

Indium(III)-Catalyzed Synthesis of *N*-Substituted Pyrroles under Solvent-Free Conditions

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Vários pirróis *N*-substituídos foram sintetizados pela reação de γ -dicetonas ($R^1C(O)CH_2CH_2C(O)R^2$; $R^1, R^2 = Me, Ph$) com aminas (RNH_2 ; $R = Alkyl, Aryl, TsNH$) ou diaminas (1,6-diaminohexano and 1,2-diaminoetano) na presença de tribrometo de índio, tricloreto de índio ou trifluorometanossulfonato de índio a temperatura ambiente e sem solventes. O protocolo envolve operações simples e os produtos são isolados em excelentes rendimentos (81-98%).

A variety of *N*-substituted pyrroles have been synthesized by reacting γ -diketones ($R^1C(O)CH_2CH_2C(O)R^2$; $R^1, R^2 = Me, Ph$) with amines (RNH_2 ; $R = Alkyl, Aryl, TsNH$) or diamines (1,6-diaminohexane and 1,2-diaminoethane) in the presence of indium tribromide, indium trichloride or indium trifluoromethanesulfonate at room temperature under solvent-free conditions. The experiment protocol features simple operations, and the products are isolated in high to excellent yields (81-98%).

Keywords: indium tribromide, indium trichloride, indium trifluoromethanesulfonate, pyrroles, solvent-free conditions

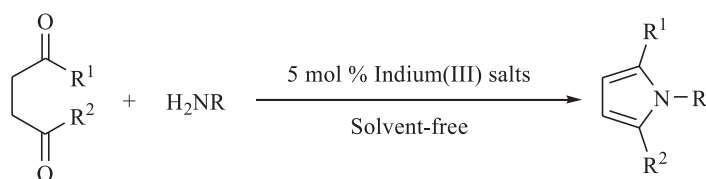
Introduction

Heterocyclic small molecules play an important role in the search for new therapeutic and drug candidates.¹ Pyrroles are an important class of heterocyclic compounds and are structural units found in a vast array of natural products, synthetic materials, and bioactive molecules, such as heme, vitamin B12, and cytochromes.² Pyrroles also play crucial roles in nonlinear optical materials as well as in supramolecular chemistry.³ Therefore, the enormous number of procedures have been developed for the construction of pyrroles. Classical methods for their preparation include the Knorr,⁴ Hantzsch,⁵ and Paal-Knorr condensation reactions.⁶⁻¹⁶ Among these methods, the most commonly used and straightforward approach for the preparation of pyrroles is the direct condensation of γ -diketones and amines (Paal-Knorr reaction) in the presence of protonic acids such as AcOH,⁶ *p*-TsOH.⁷ Some improved procedures were reported to utilize Lewis acids such as $Bi(NO_3)_3 \cdot 5H_2O$,⁸ $Sc(OTf)_3$,⁹ $SnCl_2$ ¹⁰ and heterogeneous catalyst like montmorillonite (KSF,¹¹ K10¹² and Fe(III)¹³), zirconium compounds.¹⁴ Recently, this condensation reaction has also been performed under microwave technology¹⁵ and in ionic liquid medium.¹⁶

However, there are some limitations with these methodologies such as prolonged reaction times,^{11,14,16} elevated temperatures,⁷ use of volatile organic solvents,^{8,11} the requirement of excess reagents or catalysts,¹⁰ moisture sensitive/hazardous catalysts,¹⁰ use of an additional microwave oven,¹⁵ use of costly solvent (ionic liquids),¹⁶ unsatisfactory and yields¹⁴. Thus, the development of new reagents with great efficiency, environmentally friendly, convenient procedure, and delivery of better yields methods for the synthesis of pyrroles is of great interest.

During the last decade particularly after the review by Cintas,¹⁷ indium(III) based carbon-carbon bond formation and other organic transformations have gained much attention. In accordance with the recent surge of interest in indium(III) salts has emerged as a promising catalyst for various types of organic transformations. Particularly, indium tribromide,¹⁸ indium trichloride¹⁹ and indium trifluoromethanesulfonate²⁰ as a novel type of water-tolerant green Lewis acid catalyst have received considerable attention for various transformations, because they have advantages of water stability, operational simplicity, recyclability, strong tolerance to oxygen and nitrogen-containing reaction substrates and functional groups, and it can often be used in just catalytic amounts. Recently, Zhang²¹ reported a few examples of $InBr_3$ -catalyzed organic

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Scheme 1.

reactions. Ghosh and coworkers²² reviewed systematically In(OTf)₃-catalyzed organic syntheses.

In continuation of our interest in Lewis acid-catalyzed and green chemistry organic reactions,²³ we herein wish to report a simple, practical and efficient method for the synthesis of pyrroles from γ -diketones and amines using indium(III) salt as catalyst at room temperature under solvent-free conditions (Scheme 1).

Results and Discussion

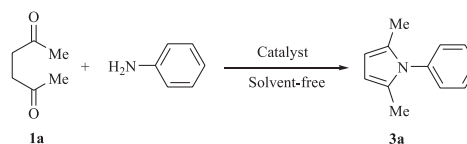
Initially, the efficacy of various catalysts was tested in the model reaction under solvent-free condition at room temperature (Table 1). The results showed that InCl₃, InBr₃ and In(OTf)₃ were superior to other Lewis acids with respect to reaction times and product yields. Entry 1 showed the blank reaction without addition of any catalyst, in this case only 29% 2,5-dimethyl-1-phenyl-1*H*-pyrrole (**3a**) was obtained after 24 h. For the sake of comparison, the reaction was carried out using other anhydrous chloride, such as ZnCl₂, NiCl₂, SrCl₂ and CuCl₂ under solvent free conditions (Entries 2-8). However, these chlorides showed lower activity than InCl₃ under same reaction conditions. We examined influence of solvents on the reaction yields. It was found that the reactions gave lower yields of the desired product in solvents such as CH₂Cl₂, H₂O, CH₃NO₂ after prolonged reaction time. (Entries 10-13, 15-18, 20-23). We also checked the reusability of the catalyst by separation and reloading in a new run and found that the catalyst could be reused three times without any decrease in the yield (Entry 19). In light of these good results, subsequent studies were carried out under the following optimized conditions: with 5 mol% InBr₃, InCl₃ or In(OTf)₃ at room temperature under solvent-free conditions.

To evaluate the scope of catalyst's application, various γ -diketones were treated with amines under the above conditions and the results presented in Table 2. The desired products were characterized by NMR, IR and mass spectrometry and also by comparison with authentic samples.

The Indium(III)-catalyzed reactions were found to be dependent on electronic and steric factors of amines.

Anilines with electron-donating groups gave a high yield (up to 98%) due to the increased electron density of the aromatic system (entries 2 and 6). Whereas anilines with strongly electron-withdrawing group (NO₂) afforded in moderate yield (71%) after 40 min (entry 7), which showed electronic effect. *ortho*-substituted anilines whatever the

Table 1. The condensation reaction of acetylacetone with aniline under various reaction conditions^a

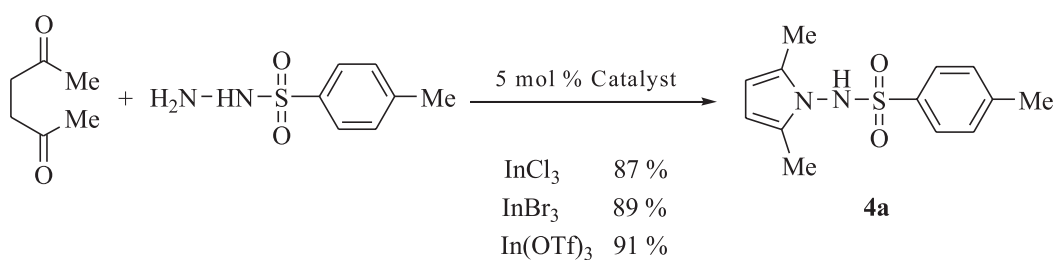


Entry	Catalyst	time/(h)	Yields/(%) ^b
1	none	24	29
2	ZnCl ₂	1.5	51
3	CoCl ₂	2	47
4	NiCl ₂	3	39
5	SrCl ₂	4	41
6	CuCl ₂	2	39
7	Cu(OAc) ₂	3	59
8	Mn(OAc) ₂	3.5	51
9	InBr ₃	0.5	93
10	InBr ₃	0.5	93 ^d
11	InBr ₃	1	84 ^e
12	InBr ₃	1	81 ^f
13	InBr ₃	1	85 ^g
14	InCl ₃	0.5	90
15	InCl ₃	0.5	92 ^d
16	InCl ₃	1	87 ^e
17	InCl ₃	1	83 ^f
18	InCl ₃	1	86 ^g
19	In(OTf) ₃ ^b	0.5	95, 92, 89
20	In(OTf) ₃	0.5	96 ^d
21	In(OTf) ₃	1	91 ^e
22	In(OTf) ₃	1	85 ^f
23	In(OTf) ₃	1	88 ^g

^aGeneral reaction conditions: acetylacetone (5 mmol), aniline (5 mmol), catalyst (5 mol%), rt. ^bIn(OTf)₃ was reused for three times. ^cIsolated yield.

^d10 mol% was used. ^e2 mL of CH₂Cl₂ were used. ^f2 mL of H₂O were used.

^g2 mL of CH₃NO₂ were used.



Scheme 2.

character of the substituted groups required longer reaction times. It was revealed that yields were significantly decreased when the sizes of the *ortho*-substituent groups were large. For example, 2,6-dimethylaniline or 2,6-diisopropylaniline (entries 4-5) were found to be less active and gave mild yields after 1 h. This may be due to the steric hindrance exhibited by the 2,6-diisopropyl and 2,6-dimethyl groups of the aniline towards the approaching acetylacetone. Moreover, we also examined the condensation reaction of aliphatic amines with acetylacetone (entries 8-18). The corresponding products (**3h-3r**) were obtained with excellent yields. In the case of 1,6-diaminohexane or 1,2-diaminoethane, two equivalents of acetylacetone were used giving products with dipyrrolyl groups **3n** or **3o** (entries 14-15).

On the other hand, it was found that heterocyclic amines (2-aminopyridine) and less nucleophilic aromatic amine (α -naphthalenamine) did not make any difference in this reaction (entries 19 and 20). It is noteworthy that optically active amines were converted into the products (**3p-3q**) without any racemization or inversion (entries 16 and 17). We also investigated the reaction of various γ -diketones such as 1,4-diphenylbutane-1,4-dione and 1-phenylpentane-1,4-dione with amines. Similarly, the corresponding pyrroles (**3u, 3v**) were obtained in high yields in the presence of InCl_3 , InBr_3 or $\text{In}(\text{OTf})_3$ at 50 °C.

Finally, we examined the condensation reactions of γ -diketones with *p*-toluenesulfonylhydrazide (Scheme 2). *N*-(2,5-Dimethyl-1*H*-pyrrol-1-yl)-4-methylbenzenesulfonamide (**4a**) were obtained with good yields (87-91%) when the reaction was performed at 70 °C in the presence of Indium(III) salts. It is found that this condensation reaction gave **4a** in moderate yield (53%) under solvent-free conditions due to poor solubility of *p*-toluenesulfonylhydrazide in γ -diketones and the yields showed significant improvement in CH_3NO_2 . Nevertheless, trace product was obtained in the absence of catalysts, which also further proved that Indium(III) salts do play an important role in this reaction.

The reaction proceeds very cleanly without the formation of any by-products except water. Because the reaction can be performed using a solvent-free procedure,

at the end of the reaction, the crude mixture can be directly charged on a chromatographic column to obtain the pure product, avoiding any tedious work up.

In summary, we have developed a facile and efficient method for the synthesis of *N*-substituted pyrroles using Indium(III) salts. The advantages of the method include (i) absence of a solvent, (ii) short reaction times, (iii) high yields, (iv) no work-up, and (v) use of trace amounts of a catalyst that could be recovered and re-used.

Experimental

Melting points were recorded on Digital Melting Point Apparatus WRS-1B and are uncorrected. ^1H NMR and ^{13}C NMR spectra were taken with a VARIAN Mercury plus-400 instrument using CDCl_3 as the solvent with tetramethylsilane (TMS) as an internal standard at room temperature. Chemical shifts are given in δ relative to TMS, the coupling constants *J* are given in Hz. IR spectra was recorded on a AVATAR 370 FI-Infrared Spectrophotometer. Mass spectra were recorded on Finnigan Trace DSQ (EI, CI) or Thermo Finnigan LCQ-Advantage (ESI).

Typical experimental procedure for the synthesis of 2,5-dimethyl-1-phenyl-1*H*-pyrrole (**3a**)

A mixture of acetylacetone (570 mg, 5 mmol) and aniline (465 mg, 5 mmol) was stirred in the presence of InCl_3 (55 mg, 5 mol%), InBr_3 (89 mg, 5 mol%) or $\text{In}(\text{OTf})_3$ (141 mg, 5 mol%) at room temperature for 30 min. After completion of the reaction (TLC), the crude products were separated by column chromatography on Et_3N pre-treated silica gel using petroleum ether/EtOAc (12:1 to 5:1) as eluent to afford a pure product **3a** in 90%, 93% or 94% yields, respectively. The spectral and analytical data of some representative compounds are given below.

2,5-dimethyl-1-phenyl-1*H*-pyrrole (**3a**)¹³


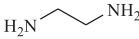
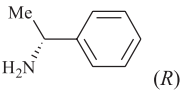
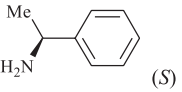
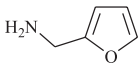
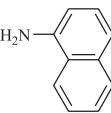
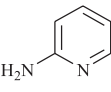
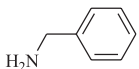
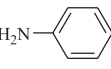
A white solid, mp 50.1-50.3 °C (46-47 °C); IR ν_{max} / cm^{-1} 3060, 2922, 1599, 1520, 1498, 1403, 1321 (film); ^1H NMR

Table 2. Indium(III)-catalyzed synthesis of pyrroles under solvent-free conditions^a

Reaction scheme: 1,2-dicarbonyl compound **1** (with substituents R¹ and R²) reacts with amine **2** (H₂NR) in the presence of 5 mol % Indium(III) catalyst under solvent-free conditions to yield *N*-substituted pyrrole **3** (with substituents R¹ and R²).

