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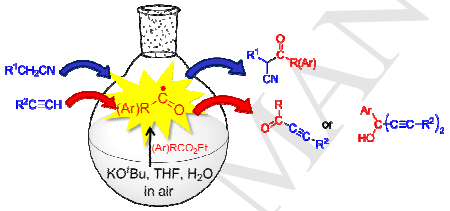

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ABSTRACT

We demonstrated the synthesis of β–ketonitriles, α,β-alkynones and biscarbinolsusing *tert*-butoxide-assisted C(C=O)-C (i.e., acyl-C) coupling of esters under ambient conditions. *tert*-Butoxide-assisted C(C=O)-C (i.e., acyl-C) coupling of esters with cyanomethylenes and acetylenes under transition metal-free ambient conditions gives β-ketonitriles, α,β-alkynones and/or aryl bis(phenylethynyl)carbinols in moderate-to-good yields. It is noteworthy that this is a rapid, facile and efficient process under ambient conditions, and use of cheap and stable starting materials.

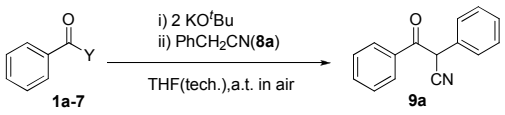
1. Introduction

β-Ketonitriles[1-3] and α,β-alkynones[4-10] are useful synthetic intermediate. They have also been used as key materials for the synthesis of various heterocycles.[1-4, 9-14] Several methods for the synthesis of β-ketonitriles and α,β-alkynones have been reported.[5-24] However, these methods suffer from one or more disadvantages such as the requirement of harsh reaction conditions and metal catalysts and/or expensive additional reagents. Therefore, significant academic efforts are underway to develop more efficient and facile method using the low-priced starting materials.

Esters are a very stable and inexpensive chemical species. They are used for a variety of purposes in synthesis. Although the ester function is an acyl source, the esters are not used generally as the acylating agents due to their low reactivity. Therefore, significant effort is ongoing in order to find more convenient and effective methods for the preparation of the corresponding acyl radicals or ions. Our research goal is the development of a convenient and efficient method for the synthesis of β-ketonitriles and α,β-alkynones using C(=O)-C (i.e., acyl-C) coupling of the esters under metal-free ambient conditions. Herein we firstly describe a synthesis of β-ketonitriles and α,β-alkynones by *tert*-butoxide-assisted C(=O)-C coupling of esters with benzyl (or alkyl) cyanides and acetylenes under transition metal-free ambient condition. Inspired by recent our report of the *tert*-butoxide-assisted amidation of esters *via* acyl radical intermediate,[25] we attempted to develop the synthetic methods using β-ketonitriles and α,β-alkynones from esters under ambient conditions.

2. Results and discussion

In order to evaluate the acyl sources under the literature conditions,[25] we first carried out the C(=O)-C coupling reactions of seven carboxylic acid derivatives, namely, ethyl benzoate (**1a**), methyl benzoate (**2**), phenyl benzoate (**3**), benzoic acid (**4**), benzoyl chloride (**5**), benzoic anhydride (**6**) and benzamide (**7**) with benzyl cyanide (**8a**). Fortunately, we found that the ethyl ester provided the corresponding 3-oxo-2,3-diphenylpropanoate (**9a**) at the best yield among the seven (Scheme 1). Whereas, the benzamide (**7**) did not convert to **9a**. Thus, we selected the ethyl esters for the *tert*-butoxide-assisted C(=O)-C coupling reactions.



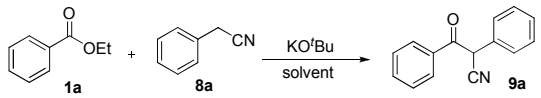
	1a	2	3	4	5	6	7
Y =	OEt	OMe	OPh	OH	Cl	O_2CPh	NH_2
9a(%)[a]	97	63	28	11	21	17	-

[a] Isolated yields. Average of two runs.

Scheme 1. *tert*-Butoxide-assisted C(=O)-C coupling of carboxylic acid derivatives **1-7** with benzyl cyanide (**8a**).

In addition, we attempted to evaluate the effect of the solvent for the reaction of ester with benzyl cyanide and phenyl acetylene. Tetrahydrofuran showed the best results in both reactions (Entry 5, Table 1; Entry 6, Table 2). Based on the literature description[25] and the results of solvent screening (Table 1 and 2), we selected the followings as an optimized conditions: ester (1 equiv.) / KOtBu (2 equiv.) / cyanide or acetylene (1 equiv.) / air / THF(tech.) / ambient temperature system.

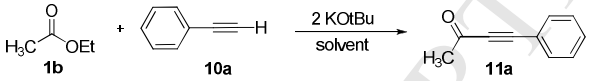
Table 1. Screening of solvents for the coupling of ethyl benzoate with benzyl cyanide and KO^{t}Bu in air at ambient temperature[a]



Entry	Solvent	Time (minute)	**9a** (%)[b]
1	*n*-hexane	40	20
2	cyclohexane	40	26
3	benzene	40	23
4	diethyl ether	40	39
5	tetrahydrofuran	30	97
6	dimethylformamide	40	10
7	dimethylsulfoxide	40	7
8	1,4-dioxane	40	8

[a] KO^{t}Bu (2 equiv., 95%), Solvent (tech. involving about 0.2% H_2O), **1a** (1 equiv.) and **8a** (1 equiv.) in air at ambient temperature. [b] All yields were isolated, pure material. Average of two runs.

Table 2. Screening of solvents for the coupling of ethyl acetate with phenyl acetylene and KO^{t}Bu in air at ambient temperature [a]

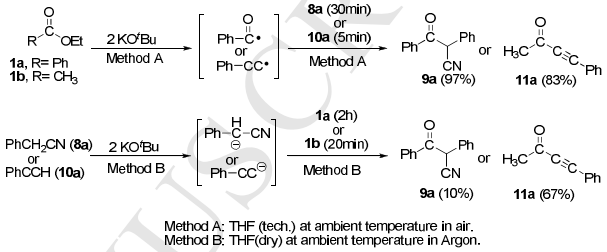


Entry	Solvent	Time (minute)	**9a** (%)[b]
1	*n*-hexane	10	2
2	toluene	10	5
3	benzene	10	no reaction
4	diethyl ether	10	4
5	methylene chloride	10	6
6	tetrahydrofuran	5	76
7	chloroform	10	no reaction
8	ethyl acetate	10	6
9	dimethyl formamide	10	50
10	1,4-dioxane	10	no reaction

[a] KO^{t}Bu (2 equiv., 95%), Solvent (tech. involving about 0.2% H_2O), **1b** (1 equiv.) and **10a** (1 equiv.) in air at ambient temperature. [b] All yields were isolated, pure material. Average of two runs.

In order to compare the yields of our reaction with the Dieckmann-type reaction,[26] we also performed two C(=O)-C couplings under the different conditions (Scheme 2).

First, C(=O)-C coupling of **1a** with **8a** under our conditions *via* benzoyl radical intermediate[25] afforded 3-oxo-2,3-diphenylpropionitrile (**9a**) at 97% yield, whereas the Dieckmann-type reaction *via* cyanophenyl methanide gave **9a** at 10% yield (Scheme 2). On the other hand, the reaction of **1a** with **8a** using KO^{t}Amyl instead of KO^{t}Bu according to the literature[14] under same conditions gave **9a** in 51% yield. In the coupling of ethyl acetate (**1b**) with phenyl acetylene (**10a**) to give 4-phenylbut-3-yn-2-one (**11a**), the yield of our process was also higher than that of the Dieckmann-type process. In the C(=O)-C coupling of the ester under our conditions, the radical path may be more favorable than the anion path.

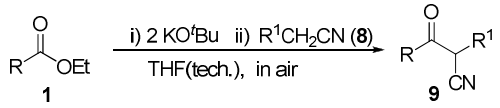


Scheme 2. Reaction of ethyl benzoate (**1a**) or ethyl acetate (**1b**) with benzyl cyanide (**8a**) or phenyl acetylene (**10a**) under our conditions and the Dieckmann-type reaction conditions

To illustrate the versatility of the *tert*-butoxide-assisted C(=O)-C coupling of esters, the C(=O)-C coupling of aliphatic and aromatic esters with aryl (or alkyl) cyanides or acetylenes was examined (Tables 3 and 4). The coupling of aromatic esters **1** and aliphatic esters with acetonitrile or butyronitrile under the above conditions afforded the corresponding β-ketonitriles **9b-9f** at 79 – 91% yields (Entries 1-5, Table 3). Aliphatic and aromatic esters were treated with benzyl cyanide (**8a**) under the same conditions to afford the corresponding β-ketonitriles **9h-9j** in good yields except for ethyl acetate (Entries 7 – 9, Table 3). Ethyl acetate (**1b**) was allowed to react with **8a** under the same conditions to afford the corresponding β-ketonitriles **9g** (26%) and ethyl 3-oxobutanoate (21%) as the by-product (Entry 6, Table 3).

In addition, the aliphatic esters such as ethyl acetate, ethyl 2-methylpropanoate, and ethyl 3-phenylpropanoate were allowed to react with phenyl acetylene (**10a**) or 1-ethynylcyclohex-1-ene (**10b**) to afford the corresponding α,β-alkynones **11a-c** and **11d** in 60 - 76% yields (Entries 1 – 3, and 5, Table 4). In contrast C(=O)-C coupling of the aromatic esters such as ethyl benzoate, ethyl 4-pyrydinecarboxylate, and ethyl 4-cyanobenzoate with 2 equiv. of phenyl acetylene (**10a**) under the same condition gave the corresponding aryl bis(phenylethynyl)carbinols **12a-12d** as over addition product instead of α,β-alkynones at 23 - 86% yields (Entries 6 – 9, Table 4). On the other hand, when ethyl 2-methylpropanoate was allowed to react with 2 equiv. of phenyl acetylene (**10a**) under the same conditions, the corresponding alkynone (36%), the carbinol (3%) and unknown products (Entry 4, Table 4) were formed. These give evidence that the carbinol was produced *via* the alkynone intermediate. When ethyl benzoates and ethyl 4-pyridinecarboxlate were made to react with 1 equiv. of phenyl acetylene (**10a**), we did not detect the corresponding α,β–alkynones. Under our conditions, the aliphatic esters underwent the substitution, whereas the aromatic esters undergo the addition of acyl radical after initial substitution. These results may be due to the different reactivity

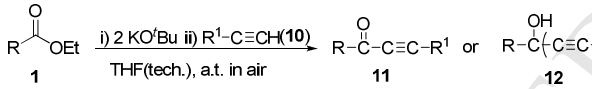
Table 3. Synthesis of β-ketonitriles by *tert*-butoxide-assisted C(=O)-C coupling of esters with nitriles and KO^{t}Bu in THF(tech.) in air at ambient temperature[a].



Entry	R	R^1	Time	**9** (%)[b]
1	Ph	H	30min	**9b** (90)
2	Ph	CH_3CH_2	30min	**9c** (82)
3	*p*-ClPh	H	30min	**9d** (91)
4	*p*-ClPh	CH_3CH_2	2h	**9e** (79)
5	*i*-Pr	H	30min	**9f** (92)
6	CH_3	Ph	7h	**9g** (26)[c]
7	*i*-Pr	Ph	8h	**9h** (75)
8	$Ph(CH_2)_2$	Ph	1h	**9i** (81)
9	4-pyridyl	Ph	1h	**9j** (90)

[a] KO^{t}Bu (2 equiv., 95%), THF (tech. involving about 0.2% H_2O), ester (1 equiv.) and cyanide (1 equiv.) in air at ambient temperature. [b] All yields were isolated, pure material. Average of two runs. [c]Ethyl 3-oxobutanoate as by-product was formed in 21% yield.

Table 4. Synthesis of α,β-alkynones or bis(phenylethnyl)carbinols by the *tert*-butoxide-assisted C(=O)-C couplings of esters with acetylenes[a]



Entry	R	R^1	Time (min)	Isolated Yield (%)[b]	
				11	**12**
1	CH_3	Ph	5	**11a** (76)	—
2	CH_3	*c*-C_6H_9[c]	6	**11b** (73)	—
3	*i*-Pr	Ph	5	**11c** (60)	—
4	*i*-Pr	Ph	30	**11c** (36)	3[d]
5	$Ph(CH_2)_2$	Ph	5	**11d** (66)	—
6	Ph	Ph	3	—	**12a** (86)
7	4-pyridyl	Ph	3	—	**12b** (73)
8	4-NCPh	Ph	3	—	**12c** (40)
9	PhCH=CH	Ph	10	—	**12d** (23)

[a]Acetylene (1 equiv. for aliphatic esters, 2 equiv. for aromatic esters) in air at ambient temperature. [b] All yields were isolated, pure material. Average of two runs. [c] 1-Cyclohexenyl. [d] 2 equiv. of phenyl acetylene was used. We also detected unknown products.

of carbonyls in the two α,β-alkynones. On the other hand, we determined the structure of **12b** according to the IR and NMR spectral data, and X-ray crystallographic data (Figure 1).

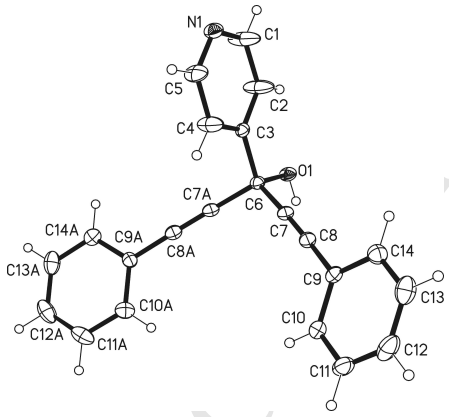


Figure 1. ORTEP diagram of **12b** (CCDC 949963)

We first carried out the *tert*-butoxide-assisted C(=O)-C coupling of the esters with benzyl (or alkyl) cyanides or acetylenes to afford the corresponding β-ketonitriles, α,β-alkynones and aryl bis(phenylethynyl)carbinols. Although metal-catalyzed C(=O)-C coupling of thioesters have been reported,[27-31] transition metal-free C(=O)-C coupling of the esters with benzyl cyanide and phenyl acetylene had not been yet achieved. The reactions in the present study are the first example (to our knowledge) of *tert*-butoxide-assisted C(=O)-C coupling of esters with alkynes and cyanomethylenes *via* the radical intermediate. The structures of all synthetic compounds were established by IR, NMR and X-ray for **12b**, also m/z of the molecular ion were obtained by HRMS.

