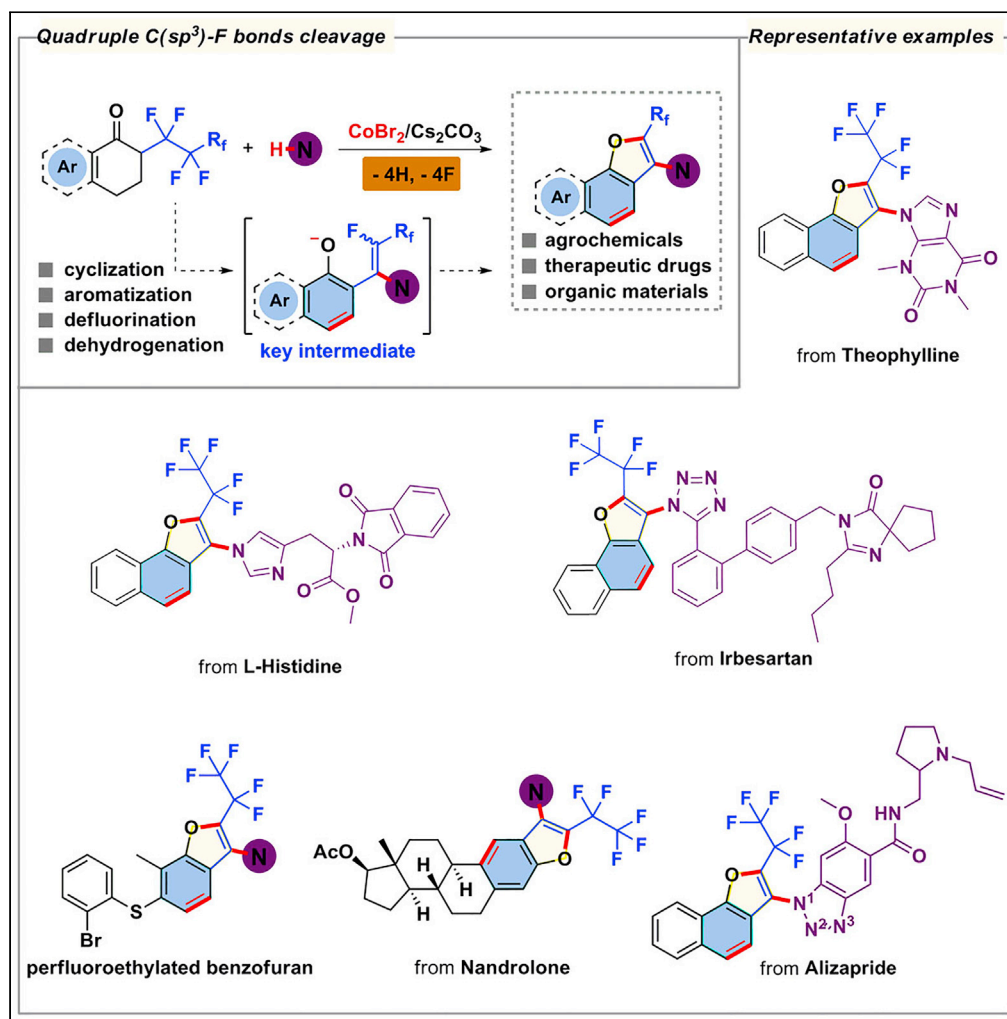


Article

Selective Quadruple C(sp³)-F Functionalization of Polyfluoroalkyl Ketones

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HIGHLIGHTS

First example of consecutive selective quadruple C(sp³)-F functionalization

Selectively and controllably partial defluorination at heteronuclear sites

Conversion to value-added chemicals by using polyfluorocarbons and nucleophiles

DFT calculations were performed to support mechanistic proposal

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Article

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Functionalization of Polyfluoroalkyl KetonesTing Xie,^{1,5} Guo-Qiang Wang,^{2,5} Ya-Wen Wang,¹ Weidong Rao,³ Haiyan Xu,⁴ Shuhua Li,^{2,*} Zhi-Liang Shen,^{1,6,*}
and Xue-Qiang Chu^{1,*}

SUMMARY

The significance of organofluorine compounds has inspired the establishment of numerous methods for the functionalization of rather inert C-F bonds. Despite advances achieved in the manipulation of C(sp²)-F bonds by employing transition-metal catalysts, such as Pd, Rh, Cu, Ni, Ru, and Ir, strategies that address the paucity of effective pathways for selective activation of multiple C(sp³)-F bonds remained challenging. In this context, we present an unprecedented coupling-aromatization-cyclization reaction of polyfluorinated ketones with diverse N- and S-nucleophiles that forms regiodefined perfluoroalkylated naphtho[1,2-b]furan/benzofuran derivatives by harnessing Co-promoted distinctive quadruple C(sp³)-F bonds cleavage relay. This chemistry involving controlled and successive selective defluorination at heteronuclear centers would greatly contribute to the preparation of drug-like heterocycles as well as the late-stage elaboration of bio-relevant compounds. Controlled experiments and DFT theoretical studies revealed that the combination of cheap cobalt salt with Cs₂CO₃ enable expeditious C-F functionalization.

INTRODUCTION

The past decades have witnessed a boom in organofluorine chemistry mainly owing to the unique physical and chemical benefits conferred by the incorporation of fluorine atom or fluorine-containing fragments into organic molecules, which have gained widespread recognition throughout drug discovery, crop protection, polymer chemistry, and materials science (Shao et al., 2015; Feng et al., 2018; Ni and Hu, 2016; Chu and Qing, 2014; Jeschke, 2004; Wang et al., 2014; Cardoso et al., 2018; Ragni et al., 2018). However, it is still challenging and highly desirable to develop reliable tools for performing controlled and selective cleavage of C-F bonds because of the notorious inertness of fluorinated entities arising from their thermodynamic stability and kinetic issues (Wang et al., 2014; Cardoso et al., 2018; Ragni et al., 2018; O'Hagan, 2008). In this context, not only C-F bond construction but also C-F bond activation and functionalization have become attractive subjects for realizing efficient preparation of oligofluorinated compounds, especially starting from readily available polyfluorinated bulk chemicals (Eisenstein et al., 2017; Ahrens et al., 2015; Amii and Uneyama, 2009).

Substantial progress has been made in the manipulation of alkenyl (Fujita et al., 2019; Hu et al., 2017, 2018; Lu et al., 2017; Thornbury and Toste, 2016; Tian et al., 2015) and aryl C(sp²)-F bonds (Shao et al., 2017; Honycutt and Hoov, 2018; Priya and Weaver, 2018; Tian et al., 2018) by means of transition-metal catalysis, photocatalysis, and electrochemical techniques (through oxidative addition, single-electron reduction, fluoride abstraction, elimination, nucleophilic substitution, etc.). Although there are many reactions involving aliphatic C-F bond activation by electrophilic compounds (Si-, B-, and P-based cations), Lewis acids, and transition metal species (Jaroschik, 2018; Shen et al., 2015; Stahl et al., 2013), selective transformations of multiple unactivated aliphatic C(sp³)-F bonds attached remote to π -system (such as benzylic and allylic moieties) is still scarce (Wang et al., 2018a, 2018b; Kojima et al., 2018; Huang and Hayashi, 2016; Choi et al., 2011; Wang and Jui, 2018; Chen et al., 2017; Romanov-Michailidis et al., 2018; Xu et al., 2015; Wang et al., 2019; Giffin et al., 2013; Pigeon et al., 2010; Gu et al., 2009; Blessley et al., 2012; Hazari et al., 2009; Xue et al., 2015) (Figure 1A). A remarkable particularity of multifluorocarbons is that their reactivity decreases along with an increase in the number of geminal fluorine atoms; this situation increases their difficulties for partial or complete defluorination through discriminating even slightly different

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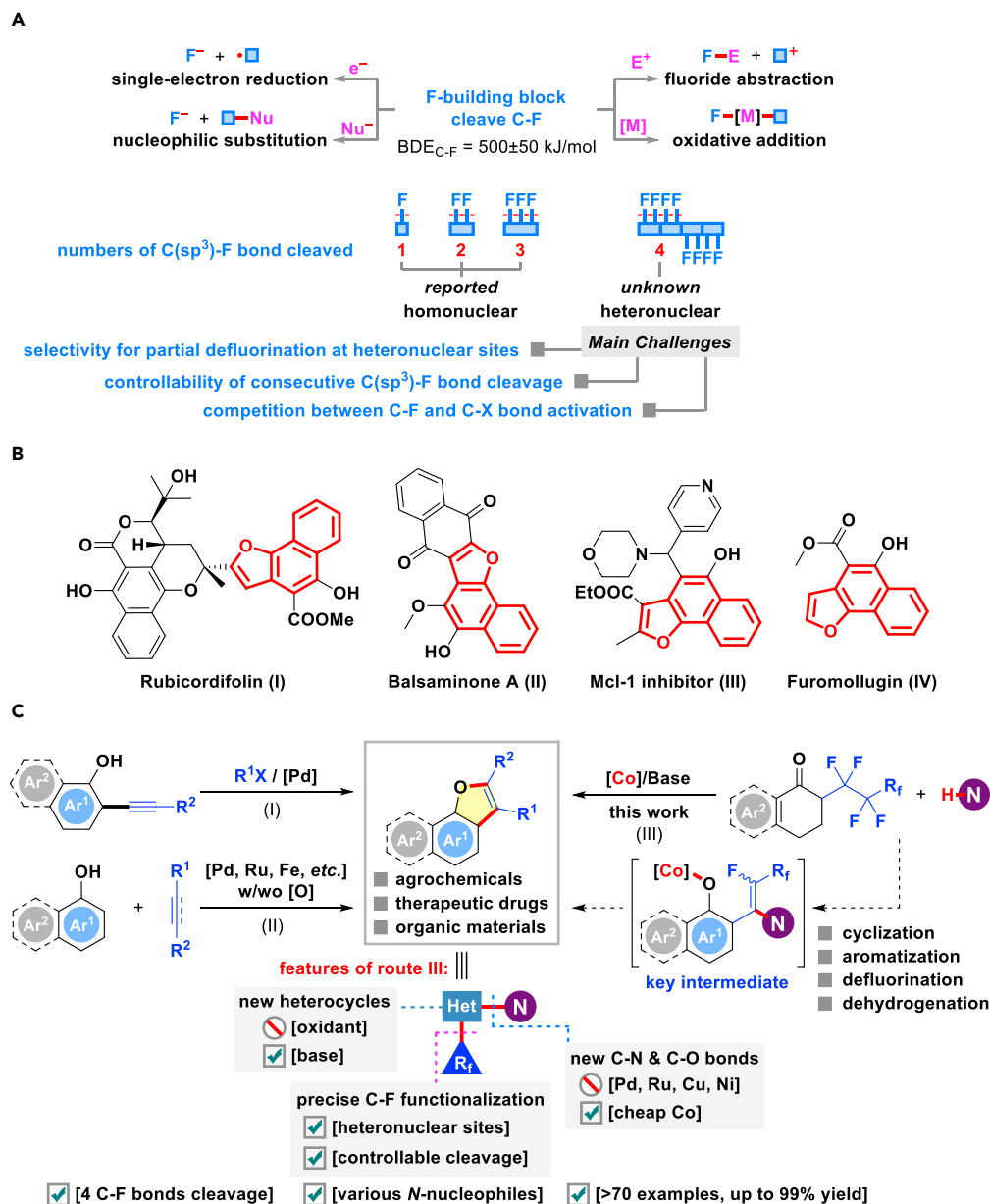


Figure 1. C(sp³)-F Bonds Cleavage Strategy

(A) Existing approaches through fluoride abstraction, oxidative addition, single-electron reduction, and nucleophilic substitution, all of which are not suitable for the multiple C-F bonds cleavage.

(B) Naphtho[1,2-b]furan skeleton in naturally occurring and pharmaceutically relevant compounds.

(C) Our strategy toward the synthesis of naphtho[1,2-b]furan or benzofuran derivatives via highly selective quadruple C(sp³)-F functionalization.

reactivity among several C-F bonds (Luo, 2007). On the other hand, although palladium- (Thornbury and Toste, 2016; Xu et al., 2015; Pigeon et al., 2010; Blessley et al., 2012; Hazari et al., 2009), ruthenium- (Tian et al., 2015, 2018; Wang et al., 2018a, 2018b; Huang and Hayashi, 2016), copper- (Hu et al., 2017, 2018; Wang et al., 2018a, 2018b; Kojima et al., 2018), nickel- (Lu et al., 2017; Honeycutt and Hoov, 2018; Tian et al., 2018; Giffin et al., 2013), and iridium-catalyzed (Priya and Weaver, 2018; Choi et al., 2011; Chen et al., 2017; Romanov-Michailidis et al., 2018) C-F functionalization have recently stimulated intense research efforts, the use of earth-abundant and cheap cobalt salts as feasible promoters for such transformations remained less explored (Kuehnel et al., 2013; Ehm et al., 2016; Andrella et al., 2019; Jaeger et al.,

2018a, 2018b; Krüger et al., 2016; Dugan et al., 2011, 2012; Li et al., 2013). Moreover, multiple defluorination of polyfluorinated molecules will also be elusive presumably due to the problems posed by the poor controllability and chemical selectivity and high bond dissociation energy. Despite the degradation of perfluoroalkyl substance (Renner, 2001), successive C(sp³)-F bond cleavage at heteronuclear sites thus far has not been successfully realized in organic synthesis (Guan et al., 1997) (Figure 1A). As a result, the exploration and discovery of multiple defluorinative reaction mode at different centers may open a new door to allow for the facile synthesis of fine chemicals with a site-selective fluoride-pattern retention and simultaneously avoid the interference from applying exogenously sensitive fluorinating sources.

Herein, we report a novel and efficient strategy involving the successive dehydrogenation and defluorination of α -polyfluoroalkyl ketones with various N-nucleophiles and S-nucleophiles for accessing modular fluoroalkylated furan derivative, which is a structural unit ubiquitously present in naturally occurring products and biologically active molecules (Kwiecien et al., 2012; Prchalova et al., 2014) (Figure 1B). Compared with typical methods relying on annulation with pre-synthesized heterocycle precursors (Figures 1C-I and 1C-II), such as naphthols and phenols (Heravi and Zadsirjan, 2015), this newly developed procedure features the following salient aspects (Figure 1C-III): (1) realizes a rationally designed aromatization-cyclization cascade along with three C(sp³)-H and four C(sp³)-F bonds cleavage under simple reaction conditions; (2) cleaves similar C(sp³)-F bonds at two different positions for the first time for heterocycle synthesis; (3) succeeds in the assembly of valuable nitrogen-containing pharmacophores with regiodefined fluoroalkyl retention (Lishchynskiy and Grushin, 2013; Xie et al., 2018; Huang et al., 2019); (4) distinguishes itself by efficient C-N or C-S/C-O couplings and concomitant formation of two five-/six-membered (hetero)aromatic rings in a one-pot operation without employing stoichiometric oxidants; (5) enables expeditious late-stage modification of biologically relevant compounds with structural complexity (Cernak et al., 2016).

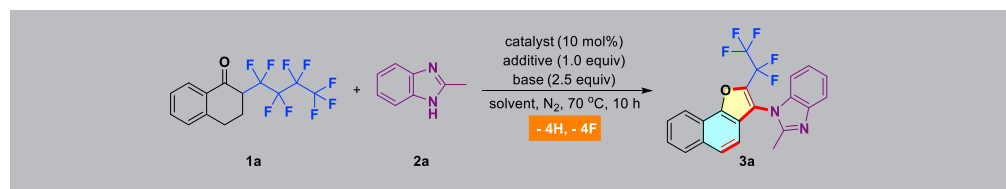
RESULTS AND DISCUSSION

Optimization of Reaction Conditions

Initially, we commenced our investigation by using 2-(perfluorobutyl)-3,4-dihydronaphthalen-1(2H)-one (**1a**) as a substrate, along with 2-methyl-1H-benzo[d]imidazole (**2a**) as a nitrogen nucleophile, in the presence of 10 mol% of CoBr₂, 1.0 equiv of ⁿBu₄NBr (TBAB), and 2.5 equiv of Cs₂CO₃ in DMSO at 70°C under N₂ for 10 h (Table 1; also see Tables S1–S5 in Supplemental Information for details). To our delight, the proposed tandem strategy could be successfully realized to afford C–N bond-forming (Bariwal and Van der Eycken, 2013) product **3a** in 74% NMR yield (70% isolated yield; Table 1, entry 1). Notably, the excellent performance of the reaction required the simultaneous use of cobalt salt, additive TBAB, and base (Mao et al., 2019; Xue et al., 2015) (Table 1, entries 2–4), as the reaction proceeded with reduced efficiency in the absence of any of them. It is noteworthy that decreasing reaction temperature even to room temperature still gave the same good yield of the product **3a** (Table 1, entry 5). In addition, in a striking comparison with other solvents, including MeCN and DMF (Table 1, entries 6–7), DMSO was found to be the best reaction medium for the transformation (Table 1, entry 5). Furthermore, careful screening of other bases and cobalt sources indicated that Cs₂CO₃ and CoBr₂ were still the base and catalyst of choices in the present reaction (Table 1, entries 8–12).

Substrate Scope Study

With the optimized reaction conditions in hand, the general applicability of this predictable and mild cascade reaction was tested with a wide range of electronically disparate nitrogen nucleophiles. As shown in Scheme 1, almost every kind of privileged N-heterocycle components in medicinal chemistry (Taylor et al., 2014), including, but not limited to, benzimidazoles (**3a–3h**, 39%–87%), imidazoles (**4a–4c**, 44%–94%), indazoles (**5a–5c**, 60%–79%), pyrazoles (**6a–6d**, 43%–92%), triazoles (**7–8**, 87%–99%), tetrazole (**9**, 39%), indoles (**10a–10d**, 57%–76%), pyrroles (**11a–11c**, 39%–66%), carbazole (**12**, 40%), and purine (**13**, 36%), could directly couple with substrate **1a** to produce pentafluoroethylated naphtho[1,2-*b*]furan in moderate to good yields. Particularly, besides the ready introduction of polyfluoroalkyl group and N-heterocycle in naphtho[1,2-*b*]furan skeleton, the present protocol also serves as an efficient method for the direct construction of naphtho[1,2-*b*]furan scaffold via defluorination and cyclization cascade, which also have its merit when compared with previous methods where preprepared or commercial naphtho[1,2-*b*]furan was directly employed for further functionalization (Heravi and Zadsirjan, 2015). Importantly, some synthetically valuable functional groups, such as halogen (Cl, Br, I), ester, nitro, formyl, keto, as well as cyano group, were amenable to the present catalytic system, which offered the synthetic potential for further elaboration. Notably, as for nucleophiles such as indazole, triazole, indole, pyrrole, and carbazole, the isolated yields



Entry	Catalyst	Additive	Base	Solvent	Yield (%) ^{a,b}
1	CoBr ₂	TBAB	Cs ₂ CO ₃	DMSO	74 (70) ^c
2	–	TBAB	Cs ₂ CO ₃	DMSO	39
3	CoBr ₂	–	Cs ₂ CO ₃	DMSO	58
4	CoBr ₂	TBAB	–	DMSO	trace
5	CoBr ₂	TBAB	Cs ₂ CO ₃	DMSO	74 (71) ^{c,d}
6	CoBr ₂	TBAB	Cs ₂ CO ₃	MeCN	55 ^d
7	CoBr ₂	TBAB	Cs ₂ CO ₃	DMF	61 ^d
8	CoBr ₂	TBAB	K ₂ CO ₃	DMSO	67 ^d
9	CoBr ₂	TBAB	Li ₂ CO ₃	DMSO	0 ^d
10	CoBr ₂	TBAB	DABCO	DMSO	<10 ^d
11	Co(OAc) ₂	TBAB	Cs ₂ CO ₃	DMSO	49 ^d
12	Co(C ₂ O ₄) ₂ ·2H ₂ O	TBAB	Cs ₂ CO ₃	DMSO	0 ^d

Table 1. Four C(sp³)-F Bonds Functionalization: Optimization of Reaction Conditions

^aReaction conditions: 2-(perfluorobutyl)-3,4-dihydronaphthalen-1(2H)-one (**1a**, 0.30 mmol), 2-methyl-1H-benzo[d]imidazole (**2a**, 0.60 mmol), catalyst (0.03 mmol), additive (0.3 mmol), and base (0.75 mmol) in solvent (2.0 mL) at 70°C for 10 h under N₂; TBAB = tetrabutylammonium bromide.

^bYields were determined by NMR analysis with 1,4-dimethoxybenzene as an internal standard.

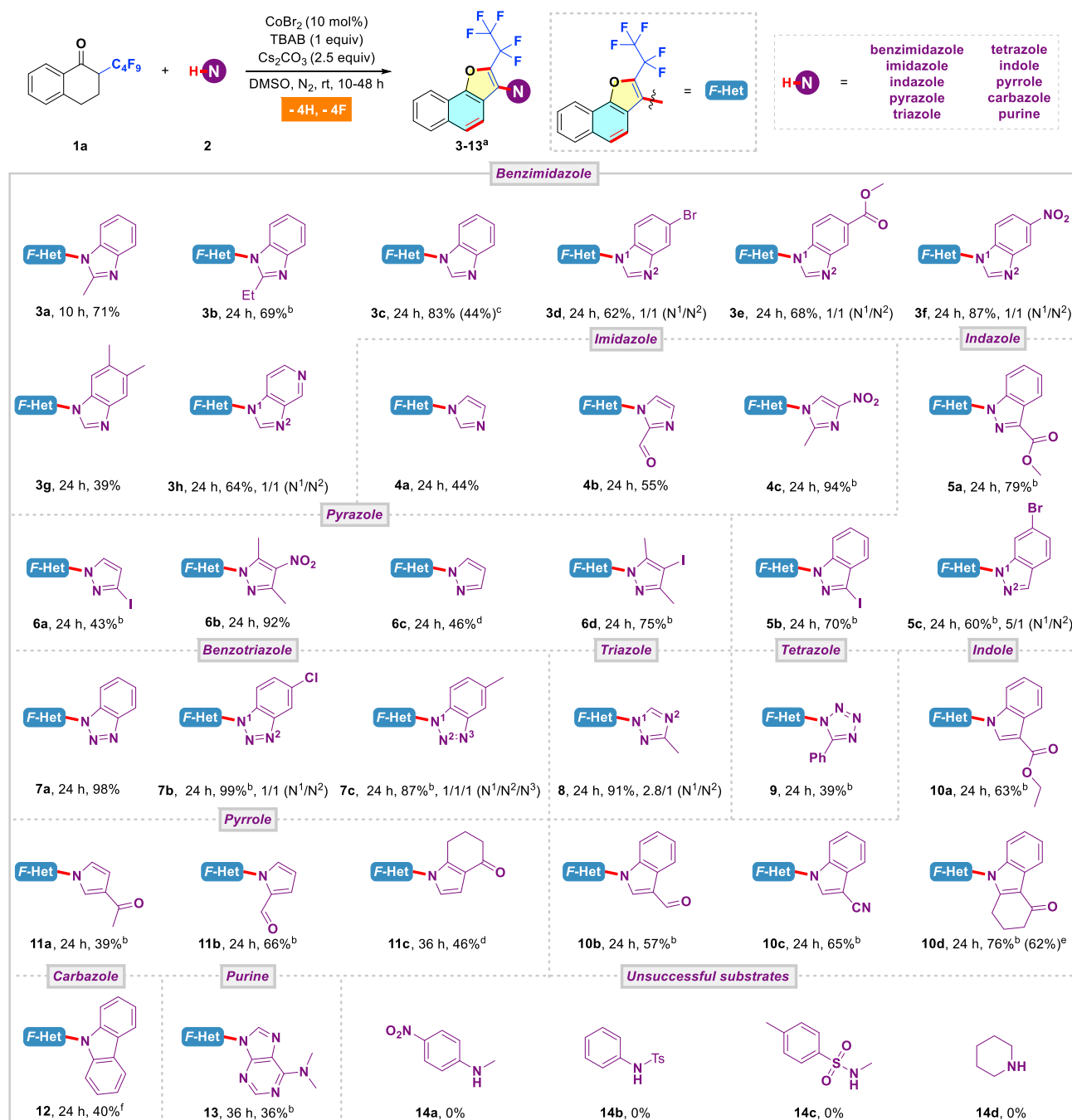
^cIsolated yield.

^dAt room temperature.

of the corresponding products could be remarkably improved by means of increasing reaction temperature and prolonging reaction time. In addition, considering the procedural simplicity and synthetically easy accessibility, a concise procedure was successfully achieved for the large-scale construction of product **10d** under slightly modified reaction conditions (62%, 0.88 g). These results clearly demonstrated the high efficiency and unique advantages of this amination protocol. However, our attempts to expand the substrate scope to anilines (**14a-14b**), sulfonamide (**14c**), and cyclic amine (**14d**) have been proven fruitless. Moreover, the structure of product **6b** was unambiguously confirmed by single crystal X-ray diffraction analysis (CCDC 1881997; [Figure 2](#); also see [Supplemental Information](#) for details).

In view of the importance of late-stage modification in drug discovery, this practical approach has been specifically evaluated with respect to representative nitrogen-containing complex molecules ([Scheme 2](#)). For example, the hypertension therapeutic dibazol could be smoothly incorporated into the naphtho [1,2-*b*]furan derivative **15a** in 38% yield. A pharmaceutical unit of telmisartan readily underwent this dehydrogenative and defluorinative reactions, leading to the desirable heterocycle **15b** in a good yield (88%). Naturally occurring substances such as L-histidine and theophylline also reacted chemoselectively with α -perfluoroalkyl ketone **1a** to furnish the corresponding products **15c** and **15d** in 35% and 49% yields, respectively. Furthermore, by using three known nitrogen-containing drugs (axitinib, alizapride, irbesartan) as viable coupling partners in the present protocol, we were also able to achieve the functionalization of these pharmaceuticals (**15e-15g**). Interestingly, the problems arising from the competitive couplings with nucleophilic amide moieties were well avoided in these cases (**15e-15f**).

Driven by the success of above reactions, subsequently we attempted to expand the substrate scope of four C(sp³)-F bonds cleavage to encompass various α -polyfluoroalkyl ketones as starting materials



Scheme 1. Four C(sp³)-F Bonds Functionalization: Substrate Scope of Various Nitrogen Nucleophiles

^aStandard reaction conditions (0.3 mmol scale); isolated yields.

^bAt 70°C.

^c10 h.

^dAt 100°C.

^e3 mmol scale reaction for 48 h.

^fAt 120°C.

(Scheme 3). A variety of ketones bearing either electron-donating groups (including MeO, OBn, Me) or electron-withdrawing groups (such as F, Cl, Br) on the phenyl rings were tolerated, affording the polycyclic products with acceptable yields (16a–16h, 36%–96% yields). However, ketone 1j was proven to be an

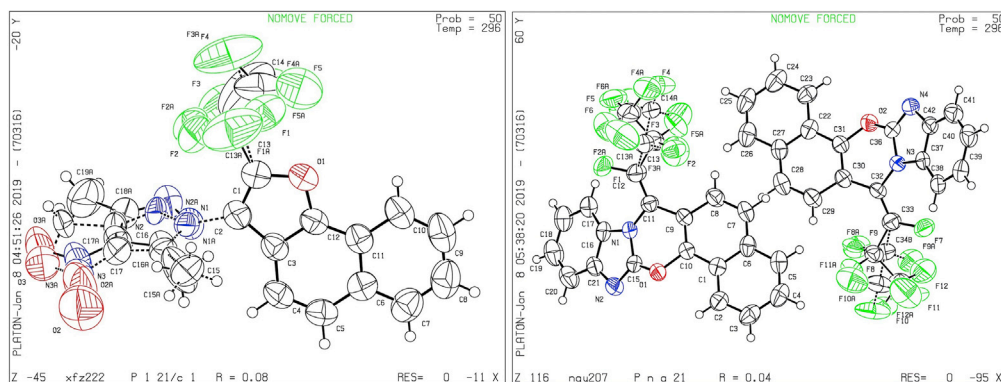


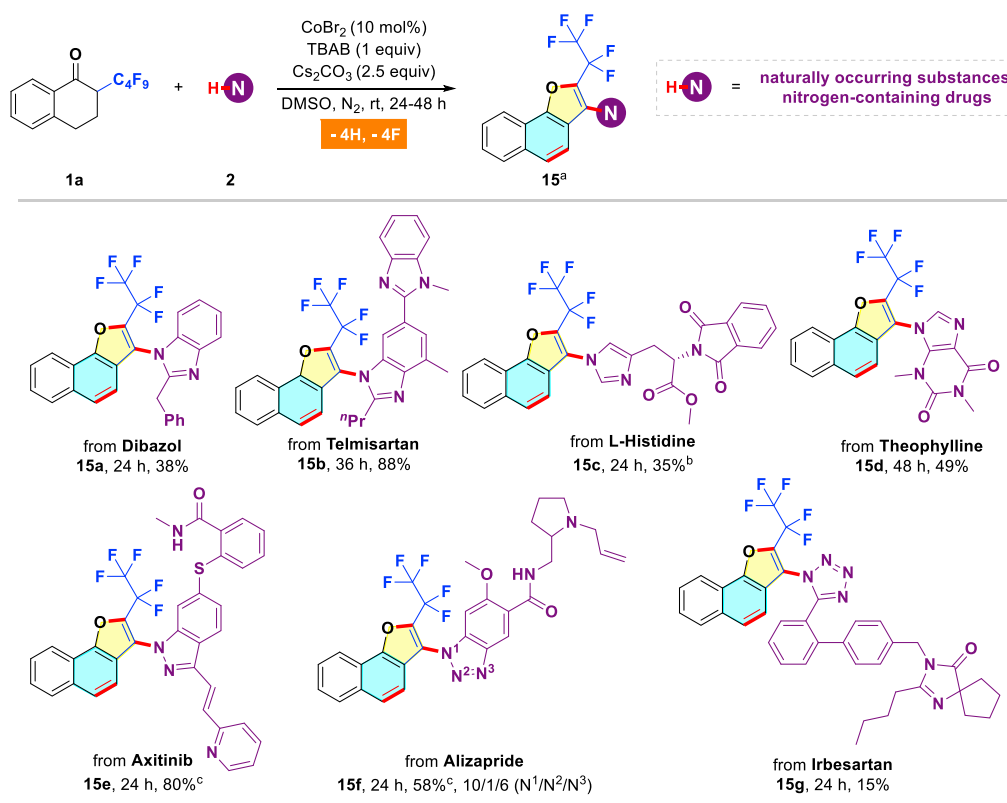
Figure 2. The X-ray Crystal Structures of Products **6b** (CCDC, 1881997, left) and **19** (CCDC, 1881996, right)

inappropriate candidate for the present reaction (**16i**), and it remained intact in the reaction. In addition, substrate **1** possessing an alkyl or aryl substituent at the C4-position underwent the aromatization-cyclization cascade with high efficiency (**16j-16k**, 59%–95% yields). In a similar manner, the reaction worked equally well with heteroaryl ketone to provide the anticipated heterocyclic variant **16l** in 96% yield. Apart from perfluorobutyl 3,4-dihydronaphthalen-1(2*H*)-one (**1a**), we were pleased to observe that the generality of this transformation could be further broadened by employing diverse perfluorobutyl cyclohex-2-en-1-one derivatives, which produced perfluoroethyl benzofuran derivatives **16m-16v** in 58%–84% yields. The substrate **1w** derived from Nandrolone could also participate into the coupling with **2s** to produce the product **16v** in 58% yield. Also, our method was able to address the paucity of process for site-selective fluoroalkylation. Interestingly, the perfluoroalkyl chain length ranging from 10 to 3 carbons only has a slight impact on the reaction outcomes (**16w-16b'**, 50%–85% yields). Furthermore, our protocol allowed convenient access to trifluoromethyl-substituted drug analogue **16b'** (Taylor et al., 2014). In view that π -conjugated benzofuran derivatives are pivotal structural constituents of optoelectronic materials and pharmaceutical molecules, the present distinctive methodology will provide chemists an attractive alternative for manufacturing these fluorinated polyfused skeletons (Tsuji and Nakamura, 2017).

The development of original and novel scaffolds is a persistent quest in medicinal chemistry. Finally, the reactions employing aryl mercaptan (**2r'-2s'**) forged the desired sulfoethers **17** and **18** containing heterocycles (Scheme 4A-I). Moreover, the use of benzoimidazole **2t'**, which possessed a halogen at the C2 position, produced an unexpected pentacyclic fused compound **19** through the removal of three fluorides [Scheme 4A-II; also see the X-ray crystal structure of compound **19** (CCDC 1881996; Figure 2) in Supplemental Information for details]. However, 1,3-bis-nucleophiles possessing a carbon atom as the tether could not participate in the designed aromatization-annulation and predominantly afforded condensed dihydrobenzoquinazoline **20** and dihydrobenzoquinoline **21** in 72% and 73% yields, respectively (Schemes 4A-III and 1A-IV). These results would significantly contribute to the mechanistic understanding of the reaction pathway.

Mechanism Study

Further insights were obtained for elementary information of the reaction mechanism via the control experiments outlined in Scheme 4B. First, no anticipated product **23** was isolated when 2-(perfluorobutyl)cyclohexan-1-one (**22**) was employed as a prefluorinated building block, revealing that the phenyl group or unsaturated C=C moiety in the α -polyfluoroalkyl ketone was essential for the established cascade defluorination (Scheme 4B-I). Next, the experiment employing seven-membered ring **24** under the standard conditions has been proven futile, indicating that the autoaromatization of the dihydronaphthalenone might become an important driving force for the successive C(sp³)-F bonds cleavage (Scheme 4B-II). Then, the significance of the nucleophiles was demonstrated through the fact that piperidine exclusively coupled with **1a**, leading to β -aminated ketone **26** in 38% yield (Scheme 4B-III; also see Scheme 1, **14d**). Moreover, it was found that α -defluorination occurred to form intermediate **27** (with TBAB, via 1,4-conjugate addition of Br anion) and **28** (without TBAB) in the absence of an *N*-nucleophile (Schemes 4B-IV and 4B-V). We believed that TBAB additive might accelerate the sequential events of C-N/C-O couplings, aromatization, and defluorination. On the other hand, the poor solubility of Cs₂CO₃ might lead to inconsistencies in mixing the



Scheme 2. Four C(sp³)-F Bonds Functionalization: Application in the Synthesis of Complex Molecules to Access Druglike Scaffolds

^aStandard reaction conditions (0.3 mmol scale); isolated yields.

^b3 equiv of **2** was used.

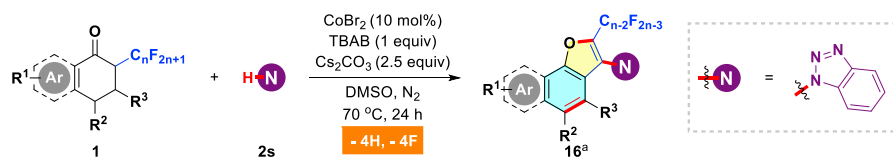
^c0.1 mmol scale.

reagents and thus poor reproducibility, and this issue could be alleviated by the addition of TBAB (Sasson and Neumann, 1997). Simultaneously, less than 5% yield of byproduct **29** was obtained under basic conditions (Scheme 4B-V). As expected, key intermediate **28** could be converted to the corresponding product **3a** in 86% yield under the standard conditions (Scheme 4B-VI).

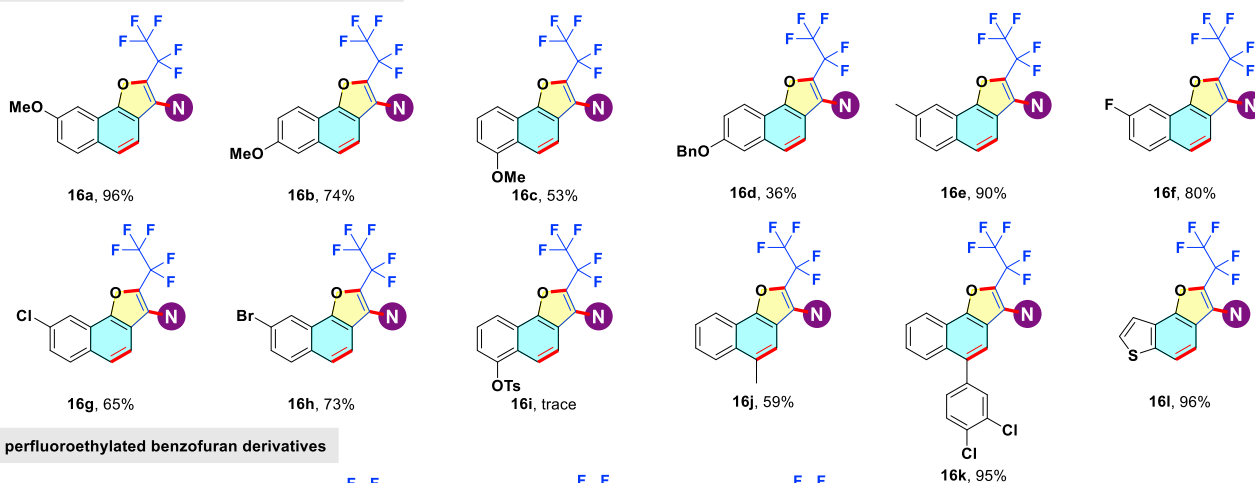
Density Functional Theory Calculations

Density functional theory (DFT) calculations with the B3LYP functional (Becke, 1993; 1988; Lee et al., 1988), including Grimme's D3 dispersion correction (DFT-D3) (Grimme et al., 2010; Goerigk and Grimme, 2011), were carried out to explore the role of Cs₂CO₃ and CoBr₂ on this quadruple C(sp³)-F bond functionalization (Data S1) [all calculations were performed with the Gaussian 09 package (Frisch et al., 2013), and optimized structures were visualized using CYLview (Legault, 2009); see Supplemental Information for computational details]. It should be noted that the desired product **3a** could be obtained in 39% yield in the absence of CoBr₂ (Table 1, entry 2). Therefore, we first investigated the possible pathway of the Cs₂CO₃-mediated defluorinative C-N/C-O coupling reaction by using 2-(perfluoropropyl)-3,4-dihydronaphthalen-1(2H)-one (**1c'**) and 2-methyl-1H-benzo[d]imidazole (**2a**) as model substrates. As indicated earlier, the perfluoroalkyl chain length only has a slight impact on the reaction outcomes. Therefore, we chose simpler **1c'** rather than **1a** as a model substrate to simplify the theoretical calculation. The calculated free energy profile and optimized transition state structures are listed in Figure 3.

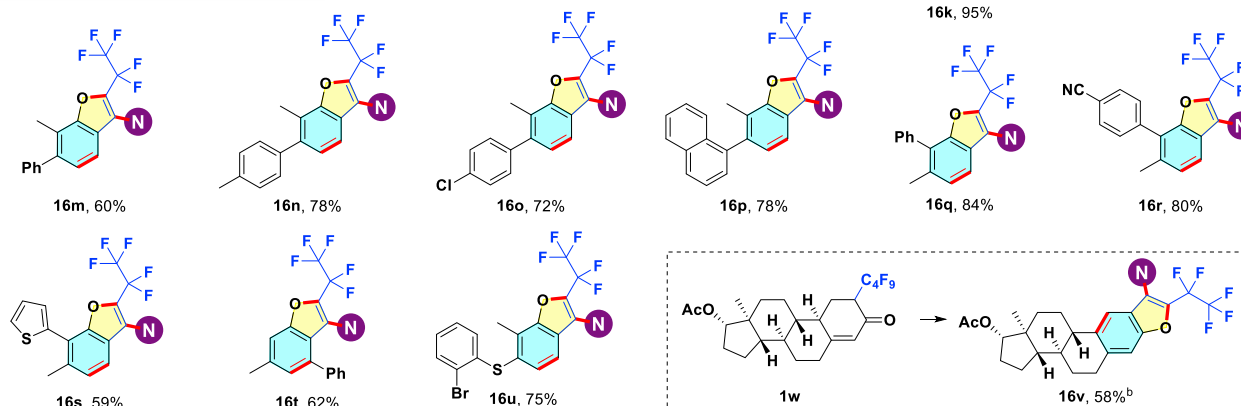
As shown in Figures 3 and 4A, the entire pathway consists of the following steps: (1) a Cs₂CO₃-assisted elimination of the first HF, proceeding through the deprotonation of the α -hydrogen of carbonyl compound **1c'** (via TS_{1c'/IN1}) and the subsequent elimination of fluorine anion (via TS_{IN1/IN2}) in an E2 elimination manner, generates an α,β -unsaturated intermediate IN2. The corresponding barrier of these two transition states



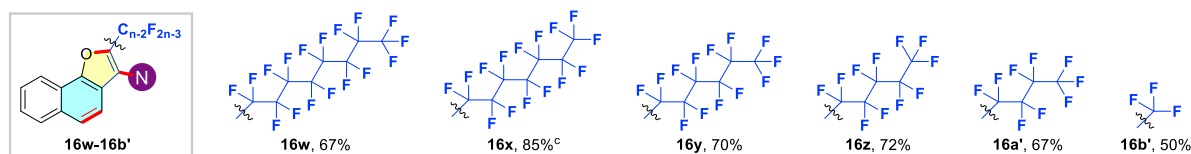
perfluoroethylated naphtho[1,2-b]furan derivatives



perfluoroethylated benzofuran derivatives



perfluoroalkylated naphtho[1,2-b]furan derivatives



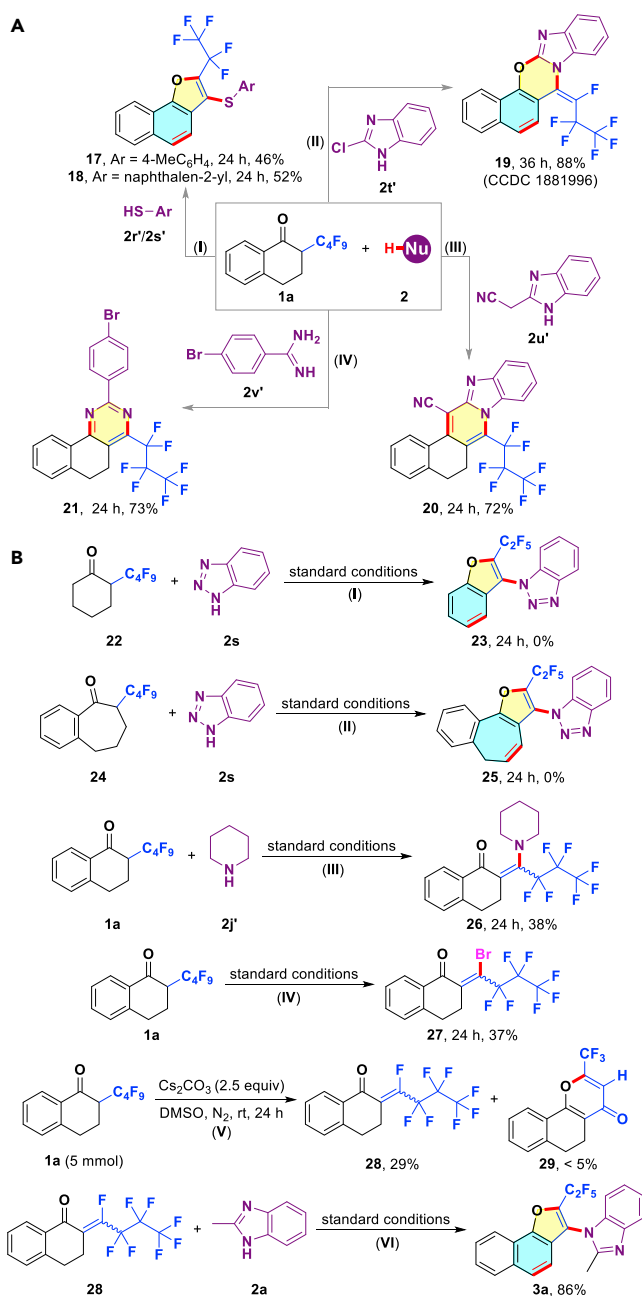
Scheme 3. Four C(sp³)-F Bonds Functionalization: Substrate Scope of Various Perfluoroalkyl Ketones

^aStandard reaction conditions (0.2 mmol scale); isolated yields.

^b0.05 mmol scale.

^c0.3 mmol scale.

are only 7.8 and 6.4 kcal/mol, respectively. (2) The nucleophilic vinylic substitution (S_NV) of **IN2**, in which the fluorine atom is replaced by a nitrogen nucleophile (**2a**), produces a C-N coupling intermediate **IN4**. The rate-determining step of this process is the π -perpendicular attack of **2a** toward **IN2** ($TS_{IN2/IN3}$, with a barrier of 15.2 kcal/mol). Abstraction of F^- by the Cs_2HCO_3 cation from the tetrahedral intermediate **IN3** forms the enamine intermediate **IN4**, which is exergonic by 16.3 kcal/mol. (3) Further elimination of the third HF proceeding through a similar deprotonation (via $TS_{IN4/IN5}$) and fluorine anion elimination sequence (via



Scheme 4. Four C(sp³)-F Bonds Functionalization with Other Mono- or Dinucleophiles and Control Experiments

(A) Four C(sp³)-F bonds cleavage with aryl mercaptan or 1,3-dinucleophiles.
 (B) Some control experiments performed for gaining more mechanistic insight.

TS_{IN5/IN6}) affords a delocalized naphthalen-1(4*H*)-one intermediate IN6. Owing to the π -conjugated effect as well as the existence of Cs⁺ ... O and Cs⁺ ... F interaction, the third C-F bond cleavage step is ready to occur (highly exergonic by about 48.6 kcal/mol) (Li et al., 2013). (4) Rearomatization of IN6 via the deprotonation of naphthalen-1(4*H*)-one (TS_{IN6/IN7}) furnishes a zwitterionic complex IN7, which could further undergo an intramolecular S_NV-type cyclization (via TS_{IN7/16b'}) to give the desired product 16b'. The whole defluorination coupling reaction is totally exergonic by 90.2 kcal/mol (relative to the separated reactants). The intramolecular cyclization reaction of IN7, involving a single-step O-nucleophilic σ -attack (TS_{IN7/16b'}), is the rate-limiting step of the reaction pathway with a barrier of 25.6 kcal/mol. It is noted that Cs₂CO₃ plays a

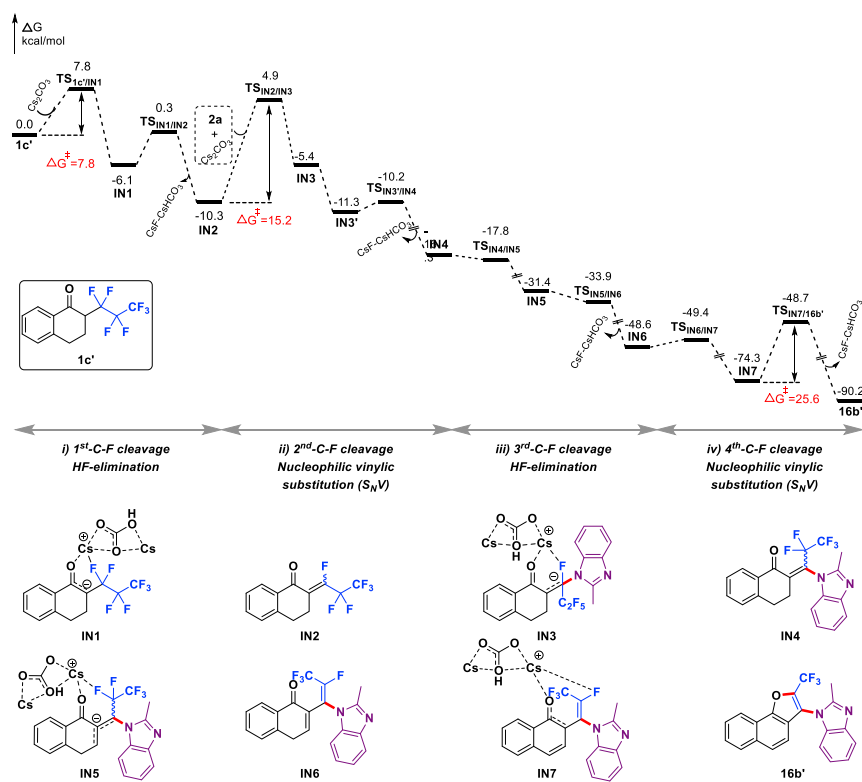


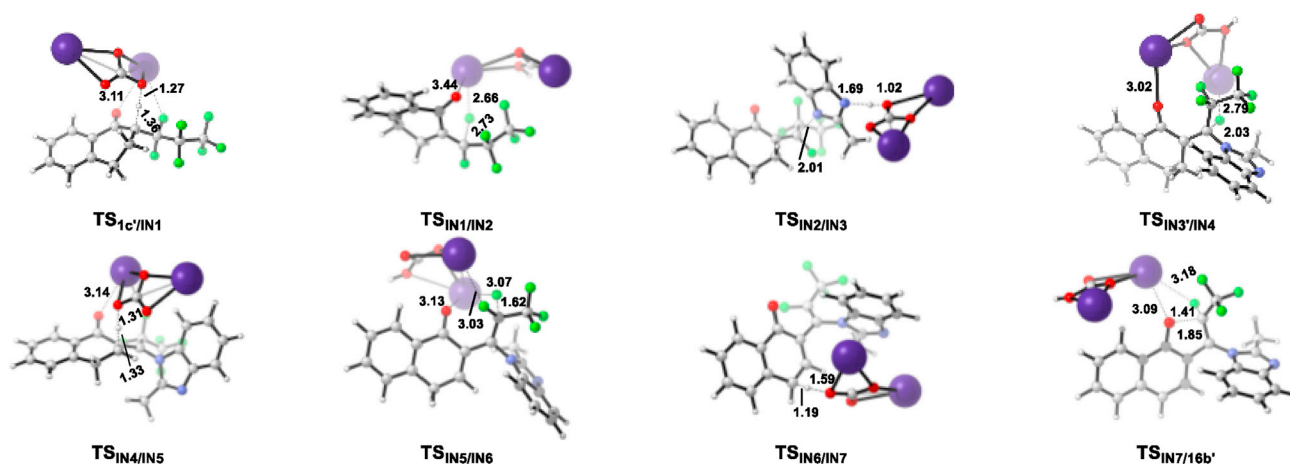
Figure 3. Free Energy Profile of the Cs_2CO_3 -Mediated Four $\text{C}(\text{sp}^3)\text{-F}$ Bonds Cleavage and C-N/O Coupling Cascade Reaction (in kcal/mol)

crucial role for facilitating both the HF elimination and the nucleophilic vinylic substitution. These computational results are consistent with experimental observations.

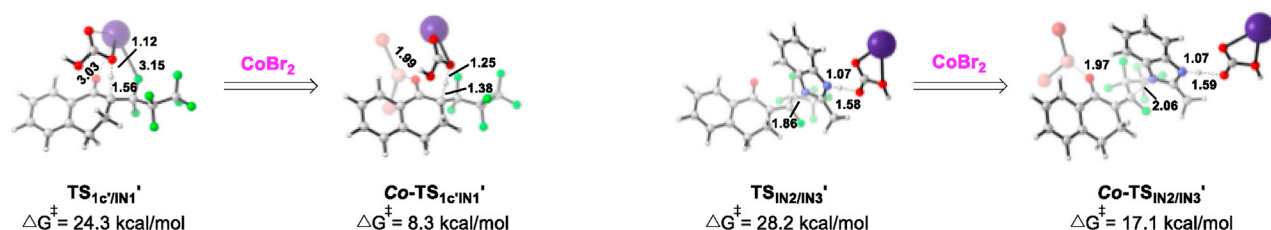
Next, we also performed DFT calculations to reveal the influence of CoBr_2 additive on this defluorination reactions. Some key steps with relatively high activation barriers discussed earlier ($\text{TS}_{\text{IN}2/\text{IN}3}$ and $\text{TS}_{\text{IN}7/16\text{b}'}$) were calculated in the presence of CoBr_2 (see Figures S235 and S236 in Supplemental Information for details). Our calculations show that CoBr_2 could lower the activation barrier of N-nucleophilic vinylic substitution step from 15.2 kcal/mol to 5.9 kcal/mol ($\text{Co-TS}_{\text{IN}2/\text{IN}3}$), which makes the intermolecular C-N bond formation more readily. However, it does not have significant influence on the rate-limiting step (26.7 kcal/mol for $\text{Co-TS}_{\text{IN}7/16\text{b}'}$, and 25.6 kcal/mol for $\text{TS}_{\text{IN}7/16\text{b}'}$). We hypothesized that the basicity of conjugated acid CsHCO_3 , which is formed with the consumption of strong base Cs_2CO_3 during the reaction process, is not sufficient to deprotonate the related substrates or intermediates in the absence of $\text{Co}(\text{II})$ salt. Both the barriers of the deprotonation of $1\text{c}'$ (via $\text{TS}_{1\text{c}'/\text{IN}1'}$) and the nucleophilic addition of nucleophile 2a toward $\text{IN}2$ (via $\text{TS}_{\text{IN}2/\text{IN}3'}$) activated by CsHCO_3 are higher than those activated by Cs_2CO_3 (24.3 kcal/mol versus 7.8 kcal/mol and 28.2 kcal/mol versus 15.2 kcal/mol) (Figure 4B). Interestingly, energy barriers of transition states with CoBr_2 , $\text{Co-TS}_{1\text{c}'/\text{IN}1'}$ and $\text{Co-TS}_{\text{IN}2/\text{IN}3'}$, are calculated to be lower in energies than those with only CsHCO_3 (8.3 kcal/mol versus 24.3 kcal/mol and 17.1 kcal/mol versus 28.2 kcal/mol). These computational results suggest that CoBr_2 might act as a Lewis acid (Stahl et al., 2013) to facilitate the base-mediated defluorinative cascade. It was found that other Lewis acid alternatives could also promote the defluorinative cascade under the optimal reaction conditions (see Table S6 in Supplemental Information for details), which is consistent with this computational result.

On the basis of the abovementioned control experiments, DFT calculations, and literature survey (Jaroschik, 2018; Shen et al., 2015; Stahl et al., 2013), a possible mechanism of the $\text{Co}(\text{II})$ -assisted/base-promoted defluorination for the formation of the observed products is described in Scheme 5. Initially, a rapid nucleophilic 1,4-addition/fluoride elimination event of the N- or S-nucleophile with α,β -unsaturated carbonyl compound A, which is *in situ* generated from substrate 1 by spontaneously removing a molecule of HF

A



B

**Figure 4. Optimized Transition State Structures**

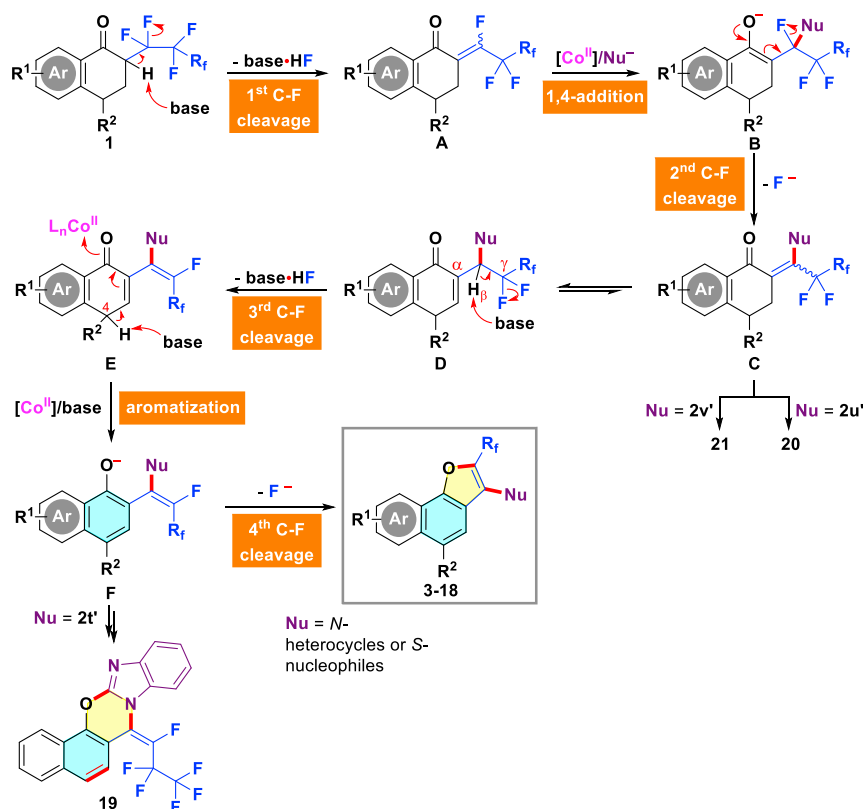
(A) Optimized transition state structures (distances are in Å).

(B) Transition state structures of CsHCO_3 -mediated deprotonation of $1c'$ and N -nucleophilic addition step of $\text{IN}2$ without or with CoBr_2 .

with the assistance of Cs_2CO_3 , occurs to give the β -coupled species **C**. Subsequently, tautomerization of nascent **C** affords a more stable endocyclic naphthalen-1(4*H*)-one **D**. Next, β,γ -desaturation readily proceeds in the presence of Cs_2CO_3 by extrusion of the third fluoride ion to produce the transient intermediate **E**, mainly owing to the π -conjugated effect. The subsequent formation of a naphthol/phenol anion **F** may be explained by a base-assisted elimination of a proton at C4-position of **E**, and autoaromatization greatly contributes to the driving force of this step (Pigeon et al., 2010). Finally, occurrence of an intramolecular O -nucleophilic vinylic substitution (Li et al., 2013) ($\text{S}_{\text{N}}\text{V}$; via intermediate **F**) delivers the ring-closure products **3-18** via readily cleaving the fourth C-F bond. On the other hand, the possibility that the reaction proceeds through 5-*endo-trig* cyclization could not be ruled out (Ichikawa et al., 2002). Alternatively, external nucleophilic attack by 2-(1*H*-benzo[d]imidazol-2-yl)acetonitrile (**2u'**) or 4-bromobenzimidamide (**2v'**), which bears two reactive sites (Schemes 4-III and 4-IV), would preferentially condense to produce conventional heterocycles **20-21** rather than undergoing successive defluorination. Notably, intramolecular nucleophilic annulation of intermediate **F** would also furnish the polycyclic fused product **19**, where the new C-O bond was forged with benzimidazole keeping γ -C-F bond intact. This result indirectly reflects the formation of intermediate **F** in the reaction. It should be mentioned that the reactions are highly regioselective because a wide variety of perfluoroalkylated naphtho[1,2-*b*]furan derivatives could be exclusively accessed even if there might potentially exist several competitive side reactions.

Conclusions

In summary, we have developed an appealing cobalt(II)/ Cs_2CO_3 -promoted quadruple defluorinative mode for accessing perfluoroalkylated naphtho[1,2-*b*]furan//benzofuran derivatives by using prefluoroalkylated ketones with various N -heterocycles, including benzimidazole, imidazole, indazole, pyrazole, triazole, tetrazole, indole, pyrrole, carbazole, and purine. This method exhibited mild reaction conditions, broad substrate scope, and good functional group compatibility. Extension of the method to other kinds of S -nucleophiles also improved the synthetic potentials of the present method in the context of diversity-oriented



Scheme 5. Proposed Mechanism

synthesis. Moreover, the method could also be applied to the late-stage functionalization of some representative nitrogen-containing druglike molecules, which might potentially find applications in medicinal chemistry and pharmaceutical industry. Controlled experiments and DFT theoretical studies revealed that the combination of cheap cobalt salt with Cs_2CO_3 enables expeditious C-F cleavage. As such, we anticipate that this strategy will provide a complementary new approach to enable the fluorine-containing modification of complex biological molecules that are not easy to achieve by using current state-of-the-art methods.

Limitations of the Study

However, the substrate scope of *N*-nucleophile is somewhat limited, as anilines, sulfonamide, and cyclic amine have been proven fruitless in the present reactions.

Resource Availability

Lead Contact

Further information and requests for resources and reagents should be directed to and will be fulfilled by the Lead Contact, Zhi-Liang Shen (ias_zlshen@njtech.edu.cn).

Materials Availability

All unique/stable reagents generated in this study are available from the Lead Contact with a completed Materials Transfer Agreement.

Data and Code Availability

The crystallography data have been deposited at the Cambridge Crystallographic Data Center (CCDC) under accession number CCDC: 1881996 (**19**) and CCDC: 1881997 (**6b**) and can be obtained free of charge from www.ccdc.cam.ac.uk/getstructures.

Original/source data for Figures 1–4, Schemes 1–5, and Table 1 in the paper are available at <https://doi.org/10.1016/j.isci.2020.101259>. Cartesian coordinate is provided as a xyz file (Data S1.xyz).

METHODS

All methods can be found in the accompanying [Transparent Methods supplemental file](#).

SUPPLEMENTAL INFORMATION

Supplemental Information can be found online at <https://doi.org/10.1016/j.isci.2020.101259>.

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AUTHOR CONTRIBUTIONS

T. X. and G.-Q.W. contributed equally to this work. T.X. and X.-Q.C. performed the experiments and analyzed the data. Y.-W.W. checked the Supporting Information. X.-Q.C. and Z.-L.S. designed the project and wrote the manuscript. The computational work was conducted by G.-Q.W. and S.L. The project was financed by W.R., Z.-L.S., H.X., and X.-Q.C. All authors discussed the experimental results and commented on the manuscript.

DECLARATION OF INTERESTS

The authors declare no competing interests.

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Supplemental Information

Selective Quadruple C(sp³)-F

Functionalization of Polyfluoroalkyl Ketones

Ting Xie, Guo-Qiang Wang, Ya-Wen Wang, Weidong Rao, Haiyan Xu, Shuhua Li, Zhi-Liang Shen, and Xue-Qiang Chu

Supplemental Figures for NMR spectrums:

Figure S1. ¹H NMR spectrum of 3a, related to Scheme 1.

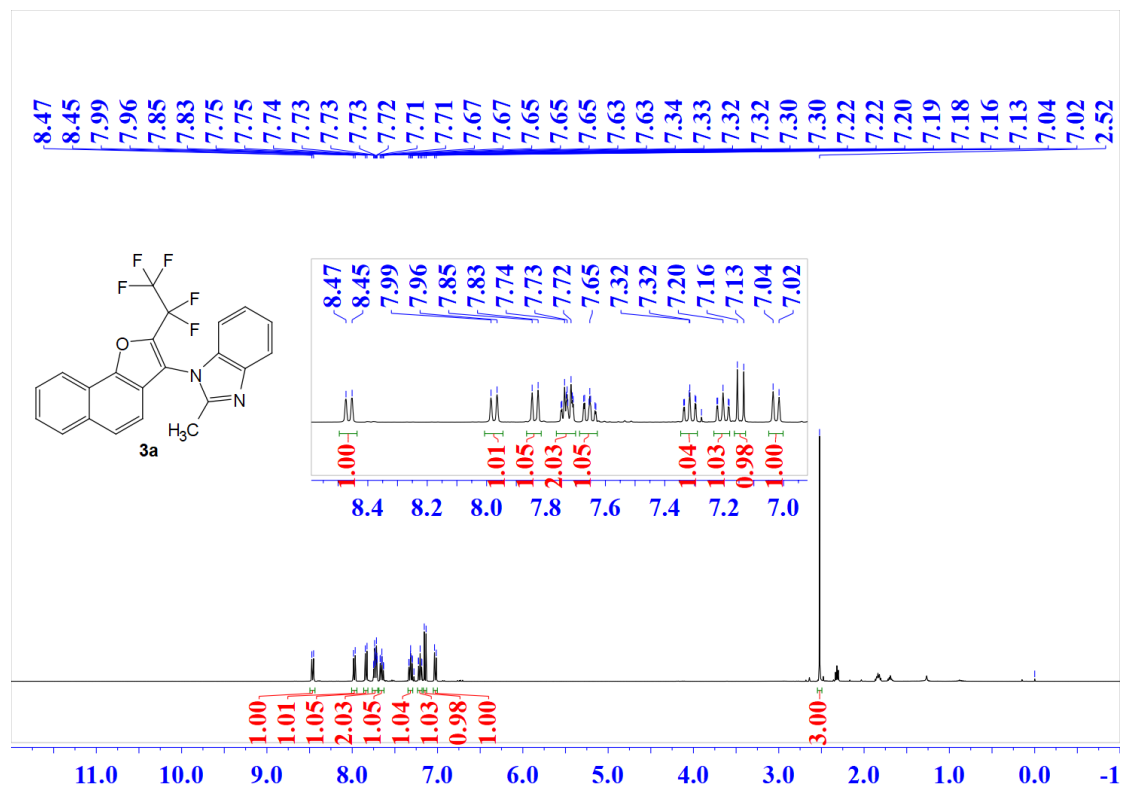


Figure S2. ¹⁹F NMR spectrum of 3a, related to Scheme 1.

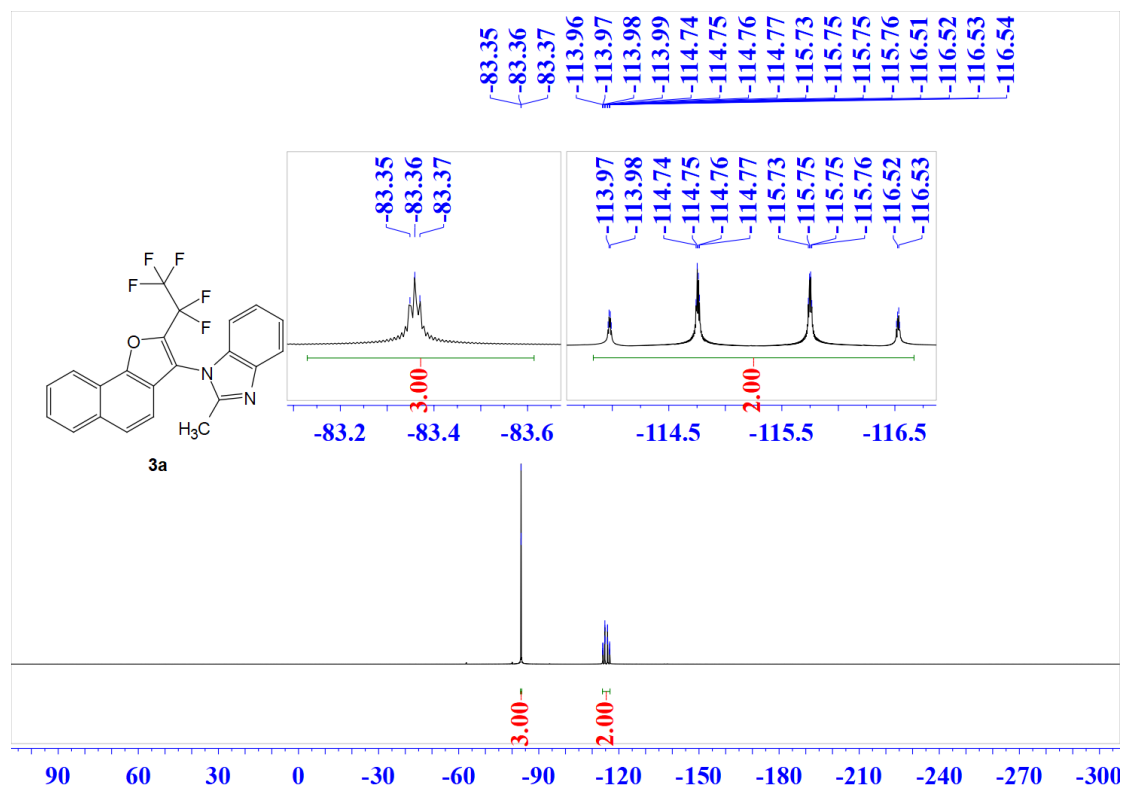


Figure S3. ¹³C NMR spectrum of **3a**, related to Scheme 1.

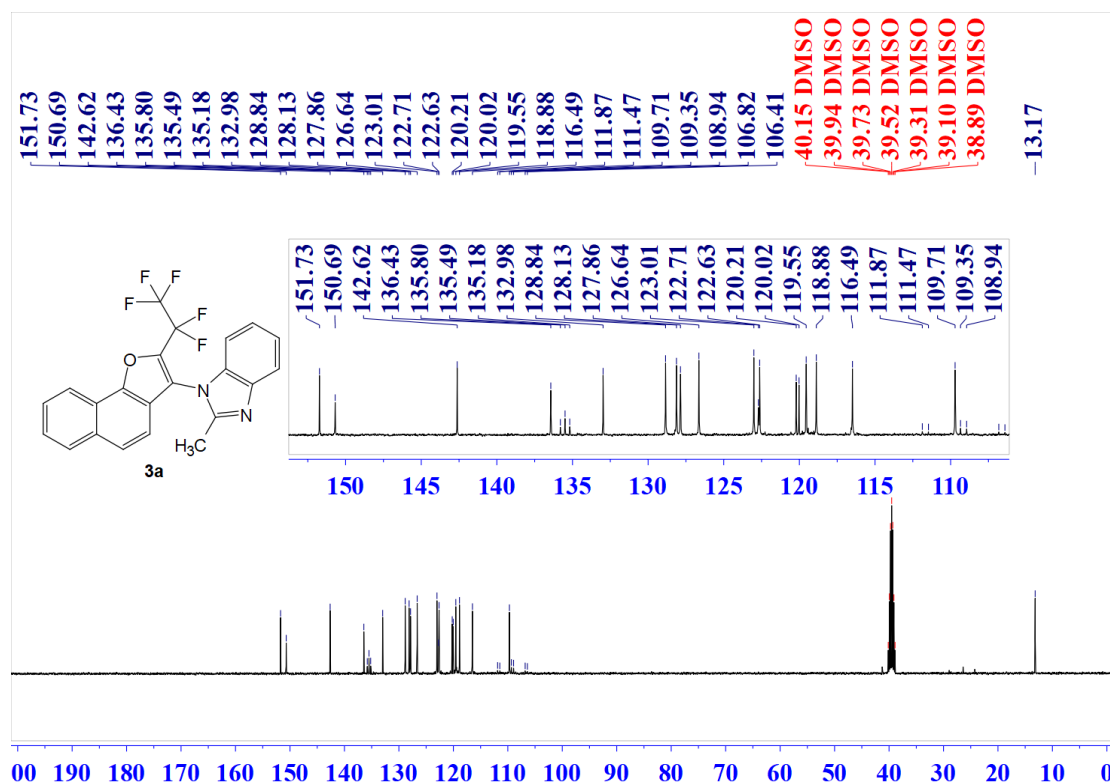


Figure S4. ¹H NMR spectrum of **3b**, related to Scheme 1.

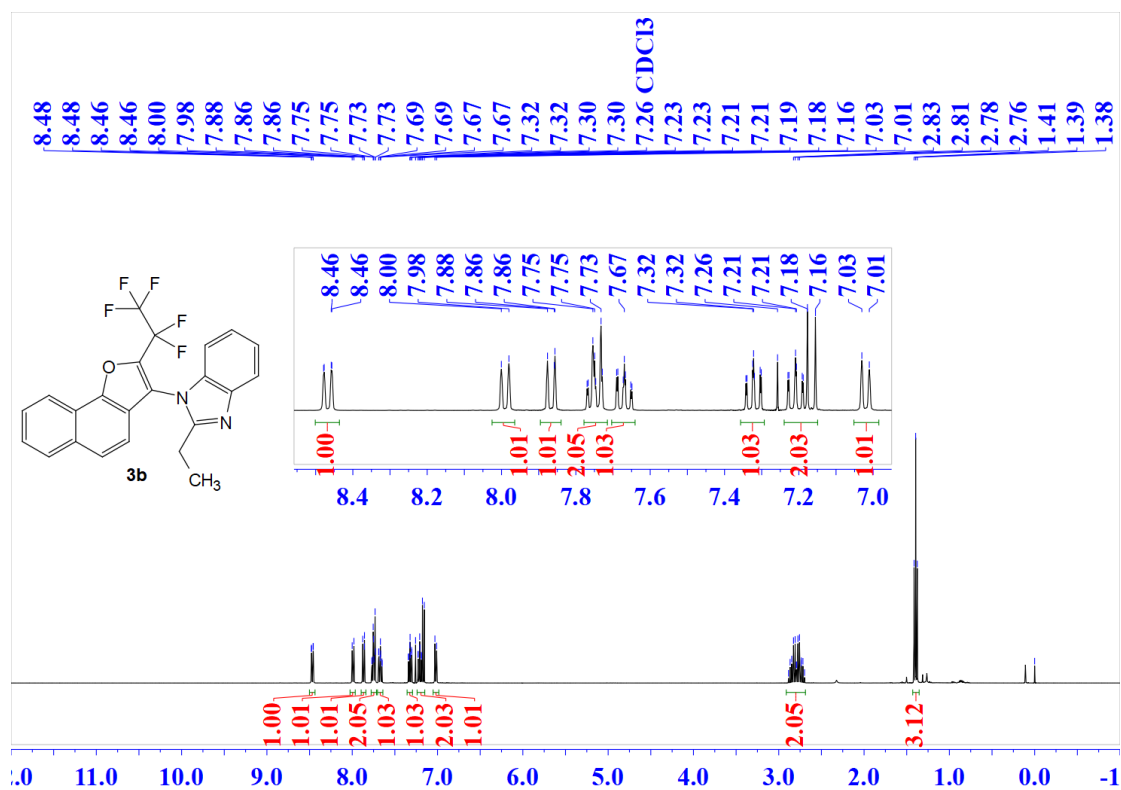


Figure S5. ^{19}F NMR spectrum of **3b**, related to Scheme 1.

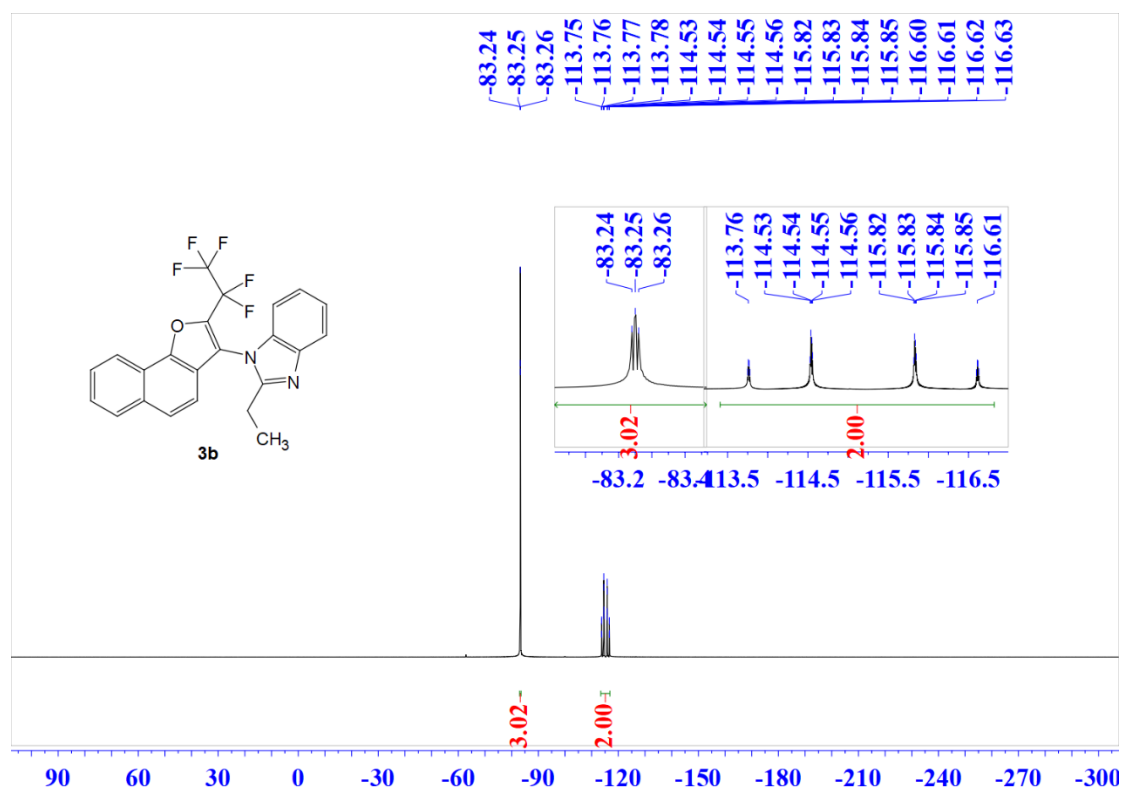


Figure S6. ^{13}C NMR spectrum of **3b**, related to Scheme 1.

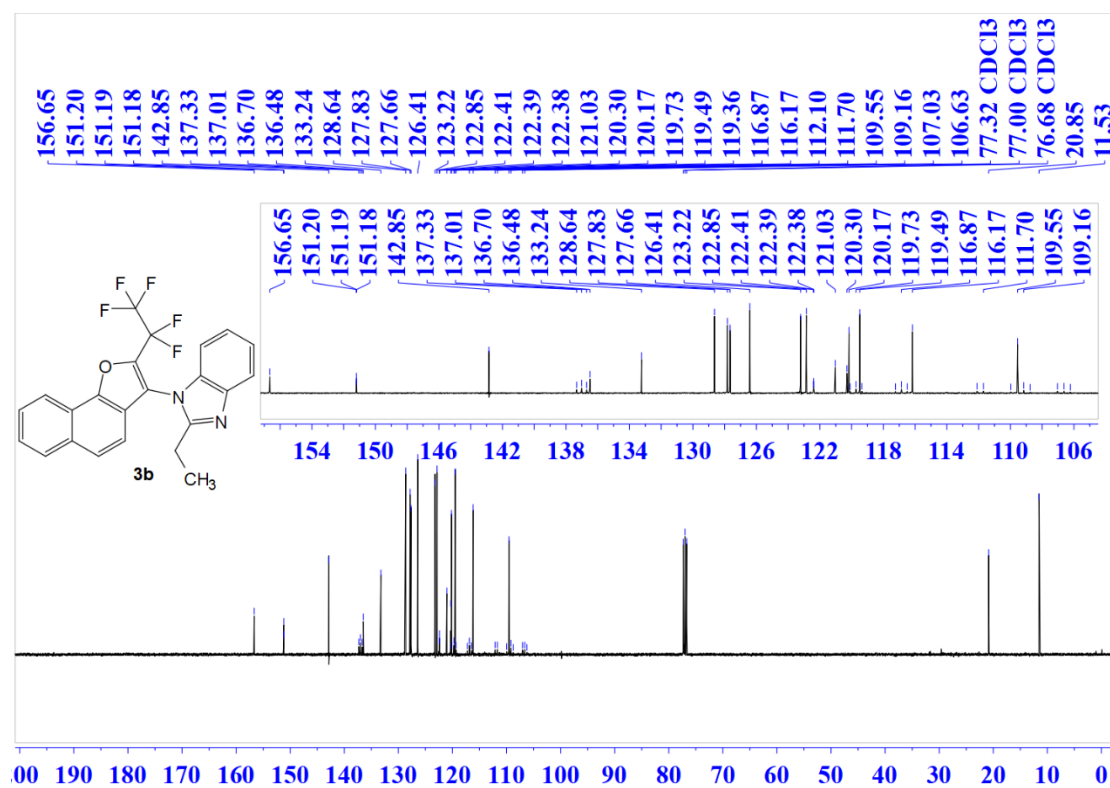


Figure S7. ¹H NMR spectrum of **3c**, related to Scheme 1.

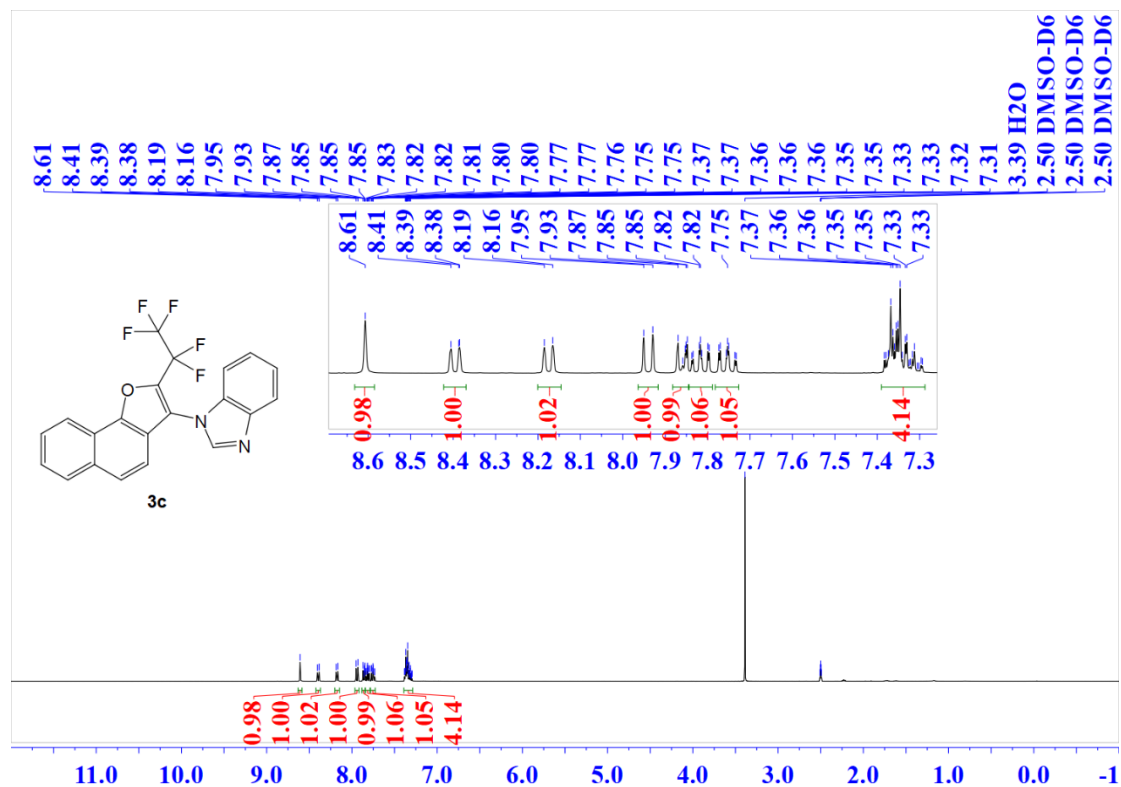


Figure S8. ¹⁹F NMR spectrum of **3c**, related to Scheme 1.

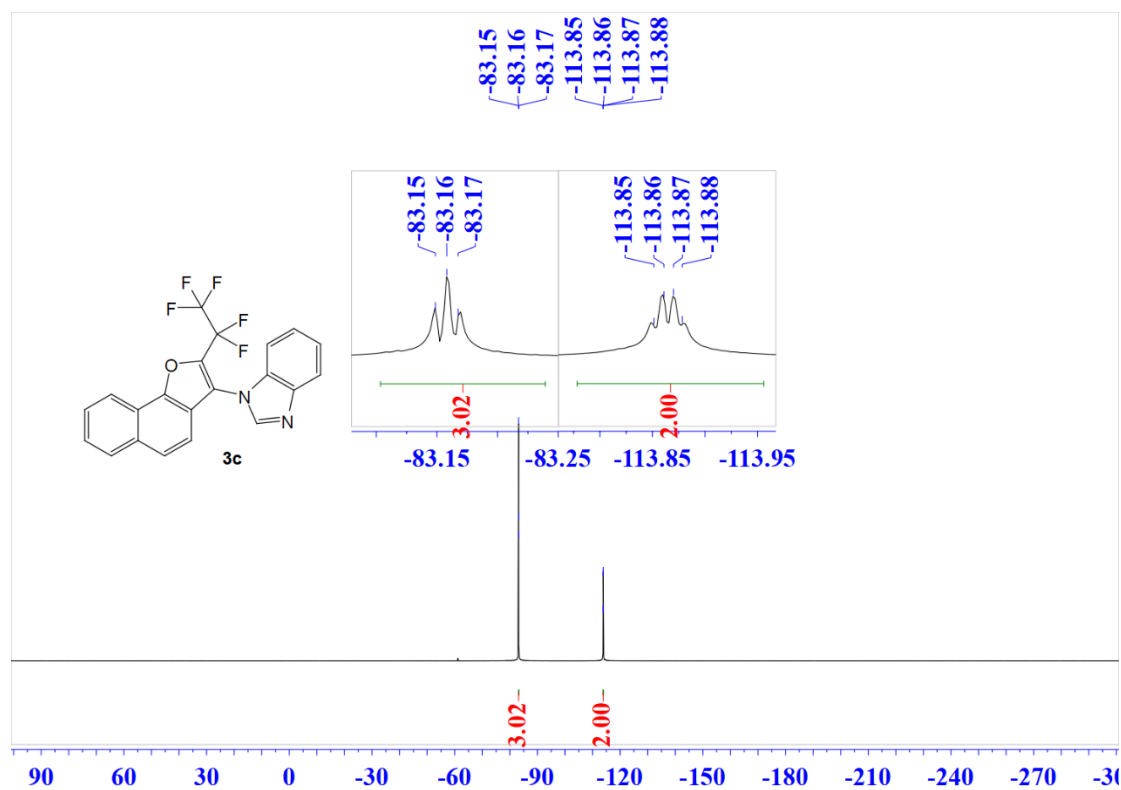


Figure S9. ¹³C NMR spectrum of **3c**, related to Scheme 1.

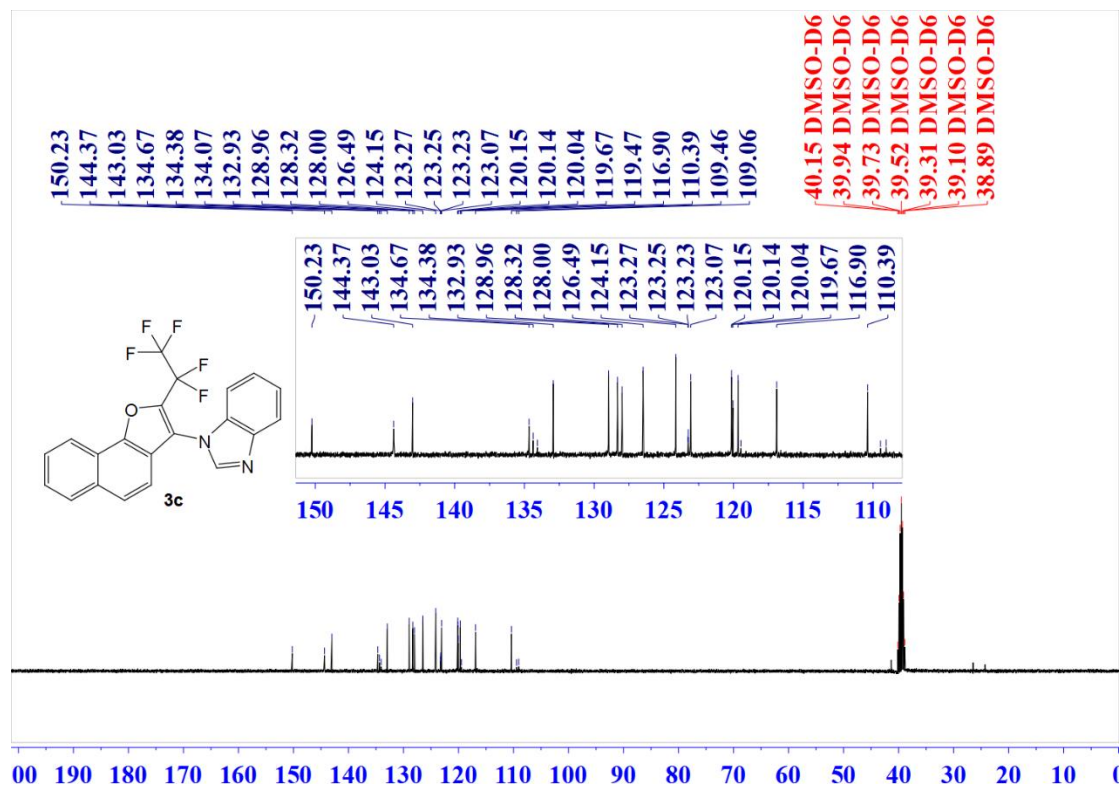


Figure S10. ¹H NMR spectrum of **3d-I** or **3d-II**, related to Scheme 1.

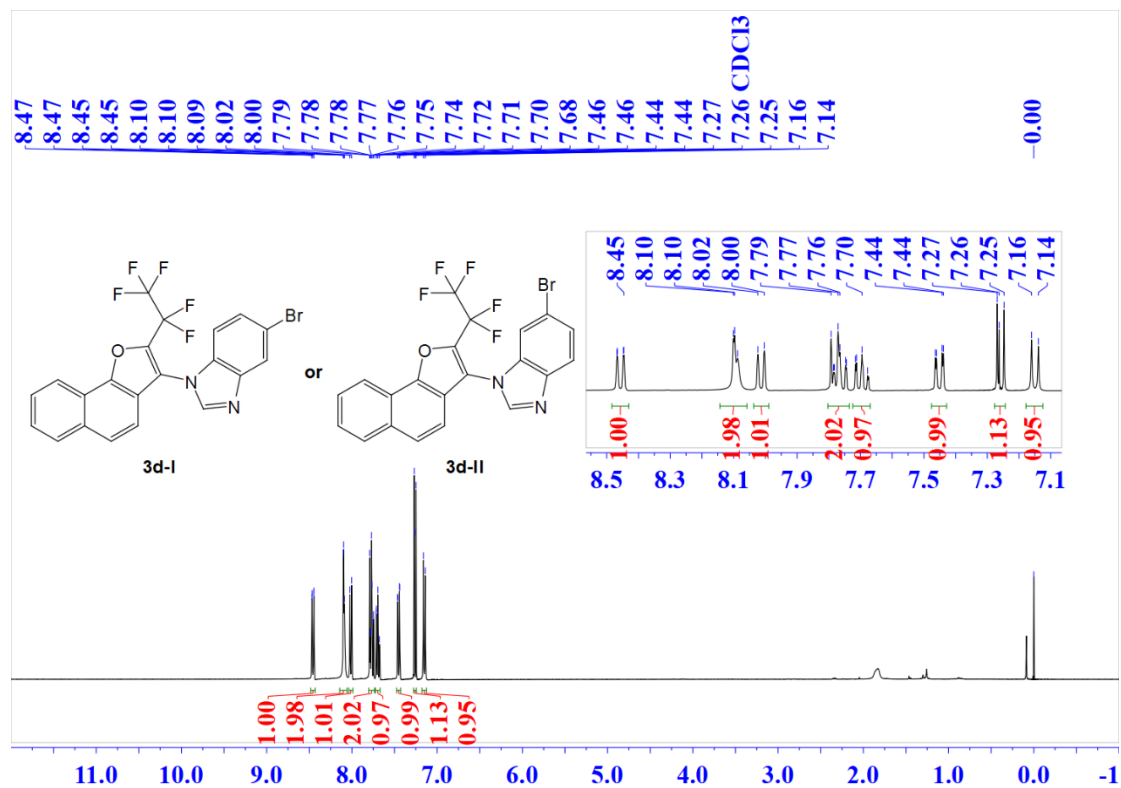


Figure S11. ^{19}F NMR spectrum of **3d-I** or **3d-II**, related to Scheme 1.

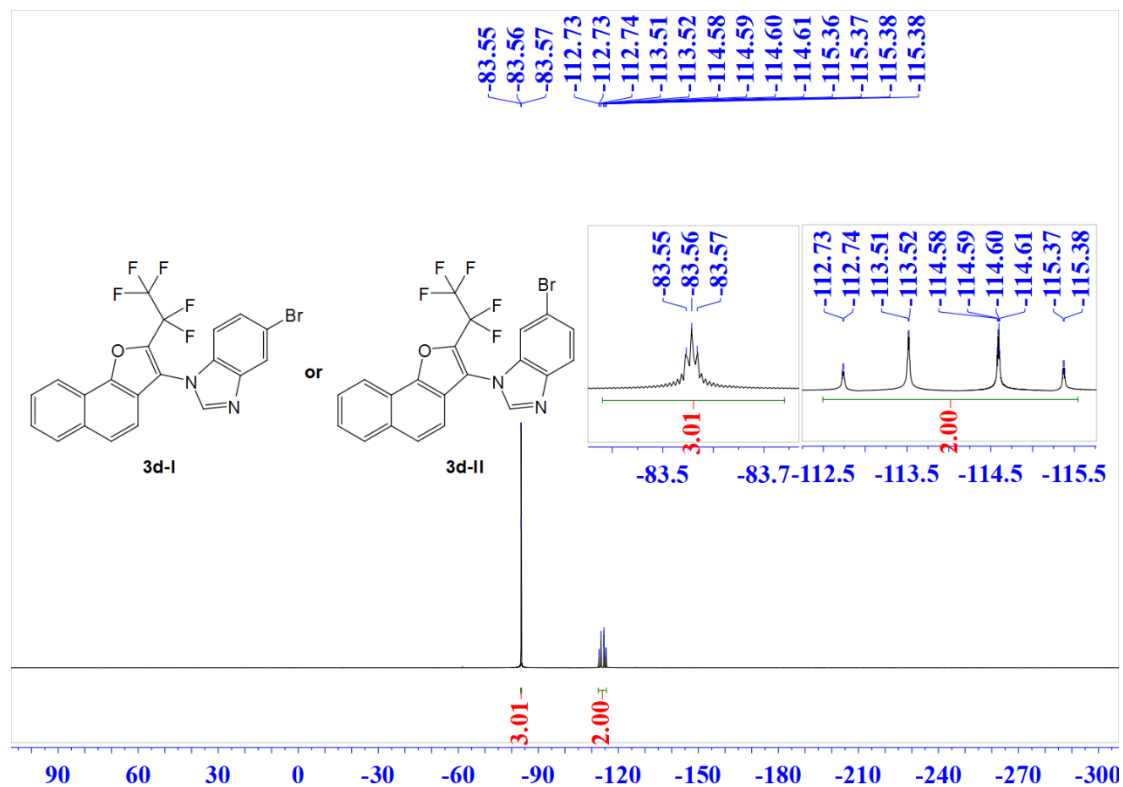


Figure S12. ^{13}C NMR spectrum of **3d-I** or **3d-II**, related to Scheme 1.

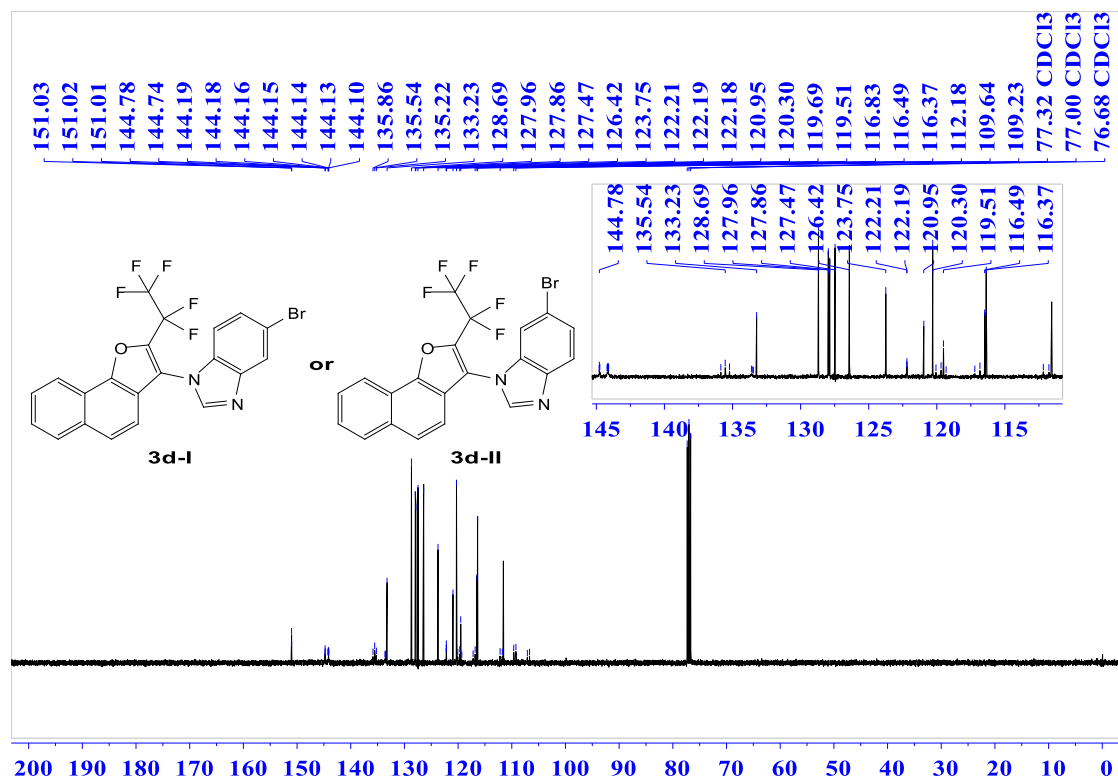


Figure S13. ¹H NMR spectrum of **3d-I** or **3d-II**, related to **Scheme 1**.

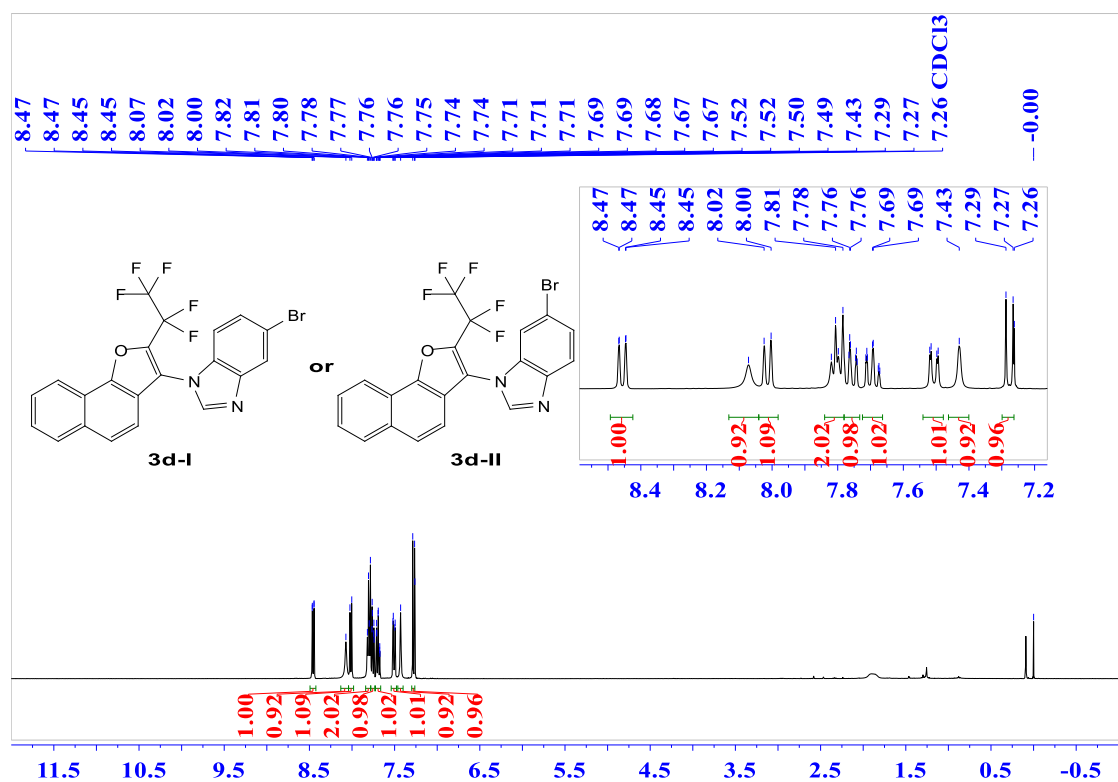


Figure S14. ¹⁹F NMR spectrum of **3d-I** or **3d-II**, related to **Scheme 1**.

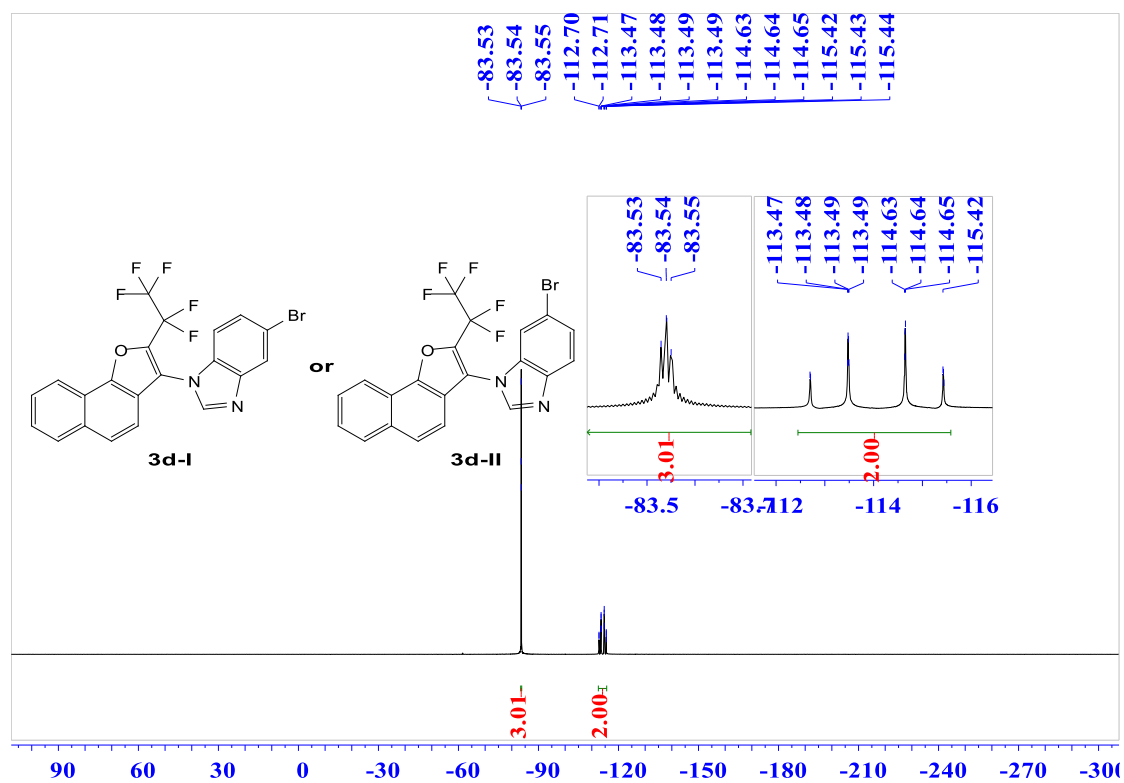


Figure S15. ^{13}C NMR spectrum of 3d-I or 3d-II, related to Scheme 1.

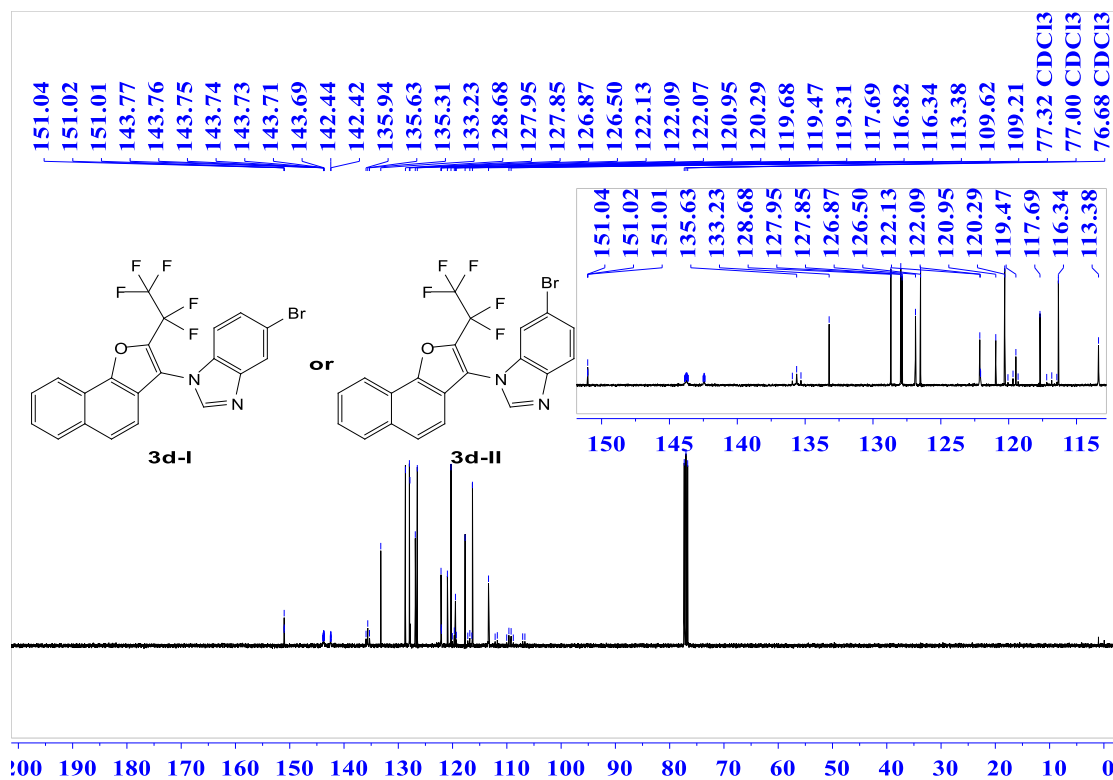


Figure S16. ^1H NMR spectrum of 3e-I and 3e-II, related to Scheme 1.

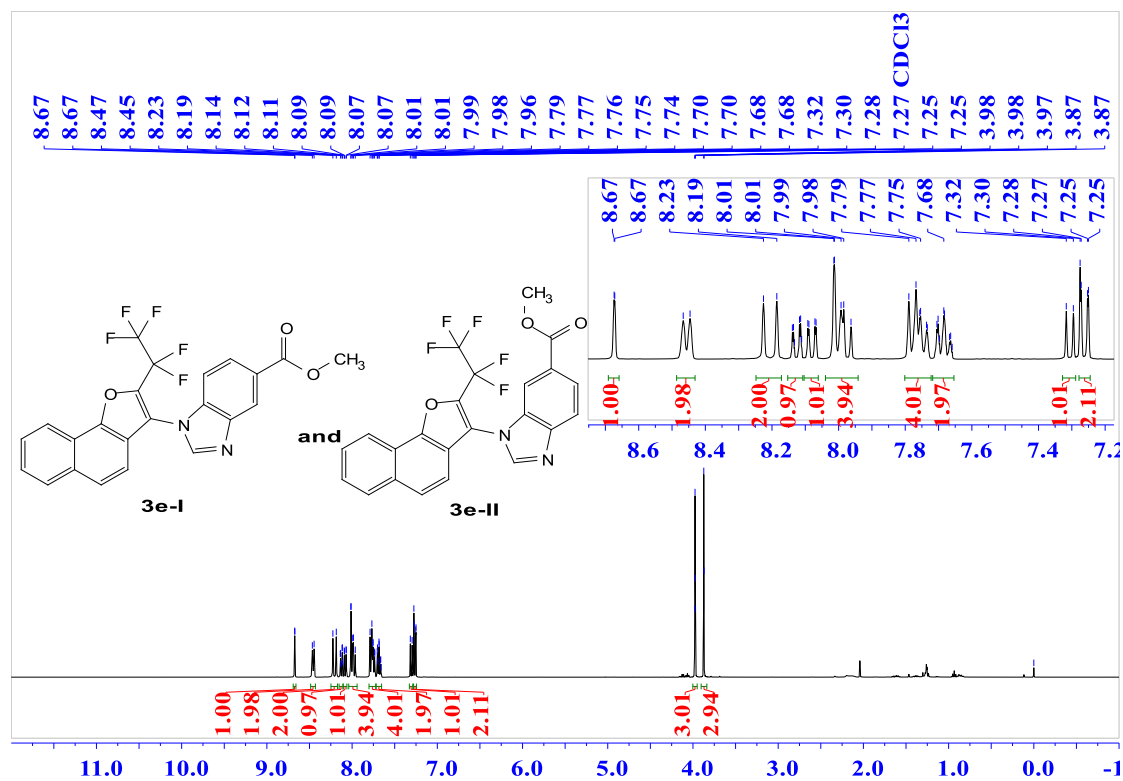


Figure S17. ^{19}F NMR spectrum of **3e-I** and **3e-II**, related to Scheme 1.

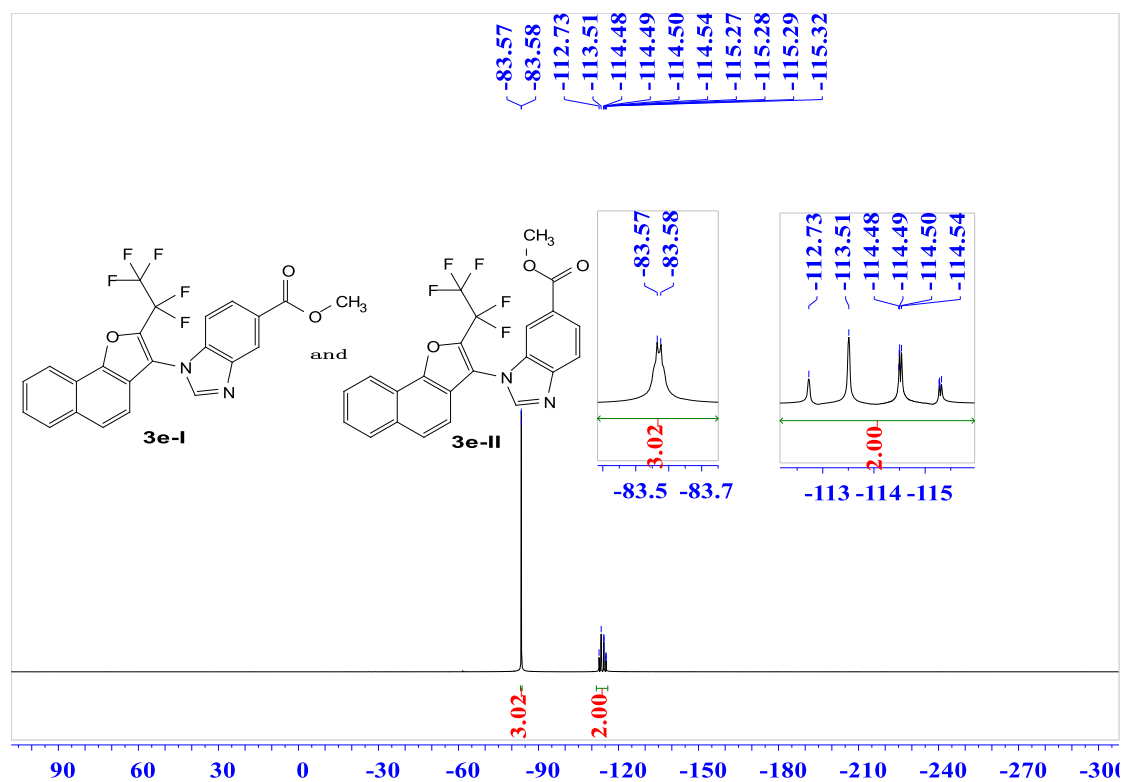


Figure S18. ^{13}C NMR spectrum of **3e-I** and **3e-II**, related to Scheme 1.

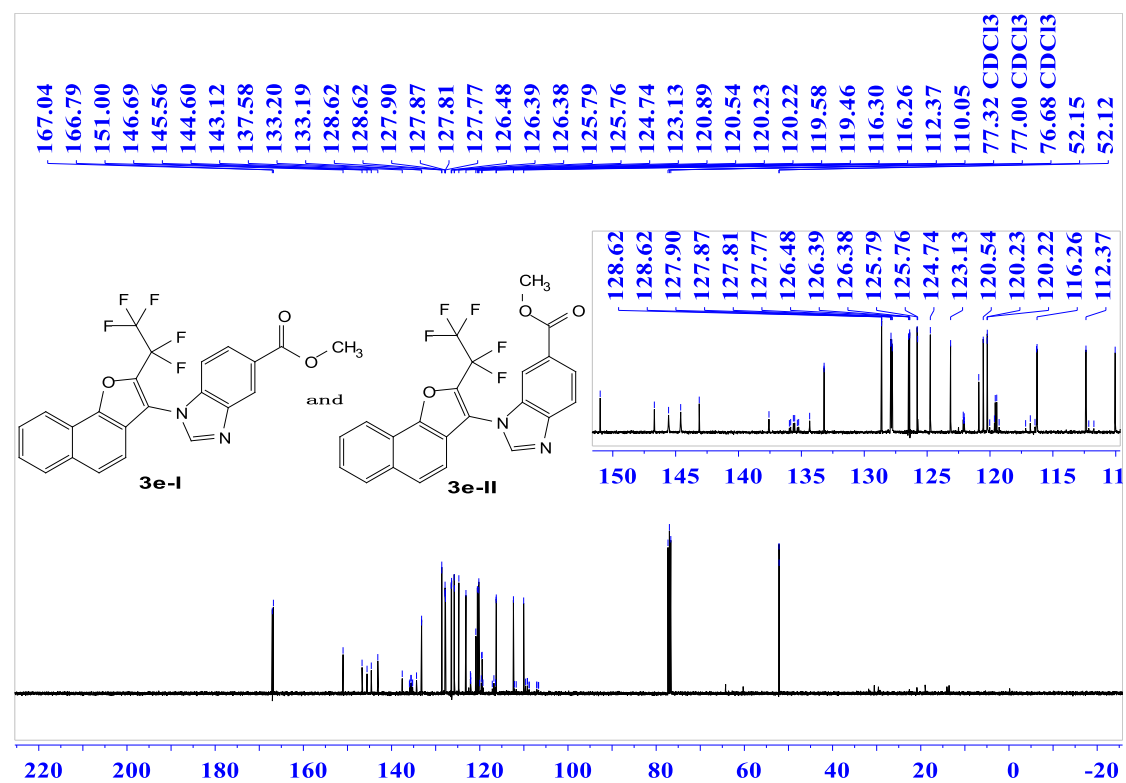


Figure S19. ¹H NMR spectrum of **3f-I** or **3f-II**, related to Scheme 1.

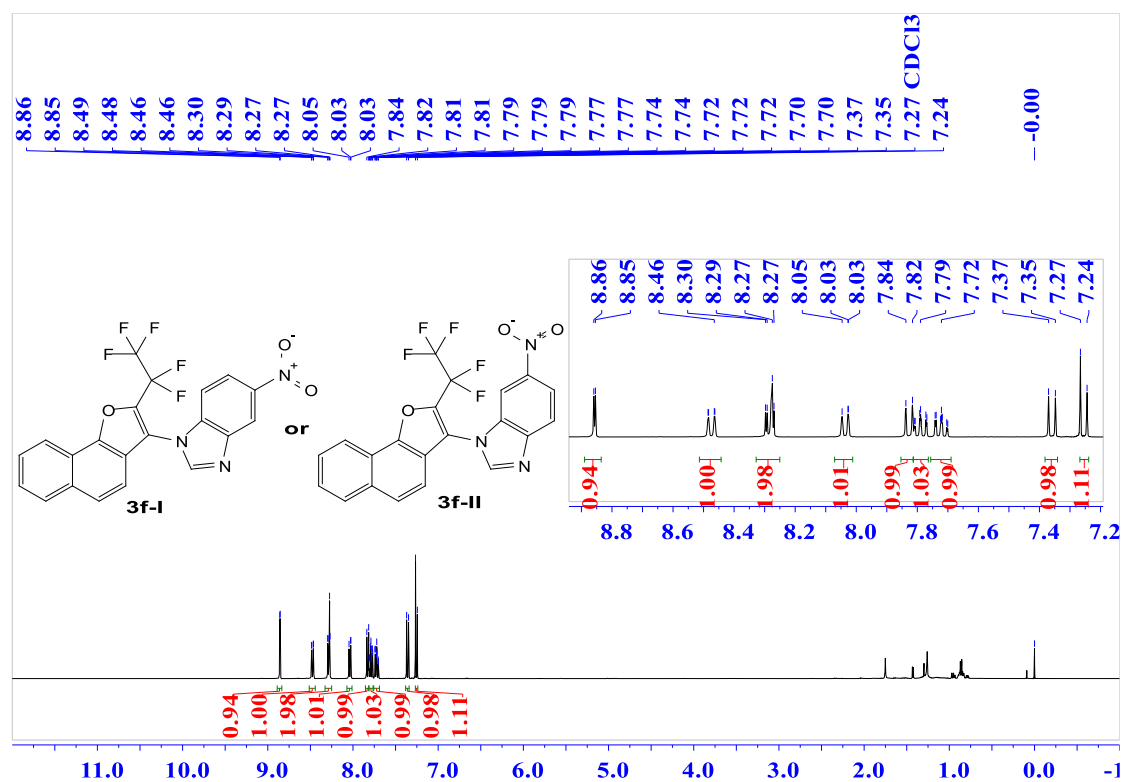


Figure S20. ¹⁹F NMR spectrum of **3f-I** or **3f-II**, related to Scheme 1.

