

Simultaneous Regioselective Synthesis of Trifluoromethyl-Containing 1,7-Phenanthrolines and Quinolines from Cyclocondensation Reaction of *N,N'*-Bis(oxotrifluoroalkenyl)-1,3-Phenylenediamines

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Este trabalho relata interessantes resultados relativos a síntese convencional de uma nova série de 2,10-dialquil(aril)-4,8-bis(trifluorometil)-1,7-fenantrolinas, em rendimentos de 22-40%, a partir das reações de ciclização de *N,N'*-bis(oxotrifluoroalquenil)-1,3-fenilenodiaminas [$1,3-C_6H_4-(NHCR=CHC(O)CF_3)_2$] em um meio fortemente ácido (PPA) e na ausência de solvente. A rota sintética também permitiu o isolamento simultâneo de uma nova série de 2-alkil(aril/heteroaril)-4-trifluorometil-7-aminoquinolinas, em 20-73% de rendimento. As enaminonas precursoras foram obtidas a partir da reação de 4-alcóxi-1,1,1-trifluor-3-alquen-2-onas [$CF_3C(O)CH=C(R)OR^1$, onde R = H, Me, Ph, 4-MePh, 4-OMePh, 4-ClPh, 4-FPh, 4-BrPh, 4-NO₂Ph, 2-furil e R¹ = Me, Et] com 1,3-fenilenodiamina em condições brandas, em rendimentos 47-91%.

This paper reports interesting results of the conventional synthesis of a new series of 2,10-dialkyl(aryl)-4,8-bis(trifluoromethyl)-1,7-phenanthrolines, in 22-40% yields, from cyclization reactions of *N,N'*-bis(oxotrifluoroalkenyl)-1,3-phenylenediamines [$1,3-C_6H_4-(NHCR=CHC(O)CF_3)_2$] in a strongly acidic medium (PPA) and absence of solvent. The synthetic route also allowed the isolation of a new series of 2-alkyl(aryl/heteroaryl)-4-trifluoromethyl-7-aminoquinolines, in 20-73% yields, simultaneously. The enaminone precursors were obtained from the reaction of 4-alkoxy-1,1,1-trifluoroalk-3-en-2-ones [$CF_3C(O)CH=C(R)OR^1$, where R = H, Me, Ph, 4-MePh, 4-OMePh, 4-ClPh, 4-FPh, 4-BrPh, 4-NO₂Ph, 2-furyl and R¹ = Me, Et] with 1,3-phenylenediamine under mild conditions, in 47-91% yields.

Keywords: enones, enaminoketones, phenanthrolines, quinolines, PPA

Introduction

Phenanthrolines are diazaphenanthrene analogs, polycyclic aromatic hydrocarbon present in sterols, sex hormones, cardiac glycosides, bile acids and in the group of morphine alkaloids.¹ Heterocycles containing nitrogen atoms such 1,10-phenanthroline,² pyronaridine³ and chloroquine-pyrazole analogs⁴ are well known for their antimalarial activity. An example of particular interest of a non-natural antimalarial agent possessing a trifluoromethyl substituted phenanthrene skeleton is halofantrine (Figure 1), an effective drug for the treatment of malaria which possesses good therapeutic effects but some important adverse effects.⁵ Furthermore, some angular and linear *N*-tricyclic similar systems have also been documented to possess antiviral activity.⁶

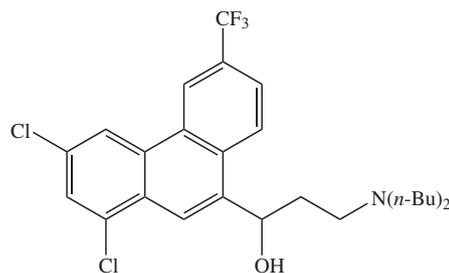


Figure 1. Chemical structure of the non-natural antimalarial halofantrine.

From a synthetic point of view, phenanthrolines obtained from phenylenediamines are of particular interest since both outer rings can be constructed simultaneously.⁷ However, phenanthrolines can be also prepared from aminoquinolines.⁸ The first phenanthroline, 1,7-phenanthroline was prepared by Skrap and Vortmann⁹ in 1882 and the method continues to be one of the best

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methods for synthesis of 1,7-phenanthrolines. A study of the Skraup reaction, when applied to *meta* and *para*-phenylenediamines, with arsenic acid as the oxidizing agent, revealed that the double Skraup reaction can be satisfactorily applied with proper observation of important factors, such as water concentration, method and time of heating.¹⁰

Recently, Jacquelin *et al.*¹¹ reported the double amination of *meta*-diiodo and dibromobenzenes by anthranilic acid derivatives using palladium and/or copper catalysis. These symmetrical and non-symmetrical phenylenediamines were submitted to a cyclization/reduction/oxidation synthetic sequence, being key precursors to polyfunctional dibenzophenanthroline carboxaldehydes.

In addition, it has been observed that the introduction of halogenated groups into organic molecules often confers significant and useful changes in their physical, chemical and biological properties.¹²⁻¹⁴ It is well known that fluorocarbons are becoming increasingly important in the medicinal, materials and agricultural fields. It has been reported that the introduction of a trifluoromethyl and its higher homologue C_nF_{2n+1} groups into a heterocycle frequently results in a much more potent activity than that of the parent compounds, a fact which is probably related to the high lipophilicity of perfluoroalkyl substituents.^{13,14}

The vast majority of organofluorine compounds are not natural products. Consequently, a synthetic methodology to incorporate fluorine and fluorine synthons must be optimized in order to prepare sophisticated fluoroorganic molecules on a practical scale. One of the most satisfactory methods for introducing a CF₃ group into heterocycles is via the trifluoromethylated building block approach.^{12,15-28} The trifluoroacetylation of enol ethers or acetals provided, in one step and in good yields, β-alkoxyvinyl trifluoromethyl ketones **1** which proved to be useful building blocks for the synthesis of many series of heterocyclic compounds.^{16,20,22-29}

Of no less importance, it is also well known that enamino-carbonyl compounds represent versatile synthetic precursors, which combine the ambident nucleophilicity of enamines with the ambident electrophilicity of enones, presenting three nucleophilic and two electrophilic sites. For this reason, enamines have found a wide application in the synthesis of various heterocycles, dyes and drugs.^{22,30-32}

Specifically, we have described the synthesis of *N*-[1-aryl(alkyl)-3-oxo-4,4-trifluoro(chloro)alken-1-yl]-*o*-phenylenediamines^{23,24} from the reactions of 4-alkoxy-1,1,1-trifluoroalk-3-en-2-ones with *o*-phenylenediamine promoting cyclization reactions for benzodiazepine and benzimidazole derivatives.

Recently, applying the method previously described by us for the preparation of some trifluoromethyl substituted

enaminoketones and their benzo[*h*]quinoline,²⁵ dihydrobenzo[*c*]acridine,²⁶ cycloalka[*b*]quinoline,²⁷ and 1,2,3,4-tetrahydroacridine derivatives,²⁸ we communicated the synthesis of only three examples of 2,8- and 4,8-bis(trifluoromethyl)-1,7-phenanthrolines and 4-(trifluoromethyl)-7-aminoquinolines where two interesting intramolecular cyclization routes were found when *N,N'*-bis(oxotrifluoroalkenyl)-1,3-phenylenediamines were heated at 165 °C in polyphosphoric acid medium.²⁹

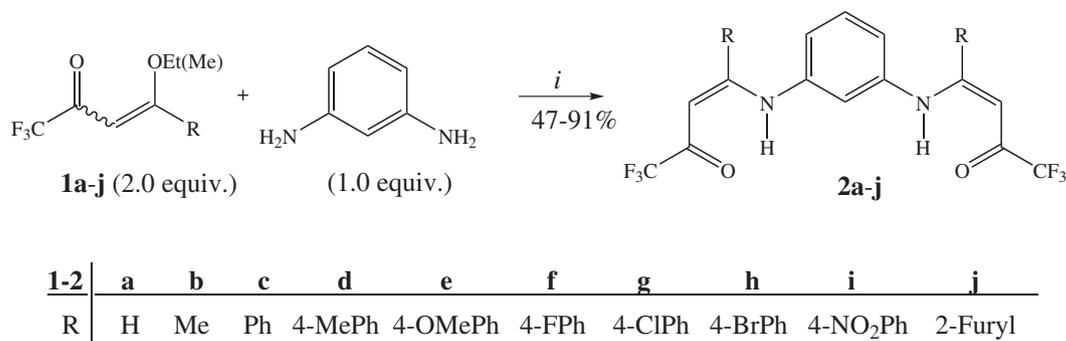
The purpose of this paper is to report the complete results of the reactions of 4-alkoxy-4-alkyl(aryl/heteroaryl)-1,1,1-trifluoroalk-3-en-2-ones (**1a-j**) with 1,3-phenylenediamine to obtain a wide series of ten examples of trifluoroacetyl substituted 1,3-phenylene-bis-enamines (**2a-j**) and also to investigate the chemical behavior of alkyl, aryl and heteroaryl-substituted enamino intermediates (**2**) for their application in the simultaneous regioselective synthesis of new 2,8- or 4,8-bis(trifluoromethyl)-2,10-bis-alkyl(aryl)-1,7-phenanthrolines (**3**) and the respective 4-(trifluoromethyl)-7-aminoquinolines (**4**) under similar reaction conditions as described previously.²⁹

Results and Discussion

Firstly, a series of ten examples of 4-alkoxy-4-alkyl(aryl/heteroaryl)-1,1,1-trifluoroalk-3-en-2-ones (**1a-j**), which are readily available 1,3-dielectrophiles (*CCC* synthetic blocks), were prepared from trifluoroacetylation reactions of enol ethers commercially available (for **1a-b**) or generated *in situ* from the respective acetophenone dimethyl acetal (for **1c-j**) with trifluoroacetic anhydride, respectively, in the presence of pyridine, as described in the literature.³³

Second, a new series of ten bis-enaminone intermediates **2a-j** was isolated in satisfactory yields of 47-91%, by the reaction of enones **1a-j** with 1,3-phenylenediamine at a molar ratio of 2:1, respectively (Scheme 1). The reactions can now be carried out in ethanol, water, water/dichloromethane (1:1) or water/chloroform (1:1) at a temperature range of 25 to 80 °C (Scheme 1). The best results were obtained when enones **1a-j** were added to 1,3-phenylenediamine, in pure ethanol for **1a-d** and **1f-j** or in water/chloroform (1:1) solution for **1e**. Good yields were also obtained under other reaction conditions tested, as above described. For example, the compounds **2b** and **2g** were obtained in good yields (85%) when the reactions were carried out in water at room temperature as solvent. However, the syntheses of enamines **2a**, **2f** and **2h** were unsuccessful in an aqueous medium.

The structures of compounds **2a-j** were easily established on the basis of ¹H and ¹³C NMR spectroscopy. In order to obtain structural information about the



Scheme 1. Reagents and conditions: (i) = ethanol, 40 °C, 2 h (**2a-d**, **f-k**) or H₂O/CHCl₃ (1:1), 60 °C, 4 h (**2e**).

configuration of the compounds **2a-j** we have performed an ¹H NMR study on (*Z,Z*)-*N,N'*-bis(3-oxo-4,4,4-trifluoro-1-buten-1-yl)-1,3-phenylenediamine (**2a**). The ¹H NMR spectrum of **2a** in CDCl₃ showed (see SI) a *cis* coupling constant for the vicinal olefin protons with *J* ca. 8 Hz, which is consistent with a *Z*-configuration as the *E*- and *Z*-forms can be easily distinguished by their ¹H NMR spectra because the N–H signals of the *E*-form (in 4–8 ppm) appeared at a much higher field than those of the *Z*-form (in 9–13 ppm), indicating the presence of an intramolecular hydrogen bonding in the latter.³⁴ The ¹H NMR chemical shifts of the enamino hydrogens (NH) for **2a-j** were observed on average of 12.20 ppm, allowing one to assume that the enaminones **2a-j** exist in the *Z,Z*-configuration in CDCl₃, which is stabilized by an intramolecular hydrogen bond (N–H...OC) in each enaminone moiety. The proposed *Z*-configuration was confirmed also by X-ray crystal diffraction³⁵ for compound **2g** (Figure 2).

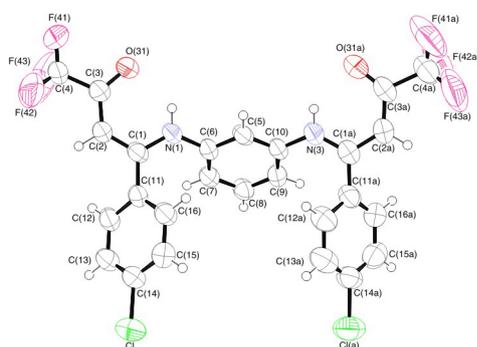


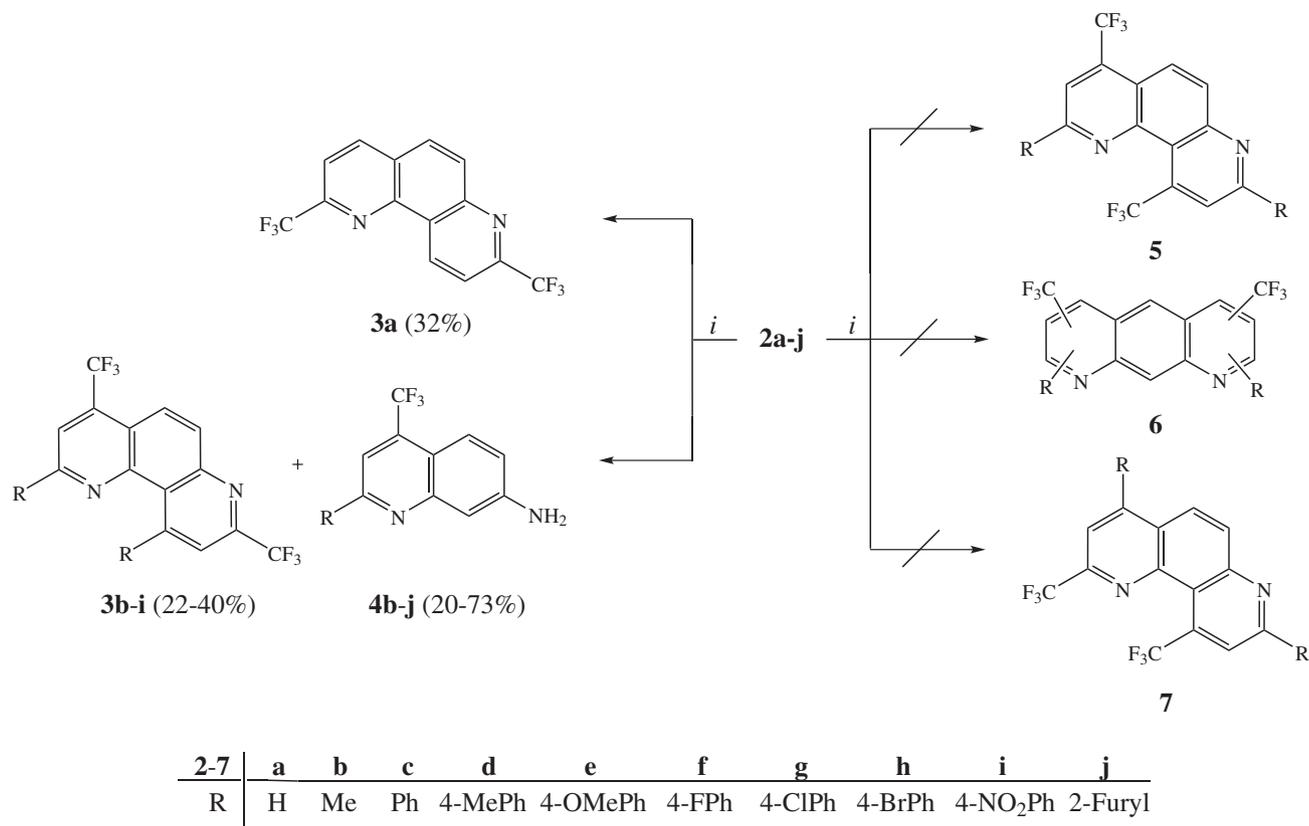
Figure 2. A perspective view of *N,N'*-bis(1-(4-chlorophenyl)-4,4,4-trifluoro-3-oxo-1-buten-1-yl)-1,3-phenylenediamine (**2g**) with atoms labeled (CCDC 699774).³⁵ Displacement ellipsoids are drawn at the in 50% probability level.

In a second reaction step, the acyclic enaminones **2a-j** were subjected to reactions carried out in the presence of a strongly acidic medium (polyphosphoric acid, PPA), in the absence of solvent. For all reactions, initially, PPA (P₂O₅ +

H₃PO₄) was prepared at 90 °C and the compounds **2a-j** were added to the acid mixture. The cyclization of **2a-j** showed that the best results were at 165 °C for 36 h, affording the corresponding new angular series of bis-trifluoromethyl-substituted 1,7-phenanthrolines **3a-i** in 22–40% yields (Scheme 2). Unfortunately, the above described general and optimized conditions allowed us to obtain only traces of the phenanthroline **3j** derived from the enaminone **2j** (2-furyl derivative).

According to the literature, it is known that the formation of two pyridine rings from derivatives of the 1,3-phenylenediamine may proceed in two possible ways to give a 1,7-phenanthroline (**3a**, **5**) or a benzodipyridine (**6**).^{8,9,29,36,37} It is also known that in the formation of cyclic compounds from phenylenediamine or quinoline derivatives, the angular structure is obtained in preference to the linear one when both are possible.^{8,9,29,36} In the present work, only derivatives of the angular structure were obtained, instead of the linear isomer bis-trifluoromethyl-substituted pyrido[*g*]quinolines (**6**) (Scheme 2). However, neither of the products isolated showed a mode of cyclization similar to that observed in the product previously identified by us as 2,8-bis(trifluoromethyl)-1,7-phenanthroline (**3a**).²⁹ Only the formation of 2,10-dialkyl(aryl)-4,8-bis(trifluoromethyl)-1,7-phenanthrolines (**3b-i**) was observed, as shown in Scheme 2.

The structures of **3a-i** were established on the basis of ¹H and ¹³C NMR spectroscopies and also confirmed by X-ray diffraction of **3a** (Figure 3) and **3c** (Figure 4). The structure pattern of compound **3a** is different from that of **3b-i**, although obtained under similar reaction conditions. For the 2,8-bis-trifluoromethyl-1,7-phenanthroline (**3a**) the two CF₃ groups occupy the nitrogen-adjacent positions, suggesting the occurrence of two retro 1,4-cyclocondensations (hydrolysis and recombination) at the same molecule **2a** during the closure of the two pyridine rings and following a mechanism already described in the literature for a single cyclocondensation reaction, which allowed the isolation of 2-trifluoromethyl-substituted quinolines^{22,37-42} and benzo[*h*]quinolines.^{37,40}



Scheme 2. Reagents and conditions: (i) = PPA, 165 °C, 36 h or PPA, 90 °C, 36 h (4j).

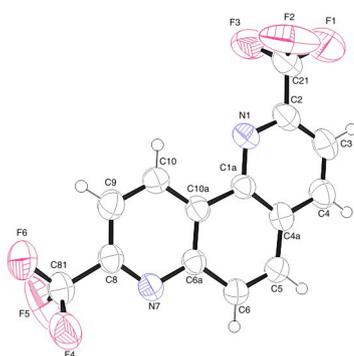


Figure 3. A perspective view of 2,8-bis(trifluoromethyl)-1,7-phenanthroline (**3a**) with atoms labeled (CCDC 699773).³⁵ Displacement ellipsoids are drawn at the in 50% probability level.

The 2,8-bis(trifluoromethyl)-1,7-phenanthroline (**3a**) showed ¹³C NMR chemical shifts at 149.6 ppm (q, ²J_{CF} 34 Hz, C-2), 147.6 ppm (q, ²J_{CF} 35 Hz, C-8) and 121.5 ppm (q, ¹J_{CF} 275 Hz, 2 CF₃). The ¹³C NMR spectra of the compounds 2,10-dialkyl(aryl)-4,8-bis(trifluoromethyl)-1,7-phenanthrolines (**3b-i**) showed chemical shifts for C-4 in the range of 133.1-136.2 ppm as a quartet with ²J_{CF} ca. 31 Hz, for C-8 in the range of 148.2-151.1 ppm as a quartet with ²J_{CF} ca. 34 Hz, for CF₃ groups in the range of 120.6-123.4 ppm as a quartet with ¹J_{CF} ca. 275 Hz. The

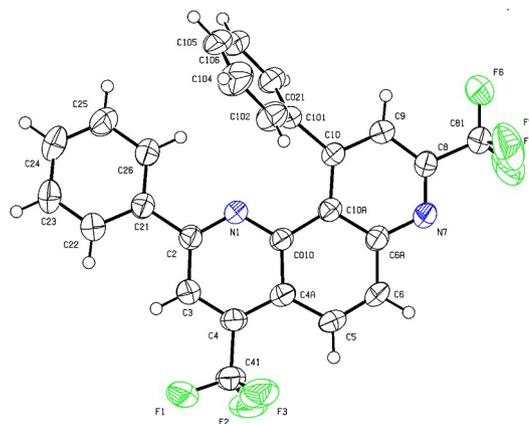


Figure 4. A perspective view of 4,8-bis(trifluoromethyl)-2,10-di(phenyl)-1,7-phenanthroline (**3c**) with atoms labeled (CCDC 740919).³⁵ Displacement ellipsoids are drawn at the in 50% probability level.

2,8-bis(trifluoromethyl)-1,7-phenanthroline (**3a**) showed ¹⁹F NMR signals at -67.12 and -67.26 ppm (CF₃-2, CF₃-8). The ¹⁹F NMR spectra for compounds 2,10-dialkyl(aryl)-4,8-bis(trifluoromethyl)-1,7-phenanthrolines (**3b, c, g**) showed signals of CF₃-4 at an average of -60.54 ppm and for CF₃-8 at an average of -67.28 ppm. The spectroscopic data agree with ¹³C NMR and ¹⁹F NMR chemical shift data for similar compounds described in the literature.^{28-31,38}

From the analysis of NMR data, we observed that one ring closure occurred by a 1,2-cyclocondensation reaction, while the other occurred by a retro 1,4-cyclocondensation. Thus, one CF₃ group is attached at the nitrogen-remote position (4-CF₃) and in the second ring and the CF₃ group is occupying the nitrogen-adjacent position (8-CF₃). These two different mechanisms are involved in the synthesis of a series of 4,8-bis(trifluoromethyl)-1,7-phenanthrolines (**3b-i**). Compounds **3** were separated from the reaction mixture by a sublimation process during the heating of the pure enaminone precursors **2**, in PPA medium.

The possible formation of the 2,10-bis(trifluoromethyl)-1,7-phenanthroline isomer (**7**, Scheme 2) was also excluded because the 5-amino-4-(trifluoromethyl)quinolines were not detected in the cyclization reactions from **2b-j**. The possible formation of the 4,10-bis(trifluoromethyl)-1,7-phenanthroline isomer (**5**) was also excluded because the CF-coupling on the NMR spectra should be present as one quartet signal for the CF₃ group and two identical quartets for C-4 and C-10 in the narrow range of δ 147-150 ppm and no quartet signals should be expected in the region of δ 134-135 ppm.

On the other hand, the cyclization reactions of the enaminones **2** by heating in acidic medium (PPA) could result in the synthesis of the linear bis-trifluoromethyl-substituted pyrido[g]quinolines (**6**), as reported in the literature (Scheme 2).³⁷ However, the NMR spectrum should show four singlets for H-3, H-5, H-7 and H-10, which were not observed, thus excluding the formation of a linear isomer (pyrido[g]quinoline). In our case, all spectroscopic data were consistent with the proposed angular structures for phenanthrolines **3a-i**, which are preferably obtained according to the literature.⁷

The 2-alkyl(aryl/heteroaryl)-7-amino-4-(trifluoromethyl) quinolines (**4b-j**, Scheme 2) were obtained in 20-73% yields, as by-products, from the reported cyclization reactions and were isolated by recrystallization after the work-up of residual reaction mixtures according to the procedure described. We have attempted unsuccessfully to obtain the phenanthrolines **3j-k** under milder reaction conditions than those described, but only quinoline **4j** was successfully isolated. The best result for **4j** was obtained when the reaction was carried out 90 °C for 24 h (73% yield).

Linderman and Kirillos³⁸ reported the synthesis of 2-CF₃-substituted quinolines and assigned the chemical shift for the CF₃ group of the ¹³C NMR spectra as quartets at δ 122.3 ppm (¹J_{CF} 275 Hz, CF₃) and at δ 148.5 ppm (²J_{CF} 34 Hz, C2). In the same letter, another intramolecular cyclization route was also described, which allowed the synthesis of the 4-(trifluoromethyl)quinoline isomer.

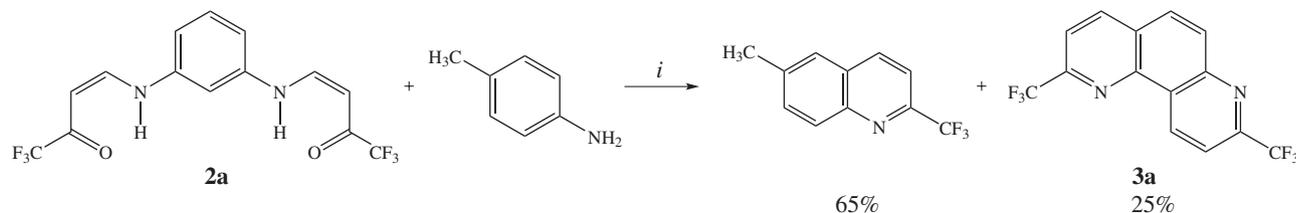
With the synthesis of 4-CF₃ quinolines, they reported the ¹³C NMR spectral data and assigned the chemical shift for the CF₃ group for this regioisomer as quartets at δ 124.2 ppm (¹J_{CF} 275 Hz, CF₃) and δ 134.8 ppm (²J_{CF} 31 Hz, C4), respectively. In some cases, the reactions resulted in mixtures of 2- and 4-CF₃ quinolines.

The structures of quinolines **4b-j** were established on the basis of ¹H and ¹³C NMR spectroscopies and literature data for similar compounds.^{36,39,40} The ¹³C NMR spectra of the compounds 2-alkyl(aryl/heteroaryl)-7-amino-4-(trifluoromethyl)quinolines (**4b-j**) showed chemical shifts for C-4 in the range of 130.7-134.5 ppm as a quartet with ²J_{CF} ca. 31 Hz and for CF₃ groups in the range of 118.3-125.5 ppm as a quartet with ¹J_{CF} ca. 275 Hz. The ¹⁹F NMR spectra of the compounds 2-alkyl(aryl/heteroaryl)-7-amino-4-(trifluoromethyl)quinolines (**4b, c, g, i**) showed signals of CF₃-4 at an average of -62.26 ppm.

Schlosser *et al.*,³⁹ who have investigated the synthesis of 2- and 4-(trifluoromethyl)quinolines and quinolinones in details, demonstrated a novel mode of isomerization and cyclization in the synthesis of 2-(trifluoromethyl)quinolines from anilines. As described, 4-anilino-1,1,1-trifluoro-3-buten-2-ones can be readily obtained from the ethyl trifluoroacetate derived 4-*tert*-butylamino-1,1,1-trifluorobut-3-en-2-one by simple amine/amine replacement. Upon heating in the presence of phosphoryl chloride, they undergo ring closure to afford 2-(trifluoromethyl)quinolines rather than the expected 4-isomers in 50% average yield.³⁹

In subsequent experiments, Schlosser *et al.*⁴¹ determined how 2-anilino vinyl perfluoroalkyl ketones can be mechanistically correlated with their cyclization products 2-(perfluoroalkyl)quinolines. Their studies demonstrated that some perfluoroalkyl-substituted 3-aminoenones, when heated in the presence of phosphoryl chloride, cleaved hydrolytically, setting free the substituted anilines and the 1,3-dicarbonyl compounds. A proved recombination of these subunits furnished unexpected 2-(CF₂)_nCF₃-quinolines.⁴¹

Then, based on experiments of Schlosser *et al.*⁴¹ to prove that a cleavage and a recombination reaction occurred on enaminones **2**, an equimolar mixture of (*Z,Z*)-*N,N'*-bis(3-oxo-4,4,4-trifluorobut-1-en-1-yl)-1,3-phenylenediamine (**2a**) and *p*-toluidine was heated at 165 °C for 36 h in the presence of PPA. The products were identified by their gas chromatographic retention times in comparison with those of authentic samples. Thus, 65% of 6-methyl-2-(trifluoromethyl)quinoline, 25% of 2,8-bis(trifluoromethyl)-1,7-phenanthroline (**3a**) and 11% of *p*-toluidine were identified after the reaction work-up (Scheme 3). Thus, we think that the mechanism suggested by Schlosser and co-workers may also explain



Scheme 3. Reagents and conditions: (i) = PPA, 165 °C, 36 h.

the unexpected findings of our work. We also think that the starting material **2a** afforded the 2,8-(CF₃) product (**3a**) “exclusively” but in only 32% yield, in absence of *p*-toluidine, because the heating in presence of PPA promoted the hydrolytic cleavage of the enaminone **2a** and a latter recombination also occurred but due to the high reaction temperature (165 °C), most of the volatile 4,4,4-trifluoro-3-oxobutanal escaped from the hot reaction mixture in the course of the recombination reaction.

The isolation of quinolines **4b-j** also suggests that a hydrolysis reaction occurred in **2b-j**, and the expected recombination of the precursors to allow the synthesis of phenanthrolines **3b-j**, due to the high reaction temperature, did not occur totally, probably because the dicarbonyl compounds evaporated from the hot reaction mixtures.