3. Conclusion

In conclusion, we developed a metal-free C(=O)-C coupling reaction of esters with benzyl (or alkyl) cyanides or acetylenes under ambient conditions to give the corresponding β-ketonitriles, α,β-alkynones, and aryl bis(phenylethynyl)carbinols. These are novel C(=O)-C coupling reaction *via* the acyl radical intermediate derived from ester under a *tert*-butoxide-assisted processes and ambient conditions. Interestingly, the decarbonylation reaction, which generates a new carbon-centered radical and carbon monoxide, was not observed under our reaction conditions. This synthetic method is rapid, convenient, and effective for a broad range of C(=O)-C coupling reactions of esters. More importantly, this process can be achieved under metal-free conditions in air using technical grade solvent. We believe that the assisted C(=O)-C coupling would be applicable in synthetic, medicinal, and industrial chemistry. Further work on the theoretical study and the exploration of the tremendous potential of esters and internal alkynes is under way in our laboratory.

4. Experimental section

4.1. General

NMR spectra were run in $CDCl_3$ or DMSO-d_6 on a 300MHz instrument and recorded at the following frequencies: proton (^{1}H,

300MHz), carbon (^{13}C, 75MHz). Chemical shifts are expressed in parts per million related to internal TMS and coupling constant (*J*) are in hertz. Infrared specta were recorded on a Fourier transform spectrometer. Mass spectra were recorded under electron ionization (EI). Melting points were determined in open glass capillaries and are uncorrected. Thin-Layer Chromatography (TLC) analyses were performed using precoated silica gel plates. Column chromatography was performed with silica gel 60 as the stationary phase. Crystallographic data for compounds **12b** (CCDC 949963) can be obtained free of charge from Cambridge Crystallographic Data Centre. X-ray diffraction data were obtained using a diffractometer equipped with a graphite monochromated MoK α (λ = 0.71073 Å) radiation source and a scintilation counter detector.

4.2. Reaction of benzoic acid derivatives with benzyl cyanide

Benzoic acid derivative (**1-7**, 6.65 mmol) was dissolved in THF (30 mL, technical grade involving 0.2% water) with stirring about 230 rpm) at room temperature for 5 minutes. Potassium *tert*-butoxide (1.57 g, 14.0 mmol, 95%) was added immediately to the above THF solution. After stirring enough the flask, benzyl cyanide (**8a**, 0.78 g, 6.65 mmol) was then added. The resulting mixture was stirred for 30 minute at room temperature. The reaction mixture was quenched by addition of water (50 mL) and then stirred for 5 minutes. After adding ethyl acetate (40 mL) and then HCl solution (1 mL, 12 M), the organic layer was separated and dried over anhydrous magnesium sulfate. The solvent was evaporated under reduced pressure, and the resulting residue was applied to the top of an open-bed silica gel column (3 × 15 cm). The column was eluted with *n*-hexane : ethyl acetate (3:1, v/v). Fractions containing the product were combined and evaporated under reduced pressure to give **9a**.

4.3. Dieckmann-type reaction of ethyl benzoate with benzyl cyanide

A mixture of benzyl cyanide (**8a**, 0.985 mL, 8.536 mmol), KO^{t}Bu (1.915g, 17.07mmol) and dry THF (30 mL) was stirred for 30 minutes at room temperature in argon atmosphere. After adding compound **1a** (1.225 mL, 8.536 mmol), the mixture was stirred for 2 hours at room temperature. Water (50 mL) and ethyl acetate (30 mL) were added into the reaction mixture with stirring. The organic layer was separated using separating funnel and dried over anhydrous magnesium sulfate. The solvent was evaporated under reduced pressure, and the resulting residue was applied to the top of an open-bed silica gel column (3 × 15 cm, *n*-hexane/ethyl acetate (3:1, v/v)). Fractions containing the product were combined and evaporated under reduced pressure to give **9a** in 10% (0.15 g) yields.

4.4. Dieckmann-type reaction of ethyl acetate with phenyl acetylene

A mixture of phenyl acetylene (**10a**, 1.24 mL, 11.34 mmol), KO^{t}Bu (1.34 g, 11.34 mmol) and dry THF (30 mL) was stirred for 20 minutes at room temperature under argon atmosphere. After adding compound **1b** (1 g, 11.34 mmol), the mixture was stirred for 20 minutes at room temperature. The reaction was quenched by addition of cold water (20 mL). The mixture was poured into mixture of ethyl acetate (80 mL). The organic layer was separated and dried over anhydrous magnesium sulfate. The solvent was evaporated under reduced pressure at 80^{o}C below to give crude **11a**. The crude product was purified by silica gel column (3 × 10 cm, *n*-hexane : ethyl acetate = 3 : 1, v/v) to give pure **11a** in 67% (0.94 g) yields.

*4.5. Typical procedure for reaction of esters with cyanides to β-ketonitilres **9** under the optimized conditions*

Ethyl ester **1** (6.65 mmol, 1 equiv.) was dissolved in THF (30 mL, technical grade involving 0.2% water) with stirring (about 230 rpm) at ambient temperature for 5 minutes. Potassium *tert*-butoxide (1.57 g, 14.0 mmol, 95%, 2 equiv.) was added immediately to the above THF solution. After stirring enough the flask, the corresponding cyanide **8** (6.65 mmol, 1 equiv) was then added. The resulting mixture was stirred at ambient temperature. The reaction mixture was quenched by addition of water (50 mL) and then stirred for 5 minutes. After adding ethyl acetate (40 mL) and then HCl solution (1 mL, 12 M), the organic layer was separated and dried over anhydrous magnesium sulfate. The solvent was evaporated under reduced pressure, and the resulting residue was applied to the top of an open-bed silica gel column (for **9a** - **9e**, **9g** - **9j** : 3 × 15 cm, *n*-hexane : ethyl acetate (3:1, v/v); for **9f** : 3.5 × 8 cm, CH_2Cl_2). Fractions containing the product were combined and evaporated under reduced pressure to give the corresponding *β*-ketonitriles.

*4.5.1. 3-Oxo-2,3-diphenylpropanenitrile (**9a**)*

Yield 97% (1.43 g), Yellow solid, mp 93-94 ^{o}C. (lit.[38] mp 93-94.5 ^{o}C), TLC (n-hexane : EtOAc, 3:1 (v/v)), R_F = 0.33, IR (KBr): 3062, 3030, 2924, 2250, 1689, 1595, 1580, 1448, 1228, 939, 763, 750 cm^{-1}, ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.66 (s, 1H), 7.34–7.58 (m, 8H), 7.93 (d, 2H, *J* = 7.7 Hz), ^{13}C NMR (75 MHz, $CDCl_3$): δ 46.6, 116.8, 128.3, 129.1, 129.2, 129.3, 129.7, 130.4, 133.6, 134.5, 189.1, HRMS(EI) *m/z*: $[M]^+$ calcd for $C_{15}H_{11}NO$ 221.0841; found, 221.0843.

*4.5.2. 3-Oxo-3-phenylpropanenitrile (**9b**)*

Yield 90% (0.87 g), Yellow solid, mp 78-79 ^{o}C. (lit.[39] 79-81 ^{o}C), TLC (CH_2Cl_2): R_F = 0.51, IR (KBr): 3362, 3076, 2953, 2922, 2262, 2254, 1691, 1651, 1596, 1582, 1450, 1393, 1311, 1219, 756 cm^{-1}, ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.13 (s, 2H), 7.44 (t, 2H, *J* = 7.8 Hz), 7.56–7.61 (m, 1H), 7.84 (d, 2H, *J* = 8.0 Hz), ^{13}C NMR (75 MHz, $CDCl_3$): δ 29.7, 114.5, 128.5, 129.1, 134.2, 134.7, 188.0, HRMS(EI) m/z: [M]+ calcd for C_9H_7NO 145.0528; found, 145.0529.

*4.5.3. 2-Ethyl-3-oxo-3-phenylpropanenitrile (**9c**)*

Yield 82% (0.94 g), Clear liquid, TLC (*n*-hexane: ethyl acetate = 3:1(v/v)): R_F = 0.51, IR (KBr): 3070, 2973, 2942, 2682, 2553, 2086, 1689, 1600, 1454, 1421, 1326, 1290, 1274, 1180, 1126, 933, 806, 707 cm^{-1}, ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.38 (t, 3H, *J* = 7.44 Hz), 1.93- 2.12 (m, 2H), 4.43-4.47 (m, 1H), 7.47-7.52 (m, 2H), 7.60-7.65 (m, 1H), 7.93-7.96 (m, 2H), ^{13}C NMR (75 MHz, $CDCl_3$): δ 11.37, 23.68, 41.56, 117.4, 128.7, 129.1, 133.9, 134.4, 191.2, HRMS(EI) *m/z*: $[M]^+$ calcd for $C_{11}H_{11}NO$ 173.0841; found, 173.0842.

*4.5.4. 3-Oxo-3-(p-chlorophenyl)propanenitrile (**9d**)*

Yield 91% (0.96 g), Light yellow solid, mp 124-126 ^{o}C. (lit.[39] 126-128 ^{o}C), TLC (CH_2Cl_2): R_F = 0.75, IR (KBr): 3088, 2951, 2920, 1686, 1589, 1401, 1327, 1219, 1095, 1004, 821 cm^{-1}, ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.08 (s, 2H), 7.51 – 7.54 (m, 2H), 7.87 – 7.90 (m, 2H), ^{13}C NMR (75 MHz, $CDCl_3$): δ 29.41, 113.5, 129.6, 129.9, 132.6, 141.5, 186.0, HRMS(EI) m/z: $[M]^+$ calcd for C_9H_6ClNO 179.0138; found, 179.0135.

*4.5.5. 2-Ethyl-3-oxo-3-(p-chlorophenyl)propanenitrile (**9e**)*

Yield 79% (0.95 g), Clear liquid, TLC (CH_2Cl_2): R_F = 0.51, IR (KBr): 3093, 2981, 2940, 2883, 1689, 1589, 1488, 1420, 1272,

1241, 1093, 1012, 850, 759 cm^{-1}, ^1H NMR (300MHz, $CDCl_3$): δ 1.15 (t, 3H, J_1 = 7.36 Hz, J_2 = 7.44 Hz), 1.94 – 2.14 (m, 2H), 4.51 – 4.49 (m, 2H), 7.46 – 7.49 (m, 2H), 7.91 (d, 2H, *J* = 8.48 Hz), ^{13}C NMR (75 MHz, $CDCl_3$): δ 11.32, 23.59, 41.60, 117.3, 129.4, 130.2, 132.3, 140.9, 190.2, HRMS(EI) *m/z*: $[M]^+$ calcd for $C_{11}H_{10}ClNO$ 207.0451; found, 207.0458.

*4.5.6. 4-Methyl-3-oxopentanenitrile (**9f**)*

Yield 92% (0.88 g), Clear liquid, TLC (CH_2Cl_2): R_F = 0.42, IR (KBr): 2975, 2931, 2881, 2260, 1724, 1625, 1465, 1390, 1305, 1045, 939, 889 cm^{-1}, ^1H NMR (300M Hz, $CDCl_3$): δ 1.11 – 1.21 (m, 6H), 2.77 – 2.82 (m, 1H), 3.68 – 3.71 (m, 2H), ^{13}C NMR (75 MHz, $CDCl_3$): δ 17.70, 30.18, 40.47, 114.3, 201.9, HRMS(EI) *m/z*: $[M]^+$ calcd for C_6H_9NO 111.0684; found, 111.0677.

*4.5.7. 3-Oxo-2-phenylbutanenitrile (**9g**)*

Yield 26% (0.47g), Light yellow solid, mp 75-77 °C. (lit.[40] 78-79 °C) , TLC (CH_2Cl_2): R_F = 0.46, IR (KBr): 3133, 3069, 2962, 2921, 2215, 1636, 1593, 1496, 1388, 1363, 1334, 1303, 1279, 1237, 1115, 1069, 1021, 916, 907, 761 cm^{-1}, ^1H NMR (300 MHz, $CDCl_3$): δ 2.27 (s, 3H), 4.70 (s, 1H), 7.40 – 7.49 (m, 5H), ^{13}C NMR (75 MHz, $CDCl_3$): δ 26.94, 51.51, 116.2, 127.9, 129.3, 129.6, 129.7, 196.4, HRMS(EI) *m/z*: $[M]^+$ calcd for $C_{10}H_9NO$ 159.0684; found, 159.0684.

*4.5.8. 4-Methyl-3-oxo-2-phenylpentanenitrile (**9h**)*

Yield 75% (0.47 g), Liquid, TLC (CH_2Cl_2): R_F = 0.76, IR (KBr): 3064, 3033, 2975, 2935, 2876, 2250, 2204, 1725, 1702, 1599, 1495, 1385, 1348, 1275, 1203, 1096, 1078, 1050, 1029, 957, 754, 716 cm^{-1}, ^1H NMR (300 MHz, $CDCl_3$): δ 0.89 (d, 3H, *J* = 6.6 Hz), 1.04 (d, 3H, *J* = 6.9 Hz), 2.77–2.84 (m, 1H), 5.00 (s, 1H), 7.28–7.39 (m, 5H), ^{13}C-NMR (75 MHz, $CDCl_3$): δ 18.3, 18.7, 19.3, 38.6, 49.0, 116.8, 128.3, 128.5, 128.9, 129.1, 129.5, 130.2, 203.2, HRMS(EI) *m/z*: $[M]^+$ calcd for $C_{12}H_{13}NO$ 187.0997; found, 187.0998.

*4.5.9. 3-Oxo-2,5-diphenylpentanenitrile (**9i**)*

Yield 81% (0.81 g), Light yellow solid, mp 73-74 °C (lit.[41] 73-74°C) TLC (*n*-hexane : EtOAc = 3:1 (v/v): R_F = 0.42, IR (KBr): 3086, 3062, 3029, 2934, 2251, 1729, 1716, 1603, 1496, 1454, 1266, 1077, 749 cm^{-1}, ^1H NMR (300 MHz, $CDCl_3$): δ 2.81–2.97 (m, 4H), 4.62 (s, 1H), 7.07 (t, 2H, *J* = 6.6 Hz), 7.19–7.25 (m, 3H), 7.31–7.33 (m, 2H), 7.38–7.40 (m, 3H), ^{13}C NMR (75 MHz, $CDCl_3$): δ 29.6, 41.2, 51.1, 116.1, 126.4, 128.0, 128.2, 128.6, 129.3, 129.5, 129.6, 139.7, 197.9, HRMS(EI) *m/z*: $[M]^+$ calcd for $C_{17}H_{15}NO$ 249.1154; found, 249.1157.