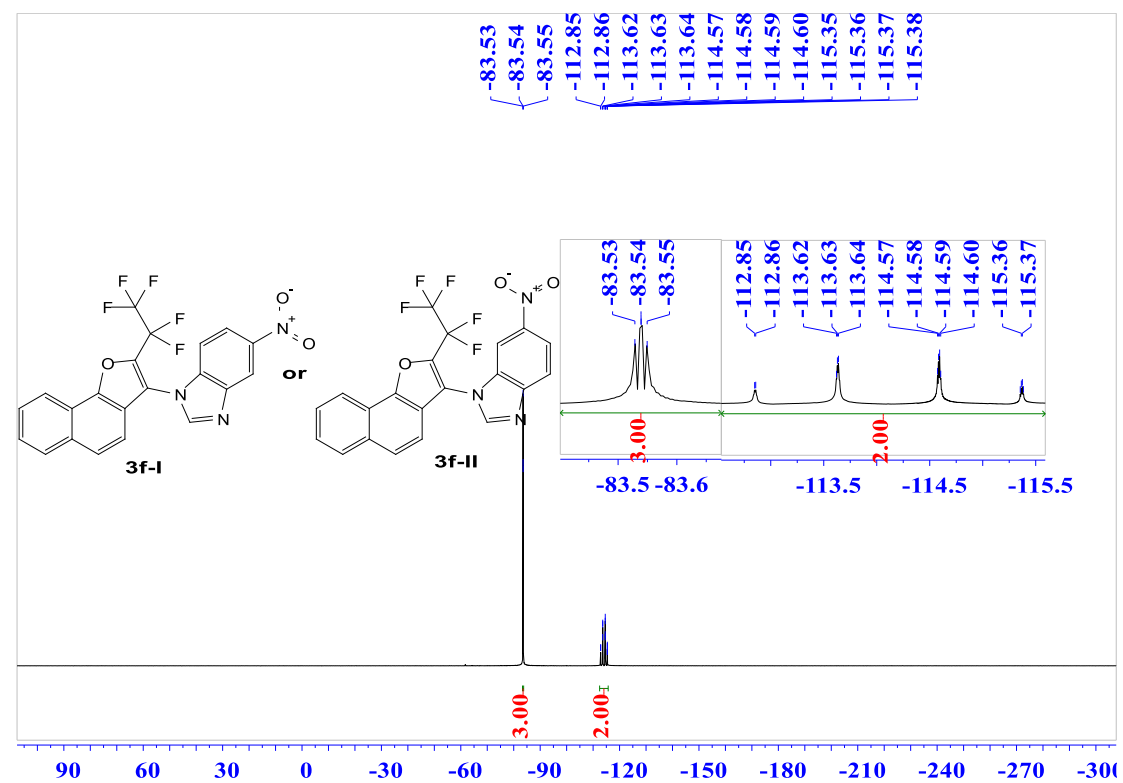


Figure S21. ¹³C NMR spectrum of **3f-I** or **3f-II**, related to Scheme 1.

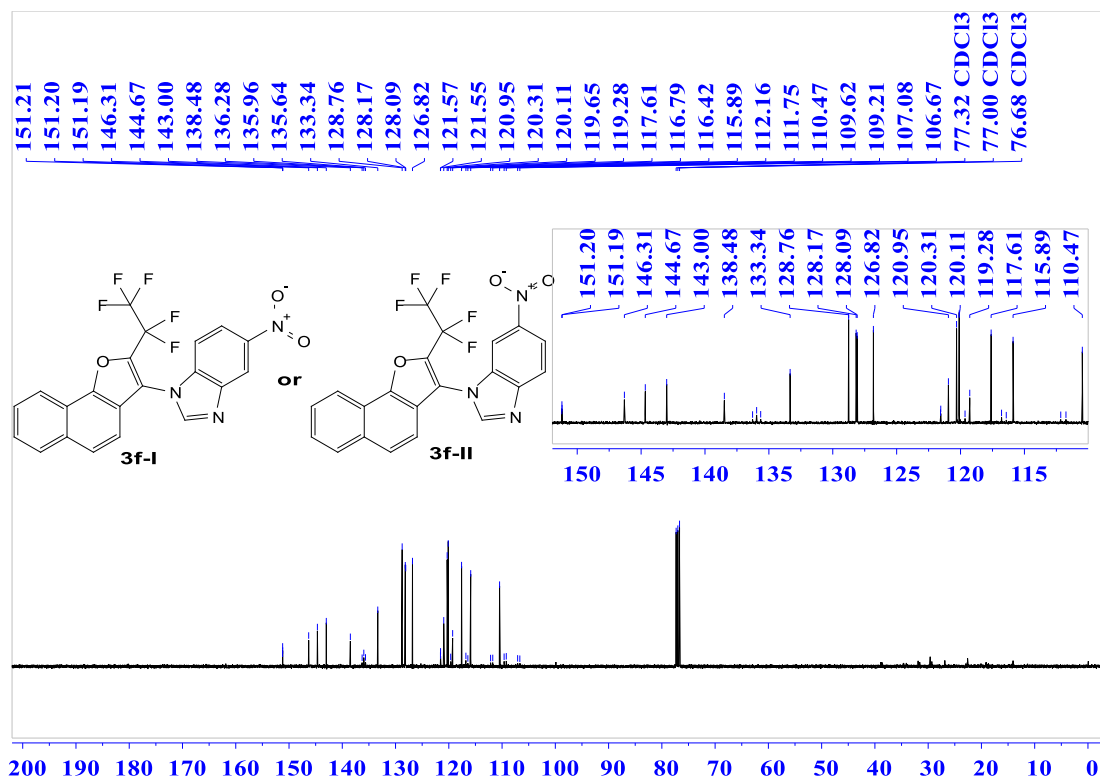


Figure S22. ¹H NMR spectrum of **3f-I** or **3f-II**, related to Scheme 1.

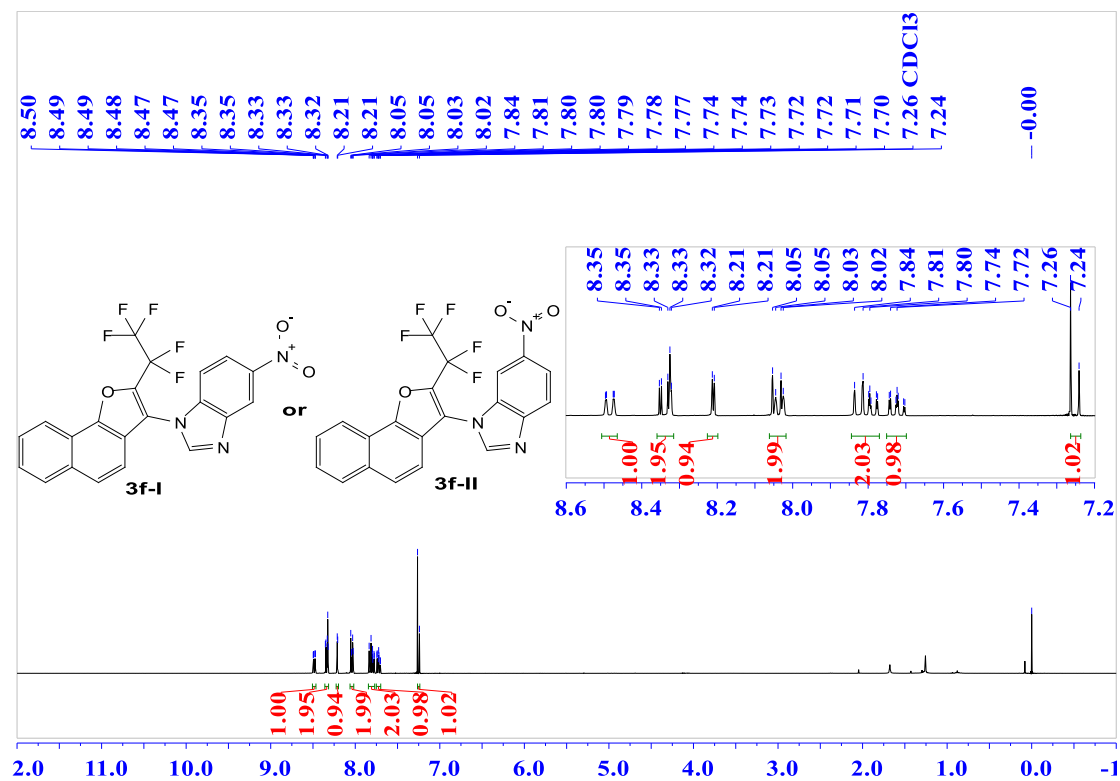


Figure S23. ^{19}F NMR spectrum of **3f-I** or **3f-II**, related to Scheme 1.

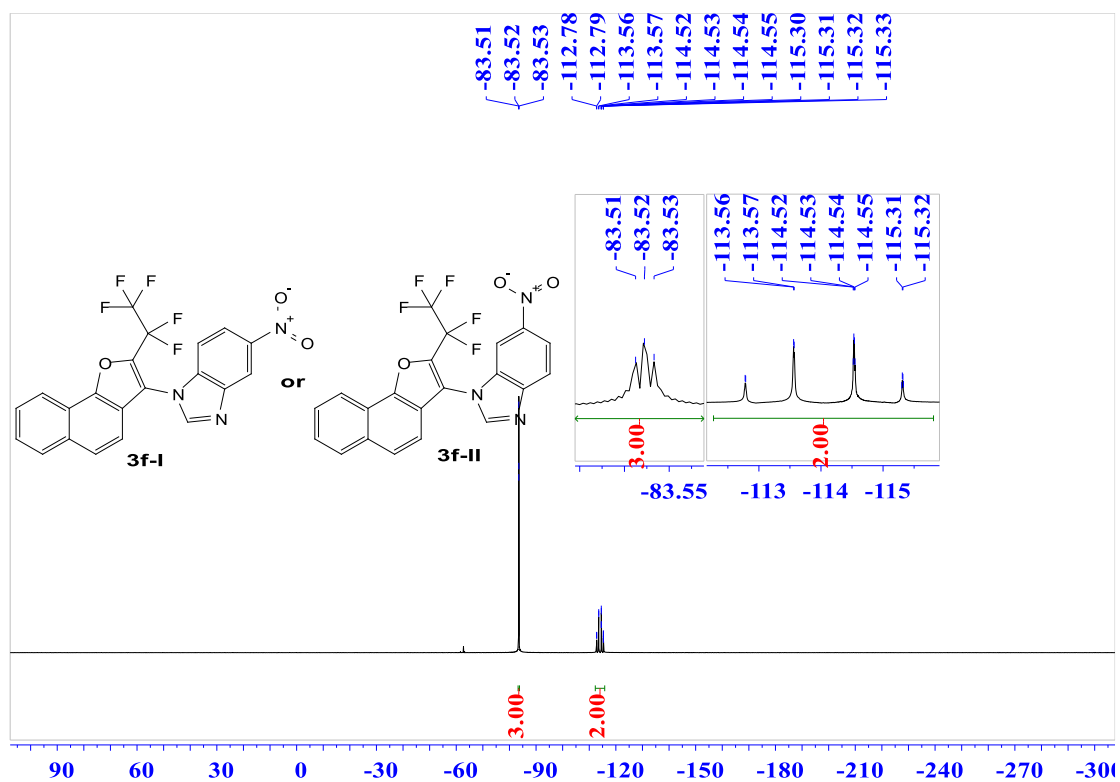


Figure S24. ^{13}C NMR spectrum of **3f-I** or **3f-II**, related to Scheme 1.

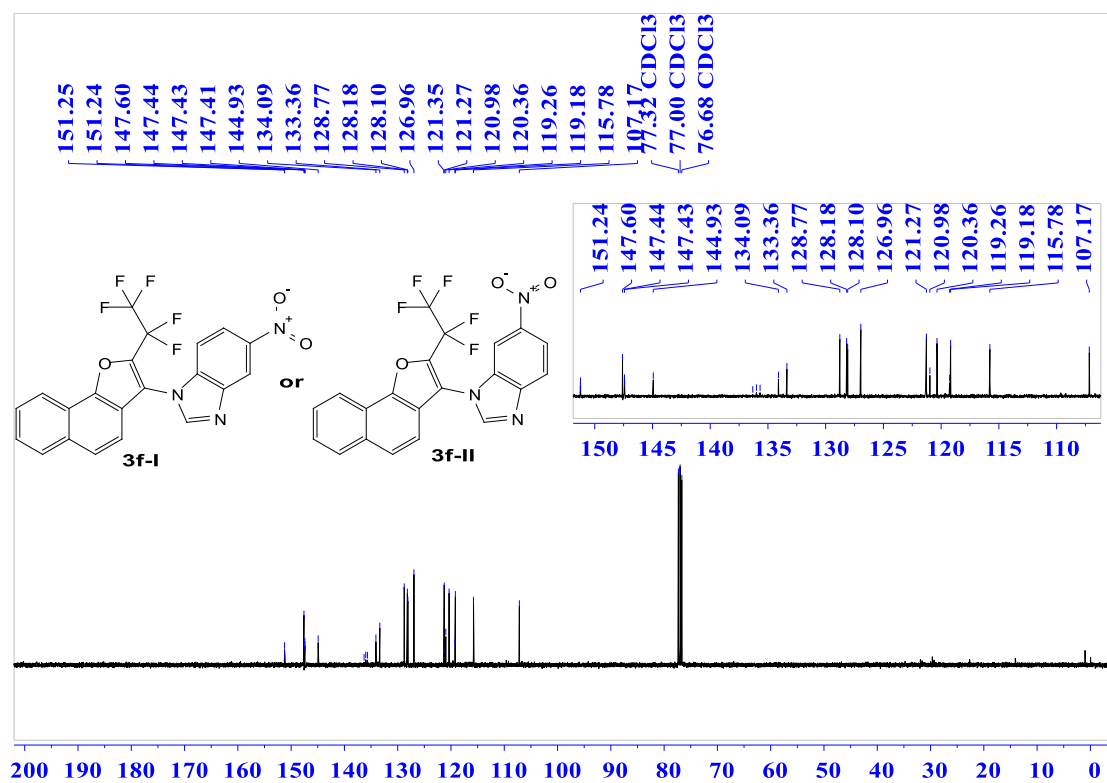


Figure S25. ¹H NMR spectrum of **3g**, related to Scheme 1.

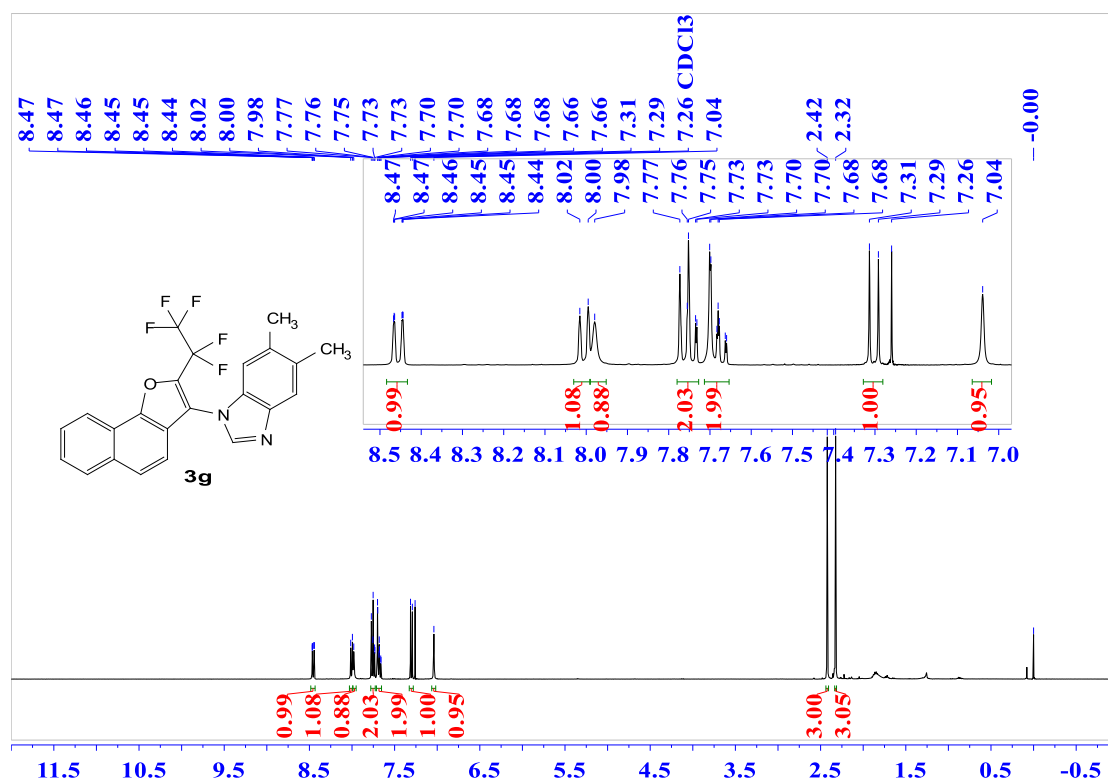


Figure S26. ¹⁹F NMR spectrum of **3g**, related to Scheme 1.

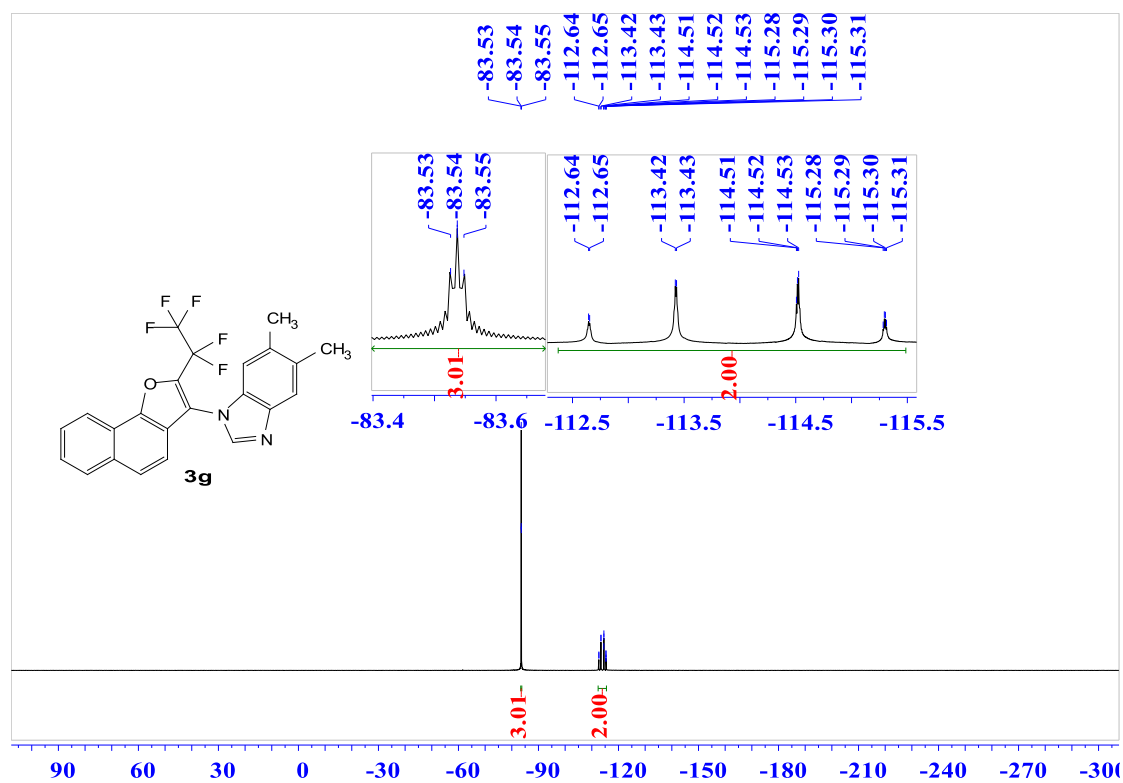


Figure S27. ^{13}C NMR spectrum of **3g**, related to Scheme 1.

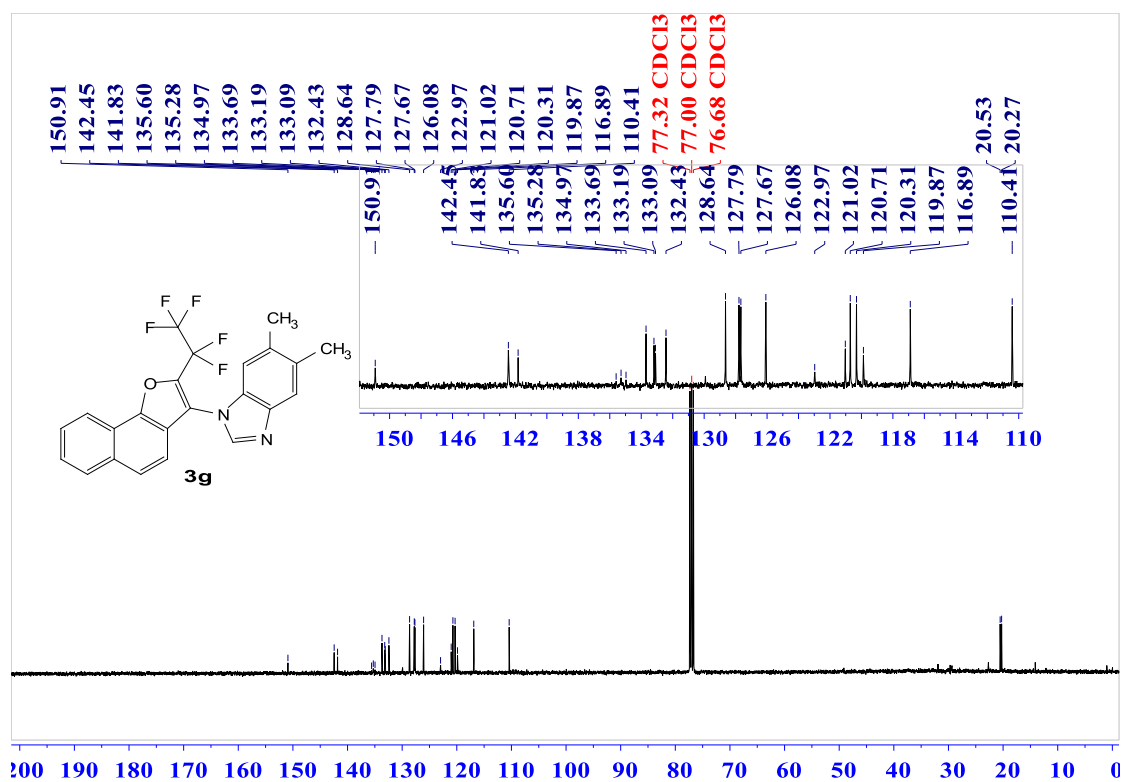


Figure S28. ^1H NMR spectrum of **3h-I** or **3h-II**, related to Scheme 1.

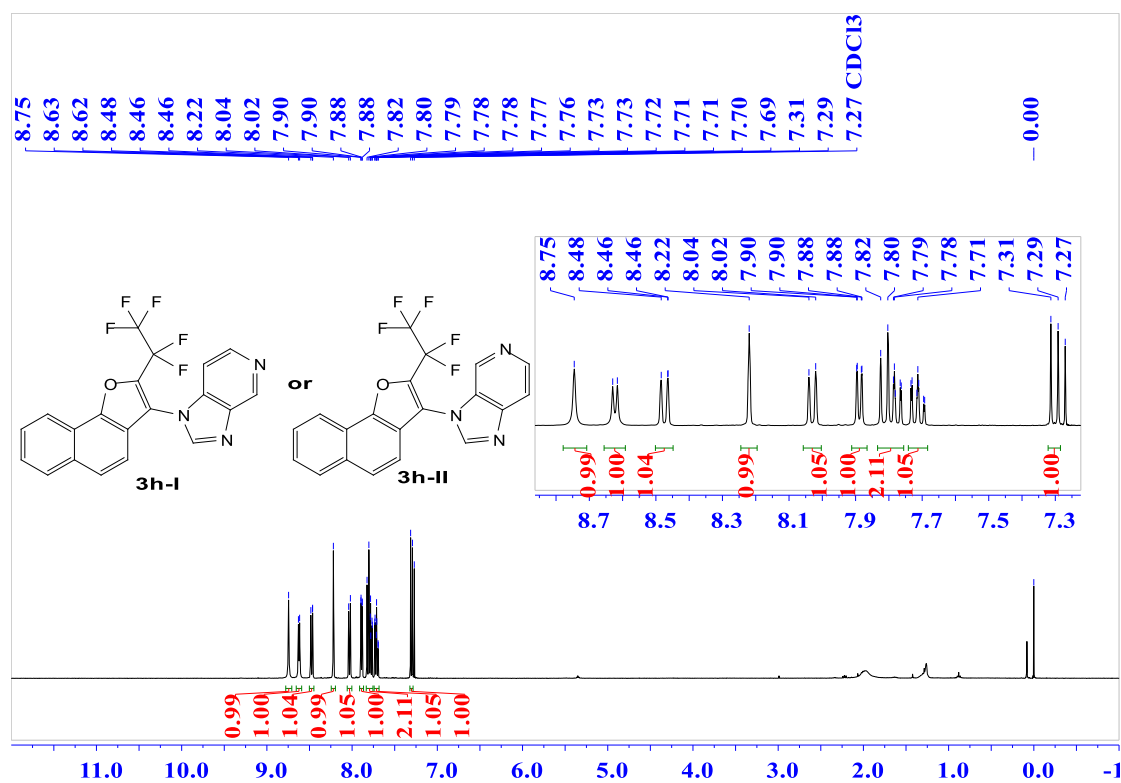


Figure S29. ^{19}F NMR spectrum of **3h-I** or **3h-II**, related to Scheme 1.

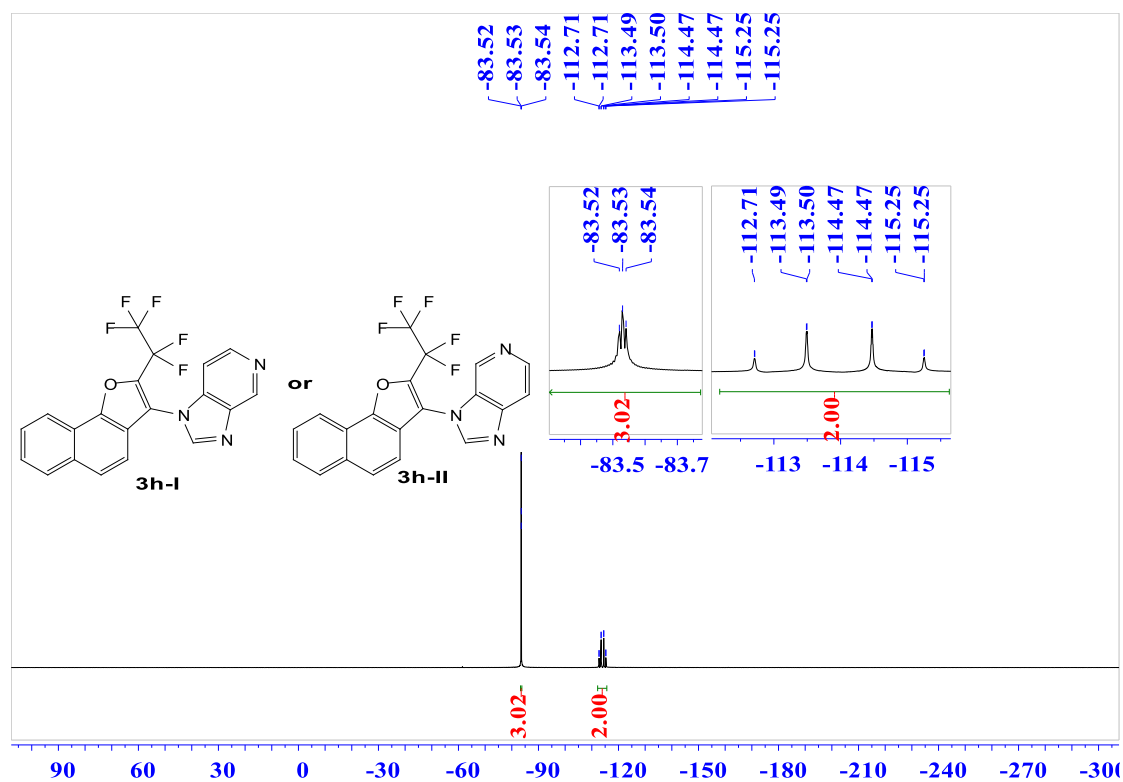


Figure S30. ^{13}C NMR spectrum of **3h-I** or **3h-II**, related to Scheme 1.

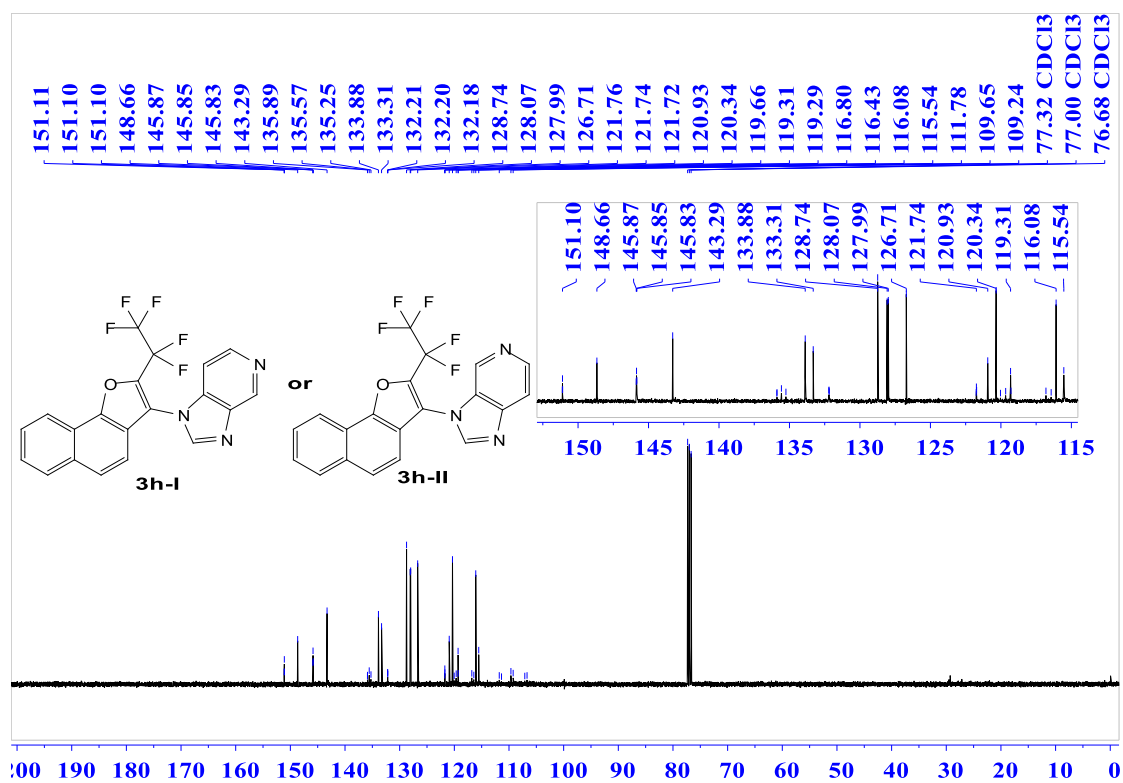


Figure S31. ¹H NMR spectrum of **3h-I** or **3h-II**, related to **Scheme 1**.

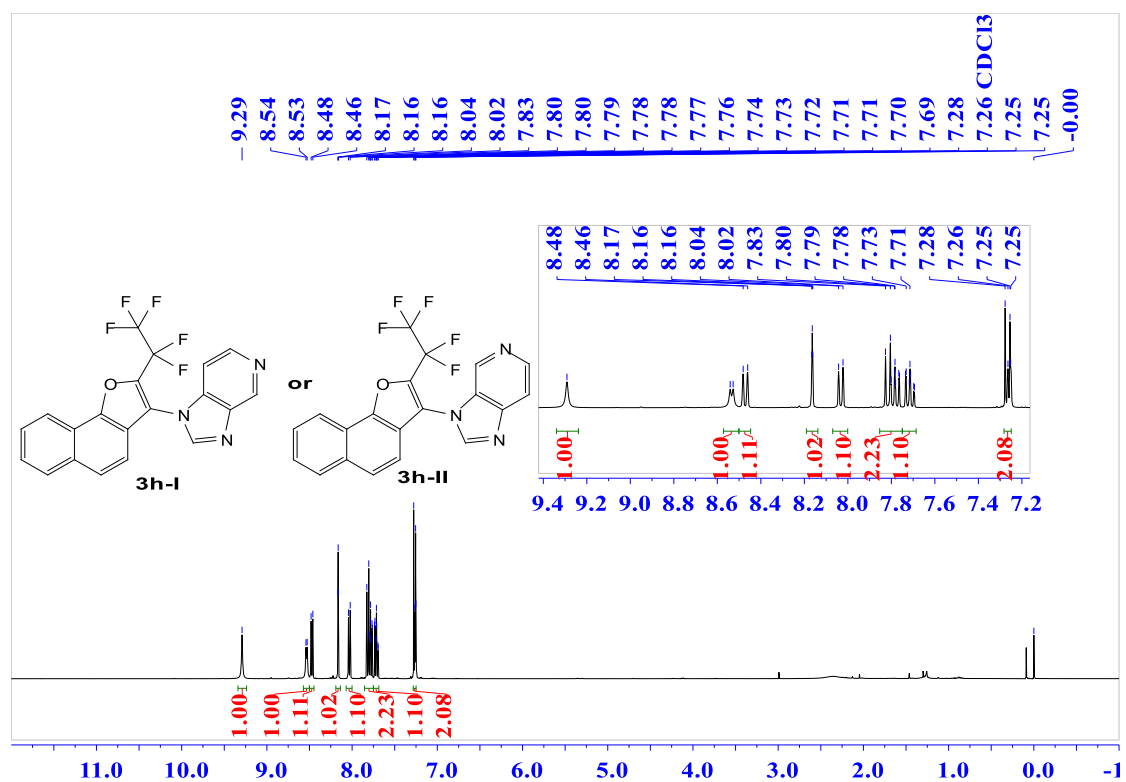


Figure S32. ¹⁹F NMR spectrum of **3h-I** or **3h-II**, related to **Scheme 1**.

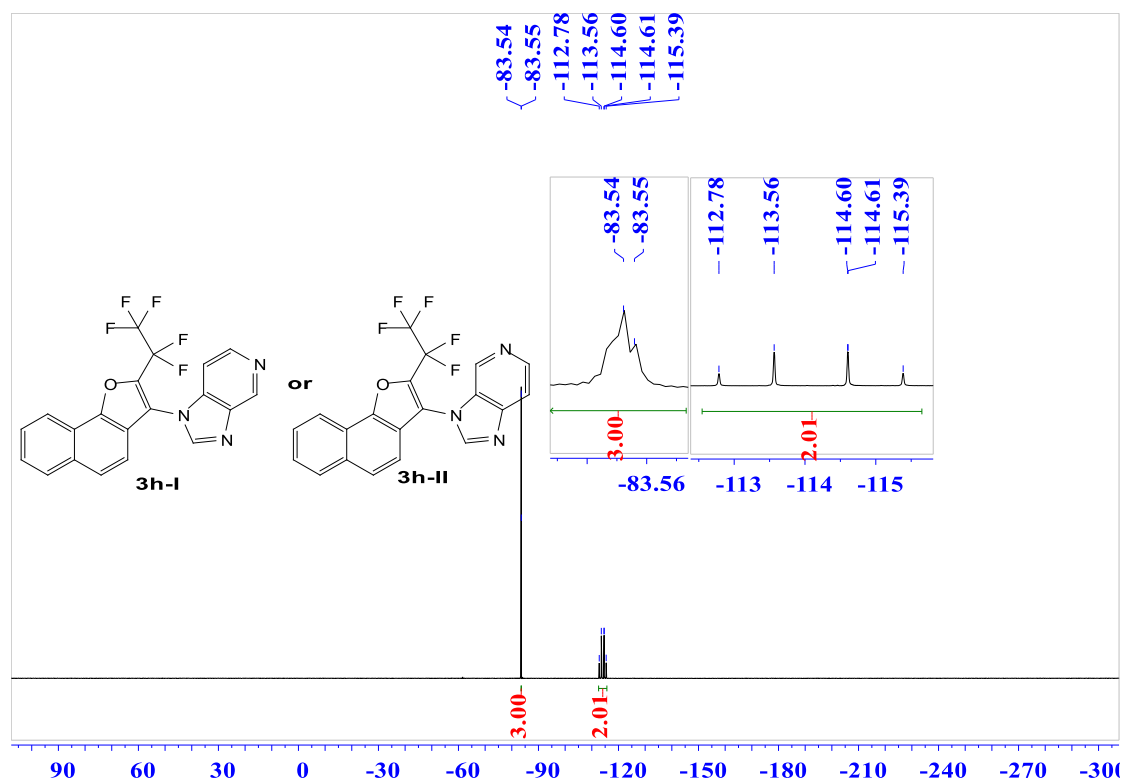


Figure S33. ^{13}C NMR spectrum of **3h-I** or **3h-II**, related to Scheme 1.

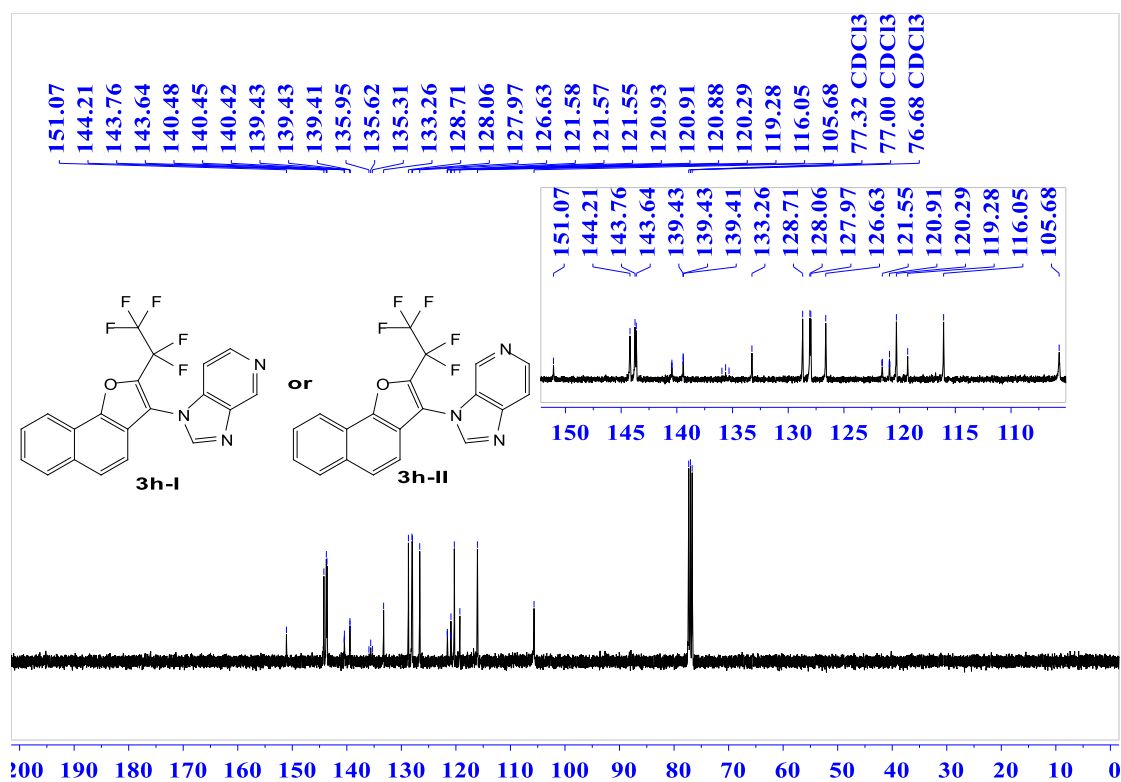


Figure S34. ^1H NMR spectrum of **4a**, related to Scheme 1.

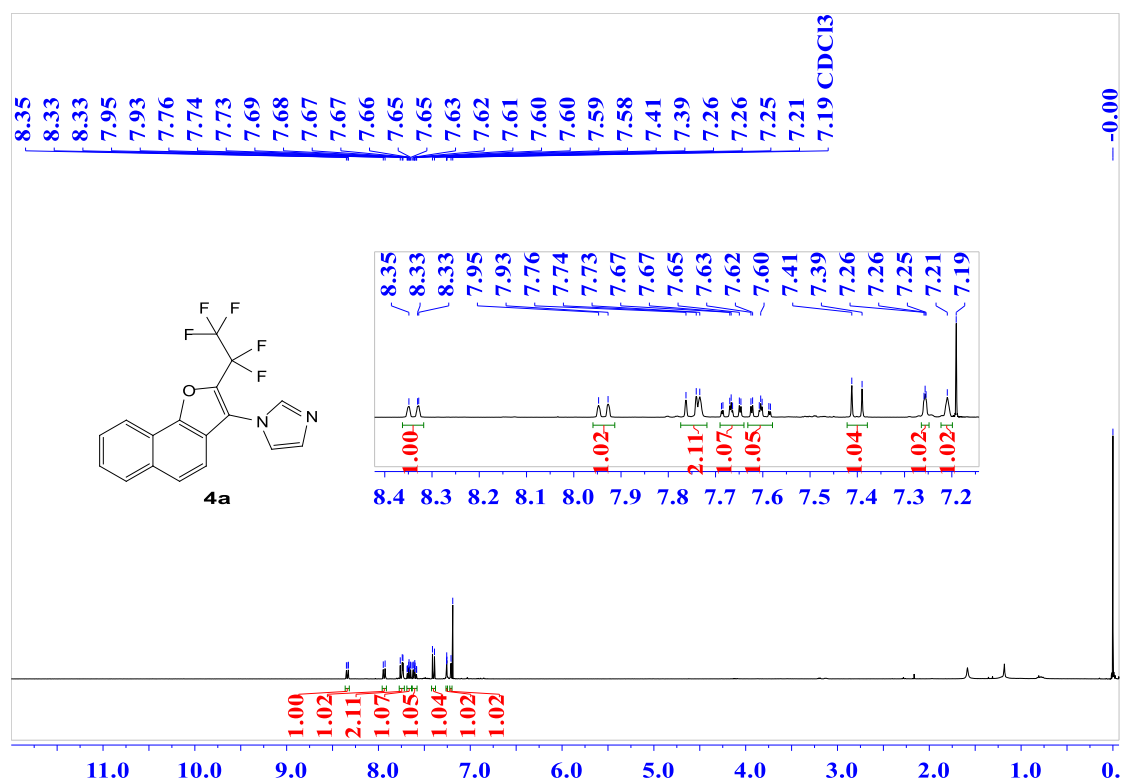


Figure S35. ^{19}F NMR spectrum of **4a**, related to Scheme 1.

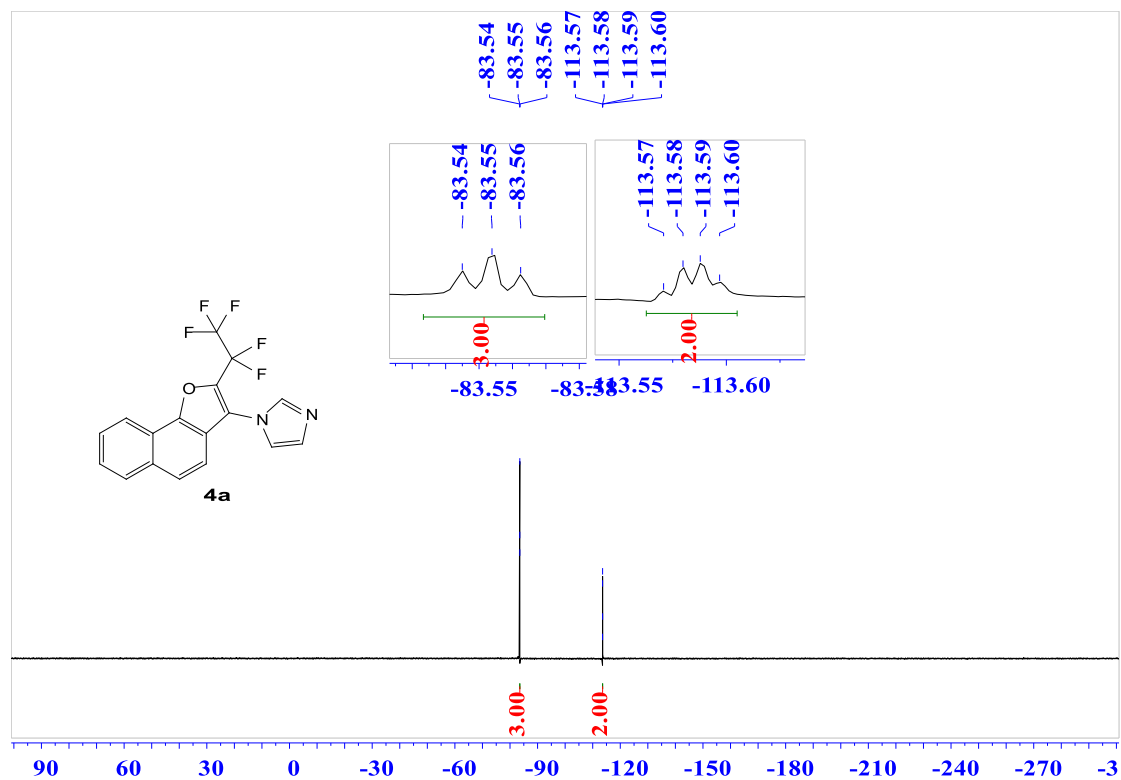


Figure S36. ^{13}C NMR spectrum of **4a**, related to Scheme 1.

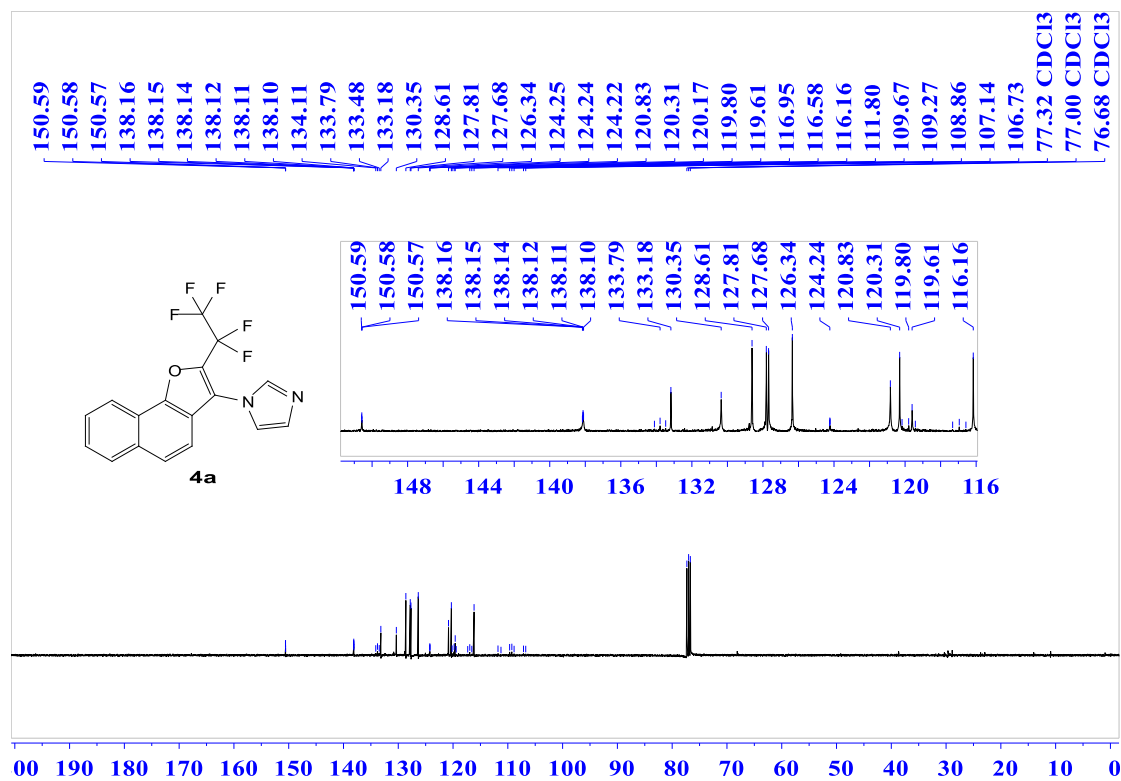


Figure S37. ¹H NMR spectrum of **4b**, related to Scheme 1.

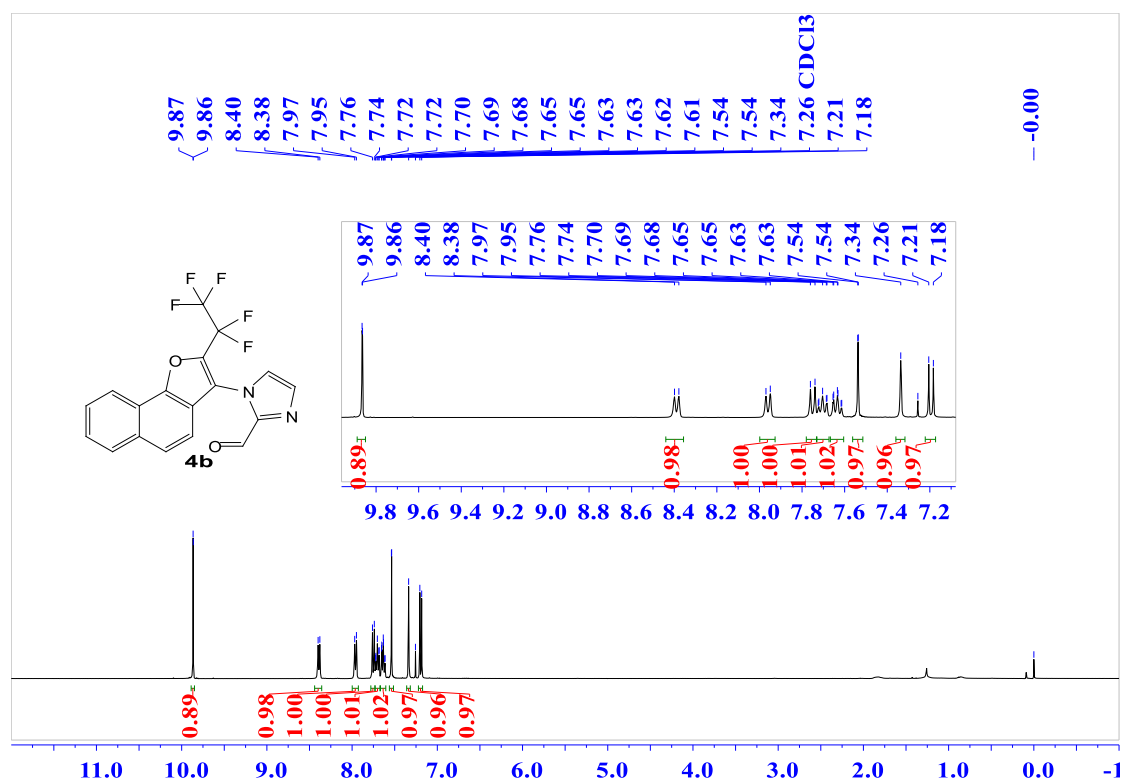


Figure S38. ¹⁹F NMR spectrum of **4b**, related to Scheme 1.

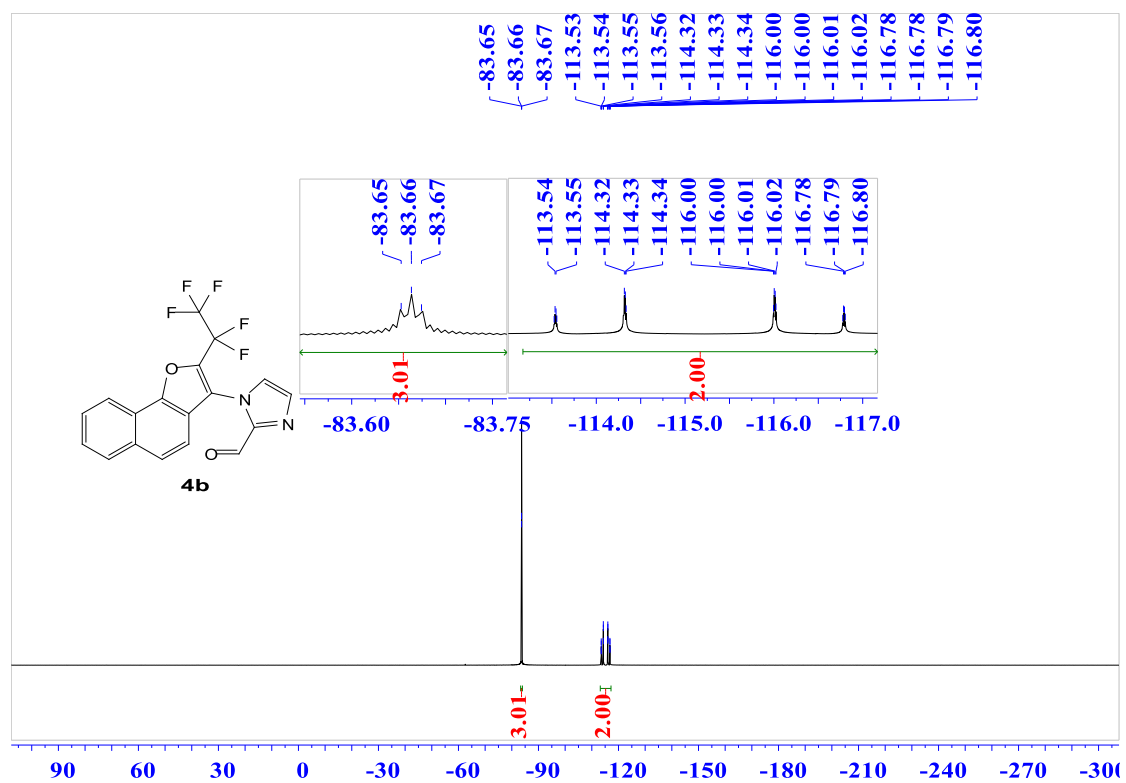


Figure S39. ¹³C NMR spectrum of **4b**, related to Scheme 1.

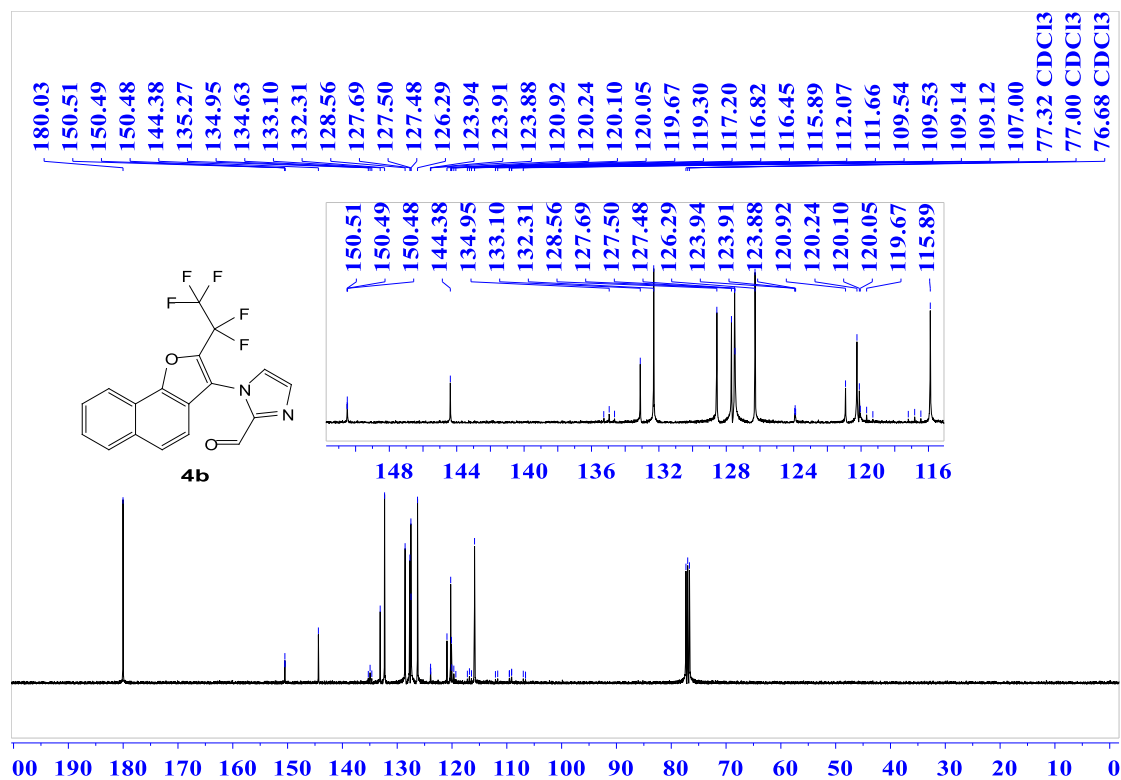


Figure S40. ¹H NMR spectrum of **4c**, related to Scheme 1.

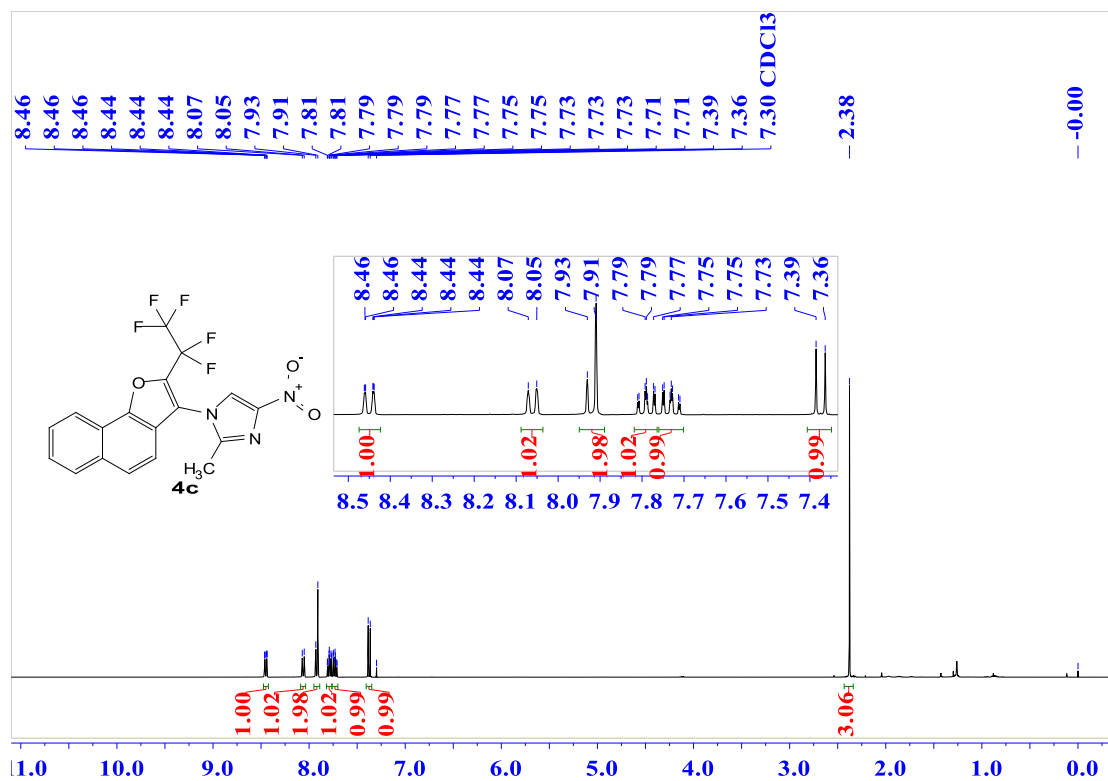


Figure S41. ^{19}F NMR spectrum of **4c**, related to Scheme 1.

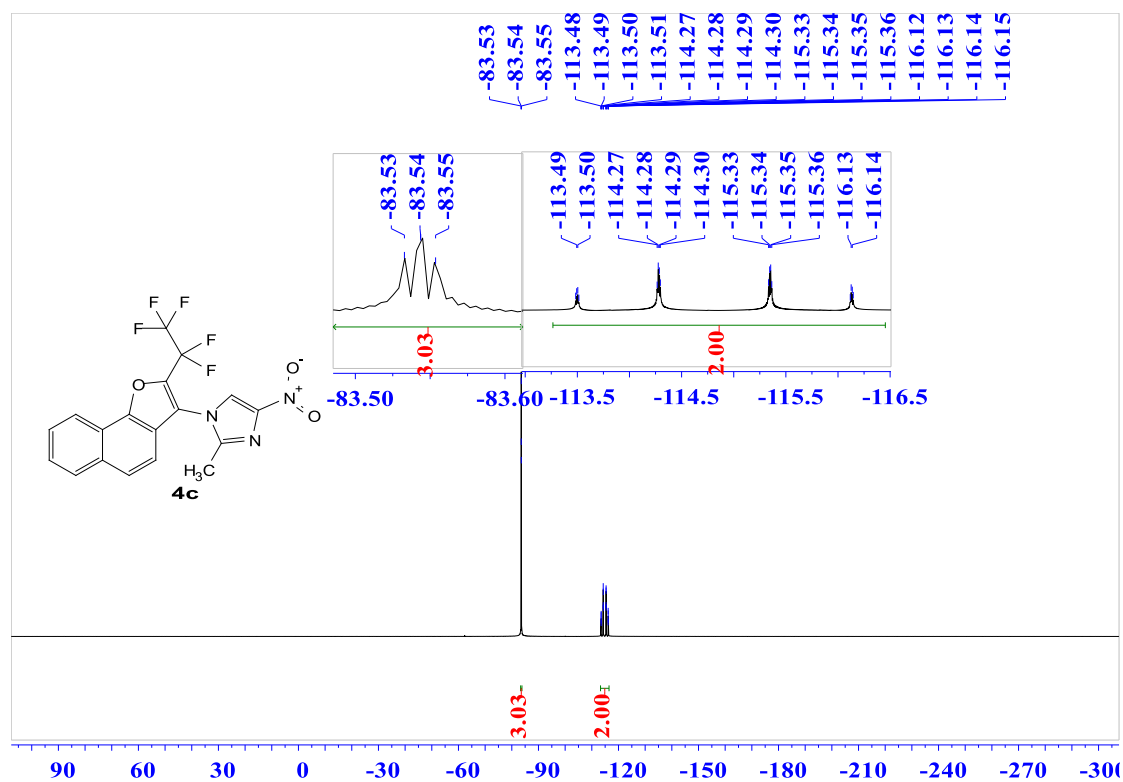


Figure S42. ^{13}C NMR spectrum of **4c**, related to Scheme 1.

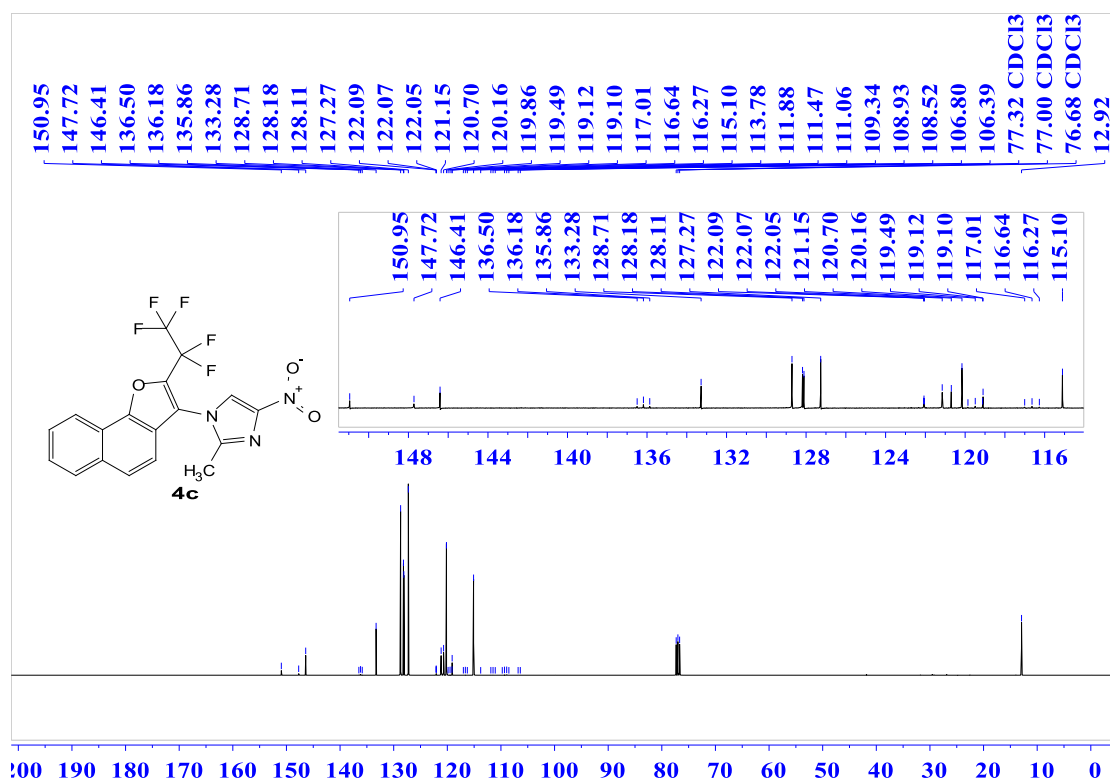


Figure S43. ^1H NMR spectrum of **5a**, related to Scheme 1.

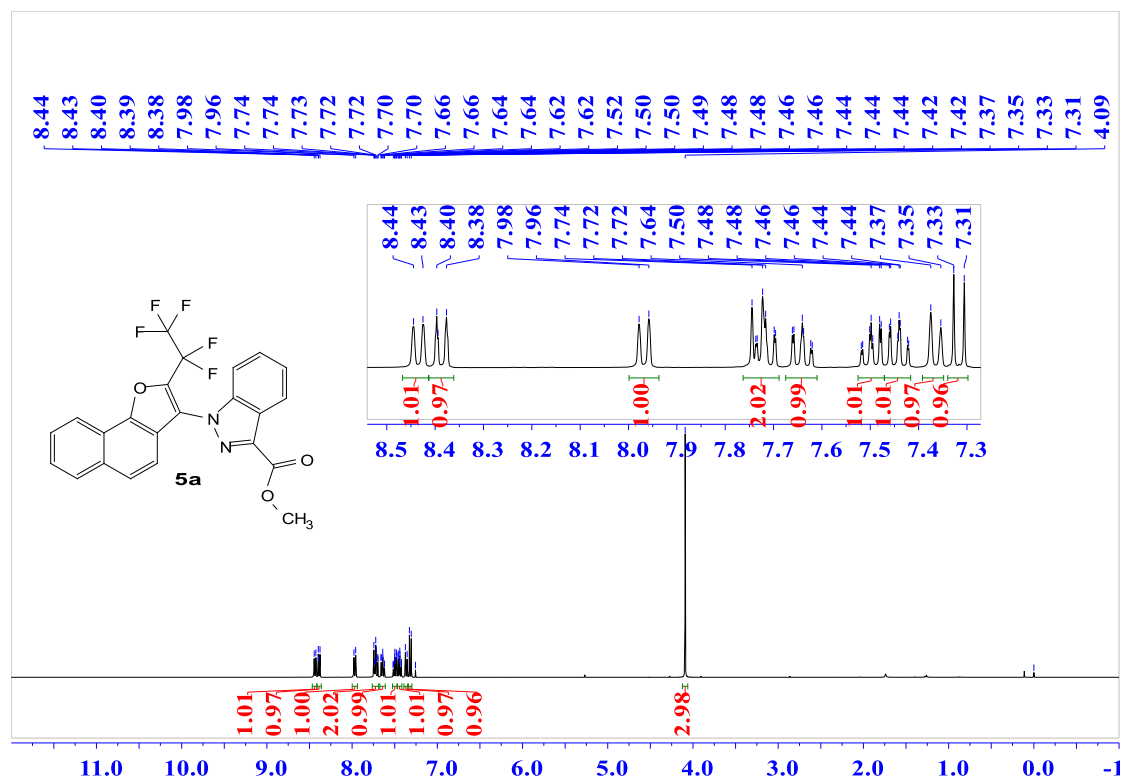


Figure S44. ^{19}F NMR spectrum of **5a**, related to Scheme 1.

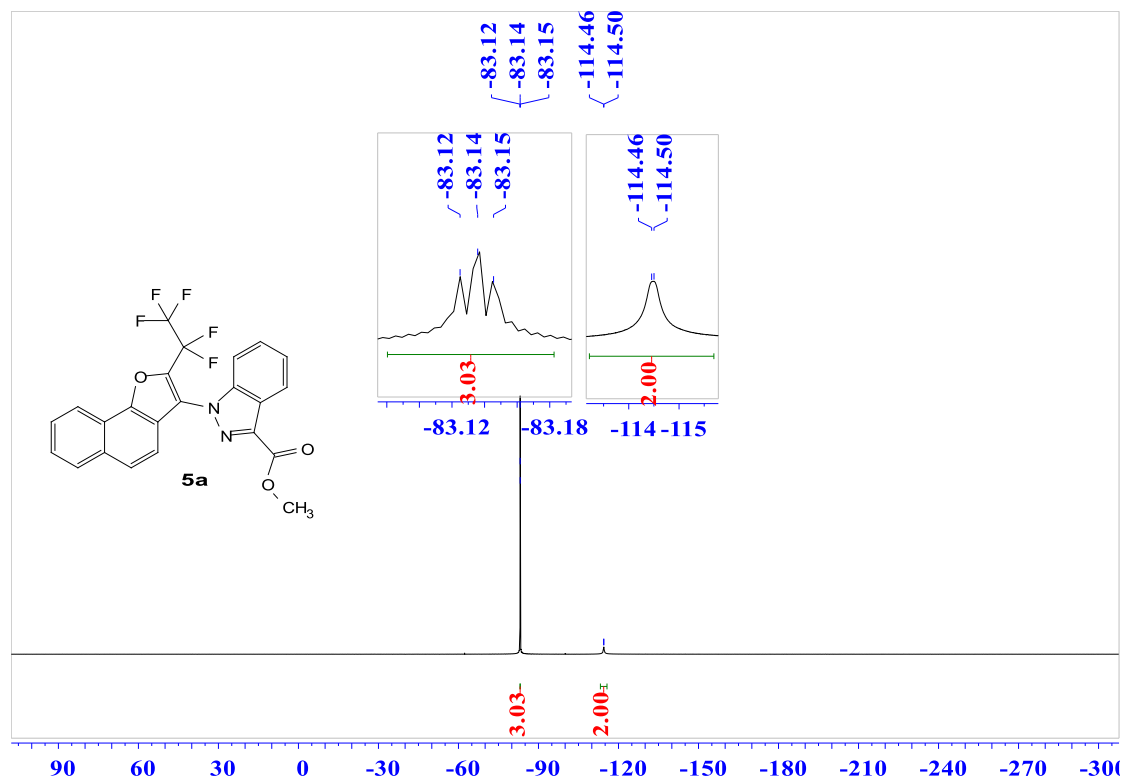


Figure S45. ¹³C NMR spectrum of **5a**, related to Scheme 1.

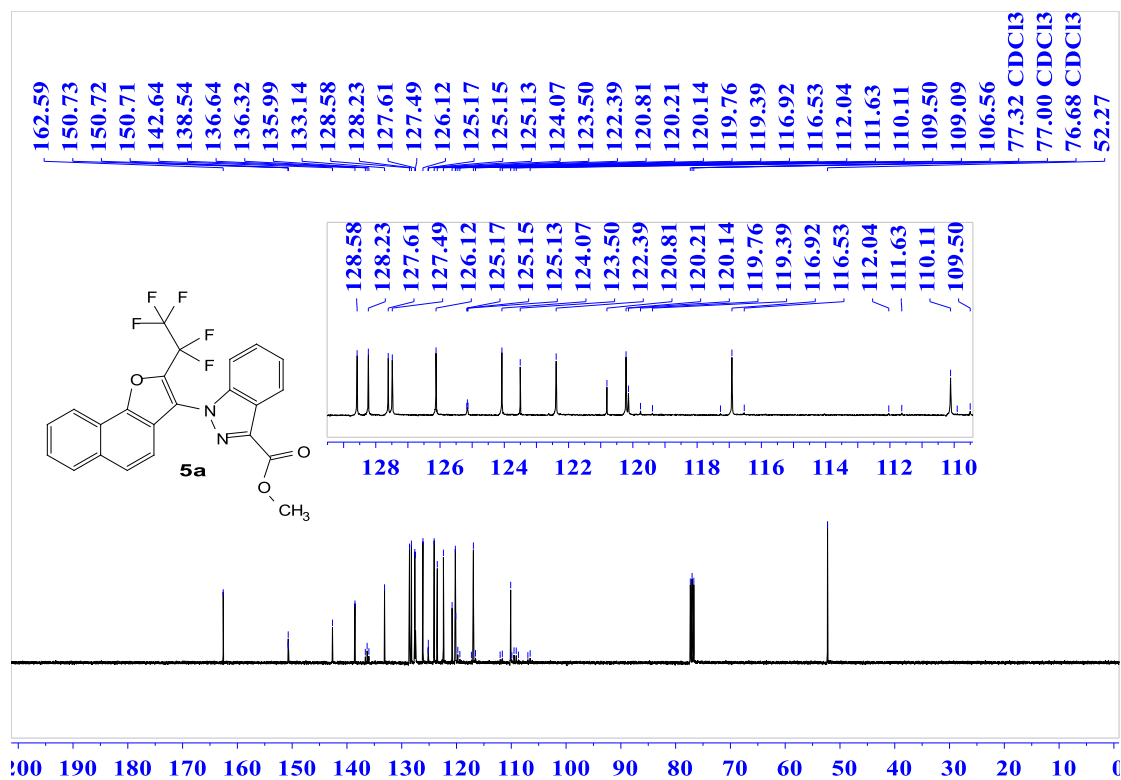


Figure S46. ¹H NMR spectrum of **5b**, related to Scheme 1.

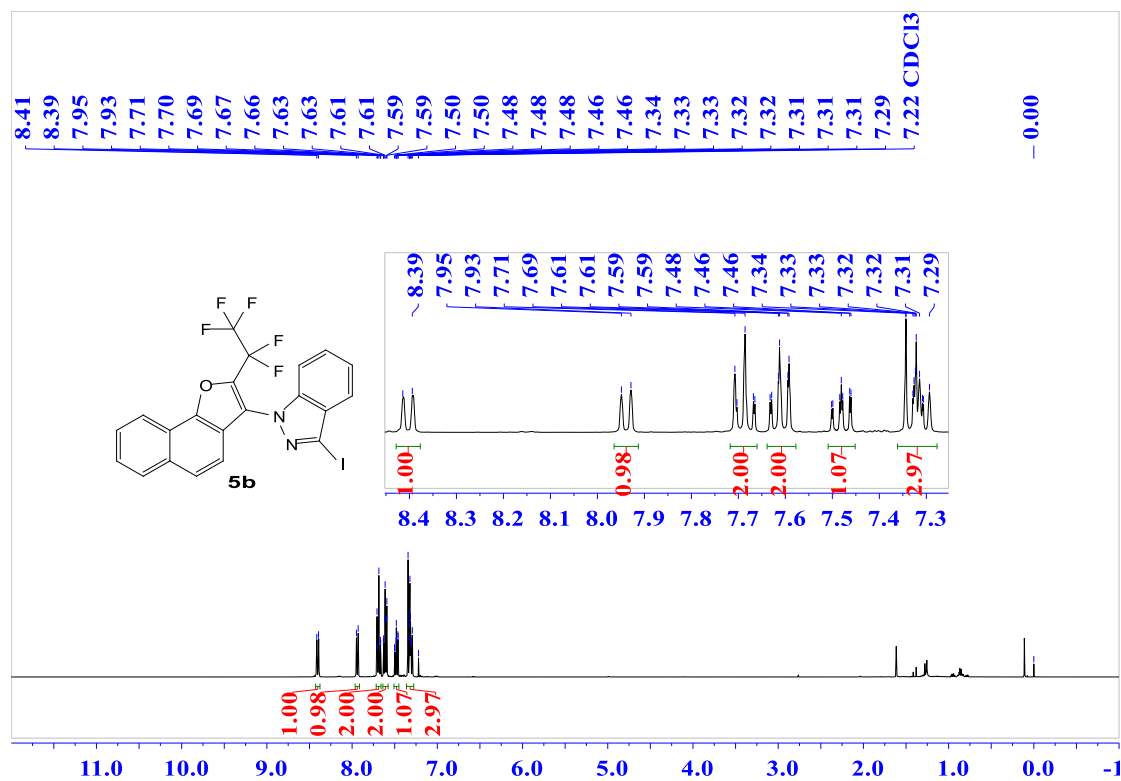


Figure S47. ^{19}F NMR spectrum of **5b**, related to Scheme 1.

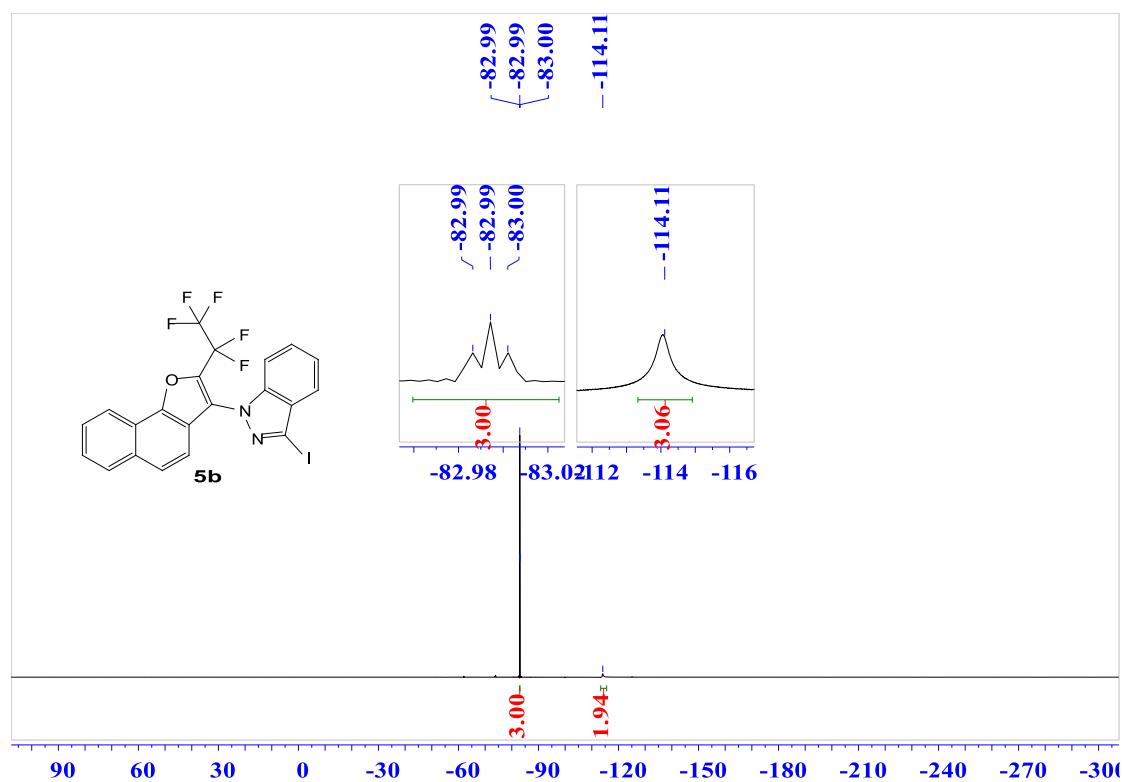


Figure S48. ^{13}C NMR spectrum of **5b**, related to Scheme 1.

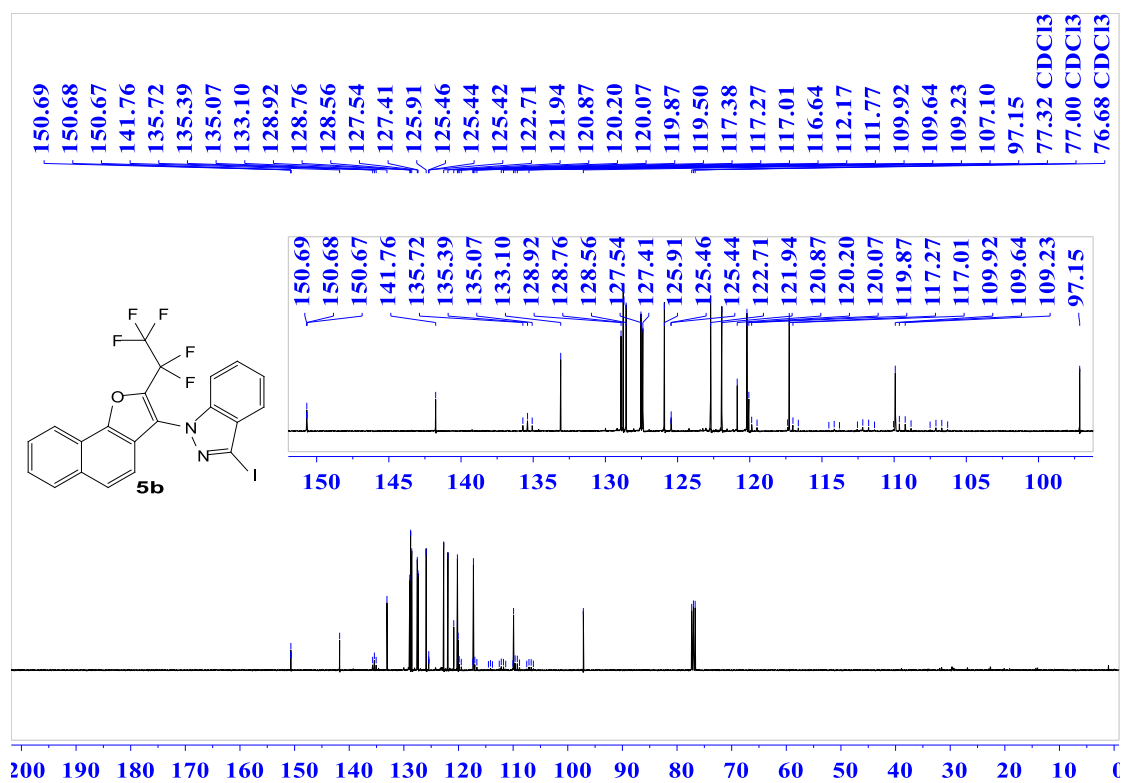


Figure S49. ¹H NMR spectrum of **5c-I**, related to Scheme 1.

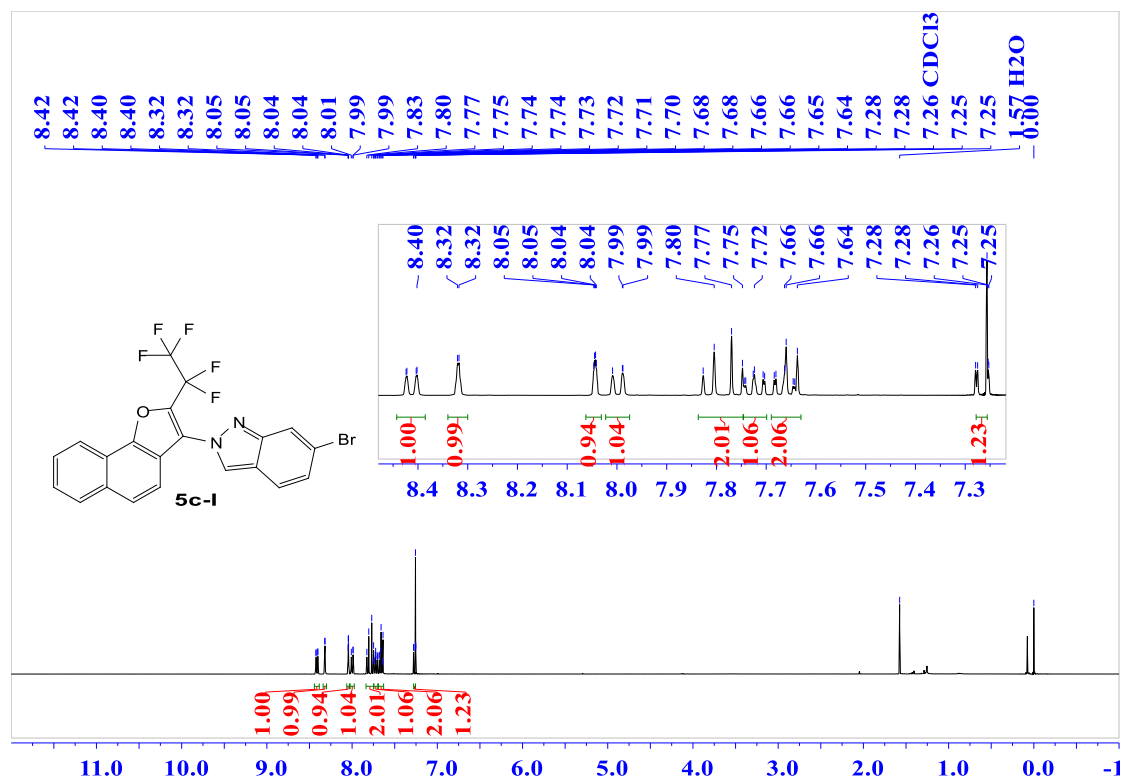


Figure S50. ¹⁹F NMR spectrum of **5c-I**, related to Scheme 1.

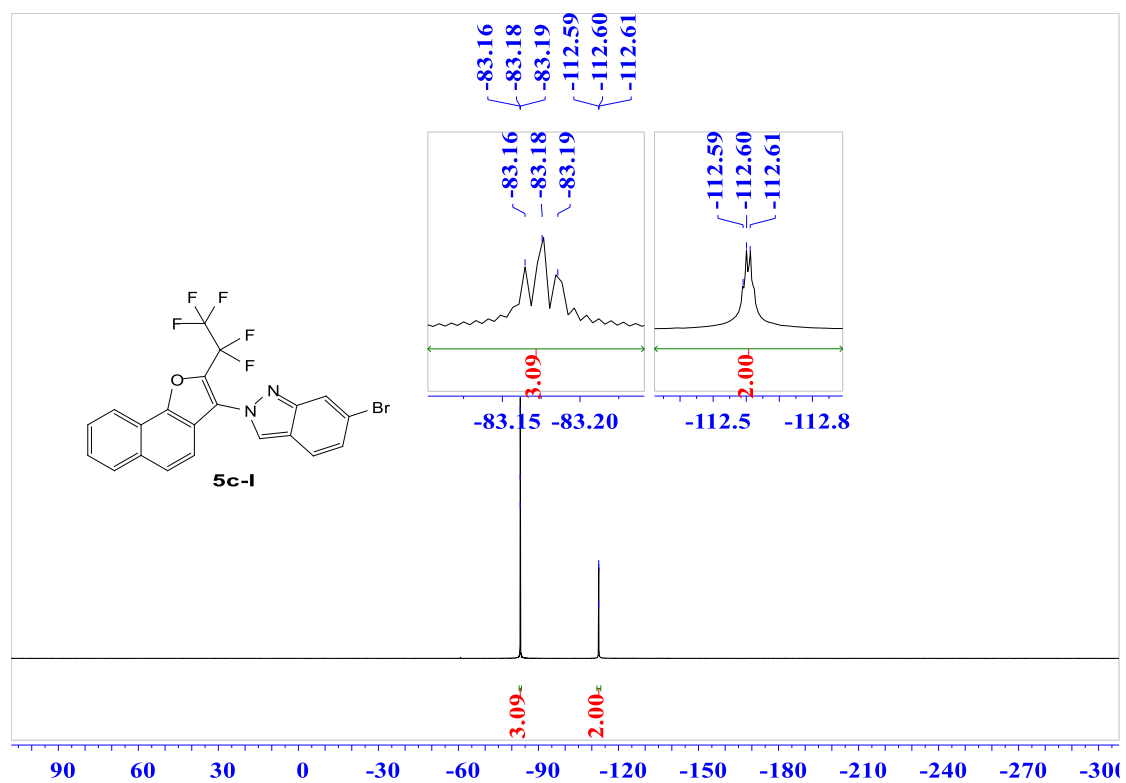


Figure S51. ¹³C NMR spectrum of **5c-I**, related to Scheme 1.

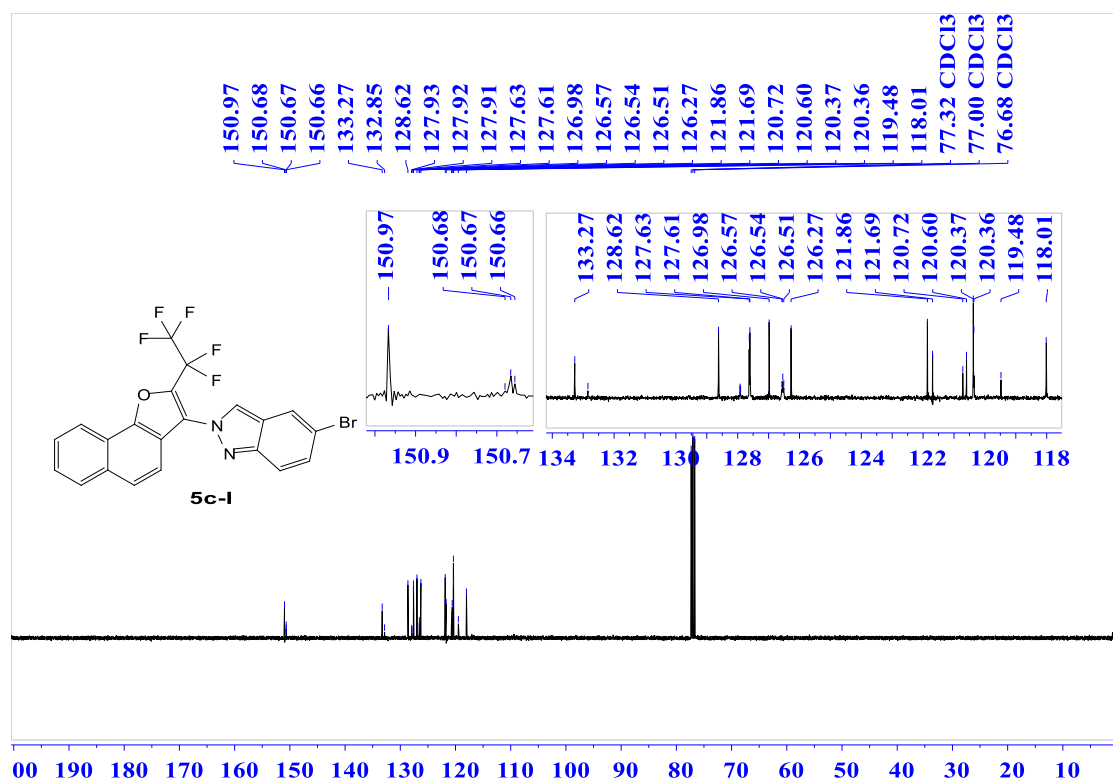


Figure S52. ¹H NMR spectrum of **5c-II**, related to Scheme 1.

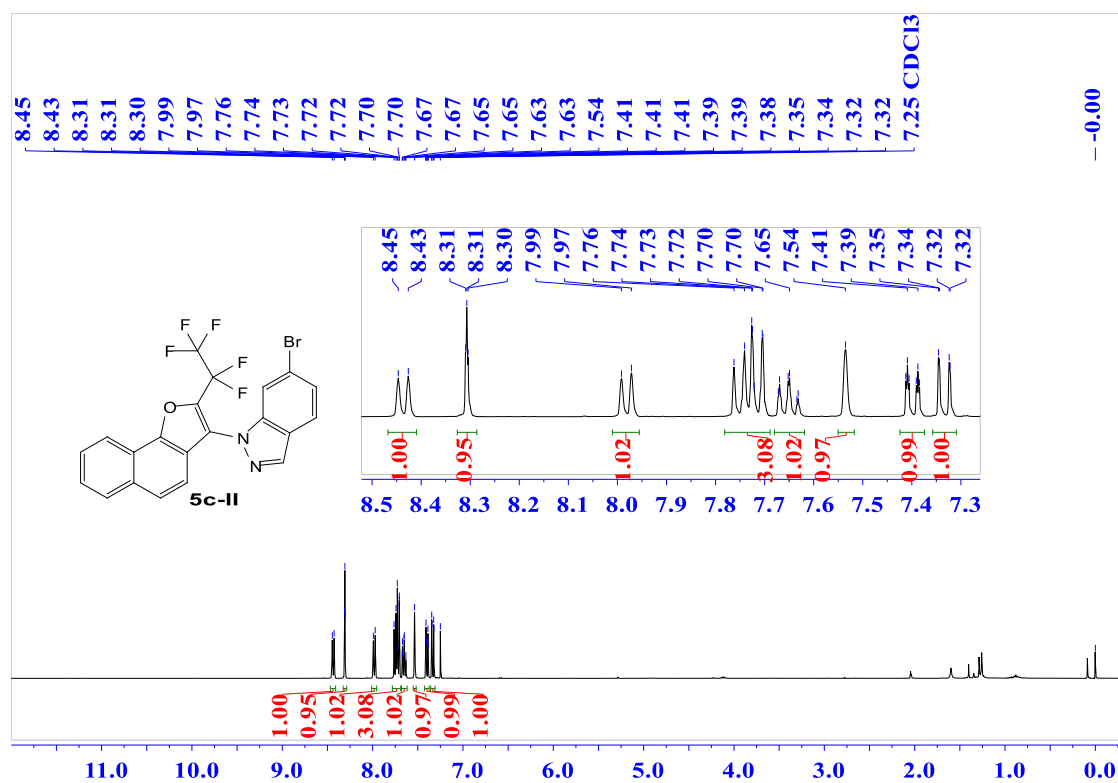


Figure S53. ^{19}F NMR spectrum of **5c-II**, related to Scheme 1.

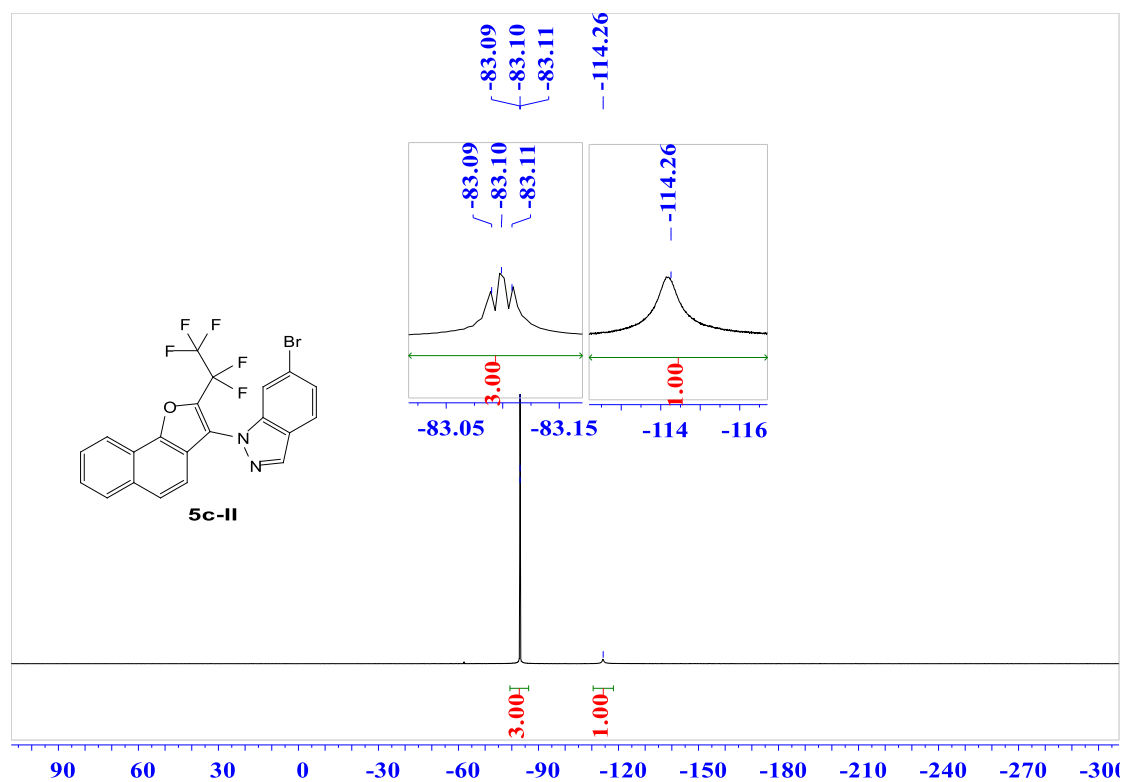


Figure S54. ^{13}C NMR spectrum of **5c-II**, related to Scheme 1.

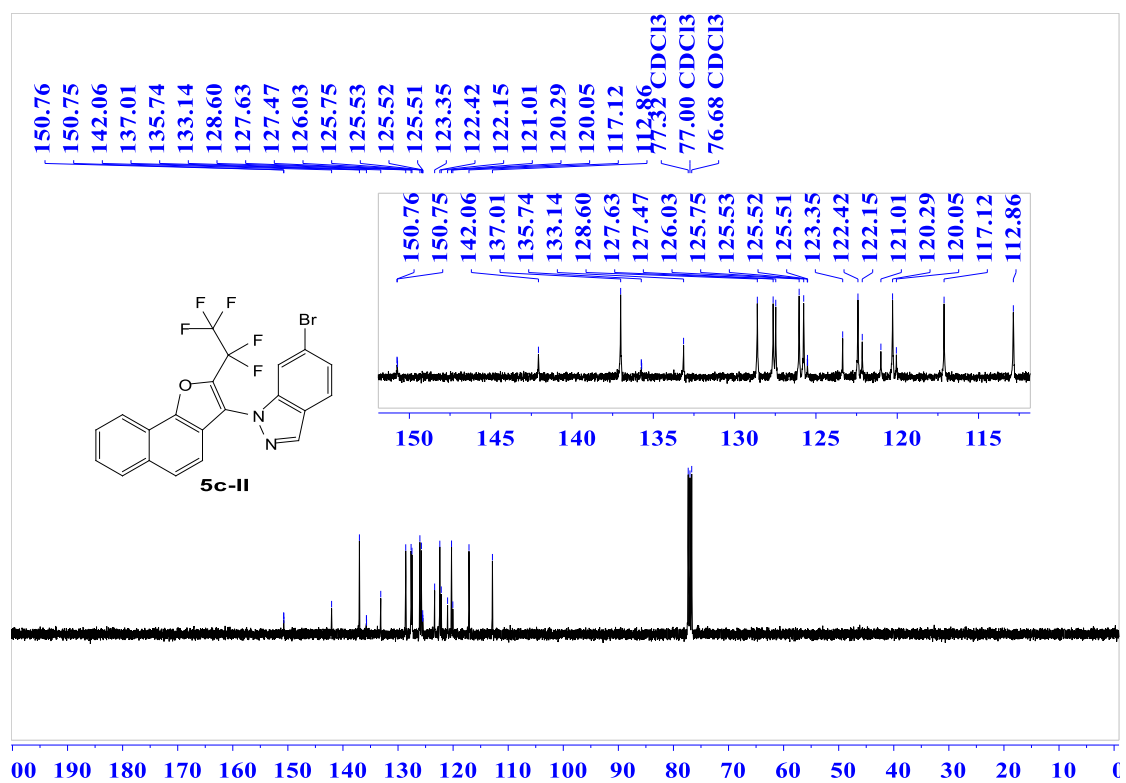


Figure S55. ¹H NMR spectrum of **6a**, related to Scheme 1.

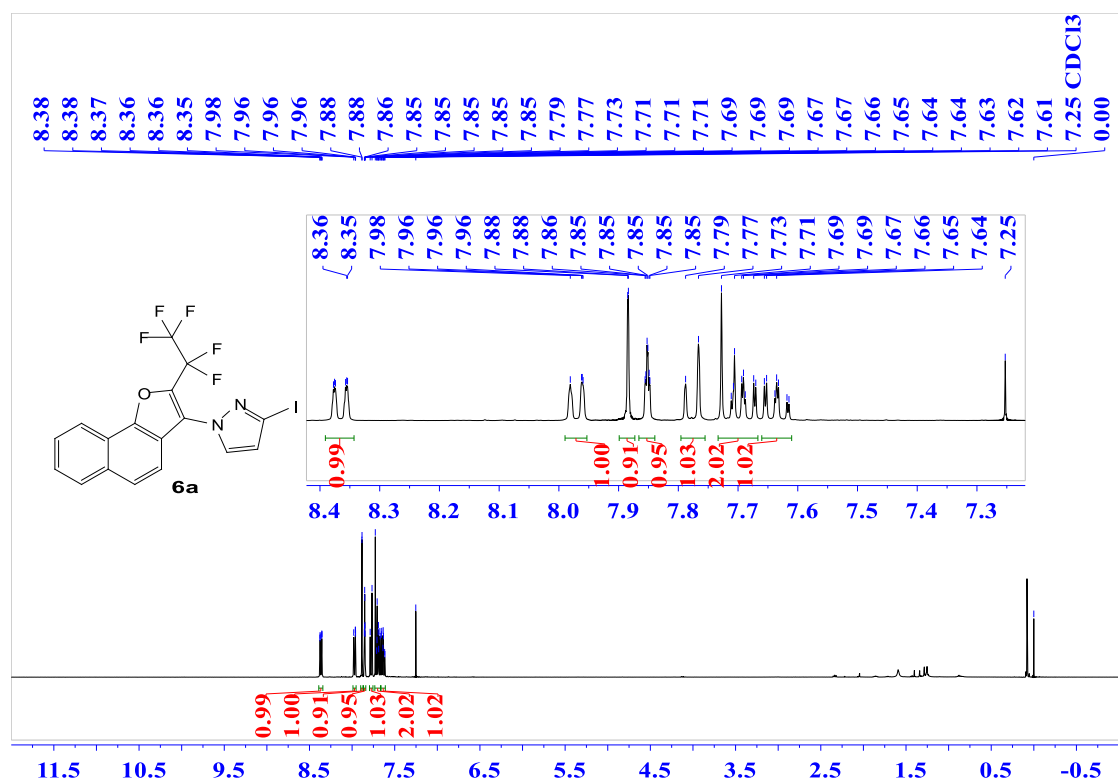


Figure S56. ¹⁹F NMR spectrum of **6a**, related to Scheme 1.

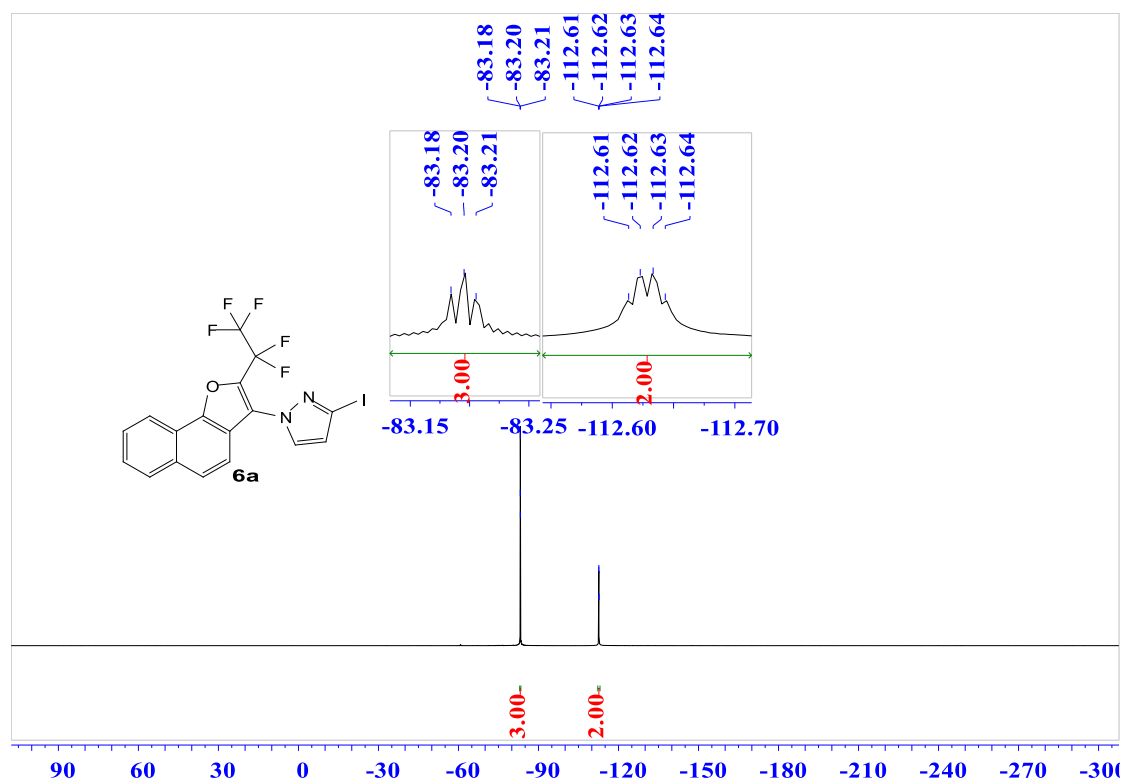


Figure S57. ¹³C NMR spectrum of **6a**, related to Scheme 1.

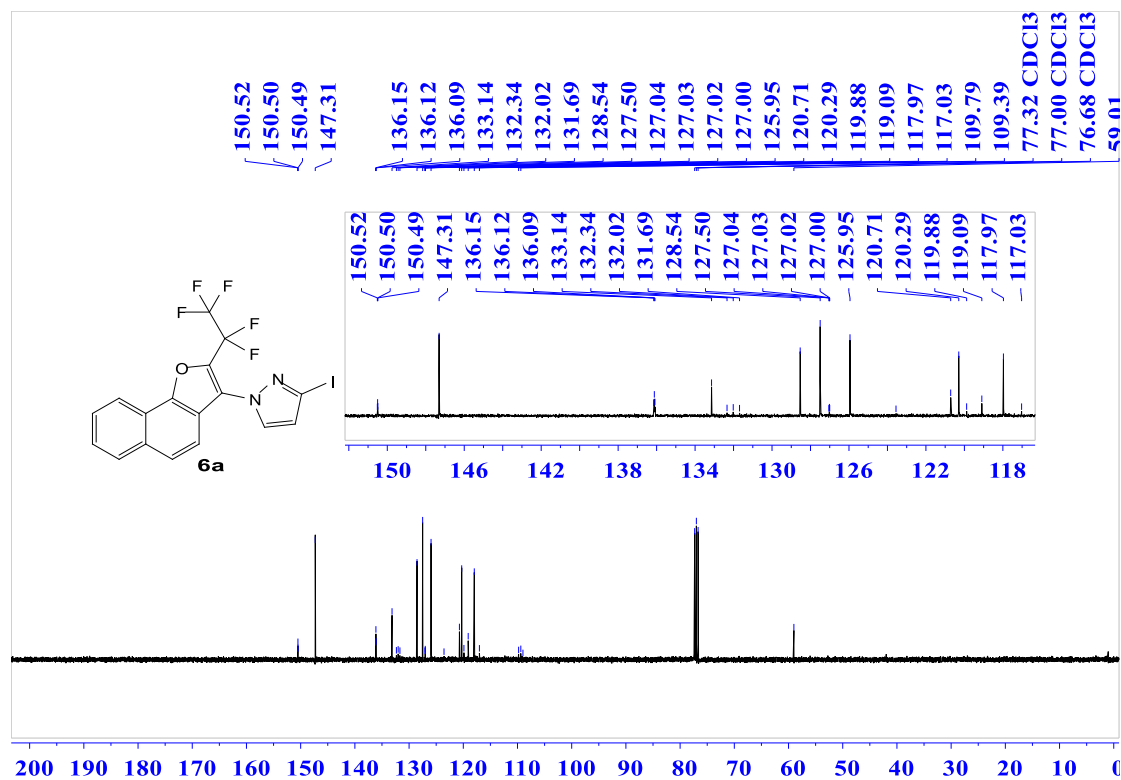


Figure S58. ¹H NMR spectrum of **6b**, related to Scheme 1.

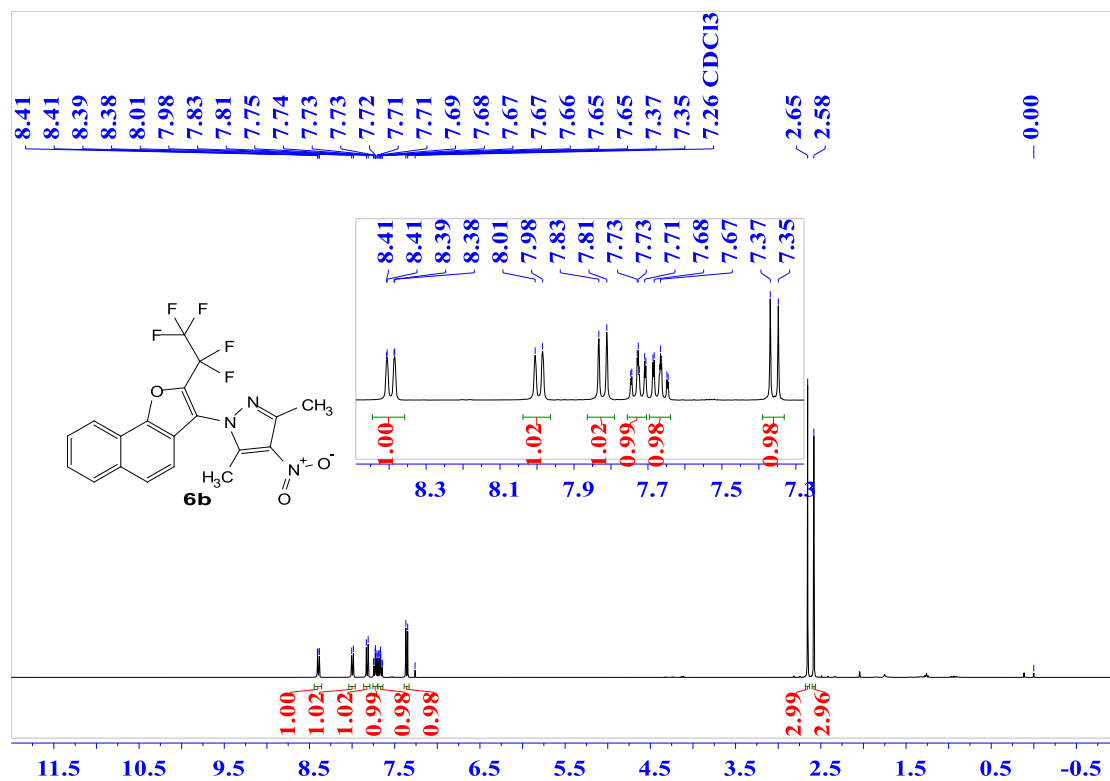


Figure S59. ^{19}F NMR spectrum of **6b**, related to Scheme 1.

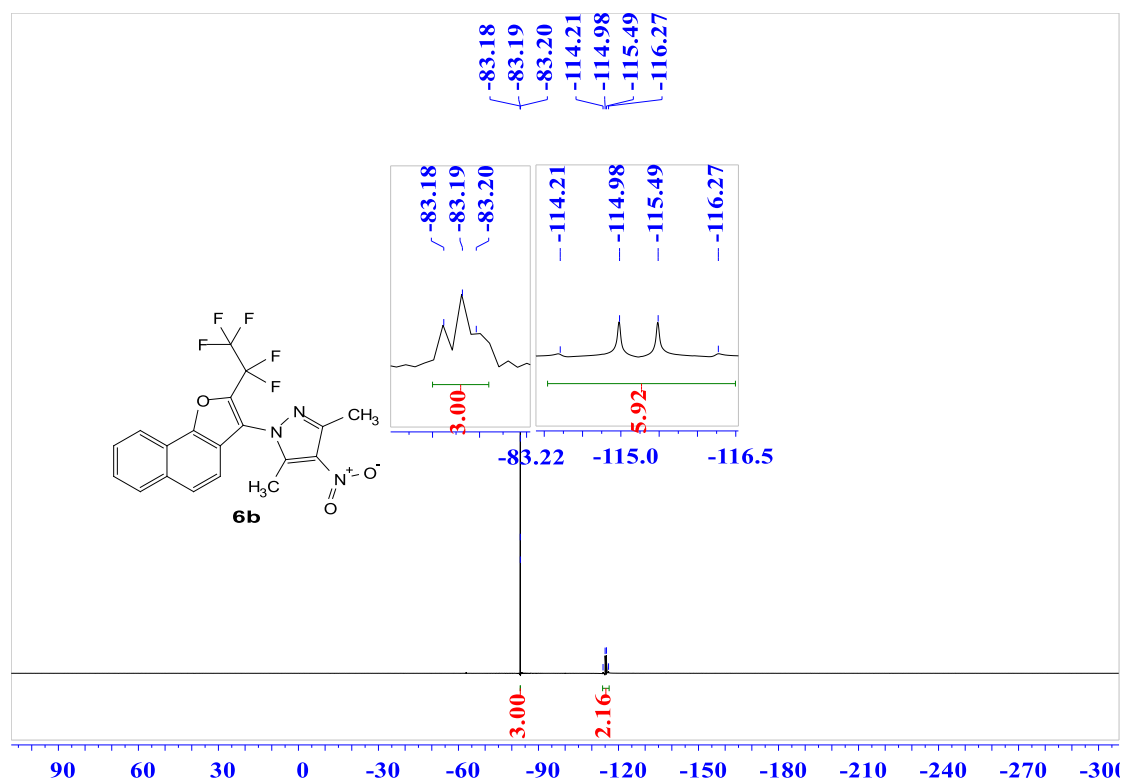


Figure S60. ^{13}C NMR spectrum of **6b**, related to Scheme 1.

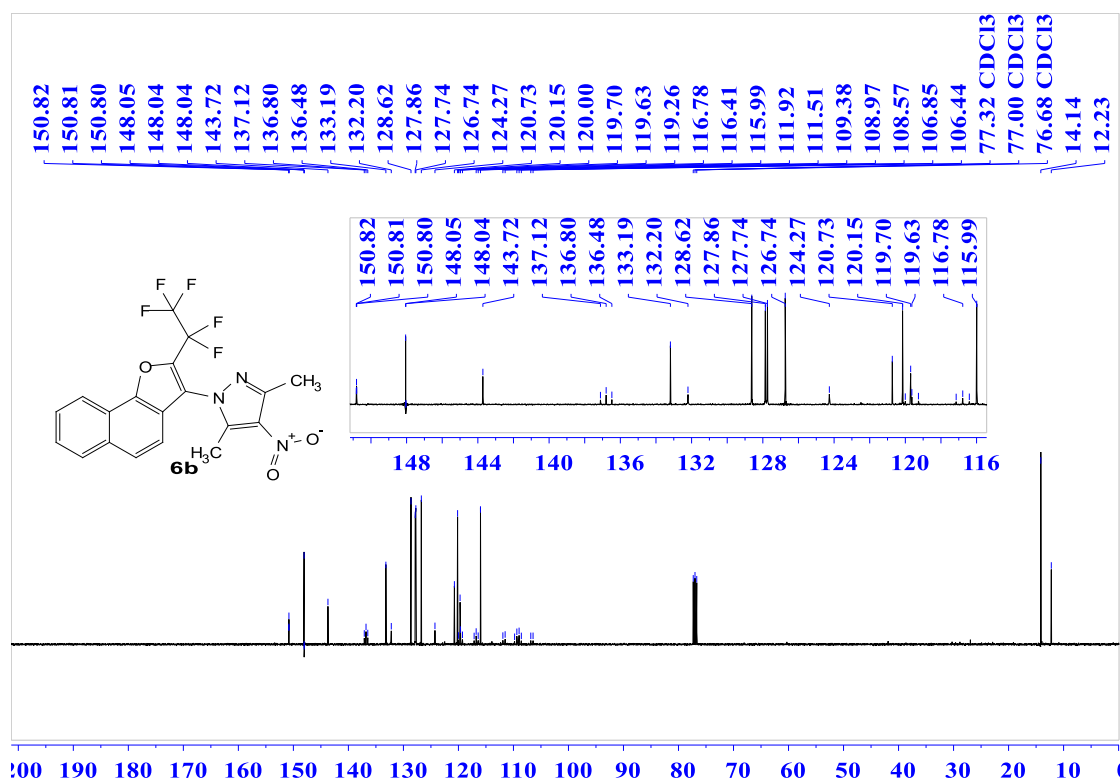


Figure S63. ¹³C NMR spectrum of **6c**, related to Scheme 1.

