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One step synthesis of 1,5-diaryl pyridin-2(1*H*)-ones from 2-aryl vinamidinium salts and *N*-aryl cyanoacetamides

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Abstract

A one step, direct method for the synthesis of 1,5-diaryl pyridin-2(1*H*)-one derivatives by condensation of 2-aryl vinamidinium salts with *N*-aryl cyanoacetamides has been developed. This method can conveniently provide the corresponding 1,5-diaryl pyridin-2(1*H*)-one derivatives with various substituents in good yields and overcome the drawbacks of existing methods such as poor substrate scope, heavy metal pollution, and low yields. The formation mechanism of the products was illustrated.

Keywords: *N*-aryl pyridin-2(1*H*)-one, perampanel, copper-catalyzed, Chan-Lam coupling, Ullmann reaction, vinamidinium salt

1. Introduction

N-aryl pyridin-2(1*H*)-one is an important component of many biologically active compounds,[1] such as perampanel, 2-(2-oxo-1-phenyl-5-pyridin-2-yl-1,2-dihydropyridin-3-yl)-benzonitrile, which is the first α-amino-3-hydroxy-5-methyl-4-isoxazole-propionic acid (AMPA) receptor inhibitor for the treatment of epilepsy and has been approved by the European Medicines Agency and US FDA in 2012.[2]

Therefore, the synthesis of these compounds is an attractive subject in organic chemistry. Conventionally, the formation of *N*-aryl pyridin-2(1*H*)-ones rely on the

copper-catalyzed C-N coupling reactions,[3] including Ullmann reaction[4] and Chan-Lam coupling reaction[5] (Fig.1). The condensation of aryl halides with pyridin-2(1*H*)-ones under the Ullmann reaction conditions usually require strong bases, ligand acceleration and high temperatures, which often result in poor substrate scope and low yields. Alternatively, the Chan-Lam coupling reaction using aryl boronic acids instead of aryl halides react with pyridin-2(1*H*)-ones in the presence of copper(II) acetate, oxygen and a base (such as pyridine) at room temperature. This method could effectively avoid the strongly aggressive conditions of Ullmann reaction, but the expensive aryl boronic acids as reaction substrates are necessary and the aftertreatment of copper salts is very troublesome. More unfortunately, the Chan-Lam coupling reaction has a reputation for erratic yields because of the effect of *ortho*-substituents on aryl boronic acids.

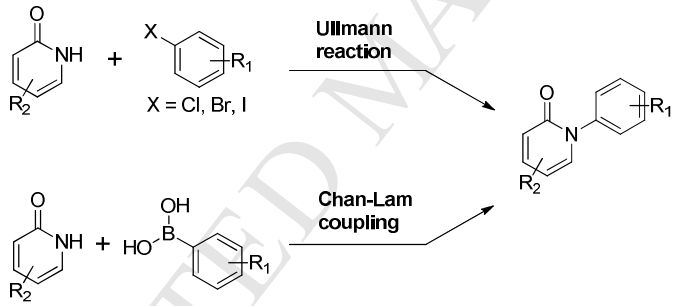
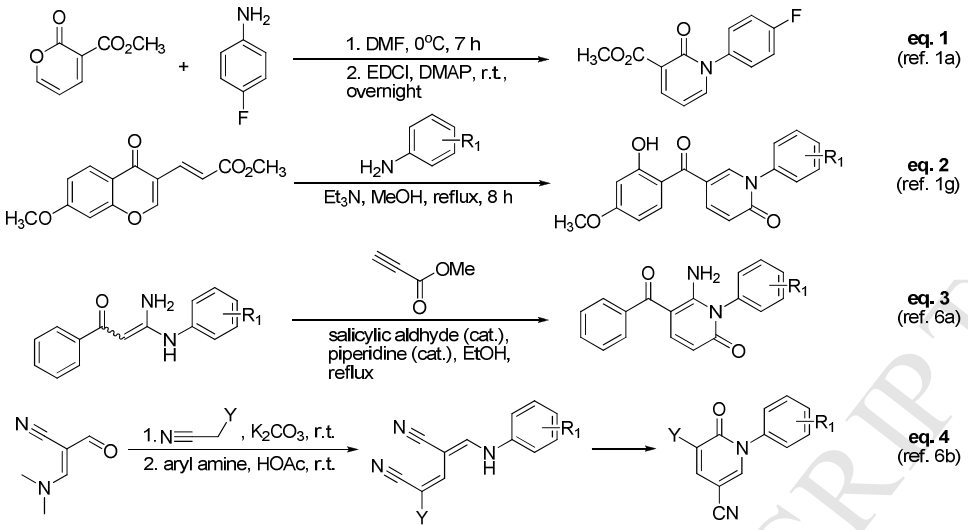


Fig. 1 Traditional strategies for the synthesis of 3-cyano-1,5-diaryl pyridin-2(1*H*)-ones.

In recent years, some non-metal catalyzed methods for the preparation of *N*-aryl pyridin-2(1*H*)-one derivatives have been reported (Scheme 1).[1a, 1g, 6] Moreover, a Diels-Alder reaction was also reported for the synthesis of these compounds.[7] Although these methods are efficient, most of them suffer from significant limitations such as the preconstruction of complex intermediates, high cost, or lack of selectivity.



Scheme 1 Non-metal catalyzed methods for the preparation of *N*-aryl pyridin-2(1*H*)-one derivatives.

We have been interested in building small molecules that contain the structure of 1,5-diaryl pyridin-2(1*H*)-one as possible therapeutic agents for human beings. When the traditional methods were used to prepare the key intermediates 3-cyano-1,5-diaryl pyridin-2(1*H*)-ones, *N*-free pyridin-2(1*H*)-ones were first synthesized, then the target compounds were obtained by the condensation of *N*-free pyridin-2(1*H*)-ones and aryl halides or aryl boronic acids. Although the *N*-free pyridin-2(1*H*)-ones could be easily obtained by the condensation of 3-(dimethylamino)-2-aryl-2-propenal with cyanoacetamide,[8] the next step of either Chan-Lam coupling reaction or Ullmann reaction was inefficient. Only a few reactions of aryl boronic acids with *N*-free pyridin-2(1*H*)-ones could afford the corresponding products in moderate yields, whereas the aryl halides didn't produce the target compounds.

In view of these disappointing results, we proposed a novel, direct method for the synthesis of 1,5-diaryl pyridin-2(1*H*)-ones by the reaction of 2-aryl vinamidinium salts with *N*-aryl cyanoacetamides to avoid the C-N coupling reaction (Fig. 2).

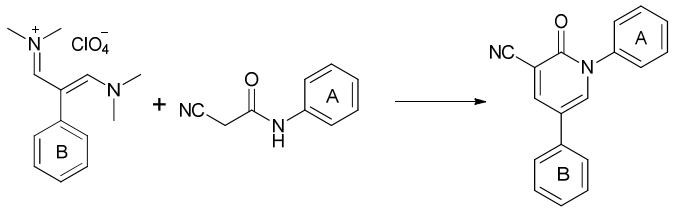


Fig. 2 Proposed strategy for the synthesis of 3-cyano-1,5-diaryl pyridin-2(1*H*)-ones.

2. Result and Discussion

In order to obtain optimal reaction conditions, (*E*)-*N*-(3-(dimethylamino)-2-phenyl-allylidene)-*N*-methylmethanaminium perchlorate (**1a**) and 2-cyano-*N*-*m*-tolylacetamide (**2c**) were employed as the model substrates (Table 1). Different base-catalyzed systems were evaluated. The mild bases such as pyridine, Et_3N and K_2CO_3 cannot trigger this reaction probably due to their alkalinity insufficient to remove the active proton of **2c**. Stronger basic systems (NaOEt/EtOH, *t*-BuOK/*t*-BuOH, NaH/DMF) were tried. NaOEt/EtOH proved to be the most suitable basic system for this reaction (entries 1-3). Further optimization of reaction conditions showed that more than 1.5 equivalent of NaOEt did not yield better results (entries 4 and 5). Finally, raising the reaction temperature could shorten the reaction time (1 h), but the yield of **4ac** decreased significantly (42%, entry 6). It was found that the combination of 1.5 equivalent of NaOEt in anhydrous ethanol afford the product **4ac** in the highest 77% yield after stirring at room temperature for 24 h (entry 4). The reaction endpoint was monitored by TLC and the product **4ac** was isolated and confirmed by NMR and HRMS.

Table 1 Synthesis conditions for the reaction of **1a** with **2c**[a]

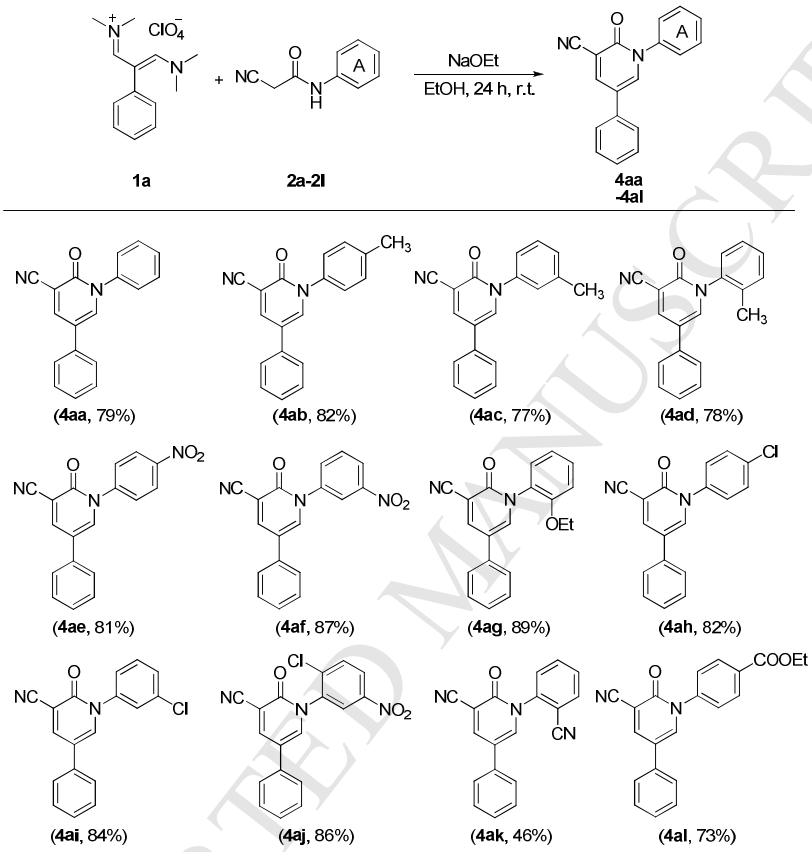
Entry	Base (equiv)	Solvent	*T* (°C)	Time (h)	Yield (%)[b]
1	NaOEt (1.1)	EtOH	rt	24	65
2	*t*-BuOK (1.5)	*t*-BuOH	0→rt	2	trace[c]
3	NaH (2.2)	DMF	0→rt	0.5	trace
4	NaOEt (1.5)	EtOH	rt	24	77

5	NaOEt (2.0)	EtOH	rt	24	74
6	NaOEt (1.5)	EtOH	reflux	1	42

[a] Unless otherwise noted, all reactions were carried out with equimolar amounts of **1a** and **2c**. [b] Isolated yield. [c] monitored by TLC.

Having set up the reaction conditions, our attention was turned to investigate the scope of application of this method. Firstly, the reactions of a variety of *N*-aryl acetamides (**2a**-**2l**) with **1a** were examined. As shown in Scheme 2, most of the 3-cyano-*N*-aryl pyridin-2(1*H*)-ones were obtained in good yields. The position of the substituents on the phenyl ring of the *N*-aryl acetamides didn't seem to play a role, and similar yields (82% for **4ab,** 77% for **4ac,** and 78% for **4ad**) were obtained from corresponding substrates bearing a methyl group at *para*- (**2b**), *meta*- (**2c**), and *ortho*-position (**2d**) of phenyl amines, respectively. The presence of electron-withdrawing groups on aryl halides and aryl boronic acids could decrease the reactivity of them, which usually resulted in poor yields of the Ullmann reaction and the Chan-Lam reaction. Therefore, *N*-aryl acetamides substituted on the phenyl ring with groups of different electronic properties were also explored, and excellent yields were obtained in most cases. As depicted in Scheme 2, the substrates **2e** and **2f** containing a nitro group (a strongly electron-withdrawing group) at the *para*- and *meta*-position of the aniline gave the corresponding 3-cyano-*N*-aryl pyridin-2(1*H*)-ones **4ae** and **4af** in 81% and 87% yields, respectively. The target compound **4ag** with a strongly electron-donating group (oxyethyl) at *ortho*-position of aniline was obtained in 89% yield. And satisfactory yields of **4ah**-**4aj** (81%, 87%, and 86%) were also obtained from the corresponding substrates **2h**, **2i**, and **2j** with electron-withdrawing groups, respectively. These results indicated that the electronic properties of phenyl amines in *N*-aryl acetamides barely affected the reaction pathway. Inexplicably, the 2-cyano-*N*-(2-cyanophenyl) acetamide **2k** was found to produce the product **4ak** only in 46% yield. In addition, in order to determine whether

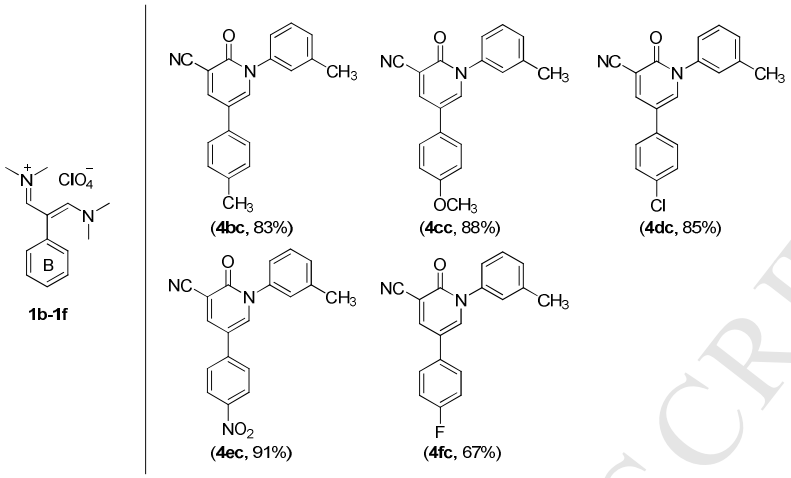
this method is suitable for base-sensitive groups, we selected the ester group (**2l**) as the model group for the reaction. A 73% yield of the corresponding pyridin-2(1*H*)-one **4al** suggested that the ester group was also well tolerated in this method.



Scheme 2 Syntheses of 1-aryl-3-cyano-5-phenyl pyridin-2(1*H*)-ones from **1a** and *N*-aryl acetamides **2a-2l**.

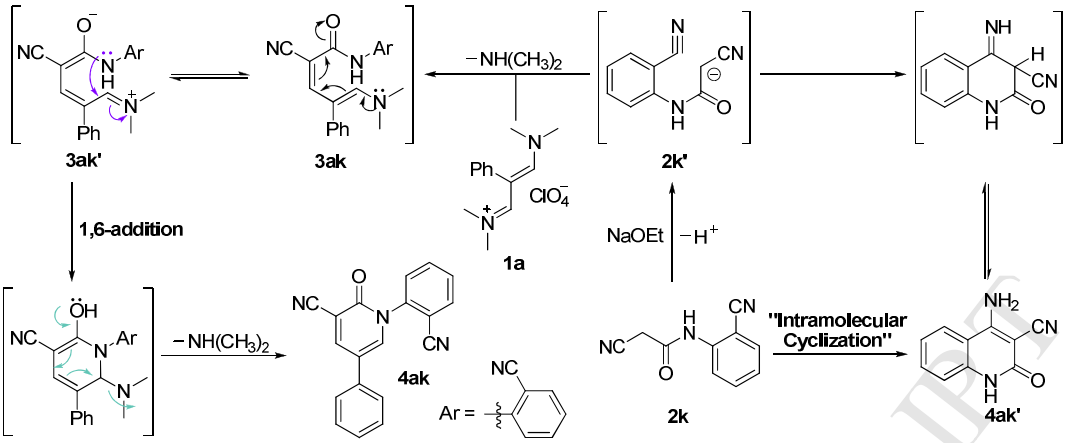
On these basis, we further explored the electronic properties of phenyl ring of the other reaction partners, 2-aryl vinamidinium salts. Five substituted 2-aryl vinamidinium salts (**1b-1f**) were selected and reacted with 2-cyano-*N*-*m*-tolylacetamide **2c**. As shown in Scheme 3, the very close yields for electron-rich substrates (**1b** and **1c**) and electron-deficient substrates (**1d** and **1e**) showed that the electron-donating substituents at the phenyl ring did not decrease the reactivity of

vinamidinium salts.



