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Facile construction of 1,2,6,7,12,12b-hexahydroindolo[*2,3-a*]quinolizines via one-pot three-component reactions of tryptamines, propiolate and *α,β*-unsaturated aromatic aldehydes or ketones

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Abstract. In the presence of anhydrous $ZnCl_2$ the one-pot three-component reaction of tryptamines, propiolates and *α,β*-unsaturated aldehydes as well as arylideneacetones afforded the functionalized 1,2,6,7,12,12b-hexahydroindolo[*2,3-a*]quinolizines in moderate to high yields and with high diastereoselectivity. The reaction mechanism involved the sequential Michael addition and Pictet-Spengler reactions of *β*-enamino ester generated *in situ*.

Keywords: multicomponent reaction; Pictet-Spengler reaction; electron-deficient alkyne; enamino ester; indolo[*2,3-a*]quinolizine.

Introduction

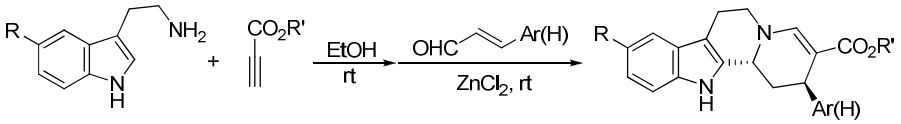
Indole alkaloids constitute an important class of natural products.[1] As one class of indole derivatives, the indolo[*2,3-a*]quinolizidine framework is a particular structural motif found within numerous natural products and pharmaceuticals.[2] Therefore, many efficient methodologies for the preparation of indolo[*2,3-a*]quinolizidine and its derivatives have been developed. The traditional synthetic methods included Bischler–Napieralski,[3] Pictet–Spengler,[4] Fischer indole synthesis [5] and others.[6] The Pictet–Spengler reaction has long been known as an efficient method for the preparation of tetrahydro-*β*-carboline frameworks.[7,8] In recent years, many developments have been made to incorporate Pictet–Spengler reaction into cascade sequence or multicomponent

reactions based on the use of tryptamine-derived substrates.[9-12] Recently Cao and Zhao[13] successfully developed an organocatalytic three-component synthesis of indoloquinolizidines based on conjugate addition of *β*-enaminoesters generated *in situ* from alkyl propiolates and *α*,*β*-enals, and subsequent substrate controlled Pictet–Spengler cyclization. In this work only aliphatic *α*,*β*-enals could give the satisfactory results, while aromatic *α*,*β*-unsaturated aldehydes were not suitable substrates for this cascade reaction. In the past few years we also reported several new domino reactions by using the *in situ* formed *β*-enamino esters derived from the reactions of arylamines with electron-deficient alkynes such as dimethyl acetylenedicarboxylate and methyl propiolate.[14,15] Encouraged by these results and hunting for new efficient multicomponent reactions, we investigated the one-pot domino reactions of tryptamines, propiolate and *α*,*β*-unsaturated aldehydes as well as arylideneacetones with catalysis of Lewis acid and successfully developed a facile synthetic procedure for the functionalized 1,2,6,7,12,12b-hexahydroindolo[*2*,*3*-*a*]quinolizines.

Results and Discussion

At first the reaction conditions were examined. According to our previously reported synthetic procedure of *β*-enamino ester from the reaction of arylamine with methyl propiolate,[15] tryptamine was treated with methyl propiolate in ethanol at room temperature rapidly to give the desired *β*-enamino ester. Then cinnamaldehyde and a Lewis acid were added and the mixture was stirred at room temperature for several hours. In the absence of Lewis catalyst, no further reaction was observed. Several Lewis acids such as $FeCl_3$, I_2, $ZnCl_2$, as well as solvent and temperature were examined to set up a standard reaction condition. The experimental results showed that the reaction proceeded with highest yields at room temperature in 48 hours when anhydrous $ZnCl_2$

Table 1 Synthesis of 1,2,6,7,12,12b-hexahydroindolo[*2,3-a*]quinolizines 1a-1q



Entry	Compd	R	R'	Ar (H)	Yield (%)
1	**1a**	H	CH_3	C_6H_5	78
2	**1b**	H	CH_3	*p*-$CH_3C_6H_4$	87
3	**1c**	H	CH_3	*m*-$CH_3C_6H_4$	81
4	**1d**	H	CH_3	*p*-$CH_3OC_6H_4$	83
5	**1e**	H	CH_3	*p*-ClC_6H_4	84
6	**1f**	H	CH_3	*m*-ClC_6H_4	77
7	**1g**	OCH_3	CH_3	C_6H_5	83
8	**1h**	OCH_3	CH_3	*p*-$CH_3C_6H_4$	86
9	**1i**	OCH_3	CH_3	*m*-$CH_3C_6H_4$	79
10	**1j**	OCH_3	CH_3	*m*-ClC_6H_4	80
11	**1k**	H	CH_3	H	80
12	**1l**	OCH_3	CH_3	H	76
13	**1m**	H	CH_2CH_3	C_6H_5	84
14	**1n**	H	CH_2CH_3	*p*-$CH_3C_6H_4$	85
15	**1o**	H	CH_2CH_3	*m*-ClC_6H_4	75
16	**1p**	OCH_3	CH_2CH_3	*p*-$CH_3C_6H_4$	81
17	**1q**	OCH_3	CH_2CH_3	*m*-ClC_6H_4	76

(1.0 mmol) was used as catalyst and ethanol as solvent. With the optimal conditions established, a variety of substituted cinnamaldehydes were employed in the reaction. All the reaction proceeded smoothly to give the corresponding 1,2,6,7,12,12b-hexahydroindolo[*2,3-a*]quinolizines (**1a-1j**) in satisfactory yields (Table 1, entries 1-10). Under this reaction condition acrolein and ethyl propiolate also afforded good yields of products (Table 1, entries 11-17). These results indicated that this one-pot domino reaction had a wide range of substrates. The structures of **1a-1q** were characterized by IR, ^1H, ^{13}C NMR, and HRMS spectra and were further confirmed by single-crystal X-ray diffraction determination of the two compounds **1a** (Fig. 1) and **1l** (Fig. 2). ^1H NMR spectra clearly showed one set of absorption peaks for each characteristic groups in the molecule, which indicated that there was only one isomer existed in each sample. As showed in

molecular structure of compound **1a** (Fig.1), the aryl group and indole moiety were in *trans*-orientation in the new formed dihydropyridyl ring. Thus compounds **1a-1q** except **1k** and **1l**, were all belonging to this *trans*-isomer. It is obvious that there is no *cis/trans*-isomers for compounds **1k** and **1l** (Fig. 2).

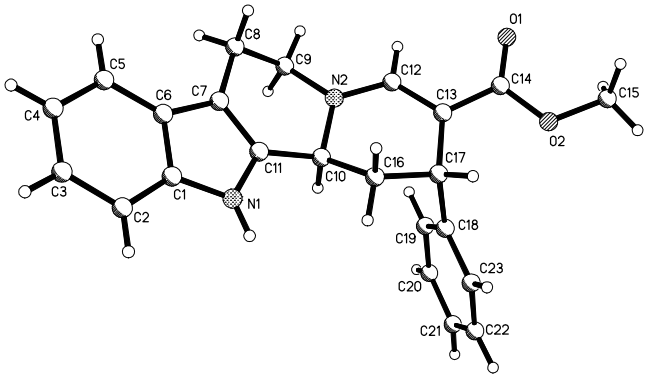


Fig. 1 Molecular structure of compound 1a

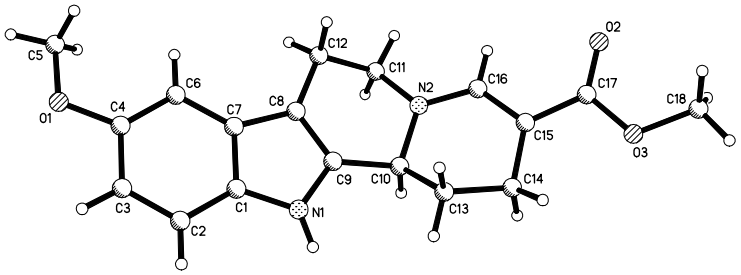
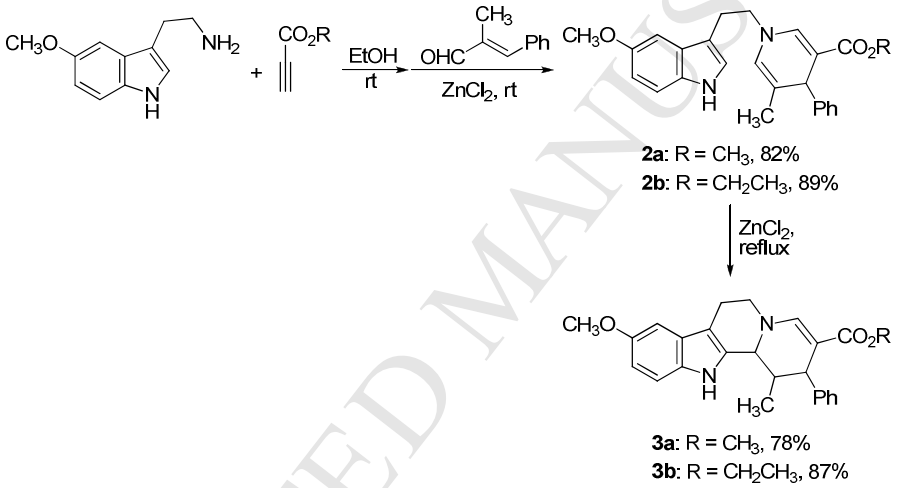


Fig. 2 Molecular structure of compound 1l

When α-methylcinnamaldehyde was used in this domino reaction under similar conditions, only the polysubstituted 1,4-dihydropyridines **2a,b were obtained** as main products at room temperature (Scheme 1). Tryptamine acted as a primary amine to construct the dihydropyridyl ring[16] and the expected Pictet-Spengler cyclization was not observed. The molecular structure of

2a was successfully determined by X-ray diffraction method (Fig. 3). We were pleased to find that **2a,b** could be transferred to indolo[*2,3-a*]quinolizines **3a,b** in alcoholic by reflux in the presence of anhydrous zinc chloride for several hours. Under this condition a intramolecular Pictet-Spengler cyclization at C-2 position of indole proceeded to give the desired cyclized products **3a,b**. This result not only indicated this one-pot domino reaction had wide range of scope, but also shed light on the mechanism of this reaction.



Scheme 1 synthesis of 1,2,6,7,12,12b-hexahydroindolo[*2,3-a*]quinolizines 3a,b

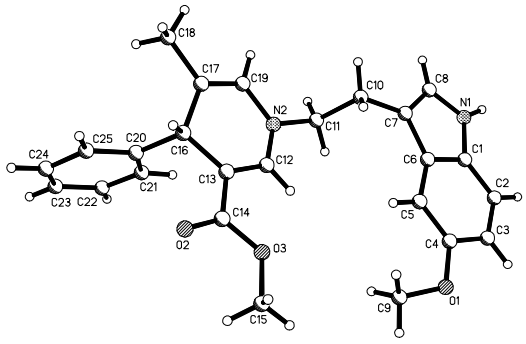
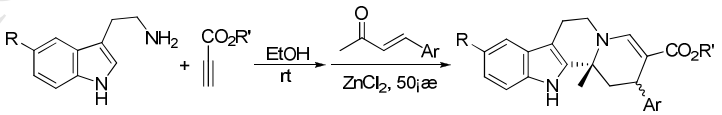


Fig. 3 Molecular structure of compound 2a

In order to further illustrate the synthetic value of this domino reaction, arylideneacetones

were employed in the reaction. At first, tryptamine was treated with methyl or ethyl propiolate in ethanol to give *β*-enamino esters. Then arylideneacetones and catalytic $ZnCl_2$ were added to the system and the mixture was heated to 50℃ for about 36 hours. After workup the expected hexahydroindolo*[2,3-a]*quinolizines **4a-4g** were obtained in 64-81% yields (Table 2). The structures of **4a-4g** were established by the spectroscopic methods and confirmed by single-crystal structure determination of compounds **4d** (Fig. 4) and **4g** (Fig. 5). ^{1}H NMR spectra of compounds **4d, 4e, 4f** and **4g** indicated that two isomers existed within each sample, which is clearly due to methyl group and aryl group in *cis* or *trans* position in tetrahydropyridyl ring. But there is only one isomer existed in compounds **4a, 4b** and **4c** from their ^{1}H NMR spectra. it is clearly to see that phenyl group exists in the *trans*-orientation to the larger indole moiety in the molecular structures of **4d** and **4g**. On the other hand the methyl and phenyl groups are in *cis*-position in the twist-chair conformation of tetrahydropyridyl ring. Thus hexahydroindolo[*2,3-a*]quinolizines **4a-4g** existed mainly in the same isomer as that of compounds **1a-1q**, in which the phenyl group and indole moiety exist in *trans*-position, while the phenyl group and indole moiety exist in *cis*-position in the minor isomer. Here the presence of methyl group might decrease the steric effect of Pictet-Spengler cyclization and caused the more easily formation of the relatively unstable *cis*-isomer.

Table 2 Synthesis of 1,2,6,7,12,12b-hexahydroindolo[*2,3-a*]quinolizines 4a-4g



4a-4g (*cis/trans*-isomer)

Entry	Compd	R	R'	Ar	Yield (%, *cis/trans*)
1	**4a**	H	CH_3	*p*-$CH_3C_6H_4$	70

2	**4b**	H	CH_3	*m*-$CH_3OC_6H_4$	72
3	**4c**	H	CH_3	*p*-BrC_6H_4	67
4	**4d**	CH_3O	CH_3	*p*-$CH_3OC_6H_4$	73 (1:8)
5	**4e**	CH_3O	CH_3	C_6H_5	81 (1:8)
6	**4f**	CH_3O	CH_3	*p*-ClC_6H_4	73 (1:5)
7	**4g**	H	CH_2CH_3	C_6H_5	64 (1:5)

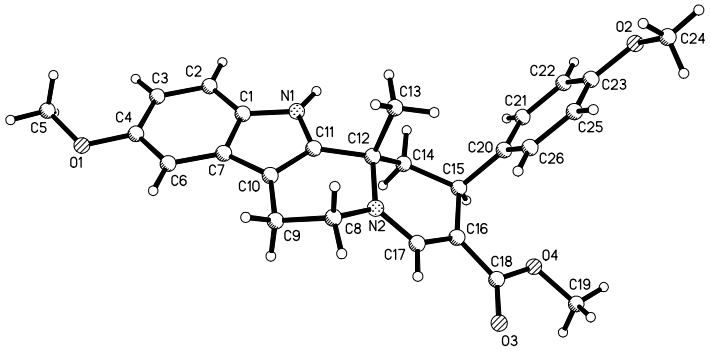


Fig. 4 Molecular structure of compound 4d (*trans*-isomer)

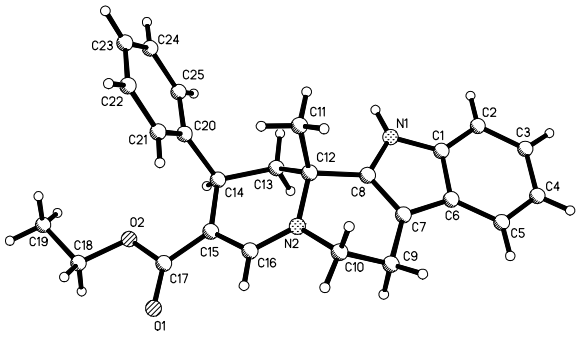
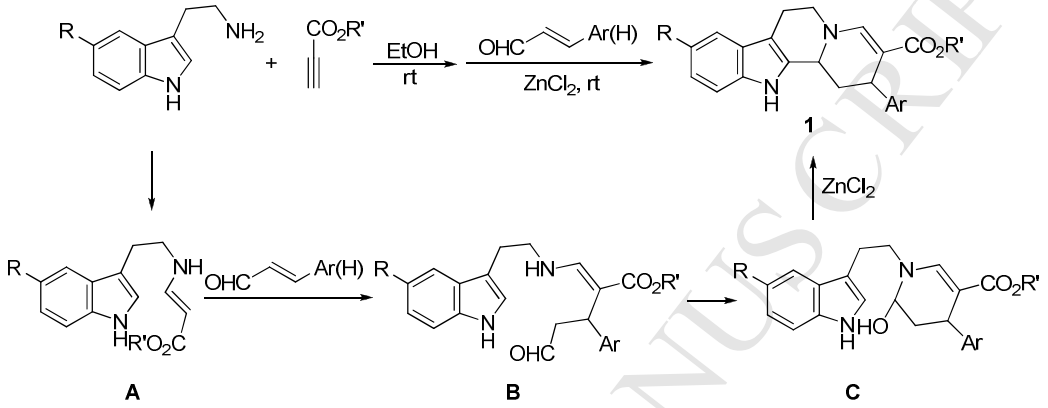


Fig. 5 Molecular structure of compound 4g (*trans*-isomer)

With regard to the mechanism of this reaction sequence (Scheme 2), we assumed that the first step was the formation of *β*-enamino ester (**A**) from the reaction of tryptamine with methyl propiolate.[15] The second step was the Michael addition of *β*-enamino ester (**A**) to α,β-unsaturated

aldehydes to give the adduct (**B**). Thirdly the intramolecular condensation of amino group with carbonyl group formed the nitrogen-containing cyclic intermediate (**C**). At last Pictet-Spengler cyclization gave the final products **1**. In the cyclization process the thermodynamically stable *trans*-isomer would be preferentially formed due to the steric effect of aryl group.



Scheme 2 The proposed mechanism for ont–pot domino reaction

In conclusion, we have developed a Lewis acid catalyzed one-pot sequential reaction of tryptamines, propiolate and α,β-unsaturated aldehydes as well as arylideneacetones for the efficient synthesis of functionalized 1,2,6,7,12,12b-hexahydroindolo[*2,3-a*]quinolizines in good yields. This protocol has advantages of mild reaction conditions, easily accessible starting materials, easy purification of the products and wide range of substrates, which makes it a useful and attractive method for the synthesis of the complex indolo[*2,3-a*]quinolizines in synthetic and medicinal chemistry. Further expansion of the reaction scope and synthetic applications of this methodology are in progress in our laboratory.

Experimental section

1. General procedure for the preparation of 1,2,6,7,12,12b-hexahydroindolo[*2,3-a*]quinolizines 1a-1q: In a round bottom flask a mixture of

tryptamines (2.0 mmol) and methyl or ethyl propiolate (2.0 mmol) in 5.0mL ethanol was stirred at room temperature for 20 minutes. Then *α*,*β*-unsaturated aldehydes (2.0 mmol) and anhydrous zinc chloride (1.0 mmol, 0.136 g) were added. The mixture was stirred at room temperature for additional 48 hours. The resulting precipitate was collected by filtration and washed with cold alcohol to give the pure product.

Methyl 2-phenyl-1,2,6,7,12,12b-hexahydroindolo[*2,3-a*]quinolizine-3-carboxylate (1a): yellow solid, 78%, m.p.279~281□; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 10.94 (s, 1H, NH), 7.88 (brs, 1H, CH), 7.40 (d, *J* = 7.8Hz, 1H, ArH), 7.36~7.34 (m, 2H, ArH), 7.27 (d, *J* = 7.8Hz, 2H, ArH), 7.23~7.21 (m, 2H, ArH), 7.02 (t, *J* = 7.2Hz, 1H, ArH), 6.96 (t, *J* = 7.2Hz, 1H, ArH), 4.21 (d, *J* = 11.4Hz, 1H, CH), 4.01~4.00 (m, 1H, CH), 3.98~3.95 (m, 1H, CH), 3.55~3.51 (m, 1H, CH), 3.49 (s, 3H, OCH_3), 2.81~2.77 (m, 1H, CH), 2.73~2.71 (m, 1H, CH), 2.57 (d, *J* = 13.2Hz, 1H, CH), 1.79 (td, J_1 = 12.6Hz, J_2 = 4.8Hz, 1H, CH); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 167.3, 147.2, 146.6, 136.2, 133.0, 128.1, 127.8, 126.3, 125.9, 121.0, 118.5, 117.7, 111.0, 106.9, 94.0, 50.2, 50.0, 47.1, 36.2, 35.7, 21.6; IR (KBr) υ: 3235, 2965, 2911, 1664, 1597, 1494, 1471, 1428, 1357, 1323, 1301, 1205, 1185, 1163, 1109, 1038, 1021, 942, 852, 790 cm^{-1}; HRMS (ESI) Calcd. for $C_{23}H_{22}N_2NaO_2$ ([M+Na]$^+$): 381.1573. Found: 381.1575.

Methyl 2-(4-methxylphenyl)-1,2,6,7,12,12b-hexahydroindolo[*2,3-a*]quinolizine-3-carboxylate (1b): yellow solid, 87%, m.p.260~262□; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 10.93 (s, 1H, NH), 7.85 (brs, 1H, CH), 7.40 (d, *J* = 7.2Hz, 1H, ArH), 7.23 (d, *J* = 7.8Hz, 1H, ArH), 7.14 (brs, 4H, ArH), 7.02~7.01 (m, 1H, ArH), 6.97~6.96 (m, 1H, ArH), 4.20 (d, *J* = 12.0Hz, 1H, CH), 3.96 (brs, 2H, CH), 3.54~3.50 (m, 1H, CH), 3.48 (s, 3H, OCH_3), 2.81~2.77 (m, 1H, CH), 2.72~2.70 (m, 1H, CH), 2.53 (d, *J* = 13.2Hz, 1H, CH), 2.29 (s, 3H, CH_3), 1.77 (t, *J* = 12.6Hz, 1H, CH); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 167.3, 147.0, 143.5, 136.2, 134.8, 133.1, 128.7, 127.6, 126.3, 120.9, 118.5, 117.6, 111.0, 106.8, 94.1, 50.1, 50.0, 47.0, 35.8, 35.7, 21.6, 20.5; IR (KBr) υ: 3252, 2959, 1668, 1560, 1510, 1427, 1358, 1321, 1302, 1206, 1184, 1165, 1109, 1039, 939, 855, 803, 777 cm^{-1}; HRMS (ESI) Calcd. for $C_{24}H_{24}N_2NaO_2$ ([M+Na]$^+$): 395.1730. Found: 395.1732.