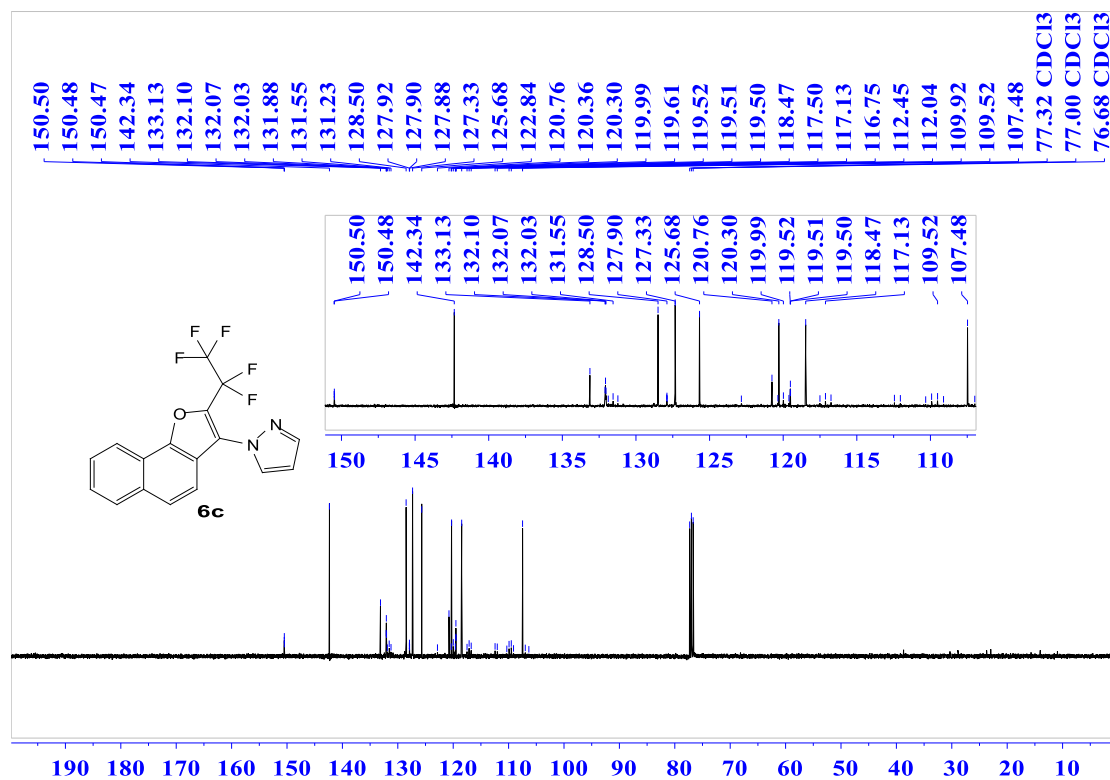


Figure S64. ¹H NMR spectrum of **6d**, related to Scheme 1.

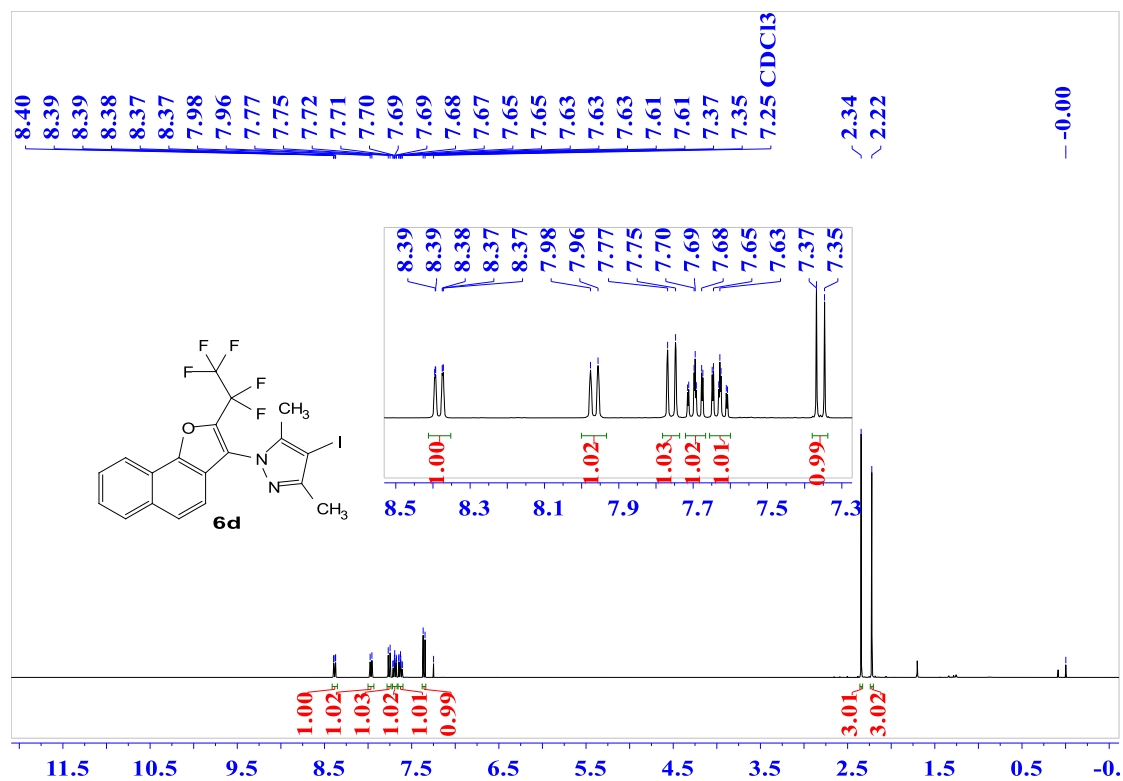


Figure S65. ^{19}F NMR spectrum of **6d**, related to Scheme 1.

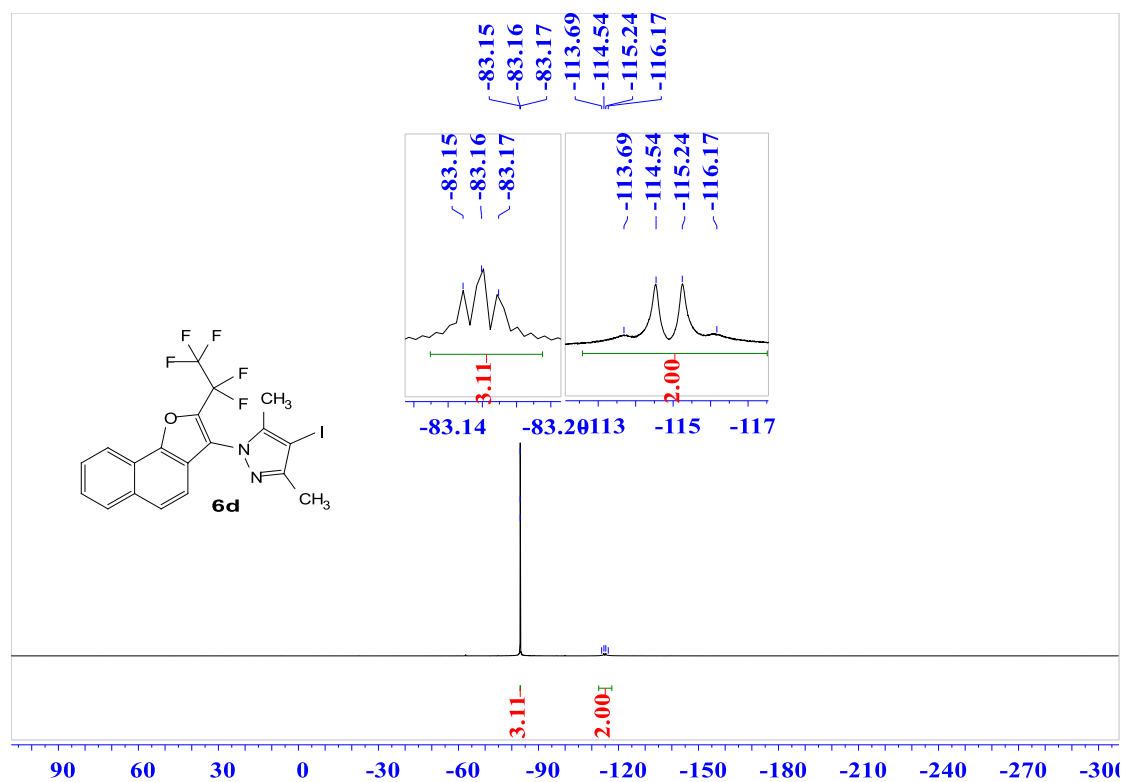


Figure S66. ^{13}C NMR spectrum of **6d**, related to Scheme 1.

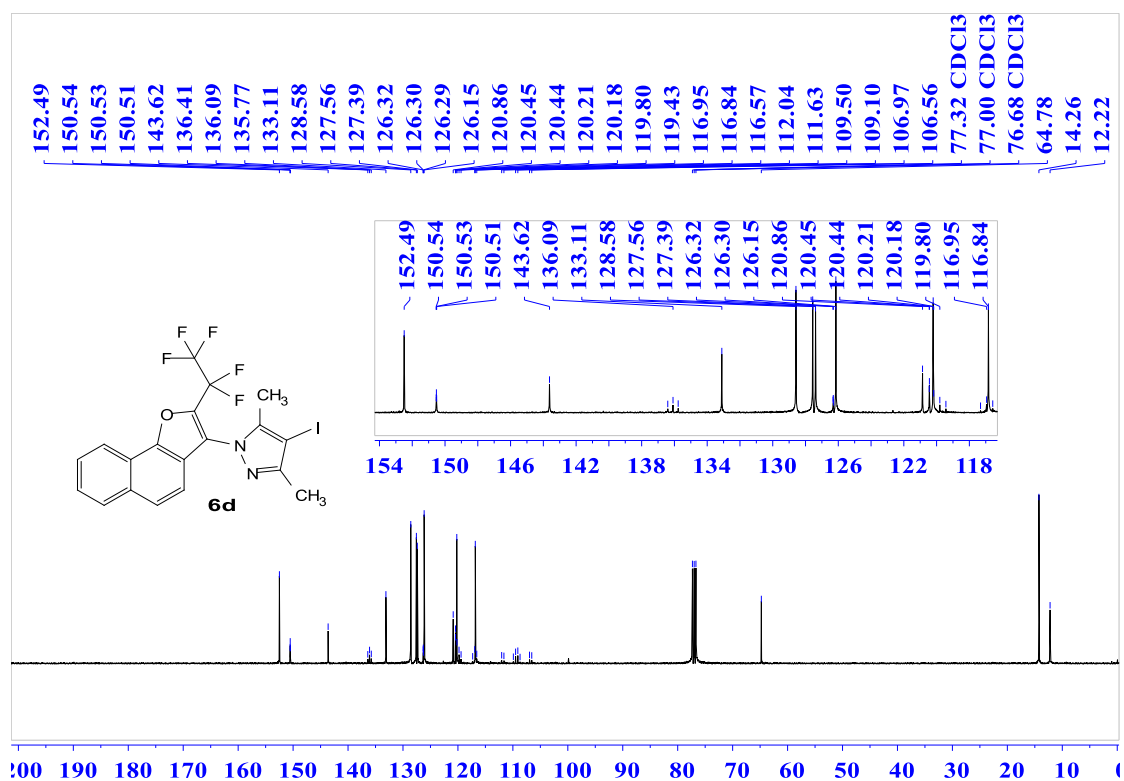


Figure S67. ¹H NMR spectrum of **7a**, related to Scheme 1.

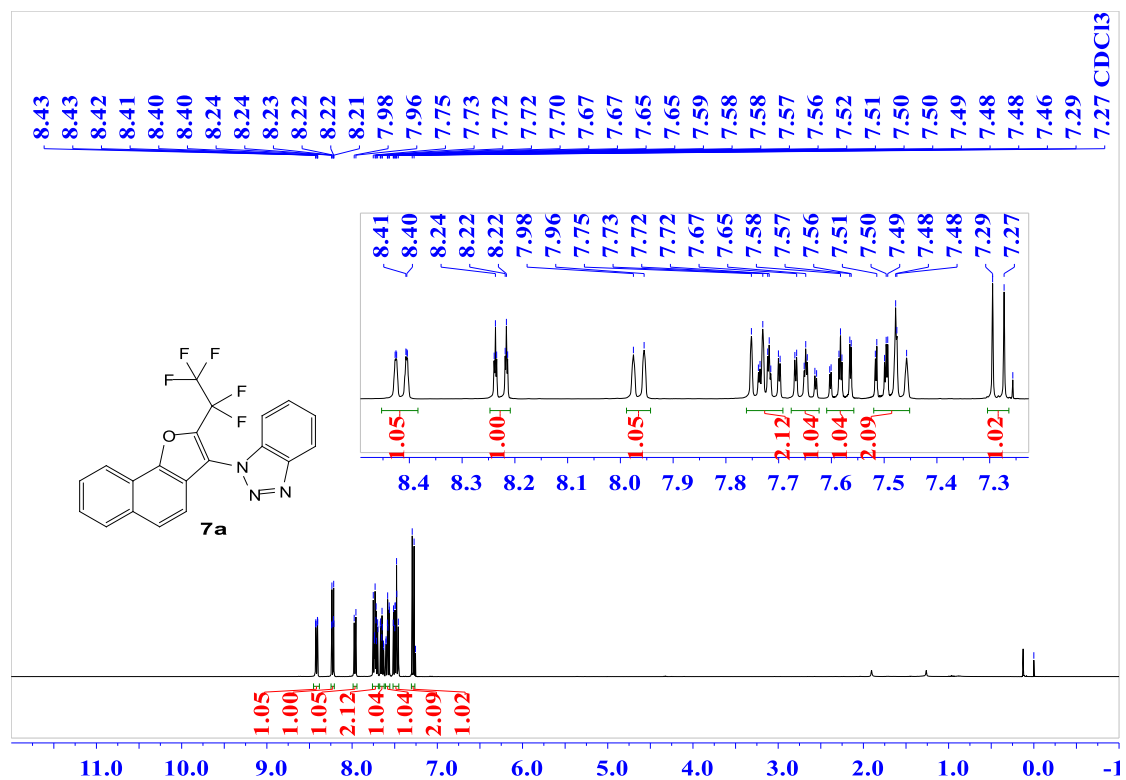


Figure S68. ¹⁹F NMR spectrum of **7a**, related to Scheme 1.

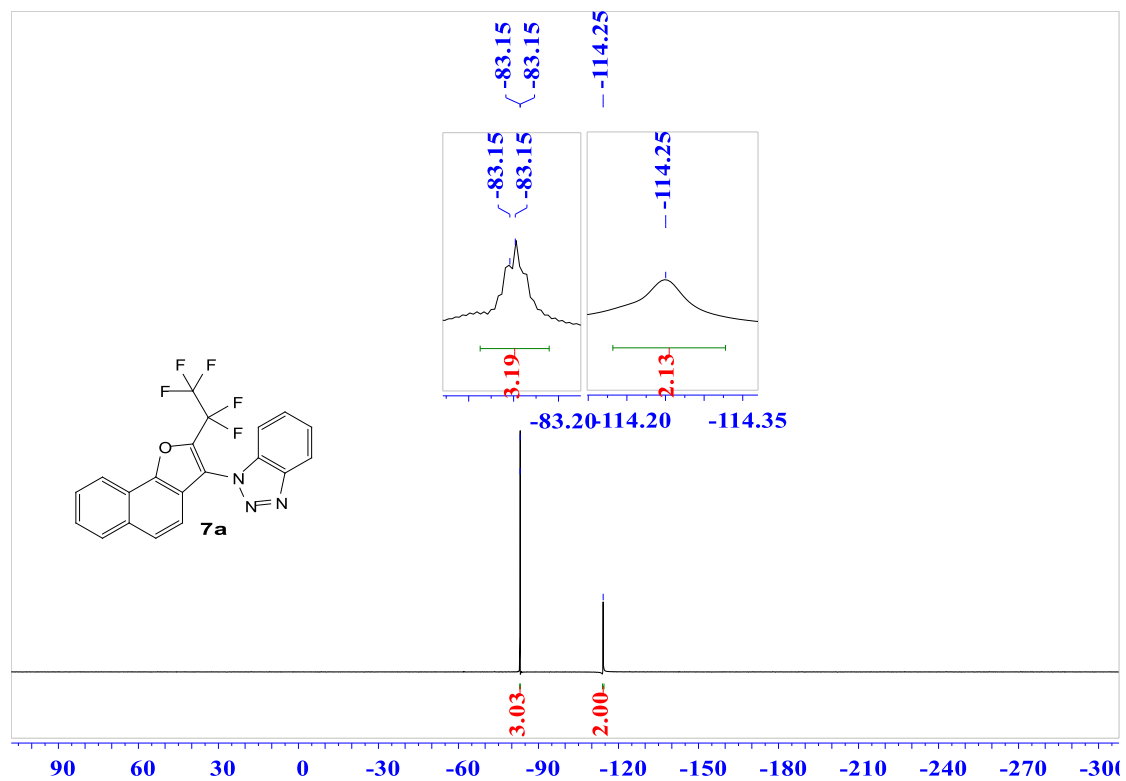


Figure S69. ¹³C NMR spectrum of **7a**, related to Scheme 1.

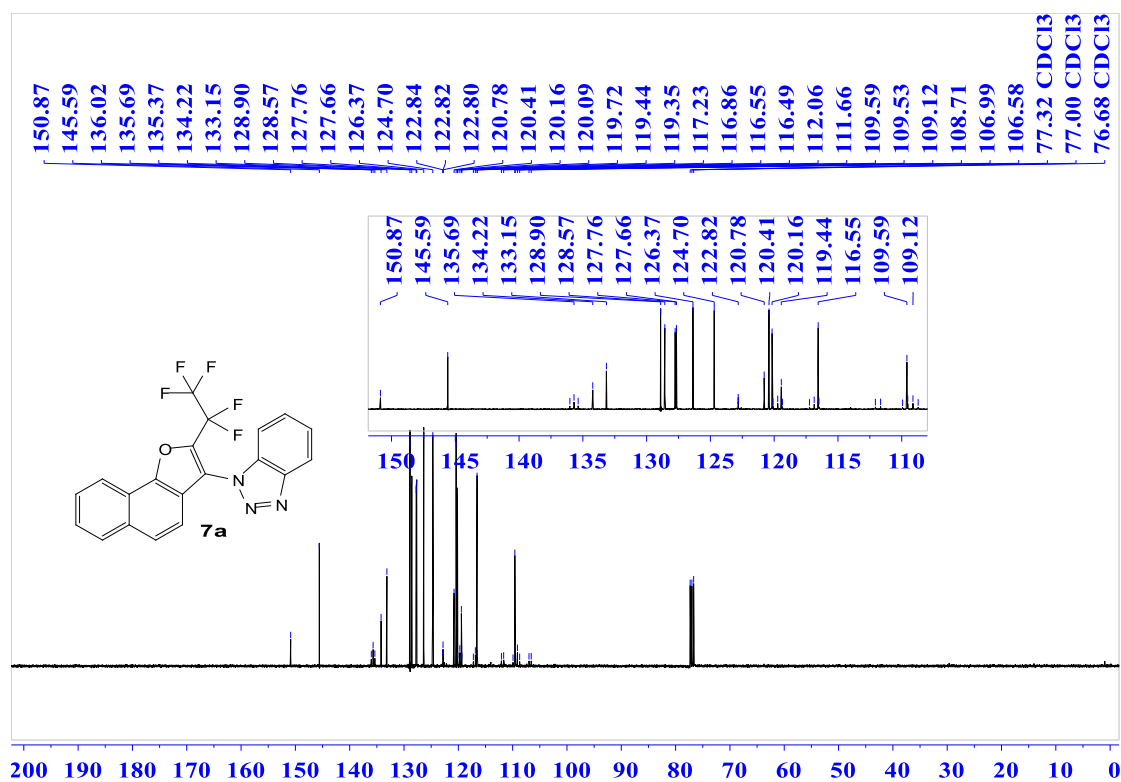


Figure S70. ¹H NMR spectrum of **7b-I** or **7b-II**, related to Scheme 1.

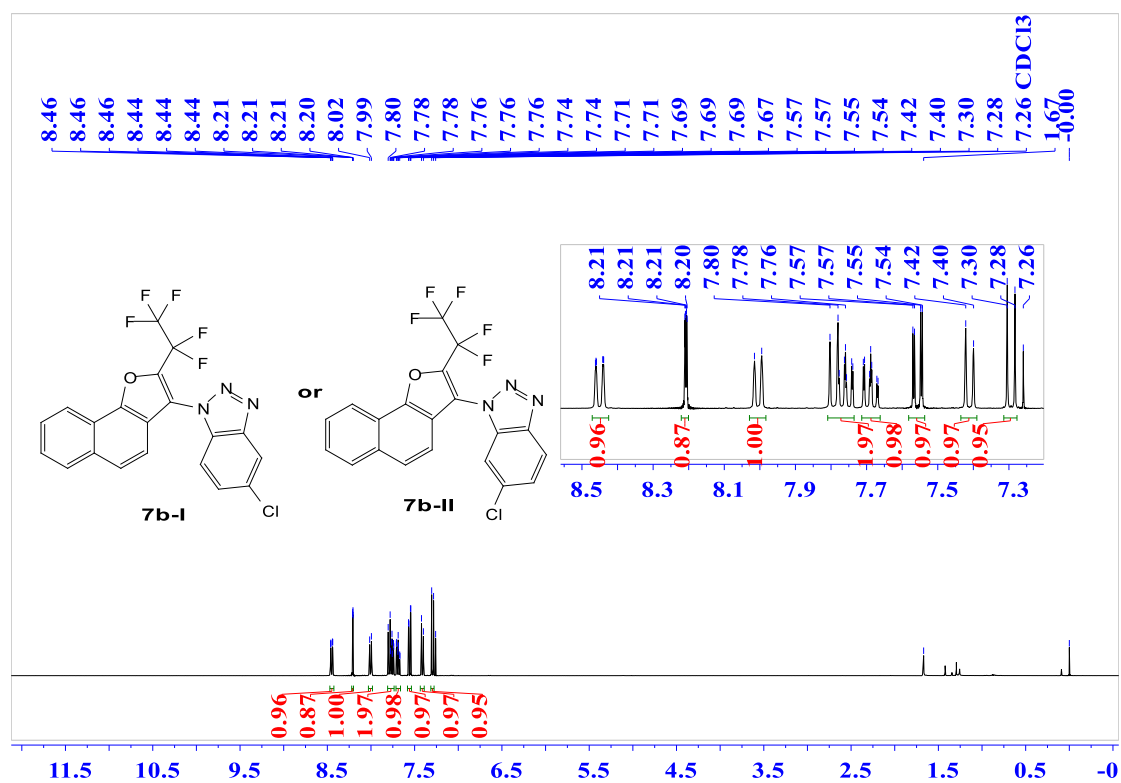


Figure S71. ^{19}F NMR spectrum of **7b-I** or **7b-II**, related to Scheme 1.

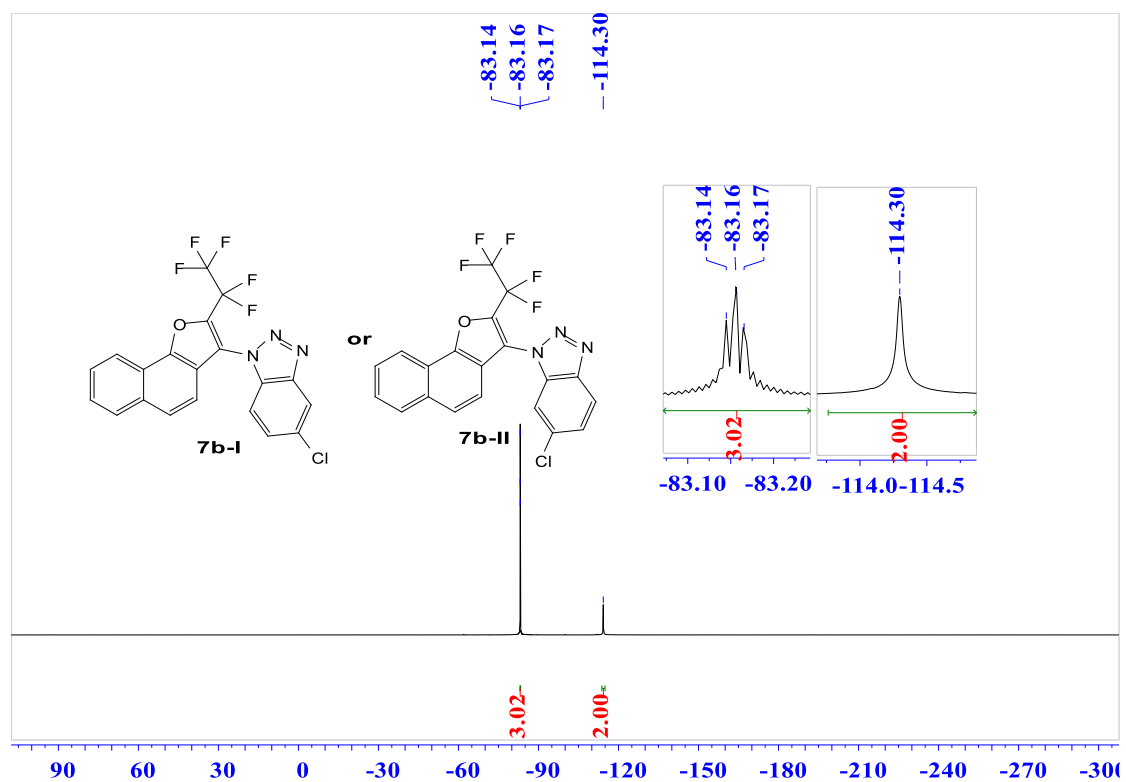


Figure S72. ^{13}C NMR spectrum of **7b-I** or **7b-II**, related to Scheme 1.

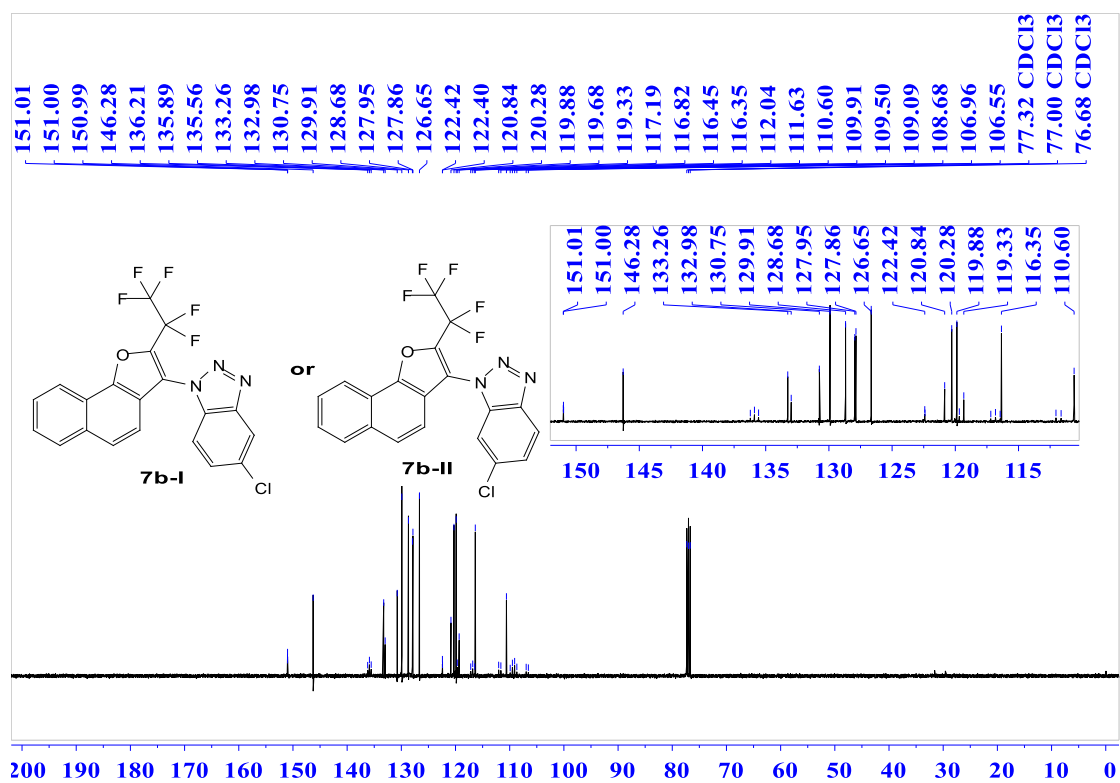


Figure S73. ¹H NMR spectrum of **7b-I** or **7b-II**, related to **Scheme 1**.

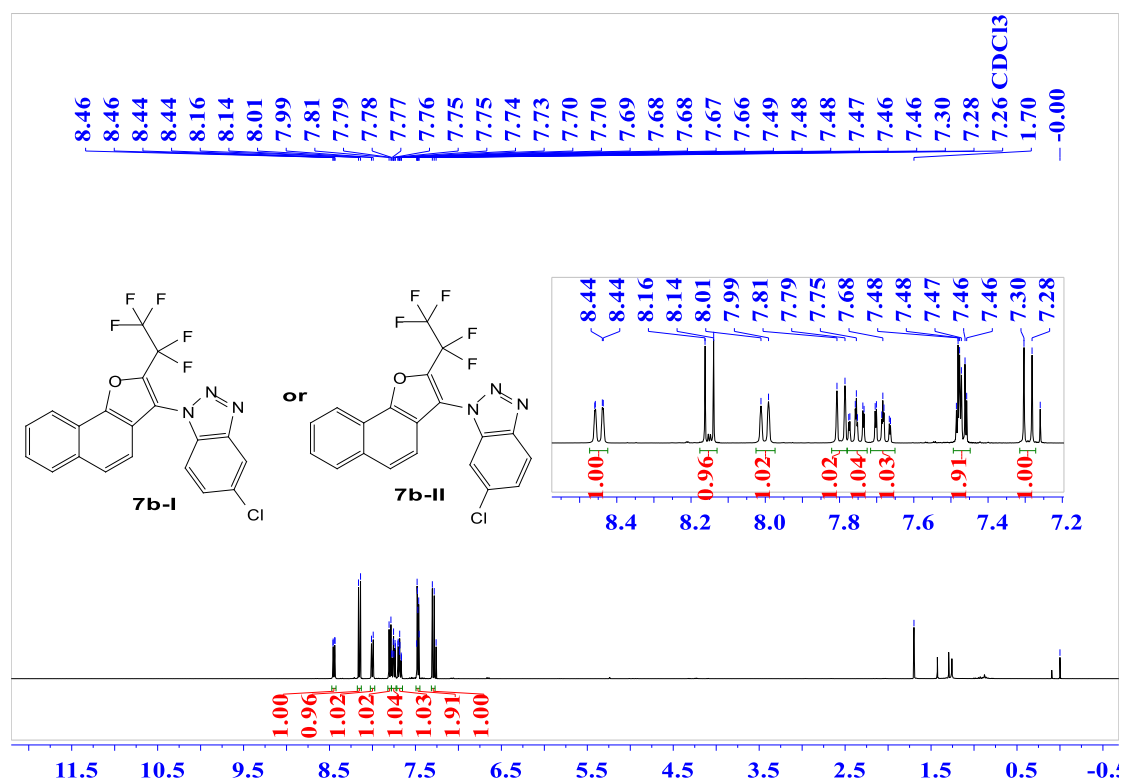


Figure S74. ¹⁹F NMR spectrum of **7b-I** or **7b-II**, related to **Scheme 1**.

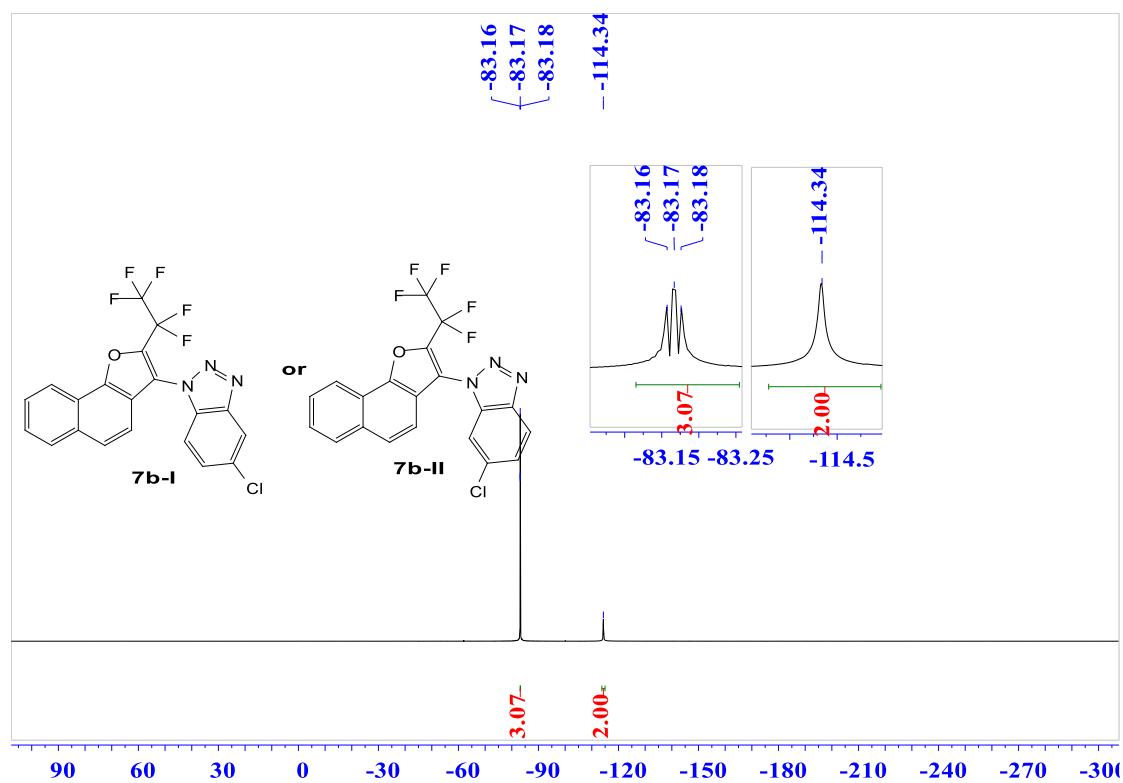


Figure S75. ^{13}C NMR spectrum of **7b-I** or **7b-II**, related to Scheme 1.

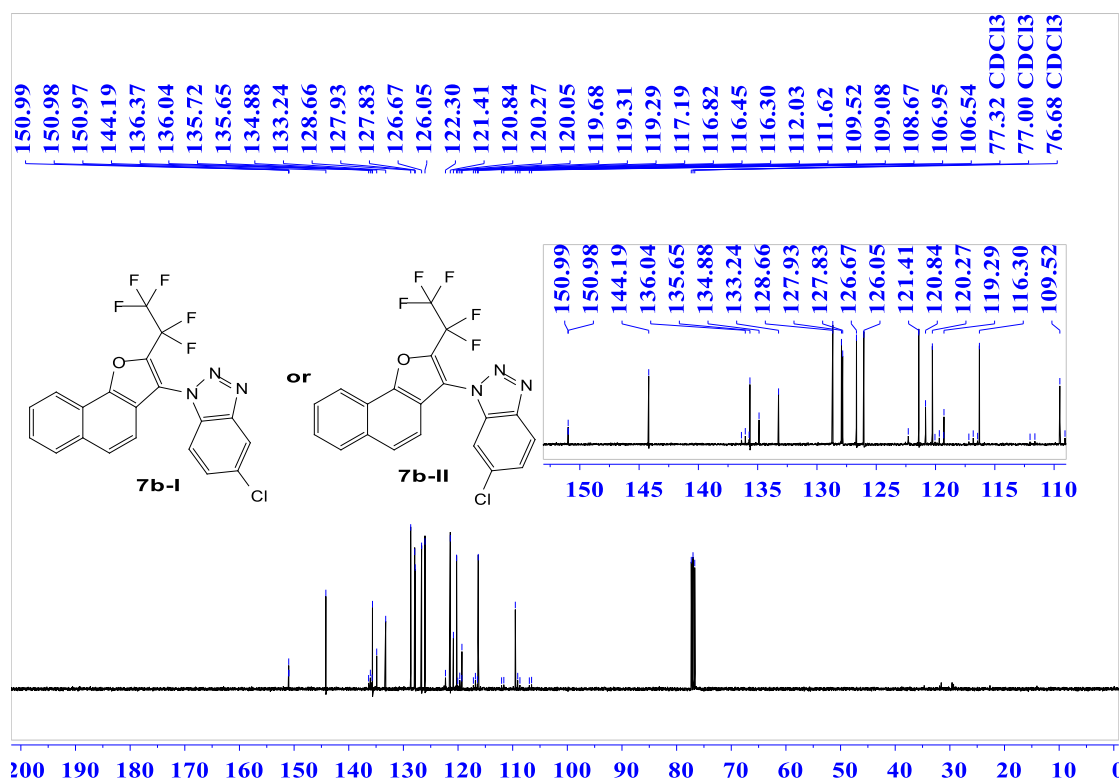


Figure S76. ^1H NMR spectrum of **7c-I**, **7c-II**, or **7c-III**, related to Scheme 1.

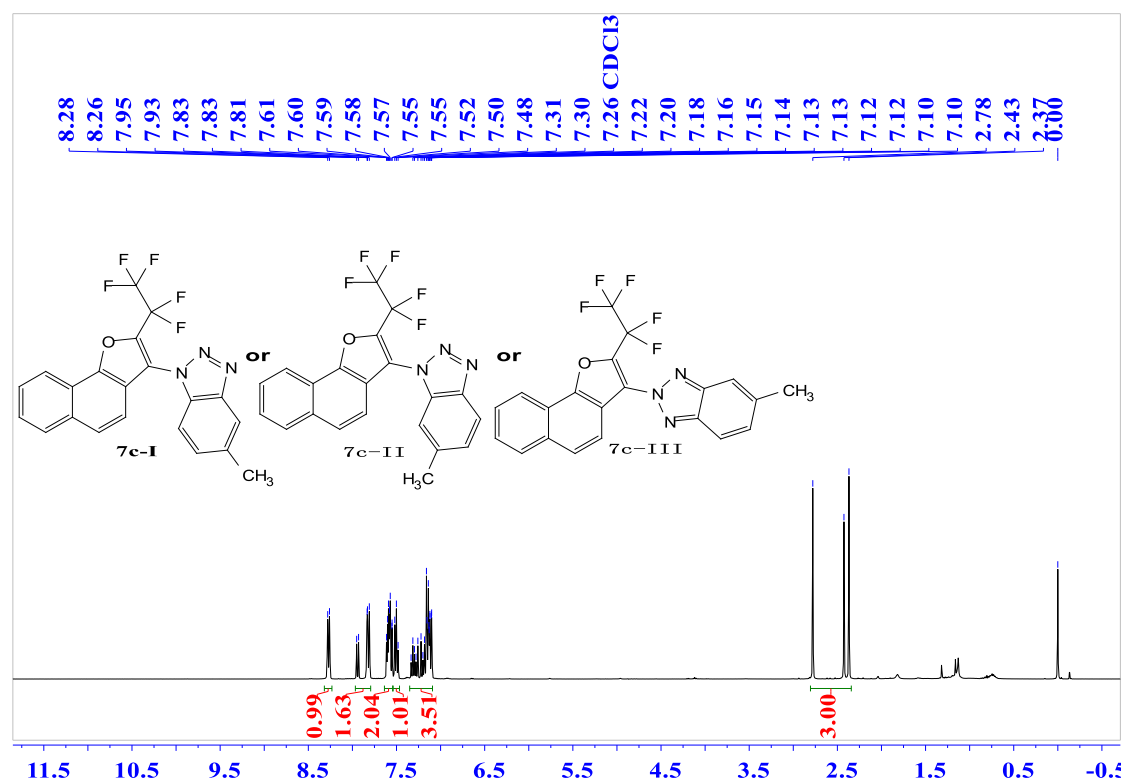


Figure S77. ^{19}F NMR spectrum of **7c-I**, **7c-II**, or **7c-III**, related to Scheme 1.

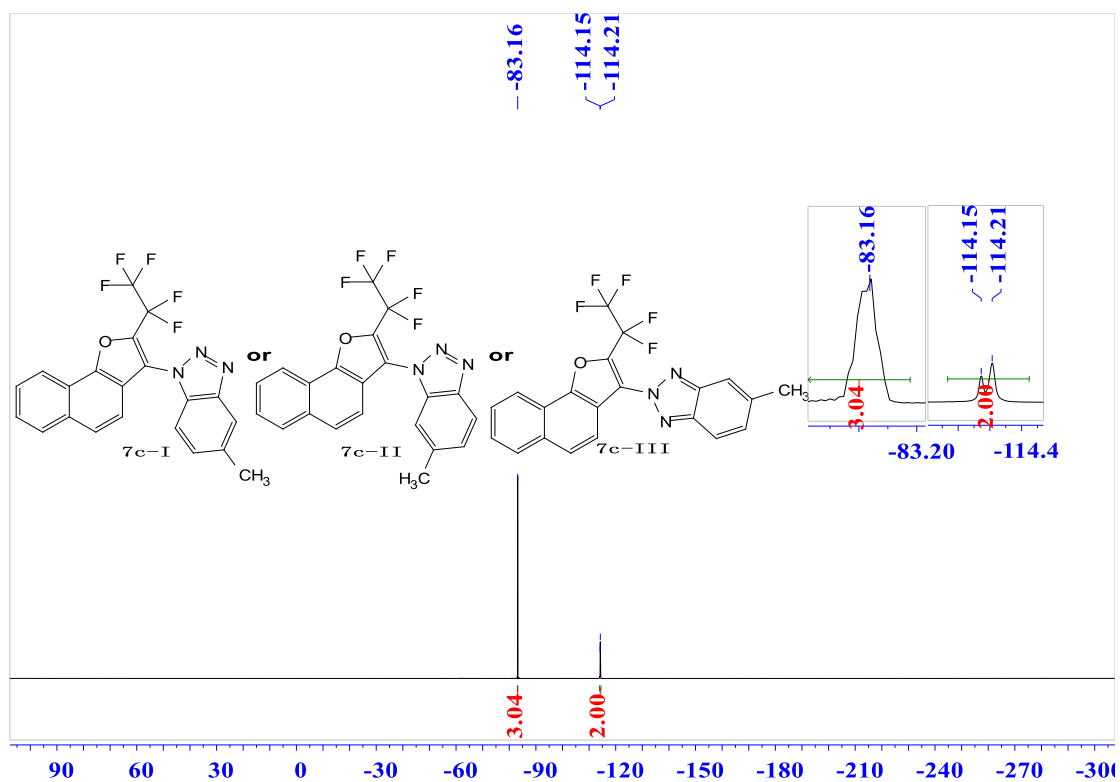


Figure S78. ^{13}C NMR spectrum of **7c-I**, **7c-II**, or **7c-III**, related to Scheme 1.

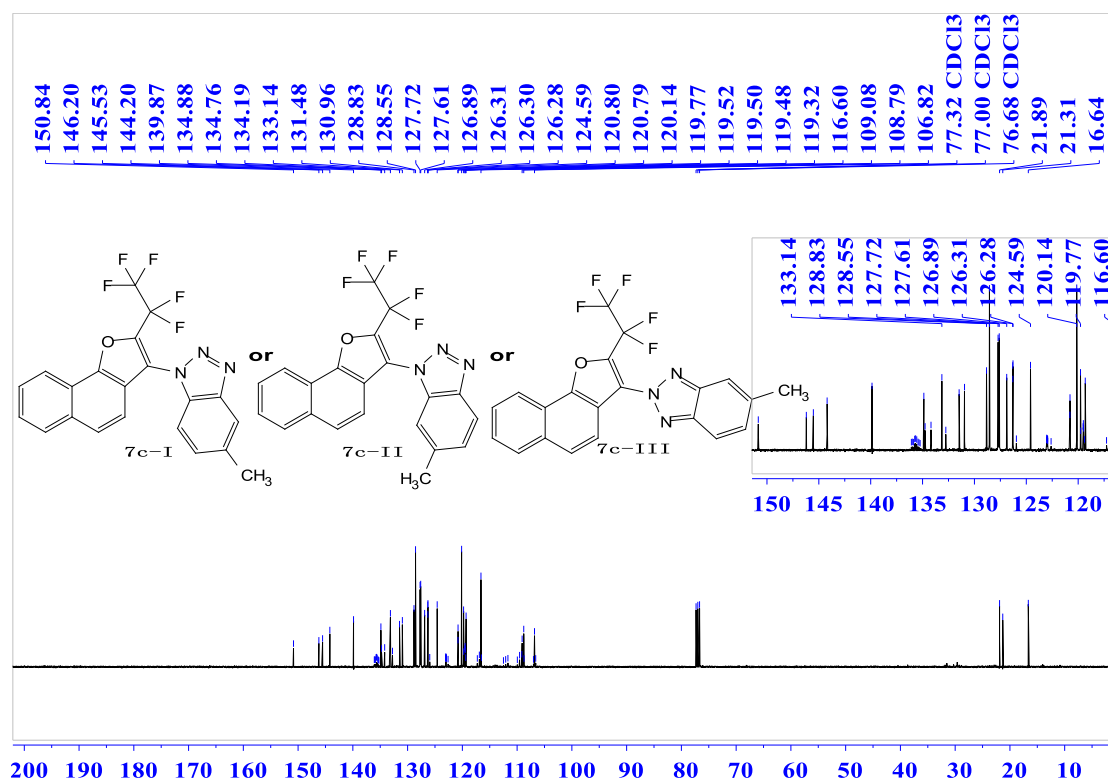


Figure S79. ¹H NMR spectrum of **8-I**, related to Scheme 1.

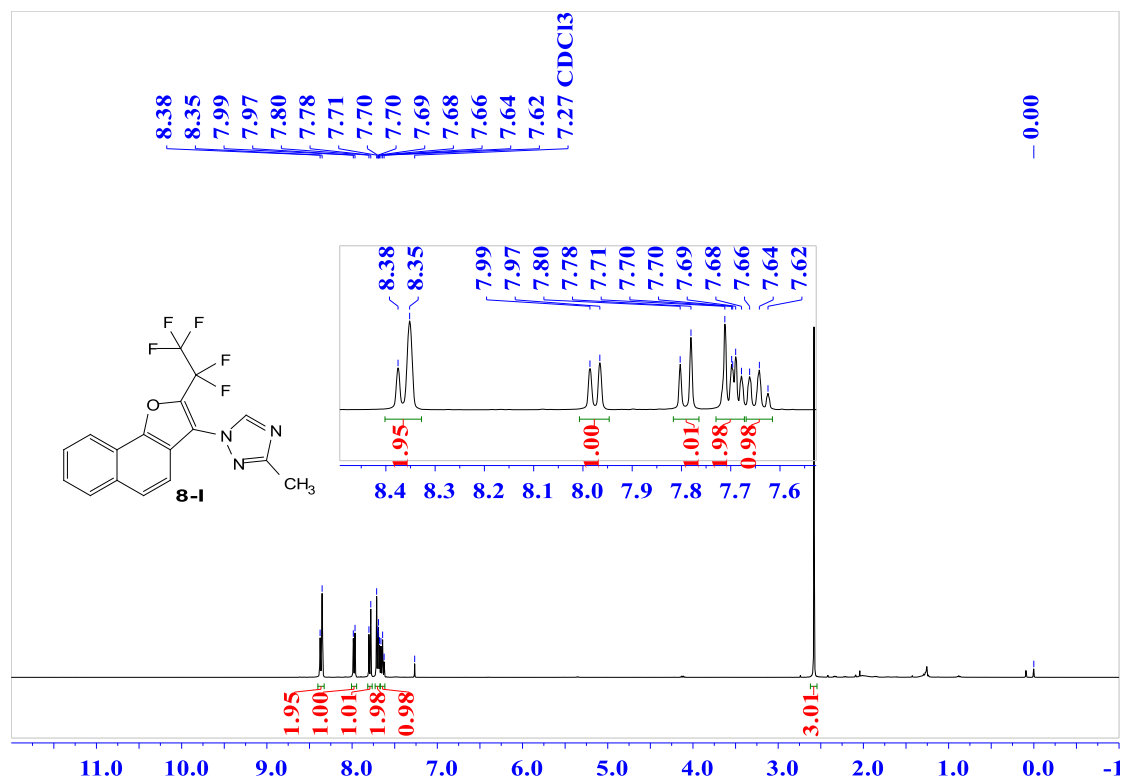


Figure S80. ¹⁹F NMR spectrum of **8-I**, related to Scheme 1.

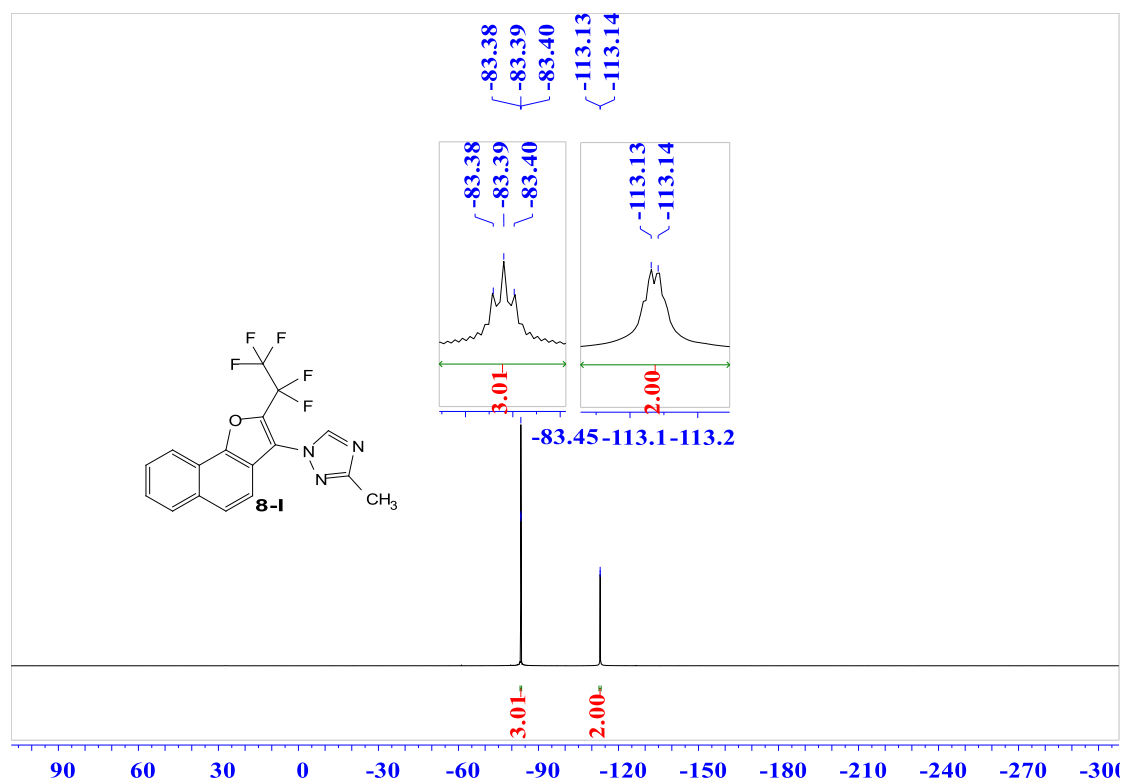


Figure S81. ¹³C NMR spectrum of **8-I**, related to Scheme 1.

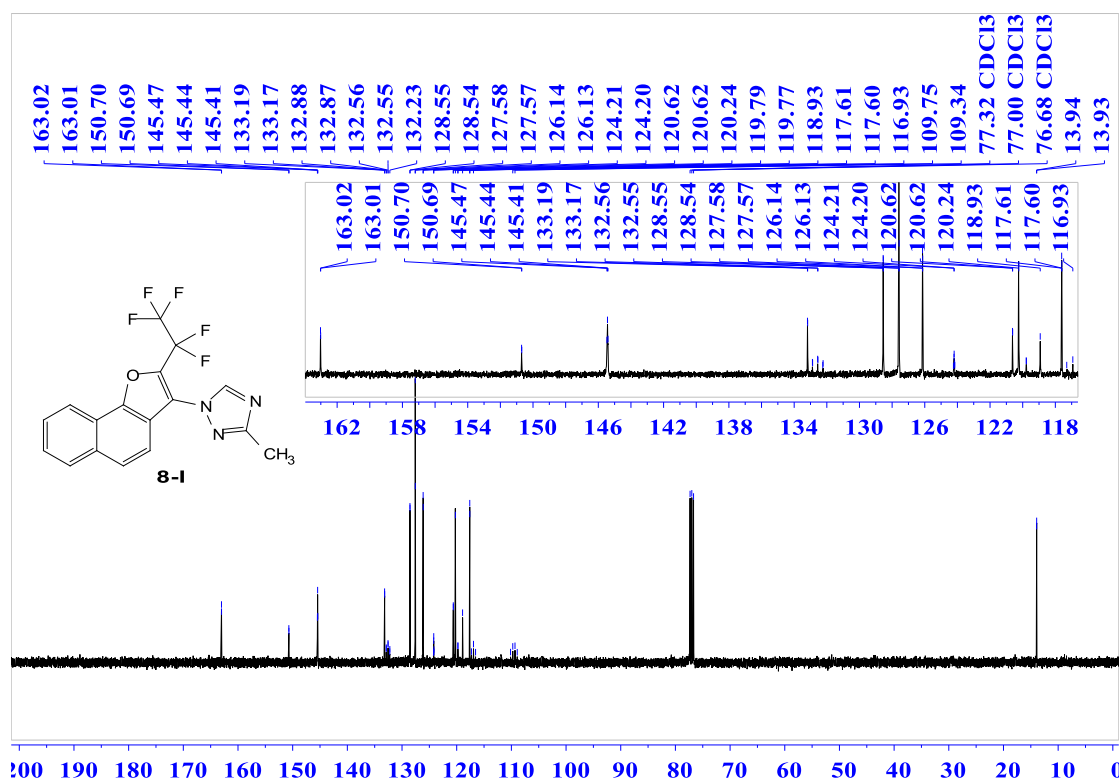


Figure S82. ¹H NMR spectrum of **8-II**, related to Scheme 1.

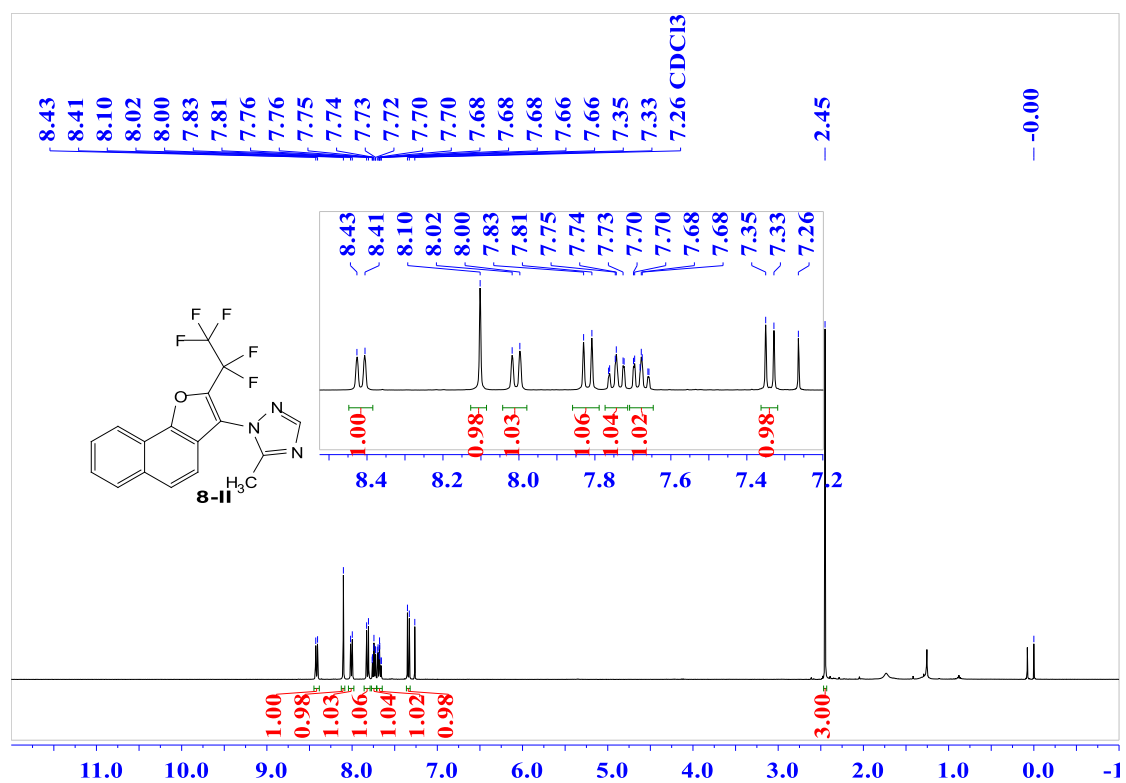


Figure S83. ^{19}F NMR spectrum of **8-II**, related to Scheme 1.

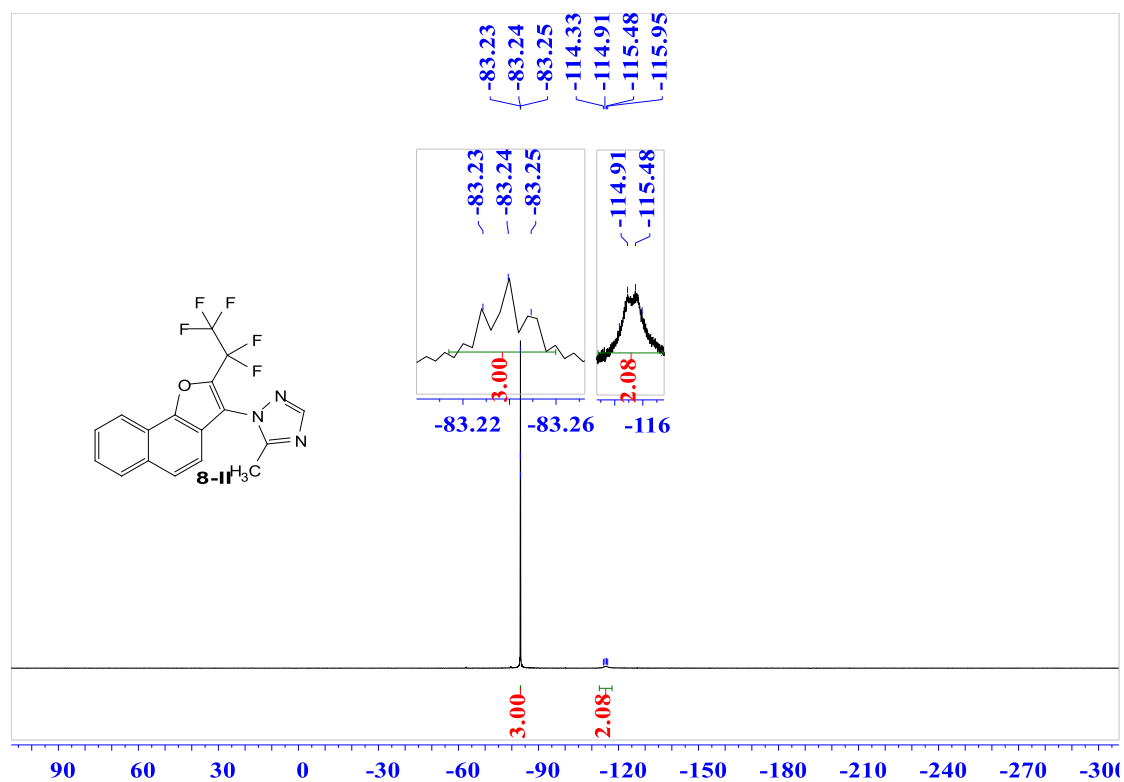


Figure S84. ^{13}C NMR spectrum of **8-II**, related to Scheme 1.

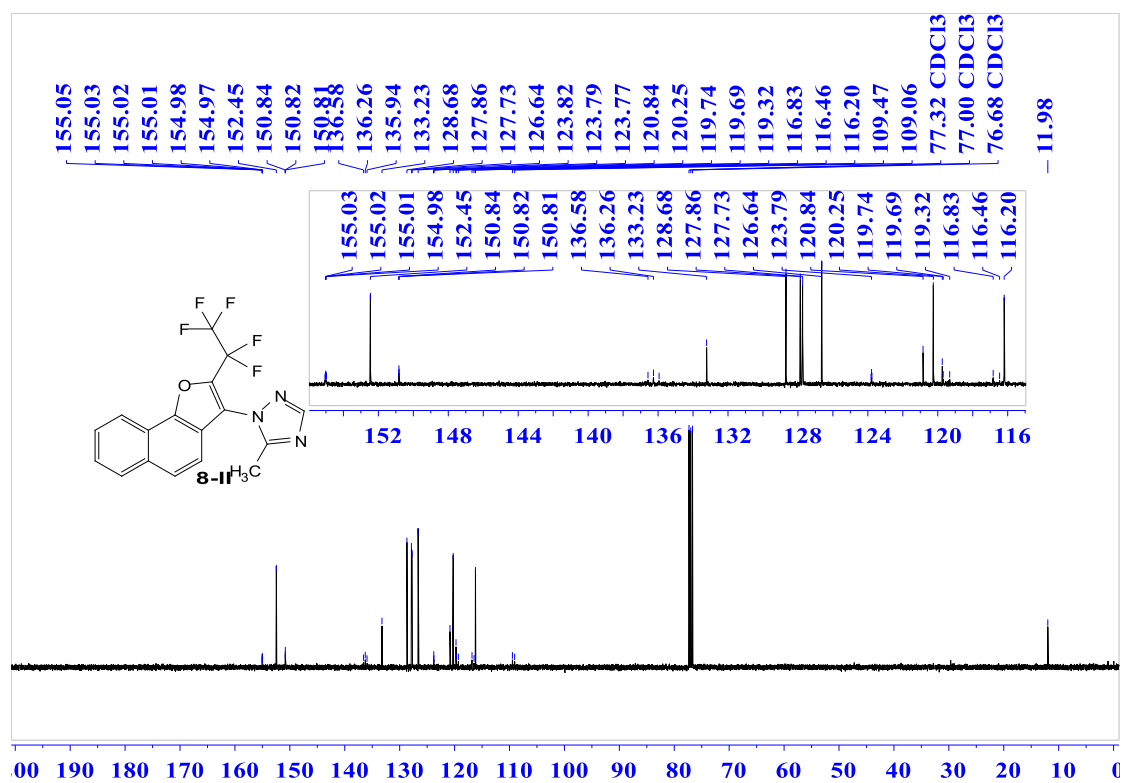


Figure S85. ¹H NMR spectrum of **9**, related to Scheme 1.

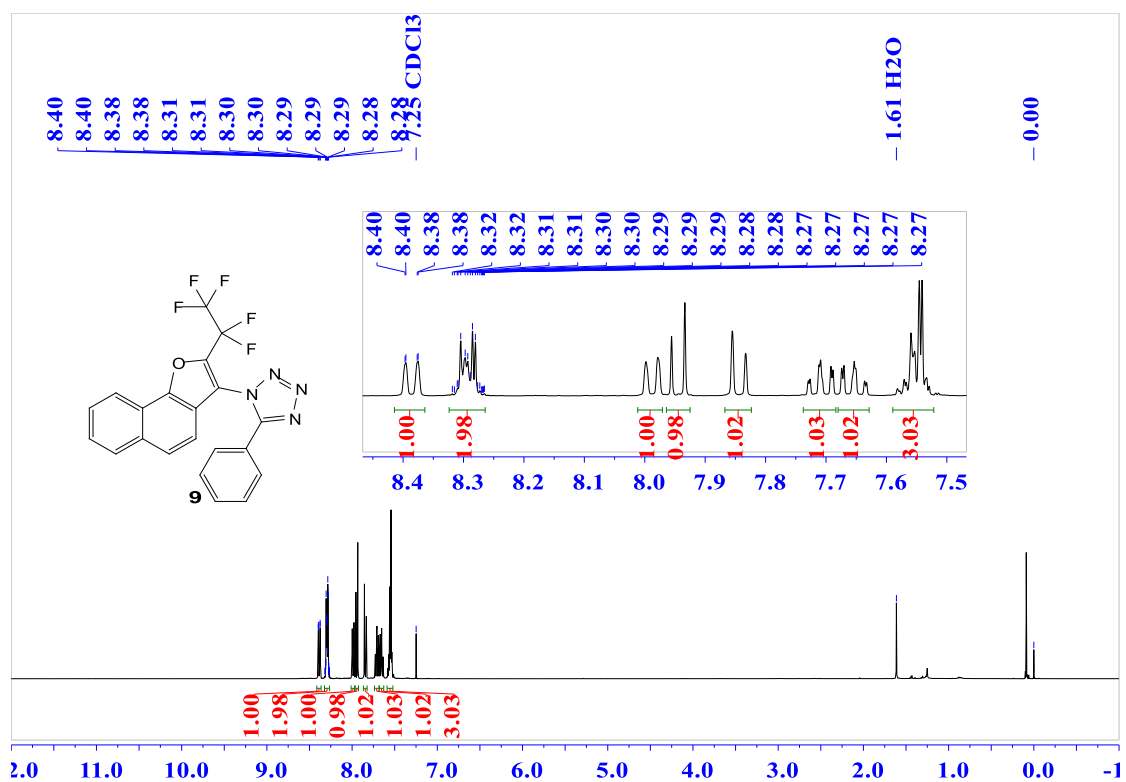


Figure S86. ¹⁹F NMR spectrum of **9**, related to Scheme 1.

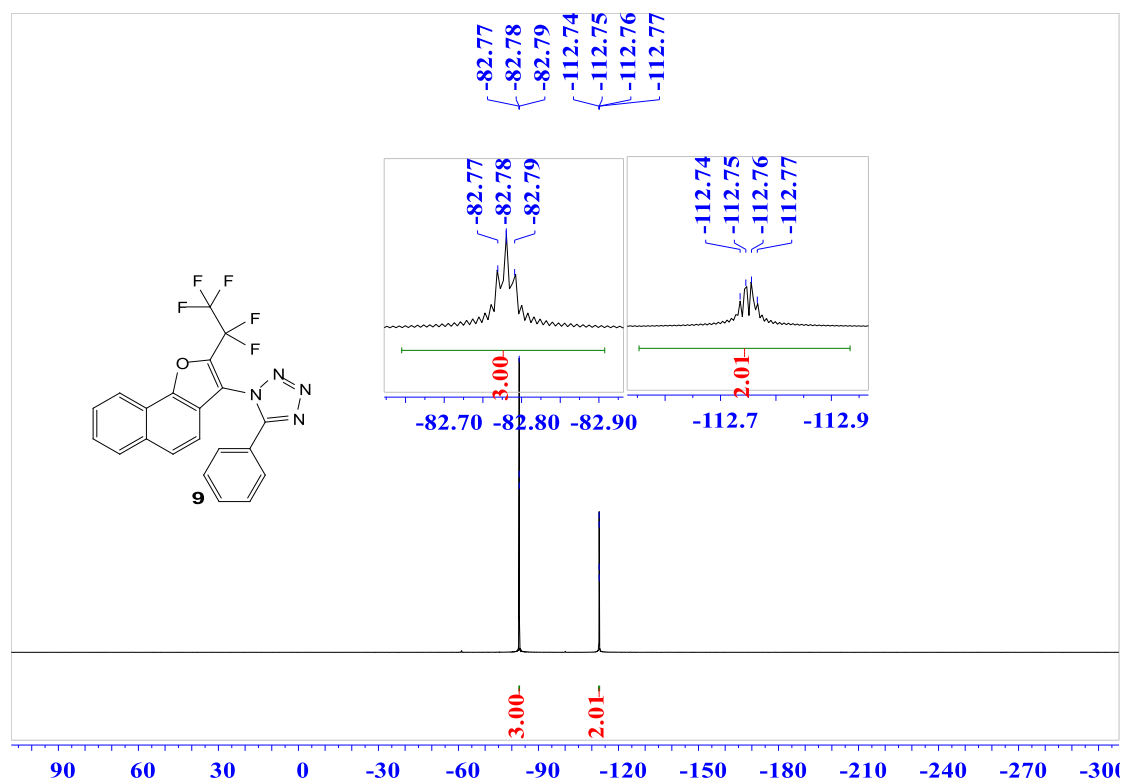


Figure S87. ^{13}C NMR spectrum of **9**, related to Scheme 1.

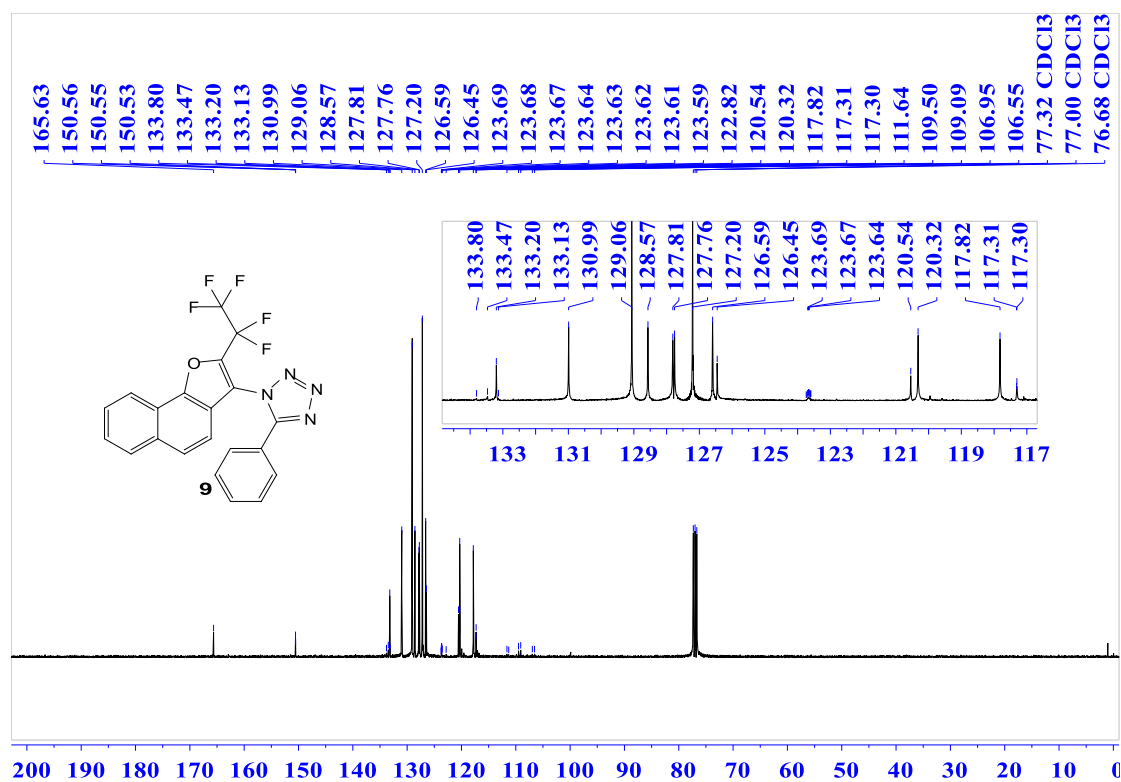


Figure S88. ^1H NMR spectrum of **10a**, related to Scheme 1.

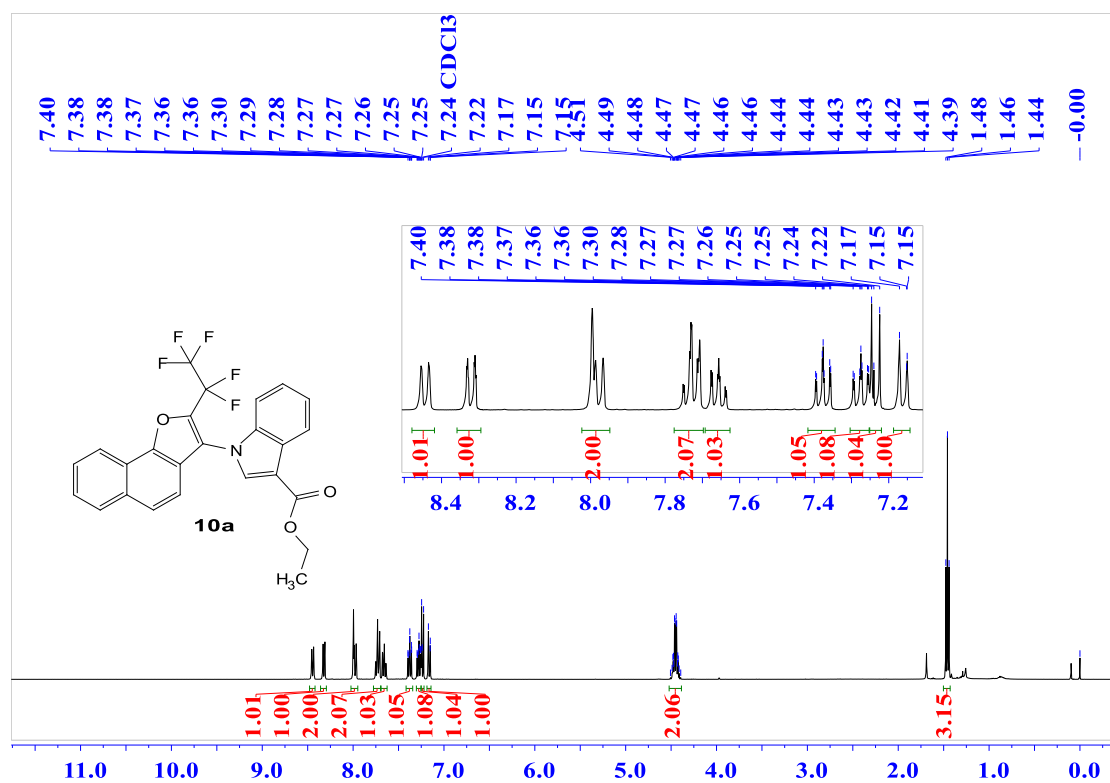


Figure S89. ^{19}F NMR spectrum of **10a**, related to Scheme 1.

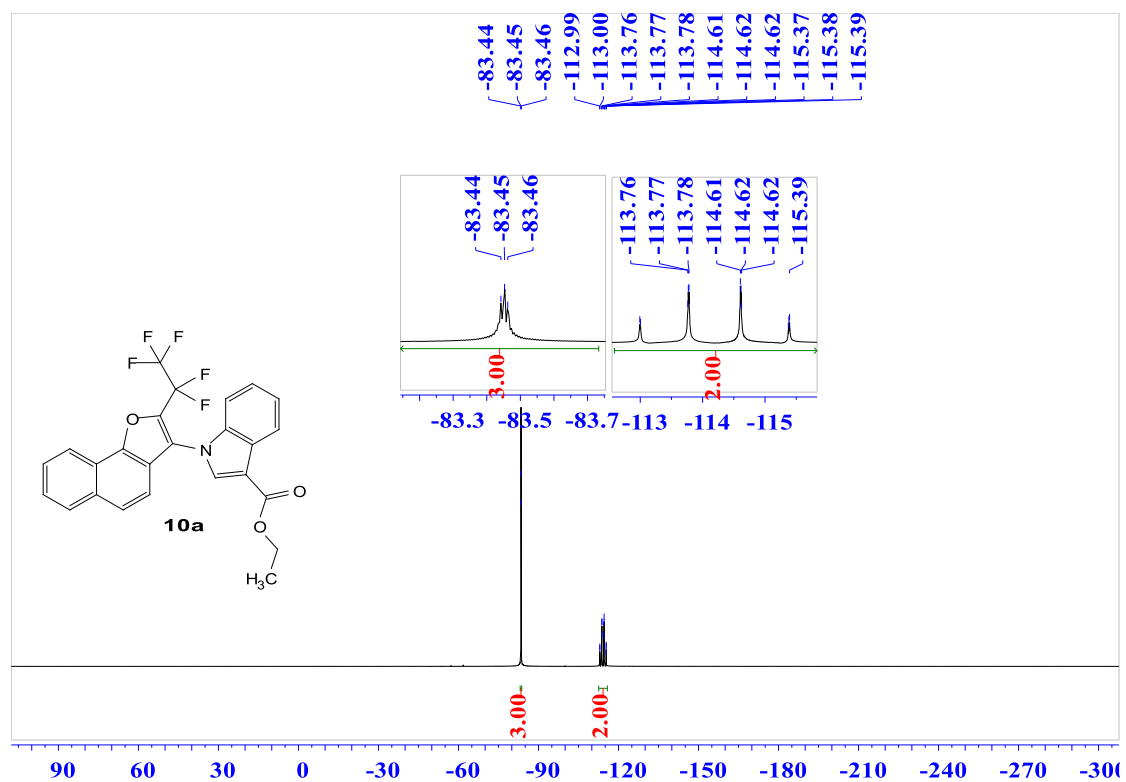


Figure S90. ^{13}C NMR spectrum of **10a**, related to Scheme 1.

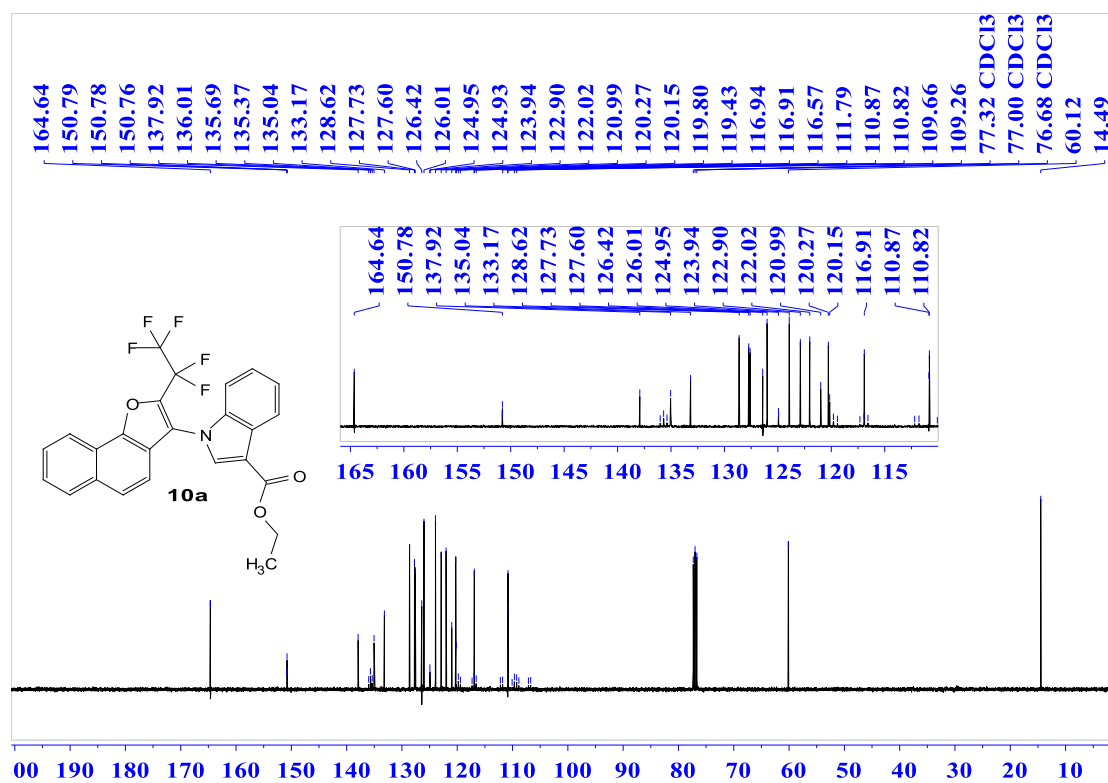


Figure S91. ¹H NMR spectrum of **10b**, related to Scheme 1.

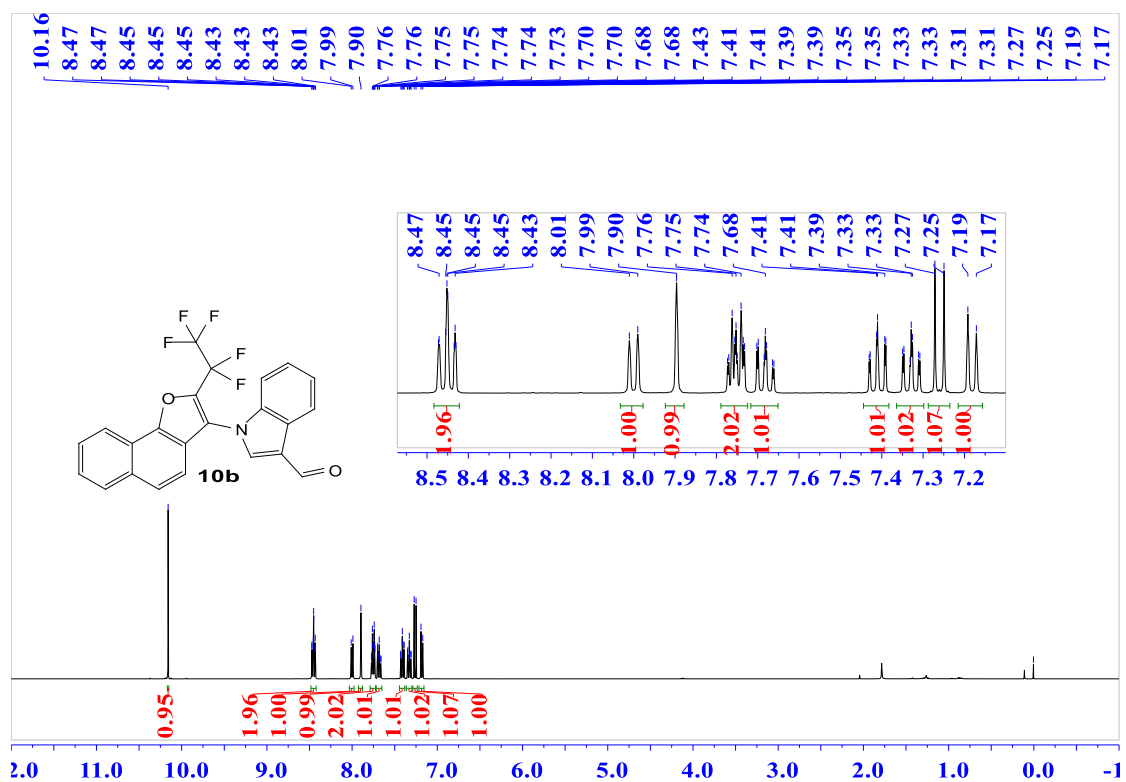


Figure S92. ¹⁹F NMR spectrum of **10b**, related to Scheme 1.

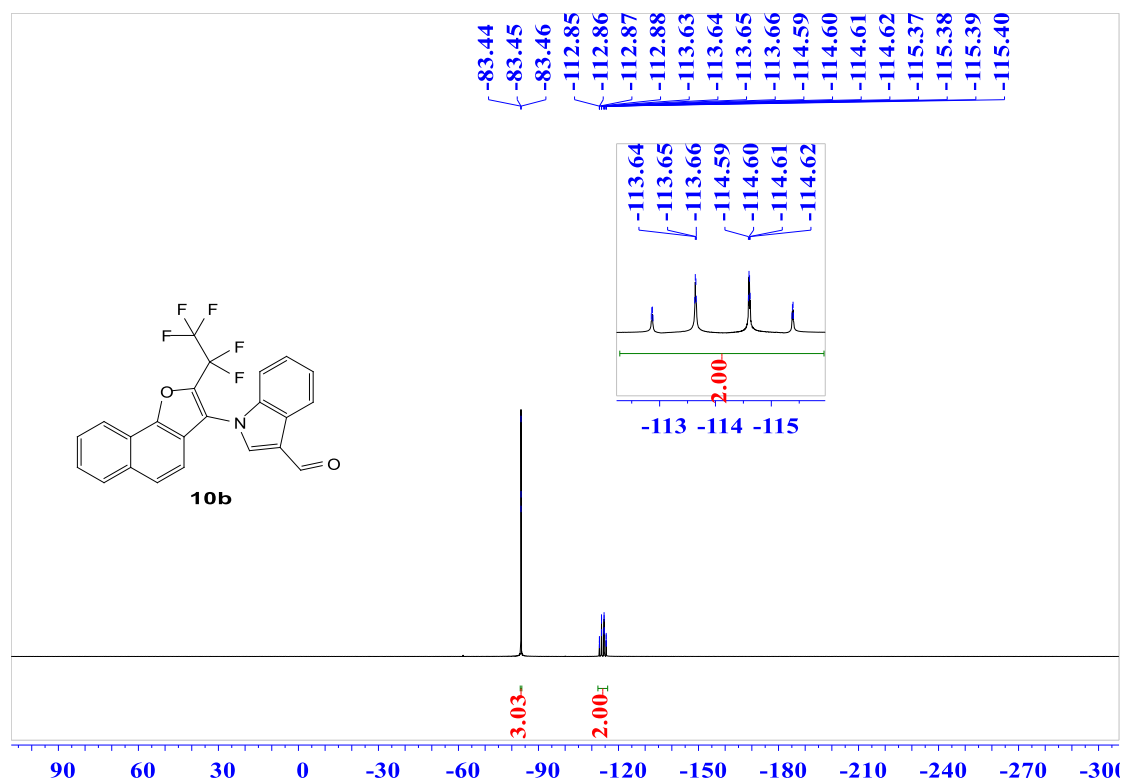


Figure S93. ¹³C NMR spectrum of **10b**, related to Scheme 1.

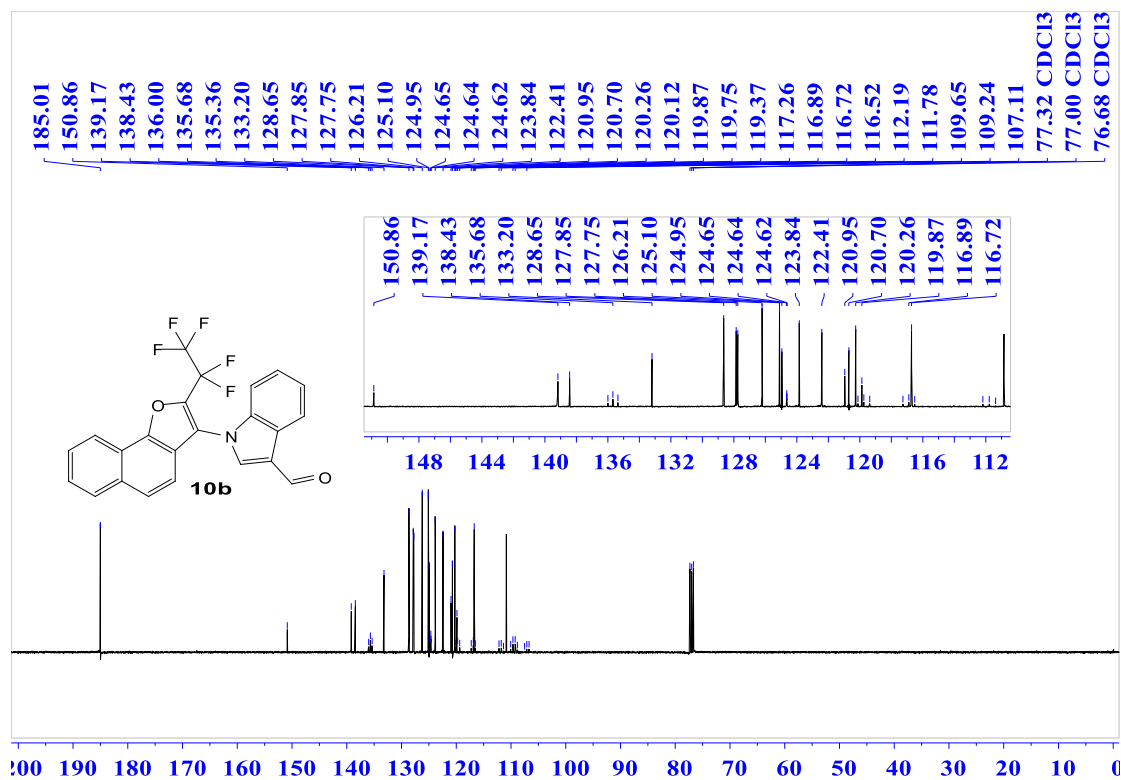


Figure S94. ¹H NMR spectrum of **10c**, related to Scheme 1.

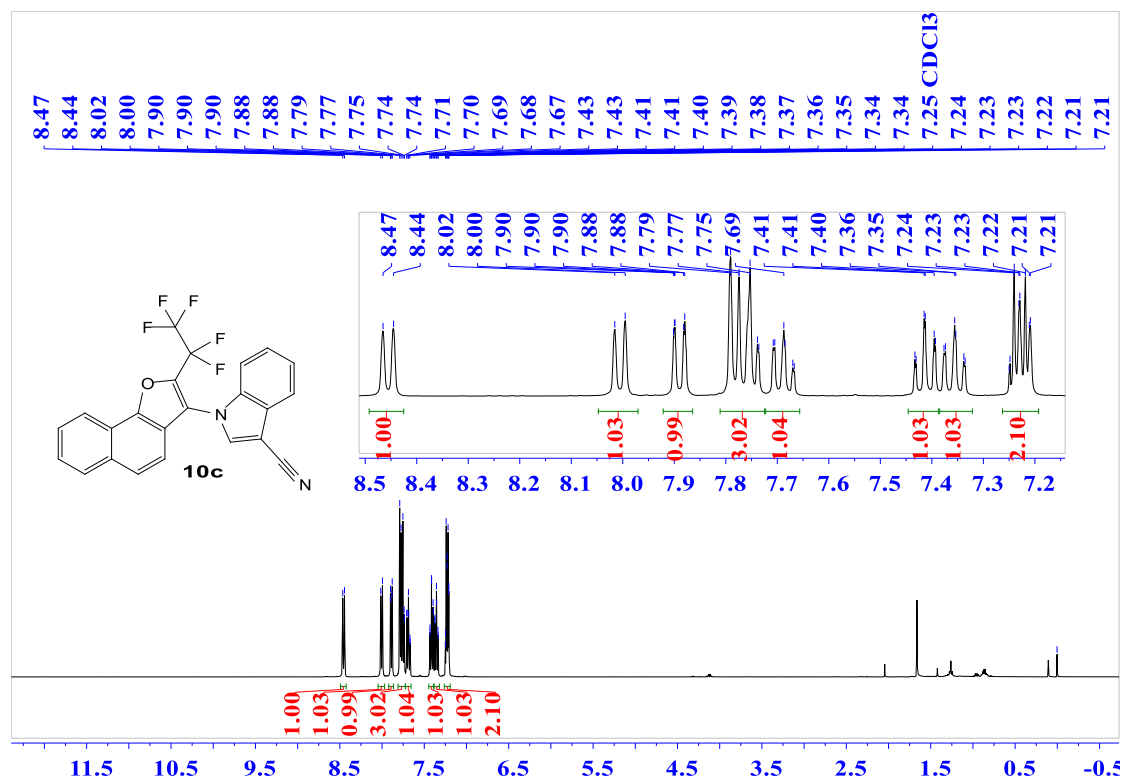


Figure S95. ¹⁹F NMR spectrum of **10c**, related to Scheme 1.

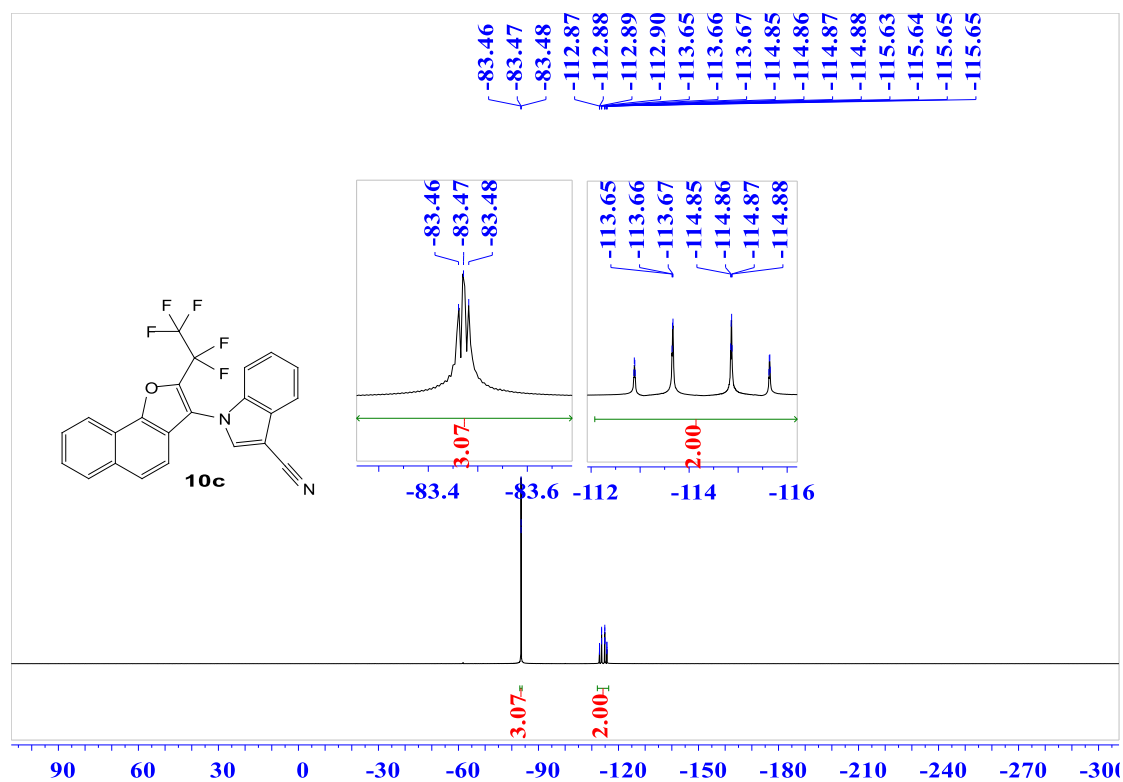


Figure S96. ¹³C NMR spectrum of **10c**, related to Scheme 1.

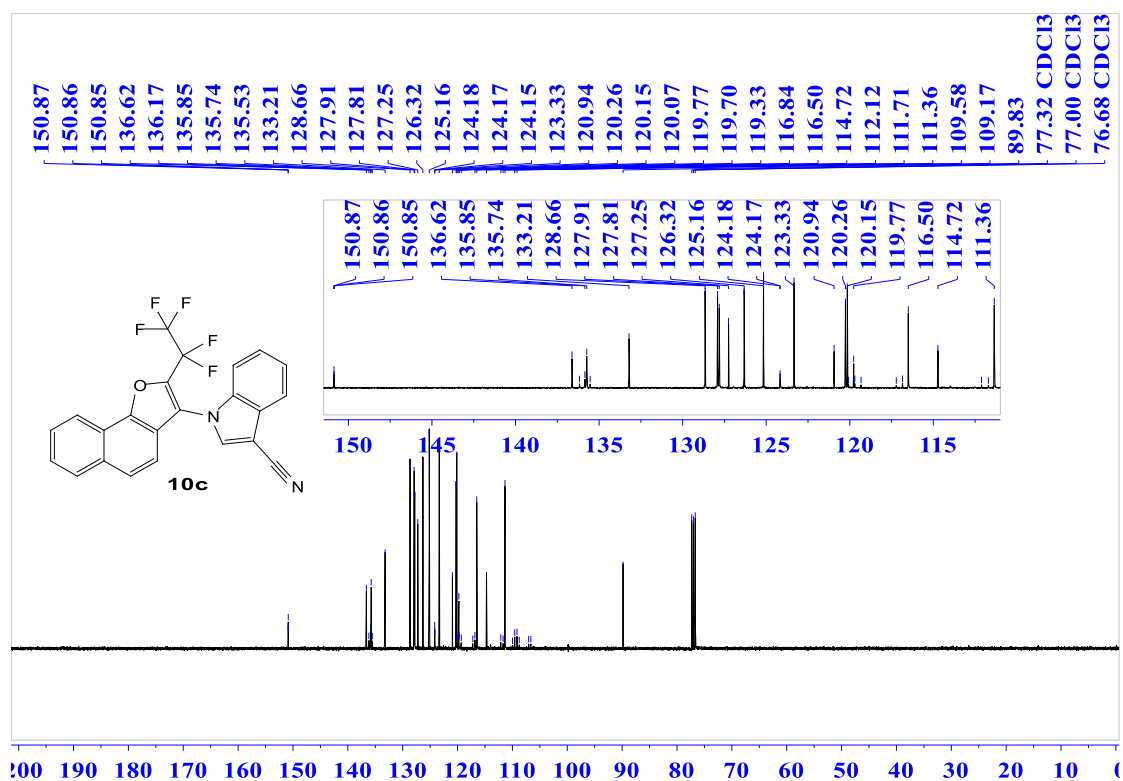


Figure S97. ¹H NMR spectrum of **10d**, related to Scheme 1.

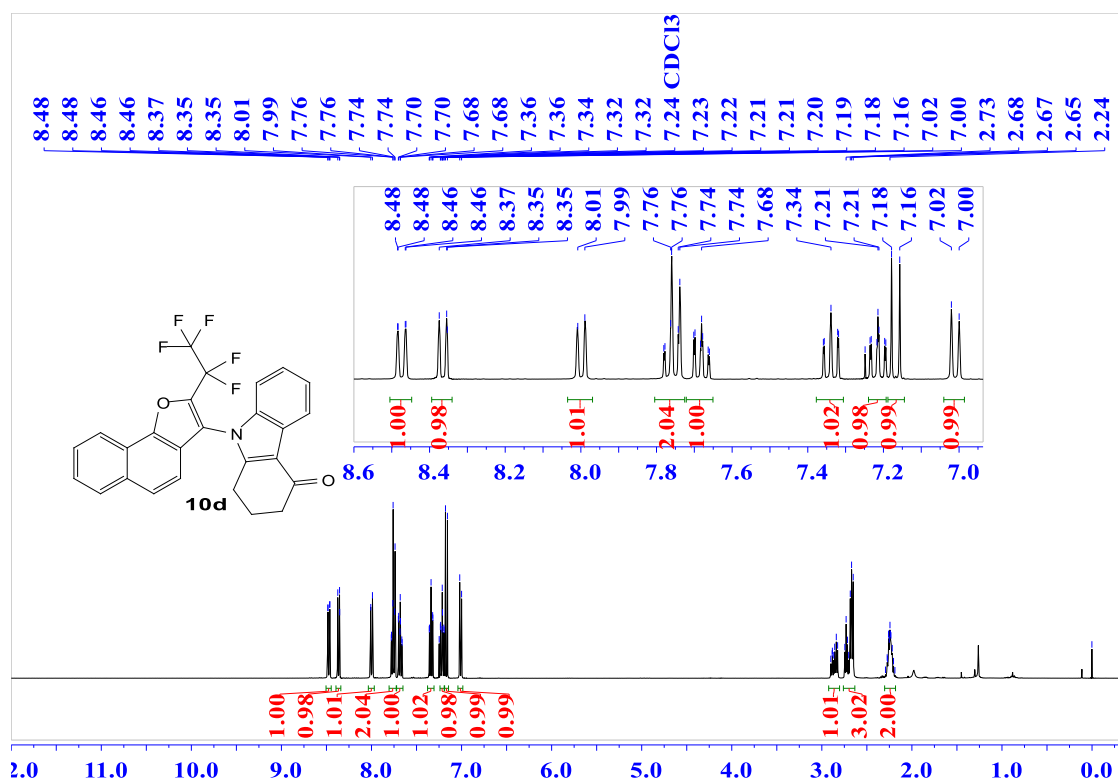


Figure S98. ¹⁹F NMR spectrum of **10d**, related to Scheme 1.

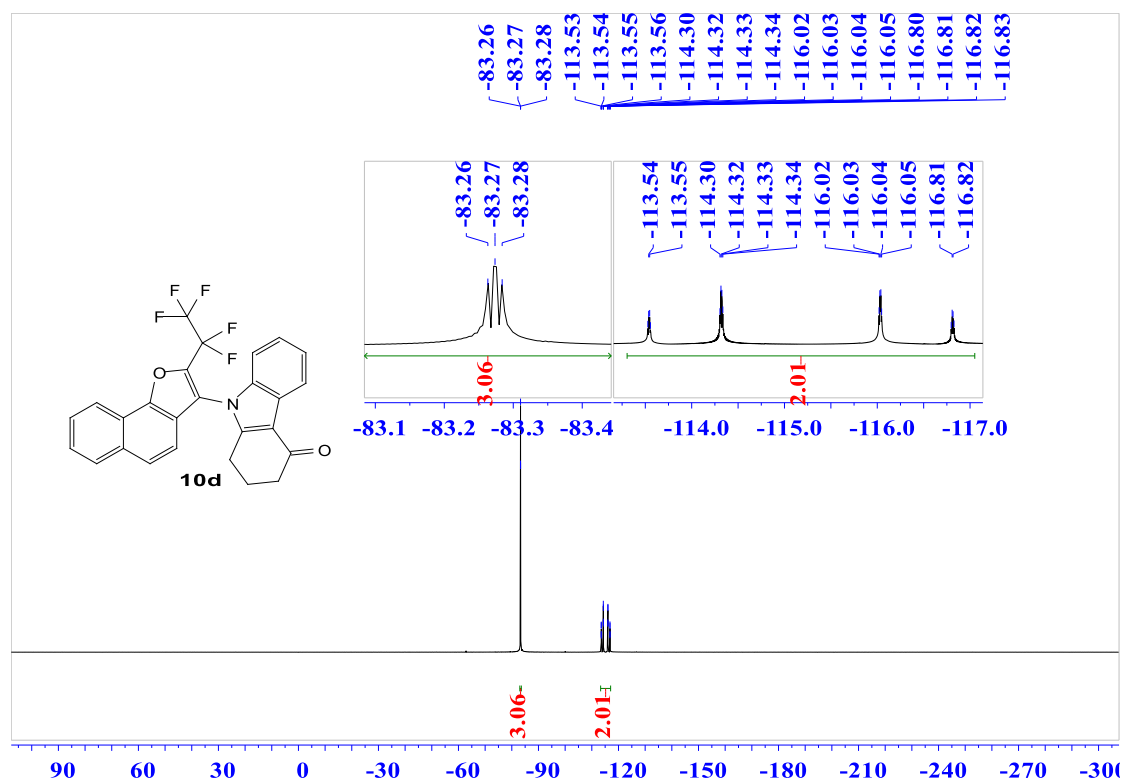


Figure S99. ¹³C NMR spectrum of **10d**, related to Scheme 1.

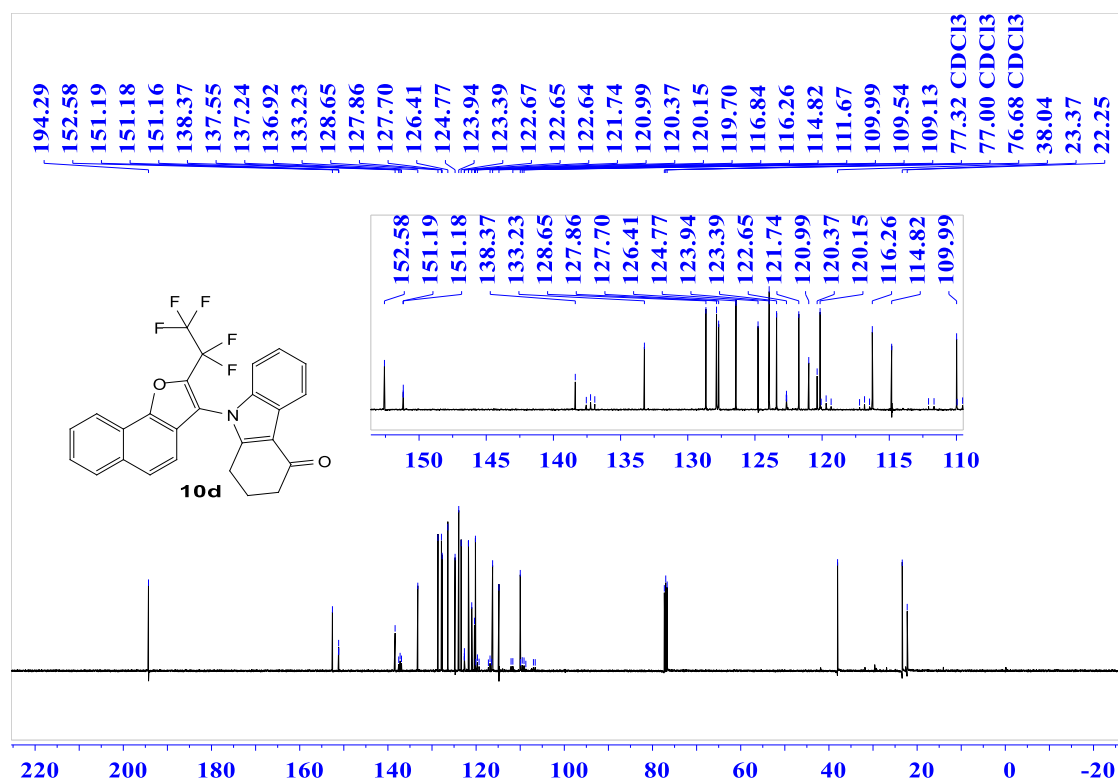


Figure S100. ¹H NMR spectrum of **11a**, related to Scheme 1.

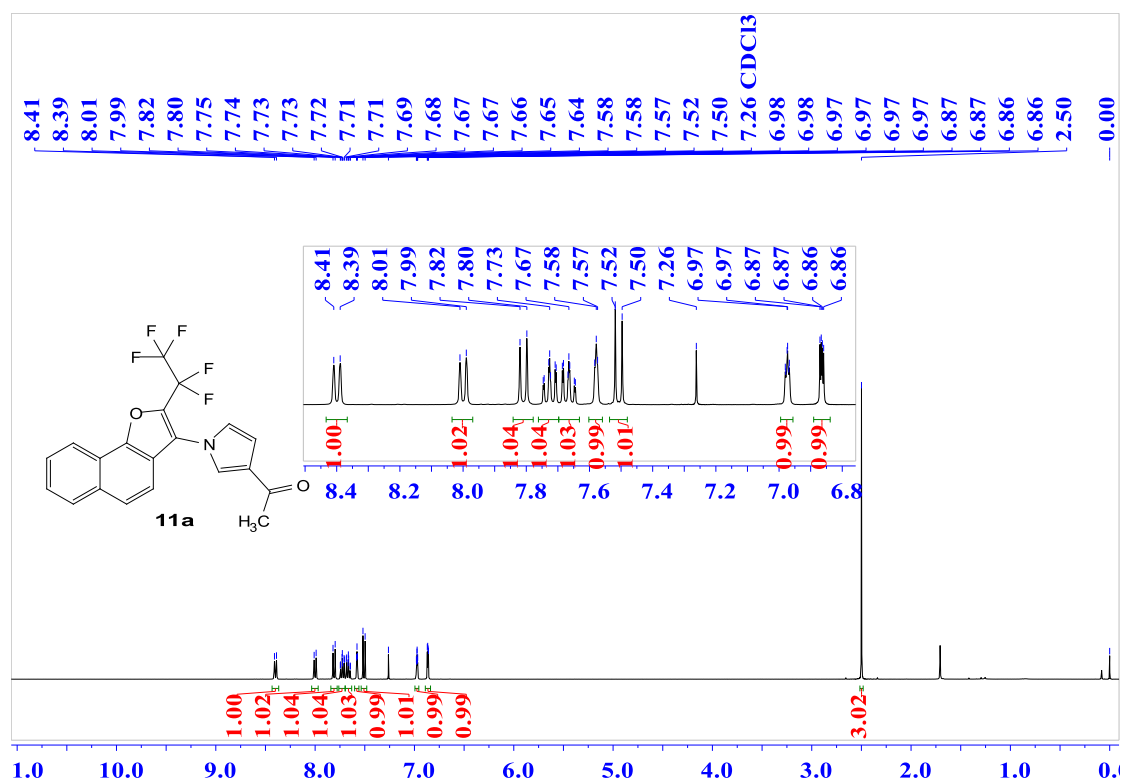


Figure S101. ^{19}F NMR spectrum of **11a**, related to Scheme 1.

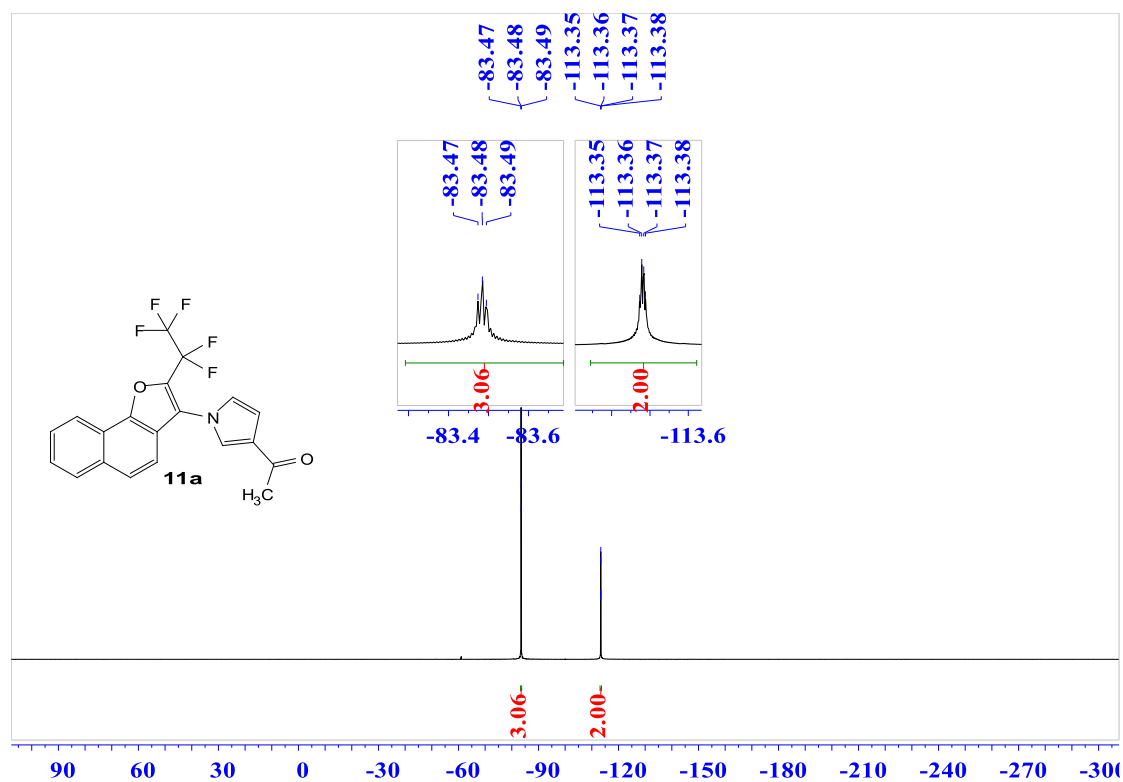


Figure S102. ^{13}C NMR spectrum of **11a**, related to Scheme 1.

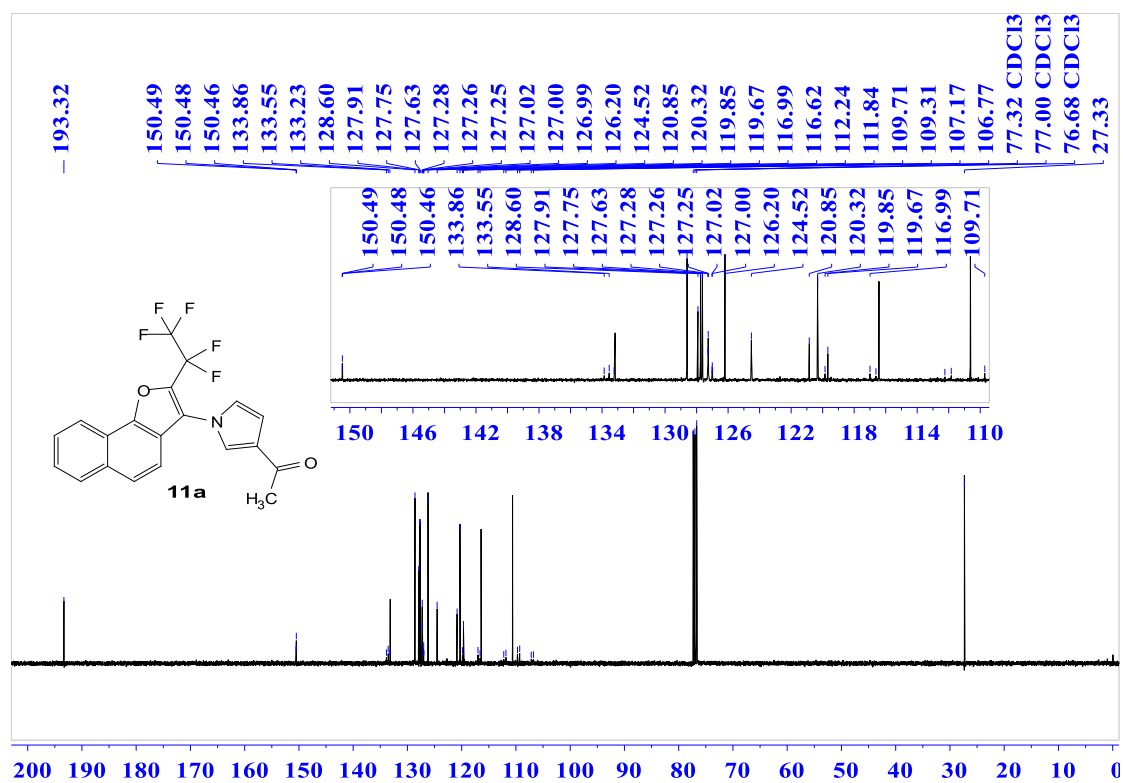


Figure S103. ¹H NMR spectrum of **11b**, related to Scheme 1.

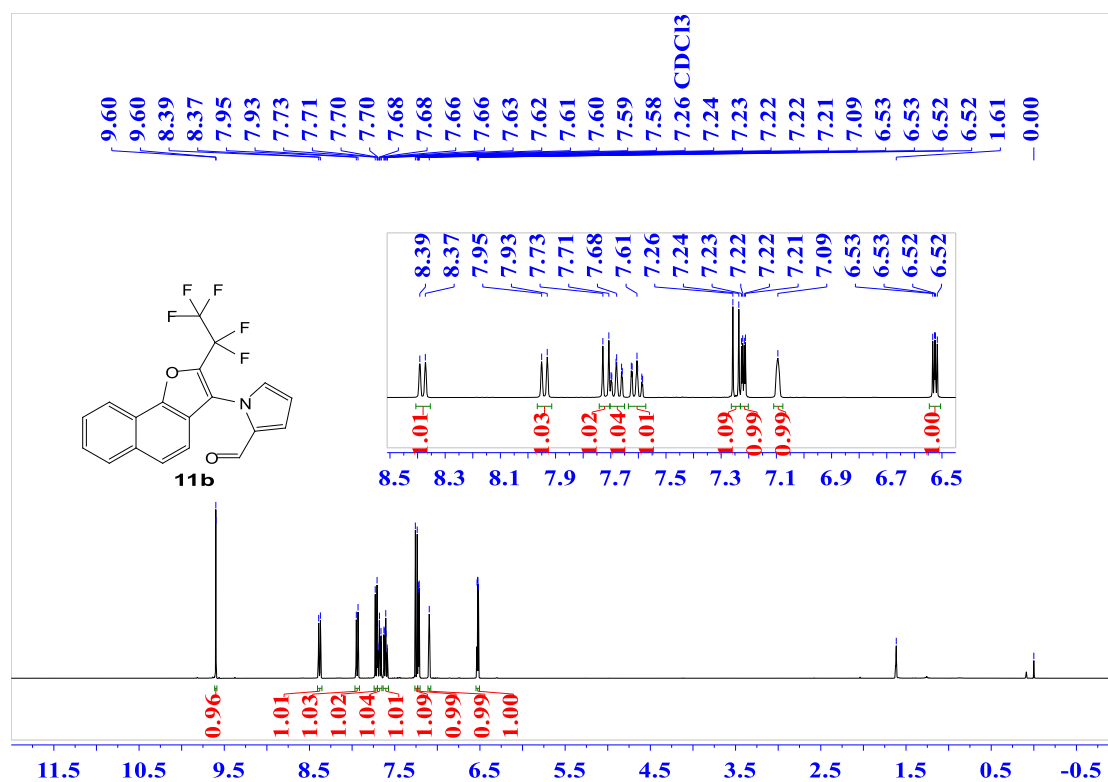


Figure S104. ¹⁹F NMR spectrum of **11b**, related to Scheme 1.