Scheme 3 1-(3-methyl) phenyl-3-cyano-5-aryl pyridin-2(1*H*)-ones prepared from **1b-1f**.

These results revealed that this approach was a general and efficient method for the synthesis of 1,5-diaryl pyridin-2(1*H*)-ones except **4ak**. We speculate that the reaction mechanism is that the 2-cyano-*N*-(2-cyanophenyl) acetamide (**2k**) was first formed the carbon-anion **2k'** in the presence of NaOEt, which could react with 2-aryl vinamidinium salt **1** to generate the intermediate **3ak**[8, 9] and further underwent a 1,6-addition followed by an elimination of dimethylamine to yield the target compound **4ak**. On the other hand, the **2k'** may convert into the compound **4ak'** under an intramolecular nucleophilic cyclization reaction. Because of the competition between the two reaction pathways, the yield of **4ak** is much lower than other compounds. In order to verify this hypothesis, the reaction mixture of **4ak** was further investigated. The molecular identification of the main byproduct **4ak'** in the reaction mixture was consistent with the product of the mechanism (Scheme 4).



Scheme 4 Proposed mechanism for the **4ak** and **4ak'**.

3. Conclusions

We have developed a direct, one step method for the synthesis of 1,5-diaryl pyridin-2(1*H*)-one derivatives with the following advantages over previous syntheses: 1) No metal catalysts such as copper salts, have been used in the synthesis, avoiding the heavy metal pollution. 2) Inexpensive and easily available starting materials, 2-aryl vinamidinium salts and *N*-aryl cyanoacetamides, were used. 3) One step reaction with satisfactory yields in most cases. In addition, the reaction conditions allowed the synthesis of some derivatives containing base sensitive groups such as ester. We believed that the proposed synthesis method could make it possible that this class of compounds prepared only in laboratory before because of the costliness can be produced on a large-scale synthesis.

4. Experimental Section

4.1. General information

Unless otherwise specified, the commercial reagents were used as received without further purification and all solvents were dried by standard methods prior to use. NMR spectra were recorded on a 300 MHz or 500 MHz spectrometer. Shifts are reported relative to tetramethylsilane; coupling constants (*J*) are given in hertz. High-resolution mass spectral (HRMS) data were acquired using ESI-TOF detection.

FTIR spectra were recorded on KBr thin film. Melting points were measured on a WRS-2A melting point apparatus and are uncorrected. Column chromatography was performed on silica gel (200-300 mesh) using CH_2Cl_2 and MeOH as eluent. *N*-aryl cyanoacetamides were provided by our laboratory. 2-aryl vinamidinium salts (**1a-1f**) were prepared according to the reported procedures.[8] Caution: Although we observed no explosive behavior with any of our perchlorate salts, it is still a potential hazard, and adequate precautions should be used when drying and using them.

4.2. General Experimental Procedure for the Synthesis of 1,5-diaryl pyridin-2(1*H*)-ones (4aa-4al, 4bc-4fc).

To a solution of NaOEt (3.0 mmol) in anhydrous ethanol (10 mL) were added amide (2.0 mmol) and 2-aryl vinamidinium salt (2.0 mmol) at room temperature. The reaction mixture was stirred at the same temperature for 24 h. After completion of the reaction, the reaction mixture was poured into water (100 mL) to precipitate the crude product, which was collected by filtration and washed with water. The residue was purified by silica gel column chromatography (CH_2Cl_2: MeOH) to afford the corresponding 1,5-diaryl-2-pyridone.

4.2.1. 2-oxo-1,5-diphenyl-1,2-dihydropyridine-3-carbonitrile (**4aa**): white solid (430 mg, 79%), m.p. 212-214 ^oC. ^1H NMR (500 MHz, $CDCl_3$): δ 8.16 (d, J = 3.0 Hz, 1H), 7.80 (d, J = 3.0 Hz, 1H), 7.48-7.55 (m, 3H), 7.39-7.47 (m, 7H). ^{13}C NMR (125 MHz, DMSO-d_6): δ 158.3, 147.5, 141.7, 139.6, 134.0, 129.0, 128.8 (d, J = 35 Hz), 127.5, 126.7, 125.7 118.4, 116.1, 104.2. IR (KBr): ν 3449, 3056, 2226, 1662, 1611, 1535, 1495, 1453, 1276, 882, 760, 694 cm^{-1}. HRMS (ESI-TOF): calcd. for $C_{18}H_{13}N_2O$ $(M + H)^+$ 273.1022, found 273.1024.

4.2.2. 2-oxo-5-phenyl-1-p-tolyl-1,2-dihydropyridine-3-carbonitrile (**4ab**): pale yellow solid (470 mg, 82%), m.p. 200-202 ^oC. ^1H NMR (300 MHz, DMSO-d_6): δ 8.69 (d, J = 2.7 Hz, 1H), 8.33 (d, J = 2.7 Hz, 1H), 7.69 (d, J = 7.8 Hz, 2H), 7.42 (t, J = 8.1 Hz, 4H), 7.34 (t, J = 7.8 Hz, 3H), 2.38 (s, 3H). ^{13}C NMR (125 MHz, DMSO-d_6): δ 158.3,

147.4, 141.9, 138.5, 137.1, 134.0, 129.4, 128.8, 127.5, 126.4, 125.7, 118.3, 116.1, 104.0, 20.5. IR (KBr): *v* 3443, 3063, 3047, 2226, 1670, 1594, 1529, 1501, 1451, 1402, 1290, 1276, 1114, 1085, 759, 694 cm^{-1}. HRMS (ESI-TOF): calcd. for $C_{19}H_{15}N_2O$ $(M + H)^+$ 287.1179, found 287.1168.

4.2.3. 2-oxo-5-phenyl-1-m-tolyl-1,2-dihydropyridine-3-carbonitrile (**4ac**): pale yellow solid (441 mg, 77%), m.p. 157-158 ^oC. ^1H NMR (300 MHz, $CDCl_3$): δ 8.15 (d, *J* = 2.7 Hz, 1H), 7.80 (d, *J* = 2.7 Hz, 1H), 7.37-7.48 (m, 6H), 7.19-7.31 (m, 3H), 2.42 (s, 3H). ^{13}C NMR (125MHz, DMSO-d_6): δ 158.4, 147.6, 141.9, 139.6, 138.8, 134.1, 129.5, 128.8 (d, *J* = 15 Hz), 127.5, 127.2, 125.8, 123.8, 118.4, 116.2, 104.2, 20.7. IR (KBr): *v* 3446, 2223, 1682, 1607, 1533, 1489, 1452, 1291, 1277, 887, 874, 780, 757, 701, 691 cm^{-1}. HRMS (ESI-TOF): calcd. for $C_{19}H_{15}N_2O$ $(M + H)^+$ 287.1179, found 287.1186.

4.2.4. 2-oxo-5-phenyl-1-o-tolyl-1,2-dihydropyridine-3-carbonitrile (**4ad**): pale yellow solid (447 mg, 78%), m.p. 206-208 ^oC. ^1H NMR (300 MHz, DMSO-d_6): δ 8.76 (d, *J* = 2.7 Hz, 1H), 8.34 (d, *J* = 2.7 Hz, 1H), 7.70 (d, *J* = 7.5 Hz, 2H), 7.31-7.44 (m, 7H), 2.11 (s, 3H). ^{13}C NMR (125 MHz, DMSO-d_6): δ 158.0, 147.8, 142.0, 139.0, 134.5, 133.9, 130.7, 129.3, 128.8, 127.6, 127.4, 127.0, 125.8, 118.6, 116.1, 104.2, 17.1. IR (KBr): *v* 3446, 3037, 2224, 1666, 1530, 1494, 1451, 1273, 776, 761, 699 cm^{-1}. HRMS (ESI-TOF): calcd. for $C_{19}H_{15}N_2O$ $(M + H)^+$ 287.1179, found 287.1187.

4.2.5. 1-(4-nitrophenyl)-2-oxo-5-phenyl-1,2-dihydropyridine-3-carbonitrile (**4ae**): yellow solid (514 mg, 81%), m.p. 262-264 ^oC. ^1H NMR (300 MHz, DMSO-d_6): δ 8.76 (d, *J* = 2.7 Hz, 1H), 8.46 (d, *J* = 2.7 Hz, 1H), 8.41 (d, *J* = 9.0 Hz, 2H), 7.91 (d, *J* = 9.0 Hz, 2H), 7.71 (d, *J* = 7.8 Hz, 2H), 7.44 (t, *J* = 7.4 Hz, 2H), 7.35 (t, *J* = 7.2 Hz, 1H). ^{13}C NMR (125 MHz, DMSO-d_6): δ 158.1, 148.2, 147.3, 144.6, 141.2, 133.9, 128.9, 128.6, 127.7, 125.8, 124.3, 118.8, 115.9, 104.5. IR (KBr): *v* 3451, 3111, 3087, 3059, 2230, 1666, 1614, 1524, 1492, 1351, 1317, 1278, 1107, 860, 766, 750, 699 cm^{-1}. HRMS (ESI-TOF): calcd. for $C_{18}H_{12}N_3O_3$ $(M + H)^+$ 318.0873, found 318.0877.

4.2.6. 1-(3-nitrophenyl)-2-oxo-5-phenyl-1,2-dihydropyridine-3-carbonitrile (**4af**): yellow solid (552 mg, 87%), m.p. 170-172 ^{o}C. ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.76 (d, J = 2.7 Hz, 1H), 8.56 (s, 1H), 8.50 (d, J = 2.7 Hz, 1H), 8.37 (dd, J = 8.4, 1.2 Hz, 1H), 8.08 (d, J = 8.7 Hz, 1H), 7.86 (t, J = 8.1 Hz, 1H), 7.71 (d, J = 8.7 Hz, 2H), 7.44 (t, J = 7.8 Hz, 2H), 7.36 (d, J = 7.2 Hz, 1H). ^{13}C NMR (125 MHz, DMSO-d_6): δ 158.3, 148.1, 147.9, 141.7, 140.2, 133.9, 130.5, 128.9, 127.7, 125.8, 123.8, 122.6, 118.7, 116.0, 104.3. IR (KBr): v 3454, 3072, 2237, 1678, 1605, 1529, 1452, 1354, 1290, 1271, 900, 826, 766, 736, 697 cm^{-1}. HRMS (ESI-TOF): calcd. for $C_{18}H_{12}N_3O_3$ $(M + H)^+$ 318.0873, found 318.0890.

4.2.7. 1-(2-ethoxyphenyl)-2-oxo-5-phenyl-1,2-dihydropyridine-3-carbonitrile (**4ag**): pale yellow solid (563 mg, 89%), m.p. 175-176 ^{o}C. ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.71 (d, J = 2.7 Hz, 1H), 8.35 (d, J = 2.7 Hz, 1H), 7.68 (d, J = 7.5 Hz, 2H), 7.40-7.51 (m, 4H), 7.34 (t, J = 7.5 Hz, 1H), 7.25 (d, J = 7.5 Hz, 1H), 7.10 (t, J = 7.5 Hz, 1H), 4.10 (q, J = 6.9 Hz, 2H), 1.20 (t, J = 6.9 Hz, 3H). ^{13}C NMR (125 MHz, DMSO-d_6): δ 158.1, 153.0, 147.8, 143.0, 134.0, 130.7, 128.9, 128.5, 127.5, 125.6, 120.5, 118.0, 116.2, 113.8, 104.0, 64.2, 14.4. IR (KBr): v 3446, 3040, 2977, 2224, 1671, 1601, 1535, 1500, 1452, 1278, 1247, 1130, 1043, 894, 770, 750, 696 cm^{-1}. HRMS (ESI-TOF): calcd. for $C_{20}H_{17}N_2O_2$ (M + H)+ 317.1285, found 317.1288.

4.2.8. 1-(4-chlorophenyl)-2-oxo-5-phenyl-1,2-dihydropyridine-3-carbonitrile (**4ah**): white solid (503 mg, 82%), m.p. 222-224 ^{o}C. ^{1}H NMR (300 MHz, DMSO-d_6): δ8.72 (d, J = 2.7 Hz, 1H), 8.39 (d, J = 2.7 Hz, 1H), 7.69 (d, J = 7.2 Hz, 2H), 7.62 (s, 4H), 7.43 (t, J = 7.8 Hz, 2H), 7.35(d, J = 7.2 Hz, 1H). ^{13}C NMR (125 MHz, DMSO-d_6): δ 158.2, 147.7, 141.6, 138.2, 133.9, 133.5, 129.0, 128.7 (d, J = 35 Hz), 127.5, 125.7, 118.5, 116.0, 104.2. IR (KBr): v 3445, 3083, 3055, 2226, 1664, 1616, 1530, 1486, 1317, 1274, 1089, 1011, 907, 834, 767, 698 cm^{-1}. HRMS (ESI-TOF): calcd. for $C_{18}H_{12}ClN_2O$ $(M + H)^+$ 307.0633, found 307.0642.

4.2.9. 1-(3-chlorophenyl)-2-oxo-5-phenyl-1,2-dihydropyridine-3-carbonitrile (**4ai**): white solid (515 mg, 84%), m.p. 188-190 ^{o}C. ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.72 (d, J = 2.7 Hz, 1H), 8.42 (d, J = 2.7 Hz, 1H), 7.75 (s, 1H), 7.71 (d, J = 7.2 Hz, 2H), 7.55-7.60 (m, 3H), 7.43 (t, J = 7.8 Hz, 2H), 7.34 (t, J = 7.2 Hz, 1H). ^{13}C NMR (125 MHz, DMSO-d_6): δ 158.2, 147.8, 141.6, 140.6, 133.9, 133.1, 130.5, 128.8 (d, J = 80 Hz), 127.5, 127.1, 125.8, 118.5, 115.9, 104.2. IR (KBr): v 3446, 3089, 3030, 2219, 1671, 1591, 1531, 1473, 1283, 868, 789, 767, 697 cm^{-1}. HRMS (ESI-TOF): calcd. for $C_{18}H_{12}ClN_2O$ $(M + H)^+$ 307.0633, found 307.0632.

4.2.10. 1-(2-chloro-5-nitrophenyl)-2-oxo-5-phenyl-1,2-dihydropyridine-3-carbonitrile (**4aj**): yellow solid (605 mg, 86%), m.p. 243-245 ^{o}C. ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.84 (d, J = 2.7 Hz, 1H), 8.77 (d, J = 2.7 Hz, 1H), 8.55 (d, J = 2.4 Hz, 1H), 8.43 (dd, J = 8.9, 2.4 Hz, 1H), 8.05 (d, J = 8.7 Hz, 1H), 7.70 (d, J = 7.2 Hz, 2H), 7.46 (t, J = 7.2 Hz, 2H), 7.37 (t, J = 7.2 Hz, 1H). ^{13}C NMR (75 MHz, DMSO-d_6): δ 157.7, 148.8, 146.7, 141.7, 138.2, 137.7, 133.7, 131.3, 129.0, 127.8, 125.8, 125.7, 125.4, 118.9 115.7, 104.4. IR (KBr): v 3456, 3095, 2228, 1663, 1528, 1352, 1284, 901, 840, 766, 741, 694 cm^{-1}. HRMS (ESI-TOF): calcd. for $C_{18}H_{11}ClN_3O_3$ $(M + H)^+$ 352.0483, found 352.0485.

