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Article

B_2O_3/Al_2O_3 as a New, Highly Efficient and Reusable Heterogeneous Catalyst for the Selective Synthesis of β-Enamino Ketones and Esters under Solvent-Free Conditions

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Óxido de boro adsorvido sobre alumina (B_2O_3/Al_2O_3) foi usado como um novo e eficiente catalisador na síntese de β-aminocetonas e ésteres pela enaminação de diferentes aminas primárias e secundárias com compostos carbonílicos sob condições livre de solvente. A importância dessa metodologia congrega grande variedade de substratos, alta eficiência, ausência de catalisador metálico, alta régio- e quimioseletividade em condições amigáveis ao ambiente. Ainda, o catalisador pode ser recuperado facilmente depois das reações e reusado sem perda de atividade.

Boron oxide adsorbed on alumina (B_2O_3/Al_2O_3) has been found to be a new and highly efficient heterogeneous catalyst for the synthesis of β-enamino ketones and esters by the enamination of various primary and secondary amines with β-dicarbonyl compounds under solvent-free conditions. The important features of this methodology are broad substrate scope, high yield, no requirement of metal catalysts, high regio- and chemoselectivity and environmental friendliness. In addition, the catalyst could be recovered easily after the reactions and reused without evident loss of reactivity.

Keywords: β-enamino ketones, β-enamino esters, β-dicarbonyl compounds, amines, B_2O_3/Al_2O_3, solvent-free

Introduction

β-Enamino carbonylic compounds represent an important class of functionalized building blocks, which become increasingly important in medicinal chemistry and organic synthesis.[1] Consequently, various approaches toward the construction of β-enamino carbonylic compounds have been explored during the past years. The direct enamination of 1,3-dicarbonyl compounds with amines is one of the most straightforward methods for the synthesis of β-enamino ketones and esters in the presence of various promoting agents.[2-19] Recent reports have described the preparation of β-enamino ketones and esters catalyzed by metal triflate.[20] Although the reported methodologies are suitable for certain synthetic conditions, some of these procedures suffered from disadvantages, such as long reaction time, low yield, use of volatile organic solvents, requirement of excess of reagents or costly catalysts, special apparatus and harsh reaction conditions. Therefore, the development of convenient, environmental friendliness, high yield and clean approaches is highly desirable.

Recently, heterogeneous organic reactions[21] have been recently performed with immobilized reagents on solid supports. These procedures offer several intrinsic advantages such as clean reactions, the easy separation of products, the recover and reuse of catalyst conveniently, the minimization of waste production, and eco-friendliness etc.

As a part of our great interest in developing novel synthetic routes for the formations of carbon-carbon and carbon-heteroatom bonds,[22] we herein reported B_2O_3/Al_2O_3 as a new, efficient and reusable heterogeneous catalyst for the enamination of β-dicarbonyl compounds with amines.

Results and Discussion

The model reaction of ethyl acetoacetate (**1a**) with aniline (**2a**) was conducted to find the optimal reaction conditions and the initial results are listed in Table 1. First, the effect of solvents was tested. Among all the solvents tested, ethanol afforded better yield than some other solvents tested. As shown in Table 1, however,

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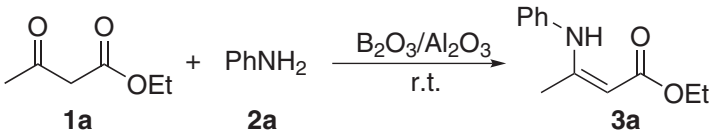
Table 1. The condensation of ethyl acetoacetate with aniline under various different reaction conditions[a]



1a **2a** **3a**

Entry	Solvent	time (h)	Yields (%)[b]
1	EtOH	1	75
2	CH_3CN	1	68
3	CH_2Cl_2	1	70
4	H_2O	1	65
5	none	1	95
6	none	2.5	96
7	none	1	85[c]
8	none	1	95[d] (22)[e]
9	none	5	40[f]

[a]All reactions were run with **1a** (1 mmol), **2a** (1.1 mmol) and B_2O_3/Al_2O_3 (0.03 g, 15% m/m) in 2 mL of solvent at room temperature. [b]Isolated yields. [c]B_2O_3/Al_2O_3 (0.01 g, 15% m/m) was used as a catalyst. [d]B_2O_3/Al_2O_3 (0.05 g, 15% m/m) was used as a catalyst. [e]In the absence of catalyst. [f]Al_2O_3 (0.03 g) was used as a catalyst.

the presence of additional solvents lowered the reaction rate (Table 1, entries 1-4). So we chose to perform this reaction under solvent-free conditions (Table 1, entry 5). In contrast, the product **3a** was obtained in 22% yield in the absence of B_2O_3/Al_2O_3 (Table 1, entry 8). When only Al_2O_3 was used as a catalyst, **3a** was obtained in 40% yield (Table 1, entry 9). On the other hand, it was found that the yield was affected by adding different amount of B_2O_3/Al_2O_3 (Table 1, entries 5, 7-8). Thus, subsequent studies were carried out under the following optimized conditions, that are, 0.03 g B_2O_3/Al_2O_3 at room temperature in the absence of solvent.

With optimal conditions in hand, the reaction of different β-dicarbonyl compounds **1** with a range of primary, secondary, and aromatic amines **2** were examined to explore the scope of the reaction.

As shown in Table 2, a series of aromatic amines bearing either electron-donating or electron-withdrawing groups on aromatic ring were investigated. The substituent groups on the aromatic ring associated with amines did not show obvious effects in terms of yields under optimal conditions. It was observed that the corresponding β-enamino ketones and esters **3** were obtained in good to excellent yields. Aliphatic amines also reacted efficiently to give products **3m**-**3p** in good yields, and the reaction time was shorter than that of aromatic amines (Table 2, entries 13-16). Moreover, secondary amines reacted to afford products **3q**-**3s** in good yields but with longer reaction times (Table 2, entries 17-19).

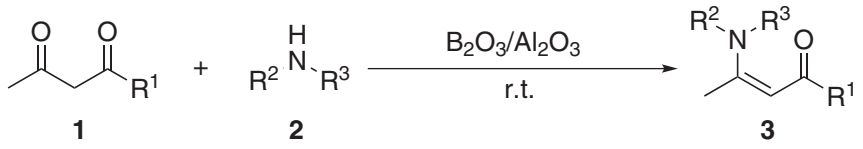
Next, we investigated the reaction of β-dicarbonyl compounds **1** with diamines **4** (Table 3). In this reaction, two equivalents of **1** were required in order to have a complete conversion of diamines. When aliphatic diamine such as 1,3-propanediamine was examined, the corresponding bis-enamine products **5a** and **5b** were obtained in 95 and 99% yields, respectively. Moreover, when aromatic diamine such as 1,4-benzenediamine was examined, the corresponding bis-enamine products **5c** and **5d** were obtained in 88 and 97% yields, respectively.

However, when more sterically hindered aromatic diamine such as 1,2-benzenediamine was examined, the reaction only gave the mono-enamine products **6a** and **6b** using two equivalents and even three equivalents of β-dicarbonyl compounds.

On the other hand, we have investigated the efficiency of this catalyst for a few representative intermolecular competition studies (Scheme 1). The different reactivity of aromatic amines and aliphatic amines were demonstrated during the reaction of β-dicarbonyl compounds such as ethyl acetoacetate and acetylacetone with equimolar mixtures of aniline and n-propylamine (selectivity in favour of n-propylamine). Analysis of the mixture after 2 h showed that only n-propylamine reacted with ethyl acetoacetate and acetylacetone.

Finally, the reusability of B_2O_3/Al_2O_3 was further investigated in subsequent reactions, taking the additions of aniline to ethyl acetoacetate as an example (Scheme 2). The catalyst was easily recovered by simple filtration after diluting of the reaction mixture with ethyl acetate and was reused after being dried under vacuum. B_2O_3/Al_2O_3 was reused for four runs without evident loss of activity.

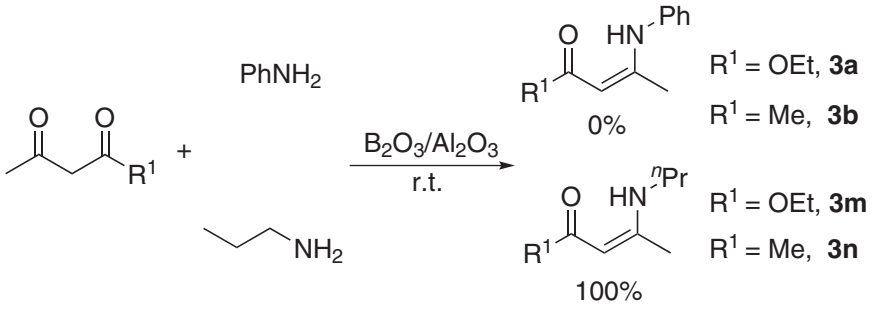
Table 2. Synthesis of β-enamino carbonylic compounds catalyzed by B_2O_3/Al_2O_3[a]



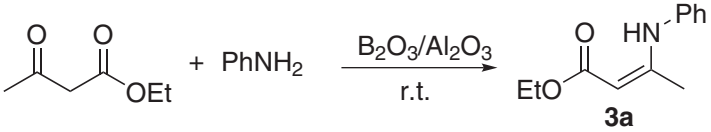
1 **2** **3**

Entry	R^1	R^2	R^3	time	Product	Yield (%)[b]
1	OEt	Ph	H	1 h	**3a**	95
2	Me	Ph	H	2 h	**3b**	87
3	OEt	α-naphtyl	H	3 h	**3c**	86
4	Me	α-naphtyl	H	4 h	**3d**	90
5	OEt	4-$CH_3C_6H_4$	H	1.5 h	**3e**	88
6	Me	4-$CH_3C_6H_4$	H	1.5 h	**3f**	86
7	OEt	2-$CH_3OC_6H_4$	H	2 h	**3g**	85
8	Me	2-$CH_3OC_6H_4$	H	2 h	**3h**	89
9	OEt	3-ClC_6H_4	H	2 h	**3i**	83
10	Me	3-ClC_6H_4	H	2 h	**3j**	71 (98)[c]
11	OEt	4-ClC_6H_4	H	1.5 h	**3k**	78 (91)[c]
12	OEt	4-BrC_6H_4	H	2 h	**3l**	73 (86)[c]
13	OEt	$CH_3CH_2CH_2$	H	20 min	**3m**	91
14	Me	$CH_3CH_2CH_2$	H	20 min	**3n**	88
15	OEt	$PhCH_2$	H	50 min	**3o**	80
16	Me	$PhCH_2$	H	50 min	**3p**	86
17	Me	CH_3CH_2	CH_3CH_2	5 h	**3q**	83
18	Me	morpholine		5 h	**3r**	83
19	OEt	morpholine		5 h	**3s**	82

[a] All reactions were run with **1** (1 mmol), **2** (1.1 mmol) and B_2O_3/Al_2O_3 (0.03 g, 15% m/m) in the absence of solvent at room temperature. [b] Isolated yields. [c] 50 °C.



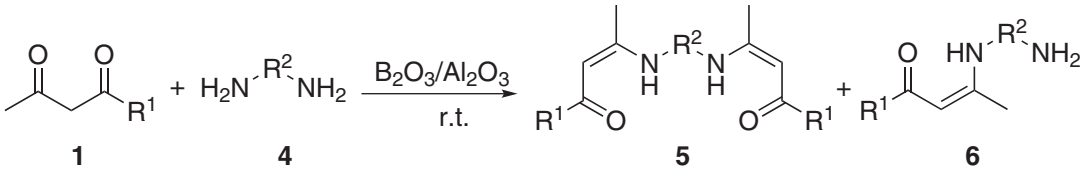
Scheme 1. Chemoselective reaction.



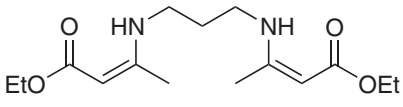
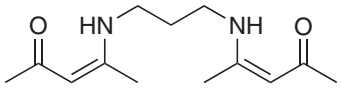
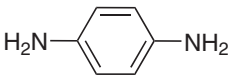
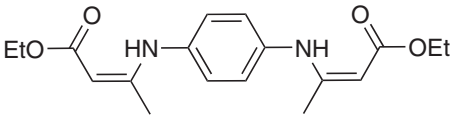
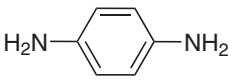
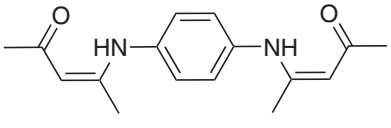
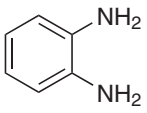
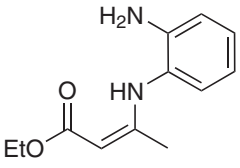
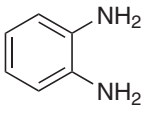
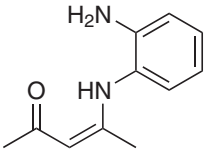
Run 1: 95%; Run 2: 95%; Run 3: 92%; Run 4: 91%

Scheme 2. Reuse of the catalyst.

Table 3. Reaction of β-dicarbonyl compounds with diamines catalyzed by B_2O_3/Al_2O_3[a]



1 **4** **5** **6**

Entry	R^1	Diamine **4**	time	Product	Yield (%)[b]
1	OEt		20 min	 **5a**	95
2	Me		5 min	 **5b**	99
3	OEt		1 h	 **5c**	88
4	Me		1 h	 **5d**	97
5	OEt		4 h	 **6a**	86
6	Me		3.5 h	 **6b**	81

[a] All reactions were run with **1** (2 mmol), **4** (1 mmol) and B_2O_3/Al_2O_3 (0.03 g, 15% m/m) in the absence of solvent at room temperature. [b] Isolated yields.

Conclusions

In conclusion, we have reported B_2O_3/Al_2O_3 as a highly efficient heterogeneous reusable catalyst for chemoselective enamination of β-dicarbonyl compounds with aliphatic and aromatic amines under solvent-free conditions. In addition, the important features of this procedure are mild reaction conditions, high yield, and operational simplicity which make it a useful and attractive strategy for the preparation of *N*-substituted β-enamino carbonylic compounds.

Experimental

Melting points were recorded on Digital Melting Point Apparatus WRS-1B and were uncorrected. ^{1}H NMR and ^{13}C NMR spectra were taken on a Bruker DPX300 spectrometer using $CDCl_3$ as the solvent with tetramethylsilane (TMS) as an internal standard at room temperature. Chemical shifts were given in δ relative to TMS, the coupling constants *J* are given in Hz.

General procedure for the preparation of β-enamino ketones and esters

To a magnetically stirred mixture of the β-dicarbonyl compounds (1 mmol) and amines (1.1 mmol), B_2O_3/Al_2O_3 (0.03 g, 15% m/m) was added and the reaction mixture was stirred at room temperature for the appropriate time. The reaction was monitored by TLC. After completion of the reaction, the reaction mixture was diluted with ethyl

acetate. The catalyst was separated by filtration, then the solution was washed with ethyl acetate (5 mL) and dried over anhydrous sodium sulfate, filtered and the solvent was evaporated under vacuum. The residue was purified by flash column chromatography to afford the desired product. The spectral and analytical data of all compounds are given in Supporting Information.

Supplementary Information

Supplementary data are available free of charge at http://jbcs.sbq.org.br, as PDF file.

Acknowledgments

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B_2O_3/Al_2O_3 as a New, Highly Efficient and Reusable Heterogeneous Catalyst for the Selective Synthesis of β-Enamino Ketones and Esters under Solvent-Free Conditions

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Description of the products

*(Z)-Ethyl 3-(phenylamino)but-2-enoate (**3a**)[1]*

Oil, IR (KBr) ν_{max}/cm^{-1}: 3456, 3258, 2979, 1610, 1495, 1442, 1370, 1270, 1162, 1056 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 10.41 (br s, 1H, NH), 7.30-7.35 (m, 2H), 7.08-7.18 (m, 3H), 4.71 (s, 1H), 4.17 (q, *J* 7.2 Hz, 2H), 2.01 (s, 3H), 1.32 (t, *J* 7.2 Hz, 3H). ^{13}C MNR (75 MHz, $CDCl_3$): δ 170.4, 158.9, 139.3, 129.0, 124.9, 124.4, 85.9, 58.7, 20.3, 14.6.

*(Z)-4-(Phenylamino)pent-3-en-2-one (**3b**)*

Solid, mp: 47-49 °C (Lit.[1] 48-49 °C); IR (KBr) ν_{max}/cm^{-1}: 3349, 2980, 1605, 1499, 1432, 1276, 1183, 1017, 746; ^{1}H NMR (300MHz, $CDCl_3$): δ 12.46 (br s, 1H, NH), 7.25-7.30 (m, 2H), 7.03-7.15 (m, 3H), 5.14 (s, 1H), 2.05 (s, 3H), 1.93 (s, 3H); ^{13}C MNR (75MHz, $CDCl_3$): δ 196.0, 160.2, 138.6, 129.0, 125.5, 124.6, 97.6, 29.1, 19.8.