The presented methodology used to obtain the intermediate 1,3-phenylene-bis-trifluoromethyl substituted enaminones (**2a-j**) showed satisfactory results. It can be affirmed through the experimental data identified by ¹H NMR and confirmed by X-ray crystal diffraction that these synthetic intermediates **2a-j** have a *Z*-configuration. The procedure of its cyclization in strongly acidic medium (PPA) proved to be feasible for the synthesis of bis-trifluoromethyl-1,7-phenanthrolines (**3a-i**). The interesting results reported herein regarding the chemical behavior of these bis-enaminones **2a-j** when subjected to the cyclization reaction showed that the mode of cyclization of unsubstituted bis-enaminone **2a** (R¹ = H) differs from that of substituted bis-enaminones (R¹ ≠ H) under the same reaction conditions.

Depending on the structure of the (*Z,Z*)-*N,N'*-bis(oxotrifluoroalkenyl)-1,3-phenylenediamines (**2**), 2,8-bis-(trifluoromethyl)-1,7-phenanthroline or a mixture of separable 4,8-bis-(trifluoromethyl)-1,7-phenanthrolines and 4-(trifluoromethyl)-7-aminoquinolines was obtained. These results reported here showed an interesting chemical behavior for the mechanism of cyclization of these new enaminoketones **2**, showing selective routes of ring closure including direct cyclocondensations, hydrolyses and recombinations, which furnished new fused bis-(trifluoromethyl)-diazatricycles. Linear bis(trifluoromethyl)-pyrido[*g*]quinolines (**6**) compounds were not isolated.

Conclusions

In summary, we have described an inexpensive and unique route to prepare 1,7-phenanthroline and 7-aminoquinoline cores simultaneously. This process might lead to greater molecular diversity of both heterocyclic series, which are of great potential interest for pharmacological and material applications.

Experimental

General

Unless otherwise indicated, all common reagents and solvents were used as obtained from commercial suppliers without further purification. The melting points (mp) were determined using a Kofler Reichert-Thermovar and Electrothermal Mel-Temp 3.0 apparatus. ¹H, ¹³C and ¹⁹F NMR spectra were acquired on a Bruker DPX 200 spectrometer (¹H at 200.13 MHz) and Bruker DPX 400 (¹H at 400.13 MHz, ¹³C at 100.32 MHz and ¹⁹F at 376.3 MHz) spectrometer, 5 mm sample tubes, 298 K, digital resolution of ± 0.01 ppm, in CDCl₃ for **1**, **2**, **3** and in DMSO-*d*₆ for **4**, using TMS as internal reference (¹H and ¹³C) or fluorobenzene as external reference (¹⁹F). Mass spectra (MS) were registered in a HP 6890 GC connected to a HP 5973 MSD and interfaced by a Pentium PC. The gas chromatograph (GC) was equipped with a split-splitless injector, autosampler, cross-linked HP-5 capillary column (30 m, 0.32 mm of internal diameter), and helium was used as the carrier gas. The diffraction (XRD) measurements were carried out by graphite-monochromatized Mo K α radiation with λ 0.71073 Å on a Bruker SMART CCD diffractometer.⁴³ The structures of **2g**, **3a** and **3c** were solved with direct methods using SHELXS-97 program,⁴⁴ and refined on F² by full-matrix least-squares by the SHELXL-97 package.⁴⁵ The absorption correction was performed by Gaussian methods.⁴⁶ Anisotropic displacement parameters for non-hydrogen atoms were applied. The hydrogen atoms were placed at calculated positions with 0.96 Å (methyl CH₃), 0.97 Å (methylene CH₂), 0.98 Å (methyne CH),

0.93 Å (aromatic CH) using a riding model. The hydrogen isotropic thermal parameters were kept equal to $U_{iso}(H) = \chi U_{eq}$ (carrier C atom), with $\chi = 1.5$ for methyl groups and $\chi = 1.2$ otherwise. The valence angles C–C–H and H–C–H of methyl groups were set to 109.5° and the H atoms were allowed to rotate around the C–C bond. A molecular graph was prepared using ORTEP3 for Windows.⁴⁷ The CHN elemental analyses were performed on a Perkin-Elmer 2400 CHN elemental analyzer (São Paulo University, USP/Brazil).

General procedure for the synthesis of N,N'-bis(1-alkyl[aryl(heteroaryl)]-4,4,4-trifluoro-3-oxo-1-buten-1-yl)-1,3-phenylenediamines (2a-j)

To a stirred solution of 1,3-phenylenediamine (0.54 g, 5 mmol) in ethanol (10 mL), **1a-j** (10 mmol) was added at room temperature. The mixture was stirred at 40 °C for 2 h. After the end of the reaction (TLC), the resulting solid products **2a-j** were isolated by filtration (1st fraction: 80%). Subsequently, the filtrates were evaporated under reduced pressure and the residues were dissolved in hot chloroform and stirred with activated charcoal. After filtration, the filtrates were evaporated under reduced pressure. Then, the crude oily products **2** were dissolved in hot ethanol and subsequently cooled (4–8 °C, 48 h) to give **2** as powders (2nd fraction: 20%). Finally, both fractions were combined and gathered and recrystallized from chloroform (26–91% yields).

*(Z,Z)-N,N'-bis(4,4,4-Trifluoro-3-oxo-1-buten-1-yl)-1,3-phenylenediamine (2a)*³²

Beige solid (1.20 g, 68% yield); mp 171–173 °C; ¹H NMR (CDCl₃) δ 11.74 (d, 2H, *J* 12 Hz, NH), 7.63 (dd, 2H, *J*₁ 8, *J*₂ 12 Hz, H-1), 7.41 (t, 1H, *J* 8 Hz, H-9), 6.95 (dd, H-8, *J*₁ 2, *J*₂ 8 Hz, 2H, H-10), 6.86 (t, 1H, *J* 2 Hz, H-6), 5.71 (d, 2H, *J* 8 Hz, H-2); ¹³C NMR (CDCl₃) δ 179.3 (q, ²*J* 34 Hz, 2 C-3), 149.3 (2 C-1), 140.3 (2 C, C-5, C-7), 131.3 (C-6), 116.5 (q, ¹*J* 289 Hz, 2 CF₃), 113.8 (2 C, C-8, C-10), 105.7 (C-9), 90.3 (2 C-2); ¹⁹F (CDCl₃) δ –75.35 (2-CF₃); GC-MS (EI, 70 eV, *m/z*) 352 (M⁺, 100), 283 (55), 213 (23), 185 (33), 107 (24), 263 (11), 69 (5%); Anal. calcd. for C₁₄H₁₀F₆N₂O₂ (352.06): C, 47.74; H, 2.86; N, 7.95%. Found: C, 48.03; H, 2.96; N, 7.85%.

(Z,Z)-N,N'-bis(5,5,5-Trifluoro-4-oxo-2-penten-2-yl)-1,3-phenylenediamine (2b)

Brown solid (1.63 g, 86% yield); mp 126–128 °C; ¹H NMR (CDCl₃) δ 12.58 (s, 2H, NH), 7.48 (t, 1H, *J* 8 Hz, H-9), 7.14 (dd, 2H, *J*₁ 2, *J*₂ 8 Hz, H-8, H-10), 7.01 (s, 1H, H-6), 5.59 (s, 2H, H-2), 2.15 (s, 6H, CH₃); ¹³C NMR

(CDCl₃) δ 177.1 (q, ²*J* 34 Hz, 2 C-3), 167.2 (2 C-1), 138.2 (2 C, C-5, C-7), 130.5 (C-6), 123.8 (2 C, C-8, C-10), 121.7 (C-9), 117.2 (q, ¹*J* 288 Hz, 2 CF₃), 91.5 (q, ³*J* 1 Hz, 2 C-2), 20.3 (2 CH₃); GC-MS (EI, 70 eV, *m/z*) 199 (100), 380 (M⁺, 75), 311 (40), 283 (55), 265 (48), 69 (7%); Anal. calcd. for C₂₆H₁₄F₆N₂O₂ (380.10): C, 50.53; H, 3.71; N, 7.37%. Found: C, 50.85; H, 3.81; N, 7.61%.

(Z,Z)-N,N'-bis(4,4,4-Trifluoro-1-phenyl-3-oxo-1-buten-1-yl)-1,3-phenylenediamine (2c)

Yellow solid (2.01 g, 80% yield); mp 190–192 °C; ¹H NMR (CDCl₃) δ 12.20 (s, 2H, NH), 7.49–7.19 (m, 10H, Ph), 6.94 (t, 1H, *J* 8 Hz, H-9), 6.52 (d, 2H, *J* 8 Hz, H-8, H-10), 6.40 (s, 1H, H-6), 5.70 (s, 2H, H-2); ¹³C NMR (CDCl₃) δ 178.1 (q, ²*J* 34 Hz, 2 C-3), 166.1 (2 C-1), 138.8 (2 C, C-5, C-7), 133.5 (2 C-Ph), 130.9 (C-6), 129.4, 128.8, 128.2 (10 C-Ph), 121.7 (2 C, C-8, C-10), 119.5 (C-9), 117.15 (q, ¹*J* 289 Hz, 2 CF₃), 93.1 (2 C-2); GC-MS (EI, 70 eV, *m/z*) 504 (M⁺, 30), 435 (22), 407 (100), 323 (30), 69 (2%); Anal. calcd. for C₂₆H₁₈F₆N₂O₂ (504.13): C, 61.91; H, 3.60; N, 5.55%. Found: C, 62.02; H, 3.75; N, 5.64%.

(Z,Z)-N,N'-bis(4,4,4-Trifluoro-1-[4-methylphenyl]-3-oxo-1-buten-1-yl)-1,3-phenylenediamine (2d)

Brown solid (2.29 g, 86% yield); mp 138–140 °C; ¹H NMR (CDCl₃) δ 12.20 (s, 2H, NH), 7.12 (d, 4H, *J* 8 Hz, Ph), 7.16 (d, 4H, *J* 8 Hz, Ph), 6.96 (t, *J* 8 Hz, 1H, H-9), 6.54 (dd, 2H, *J*₁ 2, *J*₂ 8 Hz, H-8, H-10), 6.41 (s, 1H, H-6), 5.69 (s, 2H, H-2), 2.33 (s, 6H, 2 CH₃); ¹³C NMR (CDCl₃) δ 178.0 (q, ²*J* 34 Hz, 2 C-3), 166.3 (2 C-1), 141.6 (2 C-Ph), 139.2 (2 C, C-5, C-7), 130.7 (C-6), 129.5, 129.4, 128.3 (10 C-Ph), 121.6 (2 C, C-8, C-10), 119.5 (C-9), 117.3 (q, ¹*J* 289 Hz, 2 CF₃), 93.0 (2 C-2), 21.3 (2 CH₃); GC-MS (EI, 70 eV, *m/z*) 435 (100), 532 (M⁺, 21), 463 (17), 351 (21), 222 (15), 69 (5%); Anal. calcd. for C₂₈H₂₂F₆N₂O₂ (532.16): C, 63.16; H, 4.16; N, 5.26%. Found: C, 63.02; H, 4.21; N, 5.30%.

(Z,Z)-N,N'-bis(4,4,4-Trifluoro-1-[4-methoxyphenyl]-3-oxo-1-buten-1-yl)-1,3-phenylenediamine (2e)

To a stirred solution of 1,3-phenylenediamine (0.54 g, 5 mmol) in H₂O:CHCl₃ (1:1, 10 mL), **1e** (2.60 g, 10 mmol) was added at room temperature. The mixture was stirred for 4 h at 60 °C. After the end of the reaction (TLC), the resulting residue was extracted with dichloromethane. Then the organic layer was evaporated under reduced pressure. Then, the crude oily product was dissolved in hot ethanol and subsequently cooled (4–8 °C, 48 h) to give the title compound **2e**.

Beige solid (1.32 g, 47% yield), mp 142–144 °C; ¹H NMR (CDCl₃) δ 12.22 (s, 2H, NH), 7.19 (d, 4H,

J 9 Hz, Ph), 6.98 (t, 1H, *J* 8 Hz, H₉), 6.85 (d, 4H, *J* 9 Hz, Ph), 6.55 (dd, 2H, *J*₁ 2, *J*₂ 8 Hz, H-8, H-10), 6.48 (s, 1H, H-6), 5.69 (s, 2H, H-2), 3.84 (s, 6H, 2 OCH₃); ¹³C NMR (CDCl₃) δ 177.6 (q, ²*J* 34 Hz, 2 C-3), 165.9 (2 C-1), 161.8 (2 C-Ph), 139.3 (2 C, C-5, C-7), 130.1 (4 C-Ph), 129.5 (C-6), 125.3 (2 C-Ph), 121.7 (2 C, C-8, C-10), 119.5 (C-9), 114.2 (4 C-Ph), 117.1 (q, ¹*J* 289, 2 CF₃), 92.7 (2 C-2), 55.4 (2 OCH₃); GC-MS (EI, 70 eV, *m/z*) 564 (M⁺, 21), 281 (70), 207 (100), 96 (10%); Anal. calcd. for C₂₈H₂₂F₆N₂O₄ (564.15): C, 59.58; H, 3.93; N, 4.96%. Found: C, 59.55; H, 3.89; N, 4.98%.

(Z,Z)-*N,N'*-bis(4,4,4-Trifluoro-1-[4-fluorophenyl]-3-oxo-1-buten-1-yl)-1,3-phenylenediamine (**2f**)

Beige solid (1.67 g, 62% yield); mp 177-179 °C; ¹H NMR (CDCl₃) δ 12.20 (s, 2H, NH), 7.28-7.21 (m, 4H, Ph), 7.11-6.95 (m, 4H, Ph), 6.98 (t, 1H, *J* 8 Hz, H₉), 6.53 (dd, 2H, *J*₁ 2, *J*₂ 8 Hz, H-8, H-10), 6.51 (s, 1H, H-6), 5.69 (s, 2H, H-2); ¹³C NMR (CDCl₃) δ 178.1 (q, ²*J* 34 Hz, 2 C-3), 163.9 (d, ¹*J* 253 Hz, 2 C-FPh), 164.9 (2 C-1), 138.9 (2 C, C-5, C-7), 130.5 (d, ³*J* 9 Hz, 4 C-FPh), 129.6 (C-6), 129.5 (d, ⁴*J* 3 Hz, 2 C-FPh), 122.0 (2 C, C-8, C-10), 119.7 (C-6), 117.0 (q, ¹*J* 289 Hz, 2 CF₃), 116.1 (d, ²*J* 22 Hz, 4 C-FPh), 93.2 (2 C-2); GC-MS (EI, 70 eV, *m/z*) 540 (M⁺, 20), 471 (20), 443 (100), 255 (30), 226 (30), 69 (10%); Anal. calcd. for C₂₆H₁₆F₈N₂O₂ (540.11): C, 57.79; H, 2.98; N, 5.18%. Found: C, 57.63; H, 2.99; N, 5.19%.

(Z,Z)-*N,N'*-[1-[4-Chlorophenyl]-4,4,4-trifluoro-3-oxo-1-buten-1-yl]-1,3-phenylenediamine (**2g**)

Brown solid (2.37 g, 83% yield); mp 175-177 °C; ¹H NMR (CDCl₃) δ 12.16 (s, 2H, NH), 7.34 (d, 4H, *J* 9 Hz, Ph), 7.17 (d, 4H, *J* 9 Hz, Ph), 6.99 (t, 1H, *J* 8 Hz, H-9), 6.53 (dd, 2H, *J*₁ 2, *J*₂ 8 Hz, H-8, H-10), 6.50 (s, 1H, H-6), 5.68 (s, 2H, H-2); ¹³C NMR (CDCl₃) δ 178.2 (q, ²*J* 34 Hz, 2 C-3), 164.6 (2 C-1), 138.8 (2 C, C-5, C-7), 131.9 (C-6), 129.8, 129.7, 129.6, 129.2, 128.9 (12 C-Ph), 122.2 (2 C, C-8, C-10), 119.7 (C-9), 116.9 (q, ¹*J* 289 Hz, 2 CF₃), 93.2 (2 C-2); GC-MS (EI, 70 eV, *m/z*) 572 (M⁺, 17), 475 (100), 433 (7), 391 (34), 242 (30), 213 (4), 69 (5%); Anal. calcd. for C₂₆H₁₆F₆N₂O₂ (572.05): C, 54.54; H, 2.79; N, 4.89%. Found: C, 54.57; H, 2.87; N, 4.99%.

(Z,Z)-*N,N'*-bis(1-[4-Bromophenyl]-4,4,4-trifluoro-3-oxo-1-buten-1-yl)-1,3-phenylenediamine (**2h**)

Beige solid (3.00 g, 91% yield); mp 170-172 °C; ¹H NMR (CDCl₃) δ 12.20 (s, 2H, NH), 7.51 (d, 4H, *J* 9 Hz, Ph), 7.10 (d, 4H, *J* 9 Hz, Ph), 6.99 (t, 1H, *J* 8 Hz, H-9), 6.53 (dd, 2H, *J*₁ 2, *J*₂ 8 Hz, H-8, H-10), 6.51 (s, 1H, H-6), 5.69 (s, 2H, H-2); ¹³C NMR (CDCl₃) δ 178.4 (q, ²*J* 34 Hz, 2 C-3), 164.7 (2 C-1), 138.9 (2 C, C-5, C-7),

132.4, 132.2, 131.0, 129.8 (12 C-Ph), 125.6 (C-6), 122.2 (2 C, C-8, C-10), 119.7 (C-9), 116.6 (q, ¹*J* 289 Hz, 2 CF₃), 93.3 (2 C-2); GC-MS (EI, 70 eV, *m/z*) 659 (M⁺, 17), 549 (100), 286 (30), 69 (9%); Anal. calcd. for C₂₆H₁₆Br₂F₆N₂O₂ (659.95): C, 47.16; H, 2.44; N, 4.23%. Found: C, 47.25; H, 2.45; N, 4.34%.

(Z,Z)-*N,N'*-bis(4,4,4-Trifluoro-1-(4-nitrophenyl)-3-oxo-1-buten-1-yl)-1,3-phenylenediamine (**2i**)

Beige solid (2.64 g, 89% yield); mp 220-222 °C; ¹H NMR (CDCl₃) δ 12.13 (s, 2H, NH), 8.24 (dd, 4H, *J*₁ 2, *J*₂ 8 Hz, Ph), 7.45 (dd, 4H, *J*₁ 2, *J*₂ 8 Hz, Ph), 6.95 (t, 1H, *J* 8 Hz, H-9), 6.58 (t, 1H, *J* 2 Hz, H-6), 6.46 (dd, 2H, *J*₁ 2, *J*₂ 8 Hz, H-8, H-10), 5.74 (s, 2H, H-2); ¹³C NMR (CDCl₃) δ 178.5 (q, ²*J* 34 Hz, 2 C-3), 165.4 (2 C-1), 146.3, 145.9 (4 C-Ph), 138.8 (2 C, C-5, C-7), 132.2, 129.7 (8 C-Ph), 125.6 (C-6), 122.2 (2 C, C-8, C-10), 119.8 (C-9), 117.2 (q, ¹*J* 289 Hz, 2 CF₃), 92.9 (2 C-2); GC-MS (EI, 70 eV, *m/z*) 594 (M⁺, 15), 525 (30), 497 (100), 69 (10%); Anal. calcd. for C₂₆H₁₆F₆N₄O₆ (594.10): C, 52.54; H, 2.71; N, 9.43%. Found: C, 52.60; H, 2.70; N, 9.47%.

(Z,Z)-*N,N'*-bis(4,4,4-Trifluoro-1-[2-furyl]-3-oxo-1-buten-1-yl)-1,3-phenylenediamine (**2j**)

Yellow solid (1.72 g, 71% yield); mp 210-212 °C; ¹H NMR (CDCl₃) δ 12.23 (s, 2H, NH), 7.46 (s, 2H, furyl), 7.34 (t, 1H, *J* 8 Hz, H-9), 7.04 (dd, 2H, *J*₁ 2, *J*₂ 8 Hz, H-8, H-10), 6.83 (s, 1H, H-6), 6.45-6.41 (m, 4H, furyl), 6.09 (s, 2H, H-2); ¹³C NMR (CDCl₃) δ 178.2 (q, ²*J* 34 Hz, 2 C-3), 153.9 (2 C-1), 145.8, 145.6 (4 C-furyl), 139.7 (2 C, C-5, C-7), 130.1 (C-6), 123.6 (2 C, C-8, C-10), 121.4 (C-9), 117.3 (q, ¹*J* 288 Hz, 2 CF₃), 117.2, 112.6 (4 C-furyl), 89.2 (2 C-2); GC-MS (EI, 70 eV, *m/z*) 484 (M⁺, 15), 415 (21), 387 (100), 227 (14), 69 (7%); Anal. calcd. for C₂₂H₁₄F₆N₂O₄ (484.09): C, 54.55; H, 2.91; N, 5.78%. Found: C, 54.57; H, 2.90; N, 5.82%.

General procedure for the synthesis of 2,8-bis(trifluoromethyl)-1,7-phenantrolinone (3a), 2,10-dialkyl(aryl)-4,8-bis(trifluoromethyl)-1,7-phenanthrolinones (3b-i) and 2-alkyl(aryl)-7-aminoquinolines (4b-i)

To a stirred mixture of H₃PO₄ (2 mL) and P₂O₅ (3 g) (PPA) at 90 °C, **2a-j** (2 mmol) was added. Using a 10 cm length glass adapter connecting the flask reaction and the condenser, the mixture was stirred at 165 °C for 36 h. After this time, the sublimated products **3a-i** were recovered from the adapter using chloroform and the remaining amounts of **3** in the reaction flask were also extracted with chloroform. Both organic fractions were recrystallized from chloroform (22-40% yields). To the dark residue remainder

in the reaction flask were added 20 g of crushed ice and ethyl acetate (20 mL). After stirring, the 7-aminoquinolines (**4b-j**) were isolated when the aqueous phase was extracted with ethyl acetate (6 × 20 mL) combined with NaOH sol. 40% (5 mL). The organic layer was washed with distilled water (3 × 15 mL) and dried over sodium sulfate. After filtration, the liquid phase was stirred and heated in the presence of activated charcoal, filtered again and the solvent was removed under reduced pressure. The resulting powders (**4b-j**) were recrystallized from a mixture of ethyl acetate/hexane (3:1 v/v) (20-45% yields).

*2,8-bis(Trifluoromethyl)-1,7-phenanthroline (3a)*³²

Yellow solid (0.20 g, 32% yield); mp 131-133 °C; ¹H NMR (CDCl₃) δ 9.79 (d, 1H, *J* 9 Hz, H-10), 8.48 (d, 1H, *J* 8 Hz, H-4), 8.27 (d, 1H, *J* 9 Hz, H-3), 8.11 (d, 1H, *J* 9 Hz, H-9), 8.03 (d, 1H, *J* 8 Hz, H-5), 8.01 (d, 1H, *J* 8 Hz, H-6); ¹³C NMR (CDCl₃) δ 149.6 (q, ²*J* 35 Hz, C-2), 149.0 (C-10b), 147.6 (q, ²*J* 35 Hz, C-8), 144.6 (C-6a), 137.8 (C-10), 135.2 (C-4), 130.9 (C-6), 129.7 (C-5), 128.0 (C-10a), 127.9 (C-4a), 121.5 (q, ¹*J* 275 Hz, 2 CF₃), 119.2 (C-3), 118.4 (C-9); GC-MS (EI, 70 eV, *m/z*) 316 (M⁺, 100), 297 (16), 247 (77), 227 (17), 177 (28), 69 (5%); Anal. calcd. for C₁₄H₆F₆N₂ (316.20): C, 53.18; H, 1.91; N, 8.86%. Found: C, 53.34; H 2.01; N, 8.91%.

*4,8-bis(Trifluoromethyl)-2,10-di(methyl)-1,7-phenanthroline (3b)*³²

Yellow solid (0.26 g, 38% yield); mp 147-149 °C; ¹H NMR (CDCl₃) δ 8.23 (dq, 1H, *J*₁ 2, *J*₂ 8 Hz, H-5), 8.15 (d, 1H, *J* 8 Hz, H-6), 7.74 (s, 1H, H-3), 7.70 (s, 1H, H-9), 3.33 (s, 3H, CH₃), 2.86 (s, 3H, CH₃); ¹³C NMR (CDCl₃) δ 157.1 (C-10), 151.5 (C-2), 149.6 (C-10b), 148.0 (C-6a), 147.6 (q, ²*J* 34 Hz, C-8), 134.3 (q, ²*J* 31 Hz, C-4), 130.5 (C-10a), 126.5 (C-6), 125.2 (q, ⁴*J* 3 Hz, C-5), 121.6 (q, ³*J* 5 Hz, C-3), 120.0 (C-4a), 124.0 (q, ¹*J* 275 Hz, CF₃), 123.4 (q, ¹*J* 275 Hz, CF₃), 118.5 (q, ³*J* 5 Hz, C-9), 27.2 (CH₃), 25.1 (CH₃); ¹⁹F NMR (CDCl₃) δ -60.36 (CF₃-4), -67.34 (CF₃-8); GC-MS (EI, 70 eV, *m/z*) 344 (M⁺, 100), 325 (19), 275 (19), 172 (8), 69 (6%); Anal. calcd. for C₁₆H₁₀F₆N₂ (344.25): C, 55.77; H, 2.90; N, 8.13%. Found: C, 55.48; H, 3.14; N, 8.03%.

4,8-bis(Trifluoromethyl)-2,10-di(phenyl)-1,7-phenanthroline (3c)

Yellow solid (0.37 g, 40% yield); mp 226-228 °C; ¹H NMR (CDCl₃) δ 8.39 (dq, 1H, *J*₁ 2, *J*₂ 8 Hz, H-5), 8.32 (d, 1H, *J* 9 Hz, H-6), 8.27 (s, 1H, H-3), 7.80 (s, 1H, H-9), 7.50-7.41 (m, 5H, Ph), 7.39-7.25 (m, 5H, Ph); ¹³C NMR (CDCl₃) δ 154.4 (C-10), 152.6 (C-2), 150.2 (C-10b), 148.2 (q, ²*J* 34 Hz, C-8), 146.7 (C-6a), 143.5, 136.7 (2 C-Ph), 135.2 (q, ²*J* 31 Hz, C-4), 130.7 (C-10a), 130.1, 128.7, 128.6, 127.7

(10 C-Ph), 127.3 (C-6), 127.2 (C-5), 123.4 (q, ¹*J* 275 Hz, CF₃), 122.3 (q, ³*J* 5 Hz, C-3), 122.0 (C-4a), 121.4 (q, ¹*J* 275 Hz, CF₃), 115.5 (q, ³*J* 5 Hz, C-9); ¹⁹F NMR (CDCl₃) δ -60.40 (CF₃-4), -67.38 (CF₃-8); GC-MS (EI, 70 eV, *m/z*) 468 (M⁺, 100), 449 (12), 399 (37), 226 (20), 198 (19), 137 (5%); Anal. calcd. for C₂₆H₁₄F₆N₂ (468.11): C, 66.67; H, 3.01; N, 5.98%. Found: C, 66.71; H, 3.25; N, 6.04%.

4,8-bis(Trifluoromethyl)-2,10-di(4-methylphenyl)-1,7-phenanthroline (3d)

Yellow solid (0.32 g, 28% yield); mp 230-232 °C; ¹H NMR (CDCl₃) δ 8.00 (d, 4H, *J* 8 Hz, Ph), 7.86 (d, 1H, *J*₂ 9 Hz, H-6), 7.82 (dq, 1H, *J*₁ 2, *J*₂ 8 Hz, H-5), 7.84 (s, 1H, H-3), 7.72 (s, 1H, H-9), 7.32 (d, 4H, *J* 8 Hz, Ph), 2.47 (s, 3H, CH₃), 2.42 (s, 3H, CH₃); ¹³C NMR (CDCl₃) δ 155.3 (C-10), 153.5 (C-2), 151.1 (C-10b), 149.6 (q, ²*J* 34 Hz, C-8), 147.5 (C-6a), 139.8, 136.7 (4 C-Ph), 135.2 (q, ²*J* 31 Hz, C-4), 130.1 (C-10a), 129.5, 128.3 (8 C-Ph), 125.9 (C-6), 123.4 (q, ¹*J* 275 Hz, CF₃), 121.4 (q, ¹*J* 275 Hz, CF₃), 120.5 (C-5), 120.1 (C-4a), 117.4 (q, ³*J* 3 Hz, C-3), 115.5 (q, ³*J* 5 Hz, C-9), 22.9 (CH₃), 21.1 (CH₃); GC-MS (EI, 70 eV, *m/z*) 496 (M⁺, 100), 477 (10), 427 (35%); Anal. calcd. for C₂₈H₁₈F₆N₂ (496.14): C, 67.74; H, 3.65; N, 5.64%. Found: C, 67.81; H, 3.74; N, 5.68%.

4,8-bis(Trifluoromethyl)-2,10-di(4-methoxyphenyl)-1,7-phenanthroline (3e)

Yellow solid (0.23 g, 22% yield); mp 246-248 °C; ¹H NMR (CDCl₃) δ 8.15 (dd, *J*₁ 2, *J*₂ 8 Hz, 4H, Ph), 8.97 (dq, 1H, *J*₁ 2, *J*₂ 8 Hz, H-5), 7.12 (dd, 4H, *J*₁ 2, *J*₂ 8 Hz, Ph), 7.08 (d, 1H, *J* 2 Hz, H-6), 6.98 (s, 2H, H-3, H-9), 3.89 (s, 6H, OCH₃); ¹³C NMR (CDCl₃) δ 155.5 (C-10), 153.7 (C-2), 151.3 (C-10b), 149.2 (q, ²*J* 34 Hz, C-8), 147.7 (C-6a), 144.5 (2 C-Ph), 136.2 (q, ²*J* 31 Hz, C-4), 132.7 (C-10a), 130.8, 130.6 (6 C-Ph), 129.8 (C-6), 129.4 (C-5), 128.0 (q, ³*J* 5 Hz, C-3), 127.6 (C-4a), 124.9 (4 C-Ph), 124.0 (q, ¹*J* 275 Hz, CF₃), 122.8 (q, ¹*J* 275 Hz, CF₃), 117.6 (q, ³*J* 5 Hz, C-9), 54.5 (OCH₃), 52.3 (OCH₃); GC-MS (EI, 70 eV, *m/z*) 528 (M⁺, 100), 509 (14), 459 (38%); Anal. calcd. for C₂₈H₁₈F₆N₂O₂ (528.13): C, 63.64; H, 3.43; N, 5.30%. Found: C, 63.59; H, 3.38; N, 5.41%.