Entry	R ¹	R ²	H ₂ NR	Product	Catalyst	time/(min)	Yield/(%) ^b
1	Me	Me		3a	InCl ₃	30	90
					InBr ₃	30	93
					In(OTf) ₃	30	94
2	Me	Me		3b	InCl ₃	20	92
					InBr ₃	20	94
					In(OTf) ₃	20	94
3	Me	Me		3c	InCl ₃	25	91
					InBr ₃	25	90
					In(OTf) ₃	25	92
4	Me	Me		3d	InCl ₃	60	71
					InBr ₃	60	74
					In(OTf) ₃	60	81
5	Me	Me		3e	InCl ₃	60	69
					InBr ₃	60	71
					In(OTf) ₃	60	82
6	Me	Me		3f	InCl ₃	20	93
					InBr ₃	20	94
					In(OTf) ₃	20	98
7	Me	Me		3g	InCl ₃	40	71
					InBr ₃	40	73
					In(OTf) ₃	40	87
8	Me	Me		3h	InCl ₃	35	91
					InBr ₃	35	94
					In(OTf) ₃	35	93
9	Me	Me		3i	InCl ₃	30	92
					InBr ₃	30	95
					In(OTf) ₃	30	91
10	Me	Me		3j	InCl ₃	30	90
					InBr ₃	30	93
					In(OTf) ₃	30	91
11	Me	Me		3k	InCl ₃	25	89
					InBr ₃	25	90
					In(OTf) ₃	25	92
12	Me	Me		3l	InCl ₃	30	87
					InBr ₃	30	87
					In(OTf) ₃	30	89
13	Me	Me		3m	InCl ₃	35	90
					InBr ₃	35	93
					In(OTf) ₃	35	92

Table 2. continuation

Entry	R ¹	R ²	H ₂ NR	Product	Catalyst	time/(min)	Yield/(%) ^b
14	Me	Me		3n	InCl ₃	40	88
					InBr ₃	40	87
					In(OTf) ₃	40	90
15	Me	Me		3o	InCl ₃	45	88
					InBr ₃	45	87
					In(OTf) ₃	45	92
16	Me	Me		3p	InCl ₃	40	86
					InBr ₃	40	90
					In(OTf) ₃	40	89
17	Me	Me		3q	InCl ₃	35	87
					InBr ₃	35	89
					In(OTf) ₃	35	93
18	Me	Me		3r	InCl ₃	25	90
					InBr ₃	25	89
					In(OTf) ₃	25	93
19	Me	Me		3s	InCl ₃	40	89
					InBr ₃	40	92
					In(OTf) ₃	40	90
20 ^c	Me	Me		3t	InCl ₃	35	88
					InBr ₃	35	90
					In(OTf) ₃	35	91
21 ^c	Ph	Me		3u	InCl ₃	35	87
					InBr ₃	35	87
					In(OTf) ₃	35	90
22 ^c	Ph	Ph		3v	InCl ₃	40	88
					InBr ₃	40	86
					In(OTf) ₃	40	89

^aGeneral reaction conditions: γ -diketones (5 mmol), aniline (5 mmol), catalyst (5 mol%), rt. ^bIsolated yield. ^cThe reaction was carried out at 50 °C.

(400 MHz, CDCl₃) δ 7.49-7.41 (m, 3H, ArH), 7.27-7.22 (m, 2H, ArH), 5.92 (s, 2H, pyrrole), 2.05 (s, 6H, CH₃). ¹³C NMR (100 MHz, CDCl₃) δ 139.9, 129.0, 128.8, 127.6, 105.6, 13.0; MS (EI): *m/z* (%) 171 (100) [M⁺], 156 (8). Compounds **3b-3m** and **3p-3v** were obtained following a similar procedure.

2,5-dimethyl-1-((R)-1-phenylethyl)-1H-pyrrole (**3p**)²⁴

A colorless oil, $[\alpha]_D^{20}$: +42.95(c 0.098, CH₃OH); IR ν_{\max} /cm⁻¹ 3088, 2975, 2926, 1519, 1496, 1448, 1395, 1293 (neat); ¹H NMR (400 MHz, CDCl₃) δ 7.27 (t, *J* 7.2 Hz, 2H, ArH), 7.20 (t, *J* 7.2 Hz, 2H, ArH), 7.02 (d, *J* 7.2 Hz, 2H, ArH), 5.80 (s, 2 H, pyrrole), 5.45 (q, *J* 7.2 Hz, 1H, CHCH₃), 2.06 (s, 6H, CH₃), 1.83 (d, *J* 7.2 Hz, 3H, CHCH₃). ¹³C NMR (100 MHz, CDCl₃) δ 142.3, 128.3, 128.1, 126.7,

125.9, 106.0, 52.3, 19.2, 13.7; MS (EI): *m/z* (%) 200 (52) [M+1]⁺, 199 (100), 124 (10), 96 (35).

1-(furan-2-ylmethyl)-2,5-dimethyl-1H-pyrrole (**3r**)⁹

A colorless oil, IR ν_{\max} /cm⁻¹ 3109, 2975, 2931, 1577, 1521, 1505, 1442, 1406, 1343, 1296, 1216, 1147 (neat); ¹H NMR (400 MHz, CDCl₃) δ 7.34 (s, 1H, furan), 6.31 (s, 1H, furan), 6.05 (s, 1H, furan), 5.83 (s, 2H, pyrrole), 4.93 (s, 2H, CH₂), 2.30 (s, 6H, CH₃). ¹³C NMR (100 MHz, CDCl₃) δ 151.3, 142.1, 127.9, 110.2, 106.9, 105.3, 40.5, 12.4; MS (EI): *m/z* (%) 176 (43) [M+1]⁺, 175 (100) [M⁺], 81 (13).

2-(2,5-dimethyl-1H-pyrrol-1-yl)pyridine (**3t**)¹⁴

A white solid, mp 33.2-33.9 °C; IR ν_{\max} /cm⁻¹ 3055,

2922, 1587, 1525, 1473, 1438, 1397, 1325, 1285, 1234 (film); ¹H NMR (400 MHz, CDCl₃) δ 8.62 (d, *J* 4.4 Hz, 1H, pyridine), 7.84 (t, *J* 7.8 Hz, 1H, pyridine), 7.31 (t, *J* 6.4 Hz, 1H, pyridine), 7.26-7.22 (m, 1H, pyridine), 5.91 (s, 2H, pyrrole), 2.13 (s, 6H, CH₃). ¹³C NMR (100 MHz, CDCl₃) δ 152.0, 149.2, 138.0, 128.6, 122.3, 122.0, 106.9, 13.1; MS (EI): *m/z* (%) 173 (25) [M+1]⁺, 172 (100) [M]⁺, 171 (47), 157 (25), 94 (13).

*1-benzyl-2-methyl-5-phenyl-1H-pyrrole (3u)*²⁵

A colorless oil, ¹H NMR (400 MHz, CDCl₃) δ 7.30-7.20 (m, 8H, ArH), 6.92 (d, *J* 7.2 Hz, 2H, ArH), 6.23 (d, *J* 2.8 Hz, 1H, pyrrole), 6.05 (s, 1H, pyrrole), 5.11 (s, 2H), 2.12 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 138.9, 134.6, 133.7, 130.4, 128.7, 128.6, 128.3, 126.9, 126.6, 125.6, 107.9, 107.1, 47.6, 12.5; MS (ESI): *m/z* (%) 248.2 (100) [M+1]⁺.

*1,2,5-triphenyl-1H-pyrrole (3v)*²⁶

A white solid, mp 230-232 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.26-7.03 (m, 15H, ArH), 6.5 (s, 2H, pyrrole). ¹³C NMR (100 MHz, CDCl₃) δ 138.9, 135.8, 133.2, 128.9, 128.7, 127.8, 127.2 (2C), 126.20, 109.9; MS (ESI): *m/z* (%) 296.1 (100) [M+1]⁺.

Typical experimental procedure for the synthesis of 1,6-bis(2,5-dimethyl-1H-pyrrol-1-yl)hexane (3n)

A mixture of acetonylacetone (1.14 g, 10 mmol) and 1,6-diaminohexane (580 mg, 5 mmol) was stirred in the presence of InCl₃ (55 mg, 5 mol%), InBr₃ (89 mg, 5 mol%) or In(OTf)₃ (141 mg, 5 mol%) at room temperature for 45 min. After completion of the reaction (TLC), the crude products were separated by column chromatography on Et₃N pre-treated silica gel using petroleum ether/EtOAc (15:1 to 5:1) as eluent to afford a pure product **3n** in 88, 87 or 90% yields. The spectral and analytical data of some representative compounds are given below.

*1,6-bis(2,5-dimethyl-1H-pyrrol-1-yl)hexane (3n)*²⁷

A white solid, mp 102.8-103.0 °C; IR ν_{max}/cm⁻¹ 3103, 3093, 2969, 2924, 1518, 1475, 1410, 1373, 1301 (film); ¹H NMR (400 MHz, CDCl₃) δ 5.76 (s, 4H, pyrrole), 3.70 (t, *J* 7.6 Hz, 4H), 2.20 (s, 12H, CH₃), 1.65-1.58 (m, 4H), 1.38-1.34 (m, 4H). ¹³C NMR (100 MHz, CDCl₃) δ 127.2, 105.0, 43.5, 30.9, 26.7, 12.5; MS (EI): *m/z* (%) 272 (100) [M]⁺, 257 (8), 164 (38), 108 (30), 94 (18). Compound **3o** was obtained following a similar procedure.

*N-(2,5-dimethyl-1H-pyrrol-1-yl)-4-methylbenzene-sulfonamide (4a)*²⁸

A white solid, mp 143-144 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.68 (d, *J* 8.0 Hz, 2H, ArH), 7.31 (d, *J* 8.0 Hz, 2H, ArH), 7.07 (s, 1H, NH), 5.69 (s, 2H, pyrrole), 2.45 (s, 3H, ArCH₃), 1.82 (s, 3H, CH₃). ¹³C NMR (100 MHz, CDCl₃) δ 145.0, 135.3, 129.9, 128.9, 128.4, 104.9, 21.7, 11.2; MS (ESI): *m/z* (%) 265.2 (100) [M+1]⁺.

Acknowledgments

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Supplementary Information

Supplementary data are available free of charge at <http://jbc.sqb.org.br>, as PDF file.

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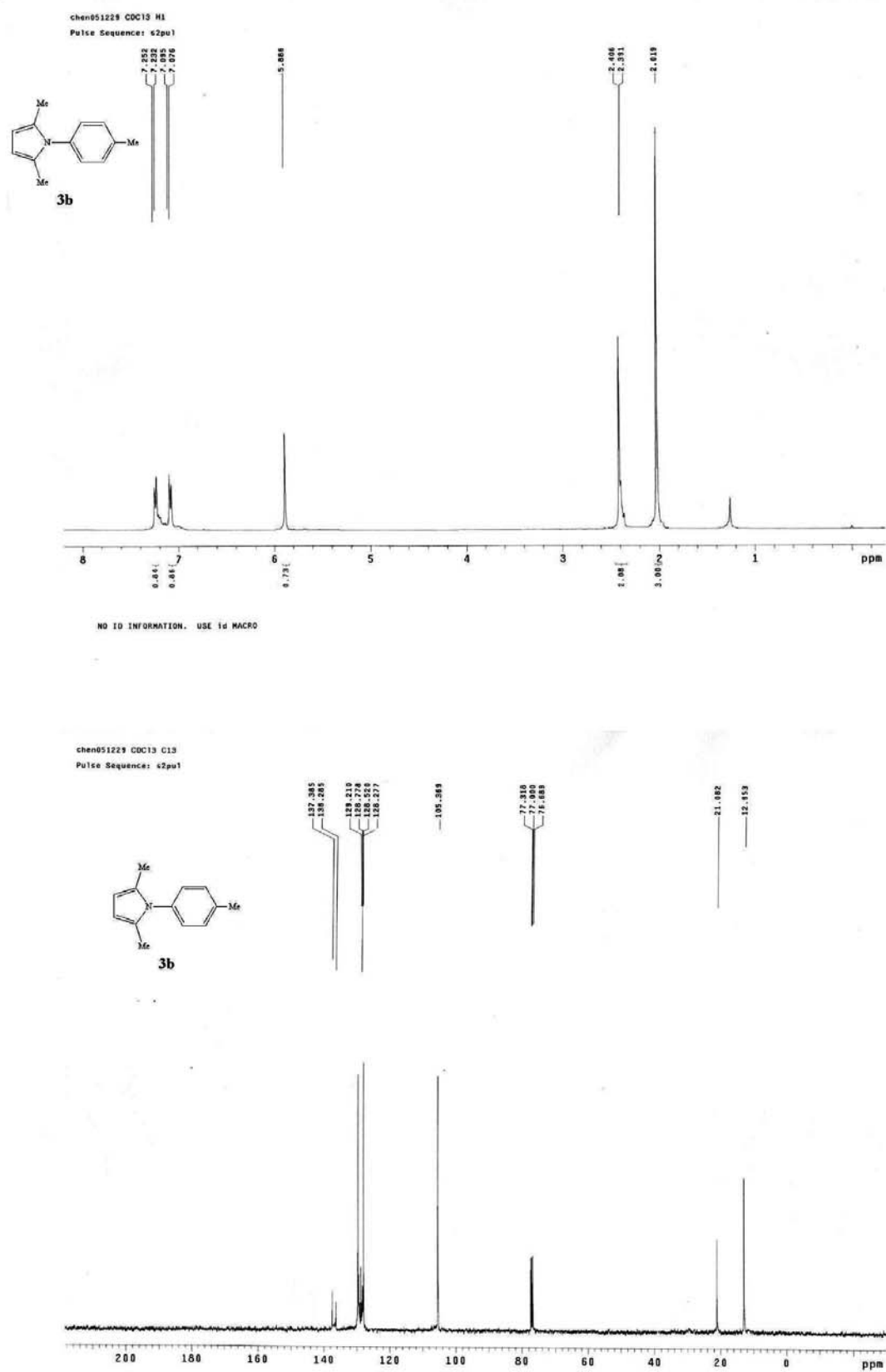


Figure S2. ¹H NMR of **3b** (400 MHz, CDCl₃) and ¹³C NMR of **3b** (100 MHz, CDCl₃).