4.2.11. 1-(2-cyanophenyl)-2-oxo-5-phenyl-1,2-dihydropyridine-3-carbonitrile (**4ak**): yellow solid (274 mg, 46%), m.p. 248-254 ^{o}C. ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.85 (d, J = 2.7 Hz, 1H), 8.58 (d, J = 2.7 Hz, 1H), 8.12 (d, J = 7.5 Hz, 1H), 7.96 (t, J = 7.8 Hz, 1H), 7.85 (d, J = 7.8 Hz, 1H), 7.71-7.79 (m, 3H), 7.46 (t, J = 7.5 Hz, 2H), 7.35-7.40 (m, 1H). ^{13}C NMR (125 MHz, DMSO-d_6): δ 158.0, 148.9, 141.6, 141.3, 134.7, 133.6 (d, J = 90 Hz), 130.2, 129.0, 127.9, 125.8, 118.9, 115.7 (d, J = 45 Hz), 111.0, 104.3. IR (KBr): v 3454, 3083, 3058, 2229, 1676, 1620, 1530, 1491, 1452, 1291, 1270, 904, 766, 703 cm^{-1}. HRMS (ESI-TOF): calcd. for $C_{19}H_{12}N_3O$ $(M + H)^+$ 298.0975, found 298.0985.

4.2.12. ethyl 4-(3-cyano-2-oxo-5-phenylpyridin-1(2H)-yl)benzoate (**4al**): yellow solid (502 mg, 73%), m.p. 230-232 ^{o}C. ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.75 (d, J = 2.7 Hz, 1H), 8.42 (d, J = 2.7 Hz, 1H), 8.12 (d, J = 8.7 Hz, 2H), 7.75 (d, J = 8.7 Hz, 2H), 7.71 (d, J = 7.5 Hz, 2H), 7.44 (t, J = 7.8 Hz, 2H), 7.33-7.38 (m, 1H), 4.37 (q, J = 7.2 Hz, 2H), 1.35 (t, J = 7.2 Hz, 3H). ^{13}C NMR (75 MHz, DMSO-d_6): δ 164.9, 158.2, 148.0, 143.3, 141.5, 134.0, 130.2, 129.9, 128.9, 127.7, 127.4, 125.9, 118.7, 116.0, 104.3, 61.0, 14.1. IR (KBr): v 3455, 2233, 1714, 1676, 1282, 1130, 1108, 865, 758 cm^{-1}. HRMS (ESI-TOF): calcd. for $C_{21}H_{17}N_2O_3$ $(M + H)^+$ 345.1234, found 345.1242.

4.2.13. 2-oxo-1-m-tolyl-5-p-tolyl-1,2-dihydropyridine-3-carbonitrile (**4bc**): yellow solid (499 mg, 83%), m.p. 188-190 ^{o}C. ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.67 (d, J = 2.7 Hz, 1H), 8.30 (d, J = 2.7 Hz, 1H), 7.58 (d, J = 8.4 Hz, 2H), 7.43 (t, J = 7.5 Hz, 1H), 7.33 (t, J = 7.5 Hz, 3H), 7.22 (d, J = 8.1 Hz, 2H), 2.38 (s, 3H), 2.31 (s, 3H). ^{13}C NMR (125 MHz, DMSO-d_6): δ 158.3, 147.4, 141.4, 139.6, 138.7, 136.9, 131.1, 129.4 (d, J = 35 Hz), 128.9, 127.2, 125.6, 123.8, 118.4, 116.2, 104.1, 20.7, 20.5. IR (KBr): v 3453, 3036, 2968, 2923, 2223, 1674, 1611, 1531, 1487, 1453, 1288, 874, 812, 778, 767, 701 cm^{-1}. HRMS (ESI-TOF): calcd. for $C_{20}H_{17}N_2O$ $(M + H)^+$ 301.1335, found 301.1346.

4.2.14. 5-(4-methoxyphenyl)-2-oxo-1-m-tolyl-1,2-dihydropyridine-3-carbonitrile (**4cc**): yellow solid (557 mg, 88%), m.p. 176-178 ^{o}C. ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.64 (d, J = 2.7 Hz, 1H), 8.26 (d, J = 2.7 Hz, 1H), 7.62 (d, J = 8.7 Hz, 2H), 7.43 (t, J = 7.5 Hz, 1H), 7.33 (t, J = 7.2 Hz, 3H), 6.97 (d, J = 8.7 Hz, 2H), 3.77 (s, 3H), 2.39 (s, 3H). ^{13}C NMR (125 MHz, DMSO-d_6): δ 158.9, 158.2, 147.4, 140.9, 139.6, 138.7, 129.4, 128.8, 127.1 (d, J = 40Hz), 126.4, 123.8, 118.3, 116.2, 114.2, 104.1, 55.1, 20.7. IR (KBr): v 3450, 2930, 2835, 2220, 1664, 1613, 1522, 1456, 1287, 1254, 1183, 1030, 830, 800, 765, 705 cm^{-1}. HRMS (ESI-TOF): calcd. for $C_{20}H_{17}N_2O_2$ $(M + H)^+$ 317.1285, found 317.1282.

4.2.15. 5-(4-chlorophenyl)-2-oxo-1-m-tolyl-1,2-dihydropyridine-3-carbonitrile (**4dc**): white solid (545 mg, 85%), m.p. 192-194 ^{o}C. ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.71 (d, J = 2.7 Hz, 1H), 8.40 (d, J = 2.7 Hz, 1H), 7.74 (d, J = 8.4 Hz, 2H), 7.47 (d, J = 8.4 Hz, 2H), 7.42 (d, J = 7.5 Hz, 1H), 7.34 (t, J = 7.2 Hz, 3H), 2.38 (s, 3H). ^{13}C NMR (125 MHz, DMSO-d_6): δ 158.3, 147.4, 142.2, 139.5, 138.7, 133.0, 132.3, 129.5, 128.8 (d, J = 75 Hz), 127.6, 127.1, 123.8, 117.2, 116.0, 104.1, 20.7. IR (KBr): v 3446, 3062, 3038, 2914, 2233, 1665, 1619, 1533, 1490, 1277, 1092, 894, 831, 789, 769, 706 cm^{-1}. HRMS (ESI-TOF): calcd. for $C_{19}H_{14}ClN_2O$ $(M + H)^+$ 321.0789, found 321.0794.

4.2.16. 5-(4-nitrophenyl)-2-oxo-1-m-tolyl-1,2-dihydropyridine-3-carbonitrile (**4ec**): yellow solid (603 mg, 91%), m.p. 270-272 ^{o}C. ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.85 (d, J = 2.7 Hz, 1H), 8.62 (d, J = 2.7 Hz, 1H), 8.25 (d, J = 9.0 Hz, 2H), 8.02 (d, J = 9.0 Hz, 2H), 7.46 (t, J = 7.5 Hz, 1H), 7.34-7.39 (m, 3H), 2.39 (s, 3H). ^{13}C NMR (125 MHz, DMSO-d_6): δ 158.3, 147.4, 146.4, 143.7, 140.8, 139.4, 138.8, 129.6, 128.9, 127.2, 126.7, 123.8 (d, J = 15Hz), 116.0 (d, J = 85Hz), 104.3, 20.7. IR (KBr): v 3454, 3084, 2919, 2227, 1678, 1598, 1513, 1343, 1319, 1283, 1212, 1112, 853, 781, 754 cm^{-1}. HRMS (ESI-TOF): calcd. for $C_{19}H_{14}N_3O_3$ $(M + H)^+$ 332.1030, found 332.1031.

4.2.17. 5-(4-fluorophenyl)-2-oxo-1-m-tolyl-1,2-dihydropyridine-3-carbonitrile (**4fc**): pale yellow solid (408 mg, 67%), m.p. 172-173 ^{o}C. ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.70 (d, J = 2.7 Hz, 1H), 8.37 (d, J = 2.7 Hz, 1H), 7.73-7.78 (m, 2H), 7.45 (t, J = 7.5 Hz, 1H), 7.32-7.37 (m, 3H), 7.27 (t, J = 8.7 Hz, 2H), 2.39 (s, 3H). ^{13}C NMR (125 MHz, DMSO-d_6): δ 162.7, 160.8, 158.3, 147.6, 141.9, 139.5, 138.7, 130.57 (d, J = 10 Hz), 129.5, 128.8, 128.0 (d, J = 30 Hz), 127.2, 123.8, 117.5, 116.1, 115.6 (d, J = 85 Hz), 104.0, 20.7. IR (KBr): v 3445, 3027, 2222, 1664, 1614, 1508, 1271, 1229, 833, 769, 698 cm^{-1}. HRMS (ESI-TOF): calcd. for $C_{19}H_{14}FN_2O$ $(M + H)^+$ 305.1085, found 305.1087.

4.2.18. 4-amino-2-oxo-1,2-dihydroquinoline-3-carbonitrile (**4ak'**). Purified by

recrystallization from DMF/EtOAc; White solid (137 mg), m.p. 284-287 ^{o}C (Lit.[10] 321-323 ^{o}C). ^{1}H NMR (300 MHz, DMSO-d_6): δ 11.22 (s, 1H), 8.12 (d, J = 8.1 Hz, 1H), 7.86 (br.s, 2H), 7.57 (t, J = 7.5 Hz, 1H), 7.23 (d, J = 8.1 Hz, 1H), 7.17 (t, J = 7.5 Hz, 1H). ^{13}C NMR (125 MHz, DMSO-d_6): δ 160.7, 158.4, 139.5, 133.0, 123.7, 121.5, 116.7, 116.2, 111.4, 77.6. IR (KBr): v 3384, 3332, 3229, 3011, 2220, 1630, 1597, 1508, 1458, 1415, 1364, 754 cm^{-1}. HRMS (ESI-TOF): calcd. for $C_{10}H_8N_3O$ $(M + H)^+$ 186.0662, found 186.0663; calcd. for $C_{10}H_7N_3ONa$ $(M + Na)^+$ 208.0481, found 208.0478.

Acknowledgments

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Supplementary data

Electronic Supplementary Information (ESI) available: Copies of the ^{1}H NMR and ^{13}C NMR spectra for all final products of **4aa-4al**, **4bc-4fc** and the compound **4ak'**.

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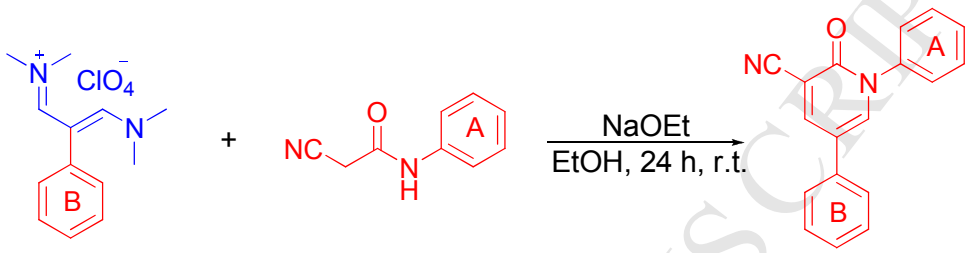
Graphical Abstract



2-aryl vinamidinium salts *N*-aryl cyanoacetamides 1,5-diaryl pyridin-2(1*H*)-ones

A simple, non-metal catalyzed method has been developed for the synthesis of 1,5-diaryl pyridin-2(1*H*)-one derivatives in good yields.

Supplementary Material

One step synthesis of 1,5-diaryl pyridin-2(1*H*)-ones from 2-aryl vinamidinium salts and *N*-aryl cyanoacetamides

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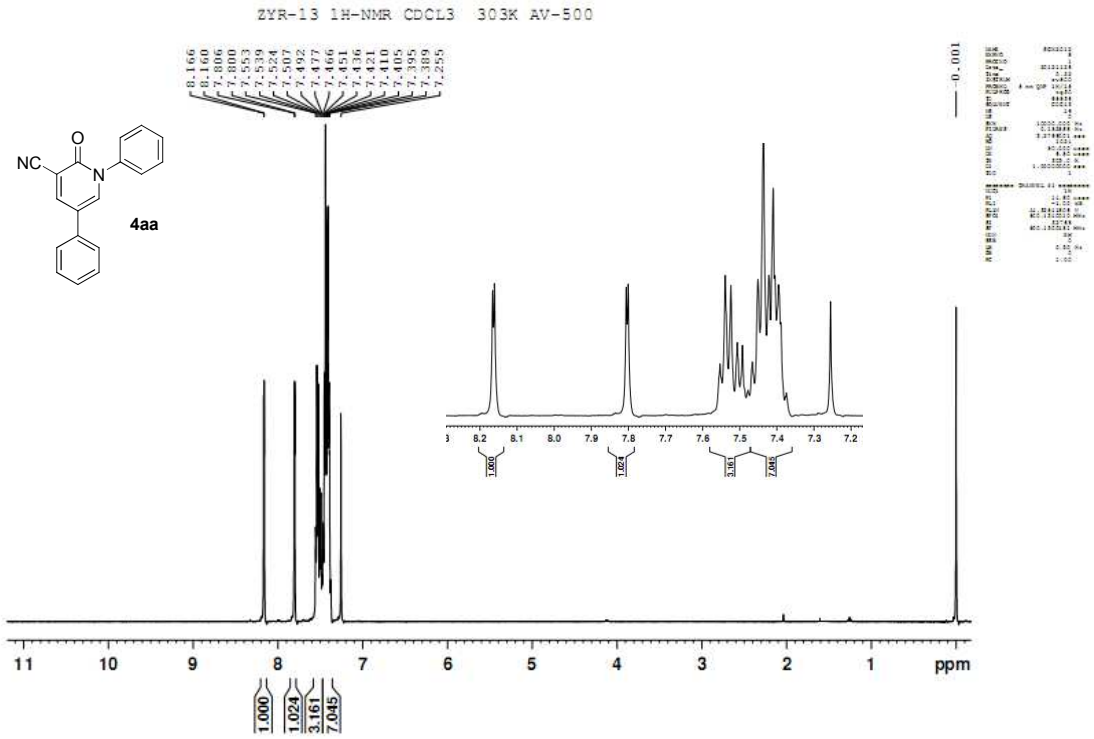
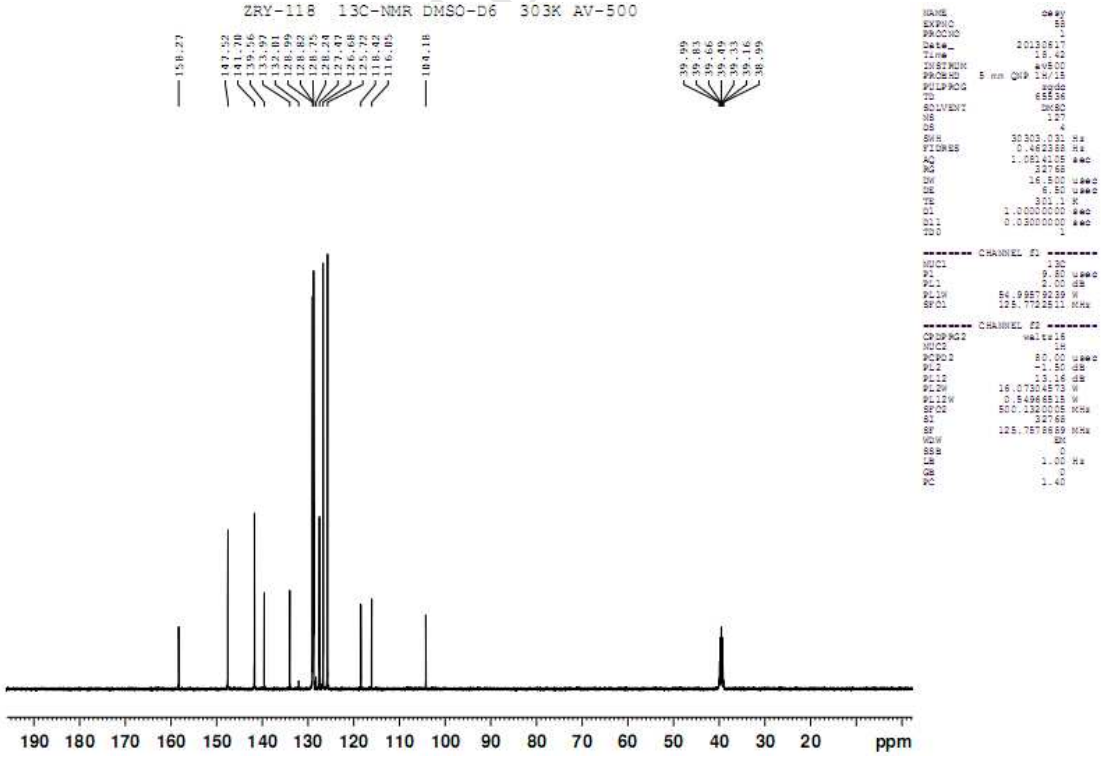
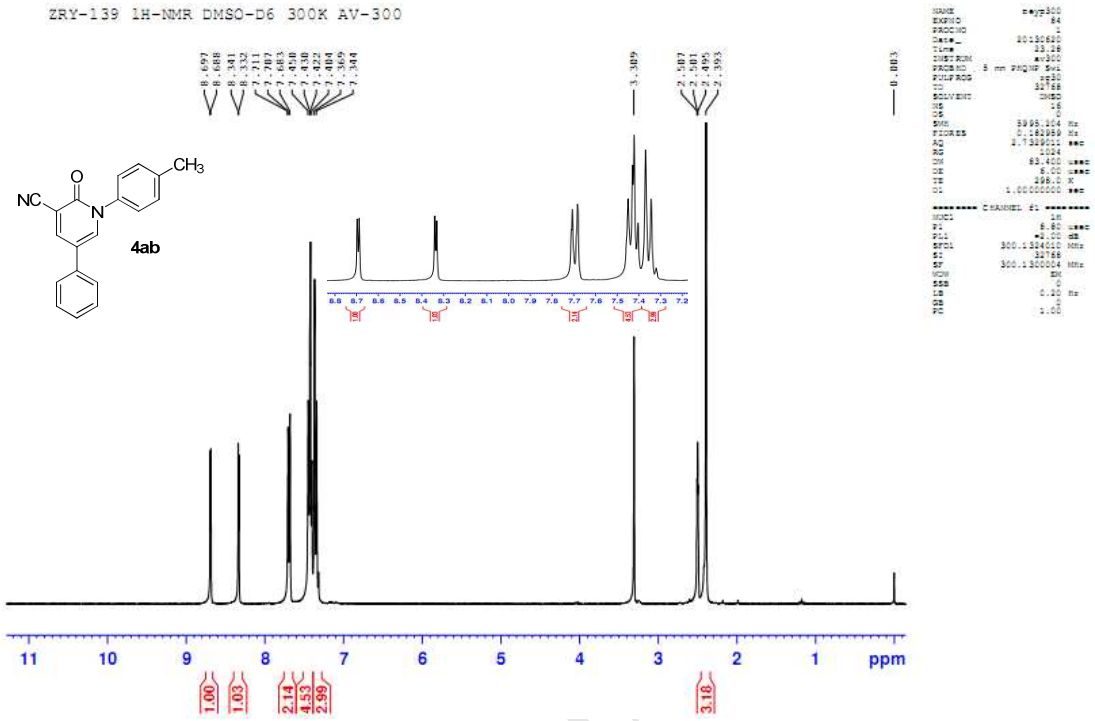
List of ^{1}H NMR and ^{13}C NMR spectra for compounds 4aa-4al, 4bc-4fc and 4ak'