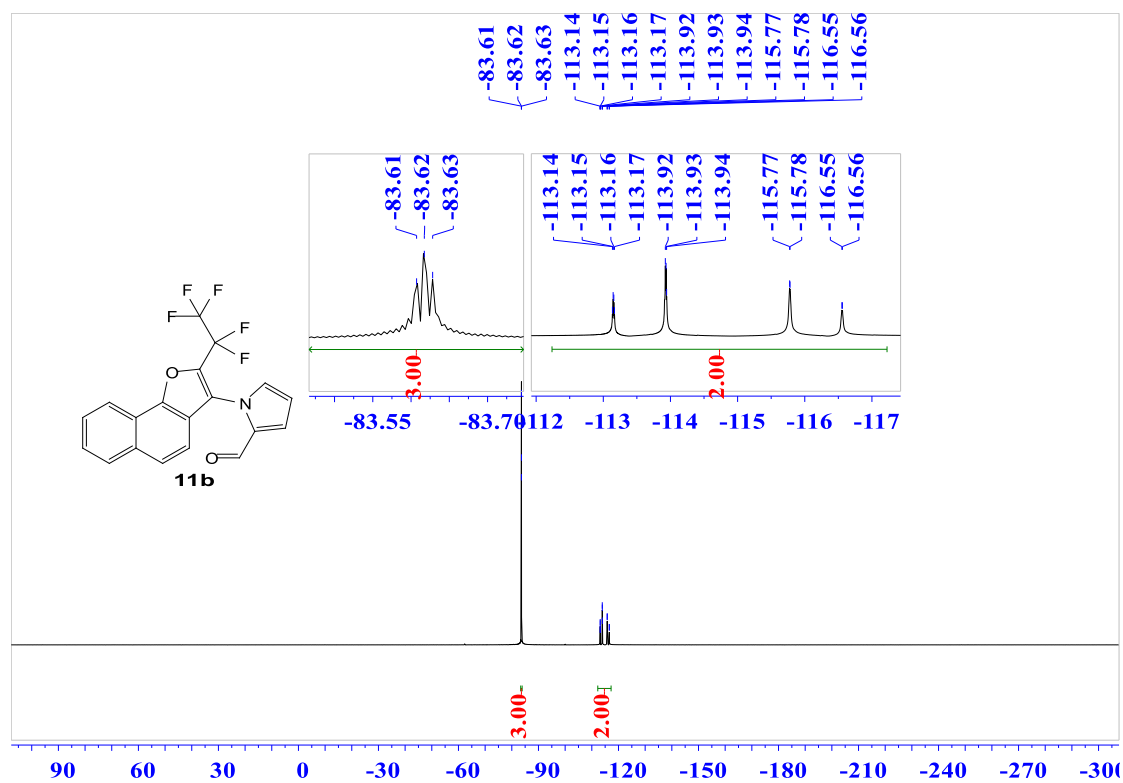


Figure S105. ¹³C NMR spectrum of **11b**, related to Scheme 1.

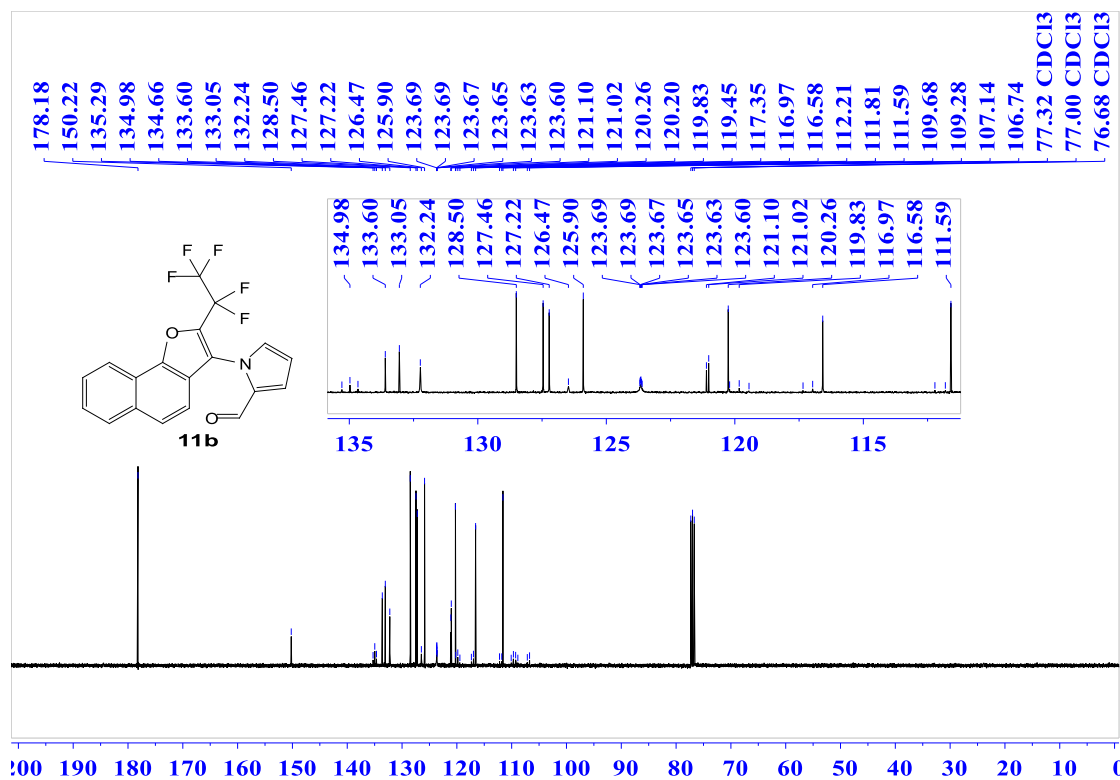


Figure S106. ¹H NMR spectrum of **11c**, related to Scheme 1.

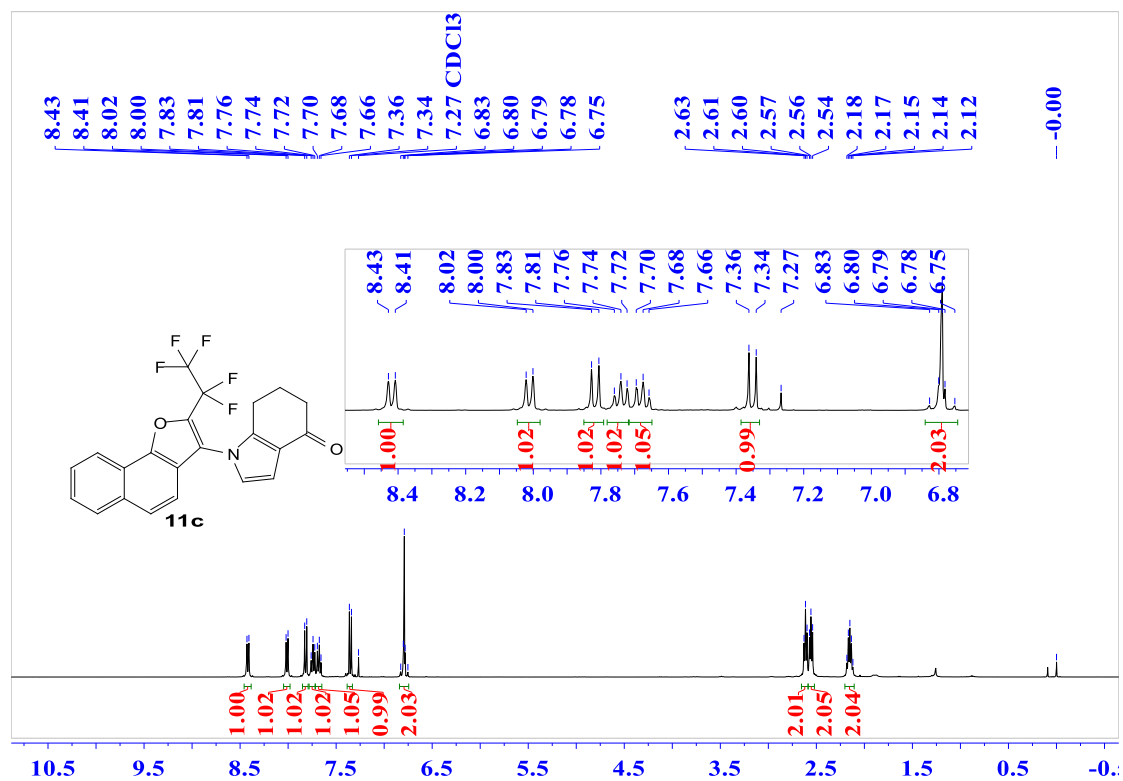


Figure S107. ¹⁹F NMR spectrum of **11c**, related to Scheme 1.

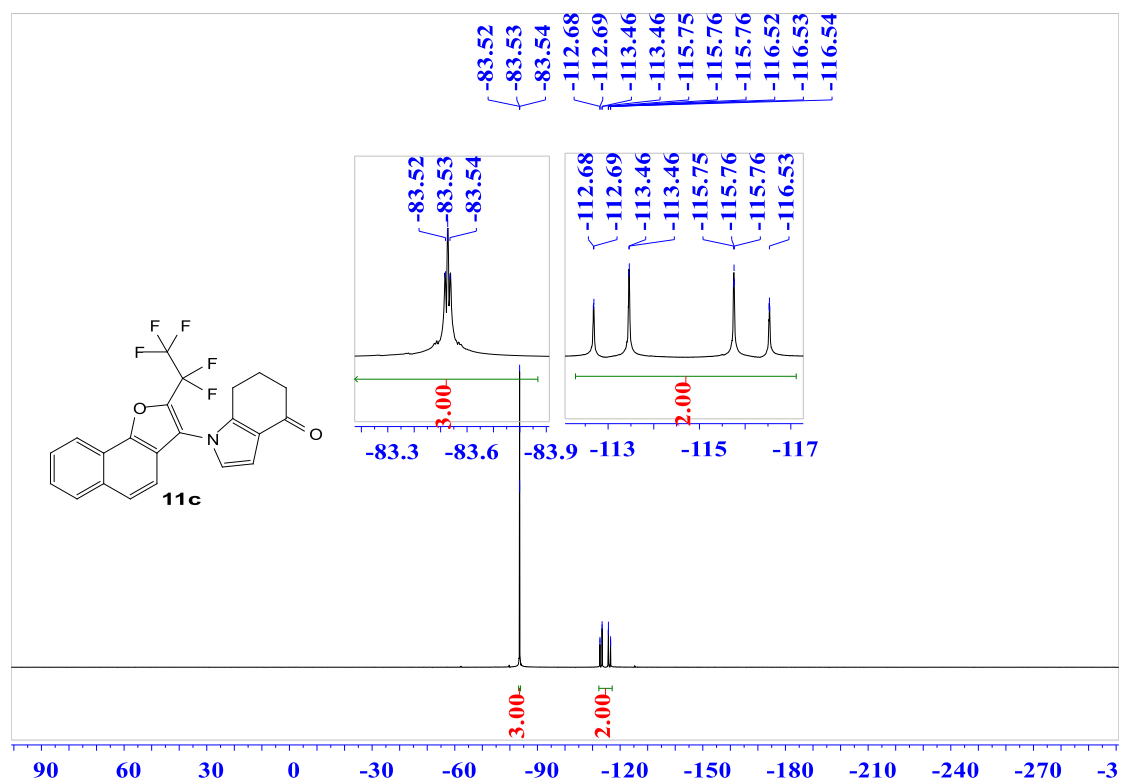


Figure S108. ¹³C NMR spectrum of **11c**, related to Scheme 1.

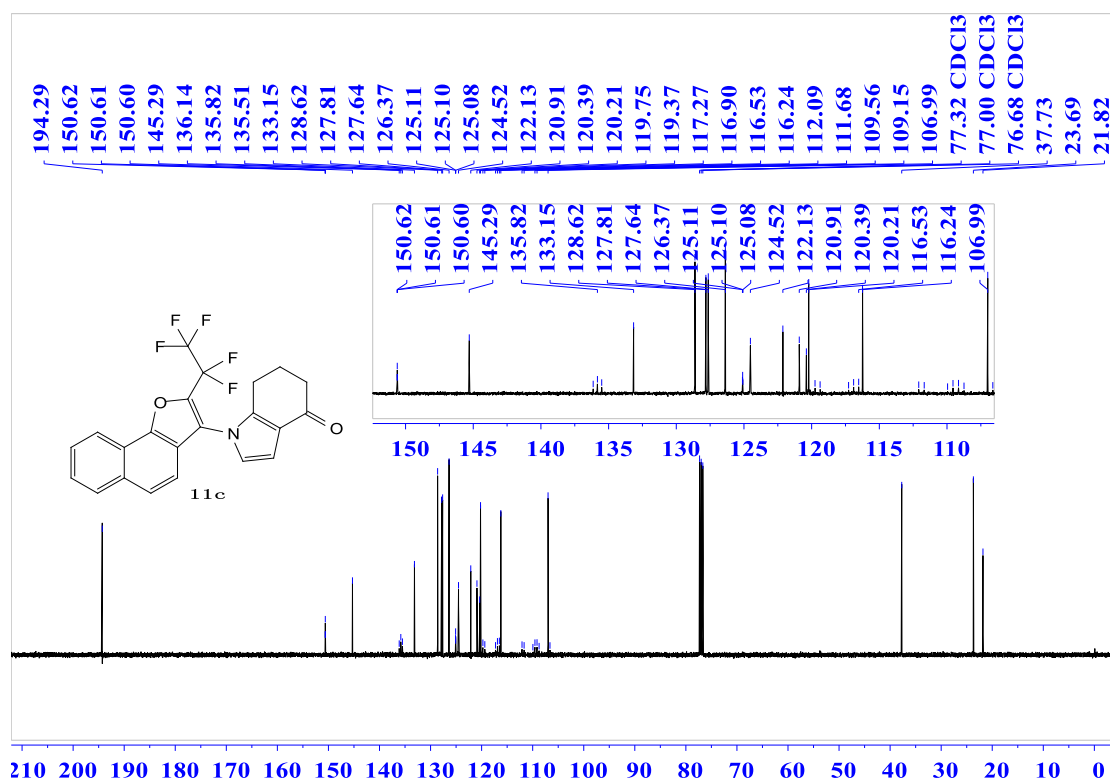


Figure S109. ¹H NMR spectrum of **12**, related to Scheme 1.

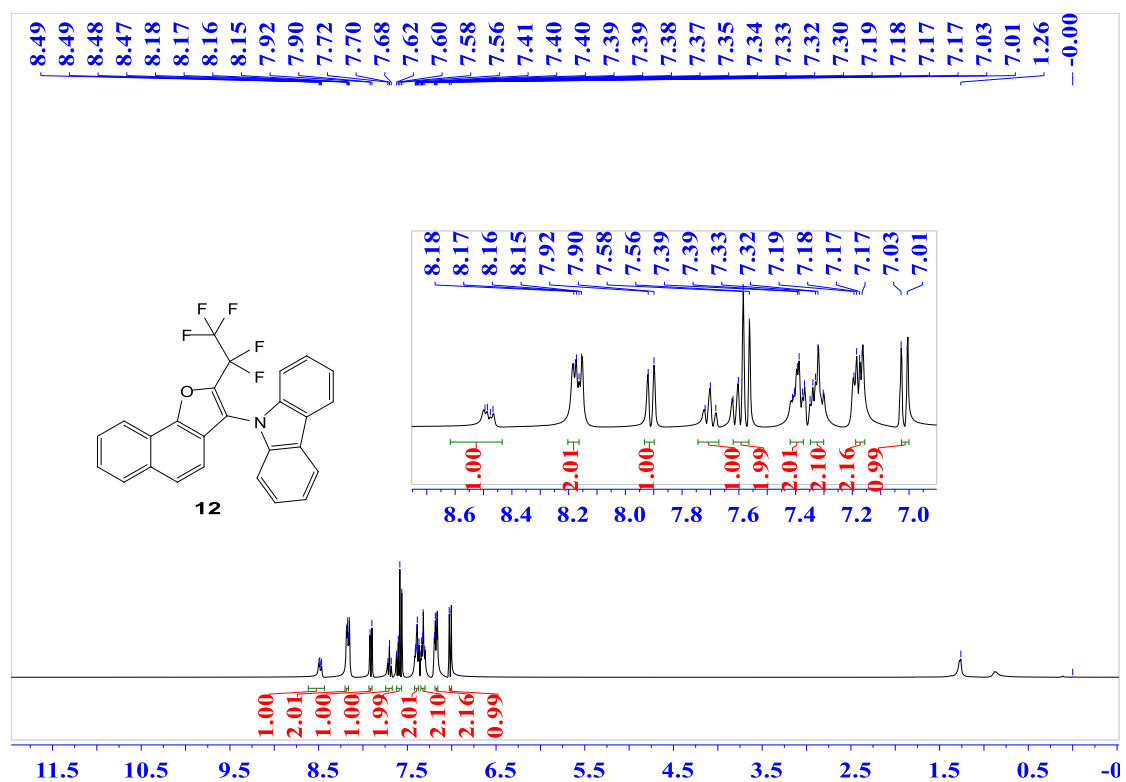


Figure S110. ¹⁹F NMR spectrum of **12**, related to Scheme 1.

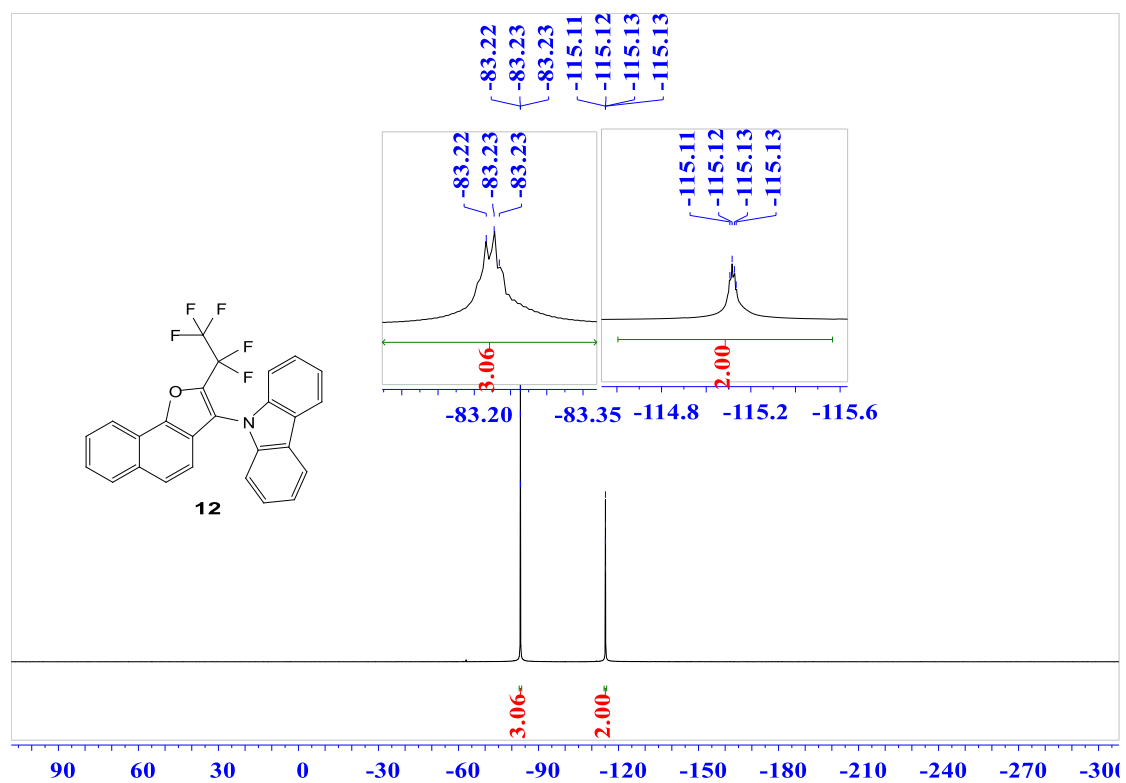


Figure S111. ^{13}C NMR spectrum of **12**, related to Scheme 1.

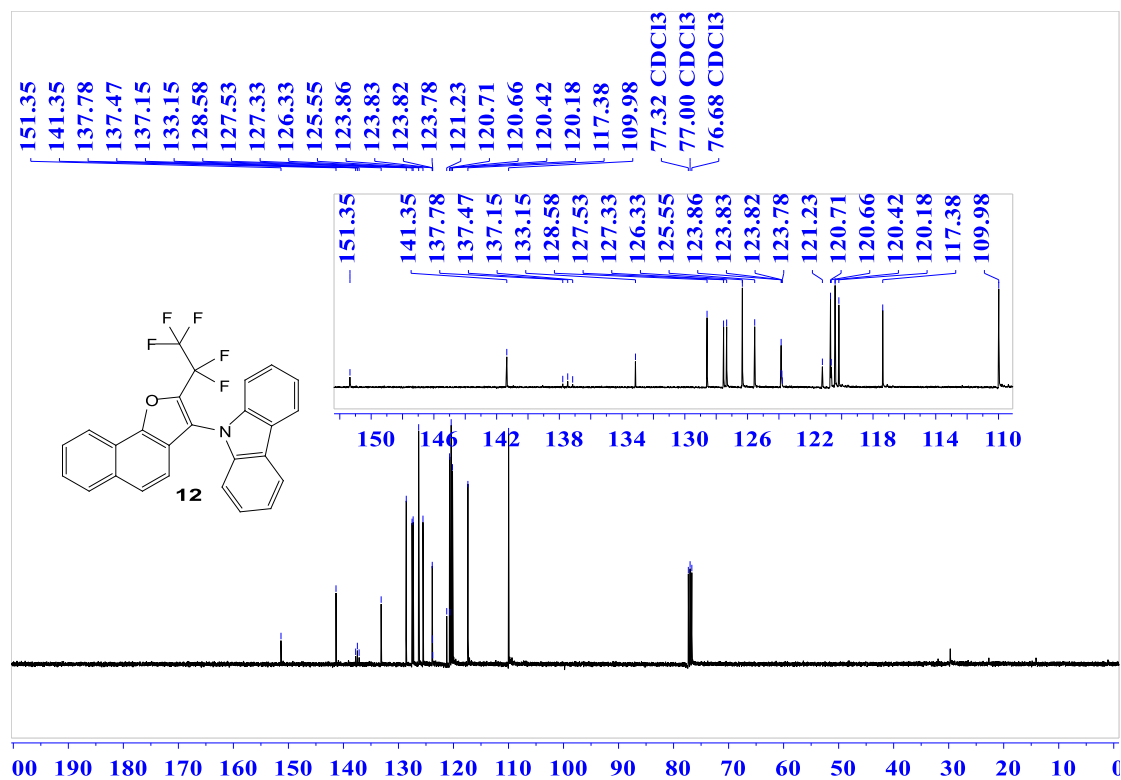


Figure S112. ^1H NMR spectrum of **13**, related to Scheme 1.

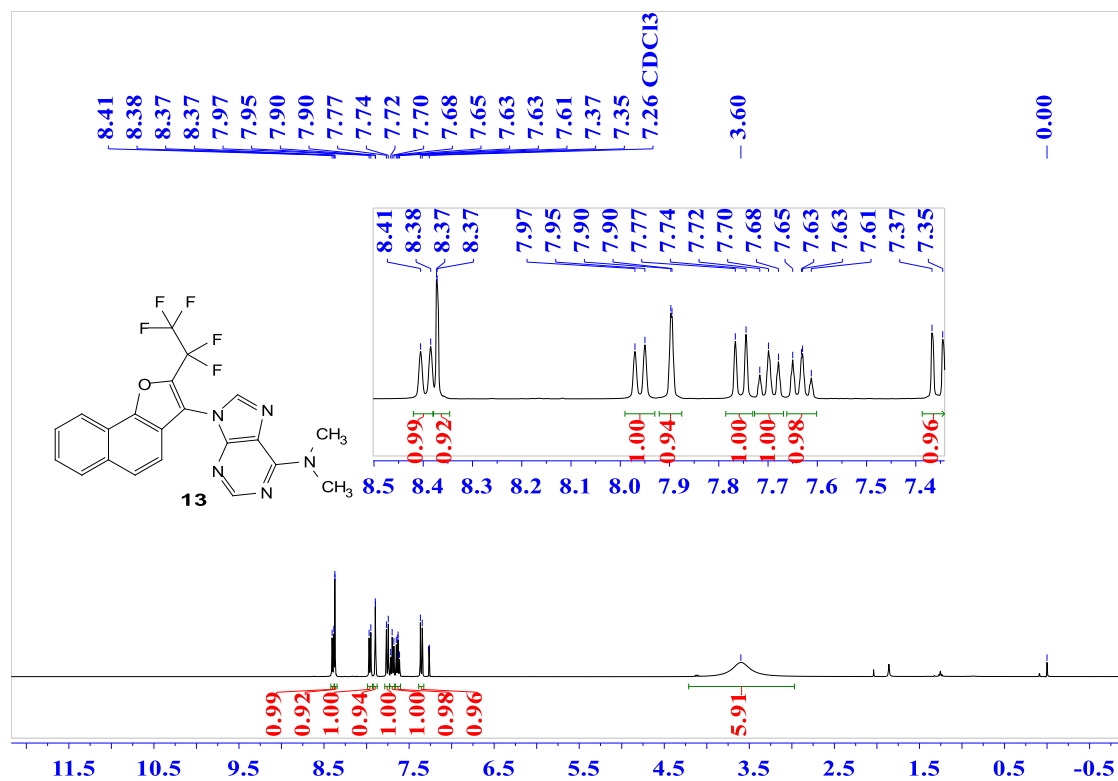


Figure S113. ^{19}F NMR spectrum of **13**, related to Scheme 1.

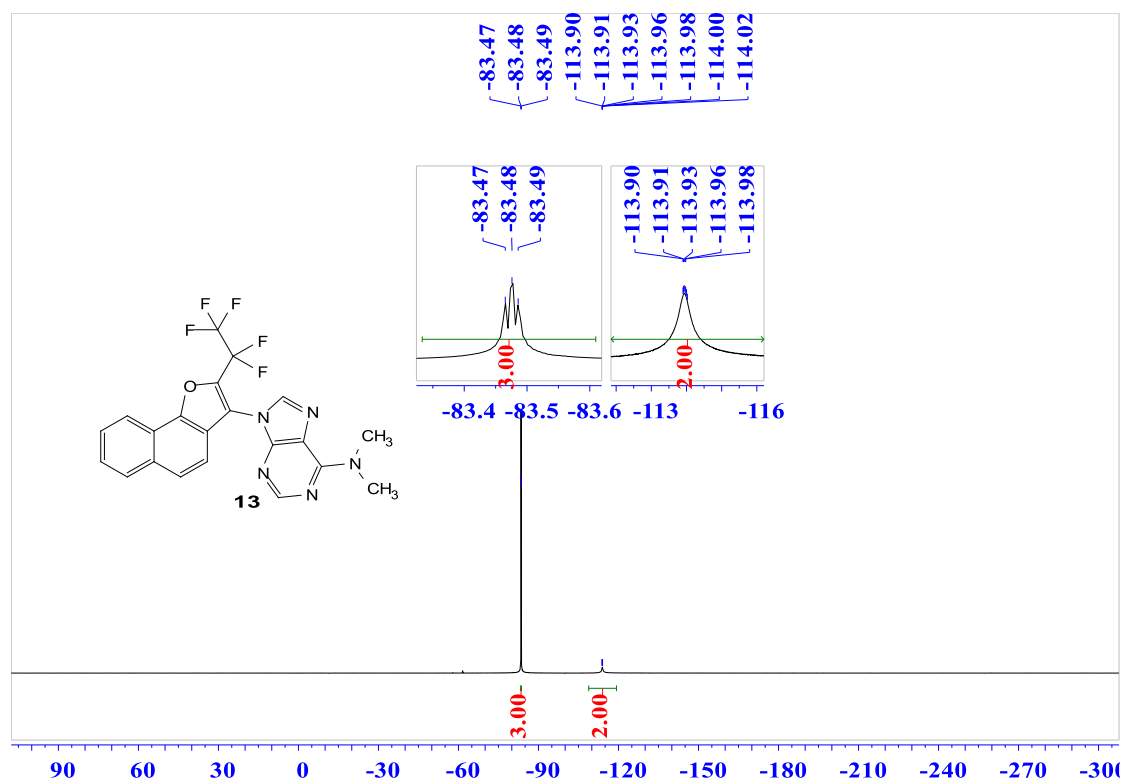


Figure S114. ^{13}C NMR spectrum of **13**, related to Scheme 1.

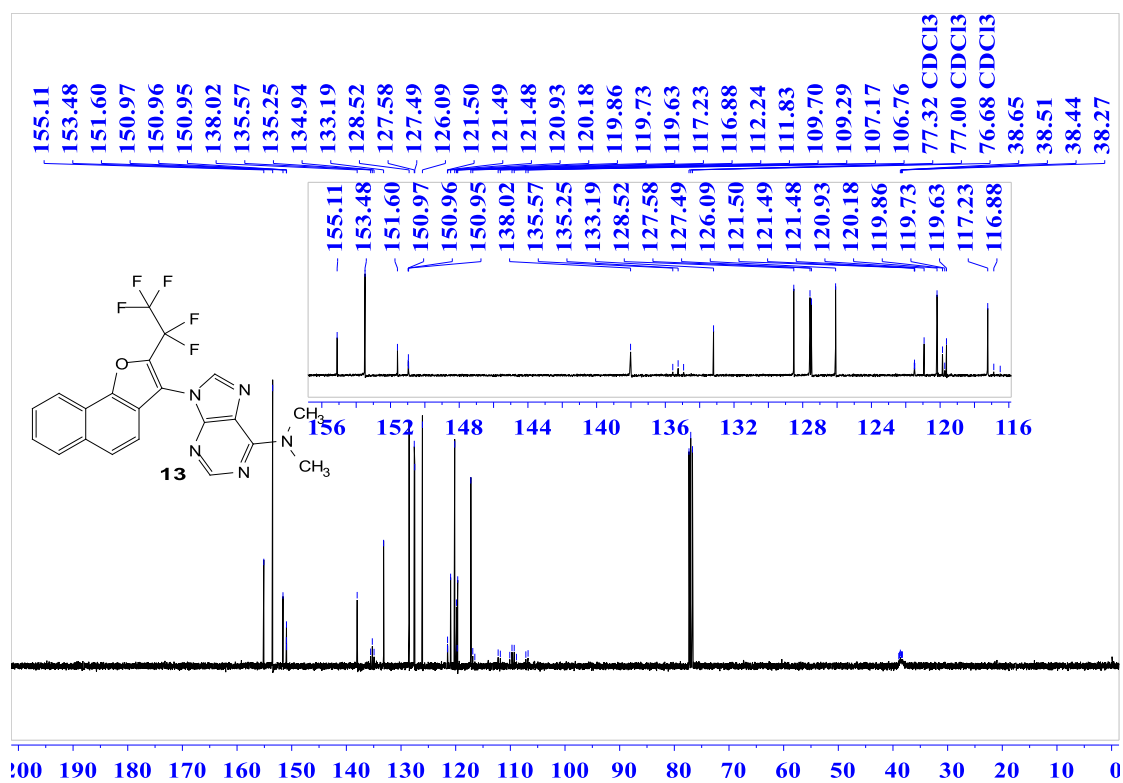


Figure S115. ¹H NMR spectrum of 15a, related to Scheme 2.

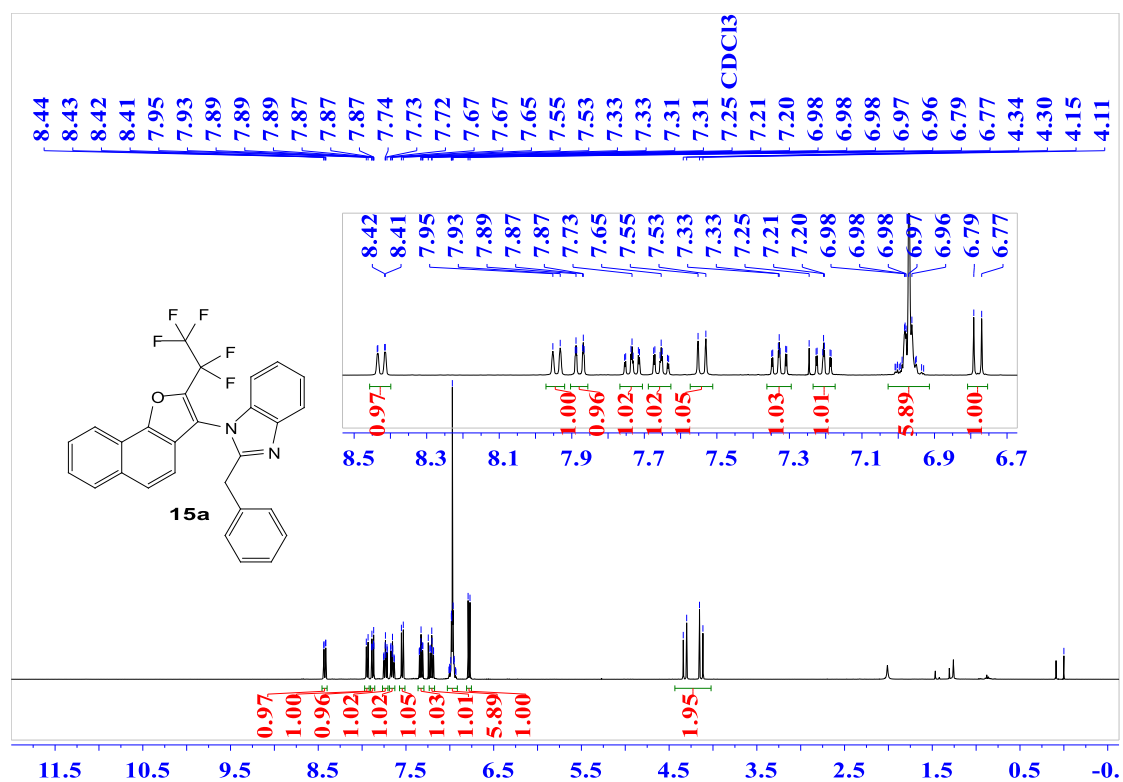


Figure S116. ¹⁹F NMR spectrum of 15a, related to Scheme 2.

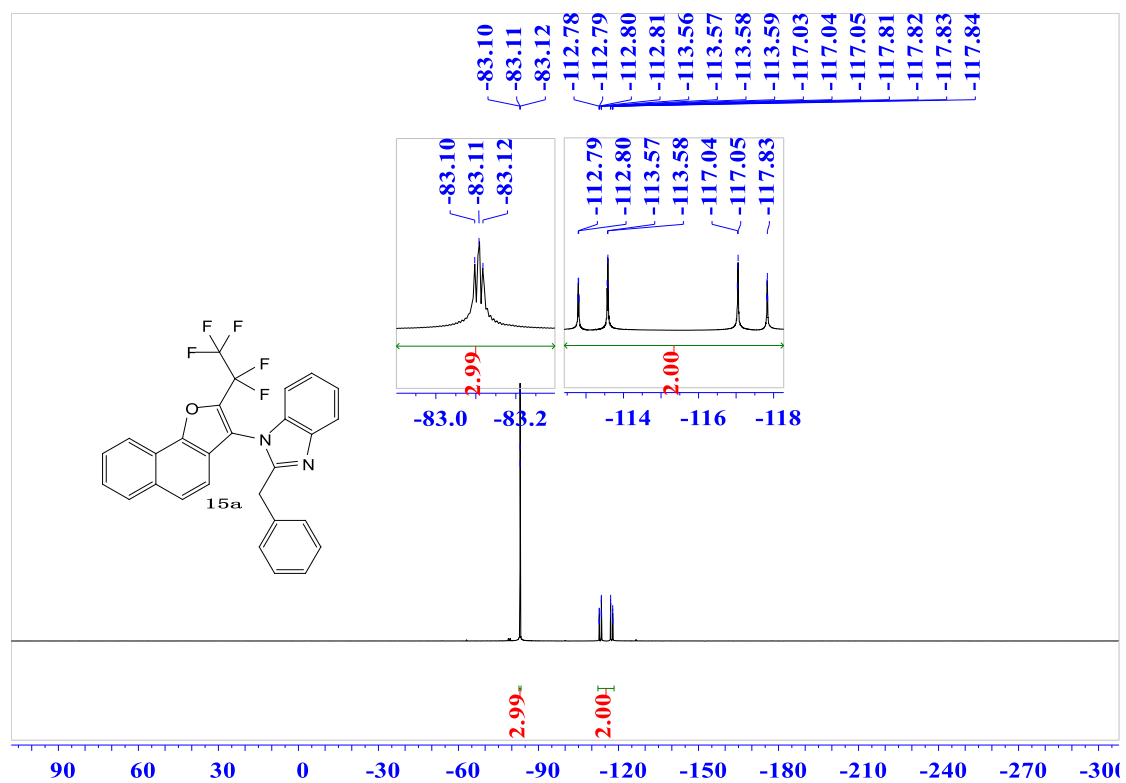


Figure S117. ^{13}C NMR spectrum of **15a**, related to Scheme 2.

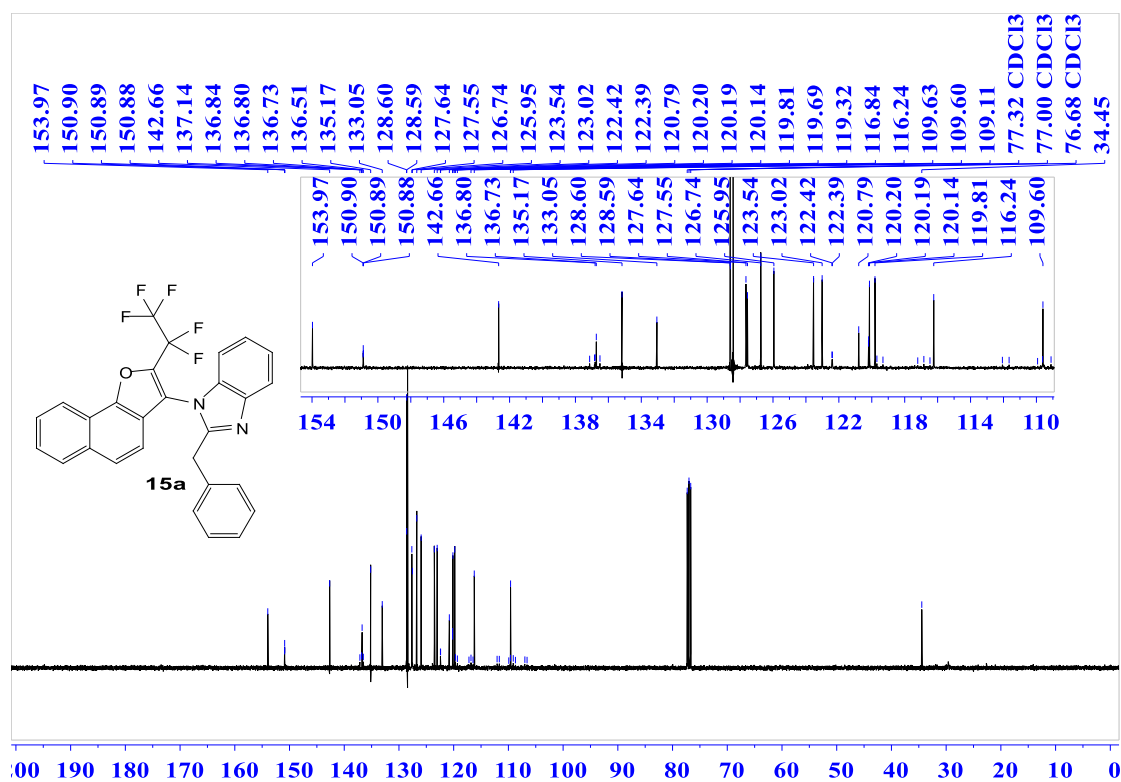


Figure S118. ^1H NMR spectrum of **15b**, related to Scheme 2.

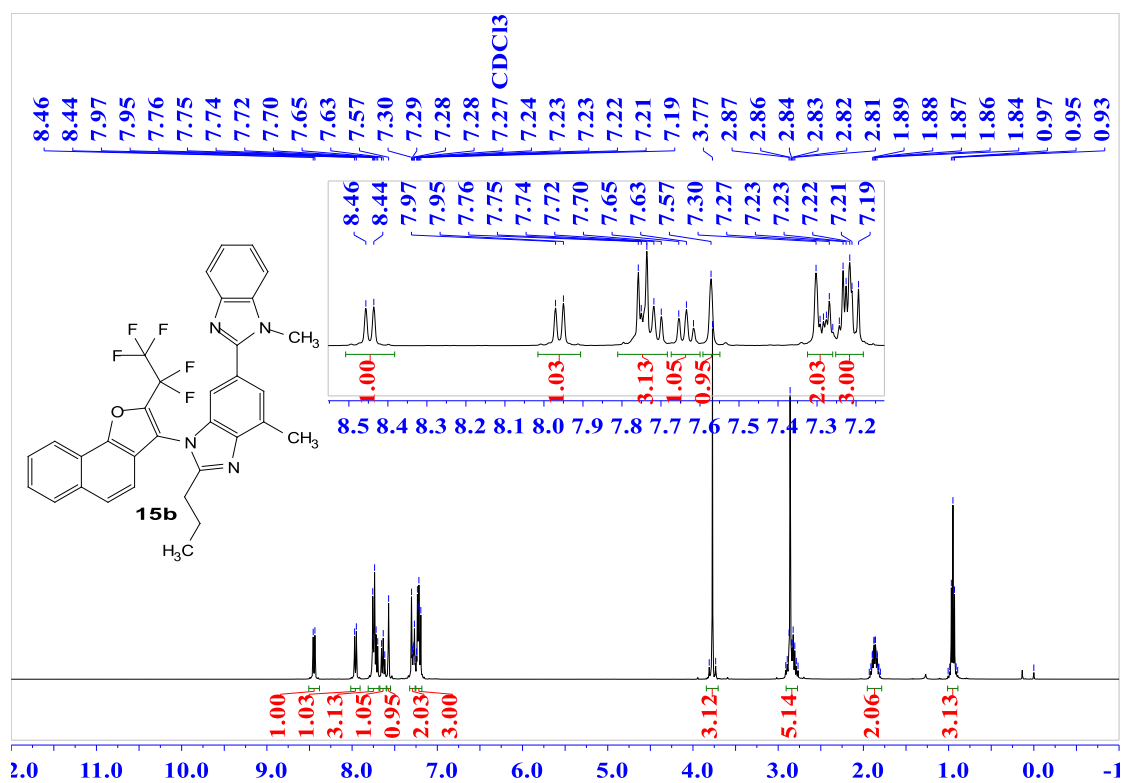


Figure S119. ^{19}F NMR spectrum of **15b**, related to Scheme 2.

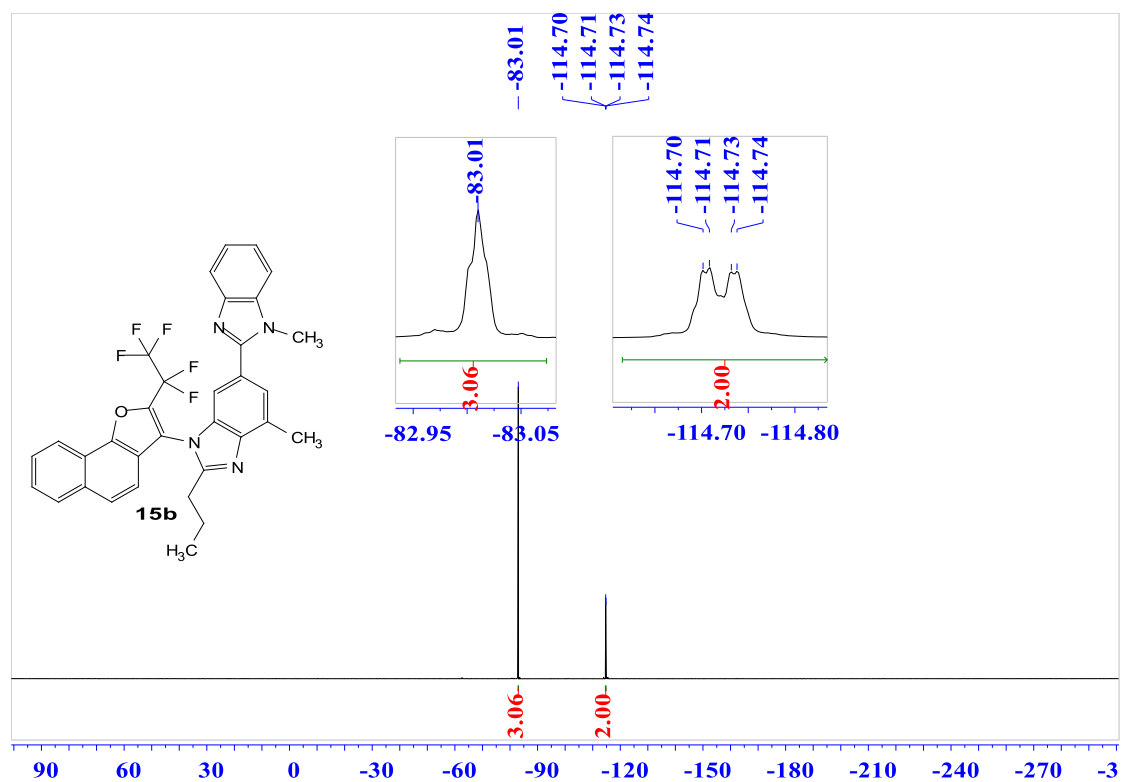


Figure S120. ^{13}C NMR spectrum of **15b**, related to Scheme 2.

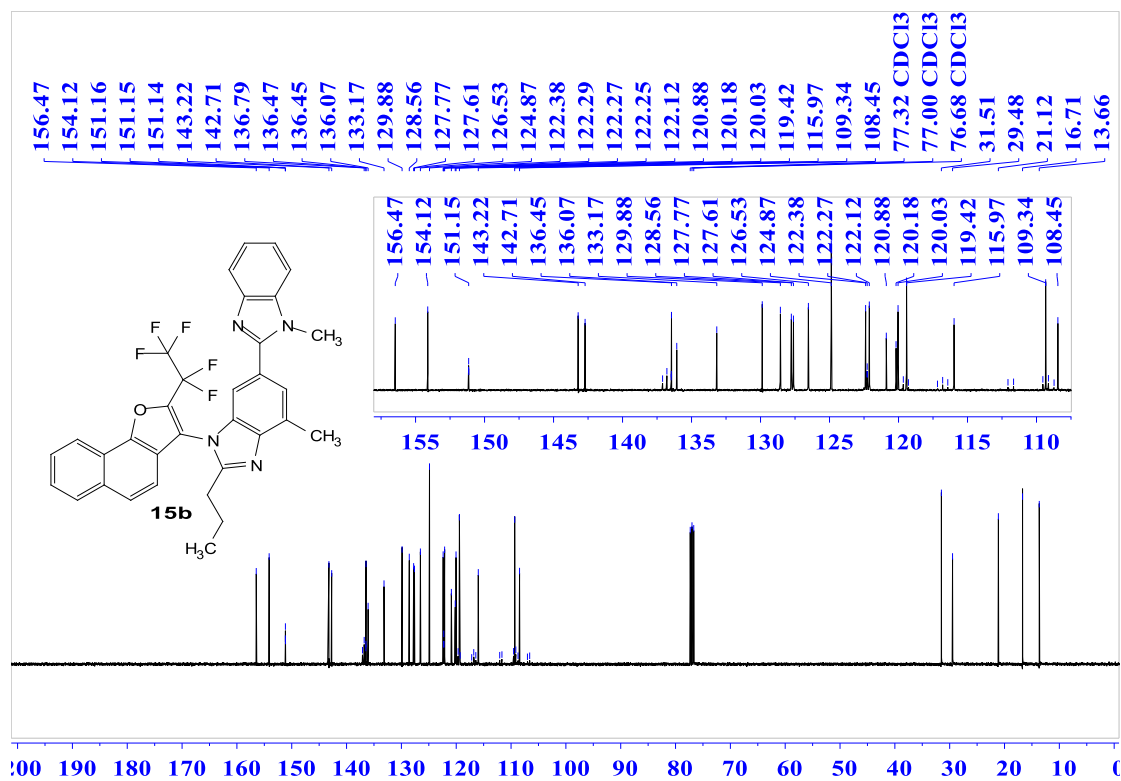


Figure S121. ¹H NMR spectrum of **15c**, related to Scheme 2.

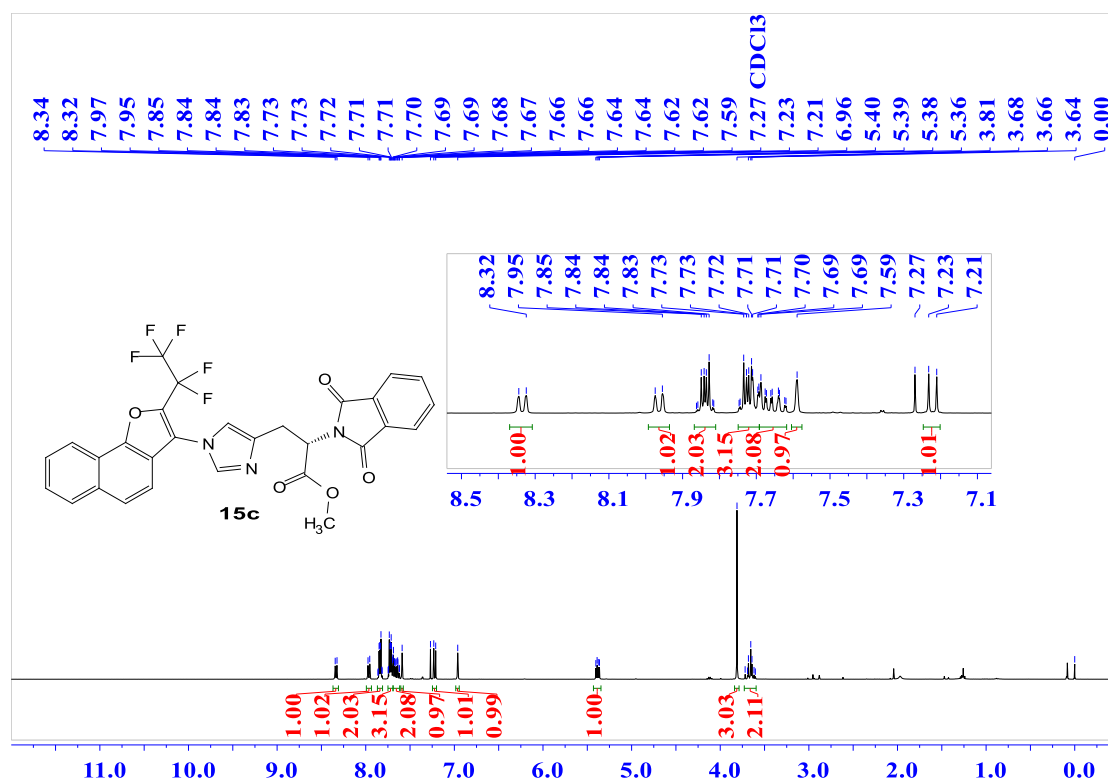


Figure S122. ¹⁹F NMR spectrum of **15c**, related to Scheme 2.

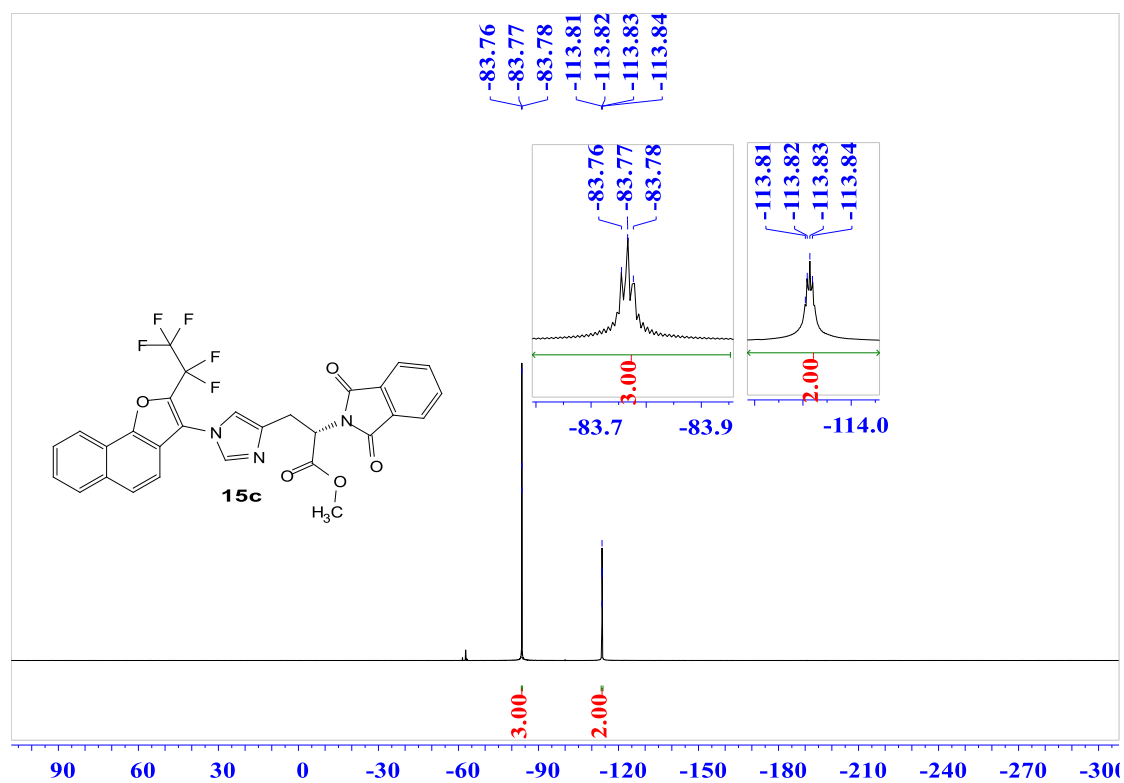


Figure S123. ¹³C NMR spectrum of **15c**, related to Scheme 2.

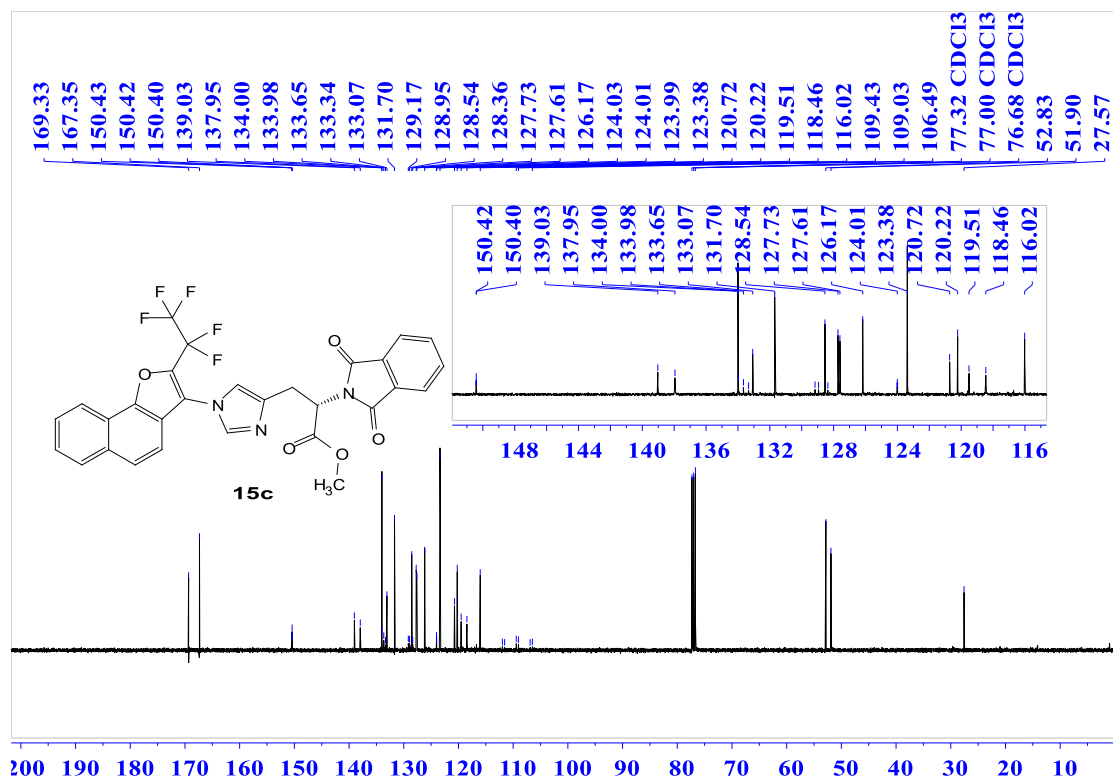


Figure S124. ¹H NMR spectrum of **15d**, related to Scheme 2.

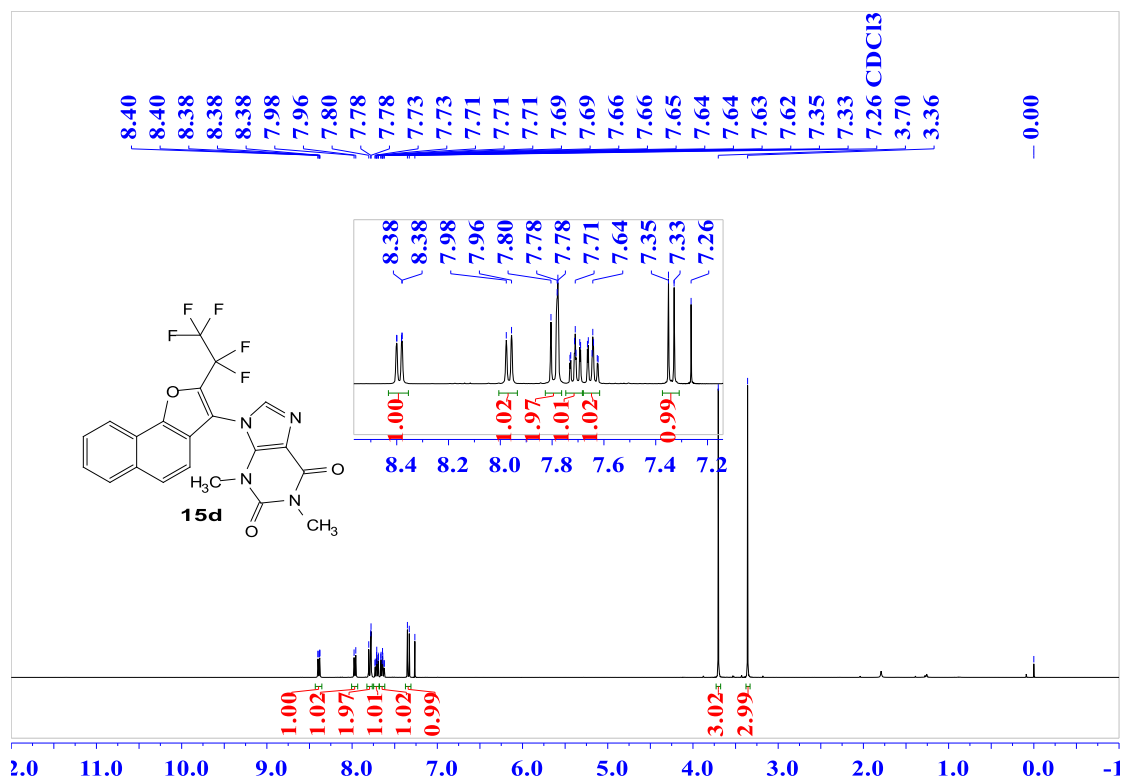


Figure S125. ¹⁹F NMR spectrum of **15d**, related to Scheme 2.

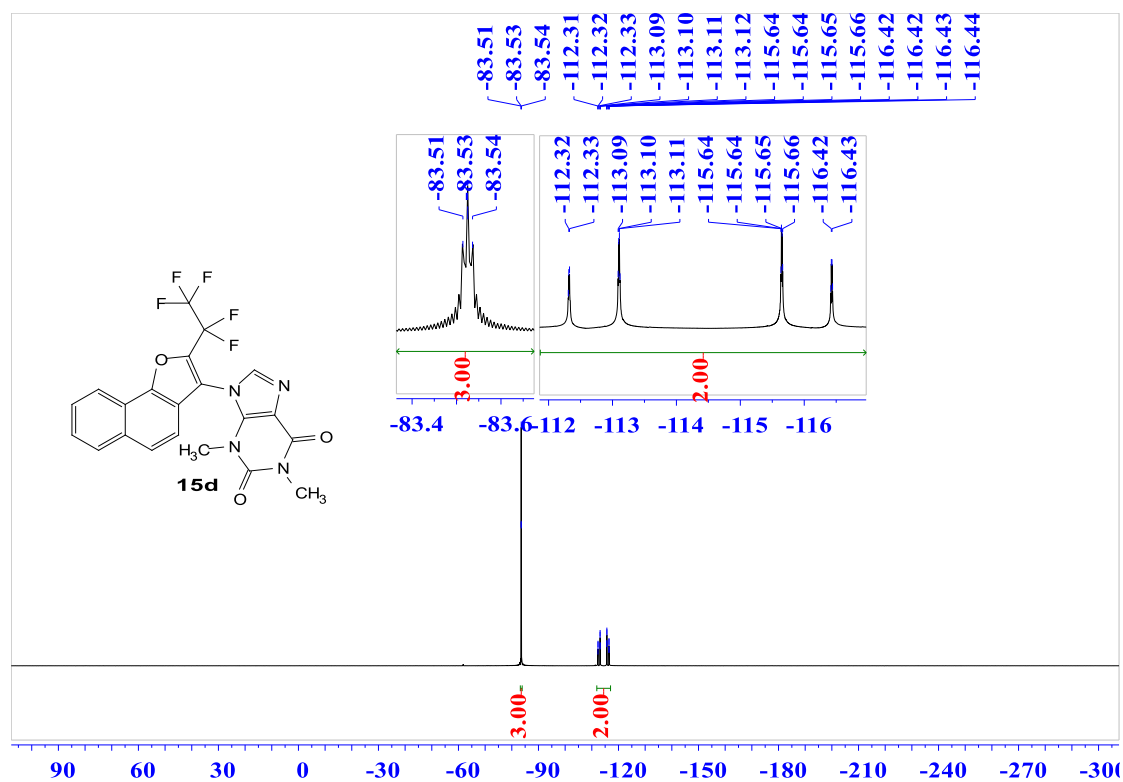


Figure S126. ¹³C NMR spectrum of **15d**, related to Scheme 2.

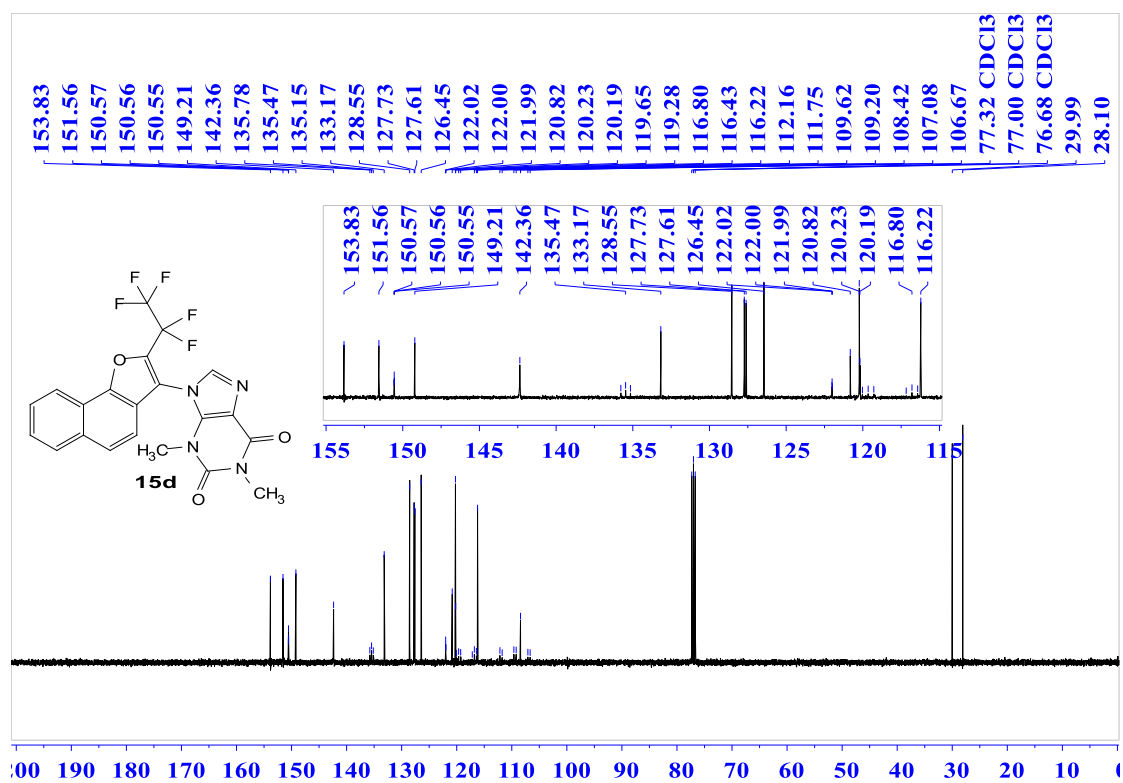


Figure S127. ¹H NMR spectrum of **15e**, related to Scheme 2.

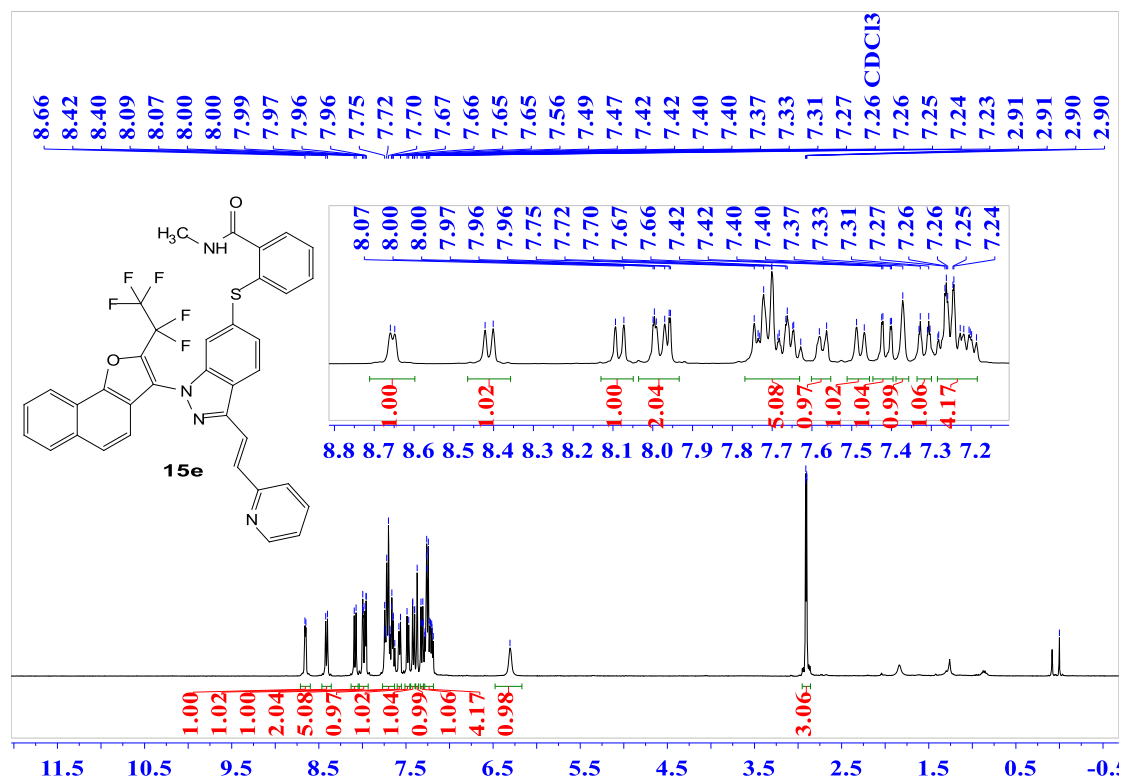


Figure S128. ¹⁹F NMR spectrum of **15e**, related to Scheme 2.

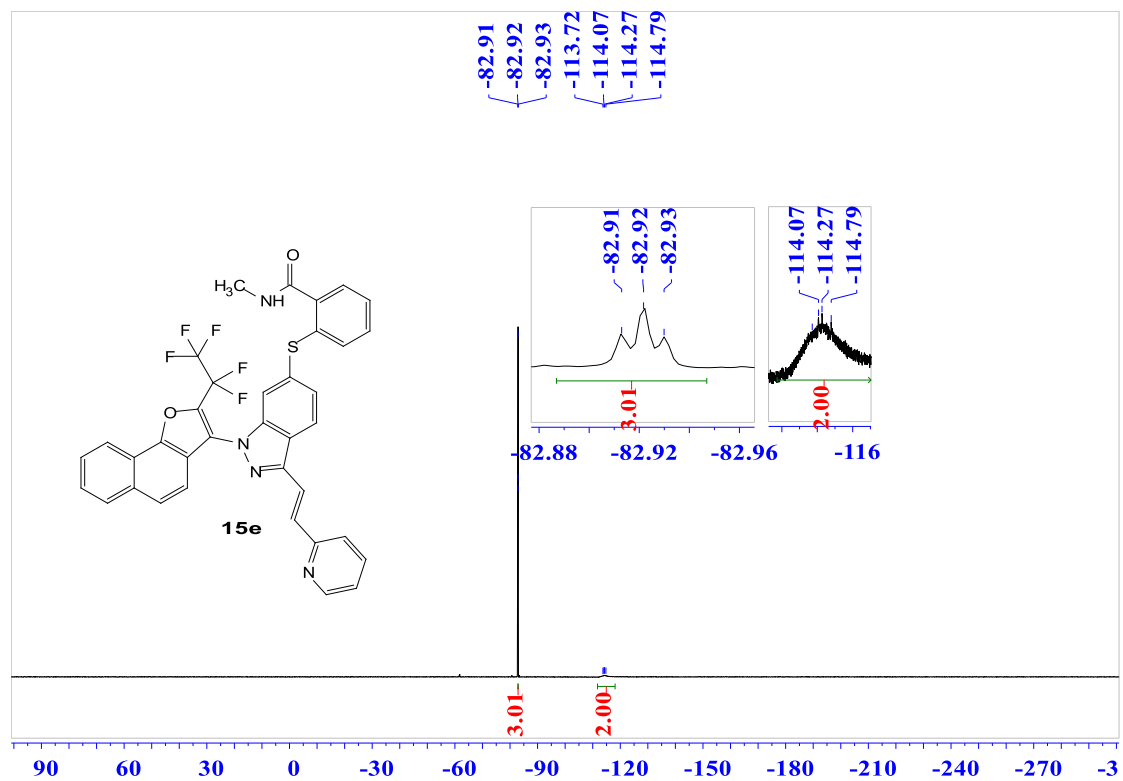


Figure S129. ¹³C NMR spectrum of **15e**, related to Scheme 2.

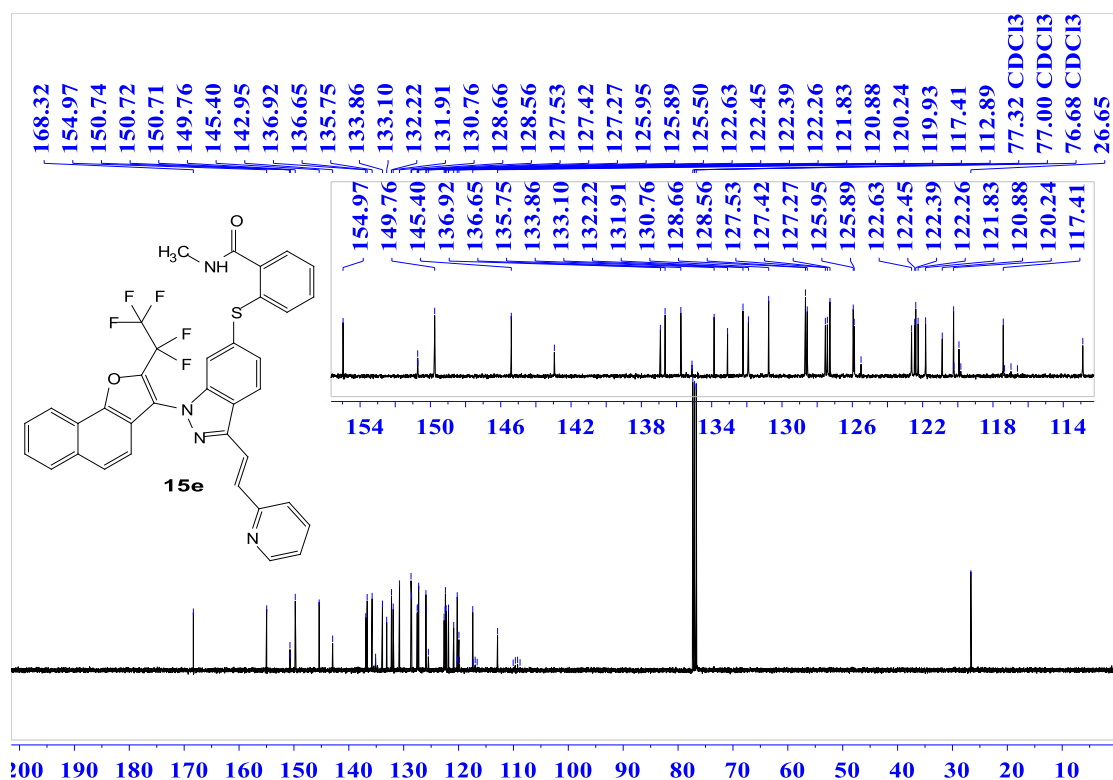


Figure S130. ¹H NMR spectrum of **15f-I**, **15f-II**, or **15f-III**, related to Scheme 2.

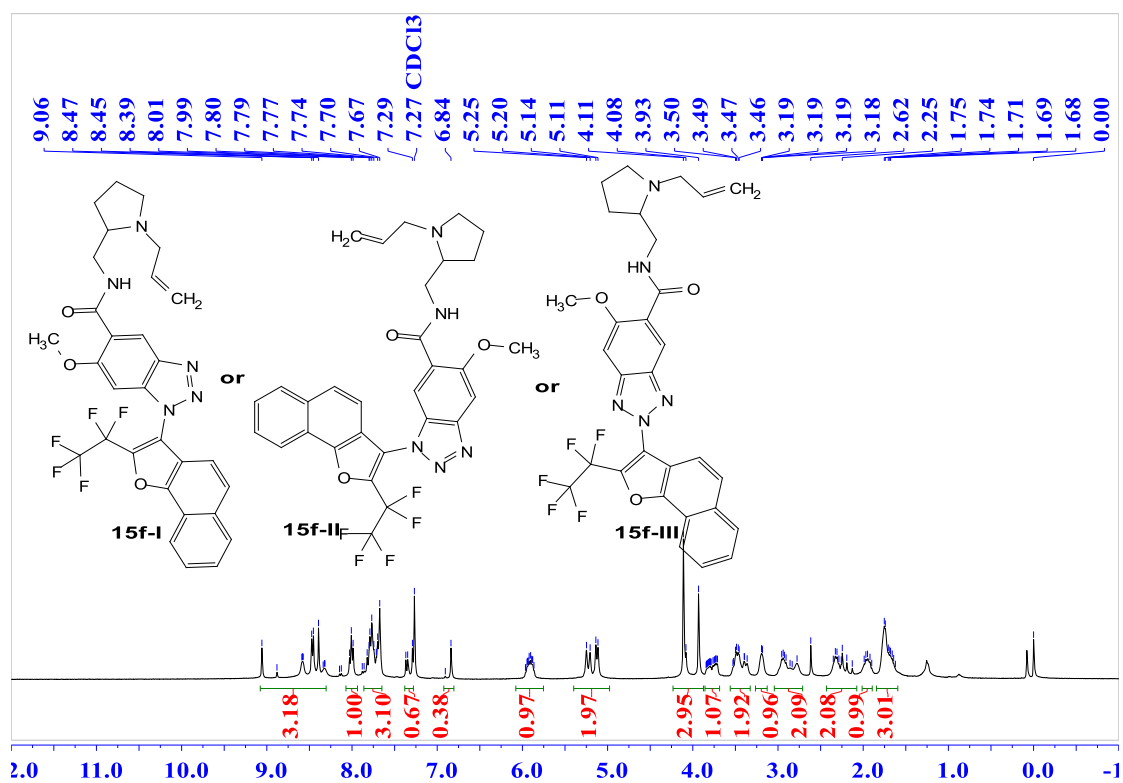


Figure S131. ^{19}F NMR spectrum of **15f-I**, **15f-II**, or **15f-III**, related to **Scheme 2**.

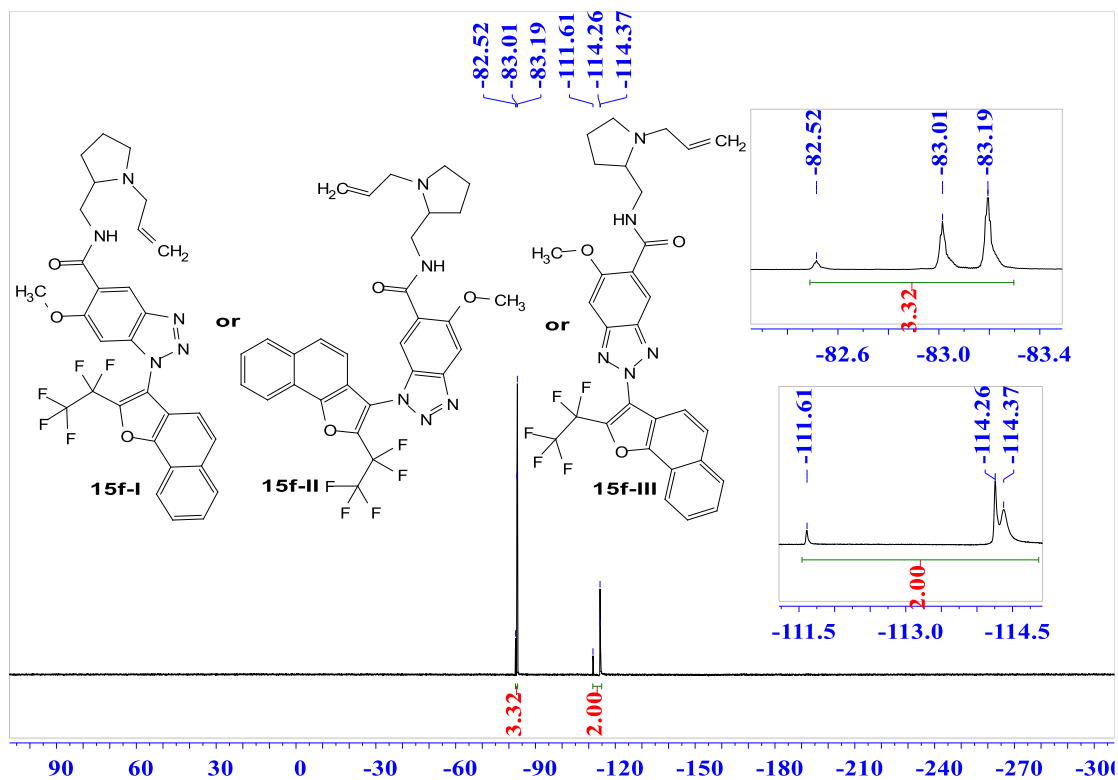


Figure S132. ^{13}C NMR spectrum of **15f-I**, **15f-II**, or **15f-III**, related to **Scheme 2**.

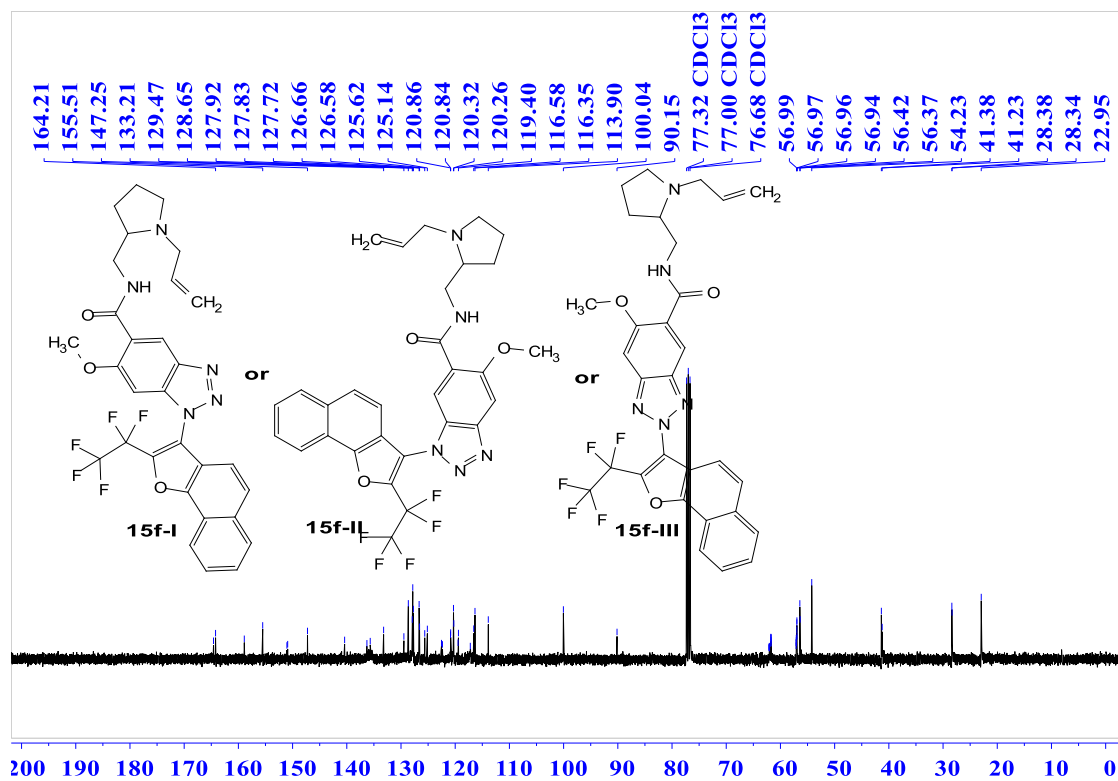


Figure S133. ¹H NMR spectrum of **15g**, related to Scheme 2.

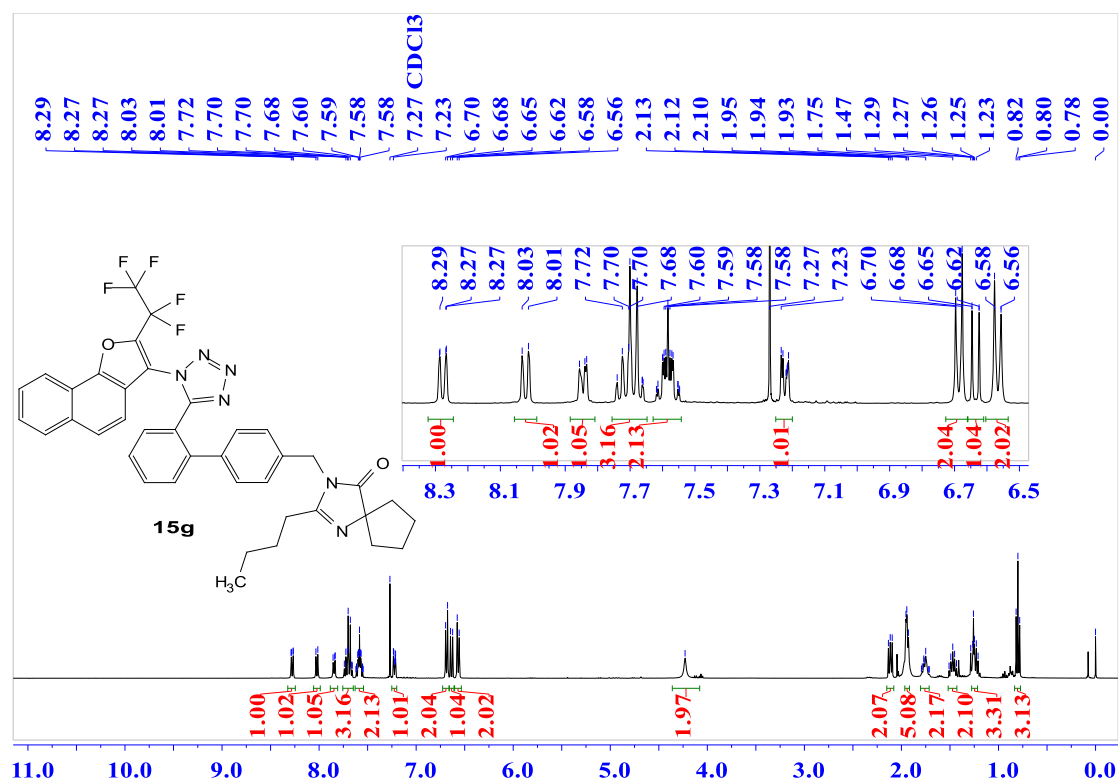


Figure S134. ¹⁹F NMR spectrum of **15g**, related to Scheme 2.

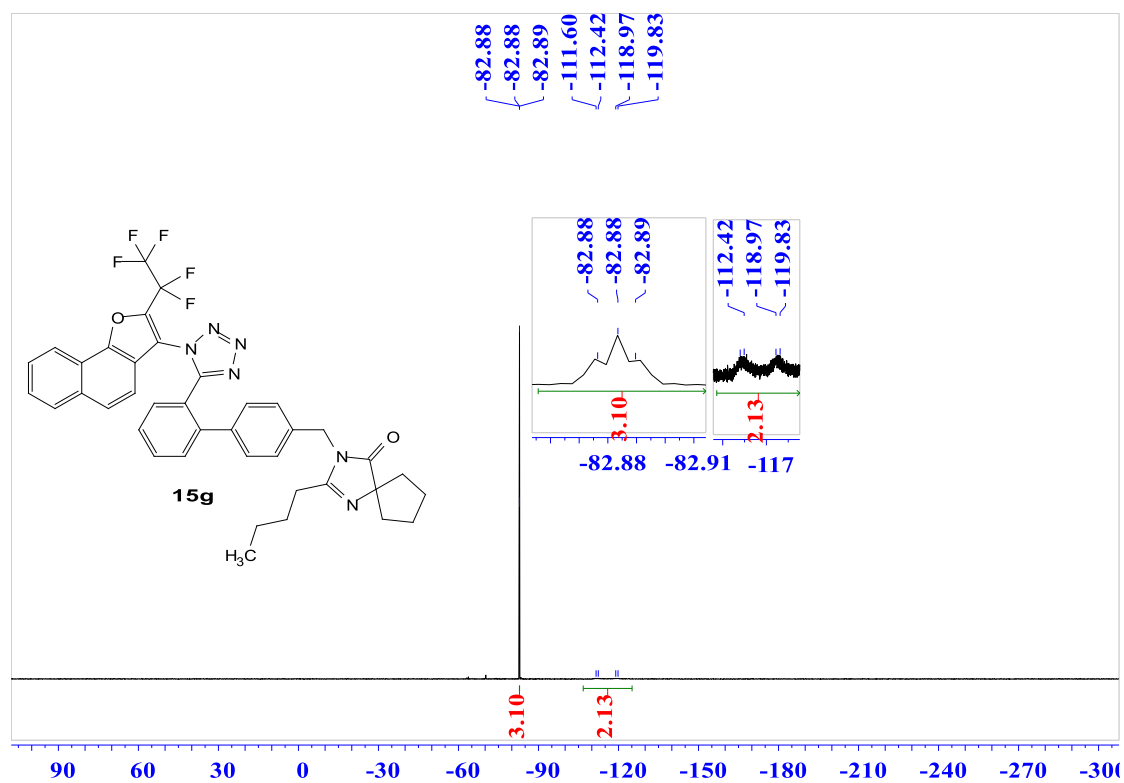


Figure S135. ^{13}C NMR spectrum of **15g**, related to Scheme 2.

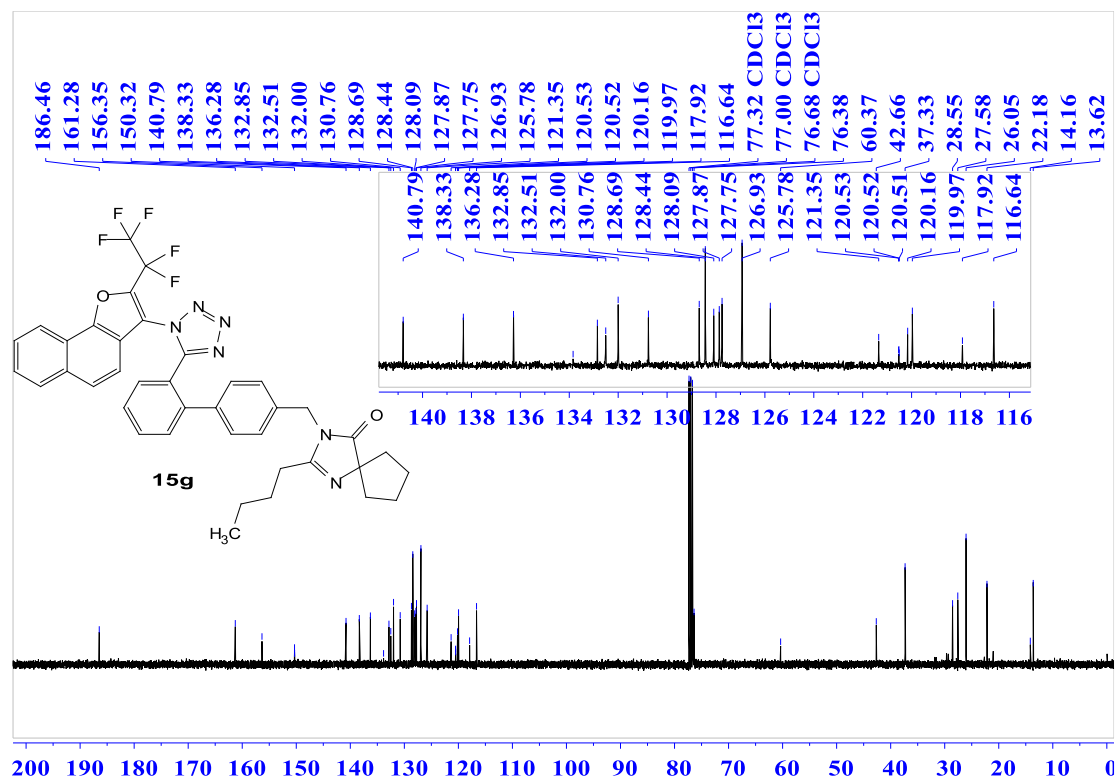


Figure S136. ^1H NMR spectrum of **16a**, related to Scheme 3.

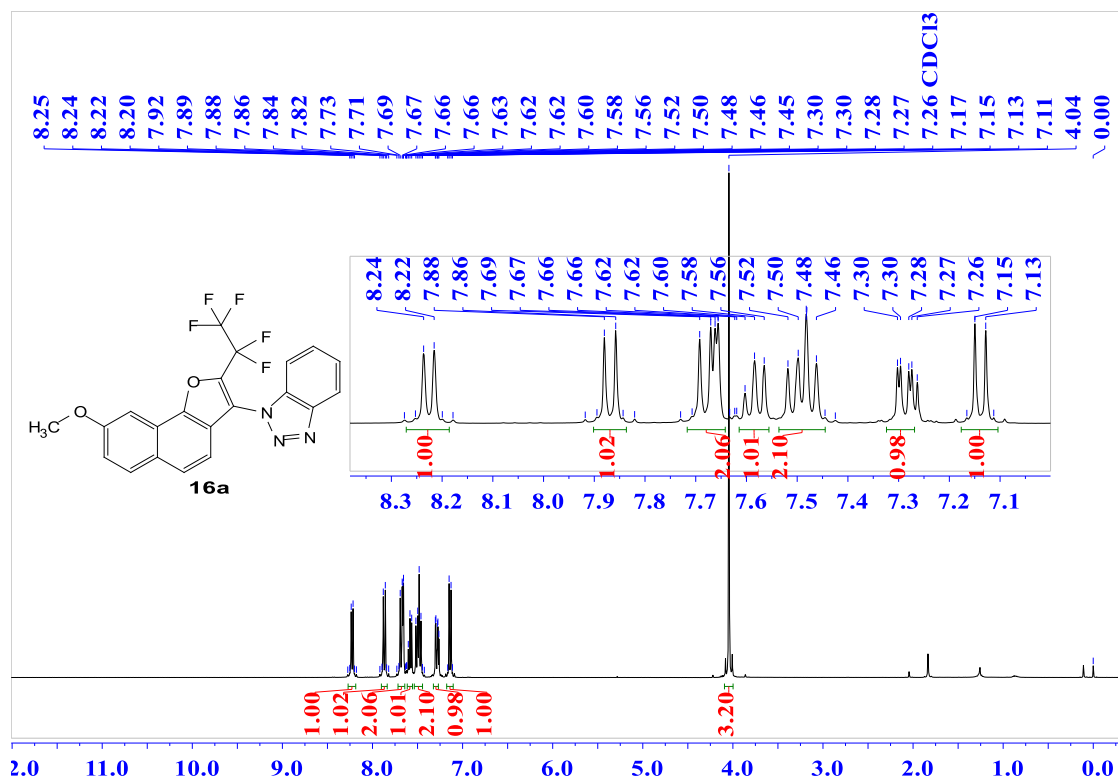


Figure S137. ^{19}F NMR spectrum of **16a**, related to Scheme 3.

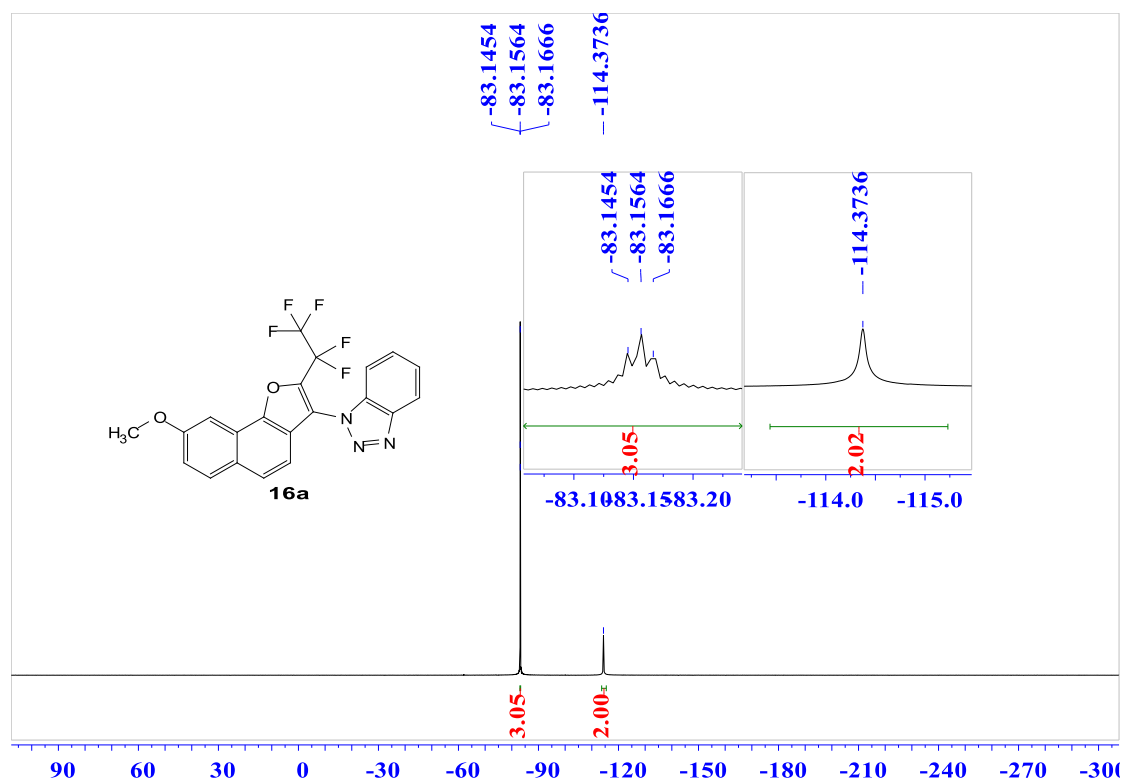


Figure S138. ^{13}C NMR spectrum of **16a**, related to Scheme 3.

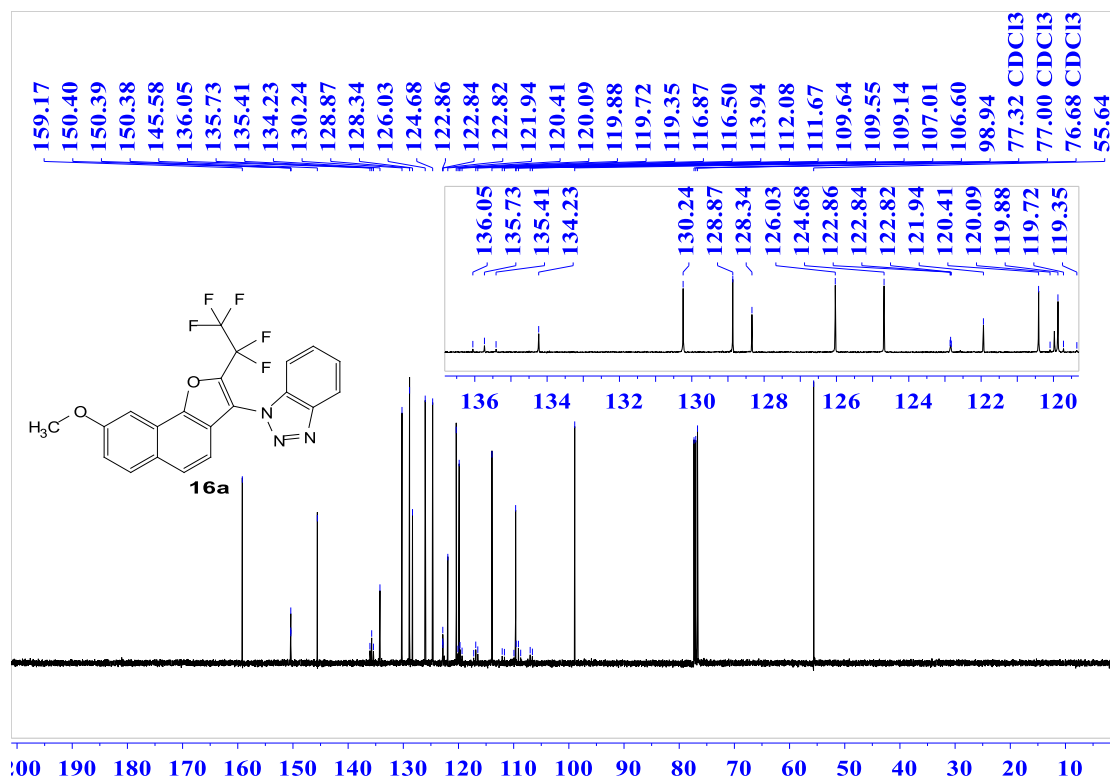


Figure S139. ¹H NMR spectrum of **16b**, related to Scheme 3.

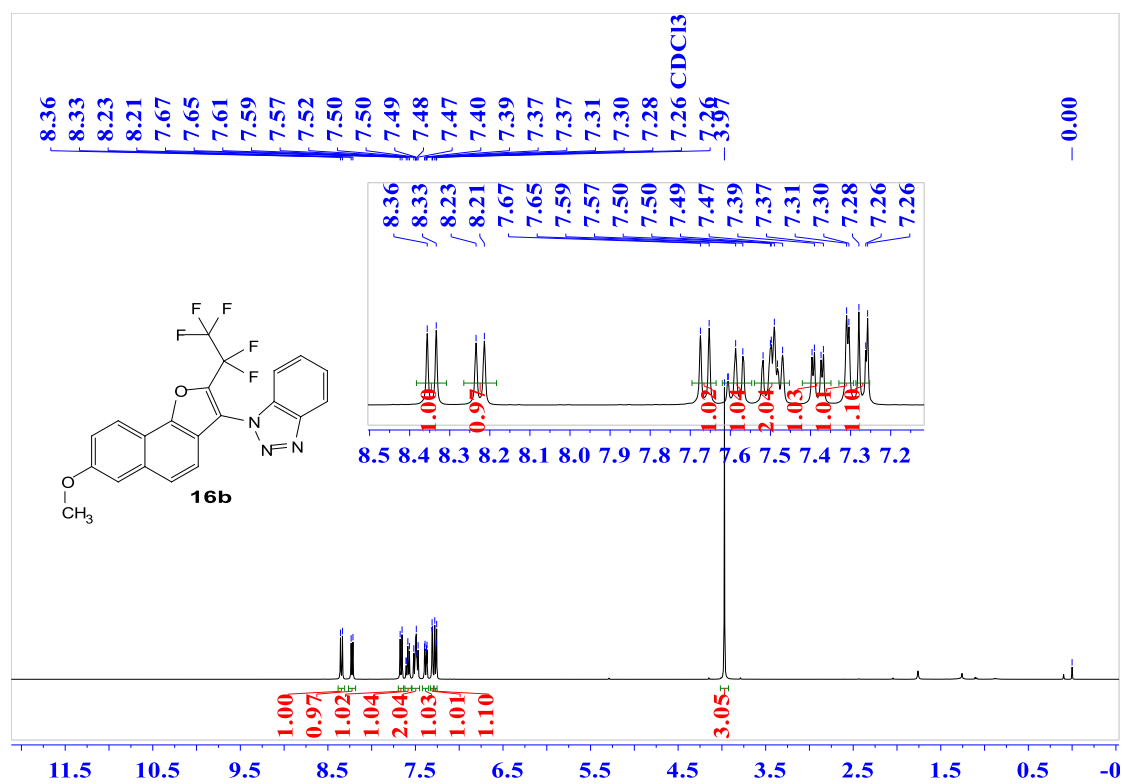


Figure S140. ¹⁹F NMR spectrum of **16b**, related to Scheme 3.

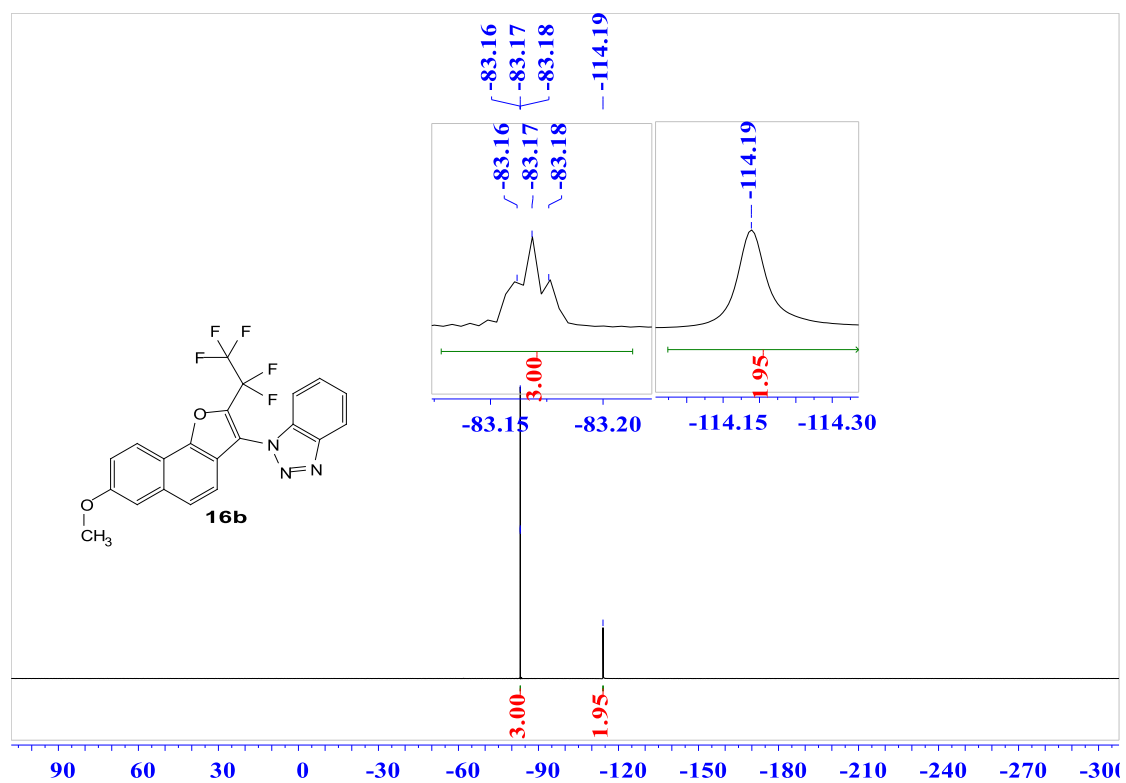


Figure S141. ¹³C NMR spectrum of **16b**, related to Scheme 3.

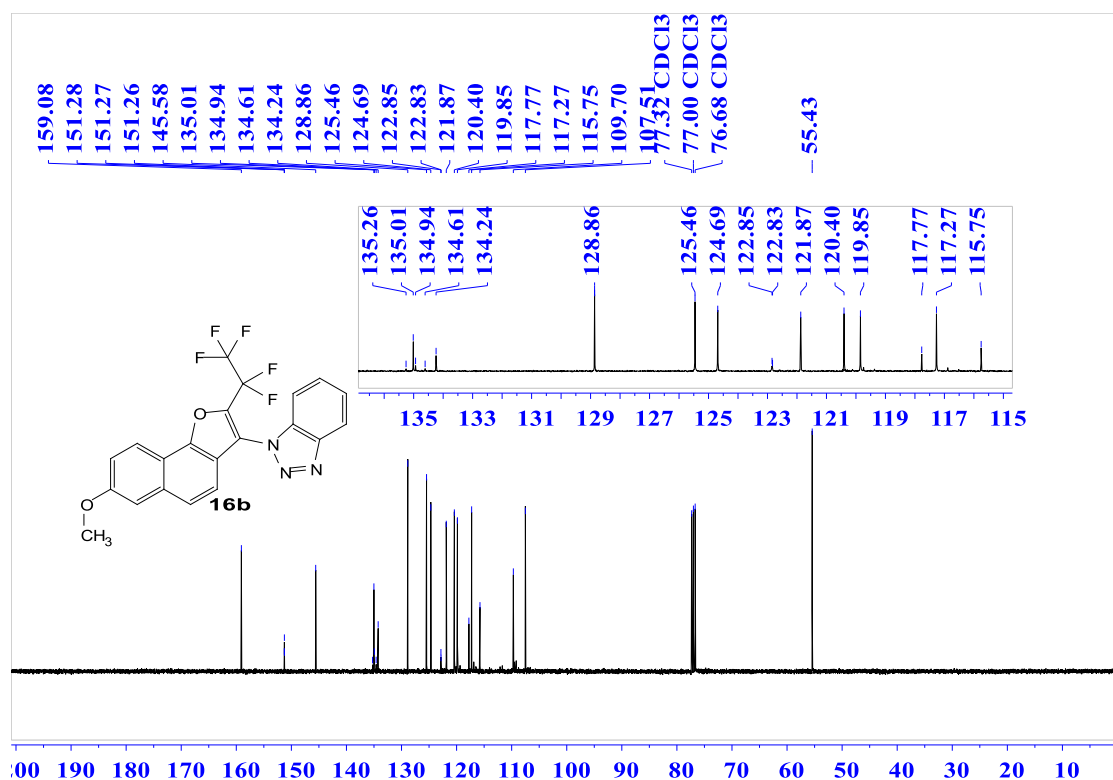


Figure S142. ¹H NMR spectrum of **16c**, related to Scheme 3.

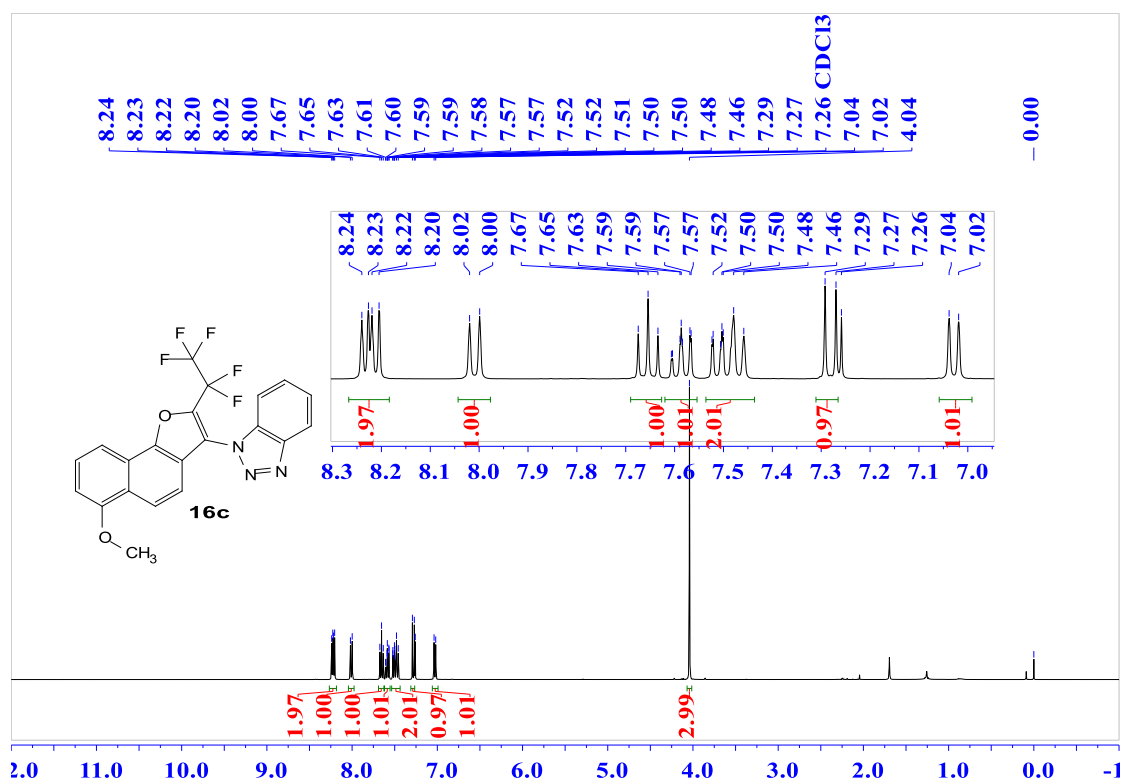


Figure S143. ^{19}F NMR spectrum of **16c**, related to Scheme 3.

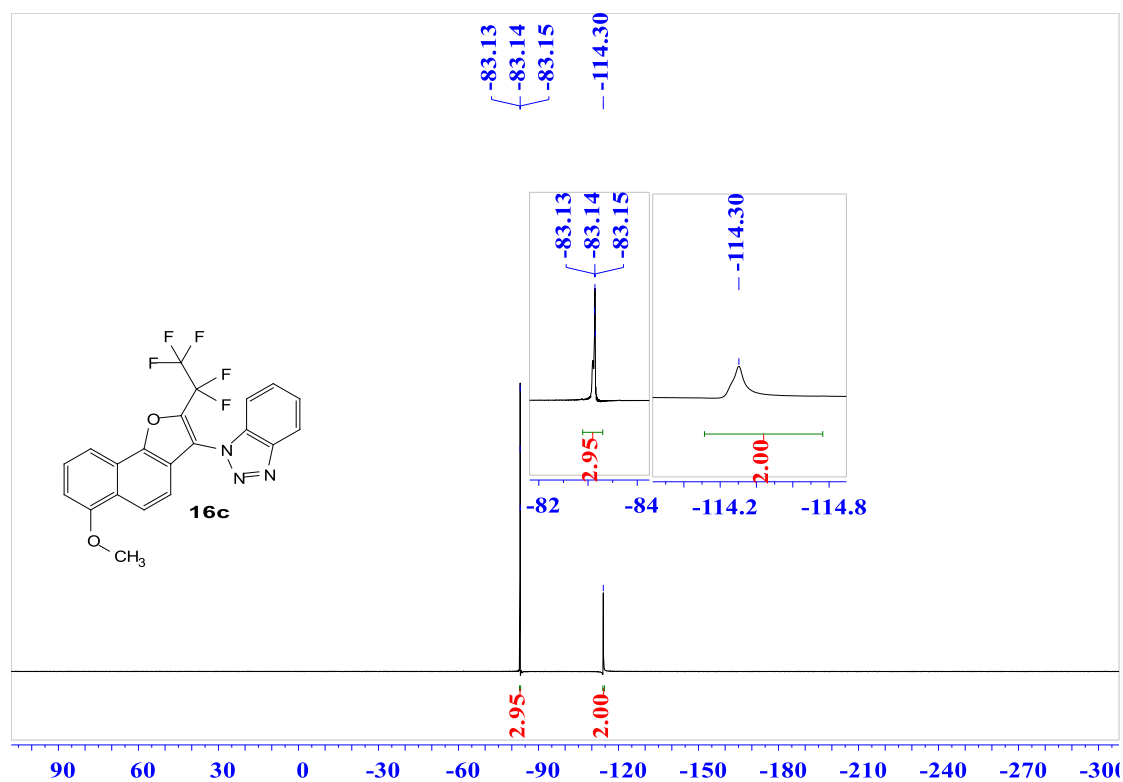


Figure S144. ^{13}C NMR spectrum of **16c**, related to Scheme 3.

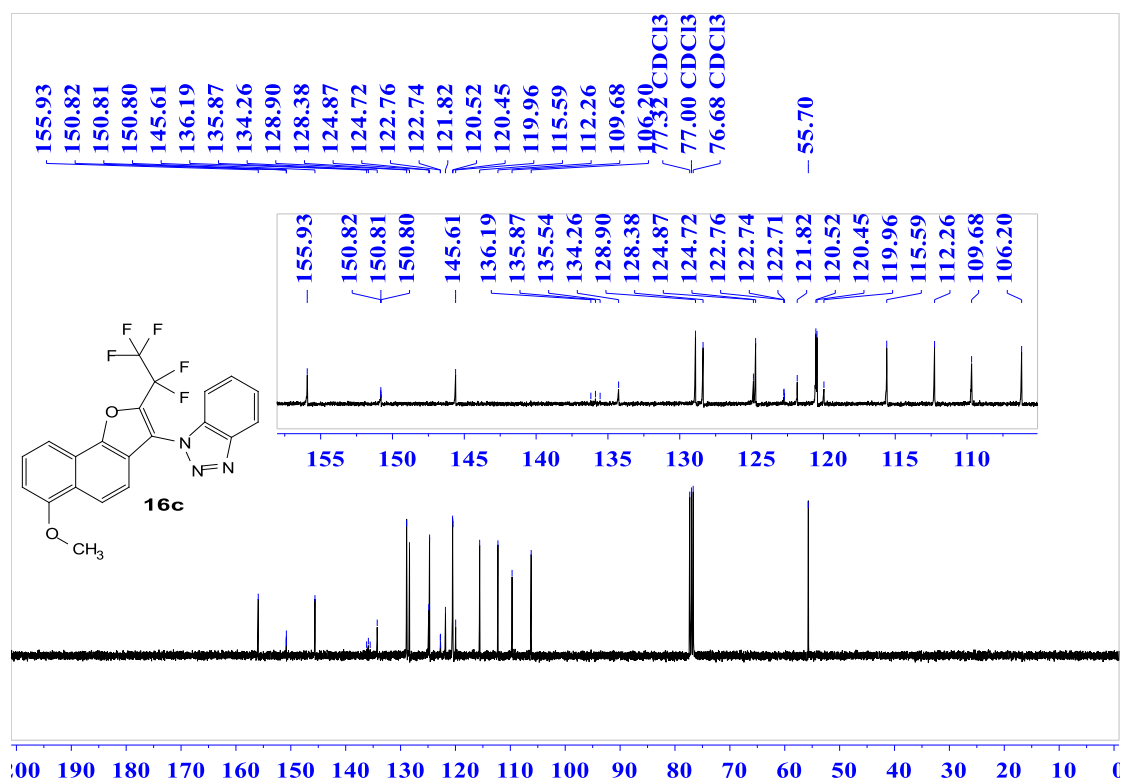


Figure S145. ¹H NMR spectrum of **16d**, related to Scheme 3.

