vapour diffusion method, and the compound was characterized by X-ray crystallography (see the Supporting Information, Section IV).

To an oven-dried 10 mL round-bottom flask charged with the **tetrameric palladacycle** (30 mg, 0.018 mmol, (0.072 mmol: tetrameric form)) and **2** (53 mg, 0.11 mmol) were added DCE (2 mL) and TFA (115 μL, 1.48 mmol). The reaction mixture was stirred at rt for 24 h. After completion of the reaction, the solvent was removed in vacuo and the residue was purified by flash column chromatography (15–20% ethyl acetate (EA) in hexane) to give **3i** (19 mg, 0.050 mmol, 69%) as a white solid.

Representative Procedure for the Synthesis of 2-(4-Methyl-2-(2,2,2-trifluoroethyl)phenyl)quinazolin-4(3*H*)-one (3a).

An oven-dried 10 mL round-bottom flask was charged with 2-(*p*-tolyl)quinazolin-4(3*H*)-one **1a** (60 mg, 0.25 mmol), **2** (182 mg, 0.38 mmol) and $Pd(OAc)_2$ (11 mg, 0.050 mmol). To this mixture were added DCE (5 mL) and TFA (396 μL, 5.0 mmol), and the reaction mixture was stirred at rt. The progress of the reaction was monitored by TLC (20% EA in hexane). After the completion of reaction, the resulting solution was diluted with dichloromethane and filtered through Celite. The reaction mixture was concentrated in vacuo and the crude residue was purified by flash column chromatography (10–15% EA in hexane) to give **3a** (73.5 mg, 0.23 mmol, 91%) as a white solid.

(1 mmol-scale) An oven-dried 25 mL round-bottom flask was charged with 2-(*p*-tolyl)quinazolin-4(3*H*)-one **1a** (236 mg, 1.0 mmol), **2** (717 mg, 1.5 mmol) and $Pd(OAc)_2$ (45 mg, 0.20 mmol). To this mixture were added DCE (15 mL) and TFA (1.55 mL, 20 mmol), and the reaction mixture was stirred at rt. The progress of the reaction was monitored by TLC (20% EA in hexane). After the completion of reaction, the resulting solution was diluted with dichloromethane and filtered through Celite. The reaction mixture was concentrated in vacuo and the crude residue was purified by flash column chromatography (10–15% EA in hexane) to give **3a** (286 mg, 0.90 mmol, 90%) as a white solid.

Representative Procedure for the Synthesis of 2-(*p*-Tolyl)-4-(2,2,2-trifluoroethoxy)quinazoline (4a).

An oven-dried 10 mL round-bottom flask was charged with **1a** (60 mg, 0.25 mmol), **2** (182 mg, 0.38 mmol) and K_2CO_3 (35 mg, 0.25 mmol). To this mixture were added MeCN (5 mL) and the system stirred at rt. The progress of the reaction was monitored by TLC (10% EA in hexane). After the completion of reaction, the solvents were evaporated to dryness and the crude residue was purified by flash column chromatography (2–5% EA in hexane) to give **4a** (75 mg, 0.24 mmol, 93%) as a white solid.

(1 mmol-scale) An oven-dried 25 mL round-bottom flask was charged with **1a** (236 mg, 1.0 mmol), **2** (717 mg, 1.5 mmol) and K_2CO_3 (138 mg, 1.0 mmol). To this mixture were added MeCN (15 mL) and the system stirred at rt. The progress of the reaction was monitored by TLC (10% EA in hexane). After the completion of reaction, the solvents were evaporated to dryness and the crude residue was purified by flash column chromatography (2–5% EA in hexane) to give **4a** (295 mg, 0.93 mmol, 93%) as a white solid.

Representative Procedure for the Synthesis of 2-(*p*-Tolyl)-3-(2,2,2-trifluoroethyl)quinazolin-4(3*H*)-one (5a).

An oven-dried Schlenk tube was charged with **1a** (60 mg, 0.25 mmol), **2** (182 mg, 0.38 mmol) and LiO*t*Bu (41 mg, 0.51 mmol). The tube was evacuated and purged with N_2 repeatedly three times. To this mixture was added degassed dry toluene (5 mL). After 12 h, the mixture was concentrated in vacuo and purified by flash column chromatography (8–10% EA in hexane) to give **5a** (72 mg, 0.23 mmol, 89%) as a colourless semi-solid.

(1 mmol-scale) An oven-dried Schlenk tube was charged with **1a** (236 mg, 1.0 mmol), **2** (717 mg, 1.5 mmol) and LiO*t*Bu (160 mg, 2.0 mmol). The tube was evacuated and purged with N_2 repeatedly three times. To this mixture was added degassed dry toluene (15 mL). After 12 h, the mixture was concentrated in vacuo and purified by flash column chromatography (8–10% EA in hexane) to give **5a** (274 mg, 0.86 mmol, 86%) as a colourless semi-solid.

Characterization Data.

*2-(4-Methyl-2-(2,2,2-trifluoroethyl)phenyl)quinazolin-4(3H)-one (**3a**)*. R_f = 0.4 (hexane:EA, 4:1); white solid (73.5 mg, 91%); mp 221−223 °C; ^{19}F NMR (377 MHz, $CDCl_3$) δ = -65.1 (t, *J* = 12 Hz); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 10.88 (s, 1H), 8.25 (d, *J* = 8 Hz, 1H), 7.82 – 7.75 (m, 2H), 7.60 (d, *J* = 8 Hz, 1H), 7.51 (t, *J* = 8 Hz, 1H), 7.34 (d, *J* = 8 Hz, 1H), 7.31 (s, 1H), 4.00 (q, *J* = 12 Hz, 2H), 2.45 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ = 163.2, 152.7, 148.8, 141.3, 135.0, 133.6, 131.7, 129.6 (q, *J* = 3 Hz), 129.5, 129.2, 127.8, 127.2, 126.5, 125.9 (q, *J* = 275 Hz), 120.8, 36.4 (q, *J* = 30 Hz), 21.5; ATR-FTIR

(cm^{-1}): 1666, 1612, 1597, 1469, 1344, 1257, 1124, 1076; HRMS (ESI+) m/z [M+H]$^+$ calcd for $C_{17}H_{14}F_3N_2O$ 319.1053; found 319.1053.

*2-(4-Ethyl-2-(2,2,2-trifluoroethyl)phenyl)quinazolin-4(3H)-one (**3b**)*. R_f = 0.4 (hexane:EA, 4:1); white solid (54 mg, 82%); mp 219−220 °C; ^{19}F NMR (377 MHz, $CDCl_3$) δ = -65.1 (t, *J* = 12 Hz); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 10.09 (s, 1H), 8.29 (d, *J* = 8 Hz, 1H), 7.81 (t, *J* = 8 Hz, 1H), 7.76 (d, *J* = 8 Hz, 1H), 7.57 (d, *J* = 8 Hz, 1H), 7.53 (t, *J* = 8 Hz, 1H), 7.36 (d *J* = 8 Hz, 1H), 7.33 (s, 1H), 4.01 (q, *J* = 12 Hz, 2H), 2.75 (q, *J* = 8 Hz, 2H), 1.29 (t, *J* = 8 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ = 162.8, 152.6, 148.7, 147.7, 135.1, 132.7, 132.0, 129.6 (q, *J* = 3 Hz), 129.1, 128.4, 127.9, 127.3, 126.6, 125.7 (q, *J* = 240 Hz), 120.9, 36.5 (q, *J* = 29 Hz), 28.8, 15.4; ATR-FTIR (cm^{-1}): 1670, 1610, 1598, 1465, 1352, 1309, 1251, 1134, 1082, 948; HRMS (ESI+) m/z [M+H]$^+$ calcd for $C_{18}H_{16}F_3N_2O$ 333.1209; found 333.1208.

*2-(4-Isopropyl-2-(2,2,2-trifluoroethyl)phenyl)quinazolin-4(3H)-one (**3c**)*. R_f = 0.4 (hexane:EA, 4:1); white solid (69 mg, 84%); mp 208−210 °C; ^{19}F NMR (377 MHz, $CDCl_3$) δ = -65.2 (t, *J* = 12 Hz); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 10.04 (s, 1H), 8.29 (d, *J* = 8 Hz, 1H), 7.81 (t, *J* = 8 Hz, 1H), 7.75 (d, *J* = 8 Hz, 1H), 7.57 (d, *J* = 8 Hz, 1H), 7.52 (t, *J* = 8 Hz, 1H), 7.38 (d, *J* = 8 Hz, 1H), 7.35 (s, 1H), 4.02 (q, *J* = 12 Hz, 2H), 3.00 (sept, *J* = 8, 4 Hz, 1H), 1.31 (s, 3H), 1.30 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ = 162.6, 152.5, 152.2, 148.7, 135.0, 132.1, 131.4, 129.6 (q, *J* = 3 Hz), 129.0, 127.9, 127.3, 127.0, 126.6, 125.9 (q, *J* = 275 Hz), 120.9, 36.6 (q, *J* = 29 Hz), 34.1, 23.8; ATR-FTIR (cm^{-1}): 1668, 1610, 1598, 1471, 1354, 1305, 1255, 1138, 1078, 1055; HRMS (ESI+) m/z [M+H]$^+$ calcd for $C_{19}H_{18}F_3N_2O$ 347.1366; found 347.1364.

*2-(4-(Tert-butyl)-2-(2,2,2-trifluoroethyl)phenyl)quinazolin-4(3H)-one (**3d**)*. R_f = 0.4 (hexane:EA, 4:1); white solid (69 mg, 87%); mp 208−209 °C; ^{19}F NMR (377 MHz, $CDCl_3$) δ = -65.2 (t, *J* = 12 Hz); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 10.11 (s, 1H), 8.28 (d, *J* = 8 Hz, 1H), 7.81 (t, *J* = 8 Hz, 1H), 7.75 (d, *J* = 8 Hz, 1H), 7.59 – 7.52 (m, 3H), 7.50 (s, 1H), 4.02 (q, *J* = 12 Hz, 2H), 1.38 (s, 9H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ = 162.9, 154.5, 152.6, 148.8, 135.0, 131.7, 130.2, 129.3 (q, *J* = 2 Hz), 128.8, 127.9, 127.3, 126.6, 125.9 (q, *J* = 276 Hz), 125.8, 120.9, 36.7 (q, *J* = 29 Hz), 35.0, 31.2; ATR-FTIR (cm^{-1}): 1670, 1610, 1599, 1564, 1467, 1355, 1284, 1255, 1120, 1085; HRMS (ESI+) m/z [M+H]$^+$ calcd for $C_{20}H_{20}F_3N_2O$ 361.1522; found 361.1521.

*2-(2-(2,2,2-Trifluoroethyl)phenyl)quinazolin-4(3H)-one (**3e**)*. R_f = 0.4 (hexane:EA, 4:1); white solid (47 mg, 86%); mp 202−203 °C; ^{19}F NMR (377 MHz, $CDCl_3$) δ = -65.1 (t, *J* = 12 Hz); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 10.89 (s, 1H), 8.26 (d, *J* = 8Hz, 1H), 7.84 – 7.76 (m, 2H), 7.71 – 7.69 (m, 1H), 7.57 – 7.50 (m, 4H), 4.02 (q, *J* = 12 Hz, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ = 163.2, 152.6, 148.7, 135.1, 134.6, 132.9, 130.9, 129.7 (q, *J* = 2 Hz), 129.3, 128.9, 127.9, 127.4, 126.6, 125.9 (q, *J* = 275 Hz), 120.9,

36.5 (q, J = 30 Hz); ATR-FTIR (cm^{-1}): 1676, 1606, 1595, 1469, 1357, 1257, 1134, 1072; HRMS (ESI+) m/z $[M+H]^+$ calcd for $C_{16}H_{12}F_3N_2O$: 305.0896; found 305.0896.

