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A Pd-Free Sonogashira Coupling Protocol Employing an In-situ-Prepared Copper/Chelating 1,2,3-Triazolylidene System

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Abstract:
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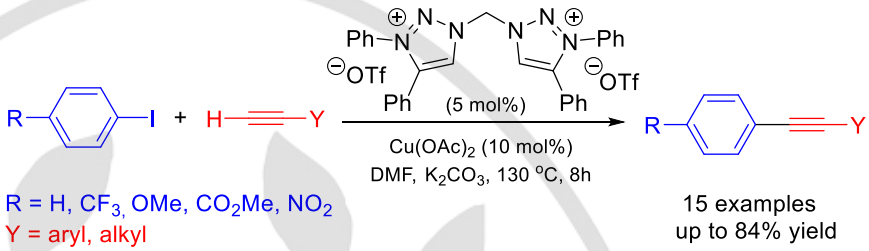

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Abstract A new, palladium-free Sonogashira coupling reaction protocol using a catalytic system that comprises a simple, cheap, widely available copper salt and a chelating 1,2,3-triazolylidene ligand precursor is reported. This protocol provides the desired coupling products in moderate to very good yields.

Key words Sonogashira coupling, palladium-free, copper, sustainability, 1,2,3-triazolylidenes

The Sonogashira coupling reaction is a metal-catalyzed cross-coupling transformation widely used in organic synthesis to form Csp^2-Csp bonds, through the coupling of aryl- or vinyl-halides with terminal alkynes, affording conjugated acetylenic compounds.[1] In 1975, two protocols were independently reported by Cassar,[2] and Dieck and Heck,[3] who used palladium catalysis for the conversion of monosubstituted acetylenes into aryl- or vinyl-substituted acetylene derivatives, through their reaction with the corresponding organohalides. In the same year, Sonogashira, Tohda and Hagihara reported an analogous, but more efficient protocol, in which the reaction was materialized in the presence of copper(I) iodide as co-catalyst under mild conditions.[4]

The Sonogashira reaction has many applications in diverse areas of organic chemistry and materials synthesis. For example, in the synthesis of natural products it is used for the preparation of compounds containing conjugated enynes or enediynes.[5] Sonogashira coupling protocols combined with reduction transformations lead to alkaloids, polyketides, or polycyclic xanthones, whereas couplings affording substituted alkynes followed by regioselective hetero-annulations are employed to synthesize indoles, oxyindoles, furans, benzofurans, or isoquinolinones.[5] Moreover, it is widely used in the synthesis of pharmaceuticals and compounds with biological activity,[6] non-linear optical materials and molecular electronics,[7] polymeric and dendrimeric materials,[8] macrocycles with acetylene links,[9] as well as polyalkynylated molecules.[10]

Sonogashira coupling protocols initially used palladium phosphine complexes as catalysts for the oxidative addition-transmetalation-reductive elimination steps, copper salts as co-catalysts (towards efficient acetylide formation), and organic amines as bases.[3,4] Later on, phosphine ligands were replaced by N-heterocyclic carbenes (NHCs), among others, given that the properties of NHCs can be easily adjusted on-demand, both sterically and electronically, and, also, because the bond between the metal and the NHC is in general stronger than the metal-phosphorus bond.[11] Nowadays, well-defined, palladium-based tailor-designed complexes, bearing either phosphine or NHC ligands, are attracting the interest of the organic and the organometallic community in this regard.[12]

Alternative, Pd-free protocols for the Sonogashira reaction have been also developed, mostly due to the fact that Pd catalysts have low sustainability and are expensive.[13] These protocols include non-conventional Pd-free couplings employing Cu-, Fe-, or Ni-based complexes as catalysts,[14a-c] transition-metal-free microwave-assisted Sonogashira reactions, using water as the solvent together with a phase-transfer agent,[15] photo-induced Sonogashira approaches,[16] or even catalytic protocols involving metal nanoparticles.[17] Recently, in the framework of our interest in sustainable catalysis,[18-23] some of us reported the development of a Pd-free Sonogashira protocol using a catalytic system comprising the widely available $CuSO_4 \bullet 5H_2O$ and a cheap, commercially-available NHC precursor salt.[24] This system can successfully employ a wide variety of terminal alkynes (electron-poor aryl, electron-rich aryl, or alkyl) with either electron-poor or electron-rich aryl iodides.

With the same mindset, we decided to explore the potential of another sustainable Sonogashira reaction protocol, employing an in-situ generated, chelating 1,2,3-triazolylidene, instead of an

NHC. Along these lines, herein we report the development of a new, user-friendly protocol for the Pd-free Sonogashira coupling reaction. This protocol requires a simple experimental setup and can be easily followed in any synthetic laboratory. After screening a number of low-cost, widely-available copper sources, in combination with the in-situ-prepared chelating 1,2,3-triazolylidene $(Trz^*_{Ph,Ph})_2CH_2$ (**L**, Figure 1),[25] the most efficient catalytic system was found to be the one employing $Cu(OAc)_2$. A number of electron-poor or electron-rich aryl iodides, along with a variety of terminal alkynes were coupled with satisfactory results.

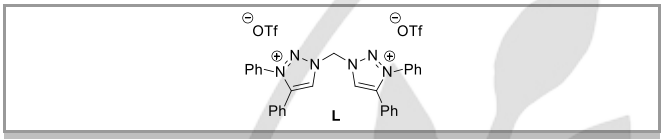
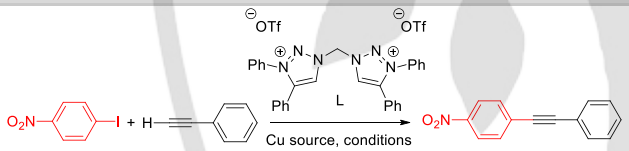


Figure 1 The chelating 1,2,3-triazolylidene ligand precursor $(Trz^*_{Ph,Ph})_2CH_2$ (**L**) utilized in the present work.

Optimization experiments towards probing efficient and straightforward catalytic conditions not requiring the formation and isolation of well-defined copper-based complex(es) were initially performed. Our studies also aimed at increasing the sustainability and selectivity of the protocol in favor of the Sonogashira product, in comparison to the simultaneously formed Glaser coupling product, as well as at the decrease of our protocol's cost. The coupling of *p*-iodonitrobenzene with phenylacetylene was chosen as the model reaction and all experiments were conducted under an inert atmosphere employing the chelating 1,2,3-triazolylidene ligand precursor $(Trz^*_{Ph,Ph})_2CH_2$ (**L**, Figure 1). Initially, we tested the catalytic activity of a wide variety of copper sources (Table 1).

Table 1 Copper source optimization.



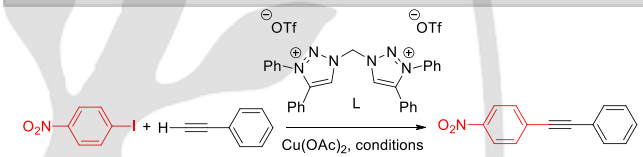
Entry	Copper Source	Product (%)*
1	$CuSO_4$ anhydrous	14%
2	$CuCl_2$ anhydrous	90%
3	$Cu(OAc)_2.xH_2O$	86%
4	$CuCl_2.2H_2O$	81%
5	$CuCO_3.Cu(OH)_2$	74%
6	Cu_2O	-
7	CuCl	84%
8	CuBr	80%
9	$CuBr_2$	87%
10	$CuI(NO_3)_2.3H_2O$	80%
11	$[Cu(CH_3CN)_4]PF_6$	91%
12	$Cu(acac)_2$	89%
13	Cu(OAc)	92%
14	$Cu(OAc)_2$	91%
15	CuI	72%

*Yields calculated by GC/MS analysis. Experimental conditions: Cu salt 20 mol%, ligand **L** 10 mol%, 1-iodo-4-nitrobenzene 0.167 mmol, phenylacetylene 0.2 mmol, K_2CO_3 2eq, solvent DMF (1 mL), temperature = 130°C, reaction time 8h.

Satisfactory catalytic activity is provided by both copper (I) and copper (II) sources, but we decided that the use of $Cu(OAc)_2$ provided the best catalytic system, taking into account the stability, cost, toxicity, and availability of this copper source, besides, of course, its catalytic efficiency. The copper and ligand loading utilized are relatively low, in comparison with our developed NHC-based catalytic system, as well as, with other published protocols.[24,26]

After also testing some inorganic and organic bases (Table 2), potassium carbonate was found to give the highest yield. Solvent optimization experiments were performed as well (Table 3). DMF and PEG 350 are the solvents providing the best results. Despite the more sustainable nature of PEG 350, we decided that DMF is superior, due to difficulties and the bad reproducibility in the isolation of the product when using PEG 350. Finally, we concluded that 130°C was the best temperature for the reaction (Table 4) and that 8 hours is the optimum reaction time (Table 5), as prolonged reaction times did not improve the results, at least in the specific transformation.

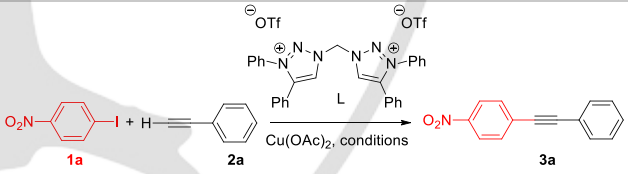
Table 2 Base optimization.



Entry	Base	Product (%)*
1	K_2CO_3	86%
2	Cs_2CO_3	56%
3	KOH	20%
4	CH_3COONa	40%
5	NEt_3	0

*Yields calculated by GC/MS analysis. Experimental conditions: $Cu(OAc)_2$ 10 mol%, ligand **L** 5 mol%, 1-iodo-4-nitrobenzene 0.167 mmol, phenylacetylene 0.2 mmol, base 2eq, solvent DMF (1 mL), temperature = 130°C, reaction time 8h.

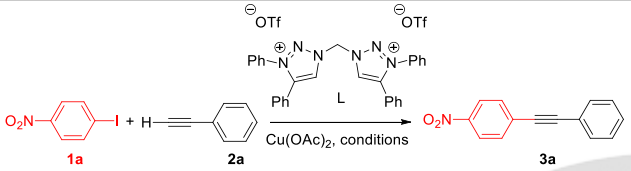
Table 3 Solvent optimization.



Entry	Solvent	Product (%)*
1	toluene	9%
2	p-cymene	17%
3	NMP	4%
4	DMF	86 (80)
5	diglyme	56%
6	1,4-dioxane	0
7	PEG 350	82%

*Yields calculated by GC/MS analysis (Isoleated yields). Experimental conditions: $Cu(OAc)_2$ 10 mol%, ligand **L** 5 mol%, 1-iodo-4-nitrobenzene 0.167 mmol, phenylacetylene 0.2 mmol, K_2CO_3 2 eq, solvent (1 mL), temperature = 130 °C, reaction time 8h

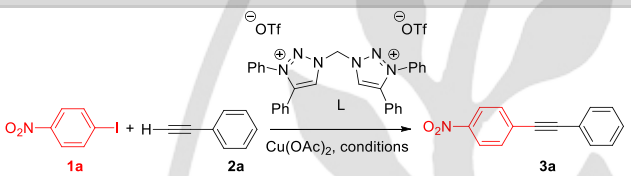
Table 4 Temperature optimization.



Entry	Temperature	Product (%)*
1	RT	No product
2	70 °C	10%
3	100 °C	57%
4	130 °C	86%

*Yields calculated by GC/MS analysis. Experimental conditions: $Cu(OAc)_2$ 10 mol%, ligand **L** 5 mol%, 1-iodo-4-nitrobenzene 0.167 mmol, phenylacetylene 0.2 mmol, K_2CO_3 2eq, solvent DMF (1 mL), temperature (°C), reaction time 8h.

Table 5 Reaction time optimization.



