Supporting Information

for

$Cu(OTf)_2$-Catalyzed Access to 2,4,5-Trisubstituted Imidazoles from Acyclic Reissert Compounds

Swetha Sathyendran,[a] Vikraman Ganesh Moorthi,[a] Sharmila Nokku,[a] Aron Manick Joel,[a] Suryanarayanan Chandrasekaran,[a] Wei-Yu Lin[b] and Gopal Chandru Senadi*[ab]

[a]Department of Chemistry, Faculty of Engineering and Technology, SRM Institute of Science and Technology, Kattankulathur - 603 203, Chengalpattu District, Tamil Nadu.

[b]Department of Medicinal and Applied Chemistry, Kaohsiung Medical University, Kaohsiung, 80708, ROC Taiwan.

Corresponding Author Email: *chandrug@srmist.edu.in*

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(1) General information

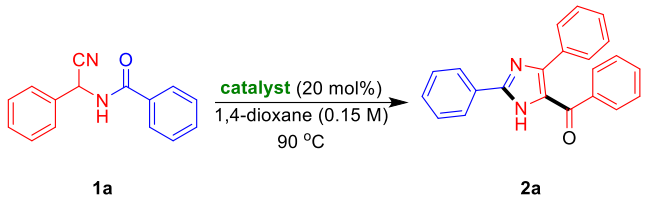
^{1}H NMR were recorded on a Bruker 500/400 MHz, Varian mercury 400/600 MHz and JEOL 400 MHz and ^{13}C NMR spectra were recorded on a Bruker 100/125 MHz, Varian mercury 100/150 MHz and JEOL 100 MHz. The chemical shift (δ) values are given in parts per million (ppm), and the coupling constants (*J*) are given in hertz (Hz). The spectra were recorded using $CDCl_3$ and DMSO-d_6 solvent. ^{1}H NMR chemical shifts are referenced to tetramethylsilane (TMS, 0 ppm) and ^{13}C NMR referenced to $CDCl_3$ (77.0 ppm) and DMSO-d_6 (39.52). The progress of the reaction was monitored by TLC using Merck pre-coated TLC sheets. The melting point of compounds were determined using digital melting point apparatus (Model 935) from Deep Vision Electronics PVT. LTD. Single crystal XRD was analyzed using Rigaku Oxford Diffraction. HRMS were measured using the Agilent G6230B Accurate Mass TOF and Waters State LC-QTOF-HRMS, Liquid chromatography-mass spectrometry using LTQ Orbitrap XL (Thermo Fisher Scientific). All quantum chemical calculations were carried out using Gaussian 16 software installed in the SRMIST-KTR Galaxy HPC server containing an Intel Xeon E5-2680v4 2.4 GHz processor of 28 cores of 16 GB RAM. Column chromatography was performed on 100–200 mesh silica gel using hexane/ethyl acetate as eluent. All commercial chemicals were purchased from Avra, SRL, TCI and BLD Pharm through vendors and Carbanio through online. The purchased commercial chemicals and solvents were used as such without any further purifications or distillation.

(2) Complete optimization studies

The reaction was initially conducted using various metal halides (20 mol%) in 1,4-dioxane at 90 °C (Table S1, entries 1-7). Among these, $FeCl_3$ afforded a good yield of 63%. However, replacement with $CoCl_2 \cdot 6H_2O$ resulted in a significant decrease in yield to 17%. Subsequently, Cu(II) halides such as $CuCl_2$ and $CuBr_2$ were evaluated, providing moderate yields of 44% and 56%, respectively. In contrast, when Cu(I) halides (CuCl and CuBr) were employed, the reaction did not proceed, likely due to the strong coordination of halide ligands in Cu(I) salts, which limits their ability to activate the nitrile functionality. Further screening with $ZnCl_2$ afforded the desired product in low yield, although the reaction progression indicates the beneficial role of a +2-oxidation state metal center. Encouraged by this observation, various metal triflates, including Fe, Cu, Sm, Ag, and Yb triflates, were investigated (entries 8-12). Among these, $Cu(OTf)_2$ exhibited a significantly higher yield, whereas the other metal triflates provided only moderate yields in the range of 48-59%. Finally, reactions performed in the

presence of Brønsted and Lewis acids such as $BF_3 \cdot OEt_2$ and triflic acid (entry 13 and 14) resulted in moderate yields of 51–62%.

Table S1. Catalyst screening[a]



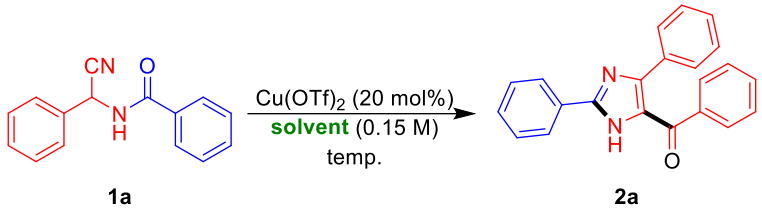
1a 2a

s.no.	catalyst (mol%)	temp. (°C)/ time (h)	yield (%)[b]
1	$FeCl_3$ (20)	90/12	63
2	$CoCl_2.6H_2O$ (20)	90/24	17
3	$CuCl_2$ (20)	90/24	44
4	$CuBr_2$ (20)	90/16	56
5[c]	CuCl (20)	90/24	nr
6[c]	CuBr (20)	90/24	nr
7	$ZnCl_2$ (20)	90/24	31
8	$Fe(OTf)_2$ (20)	90/12	59
9	**$Cu(OTf)_2$ (20)**	**90/8**	**73**
10	$Sm(OTf)_3$ (20)	90/24	48
11	AgOTf (20)	90/24	54
12	$Yb(OTf)_3$ (20)	90/24	51
13	BF_3 etherate (20)	90/24	62
14	Triflic acid (20)	90/24	51

[a]Reaction Conditions: All reactions were carried out using **1a** (0.5 mmol), 1,4-dioxane (0.15 M) and catalyst (20 mol%) in a sealed vial at indicated temperature and time unless otherwise noted. [b]Isolated yield. [c]The reaction was carefully kept for three independent trials and the unreacted starting materials were recovered.

Upon identifying $Cu(OTf)_2$ as the most effective catalyst, it was selected as the standard condition for further optimization, and a range of solvents was subsequently screened. As shown in Table S2 (entry 1), replacing 1,4-dioxane with ethanol led to a significant decrease in yield to 42%. Similarly, lower yields were consistently observed with other solvents such as isopropanol (IPA), ethyl acetate, and acetonitrile, with yields ranging from 19% to 38%. Although ethylene glycol provided a comparatively improved yield of 61%, it remained inferior to that obtained with 1,4-dioxane.

Table S2. Solvent screening[a]



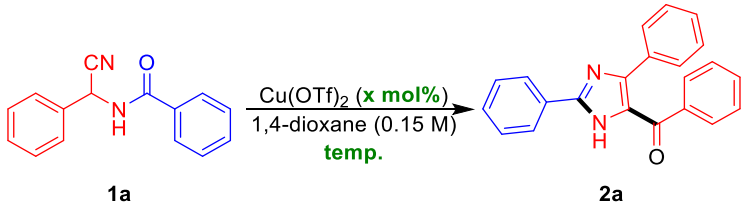
1a 2a

s.no.	solvent	catalyst (mol%)	temp. (°C) / time (h)	yield (%)[b]
1	ethanol	$Cu(OTf)_2$ (20)	80/24	42
2	IPA	$Cu(OTf)_2$ (20)	80/24	38
3	ethyl acetate	$Cu(OTf)_2$ (20)	80/24	34
4	acetonitrile	$Cu(OTf)_2$ (20)	80/24	19
5	ethylene glycol	$Cu(OTf)_2$ (20)	100/12	61

[a]Reaction Conditions: All reactions were carried out using **1a** (0.5 mmol), Solvent (0.15 M) and $Cu(OTf)_2$ (20 mol%) in a sealed vial at indicated temperature and time unless otherwise noted. [b]Isolated yield.

After identifying the optimal catalyst and solvent, we next investigated the effect of catalyst loading to maximize the reaction yield. Initially, reducing the catalyst loading to 10 mol% (entry 1) resulted in a decreased yield of 61%. Increasing the catalyst loading to 15 mol% (entry 2) led to a slight improvement, affording a yield of 64%, indicating that higher catalyst loading is beneficial. Under the standard condition of 20 mol%, the reaction delivered the maximum yield. Further increasing the catalyst loading to 25 mol% (entry 3) afforded a yield of approximately 72%, which is comparable to that obtained under the standard conditions. Therefore, 20 mol% was selected as the optimal catalyst loading. Subsequently, the effect of temperature was examined. Lowering the reaction temperature to 70 °C resulted in a reduced yield of 58%, whereas increasing the temperature to 110 °C afforded a yield of 74%, which is comparable to that obtained at 90 °C. Accordingly, 90 °C was retained as the optimal reaction temperature.

Table S3. Catalyst loading and temperature studies[a]



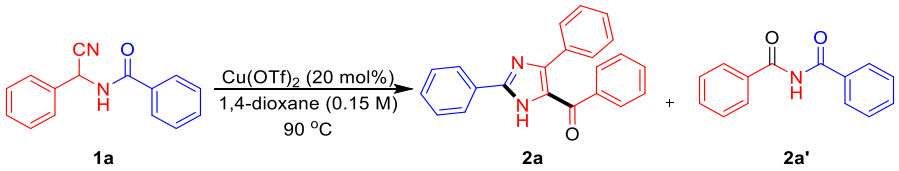
1a 2a

s.no.	solvent	catalyst (mol%)	temp. (°C) / time (h)	yield(%)[b]
1	1,4-dioxane	$Cu(OTf)_2$ (10)	90/24	61
2	1,4-dioxane	$Cu(OTf)_2$ (15)	90/24	64
3	1,4-dioxane	$Cu(OTf)_2$ (25)	90/8	72
5	1,4-dioxane	$Cu(OTf)_2$ (20)	70/24	58
6	1,4-dioxane	$Cu(OTf)_2$ (20)	110/8	74

[a]Reaction Conditions: All reactions were carried out using **1a** (0.5 mmol), Solvent (0.15 M) and $Cu(OTf)_2$ (x mol%) in a sealed vial at indicated temperature and time unless otherwise noted. [b]Isolated yield.

The effect of reaction atmosphere was subsequently investigated (Table S4). Conducting the reaction under open-air conditions (entry 1), instead of in a sealed system, resulted in a decreased yield of 64%. The addition of 5.0 equiv. of H_2O (entry 2) did not significantly affect the yield. When a mixed solvent system of H_2O/1,4-dioxane (3:2) was employed (entry 3), a slight decrease in yield to 67% was observed. Notably, performing the reaction under an O_2 atmosphere (entry 4) led to a substantial reduction in yield to 47%, along with the formation of an oxidative decyanative imide product **2a"** in 25% yield. In contrast, conducting the reaction under an N_2 atmosphere (entry 5) further diminished the yield to 29%. However, when the reaction under N_2 was supplemented with H_2O (entries 6 and 7), the yield improved to 56% and 68% with 5.0 and 10 equiv. of H_2O, respectively. These observations suggest that water plays a crucial role in facilitating the reaction toward the formation of product **2a**.

Table S4. Other parameters studies[a]



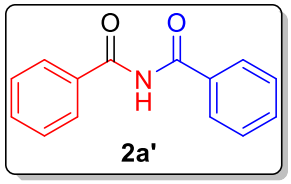
1a 2a 2a'

s.no.	solvent	temp. (°C) / time (h)	yield (%)[b] (2a/2a')
1	1,4-dioxane (open air)	90/12	64/0
2	1,4-dioxane (5.0 equiv. H_2O)	90/12	73/0
3	H_2O:1,4-dioxane (3:2 ratio)	90/12	67/0
4	1,4-dioxane (degassed, O_2 atm.)	90/12	47/25
5	1,4-dioxane (N_2 atm.)	90/24	29/0

6	1,4-dioxane (N_2 atm.) in 5 equiv. of H_2O	90/12	56
7	1,4-dioxane (N_2 atm.) in 10 equiv. of H_2O	90/12	68

[a]Reaction Conditions: All reactions were carried out using **1a** (0.5 mmol), Solvent (0.15 M) and $Cu(OTf)_2$ (20 mol%) in a sealed vial at indicated temperature and time unless otherwise noted. [b]Isolated yield.

***N*-benzoylbenzamide (2a').**[1] A 15 mL vial was charged with **1a** (118 mg, 0.5 mmol) and



$Cu(OTf)_2$ (20 mol%) in 1,4-dioxane (3.3 mL, 0.15 M) under degassed O_2 atmosphere. The reaction mixture was allowed to stir at 90 °C in oil bath in sealed vial until the completion of reaction by TLC chromatography (12 h). The reaction mixture was cooled to room temperature, diluted with 10 mL of water. The water layer was extracted with (3 x 15 mL) of ethyl acetate and the combined ethyl acetate layer was given brine wash (2 x 10 mL). The final ethyl acetate layer was dried over Na_2SO_4 and concentrated under reduced pressure to get the crude compound. The obtained crude was purified using column chromatography on silica gel (EA/Hex=20%) to afford **2a'** as white solid (28 mg, 25% yield); mp 155-156 °C (lit. 156-157 °C)[1]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.48 (s, 1H), 7.82 (d, J = 8Hz, 4H), 7.53-7.49 (m, 2H), 7.40 (t, J = 7.8Hz, 4H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 166.7, 133.3, 132.9, 128.6, 128.0.

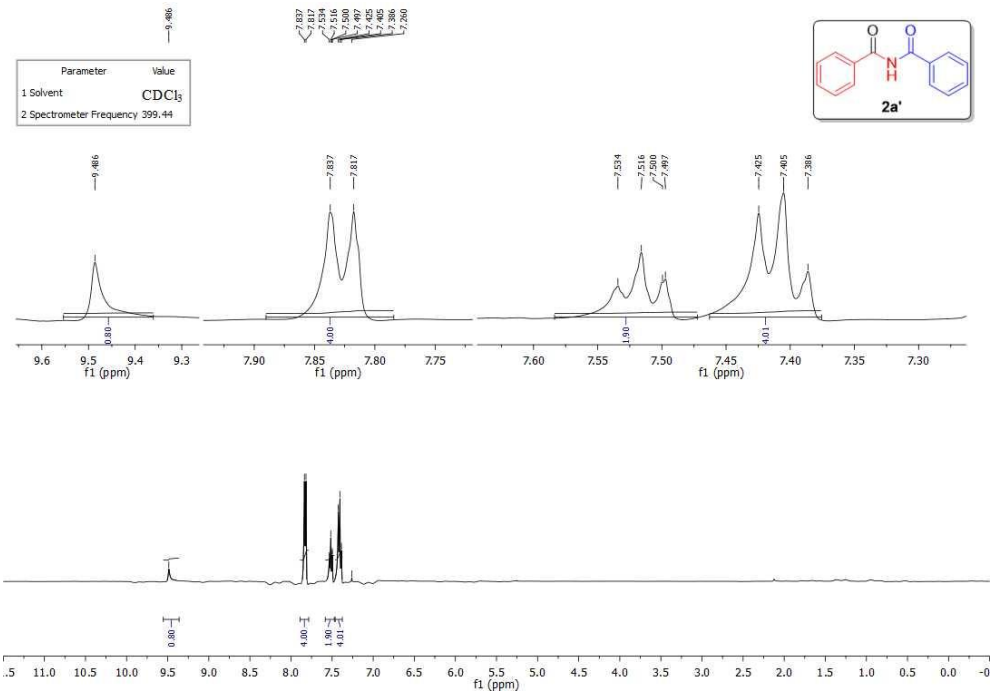


Fig. S1. ^{1}H NMR for *N*-benzoylbenzamide **(2a').**

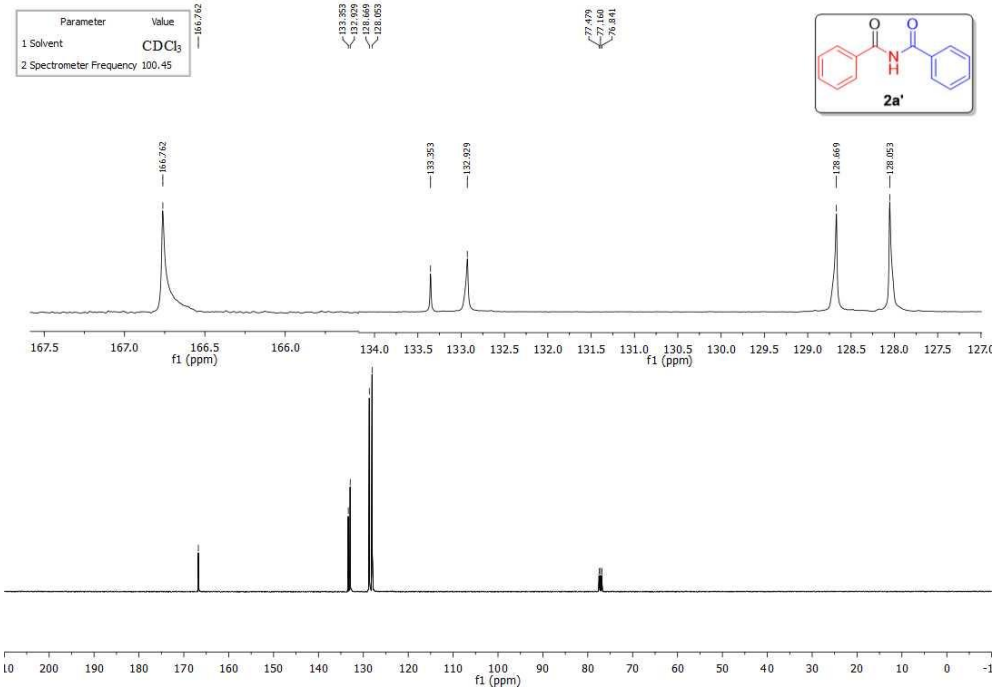


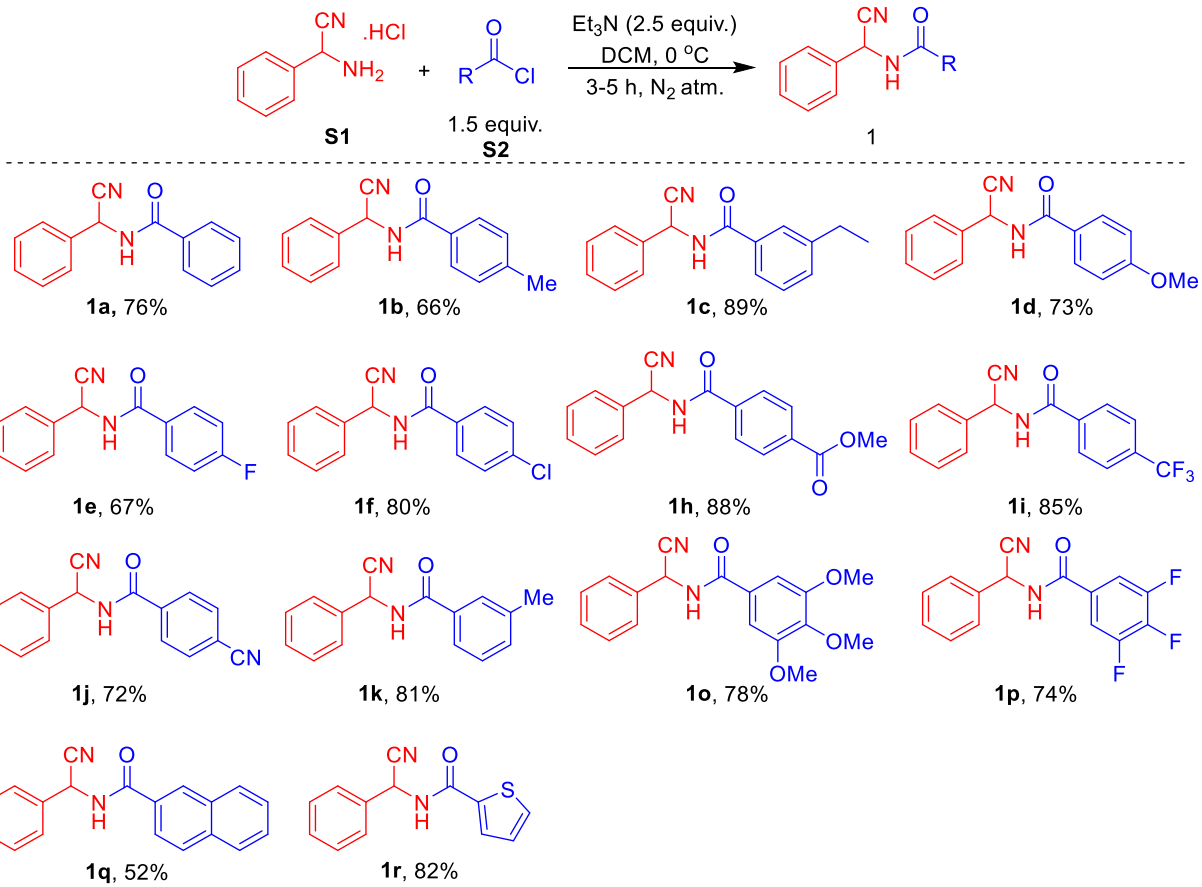
Fig. S2. ^{13}C NMR for *N*-benzoylbenzamide **(2a').**

(3) Experimental procedure for synthesis of *N*-acyl-*α*-aminonitriles

All starting materials are synthesized by Method A or Method B. The starting material 2-amino-2-phenylacetonitrile **3** was purchased as a hydrochloride salt and used as such for the preparation of *N*-acyl-*α*-aminonitrile **1**.

Method A: To the solution of 2-amino-2-phenylacetonitrile **S1** (1.0 equiv.) in DCM, triethylamine (2.5 equiv.) was added and stirred at 0~5 °C in nitrogen atmosphere for 10~15 mins. To this stirred reaction mixture acid chlorides **S2** (1.5 equiv.) in DCM was added and continued stirring at 0~5 °C in nitrogen atmosphere for 3~5 h. After the completion of the reaction, DCM was evaporated under rotary vacuum. Then the crude product was diluted with water (30 mL) followed by extraction with ethyl acetate (3 x 20 mL). The obtained organic layer was given brine wash (20 mL), dried over Na_2SO_4 and concentrated under rotary vacuum. The obtained crude was purified using column chromatography by eluting EA/Hex to afford the pure *N*-acyl-*α*-aminonitriles **1a-f, 1h-k** and **1o-r** in **52-89%** yields.

(a) Substrate scope for method A

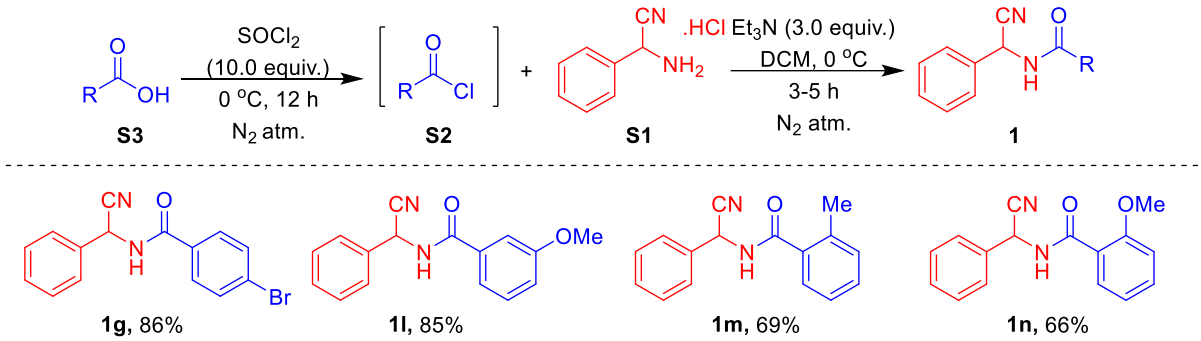


[a]Reaction Conditions: All reactions were carried out using **S1** (2 mmol), **S2** (3 mmol), DCM (0.15 M) and Et_3N (5 mmol) in a sealed vial at 0 °C under nitrogen atmosphere and time unless otherwise noted. [b]Isolated yield.

Method B: To the 100 mL round bottom flask charged with acid **S3** (2 mmol) in nitrogen atmosphere, thionyl chloride (10.0 equiv.) was added at 0 °C and stirred for 12 h. After complete formation of acid chloride confirmed by thin layer chromatography, excess $SOCl_2$ was removed in rotary vacuum under nitrogen atmosphere and quenched with sodium

bicarbonate. To this reaction mixture 2-amino-2-phenylacetonitrile **S1** (1.0 equiv.) and triethylamine (2.5 equiv.) in DCM was added and stirred at 0~5 °C in nitrogen atmosphere for 3~5 h. After the completion of the reaction, DCM was evaporated under rotary vacuum. Then the crude product was diluted with water (30 mL) followed by extraction with ethyl acetate (3 x 20 mL). The obtained organic layer was given brine wash (20 mL), dried over Na_2SO_4 and concentrated under rotary vacuum. The obtained crude was purified using column chromatography by eluting EA/Hex to afford the pure *N*-acyl-*α*-aminonitriles **1g, 1l-n** in **66-86%** yields.

(b) Substrate scope for method B

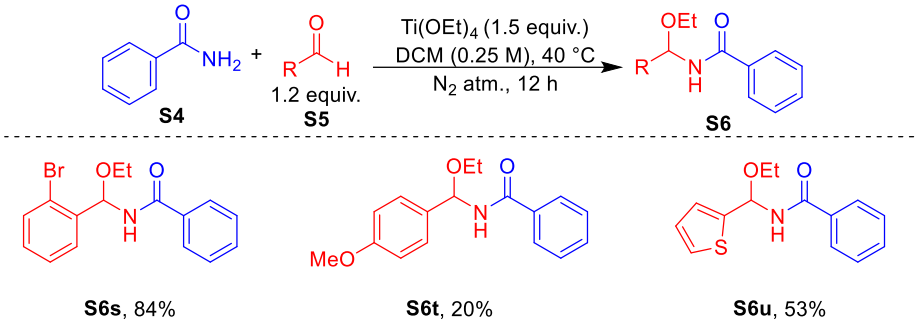


[a]Reaction Conditions: All reactions were carried out using **S3** (2 mmol), $SOCl_2$ (10 equiv.), **S1** (2 mmol), DCM (0.15 M) and Et_3N (5 mmol) at 0 °C under nitrogen atmosphere for indicated time unless otherwise noted. [b]Isolated yield.

Note: Among the starting materials synthesized, few are reported and few are new. For known starting materials respective literatures are mentioned (**1a**[2], **1b**[3], **1d**[2], **1e**[2], **1f**[4], **1g**[2], **1i**[3], **1r**[3], **1s**[5] **and 1u**[5]) and for unknown compounds (**1c, 1h, 1j, 1k, 1l, 1o, 1p, 1q and 1t**) proton, carbon and HRMS data has been taken and including in this supporting material.

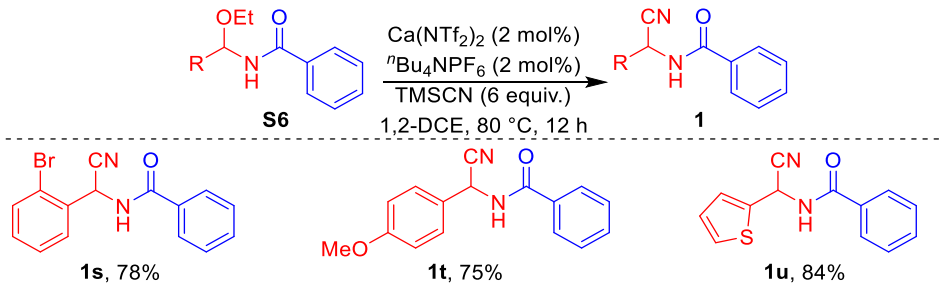
Method C (Step-1) By following the reported literature,[5] amide **S4** (1.0 equiv.) and aldehyde **S5** (1.2 equiv.) were dissolved in anhydrous DCM (0.25 M) under a nitrogen atmosphere. To this solution, $Ti(OEt)_4$ (1.5 equiv.) was added dropwise, and the reaction mixture was stirred at 40 °C overnight (with a condenser attached for reactions conducted at 40 °C). Upon completion, the mixture was diluted with ethanol and quenched by the slow addition of 0.5 M K_2CO_3 solution. The resulting precipitate was removed by filtration through Celite and washed three times with ethanol. The filtrate was then concentrated under reduced pressure, and the crude solid was purified by flash column chromatography (EA/Hex) to afford the desired products **S6**.

(c) Substrate scope for method C (Step-1)



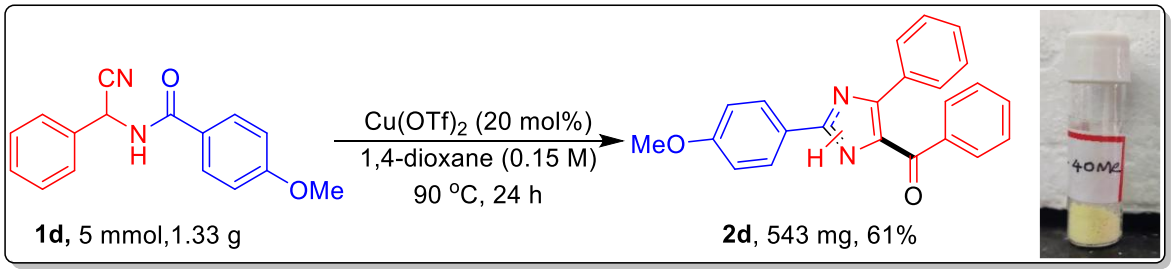
Method C (Step-2): The *N*-acyl-N,O-acetal **S6** (1 equiv.) was placed in a screw-top vial equipped with a Teflon-lined cap, followed by the addition of trimethylsilyl cyanide (TMSCN, 6 equiv.), $Ca(NTf_2)_2$ (2 mol%), and $^nBu_4NPF_6$ (2 mol%) in 1,2-dichloroethane (0.2 M). The reaction mixture was stirred at 80 °C until complete consumption of the starting material was confirmed by TLC (typically 12 h). Upon completion, the reaction was quenched with saturated aqueous $NaHCO_3$ and extracted with DCM (3 x 20 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification by flash column chromatography (EA/Hex) afforded the pure *N*-acyl-*α*-aminonitriles **1s-u** in **75-84%** yields.

(d) Substrate scope for method C (Step-2)



(4) Gram-scale synthesis of 2d and 2h

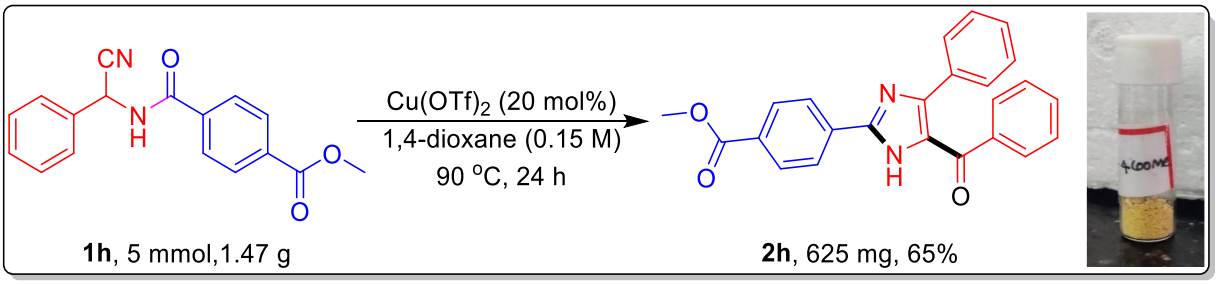
(a) Synthesis of (2-(4-methoxyphenyl)-4-phenyl-1*H*-imidazol-5-yl)(phenyl)methanone (2d)



A 100 mL round bottom was charged with **1d** (1.0 equiv., 5 mmol) and $Cu(OTf)_2$ (20 mol%) in 1,4-dioxane (0.15 M). The reaction mixture was allowed to stir at 90 °C in oil bath in the

sealed RB until the completion of reaction by TLC chromatography (~24 h). The reaction mixture was cooled to room temperature, diluted with 100 mL of water. The water layer was extracted with (3 x 150 mL) of ethyl acetate and the combined ethyl acetate layer was given brine wash (2 x 100 mL). The final ethyl acetate layer was dried over Na_2SO_4 and concentrated under reduced pressure to get the crude compound. The obtained crude was purified using column chromatography by eluting EA/Hex to obtain pale yellow solid of (2-(4-methoxyphenyl)-4-phenyl-1*H*-imidazol-5-yl)(phenyl)methanone **2d** (543 mg, 61% yield).

(b) Synthesis of methyl 4-(5-benzoyl-4-phenyl-1*H*-imidazol-2-yl)benzoate (2h)



A 100 mL round bottom was charged with **1h** (1.0 equiv., 5 mmol) and $Cu(OTf)_2$ (20 mol%) in 1,4-dioxane (0.15 M). The reaction mixture was allowed to stir at 90 °C in oil bath in the sealed RB until the completion of reaction by TLC chromatography (~24 h). The reaction mixture was cooled to room temperature, diluted with 100 mL of water. The water layer was extracted with (3 x 150 mL) of ethyl acetate and the combined ethyl acetate layer was given brine wash (2 x 100 mL). The final ethyl acetate layer was dried over Na_2SO_4 and concentrated under reduced pressure to get the crude compound. The obtained crude was purified using column chromatography by eluting EA/Hex to obtain yellow solid of methyl 4-(5-benzoyl-4-phenyl-1*H*-imidazol-2-yl)benzoate **2h** (625mg, 65% yield).

(5) Reaction monitoring of substrates by TLC

Initially, the reaction progress was monitored using a hexane/ethyl acetate solvent system. However, both the starting material and product exhibited similar R_f values and required multiple elutions with the gradual addition of ethyl acetate for partial separation. This made it difficult to clearly distinguish the consumption of the starting material and the formation of the product. To overcome this challenge, various solvent systems were screened to achieve better resolution. Among them, the dichloromethane/hexane (DCM/Hex) system provided distinct separation between the starting material and product, as illustrated in Fig. S3.

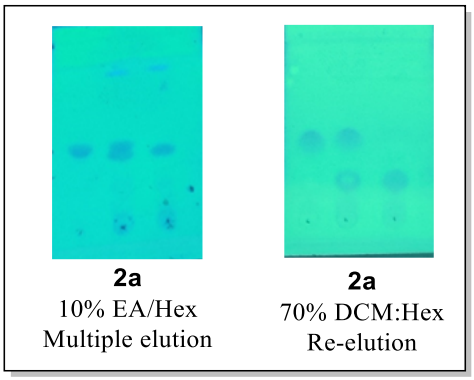
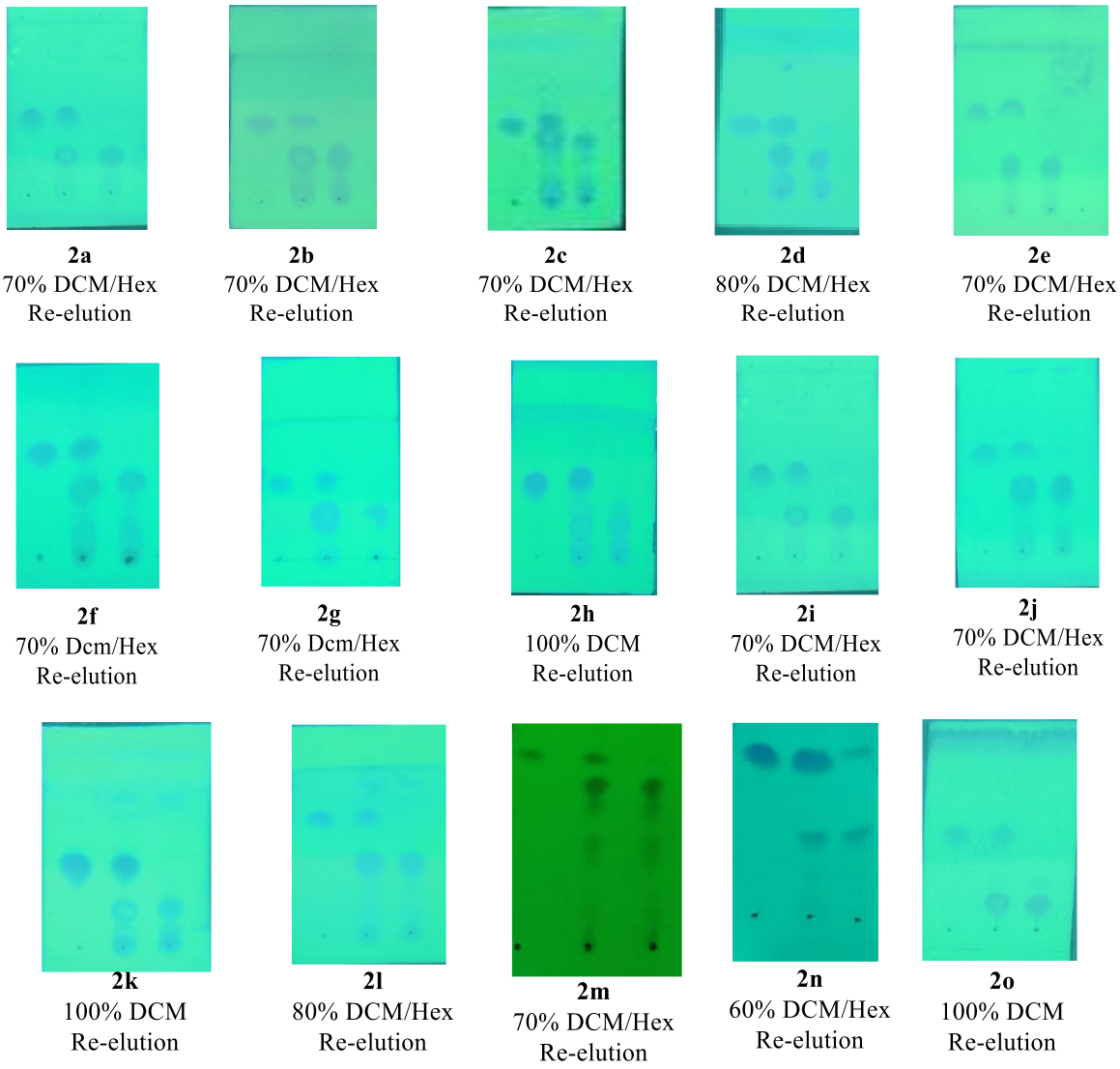


Fig. S3. TLC separation with EA/Hex and DCM/Hex solvent systems.

Hence, this issue was resolved, and the DCM/hexane solvent system was subsequently adopted for monitoring the reaction progress by TLC throughout the project. The optimized TLC systems used for each synthesized substrate are provided below.



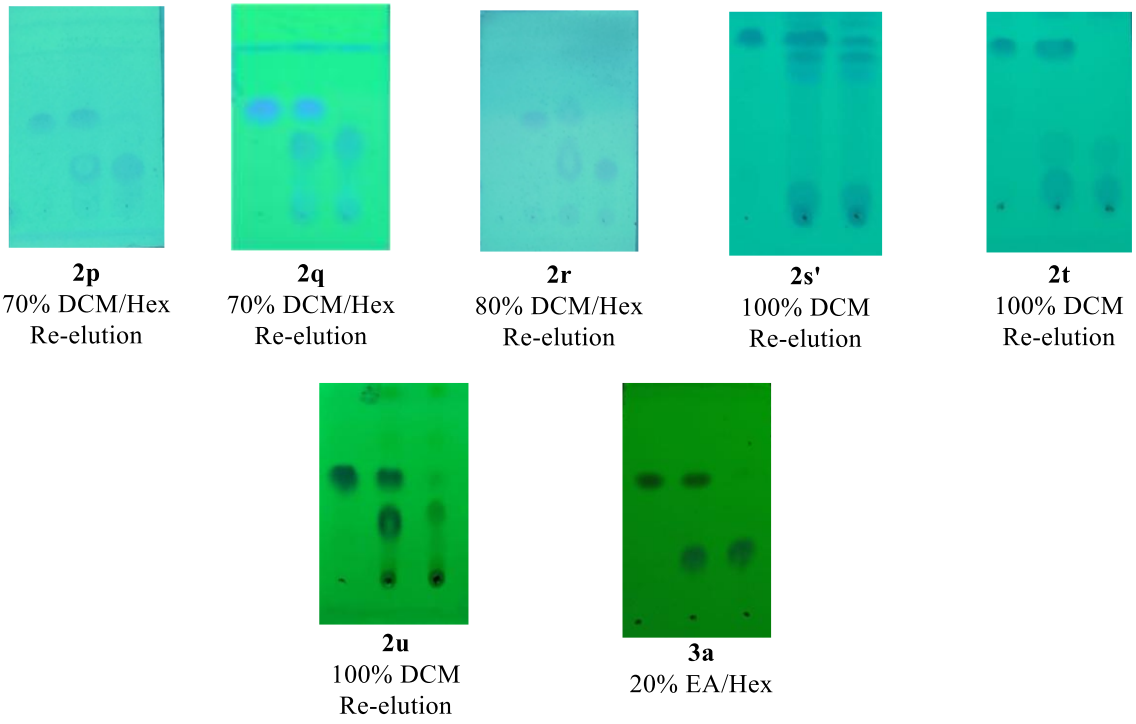


Fig. S4. TLC of substrates.

(6) Single crystal XRD data

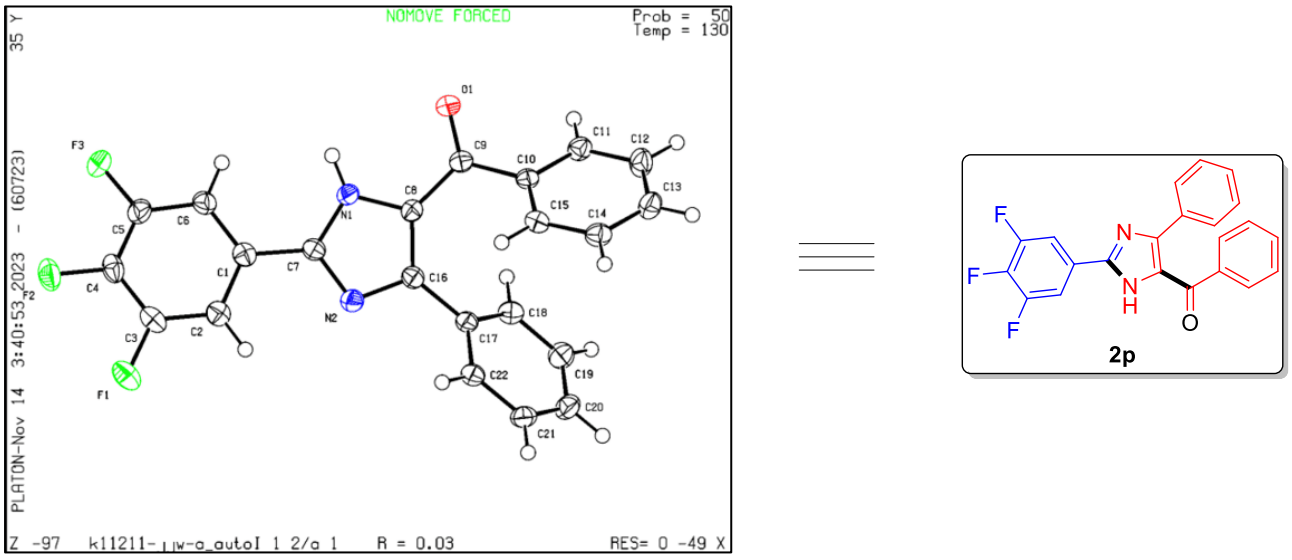
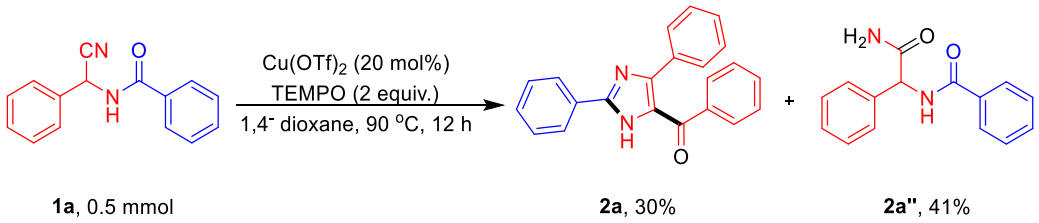


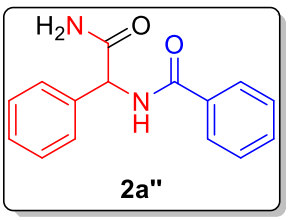
Fig. S5. ORTEP diagram of phenyl(4-phenyl-2-(3,4,5-trifluorophenyl)-1*H*-imidazol-5-yl)methanone **2p** with the atom-numbering scheme; displacement ellipsoids are shown at the 50% probability level.

(7) Radical scavenging experiment

The *N*-acyl-α-aminonitrile **1a** (0.5 mmol) was subjected to reaction with $Cu(OTf)_2$ (20 mol%) and TEMPO (2.0 equiv.) in 1,4-dioxane at 90 °C for 12 h, affording the imidazole product **2a** in 30% yield, accompanied by the nitrile-hydrolyzed product **2a"** in 41% yield.



***N*-(2-amino-2-oxo-1-phenylethyl)benzamide (2a'').**[1] A 15 mL vial was charged with **1a** (118 mg, 0.5 mmol), TEMPO (2.0 equiv.) and $Cu(OTf)_2$ (20 mol%) in 1,4-dioxane (3.3 mL, 0.15 M). The reaction mixture was allowed to stir at 90 °C in oil bath in sealed vial until the completion of reaction by TLC chromatography (12 h). The reaction mixture was cooled to room temperature, diluted with 10 mL of water. The water layer was extracted with (3 x 15 mL) of ethyl acetate and the combined ethyl acetate layer was given



brine wash (2 x 10 mL). The final ethyl acetate layer was dried over Na_2SO_4 and concentrated under reduced pressure to get the crude compound. The obtained crude was purified using column chromatography on silica gel (EA/Hex=70%) to afford **2a** as white solid (52 mg, 41% yield); mp 187-188 °C (lit. 189-191 °C)[1]; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.67 (d, *J* = 7.8 Hz, 1H), 7.91-7.90 (m, 2H), 7.72 (s, 1H), 7.54-7.52 (m, 3H), 7.46 (t, *J* = 7.5 Hz, 2H), 7.35 (t, *J* = 7.5 Hz, 2H), 7.29 (t, 7.5 Hz, 1H), 7.25 (s, 1H), 5.61 (d, *J* = 7.8 Hz, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 150 MHz): δ 171.8, 166.1, 138.7, 133.9, 131.5, 128.4, 128.3, 127.7, 127.6, 127.5, 56.9.

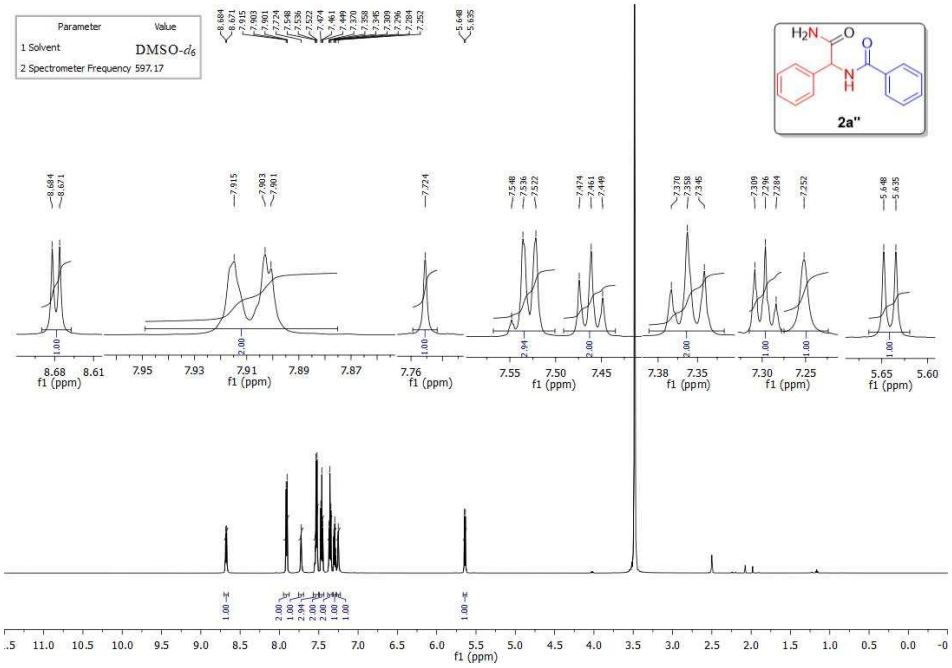


Fig. S6. ^{1}H NMR spectra *of N*-(2-amino-2-oxo-1-phenylethyl)benzamide **(2a").**

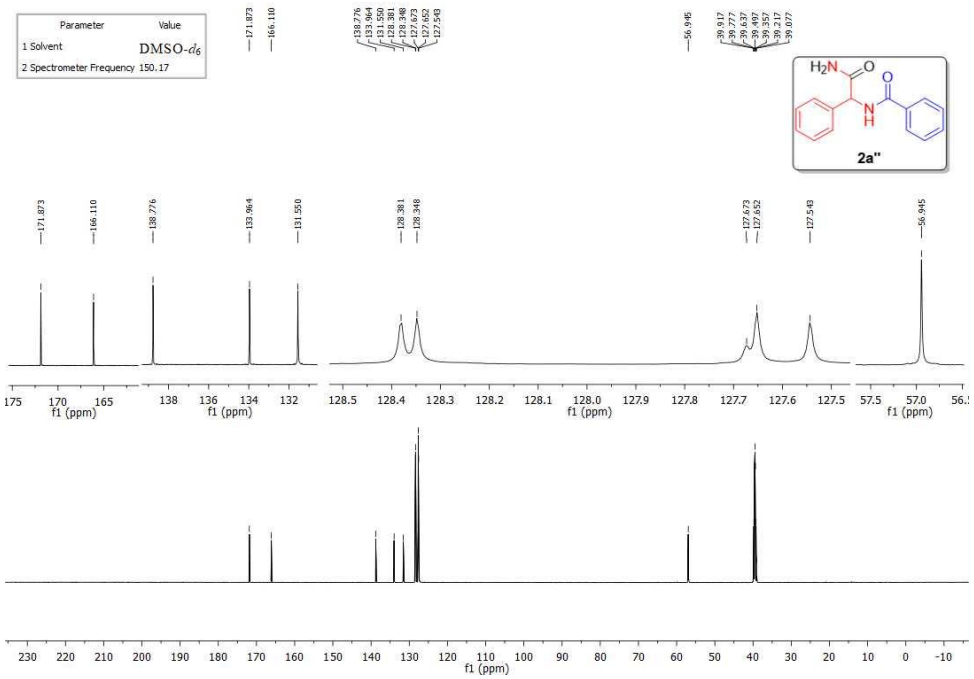
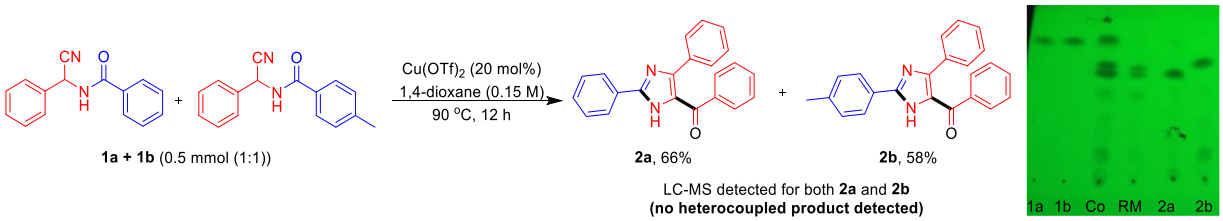


Fig. S7. ^{13}C NMR spectra of *N*-(2-amino-2-oxo-1-phenylethyl)benzamide **(2a").**

(8) Cross-Over (heterocoupling) studies

(a) Cross-over experiment between 1a+1b

To probe this possibility, cross-over experiments were performed using two different substrates, **1a** and **1b** (bearing an electron-donating group), under the standard reaction conditions. In this case, the reaction proceeded smoothly to afford the corresponding products **2a** and **2b**, respectively. Notably, only the homocoupling products were observed, while no cross-over (heterocoupling) products were detected under these conditions, indicating that the reaction likely proceeds without intermolecular exchange between different substrates. The structures of the products were confirmed by LC–MS analysis of the reaction mixture, which showed the presence of only the expected homo-coupled species.



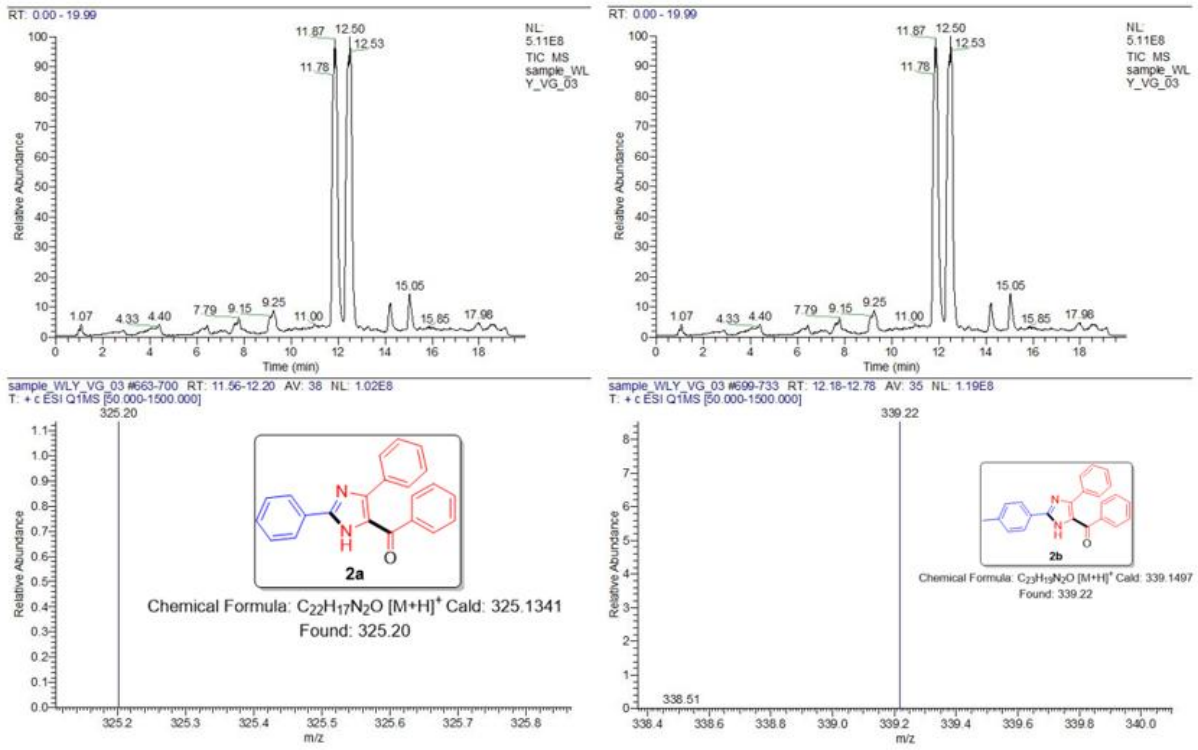
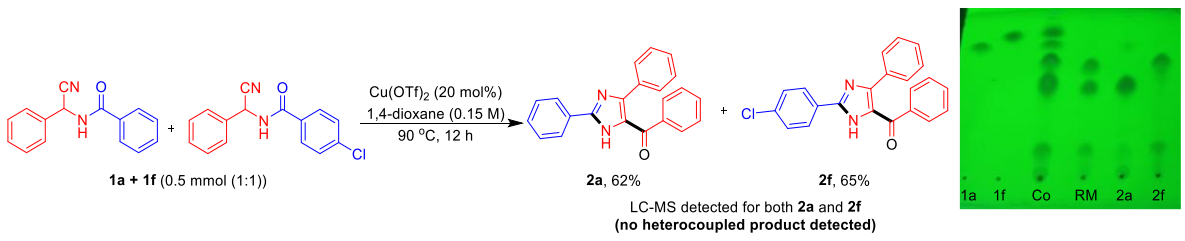


Fig. S8. LC-MS data of cross-coupling reaction with 1a+1b under standard conditions.

(b) Cross-over experiment between 1a+1f

Later, the cross-over experiments were performed using two different substrates, **1a** and **1f** (bearing a halogen group), under the standard reaction conditions. In this case, the reaction proceeded smoothly to afford the corresponding products **2a** and **2f**, respectively. Notably, only the homocoupling products were observed, while no cross-over (heterocoupling) products were detected under these conditions, indicating that the reaction likely proceeds without intermolecular exchange between different substrates. The structures of the products were confirmed by LC–MS analysis of the reaction mixture, which showed the presence of only the expected homo-coupled species.



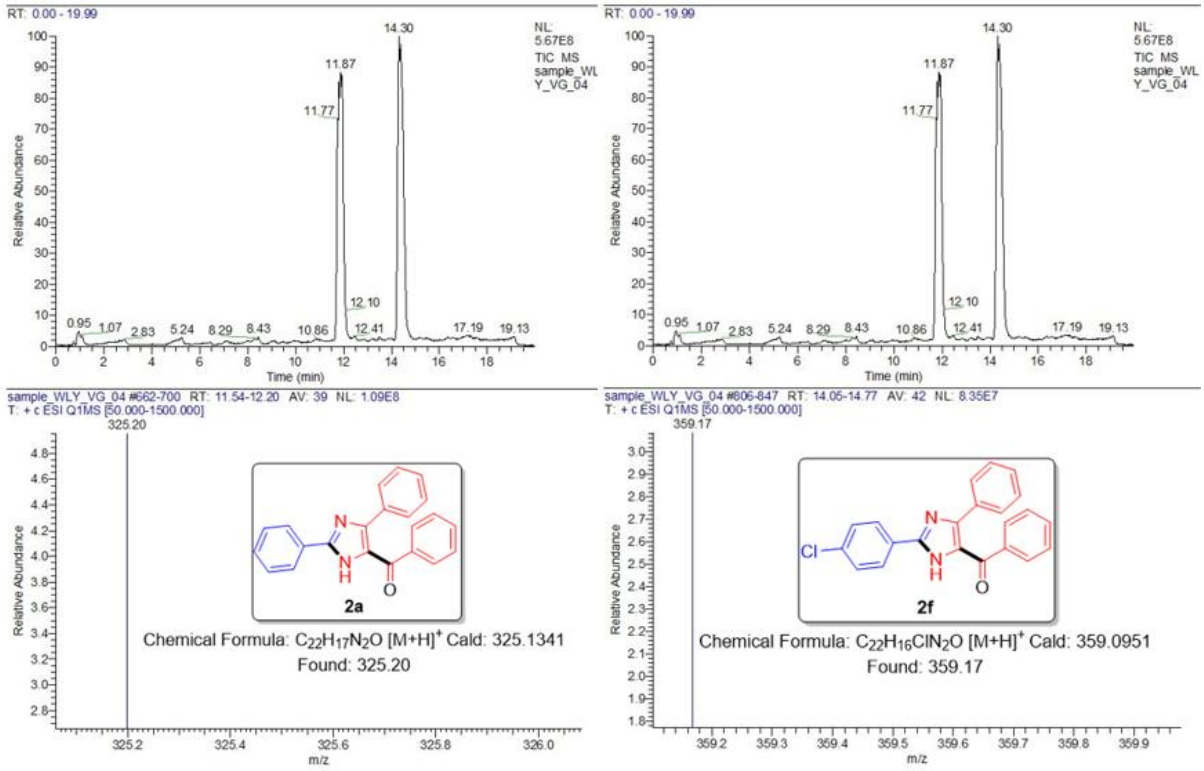
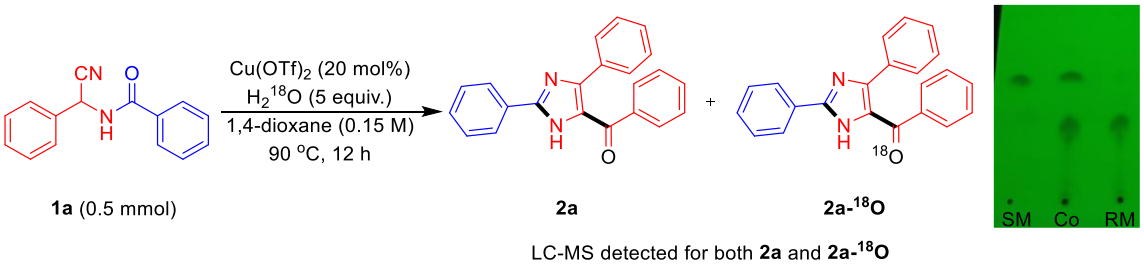


Fig. S9. LC-MS data of cross-coupling reaction with 1a+1f under standard conditions.

(9) Isotopic labelling ($H_2{}^{18}O$) studies for confirming the role of H_2O

To elucidate the role of water in product formation, an isotopic labelling experiment was performed using $H_2{}^{18}O$ in undried 1,4-dioxane to assess the influence of residual moisture. The reaction afforded a mixture of isotopically labelled and unlabelled products, as indicated by the presence of corresponding mass peaks in LC–MS analysis. This partial incorporation of ^{18}O suggests that water participates in the reaction pathway, while the formation of unlabelled product indicates the contribution of water generated during the course of the reaction as well as the moisture from solvent system.