2-(4-Methoxy-2-(2,2,2-trifluoroethyl)phenyl)quinazolin-4(3H)-one ***(3f)***. R_f = 0.30 (hexane:EA, 4:1); white solid (42 mg, 63%); mp 224−225 °C; ^{19}F NMR (377 MHz, $CDCl_3$) δ = -64.9 (t, J = 12 Hz); ^1H NMR (400 MHz, $CDCl_3$) δ = 10.77 (s, 1H), 8.26 (d, J = 8 Hz, 1H), 7.82 – 7.74 (m, 2H), 7.65 (d, J = 12 Hz, 1H), 7.51 (t, J = 8 Hz, 1H), 7.05 (t, J = 8 Hz, 1H), 7.03 (s, 1H), 4.05 (q, J = 12 Hz, 2H), 3.90 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ = 163.4, 161.3, 152.5, 148.9, 135.0, 131.7 (q, J = 3 Hz), 130.9, 127.8, 127.1, 126.9, 126.5, 125.9 (q, J = 276 Hz) 120.7, 118.8, 113.7, 55.6, 36.7 (q, J = 30 Hz); ATR-FTIR (cm^{-1}): 1674, 1608, 1570, 1465, 1355, 1253, 1240, 1132, 1085, 1072; HRMS (ESI+) m/z $[M+H]^+$ calcd for $C_{17}H_{14}F_3N_2O_2$ 335.1002; found 335.1002.

2-(4-Fluoro-2-(2,2,2-trifluoroethyl)phenyl)quinazolin-4(3H)-one ***(3g)***. R_f = 0.40 (hexane:EA, 4:1); white solid (52 mg, 70%); mp 228−229 °C; ^{19}F NMR (377 MHz, $CDCl_3$) δ = -66.0 (t, J = 12 Hz), -108.2 – -102.3 (m); ^1H NMR (400 MHz, $CDCl_3$) δ = 10.71 (s, 1H), 8.28 (d, J = 8 Hz, 1H), 7.83 (t, J = 8 Hz, 1H), 7.77 (d, J = 8 Hz, 1H), 7.71 (dd, J = 8 Hz, 1H), 7.55 (t, J = 8 Hz, 1H), 7.29 – 7.24 (m, 2H), 4.03 (q, J = 12 Hz, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ = 164.9, 163.2, 162.4, 151.7, 148.6, 135.2, 132.6 (q, J = 5 Hz), 131.4 (d, J = 9 Hz), 130.8 (d, J = 3 Hz), 127.7 (d, J = 28 Hz), 126.6, 125.5 (d, J = 276 Hz), 120.8, 119.9 (d, J = 22 Hz), 116.0 (d, J = 21 Hz), 36.6 (q, J = 30 Hz); ATR-FTIR (cm^{-1}): 1674, 1585, 1469, 1354, 1298, 1255, 1220, 1145, 1076; HRMS (ESI+) m/z $[M+H]^+$ calcd for $C_{16}H_{11}F_4N_2O$: 323.0802; found 323.0802.

2-(4-Chloro-2-(2,2,2-trifluoroethyl)phenyl)quinazolin-4(3H)-one ***(3h)***. R_f = 0.40 (hexane:EA, 4:1); white solid (49 mg, 69%); mp 237−238 °C; ^{19}F NMR (377 MHz, $CDCl_3$) δ = -65.0 (t, J = 12 Hz); ^1H NMR (400 MHz, $CDCl_3$) δ = 11.15 (s, 1H), 8.27 (d, J = 8 Hz, 1H), 7.83 (t, J = 8 Hz, 1H), 7.77 (d, J = 8 Hz, 1H), 7.69 (d, J = 12 Hz, 1H), 7.58 – 7.53 (m, 3H), 4.03 (q, J = 12 Hz, 2 H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ = 163.4, 151.6, 148.6, 137.1, 135.3, 132.9, 132.9, 131.7 (q, J = 3 Hz), 130.7, 129.1, 127.9, 127.7, 126.6, 125.6 (q, J = 275 Hz), 120.8, 36.4 (q, J = 30 Hz); ATR-FTIR (cm^{-1}): 1676, 1606, 1568, 1469, 1377, 1298, 1246, 1138, 1091; HRMS (ESI+) m/z $[M+H]^+$ calcd for $C_{16}H_{11}ClF_3N_2O$: 339.0507; found 339.0506.

2-(4-Bromo-2-(2,2,2-trifluoroethyl)phenyl)quinazolin-4(3H)-one ***(3i)***. R_f = 0.40 (hexane:EA, 4:1); white solid (48 mg, 69%); mp 237−238 °C; ^{19}F NMR (377 MHz, $CDCl_3$) δ = -65.0 (t, J = 12 Hz); ^1H NMR (400 MHz, $CDCl_3$) δ = 10.80 (s, 1H), 8.28 (d, J = 8 Hz, 1H), 7.84 – 7.81 (m, 1H), 7.76 (s, 1H), 7.72 – 7.69 (m, 2H), 7.60 – 7.54 (m, 2H), 4.02 (q, J = 12 Hz, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ = 163.2, 151.6, 148.5, 135.8, 135.3, 133.4, 132.1, 131.8 (q, J = 3 Hz), 130.7, 127.9, 127.7, 126.6, 125.6 (q,

J = 276 Hz), 125.3, 120.8, 36.3 (q, *J* = 30 Hz); ATR-FTIR (cm^{-1}): 1678, 1606, 1566, 1469, 1375, 1300, 1244, 1138, 1091; HRMS (ESI+) m/z $[M+H]^+$ calcd for $C_{16}H_{11}BrF_3N_2O$: 383.0001; found 383.0001.

*2-(4-Iodo-2-(2,2,2-trifluoroethyl)phenyl)quinazolin-4(3H)-one (**3j**)*. R_f = 0.45 (hexane:EA, 4:1); white solid (44 mg, 85%); mp 226−227 °C; ^{19}F NMR (377 MHz, $CDCl_3$) δ = -65.0 (t, *J* = 12 Hz); ^1H NMR (400 MHz, $CDCl_3$) δ = 11.12 (s, 1H), 8.26 (d, *J* = 8 Hz, 1H), 7.92 – 7.81 (m, 3H), 7.76 (d, *J* = 8 Hz, 1H), 7.56 (t, *J* = 8 Hz, 1H), 7.46 (d, *J* = 12 Hz, 1H), 4.00 (q, *J* = 12 Hz, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ = 163.4, 151.8, 148.6, 141.7, 138.0, 135.3, 134.0, 131.7 (q, *J* = 3 Hz), 130.7, 127.9, 127.7, 126.6, 125.6 (q, *J* = 276 Hz),120.8, 97.3, 36.1 (q, *J* = 30 Hz); ATR-FTIR (cm^{-1}): 1680, 1597, 1546, 1477, 1363, 1282, 1246, 1136, 1070; HRMS (ESI+) m/z $[M+H]^+$ calcd for $C_{16}H_{11}F_3IN_2O$: 430.9863; found 430.9863.

*2-(3,5-Difluoro-2-(2,2,2-trifluoroethyl)phenyl)quinazolin-4(3H)-one (**3k**)*. R_f = 0.35 (hexane:EA, 4:1); white solid (29 mg, 44%); mp 233−235 °C; ^{19}F NMR (377 MHz, $CDCl_3$) δ = -65.6 (m), -107.4 – -107.5 (m), -107.7 – -107.8 (m); ^1H NMR (400 MHz, $CDCl_3$) δ = 11.48 (s, 1H), 8.29 (d, *J* = 8 Hz, 1H), 7.87 (t, *J* = 8 Hz, 1H), 7.78 (d, *J* = 8 Hz, 1H), 7.58 (t, *J* = 8 Hz, 1H), 7.38 (d, *J* = 8 Hz, 1H), 7.11 (d, *J* = 8 Hz, 1H), 4.15 (q, *J* = 12 Hz, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ = 163.5, 162.7 (d, *J* = 265 Hz), 162.6 (d, *J* = 237 Hz), 150.5 (t, *J* = 3 Hz), 148.4, 137.1 (q, *J* = 4 Hz), 135.4, 128.0 (d, *J* = 7 Hz), 126.7, 125.4 (q, *J* = 276 Hz), 120.9, 114.0 (d, *J* = 20 Hz), 113.2 (dd, $J_1 = J_2$ = 24 Hz), 106.6 (d, *J* = 24 Hz), 106.3 (d, *J* = 24 Hz), 37.0 (q, *J* = 31 Hz); ATR-FTIR (cm^{-1}): 1674, 1608, 1506, 1467, 1373, 1336, 1247, 1126, 1089; HRMS (ESI+) m/z $[M+H]^+$ calcd for $C_{16}H_{10}F_5N_2O$ 341.0708; found 341.0708.

*2-(4-Nitro-2-(2,2,2-trifluoroethyl)phenyl)quinazolin-4(3H)-one (**3l**)*. R_f = 0.30 (hexane:EA, 7:3); white solid (23 mg, 61%); mp 246−248 °C; ^{19}F NMR (377 MHz, $CDCl_3$) δ = -64.9 (t, *J* = 12 Hz); ^1H NMR (400 MHz, $CDCl_3$) δ = 11.04 (s, 1H), 8.45 – 8.42 (m, 2H), 8.30 (d, *J* = 8 Hz, 1H), 7.93 (d, *J* = 8 Hz, 1H), 7.88 (t, *J* = 8 Hz, 1H), 7.80 (d, *J* = 8 Hz, 1H), 7.61 (t, *J* = 8 Hz, 1H), 4.15 (q, *J* = 12 Hz, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ = 161.7, 151.9, 148.1, 148.0, 140.3, 134.7, 132.0, 131.5 (q, *J* = 3 Hz), 127.5, 127.4, 126.8, 125.9 (q, *J* = 276 Hz), 125.8, 123.2, 121.2, 34.8 (q, *J* = 29 Hz); ATR-FTIR (cm^{-1}): 1678, 1599, 1523, 1469, 1344, 1294, 1246, 1130, 1089; HRMS (ESI+) m/z $[M+H]^+$ calcd for $C_{16}H_{11}F_3N_3O_3$: 350.0747; found 350.0747.

*2-(2-(2,2,2-Trifluoroethyl)-4-(trifluoromethyl)phenyl)quinazolin-4(3H)-one (**3m**)*. R_f = 0.30 (hexane:EA, 7:3); white solid (49 mg, 54%); mp 230−232 °C; ^{19}F NMR (377 MHz, $CDCl_3$) δ = -63.0, -65.1 (t, *J* = 12 Hz); ^1H NMR (400 MHz, $CDCl_3$) δ = 11.42 (s, 1H), 8.25 (d, J = 8 Hz, 1H), 7.90 – 7.78 (m, 4H), 7.79 (s, 1H), 7.58 (t, *J* = 8 Hz, 1H), 4.1 (q, *J* = 30 Hz, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ = 163.5, 151.3, 148.5, 137.8, 135.4, 132.9 (q, *J* = 33 Hz), 131.0 (q, *J* = 3 Hz), 130.2, 129.6 (q, *J* = 3 Hz), 128.0, 127.9, 126.6, 125.9 (q, *J* = 203 Hz), 125.8 (q, *J* = 4 Hz), 123.1 (q, *J* = 199 Hz), 120.9, 36.6 (q, *J* =

30 Hz); ATR-FTIR (cm^{-1}): 1680, 1602, 1446, 1344, 1325, 1247, 1138, 1120, 1070; HRMS (ESI+) m/z $[M+H]^+$ calcd for $C_{17}H_{11}F_6N_2O$: 373.0770; found 373.0770.

*2-(3-(2,2,2-Trifluoroethyl)-[1,1'-biphenyl]-4-yl)quinazolin-4(3H)-one (**3o**)*. R_f = 0.35 (hexane:EA, 4:1); white solid (61 mg, 89%); mp 212−214 °C; ^{19}F NMR (377 MHz, $CDCl_3$) δ = -65.0 (t, *J* = 12 Hz); ^1H NMR (400 MHz, $CDCl_3$) δ = 10.05 (s, 1H), 8.32 (d, *J* = 8 Hz, 1H), 7.85 – 7.72 (m, 5H), 7.67 – 7.64 (m, 2H), 7.55 – 7.51 (m, 3H), 7.49 – 7.44 (m, 1H), 4.11 (q, *J* = 12 Hz, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ = 162.7, 152.2, 148.7, 144.0, 139.4, 135.1, 133.2, 131.7, 130.2 (q, *J* = 3 Hz), 129.5, 129.2, 128.5, 127.9, 127.6. 127.5, 127.4, 126.6, 125.9 (q, *J* = 275 Hz), 121.0, 36.6 (q, *J* = 30 Hz); ATR-FTIR (cm^{-1}): 1647, 1600, 1554, 1471, 1440, 1361, 1292, 1263, 1136, 1082; HRMS (ESI+) m/z $[M+H]^+$ calcd for $C_{22}H_{16}F_3N_2O$ 381.1209; found 381.1206.