*(Z)-Ethyl 3-(naphthalen-1-ylamino)but-2-enoate (**3c**)[2]*

Oil; IR (KBr) ν_{max}/cm^{-1}:: 3246, 3056, 2978, 1605, 1441, 1384, 1266, 1165, 785; ^{1}H NMR (300MHz, $CDCl_3$): δ 10.61 (br s, 1H, NH), 8.06-8.09 (m, 1H), 7.86-7.89 (m, 1H), 7.75 (d, *J* 8.4 Hz, 1H), 7.26-7.57 (m, 4H), 4.83 (s, 1H), 4.23 (q, *J* 7.2Hz, 2H), 1.86 (s, 3H), 1.34 (q, *J* 7.2Hz, 3H); ^{13}C MNR (75MHz, $CDCl_3$): δ 170.7, 160.5, 135.3, 134.3, 130.4, 128.2, 126.7, 126.5, 126.4, 125.3, 123.6, 122.7, 85.7, 58.8, 20.04, 14.7.

*(Z)-4-(Naphthalen-1-ylamino)pent-3-en-2-one (**3d**)*

Solid, mp: 61-63 °C (Lit.[3] 51-53 °C); IR (KBr) ν_{max}/cm^{-1}: 3430, 2972, 1600, 1550, 1425, 1278, 1078, 1015, 774; ^{1}H NMR (300MHz, $CDCl_3$): δ 12.76 (br s, 1H, NH), 8.02-8.05 (m, 1H), 7.87-7.90 (m, 1H), 7.77 (d, *J* 8.4Hz, 1H), 7.27-7.56 (m, 4H), 5.32 (s, 1H), 2.18 (s, 3H), 1.88 (s, 3H); ^{13}C MNR (75MHz, $CDCl_3$): δ 196.6, 161.9, 134.8, 134.2, 123.0, 128.2, 126.9, 126.9, 126.5, 125.5, 123.4, 122.8, 97.4, 29.2, 19.6.

*(Z)-Ethyl 3-(p-toluidino)but-2-enoate (**3e**)[1]*

Oil; IR (KBr) ν_{max}/cm^{-1}: 3257, 3189, 2979, 1615, 1509, 1441, 1271, 1161, 1059, 792; ^{1}H NMR (300MHz, $CDCl_3$): δ 10.28 (br s, 1H, NH), 7.10-7.13 (m, 2H), 6.96-6.99 (m, 2H), 4.66 (s, 1H), 4.14 (q, *J* 7.2Hz, 2H), 2.33 (s, 3H), 1.95 (s, 3H), 1.28 (t, *J* 7.2Hz, 3H); ^{13}C MNR (75MHz, $CDCl_3$): δ 170.5, 158.8, 136.7, 134.9, 129.6, 124.7, 85.3, 58.7, 20.9, 20.3, 14.6.

*(Z)-4-(p-Toluidino)pent-3-en-2-one (**3f**)*

Solid, mp: 66-67 °C (Lit.[4] 68-69 °C); IR (KBr) ν_{max}/cm^{-1}: 3448, 2922, 1607, 1508, 1434, 1276, 1178, 1013, 822, 753; ^{1}H NMR (300MHz, $CDCl_3$): δ 12.40 (br s, 1H, NH), 7.14 (d, *J* 8.4Hz, 2H), 7.00 (d, *J* 8.4Hz, 2H), 5.16 (s, 1H), 2.34 (s, 3H), 2.09 (s, 3H), 1.96 (s, 3H); ^{13}C MNR (75MHz, $CDCl_3$): δ 195.9, 160.7, 136.1, 135.5, 129.6, 124.8, 97.2, 29.1, 20.9, 19.7.

*(Z)-Ethyl 3-(2-methoxyphenylamino)but-2-enoate (**3g**)[5]*

Oil; IR (KBr) ν_{max}/cm^{-1}: 3262, 2976, 1614, 1464, 1376, 1220, 1161, 1037, 746; ^{1}H NMR (300MHz, $CDCl_3$): δ 10.28 (br s, 1H, NH), 7.08-7.14 (m, 2H), 6.88-6.92 (m, 2H), 4.71 (s, 1H), 4.16 (q, *J* 7.2Hz, 2H), 3.86 (s, 3H), 2.01 (s, 3H), 1.28 (t, *J* 7.2Hz, 3H); ^{13}C MNR (75MHz, $CDCl_3$): δ 170.2, 158.9, 152.6, 128.6, 125.3, 124.4, 120.3, 111.0, 86.3, 58.7, 55.7, 20.4, 14.6.

*(Z)-4-(2-Methoxyphenylamino)pent-3-en-2-one (**3h**)[5]*

Oil; IR (KBr) ν_{max}/cm^{-1}: 3456, 2949, 2841, 1607, 1481, 1344, 1274, 1180, 1025, 747; ^{1}H NMR (300MHz, $CDCl_3$): δ 12.32 (br s, 1H, NH), 7.01-7.18 (m, 2H), 6.87-6.93 (m, 2H), 5.20 (s, 1H), 3.86 (s, 3H), 2.10 (s, 3H), 1.99 (s, 3H); ^{13}C MNR (75MHz, $CDCl_3$): δ 195.9, 160.4, 152.8, 128.0, 126.2, 125.0, 120.3, 111.2, 97.8, 55.7, 29.1, 20.0.

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*(Z)-Ethyl 3-(3-chlorophenylamino)but-2-enoate (**3i**)*[6]

Oil; IR (KBr) ν_{max}/cm^{-1}: 3190, 2979, 1637, 1476, 1370, 1270, 1164, 1074, 784; ^{1}H NMR (300MHz, $CDCl_3$): δ 10.42 (br s, 1H, NH), 7.10-7.22 (m, 3H), 6.94-6.96 (m, 1H), 4.72 (s, 1H), 4.15 (q, *J* 7.2Hz, 2H), 2.02 (s, 3H), 1.28 (t, *J* 7.2Hz, 3H); ^{13}C MNR (75MHz, $CDCl_3$): δ 170.3, 158.0, 140.7, 134.6, 130.0, 124.7, 123.9, 122.1, 87.5, 59.0, 20.4, 14.6.

*(Z)-4-(3-Chlorophenylamino)pent-3-en-2-one (**3j**)*

Solid, mp: 37-39 °C (Lit.[1] 39-40 °C); IR (KBr) ν_{max}/cm^{-1}: 3428, 2978, 1578, 1491, 1429, 1276, 1186, 1020, 937, 772; ^{1}H NMR (300MHz, $CDCl_3$): δ 12.47 (br s, 1H, NH), 6.98-7.29 (m, 4H), 5.22 (s, 1H), 2.11 (s, 3H), 2.02 (s, 3H); ^{13}C MNR (75MHz, $CDCl_3$): δ 196.4, 157.8, 140.2, 128.1, 127.5, 124.9, 118.3, 115.7, 97.0, 43.2, 19.3.

*(Z)-Ethyl 3-(4-chlorophenylamino)but-2-enoate (**3k**)*

Solid, mp: 52-54 °C (Lit.[1] 54-55 °C); IR (KBr) ν_{max}/cm^{-1}: 3457, 2980, 1633, 1491, 1383, 1272, 1160, 787; ^{1}H NMR (300MHz, $CDCl_3$): δ 10.34 (br s, 1H, NH), 7.22-7.26 (m, 2H), 6.97-6.99 (m, 2H), 4.69 (s, 1H), 4.12 (q, *J* 7.2Hz, 2H), 1.95 (s, 3H), 1.26 (t, *J* 7.2Hz, 3H); ^{13}C MNR (75MHz, $CDCl_3$): δ 170.4, 158.3, 138.0, 130.2, 129.2, 125.5, 86.9, 58.9, 20.2, 14.6.

*(Z)-Ethyl 3-(4-bromophenylamino)but-2-enoate (**3l**)*

Solid, mp: 53-55 °C (Lit.[3] 54-55 °C); IR (KBr) ν_{max}/cm^{-1}: 3451, 3273, 2924, 1622, 1482, 1358, 1269, 1163, 1059, 786; ^{1}H NMR (300MHz, $CDCl_3$): δ 10.35 (br s, 1H, NH), 7.38-7.43 (m, 2H), 6.91-6.96 (m, 2H), 4.70 (s, 1H), 4.12 (q, *J* 7.2Hz, 2H), 1.97 (s, 3H), 1.26 (t, *J* 7.2Hz, 3H); ^{13}C MNR (75MHz, $CDCl_3$): δ 170.3, 158.2, 138.5, 132.1, 125.7, 117.9, 87.0, 58.9, 20.3, 14.6.

*(Z)-Ethyl 3-(propylamino)but-2-enoate (**3m**)*[7]

Oil; IR (KBr) ν_{max}/cm^{-1}: 3285, 2965, 1609, 1448, 1270, 1160, 1065, 784, 695; ^{1}H NMR (300MHz, $CDCl_3$): δ 8.51 (br s, 1H, NH), 4.36 (s, 1H), 4.00-4.03 (m, 2H), 3.07-3.11 (m, 2H), 1.85 (s, 3H), 1.49-1.53 (m, 2H), 1.16-1.18 (m, 3H), 0.90-0.91 (m, 3H); ^{13}C MNR (75MHz, $CDCl_3$): δ 170.5, 161.8, 81.6, 58.0, 44.5, 23.5, 19.2, 14.5, 11.2.

*(Z)-4-(Propylamino)pent-3-en-2-one (**3n**)*[8]

Oil; IR (KBr) ν_{max}/cm^{-1}: 3451, 2960, 1603, 1443, 1359, 1295, 740, 647; ^{1}H NMR (300MHz, $CDCl_3$): δ 10.85 (br s, 1H, NH), 4.93 (s, 1H), 3.14-3.21 (m, 2H), 1.98 (s, 3H), 1.90 (s, 3H), 1.53-1.62 (m, 2H), 0.93-0.98 (m, 3H); ^{13}C MNR (75MHz, $CDCl_3$): δ 194.8, 163.1, 95.0, 44.8, 28.7, 23.3, 18.8, 11.3.

*(Z)-Ethyl 3-(benzylamino)but-2-enoate (**3o**)*[5]

Oil; IR (KBr) ν_{max}/cm^{-1}: 3289, 2977, 1605, 1499, 1445, 1280, 1169, 1113, 786, 697; ^{1}H NMR (300MHz, $CDCl_3$): δ 8.96 (br s, 1H, NH), 7.24-7.37 (m, 5H), 4.54 (s, 1H), 4.43 (d, *J* 6.3Hz, 2H), 4.10 (q, *J* 7.2Hz, 2H), 1.92 (s, 3H), 1.26 (t, *J* 7.2Hz, 3H); ^{13}C MNR (75MHz, $CDCl_3$): δ 170.5, 161.7, 138.7, 128.7, 127.2, 126.6, 83.1, 58.3, 46.7, 19.3, 14.5.

*(Z)-4-(Benzylamino)pent-3-en-2-one (**3p**)*[5]

Oil; IR (KBr) ν_{max}/cm^{-1}: 3446, 2926, 1605, 1509, 1441, 1360, 1295, 1104, 1023, 739; ^{1}H NMR (300MHz, $CDCl_3$): δ 11.16 (br s, 1H, NH), 7.24-7.36 (m, 5H), 5.04 (s, 1H), 4.45 (d, *J* 6.3Hz, 2H), 2.03 (s, 3H) 1.91 (s, 3H); ^{13}C MNR (75MHz, $CDCl_3$): δ 195.3, 163.0, 138.0, 128.7, 127.3, 126.6, 95.8, 46.6, 28.8, 18.8.

*4-(Diethylamino)pent-3-en-2-one (**3q**)*[9]

Oil; IR (KBr) ν_{max}/cm^{-1}: 2975, 1628, 1538, 1439, 1355, 1193; ^{1}H NMR (300MHz, $CDCl_3$): δ 5.07 (s, 1H), 3.25-3.32 (m, 4H), 2.51 (s, 3H), 2.05 (s, 3H), 1.13-1.18 (m, 6H); ^{13}C MNR (75MHz, $CDCl_3$): δ 194.1, 160.0, 93.8, 43.7, 15.1, 12.4.

*4-Morpholinopent-3-en-2-one (**3r**)*[1]

Oil; IR (KBr) ν_{max}/cm^{-1}: 2964, 2854, 1640, 1544, 1431, 1257, 1184, 1119; ^{1}H NMR (300MHz, $CDCl_3$): δ 5.21 (s, 1H), 3.64-3.71 (m, 4H), 3.26-3.30 (m, 4H), 2.43 (s, 3H), 1.97 (s, 3H); ^{13}C MNR (75MHz, $CDCl_3$): δ 195.5, 160.6, 96.9, 66.5, 45.8, 30.7, 15.1.

*Ethyl 3-morpholinobut-2-enoate (**3s**)*[9]

Oil; IR (KBr) ν_{max}/cm^{-1}: 2970, 2854, 1688, 1584, 1435, 1259, 1144, 998, 805; ^{1}H NMR (300MHz, $CDCl_3$): δ 4.78 (s, 1H), 4.06-4.12 (m, 2H), 3.69-3.73 (m, 4H), 3.19-3.23 (m, 4H), 2.40 (s, 3H), 1.22-1.27 (m, 3H); ^{13}C MNR (75MHz, $CDCl_3$): δ 168.6, 160.9, 88.1, 66.0, 58.4, 46.1, 15.0, 14.2.

*(2Z, 2'Z)-Diethyl 3, 3'-(propane-1, 3-diylbis(azanediyl)) dibut-2-enoate (**5a**)*[1]

Oil; IR (KBr) ν_{max}/cm^{-1}: 3283, 3193, 2977, 2248, 1604, 1270, 913, 787, 726, 554; ^{1}H NMR (300MHz, $CDCl_3$): δ 8.47 (br s, 2H, NH), 4.37 (s, 2H), 3.98 (q, *J* 7.2Hz, 4H), 3.22 (q, *J* 6.3Hz, 4H), 1.82 (s, 6H), 1.74-1.76 (m, 2H), 1.15 (t, *J* 7.2Hz, 6H); ^{13}C MNR (75MHz, $CDCl_3$): δ 170.5, 161.7, 82.6, 58.2, 39.7, 30.9, 19.2, 14.5.

*(3Z, 3'Z)-4, 4'-(Propane-1, 3-diylbis(azanediyl))dipent-3-en-2-one (**5b**)*

Solid, mp: 43-45 °C (Lit.[10] 50-52 °C); IR (KBr) ν_{max}/cm^{-1}: 3442, 2940, 1606, 1438, 1363, 1294, 1123, 1016, 742; ^{1}H NMR (300MHz, $CDCl_3$): δ 10.87 (br s, 1H, NH), 4.98 (s,

1H), 3.32-3.38 (m, 2H), 1.99 (s, 3H), 1.92 (s, 3H), 1.85-1.89 (m, 1H); ^{13}C MNR (75MHz, $CDCl_3$): δ 195.2, 163.2 95.6, 39.6, 30.2, 28.8, 18.8.

*(2Z,2'Z)-Diethyl 3,3'-(1,4-phenylenebis(azanediyl))dibut-2-enoate (**5c**)*[27]

Solid, mp: 135-137 °C (Lit.[11] 135 °C); IR (KBr) ν_{max}/cm^{-1}: 2450, 2979, 2929, 1617, 1484, 1385, 1256, 1056, 780, 679; ^{1}H NMR (300MHz, $CDCl_3$): δ 10.34 (br s, 2H, NH), 7.04 (s, 4H), 4.70 (s, 2H), 4.15 (q, *J* 7.2Hz, 4H), 2.00 (s, 6H), 1.29 (d, *J* 7.2Hz, 6H); ^{13}C MNR (75MHz, $CDCl_3$): δ 170.3, 158.7, 136.2, 124.9, 86.2, 58.7, 20.2, 14.5.

*(3Z,3'Z)-4,4'-(1,4-Phenylenebis(azanediyl))dipent-3-en-2-one (**5d**)*[28]

Solid, mp: 185-187 °C (Lit.[12] 172 °C); IR (KBr) ν_{max}/cm^{-1}: 3442, 2926, 1614, 1568, 1492, 1430, 1267, 1177, 1008, 865, 737; ^{1}H NMR (300MHz, $CDCl_3$): δ 11.96 (br s, 2H, NH), 7.07 (s, 4H), 5.19 (s, 2H), 2.10 (s, 6H), 2.00 (s, 6H); ^{13}C MNR (75MHz, $CDCl_3$): δ 196.3, 159.8, 136.1, 125.1, 97.8, 29.1, 19.8.