Methyl 2-(3-methxylphenyl)-1,2,6,7,12,12b-hexahydroindolo[*2,3-a*]quinolizine-3-carboxylate (1c): yellow solid, 81%, m.p.282~284□; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 10.94 (s, 1H, NH), 7.87 (brs, 1H, CH), 7.40 (d, *J* = 7.8Hz, 1H, ArH), 7.23~7.21 (m, 2H, ArH), 7.09 (brs, 1H, ArH), 7.04~7.02 (m, 3H, ArH), 6.97~6.95 (m, 1H, ArH), 4.22 (d, *J* = 11.4Hz, 1H, CH), 3.96 (brs, 2H,

CH), 3.56~3.52 (m, 1H, CH), 3.48 (s, 3H, OCH_3), 2.79~2.77 (m, 1H, CH), 2.73~2.70 (m, 1H, CH), 2.54 (d, *J* = 12.6Hz, 1H, CH), 2.33 (s, 3H, CH_3), 1.79~1.76 (m, 1H, CH); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 167.3, 147.1, 146.6, 137.1, 136.2, 133.1, 128.4, 128.0, 126.6, 126.3, 124.8, 120.9, 118.5, 117.6, 111.0, 106.9, 94.0, 50.1, 50.0, 47.0, 36.1, 35.7, 21.6, 21.2; IR (KBr) υ: 3451, 3236, 2908, 2849, 1667, 1599, 1424, 1354, 1320, 1302, 1231, 1214, 1199, 1184, 1169, 1110, 1063, 1038, 924, 882, 778 cm^{-1}; HRMS (ESI) Calcd. for $C_{24}H_{24}N_2NaO_2$ ($[M+Na]^+$): 395.1730. Found: 395.1728.

Methyl 2-(4-methoxyphenyl)-1,2,6,7,12,12b-hexahydroindolo[*2,3-a*]quinolizine-3-carboxylate (1d): yellow solid, 83%, m.p.256~257□; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 10.91 (s, 1H, NH), 7.84 (brs, 1H, CH), 7.40 (d, *J* = 7.8Hz, 1H, ArH), 7.23 (d, *J* = 7.8Hz, 1H, ArH), 7.17 (d, *J* = 7.8Hz, 2H, ArH), 7.02 (t, *J* = 7.2Hz, 1H, ArH), 6.96 (t, *J* = 7.2Hz, 1H, ArH), 6.90 (d, *J* = 7.8Hz, 2H, ArH), 4.20 (d, *J* = 11.4Hz, 1H, CH), 3.95~3.94 (m, 2H, CH), 3.74 (s, 3H, OCH_3), 3.54~3.52 (m, 1H, CH), 3.49 (s, 3H, OCH_3), 2.81~2.77 (m, 1H, CH), 2.73~2.70 (m, 1H, CH), 2.53 (d, *J* = 12.6Hz, 1H, CH), 1.75 (td, J_1 = 12.6Hz, J_2 = 3.6Hz, 1H, CH); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 167.3, 157.6, 147.0, 138.4, 136.2, 133.1, 128.6, 126.3, 120.9, 118.5, 117.6, 113.5, 111.0, 106.8, 94.3, 55.0, 50.1, 50.0, 47.0, 35.9, 35.3, 21.6; IR (KBr) υ: 3449, 2958, 1663, 1598, 1509, 1429, 1358, 1323, 1303, 1277, 1250, 1207, 1186, 1109, 1037, 832 cm^{-1}; HRMS (ESI) Calcd. for $C_{24}H_{24}N_2NaO_3$ ($[M+Na]^+$): 411.1679. Found: 411.1682.

Methyl 2-(4-chlorophenyl)-1,2,6,7,12,12b-hexahydroindolo[*2,3-a*]quinolizine-3-carboxylate (1e): yellow solid, 84%, m.p.267~268□; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 10.93 (s, 1H, NH), 7.88 (brs, 1H, CH), 7.41~7.40 (m, 3H, ArH), 7.30~7.28 (m, 2H, ArH), 7.24 (d, *J* = 6.6Hz, 1H, ArH), 7.03 (brs, 1H, ArH), 6.96 (brs, 1H, ArH), 4.20 (d, *J* = 10.2Hz, 1H, CH), 4.00~3.95 (m, 2H, CH), 3.53 (brs, 1H, CH), 3.49 (s, 3H, OCH_3), 2.79~2.71 (m, 2H, CH), 2.55 (d, *J* = 12.6Hz, 1H, CH), 1.79 (brs, 1H, CH); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 167.2, 147.3, 145.6, 136.2, 132.9, 130.5, 129.6, 128.0, 126.3, 120.9, 118.5, 117.8, 111.0, 106.9, 93.6, 50.1, 50.0, 46.9, 35.6, 21.6; IR (KBr) υ: 3447, 3232, 2962, 2822, 1669, 1599, 1489, 1427, 1356, 1320, 1304, 1207, 1185, 1164, 1111, 1037, 1012, 876, 854, 832, 796, 758 cm^{-1}; HRMS (ESI) Calcd. for $C_{23}H_{21}ClN_2NaO_2$ ($[M+Na]^+$): 415.1184. Found: 415.1184.

Methyl 2-(3-chlorophenyl)-1,2,6,7,12,12b-hexahydroindolo[*2,3-a*]quinolizine-3-carboxylate (1f): yellow solid, 77%, m.p.258~260□; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 10.95 (s, 1H, NH),

7.90 (brs, 1H, CH), 7.40~7.38 (m, 2H, ArH), 7.32~7.30 (m, 2H, ArH), 7.23 (brs, 2H, ArH), 7.03 (brs, 1H, ArH), 6.96 (brs, 1H, ArH), 4.20 (d, *J* = 10.8Hz, 1H, CH), 4.02 (brs, 1H, CH), 3.98~3.96 (m, 1H, CH), 3.55~3.53 (m, 1H, CH), 3.50 (s, 3H, OCH_3), 2.78~2.77 (m, 1H, CH), 2.73~2.71 (m, 1H, CH), 2.59 (d, *J* = 12.0Hz, 1H, CH), 1.79 (brs, 1H, CH); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 167.2, 149.2, 147.5, 136.2, 132.9, 132.8, 130.0, 127.6, 126.5, 126.3, 126.0, 121.0, 118.5, 117.7, 111.0, 106.9, 93.2, 50.2, 50.1, 47.0, 35.9, 35.5, 21.5; IR (KBr) υ: 3497, 3263, 2919, 2853, 2809, 1668, 1600, 1472, 1424, 1355, 1324, 1302, 1205, 1184, 1167, 1113, 1038, 890, 862, 773 cm^{-1}; HRMS (ESI) Calcd. for $C_{23}H_{21}ClN_2NaO_2$ ($[M+Na]^+$): 415.1184. Found: 415.1184.

Methyl 9-methoxy-2-phenyl-1,2,6,7,12,12b-hexahydroindolo[*2,3-a*]quinolizine-3-carboxylate (1g): yellow solid, 83%, m.p.252~253□; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 10.76 (s, 1H, NH), 7.87 (brs, 1H, CH), 7.36~7.33 (m, 2H, ArH), 7.26 (d, *J* = 6.6Hz, 2H, ArH), 7.21 (t, *J* = 7.2Hz, 1H, ArH), 7.11 (d, *J* = 8.4Hz, 1H, ArH), 6.90 (brs, 1H, ArH), 6.67~6.65 (m, 1H, ArH), 4.19 (d, *J* = 12.0Hz, 1H, CH), 4.00~3.99 (m, 1H, CH), 3.97~3.94 (m, 1H, CH), 3.73 (s, 3H, OCH_3), 3.55~3.50 (m, 1H, CH), 3.48 (s, 3H, OCH_3), 2.79~2.74 (m, 1H, CH), 2.69 (d, *J* = 12.6Hz, 1H, CH), 2.54 (d, *J* = 12.6Hz, 1H, CH), 1.78 (td, J_1 = 12.6Hz, J_2 = 4.8Hz, 1H, CH); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 167.3, 153.2, 147.2, 146.5, 133.7, 131.2, 128.1, 127.8, 126.6, 125.9, 111.6, 110.7, 106.7, 99.9, 93.9, 55.4, 50.2, 50.0, 47.1, 36.1, 35.7, 21.7; IR (KBr) υ: 3244, 2913, 2826, 1665, 1584, 1490, 1444, 1426, 1362, 1321, 1301, 1222, 1205, 1179, 1159, 1106, 1061, 1036, 945, 934, 805, 756 cm^{-1}; HRMS (ESI) Calcd. for $C_{24}H_{24}N_2NaO_3$ ($[M+Na]^+$): 411.1679. Found: 411.1670.

Methyl 9-methoxy-2-(4-methylphenyl)-1,2,6,7,12,12b-hexahydroindolo[*2,3-a*]quinolizine-3-carboxylate (1h): yellow solid, 86%, m.p.238~240□; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 10.76 (s, 1H, NH), 7.85 (brs, 1H, CH), 7.14 (brs, 4H, CH), 7.12~7.10 (m, 1H, ArH), 6.90 (brs, 1H, CH), 6.66 (d, *J* = 9.0Hz, 1H, ArH), 4.17 (d, *J* = 12.0Hz, 1H, CH), 3.95 (brs, 2H, CH), 3.73 (s, 3H, OCH_3), 3.53~3.51 (m, 1H, CH), 3.48 (s, 3H, OCH_3), 2.78~2.74 (m, 1H, CH), 2.70~2.67 (m, 1H, CH), 2.46 (brs, 1H, CH), 2.28 (s, 3H, CH_3), 1.76 (t, *J* = 12.0Hz, 1H, CH); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 167.3, 153.2, 147.0, 143.6, 134. 8, 133.8, 131.3, 128.7, 127.6, 126.6, 111.6, 110.7, 106.7, 99.9, 94.1, 55.3, 50.2, 50.0, 47.1, 35.8, 35.7, 21.7, 20.5; IR (KBr) υ: 3237, 2945, 1665, 1583, 1510, 1485, 1452, 1432, 1373, 1318, 1296, 1205, 1181, 1163, 1135, 1106, 1026, 855, 823, 802, 774 cm^{-1}; HRMS (ESI) Calcd. for $C_{25}H_{26}N_2NaO_3$ ($[M+Na]^+$): 425.1836. Found: 425.1826.

Methyl 9-methoxy-2-(3-methylphenyl)-1,2,6,7,12,12b-hexahydroindolo[*2,3-a*]quinolizine-3-

carboxylate (1i): yellow solid, 79%, m.p.226~228□; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 10.77 (s, 1H, NH), 7.86 (brs, 1H, CH), 7.22 (brs, 1H, ArH), 7.11~7.08 (m, 2H, ArH), 7.02 (brs, 2H, CH), 6.90 (brs, 1H, CH), 6.66~6.65 (m, 1H, ArH), 4.19 (d, *J* = 10.2Hz, 1H, CH), 3.95 (brs, 2H, CH), 3.73 (s, 3H, OCH_3), 3.56~3.53 (m, 1H, CH), 3.48 (s, 3H, OCH_3), 2.76~2.68 (m, 2H, CH), 2.54 (brs, 1H, CH), 2.32 (s, 3H, CH_3), 1.76 (brs, 1H, CH); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 167.3, 153.2, 147.1, 146.6, 137.1, 133.7, 131.2, 128.4, 128.0, 126.6, 124.8, 111.6, 110.7, 106.7, 99.9, 94.0, 55.3, 50.2, 50.0, 47.1, 36.1, 35.7, 21.7, 21.2; IR (KBr) υ: 3236, 2947, 2847, 1663, 1584, 1483, 1435, 1361, 1317, 1301, 1214, 1196, 1182, 1160, 1107, 1058, 1034, 888, 831, 800, 776 cm^{-1}; HRMS (ESI) Calcd. for $C_{25}H_{26}N_2NaO_3$ ([M+Na]$^+$): 425.1836. Found: 425.1827.

Methyl 9-methoxy-2-(3-chlorophenyl)-1,2,6,7,12,12b-hexahydroindolo[*2,3-a*]quinolizine-3-carboxylate (1j): white solid, 80%, m.p.244~245℃; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 10.75 (s, 1H, NH), 7.88 (brs, 1H, CH), 7.37 (t, *J* = 7.2Hz, 1H, ArH), 7.31 (brs, 1H, ArH), 7.28 (d, *J* = 7.8Hz, 1H, ArH), 7.21 (d, *J* = 7.8Hz, 1H, ArH), 7.12 (t, *J* = 8.4Hz, 1H, ArH), 6.91 (brs, 1H, ArH), 6.67 (d, *J* = 8.4Hz, 1H, ArH), 4.17 (d, *J* = 11.4Hz, 1H, CH), 4.01 (brs, 1H, CH), 3.96~3.94 (m, 1H, CH), 3.73 (s, 3H, OCH_3), 3.56~3.52 (m, 1H, CH), 3.50 (s, 3H, OCH_3), 2.78~2.74 (m, 1H, CH), 2.70~2.68 (m, 1H, CH), 2.55 (d, *J* = 12.6Hz, 1H, CH), 1.88~1.77 (m, 1H, CH); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 167.2, 153.2, 149.2, 147.5, 133.5, 132.9, 131.2, 130.0, 127.6, 126.6, 126.4, 125.9, 111.6, 110.8, 106.8, 100.0, 93.2, 55.4, 50.2, 50.1, 47.0, 35.9, 35.5, 21.6; IR (KBr) υ: 3499, 3244, 2950, 2838, 1666, 1586, 1484, 1429, 1360, 1335, 1312, 1207, 1183, 1161, 1110, 1061, 1034, 888, 858, 832, 797, 768 cm^{-1}; HRMS (ESI) Calcd. for $C_{24}H_{23}ClN_2NaO_3$ ([M+Na]$^+$): 445.1289. Found: 445.1284.

Methyl 1,2,6,7,12,12b-hexahydroindolo[*2,3-a*]quinolizine-3-carboxylate (1k): yellow solid, 80%, m.p.156~158□; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 10.96 (s, 1H, NH), 7.53 (brs, 1H, CH), 7.41 (d, *J* = 7.8Hz, 1H, ArH), 7.32 (d, *J* = 7.2Hz, 1H, ArH), 7.07~7.05 (m, 1H, ArH), 6.99~6.98 (m, 1H, ArH), 4.99 (d, *J* = 10.2Hz, 1H, CH), 3.82 (d, *J* = 12.0Hz, 1H, CH), 3.56 (s, 3H, OCH_3), 3.46~3.43 (m, 1H, CH), 2.78~2.74 (m, 1H, CH), 2.71~2.69 (m, 1H, CH), 2.57 (d, *J* = 12.0Hz, 1H, CH), 2.39~2.36 (m, 1H, CH), 2.31~2.27 (m, 1H, CH), 1.60~1.58 (m, 1H, CH); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 167.6, 146.5, 136.1, 133.6, 126.4, 120.9, 118.5, 117.7, 111.1, 106.5, 93.4, 51.5, 50.0, 49.9, 27.4, 21.6, 20.1; IR (KBr) υ: 3293, 2938, 2849, 1654, 1610, 1493, 1439, 1418,

1356, 1332, 1301, 1244, 1205, 1182, 1154, 1095, 1063, 1037, 1002, 933, 829 cm^{-1}; HRMS (ESI) Calcd. for $C_{17}H_{18}N_2NaO_2$ ($[M+Na]^+$): 305.1260. Found: 305.1255.

Methyl 9-methoxy-1,2,6,7,12,12b-hexahydroindolo[*2,3-a*]quinolizine-3-carboxylate (1l): yellow solid, 76%, m.p.204~206℃; ^1H NMR (600 MHz, DMSO-d_6) δ: 10.78 (s, 1H, NH), 7.52 (brs, 1H, CH), 7.20 (d, *J* = 8.4Hz, 1H, ArH), 6.91 (brs, 1H, ArH), 6.70 (d, *J* = 8.4Hz, 1H, ArH), 4.46 (d, *J* = 10.2Hz, 1H, CH), 3.81 (d, *J* = 12.0Hz, 1H, CH), 3.74 (s, 3H, OCH_3), 3.55 (s, 3H, OCH_3), 3.45~3.41 (m, 1H, CH), 2.75~2.71 (m, 1H, CH), 2.68~2.66 (m, 1H, CH), 2.54 (d, *J* = 12.0Hz, 1H, CH), 2.38~2.35 (m, 1H, CH), 2.29~2.25 (m, 1H, CH), 1.59~1.57 (m, 1H, CH); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 167.6, 153.2, 146.5, 134.3, 131.2, 126.7, 111.7, 110.7, 106.4, 100.0, 93.4, 55.3, 51.6, 50.0, 27.4, 21.7, 20.1; IR (KBr) υ: 3229, 2942, 2902, 2843, 1664, 1587, 1487, 1436, 1356, 1303, 1211, 1180, 1151, 1106, 1060, 1031, 940, 913, 834, 794 cm^{-1}; HRMS (ESI) Calcd. for $C_{18}H_{20}N_2NaO_3$ ($[M+Na]^+$): 335.1366. Found: 335.1364.

Ethyl 2-phenyl-1,2,6,7,12,12b-hexahydroindolo[*2,3-a*]quinolizine-3-carboxylate (1m): yellow solid, 84%, m.p.256~258℃; ^1H NMR (600 MHz, DMSO-d_6) δ: 10.92 (s, 1H, NH), 7.84 (brs, 1H, CH), 7.40 (d, *J* = 7.2Hz, 1H, ArH), 7.34~7.33 (m, 2H, ArH), 7.27~7.26 (m, 2H, ArH), 7.23~7.22 (m, 2H, ArH), 7.02 (t, *J* = 6.6Hz, 1H, ArH), 6.97~6.96 (m, 1H, ArH), 4.22 (d, *J* = 11.4Hz, 1H, CH), 4.00~3.96 (m, 4H, CH), 3.55~3.52 (m, 1H, CH), 2.80~2.78 (m, 1H, CH), 2.73~2.71 (m, 1H, CH), 2.57 (d, *J* = 12.6Hz, 1H, CH), 1.82~1.79 (m, 1H, CH), 1.10 (brs, 3H, CH_3); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 166.8, 146.9, 146.7, 136.2, 133.1, 128.1, 127.9, 127.8, 126.3, 125.8, 120.9, 118.5, 117.7, 111.0, 106.9, 94.4, 58.1, 50.2, 47.1, 36.2, 35.7, 21.6, 14.6; IR (KBr) υ: 3450, 3232, 2978, 2911, 2851, 1663, 1588, 1494, 1473, 1438, 1363, 1320, 1300, 1209, 1185, 1166, 1108, 1039, 1018, 940, 789 cm^{-1}; HRMS (ESI) Calcd. for $C_{24}H_{24}N_2NaO_2$ ($[M+Na]^+$): 395.1730. Found: 395.1727.

Ethyl 2-(4-methylphenyl)-1,2,6,7,12,12b-hexahydroindolo[*2,3-a*]quinolizine-3-carboxylate (1n): yellow solid, 85%, m.p.226~227℃; ^1H NMR (600 MHz, DMSO-d_6) δ: 10.91 (s, 1H, NH), 7.82 (brs, 1H, CH), 7.39 (d, *J* = 7.8Hz, 1H, ArH), 7.23 (d, *J* = 8.4Hz, 1H, ArH), 7.14 (brs, 4H, ArH), 7.02 (t, *J* = 7.8Hz, 1H, ArH), 6.95 (t, *J* = 7.2Hz, 1H, ArH), 4.20 (d, *J* = 12.0Hz, 1H, CH), 3.97~3.92 (m, 4H, CH), 3.54~3.50 (m, 1H, CH), 2.82~2.78 (m, 1H, CH), 2.72~2.70 (m, 1H, CH), 2.53 (d, *J* = 13.2Hz, 1H, CH), 2.29 (s, 3H, CH_3), 1.77 (td, J_1 = 12.6Hz, J_2 = 4.8Hz, 1H, CH), 1.10

(t, J = 7.2Hz, 3H, CH_3); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 166.8, 146.8, 143.6, 136.2, 134.8, 133.1, 128.7, 127.6, 126.3, 120.9, 118.5, 117.6, 111.0, 106.9, 94.6, 58.0, 50.1, 47.1, 35.8, 35.7, 21.6, 20.5, 14.6; IR (KBr) υ: 3449, 2967, 2915, 2852, 2804, 1662, 1587, 1509, 1473, 1442, 1363, 1320, 1301, 1208, 1166, 1107, 1040, 1016, 940, 875, 808, 775 cm^{-1}; HRMS (ESI) Calcd. for $C_{25}H_{26}N_2NaO_2$ ([M+Na]$^+$): 409.1886. Found: 409.1885.

Ethyl 2-(3-chlorophenyl)-1,2,6,7,12,12b-hexahydroindolo[*2,3-a*]quinolizine-3-carboxylate (1o): yellow solid, 75%, m.p. >300℃; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 10.93 (s, 1H, NH), 7.86 (brs, 1H, CH), 7.41~7.39 (m, 1H, ArH), 7.37 (d, J = 7.8Hz, 1H, ArH), 7.31 (brs, 1H, ArH), 7.28 (d, J = 7.8Hz, 1H, ArH), 7.23 (t, J = 7.8Hz, 2H, ArH), 7.04~7.39 (m, 1H, ArH), 6.97~6.95 (m, 1H, ArH), 4.21 (d, J = 12.0Hz, 1H, CH), 4.02~3.98 (m, 2H, CH), 3.97~3.94 (m, 2H, CH), 3.58~3.53 (m, 1H, CH), 2.82~2.77 (m, 1H, CH), 2.72 (d, J = 12.0Hz, 1H, CH), 2.59 (d, J = 13.2Hz, 1H, CH), 1.80 (td, J_1 = 12.6Hz, J_2 = 5.4Hz, 1H, CH), 1.11 (t, J = 7.2Hz, 3H, CH_3); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 166.7, 149.3, 147.3, 136.2, 132.9, 129.9, 127.7, 126.5, 126.3, 125.9, 1209, 118.5, 117.7, 111.0, 106.9, 93.6, 58.1, 50.2, 47.0, 36.0, 35.4, 21.5, 14.6; IR (KBr) υ: 3448, 2990, 2914, 1660, 1586, 1474, 1440, 1363, 1325, 1303, 1193, 1165, 1108, 1038, 886, 776 cm^{-1}; HRMS (ESI) Calcd. for $C_{24}H_{23}ClN_2NaO_2$ ([M+Na]$^+$): 429.1340. Found: 429.1334.