*2-(5-Bromo-2-(2,2,2-trifluoroethyl)phenyl)quinazolin-4(3H)-one (**3p**)*. R_f = 0.40 (hexane:EA, 4:1); white solid (45 mg, 64%); mp 239−240 °C; ^{19}F NMR (377 MHz, $CDCl_3$) δ = -65.0 (t, *J* = 12 Hz); ^1H NMR (400 MHz, $CDCl_3$) δ = 11.13 (s, 1H), 8.38 (d, *J* = 8 Hz, 1H), 7.94 (s, 1H), 7.84 (t, *J* = 8 Hz, 1H), 7.78 (d, *J* = 8 Hz, 1H), 7.70 (dd, *J* = 8, 2 Hz, 1H), 7.57 (t, *J* = 8 Hz, 1H), 7.40 (d, *J* = 8 Hz, 1H), 4.01 (q, *J* = 11 Hz, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ = 163.4, 151.1, 148.5, 136.1, 135.3, 134.3, 134.0, 132.6, 128.8 (q, *J* = 3 Hz), 127.9, 127.8, 126.8, 125.5 (q, *J* = 276 Hz), 122.9, 120.9, 36.2 (q, *J* = 29 Hz); ATR-FTIR (cm^{-1}): 1676, 1608, 1585, 1469, 1373, 1278, 1246, 1128, 1085; HRMS (ESI+) m/z $[M+H]^+$ calcd for $C_{16}H_{11}BrF_3N_2O$ 383.0001; found 383.0001.

*2-(2,4-Dimethyl-6-(2,2,2-trifluoroethyl)phenyl)quinazolin-4(3H)-one (**3p'**)*. R_f = 0.45 (hexane:EA, 4:1); white solid (65 mg, 83%); mp 212−214 °C; ^{19}F NMR (377 MHz, $CDCl_3$) δ = -64.9 (t, *J* = 12 Hz); ^1H NMR (400 MHz, $CDCl_3$) δ = 9.83 (s, 1H), 8.26 (d, *J* = 8 Hz, 1H), 7.84 – 7.76 (m, 2H), 7.54 (t, *J* = 8 Hz, 1H), 7.13 (s, 2H), 3.44 (q, *J* = 12 Hz, 2H), 2.39 (s, 3H), 2.27 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ = 162.2, 152.6, 148.8, 140.5, 136.8, 135.1, 132.3, 131.5, 129.9, 128.6 (q, *J* = 3 Hz), 127.9, 127.5, 126.7, 125.6 (q, *J* = 275 Hz), 121.1, 36.9 (q, *J* = 30 Hz), 21.38, 19.88; ATR-FTIR (cm^{-1}): 1667, 1609, 1449, 1302, 1256, 1136, 1089; HRMS (ESI+) m/z $[M+H]^+$ calcd for $C_{18}H_{16}F_3N_2O$ 333.1209; found 333.1209.

*2-(2-Fluoro-6-(2,2,2-trifluoroethyl)phenyl)quinazolin-4(3H)-one (**3p''**)*. R_f = 0.40 (hexane:EA, 4:1); white solid (48 mg, 62%); mp 174−176 °C; ^{19}F NMR (377 MHz, $CDCl_3$) δ = -65.2 (t, *J* = 12 Hz), -113.3 – -113.34 (m); ^1H NMR (400 MHz, $CDCl_3$) δ = 9.95 (s, 1H), 8.29 (d, *J* = 8 Hz, 1H), 7.83 (t, *J* = 8 Hz, 1H), 7.77 (d, *J* = 8 Hz, 1H), 7.58 – 7.51 (m, 2H), 7.32 (d, *J* = 8 Hz, 1H), 7.27 – 7.23 (m, 1H), 3.82 (q, *J* = 8 Hz, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ = 162.0, 160.6 (d, *J* = 248 Hz), 148.6, 147.8, 135.1, 132.3 (d, *J* = 9 Hz), 131.9 (q, *J* = 3 Hz), 128.2 (d, *J* = 3 Hz), 127.9 (d, *J* = 5 Hz), 126.8, 124.5 (q, *J* = 275 Hz), 124.0, 123.1 (d, *J* = 15 Hz), 121.4, 116.4 (d, *J* = 22 Hz), 36.4 (q, *J* = 28 Hz); ATR-FTIR (cm^{-1}): 1670,

1602, 1465, 1305, 1256, 1141, 1082; HRMS (ESI+) m/z $[M+H]^+$ calcd for $C_{16}H_{11}F_4N_2O$ 323.0802; found 323.0804.

*5-Methoxy-2-(2-(2,2,2-trifluoroethyl)phenyl)quinazolin-4(3H)-one (**3q**)*. R_f = 0.40 (hexane:EA, 7:3); white solid (19 mg, 36%) (49% based on recovered starting materials using 5.0 equiv TFA); mp 191−192 °C; ^{19}F NMR (377 MHz, $CDCl_3$) δ = -65.2 (t, *J* = 12 Hz); ^1H NMR (400 MHz, $CDCl_3$) δ = 9.22 (s, 1H), 7.70 (t, *J* = 8 Hz, 1H), 7.60 – 7.48 (m, 4H), 7.34 (d, *J* = 12 Hz, 1H), 6.96 (d, *J* = 8Hz, 1H), 4.03 (s, 3H), 3.98 (q, *J* = 12 Hz, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ = 160.7, 160.4, 152.8, 151.1, 135.4, 134.4, 133.0, 131.1, 129.6 (q, *J* = 3 Hz), 129.0, 128.7,121.5 (q, *J* = 274 Hz), 120.1, 110.9, 108.7, 56.6, 36.5 (q, *J* = 29 Hz); ATR-FTIR (cm^{-1}): 1668, 1602, 1568, 1471, 1367, 1307, 1259, 1130, 1105, 1082; HRMS (ESI+) m/z $[M+H]^+$ calcd for $C_{17}H_{14}F_3N_2O_2$ 335.1002; found 335.1002.

*5-Fluoro-2-(2-(2,2,2-trifluoroethyl)phenyl)quinazolin-4(3H)-one (**3r**)*. R_f = 0.40 (hexane:EA, 4:1); white solid (56 mg, 87%); mp 222−224 °C; ^{19}F NMR (377 MHz, $CDCl_3$) δ = -65.1 (t, *J* = 12 Hz), -109.7 – -109.8 (m); ^1H NMR (400 MHz, $CDCl_3$) δ = 10.50 (s, 1H), 7.77 – 7.71 (m, 2H), 7.57 – 7.55 (m, 4H), 7.17 (t, *J* = 8 Hz, 1H), 4.02 (q, *J* = 8 Hz, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ = 161.5 (d, J = 260 Hz), 153.5, 150.6, 135.5, 135.4, 133.9, 133.1, 131.3, 129.7 (q, $J_{C,F}$ = 3 Hz), 129.2, 129.1, 127.2, 125.8 (q, *J* = 275 Hz), 123.8 (d, *J* = 5 Hz), 114.1 (d, *J* = 20 Hz), 36.5 (q, *J* = 29 Hz); ATR-FTIR (cm^{-1}): 1668, 1614, 1469, 1425, 1361, 1249, 1130, 1091; HRMS (ESI+) m/z $[M+H]^+$ calcd for $C_{16}H_{11}F_4N_2O$: 323.0802; found 323.0802.

*5-Chloro-2-(2-(2,2,2-trifluoroethyl)phenyl)quinazolin-4(3H)-one (**3s**)*. R_f = 0.40 (hexane:EA, 4:1); white solid (41 mg, 60%); mp 235−237 °C; ^{19}F NMR (377 MHz, $CDCl_3$) δ = -65.1 (t, *J* = 12 Hz); ^1H NMR (400 MHz, $CDCl_3$) δ = 10.33 (s, 1H), 7.73 – 7.63 (m, 3H), 7.58 – 7.50 (m, 4H), 4.01 (q, *J* = 12 Hz, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ = 161.2, 153.2, 151.1, 134.5, 133.9, 133.1, 131.3, 130.1, 129.7 (q, *J* = 3 Hz), 129.3, 129.2, 129.1, 127.2, 125.8 (q, *J* = 274 Hz), 118.2, 36.6 (q, *J* = 29 Hz); ATR-FTIR (cm^{-1}): 1664, 1597, 1460, 1369, 1301, 1249, 1120, 1091, 1070; HRMS (ESI+) m/z $[M+H]^+$ calcd for $C_{16}H_{11}ClF_3N_2O$: 339.0507; found 339.0504.

*6-Fluoro-2-(2-(2,2,2-trifluoroethyl)phenyl)quinazolin-4(3H)-one (**3t**)*. R_f = 0.35 (hexane:EA, 4:1); white solid (59 mg, 78%); mp 210−212 °C; ^{19}F NMR (377 MHz, $CDCl_3$) δ = -65.2 (t, *J* = 12 Hz), -111.7 – -111. 8 (m); ^1H NMR (400 MHz, $CDCl_3$) δ = 11.08 (s, 1H), 7.84 (dd, J_1 = 4 Hz, J_2 = 4 Hz, 1H), 7.78 (dd, J_1 = 4 Hz, J_2 = 4 Hz, 1H), 7.71 – 7.69 (m, 1H), 7.58 – 7.51 (m, 4H), 4.00 (q, *J* = 12 Hz, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ = 162.7 (d, *J* = 3 Hz), 161.2 (d, *J* = 248 Hz), 152.0 (d, *J* = 2 Hz), 145.4 (d, *J* = 2 Hz), 134.3, 132.9, 131.1, 130.3 (d, *J* = 8 Hz), 129.6 (q, *J* = 3 Hz), 129.4, 128.9, 125.8 (q, *J* = 276 Hz), 123.7 (d, *J* = 24 Hz), 122.1 (d, *J* = 9 Hz), 111.5 (d, *J* = 23 Hz), 36.5 (q, *J* = 29 Hz); ATR-FTIR (cm^{-1}):

1676, 1612, 1479, 1379, 1259, 1199, 1122, 1093; HRMS (ESI+) m/z $[M+H]^+$ calcd for $C_{16}H_{11}F_4N_2O$: 323.0802; found 323.0802.

6-Bromo-2-(2-(2,2,2-trifluoroethyl)phenyl)quinazolin-4(3H)-one (***3u***). R_f = 0.35 (hexane:EA, 4:1); white solid (58 mg, 90%); mp 206−208 °C; ^{19}F NMR (377 MHz, $CDCl_3$) δ = -65.2 (t, J = 12 Hz); ^1H NMR (400 MHz, $CDCl_3$) δ = 10.79 (s, 1H), 8.36 (s, 1H), 7.89 (dd, $J_1 = J_2$ = 4 Hz, 1H), 7.69 – 7.63 (m, 2H), 7.59 – 7.51 (m, 3H), 4.00 (q, J = 12 Hz, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ = 162.0, 153.0, 147.5, 138.3, 134.2, 133.2, 131.3, 129.7, 129.6 (q, J = 3 Hz), 129.2, 129.1, 129.0, 125.9 (q, J = 275 Hz), 122.2, 121.0, 36.5 (q, J = 30 Hz); ATR-FTIR (cm^{-1}): 1674, 1602, 1471, 1361, 1282, 1246, 1134, 1068; HRMS (ESI+) m/z $[M+H]^+$ calcd for $C_{16}H_{11}BrF_3N_2O$ 383.0001; found 383.0001.