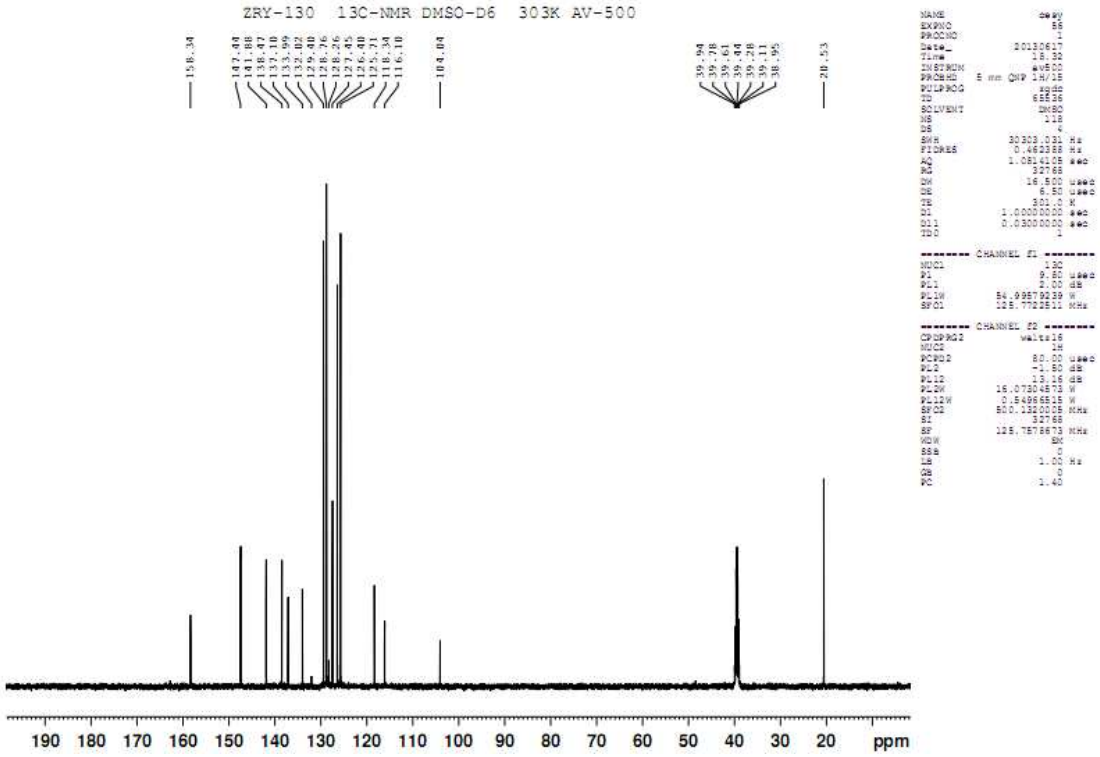
^{1}H NMR and ^{13}C NMR of 4aa





^{1}H NMR and ^{13}C NMR of 4ab





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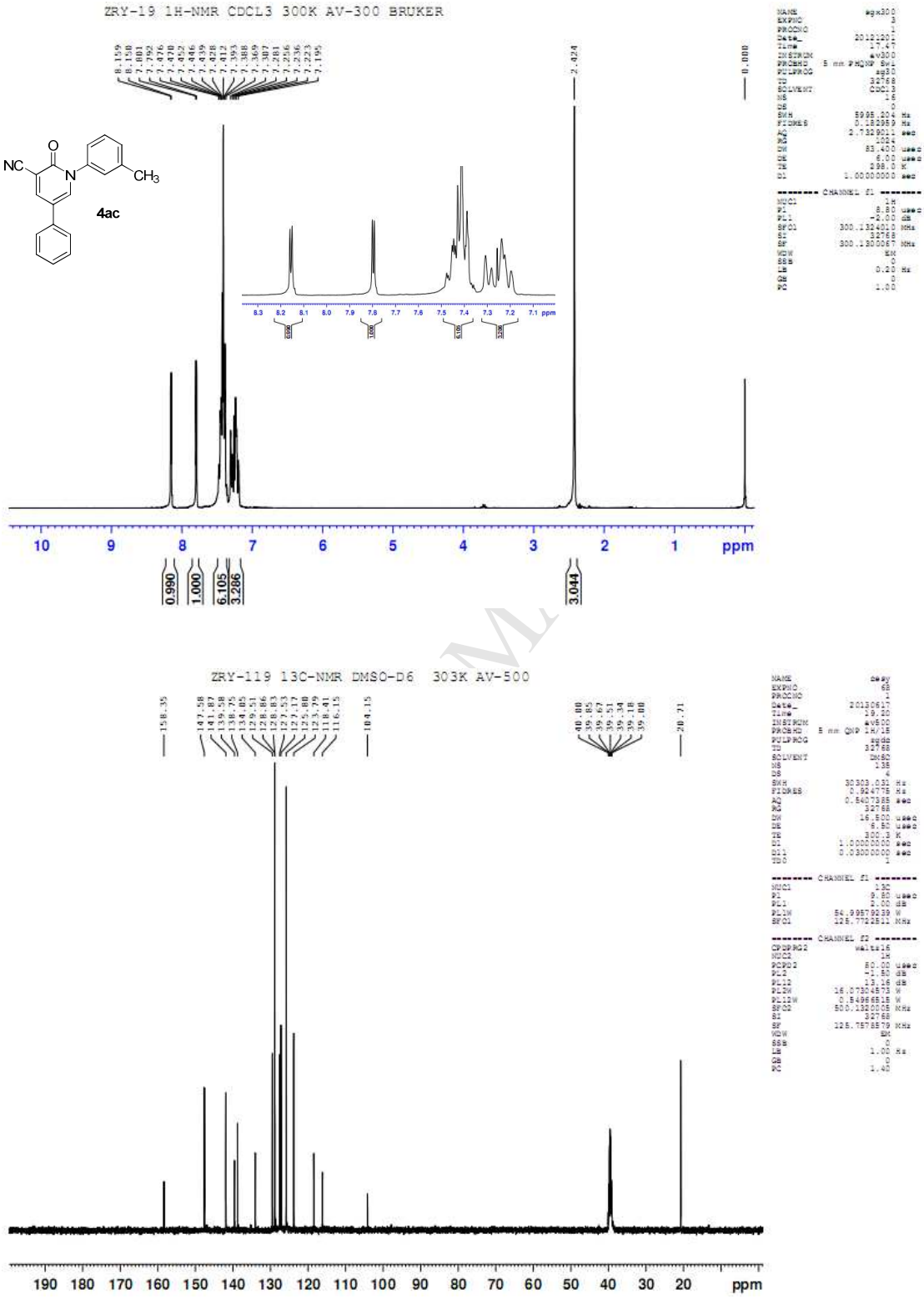
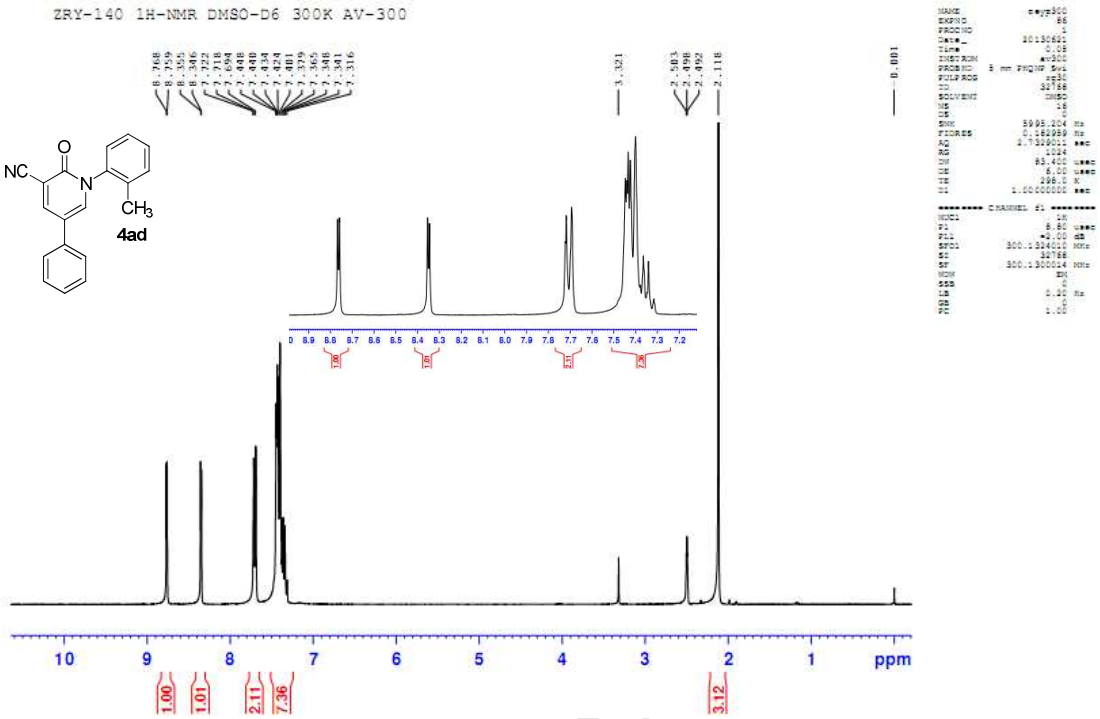
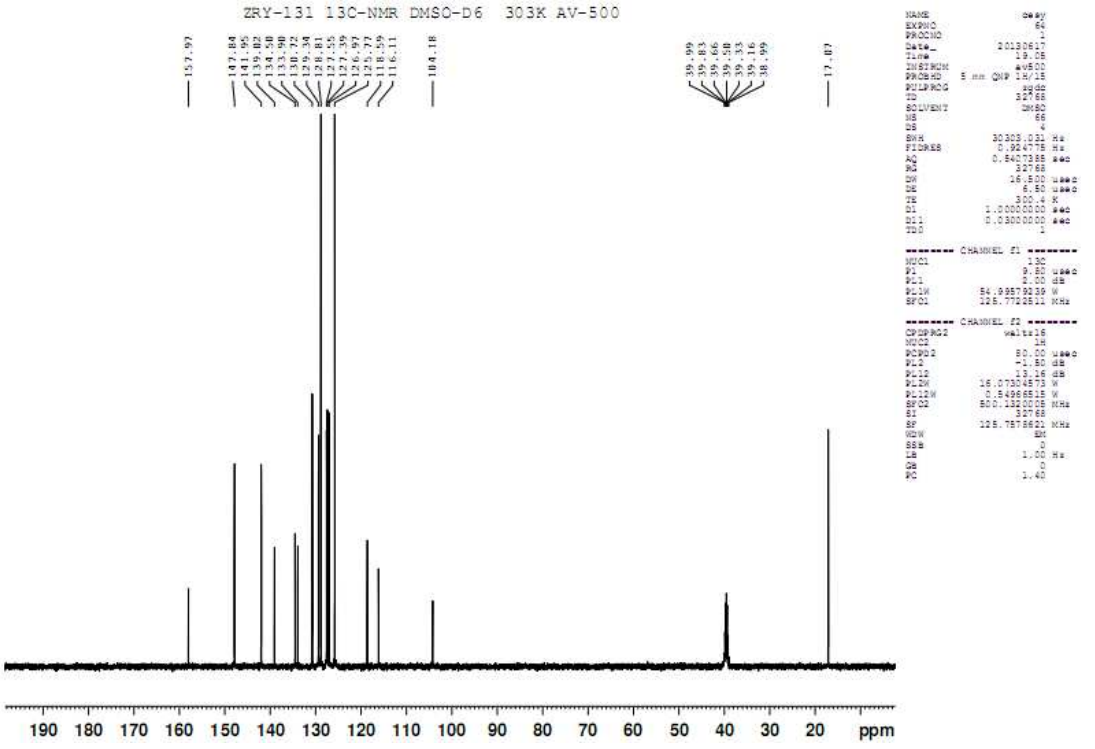
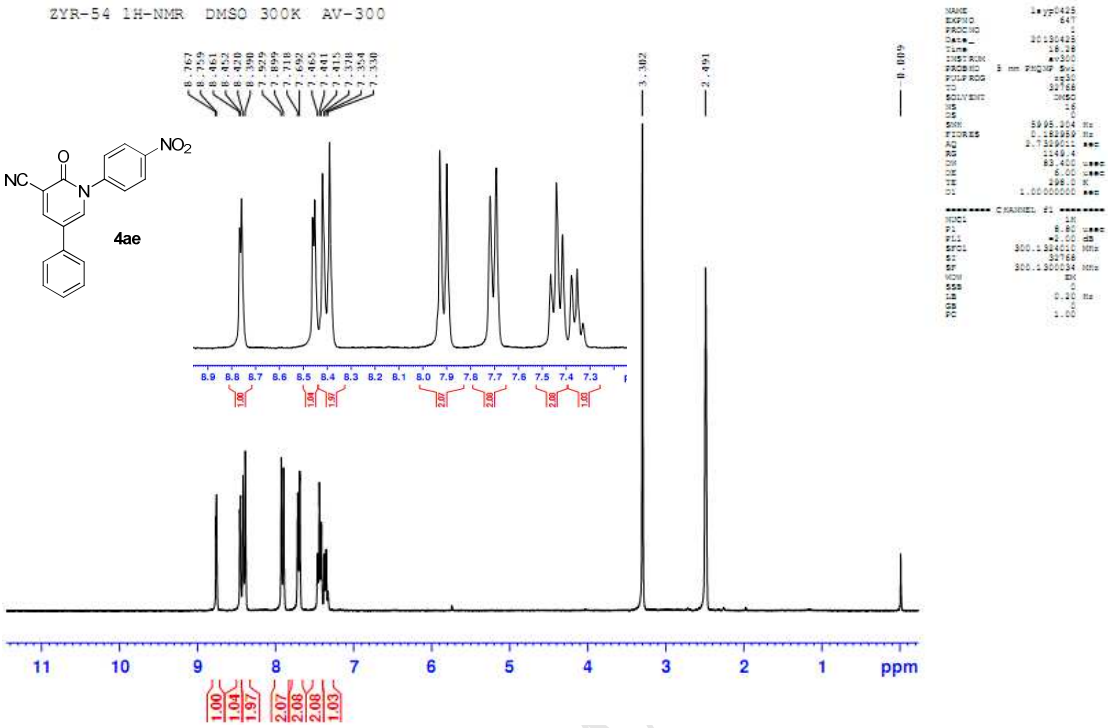