*(Z)-Ethyl 3-(2-aminophenylamino)but-2-enoate (**6a**)*[29]

Solid, mp: 77-79 °C (Lit.[13] 85 °C); IR (KBr) ν_{max}/cm^{-1}: 3408, 3285, 2965, 1609, 1448, 1270, 1159, 1065, 784, 695; ^{1}H NMR (300MHz, $CDCl_3$): δ 9.70 (br s, 1H, NH), 7.04-7.10 (m, 2H), 6.68-6.76 (m, 2H), 4.72 (s, 1H), 4.15 (q, *J* 7.2Hz, 2H), 3.84 (br s, 2H, NH), 1.80 (s, 3H), 1.28 (t, *J* 7.2Hz, 3H); ^{13}C MNR (75MHz, $CDCl_3$): δ 170.6, 161.5, 143.5, 128.6, 128.0, 124.7, 118.3, 115.6, 85.1, 58.7, 19.7, 14.6.

*(Z)-4-(2-Aminophenylamino)pent-3-en-2-one (**6b**)*

Solid, mp: 129-131 °C (Lit.[6] not reported); IR (KBr) ν_{max}/cm^{-1}: 3759, 3445, 2931, 1624, 1426, 1256, 1255, 1114, 765; ^{1}H NMR (300MHz, $CDCl_3$): δ 12.47 (br s, 1H, NH), 6.98-7.28 (m, 4H), 5.21 (s, 1H), 2.10 (s, 3H), 2.02 (s, 3H); ^{13}C MNR (75MHz, $CDCl_3$): δ 196.7, 159.3, 140.1, 134.6, 130.1, 125.4, 124.5, 122.6, 98.4, 29.3, 19.9.

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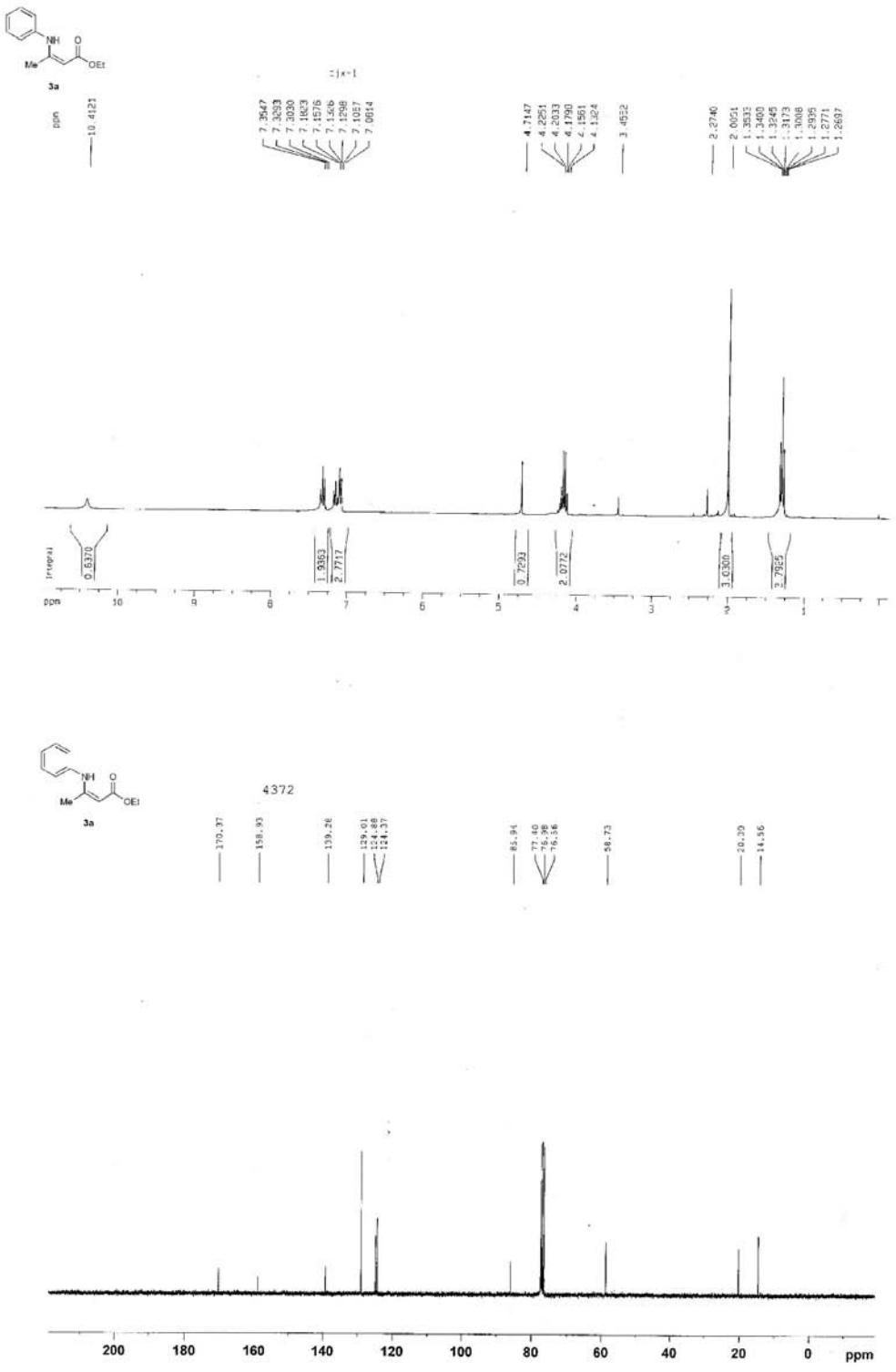

Figure S1. ^{1}H NMR of **3a** (300 MHz, $CDCl_3$) and ^{13}C NMR of **3a** (75 MHz, $CDCl_3$).

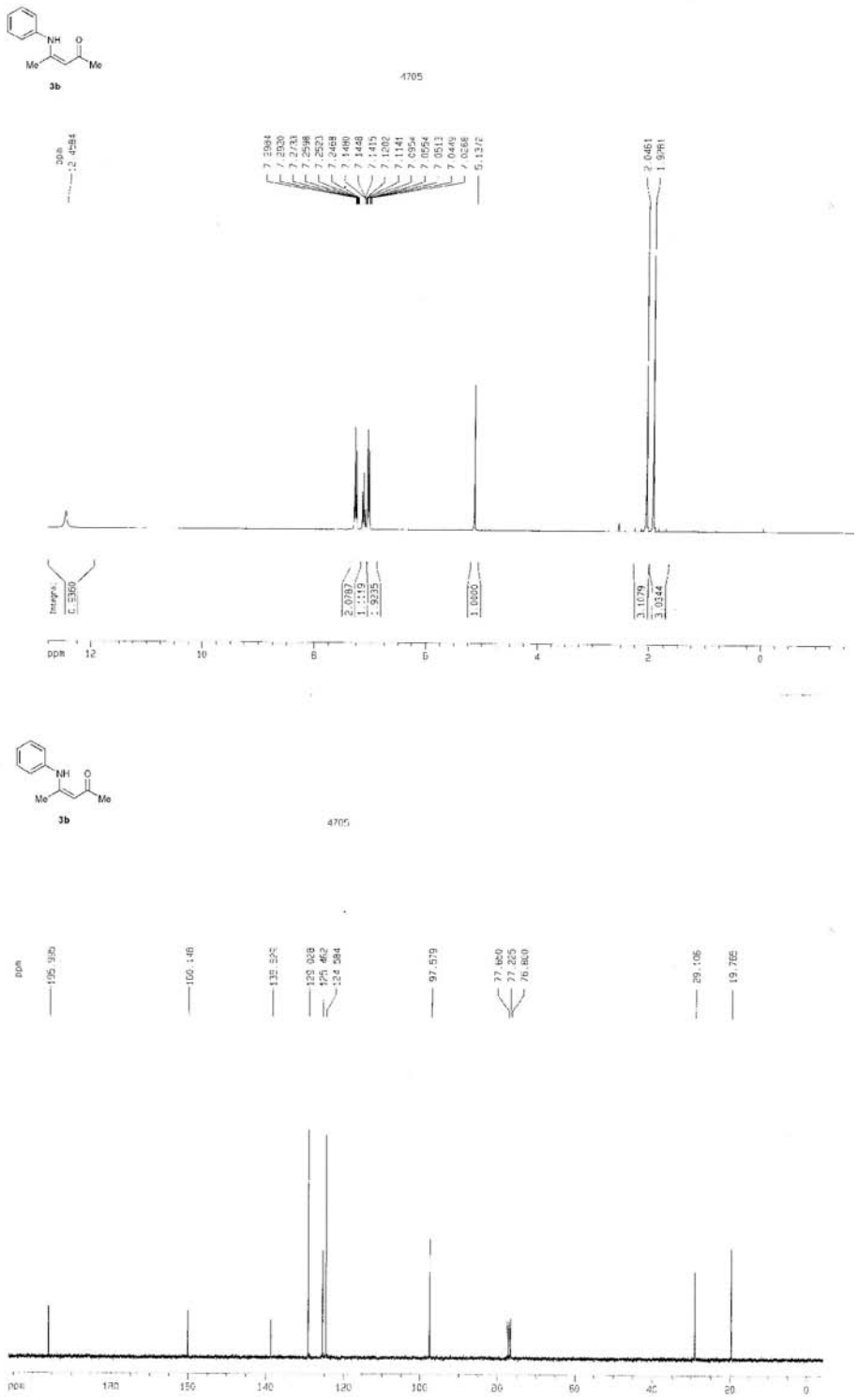

Figure S2. ^{1}H NMR of **3b** (300 MHz, $CDCl_3$) and ^{13}C NMR of **3b** (75 MHz, $CDCl_3$).

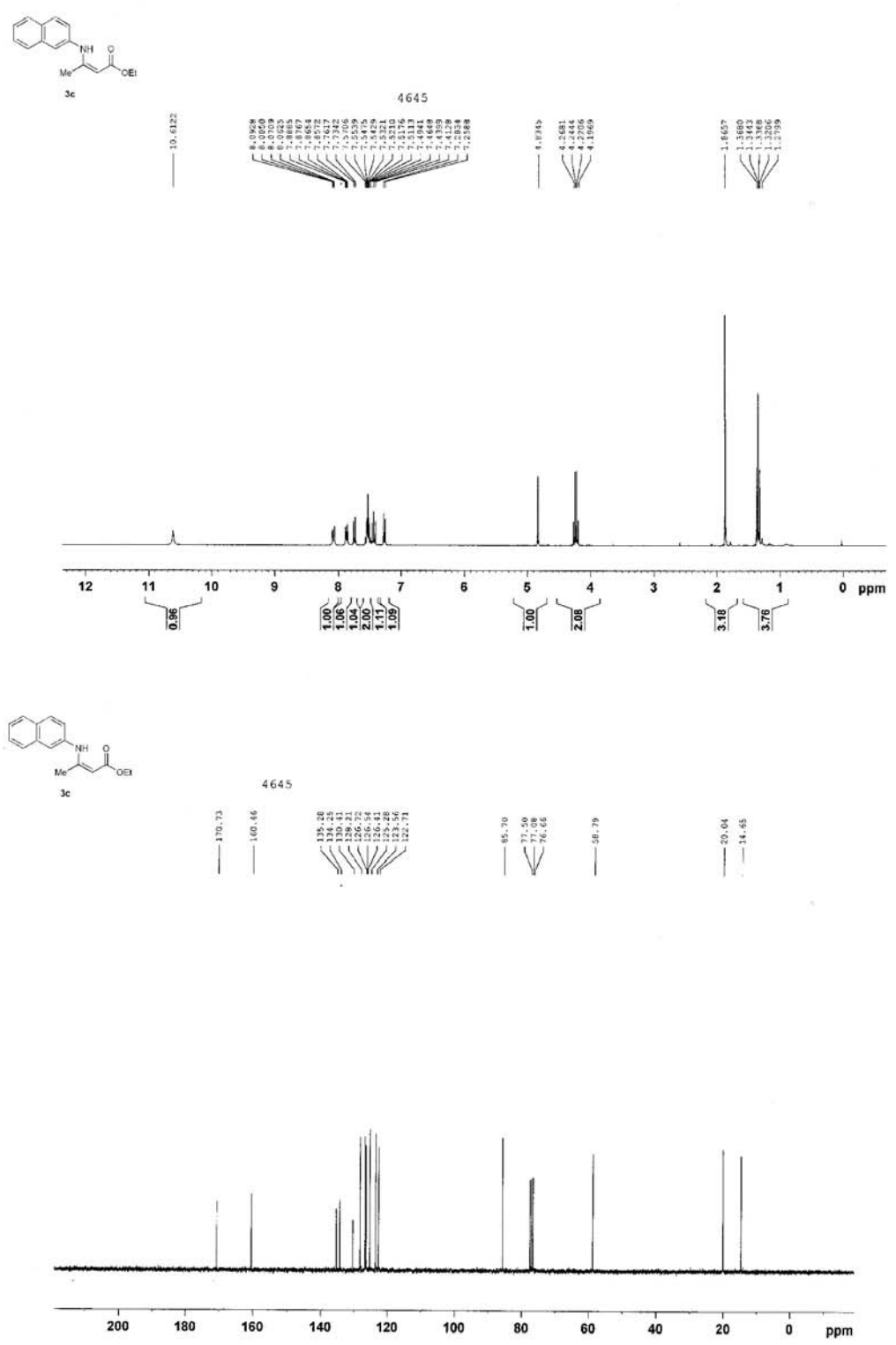

Figure S3. ^{1}H NMR of **3c** (300 MHz, $CDCl_3$) and ^{13}C NMR of **3c** (75 MHz, $CDCl_3$).

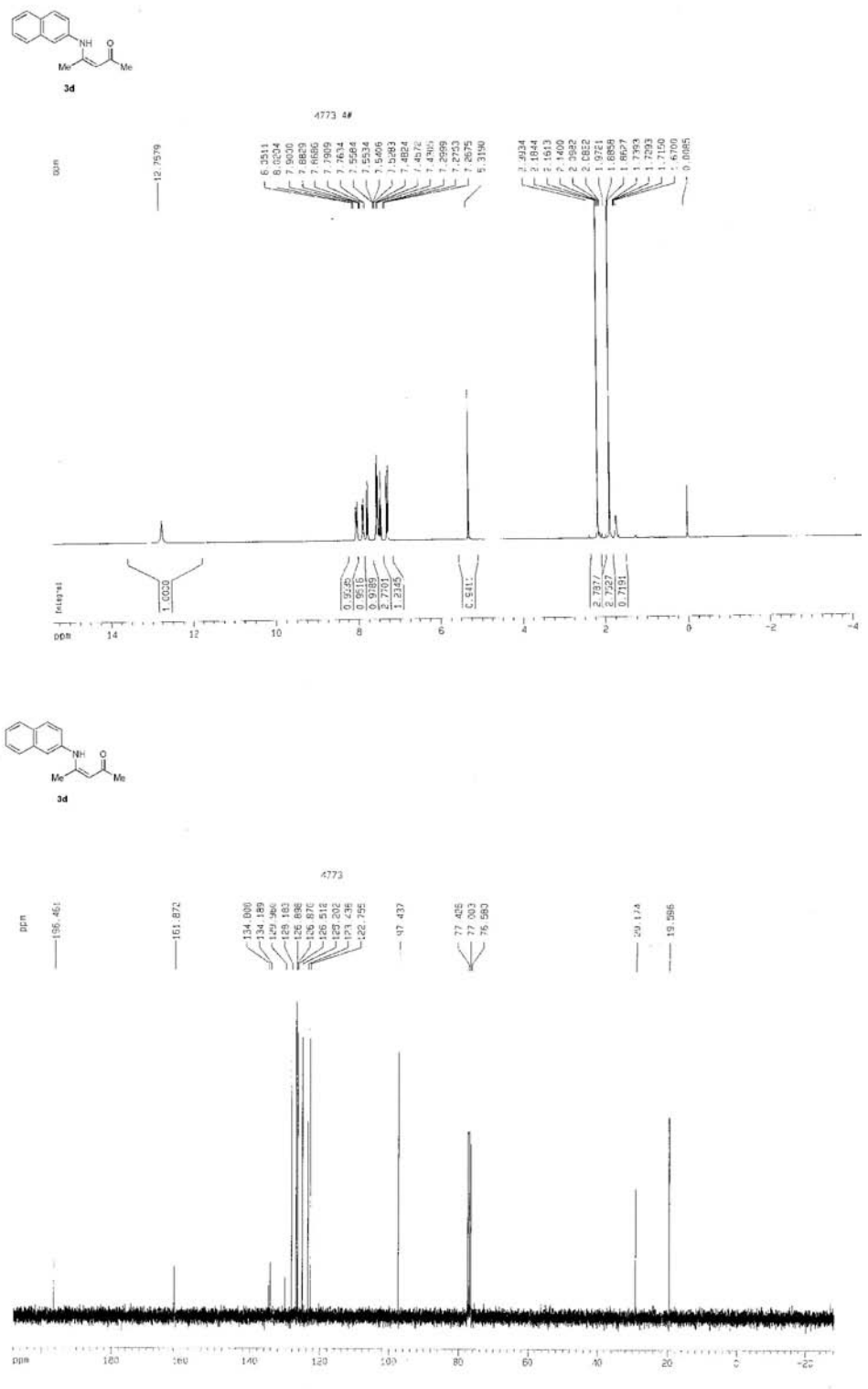

Figure S4. ^{1}H NMR of **3d** (300 MHz, $CDCl_3$) and ^{13}C NMR of **3d** (75 MHz, $CDCl_3$).