LC-MS detected for both **2a** and **2a-^{18}O**

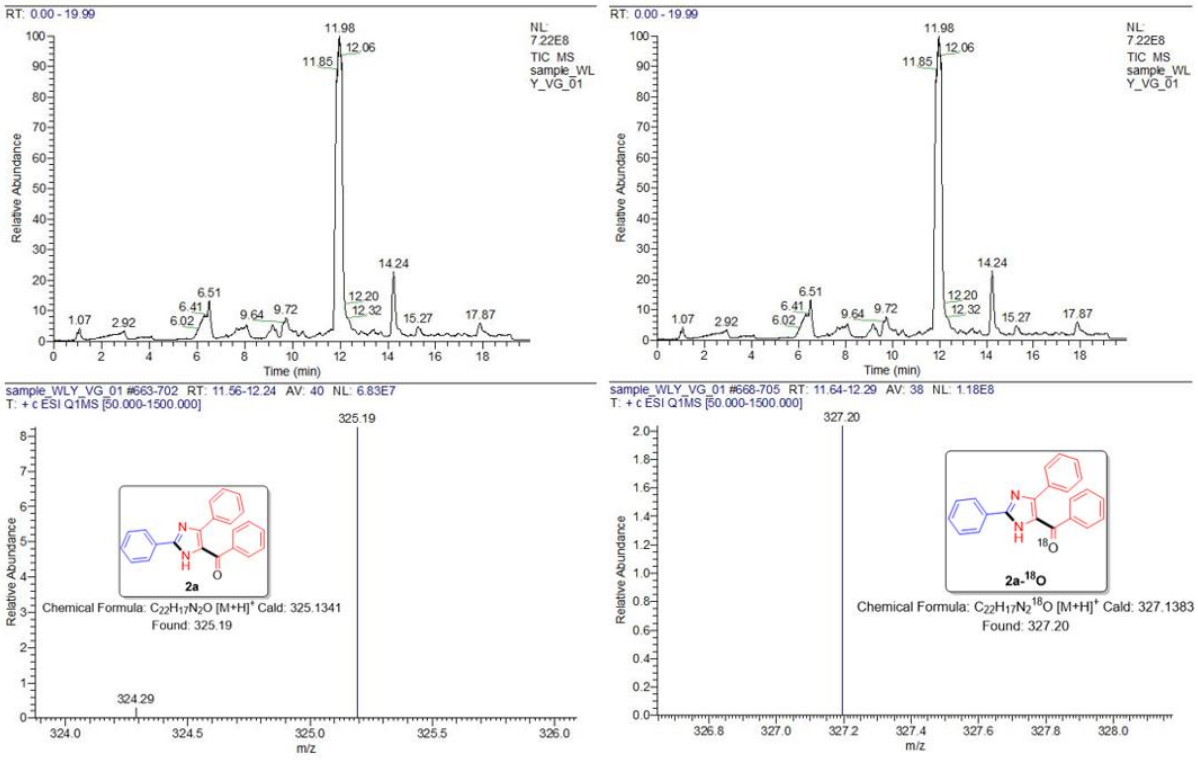
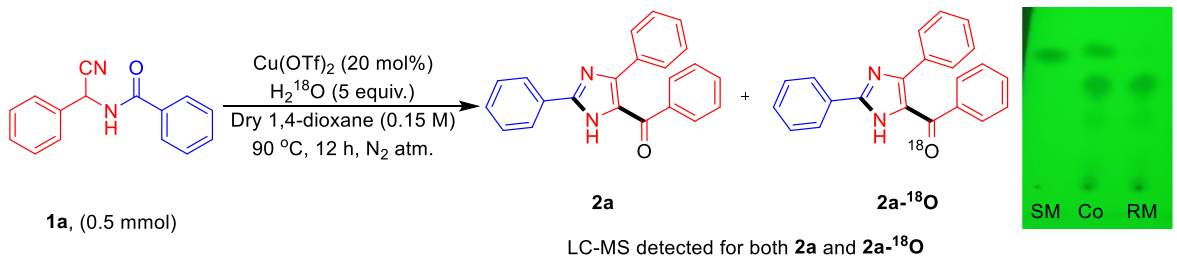


Fig. S10. LC-MS data for $H_2{}^{18}O$ reaction in undried 1,4-dioxane.

To further examine the role of water, the isotopic labelling experiment was repeated using $H_2{}^{18}O$ in rigorously dried 1,4-dioxane. Under these conditions, LC–MS analysis still revealed a similar distribution of isotopically labelled and unlabelled mass peaks. This observation indicates that, despite minimizing external moisture, incomplete ^{18}O incorporation persists, suggesting the involvement of water generated during the course of the reaction progress. These results further support the participation of water in the reaction.



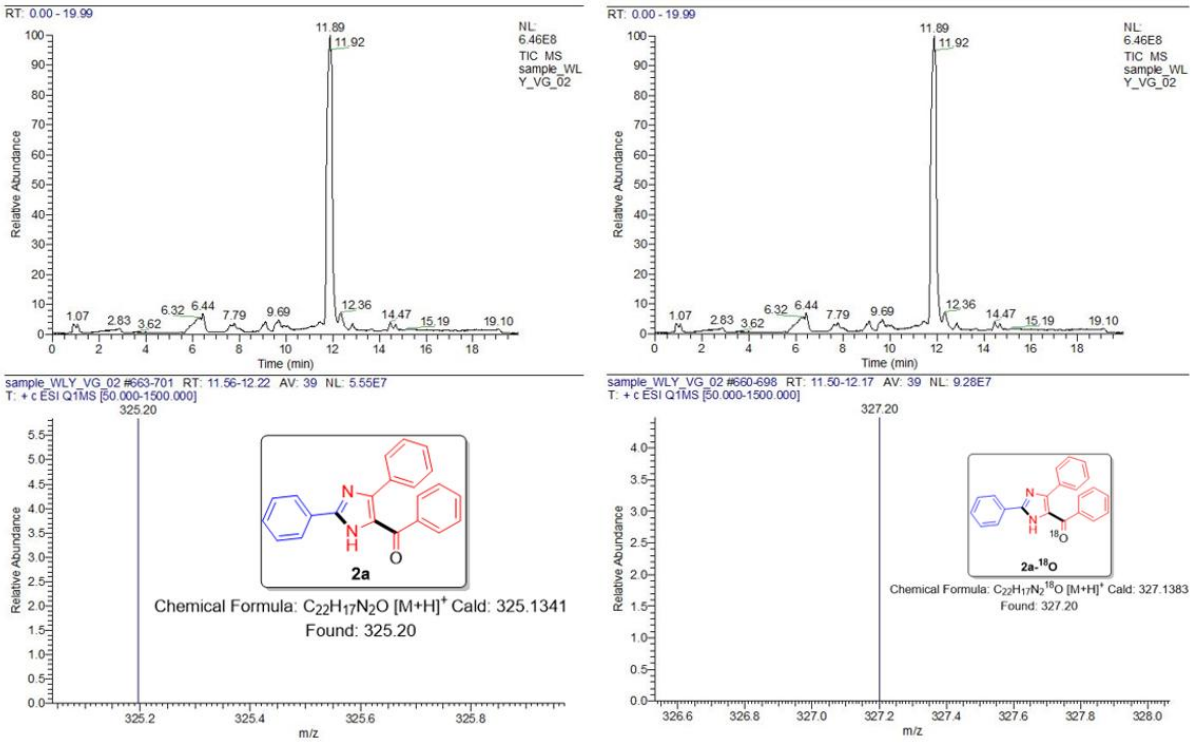
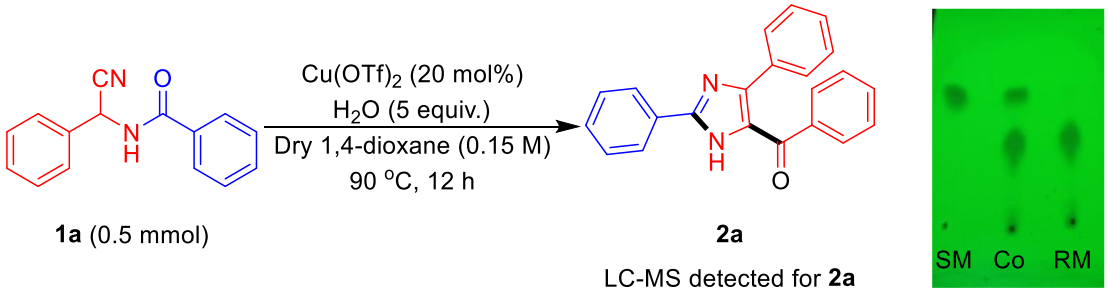


Fig. S11. LC-MS data for $H_2{}^{18}O$ reaction in dry 1,4-dioxane.

In a separate control experiment, the reaction was carried out in rigorously dried 1,4-dioxane in the presence of normal H_2O for comparison. Under these conditions, LC–MS analysis of the reaction mixture revealed the exclusive formation of the unlabelled product, with no evidence of isotopic mass incorporation. This result confirms that the mass shifts observed in the $H_2{}^{18}O$ experiment arise specifically from ^{18}O incorporation.



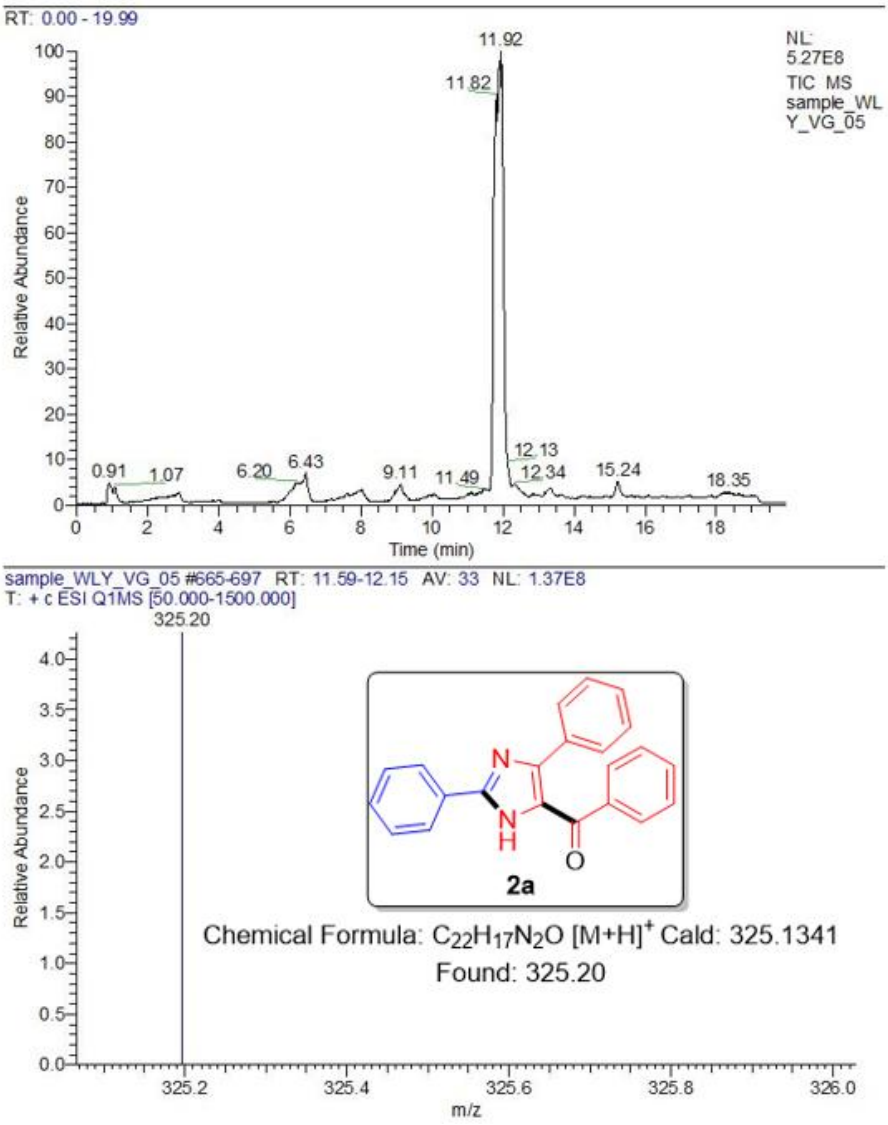


Fig. S12. LC-MS data for H_2O reaction in dry 1,4-dioxane.

(10) DFT Computational studies

All quantum chemical calculations were carried out using Gaussian 16 software[6] installed in the SRMIST-KTR Galaxy HPC server containing an Intel Xeon E5-2680v4 2.4 GHz processor of 28 cores of 16 GB RAM. The input files for it were generated using Gaussview 6 software. The molecular electrostatic potential (MEP surface) and frontier molecular orbital analysis (HOMO-LUMO) were done using the Cubegen utility of Gaussian 16 and visualized with GaussView. Since the copper(II) trifluoromethanesulfonate [$Cu(CF_3SO_3)_2$ or $Cu(OTf)_2$] has a spin of doublet, the UB3LYP functional is used in conjunction with the def2-TZVP basis set.[7,8] Solvent effects were incorporated through the CPCM implicit solvation model, using 1,4-dioxane to reproduce the experimental reaction medium. No symmetry constraints were imposed during the geometry optimizations. The reported Gibbs free energies were obtained

from the sum of electronic and thermal free energies derived from the frequency calculations. To investigate the feasibility of the proposed ring-closure process leading from intermediate **A** to intermediate **B**, a ModRedundant relaxed scan was employed along the key bond-forming coordinate to generate an approximate transition-state guess, followed by full transition-state optimization using the Opt=(TS,CalcFC,NoEigenTest) procedure.

To support this density functional theory (DFT) calculations were performed at UB3LYP/def2-TZVP level, utilizing a 1,4-dioxane implicit solvation model. The preferential binding mechanism of $Cu(OTf)_2$ to the substrate nitrogen and oxygen sites were examined. The computed binding free energies indicate that the nitrogen coordination is more favourable ($\Delta G = -8.04$ kcal/mol) than oxygen coordination ($\Delta G = -3.35$ kcal/mol).

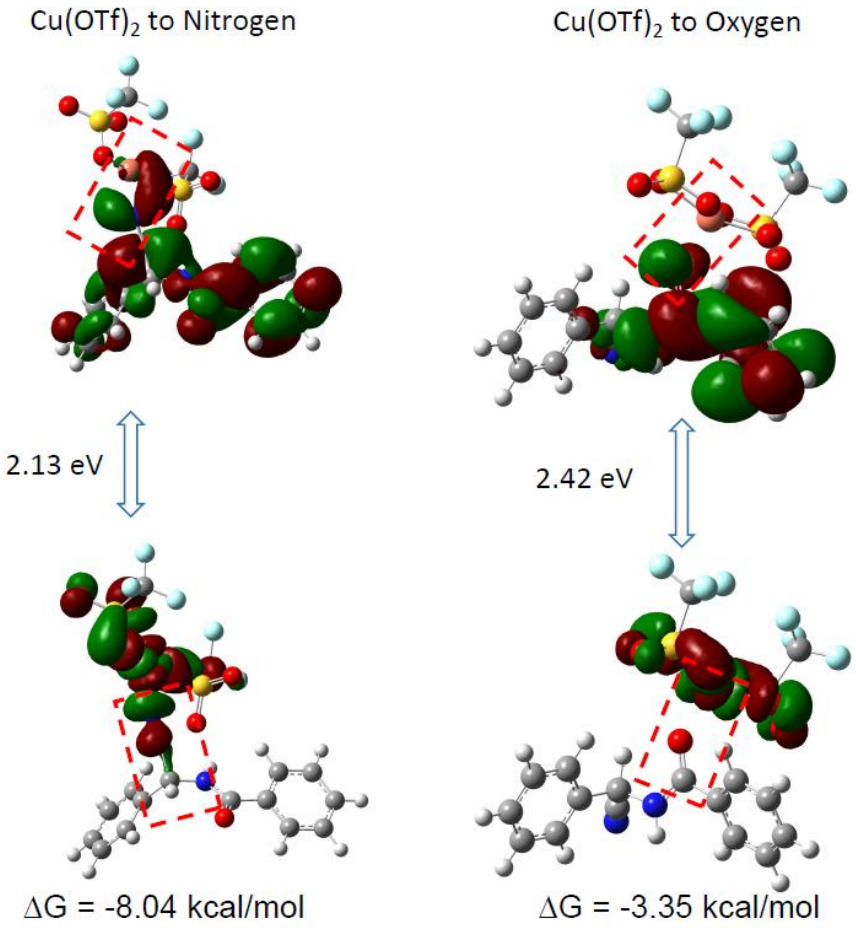


Fig. S13. Frontier molecular orbitals (HOMO and LUMO) of the substrate $Cu(OTf)_2$ complexes for coordination at nitrile nitrogen and oxygen sites.

Molecular electrostatic potential (MEP) analysis shows a higher negative electrostatic potential over the nitrogen hetero-atom (Fig. S14.). Furthermore, the frontier molecular orbital analysis

shows the overlap of HOMO-LUMO orbital between nitrogen and $Cu(OTf)_2$ with smaller bandgap of 2.13 eV as shown in Fig. S13.

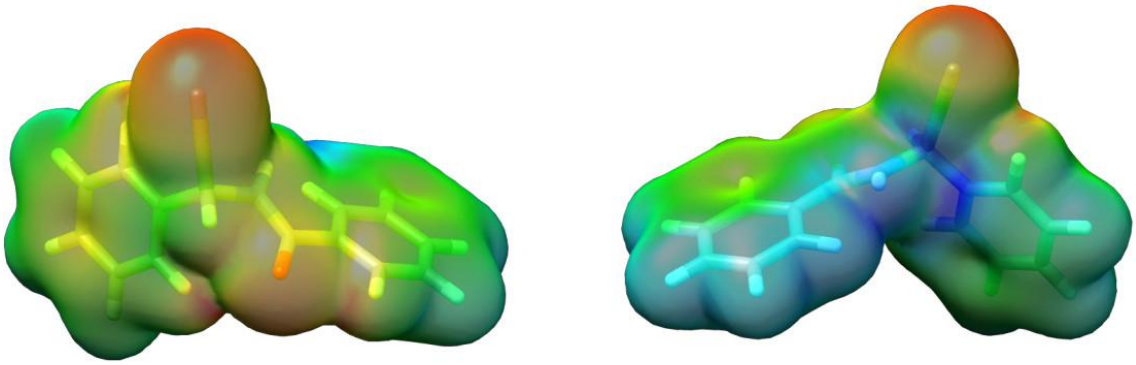


Fig. S14. Molecular electrostatic potential (MEP) surface mapped onto the electron density of the substrate. The colour scale ranges from electron-rich regions (red, negative potential) to electron-deficient regions (blue, positive potential).

The lowest bandgap and high binding free energy suggest that nitrogen is the most likely binding pathway in the reaction mechanism. To assess the ring closure mechanism or stability of cyclized intermediate **B**, a transition state free energy calculation is performed. The process occurs through a transition state **A** with an activation free energy of $\Delta G^{\#}$ = 23.4 kcal/mol, leading to intermediate **B**, which is thermodynamically stabilized by −4.46 kcal/mol compared to the initial reactant complex **1**. Upon cyclization, the Cu–O bond distances linked to one of the triflate ligands show slight elongation (2.05 Å and 1.92 Å), whereas the Cu–N bond distance decreases to 1.96 Å, suggesting increased coordination between the metal center and the substrate, indicative of a Lewis acid type catalytic mechanism for $Cu(OTf)_2$

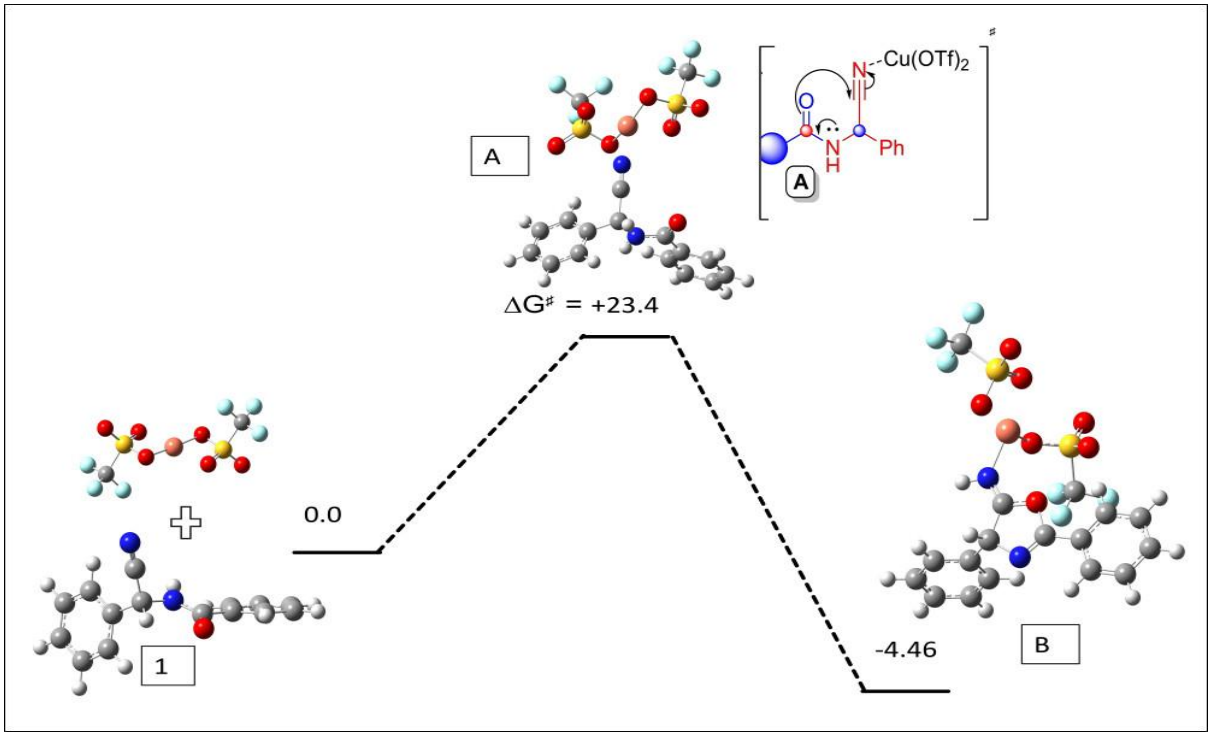
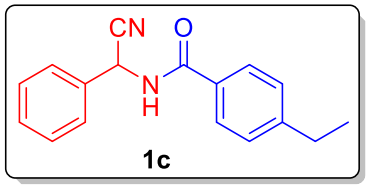


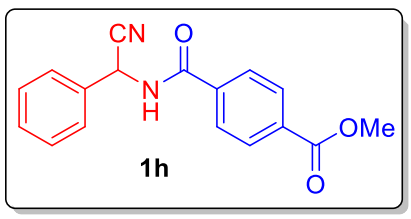
Fig. S15. Computed free-energy profile for the $Cu(OTf)_2$-mediated cyclization pathway leading to intermediate **B**. For more detail check the mechanism (Scheme 3) in the manuscript.

(11) Spectral characterization of starting materials

***N*-(cyano(phenyl)methyl)-3-ethylbenzamide (1c).** A 2 mmol scale reaction was carried out according to the general procedure (Method A), and the title compound was isolated by column chromatography on silica gel (EA/Hex=8%) to afford **1c** as white solid (420 mg, 89% yield); Mp. 121-123 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.72 (d, J = 8.2 Hz, 2H), 7.55 (dd, J = 7.4, 1.5 Hz, 2H), 7.46-7.42 (m, 3H), 7.27 (d, J = 8.7 Hz, 2H), 6.75 (d, J = 8.2 Hz, 1H), 6.35 (d, J = 8.4 Hz, 1H), 2.70 (q, J = 7.6 Hz, 2H), 1.24 (t, J = 7.6 Hz, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 166.6, 149.3, 133.4, 129.8, 129.4, 129.3, 128.2, 127.5, 127.1, 117.6, 44.4, 28.8, 15.2. HRMS (ESI) calculated for $C_{17}H_{16}N_2ONa$ $[M+Na]^+$: 287.1154 found 287.1154.

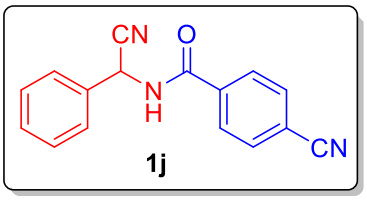


Methyl 4-((cyano(phenyl)methyl)carbamoyl)benzoate (1h). A 2 mmol scale reaction was carried out according to the general procedure (Method A), and the title compound was isolated by column chromatography on silica gel (EA/Hex=18%) to afford **1h** as white solid (459 mg, 88% yield); Mp. 173-1175 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.10-8.07 (m, 2H), 7.86-7.84 (m, 2H), 7.56-7.54 (m, 2H), 7.46-

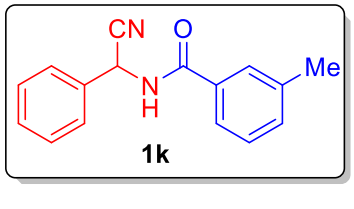


7.44 (m, 3H), 6.99 (d, J = 8.2 Hz, 1H), 6.33 (d, J = 8.2 Hz, 1H), 3.94 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 166.1, 165.8, 136.3, 133.5, 132.9, 129.9, 129.7, 129.5, 127.4, 127.1, 117.3, 52.5, 44.7. HRMS (ESI) calculated for $C_{17}H_{14}N_2O_3Na$ $[M+Na]^+$: 317.0896 found 317.0896.

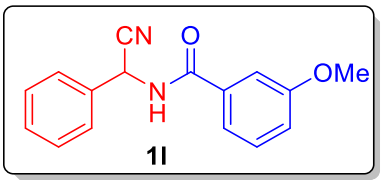
4-Cyano-*N*-(cyano(phenyl)methyl)benzamide (1j). A 2 mmol scale reaction was carried out according to the general procedure (Method A), and the title compound was isolated by column chromatography on silica gel (EA/Hex=18%) to afford **1j** as yellow solid (335 mg, 72% yield); Mp. 173-175 °C; ^1H NMR (500 MHz, $CDCl_3$): δ 7.91 (d, J = 8.4 Hz, 2H), 7.75 (d, J = 8.4 Hz, 2H), 7.55-7.53 (m, 2H), 7.47-7.45 (m, 3H), 6.98 (d, J = 8.0 Hz, 1H), 6.30 (d, J = 8.1 Hz, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 164.8, 136.2, 132.7, 132.6, 129.9, 129.6, 128.1, 127.2, 117.7, 117.1, 116.0, 44.8. HRMS (ESI) calculated for $C_{16}H_{11}N_3ONa$ $[M+Na]^+$: 284.0794 found 284.0795.



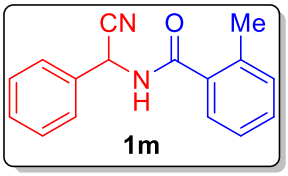
***N*-(cyano(phenyl)methyl)-3-methylbenzamide (1k).** A 2 mmol scale reaction was carried out according to the general procedure (Method A), and the title compound was isolated by column chromatography on silica gel (EA/Hex=8%) to afford **1k** as yellow solid (364 mg, 81% yield); Mp. 140-1142 °C; ^1H NMR (500 MHz, $CDCl_3$): δ 7.62 (s, 1H), 7.58-7.54 (m, 3H), 7.47-7.42 (m, 3H), 7.36-7.31 (m, 2H), 6.35 (d, J = 8.4 Hz, 1H), 2.39 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 166.6, 138.8, 133.3, 133.2, 132.4, 129.6, 129.5, 128.7, 128.0, 127.1, 124.2, 117.4, 44.5, 21.3. HRMS (ESI) calculated for $C_{16}H_{14}N_2ONa$ $[M+Na]^+$: 273.0098 found 273.0997.



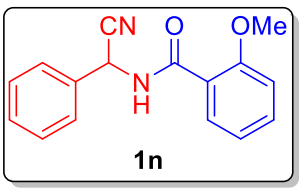
***N*-(cyano(phenyl)methyl)-3-methoxybenzamide (1l).** A 2 mmol scale reaction was carried out according to the general procedure (Method B), and the title compound was isolated by column chromatography on silica gel (EA/Hex=12%) to afford **1l** as pale yellow solid (403 mg, 85% yield); Mp. 188-190 °C; ^1H NMR (500 MHz, $CDCl_3$): δ 7.55-7.54 (m, 2H), 7.45-7.44 (m, 3H), 7.37-7.28 (m, 3H), 7.09-7.07 (m, 1H), 6.33 (d, J = 8.3 Hz, 1H), 3.84 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 166.5, 159.9, 133.8, 133.2, 129.8, 129.5, 129.4, 127.1, 119.2, 118.7, 117.5, 112.6, 55.5, 44.6. HRMS (ESI) calculated for $C_{16}H_{14}N_2O_2Na$ $[M+Na]^+$: 289.0947 found 289.0947.



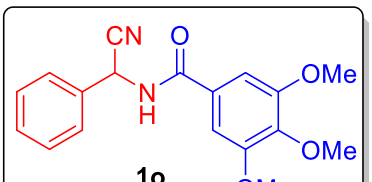
***N*-(cyano(phenyl)methyl)-2-methylbenzamide (1m).** A 2 mmol scale reaction was carried out according to the general procedure (Method B), and the title compound was isolated by column chromatography on silica gel (EA/Hex=10%) to afford **1m** as white solid (347 mg, 69% yield); Mp. 138-139 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.50-7.47 (m, 2H), 7.44-7.39 (m, 3H), 7.33-7.29 (m, 2H), 7.20-7.13 (m, 2H), 6.77 (d, *J* = 8.4 Hz, 1H), 6.20 (d, *J* = 8.4 Hz, 1H), 2.38 (, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 168.9, 136.7, 133.9, 133.2, 131.2, 130.7, 129.5, 129.3, 126.9, 126.8, 125.8, 117.3, 44.2, 19.8. HRMS (ESI) calculated for $C_{16}H_{14}N_2ONa$ $[M+Na]^+$: 273.1003 found 273.1015.



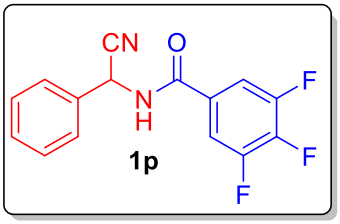
***N*-(cyano(phenyl)methyl)-2-methoxybenzamide (1n).** A 2 mmol scale reaction was carried out according to the general procedure (Method B), and the title compound was isolated by column chromatography on silica gel (EA/Hex=10%) to afford **1n** as white solid (350 mg, 66% yield); Mp. 105-106 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.52 (d, *J* = 7.5 Hz, 1H), 8.24 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.56-7.55 (m, 2H), 7.50-7.48 (m, 1H), 7.47-7.40 (m, 3H), 7.13-7.09 (m, 1H), 6.98 (d, *J* = 8.5 Hz, 1H), 6.40 (d, *J* = 8.5 Hz, 1H), 3.91 (s, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 164.7, 157.6, 133.9, 133.7, 132.7, 129.3, 126.8, 121.6, 119.6, 117.8, 111.5, 56.1, 44.2. HRMS (ESI) calculated for $C_{16}H_{14}KN_2O_2$ $[M+K]^+$: 305.0692 found 305.0712.



***N*-(cyano(phenyl)methyl)-3,4,5-trimethoxybenzamide (1o).** A 2 mmol scale reaction was carried out according to the general procedure (Method A), and the title compound was isolated by column chromatography on silica gel (EA/Hex=20%) to afford **1o** as white solid (456 mg, 78% yield); Mp. 192-194 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.56-7.55 (m, 2H), 7.47-7.44 (m, 3H), 7.02 (s, 2H), 6.76 (d, *J* = 8.3 Hz, 1H), 6.36 (d, *J* = 8.3 Hz, 1H), 3.89 (s, 6H), 3.88 (s, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 166.2, 153.3, 141.8, 133.3, 129.7, 129.5, 127.6, 127.1, 117.6, 104.8, 60.9, 56.4, 44.7. HRMS (ESI) calculated for $C_{18}H_{18}N_2O_4Na$ $[M+Na]^+$: 349.1158 found 349.1157.

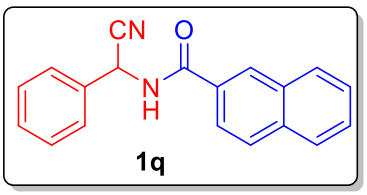


***N*-(cyano(phenyl)methyl)-3,4,5-trifluorobenzamide (1p).** A 2 mmol scale reaction was carried out according to the general procedure (Method A), and the title compound was isolated by column chromatography on silica gel (EA/Hex=7%) to afford **1p** as white solid (387 mg, 74% yield); Mp. 176-177 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.54-7.53 (m, 2H), 7.49-7.46 (m, 5H), 6.75 (s, 1H), 6.26 (d, *J* = 8.1 Hz, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100



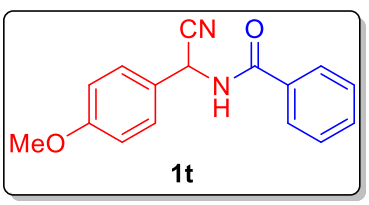
MHz): δ 163.5, 152.1 (dd, J_{CF} = 9.9, 3.3 Hz), 149.62 (dd, J_{CF} = 10, 3.5 Hz), 143.43 (t, J_{CF} = 15.3 Hz), 140.87 (t, J_{CF} = 15.1 Hz), 133.83, 129.28, 129.14, 128.83, 127.25, 117.80, 112.99 (dd, J_{CF} = 16.4, 6.2 Hz), 44.51. HRMS (ESI) calculated for $C_{15}H_9F_3N_2ONa$ $[M+Na]^+$: 313.0559 found 313.0558.

***N*-(cyano(phenyl)methyl)-2-naphthamide (1q).** A 2 mmol scale reaction was carried out according to the general procedure (Method A), and the title compound was isolated by column chromatography on silica gel (EA/Hex=10%) to afford **1q** as white solid (267 mg, 52% yield); Mp. 171-174 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.32 (s, 1H), 7.92 (d, J = 8 Hz, 2H), 7.88 (d, J = 8 Hz, 1H), 7.84 (dd, J = 8.5, 1.5 Hz, 1H), 7.61-7.54 (m, 4H), 7.50-7.45 (m, 3H), 6.81 (d, J = 8 Hz, 1H), 6.42 (d, J = 8.5 Hz, 1H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 166.5, 135.1, 133.2, 132.4, 129.7, 129.6, 129.5, 129.0, 128.8, 128.2, 128.1, 127.8,127.2, 127.1, 123.3, 117.4, 44.7. HRMS (ESI) calculated for $C_{19}H_{14}N_2ONa$ $[M+Na]^+$: 309.0998 found 309.0997.



1q

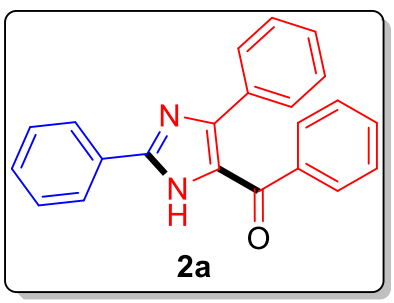
***N*-(cyano(4-methoxyphenyl)methyl)benzamide (1t).** A 2 mmol scale reaction was carried out according to the general procedure (Method C), and the title compound was isolated by column chromatography on silica gel (EA/Hex=30%) to afford **1t** as off-white solid (400 mg, 75% yield); Mp. 151-152 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.78-7.76 (m, 2H), 7.52 (t, J = 7.5 Hz, 1H), 7.45-7.40 (m, 4H), 6.99-6.96 (m, 1H), 6.92 (d, J = 9.0 Hz, 2H), 6.22 (d, J = 8 Hz, 1H), 3.80 (s, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$, 120 MHz): δ 166.5, 160.4, 132.4, 128.7, 128.5, 127.3, 125.2, 117.7, 114.7, 55.4, 44.1. HRMS (ESI) calculated for $C_{16}H_{14}N_2O_2Na$ $[M+Na]^+$: 289.0953 found 289.0944.



1t

(12) Experimental procedures and spectral characterization of 2a-2u & 3a

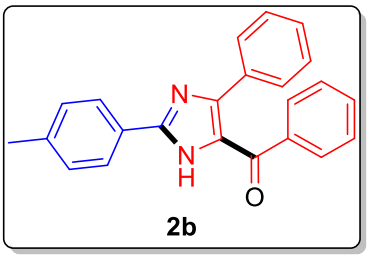
(2,4-Diphenyl-1*H*-imidazol-5-yl)(phenyl)methanone (2a).[9] A 15 mL vial was charged with **1a** (118 mg, 0.5 mmol) and $Cu(OTf)_2$ (20 mol%) in 1,4-dioxane (3.3 mL, 0.15 M). The reaction mixture was allowed to stir at 90 °C in oil bath in sealed vial until the completion of reaction by TLC chromatography (7 h). The reaction mixture was cooled to room temperature, diluted with 10 mL of water. The water layer was extracted with (3 x 15 mL) of ethyl acetate and the combined ethyl acetate layer was given brine wash (2 x 10 mL). The final



2a

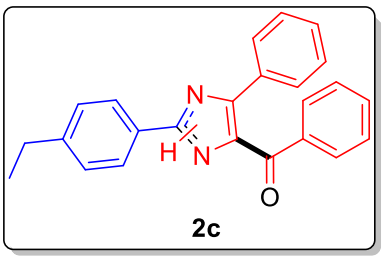
ethyl acetate layer was dried over Na_2SO_4 and concentrated under reduced pressure to get the crude compound. The obtained crude was purified using column chromatography on silica gel (EA/Hex=7%) to afford **2a** as white solid (59 mg, 73% yield); Mp. 185-186 °C (lit. 188-190 °C)[9]; ^{1}H NMR (500 MHz, $CDCl_3$): δ 11.12 (s, 1H), 8.12 (s, 2H), 7.58 (s, 2H), 7.48- 7.46 (m, 3H), 7.33 (s, 3H), 7.15-7.12 (m, 5H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 187.8, 149.3, 136.9, 132.9, 132.3, 130.2, 130.1, 129.8, 129.7, 128.9, 128.6, 128.4, 128.2, 127.9, 127.8, 126.7.

Phenyl(4-phenyl-2-(*p*-tolyl)-1*H*-imidazol-5-yl)methanone (2b).[9] A 15 mL vial was charged with **1b** (125 mg, 0.5 mmol) and $Cu(OTf)_2$ (20 mol%) in 1,4-dioxane (3.3 mL, 0.15 M). The reaction mixture was allowed to stir at 90 °C in oil bath in sealed vial until the completion of reaction by TLC chromatography (12 h). The reaction mixture was cooled to room temperature, diluted with 10 mL of water. The water layer was extracted with (3 x 15 mL) of ethyl acetate and the combined ethyl acetate layer was given brine wash (2 x 10 mL). The final ethyl acetate layer was dried over Na_2SO_4 and concentrated under reduced pressure to get the crude compound. The obtained crude was purified using column chromatography on silica gel (EA/Hex=6%) to afford **2b** as white solid (57 mg, 67% yield); Mp. 149-151 °C (lit. 147-150 °C)[9]; ^{1}H NMR (500 MHz, $CDCl_3$): δ 11.33 (s, 1H), 8.05 (d, J = 6.9 Hz, 2H), 7.58 (d, J = 6.5 Hz, 2H), 7.35-7.31 (m, 3H), 7.27 (d, J = 1.5 Hz, 2H), 7.15 (s, 3H), 7.11 (d, J = 6.5 Hz, 2H), 2.43 (s, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 187.5, 149.4, 140.5, 137.2, 132.9, 132.2, 130.2, 129.8, 129.7, 129.6, 129.2.128.2, 127.9, 127.8, 126.6, 125.8, 21.5.



2b

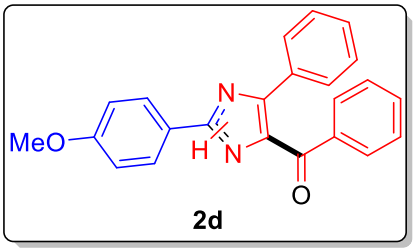
(2-(4-Ethylphenyl)-4-phenyl-1*H*-imidazol-5-yl)(phenyl)methanone (2c). A 15 mL vial was charged with **1c** (132 mg, 0.5 mmol) and $Cu(OTf)_2$ (20 mol%) in 1,4-dioxane (3.3 mL, 0.15 M). The reaction mixture was allowed to stir at 90 °C in oil bath in sealed vial until the completion of reaction by TLC chromatography (12 h). The reaction mixture was cooled to room temperature, diluted with 10 mL of water. The water layer was extracted with (3 x 15 mL) of ethyl acetate and the combined ethyl acetate layer was given brine wash (2 x 10 mL). The final ethyl acetate layer was dried over Na_2SO_4 and concentrated under reduced pressure to get the crude compound. The obtained crude was purified using column chromatography on silica gel (EA/Hex=8%) to afford **2c** as white solid (59 mg, 67% yield); Mp. 157-160 °C; *In $CDCl_3$, additional signals observed in the* ^{1}H *NMR spectrum are attributed to the presence of N1–N3 tautomeric forms.* ^{1}H NMR (500 MHz, $CDCl_3$): δ 11.52-11.39 (m, 1H), 8.07 (s, 2H), 7.58 (d, J = 7.5 Hz, 2H),



2c

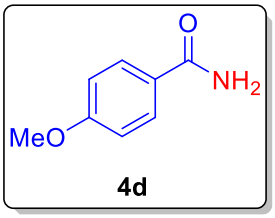
7.35-7.30 (m, 3H), 7.26 (s, 2H), 7.15-7.12 (m, 3H), 7.10-7.07 (m, 2H), 2.71 (q, J = 7.1 Hz, 2H), 1.28 (t, J = 7.5 Hz, 3H); $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 100 MHz): δ 187.2, 150.5, 149.8, 146.5, 137.1, 133.7, 131.9, 129.7, 129.4, 128.2, 127.8, 127.7, 127.6, 127.2, 126.5, 126.1, 28.6, 15.1. HRMS (ESI) calculated for $C_{24}H_{21}N_2O$ $[M+H]^+$: 353.1648 found 353.1646.

(2-(4-Methoxyphenyl)-4-phenyl-1*H*-imidazol-5-yl)(phenyl)methanone (2d).[9] A 15 mL vial



2d

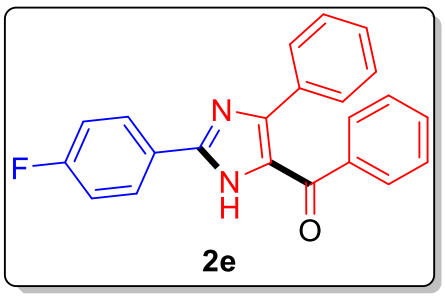
was charged with **1d** (133 mg, 0.5 mmol) and $Cu(OTf)_2$ (20 mol%) in 1,4-dioxane (3.3 mL, 0.15 M). The reaction mixture was allowed to stir at 90 °C in oil bath in sealed vial until the completion of reaction by TLC chromatography (20 h). The reaction mixture was cooled to room temperature, diluted with 10 mL of water. The water layer was extracted with (3 x 15 mL) of ethyl acetate and the combined ethyl acetate layer was given brine wash (2 x 10 mL). The final ethyl acetate layer was dried over Na_2SO_4 and concentrated under reduced pressure to get the crude compound. The obtained crude was purified using column chromatography on silica gel (EA/Hex=15%) to afford **2d** as pale yellow solid (57 mg, 64% yield); Mp. 163-165 °C (lit. 159-162 °C)[9]; *In $CDCl_3$, additional signals observed in the* ^{1}H *NMR spectrum are attributed to the presence of N1–N3 tautomeric forms*. ^{1}H NMR (500 MHz, $CDCl_3$): δ 11.72-11.66 (m, 1H), 8.14-8.13 (m, 2H), 7.57 (d, J = 7.5 Hz, 2H), 7.35-7.29 (m, 3H), 7.11 (dt, J = 15.2, 7.6 Hz, 5H), 6.92-6.90 (m, 2H), 3.85 (s, 3H); $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 125 MHz): δ 187.3, 161.1, 150.8, 149.9, 137.3, 133.8, 132.0, 129.8, 129.5, 128.2, 127.9, 127.8, 127.7, 127.3, 121.5, 114.2, 55.3. HRMS (ESI) calculated for $C_{23}H_{19}N_2O_2$ $[M+H]^+$: 355.1441 found 355.1438.



4d

By following the mentioned protocol, we have obtained 4-methoxybenzamide (**4d).**[10] as our by-product (The yield was not determined); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.78 (d, J = 8.5 Hz, 2H), 6.93 (d, J = 9 Hz, 2H), 3.86 (s, 3H).

(2-(4-Fluorophenyl)-4-phenyl-1*H*-imidazol-5-yl)(phenyl)methanone (2e).[9] A 15 mL vial

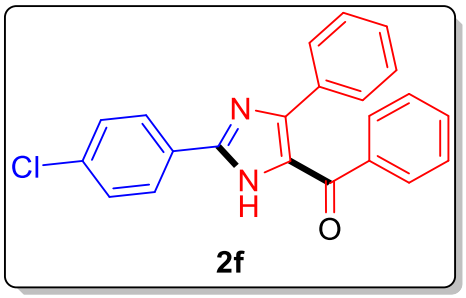


2e

was charged with **1e** (127 mg, 0.5 mmol) and $Cu(OTf)_2$ (20 mol%) in 1,4-dioxane (3.3 mL, 0.15 M). The reaction mixture was allowed to stir at 90 °C in oil bath in sealed vial until the completion of reaction by TLC chromatography (7 h). The reaction mixture was cooled to room temperature, diluted with 10 mL of water. The water layer was extracted with (3 x 15 mL) of ethyl acetate and the combined ethyl acetate

layer was given brine wash (2 x 10 mL). The final ethyl acetate layer was dried over Na_2SO_4 and concentrated under reduced pressure to get the crude compound. The obtained crude was purified using column chromatography on silica gel (EA/Hex=8%) to afford **2e** as pale yellow solid (63 mg, 74% yield); Mp. 188-189 °C (lit. 191-193 °C)[9]; ^{1}H NMR (500 MHz, $CDCl_3$): δ 12.21 (s, 1H), 8.23 (s, 2H), 7.57 (d, J = 7 Hz, 2H), 7.36 (t, J = 7 Hz, 1H), 7.29 (d, J = 7 Hz, 2H), 7.16-7.15 (m, 3H), 7.10 – 7.04 (m, 4H); ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz): δ 187.8, 163.8 (d, J_{CF} = 249.5 Hz), 151.0, 149.2, 137.2, 133.6, 132.3, 129.8, 129.5, 128.8 (d, J_{CF} = 8.1 Hz), 128.1, 127.9, 127.8, 127.7, 125.2, 115.9 (d, J_{CF} = 21.7 Hz).

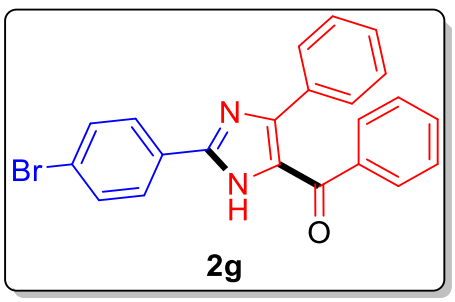
(2-(4-Chlorophenyl)-4-phenyl-1*H*-imidazol-5-yl)(phenyl)methanone (2f).[9] A 15 mL vial



2f

was charged with **1f** (135 mg, 0.5 mmol) and $Cu(OTf)_2$ (20 mol%) in 1,4-dioxane (3.3 mL, 0.15 M). The reaction mixture was allowed to stir at 90 °C in oil bath in sealed vial until the completion of reaction by TLC chromatography (7 h). The reaction mixture was cooled to room temperature, diluted with 10 mL of water. The water layer was extracted with (3 x 15 mL) of ethyl acetate and the combined ethyl acetate layer was given brine wash (2 x 10 mL). The final ethyl acetate layer was dried over Na_2SO_4 and concentrated under reduced pressure to get the crude compound. The obtained crude was purified using column chromatography on silica gel (EA/Hex=6%) to afford **2f** as pale yellow solid (65 mg, 72% yield); Mp. 183-185 °C (lit. 186-189 °C)[9]; ^{1}H NMR (500 MHz, $CDCl_3$): δ 12.11 (s, 1H), 8.17 (d, J = 8.5 Hz, 2H), 7.57 (d, J = 7 Hz, 2H), 7.36 (d, J = 8.5 Hz, 3H), 7.29 (d, J = 7 Hz, 2H), 7.18-7.14 (m, 3H), 7.09 (t, J = 7.5 Hz, 2H); ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz): δ 187.8, 151.0, 148.9, 137.1, 136.1, 133.5, 132.4, 129.8, 129.5, 129.1, 128.1, 128.0, 127.9, 127.87, 127.80, 127.4.

(2-(4-Bromophenyl)-4-phenyl-1*H*-imidazol-5-yl)(phenyl)methanone (2g).[9] A 15 mL vial

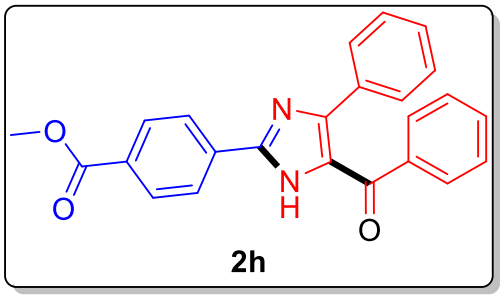


2g

was charged with **1g** (157.5 mg, 0.5 mmol) and $Cu(OTf)_2$ (20 mol%) in 1,4-dioxane (3.3 mL, 0.15 M). The reaction mixture was allowed to stir at 90 °C in oil bath in sealed vial until the completion of reaction by TLC chromatography (11 h). The reaction mixture was cooled to room temperature, diluted with 10 mL of water. The water layer was extracted with (3 x 15 mL) of ethyl acetate and the combined ethyl acetate layer was given brine wash (2 x 10 mL). The final ethyl acetate layer was dried over Na_2SO_4 and concentrated under reduced pressure to get the crude compound. The obtained crude was

purified using column chromatography on silica gel (EA/Hex=7%) to afford **2g** as white solid (75 mg, 74% yield); Mp. 182-184 °C (lit. 178-180 °C)[9]; ^{1}H NMR (500 MHz, $CDCl_3$): δ 11.60 (s, 1H), 8.05 (d, *J* = 8.5 Hz, 2H), 7.57-7.55 (m, 4H), 7.36 (t, *J* = 7.5 Hz, 1H), 7.30-7.28 (m, 2H), 7.17-7.14 (m, 3H), 7.10 (t, *J* = 7.3 Hz, 2H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 187.7, 159.4, 150.8, 148.8, 137.0, 133.5, 132.4, 132.2, 129.8, 129.5, 128.1, 127.9, 127.8, 127.7, 124.5.

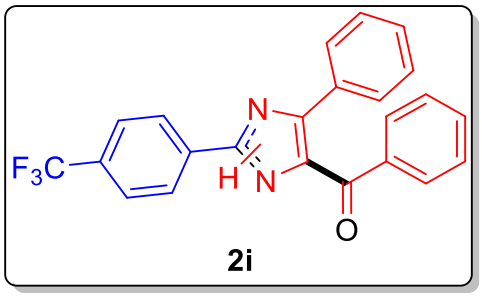
Methyl 4-(5-benzoyl-4-phenyl-1*H*-imidazol-2-yl)benzoate (2h). A 15 mL vial was charged



2h

with **1h** (147 mg, 0.5 mmol) and $Cu(OTf)_2$ (20 mol%) in 1,4-dioxane (3.3 mL, 0.15 M). The reaction mixture was allowed to stir at 90 °C in oil bath in sealed vial until the completion of reaction by TLC chromatography (15 h). The reaction mixture was cooled to room temperature, diluted with 10 mL of water. The water layer was extracted with (3 x 15 mL) of ethyl acetate and the combined ethyl acetate layer was given brine wash (2 x 10 mL). The final ethyl acetate layer was dried over Na_2SO_4 and concentrated under reduced pressure to get the crude compound. The obtained crude was purified using column chromatography on silica gel (EA/Hex=18%) to afford **2h** as white solid (57 mg, 60% yield); Mp. 213-214 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 11.62 (s, 1H), 8.25 (d, *J* = 8.0 Hz, 2H), 8.12 (d, *J* = 8.4 Hz, 2H), 7.59 (d, *J* = 7.4 Hz, 2H), 7.38-7.31 (m, 3H), 7.18-7.16 (m, 3H), 7.13-7.10 (m, 2H), 3.96 (s, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 187.9, 166.5, 147.7, 137.0, 132.6, 131.2, 130.2, 129.9, 129.8, 129.7, 128.6, 128.4, 128.0, 127.9, 126.9, 126.5, 52.4. HRMS (ESI) calculated for $C_{24}H_{17}N_2O_3$ [M-H]$^-$: 381.1239 found 381.1281.

Phenyl(4-phenyl-2-(4-(trifluoromethyl)phenyl)-1*H*-imidazol-5-yl)methanone (2i). A 15

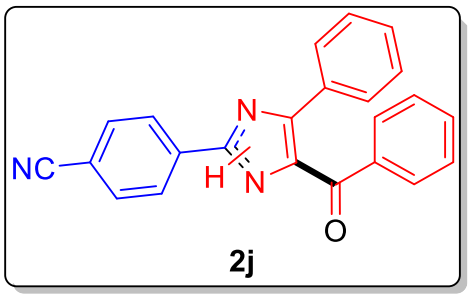


2i

mL vial was charged with **1i** (152 mg, 0.5 mmol) and $Cu(OTf)_2$ (20 mol%) in 1,4-dioxane (3.3 mL, 0.15 M). The reaction mixture was allowed to stir at 90 °C in oil bath in sealed vial until the completion of reaction by TLC chromatography (14 h). The reaction mixture was cooled to room temperature, diluted with 10 mL of water. The water layer was extracted with (3 x 15 mL) of ethyl acetate and the combined ethyl acetate layer was given brine wash (2 x 10 mL). The final ethyl acetate layer was dried over Na_2SO_4 and concentrated under reduced pressure to get the crude compound. The obtained crude was purified using column chromatography on silica gel (EA/Hex=7%) to afford **2i** as white solid (77 mg, 78% yield); Mp. 220-222 °C; *In $CDCl_3$, additional signals observed in the* ^{1}H *NMR spectrum are attributed to the presence of N1–N3 tautomeric forms.*^{1}H NMR (500

MHz, $CDCl_3$): δ 12.09 (s, 1H), 8.33 (d, J = 8.0 Hz, 2H), 7.65 (d, J = 8.0 Hz, 2H), 7.58 (d, J = 8 Hz, 2H), 7.38 (t, J = 7.5 Hz, 1H), 7.31 (d, J = 7.0 Hz, 2H), 7.16 (t, J = 7.5 Hz, 3H), 7.12-7.09 (m, 2H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ 188.1, 147.9, 137.0, 132.6, 132.1, 132.0, 131.8, 131.4, 131.1, 129.7 (d, J_{CF} = 3.9 Hz), 128.4, 128.0, 127.9, 126.9, 125.8 (q, J_{CF} = 3.6 Hz), 125.2, 122.5, 119.8; ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.5. HRMS (ESI) calculated for $C_{23}H_{16}F_3N_2O$ $[M+H]^+$: 393.1209 found 393.1208.

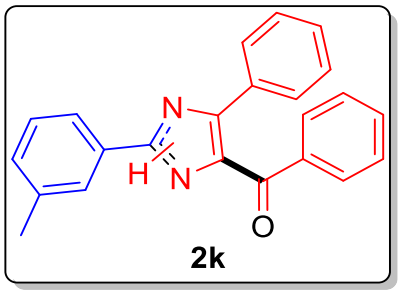
4-(5-Benzoyl-4-phenyl-1*H*-imidazol-2-yl)benzonitrile (2j). A 15 mL vial was charged with



2j

1j (133 mg, 0.5 mmol) and $Cu(OTf)_2$ (20 mol%) in 1,4-dioxane (3.3 mL, 0.15 M). The reaction mixture was allowed to stir at 90 °C in oil bath in sealed vial until the completion of reaction by TLC chromatography (20 h). The reaction mixture was cooled to room temperature, diluted with 10 mL of water. The water layer was extracted with (3 x 15 mL) of ethyl acetate and the combined ethyl acetate layer was given brine wash (2 x 10 mL). The final ethyl acetate layer was dried over Na_2SO_4 and concentrated under reduced pressure to get the crude compound. The obtained crude was purified using column chromatography on silica gel (EA/Hex=18%) to afford **2j** as pale orange solid (61 mg, 70% yield); Mp. 195-197 °C; *In DMSO-d_6, additional signals observed in the* ^1H *and* ^{13}C *NMR spectra are attributed to the presence of N1–N3 tautomeric forms*. ^1H NMR (500 MHz, DMSO-d_6): δ 13.76-13.53 (m, 1H), 8.39-8.25 (m, 2H), 8.12 (d, J = 4.5 Hz, 1H), 7.97 (d, J = 8 Hz, 2H), 7.73-7.17 (m, 9H); $^{13}C\{^1H\}$ NMR (DMSO-d_6, 125 MHz): δ 188.8, 186.9, 144.0, 139.9, 138.6, 137.0, 134.1, 133.3, 132.7, 130.7, 129.7, 129.4, 129.3, 128.5, 128.4, 126.6, 119.2, 111.4. HRMS (ESI) calculated for $C_{23}H_{16}N_3O$ $[M+H]^+$: 350.1287 found 350.1286.

Phenyl(4-phenyl-2-(*m*-tolyl)-1*H*-imidazol-5-yl)methanone (2k). A 15 mL vial was charged

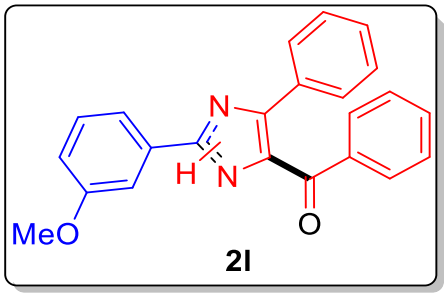


2k

with **1k** (125 mg, 0.5 mmol) and $Cu(OTf)_2$ (20 mol%) in 1,4-dioxane (3.3 mL, 0.15 M). The reaction mixture was allowed to stir at 90 °C in oil bath in sealed vial until the completion of reaction by TLC chromatography (12 h). The reaction mixture was cooled to room temperature, diluted with 10 mL of water. The water layer was extracted with (3 x 15 mL) of ethyl acetate and the combined ethyl acetate layer was given brine wash (2 x 10 mL). The final ethyl acetate layer was dried over Na_2SO_4 and concentrated under reduced pressure to get the crude compound. The obtained crude was purified using column chromatography on silica gel (EA/Hex=8%) to afford **2k** as white solid (56 mg, 66% yield); Mp. 137-138 °C; *In $CDCl_3$,*

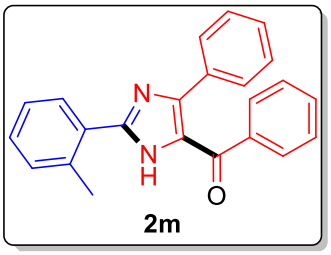
additional signals observed in the ^{1}H *NMR spectrum are attributed to the presence of N1–N3 tautomeric forms*. ^{1}H NMR (500 MHz, $CDCl_3$): δ 11.81-11.74 (m, 1H), 8.01 (s, 1H), 7.96 (d, *J* = 7.5 Hz, 1H), 7.59 (d, *J* = 7.5 Hz, 2H), 7.37-7.32 (m, 4H), 7.29-7.27 (m, 1H), 7.16-7.10 (m, 5H), 2.41 (s, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz): δ 187.4, 150.5, 149.4, 138.7, 137.1, 133.8, 132.2, 130.9, 129.8, 129.5, 128.8, 128.7, 128.0, 127.9, 127.8, 127.5, 127.3, 123.5, 21.3. HRMS (ESI) calculated for $C_{23}H_{19}N_2O$ $[M+H]^+$: 339.1491 found 339.1490.

(2-(3-Methoxyphenyl)-4-phenyl-1*H*-imidazol-5-yl)(phenyl)methanone (2l). A 15 mL vial was charged with **1l** (133 mg, 0.5 mmol) and $Cu(OTf)_2$ (20 mol%) in 1,4-dioxane (3.3 mL, 0.15 M). The reaction mixture was allowed to stir at 90 °C in oil bath in sealed vial until the completion of reaction by TLC chromatography (16 h). The reaction mixture was cooled to room temperature, diluted with 10 mL of water. The water layer was extracted with (3 x 15 mL) of ethyl acetate and the combined ethyl acetate layer was given brine wash (2 x 10 mL). The final ethyl acetate layer was dried over Na_2SO_4 and concentrated under reduced pressure to get the crude compound. The obtained crude was purified using column chromatography on silica gel (EA/Hex=12%) to afford **2l** as white solid (58 mg, 65% yield); Mp. 157-160 °C; *In CDCl₃+DMSO-d₆, additional signals observed in the* ^{1}H *and* ^{13}C *NMR spectrum are attributed to the presence of N1–N3 tautomeric forms*. ^{1}H NMR (500 MHz, $CDCl_3$): δ 12.71 (d, *J* = 29.5 Hz, 1H), 8.17 (d, *J* = 7.5 Hz, 1H), 7.83 (d, *J* = 7 Hz, 1H), 7.72 (d, *J* = 8Hz, 1H), 7.66 (d, *J* = 7 Hz, 1H), 7.56 (d, *J* = 7.5 Hz, 1H), 7.40-7.29 (m, 5H), 7.14-7.06 (m, 3H), 6.93 (dd, *J* = 22.5, 8 Hz, 1H), 3.87 (d, *J* = 13.5 Hz, 3H) ; ^{13}C{^{1}H} NMR ($CDCl_3$ + DMSO-*d*$_6$, 125 MHz): δ 189.3, 186.9, 159.8, 149.3, 149.2, 146.0, 131.9, 131.8, 131.2, 130.6, 130.0, 129.7, 129.6, 129.4, 128.5, 127.9, 127.72, 127.70, 127.6, 119.1, 118.4, 116.1, 114.9, 111.3, 111.0, 55.4, 55.3. HRMS (ESI) calculated for $C_{23}H_{19}N_2O_2$ $[M+H]^+$: 355.1441 found 355.1439.



2l

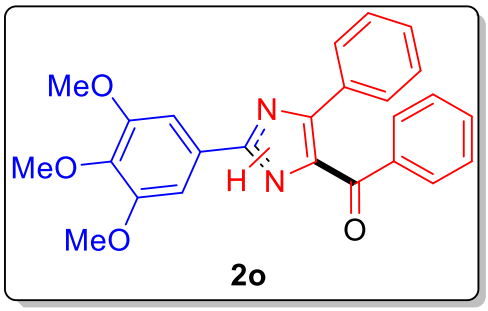
Phenyl(4-phenyl-2-(*o*-tolyl)-1*H*-imidazol-5-yl)methanone (2m). A 15 mL vial was charged with **1m** (125 mg, 0.5 mmol) and $Cu(OTf)_2$ (20 mol%) in 1,4-dioxane (3.3 mL, 0.15 M). The reaction mixture was allowed to stir at 90 °C in oil bath in sealed vial until the completion of reaction by TLC chromatography (12 h). The reaction mixture was cooled to room temperature, diluted with 10 mL of water. The water layer was extracted with (3 x 15 mL) of ethyl acetate and the combined ethyl acetate layer was given brine wash (2 x 10 mL). The final ethyl acetate layer was dried over Na_2SO_4



2m

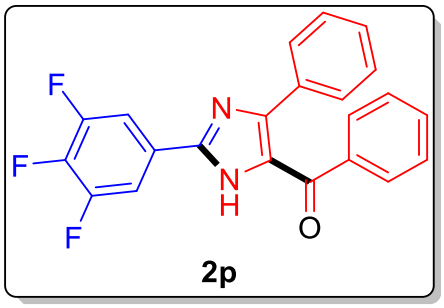
and concentrated under reduced pressure to get the crude compound. The obtained crude was purified using column chromatography on silica gel (EA/Hex=15%) to afford **2m** as pale-yellow solid (55 mg, 65% yield); Mp. 129-130 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.67 (s, 1H), 7.71 (d, *J* = 7.2 Hz, 1H), 7.63-7.34 (m, 6H), 7.32-7.26 (m, 2H), 7.25-7.17 (m, 5H), 2.64 (s, 3H); ^{13}C{^{1}H} NMR (DMSO-*d*$_6$, 100 MHz): δ 188.8, 146.1, 138.9, 138.3, 137.0, 136.0, 132.4, 131.5, 130.6, 130.0, 129.7, 129.6, 129.5, 129.3, 128.9, 128.4, 128.2, 126.2, 21.3. HRMS (ESI) calculated for $C_{23}H_{19}N_2O$ $[M+H]^+$: 339.1497 found 339.1521.