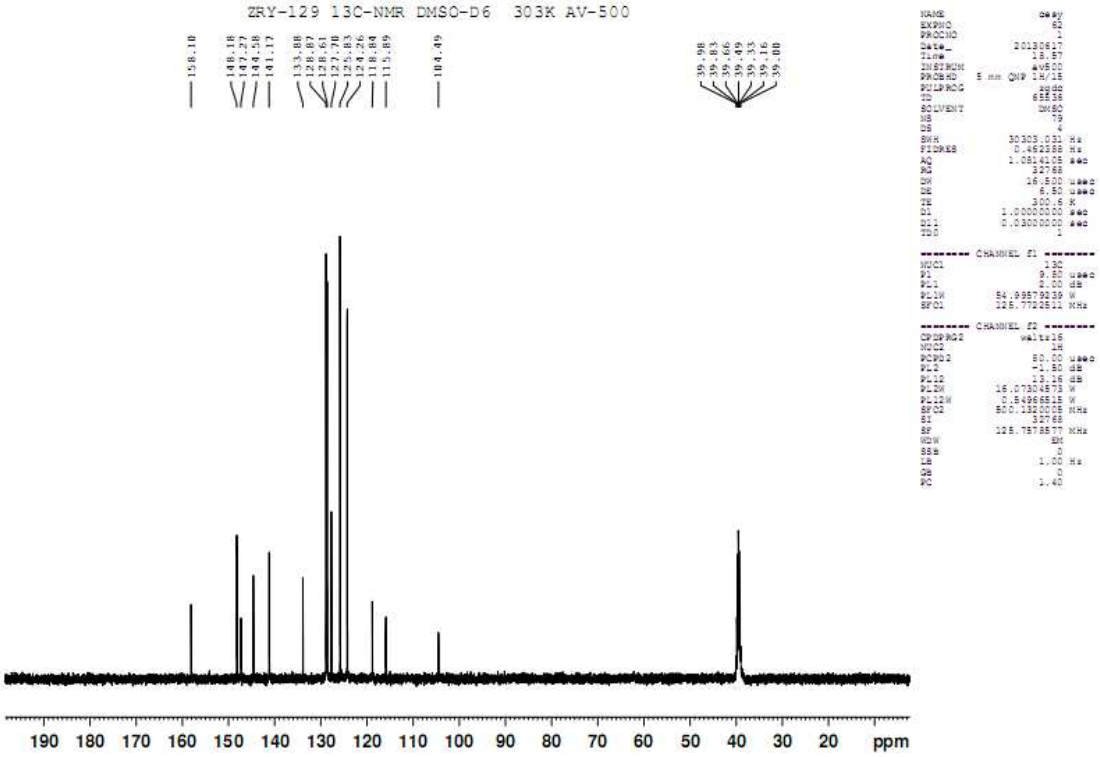
^{1}H NMR and ^{13}C NMR of 4ad





^{1}H NMR and ^{13}C NMR of 4ae





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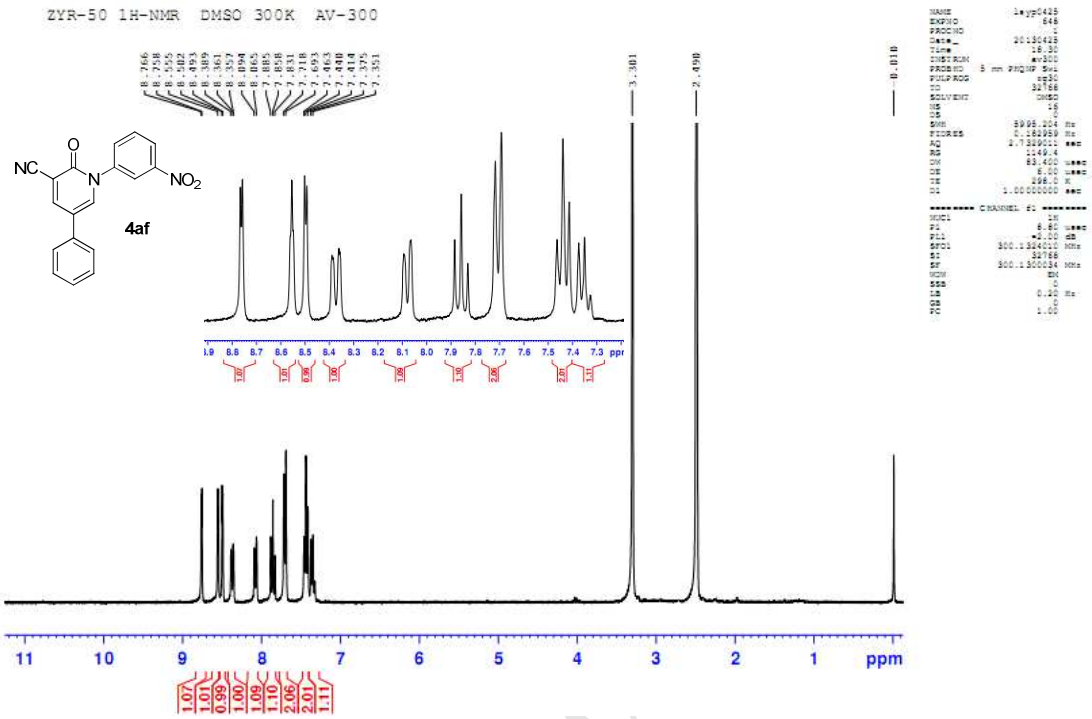

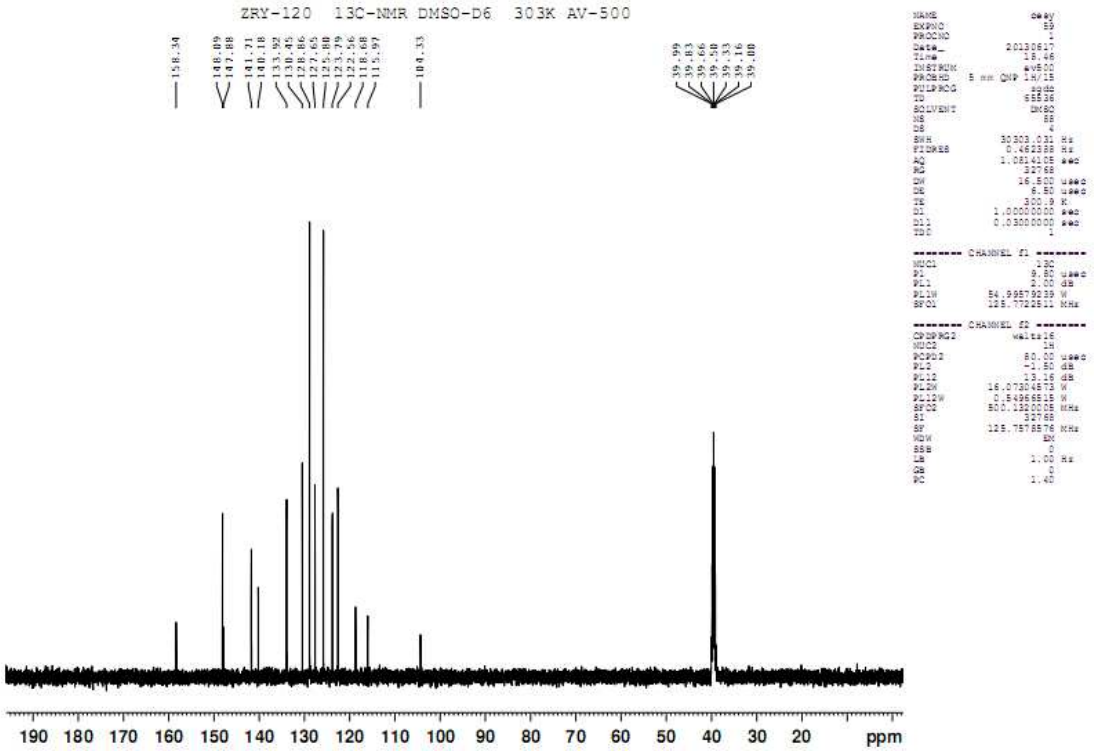

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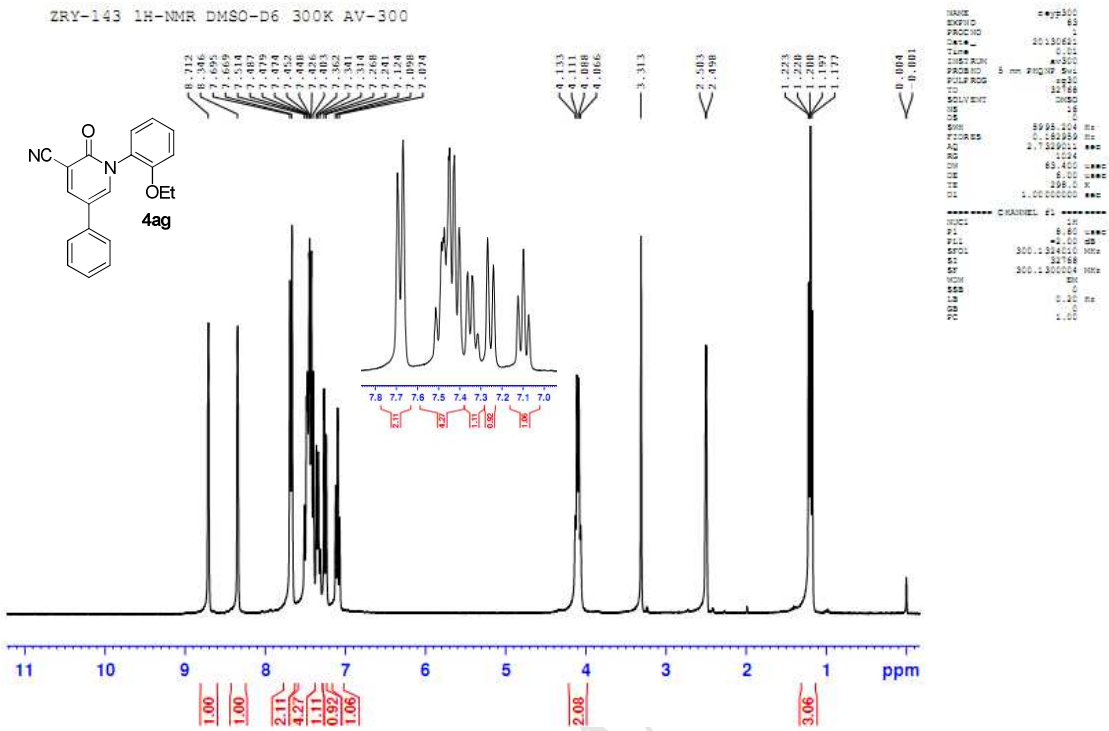