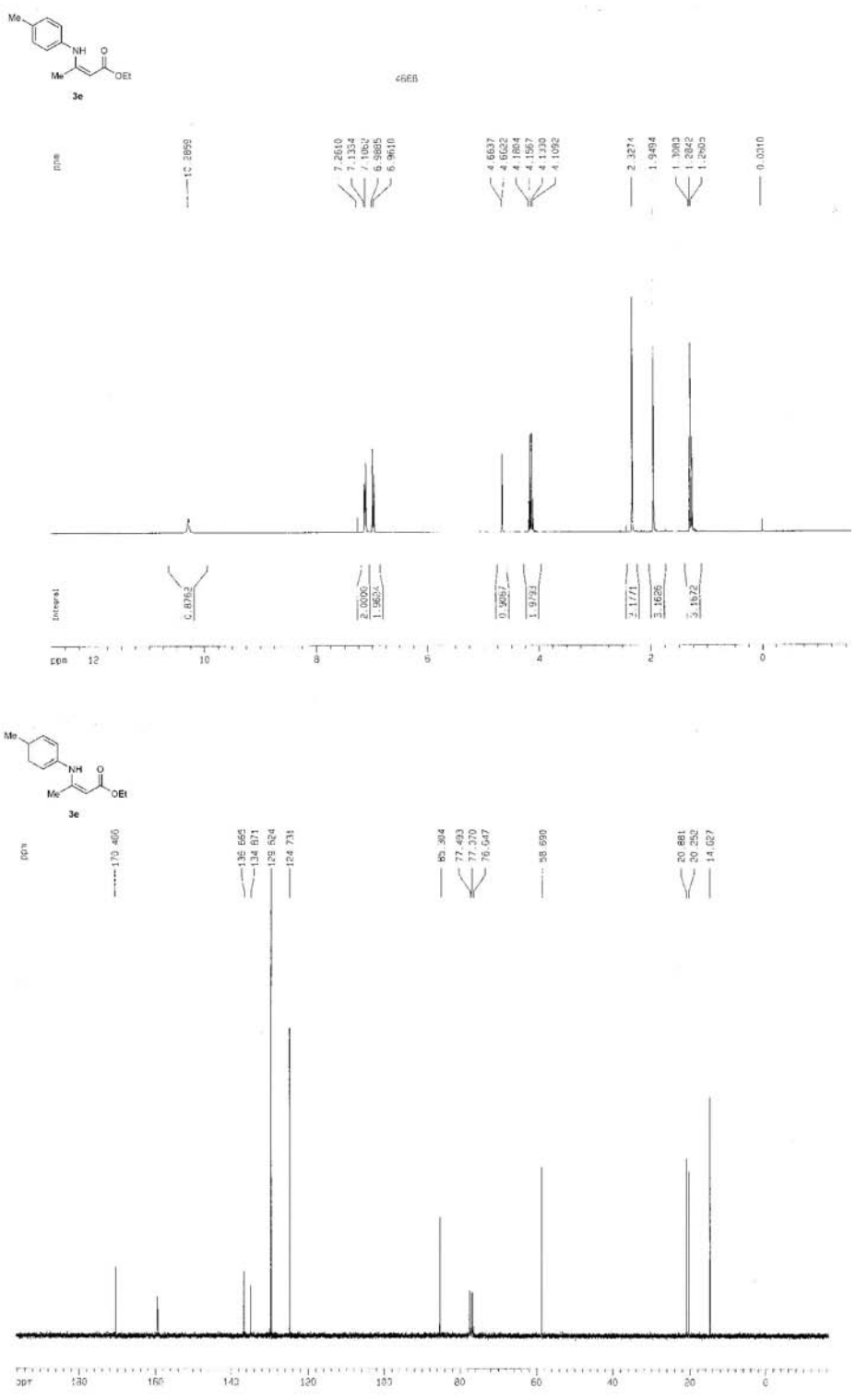

Figure S5. ^{1}H NMR of **3e** (300 MHz, $CDCl_3$) and ^{13}C NMR of **3e** (75 MHz, $CDCl_3$).

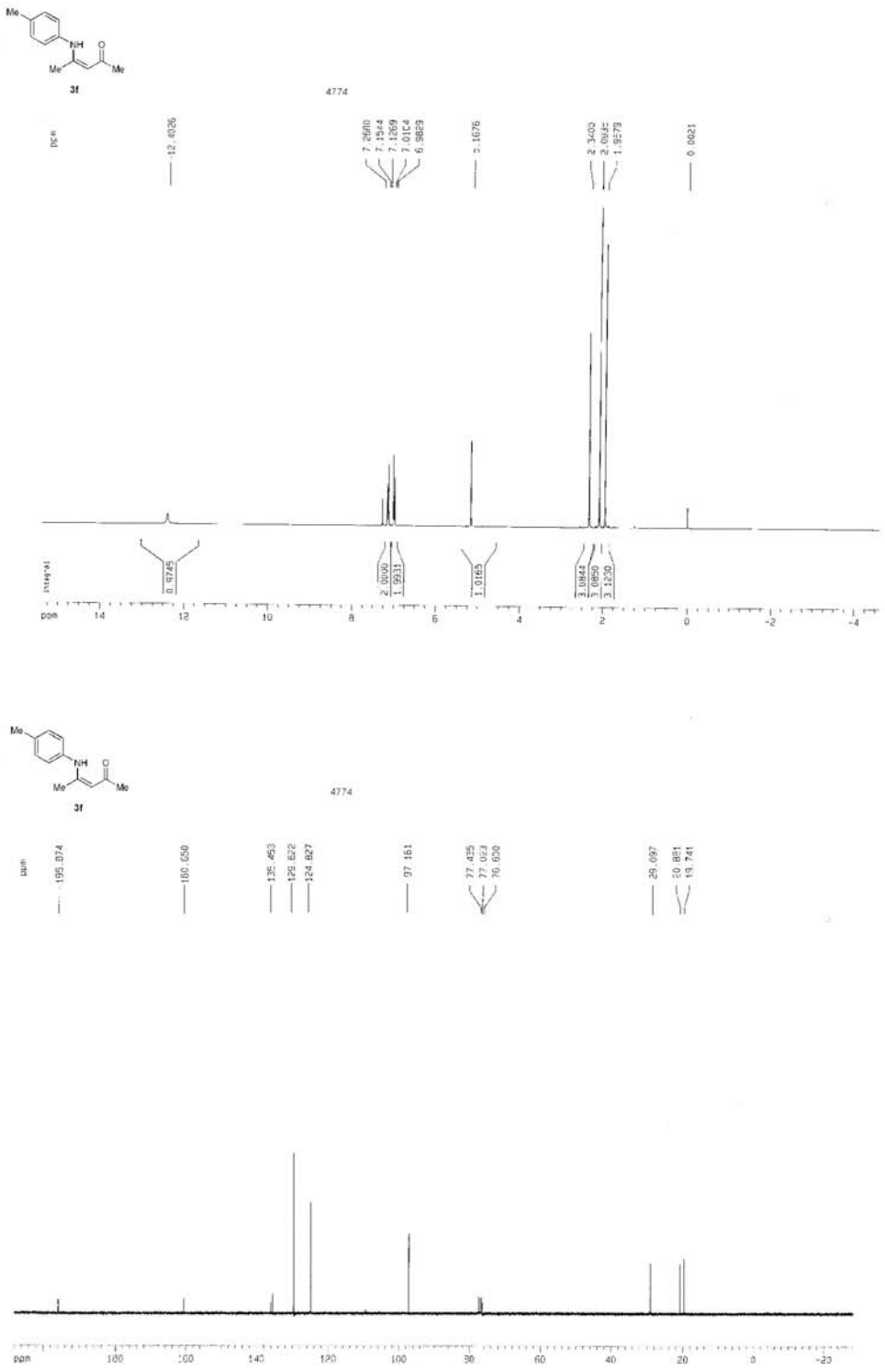

Figure S6. ^{1}H NMR of **3f** (300 MHz, $CDCl_3$) and ^{13}C NMR of **3f** (75 MHz, $CDCl_3$).

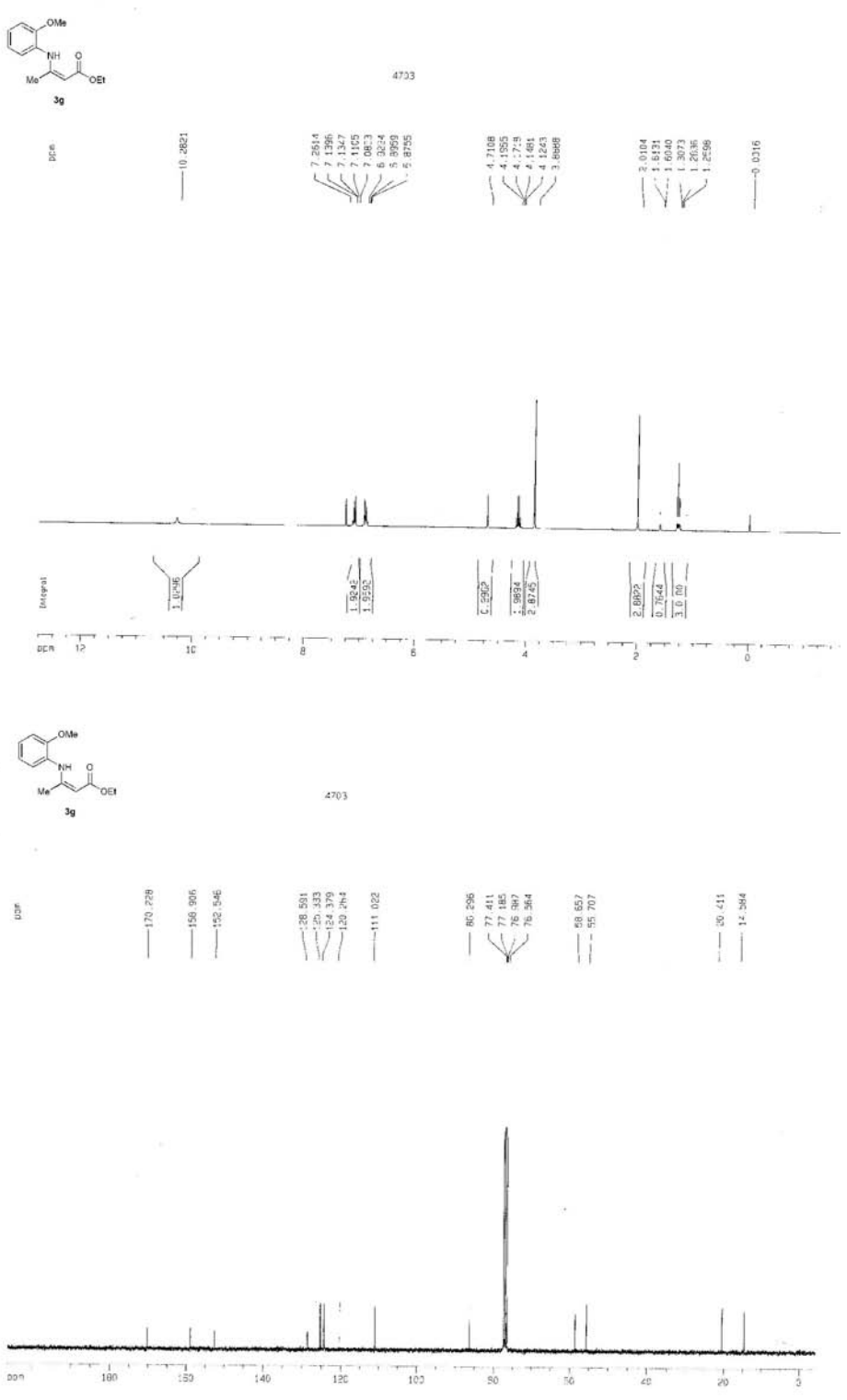

Figure S7. ^{1}H NMR of **3g** (300 MHz, $CDCl_3$) and ^{13}C NMR of **3g** (75 MHz, $CDCl_3$).

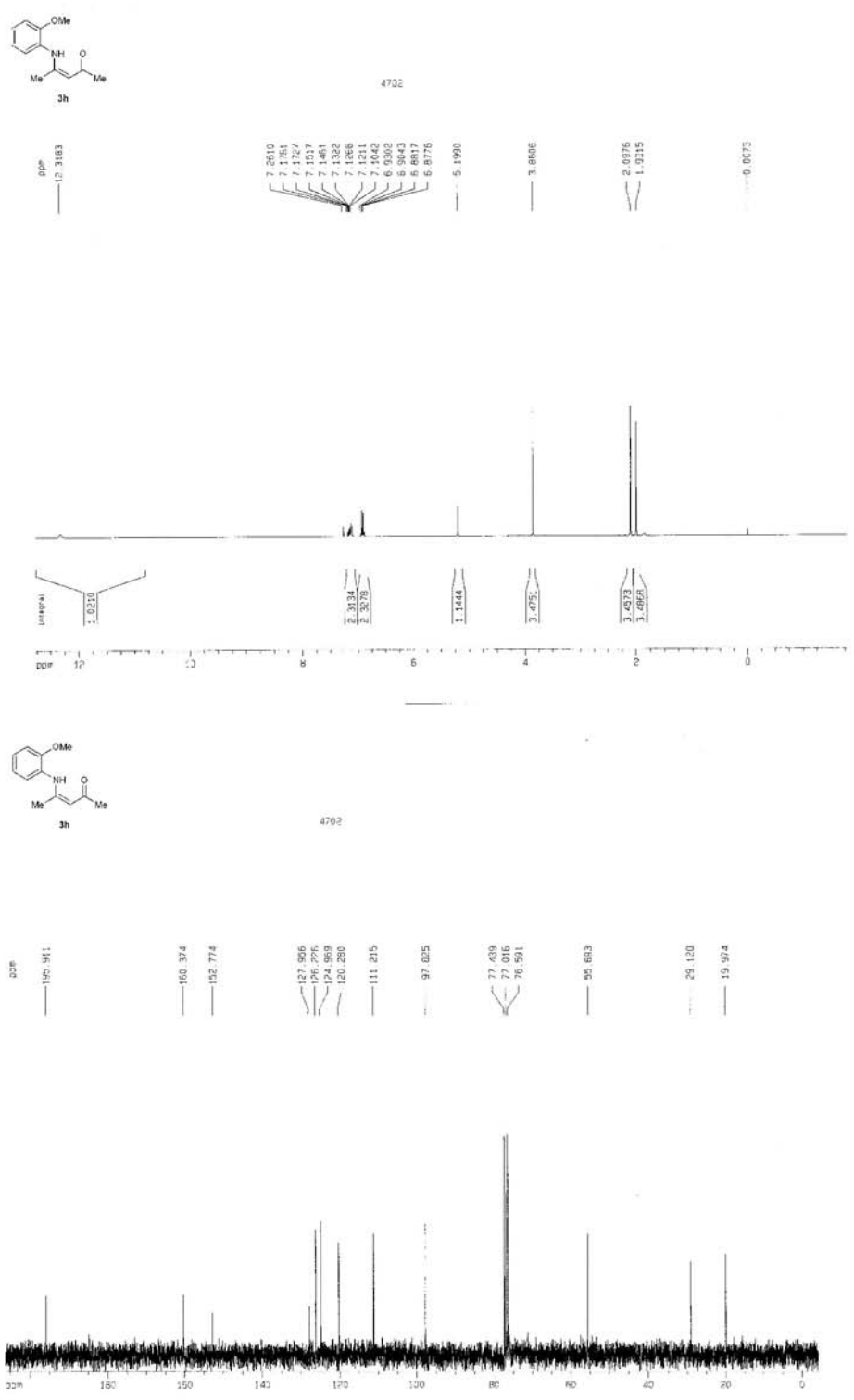

Figure S8. ^{1}H NMR of **3h** (300 MHz, $CDCl_3$) and ^{13}C NMR of **3h** (75 MHz, $CDCl_3$).