Ethyl 9-methoxy-2-(4-methoxyphenyl)-1,2,6,7,12,12b-hexahydroindolo[*2,3-a*]quinolizine-3-carboxylate (1p): white solid, 81%, m.p.249~250℃; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 10.72 (s, 1H, NH), 7.81 (brs, 1H, CH), 7.13~7.10 (m, 5H, ArH), 6.90 (brs, 1H, ArH), 6.66 (d, J = 7.8Hz, 1H, ArH), 4.17 (d, J = 10.8Hz, 1H, CH), 3.94 (brs, 4H, CH), 3.73 (s, 3H, 0CH_3), 3.53~3.49 (m, 1H, CH), 2.77~2.75 (m, 1H, CH), 2.69~2.67 (m, 1H, CH), 2.54 (brs, 1H, CH), 2.28 (s, 3H, CH_3), 1.76 (brs, 1H, CH), 1.10 (brs, 3H, CH); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 166.8, 153.2, 146.8, 143.7, 134.7, 133.8, 131.2, 128.7, 127.6, 126.6, 111.6, 110.7, 106.7, 99.9, 94.5, 58.0, 56.0, 55.3, 50.2, 47.1, 35.8, 21.7, 20.5, 18.5, 14.6; IR (KBr) υ: 3453, 2982, 2907, 2828, 1660, 1583, 1484, 1443, 1365, 1318, 1298, 1209, 1162, 1107, 1035, 821, 799, 776 cm^{-1}; HRMS (ESI) Calcd. for $C_{26}H_{28}N_2NaO_3$ ([M+Na]$^+$): 439.1992. Found: 439.1988.

Ethyl 9-methoxy-2-(3-chlorophenyl)-1,2,6,7,12,12b-hexahydroindolo[*2,3-a*]quinolizine-3-carboxylate (1q): white solid, 76%, m.p.241~243℃; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 10.75 (s, 1H, NH), 7.85 (brs, 1H, CH), 7.37 (t, J = 7.8Hz, 1H, ArH), 7.30~7.27 (m, 2H, ArH), 7.22 (d, J =

7.8Hz, 1H, ArH), 7.12 (d, *J* = 8.4Hz, 1H, ArH), 6.91 (brs, 1H, ArH), 6.67 (d, *J* = 8.4Hz, 1H, ArH), 4.18 (d, *J* = 12.0Hz, 1H, CH), 4.01~3.97 (m, 2H, CH), 3.96~3.93 (m, 2H, CH), 3.73 (s, 3H, $0CH_3$), 3.57~3.52 (m, 1H, CH), 2.79~2.74 (m, 1H, CH), 2.69 (d, *J* = 12.6Hz, 1H, CH), 2.56 (d, *J* = 13.2Hz, 1H, CH), 1.79 (td, J_1 = 12.6Hz, J_2 = 5.4Hz, 1H, CH), 1.11 (t, *J* = 7.2Hz, 3H, CH_3); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 166.7, 153.2, 149.3, 147.3, 133.5, 132.9, 131.2, 129.9, 127.6, 126.6, 126.4, 125.9, 111.6, 110.7, 106.8, 100.0, 93.6, 58.1, 55.3, 50.2, 47.1, 36.0, 35.4, 21.6, 14.5; IR (KBr) υ: 3449, 2956, 2836, 1660, 1586, 1480, 1438, 1365, 1305, 1210, 1162, 1108, 1037, 889, 830, 775 cm^{-1}; HRMS (ESI) Calcd. for $C_{25}H_{25}ClN_2NaO_3$ ($[M+Na]^+$): 459.1446. Found: 459.1440.

2. General procedure for the preparation of 1,4-dihydropyridines 2a,b and 1,2,6,7,12,12b-hexahydroindolo[*2,3-a*]quinolizines 3a,b: The same procedure as described above was used by using *α*-methylcinnamaldehyde. A mixture of 5-methoxytryptamine (2.0 mmol) and methyl or ethyl propiolate (2.0 mmol) in 5.0mL ethanol was stirred at room temperature for 20 minutes. Then *α*-methylcinnamaldehyde (2.0 mmol) and anhydrous zinc chloride (1.0 mmol, 0.136 g) were added. The mixture was stirred at room temperature for additional 48 hours. The resulting precipitates were collected by filtration and washed with cold alcohol to give the pure product. Then a solution of compound **2a** in a mixture of methanol and toluene (V/V = 1:1) containing zinc chloride was refluxed for 48 hours to give the product **3a**. On the other hand a solution of compound **2b** in ethanol containing zinc chloride was refluxed for 48 hours to give the product **3b**.

Methyl 1-[2-(5-Methoxy-1H-indol-3-yl)-ethyl]-5-methyl-4-phenyl-1,4-dihydropyridine-3-carboxylate (2a): white solid, 82%, m.p.158~159℃; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 10.72 (s, 1H, NH), 7.27 (brs, 1H, CH), 7.24 (d, *J* = 9.0Hz, 1H, ArH), 7.18~7.16 (m, 3H, ArH), 7.11~7.10 (m, 2H, ArH), 7.08~7.06 (m, 2H, ArH), 6.73 (d, *J* = 9.0Hz, 1H, ArH), 6.09 (brs, 1H, CH), 4.13 (brs, 1H, CH), 3.77 (s, 3H, OCH_3), 3.70~3.66 (m, 1H, CH), 3.63~3.60 (m, 1H, CH), 3.41 (s, 3H, OCH_3), 2.97~2.96 (m, 2H, CH), 1.43 (s, 3H, CH_3); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 167.3, 153.1, 146.5, 139.9, 131.4, 127.8, 127.6, 127.5, 125.9, 124.0, 123.1, 115.0, 112.0, 111.1, 110.2, 100.4, 98.2, 55.4, 53.7, 50.1, 43.4, 25.6, 18.5; IR (KBr) υ: 3343, 3074, 2989, 2849,1686, 1660, 1597, 1450, 1421, 1367, 1312, 1260, 1193, 1158, 1093, 1024, 923, 844, 825, 795, 762 cm^{-1}; HRMS (ESI) Calcd. for $C_{25}H_{26}N_2NaO_3$ ($[M+Na]^+$): 425.1836. Found: 425.1832.

Ethyl 1-[2-(5-Methoxy-1H-indol-3-yl)-ethyl]-5-methyl-4-phenyl-1,4-dihydropyridine-3-carboxylate (2b): white solid, 89%, m.p.138~140℃; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 10.74 (s, 1H, NH), 7.25~7.21 (m, 2H, CH, ArH), 7.19~7.16 (m, 3H, ArH), 7.11~7.06 (m, 4H, ArH), 6.74~6.72 (m, 1H, ArH), 6.10 (brs, 1H, CH), 4.12 (brs, 1H, CH), 3.90~3.87 (m, 1H, CH), 3.83~3.79 (m, 1H, CH), 3.77 (s, 3H, OCH_3), 3.69~3.61 (m, 2H, CH), 2.99~2.94 (m, 2H, CH), 1.42 (s, 3H, CH_3), 1.02 (t, J = 6.6Hz, 3H, CH_3); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 166.9, 153.1, 146.6, 139.7, 131.5, 127.7, 127.6, 127.5, 125.8, 124.0, 123.1, 114.9, 112.0, 111.1, 110.3, 100.4, 98.6, 58.3, 55.4, 53.7, 43.5, 25.6, 18.5, 14.2; IR (KBr) υ: 3437, 3075, 2989, 1687, 1661, 1597, 1487, 1455, 1430, 1371, 1307, 1261, 1240, 1216, 1190, 1158, 1092, 1027, 976, 922, 843, 794, 758 cm^{-1}; HRMS (ESI) Calcd. for $C_{26}H_{28}N_2NaO_3$ ($[M+Na]^+$): 439.1992. Found: 439.1993.

Methyl 9-methoxy-1-methyl-2-phenyl-1,2,6,7,12,12b-hexahydroindolo[*2,3-a*]quinolizine-3-carboxylate (3a): white solid, 78%, m.p.264~265℃; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 10.25 (s, 1H, NH), 7.27 (brs, 1H, CH), 7.32~7.29 (m, 2H, ArH), 7.22~7.19 (m, 3H, ArH), 7.15 (d, J = 8.4Hz, 1H, ArH), 6.93 (brs, 1H, ArH), 6.68~6.66 (m, 1H, ArH), 4.31 (d, J = 13.8Hz, 1H, CH), 3.94~3.91 (m, 1H, CH), 3.78~3.77 (m, 1H, CH), 3.74 (s, 3H, OCH_3), 3.45 (s, 3H, OCH_3), 3.42~3.41 (m, 1H, CH), 2.77~2.73 (m, 2H, CH), 1.94~1.91 (m, 1H, CH), 1.02 (d, J = 6.6Hz, 3H, CH_3); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 166.9, 153.2, 146.7, 143.0, 132.7, 131.4, 129.4, 127.6, 126.5, 126.0, 111.8, 110.9, 99.8, 96.5, 55.4, 53.6, 51.7, 49.9, 43.9, 37.2, 22.3, 16.3; IR (KBr) υ: 3313, 3029, 2999, 2956, 2918, 2824, 1657, 1624, 1485, 1459, 1415, 1335, 1245, 1214, 1178, 1154, 1122, 1095, 1033, 993, 938, 916, 879, 848, 795, 754 cm^{-1}; HRMS (ESI) Calcd. for $C_{25}H_{26}N_2NaO_3$ ($[M+Na]^+$): 425.1836. Found: 425.1837.

Ethyl 9-methoxy-1-methyl-2-phenyl-1,2,6,7,12,12b-hexahydroindolo[*2,3-a*]quinolizine-3-carboxylate (3b): white solid, 87%, m.p.226~228℃; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 10.28 (s, 1H, NH), 7.81 (brs, 1H, CH), 7.32~7.29 (m, 2H, ArH), 7.22~7.19 (m, 3H, ArH), 7.15 (d, J = 8.4Hz, 1H, ArH), 6.93 (brs, 1H, ArH), 6.68~6.66 (m, 1H, ArH), 4.34~3.31 (m, 1H, CH), 3.93~3.89 (m, 3H, CH), 3.77~3.76 (m, 1H, CH), 3.74 (s, 3H, OCH_3), 3.45~3.42 (m, 1H, CH), 2.79~2.73 (m, 2H, CH), 1.94~1.93 (m, 1H, CH), 1.07~1.05 (m, 3H, CH_3), 1.02 (d, J = 6.6Hz, 3H, CH_3); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 166.5, 153.2, 146.5, 143.1, 132.8, 131.4, 129.4, 127.5, 126.5, 125.9, 111.8, 110.9, 109.2, 99.8, 96.8, 58.0, 55.4, 53.7, 51.7, 43.9, 37.1, 22.3, 18.5, 16.3,

14.5; IR (KBr) υ: 3108, 1728, 1587, 1487, 1460, 1367, 1312, 1244, 1213, 1160, 1123, 1032, 909, 843, 783, 750 cm^{-1}; HRMS (ESI) Calcd. for $C_{26}H_{28}N_2NaO_3$ ($[M+Na]^+$): 439.1992. Found: 439.1997.

2. General procedure for the preparations of 1,2,6,7,12,12b-hexahydroindolo[*2,3-a*]quinolizines 4a-4g: A mixture of tryptamines (2.0 mmol) and methyl or ethyl propiolate (2.0 mmol) in 10.0mL ethanol was stirred at room temperature for 20 minutes. Then arylideneacetones (2.0 mmol) and anhydrous zinc chloride (1.0 mmol, 0.136 g) were added to it. The solution was stirred at about 50C for additional 36 hours. The solvent was removed by rotator evaporation and the residue was titrated with cold alcohol to give the pure product.

Methyl 12b-methyl-2-(4-methylphenyl)-1,2,6,7,12,12b-hexahydroindolo[*2,3-a*]quinolizine-3-carboxylate (4a): white solid, 70%, m.p.288~290℃; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 10.97 (s, 1H, NH), 7.82 (brs, 1H, CH), 7.39 (d, *J* = 7.2Hz, 1H, ArH), 7.28 (d, *J* = 7.8Hz, 1H, ArH), 7.16 (d, *J* = 7.8Hz, 2H, ArH), 7.12 (d, *J* = 7.2Hz, 2H, ArH), 7.04 (t, *J* = 7.2Hz, 1H, ArH), 6.96 (t, *J* = 7.2Hz, 1H, ArH), 3.98~3.97 (m, 1H, CH), 3.83~3.81 (m, 1H, CH), 3.63~3.59 (m, 1H, CH), 3.50 (s, 3H, OCH_3), 2.88 (d, *J* = 13.8Hz, 1H, CH), 2.77~2.73 (m, 1H, CH), 2.67 (d, *J* = 12.6Hz, 1H, CH), 2.28 (s, 3H, CH_3), 1.97~1.93 (m, 1H, CH), 0.99 (s, 3H, CH_3); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 167.7, 146.7, 142.3, 139.0, 135.9, 134.2, 128.5, 127.4, 126.0, 120.9, 118.5, 117.9, 111.0, 104.3, 92.7, 54.2, 50.0, 47.6, 40.5, 34.6, 24.3, 21.9, 20.5; IR (KBr) υ: 3446, 2916, 2849, 1664, 1582, 1425, 1353, 1311, 1217, 1183, 1142, 1093, 1039, 923, 853, 818, 795, 774 cm^{-1}; HRMS (ESI) Calcd. for $C_{25}H_{26}N_2NaO_2$ ($[M+Na]^+$): 409.1886. Found: 409.1878.

Methyl 12b-methyl-2-(3-methoxyphenyl-1,2,6,7,12,12b-hexahydroindolo[*2,3-a*]quinolizine-3-carboxylate (4b): white solid, 72%, m.p.272~274℃; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 10.99 (s, 1H, NH), 7.83 (brs, 1H, CH), 7.39 (d, *J* = 7.2Hz, 1H, ArH), 7.28 (d, *J* = 8.4Hz, 1H, ArH), 7.23 (t, *J* = 7.8Hz, 1H, ArH), 7.05 (t, *J* = 7.8Hz, 1H, ArH), 6.96 (t, *J* = 7.2Hz, 1H, ArH), 6.87~6.84 (m, 2H, ArH), 6.75 (d, *J* = 7.2Hz, 1H, ArH), 3.99~3.98 (m, 1H, CH), 3.85~3.82 (m, 1H, CH), 3.76 (s, 3H, OCH_3), 3.64~3.60 (m, 1H, CH), 3.52 (s, 3H, OCH_3), 2.91 (d, *J* = 13.8Hz, 1H, CH), 2.77~2.72 (m, 1H, CH), 2.69~2.66 (m, 1H, CH), 1.95 (dd, J_1 = 13.8Hz, J_2 = 6.6Hz, 1H, CH), 1.02 (s, 3H, CH_3); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 167.7, 159.1, 147.1, 146.7, 139.0, 135.9, 128.9, 126.0, 120.9,

119.9, 118.5, 117.9, 113.9, 111.0, 110.2, 104.3, 92.5, 54.9, 54.2, 50.1, 47.6, 35.0, 24.2, 21.9; IR (KBr) υ: 3452, 2930, 2853, 1637, 1485, 1424, 1383, 1349, 1308, 1268, 1221, 1185, 1141, 1092, 1053, 879, 776 cm^{-1}; HRMS (ESI) Calcd. for $C_{25}H_{26}N_2NaO_3$ ($[M+Na]^+$): 425.1836. Found: 425.1831.

Methyl 9-methoxy-12b-methyl-2-(4-bromophenyl)-1,2,6,7,12,12b-hexahydroindolo[*2,3-a*]-quinolizine-3-carboxylate (4c): white solid, 67%, m.p.299~300℃; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 11.00 (s, 1H, NH), 7.86 (brs, 1H, CH), 7.52~7.51 (m, 2H, ArH), 7.40~7.39 (m, 1H, ArH), 7.29~7.25 (m, 3H, ArH), 7.05~6.96 (m, 2H, ArH), 3.98 (brs, 1H, CH), 3.84 (brs, 1H, CH), 3.62 (brs, 1H, CH), 3.52 (s, 3H, OCH_3), 2.87 (d, *J* = 12.0Hz, 1H, CH), 2.75~2.68 (m, 2H, CH), 1.98 (brs, 1H, CH), 1.00 (s, 3H, CH_3); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 167.6, 146.9, 144.9, 138.8, 135.9, 130.7, 129.9, 126.0, 120.9, 118.5, 117.9, 111.0, 104.3, 92.0, 54.2, 50.1, 47.6, 34.7, 24.3, 21.9; IR (KBr) υ: 3448, 2926, 2854, 2025, 1663, 1582, 1485, 1426, 1353, 1309, 1219, 1185, 1143, 1094, 1039, 1011, 823, 782 cm^{-1}; HRMS (ESI) Calcd. for $C_{24}H_{23}BrN_2NaO_2$ ($[M+Na]^+$): 473.0835. Found: 473.0822.

Methyl 9-methoxy-12b-methyl-2-(4-methoxyphenyl-1,2,6,7,12,12b-hexahydroindolo[*2,3-a*]-quinolizine-3-carboxylate (4d): white solid, 73%, m.p.266~267℃; ^{1}H NMR (600 MHz, DMSO-d_6) δ: *cis/trans* = 1:8; *trans-isomer*: 10.80 (s, 1H, NH), 7.81 (brs, 1H, CH), 7.16 (brs, 3H, ArH), 6.89 (brs, 3H, ArH), 6.68 (d, *J* = 7.2Hz, 1H, ArH), 4.18 (d, *J* = 12.0Hz, 1H, CH), 3.99~3.94 (m, 1H, CH), 3.81~3.80 (m, 1H, CH), 3.73 (s, 6H, $0CH_3$), 3.51 (s, 3H, $0CH_3$), 2.83 (d, *J* = 13.2Hz, 1H, CH), 2.71~2.70 (m, 1H, CH), 2.65 (d, *J* = 13.2Hz, 1H, CH), 1.92~1.91 (m, 1H, CH), 0.98 (s, 3H, CH_3); *cis-isomer*: 7.78 (brs, 1H, CH), 3.94 (s, 3H, OCH_3); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 167.7, 157.1, 153.2, 146.7, 139.8, 137.2, 130.9, 128.4, 126.3, 113.4, 113.3, 111.6, 110.7, 104.2, 100.1, 92.8, 55.4, 54.9, 54.2, 50.0, 47.6, 40.6, 34.2, 24.4, 22.0; IR (KBr) υ: 3451, 3240, 2949, 2831, 1662, 1579, 1510, 1461, 1426, 1357, 1314, 1253, 1216, 1180, 1139, 1091, 1036, 984, 910, 829, 774 cm^{-1}; HRMS (ESI) Calcd. for $C_{26}H_{28}N_2NaO_4$ ($[M+Na]^+$): 455.1941. Found: 455.1937.

Methyl 9-methoxy-12b-methyl-2-phenyl-1,2,6,7,12,12b-hexahydroindolo[*2,3-a*]quinolizine-3-carboxylate (4e): white solid, 81%, m.p. >300℃; ^{1}H NMR (600 MHz, DMSO-d_6) δ: *cis/trans* = 1:8; *trans-isomer*: 10.81 (s, 1H, NH), 7.84 (brs, 1H, CH), 7.33~7.27 (m, 4H, ArH), 7.17~7.15 (m, 2H, ArH), 6.89 (brs, 1H, ArH), 6.69~6.67 (m, 1H, ArH), 4.02~3.98 (m, 1H, CH), 3.83~3.80 (m,

1H, CH), 3.73 (s, 3H, 0CH_3), 3.63~3.59 (m, 1H, CH), 3.51 (s, 3H, 0CH_3), 2.89~2.85 (m, 1H, CH), 2.75~2.63 (m, 2H, CH), 2.00~1.96 (m, 1H, CH), 0.97 (s, 3H, CH_3); *cis-isomer*: 7.78 (brs, 1H, CH), 3.94 (s, 3H, OCH_3); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 167.6, 153.2, 146.9, 144.5, 139.5, 131.0, 129.9, 129.4, 127.8, 126.4, 111.6, 110.8, 104.3, 100.3, 92.2, 55.4, 54.3, 50.0, 47.7, 40.4, 34.6, 24.4, 22.0; IR (KBr) υ: 3453, 3291, 2976, 2924, 2865, 2828, 2733, 1647, 1610, 1488, 1436, 1416, 1329, 1311, 1219, 1183, 1139, 1113, 1091, 1030, 1012, 952, 913, 889, 822, 797, 783 cm^{-1}; HRMS (ESI) Calcd. for $C_{25}H_{26}N_2NaO_3$ ($[M+Na]^+$): 425.1836. Found: 425.1840.

Methyl 9-methoxy-12b-methyl-2-(4-chlorophenyl)-1,2,6,7,12,12b-hexahydroindolo[*2,3-a*]-quinolizine-3-carboxylate (4f): white solid, 73%, m.p. **>** 300℃; ^{1}H NMR (600 MHz, DMSO-d_6) δ: *cis/trans* = 1:5; *trans-isomer*: 10.81 (s, 1H, NH), 7.84 (brs, 1H, CH), 7.38 (d, *J* = 7.8Hz, 2H, ArH), 7.29 (d, *J* = 7.8Hz, 2H, ArH), 7.17 (d, *J* = 9.0Hz, 1H, ArH), 6.90 (brs, 1H, ArH), 6.69 (d, *J* = 8.4Hz, 1H, ArH), 3.99~3.98 (m, 1H, CH), 3.84~3.81 (m, 1H, CH), 3.74 (s, 3H, 0CH_3), 3.63~3.59 (m, 1H, CH), 3.52 (s, 3H, 0CH_3), 2.86~2.82 (m, 1H, CH), 2.75~2.70 (m, 1H, CH), 2.68~2.64 (m, 1H, CH), 1.99~1.98 (m, 1H, CH), 0.98 (s, 3H, CH_3); *cis-isomer*: 7.81 (brs, 1H, CH); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 167.7, 153.2, 146.7, 145.4, 139.7, 131.0, 127.9, 127.8, 127.5, 126.4, 125.4, 111.6, 110.7, 104.2, 100.2, 92.6, 55.4, 54.3, 50.0, 47.7, 40.6, 35.1, 24.3, 22.0; IR (KBr) υ: 3446, 3273, 2950, 2926, 2864, 2826, 1642, 1611, 1489, 1418, 1335, 1315, 1219, 1185, 1139, 1093, 1033, 953, 914, 879, 829, 800, 769 cm^{-1}; HRMS (ESI) Calcd. for $C_{25}H_{25}ClN_2NaO_3$ ($[M+Na]^+$): 459.1992. Found: 459.1945.