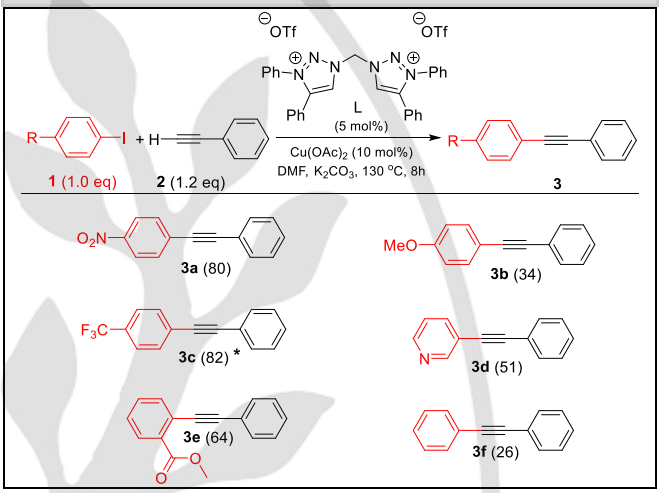
Entry	Time	Product (%)*
1	2 hrs	21
2	4 hrs	48
3	6 hrs	77 (69)
4	8 hrs	86
5	10 hrs	85
6	14 hrs	86

*Yields calculated by GC/MS analysis (Isoleated yields). Experimental conditions: $Cu(OAc)_2$ 10 mol%, ligand **L** 5 mol%, 1-iodo-4-nitrobenzene 0.167 mmol, phenylacetylene 0.2 mmol, K_2CO_3 2eq, solvent DMF (1 mL), temperature 130 °C, reaction time (h).

As mentioned above, one of the known byproducts of the Sonogashira reaction is the Glaser coupling product (coupling of two terminal alkynes / homocoupling).[24,27] In our protocol discussed herein, the Glaser product is formed as well, however, in very low yields. Specifically, in all of the reactions conducted, the ratio of the Sonogashira coupling product versus the Glaser coupling product is below 5.3/1. Moreover, although *p*-iodonitrobenzene and phenylacetylene are known to provide both the corresponding Sonogashira and Glaser products, simply in the presence of some copper sources (albeit in low yields and in non-favorable Sonogashira/Glaser ratios),[24] and this was confirmed in our present study, when we ran some blank tests only with $Cu(OAc)_2$, the Sonogashira product yield obtained in this way is inferior to that of our optimized system (including **L**), even concerning this exceptional substrate case (Sonogashira/homocoupling product yield was 38 %/14 % under otherwise identical to the substrate scope reaction conditions). Along these lines, only traces of the Sonogashira product were observed in the absence of ligand **L** in the coupling of *p*-iodoanisole with phenylacetylene. Finally, a blank experiment carried out in the coupling of phenylacetylene with *p*-iodonitrobenzene in the absence of a copper source did not provide any product.

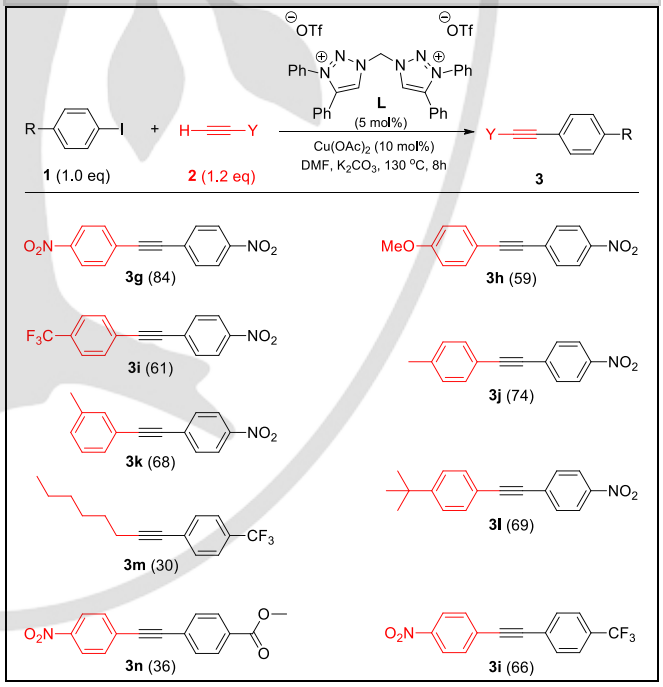
After the optimum catalytic system and reaction conditions were determined, we studied our protocol's substrate scope. As already shown in the optimization studies above, concerning *p*-iodonitrobenzene, aryl iodides bearing electron withdrawing groups afford the desired cross-coupling product in very good isolated yields (**3a**, **3c**, and **3e**, Table 6). Aryl iodides having no substituents (**3f**), heterocyclic rings (**3d**), or electron donating substituents (**3b**) provide moderate to good isolated yields (Table 6). Aryl bromides (bromobenzene, 4-bromobenzotrifluoride) and aryl chlorides (chlorobenzene) are not amenable to this protocol, as concerns their attempted coupling with phenylacetylene, providing very low yields of the desired cross-coupled products, or no product at all.

Table 6 Aryl halide Sonogashira reaction scope.



Experimental conditions: $Cu(OAc)_2$ 10 mol%, ligand **L** 5 mol%, aryl halide 0.167 mmol, phenylacetylene 0.2 mmol, K_2CO_3 2eq, solvent DMF 1 mL, temperature =130 °C, reaction time 8h. *2x catalyst loading: $Cu(OAc)_2$ 20 mol%, ligand 10 mol% (with $Cu(OAc)_2$ 10 mol%, ligand 5 mol%: 61% isolated yield).

Table 7 Terminal alkyne Sonogashira reaction scope.



Experimental conditions: $Cu(OAc)_2$ 10 mol%, ligand **L** 5 mol%, aryl halide 0.167 mmol, terminal alkyne 0.2 mmol, K_2CO_3 2eq, solvent DMF 1 mL, temperature =130 °C, reaction time 8h.

We then investigated the substrate scope of our protocol with regards to the terminal alkynes. Given that the aryl halide scope

study showed that electron donating groups result in moderate to good yields, we only studied the coupling of aryl halides bearing electron withdrawing groups (Table 7). More specifically, both alkyl- and aryl-substituted terminal alkynes, bearing either electron-donating or electron-withdrawing groups on the phenyl ring, afforded good to very good isolated yields. This result suggests that the electronic characteristics of the aromatic terminal alkynes employed do not play a significant role in the outcome of the reaction, at least at the extent of the analogous influence shown by the electronic characteristics of the aryl halide.

To probe the possible intervention of radical species in our catalytic protocol, we performed a reaction in the presence of a radical scavenger and another in the presence of a radical initiator. More specifically, utilization of one of the most widely-used radical scavengers, 2,2,6,6-tetramethylpiperidine 1-oxyl (TEMPO), afforded almost identical results with our typical protocol, revealing that the absence of radical species does not negatively affect the reaction's yield. As radical initiator we used azobisisobutyronitrile (AIBN). Again, we did not observe any change in the reaction's yield, thus excluding the presence of free radical species in the reaction. The mechanism we propose for this transformation is similar to those of analogous, copper-based catalytic systems, including copper acetylide formation, oxidative addition to the organohalide, and, eventually, reductive elimination of the cross-coupled product.[24,28,29] This Cu(I)/Cu(III) catalytic cycle[30] requires, in the present case, the in-situ reduction of Cu(II) to Cu(I), which can take place by the solvent or the ligand.[24]

Finally, we decided to study the catalytic efficiency of a pre-formed, well-defined copper complex that could possibly form and function under the catalytic reaction conditions employed, in order to compare it with the in-situ generated catalytic system. Several attempts were made to prepare such a complex: reactions of anhydrous copper(II) acetate or copper(II) triflate as the copper source, in the presence of the 1,2,3-triazolylidene $(Trz^*_{Ph,Ph})_2CH_2$ (**L**, Figure 1) in various solvents of different polarity and coordinating ability (CH_2Cl_2, CH_3OH, CH_3CN, DMF, or THF), with different bases (anhydrous sodium acetate, sodium acetate trihydrate, anhydrous potassium carbonate, or potassium *tert*-butoxide) were all unsuccessful. Performing the complexation reactions at room temperature or under heating also did not yield a well-defined compound. Transmetalation of the 1,2,3-triazolylidene using silver(I) salts was unsuccessful as well. In all cases, the products of the reactions were inorganic salts of copper with carbonate, acetate, or triflate counter-anions. To this end, dicopper(I)-dimesoionic carbene complex **4** (Figure 2), that is, a binuclear complex with one bridging mesoionic dicarbene ligand and one bridging acetate, previously reported by some of us,[31] was alternatively used, as a well-defined catalyst possibly resembling our in-situ prepared system. Although the Sonogashira coupling was successful (GC/MS yield using the well-defined complex 46% vs GC/MS yield using our protocol 91%), the results were significantly inferior compared to that of the in-situ prepared system, as both the Sonogashira product yield and the Sonogashira/Glaser products ratio (3/2) were lower in the case of complex **4**.

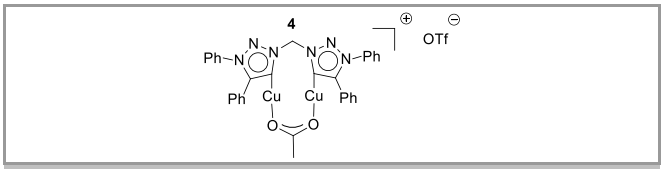


Figure 2 Well-defined dicopper(I)-dimesoionic carbene complex **4** tested for its catalytic activity under the optimized conditions.

Summing up, herein we have reported the development of a user-friendly, sustainable protocol for the Pd-free Sonogashira coupling reaction. Reaction conditions were optimized with regards to the copper source, the base, the solvent, the temperature, and the reaction time utilized. The final catalytic system was chosen on the basis of its efficiency, components stability, cost, toxicity, and availability. It is formed in-situ and the necessary catalyst loading is relatively low, when compared to analogous systems. The reaction scope of the organohalides and the terminal alkynes amenable to this system was investigated by employing a variety of substrates. Aryl bromides and aryl chlorides are, in general, innocent bystanders. On the other hand, aryl iodides bearing electron-withdrawing groups provide very good isolated yields, while aryl iodides bearing electron-donating groups provide moderate to good yields. With regards to the various terminal alkynes studied, the results are very good with aryl substituted terminal alkynes bearing either electron withdrawing or electron donating substituents. Alkyl substituted terminal alkynes afford the desired product in moderate yields.

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Supporting Information

YES (this text will be updated with links prior to publication)

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(32) **General catalytic protocol procedure**
A dry Schlenk tube equipped with a magnetic stirrer is loaded under argon with $Cu(OAc)_2$ (10 mol%, 0.0167 mmol), ligand **L** (5 mol%, 0.0084 mmol), K_2CO_3 (0,33 mmol), the aryl halide (0.167 mmol) and DMF (1 mL). The above mixture is degassed with a slow bubbling flow of argon for 20 minutes. The terminal alkyne (0.2 mmol) is then added and the reaction mixture is sealed under an argon atmosphere. The Schlenk tube is transferred in a preheated oil bath (130°C) and the reaction mixture is stirred for 8h. Then, the reaction is cooled to room temperature and transferred in a 100 mL separating funnel with 20 mL of H_2O. The mixture is extracted with ethyl acetate (3X10mL). The organic layers are combined, washed with brine (15 mL), and dried over $MgSO_4$. The dry organic layer is filtered and the solvent is removed in a rotary evaporator. Products are separated with gradient column chromatography using CH_2Cl_2/petroleum ether.
1-Nitro-4-(phenylethynyl)benzene (3a). Prepared according to the general procedure and obtained as a yellow solid in 80% yield (30 mg, 0.134 mmol). ^{1}H NMR (200 MHz, $CDCl_3$) δ 8.23 (d, *J* = 9.0 Hz, 2H), 7.67 (d, *J* = 9.0 Hz, 2H), 7.61 – 7.52 (m, 2H), 7.44 – 7.34 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 147.14, 132.43, 132.00, 130.43, 129.43, 128.69, 123.80, 122.26, 94.86, 87.70.