4,8-bis(Trifluoromethyl)-2,10-di(4-fluorophenyl)-1,7-phenanthroline (3f)

Yellow solid (0.29 g, 29% yield); mp 234-236 °C; ¹H NMR (CDCl₃) δ 8.15-8.08 (m, 2H, Ph), 7.86 (dq, 1H, *J*₁ 2, *J*₂ 8 Hz, H-5), 7.76 (s, 1H, H-6), 7.43-7.39 (m, 2H, Ph), 7.23 (s, 1H, H-3), 7.19-7.14 (m, 2H, Ph), 7.01 (s, 1H, H-9), 7.01-6.94 (m, 2H, Ph); ¹³C NMR (CDCl₃) δ 162.3 (d, ¹*J* 253 Hz, 2 C-FPh), 155.1 (C-10), 154.2 (C-2), 153.3 (C-10b), 148.6 (q, ²*J* 34 Hz, C-8), 146.1 (C-6a), 133.1

(q, 2J 31 Hz, C-4), 130.3 (d, 4J 3 Hz, 2 C-FPh), 129.1 (C-10a), 128.3 (d, 3J 8 Hz, 4 C-FPh), 122.2 (C-6), 123.4 (q, 1J 275 Hz, CF₃), 121.4 (q, 1J 275 Hz, CF₃), 117.6 (q, 3J 5 Hz, C-5), 115.4 (C-4a), 114.4 (d, 2J 22 Hz, 4 C-FPh), 114.2 (C-3), 112.8 (C-9); GC-MS (EI, 70 eV, m/z) 503 (M⁺, 100), 485 (7), 435 (18), 409 (16%); Anal. calcd. for C₂₆H₁₂F₈N₂ (504.09): C, 61.91; H, 2.40; N, 5.55%. Found: C, 61.95; H, 2.53; N, 5.64%.

2,10-di(4-Chlorophenyl)-4,8-bis(trifluoromethyl)-1,7-phenanthroline (3g)

Yellow solid (0.37 g, 35% yield); mp 236-238 °C; ¹H NMR (CDCl₃) δ 8.39 (dq, 1H, J_1 2, J_2 8 Hz, H-5), 8.34 (d, 1H, J 2 Hz, H-6), 8.23 (s, 1H, H-3), 7.76 (s, 1H, H-9), 7.49-7.46 (m, 2H, Ph), 7.37-7.35 (m, 4H, Ph), 7.24-7.21 (m, 2H, Ph); ¹³C NMR (CDCl₃) δ 153.2 (C-10), 152.5 (C-2), 151.6 (C-10b), 151.1 (q, 2J 34 Hz, C-8), 148.2 (C-6a), 137.8, 135.3 (4 C-Ph), 134.1 (q, 2J 31 Hz, C-4), 131.5 (C-10a), 130.9, 169.7 (8 C-Ph), 128.0 (C-6), 126.4 (C-5), 123.6 (q, 1J 275 Hz, CF₃), 121.5 (q, 1J 275 Hz, CF₃), 119.5 (q, 3J 5 Hz, C-3), 119.3 (C-4a), 118.1 (q, 3J 5 Hz, C-9); ¹⁹F NMR (CDCl₃) δ -60.59 (CF₃-4), -67.57 (CF₃-8); GC-MS (EI, 70 eV, m/z) 535 (M⁺, 100), 501 (20), 467 (12), 425 (12), 232.6 (14), 198 (14), 138 (5%); Anal. calcd. for C₂₆H₁₄F₆N₂ (536.02): C, 58.12; H, 2.25; N, 5.21%. Found: C, 58.21; H, 2.32; N, 5.18%.

2,10-di(4-Bromophenyl)-4,8-bis(trifluoromethyl)-1,7-phenanthroline (3h)

Yellow solid (0.43 g, 33% yield); mp 262-264 °C; ¹H NMR (CDCl₃) δ 8.35 (s, 1H, H-3), 8.22 (s, 1H, H-9), 7.95 (dq, 1H, J_1 2, J_2 8 Hz, H-5), 7.78 (d, 1H, J 2 Hz, H-6), 7.58 (dd, 4H, J_1 2, J_2 8 Hz, Ph), 7.21 (dd, 4H, J_1 2, J_2 8 Hz, Ph); ¹³C NMR (CDCl₃) δ 152.8 (C-10), 152.2 (C-2), 151.2 (C-10b), 149.3 (q, 2J 34 Hz, C-8), 137.5 (C-6a), 134.9 (2 C-Ph), 133.8 (q, 2J 31 Hz, C-4), 132.0 (C-10a), 131.2, 130.6, 129.3 (10 C-Ph), 127.7 (C-6), 125.6 (C-5), 123.5 (q, 1J 275 Hz, CF₃), 121.5 (q, 1J 275 Hz, CF₃), 119.4 (q, 3J 5 Hz, C-3), 118.9 (C-4a), 117.8 (q, 3J 5 Hz, C-9); GC-MS (EI, 70 eV, m/z) 625 (M⁺, 100), 554 (23), 468 (5), 69 (8%); Anal. calcd. for C₂₆H₁₂Br₂F₆N₂ (623.93): C, 49.87; H, 1.93; N, 4.47%. Found: C, 49.83; H, 2.01; N, 4.58%.

4,8-bis(Trifluoromethyl)-2,10-di(4-nitrophenyl)-1,7-phenanthroline (3i)

Yellow solid (0.29 g, 23% yield); mp 249-251 °C; ¹H NMR (CDCl₃) δ 8.37 (dd, 4H, J_1 2, J_2 8 Hz, Ph), 8.12 (dd, 4H, J_1 2, J_2 8 Hz, Ph), 7.97 (dq, 1H, J_1 2, J_2 8 Hz, H-5), 7.90 (s, 1H, H-3), 7.37 (s, 1H, H-9), 7.13 (dd, 1H, J_1 2, J_2 8 Hz, H-6); ¹³C NMR (CDCl₃) δ 155.5 (C-10), 153.9 (C-2), 152.0 (C-10b), 150.4 (q, 2J 34 Hz, C-8),

147.8 (C-6a), 147.4, 143.9 (4 C-Ph), 134.3 (q, 2J 31 Hz, C-4), 131.4 (C-10a), 130.0 (4 C-Ph), 126.5 (C-6), 125.2 (q, 4J 3 Hz, C-5), 124.5 (4 C-Ph), 123.4 (q, 1J 275 Hz, CF₃), 121.5 (q, 1J 275 Hz, CF₃), 121.6 (q, 3J 5 Hz, C-3), 120.9 (C-4a), 118.4 (q, 3J 5 Hz, C-9); GC-MS (EI, 70 eV, m/z) 558 (M⁺, 100), 539 (18), 489 (30), 69 (10%); Anal. calcd. for C₂₆H₁₂F₆N₄O₄ (558.08): C, 55.92; H, 2.17; N, 10.03%. Found: C, 55.88; H, 2.28; N, 10.21%.

4-Trifluoromethyl-2-methyl-7-aminoquinoline (4b)³²

Brown solid (0.18 g, 40% yield); mp 174-176 °C; ¹H NMR (CDCl₃) δ 7.87 (dq, 1H, J_1 2, J_2 9 Hz, H-5), 7.30 (s, 1H, H-3), 7.21 (d, 1H, J 2 Hz, H-8), 7.02 (dd, 1H, J_1 2, J_2 9 Hz, H-6), 4.18 (s, 2H, NH), 2.72 (s, 3H, CH₃); ¹³C NMR (DMSO-*d*₆) δ 158.1 (C-2), 150.7 (C-8a), 150.6 (C-7), 132.2 (q, 2J 30 Hz, C-4), 123.6 (C-5), 119.5 (C-6), 118.3 (q, 1J 275 Hz, CF₃), 113.5 (q, 3J 5 Hz, C-3), 112.2 (C-4a), 106.8 (C-8), 24.7 (CH₃); ¹⁹F NMR (376 MHz, CDCl₃) δ -61.25 (CF₃-4); GC-MS (EI, 70 eV, m/z) 226 (M⁺, 100), 210 (7), 199 (31), 157 (8), 142 (7), 69 (6%); Anal. calcd. for C₁₁H₉F₃N₂ (226.07): C, 58.41; H, 4.01; N, 12.38%. Found: C, 58.04; H, 4.01; N, 12.01%.

4-Trifluoromethyl-2-phenyl-7-aminoquinoline (4c)

Brown solid (0.22 g, 38% yield); mp 139-141 °C; ¹H NMR (DMSO-*d*₆) δ 8.25 (dd, 2H, J_1 2, J_2 8 Hz, Ph), 7.95 (s, 1H, H-3), 7.79 (dq, 2H, J_1 2, J_2 8 Hz, H-5), 7.57-7.51 (m, 3H, Ph), 7.21 (d, 1H, J 2 Hz, H-6), 7.16 (s, 1H, H-8), 6.15 (s, 2H, NH₂); ¹³C NMR (DMSO-*d*₆) δ 155.4 (C-2), 151.0 (C-8a), 150.9 (C-7), 138.1 (C-Ph), 130.7 (q, 2J 30 Hz, C-4), 129.6, 128.7, 127.0 (5 C-Ph), 123.8 (q, 1J 275 Hz, CF₃), 123.7 (C-5), 120.5 (C-6), 113.0 (C-4a), 110.0 (q, 3J 5 Hz, C-3), 107.3 (C-8); ¹⁹F NMR (CDCl₃) δ -61.28 (CF₃-4); GC-MS (EI, 70 eV, m/z) 288 (M⁺, 100), 273 (5), 219 (20), 203 (5%); Anal. calcd. for C₁₆H₁₁F₃N₂ (288.09): C, 66.66; H, 3.85; N, 9.72%. Found: C, 66.32; H, 3.75; N, 9.64%.

4-Trifluoromethyl-2-(4-methylphenyl)-7-aminoquinoline (4d)

Yellow brown (0.14 g, 24% yield); mp 156-158 °C; ¹H NMR (CDCl₃) δ 8.03 (d, 2H, J 8 Hz, Ph), 7.91 (dq, 2H, J_1 2, J_2 9 Hz, H-5), 7.86 (s, 1H, H-3), 7.34 (d, 2H, J 2 Hz, Ph), 7.31 (s, 1H, H-8), 7.04 (dd, 1H, J_1 2, J_2 9 Hz, H-6), 4.16 (s, 2H, NH₂), 2.43 (s, 3H, 2 CH₃); ¹³C NMR (DMSO-*d*₆) δ 156.9 (C-2), 150.9 (C-8a), 148.2 (C-7), 139.8, 136.0 (2 C-Ph), 134.5 (q, 2J 31 Hz, C-4), 129.5, 127.2 (4 C-Ph), 124.8 (C-5), 123.7 (q, 1J 275 Hz, CF₃), 119.4 (C-6), 115.2 (C-4a), 112.1 (q, 3J 5 Hz, C-3), 110.0 (C-8), 21.2 (CH₃); GC-MS (EI, 70 eV, m/z) 302 (M⁺, 100), 233 (23), 69 (10%); Anal. calcd. for C₁₇H₁₃F₃N₂ (302.10): C, 67.54; H, 4.33; N, 9.27%. Found: C, 67.14; H, 4.19; N, 8.90%.

4-Trifluoromethyl-2-(4-methoxyphenyl)-7-aminoquinoline (4e)

Brown solid (0.13 g, 20% yield); mp 173-175 °C; ¹H NMR (CDCl₃) δ 8.22 (dd, 2H, *J*₁ 2, *J*₂ 8 Hz, Ph), 7.89 (s, 1H, H-3), 7.80 (dq, 1H, *J*₁ 2, *J*₂ 9 Hz, H-5), 7.21 (s, 1H, H-8), 7.18 (dd, 1H, *J*₁ 2, *J*₂ 9 Hz, H-6), 7.10 (dd, 2H, *J*₁ 2, *J*₂ 8 Hz, Ph), 5.98 (s, 2H, NH₂), 3.85 (s, 3H, OCH₃); ¹³C NMR (DMSO-*d*₆) δ 160.5 (C-2), 154.9 (C-8a), 150.6 (C-7), 132.8 (q, ²*J* 31 Hz, C-4), 130.4, 128.2 (3 C-Ph), 123.6 (q, ¹*J* 275, CF₃), 123.4 (q, ⁴*J* 2 Hz, C-5), 119.7 (C-6), 113.9 (3 C-Ph), 112.5 (4a), 109.6 (q, ³*J* 5 Hz, C-3), 107.5 (C-8), 54.9 (2 OCH₃); GC-MS (EI, 70 eV, *m/z*) 318 (M⁺, 100), 233 (5), 249 (29), 69 (12%); Anal. calcd. for C₁₇H₁₃F₃N₂O (318.10): 64.15; H, 4.12; N, 8.80%. Found: C, 63.89; H, 3.98; N, 8.80%.

4-Trifluoromethyl-2-(4-fluorophenyl)-7-aminoquinoline (4f)

Yellow solid (0.27 g, 45% yield); mp 191-193 °C; ¹H NMR (DMSO-*d*₆) δ 8.33-8.29 (m, 2H, Ph), 7.93 (s, 1H, H-3), 7.79 (dq, 1H, *J*₁ 2, *J*₂ 8 Hz, H-5), 7.37-7.33 (m, 2H, Ph), 7.21 (d, 1H, *J* 2 Hz, H-6), 7.18 (s, 1H, H-8), 6.10 (s, 2H, NH₂); ¹³C NMR (DMSO-*d*₆) δ 163.1 (d, ¹*J* 248 Hz, C-FPh), 154.3 (C-2), 150.8 (C-8a), 150.6 (C-7), 134.4 (d, ⁴*J* 3 Hz, C-FPh), 133.1 (q, ²*J* 31 Hz, C-4), 129.1 (d, ³*J* 8 Hz, 2 C-FPh), 123.5 (q, ¹*J* 275 Hz, CF₃), 123.4 (C-5), 120.3 (C-6), 115.3 (d, ²*J* 22 Hz, 2 C-FPh), 112.8 (C-4a), 109.9 (q, ³*J* 5 Hz, C-3), 107.2 (C-8); GC-MS (EI, 70 eV, *m/z*) 306 (M⁺, 100), 237 (22), 142 (8), 69 (16%); Anal. calcd. for C₁₆H₁₀F₄N₂ (306.08): C, 62.75; H, 3.29; N, 9.15%. Found: C, 62.58; H, 3.14; N, 9.01%.

2-(4-Chlorophenyl)-4-trifluoromethyl-7-aminoquinoline (4g)

Yellow solid (0.22 g, 35% yield); mp 178-180 °C; ¹H NMR (CDCl₃) δ 8.09 (dd, 2H, *J*₁ 2, *J*₂ 8 Hz, Ph), 7.93 (dq, 1H, *J*₁ 2, *J*₂ 8 Hz, H-5), 7.83 (s, 1H, H-3), 7.50 (dd, 2H, *J*₁ 2, *J*₂ 8 Hz, Ph), 7.33 (d, 1H, *J* 2 Hz, H-8), 7.07 (dd, 1H, *J*₁ 2, *J*₂ 9 Hz, H-6), 4.20 (s, 2H, NH₂); ¹³C NMR (DMSO-*d*₆) δ 154.2 (C-2), 151.1 (C-8a), 150.7 (C-7), 136.8, 134.6 (2 C-Ph), 133.3 (q, ²*J* 31 Hz, C-4), 128.8, 128.7 (4 C-Ph), 125.1 (C-5), 125.5 (q, ¹*J* 275 Hz, CF₃), 122.3 (C-6), 119.6 (C-4a), 110.0 (q, ³*J* 5 Hz, C-3), 107.1 (C-8); ¹⁹F NMR (CDCl₃) δ -61.30 (CF₃-4); GC-MS (EI, 70 eV, *m/z*) 322 (M⁺, 100), 303 (4), 283 (4), 253 (4), 239 (16%); Anal. calcd. for C₁₆H₁₀ClF₃N₂ (322.05): C, 59.55; H, 3.12; N, 8.68%. Found: C, 59.63; H, 3.07; N, 8.61%.

2-(4-Bromophenyl)-4-trifluoromethyl-7-aminoquinoline (4h)

Yellow solid (0.24 g, 33% yield); mp 177-179 °C; ¹H NMR (CDCl₃) δ 8.03 (dd, 2H, *J*₁ 2, *J*₂ 8 Hz, Ph), 7.93

(dq, 1H, *J*₁ 2, *J*₂ 8 Hz, H-5), 7.83 (s, 1H, H-3), 7.65 (dd, 2H, *J*₁ 2, *J*₂ 8 Hz, Ph), 7.33 (d, 1H, *J* 2 Hz, H-8), 7.07 (dd, 1H, *J*₁ 2, *J*₂ 8 Hz, H-6), 4.20 (s, 2H, NH₂); ¹³C NMR (DMSO-*d*₆) δ 154.1 (C-2), 150.9 (C-8a), 150.6 (C-7), 137.1 (C-Ph), 133.2 (q, ²*J* 31 Hz, C-4), 131.4, 128.8, 123.5 (5 C-Ph), 123.6 (q, ¹*J* 275 Hz, CF₃), 123.2 (C-5), 120.6 (C-6), 113.0 (C-4a), 109.8 (q, ³*J* 5 Hz, C-3), 107.1 (C-8); GC-MS (EI, 70 eV, *m/z*) 366 (M⁺, 100), 347 (6), 297 (14), 280 (4), 69 (5%); Anal. calcd. for C₁₆H₁₀BrF₃N₂ (366.00): C, 52.34; H, 2.75; N, 7.63%. Found: C, 52.40; H, 2.71; N, 7.58%.

4-Trifluoromethyl-2-(4-nitrophenyl)-7-aminoquinoline (4i)

Beige solid (0.14 g, 21% yield); mp 199-201 °C; ¹H NMR (CDCl₃) δ 7.98 (d, 2H, *J* 8 Hz, Ph), 7.87 (d, 1H, *J* 8 Hz, H-5), 7.80 (s, 1H, H-3), 7.30 (d, 1H, *J* 2 Hz, H-8), 7.00 (d, 1H, *J* 2 Hz, H-6), 6.79 (d, 2H, *J* 8 Hz, Ph), 5.34 (s, 2H, NH₂); ¹³C NMR (DMSO-*d*₆) δ 153.3 (C-2), 151.4 (C-8a), 150.8 (C-7), 148.1, 143.9 (2 C-Ph), 133.5 (q, ²*J* 31 Hz, C-4), 128.4, 123.9 (4 C-Ph), 123.8 (q, ¹*J* 275 Hz, CF₃), 123.7 (C-5), 121.6 (C-6), 113.5 (C-4a), 110.7 (q, ³*J* 5 Hz, C-3), 107.0 (C-8); ¹⁹F NMR (CDCl₃) δ -61.23 (CF₃-4); GC-MS (EI, 70 eV, *m/z*) 333 (M⁺, 100), 314 (7), 264 (18), 248 (5), 69 (5%); Anal. calcd. for C₁₆H₁₀F₃N₃O₂ (333.07): C, 57.66; H, 3.02; N, 12.61%. Found: C, 57.52; H, 2.87; N, 12.68%.

4-Trifluoromethyl-2-(2-furyl)-7-aminoquinoline (4j)

To a stirred mixture of H₃PO₄ (0.8 mL) and P₂O₅ (1.2 g) (PPA) at 90 °C, **2j** (2 mmol) was added. Using an 10 cm length glass adapter connecting the flask reaction and the condenser, the mixture was stirred at 90 °C for 36 h. Then, to the dark residue in the reaction flask was added 20 g of crushed ice and ethyl acetate (20 mL). After stirring, the 7-aminoquinoline **4j** was isolated when the aqueous phase was extracted with ethyl acetate (6 × 20 mL) combined with NaOH solution 40% (5 mL). The organic layer was washed with distilled water (3 × 15 mL) and dried over sodium sulfate. After filtration, the liquid phase was stirred and heated in the presence of activated charcoal, filtered again and the solvent removed under reduced pressure.

Yellow solid (0.40 g, 73% yield), mp 235-238 °C; ¹H NMR (DMSO-*d*₆) δ 7.96 (d, 1H, *J* 1 Hz, furyl), 7.79 (s, 1H, H-3), 7.75 (d, 1H, *J* 2 Hz, H-5), 7.43 (d, 1H, *J* 3 Hz, furyl), 7.19 (dd, 1H, *J*₁ 2, *J*₂ 9 Hz, H-6), 7.11 (d, 1H, *J* 2 Hz, H-8), 6.75-6.72 (m, 1H, *J* 2 Hz, furyl), 6.20 (s, 2H, NH₂); ¹³C NMR (DMSO-*d*₆) δ 152.5 (C-2), 151.2 (C-8a), 150.7 (C-7), 147.7, 145.0 (2 C-furyl), 133.0 (q, ²*J* 31 Hz, C-4), 123.9 (C-5), 123.6 (q, ¹*J* 275 Hz, CF₃), 120.3 (C-6), 112.7 (C-4a), 112.6, 110.9 (2 C-furyl), 108.8 (q, ³*J* 5 Hz, C-3), 106.8 (C-8); CG-MS (EI, 70 eV, *m/z*) 278 (M⁺, 100), 250 (11), 69 (4%); Anal. calcd. for

C₁₄H₉F₃N₂O (278.07): C, 60.44; H, 3.26; N, 10.07%. Found: C, 60.48; H, 3.25; N, 10.01%.

Supplementary Information

NMR spectra are available free of charge at <http://jbcs.sbq.org.br> as PDF file.

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Supplementary Information

Simultaneous Regioselective Synthesis of Trifluoromethyl-Containing 1,7-Phenanthrolines and Quinolines from Cyclocondensation Reaction of *N,N'*-Bis(oxotrifluoroalkenyl)-1,3-Phenylenediamines

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NMR spectra of compounds

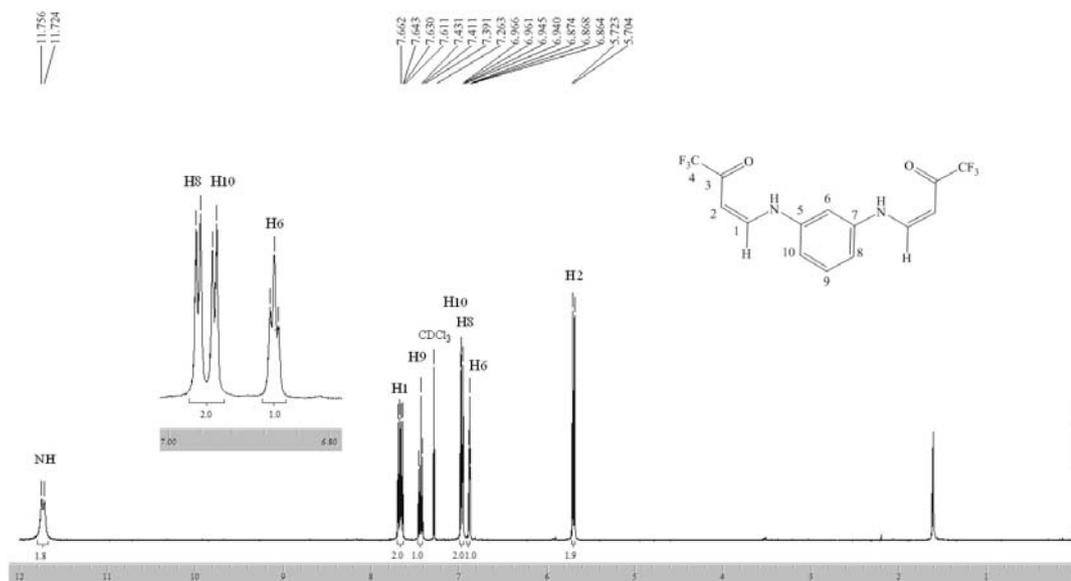


Figure S1. ¹H NMR (100 MHz, CDCl₃) spectrum of (Z,Z)-*N,N'*-bis(4,4,4-trifluoro-3-oxo-1-buten-1-yl)-1,3-phenylenediamine (**2a**).

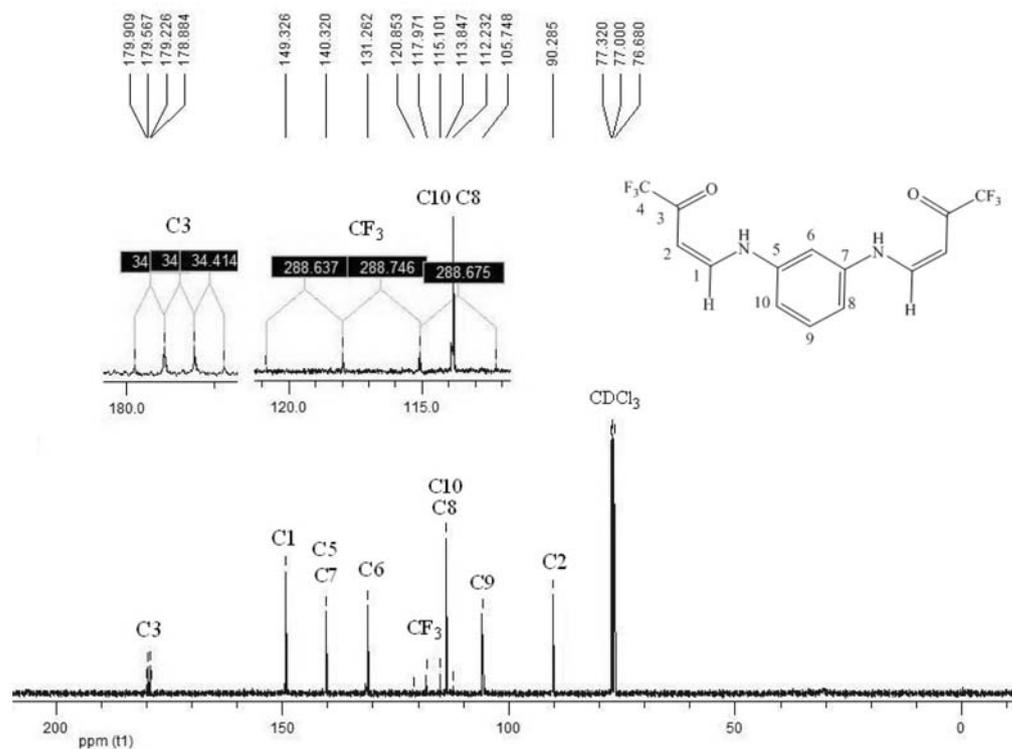


Figure S2. ^{13}C NMR (200 MHz, CDCl_3) spectrum of *(Z,Z)*-*N,N'*-bis(4,4,4-trifluoro-3-oxo-1-buten-1-yl)-1,3-phenylenediamine (**2a**).



Figure S3. ^{19}F NMR (376 MHz, CDCl_3) spectrum of *(Z,Z)*-*N,N'*-bis(4,4,4-trifluoro-3-oxo-1-buten-1-yl)-1,3-phenylenediamine (**2a**).

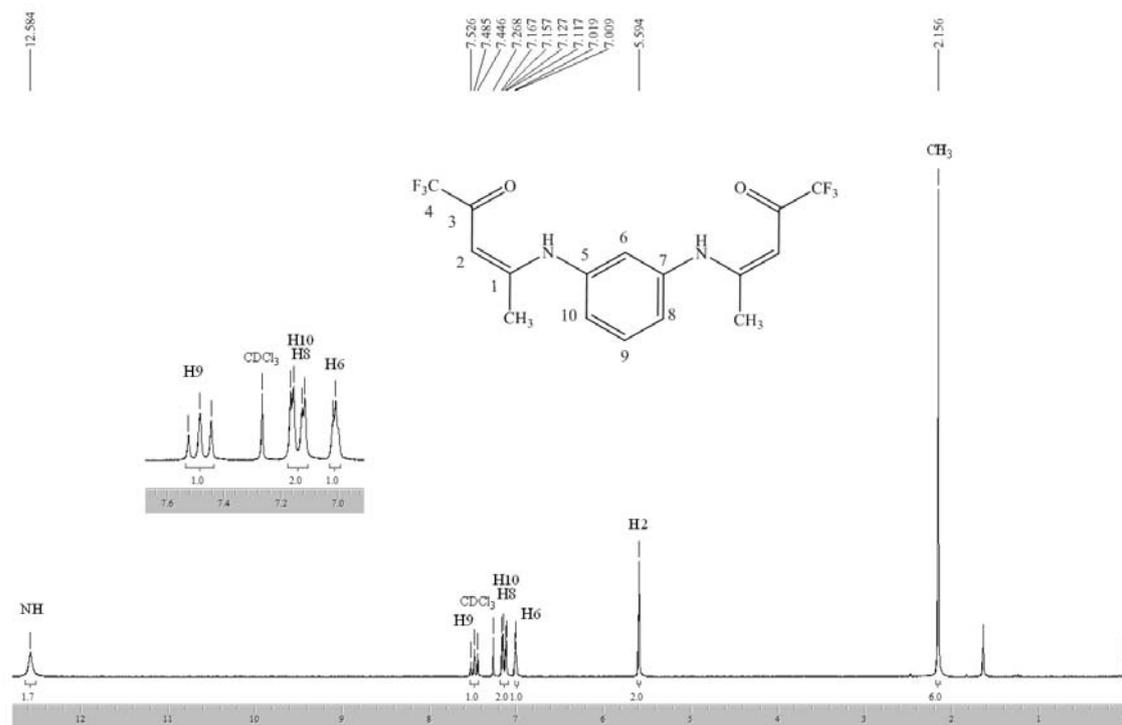


Figure S4. ^1H NMR (100 MHz, CDCl_3) spectrum of (Z,Z) - N,N' -bis(5,5,5-trifluoro-4-oxo-2-penten-2-yl)-1,3-phenylenediamine (**2b**).