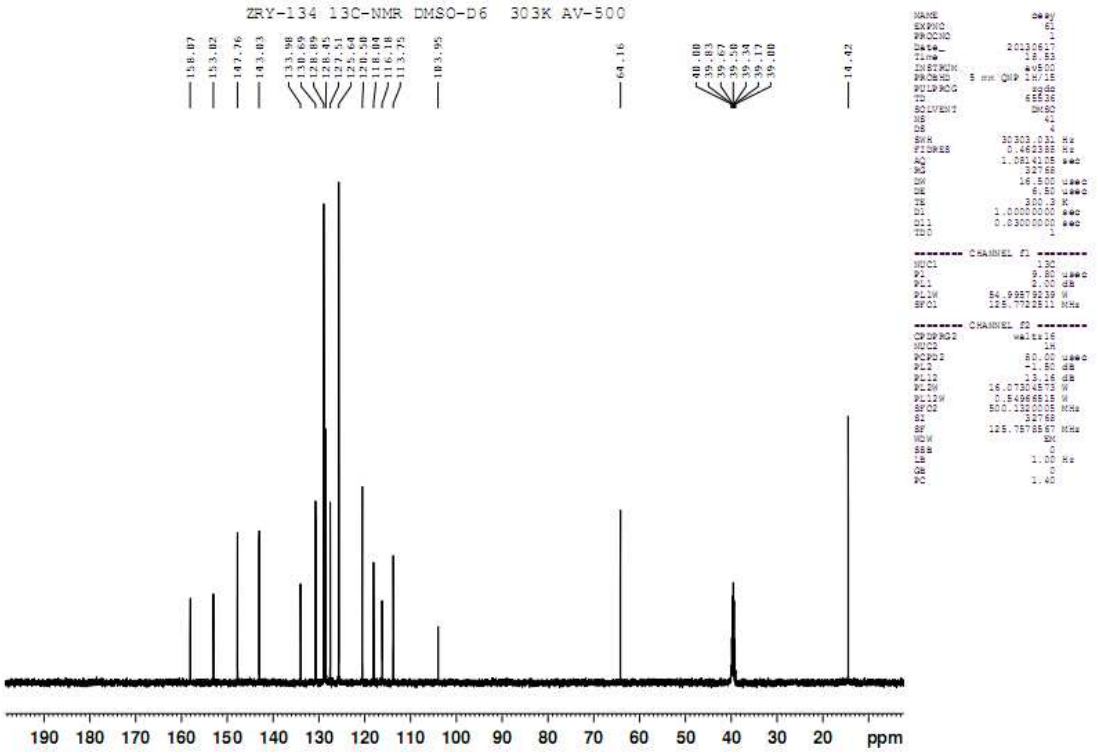

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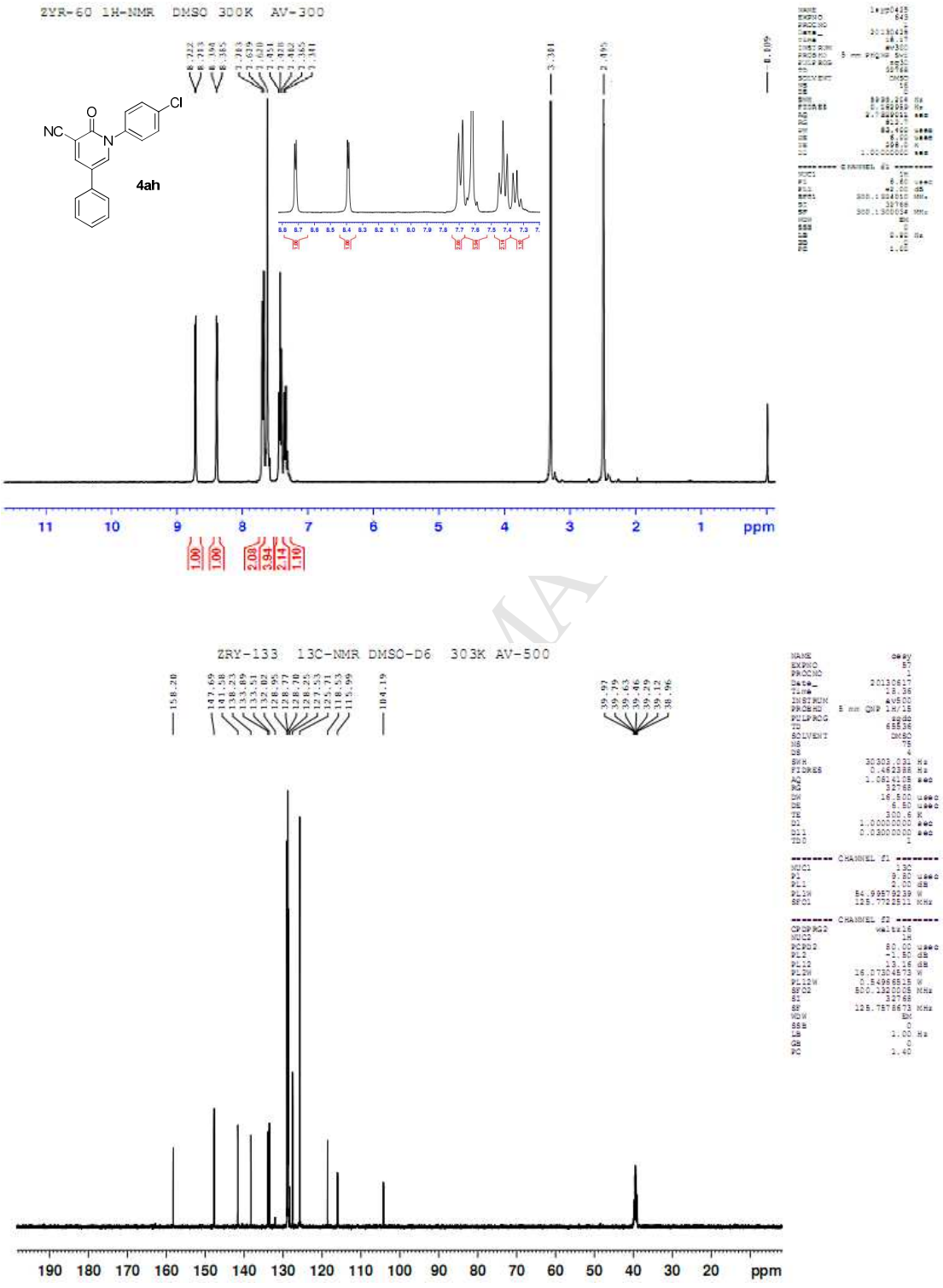
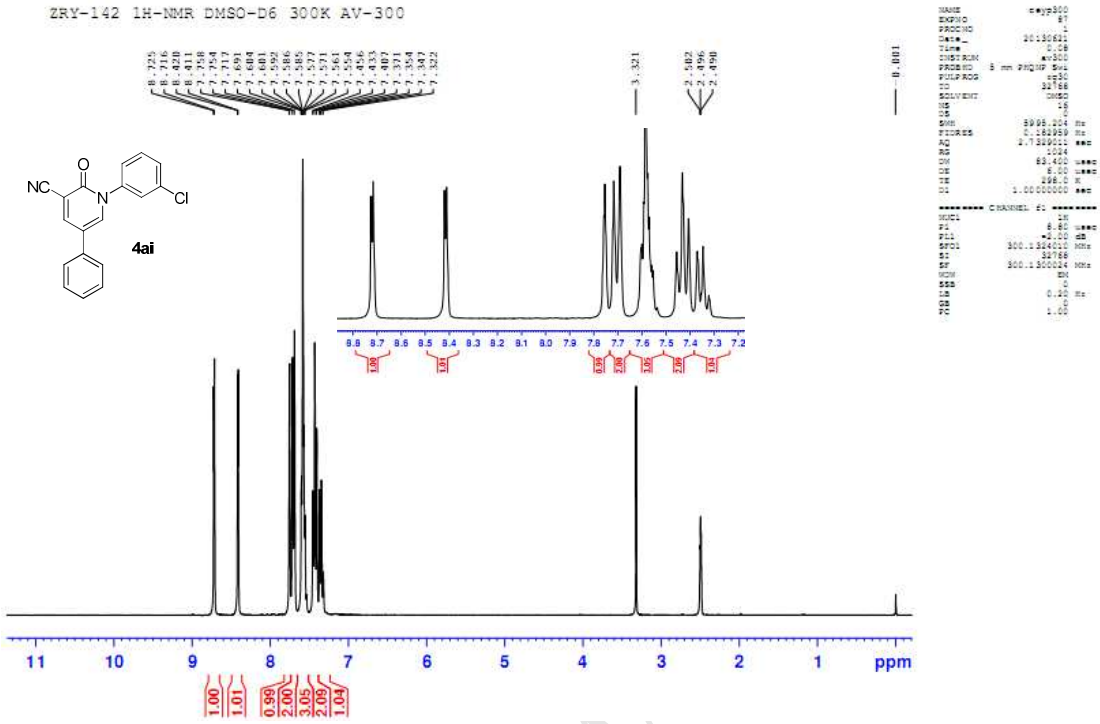
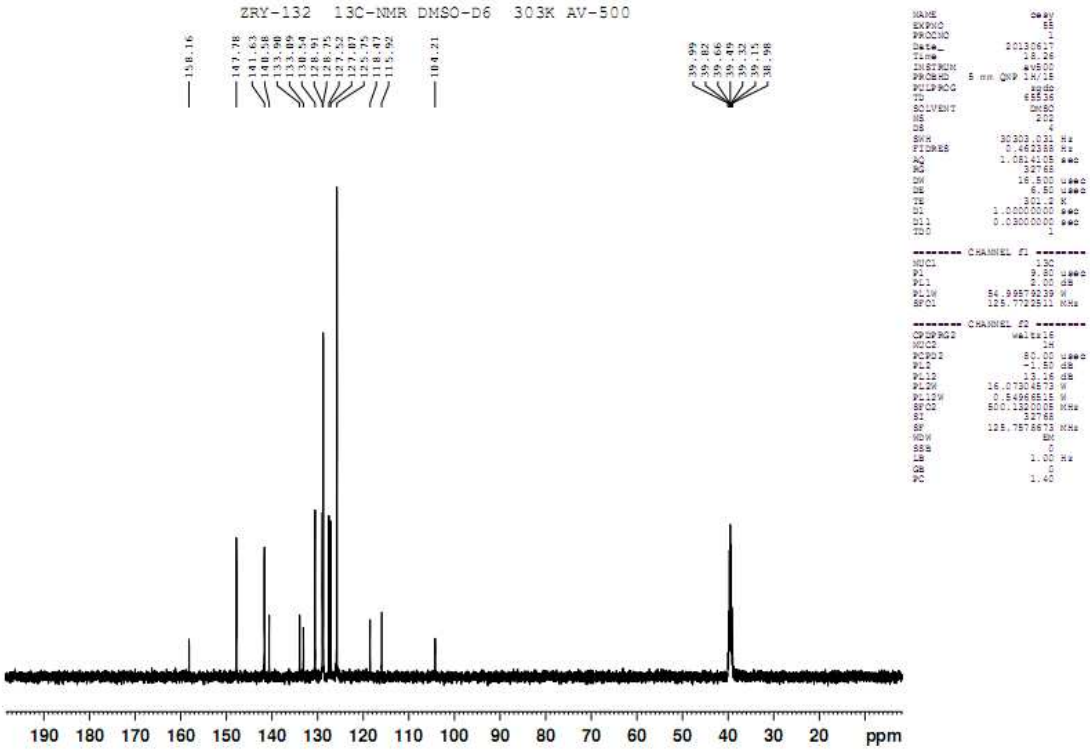
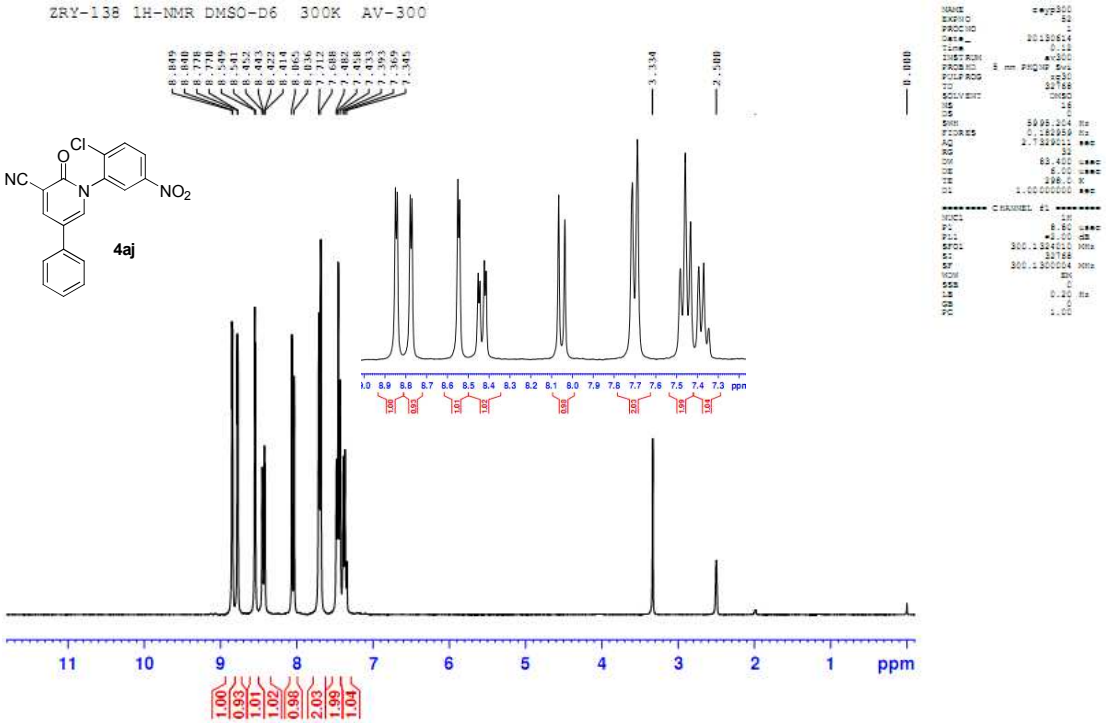