*4.5.10. 3-Oxo-2-phenyl-3-(pyridine-4-yl)propanenitrile (**9j**)*

Yield 90% (1.32 g), Light yellow solid, mp 113-115 °C, TLC (EtOAc): R_F = 0.13, IR (KBr): 3092, 3053, 2200, 1605, 1593, 1305, 1017, 759 cm^{-1}, ^1H NMR (300 MHz, DMSO-d_6): δ 7.20-7.31 (m, 2H), 7.40-7.46 (m, 2H), 7.68 (d, 2H, *J* = 4.5 Hz), 7.79 (t, 2H, *J* = 7.9 Hz), 8.77-8.79 (m, 2H), ^{13}C NMR (75 MHz, DMSO-d_6): δ 89.2, 120.9, 123.5, 127.5, 127.7, 128.9, 129.1, 133.0, 150.1, 166.2, HRMS(EI) m/z: $[M]^+$ calcd for $C_{14}H_{10}N_2O$ 222.0793; found, 222.0795.

*4.6. General procedure for reaction of esters and acetylenes to α,β-alkynones **11**.*

Potassium *tert*-butoxide (2.68 g, 23.89 mmol, 95%, 2 equiv) was dissolved in THF (30mL, technical grade involving 0.2% water) and the THF solution of ethyl ester **1** and acetylene **10**, which was dissolved ester **1** (11.34 mmol, 1 equiv) and acetylene **10** (11.34 mmol, 1 equiv) in THF (10 mL), was dropped immediately for 1 minute in above solution at ambient temperature (for **11a-11c**) or -15°C icebath (for **11d**). After stirring at ambient temperature, the reaction mixture was quenched by addition of water (20 mL). The mixture was poured into mixture of ethyl acetate (60 mL) and ice powder (25-30 g). The organic layer was separated and dried over anhydrous magnesium sulfate. The solvent was evaporated under reduced pressure at 80°C (for **11a**, **11b**) or 40°C (for **11c**, **11d**) below and the resulting residue was applied to the top of an open-bed silica gel column (for **11a-11c**: 3 × 8 cm, *n*-hexane : ethyl acetate (3:1, v/v); **11d** : 3 × 5 cm, *n*-hexane : ethyl acetate (10:1, v/v). Fractions containing the product were combined and evaporated under reduced pressure to give the corresponding *α,β*-Alkynones.

*4.6.1. 4-Phenylbut-3-yn-2-one (**11a**)*

Yield 76% (1.24 g), Yellow liquid, TLC (*n*-hexane : EtOAc, 3:1 (v/v)): R_F = 0.62, IR (KBr): 3060, 2978, 2201, 1673, 1488, 1442, 1358, 1280, 1156, 976, 757 cm^{-1}, ^1H-NMR (300 MHz, DMSO-d_6): δ 2.41 (s, 3H), 7.41–7.61 (m, 5H), ^{13}C-NMR (75 MHz, DMSO-d_6): δ 33.0, 88.6, 89.6, 119.6, 129.3, 131.4, 133.2, 184.3, HRMS(EI) m/z: [M]+ calcd for $C_{10}H_8O$ 144.0575; found, 144.0577.

*4.6.2. 4-Cyclohexenylbut-3-yn-2-one (**11b**).*

Yield 73% (0.62 g), Liquid, TLC (*n*-hexane : EtOAc, 3:1 (v/v)): R_F = 0.74, IR (KBr): 3008, 2990, 2941, 2913, 2867, 2185, 1759, 1727, 1700, 1677, 1662, 1645, 1568, 1541, 1358, 1275, 1260, 1175, 1133, 1047, 1018, 981, 961, 922, 845, 763, 749 cm^{-1}, ^1H NMR (300 MHz, $CDCl_3$), δ 1.58-1.71 (m, 4H), 2.14-2.19 (m, 4H), 2.36 (s, 3H), 6.44-6.47 (m, 1H), ^{13}C NMR (75 MHz, $CDCl_3$): δ 21.1, 21.9, 26.1, 28.3, 32.7, 86.6, 92.9, 118.9, 142.4, 184.8, HRMS(EI) *m/z*: $[M]^+$ calcd for $C_{10}H_{12}O$ 148.0888; found, 148.0874.

*4.6.3. 1-Phenyl-4-methylpent-1-yn-3-one (**11c**)*

Yield: 60% (0.89 g), Liquid, TLC (*n*-hexane : EtOAc, 3:1 (v/v)): R_F = 0.58, IR (KBr): 3320, 3058, 2972, 2933, 2872, 2199, 1667, 1597, 1573, 1488, 1465, 1444, 1384, 1337, 1280, 1257, 1179, 1158, 1124, 1054, 996, 961, 920, 891, 814, 757, 728 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 1.24–1.34 (m, 6H), 2.70-2.79 (m, 1H), 7.34–7.43 (m, 3H), 7.54–7.57 (m, 2H), ^{13}C NMR (75 MHz, $CDCl_3$): δ 18.0, 43.1, 86.8, 91.6, 120.1, 128.6, 130.6, 132.5, 132.9, 192.0, HRMS(EI) *m/z*: $[M]^+$ calcd for $C_{12}H_{12}O$ 172.0888; found, 172.0885.

*4.6.4. 1,5-Diphenylpent-1-yn-3-one (**11d**)*

Yield 66% (0.86g),Colorless liquid, TLC (*n*-hexane : EtOAc, 10:1 (v/v)): R_F = 0.39, IR (KBr): 3060, 3027, 3005, 2988, 2925, 2202, 1699, 1670, 1490, 1454, 1362, 1276, 1262, 1092, 1071, 912, 747, 700 cm^{-1}, ^1H NMR (300 MHz, $CDCl_3$): δ 3.01–3.10 (m, 4H), 7.20–7.25 (m, 2H), 7.26–7.48 (m, 6H), 7.56–7.60 (m, 2H), ^{13}C NMR (75 MHz, $CDCl_3$): δ 30.0, 47.0, 87.8, 91.2, 120.0, 126.3, 128.3, 128.5, 128.6, 130.7, 133.0, 140.2, 186.8, HRMS(EI) *m/z*: $[M]^+$ calcd for $C_{17}H_{14}O$ 234.1045; found, 234.1044.

*4.7. General procedure for reaction of esters and acetylenes to biscarbinols **12**.*

Ethyl ester (**1**, 6.65 mmol) was dissolved in cold THF (30 mL, technical grade involving 0.2% water, cooling in ice bath for 5 minute). Potassium *tert*-butoxide (1.57 g, 14.0 mmol, 95%) and acetylene (**10**, 13.3 mmol) were added immediately. After the reaction was quenched by addition of water (20 mL) was then added. The reaction mixture was poured into the mixture of ethyl acetate (60 mL)/ice powder (25-30 g). The organic layer was separated and dried over anhydrous magnesium sulfate. After evaporating the solvent under reduced pressure at 60 °C below, the residue was applied to the top of an open-bed silica gel column (for **12a**,**12c**, **12d**: 4.5 × 15 cm, *n*-hexane : ethyl acetate (3:1, v/v)) or washed with *n*-hexane (50 mL, for **12b**) to give **12**

*4.7.1. 1,3,5-Triphenylpenta-1,4-diyn-3-ol (**12a**)*

Yield 86% (1.72 g) ,Orange liquid, TLC (*n*-hexane : EtOAc, 3:1 (v/v)): R_F = 0.51, IR (KBr): 3534, 3401, 3080, 3060, 3032, 2925, 2852, 2228, 1954, 1884, 1809, 1689, 1597, 1489, 1449, 1265, 1176, 1051, 1029, 940, 917, 775 cm^{-1}, ^1H NMR (300 MHz, DMSO-d_6): δ 7.32 (bs, OH, D_2O exchangeable), 7.37–7.52 (m, 13H), 7.82–7.85 (m, 2H), ^{13}C NMR (75 MHz, DMSO-d_6): δ 64.7, 83.8, 91.3, 121.9, 126.0, 128.6, 128.8, 129.2, 129.5, 131.9, 143.6, HRMS(EI) *m/z*: $[M-H]^+$ calcd. for $C_{23}H_{15}O$ 307.1123; found, 307.1124

*4.7.2. 1,5-Diphenyl-3-(pyridine-4-yl)penta-1,4-diyn-3-ol (**12b**)*

Yield 73% (1.48 g), White solid, mp 195-196 °C, TLC (*n*-hexane : EtOAc, 3:1 (v/v)): R_F = 0.38, IR (KBr): 3092, 3054, 2786, 2655, 2437, 2226, 1603, 1566, 1487, 1441, 1414, 1321, 1263, 1220, 1190, 1098, 1058, 1008, 998, 963, 921, 821, 767, 750 cm^{-1}, ^1H NMR (300 MHz, DMSO-d6): δ 7.39–7.43 (m, 6H), 7.50–7.53 (m, 4H), 7.65 (bs, OH, D_2O exchangeable), 7.78–7.80 (m, 2H), 8.67–8.69 (m, 2H), ^{13}C NMR (75 MHz, DMSO-d_6): δ 64.0, 84.5, 90.0, 120.8, 121.5, 129.2, 129.8, 132.0, 150.5, 151.9, HRMS(EI) *m/z*: $[M-H]^+$ calcd for $C_{22}H_{14}NO$ 308.1075; found, 308.1070.

*4.7.3. 1-Cyanophenyl-3,5-diphenylpenta-1,4-diyn-3-ol (**12c**)*

Yield 40% (0.78 g), Light ivory solid, mp 132– 134 °C. TLC (*n*-hexane : EtOAc, 3:1 (v/v)): R_F = 0.51, IR (KBr): 3411, 3097, 3079, 3057, 3022, 2990, 2816, 2229, 1598, 1573, 1489, 1443, 1402, 1265, 1186, 1167, 1069, 1035, 1019, 997, 942, 843, 755 cm^{-1}, ^1H NMR (300 MHz, DMSO-d_6): δ 7.37–7.44 (m, 6H), 7.46–7.53(m, 4H), 7.65 (bs, OH, D_2O exchangeable), 7.92–8.02 (m, 4H), ^{13}C NMR (75 MHz, DMSO-d_6): δ 64.4, 84.6, 90.2, 111.6, 119.0, 121.5, 127.0, 129.2, 129.8, 131.9, 133.1, 148.6, HRMS(EI) *m/z*: $[M]^+$ for $C_{24}H_{15}NO$ 333.1154; found, 333.1153.

*4.7.4. 1,5-Diphenyl-3-(phenylethynyl)pent-1-en-4-yn-3-ol (**12d**)*

Yield 23% (0.43 g), Liquid, TLC (*n*-hexane : EtOAc, 3:1 (v/v)): R_F = 0.44, IR (KBr, CH_2Cl_2): 3418, 2226, 1642, 1601, 1489, 1444, 1366, 1272, 1099, 1031, 991, 963, 755 cm^{-1}, ^1H NMR (300 MHz, $CDCl_3$): δ 3.08 (bs, 1H, D_2O exchangeable), 6.53 (d, 1H, *J* = 15.6 Hz), 7.15 (d, 2H, *J* = 15.6 Hz), 7.26 – 7.34 (m, 9H), 7.44-7.47 (m, 2H), 7.50-7.53(m, 4H), ^{13}C NMR (75 MHz, $CDCl_3$): δ 64.27, 85.22, 87.87, 122.0, 127.2, 128.4, 128.7, 128.9, 129.6, 131.0, 132.0, 135.8, HRMS (EI) *m/z*: $[M-H]^+$ for $C_{25}H_{17}O$ 333.1279; found, 333.1281.

References

1. Elnagdi, M. H.; Elmoghayar, M. R. H.; Elgemeie, G. E. H. *Synthesis*, **1984**, 1.
2. Laufer, S. A.; Zimmermann, W.; Ruff, K. J. *J. Med. Chem*. **2004**, *47*, 6311.
3. Hauser, C. R.; Eby, C. J. *J. Am. Chem. Soc*. **1957**, *79*, 728.
4. Cao, H.; Jiang, H.; Mai, R.; Zhu, S.; Qi, C. *Adv. Synth. Catal.* **2010**, 143.
5. Lakshmi, B. V.; Kazmaier, U. *Synlett* **2010**, 407.
6. Yoshikawa, T.; Mori, S.; Shindo, M. *J. Am. Chem. Soc*. **2009**, *131*, 2092.
7. Baxendale, I. R.; Schou, S. C.; Sedelmeier, J. Ley, S. V. *Chem. Eur. J*. **2010**, *16*, 89.
8. Sheng, H.; Lin, S.; Huang, Y. *Tetrahedron Lett.* **1986**, *27*(40), 4893.
9. Sydnes, L. K.; Holmelid, B.; Sengee, M.; Hanstein, M. *J. Org. Chem*. **2009**,*74*, 3430.
10. Payette, J. N.; Yamamoto, H. *Angew. Chem. Int. Ed*. **2009**, *48*, 8060.
11. Sheng, H.; Lin, S.; Huang, Y. *Synthesis* **1987**, 1022.
12. Beech. W. F.; Piggott, H. A. *J. Chem. Soc*. **1955**, 423.
13. Fleming, F. F.; Iyer, P. S. *Synthesis*, **2006**, 893.
14. Ji, Y.; Trenkle, W. C.; Viwles, J. V. *Org. Lett*. **2006**, *8*, 1161.
15. Katritzky, A. R.; Abdel-Fatth, A. A. A.; Wang, M. *J. Org. Chem*. **2003**, *68*, 4932.
16. Cahiez, G.; Gager, O.; Moyeux, A.; Laboue-Bertrand, B. *Synthesis* **2010**, 4213.
17. Aijou, A. N.; Ferguson, G. *Tetrahedron Lett*. **2006**, *47*, 3719.
18. Maeda, Y.; Kakiuchi, N.; Matsumura, S.; Nishimura, T.; Kawamura, T.; Uemura, S. *J. Org. Chem*. **2002**, *67*, 6718.
19. Dieter, R. K. *Tetrahedron* **1999**, *55*, 4177.
20. Oh, C. H.; Reddy, V. R. *Tetrahedron Lett*. **2004**, *45*, 8545.
21. Marko, I. E.; Southern, J. M. *J. Org. Chem*. **1990**, *55*, 3368.
22. Auge, J.; Lubin-Germain, N.; Seghrouchni, L. *Tetrahedron Lett*. **2003**, *44*, 819.
23. Liu, J.; Xie, X.; Ma, S. *Synthesis* **2012**, *44*, 1569.
24. Ajjou, A. N.; Ferguson, G. *Tetrahedron Lett*. **2006**, *47*, 3719.
25. Kim, B. R.; Lee, H. G.; Kang, S. B.; Sung, G. H.; Kim, J. J.; Park, J. K.; Lee, S. G.; Yoon, Y. J. *Synthesis* **2012**, *44*, 42.
26. Kurti, L.; Czako, B. "Strategic Applications of Named Reactions in Organic Synthesis", Elsevier Academic Press, Amsterdam, **2005**, pp138-139.
27. Liebeskind, L. S.; Srogl, J. *J. Am. Chem. Soc*. **2000**, *122*(45), 11260.
28. Procopcova, H.; Kappe, C. O. *Angew. Chem.Int. Ed.* **2008**, *47*, 3674.
29. Ngai, M. –Y.; Kong, J. –R.; Krische, M. J. *J. Org. Chem*. **2007**, *72*(4), 1063.
30. Yang, H.; Li, H.; Wittenberg, R.; Egi, M.; Huang, W.; Liebeskind, L. S. *J. Am. Chem. Soc*. **2007**, *129*(5), 1132.
31. Villalobos, J. M.; Srogl, J.; Liebeskind, L. S. *J. Am. Chem. Soc*. **2007**, *129*(51), 15734.
32. Hanson, S. K.; Wu, R.; "Pete" Silks, L. A. *Org. Lett.* **2011**, *13*, 1908.
33. Caldwell, S. E; Porter, N. A.; *J. Am. Chem. Soc*. **1995**, *117*, 8676.
34. Nakanishi, W.; Ikeda, Y.; Iwamura, H. *J. Org. Chem*. **1982**, *47*, 2275.
35. Staab, H. A.; Rohr, W.; Graf, F. *Chem. Ber*. **1965**, *98*, 1122.
36. Hamada, Y.; Mizuno, A.; Ohno, T.; Shiori, T. *Chem. Pharm. Bull.* **1984**, *32*, 3683.
37. Stepanov, F. N.; Vul'fson, N. S. Org. Poluprod. i Krasiteli, Nauch.-Issledovatel. Inst. Org. Poluprod. i Krasitelei im. K. E. Voroshilova, Sbornik Statei. **1959**, 1, 222.
38. Takahashi, K; Yamada, K; Iida, H. *Bull. Chem. Soc. Jpn*. **1978**, *51*(11), 3389.
39. Al-Qalaf, F.; Mandani, F.; Abdelkhalik, M. M.; Bassam, A. A. *Molecules*, **2009**, *14*(1),78.
40. Kamila, S.; Koh, B.; Biehl, E. R. *Synth. Commun*. **2005**, *36*(23), 3493.
41. Ruggli, P.; Weis, P.; Rupe, H. *Helv. Chim. Acta*. **1946**, *29*, 1788.