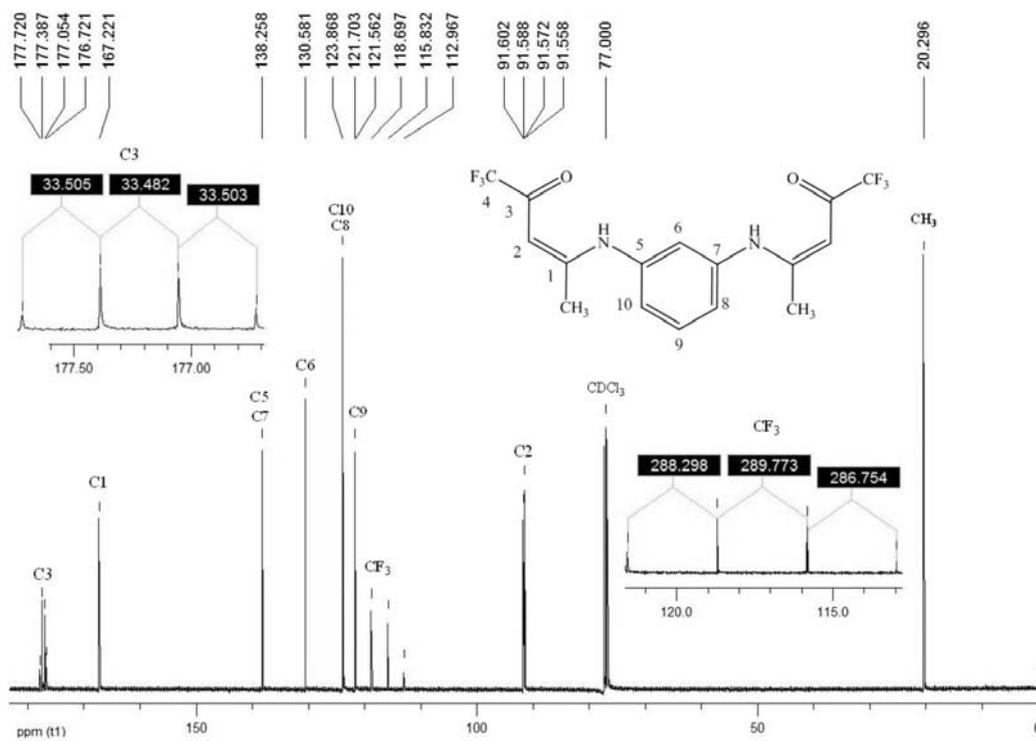


Figure S5. ^{13}C NMR (200 MHz, CDCl_3) spectrum of (Z,Z) - N,N' -bis(5,5,5-trifluoro-4-oxo-2-penten-2-yl)-1,3-phenylenediamine (**2b**).

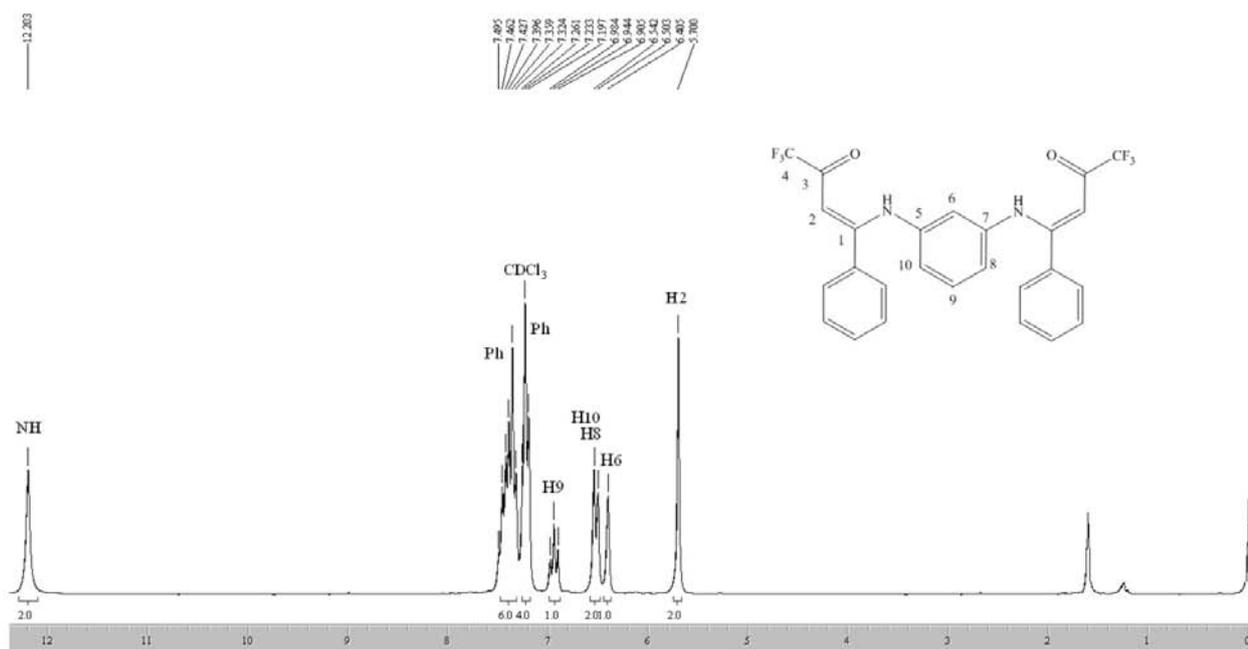


Figure S6. ¹H NMR (100 MHz, CDCl₃) spectrum of (Z,Z)-N,N'-bis(4,4,4-trifluoro-1-phenyl-3-oxo-1-buten-1-yl)-1,3-phenylenediamine (**2c**).

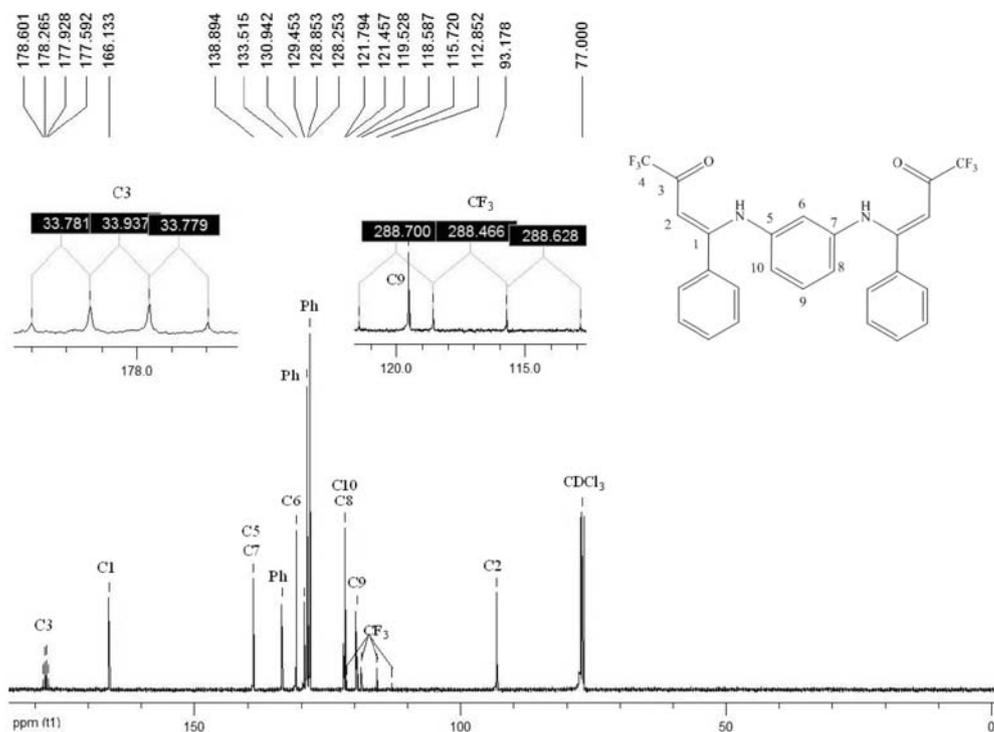


Figure S7. ¹³C NMR (200 MHz, CDCl₃) spectrum of (Z,Z)-N,N'-bis(4,4,4-trifluoro-1-phenyl-3-oxo-1-buten-1-yl)-1,3-phenylenediamine (**2c**).

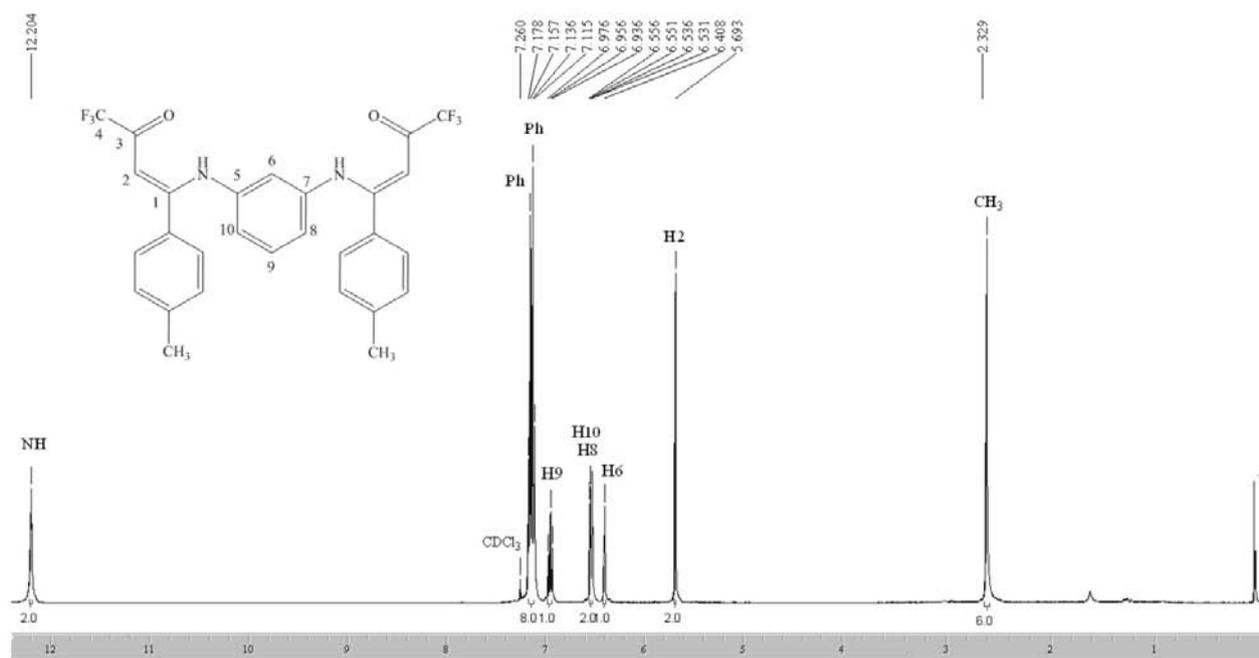


Figure S8. ^1H NMR (100 MHz, CDCl_3) spectrum of (*Z,Z*)-*N,N'*-bis(4,4,4-trifluoro-1-[4-methylphenyl]-3-oxo-1-buten-1-yl)-1,3-phenylenediamine (**2d**).

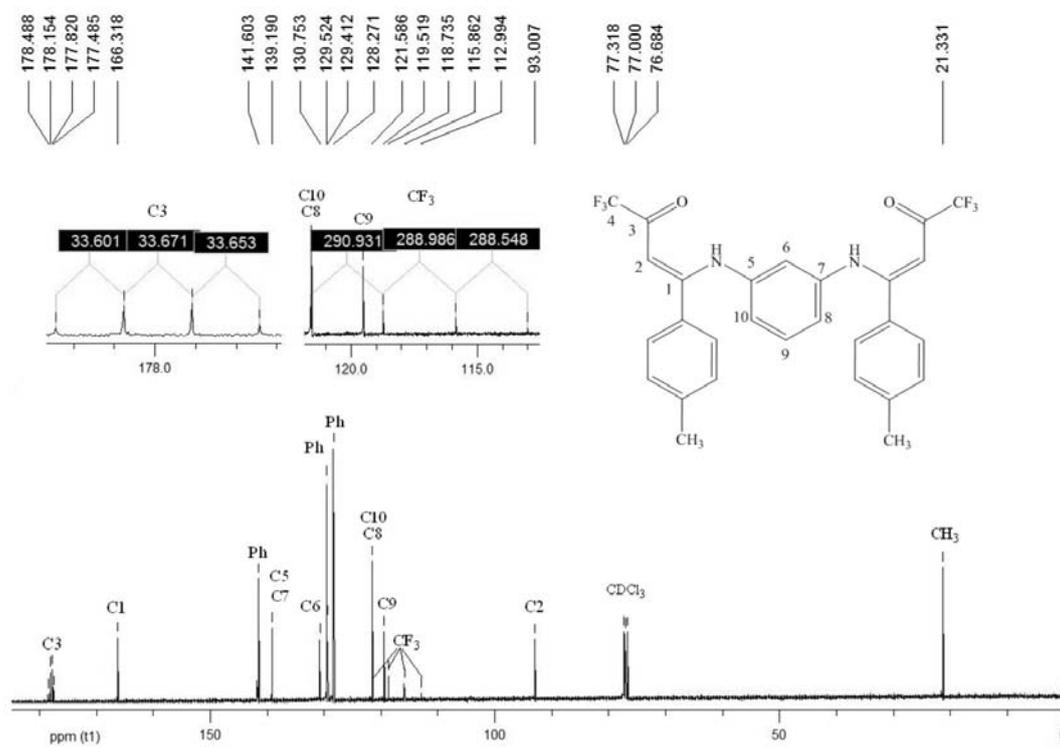


Figure S9. ^{13}C NMR (200 MHz, CDCl_3) spectrum of (*Z,Z*)-*N,N'*-bis(4,4,4-trifluoro-1-[4-methylphenyl]-3-oxo-1-buten-1-yl)-1,3-phenylenediamine (**2d**).

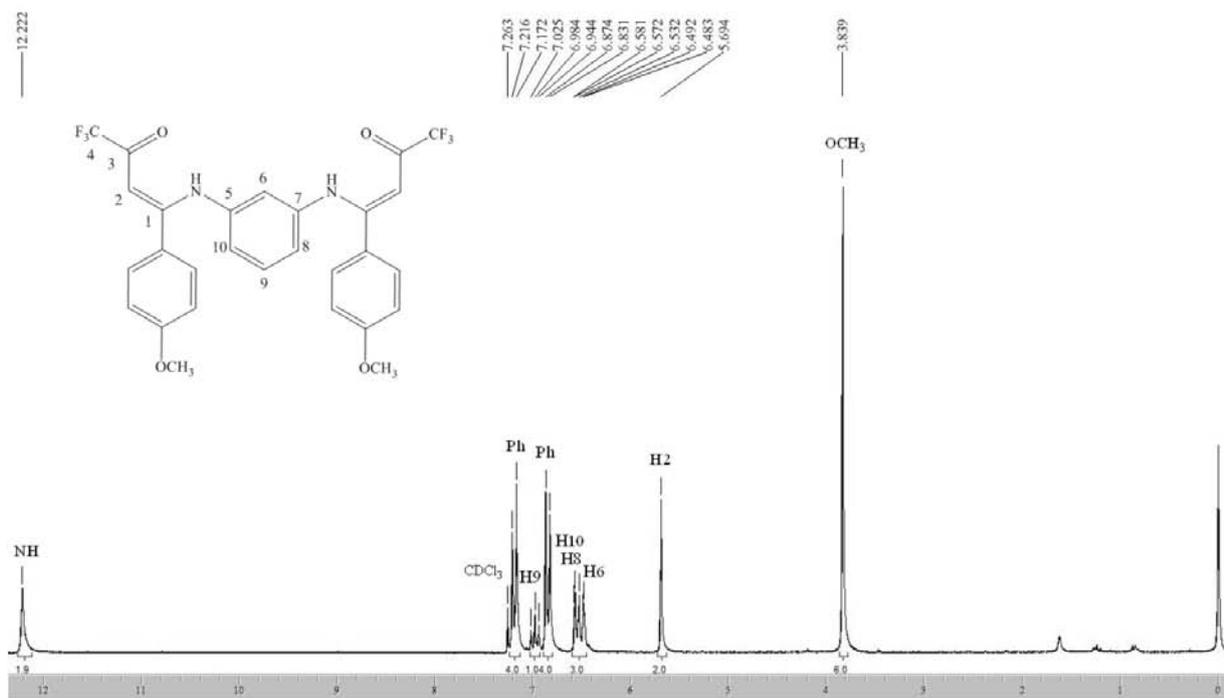


Figure S10. ^1H NMR (100 MHz, CDCl_3) spectrum of *(Z,Z)*-*N,N'*-bis(4,4,4-trifluoro-1-[4-methoxyphenyl]-3-oxo-1-buten-1-yl)-1,3-phenylenediamine (**2e**).

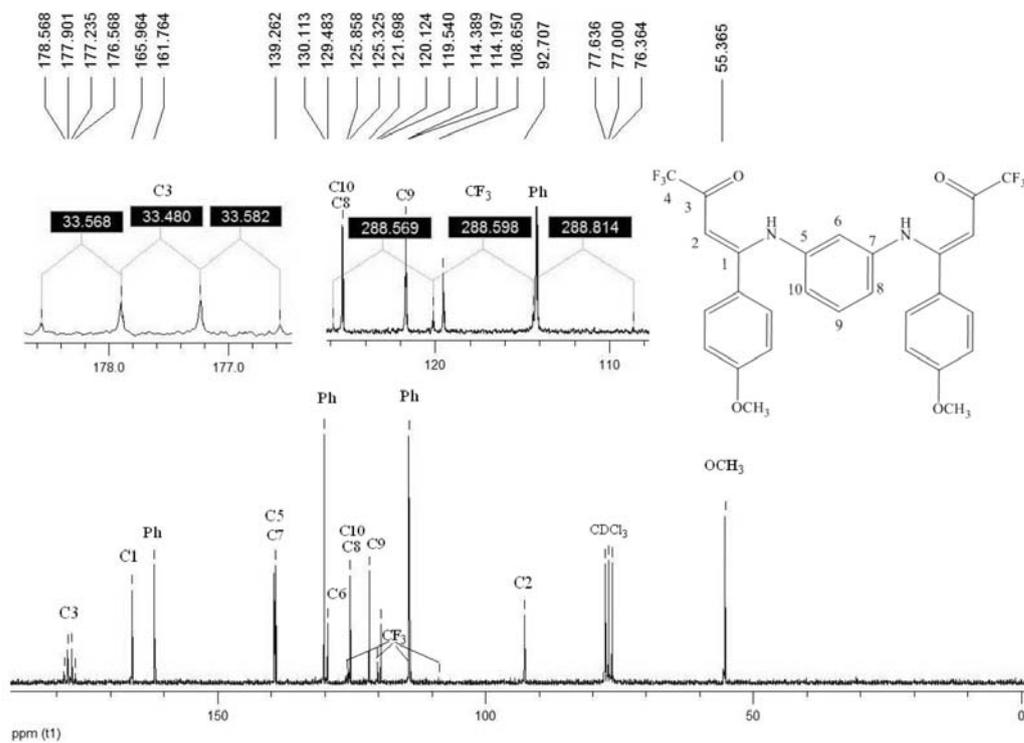


Figure S11. ^{13}C NMR (200 MHz, CDCl_3) spectrum of *(Z,Z)*-*N,N'*-bis(4,4,4-trifluoro-1-[4-methoxyphenyl]-3-oxo-1-buten-1-yl)-1,3-phenylenediamine (**2e**).

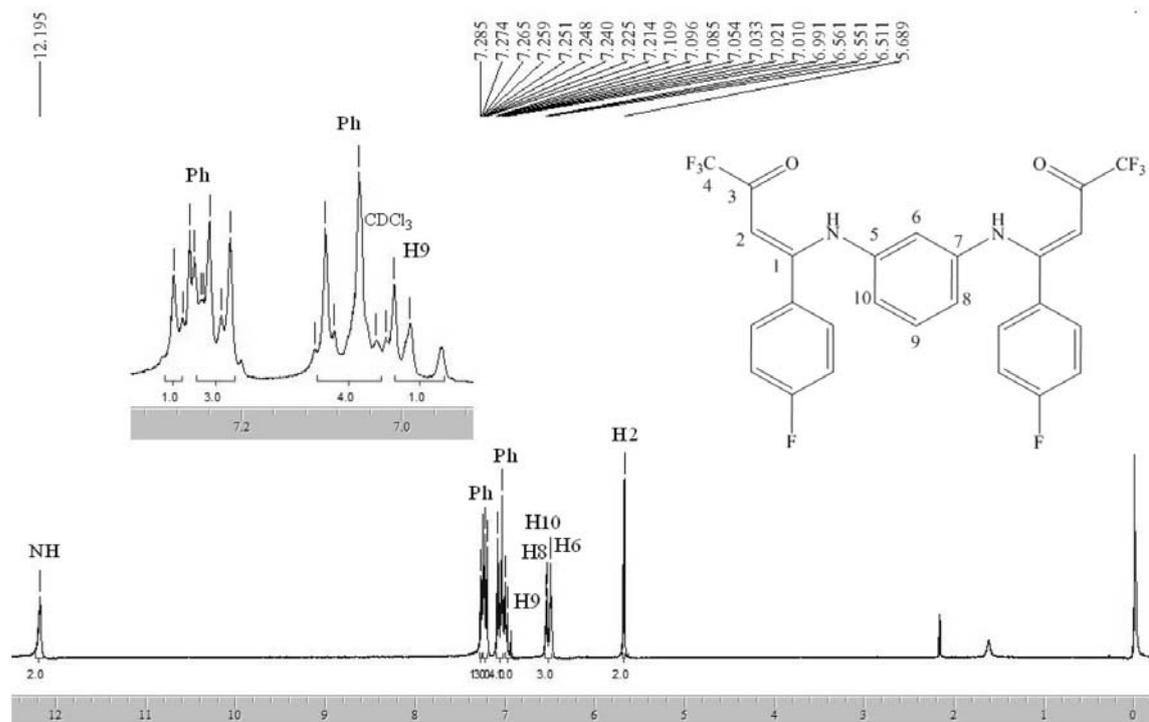


Figure S12. ^1H NMR (100 MHz, CDCl_3) spectrum of (Z,Z) - N,N' -bis(4,4,4-trifluoro-1-[4-fluorophenyl]-3-oxo-1-buten-1-yl)-1,3-phenylenediamine (**2f**).

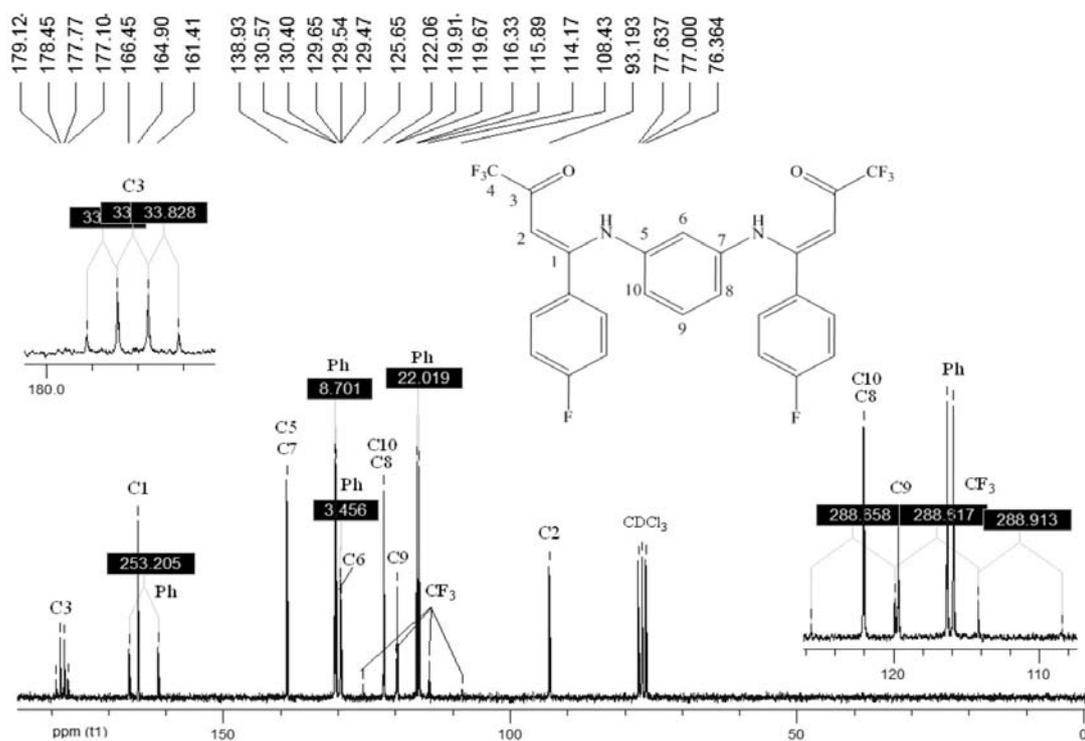


Figure S13. ^{13}C NMR (200 MHz, CDCl_3) spectrum of (Z,Z) - N,N' -bis(4,4,4-trifluoro-1-[4-fluorophenyl]-3-oxo-1-buten-1-yl)-1,3-phenylenediamine (**2f**).

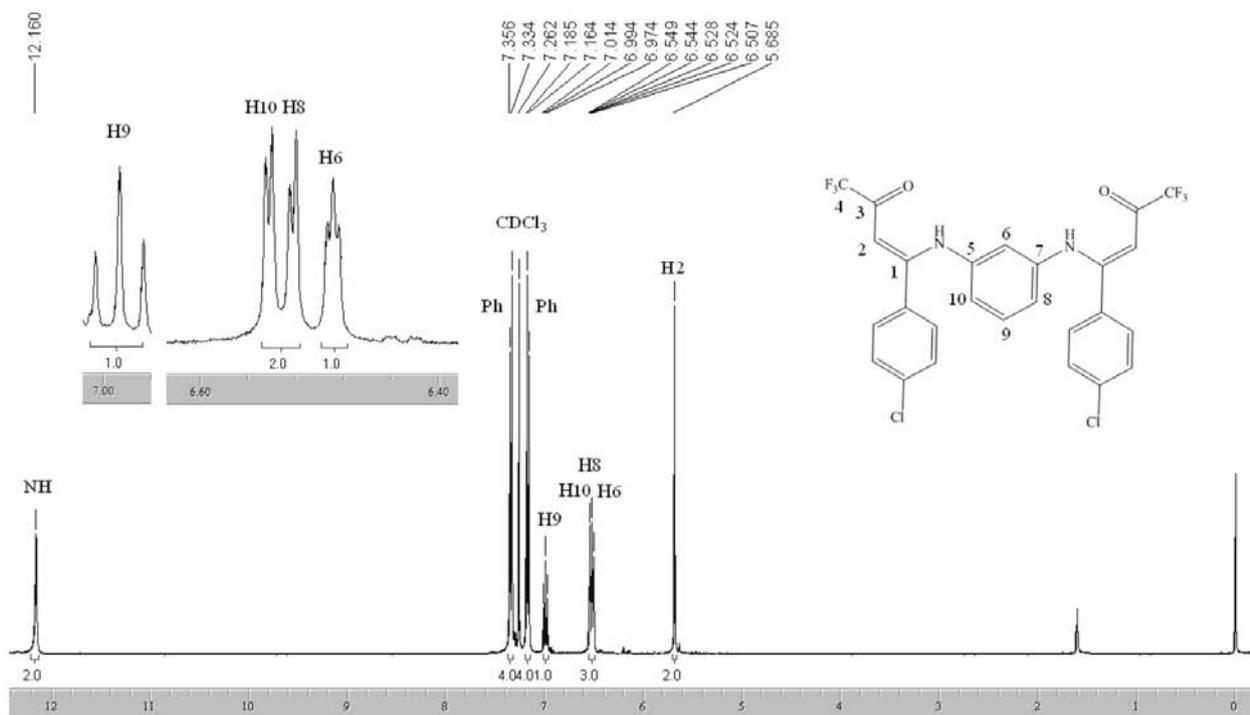


Figure S14. ^1H NMR (100 MHz, CDCl_3) spectrum of (Z,Z)-N,N'-[1-[4-chlorophenyl]-4,4,4-trifluoro-3-oxo-1-buten-1-yl]-1,3-phenylenediamine (**2g**).

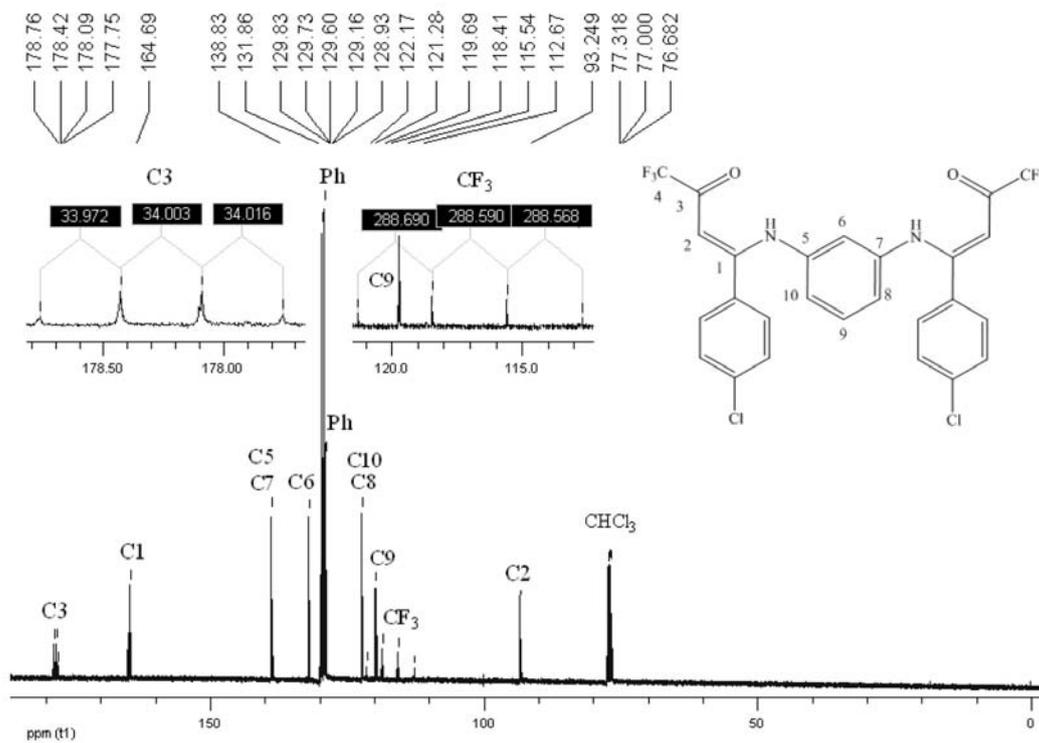


Figure S15. ^{13}C NMR (200 MHz, CDCl_3) spectrum of (Z,Z)-N,N'-[1-[4-chlorophenyl]-4,4,4-trifluoro-3-oxo-1-buten-1-yl]-1,3-phenylenediamine (**2g**).