6-Methyl-2-(2-(2,2,2-trifluoroethyl)phenyl)quinazolin-4(3H)-one (***3v***). R_f = 0.45 (hexane:EA, 4:1); white solid (42 mg, 56%); mp 231−233 °C; ^{19}F NMR (377 MHz, $CDCl_3$) δ = -65.2 (t, J = 12 Hz); ^1H NMR (400 MHz, $CDCl_3$) δ = 9.97 (s, 1H), 8.09 (s, 1H), 7.68 – 7.62 (m, 3H), 7.55 – 7.50 (m, 3H), 3.99 (q, J = 12 Hz, 2H), 2.52 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ = 162.7, 151.5, 146.6, 137.9, 136.6, 134.8, 132.9, 130.9, 129.6 (q, J = 3 Hz), 129.0, 128.9, 127.7, 126.0, 125.8 (q, J = 275 Hz), 120.7, 36.5 (q, J = 30 Hz), 21.5; ATR-FTIR (cm^{-1}): 1668, 1610, 1593, 1489, 1357, 1251, 1134, 1078; HRMS (ESI+) m/z $[M+H]^+$ calcd for $C_{17}H_{14}F_3N_2O$ 319.1053; found 319.1051.

7-Fluoro-2-(2-(2,2,2-trifluoroethyl)phenyl)quinazolin-4(3H)-one (***3w***). R_f = 0.45 (hexane:EA, 4:1); white solid (42 mg, 48%); mp 218−220 °C; ^{19}F NMR (377 MHz, $CDCl_3$) δ = -65.2 (t, J = 12 Hz), -102.1 (m); ^1H NMR (400 MHz, $CDCl_3$) δ = 10.43 (s, 1H), 8.28 (dd, J_1 = 8 Hz, J_2 = 8 Hz, 1H), 7.67 – 7.65 (m, 1H), 7.56 – 7.53 (m, 3H), 7.42 (dd, J_1 = 4 Hz, J_2 = 4 Hz, 1H), 7.27 – 7.22 (m, 1H), 4.00 (q, J = 12 Hz, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ = 168.3, 165.7, 162.3, 153.9, 150.9 (d, J = 13 Hz), 134.3, 133.0, 131.2, 129.7 (q, J = 3 Hz), 129.7 (d, J = 10 Hz), 129.1 (d, J = 22 Hz), 125.8 (q, J = 275 Hz), 117.6, 116.2 (d, J = 23 Hz), 113.3 (d, J = 21 Hz), 36.5 (q, J = 29 Hz); ATR-FTIR (cm^{-1}): 1678, 1608, 1573, 1448, 1359, 1261, 1132, 1078; HRMS (ESI+) m/z $[M+H]^+$ calcd for $C_{16}H_{11}F_4N_2O$: 323.0802; found 323.0800.

7-Chloro-5-methyl-2-(2-(2,2,2-trifluoroethyl)phenyl)quinazolin-4(3H)-one (***3x***). R_f = 0.45 (hexane:EA, 4:1); white solid (33 mg, 72%); mp 248−250 °C; ^{19}F NMR (377 MHz, $CDCl_3$) δ = -65.2 (t, J = 12 Hz); ^1H NMR (400 MHz, $CDCl_3$) δ = 10.77 (s, 1H), 7.71 – 7.69 (m, 1H), 7.59 – 7.49 (m, 3H), 7.24 (s, 1H), 4.01 (q, J = 12 Hz, 2H), 2.78 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ = 163.5, 153.5, 151.3, 143.2, 140.1, 134.0, 132.9, 131.1, 130.0, 129.7 (q, J = 3 Hz), 129.2, 128.8, 125.8 (q, J = 275 Hz), 125.5, 117.8, 36.5 (q, J = 30 Hz), 22.7; ATR-FTIR (cm^{-1}): 1666, 1589, 1508, 1442, 1352, 1259, 1128, 1066; HRMS (ESI+) m/z $[M+H]^+$ calcd for $C_{17}H_{13}ClF_3N_2O$: 353.0663; found 353.0661.

*6,7-Dimethyl-2-(2-(2,2,2-trifluoroethyl)phenyl)quinazolin-4(3H)-one (**3y**)*. R_f = 0.45 (hexane:EA, 4:1); white solid (51 mg, 87%); mp 249−251 °C; ^{19}F NMR (377 MHz, $CDCl_3$) δ = -65.2 (t, *J* = 12 Hz); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 10.21 (s, 1H), 8.02 (s, 1H), 7.65 – 7.63 (m, 1H), 7.54 – 7.50 (m, 4H), 4.00 (q, *J* = 12 Hz, 2H), 2.43 (s, 3H), 2.42 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ = 162.4, 151.5, 147.0, 145.5, 137.3, 134.9, 132.9, 130.9, 129.6 (q, *J* = 2 Hz), 129.0, 128.9, 128.1, 126.4, 125.8 (q, *J* = 275 Hz), 118.7, 36.4 (q, *J* = 30 Hz), 20.6, 19.9; ATR-FTIR (cm^{-1}): 1666, 1610, 1593, 1469, 1365, 1303, 1251, 1132, 1085; HRMS (ESI+) m/z $[M+H]^+$ calcd for $C_{18}H_{16}F_3N_2O$: 333.1209; found 333.1209.

*8-Nitro-2-(2-(2,2,2-trifluoroethyl)phenyl)quinazolin-4(3H)-one (**3z**)*. R_f = 0.40 (hexane:EA, 7:3); white solid (51 mg, 84%); mp 264−266 °C; ^{19}F NMR (377 MHz, $CDCl_3$) δ = -65.4 (t, *J* = 8 Hz); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 9.66 (s, 1H), 8.52 (d, *J* = 8 Hz, 1H), 8.15 (d, *J* = 8 Hz, 1H), 7.64 – 7.54 (m, 5H), 4.2 (q, *J* = 12 Hz, 2H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ = 160.7, 156.1, 146.4, 140.1, 133.4, 132.7, 131.0, 130.5, 129.7, 129.4 (q, *J* = 3 Hz), 128.4, 128.3, 126.4, 126.3 (q, *J* = 276 Hz), 122.4, 34.7 (q, *J* = 29 Hz); ATR-FTIR (cm^{-1}): 1668, 1610, 1521, 1435, 1354, 1303, 1257, 1141, 1068; HRMS (ESI+) m/z $[M+H]^+$ calcd for $C_{16}H_{11}F_3N_3O_3$: 350.0747; found 350.0747.

*2-(p-Tolyl)-4-(2,2,2-trifluoroethoxy)quinazoline (**4a**)*. R_f = 0.70 (hexane:EA, 9:1); white solid (75 mg, 93%); mp 137−138 °C; ^{19}F NMR (377 MHz, $CDCl_3$) δ = -73.3 (t, *J* = 8 Hz); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.44 (d, *J* = 8 Hz, 2H), 8.20 (d, *J* = 8 Hz, 1H), 8.02 (d, *J* = 8 Hz, 1H), 7.87 (t, *J* = 8 Hz, 1H), 7.56 (d, *J* = 8 Hz, 1H), 7.32 (d, *J* = 8 Hz, 2H), 5.12 (q, *J* = 8 Hz, 2H), 2.45 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ = 165.1, 159.7, 152.4, 141.3, 134.8, 134.3, 129.4, 128.5, 128.1, 126.9, 123.5 (q, *J* = 276 Hz), 123.4, 114.5, 62.7 (q, *J* = 37 Hz), 21.6; ATR-FTIR (cm^{-1}): 1624, 1573, 1494, 1454, 1423, 1350, 1278, 1165, 1091; HRMS (ESI+) m/z $[M+H]^+$ calcd for $C_{17}H_{14}F_3N_2O$ 319.1053; found 319.1053.

*2-(4-Ethylphenyl)-4-(2,2,2-trifluoroethoxy)quinazoline (**4b**)*. R_f = 0.70 (hexane:EA, 9:1); white solid (57.9 mg, 87%); mp 112−114 °C; ^{19}F NMR (377 MHz, $CDCl_3$) δ = -73.3 (t, *J* = 8 Hz); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.46 (d, *J* = 8 Hz, 2H), 8.20 (d, *J* = 8 Hz, 1H), 8.02 (d, *J* = 8 Hz, 1H), 7.87 (t, *J* = 8 Hz, 1H), 7.56 (t, *J* = 8 Hz, 1H), 7.35 (d, *J* = 8 Hz, 2H), 5.13 (q, *J* = 8 Hz, 2H), 2.75 (q, *J* = 8 Hz, 2H), 1.30 (t, *J* = 8 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ = 165.0, 159.6, 152.4, 147.5, 135.1, 134.2, 128.6, 128.2, 128.1, 126.9, 123.6 (q, *J* = 275 Hz), 123.3, 114.5, 62.7 (q, *J* = 36 Hz), 29.0, 15.5; ATR-FTIR (cm^{-1}): 1624, 1579, 1558, 1494, 1421, 1352, 1267, 1165, 1091; HRMS (ESI+) m/z $[M+H]^+$ calcd for $C_{18}H_{16}F_3N_2O$ 333.1209; found 333.1209.

*2-(4-Isopropylphenyl)-4-(2,2,2-trifluoroethoxy)quinazoline (**4c**)*. R_f = 0.70 (hexane:EA, 9:1); white solid (64 mg, 97%); mp 94−96 °C; ^{19}F NMR (377 MHz, $CDCl_3$) δ = -73.3 (t, *J* = 8 Hz); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.47 (d, *J* = 8 Hz, 2H), 8.19 (d, *J* = 8 Hz, 1H), 8.02 (d, *J* = 8 Hz, 1H), 7.86 (t, *J* = 8 Hz,

1H), 7.55 (t, *J* = 8 Hz, 1H), 7.38 (d, *J* = 8 Hz, 2H), 5.11 (q, *J* = 8 Hz, 2H), 3.01 (sept, *J* = 8 Hz, 1H), 1.32 (d, *J* = 8 Hz, 6H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ = 165.0, 159.7, 152.4, 152.1, 135.3, 134.2, 128.6, 128.1, 126.9, 126.8, 123.6 (q, *J* = 275 Hz), 123.3, 114.5, 62.6 (q, *J* = 37 Hz), 34.2, 24.0; ATR-FTIR (cm^{-1}): 1622, 1585, 1556, 1492, 1417, 1348, 1273, 1163, 1089; HRMS (ESI+) m/z $[M+H]^+$ calcd for $C_{19}H_{18}F_3N_2O$ 347.1366; found 347.1366.

*2-(4-(Tert-butyl)phenyl)-4-(2,2,2-trifluoroethoxy)quinazoline (**4d**)*. R_f = 0.70 (hexane:EA, 9:1); white solid (60 mg, 93%); mp 108−110 °C; ^{19}F NMR (377 MHz, $CDCl_3$) δ = -73.3 (t, *J* = 8 Hz); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.47 (d, *J* = 8 Hz, 2H), 8.20 (d, *J* = 8 Hz, 1H), 8.02 (d, *J* = 8 Hz, 1H), 7.86 (t, *J* = 8 Hz, 1H), 7.57 – 7.53 (m, 3H), 5.11 (q, *J* = 8 Hz, 2H), 1.40 (s, 9H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ = 165.0, 159.6, 154.3, 152.4, 134.9, 134.2, 128.3, 128.2, 126.9, 125.6, 123.6 (q, *J* = 276 Hz), 123.3, 114.5, 62.6 (q, *J* = 6 Hz), 35.0, 31.4; ATR-FTIR (cm^{-1}): 1625, 1577, 1494, 1419, 1350, 1267, 1168, 1109, 1089; HRMS (ESI+) m/z $[M+H]^+$ calcd for $C_{20}H_{20}F_3N_2O$ 361.1522; found 361.1522.

*2-Phenyl-4-(2,2,2-trifluoroethoxy)quinazoline (**4e**)*. R_f = 0.70 (hexane:EA, 9:1); white solid (48 mg, 88%); mp 123−124 °C; ^{19}F NMR (377 MHz, $CDCl_3$) δ = -73.3 (t, *J* = 8 Hz); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.57 – 8.54 (m, 2H), 8.22 (d, *J* = 8 Hz, 1H), 8.04 (d, *J* = 8 Hz, 1H), 7.88 (t, *J* = 4 Hz, 1H), 7.60 – 7.56 (m, 1H), 7.54 – 7.51 (m, 3H), 5.14 (q, *J* = 8 Hz, 2H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ = 165.2, 159.6, 152.4, 137.5, 134.3, 131.0, 128.6, 128.5, 128.2, 127.2, 123.5 (q, *J* = 275 Hz), 114.6, 62.7 (q, *J* = 36 Hz); ATR-FTIR (cm^{-1}): 1620, 1575, 1498, 1419, 1352, 1263, 1163, 1118, 1091; HRMS (ESI+) m/z $[M+H]^+$ calcd for $C_{16}H_{12}F_3N_2O$: 305.0896; found 305.0896.