Supporting Information

for

A Pd-Free Sonogashira Coupling Protocol Employing an In-situ-Prepared Copper/Chelating 1,2,3-Triazolylidene System

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Prof. Dr. G. C. Vougioukalakis: vougiouk@chem.uoa.gr

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General Reagent Information

All chemicals were obtained from commercial sources and were used without any further purification. All reactions were carried out under an atmosphere of

argon. The course of the reactions was followed by either GC-MS or thin layer chromatography (TLC), using aluminium sheets (0.2 mm) coated with silica gel 60 with fluorescence material that absorbs at 254 nm (silica gel 60 F254). The purification of the products was carried out by flash column chromatography, using silica gel 60 (230-400 mesh).

General Analytical Information

^{1}H, ^{13}C and ^{19}F NMR spectra were measured on a Varian Mercury 200 MHz, or a Brucker Avance 400 MHz instrument, using $CDCl_3$ as the solvent and its residual solvent peak as a reference. NMR spectroscopic data are given in the order: chemical shift, multiplicity (s, singlet, br. s, broad singlet, d, doublet, t, triplet, q, quartet, m, multiplet), coupling constant in Hertz (Hz), and number of protons. The GC-MS spectra were recorded with a Shimandzu® GCMS-QP2010 Plus, Chromatograph Mass Spectrometer using a MEGA® (MEGA-5, F.T: 0.25 μm, I.D.: 0.25 mm, L: 30 m, Tmax: 350 ^{o}C, Column ID# 11475) column, using *n*-octane as the internal standard.

General Catalytic Protocol Procedure

A dry Schlenk tube equipped with a magnetic stirrer is loaded under argon with $Cu(OAc)_2$ (10 mol%, 0.0167 mmol), ligand **L** (5 mol%, 0.0084 mmol), K_2CO_3 (0,33 mmol), the aryl halide (0.167 mmol) and DMF (1 mL). The above mixture is degassed with a slow bubbling flow of argon for 20 minutes. The terminal alkyne (0.2 mmol) is then added and the reaction mixture is sealed under an argon atmosphere. The Schlenk tube is transferred in a preheated oil bath (130^{o}C) and the reaction mixture is stirred for 8h. Then, the reaction is cooled to room temperature and transferred in a 100 mL separating funnel with 20 mL of H_2O. The mixture is extracted with ethyl acetate (3X10mL). The organic layers are combined, washed with brine (15 mL), and dried over $MgSO_4$. The dry organic layer is filtered and the solvent is removed in a rotary evaporator. Products are separated with gradient column chromatography using CH_2Cl_2/petroleum ether.

Compounds Characterization Data

(Trz*$_{Ph,Ph}$)$_2$CH$_2$ (L). ^{1}H NMR (400 MHz, acetone-*d6*): δ 9.69 (s, 2H, triazole-5*H*), 8.09 (s, 2H, N-C*H*$_2$-N), 7.82 – 7.79 (m, 2H, aryl-*H*), 7.77 – 7.73 (m 8H, aryl-*H*), 7.68 – 7.63 (m, 2H, aryl-*H*), 7.60 – 7.54 (m, 4H, aryl-*H*), 7.50 – 7.46 (m, 4H, aryl-*H*). ^{13}C NMR (100 MHz, acetone-*d6*): δ 145.6 (triazole-5*C*), 135.1, 133.3, 132.6, 132.1, 130.9, 129.9, 127.4, 123.3 (all aryl-*C*), 65.8 (N-*C*H$_2$-N). MS (ESI): m/z found 228.1044 calcd 228.1026 for $[C_{29}H_{24}N_6]^{2+}$.

Well-defined dicopper(I)-dimesoionic carbene complex (4). ^{1}H NMR (400 MHz, CD_2Cl_2) δ 7.75–7.28 (m, 22H, aryl-H + methylene-H), 2.09 (s, 3H, acetate-H). ^{13}C NMR (101 MHz, CD_2Cl_2) δ 83.38 (Carbene), 149.79, 135.15,132.07, 130.93, 130.49, 130.10, 129.69, 127.22, 125.85, 70.50, 68.31 (THF), 31.17, 26.14 (THF), 22.63. Anal. Calcd (%) for $[C_{32}H_{25}N_6Cu_2O_5F_3S{\cdot}0.60\ C_4H_8O]$ C 49.6, H 3.61, N 10.09; Found C 49.21, H 3.627, N 9.747. ESI-MS: m/z: [M–OTf] + Calcd 639.063, Found 639.062.

1-Nitro-4-(phenylethynyl)benzene (3a). Prepared according to the general procedure and obtained as a yellow solid in 80% yield (30 mg, 0.134 mmol). ^{1}H NMR (200 MHz, $CDCl_3$) δ 8.23 (d, *J* = 9.0 Hz, 2H), 7.67 (d, *J* = 9.0 Hz, 2H), 7.61 – 7.52 (m, 2H), 7.44 – 7.34 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 147.14, 132.43, 132.00, 130.43, 129.43, 128.69, 123.80, 122.26, 94.86, 87.70.

1-Methoxy-4-(phenylethynyl)benzene (3b). Prepared according to the general procedure and obtained as a white solid in 34% yield (12 mg, 0.057 mmol). ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.60 – 7.41 (m, 4H), 7.38 – 7.30 (m, 3H), 6.90 (d, *J* = 8.8 Hz, 2H), 3.82 (s, 3H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 159.66, 133.12, 131.51, 128.39, 128.01, 123.64, 115.37, 114.05, 89.51, 88.17, 55.29.

1-(Phenylethynyl)-4-(trifluoromethyl)benzene (3c). Prepared according to the general procedure and obtained as a yellow solid in 61% yield (25 mg, 0.102 mmol). ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.66 – 7.59 (m, 4H), 7.58 – 7.51 (m, 2H), 7.42 – 7.34 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 131.96, 131.90, 130.07 (q, *J* = 32.6 Hz), 128.98, 128.60, 127.29, 125.48 (q, *J* = 3.8 Hz), 124.21 (q, *J* = 270.2 Hz), 122.72, 91.91, 88.12.

3-(Phenylethynyl)pyridine (3d). Prepared according to the general procedure and obtained as a yellow solid in 51% yield (15 mg, 0.085 mmol). ^{1}H NMR (200 MHz, $CDCl_3$) δ 8.82 – 8.73 (m, 1H), 8.60 – 8.51 (m, 1H), 7.88 – 7.75 (m, 1H), 7.59 – 7.48 (m, 2H), 7.44 – 7.27 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 152.43, 148.71, 138.56, 131.85, 128.96, 128.60, 123.19, 122.70, 120.67, 92.79, 86.09.

Methyl 2-(phenylethynyl)benzoate (3e). Prepared according to the general procedure and obtained as a yellow oil in 64% yield (25 mg, 0.107 mmol). ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.98 (d, *J* = 7.7 Hz, 1H), 7.65 (d, *J* = 7.7 Hz, 1H), 7.61 – 7.53 (m, 2H), 7.52 – 7.41 (m, 1H), 7.40 – 7.29 (m, 4H), 3.97 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.86, 134.11, 132.00, 131.87, 131.82, 130.60, 128.65, 128.49, 128.02, 123.84, 123.45, 94.46, 88.35, 52.32.

1,2-Diphenylethyne (3f). Prepared according to the general procedure and obtained as a white solid in 16% yield (5 mg, 0.027 mmol). ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.73 – 7.61 (m, 4H), 7.48 – 7.36 (m, 6H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 131.71, 128.45, 128.36, 123.39, 89.53.

1,2-bis(4-nitrophenyl)ethyne (3g). Prepared according to the general procedure and obtained as a white solid in 16% yield (5 mg, 0.027 mmol). ^{1}H NMR (200 MHz, $CDCl_3$) δ 8.26 (d, *J* = 8.8 Hz, 4H), 7.71 (d, *J* = 8.8 Hz, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 147.81, 132.77, 129.02, 123.94, 92.14.

1-Methoxy-4-((4-nitrophenyl)ethynyl)benzene (3h). Prepared according to the general procedure and obtained as a yellow solid in 59% yield (25 mg, 0.1 mmol). ^{1}H NMR (200 MHz, $CDCl_3$) δ 8.20 (d, *J* = 8.9 Hz, 2H), 7.63 (d, *J* = 8.9 Hz, 2H), 7.50 (d, *J* = 8.8 Hz, 2H), 6.91 (d, *J* = 8.8 Hz, 2H), 3.85 (s, 3H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 160.53, 146.79, 133.58, 132.12, 130.83, 123.77, 114.34, 114.23, 95.28, 86.77, 55.51.

1-Nitro-4-((4-(trifluoromethyl)phenyl)ethynyl)benzene (3i). Prepared according to the general procedure and obtained as a yellow solid in 61% yield / 66% yield (26 mg, 0.09 mmol / 32 mg, 0,11 mmol). ^{1}H NMR (200 MHz, $CDCl_3$) δ 8.29 – 8.14 (m, 2H), 7.74 – 7.57 (m, 6H). ^{13}C NMR (101 MHz, CDCl3): δ 147.55, 132.65, 132.24, 131.06 (q, *J* = 32.8 Hz), 129.56, 126.05, 125.64 (q, *J* = 3.7 Hz), 123.91 (q, *J* = 271.2 Hz), 123.87, 92.94, 89.67.

1-methyl-4-((4-nitrophenyl)ethynyl)benzene (3j). Prepared according to the general procedure and obtained as a yellow solid in 74% yield (29 mg, 0.12 mmol). ^{1}H NMR (200 MHz, $CDCl_3$) δ 8.21 (d, *J* = 8.9 Hz, 2H), 7.64 (d, *J* = 8.9 Hz, 2H), 7.45 (d, *J* = 8.1 Hz, 2H), 7.19 (d, *J* = 7.9 Hz, 2H), 2.39 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 146.97, 139.80, 132.29, 131.90, 130.66, 129.45, 123.75, 119.16, 95.24, 87.22, 21.32

1-Methyl-3-(2-(4-nitrophenyl)ethynyl)benzene (3k). Prepared according to the general procedure and obtained as a yellow solid in 68% yield (27 mg, 0.11 mmol). ^{1}H NMR (200 MHz, $CDCl_3$) δ 8.21 (d, *J* = 8.8 Hz, 2H), 7.65 (d, *J* = 8.9 Hz, 2H), 7.42 – 7.32 (m, 2H), 7.28 – 7.24 (m, 1H), 7.23 – 7.17 (m, 1H), 2.37 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 147.08, 138.45, 132.54, 132.39, 130.54, 130.35, 129.09, 128.59, 123.79, 122.05, 95.14, 87.39, 21.38.