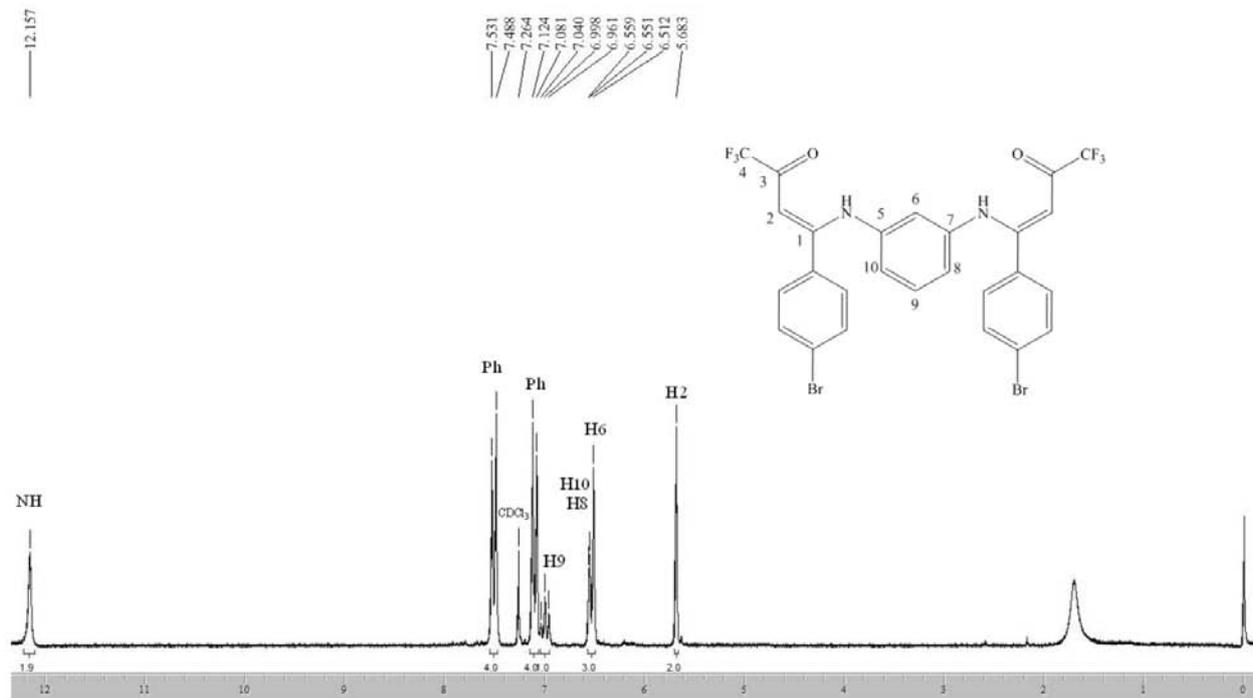


Figure S16. ^1H NMR (100 MHz, CDCl_3) spectrum of (Z,Z) - N,N' -bis(1-[4-bromophenyl]-4,4,4-trifluoro-3-oxo-1-buten-1-yl)-1,3-phenylenediamine (**2h**).

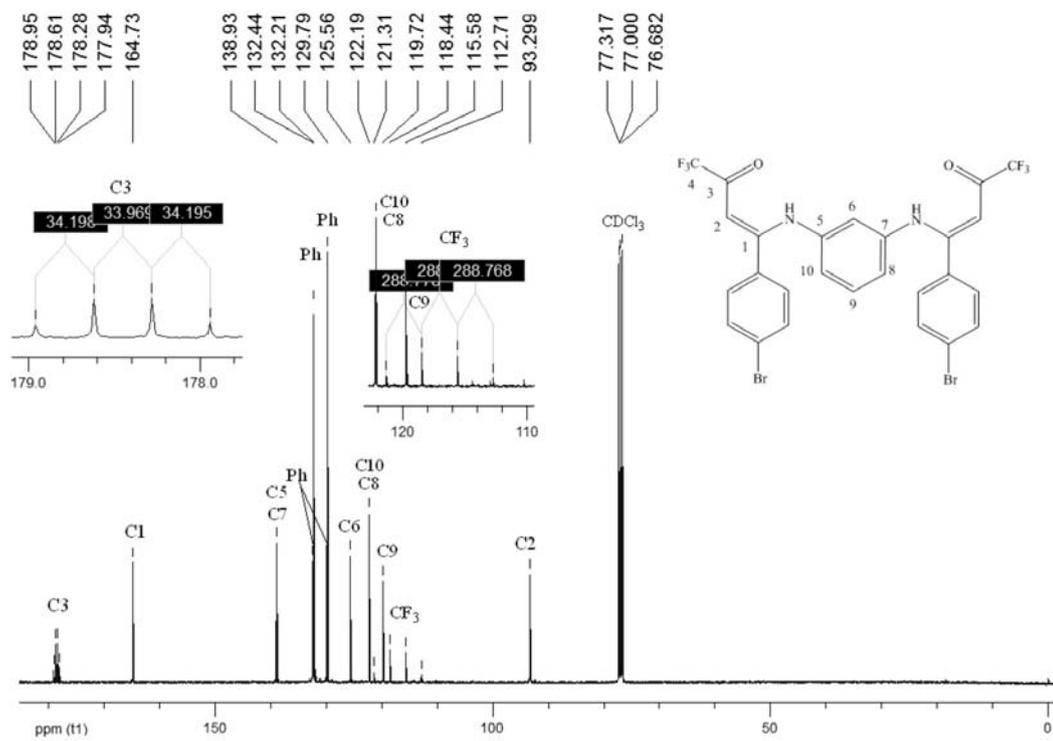


Figure S17. ^{13}C NMR (200 MHz, CDCl_3) spectrum of (Z,Z) - N,N' -bis(1-[4-bromophenyl]-4,4,4-trifluoro-3-oxo-1-buten-1-yl)-1,3-phenylenediamine (**2h**).

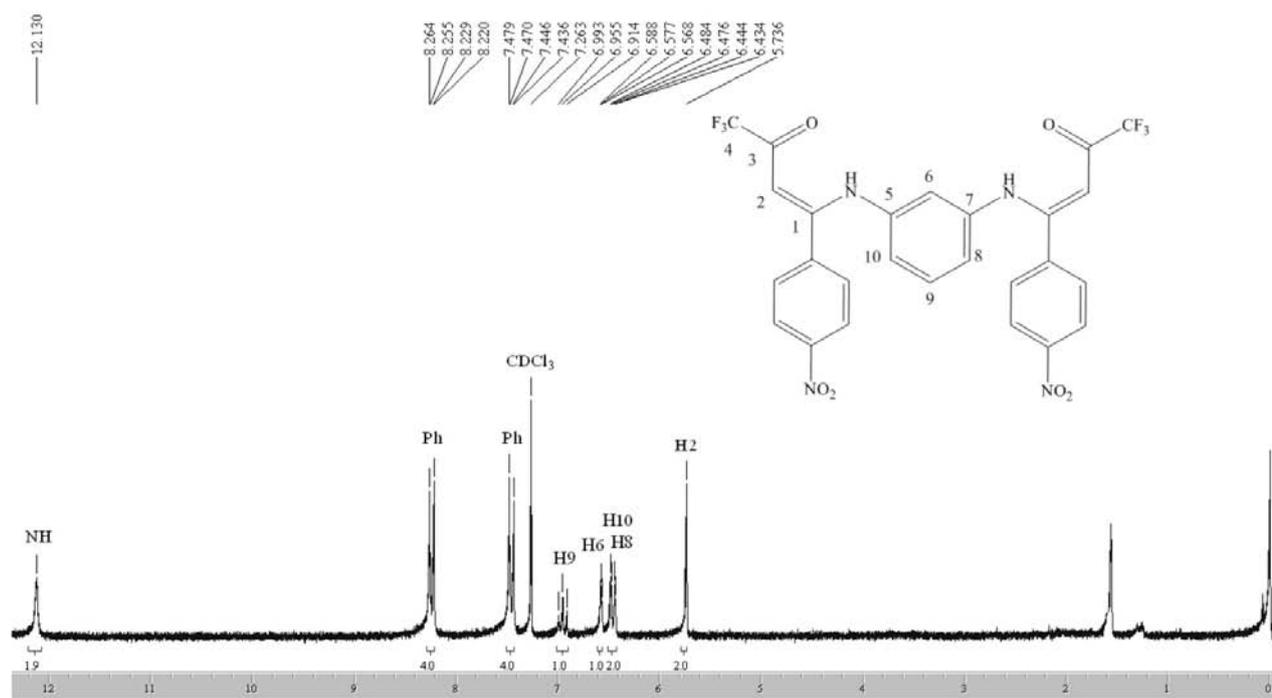


Figure S18. ^1H NMR (100 MHz, CDCl_3) spectrum of (Z,Z)-N,N'-bis(4,4,4-trifluoro-1-(4-nitrophenyl)-3-oxo-1-buten-1-yl)-1,3-phenylenediamine (**2i**).

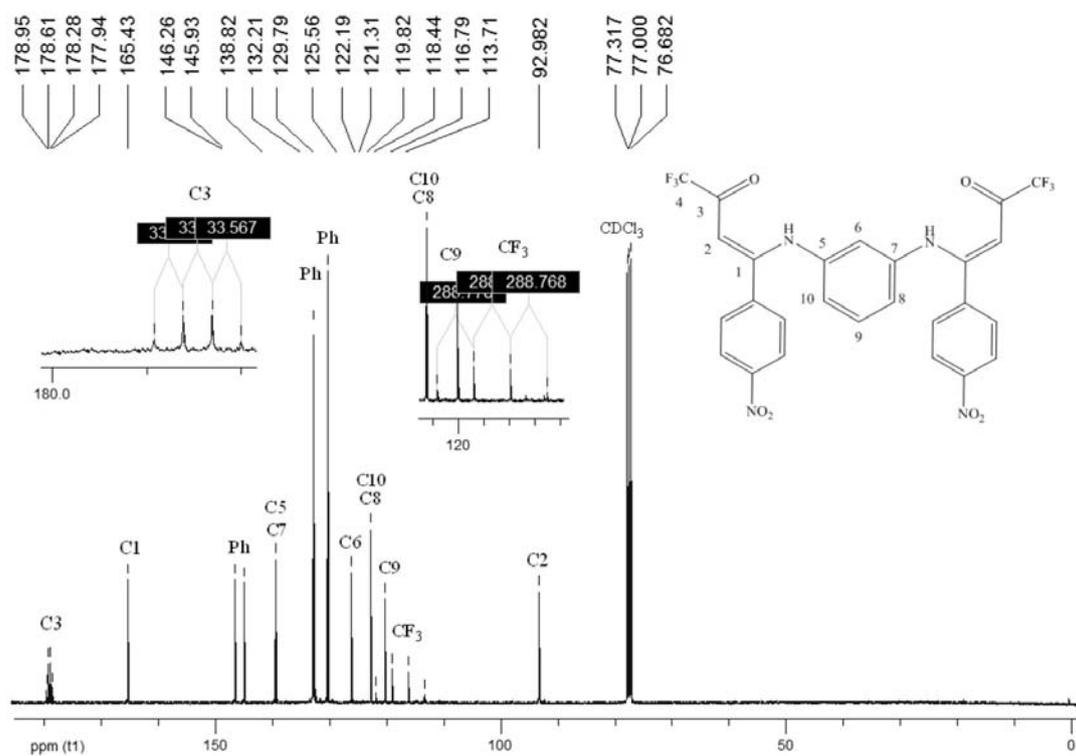


Figure S19. ^{13}C NMR (200 MHz, CDCl_3) spectrum of (Z,Z)-N,N'-bis(4,4,4-trifluoro-1-(4-nitrophenyl)-3-oxo-1-buten-1-yl)-1,3-phenylenediamine (**2i**).

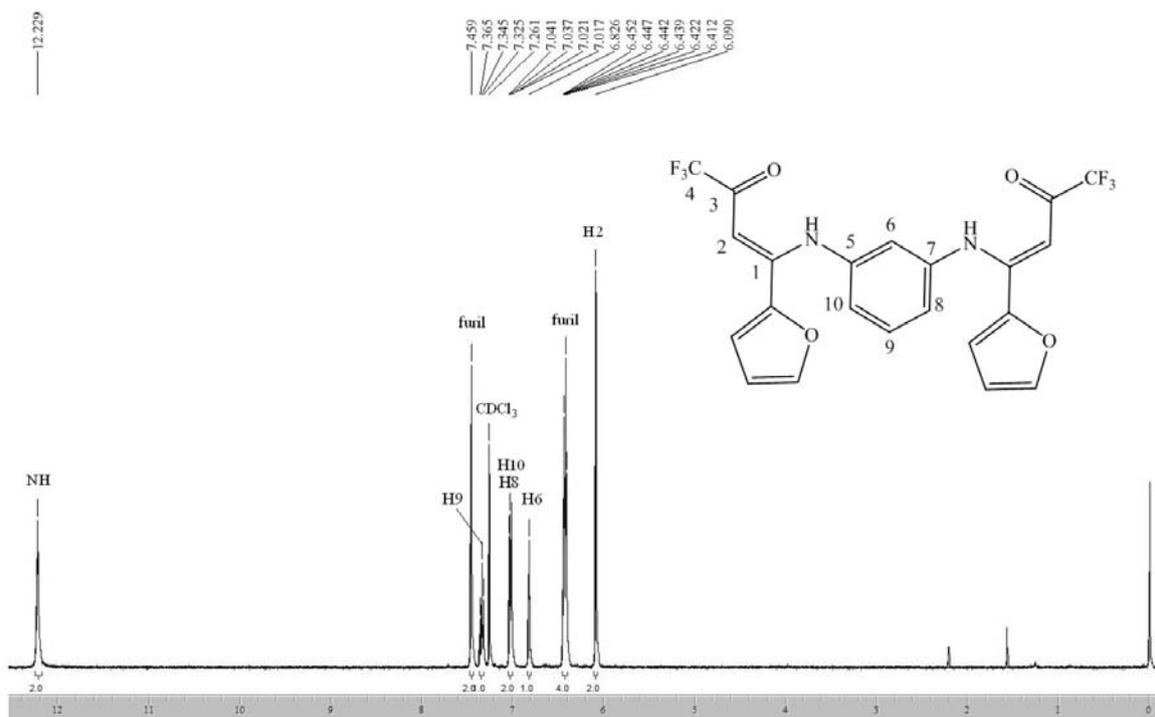


Figure S20. ^1H NMR (100 MHz, CDCl_3) spectrum of (Z,Z)-*N,N'*-bis(4,4,4-trifluoro-1-[2-furyl]-3-oxo-1-buten-1-yl)-1,3-phenylenediamine (**2j**).

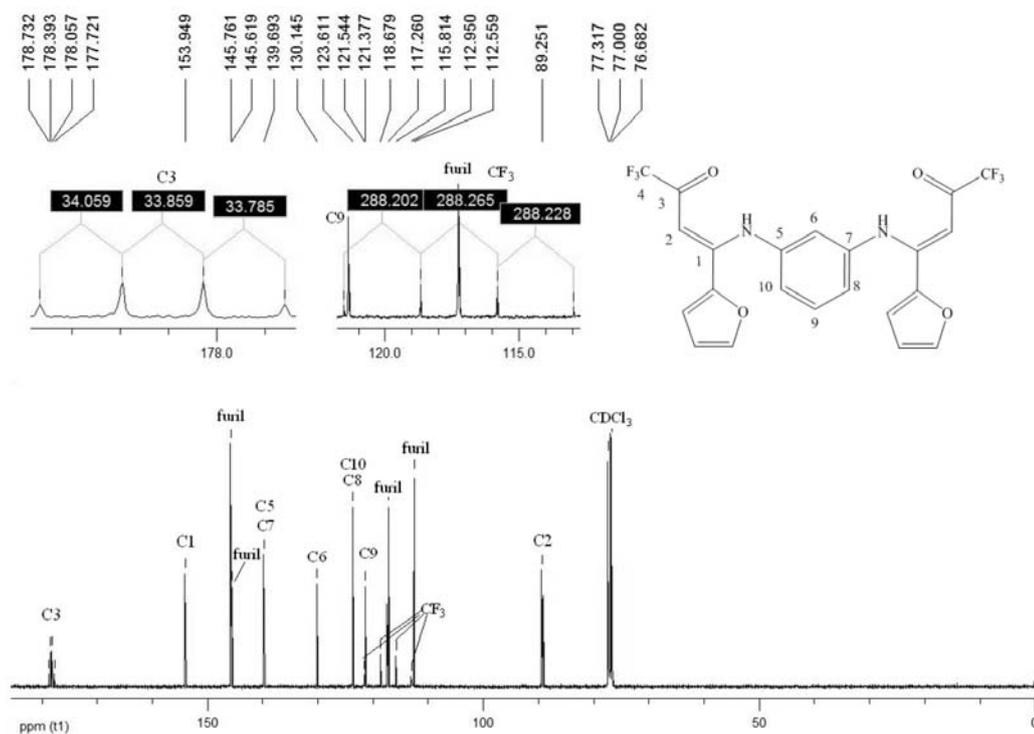


Figure S21. ^{13}C NMR (200 MHz, CDCl_3) spectrum of (Z,Z)-*N,N'*-bis(4,4,4-trifluoro-1-[2-furyl]-3-oxo-1-buten-1-yl)-1,3-phenylenediamine (**2j**).

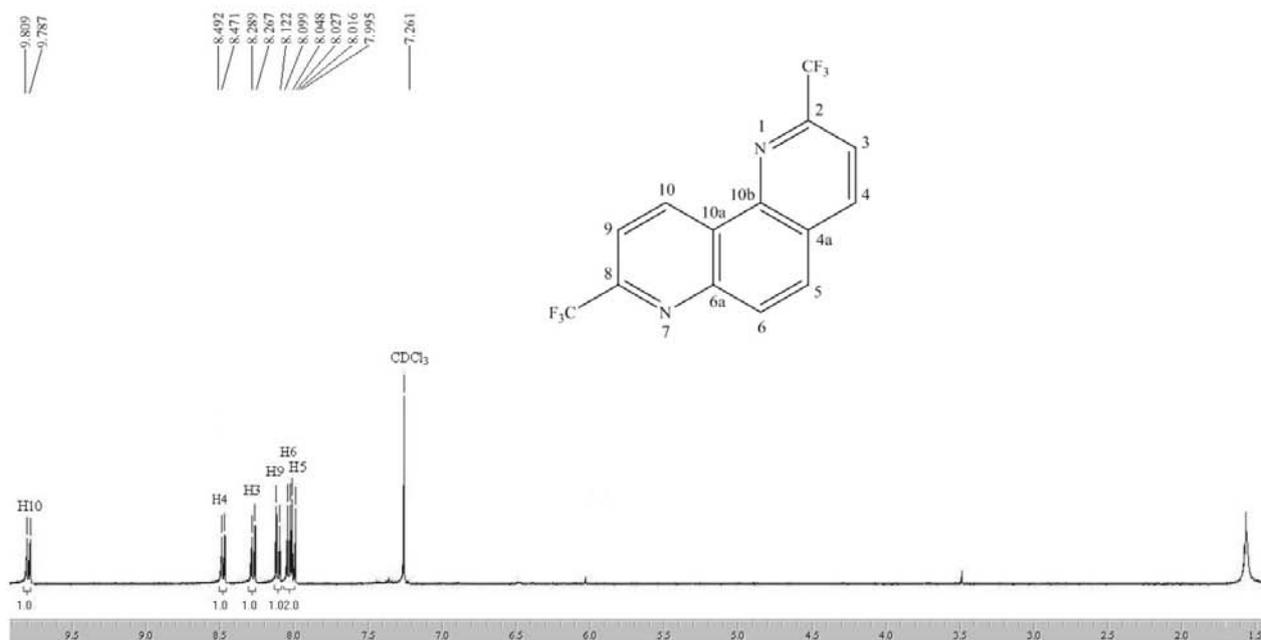


Figure S22. ¹H NMR (100 MHz, CDCl₃) spectrum of 2,8-bis(trifluoromethyl)-1,7-phenanthroline (**3a**).

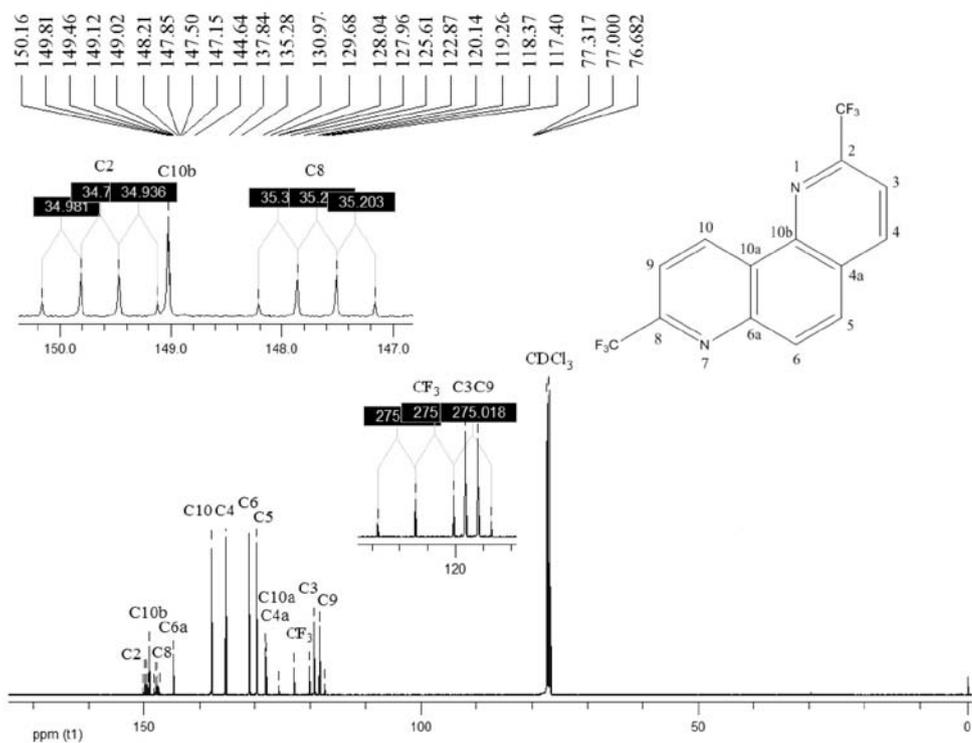


Figure S23. ¹³C NMR (200 MHz, CDCl₃) spectrum of 2,8-bis(trifluoromethyl)-1,7-phenanthroline (**3a**).

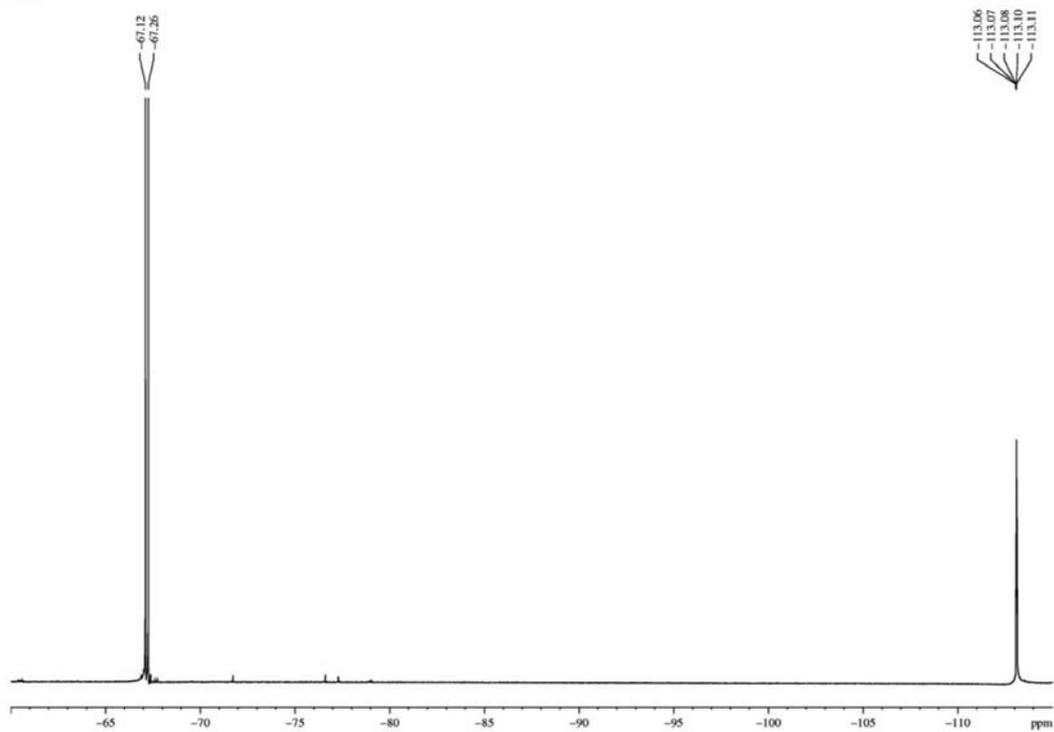


Figure S24. ^{19}F NMR (376 MHz, CDCl_3) spectrum of 2,8-bis(trifluoromethyl)-1,7-phenanthroline (**3a**).

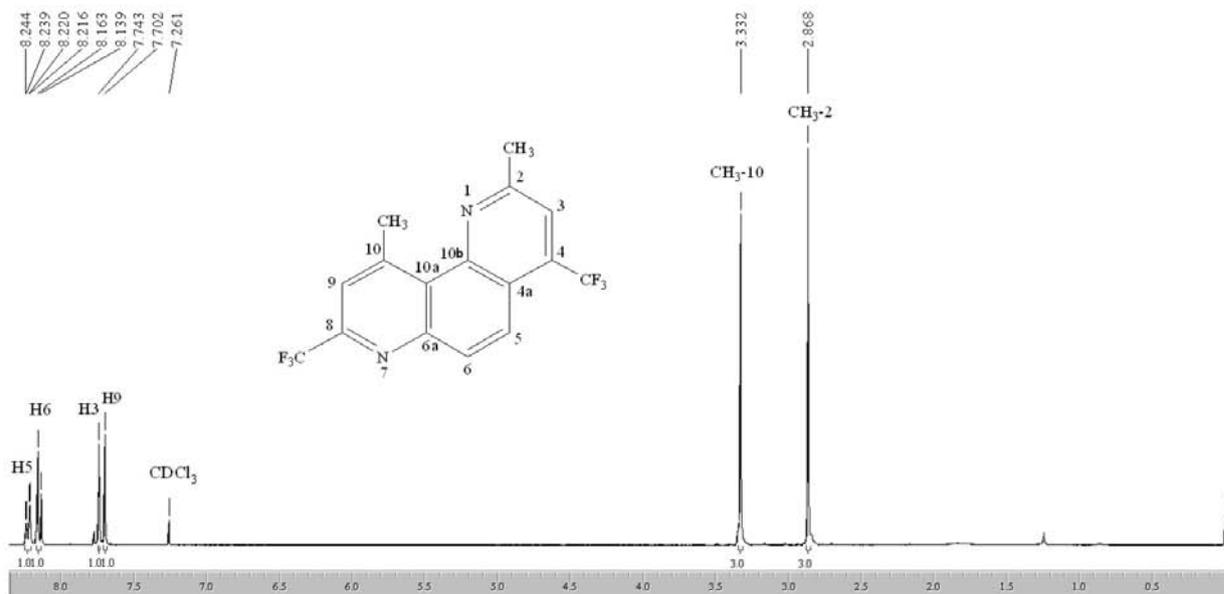


Figure S25. ^1H NMR (100 MHz, CDCl_3) spectrum of 4,8-bis(trifluoromethyl)-2,10-di(methyl)-1,7-phenanthroline (**3b**).

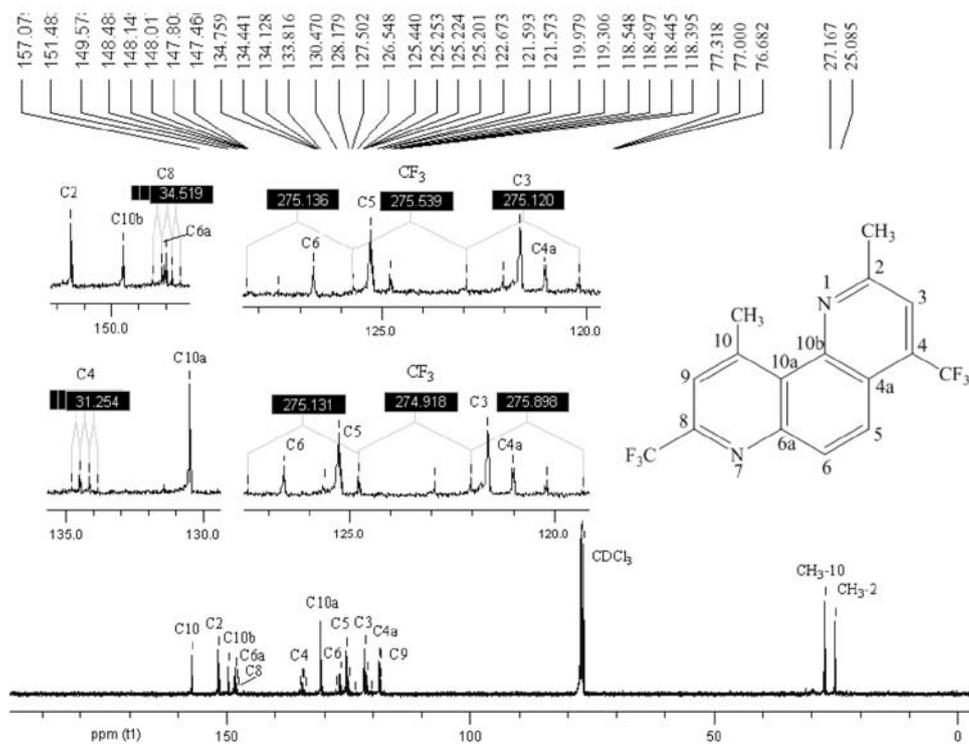


Figure S26. ^{13}C NMR (200 MHz, CDCl_3) spectrum of 4,8-bis(trifluoromethyl)-2,10-di(methyl)-1,7-phenanthroline (**3b**).