Ethyl 9-methoxy-12b-methyl-2-phenyl-1,2,6,7,12,12b-hexahydroindolo[*2,3-a*]quinolizine-3-carboxylate (4g): white solid, 64%, m.p.266~268℃; ^{1}H NMR (600 MHz, DMSO-d_6) δ: *cis/trans* = 1:5; *trans-isomer*: 10.98 (s, 1H, NH), 7.81 (brs, 1H, CH), 7.41~7.38 (m, 1H, ArH), 7.33~7.28 (m, 5H, ArH), 7.18~7.15 (m, 1H, ArH), 7.06~7.02 (m, 1H, ArH), 6.96 (t, *J* = 7.2Hz, 1H, ArH), 4.01~3.98 (m, 3H, CH), 3.83~3.81 (m, 1H, CH), 3.65~3.60 (m, 1H, CH), 2.89 (d, *J* = 13.2Hz, 1H, CH), 2.76~2.73 (m, 1H, CH), 2.69~2.66 (m, 1H, CH), 2.00 (dd, J_1 = 13.2Hz, J_2 = 6.6Hz, 1H, CH), 1.10 (t, *J* = 6.6Hz, 3H, CH_3), 0.99 (s, 3H, CH_3); *cis-isomer*: 10.87 (s, 1H, NH), 7.66 (brs, 1H, CH), 7.24~7.23 (m, 1H, ArH), 7.20~7.19 (m, 1H, ArH), 7.12~7.09 (m, 3H, ArH), 3.80~3.77 (m, 2H, CH), 3.73~2.70 (m, 1H, CH), 3.69~3.67 (m, 1H, CH), 3.29 (brs, 1H, CH), 2.81~2.77 (m, 1H, CH), 2.61~2.58 (m, 1H, CH), 1.55 (s, 3H, CH_3), 0.85 (t, *J* = 6.6Hz, 3H, CH_3); ^{13}C NMR (150 MHz,

DMSO-d_6) δ: 167.2, 146.6, 145.5, 139.0, 135.9, 127.8, 127.5, 126.6, 126.1, 125.3, 125.2, 120.9, 118.5, 117.9, 111.0, 104.3, 93.2, 58.0, 54.2, 47.6, 40.6, 35.1, 24.3, 21.9, 14.6; IR (KBr) υ: 3417, 3241, 2978, 2911, 2856, 1664, 1585, 1445, 1363, 1308, 1221, 1187, 1142, 1090, 1038, 960, 923, 882 cm^{-1}; HRMS (ESI) Calcd. for $C_{25}H_{26}N_2NaO_2$ ($[M+Na]^+$): 409.1886. Found: 409.1893.

Supporting Information: The Detailed experiments and characterization data for all compounds can be found in Supporting Information. Crystallographic data **1a** (CCDC 916908), **1c** (CCDC 916909), **3a** (CCDC 916911), **4d** (CCDC 916910) and **4g** (CCDC 932055) have been deposited at the Cambridge Crystallographic Database Centre. These data can be obtained free of charge via www.ccdc.ac.ck./data_request/cif.

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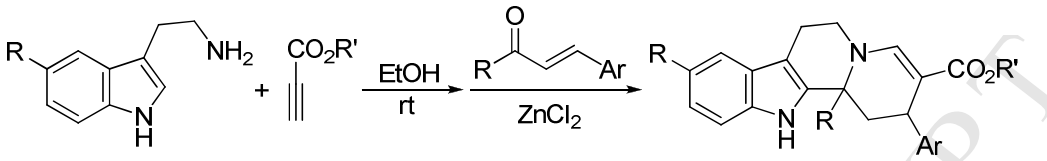
Graphic abstract

Facile construction of 1,2,6,7,12,12b-hexahydroindolo[2,3-a]quinolizines via one-pot three-component reactions of tryptamines, propiolate and

α,β-unsaturated aromatic aldehydes or ketones

Jing Sun, Li-Li Zhang, Chao-Guo Yan*



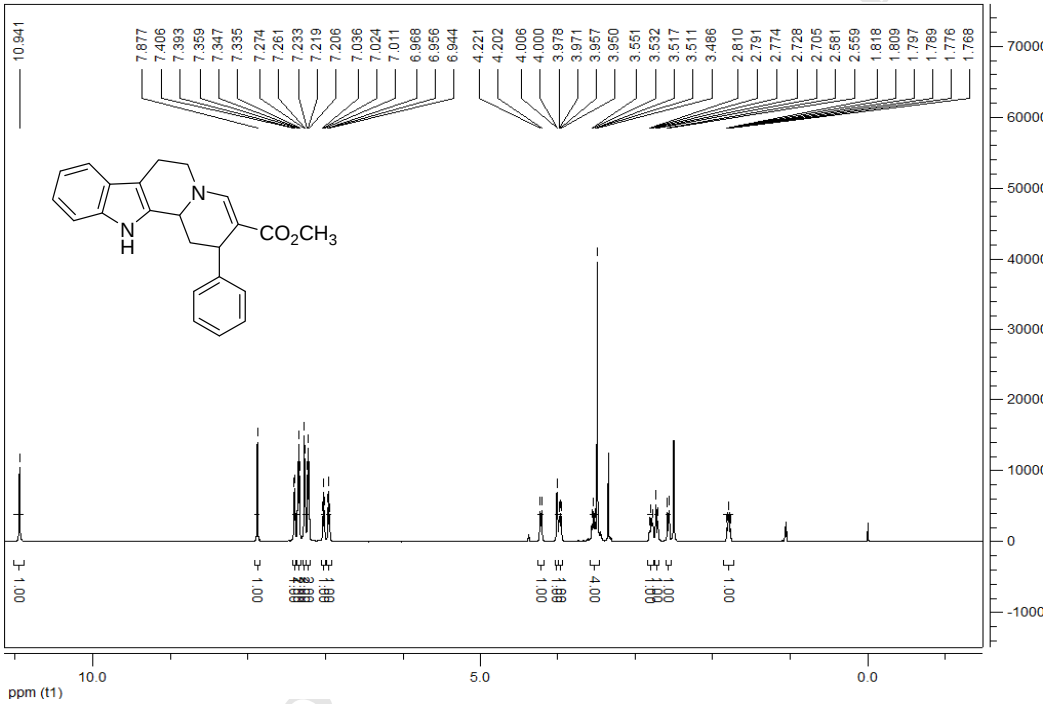
Facile construction of 1,2,6,7,12,12b-hexahydroindolo[2,3-a]quinolizines via domino Pictet-Spengler reaction of tryptamines, propiolate and α,β-unsaturated aldehydes or ketones

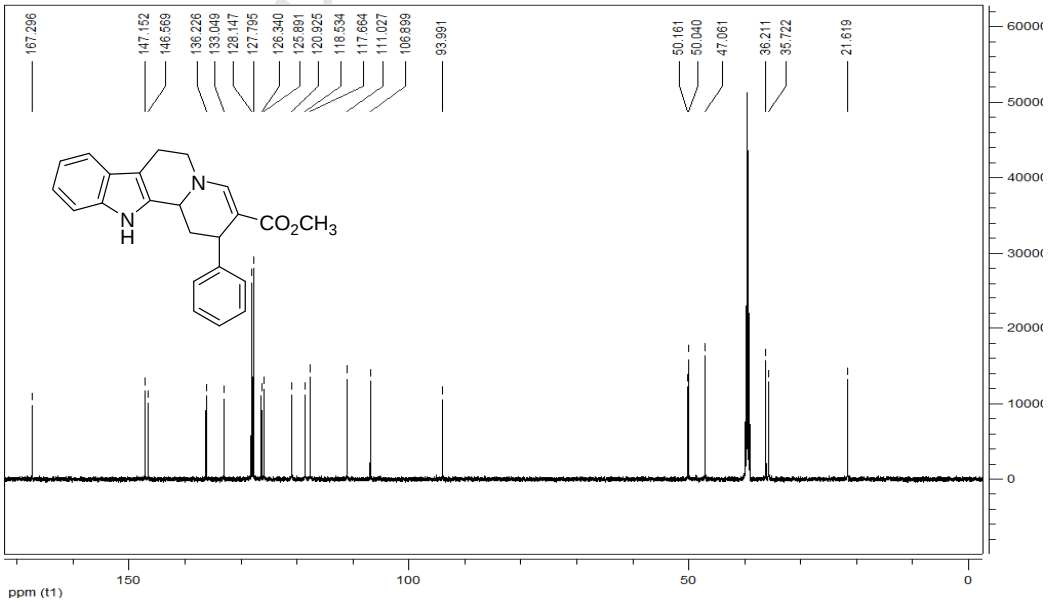
Jing Sun, Li-Li Zhang, Chao-Guo Yan*

Supporting Information

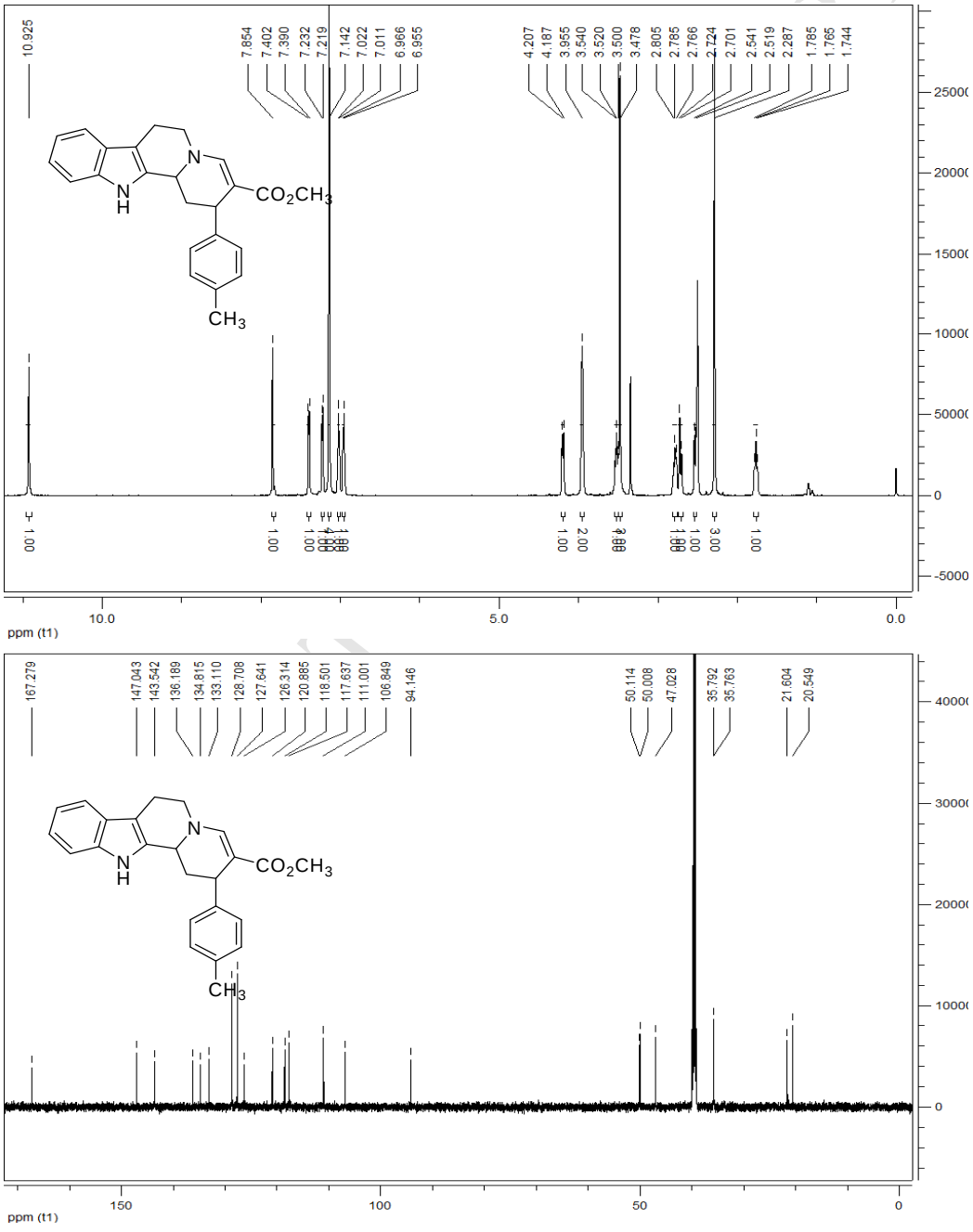
1. General procedure for the preparation of 1,2,6,7,12,12b-hexahydroindolo[2,3-a]-quinolizines 1a-1q: In a round bottom flask a mixture of tryptamines (2.0 mmol) and methyl or ethyl propiolate (2.0 mmol) in 5.0mL ethanol was stirred at room temperature for 20 minuts. Then *α,β*-unsaturated aldehydes (2.0 mmol) and anhydrous zinc chloride (1.0 mmol, 0.136 g) were added to it. The solution was stirred at room temperature for additional 48 hours. The resulting precipitates were collected by filtration and washed with cold alcohol to give the pure product.

methyl 2-phenyl-1,2,6,7,12,12b-hexahydroindolo[2,3-a]quinolizine-3-carboxylate (1a): yellow solid, 78%, m.p.279~281□; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 10.94 (s, 1H, NH), 7.88 (brs, 1H, CH), 7.40 (d, J = 7.8Hz, 1H, ArH), 7.36~7.34 (m, 2H, ArH), 7.27 (d, J = 7.8Hz, 2H, ArH), 7.23~7.21 (m, 2H, ArH), 7.02 (t, J = 7.2Hz, 1H, ArH), 6.96 (t, J = 7.2Hz, 1H, ArH), 4.21 (d, J = 11.4Hz, 1H, CH), 4.01~4.00 (m, 1H, CH), 3.98~3.95 (m, 1H, CH), 3.55~3.51 (m, 1H, CH), 3.49 (s, 3H, OCH_3), 2.81~2.77 (m, 1H, CH), 2.73~2.71 (m, 1H, CH), 2.57 (d, J = 13.2Hz, 1H, CH), 1.79 (td, J_1 = 12.6Hz, J_2 = 4.8Hz, 1H, CH); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 167.3, 147.2, 146.6, 136.2, 133.0, 128.1, 127.8, 126.3, 125.9, 121.0, 118.5, 117.7, 111.0, 106.9, 94.0, 50.2, 50.0, 47.1, 36.2, 35.7, 21.6; IR (KBr) υ: 3235, 2965, 2911, 1664, 1597, 1494, 1471, 1428, 1357, 1323, 1301, 1205, 1185, 1163, 1109, 1038, 1021, 942, 852, 790 cm^{-1}; HRMS (ESI) Calcd. for $C_{23}H_{22}N_2NaO_2$ ([M+Na]$^+$): 381.1573. Found: 381.1575.

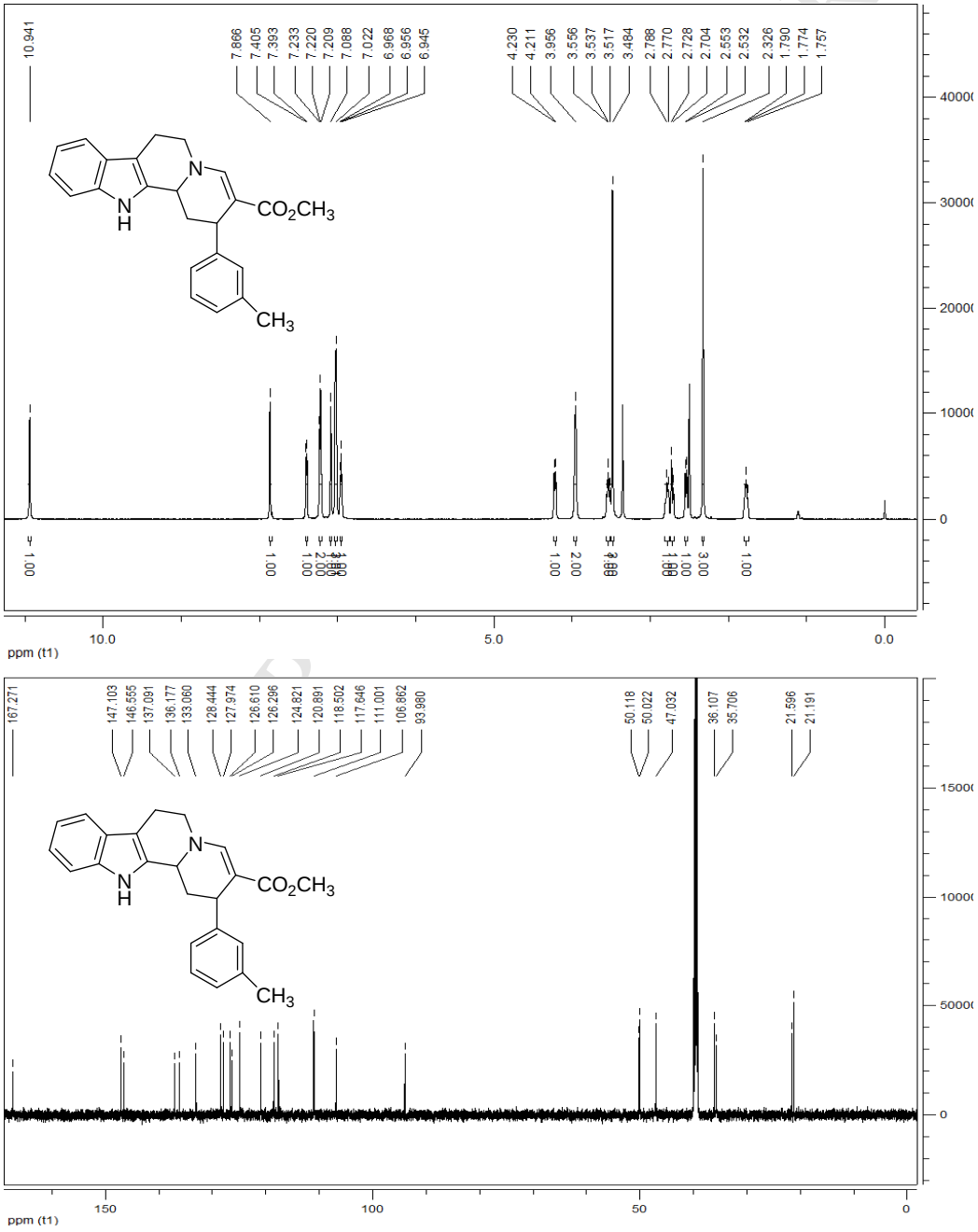




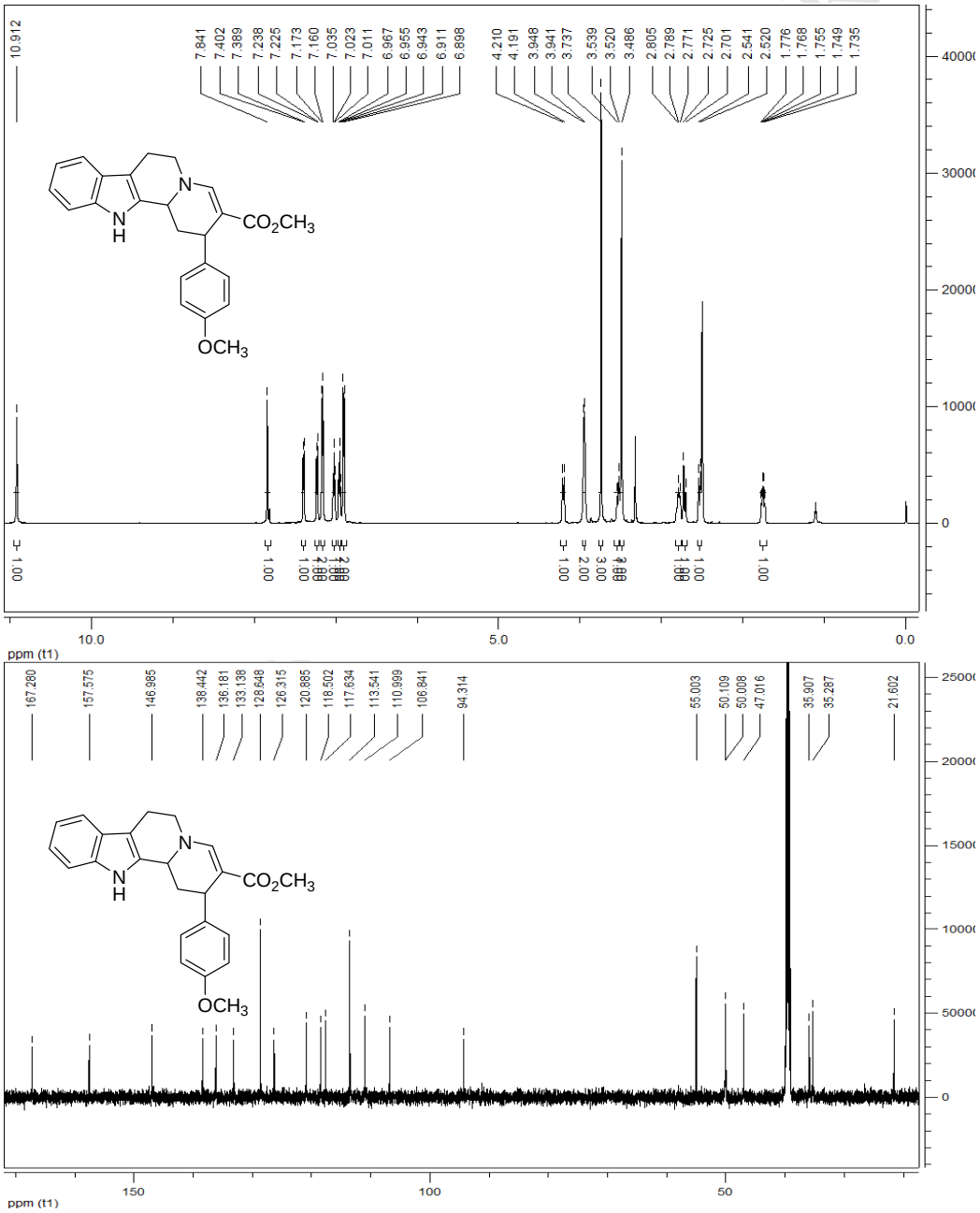
methyl 2-(4-methxylphenyl)-1,2,6,7,12,12b-hexahydroindolo[2,3-a]quinolizine-3-carboxylate (1b): yellow solid, 87%, m.p.260~262□; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 10.93 (s, 1H, NH), 7.85 (brs, 1H, CH), 7.40 (d, J = 7.2Hz, 1H, ArH), 7.23 (d, J = 7.8Hz, 1H, ArH), 7.14 (brs, 4H, ArH), 7.02~7.01 (m, 1H, ArH), 6.97~6.96 (m, 1H, ArH), 4.20 (d, J = 12.0Hz, 1H, CH), 3.96 (brs, 2H, CH), 3.54~3.50 (m, 1H, CH), 3.48 (s, 3H, OCH_3), 2.81~2.77 (m, 1H, CH), 2.72~2.70 (m, 1H, CH), 2.53 (d, J = 13.2Hz, 1H, CH), 2.29 (s, 3H, CH_3), 1.77 (t, J = 12.6Hz, 1H, CH); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 167.3, 147.0, 143.5, 136.2, 134.8, 133.1, 128.7, 127.6, 126.3, 120.9, 118.5, 117.6, 111.0, 106.8, 94.1, 50.1, 50.0, 47.0, 35.8, 35.7, 21.6, 20.5; IR (KBr) υ: 3252, 2959, 1668, 1560, 1510, 1427, 1358, 1321, 1302, 1206, 1184, 1165, 1109, 1039, 939, 855, 803, 777 cm^{-1}; HRMS (ESI) Calcd. for $C_{24}H_{24}N_2NaO_2$ ([M+Na]$^+$): 395.1730. Found: 395.1732.