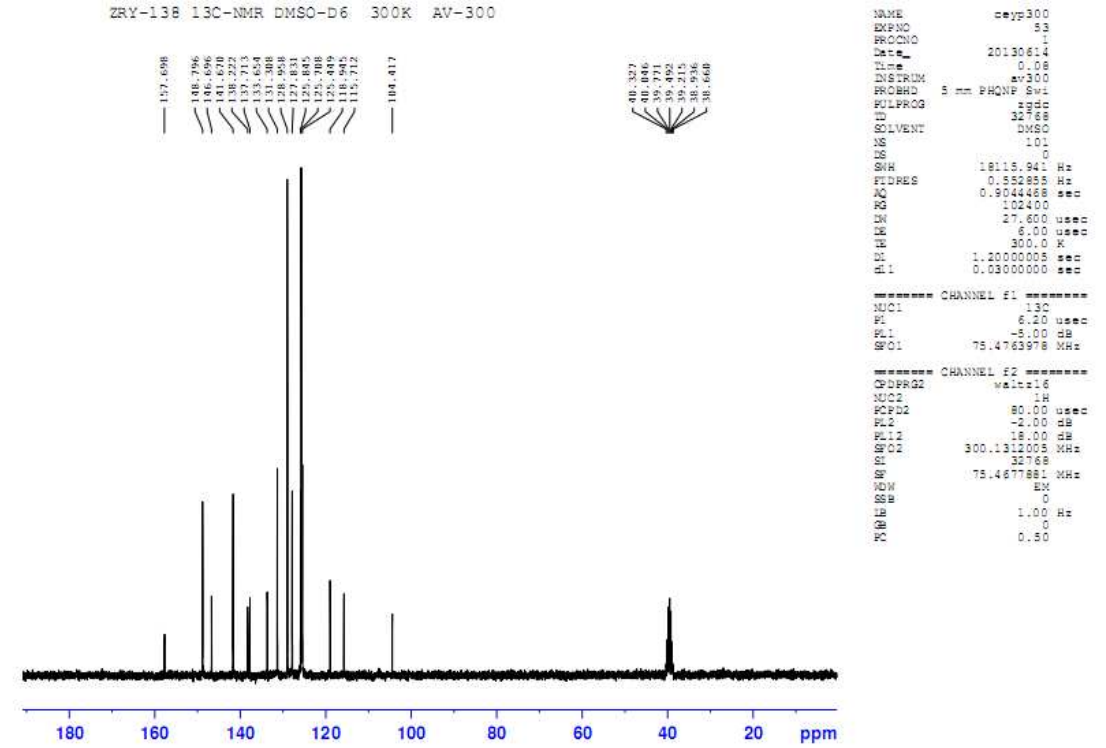
^{1}H NMR and ^{13}C NMR of 4ai



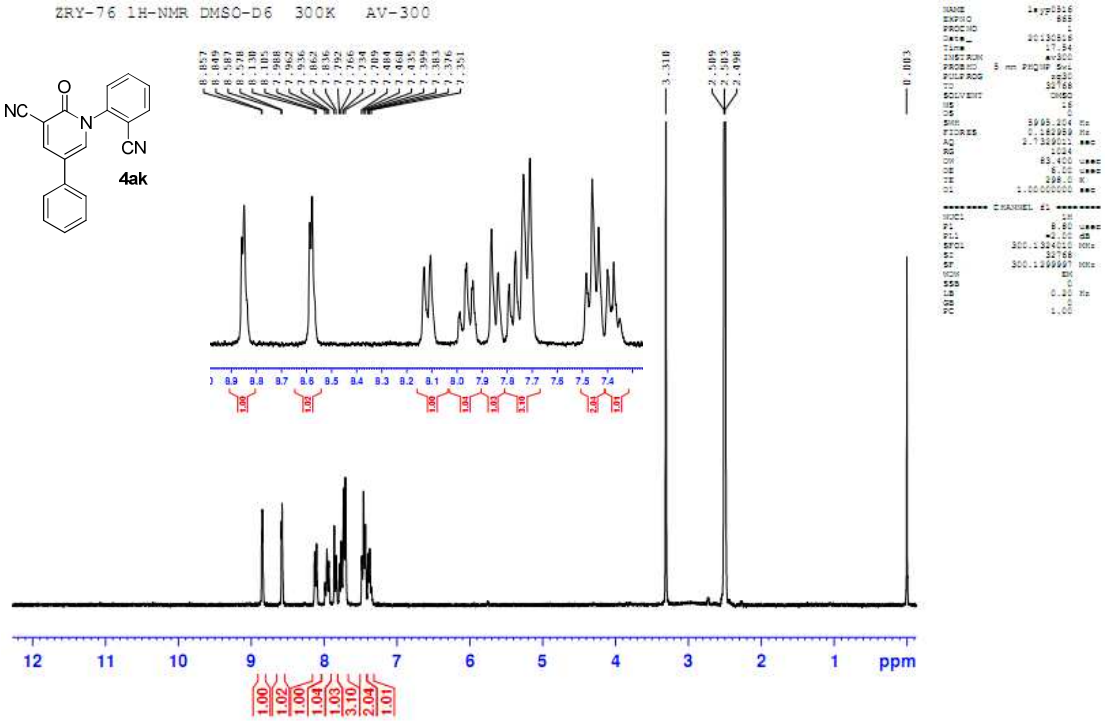


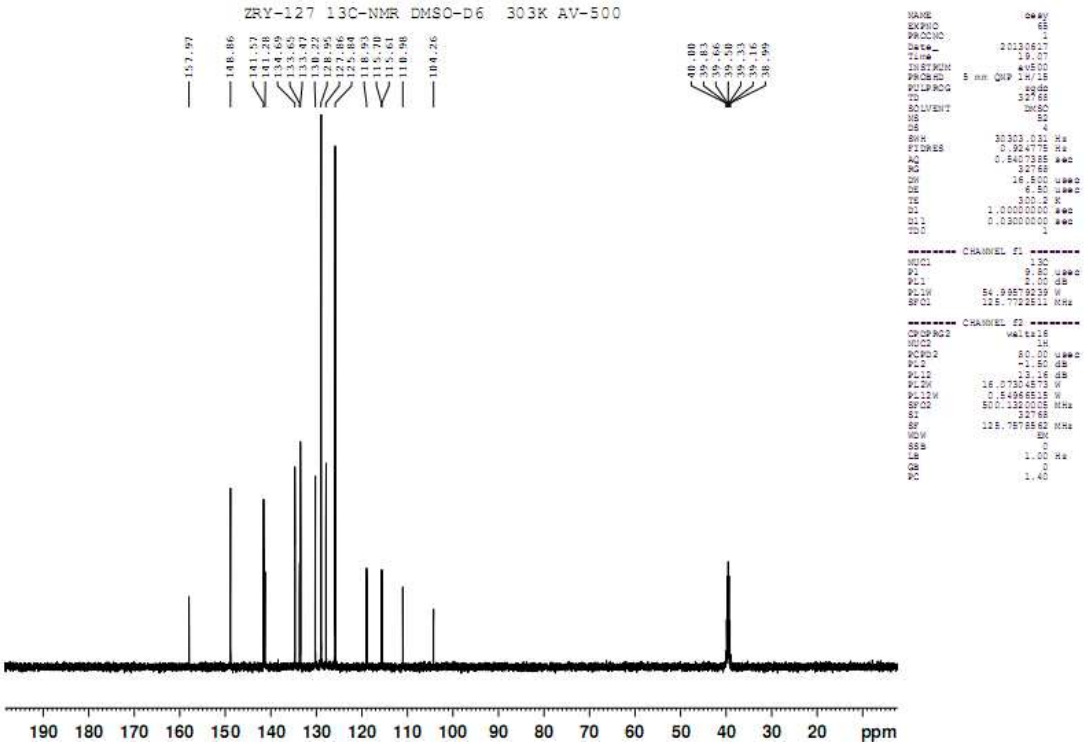
^{1}H NMR and ^{13}C NMR of 4aj



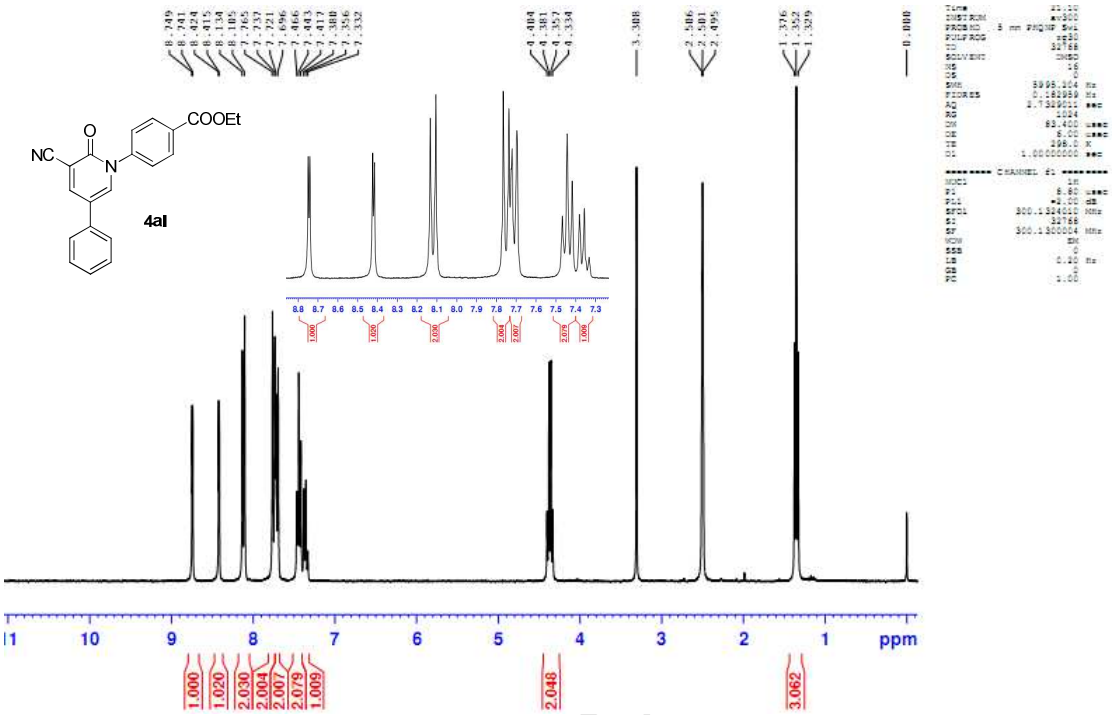


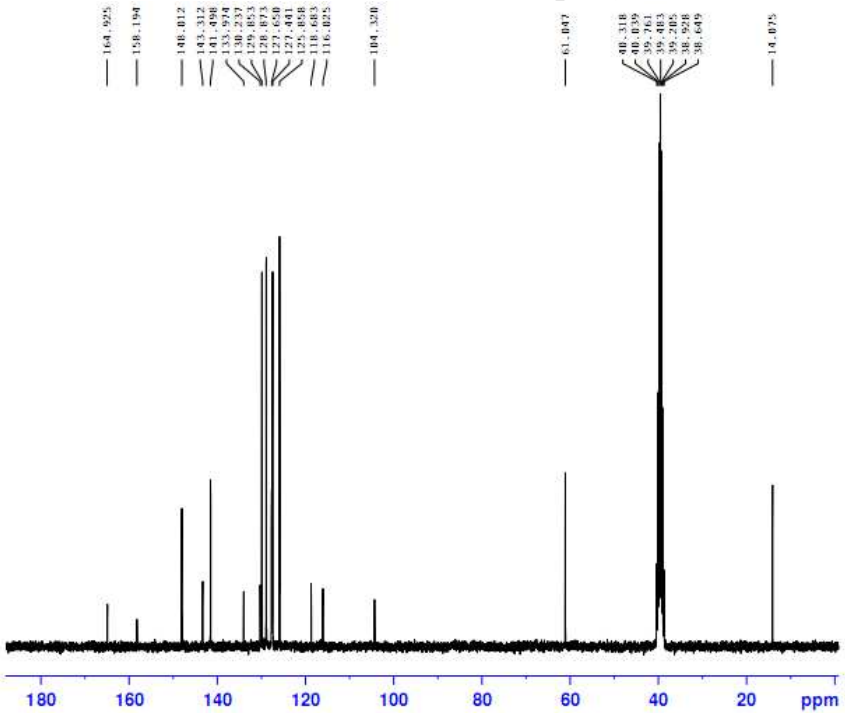
^{1}H NMR and ^{13}C NMR of 4ak



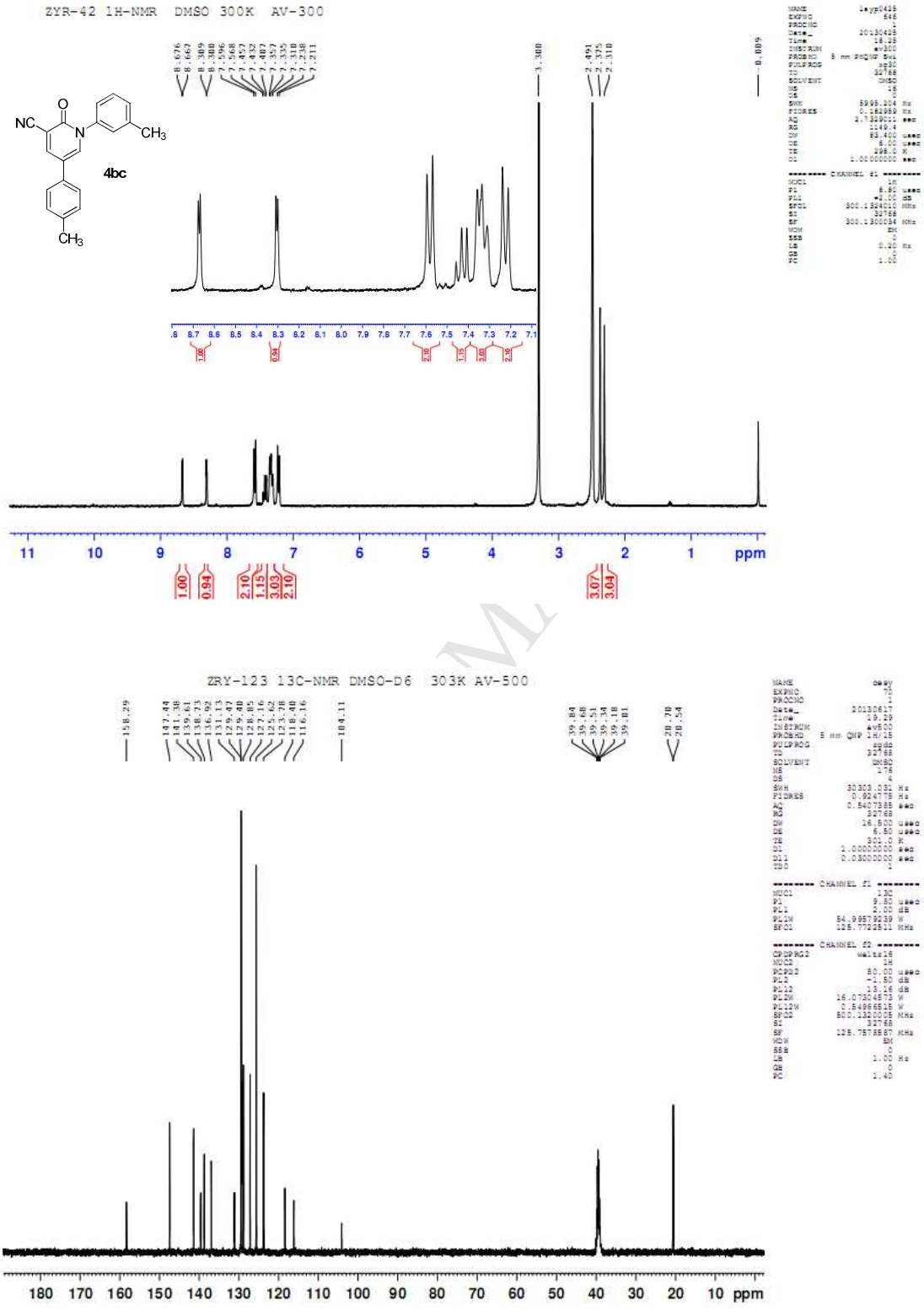


^{1}H NMR and ^{13}C NMR of 4al

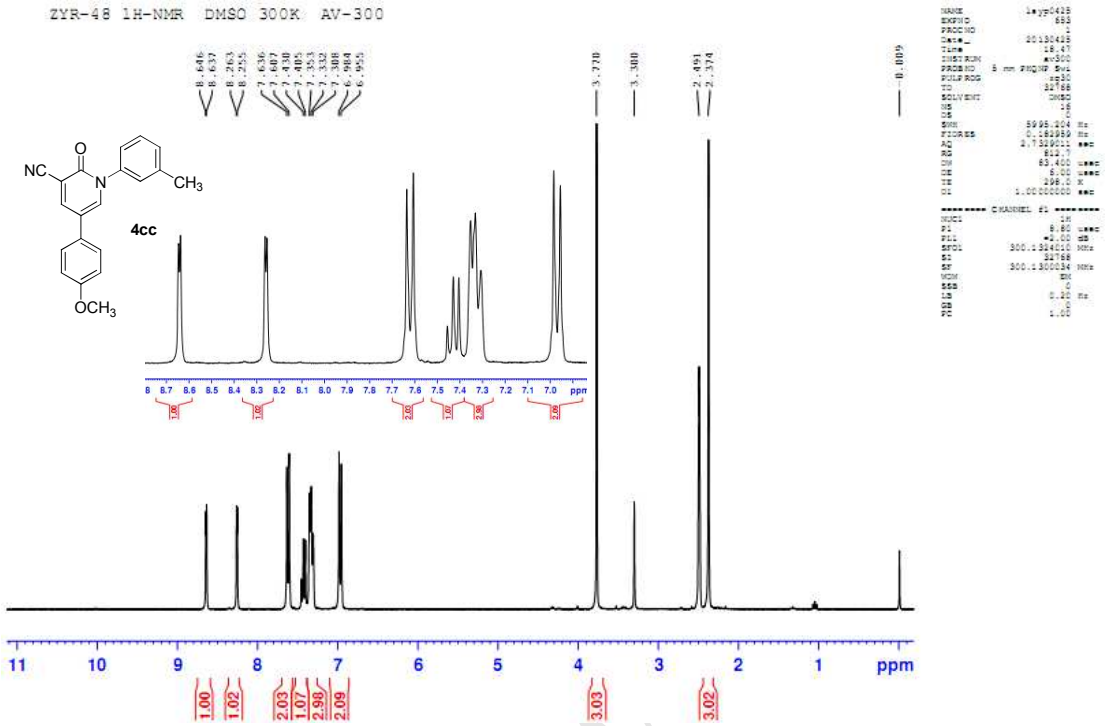