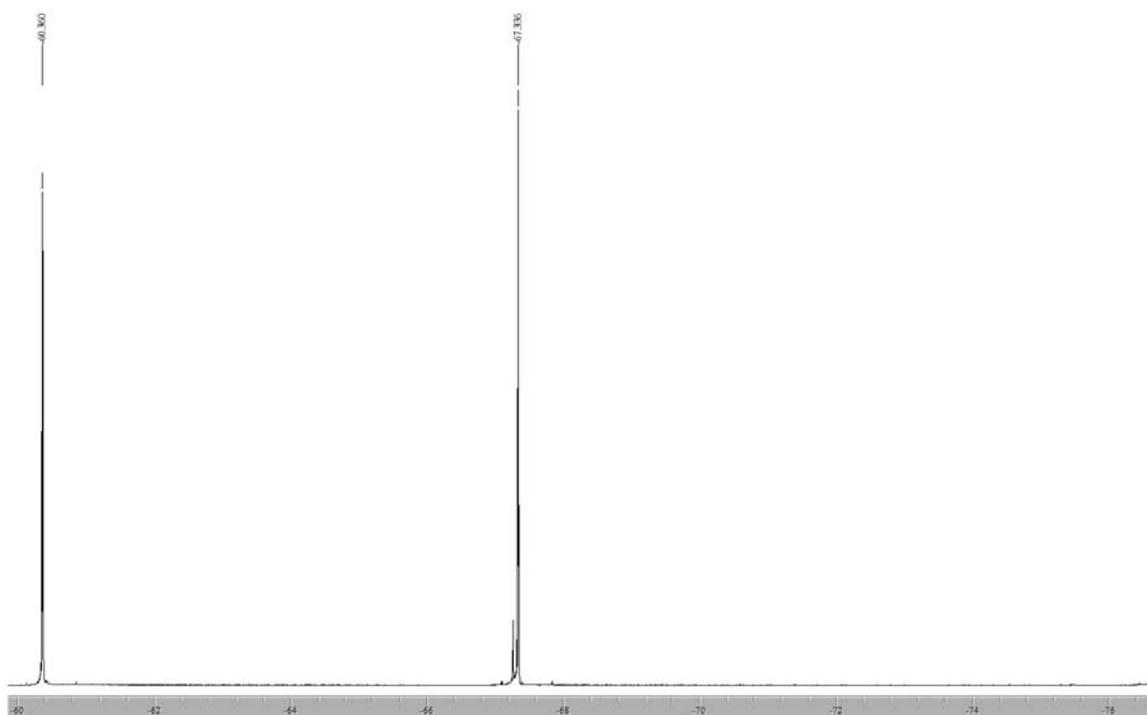


Figure S27. ^{19}F NMR (376 MHz, CDCl_3) spectrum of 4,8-bis(trifluoromethyl)-2,10-di(methyl)-1,7-phenanthroline (**3b**).

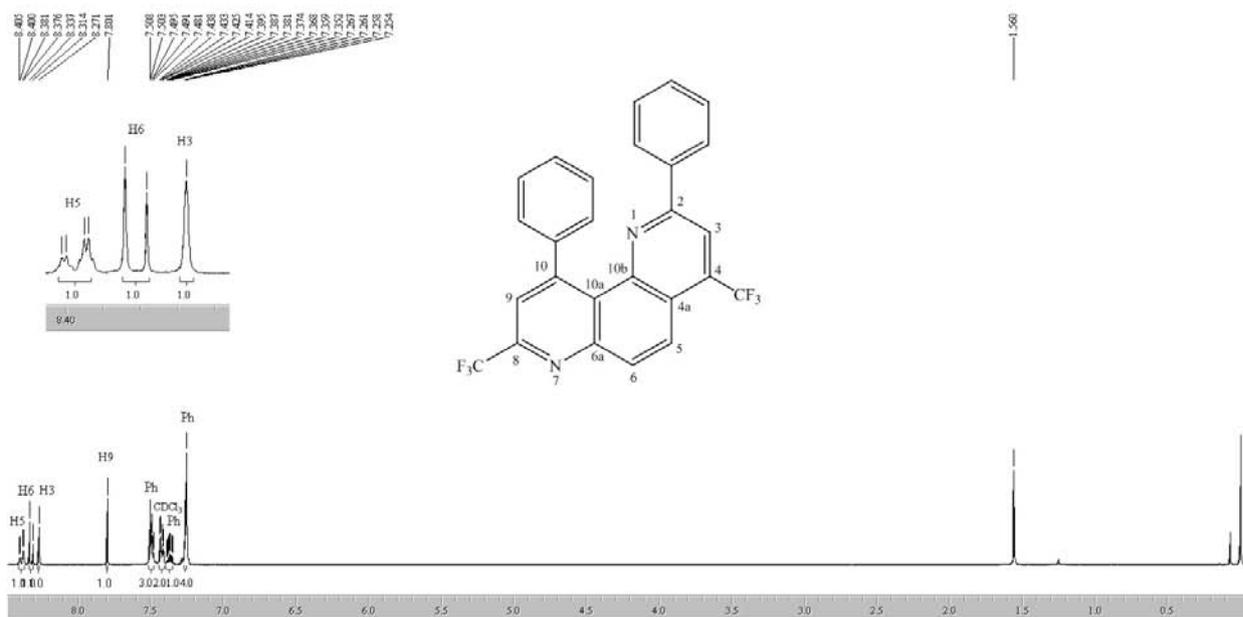


Figure S28. ^1H NMR (100 MHz, CDCl_3) spectrum of 4,8-bis(trifluoromethyl)-2,10-di(phenyl)-1,7-phenanthroline (**3c**).

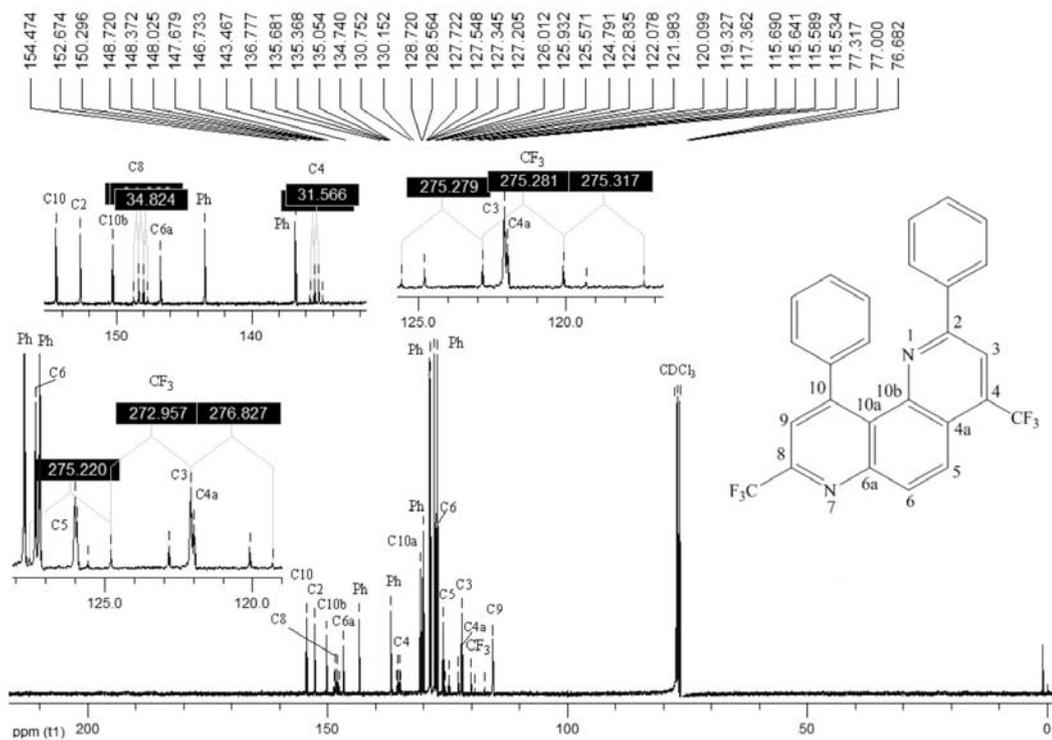


Figure S29. ^{13}C NMR (200 MHz, CDCl_3) spectrum of 4,8-bis(trifluoromethyl)-2,10-di(phenyl)-1,7-phenanthroline (**3c**).

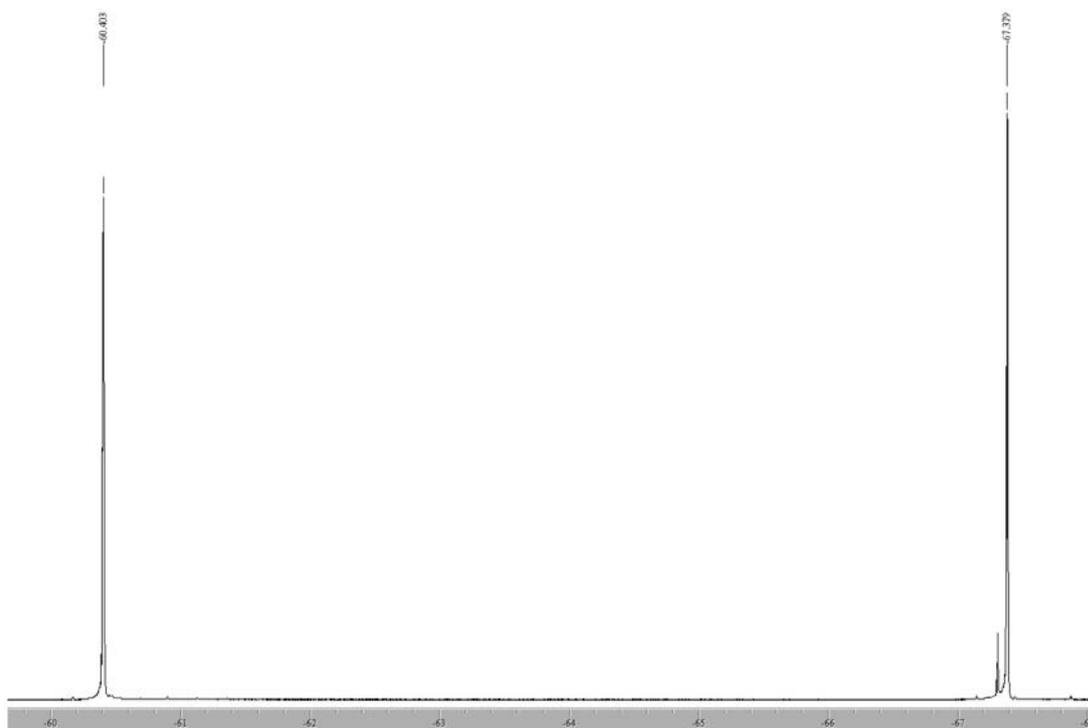


Figure S30. ^{19}F NMR (376 MHz, CDCl_3) spectrum of 4,8-bis(trifluoromethyl)-2,10-di(phenyl)-1,7-phenanthroline (**3c**).

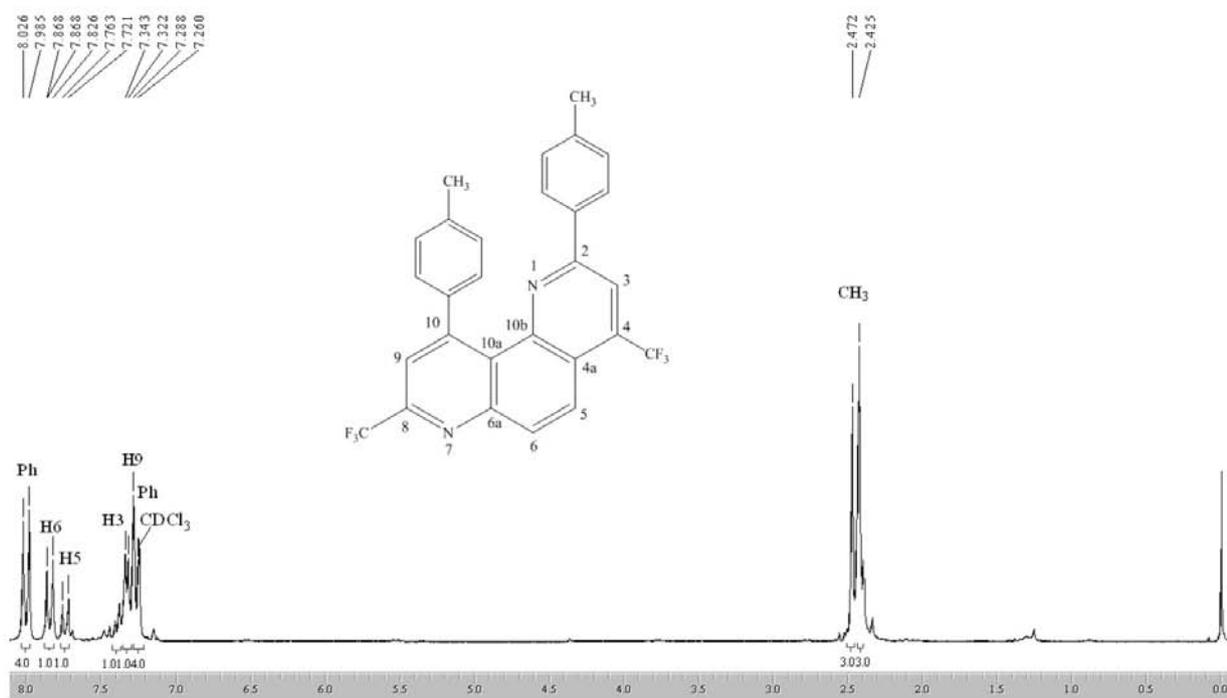


Figure S31. ^1H NMR (100 MHz, CDCl_3) spectrum of 4,8-bis(trifluoromethyl)-2,10-di(4-methylphenyl)-1,7-phenanthroline (**3d**).

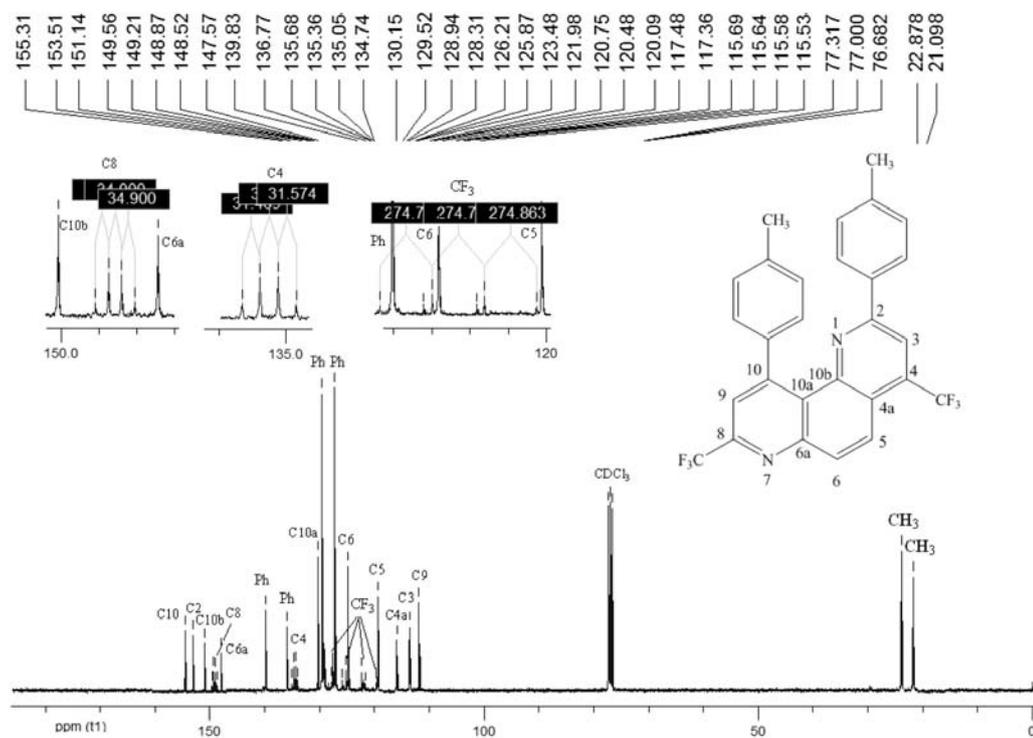


Figure S32. ^{13}C NMR (200 MHz, CDCl_3) spectrum of 4,8-bis(trifluoromethyl)-2,10-di(4-methylphenyl)-1,7-phenanthroline (**3d**).

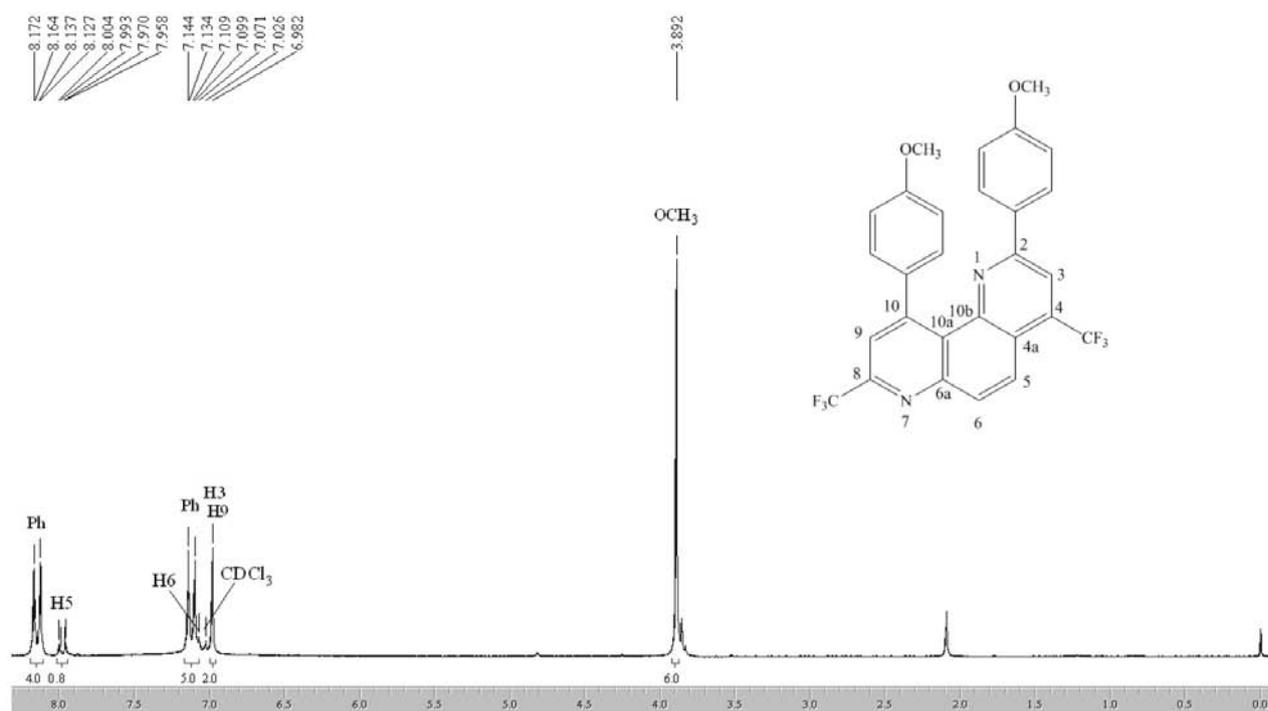


Figure S33. ^1H NMR (100 MHz, CDCl_3) spectrum of 4,8-bis(trifluoromethyl)-2,10-di(4-methoxyphenyl)-1,7-phenanthroline (**3e**).

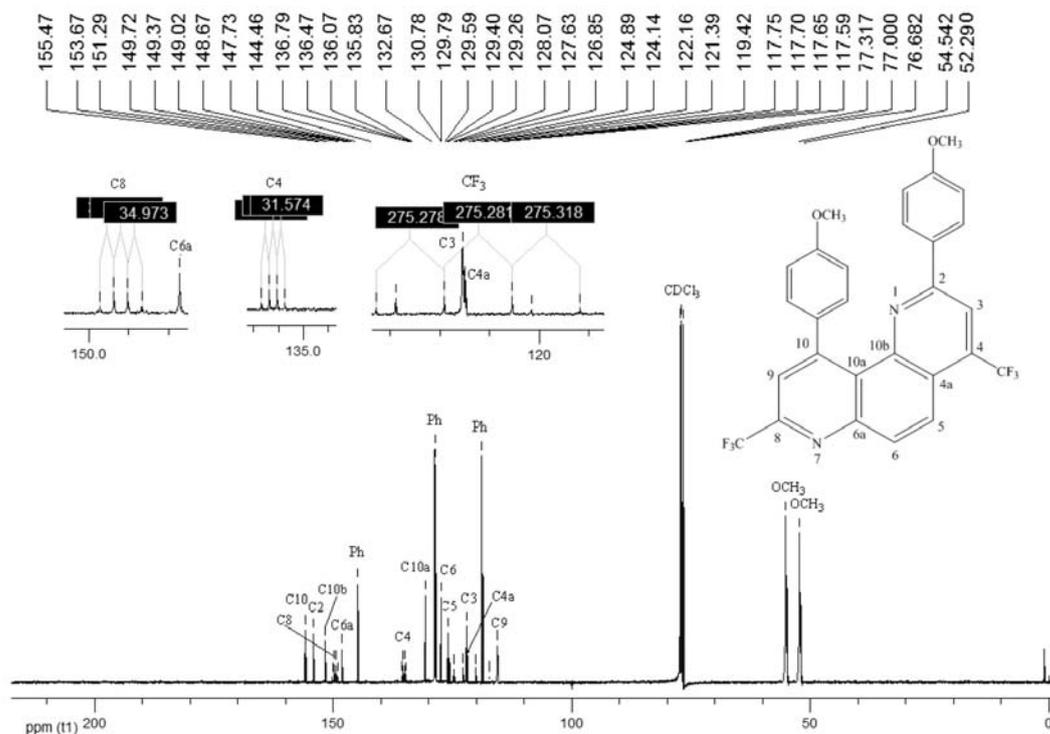


Figure S34. ^{13}C NMR (200 MHz, CDCl_3) spectrum of 4,8-bis(trifluoromethyl)-2,10-di(4-methoxyphenyl)-1,7-phenanthroline (**3e**).

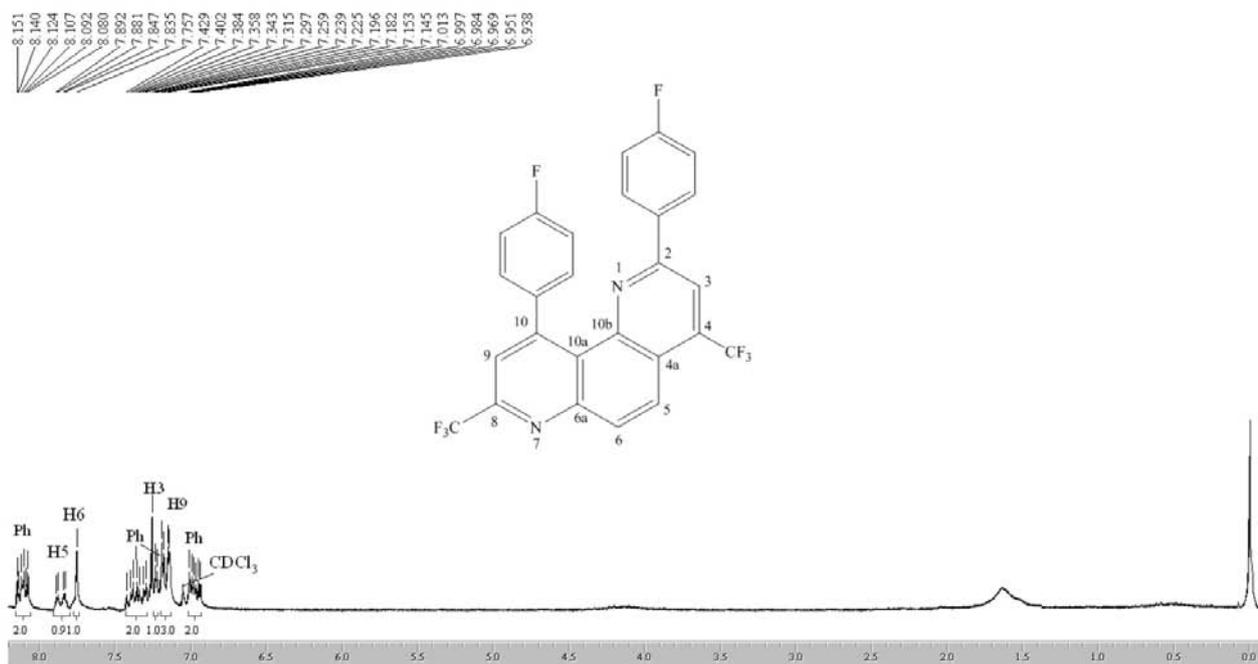


Figure S35. ^1H NMR (100 MHz, CDCl_3) spectrum of 4,8-bis(trifluoromethyl)-2,10-di(4-fluorophenyl)-1,7-phenanthroline (**3f**).

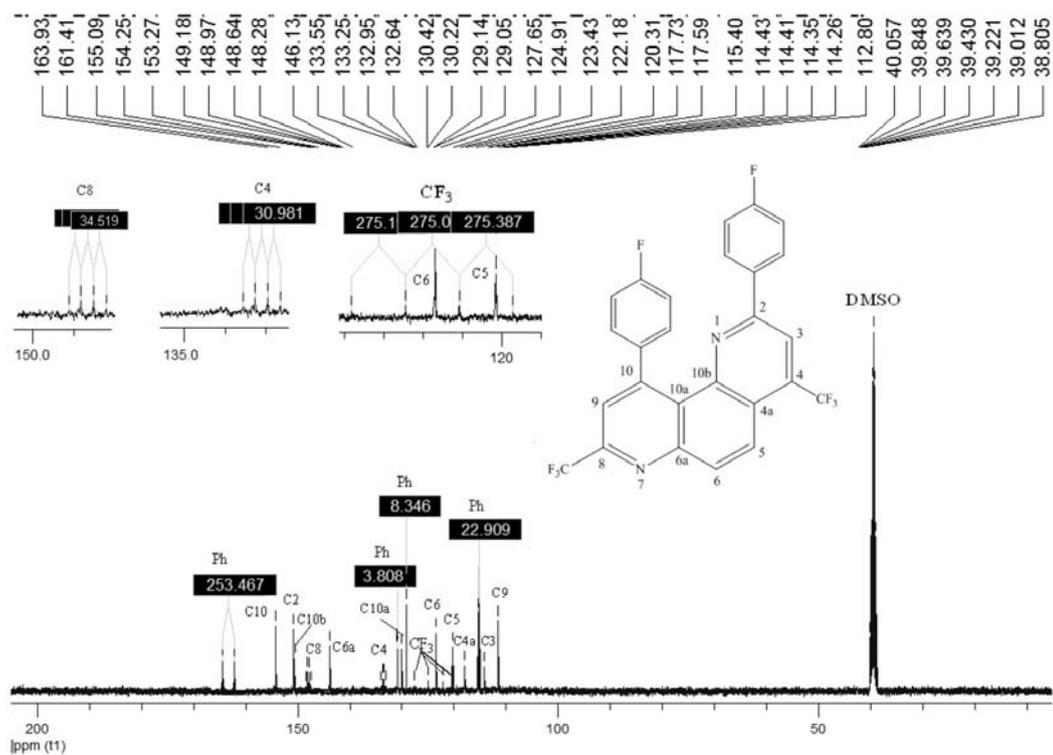


Figure S36. ^{13}C NMR (200 MHz, CDCl_3) spectrum of 4,8-bis(trifluoromethyl)-2,10-di(4-fluorophenyl)-1,7-phenanthroline (**3f**).