Supporting Information

Synthesis of *β*-Ketonitriles, *α,β*-Alkynones and Biscabinols from Esters Using *tert*-Butoxide-assisted C(=O)-C (i.e., acyl-C) Coupling under Ambient Conditions

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Contents **Section**

1. Spectral data for compounds 9, 11 and 12

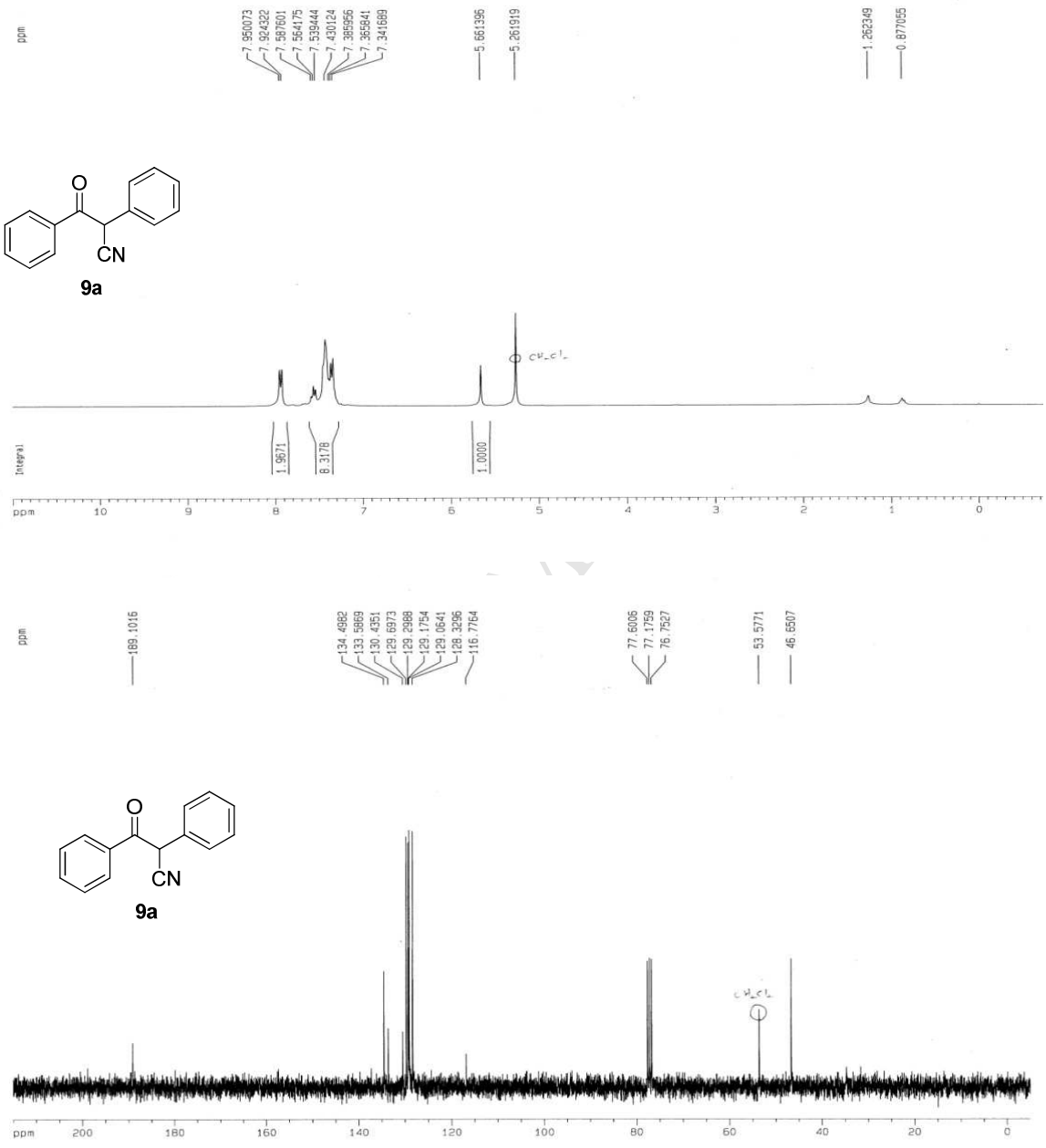

Figure 1. ^{1}H(top) and ^{13}C NMR(bottom) spectra in $CDCl_3$ of compound **9a**.

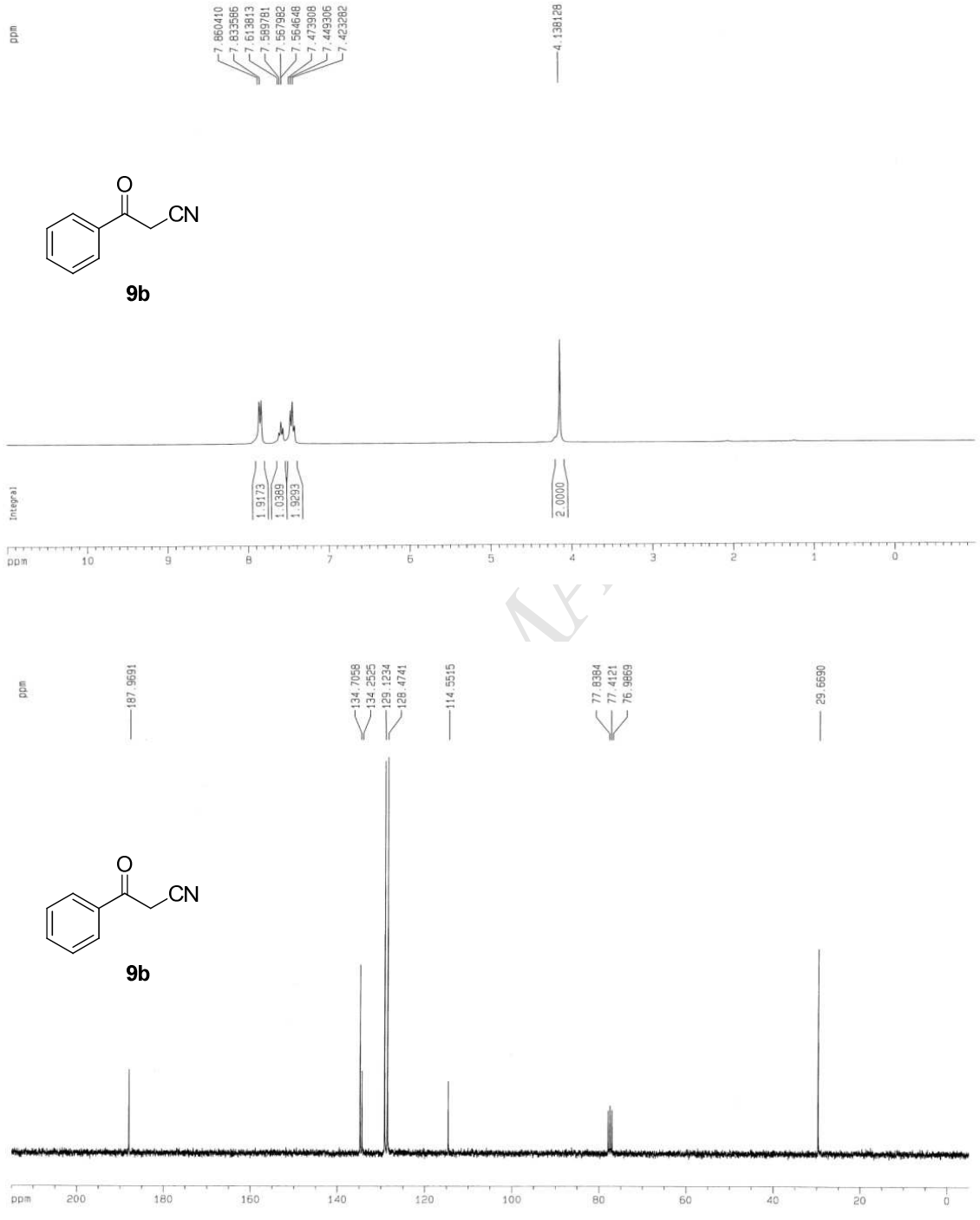

Figure 2. ^{1}H(top) and ^{13}C NMR(bottom) spectra in $CDCl_3$ of compound **9b**.

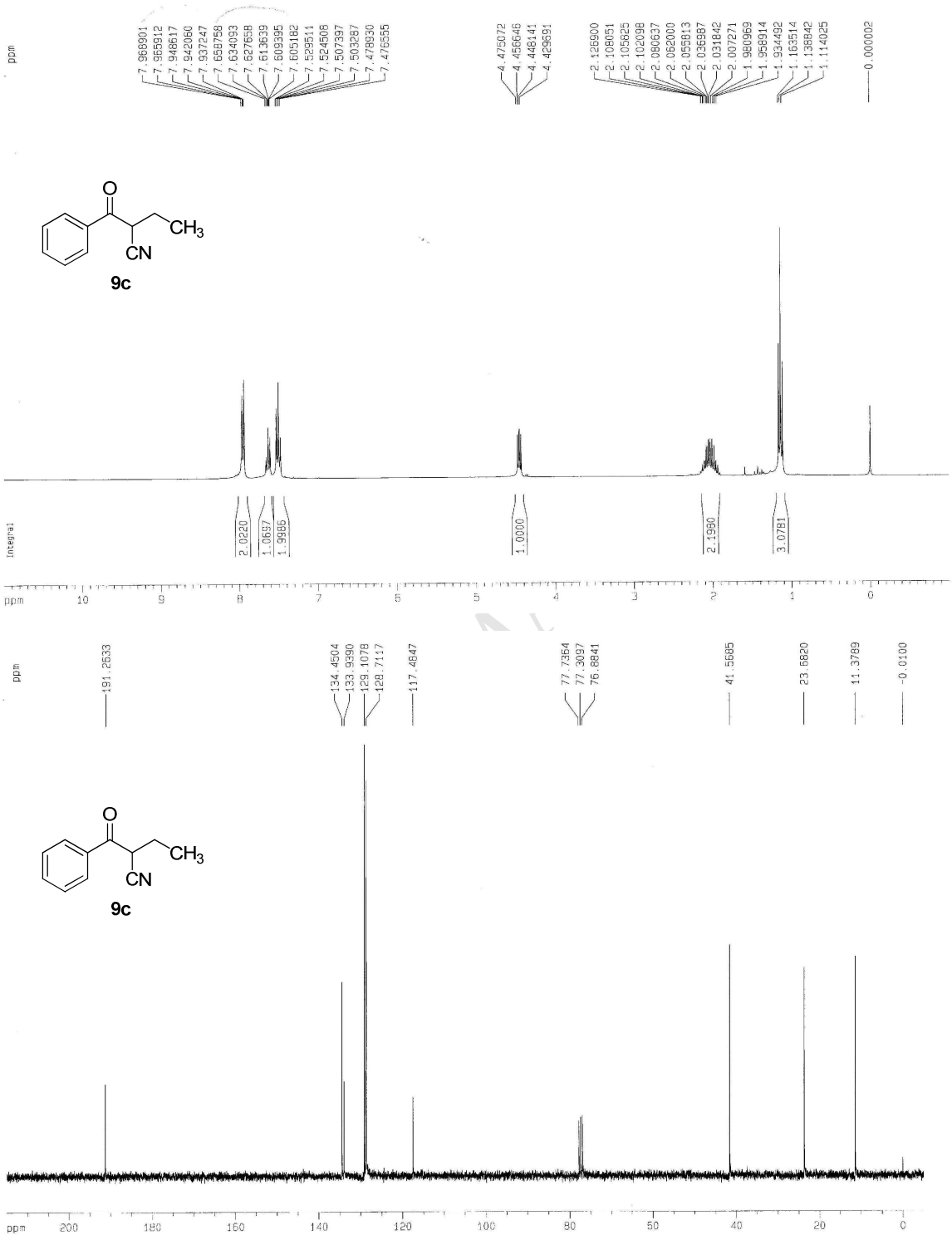

Figure 3. ^{1}H(top) and ^{13}C NMR(bottom) spectra in $CDCl_3$ of compound **9c**.