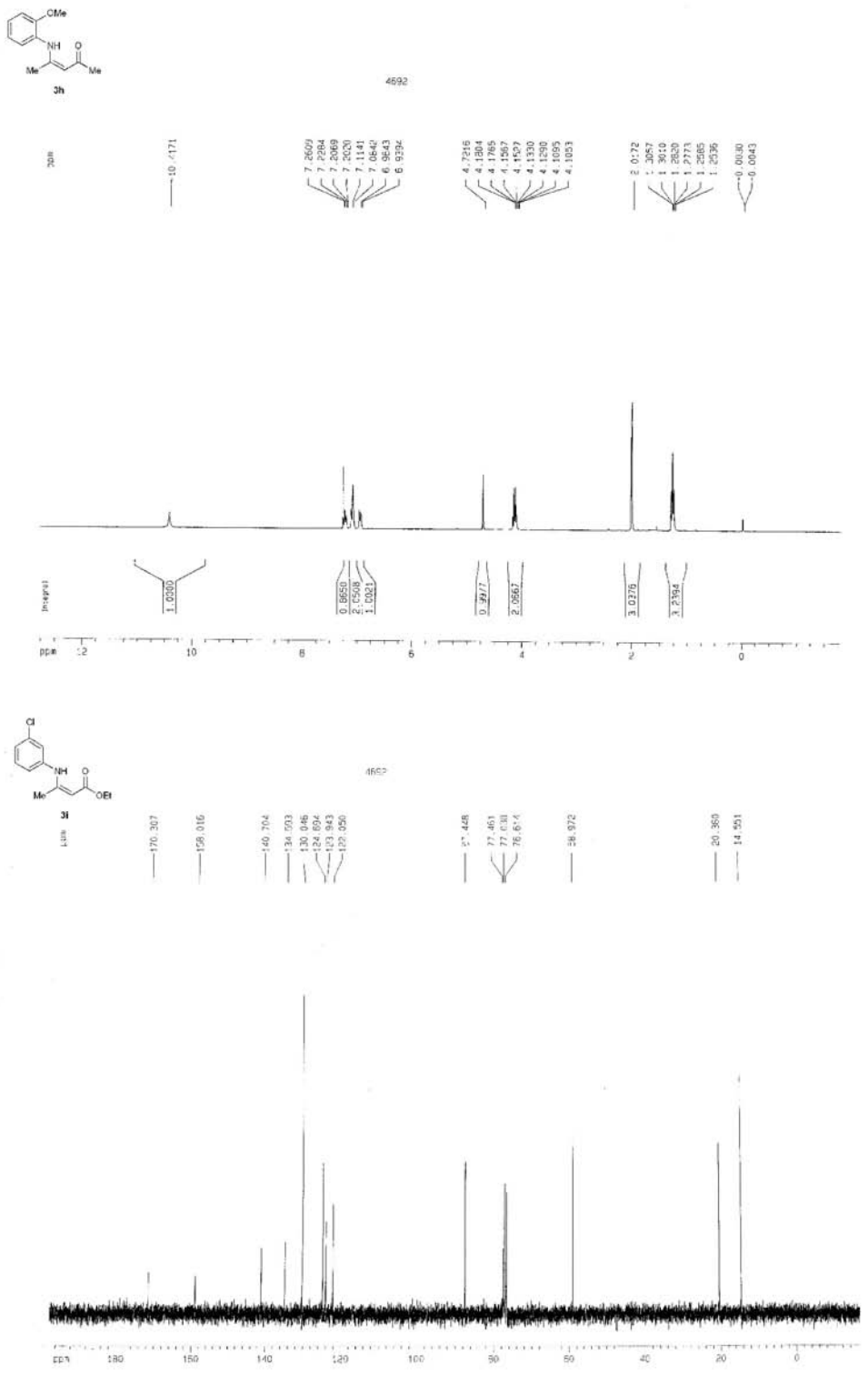

Figure S9. ^{1}H NMR of **3i** (300 MHz, $CDCl_3$) and ^{13}C NMR of **3i** (75 MHz, $CDCl_3$).

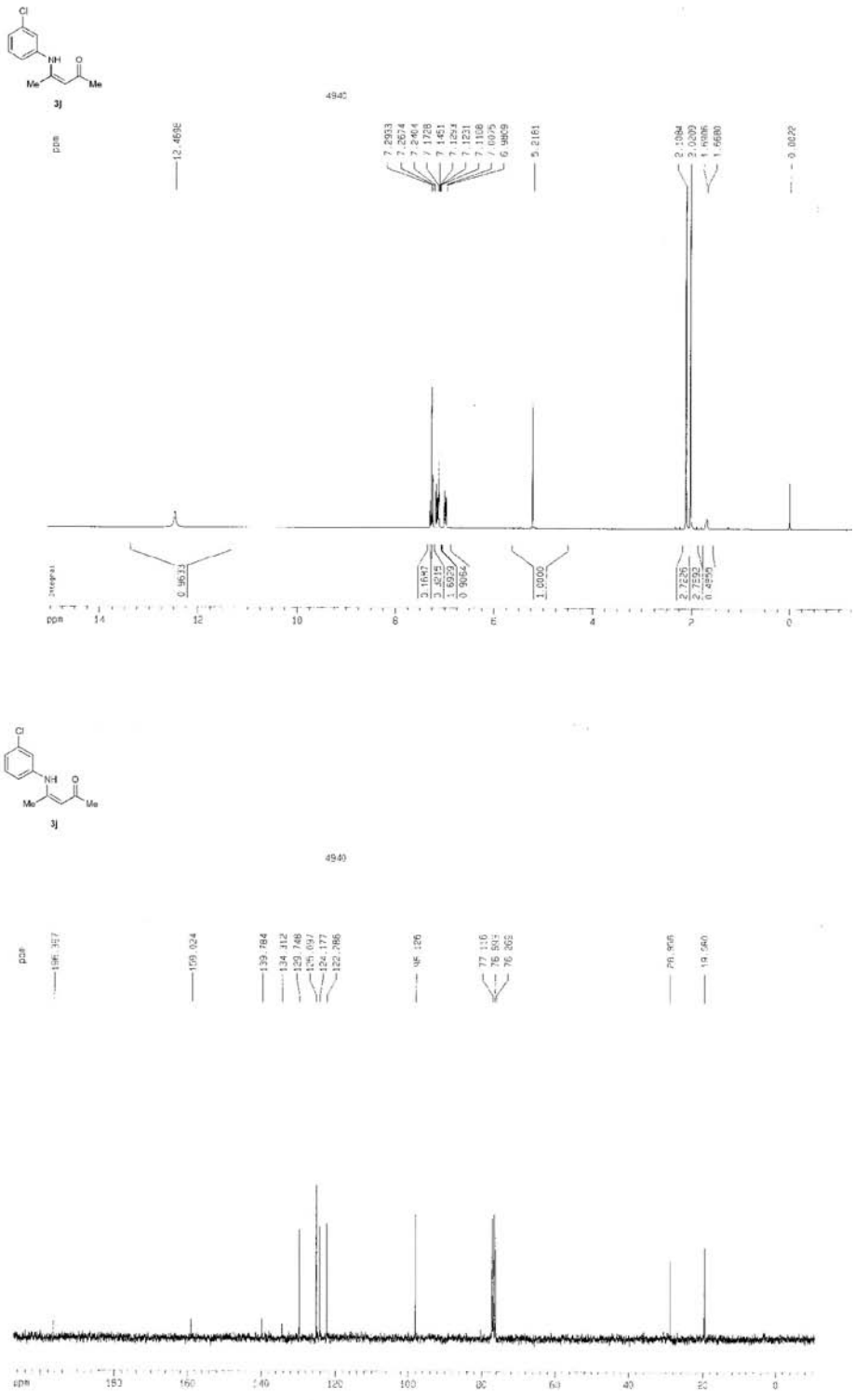

Figure S10. ^{1}H NMR of **3j** (300 MHz, $CDCl_3$) and ^{13}C NMR of **3j** (75 MHz, $CDCl_3$).

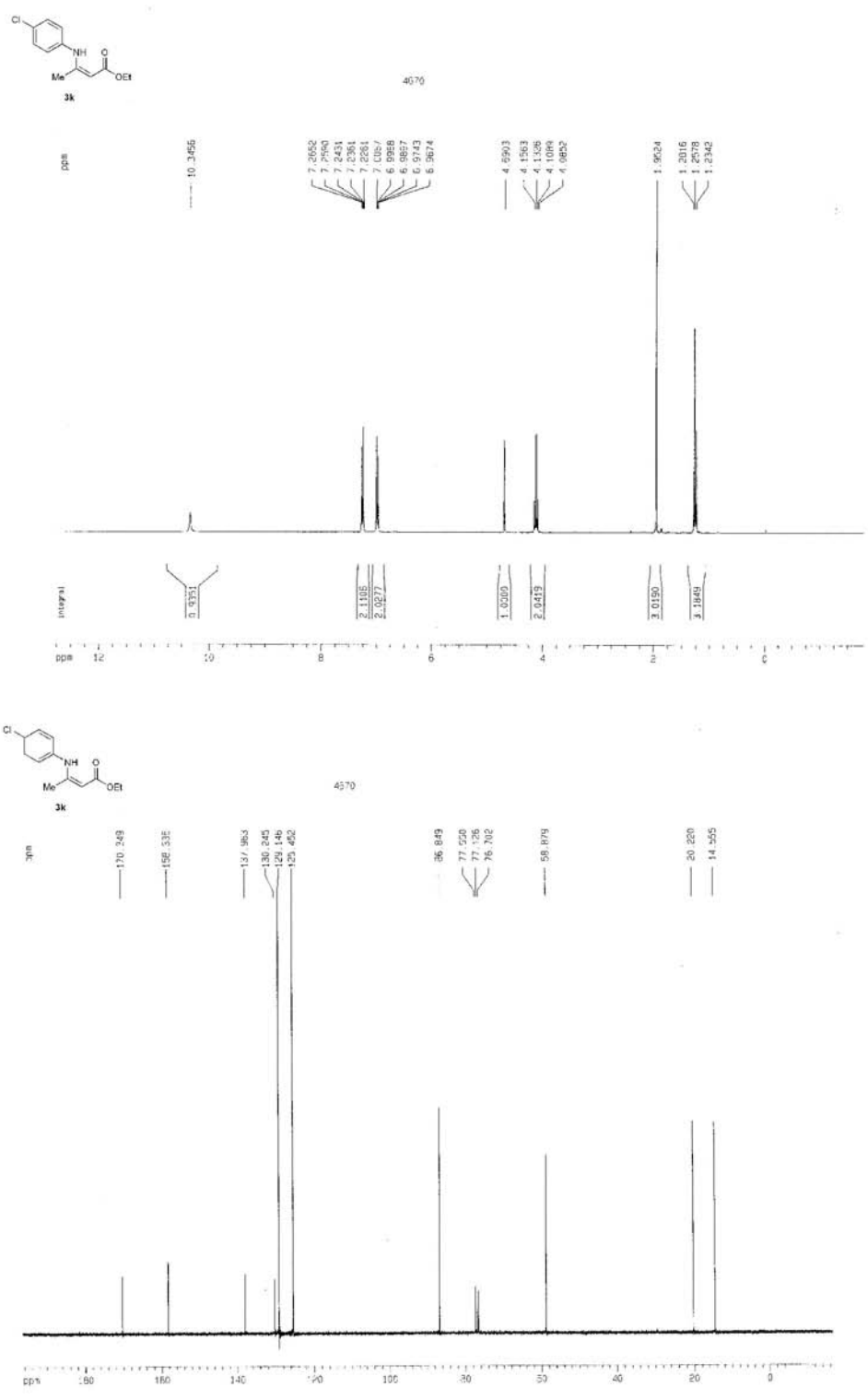

Figure S11. ^{1}H NMR of **3k** (300 MHz, $CDCl_3$) and ^{13}C NMR of **3k** (75 MHz, $CDCl_3$).

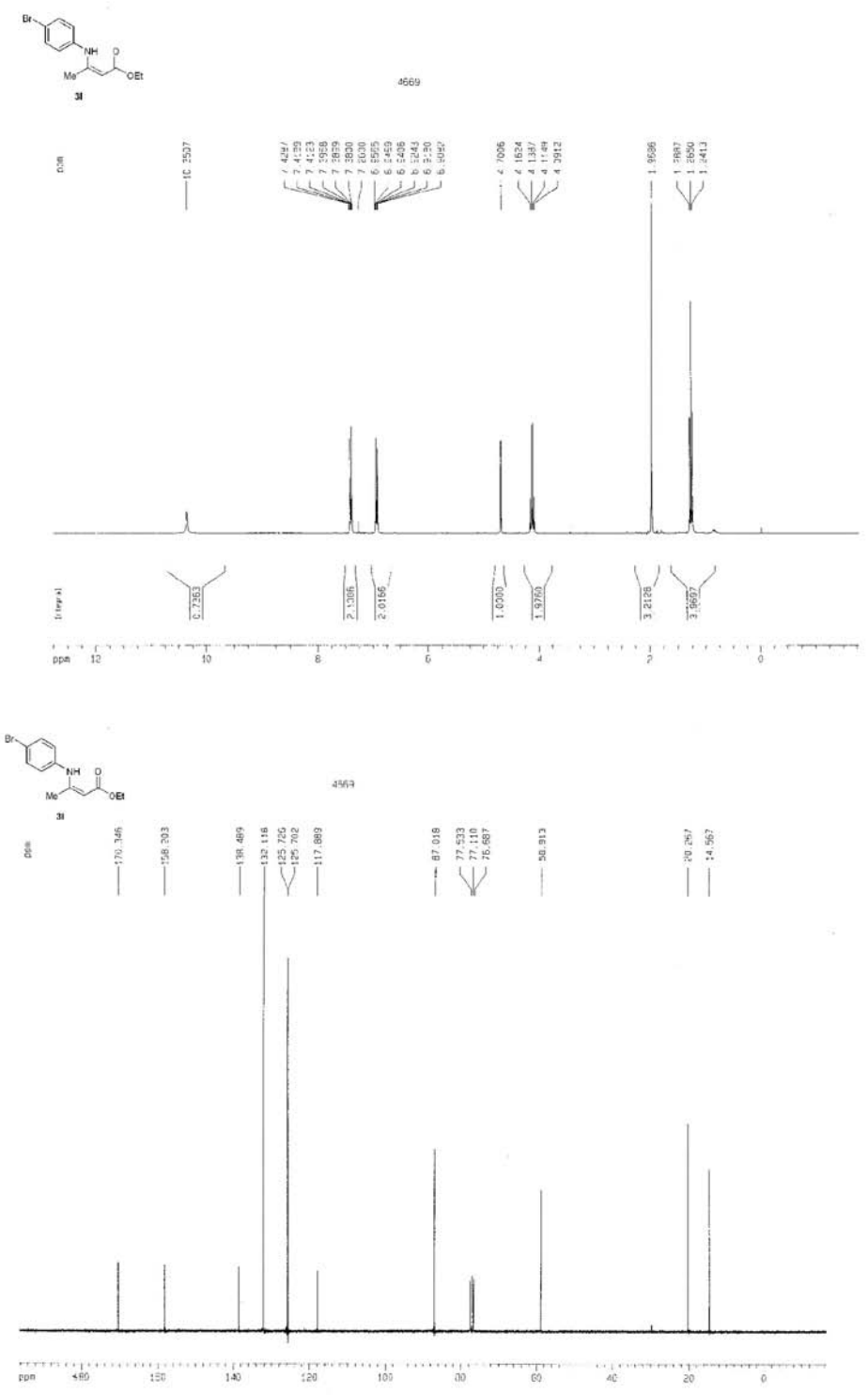

Figure S12. ^{1}H NMR of **3l** (300 MHz, $CDCl_3$) and ^{13}C NMR of **3l** (75 MHz, $CDCl_3$).