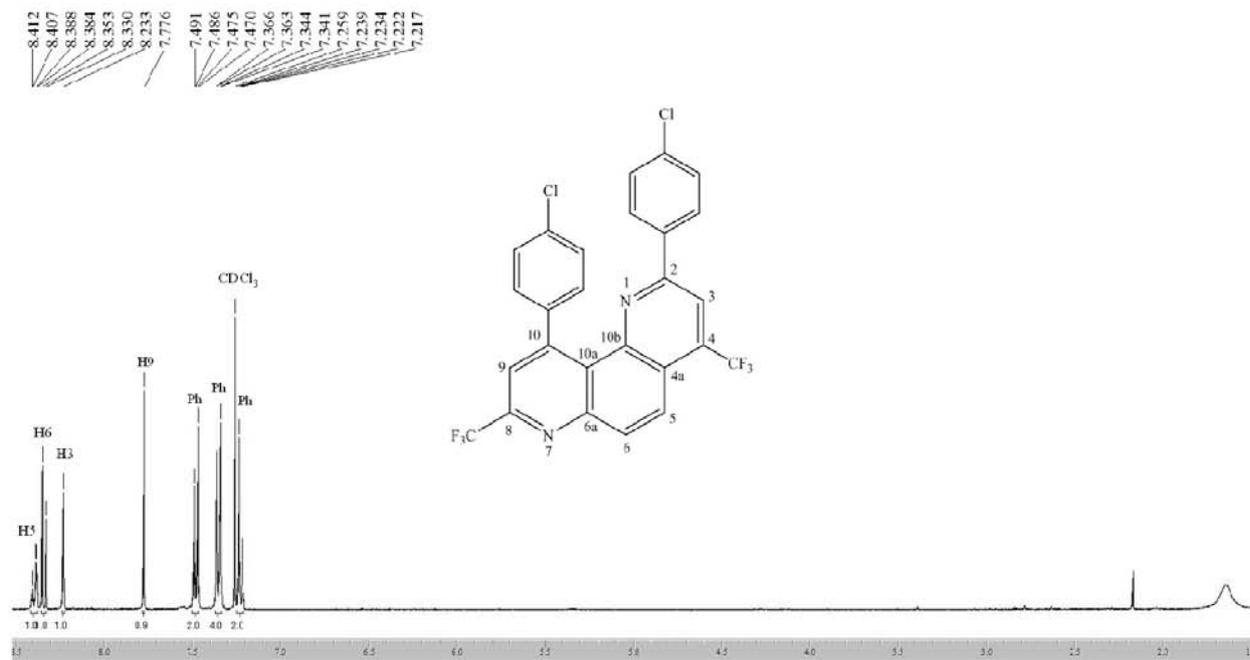


Figure S37. ^1H NMR (100 MHz, CDCl_3) spectrum of 2,10-di(4-chlorophenyl)-4,8-bis(trifluoromethyl)-1,7-phenanthroline (**3g**).

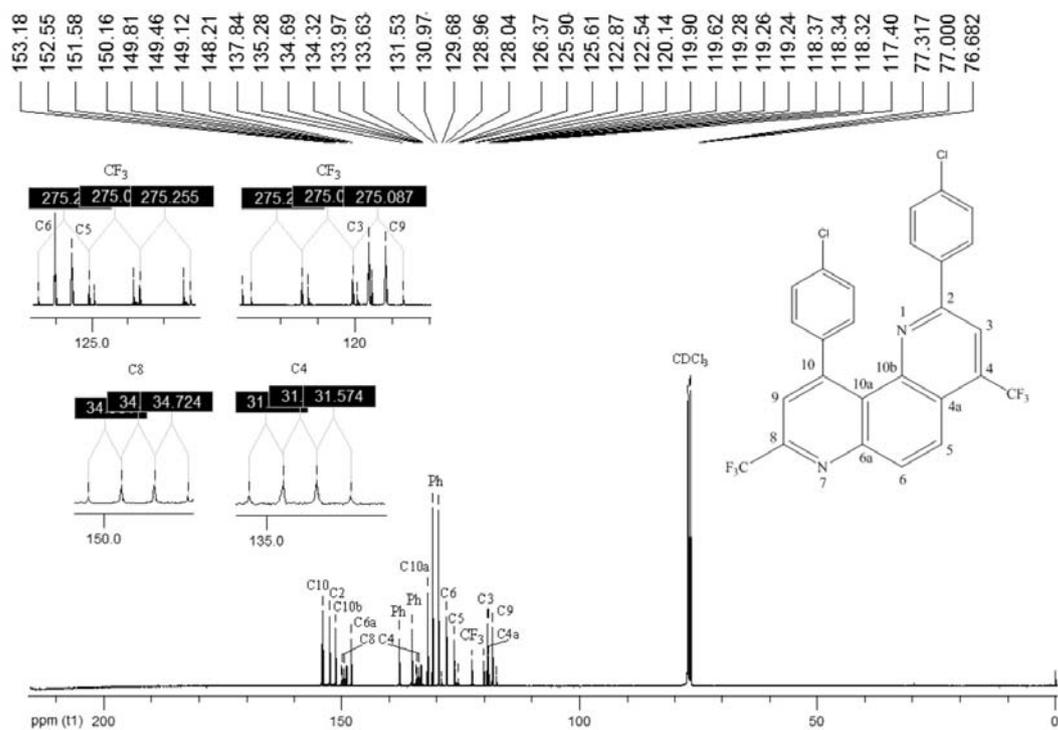


Figure S38. ¹³C NMR (200 MHz, CDCl₃) spectrum of 2,10-di(4-chlorophenyl)-4,8-bis(trifluoromethyl)-1,7-phenanthroline (**3g**).

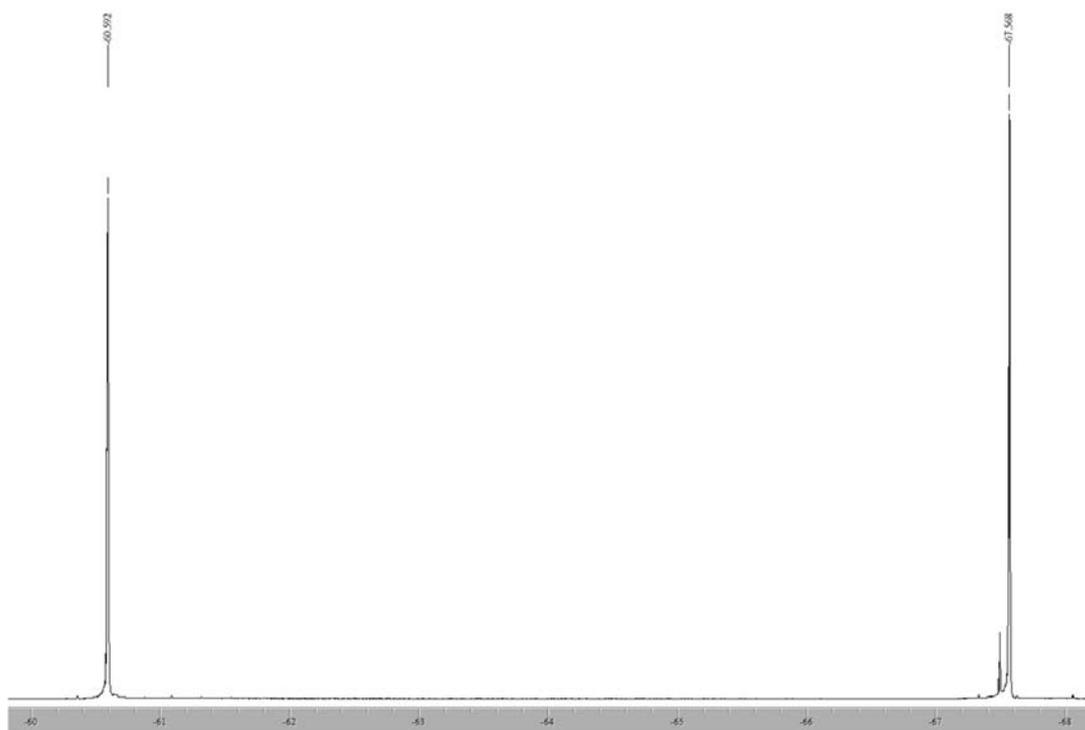


Figure S39. ¹⁹F NMR (376 MHz, CDCl₃) spectrum of 2,10-di(4-chlorophenyl)-4,8-bis(trifluoromethyl)-1,7-phenanthroline (**3g**).

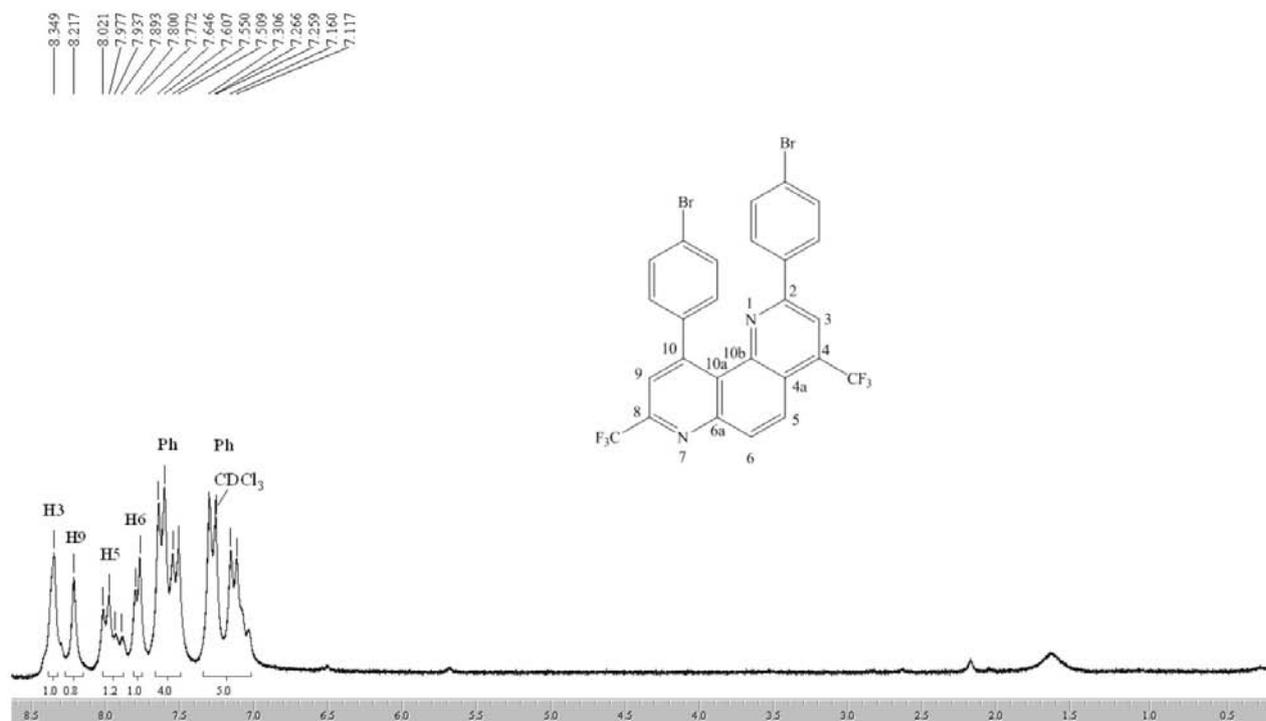


Figure S40. ¹H NMR (100 MHz, CDCl₃) spectrum of 2,10-di(4-bromophenyl)-4,8-bis(trifluoromethyl)-1,7-phenanthroline (**3h**).

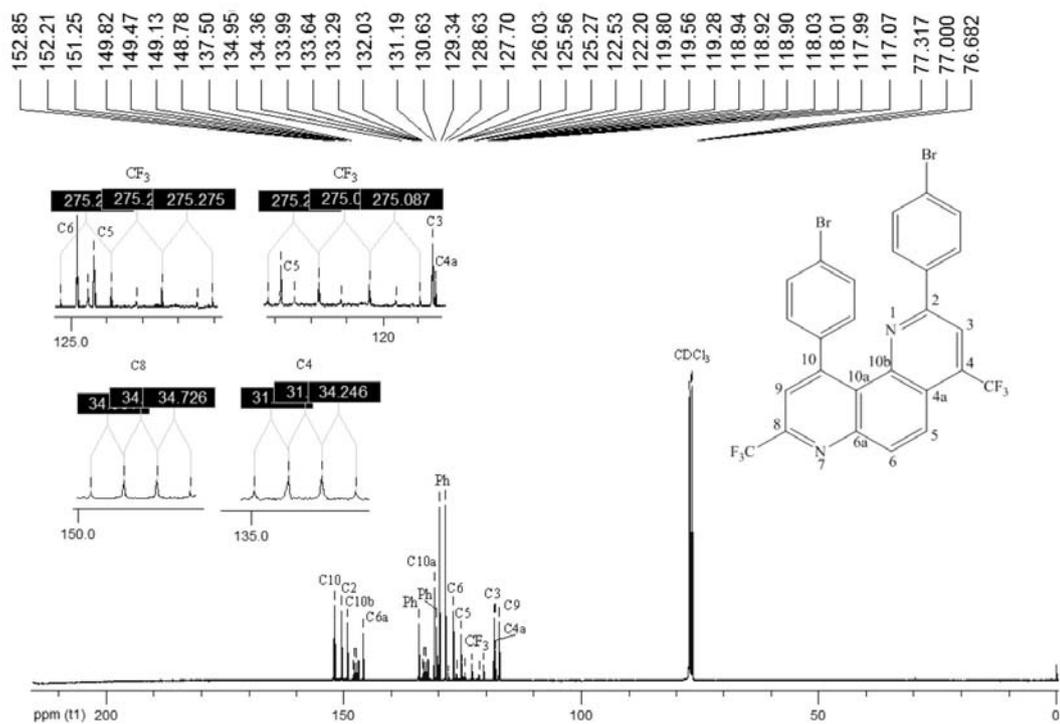


Figure S41. ¹³C NMR (200 MHz, CDCl₃) spectrum of 2,10-di(4-bromophenyl)-4,8-bis(trifluoromethyl)-1,7-phenanthroline (**3h**).

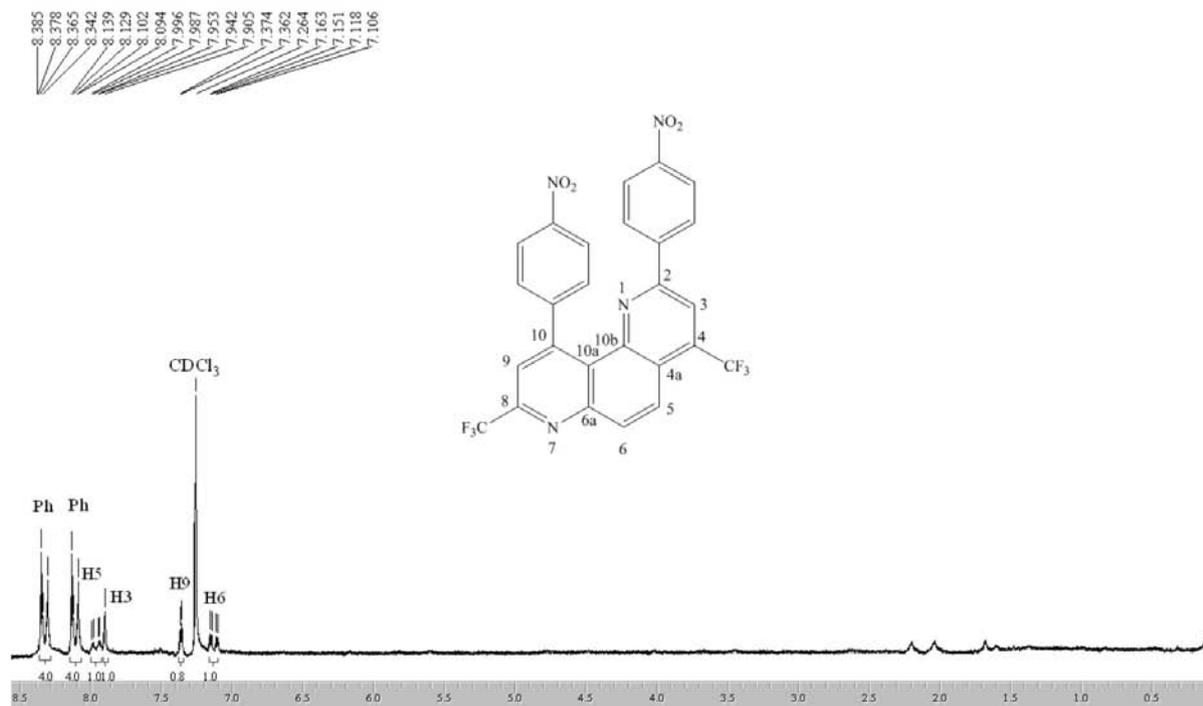


Figure S42. ¹H NMR (100 MHz, CDCl₃) spectrum of 4,8-bis(trifluoromethyl)-2,10-di(4-nitrophenyl)-1,7-phenanthroline (3i).

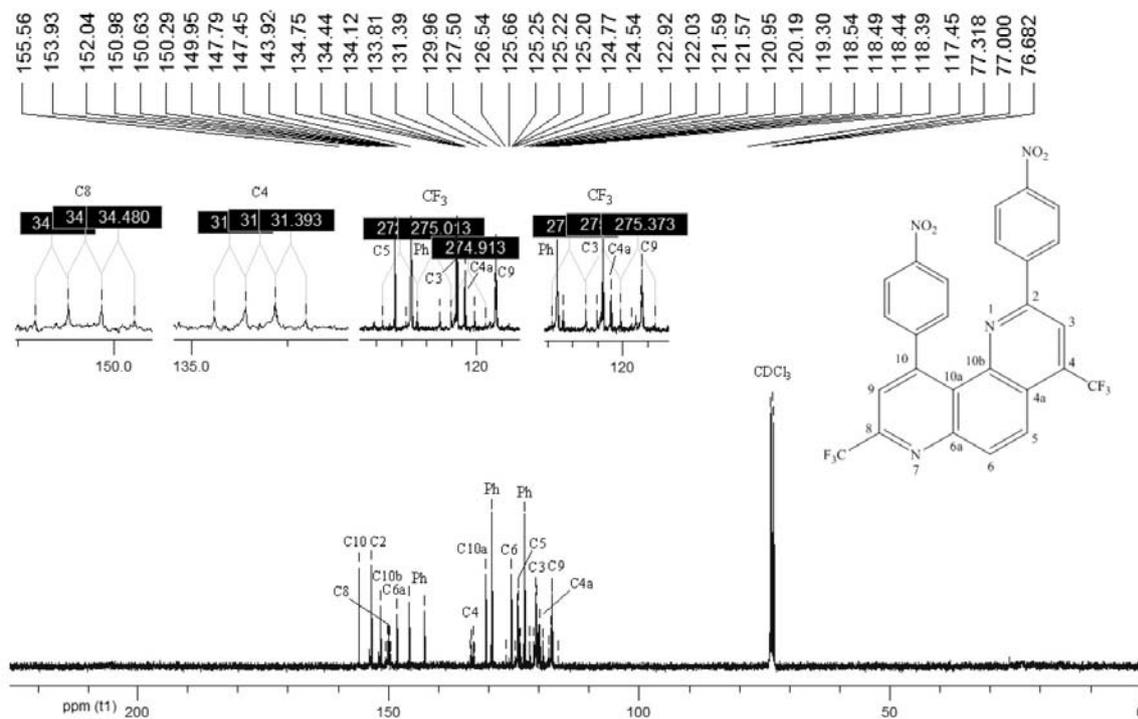


Figure S43. ¹³C NMR (200 MHz, CDCl₃) spectrum of 4,8-bis(trifluoromethyl)-2,10-di(4-nitrophenyl)-1,7-phenanthroline (3i).

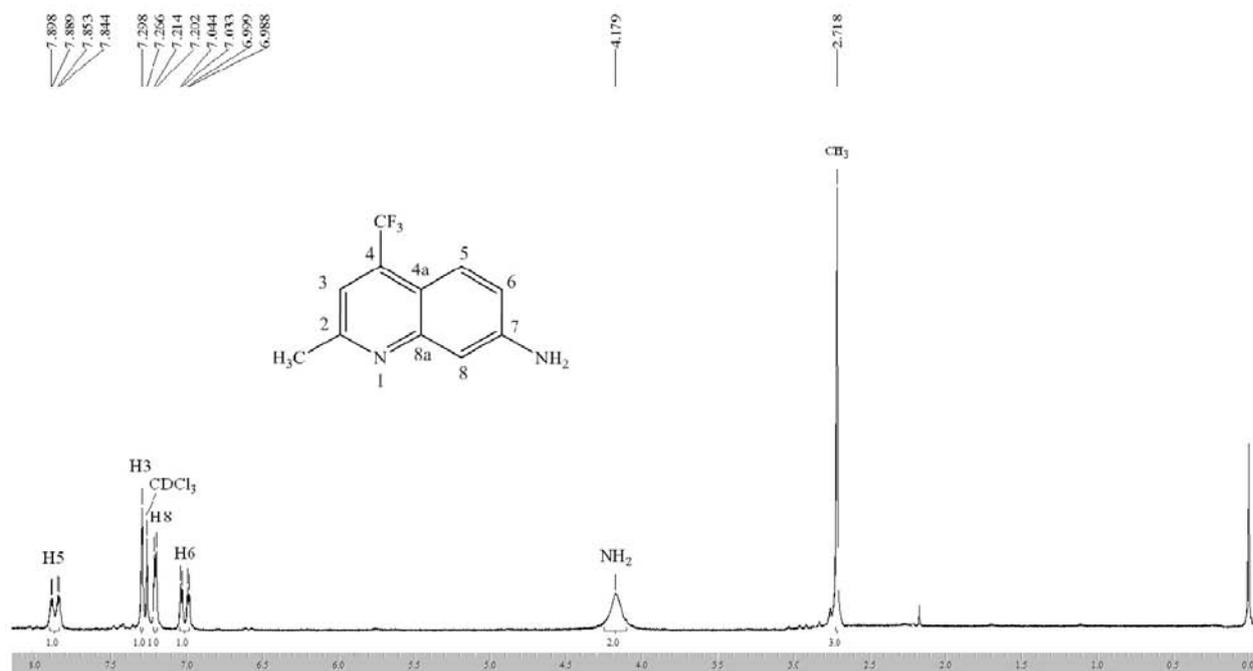


Figure S44. ¹H NMR (100 MHz, CDCl₃) spectrum of 4-trifluoromethyl-2-methyl-7-aminoquinoline (**4b**).

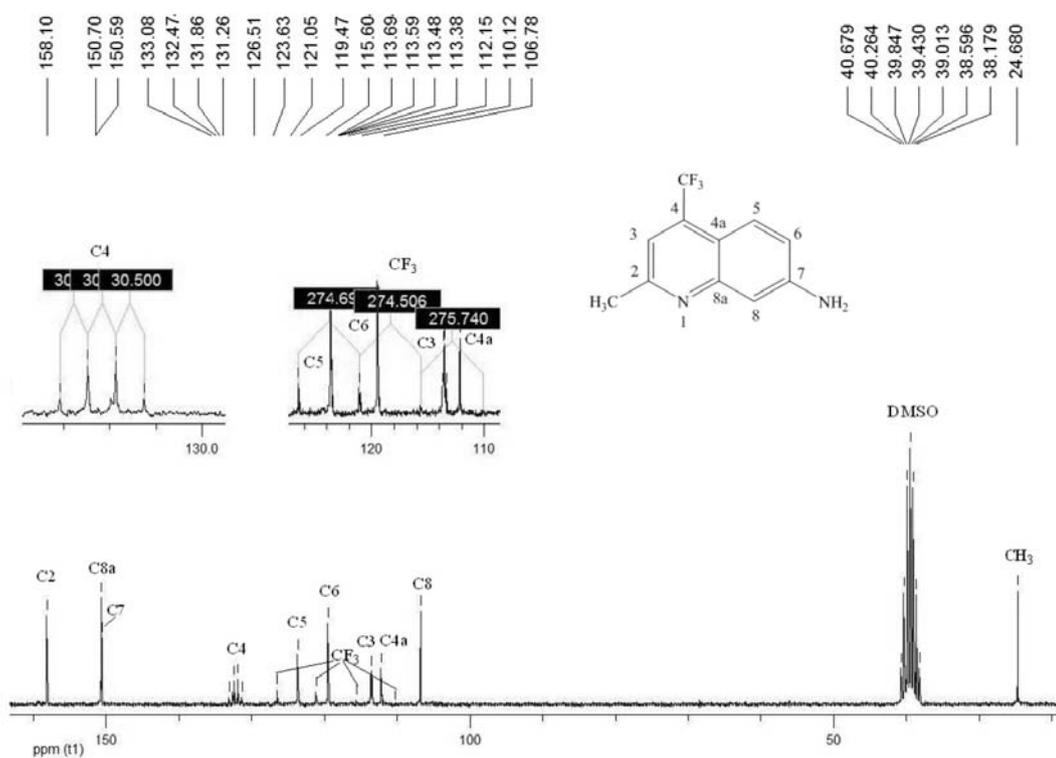


Figure S45. ¹³C NMR (200 MHz, DMSO-*d*₆) spectrum of 4-trifluoromethyl-2-methyl-7-aminoquinoline (**4b**).

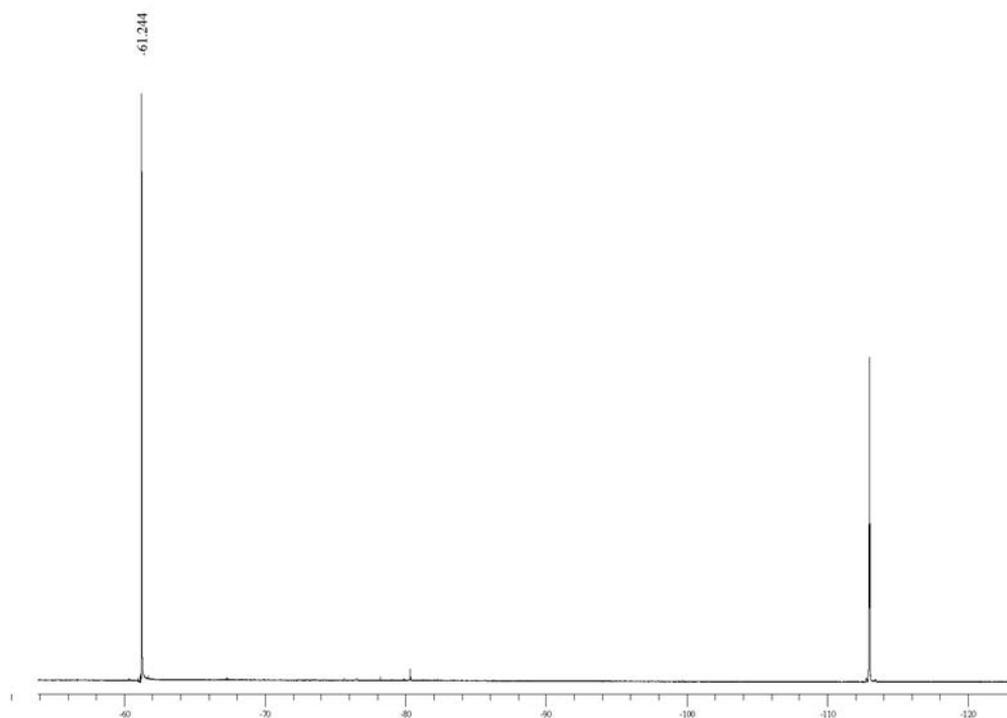


Figure S46. ^{19}F NMR (376 MHz, CDCl_3) spectrum of 4-trifluoromethyl-2-methyl-7-aminoquinoline (**4b**).

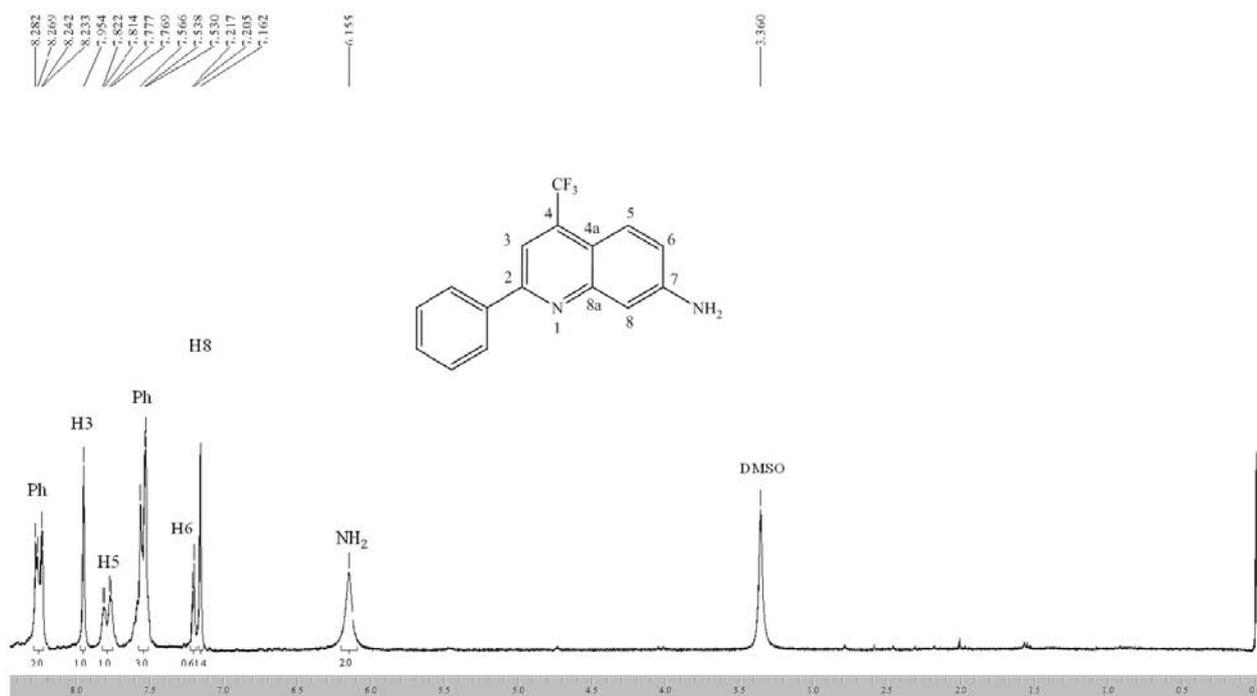


Figure S47. ^1H NMR (100 MHz, $\text{DMSO}-d_6$) spectrum of 4-trifluoromethyl-2-phenyl-7-aminoquinoline (**4c**).