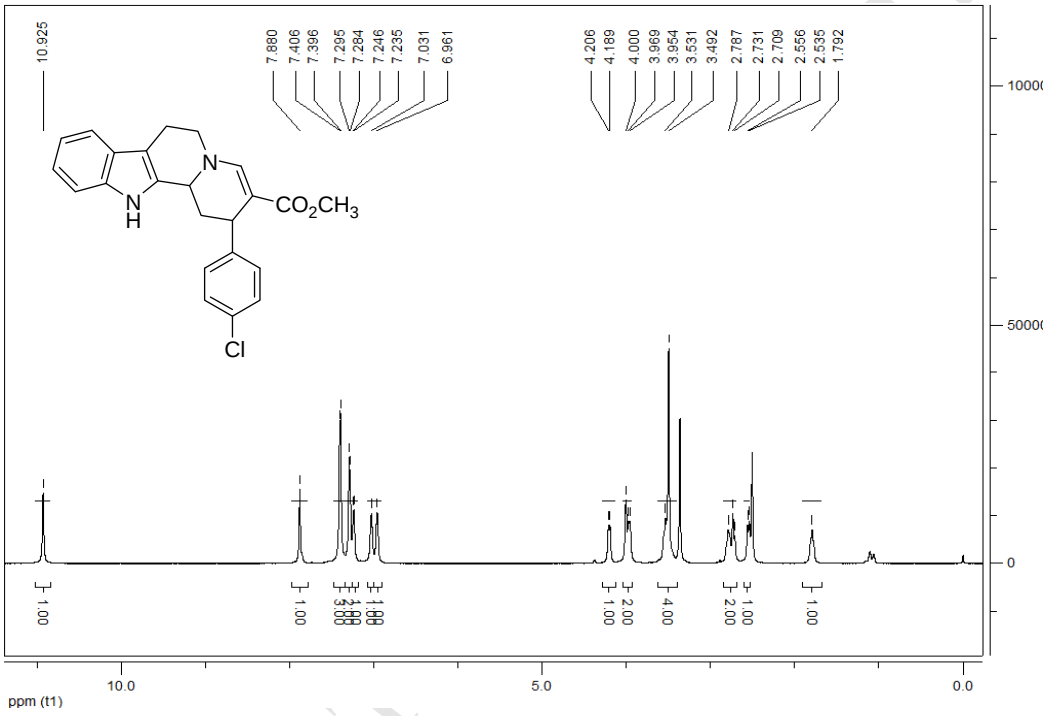
methyl 2-(3-methxylphenyl)-1,2,6,7,12,12b-hexahydroindolo[2,3-a]quinolizine-3-carboxylate (1c): yellow solid, 81%, m.p.282~284□; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 10.94 (s, 1H, NH), 7.87 (brs, 1H, CH), 7.40 (d, *J* = 7.8Hz, 1H, ArH), 7.23~7.21 (m, 2H, ArH), 7.09 (brs, 1H, ArH), 7.04~7.02 (m, 3H, ArH), 6.97~6.95 (m, 1H, ArH), 4.22 (d, *J* = 11.4Hz, 1H, CH), 3.96 (brs, 2H, CH), 3.56~3.52 (m, 1H, CH), 3.48 (s, 3H, OCH_3), 2.79~2.77 (m, 1H, CH), 2.73~2.70 (m, 1H, CH), 2.54 (d, *J* = 12.6Hz, 1H, CH), 2.33 (s, 3H, CH_3), 1.79~1.76 (m, 1H, CH); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 167.3, 147.1, 146.6, 137.1, 136.2, 133.1, 128.4, 128.0, 126.6, 126.3, 124.8, 120.9, 118.5, 117.6, 111.0, 106.9, 94.0, 50.1, 50.0, 47.0, 36.1, 35.7, 21.6, 21.2; IR (KBr) υ: 3451, 3236, 2908, 2849, 1667, 1599, 1424, 1354, 1320, 1302, 1231, 1214, 1199, 1184, 1169, 1110, 1063, 1038, 924, 882, 778 cm^{-1}; HRMS (ESI) Calcd. for $C_{24}H_{24}N_2NaO_2$ ([M+Na]$^+$): 395.1730. Found: 395.1728.

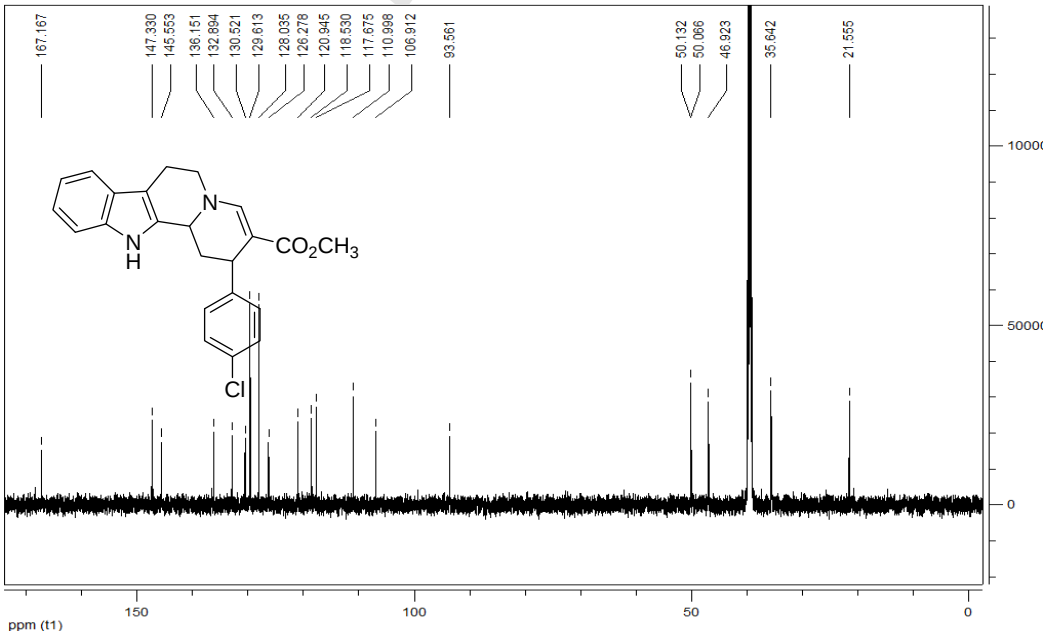


methyl 2-(4-methoxyphenyl)-1,2,6,7,12,12b-hexahydroindolo[2,3-a]quinolizine-3-carboxylate (1d): yellow solid, 83%, m.p.256~257□; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 10.91 (s, 1H, NH), 7.84 (brs, 1H, CH), 7.40 (d, J = 7.8Hz, 1H, ArH), 7.23 (d, J = 7.8Hz, 1H, ArH), 7.17 (d, J = 7.8Hz, 2H, ArH), 7.02 (t, J = 7.2Hz, 1H, ArH), 6.96 (t, J = 7.2Hz, 1H, ArH), 6.90 (d, J = 7.8Hz, 2H, ArH), 4.20 (d, J = 11.4Hz, 1H, CH), 3.95~3.94 (m, 2H, CH), 3.74 (s, 3H, OCH_3), 3.54~3.52 (m, 1H, CH), 3.49 (s, 3H, OCH_3), 2.81~2.77 (m, 1H, CH), 2.73~2.70 (m, 1H, CH), 2.53 (d, J = 12.6Hz, 1H, CH), 1.75 (td, J_1 = 12.6Hz, J_2 = 3.6Hz, 1H, CH); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 167.3, 157.6, 147.0, 138.4, 136.2, 133.1, 128.6, 126.3, 120.9, 118.5, 117.6, 113.5, 111.0, 106.8, 94.3, 55.0, 50.1, 50.0, 47.0, 35.9, 35.3, 21.6; IR (KBr) υ: 3449, 2958, 1663, 1598, 1509, 1429, 1358, 1323, 1303, 1277, 1250, 1207, 1186, 1109, 1037, 832 cm^{-1}; HRMS (ESI) Calcd. for $C_{24}H_{24}N_2NaO_3$ ([M+Na]$^+$): 411.1679. Found: 411.1682.

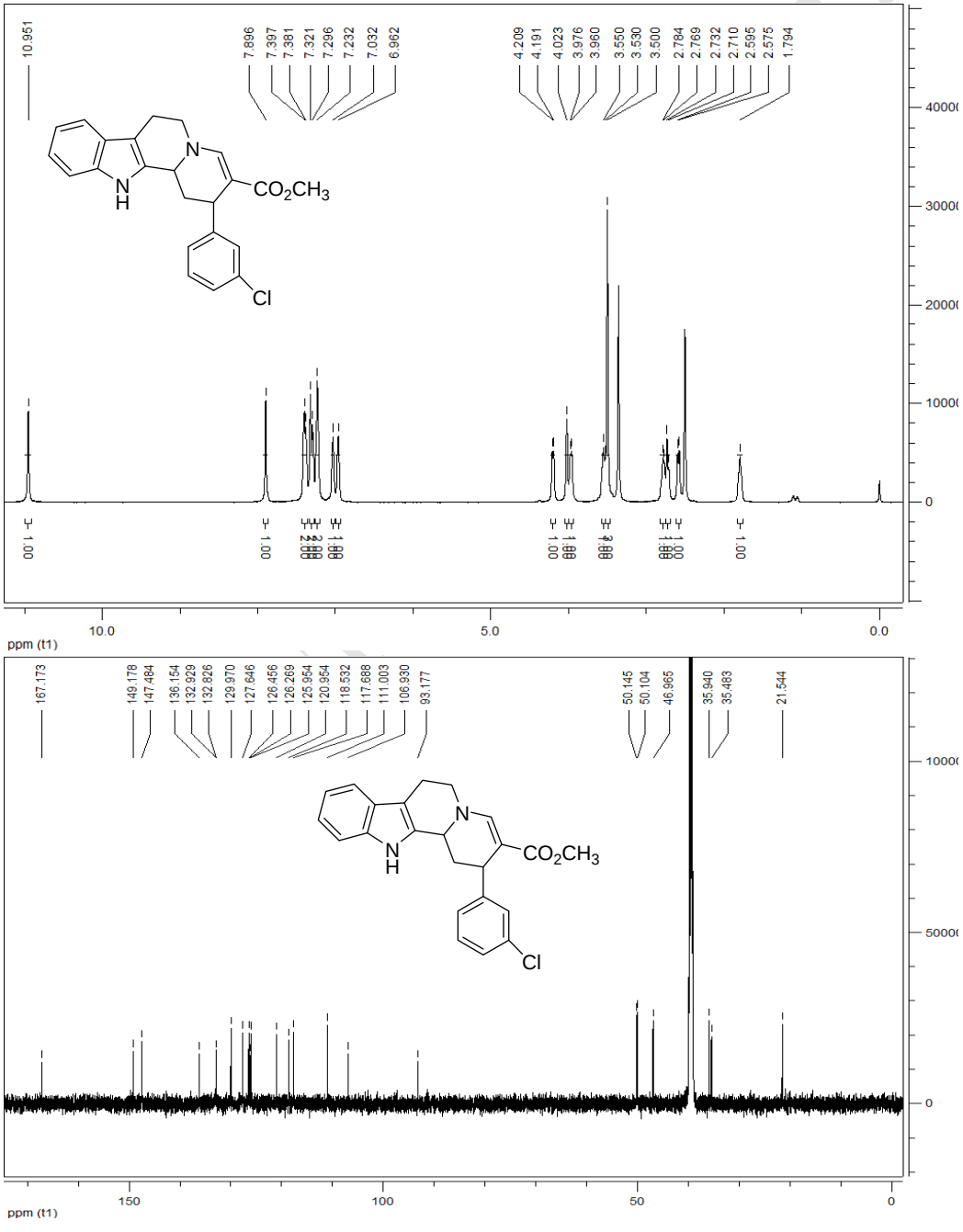


methyl 2-(4-chlorophenyl)-1,2,6,7,12,12b-hexahydroindolo[2,3-a]quinolizine-3-carboxylate (1e): yellow solid, 84%, m.p.267~268□; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 10.93 (s, 1H, NH), 7.88 (brs, 1H, CH), 7.41~7.40 (m, 3H, ArH), 7.30~7.28 (m, 2H, ArH), 7.24 (d, J = 6.6Hz, 1H, ArH), 7.03 (brs, 1H, ArH), 6.96 (brs, 1H, ArH), 4.20 (d, J = 10.2Hz, 1H, CH), 4.00~3.95 (m, 2H, CH), 3.53 (brs, 1H, CH), 3.49 (s, 3H, OCH_3), 2.79~2.71 (m, 2H, CH), 2.55 (d, J = 12.6Hz, 1H, CH), 1.79 (brs, 1H, CH); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 167.2, 147.3, 145.6, 136.2, 132.9, 130.5, 129.6, 128.0, 126.3, 120.9, 118.5, 117.8, 111.0, 106.9, 93.6, 50.1, 50.0, 46.9, 35.6, 21.6; IR (KBr) υ: 3447, 3232, 2962, 2822, 1669, 1599, 1489, 1427, 1356, 1320, 1304, 1207, 1185, 1164, 1111, 1037, 1012, 876, 854, 832, 796, 758 cm^{-1}; HRMS (ESI) Calcd. for $C_{23}H_{21}ClN_2NaO_2$ ([M+Na]$^+$): 415.1184. Found: 415.1184.

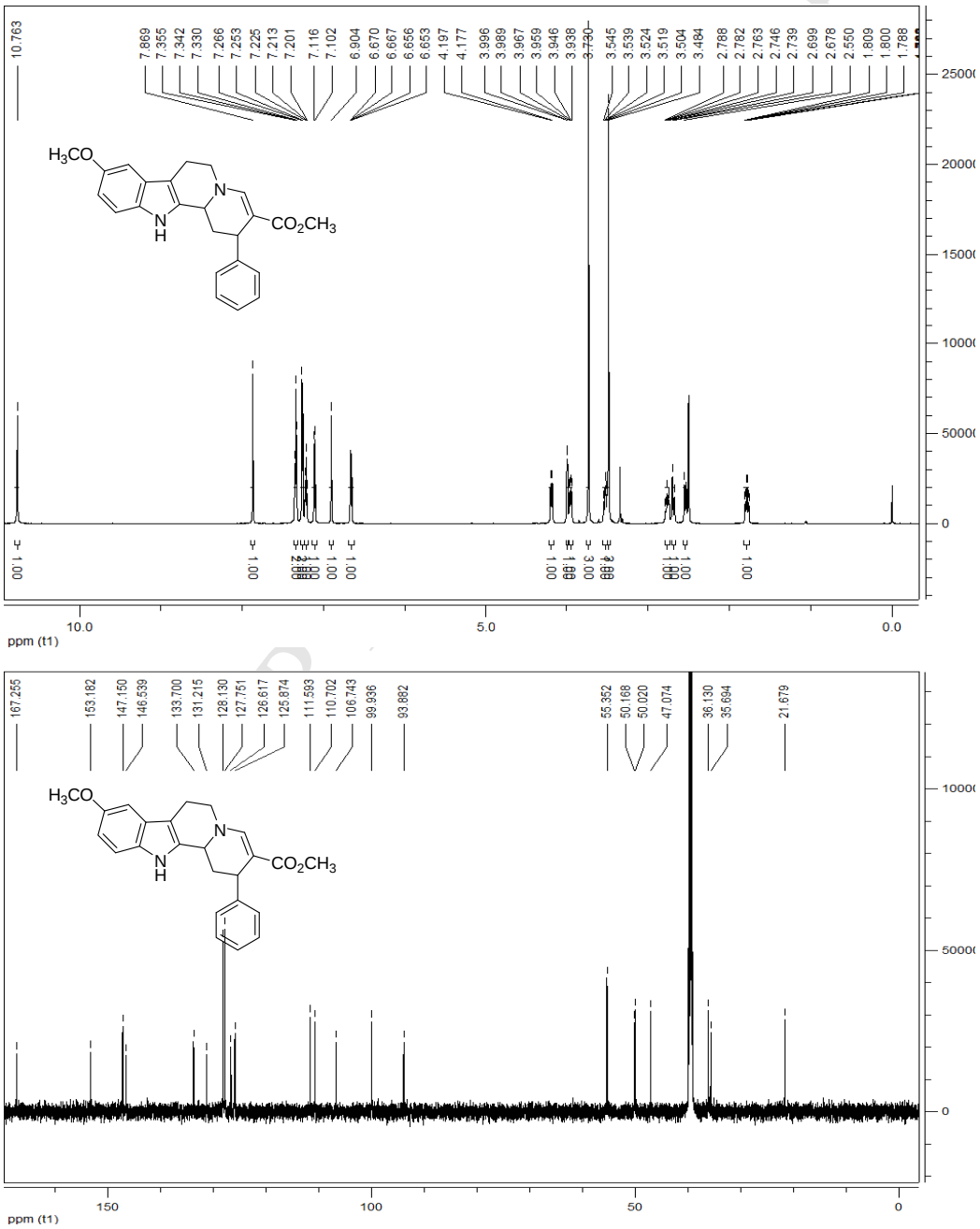




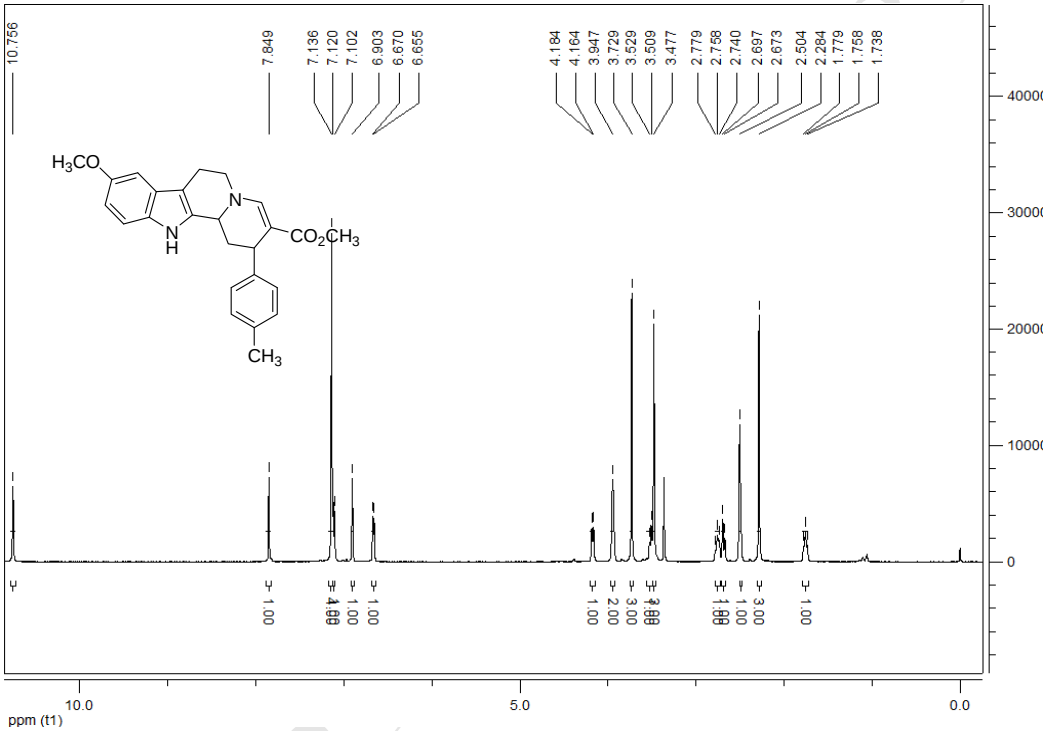
methyl 2-(3-chlorophenyl)-1,2,6,7,12,12b-hexahydroindolo[2,3-a]quinolizine-3-carboxylate (1f): yellow solid, 77%, m.p.258~260□; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 10.95 (s, 1H, NH), 7.90 (brs, 1H, CH), 7.40~7.38 (m, 2H, ArH), 7.32~7.30 (m, 2H, ArH), 7.23 (brs, 2H, ArH), 7.03 (brs, 1H, ArH), 6.96 (brs, 1H, ArH), 4.20 (d, J = 10.8Hz, 1H, CH), 4.02 (brs, 1H, CH), 3.98~3.96 (m, 1H, CH), 3.55~3.53 (m, 1H, CH), 3.50 (s, 3H, OCH_3), 2.78~2.77 (m, 1H, CH), 2.73~2.71 (m, 1H, CH), 2.59 (d, J = 12.0Hz, 1H, CH), 1.79 (brs, 1H, CH); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 167.2, 149.2, 147.5, 136.2, 132.9, 132.8, 130.0, 127.6, 126.5, 126.3, 126.0, 121.0, 118.5, 117.7, 111.0, 106.9, 93.2, 50.2, 50.1, 47.0, 35.9, 35.5, 21.5; IR (KBr) υ: 3497, 3263, 2919, 2853, 2809, 1668, 1600, 1472, 1424, 1355, 1324, 1302, 1205, 1184, 1167, 1113, 1038, 890, 862, 773 cm^{-1}; HRMS (ESI) Calcd. for $C_{23}H_{21}ClN_2NaO_2$ ([M+Na]$^+$): 415.1184. Found: 415.1184.

