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PII: S0040-4020(14)00583-3

DOI: 10.1016/j.tet.2014.04.061

Reference: TET 25511

To appear in: *Tetrahedron*

Received Date: 22 March 2014

Revised Date: 21 April 2014

Accepted Date: 22 April 2014

Please cite this article as: Umeda R, Mashino T, Nishiyama Y, Synthesis of multisubstituted 1*H*-pyrrole: selenium-catalyzed reaction of γ-nitro substituted carbonyl compounds and carbon monoxide, *Tetrahedron* (2014), doi: 10.1016/j.tet.2014.04.061.

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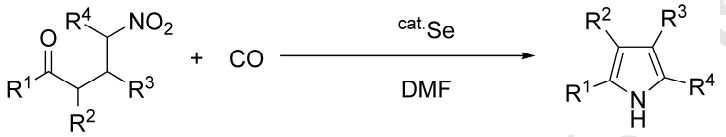

Tetrahedron
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ARTICLE INFO

Article history:
Received
Received in revised form
Accepted
Available online

Keywords:
Pyrrole
Selenium
Carbon Monoxide
γ-Nitro Substituted Carbonyl Compound

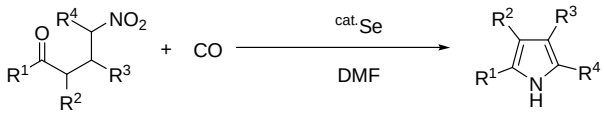
ABSTRACT

The novel and efficient selenium-catalyzed reductive *N*-heterocyclization of γ-nitro substituted carbonyl compounds with carbon monoxide has been developed. Various multisubstituted 1*H*-pyrroles can be easily prepared by this protocol. The one-pot synthesis of ethyl 1*H*-pyrrole-3-carboxylate derivatives was also successfully attained by the selenium-catalyzed reaction of β-ketoester, vinyl nitro compounds, and carbon monoxide.

1. Introduction

The pyrrole ring is a one of key structural elements in numerous natural products,[1,2] synthetic medicinal agents,[3,4] and novel materials.[5] These widespread applications have triggered the development of various synthetic methods of pyrroles. However, it often poses difficult problems of regioselectivity and is often complicated by the low chemical stability of many pyrroles derivatives on the reaction conditions. Thus, the development of a simple and convenient synthetic method of various type of multisubstituted 1*H*-pyrroles is of continuous interest.[6-8]

Recently, we and Chinese chemists have shown that elemental selenium acts as a unique catalyst for the reductive cyclization and reductive carbonylation of aromatic nitro compounds with carbon monoxide giving the corresponding nitrogen-containing heterocyclic compounds.[9,10] Based on the continuous study of the utilization of carbon monoxide in organic synthesis, we now show a convenient synthetic method of various multisubstituted 1*H*-pyrroles by the reaction of γ-nitro substituted ketones, which are easily prepared by the Michael addition reaction of alkyl nitro compounds with α,β-unsaturated carbonyl compounds, and carbon monoxide in the presence of the selenium catalyst (Scheme 1).[11,12]



Scheme 1.

2. Results and discussion

When 4-nitro-1,3-diphenylbutan-1-one (**1a**) was reacted with carbon monoxide (30 atm) in the presence of a catalytic amount of selenium (25 mol%) and 1-methylpyrrolidine as a base in DMF solvent at 150 ºC for 5 h, 2,4-diphenyl-1*H*-pyrrole (**2a**) was formed in 81% yield (entry 5 in Table 1). To determine the optimized reaction conditions, **1a** was allowed to react with carbon monoxide in the presence of the selenium catalyst under various reaction conditions, and these results are shown in Table 1. When other amines, such as triethylamine, DBU, and an inorganic base, K_2CO_3, instead of 1-methylpyrrolidine were used as a base, the yields of **2a** decreased due to the formation of 4-oxo-2,4-diphenylbutanenitrile (**3a**), 4-oxo-2,4-diphenylbutanal oxime (**4a**) or 1,3-diphenylpropane-1-one (**5a**)[13] as by-products (entries 7-9). In the case of dimethylacetamide (DMA), acetonitrile, and THF solvents, the yields of **2a** slightly decreased (entries 10-12). The yield of **2a** was diminished, when the reaction was carried out at lower reaction temperatures (30, 50, 80, and 120 ºC) and a lower CO pressure (10 atm) (entries 1-4

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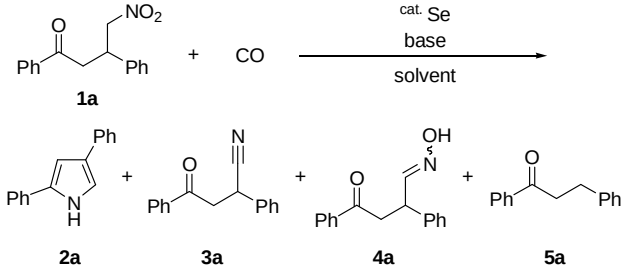
and 6). It is interesting to note that, at 30 and 50 ºC, oxime **4a** was obtained as the main product (entries 1 and 2).

Table 1. Optimized reaction conditions[a]



Entry	Solvent	Base	Temp. ℃	Yield (%)[b] 2a	3a	4a	5a
1	DMF		30	17	15	51	0
2	DMF		50	25	16	37	0
3	DMF		80	43	12	13	3
4	DMF		120	71	7	0	8
5	DMF		150	81 (62)	0	0	13
6[c]	DMF		150	71	0	0	10
7	DMF	Et_3N	150	23	25	15	31
8	DMF	DBU	150	40	0	0	55
9	DMF	K_2CO_3	150	29	11	0	10
10	DMA		150	67	5	0	10
11	THF		150	43	3	6	17
12	CH_3CN		150	64	4	4	12

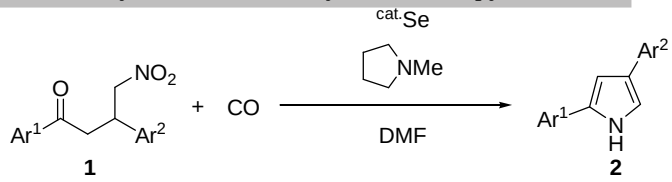
[a] Reaction conditions: **1a** (0.4 mmol), selenium (0.1 mmol), base (2.5 mmol), and solvent (2.5 mL) under CO (30 atm) for 5 h.

[b] ^{1}H-NMR yields. The number in parenthesis shows isolated yield.

[c] Under CO (10 atm).

In order to elucidate the scope and limitation of the protocol, various 4-nitro-1,3-diarylbutan-1-ones were treated with carbon monoxide in the presence of the selenium catalyst (25 mol%) under the same reaction conditions as that of entry 5 in Table 1. These results are shown in Table 2. 4-Nitro-1-(4-methylphenyl)- and 4-nitro-1-(3-methylphenyl)-3-phenylbutane-1-one bearing an electron donating group gave the corresponding 2-aryl-4-diphenyl-1*H*-pyrroles, **2b** and **2c**, in 61 and 68% yields, respectively (entries 1 and 2). In the case of 4-nitro-1-(4-methoxyphenyl)-3-phenylbutan-1-one, the yield of 2-(4-methoxyphenyl)-3-phenyl-1*H*-pyrrole (**2e**) decreased; however, the yield of **2e** was improved by extending the reaction time (10 h) (entry 4). For the reaction of 1-nitro-1-(4-chlorophenyl)-3-phenylbutan-1-one, in which the electron withdrawing group was substituted on the aromatic ring, **2f** was also obtained in a moderate yield (entry 5). Similarly, the reductive *N*-heterocyclization of the 3-aryl substituted 4-nitro-1-phenylbutan-1-ones with carbon monoxide smoothly proceeded to give the 2-phenyl-4-aryl substituted 1*H*-pyrroles, **2g**-**2k**, in moderate yields (entries 6-10). Even when the sterically hindered 1,3-diaryl substituted 4-nitroketones, such as 4-nitro-1-(2-methylphenyl)-3-phenylbutane-1-one, was used as the substrate, **2d** was obtained in 57% yield (entry 3).

Table 2. Synthesis of 2,4-diaryl substituted pyrroles[a]



Entry	Ar^1	Ar^2	Yield (%)[b]
1	4-$CH_3C_6H_4$	Ph	**2b** 56 (61)
2	3-$CH_3C_6H_4$	Ph	**2c** 64 (68)
3[c]	2-$CH_3C_6H_4$	Ph	**2d** 30 (57)
4[c]	4-$CH_3OC_6H_4$	Ph	**2e** 58 (66)
5	4-ClC_6H_4	Ph	**2f** 43 (64)
6	Ph	4-$CH_3C_6H_4$	**2g** 54 (63)
7	Ph	3-$CH_3C_6H_4$	**2h** 50 (59)
8	Ph	2-$CH_3C_6H_4$	**2i** 32 (51)
9	Ph	4-$CH_3OC_6H_4$	**2j** 44 (45)
10	Ph	4-ClC_6H_4	**2k** 66 (79)

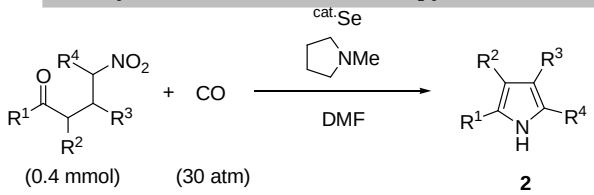
[a] Reaction conditions: **1a** (0.4 mmol), selenium (0.1 mmol), 1-methylpyrrolidine (2.5 mmol), and DMF (2.5 mL) under CO (30 atm) at 150 ºC for 5 h.

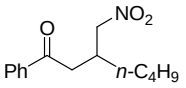
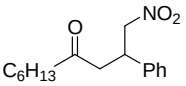
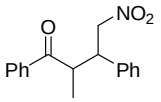
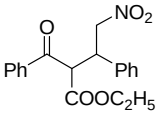
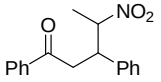
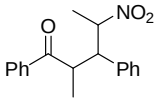
[b] Isolated yields. The numbers in parenthesis show the ^{1}H-NMR yields.

[c] For 10 h.

The synthesis of 4-alkyl-2-phenyl- and 2-alkyl-4-phenyl-1*H*-pyrroles, **2l** and **2m**, was successfully achieved by the selenium-catalyzed reaction of the corresponding γ-nitro substituted ketones and carbon monoxide (entries 1 and 2 in Table 3). The 2,3,4- and 2,3,5-tri- and 2,3,4,5-tetrasubstituted 1*H*-pyrroles, **2n**-**2q**, were also synthesized by the selenium-catalyzed reductive *N*-heterocyclization of the corresponding γ-nitro substituted ketones with carbon monoxide (entries 3-6). In the case of the synthesis of **2o** by the reaction using ethyl 2-acetoxy-4-nitro-3-phenylbutanoate, the ester group was inactive under the reaction conditions (entry 4).

Table 3. Synthesis of multisubstituted pyrroles[a]



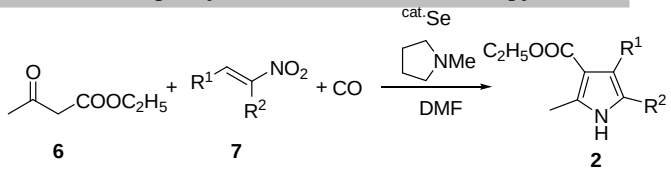
Entry	γ-Nitoro carbonyl compound	Yield (%)[b]
1		**2l**, 31%
2		**2m**, 53%
3		**2n**, 53%
4		**2o**, 60%
5		**2p**, 36%
6		**2q**, 25%

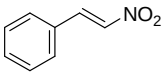
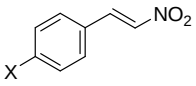
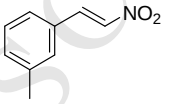
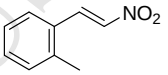
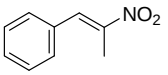
[a] Reaction conditions: γ-nitro carbonyl compound (0.4 mmol), selenium (0.1 mmol), 1-methylpyrrolidine (2.5 mmol), and DMF (2.5 mL) under CO (30 atm) at 150 ºC for 5 h.

[b] Isolated yields.

Next, we investigated the one-pot synthesis of 1*H*-pyrrole bearing an ethyl ester group by the selenium-catalyzed reaction of ethyl acetoacetate (**6**), β-nitrostyrene (**7a**) and carbon monoxide. When **6** was allowed to react with **7a** under the pressure of carbon monoxide (30 atm) in the presence of a catalytic amount of selenium (25 mol%) and 1-methylpyrrolidine as the base in DMF solvent at 120 ºC for 5 h, the one-pot synthesis of 1*H*-pyrrole bearing ethyl ester group was successfully attained to give ethyl 2-methyl-4-phenyl-1*H*-pyrrole-3-carboxylate (**2o**) in 58% yield (entry 1 in Table 4). 1-Methyl-, 1-methoxy-, 1-chloro-4-(2-nitroethenyl)benzenes, and 1-methyl-3-(2-nitroethenyl)benzene gave the corresponding 2-methyl-4-aryl-1*H*-pyrrole-3-carboxylates, **2r**-**2u**, in 59, 58, 55 and 63% yields, respectively (entries 2-5). For the sterically hindered β-nitrostyrene, such as 1-methyl-2-(2-nitroethenyl)benzene and 2-nitro-1-phenyl-1-propene, the yields of products, **2v** and **2w**, were slightly decreased (entries 6 and 7).

Table 4. One-pot synthesis of multisubstituted pyrroles[a]

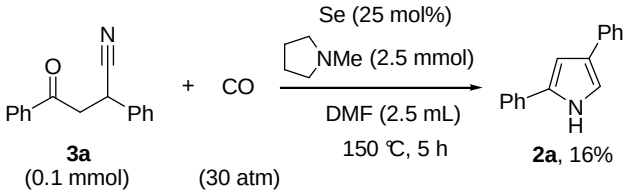


Entry	Vinyl nitro compound	Yield (%)[b]
1		**2o** 58
2	 X = CH_3	**2r** 59
3	X = CH_3O	**2s** 58
4	X = Cl	**2t** 55
5		**2u** 63
6		**2v** 39
7		**2w** 16

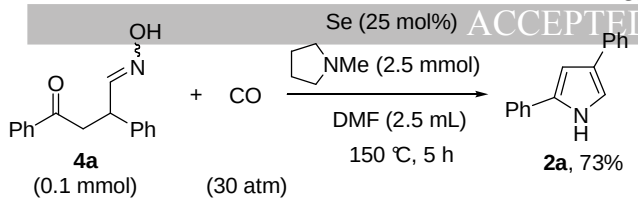
[a] Reaction conditions: 6 (0.4 mmol), 7 (0.4 mmol), selenium (0.1 mmol), 1-methylpyrrolidine (2.5 mmol), and DMF (2.5 mL) under CO (30 atm) at 120 ºC for 5 h.

[b] Isolated yields.