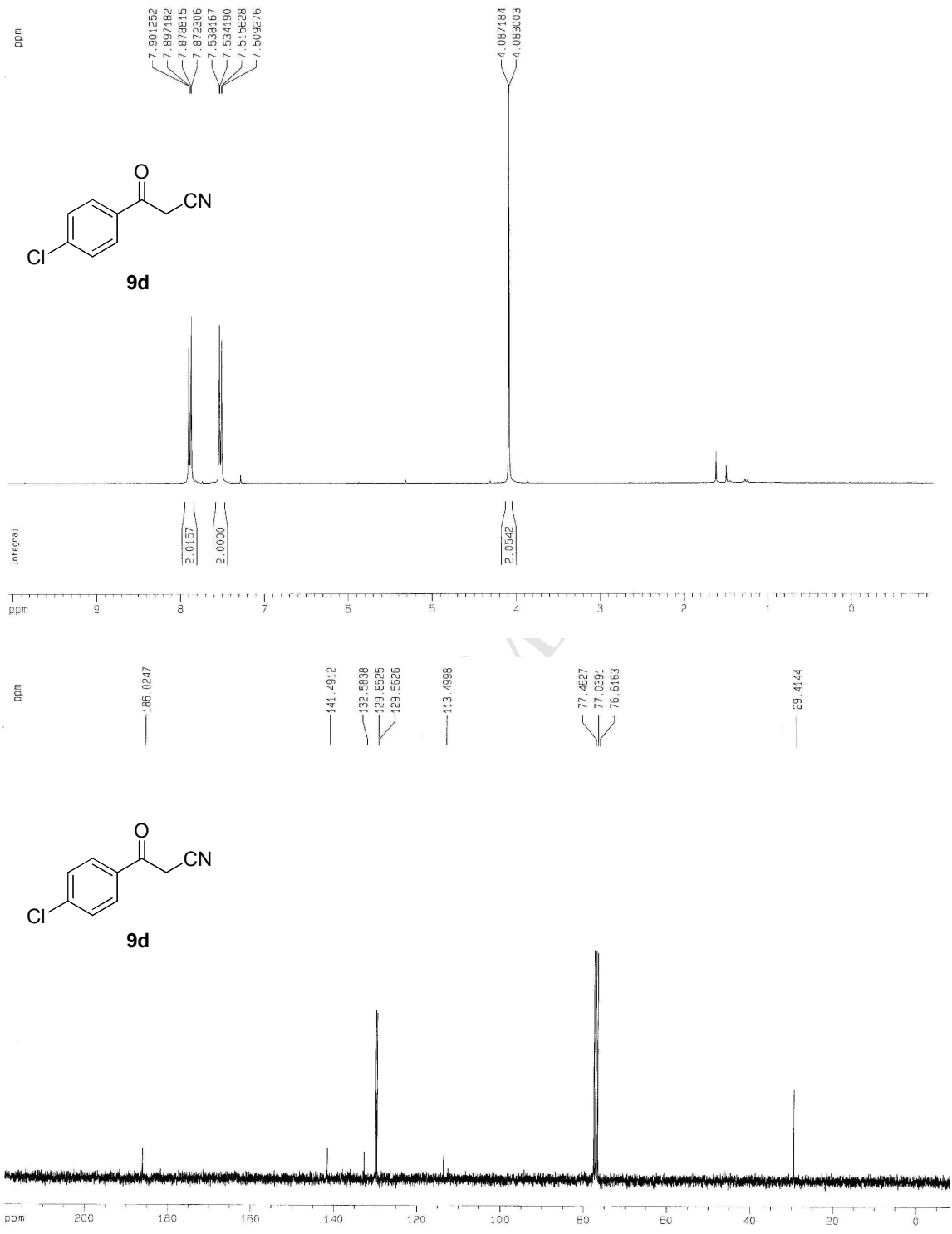

Figure 4. ^{1}H(top) and ^{13}C NMR(bottom) spectra in $CDCl_3$ of compound **9d**

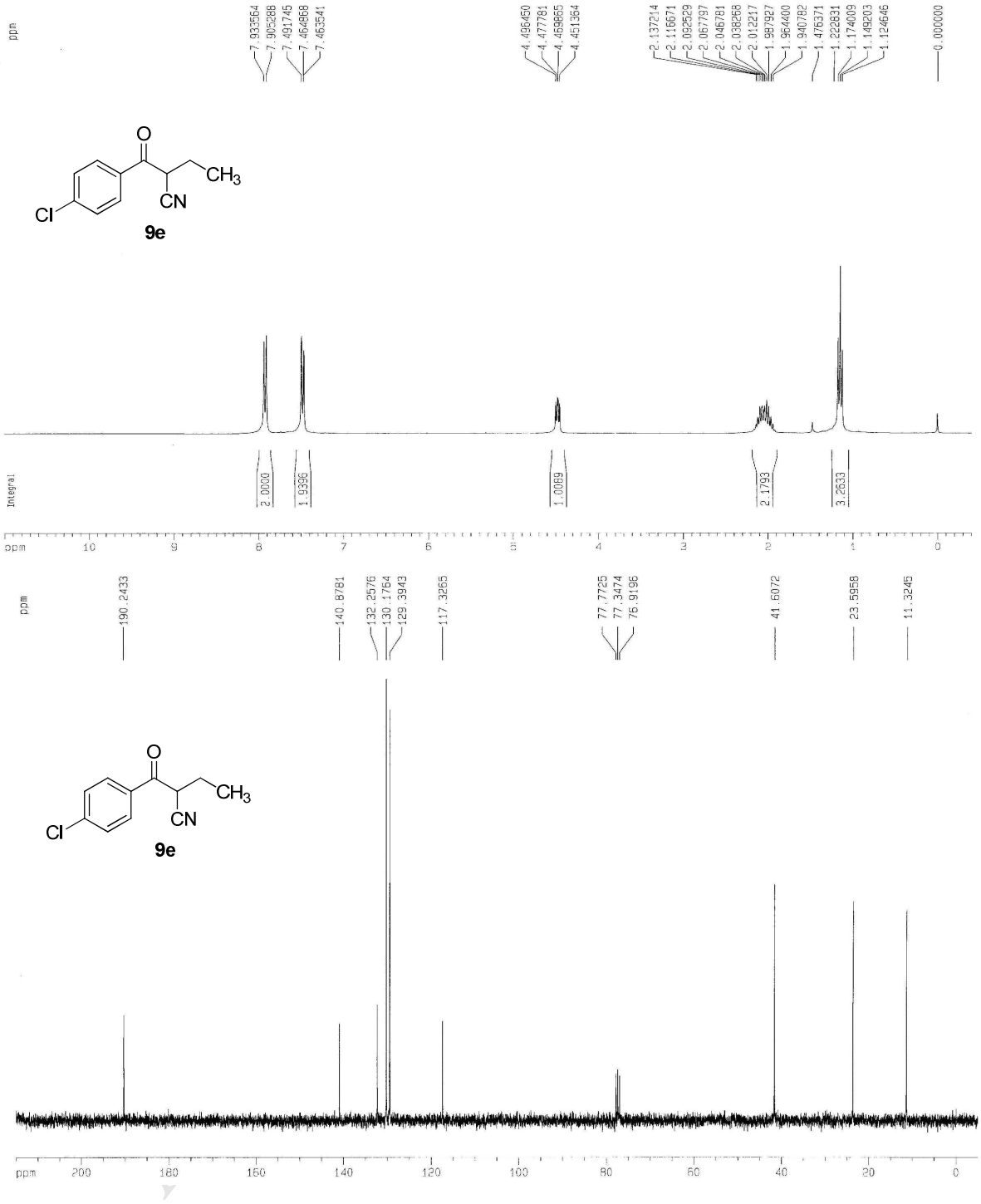

Figure 5. ^{1}H(top) and ^{13}C NMR(bottom) spectra in $CDCl_3$ of compound **9e**.

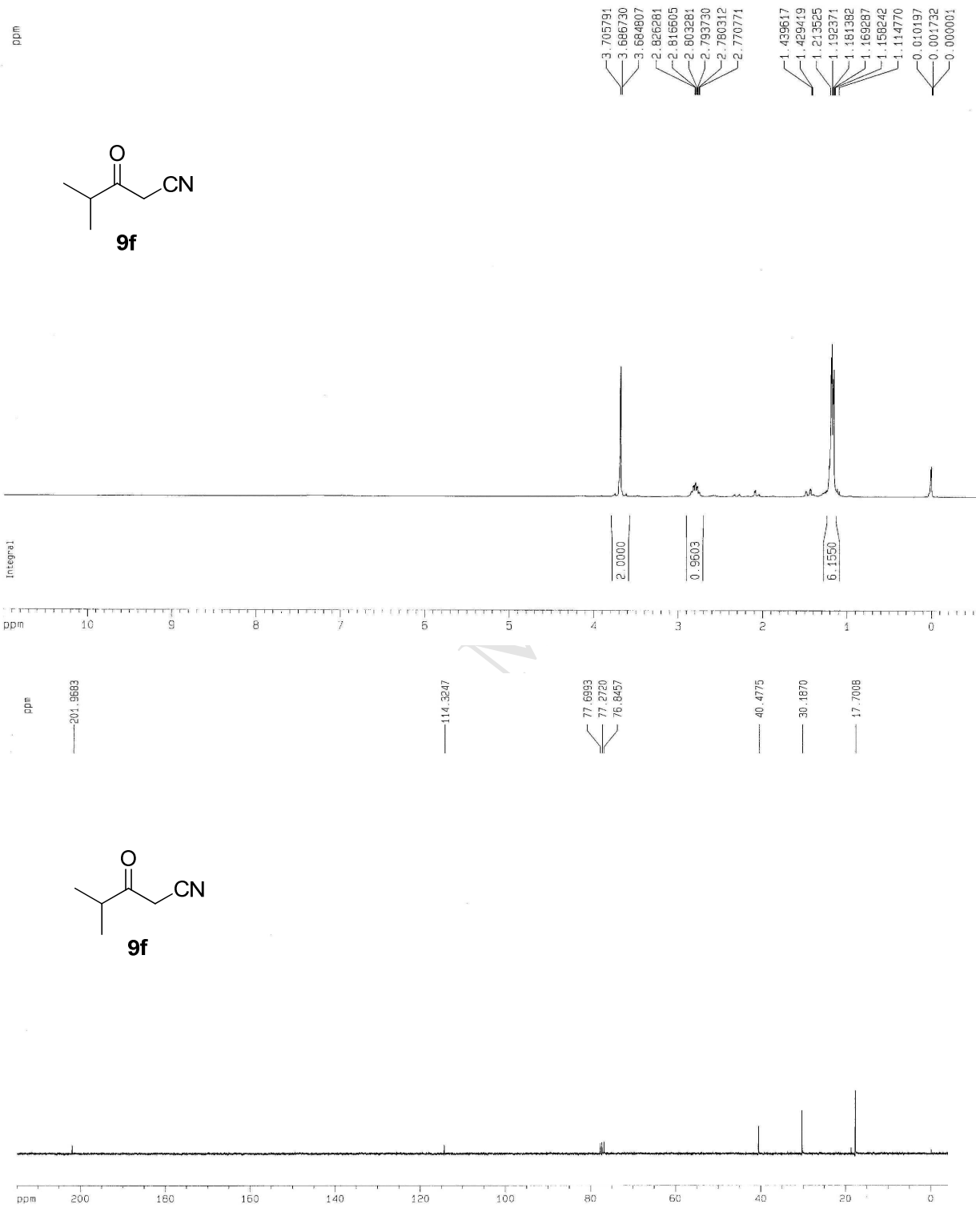

Figure 6. ^{1}H(top) and ^{13}C NMR(bottom) spectra in $CDCl_3$ of compound **9f**.

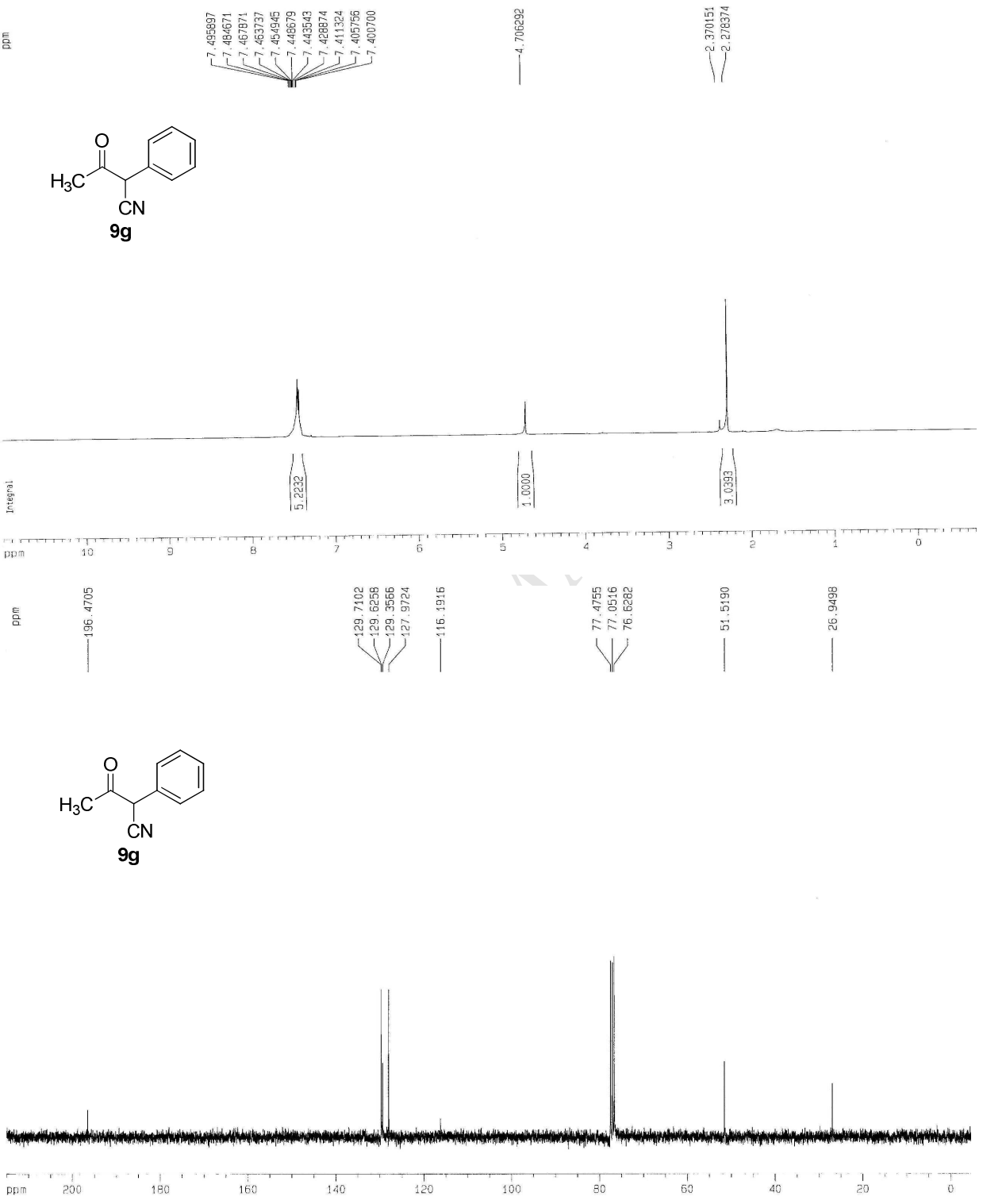

Figure 7. ^{1}H(top) and ^{13}C NMR(bottom) spectra in $CDCl_3$ of compound **9g**.