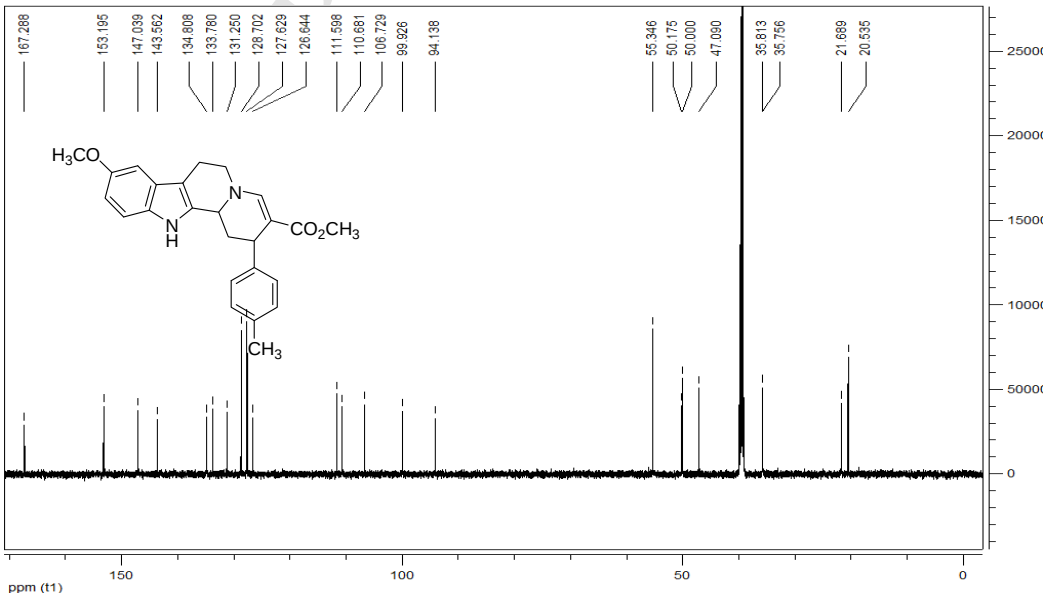


methyl 9-methoxy-2-phenyl-1,2,6,7,12,12b-hexahydroindolo[2,3-a]quinolizine-3-carboxylate (1g): yellow solid, 83%, m.p.252~253□; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 10.76 (s, 1H, NH), 7.87 (brs, 1H, CH), 7.36~7.33 (m, 2H, ArH), 7.26 (d, J = 6.6Hz, 2H, ArH), 7.21 (t, J = 7.2Hz, 1H, ArH), 7.11 (d, J = 8.4Hz, 1H, ArH), 6.90 (brs, 1H, ArH), 6.67~6.65 (m, 1H, ArH), 4.19 (d, J = 12.0Hz, 1H, CH), 4.00~3.99 (m, 1H, CH), 3.97~3.94 (m, 1H, CH), 3.73 (s, 3H, OCH_3), 3.55~3.50 (m, 1H, CH), 3.48 (s, 3H, OCH_3), 2.79~2.74 (m, 1H, CH), 2.69 (d, J = 12.6Hz, 1H, CH), 2.54 (d, J = 12.6Hz, 1H, CH), 1.78 (td, J_1 = 12.6Hz, J_2 = 4.8Hz, 1H, CH); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 167.3, 153.2, 147.2, 146.5, 133.7, 131.2, 128.1, 127.8, 126.6, 125.9, 111.6, 110.7, 106.7, 99.9, 93.9, 55.4, 50.2, 50.0, 47.1, 36.1, 35.7, 21.7; IR (KBr) υ: 3244, 2913, 2826, 1665, 1584, 1490, 1444, 1426, 1362, 1321, 1301, 1222, 1205, 1179, 1159, 1106, 1061, 1036, 945, 934, 805, 756 cm^{-1}; HRMS (ESI) Calcd. for $C_{24}H_{24}N_2NaO_3$ ([M+Na]$^+$): 411.1679. Found: 411.1670.

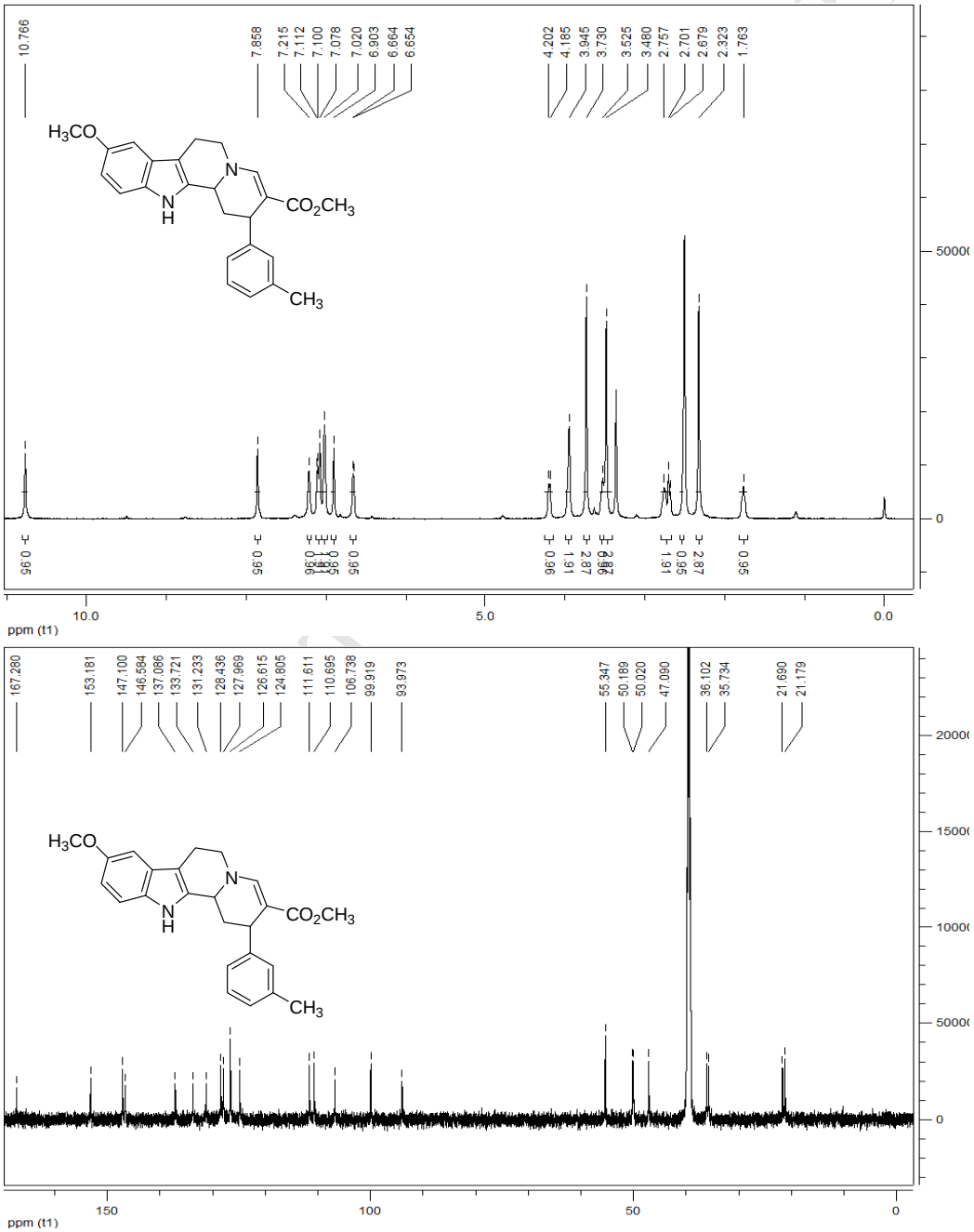


methyl 9-methoxy-2-(4-methylphenyl)-1,2,6,7,12,12b-hexahydroindolo[2,3-a]quinolizine-3-carboxylate (1h): yellow solid, 86%, m.p.238~240□; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 10.76 (s, 1H, NH), 7.85 (brs, 1H, CH), 7.14 (brs, 4H, CH), 7.12~7.10 (m, 1H, ArH), 6.90 (brs, 1H, CH), 6.66 (d, J = 9.0Hz, 1H, ArH), 4.17 (d, J = 12.0Hz, 1H, CH), 3.95 (brs, 2H, CH), 3.73 (s, 3H, OCH_3), 3.53~3.51 (m, 1H, CH), 3.48 (s, 3H, OCH_3), 2.78~2.74 (m, 1H, CH), 2.70~2.67 (m, 1H, CH), 2.46 (brs, 1H, CH), 2.28 (s, 3H, CH_3), 1.76 (t, J = 12.0Hz, 1H, CH); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 167.3, 153.2, 147.0, 143.6, 134. 8, 133.8, 131.3, 128.7, 127.6, 126.6, 111.6, 110.7, 106.7, 99.9, 94.1, 55.3, 50.2, 50.0, 47.1, 35.8, 35.7, 21.7, 20.5; IR (KBr) υ: 3237, 2945, 1665, 1583, 1510, 1485, 1452, 1432, 1373, 1318, 1296, 1205, 1181, 1163, 1135, 1106, 1026, 855, 823, 802, 774 cm^{-1}; HRMS (ESI) Calcd. for $C_{25}H_{26}N_2NaO_3$ ([M+Na]$^+$): 425.1836. Found: 425.1826.

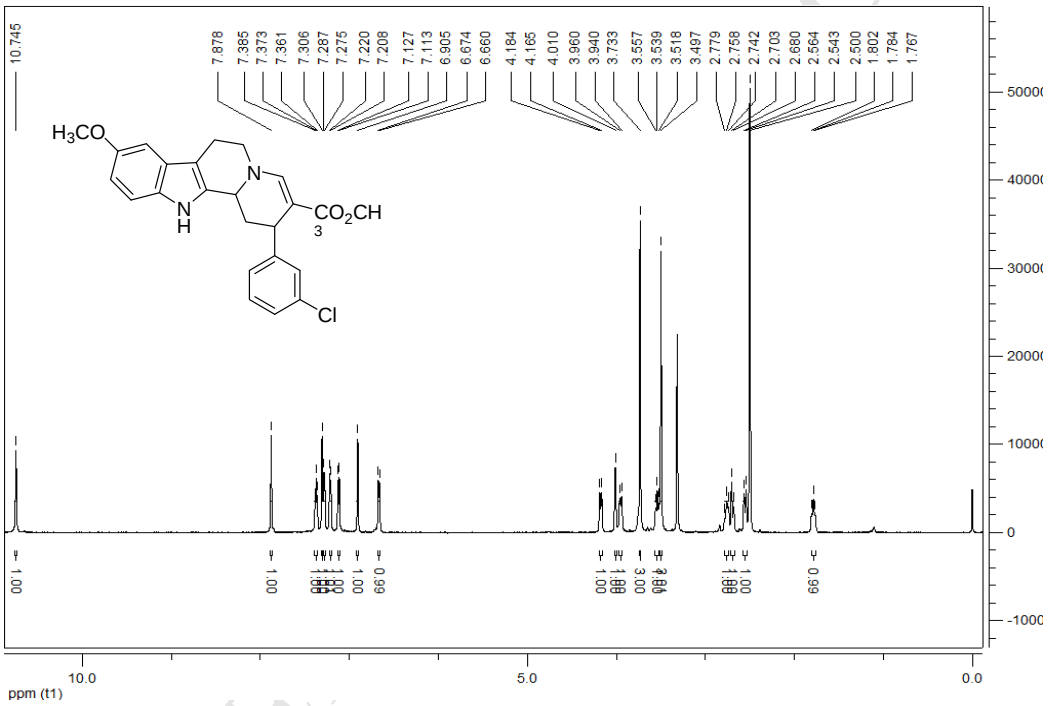


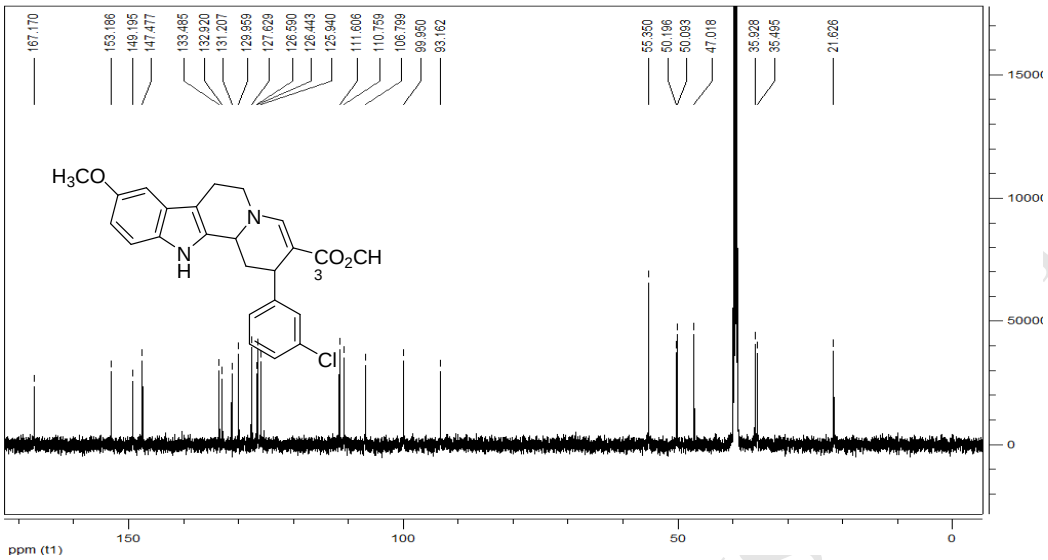


methyl 9-methoxy-2-(3-methylphenyl)-1,2,6,7,12,12b-hexahydroindolo[2,3-a]quinolizine-3-carboxylate (1i): yellow solid, 79%, m.p.226~228□; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 10.77 (s, 1H, NH), 7.86 (brs, 1H, CH), 7.22 (brs, 1H, ArH), 7.11~7.08 (m, 2H, ArH), 7.02 (brs, 2H, CH), 6.90 (brs, 1H, CH), 6.66~6.65 (m, 1H, ArH), 4.19 (d, J = 10.2Hz, 1H, CH), 3.95 (brs, 2H, CH), 3.73 (s, 3H, OCH_3), 3.56~3.53 (m, 1H, CH), 3.48 (s, 3H, OCH_3), 2.76~2.68 (m, 2H, CH), 2.54 (brs, 1H, CH), 2.32 (s, 3H, CH_3), 1.76 (brs, 1H, CH); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 167.3, 153.2, 147.1, 146.6, 137.1, 133.7, 131.2, 128.4, 128.0, 126.6, 124.8, 111.6, 110.7, 106.7, 99.9, 94.0, 55.3, 50.2, 50.0, 47.1, 36.1, 35.7, 21.7, 21.2; IR (KBr) υ: 3236, 2947, 2847, 1663, 1584, 1483, 1435, 1361, 1317, 1301, 1214, 1196, 1182, 1160, 1107, 1058, 1034, 888, 831, 800, 776 cm^{-1}; HRMS (ESI) Calcd. for $C_{25}H_{26}N_2NaO_3$ ([M+Na]$^+$): 425.1836. Found: 425.1827.

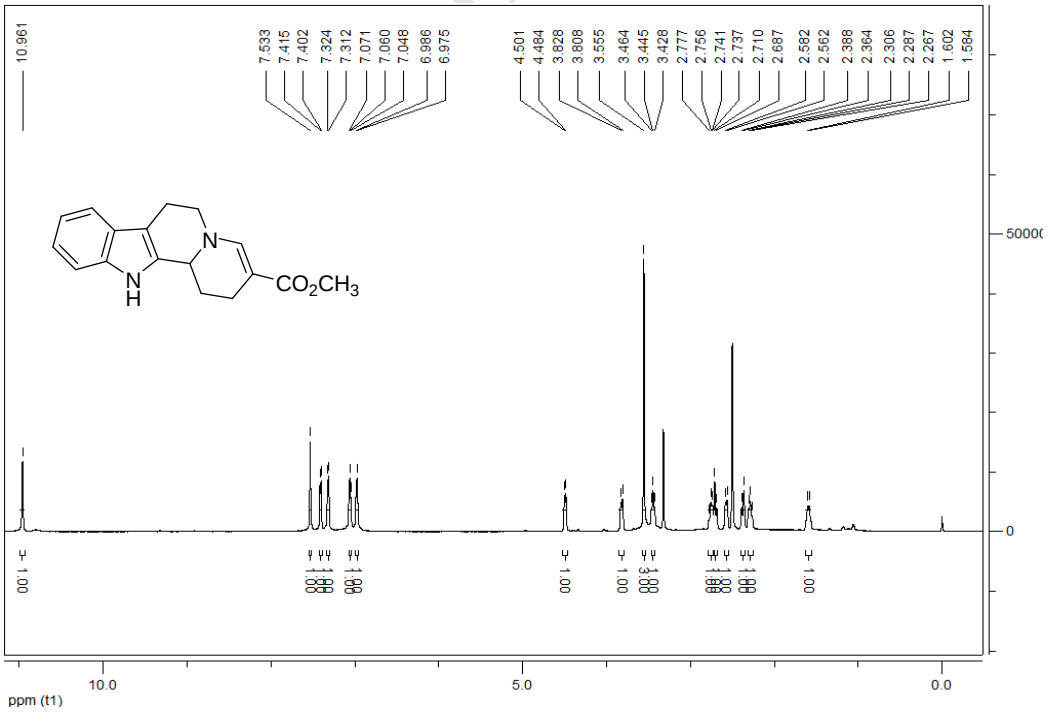


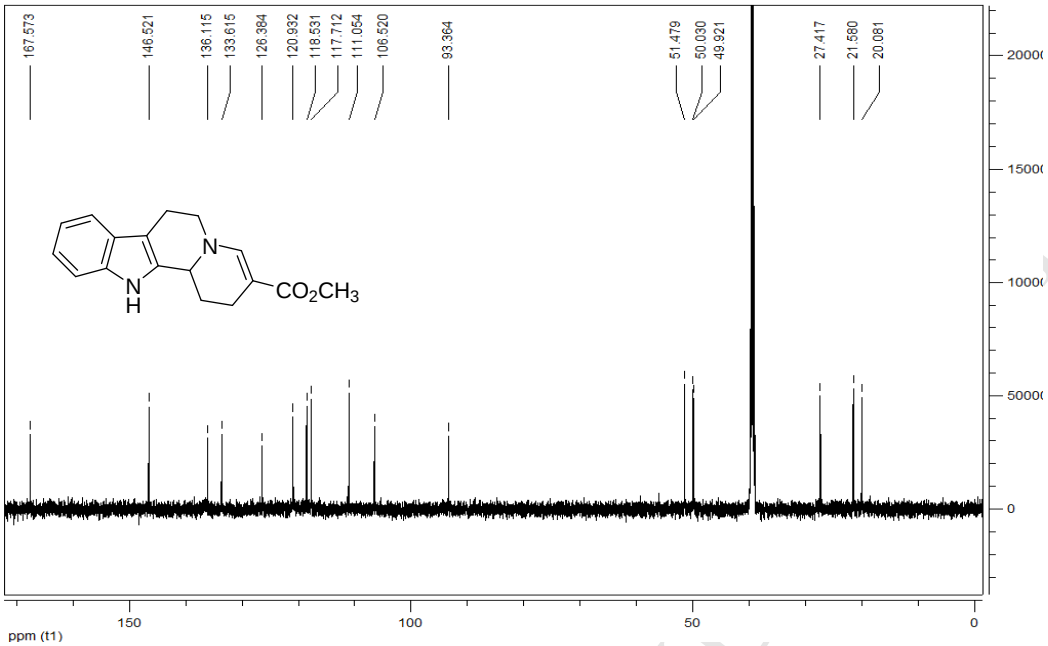
methyl 9-methoxy-2-(3-chlorophenyl)-1,2,6,7,12,12b-hexahydroindolo[2,3-a]quinolizine-3-carboxylate (1j): white solid, 80%, m.p.244~245℃; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 10.75 (s, 1H, NH), 7.88 (brs, 1H, CH), 7.37 (t, *J* = 7.2Hz, 1H, ArH), 7.31 (brs, 1H, ArH), 7.28 (d, *J* = 7.8Hz, 1H, ArH), 7.21 (d, *J* = 7.8Hz, 1H, ArH), 7.12 (t, *J* = 8.4Hz, 1H, ArH), 6.91 (brs, 1H, ArH), 6.67 (d, *J* = 8.4Hz, 1H, ArH), 4.17 (d, *J* = 11.4Hz, 1H, CH), 4.01 (brs, 1H, CH), 3.96~3.94 (m, 1H, CH), 3.73 (s, 3H, OCH_3), 3.56~3.52 (m, 1H, CH), 3.50 (s, 3H, OCH_3), 2.78~2.74 (m, 1H, CH), 2.70~2.68 (m, 1H, CH), 2.55 (d, *J* = 12.6Hz, 1H, CH), 1.88~1.77 (m, 1H, CH); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 167.2, 153.2, 149.2, 147.5, 133.5, 132.9, 131.2, 130.0, 127.6, 126.6, 126.4, 125.9, 111.6, 110.8, 106.8, 100.0, 93.2, 55.4, 50.2, 50.1, 47.0, 35.9, 35.5, 21.6; IR (KBr) υ: 3499, 3244, 2950, 2838, 1666, 1586, 1484, 1429, 1360, 1335, 1312, 1207, 1183, 1161, 1110, 1061, 1034, 888, 858, 832, 797, 768 cm^{-1}; HRMS (ESI) Calcd. for $C_{24}H_{23}ClN_2NaO_3$ ([M+Na]$^+$): 445.1289. Found: 445.1284.