*2-(4-Methoxyphenyl)-4-(2,2,2-trifluoroethoxy)quinazoline (**4f**)*. R_f = 0.50 (hexane:EA, 9:1); white solid (61 mg, 92%); mp 125−127 °C; ^{19}F NMR (377 MHz, $CDCl_3$) δ = -73.3 (t, *J* = 8 Hz); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.50 (d, *J* = 8 Hz, 2H), 8.17 (d, *J* = 8 Hz, 1H), 7.98 (d, *J* = 8 Hz), 7.84 (t, *J* = 8 Hz, 1H), 7.53 (t, *J* = 8 Hz, 1H), 7.02 (d, *J* = 8 Hz, 2H), 5.10 (q, *J* = 8 Hz, 2H), 3.90 (s, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ = 165.0, 162.1, 159.3, 152.5, 134.2, 130.2, 127.9, 126.6, 123.6 (q, *J* = 275 Hz), 123.4, 114.3, 113.9, 62.6 (q, *J* = 36 Hz), 55.5; ATR-FTIR (cm^{-1}): 1622, 1579, 1517, 1456, 1354, 1251, 1159, 1159, 1091; HRMS (ESI+) m/z $[M+H]^+$ calcd for $C_{17}H_{14}F_3N_2O_2$ 335.1002; found 335.1002.

*2-(4-Fluorophenyl)-4-(2,2,2-trifluoroethoxy)quinazoline (**4g**)*. R_f = 0.70 (hexane:EA, 9:1); white solid (44 mg, 93%); mp 131−133 °C; ^{19}F NMR (377 MHz, $CDCl_3$) δ = -73.3 (t, *J* = 8 Hz), -110.02 – -110.10 (m); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.58 – 8.54 (m, 2H), 8.21 (d, *J* = 8 Hz, 1H), 8.01 (d, *J* = 8 Hz, 1H), 7.88 (t, *J* = 8 Hz, 1H), 7.58 (t, *J* = 8 Hz, 1H), 7.21 – 7.17 (m, 2H), 5.11 (q, *J* = 8 Hz, 2H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ = 165.2, 164.9 (d, *J* = 248 Hz), 158.6, 152.3, 134.4, 133.7 (d, *J* = 3 Hz), 130.7 (d, *J* = 9 Hz), 128.1, 127.2, 123.5 (q, *J* = 276 Hz), 123.4, 115.6 (d, *J* = 21 Hz), 114.5, 62.6 (q, *J* = 36 Hz);

ATR-FTIR (cm^{-1}): 1622, 1577, 1514, 1498, 1404, 1348, 1276, 1163, 1089; HRMS (ESI+) m/z $[M+H]^+$ calcd for $C_{16}H_{11}F_4N_2O$: 323.0802; found 323.0799.

*2-(4-Chlorophenyl)-4-(2,2,2-trifluoroethoxy)quinazoline (**4h**)*. R_f = 0.70 (hexane:EA, 9:1); white solid (58.9 mg, 89%); mp 128−130 °C; ^{19}F NMR (377 MHz, $CDCl_3$) δ = - 73.3 (t, *J* = 8 Hz); ^1H NMR (400 MHz, $CDCl_3$) δ = 8.50 (d, *J* = 8 Hz, 2H), 8.22 (d, *J* = 8 Hz, 1H), 8.02 (d, *J* = 8 Hz, 1H), 7.89 (t, *J* = 8 Hz, 1H), 7.60 (t, *J* = 8 Hz, 1H), 7.49 (d, *J* = 8 Hz, 2H), 5.1 (q, *J* = 8 Hz, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ = 165.2, 158.4, 152.2, 137.1, 136.0, 134.4, 129.8, 128.8, 128.2, 127.3, 123.5 (q, *J* = 276 Hz), 123.4, 114.5, 62.8 (q, *J* = 36 Hz); ATR-FTIR (cm^{-1}): 1624, 1585, 1575, 1498, 1421, 1402, 1267, 1159, 1091; HRMS (ESI+) m/z $[M+H]^+$ calcd for $C_{16}H_{11}ClF_3N_2O$: 339.0507; found 339.0507.

*2-(4-Bromophenyl)-4-(2,2,2-trifluoroethoxy)quinazoline (**4i**)*. R_f = 0.70 (hexane:EA, 9:1); white solid (47.5 mg, 75%); mp 124−125 °C; ^{19}F NMR (377 MHz, $CDCl_3$) δ = -73.3 (t, *J* = 8 Hz); ^1H NMR (400 MHz, $CDCl_3$) δ = 8.43 (d, *J* = 8 Hz, 2H), 8.22 (d, *J* = 8 Hz, 1H), 8.02 (d, *J* = 8 Hz, 1H), 7.65 (d, *J* = 8 Hz, 2H), 7.60 (t, *J* = 8 Hz, 1H), 5.11 (q, *J* = 8 Hz, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ = 165.2, 158.5, 152.2, 136.4, 134.5, 131.8, 130.1, 128.2, 127.4, 125.7, 123.5 (q, *J* = 276 Hz), 123.4, 114.6, 62.8 (q, *J* = 36 Hz); ATR-FTIR (cm^{-1}): 1622, 1573, 1556, 1496, 1400, 1348, 1271, 1161, 1089; HRMS (ESI+) m/z $[M+H]^+$ calcd for $C_{16}H_{11}BrF_3N_2O$: 383.0001; found 383.0001.

*2-(4-Iodophenyl)-4-(2,2,2-trifluoroethoxy)quinazoline (**4j**)*. R_f = 0.70 (hexane:EA, 9:1); white solid (38.2 mg, 68%); mp 133−135 °C; ^{19}F NMR (377 MHz, $CDCl_3$) δ = -73.3 (t, *J* = 8 Hz); ^1H NMR (400 MHz, $CDCl_3$) δ = 8.24 (d, *J* = 8 Hz, 2H), 8.18 (d, *J* = 8 Hz, 1H), 7.88 – 7.82 (m, 3H), 7.57 (t, *J* = 8 Hz, 1H), 5.07 (q, *J* = 8 Hz, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ = 165.1, 158.6, 152.2, 137.8, 137.0, 134.4, 130.1, 128.2, 127.4, 123.5 (q, *J* = 276 Hz), 123.4, 114.6, 98.0, 62.8 (q, *J* = 36 Hz); ATR-FTIR (cm^{-1}): 1622, 1581, 1494, 1419, 1348, 1261, 1182, 1155, 1085; HRMS (ESI+): m/z $[M+H]^+$ calcd for $C_{16}H_{11}F_3IN_2O$: 430.9863, found 430.9850.

*2-(3,5-Difluorophenyl)-4-(2,2,2-trifluoroethoxy)quinazoline (**4k**)*. R_f = 0.70 (hexane:EA, 9:1); white solid (62.8 mg, 95%); mp 138−139 °C; ^{19}F NMR (377 MHz, $CDCl_3$) δ = -73.3 (t, *J* = 8 Hz), -109.7 – -109.8 (m); ^1H NMR (400 MHz, $CDCl_3$) δ = 8.18 (d, *J* = 8 Hz, 1H), 8.03 – 7.98 (m, 3H), 7.90 – 7.86 (m, 1H), 7.61 – 7.57 (m, 1H), 6.94 – 6.89 (m, 1H), 5.06 (q, *J* = 8 Hz, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ = 165.3, 164.5 (d, *J* = 12 Hz), 162.1 (d, *J* = 12 Hz), 157.1 (t, *J* = 4 Hz), 152.0, 141.0 (t, *J* = 10 Hz), 134.6, 128.3, 127.8, 123.5 (q, *J* = 276 Hz), 123.4, 114.8, 111.2 (d, *J* = 26 Hz), 111.1 (d, *J* = 12 Hz), 106.0 (t, *J* = 26 Hz), 62.9 (q, *J* = 36 Hz); ATR-FTIR (cm^{-1}): 1629, 1598, 1564, 1494, 1421, 1355, 1269, 1168, 1111, 1080, 1024; HRMS (ESI+) m/z $[M+H]^+$ calcd for $C_{16}H_{10}F_5N_2O$: 341.0708; found: 341.0704.

*2-(4-Nitrophenyl)-4-(2,2,2-trifluoroethoxy)quinazoline (**4l**)*. R_f = 0.60 (hexane:EA, 9:1); white solid (66 mg, 84%); mp 166−167 °C; ^{19}F NMR (377 MHz, $CDCl_3$) δ = -73.3 (t, *J* = 8 Hz); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.72 (d, *J* = 8 Hz, 2H), 8.35 (d, *J* = 8 Hz, 2H), 8.26 (d, *J* = 8 Hz, 1H), 8.07 (d, *J* = 8 Hz, 1H), 7.94 (t, *J* = 8 Hz, 1H), 7.66 (t, *J* = 8 Hz, 1H), 5.14 (q, *J* = 8 Hz, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ = 165.5, 157.2, 152.1, 149.4, 143.3, 134.8, 129.3, 128.5, 128.2, 123.8, 123.5, 123.4 (q, *J* = 276 Hz), 114.8, 63.0 (q, *J* = 36 Hz); ATR-FTIR (cm^{-1}): 1622, 1575, 1519, 1423, 1344, 1271, 1178, 1155, 1122, 1089; HRMS (ESI+) m/z $[M+H]^+$ calcd for $C_{16}H_{11}F_3N_3O_3$: 350.0747; found 350.0747.

*4-(2,2,2-Trifluoroethoxy)-2-(4-(trifluoromethyl)phenyl)quinazoline (**4m**)*. R_f = 0.70 (hexane:EA, 9:1); white solid (58 mg, 95%); mp 146−147 °C; ^{19}F NMR (377 MHz, $CDCl_3$) δ = -62.7, -73.3 (t, *J* = 8 Hz); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.67 (d, *J* = 8 Hz, 2H), 8.24 (d, *J* = 8 Hz, 1H), 8.06 (d, *J* = 8 Hz, 1H), 7.94 – 7.90 (m, 1H), 7.77 (d, *J* = 8 Hz, 2H), 7.65 – 7.61 (m, 1H), 5.13 (q, *J* = 8 Hz, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ = 165.3, 158.1, 152.2, 140.8, 134.6, 132.9 (q, *J* = 32 Hz), 128.8, 128.4, 127.8, 125.6 (q, *J* = 4 Hz), 123.5, 123.4 (q, *J* = 275 Hz), 122.9, 114.8, 62.9 (q, *J* = 37 Hz); ATR-FTIR (cm^{-1}): 1624, 1577, 1558, 1494, 1423, 1321, 1267, 1161, 1116, 1091, 1064; HRMS (ESI+) m/z $[M+H]^+$ calcd for $C_{17}H_{11}F_6N_2O$: 373.0770; found 373.0770.

*4-(4-(2,2,2-Trifluoroethoxy)quinazolin-2-yl)benzonitrile (**4n**)*. R_f = 0.70 (hexane:EA, 9:1); white solid (60.9 mg, 91%); mp 174−176 °C; ^{19}F NMR (377 MHz, $CDCl_3$) δ = -73.3 (t, *J* = 8 Hz); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.68 (t, *J* = 12 Hz, 2H), 8.25 (d, *J* = 8 Hz, 1H), 8.06 (d, *J* = 8 Hz, 1H), 7.93 (t, *J* = 8 Hz, 1H), 7.81 (d, *J* = 8 Hz, 2H), 7.65 (t, *J* = 8 Hz, 1H), 5.13 (q, *J* = 8 Hz, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ = 165.3, 157.4, 152.0, 141.5, 134.7, 132.3, 128.9, 128.4, 128.0, 123.5, 123.4 (q, *J* = 275 Hz), 118.8, 114.8, 114.1, 62.9 (q, *J* = 37 Hz); ATR-FTIR (cm^{-1}): 2227, 1618, 1573, 1492, 1425, 1352, 1282, 1259, 1165, 1091; HRMS (ESI+) m/z $[M+H]^+$ calcd for $C_{17}H_{11}F_3N_3O$: 330.0849; found 330.0849.