Phenyl(4-phenyl-2-(3,4,5-trimethoxyphenyl)-1*H*-imidazol-5-yl)methanone (2o). A 15 mL vial was charged with **1o** (163 mg, 0.5 mmol) and $Cu(OTf)_2$ (20 mol%) in 1,4-dioxane (3.3 mL, 0.15 M). The reaction mixture was allowed to stir at 90 °C in oil bath in sealed vial until the completion of reaction by TLC chromatography (20 h). The reaction mixture was cooled to room temperature, diluted with 10 mL of water. The water layer was extracted with (3 x 15 mL) of ethyl acetate and the combined ethyl acetate layer was given brine wash (2 x 10 mL). The final ethyl acetate layer was dried over Na_2SO_4 and concentrated under reduced pressure to get the crude compound. The obtained crude was purified using column chromatography on silica gel (EA/Hex=20%) to afford **2o** as pale yellow solid (74 mg, 71% yield); Mp. 201-204 °C; *In DMSO-d*$_6$*, additional signals observed in the* ^{1}H *and* ^{13}C *NMR spectra are attributed to the presence of N1–N3 tautomeric forms.*^{1}H NMR (500 MHz, DMSO-*d*$_6$): δ 13.47-13.19 (m, 1H), 8.10 (d, *J* = 7.5 Hz, 2H), 7.68 (d, *J* = 7 Hz, 5H), 7.61 (s, 1H), 7.56 (t, *J* = 7.5 Hz, 1H), 7.50-7.44 (m, 3H), 7.43-7.39 (m, 2H), 7.31 (d, *J* = 7 Hz, 1H), 7.21 (t, *J* = 7.2 Hz, 1H), 7.16-7.10 (m, 1H), 3.87 (d, *J* = 14 Hz, 6H), 3.73 (d, *J* = 8 Hz, 3H); ^{13}C{^{1}H} NMR (DMSO-*d*$_6$, 125 MHz): δ 188.9, 186.7, 153.7, 153.6, 148.9, 148.5, 145.8, 139.1, 138.9, 138.8, 138.7, 138.0, 136.3, 134.4, 132.6, 130.7, 130.1, 129.8, 129.7, 129.6, 129.0, 128.6, 128.43, 128.41, 128.04, 128.01, 127.7, 125.5, 125.0, 106.6, 104.2, 103.6, 60.6, 56.5. HRMS (ESI) calculated for $C_{25}H_{23}N_2O_4$ $[M+H]^+$: 415.1652 found 415.1649.



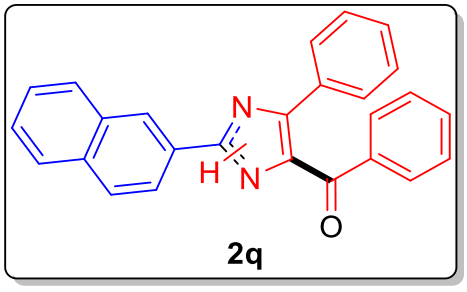
2o

Phenyl(4-phenyl-2-(3,4,5-trifluorophenyl)-1*H*-imidazol-5-yl)methanone (2p). A 15 mL vial was charged with **1p** (145 mg, 0.5 mmol) and $Cu(OTf)_2$ (20 mol%) in 1,4-dioxane (3.3 mL, 0.15 M). The reaction mixture was allowed to stir at 90 °C in oil bath in sealed vial until the completion of reaction by TLC chromatography (12 h). The reaction mixture was cooled to room temperature, diluted with 10 mL of water. The water layer was extracted with (3 x 15 mL) of ethyl acetate and the combined ethyl acetate layer was given brine wash (2 x 10 mL). The final ethyl acetate layer was dried over Na_2SO_4 and concentrated under reduced pressure to get the crude compound. The obtained crude was purified using column chromatography on silica gel (EA/Hex=7%) to afford **2p** as white solid (72 mg, 76% yield); Mp. 224-226 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 12.48 (s, 1H), 8.03 (t, *J* = 6.2 Hz, 2H), 7.60 (d, *J* = 7.4 Hz, 2H), 7.36 (t, *J* = 7.2 Hz, 1H), 7.28 (d, *J* = 7.3 Hz, 2H), 7.16 (t, *J* = 6.7 Hz, 3H), 7.12-7.09 (m, 2H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ 189.1, 153.2 (d, J_{CF} = 7.7 Hz), 151.8, 150.79 (d, J_{CF} = 7.7 Hz), 147.6, 142.6 (t, J_{CF} = 17.9 Hz), 140.1 (t, J_{CF} = 15.3 Hz), 137.3, 133.7, 133.1, 130.1 (d, J_{CF} = 15.6 Hz), 128.7, 128.5, 128.3, 125.6, 111.7 (d, J_{CF} = 22.2 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -132.9, -157.3. HRMS (ESI) calculated for $C_{22}H_{14}F_3N_2O$ $[M+H]^+$: 379.1052 found 379.1050.



2p

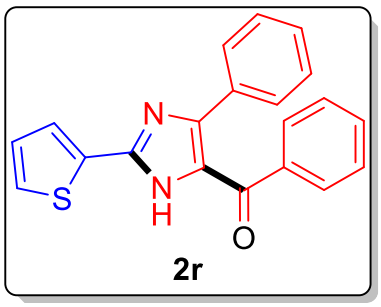
(2-Naphthalen-2-yl)-4-phenyl-1*H*-imidazol-5-yl)(phenyl)methanone (2q). A 15 mL vial was charged with **1q** (143 mg, 0.5 mmol) and $Cu(OTf)_2$ (20 mol%) in 1,4-dioxane (3.3 mL, 0.15 M). The reaction mixture was allowed to stir at 90 °C in oil bath in sealed vial until the completion of reaction by TLC chromatography (10 h). The reaction mixture was cooled to room temperature, diluted with 10 mL of water. The water layer was extracted with (3 x 15 mL) of ethyl acetate and the combined ethyl acetate layer was given brine wash (2 x 10 mL). The final ethyl acetate layer was dried over Na_2SO_4 and concentrated under reduced pressure to get the crude compound. The obtained crude was purified using column chromatography on silica gel (EA/Hex=10%) to afford **2q** as white solid (58 mg, 62% yield); Mp. 148-149 °C; *In $CDCl_3$+DMSO-d_6, additional signals observed in the* ^{1}H *and* ^{13}C *NMR spectrum are attributed to the presence of N1–N3 tautomeric forms*. ^{1}H NMR (500 MHz, $CDCl_3$): δ 12.67-12.55 (m, 1H), 8.75-8.59 (m, 1H), 8.33-8.15 (m, 2H), 7.91-7.84 (m, 3H), 7.68 (d, *J* = 6 Hz, 1H), 7.58 (d, *J* = 7 Hz, 1H), 7.51-7.49 (m, 2H), 7.42-7.30 (m, 4H), 7.12-7.09 (m, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$ + DMSO-d_6, 125 MHz): δ 189.5,



2q

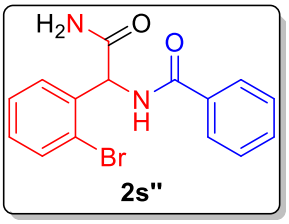
187.0, 149.8, 149.6, 146.2, 139.1, 138.5, 137.5, 136.6, 134.0, 133.8, 133.4, 133.1, 131.9, 130.7, 129.7, 129.5, 129.4, 128.6, 128.5, 128.4, 128.3, 128.2, 128.0, 127.8, 127.74, 127.71, 126.8, 126.56, 126.51, 126.4, 125.0, 123.9. HRMS (ESI) calculated for $C_{26}H_{17}N_2O$ $[M-H]^-$: 373.1340 found 373.1367.

Phenyl(4-phenyl-2-(thiophen-2-yl)-1*H*-imidazol-5-yl)methanone (2r). A 15 mL vial was charged with **1r** (121 mg, 0.5 mmol) and $Cu(OTf)_2$ (20 mol%) in 1,4-dioxane (3.3 mL, 0.15 M). The reaction mixture was allowed to stir at 90 °C in oil bath in sealed vial until the completion of reaction by TLC chromatography (7 h). The reaction mixture was cooled to room temperature, diluted with 10 mL of water. The water layer was extracted with (3 x 15 mL) of ethyl acetate and the combined ethyl acetate layer was given brine wash (2 x 10 mL). The final ethyl acetate layer was dried over Na_2SO_4 and concentrated under reduced pressure to get the crude compound. The obtained crude was purified using column chromatography on silica gel (EA/Hex=10%) to afford **2r** as yellow solid (56 mg, 68% yield); Mp. 174-177 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 11.64 (s, 1H), 7.83 (s, 1H), 7.56 (d, J = 4.5 Hz, 2H), 7.43 (d, J = 2.5 Hz, 1H), 7.33-7.28 (m, 3H), 7.13-7.08 (m, 6H) ; ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz): δ 187.3, 150.6, 145.5, 137.0, 133.4, 132.2, 132.1, 129.8, 129.5, 128.3, 128.1, 128.0, 127.9, 127.8, 127.1, 126.9. HRMS (ESI) calculated for $C_{20}H_{15}N_2OS$ $[M+H]^+$: 331.0899 found 331.0898.



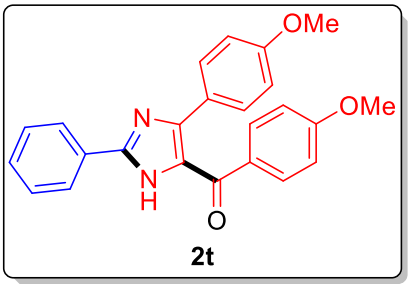
2r

***N*-(2-amino-1-(2-bromophenyl)-2-oxoethyl)benzamide (2s").** A 15 mL vial was charged with **1s** (157.5 mg, 0.5 mmol) and $Cu(OTf)_2$ (20 mol%) in 1,4-dioxane (3.3 mL, 0.15 M). The reaction mixture was allowed to stir at 90 °C in oil bath in sealed vial until the completion of reaction by TLC chromatography (12 h). The reaction mixture was cooled to room temperature, diluted with 10 mL of water. The water layer was extracted with (3 x 15 mL) of ethyl acetate and the combined ethyl acetate layer was given brine wash (2 x 10 mL). The final ethyl acetate layer was dried over Na_2SO_4 and concentrated under reduced pressure to get the crude compound. The obtained crude was purified using column chromatography on silica gel (DCM=10%) to afford **2s"** as white solid (87 mg, 52% yield); Mp. 185-186 °C; ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.98 (d, J = 7.5 Hz, 1H), 7.92 (d, J = 7.0 Hz, 2H), 7.65-7.62 (m, 2H), 7.46 (t, J = 7.7 Hz, 2H), 7.40 (t, J = 7.5 Hz, 1H), 7.36 (s, 1H), 7.28-7.25 (m, 1H), 5.85 (d, J = 7.5 Hz, 1H); ^{13}C{^{1}H} NMR (DMSO-d_6, 125 MHz): δ 171.4, 166.6, 138.2, 134.2, 133.0, 131.8, 130.2, 130.0, 128.5, 128.2, 128.1, 124.9, 57.5. HRMS (ESI) calculated for $C_{15}H_{13}N_2O_2BrNa$ $[M+Na]^+$: 355.0058 found 355.0054.



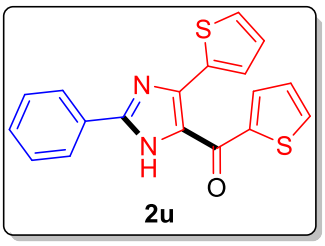
2s"

(4-Methoxyphenyl)(4-(4-methoxyphenyl)-2-phenyl-1*H*-imidazol-5-yl)methanone (2t). A 15 mL vial was charged with **1t** (133 mg, 0.5 mmol) and $Cu(OTf)_2$ (20 mol%) in 1,4-dioxane (3.3 mL, 0.15 M). The reaction mixture was allowed to stir at 90 °C in oil bath in sealed vial until the completion of reaction by TLC chromatography (12 h). The reaction mixture was cooled to room temperature, diluted with 10 mL of water. The water layer was extracted with (3 x 15 mL) of ethyl acetate and the combined ethyl acetate layer was given brine wash (2 x 10 mL). The final ethyl acetate layer was dried over Na_2SO_4 and concentrated under reduced pressure to get the crude compound. The obtained crude was purified using column chromatography on silica gel (DCM=10%) to afford **2t** as pale-yellow solid (52 mg, 54% yield); Mp. 166-167 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 11.65 (s, 1H), 8.10 (s, 2H), 7.68 (s, 2H), 7.43-7.41 (m, 3H), 7.33 (d, *J* = 8 Hz, 2H), 6.68 (d, *J* = 8.5 Hz, 4H), 3.77 (s, 3H), 3.74 (s, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz): δ 186.4, 163.0, 159.4, 148.9, 148.3, 132.3, 130.9, 129.7, 129.1, 128.8, 126.3, 113.4, 113.2, 55.4, 55.2. HRMS (ESI) calculated for $C_{24}H_{21}N_2O_3$ $[M+H]^+$: 385.1552 found 385.1569.



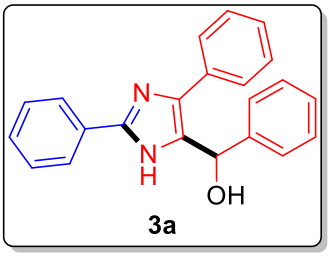
2t

(2-Phenyl-4-(thiophen-2-yl)-1*H*-imidazol-5-yl)(thiophen-2-yl)methanone (2u). A 15 mL vial was charged with **1u** (121 mg, 0.5 mmol) and $Cu(OTf)_2$ (20 mol%) in 1,4-dioxane (3.3 mL, 0.15 M). The reaction mixture was allowed to stir at 90 °C in oil bath in sealed vial until the completion of reaction by TLC chromatography (12 h). The reaction mixture was cooled to room temperature, diluted with 10 mL of water. The water layer was extracted with (3 x 15 mL) of ethyl acetate and the combined ethyl acetate layer was given brine wash (2 x 10 mL). The final ethyl acetate layer was dried over Na_2SO_4 and concentrated under reduced pressure to get the crude compound. HRMS (ESI) calculated for $C_{18}H_{13}N_2OS_2$ $[M+H]^+$: 337.0469 found 337.0480.



2u

(2,4-Diphenyl-1*H*-imidazol-5-yl)(phenyl)methanol (3a). A 15ml vial was charged with **2a** (81mg, 0.25 mmol) and $NaBH_4$ (2 equiv.) in methanol (1.3 ml, 0.15 M). The reaction mixture was allowed to stir at room temperature in a vial until the completion of reaction by TLC chromatography (2 hours). Reaction mixture was diluted with 10 ml of water. The water layer was extracted with (3 x 10ml) of ethyl acetate and combined ethyl acetate layer was given brine wash (2 x 10 mL). The final ethyl acetate layer was dried over Na_2SO_4 and concentrated under reduced pressure to get the crude compound.



3a

The obtained crude was purified using column chromatography on silica gel (EA/Hex=20%) to afford **3a** as pale yellow solid (69 mg, 84% yield); Mp. 128-129 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.62-7.61 (m, 2H), 7.34-7.33 (m, 2H), 7.26-7.17 (m, 10H), 5.86 (s, 1H); $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 150 MHz): δ 145.9, 142.0, 134.6, 133.0, 132.1, 129.2, 128.7, 128.6, 128.4, 128.3, 127.5, 127.3, 127.1, 126.6, 125.3, 67.8. HRMS (ESI) calculated for $C_{22}H_{19}N_2O$ $[M+H]^+$: 327.1497 found 327.1494.

(13) References

1. V. G. Moorthi, V. T. Seenivasan, S. Nokku, A. M. Joel, W. -Y. Lin and G. C. Senadi, *Chem. Commun.*, 2026, **62**, 5477-5481.
2. M. J. Thompson, H. Adams and B. Chen, *J. Org. Chem*., 2009, **74**, 3856–3865.
3. P. M. O'Brien, D. R. Sliskovic, J. Blankley, B. D. Roth, M. W. Wilson, K. L. Hamelehle, B. R. Krause and R. L. Stanfield. *J. Med. Chem*., 1994, **37**, 1810–1822.
4. G. Kille and J. -P. Fleury, *Bull. Soc. Chim. Fr*. 1968, 4631–4636.
5. A. J. Basson, M. P. Cameron and M. G. McLaughlin, *Chem. Commun*., 2025, **61**, 5739–5741.
6. M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, G. A. Petersson, H. Nakatsuji, X. Li, M. Caricato, A. V. Marenich, J. Bloino, B. G. Janesko, R. Gomperts, B. Mennucci, H. P. Hratchian, J. V. Ortiz, A. F. Izmaylov, J. L. Sonnenberg, D. Williams-Young, F. Ding, F. Lipparini, J. Egidi, J. Goings, B. Peng, A. Petrone, T. Henderson, D. Ranasinghe, V. G. Zakrzewski, J. Gao, N. Rega, G. Zheng, W. Liang, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, K. Throssell, J. A. Montgomery Jr., J. E. Peralta, F. Ogliaro, M. J. Bearpark, J. J. Heyd, E. N. Brothers, K. N. Kudin, V. N. Staroverov, T. A. Keith, R. Kobayashi, J. Normand, K. Raghavachari, A. P. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, J. M. Millam, M. Klene, C. Adamo, R. Cammi, J. W. Ochterski, R. L. Martin, K. Morokuma, O. Farkas, J. B. Foresman and D. J. Fox, *Gaussian 16*, *Revision C.01*, Gaussian, Inc., Wallingford CT, 2016.
7. I. Shimizu, Y. Morimoto, D. Faltermeier, M. Kerscher, S. Paria, T. Abe, H. Sugimoto, N. Fujieda, K. Asano, T. Suzuki, P. Comba and S. Itoh, *Inorg. Chem.*, 2017, **56**, 9634-9645.
8. N. Dhama, M. K. Tiwari, V. K. Vishvakarma, R. Yadav, M. Kumar and D. T. Masram, *Inorg. Chim. Acta*, 2026, **589**, 122928.

9. P. Wu, X. Zhang, B. Chen, *Tetrahedron Lett*., 2019, **60**, 1103–1107.
10. S. Hanada, Y. Motoyama and H. Nagashima, *Eur. J. Org. Chem*., 2008, ***2008***, 4097-4100.

(14) Copies of ^{1}H, ^{13}C, ^{19}F and HRMS spectra

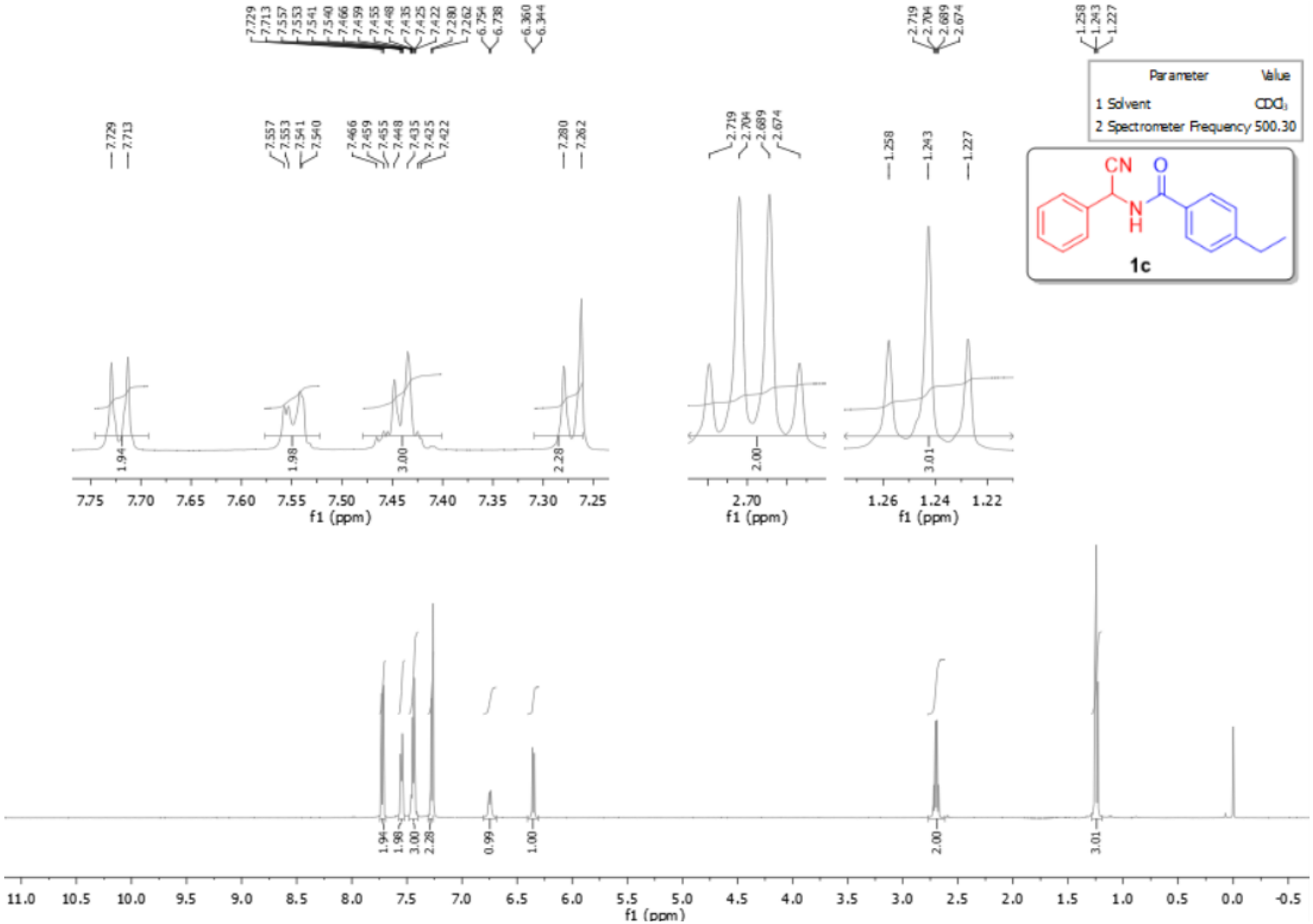


Fig. S16. ^{1}H NMR spectra of *N*-(cyano(phenyl)methyl)-3-ethylbenzamide (**1c**).

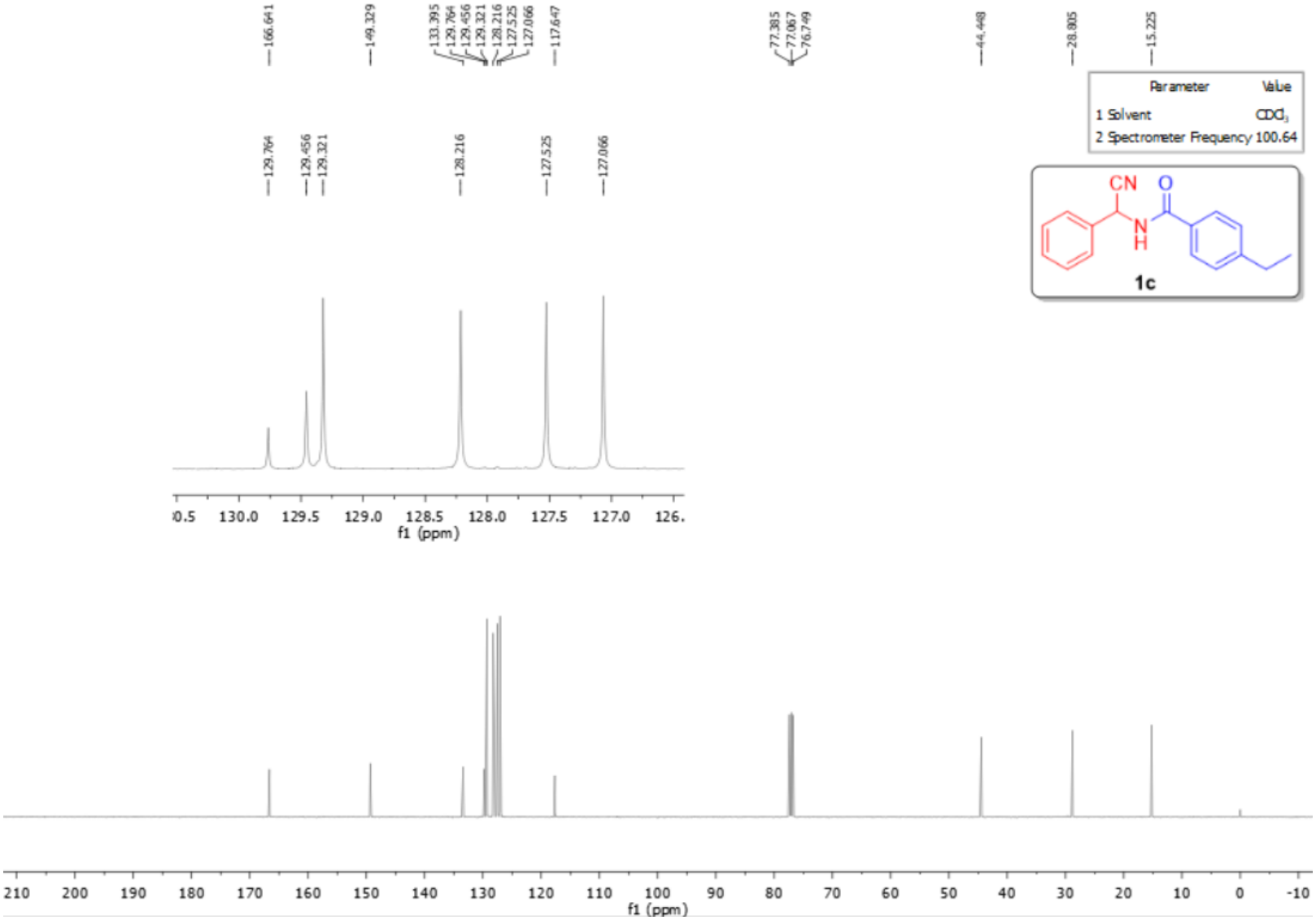
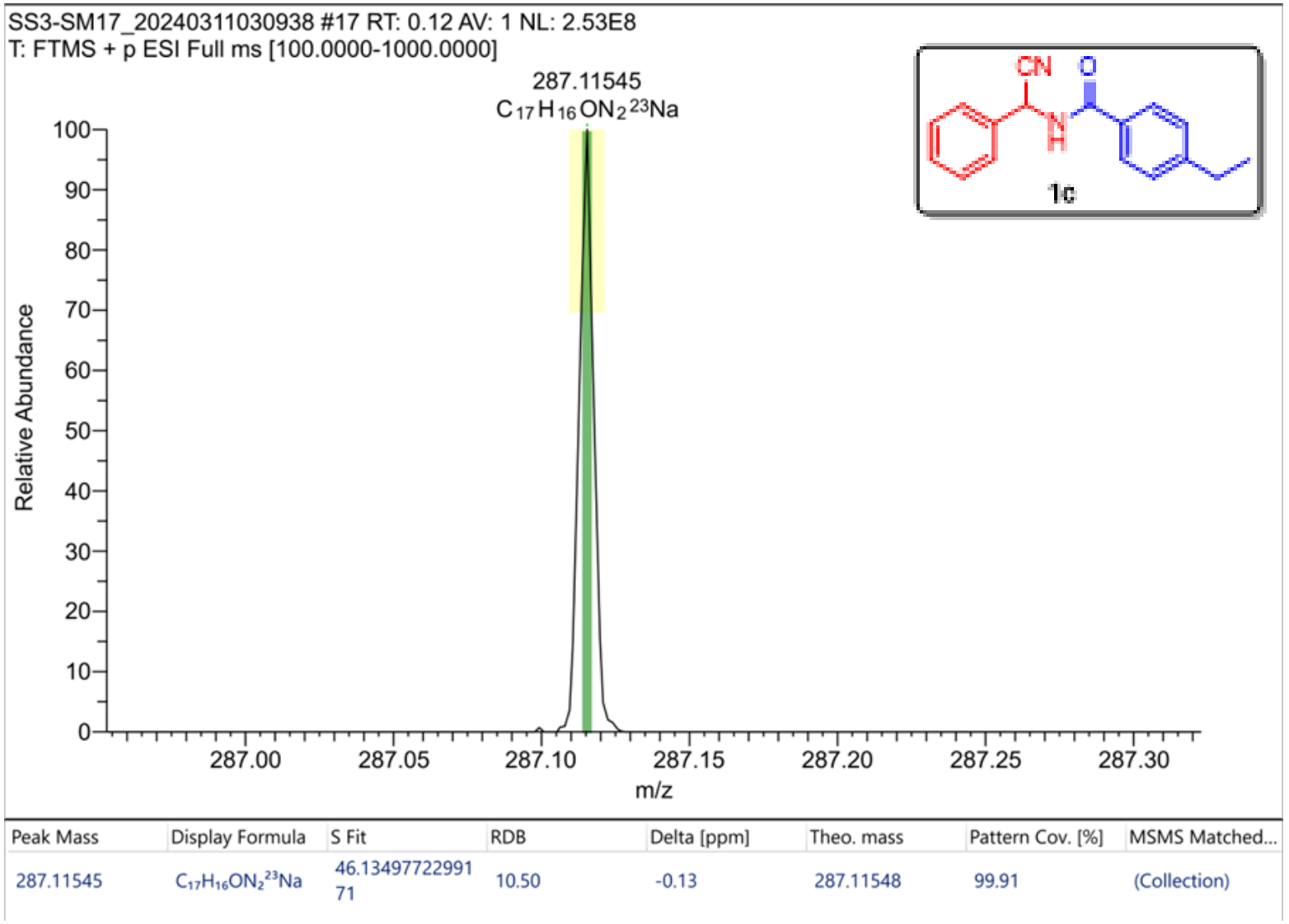


Fig. S17. ^{13}C NMR spectra of *N*-(cyano(phenyl)methyl)-3-ethylbenzamide (**1c**).



Peak Mass	Display Formula	S Fit	RDB	Delta [ppm]	Theo. mass	Pattern Cov. [%]	MSMS Matched...
287.11545	$C_{17}H_{16}ON_2{}^{23}Na$	46.1349772299171	10.50	-0.13	287.11548	99.91	(Collection)

Fig. S18. HRMS data of *N*-(cyano(phenyl)methyl)-3-ethylbenzamide (**1c**).

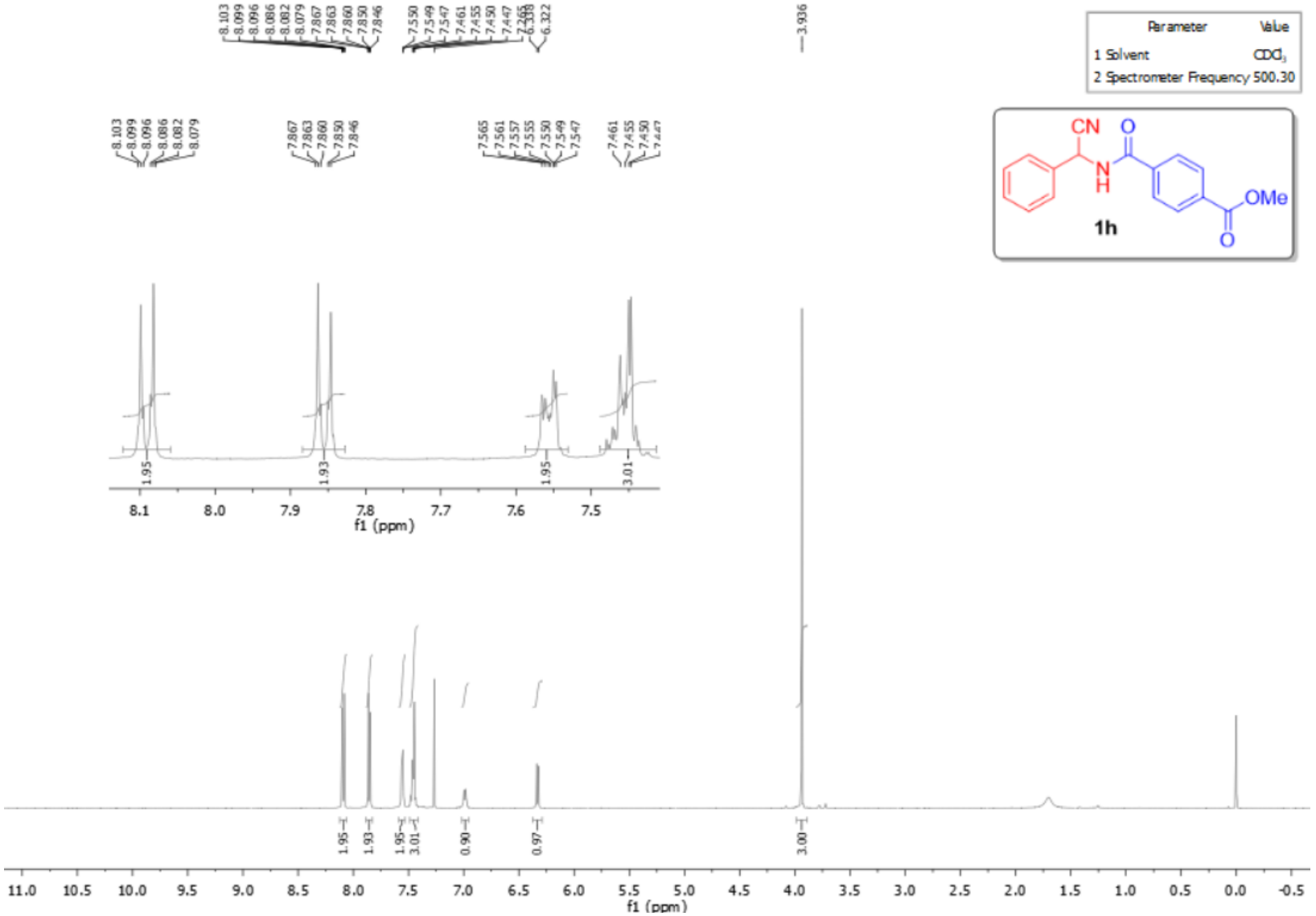


Fig. S19. [1]H NMR spectra of methyl 4-((cyano(phenyl)methyl)carbamoyl)benzoate **(1h).**

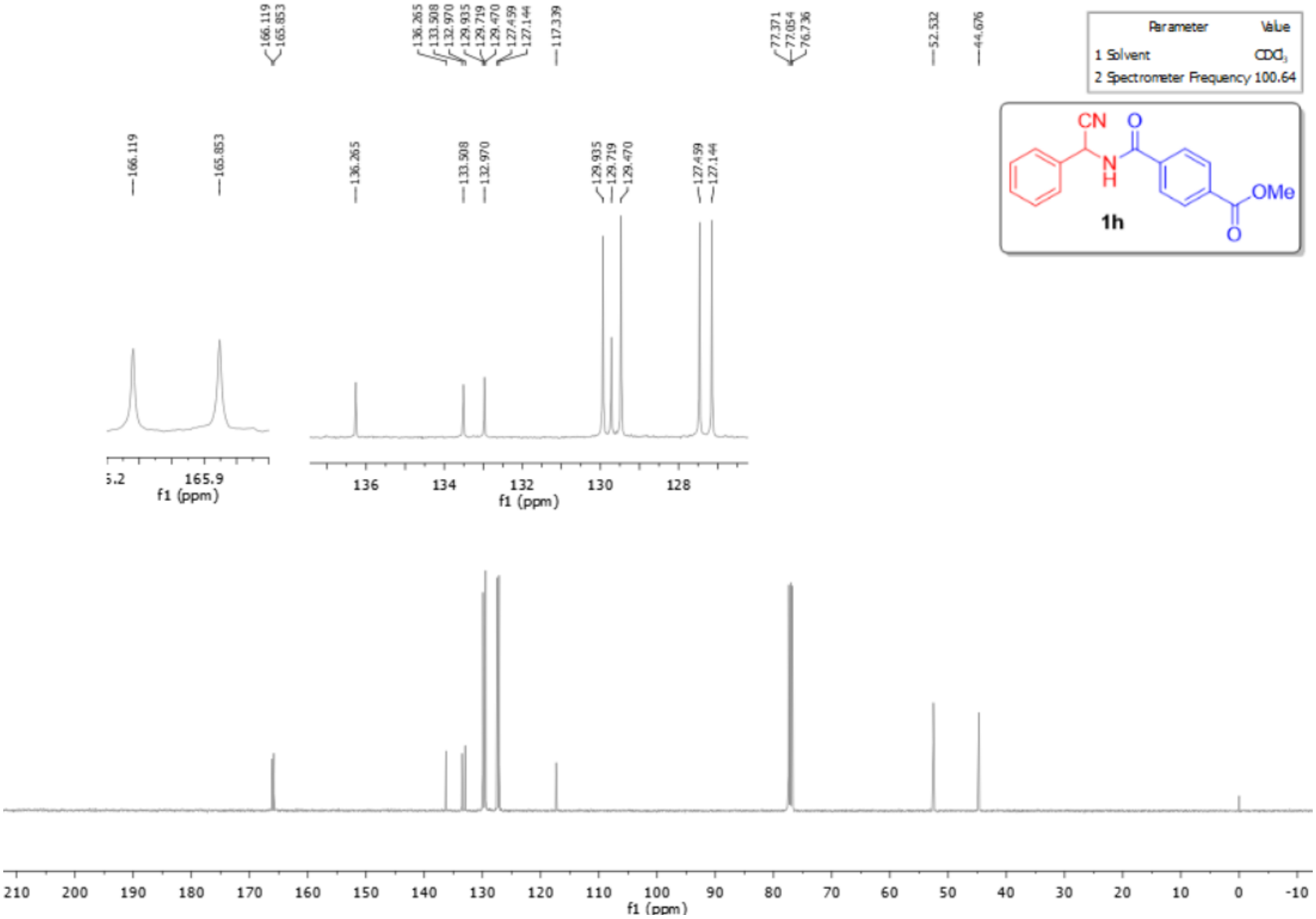
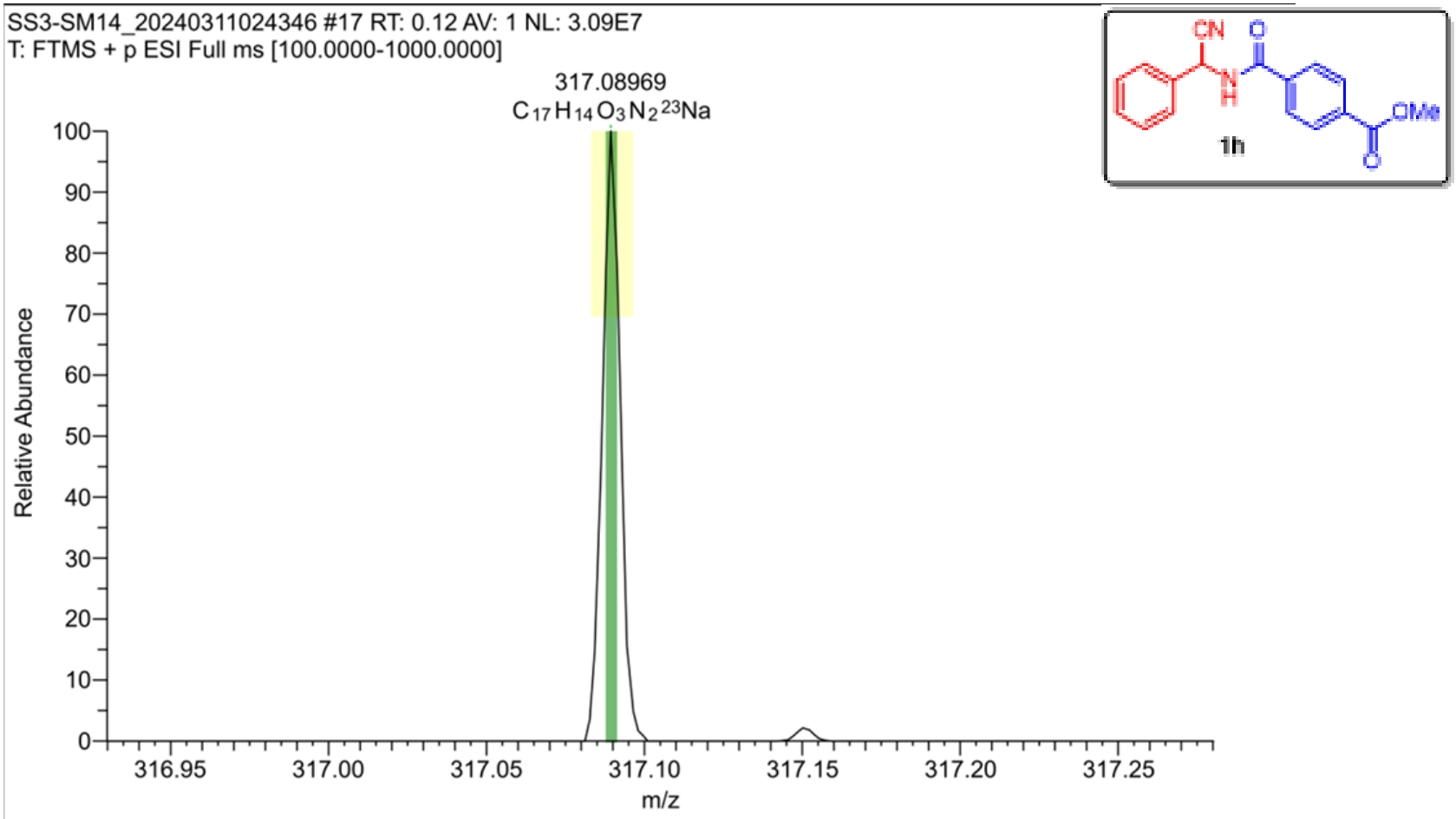


Fig. S20. ^{13}C NMR spectra of methyl 4-((cyano(phenyl)methyl)carbamoyl)benzoate **(1h).**



Peak Mass	Display Formula	S Fit	RDB	Delta [ppm]	Theo. mass	Pattern Cov. [%]	MSMS Matched...
317.08969	$C_{17}H_{14}O_3N_2{}^{23}Na$	49.1720294955561	11.50	0.09	317.08966	99.85	(Collection)

Fig. S21. HRMS data of methyl 4-((cyano(phenyl)methyl)carbamoyl)benzoate **(1h).**

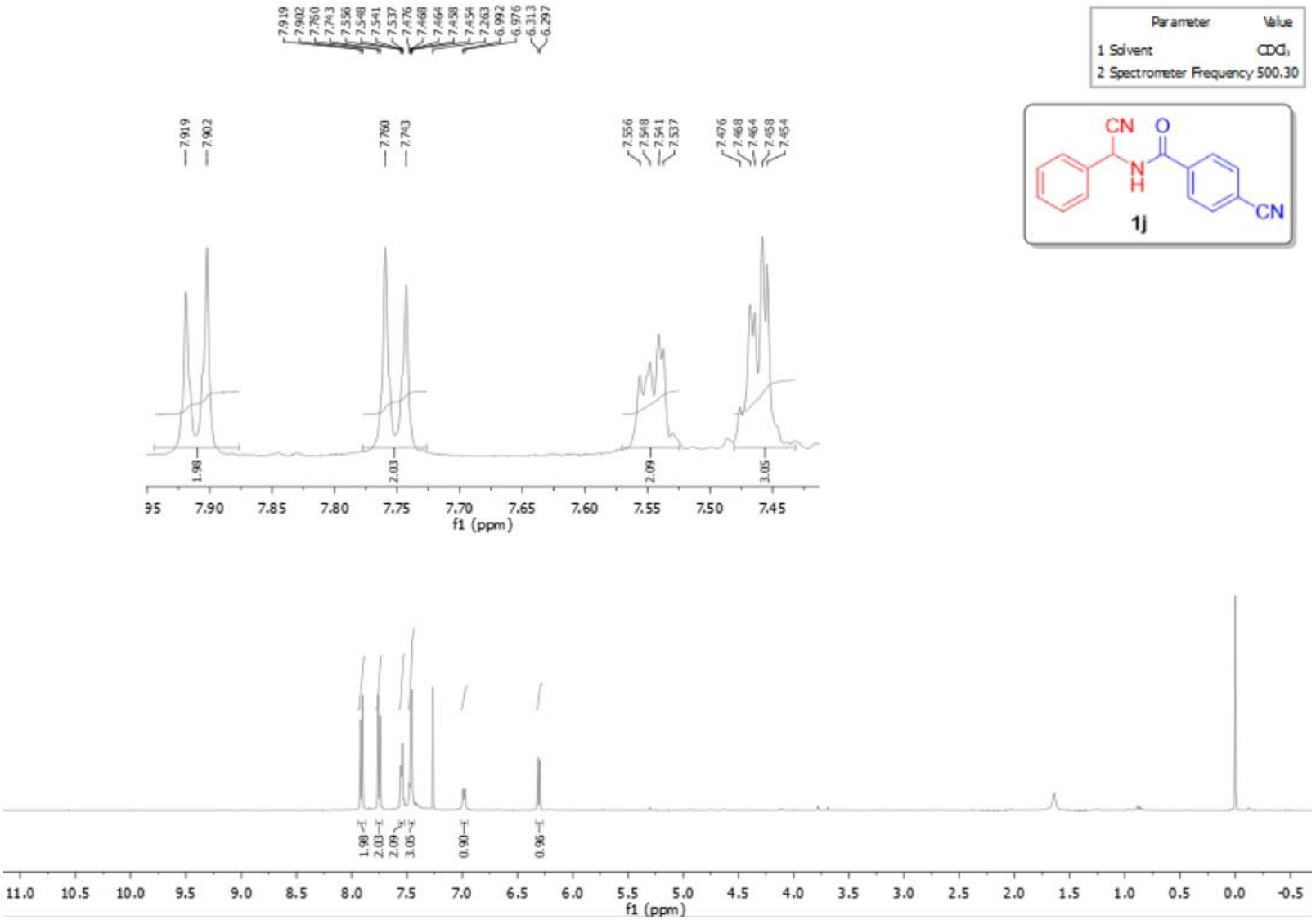


Fig. S22. [1]H NMR spectra of 4-cyano-*N*-(cyano(phenyl)methyl)benzamide **(1j).**

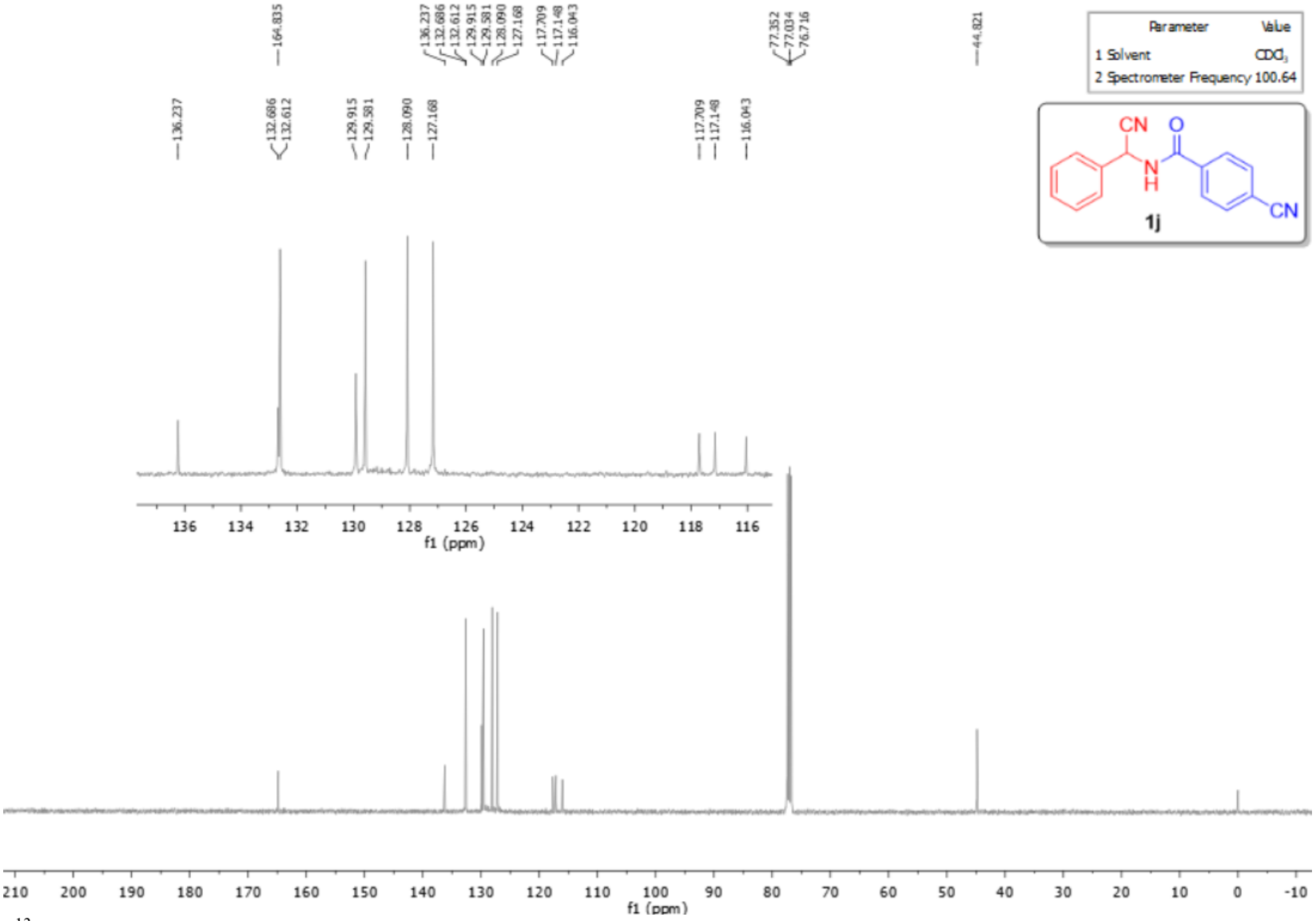
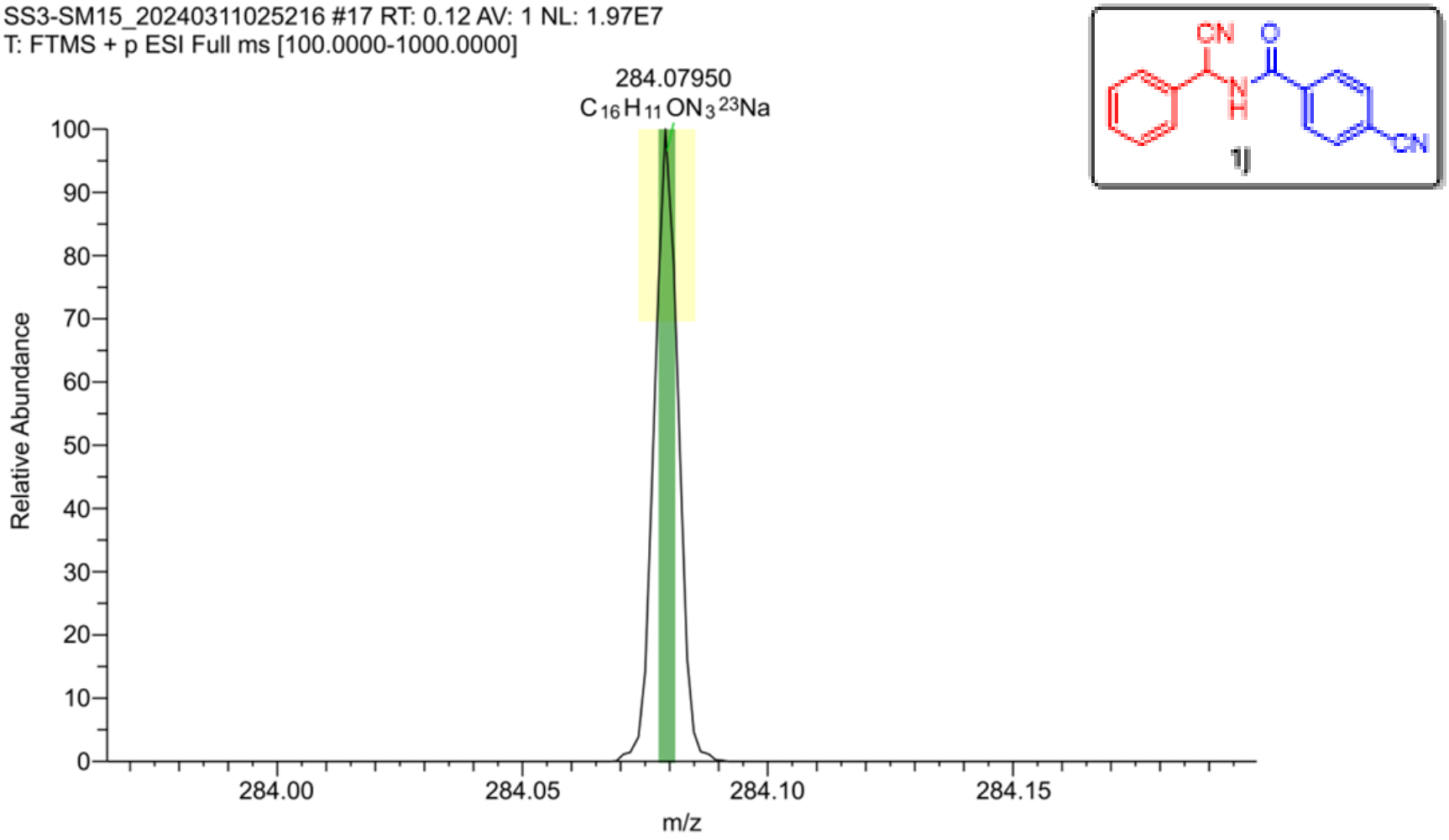


Fig. S23. ^{13}C NMR spectra of 4-cyano-*N*-(cyano(phenyl)methyl)benzamide **(1j).**



Peak Mass	Display Formula	S Fit	RDB	Delta [ppm]	Theo. mass	Pattern Cov. [%]	MSMS Matched...
284.07950	$C_{16}H_{11}ON_3{}^{23}Na$	40.6752905458662	12.50	0.23	284.07943	98.71	(Collection)

Fig. S24. HRMS data of 4-cyano-*N*-(cyano(phenyl)methyl)benzamide **(1j).**

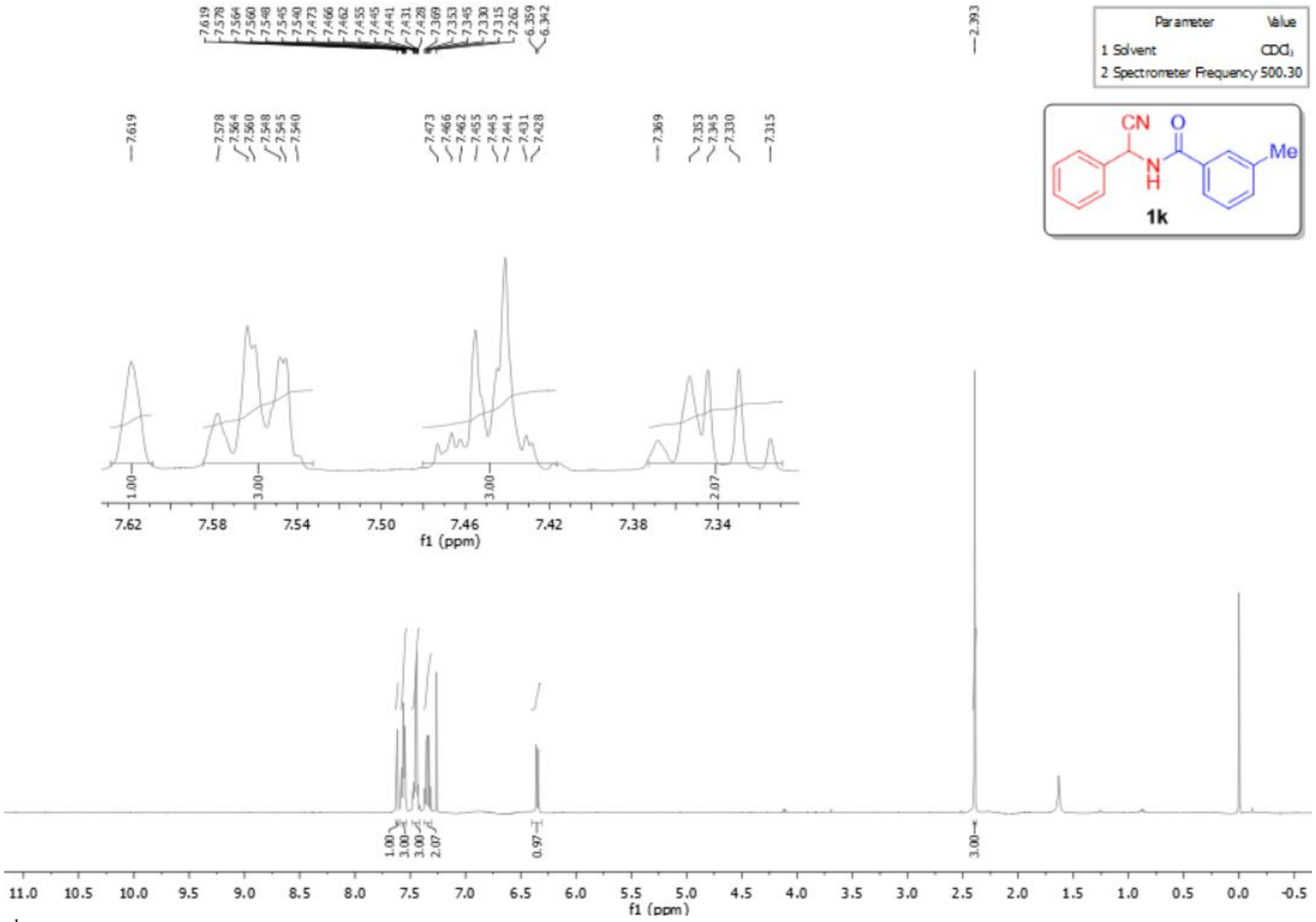


Fig. S25. ^{1}H NMR spectra of *N*-(cyano(phenyl)methyl)-3-methylbenzamide **(1k).**

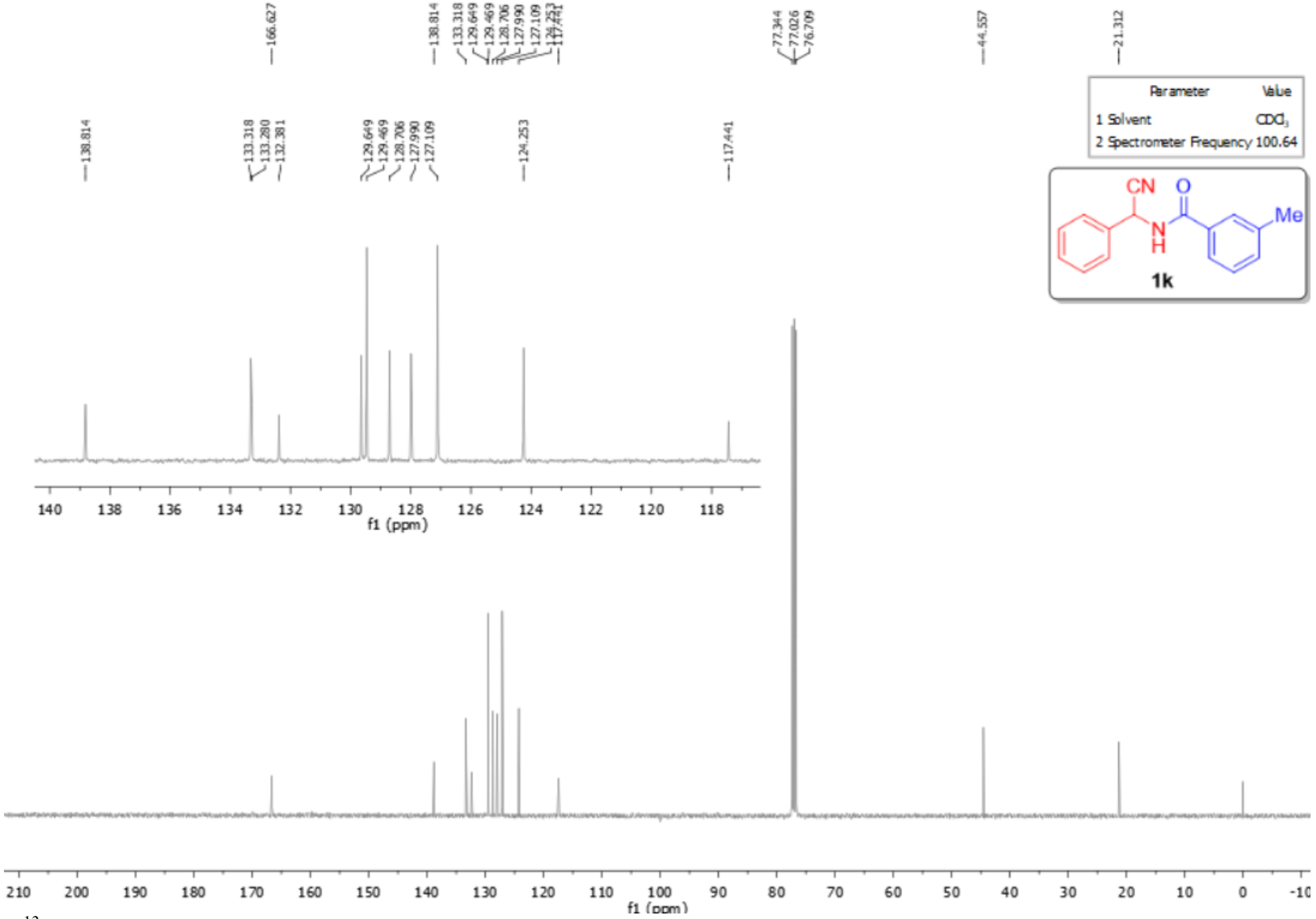
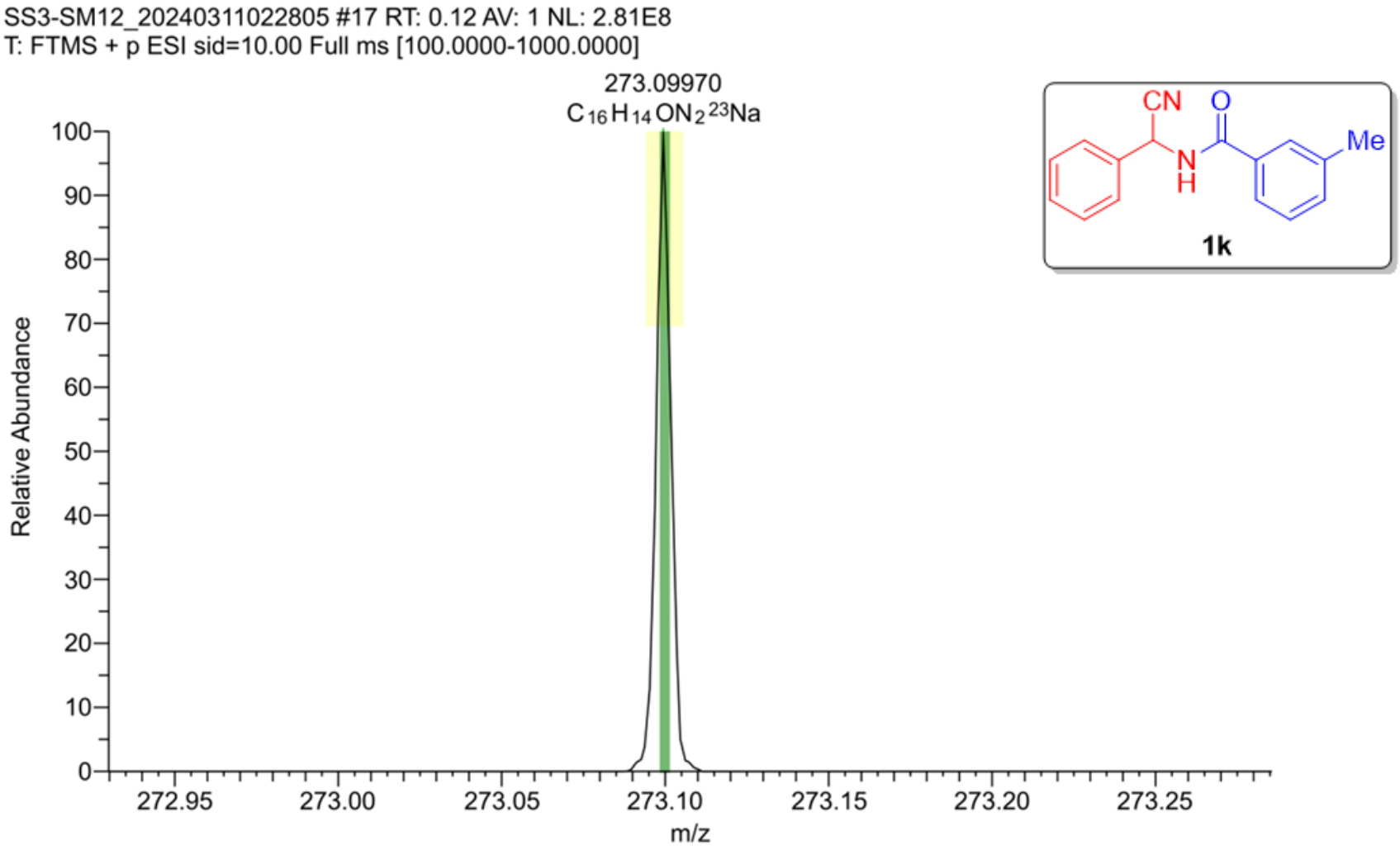