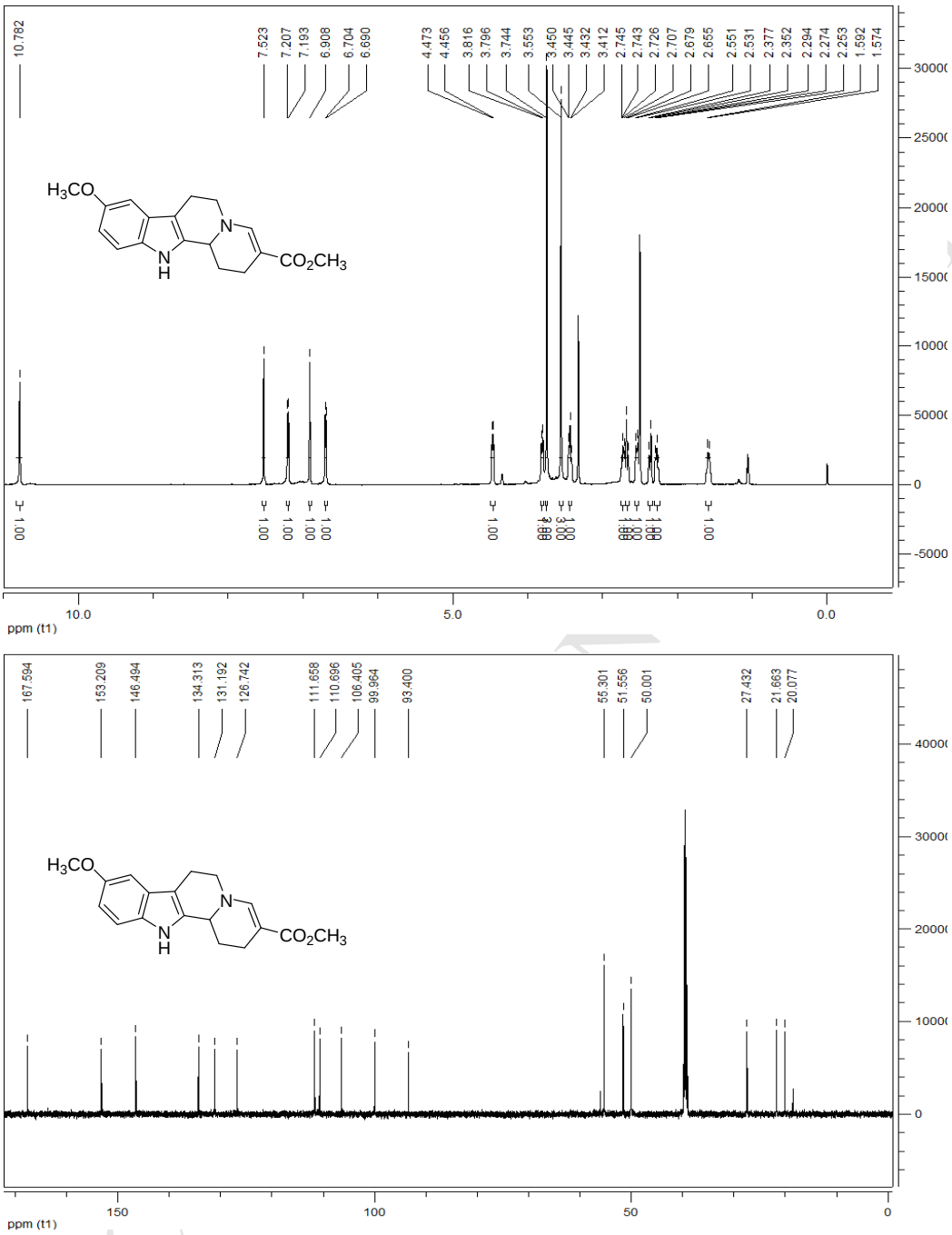
methyl 1,2,6,7,12,12b-hexahydroindolo[2,3-a]quinolizine-3-carboxylate (1k): yellow solid, 80%, m.p.156~158□; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 10.96 (s, 1H, NH), 7.53 (brs, 1H, CH), 7.41 (d, J = 7.8Hz, 1H, ArH), 7.32 (d, J = 7.2Hz, 1H, ArH), 7.07~7.05 (m, 1H, ArH), 6.99~6.98 (m, 1H, ArH), 4.99 (d, J = 10.2Hz, 1H, CH), 3.82 (d, J = 12.0Hz, 1H, CH), 3.56 (s, 3H, OCH_3), 3.46~3.43 (m, 1H, CH), 2.78~2.74 (m, 1H, CH), 2.71~2.69 (m, 1H, CH), 2.57 (d, J = 12.0Hz, 1H, CH), 2.39~2.36 (m, 1H, CH), 2.31~2.27 (m, 1H, CH), 1.60~1.58 (m, 1H, CH); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 167.6, 146.5, 136.1, 133.6, 126.4, 120.9, 118.5, 117.7, 111.1, 106.5, 93.4, 51.5, 50.0, 49.9, 27.4, 21.6, 20.1; IR (KBr) υ: 3293, 2938, 2849, 1654, 1610, 1493, 1439, 1418, 1356, 1332, 1301, 1244, 1205, 1182, 1154, 1095, 1063, 1037, 1002, 933, 829 cm^{-1}; HRMS (ESI) Calcd. for $C_{17}H_{18}N_2NaO_2$ ([M+Na]$^+$): 305.1260. Found: 305.1255.





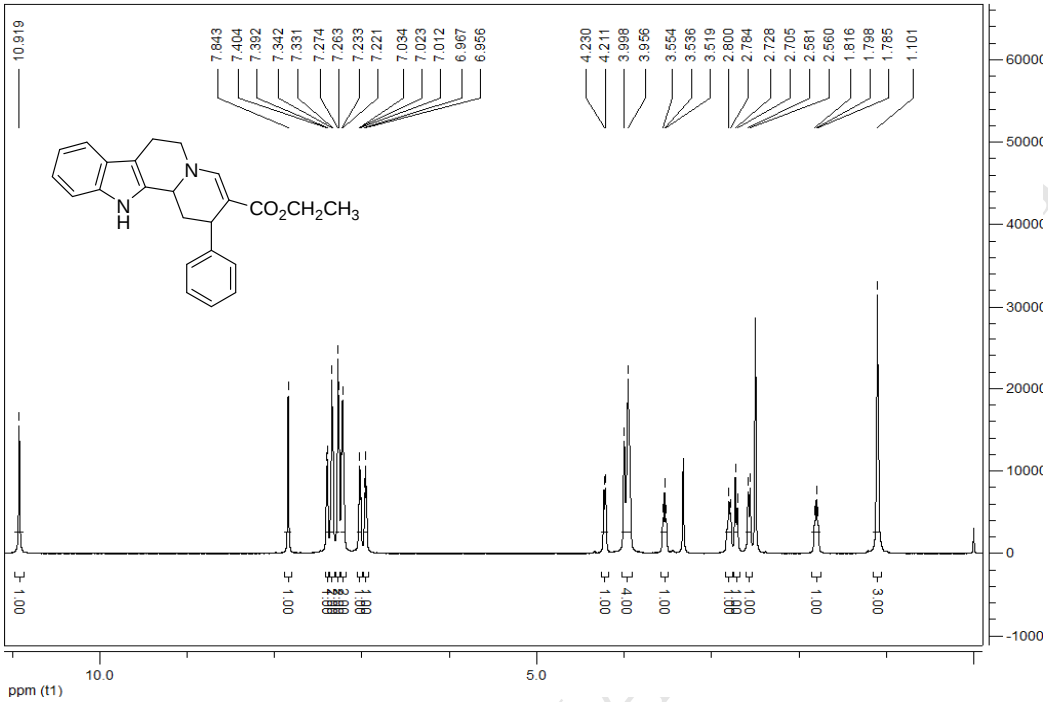
methyl 9-methoxy-1,2,6,7,12,12b-hexahydroindolo[2,3-a]quinolizine-3-carboxylate (1l):

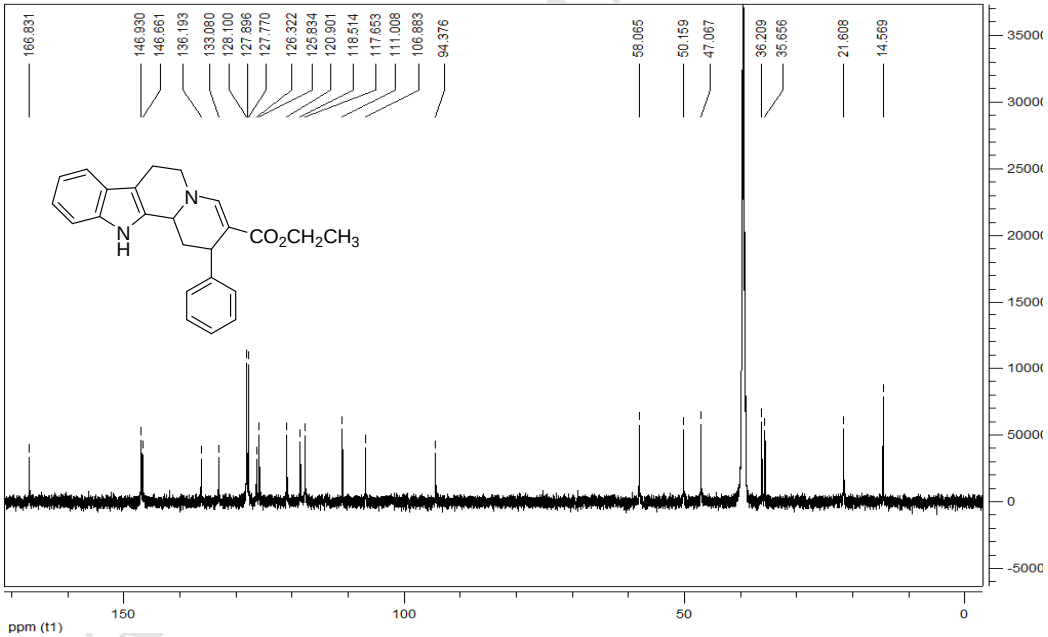
yellow solid, 76%, m.p.204~206℃; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 10.78 (s, 1H, NH), 7.52 (brs, 1H, CH), 7.20 (d, J = 8.4Hz, 1H, ArH), 6.91 (brs, 1H, ArH), 6.70 (d, J = 8.4Hz, 1H, ArH), 4.46 (d, J = 10.2Hz, 1H, CH), 3.81 (d, J = 12.0Hz, 1H, CH), 3.74 (s, 3H, OCH_3), 3.55 (s, 3H, OCH_3), 3.45~3.41 (m, 1H, CH), 2.75~2.71 (m, 1H, CH), 2.68~2.66 (m, 1H, CH), 2.54 (d, J = 12.0Hz, 1H, CH), 2.38~2.35 (m, 1H, CH), 2.29~2.25 (m, 1H, CH), 1.59~1.57 (m, 1H, CH); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 167.6, 153.2, 146.5, 134.3, 131.2, 126.7, 111.7, 110.7, 106.4, 100.0, 93.4, 55.3, 51.6, 50.0, 27.4, 21.7, 20.1; IR (KBr) υ: 3229, 2942, 2902, 2843, 1664, 1587, 1487, 1436, 1356, 1303, 1211, 1180, 1151, 1106, 1060, 1031, 940, 913, 834, 794 cm^{-1}; HRMS (ESI) Calcd. for $C_{18}H_{20}N_2NaO_3$ ($[M+Na]^+$): 335.1366. Found: 335.1364.



ethyl 2-phenyl-1,2,6,7,12,12b-hexahydroindolo[2,3-a]quinolizine-3-carboxylate (1m): yellow solid, 84%, m.p.256~258℃; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 10.92 (s, 1H, NH), 7.84 (brs, 1H, CH), 7.40 (d, J = 7.2Hz, 1H, ArH), 7.34~7.33 (m, 2H, ArH), 7.27~7.26 (m, 2H, ArH), 7.23~7.22 (m, 2H, ArH), 7.02 (t, J = 6.6Hz, 1H, ArH), 6.97~6.96 (m, 1H, ArH), 4.22 (d, J = 11.4Hz, 1H, CH), 4.00~3.96 (m, 4H, CH), 3.55~3.52 (m, 1H, CH), 2.80~2.78 (m, 1H, CH), 2.73~2.71 (m, 1H, CH), 2.57 (d, J = 12.6Hz, 1H, CH), 1.82~1.79 (m, 1H, CH), 1.10 (brs, 3H, CH_3); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 166.8, 146.9, 146.7, 136.2, 133.1, 128.1, 127.9, 127.8, 126.3, 125.8, 120.9, 118.5, 117.7, 111.0, 106.9, 94.4, 58.1, 50.2, 47.1, 36.2, 35.7, 21.6, 14.6; IR (KBr) υ: 3450, 3232, 2978,

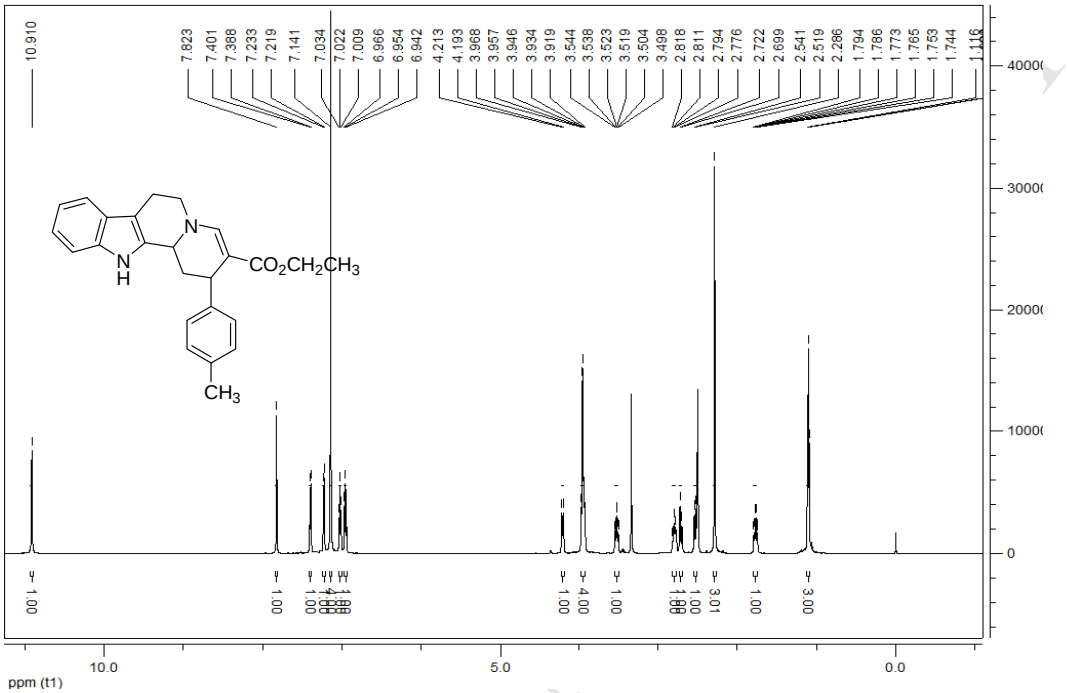
2911, 2851, 1663, 1588, 1494, 1473, 1438, 1363, 1320, 1300, 1209, 1185, 1166, 1108, 1039, 1018, 940, 789 cm^{-1}; HRMS (ESI) Calcd. for $C_{24}H_{24}N_2NaO_2$ ($[M+Na]^+$): 395.1730. Found: 395.1727.

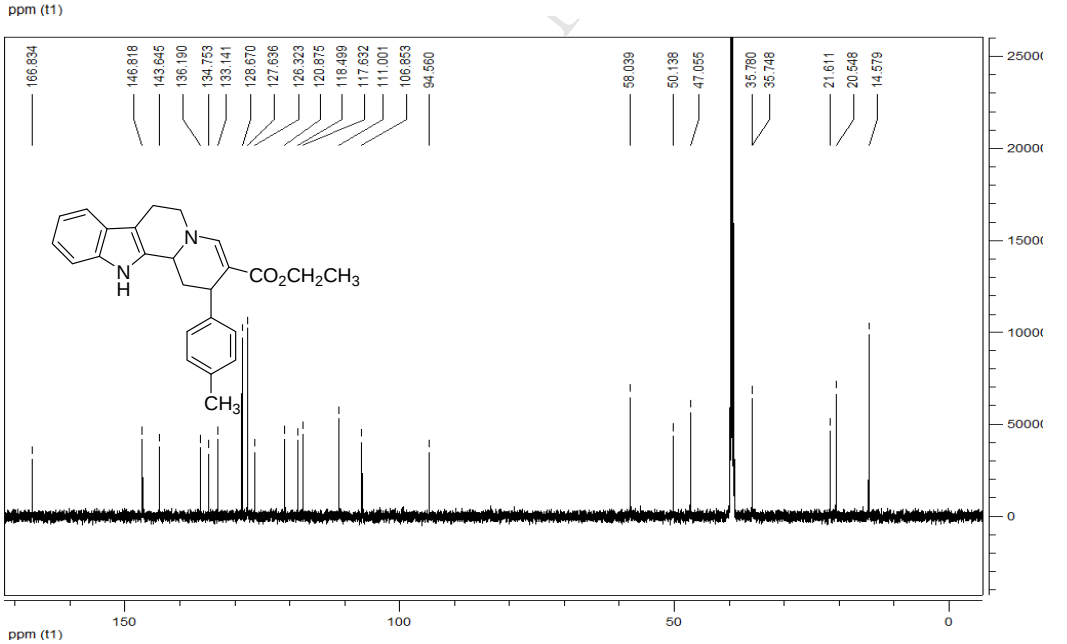




ethyl 2-(4-methylphenyl)-1,2,6,7,12,12b-hexahydroindolo[2,3-a]quinolizine-3-carboxylate (1n): yellow solid, 85%, m.p.226~227℃; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 10.91 (s, 1H, NH), 7.82 (brs, 1H, CH), 7.39 (d, J = 7.8Hz, 1H, ArH), 7.23 (d, J = 8.4Hz, 1H, ArH), 7.14 (brs, 4H, ArH), 7.02 (t, J = 7.8Hz, 1H, ArH), 6.95 (t, J = 7.2Hz, 1H, ArH), 4.20 (d, J = 12.0Hz, 1H, CH), 3.97~3.92 (m, 4H, CH), 3.54~3.50 (m, 1H, CH), 2.82~2.78 (m, 1H, CH), 2.72~2.70 (m, 1H, CH), 2.53 (d, J = 13.2Hz, 1H, CH), 2.29 (s, 3H, CH_3), 1.77 (td, J_1 = 12.6Hz, J_2 = 4.8Hz, 1H, CH), 1.10

(t, J = 7.2Hz, 3H, CH_3); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 166.8, 146.8, 143.6, 136.2, 134.8, 133.1, 128.7, 127.6, 126.3, 120.9, 118.5, 117.6, 111.0, 106.9, 94.6, 58.0, 50.1, 47.1, 35.8, 35.7, 21.6, 20.5, 14.6; IR (KBr) υ: 3449, 2967, 2915, 2852, 2804, 1662, 1587, 1509, 1473, 1442, 1363, 1320, 1301, 1208, 1166, 1107, 1040, 1016, 940, 875, 808, 775 cm^{-1}; HRMS (ESI) Calcd. for $C_{25}H_{26}N_2NaO_2$ ($[M+Na]^+$): 409.1886. Found: 409.1885.