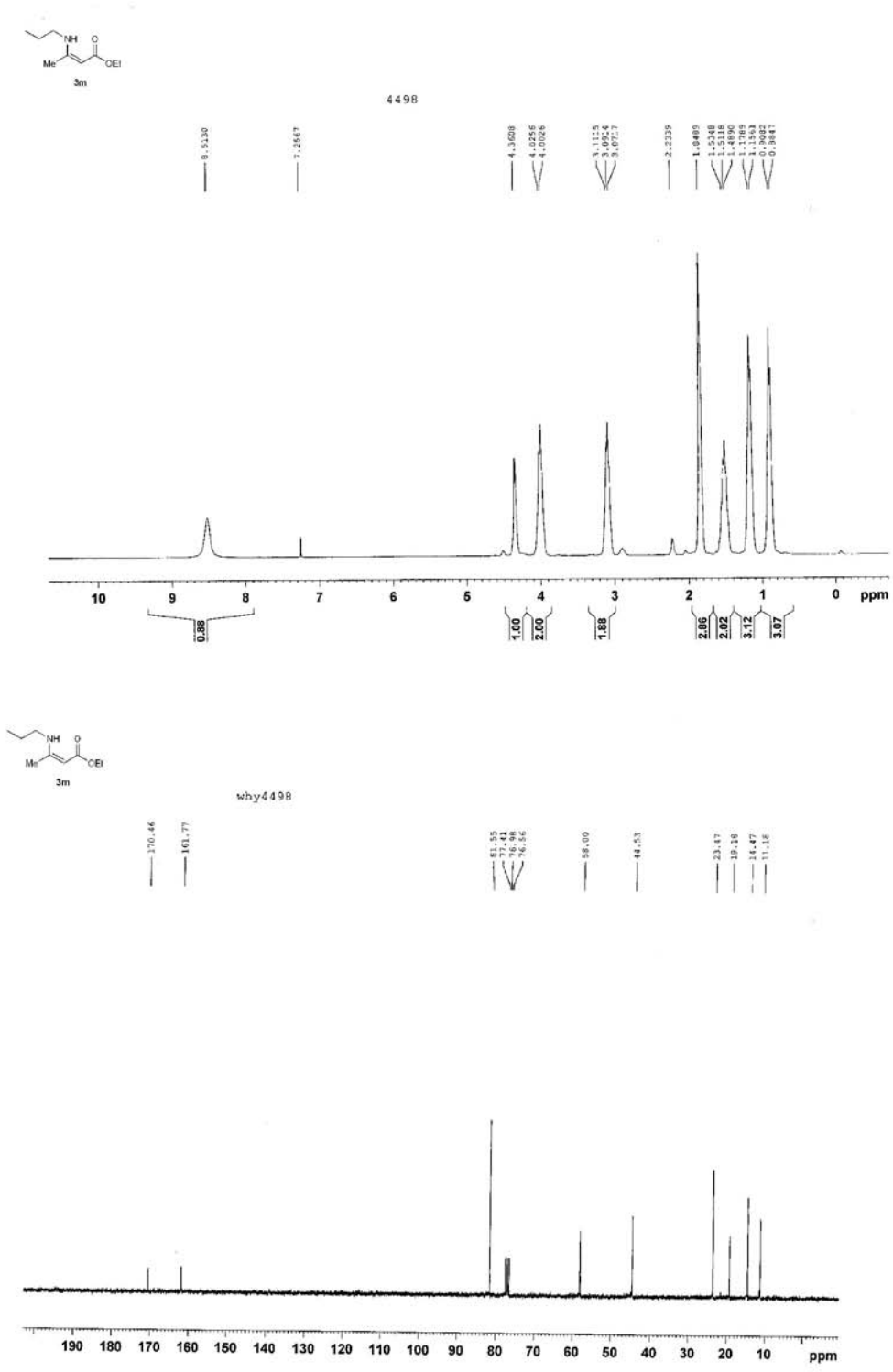

Figure S13. ^{1}H NMR of **3m** (300 MHz, $CDCl_3$) and ^{13}C NMR of **3m** (75 MHz, $CDCl_3$).

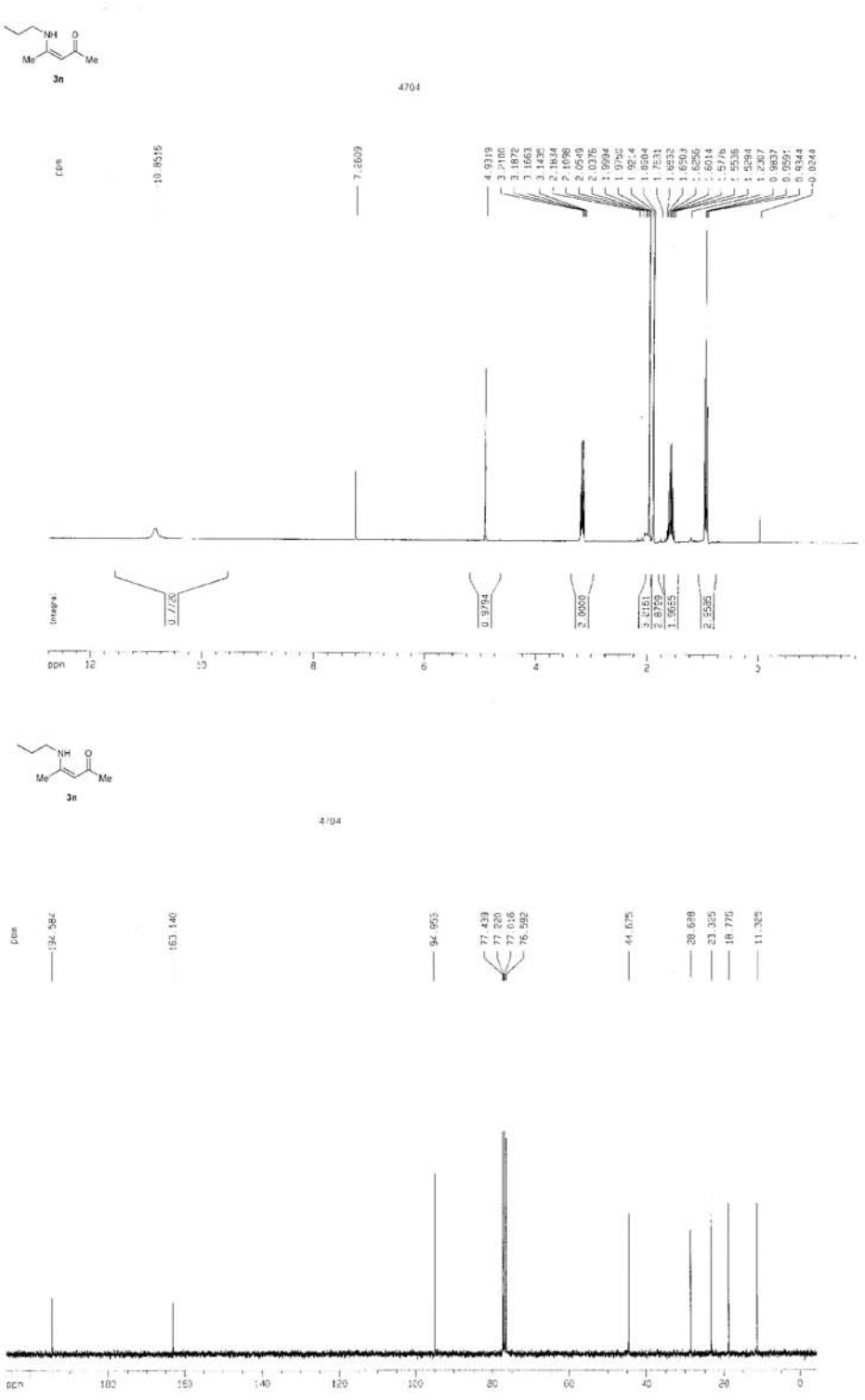

Figure S14. ^{1}H NMR of **3n** (300 MHz, $CDCl_3$) and ^{13}C NMR of **3n** (75 MHz, $CDCl_3$).

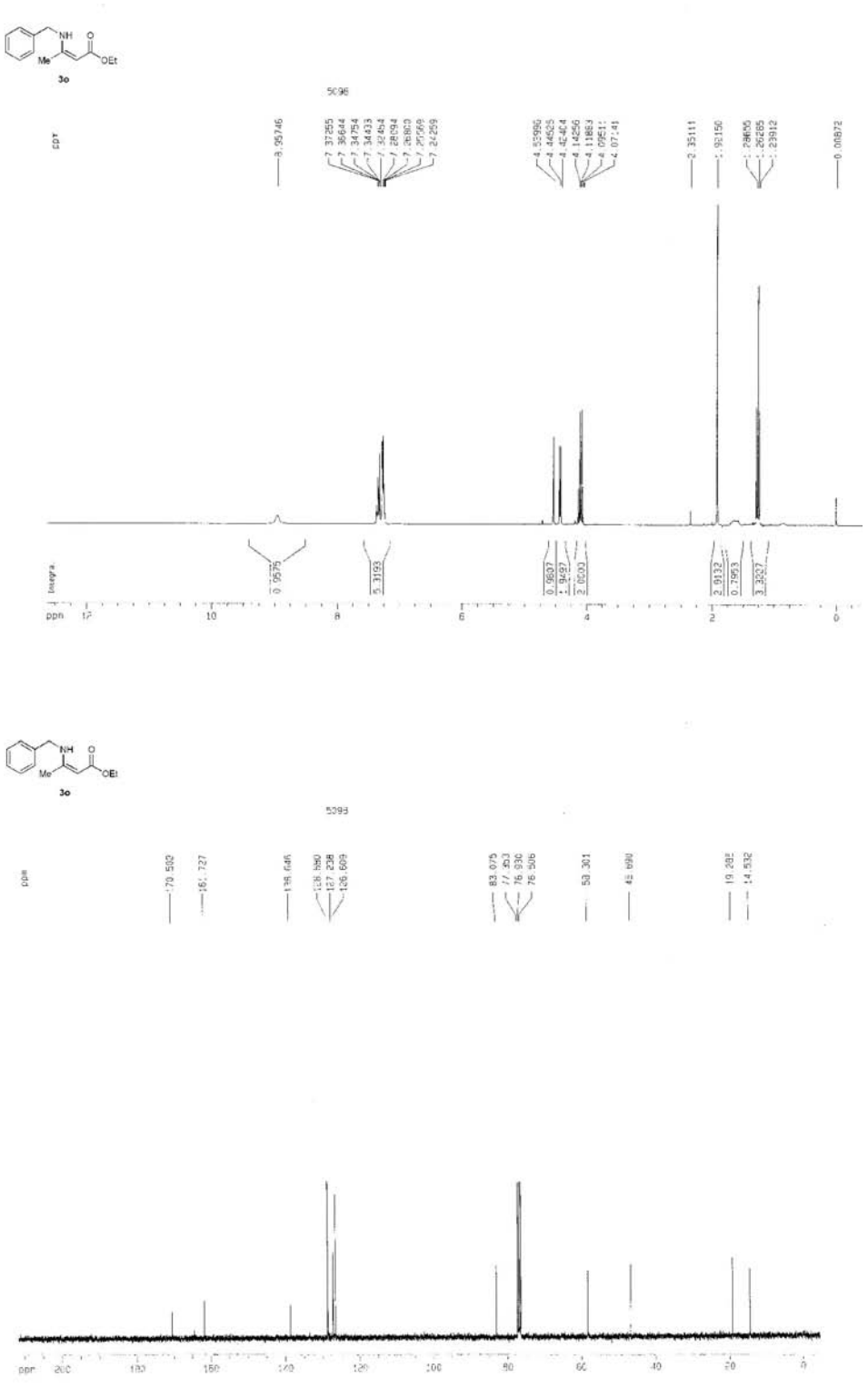

Figure S15. ^{1}H NMR of **3o** (300 MHz, $CDCl_3$) and ^{13}C NMR of **3o** (75 MHz, $CDCl_3$).

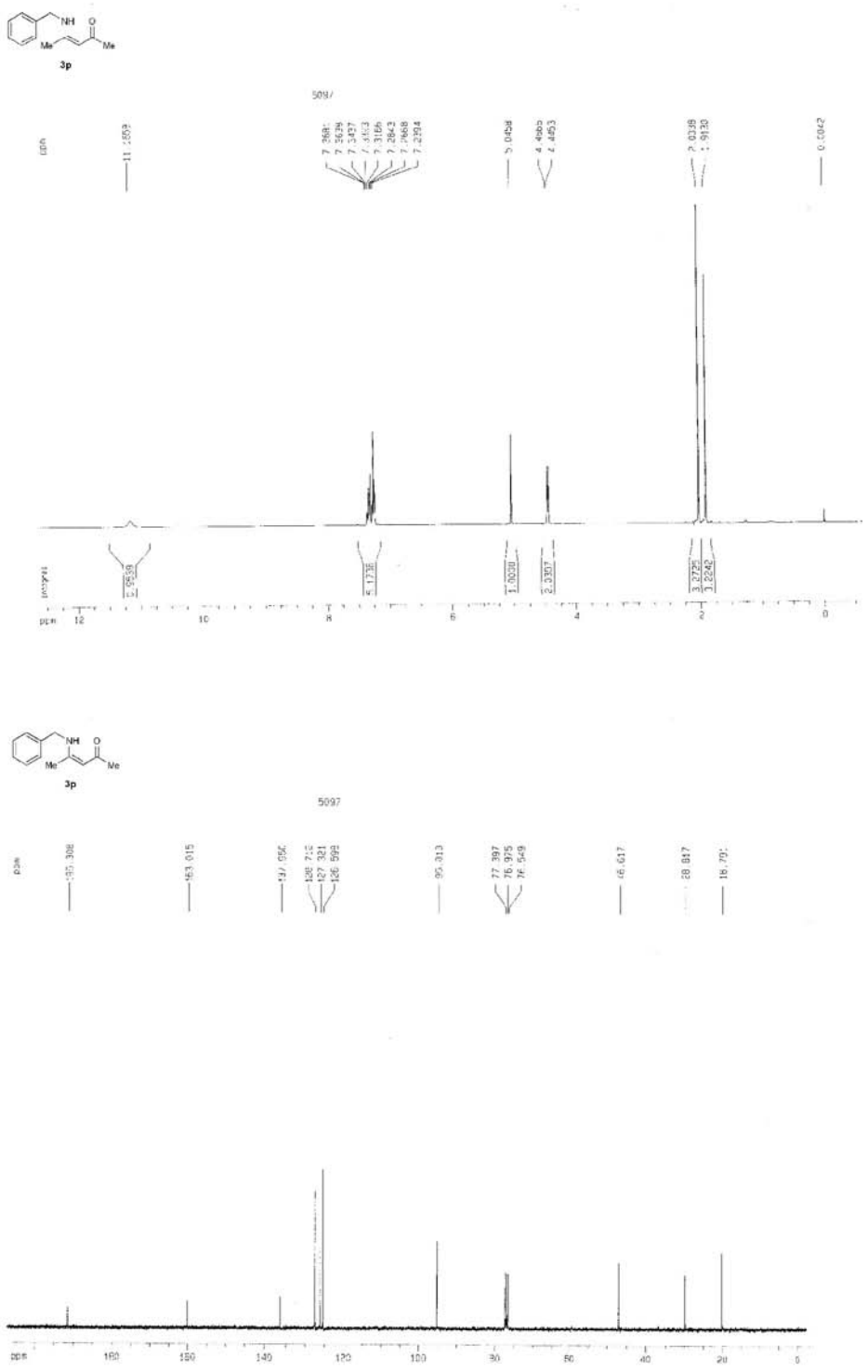

Figure S16. ^{1}H NMR of **3p** (300 MHz, $CDCl_3$) and ^{13}C NMR of **3p** (75 MHz, $CDCl_3$).

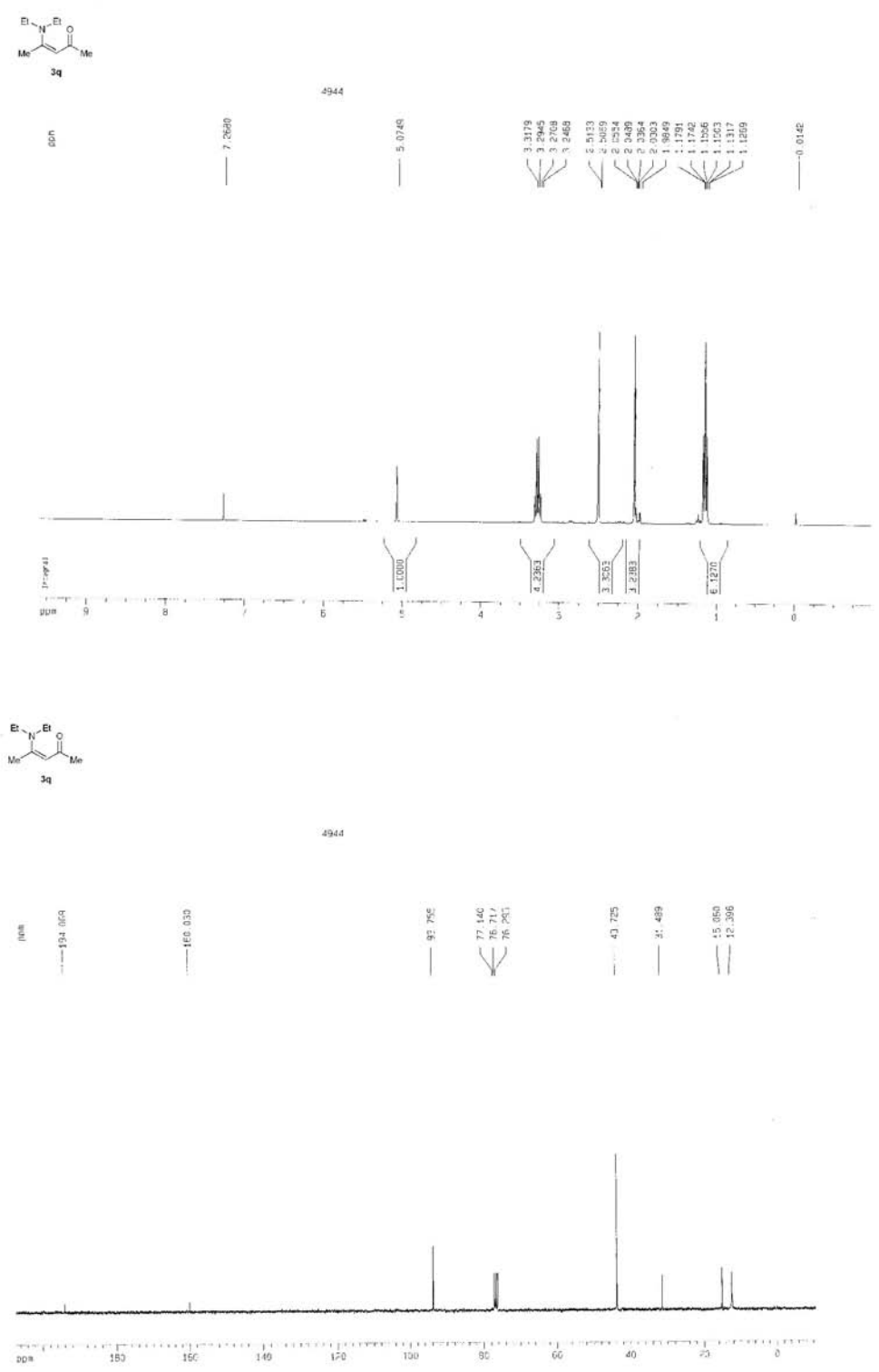

Figure S17. ^{1}H NMR of **3q** (300 MHz, $CDCl_3$) and ^{13}C NMR of **3q** (75 MHz, $CDCl_3$).