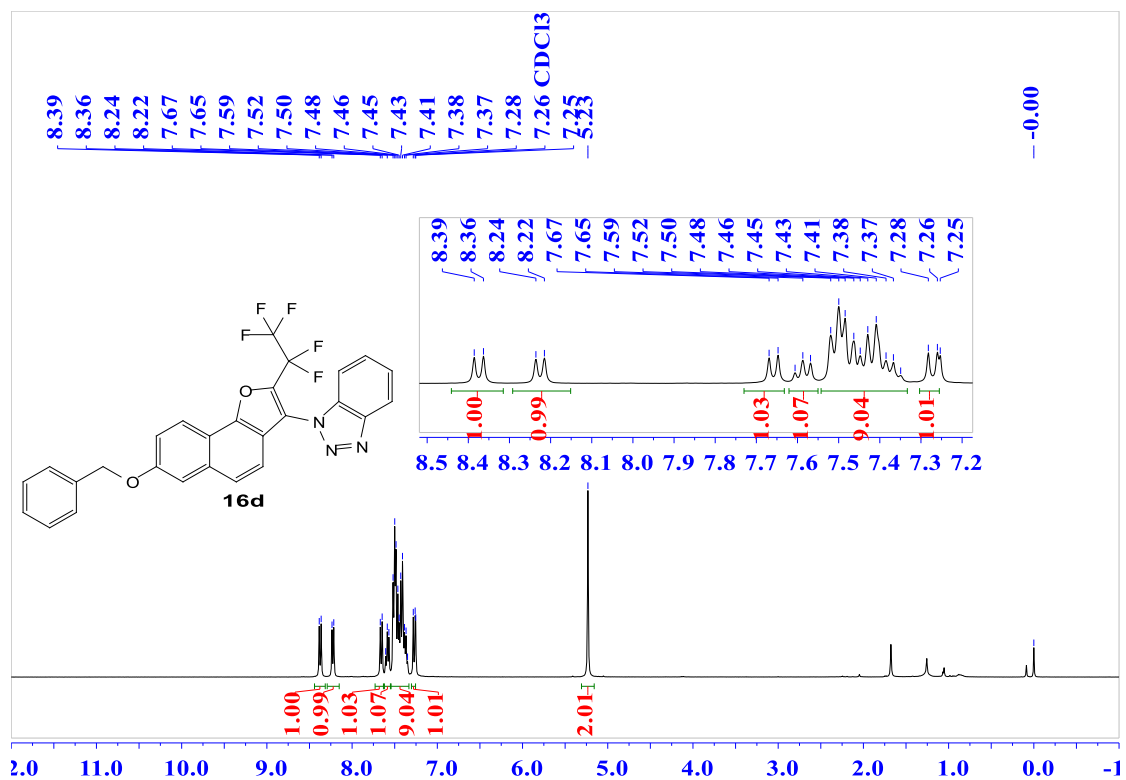


Figure S146. ¹⁹F NMR spectrum of **16d**, related to Scheme 3.

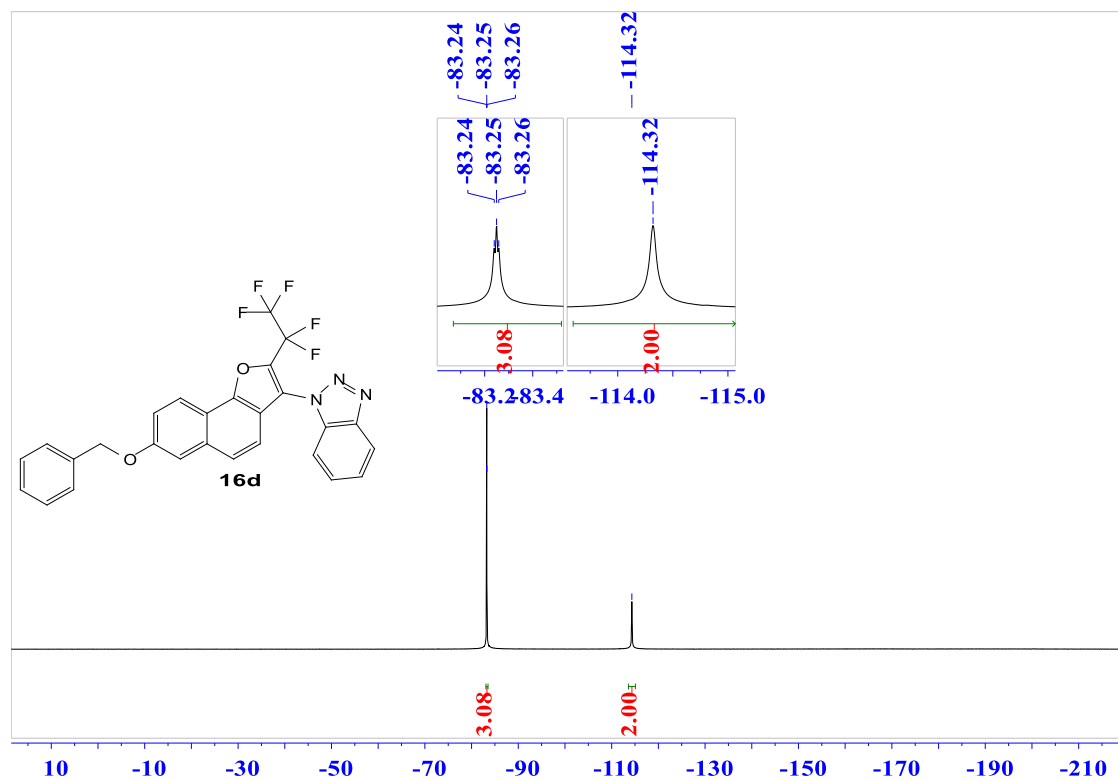


Figure S147. ¹³C NMR spectrum of **16d**, related to Scheme 3.

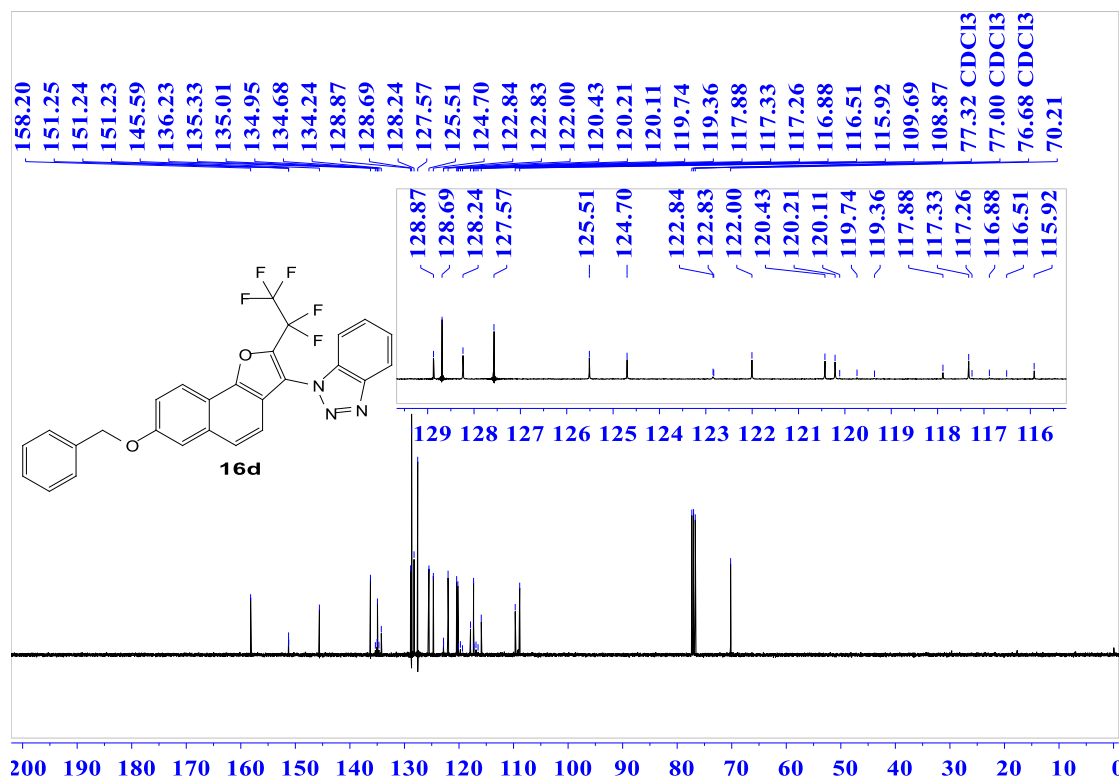


Figure S148. ¹H NMR spectrum of **16e**, related to Scheme 3.

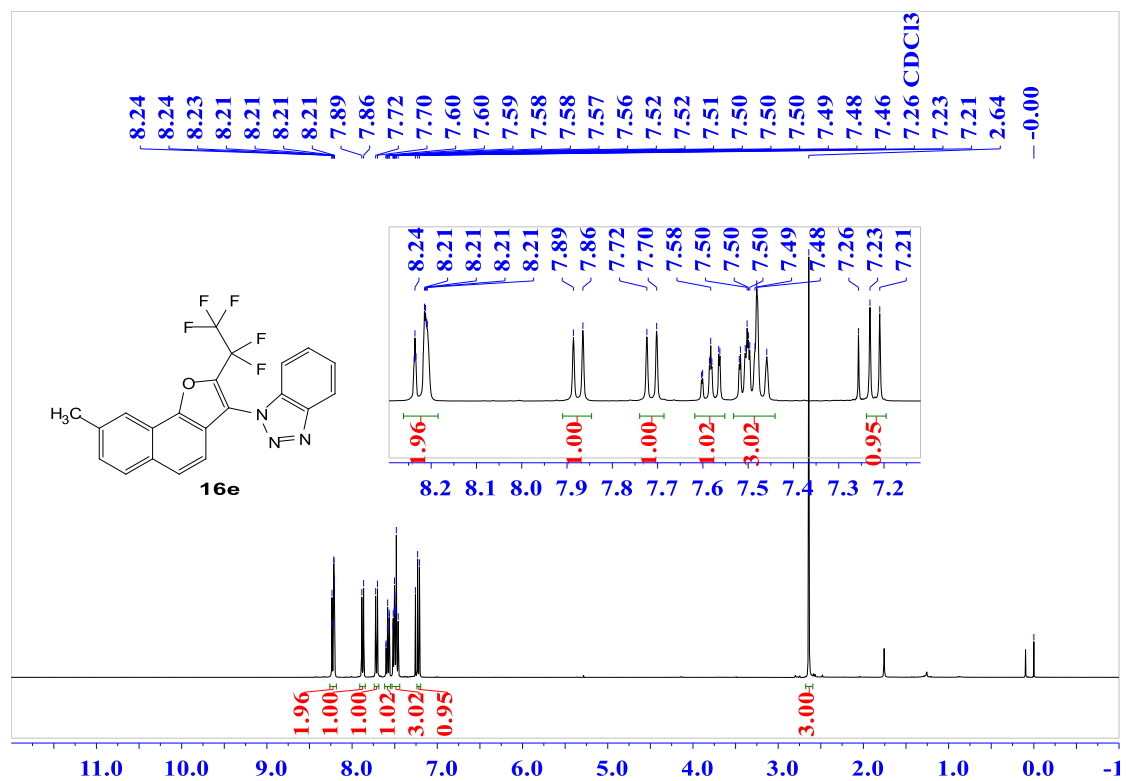


Figure S149. ^{19}F NMR spectrum of **16e**, related to Scheme 3.

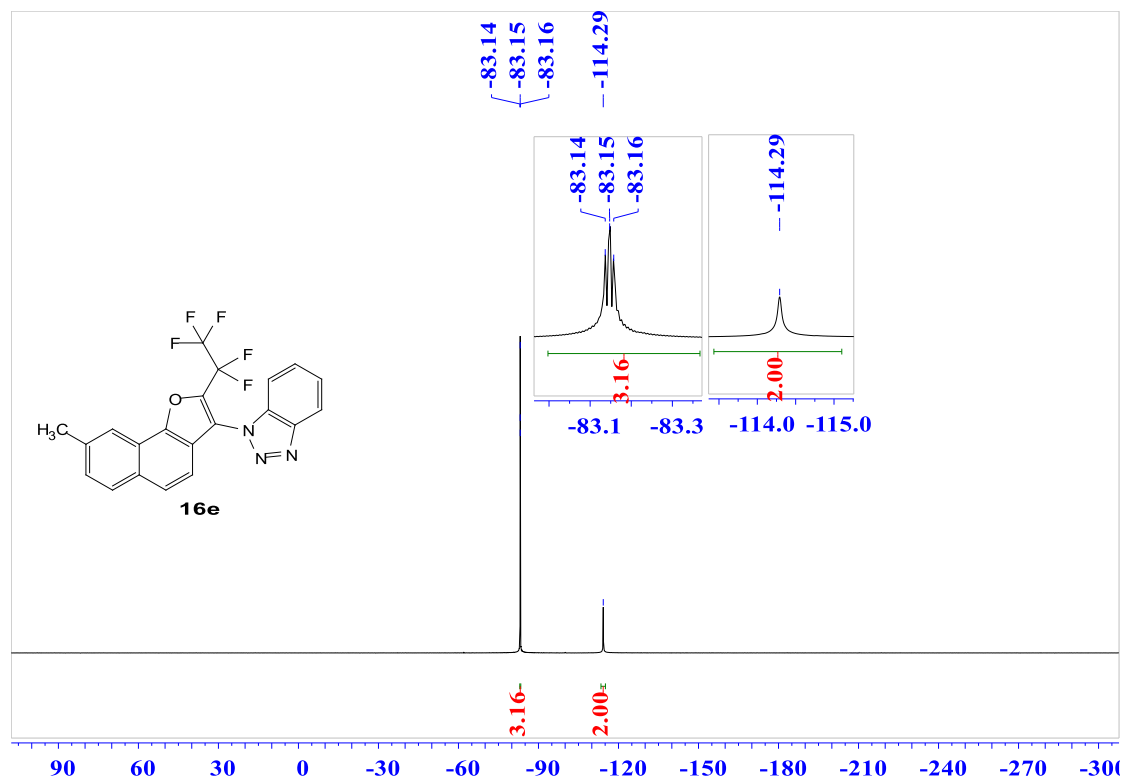


Figure S150. ^{13}C NMR spectrum of **16e**, related to Scheme 3.

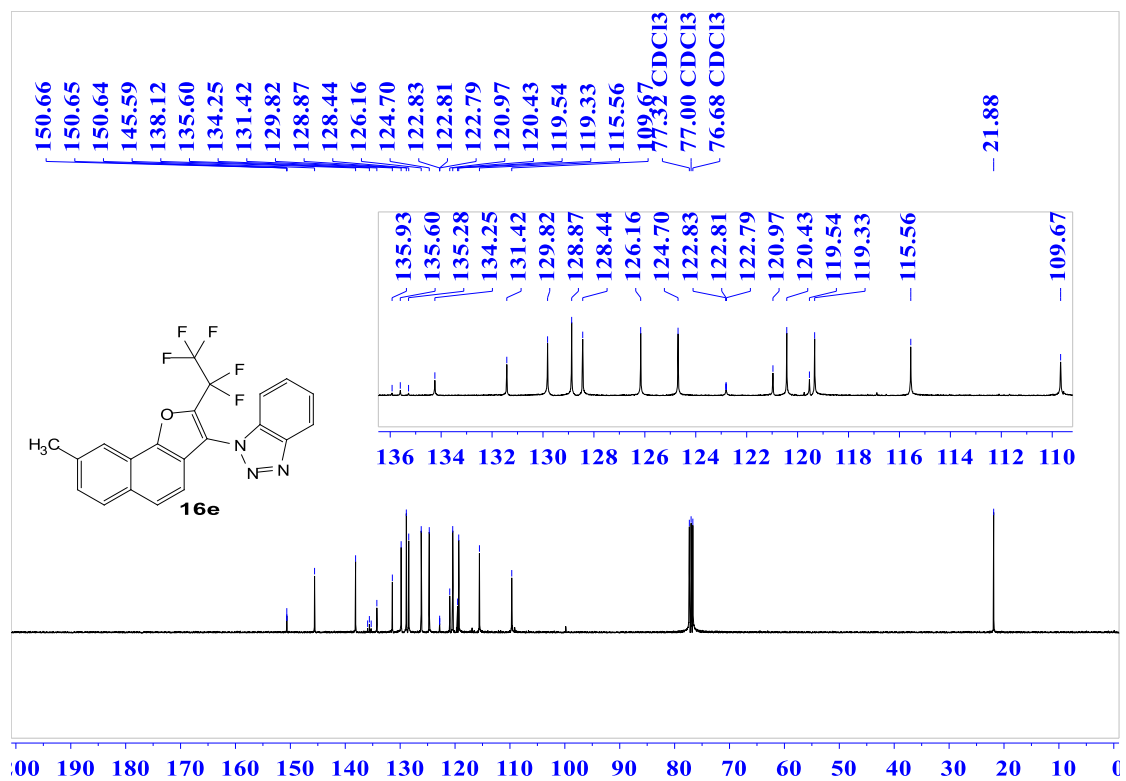


Figure S151. ¹H NMR spectrum of **16f**, related to Scheme 3.

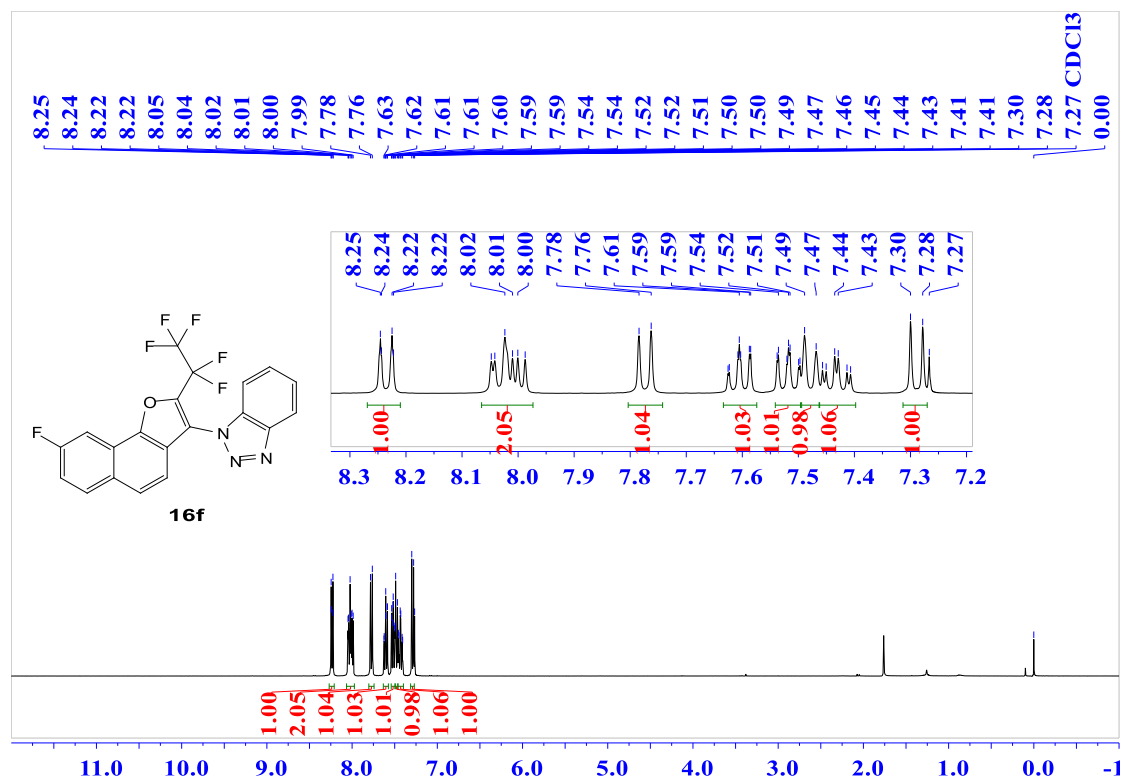


Figure S152. ¹⁹F NMR spectrum of **16f**, related to Scheme 3.

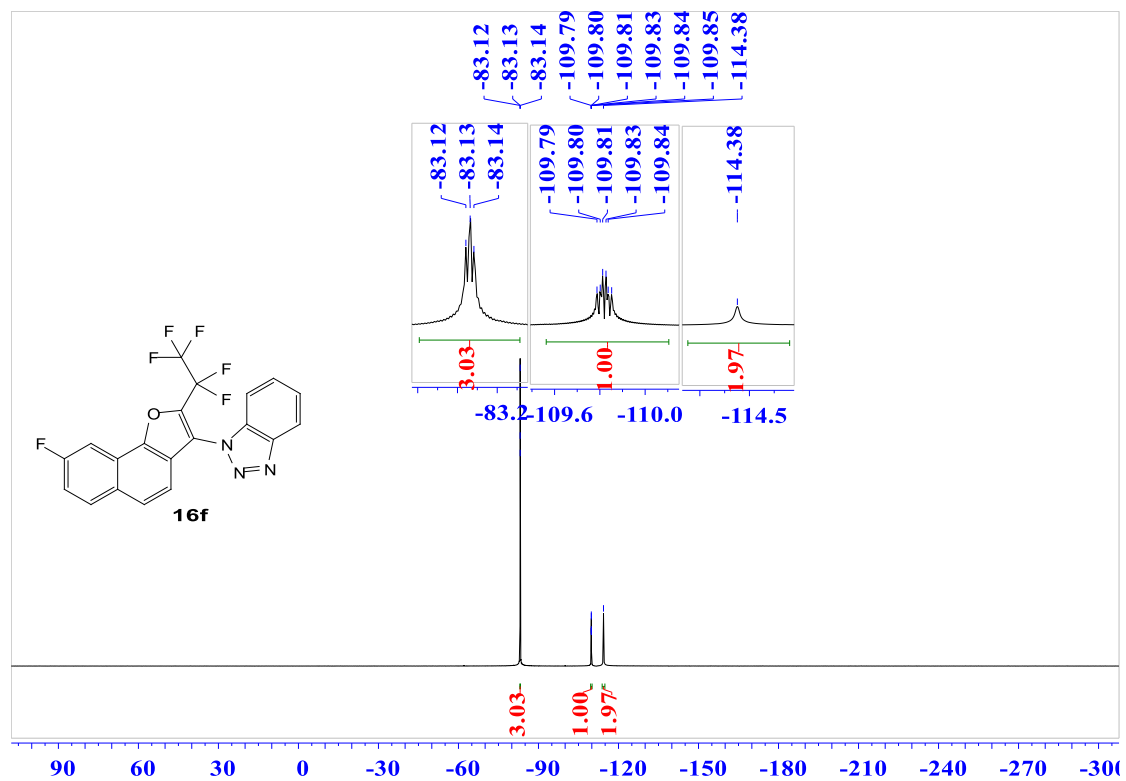


Figure S153. ¹³C NMR spectrum of **16f**, related to Scheme 3.

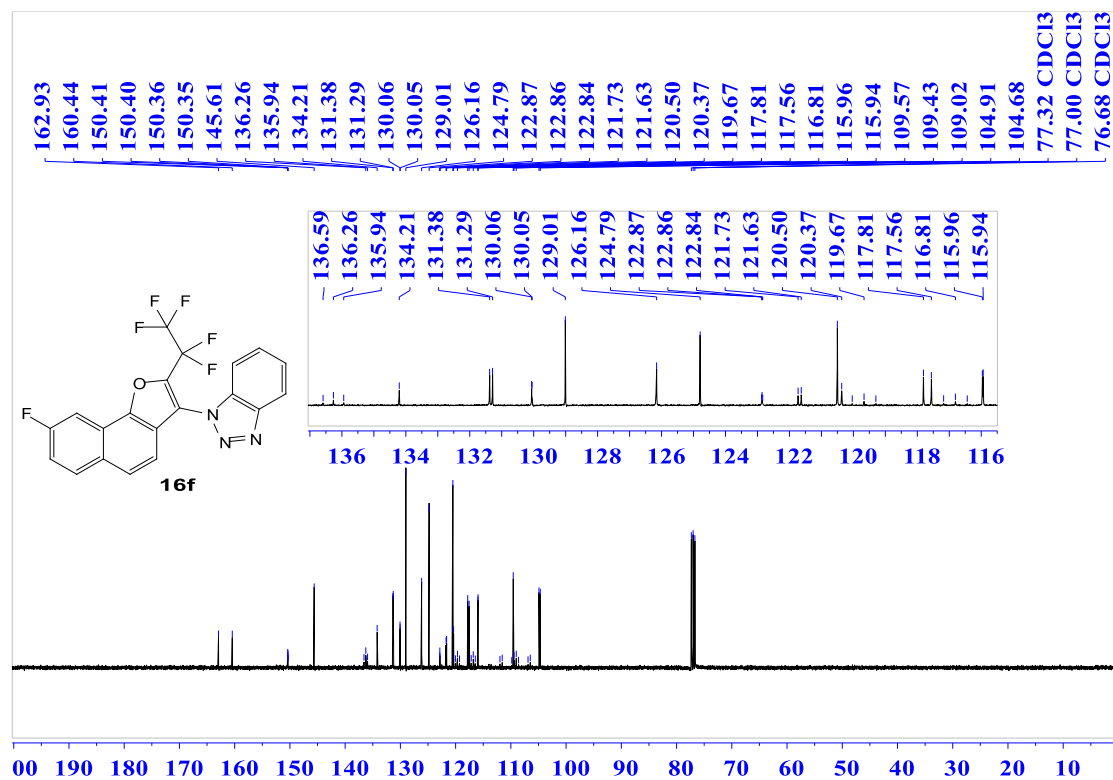


Figure S154. ¹H NMR spectrum of **16g**, related to Scheme 3.

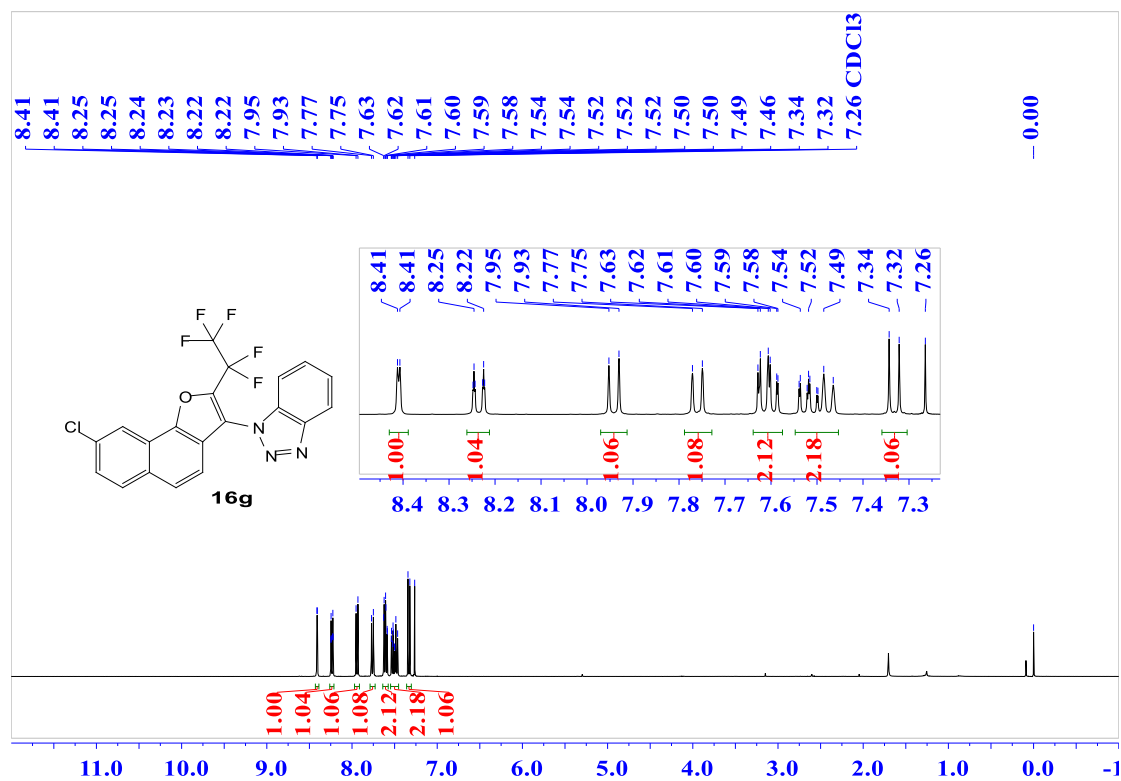


Figure S155. ¹⁹F NMR spectrum of **16g**, related to Scheme 3.

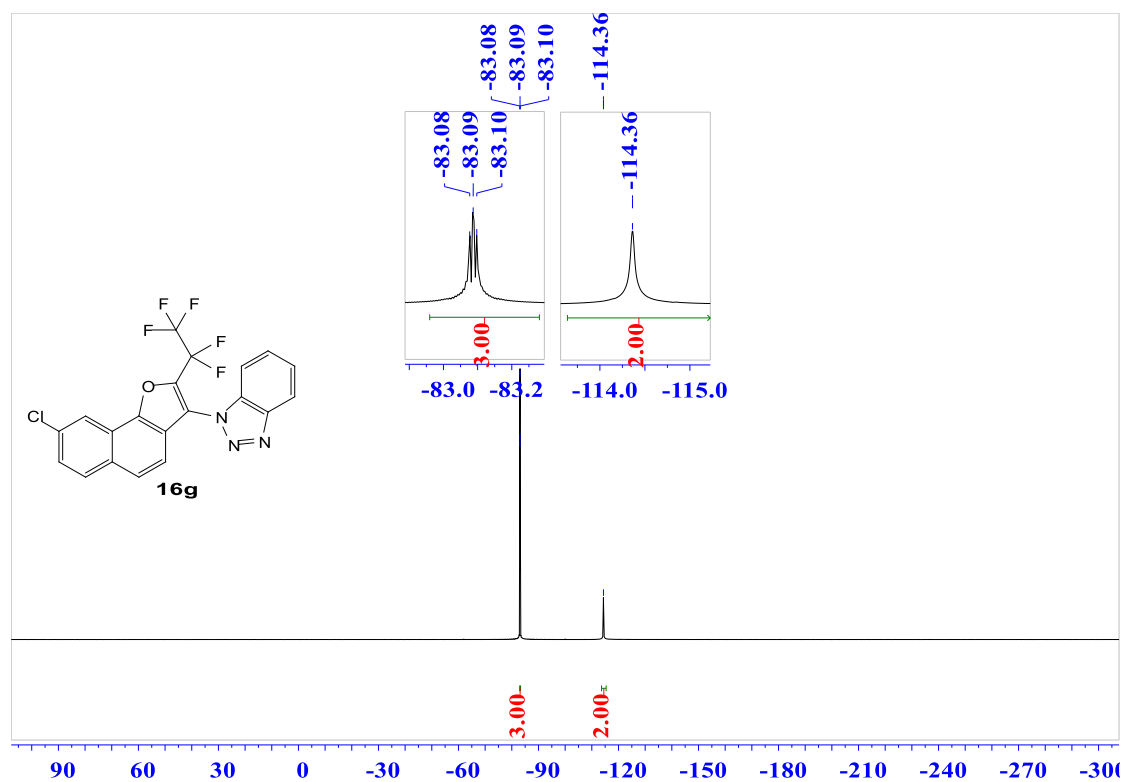


Figure S156. ¹³C NMR spectrum of **16g**, related to Scheme 3.

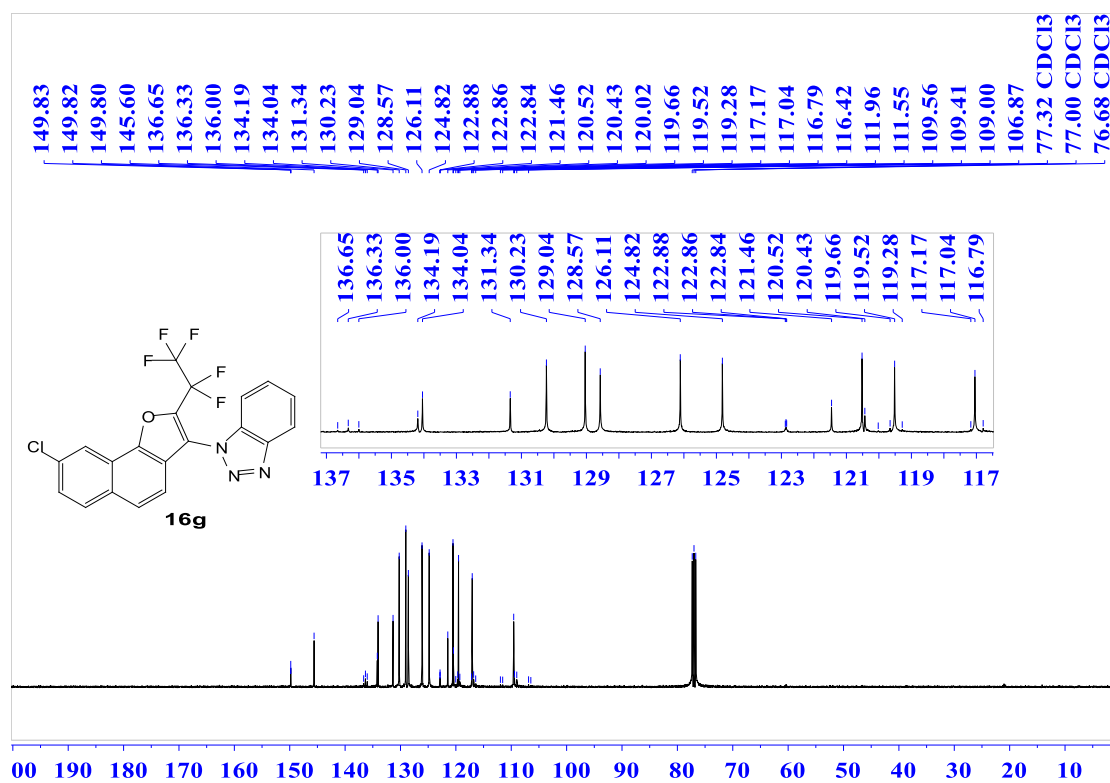


Figure S157. ¹H NMR spectrum of **16g**, related to Scheme 3.

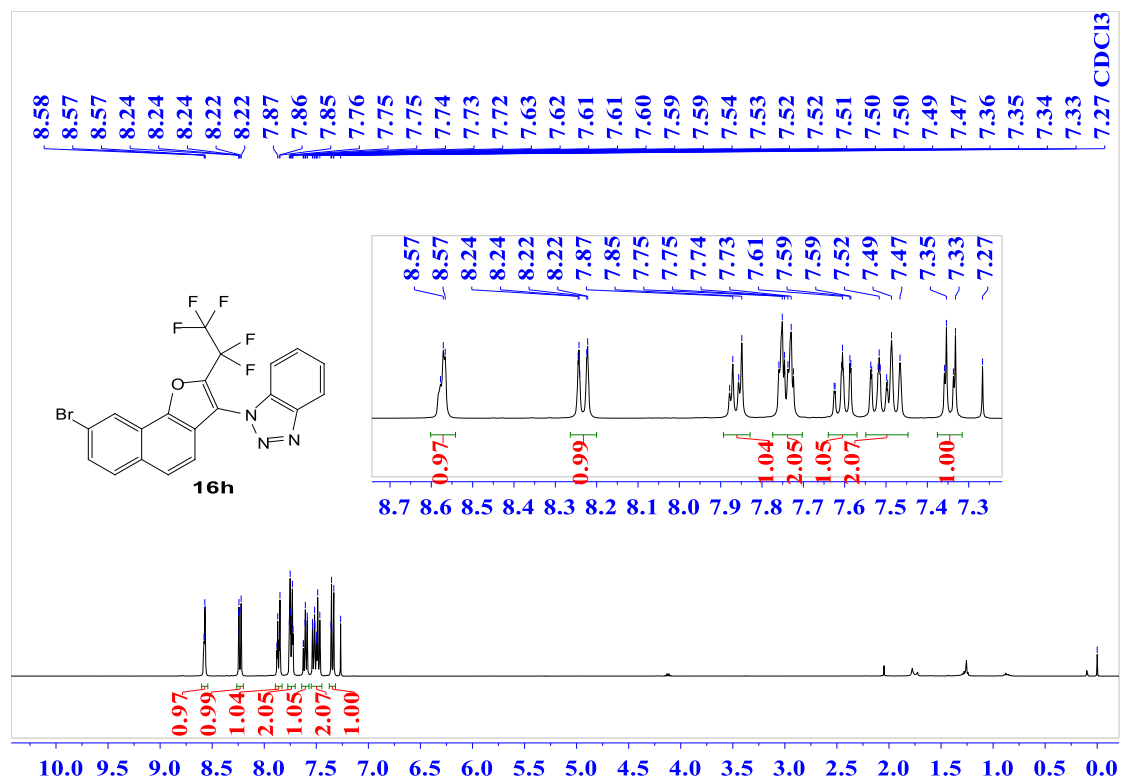


Figure S158. ¹⁹F NMR spectrum of **16h**, related to Scheme 3.

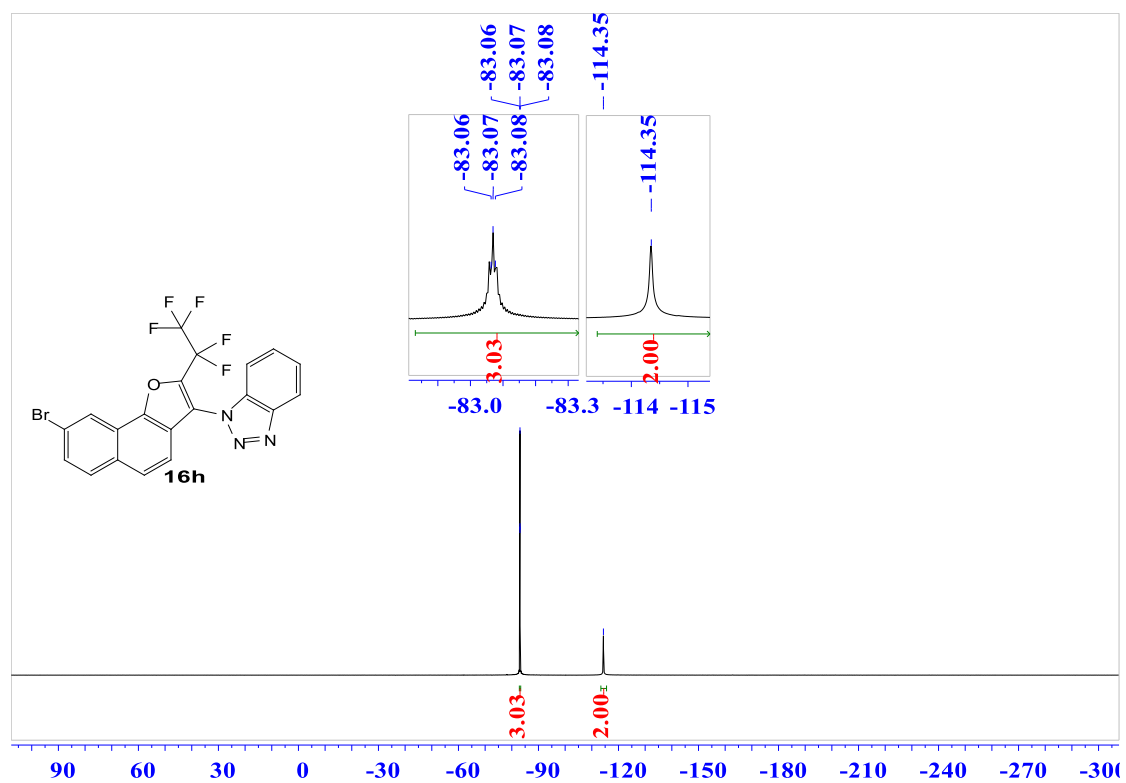


Figure S159. ¹³C NMR spectrum of **16h**, related to Scheme 3.

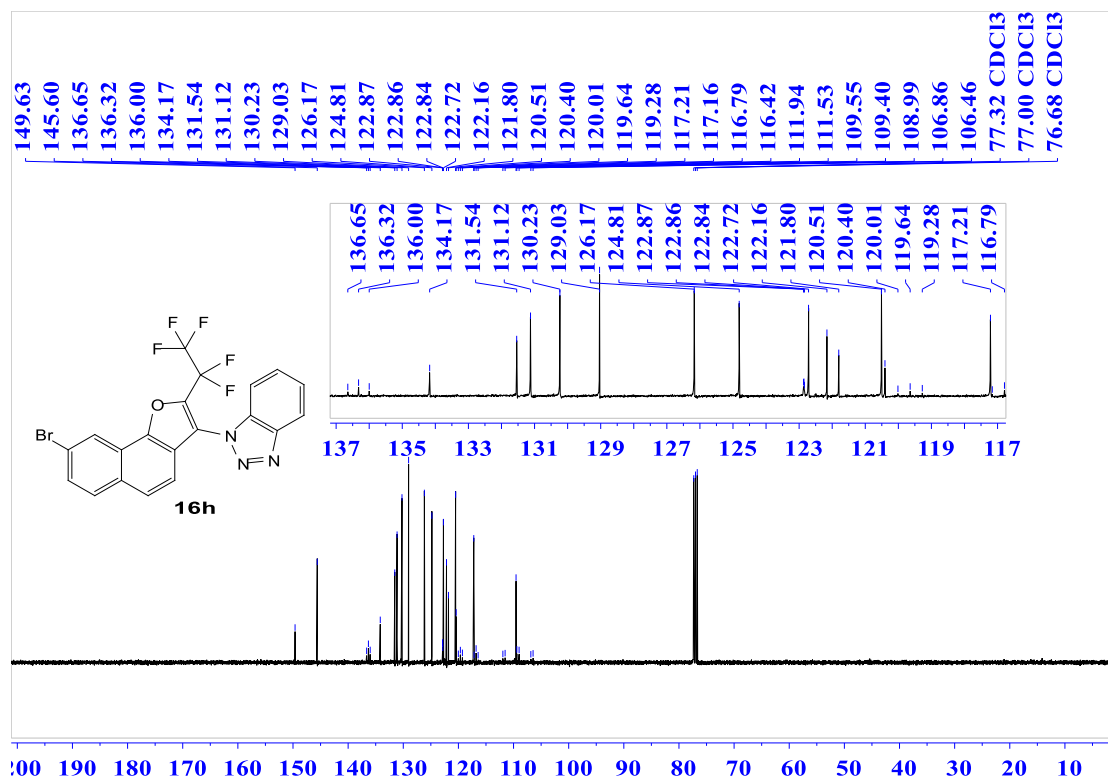


Figure S160. ¹H NMR spectrum of **16j**, related to Scheme 3.

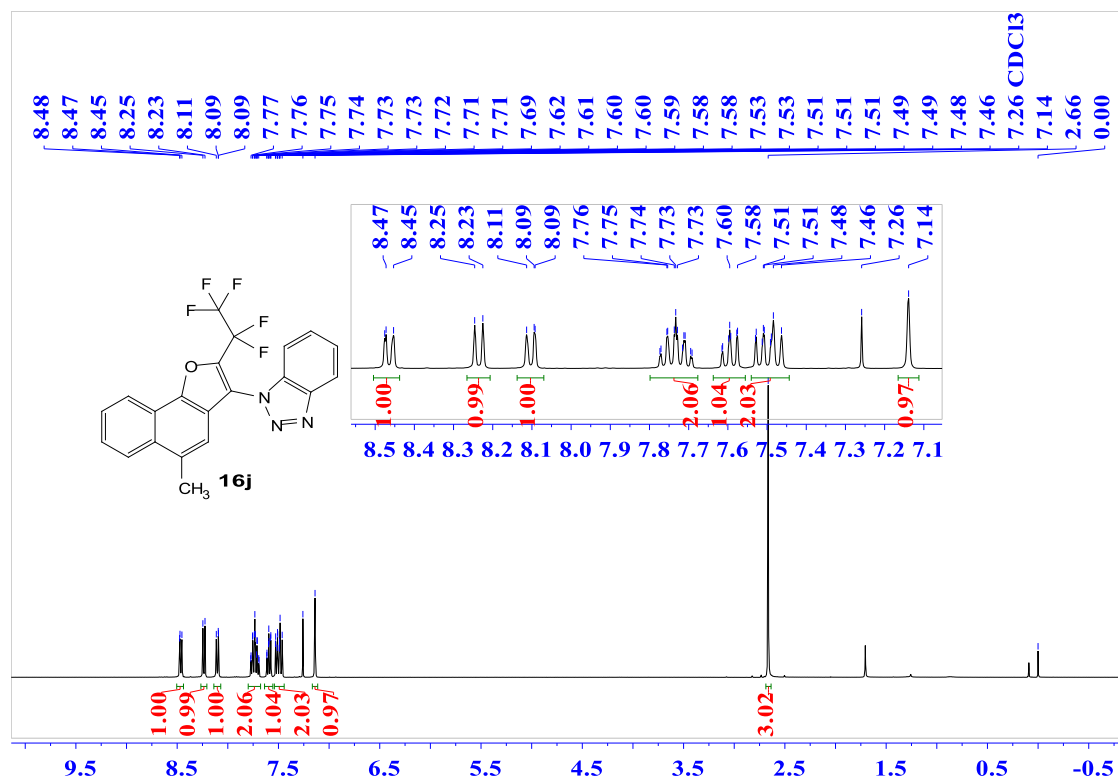


Figure S161. ^{19}F NMR spectrum of **16j**, related to Scheme 3.

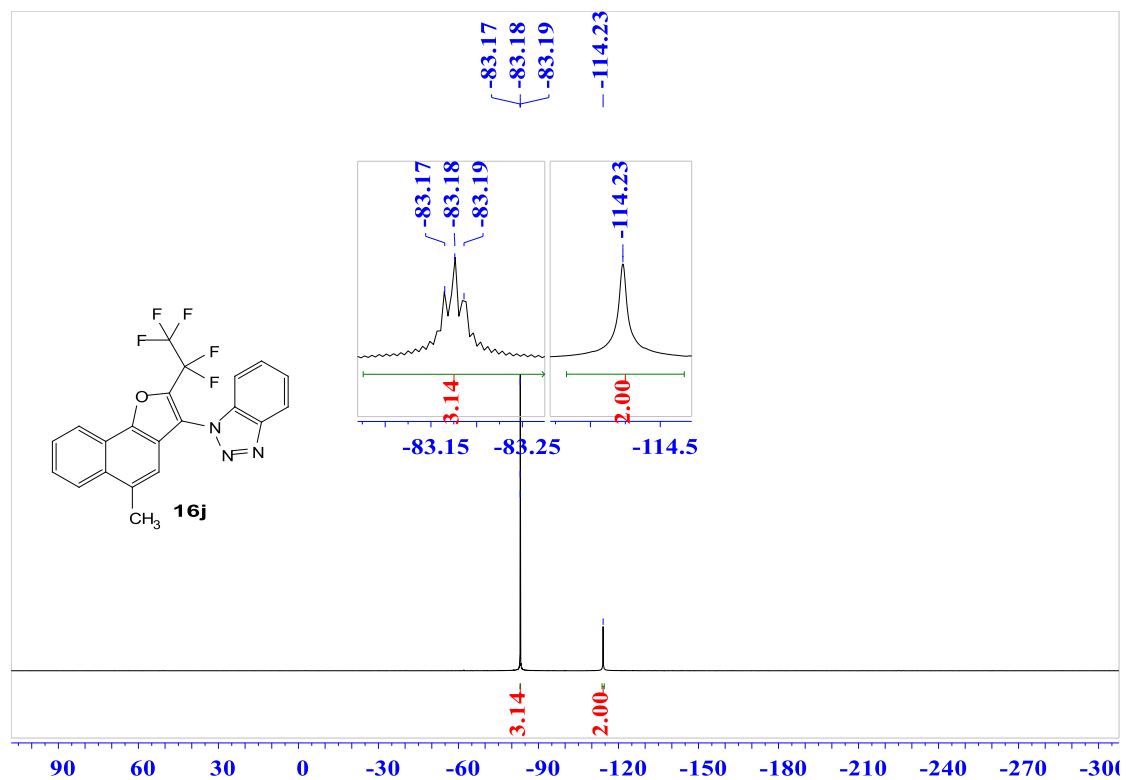


Figure S162. ^{13}C NMR spectrum of **16j**, related to Scheme 3.

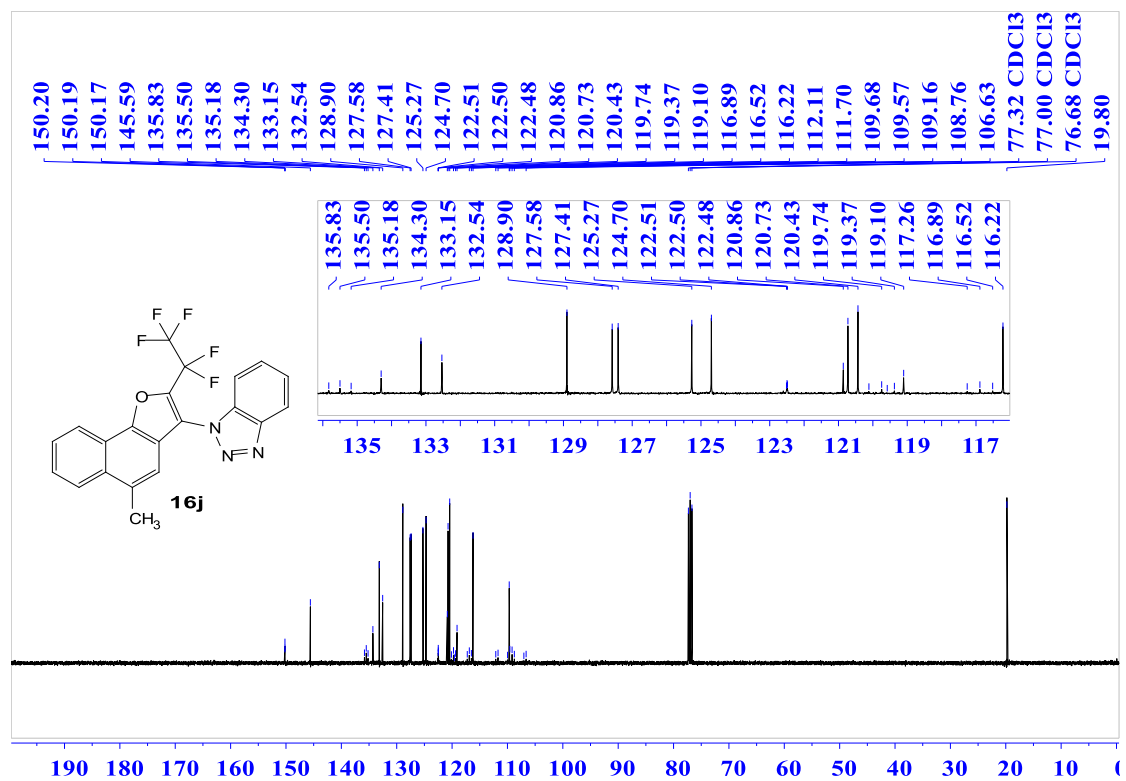


Figure S163. ¹H NMR spectrum of **16k**, related to Scheme 3.

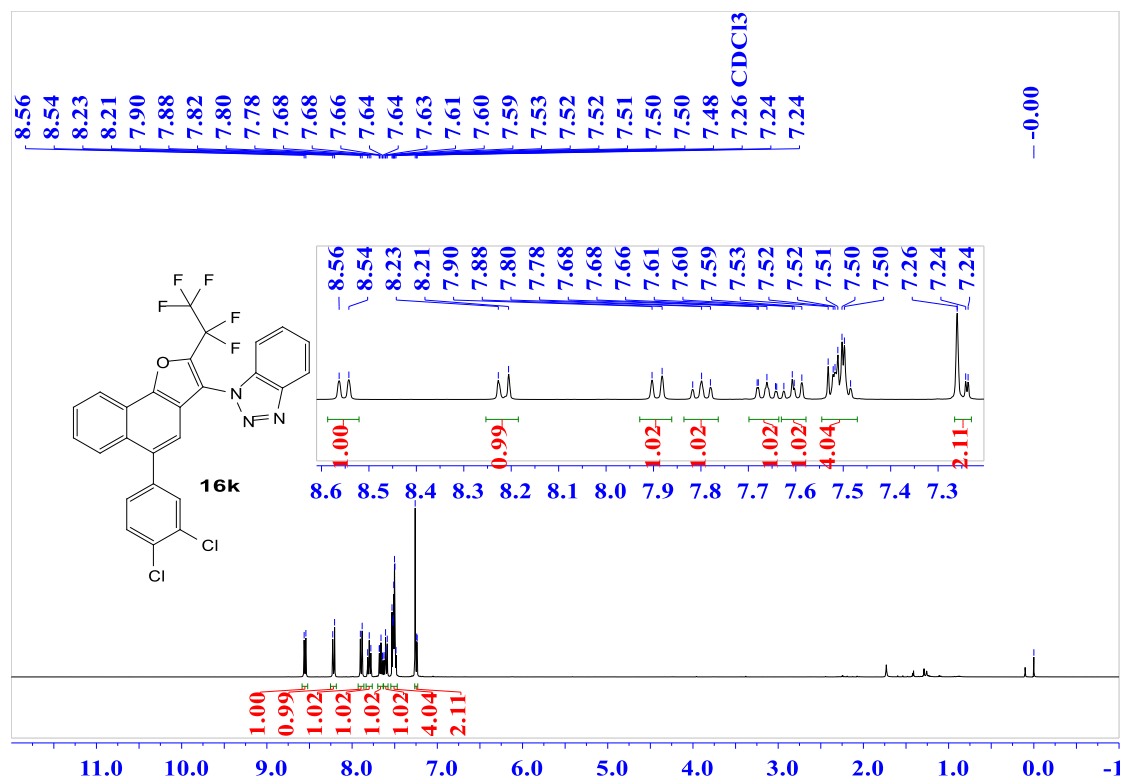


Figure S164. ¹⁹F NMR spectrum of **16k**, related to Scheme 3.

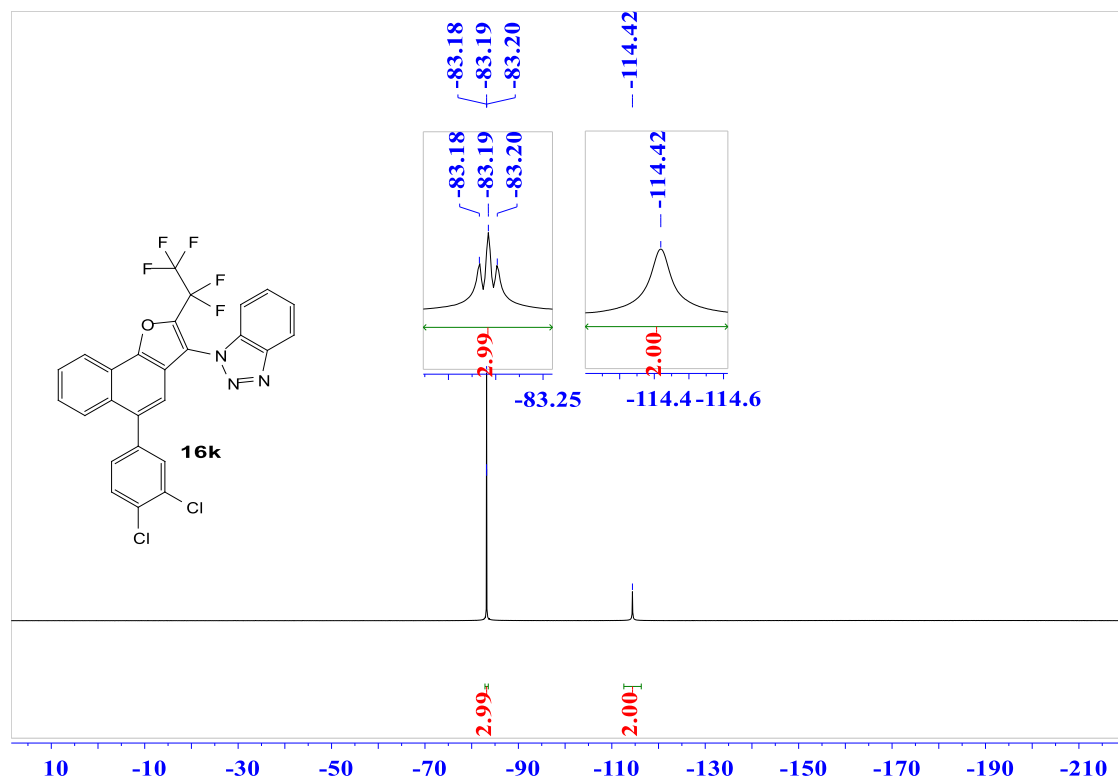


Figure S165. ^{13}C NMR spectrum of **16k**, related to Scheme 3.

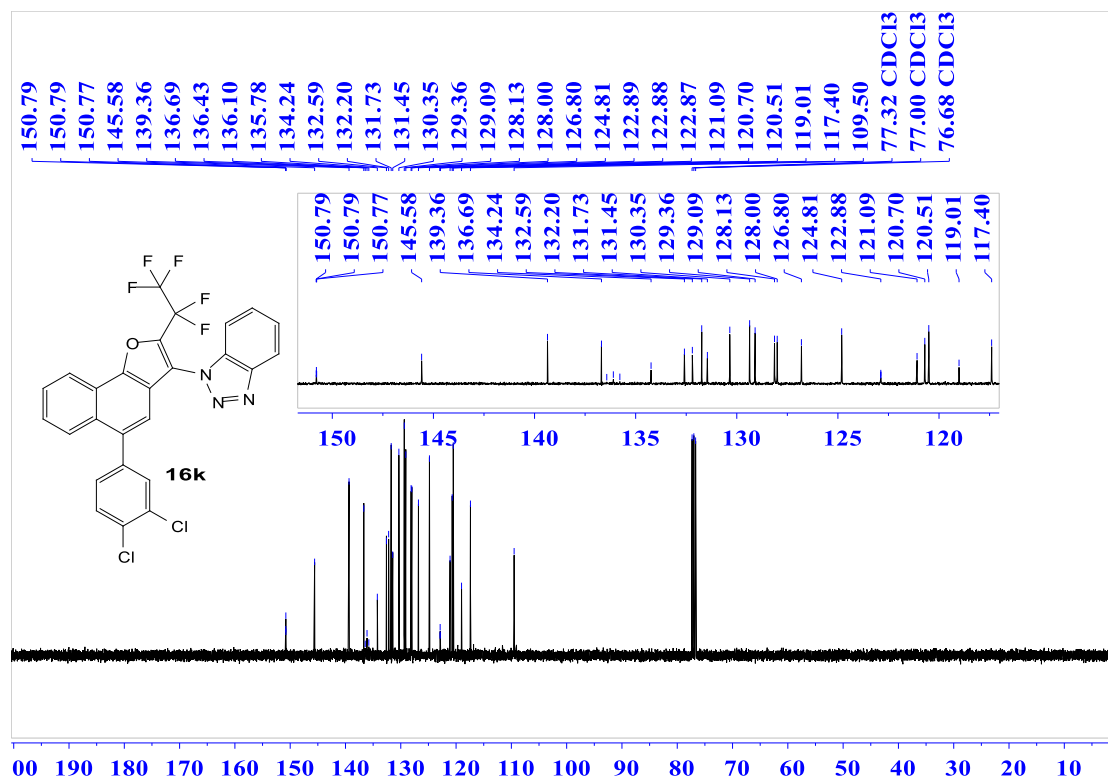


Figure S166. ^1H NMR spectrum of **16l**, related to Scheme 3.

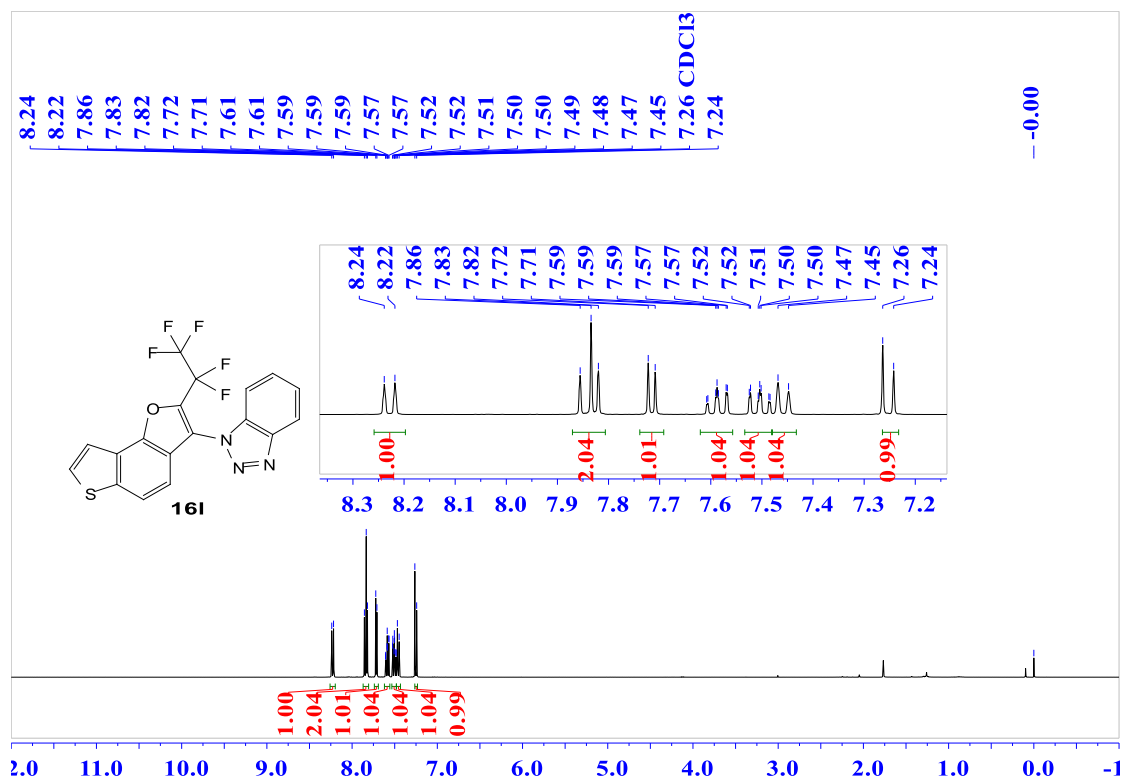


Figure S167. ^{19}F NMR spectrum of **16l**, related to Scheme 3.

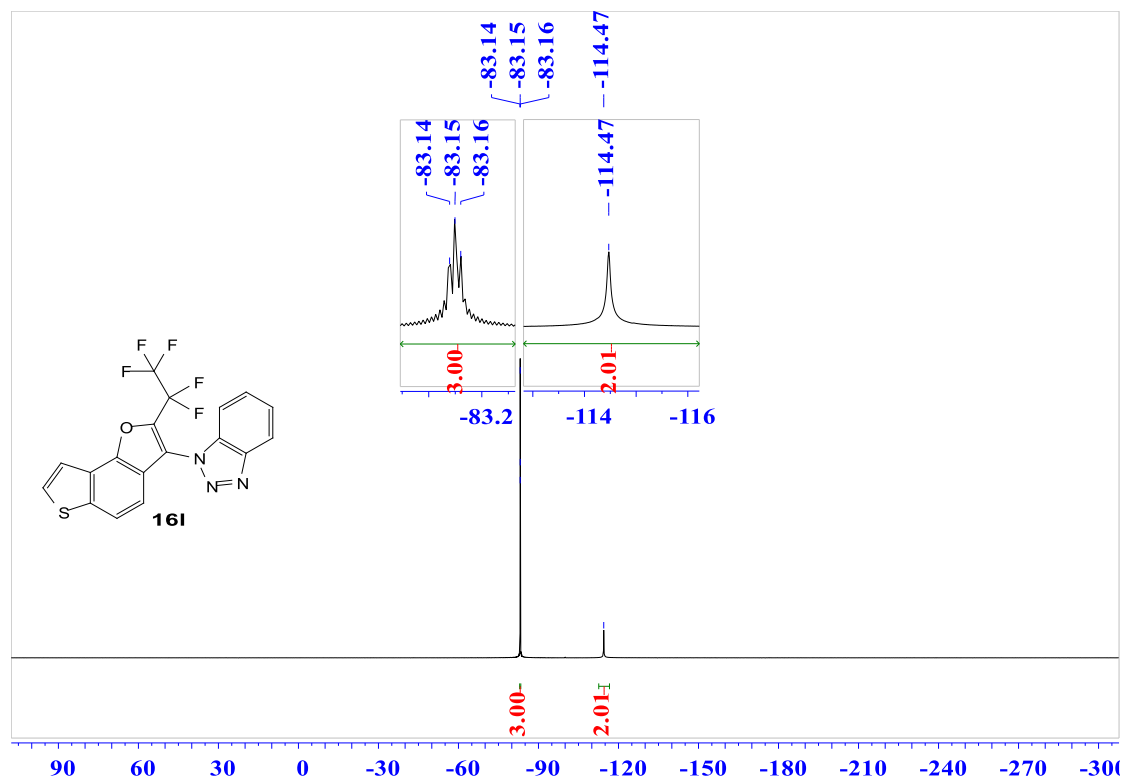


Figure S168. ^{13}C NMR spectrum of **16l**, related to Scheme 3.

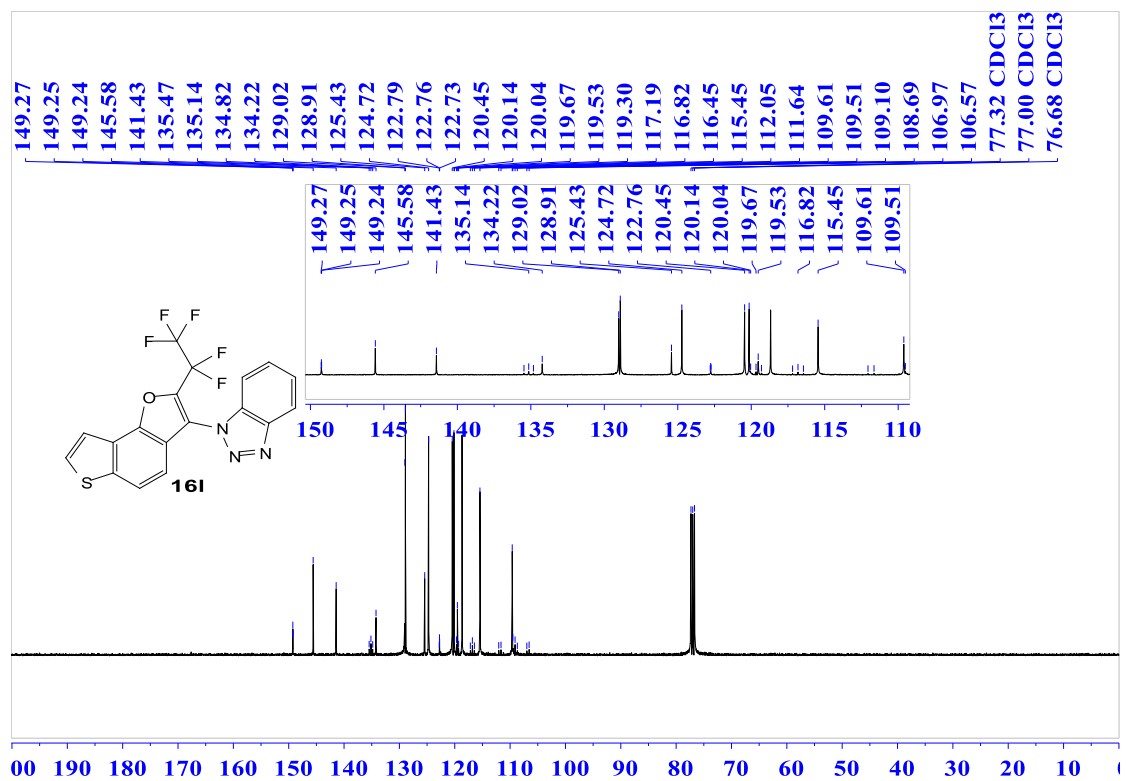


Figure S169. ¹H NMR spectrum of **16m**, related to Scheme 3.

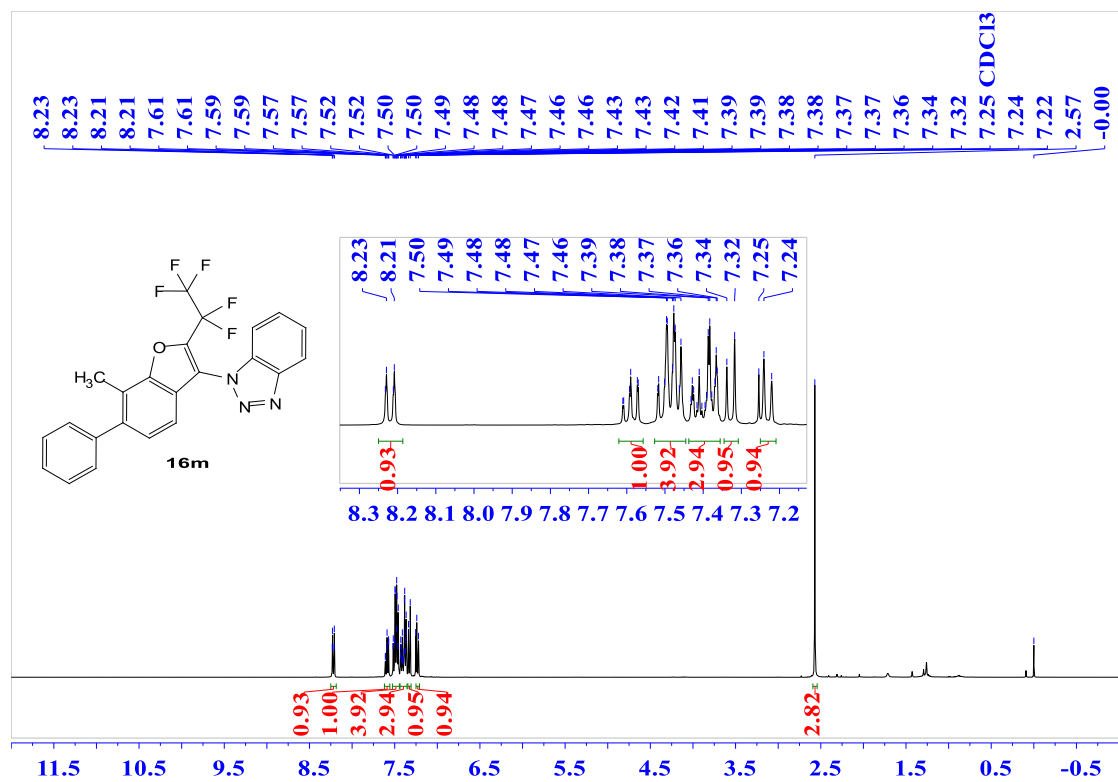


Figure S170. ¹⁹F NMR spectrum of **16m**, related to Scheme 3.

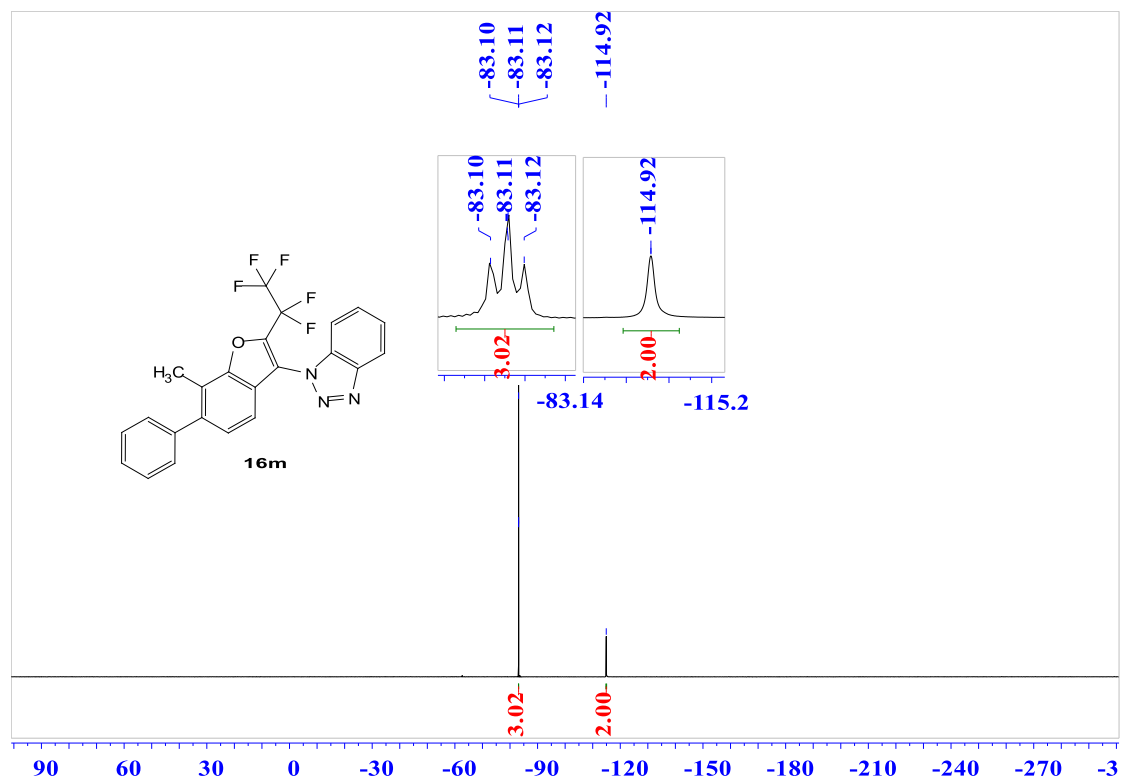


Figure S171. ¹³C NMR spectrum of **16m**, related to Scheme 3.

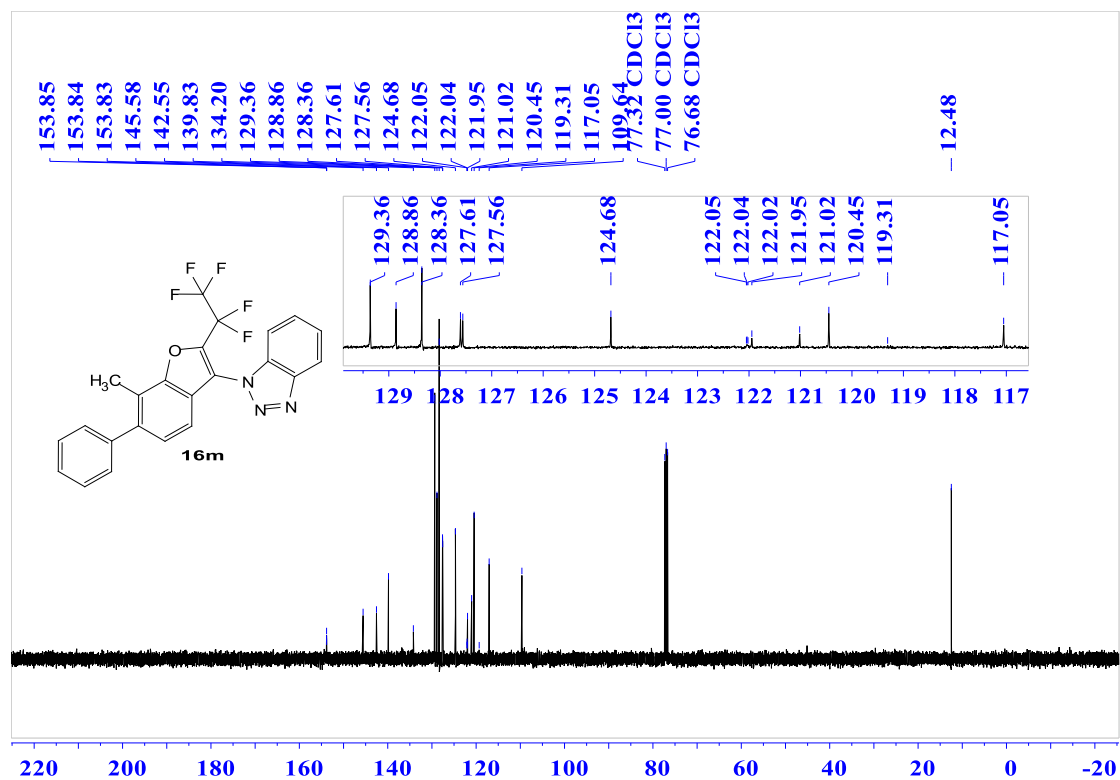


Figure S172. ¹H NMR spectrum of **16n**, related to Scheme 3.

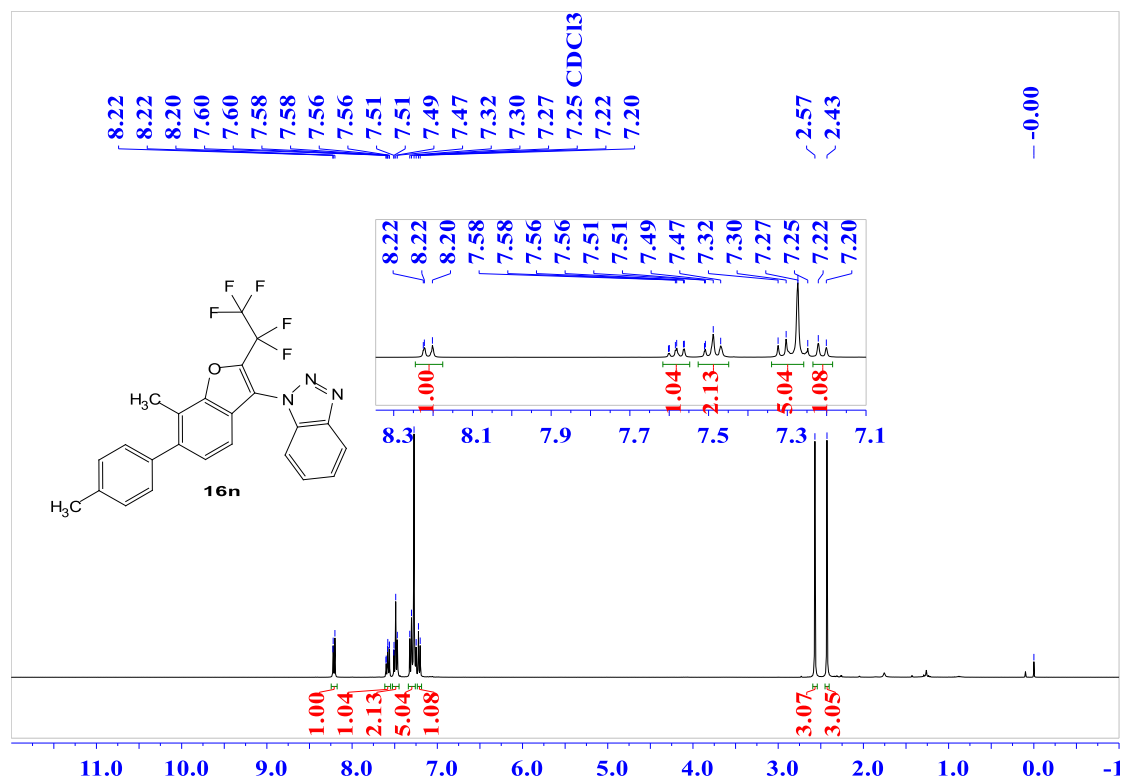


Figure S173. ¹⁹F NMR spectrum of **16n**, related to Scheme 3.

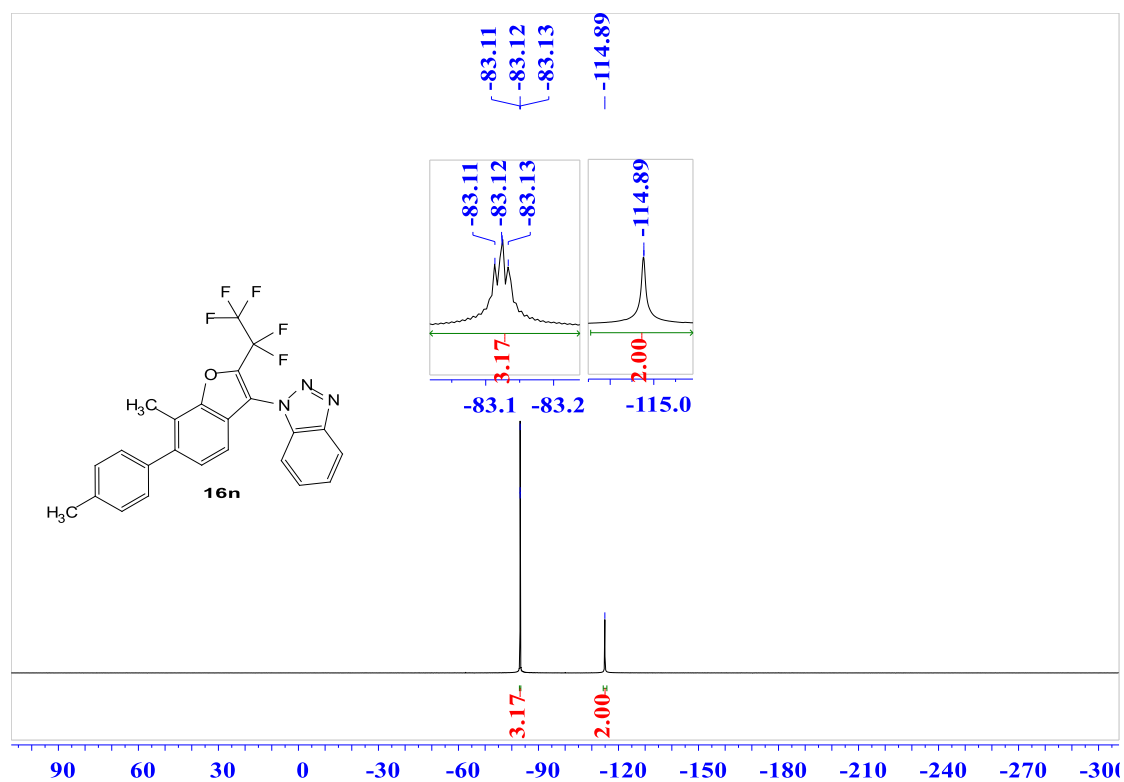


Figure S174. ¹³C NMR spectrum of **16n**, related to Scheme 3.

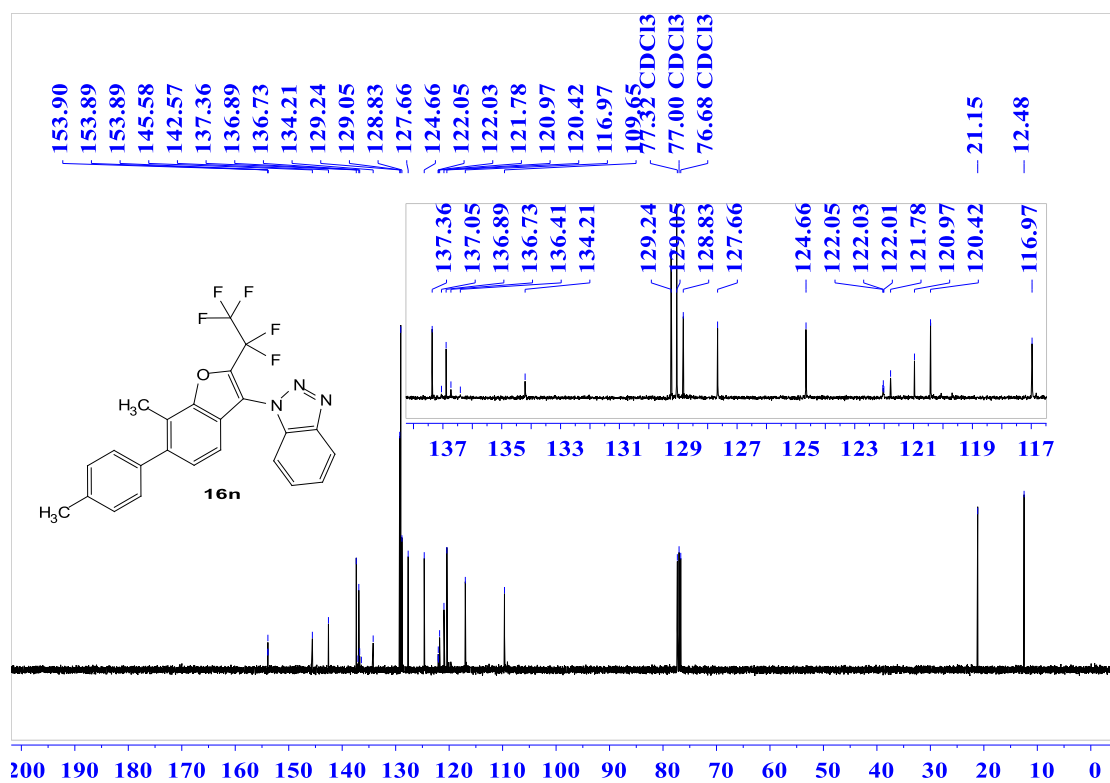


Figure S175. ¹H NMR spectrum of **16o**, related to Scheme 3.

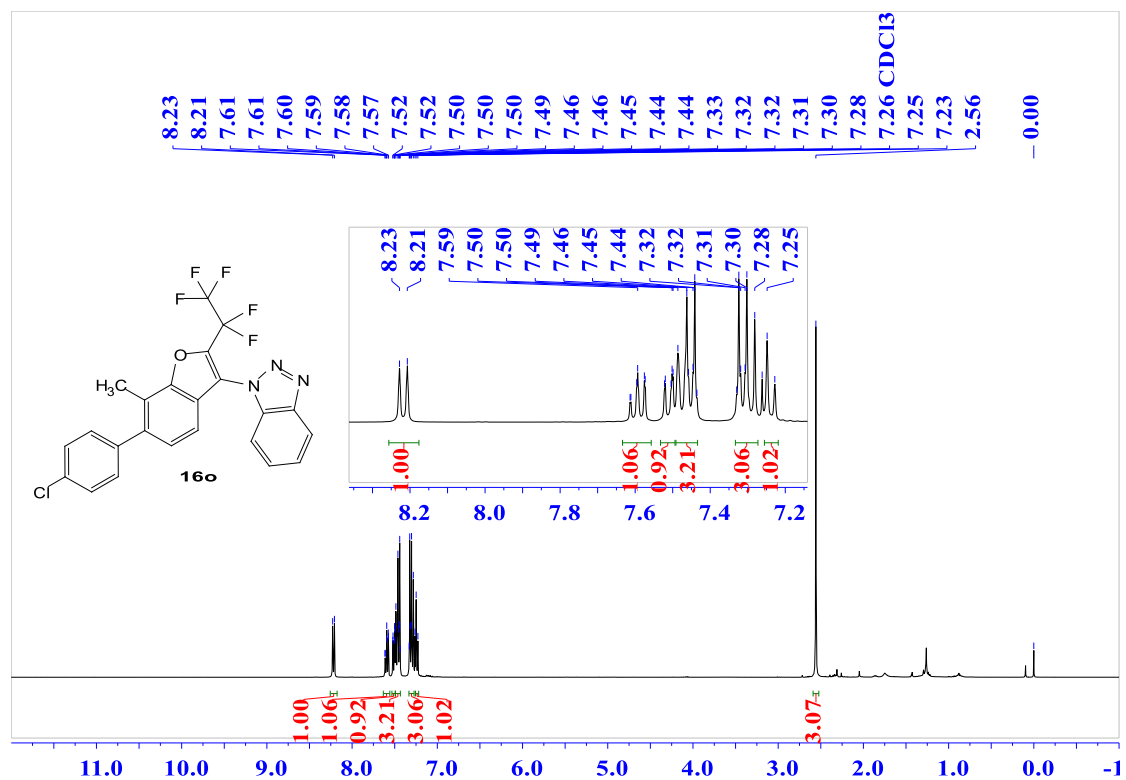


Figure S176. ¹⁹F NMR spectrum of **16o**, related to Scheme 3.

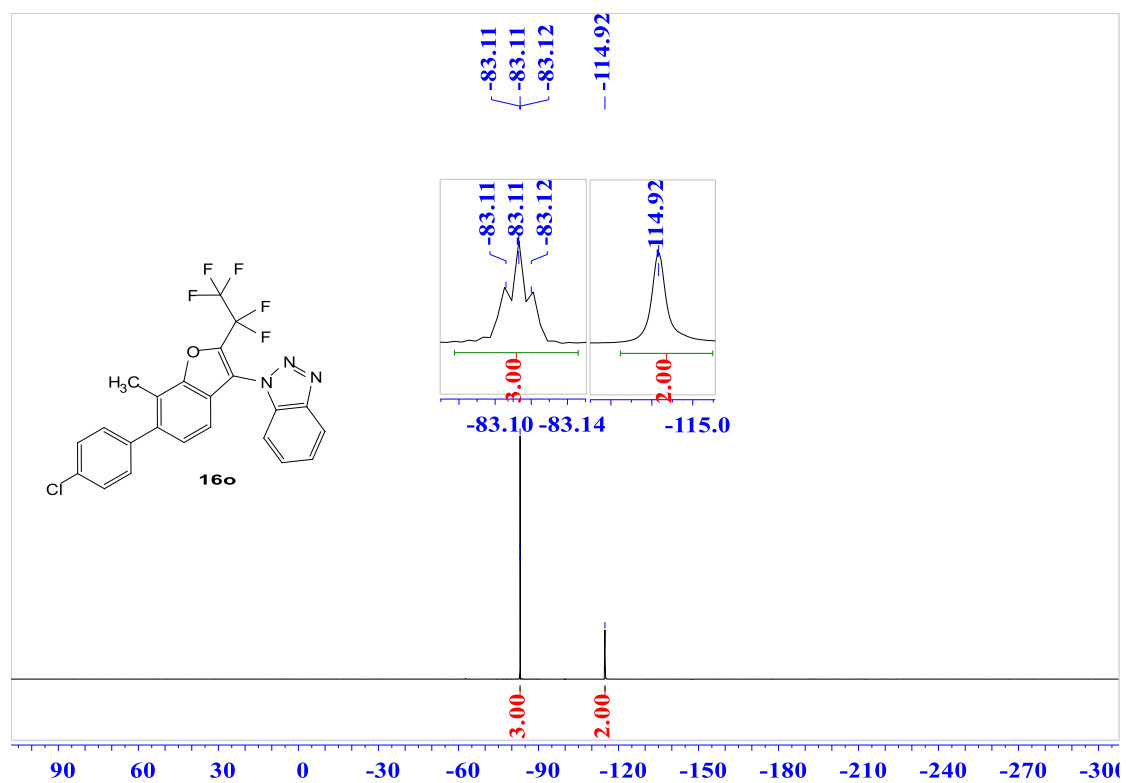


Figure S177. ^{13}C NMR spectrum of **16o**, related to Scheme 3.

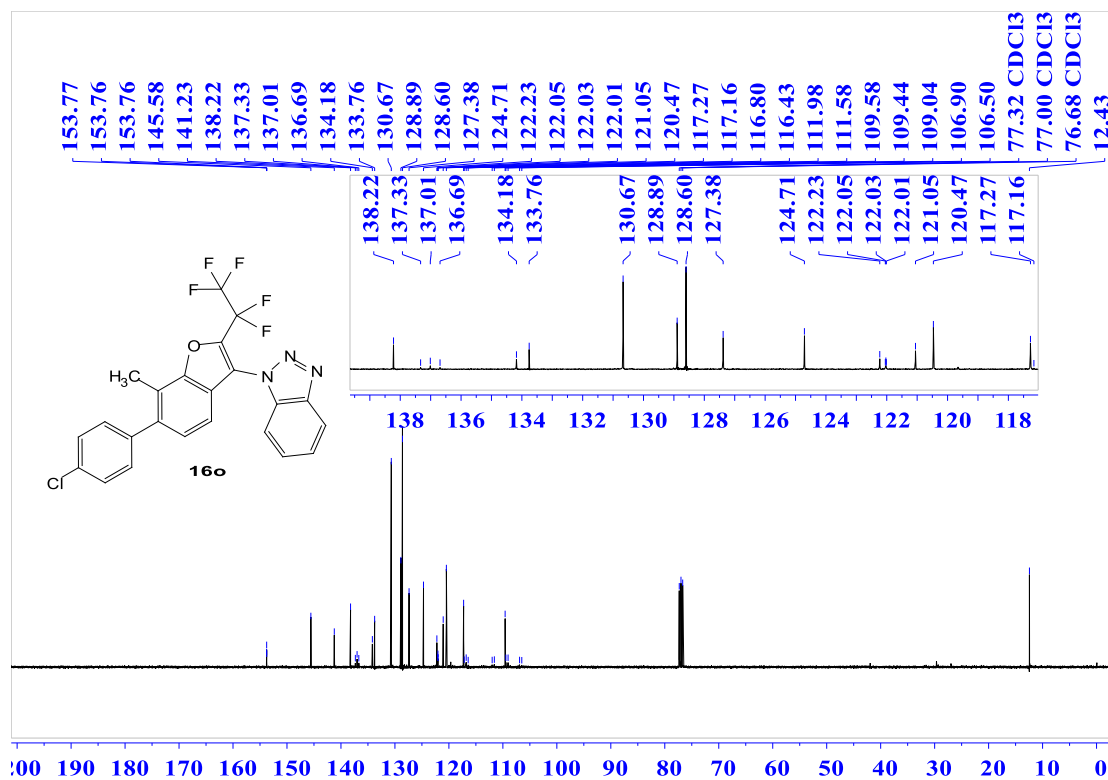


Figure S178. ^1H NMR spectrum of **16p**, related to Scheme 3.

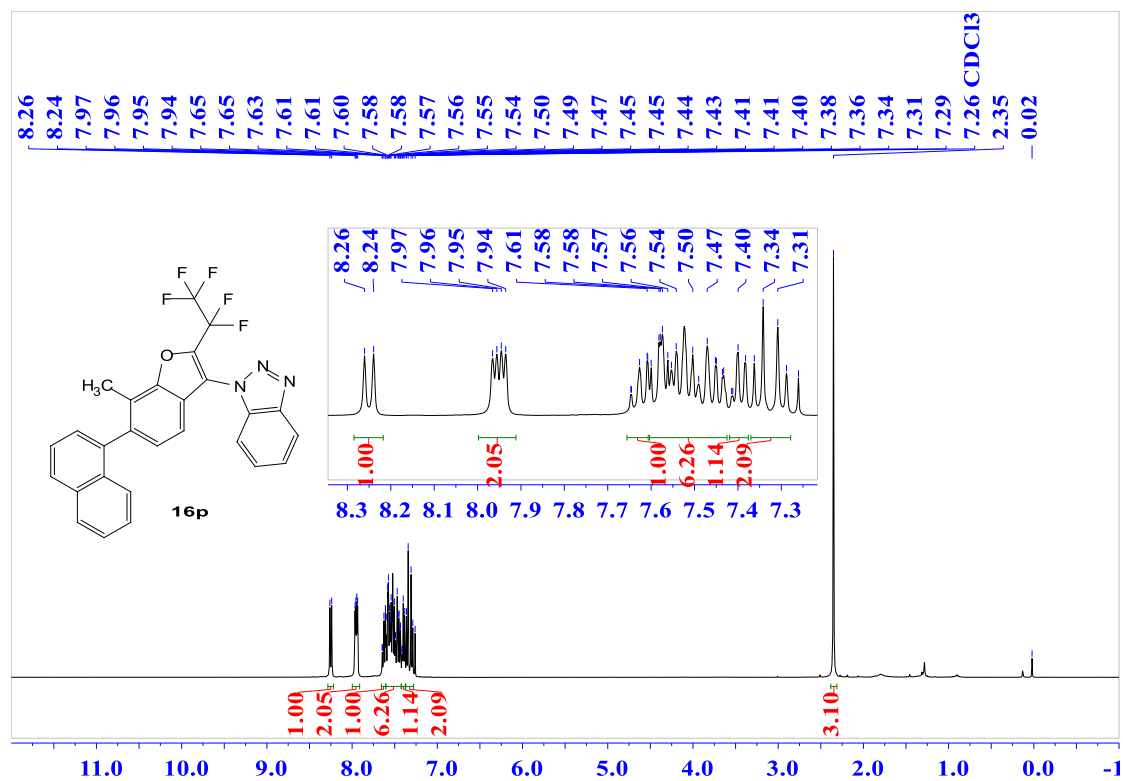


Figure S179. ^{19}F NMR spectrum of **16p**, related to Scheme 3.

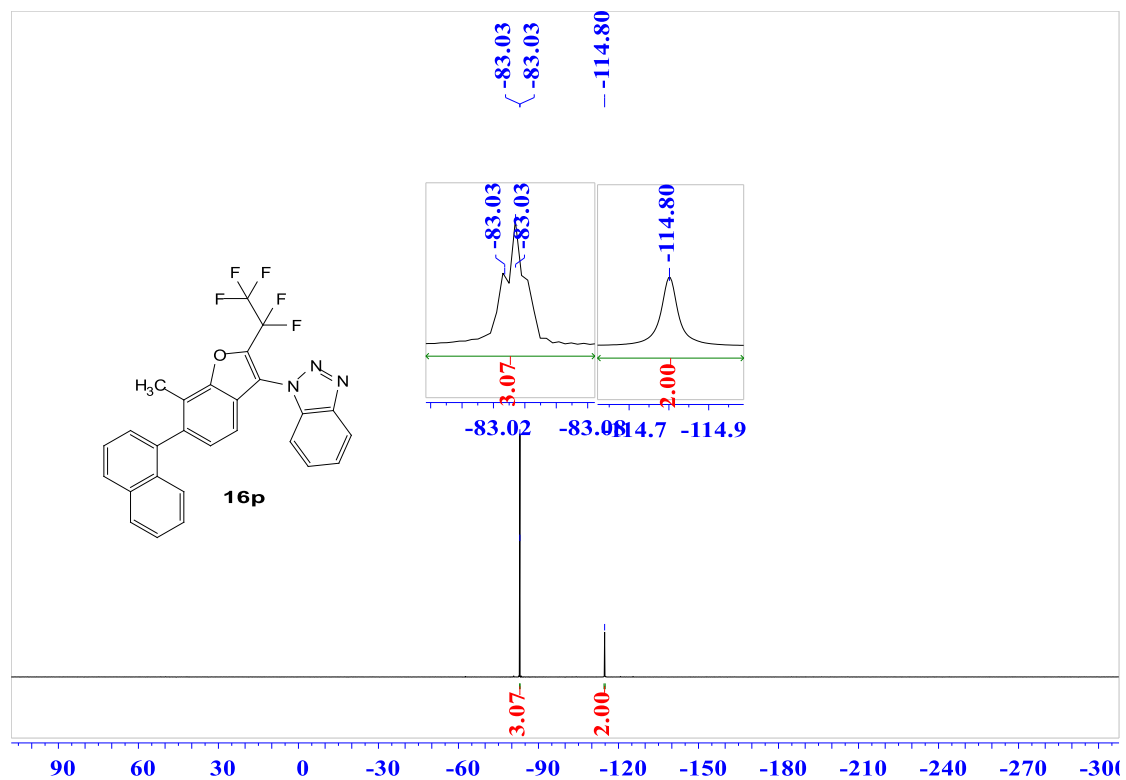


Figure S180. ^{13}C NMR spectrum of **16p**, related to Scheme 3.

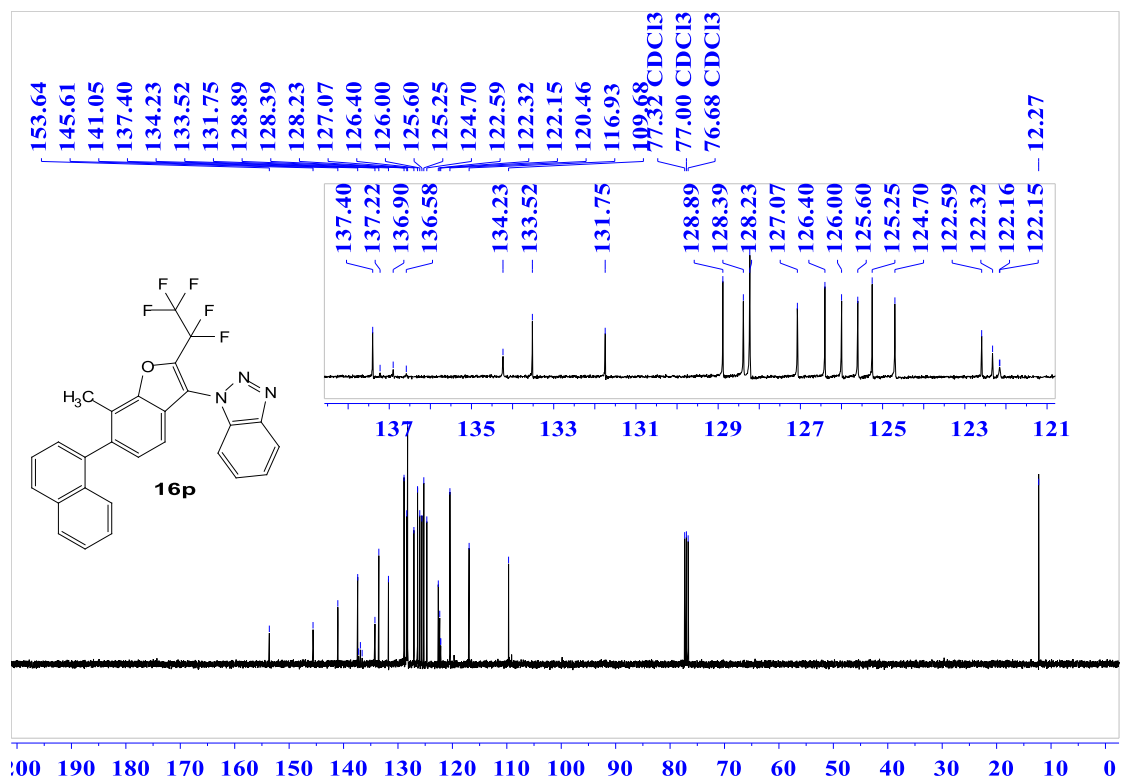


Figure S181. ¹H NMR spectrum of **16q**, related to Scheme 3.

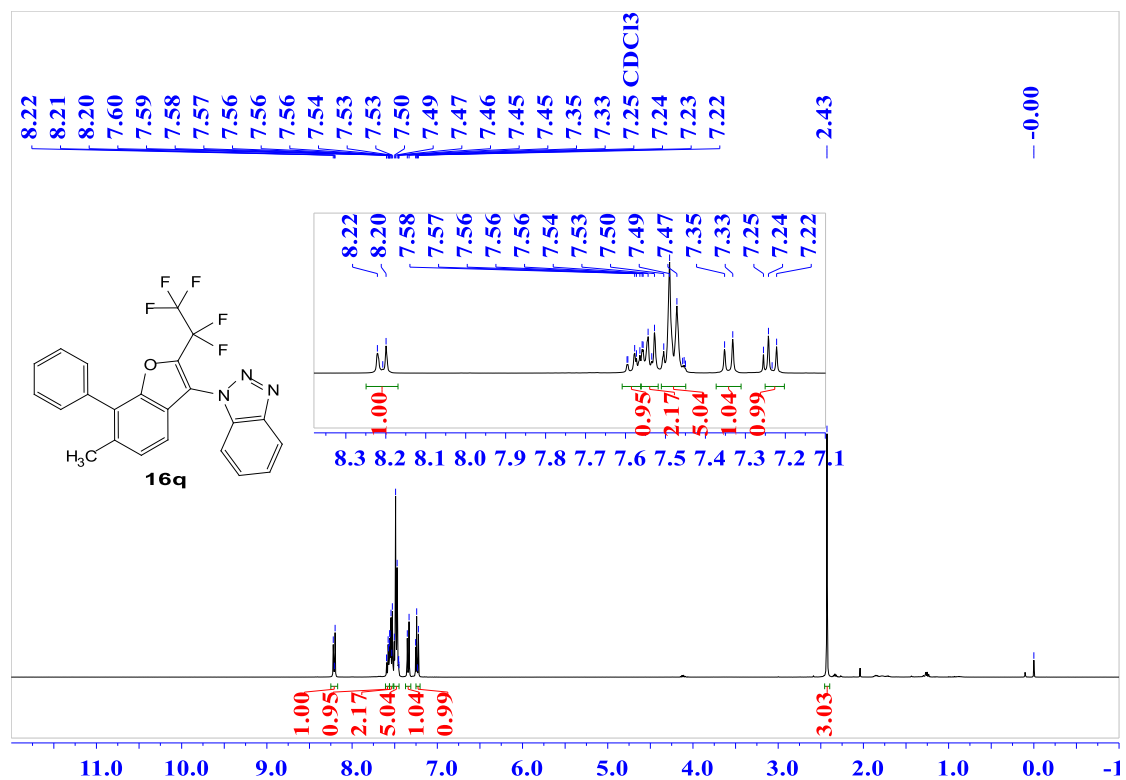


Figure S182. ¹⁹F NMR spectrum of **16q**, related to Scheme 3.

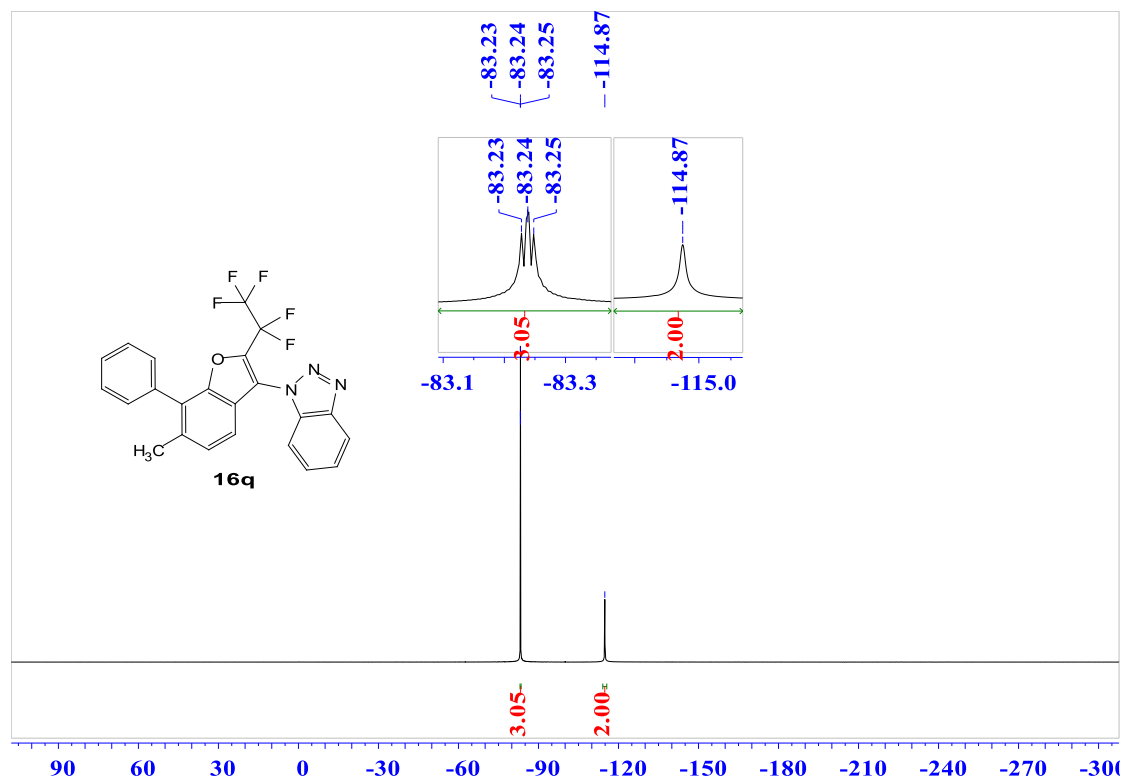


Figure S183. ¹³C NMR spectrum of **16q**, related to Scheme 3.

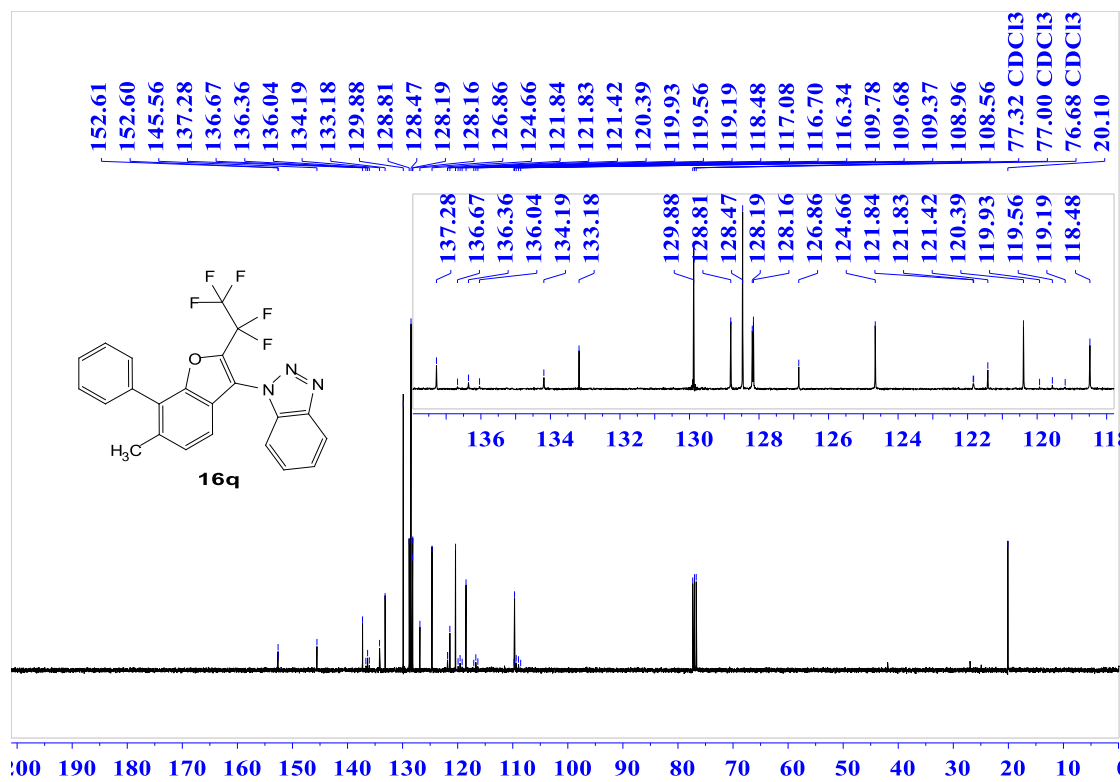


Figure S184. ¹H NMR spectrum of **16r**, related to Scheme 3.

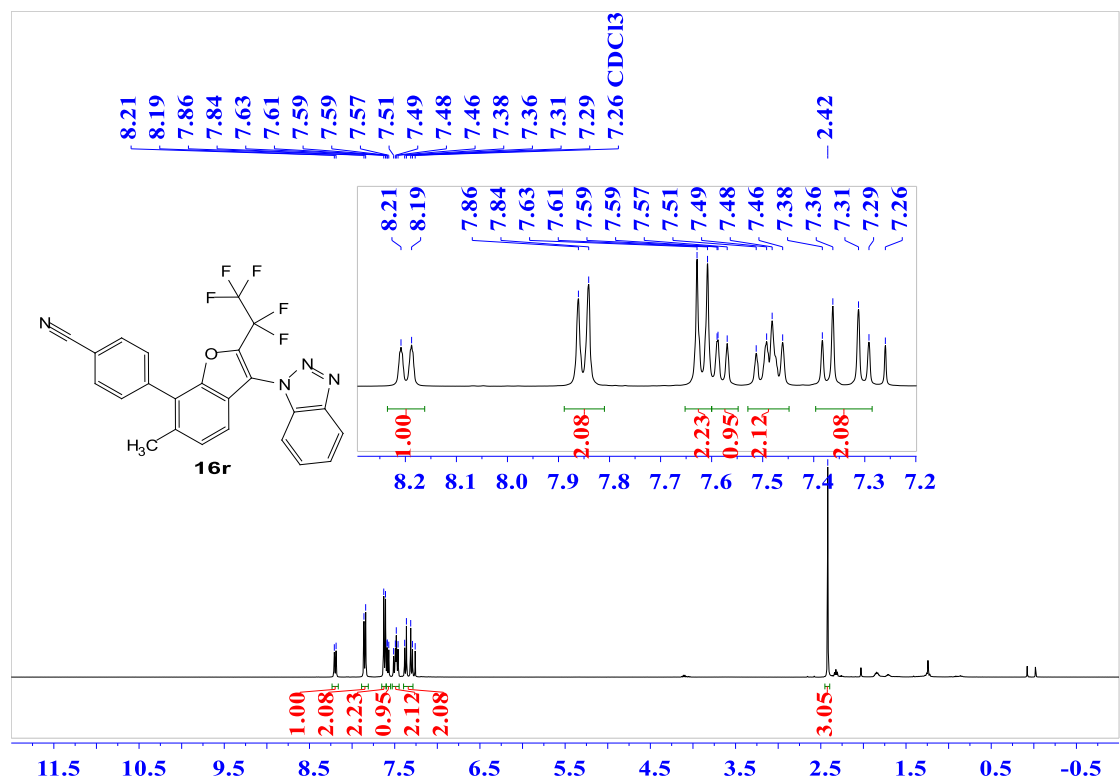


Figure S185. ^{19}F NMR spectrum of **16r**, related to Scheme 3.

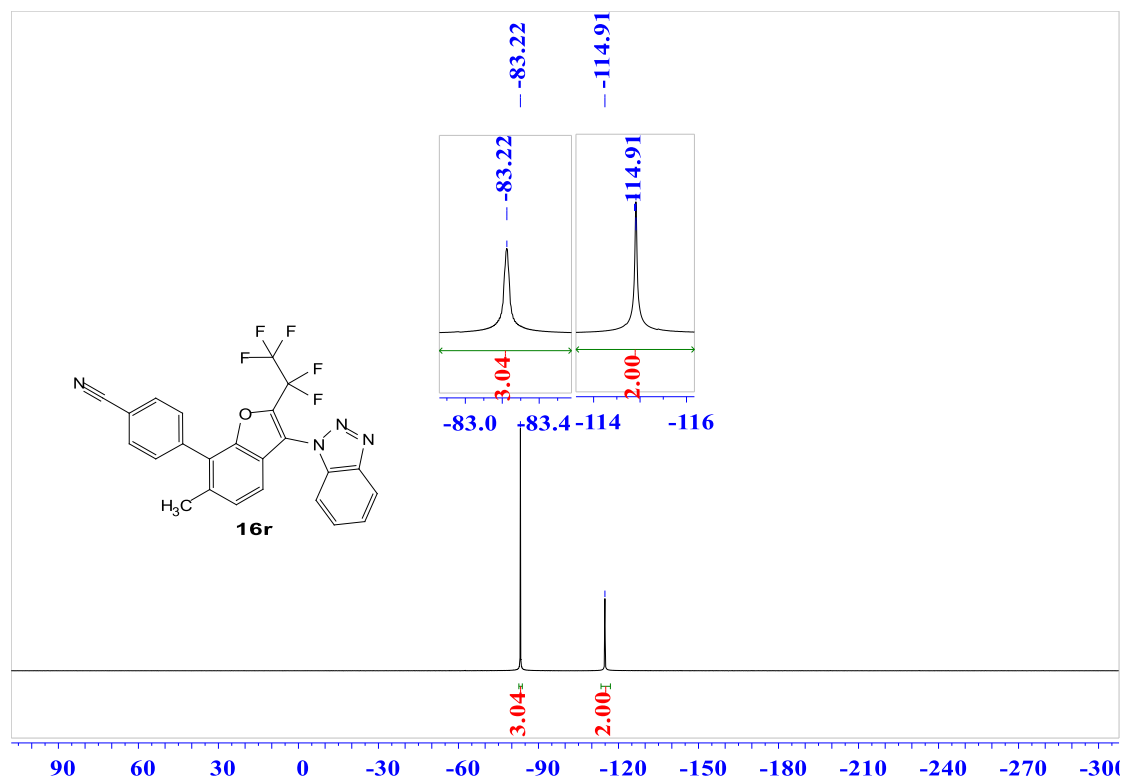


Figure S186. ^{13}C NMR spectrum of **16r**, related to Scheme 3.