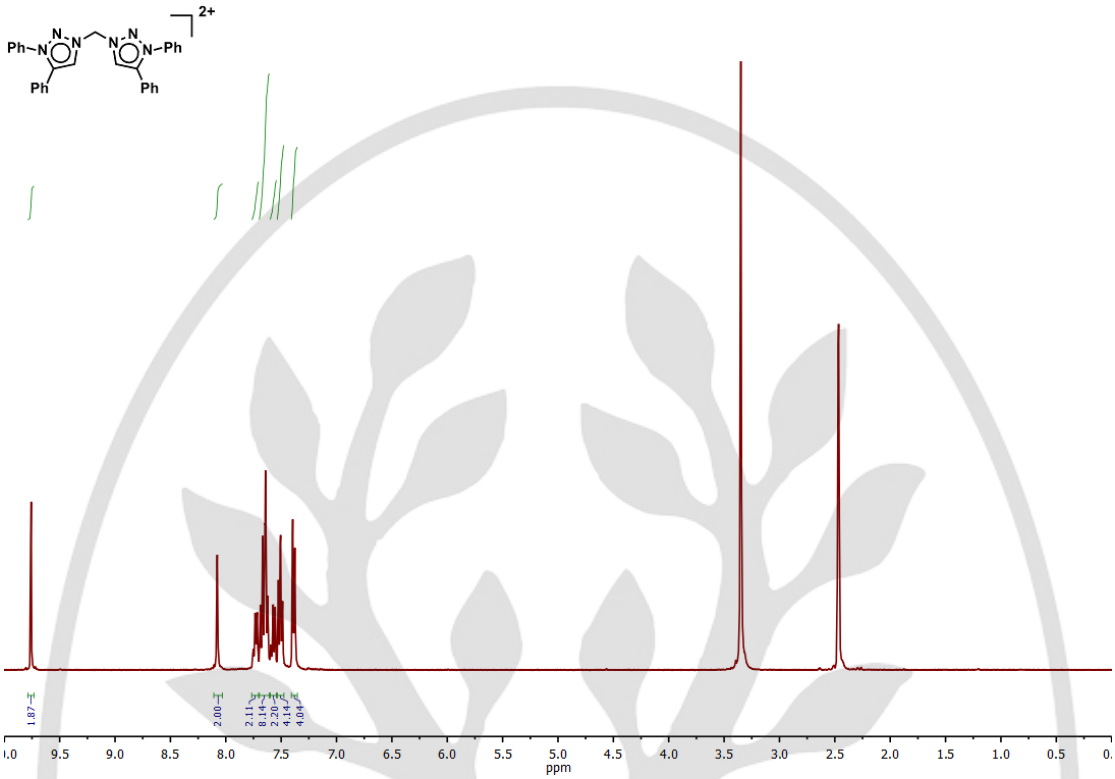
1-(tert-butyl)-4-((4-nitrophenyl)ethynyl)benzene (3l). Prepared according to the general procedure and obtained as a pale-yellow solid in 69% yield (32 mg, 0.115 mmol). ^{1}H NMR (200 MHz, $CDCl_3$) δ 8.25 – 8.12 (m, 2H), 7.71 – 7.60 (m, 2H), 7.54 – 7.45 (m, 2H), 7.44 – 7.37 (m, 2H), 1.34 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 152.92, 146.98, 132.33, 131.76, 130.70, 125.71, 123.76, 119.20, 95.23, 87.21, 35.07, 31.27.

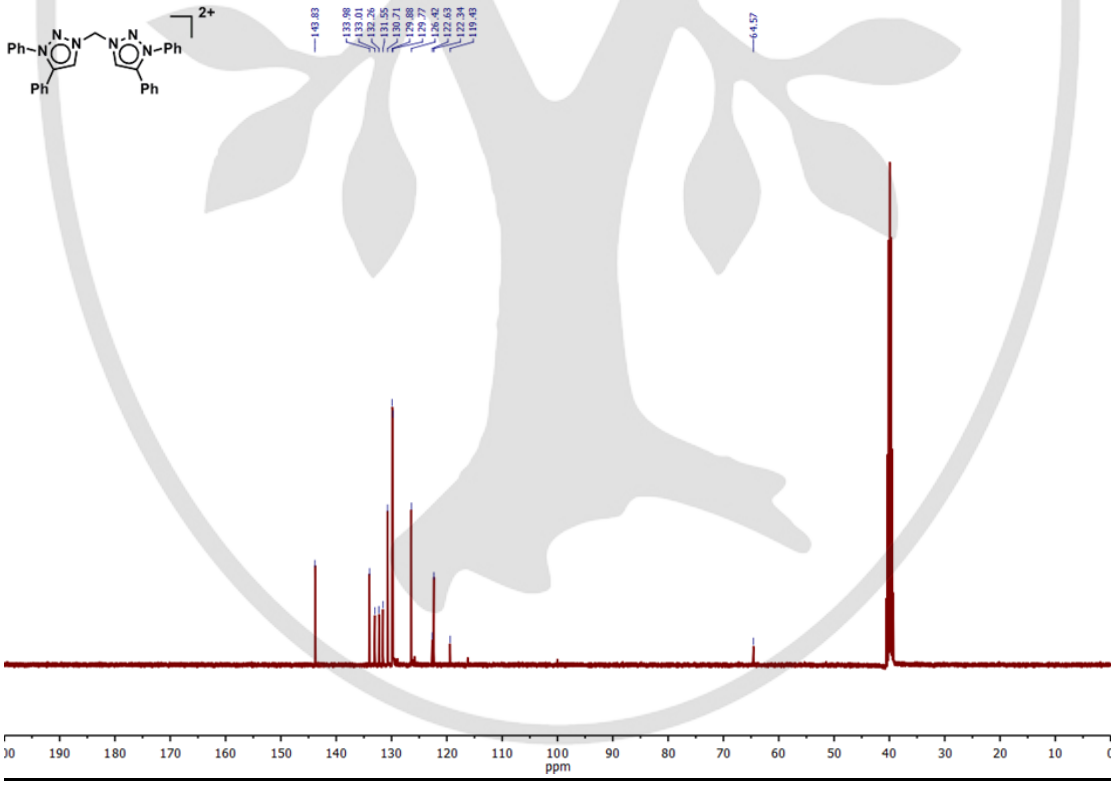
1-(oct-1-yn-1-yl)-4-(trifluoromethyl)benzene (3m). Prepared according to the general procedure and obtained as a yellow oil in 30% yield (12.5 mg, 0.05 mmol). ^{1}H NMR (200 MHz $CDCl_3$) δ 7.54 (d, *J* = 8.7 Hz, 2H), 7.48 (d, *J* = 8.7 Hz, 2H), 2.43 (t, *J* = 7.0 Hz, 2H), 1.71 – 1.55 (m, 2H), 1.52 – 1.41 (m, 2H), 1.39 – 1.29 (m, 4H), 0.92 (t, *J* = 6.7 Hz, 3H). ^{13}C NMR ($CDCl_3$): δ 131.92, 129.43 (q, *J* = 32.6 Hz), 128.27, 125.29 (q, *J* = 3.7 Hz), 124.2 (q, *J* = 280 Hz), 93.53, 79.68, 31.51, 28.77, 28.70, 22.71, 19.59, 14.17.

Methyl 2-((4-nitrophenyl)ethynyl)benzoate (3n). Prepared according to the general procedure and obtained as a yellow solid in 36% yield (17 mg, 0.06 mmol). ^{1}H NMR (200 MHz, $CDCl_3$) δ 8.27 – 8.19 (m, 2H), 8.07 – 8.00 (m, 1H), 7.76 – 7.65 (m, 3H), 7.59 – 7.41 (m, 2H), 3.97 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.34, 147.33, 134.36, 132.58, 132.20, 132.08, 130.84, 130.45, 129.05, 123.79, 122.85, 93.55, 92.29, 52.46.

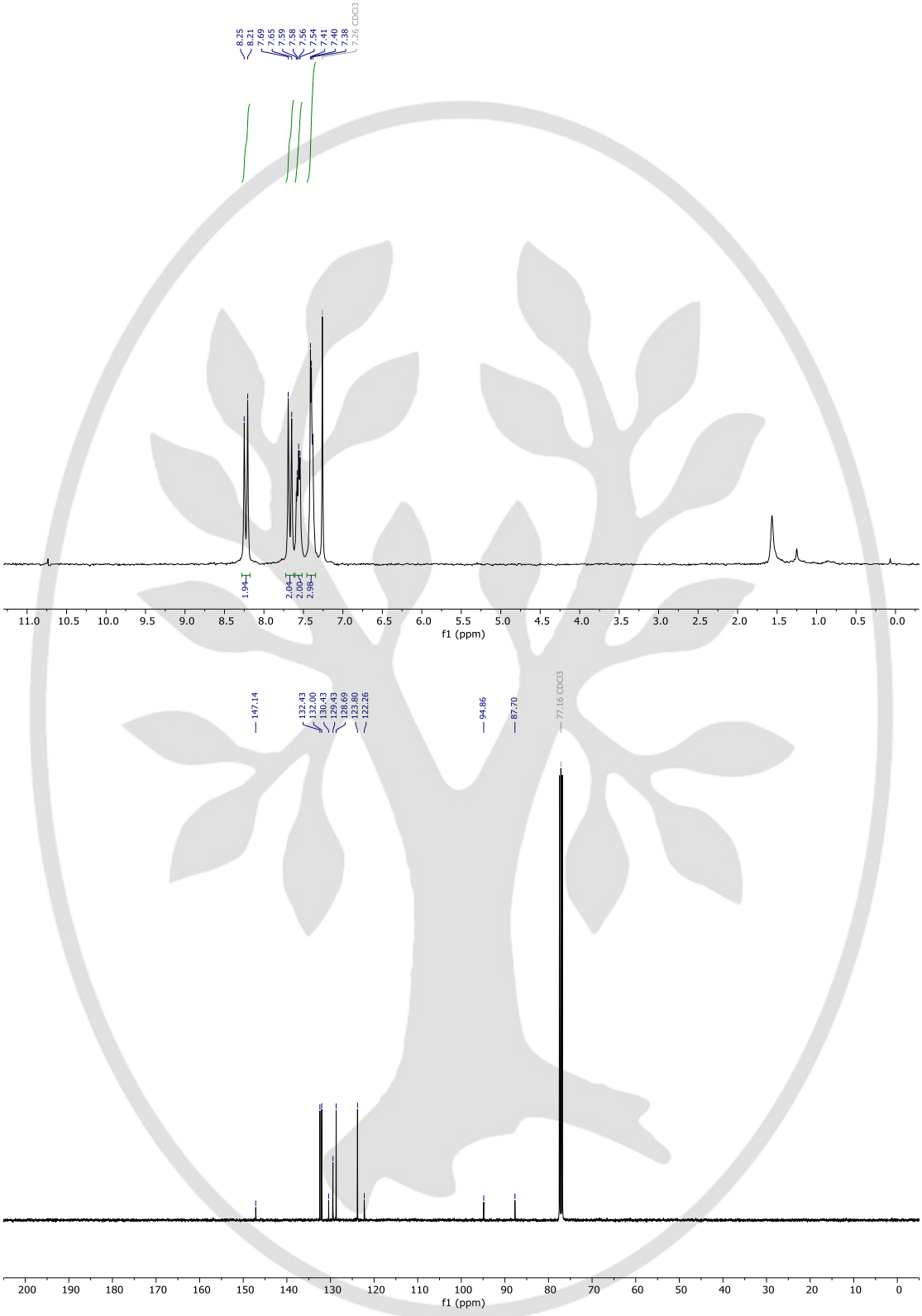
^{1}H and ^{13}C NMR Spectra

$(Trz^{*}_{Ph,Ph})_2CH_2$ (L)





1-Nitro-4-(phenylethynyl)benzene (3a)