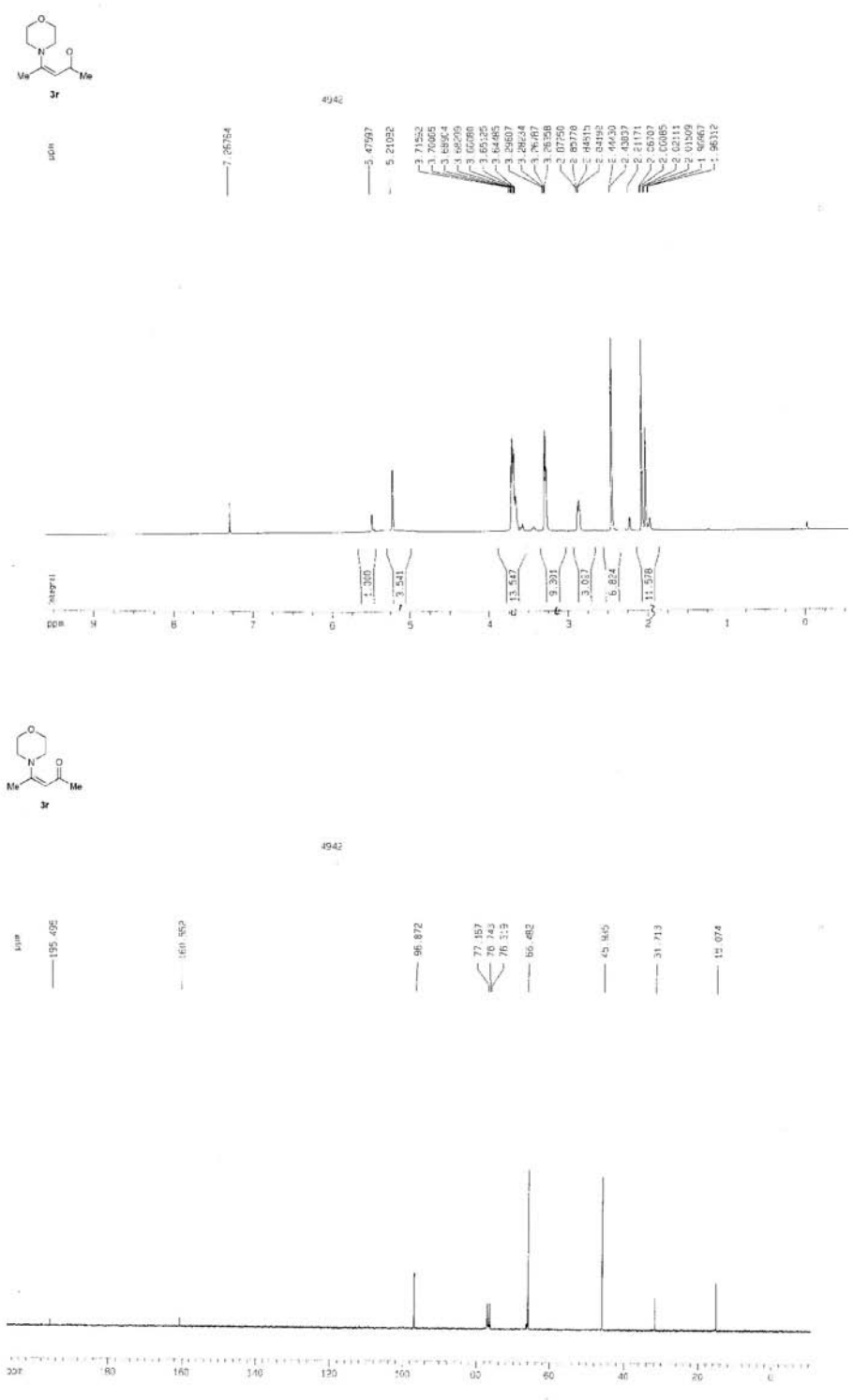

Figure S18. ^{1}H NMR of **3r** (300 MHz, $CDCl_3$) and ^{13}C NMR of **3r** (75 MHz, $CDCl_3$).

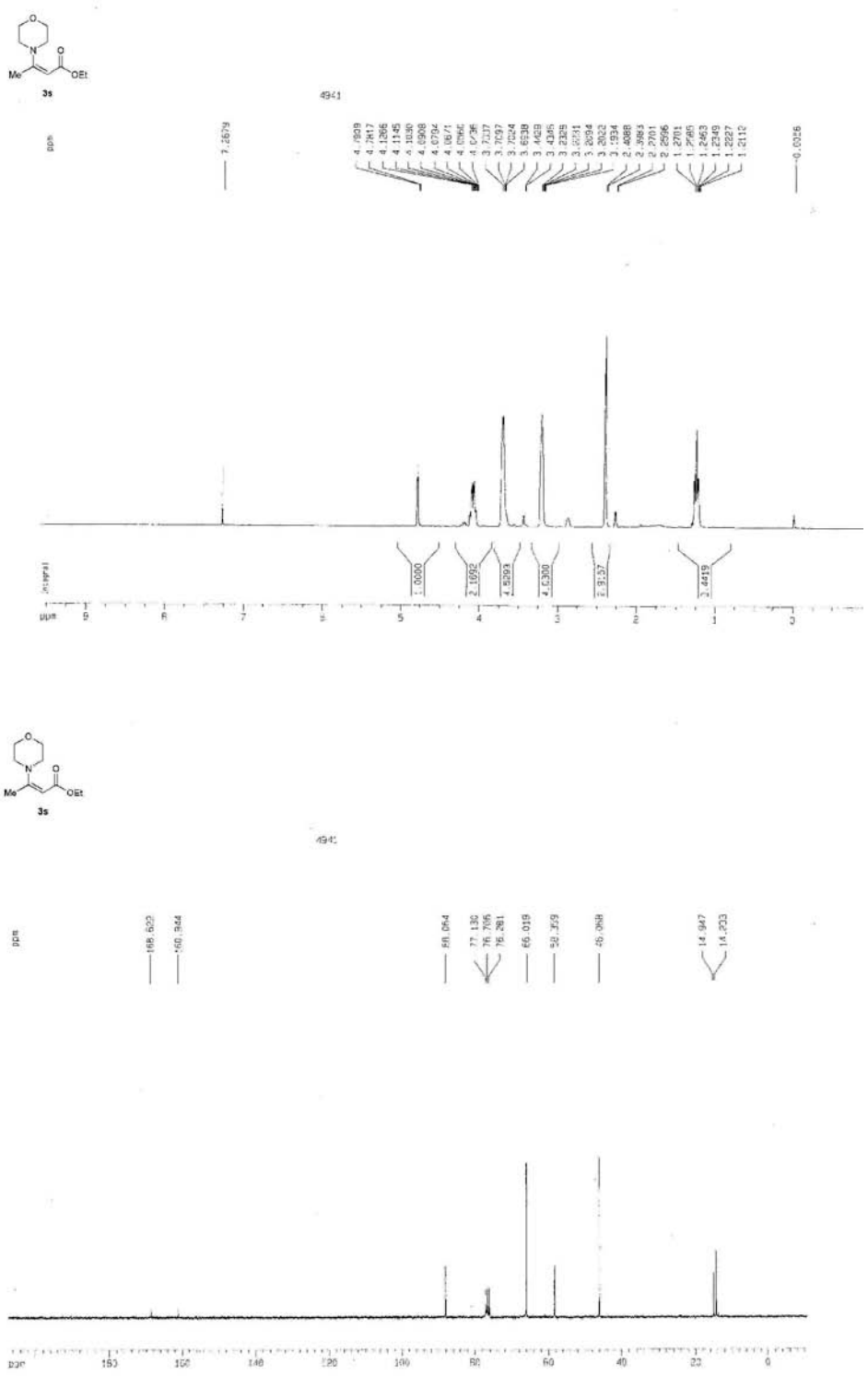

Figure S19. ^{1}H NMR of **3s** (300 MHz, $CDCl_3$) and ^{13}C NMR of **3s** (75 MHz, $CDCl_3$).

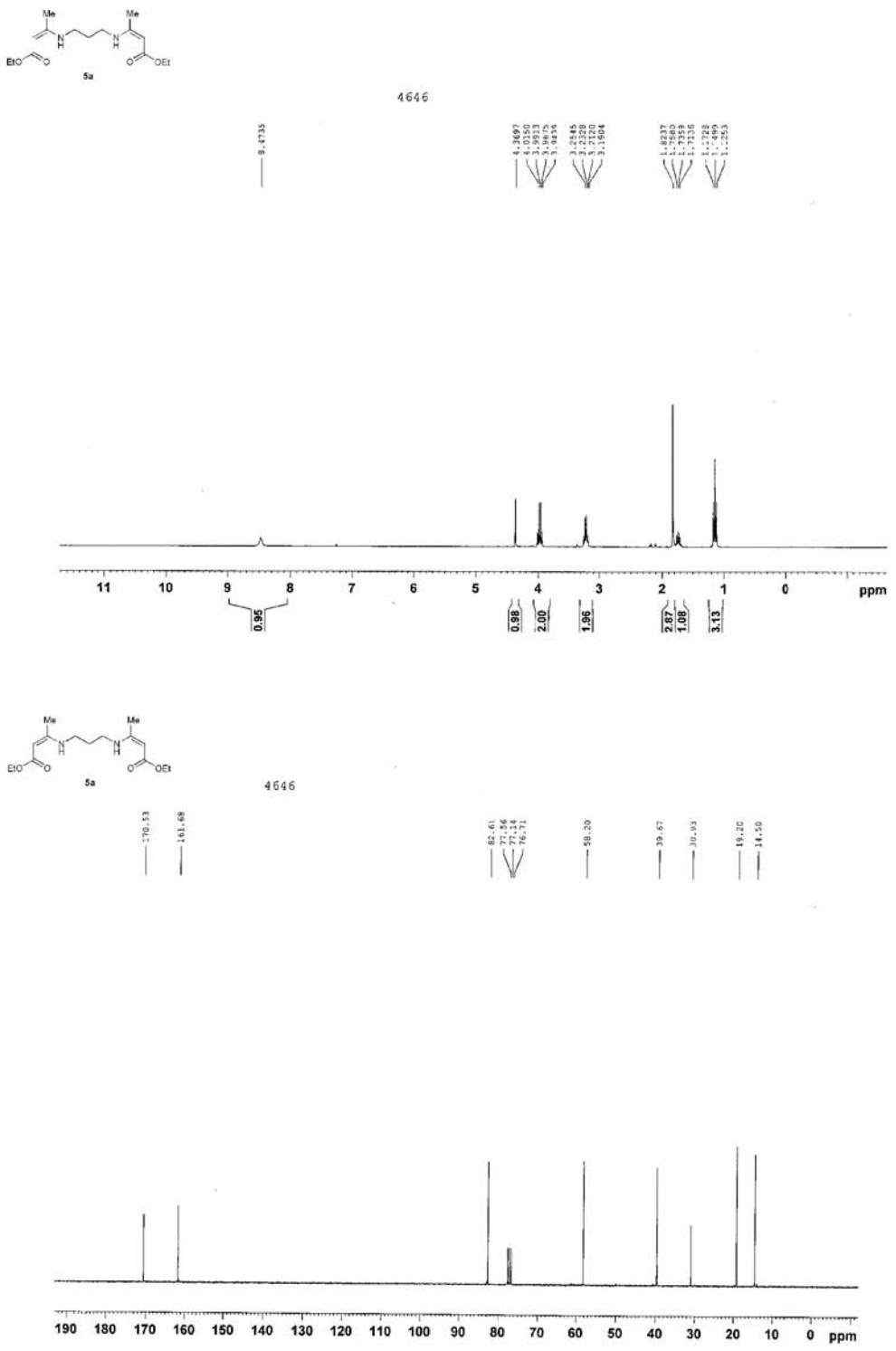

Figure S20. ^{1}H NMR of **5a** (300 MHz, $CDCl_3$) and ^{13}C NMR of **5a** (75 MHz, $CDCl_3$).

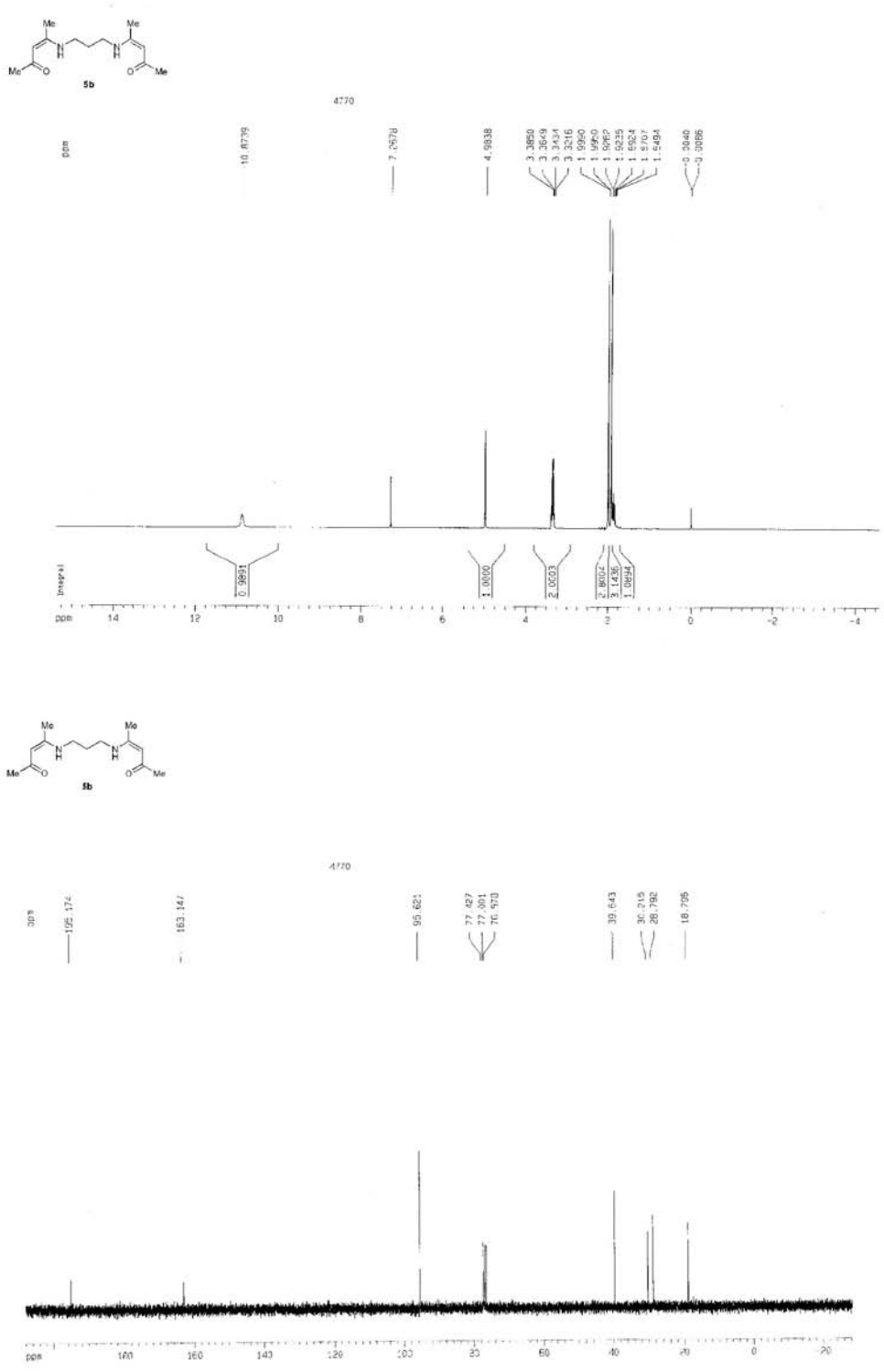

Figure S21. ^{1}H NMR of **5b** (300 MHz, $CDCl_3$) and ^{13}C NMR of **5b** (75 MHz, $CDCl_3$).