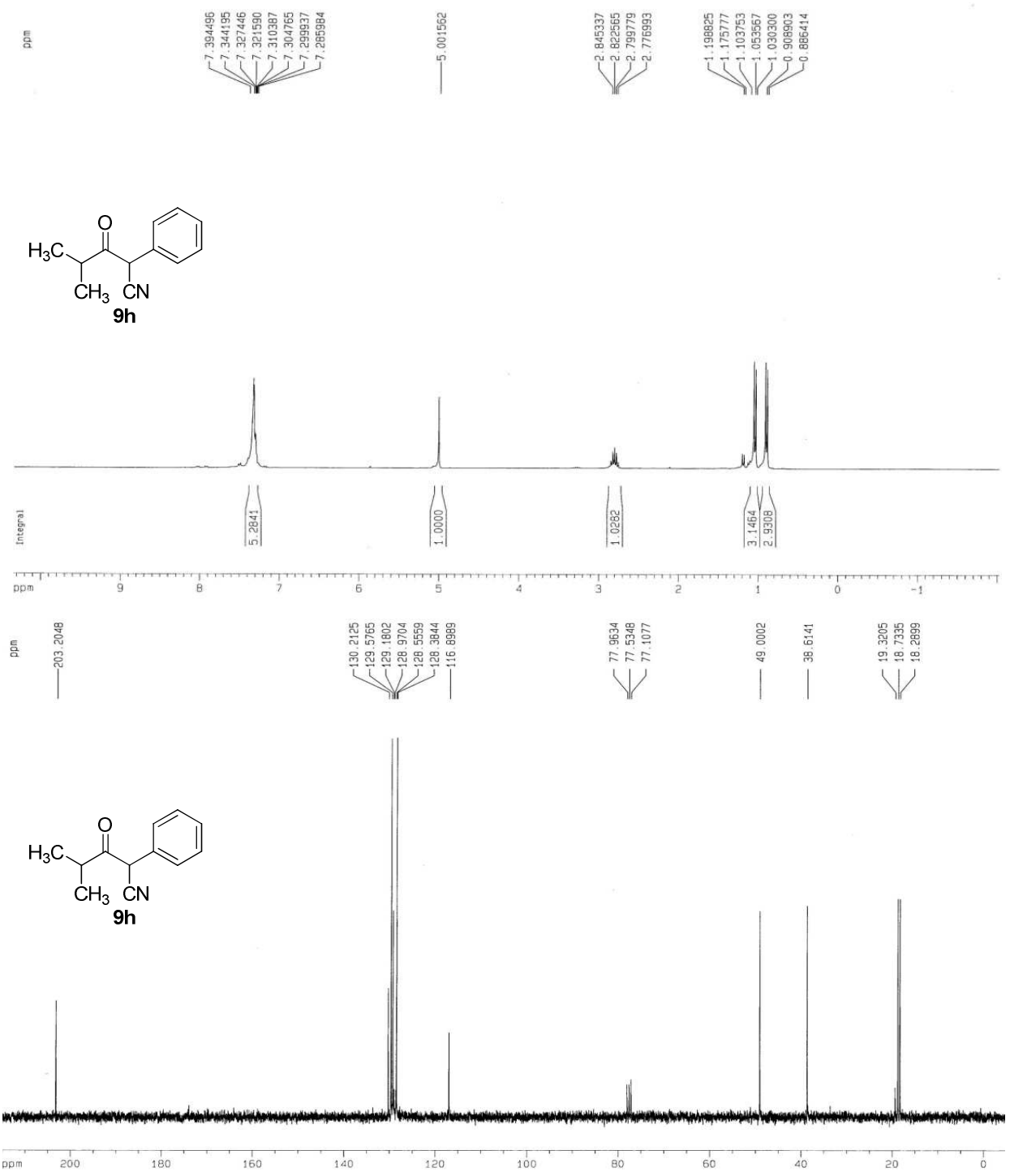

Figure 8. ^{1}H(top) and ^{13}C NMR(bottom) spectra in $CDCl_3$ of compound **9h**.

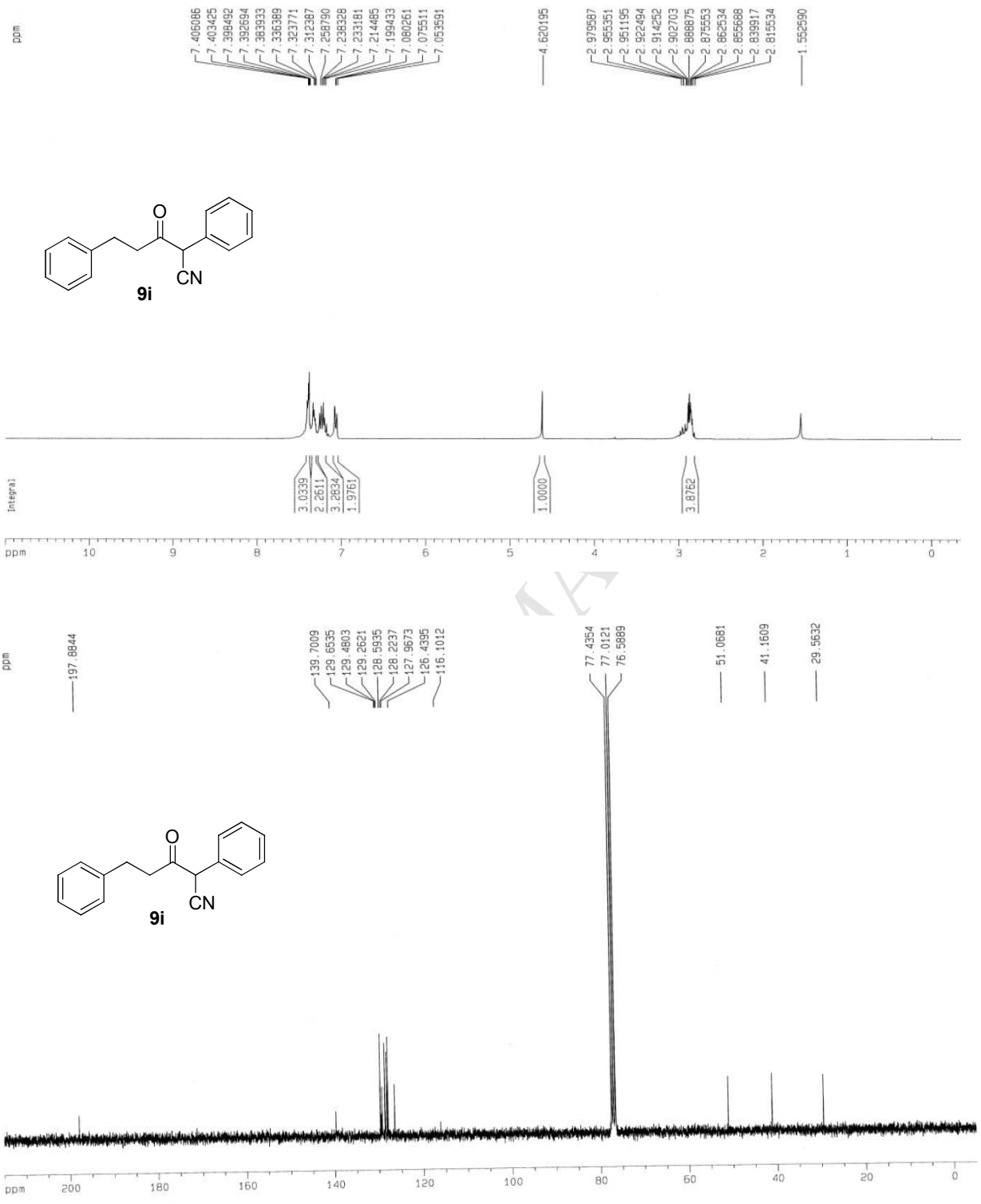

Figure 9. ^{1}H(top) and ^{13}C NMR(bottom) spectra in $CDCl_3$ of compound **9i**.

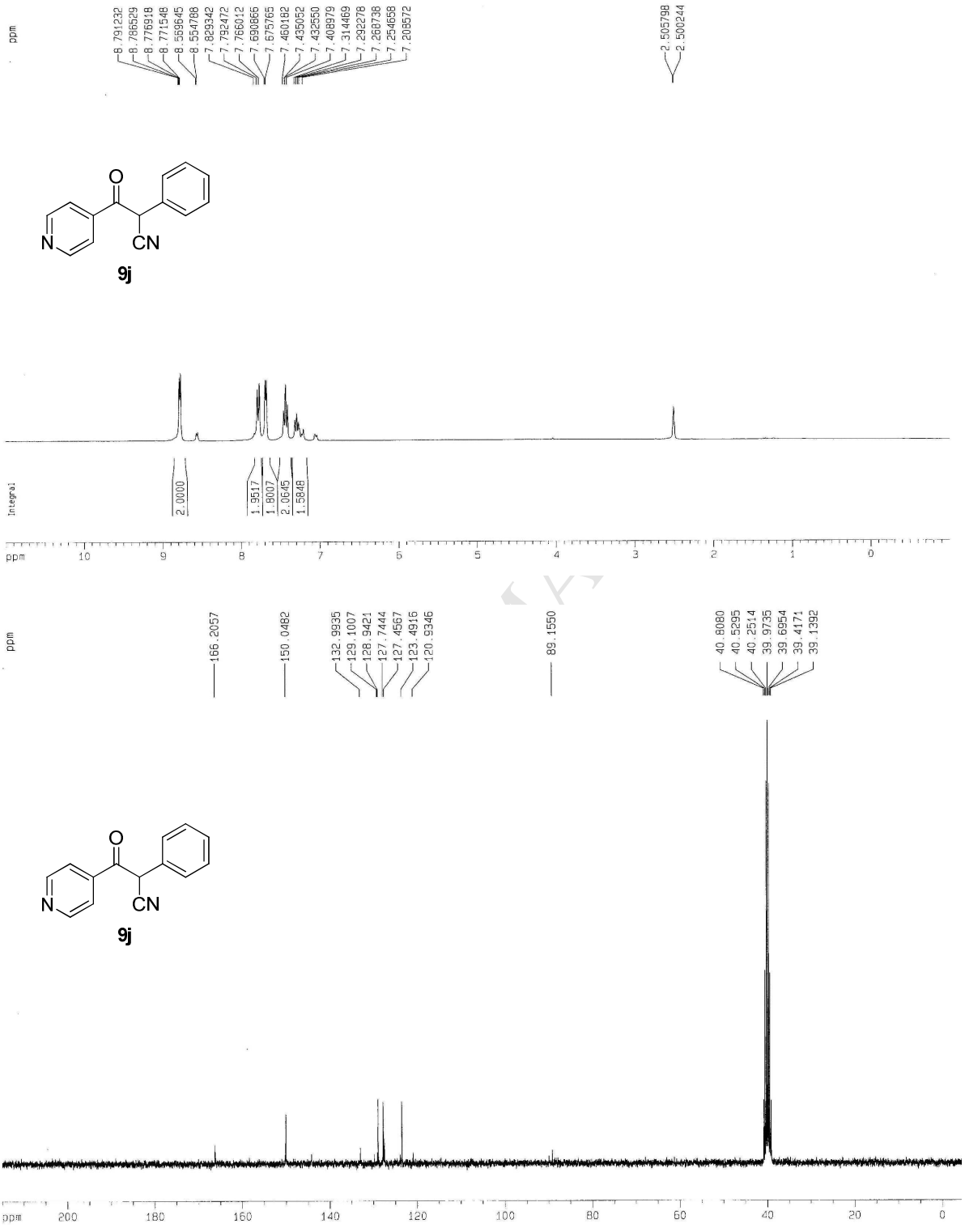

Figure 10. ^{1}H(top) and ^{13}C NMR(bottom) spectra in $CDCl_3$ of compound **9j**.

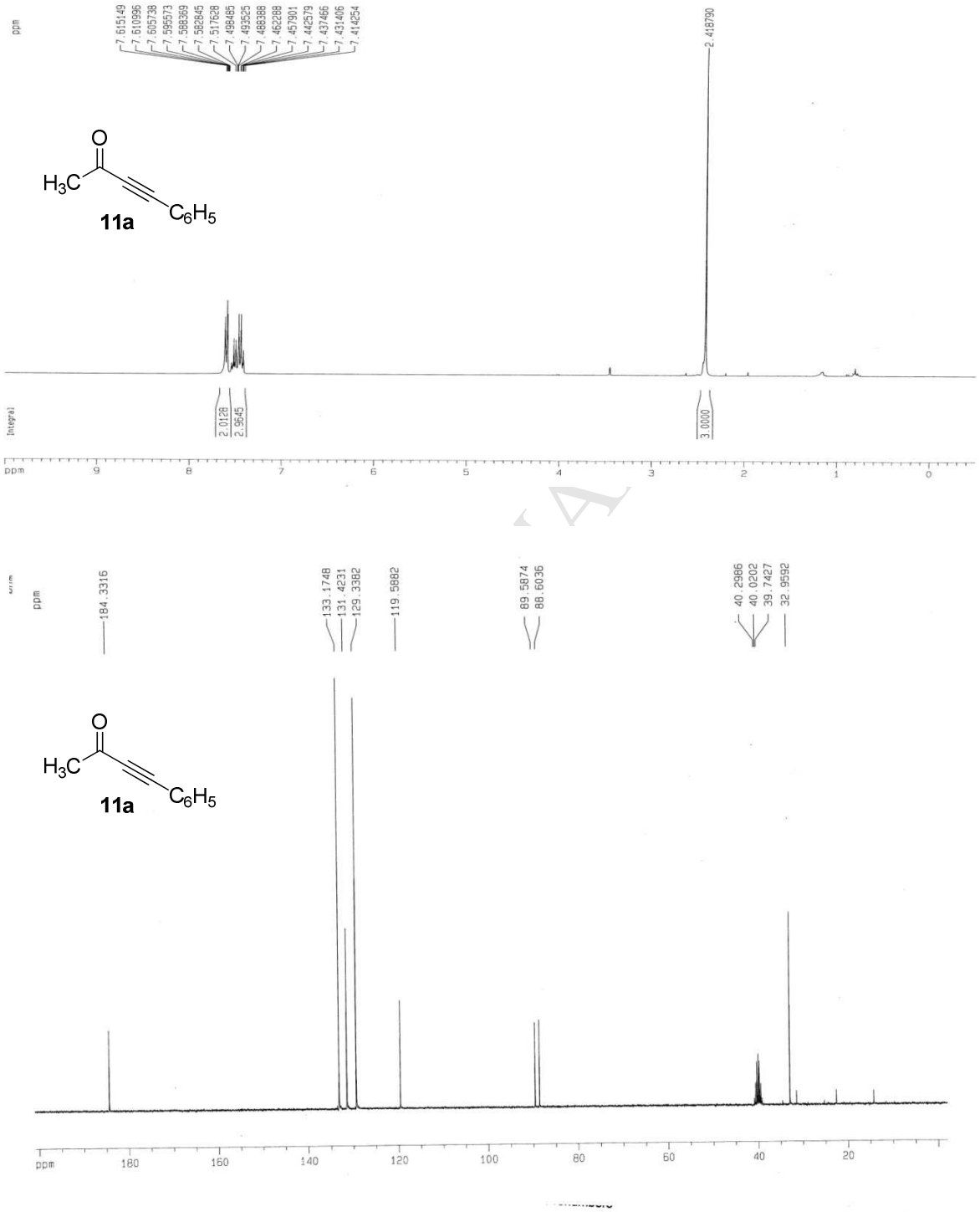

Figure 11. ^{1}H(top) and ^{13}C NMR(bottom) spectra in DMSO-d_6 of compound **11a**.