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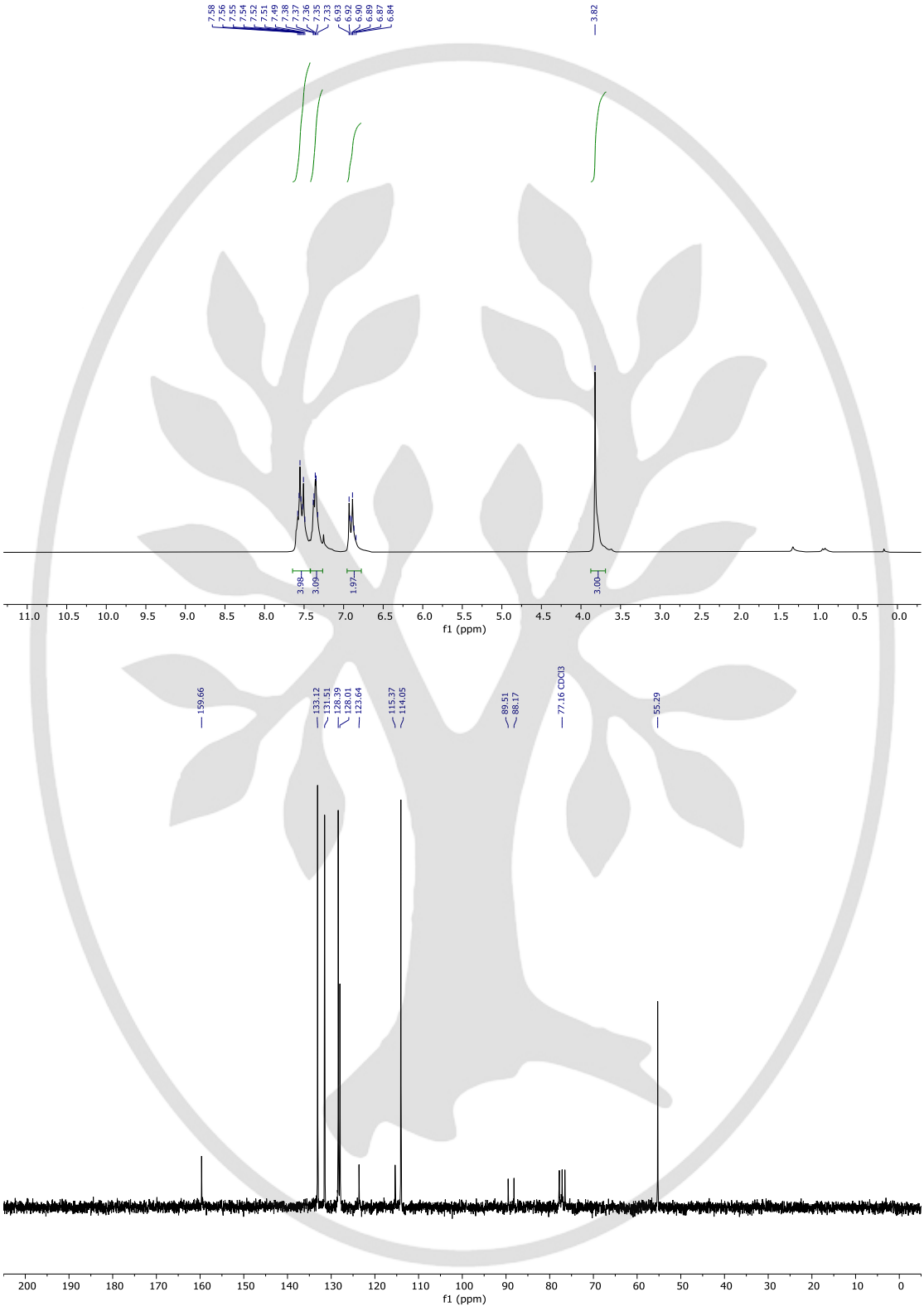

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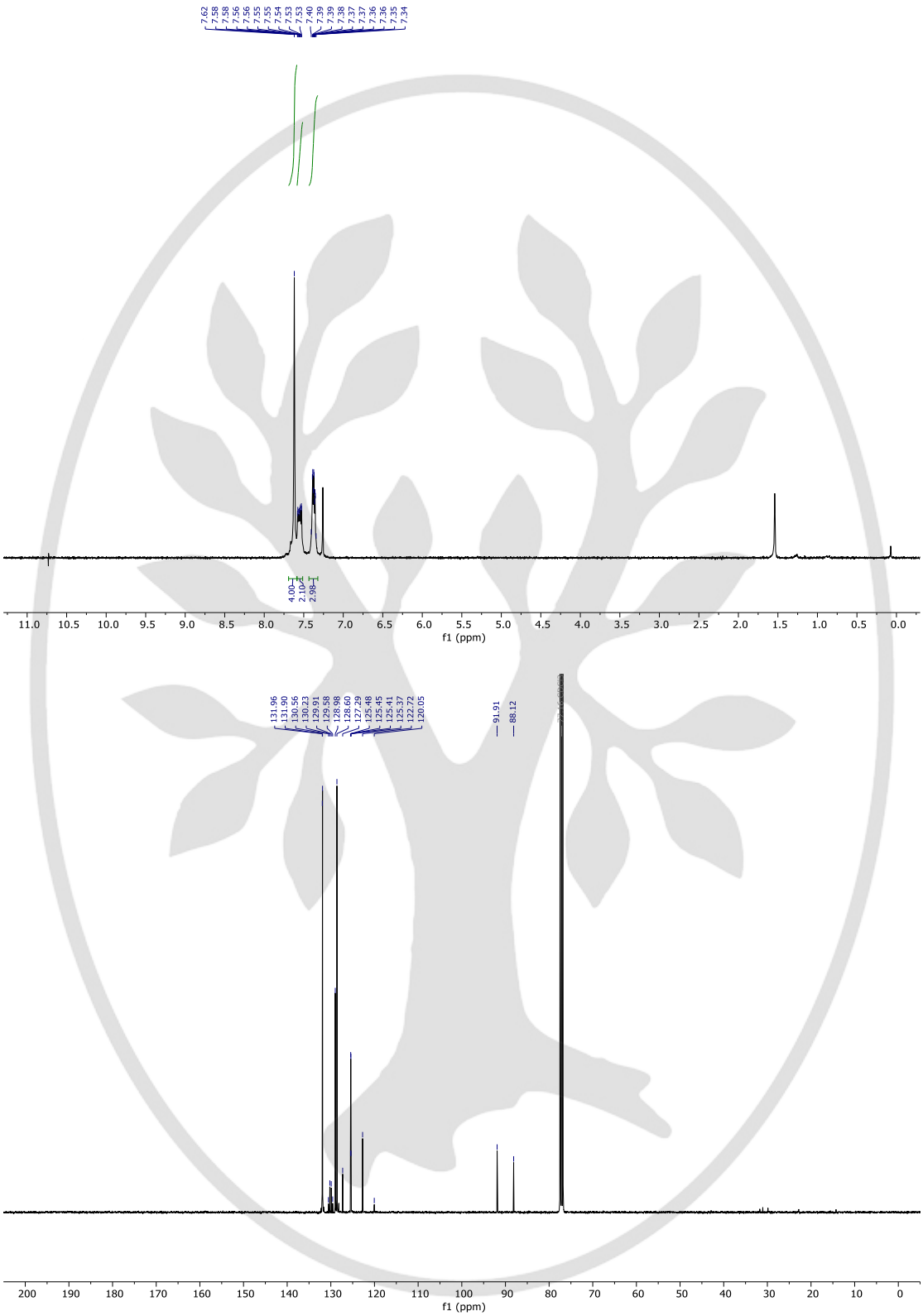

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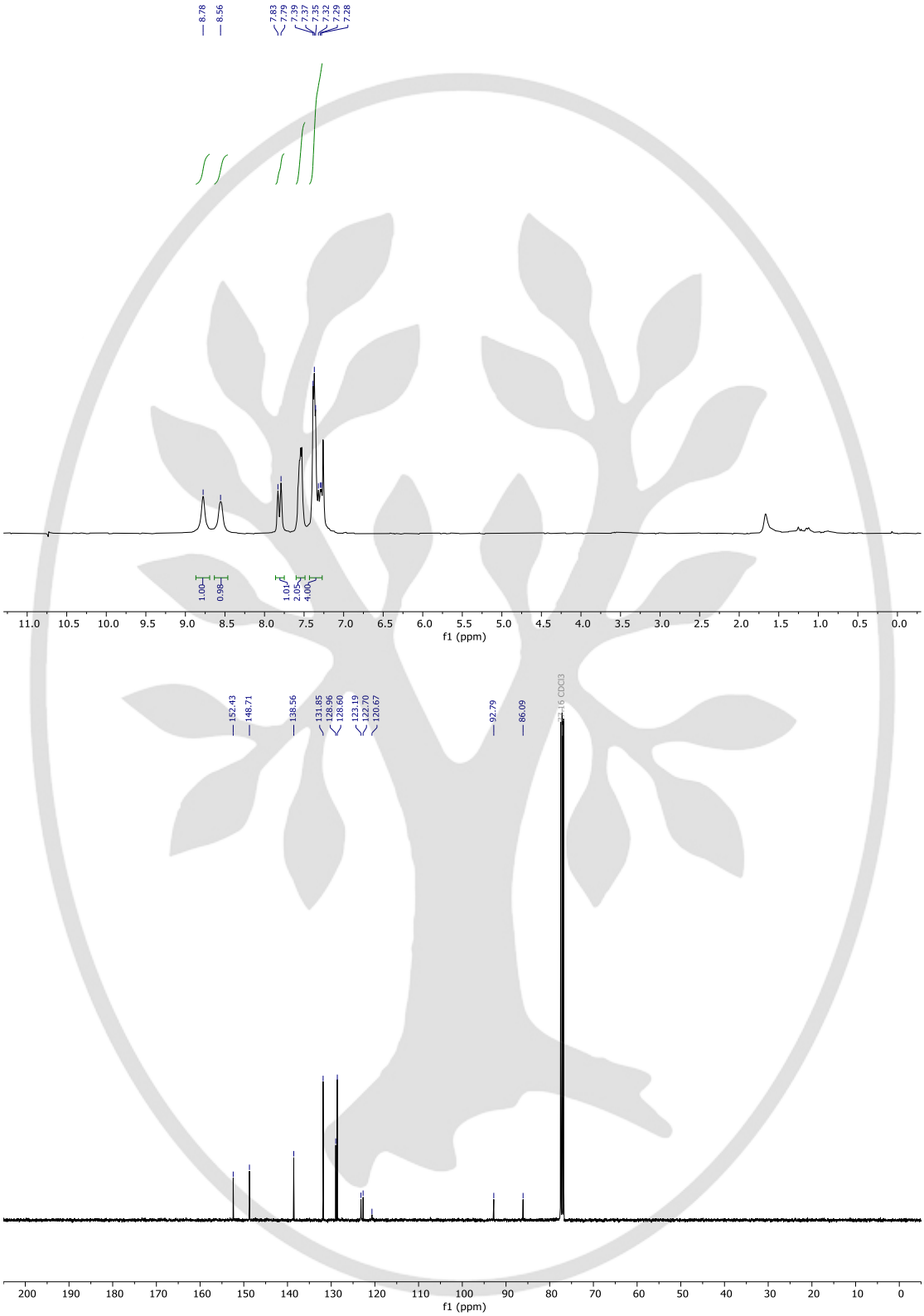