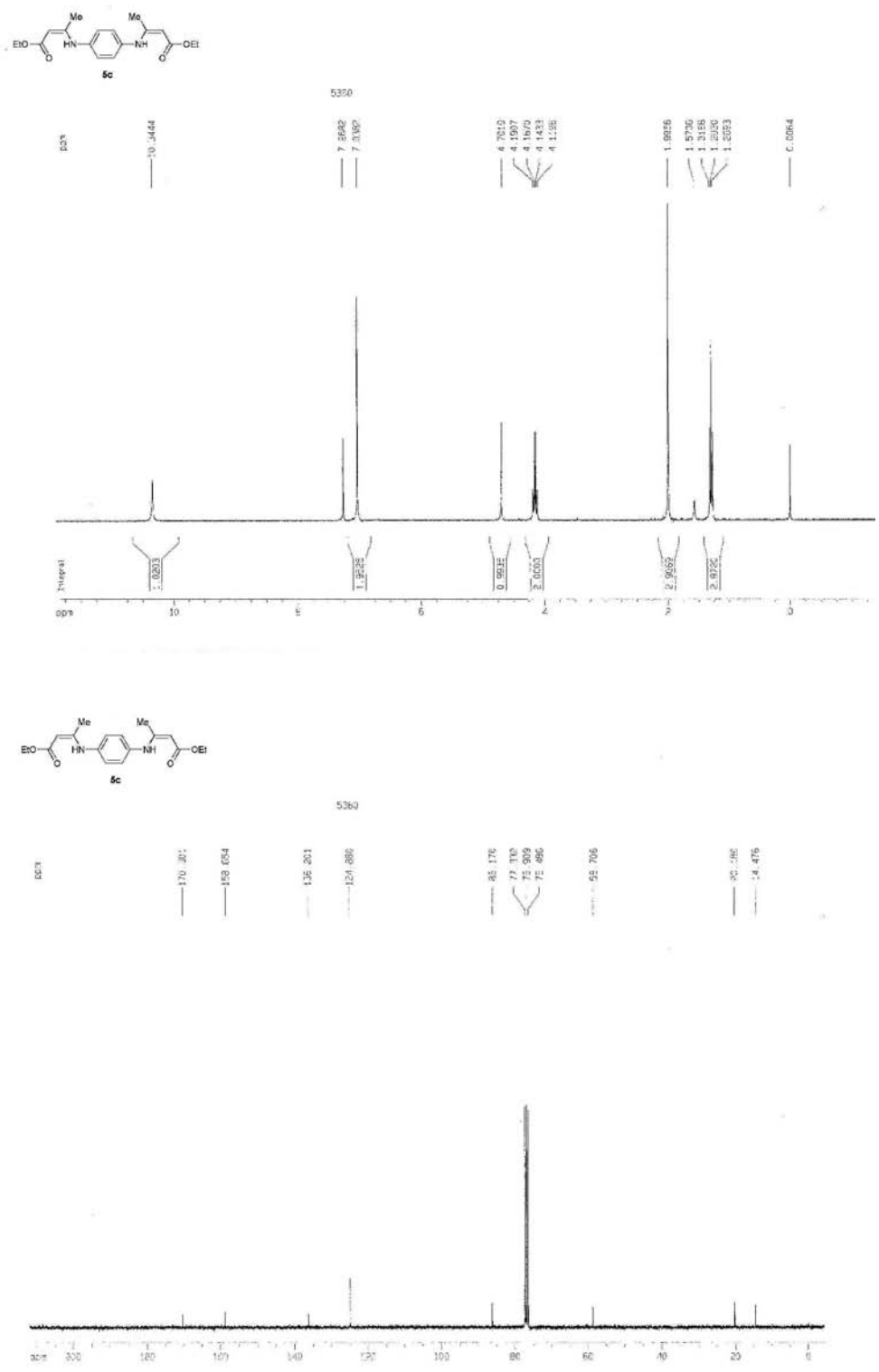

Figure S22. ^{1}H NMR of **5c** (300 MHz, $CDCl_3$) and ^{13}C NMR of **5c** (75 MHz, $CDCl_3$).

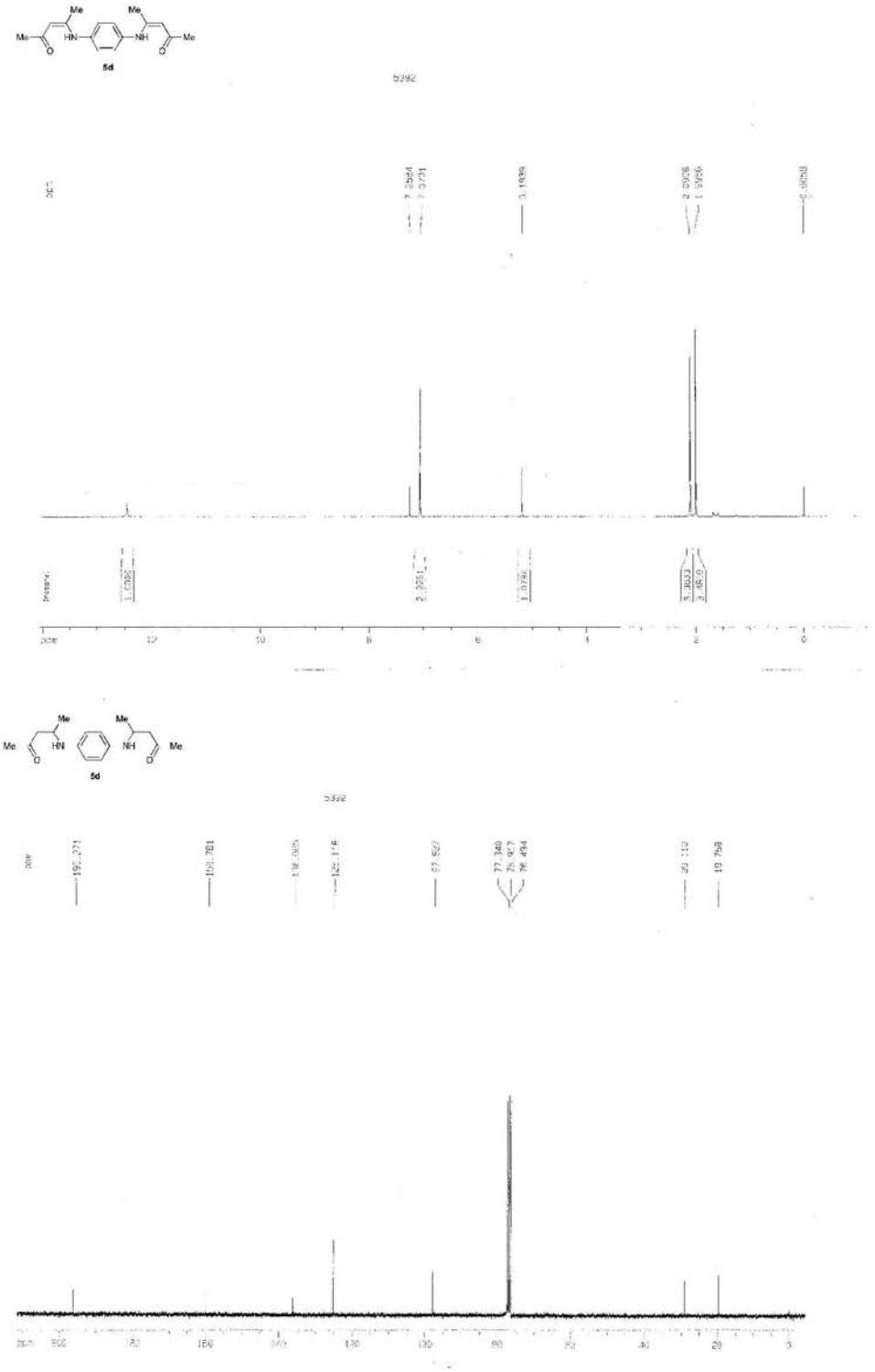

Figure S23. ^{1}H NMR of **5d** (300 MHz, $CDCl_3$) and ^{13}C NMR of **5d** (75 MHz, $CDCl_3$).

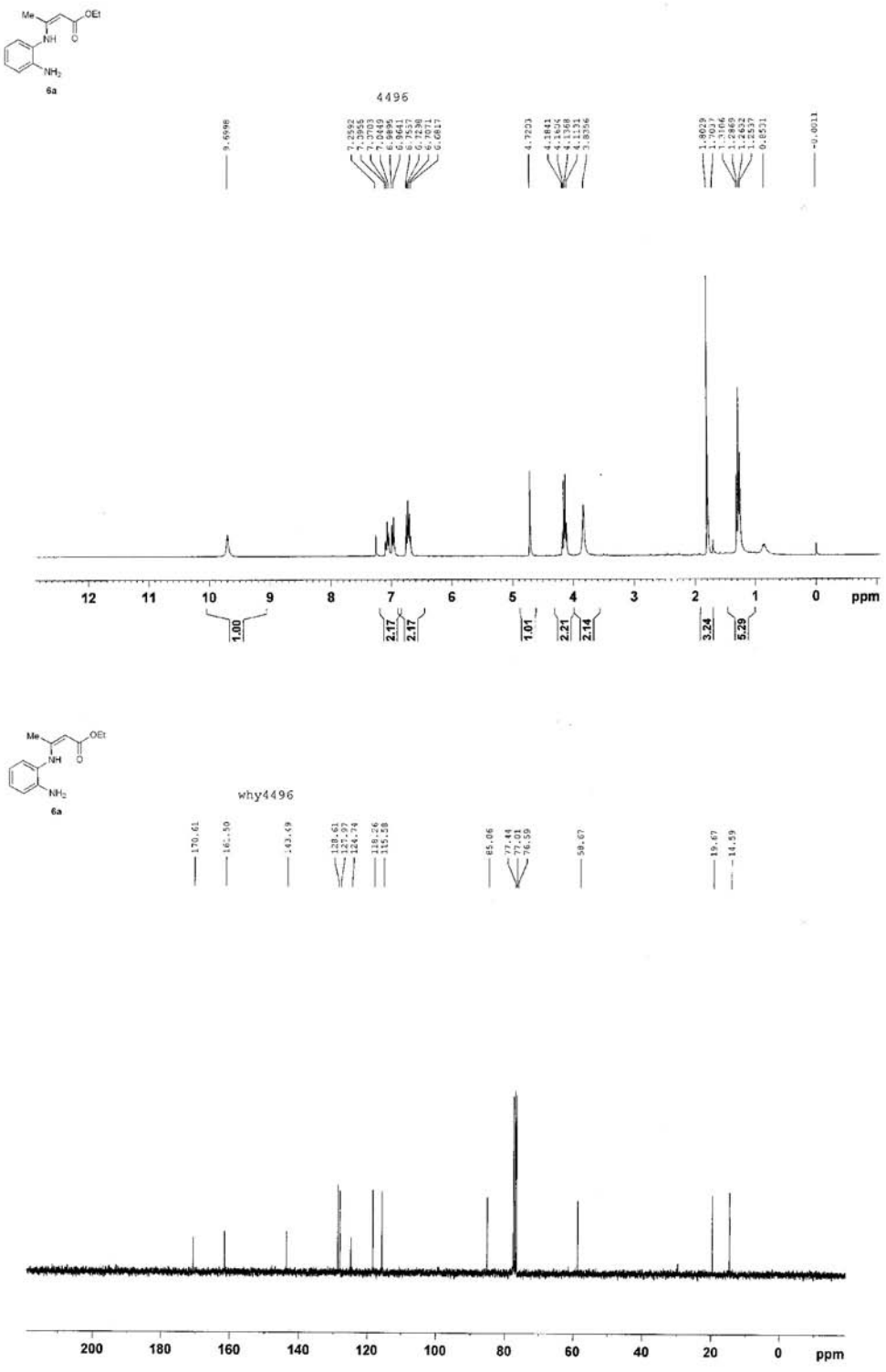

Figure S24. ^{1}H NMR of **6a** (300 MHz, $CDCl_3$) and ^{13}C NMR of **6a** (75 MHz, $CDCl_3$).

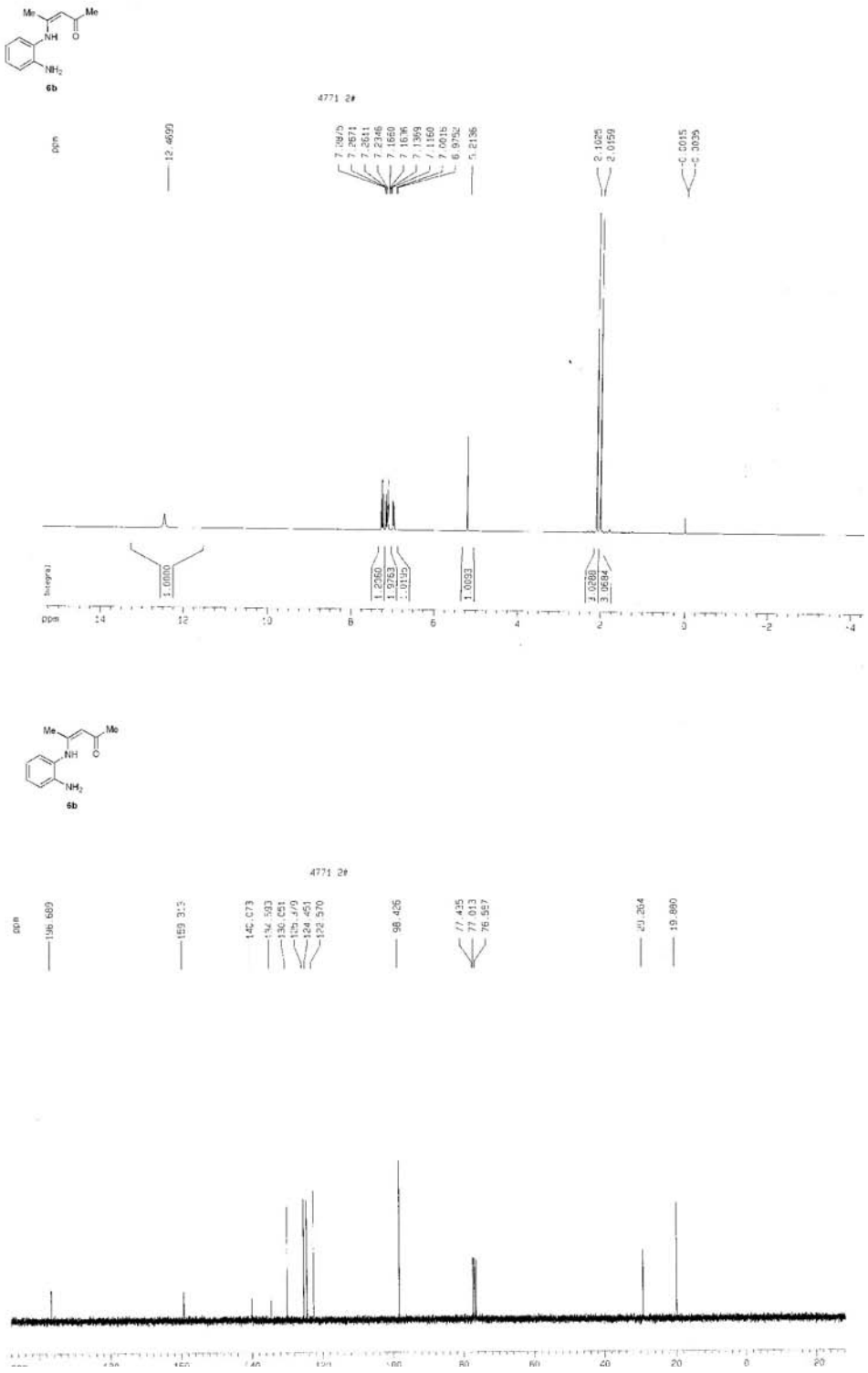

Figure S25. ^{1}H NMR of **6b** (300 MHz, $CDCl_3$) and ^{13}C NMR of **6b** (75 MHz, $CDCl_3$).