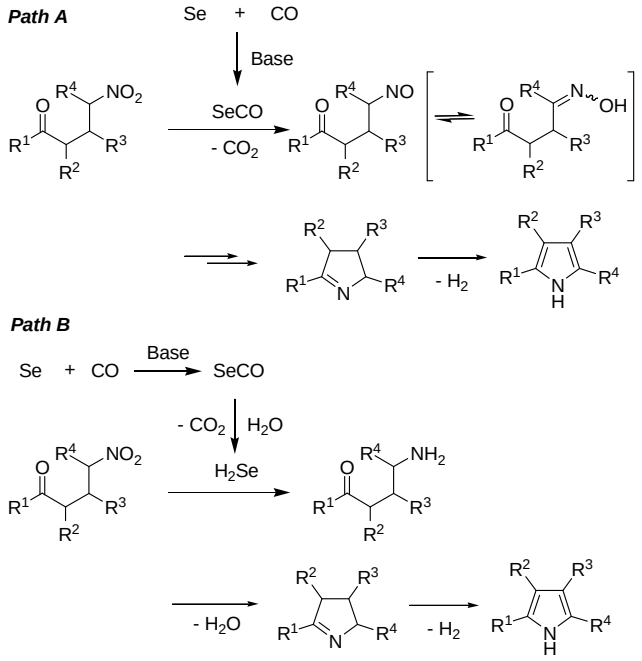
For the reaction, 4-oxo-2,4-diphenylbutanenitrile (**3a**) and 4-oxo-2,4-diphenylbutanal oxime (**4a**) were formed as by-products (Table 1). Based on these results, we proposed that these compounds were intermediates for the selenium-catalyzed synthesis of multisubstituted 1*H*-pyrroles by the reaction of the γ-nitro substituted ketones with carbon monoxide. To obtain information on the reaction pathway, the nitrile **3a** and oxime **4a** were separately treated with carbon monoxide in the presence of a catalytic amount of selenium at 150 ºC for 5 h. For the reaction of **3a**, **3a** was recovered in 67% yield with a small amount of the 1*H*-pyrrole **2a** (16%) (Scheme 2). On the other hand, in the case of **4a**, **2a** was obtained in 73% yield (Scheme 3). From these results, it was suggested that the oxime may be an important intermediate during the reaction.



Scheme 2

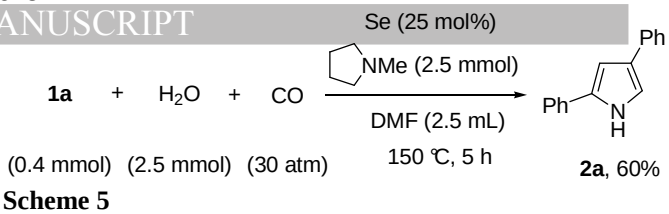


Scheme 3



Scheme 4

We cannot explain the reaction pathway in detail, but a plausible reaction pathway is shown in Scheme 4. A method for the preparation of the carbonyl selenide (SeCO) via the acidolysis of secondary amine salts of the selenocarbamates generated by the reaction of elemental selenium with carbon monoxide and secondary amine has already been shown.[14] It was proposed that the reductive deoxygenation of the nitro group of the γ-nitro substituted ketones with SeCO to generate the nitroso is the first step in this reaction (path A in Scheme 4). The tautomerization of the nitroso compounds smoothly proceeded under mild conditions to produce the oximes.[15] When the reaction was carried out under harsh reaction conditions, the deoxygenation of the nitroso, intramolecular cyclization, followed by dehydrogenation proceeded to form the 1*H*-pyrroles.[16] On the other hand, a method for the preparation of the hydrogen selenide amine salt by the reaction of elemental selenium with carbon monoxide and water in the presence of tertiary amine has already been shown.[17] Based on the result, it was also proposed that reduction of the nitro group to the amino group by the hydrogen selenide amine salt, which was generated in situ by the reaction of selenium, carbon monoxide, and water in the presence of 1-methylpyrrolidine, is a key step of the reaction (path B in Scheme 4).[18] When the reaction of 4-nitro-1,3-diphenyl-butan-1-one (**1a**) was carried out in the presence of H_2O (2.5 mmol), 2,4-diphenyl-1*H*-pyrrole (**2a**) was then formed in 60% yield (Scheme 5). Based on the result, path B including the reduction of nitro compound by hydrogen selenide, giving the corresponding amine intermediate, cannot ruled out.



Scheme 5

3. Conclusion

In conclusion, the selenium-catalyzed reaction of γ-nitro substituted carbonyl compounds with carbon monoxide gave the corresponding multisubstituted 1*H*-pyrrole. The possibility of the carbon monoxide-selenium catalytic system for the synthesis of *N*-heterocyclic compounds is currently under investigation.

4. Experimental section

4.1. Reagents. The selenium and carbon monoxide were commercially available and were used without further purification. The γ-nitro substituted carbonyl compounds were synthesized by the Michael addition of nitromethane or nitroethane to α,β-unsaturated carbonyl compounds. All other chemical agents were commercially obtained and purified by distillation prior to use if necessary.

4.2. General Procedure for Selenium-Catalyzed Reaction of γ-Nitro Substituted Carbonyl Compounds with Carbon Monoxide. To an autoclave, γ-nitro substituted carbonyl compounds (0.4 mmol), selenium (8 mg, 0.1 mmol), and 1-methylpyrrolidine (211 mg, 2.5 mmol), were added to DMF (2.5 mL). The apparatus was then flushed several times with carbon monoxide and fully charged with carbon monoxide (30 atm) at room temperature. The reaction was carried out at 150 °C for 5 h. The reaction apparatus was then cooled to room temperature. After the evacuation of the excess carbon monoxide, the solution was extracted with ethyl acetate. The organic layer was dried over $MgSO_4$. The resulting mixture was filtered, and the filtrate was concentrated. Purification of the residue by silica gel column chromatography afforded the pyrrole. (*Caution:* The prepared pyrroles slowly decomposed during the purification and storing in solution.) The structures of the products were assigned by their ^{1}H- and ^{13}C-NMR, and mass spectra. The product was characterized by comparing its spectral data with those of an authentic sample or previous reports on **2a**,[8g] **2b**,[8g] **2e**,[19] **2f**,[8g] **2g**,[8g] **2j**,[20] **2k**,[8g] **2l**,[21] **2o**,[22] **2p**,[23] **2q**,[24] **3a**,[25] and **5a**.[26]

4-Phenyl-2-*m*-tolyl-1*H*-pyrrole (**2c**): m.p. 139-142 °C; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.40 (s, 1H), 7.56 (d, *J* = 7.7 Hz, 2H), 7.37-7.23 (m, 5H), 7.19 (t, *J* = 7.2 Hz, 1H), 7.10 (s, 1H), 6.81 (s, 1H), 2.38 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 138.5, 135.5, 133.2, 132.4, 128.8, 128.6, 127.3, 126.5, 125.7, 125.1, 124.6, 120.9, 115.4, 103.8, 21.5; IR (KBr): 3428, 1606, 1489, 1433, 1133, 924, 807, 793, 779, 756, 693 cm^{-1}; MS (EI) *m/z* 233 (M^+).

4-Phenyl-2-*o*-tolyl-1*H*-pyrrole (**2d**): m.p. 83-84 °C; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.26 (s, 1H), 7.57 (dd, *J* = 8.4 Hz, 1.1 Hz, 2H), 7.39-7.34 (m, 3H), 7.29-7.14 (m, 5H), 6.64 (dd, *J* = 2.7 Hz, 1.4 Hz, 1H), 2.50 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 135.7, 135.2, 132.6, 132.4, 131.1, 128.6, 127.9, 127.0, 126.1, 125.8, 125.6, 125.2, 114.7, 106.8, 21.2; IR (KBr): 3419, 3059, 1690, 1600, 1488, 1129, 929, 757 cm^{-1}; MS (EI) *m/z* 233 (M^+).

2-Phenyl-4-*m*-tolyl-1*H*-pyrrole (**2h**): m.p. 145-147 °C (Lit.[8g] 117-118 °C); ^{1}H-NMR (400 MHz $CDCl_3$) δ 8.40 (s, 1H), 7.50 (d, *J* = 7.2 Hz, 2H), 7.40-7.36 (m, 4H), 7.27-7.21 (m, 2H), 7.10 (t, *J* = 2.0 Hz, 1H), 7.02 (d, *J* = 7.7 Hz, 1H), 6.82 (dd, *J* = 2.5 Hz, 1.6 Hz, 1H), 2.38 (s, 3H); ^{13}C-NMR (100 MHz $CDCl_3$) δ 138.1,

135.4, 132.9, 132.5, 128.9, 128.5, 126.6, 126.5, 126.4, 125.9, 123.8, 122.3, 115.6, 104.0, 21.5; IR (KBr): 3403, 3031, 2919, 1603, 1487, 1136, 811, 790 cm^{-1}; MS (EI) *m/z* 233 (M^+).

2-Phenyl-4-*o*-tolyl-1*H*-pyrrole (**2i**): m.p. 108-109 °C (Lit.[8g] 154-155 °C); ^{1}H-NMR (400 MHz $CDCl_3$) δ 8.40 (s, 1H), 7.49 (d, *J* = 7.7 Hz, 2H), 7.43-7.35 (m, 3H), 7.20 (tt, *J* = 13.4 Hz, 6.1 Hz, 4H), 6.90 (s, 1H), 6.68 (s, 1H), 2.46 (s, 3H); ^{13}C-NMR (100 MHz $CDCl_3$) δ 135.5, 135.3, 132.5, 131.8, 130.6, 129.2, 128.9, 126.3, 126.1, 126.0, 125.8, 123.8, 117.7, 106.9, 21.4; IR (KBr): 3372, 3013, 2950, 1604, 1488, 1455, 1135, 814, 762 cm^{-1}; MS (EI) *m/z* 233 (M^+).

2-Hexyl-4-phenyl-1*H*-pyrrole (**2m**): ^{1}H-NMR (400 MHz $CDCl_3$) δ 7.82 (s, 1H), 7.49 (t, *J* = 7.7 Hz, 2H), 7.30 (t, *J* = 7.7 Hz, 2H), 7.13 (t, *J* = 7.2 Hz, 1H), 6.90 (s, 1H), 6.22 (s, 1H), 2.56 (t, *J* = 7.7 Hz, 2H), 1.65-1.58 (m, 2H), 1.33 (m, 6H), 0.89 (t, *J* = 6.6 Hz, 3H); ^{13}C-NMR (100 MHz $CDCl_3$) δ 136.0, 134.0, 128.5, 125.2, 125.0, 124.8, 112.7, 31.6, 29.5, 29.0, 27.8, 22.6, 14.1. IR (KBr): 3370, 2927, 1683, 1604, 1525, 1454, 795, 763, 695 cm^{-1}; MS (EI) *m/z* 227 (M^+).

3-Methyl-2,4-diphenyl-1*H*-pyrrole (**2n**): m.p. 119-123 °C; ^{1}H-NMR (400 MHz $CDCl_3$) δ 8.17 (s, 1H), 7.48-7.38 (m, 8H), 7.29-7.23 (m, 2H), 6.92 (d, *J* = 2.4 Hz, 1H), 2.34 (s, 1H); ^{13}C-NMR (100 MHz $CDCl_3$) δ 136.2, 133.5, 129.7, 128.7, 128.3, 128.2, 126.9, 126.8, 126.3, 125.7, 115.9, 113.9, 11.5; IR (KBr): 3454, 3056, 1692, 1603, 1492, 1449, 766, 755, 699 cm^{-1}; MS (EI) *m/z* 233 (M^+).

4-Oxo-2,4-diphenylbutanal oxime (**4a**): m.p. 119-120 °C; ^{1}H-NMR (400 MHz $CDCl_3$) δ 7.94 (dd, *J* = 8.4, 1.1 Hz, 2H), 7.61 (d, J = 4.5 Hz, 1H), 7.55 (t, *J* = 7.5 Hz, 1H), 7.44 (t, *J* = 7.7 Hz, 2H), 7.36-7.24 (m, 6H), 4.39-4.35 (m, 1H), 3.78 (dd, *J* = 17.2, 8.2 Hz, 1H), 3.26 (dd, *J* = 17.2, 5.7 Hz, 1H); ^{13}C-NMR (100 MHz $CDCl_3$) δ197.5, 152.6, 140.0, 136.8, 133.1, 128.8, 128.6, 128.2, 128.1, 127.3, 41.2, 41.3; IR (KBr): 3268, 2913, 1690, 1449, 936, 703 cm^{-1}; MS (EI) *m/z* 235 (M^+- H_2O).

4.3. General Procedure for Selenium-Catalyzed Reaction of Ethyl 3-Oxobutanoate, Nitro Vinyl Compounds and Carbon Monoxide. To an autoclave, ethyl acetoacetate (52 mg, 0.4 mmol), vinyl nitro compound (0.4 mmol), selenium (8 mg, 0.1 mmol), and 1-methylpyrrolidine (212 mg, 2.5 mmol), were added to DMF (2.5 mL). The apparatus was then flushed several times with carbon monoxide and fully charged with carbon monoxide (30 atm) at room temperature. The reaction was carried out at 120 °C for 5 h. The reaction apparatus was then cooled to room temperature. After the evacuation of the excess carbon monoxide, the solution was extracted with ethyl acetate. The organic layer was dried over $MgSO_4$. The resulting mixture was filtered, and the filtrate was concentrated. Purification of the residue by silica gel column chromatography afforded the pyrrole. (*Caution:* The prepared pyrroles slowly decomposed during the purification and storing in solution.) The structures of the products were assigned by their ^{1}H- and ^{13}C-NMR, and mass spectra. The product was characterized by comparing its spectral data with those of an authentic sample or previous reports on **2s**[27] and **2w**.[28]

Ethyl 4-(4-chlorophenyl)-2-methyl-1*H*-pyrrole-3-carboxylate (**2r**): m.p. 165-168 °C; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.18 (s, 1H), 7.33-7.26 (m, 4H), 6.58 (d, *J* = 2.3 Hz, 1H), 4.18 (q, *J* = 7.2 Hz, 2H), 2.55 (s, 3H), 1.18 (t, *J* = 7.2 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 165.6, 136.3, 134.3, 132.0, 130.1, 127.6, 126.1, 115.4, 109.9, 59.4, 14.2, 14.0; IR (KBr): 3282, 1658, 1298, 1137, 797, 750 cm^{-1}; MS (EI) *m/z* 263 (M^+).

Ethyl 2-methyl-4-*p*-tolyl-1*H*-pyrrole-3-carboxylate (**2t**): m.p. 127-128°C; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.24 (s, 1 H), 7.28 (d, *J* = 8.3 Hz, 2H), 7.13 (d, *J* = 7.7 Hz, 2H), 6.54 (d, *J* = 2.3 Hz, 1H), 4.18 (q, *J* = 7.1 Hz, 2H), 2.52 (s, 3H), 2.35 (s, 3H), 1.18 (t, *J* = 7.0 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 165.8, 135.9, 135.7, 132.8, 129.2, 128.2, 127.2, 115.2, 110.0, 59.3, 21.1, 14.2, 14.0; IR (KBr): 3335, 1663, 1441, 1292, 1133, 787 cm^{-1}. MS (EI) *m/z* 243 (M^+).

Ethyl 2-methyl-4-*m*-tolyl-1*H*-pyrrole-3-carboxylate (**2u**): m.p. 89-90 °C; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.36 (s, 1 H), 7.25-7.18 (m, 3H), 7.06 (d, *J* = 6.8 Hz, 1H), 6.53 (d, *J* = 2.3 Hz, 1H), 4.17 (q, *J* = 7.2 Hz, 2H), 2.51 (s, 3H), 2.35 (s, 3H), 1.16 (t, *J* = 7.2 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 165.9, 136.8, 136.1, 135.7, 130.0, 127.4, 127.2, 126.9, 126.4, 115.3, 109.9, 59.3, 21.4, 14.1, 13.9; IR (KBr): 3337, 1669, 1442, 1301, 1136, 782 cm^{-1}; MS (EI) *m/z* 243 (M^+).