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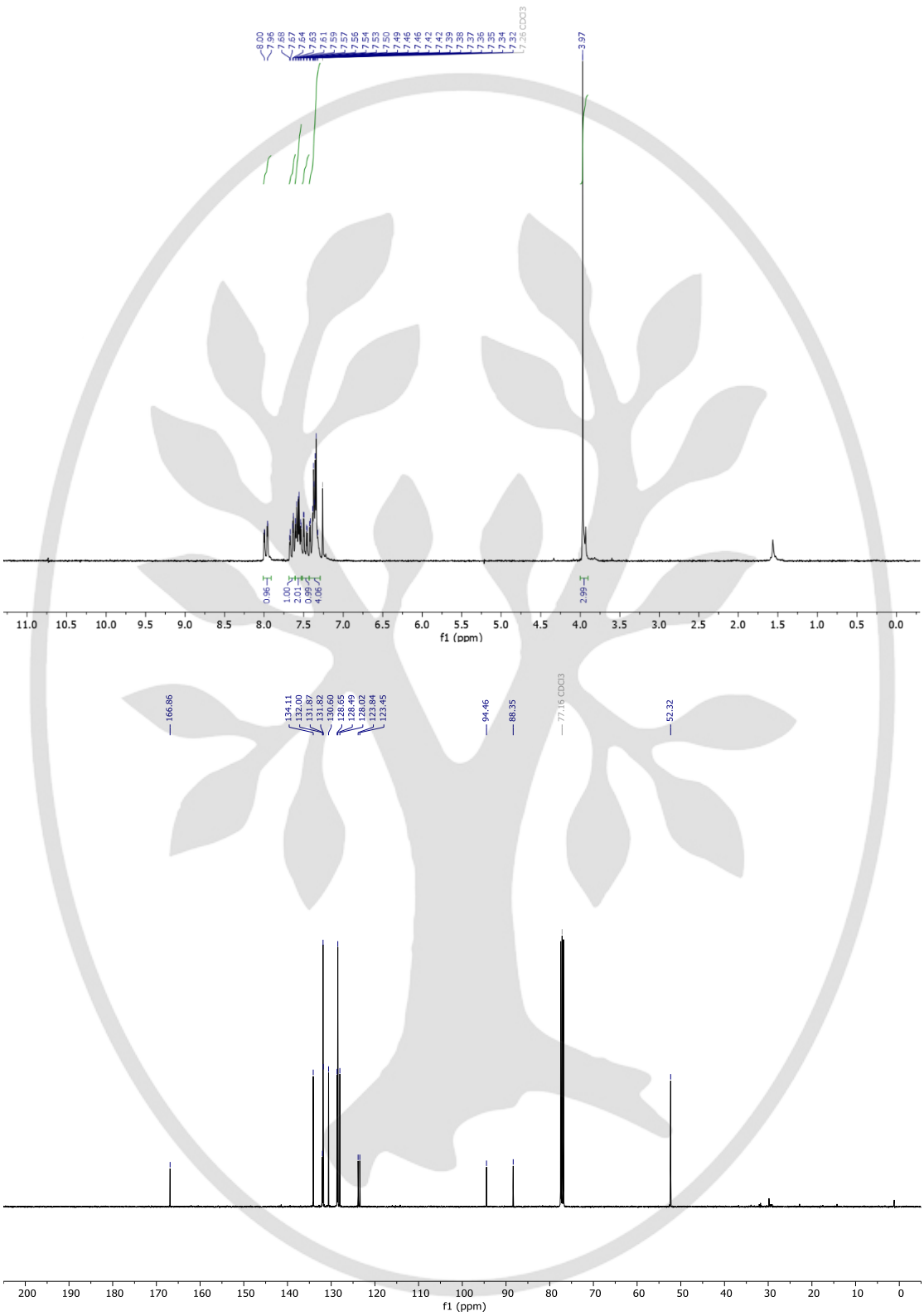
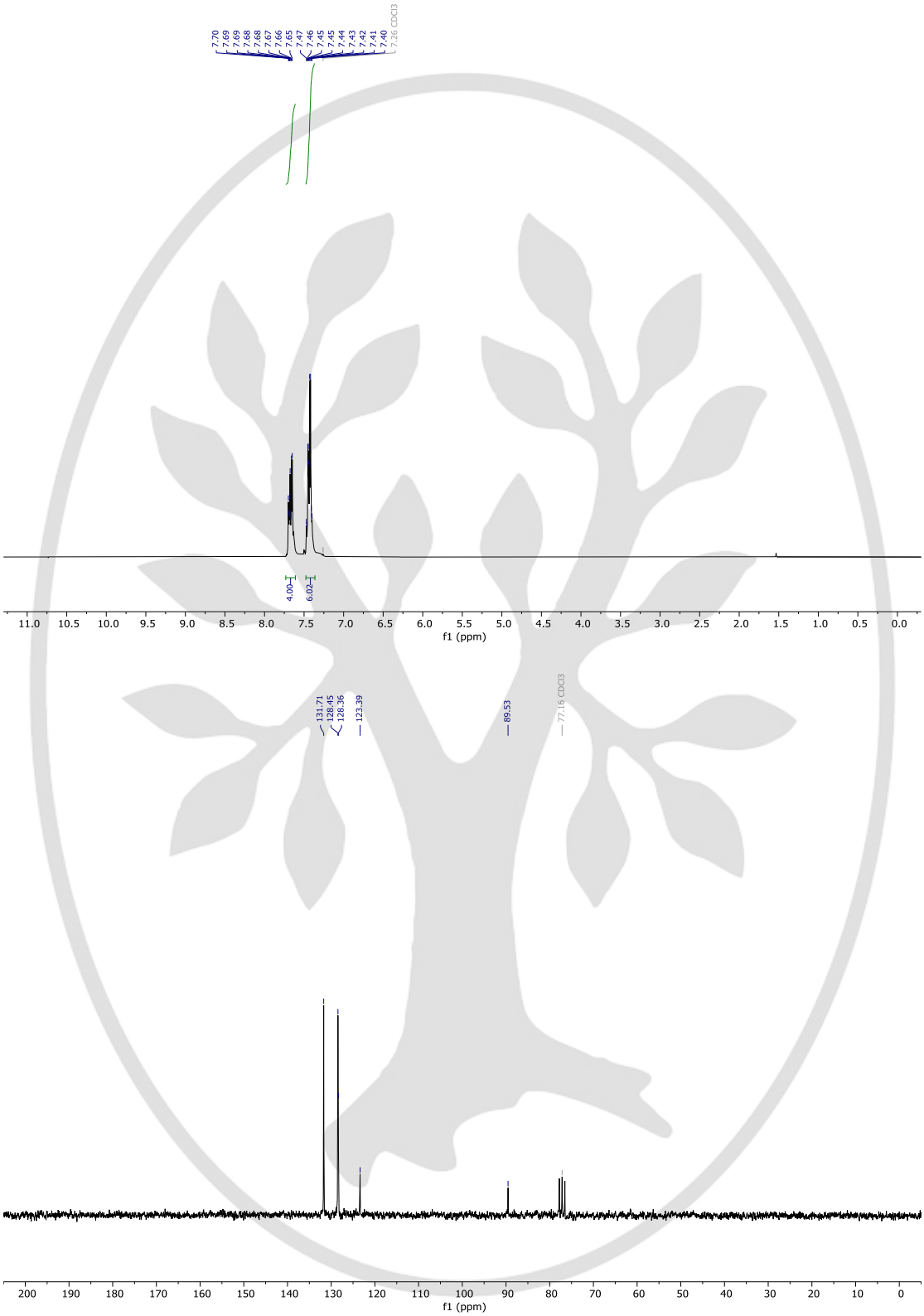
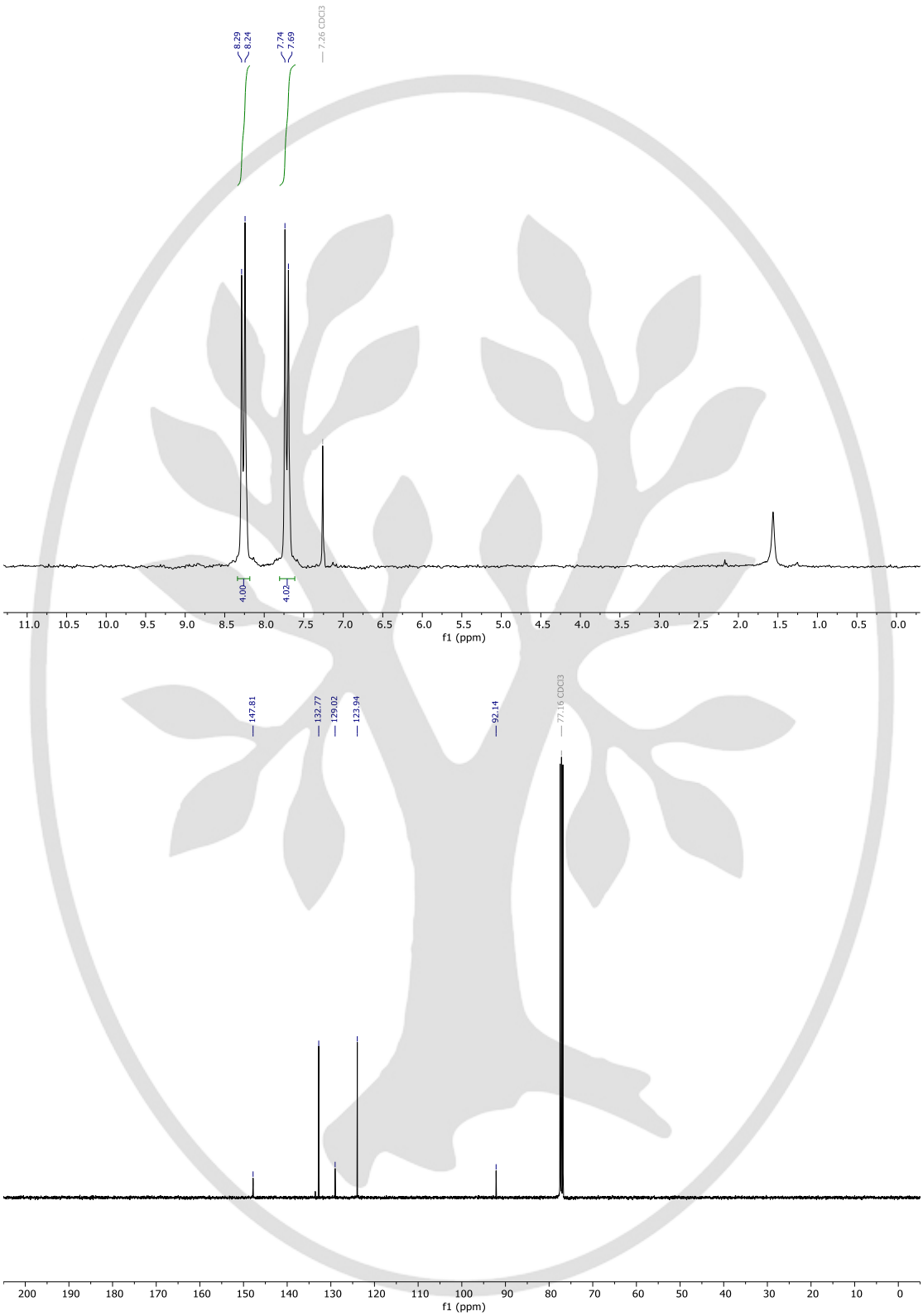


1,2-Diphenylethyne (3f)



1,2-bis(4-nitrophenyl)ethyne (3g)