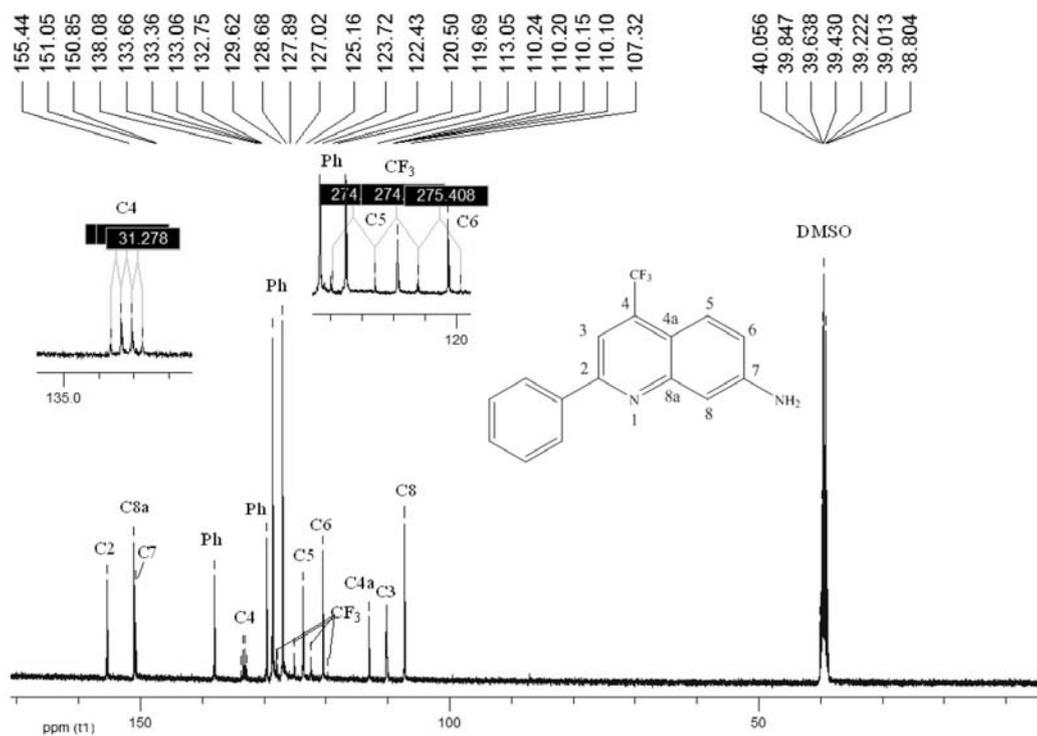


Figure S48. ^{13}C NMR (200 MHz, $\text{DMSO-}d_6$) spectrum of 4-trifluoromethyl-2-phenyl-7-aminoquinoline (**4c**).



Figure S49. ^{19}F NMR (376 MHz, CDCl_3) spectrum of 4-trifluoromethyl-2-phenyl-7-aminoquinoline (**4c**).

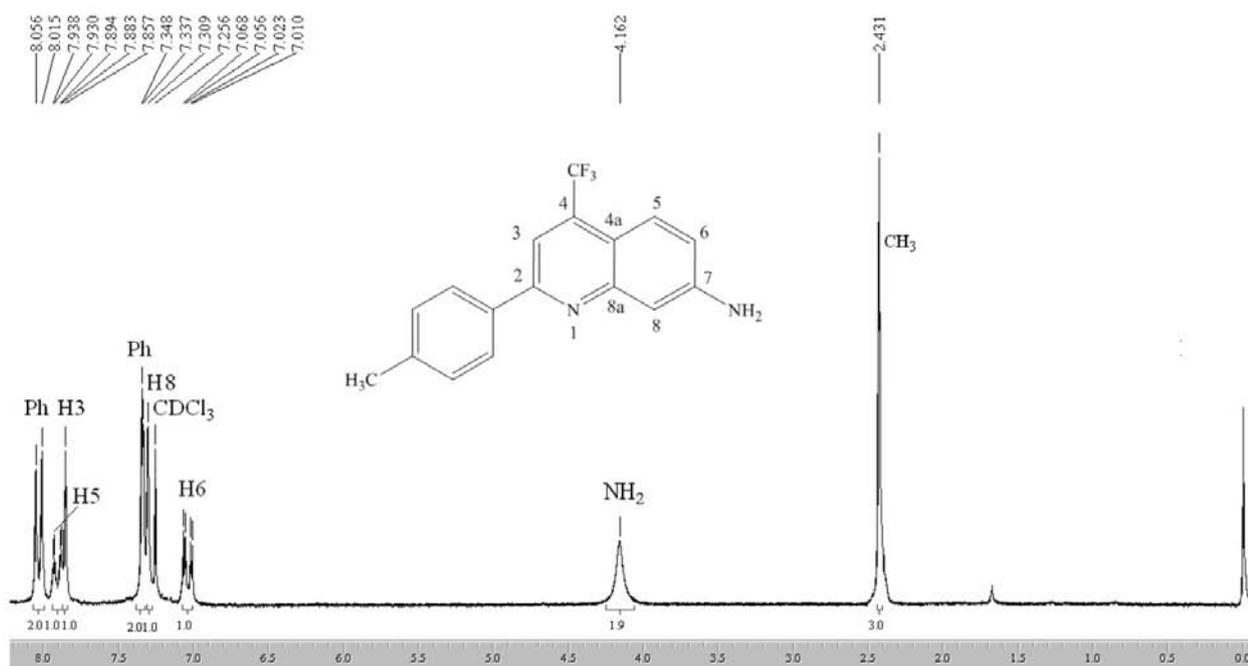


Figure S50. ^1H NMR (100 MHz, CDCl_3) spectrum of 4-trifluoromethyl-2-(4-methylphenyl)-7-aminoquinoline (**4d**).

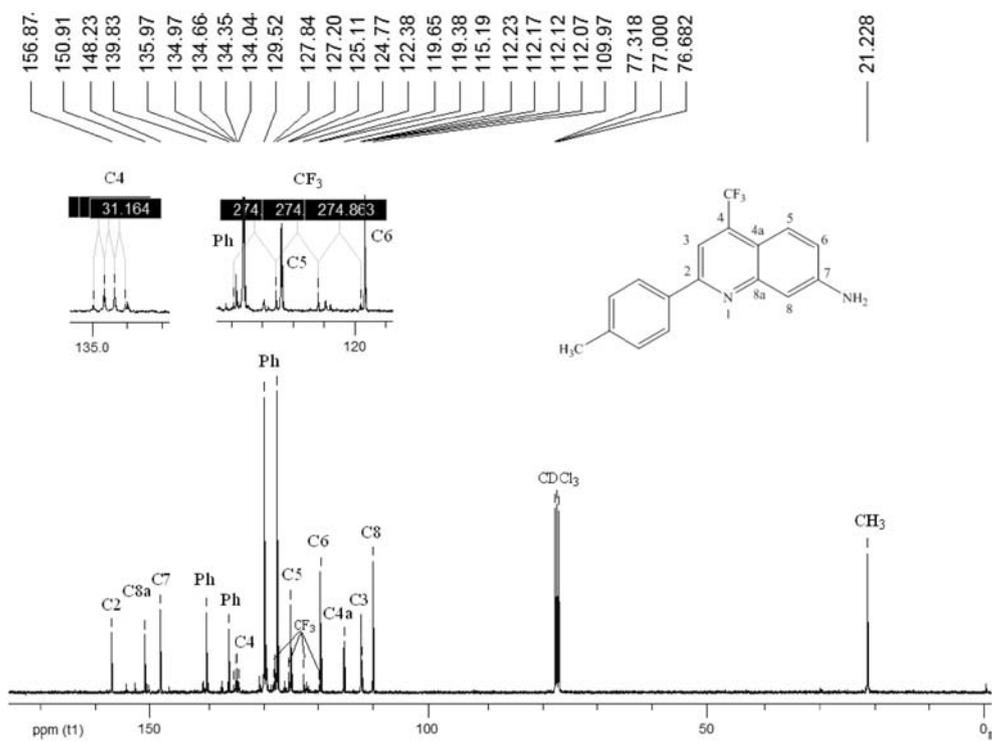


Figure S51. ^{13}C NMR (200 MHz, CDCl_3) spectrum of 4-trifluoromethyl-2-(4-methylphenyl)-7-aminoquinoline (**4d**).

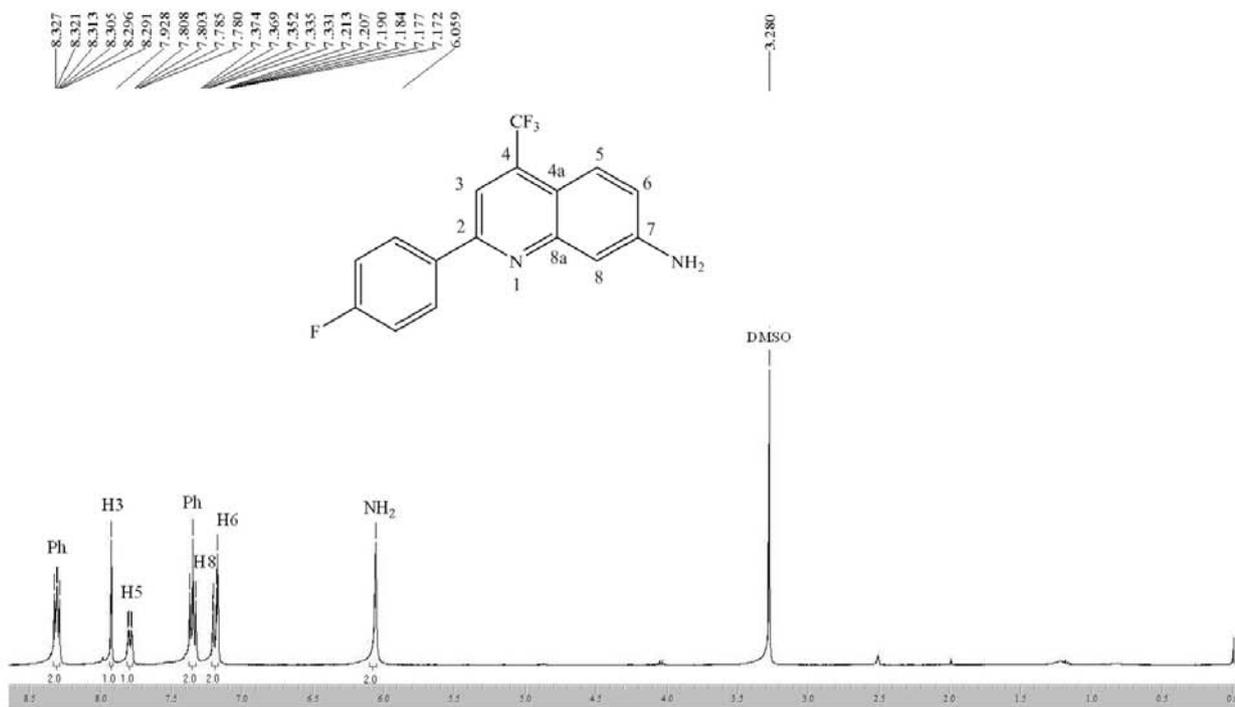


Figure S54. ^1H NMR (100 MHz, $\text{DMSO-}d_6$) spectrum of 4-trifluoromethyl-2-(4-fluorophenyl)-7-aminoquinoline (**4f**).

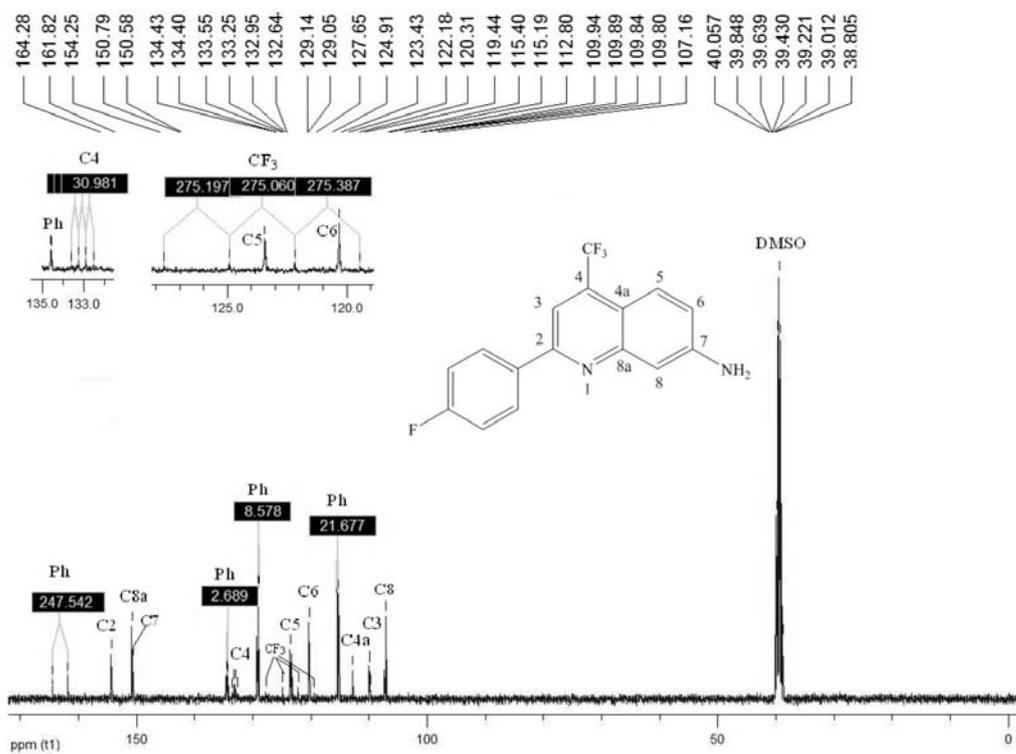


Figure S55. ^{13}C NMR (200 MHz, $\text{DMSO-}d_6$) spectrum of 4-trifluoromethyl-2-(4-fluorophenyl)-7-aminoquinoline (**4f**).

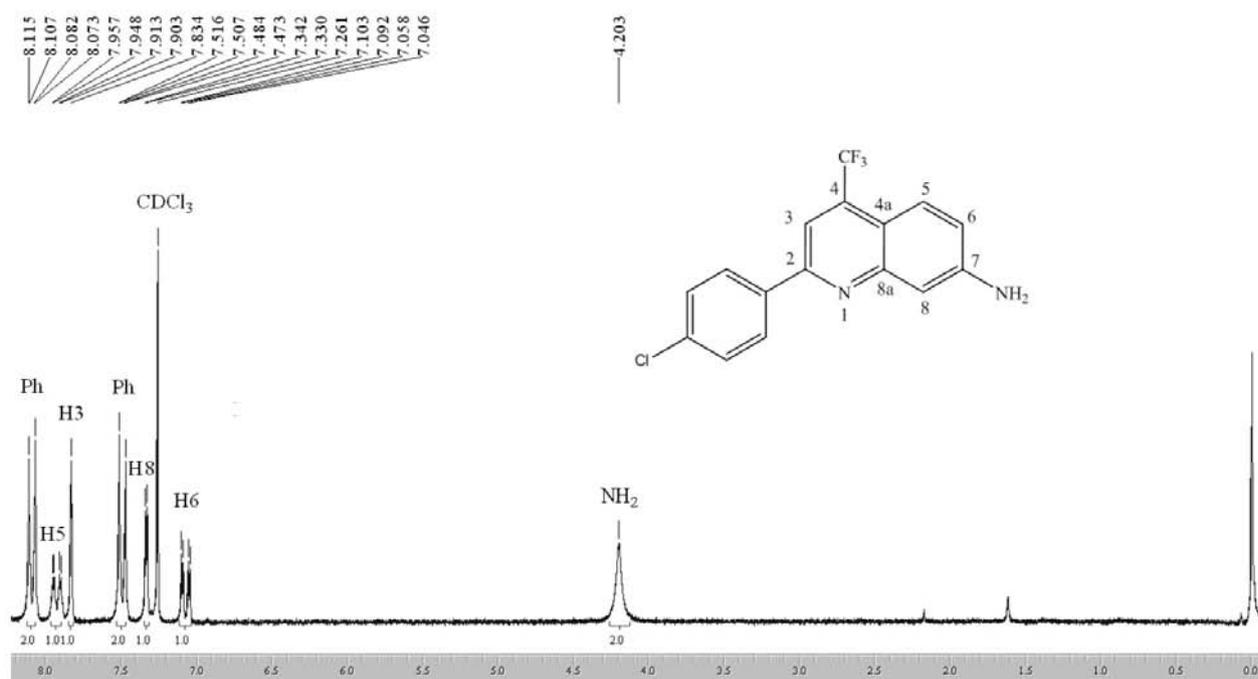


Figure S56. ¹H NMR (100 MHz, CDCl₃) spectrum of 2-(4-chlorophenyl)-4-trifluoromethyl-7-aminoquinoline (**4g**).

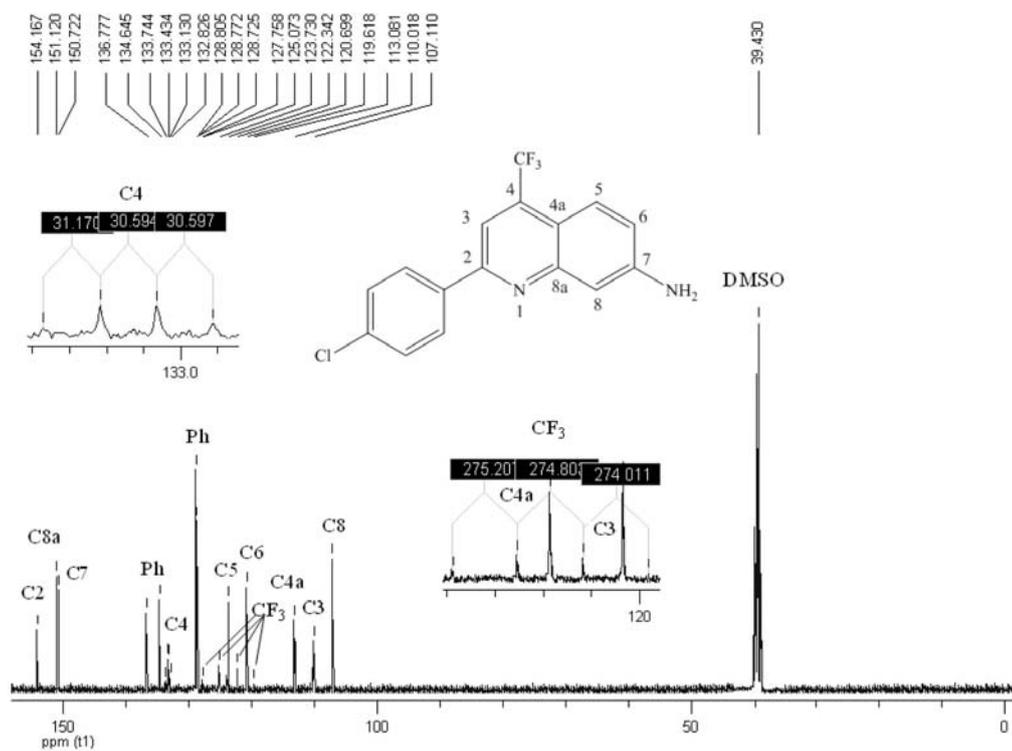


Figure S57. ¹³C NMR (200 MHz, DMSO-*d*₆) spectrum of 2-(4-chlorophenyl)-4-trifluoromethyl-7-aminoquinoline (**4g**).

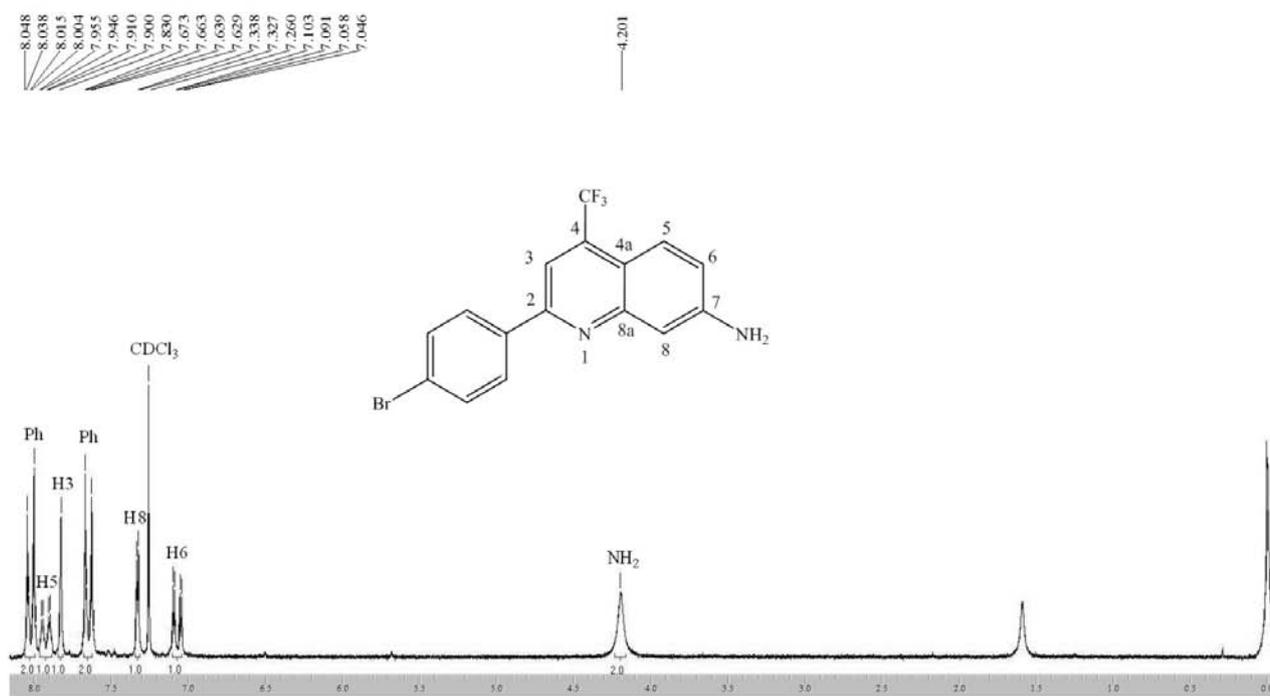


Figure S58. ¹H NMR (100 MHz, CDCl₃) spectrum of 2-(4-bromophenyl)-4-trifluoromethyl-7-aminoquinoline (4h).

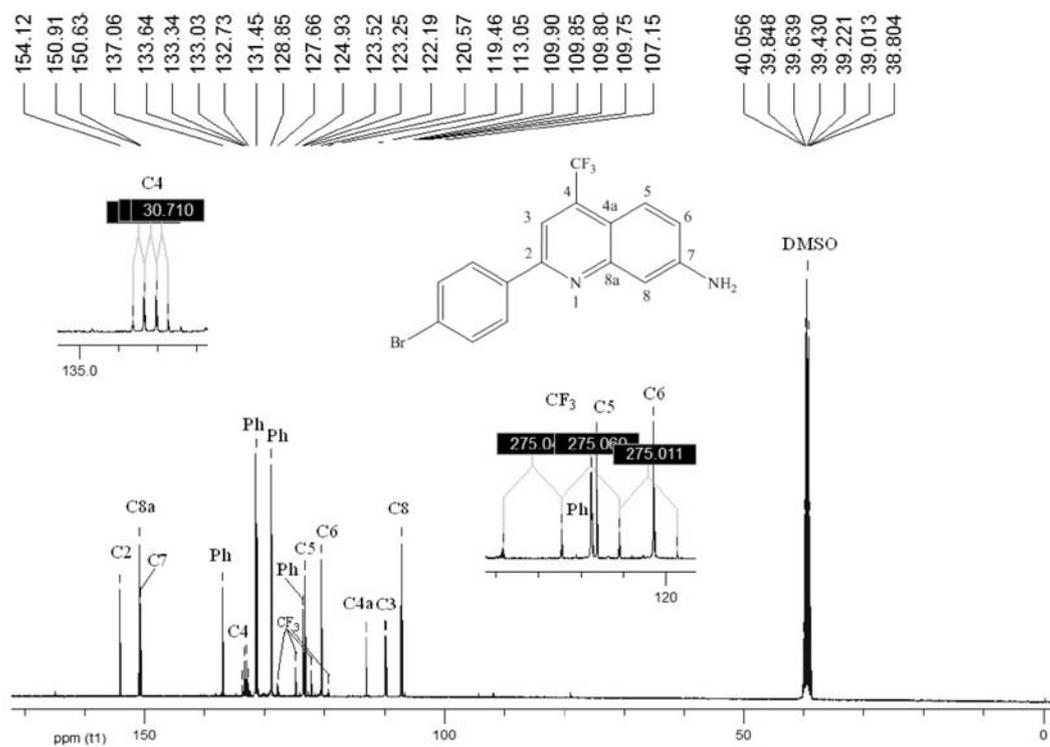


Figure S59. ¹³C NMR (200 MHz, DMSO-*d*₆) spectrum of 2-(4-bromophenyl)-4-trifluoromethyl-7-aminoquinoline (4h).

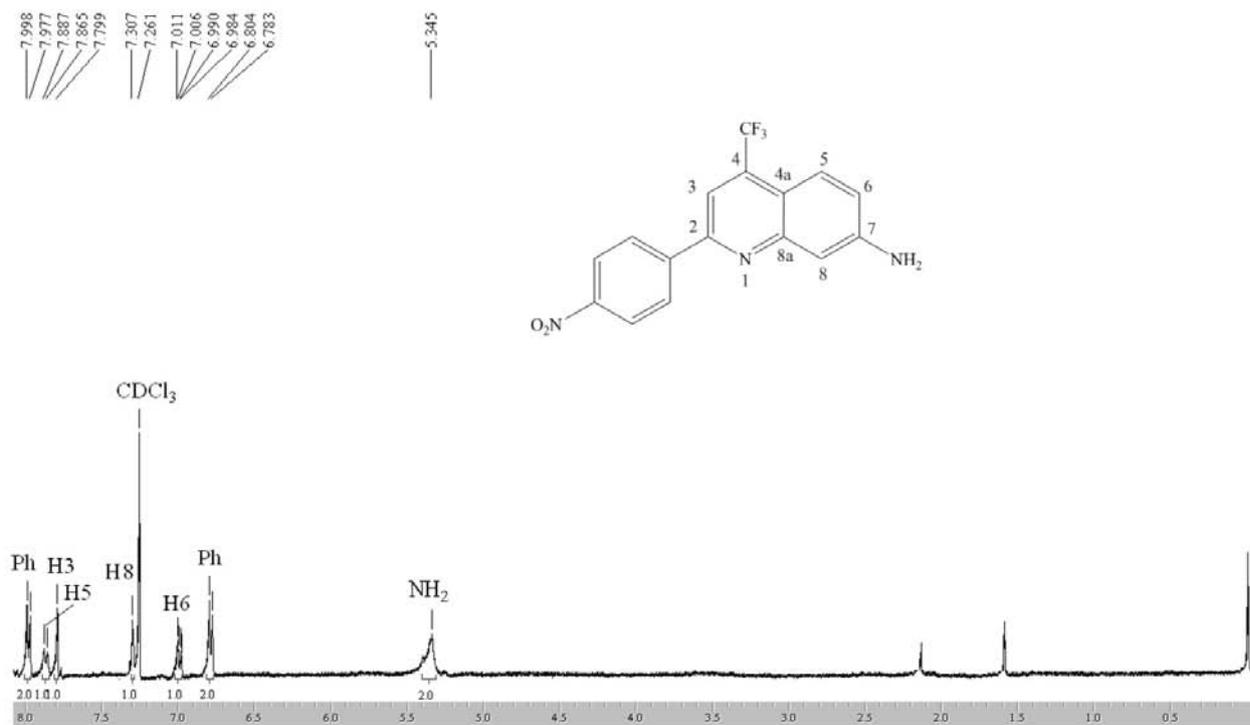


Figure S60. ¹H NMR (100 MHz, CDCl₃) spectrum of 4-trifluoromethyl-2-(4-nitrophenyl)-7-aminoquinoline (**4i**).

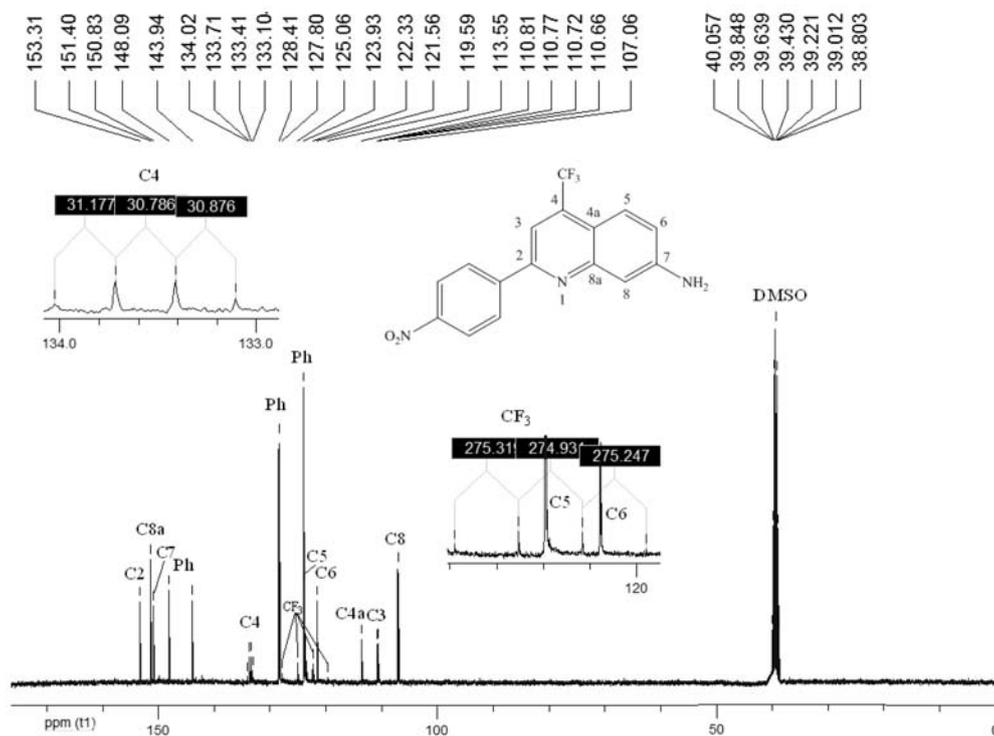


Figure S61. ¹³C NMR (200 MHz, DMSO-*d*₆) spectrum of 4-trifluoromethyl-2-(4-nitrophenyl)-7-aminoquinoline (**4i**).