*2-([1,1'-Biphenyl]-4-yl)-4-(2,2,2-trifluoroethoxy)quinazoline (**4o**)*. R_f = 0.70 (hexane:EA, 9:1); white solid (49 mg, 77%); mp 132−134 °C; ^{19}F NMR (377 MHz, $CDCl_3$) δ = -73.3 (t, *J* = 8 Hz); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.63 (d, *J* = 8 Hz, 2H), 8.22 (d, *J* = 8 Hz, 1H), 8.05 (d, *J* = 8 Hz, 1H), 7.91 – 7.87 (m, 1H), 7.76 (d, *J* = 8 Hz, 2H), 7.70 (d, *J* = 8 Hz, 2H), 7.61 – 7.57 (m, 1H), 7.49 (t, *J* = 8 Hz, 2H), 7.41 – 7.38 (m, 1H), 5.15 (q, *J* = 8 Hz, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ = 165.1, 159.3, 152.4, 143.6, 140.7, 136.5, 134.3, 129.1, 129.0, 128.2, 127.8, 127.4, 127.3, 126.6, 123.6 (q, *J* = 276 Hz), 123.4, 114.6, 62.7 (q, *J* = 36 Hz); ATR-FTIR (cm^{-1}): 1622, 1577, 1552, 1492, 1419, 1400, 1350, 1269, 1170, 1141, 1089; HRMS (ESI+) m/z $[M+H]^+$ calcd for $C_{22}H_{16}F_3N_2O$ 381.1209; found 381.1209.

*2-(3-Bromophenyl)-4-(2,2,2-trifluoroethoxy)quinazoline (**4p**)*. R_f = 0.70 (hexane:EA, 9:1); white solid (54 mg, 86%); mp 140−142 °C; ^{19}F NMR (377 MHz, $CDCl_3$) δ = -73.3 (t, *J* = 8 Hz); ^{1}H NMR (400 MHz,

$CDCl_3$) δ = 8.68 (s, 1H), 8.48 (d, *J* = 8 Hz, 1H), 8.21 (d, *J* = 8 Hz, 1H), 8.03 (d, *J* = 12 Hz, 1H), 7.89 (t, *J* = 8 Hz, 1H), 7.64 – 7.58 (m, 2H), 7.38 (t, *J* = 8 Hz, 1H), 5.11 (q, *J* = 8 Hz, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ = 165.2, 158.0, 152.2, 139.6, 134.5, 133.8, 131.4, 130.1, 128.3, 127.5, 127.1, 123.5 (q, *J* = 275 Hz), 123.4, 122.9, 114.7, 62.9 (q, *J* = 36 Hz); ATR-FTIR (cm^{-1}): 1622, 1583, 1556, 1496, 1417, 1350, 1267, 1168, 1099; HRMS (ESI+) m/z $[M+H]^+$ calcd for $C_{16}H_{11}BrF_3N_2O$: 383.0001; found 383.0001.

5-Fluoro-2-phenyl-4-(2,2,2-trifluoroethoxy)quinazoline ***(4r)***. R_f = 0.70 (hexane:EA, 9:1); white solid (59.3 mg, 88%); mp 138−140 °C; ^{19}F NMR (377 MHz, $CDCl_3$) δ = -73.2 (t, *J* = 8 Hz), -107.6 – -107.7 (m); ^1H NMR (400 MHz, $CDCl_3$) δ = 8.50 – 8.48 (m, 2H), 7.80 – 7.72 (m, 2H), 7.52 – 7.50 (m, 3H), 7.19 – 7.15 (m, 1H), 5.07 (q, *J* = 8 Hz, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ = 164.1 (d, *J* = 5 Hz), 160.0 (d, *J* = 2 Hz), 159.5, 156.9, 154.1, 136.8, 134.2 (d, *J* = 10 Hz), 131.3, 128.6 (d, *J* = 4 Hz), 124.1 (d, *J* = 4 Hz), 123.4 (q, *J* = 275 Hz), 112.6 (d, *J* = 21 Hz), 105.3 (d, *J* = 12 Hz), 62.9 (q, *J* = 37 Hz); ATR-FTIR (cm^{-1}): 1627, 1577, 1489, 1415, 1334, 1269, 1163, 1114, 1064; HRMS (ESI+) m/z $[M+H]^+$ calcd for $C_{16}H_{11}F_4N_2O$ 323.0802; found 323.0801.

5-Chloro-2-phenyl-4-(2,2,2-trifluoroethoxy)quinazoline ***(4s)***. R_f = 0.70 (hexane:EA, 9:1); white solid (25 mg, 83%); mp 132−133 °C; ^{19}F NMR (377 MHz, $CDCl_3$) δ = -73.0 (t, *J* = 8 Hz); ^1H NMR (400 MHz, $CDCl_3$) δ = 8.49 – 8.46 (m, 2H), 7.88 (d, *J* = 8 Hz, 1H), 7.67 (t, *J* = 8 Hz, 1H), 7.55 – 7.49 (m, 4H), 5.02 (q, *J* = 8 Hz, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ = 164.3, 159.4, 154.4, 136.7, 133.5, 131.3, 130.7, 129.6, 128.6, 128.5, 127.4, 123.5 (q, *J* = 276 Hz), 113.2, 63.1 (q, *J* = 37 Hz); ATR-FTIR (cm^{-1}): 1625, 1608, 1570, 1485, 1396, 1332, 1261, 1165, 1064; HRMS (ESI+) m/z $[M+H]^+$ calcd for $C_{16}H_{11}ClF_3N_2O$: 339.0507; found 339.0506.

6-Fluoro-2-phenyl-4-(2,2,2-trifluoroethoxy)quinazoline ***(4t)***. R_f = 0.70 (hexane:EA, 9:1); white solid (67.1 mg, 98%); mp 121−123 °C; ^{19}F NMR (377 MHz, $CDCl_3$) δ = -73.3 (t, *J* = 8 Hz), -110.7 – -110.8 (m); ^1H NMR (400 MHz, $CDCl_3$) δ = 8.53 (dd, $J_1 = J_2$ = 4 Hz, 2H), 8.05 (dd, J_1 = 4 Hz, J_2 = 8 Hz, 1H), 7.82 (dd, $J_1 = J_2$ = 4 Hz, 1H), 7.67 – 7.62 (m, 1H), 7.53 – 7.52 (m, 3H), 5.13 (q, *J* = 8 Hz, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ = 164.8 (d, *J* = 5 Hz), 161.8, 159.3, 159.1 (d, *J* = 3 Hz), 149.4, 137.2, 131.0, 130.8 (d, *J* = 8 Hz), 128.5 (d, *J* = 25 Hz), 124.3 (d, *J* = 25 Hz), 123.4 (q, *J* = 276 Hz), 115.1 (d, *J* = 9 Hz), 107.5 (d, *J* = 23 Hz), 62.8 (q, *J* = 36 Hz); ATR-FTIR (cm^{-1}): 1629, 1591, 1504, 1421, 1271, 1240, 1165, 1100, 1085; HRMS (ESI+) m/z $[M+H]^+$ calcd for $C_{16}H_{11}F_4N_2O$ 323.0802; found 323.0799.

6-Bromo-2-phenyl-4-(2,2,2-trifluoroethoxy)quinazoline ***(4u)***. R_f = 0.70 (hexane:EA, 9:1); white solid (35.9 mg, 88%); mp 174−176 °C; ^{19}F NMR (377 MHz, $CDCl_3$) δ = -73.2 (t, *J* = 8 Hz); ^1H NMR (400 MHz, $CDCl_3$) δ = 8.51 (d, *J* = 8 Hz, 2H), 8.31 (s, 1H), 7.94 – 7.86 (m, 2H), 7.52 – 7.51 (m, 3H), 5.09 (q, *J*

= 8 Hz, 2H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ = 164.1, 159.8, 151.0, 137.8, 137.1, 131.2, 129.9, 128.7, 128.5, 125.8, 123.4 (q, *J* = 275 Hz), 120.6, 115.6, 62.9 (q, *J* = 36 Hz); ATR-FTIR (cm^{-1}): 1616, 1570, 1558, 1485, 1411, 1267, 1155, 1130, 1091; HRMS (ESI+) m/z $[M+H]^+$ calcd for $C_{16}H_{11}BrF_3N_2O$: 383.0001; found 383.0001.

*6-Methyl-2-phenyl-4-(2,2,2-trifluoroethoxy)quinazoline (**4v**)*. R_f = 0.70 (hexane:EA, 9:1); white solid (54.2 mg, 80%); mp 162−163 °C; ^{19}F NMR (377 MHz, $CDCl_3$) δ = -73.3 (t, *J* = 8 Hz); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.53 (d, *J* = 8 Hz, 2H), 7.94 – 7.91 (m, 2H), 7.69 (d, *J* = 8 Hz, 1H), 7.52 – 7.50 (m, 3H), 5.10 (q, *J* = 8 Hz, 2H), 2.55 (s, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ = 164.6, 158.7, 150.8, 137.6, 137.4, 136.3, 130.7, 128.6, 128.4, 127.9, 123.6 (q, *J* = 276 Hz), 122.2, 114.4, 62.6 (q, *J* = 36 Hz), 21.8; ATR-FTIR (cm^{-1}): 1627, 1589, 1573, 1506, 1425, 1348, 1321, 1269, 1161, 1091; HRMS (ESI+) m/z $[M+H]^+$ calcd for $C_{17}H_{14}F_3N_2O$ 319.1053; found 319.1050.

*7-Fluoro-2-phenyl-4-(2,2,2-trifluoroethoxy)quinazoline (**4w**)*. R_f = 0.70 (hexane:EA, 9:1); white solid (57.7 mg, 86%); mp 124−125 °C; ^{19}F NMR (377 MHz, $CDCl_3$) δ = -73.3 (t, *J* = 8 Hz), -102.4 (m); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.24 (d, *J* = 8 Hz, 2H), 7.91 (dd, *J* = 4 Hz, 1H), 7.35 (dd, *J* = 4 Hz, 1H), 7.26 – 7.24 (m, 3H), 7.03 (dt, J_1 = 4 Hz, J_2 = 4 Hz, 1H), 4.8 (q, *J* = 8 Hz, 2H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ = 166.3 (d, *J* = 254 Hz), 164.8, 160.6, 154.2 (d, *J* = 14 Hz), 137.1, 131.2, 128.6, 126.0 (d, *J* = 10 Hz), 123.5 (q, *J* = 276 Hz), 117.1 (d, *J* = 24 Hz), 112.4 (d, *J* = 21 Hz), 111.4 (d, *J* = 1 Hz), 62.7 (q, *J* = 37 Hz); ATR-FTIR (cm^{-1}): 1627, 1579, 1490, 1456, 1419, 1394, 1355, 1267, 1163, 1085; HRMS (ESI+) m/z $[M+H]^+$ calcd for $C_{16}H_{11}F_4N_2O$ 323.0802; found 323.0802.

*6,7-Dimethyl-2-phenyl-4-(2,2,2-trifluoroethoxy)quinazoline (**4y**)*. R_f = 0.70 (hexane:EA, 9:1); white solid (15.8 mg, 78%); mp 148−150 °C; ^{19}F NMR (377 MHz, $CDCl_3$) δ = -73.3 (t, *J* = 8 Hz); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.53 – 8.50 (m, 2H), 7.88 (s, 1H), 7.78 (s, 1H), 7.52 – 7.49 (m, 3H), 5.08 (q, *J* = 8 Hz, 2H), 2.47 (s, 3H), 2.44 (s, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ = 164.4, 158.7, 151.3, 145.0, 137.8, 137.2, 130.6, 128.5, 128.3, 127.7, 123.7 (q, *J* = 275 Hz), 112.7, 62.5 (q, *J* = 36 Hz), 20.8. 20.2 ATR-FTIR (cm^{-1}): 1631, 1593, 1579, 1558, 1489, 1427, 1348, 1269, 1163, 1097; HRMS (ESI+) m/z $[M+H]^+$ calcd for $C_{18}H_{16}F_3N_2O$: 333.1209; found 333.1209.