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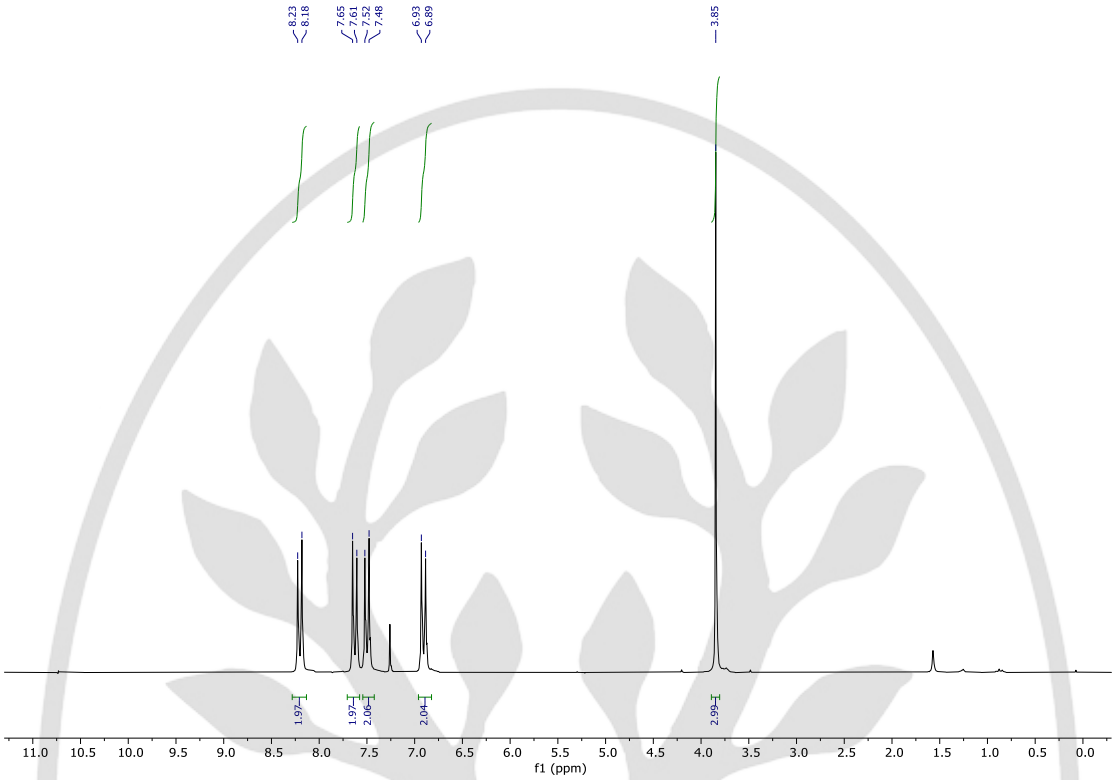

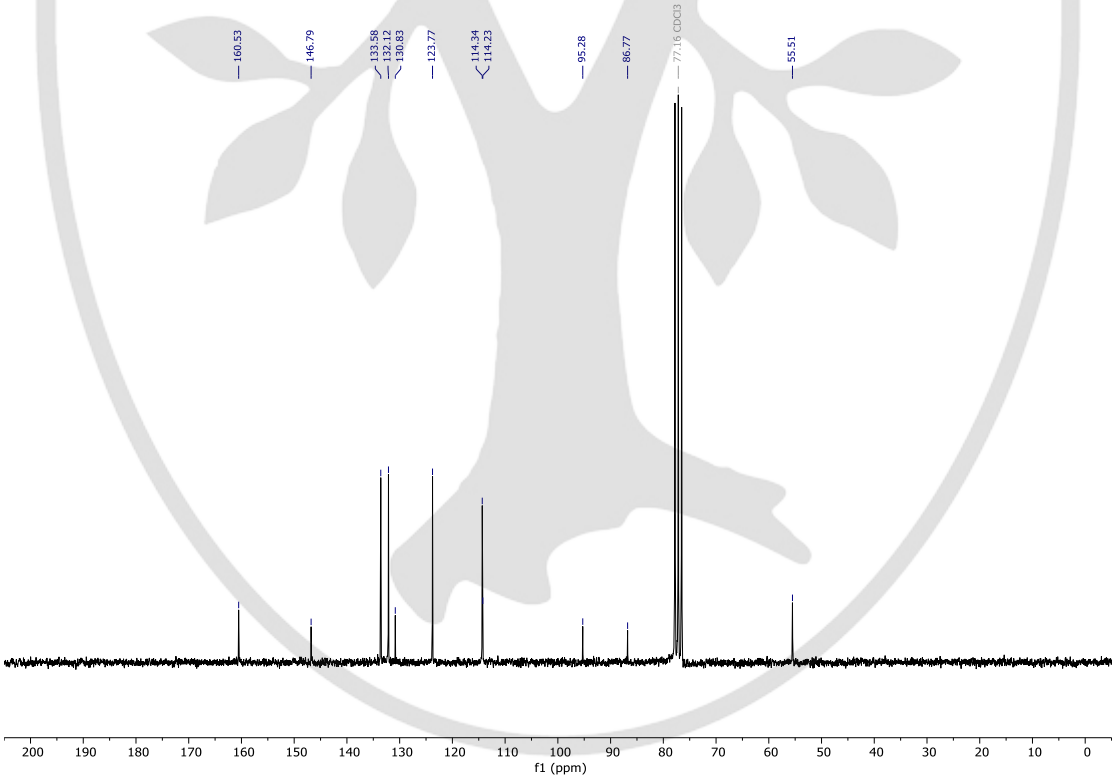

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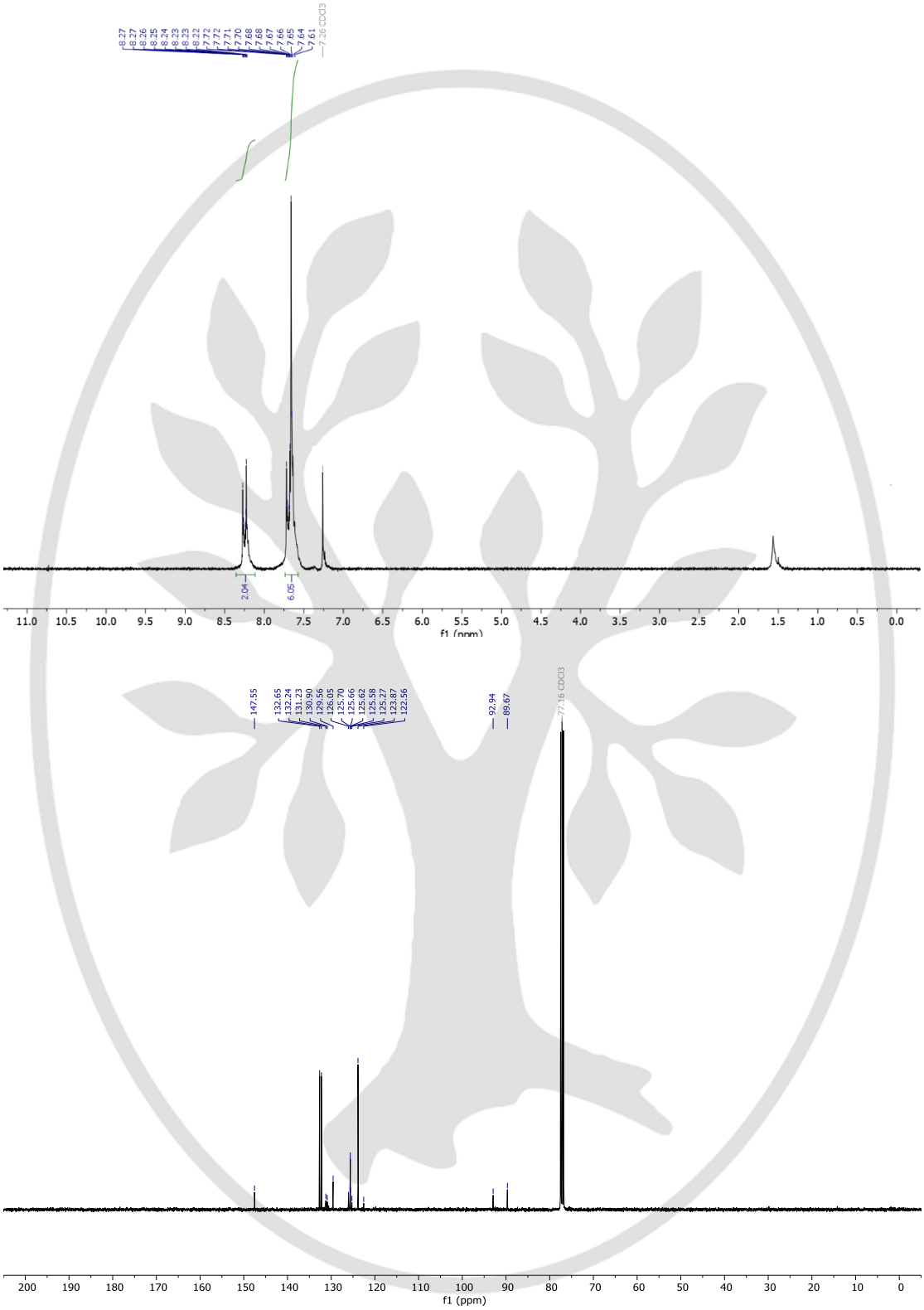

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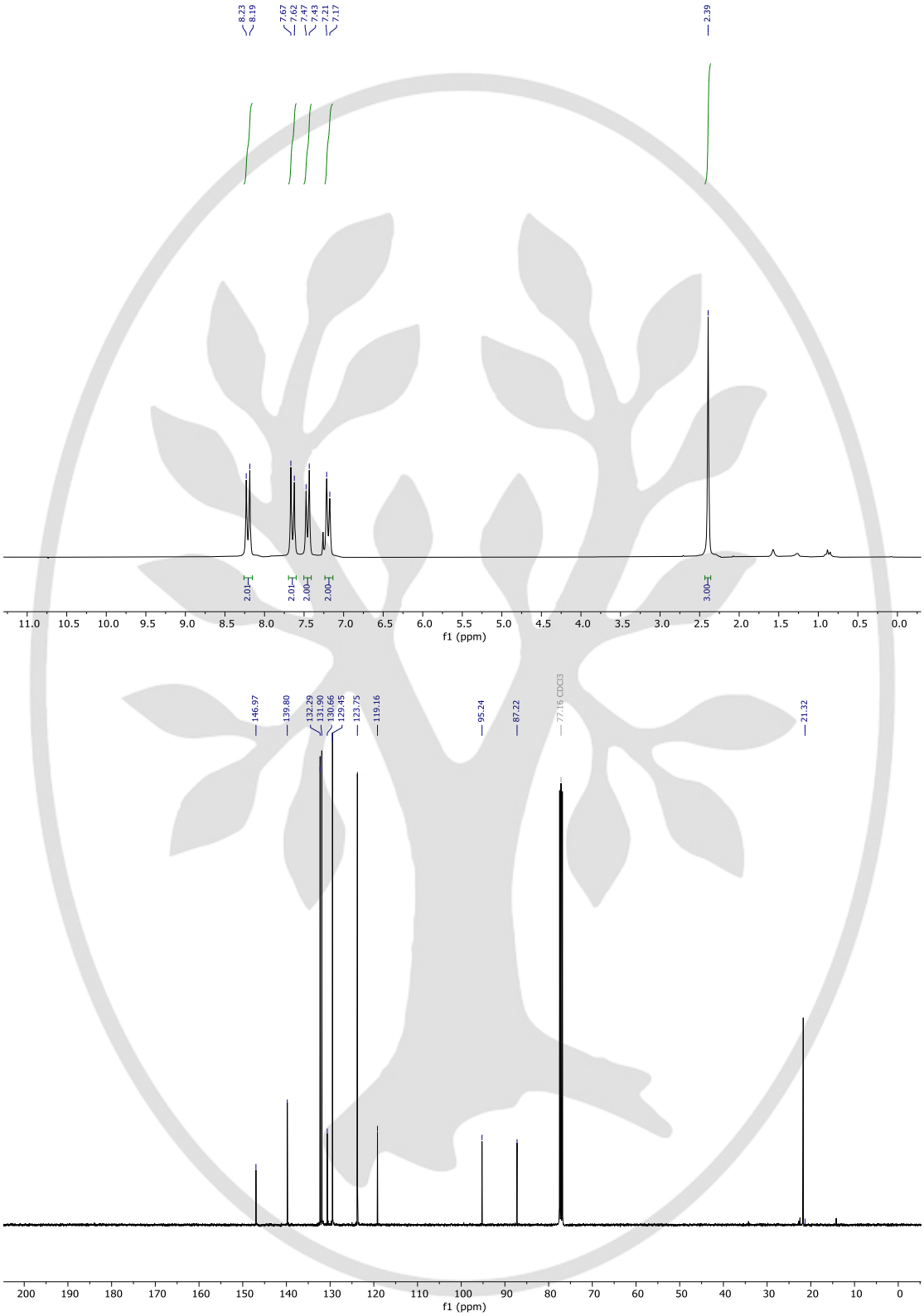