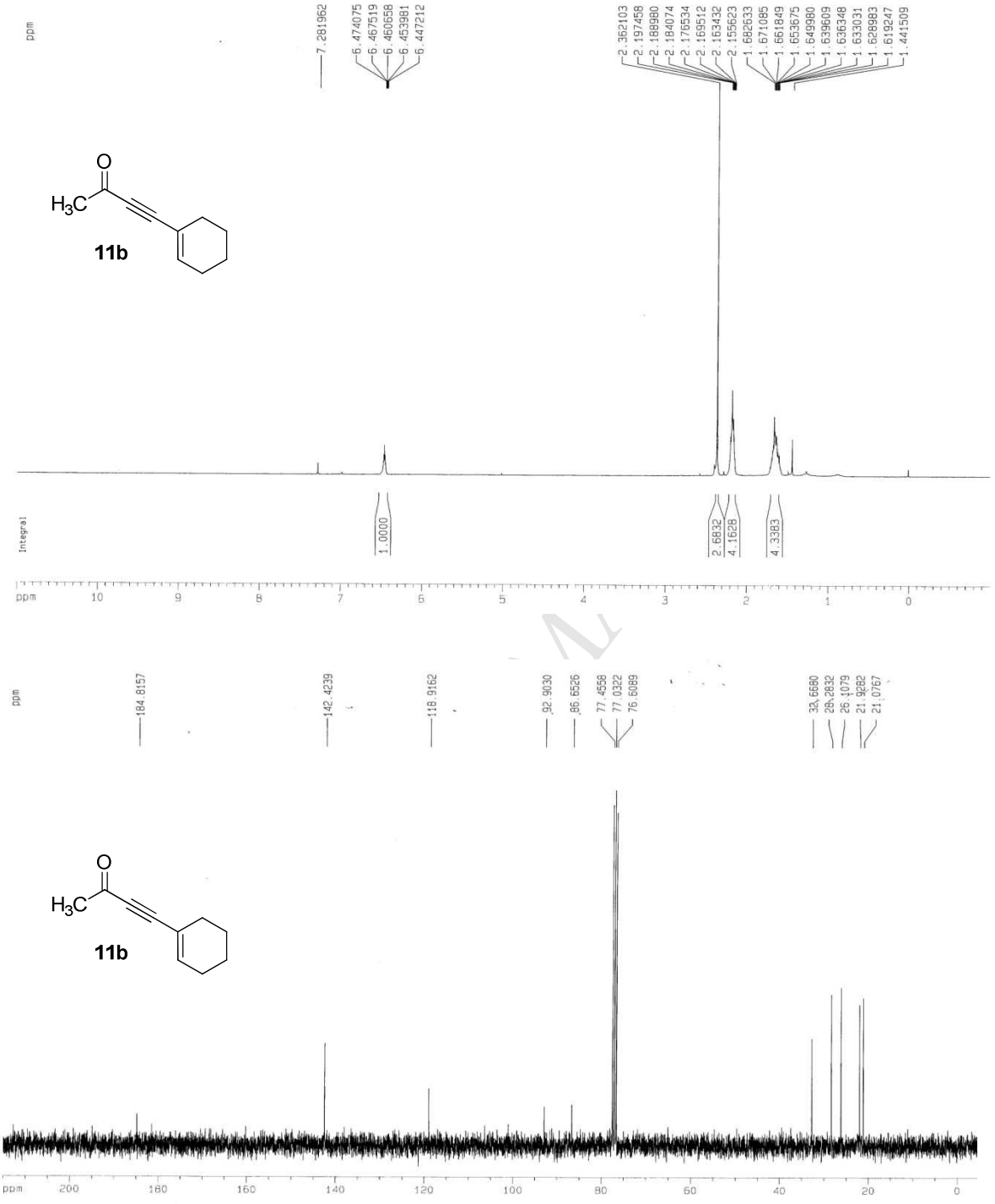

Figure 12. ^{1}H(top) and ^{13}C NMR(bottom) spectra in $CDCl_3$ of compound **11b**.

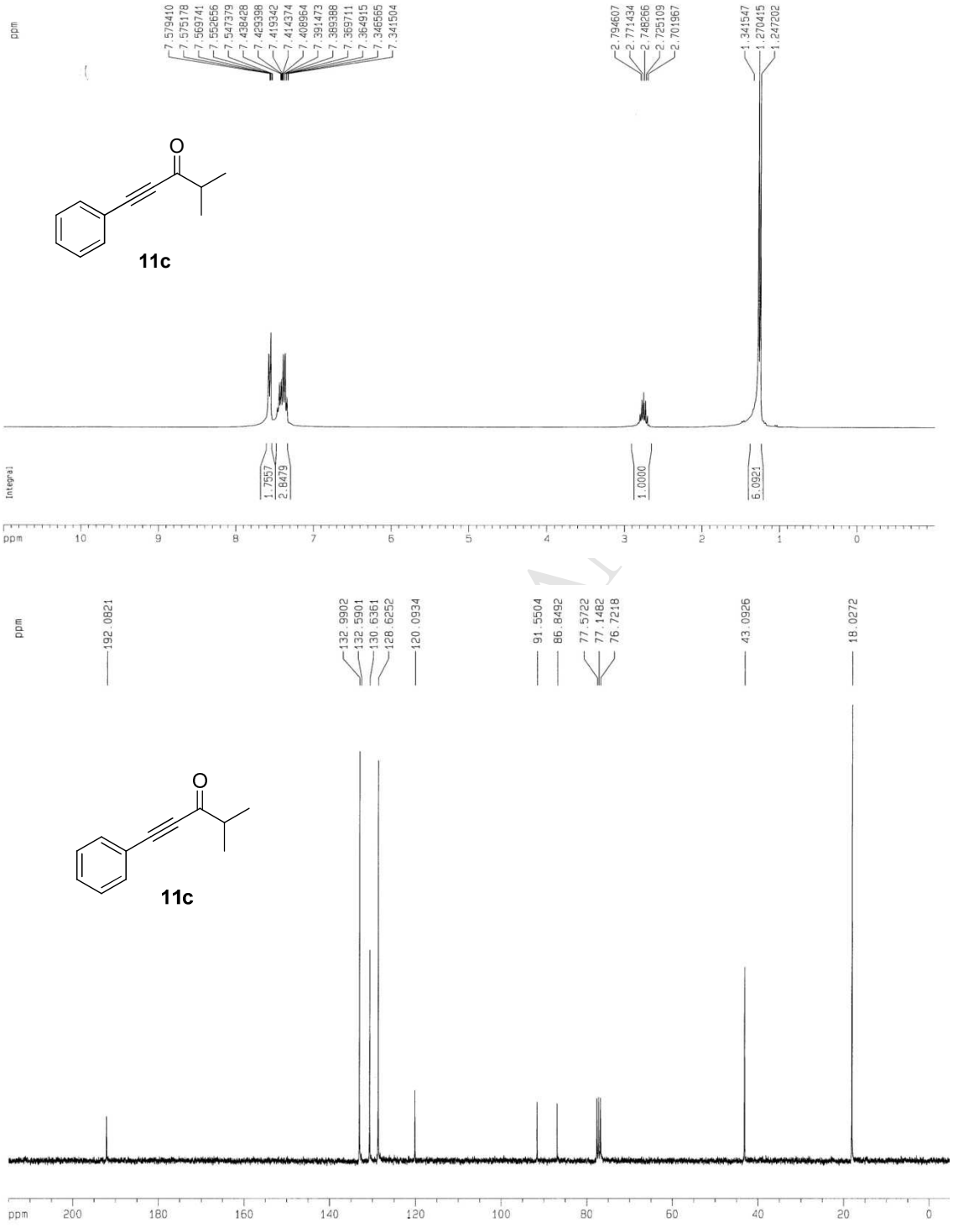

Figure 13. ^{1}H(top) and ^{13}C NMR(bottom) spectra in $CDCl_3$ of compound **11c**.

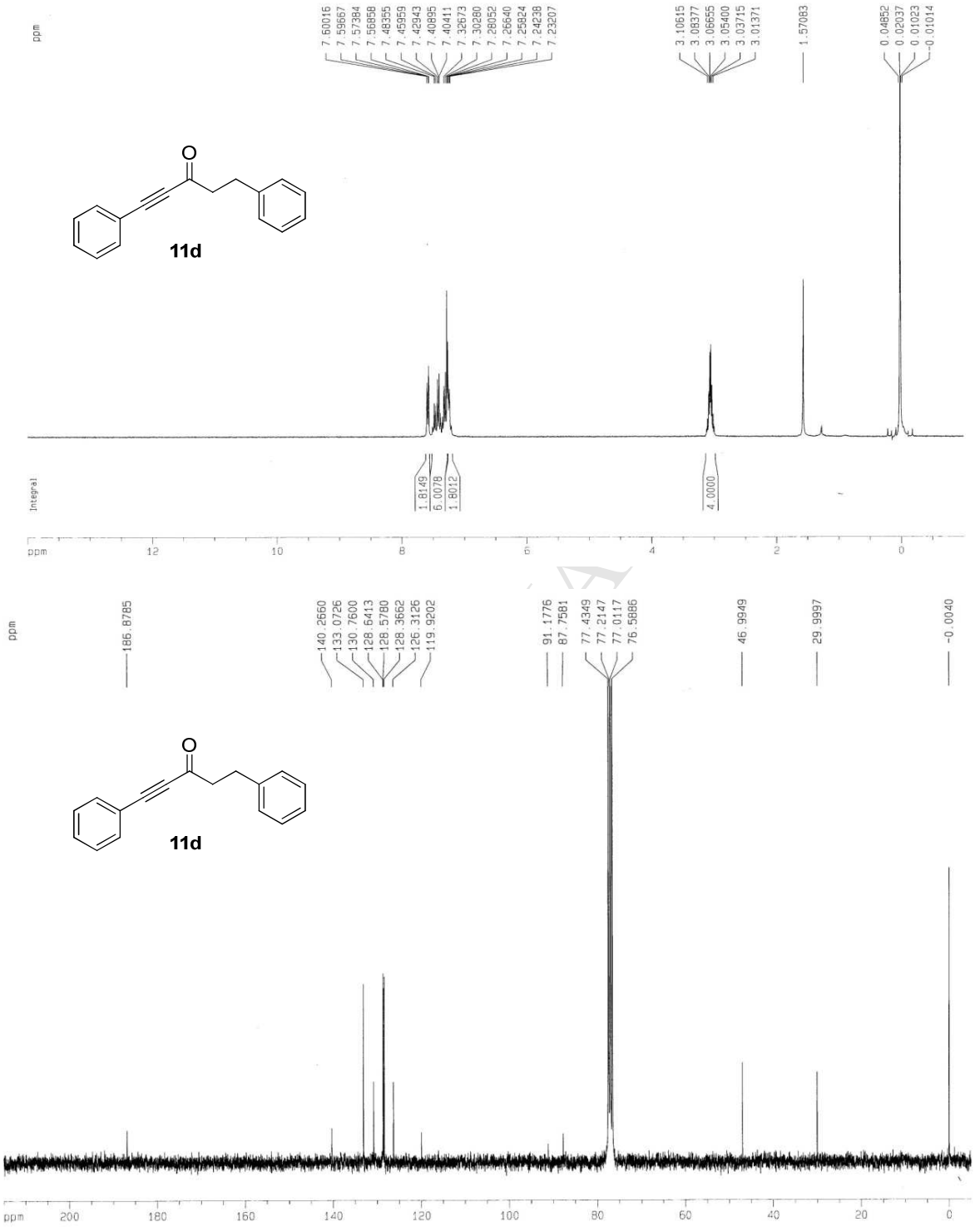

Figure 14. ^{1}H(top) and ^{13}C NMR(bottom) spectra in $CDCl_3$ of compound **11d**.