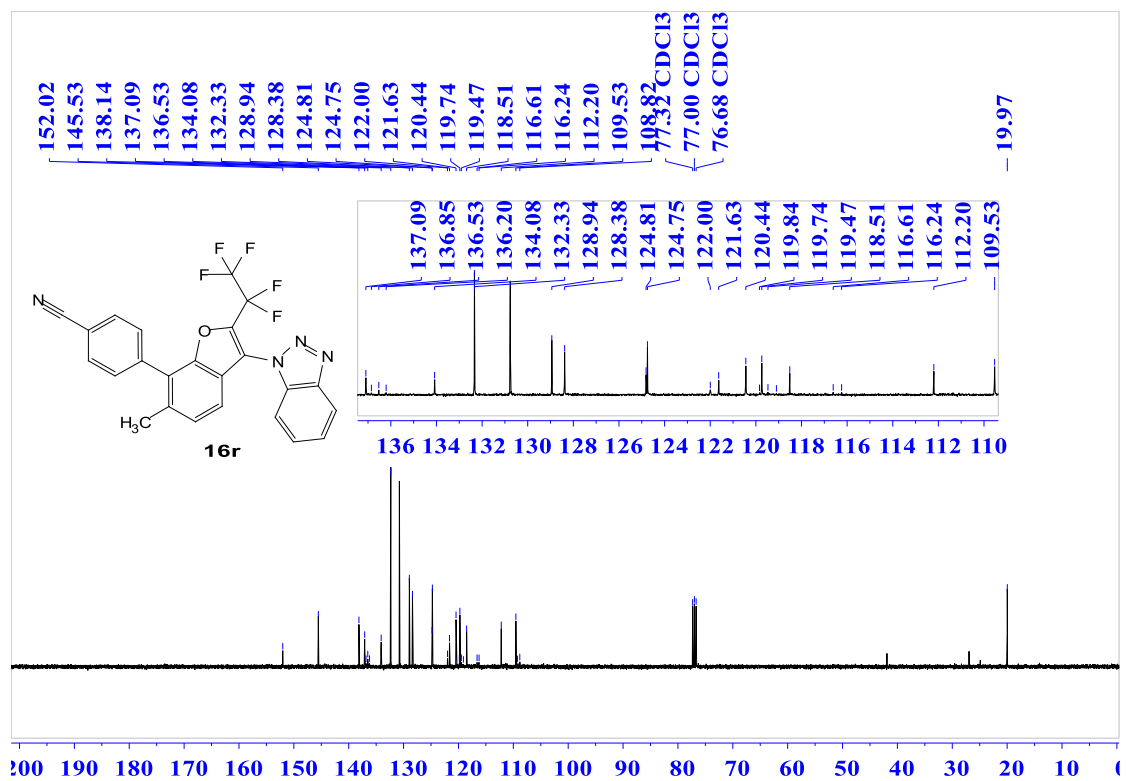


Figure S189. ¹³C NMR spectrum of **16s**, related to Scheme 3.

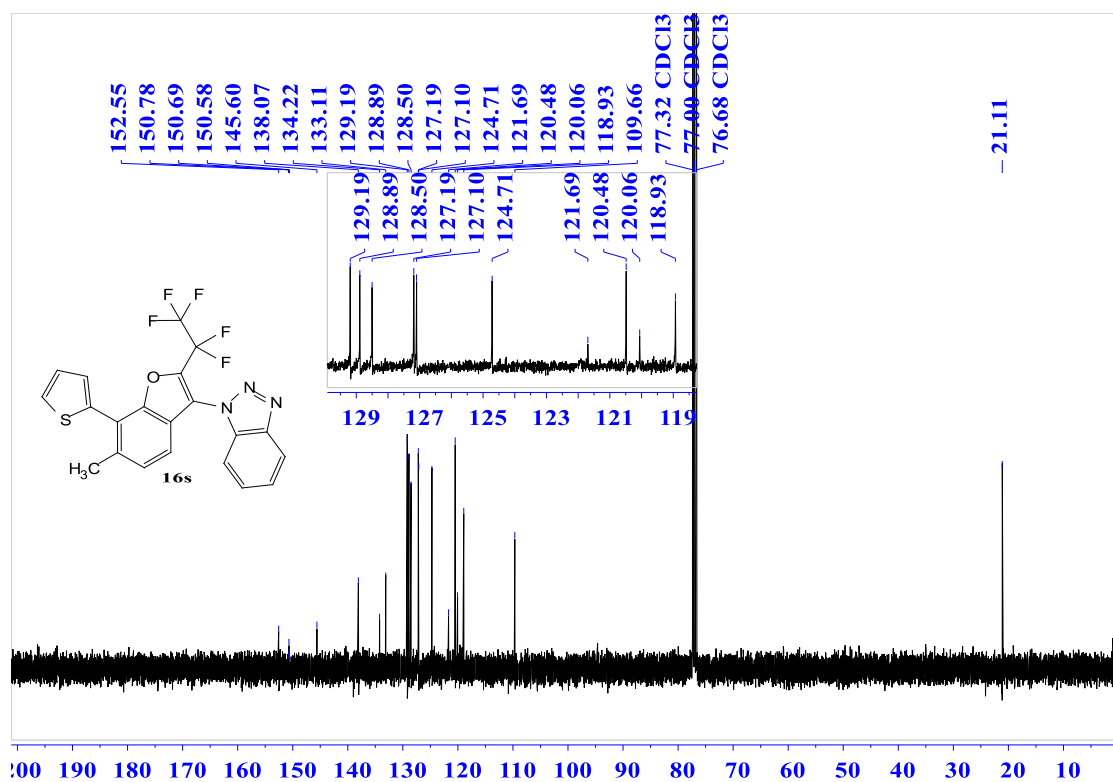


Figure S190. ¹H NMR spectrum of **16t**, related to Scheme 3.

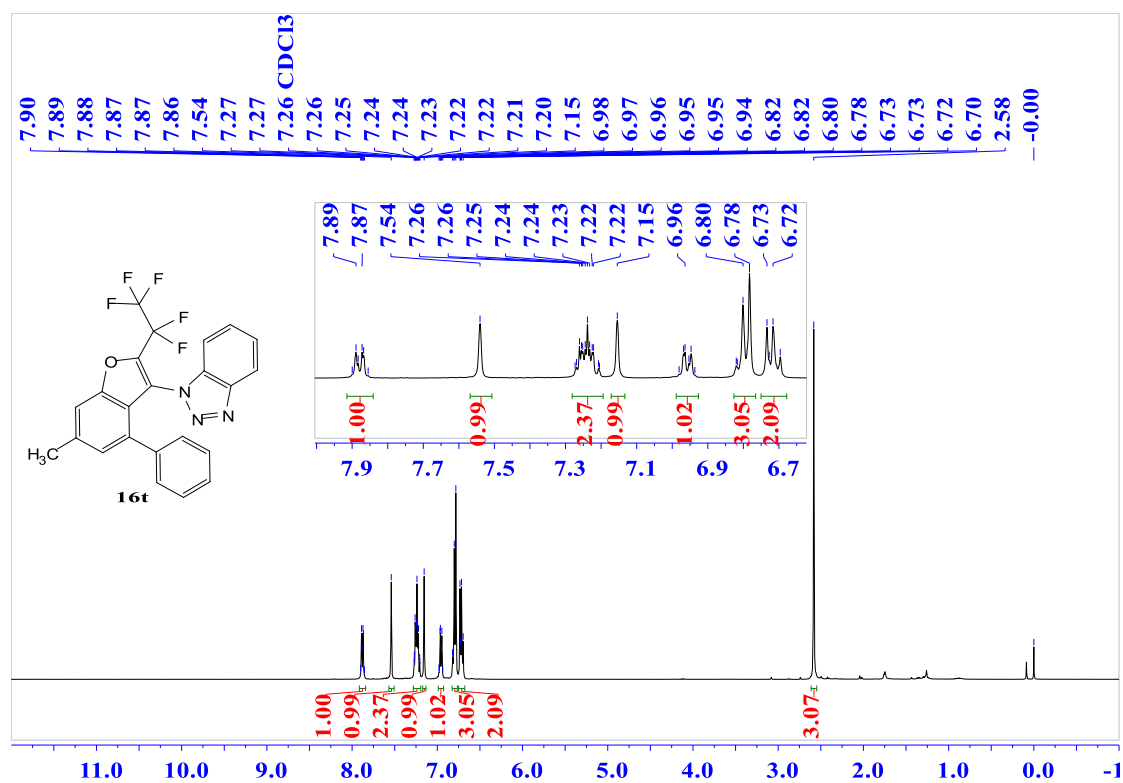


Figure S191. ¹⁹F NMR spectrum of **16t**, related to Scheme 3.

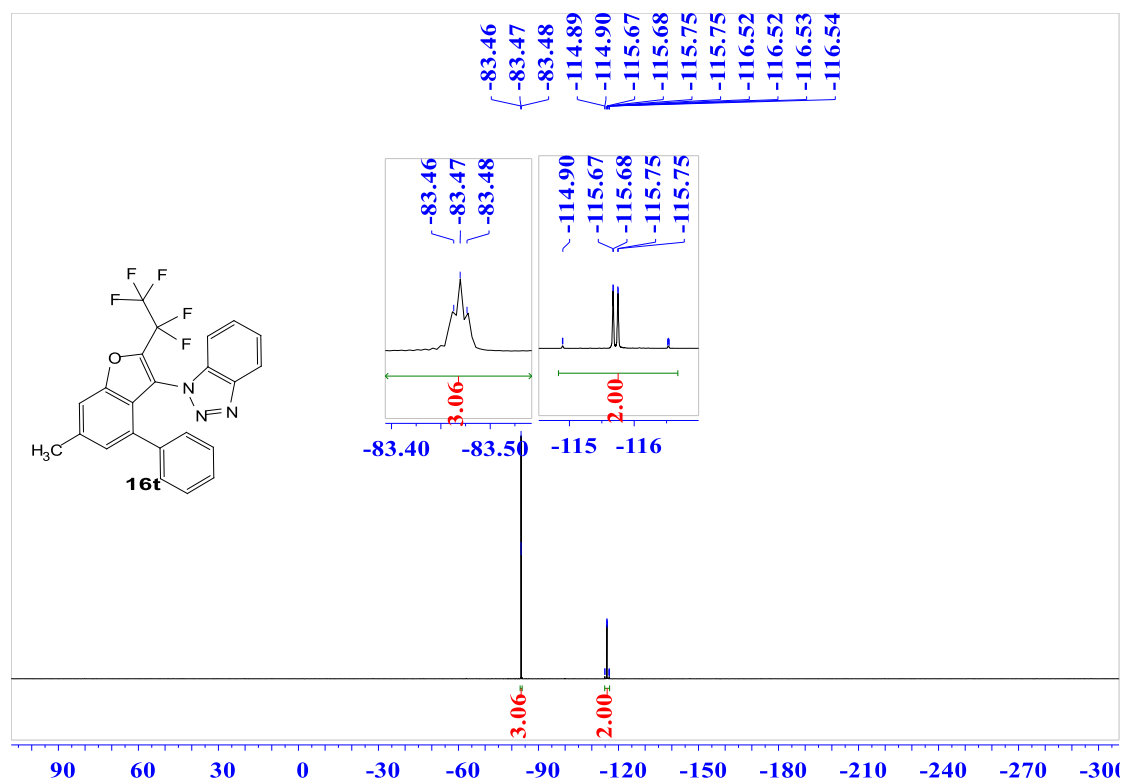


Figure S192. ¹³C NMR spectrum of **16t**, related to Scheme 3.

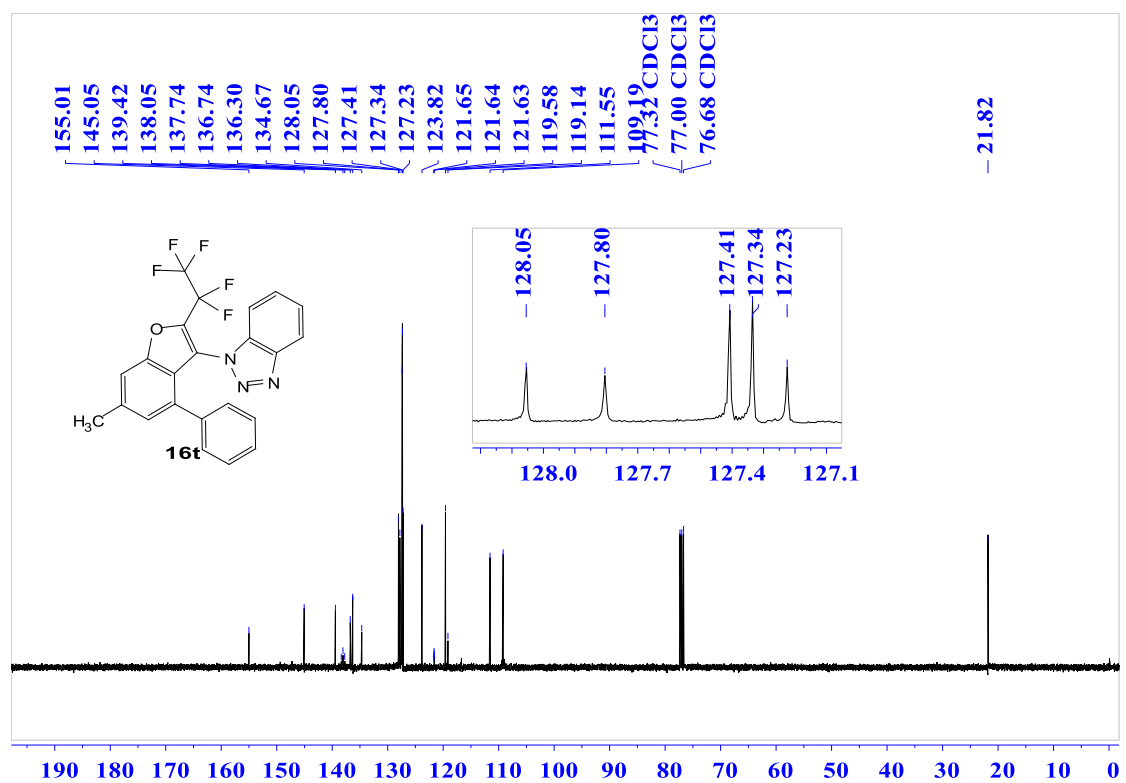


Figure S193. ¹H NMR spectrum of **16u**, related to Scheme 3.

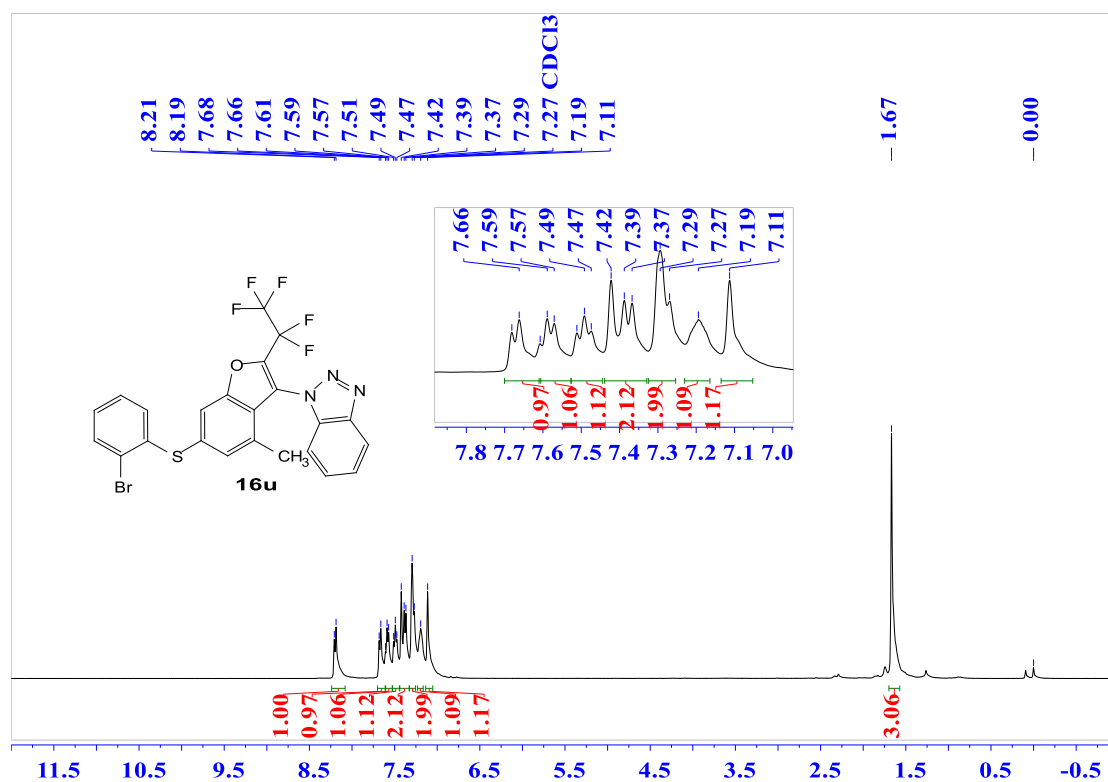


Figure S194. ¹⁹F NMR spectrum of **16u**, related to Scheme 3.

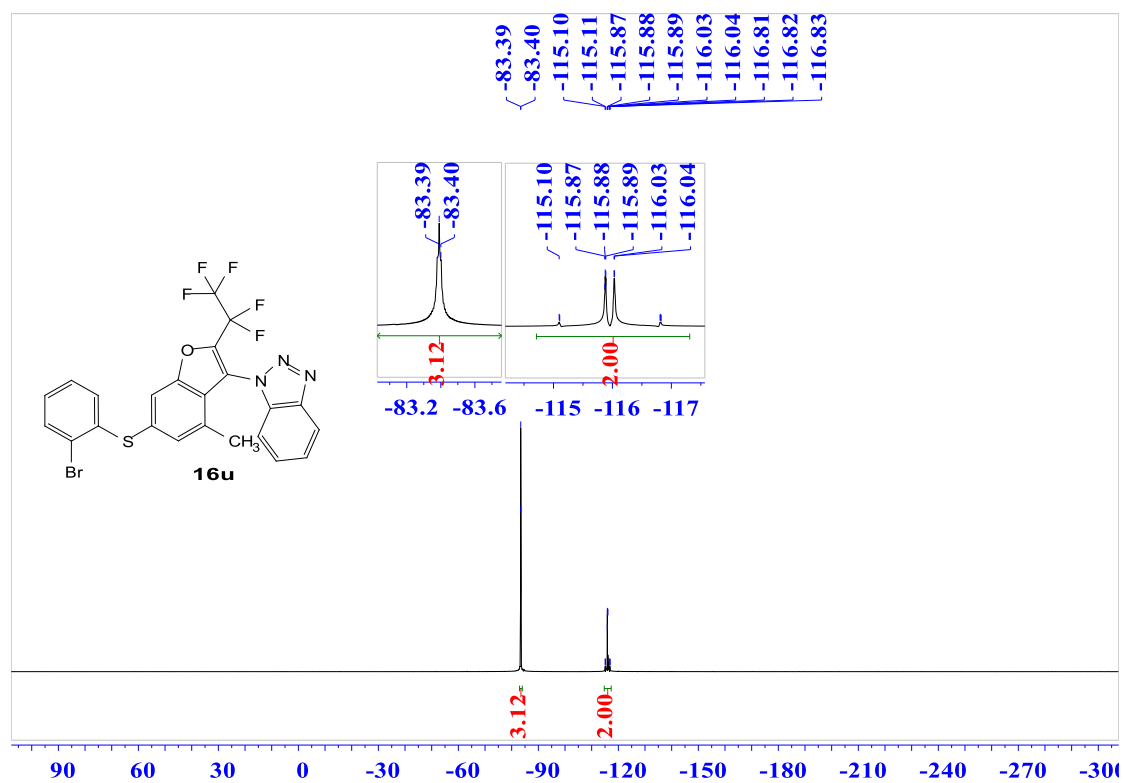


Figure S195. ¹³C NMR spectrum of **16u**, related to Scheme 3.

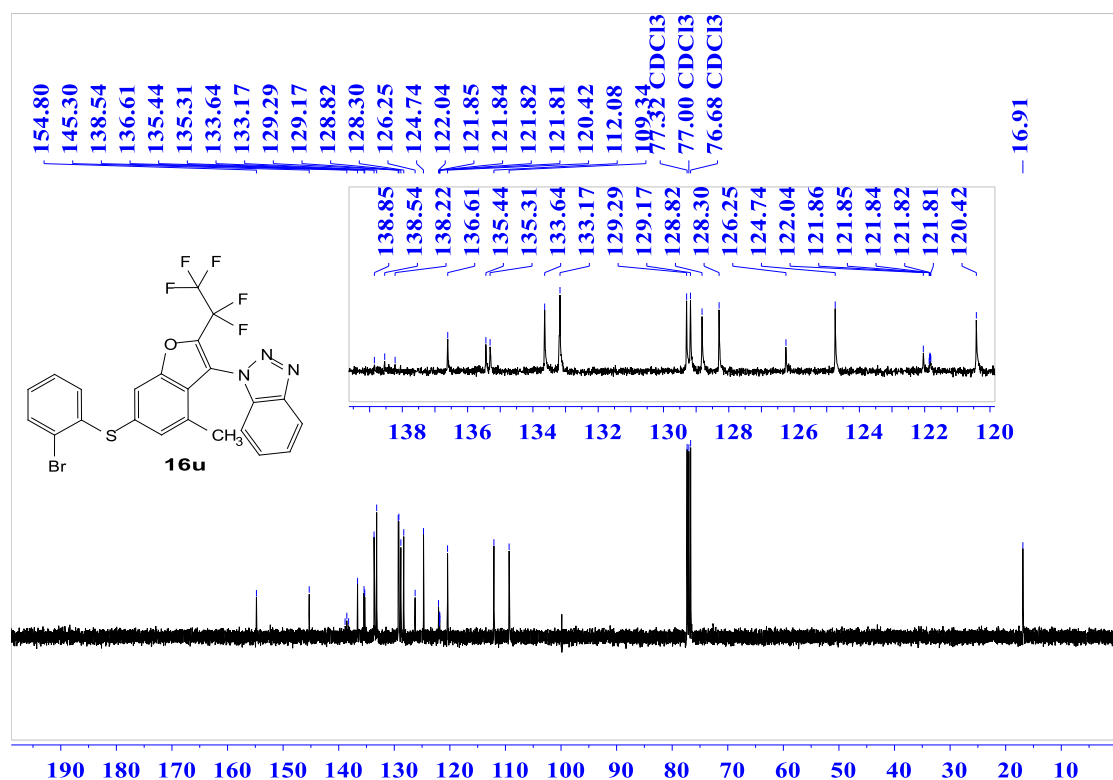


Figure S196. ¹H NMR spectrum of **16v**, related to Scheme 3.

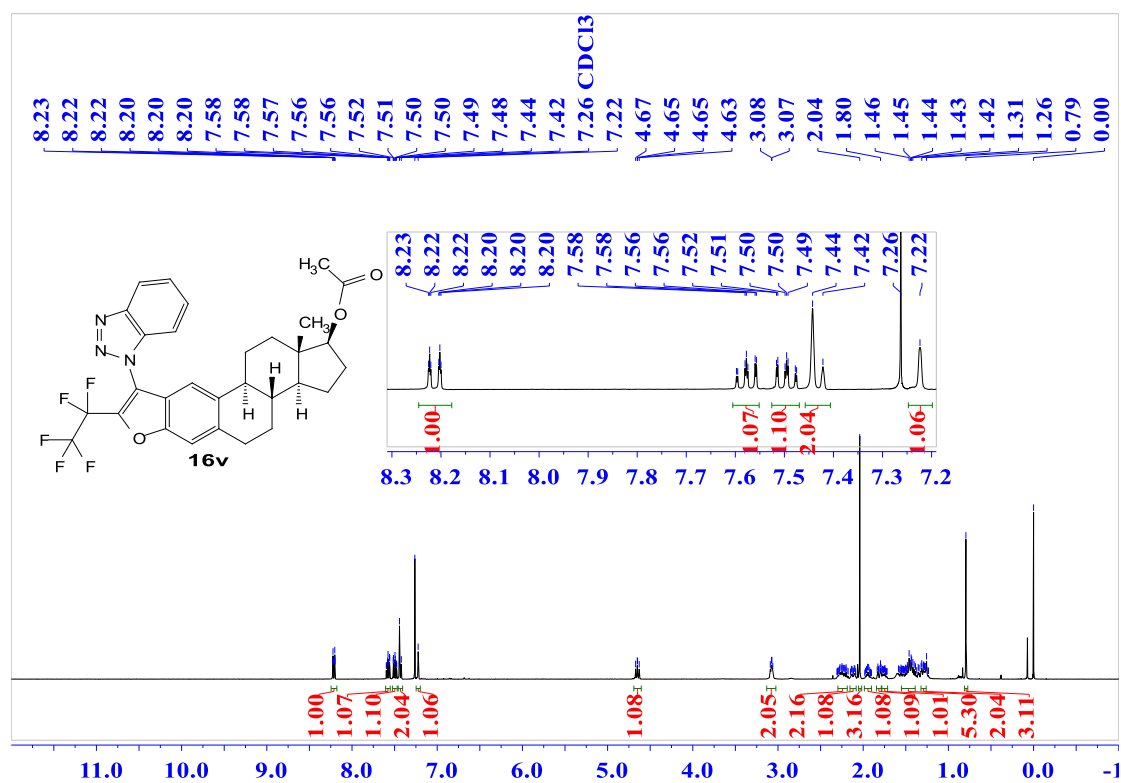


Figure S197. ^{19}F NMR spectrum of **16v**, related to Scheme 3.

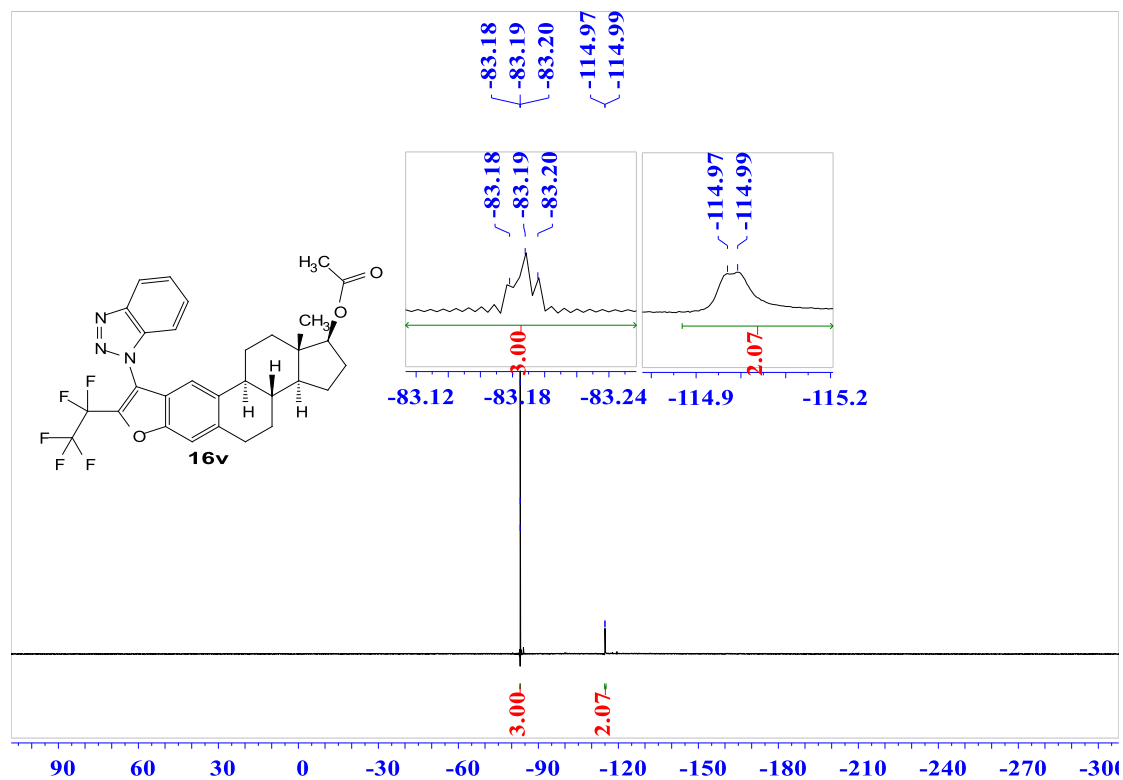


Figure S198. ^{13}C NMR spectrum of **16v**, related to Scheme 3.

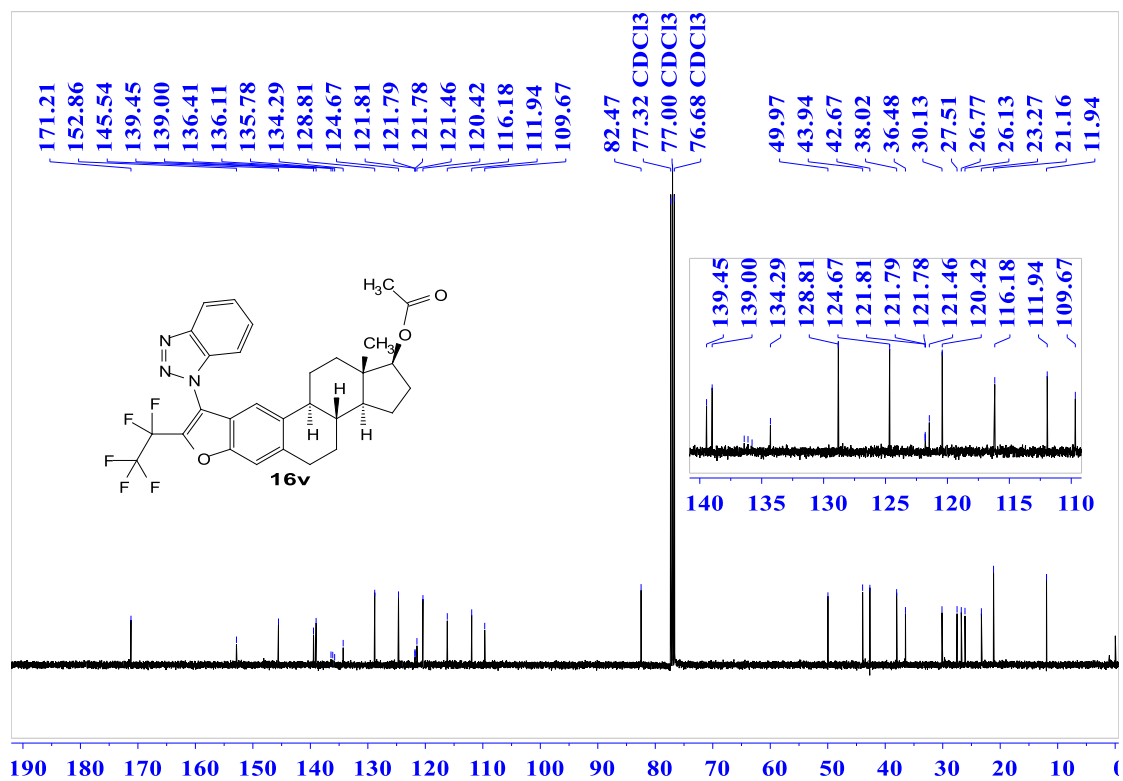


Figure S199. ¹H NMR spectrum of **16w**, related to Scheme 3.

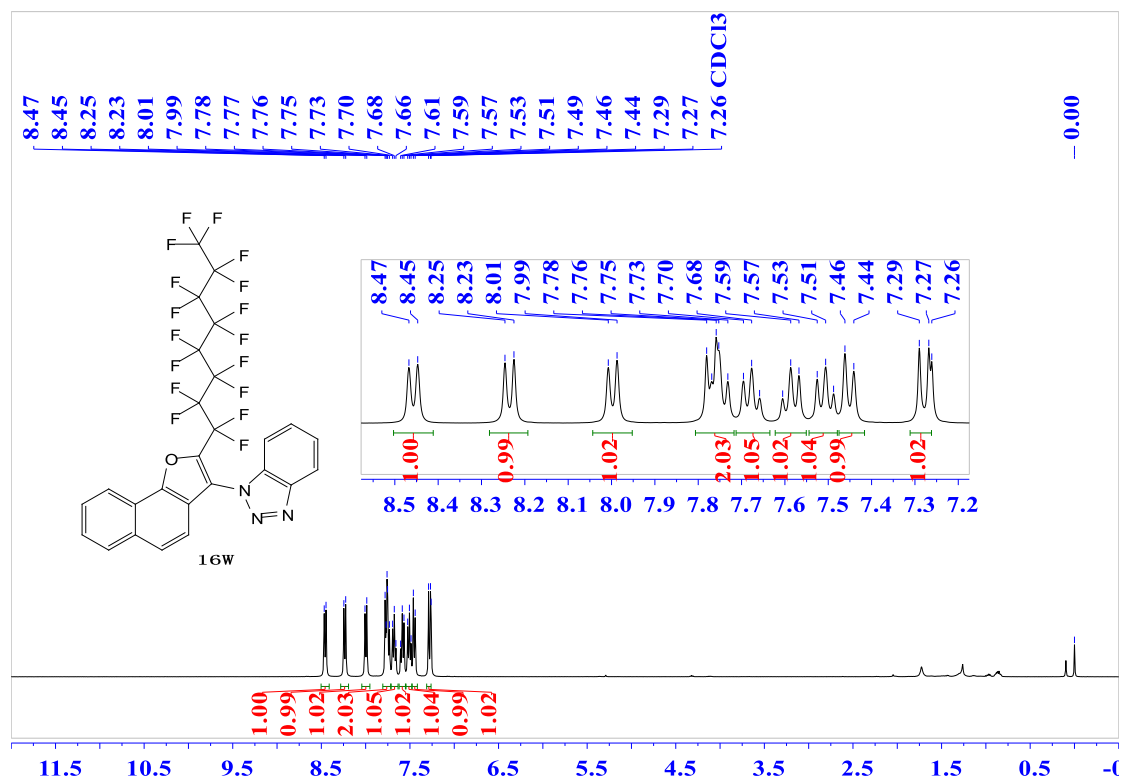


Figure S200. ¹⁹F NMR spectrum of **16w**, related to Scheme 3.

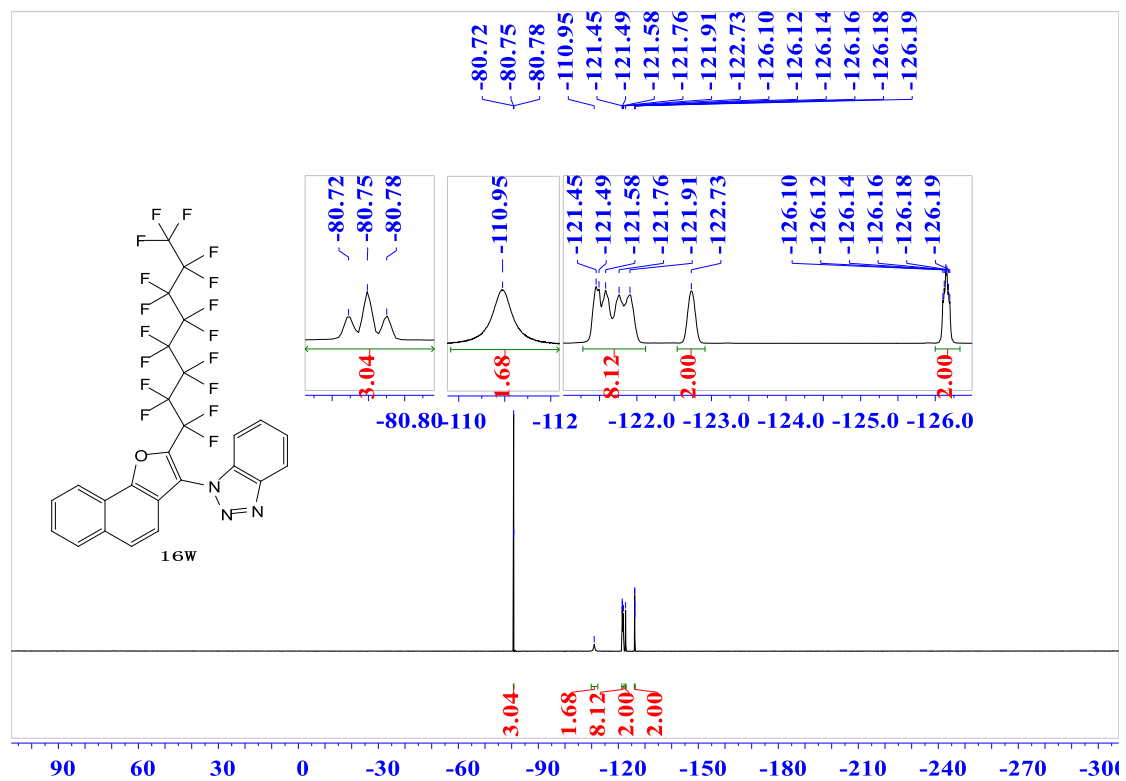


Figure S201. ^{13}C NMR spectrum of **16w**, related to Scheme 3.

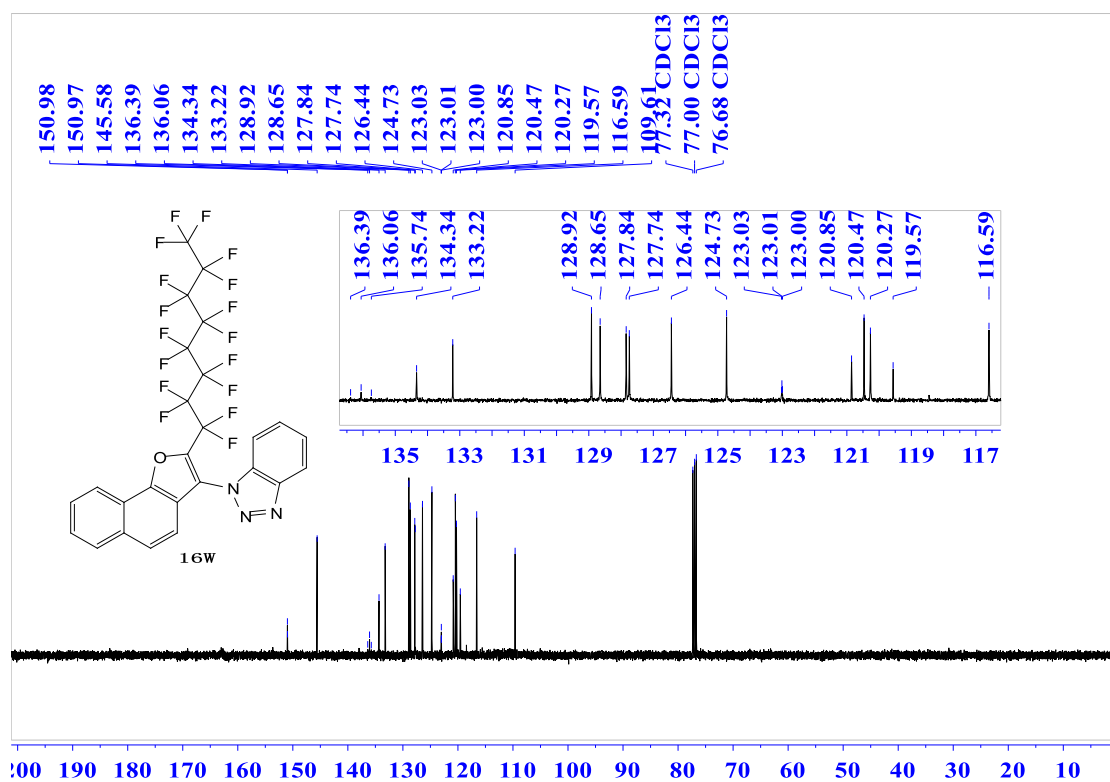


Figure S202. ^1H NMR spectrum of **16x**, related to Scheme 3.

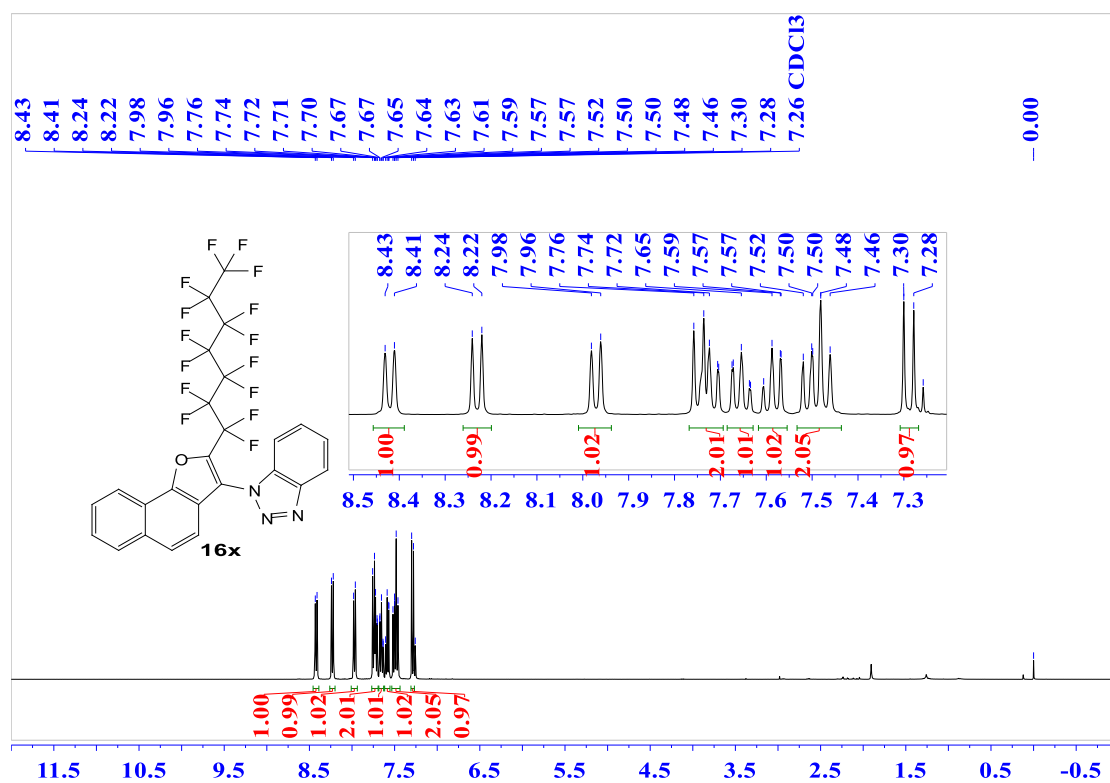


Figure S203. ¹⁹F NMR spectrum of **16x**, related to Scheme 3.

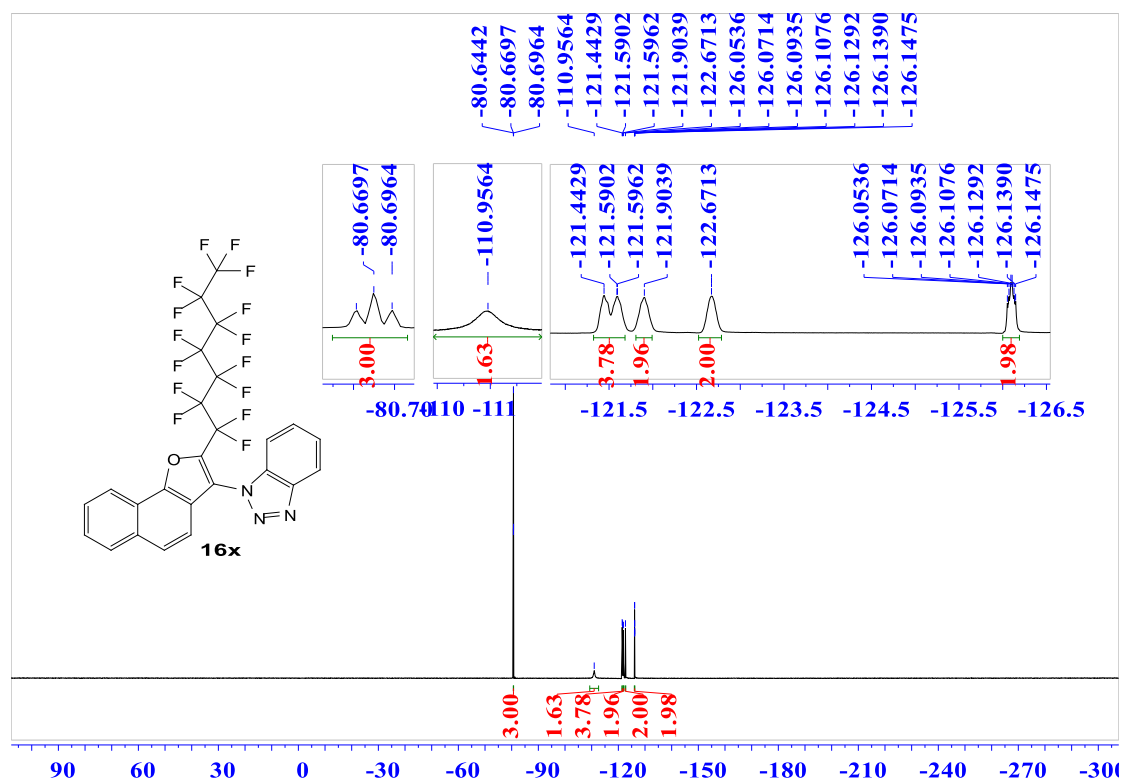


Figure S204. ¹³C NMR spectrum of **16x**, related to Scheme 3.

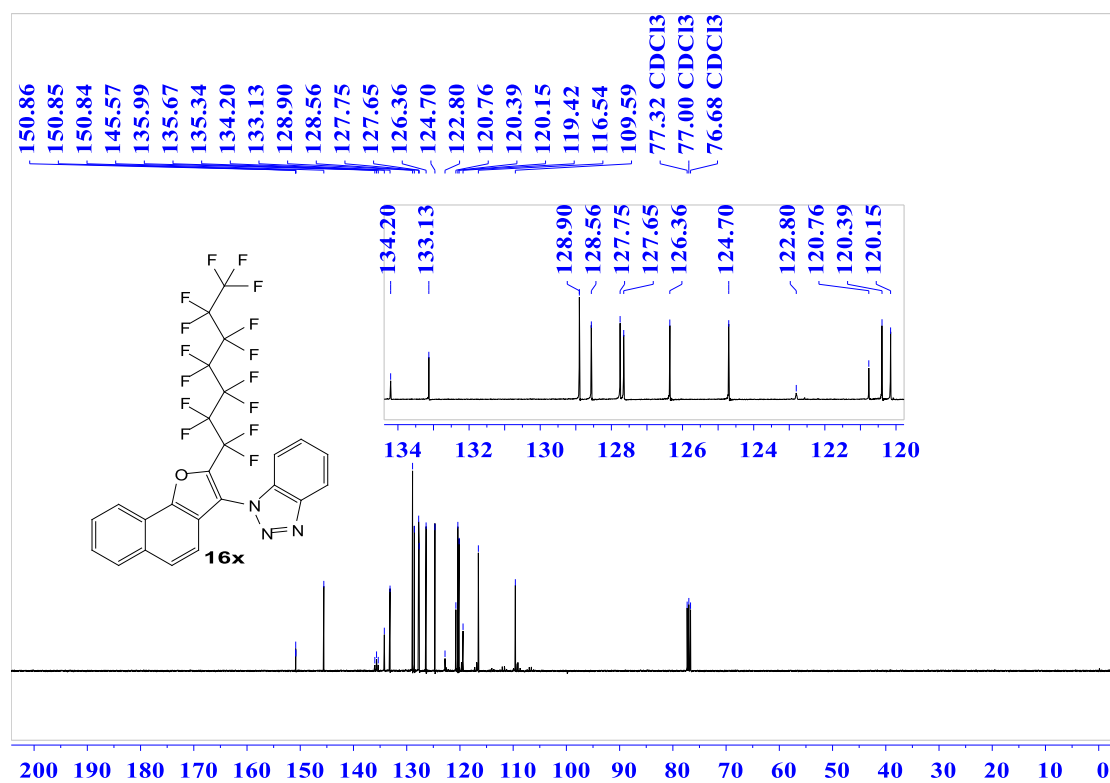


Figure S205. ¹H NMR spectrum of **16y**, related to Scheme 3.

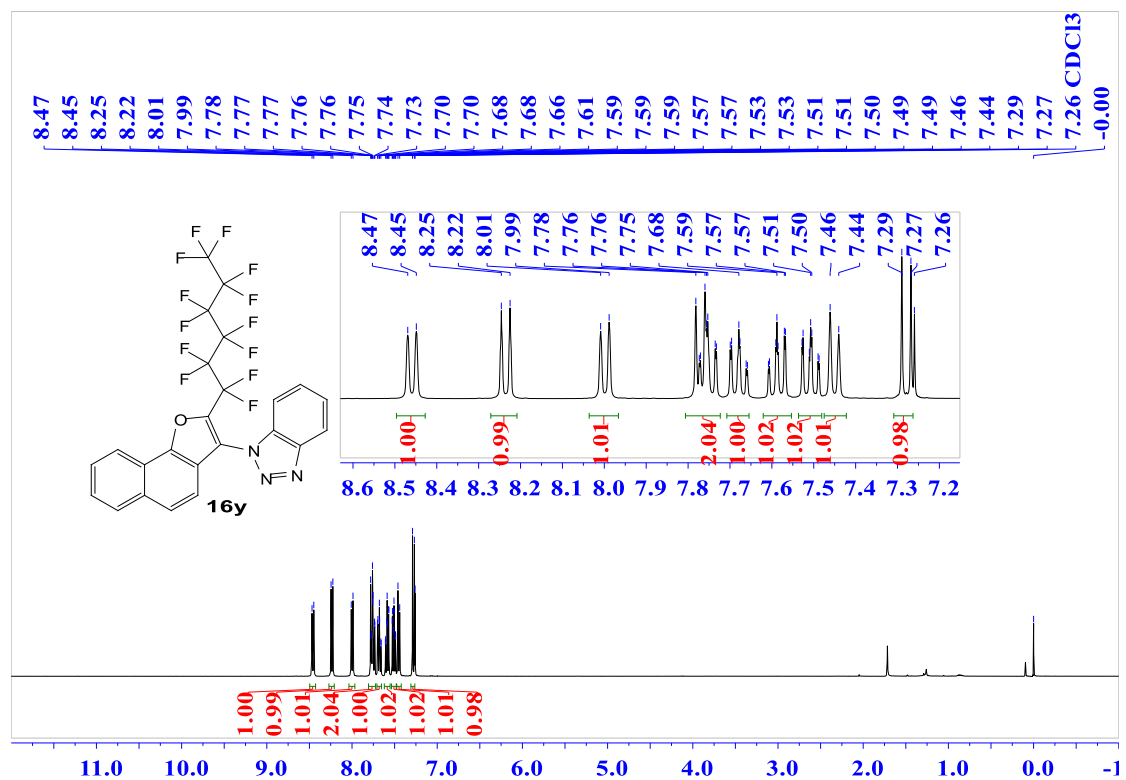


Figure S206. ¹⁹F NMR spectrum of **16y**, related to Scheme 3.

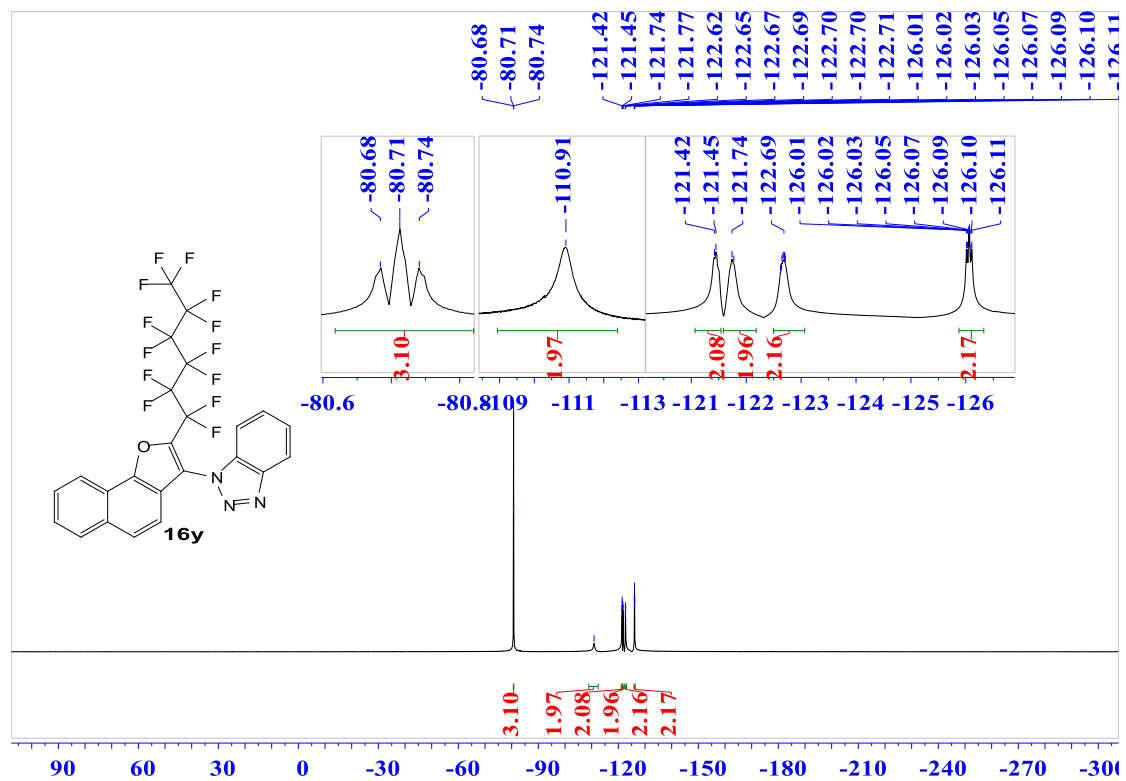


Figure S207. ^{13}C NMR spectrum of **16y**, related to Scheme 3.

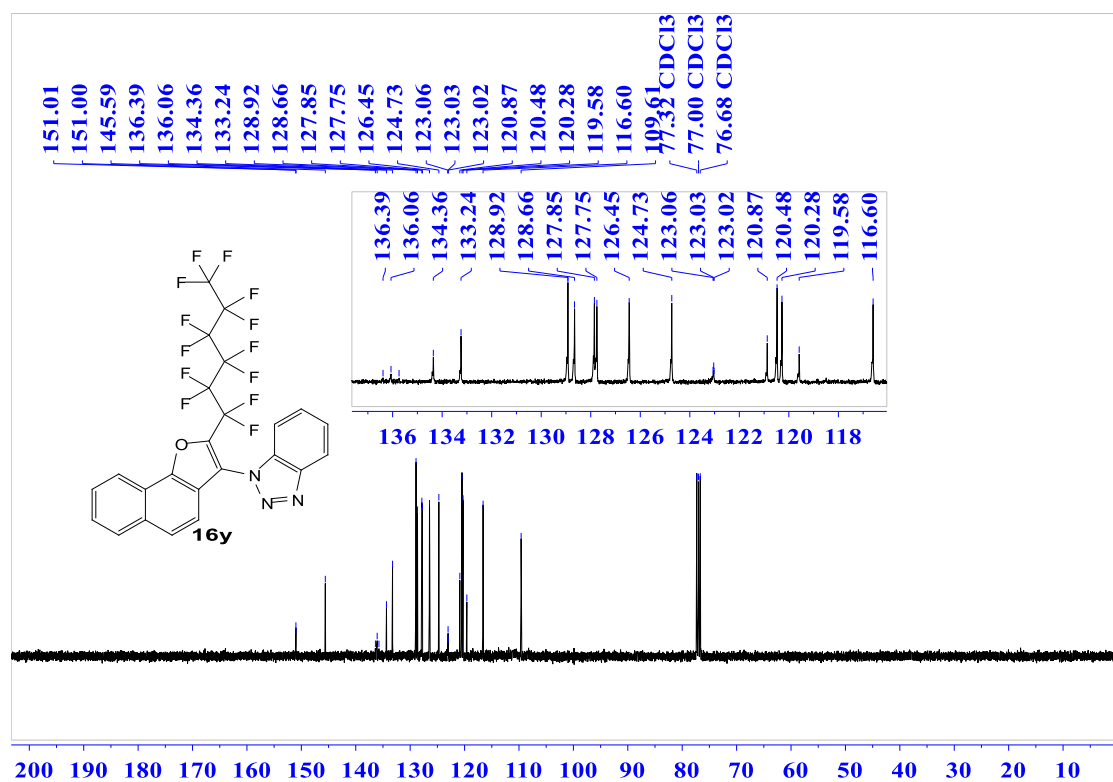


Figure S208. ^1H NMR spectrum of **16z**, related to Scheme 3.

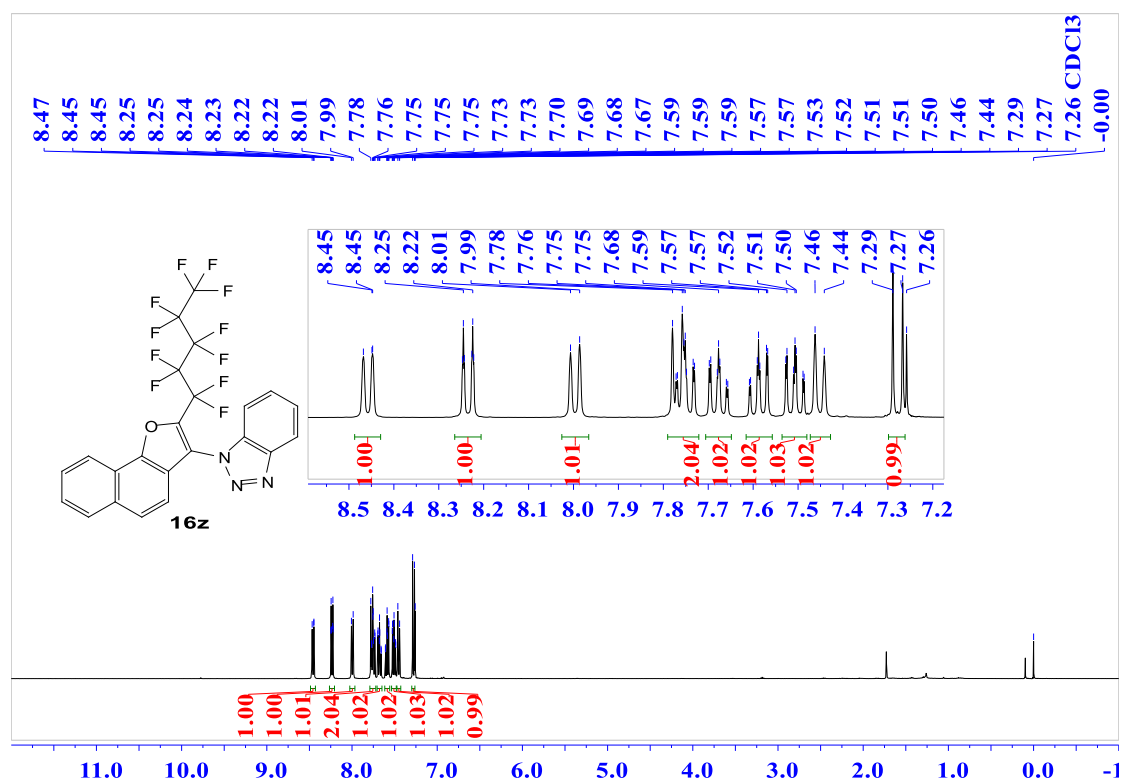


Figure S209. ¹⁹F NMR spectrum of **16z**, related to Scheme 3.

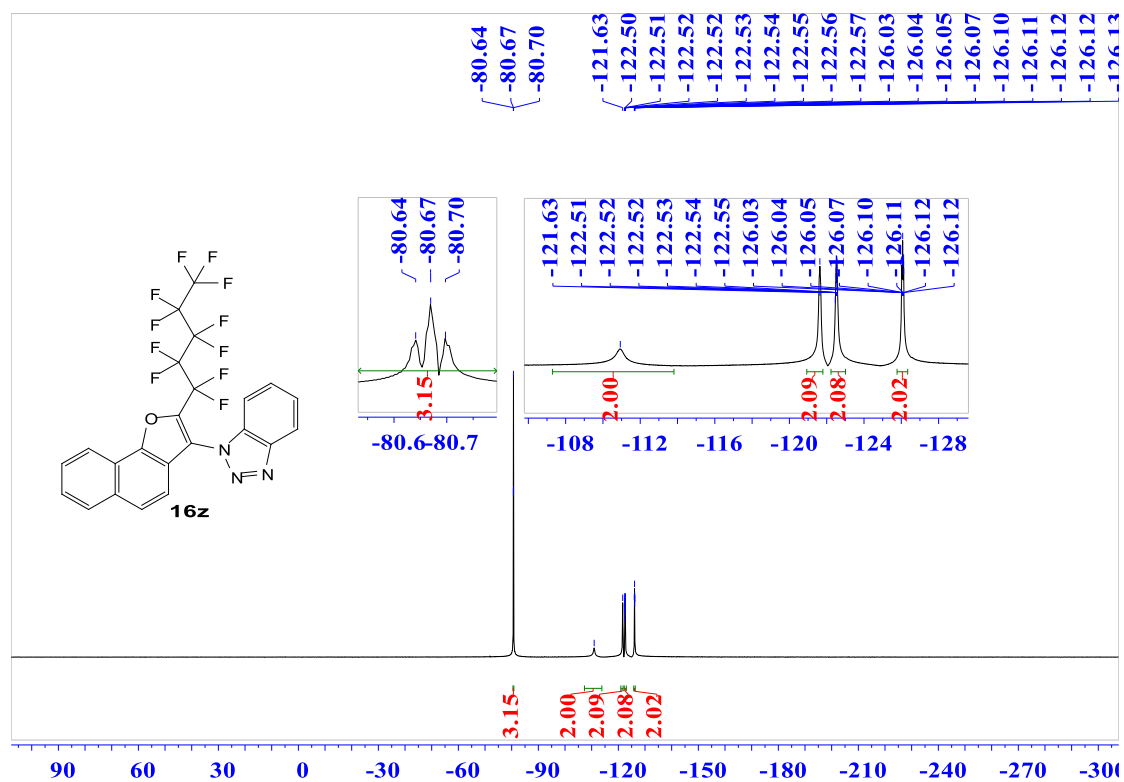


Figure S210. ¹³C NMR spectrum of **16z**, related to Scheme 3.

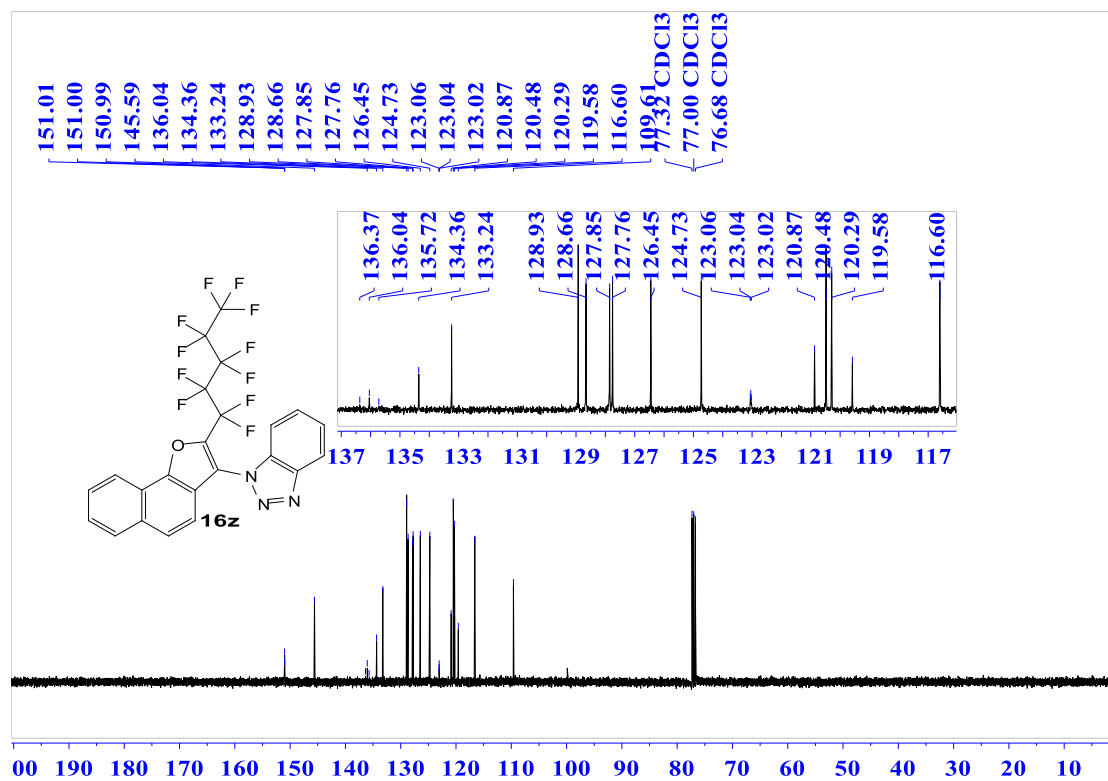


Figure S211. ¹H NMR spectrum of **16a'**, related to Scheme 3.

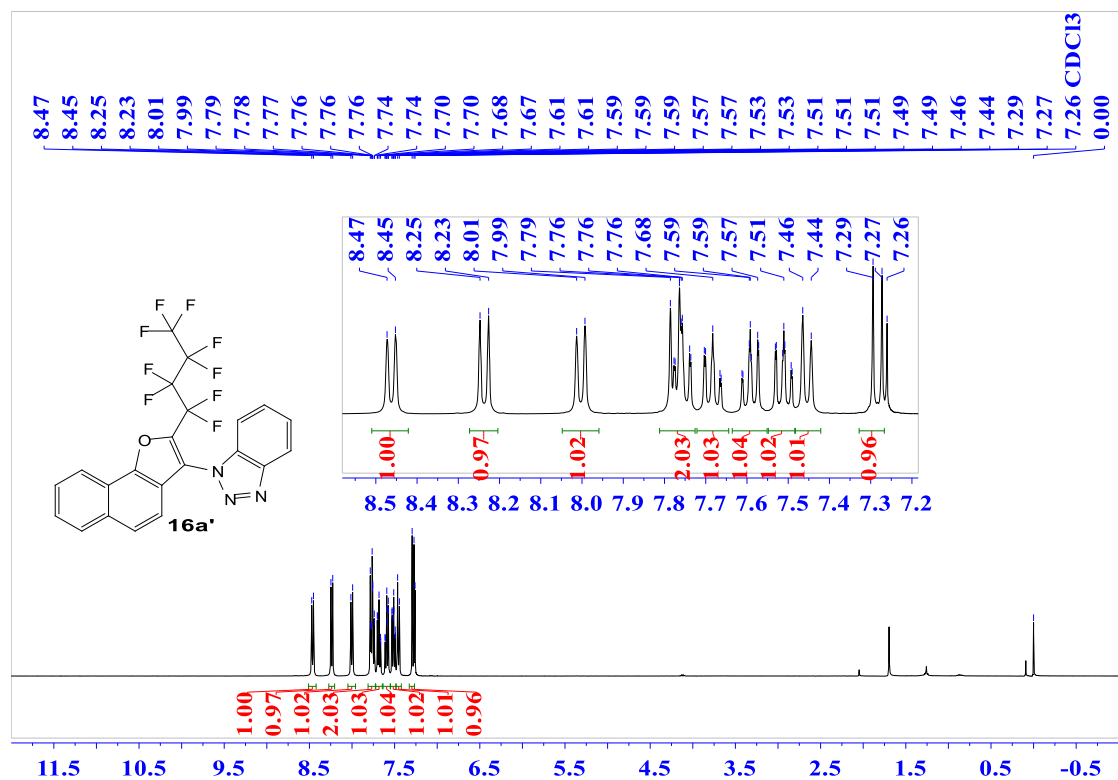


Figure S212. ¹⁹F NMR spectrum of **16a'**, related to Scheme 3.

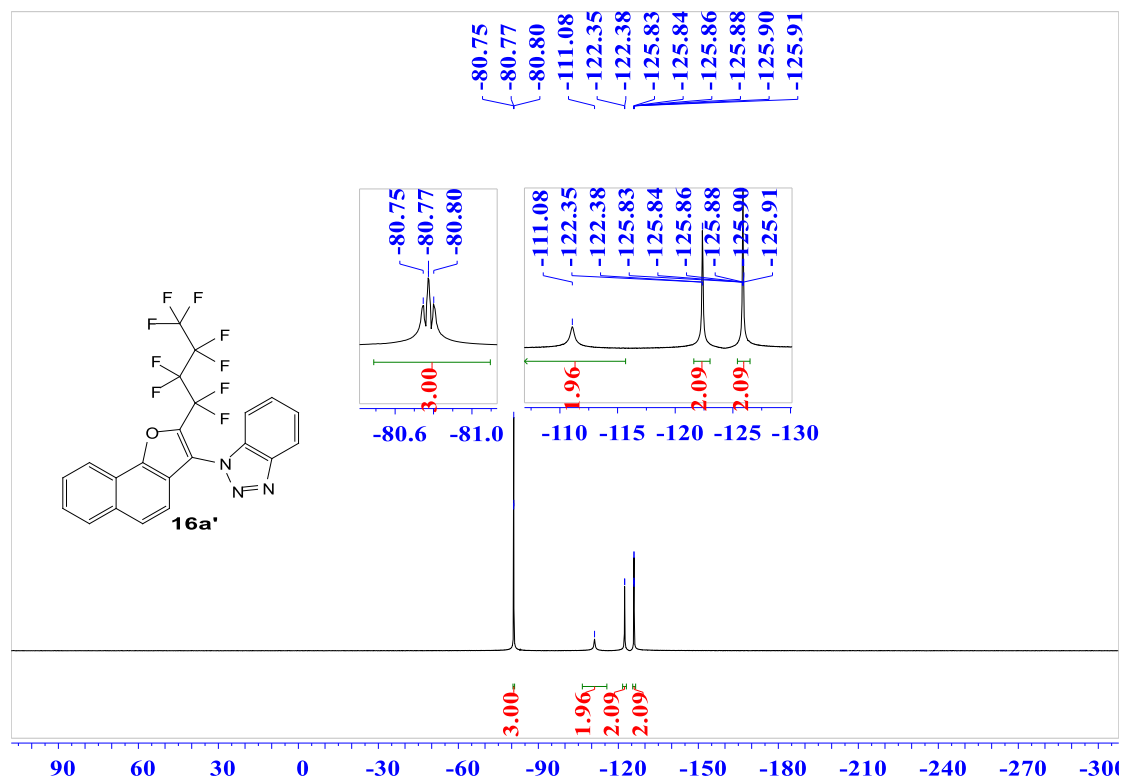


Figure S213. ^{13}C NMR spectrum of **16a'**, related to Scheme 3.

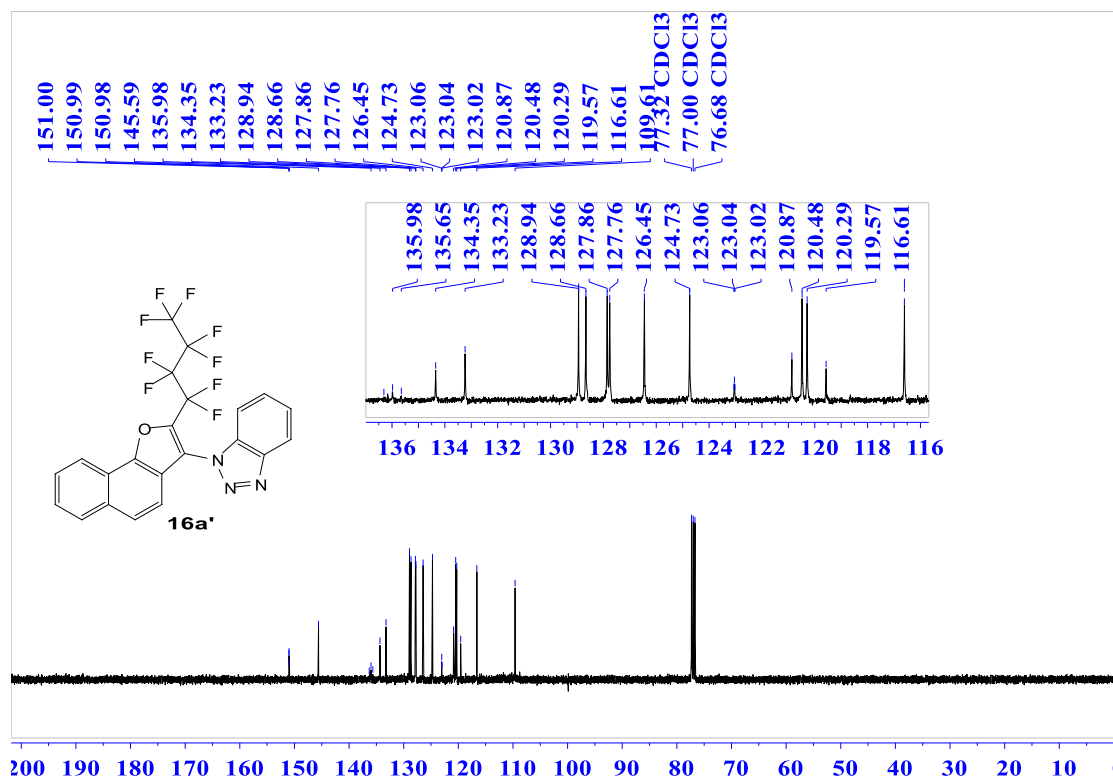


Figure S214. ^1H NMR spectrum of **16b'**, related to Scheme 3.

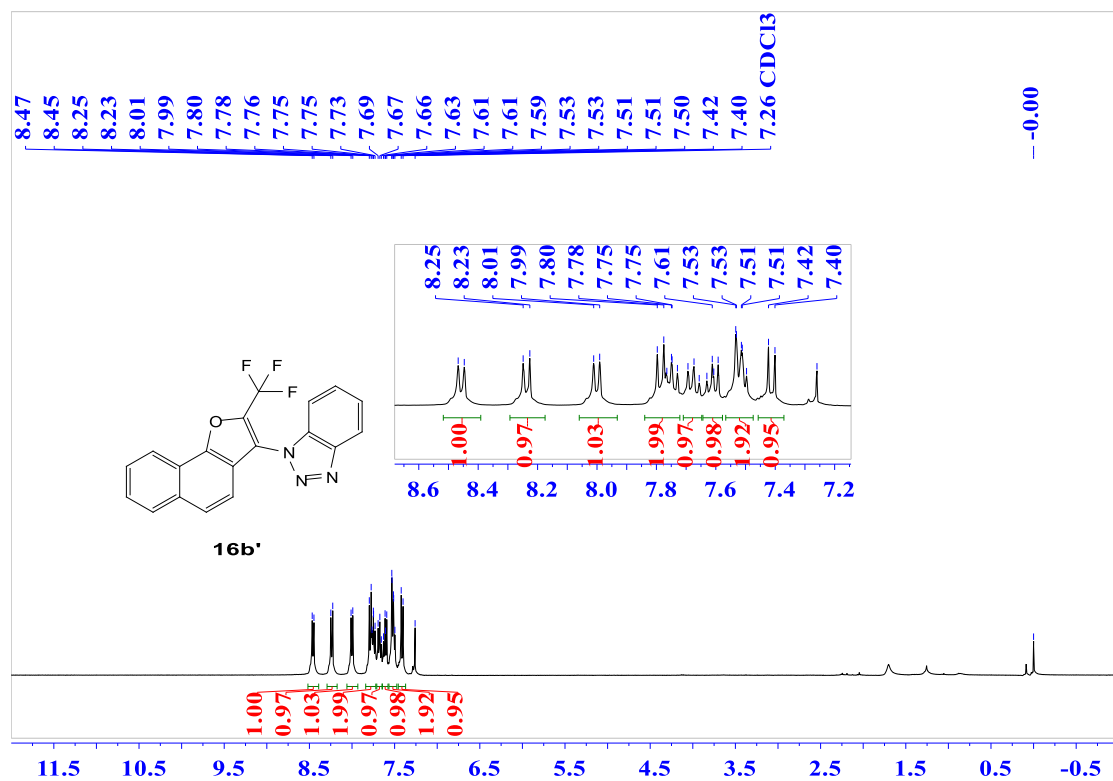


Figure S215. ^{19}F NMR spectrum of **16b'**, related to Scheme 3.

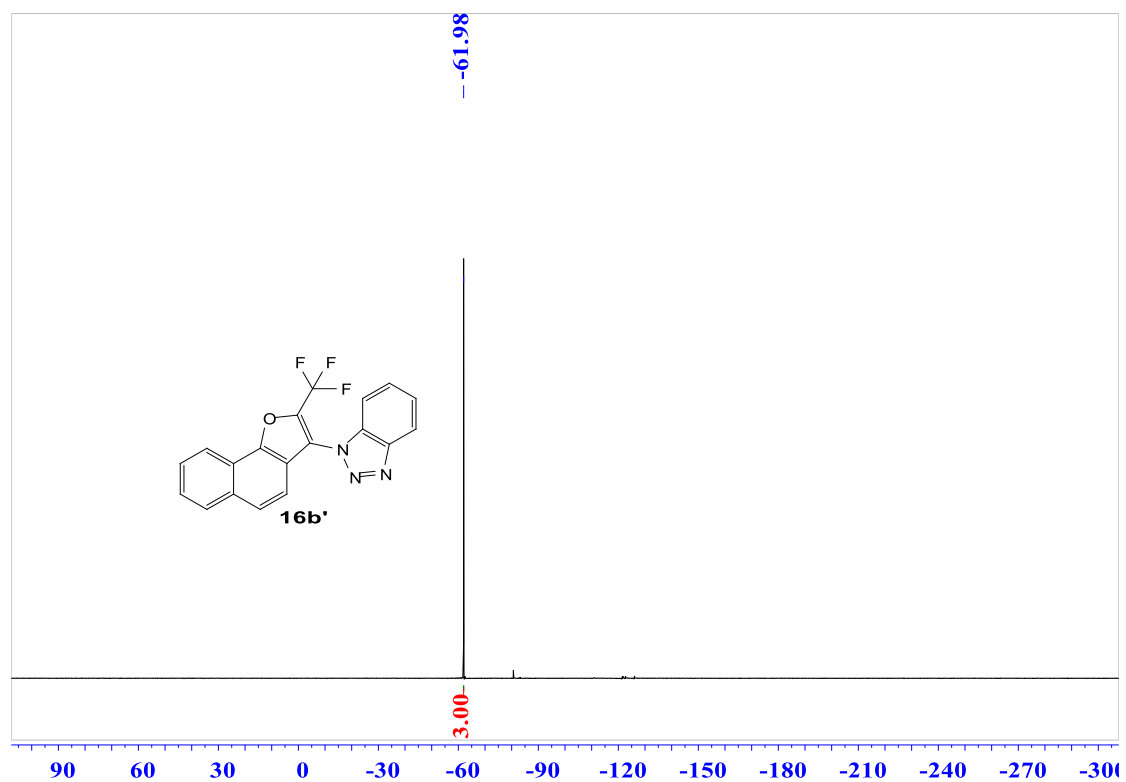


Figure S216. ^{13}C NMR spectrum of **16b'**, related to Scheme 3.

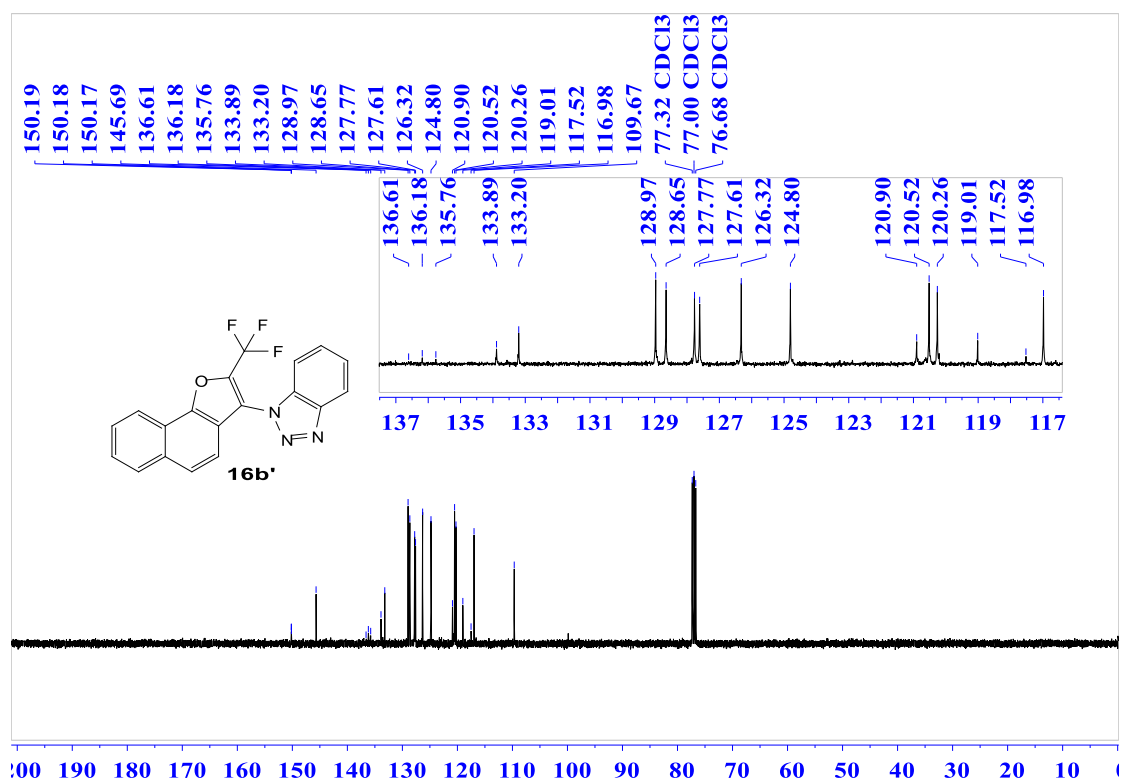


Figure S217. ¹H NMR spectrum of **17**, related to Scheme 4.

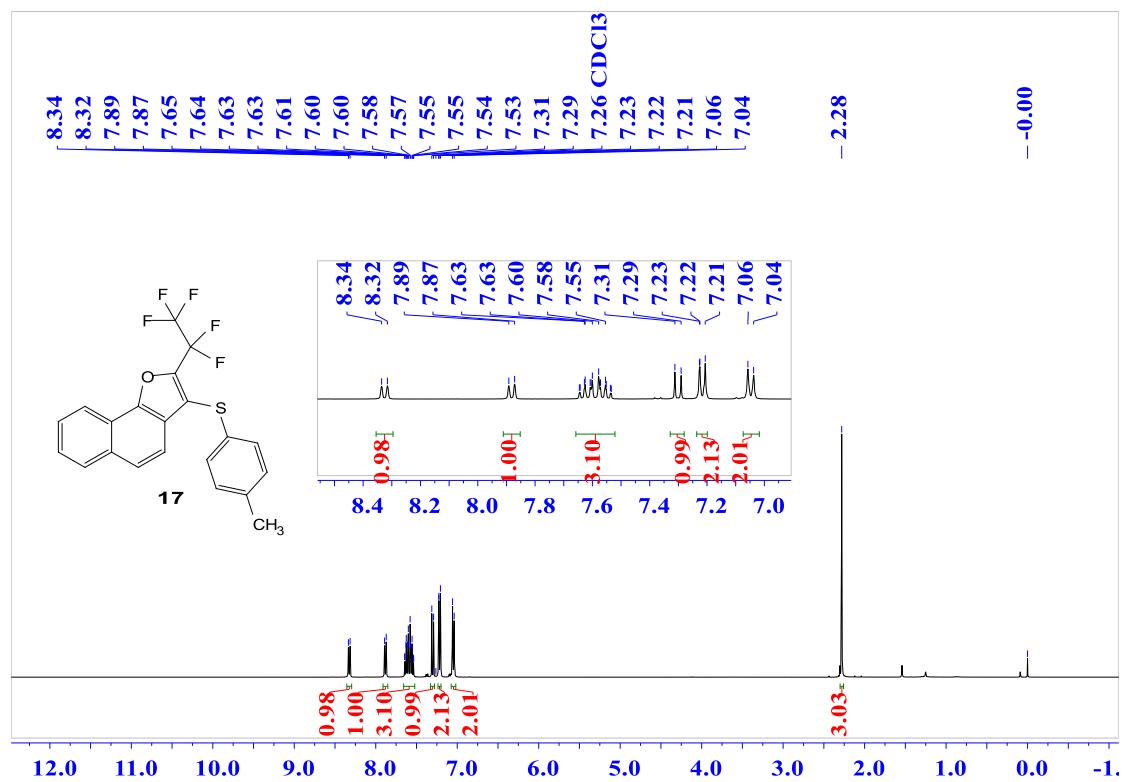


Figure S218. ¹⁹F NMR spectrum of **17**, related to Scheme 4.

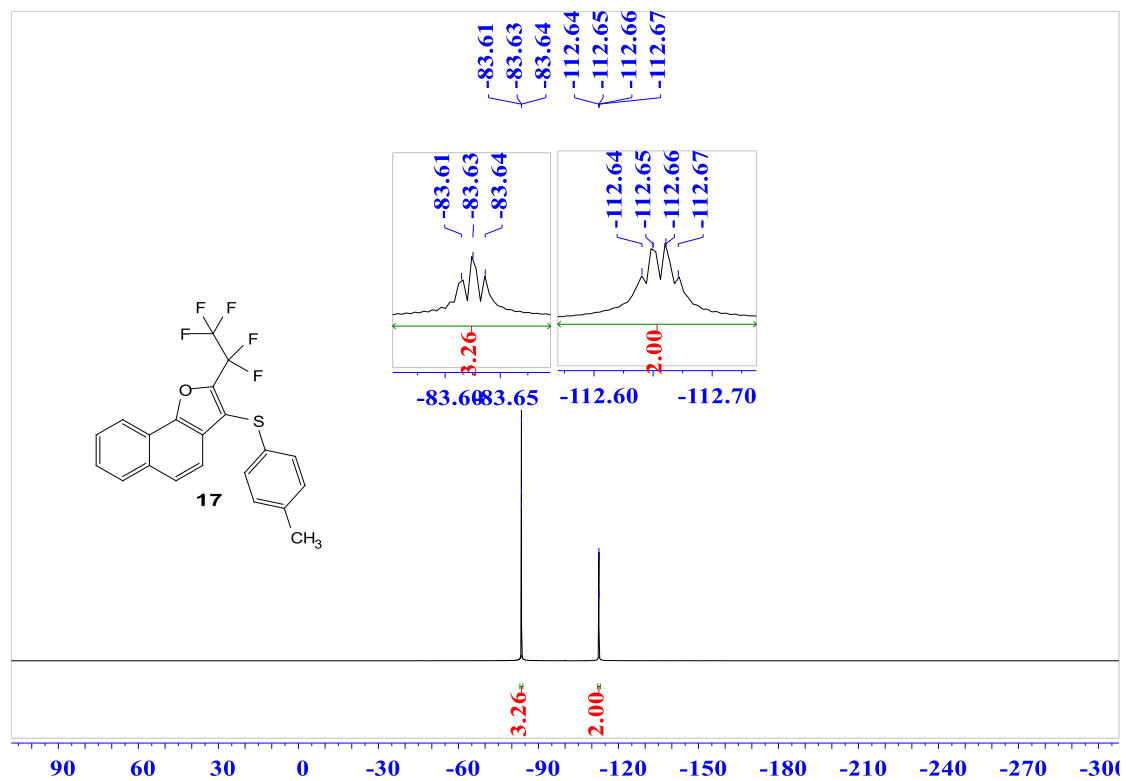


Figure S219. ¹³C NMR spectrum of **17**, related to Scheme 4.

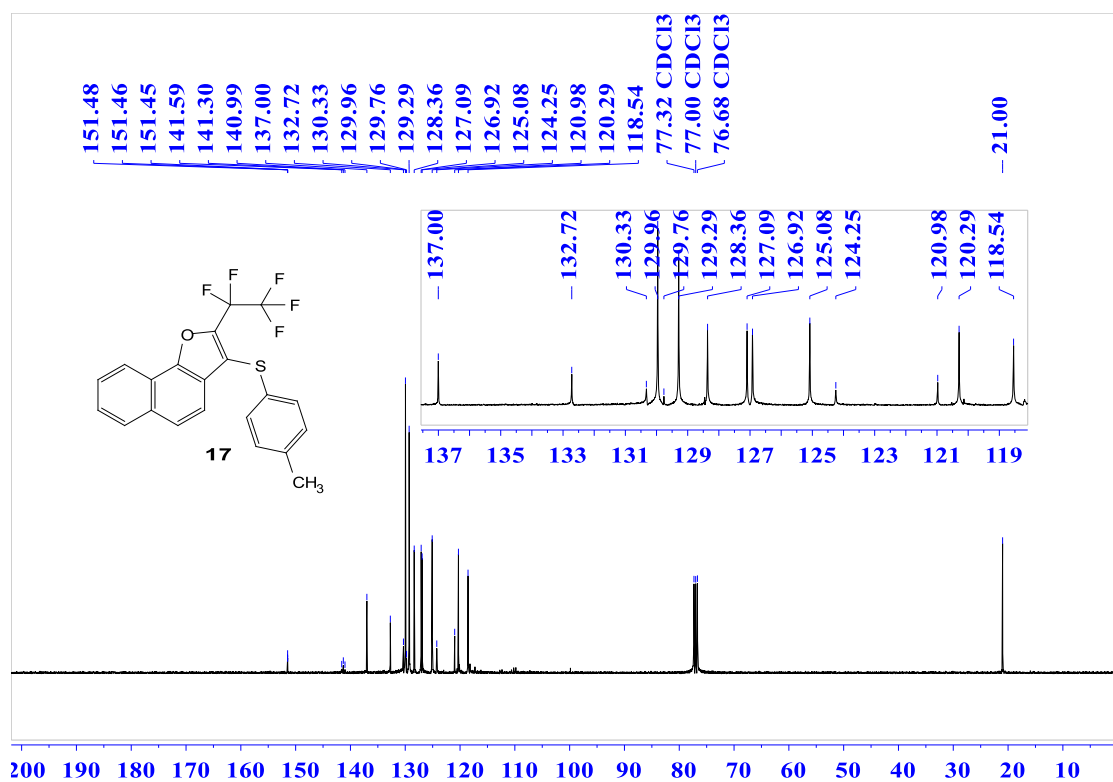


Figure S220. ¹H NMR spectrum of **18**, related to Scheme 4.

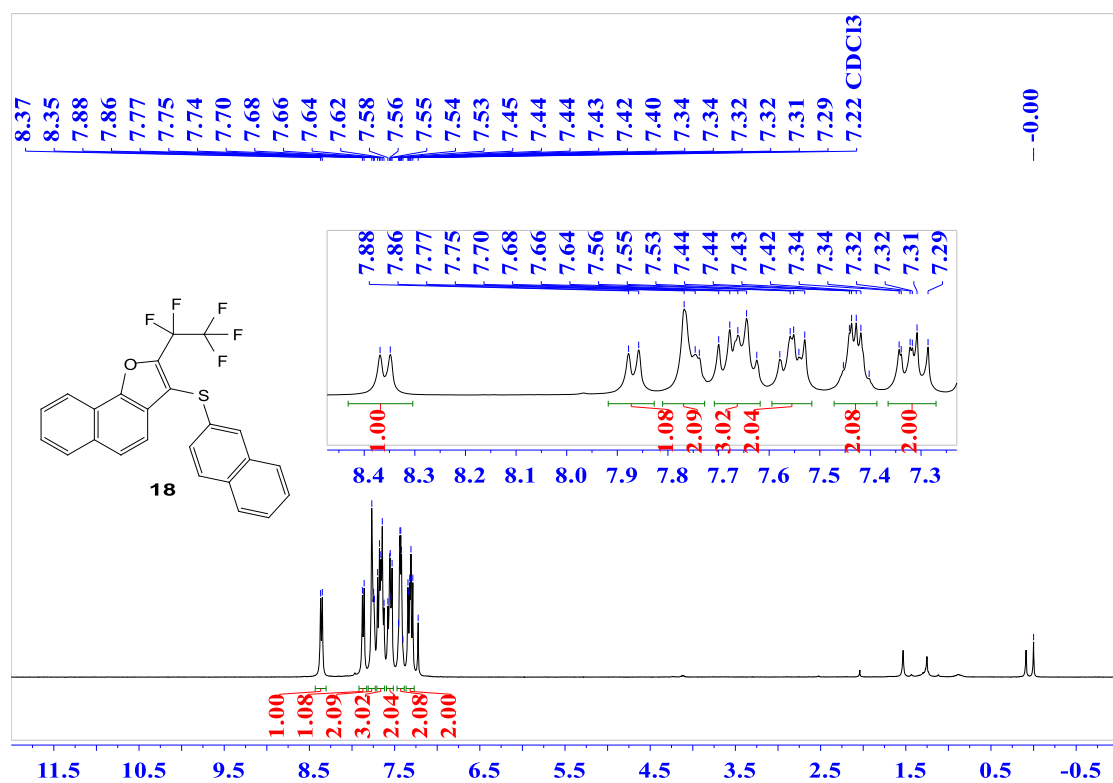


Figure S221. ¹⁹F NMR spectrum of **18**, related to Scheme 4.

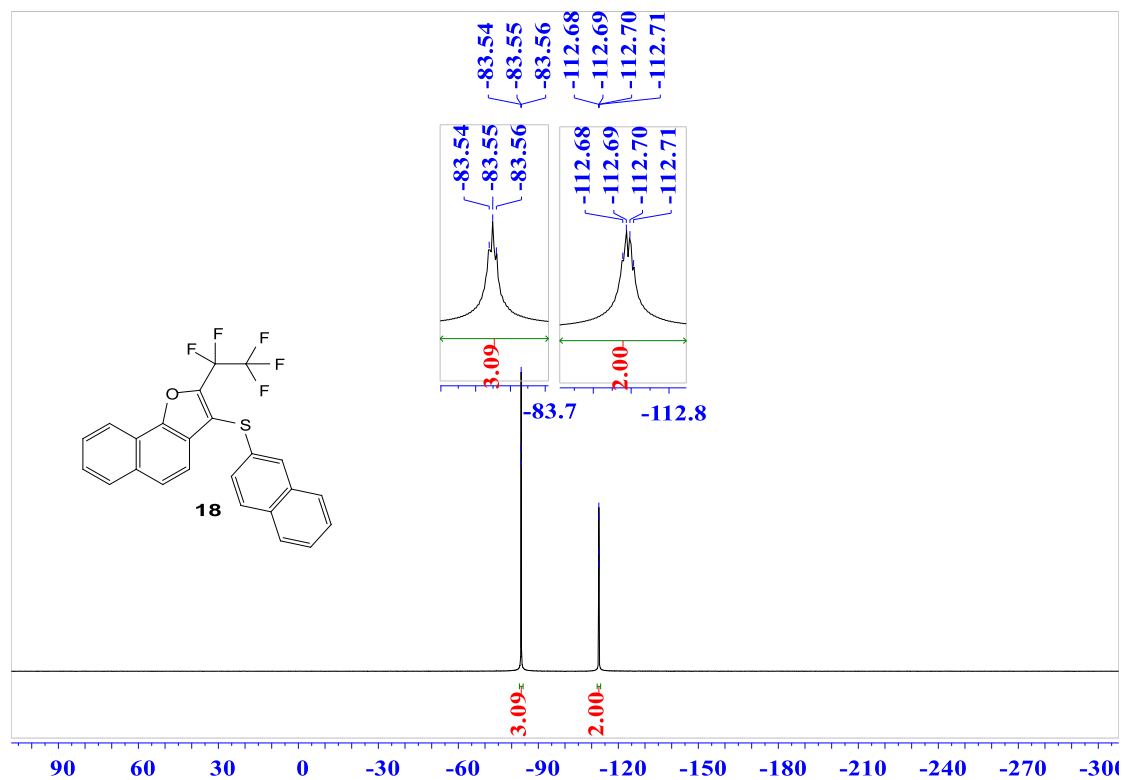


Figure S222. ¹³C NMR spectrum of **18**, related to Scheme 4.

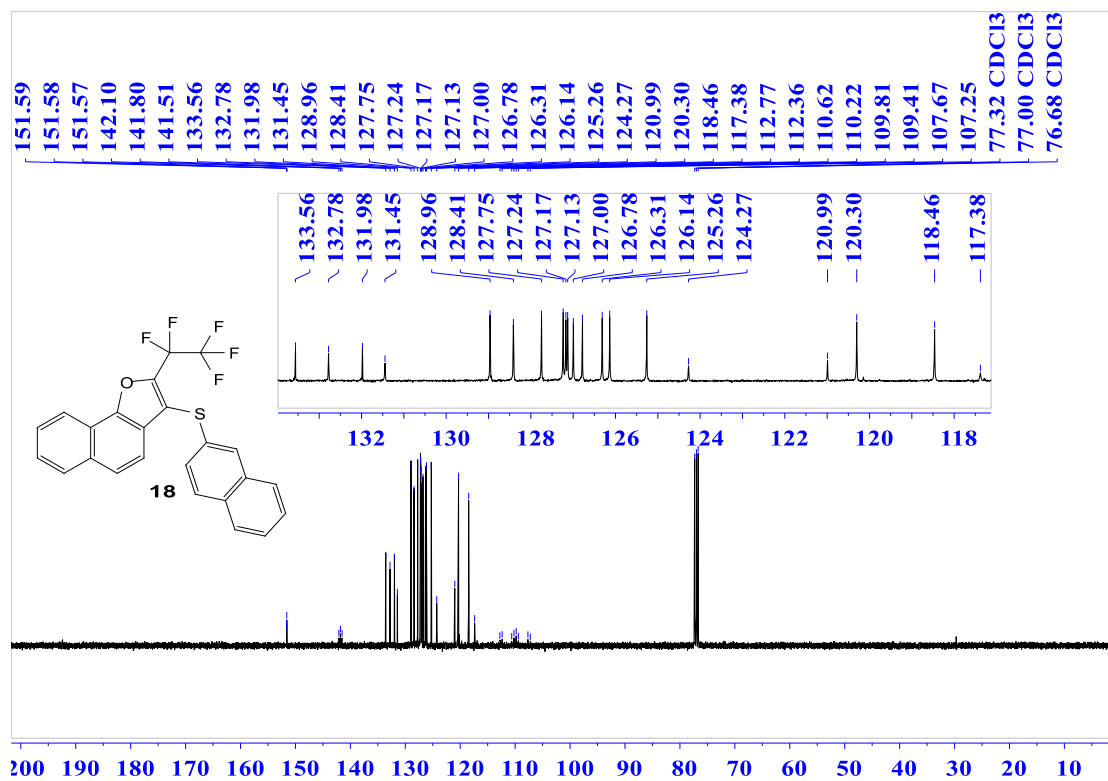


Figure S223. ¹H NMR spectrum of **19**, related to Scheme 4.

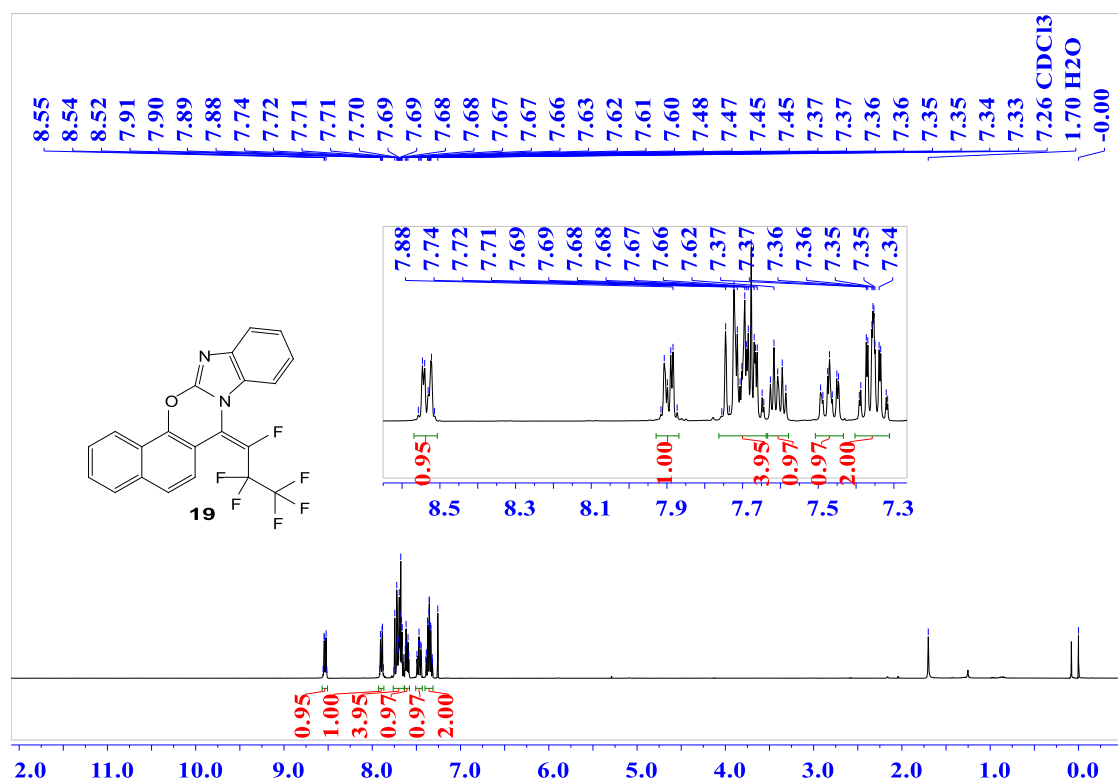


Figure S224. ¹⁹F NMR spectrum of **19**, related to Scheme 4.

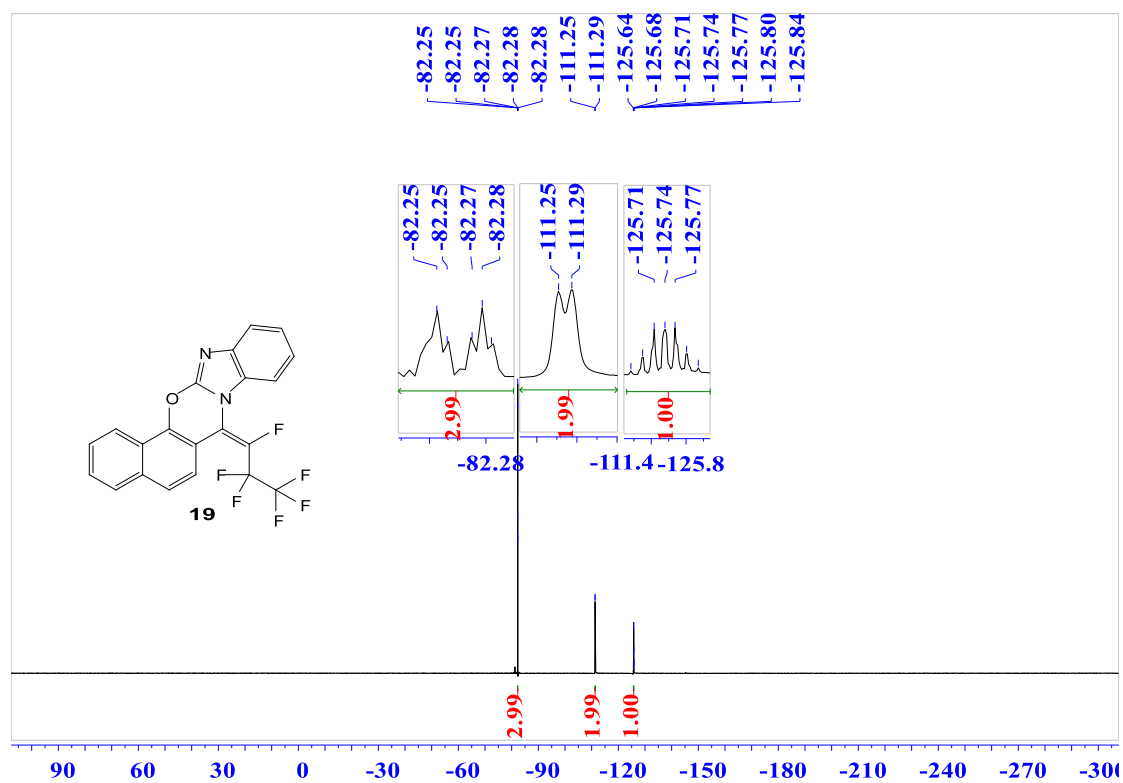


Figure S225. ¹³C NMR spectrum of **19**, related to Scheme 4.

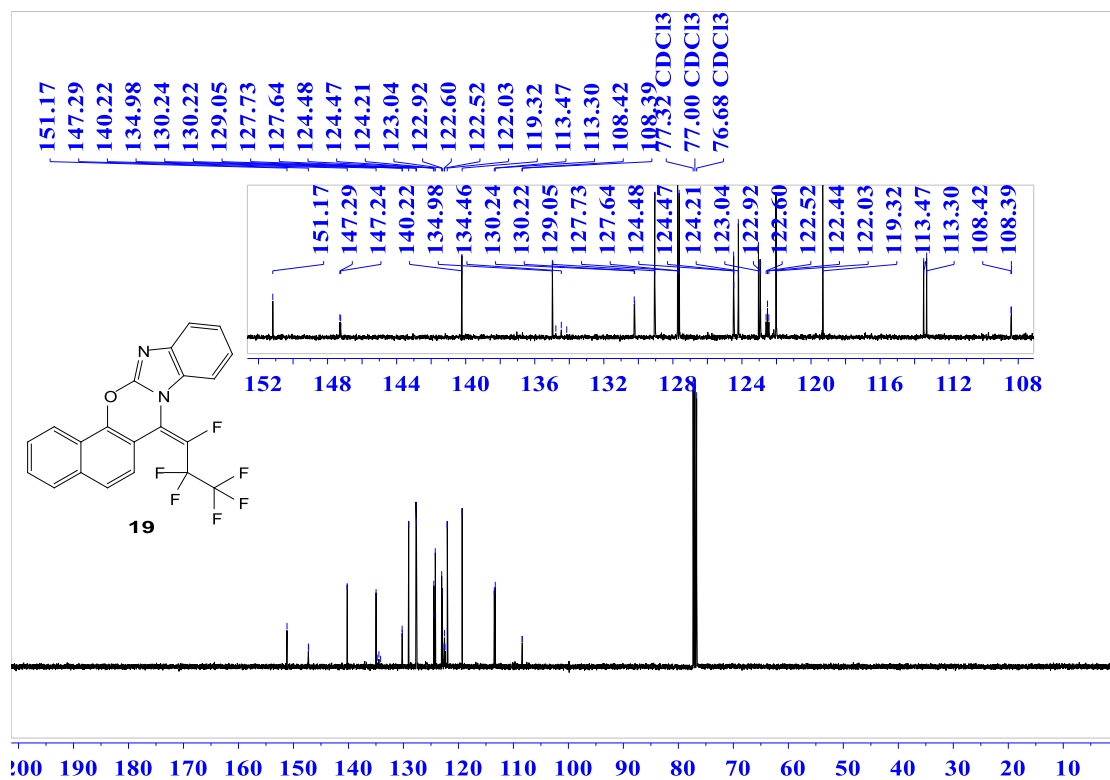


Figure S226. ¹H NMR spectrum of **20**, related to Scheme 4.

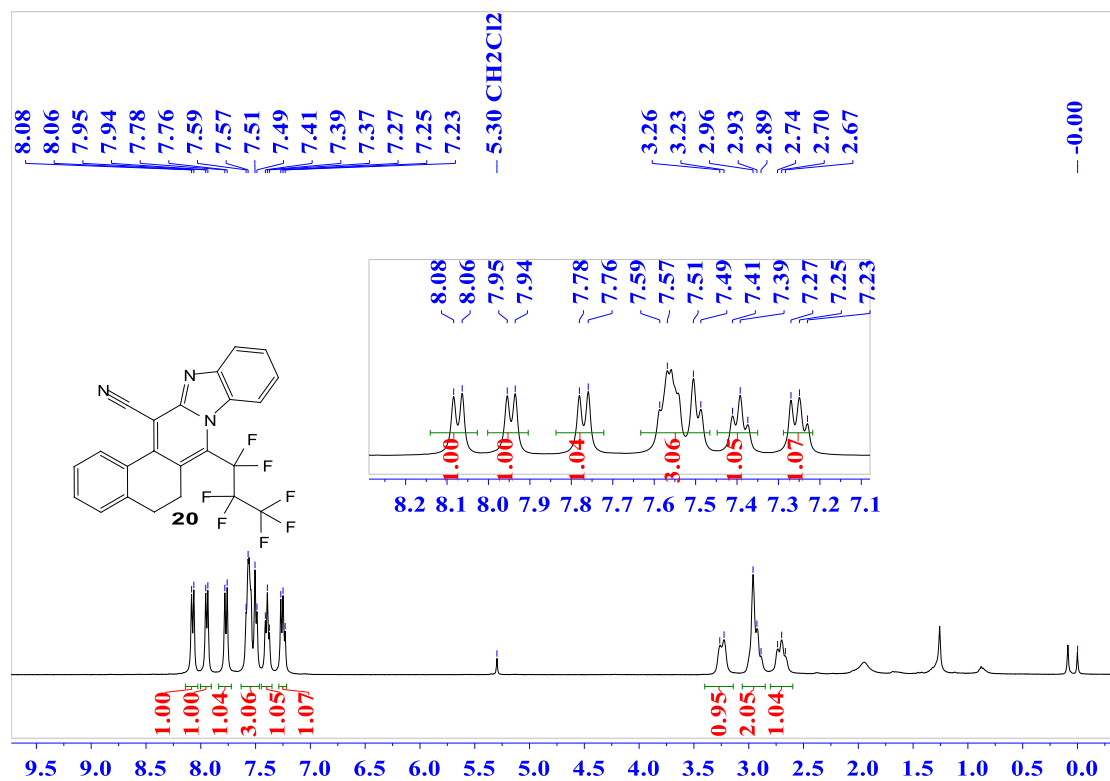


Figure S227. ^{19}F NMR spectrum of **20**, related to Scheme 4.

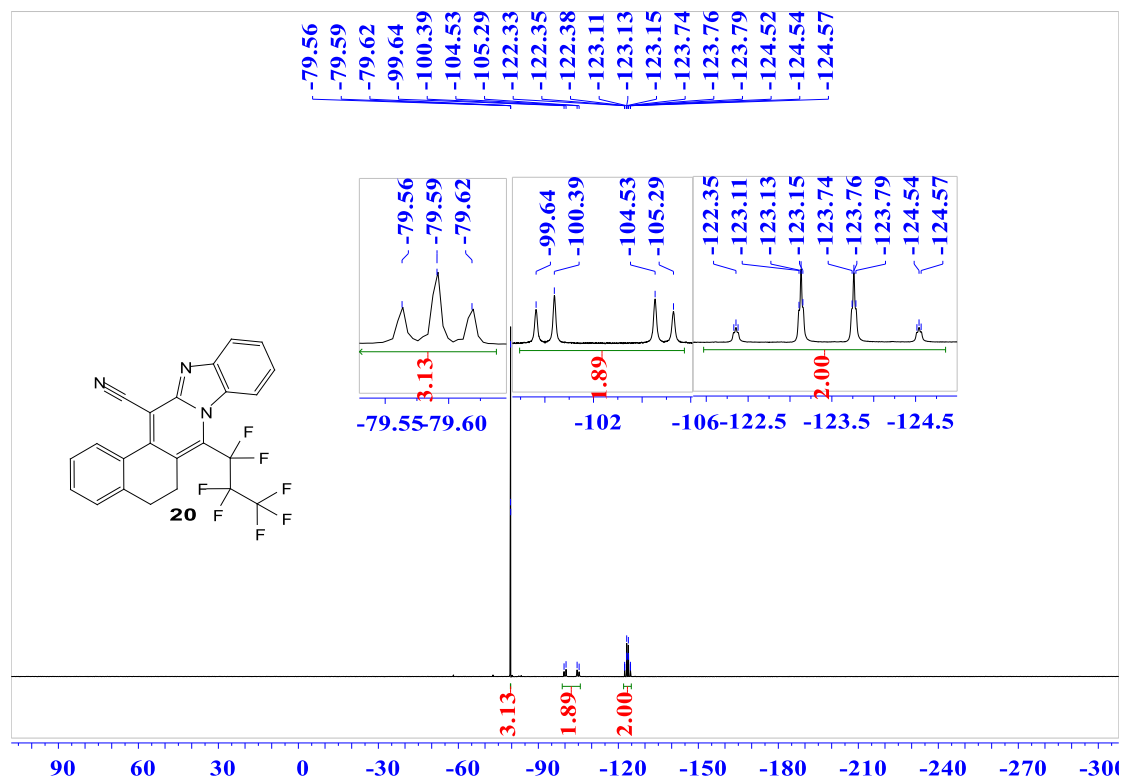


Figure S228. ^{13}C NMR spectrum of **20**, related to Scheme 4.

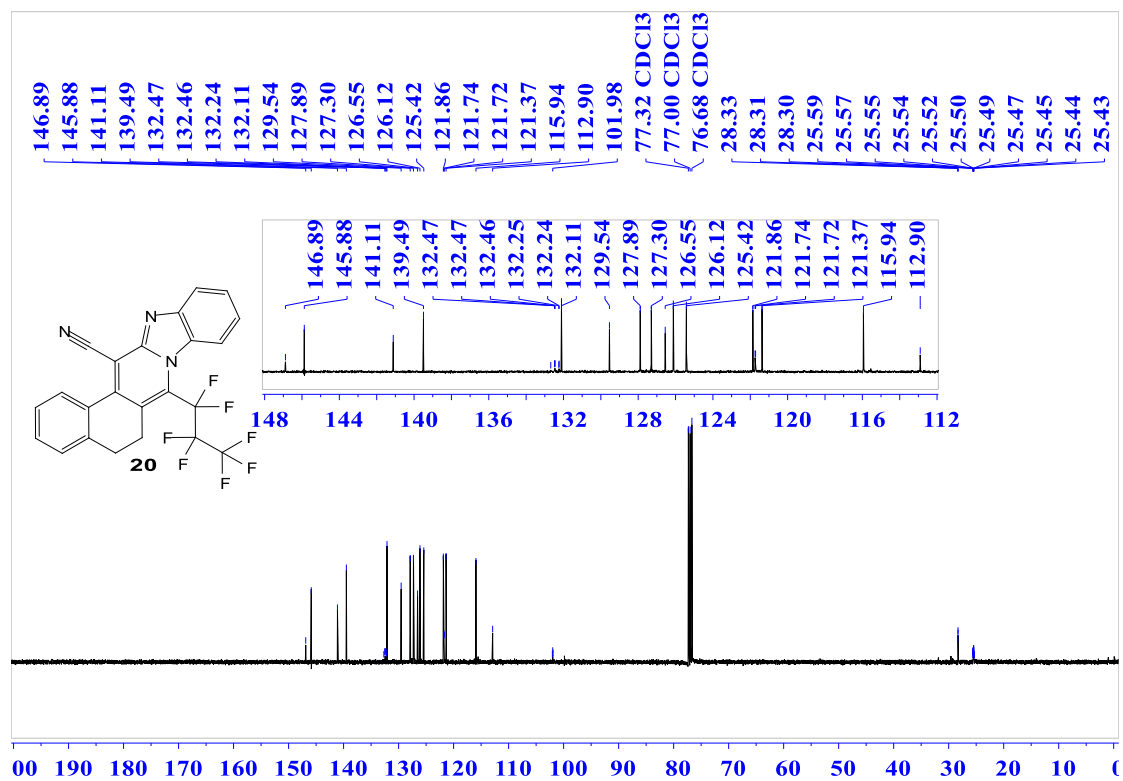


Figure S229. ¹H NMR spectrum of **21**, related to Scheme 4.

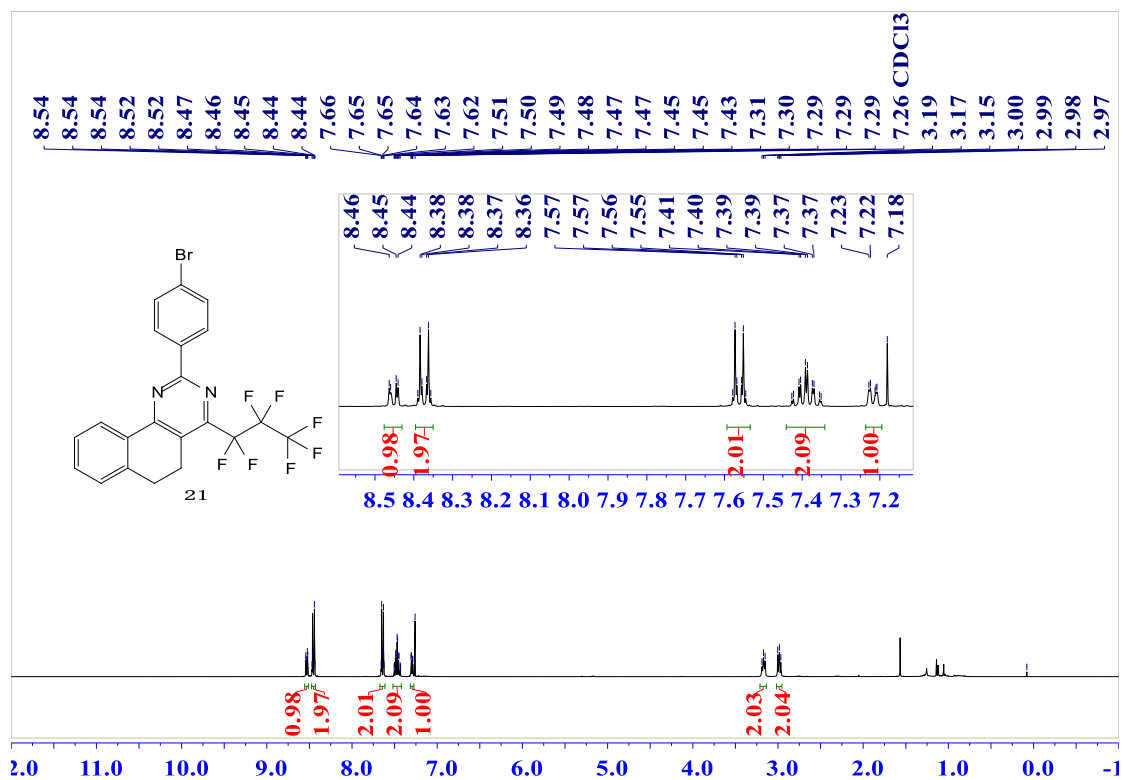


Figure S230. ¹⁹F NMR spectrum of **21**, related to Scheme 4.