Ethyl 2-methyl-4-*o*-tolyl-1*H*-pyrrole-3-carboxylate (**2v**): m.p. 128-130 °C; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.23 (s, 1 H), 7.20-7.13 (m, 4H), 6.45 (d, *J* = 2.3 Hz, 1H), 4.03 (q, *J* = 7.2 Hz, 2H), 2.56 (s, 3H), 2.16 (s, 3H), 0.98 (t, *J* = 7.0 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 165.7, 137.4, 136.3, 135.4, 130.2, 129.0, 126.7, 126.1, 124.8, 114.9, 111.1, 59.0, 20.3, 13.8, 13.8; IR (KBr): 3352, 1667, 1440, 1296, 1141, 759 cm^{-1}; MS (EI) *m/z* 243 (M^+).

Acknowledgment

This work was financially supported by the MEXT-Supported Program for the Strategic Research Foundation at Private Universities, Grant-in-Aid for Scientific Research, and the Kansai University Research Grants: Grant-in-Aid for Encouragement of Scientists.

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Supplementary Material

Supplementary data for new compounds of ^{1}H and ^{13}C NMR spectra can be found, in the online version, at doi: /

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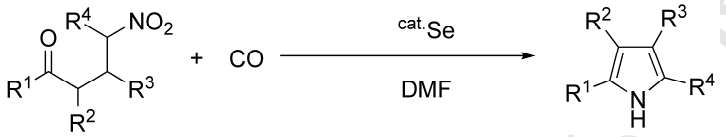

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ARTICLE INFO

Article history:
Received
Received in revised form
Accepted
Available online

Keywords:
Pyrrole
Selenium
Carbon Monoxide
γ-Nitro Substituted Carbonyl Compound

ABSTRACT

The novel and efficient selenium-catalyzed reductive *N*-heterocyclization of γ-nitro substituted carbonyl compounds with carbon monoxide has been developed. Various multisubstituted 1*H*-pyrroles can be easily prepared by this protocol. The one-pot synthesis of ethyl 1*H*-pyrrole-3-carboxylate derivatives was also successfully attained by the selenium-catalyzed reaction of β-ketoester, vinyl nitro compounds, and carbon monoxide.

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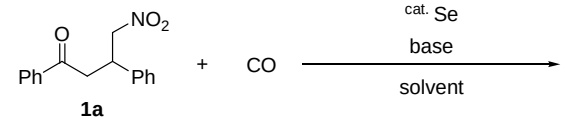
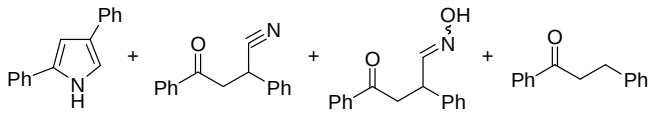
Table 1. Optimized reaction conditions[a]





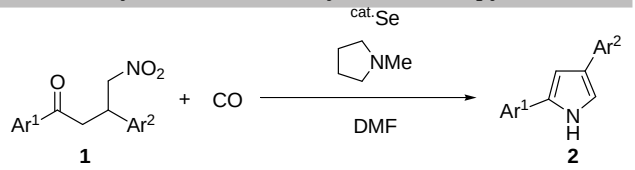
Entry	Solvent	Base	Temp. °C	Yield (%)[b] 2a	3a	4a	5a
1	DMF		30	17	15	51	0
2	DMF		50	25	16	37	0
3	DMF		80	43	12	13	3
4	DMF		120	71	7	0	8
5	DMF		150	81(62)	0	0	13
6	DMF		150	71	0	0	10
7	DMF	Et_3N	150	23	25	15	31
8	DMF	DBU	150	40	2	0	55
9	DMF	K_2CO_3	150	29	11	0	10
10	DMA		150	67	5	0	10
11	THF		150	43	3	6	17
12	CH_3CN		150	64	4	4	12

[a] Reaction conditions: **1a** (0.4 mmol), selenium (0.1 mmol), base (2.5 mmol), and solvent (2.5 mL) under CO (30 atm) for 5 h.

[b] ^{1}H-NMR yields. The number in parenthesis shows isolated yield.

[c] Under CO (10 atm).

Table 2. Synthesis of 2,4-diaryl substituted pyrroles[a]



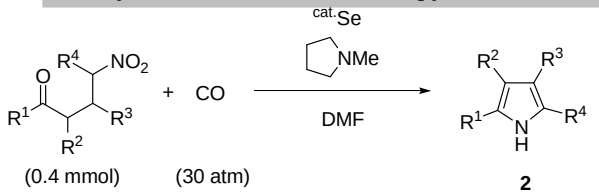
Entry	Ar^1	Ar^2	Yield (%)[b]
1	4-$CH_3C_6H_4$	Ph	**2b** 56 (61)
2	3-$CH_3C_6H_4$	Ph	**2c** 64 (68)
3	2-$CH_3C_6H_4$	Ph	**2d** 30 (57)
4	4-$CH_3OC_6H_4$	Ph	**2e** 58 (66)
5	4-ClC_6H_4	Ph	**2f** 43 (64)
6	Ph	4-$CH_3C_6H_4$	**2g** 54 (63)
7	Ph	3-$CH_3C_6H_4$	**2h** 50 (59)
8	Ph	2-$CH_3C_6H_4$	**2i** 32 (51)
9	Ph	4-$CH_3OC_6H_4$	**2j** 44 (45)
10	Ph	4-ClC_6H_4	**2k** 66 (79)

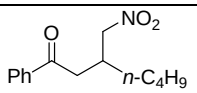
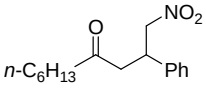
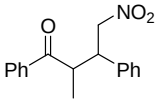
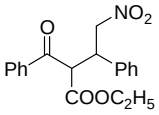
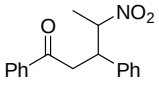
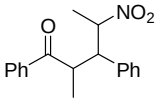
[a] Reaction conditions: **1a** (0.4 mmol), selenium (0.1 mmol), 1-methylpyrrolidine (2.5 mmol), and DMF (2.5 mL) under CO (30 atm) at 150 °C for 5 h.

[b] Isolated yields. The numbers in parenthesis show the ^{1}H-NMR yields.

[c] For 10 h.

Table 3. Synthesis of multisubstituted pyrroles[a]

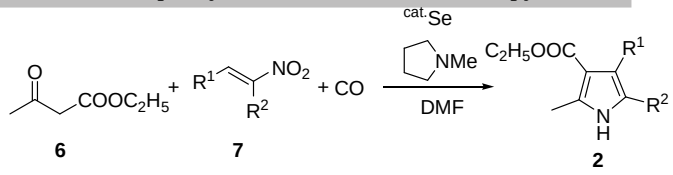


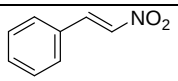
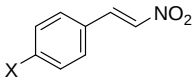
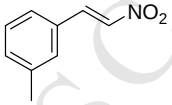
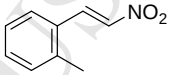
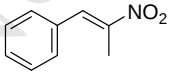
Entry	γ-Nitro carbonyl compound	Yield (%)[b]
1		**2l**, 31
2		**2m**, 53
3		**2n**, 53
4		**2o**, 60
5		**2p**, 36
6		**2q**, 25

[a] Reaction conditions: γ-nitro carbonyl compound (0.4 mmol), selenium (0.1 mmol), 1-methylpyrrolidine (2.5 mmol), and DMF (2.5 mL) under CO (30 atm) at 150 ºC for 5 h.

[b] Isolated yields.

Table 4. One-pot synthesis of multisubstituted pyrroles[a]



Entry	Vinyl nitro carbonyl compound	Yield (%)[b]
1		**2l**, 58
2	X = CH_3 	**2n**, 59
3	X = CH_3O	**2o**, 58
4	X = Cl	**2p**, 55
5		**2q**, 63
6		**2m**, 39
7		**2m**, 16

[a] Reaction conditions: 6 (0.4 mmol), 7 (0.4 mmol), selenium (0.1 mmol), 1-methylpyrrolidine (2.5 mmol), and DMF (2.5 mL) under CO (30 atm) at 120 ºC for 5 h.

[b] Isolated yields.

Supplementary Material

Synthesis of multisubstituted 1*H*-pyrrole: selenium-catalyzed reaction of γ-nitro substituted carbonyl compounds and carbon monoxide

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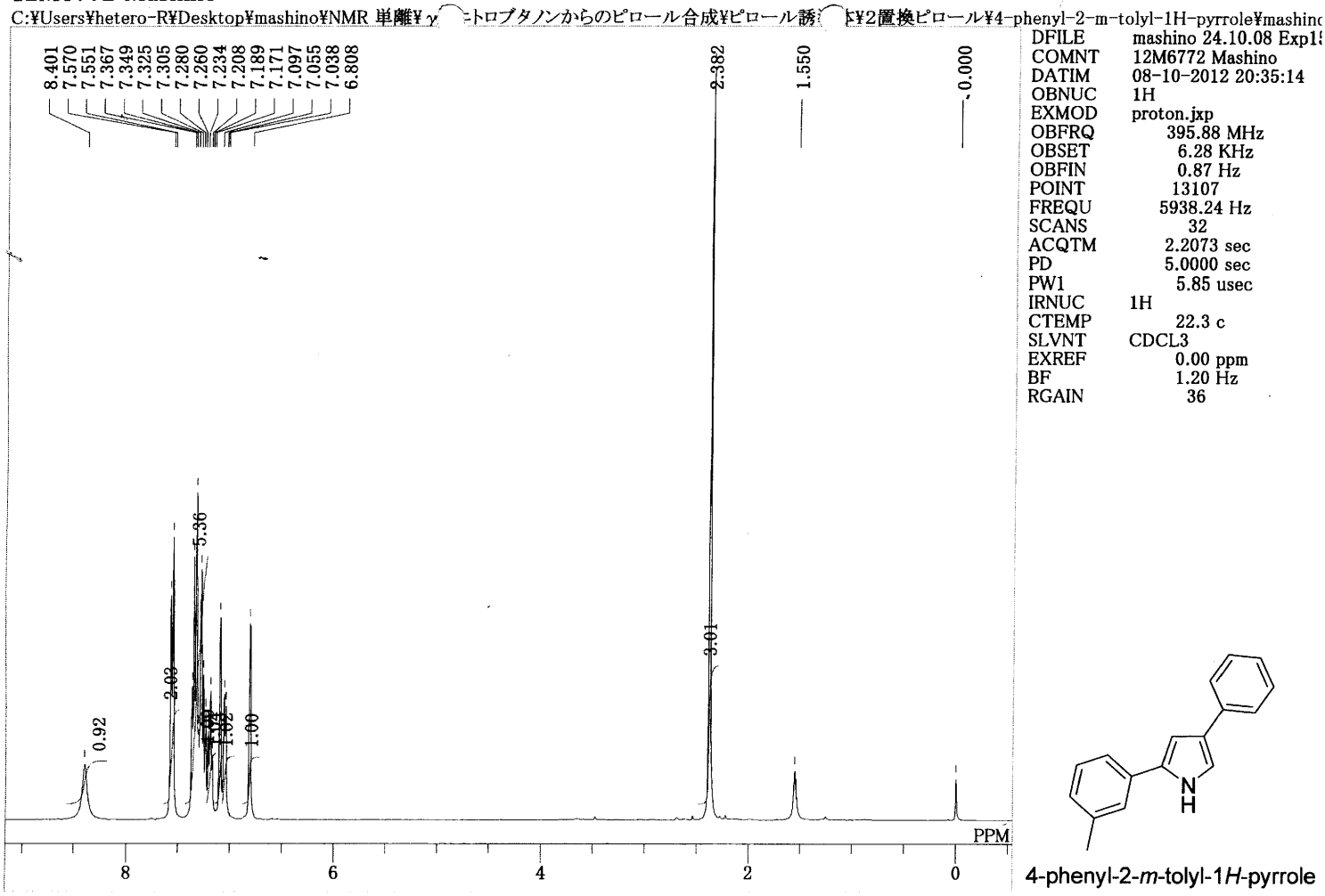
CONTENTS of the Supplementary Material