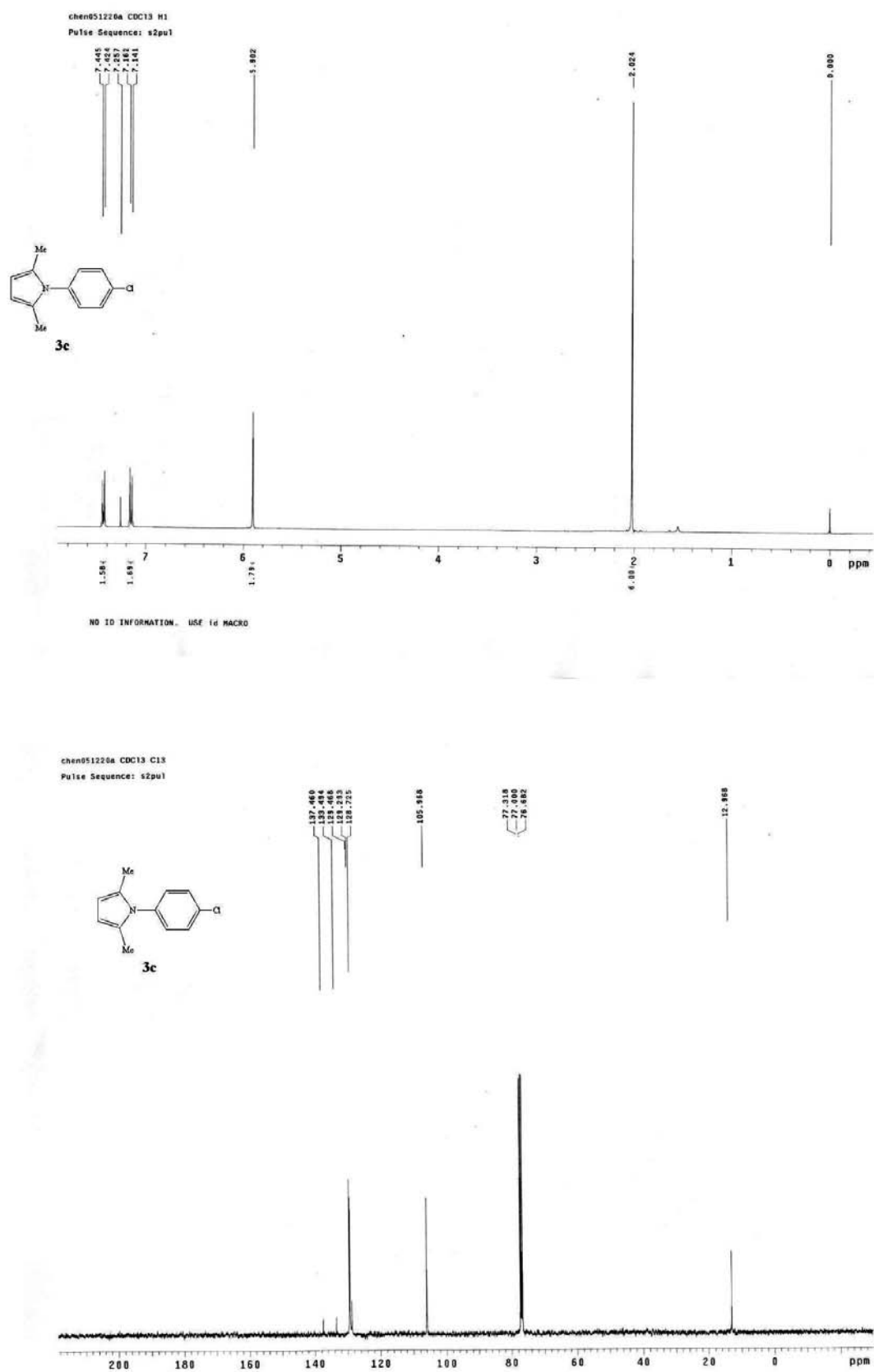


Figure S3. ¹H NMR of **3c** (400 MHz, CDCl₃) and ¹³C NMR of **3c** (100 MHz, CDCl₃).

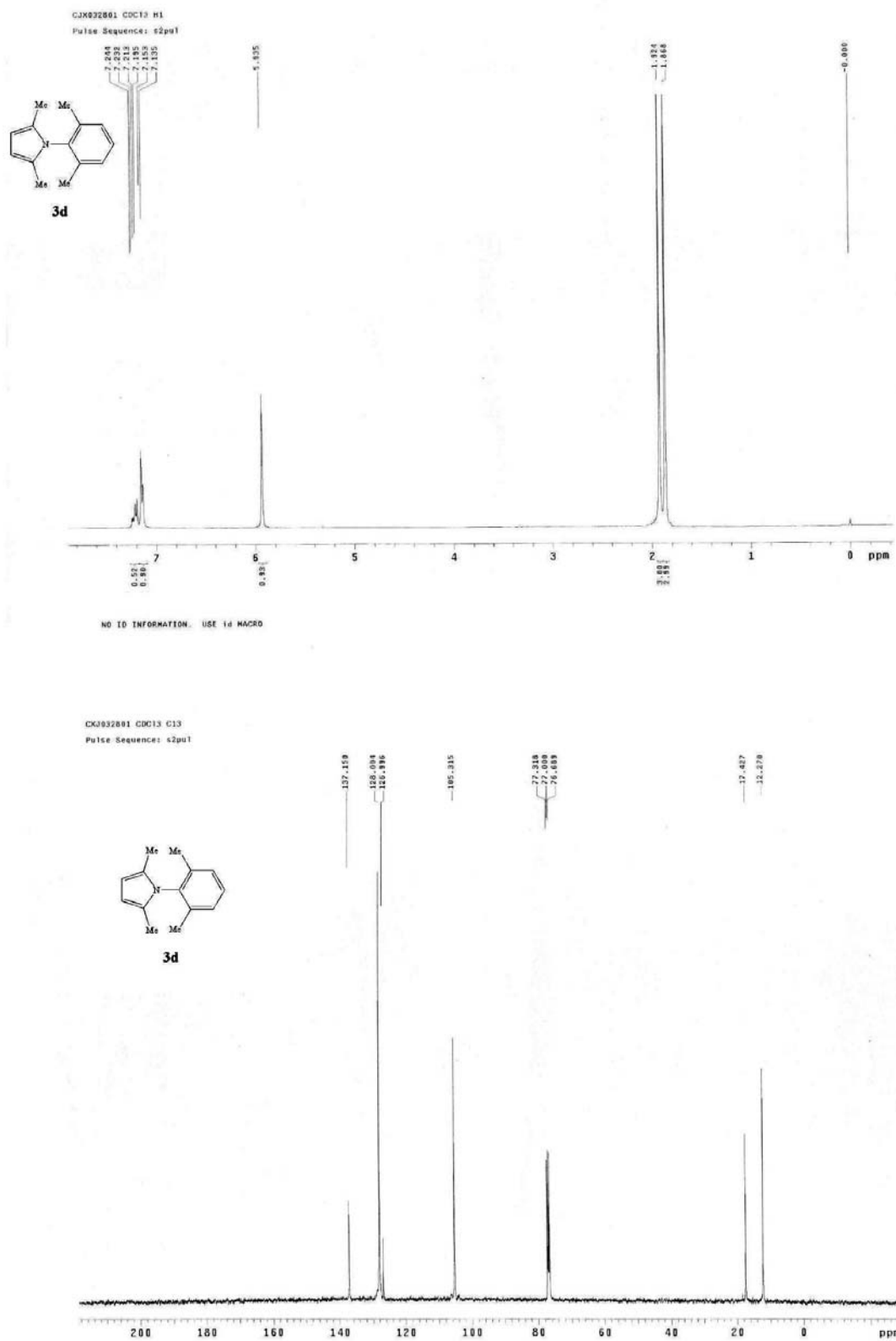


Figure S4. ¹H NMR of **3d** (400 MHz, CDCl₃) and ¹³C NMR of **3d** (100 MHz, CDCl₃).

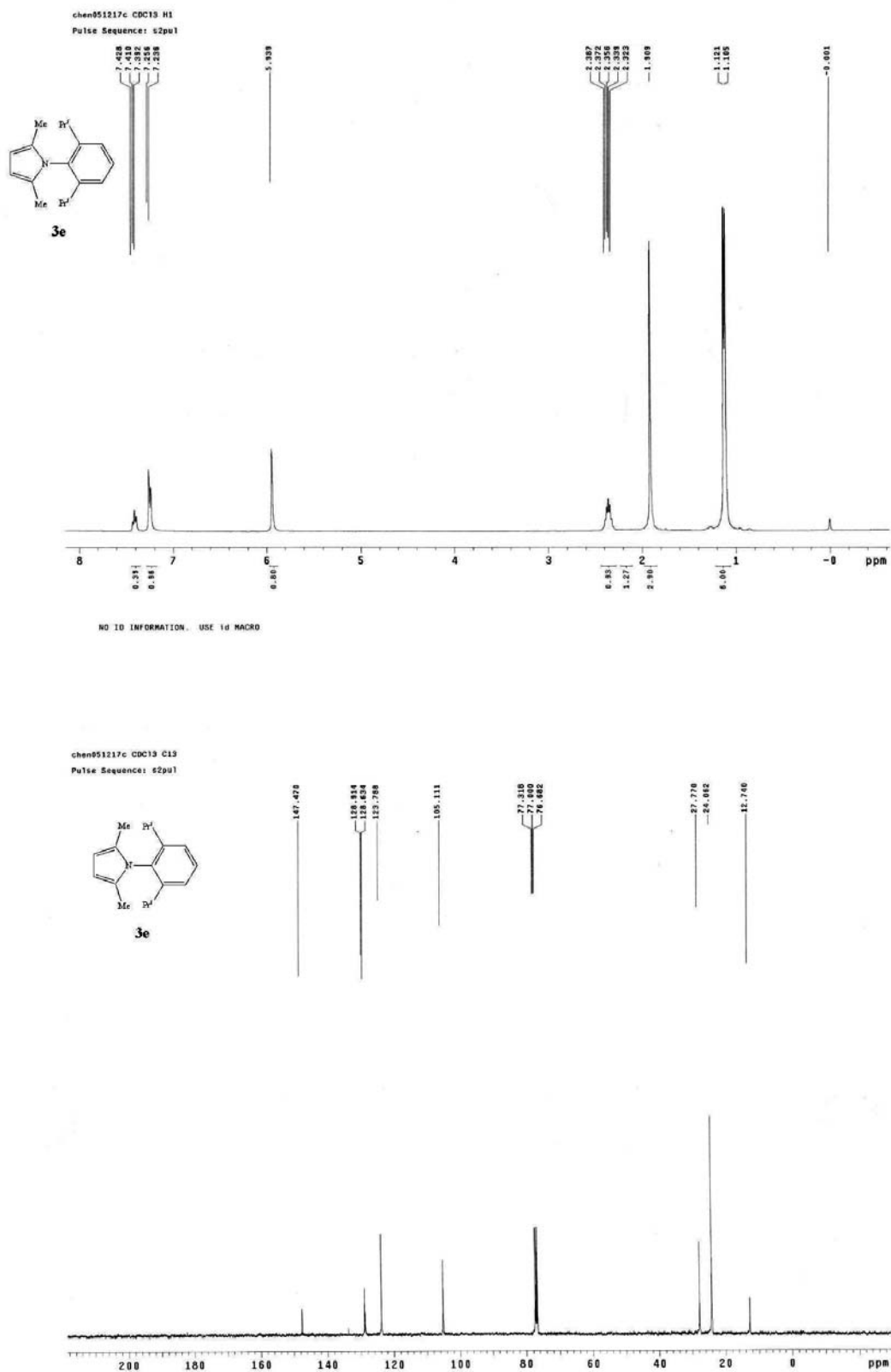


Figure S5. ^1H NMR of **3e** (400 MHz, CDCl_3) and ^{13}C NMR of **3e** (100 MHz, CDCl_3).

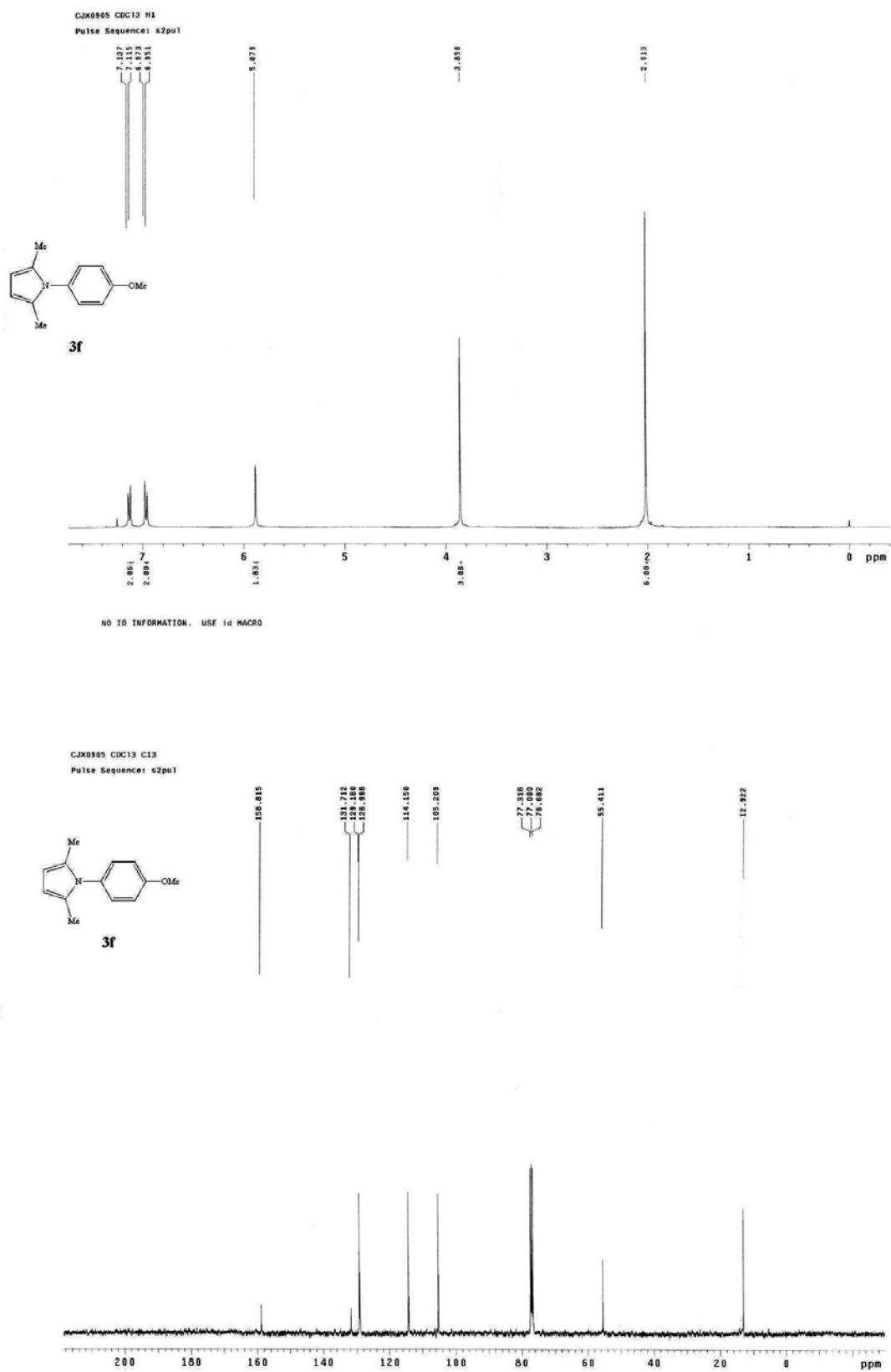


Figure S6. ¹H NMR of **3f** (400 MHz, CDCl₃) and ¹³C NMR of **3f** (100 MHz, CDCl₃).