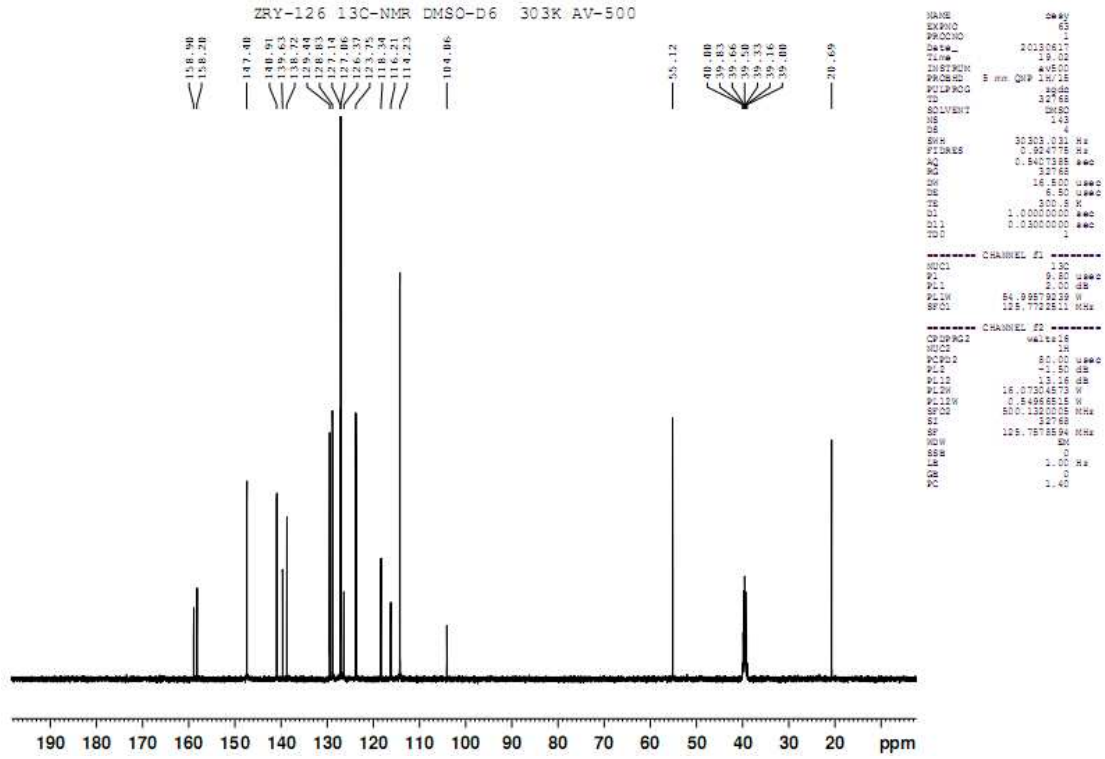


^{1}H NMR and ^{13}C NMR of 4bc

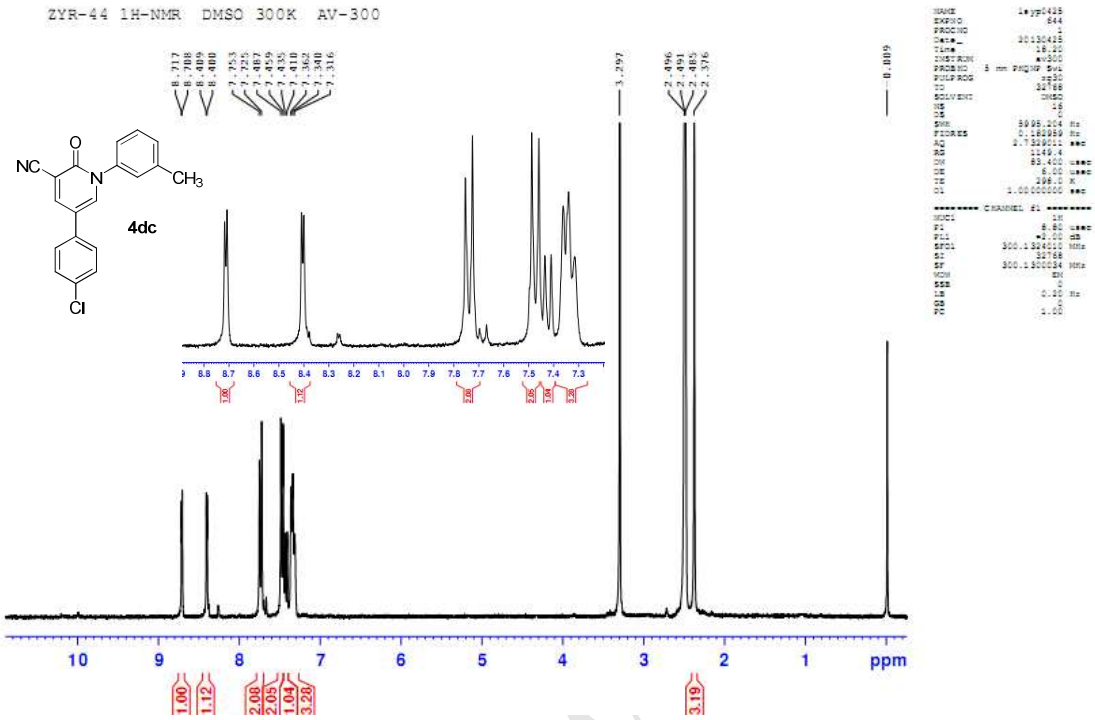


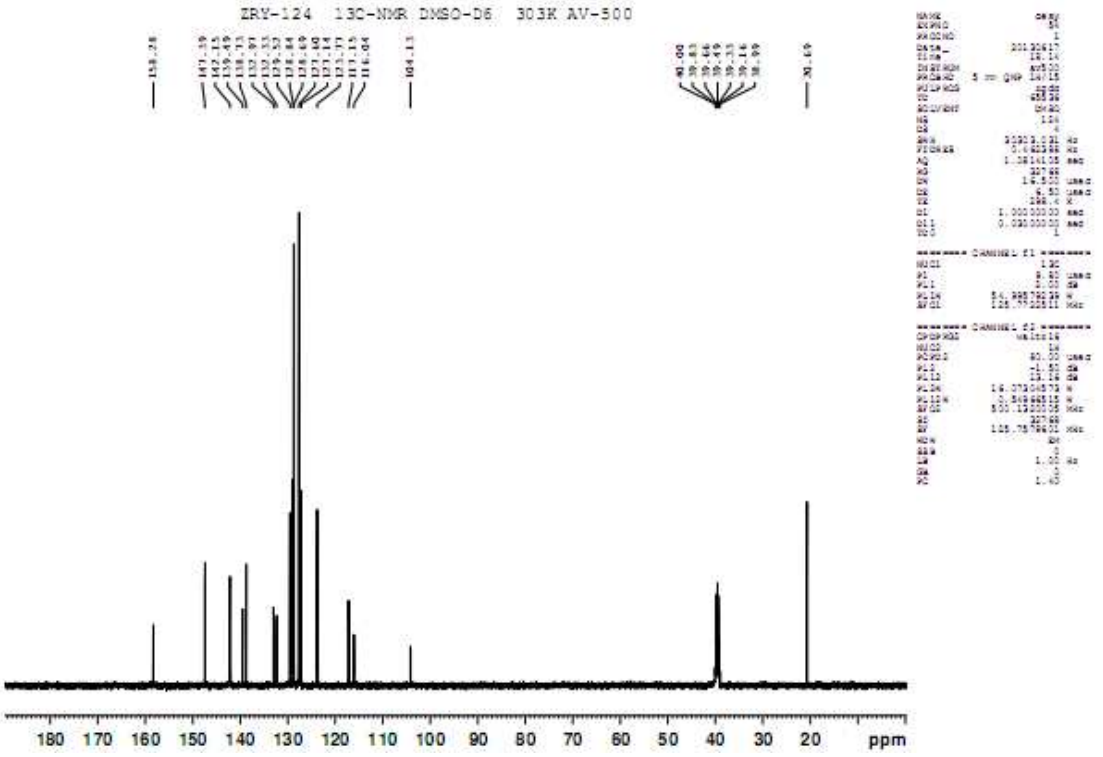
^{1}H NMR and ^{13}C NMR of 4cc



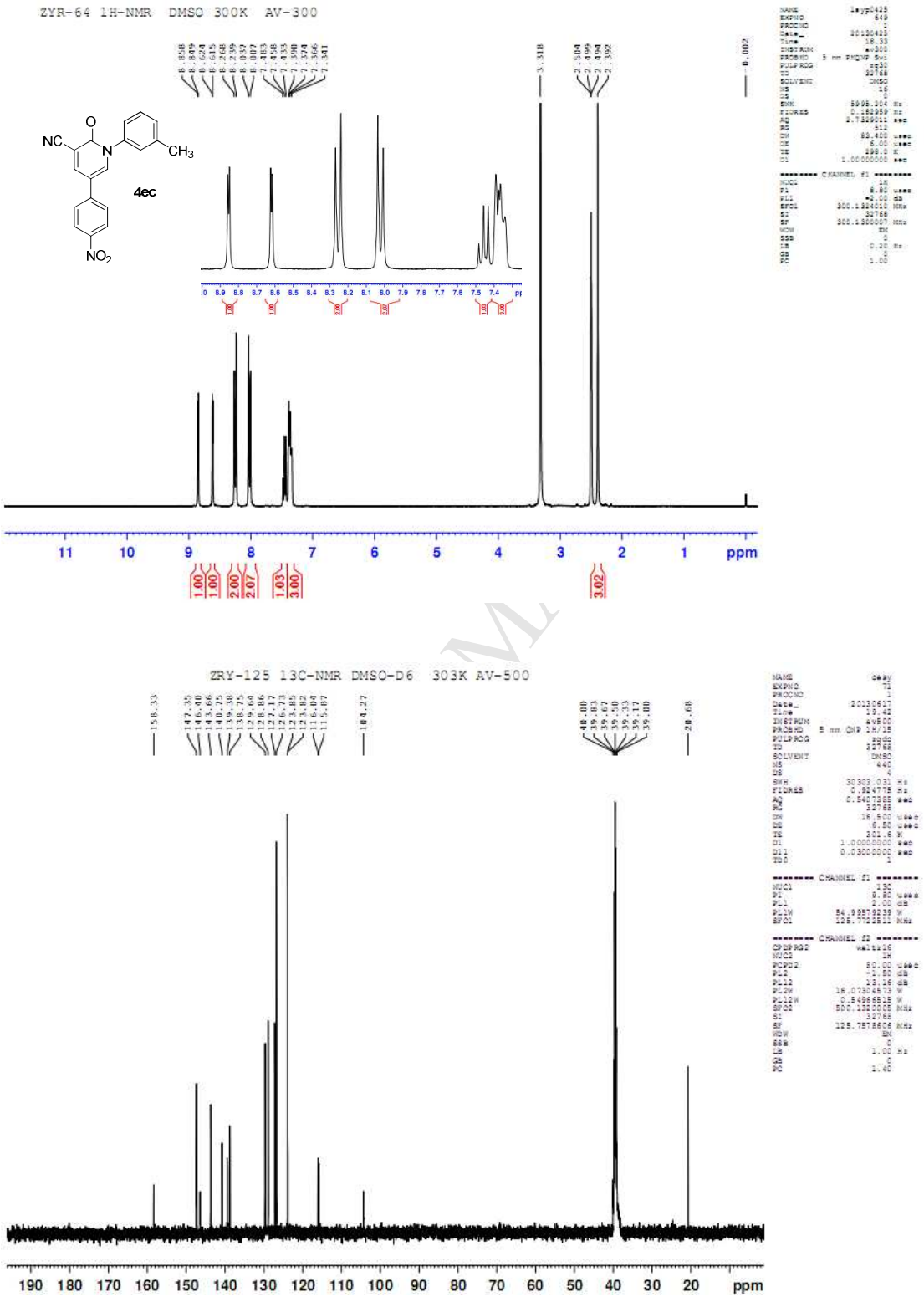


^{1}H NMR and ^{13}C NMR of 4dc

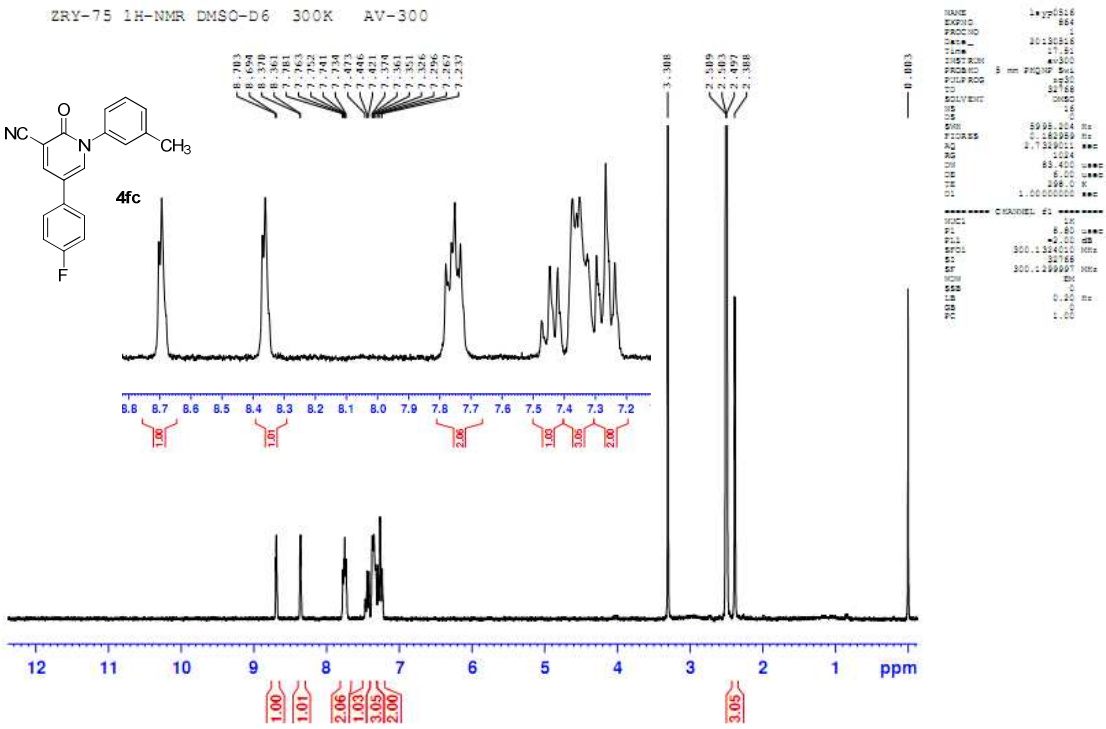


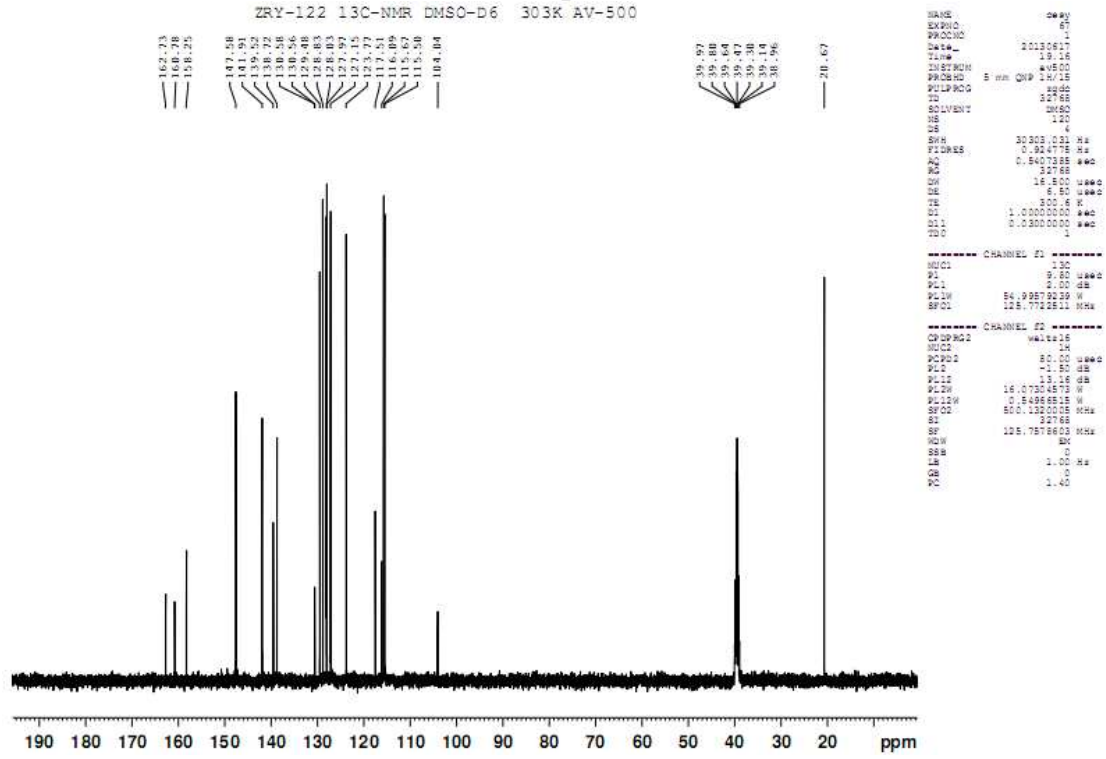


^{1}H NMR and ^{13}C NMR of 4ec



^{1}H NMR and ^{13}C NMR of **4fc**





^{1}H NMR and ^{13}C NMR of 4ak'