Fig. S26. ^{13}C NMR spectra of *N*-(cyano(phenyl)methyl)-3-methylbenzamide **(1k).**



Peak Mass	Display Formula	S Fit	RDB	Delta [ppm]	Theo. mass	Pattern Cov. [%]	MSMS Matched...
273.09970	$C_{16}H_{14}ON_2{}^{23}Na$	90.6848325038481	10.50	-0.49	273.09983	100	(Collection)

Fig. S27. HRMS data of *N*-(cyano(phenyl)methyl)-3-methylbenzamide **(1k).**

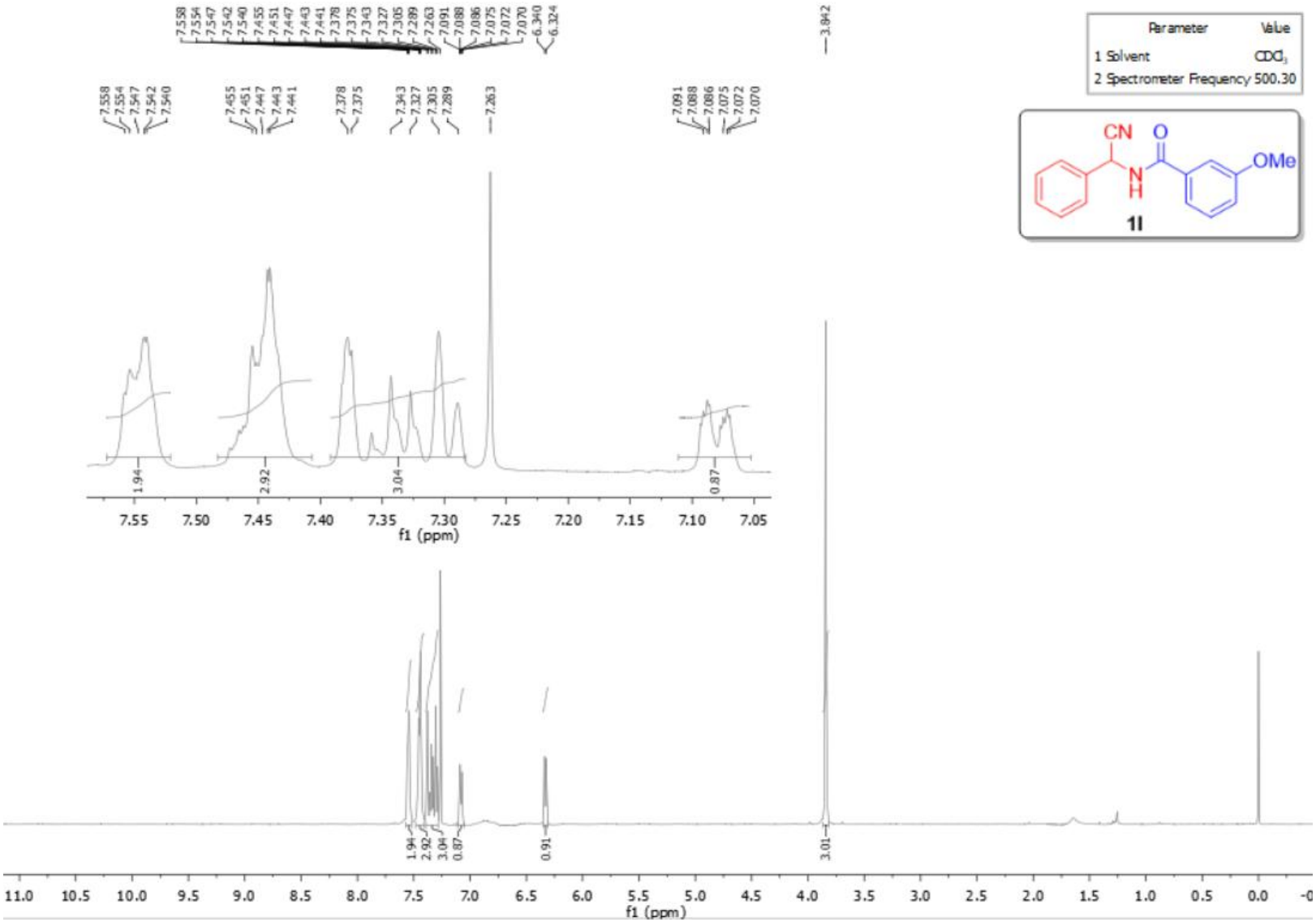


Fig. S28. [1]H NMR spectra of *N*-(cyano(phenyl)methyl)-3-methoxybenzamide **(1l).**

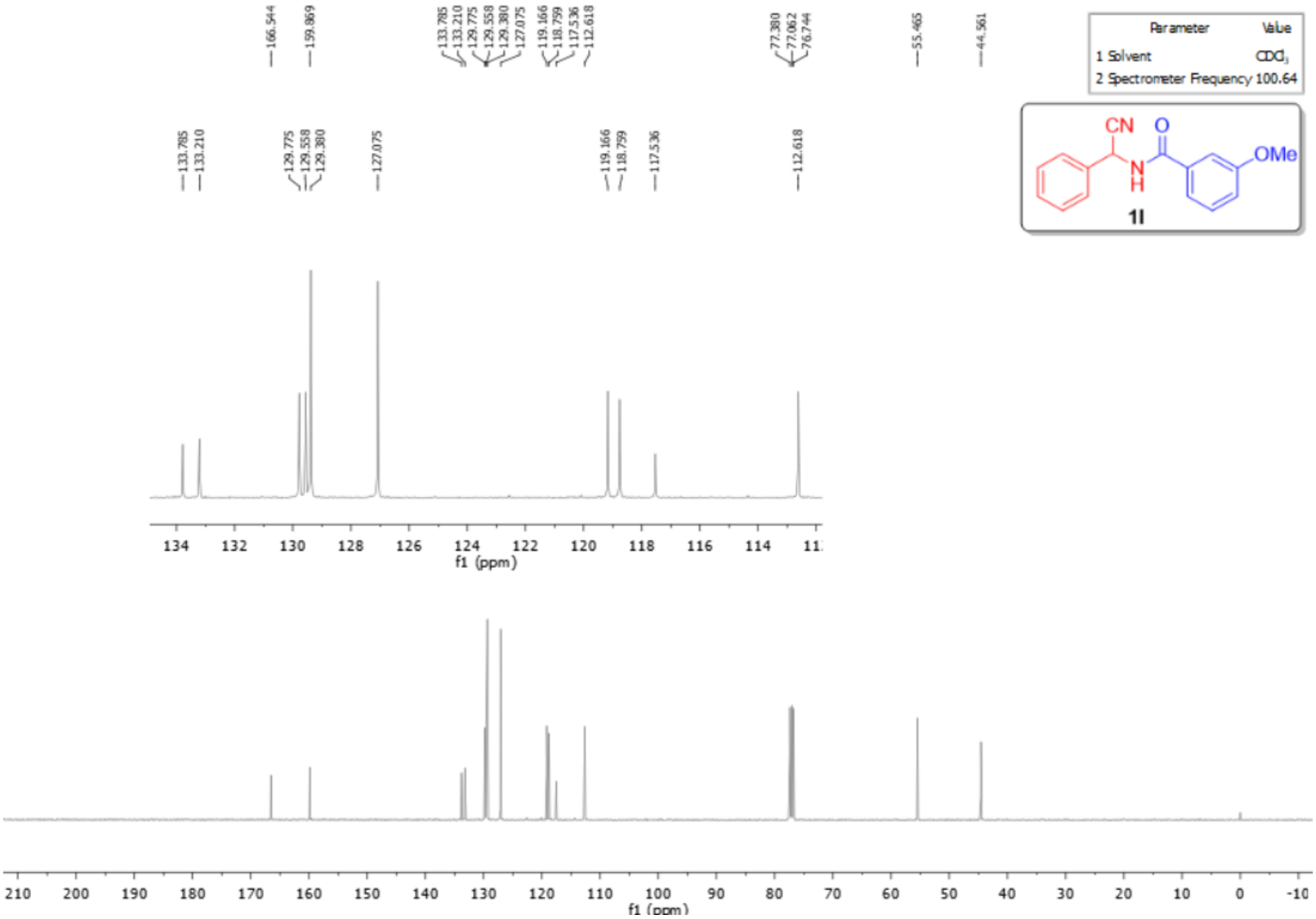
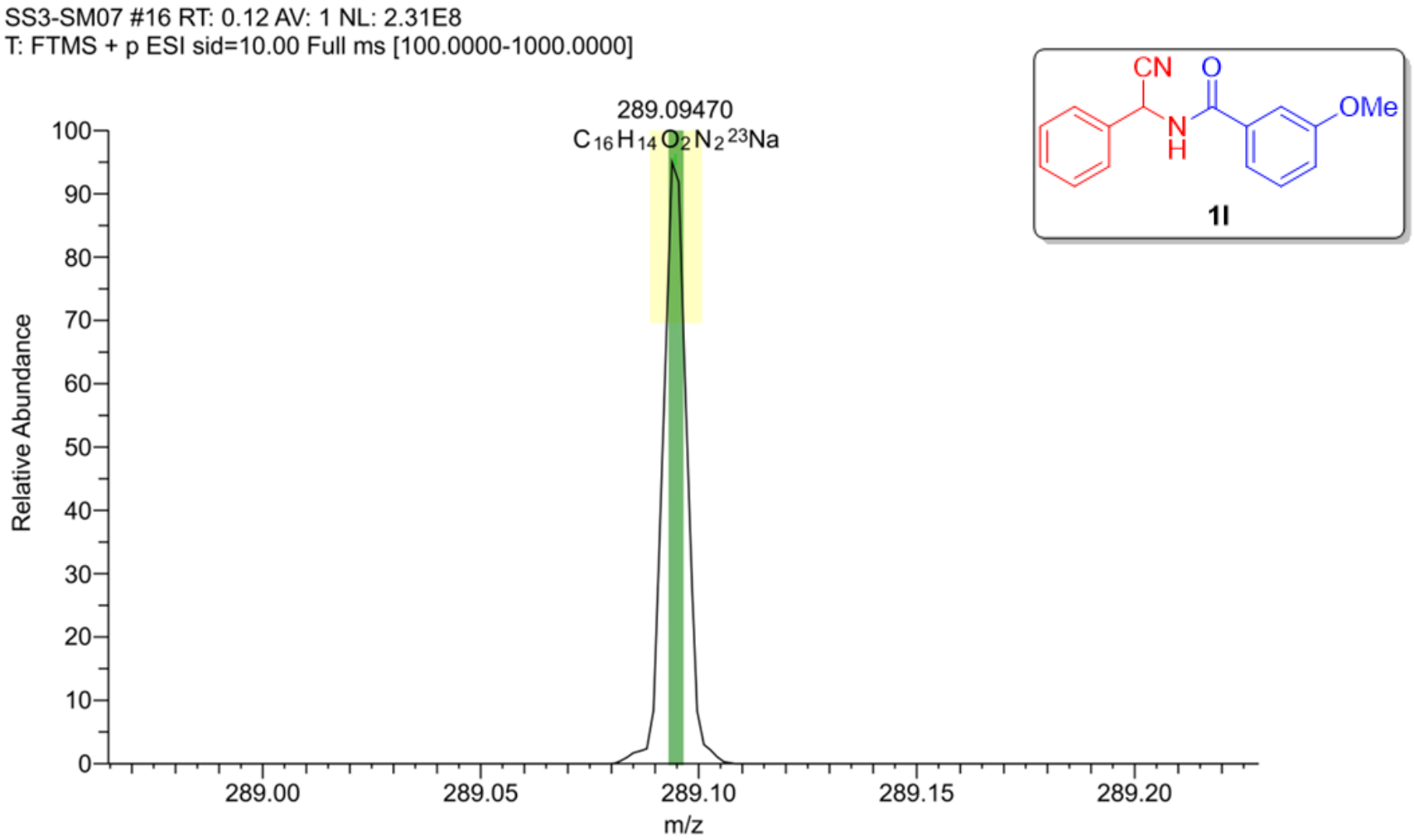


Fig. S29. ^{13}C NMR spectra of *N*-(cyano(phenyl)methyl)-3-methoxybenzamide **(1l).**



Peak Mass	Display Formula	S Fit	RDB	Delta [ppm]	Theo. mass	Pattern Cov. [%]	MSMS Matched...
289.09470	$C_{16}H_{14}O_2N_2{}^{23}Na$	45.2027812758422	10.50	-0.18	289.09475	99.9	(Collection)

Fig. S30. HRMS data of *N*-(cyano(phenyl)methyl)-3-methoxybenzamide **(1l).**

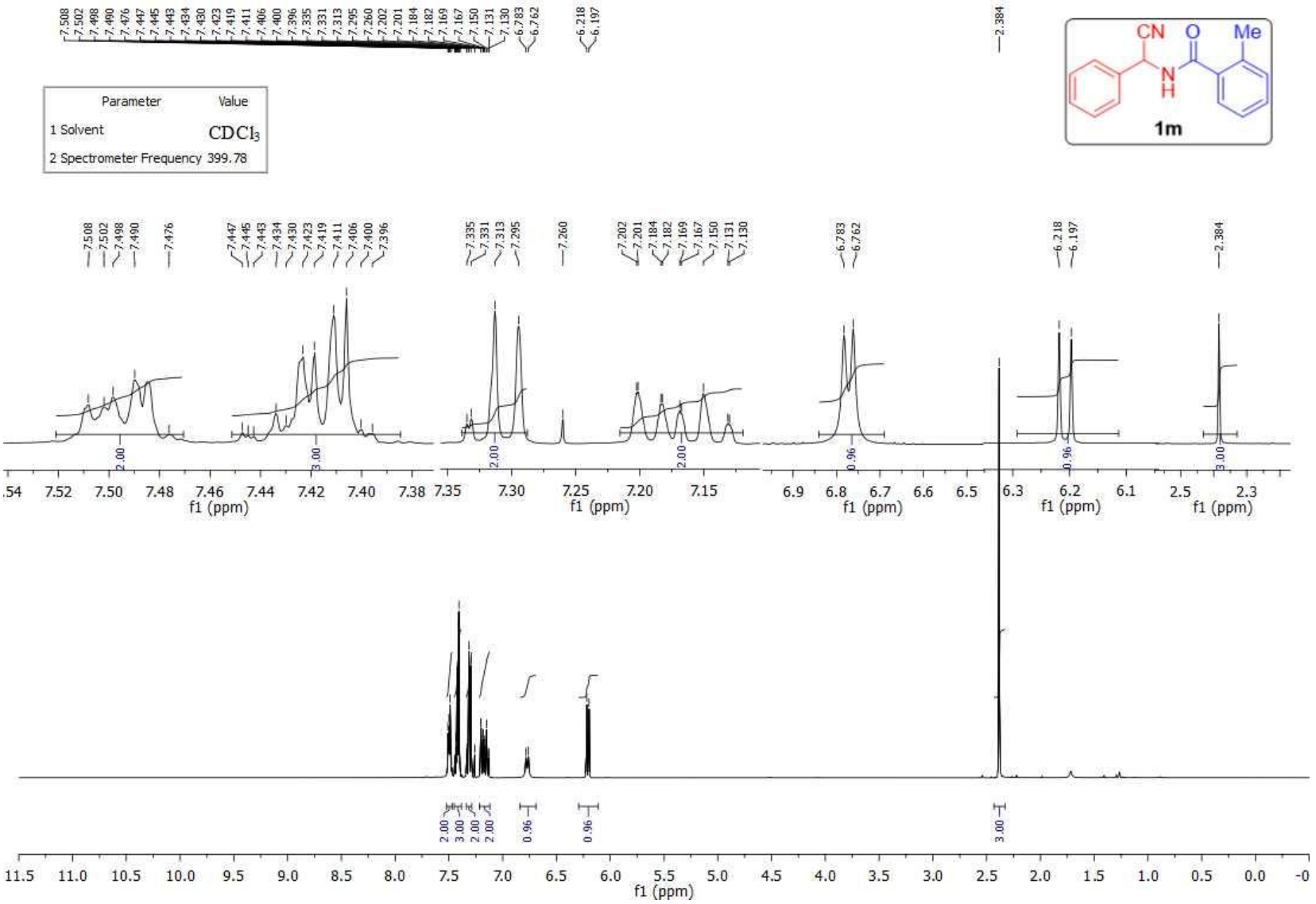


Fig. S31. [1]H NMR spectra of *N*-(cyano(phenyl)methyl)-2-methylbenzamide **(1m).**

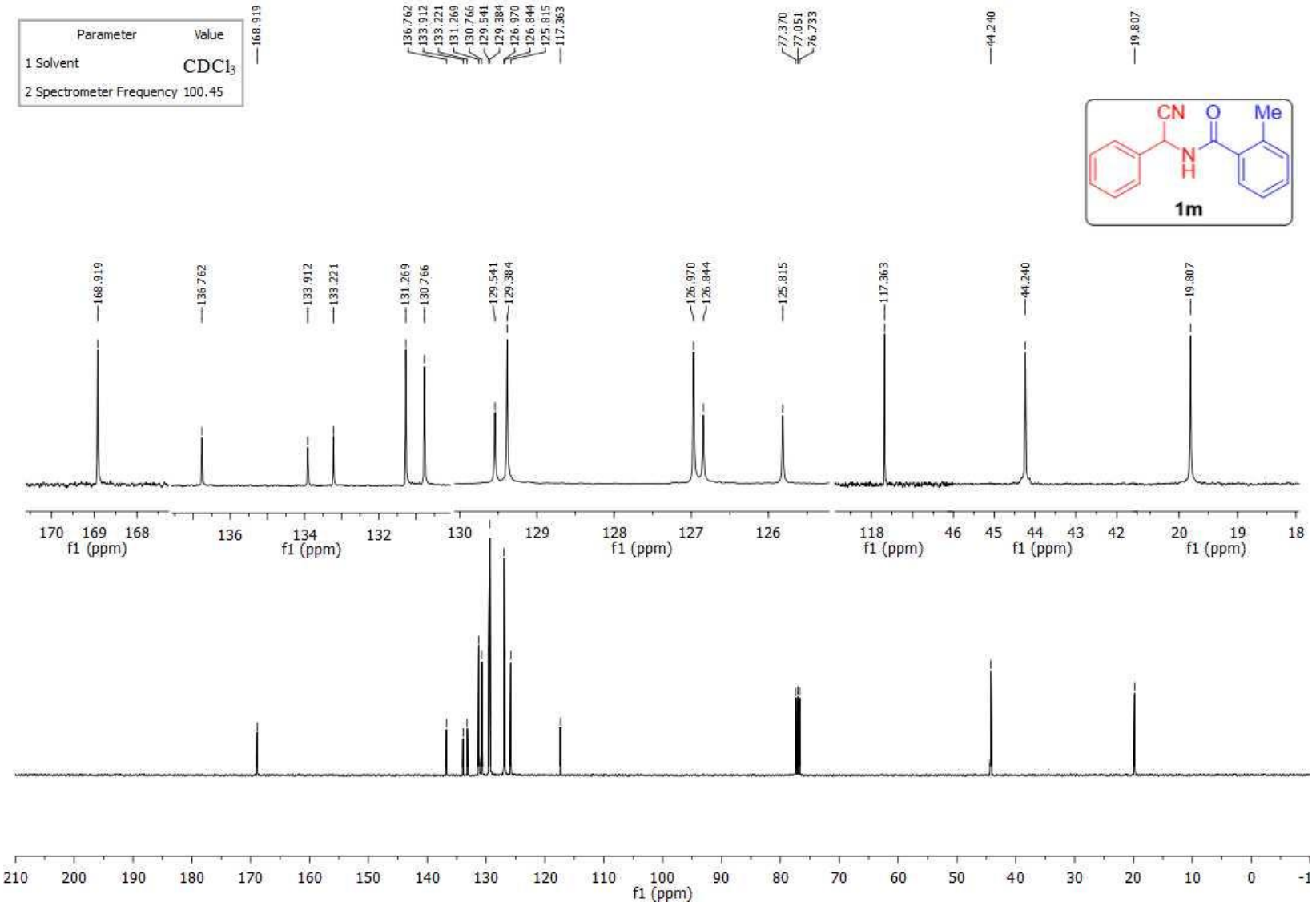


Fig. S32. ^{13}C NMR spectra of *N*-(cyano(phenyl)methyl)-2-methylbenzamide **(1m).**

Sample Name	2ME_MeOH_Positive	**Position**		**Instrument Name**	CY-E-HRMS-01
User Name		**Inj Vol**	Unknown / Injection Program	**InjPosition**	
Sample Type	Sample	**IRM Calibration Status**	Success	**Data Filename**	2ME_MeOH_Positive.d
ACQ Method	TEST.m	**Comment**		**Acquired Time**	2/28/2026 11:34:19 AM (UTC+05:30)

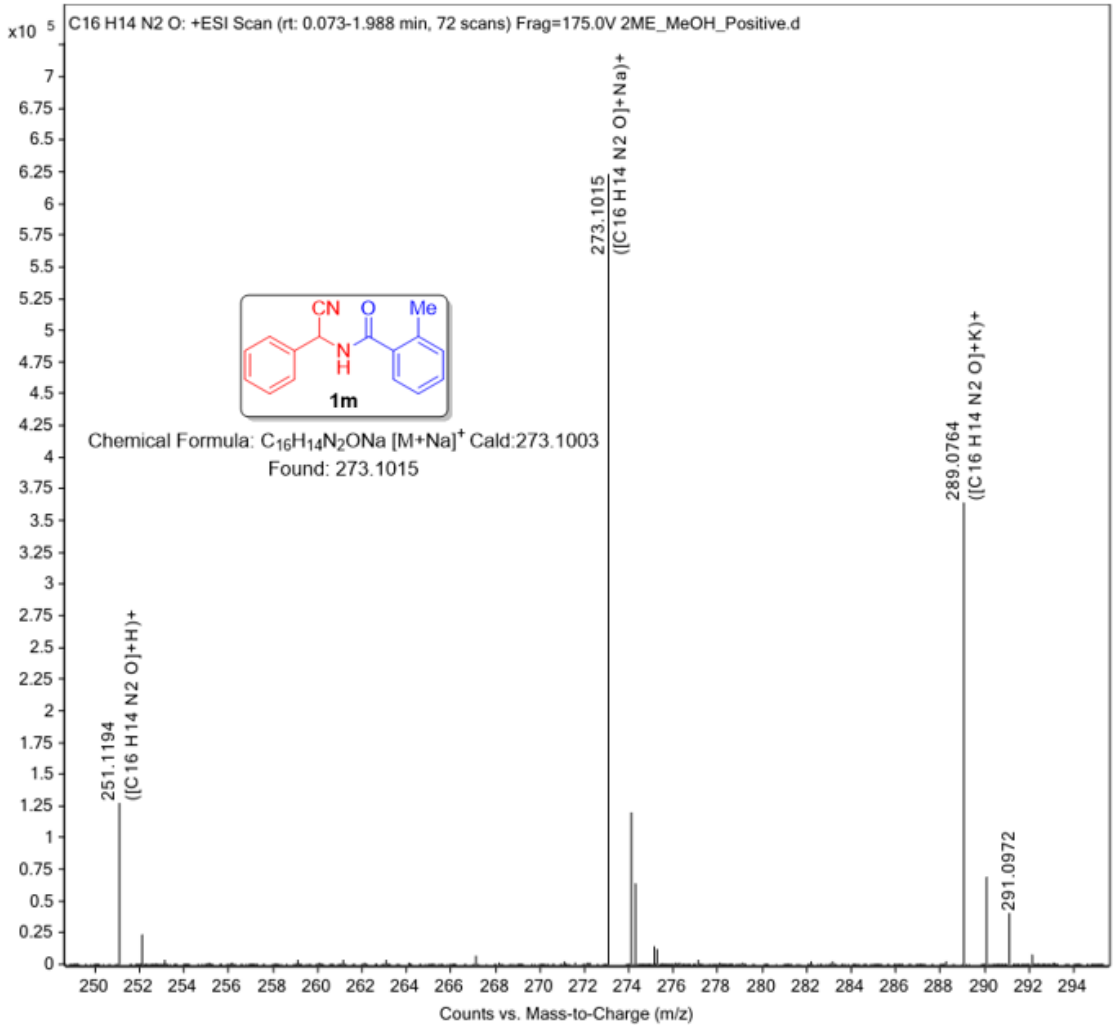


Fig. S33. HRMS data of *N*-(cyano(phenyl)methyl)-2-methylbenzamide **(1m).**

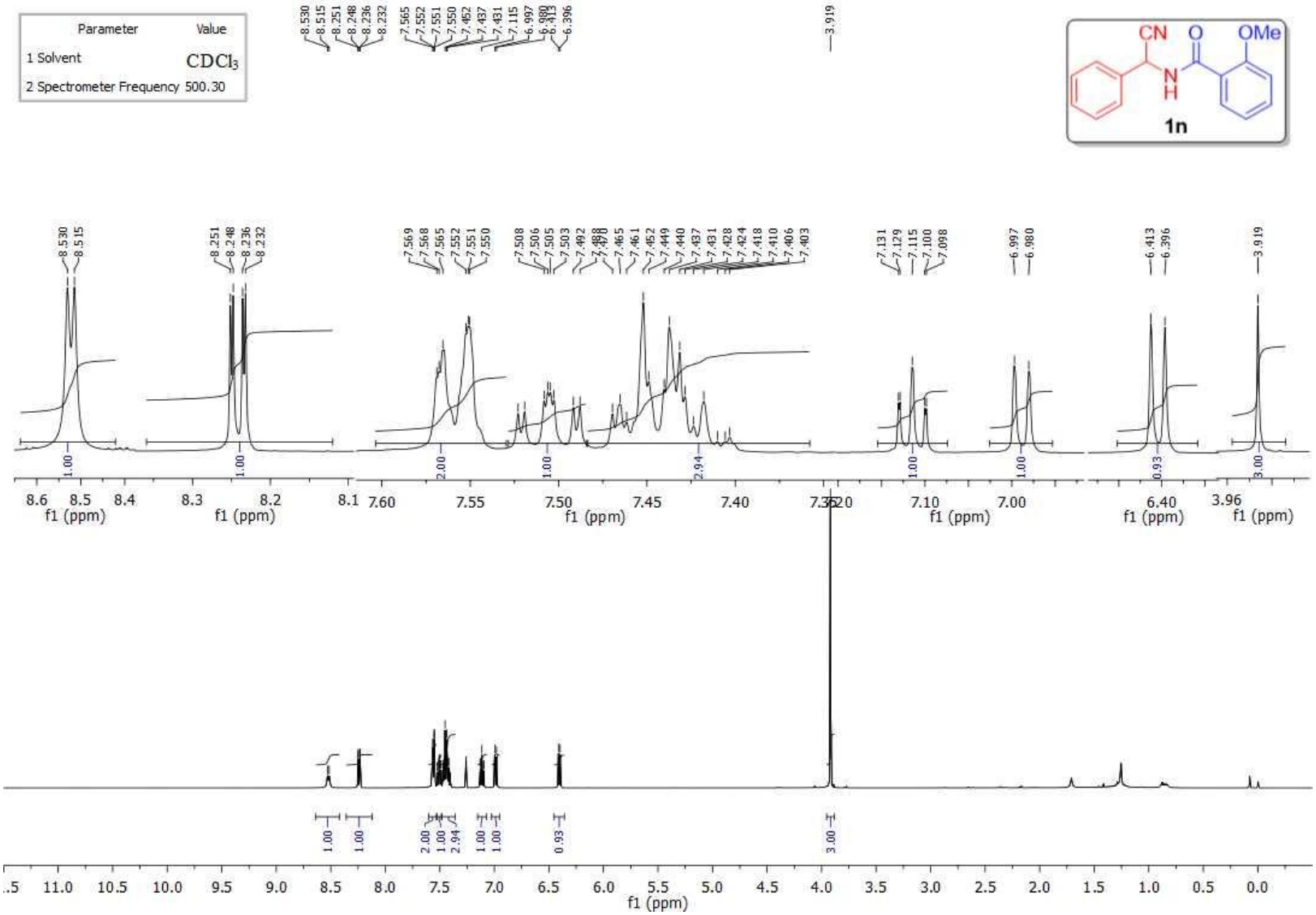


Fig. S34. ^{1}H NMR spectra of *N*-(cyano(phenyl)methyl)-2-methoxybenzamide **(1n).**

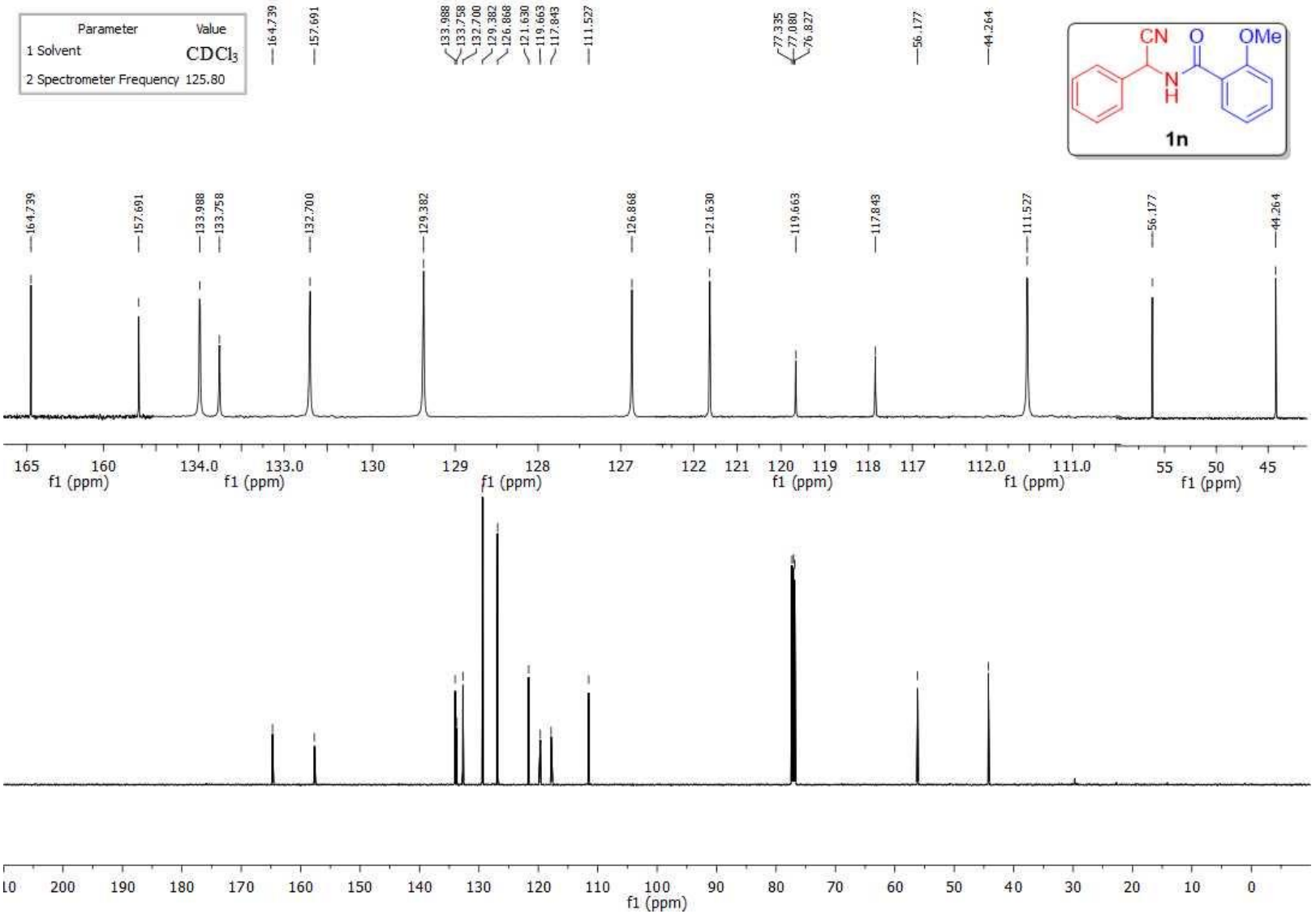


Fig. S35. ^{13}C NMR spectra of *N*-(cyano(phenyl)methyl)-2-methoxybenzamide **(1n).**

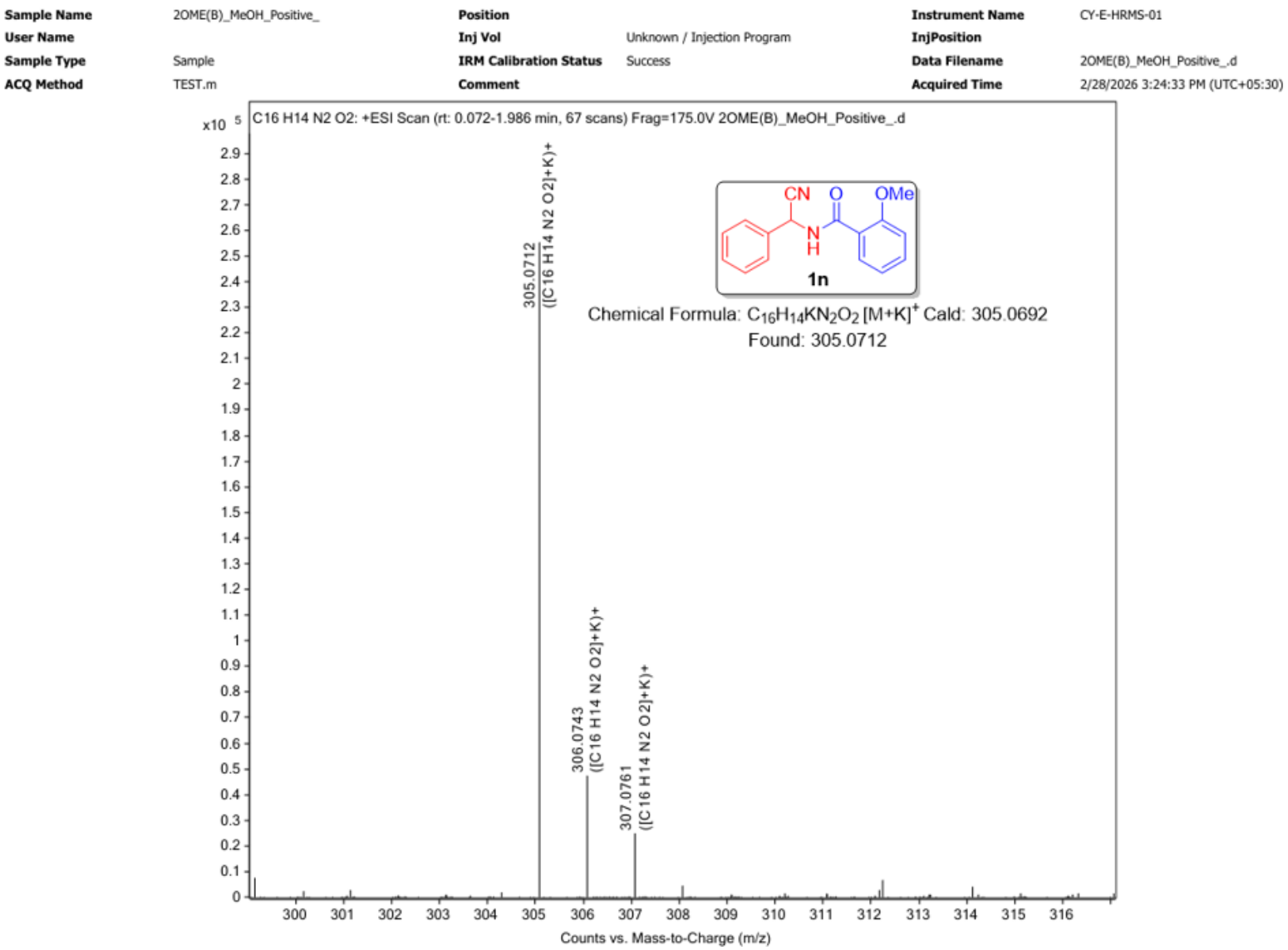


Fig. S36. HRMS data of *N*-(cyano(phenyl)methyl)-2-methoxybenzamide **(1n).**

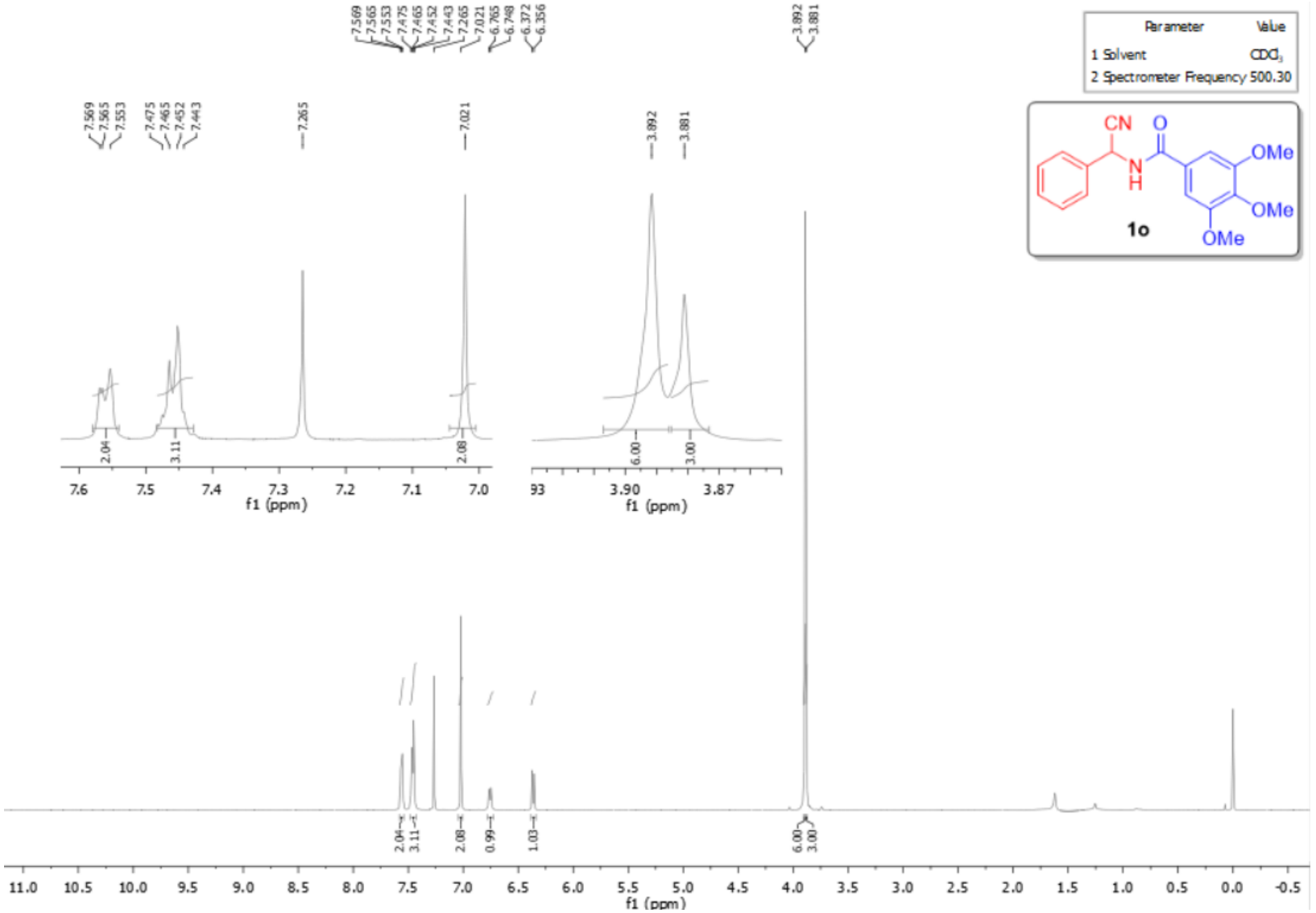


Fig. S37. ^{1}H NMR spectra of *N*-(cyano(phenyl)methyl)-3,4,5-trimethoxybenzamide **(1o).**

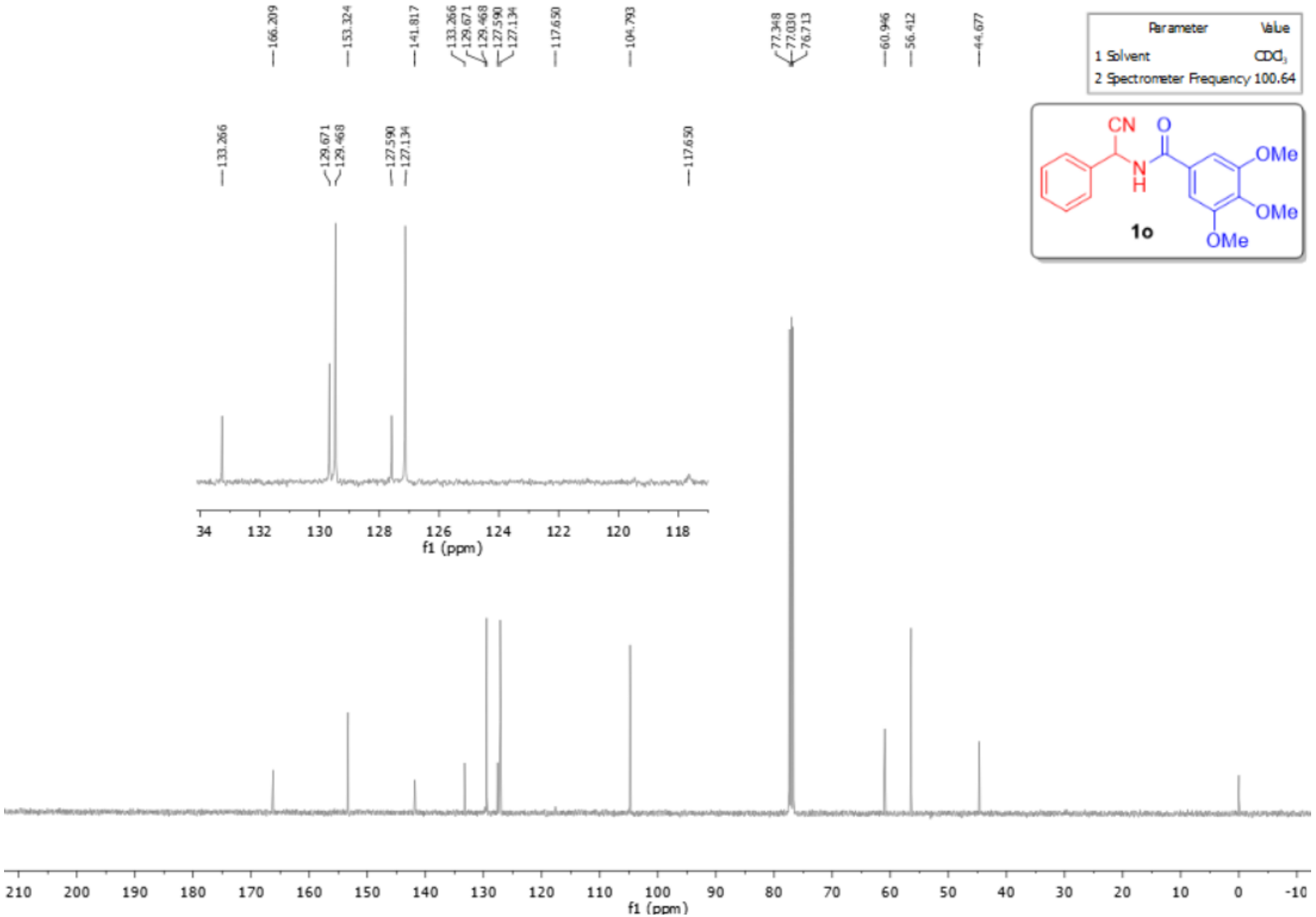
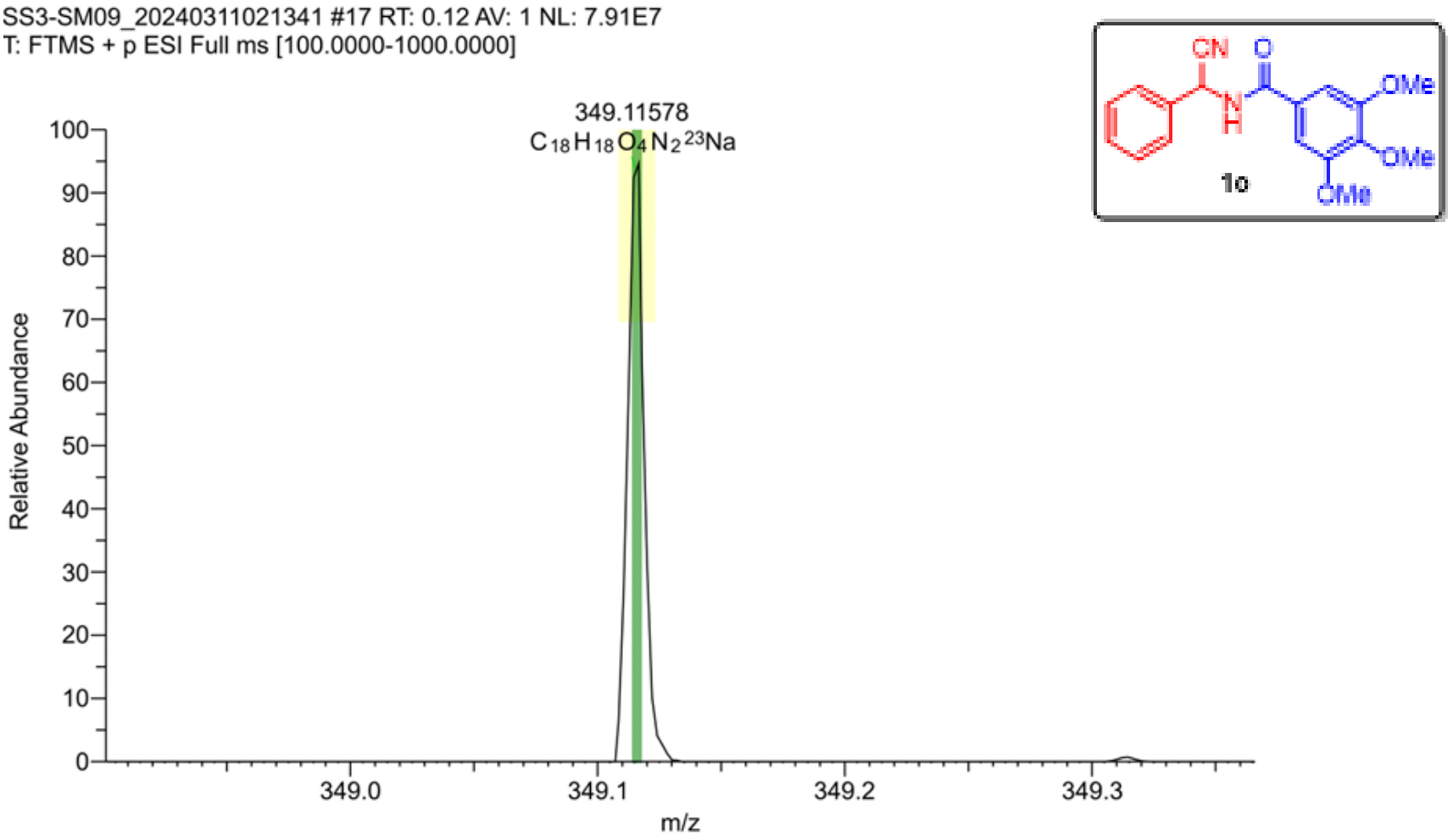


Fig. S38. ^{13}C NMR spectra of *N*-(cyano(phenyl)methyl)-3,4,5-trimethoxybenzamide **(1o).**



Peak Mass	Display Formula	S Fit	RDB	Delta [ppm]	Theo. mass	Pattern Cov. [%]	MSMS Matched...
349.11578	$C_{18}H_{18}O_4N_2{}^{23}Na$	81.59540785754 36	10.50	-0.27	349.11588	100	(Collection)

Fig. S39. HRMS data of *N*-(cyano(phenyl)methyl)-3,4,5-trimethoxybenzamide **(1o).**

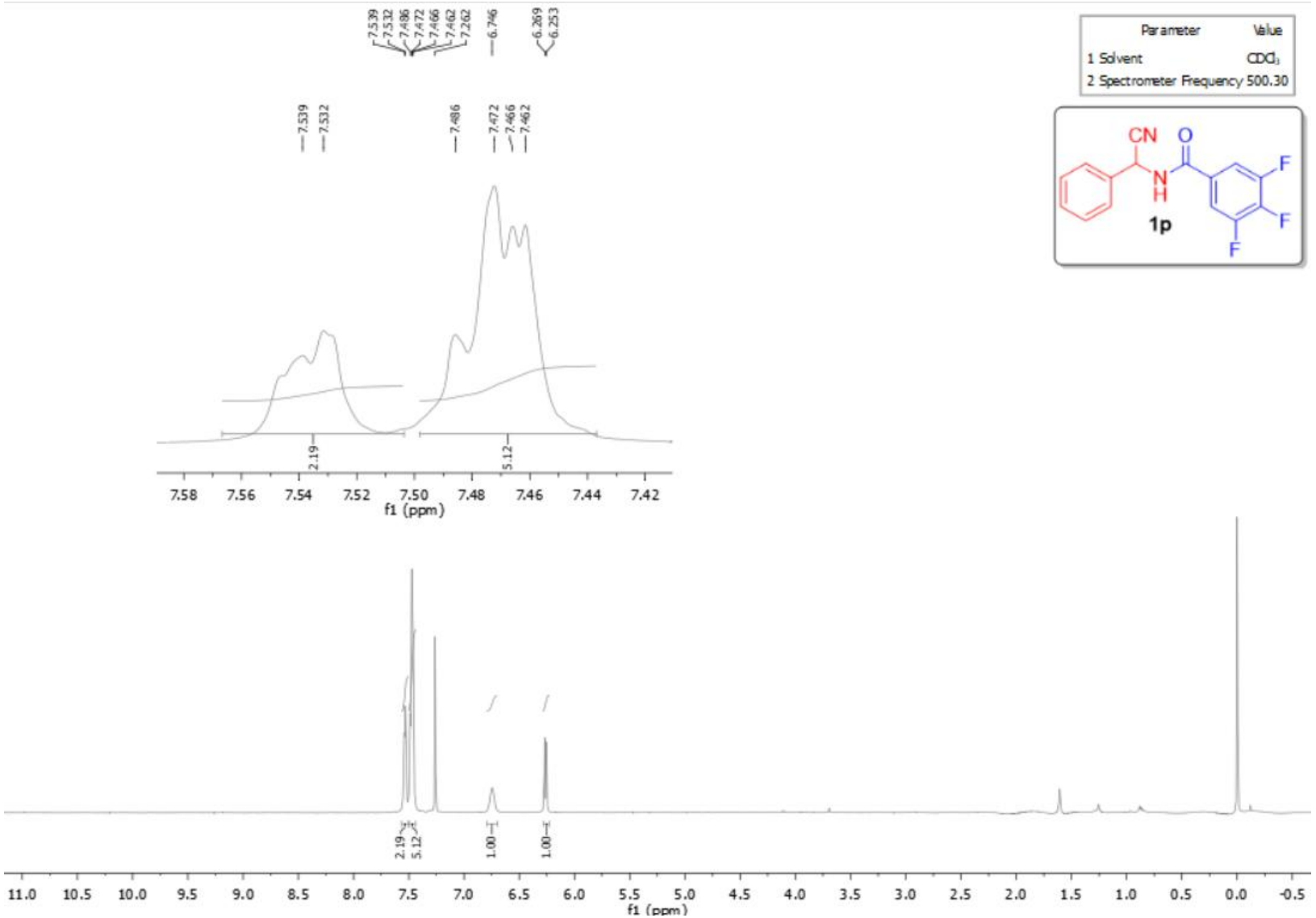


Fig. S40. ^{1}H NMR spectra of *N*-(cyano(phenyl)methyl)-3,4,5-trifluorobenzamide **(1p).**

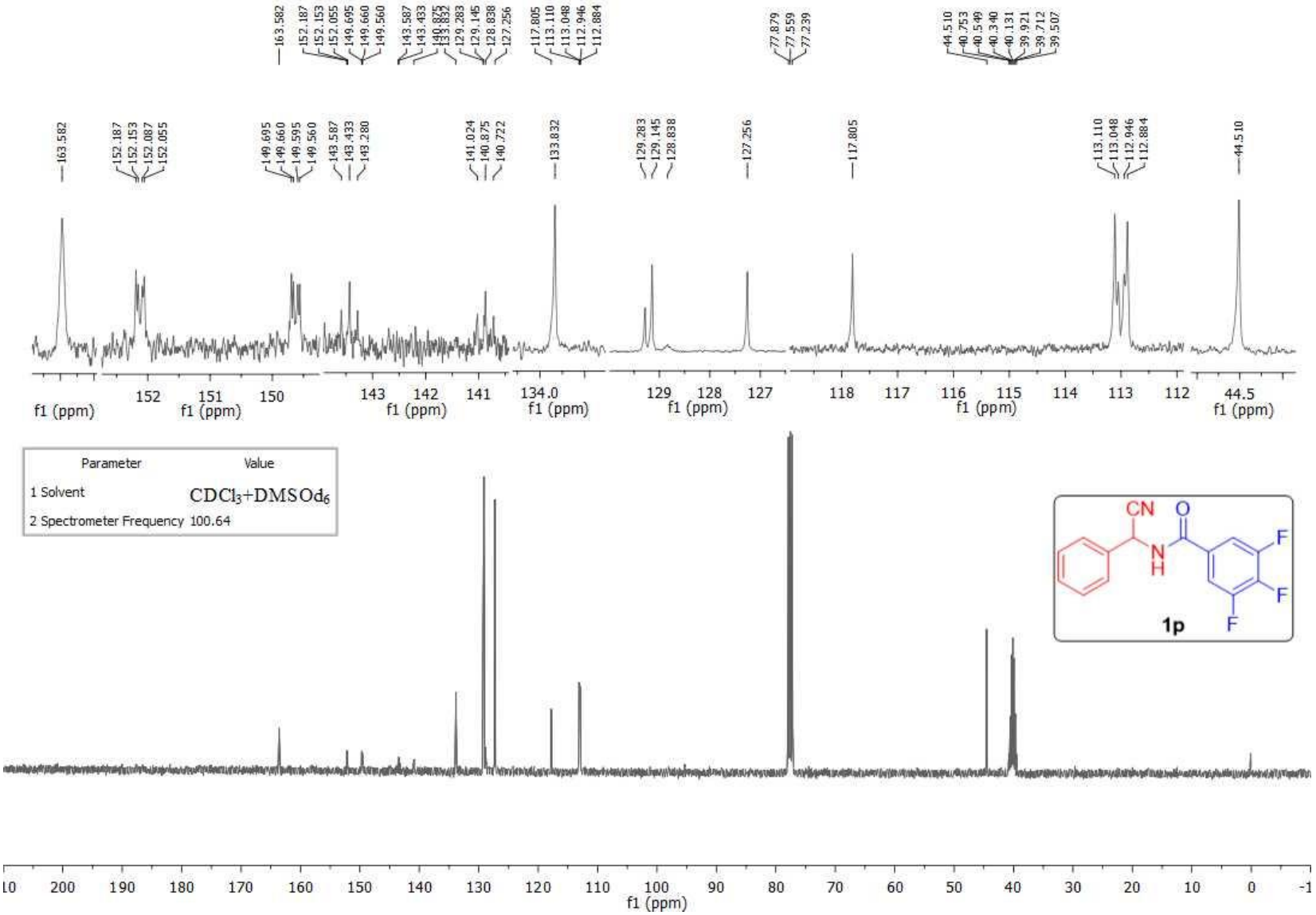
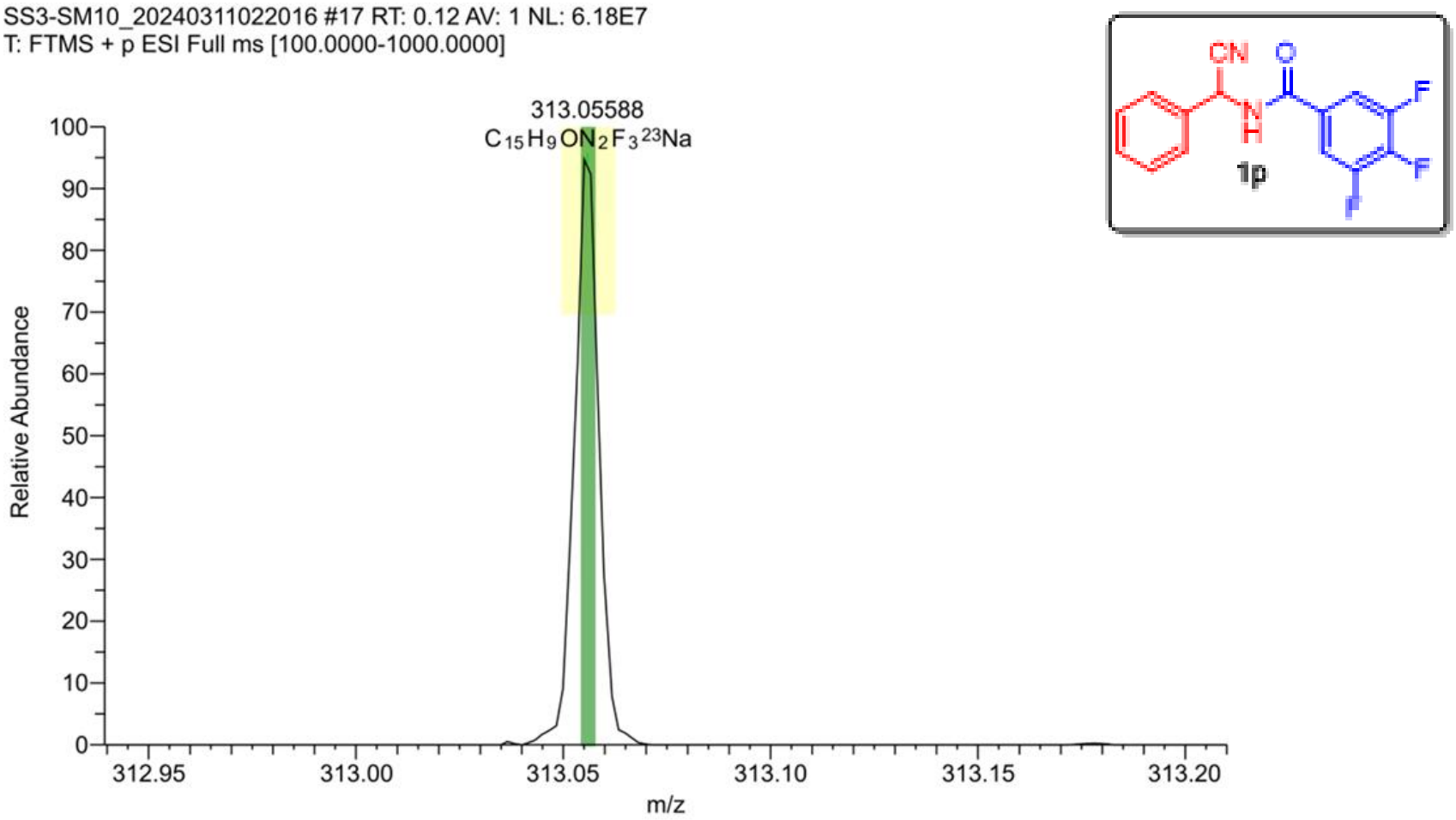


Fig. S41. ^{13}C NMR spectra of *N*-(cyano(phenyl)methyl)-3,4,5-trifluorobenzamide **(1p).**



Peak Mass	Display Formula	S Fit	RDB	Delta [ppm]	Theo. mass	Pattern Cov. [%]	MSMS Matched...
313.05588	$C_{15}H_9ON_2F_3{}^{23}Na$	79.59733154939 13	10.50	-0.13	313.05592	100	(Collection)

Fig. S42. HRMS data of *N*-(cyano(phenyl)methyl)-3,4,5-trifluorobenzamide **(1p).**