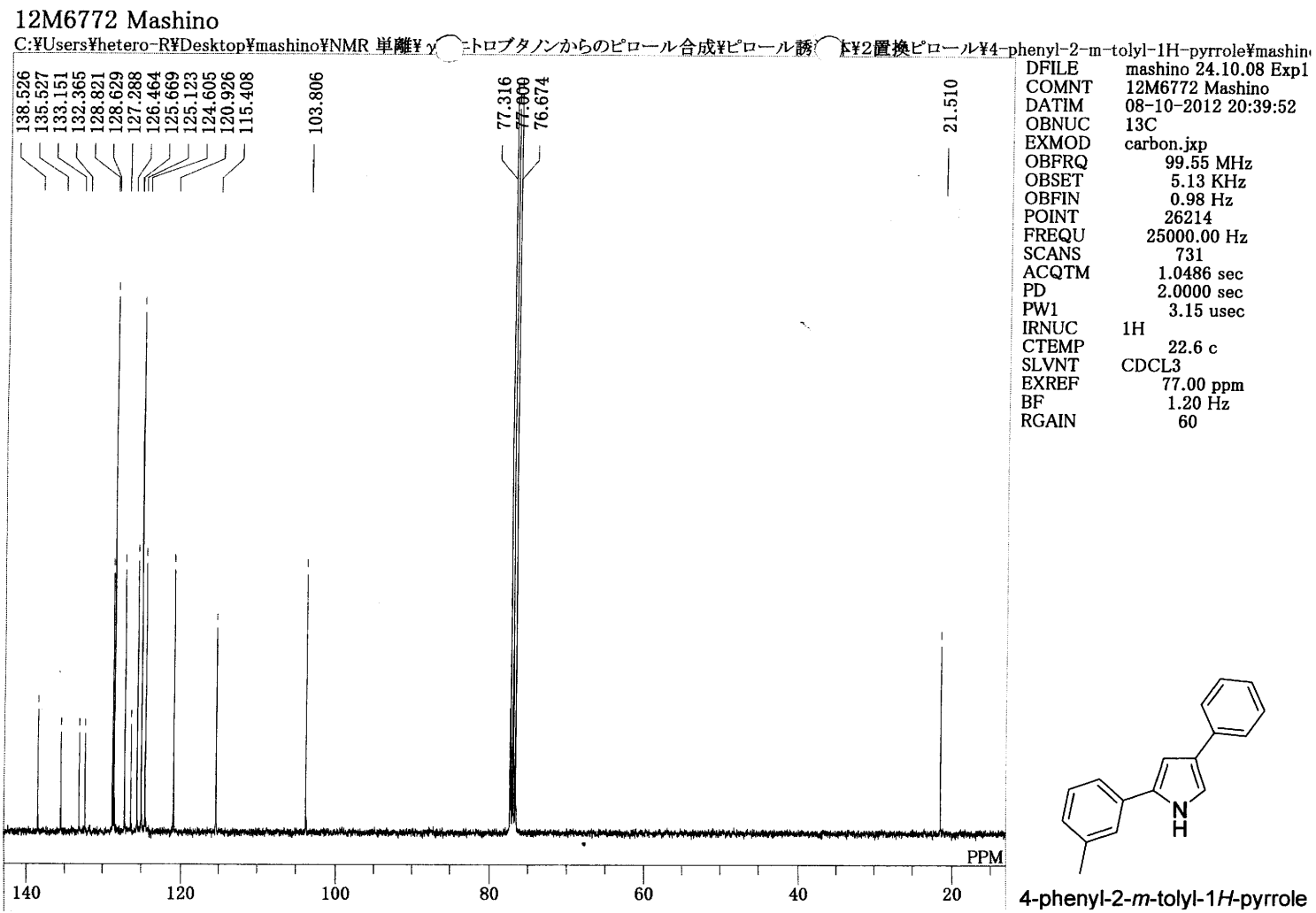
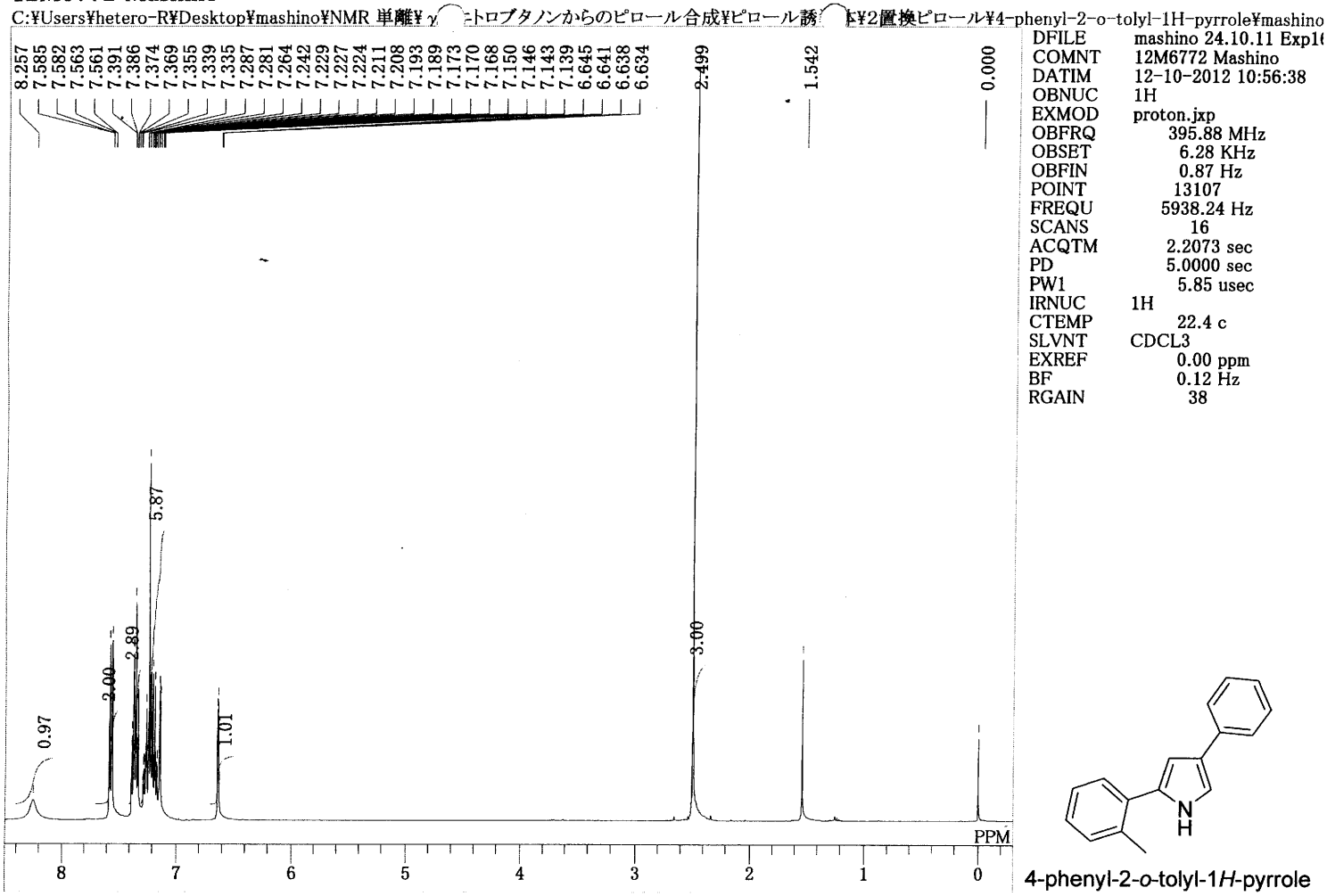


Fig. S1. ^{1}H (400 MHz) and ^{13}C (100 MHz) NMR spectra of **2c** in $CDCl_3$



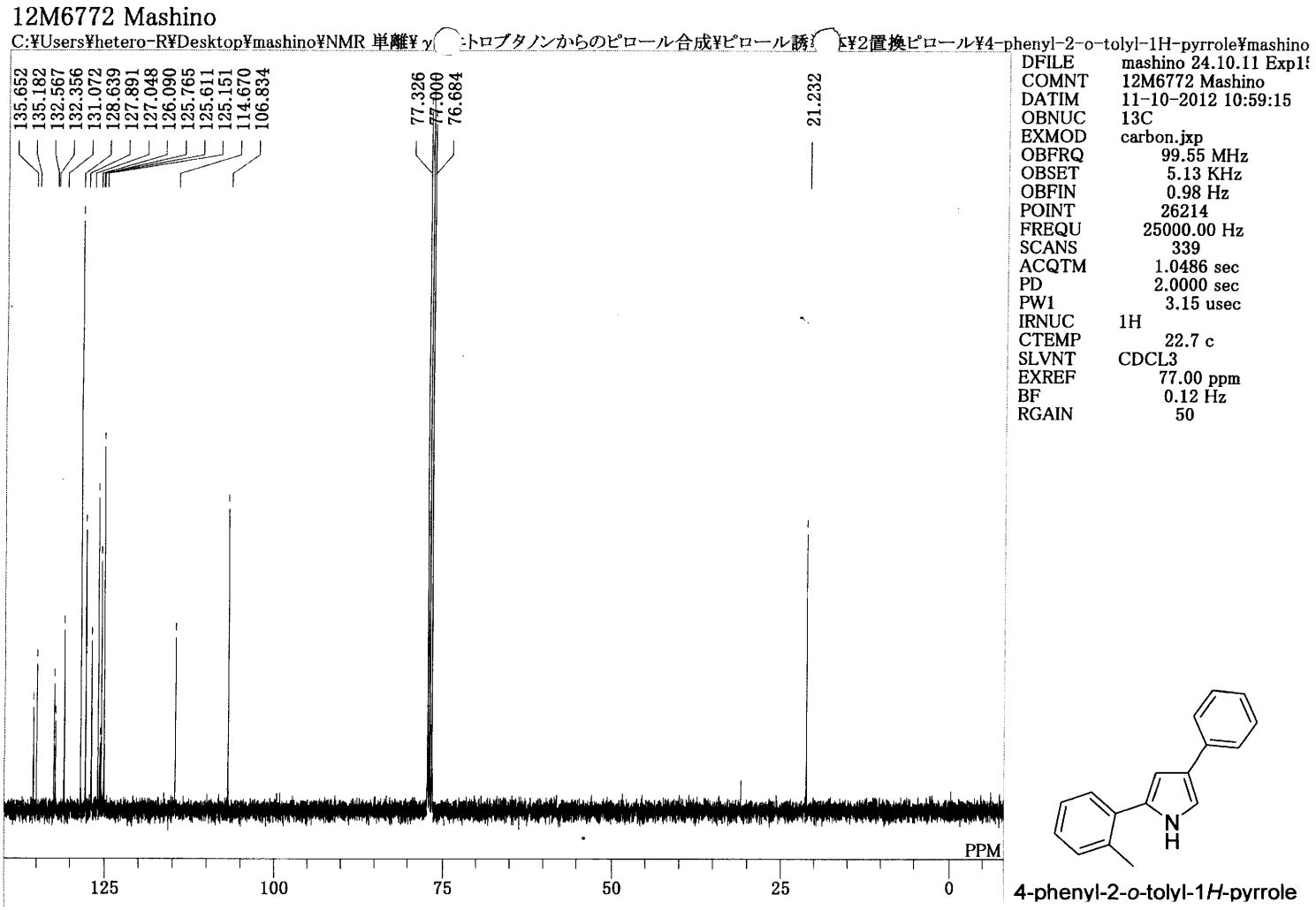
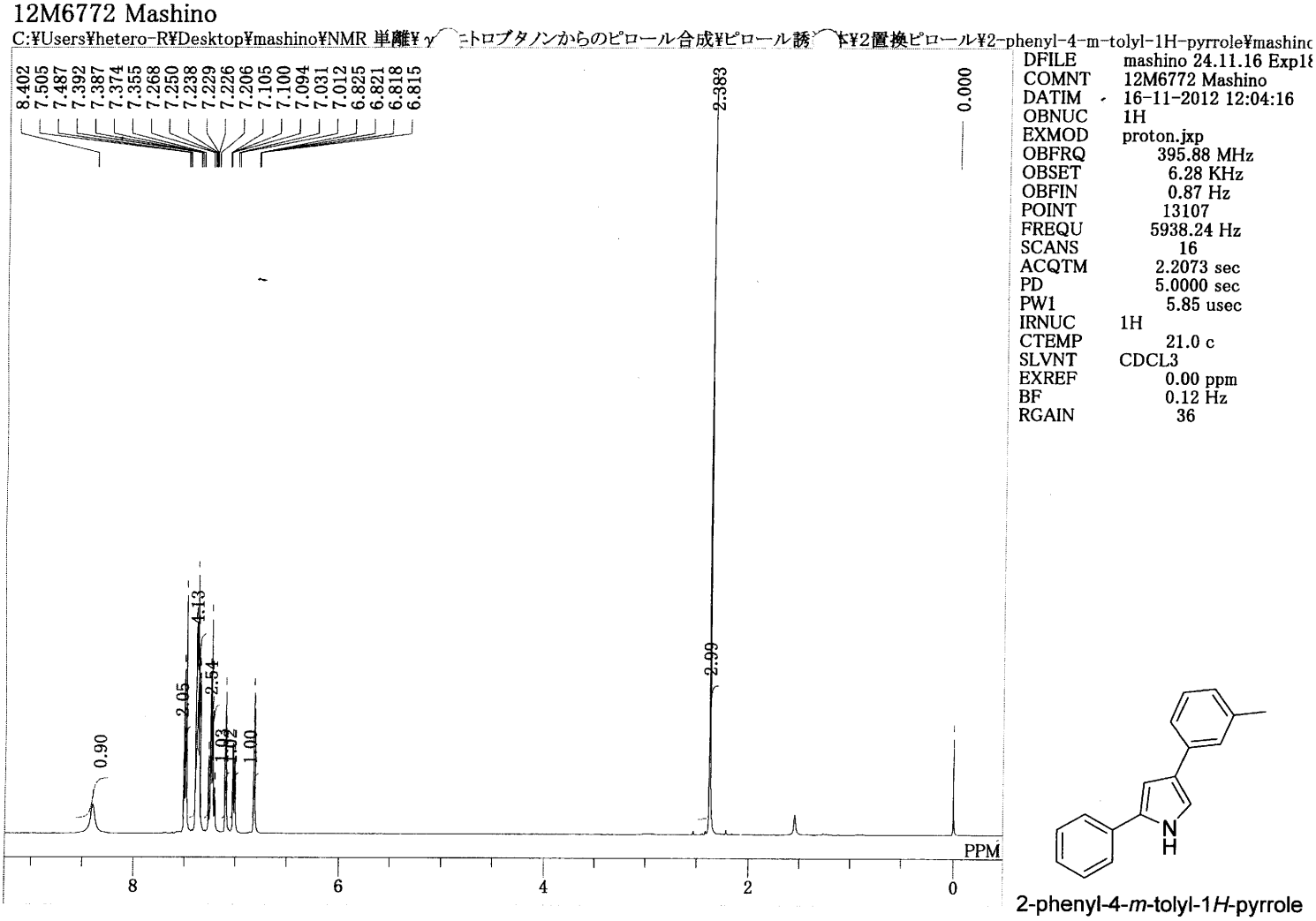
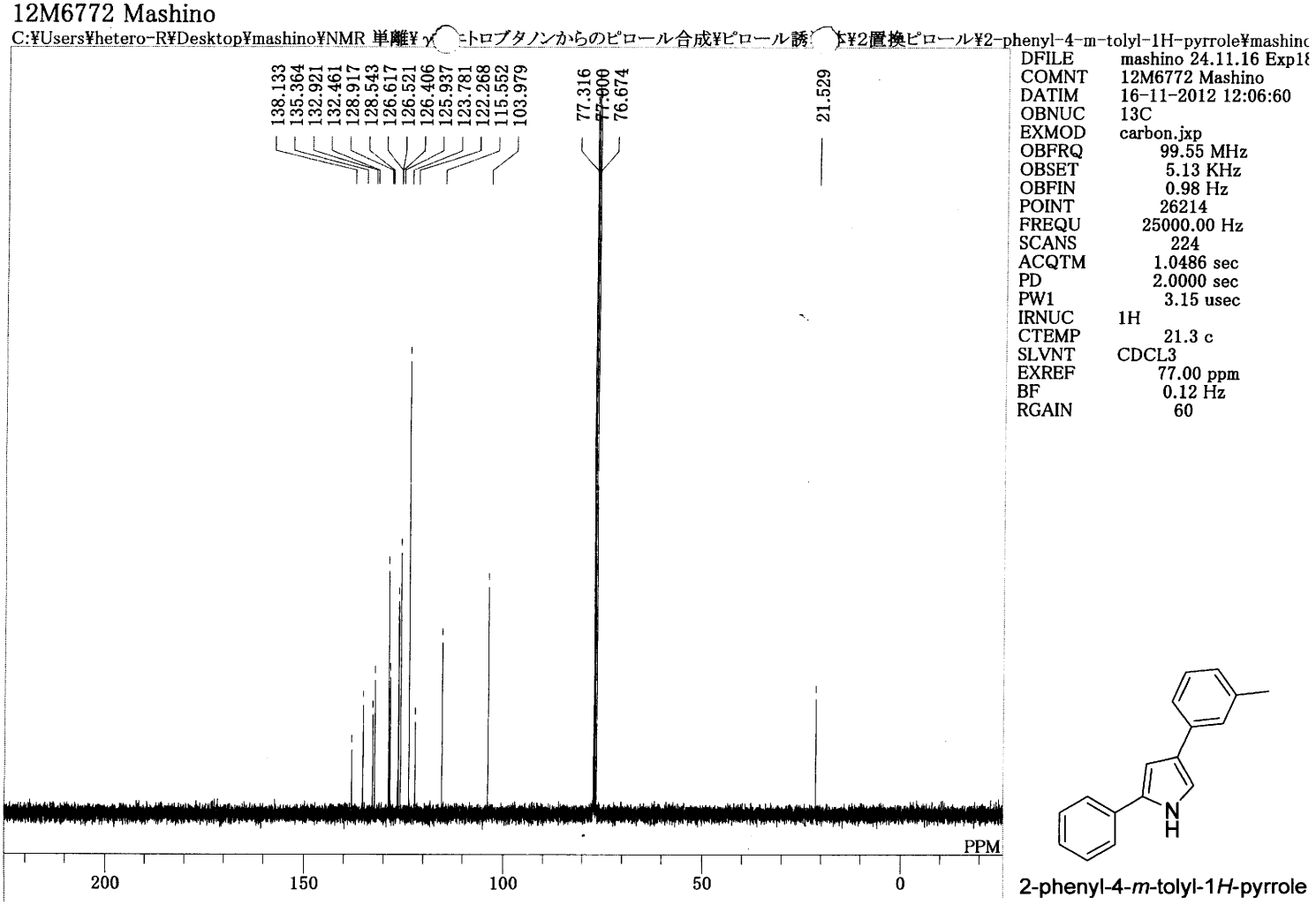