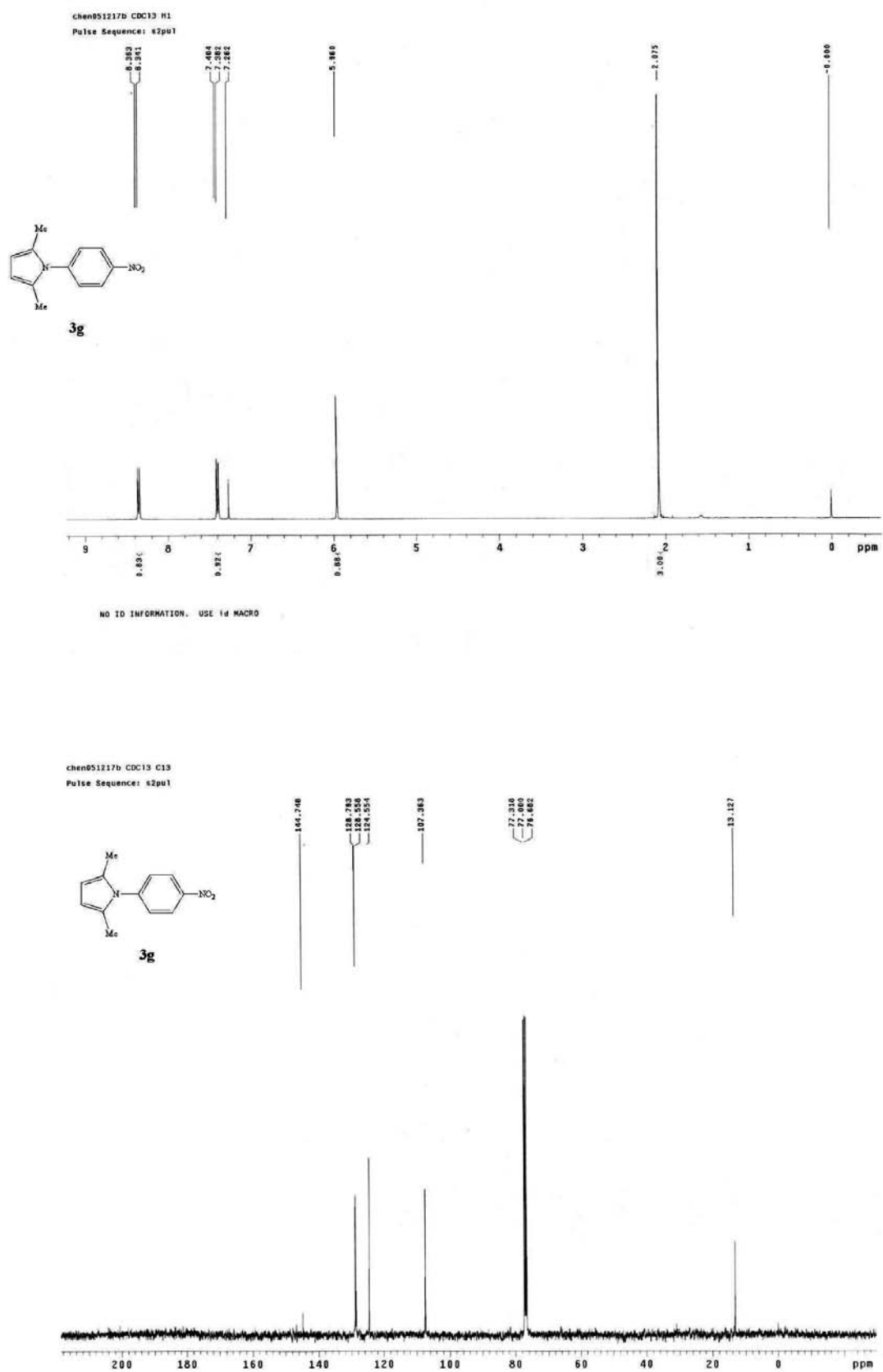


Figure S7. ¹H NMR of **3g** (400 MHz, CDCl₃) and ¹³C NMR of **3g** (100 MHz, CDCl₃).

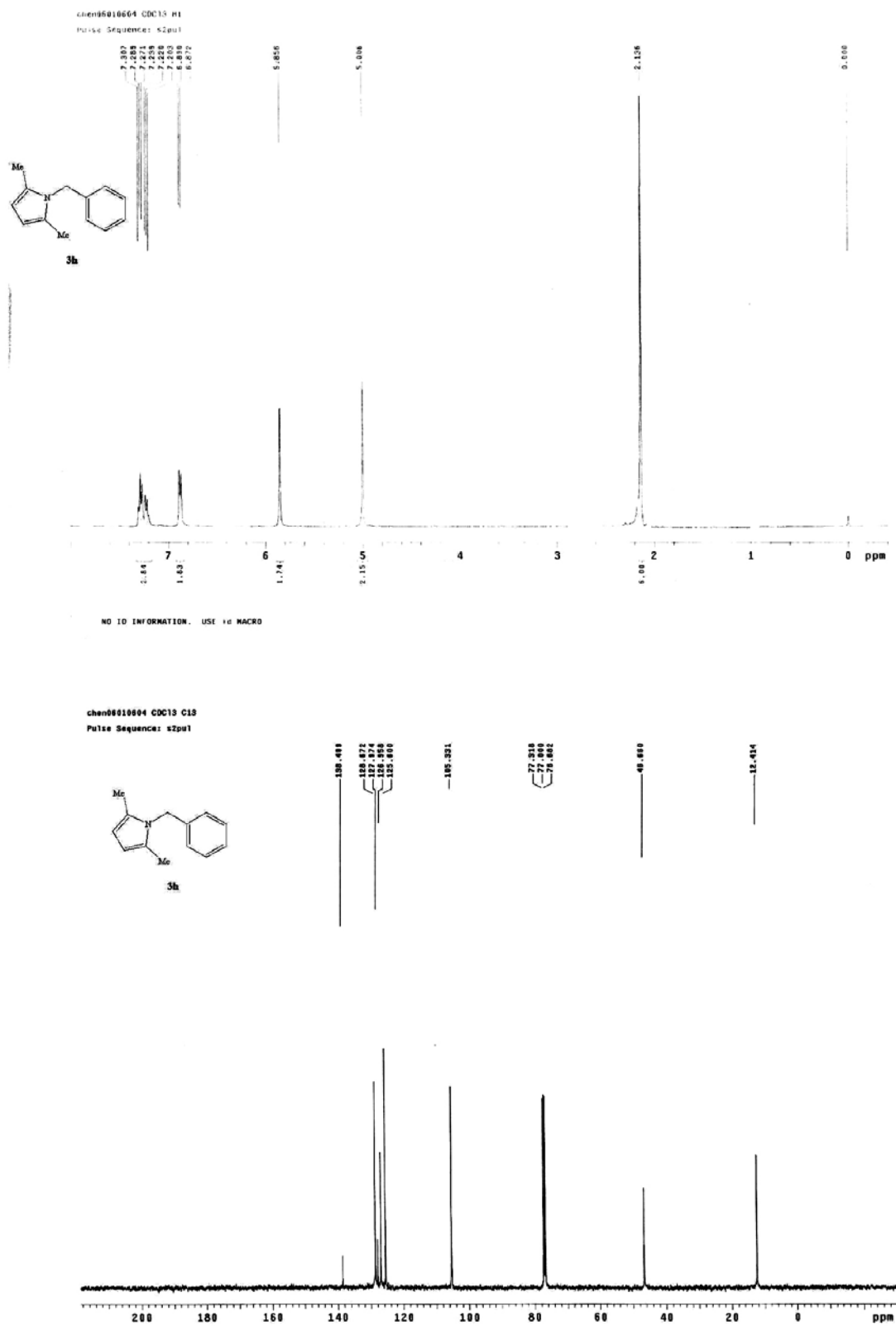


Figure S8. ¹H NMR of **3h** (400 MHz, CDCl₃) and ¹³C NMR of **3h** (100 MHz, CDCl₃).

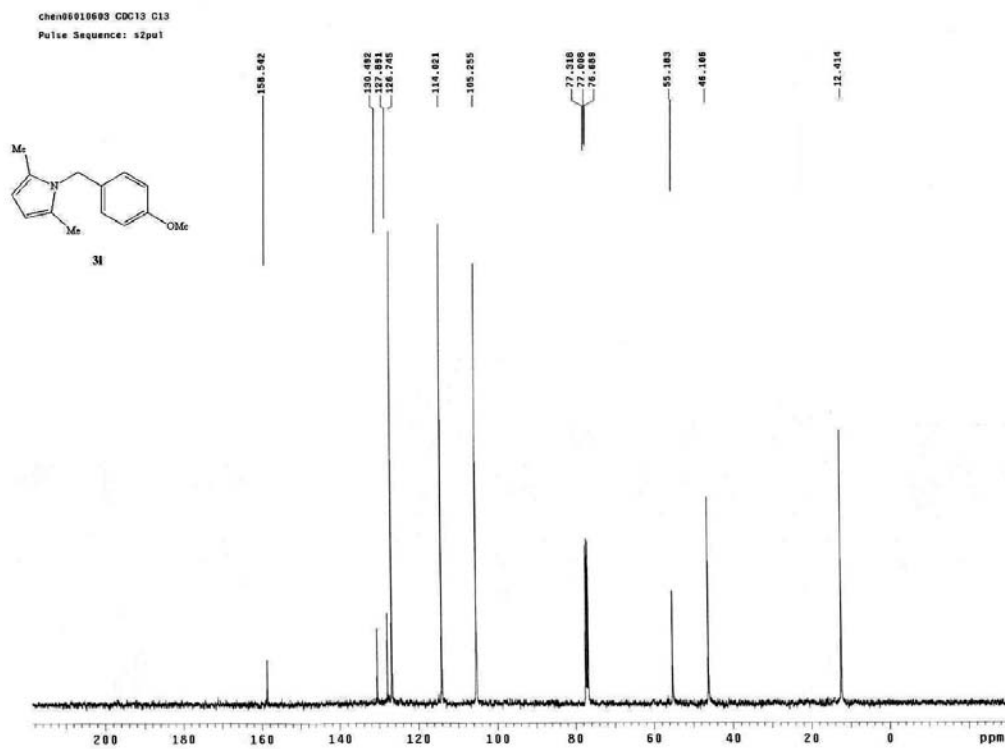
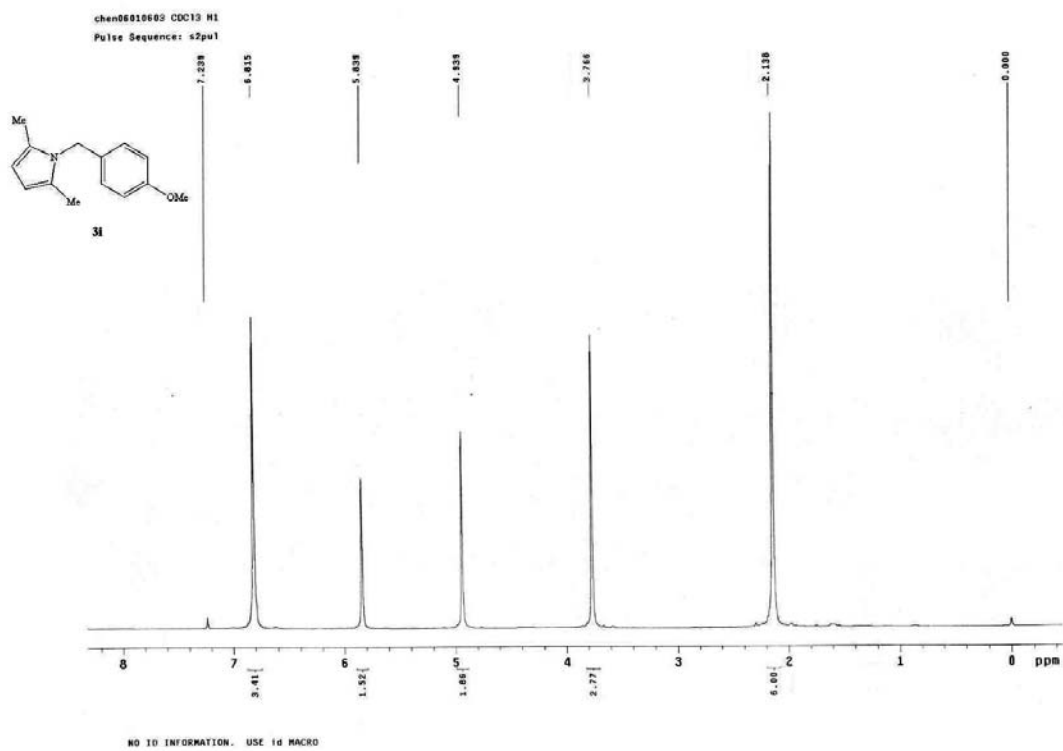


Figure S9. ^1H NMR of **3i** (400 MHz, CDCl_3) and ^{13}C NMR of **3i** (100 MHz, CDCl_3).