*8-Nitro-2-phenyl-4-(2,2,2-trifluoroethoxy)quinazoline (**4z**)*. R_f = 0.70 (hexane:EA, 4:1); white solid (28 mg, 61%); mp 213−215 °C; ^{19}F NMR (377 MHz, $CDCl_3$) δ = -73.2 (t, *J* = 8 Hz); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.55 (d, *J* = 8 Hz, 2H), 8.41 (d, *J* = 8 Hz, 1H), 8.23 (d, *J* = 8 Hz, 1H), 7.62 (t, *J* = 8 Hz, 1H), 7.54 – 7.48 (m, 3H), 5.14 (q, *J* = 8 Hz); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ = 164.9, 161.6, 146.8, 144.3, 136.3, 132.0, 129.1, 128.7, 127.9, 125.6, 123.2 (q, *J* = 276 Hz), 115.7, 63.2 (q, *J* = 37 Hz); ATR-FTIR

(cm^{-1}): 1627, 1575, 1531, 1487, 1419, 1352, 1327, 1267, 1165, 1097; HRMS (ESI+) m/z [M+H]$^+$ calcd for $C_{16}H_{11}F_3N_3O_3$: 350.0747; found 350.0747.

*2-(p-Tolyl)-3-(2,2,2-trifluoroethyl)quinazolin-4(3H)-one (**5a**)*. R_f = 0.50 (hexane:EA, 4:1); colourless semi-solid (72 mg, 89%); ^{19}F NMR (377 MHz, $CDCl_3$) δ = -68.4 (t, *J* = 8 Hz); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.33 (d, *J* = 8 Hz, 1H), 7.80 – 7.75 (m, 2H), 7.53 (t, *J* = 8 Hz, 1H), 7.41 – 7.32 (m, 4H), 4.84 (q, *J* = 8 Hz, 2H), 2.44 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ = 162.1, 155.4, 146.9, 140.7, 135.2, 131.6, 129.8, 128.1, 127.9, 127.7, 127.3, 123.3 (q, *J* = 279 Hz), 120.3, 45.3 (q, *J* = 35 Hz), 21.5; ATR-FTIR (cm^{-1}): 1672, 1587, 1469, 1415, 1365, 1257, 1161, 1082; HRMS (ESI+) m/z [M+H]$^+$ calcd for $C_{17}H_{14}F_3N_2O$ 319.1053; found 319.1053.

*2-(4-Ethylphenyl)-3-(2,2,2-trifluoroethyl)quinazolin-4(3H)-one (**5b**)*. R_f = 0.50 (hexane:EA, 4:1); colourless semi-solid (57 mg, 89%); ^{19}F NMR (377 MHz, $CDCl_3$) δ = -68.4 (t, *J* = 8 Hz); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.34 (d, *J* = 8 Hz, 1H), 7.82 – 7.74 (m, 2H), 7.54 (t, *J* = 8 Hz, 1H), 7.44 – 7.35 (m, 4H), 4.85 (q, *J* = 8 Hz, 2H), 2.74 (q, *J* = 8 Hz, 2H), 1.28 (t, *J* = 8 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ = 162.1, 155.4, 146.9, 135.2, 131.8, 128.7, 128.2, 127.9, 127.7, 127.5, 127.3, 123.3 (q, *J* = 279 Hz), 120.3, 45.3 (q, *J* = 35 Hz), 28.9, 15.4; ATR-FTIR (cm^{-1}): 1697, 1591, 1473, 1417, 1367, 1253, 1163, 1087; HRMS (ESI+) m/z [M+H]$^+$ calcd for $C_{18}H_{16}F_3N_2O$ 333.1209; found 333.1209.

*2-(4-Isopropylphenyl)-3-(2,2,2-trifluoroethyl)quinazolin-4(3H)-one (**5c**)*. R_f = 0.50 (hexane:EA, 4:1); white solid (57 mg, 90%); mp 139−140 °C; ^{19}F NMR (377 MHz, $CDCl_3$) δ = -68.4 (t, *J* = 8 Hz); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.33 (d, *J* = 8 Hz, 1H), 7.81 – 7.73 (m, 2H), 7.53 (t, *J* = 8 Hz, 1H), 7.45 – 7.37 (m, 4H), 4.85 (q, *J* = 8 Hz, 2H), 2.99 (sept, *J* = 8 Hz, 1H), 1.29 (d, *J* = 8 Hz, 6H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ = 162.1, 155.5, 151.4, 146.9, 135.2, 131.9, 128.1, 127.8, 127.6, 127.5, 127.3, 123.3 (q, *J* = 280 Hz), 120.3, 45.3 (q, *J* = 35 Hz), 34.2, 23.9; ATR-FTIR (cm^{-1}): 1699, 1589, 1475, 1415, 1365, 1261, 1157, 1085; HRMS (ESI+) m/z [M+H]$^+$ calcd for $C_{19}H_{18}F_3N_2O$ 347.1366; found 347.1366.

*2-(4-(Tert-butyl)phenyl)-3-(2,2,2-trifluoroethyl)quinazolin-4(3H)-one (**5d**)*. R_f = 0.50 (hexane:EA, 4:1); white solid (95 mg, 91%); mp 147−148 °C; ^{19}F NMR (377 MHz, $CDCl_3$) δ = -68.3 (t, *J* = 8 Hz); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.33 (d, *J* = 8 Hz, 1H), 7.80 – 7.73 (m, 2H), 7.55 – 7.44 (m, 5H), 4.85 (q, *J* = 8 Hz, 2H), 1.36 (s, 9H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ = 162.0, 155.4, 153.7, 146.9, 135.1, 131.5, 127.9, 127.8, 127.6, 127.2, 126.1, 123.3 (q, *J* = 280 Hz), 120.3, 45.3 (q, *J* = 35 Hz), 35.0, 31.2; ATR-FTIR (cm^{-1}): 1695, 1587, 1475, 1415, 1365, 1261, 1155, 1083; HRMS (ESI+) m/z [M+H]$^+$ calcd for $C_{20}H_{20}F_3N_2O$ 361.1522; found 361.1522.

*2-Phenyl-3-(2,2,2-trifluoroethyl)quinazolin-4(3H)-one (**5e**)*. R_f = 0.50 (hexane:EA, 4:1); colourless semi-solid (48 mg, 82%); ^{19}F NMR (377 MHz, $CDCl_3$) δ = -68.4 (t, *J* = 8 Hz); ^{1}H NMR (400 MHz,

$CDCl_3$) δ = 8.34 (d, *J* = 8 Hz, 1H), 7.82 – 7.74 (m, 2H), 7.56 – 7.51 (m, 6H), 4.82 (q, *J* = 8 Hz, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ = 161.9, 155.2, 146.8, 135.2, 134.4, 130.4, 129.2, 128.2, 127.9, 127.8, 127.3, 123.2 (q, *J* = 279 Hz), 120.3, 45.2 (q, *J* = 35 Hz); ATR-FTIR (cm^{-1}): 1695, 1593, 1473, 1369, 1332, 1261, 1165, 1087; HRMS (ESI+) m/z $[M+H]^+$ calcd for $C_{16}H_{12}F_3N_2O$: 305.0896; found 305.0896.

*2-(4-Methoxyphenyl)-3-(2,2,2-trifluoroethyl)quinazolin-4(3H)-one (**5f**)*. R_f = 0.40 (hexane:EA, 4:1); colourless semi-solid (65 mg, 61%); ^{19}F NMR (377 MHz, $CDCl_3$) δ = -68.4 (t, *J* = 8 Hz); ^1H NMR (400 MHz, $CDCl_3$) δ = 8.33 (d, *J* = 8 Hz, 1H), 7.82-7.73 (m, 2H), 7.54 (t, *J* = 8 Hz, 1H), 7.46 (d, *J* = 8 Hz, 2H), 7.04 (d, *J* = 8 Hz, 2H), 4.85 (q, *J* = 8 Hz, 2H), 3.88 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ = 162.2, 161.1, 155.2, 146.9, 135.2, 129.8, 127.8, 127.6, 127.3, 126.8, 123.3 (q, *J* = 279 Hz), 120.2, 114.6, 55.6, 45.8 (q, *J* = 35 Hz); ATR-FTIR (cm^{-1}): 1689, 1589, 1510, 1473, 1373, 1249, 1145, 1085; HRMS (ESI+) m/z $[M+H]^+$ calcd for $C_{17}H_{14}F_3N_2O_2$ 335.1002; found 335.1002.

*2-(4-Fluorophenyl)-3-(2,2,2-trifluoroethyl)quinazolin-4(3H)-one (**5g**)*. R_f = 0.45 (hexane:EA, 4:1); colourless semi-solid (41 mg, 75%); ^{19}F NMR (377 MHz, $CDCl_3$) δ = -68.5 (t, *J* = 8 Hz), -108.9 – -109.0 (m); ^1H NMR (400 MHz, $CDCl_3$) δ = 8.36 (d, *J* = 8 Hz, 1H), 7.85 – 7.81 (m, 1H), 7.76 (t, *J* = 8 Hz, 1H), 7.60 – 7.53 (m, 3H), 7.28 – 7.24 (m, 2H), 4.83 (q, *J* = 8 Hz, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ = 163.7 (d, *J* = 250 Hz), 161.9, 154.2, 146.6, 135.4, 130.6 (d, *J* = 4 Hz), 130.5 (d, *J* = 9 Hz), 128.0, 127.9, 127.4, 123.3 (q, *J* = 280 Hz), 120.3, 116.5 (d, *J* = 22 Hz), 45.3 (q, *J* = 35 Hz); ATR-FTIR (cm^{-1}): 1687, 1604, 1510, 1471, 1369, 1257, 1222, 1166, 1085; HRMS (ESI+) m/z $[M+H]^+$ calcd for $C_{16}H_{11}F_4N_2O$ 323.0802; found 323.0802.

*2-(4-Chlorophenyl)-3-(2,2,2-trifluoroethyl)quinazolin-4(3H)-one (**5h**)*. R_f = 0.45 (hexane:EA, 4:1); colourless semi-solid (59 mg, 76%); ^{19}F NMR (377 MHz, $CDCl_3$) δ = -68.5 (t, *J* = 8 Hz); ^1H NMR (400 MHz, $CDCl_3$) δ = 8.33 (d, *J* = 8 Hz, 1H), 7.81 (t, *J* = 8 Hz, 1H), 7.73 (d, *J* = 8 Hz, 1H), 7.57 – 7.46 (m, 5H), 4.85 (q, *J* = 8 Hz, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ = 161.8, 154.1, 146.6, 136.7, 135.4, 132.8, 129.7, 129.5, 128.0, 127.9, 127.3, 123.2 (q, *J* = 279 Hz), 120.3, 45.2 (q, *J* = 35 Hz); ATR-FTIR (cm^{-1}): 1687, 1600, 1492, 1473, 1367, 1330, 1257, 1157, 1091; HRMS (ESI+) m/z $[M+H]^+$ calcd for $C_{16}H_{11}ClF_3N_2O$: 339.0507; found 339.0507.

*2-(4-Bromophenyl)-3-(2,2,2-trifluoroethyl)quinazolin-4(3H)-one (**5i**)*. R_f = 0.45 (hexane:EA, 4:1); white solid (55 mg, 84%); mp 149−150 °C; ^{19}F NMR (377 MHz, $CDCl_3$) δ = -68.5 (t, *J* = 8 Hz); ^1H NMR (400 MHz, $CDCl_3$) δ = 8.34 (d, *J* = 8 Hz, 1H), 7.81 (t, *J* = 8 Hz, 1H), 7.75 – 7.67 (m, 3H), 7.56 (t, *J* = 8 Hz, 1H), 7.41 (t, *J* = 12 Hz, 2H), 4.85 (q, *J* = 8 Hz, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ = 161.8, 154.1, 146.6, 135.4, 133.3, 132.5, 129.9, 128.1, 127.9, 127.4, 125.0, 123.2 (q, *J* = 280 Hz), 120.3, 45.2 (q,

J = 35 Hz); ATR-FTIR (cm^{-1}): 1687, 1597, 1475, 1371, 1261, 11661, 1147, 1084; HRMS (ESI+) m/z $[M+H]^+$ calcd for $C_{16}H_{11}BrF_3N_2O$ 383.0001; found 383.0001.