Fig. S2. ^{1}H (400 MHz) and ^{13}C (100 MHz) NMR spectra of **2d** in $CDCl_3$

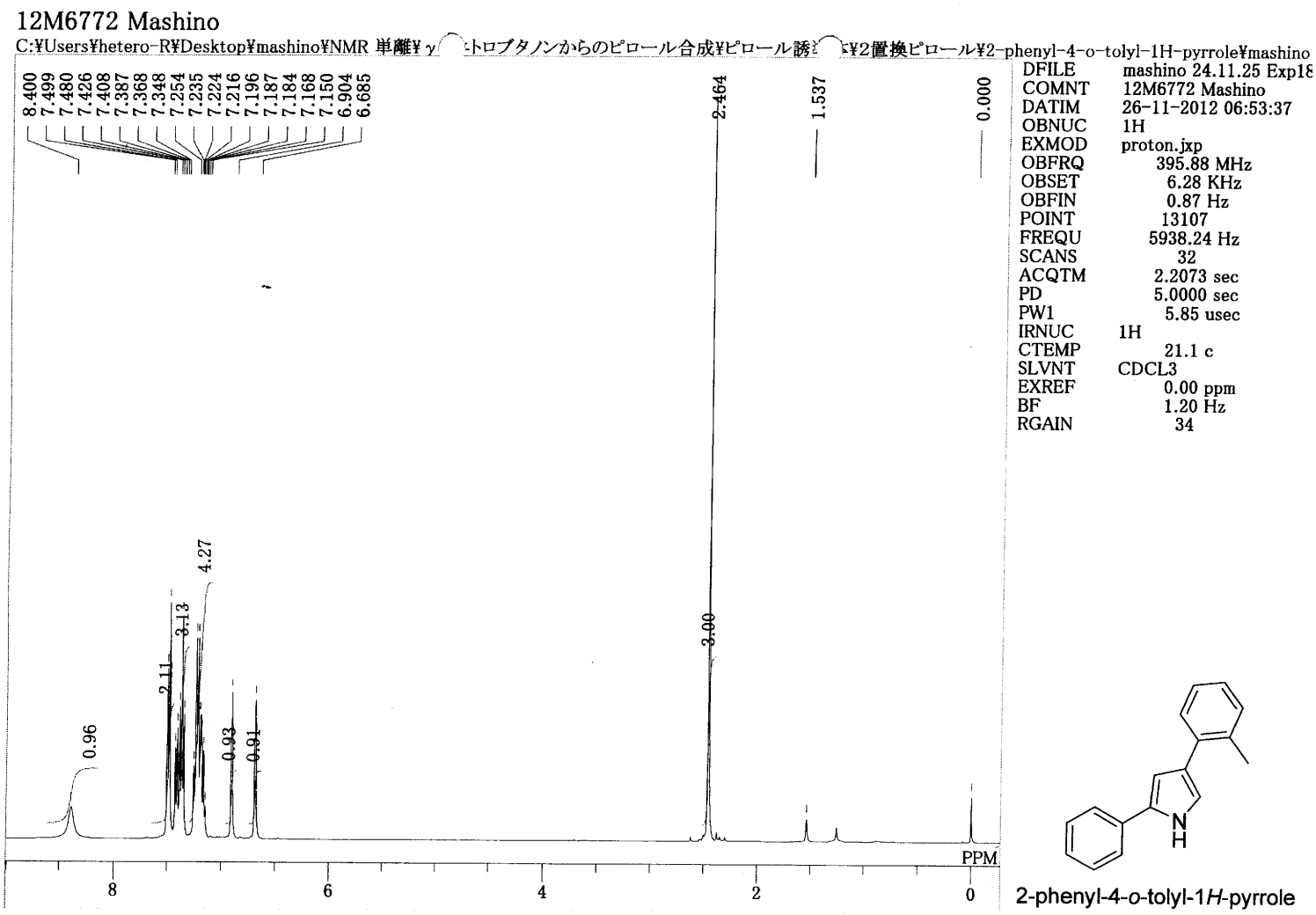


2-phenyl-4-*m*-tolyl-1*H*-pyrrole



2-phenyl-4-*m*-tolyl-1*H*-pyrrole

Fig. S3. ^{1}H (400 MHz) and ^{13}C (100 MHz) NMR spectra of **2h** in $CDCl_3$



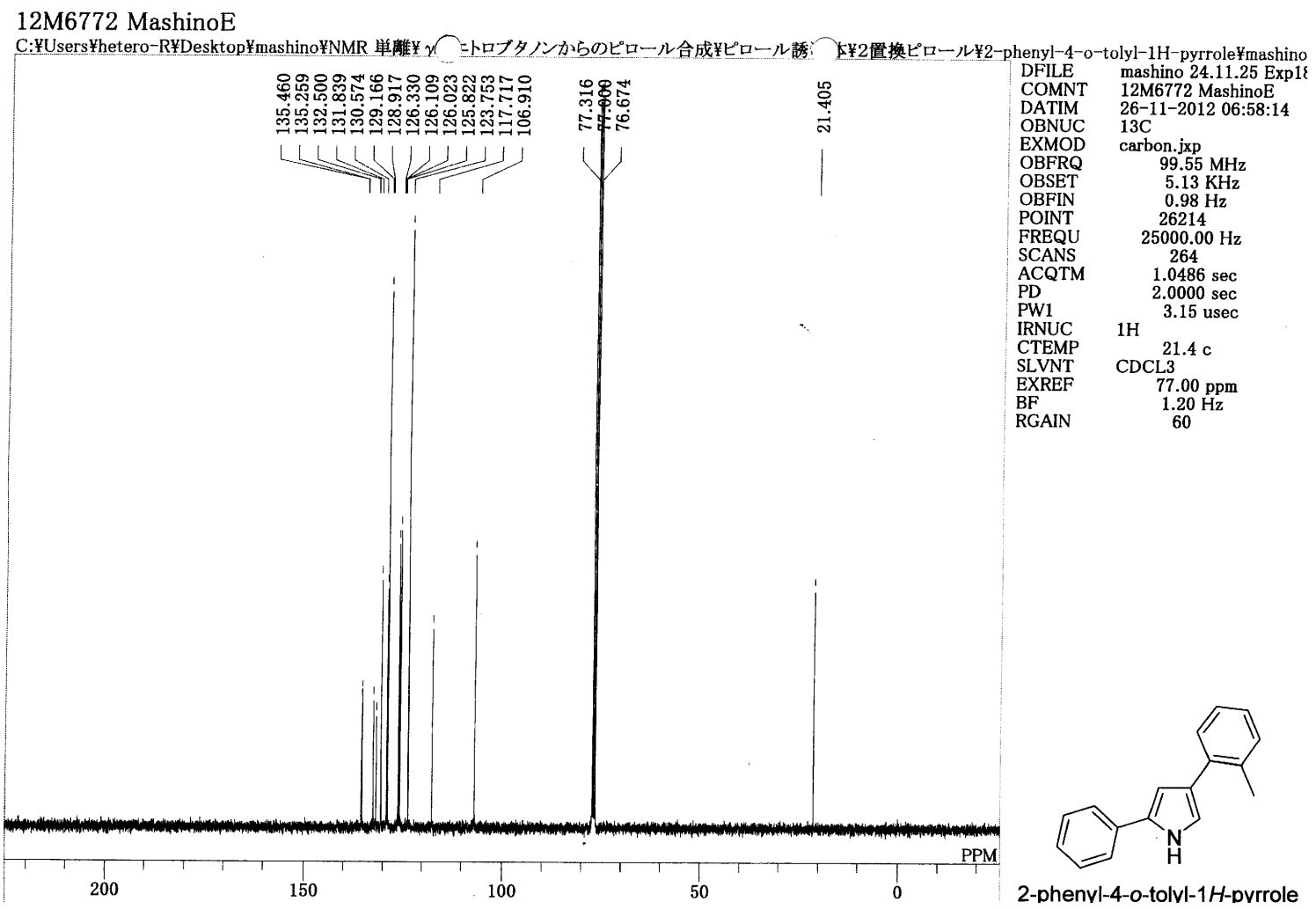
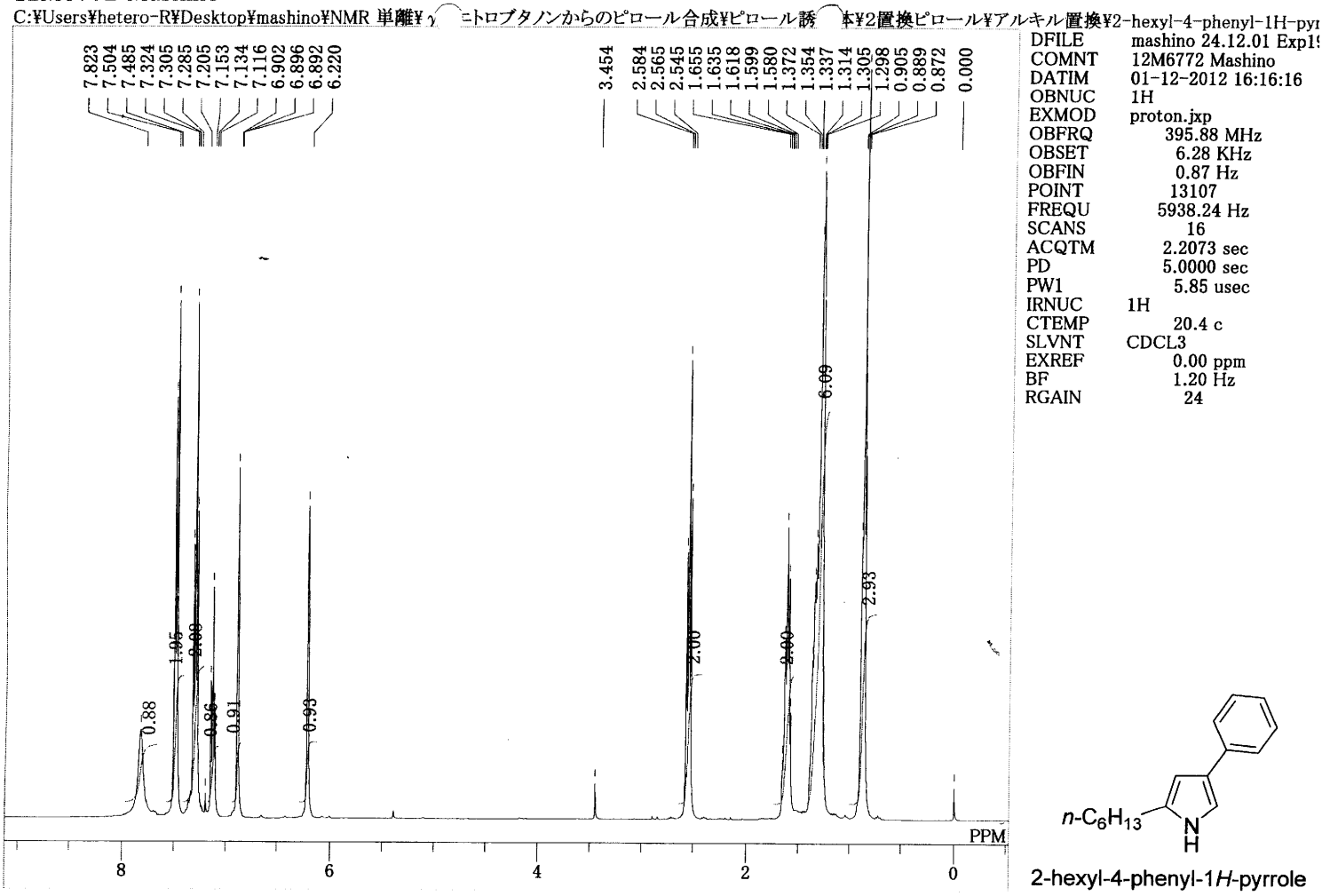