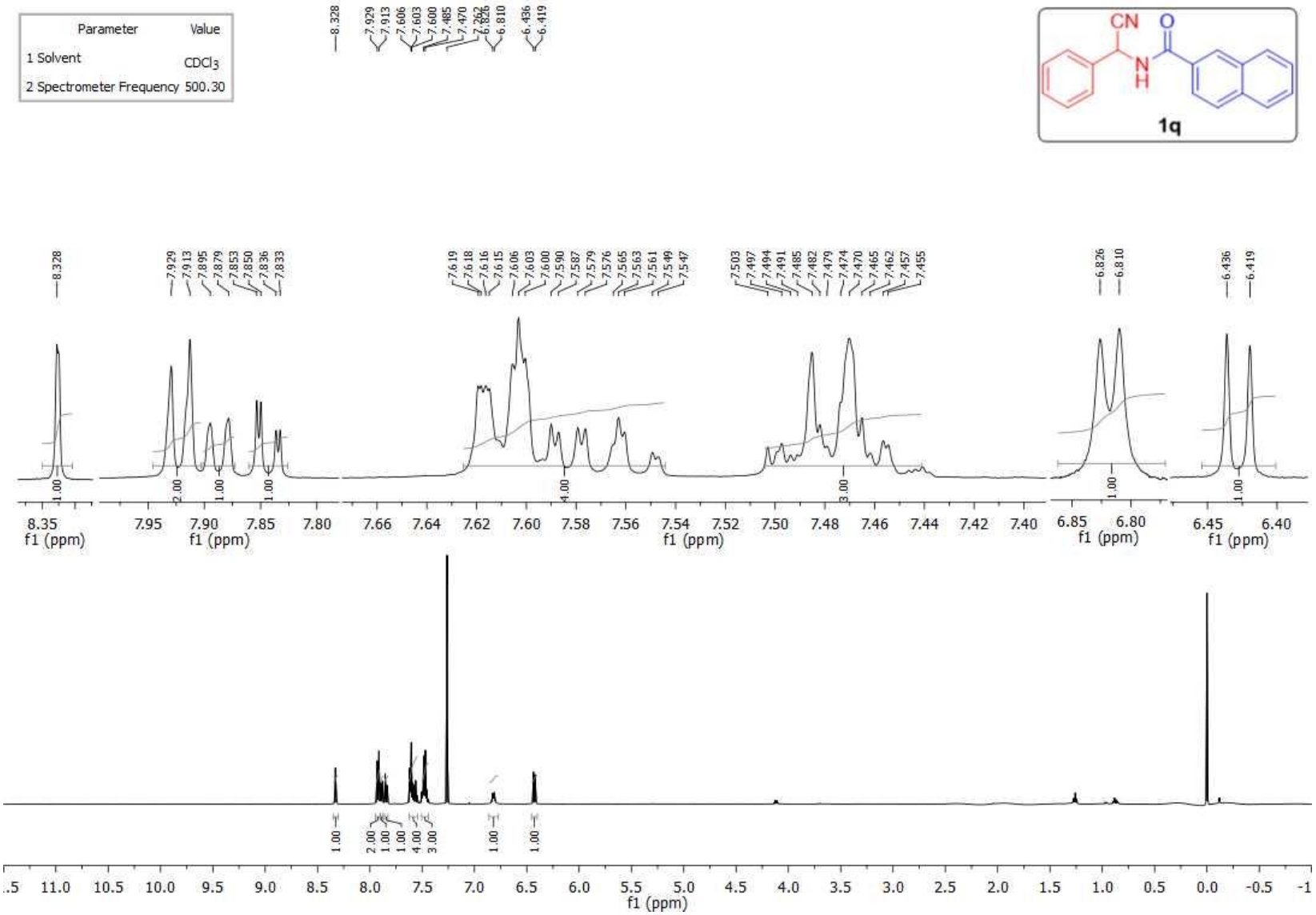


Fig. S43. [1]H NMR spectra of *N*-(cyano(phenyl)methyl)-2-naphthamide **(1q).**

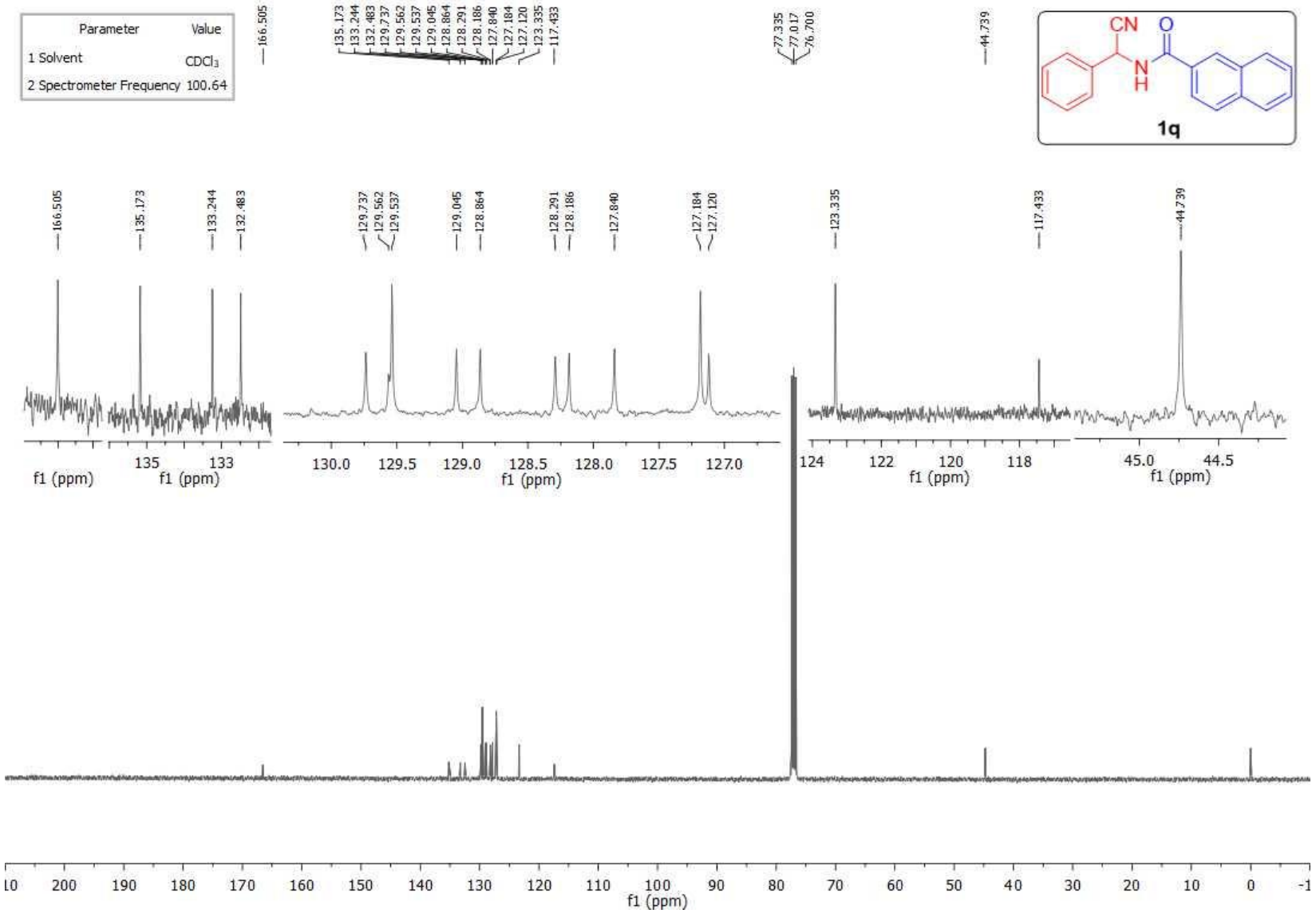
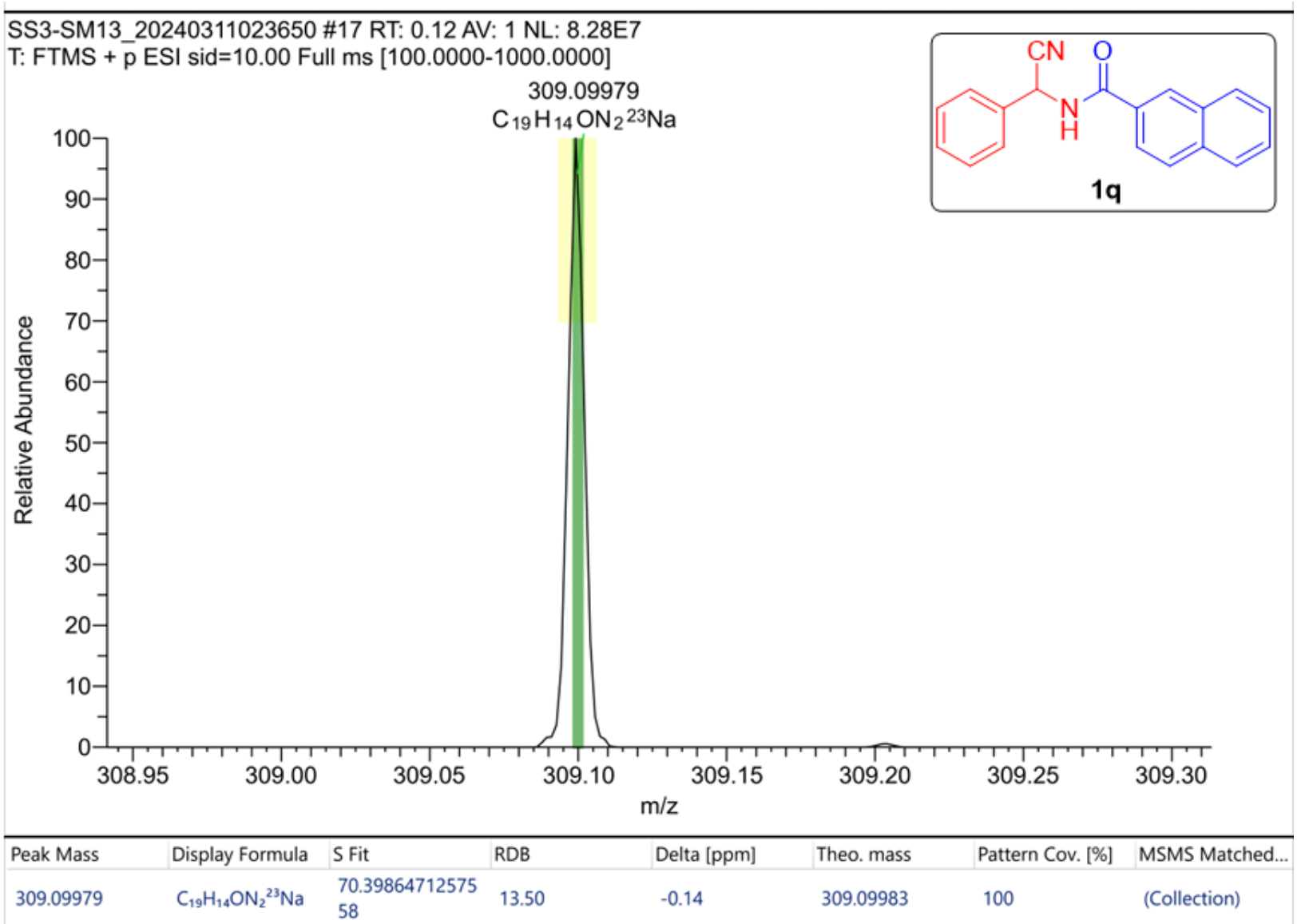


Fig. S44. ^{13}C NMR spectra of *N*-(cyano(phenyl)methyl)-2-naphthamide **(1q).**



Peak Mass	Display Formula	S Fit	RDB	Delta [ppm]	Theo. mass	Pattern Cov. [%]	MSMS Matched...
309.09979	$C_{19}H_{14}ON_2{}^{23}Na$	70.3986471257558	13.50	-0.14	309.09983	100	(Collection)

Fig. S45. HRMS data of *N*-(cyano(phenyl)methyl)-2-naphthamide **(1q).**

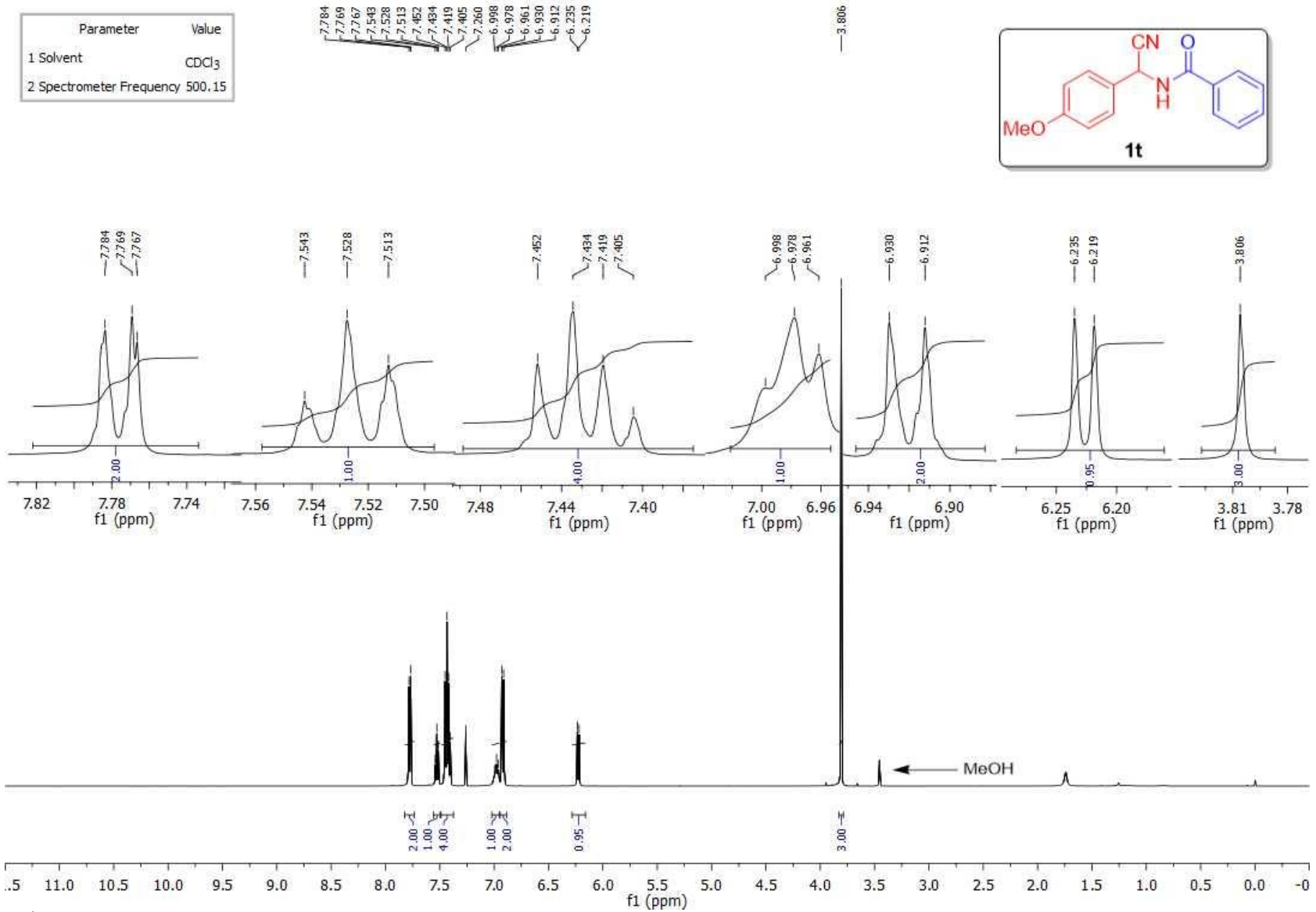


Fig. S46. ^{1}H NMR spectra of *N*-(cyano(4-methoxyphenyl)methyl)benzamide **(1t).**

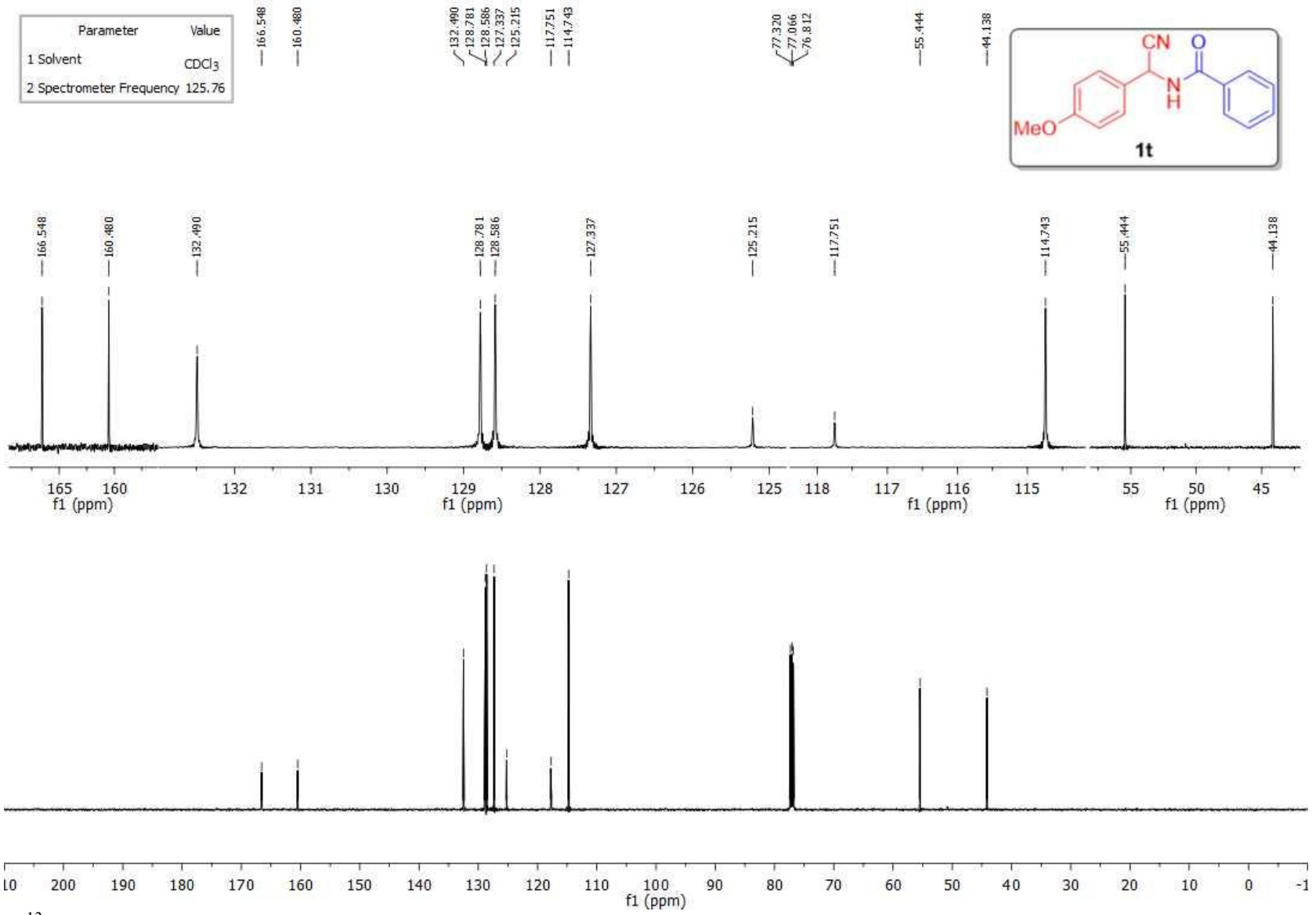


Fig. S47. ^{13}C NMR spectra of *N*-(cyano(4-methoxyphenyl)methyl)benzamide **(1t).**

Sample Name	4 OME CN_MeOH_Positive	**Position**		**Instrument Name**	CY-E-HRMS-01
User Name		**Inj Vol**	Unknown / Injection Program	**InjPosition**	
Sample Type	Sample	**IRM Calibration Status**	Success	**Data Filename**	4 OME CN_MeOH_Positive.d
ACQ Method	TEST.m	**Comment**		**Acquired Time**	4/1/2026 11:53:59 AM (UTC+05:30)

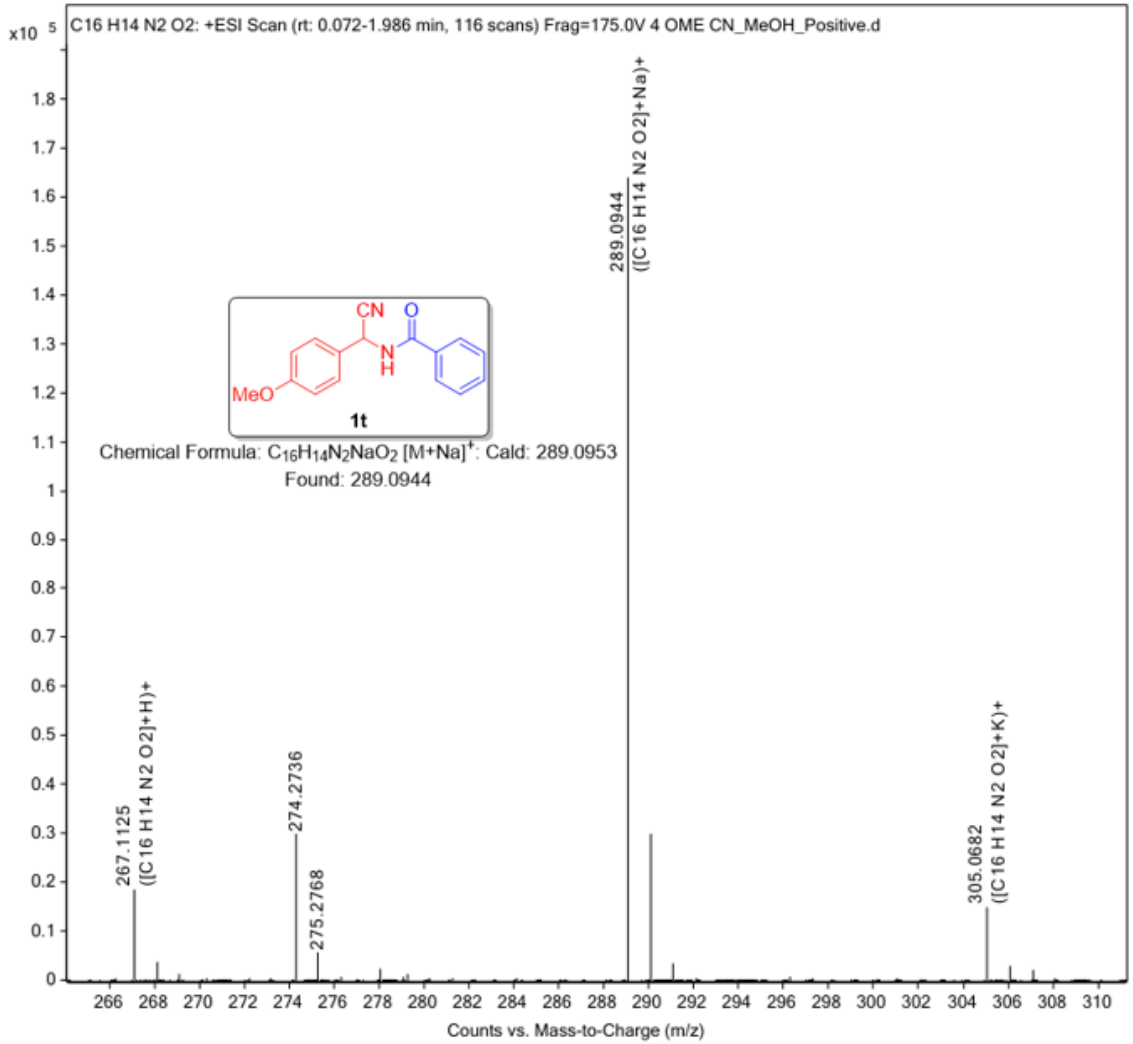


Fig. S48. HRMS data of *N*-(cyano(4-methoxyphenyl)methyl)benzamide **(1t).**

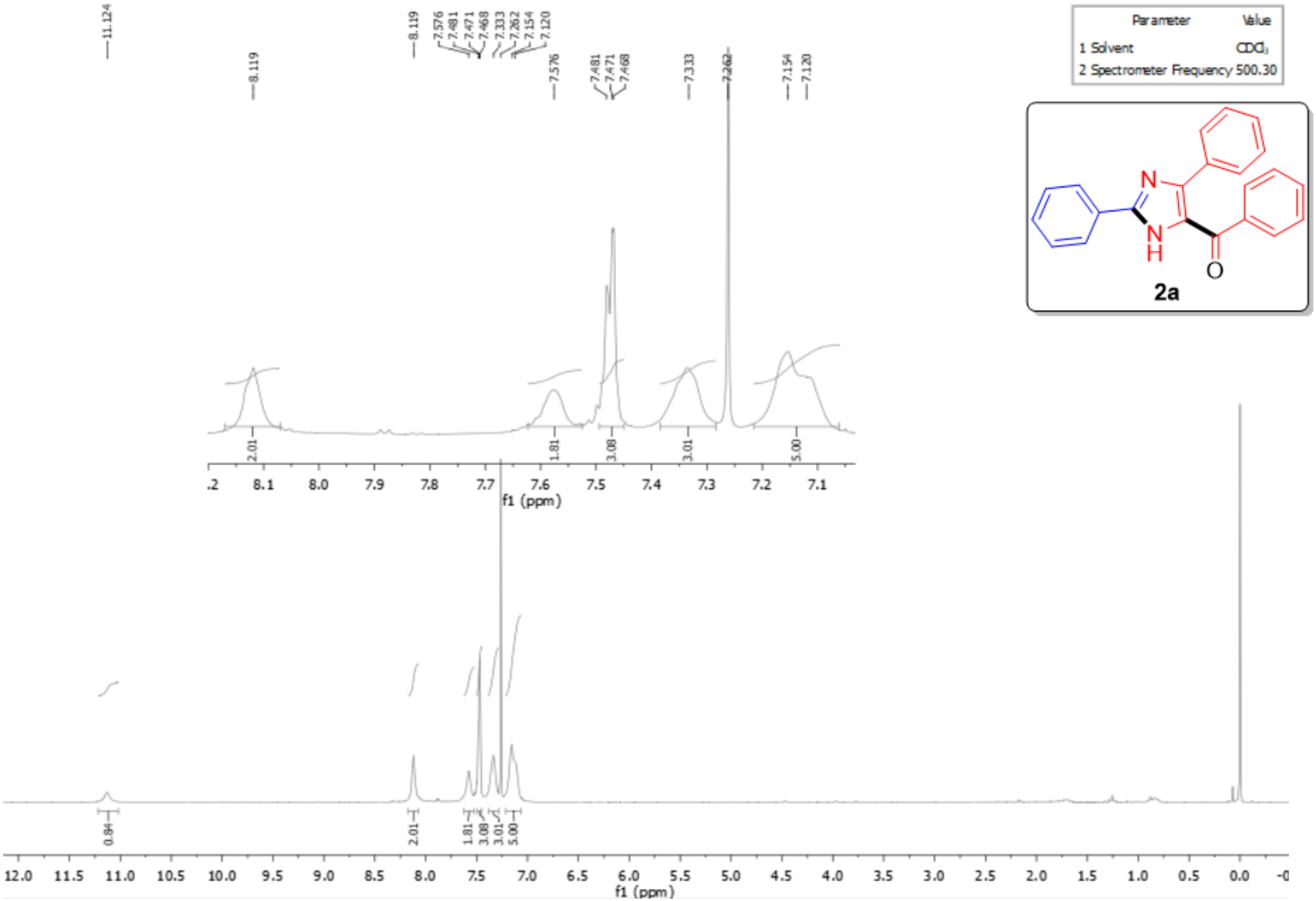


Fig. S49. ^{1}H NMR spectra of (2,4-diphenyl-1*H*-imidazol-5-yl)(phenyl)methanone **(2a).**

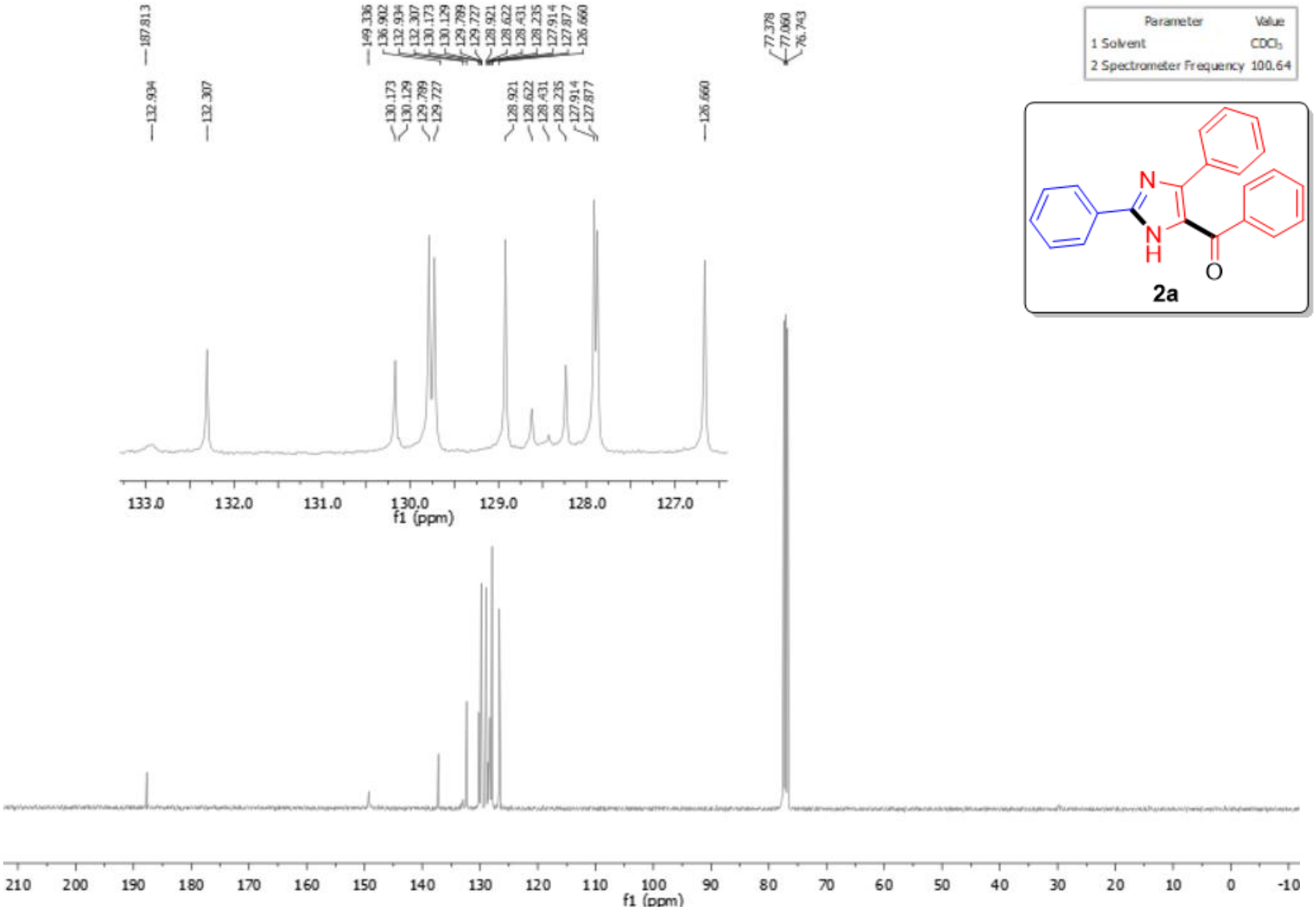


Fig. S50. ^{13}C NMR spectra of (2,4-diphenyl-1*H*-imidazol-5-yl)(phenyl)methanone **(2a).**

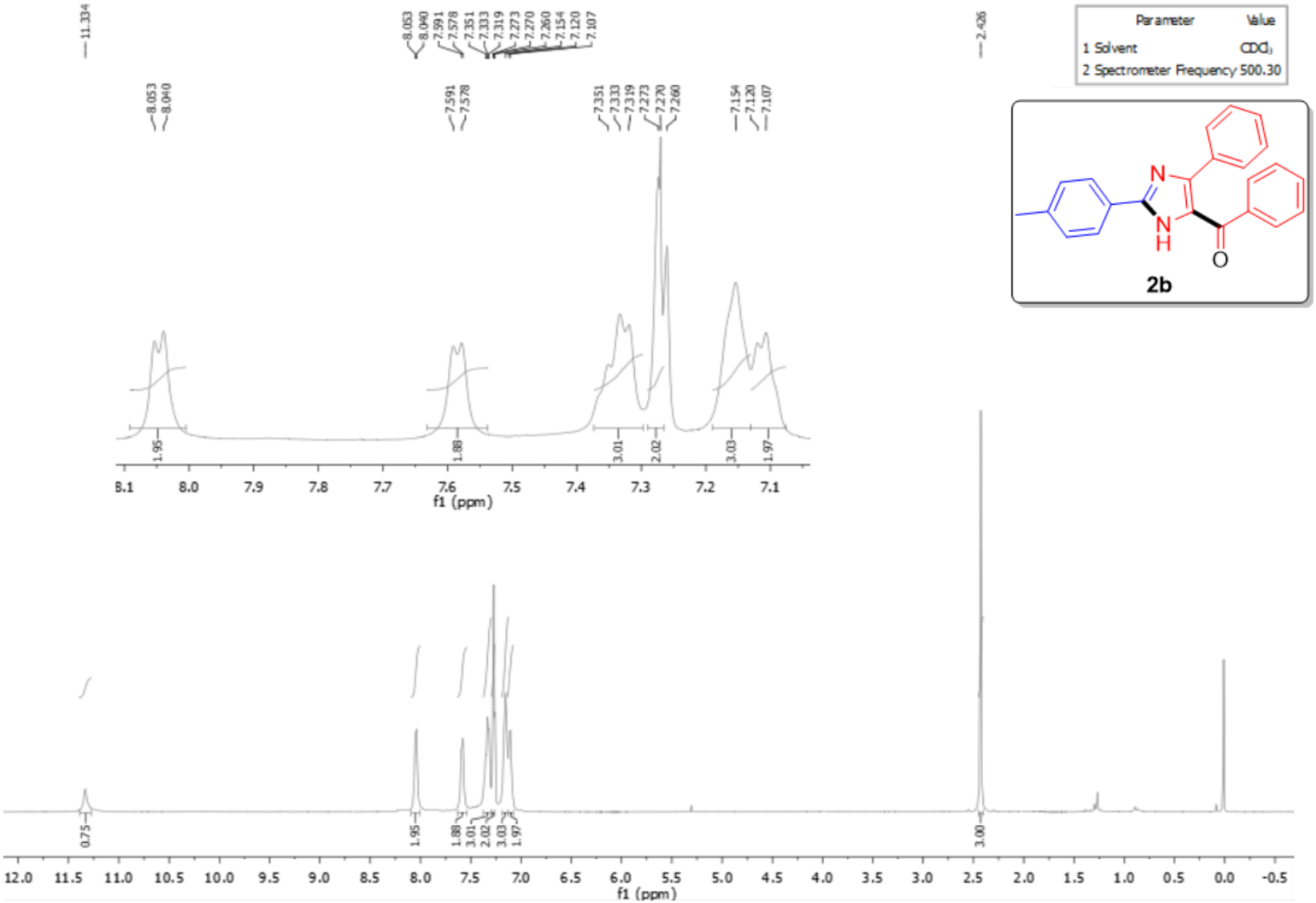


Fig. S51. [1]H NMR spectra of phenyl(4-phenyl-2-(*p*-tolyl)-1*H*-imidazol-5-yl)methanone **(2b).**

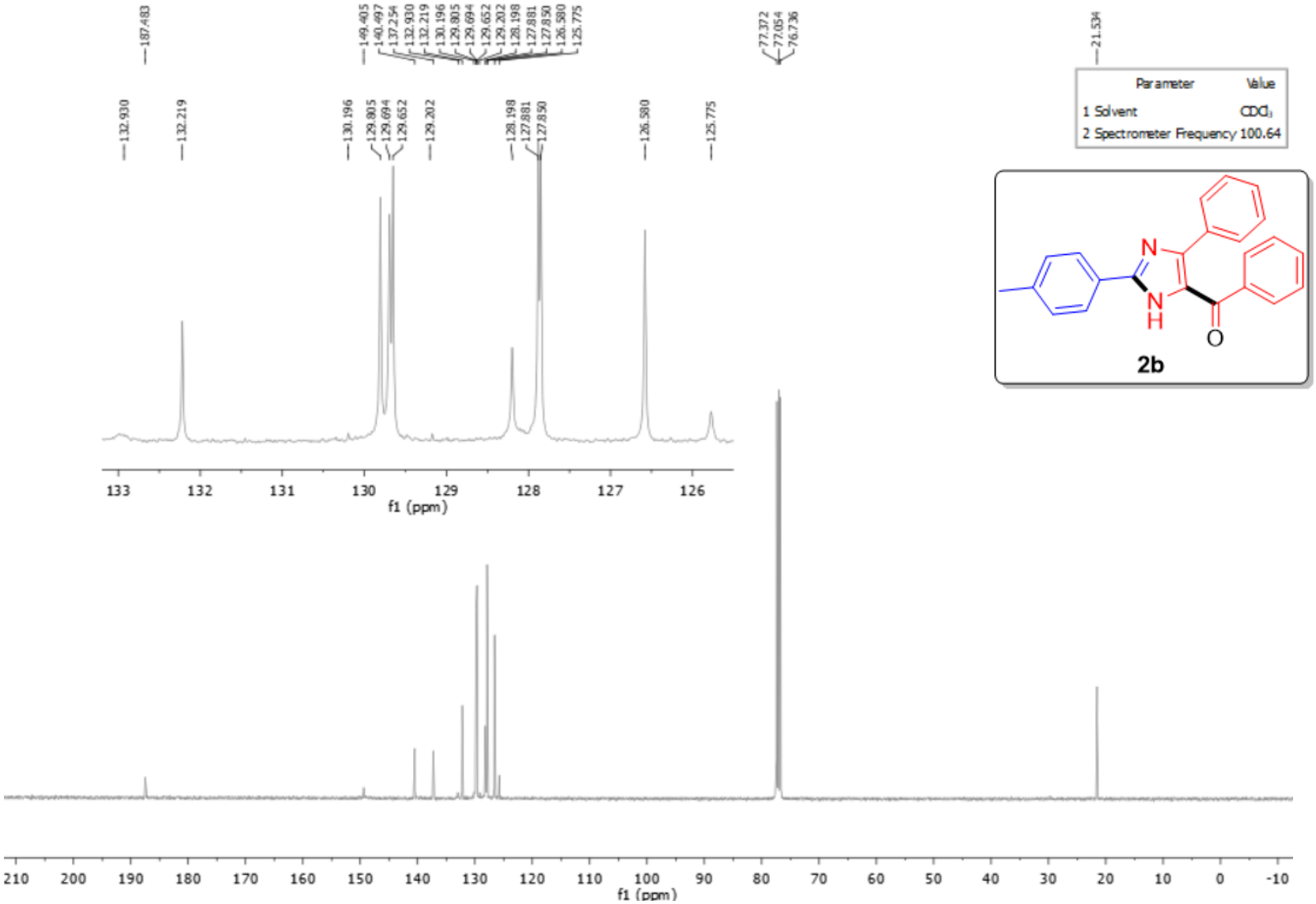


Fig. S52. ^{13}C NMR spectra of phenyl(4-phenyl-2-(*p*-tolyl)-1*H*-imidazol-5-yl)methanone **(2b).**

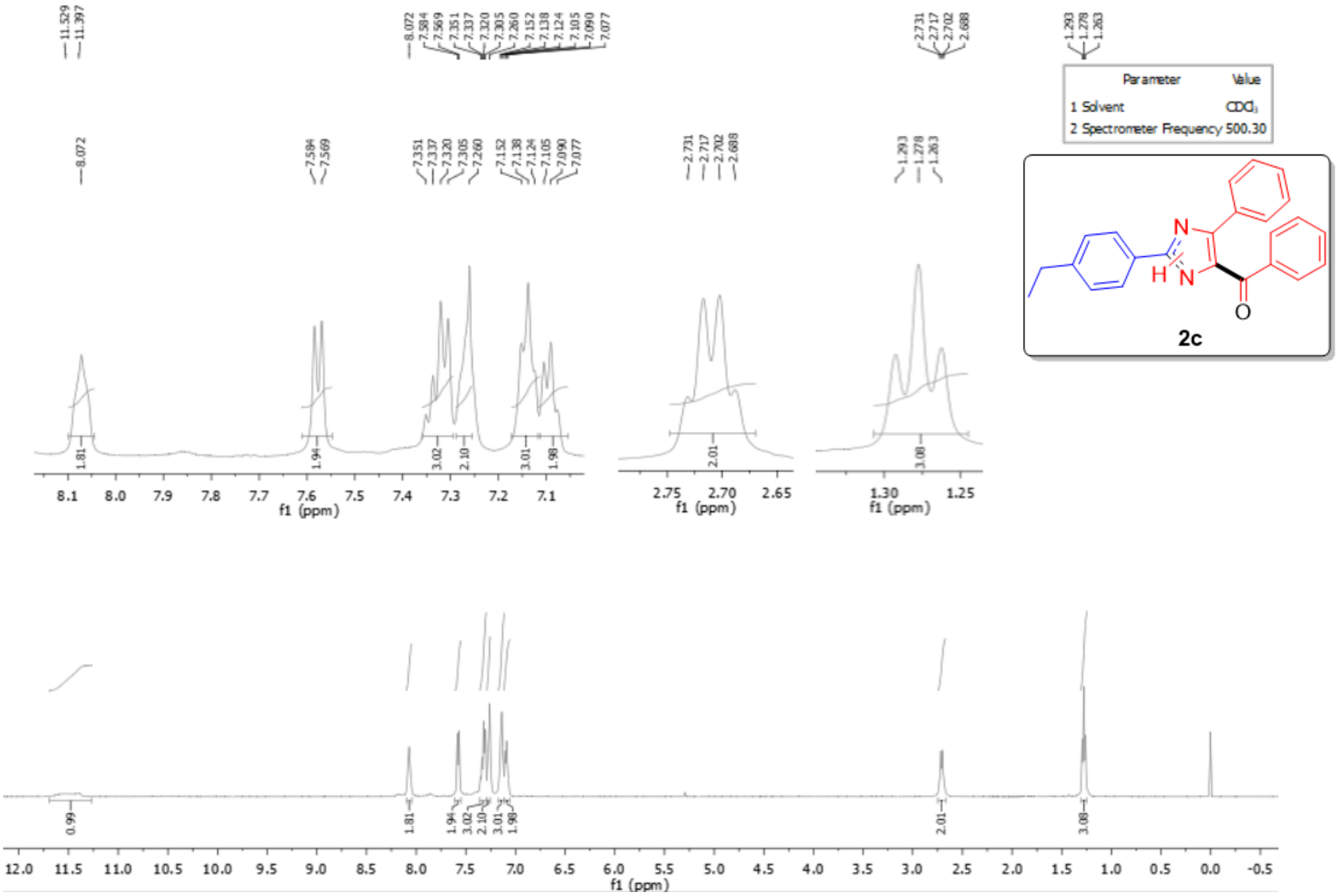


Fig. S53. [1]H NMR spectra of (2-(4-ethylphenyl)-4-phenyl-1*H*-imidazol-5-yl)(phenyl)methanone **(2c).**

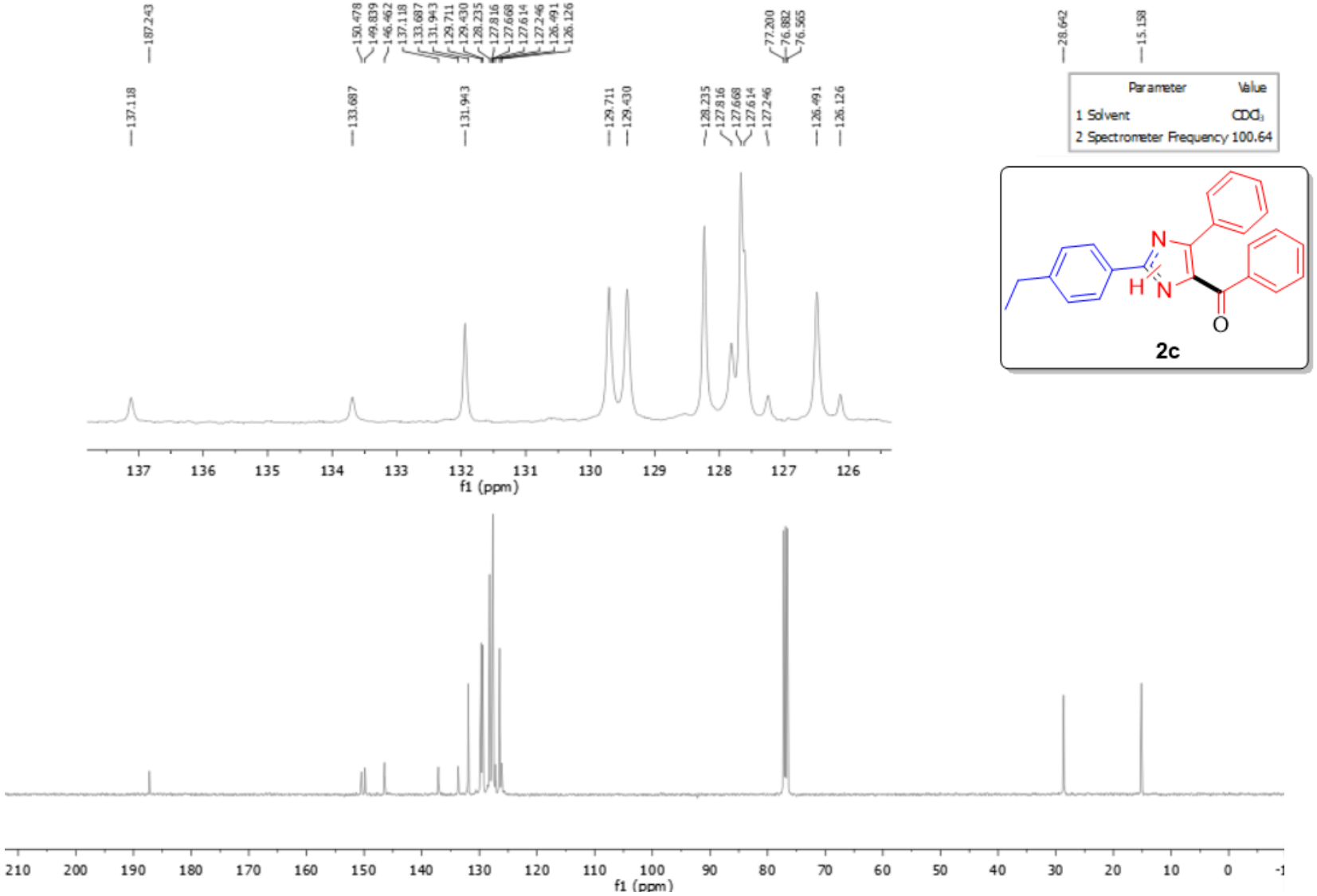
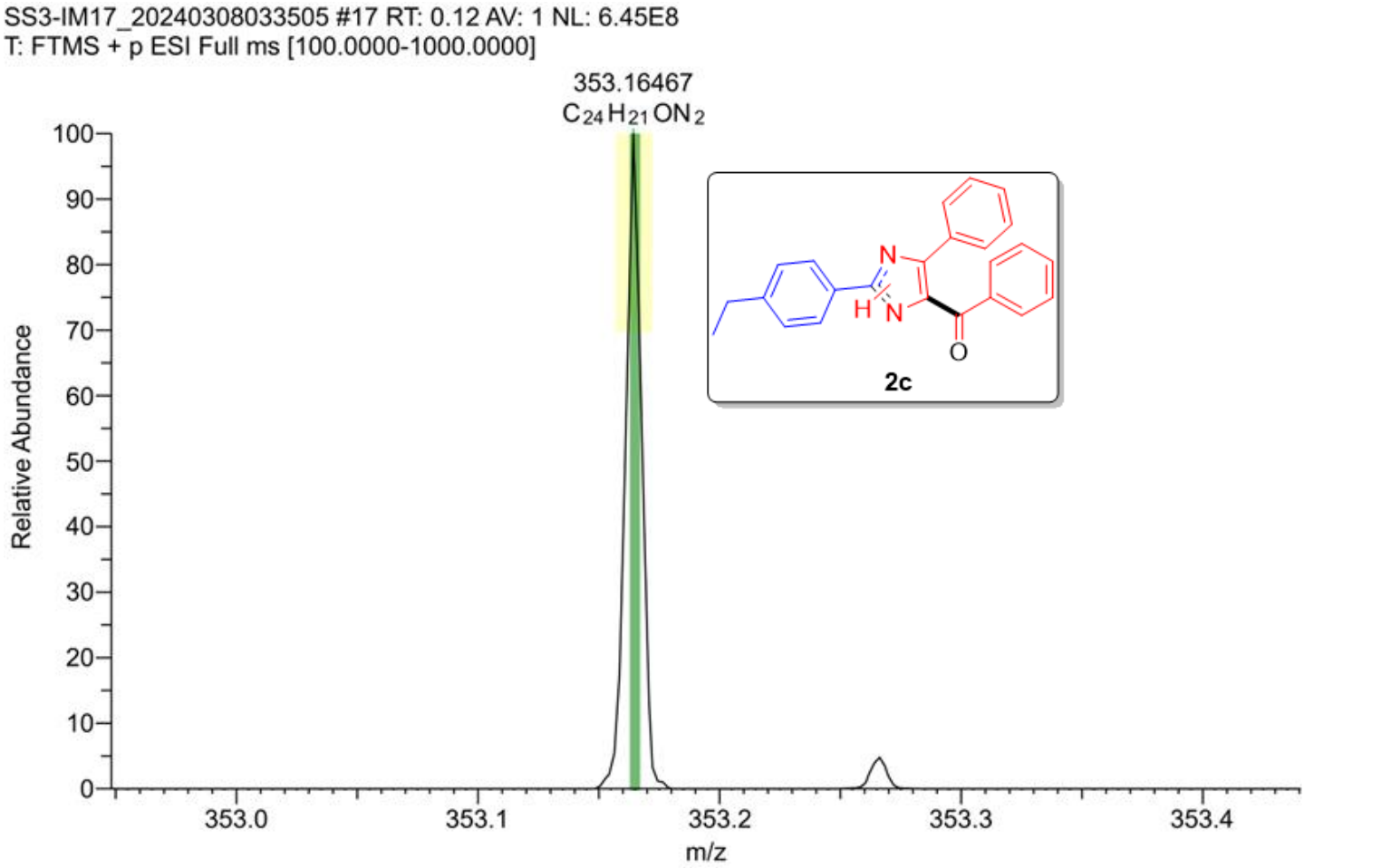


Fig. S54. ^{13}C NMR spectra of (2-(4-ethylphenyl)-4-phenyl-1*H*-imidazol-5-yl)(phenyl)methanone **(2c).**



Peak Mass	Display Formula	S Fit	RDB	Delta [ppm]	Theo. mass	Pattern Cov. [%]	MSMS Matched...
353.16467	$C_{24}H_{21}ON_2$	87.3560596768266	15.50	-0.47	353.16484	100	(Collection)

Fig. S55. HRMS data of (2-(4-ethylphenyl)-4-phenyl-1*H*-imidazol-5-yl)(phenyl)methanone **(2c).**

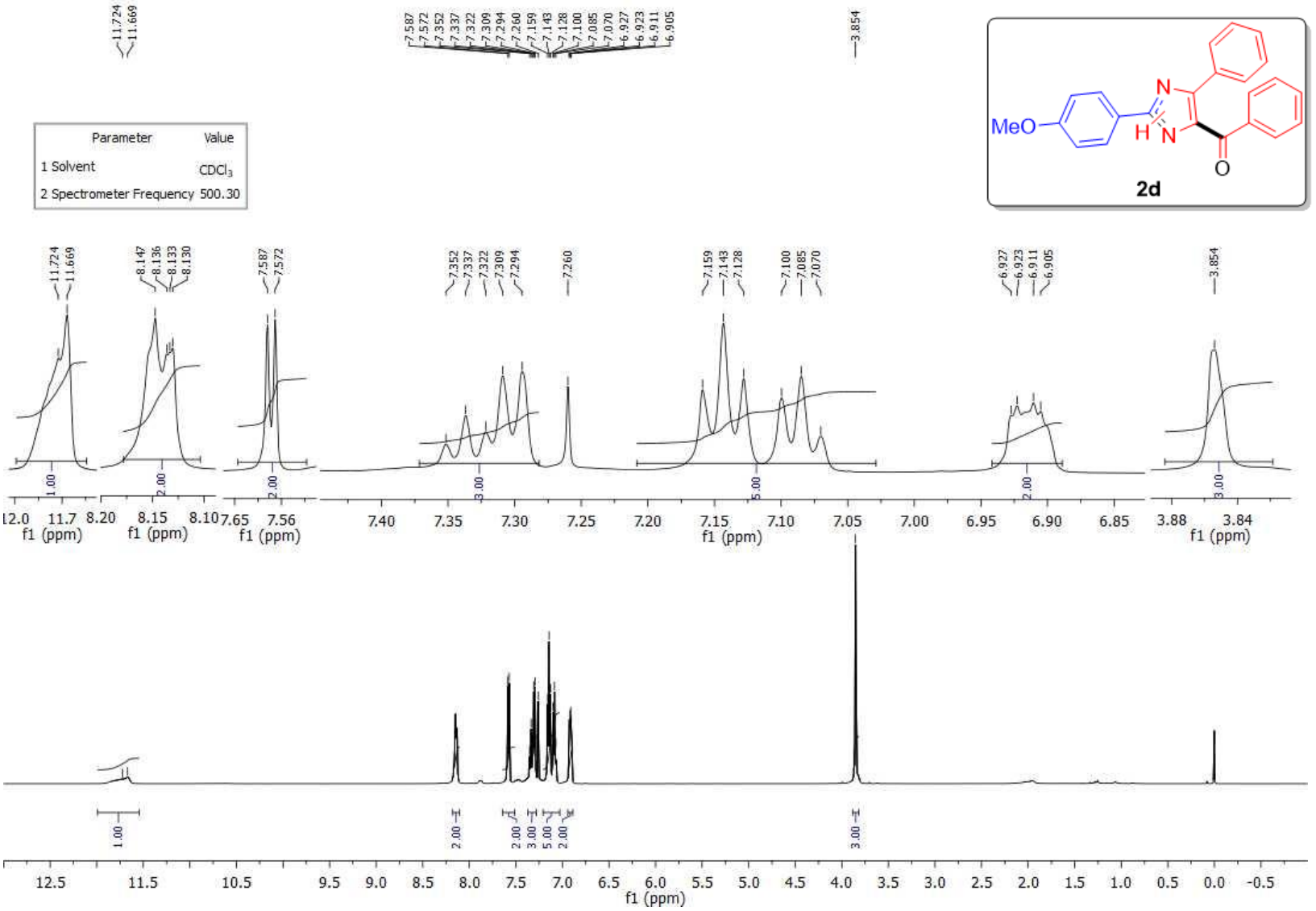


Fig. S56. ^{1}H NMR spectra of (2-(4-methoxyphenyl)-4-phenyl-1*H*-imidazol-5-yl)(phenyl)methanone **(2d).**

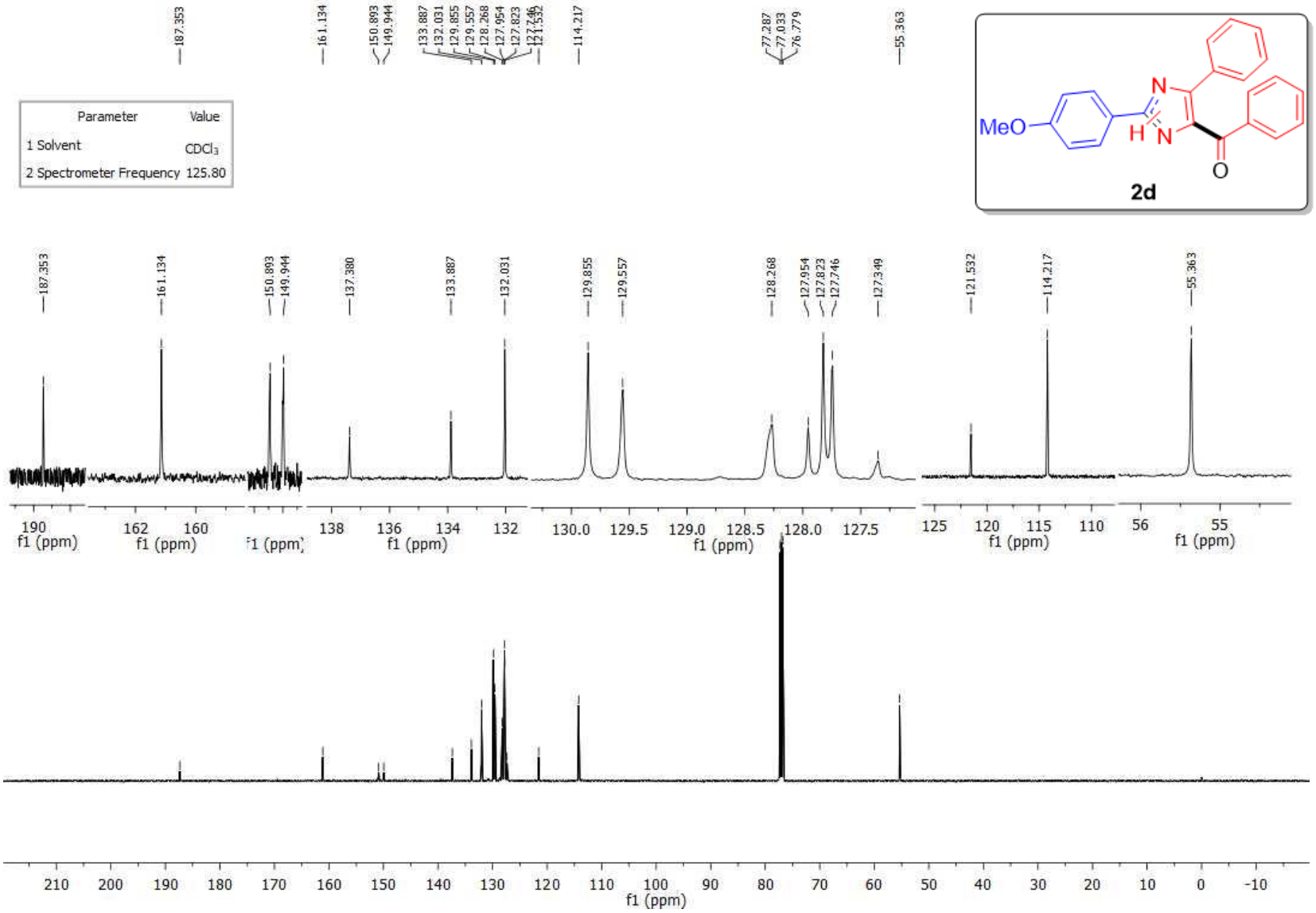
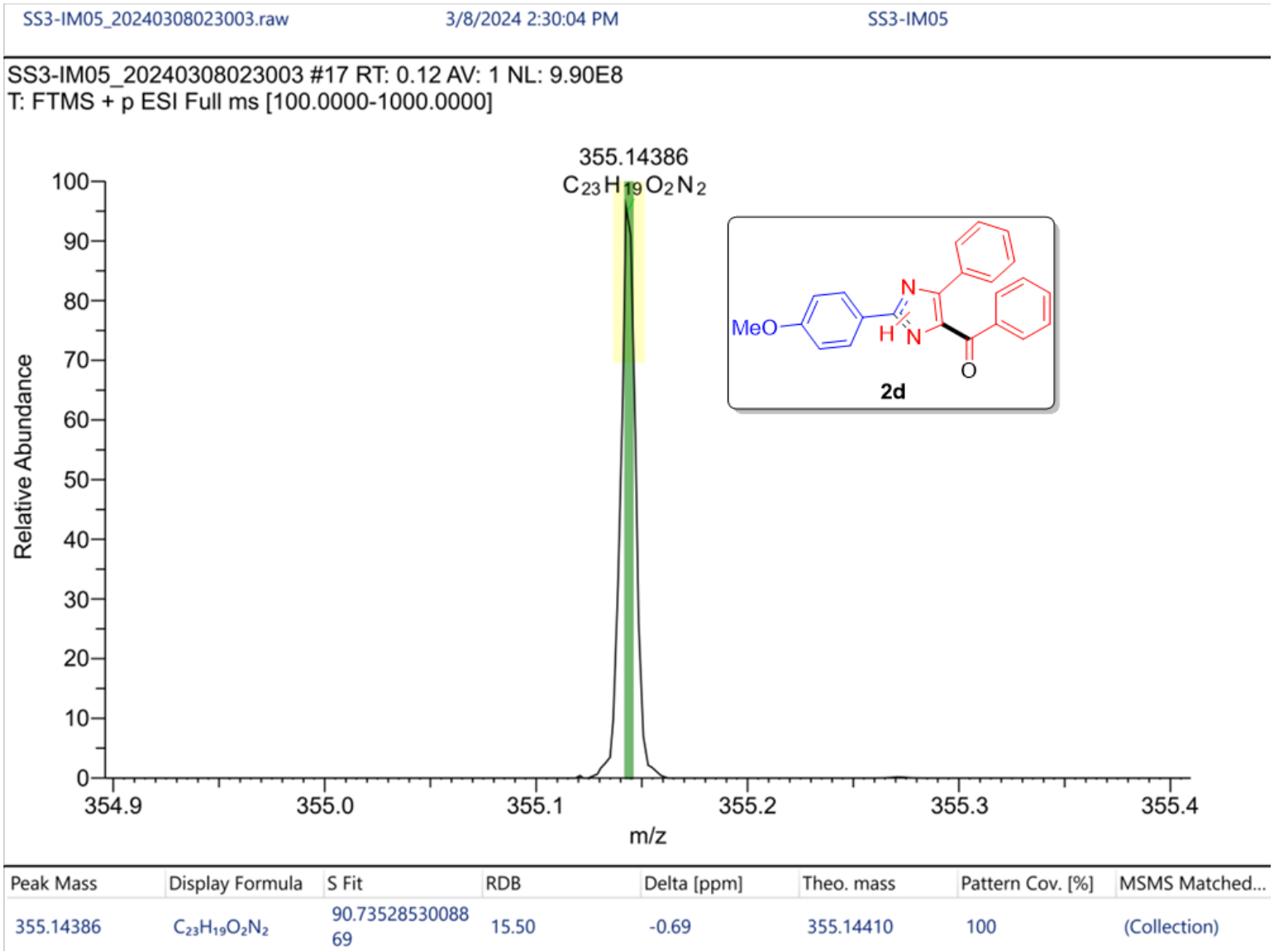


Fig. S57. ^{13}C NMR spectra of (2-(4-methoxyphenyl)-4-phenyl-1*H*-imidazol-5-yl)(phenyl)methanone **(2d).**



Peak Mass	Display Formula	S Fit	RDB	Delta [ppm]	Theo. mass	Pattern Cov. [%]	MSMS Matched...
355.14386	$C_{23}H_{19}O_2N_2$	90.7352853008869	15.50	-0.69	355.14410	100	(Collection)

Fig. S58. HRMS data of (2-(4-methoxyphenyl)-4-phenyl-1*H*-imidazol-5-yl)(phenyl)methanone **(2d).**