*2-(4-Iodophenyl)-3-(2,2,2-trifluoroethyl)quinazolin-4(3H)-one (**5j**)*. R_f = 0.50 (hexane:EA, 4:1); white solid (42 mg, 67%); mp 141−142 °C; ^{19}F NMR (377 MHz, $CDCl_3$) δ = -68.5 (t, *J* = 8 Hz); ^1H NMR (400 MHz, $CDCl_3$) δ = 8.33 (d, *J* = 8 Hz, 1H), 7.90 (d, *J* = 8 Hz, 2H), 7.83 – 7.79 (m, 1H), 7.73 (d, *J* = 8 Hz, 1H), 7.58 – 7.54 (m, 1H), 7.26 (d, *J* = 8 Hz, 2H), 4.85 (q, *J* = 8 Hz, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ = 161.8, 154.2, 146.7, 138.4, 135.4, 133.9, 129.8, 128.0, 127.9, 127.4, 123.2 (q, *J* = 279 Hz), 120.3, 96.9, 45.2 (q, *J* = 35 Hz); ATR-FTIR (cm^{-1}): 1684, 1595, 1475, 1400, 1369, 1261, 1182, 1163, 1149, 1084; HRMS (ESI+) m/z $[M+H]^+$ calcd for $C_{16}H_{11}F_3IN_2O$ 430.9863; found 430.9863.

*2-(3,5-Difluorophenyl)-3-(2,2,2-trifluoroethyl)quinazolin-4(3H)-one (**5k**)*. R_f = 0.4 (hexane:EA, 4:1); colourless semi-solid (32 mg, 57%); ^{19}F NMR (377 MHz, $CDCl_3$) δ = -68.51 (t, *J* = 8 Hz), -106.4 (m); ^1H NMR (400 MHz, $CDCl_3$) δ = 8.34 (d, *J* = 8 Hz, 1H), 7.83 (t, *J* = 8 Hz, 1H), 7.74 (d, *J* = 8 Hz, 1H), 7.58 (t, *J* = 8 Hz, 1H), 7.10 – 7.07 (m, 2H), 7.04 – 6.99 (m, 1H), 4.81 (q, *J* = 8 Hz, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ = 164.5 (d, *J* = 12 Hz), 162.0 (d, *J* = 13 Hz), 161.5, 152.6 (t, *J* = 3 Hz), 146.4, 137.0 (t, *J* = 9 Hz), 135.5, 128.4, 128.0, 127.5, 123.1 (q, *J* = 279 Hz), 120.4, 112.1 (d, *J* = 27 Hz), 112.0 (d, *J* = 11 Hz), 106.3 (t, *J* = 24 Hz), 45.2 (q, *J* = 36 Hz); ATR-FTIR (cm^{-1}): 1699, 1589, 1469, 1438, 1375, 1330, 1259, 1161, 1130, 1093; HRMS (ESI+) m/z $[M+H]^+$ calcd for $C_{16}H_{10}F_5N_2O$: 341.0708; found: 341.0708.

*3-(2,2,2-Trifluoroethyl)-2-(4-(trifluoromethyl)phenyl)quinazolin-4(3H)-one (**5m**)*. R_f = 0.35 (hexane:EA, 4:1); colourless semi-solid (46 mg, 74%); ^{19}F NMR (377 MHz, $CDCl_3$) δ = -63.0, -68.6 (t, *J* = 8 Hz); ^1H NMR (400 MHz, $CDCl_3$) δ = 8.35 (d, *J* = 8 Hz, 1H), 7.85 – 7.81 (m, 3H), 7.74 (d, *J* = 8 Hz, 1H), 7.68 (d, *J* = 8 Hz, 2H), 7.58 (t, *J* = 8 Hz, 1H), 4.79 (q, *J* = 8 Hz, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ = 161.6, 153.7, 146.6, 137.9, 135.5, 132.5 (q, *J* = 33 Hz), 128.9, 128.3, 128.0, 127.4, 126.3 (q, *J* = 3 Hz), 123.7 (q, *J* = 271 Hz), 123.1 (q, *J* = 280 Hz), 120.4, 45.2 (q, *J* = 35 Hz); ATR-FTIR (cm^{-1}): 1695, 1595, 1572, 1475, 1375, 1325, 1261, 1163, 1130, 1085; HRMS (ESI+) m/z $[M+H]^+$ calcd for $C_{17}H_{11}F_6N_2O$: 373.0770; found 373.0770.

*4-(4-Oxo-3-(2,2,2-trifluoroethyl)-3,4-dihydroquinazolin-2-yl)benzonitrile (**5n**)*. R_f = 0.30 (hexane:EA, 4:1); colourless semi-solid (29 mg, 43%); ^{19}F NMR (377 MHz, $CDCl_3$) δ = -68.6 (t, *J* = 8 Hz); ^1H NMR (400 MHz, $CDCl_3$) δ = 8.35 (d, *J* = 8 Hz, 1H), 7.87 – 7.82 (m, 3H), 7.73 (d, *J* = 8 Hz, 1H), 7.67 (d, *J* = 8 Hz, 2H), 7.59 (t, *J* = 8 Hz, 1H), 4.77 (q, *J* = 8 Hz, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ = 161.5, 153.1, 146.4, 138.5, 135.6, 133.0, 129.2, 128.4, 128.0, 127.5, 123.0 (q, *J* = 279 Hz), 120.4, 117.8, 114.5, 45.1 (q, *J* = 35 Hz); ATR-FTIR (cm^{-1}): 2235, 1689, 1591, 1506, 1471, 1371, 1255, 1165, 1087; HRMS (ESI+) m/z $[M+H]^+$ calcd for $C_{17}H_{11}F_3N_3O$: 330.0849; found 330.0849.

*2-([1,1'-Biphenyl]-4-yl)-3-(2,2,2-trifluoroethyl)quinazolin-4(3H)-one (**5o**)*. R_f = 0.40 (hexane:EA, 4:1); white solid (49 mg, 76%); mp 174−176 °C; ^{19}F NMR (377 MHz, $CDCl_3$) δ = -68.4 (t, *J* = 8 Hz); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.37 (d, *J* = 8 Hz, 1H), 7.85 – 7.75 (m, 4H), 7.66 – 7.54 (m, 5H), 7.50 (t, *J* = 8 Hz, 2H), 7.44 – 7.39 (m, 1H), 4.90 (q, *J* = 8 Hz, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ = 162.0, 155.1, 146.9, 143.4, 140.0, 135.3, 133.2, 129.1, 128.7, 128.2, 127.9, 127.8, 127.5, 127.4, 127.3, 123.3 (q, *J* = 279 Hz), 120.3, 45.4 (q, *J* = 35 Hz); ATR-FTIR (cm^{-1}): 1697, 1591, 1521, 1471, 1417, 1367, 1336, 1247, 1186, 1147, 1087; HRMS (ESI+) m/z $[M+H]^+$ calcd for $C_{22}H_{16}F_3N_2O$ 381.1209; found 381.1209.

*2-(3-Bromophenyl)-3-(2,2,2-trifluoroethyl)quinazolin-4(3H)-one (**5p**)*. R_f = 0.50 (hexane:EA, 4:1); white solid (31 mg, 61%); mp 116−118 °C; ^{19}F NMR (377 MHz, $CDCl_3$) δ = -68.4 (t, *J* = 8 Hz); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.34 (d, *J* = 8 Hz, 1H), 7.84 – 7.80 (m, 1H), 7.76 – 7.73 (m, 1H), 7.70 – 7.68 (m, 2H), 7.59 – 7.55 (m, 1H), 7.47 – 7.40 (m, 2H), 4.80 (q, *J* = 8 Hz, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ = 161.7, 153.5, 146.6, 136.2, 135.4, 133.6, 131.3, 130.7, 128.1, 127.9, 127.4, 126.8, 123.3, 123.2 (q, *J* = 280 Hz), 120.4, 45.3 (q, *J* = 36 Hz); ATR-FTIR (cm^{-1}): 1695, 1589, 1473, 1419, 1369, 1330, 1261, 1163, 1087; HRMS (ESI+) m/z $[M+H]^+$ calcd for $C_{16}H_{11}BrF_3N_2O$: 383.0001; found 383.0001.

*5-Fluoro-2-phenyl-3-(2,2,2-trifluoroethyl)quinazolin-4(3H)-one (**5r**)*. R_f = 0.50 (hexane:EA, 4:1); colourless semi-solid (30 mg, 70%); ^{19}F NMR (377 MHz, $CDCl_3$) δ = -68.3 (t, *J* = 8 Hz), -109.4 – -109.5 (m); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.76 – 7.71 (m, 1H), 7.56 – 7.49 (m, 6H), 7.22 – 7.17 (m, 1H), 4.80 (q, *J* = 8 Hz, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ = 161.4 (d, *J* = 266 Hz), 158.8 (d, *J* = 4 Hz), 156.2, 148.6, 135.8 (d, *J* = 10 Hz), 134.1, 130.6, 129.3, 128.1, 123.8 (d, *J* = 4 Hz), 123.1 (q, *J* = 279 Hz), 114.5 (d, *J* = 21 Hz), 110.1 (d, *J* = 6 Hz), 45.5 (q, *J* = 36 Hz); ATR-FTIR (cm^{-1}): 1676, 1593, 1566, 1473, 1413, 1363, 1311, 1243, 1155, 1095; HRMS (ESI+) m/z $[M+H]^+$ calcd for $C_{16}H_{11}F_4N_2O$ 323.0802; found 323.0802.

*7-Fluoro-2-phenyl-3-(2,2,2-trifluoroethyl)quinazolin-4(3H)-one (**5w**)*. R_f = 0.50 (hexane:EA, 4:1); colourless semi-solid (39 mg, 60%); ^{19}F NMR (377 MHz, $CDCl_3$) δ = -68.4 (t, *J* = 8 Hz), -101.6 (m); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.08 (dd, $J_1 = J_2$ = 4 Hz, 1H), 7.30 – 7.25 (m, 5H), 7.13 (dd, $J_1 = J_2$ = 4 Hz, 1H), 6.99 (td, $J_1 = J_2$ = 4 Hz, 1H), 4.55 (q, *J* = 8 Hz, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ = 167.1 (d, *J* = 254 Hz), 161.2, 156.5, 149.0 (d, *J* = 13 Hz), 134.2, 130.6, 130.2 (d, *J* = 11 Hz), 129.2. 128.1, 123.2 (q, *J* = 279 Hz), 117.1 (d, *J* = 2 Hz), 116.6 (d, *J* = 24 Hz), 113.4 (d, *J* = 22 Hz), 45.3 (q, *J* = 35 Hz); ATR-FTIR (cm^{-1}): 1687, 1593, 1573, 1479, 1369, 1342, 1259, 1138, 1080; HRMS (ESI+) m/z $[M+H]^+$ calcd for $C_{16}H_{11}F_4N_2O$ 323.0802; found 323.0802.

*7-Fluoro-5-methyl-2-phenyl-3-(2,2,2-trifluoroethyl)quinazolin-4(3H)-one (**5w'**)*. R_f = 0.50 (hexane:EA, 4:1); colourless semi-solid (44 mg, 71%); ^{19}F NMR (377 MHz, $CDCl_3$) δ = -68.3 (t, *J* = 8

Hz), -103.3 – -103.4 (m); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.55 – 7.48 (m, 5H), 7.24 – 7.21 (m, 1H), 7.04 – 7.01 (m, 1H), 4.76 (q, *J* = 8 Hz, 2H), 2.90 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ = 165.7 (d, *J* = 253 Hz), 161.5, 156.2, 150.6 (d, *J* = 14 Hz), 145.4 (d, *J* = 10 Hz), 134.3, 130.5, 129.2, 128.0, 123.2 (q, *J* = 279 Hz), 118.5 (d, *J* = 23 Hz), 115.7 (d, *J* = 2 Hz), 111.5 (d, *J* = 21 Hz), 45.2 (q, *J* = 35 Hz), 23.4; ATR-FTIR (cm^{-1}): 1676, 1602, 1577, 1446, 1375, 1300, 1263, 1195, 1138, 1097; HRMS (ESI+) m/z $[M+H]^+$ calcd for $C_{17}H_{13}F_4N_2O$ 337.0959; found 337.0959.

ASSOCIATED CONTENT

Supporting Information

Electronic spectroscopic studies, melting points, and ^{1}H, ^{13}C, ^{19}F NMR spectra (DOCX)

X-ray single crystal diffraction data for **tetrameric palladacycle**, **3a**, **4e** and **5d** (CIF).

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