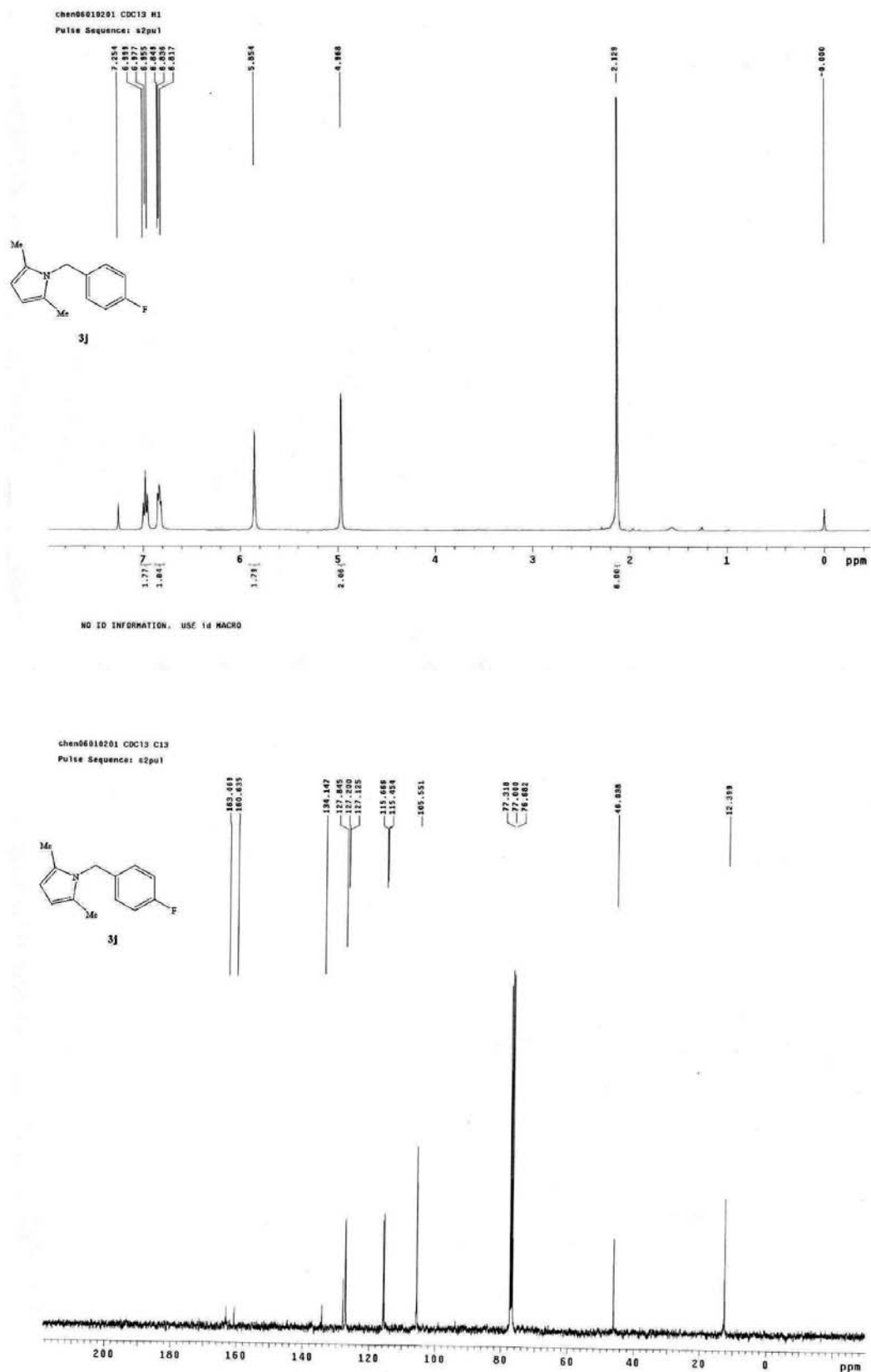


Figure S10. ¹H NMR of **3j** (400 MHz, CDCl₃) and ¹³C NMR of **3j** (100 MHz, CDCl₃).

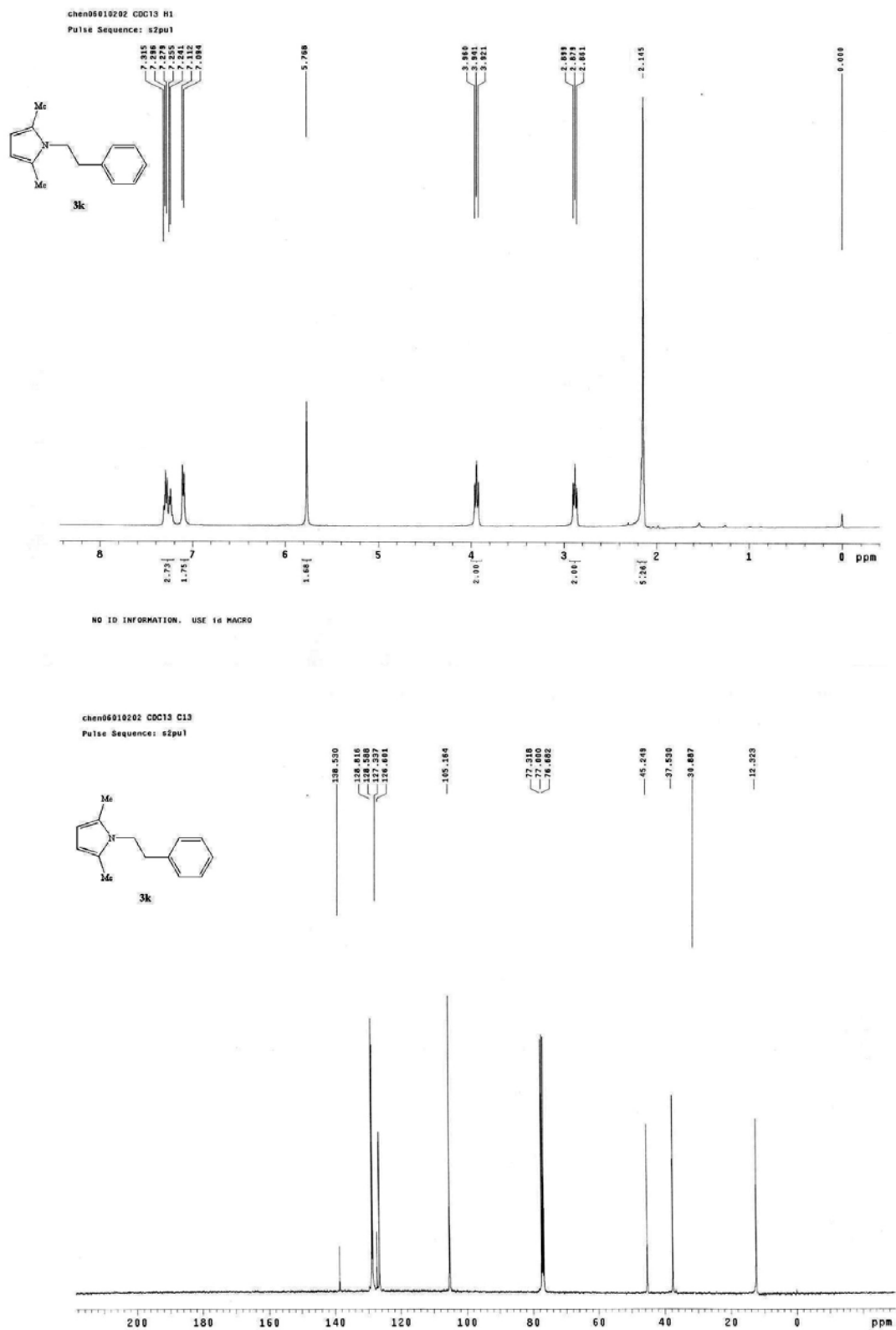


Figure S11. ¹H NMR of **3k** (400 MHz, CDCl₃) and ¹³C NMR of **3k** (100 MHz, CDCl₃).

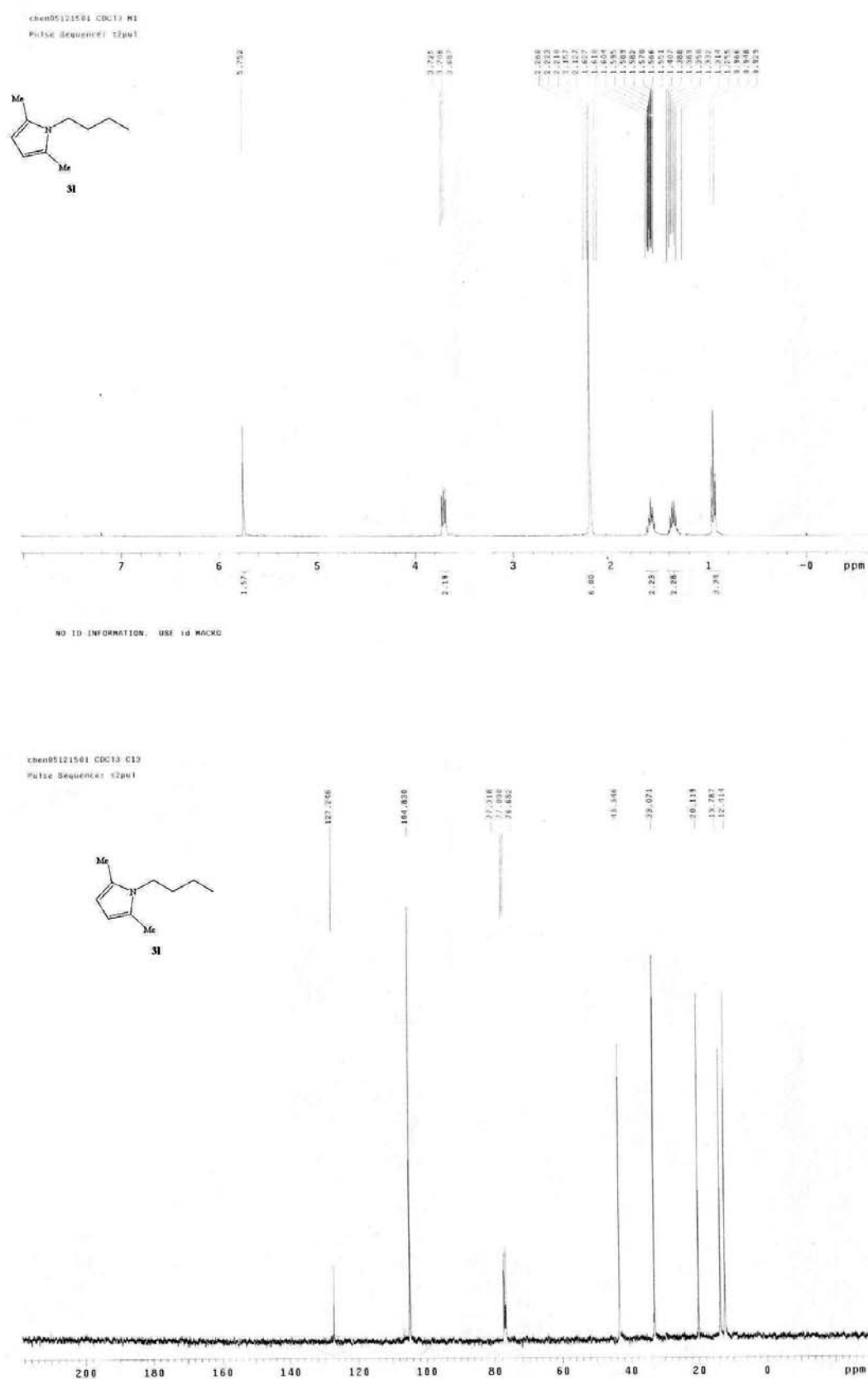


Figure S12. ^1H NMR of **31** (400 MHz, CDCl_3) and ^{13}C NMR of **31** (100 MHz, CDCl_3).