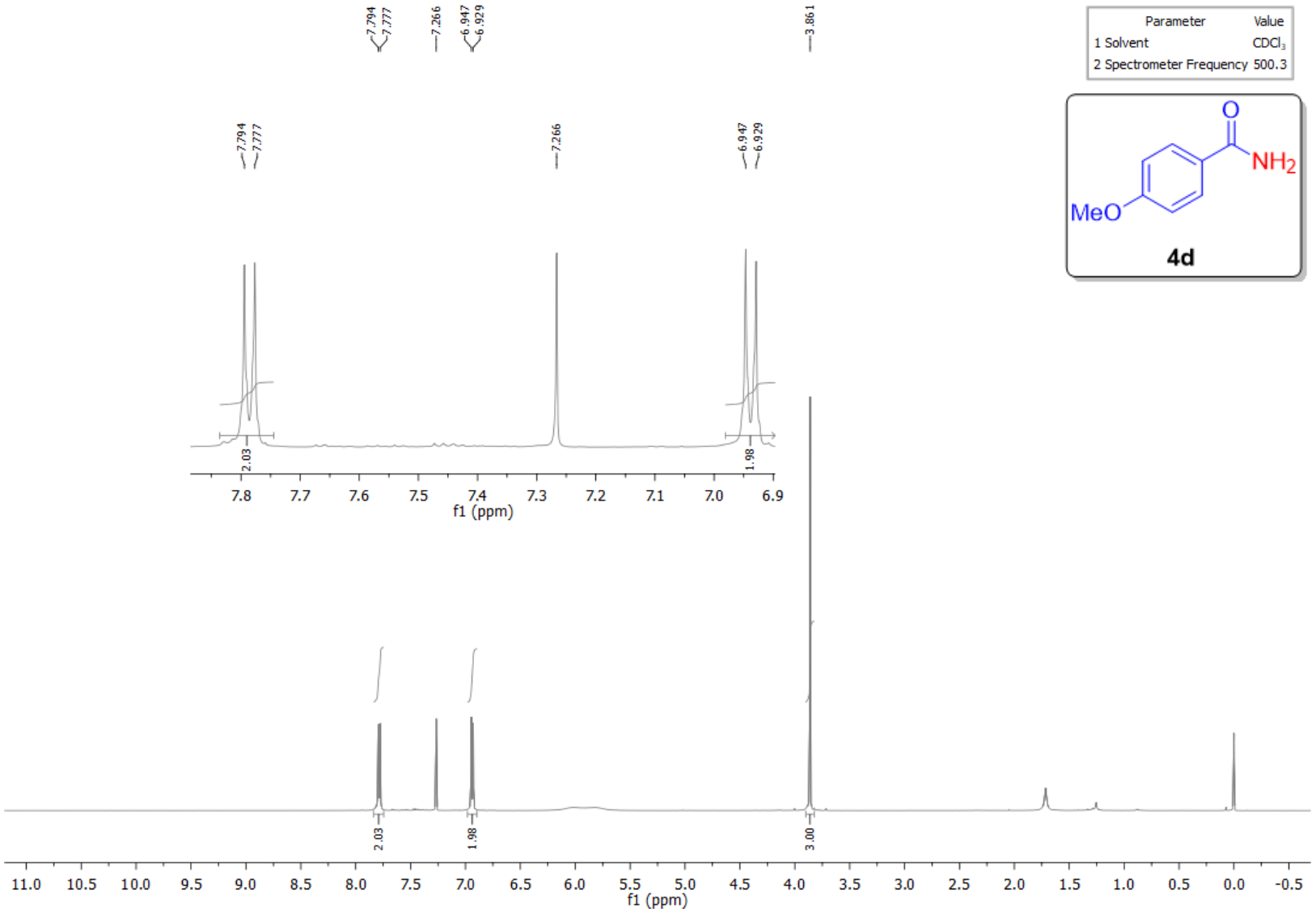


Fig. S59. [1]H NMR spectra of 4-methoxybenzamide **(4d).**

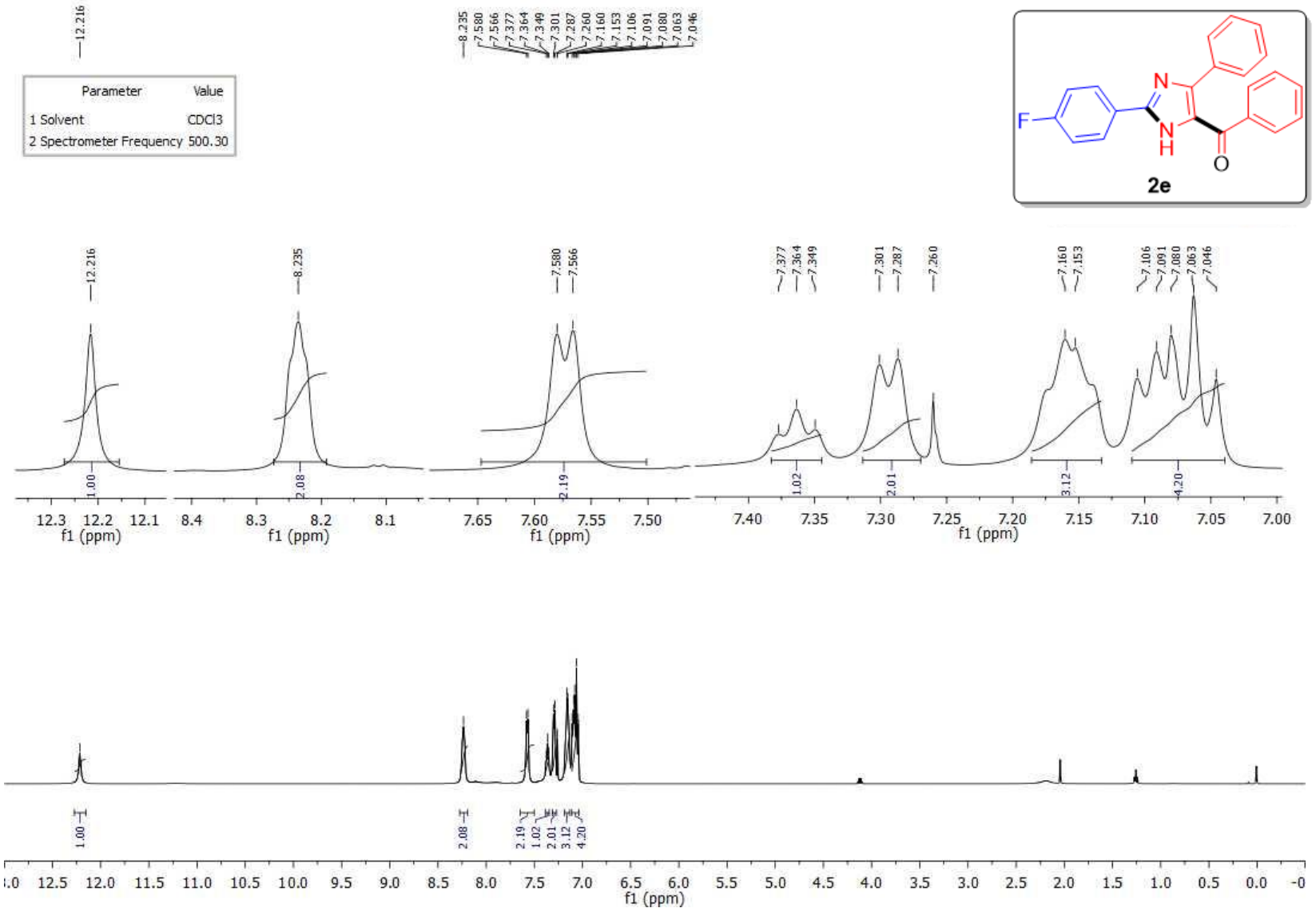


Fig. S60. [1]H NMR spectra of (2-(4-fluorophenyl)-4-phenyl-1*H*-imidazol-5-yl)(phenyl)methanone **(2e).**

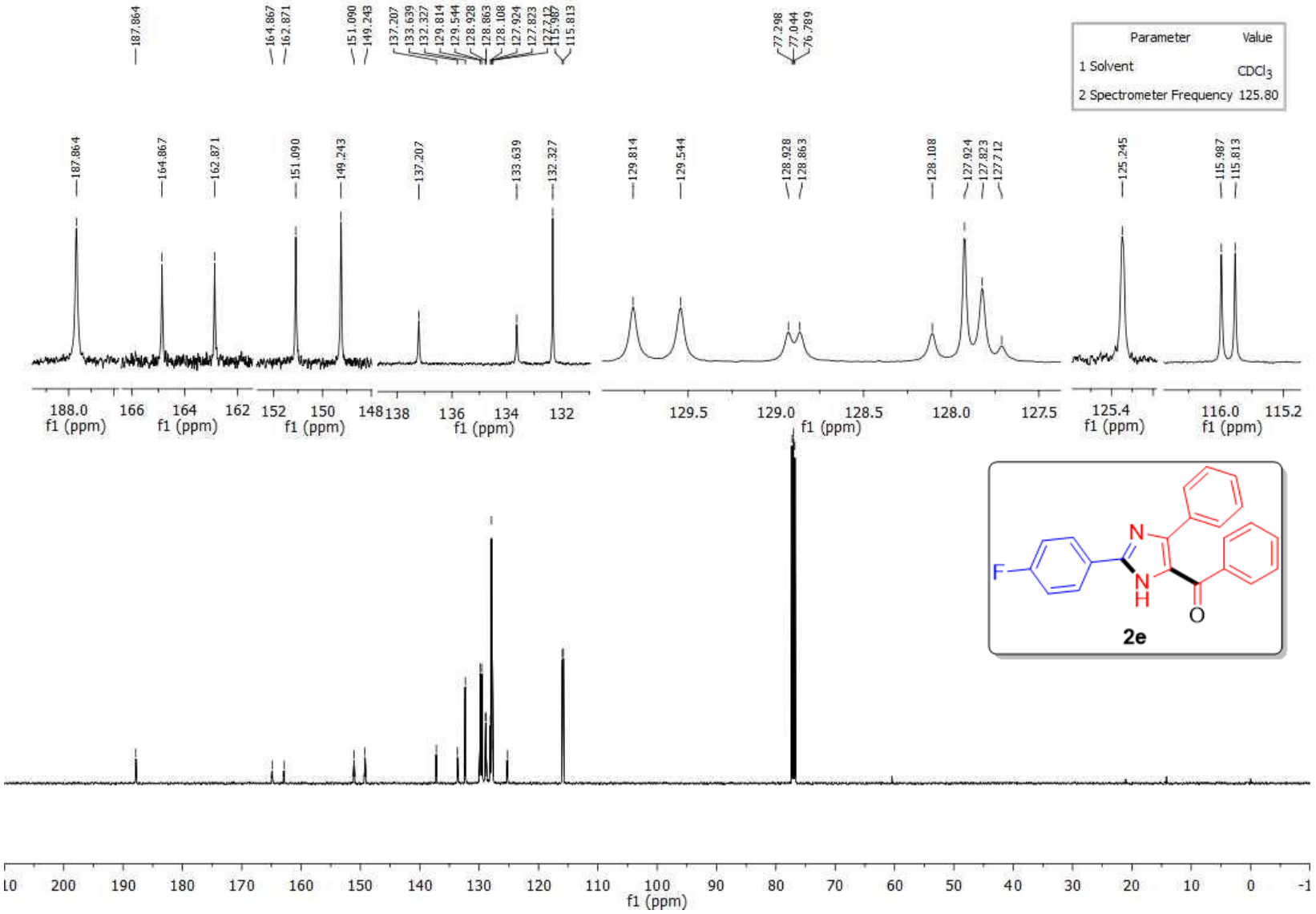


Fig. S61. ^{13}C NMR spectra of (2-(4-fluorophenyl)-4-phenyl-1*H*-imidazol-5-yl)(phenyl)methanone **(2e).**

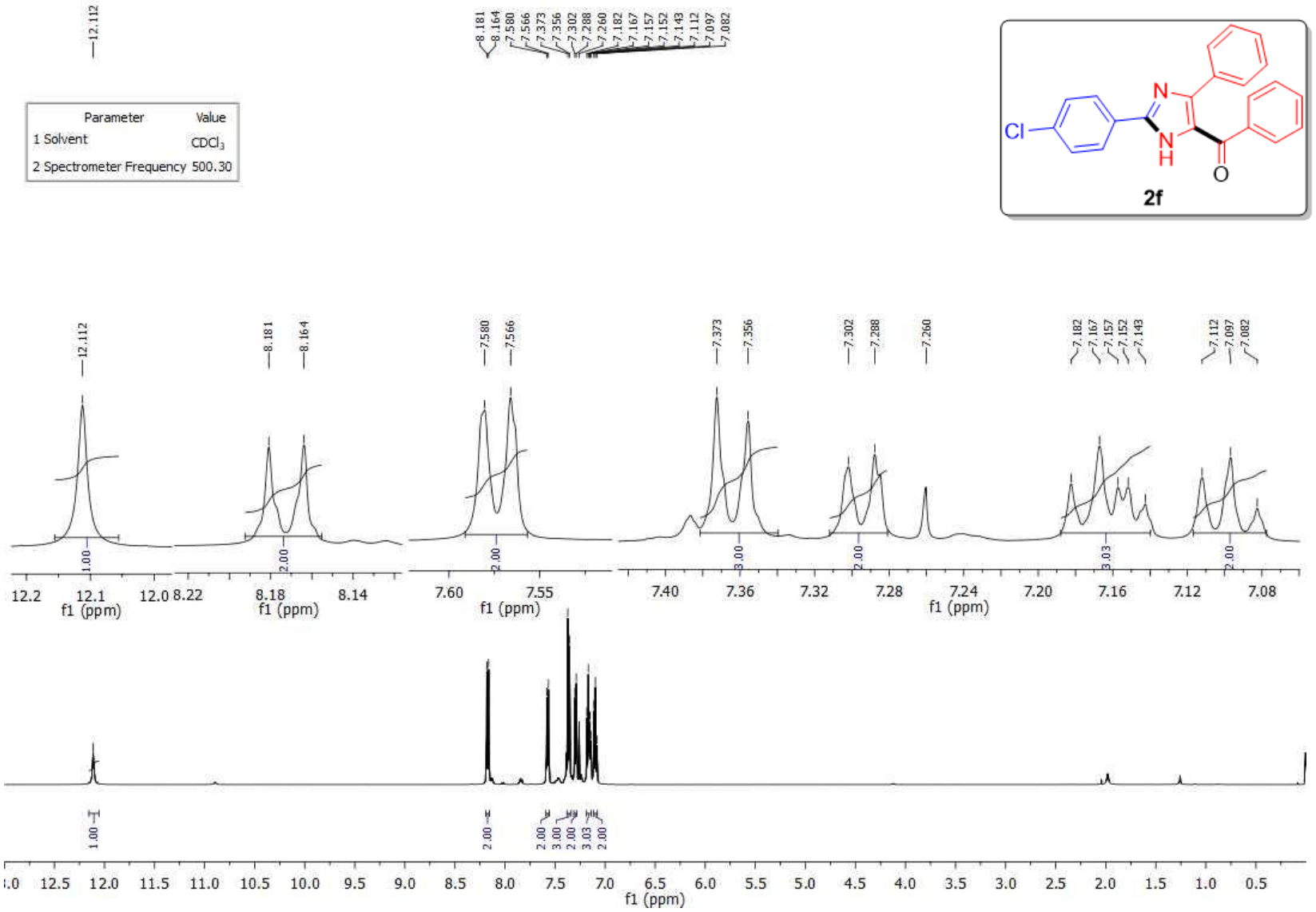


Fig. S62. ^{1}H NMR spectra of (2-(4-chlorophenyl)-4-phenyl-1*H*-imidazol-5-yl)(phenyl)methanone **(2f).**

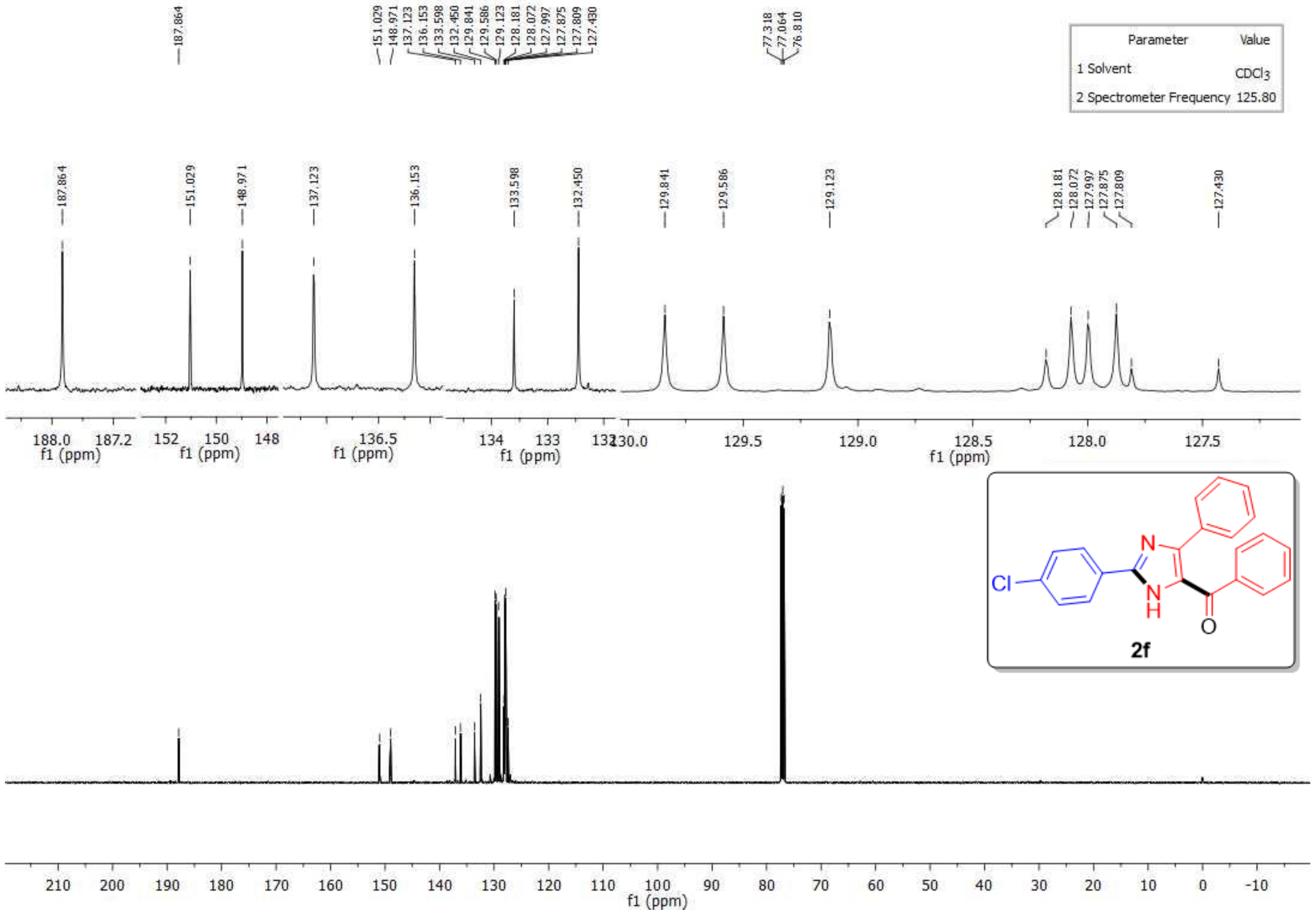


Fig. S63. ^{13}C NMR spectra of (2-(4-chlorophenyl)-4-phenyl-1*H*-imidazol-5-yl)(phenyl)methanone **(2f).**

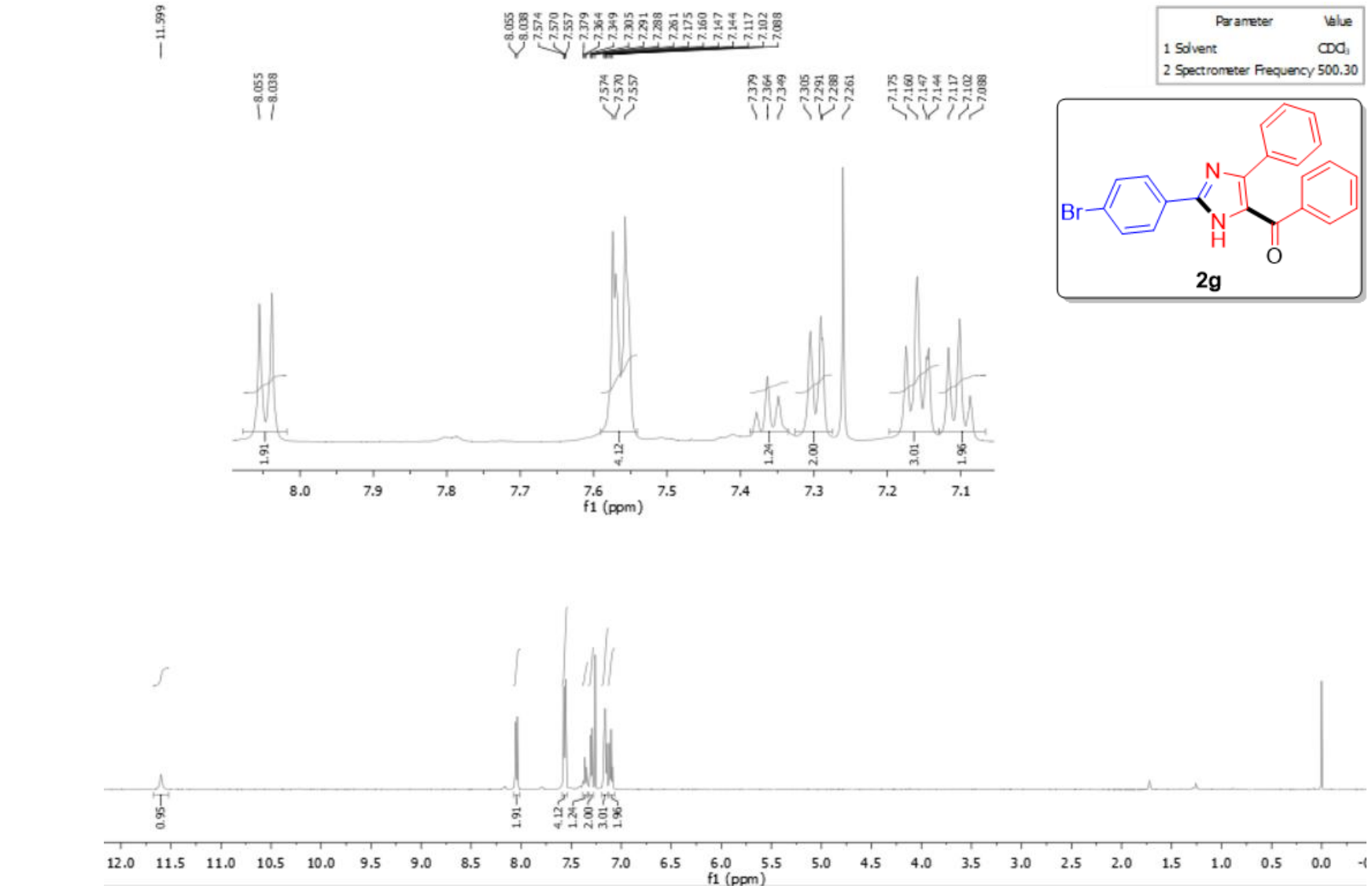


Fig. S64. ^{1}H NMR spectra of (2-(4-bromophenyl)-4-phenyl-1*H*-imidazol-5-yl)(phenyl)methanone **(2g).**

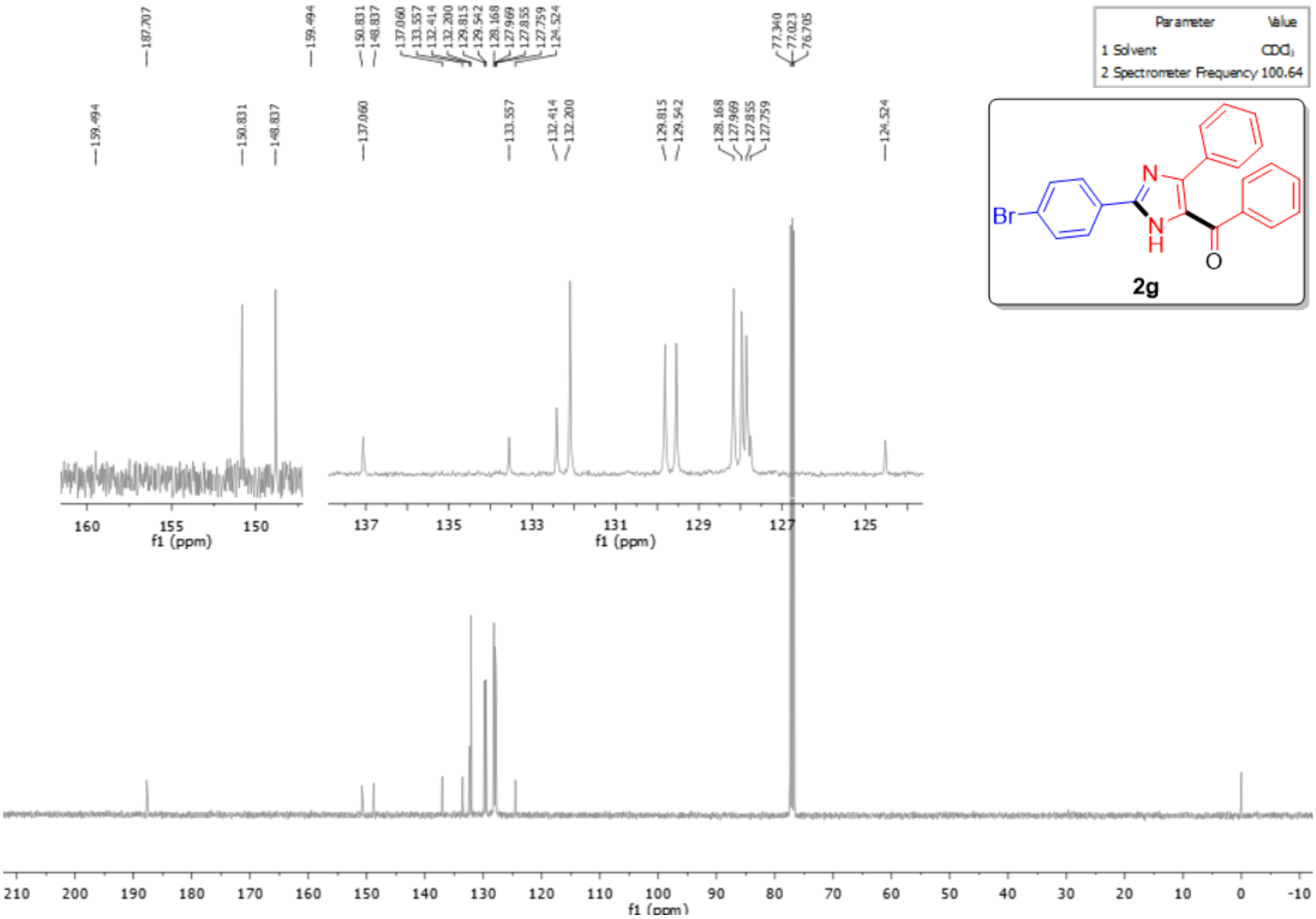


Fig. S65. ^{13}C NMR spectra of (2-(4-bromophenyl)-4-phenyl-1*H*-imidazol-5-yl)(phenyl)methanone **(2g).**

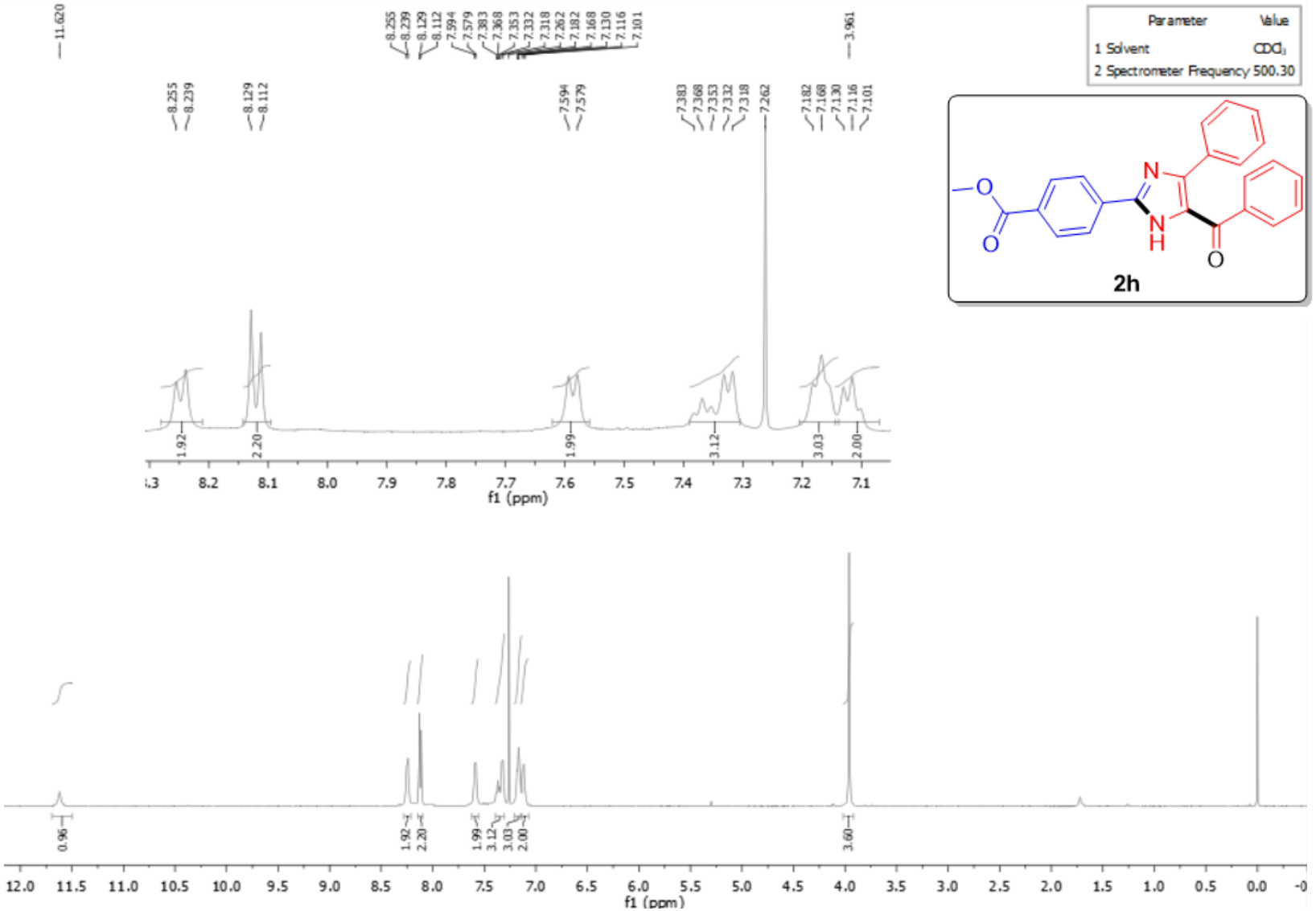


Fig. S66. ^{1}H NMR spectra of methyl 4-(5-benzoyl-4-phenyl-1*H*-imidazol-2-yl)benzoate **(2h).**

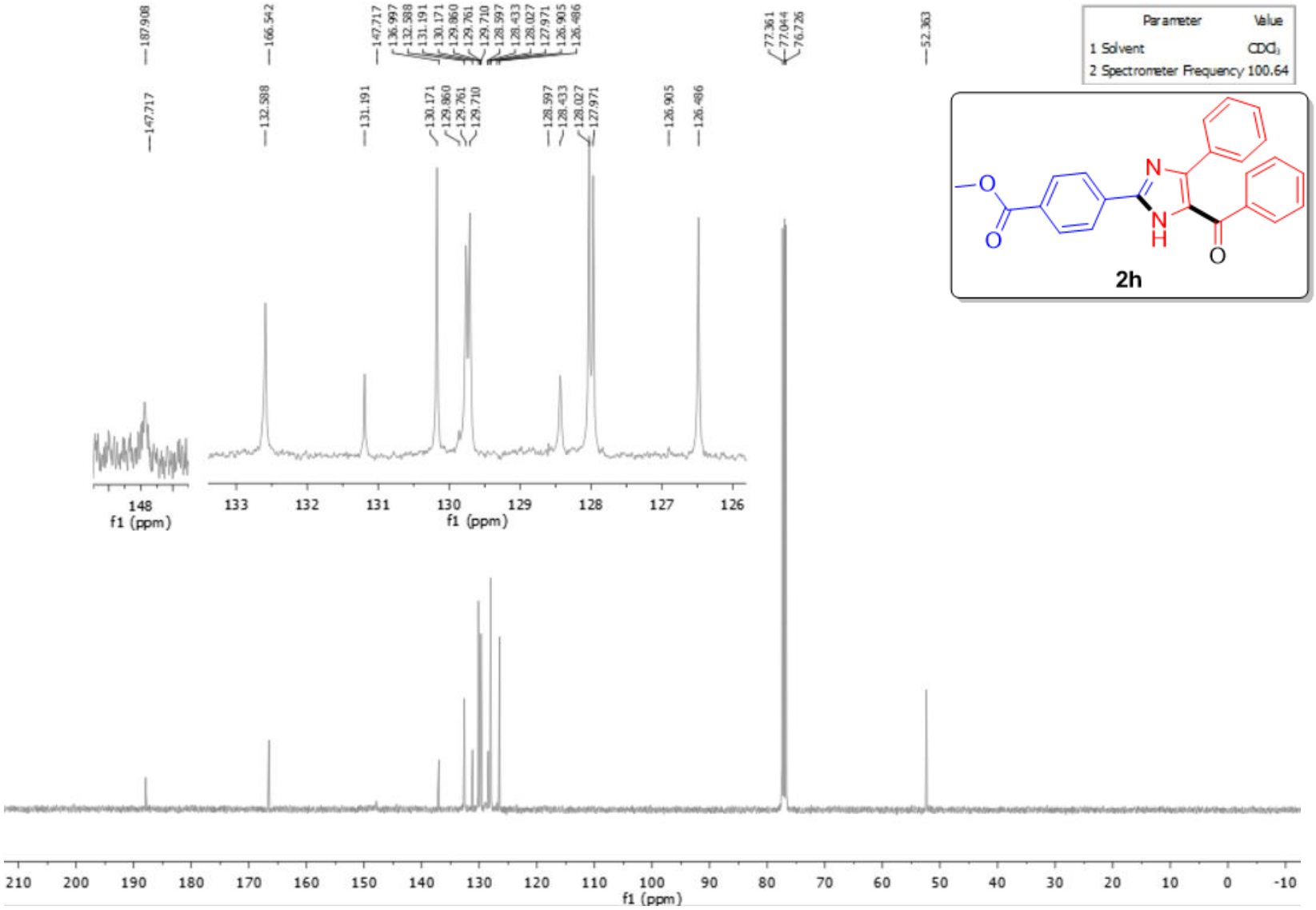


Fig. S67. ^{13}C NMR spectra of methyl 4-(5-benzoyl-4-phenyl-1*H*-imidazol-2-yl)benzoate **(2h).**

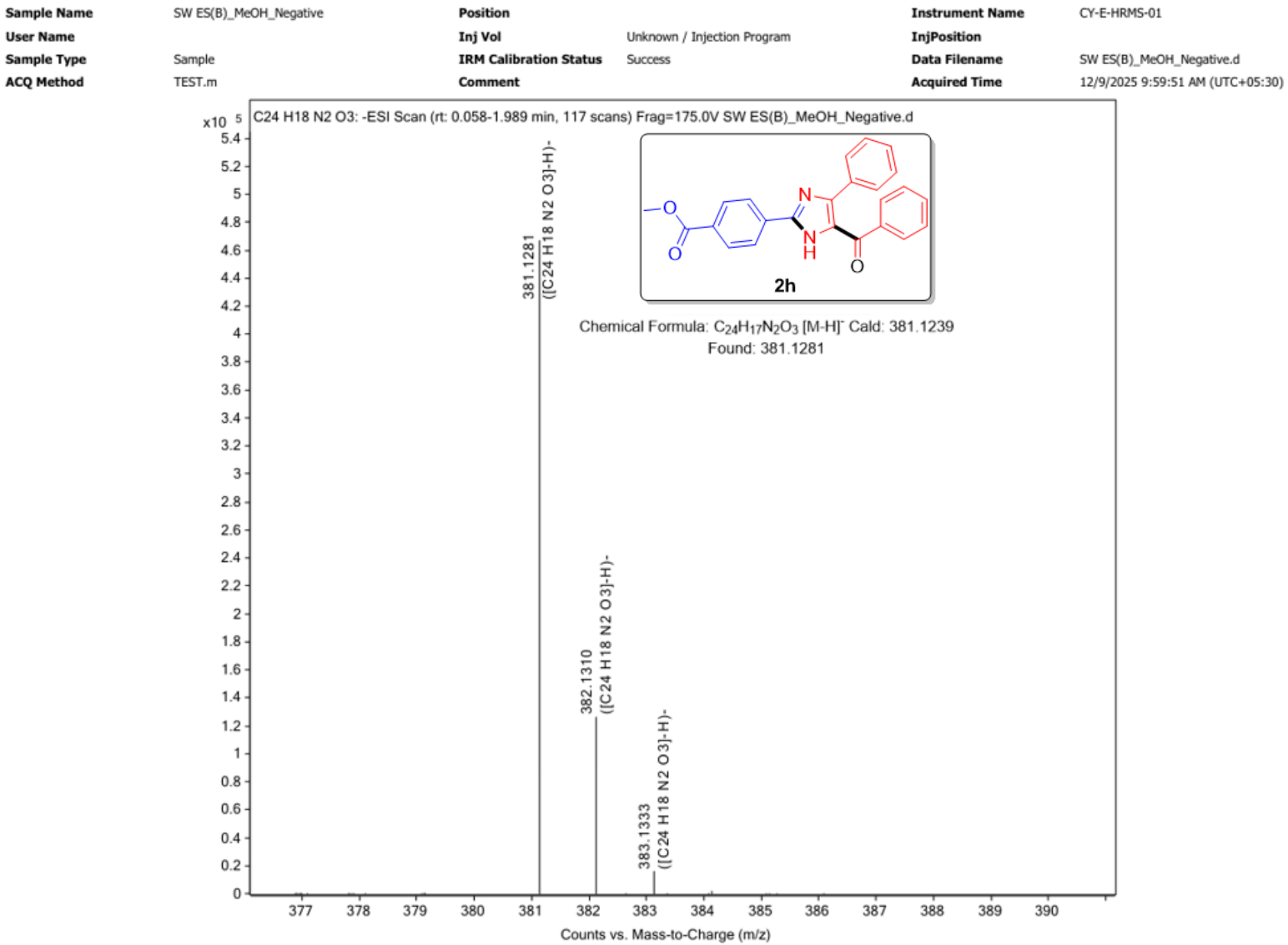


Fig. S68. HRMS data of methyl 4-(5-benzoyl-4-phenyl-1*H*-imidazol-2-yl)benzoate **(2h).**

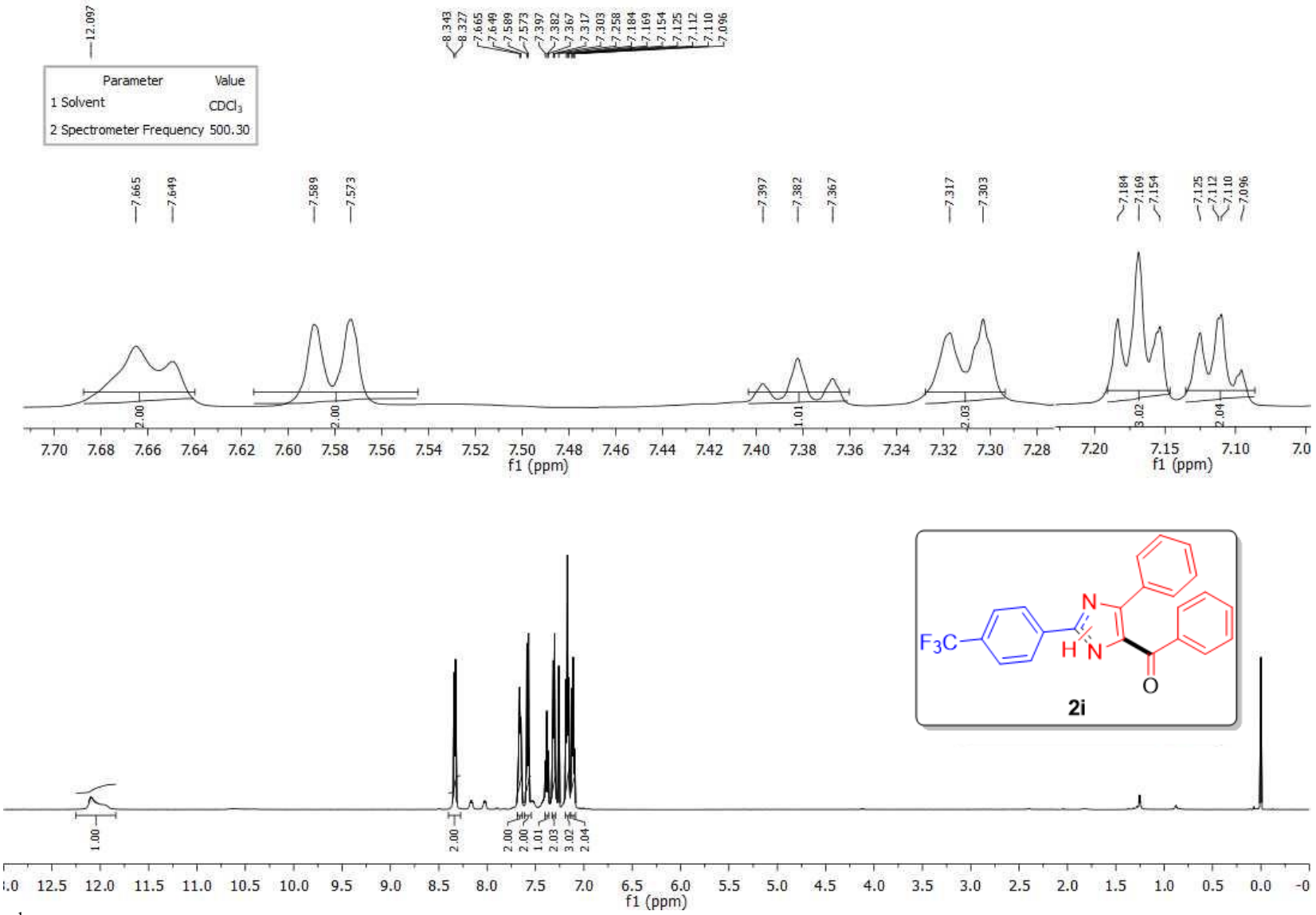


Fig. S69. [1]H NMR spectra of phenyl(4-phenyl-2-(4-(trifluoromethyl)phenyl)-1*H*-imidazol-5-yl)methanone **(2i).**

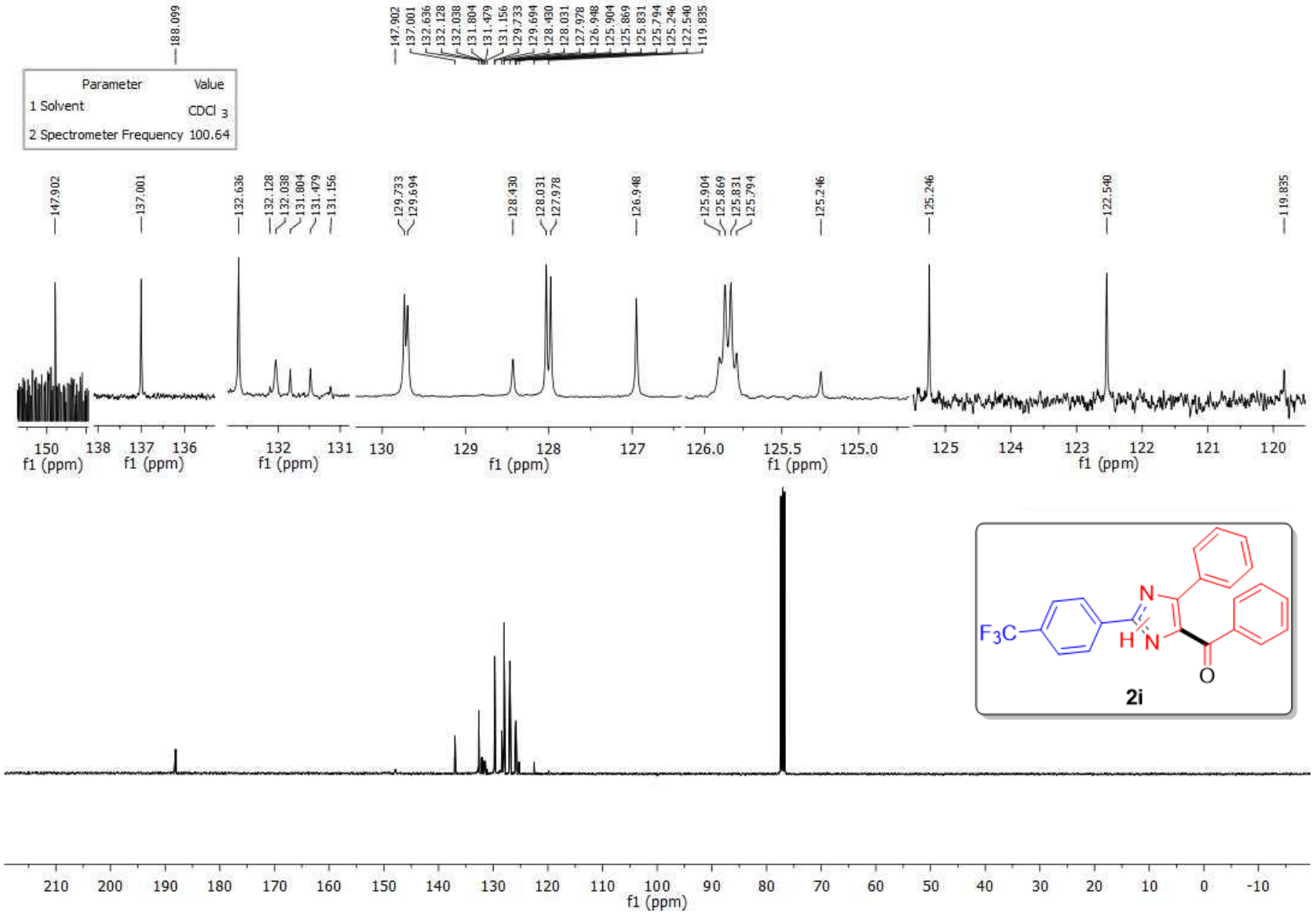


Fig. S70. ^{13}C NMR spectra of phenyl(4-phenyl-2-(4-(trifluoromethyl)phenyl)-1*H*-imidazol-5-yl)methanone **(2i).**

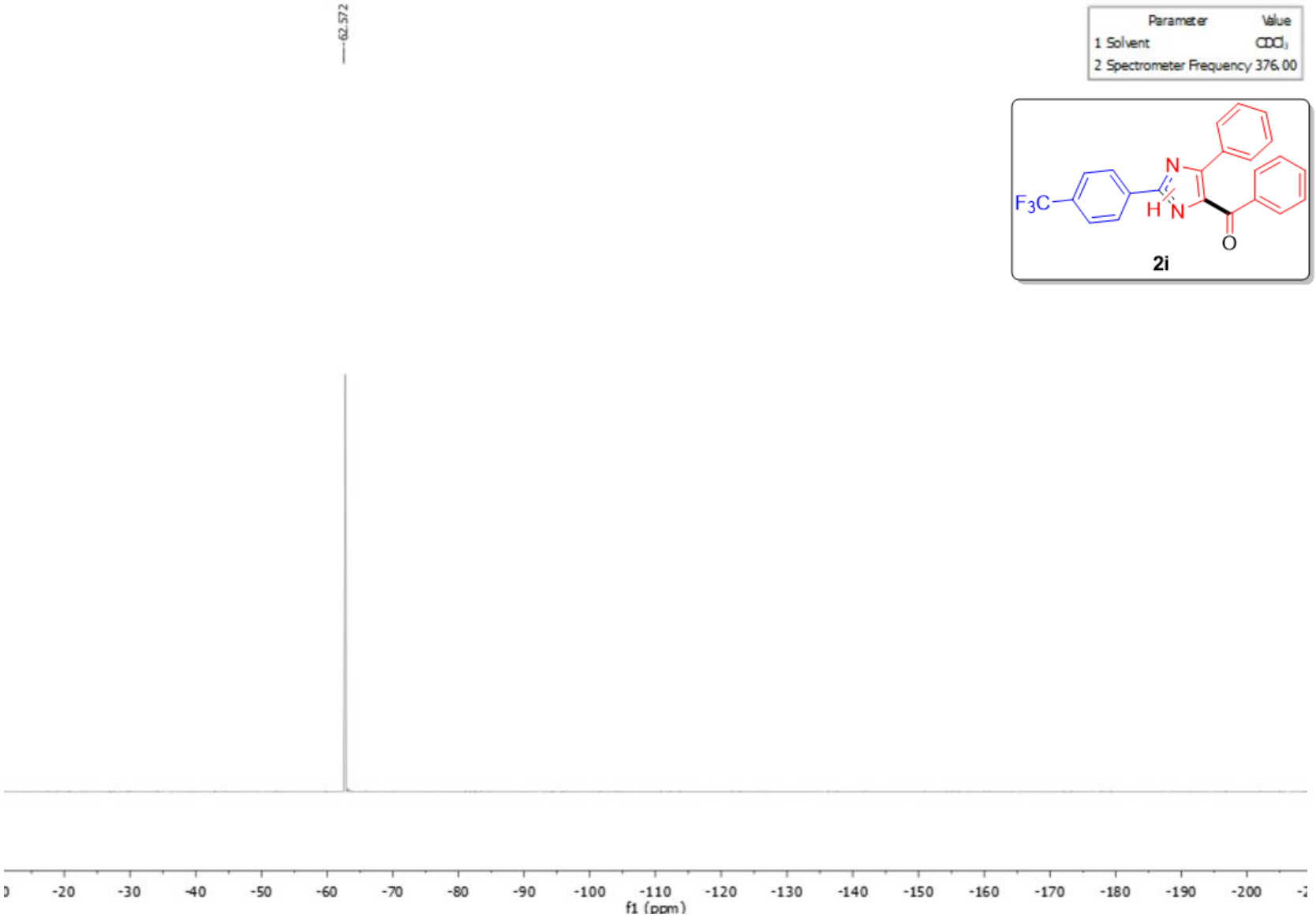
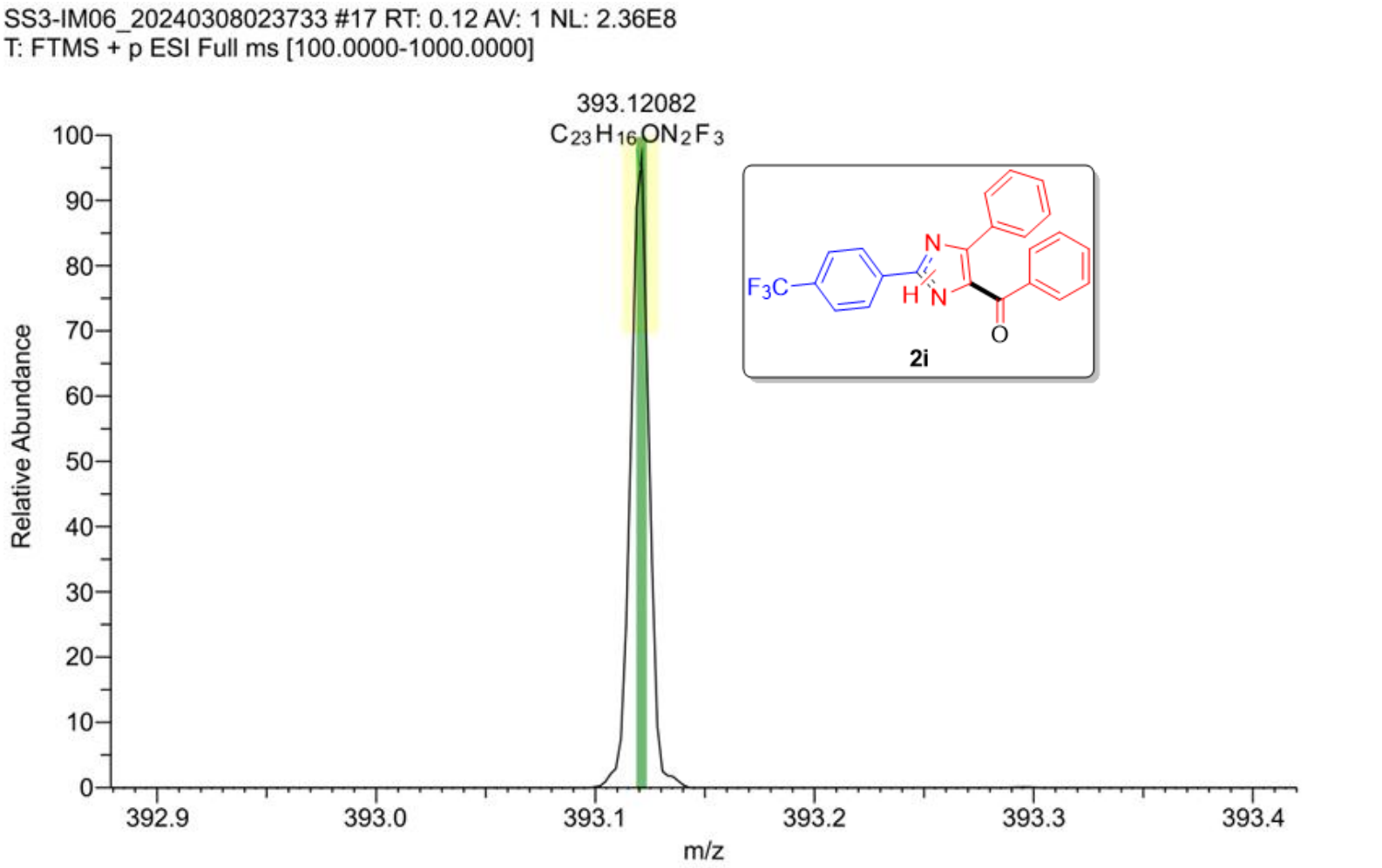


Fig. S71. ^{19}F NMR spectra of phenyl(4-phenyl-2-(4-(trifluoromethyl)phenyl)-1*H*-imidazol-5-yl)methanone **(2i).**



Peak Mass	Display Formula	S Fit	RDB	Delta [ppm]	Theo. mass	Pattern Cov. [%]	MSMS Matched...
393.12082	$C_{23}H_{16}ON_2F_3$	77.5882926069905	15.50	-0.27	393.12092	100	(Collection)

Fig. S72. HRMS data of phenyl(4-phenyl-2-(4-(trifluoromethyl)phenyl)-1*H*-imidazol-5-yl)methanone **(2i).**

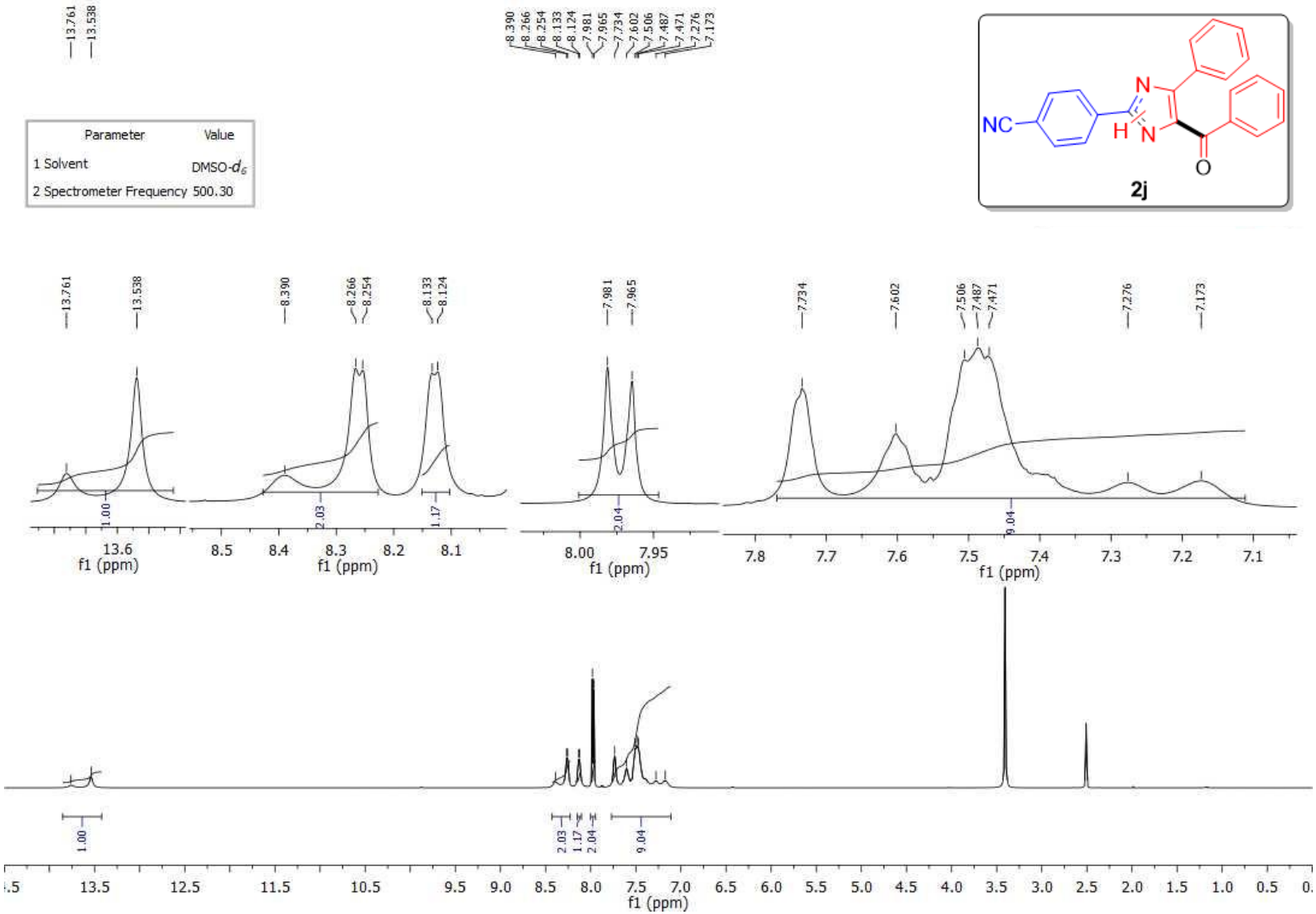


Fig. S73. ^{1}H NMR spectra of 4-(5-benzoyl-4-phenyl-1*H*-imidazol-2-yl)benzonitrile **(2j).**

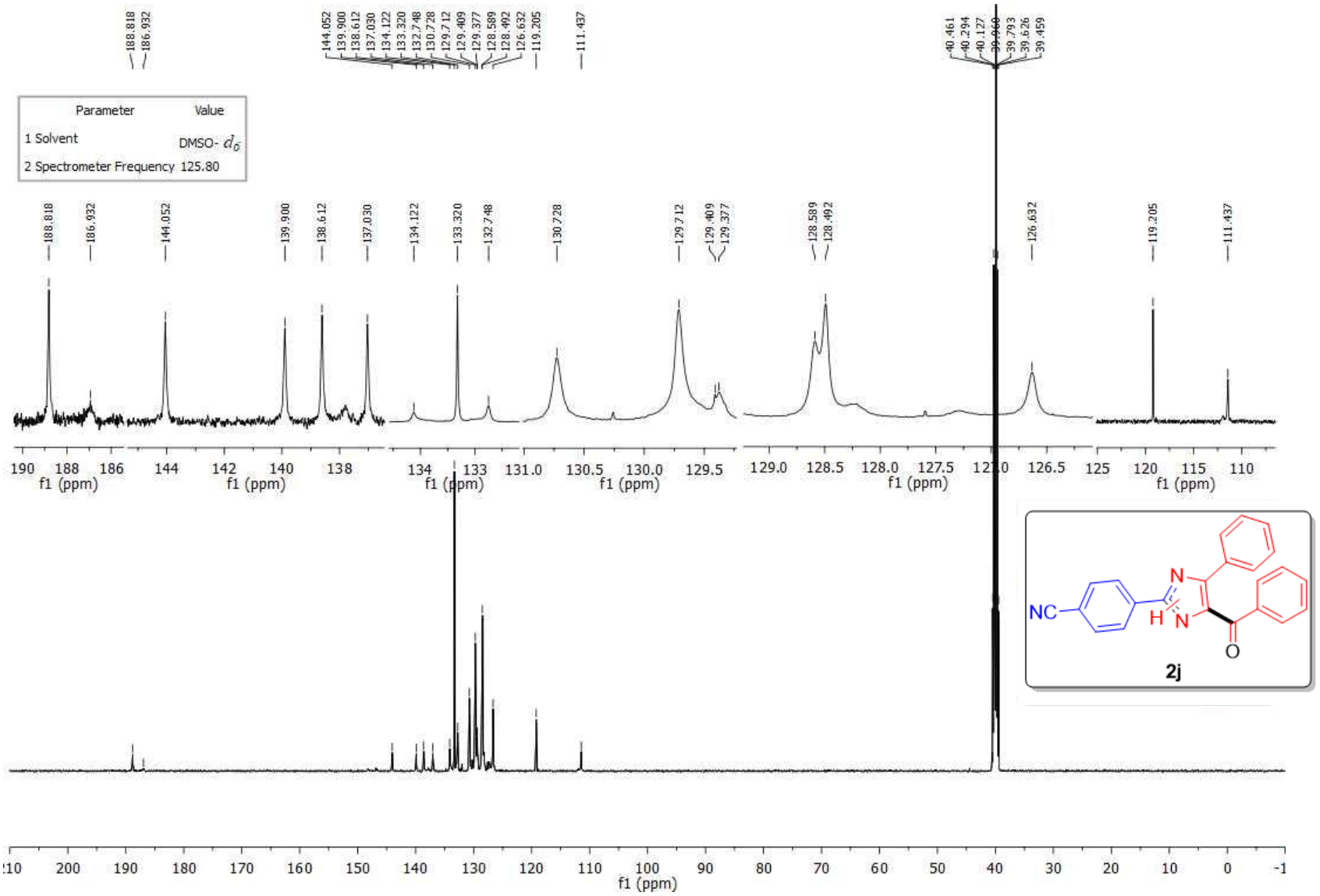
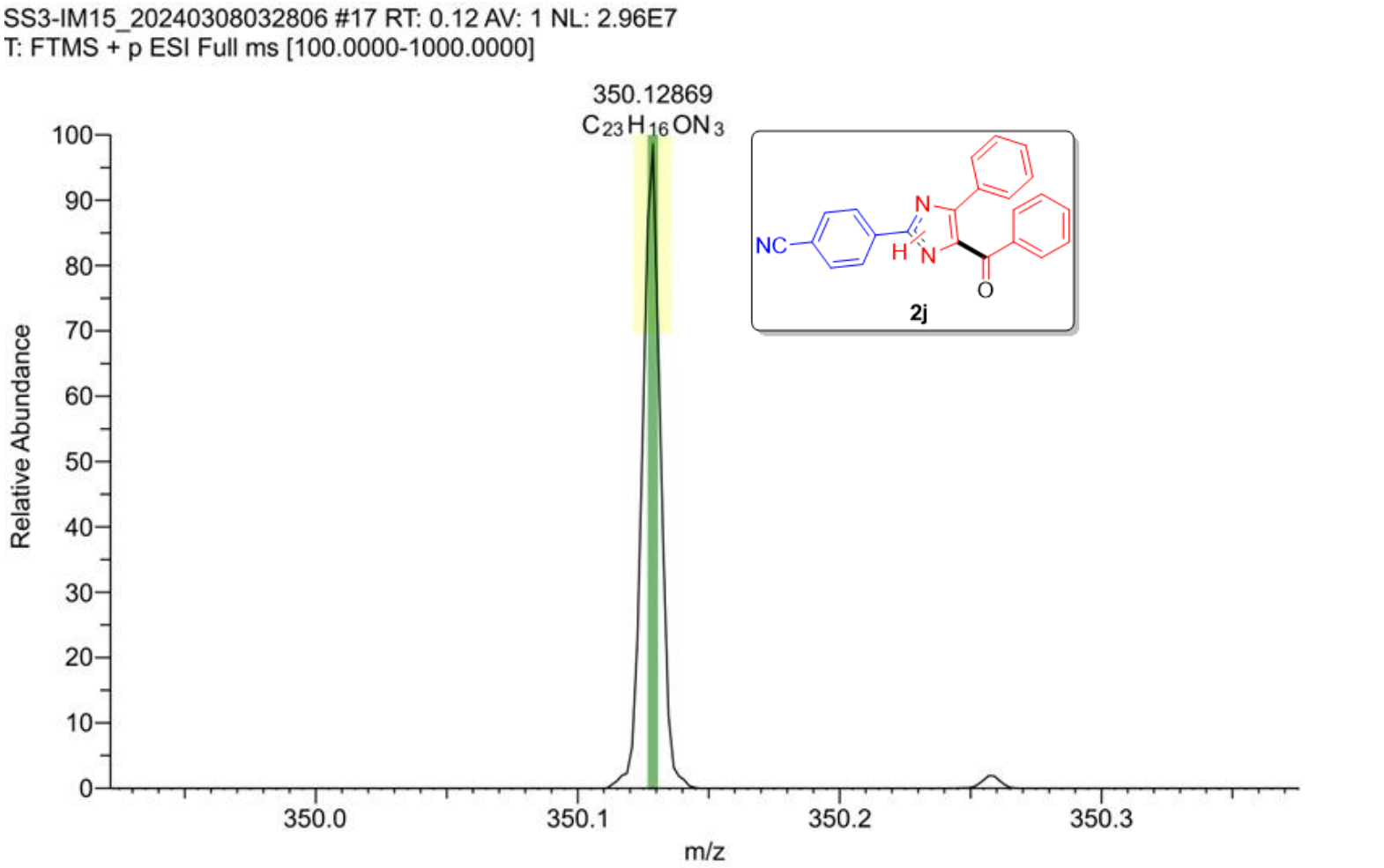