Fig. S4. ^{1}H (400 MHz) and ^{13}C (100 MHz) NMR spectra of **2i** in $CDCl_3$



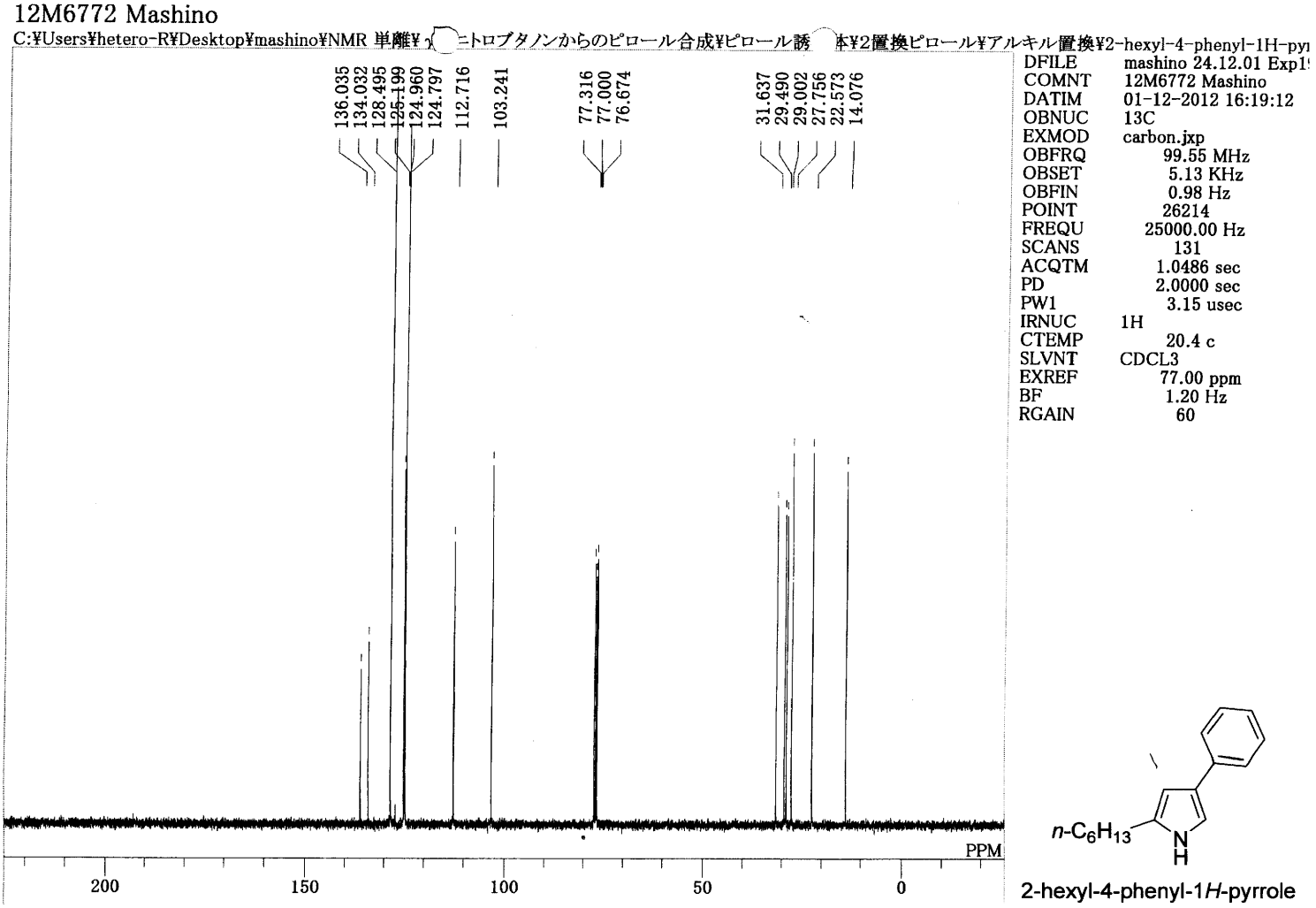
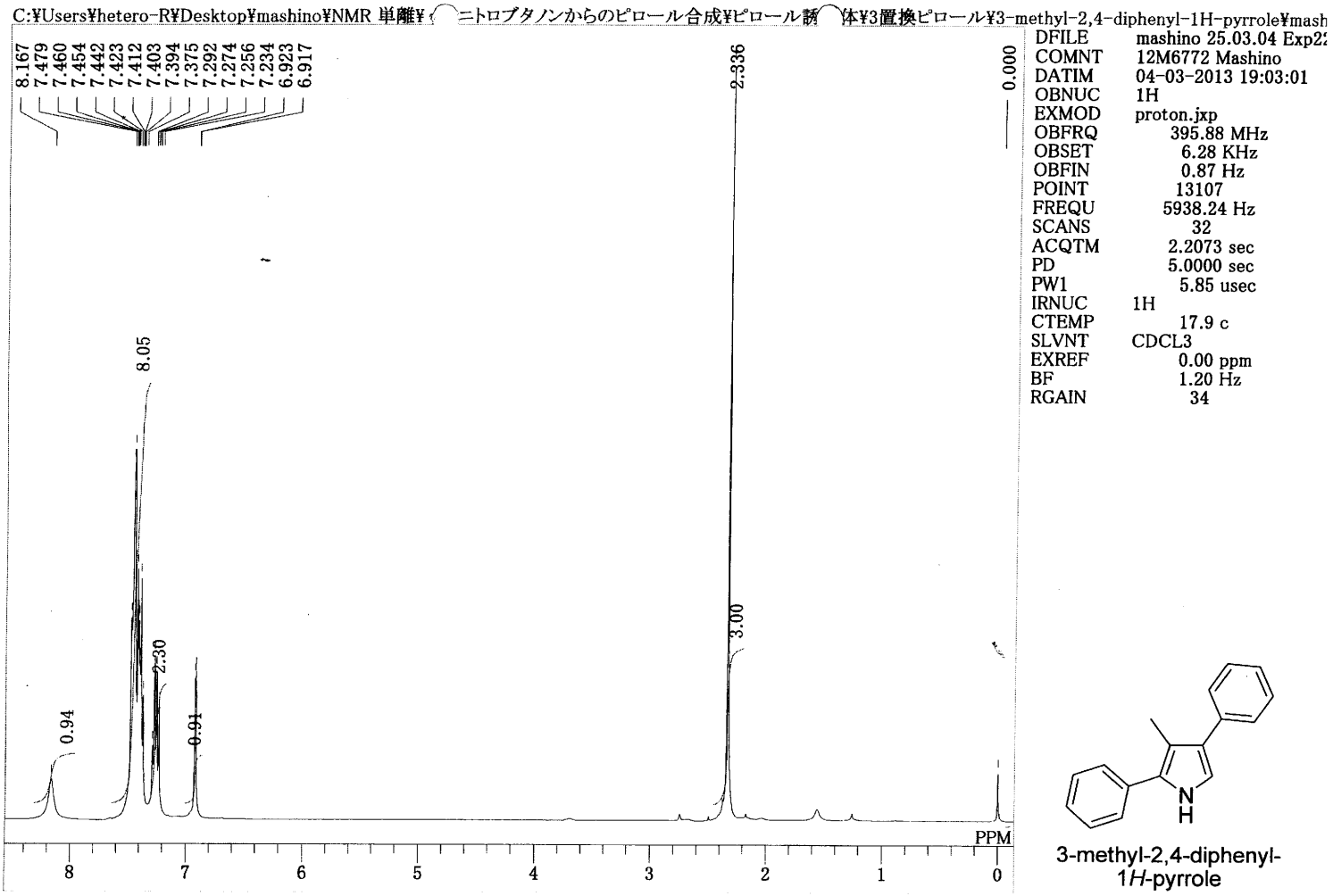


Fig. S5. ^{1}H (400 MHz) and ^{13}C (100 MHz) NMR spectra of **2m** in $CDCl_3$



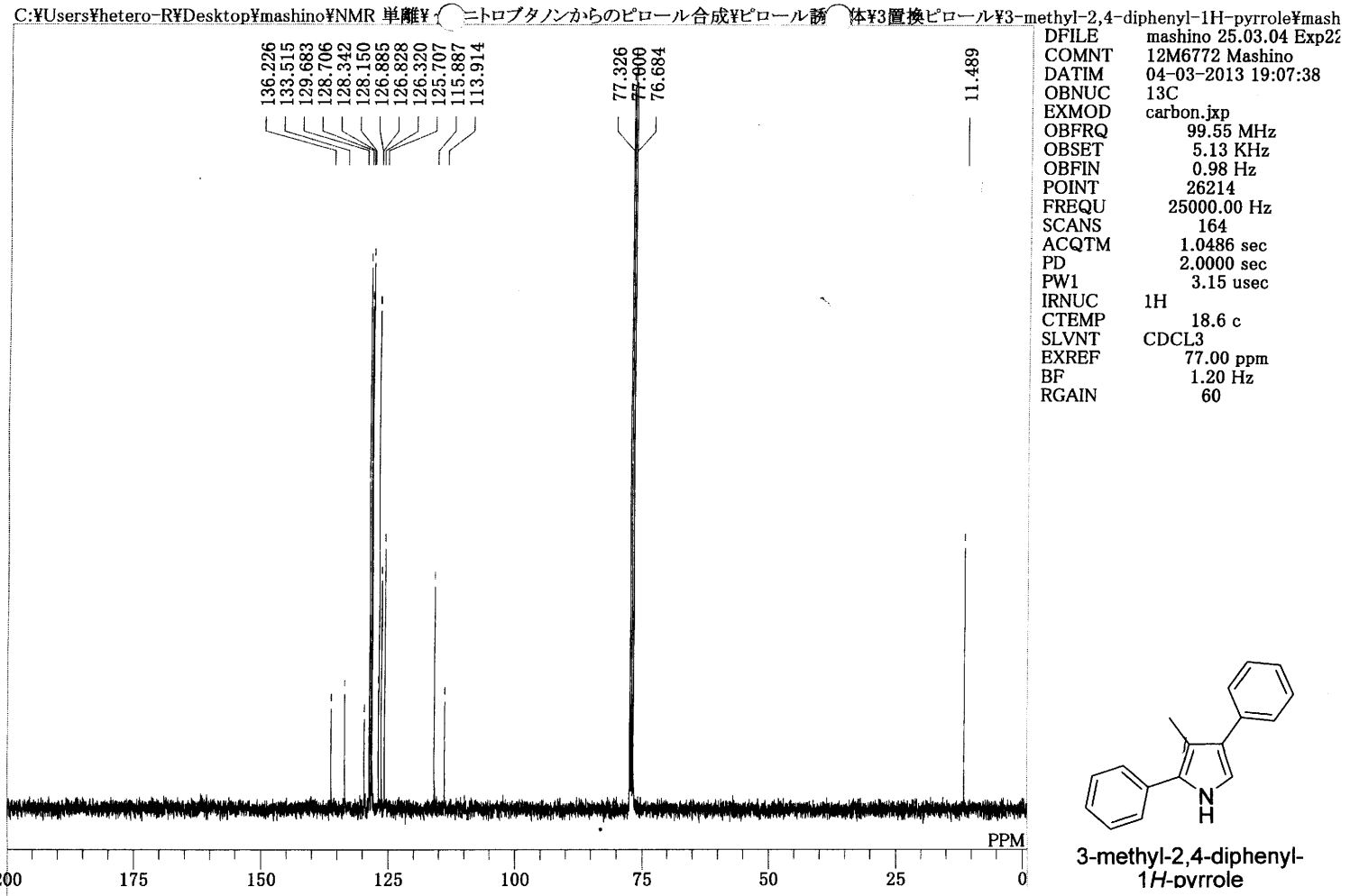
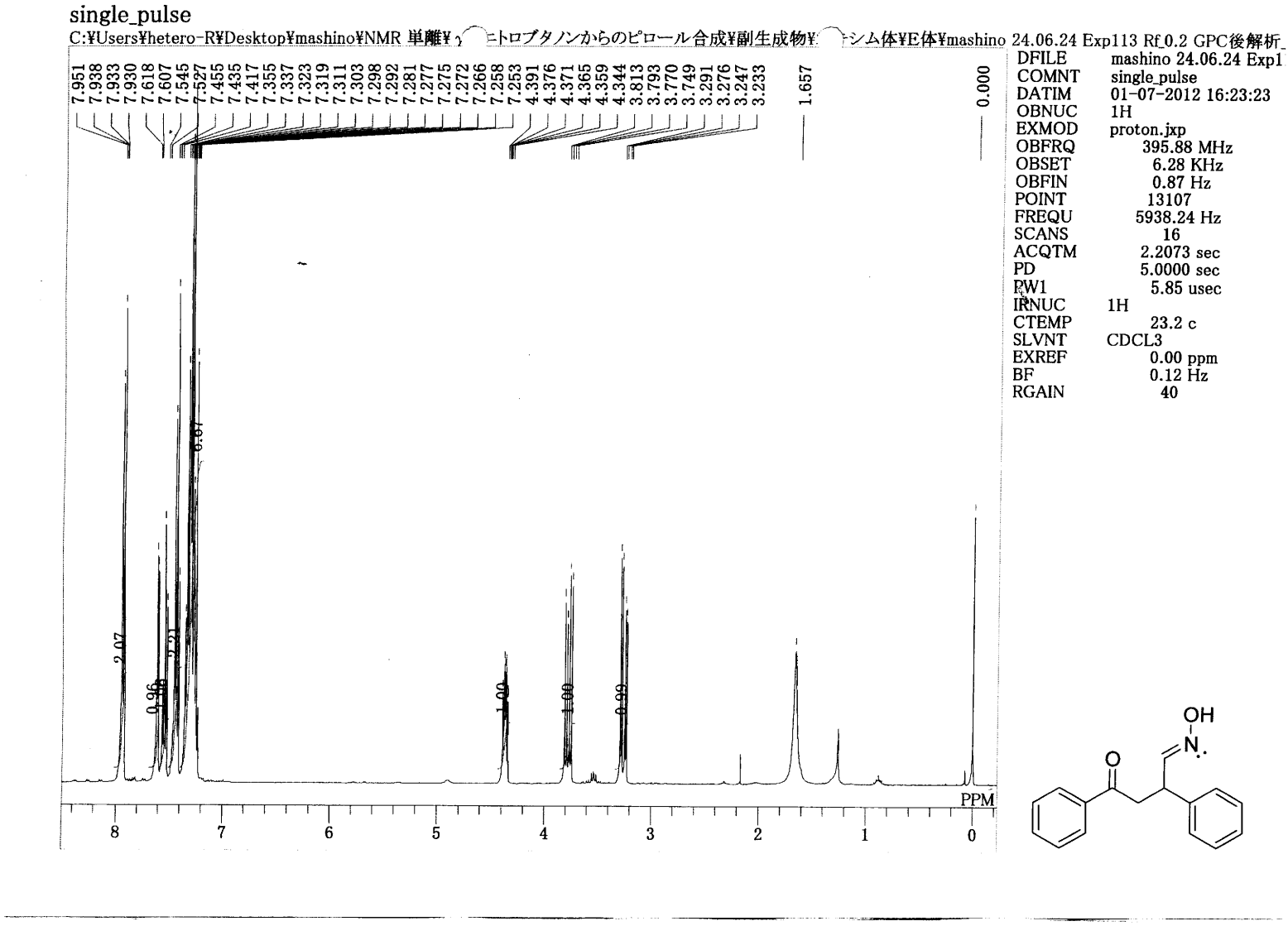