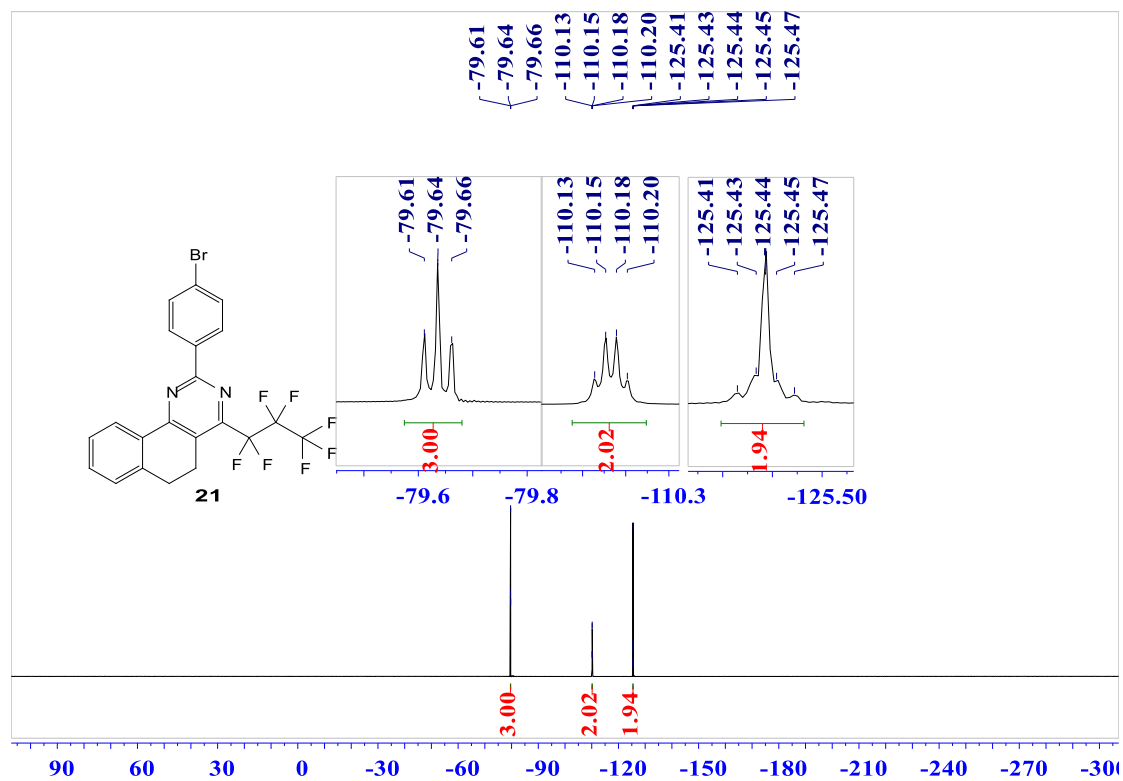
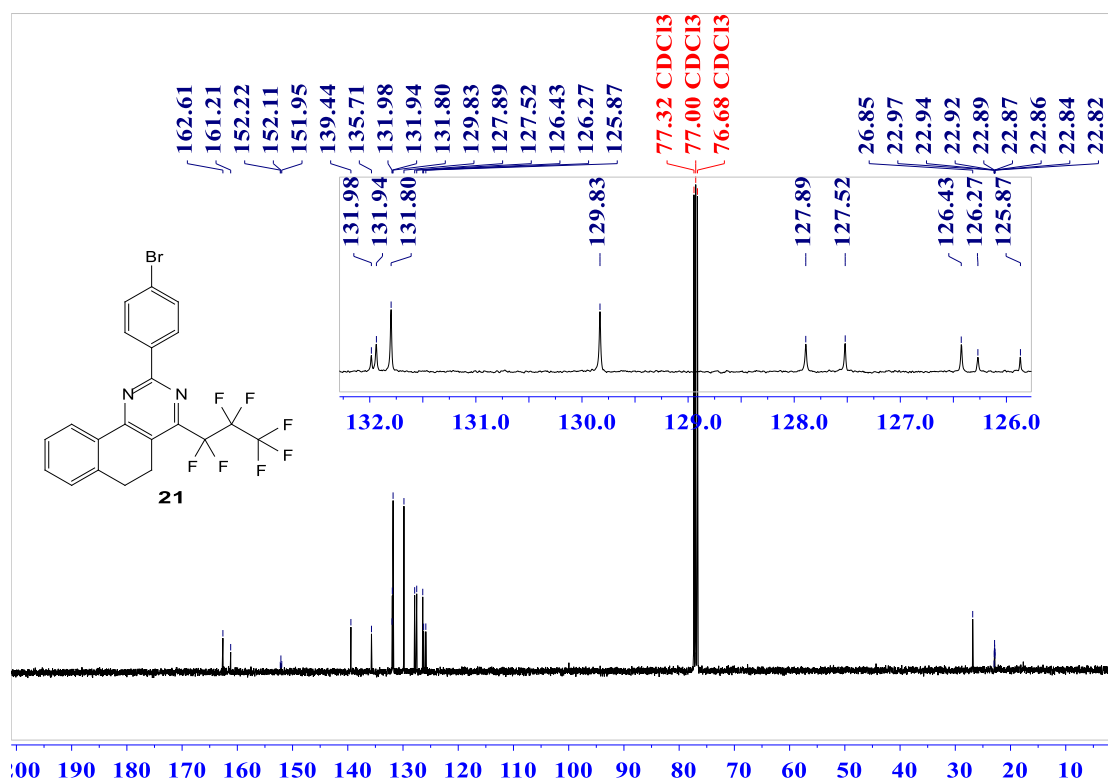
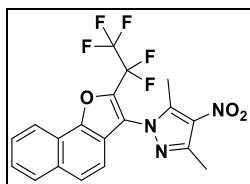


Figure S231. ^{13}C NMR spectrum of **21**, related to Scheme 4.



Supplemental figures for X-Ray structures

Figure S232. X-Ray crystal data of **6b**, related to **Figure 2**.



Compound: 3,5-dimethyl-4-nitro-1-(2-(perfluoroethyl)naphtho[1,2-b]furan-3-yl)-1H-pyrazole (**6b**)

Crystal Number: CCDC 1881997

Chemical Formula: C₁₉H₁₂F₅N₃O₃

Formula weight: 425.3150

Space Group: P 21/c

Cell: a = 18.612(4) b = 13.533(3) c = 7.5759(17)

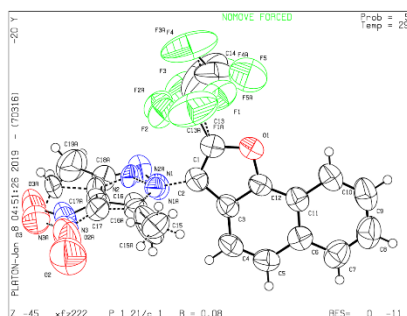
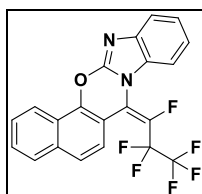


Figure S233. X-Ray crystal data of **19**, related to **Figure 2**.



Compound: (Z)-7-(perfluoropropylidene)-7H-benzo[4,5]imidazo[2,1-b]naphtho[2,1-e][1,3]oxazine (**19**)

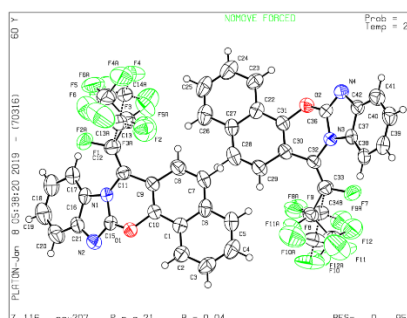
Crystal Number: CCDC 1881996

Chemical Formula: C₂₁H₁₀F₆N₂O

Formula weight: 420.3144

Space Group: P n a 21

Cell: a = 8.920(8) b = 12.280(11) c = 32.31(3)



Notice: these structures were collected at room temperature, where the disorder in the fluorinated groups is severe and can hardly be modelled.

Supplemental figures for computational details and discussion

All calculations were performed with the Gaussian 09 package (Frischet al., 2013). Geometry optimizations and frequency calculations were performed at the UB3LYP (Becke, 1988; Lee et al., 1988; Becke, 1993)/def2-SVP level (Weigend et al., 2005) in conjunction with the polarizable continuum model (PCM) (Tomasi et al. 1994) to account for the solvation effects of dimethyl sulfoxide (DMSO). To get more accurate energies, single point energies were computed at the UB3LYP/def2-TZVP (Weigend et al., 2005) level combined with Grimme's DFT empirical dispersion correction (DFT-D3) for all the species (Grimme et al., 2010; Goerigk et al., 2011). The 3D structures of the optimized species were generated using CYLview (Legault, 2009). Activation free energy barriers reported here are defined as the free energy difference between the transition state and the lowest-energy stationary point or separated reactants before it along the reaction pathways.

Figure S234. 3D structures of the species involved in the Cs_2CO_3 -mediated four $\text{C}(\text{sp}^3)$ -F bonds cleavage and C-N/O coupling reaction of **1c'** and **2a**, related to **Figure 3** and **4**.

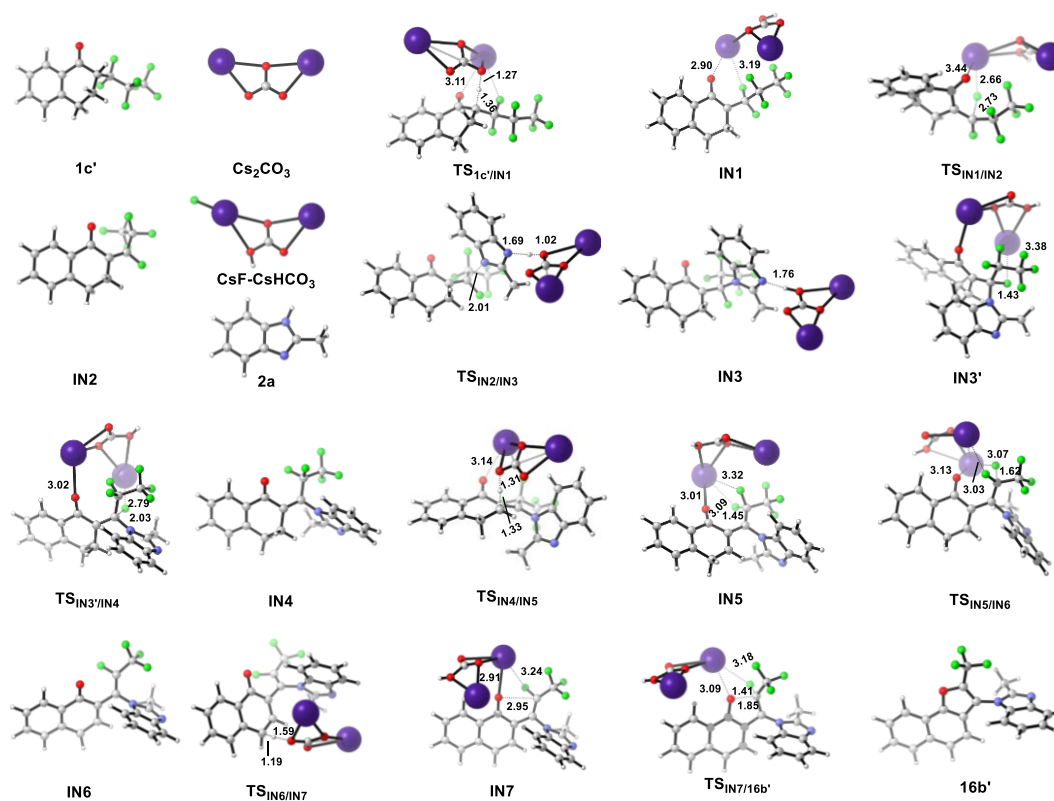


Figure S235. Transition state structures of Cs₂CO₃-mediated nucleophilic addition of **2a** to **IN2** without or with CoBr₂, related to **Figure 3** and **4**.

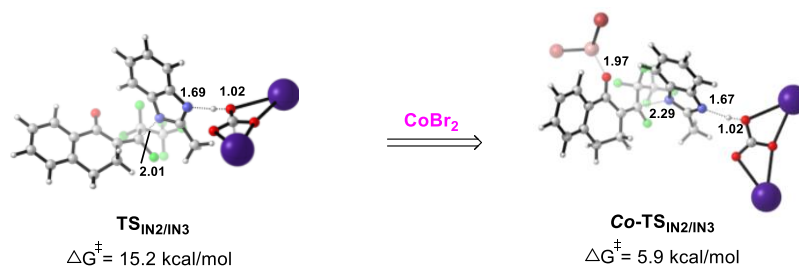


Figure S236. Transition state structures of Cs₂CO₃-mediated intramolecular cyclization reaction of **IN7** without or with CoBr₂, related to **Figure 3** and **4**.

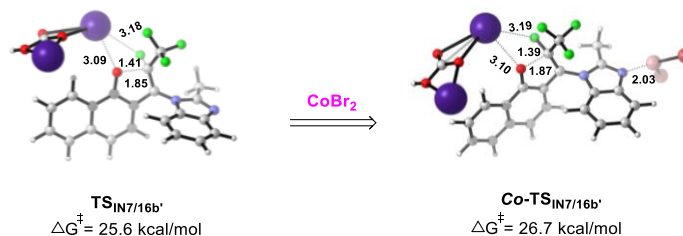
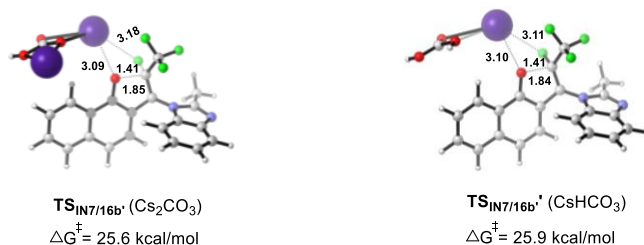


Figure S237. Cs₂CO₃- and CsHCO₃-mediated intramolecular cyclization reaction of **IN7**, related to **Figure 3** and **4**.



The CsHCO₃-mediated intramolecular cyclization reaction of **IN7** (rate-limiting step) was also investigated. As shown in Figure S237, the corresponding transition states, **TS_{IN7/16b'}** and **TS_{IN7/16b'}**, have almost similar activation barriers with Cs₂CO₃ and CsHCO₃. This result indicates that the base does not have significant influence on this process.

Figure S238. Various α -perfluoroalkyl ketones, related to Scheme 1-5.

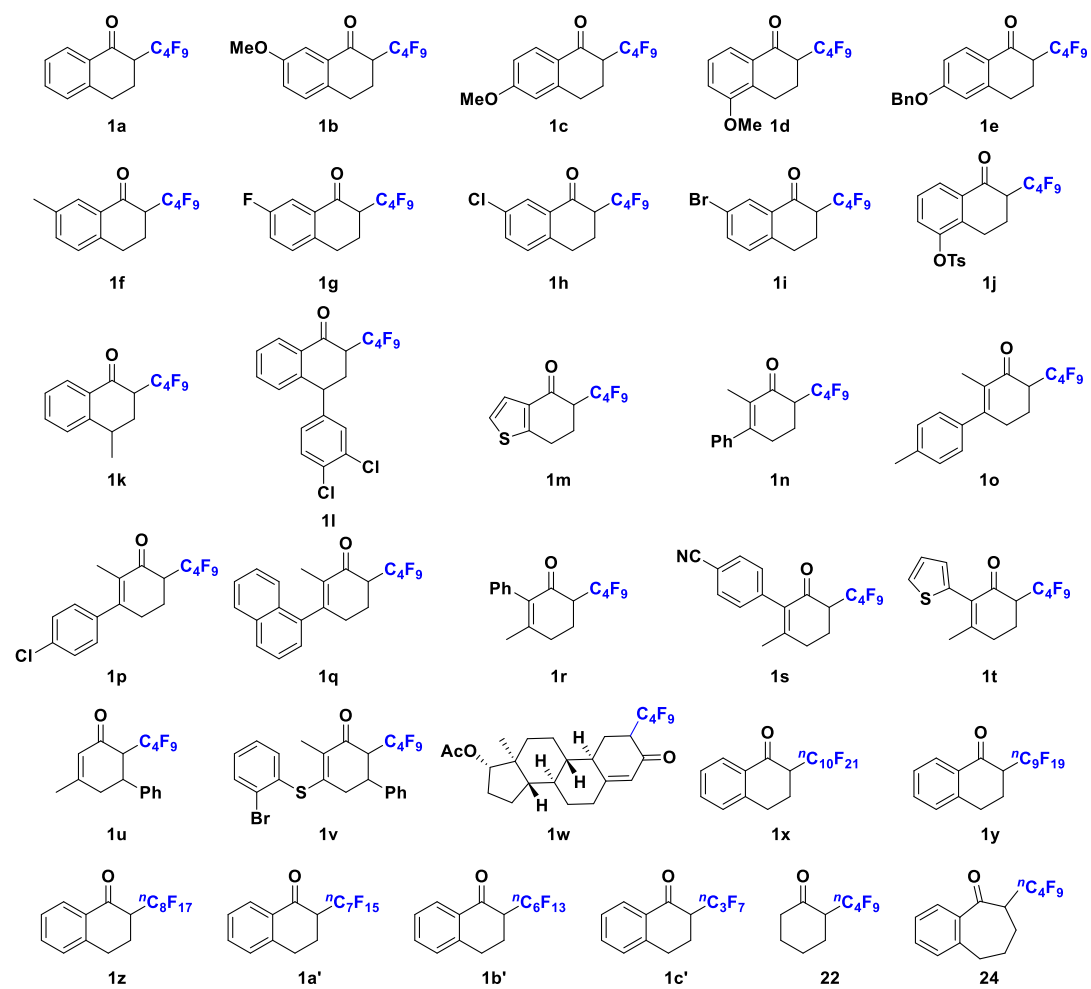
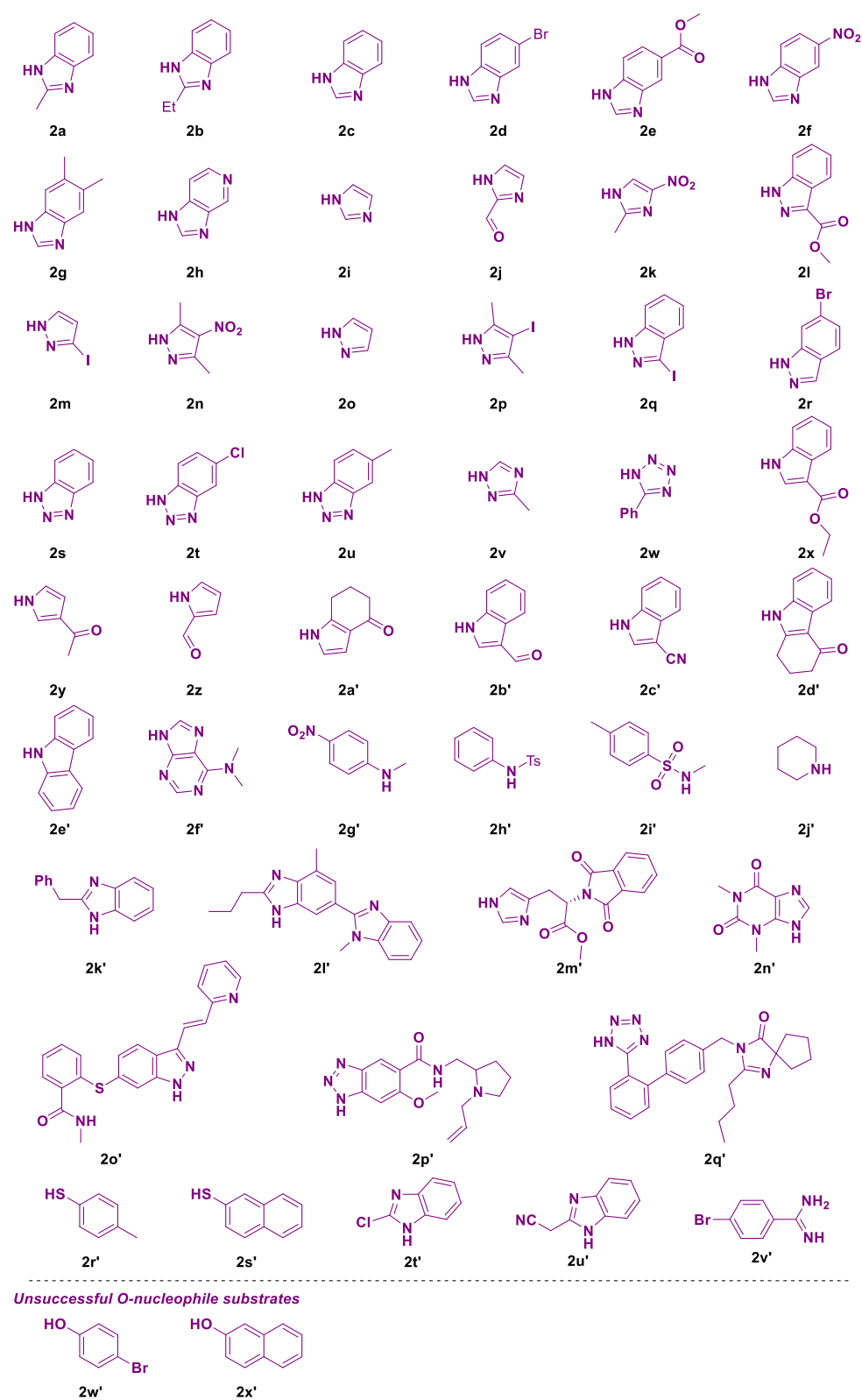
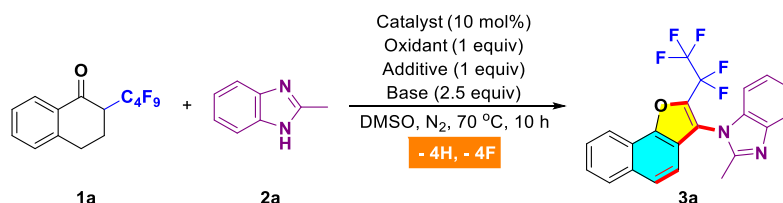


Figure S239. Various nucleophiles, related to Scheme 1-5.



Optimization of reaction conditions

Table S1. Initial attempts for the designed reaction^[a], related to **Table 1**.



Entry	Catalyst	Additive	Oxidant	Base	Yield of 3a (%) ^[b]
1	CoBr ₂	TBAB	K ₂ S ₂ O ₈	Cs ₂ CO ₃	55 (52) ^[c]
2	CoBr₂	TBAB	--	Cs₂CO₃	74 (70)^[c]
3	--	TBAB	K ₂ S ₂ O ₈	Cs ₂ CO ₃	39
4	--	TBAB	--	Cs ₂ CO ₃	39
5	CoBr ₂	--	--	Cs ₂ CO ₃	58
6	CoBr ₂	TBAB	K ₂ S ₂ O ₈	--	trace

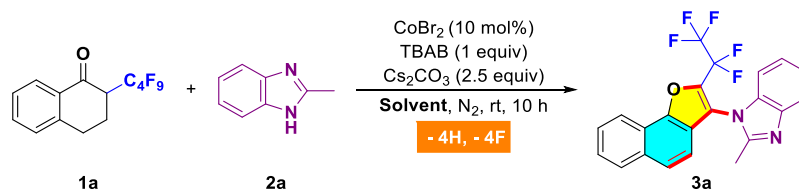
^[a] Reaction conditions: 2-(perfluorobutyl)-3,4-dihydronaphthalen-1(2H)-one (**1a**, 0.30 mmol), 2-methyl-1H-benzo[d]imidazole (**2a**, 0.60 mmol), catalyst (0.03 mmol), oxidant (0.3 mmol), additive (0.3 mmol), and base (0.75 mmol) in DMSO (2.0 mL) at 70 °C under N₂ for 10 h. ^[b] Yields were determined by NMR analysis with 1,4-dimethoxybenzene as an internal standard. ^[c] Isolated yield.

Table S2. Optimization of the reaction temperature^[a], related to **Table 1**.



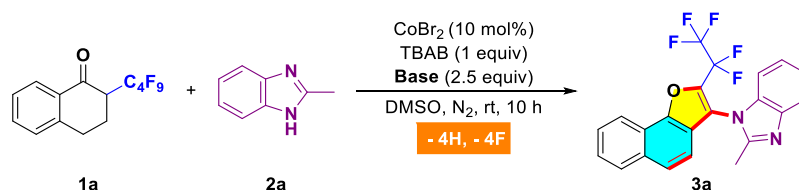
Entry	Temperature (°C)	Yield of 3a (%) ^[b]
1	rt	74 (71)^[c]
2	50	55
3	70	74
4	100	46

^[a] Reaction conditions: 2-(perfluorobutyl)-3,4-dihydronaphthalen-1(2H)-one (**1a**, 0.30 mmol), 2-methyl-1H-benzo[d]imidazole (**2a**, 0.60 mmol), CoBr₂ (0.03 mmol), TBAB (0.3 mmol), and Cs₂CO₃ (0.75 mmol) in DMSO (2.0 mL) under N₂ for 10 h. ^[b] Yields were determined by NMR analysis with 1,4-dimethoxybenzene as an internal standard. ^[c] Isolated yield.

Table S3. Optimization of the reaction solvent^[a], related to **Table 1**.

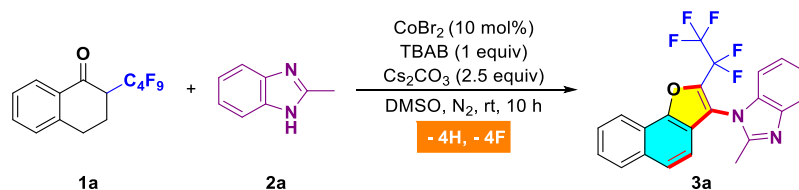
Entry	Solvent	Yield of 3a (%) ^[b]
1	DMSO	74 (71)^[c]
2	MeCN	55
3	MeNO ₂	0
4	DCM	66
5	DMF	61

^[a] Reaction conditions: 2-(perfluorobutyl)-3,4-dihydronaphthalen-1(2H)-one (**1a**, 0.30 mmol), 2-methyl-1H-benzo[d]imidazole (**2a**, 0.60 mmol), CoBr_2 (0.03 mmol), TBAB (0.3 mmol), and Cs_2CO_3 (0.75 mmol) in solvent (2.0 mL) at room temperature under N_2 for 10 h. ^[b] Yields were determined by NMR analysis with 1,4-dimethoxybenzene as an internal standard. ^[c] Isolated yield.

Table S4. Optimization of the reaction base^[a], related to **Table 1**.

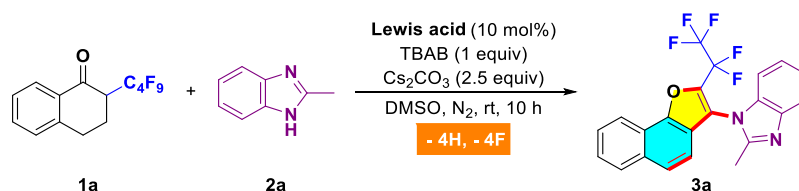
Entry	Base	Yield of 3a (%) ^[b]
1	Cs_2CO_3	74 (71)^[c]
2	K_2CO_3	67
3	Li_2CO_3	0
4	^t BuONa	62
5	DABCO	<10
6	LiOH	56

^[a] Reaction conditions: 2-(perfluorobutyl)-3,4-dihydronaphthalen-1(2H)-one (**1a**, 0.30 mmol), 2-methyl-1H-benzo[d]imidazole (**2a**, 0.60 mmol), CoBr_2 (0.03 mmol), TBAB (0.3 mmol), and base (0.75 mmol) in DMSO (2.0 mL) at room temperature under N_2 for 10 h. ^[b] Yields were determined by NMR analysis with 1,4-dimethoxybenzene as an internal standard. ^[c] Isolated yield.

Table S5. Optimization of the reaction catalyst^[a], related to **Table 1**.

Entry	Catalyst	Yield of 3a (%) ^[b]
1	CoBr₂	74 (71)^[c]
2	Co(OAc) ₂	49
3	CoCl₂·6H₂O	75 (72)^[c]
4	Co(C ₂ O ₄) ₂ ·2H ₂ O	0
5	CuBr ₂	70

^[a] Reaction conditions: 2-(perfluorobutyl)-3,4-dihydronaphthalen-1(2H)-one (**1a**, 0.30 mmol), 2-methyl-1H-benzo[d]imidazole (**2a**, 0.60 mmol), catalyst (0.03 mmol), TBAB (0.3 mmol), and Cs₂CO₃ (0.75 mmol) in DMSO (2.0 mL) at room temperature under N₂ for 10 h. ^[b] Yields were determined by NMR analysis with 1,4-dimethoxybenzene as an internal standard. ^[c] Isolated yield.

Table S6. Other Lewis acids as catalysts^[a], related to **Table 1**.

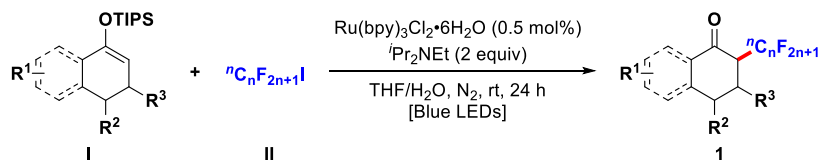
Entry	Lewis acid	Yield of 3a (%) ^[b]
1	--	39
2	CoBr ₂	74
3	BF ₃ Et ₂ O	60
4	AlCl ₃	74
5	NiBr ₂	50
6	InBr ₃	72
7	ZnBr ₂	66
8	GaBr ₃	75
9	Fe(OTf) ₃	71
10	FeCl ₂	63
11	Fe(acac) ₃	44

^[a] Reaction conditions: 2-(perfluorobutyl)-3,4-dihydronaphthalen-1(2H)-one (**1a**, 0.30 mmol), 2-methyl-1H-benzo[d]imidazole (**2a**, 0.60 mmol), Lewis acid (0.03 mmol), TBAB (0.3 mmol), and Cs₂CO₃ (0.75 mmol) in DMSO (2.0 mL) at room temperature under N₂ for 10 h. ^[b] Yields were determined by NMR analysis with 1,4-dimethoxybenzene as an internal standard.

Preparation of Substrates

General procedures for the synthesis of α -perfluoroalkyl ketones

Figure S240. General procedure A (Pham et al., 2011), related to Scheme 1-4.



According to MacMillan's reported method, a solution of enolsilane **I** (1.2 mmol), Ru(bpy)₃Cl₂·6H₂O (4.5 mg, 0.006 mmol, 0.5 mol%), *N*-ethyl-*N*-isopropylpropan-2-amine (424.0 μ L, 2.4 mmol), perfluoroalkyl iodide **II** (12 mmol), H₂O (32.0 μ L, 17.8 mmol) in THF (6.0 mL) was stirred under nitrogen atmosphere (by 3 times' vacuum evacuation/N₂ backfill cycles) by irradiation with 8 W Blue LEDs at room temperature for 24 h. Upon completion of the reaction (indicated by TLC), solvent was removed under vacuum and the residue was purified by flash silica gel column chromatography (300-400 mesh) using petroleum ether/ethyl acetate (1:500) as eluent to afford the α -perfluoroalkyl ketone **1**.

Representative examples:

2-(Perfluorobutyl)-3,4-dihydronaphthalen-1(2H)-one (**1a**) (Lee et al., 1988)

¹H NMR (400 MHz, CDCl₃): δ = 8.08 – 8.01 (m, 1H), 7.57 – 7.49 (m, 1H), 7.35 (t, *J* = 7.6 Hz, 1H), 7.28 (s, 1H), 3.49 – 3.35 (m, 1H), 3.23 – 3.15 (m, 1H), 3.08 – 2.98 (m, 1H), 2.55 – 2.36 (m, 2H) ppm.

¹⁹F NMR (376 MHz, CDCl₃): δ = -80.45 – -81.25 (m, 3F), -108.96 – -113.38 (m, 2F), -118.78 – -121.94 (m, 2F), -125.80 – -126.50 (m, 2F) ppm.

¹³C NMR (100 MHz, CDCl₃): δ = 190.3 (m), 142.9, 134.2, 132.3 (m), 128.7, 127.9, 127.0, 49.3 (t, *J* = 20.3 Hz), 27.1, 22.9 (m) ppm; carbons corresponding to the C₄F₉ group cannot be identified due to C-F coupling.

2-Methyl-4-(perfluorobutyl)-5,6-dihydro-[1,1'-biphenyl]-3(4H)-one (**1n**)

¹H NMR (400 MHz, CDCl₃): δ = 7.43 – 7.38 (m, 2H), 7.37 – 7.32 (m, 1H), 7.23 – 7.19 (m, 2H), 3.39 – 3.24 (m, 1H), 2.88 – 2.76 (m, 1H), 2.73 – 2.64 (m, 1H), 2.48 – 2.34 (m, 2H), 1.76 (t, *J* = 1.7 Hz, 3H) ppm.

¹⁹F NMR (376 MHz, CDCl₃): δ = -80.67 – -81.08 (m, 3F), -108.12 – -114.26 (m, 2F), -119.45 – -122.63 (m, 2F), -125.74 – -126.38 (m, 2F) ppm.

¹³C NMR (100 MHz, CDCl₃): δ = 191.6, 156.5, 140.3, 132.2, 128.5, 128.3, 126.9, 47.6 (t, J = 20.3 Hz), 30.7, 22.0, 13.1 ppm; carbons corresponding to the C₄F₉ group cannot be identified due to C-F coupling.

2,4'-Dimethyl-4-(perfluorobutyl)-5,6-dihydro-[1,1'-biphenyl]-3(4H)-one (1o)

¹H NMR (400 MHz, CDCl₃): δ = 7.25 – 7.20 (m, 2H), 7.13 – 7.08 (m, 2H), 3.36 – 3.22 (m, 1H), 2.87 – 2.75 (m, 1H), 2.72 – 2.60 (m, 1H), 2.38 (s, 3H) ppm.

¹⁹F NMR (376 MHz, CDCl₃): δ = -80.77 (t, J = 9.8 Hz, 3F), -109.70 – -114.25 (m, 2F), -119.29 – -122.06 (m, 2F), -125.98 (t, J = 15.4 Hz, 2F) ppm.

¹³C NMR (100 MHz, CDCl₃): δ = 191.7 (t, J = 1.4 Hz), 156.6, 138.4, 137.3, 132.1, 129.1, 127.0, 47.6 (t, J = 20.2 Hz), 30.7, 22.0 (m), 21.2, 13.3 ppm; carbons corresponding to the C₄F₉ group cannot be identified due to C-F coupling.

4'-Chloro-2-methyl-4-(perfluorobutyl)-5,6-dihydro-[1,1'-biphenyl]-3(4H)-one (1p)

¹H NMR (400 MHz, CDCl₃): δ = 7.34 (d, J = 8.4 Hz, 2H), 7.14 (d, J = 8.4 Hz, 2H), 3.35 – 3.20 (m, 1H), 2.83 – 2.71 (m, 1H), 2.70 – 2.58 (m, 1H), 2.46 – 2.29 (m, 2H), 1.79 (s, 3H) ppm.

¹⁹F NMR (376 MHz, CDCl₃): δ = -80.80 – -80.92 (m, 3F), -110.28 – -114.09 (m, 2F), -119.53 – -121.96 (m, 2F), -125.96 – -126.14 (m, 2F) ppm.

¹³C NMR (100 MHz, CDCl₃): δ = 191.2, 154.9, 138.6, 134.2, 132.4, 128.6, 128.4, 47.6 (t, J = 20.6 Hz), 30.4, 21.8, 12.9 ppm; carbons corresponding to the C₄F₉ group cannot be identified due to C-F coupling.

2-Methyl-3-(naphthalen-1-yl)-6-(perfluorobutyl)cyclohex-2-en-1-one (1q)

¹H NMR (400 MHz, CDCl₃): δ = 7.93 – 7.86 (m, 1H), 7.83 (d, J = 8.3 Hz, 1H), 7.69 – 7.56 (m, 1H), 7.54 – 7.46 (m, 3H), 7.24 – 7.18 (m, 1H), 3.55 – 3.31 (m, 1H), 2.96 – 2.78 (m, 1H), 2.78 – 2.58 (m, 1H), 2.50 (d, J = 5.4 Hz, 2H), 1.56 (s, 3H) ppm.

¹⁹F NMR (376 MHz, CDCl₃): δ = -80.80 (s, 3F), -109.50 – -113.97 (m, 2F), -119.36 – -122.12 (m, 2F), -125.92 (t, J = 12.4 Hz, 2F) ppm.

¹³C NMR (100 MHz, CDCl₃): δ = 191.3 (m), 156.2 (d, *J* = 18.6 Hz), 138.1 (d, *J* = 5.1 Hz), 134.2 (d, *J* = 9.4 Hz), 133.6, 129.1 (d, *J* = 9.3 Hz), 128.7 (d, *J* = 9.2 Hz), 128.2 (d, *J* = 7.5 Hz), 126.8 (d, *J* = 16.2 Hz), 126.2 (d, *J* = 5.1 Hz), 125.4 (d, *J* = 11.6 Hz), 124.3 (d, *J* = 4.8 Hz), 123.6 (d, *J* = 3.6 Hz), 47.7 (q, *J* = 20.0 Hz), 31.1 (d, *J* = 23.2 Hz), 22.3 (m), 12.9 ppm; carbons corresponding to the C₄F₉ group cannot be identified due to C-F coupling.

6-Methyl-3-(perfluorobutyl)-4,5-dihydro-[1,1'-biphenyl]-2(3H)-one (1r)

¹H NMR (400 MHz, CDCl₃): δ = 7.40 – 7.32 (m, 2H), 7.31 – 7.25 (m, 1H), 7.04 (d, *J* = 7.1 Hz, 2H), 3.40 – 3.19 (m, 1H), 2.73 – 2.59 (m, 1H), 2.56 – 2.43 (m, 1H), 2.42 – 2.30 (m, 2H), 1.81 (s, 3H) ppm.

¹⁹F NMR (376 MHz, CDCl₃): δ = -80.91 (s, 3F), -110.17 – -113.94 (m, 2F), -119.49 – -122.08 (m, 2F), -126.06 (t, *J* = 14.9 Hz, 2F) ppm.

¹³C NMR (100 MHz, CDCl₃): δ = 189.8 (m), 157.5, 137.9 (d, *J* = 1.1 Hz), 135.1, 129.8, 128.0, 127.3, 47.7 (t, *J* = 21.0 Hz), 30.1, 22.4, 21.4 (m) ppm; carbons corresponding to the C₄F₉ group cannot be identified due to C-F coupling.

6'-Methyl-2'-oxo-3'-(perfluorobutyl)-2',3',4',5'-tetrahydro-[1,1'-biphenyl]-4-carbonitrile (1s)

¹H NMR (400 MHz, CDCl₃): δ = 7.66 (d, *J* = 7.6 Hz, 2H), 7.18 (d, *J* = 7.5 Hz, 2H), 3.43 – 3.26 (m, 1H), 2.82 – 2.67 (m, 1H), 2.64 – 2.52 (m, 1H), 2.46 – 2.37 (m, 2H), 1.85 (s, 3H) ppm.

¹⁹F NMR (376 MHz, CDCl₃): δ = -80.83 (t, *J* = 9.7 Hz, 3F), -110.32 – -113.64 (m, 2F), -119.39 – -122.20 (m, 2F), -126.01 (t, *J* = 15.1 Hz, 2F) ppm.

¹³C NMR (100 MHz, CDCl₃): δ = 189.2 (t, *J* = 2.1 Hz), 158.9, 140.1, 136.5 (d, *J* = 2.0 Hz), 131.9, 130.8, 118.7, 111.3, 47.5 (t, *J* = 21.4 Hz), 30.2, 22.4, 21.3 (m) ppm; carbons corresponding to the C₄F₉ group cannot be identified due to C-F coupling.

3-Methyl-6-(perfluorobutyl)-2-(thiophen-2-yl)cyclohex-2-en-1-one (1t)

¹H NMR (400 MHz, CDCl₃): δ = 7.37 (d, *J* = 4.9 Hz, 1H), 7.04 (t, *J* = 4.1 Hz, 1H), 6.84 (d, *J* = 2.5 Hz, 1H), 3.41 – 3.25 (m, 1H), 2.80 – 2.67 (m, 1H), 2.63 – 2.50 (m, 1H), 2.43 – 2.33 (m, 2H), 2.01 (s, 3H) ppm.

¹⁹F NMR (376 MHz, CDCl₃): δ = -80.09 (t, *J* = 9.8 Hz, 3F), -109.64 – -113.10 (m, 2F), -118.74

- -121.25 (m, 2F), -125.28 (t, $J = 15.1$ Hz, 2F) ppm.

^{13}C NMR (100 MHz, CDCl_3): $\delta = 189.1$ (m), 160.1, 134.6, 131.1, 128.4, 126.5, 126.4, 47.8 (t, $J = 21.3$ Hz), 30.8 (t, $J = 1.5$ Hz), 23.0, 21.3 (m) ppm; carbons corresponding to the C_4F_9 group cannot be identified due to C-F coupling.

5-Methyl-2-(perfluorobutyl)-1,6-dihydro-[1,1'-biphenyl]-3(2H)-one (1u)

^1H NMR (400 MHz, CDCl_3): $\delta = 7.31 - 7.18$ (m, 3H), 7.11 (d, $J = 7.3$ Hz, 2H), 6.12 (s, 1H), 4.00 - 3.89 (m, 1H), 3.47 - 3.26 (m, 1H), 3.03 (dd, $J = 19.7, 5.2$ Hz, 1H), 2.55 (d, $J = 19.8$ Hz, 1H), 2.03 (s, 3H) ppm.

^{19}F NMR (376 MHz, CDCl_3): $\delta = -80.81 - -81.32$ (m, 3F), -110.57 - -112.97 (m, 2F), -119.91 - -122.06 (m, 2F), -124.76 - -127.17 (m, 2F) ppm.

^{13}C NMR (100 MHz, CDCl_3): $\delta = 189.6$ (m), 161.6, 142.0, 128.9, 128.9, 127.3 (t, $J = 1.9$ Hz), 126.8, 52.6 (t, $J = 20.1$ Hz), 37.4 (t, $J = 1.7$ Hz), 34.2, 24.1 (m) ppm; carbons corresponding to the C_4F_9 group cannot be identified due to C-F coupling.

3-((2-Bromophenyl)thio)-5-methyl-6-(perfluorobutyl)cyclohex-2-en-1-one (1v)

^1H NMR (400 MHz, CDCl_3): $\delta = 7.74$ (d, $J = 7.6$ Hz, 1H), 7.66 - 7.60 (m, 1H), 7.42 - 7.30 (m, 2H), 5.50 (d, $J = 2.0$ Hz, 1H), 3.12 - 2.80 (m, 3H), 2.27 (d, $J = 18.4$ Hz, 1H), 1.20 (d, $J = 7.1$ Hz, 3H) ppm.

^{19}F NMR (376 MHz, CDCl_3): $\delta = -80.74 - -80.90$ (m, 3F), -109.53 - -114.50 (m, 2F), -120.05 - -122.55 (m, 2F), -125.68 - -126.00 (m, 2F) ppm.

^{13}C NMR (100 MHz, CDCl_3): $\delta = 186.8$ (m), 163.1, 137.7, 134.3, 132.1, 130.5, 128.8, 128.7, 120.1 (d, $J = 1.7$ Hz), 53.0 (t, $J = 20.1$ Hz), 33.6 (t, $J = 2.6$ Hz), 27.7 (m), 19.9 (d, $J = 0.9$ Hz) ppm; carbons corresponding to the C_4F_9 group cannot be identified due to C-F coupling.

(8R,9S,10R,13S,14S,17S)-13-Methyl-3-oxo-2-(perfluorobutyl)-

2,3,6,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-17-yl acetate (1w)

^1H NMR (400 MHz, CDCl_3): $\delta = 5.96$ (s, 1H), 4.67 - 4.57 (m, 1H), 3.18 (t, $J = 17.9$ Hz, 1H), 2.68 - 2.47 (m, 2H), 2.35 - 2.25 (m, 2H), 2.24 - 2.13 (m, 1H), 2.05 (s, 3H), 1.91 - 1.75 (m, 4H), 1.72

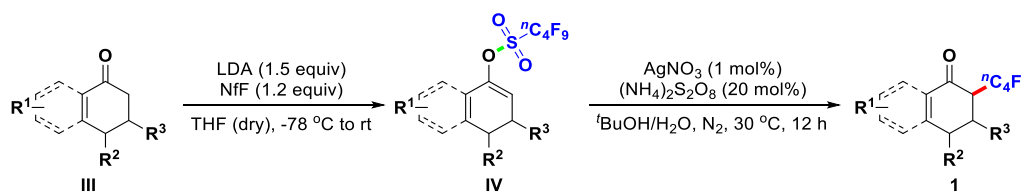
– 1.60 (m, 2H), 1.58 – 1.48 (m, 1H), 1.41 – 1.24 (m, 4H), 1.14 – 1.05 (m, 2H), 0.86 (s, 3H) ppm.

¹⁹F NMR (376 MHz, CDCl₃): δ = -80.82 (t, J = 9.5 Hz, 3F), -110.30 – -113.92 (m, 2F), -120.11 – -122.69 (m, 2F), -125.83 (t, J = 15.1 Hz, 2F) ppm.

¹³C NMR (100 MHz, CDCl₃): δ = 190.6 (m), 171.2, 167.9, 124.3 (d, J = 1.5 Hz), 82.4, 50.2, 49.4, 46.5 (t, J = 20.4 Hz), 42.6, 40.0, 39.9 (t, J = 1.4 Hz), 36.4, 35.5, 30.7, 27.4, 26.4 (m), 25.7, 23.3, 21.1, 12.0 ppm; carbons corresponding to the C₄F₉ group cannot be identified due to C-F coupling.

2-(Perfluorobutyl)-3,4-dihydronaphthalen-1(2*H*)-one (**1a**), 6-(benzyloxy)-2-(perfluorobutyl)-3,4-dihydronaphthalen-1(2*H*)-one (**1e**), 5-oxo-6-(perfluorobutyl)-5,6,7,8-tetrahydronaphthalen-1-yl 4-methylbenzenesulfonate (**1j**), 5-(perfluorobutyl)-6,7-dihydrobenzo[*b*]thiophen-4(5*H*)-one (**1m**), 2-methyl-4-(perfluorobutyl)-5,6-dihydro-[1,1'-biphenyl]-3(4*H*)-one (**1n**), 2,4'-dimethyl-4-(perfluorobutyl)-5,6-dihydro-[1,1'-biphenyl]-3(4*H*)-one (**1o**), 4'-chloro-2-methyl-4-(perfluorobutyl)-5,6-dihydro-[1,1'-biphenyl]-3(4*H*)-one (**1p**), 2-methyl-3-(naphthalen-1-yl)-6-(perfluorobutyl)cyclohex-2-en-1-one (**1q**), 6-methyl-3-(perfluorobutyl)-4,5-dihydro-[1,1'-biphenyl]-2(3*H*)-one (**1r**), 6'-methyl-2'-oxo-3'-(perfluorobutyl)-2',3',4',5'-tetrahydro-[1,1'-biphenyl]-4-carbonitrile (**1s**), 3-methyl-6-(perfluorobutyl)-2-(thiophen-2-yl)cyclohex-2-en-1-one (**1t**), 5-methyl-2-(perfluorobutyl)-1,6-dihydro-[1,1'-biphenyl]-3(2*H*)-one (**1u**), 3-((2-bromophenyl)thio)-5-methyl-6-(perfluorobutyl)cyclohex-2-en-1-one (**1v**), 2-(perfluorodecyl)-3,4-dihydronaphthalen-1(2*H*)-one (**1x**), 2-(perfluorononyl)-3,4-dihydronaphthalen-1(2*H*)-one (**1y**), 2-(perfluorooctyl)-3,4-dihydronaphthalen-1(2*H*)-one (**1z**), 2-(perfluoroheptyl)-3,4-dihydronaphthalen-1(2*H*)-one (**1a'**), 2-(perfluorohexyl)-3,4-dihydronaphthalen-1(2*H*)-one (**1b'**), and 2-(perfluoropropyl)-3,4-dihydronaphthalen-1(2*H*)-one (**1c'**) were synthesized according to general procedure A.

Figure S241. General procedure B (Su et al., 2017; Xie et al., 2018), related to **Scheme 1-4**.



Step 1: The solution of ketone **III** (5 mmol) in dry THF (25 mL) was cooled to -78 °C and then lithium diisopropylamide (LDA, 3.75 mL, 7.5 mmol, 2.0 mol/L in THF/hexane) was dropwise added to the reaction mixture. Nonafluorobutanesulfonyl fluoride (1.1 mL, 6 mmol) was added slowly by a syringe over 10 min. The reaction mixture was warmed to room temperature and stirred overnight. The reaction was then quenched by saturated NH₄Cl solution (20 mL) and diluted with EtOAc (20 mL). The organic layer was washed with saturated brine twice, dried over MgSO₄, filtered, and concentrated under reduced pressure. The crude product was purified by flash column chromatography (300-400 mesh) on Et₃N-treated silica gel eluting with petroleum ether to afford enol nonaflate **IV**.

Step 2: A solution of enol nonaflate **IV** (0.8 mmol), (NH₄)₂S₂O₈ (0.16 mmol, 37 mg), and AgNO₃ (0.008 mmol, 1.4 mg) in tBuOH (2.0 mL) and H₂O (2.0 mL) was stirred vigorously under nitrogen atmosphere (by 3 times' vacuum evacuation/N₂ backfill cycles) at 30 °C for 12 h. Upon completion of the reaction (indicated by TLC), the reaction mixture was diluted with dichloromethane. The organic layer was separated and the aqueous layer was washed with dichloromethane (3×10 mL). The combined organic layers were dried over Na₂SO₄. The solvent was removed under vacuum and the residue was purified by flash silica gel column chromatography (300-400 mesh) using petroleum ether/ethyl acetate as eluent to afford α -perfluoroalkyl ketone **1**.

Representative examples:

6-Methoxy-2-(perfluorobutyl)-3,4-dihydronaphthalen-1(2H)-one (**1b**)

¹H NMR (400 MHz, CDCl₃): δ = 8.02 (d, *J* = 8.8 Hz, 1H), 6.86 (dd, *J* = 8.8, 2.5 Hz, 1H), 6.70 (d, *J* = 2.4 Hz, 1H), 3.87 (s, 3H), 3.44 – 3.30 (m, 1H), 3.20 – 3.10 (m, 1H), 3.00 – 2.91 (m, 1H), 2.50 – 2.34 (m, 2H) ppm.

¹⁹F NMR (376 MHz, CDCl₃): δ = -80.45 – -81.24 (m, 3F), -108.98 – -113.48 (m, 2F), -118.81 –

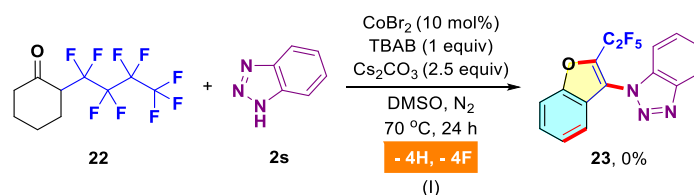
-121.88 (m, 2F), -125.99 – -126.55 (m, 2F) ppm.

¹³C NMR (100 MHz, CDCl₃): δ = 188.8 (m), 164.1, 145.5, 130.3, 125.8, 113.7, 112.3, 55.4, 48.9 (t, *J* = 20.4 Hz), 27.3, 23.0 ppm; carbons corresponding to the C₄F₉ group cannot be identified due to C-F coupling.

7-Methoxy-2-(perfluorobutyl)-3,4-dihydronaphthalen-1(2*H*)-one (**1b**), 6-methoxy-2-(perfluorobutyl)-3,4-dihydronaphthalen-1(2*H*)-one (**1c**), 5-methoxy-2-(perfluorobutyl)-3,4-dihydronaphthalen-1(2*H*)-one (**1d**), 7-methyl-2-(perfluorobutyl)-3,4-dihydronaphthalen-1(2*H*)-one (**1f**), 7-fluoro-2-(perfluorobutyl)-3,4-dihydronaphthalen-1(2*H*)-one (**1g**), 7-chloro-2-(perfluorobutyl)-3,4-dihydronaphthalen-1(2*H*)-one (**1h**), 7-bromo-2-(perfluorobutyl)-3,4-dihydronaphthalen-1(2*H*)-one (**1i**), 4-methyl-2-(perfluorobutyl)-3,4-dihydronaphthalen-1(2*H*)-one (**1k**), 4-(3,4-dichlorophenyl)-2-(perfluorobutyl)-3,4-dihydronaphthalen-1(2*H*)-one (**1l**), 2-(perfluorobutyl)cyclohexan-1-one (**22**), and 6-(perfluorobutyl)-6,7,8,9-tetrahydro-5*H*-benzo[7]annulen-5-one (**24**) were synthesized according to general procedure B.

Mechanistic studies

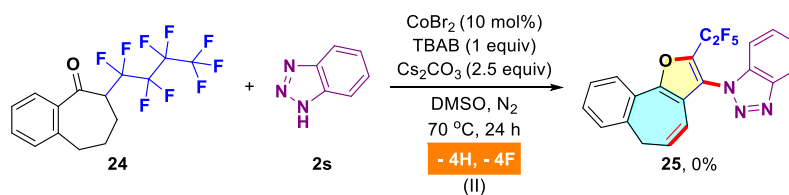
Figure S242. Control experiment of 2-(perfluorobutyl)cyclohexan-1-one (22) with 1*H*-benzo[*d*][1,2,3]triazole (2s), related to Scheme 4.



A solution of 2-(perfluorobutyl)cyclohexan-1-one (**22**, 95 mg, 0.3 mmol), 1*H*-benzo[*d*][1,2,3]triazole (**2s**, 71 mg, 0.6 mmol), CoBr₂ (66 mg, 0.03 mmol), tetrabutylammonium bromide (97 mg, 0.3 mmol, TBAB), and Cs₂CO₃ (244 mg, 0.75 mmol) in DMSO (2.0 mL) was stirred under nitrogen atmosphere at 70 °C for 24 h. No target product **23** was obtained. **This result suggested that the phenyl moiety or unsaturated C=C bond in the α-perfluoroalkyl ketone was essential for the established reaction.**

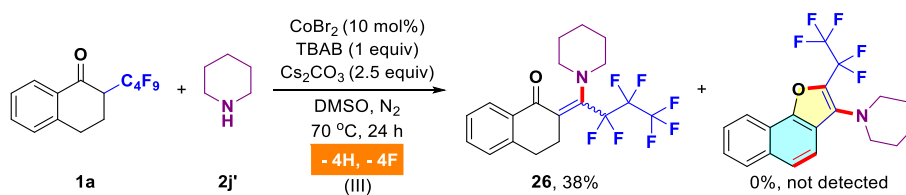
Figure S243. Control experiment of 6-(perfluorobutyl)-6,7,8,9-tetrahydro-5*H*-

benzo[7]annulen-5-one (**24**) with 1*H*-benzo[*d*][1,2,3]triazole (**2s**), related to Scheme 4.



A solution of 6-(perfluorobutyl)-6,7,8,9-tetrahydro-5*H*-benzo[7]annulen-5-one (**24**, 114 mg, 0.3 mmol), 1*H*-benzo[*d*][1,2,3]triazole (**2s**, 71 mg, 0.6 mmol), CoBr₂ (66 mg, 0.03 mmol), tetrabutylammonium bromide (97 mg, 0.3 mmol, TBAB), and Cs₂CO₃ (244 mg, 0.75 mmol) in DMSO (2.0 mL) was stirred under nitrogen atmosphere at 70 °C for 24 h. No target product **25** was obtained. **This result suggested that the aromatization was the important driving force for the C-F cleavage reaction.**

Figure S244. Control experiment of 2-(perfluorobutyl)-3,4-dihydronaphthalen-1(2*H*)-one (1a**) with 1*H*-benzo[*d*][1,2,3]triazole (**2j'**), related to Scheme 4.**



A solution of 2-(perfluorobutyl)-3,4-dihydronaphthalen-1(2*H*)-one (**1a**, 109 mg, 0.3 mmol), piperidine (**2j'**, 64 mg, 0.75 mmol), CoBr₂ (66 mg, 0.03 mmol), tetrabutylammonium bromide (97 mg, 0.3 mmol, TBAB), and Cs₂CO₃ (244 mg, 0.75 mmol) in DMSO (2.0 mL) was stirred under nitrogen atmosphere at 70 °C for 24 h. The reaction was then quenched by saturated NH₄Cl solution (20 mL) and diluted with EtOAc (20 mL). The organic layer was washed with saturated brine twice, dried over MgSO₄, filtered, and concentrated under reduced pressure. The crude product was purified by flash column chromatography (300-400 mesh) using petroleum ether/ethyl acetate (500/1~200/1) as eluent to afford the pure product **26** (46 mg, 38%). No target product was obtained. **This result suggested that the nucleophile was also essential for the aromatization/cyclization and successive dehydrogenation/defluorination.**

Figure S245. Compound 26, related to Scheme 4.

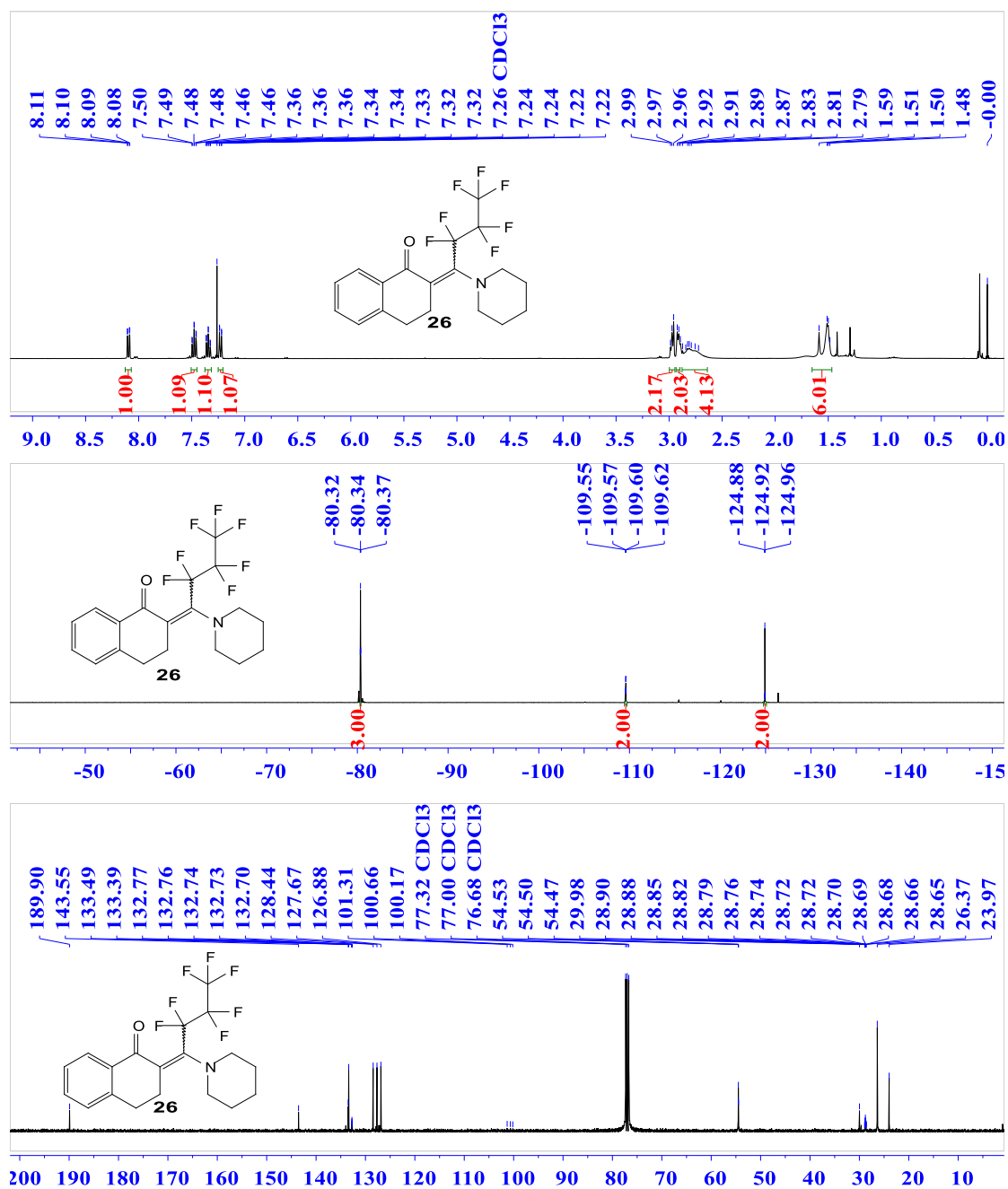
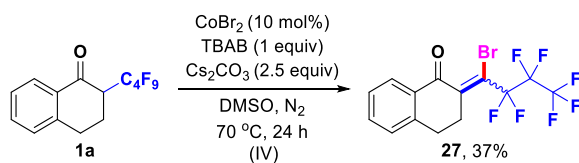


Figure S246. Detection of the by-product 2-(1-bromo-2,2,3,3,4,4,4-heptafluorobutylidene)-3,4-dihydronaphthalen-1(2H)-one (27), related to Scheme 4.



A solution of 2-(perfluorobutyl)-3,4-dihydronaphthalen-1(2H)-one (**1a**, 109 mg, 0.3 mmol), CoBr₂ (66 mg, 0.03 mmol), tetrabutylammonium bromide (97 mg, 0.3 mmol, TBAB), and

Cs₂CO₃ (244 mg, 0.75 mmol) in DMSO (2.0 mL) was stirred under nitrogen atmosphere at 70 °C for 24 h. The reaction was then quenched by saturated NH₄Cl solution (20 mL) and diluted with EtOAc (20 mL). The organic layer was washed with saturated brine twice, dried over MgSO₄, filtered, and concentrated under reduced pressure. The crude product was purified by flash column chromatography (300-400 mesh) using petroleum ether/ethyl acetate (500/1~200/1) as eluent to afford the pure product **27** (45 mg, 37%). **This result suggested that TBAB might participate in the reaction process.**

Figure S247. Compound **27**, related to Scheme 4.

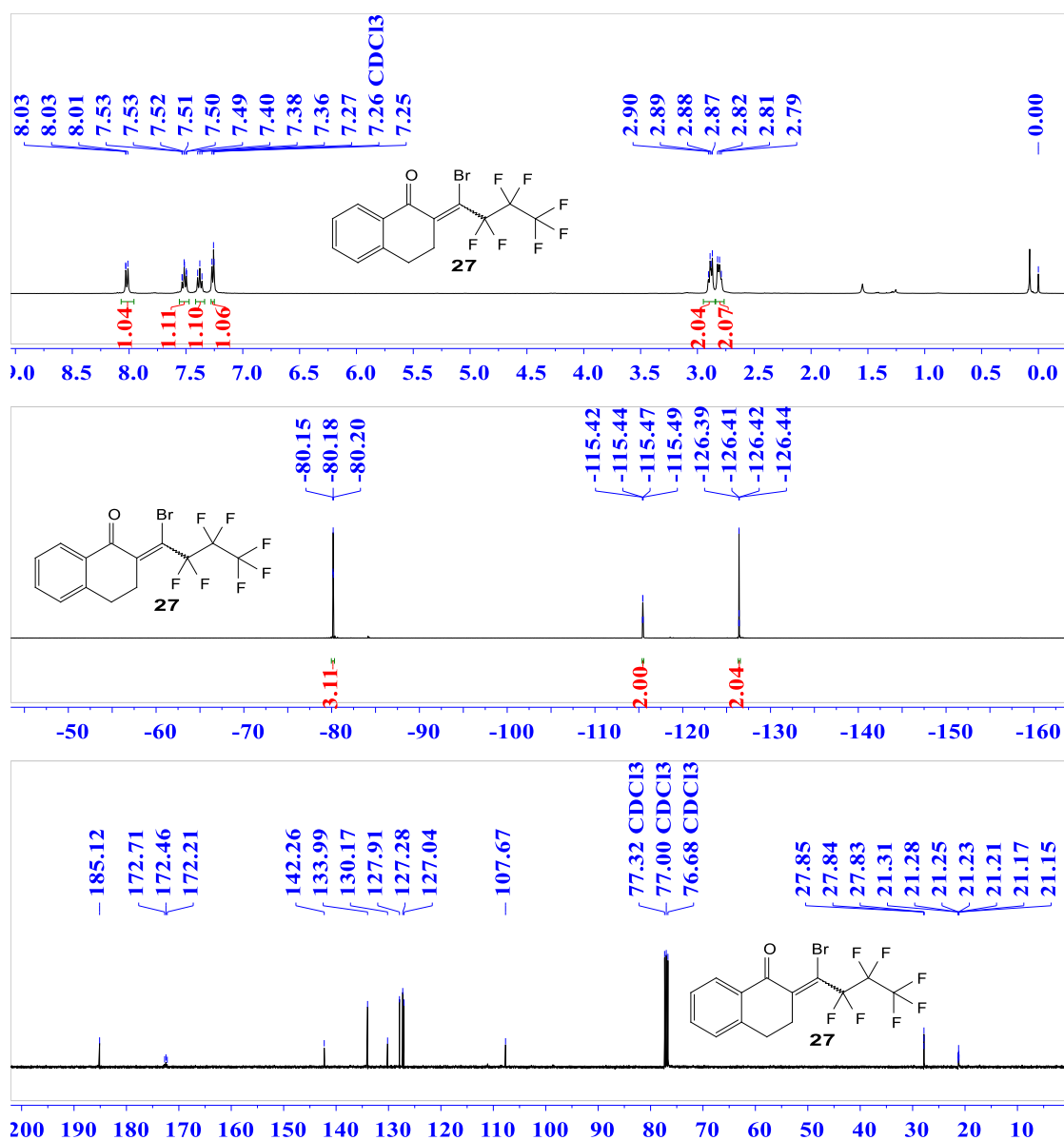
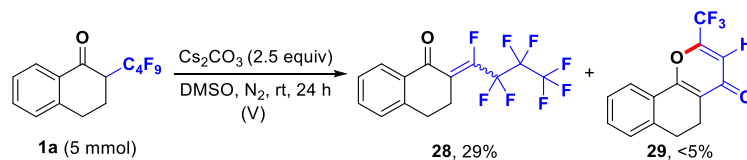
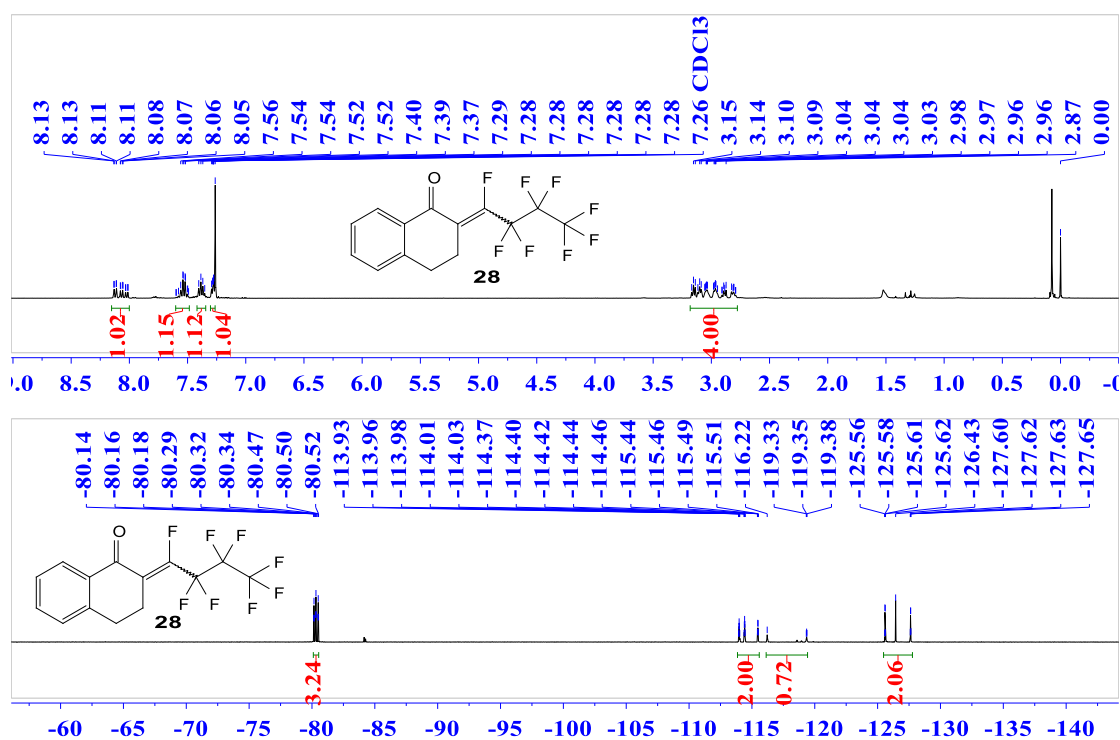


Figure S248. Detection of the intermediate 2-(perfluorobutylidene)-3,4-dihydronaphthalen-1(2H)-one (28) and byproduct 2-(trifluoromethyl)-5,6-dihydro-4H-benzo[h]chromen-4-one (29), related to Scheme 4.



A solution of 2-(perfluorobutyl)-3,4-dihydronaphthalen-1(2H)-one (**1a**, 1.82 g, 5 mmol), Cs_2CO_3 (4.1 g, 12.5 mmol) in DMSO (20.0 mL) was stirred under nitrogen atmosphere at room temperature for 24 h. The reaction was then quenched by saturated NH_4Cl solution (20 mL) and diluted with EtOAc (20 mL). The organic layer was washed with saturated brine twice, dried over MgSO_4 , filtered, and concentrated under reduced pressure. The crude product was purified by flash column chromatography (300-400 mesh) using petroleum ether/ethyl acetate (500/1~200/1) as eluent to afford the pure product **28** (499 mg, 29%) and byproduct **29** (<5%). This result suggested that compound **28** was the possible reaction intermediate.

Figure S249. Compound 28, related to Scheme 4.



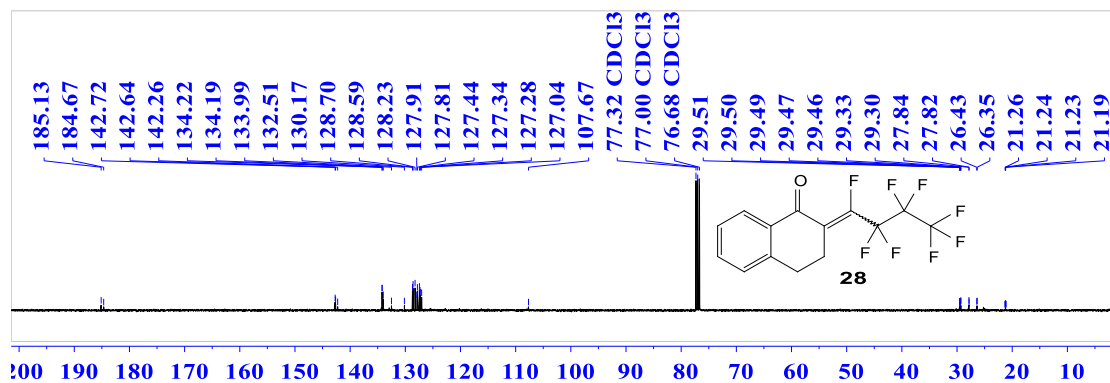


Figure S250. Compound 29, related to Scheme 4.

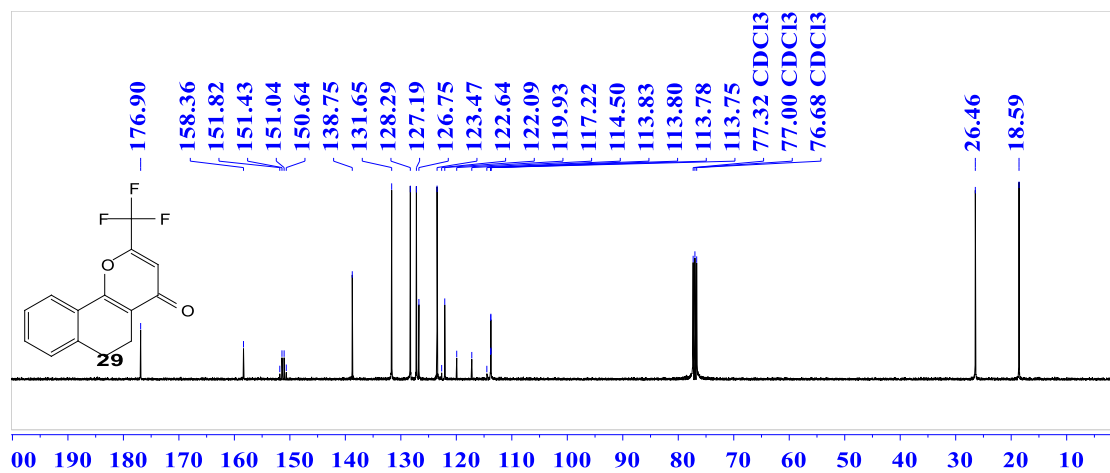
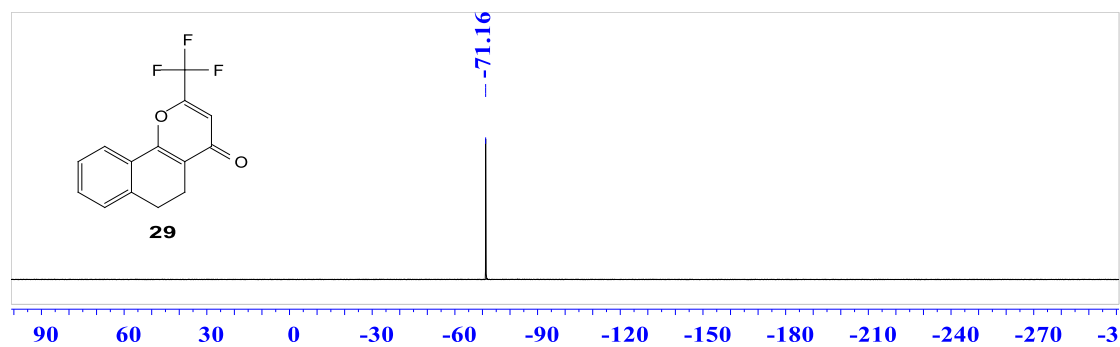
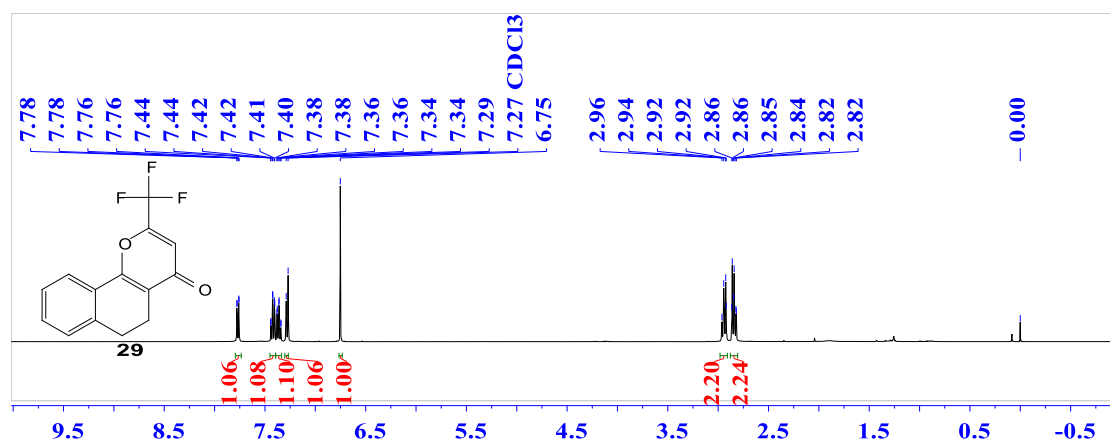
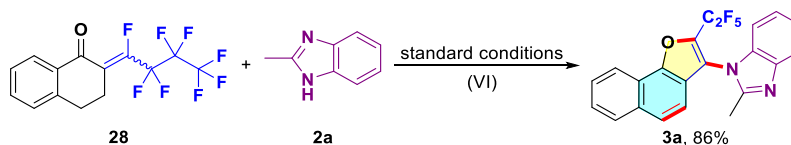


Figure S251. The reaction of 2-(perfluorobutylidene)-3,4-dihydronaphthalen-1(2*H*)-one (**28**) with 2-methyl-1*H*-benzo[*d*]imidazole (**2a**), related to **Scheme 4**.



A solution of 2-(perfluorobutyl)-3,4-dihydronaphthalen-1(2*H*)-one (**28**, 103 mg, 0.3 mmol), 2-methyl-1*H*-benzo[*d*]imidazole (**2a**, 79 mg, 0.6 mmol), CoBr₂ (66 mg, 0.03 mmol), tetrabutylammonium bromide (97 mg, 0.3 mmol, TBAB), and Cs₂CO₃ (244 mg, 0.75 mmol) in DMSO (2.0 mL) was stirred under nitrogen atmosphere at 70 °C for 24 h. The reaction was then quenched by saturated NH₄Cl solution (20 mL) and diluted with EtOAc (20 mL). The organic layer was washed with saturated brine twice, dried over MgSO₄, filtered, and concentrated under reduced pressure. The crude product was purified by flash column chromatography (300-400 mesh) using petroleum ether/ethyl acetate (100/1~20/1) as eluent to afford the pure product **3a** (107 mg, 86%). **This result suggested that compound 28 was the possible reaction intermediate.**

Transparent Methods

General information

Unless otherwise stated, all reagents were purchased from commercial suppliers and used without further purification. All reactions were carried out under N₂ atmosphere using undistilled solvent. Melting points were recorded on an Electrothermal digital melting point apparatus. IR spectra were recorded on a FT-IR spectrophotometer using KBr optics. ¹H, ¹⁹F, and ¹³C NMR spectra were recorded in CDCl₃ or DMSO-*d*₆ on Bruker Avance or Joel 400 MHz spectrometers. The chemical shifts (δ) are reported in ppm and coupling constants (*J*) in Hz. High resolution mass spectra (HRMS) were obtained using a commercial apparatus (ESI or EI Source). Column chromatography was generally performed on silica gel (300-400 mesh) or alkali alumina (200-300 mesh) and reactions were monitored by thin layer chromatography (TLC) using UV light to visualize the course of the reactions.

General procedures for the synthesis of perfluoroalkylated naphtho[1,2-*b*]furan/benzofuran derivatives, related to Scheme 1-4.

A solution of α -perfluoroalkyl ketone **1** (0.3 mmol), *N*-heterocycle **2a-2v'** (0.6-0.9 mmol), CoBr₂ (66 mg, 0.03 mmol), tetrabutylammonium bromide (97 mg, 0.3 mmol, TBAB), and Cs₂CO₃ (244 mg, 0.75 mmol) in DMSO (2.0 mL) was stirred under nitrogen atmosphere at room temperature to 120 °C for 10-48 h. The reaction was then quenched by saturated NH₄Cl solution (20 mL) and diluted with EtOAc (20 mL). The organic layer was washed with saturated brine twice, dried over MgSO₄, filtered, and concentrated under reduced pressure. The crude product was purified by flash column chromatography (300-400 mesh) using petroleum ether/ethyl acetate or dichloromethane/methanol as eluent to afford the pure products **3-16**.

Large scale synthesis of perfluoroalkylated naphtho[1,2-*b*]furan **10d**, related to Scheme 1.

A solution of 2-(perfluorobutyl)-3,4-dihydronaphthalen-1(2*H*)-one (**1a**, 1.09 g, 3 mmol), 1,2,3,9-tetrahydro-4*H*-carbazol-4-one (**2d'**, 1.67 g, 9 mmol), CoBr₂ (0.07 g, 0.3 mmol), tetrabutylammonium bromide (0.97 g, 3 mmol, TBAB), and Cs₂CO₃ (2.44 g, 7.5 mmol) in DMSO (10.0 mL) was stirred under nitrogen atmosphere at 100 °C for 48 h. The reaction was then quenched by saturated NH₄Cl solution (50 mL) and diluted with EtOAc (50 mL). The organic layer was washed with saturated brine twice, dried over MgSO₄, filtered, and concentrated under reduced pressure. The crude product was purified by flash column chromatography (300-

400 mesh) using petroleum ether/ethyl acetate (6/1) as eluent to afford the pure product **10d** (0.87 g, 62%).

General procedure for the synthesis of perfluoroalkylated naphtho[1,2-*b*]furan 17-18, related to **Scheme 4**.

A solution of 2-(perfluorobutyl)-3,4-dihydronaphthalen-1(2*H*)-one (**1a**, 109 mg, 0.3 mmol), 4-methylbenzenethiol (**2r'**, 75 mg, 0.6 mmol) or naphthalene-2-thiol (**2s'**, 96 mg, 0.6 mmol), CoBr₂ (66 mg, 0.03 mmol), tetrabutylammonium bromide (97 mg, 0.3 mmol, TBAB), and Cs₂CO₃ (244 mg, 0.75 mmol) in DMSO (2.0 mL) was stirred under nitrogen atmosphere at 70 °C for 24 h. The reaction was then quenched by saturated NH₄Cl solution (20 mL) and diluted with EtOAc (20 mL). The organic layer was washed with saturated brine twice, dried over MgSO₄, filtered, and concentrated under reduced pressure. The crude product was purified by flash column chromatography (300-400 mesh) using petroleum ether as eluent to afford the pure product **17** (56 mg, 46%) or **18** (69 mg, 52%).

General procedure for the synthesis of perfluoroalkylated benzo[4,5]imidazo[2,1-*b*]naphtho[2,1-*e*][1,3]oxazine 19, related to **Scheme 4**.

A solution of 2-(perfluorobutyl)-3,4-dihydronaphthalen-1(2*H*)-one (**1a**, 109 mg, 0.3 mmol), 2-chloro-1*H*-benzo[*d*]imidazole (**2t'**, 92 mg, 0.6 mmol), CoBr₂ (66 mg, 0.03 mmol), tetrabutylammonium bromide (97 mg, 0.3 mmol, TBAB), and Cs₂CO₃ (244 mg, 0.75 mmol) in DMSO (2.0 mL) was stirred under nitrogen atmosphere at 70 °C for 36 h. The reaction was then quenched by saturated NH₄Cl solution (20 mL) and diluted with EtOAc (20 mL). The organic layer was washed with saturated brine twice, dried over MgSO₄, filtered, and concentrated under reduced pressure. The crude product was purified by flash column chromatography (300-400 mesh) using petroleum ether/ethyl acetate (50/1~3/1) as eluent to afford the pure product **19** (111 mg, 88%).

General procedure for the synthesis of perfluoroalkylated benzo[4,5]imidazo[1,2-*b*]isoquinoline 20, related to **Scheme 4**.

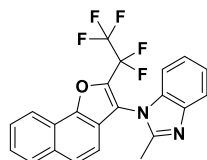
A solution of 2-(perfluorobutyl)-3,4-dihydronaphthalen-1(2*H*)-one (**1a**, 109 mg, 0.3 mmol), 2-

(1*H*-benzo[*d*]imidazol-2-yl)acetonitrile (**2u'**, 94 mg, 0.6 mmol), CoBr₂ (66 mg, 0.03 mmol), tetrabutylammonium bromide (97 mg, 0.3 mmol, TBAB), and Cs₂CO₃ (244 mg, 0.75 mmol) in DMSO (2.0 mL) was stirred under nitrogen atmosphere at 70 °C for 24 h. The reaction was then quenched by saturated NH₄Cl solution (20 mL) and diluted with EtOAc (20 mL). The organic layer was washed with saturated brine twice, dried over MgSO₄, filtered, and concentrated under reduced pressure. The crude product was purified by flash column chromatography (300-400 mesh) using petroleum ether/ethyl acetate (50/1~3/1) as eluent to afford the pure product **20** (100 mg, 72%).

General procedure for the synthesis of perfluoroalkylated dihydrobenzo[*h*]quinazoline **21, related to Scheme 4.**

A solution of 2-(perfluorobutyl)-3,4-dihydronaphthalen-1(2*H*)-one (**1a**, 109 mg, 0.3 mmol), 4-bromobenzimidamide (**2v'**, 119 mg, 0.6 mmol), CoBr₂ (66 mg, 0.03 mmol), tetrabutylammonium bromide (97 mg, 0.3 mmol, TBAB), and Cs₂CO₃ (244 mg, 0.75 mmol) in DMSO (2.0 mL) was stirred under nitrogen atmosphere at 70 °C for 24 h. The reaction was then quenched by saturated NH₄Cl solution (20 mL) and diluted with EtOAc (20 mL). The organic layer was washed with saturated brine twice, dried over MgSO₄, filtered, and concentrated under reduced pressure. The crude product was purified by flash column chromatography (300-400 mesh) using petroleum ether/ethyl acetate (50/1~20/1) as eluent to afford the pure product **21** (111 mg, 73%).

Characterization data for perfluoroalkylated naphtho[1,2-*b*]furan derivatives



2-Methyl-1-(2-(perfluoroethyl)naphtho[1,2-*b*]furan-3-yl)-1*H*-benzo[*d*]imidazole (3a**):**

Yield = 71% (89 mg), 0.3 mmol scale. Yellow oil.

IR (KBr): $\nu = 3063, 1625, 1538, 812, 744 \text{ cm}^{-1}$.

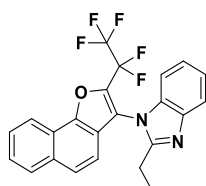
¹H NMR (400 MHz, CDCl₃): $\delta = 8.46$ (d, $J = 8.2$ Hz, 1H), 7.98 (d, $J = 8.1$ Hz, 1H), 7.84 (d, $J = 8.0$ Hz, 1H), $7.77 - 7.70$ (m, 2H), $7.67 - 7.63$ (m, 1H), 7.32 (td, $J = 7.8, 1.1$ Hz, 1H), $7.23 - 7.18$

(m, 1H), 7.14 (d, $J = 8.7$ Hz, 1H), 7.03 (d, $J = 8.0$ Hz, 1H), 2.52 (s, 3H) ppm.

^{19}F NMR (376 MHz, CDCl_3): $\delta = -83.36$ (t, $J = 4.0$ Hz, 3F), $-113.83 - -116.67$ (m, 2F) ppm.

^{13}C NMR (100 MHz, $\text{DMSO-}D_6$): $\delta = 151.7, 150.7, 142.6, 136.4, 135.5$ (t, $J = 31.0$ Hz), 133.0, 128.8, 128.1, 127.9, 126.6, 123.0, 122.7, 122.6, 120.2, 120.0, 119.5, 118.9, 116.5, 109.7, 13.2 ppm; carbons corresponding to the C_2F_5 group cannot be identified due to C-F coupling.

HRMS m/z : calcd for $\text{C}_{22}\text{H}_{14}\text{F}_5\text{N}_2\text{O}$ $[\text{M}+\text{H}]^+$ 417.1021, found: 417.1026.



2-Ethyl-1-(2-(perfluoroethyl)naphtho[1,2-*b*]furan-3-yl)-1*H*-benzo[*d*]imidazole (3b):

Yield = 69% (89 mg), 0.3 mmol scale. Yellow solid. M.p. 70.8–72.2 °C.

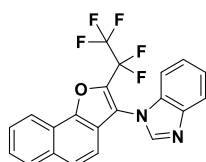
IR (KBr): $\nu = 3064, 1616, 1535, 818, 747$ cm^{-1} .

^1H NMR (400 MHz, CDCl_3): $\delta = 8.50 - 8.44$ (m, 1H), 7.99 (d, $J = 8.2$ Hz, 1H), 7.90 – 7.84 (m, 1H), 7.78 – 7.72 (m, 2H), 7.70 – 7.64 (m, 1H), 7.35 – 7.29 (m, 1H), 7.24 – 7.15 (m, 2H), 7.02 (d, $J = 8.0$ Hz, 1H), 2.91 – 2.69 (m, 2H), 1.39 (t, $J = 7.5$ Hz, 3H) ppm.

^{19}F NMR (376 MHz, CDCl_3): $\delta = -82.99 - -83.53$ (m, 3F), $-113.41 - -116.82$ (m, 2F) ppm.

^{13}C NMR (100 MHz, CDCl_3): $\delta = 156.7, 151.2$ (t, $J = 1.4$ Hz), 142.8, 137.0 (t, $J = 31.5$ Hz), 136.5, 133.2, 128.6, 127.8, 127.7, 126.4, 123.2, 122.9, 122.4 (t, $J = 1.5$ Hz), 121.0, 120.3, 120.2, 119.5, 116.2, 109.5, 20.8, 11.5 ppm; carbons corresponding to the C_2F_5 group cannot be identified due to C-F coupling.

HRMS m/z : calcd for $\text{C}_{23}\text{H}_{16}\text{F}_5\text{N}_2\text{O}$ $[\text{M}+\text{H}]^+$ 431.1177, found: 431.1183.



1-(2-(Perfluoroethyl)naphtho[1,2-*b*]furan-3-yl)-1*H*-benzo[*d*]imidazole (3c):

Yield = 83% (100 mg), 0.3 mmol scale. Yellow oil.

IR (KBr): $\nu = 3120, 1628, 1614, 829, 746$ cm^{-1} .

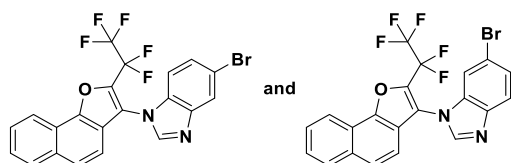
^1H NMR (400 MHz, $\text{DMSO-}D_6$): $\delta = 8.61$ (s, 1H), 8.42 – 8.37 (m, 1H), 8.18 (d, $J = 8.0$ Hz, 1H),

7.94 (d, $J = 8.6$ Hz, 1H), 7.88 – 7.85 (m, 1H), 7.84 – 7.79 (m, 1H), 7.78 – 7.72 (m, 1H), 7.39 – 7.29 (m, 4H) ppm.

^{19}F NMR (376 MHz, DMSO- D_6): $\delta = -83.16$ (t, $J = 3.5$ Hz, 3F), -113.87 (q, $J = 3.4$ Hz, 2F) ppm.

^{13}C NMR (100 MHz, DMSO- D_6): $\delta = 150.2, 144.4, 143.0, 134.7, 134.4$ (t, $J = 31.0$ Hz), 132.9, 129.0, 128.3, 128.0, 126.5, 124.1, 123.3 (t, $J = 1.8$ Hz), 123.1, 120.1, 120.1, 120.0, 119.7, 116.9, 110.4 ppm; carbons corresponding to the C_2F_5 group cannot be identified due to C-F coupling.

HRMS m/z : calcd for $\text{C}_{21}\text{H}_{12}\text{F}_5\text{N}_2\text{O}$ $[\text{M}+\text{H}]^+$ 403.0864, found: 403.0866.



5-Bromo-1-(2-(perfluoroethyl)naphtho[1,2-*b*]furan-3-yl)-1H-benzo[*d*]imidazole (3d-I) and 6-bromo-1-(2-(perfluoroethyl)naphtho[1,2-*b*]furan-3-yl)-1H-benzo[*d*]imidazole (3d-II):

3d-I and its isomer **3d-II** were separable but unidentified regioisomers.

Total yield = 62% (90 mg, **3d-I/3d-II** = 1/1), 0.3 mmol scale.

Isomer I: Yellow solid. M.p. 108.8–110.6 °C.

IR (KBr): $\nu = 3069, 1719, 1491, 818, 792$ cm^{-1} .

^1H NMR (400 MHz, CDCl_3): $\delta = 8.48 - 8.43$ (m, 1H), 8.14 – 8.06 (m, 2H), 8.04 – 7.99 (m, 1H), 7.80 – 7.74 (m, 2H), 7.72 – 7.67 (m, 1H), 7.45 (dd, $J = 8.6, 1.6$ Hz, 1H), 7.28 – 7.24 (m, 1H), 7.15 (d, $J = 8.6$ Hz, 1H) ppm.

^{19}F NMR (376 MHz, CDCl_3): $\delta = -83.56$ (t, $J = 4.1$ Hz, 3F), $-112.49 - -115.54$ (m, 2F) ppm.

^{13}C NMR (100 MHz, CDCl_3): $\delta = 151.0$ (t, $J = 1.3$ Hz), 144.8 (t, $J = 3.3$ Hz), 144.1 (m), 135.5 (t, $J = 31.8$ Hz), 133.6, 133.2, 128.7, 128.0, 127.9, 127.5, 126.4, 123.7, 122.2 (t, $J = 1.5$ Hz), 121.0, 120.3, 119.5, 116.5, 116.4, 111.6 ppm; carbons corresponding to the C_2F_5 group cannot be identified due to C-F coupling.

HRMS m/z : calcd for $\text{C}_{21}\text{H}_{11}\text{BrF}_5\text{N}_2\text{O}$ $[\text{M}+\text{H}]^+$ 480.9975, found: 480.9975.

Isomer II: Yellow solid. M.p. 108.6–109.6 °C.

IR (KBr): $\nu = 3047, 1620, 1529, 811, 749$ cm^{-1} .

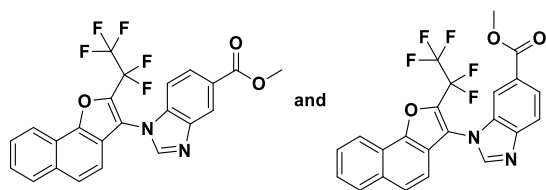
^1H NMR (400 MHz, CDCl_3): $\delta = 8.49 - 8.42$ (m, 1H), 8.07 (s, 1H), 8.01 (d, $J = 8.5$ Hz, 1H), 7.80 (dd, $J = 8.7, 5.3$ Hz, 2H), 7.75 (dt, $J = 8.1, 0.9$ Hz, 1H), 7.72 – 7.66 (m, 1H), 7.51 (dd, $J = 8.6,$

1.6 Hz, 1H), 7.43 (s, 1H), 7.28 (d, $J = 8.7$ Hz, 1H) ppm.

^{19}F NMR (376 MHz, CDCl_3): $\delta = -83.54$ (t, $J = 3.9$ Hz, 3F), $-112.45 - -115.58$ (m, 2F) ppm.

^{13}C NMR (100 MHz, CDCl_3): $\delta = 151.0$ (t, $J = 1.2$ Hz), 143.8 (m), 142.4 (m), 135.6 (t, $J = 31.9$ Hz), 133.2, 128.7, 128.0, 127.9, 126.9, 126.5, 122.1, 122.1 (t, $J = 1.9$ Hz), 121.0, 120.3, 119.5, 117.7, 116.3, 113.4 ppm; carbons corresponding to the C_2F_5 group cannot be identified due to C-F coupling.

HRMS m/z : calcd for $\text{C}_{21}\text{H}_{11}\text{BrF}_5\text{N}_2\text{O}$ $[\text{M}+\text{H}]^+$ 480.9969, found: 480.9965.



Methyl 1-(2-(perfluoroethyl)naphtho[1,2-*b*]furan-3-yl)-1*H*-benzo[*d*]imidazole-5-carboxylate (3e-I) and methyl 1-(2-(perfluoroethyl)naphtho[1,2-*b*]furan-3-yl)-1*H*-benzo[*d*]imidazole-6-carboxylate (3e-II):

3e-I and its isomer **3e-II** were inseparable regioisomers.

Total yield = 68% (94 mg, **3e-I/3e-II** = 1/1), 0.3 mmol scale. Yellow solid.

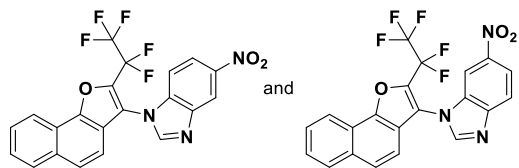
Isomer I & II: IR (KBr): $\nu = 3187, 1719, 1620, 1529, 811, 749$ cm^{-1} .

^1H NMR (400 MHz, CDCl_3): $\delta = 8.69 - 8.66$ (m, 1H), 8.48 - 8.43 (m, 2H), 8.21 (d, $J = 16.0$ Hz, 2H), 8.15 - 8.10 (m, 1H), 8.09 - 8.06 (m, 1H), 8.04 - 7.94 (m, 4H), 7.80 - 7.72 (m, 4H), 7.72 - 7.65 (m, 2H), 7.31 (d, $J = 8.5$ Hz, 1H), 7.28 - 7.24 (m, 2H), 3.98 (t, $J = 1.2$ Hz, 3H), 3.87 (t, $J = 1.2$ Hz, 3H) ppm.

^{19}F NMR (376 MHz, CDCl_3): $\delta = -83.27 - -83.87$ (m, 3F), $-111.73 - -115.99$ (m, 2F) ppm.

^{13}C NMR (100 MHz, CDCl_3): $\delta = 167.0, 166.8, 151.0, 146.7, 145.6, 144.6, 144.6, 143.1, 137.6, 135.6$ (t, $J = 31.5$ Hz), 135.5 (t, $J = 31.6$ Hz), 134.3, 133.2, 133.2, 128.6, 128.6, 127.9, 127.9, 127.8, 127.8, 126.5, 126.4, 126.4, 125.8, 125.8, 124.7, 123.1, 122.1 (t, $J = 1.7$ Hz), 122.1 (t, $J = 1.5$ Hz), 120.9, 120.5, 120.2, 120.2, 119.6, 119.5, 116.3, 116.3, 112.4, 110.0, 52.1, 52.1 ppm; carbons corresponding to the C_2F_5 group cannot be identified due to C-F coupling.

HRMS m/z : calcd for $\text{C}_{23}\text{H}_{14}\text{F}_5\text{N}_2\text{O}_3$ $[\text{M}+\text{H}]^+$ 461.0919, found: 461.0925.



5-Nitro-1-(2-(perfluoroethyl)naphtho[1,2-*b*]furan-3-yl)-1*H*-benzo[*d*]imidazole (3f-I) and 6-nitro-1-(2-(perfluoroethyl)naphtho[1,2-*b*]furan-3-yl)-1*H*-benzo[*d*]imidazole (3f-II):

3f-I and its isomer **3f-II** were separable but unidentified regioisomers.

Yield = 87% (117 mg, **3f-I/3f-II** = 1/1), 0.3 mmol scale.

Isomer I: Yellow solid. M.p. 131.4–132.6 °C.

IR (KBr): ν = 3071, 1629, 1523, 1345, 801, 739 cm^{-1} .

$^1\text{H NMR}$ (400 MHz, CDCl_3): δ = 8.86 (d, J = 2.1 Hz, 1H), 8.51 – 8.44 (m, 1H), 8.33 – 8.25 (m, 2H), 8.07 – 8.01 (m, 1H), 7.83 (d, J = 8.7 Hz, 1H), 7.81 – 7.76 (m, 1H), 7.75 – 7.69 (m, 1H), 7.36 (d, J = 9.0 Hz, 1H), 7.26 (d, J = 8.7 Hz, 1H) ppm.

$^{19}\text{F NMR}$ (376 MHz, CDCl_3): δ = -83.32 – -83.75 (m, 3F), -112.46 – -115.70 (m, 2F) ppm.

$^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ = 151.2 (t, J = 1.1 Hz), 146.3, 144.7, 143.0, 138.5, 136.0 (t, J = 31.7 Hz), 133.3, 128.8, 128.2, 128.1, 126.8, 121.6 (t, J = 1.7 Hz), 120.9, 120.3, 120.1, 119.3, 117.6, 115.9, 110.5 ppm; carbons corresponding to the C_2F_5 group cannot be identified due to C-F coupling.

HRMS m/z : calcd for $\text{C}_{21}\text{H}_{11}\text{F}_5\text{N}_3\text{O}_3$ [$\text{M}+\text{H}$] $^+$ 448.0721, found: 448.0719.

Isomer II: Yellow solid. M.p. 131.6–132.9 °C.

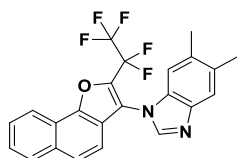
IR (KBr): ν = 3319, 1770, 1633, 1523, 803, 732 cm^{-1} .

$^1\text{H NMR}$ (400 MHz, CDCl_3): δ = 8.51 – 8.46 (m, 1H), 8.36 – 8.32 (m, 2H), 8.21 (d, J = 2.1 Hz, 1H), 8.06 – 8.02 (m, 2H), 7.84 – 7.77 (m, 2H), 7.75 – 7.70 (m, 1H), 7.24 (s, 1H) ppm.

$^{19}\text{F NMR}$ (376 MHz, CDCl_3): δ = -83.25 – -83.78 (m, 3F), -112.27 – -115.81 (m, 2F) ppm.

$^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ = 151.2 (t, J = 1.3 Hz), 147.6, 147.4 (t, J = 1.7 Hz), 144.9, 136.0 (t, J = 31.5 Hz), 134.1, 133.4, 128.8, 128.2, 128.1, 127.0, 121.3, 121.3, 121.0, 120.4, 119.3, 119.2, 115.8, 107.2 ppm; carbons corresponding to the C_2F_5 group cannot be identified due to C-F coupling.

HRMS m/z : calcd for $\text{C}_{21}\text{H}_{11}\text{F}_5\text{N}_3\text{O}_3$ [$\text{M}+\text{H}$] $^+$ 448.0715, found: 448.0719.



5,6-Dimethyl-1-(2-(perfluoroethyl)naphtho[1,2-*b*]furan-3-yl)-1*H*-benzo[*d*]imidazole (3g):

Yield = 39% (50 mg), 0.3 mmol scale. Colorless oil.

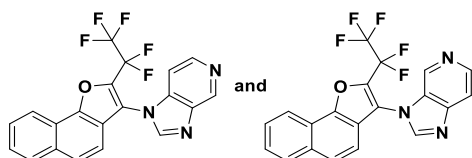
IR (KBr): $\nu = 2924, 1628, 1496, 810, 757 \text{ cm}^{-1}$.

$^1\text{H NMR}$ (400 MHz, CDCl_3): $\delta = 8.48 - 8.43$ (m, 1H), 8.01 (d, $J = 8.1 \text{ Hz}$, 1H), 7.98 (s, 1H), 7.78 – 7.73 (m, 2H), 7.71 – 7.65 (m, 2H), 7.30 (d, $J = 8.7 \text{ Hz}$, 1H), 7.04 (s, 1H), 2.42 (s, 3H), 2.32 (s, 3H) ppm.

$^{19}\text{F NMR}$ (376 MHz, CDCl_3): $\delta = -83.54$ (t, $J = 4.1 \text{ Hz}$, 3F), $-112.37 - -115.49$ (m, 2F) ppm.

$^{13}\text{C NMR}$ (100 MHz, CDCl_3): $\delta = 150.9, 142.4, 141.8, 135.3$ (t, $J = 31.7 \text{ Hz}$), 133.7, 133.2, 133.1, 132.4, 128.6, 127.8, 127.7, 126.1, 123.0 (t, $J = 2.0 \text{ Hz}$), 121.0, 120.7, 120.3, 119.9, 116.9, 110.4, 20.5, 20.3 ppm; carbons corresponding to the C_2F_5 group cannot be identified due to C-F coupling.

HRMS m/z : calcd for $\text{C}_{23}\text{H}_{16}\text{F}_5\text{N}_2\text{O}$ $[\text{M}+\text{H}]^+$ 431.1177, found: 431.1179.



1-(2-(Perfluoroethyl)naphtho[1,2-*b*]furan-3-yl)-1*H*-imidazo[4,5-*c*]pyridine (3h-I) and 3-(2-(perfluoroethyl)naphtho[1,2-*b*]furan-3-yl)-3*H*-imidazo[4,5-*c*]pyridine (3h-II):

3h-I and its isomer **3h-II** were separable but unidentified regioisomers.

Total yield = 64% (77 mg, **3h-I/3h-II** = 1/1), 0.3 mmol scale.

Isomer I: Brown solid. M.p. 130.9–132.3 °C.

IR (KBr): $\nu = 3053, 1629, 1609, 823, 751 \text{ cm}^{-1}$.

$^1\text{H NMR}$ (400 MHz, CDCl_3): $\delta = 8.75$ (s, 1H), 8.62 (d, $J = 5.6 \text{ Hz}$, 1H), 8.50 – 8.45 (m, 1H), 8.22 (s, 1H), 8.03 (d, $J = 8.1 \text{ Hz}$, 1H), 7.91 – 7.87 (m, 1H), 7.83 – 7.76 (m, 2H), 7.74 – 7.68 (m, 1H), 7.30 (d, $J = 8.7 \text{ Hz}$, 1H) ppm.

$^{19}\text{F NMR}$ (376 MHz, CDCl_3): $\delta = -83.27 - -83.77$ (m, 3F), $-112.19 - -115.63$ (m, 2F) ppm.

$^{13}\text{C NMR}$ (100 MHz, CDCl_3): $\delta = 151.1$ (t, $J = 1.1 \text{ Hz}$), 148.7, 145.9 (t, $J = 2.0 \text{ Hz}$), 143.3, 135.6

(t, $J = 32.0$ Hz), 133.9, 133.3, 132.2 (t, $J = 1.6$ Hz), 128.7, 128.1, 128.0, 126.7, 121.7 (t, $J = 1.5$ Hz), 120.9, 120.3, 119.3, 116.1, 115.5 ppm; carbons corresponding to the C_2F_5 group cannot be identified due to C-F coupling.

HRMS m/z : calcd for $C_{20}H_{11}F_5N_3O$ $[M+H]^+$ 404.0823, found: 404.0829.

Isomer II: Yellow solid. M.p. 170.6–171.7 °C.

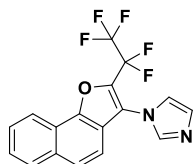
IR (KBr): $\nu = 3462, 1632, 1607, 816, 750$ cm^{-1} .

1H NMR (400 MHz, $CDCl_3$): $\delta = 9.29$ (s, 1H), 8.53 (d, $J = 5.4$ Hz, 1H), 8.47 (d, $J = 8.3$ Hz, 1H), 8.16 (d, $J = 1.0$ Hz, 1H), 8.03 (d, $J = 8.1$ Hz, 1H), 7.85 – 7.75 (m, 2H), 7.74 – 7.68 (m, 1H), 7.28 – 7.25 (m, 2H) ppm.

^{19}F NMR (376 MHz, $CDCl_3$): $\delta = -83.55$ (d, $J = 2.8$ Hz, 3F), -112.55 – -115.65 (m, 2F) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 151.1, 144.2, 143.8, 143.6, 140.4$ (m), 139.4 (t, $J = 2.1$ Hz), 135.6 (t, $J = 30.9$ Hz), 133.3, 128.7, 128.1, 128.0, 126.6, 121.6 (m), 120.9, 120.3, 119.3, 116.1, 105.7 ppm; carbons corresponding to the C_2F_5 group cannot be identified due to C-F coupling.

HRMS m/z : calcd for $C_{20}H_{11}F_5N_3O$ $[M+H]^+$ 404.0817, found: 404.0825.



1-(2-(Perfluoroethyl)naphtho[1,2-*b*]furan-3-yl)-1*H*-imidazole (4a):

Yield = 44% (47 mg), 0.3 mmol scale. Yellow oil.

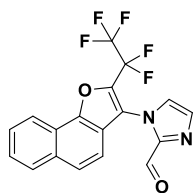
IR (KBr): $\nu = 2963, 1630, 1492, 809, 748$ cm^{-1} .

1H NMR (400 MHz, $CDCl_3$): $\delta = 8.36$ – 8.32 (m, 1H), 7.94 (d, $J = 8.0$ Hz, 1H), 7.77 – 7.72 (m, 2H), 7.69 – 7.64 (m, 1H), 7.63 – 7.58 (m, 1H), 7.40 (d, $J = 8.7$ Hz, 1H), 7.26 – 7.25 (m, 1H), 7.21 (s, 1H) ppm.

^{19}F NMR (376 MHz, $CDCl_3$): $\delta = -83.55$ (t, $J = 3.3$ Hz, 3F), -113.56 – -113.62 (m, 2F) ppm.

^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 150.6$ (t, $J = 1.3$ Hz), 138.1, 138.1, 133.8 (t, $J = 31.5$ Hz), 133.2, 130.4, 128.6, 127.8, 127.7, 126.3, 124.2 (t, $J = 1.4$ Hz), 120.8, 120.3, 119.6, 116.2 ppm; carbons corresponding to the C_2F_5 group cannot be identified due to C-F coupling.

HRMS m/z : calcd for $C_{17}H_{10}F_5N_2O$ $[M+H]^+$ 353.0708, found: 353.0710.



1-(2-(Perfluoroethyl)naphtho[1,2-*b*]furan-3-yl)-1*H*-imidazole-2-carbaldehyde (4b):

Yield = 55% (63 mg), 0.3 mmol scale. White solid. M.p. 177.5–178.8 °C.

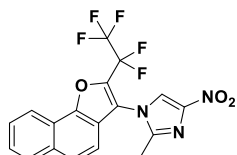
IR (KBr): $\nu = 3441, 1770, 1690, 1634, 826, 776 \text{ cm}^{-1}$.

¹H NMR (400 MHz, CDCl₃): $\delta = 9.86$ (d, $J = 0.9$ Hz, 1H), 8.39 (d, $J = 8.2$ Hz, 1H), 7.96 (d, $J = 8.2$ Hz, 1H), 7.75 (d, $J = 8.7$ Hz, 1H), 7.73 – 7.67 (m, 1H), 7.67 – 7.60 (m, 1H), 7.54 (d, $J = 1.0$ Hz, 1H), 7.34 (s, 1H), 7.19 (d, $J = 8.7$ Hz, 1H) ppm.

¹⁹F NMR (376 MHz, CDCl₃): $\delta = -83.66$ (t, $J = 4.1$ Hz, 3F), -113.17 – -117.19 (m, 2F) ppm.

¹³C NMR (100 MHz, CDCl₃): $\delta = 180.0, 150.5$ (t, $J = 1.4$ Hz), 144.4, 134.9 (t, $J = 31.6$ Hz), 133.1, 132.3, 128.6, 127.7, 127.5, 127.5, 126.3, 123.9 (t, $J = 2.6$ Hz), 120.9, 120.2, 120.1, 115.9 ppm; carbons corresponding to the C₂F₅ group cannot be identified due to C-F coupling.

HRMS m/z : calcd for C₁₈H₁₀F₅N₂O₂ [M+H]⁺ 381.0657, found: 381.0660.



2-Methyl-4-nitro-1-(2-(perfluoroethyl)naphtho[1,2-*b*]furan-3-yl)-1*H*-imidazole (4c):

Yield = 94% (116 mg), 0.3 mmol scale. White solid. M.p. 112.5–113.7 °C.

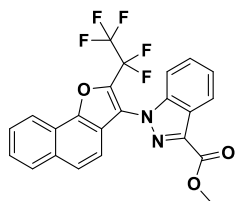
IR (KBr): $\nu = 3160, 1629, 1547, 819, 753 \text{ cm}^{-1}$.

¹H NMR (400 MHz, CDCl₃): $\delta = 8.47 - 8.42$ (m, 1H), 8.06 (d, $J = 8.0$ Hz, 1H), 7.92 (d, $J = 8.4$ Hz, 2H), 7.82 – 7.76 (m, 1H), 7.76 – 7.70 (m, 1H), 7.37 (d, $J = 8.7$ Hz, 1H), 2.38 (s, 3H) ppm.

¹⁹F NMR (376 MHz, CDCl₃): $\delta = -83.30 - -83.81$ (m, 3F), -113.27 – -116.45 (m, 2F) ppm.

¹³C NMR (100 MHz, CDCl₃): $\delta = 151.0$ (t, $J = 1.4$ Hz), 147.7, 146.4, 136.2 (t, $J = 31.6$ Hz), 133.3, 128.7, 128.2, 128.1, 127.3, 122.1 (t, $J = 2.2$ Hz), 121.2, 120.7, 120.2, 119.1, 115.1, 12.9 ppm; carbons corresponding to the C₂F₅ group cannot be identified due to C-F coupling.

HRMS m/z : calcd for C₁₈H₁₁F₅N₃O₃ [M+H]⁺ 412.0715, found: 412.0717.



Methyl 1-(2-(perfluoroethyl)naphtho[1,2-*b*]furan-3-yl)-1*H*-indazole-3-carboxylate (5a):

Yield = 79% (109 mg), 0.3 mmol scale. White solid. M.p. 142.6–143.4 °C.

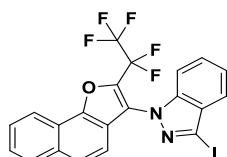
IR (KBr): $\nu = 3071, 1710, 1629, 817, 750 \text{ cm}^{-1}$.

¹H NMR (400 MHz, CDCl₃): $\delta = 8.43$ (d, $J = 7.8$ Hz, 1H), 8.41 – 8.36 (m, 1H), 7.97 (d, $J = 8.1$ Hz, 1H), 7.76 – 7.69 (m, 2H), 7.67 – 7.61 (m, 1H), 7.53 – 7.45 (m, 1H), 7.47 – 7.41 (m, 1H), 7.36 (d, $J = 8.3$ Hz, 1H), 7.32 (d, $J = 8.7$ Hz, 1H), 4.09 (s, 3H) ppm.

¹⁹F NMR (376 MHz, CDCl₃): $\delta = -83.08 - -83.18$ (m, 3F), $-113.22 - -115.69$ (m, 2F) ppm.

¹³C NMR (100 MHz, CDCl₃): $\delta = 162.6, 150.7$ (t, $J = 1.3$ Hz), 142.6, 138.5, 136.3 (t, $J = 32.5$ Hz), 133.1, 128.6, 128.2, 127.6, 127.5, 126.1, 125.1 (t, $J = 1.9$ Hz), 124.1, 123.5, 122.4, 120.8, 120.2, 120.1, 116.9, 110.1, 52.3 ppm; carbons corresponding to the C₂F₅ group cannot be identified due to C-F coupling.

HRMS m/z: calcd for C₂₃H₁₄F₅N₂O₃ [M+H]⁺ 461.0919, found: 461.0919.



3-Iodo-1-(2-(perfluoroethyl)naphtho[1,2-*b*]furan-3-yl)-1*H*-indazole (5b):

Yield = 70% (111 mg), 0.3 mmol scale. Brown solid. M.p. 49.8–51.7 °C.

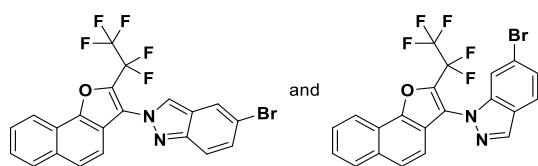
IR (KBr): $\nu = 3066, 1756, 1613, 810, 746 \text{ cm}^{-1}$.

¹H NMR (400 MHz, CDCl₃): $\delta = 8.40$ (d, $J = 8.1$ Hz, 1H), 7.94 (d, $J = 8.1$ Hz, 1H), 7.72 – 7.66 (m, 2H), 7.64 – 7.58 (m, 2H), 7.51 – 7.45 (m, 1H), 7.36 – 7.28 (m, 3H) ppm.

¹⁹F NMR (376 MHz, CDCl₃): $\delta = -82.99$ (t, $J = 2.9$ Hz, 3F), -114.11 (s, 2F) ppm.

¹³C NMR (100 MHz, CDCl₃): $\delta = 150.7$ (t, $J = 1.0$ Hz), 141.8, 135.4 (t, $J = 32.3$ Hz), 133.1, 128.9, 128.8, 128.6, 127.5, 127.4, 125.9, 125.4 (t, $J = 1.9$ Hz), 122.7, 121.9, 120.9, 120.2, 120.1, 117.3, 109.9, 97.1 ppm; carbons corresponding to the C₂F₅ group cannot be identified due to C-F coupling.

HRMS m/z: calcd for C₂₁H₁₁F₅IN₂O [M+H]⁺ 528.9831, found: 528.9831.



5-Bromo-2-(2-(perfluoroethyl)naphtho[1,2-*b*]furan-3-yl)-2*H*-indazole (5c-I) and 6-bromo-1-(2-(perfluoroethyl)naphtho[1,2-*b*]furan-3-yl)-1*H*-indazole (5c-II):

5c-I and its isomer **5c-II** were separable and identified regioisomers.