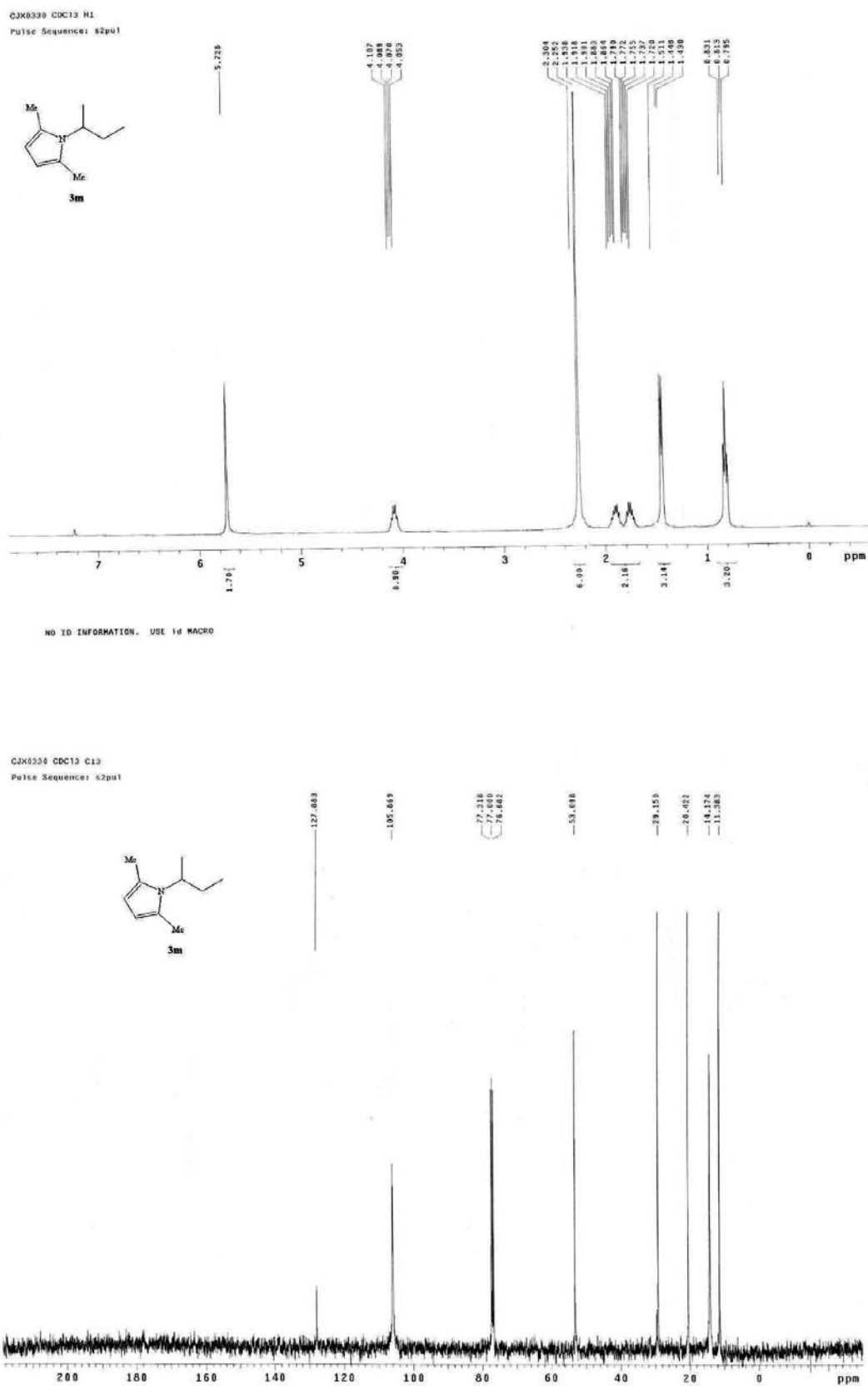


Figure S13. ¹H NMR of **3m** (400 MHz, CDCl₃) and ¹³C NMR of **3m** (100 MHz, CDCl₃).

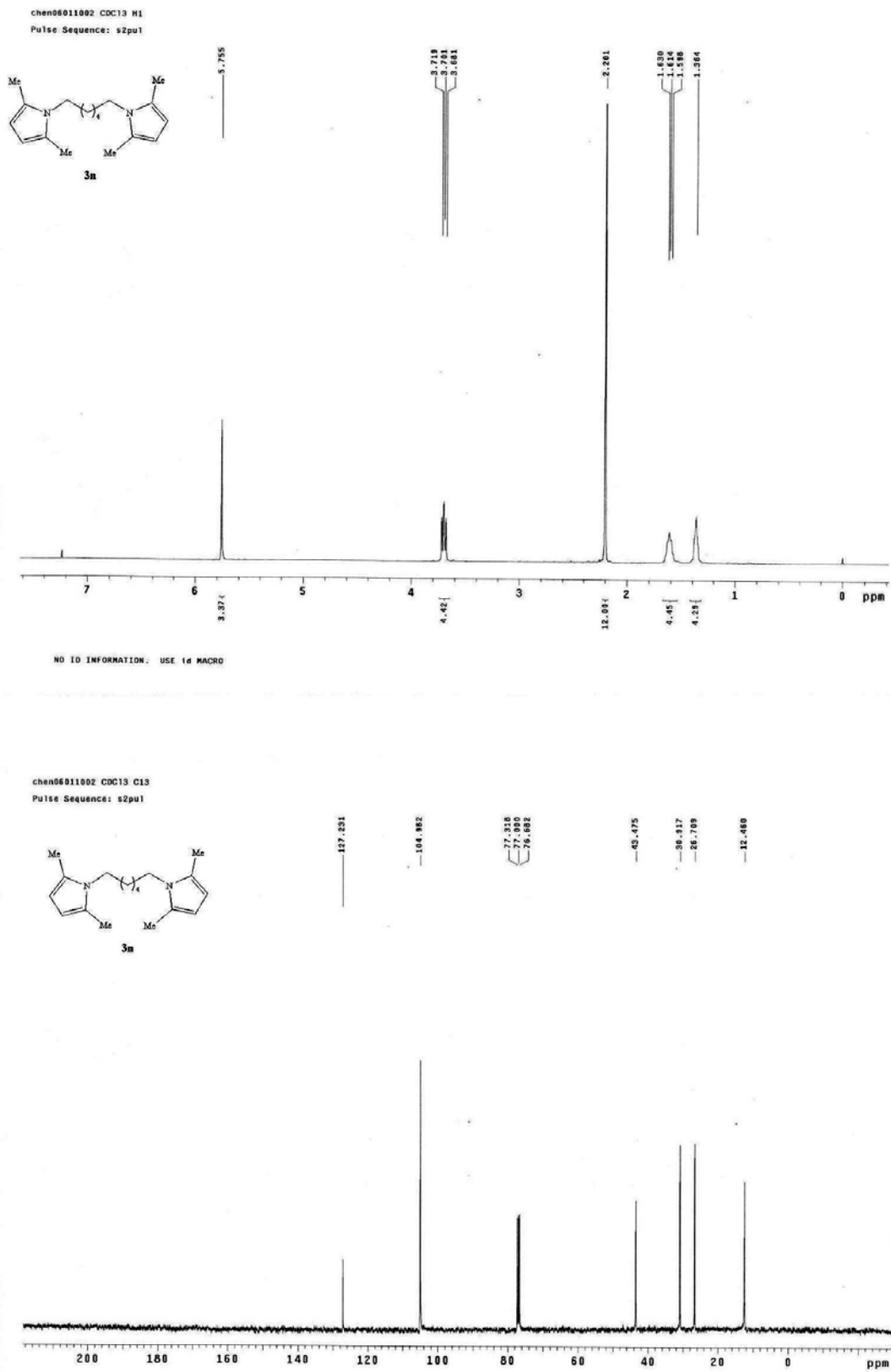


Figure S14. ^1H NMR of **3n** (400 MHz, CDCl_3) and ^{13}C NMR of **3n** (100 MHz, CDCl_3).

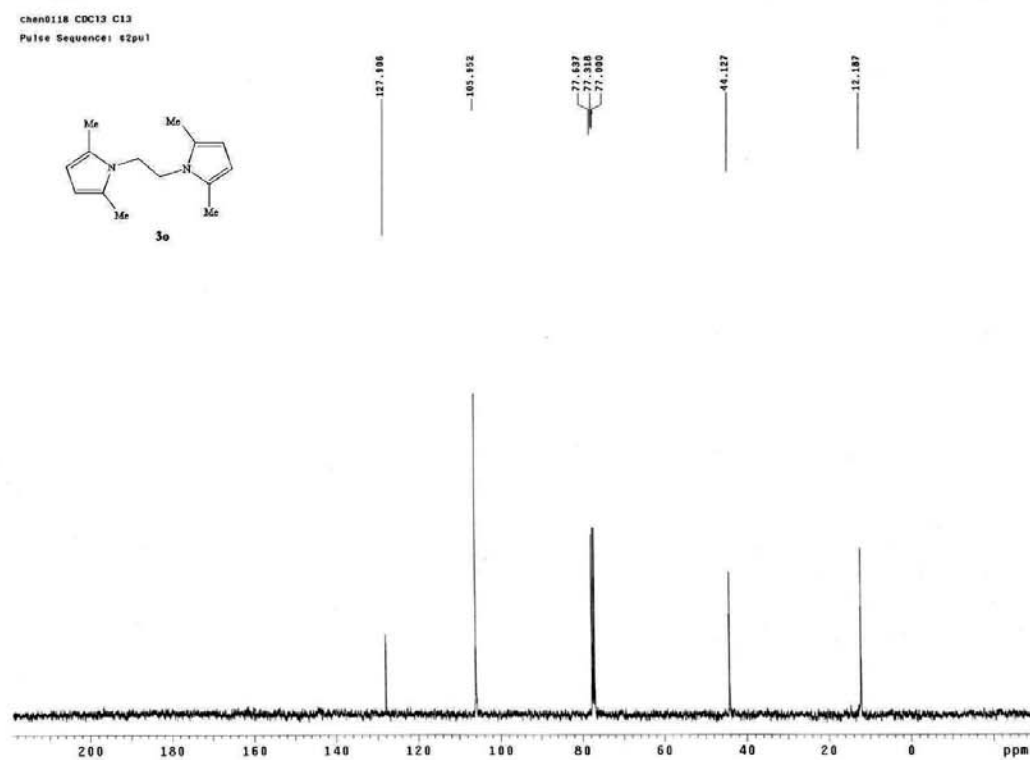
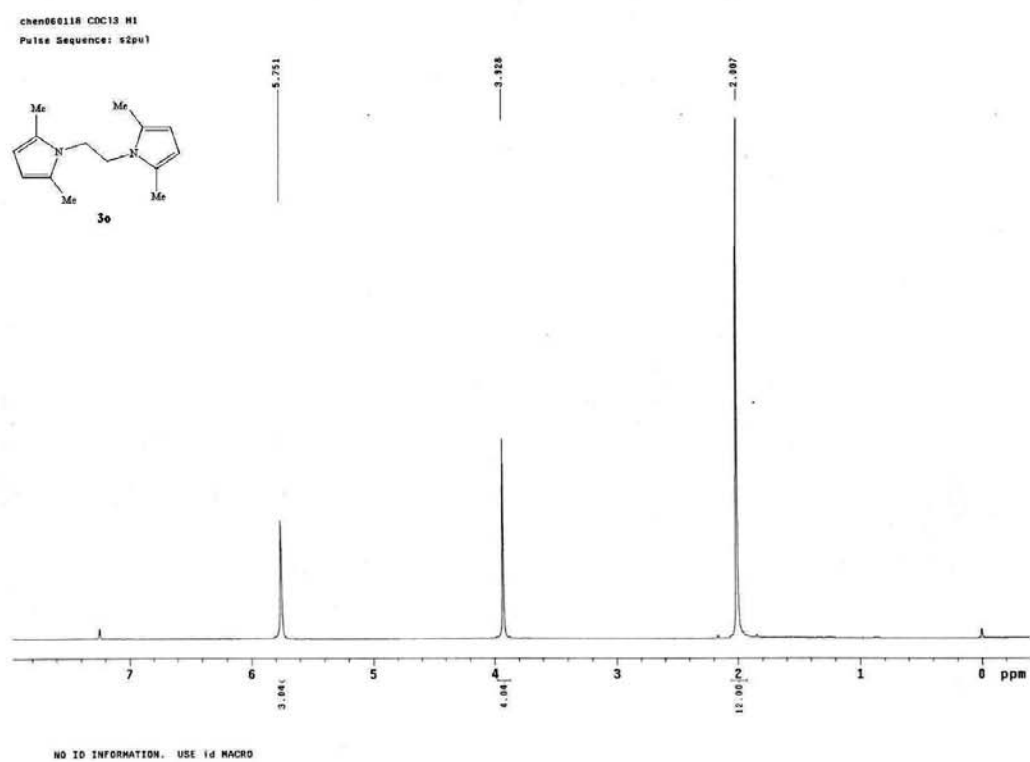


Figure S15. ^1H NMR of **3o** (400 MHz, CDCl_3) and ^{13}C NMR of **3o** (100 MHz, CDCl_3).

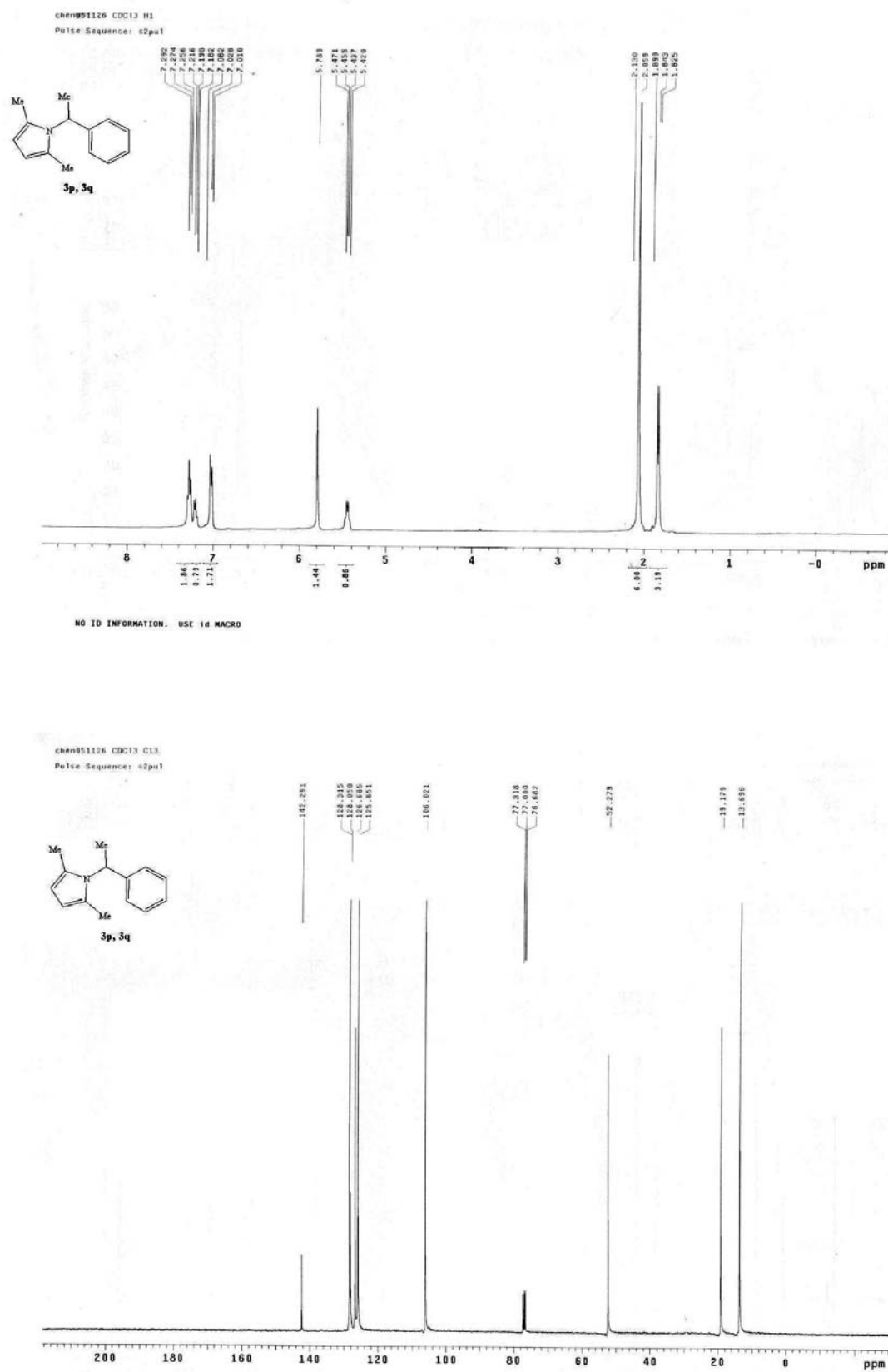
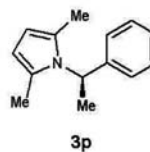


Figure S16. ¹H NMR of **3p** or **3q** (400 MHz, CDCl₃) and ¹³C NMR of **3p** or **3q** (100 MHz, CDCl₃).