Fig. S6. ^{1}H (400 MHz) and ^{13}C (100 MHz) NMR spectra of **2n** in $CDCl_3$



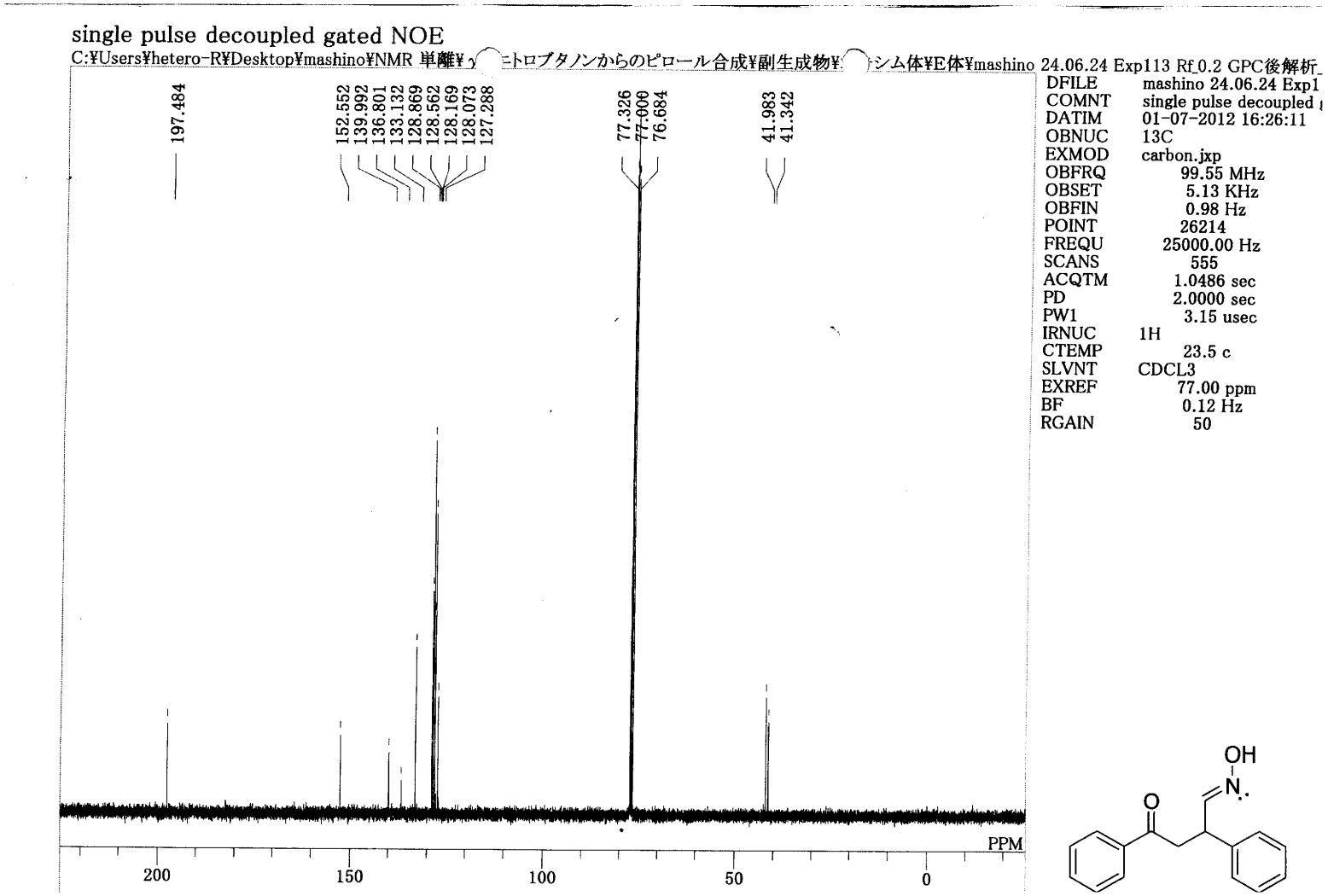
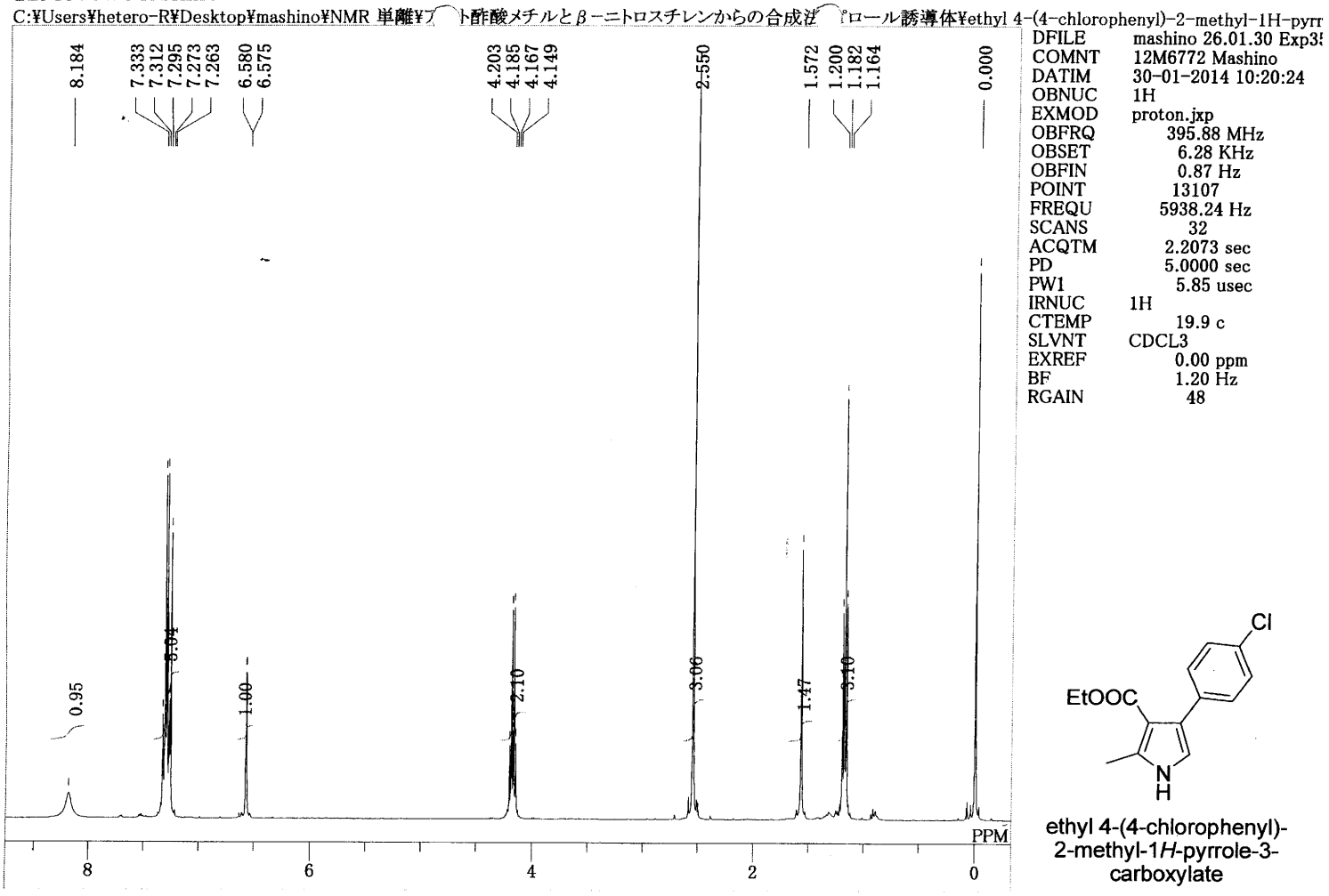


Fig. S7. ^{1}H (400 MHz) and ^{13}C (100 MHz) NMR spectra of **4a** in $CDCl_3$



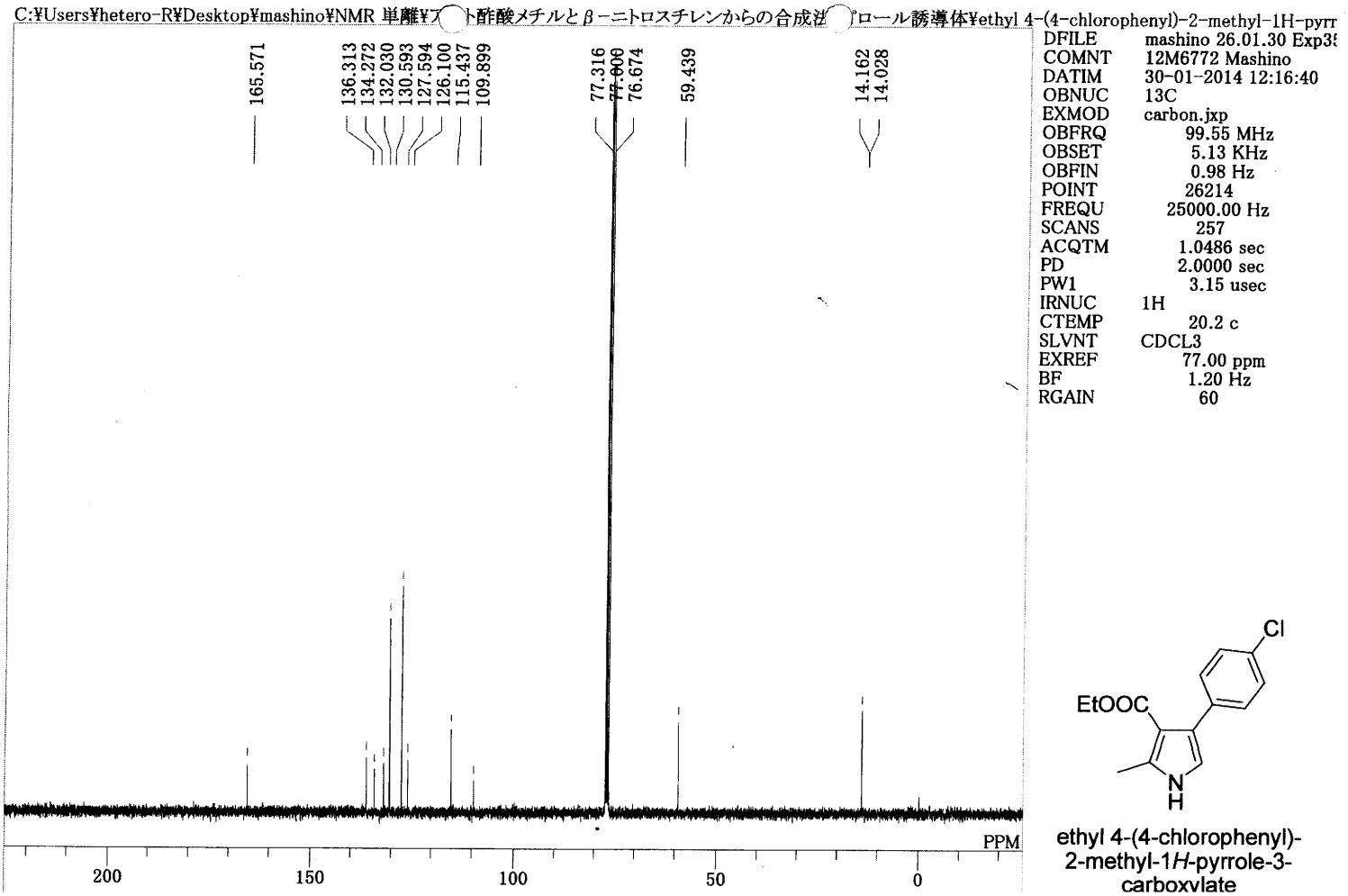
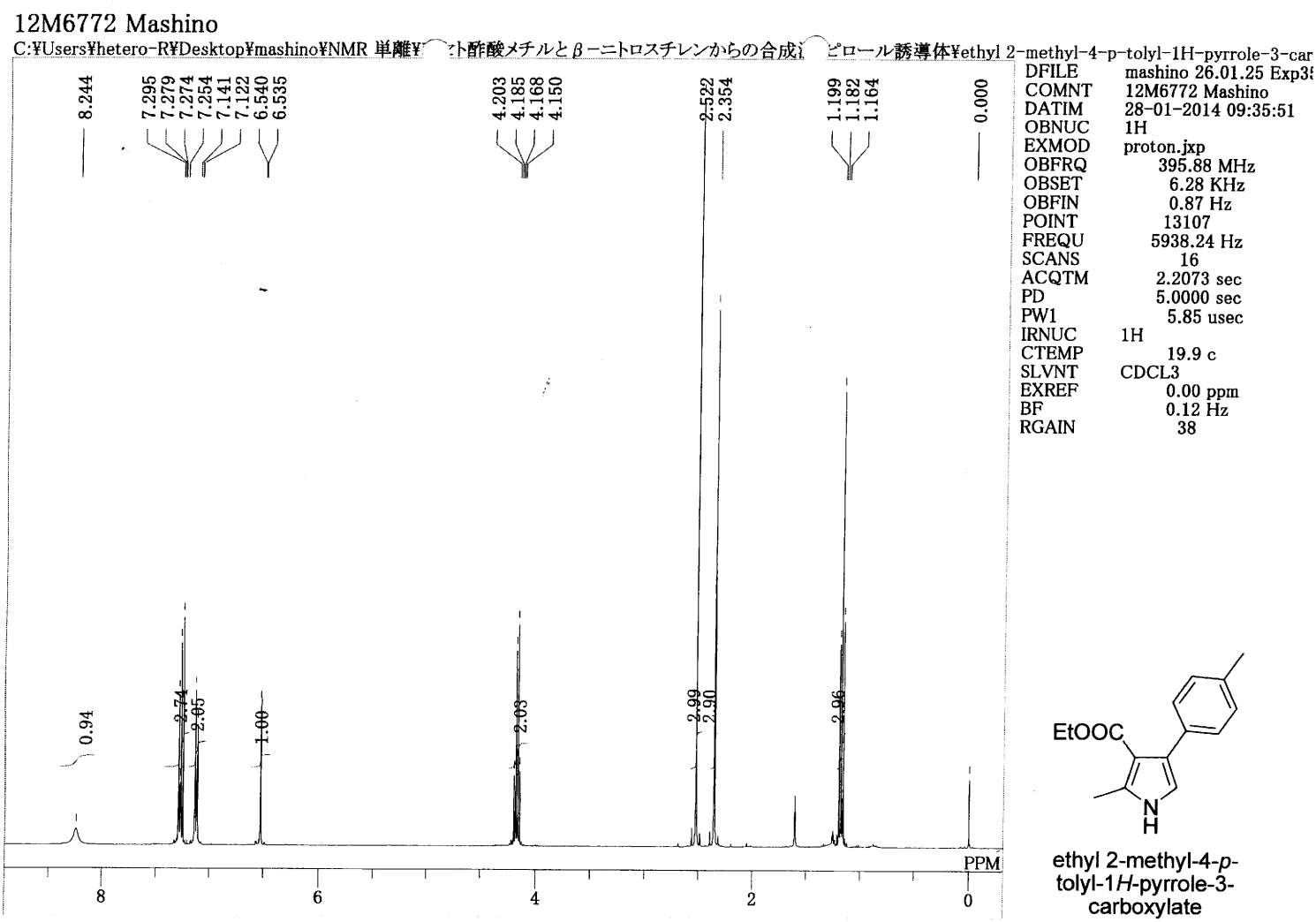


Fig. S8. ^{1}H (400 MHz) and ^{13}C (100 MHz) NMR spectra of **2r** in $CDCl_3$



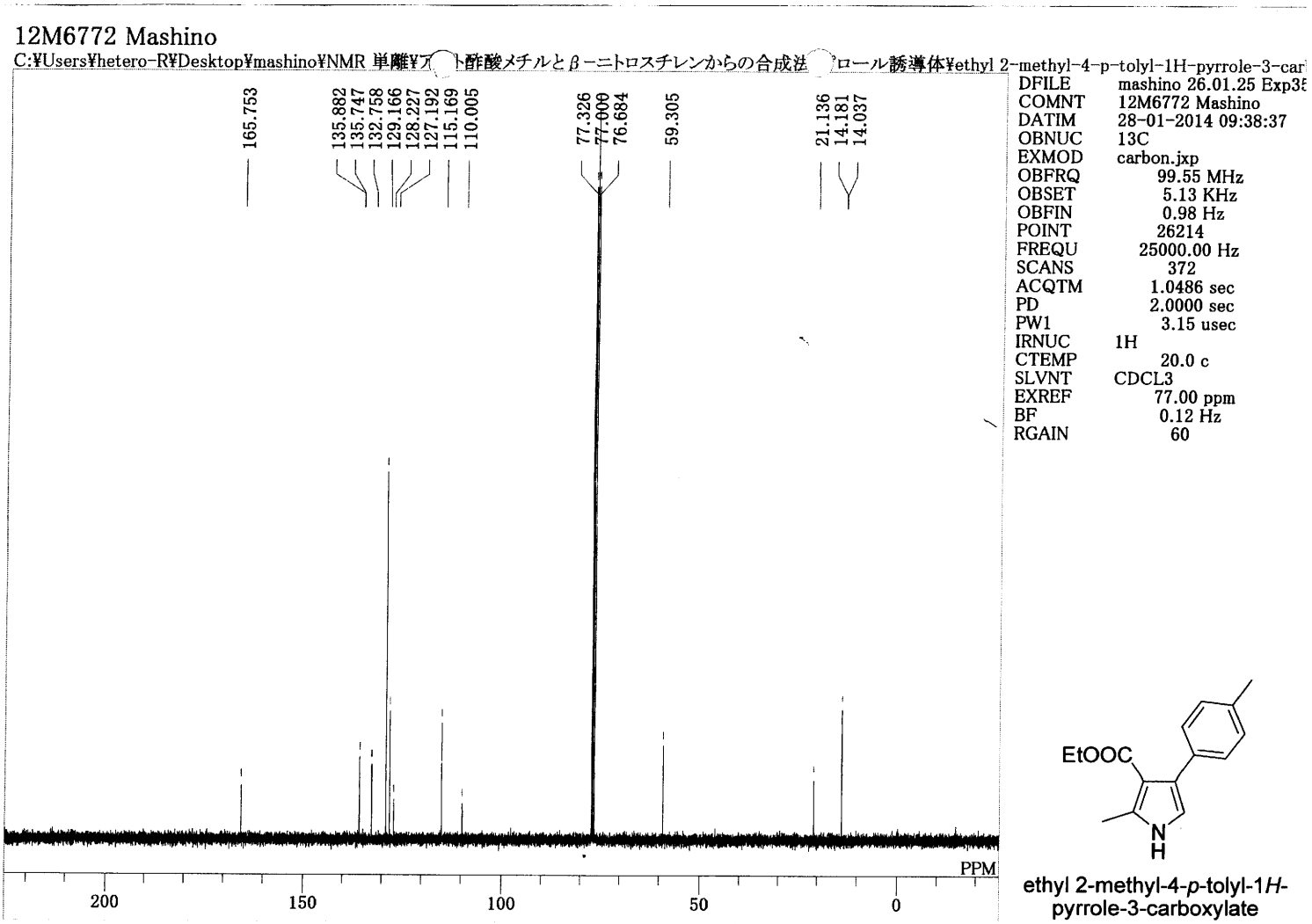
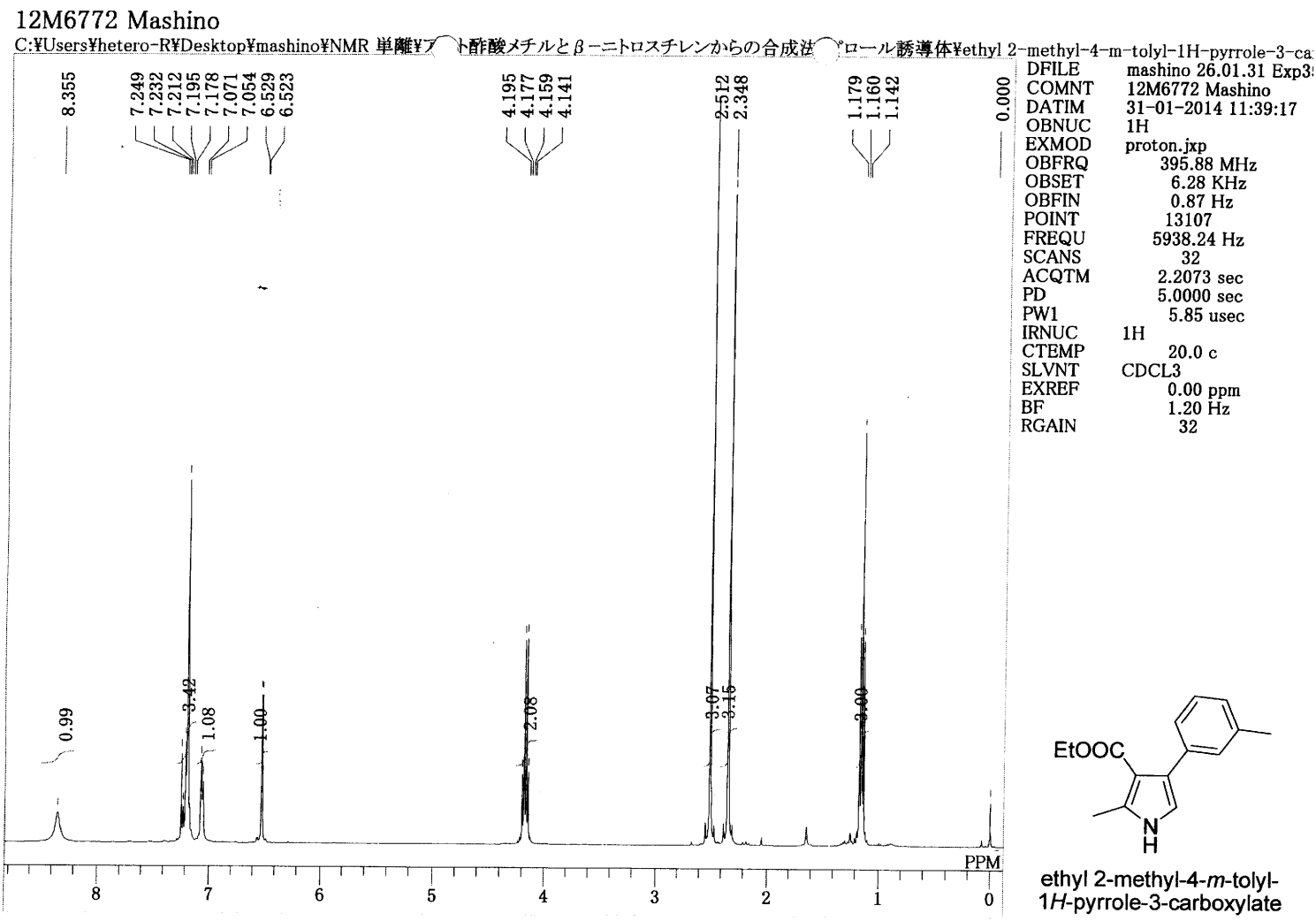