Total yield = 60% (87 mg, **5c-I/5c-II** = 1:2), 0.3 mmol scale.

5c-I: Yellow solid. M.p. 120.3–123.0 °C.

IR (KBr): $\nu = 3440, 1626, 1536, 801, 756 \text{ cm}^{-1}$.

¹H NMR (400 MHz, CDCl₃): $\delta = 8.44 - 8.39$ (m, 1H), $8.34 - 8.30$ (m, 1H), $8.06 - 8.03$ (m, 1H), $8.02 - 7.97$ (m, 1H), $7.84 - 7.75$ (m, 2H), $7.75 - 7.70$ (m, 1H), $7.69 - 7.63$ (m, 2H), 7.27 (d, $J = 7.5 \text{ Hz}$, 1H) ppm.

¹⁹F NMR (376 MHz, CDCl₃): $\delta = -83.18$ (t, $J = 4.0 \text{ Hz}$, 3F), $-111.91 - -113.37$ (m, 2F) ppm.

¹³C NMR (100 MHz, CDCl₃): $\delta = 151.0, 150.7$ (t, $J = 1.0 \text{ Hz}$), $133.3, 132.8, 128.6, 127.9$ (t, $J = 1.4 \text{ Hz}$), $127.6, 127.6, 127.0, 126.5$ (t, $J = 3.3 \text{ Hz}$), $126.3, 121.9, 121.7, 120.7, 120.6, 120.4, 120.4, 119.5, 118.0$ ppm; carbons corresponding to the C₂F₅ group cannot be identified due to C-F coupling.

HRMS m/z: calcd for C₂₁H₁₁BrF₅N₂O [M+H]⁺ 480.9975, found: 480.9975.

5c-II: Yellow solid. M.p. 132.1–133.8 °C.

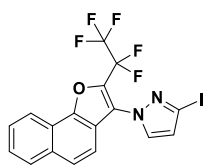
IR (KBr): $\nu = 3451, 1630, 1478, 810, 749 \text{ cm}^{-1}$.

¹H NMR (400 MHz, CDCl₃): $\delta = 8.44$ (d, $J = 8.2 \text{ Hz}$, 1H), 8.31 (t, $J = 1.0 \text{ Hz}$, 1H), 7.98 (d, $J = 8.1 \text{ Hz}$, 1H), $7.78 - 7.69$ (m, 3H), $7.68 - 7.62$ (m, 1H), 7.54 (s, 1H), $7.42 - 7.37$ (m, 1H), $7.35 - 7.31$ (m, 1H) ppm.

¹⁹F NMR (376 MHz, CDCl₃): $\delta = -83.10$ (t, $J = 3.4 \text{ Hz}$, 3F), -114.26 (s, 2F) ppm.

¹³C NMR (100 MHz, CDCl₃): $\delta = 150.7$ (t, $J = 1.9 \text{ Hz}$), $142.1, 137.0, 135.7$ (t, $J = 1.3 \text{ Hz}$), $133.1, 128.6, 127.6, 127.5, 126.0, 125.8, 125.5$ (t, $J = 1.0 \text{ Hz}$), $123.4, 122.4, 122.2, 121.0, 120.3, 120.1, 117.1, 112.9$ ppm; carbons corresponding to the C₂F₅ group cannot be identified due to C-F coupling.

HRMS m/z: calcd for C₂₁H₁₁BrF₅N₂O [M+H]⁺ 480.9969, found: 480.9975.



3-iodo-1-(2-(perfluoroethyl)naphtho[1,2-*b*]furan-3-yl)-1*H*-pyrazole (6a):

Yield = 43% (62 mg), 0.3 mmol scale. Yellow solid. M.p. 82.8–83.3 °C.

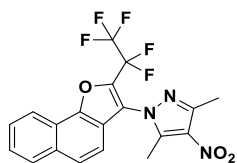
IR (KBr): $\nu = 3447, 1633, 1475, 811, 741 \text{ cm}^{-1}$.

¹H NMR (400 MHz, CDCl₃): $\delta = 8.39 - 8.34$ (m, 1H), 7.99 – 7.95 (m, 1H), 7.88 (d, $J = 0.4$ Hz, 1H), 7.86 – 7.84 (m, 1H), 7.78 (d, $J = 8.6$ Hz, 1H), 7.73 – 7.67 (m, 2H), 7.66 – 7.61 (m, 1H) ppm.

¹⁹F NMR (376 MHz, CDCl₃): $\delta = -83.20$ (t, $J = 4.0$ Hz, 3F), $-112.24 - -113.07$ (m, 2F) ppm.

¹³C NMR (100 MHz, CDCl₃): $\delta = 150.5$ (t, $J = 1.3$ Hz), 147.3, 136.1 (t, $J = 3.3$ Hz), 133.1, 132.0 (t, $J = 32.2$ Hz), 128.5, 127.5, 127.0 (m), 125.9, 120.7, 120.3, 119.9, 119.1, 118.0, 59.0 ppm; carbons corresponding to the C₂F₅ group cannot be identified due to C-F coupling.

HRMS m/z : calcd for C₁₇H₉F₅IN₂O [M+H]⁺ 478.9674, found: 478.9675.



3,5-Dimethyl-4-nitro-1-(2-(perfluoroethyl)naphtho[1,2-*b*]furan-3-yl)-1*H*-pyrazole (6b):

Yield = 92% (117 mg), 0.3 mmol scale. White solid. M.p. 155.0–156.2 °C.

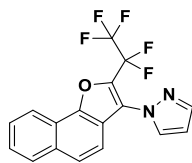
IR (KBr): $\nu = 3447, 1633, 1532, 811, 742 \text{ cm}^{-1}$.

¹H NMR (400 MHz, CDCl₃): $\delta = 8.45 - 8.36$ (m, 1H), 7.99 (d, $J = 8.0$ Hz, 1H), 7.82 (d, $J = 8.6$ Hz, 1H), 7.75 – 7.70 (m, 1H), 7.69 – 7.64 (m, 1H), 7.36 (d, $J = 8.7$ Hz, 1H), 2.65 (s, 3H), 2.58 (s, 3H) ppm.

¹⁹F NMR (376 MHz, CDCl₃): $\delta = -83.19$ (t, $J = 2.6$ Hz, 3F), $-114.21 - -116.27$ (m, 2F) ppm.

¹³C NMR (100 MHz, CDCl₃): $\delta = 150.8$ (t, $J = 1.1$ Hz), 148.1, 143.7, 136.8 (t, $J = 32.1$ Hz), 133.2, 132.2, 128.6, 127.9, 127.7, 126.7, 124.3 (t, $J = 1.8$ Hz), 120.7, 120.2, 119.7, 116.0, 14.1, 12.2 ppm; carbons corresponding to the C₂F₅ group cannot be identified due to C-F coupling.

HRMS m/z : calcd for C₁₉H₁₃F₅N₃O₃ [M+H]⁺ 426.0872, found: 426.0880.



1-(2-(Perfluoroethyl)naphtho[1,2-*b*]furan-3-yl)-1*H*-pyrazole (6c):

Yield = 46% (49 mg), 0.3 mmol scale. White solid. M.p. 78.9–79.1 °C.

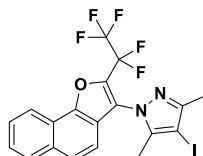
IR (KBr): $\nu = 3077, 1634, 1532, 811, 742 \text{ cm}^{-1}$.

¹H NMR (400 MHz, CDCl₃): $\delta = 8.37$ (d, $J = 8.1$ Hz, 1H), 7.96 (d, $J = 8.0$ Hz, 1H), 7.89 (d, $J = 1.6$ Hz, 1H), 7.85 – 7.81 (m, 1H), 7.81 – 7.74 (m, 2H), 7.72 – 7.58 (m, 2H), 6.55 (t, $J = 2.1$ Hz, 1H) ppm.

¹⁹F NMR (376 MHz, CDCl₃): $\delta = -83.25$ (t, $J = 2.3$ Hz, 3F), $-112.49 - -112.62$ (m, 2F) ppm.

¹³C NMR (100 MHz, CDCl₃): $\delta = 150.5$ (t, $J = 1.3$ Hz), 142.3, 133.1, 132.1 (t, $J = 1.3$ Hz), 131.6 (t, $J = 32.8$ Hz), 128.5, 127.9 (t, $J = 2.1$ Hz), 127.3, 125.7, 122.8, 120.8, 120.3, 119.5 (t, $J = 1.0$ Hz), 118.5, 107.5 ppm; carbons corresponding to the C₂F₅ group cannot be identified due to C-F coupling.

HRMS m/z : calcd for C₁₇H₁₀F₅N₂O [M+H]⁺ 353.0708, found: 353.0714.



4-iodo-3,5-dimethyl-1-(2-(perfluoroethyl)naphtho[1,2-*b*]furan-3-yl)-1*H*-pyrazole (6d):

Yield = 75% (114 mg), 0.3 mmol scale. White solid. M.p. 80.3–81.8 °C.

IR (KBr): $\nu = 3134, 1628, 1543, 804, 744 \text{ cm}^{-1}$.

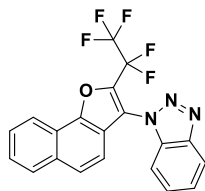
¹H NMR (400 MHz, CDCl₃): $\delta = 8.41 - 8.35$ (m, 1H), 7.97 (d, $J = 8.1$ Hz, 1H), 7.76 (d, $J = 8.6$ Hz, 1H), 7.72 – 7.67 (m, 1H), 7.65 – 7.60 (m, 1H), 7.36 (d, $J = 8.7$ Hz, 1H), 2.34 (s, 3H), 2.22 (s, 3H) ppm.

¹⁹F NMR (376 MHz, CDCl₃): $\delta = -83.13 - -83.20$ (m, 3F), $-112.58 - -117.51$ (m, 2F) ppm.

¹³C NMR (100 MHz, CDCl₃): $\delta = 152.5, 150.5$ (t, $J = 1.4$ Hz), 143.6, 136.1 (t, $J = 32.0$ Hz), 133.1, 128.6, 127.6, 127.4, 126.3 (t, $J = 1.8$ Hz), 126.1, 120.9, 120.4 (t, $J = 0.9$ Hz), 120.2, 116.8, 64.8, 14.3, 12.2 ppm; carbons corresponding to the C₂F₅ group cannot be identified due to C-F

coupling.

HRMS m/z: calcd for C₁₉H₁₃F₅IN₂O [M+H]⁺ 506.9987, found: 506.9995.



1-(2-(Perfluoroethyl)naphtho[1,2-*b*]furan-3-yl)-1*H*-benzo[*d*][1,2,3]triazole (7a):

Yield = 98% (119 mg), 0.3 mmol scale. Pink solid. M.p. 71.1–73.2 °C.

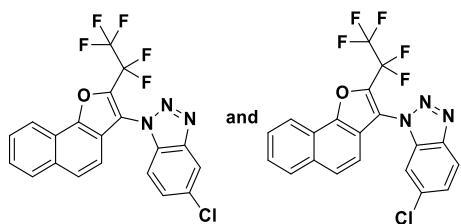
IR (KBr): ν = 3056, 1634, 1492, 811, 747 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ = 8.45 – 8.38 (m, 1H), 8.25 – 8.20 (m, 1H), 7.97 (d, *J* = 8.1 Hz, 1H), 7.76 – 7.69 (m, 2H), 7.67 – 7.62 (m, 1H), 7.61 – 7.55 (m, 1H), 7.52 – 7.45 (m, 2H), 7.28 (d, *J* = 8.7 Hz, 1H) ppm.

¹⁹F NMR (376 MHz, CDCl₃): δ = -83.15 (d, *J* = 2.3 Hz, 3F), -114.25 (s, 2F) ppm.

¹³C NMR (100 MHz, CDCl₃): δ = 150.9 (t, *J* = 1.2 Hz), 145.6, 135.7 (t, *J* = 32.3 Hz), 134.2, 133.1, 128.9, 128.6, 127.8, 127.7, 126.4, 124.7, 122.8, 120.8 (t, *J* = 1.9 Hz), 120.4, 120.2, 119.4, 116.6, 109.6 ppm; carbons corresponding to the C₂F₅ group cannot be identified due to C-F coupling.

HRMS m/z: calcd for C₂₀H₁₁F₅N₃O [M+H]⁺ 404.0817, found: 404.0826.



5-Chloro-1-(2-(perfluoroethyl)naphtho[1,2-*b*]furan-3-yl)-1*H*-benzo[*d*][1,2,3]triazole (7b-I) and 6-chloro-1-(2-(perfluoroethyl)naphtho[1,2-*b*]furan-3-yl)-1*H*-benzo[*d*][1,2,3]triazole (7b-II):

7b-I and its isomer **7b-II** were separable but unidentified regioisomers.

Total yield = 99% (130 mg, **7b-I/7b-II** = 1/1), 0.3 mmol scale.

Isomer I: White solid. M.p. 117.8–120.1 °C.

IR (KBr): ν = 3065, 1632, 1610, 809, 759 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ = 8.47 – 8.42 (m, 1H), 8.21 (dd, *J* = 1.8, 0.7 Hz, 1H), 8.00 (d, *J* = 8.1 Hz, 1H), 7.81 – 7.74 (m, 2H), 7.71 – 7.66 (m, 1H), 7.56 (dd, *J* = 8.8, 1.8 Hz, 1H), 7.41 (d, *J* = 8.8 Hz, 1H), 7.29 (d, *J* = 8.7 Hz, 1H) ppm.

¹⁹F NMR (376 MHz, CDCl₃): δ = -83.16 (t, *J* = 3.9 Hz, 3F), -114.30 (s, 2F) ppm.

¹³C NMR (100 MHz, CDCl₃): δ = 151.0 (t, *J* = 1.1 Hz), 146.3, 135.9 (t, *J* = 32.5 Hz), 133.3, 133.0, 130.8, 129.9, 128.7, 128.0, 127.9, 126.7, 122.4 (t, *J* = 1.8 Hz), 120.8, 120.3, 119.9, 119.3, 116.4, 110.6 ppm; carbons corresponding to the C₂F₅ group cannot be identified due to C-F coupling.

HRMS *m/z*: calcd for C₂₀H₁₀ClF₅N₃O [M+H]⁺ 438.0433, found: 438.0432.

Isomer II: White solid. M.p. 118.9–120.0 °C.

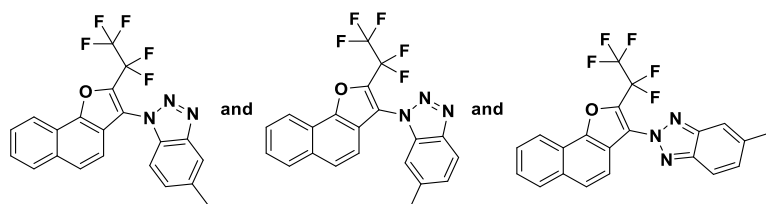
IR (KBr): ν = 3069, 1633, 1532, 811, 742 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ = 8.47 – 8.42 (m, 1H), 8.15 (d, *J* = 9.3 Hz, 1H), 8.00 (d, *J* = 8.1 Hz, 1H), 7.80 (d, *J* = 8.6 Hz, 1H), 7.78 – 7.72 (m, 1H), 7.71 – 7.65 (m, 1H), 7.49 – 7.45 (m, 2H), 7.29 (d, *J* = 8.7 Hz, 1H) ppm.

¹⁹F NMR (376 MHz, CDCl₃): δ = -83.12 – -83.25 (m, 3F), -114.34 (s, 2F) ppm.

¹³C NMR (100 MHz, CDCl₃): δ = 151.0 (t, *J* = 1.0 Hz), 144.2, 136.0 (t, *J* = 32.5 Hz), 135.7, 134.9, 133.2, 128.7, 127.9, 127.8, 126.7, 126.0, 122.3 (t, *J* = 2.1 Hz), 121.4, 120.8, 120.3, 119.3, 116.3, 109.5 ppm; carbons corresponding to the C₂F₅ group cannot be identified due to C-F coupling.

HRMS *m/z*: calcd for C₂₀H₁₀ClF₅N₃O [M+H]⁺ 438.0427, found: 438.0430.



5-Methyl-1-(2-(perfluoroethyl)naphtho[1,2-*b*]furan-3-yl)-1*H*-benzo[*d*][1,2,3]triazole (7c-I), 6-methyl-1-(2-(perfluoroethyl)naphtho[1,2-*b*]furan-3-yl)-1*H*-benzo[*d*][1,2,3]triazole (7c-II), and 5-methyl-2-(2-(perfluoroethyl)naphtho[1,2-*b*]furan-3-yl)-2*H*-benzo[*d*][1,2,3]triazole (7c-III):

7c-I, 7c-II and its isomer **7c-III** were inseparable and unidentified regioisomers.

Total yield = 87% (109 mg, **7c-I/7c-II/7c-III** = 1/1/1), 0.3 mmol scale. Yellow solid.

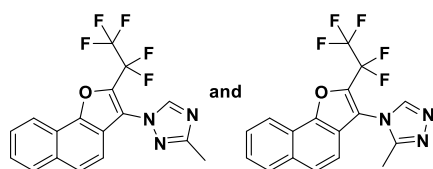
IR (KBr): ν = 2962, 1632, 1496, 809, 722 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ = 8.27 (d, *J* = 8.1 Hz, 1H), 7.97 – 7.79 (m, 1.5H), 7.64 – 7.54 (m, 2H), 7.50 (t, *J* = 7.5 Hz, 1H), 7.35 – 7.09 (m, 3.5H), 2.81 – 2.34 (m, 3H) ppm.

¹⁹F NMR (376 MHz, CDCl₃): δ = -83.11 – -83.19 (m, 3F), -114.18 (d, *J* = 25.9 Hz, 2F) ppm.

¹³C NMR (100 MHz, CDCl₃): δ = 150.8, 146.2, 145.5, 144.2, 139.9, 135.8 (t, *J* = 32.1 Hz), 135.7 (t, *J* = 32.1 Hz), 135.6 (t, *J* = 32.1 Hz), 134.9, 134.8, 134.2, 133.1, 132.8, 131.5, 131.0, 128.8, 128.6, 127.7, 127.6, 126.9, 126.3, 126.3, 126.3, 126.0, 124.6, 123.0 (t, *J* = 1.4 Hz), 123.0 (t, *J* = 1.4 Hz), 122.9 (t, *J* = 1.4 Hz), 122.6, 120.8, 120.8, 120.1, 119.8, 119.8, 119.5, 119.5, 119.5, 119.3, 116.6, 109.1, 108.8, 106.8, 21.9, 21.3, 16.6 ppm; carbons corresponding to the C₂F₅ group cannot be identified due to C-F coupling.

HRMS *m/z*: calcd for C₂₁H₁₃F₅N₃O [M+H]⁺ 418.0973, found: 418.0991.



3-Methyl-1-(2-(perfluoroethyl)naphtho[1,2-*b*]furan-3-yl)-1*H*-1,2,4-triazole (8-I) and **3-methyl-4-(2-(perfluoroethyl)naphtho[1,2-*b*]furan-3-yl)-4*H*-1,2,4-triazole (8-II)**:

8-I and its isomer **8-II** were separable and identified regioisomers.

Total yield = 91% (100 mg, **8-I/8-II** = 2.8/1), 0.3 mmol scale.

Isomer 8-I: White solid. M.p. 143.0–144.3 °C.

IR (KBr): ν = 3119, 1653, 1635, 811, 729 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ = 8.36 (d, *J* = 9.4 Hz, 2H), 7.98 (d, *J* = 8.0 Hz, 1H), 7.79 (d, *J* = 8.8 Hz, 1H), 7.73 – 7.67 (m, 2H), 7.64 (t, *J* = 7.5 Hz, 1H), 2.58 (s, 3H) ppm.

¹⁹F NMR (376 MHz, CDCl₃): δ = -83.39 (t, *J* = 4.2 Hz, 3F), -112.68 – -113.49 (m, 2F) ppm.

¹³C NMR (100 MHz, CDCl₃): δ = 163.0, 150.7, 145.5 (t, *J* = 3.6 Hz), 133.2, 132.6 (t, *J* = 32.1 Hz), 128.5, 127.6, 127.6, 126.1, 124.2 (m), 120.6, 120.2, 118.9, 117.6, 13.9 ppm; carbons corresponding to the C₂F₅ group cannot be identified due to C-F coupling.

HRMS *m/z*: calcd for C₁₇H₁₁F₅N₃O [M+H]⁺ 368.0823, found: 368.0830.

Isomer 8-II: White solid. M.p. 144.2–145.5 °C.

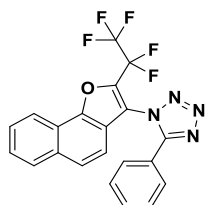
IR (KBr): ν = 3057, 1750, 1528, 803, 748 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ = 8.45 – 8.38 (m, 1H), 8.10 (s, 1H), 8.01 (d, *J* = 8.1 Hz, 1H), 7.82 (d, *J* = 8.7 Hz, 1H), 7.77 – 7.71 (m, 1H), 7.71 – 7.65 (m, 1H), 7.34 (d, *J* = 8.7 Hz, 1H), 2.45 (s, 3H) ppm.

¹⁹F NMR (376 MHz, CDCl₃): δ = -83.24 (t, *J* = 3.9 Hz, 3F), -112.81 – -117.59 (m, 2F) ppm.

¹³C NMR (100 MHz, CDCl₃): δ = 155.0 (m), 152.5, 150.8 (t, *J* = 1.2 Hz), 136.3 (t, *J* = 31.6 Hz), 133.2, 128.7, 127.9, 127.7, 126.6, 123.8 (t, *J* = 2.2 Hz), 120.8, 120.3, 119.7, 116.2, 12.0 ppm; carbons corresponding to the C₂F₅ group cannot be identified due to C-F coupling.

HRMS *m/z*: calcd for C₁₇H₁₁F₅N₃O [M+H]⁺ 368.0817, found: 368.0833.



1-(2-(Perfluoroethyl)naphtho[1,2-*b*]furan-3-yl)-5-phenyl-1*H*-tetrazole (9):

Yield = 39% (50 mg), 0.3 mmol scale. Yellow solid. M.p. 131.7–132.5 °C.

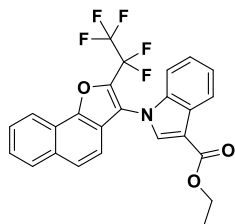
IR (KBr): *ν* = 3423, 1620, 1536, 819, 728 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ = 8.41 – 8.36 (m, 1H), 8.32 – 8.26 (m, 2H), 7.99 (d, *J* = 7.3 Hz, 1H), 7.96 – 7.92 (m, 1H), 7.84 (d, *J* = 8.7 Hz, 1H), 7.74 – 7.68 (m, 1H), 7.68 – 7.63 (m, 1H), 7.59 – 7.52 (m, 3H) ppm.

¹⁹F NMR (376 MHz, CDCl₃): δ = -82.78 (t, *J* = 4.1 Hz, 3F), -112.60 – -112.98 (m, 2F) ppm.

¹³C NMR (100 MHz, CDCl₃): δ = 165.6, 150.5 (t, *J* = 1.4 Hz), 133.5 (t, *J* = 33.4 Hz), 133.2, 131.0, 129.1, 128.6, 127.8, 127.8, 127.2, 126.6, 126.5, 123.7 (m), 120.5, 120.3, 117.8, 117.3 (t, *J* = 1.0 Hz) ppm; carbons corresponding to the C₂F₅ group cannot be identified due to C-F coupling.

HRMS *m/z*: calcd for C₂₁H₁₂F₅N₄O [M+H]⁺ 431.0926, found: 431.0921.



Ethyl 1-(2-(perfluoroethyl)naphtho[1,2-*b*]furan-3-yl)-1*H*-indole-3-carboxylate (10a):

Yield = 63% (89 mg), 0.3 mmol scale. Yellow solid. M.p. 134.0–135.2 °C.

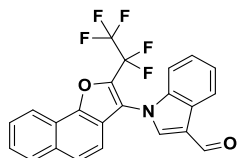
IR (KBr): $\nu = 3066, 1626, 1540, 808, 751 \text{ cm}^{-1}$.

¹H NMR (400 MHz, CDCl₃): $\delta = 8.44$ (d, $J = 7.9 \text{ Hz}$, 1H), 8.32 (d, $J = 7.6 \text{ Hz}$, 1H), 7.98 (d, $J = 10.9 \text{ Hz}$, 2H), 7.73 (t, $J = 8.1 \text{ Hz}$, 2H), $7.69 - 7.62$ (m, 1H), $7.41 - 7.34$ (m, 1H), $7.30 - 7.25$ (m, 1H), $7.25 - 7.22$ (m, 1H), $7.19 - 7.14$ (m, 1H), $4.52 - 4.39$ (m, 2H), 1.46 (t, $J = 7.1 \text{ Hz}$, 3H) ppm.

¹⁹F NMR (376 MHz, CDCl₃): $\delta = -83.14 - -83.73$ (m, 3F), $-112.59 - -115.84$ (m, 2F) ppm.

¹³C NMR (100 MHz, CDCl₃): $\delta = 164.6, 150.8$ (t, $J = 1.3 \text{ Hz}$), $137.9, 135.7$ (t, $J = 31.8 \text{ Hz}$), $135.0, 133.2, 128.6, 127.7, 127.6, 126.4, 126.0, 124.9$ (t, $J = 1.8 \text{ Hz}$), $123.9, 122.9, 122.0, 121.0, 120.3, 120.2, 116.9, 110.9, 110.8, 60.1, 14.5$ ppm; carbons corresponding to the C₂F₅ group cannot be identified due to C-F coupling.

HRMS m/z: calcd for C₂₅H₁₇F₅NO₃ [M+H]⁺ 474.1123, found: 474.1126.



1-(2-(Perfluoroethyl)naphtho[1,2-*b*]furan-3-yl)-1*H*-indole-3-carbaldehyde (10b):

Yield = 57% (74 mg), 0.3 mmol scale. Light brown solid. M.p. 150.5–152.2 °C.

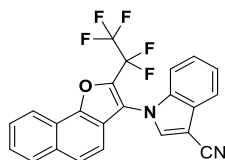
IR (KBr): $\nu = 3104, 1676, 1626, 1611, 805, 755 \text{ cm}^{-1}$.

¹H NMR (400 MHz, CDCl₃): $\delta = 10.16$ (s, 1H), $8.48 - 8.42$ (m, 2H), 8.00 (d, $J = 8.1 \text{ Hz}$, 1H), 7.90 (s, 1H), $7.79 - 7.72$ (m, 2H), $7.71 - 7.65$ (m, 1H), $7.44 - 7.38$ (m, 1H), $7.36 - 7.30$ (m, 1H), 7.26 (d, $J = 8.7 \text{ Hz}$, 1H), 7.18 (d, $J = 8.2 \text{ Hz}$, 1H) ppm.

¹⁹F NMR (376 MHz, CDCl₃): $\delta = -83.45$ (t, $J = 4.0 \text{ Hz}$, 3F), $-112.29 - -115.94$ (m, 2F) ppm.

¹³C NMR (100 MHz, CDCl₃): $\delta = 185.0, 150.9$ (t, $J = 1.0 \text{ Hz}$), $139.2, 138.4, 135.7$ (t, $J = 31.7 \text{ Hz}$), $133.2, 128.6, 127.9, 127.7, 126.2, 125.1, 125.0, 124.6$ (t, $J = 1.6 \text{ Hz}$), $123.8, 122.4, 121.0, 120.7, 120.3, 119.9, 116.7, 110.8$ ppm; carbons corresponding to the C₂F₅ group cannot be identified due to C-F coupling.

HRMS m/z: calcd for C₂₃H₁₃F₅NO₂ [M+H]⁺ 430.0861, found: 430.0871.



1-(2-(Perfluoroethyl)naphtho[1,2-*b*]furan-3-yl)-1*H*-indole-3-carbonitrile (10c):

Yield = 65% (83 mg), 0.3 mmol scale. White solid. M.p. 169.8–171.3 °C.

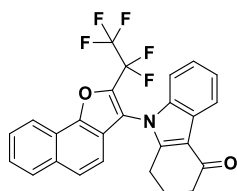
IR (KBr): $\nu = 3118, 2228, 1748, 1471, 804, 746 \text{ cm}^{-1}$.

¹H NMR (400 MHz, CDCl₃): $\delta = 8.46$ (d, $J = 8.2$ Hz, 1H), 8.01 (d, $J = 8.1$ Hz, 1H), $7.92 - 7.86$ (m, 1H), $7.80 - 7.73$ (m, 3H), $7.72 - 7.66$ (m, 1H), $7.45 - 7.39$ (m, 1H), $7.38 - 7.33$ (m, 1H), $7.26 - 7.19$ (m, 2H) ppm.

¹⁹F NMR (376 MHz, CDCl₃): $\delta = -83.01 - -83.86$ (m, 3F), $-112.07 - -116.33$ (m, 2F) ppm.

¹³C NMR (100 MHz, CDCl₃): $\delta = 150.9$ (t, $J = 1.1$ Hz), $136.6, 135.9$ (t, $J = 31.9$ Hz), $135.7, 133.2, 128.7, 127.9, 127.8, 127.3, 126.3, 125.2, 124.2$ (t, $J = 1.3$ Hz), $123.3, 120.9, 120.3, 120.1, 119.8, 116.5, 114.7, 111.4, 89.8$ ppm; carbons corresponding to the C₂F₅ group cannot be identified due to C-F coupling.

HRMS m/z : calcd for C₂₃H₁₂F₅N₂O [M+H]⁺ 427.0864, found: 427.0870.



9-(2-(Perfluoroethyl)naphtho[1,2-*b*]furan-3-yl)-1,2,3,9-tetrahydro-4*H*-carbazol-4-one

(10d):

Yield = 76% (107 mg), 0.3 mmol scale. Light brown solid. M.p. 150.8–151.3 °C.

IR (KBr): $\nu = 3116, 1721, 1659, 1617, 810, 749 \text{ cm}^{-1}$.

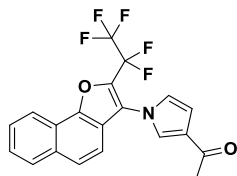
¹H NMR (400 MHz, CDCl₃): $\delta = 8.50 - 8.45$ (m, 1H), $8.39 - 8.34$ (m, 1H), 8.00 (d, $J = 7.5$ Hz, 1H), $7.80 - 7.73$ (m, 2H), $7.71 - 7.65$ (m, 1H), $7.38 - 7.31$ (m, 1H), $7.24 - 7.19$ (m, 1H), 7.17 (d, $J = 8.7$ Hz, 1H), 7.01 (d, $J = 8.2$ Hz, 1H), $2.92 - 2.80$ (m, 1H), $2.76 - 2.63$ (m, 3H), $2.30 - 2.18$ (m, 2H) ppm.

¹⁹F NMR (376 MHz, CDCl₃): $\delta = -83.01 - -83.57$ (m, 3F), $-113.30 - -117.05$ (m, 2F) ppm.

¹³C NMR (100 MHz, CDCl₃): $\delta = 194.3, 152.6, 151.2$ (t, $J = 1.2$ Hz), $138.4, 137.2$ (t, $J = 31.4$ Hz), $133.2, 128.6, 127.9, 127.7, 126.4, 124.8, 123.9, 123.4, 122.7$ (t, $J = 1.6$ Hz), $121.7, 121.0,$

120.4, 120.2, 116.3, 114.8, 110.0, 38.0, 23.4, 22.2 ppm; carbons corresponding to the C₂F₅ group cannot be identified due to C-F coupling.

HRMS m/z: calcd for C₂₆H₁₇F₅NO₂ [M+H]⁺ 470.1174, found: 470.1184.



1-(1-(2-(Perfluoroethyl)naphtho[1,2-*b*]furan-3-yl)-1*H*-pyrrol-3-yl)ethan-1-one (11a):

Yield = 39% (46 mg), 0.3 mmol scale. White solid. M.p. 98.1–98.7 °C.

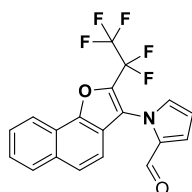
IR (KBr): $\nu = 3141, 1667, 1629, 810, 759 \text{ cm}^{-1}$.

¹H NMR (400 MHz, CDCl₃): $\delta = 8.40$ (d, $J = 8.1$ Hz, 1H), 8.00 (d, $J = 8.0$ Hz, 1H), 7.81 (d, $J = 8.7$ Hz, 1H), $7.75 - 7.69$ (m, 1H), $7.69 - 7.63$ (m, 1H), 7.58 (t, $J = 1.8$ Hz, 1H), 7.51 (d, $J = 8.7$ Hz, 1H), $7.00 - 6.96$ (m, 1H), $6.88 - 6.84$ (m, 1H), 2.50 (s, 3H) ppm.

¹⁹F NMR (376 MHz, CDCl₃): $\delta = -83.48$ (t, $J = 4.0$ Hz, 3F), -113.36 (q, $J = 3.7$ Hz, 2F) ppm.

¹³C NMR (100 MHz, CDCl₃): $\delta = 193.3, 150.5$ (t, $J = 1.0$ Hz), 133.5 (t, $J = 31.9$ Hz), $133.2, 128.6, 127.9, 127.8, 127.6, 127.3$ (t, $J = 1.5$ Hz), 127.0 (t, $J = 1.9$ Hz), $126.2, 124.5, 120.8, 120.3, 119.7, 116.4, 110.6, 27.3$ ppm; carbons corresponding to the C₂F₅ group cannot be identified due to C-F coupling.

HRMS m/z: calcd for C₂₀H₁₃F₅NO₂ [M+H]⁺ 394.0861, found: 394.0869.



1-(2-(Perfluoroethyl)naphtho[1,2-*b*]furan-3-yl)-1*H*-pyrrole-2-carbaldehyde (11b):

Yield = 66% (75 mg), 0.3 mmol scale. Yellow solid. M.p. 119.0–119.4 °C.

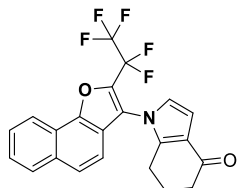
IR (KBr): $\nu = 3137, 1672, 1537, 815, 768 \text{ cm}^{-1}$.

¹H NMR (400 MHz, CDCl₃): $\delta = 9.61 - 9.59$ (m, 1H), $8.41 - 8.35$ (m, 1H), 7.94 (d, $J = 8.1$ Hz, 1H), 7.72 (d, $J = 8.6$ Hz, 1H), $7.70 - 7.65$ (m, 1H), $7.63 - 7.57$ (m, 1H), 7.25 (d, $J = 8.6$ Hz, 1H), $7.23 - 7.20$ (m, 1H), 7.09 (s, 1H), 6.53 (dd, $J = 4.0, 2.7$ Hz, 1H) ppm.

¹⁹F NMR (376 MHz, CDCl₃): δ = -83.62 (t, J = 3.9 Hz, 3F), -112.24 – -117.23 (m, 2F) ppm.

¹³C NMR (100 MHz, CDCl₃): δ = 178.2, 150.2 (t, J = 1.2 Hz), 135.0 (t, J = 31.2 Hz), 133.6, 133.1, 132.2, 128.5, 127.5, 127.2, 126.5 (t, J = 2.3 Hz), 125.9, 123.7 (m), 121.1, 121.0, 120.3, 116.6, 111.6 ppm; carbons corresponding to the C₂F₅ group cannot be identified due to C-F coupling.

HRMS m/z: calcd for C₁₉H₁₁F₅NO₂ [M+H]⁺ 380.0704, found: 380.0704.



1-(2-(Perfluoroethyl)naphtho[1,2-*b*]furan-3-yl)-1,5,6,7-tetrahydro-4*H*-indol-4-one (11c):

Yield = 46% (78 mg), 0.3 mmol scale. Yellow solid. M.p. 113.4–114.9 °C.

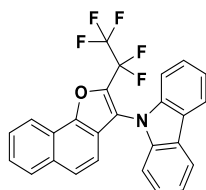
IR (KBr): ν = 2951, 1668, 1627, 809, 748 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ = 8.46 – 8.38 (m, 1H), 8.01 (d, J = 8.1 Hz, 1H), 7.82 (d, J = 8.7 Hz, 1H), 7.74 (t, J = 7.5 Hz, 1H), 7.68 (t, J = 7.6 Hz, 1H), 7.35 (d, J = 8.7 Hz, 1H), 6.80 (d, J = 4.2 Hz, 2H), 2.61 (t, J = 6.3 Hz, 2H), 2.59 – 2.52 (m, 2H), 2.15 (p, J = 6.3 Hz, 2H) ppm.

¹⁹F NMR (376 MHz, CDCl₃): δ = -83.53 (t, J = 3.2 Hz, 3F), -112.29 – -117.12 (m, 2F) ppm.

¹³C NMR (100 MHz, CDCl₃): δ = 194.3, 150.6 (t, J = 1.3 Hz), 145.3, 135.8 (t, J = 31.5 Hz), 133.2, 128.6, 127.8, 127.6, 126.4, 125.1 (t, J = 1.8 Hz), 124.5, 122.1, 120.9, 120.4, 120.2, 116.2, 107.0, 37.7, 23.7, 21.8 ppm; carbons corresponding to the C₂F₅ group cannot be identified due to C-F coupling.

HRMS m/z: calcd for C₂₂H₁₅F₅NO₂ [M+H]⁺ 420.1017, found: 420.1018.



9-(2-(Perfluoroethyl)naphtho[1,2-*b*]furan-3-yl)-9*H*-carbazole (12):

Yield = 40% (54 mg), 0.3 mmol scale. Yellow solid. M.p. 111.8–112.3 °C.

IR (KBr): ν = 3363, 1790, 1620, 812, 746 cm⁻¹.

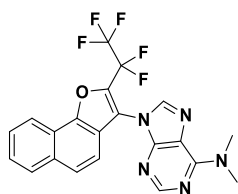
¹H NMR (400 MHz, CDCl₃): δ = 8.53 – 8.43 (m, 1H), 8.20 – 8.16 (m, 2H), 7.91 (d, J = 8.2 Hz,

1H), 7.70 (t, $J = 7.5$ Hz, 1H), 7.59 (d, $J = 6.9$ Hz, 2H), 7.42 – 7.36 (m, 2H), 7.35 – 7.30 (m, 2H), 7.19 – 7.16 (m, 2H), 7.01 (s, 1H) ppm.

^{19}F NMR (376 MHz, CDCl_3): $\delta = -82.76 - -83.72$ (m, 3F), $-114.60 - -115.57$ (m, 2F) ppm.

^{13}C NMR (100 MHz, CDCl_3): $\delta = 151.4, 141.4, 137.5$ (t, $J = 31.6$ Hz), 133.1, 128.6, 127.5, 127.3, 126.3, 125.5, 123.9, 123.8 (t, $J = 1.8$ Hz), 121.2, 120.7, 120.7, 120.4, 120.2, 117.4, 110.0 ppm; carbons corresponding to the C_2F_5 group cannot be identified due to C-F coupling.

HRMS m/z : calcd for $\text{C}_{26}\text{H}_{15}\text{F}_5\text{NO}$ $[\text{M}+\text{H}]^+$ 452.1068, found: 452.1070.



***N,N*-Dimethyl-9-(2-(perfluoroethyl)naphtho[1,2-*b*]furan-3-yl)-9*H*-purin-6-amine (13):**

Yield = 36% (48 mg), 0.3 mmol scale. Yellow solid. M.p. 175.2–175.6 °C.

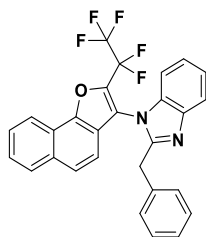
IR (KBr): $\nu = 2934, 1614, 1566, 820, 745$ cm^{-1} .

^1H NMR (400 MHz, CDCl_3): $\delta = 8.40$ (d, $J = 8.2$ Hz, 1H), 8.38 – 8.35 (m, 1H), 7.96 (d, $J = 8.1$ Hz, 1H), 7.92 – 7.88 (m, 1H), 7.76 (d, $J = 8.7$ Hz, 1H), 7.70 (t, $J = 7.6$ Hz, 1H), 7.66 – 7.60 (m, 1H), 7.36 (d, $J = 8.7$ Hz, 1H), 3.60 (s, 6H) ppm.

^{19}F NMR (376 MHz, CDCl_3): $\delta = -83.33 - -83.61$ (m, 3F), $-108.83 - -109.25$ (m, 2F) ppm.

^{13}C NMR (100 MHz, CDCl_3): $\delta = 155.1, 153.5, 151.6, 151.0$ (t, $J = 1.1$ Hz), 138.0, 135.3 (t, $J = 31.2$ Hz), 133.2, 128.5, 127.6, 127.5, 126.1, 121.5 (t, $J = 1.3$ Hz), 120.9, 120.2, 119.9, 119.6, 117.2, 116.9, 38.6 ppm; carbons corresponding to the C_2F_5 group cannot be identified due to C-F coupling.

HRMS m/z : calcd for $\text{C}_{21}\text{H}_{15}\text{F}_5\text{N}_5\text{O}$ $[\text{M}+\text{H}]^+$ 448.1191, found: 448.1196.



2-Benzyl-1-(2-(perfluoroethyl)naphtho[1,2-*b*]furan-3-yl)-1*H*-benzo[*d*]imidazole (15a):

Yield = 38% (56 mg), 0.3 mmol scale. Yellow oil.

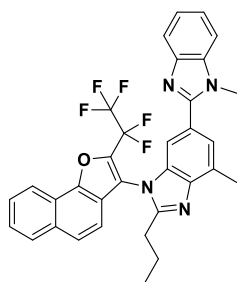
IR (KBr): $\nu = 2993, 1620, 1492, 812, 746 \text{ cm}^{-1}$.

$^1\text{H NMR}$ (400 MHz, CDCl_3): $\delta = 8.46 - 8.40$ (m, 1H), 7.94 (d, $J = 8.1 \text{ Hz}$, 1H), 7.90 – 7.86 (m, 1H), 7.76 – 7.70 (m, 1H), 7.68 – 7.62 (m, 1H), 7.54 (d, $J = 8.6 \text{ Hz}$, 1H), 7.36 – 7.30 (m, 1H), 7.23 – 7.18 (m, 1H), 7.03 – 6.91 (m, 6H), 6.78 (d, $J = 8.7 \text{ Hz}$, 1H), 4.43 – 4.02 (m, 2H) ppm.

$^{19}\text{F NMR}$ (376 MHz, CDCl_3): $\delta = -82.68 - -83.46$ (m, 3F), $-112.29 - -118.35$ (m, 2F) ppm.

$^{13}\text{C NMR}$ (100 MHz, CDCl_3): $\delta = 154.0, 150.9$ (t, $J = 1.1 \text{ Hz}$), 142.7, 136.8 (m), 136.7, 135.2, 133.1, 128.6, 128.6, 128.4, 127.6, 127.6, 126.7, 125.9, 123.5, 123.0, 122.4 (d, $J = 2.6 \text{ Hz}$), 120.8, 120.2 (d, $J = 0.7 \text{ Hz}$), 120.1, 119.8, 116.2, 109.6, 34.5 ppm; carbons corresponding to the C_2F_5 group cannot be identified due to C-F coupling.

HRMS m/z: calcd for $\text{C}_{28}\text{H}_{18}\text{F}_5\text{N}_2\text{O}$ $[\text{M}+\text{H}]^+$ 493.1334, found: 493.1336.



1,7'-Dimethyl-3'-(2-(perfluoroethyl)naphtho[1,2-b]furan-3-yl)-2'-propyl-1H,3'H-2,5'-bibenzo[d]imidazole (15b):

Yield = 88% (156 mg), 0.3 mmol scale. Yellow solid. M.p. 121.3–121.7 °C.

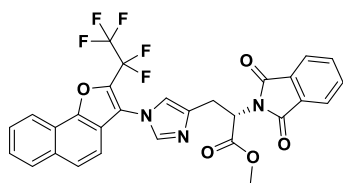
IR (KBr): $\nu = 2967, 1624, 1529, 814, 745 \text{ cm}^{-1}$.

$^1\text{H NMR}$ (400 MHz, CDCl_3): $\delta = 8.51 - 8.38$ (m, 1H), 8.02 – 7.91 (m, 1H), 7.81 – 7.68 (m, 3H), 7.64 (t, $J = 7.6 \text{ Hz}$, 1H), 7.57 (s, 1H), 7.32 – 7.26 (m, 2H), 7.25 – 7.18 (m, 3H), 3.77 (s, 3H), 2.91 – 2.77 (m, 5H), 1.95 – 1.79 (m, 2H), 0.95 (t, $J = 7.4 \text{ Hz}$, 3H) ppm.

$^{19}\text{F NMR}$ (376 MHz, CDCl_3): $\delta = -83.01$ (s, 3F), $-114.62 - -114.84$ (m, 2F) ppm.

$^{13}\text{C NMR}$ (100 MHz, CDCl_3): $\delta = 156.5, 154.1, 151.2$ (t, $J = 1.1 \text{ Hz}$), 143.2, 142.7, 136.8 (t, $J = 31.8 \text{ Hz}$), 136.5, 136.1, 133.2, 129.9, 128.6, 127.8, 127.6, 126.5, 124.9, 122.4, 122.3 (t, $J = 1.6 \text{ Hz}$), 122.1, 120.9, 120.2, 120.0, 119.4, 116.0, 109.3, 108.5, 31.5, 29.5, 21.1, 16.7, 13.7 ppm; carbons corresponding to the C_2F_5 group cannot be identified due to C-F coupling.

HRMS m/z: calcd for $\text{C}_{33}\text{H}_{26}\text{F}_5\text{N}_4\text{O}$ $[\text{M}+\text{H}]^+$ 589.2021, found: 589.2028.



Methyl (S)-2-(1,3-dioxoisoindolin-2-yl)-3-(1-(2-(perfluoroethyl)naphtho[1,2-*b*]furan-3-yl)-1*H*-imidazol-4-yl)propanoate (15c):

Yield = 35% (61 mg), 0.3 mmol scale. Yellow oil.

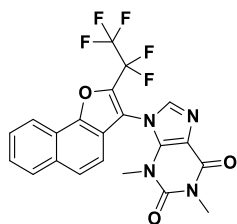
IR (KBr): $\nu = 2956, 1717, 1631, 814, 718 \text{ cm}^{-1}$.

¹H NMR (400 MHz, CDCl₃): $\delta = 8.33$ (d, $J = 8.1$ Hz, 1H), 7.96 (d, $J = 7.8$ Hz, 1H), $7.87 - 7.81$ (m, 2H), $7.75 - 7.69$ (m, 3H), $7.69 - 7.62$ (m, 2H), 7.59 (s, 1H), 7.22 (d, $J = 8.7$ Hz, 1H), 6.96 (s, 1H), $5.42 - 5.35$ (m, 1H), 3.81 (s, 3H), $3.73 - 3.59$ (m, 2H) ppm.

¹⁹F NMR (376 MHz, CDCl₃): $\delta = -83.77$ (t, $J = 4.0$ Hz, 3F), $-113.50 - -114.18$ (m, 2F) ppm.

¹³C NMR (100 MHz, CDCl₃): $\delta = 169.3, 167.3, 150.4$ (t, $J = 1.2$ Hz), $139.0, 137.9, 134.0, 133.7$ (t, $J = 31.9$ Hz), $133.1, 131.7, 128.5, 127.7, 127.6, 126.2, 124.0$ (t, $J = 2.0$ Hz), $123.4, 120.7, 120.2, 119.5, 118.5, 116.0, 52.8, 51.9, 27.6$ ppm; carbons corresponding to the C₂F₅ group cannot be identified due to C-F coupling.

HRMS m/z : calcd for C₂₉H₁₉F₅N₃O₅ [M+H]⁺ 584.1239, found: 584.1245.



1,3-Dimethyl-9-(2-(perfluoroethyl)naphtho[1,2-*b*]furan-3-yl)-3,9-dihydro-1*H*-purine-2,6-dione (15d):

Yield = 49% (68 mg), 0.3 mmol scale. Yellow solid. M.p. 236.5–237.1 °C.

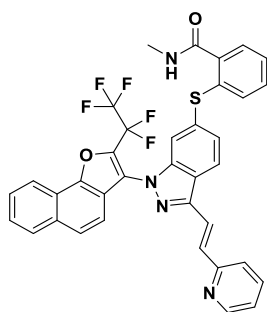
IR (KBr): $\nu = 3125, 1712, 1676, 818, 748 \text{ cm}^{-1}$.

¹H NMR (400 MHz, CDCl₃): $\delta = 8.43 - 8.35$ (m, 1H), 7.97 (d, $J = 8.1$ Hz, 1H), $7.83 - 7.76$ (m, 2H), $7.74 - 7.68$ (m, 1H), $7.67 - 7.61$ (m, 1H), 7.34 (d, $J = 8.7$ Hz, 1H), 3.70 (s, 3H), 3.36 (s, 3H) ppm.

¹⁹F NMR (376 MHz, CDCl₃): δ = -83.53 (t, *J* = 4.1 Hz, 3F), -111.87 – -117.02 (m, 2F) ppm.

¹³C NMR (100 MHz, CDCl₃): δ = 153.8, 151.6, 150.6 (t, *J* = 1.2 Hz), 149.2, 142.4, 135.5 (t, *J* = 31.1 Hz), 133.2, 128.5, 127.7, 127.6, 126.4, 122.0 (t, *J* = 1.2 Hz), 120.8, 120.2, 120.2, 116.2, 108.4, 30.0, 28.1 ppm; carbons corresponding to the C₂F₅ group cannot be identified due to C-F coupling.

HRMS m/z: calcd for C₂₁H₁₄F₅N₄O₃ [M+H]⁺ 465.0981, found: 465.0986.



(E)-N-Methyl-2-((1-(2-(perfluoroethyl)naphtho[1,2-b]furan-3-yl)-3-(2-(pyridin-2-yl)vinyl)-1H-indazol-6-yl)thio)benzamide (15e):

Yield = 80% (54 mg), 0.1 mmol scale. Yellow solid. M.p. 113.1–113.5 °C.

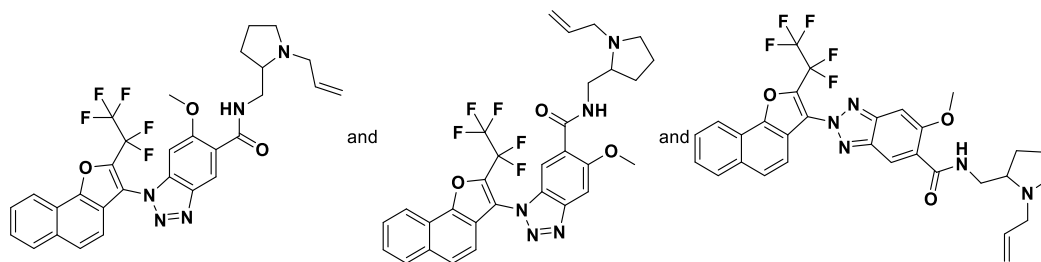
IR (KBr): ν = 3072, 1676, 1623, 802, 760 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ = 8.65 (d, *J* = 4.4 Hz, 1H), 8.41 (d, *J* = 8.1 Hz, 1H), 8.08 (d, *J* = 8.4 Hz, 1H), 8.04 – 7.93 (m, 2H), 7.77 – 7.63 (m, 5H), 7.57 (d, *J* = 7.3 Hz, 1H), 7.48 (d, *J* = 7.8 Hz, 1H), 7.44 – 7.39 (m, 1H), 7.37 (s, 1H), 7.34 – 7.30 (m, 1H), 7.28 – 7.18 (m, 4H), 6.31 (s, 1H), 2.91 (dd, *J* = 4.8, 1.1 Hz, 3H) ppm.

¹⁹F NMR (376 MHz, CDCl₃): δ = -82.92 (t, *J* = 3.2 Hz, 3F), -111.73 – -118.12 (m, 2F) ppm.

¹³C NMR (100 MHz, CDCl₃): δ = 168.3, 155.0, 150.7 (t, *J* = 1.4 Hz), 149.8, 145.4, 142.9, 136.9, 136.7, 135.8, 135.1 (t, *J* = 33.1 Hz), 133.9, 133.1, 132.2, 131.9, 130.8, 128.7, 128.6, 127.5, 127.4, 127.3, 125.9, 125.9, 125.5 (t, *J* = 1.5 Hz), 122.6, 122.4, 122.4, 122.3, 121.8, 120.9, 120.2, 119.9, 117.4, 112.9, 26.6 ppm; carbons corresponding to the C₂F₅ group cannot be identified due to C-F coupling.

HRMS m/z: calcd for C₃₆H₂₄F₅N₄O₂S [M+H]⁺ 671.1535, found: 671.1539.



***N*-((1-allylpyrrolidin-2-yl)methyl)-6-methoxy-1-(2-(perfluoroethyl)naphtho[1,2-*b*]furan-3-yl)-1*H*-benzo[*d*][1,2,3]triazole-5-carboxamide (15f-I), *N*-((1-allylpyrrolidin-2-yl)methyl)-5-methoxy-1-(2-(perfluoroethyl)naphtho[1,2-*b*]furan-3-yl)-1*H*-benzo[*d*][1,2,3]triazole-6-carboxamide (15f-II), and *N*-((1-allylpyrrolidin-2-yl)methyl)-6-methoxy-2-(2-(perfluoroethyl)naphtho[1,2-*b*]furan-3-yl)-2*H*-benzo[*d*][1,2,3]triazole-5-carboxamide (15f-III):**

15f-I, 15f-II and its isomer **15f-III** were inseparable and unidentified regioisomers.

Total yield = 58% (35 mg, **15f-I/15f-II/15f-III** = 10/6/1), 0.1 mmol scale. Yellow solid.

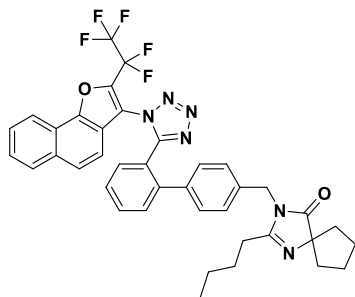
IR (KBr): ν = 2967, 1659, 1525, 807, 757 cm^{-1} .

$^1\text{H NMR}$ (400 MHz, CDCl_3): δ = 9.08 – 8.30 (m, 3H), 8.01 (t, J = 8.3 Hz, 1H), 7.90 – 7.64 (m, 3H), 7.38 – 7.28 (m, 0.6H), 6.84 (s, 0.4H), 6.08 – 5.75 (m, 1H), 5.40 – 5.00 (m, 2H), 4.20 – 3.89 (m, 3H), 3.86 – 3.69 (m, 1H), 3.56 – 3.33 (m, 2H), 3.26 – 3.13 (m, 1H), 3.04 – 2.71 (m, 2H), 2.43 – 2.08 (m, 2H), 2.01 – 1.89 (m, 1H), 1.82 – 1.60 (m, 3H) ppm.

$^{19}\text{F NMR}$ (376 MHz, CDCl_3): δ = -82.49 – -83.30 (m, 3F), -111.54 – -114.87 (m, 2F) ppm.

$^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ = 164.6, 164.2, 158.9, 155.5, 151.0 (t, J = 1.4 Hz), 150.9 (t, J = 1.4 Hz), 147.2, 140.4, 136.3 (m), 135.7 (m), 133.2, 129.5, 128.6, 127.9, 127.8, 127.7, 126.7, 126.6, 125.6, 125.1, 122.5 (t, J = 1.5 Hz), 122.4 (t, J = 1.5 Hz), 120.9, 120.8, 120.3, 120.3, 119.5, 119.4, 116.6, 116.3, 113.9, 100.0, 90.1, 62.1 (m), 61.7 (m), 57.1 (m), 57.0 (m), 56.4, 56.4, 54.2, 41.4, 41.2, 28.4, 28.3, 23.0 ppm; carbons corresponding to the C_2F_5 group cannot be identified due to C-F coupling.

HRMS m/z : calcd for $\text{C}_{30}\text{H}_{27}\text{F}_5\text{N}_5\text{O}_3$ $[\text{M}+\text{H}]^+$ 600.2029, found: 600.2036.



2-Butyl-3-((2'-(1-(2-(perfluoroethyl)naphtho[1,2-*b*]furan-3-yl)-1*H*-tetrazol-5-yl)-[1,1'-biphenyl]-4-yl)methyl)-1,3-diazaspiro[4.4]non-1-en-4-one (15g):

Yield = 15% (32 mg), 0.3 mmol scale. Yellow solid. M.p. 184.6–185.9 °C.

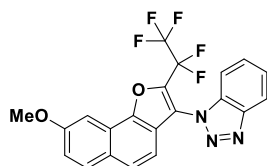
IR (KBr): $\nu = 2962, 1727, 1629, 808, 758 \text{ cm}^{-1}$.

¹H NMR (400 MHz, CDCl₃): $\delta = 8.32 - 8.24$ (m, 1H), 8.02 (d, $J = 7.8$ Hz, 1H), 7.88 – 7.81 (m, 1H), 7.76 – 7.65 (m, 3H), 7.63 – 7.54 (m, 2H), 7.25 – 7.20 (m, 1H), 6.69 (d, $J = 8.0$ Hz, 2H), 6.64 (d, $J = 8.8$ Hz, 1H), 6.57 (d, $J = 8.0$ Hz, 2H), 4.23 (s, 2H), 2.15 – 2.08 (m, 2H), 1.97 – 1.92 (m, 5H), 1.80 – 1.71 (m, 2H), 1.52 – 1.42 (m, 2H), 1.28 – 1.22 (m, 3H), 0.80 (t, $J = 7.3$ Hz, 3H) ppm.

¹⁹F NMR (376 MHz, CDCl₃): $\delta = -82.88$ (t, $J = 2.5$ Hz, 3F), $-106.78 - -125.10$ (m, 2F) ppm.

¹³C NMR (100 MHz, CDCl₃): $\delta = 186.5, 161.3, 156.3, 150.3$ (t, $J = 1.3$ Hz), 140.8, 138.3, 136.3, 133.8 (t, $J = 32.1$ Hz), 132.9, 132.5, 132.0, 130.8, 128.7, 128.4, 128.1, 127.9, 127.8, 126.9, 125.8, 121.3, 120.5 (t, $J = 1.3$ Hz), 120.2, 120.0, 117.9, 116.6, 76.4, 60.4, 42.7, 37.3, 28.5, 27.6, 26.0, 22.2, 14.2, 13.6 ppm; carbons corresponding to the C₂F₅ group cannot be identified due to C-F coupling.

HRMS *m/z*: calcd for C₃₉H₃₄F₅N₆O₂ [M+H]⁺ 713.2658, found: 713.2661.



1-(8-Methoxy-2-(perfluoroethyl)naphtho[1,2-*b*]furan-3-yl)-1*H*-benzo[*d*][1,2,3]triazole (16a):

Yield = 96% (83 mg), 0.2 mmol scale. White solid. M.p. 176.8–177.5 °C.

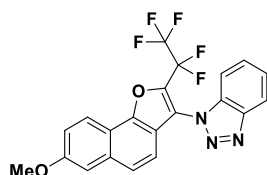
IR (KBr): $\nu = 3074, 1636, 1601, 836, 753 \text{ cm}^{-1}$.

¹H NMR (400 MHz, CDCl₃): δ = 8.23 (d, *J* = 8.3 Hz, 1H), 7.87 (d, *J* = 9.0 Hz, 1H), 7.72 – 7.64 (m, 2H), 7.61 – 7.56 (m, 1H), 7.54 – 7.44 (m, 2H), 7.29 (dd, *J* = 8.9, 2.4 Hz, 1H), 7.14 (d, *J* = 8.6 Hz, 1H), 4.04 (s, 3H) ppm.

¹⁹F NMR (376 MHz, CDCl₃): δ = -83.16 (t, *J* = 4.0 Hz, 3F), -114.37 (s, 2F) ppm.

¹³C NMR (100 MHz, CDCl₃): δ = 159.2, 150.4 (t, *J* = 0.9 Hz), 145.6, 135.7 (t, *J* = 32.1 Hz), 134.2, 130.2, 128.9, 128.3, 126.0, 124.7, 122.8 (t, *J* = 1.4 Hz), 121.9, 120.4, 120.0, 119.9, 113.9, 109.6, 98.9, 55.6 ppm; carbons corresponding to the C₂F₅ group cannot be identified due to C-F coupling.

HRMS *m/z*: calcd for C₂₁H₁₃F₅N₃O₂ [M+H]⁺ 434.0922, found: 434.0927.



1-(7-Methoxy-2-(perfluoroethyl)naphtho[1,2-*b*]furan-3-yl)-1*H*-benzo[*d*][1,2,3]triazole

(16b):

Yield = 74% (64 mg), 0.2 mmol scale. Yellow solid. M.p. 134.0–135.2 °C.

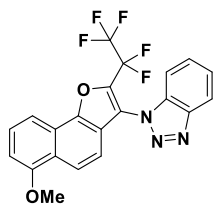
IR (KBr): ν = 3066, 1626, 1540, 808, 751 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ = 8.34 (d, *J* = 9.0 Hz, 1H), 8.22 (d, *J* = 8.3 Hz, 1H), 7.66 (d, *J* = 8.7 Hz, 1H), 7.62 – 7.55 (m, 1H), 7.54 – 7.45 (m, 2H), 7.38 (dd, *J* = 9.0, 2.4 Hz, 1H), 7.31 (d, *J* = 2.3 Hz, 1H), 7.29 – 7.25 (m, 1H), 3.97 (s, 3H) ppm.

¹⁹F NMR (376 MHz, CDCl₃): δ = -83.17 (t, *J* = 2.6 Hz, 3F), -114.19 (s, 2F) ppm.

¹³C NMR (100 MHz, CDCl₃): δ = 159.1, 151.3 (t, *J* = 1.1 Hz), 145.6, 135.0, 134.9 (t, *J* = 32.4 Hz), 134.2, 128.9, 125.5, 124.7, 122.8 (t, *J* = 1.7 Hz), 121.9, 120.4, 119.8, 117.8, 117.3, 115.8, 109.7, 107.5, 55.4 ppm; carbons corresponding to the C₂F₅ group cannot be identified due to C-F coupling.

HRMS *m/z*: calcd for C₂₁H₁₃F₅N₃O₂ [M+H]⁺ 434.0922, found: 434.0926.



1-(6-Methoxy-2-(perfluoroethyl)naphtho[1,2-*b*]furan-3-yl)-1*H*-benzo[*d*][1,2,3]triazole

(16c):

Yield = 53% (46 mg, 0.2 mmol scale). White solid. M.p. 137.0–138.9 °C.

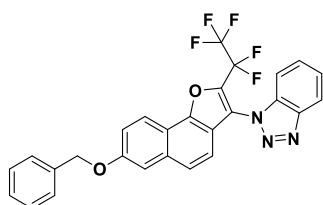
IR (KBr): $\nu = 2944, 1634, 1533, 796, 721 \text{ cm}^{-1}$.

¹H NMR (400 MHz, CDCl₃): $\delta = 8.22$ (dd, $J = 8.5, 5.6 \text{ Hz}$, 2H), 8.01 (d, $J = 8.3 \text{ Hz}$, 1H), 7.65 (t, $J = 8.1 \text{ Hz}$, 1H), $7.62 - 7.55$ (m, 1H), $7.54 - 7.44$ (m, 2H), 7.28 (d, $J = 8.9 \text{ Hz}$, 1H), 7.03 (d, $J = 7.8 \text{ Hz}$, 1H), 4.04 (s, 3H) ppm.

¹⁹F NMR (376 MHz, CDCl₃): $\delta = -82.89 - -83.30$ (m, 3F), -114.30 (s, 2F) ppm.

¹³C NMR (100 MHz, CDCl₃): $\delta = 155.9, 150.8$ (t, $J = 1.3 \text{ Hz}$), $145.6, 135.9$ (t, $J = 32.4 \text{ Hz}$), $134.3, 128.9, 128.4, 124.9, 124.7, 122.7$ (t, $J = 1.4 \text{ Hz}$), $121.8, 120.5, 120.4, 120.0, 115.6, 112.3, 109.7, 106.2, 55.7$ ppm; carbons corresponding to the C₂F₅ group cannot be identified due to C-F coupling.

HRMS m/z: calcd for C₂₁H₁₃F₅N₃O₂ [M+H]⁺ 434.0922, found: 434.0927.



1-(7-(Benzyloxy)-2-(perfluoroethyl)naphtho[1,2-*b*]furan-3-yl)-1*H*-benzo[*d*][1,2,3]triazole

(16d):

Yield = 36% (37 mg), 0.2 mmol scale. Light yellow solid. M.p. 109.7–111.1 °C.

IR (KBr): $\nu = 2907, 1641, 1612, 800, 746 \text{ cm}^{-1}$.

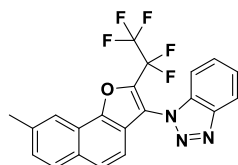
¹H NMR (400 MHz, CDCl₃): $\delta = 8.37$ (d, $J = 9.0 \text{ Hz}$, 1H), 8.23 (d, $J = 8.3 \text{ Hz}$, 1H), 7.66 (d, $J = 8.7 \text{ Hz}$, 1H), $7.62 - 7.55$ (m, 1H), $7.54 - 7.34$ (m, 9H), 7.28 (s, 1H), 5.23 (s, 2H) ppm.

¹⁹F NMR (376 MHz, CDCl₃): $\delta = -83.07 - -83.52$ (m, 3F), -114.32 (s, 2F) ppm.

¹³C NMR (100 MHz, CDCl₃): $\delta = 158.2, 151.2$ (t, $J = 1.2 \text{ Hz}$), $145.6, 136.2, 135.0, 134.9, 134.2, 128.9, 128.7, 128.2, 127.6, 125.5, 124.7, 122.8$ (t, $J = 1.5 \text{ Hz}$), $122.0, 120.4, 120.2, 117.9, 117.3,$

115.9, 109.7, 108.9, 70.2 ppm; carbons corresponding to the C₂F₅ group cannot be identified due to C-F coupling.

HRMS m/z: calcd for C₂₇H₁₇F₅N₃O₂ [M+H]⁺ 510.1235, found: 510.1242.



1-(8-Methyl-2-(perfluoroethyl)naphtho[1,2-*b*]furan-3-yl)-1*H*-benzo[*d*][1,2,3]triazole (16e):

Yield = 90% (75 mg), 0.2 mmol scale. Yellow solid. M.p. 150.5–151.4 °C.

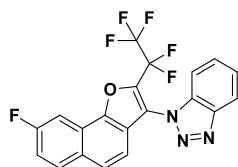
IR (KBr): ν = 2920, 1630, 1615, 830, 749 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ = 8.26 – 8.18 (m, 2H), 7.88 (d, *J* = 8.4 Hz, 1H), 7.71 (d, *J* = 8.6 Hz, 1H), 7.61 – 7.55 (m, 1H), 7.53 – 7.44 (m, 3H), 7.22 (d, *J* = 8.7 Hz, 1H), 2.64 (s, 3H) ppm.

¹⁹F NMR (376 MHz, CDCl₃): δ = -83.00 – -83.37 (m, 3F), -114.29 (s, 2F) ppm.

¹³C NMR (100 MHz, CDCl₃): δ = 150.7 (t, *J* = 1.4 Hz), 145.6, 138.1, 135.6 (t, *J* = 32.4 Hz), 134.2, 131.4, 129.8, 128.9, 128.4, 126.2, 124.7, 122.8 (t, *J* = 1.6 Hz), 121.0, 120.4, 119.5, 119.3, 115.6, 109.7, 21.9 ppm; carbons corresponding to the C₂F₅ group cannot be identified due to C-F coupling.

HRMS m/z: calcd for C₂₁H₁₃F₅N₃O [M+H]⁺ 418.0973, found: 418.0979.



1-(8-Fluoro-2-(perfluoroethyl)naphtho[1,2-*b*]furan-3-yl)-1*H*-benzo[*d*][1,2,3]triazole (16f):

Yield = 80% (67 mg), 0.2 mmol scale. Colorless oil.

IR (KBr): ν = 3073, 1629, 1596, 832, 734 cm⁻¹.

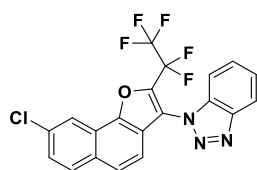
¹H NMR (400 MHz, CDCl₃): δ = 8.27 – 8.21 (m, 1H), 8.07 – 7.97 (m, 2H), 7.77 (d, *J* = 8.7 Hz, 1H), 7.63 – 7.58 (m, 1H), 7.55 – 7.50 (m, 1H), 7.48 (d, *J* = 8.3 Hz, 1H), 7.46 – 7.40 (m, 1H), 7.29 (d, *J* = 8.7 Hz, 1H) ppm.

¹⁹F NMR (376 MHz, CDCl₃): δ = -83.00 – -83.26 (m, 3F), -109.58 – -110.06 (m, 1F), -114.38 (s,

2F) ppm.

¹³C NMR (100 MHz, CDCl₃): δ = 161.7 (d, J = 248.8 Hz), 150.4 (dt, J = 5.3, 1.2 Hz), 145.6, 136.3 (t, J = 32.4 Hz), 134.2, 131.3 (d, J = 9.2 Hz), 130.1 (d, J = 1.4 Hz), 129.0, 126.2 (d, J = 1.2 Hz), 124.8, 122.9 (t, J = 1.4 Hz), 121.7 (d, J = 10.0 Hz), 120.5, 120.4, 117.7 (d, J = 24.8 Hz), 116.0 (d, J = 2.6 Hz), 109.6, 104.8 (d, J = 23.4 Hz) ppm; carbons corresponding to the C₂F₅ group cannot be identified due to C-F coupling.

HRMS m/z : calcd for C₂₀H₁₀F₆N₃O [M+H]⁺ 422.0723, found: 422.0726.



1-(8-Chloro-2-(perfluoroethyl)naphtho[1,2-*b*]furan-3-yl)-1*H*-benzo[*d*][1,2,3]triazole (16g):

Yield = 65% (57 mg), 0.2 mmol scale. White solid. M.p. 135.7–137.1 °C.

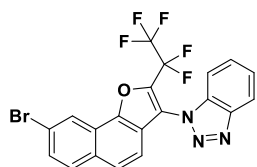
IR (KBr): ν = 3066, 1749, 1491, 812, 748 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ = 8.41 (d, J = 2.1 Hz, 1H), 8.25 – 8.21 (m, 1H), 7.94 (d, J = 8.7 Hz, 1H), 7.76 (d, J = 8.6 Hz, 1H), 7.64 – 7.58 (m, 2H), 7.55 – 7.45 (m, 2H), 7.33 (d, J = 8.7 Hz, 1H) ppm.

¹⁹F NMR (376 MHz, CDCl₃): δ = -82.96 – -83.28 (m, 3F), -114.36 (s, 2F) ppm.

¹³C NMR (100 MHz, CDCl₃): δ = 149.8 (t, J = 1.4 Hz), 145.6, 136.3 (t, J = 32.5 Hz), 134.2, 134.0, 131.3, 130.2, 129.0, 128.6, 126.1, 124.8, 122.9 (t, J = 2.0 Hz), 121.5, 120.5, 120.4, 119.5, 117.0, 109.6 ppm; carbons corresponding to the C₂F₅ group cannot be identified due to C-F coupling.

HRMS m/z : calcd for C₂₀H₁₀ClF₅N₃O [M+H]⁺ 438.0427, found: 438.0437.



1-(8-Bromo-2-(perfluoroethyl)naphtho[1,2-*b*]furan-3-yl)-1*H*-benzo[*d*][1,2,3]triazole (16h):

Yield = 73% (70 mg), 0.2 mmol scale. Light brown solid. M.p. 156.1–156.7 °C.

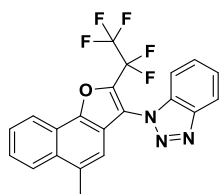
IR (KBr): ν = 3067, 1630, 1611, 803, 733 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ = 8.60 – 8.54 (m, 1H), 8.26 – 8.20 (m, 1H), 7.89 – 7.83 (m, 1H), 7.77 – 7.70 (m, 2H), 7.64 – 7.57 (m, 1H), 7.55 – 7.45 (m, 2H), 7.37 – 7.32 (m, 1H) ppm.

¹⁹F NMR (376 MHz, CDCl₃): δ = -83.07 (t, *J* = 2.5 Hz, 3F), -114.35 (s, 2F) ppm.

¹³C NMR (100 MHz, CDCl₃): δ = 149.6 (t, *J* = 1.4 Hz), 145.6, 136.3 (t, *J* = 32.2 Hz), 134.2, 131.5, 131.1, 130.2, 129.0, 126.2, 124.8, 122.9 (t, *J* = 1.5 Hz), 122.7, 122.2, 121.8, 120.5, 120.4, 117.2, 109.5 ppm; carbons corresponding to the C₂F₅ group cannot be identified due to C-F coupling.

HRMS *m/z*: calcd for C₂₀H₁₀BrF₅N₃O [M+H]⁺ 481.9922, found: 481.9924.



1-(5-Methyl-2-(perfluoroethyl)naphtho[1,2-*b*]furan-3-yl)-1*H*-benzo[*d*][1,2,3]triazole (16j):

Yield = 59% (49 mg), 0.2 mmol scale. White solid. M.p. 122.9–124.2 °C.

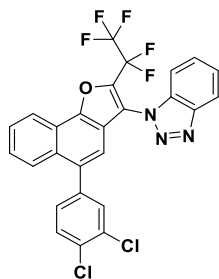
IR (KBr): *ν* = 3071, 1630, 1613, 785, 756 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ = 8.50 – 8.44 (m, 1H), 8.24 (d, *J* = 8.3 Hz, 1H), 8.10 (d, *J* = 7.7 Hz, 1H), 7.80 – 7.68 (m, 2H), 7.64 – 7.56 (m, 1H), 7.54 – 7.44 (m, 2H), 7.14 (s, 1H), 2.66 (s, 3H) ppm.

¹⁹F NMR (376 MHz, CDCl₃): δ = -83.18 (t, *J* = 4.0 Hz, 3F), -114.23 (s, 2F) ppm.

¹³C NMR (100 MHz, CDCl₃): δ = 150.2 (t, *J* = 1.3 Hz), 145.6, 135.5 (t, *J* = 32.5 Hz), 134.3, 133.1, 132.5, 128.9, 127.6, 127.4, 125.3, 124.7, 122.5 (t, *J* = 1.3 Hz), 120.9, 120.7, 120.4, 119.1, 116.2, 109.7, 19.8 ppm; carbons corresponding to the C₂F₅ group cannot be identified due to C-F coupling.

HRMS *m/z*: calcd for C₂₁H₁₃F₅N₃O [M+H]⁺ 418.0973, found: 418.0982.



1-(5-(3,4-Dichlorophenyl)-2-(perfluoroethyl)naphtho[1,2-*b*]furan-3-yl)-1*H*-

benzo[d][1,2,3]triazole (16k):

Yield = 95% (104 mg), 0.2 mmol scale. White solid. M.p. 173.0–174.1 °C.

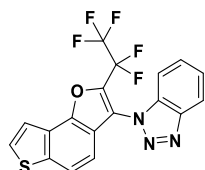
IR (KBr): $\nu = 3068, 1639, 1591, 819, 756 \text{ cm}^{-1}$.

¹H NMR (400 MHz, CDCl₃): $\delta = 8.55$ (d, $J = 8.2$ Hz, 1H), 8.25 – 8.19 (m, 1H), 7.89 (d, $J = 8.5$ Hz, 1H), 7.80 (t, $J = 7.5$ Hz, 1H), 7.70 – 7.64 (m, 1H), 7.63 – 7.57 (m, 1H), 7.55 – 7.47 (m, 4H), 7.25 (d, $J = 7.2$ Hz, 2H) ppm.

¹⁹F NMR (376 MHz, CDCl₃): $\delta = -83.19$ (t, $J = 3.6$ Hz, 3F), -114.42 (s, 2F) ppm.

¹³C NMR (100 MHz, CDCl₃): $\delta = 150.8$ (t, $J = 1.2$ Hz), 145.6, 139.4, 136.7, 136.1 (t, $J = 32.5$ Hz), 134.2, 132.6, 132.2, 131.7, 131.5, 130.3, 129.4, 129.1, 128.1, 128.0, 126.8, 124.8, 122.9 (t, $J = 1.1$ Hz), 121.1, 120.7, 120.5, 119.0, 117.4, 109.5 ppm; carbons corresponding to the C₂F₅ group cannot be identified due to C-F coupling.

HRMS m/z: calcd for C₂₆H₁₃Cl₂F₅N₃O [M+H]⁺ 548.0350, found: 548.0358.



1-(2-(Perfluoroethyl)thieno[2,3-g]benzofuran-3-yl)-1H-benzo[d][1,2,3]triazole (16l):

Yield = 96% (79 mg), 0.2 mmol scale. Yellow solid. M.p. 111.7–112.9 °C.

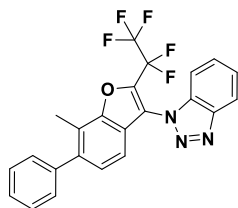
IR (KBr): $\nu = 3068, 1630, 1612, 797, 748 \text{ cm}^{-1}$.

¹H NMR (400 MHz, CDCl₃): $\delta = 8.23$ (d, $J = 8.3$ Hz, 1H), 7.87 – 7.81 (m, 2H), 7.72 (d, $J = 5.5$ Hz, 1H), 7.62 – 7.56 (m, 1H), 7.53 – 7.48 (m, 1H), 7.46 (d, $J = 8.2$ Hz, 1H), 7.25 (d, $J = 8.6$ Hz, 1H) ppm.

¹⁹F NMR (376 MHz, CDCl₃): $\delta = -83.15$ (t, $J = 3.9$ Hz, 3F), -114.47 (s, 2F) ppm.

¹³C NMR (100 MHz, CDCl₃): $\delta = 149.3$ (t, $J = 1.4$ Hz), 145.6, 141.4, 135.1 (t, $J = 32.3$ Hz), 134.2, 129.0, 128.9, 125.4, 124.7, 122.8 (t, $J = 1.5$ Hz), 120.5, 120.1, 119.5, 118.7, 115.4, 109.6 ppm; carbons corresponding to the C₂F₅ group cannot be identified due to C-F coupling.

HRMS m/z: calcd for C₁₈H₉F₅N₃OS [M+H]⁺ 410.0381, found: 410.0384.



1-(7-Methyl-2-(perfluoroethyl)-6-phenylbenzofuran-3-yl)-1H-benzo[d][1,2,3]triazole (16m):

Yield = 60% (53 mg), 0.2 mmol scale. Yellow oil.

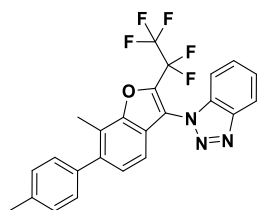
IR (KBr): $\nu = 3062, 1637, 1613, 772, 743 \text{ cm}^{-1}$.

$^1\text{H NMR}$ (400 MHz, CDCl_3): $\delta = 8.25 - 8.19$ (m, 1H), 7.62 – 7.56 (m, 1H), 7.53 – 7.45 (m, 4H), 7.44 – 7.36 (m, 3H), 7.33 (d, $J = 8.2 \text{ Hz}$, 1H), 7.23 (d, $J = 8.2 \text{ Hz}$, 1H), 2.57 (s, 3H) ppm.

$^{19}\text{F NMR}$ (376 MHz, CDCl_3): $\delta = -83.11$ (t, $J = 3.1 \text{ Hz}$, 3F), -114.92 (s, 2F) ppm.

$^{13}\text{C NMR}$ (100 MHz, CDCl_3): $\delta = 153.8$ (t, $J = 1.1 \text{ Hz}$), 145.6, 142.5, 139.8, 136.8 (t, $J = 32.0 \text{ Hz}$), 134.2, 129.4, 128.9, 128.4, 127.6, 127.6, 124.7, 122.0 (t, $J = 1.0 \text{ Hz}$), 121.9, 121.0, 120.4, 117.1, 109.6, 12.5 ppm; carbons corresponding to the C_2F_5 group cannot be identified due to C-F coupling.

HRMS m/z : calcd for $\text{C}_{23}\text{H}_{15}\text{F}_5\text{N}_3\text{O}$ $[\text{M}+\text{H}]^+$ 444.1130, found: 444.1128.



1-(7-Methyl-2-(perfluoroethyl)-6-(p-tolyl)benzofuran-3-yl)-1H-benzo[d][1,2,3]triazole

(16n):

Yield = 78% (71 mg), 0.2 mmol scale. Yellow oil.

IR (KBr): $\nu = 2927, 1682, 1623, 766, 746 \text{ cm}^{-1}$.

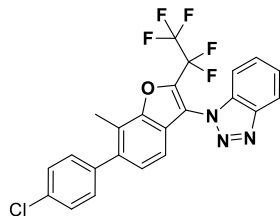
$^1\text{H NMR}$ (400 MHz, CDCl_3): $\delta = 8.25 - 8.18$ (m, 1H), 7.62 – 7.55 (m, 1H), 7.53 – 7.45 (m, 2H), 7.34 – 7.26 (m, 5H), 7.21 (d, $J = 8.2 \text{ Hz}$, 1H), 2.57 (s, 3H), 2.43 (s, 3H) ppm.

$^{19}\text{F NMR}$ (376 MHz, CDCl_3): $\delta = -82.86 - -83.38$ (m, 3F), -114.89 (s, 2F) ppm.

$^{13}\text{C NMR}$ (100 MHz, CDCl_3): $\delta = 153.9$ (t, $J = 1.0 \text{ Hz}$), 145.6, 142.6, 137.4, 136.9, 136.7 (t, $J = 31.9 \text{ Hz}$), 134.2, 129.2, 129.1, 128.8, 127.7, 124.7, 122.0 (t, $J = 1.7 \text{ Hz}$), 121.8, 121.0, 120.4, 117.0, 109.6, 21.1, 12.5 ppm; carbons corresponding to the C_2F_5 group cannot be identified

due to C-F coupling.

HRMS m/z: calcd for C₂₄H₁₇F₅N₃O [M+H]⁺ 458.1286, found: 458.1287.



1-(6-(4-Chlorophenyl)-7-methyl-2-(perfluoroethyl)benzofuran-3-yl)-1H-benzo[d][1,2,3]triazole (16o):

Yield = 72% (69 mg), 0.2 mmol scale. Yellow solid. M.p. 95.5–96.3 °C.

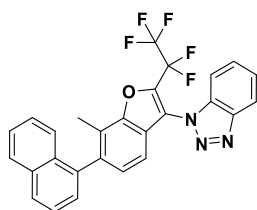
IR (KBr): $\nu = 3066, 1634, 1614, 747, 729 \text{ cm}^{-1}$.

¹H NMR (400 MHz, CDCl₃): $\delta = 8.22$ (d, $J = 8.3$ Hz, 1H), 7.63 – 7.56 (m, 1H), 7.53 – 7.50 (m, 1H), 7.49 – 7.43 (m, 3H), 7.33 – 7.27 (m, 3H), 7.24 (d, $J = 8.2$ Hz, 1H), 2.56 (s, 3H) ppm.

¹⁹F NMR (376 MHz, CDCl₃): $\delta = -83.11$ (t, $J = 2.6$ Hz, 3F), -114.92 (s, 2F) ppm.

¹³C NMR (100 MHz, CDCl₃): $\delta = 153.8$ (t, $J = 1.0$ Hz), 145.6, 141.2, 138.2, 137.0 (t, $J = 31.9$ Hz), 134.2, 133.8, 130.7, 128.9, 128.6, 127.4, 124.7, 122.2, 122.0 (t, $J = 1.8$ Hz), 121.1, 120.5, 117.3, 109.6, 12.4 ppm; carbons corresponding to the C₂F₅ group cannot be identified due to C-F coupling.

HRMS m/z: calcd for C₂₃H₁₄ClF₅N₃O [M+H]⁺ 478.0740, found: 478.0743.



1-(7-Methyl-6-(naphthalen-1-yl)-2-(perfluoroethyl)benzofuran-3-yl)-1H-benzo[d][1,2,3]triazole (16p):

Yield = 78% (77 mg), 0.2 mmol scale. Yellow solid. M.p. 68.1–68.3 °C.

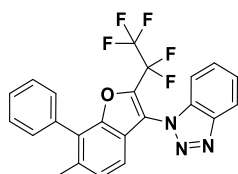
IR (KBr): $\nu = 3062, 1636, 1593, 746, 731 \text{ cm}^{-1}$.

¹H NMR (400 MHz, CDCl₃): $\delta = 8.25$ (d, $J = 8.3$ Hz, 1H), 7.95 (dd, $J = 8.1, 4.0$ Hz, 2H), 7.66 – 7.61 (m, 1H), 7.60 – 7.43 (m, 6H), 7.42 – 7.38 (m, 1H), 7.37 – 7.28 (m, 2H), 2.35 (s, 3H) ppm.

¹⁹F NMR (376 MHz, CDCl₃): δ = -83.03 (d, J = 2.6 Hz, 3F), -114.80 (s, 2F) ppm.

¹³C NMR (100 MHz, CDCl₃): δ = 153.6, 145.6, 141.1, 137.4, 136.9 (t, J = 31.9 Hz), 134.2, 133.5, 131.7, 128.9, 128.4, 128.2, 127.1, 126.4, 126.0, 125.6, 125.3, 124.7, 122.6, 122.3, 122.2, 122.1, 120.5, 116.9, 109.7, 12.3 ppm; carbons corresponding to the C₂F₅ group cannot be identified due to C-F coupling.

HRMS m/z: calcd for C₂₇H₁₇F₅N₃O [M+H]⁺ 494.1286, found: 494.1287.



1-(6-Methyl-2-(perfluoroethyl)-7-phenylbenzofuran-3-yl)-1H-benzo[d][1,2,3]triazole (16q):

Yield = 84% (74 mg), 0.2 mmol scale. Yellow solid. M.p. 67.7–68.1 °C.

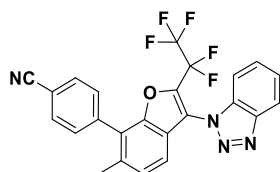
IR (KBr): ν = 3060, 1636, 1612, 748, 723 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ = 8.21 (d, J = 8.7 Hz, 1H), 7.61 – 7.56 (m, 1H), 7.55 – 7.52 (m, 2H), 7.51 – 7.45 (m, 5H), 7.34 (d, J = 8.2 Hz, 1H), 7.23 (d, J = 8.1 Hz, 1H), 2.43 (s, 3H) ppm.

¹⁹F NMR (376 MHz, CDCl₃): δ = -83.09 – -83.50 (m, 3F), -114.87 (s, 2F) ppm.

¹³C NMR (100 MHz, CDCl₃): δ = 152.6 (t, J = 1.2 Hz), 145.6, 137.3, 136.4 (t, J = 31.5 Hz), 134.2, 133.2, 129.9, 128.8, 128.5, 128.2, 128.2, 126.9, 124.7, 121.8 (t, J = 1.1 Hz), 121.4, 120.4, 118.5, 109.7, 20.1 ppm; carbons corresponding to the C₂F₅ group cannot be identified due to C-F coupling.

HRMS m/z: calcd for C₂₃H₁₅F₅N₃O [M+H]⁺ 444.1130, found: 444.1132.



4-(3-(1H-benzo[d][1,2,3]triazol-1-yl)-6-methyl-2-(perfluoroethyl)benzofuran-7-yl)benzonitrile (16r):

Yield = 80% (75 mg), 0.2 mmol scale. Yellow solid. M.p. 93.6–94.3 °C.

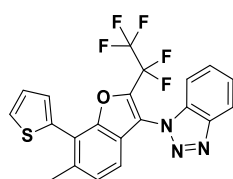
IR (KBr): ν = 2992, 2228, 1637, 1607, 767 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ = 8.20 (d, *J* = 8.3 Hz, 1H), 7.85 (d, *J* = 8.0 Hz, 2H), 7.62 (d, *J* = 8.2 Hz, 2H), 7.60 – 7.55 (m, 1H), 7.53 – 7.45 (m, 2H), 7.40 – 7.29 (m, 2H), 2.42 (s, 3H) ppm.

¹⁹F NMR (376 MHz, CDCl₃): δ = -83.22 (s, 3F), -114.91 (s, 2F) ppm.

¹³C NMR (100 MHz, CDCl₃): δ = 152.0, 145.5, 138.1, 137.1, 136.5 (t, *J* = 32.3 Hz), 134.1, 132.3, 130.8, 128.9, 128.4, 124.8, 124.8, 122.0, 121.6, 120.4, 119.7, 118.5, 112.2, 109.5, 20.0 ppm; carbons corresponding to the C₂F₅ group cannot be identified due to C-F coupling.

HRMS *m/z*: calcd for C₂₄H₁₄F₅N₄O [M+H]⁺ 469.1082, found: 469.1082.



1-(6-Methyl-2-(perfluoroethyl)-7-(thiophen-2-yl)benzofuran-3-yl)-1H-

benzo[d][1,2,3]triazole (16s):

Yield = 59% (53 mg), 0.2 mmol scale. Yellow solid. M.p. 114.9– 115.8 °C.

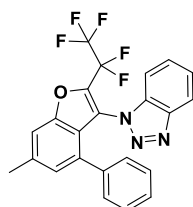
IR (KBr): ν = 2962, 1639, 1613, 745, 701 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ = 8.26 – 8.19 (m, 1H), 7.62 – 7.56 (m, 2H), 7.54 – 7.44 (m, 2H), 7.40 – 7.32 (m, 2H), 7.27 – 7.22 (m, 2H), 2.61 (s, 3H) ppm.

¹⁹F NMR (376 MHz, CDCl₃): δ = -82.27 – -84.16 (m, 3F), -114.79 (s, 2F) ppm.

¹³C NMR (100 MHz, CDCl₃): δ = 152.5, 150.7 (t, *J* = 1.1 Hz), 145.6, 138.1, 136.1 (t, *J* = 32.0 Hz), 134.2, 133.1, 129.2, 128.9, 128.5, 127.2, 127.1, 124.7, 121.7, 120.5, 120.1, 118.9, 109.7, 21.1 ppm; carbons corresponding to the C₂F₅ group cannot be identified due to C-F coupling.

HRMS *m/z*: calcd for C₂₁H₁₃F₅N₃OS [M+H]⁺ 450.0694, found: 450.0692.



1-(6-Methyl-2-(perfluoroethyl)-4-phenylbenzofuran-3-yl)-1H-benzo[d][1,2,3]triazole (16t):

Yield = 62% (55 mg), 0.2 mmol scale. Yellow solid. M.p. 104.8– 105.4 °C.

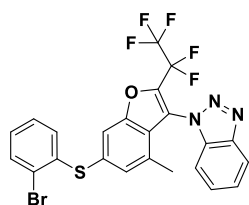
IR (KBr): $\nu = 3034, 1635, 1621, 756, 745 \text{ cm}^{-1}$.

$^1\text{H NMR}$ (400 MHz, CDCl_3): $\delta = 7.91 - 7.85$ (m, 1H), 7.54 (s, 1H), 7.28 – 7.19 (m, 2H), 7.15 (s, 1H), 6.99 – 6.93 (m, 1H), 6.79 (d, $J = 7.3 \text{ Hz}$, 3H), 6.75 – 6.68 (m, 2H), 2.58 (s, 3H) ppm.

$^{19}\text{F NMR}$ (376 MHz, CDCl_3): $\delta = -83.47$ (t, $J = 2.5 \text{ Hz}$, 3F), -115.71 (dd, $J = 28.2, 2.6 \text{ Hz}$, 2F) ppm.

$^{13}\text{C NMR}$ (100 MHz, CDCl_3): $\delta = 155.0, 145.0, 139.4, 138.1$ (t, $J = 30.0 \text{ Hz}$), 136.7, 136.3, 134.7, 128.1, 127.8, 127.4, 127.3, 127.2, 123.8, 121.6 (m), 119.6, 119.1, 111.6, 109.2, 21.8 ppm; carbons corresponding to the C_2F_5 group cannot be identified due to C-F coupling.

HRMS m/z : calcd for $\text{C}_{23}\text{H}_{15}\text{F}_5\text{N}_3\text{O}$ $[\text{M}+\text{H}]^+$ 444.1130, found: 444.1127.



1-(6-((2-Bromophenyl)thio)-4-methyl-2-(perfluoroethyl)benzofuran-3-yl)-1H-benzo[d][1,2,3]triazole (16u):

Yield = 75% (83 mg), 0.2 mmol scale. Yellow oil.

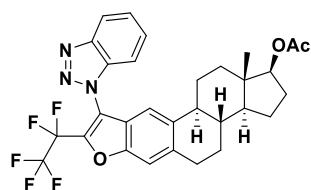
IR (KBr): $\nu = 3063, 1633, 1609, 783, 744 \text{ cm}^{-1}$.

$^1\text{H NMR}$ (400 MHz, CDCl_3): $\delta = 8.20$ (d, $J = 8.3 \text{ Hz}$, 1H), 7.70 – 7.61 (m, 1H), 7.58 (d, $J = 7.3 \text{ Hz}$, 1H), 7.53 – 7.44 (m, 1H), 7.43 – 7.33 (m, 2H), 7.28 (d, $J = 9.9 \text{ Hz}$, 2H), 7.19 (s, 1H), 7.11 (s, 1H), 1.67 (s, 3H) ppm.

$^{19}\text{F NMR}$ (376 MHz, CDCl_3): $\delta = -82.95 - -83.97$ (m, 3F), $-114.71 - -117.31$ (m, 2F) ppm.

$^{13}\text{C NMR}$ (100 MHz, CDCl_3): $\delta = 154.8, 145.3, 138.5$ (t, $J = 31.6 \text{ Hz}$), 136.6, 135.4, 135.3, 133.6, 133.2, 133.2, 129.3, 129.2, 128.8, 128.3, 126.2, 124.7, 122.0, 121.8 (m), 120.4, 112.1, 109.3, 16.9 ppm; carbons corresponding to the C_2F_5 group cannot be identified due to C-F coupling.

HRMS m/z : calcd for $\text{C}_{23}\text{H}_{14}\text{BrF}_5\text{N}_3\text{OS}$ $[\text{M}+\text{H}]^+$ 553.9956, found: 553.9954.



(1S,3aS,3bR,10bS,12aS)-9-(1H-Benzo[d][1,2,3]triazol-1-yl)-12a-methyl-8-(perfluoroethyl)-2,3,3a,3b,4,5,10b,11,12,12a-decahydro-1H-cyclopenta[7,8]phenanthro[2,3-b]furan-1-yl acetate (16v):

Yield = 58% (17 mg), 0.05 mmol scale. Yellow solid. M.p. 96.1–96.5 °C.

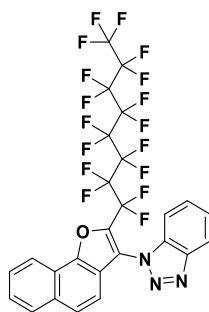
IR (KBr): $\nu = 3441, 2930, 1736, 1633, 745 \text{ cm}^{-1}$.

¹H NMR (400 MHz, CDCl₃): $\delta = 8.25 - 8.18$ (m, 1H), 7.61 – 7.55 (m, 1H), 7.52 – 7.47 (m, 1H), 7.46 – 7.41 (m, 2H), 7.22 (s, 1H), 4.65 (dd, $J = 9.1, 7.8$ Hz, 1H), 3.13 – 3.03 (m, 2H), 2.30 – 2.19 (m, 2H), 2.16 – 2.08 (m, 1H), 2.04 (s, 3H), 1.99 – 1.90 (m, 1H), 1.84 – 1.78 (m, 1H), 1.77 – 1.71 (m, 1H), 1.55 – 1.39 (m, 5H), 1.32 – 1.26 (m, 2H), 0.79 (s, 3H) ppm.

¹⁹F NMR (376 MHz, CDCl₃): $\delta = -83.19$ (t, $J = 3.3$ Hz, 3F), -114.87 – -115.40 (m, 2F) ppm.

¹³C NMR (100 MHz, CDCl₃): $\delta = 171.2, 152.9, 145.5, 139.5, 139.0, 136.1$ (t, $J = 30.5$ Hz), 134.3, 128.8, 124.7, 121.8 (t, $J = 1.7$ Hz), 121.5, 120.4, 116.2, 111.9, 109.7, 82.5, 50.0, 43.9, 42.7, 38.0, 36.5, 30.1, 27.5, 26.8, 26.1, 23.3, 21.2, 11.9 ppm; carbons corresponding to the C₂F₅ group cannot be identified due to C-F coupling.

HRMS m/z: calcd for C₃₀H₂₉F₅N₃O₃ [M+H]⁺ 574.2124, found: 574.2128.



1-(2-(Perfluorooctyl)naphtho[1,2-b]furan-3-yl)-1H-benzo[d]imidazole (16w):

Yield = 67% (94 mg), 0.2 mmol scale. Yellow solid. M.p. 125.5–126.6 °C.

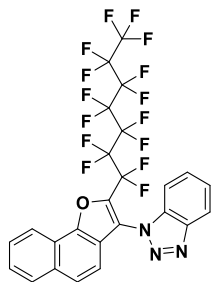
IR (KBr): $\nu = 3057, 1749, 1650, 815, 747 \text{ cm}^{-1}$.

¹H NMR (400 MHz, CDCl₃): $\delta = 8.46$ (d, $J = 8.1$ Hz, 1H), 8.24 (d, $J = 8.3$ Hz, 1H), 8.00 (d, $J = 8.1$ Hz, 1H), 7.81 – 7.72 (m, 2H), 7.68 (t, $J = 7.4$ Hz, 1H), 7.59 (t, $J = 7.5$ Hz, 1H), 7.51 (t, $J = 7.5$ Hz, 1H), 7.45 (d, $J = 8.2$ Hz, 1H), 7.28 (d, $J = 8.7$ Hz, 1H) ppm.

¹⁹F NMR (376 MHz, CDCl₃): $\delta = -80.75$ (t, $J = 9.9$ Hz, 3F), -110.95 (s, 2F), -121.28 – -122.12 (m, 8F), -122.73 (s, 2F), -126.01 – -126.28 (m, 2F) ppm.

¹³C NMR (100 MHz, CDCl₃): δ = 151.0 (t, J = 1.4 Hz), 145.6, 136.1 (t, J = 32.8 Hz), 134.3, 133.2, 128.9, 128.6, 127.8, 127.7, 126.4, 124.7, 123.0 (t, J = 1.9 Hz), 120.9, 120.5, 120.3, 119.6, 116.6, 109.6 ppm; carbons corresponding to the C₈F₁₇ group cannot be identified due to C-F coupling.

HRMS m/z: calcd for C₂₆H₁₁F₁₇N₃O [M+H]⁺ 704.0625, found: 704.0640.



1-(2-(Perfluoroheptyl)naphtho[1,2-*b*]furan-3-yl)-1*H*-benzo[*d*]imidazole (16x):

Yield = 85% (167 mg), 0.2 mmol scale. Yellow solid. M.p. 119.4–119.7 °C.

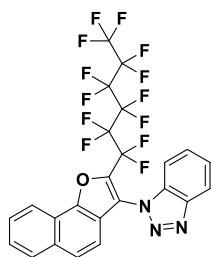
IR (KBr): ν = 3072, 1631, 1613, 810, 749 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ = 8.42 (d, J = 8.1 Hz, 1H), 8.23 (d, J = 8.3 Hz, 1H), 7.97 (d, J = 8.1 Hz, 1H), 7.77 – 7.69 (m, 2H), 7.69 – 7.63 (m, 1H), 7.62 – 7.55 (m, 1H), 7.53 – 7.44 (m, 2H), 7.29 (d, J = 8.7 Hz, 1H) ppm.

¹⁹F NMR (376 MHz, CDCl₃): δ = -80.67 (t, J = 9.8 Hz, 3F), -110.96 (s, 2F), -121.32 – -121.68 (m, 2F), -121.90 (s, 2F), -122.67 (s, 2F), -126.00 – -126.20 (m, 2F) ppm.

¹³C NMR (100 MHz, CDCl₃): δ = 150.9 (t, J = 1.3 Hz), 145.6, 135.7 (t, J = 32.3 Hz), 134.2, 133.1, 128.9, 128.6, 127.8, 127.7, 126.4, 124.7, 122.8 (t, J = 1.6 Hz), 120.8, 120.4, 120.2, 119.4, 116.5, 109.6 ppm; carbons corresponding to the C₇F₁₅ group cannot be identified due to C-F coupling.

HRMS m/z: calcd for C₂₅H₁₁F₁₅N₃O [M+H]⁺ 654.0657, found: 654.0660.



1-(2-(Perfluorohexyl)naphtho[1,2-*b*]furan-3-yl)-1*H*-benzo[*d*]imidazole (16y):

Yield = 70% (84 mg), 0.2 mmol scale). White solid. M.p. 105.7–106.2 °C.

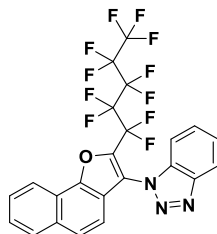
IR (KBr): $\nu = 3073, 1627, 1533, 805, 720 \text{ cm}^{-1}$.

$^1\text{H NMR}$ (400 MHz, CDCl_3): $\delta = 8.46$ (d, $J = 8.2 \text{ Hz}$, 1H), 8.24 (d, $J = 8.3 \text{ Hz}$, 1H), 8.00 (d, $J = 8.1 \text{ Hz}$, 1H), $7.81 - 7.72$ (m, 2H), $7.71 - 7.65$ (m, 1H), $7.62 - 7.55$ (m, 1H), $7.54 - 7.48$ (m, 1H), 7.45 (d, $J = 8.2 \text{ Hz}$, 1H), 7.28 (d, $J = 8.7 \text{ Hz}$, 1H) ppm.

$^{19}\text{F NMR}$ (376 MHz, CDCl_3): $\delta = -80.71$ (t, $J = 10.7 \text{ Hz}$, 3F), -110.91 (s, 2F), $-121.07 - -121.54$ (m, 2F), $-121.59 - -122.18$ (m, 2F), $-122.50 - -123.07$ (m, 2F), $-125.87 - -126.33$ (m, 2F) ppm.

$^{13}\text{C NMR}$ (100 MHz, CDCl_3): $\delta = 151.0$ (t, $J = 1.0 \text{ Hz}$), 145.6 , 136.1 (t, $J = 32.3 \text{ Hz}$), 134.4 , 133.2 , 128.9 , 128.7 , 127.9 , 127.8 , 126.4 , 124.7 , 123.0 (t, $J = 1.0 \text{ Hz}$), 120.9 , 120.5 , 120.3 , 119.6 , 116.6 , 109.6 ppm; carbons corresponding to the C_6F_{13} group cannot be identified due to C-F coupling.

HRMS m/z : calcd for $\text{C}_{24}\text{H}_{11}\text{F}_{13}\text{N}_3\text{O}$ $[\text{M}+\text{H}]^+$ 604.0689, found: 604.0698.



1-(2-(Perfluoropentyl)naphtho[1,2-*b*]furan-3-yl)-1*H*-benzo[*d*][1,2,3]triazole (16z):

Yield = 72% (80 mg), 0.2 mmol scale. Yellow solid. M.p. 118.6–120.5 °C.

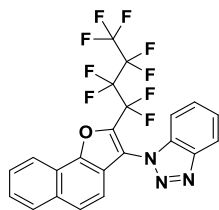
IR (KBr): $\nu = 3056, 1629, 1533, 814, 746 \text{ cm}^{-1}$.

$^1\text{H NMR}$ (400 MHz, CDCl_3): $\delta = 8.49 - 8.43$ (m, 1H), $8.26 - 8.20$ (m, 1H), 8.00 (d, $J = 8.1 \text{ Hz}$, 1H), $7.79 - 7.72$ (m, 2H), $7.71 - 7.65$ (m, 1H), $7.62 - 7.56$ (m, 1H), $7.53 - 7.48$ (m, 1H), 7.45 (d, $J = 8.2 \text{ Hz}$, 1H), 7.28 (d, $J = 8.7 \text{ Hz}$, 1H) ppm.

$^{19}\text{F NMR}$ (376 MHz, CDCl_3): $\delta = -80.67$ (t, $J = 10.6 \text{ Hz}$, 3F), -110.93 (s, 2F), -121.63 (s, 2F), $-122.23 - -123.01$ (m, 2F), $-125.77 - -126.34$ (m, 2F) ppm.

$^{13}\text{C NMR}$ (100 MHz, CDCl_3): $\delta = 151.0$ (t, $J = 1.1 \text{ Hz}$), 145.6 , 136.0 (t, $J = 32.6 \text{ Hz}$), 134.4 , 133.2 , 128.9 , 128.7 , 127.9 , 127.8 , 126.5 , 124.7 , 123.0 (t, $J = 2.0 \text{ Hz}$), 120.9 , 120.5 , 120.3 , 119.6 , 116.6 , 109.6 ppm; carbons corresponding to the C_5F_{11} group cannot be identified due to C-F coupling.

HRMS m/z : calcd for $\text{C}_{23}\text{H}_{11}\text{F}_{11}\text{N}_3\text{O}$ $[\text{M}+\text{H}]^+$ 554.0721, found: 554.0722.



1-(2-(Perfluorobutyl)naphtho[1,2-*b*]furan-3-yl)-1*H*-benzo[*d*][1,2,3]triazole (16a'):

Yield = 67% (67 mg), 0.2 mmol scale. White solid. M.p. 112.7–114.1 °C.

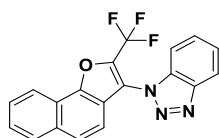
IR (KBr): $\nu = 3075, 1629, 1491, 805, 732 \text{ cm}^{-1}$.

¹H NMR (400 MHz, CDCl₃): $\delta = 8.46$ (d, $J = 8.1$ Hz, 1H), 8.24 (d, $J = 8.3$ Hz, 1H), 8.00 (d, $J = 8.1$ Hz, 1H), 7.81 – 7.73 (m, 2H), 7.72 – 7.64 (m, 1H), 7.63 – 7.56 (m, 1H), 7.54 – 7.48 (m, 1H), 7.45 (d, $J = 8.2$ Hz, 1H), 7.28 (d, $J = 8.7$ Hz, 1H) ppm.

¹⁹F NMR (376 MHz, CDCl₃): $\delta = -80.77$ (t, $J = 10.3$ Hz, 3F), -111.08 (s, 2F), -121.61 – -123.02 (m, 2F), -125.87 (td, $J = 13.2, 5.9$ Hz, 2F) ppm.

¹³C NMR (100 MHz, CDCl₃): $\delta = 151.0$ (t, $J = 1.6$ Hz), 145.6, 136.0 (t, $J = 33.2$ Hz), 134.3, 133.2, 128.9, 128.7, 127.9, 127.8, 126.4, 124.7, 123.0 (t, $J = 2.2$ Hz), 120.9, 120.5, 120.3, 119.6, 116.6, 109.6 ppm; carbons corresponding to the C₄F₉ group cannot be identified due to C-F coupling.

HRMS *m/z*: calcd for C₂₂H₁₁F₉N₃O [M+H]⁺ 504.0753, found: 504.0762.



1-(2-(Trifluoromethyl)naphtho[1,2-*b*]furan-3-yl)-1*H*-benzo[*d*][1,2,3]triazole (16b'):

Yield = 50% (35 mg), 0.2 mmol scale. Yellow solid. M.p. 86.1–87.3 °C.

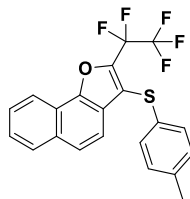
IR (KBr): $\nu = 3063, 1627, 1613, 808, 745 \text{ cm}^{-1}$.

¹H NMR (400 MHz, CDCl₃): $\delta = 8.46$ (d, $J = 8.2$ Hz, 1H), 8.24 (d, $J = 9.0$ Hz, 1H), 8.00 (d, $J = 8.1$ Hz, 1H), 7.84 – 7.72 (m, 2H), 7.71 – 7.65 (m, 1H), 7.64 – 7.58 (m, 1H), 7.57 – 7.47 (m, 2H), 7.41 (d, $J = 8.7$ Hz, 1H) ppm.

¹⁹F NMR (376 MHz, CDCl₃): $\delta = -61.98$ (s, 3F) ppm.

¹³C NMR (100 MHz, CDCl₃): $\delta = 150.2$ (t, $J = 1.0$ Hz), 145.7, 136.2 (t, $J = 32.1$ Hz), 133.9, 133.2, 129.0, 128.6, 127.8, 127.6, 126.3, 124.8, 120.9, 120.5, 120.3, 120.3 (q, $J = 297.3$ Hz), 119.0, 117.5, 117.0, 109.7 ppm

HRMS m/z: calcd for C₁₉H₁₁F₃N₃O [M+H]⁺ 354.0849, found: 354.0850.



2-(Perfluoroethyl)-3-(p-tolylthio)naphtho[1,2-b]furan (17):

Yield = 46% (56 mg), 0.3 mmol scale. White solid. M.p. 101.0–102.7 °C.

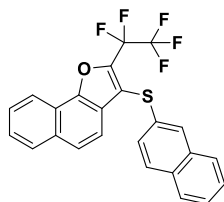
IR (KBr): ν = 3060, 1771, 1579, 810, 720 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ = 8.35 – 8.30 (m, 1H), 7.88 (d, *J* = 8.1 Hz, 1H), 7.66 – 7.52 (m, 3H), 7.30 (d, *J* = 8.7 Hz, 1H), 7.24 – 7.20 (m, 2H), 7.05 (d, *J* = 8.0 Hz, 2H), 2.28 (s, 3H) ppm.

¹⁹F NMR (376 MHz, CDCl₃): δ = -83.63 (t, *J* = 4.1 Hz, 3F), -112.18 – -113.16 (m, 2F) ppm.

¹³C NMR (100 MHz, CDCl₃): δ = 151.5 (t, *J* = 1.3 Hz), 141.3 (t, *J* = 29.6 Hz), 137.0, 132.7, 130.3, 130.0, 129.8, 129.3, 128.4, 127.1, 126.9, 125.1, 124.2, 121.0, 120.3, 118.5, 21.0 ppm; carbons corresponding to the C₂F₅ group cannot be identified due to C-F coupling.

HRMS m/z: calcd for C₂₁H₁₄F₅OS [M+H]⁺ 409.0680, found: 409.0685.



3-(Naphthalen-2-ylthio)-2-(perfluoroethyl)naphtho[1,2-b]furan (18):

Yield = 52% (69 mg), 0.3 mmol scale. White solid. M.p. 135.1–135.8 °C.

IR (KBr): ν = 3366, 1771, 1579, 1501, 810, 747 cm⁻¹.

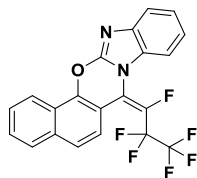
¹H NMR (400 MHz, CDCl₃): δ = 8.36 (d, *J* = 8.1 Hz, 1H), 7.87 (d, *J* = 8.0 Hz, 1H), 7.81 – 7.73 (m, 2H), 7.71 – 7.61 (m, 3H), 7.59 – 7.52 (m, 2H), 7.46 – 7.38 (m, 2H), 7.37 – 7.27 (m, 2H) ppm.

¹⁹F NMR (376 MHz, CDCl₃): δ = -82.90 – -84.28 (m, 3F), -112.06 – -113.36 (m, 2F) ppm.

¹³C NMR (100 MHz, CDCl₃): δ = 151.6 (t, *J* = 1.0 Hz), 141.8 (t, *J* = 29.9 Hz), 133.6, 132.8, 132.0, 131.4, 129.0, 128.4, 127.7, 127.2, 127.2, 127.1, 127.0, 126.8, 126.3, 126.1, 125.3, 124.3, 121.0, 120.3, 118.5, 117.4 ppm; carbons corresponding to the C₂F₅ group cannot be identified due to

C-F coupling.

HRMS m/z: calcd for C₂₄H₁₄F₅OS [M+H]⁺ 445.0680, found: 445.0685.



(Z)-7-(Perfluoropropylidene)-7H-benzo[4,5]imidazo[2,1-b]naphtho[2,1-e][1,3]oxazine (19):

Yield = 88% (111 mg), 0.3 mmol scale. Yellow solid. M.p. 234.8–235.1 °C.

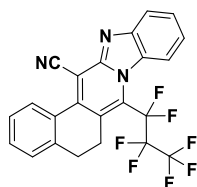
IR (KBr): ν = 3064, 1676, 1623, 801, 745 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ = 8.57 – 8.51 (m, 1H), 7.92 – 7.86 (m, 1H), 7.76 – 7.64 (m, 4H), 7.63 – 7.58 (m, 1H), 7.50 – 7.43 (m, 1H), 7.40 – 7.31 (m, 2H) ppm.

¹⁹F NMR (376 MHz, CDCl₃): δ = -82.22 – -82.30 (m, 3F), -111.27 (d, J = 12.4 Hz, 2F), -125.75 (dq, J = 25.1, 12.5 Hz, 1F) ppm.

¹³C NMR (100 MHz, CDCl₃): δ = 151.2, 147.3 (d, J = 4.8 Hz), 140.2, 135.0, 134.5 (t, J = 31.3 Hz), 130.2 (t, J = 2.5 Hz), 129.0, 127.7, 127.6, 124.5 (t, J = 0.9 Hz), 124.2, 123.0, 122.9 (d, J = 2.6 Hz), 122.5 (t, J = 7.9 Hz), 122.0, 119.3, 113.4 (d, J = 17.2 Hz), 108.4 (d, J = 2.4 Hz) ppm; carbons corresponding to the C₃F₆ group cannot be identified due to C-F coupling.

HRMS m/z: calcd for C₂₁H₁₁F₆N₂O [M+H]⁺ 421.0770, found: 421.0769.



7-(Perfluoropropyl)-5,6-dihydrobenzo[f]benzo[4,5]imidazo[1,2-b]isoquinoline-14-carbonitrile (20):

Yield = 72% (100 mg), 0.3 mmol scale. Yellow solid. M.p. 257.9–258.2 °C.

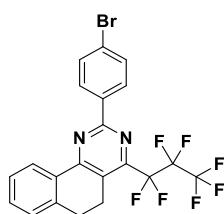
IR (KBr): ν = 2901, 2230, 1602, 1475, 742, 721 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ = 8.07 (d, J = 8.2 Hz, 1H), 7.95 (d, J = 7.7 Hz, 1H), 7.77 (d, J = 8.5 Hz, 1H), 7.63 – 7.47 (m, 3H), 7.39 (t, J = 7.4 Hz, 1H), 7.29 – 7.22 (m, 1H), 3.24 (d, J = 15.6 Hz, 1H), 2.94 (d, J = 14.2 Hz, 2H), 2.70 (t, J = 14.3 Hz, 1H) ppm.

¹⁹F NMR (376 MHz, CDCl₃): δ = -79.59 (t, J = 10.4 Hz, 3F), -98.9 – -105.8 (m, 2F), -121.97 – -124.86 (m, 2F) ppm.

¹³C NMR (100 MHz, CDCl₃): δ = 146.9, 145.9, 141.1, 139.5, 132.5 (t, J = 23.1 Hz), 132.1, 129.5, 127.9, 127.3, 126.6, 126.1, 125.4, 121.9, 121.7 (d, J = 2.8 Hz), 121.4, 115.9, 112.9, 102.0 (t, J = 5.5 Hz), 28.3 (t, J = 1.5 Hz), 25.5 (m) ppm; carbons corresponding to the C₃F₇ group cannot be identified due to C-F coupling.

HRMS m/z: calcd for C₂₃H₁₃F₇N₃ [M+H]⁺ 464.0992, found: 464.0995.



2-(4-Bromophenyl)-4-(perfluoropropyl)-5,6-dihydrobenzo[*h*]quinazoline (21):

Yield = 73% (111 mg), 0.3 mmol scale. White solid. M.p. 111.1–112.9 °C.

IR (KBr): ν = 3072, 2943, 1556, 1399, 1227, 930, 770, 743, 606 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ = 8.53 (dd, J = 7.4, 1.7 Hz, 1H), 8.47 – 8.43 (m, 2H), 7.67 – 7.61 (m, 2H), 7.51 – 7.43 (m, 2H), 7.32 – 7.27 (m, 1H), 3.21 – 3.14 (m, 2H), 3.00 – 2.97 (m, 2H) ppm.

¹⁹F NMR (376 MHz, CDCl₃): δ = -79.64 (t, J = 9.5 Hz, 3F), -110.17 (q, J = 9.6 Hz, 2F), -125.41 – -125.47 (d, J = 3.6 Hz, 2F) ppm.

¹³C NMR (100 MHz, CDCl₃): δ = 162.6, 161.2, 152.1 (t, J_{C-F} = 25.3 Hz), 139.4, 135.7, 132.0, 131.9, 131.8, 129.8, 127.9, 127.5, 126.4, 126.3, 125.9, 26.8, 22.9 (m) ppm; carbons corresponding to the C₃F₇ group cannot be identified due to C-F coupling.

HRMS m/z: calcd for C₂₁H₁₃BrF₇N₂ [M+H]⁺ 505.0145, found: 505.0163.

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