Fig. S74. ^{13}C NMR spectra of 4-(5-benzoyl-4-phenyl-1*H*-imidazol-2-yl)benzonitrile **(2j).**



Peak Mass	Display Formula	S Fit	RDB	Delta [ppm]	Theo. mass	Pattern Cov. [%]	MSMS Matched..
350.12869	$C_{23}H_{16}ON_3$	81.9562264355416	17.50	-0.27	350.12879	100	(Collection)

Fig. S75. HRMS data of 4-(5-benzoyl-4-phenyl-1*H*-imidazol-2-yl)benzonitrile **(2j).**

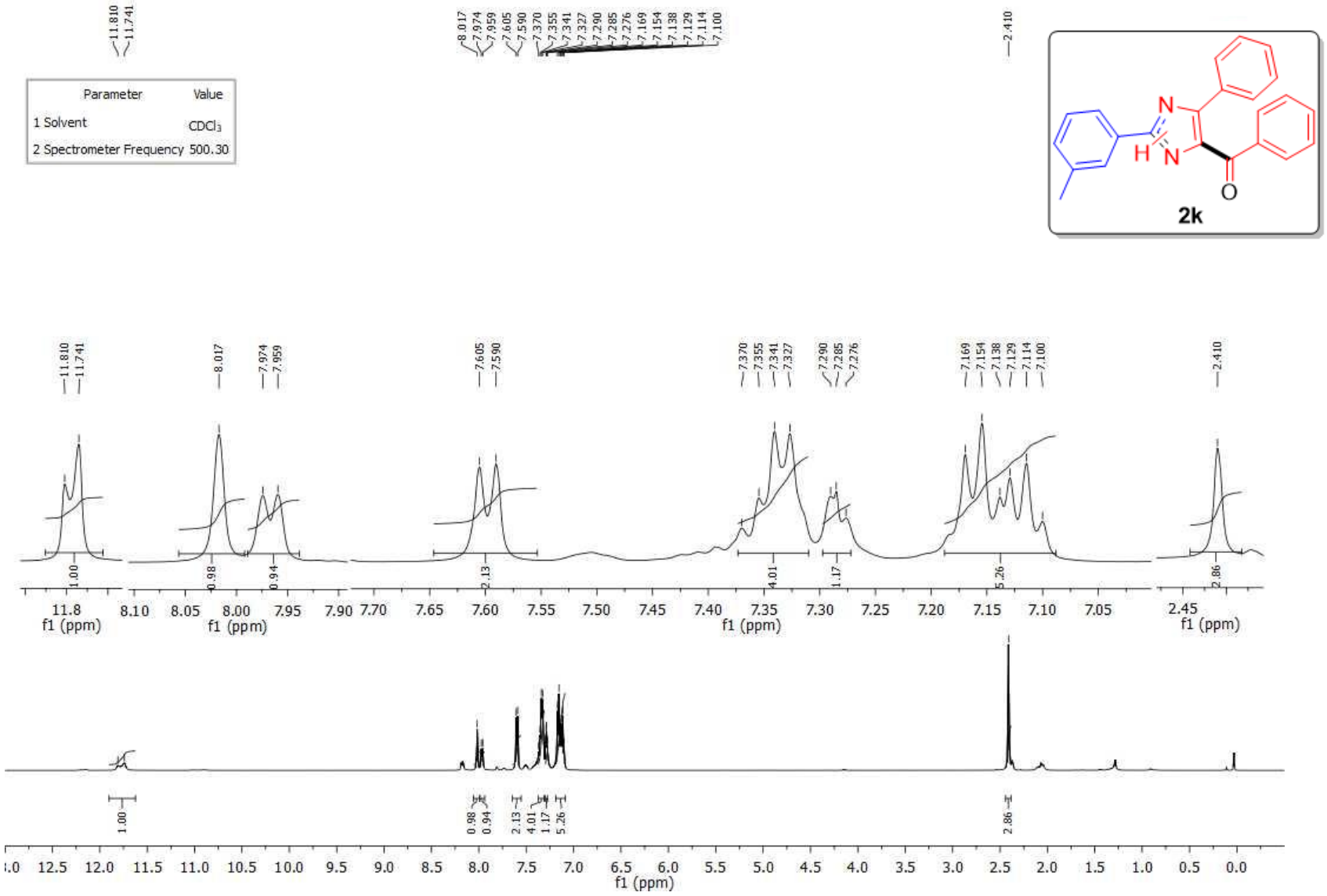


Fig. S76. ^{1}H NMR spectra of phenyl(4-phenyl-2-(*m*-tolyl)-1*H*-imidazol-5-yl)methanone **(2k).**

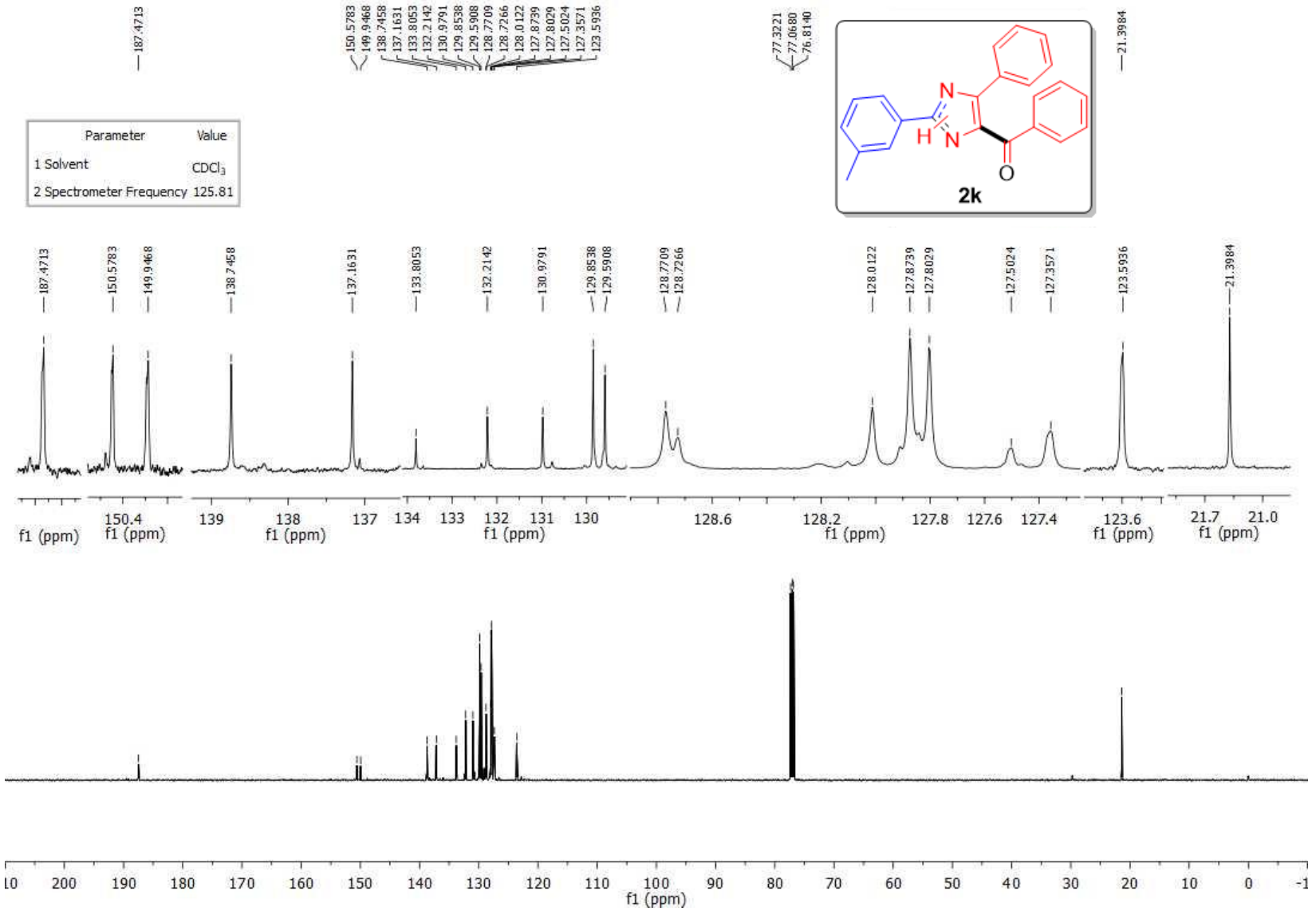
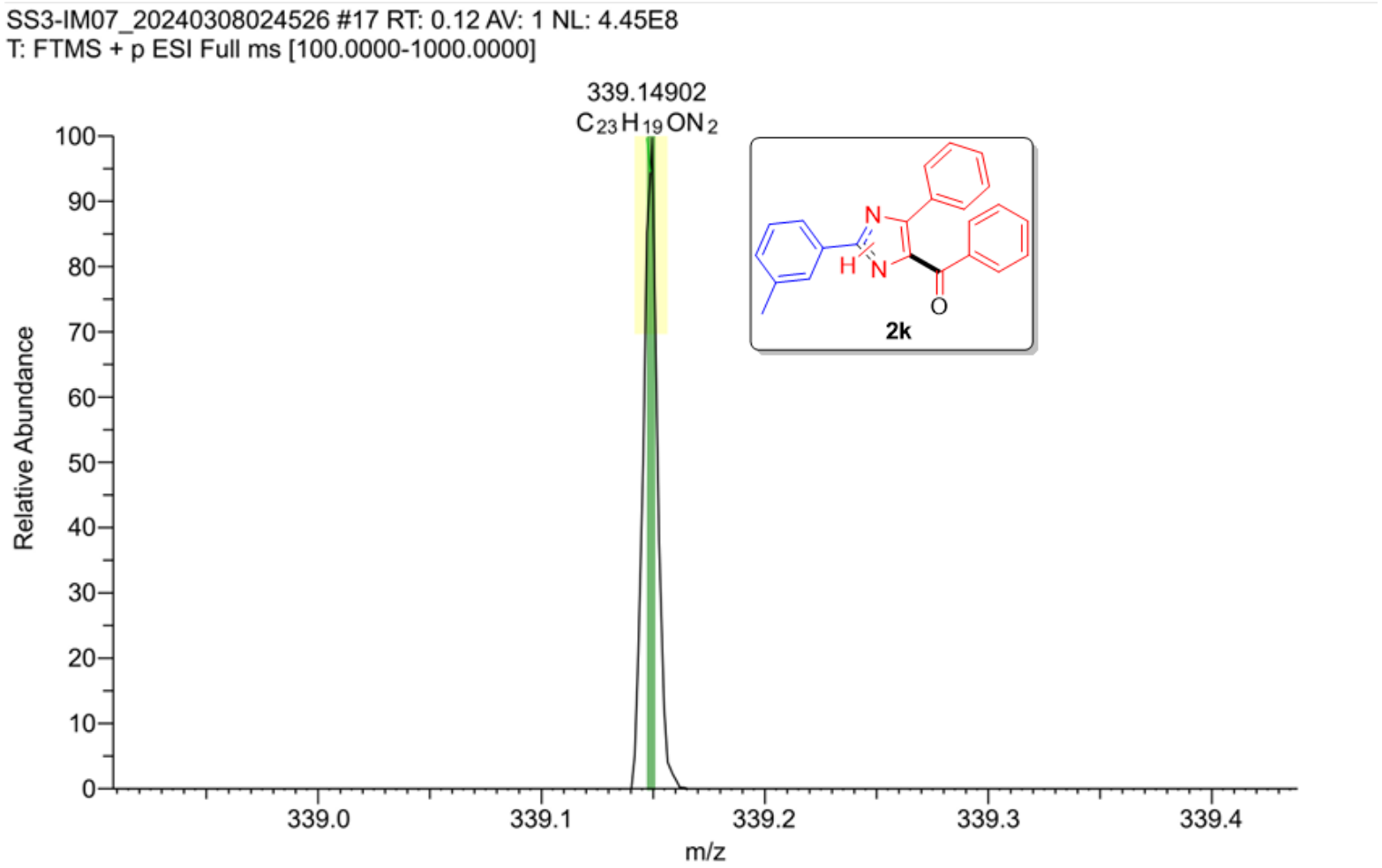


Fig. S77. ^{13}C NMR spectra of phenyl(4-phenyl-2-(*m*-tolyl)-1*H*-imidazol-5-yl)methanone **(2k).**



Peak Mass	Display Formula	S Fit	RDB	Delta [ppm]	Theo. mass	Pattern Cov. [%]	MSMS Matched...
339.14902	$C_{23}H_{19}ON_2$	80.82674437068 39	15.50	-0.51	339.14919	100	(Collection)

Fig. S78. HRMS data of phenyl(4-phenyl-2-(*m*-tolyl)-1*H*-imidazol-5-yl)methanone **(2k).**

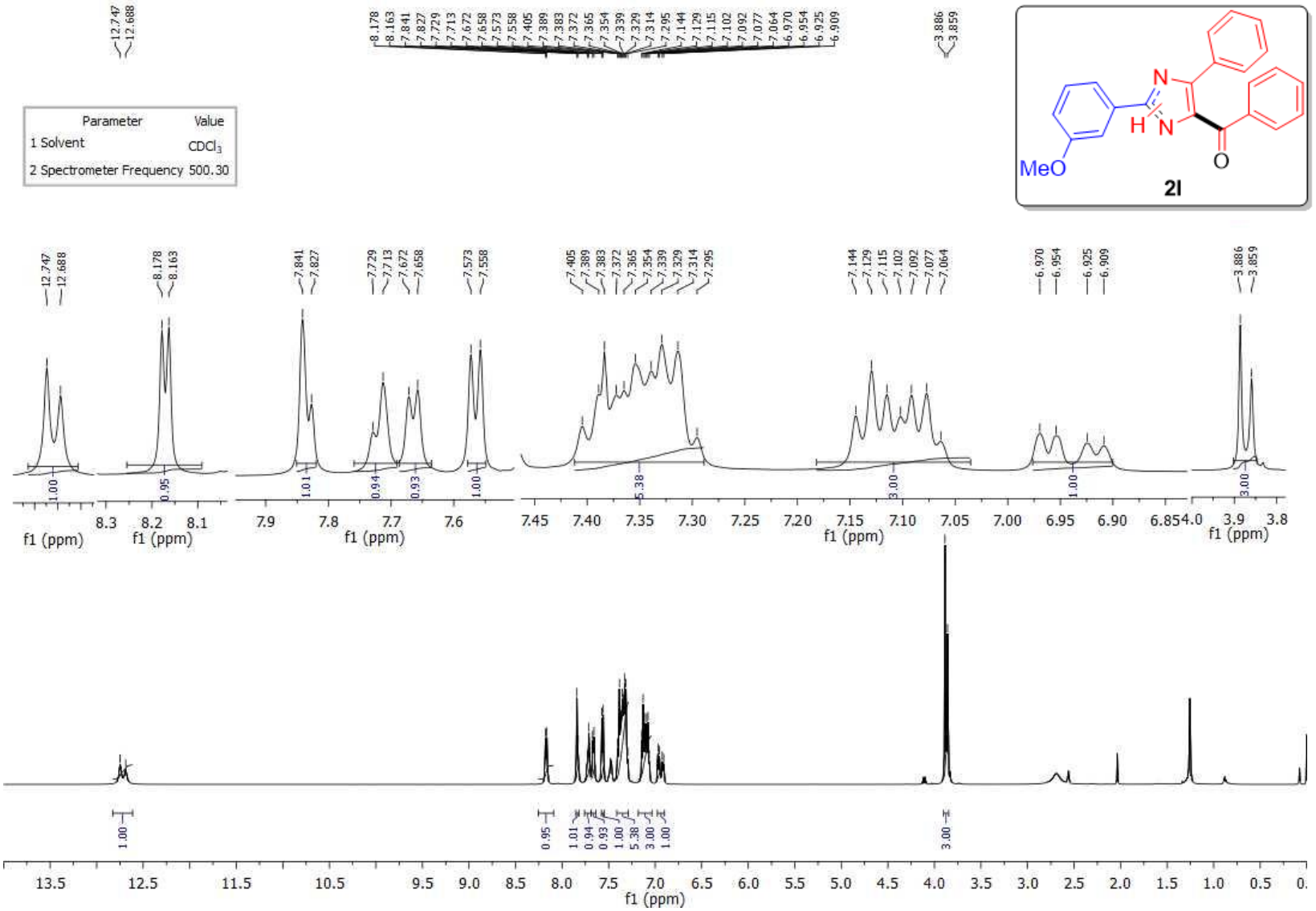


Fig. S79. ^{1}H NMR spectra of **(**2-(3-methoxyphenyl)-4-phenyl-1*H*-imidazol-5-yl)(phenyl)methanone **(2l).**

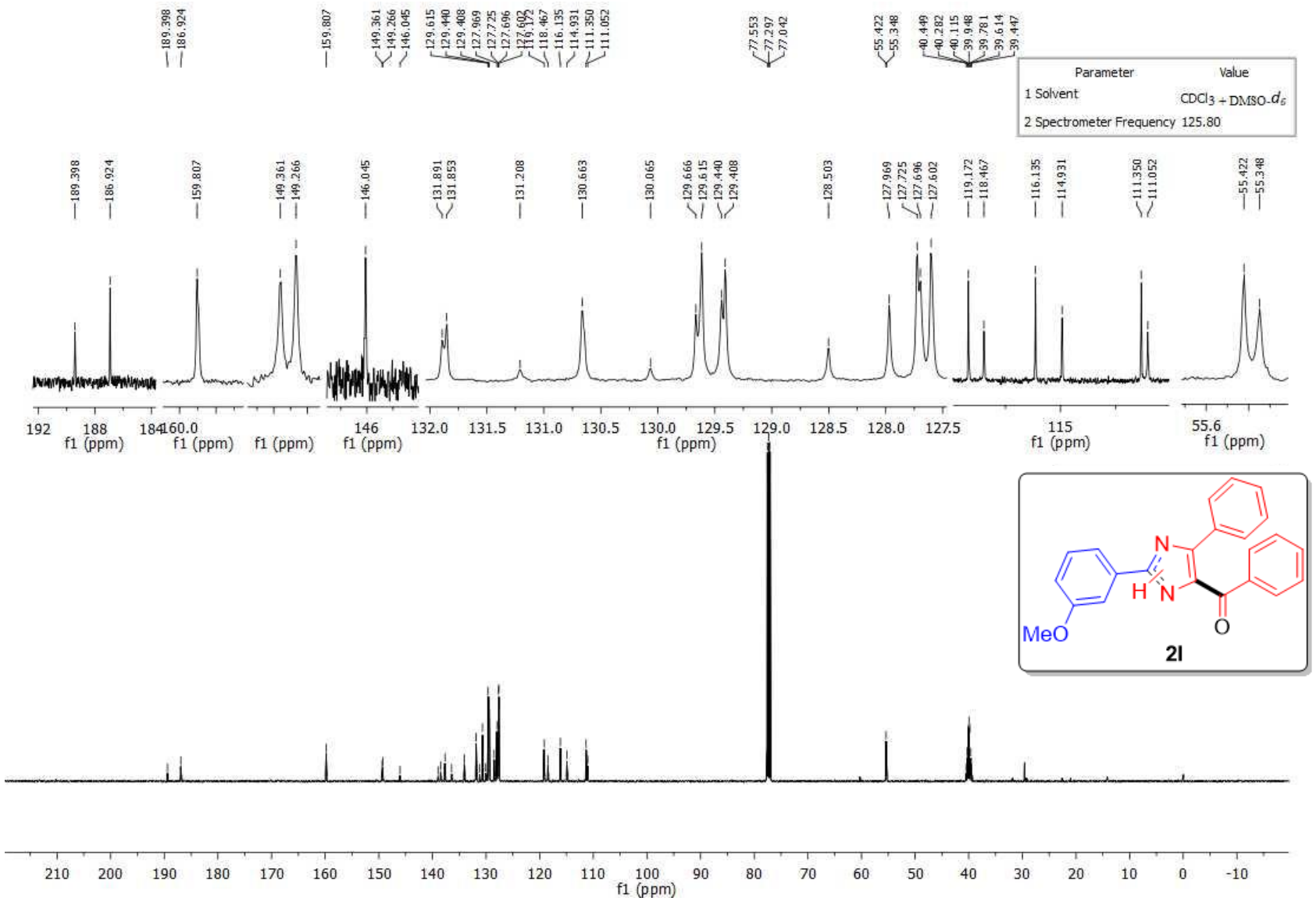
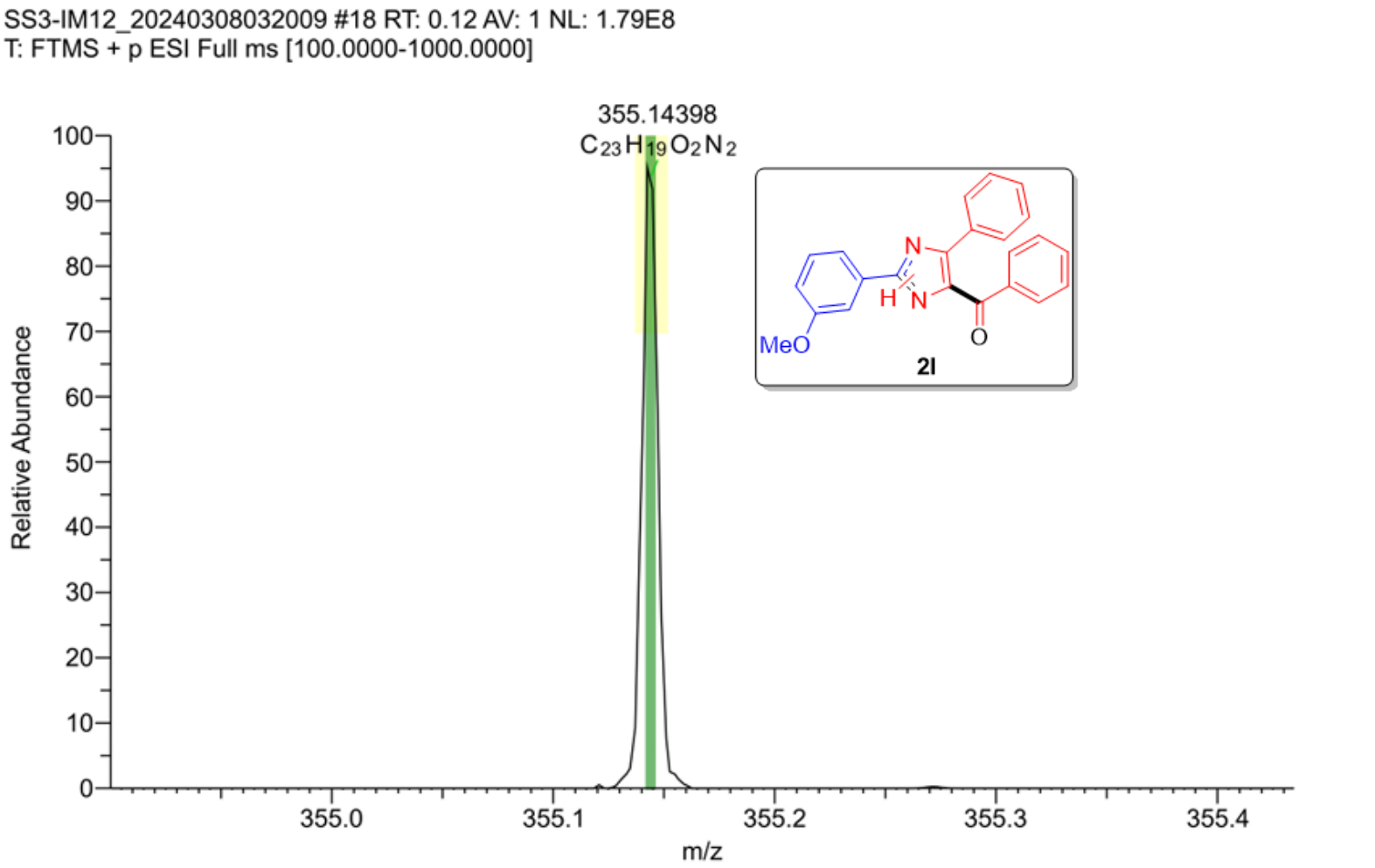


Fig. S80. ^{13}C NMR spectra of **(**2-(3-methoxyphenyl)-4-phenyl-1*H*-imidazol-5-yl)(phenyl)methanone **(2l).**



Peak Mass	Display Formula	S Fit	RDB	Delta [ppm]	Theo. mass	Pattern Cov. [%]	MSMS Matched..
355.14398	$C_{23}H_{19}O_2N_2$	82.5906914867039	15.50	-0.34	355.14410	100	(Collection)

Fig. S81. HRMS data of **(**2-(3-methoxyphenyl)-4-phenyl-1*H*-imidazol-5-yl)(phenyl)methanone **(2l).**

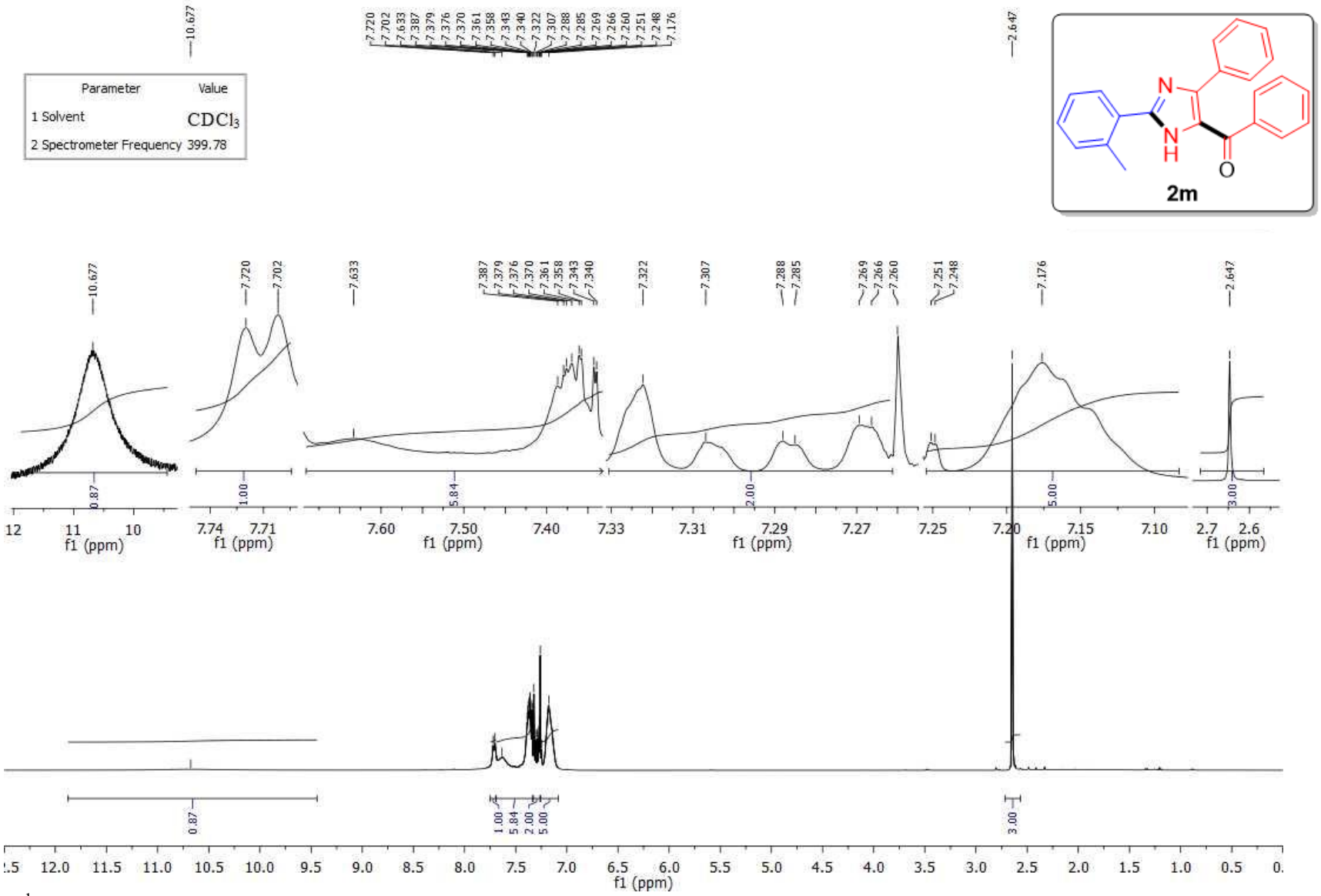


Fig. S82. ^{1}H NMR spectra of phenyl(4-phenyl-2-(*o*-tolyl)-1*H*-imidazol-5-yl)methanone **(2m).**

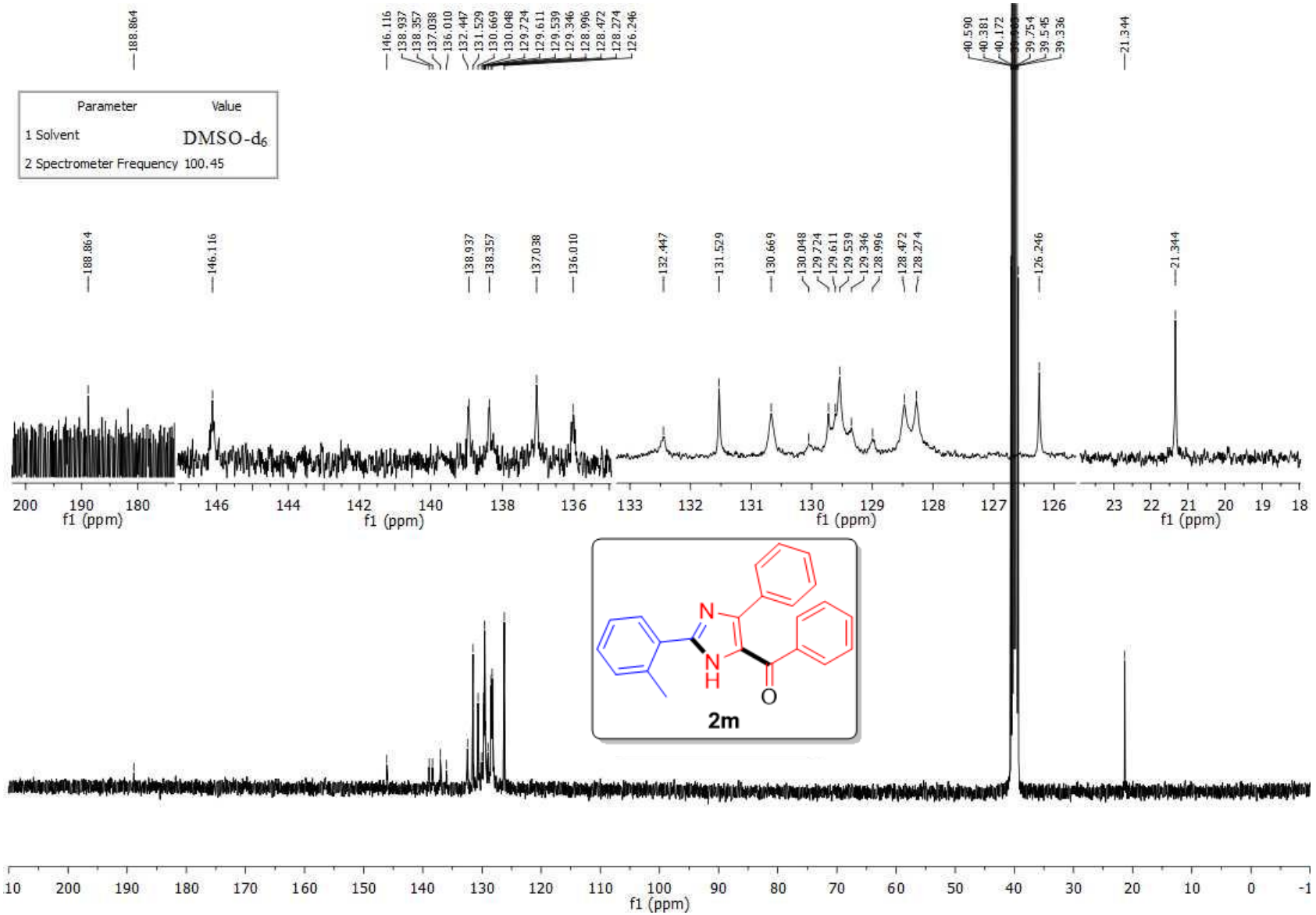
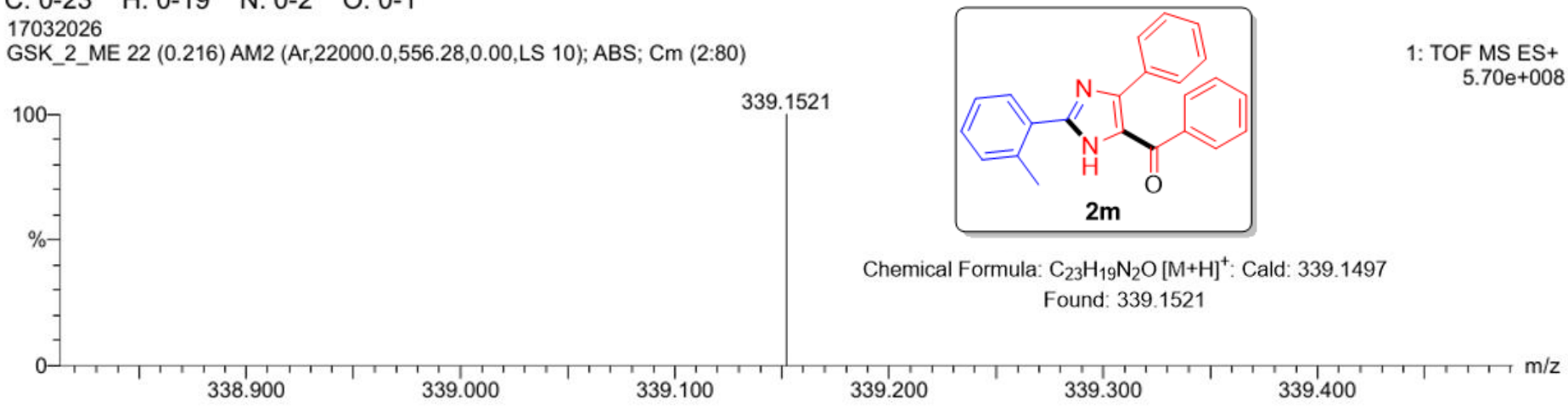


Fig. S83. ^{13}C NMR spectra of phenyl(4-phenyl-2-(*o*-tolyl)-1*H*-imidazol-5-yl)methanone **(2m).**

Single Mass Analysis
Tolerance = 200.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
2 formula(e) evaluated with 1 results within limits (up to 1 best isotopic matches for each mass)
Elements Used:
C: 0-23 H: 0-19 N: 0-2 O: 0-1
17032026
GSK_2_ME 22 (0.216) AM2 (Ar,22000.0,556.28,0.00,LS 10); ABS; Cm (2:80)



Chemical Formula: $C_{23}H_{19}N_2O$ $[M+H]^+$: Cald: 339.1497
Found: 339.1521

Minimum:				-1.5				
Maximum:		5.0	200.0	50.0				
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
339.1521	339.1497	2.4	7.1	15.5	53.9	n/a	n/a	C23 H19 N2 O

Fig. S84. HRMS data of phenyl(4-phenyl-2-(*o*-tolyl)-1*H*-imidazol-5-yl)methanone **(2m).**

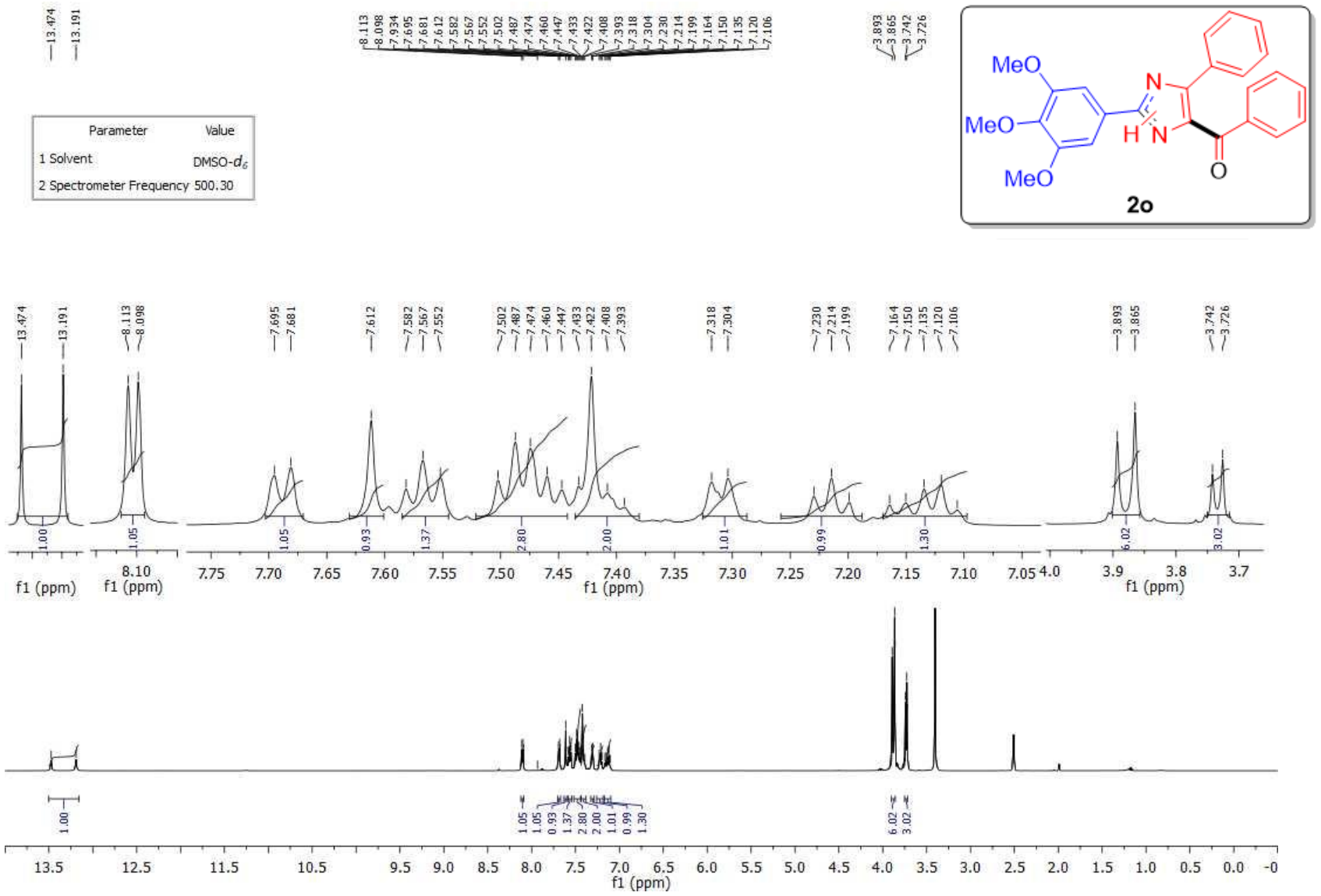


Fig. S85. ^{1}H NMR spectra of phenyl(4-phenyl-2-(3,4,5-trimethoxyphenyl)-1*H*-imidazol-5-yl)methanone **(2o).**

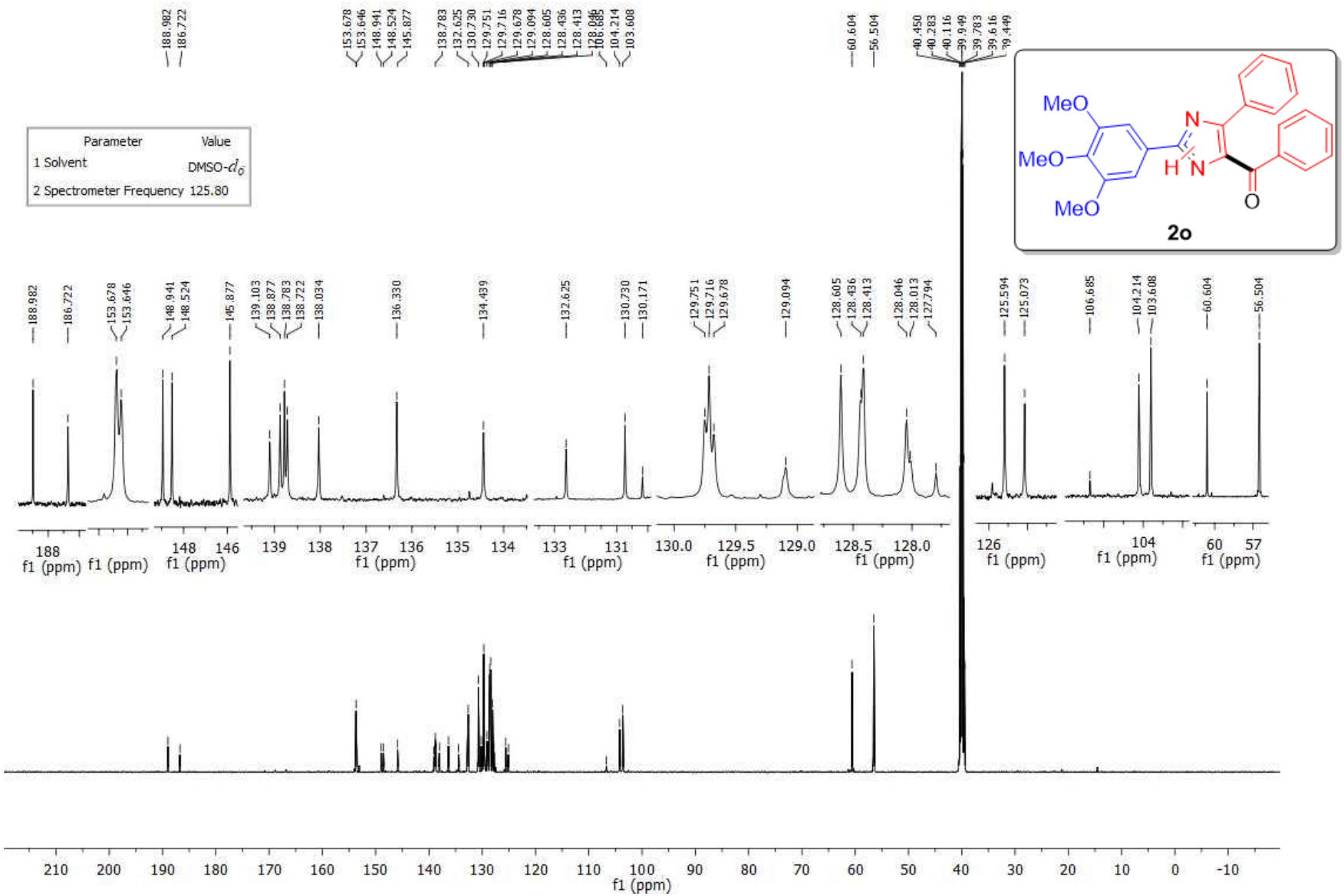
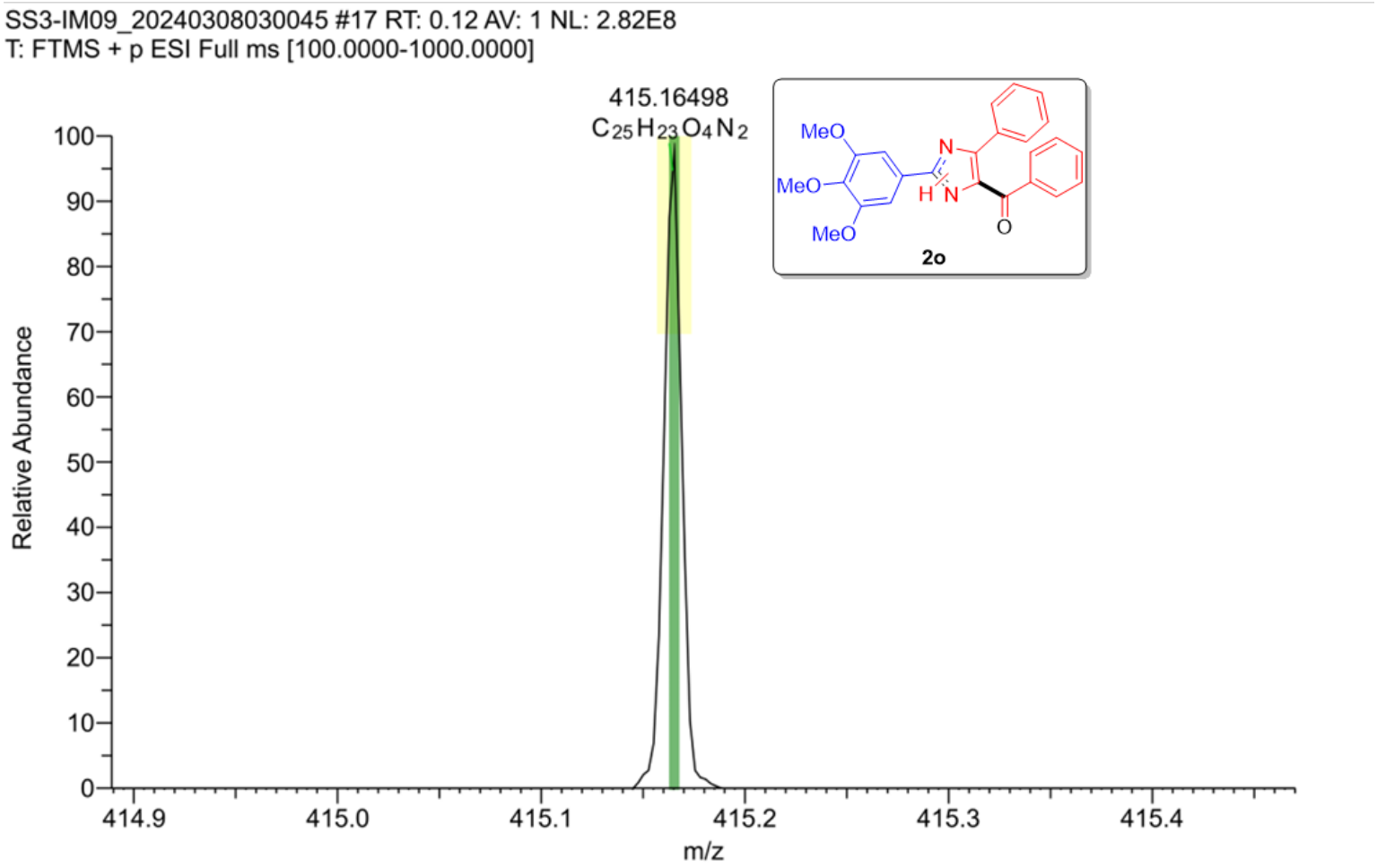


Fig. S86. ^{13}C NMR spectra of phenyl(4-phenyl-2-(3,4,5-trimethoxyphenyl)-1*H*-imidazol-5-yl)methanone **(2o).**



Peak Mass	Display Formula	S Fit	RDB	Delta [ppm]	Theo. mass	Pattern Cov. [%]	MSMS Matched..
415.16498	$C_{25}H_{23}O_4N_2$	87.5435824827319	15.50	-0.62	415.16523	100	(Collection)

Fig. S87. HRMS data of phenyl(4-phenyl-2-(3,4,5-trimethoxyphenyl)-1*H*-imidazol-5-yl)methanone **(2o).**

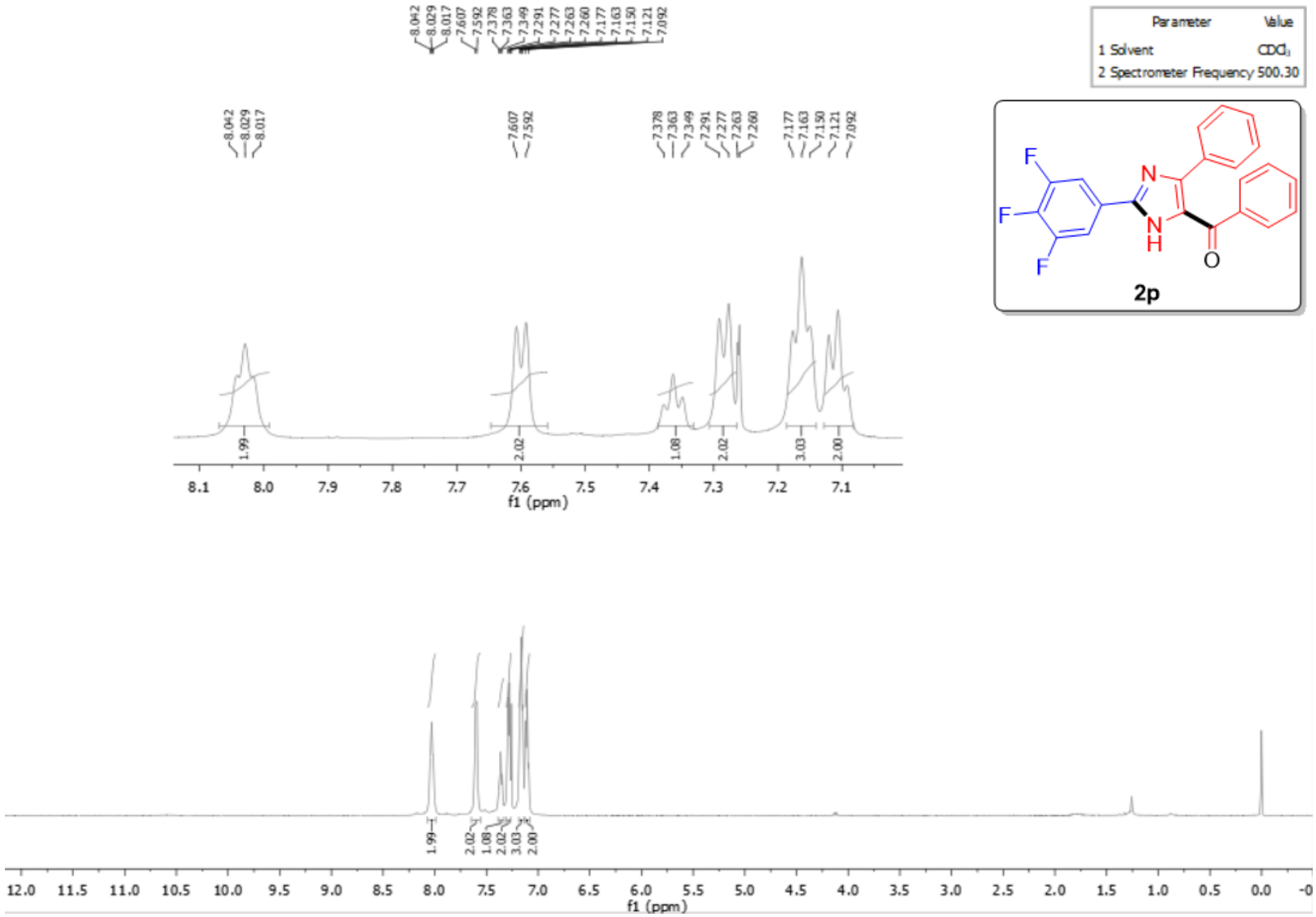


Fig. S88. ^{1}H NMR spectra of phenyl(4-phenyl-2-(3,4,5-trifluorophenyl)-1*H*-imidazol-5-yl)methanone **(2p).**

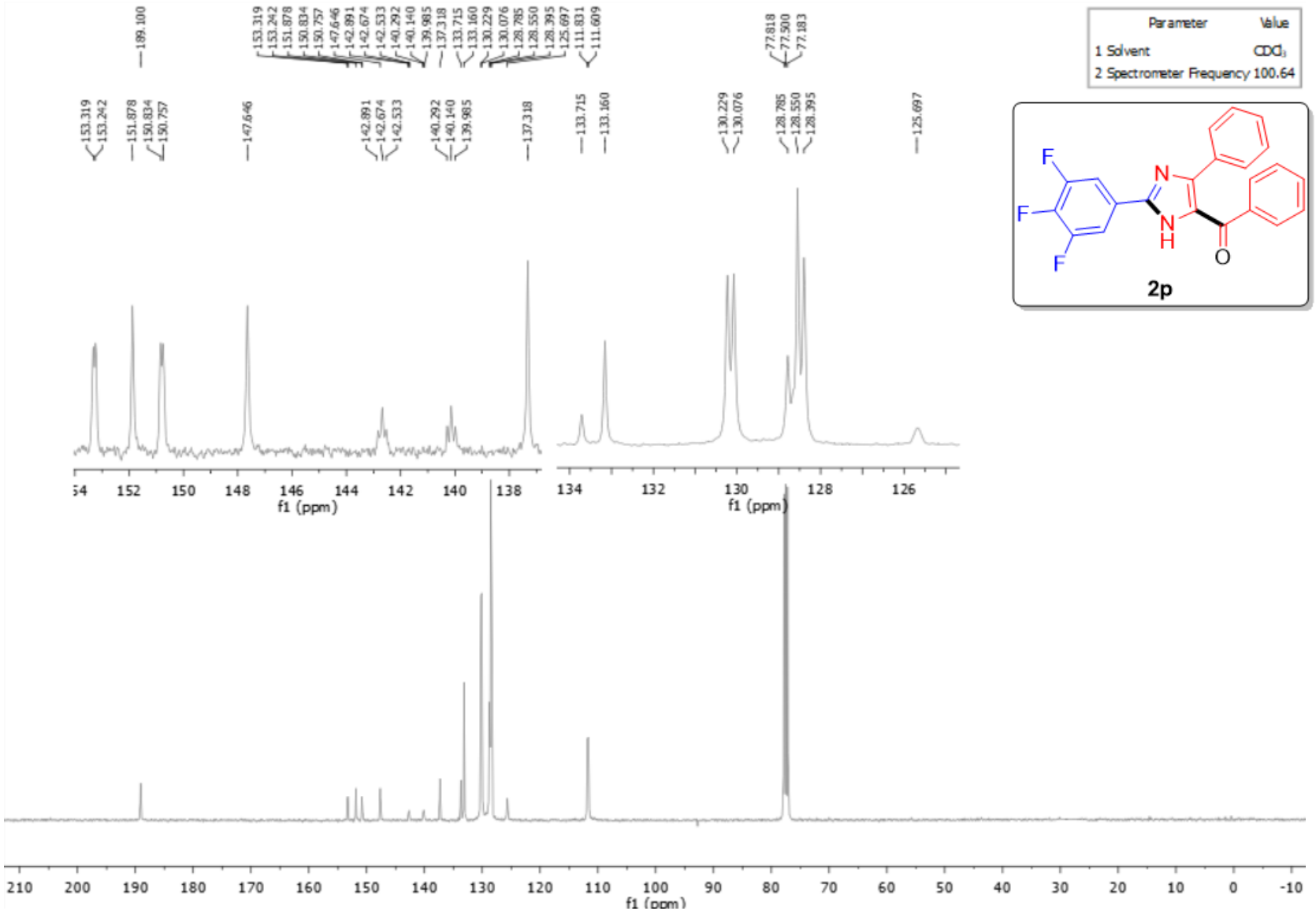


Fig. S89. ^{13}C NMR spectra of phenyl(4-phenyl-2-(3,4,5-trifluorophenyl)-1*H*-imidazol-5-yl)methanone **(2p).**

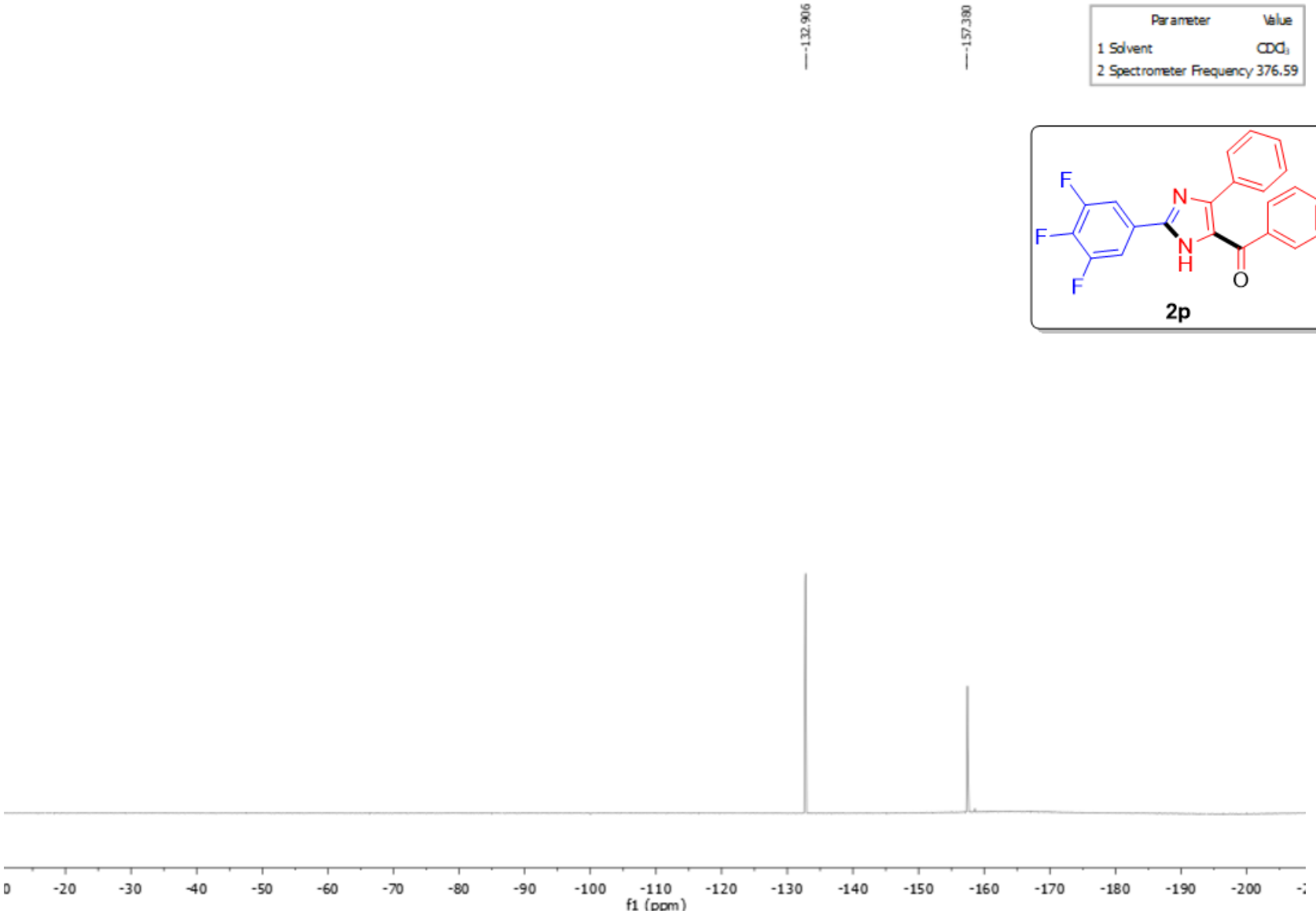
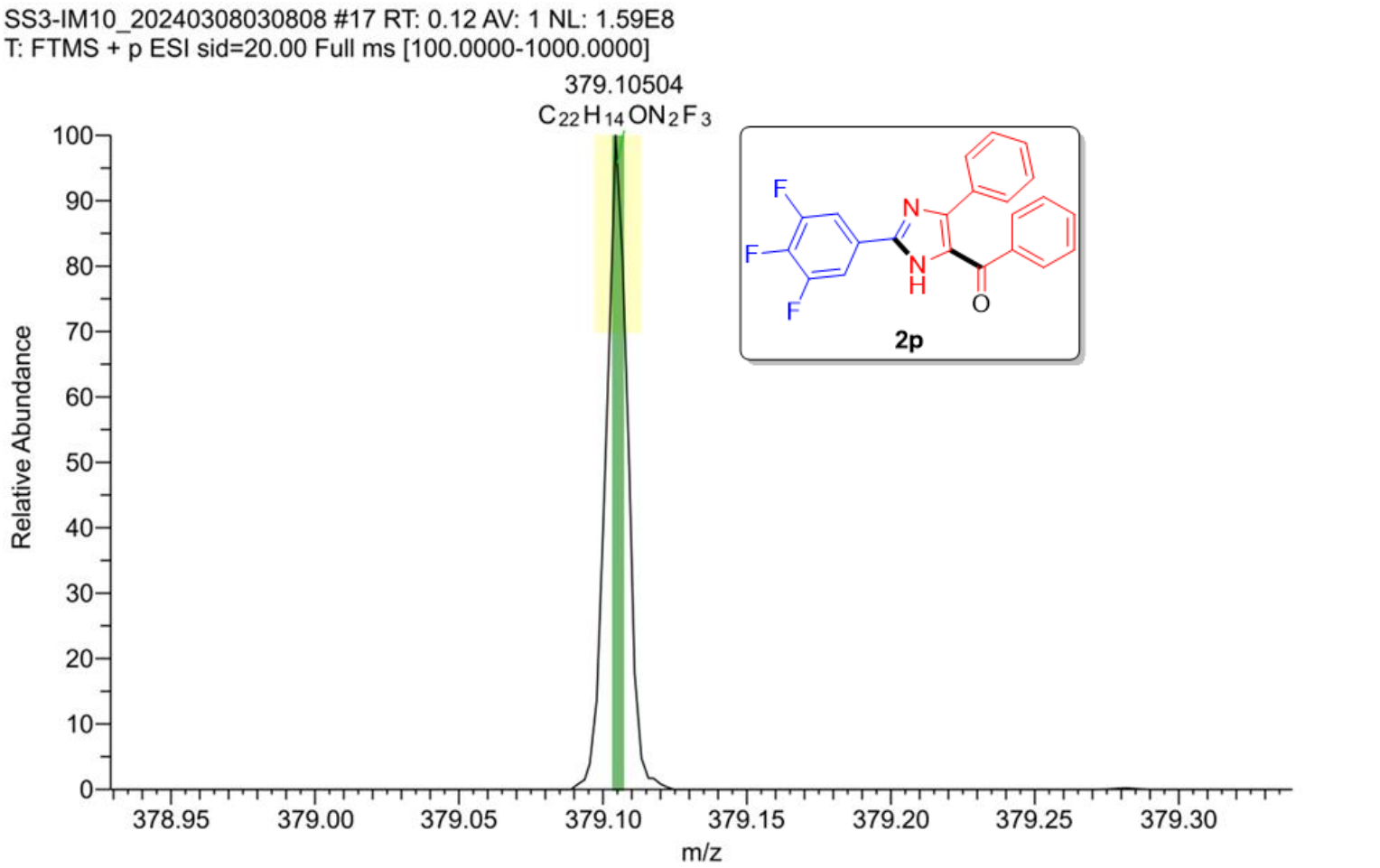