Fig. S9. ^{1}H (400 MHz) and ^{13}C (100 MHz) NMR spectra of **2t** in $CDCl_3$



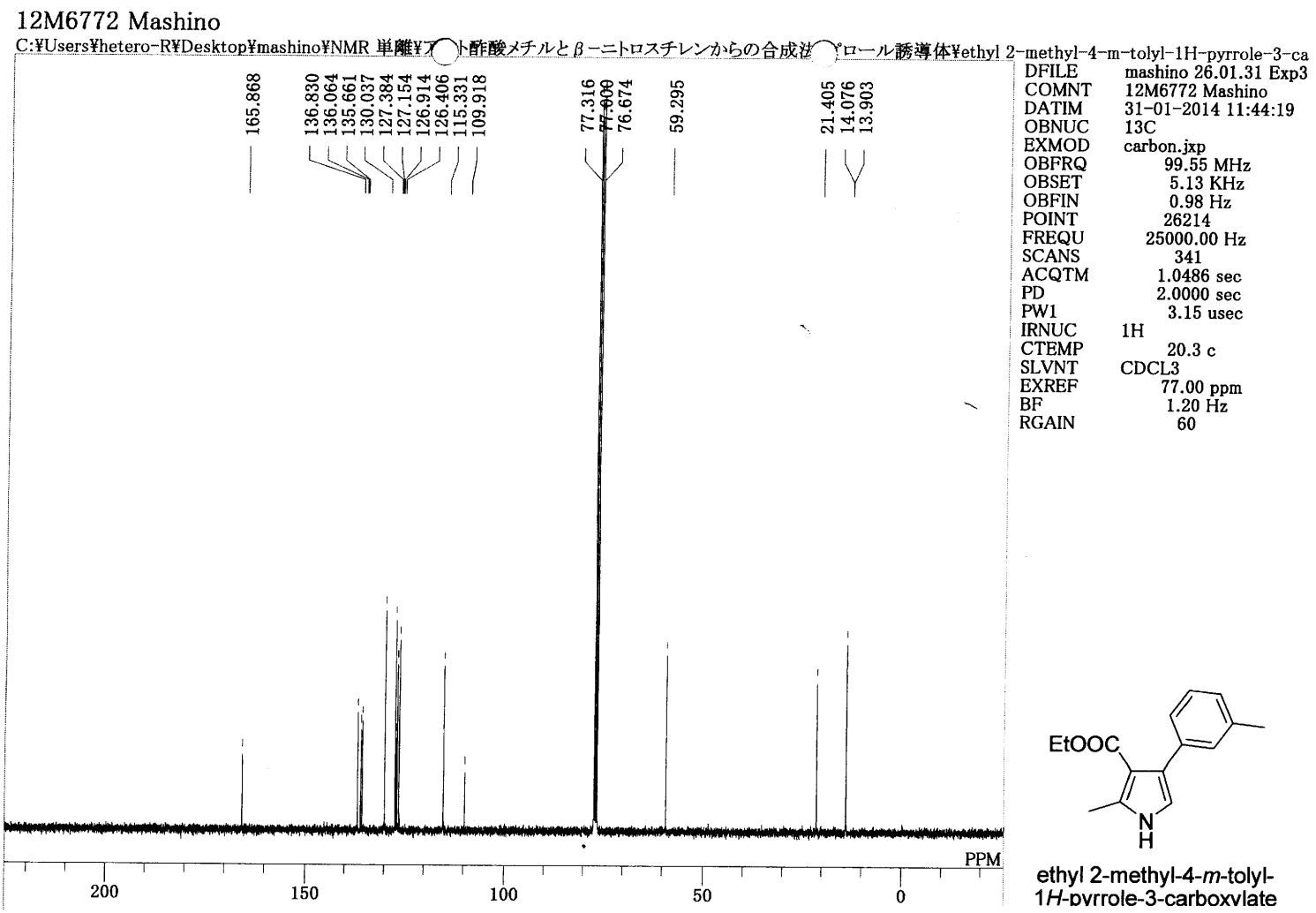
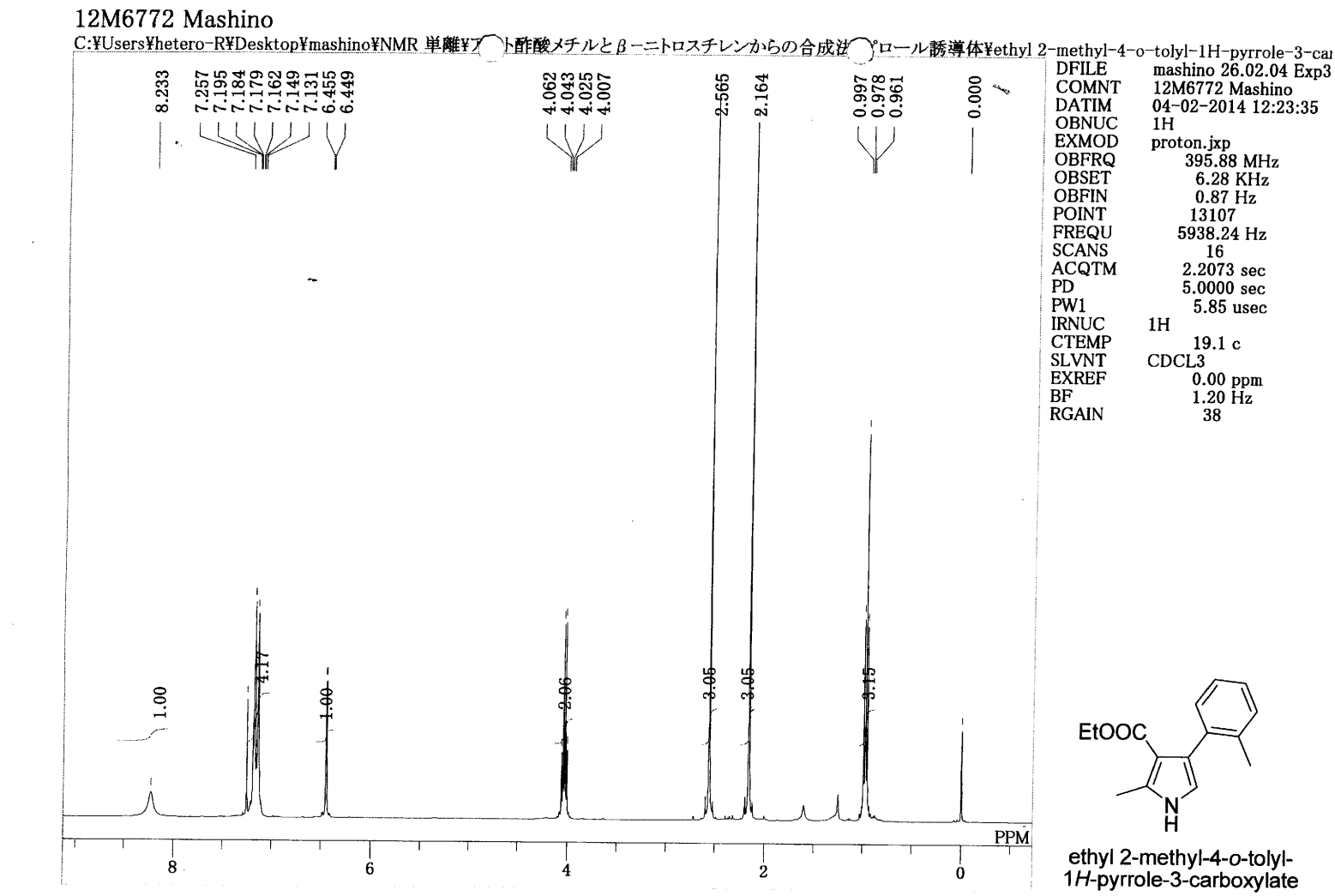


Fig. S10. ^{1}H (400 MHz) and ^{13}C (100 MHz) NMR spectra of **2u** in $CDCl_3$



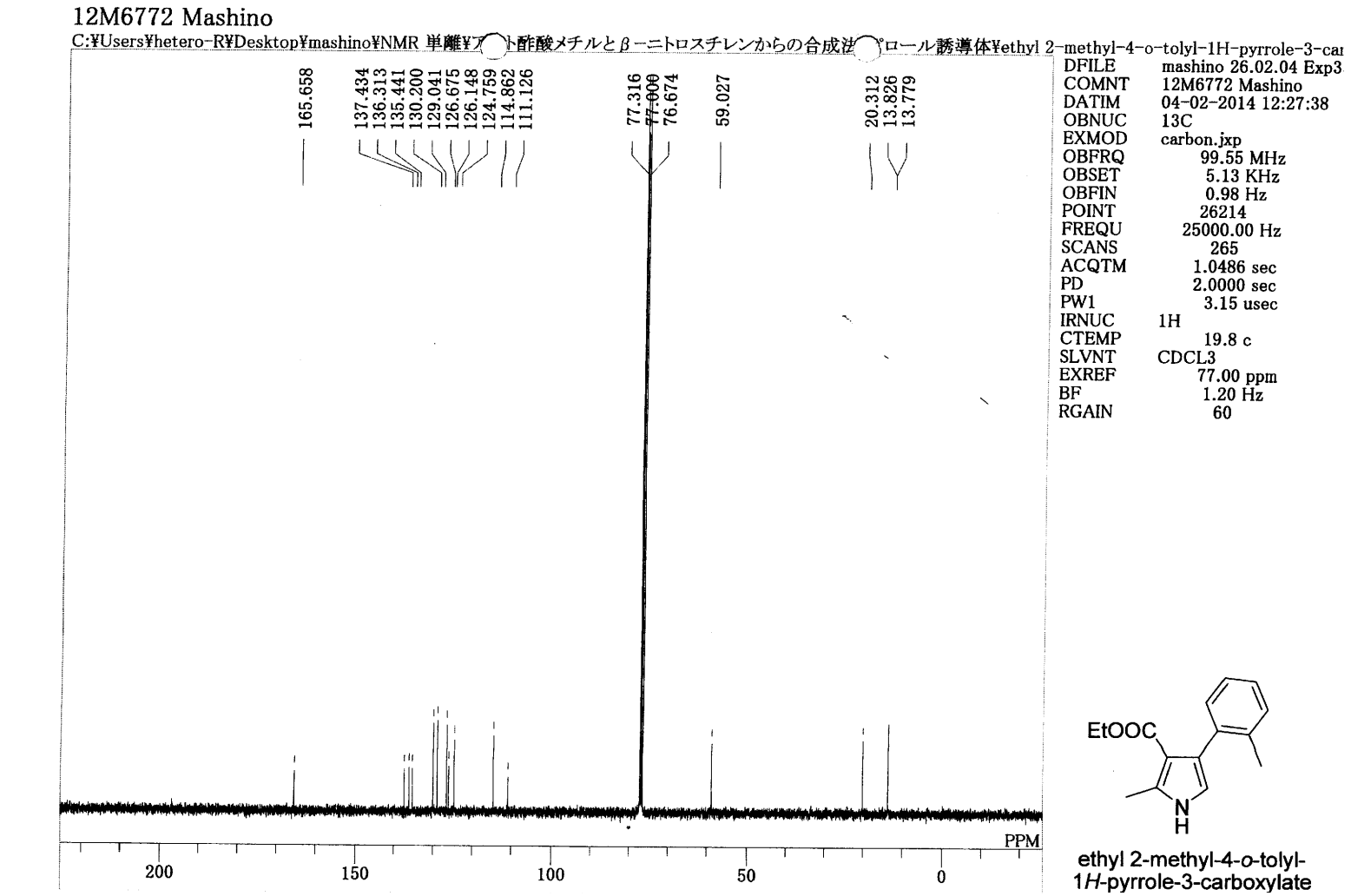


Fig. S11. ^{1}H (400 MHz) and ^{13}C (100 MHz) NMR spectra of **2v** in $CDCl_3$