Sat Jan 7, 2006
17:12
RUDOLPH RESEARCH
AUTOPOL IV
Serial No. 2513

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Wavelength : 589 nm
Concentration : 0.098%
Cell Length : 50.000 mm
Response Time : 2 sec
Sample Name : Disabled
Temp.-Chamber : 16.0°C

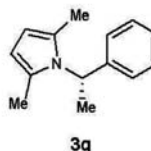


Meas.	Optical Rotation	Meas. Limits
42.951	0.021 deg.Arc	
42.951	0.021 deg.Arc	
42.951	0.021 deg.Arc	
42.951	0.021 deg.Arc	
42.951	0.021 deg.Arc	
42.951	0.021 deg.Arc	
42.951	0.021 deg.Arc	
42.951	0.021 deg.Arc	
42.951	0.021 deg.Arc	

Figure S17. Optical Rotation of 3p.

Sat Jan 7, 2006
16:41
RUDOLPH RESEARCH
AUTOPOL IV
Serial No. 2513

Meas. Type : Sp. Rot.
Wavelength : 589 nm
Concentration : 0.098%
Cell Length : 50.000 mm
Response Time : 2 sec
Sample Name : Disabled
Temp.-Chamber : 16.9°C



Meas.	Optical Rotation	Meas. Limits
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-42.955	-0.021 deg.Arc	
-42.955	-0.021 deg.Arc	
-42.955	-0.021 deg.Arc	
-42.955	-0.021 deg.Arc	
-42.955	-0.021 deg.Arc	
-42.955	-0.021 deg.Arc	
-42.955	-0.021 deg.Arc	
-42.955	-0.021 deg.Arc	

Figure S18. Optical Rotation of 3q.

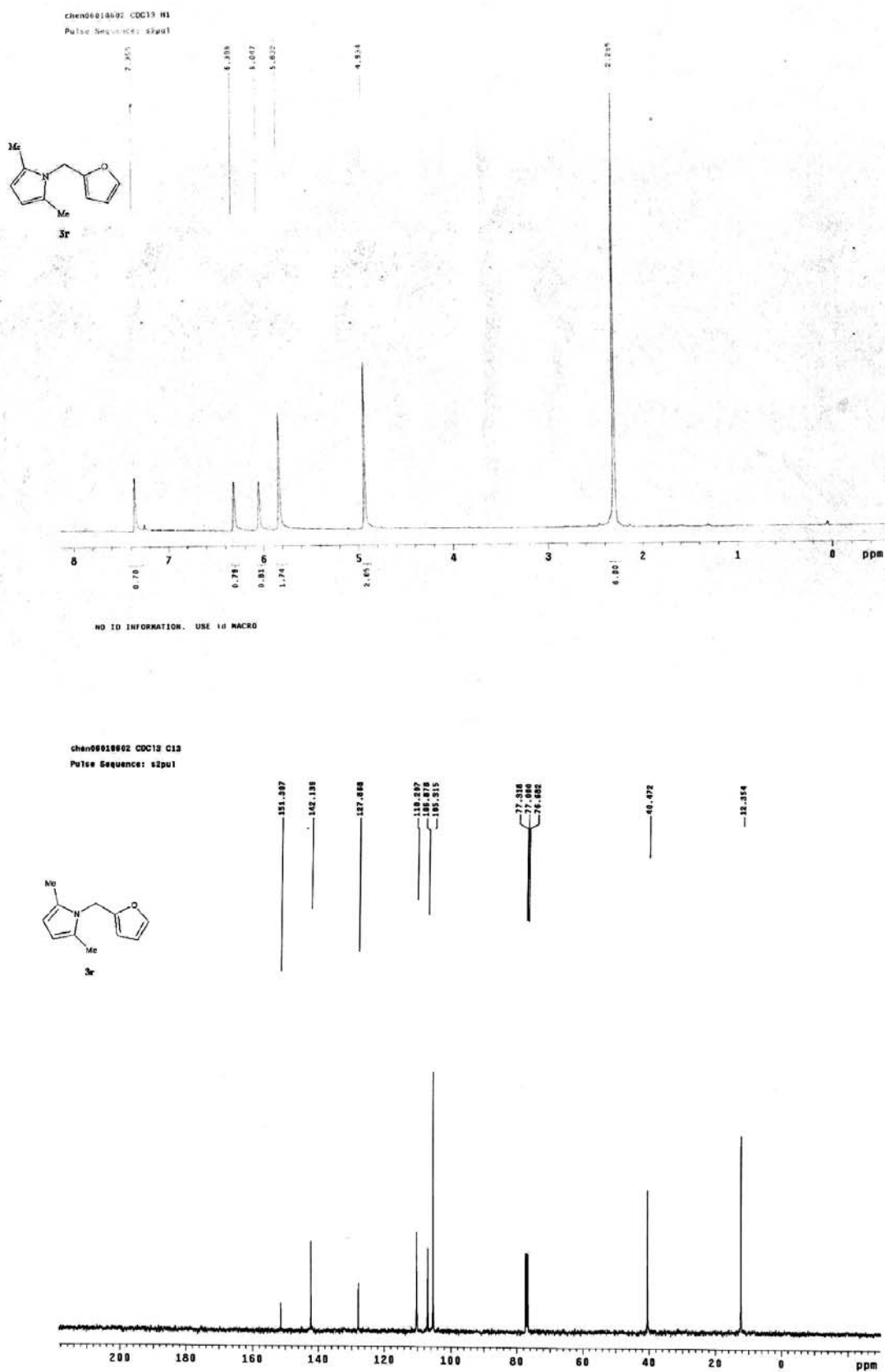


Figure S19. ¹H NMR of **3r** (400 MHz, CDCl₃) and ¹³C NMR of **3r** (100 MHz, CDCl₃).

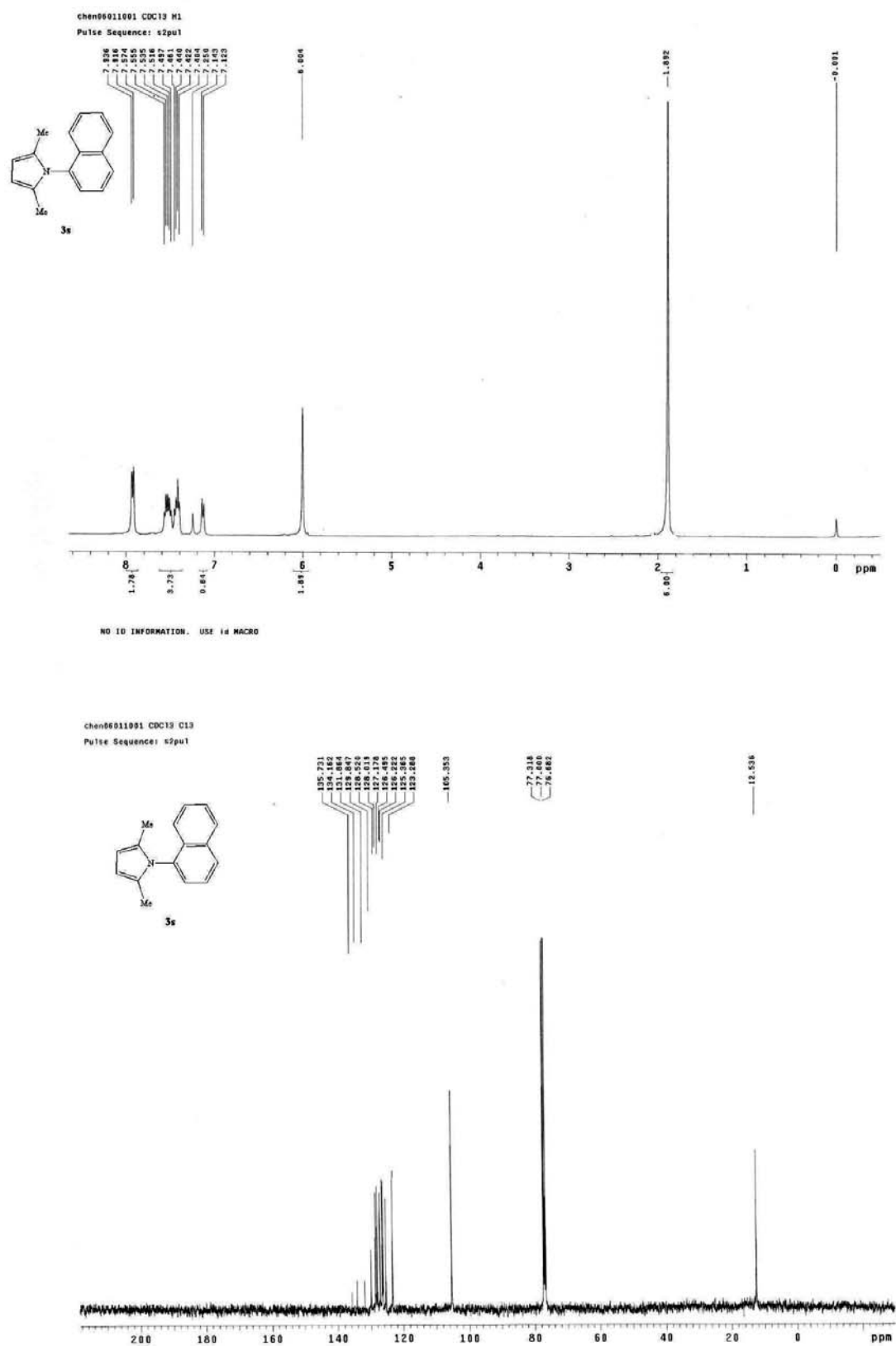
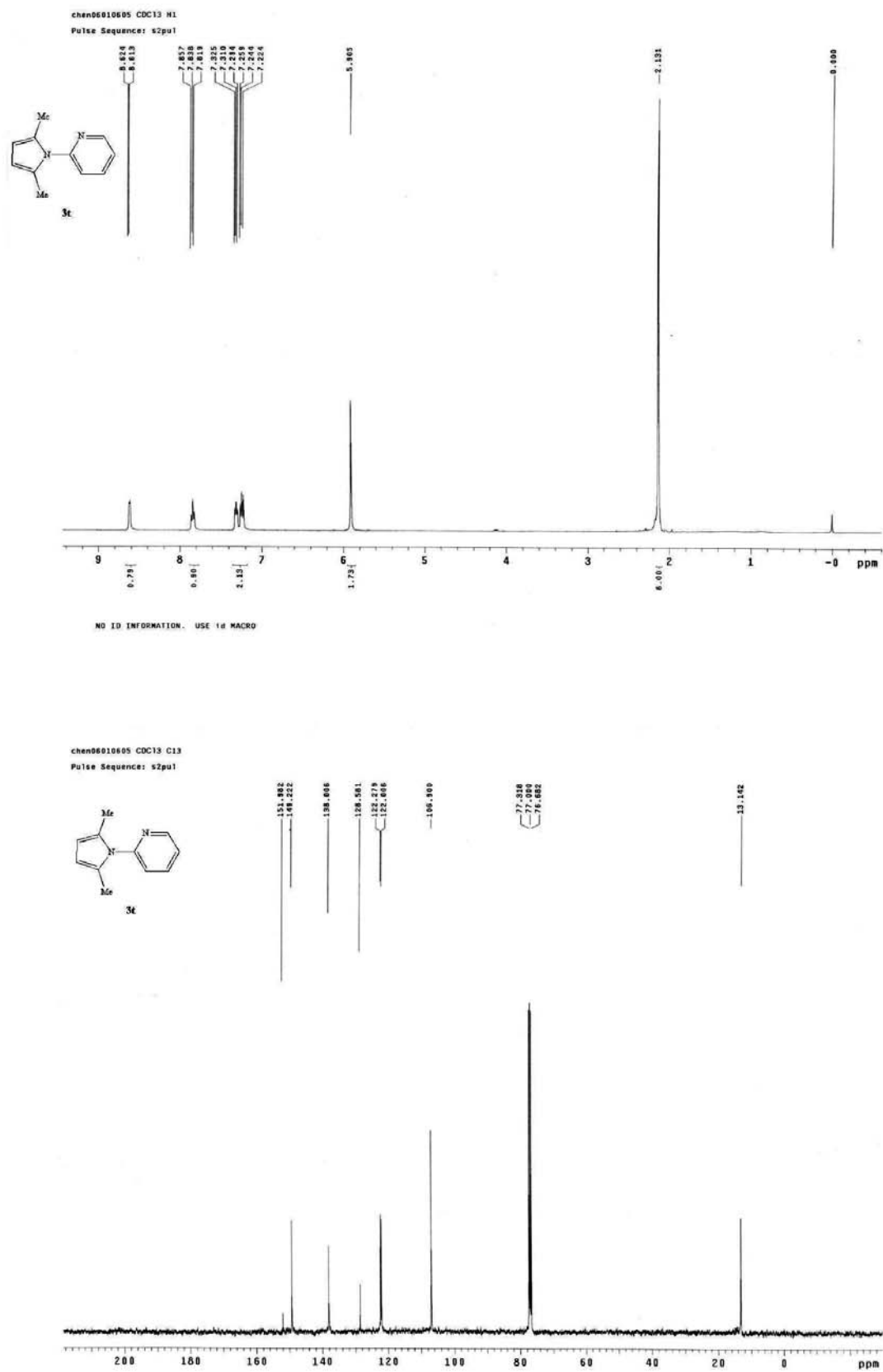


Figure S20. ¹H NMR of **3s** (400 MHz, CDCl₃) and ¹³C NMR of **3s** (100 MHz, CDCl₃).