Fig. S90. ^{19}F NMR spectra of phenyl(4-phenyl-2-(3,4,5-trifluorophenyl)-1*H*-imidazol-5-yl)methanone **(2p).**



Peak Mass	Display Formula	S Fit	RDB	Delta [ppm]	Theo. mass	Pattern Cov. [%]	MSMS Matched...
379.10504	$C_{22}H_{14}ON_2F_3$	68.0642307650086	15.50	-0.61	379.10527	100	(Collection)

Fig. S91. HRMS data of phenyl(4-phenyl-2-(3,4,5-trifluorophenyl)-1*H*-imidazol-5-yl)methanone **(2p).**

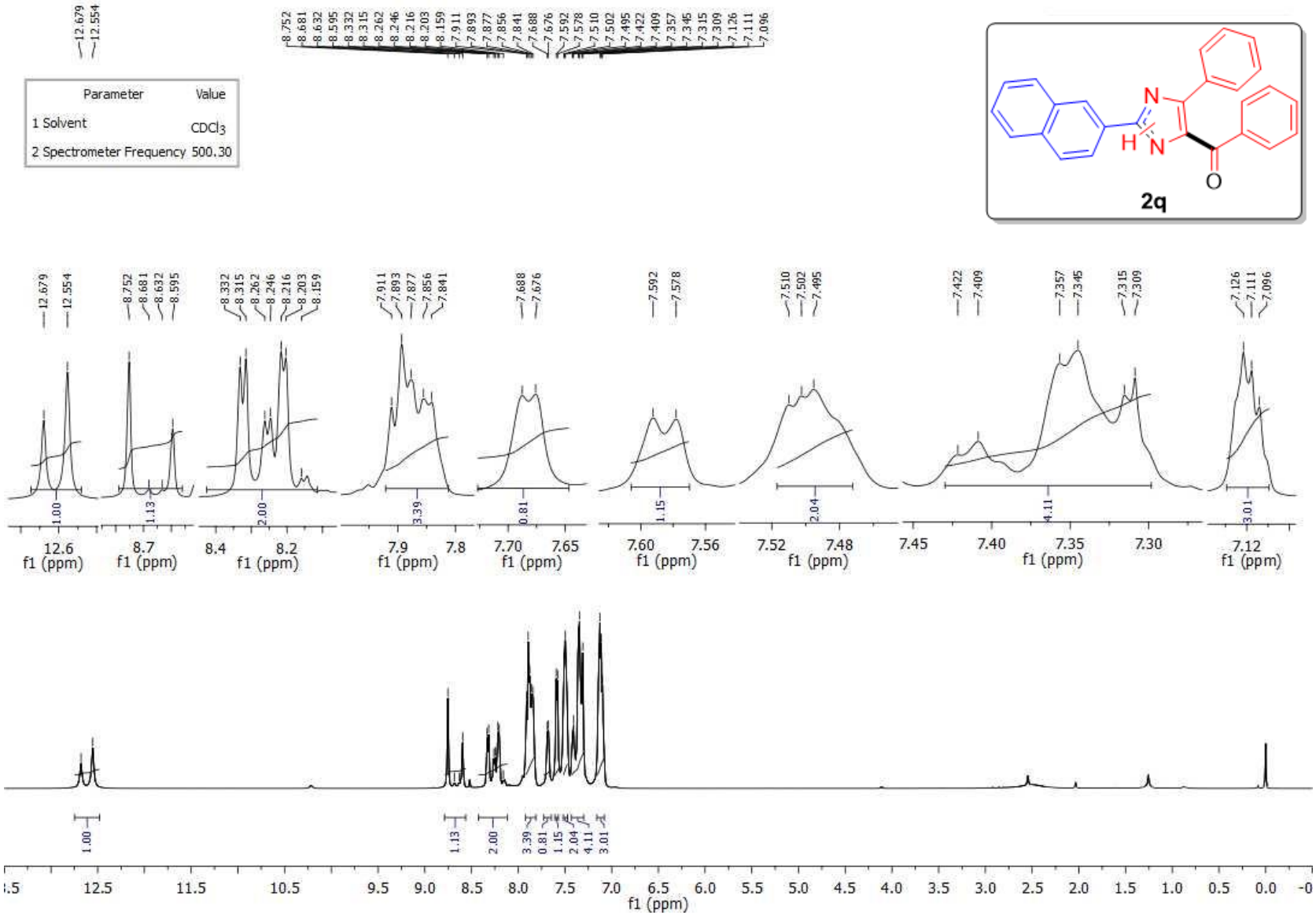


Fig. S92. ^{1}H NMR spectra of (2-(naphthalen-2-yl)-4-phenyl-1*H*-imidazol-5-yl)(phenyl)methanone **(2q).**

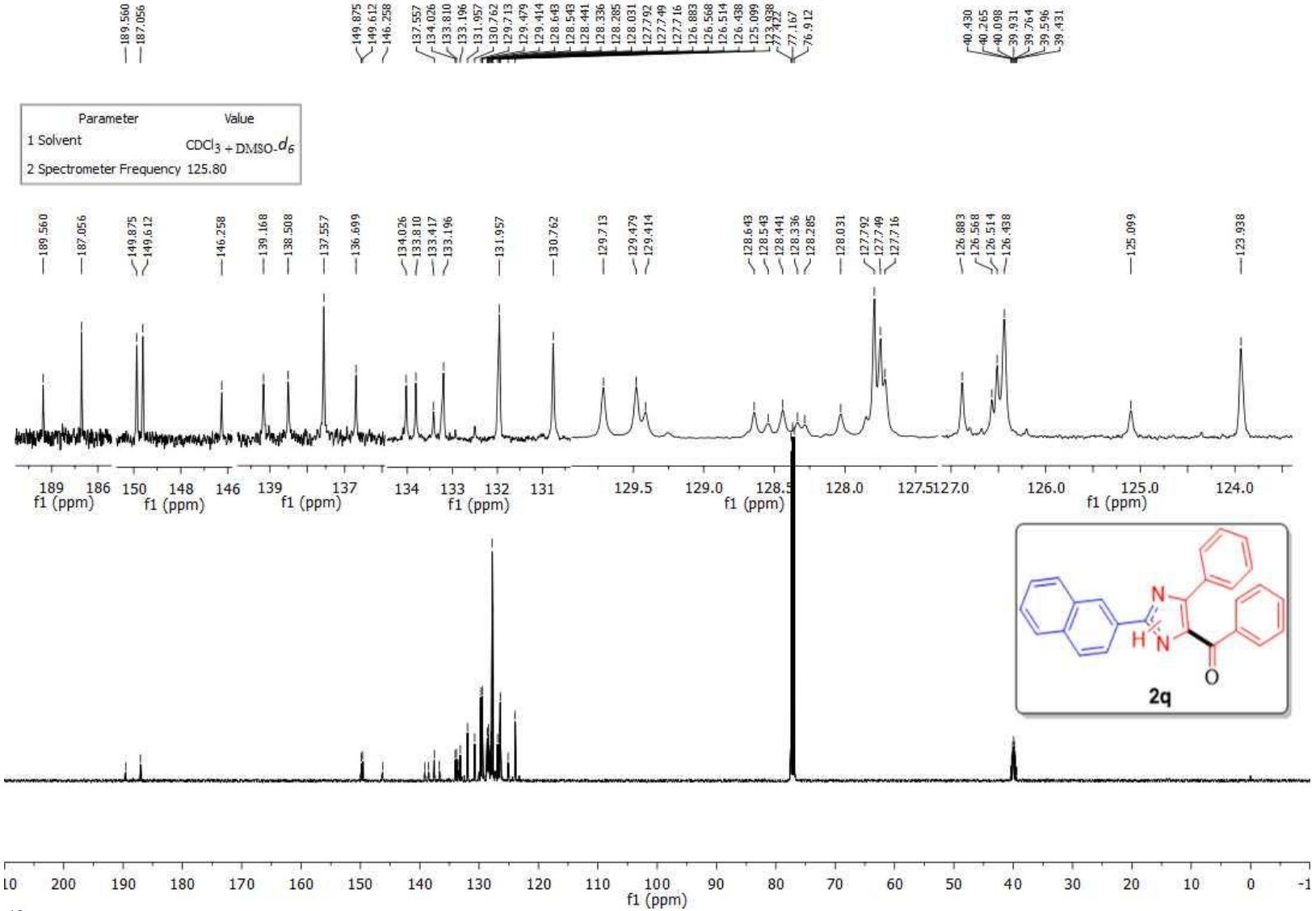


Fig. S93. ^{13}C NMR spectra of (2-(naphthalen-2-yl)-4-phenyl-1*H*-imidazol-5-yl)(phenyl)methanone **(2q).**

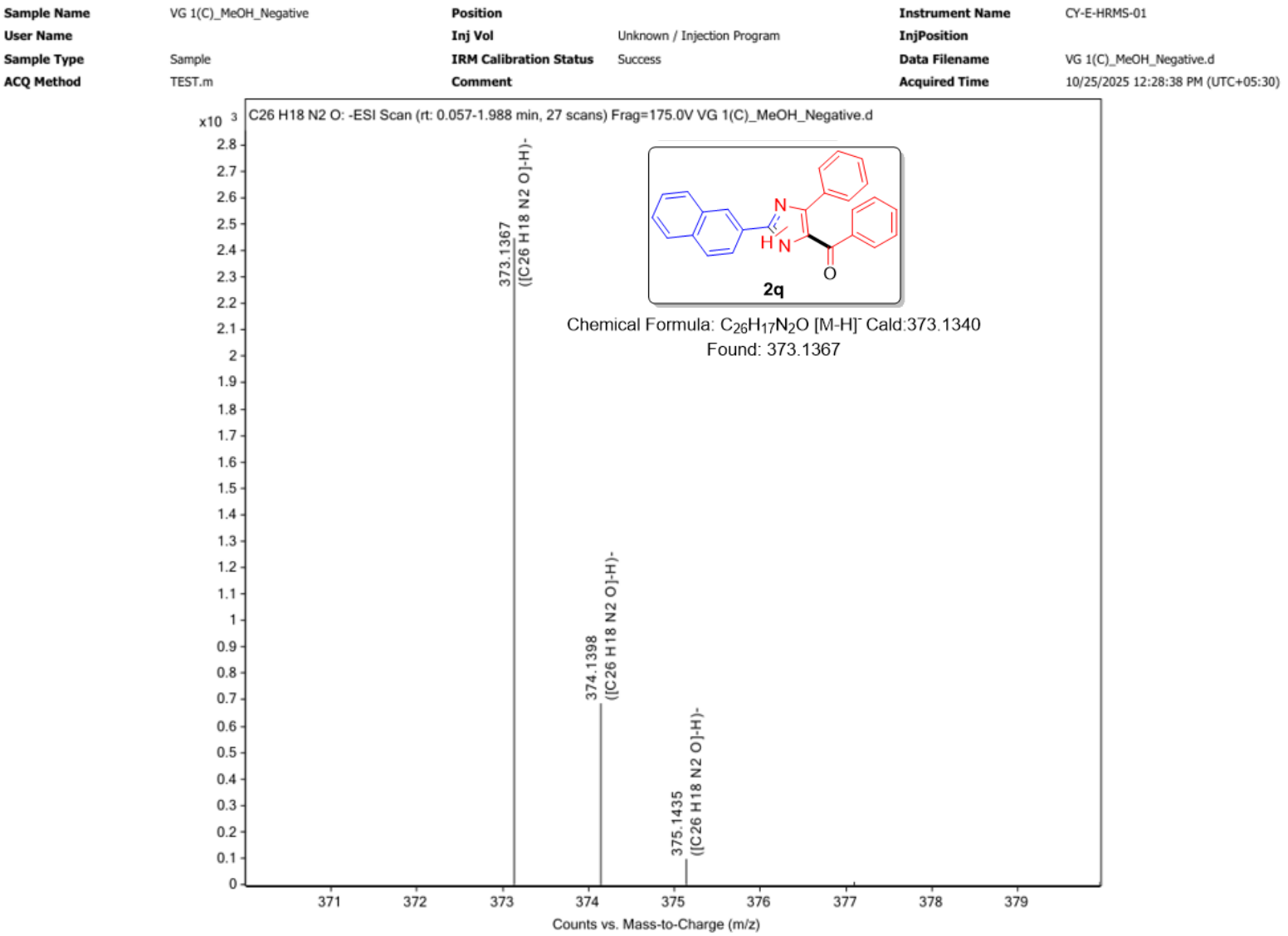


Fig. S94. HRMS data of (2-(naphthalen-2-yl)-4-phenyl-1*H*-imidazol-5-yl)(phenyl)methanone **(2q).**

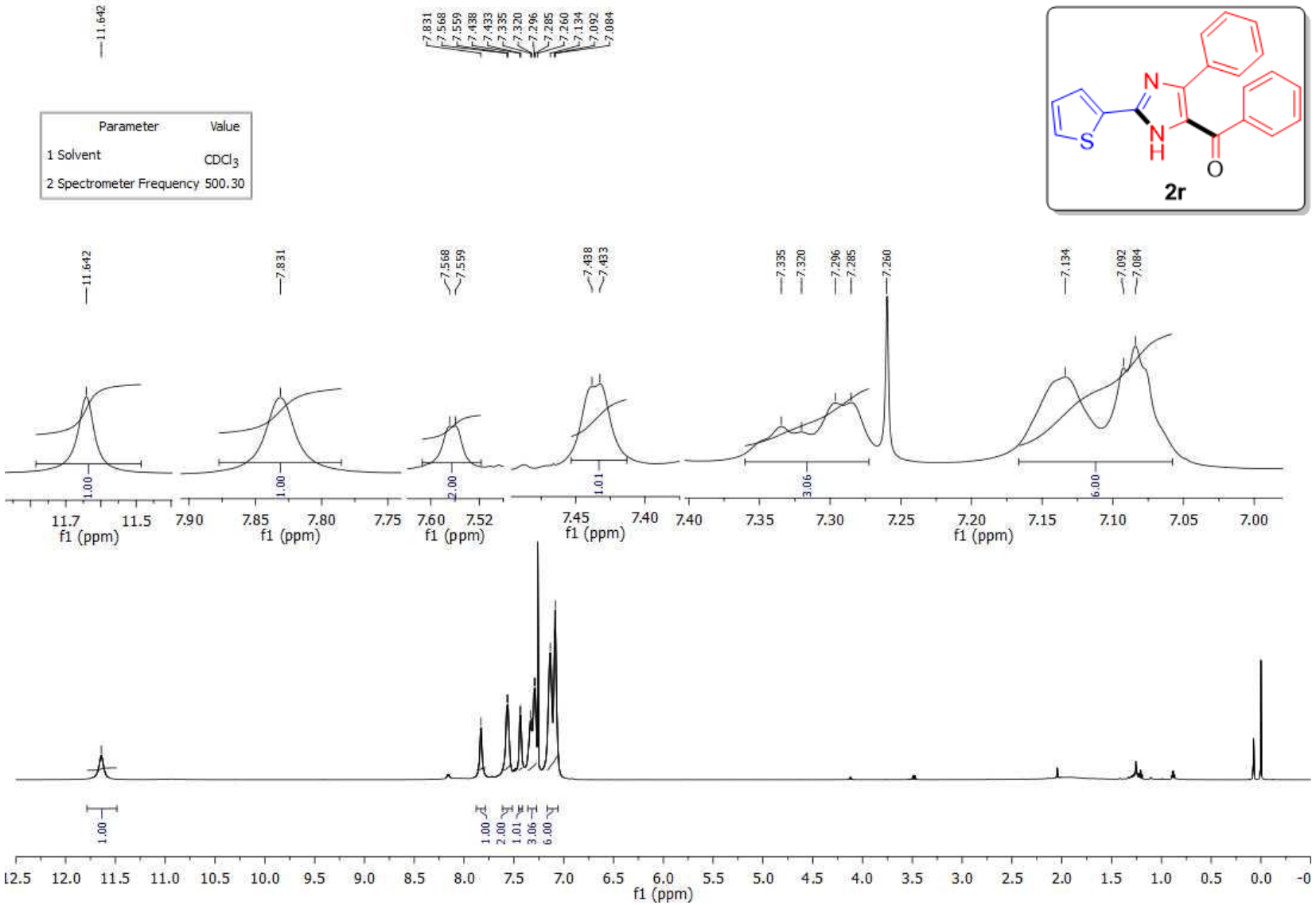


Fig. S95. ^{1}H NMR spectra of phenyl(4-phenyl-2-(thiophen-2-yl)-1*H*-imidazol-5-yl)methanone **(2r).**

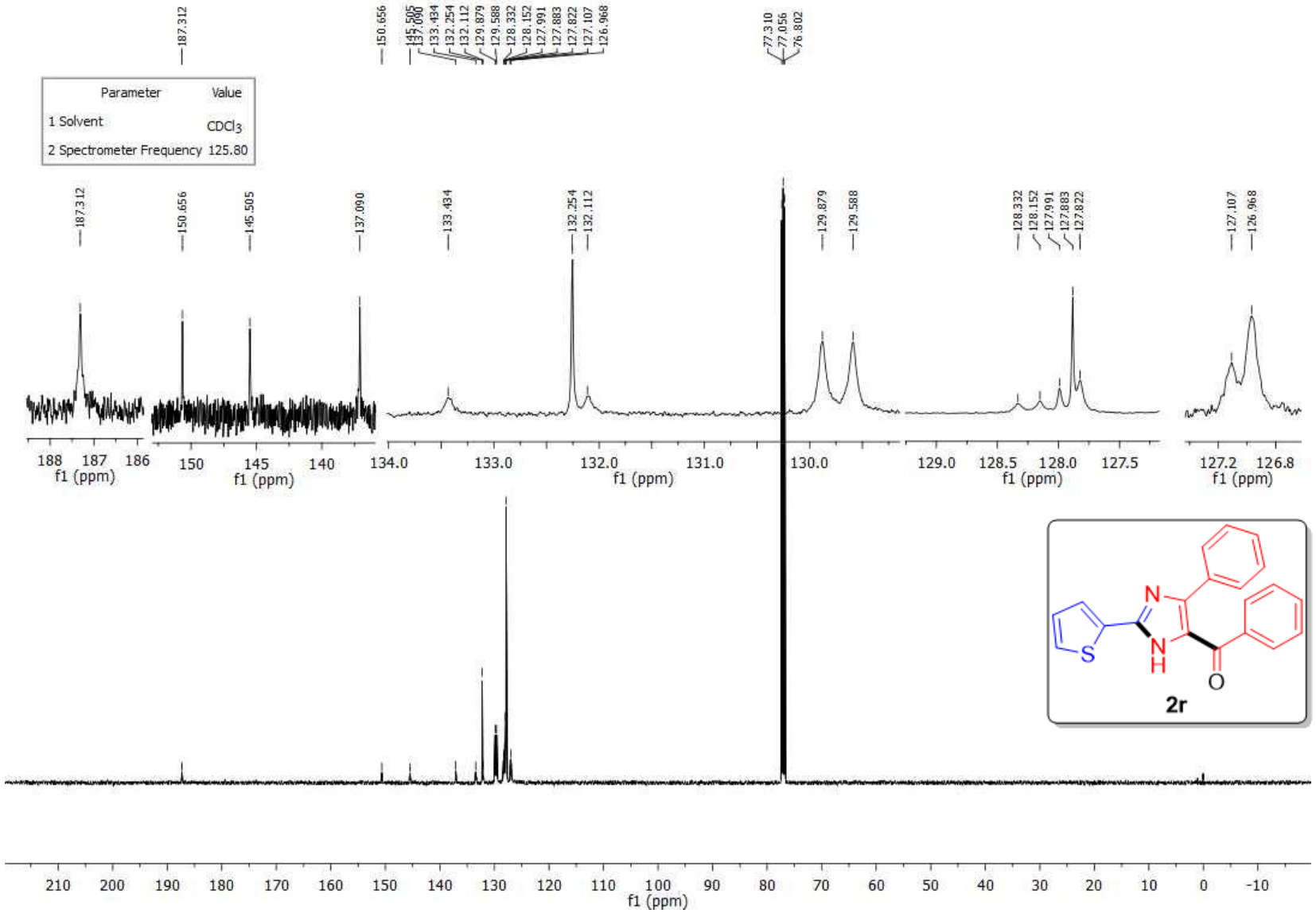
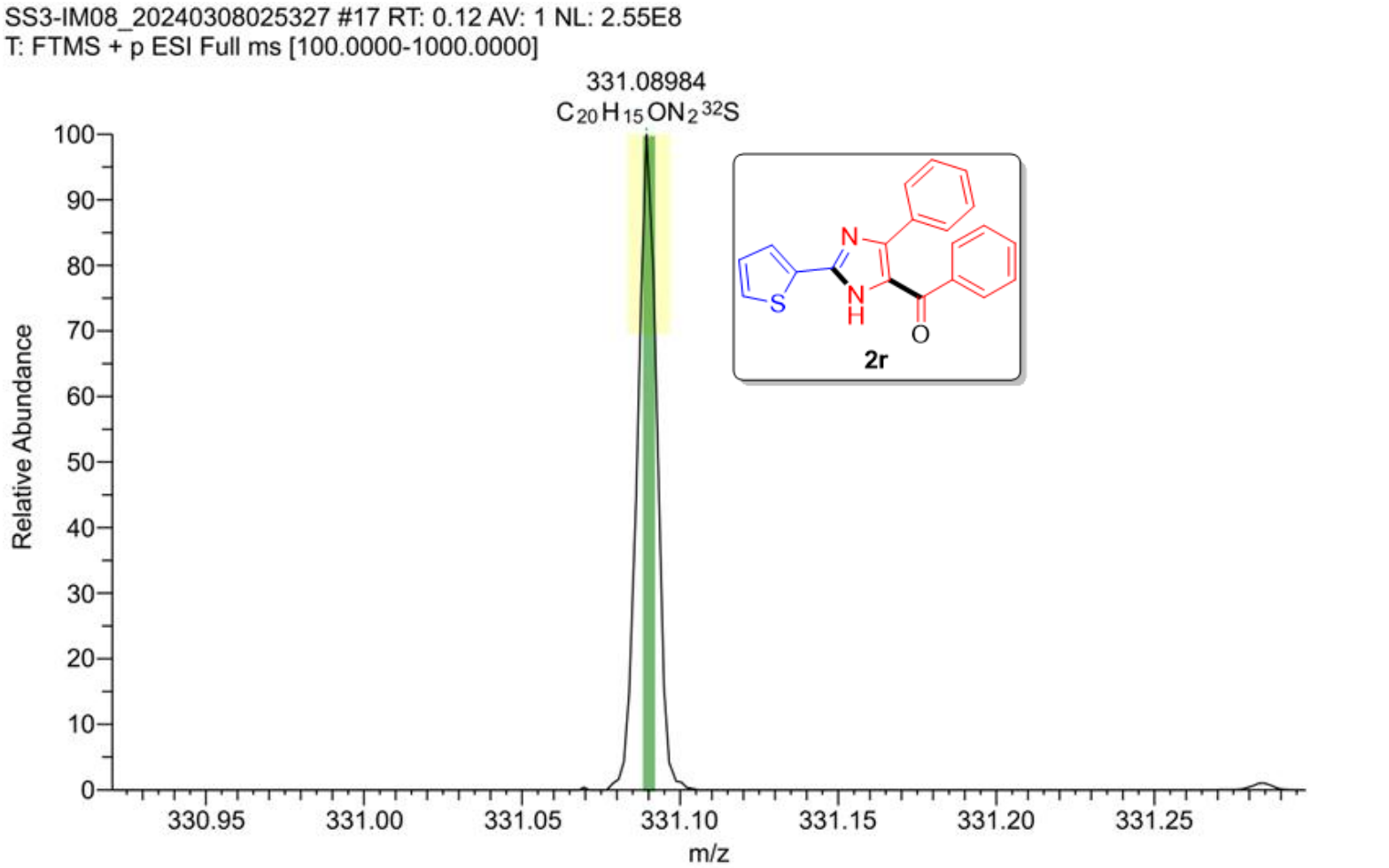


Fig. S96. ^{13}C NMR spectra of phenyl(4-phenyl-2-(thiophen-2-yl)-1*H*-imidazol-5-yl)methanone **(2r).**



Peak Mass	Display Formula	S Fit	RDB	Delta [ppm]	Theo. mass	Pattern Cov. [%]	MSMS Matched...
331.08984	$C_{20}H_{15}ON_2{}^{32}S$	53.390470068323	14.50	-0.35	331.08996	99.85	(Collection)

Fig. S97. HRMS data of phenyl(4-phenyl-2-(thiophen-2-yl)-1*H*-imidazol-5-yl)methanone **(2r).**

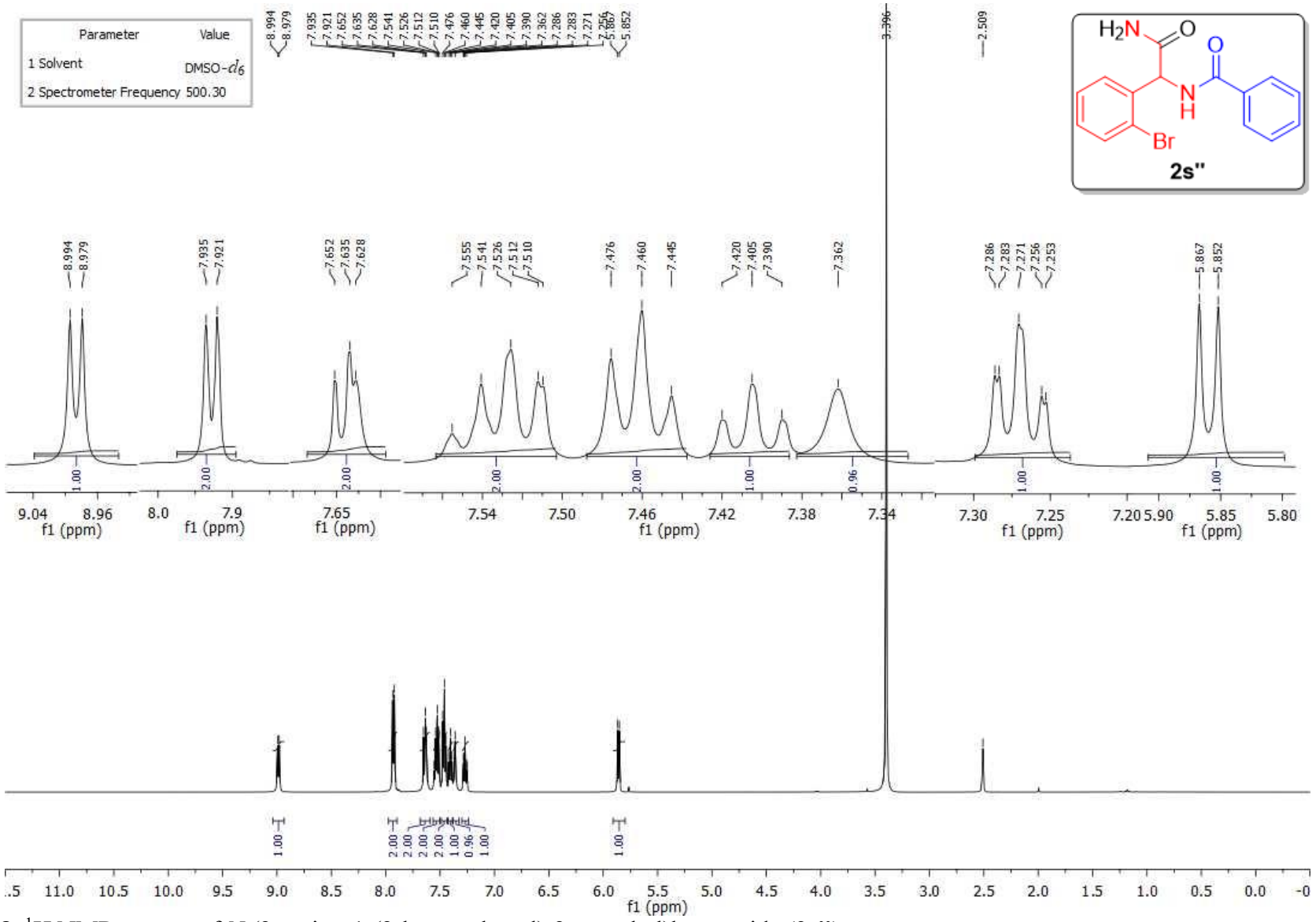


Fig. S98. [1]H NMR spectra of *N*-(2-amino-1-(2-bromophenyl)-2-oxoethyl)benzamide **(2s").**

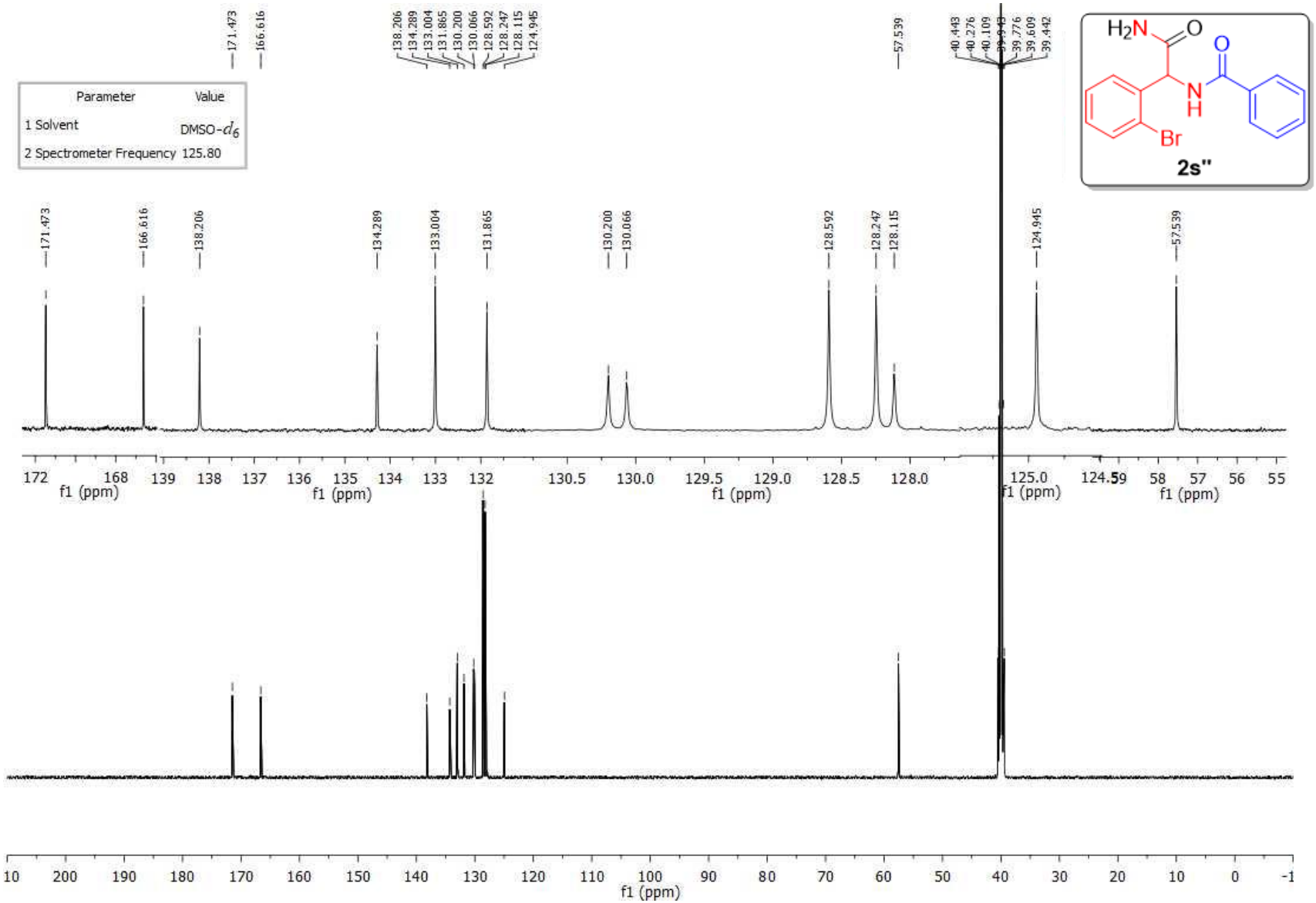


Fig. S99. ^{13}C NMR spectra of *N*-(2-amino-1-(2-bromophenyl)-2-oxoethyl)benzamide **(2s'').**

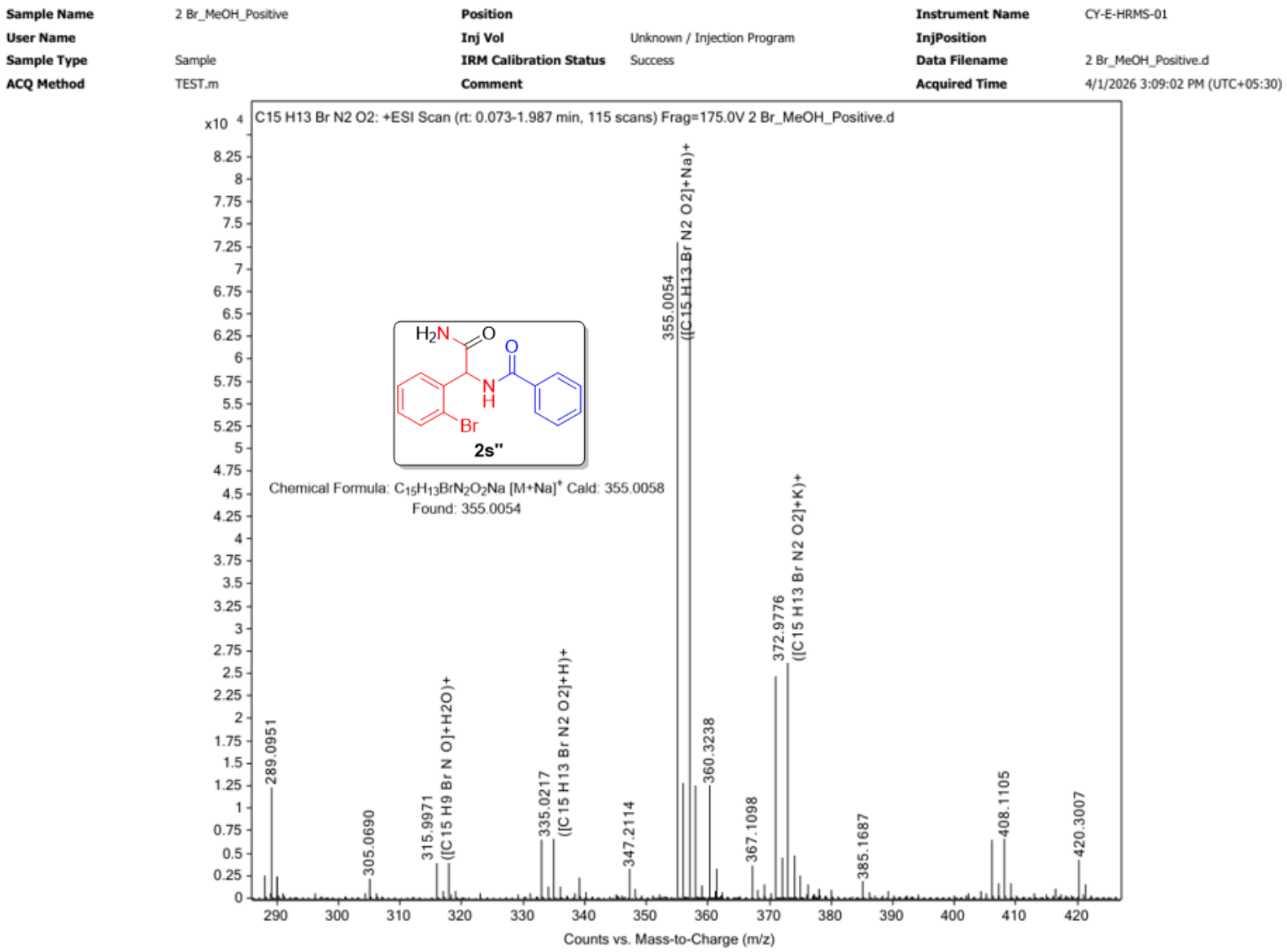


Fig. S100. HRMS data of *N*-(2-amino-1-(2-bromophenyl)-2-oxoethyl)benzamide **(2s'').**

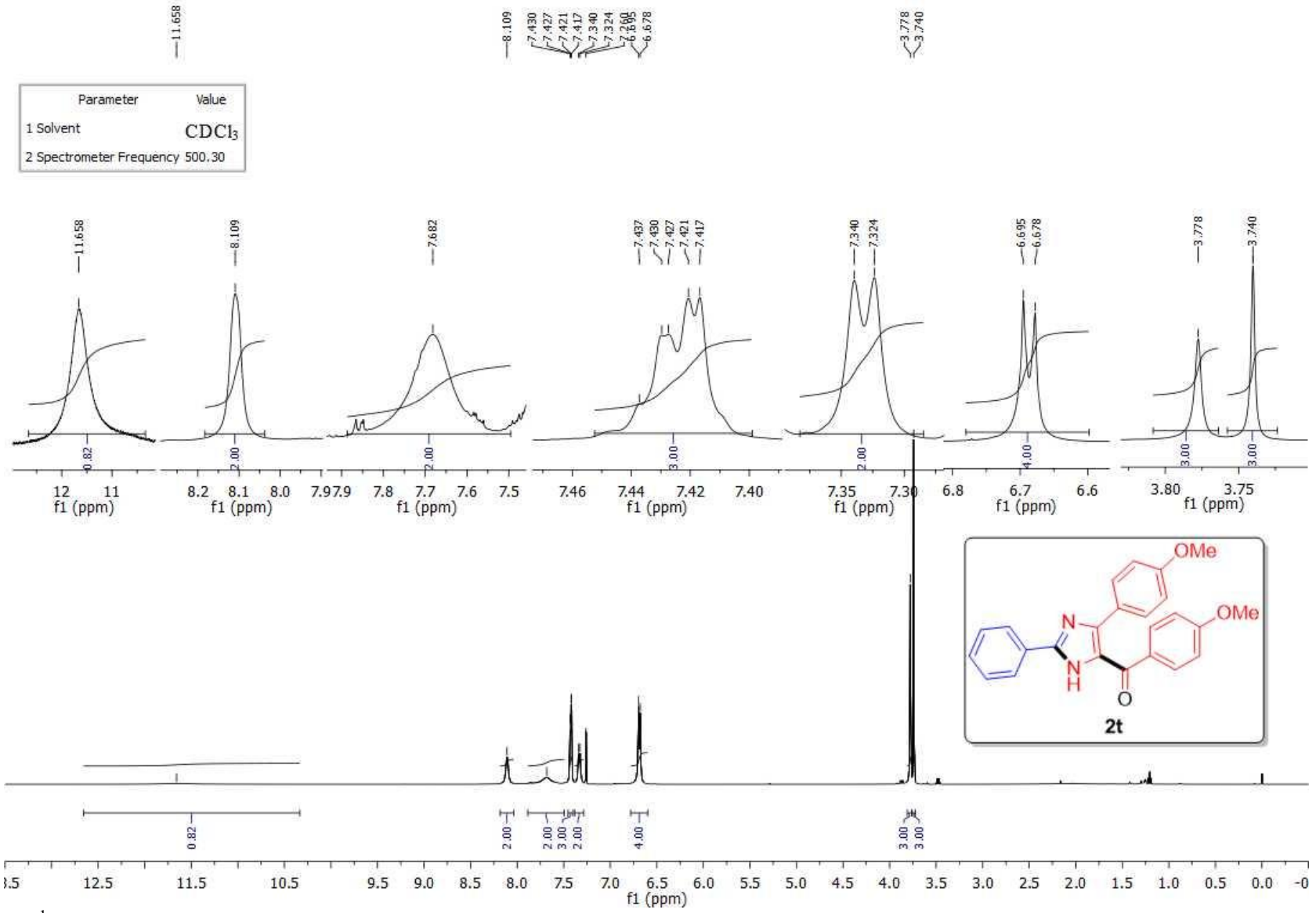


Fig. S101. [1]H NMR spectra of (4-methoxyphenyl)(4-(4-methoxyphenyl)-2-phenyl-1*H*-imidazol-5-yl)methanone **(2t).**

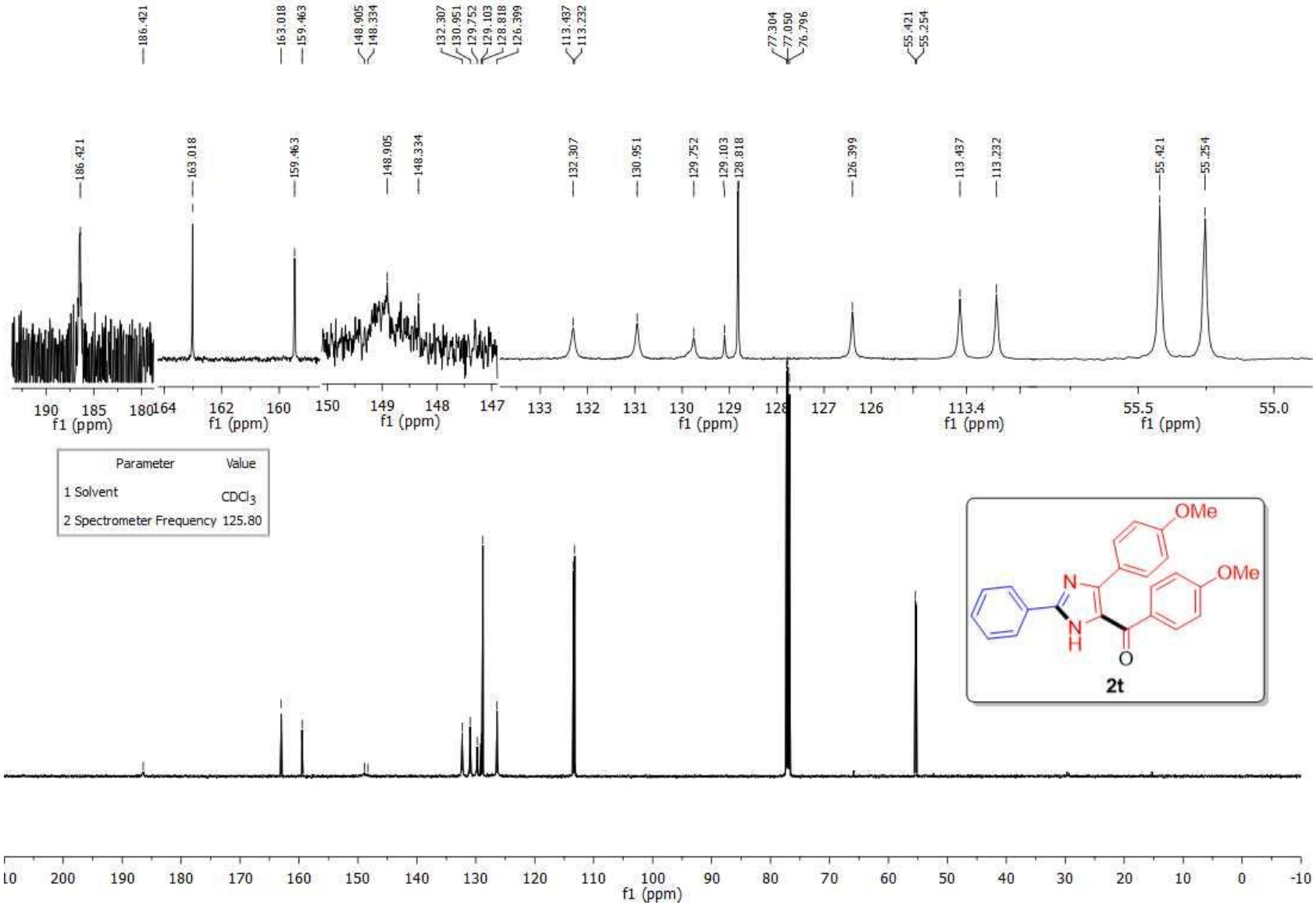
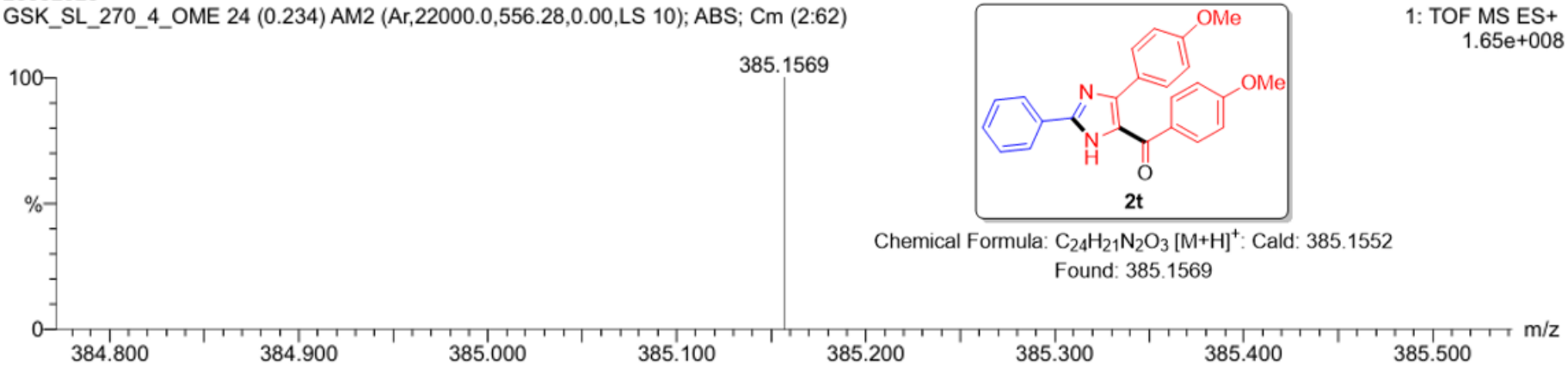


Fig. S102. ^{13}C NMR spectra of (4-methoxyphenyl)(4-(4-methoxyphenyl)-2-phenyl-1*H*-imidazol-5-yl)methanone **(2t).**

Single Mass Analysis
Tolerance = 200.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
7 formula(e) evaluated with 1 results within limits (up to 1 best isotopic matches for each mass)
Elements Used:
C: 0-24 H: 0-21 N: 0-2 O: 0-3
26032026
GSK_SL_270_4_OME 24 (0.234) AM2 (Ar,22000.0,556.28,0.00,LS 10); ABS; Cm (2:62)



Chemical Formula: $C_{24}H_{21}N_2O_3$ $[M+H]^+$: Cald: 385.1552
Found: 385.1569

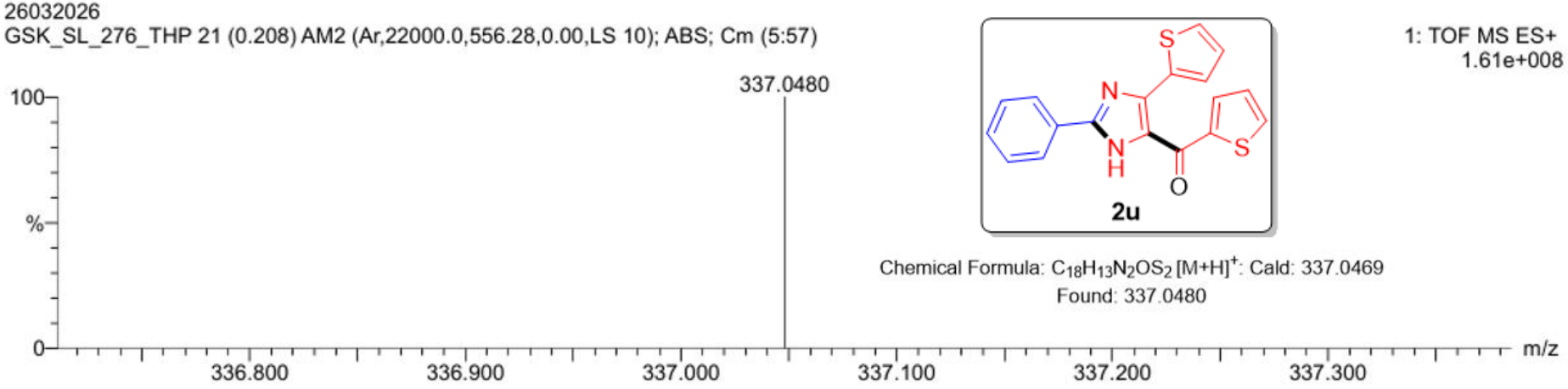
Minimum:				-1.5				
Maximum:		5.0	200.0	50.0				
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
385.1569	385.1552	1.7	4.4	15.5	51.4	n/a	n/a	C24 H21 N2 O3

Fig. S103. HRMS data of (4-methoxyphenyl)(4-(4-methoxyphenyl)-2-phenyl-1*H*-imidazol-5-yl)methanone **(2t).**

Single Mass Analysis
Tolerance = 200.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
13 formula(e) evaluated with 1 results within limits (up to 1 best isotopic matches for each mass)
Elements Used:
C: 0-18 H: 0-13 N: 0-2 O: 0-1 S: 0-2

26032026
GSK_SL_276_THP 21 (0.208) AM2 (Ar,22000.0,556.28,0.00,LS 10); ABS; Cm (5:57)



Minimum:				-1.5				
Maximum:		5.0	200.0	50.0				
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
337.0480	337.0469	1.1	3.3	13.5	51.3	n/a	n/a	C18 H13 N2 O S2

Fig. S104. HRMS data of (2-phenyl-4-(thiophen-2-yl)-1*H*-imidazol-5-yl)(thiophen-2-yl)methanone **(2u).**

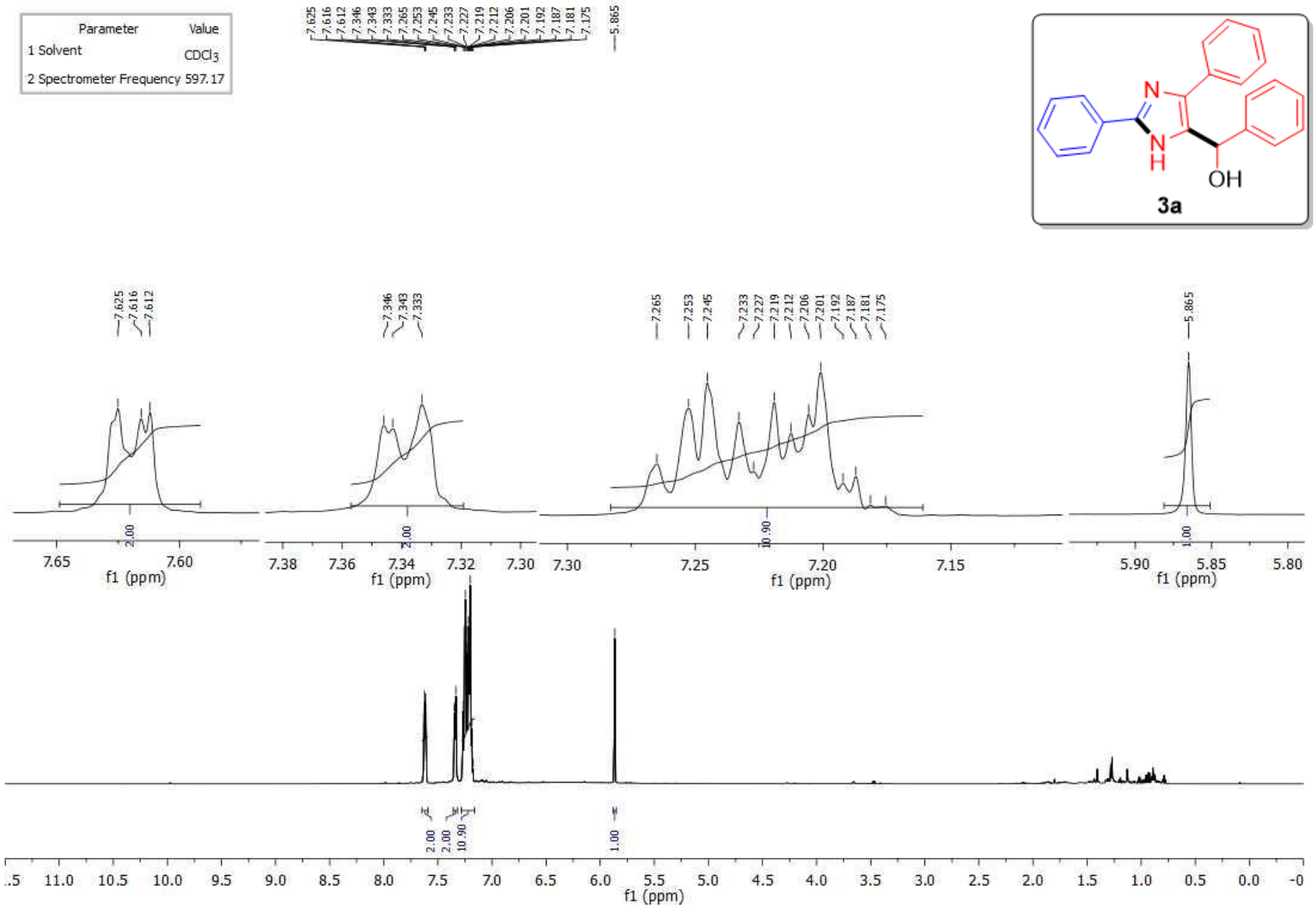


Fig. S105. ^{1}H NMR spectra of (2,4-diphenyl-1*H*-imidazol-5-yl)(phenyl)methanol **(3a).**

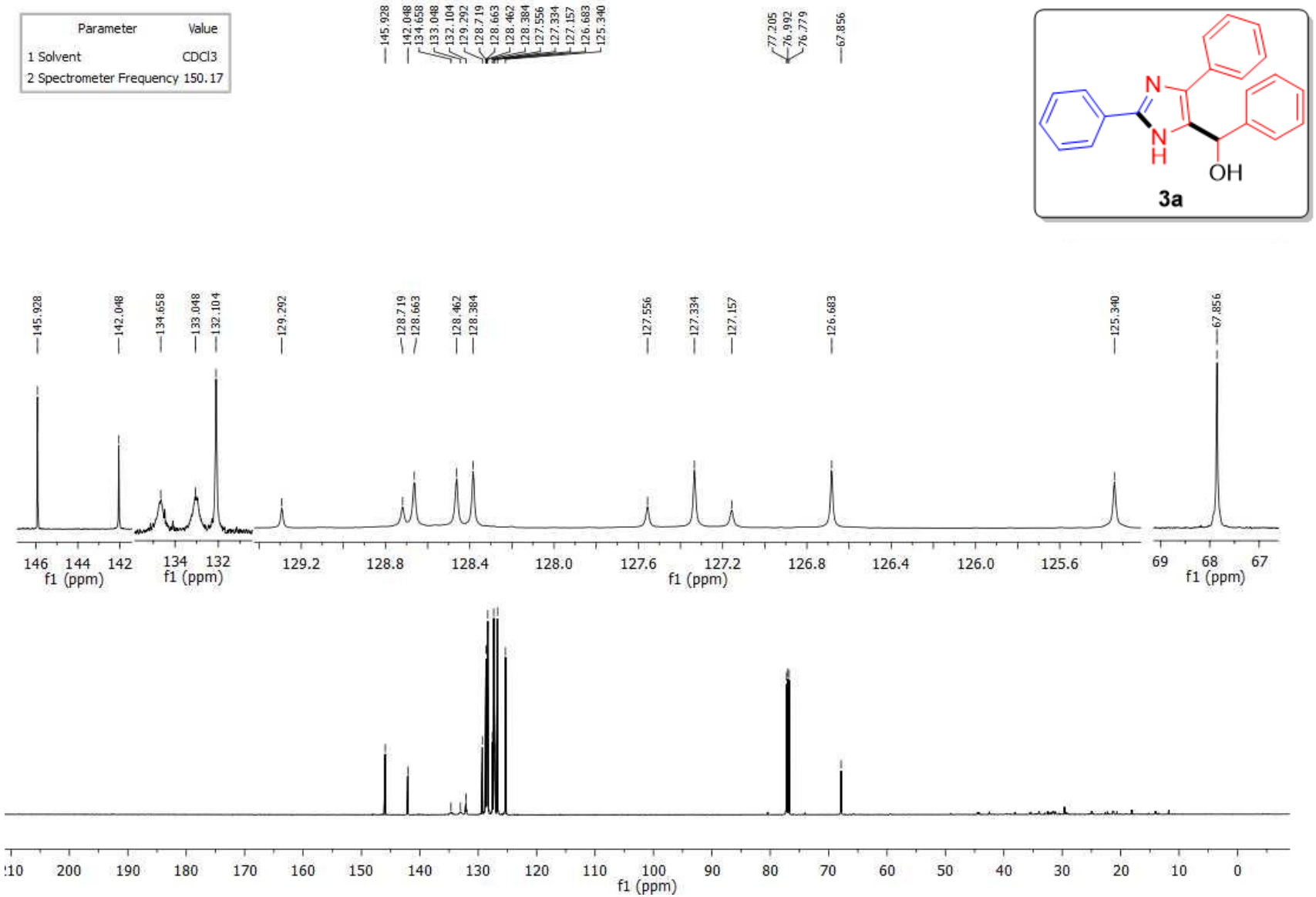


Fig. S106. ^{13}C NMR spectra of (2,4-diphenyl-1*H*-imidazol-5-yl)(phenyl)methanol **(3a).**

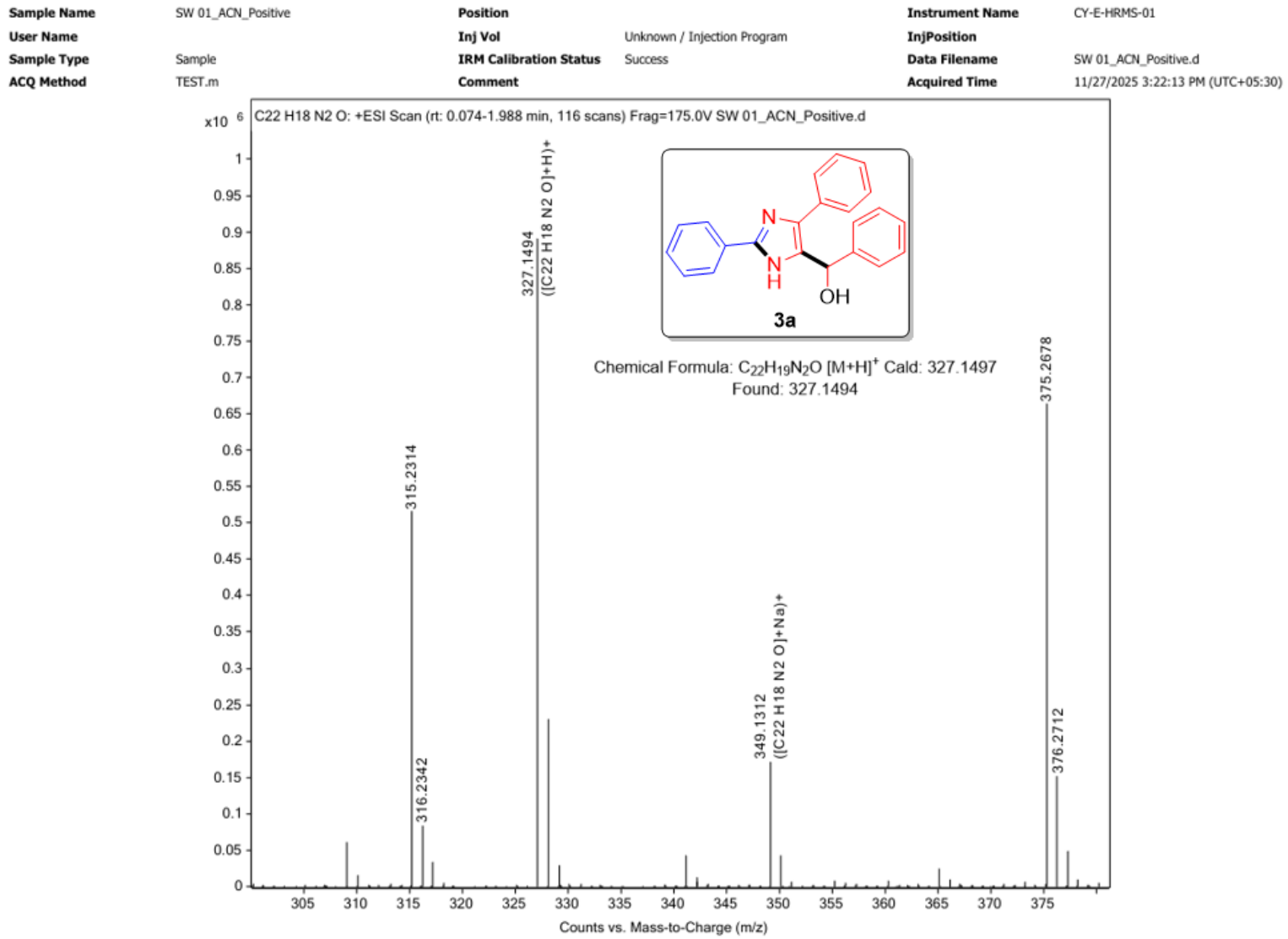


Fig. S107. HRMS data of (2,4-diphenyl-1*H*-imidazol-5-yl)(phenyl)methanol **(3a).**