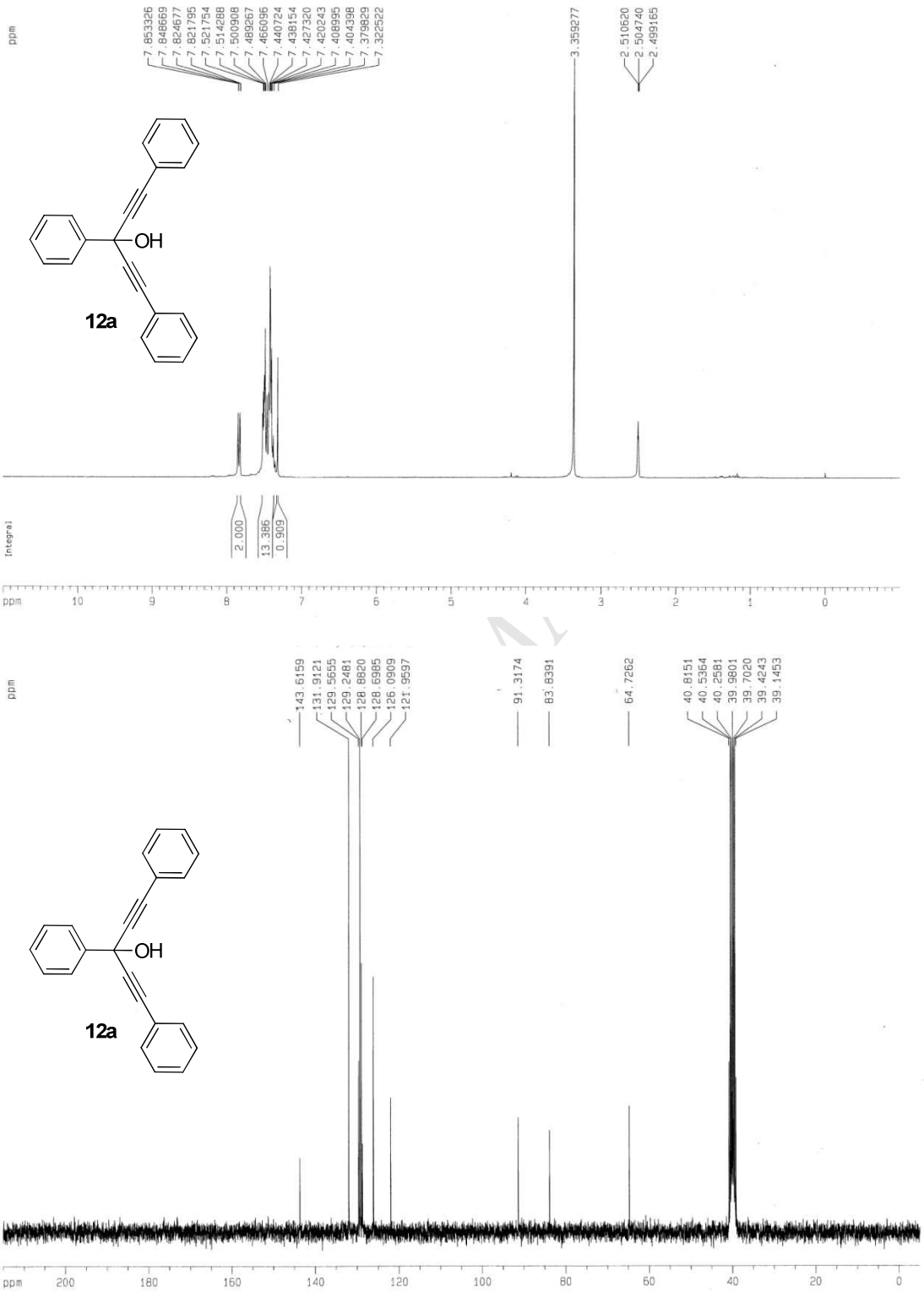

Figure 15. ^{1}H(top) and ^{13}C NMR(bottom) spectra in DMSO-d_6 of compound **12a**.

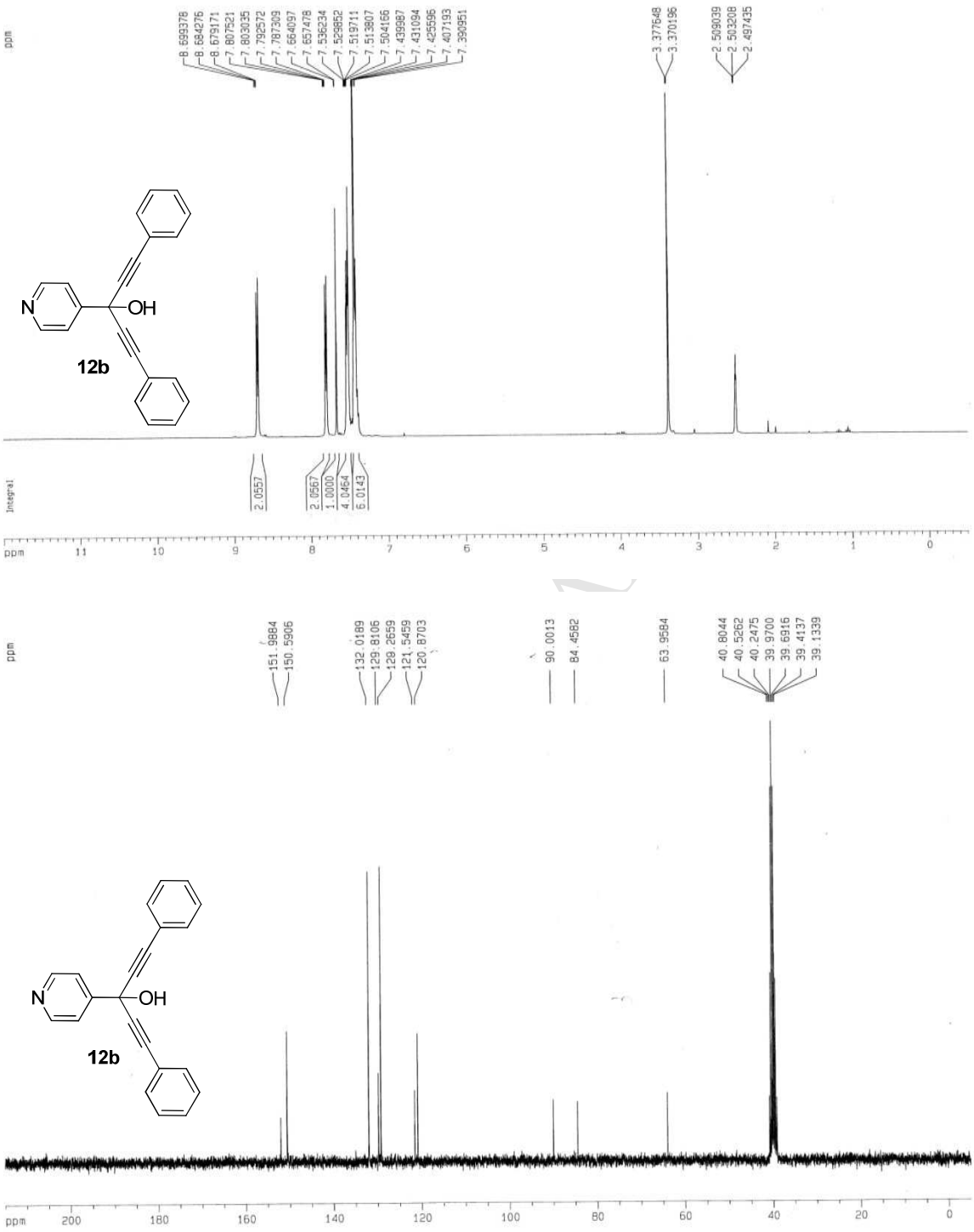

Figure 16. ^{1}H(top) and ^{13}C NMR(bottom) spectra in DMSO-d_6 of compound **12b**.

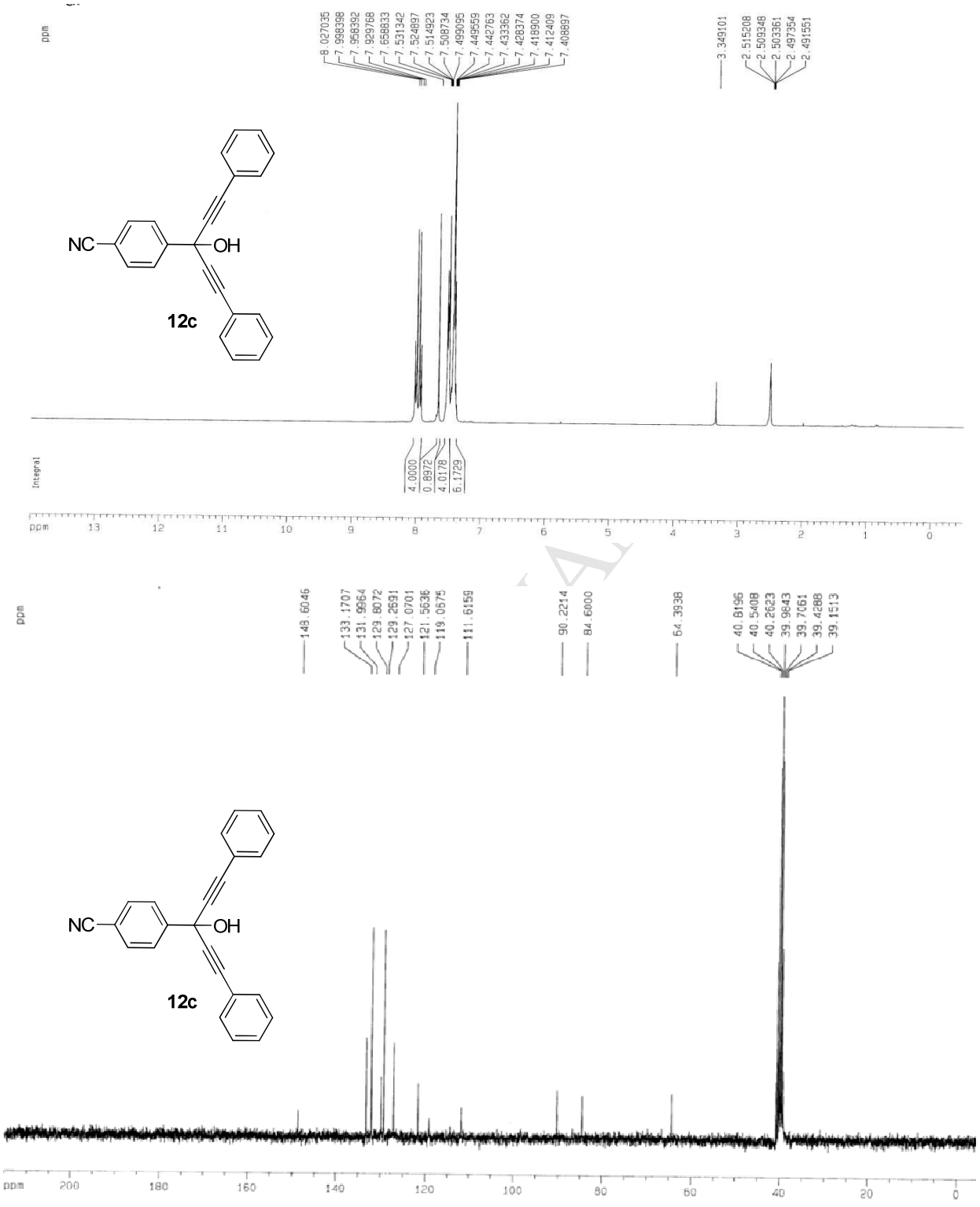

Figure 17. ^{1}H(top) and ^{13}C NMR(bottom) spectra in DMSO-d_6 of compound **12c**.

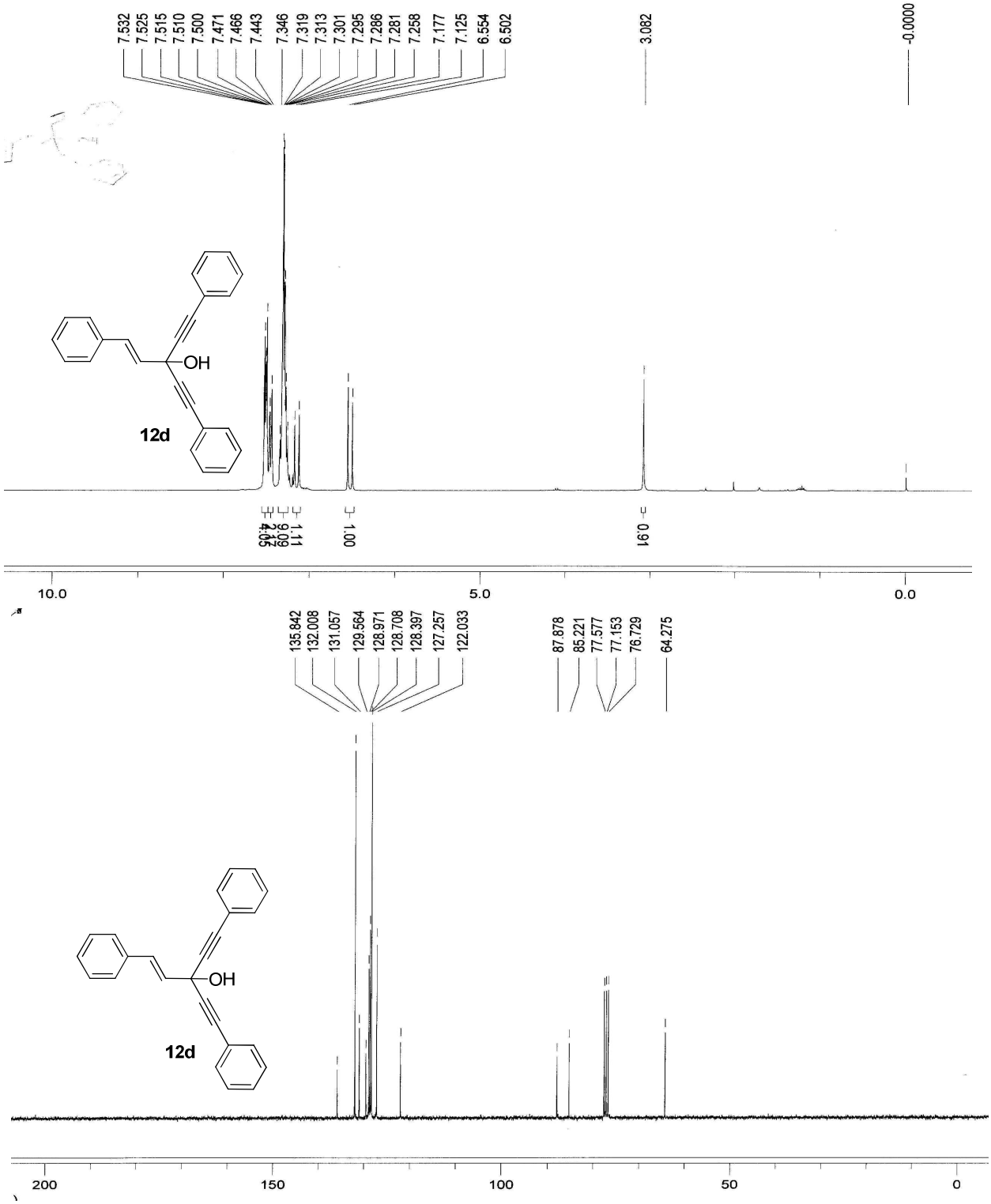

Figure 18. ^{1}H(top) and ^{13}C NMR(bottom) spectra in DMSO-d_6 of compound **12d**.