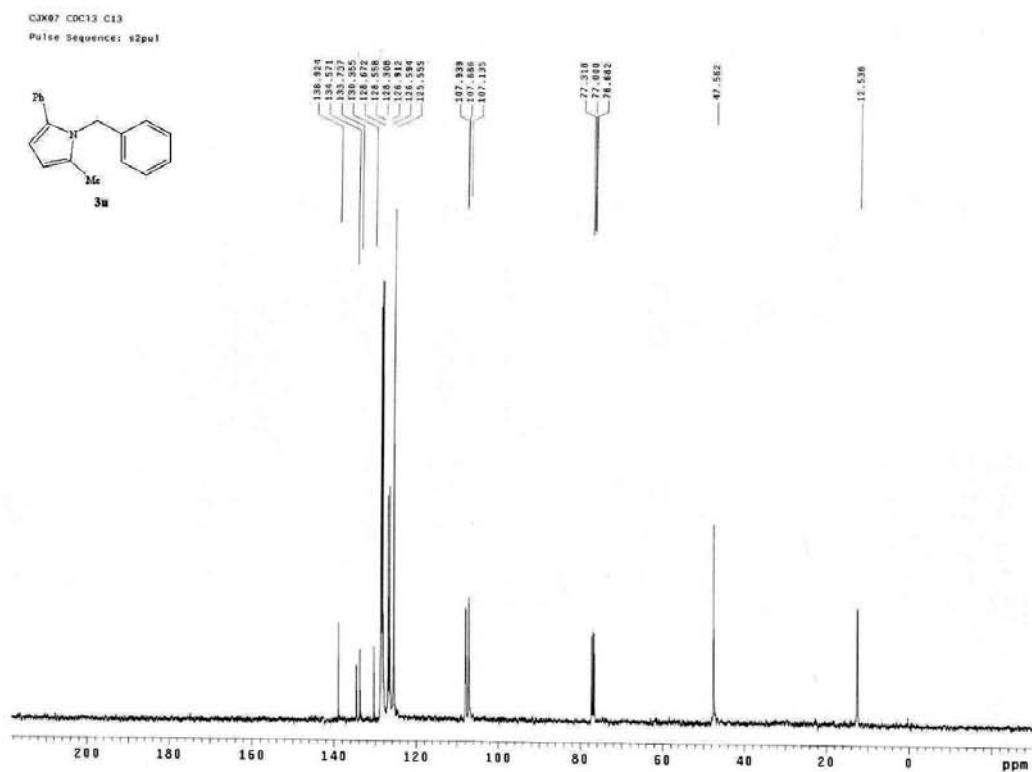
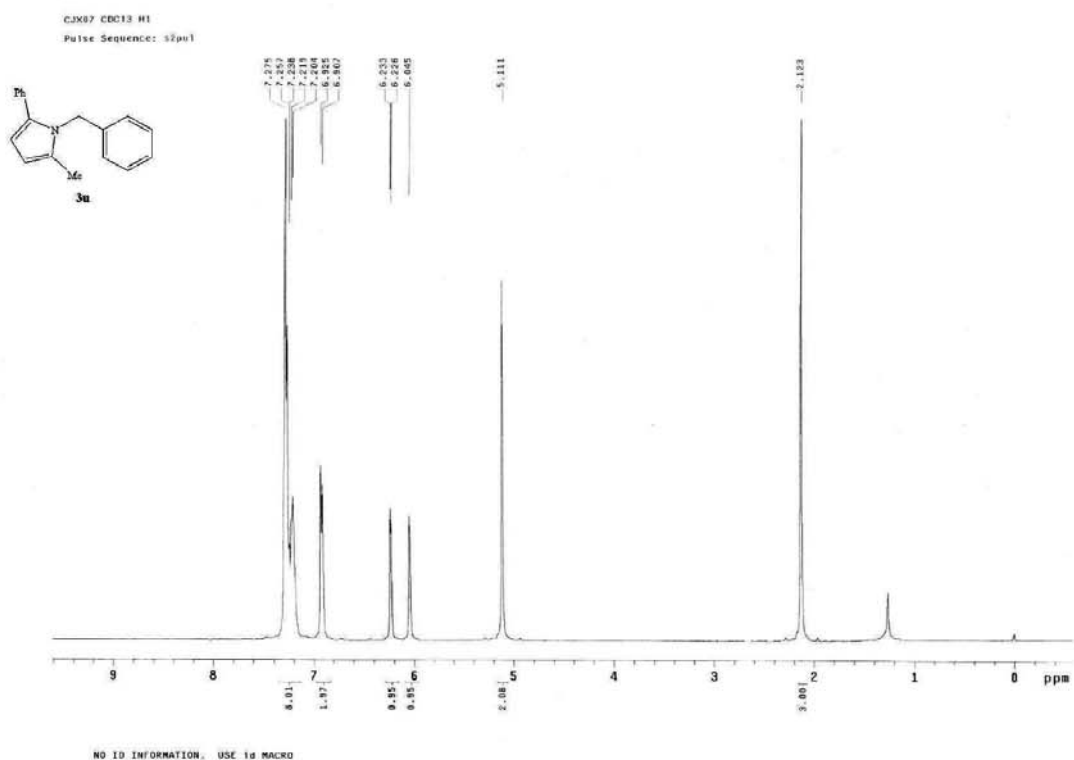


Figure S122. ¹H NMR of **3u** (400 MHz, CDCl₃) and ¹³C NMR of **3u** (100 MHz, CDCl₃).

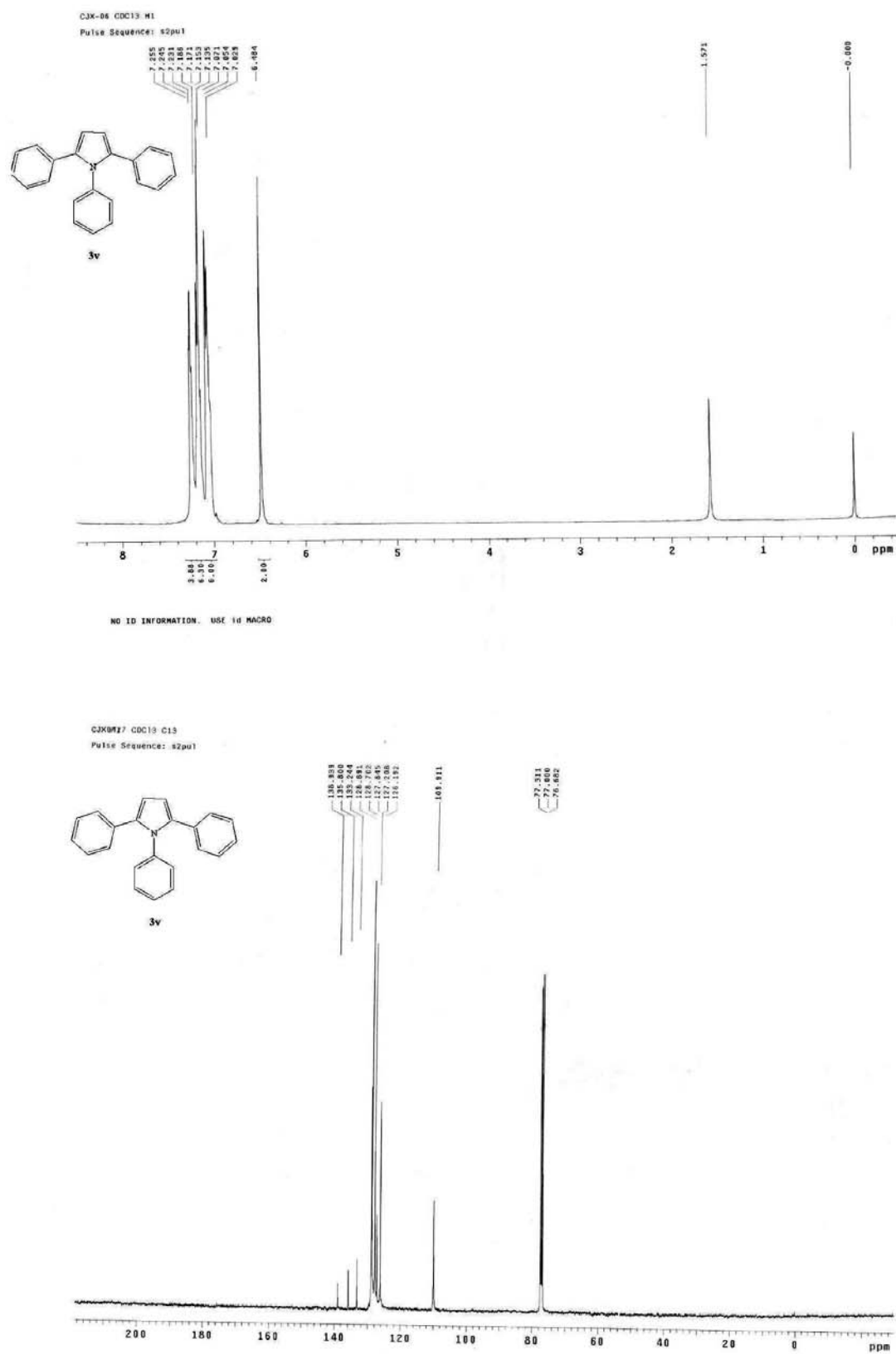


Figure S23. ¹H NMR of **3v** (400 MHz, CDCl₃) and ¹³C NMR of **3v** (100 MHz, CDCl₃).

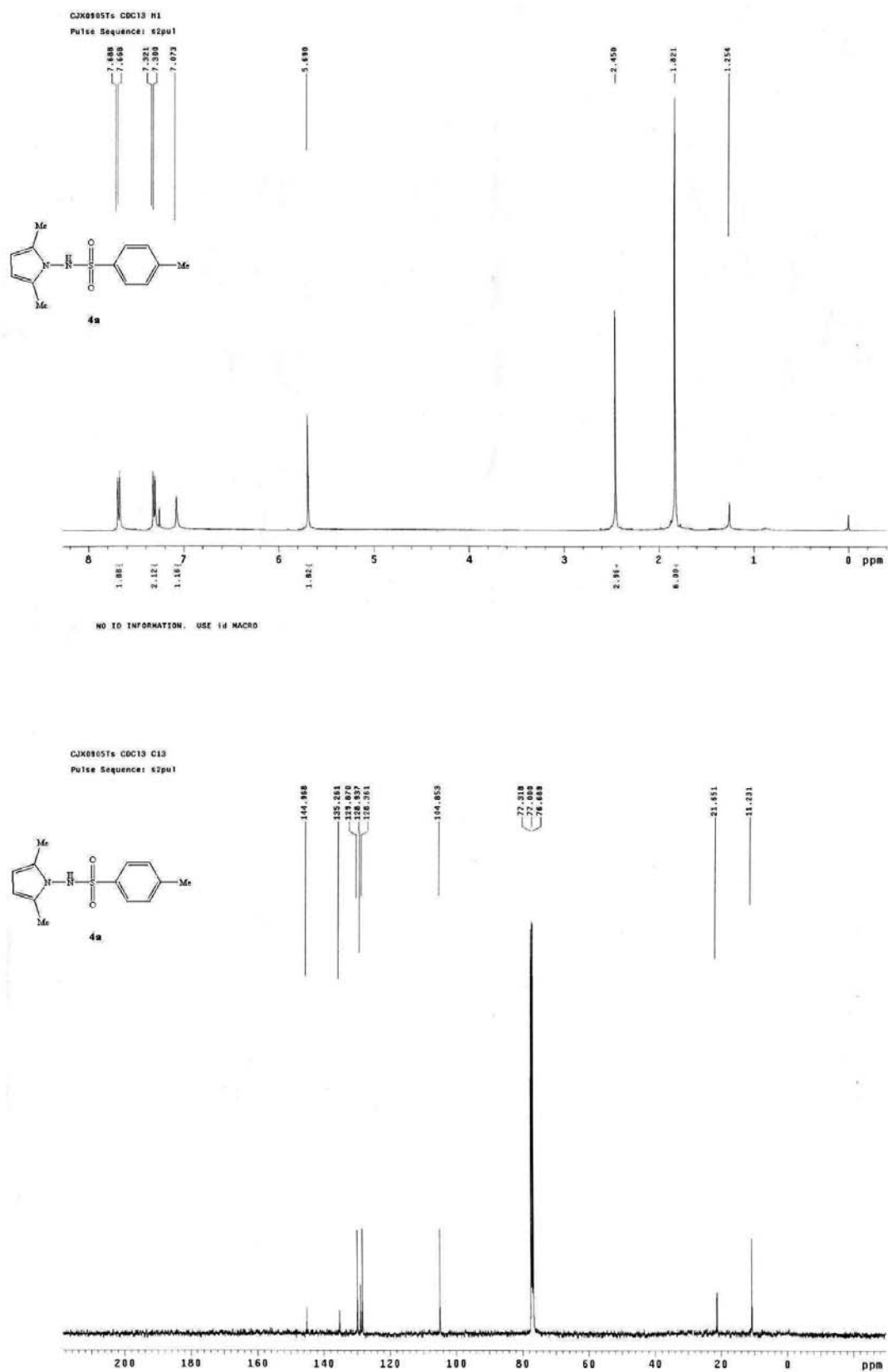


Figure S24. ^1H NMR of **4a** (400 MHz, CDCl_3) and ^{13}C NMR of **4a** (100 MHz, CDCl_3).