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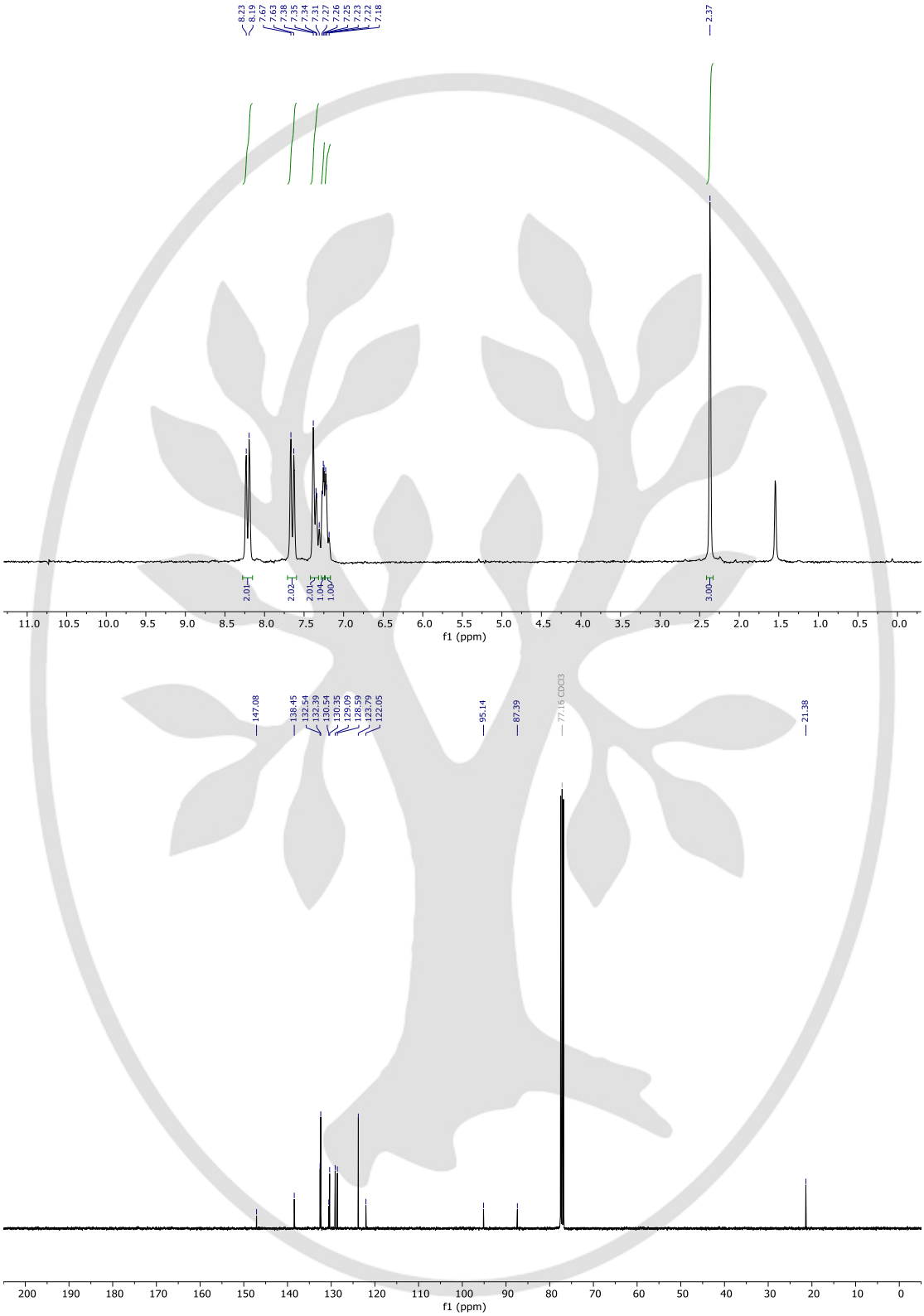

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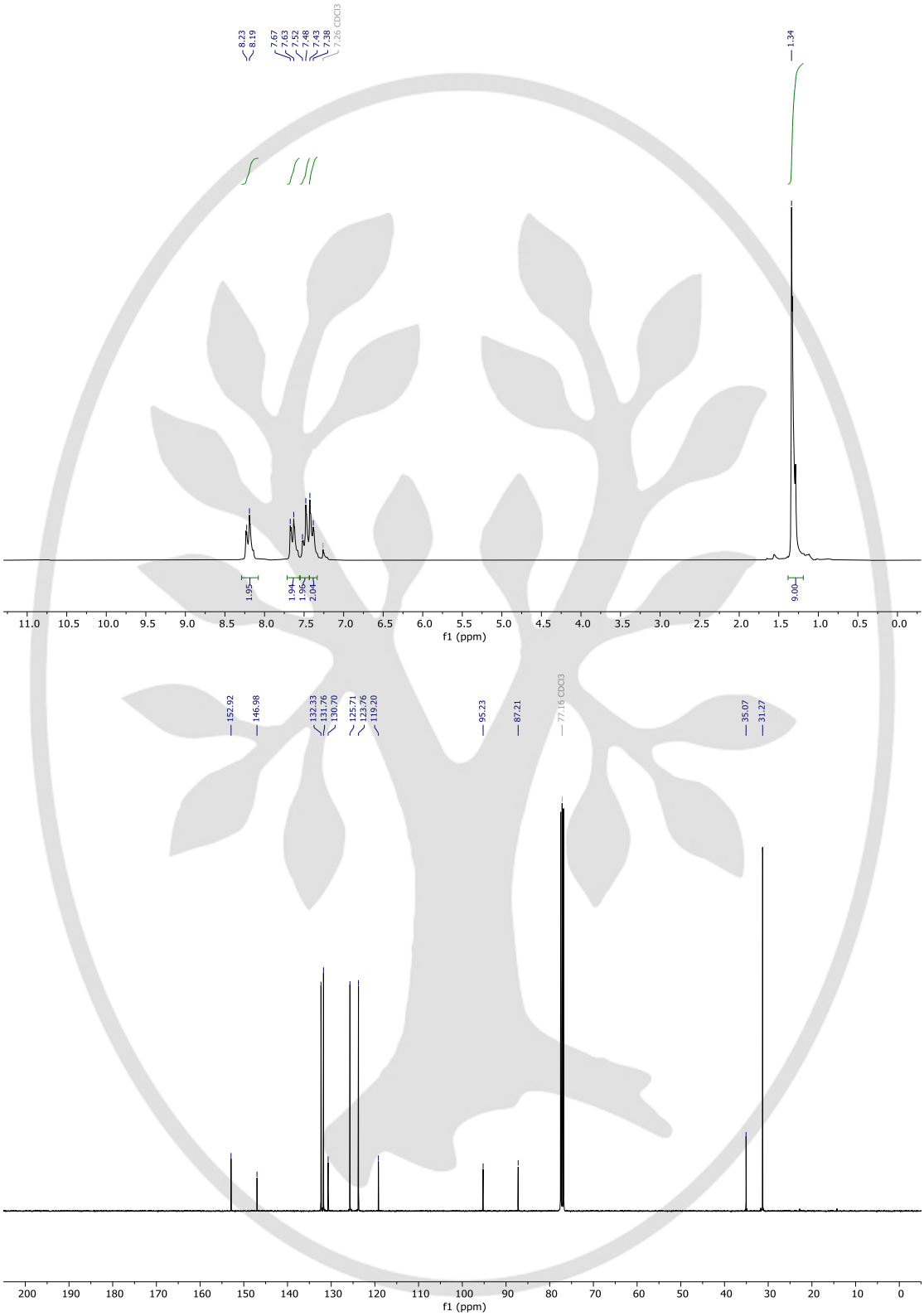
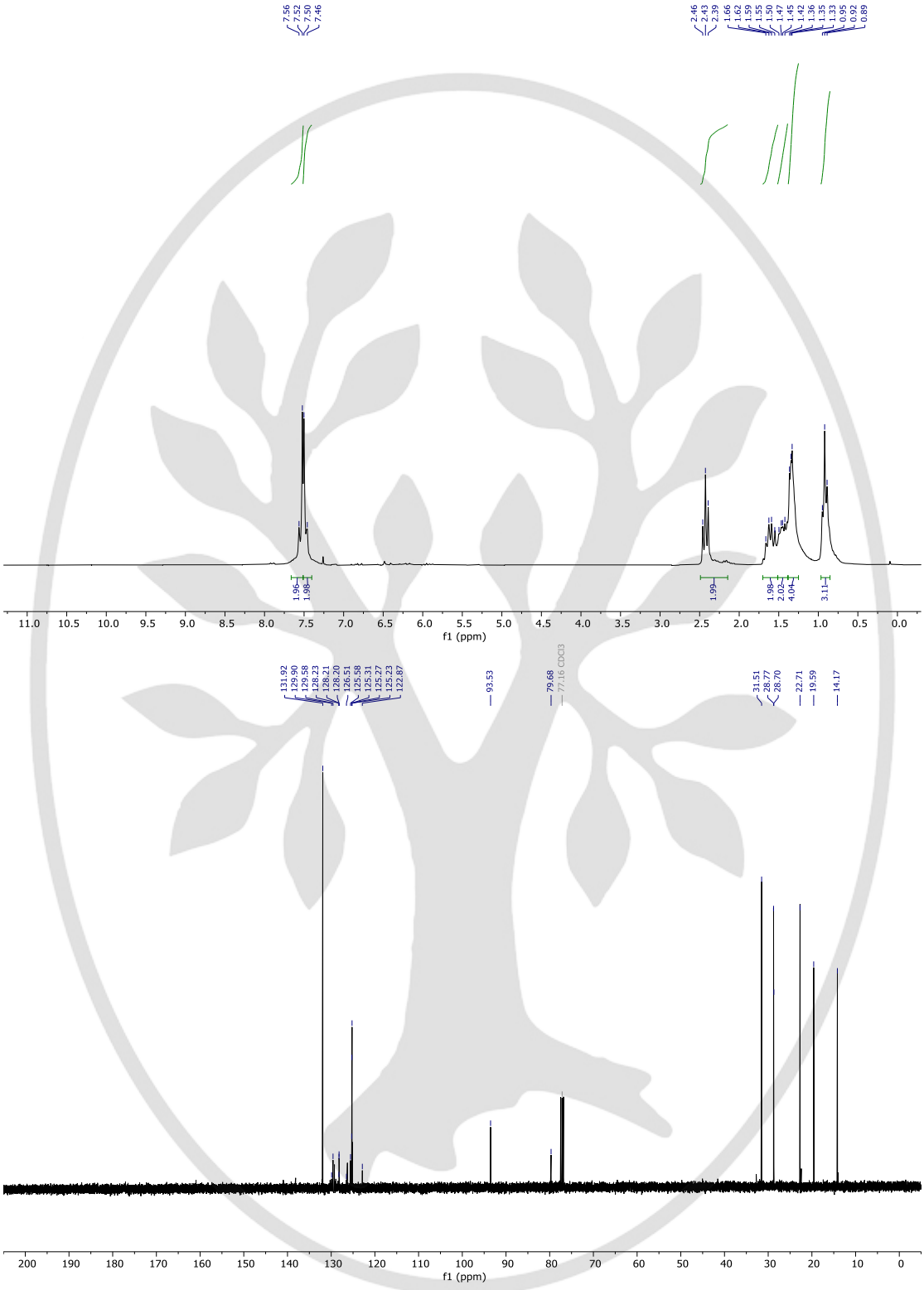


1-(oct-1-yn-1-yl)-4-(trifluoromethyl)benzene (3m)



Methyl 2-((4-nitrophenyl)ethynyl)benzoate (3n)