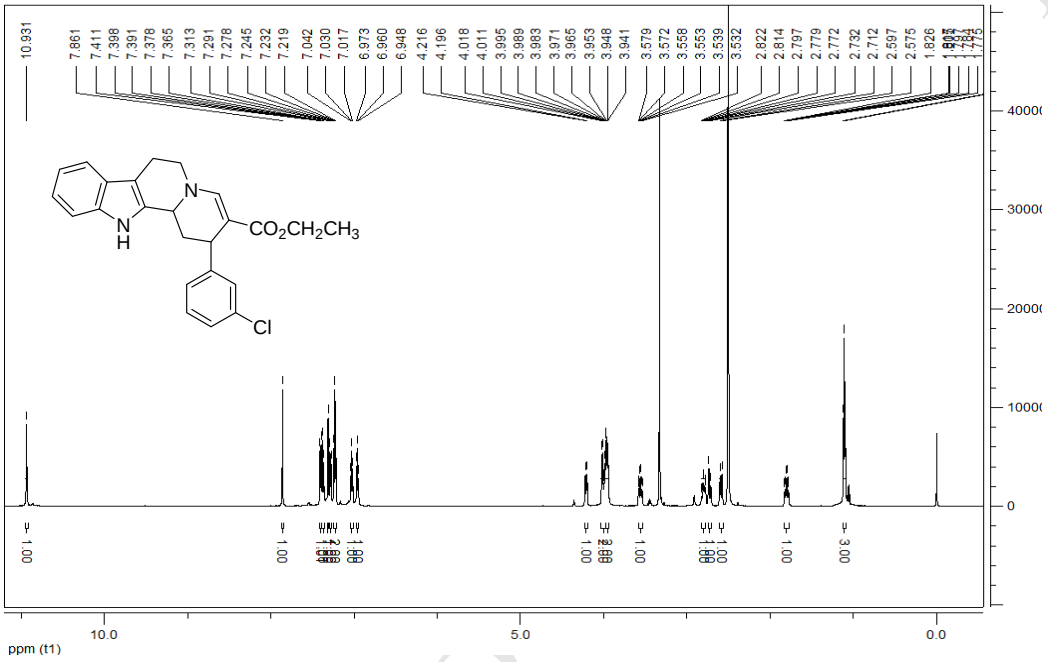


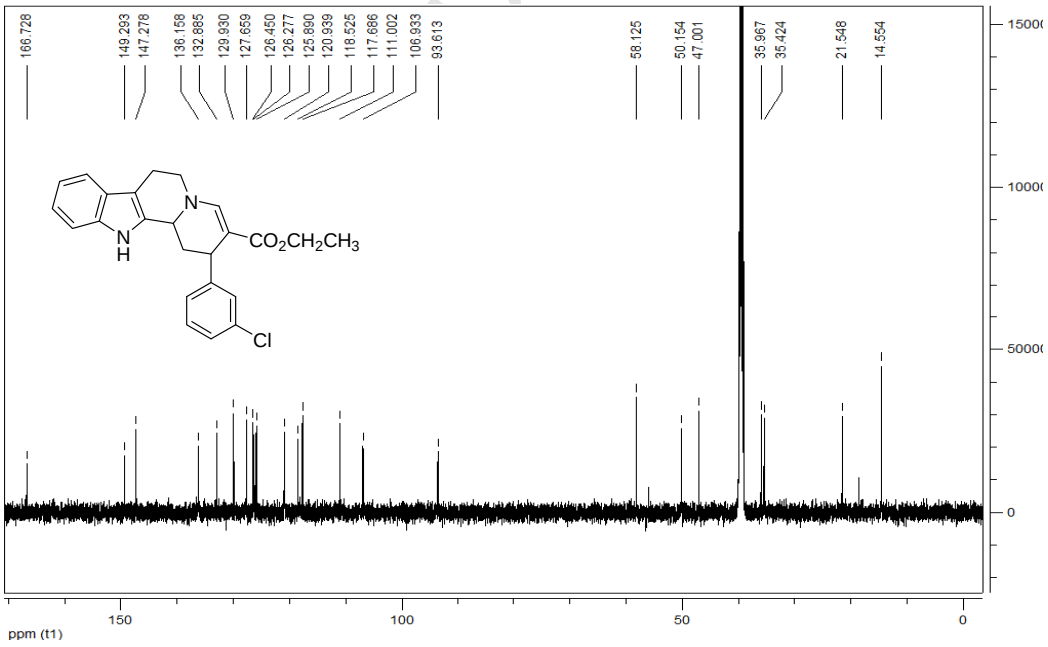


ethyl 2-(3-chlorophenyl)-1,2,6,7,12,12b-hexahydroindolo[2,3-a]quinolizine-3-carboxylate (1o):

yellow solid, 75%, m.p. > 300℃; ^1H NMR (600 MHz, DMSO-d_6) δ: 10.93 (s, 1H, NH), 7.86 (brs, 1H, CH), 7.41~7.39 (m, 1H, ArH), 7.37 (d, J = 7.8Hz, 1H, ArH), 7.31 (brs, 1H, ArH), 7.28 (d, J = 7.8Hz, 1H, ArH), 7.23 (t, J = 7.8Hz, 2H, ArH), 7.04~7.39 (m, 1H, ArH), 6.97~6.95 (m, 1H, ArH),

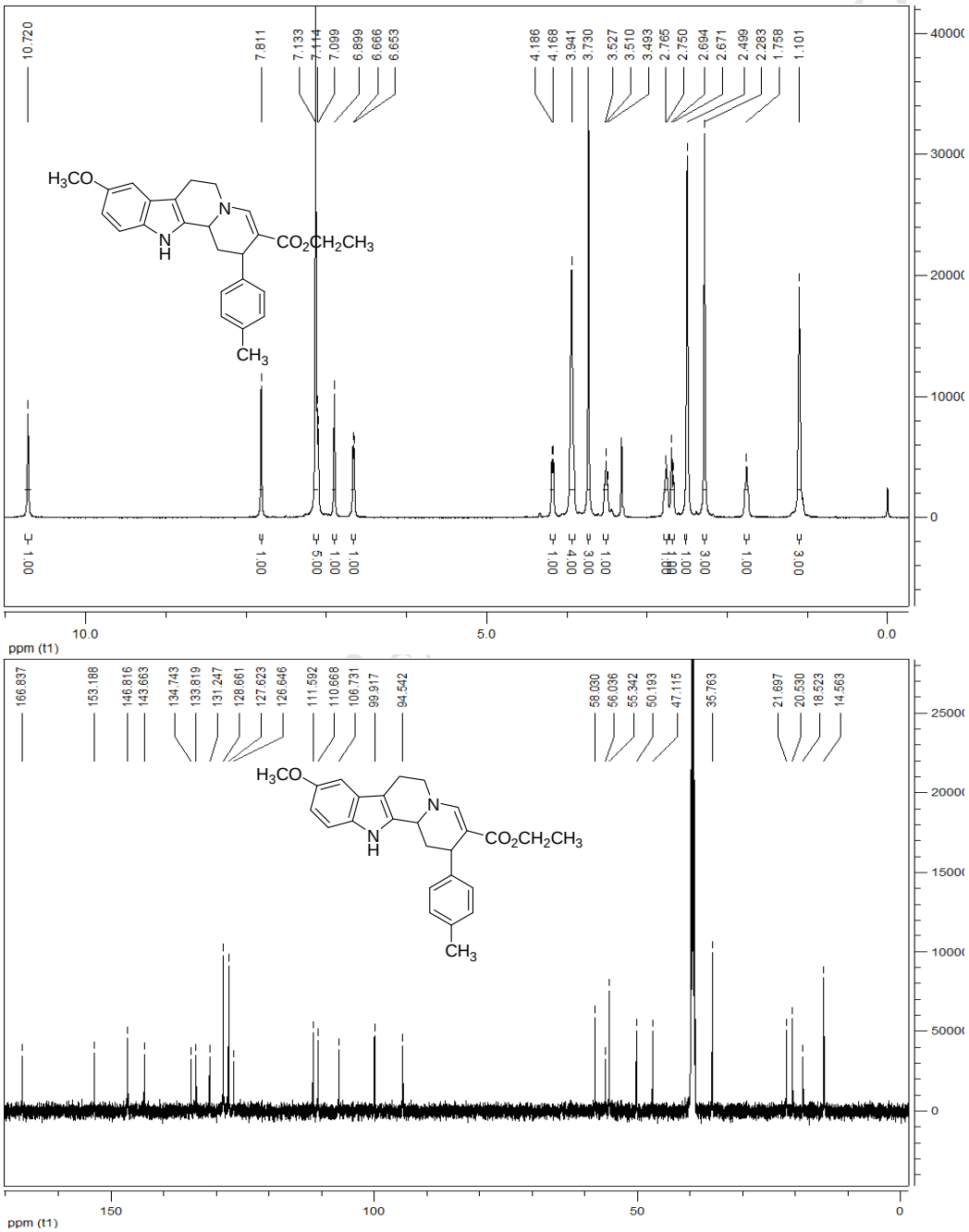
4.21 (d, *J* = 12.0Hz, 1H, CH), 4.02~3.98 (m, 2H, CH), 3.97~3.94 (m, 2H, CH), 3.58~3.53 (m, 1H, CH), 2.82~2.77 (m, 1H, CH), 2.72 (d, *J* = 12.0Hz, 1H, CH), 2.59 (d, *J* = 13.2Hz, 1H, CH), 1.80 (td, J_1 = 12.6Hz, J_2 = 5.4Hz, 1H, CH), 1.11 (t, *J* = 7.2Hz, 3H, CH_3); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 166.7, 149.3, 147.3, 136.2, 132.9, 129.9, 127.7, 126.5, 126.3, 125.9, 1209, 118.5, 117.7, 111.0, 106.9, 93.6, 58.1, 50.2, 47.0, 36.0, 35.4, 21.5, 14.6; IR (KBr) υ: 3448, 2990, 2914, 1660, 1586, 1474, 1440, 1363, 1325, 1303, 1193, 1165, 1108, 1038, 886, 776 cm^{-1}; HRMS (ESI) Calcd. for $C_{24}H_{23}ClN_2NaO_2$ ([M+Na]$^+$): 429.1340. Found: 429.1334.





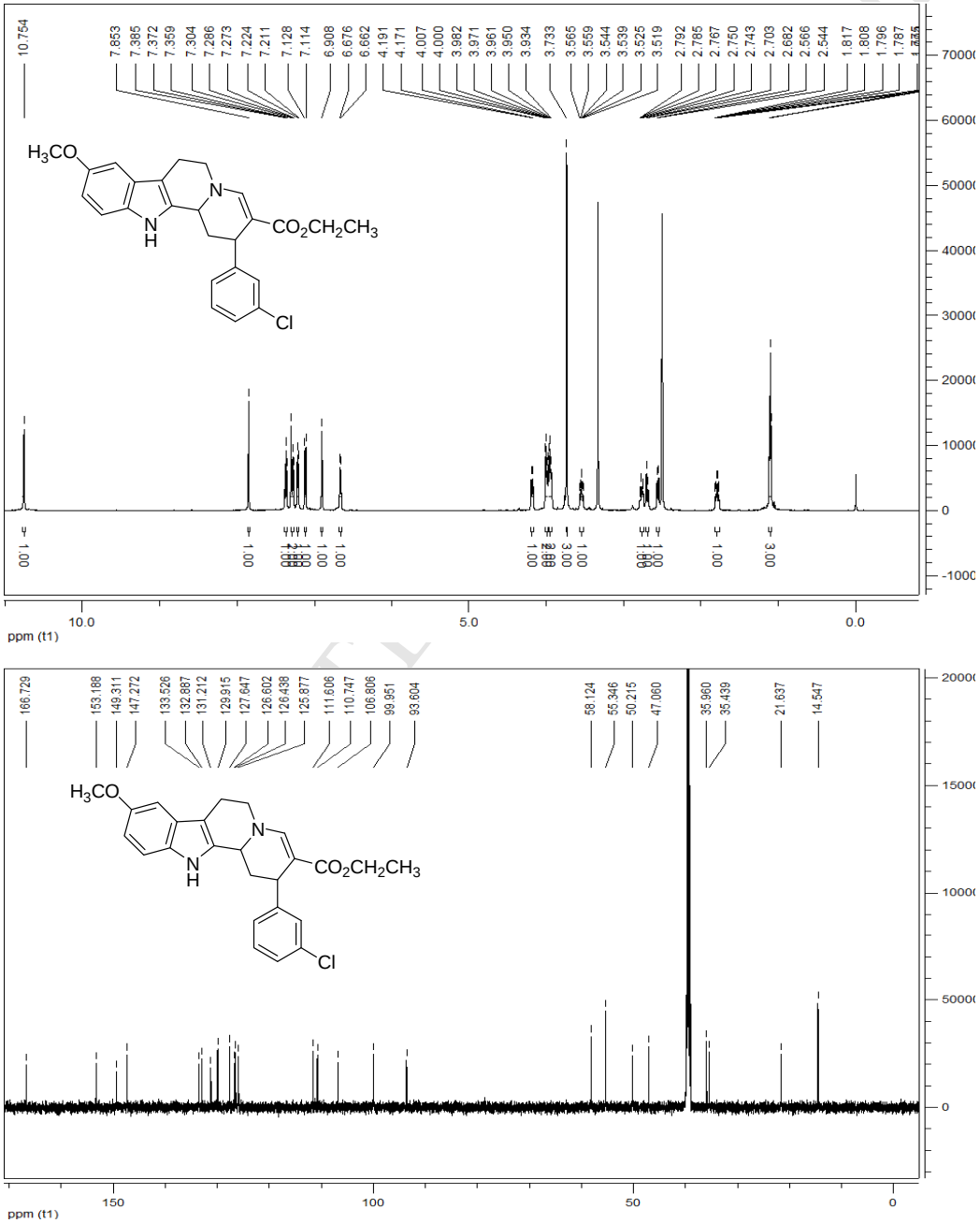
ethyl 9-methoxy-2-(4-methoxyphenyl)-1,2,6,7,12,12b-hexahydroindolo[2,3-a]quinolizine-3-carboxylate (1p): white solid, 81%, m.p.249~250℃; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 10.72 (s,

1H, NH), 7.81 (brs, 1H, CH), 7.13~7.10 (m, 5H, ArH), 6.90 (brs, 1H, ArH), 6.66 (d, *J* = 7.8Hz, 1H, ArH), 4.17 (d, *J* = 10.8Hz, 1H, CH), 3.94 (brs, 4H, CH), 3.73 (s, 3H, $0CH_3$), 3.53~3.49 (m, 1H, CH), 2.77~2.75 (m, 1H, CH), 2.69~2.67 (m, 1H, CH), 2.54 (brs, 1H, CH), 2.28 (s, 3H, CH_3), 1.76 (brs, 1H, CH), 1.10 (brs, 3H, CH); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 166.8, 153.2, 146.8, 143.7, 134.7, 133.8, 131.2, 128.7, 127.6, 126.6, 111.6, 110.7, 106.7, 99.9, 94.5, 58.0, 56.0, 55.3, 50.2, 47.1, 35.8, 21.7, 20.5, 18.5, 14.6; IR (KBr) υ: 3453, 2982, 2907, 2828, 1660, 1583, 1484, 1443, 1365, 1318, 1298, 1209, 1162, 1107, 1035, 821, 799, 776 cm^{-1}; HRMS (ESI) Calcd. for $C_{26}H_{28}N_2NaO_3$ ($[M+Na]^+$): 439.1992. Found: 439.1988.



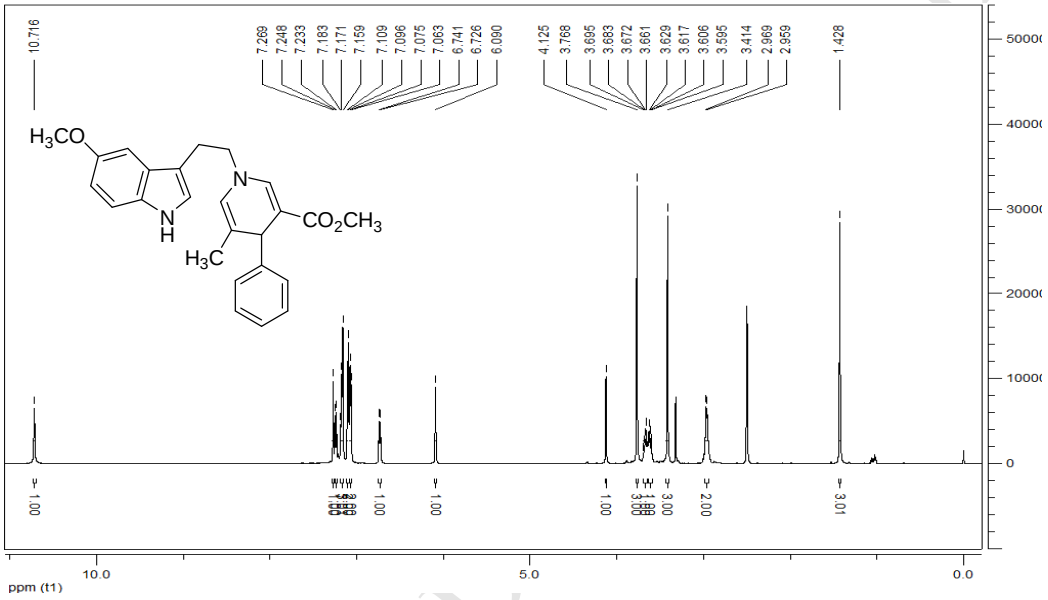
ethyl 9-methoxy-2-(3-chlorophenyl)-1,2,6,7,12,12b-hexahydroindolo[2,3-a]quinolizine-3-carboxylate (1q): white solid, 76%, m.p.241~243℃; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 10.75 (s,

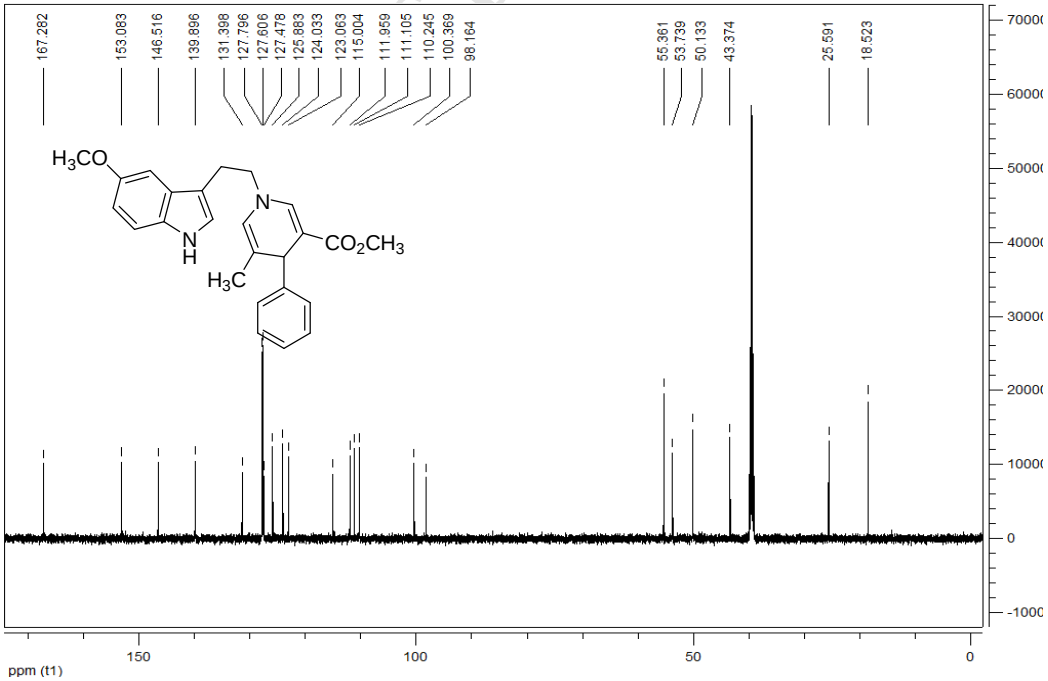
1H, NH), 7.85 (brs, 1H, CH), 7.37 (t, *J* = 7.8Hz, 1H, ArH), 7.30~7.27 (m, 2H, ArH), 7.22 (d, *J* = 7.8Hz, 1H, ArH), 7.12 (d, *J* = 8.4Hz, 1H, ArH), 6.91 (brs, 1H, ArH), 6.67 (d, *J* = 8.4Hz, 1H, ArH), 4.18 (d, *J* = 12.0Hz, 1H, CH), 4.01~3.97 (m, 2H, CH), 3.96~3.93 (m, 2H, CH), 3.73 (s, 3H, $0CH_3$), 3.57~3.52 (m, 1H, CH), 2.79~2.74 (m, 1H, CH), 2.69 (d, *J* = 12.6Hz, 1H, CH), 2.56 (d, *J* = 13.2Hz, 1H, CH), 1.79 (td, J_1 = 12.6Hz, J_2 = 5.4Hz, 1H, CH), 1.11 (t, *J* = 7.2Hz, 3H, CH_3); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 166.7, 153.2, 149.3, 147.3, 133.5, 132.9, 131.2, 129.9, 127.6, 126.6, 126.4, 125.9, 111.6, 110.7, 106.8, 100.0, 93.6, 58.1, 55.3, 50.2, 47.1, 36.0, 35.4, 21.6, 14.5; IR (KBr) υ: 3449, 2956, 2836, 1660, 1586, 1480, 1438, 1365, 1305, 1210, 1162, 1108, 1037, 889, 830, 775 cm^{-1}; HRMS (ESI) Calcd. for $C_{25}H_{25}ClN_2NaO_3$ ($[M+Na]^+$): 459.1446. Found: 459.1440.



Methyl 1-[2-(5-Methoxy-1H-indol-3-yl)-ethyl]-5-methyl-4-phenyl-1,4-dihydropyridine-3-

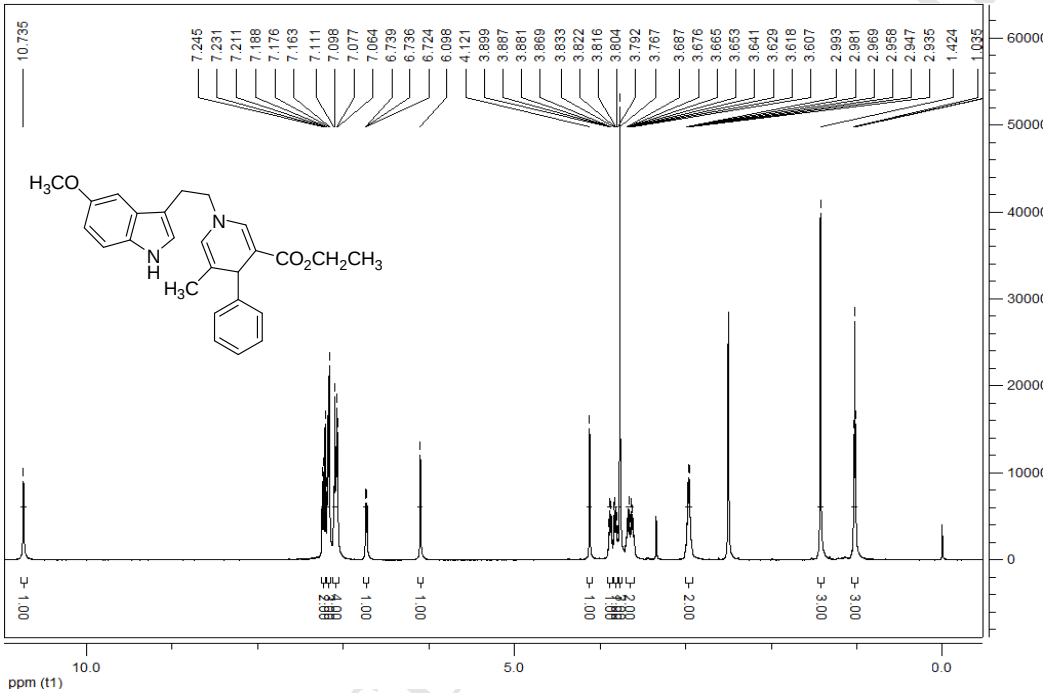
carboxylate (2a): white solid, 82%, m.p.158~159□; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 10.72 (s, 1H, NH), 7.27 (brs, 1H, CH), 7.24 (d, J = 9.0Hz, 1H, ArH), 7.18~7.16 (m, 3H, ArH), 7.11~7.10 (m, 2H, ArH), 7.08~7.06 (m, 2H, ArH), 6.73 (d, J = 9.0Hz, 1H, ArH), 6.09 (brs, 1H, CH), 4.13 (brs, 1H, CH), 3.77 (s, 3H, OCH_3), 3.70~3.66 (m, 1H, CH), 3.63~3.60 (m, 1H, CH), 3.41 (s, 3H, OCH_3), 2.97~2.96 (m, 2H, CH), 1.43 (s, 3H, CH_3); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 167.3, 153.1, 146.5, 139.9, 131.4, 127.8, 127.6, 127.5, 125.9, 124.0, 123.1, 115.0, 112.0, 111.1, 110.2, 100.4, 98.2, 55.4, 53.7, 50.1, 43.4, 25.6, 18.5; IR (KBr) υ: 3343, 3074, 2989, 2849,1686, 1660, 1597, 1450, 1421, 1367, 1312, 1260, 1193, 1158, 1093, 1024, 923, 844, 825, 795, 762 cm^{-1}; HRMS (ESI) Calcd. for $C_{25}H_{26}N_2NaO_3$ ([M+Na]$^+$): 425.1836. Found: 425.1832.

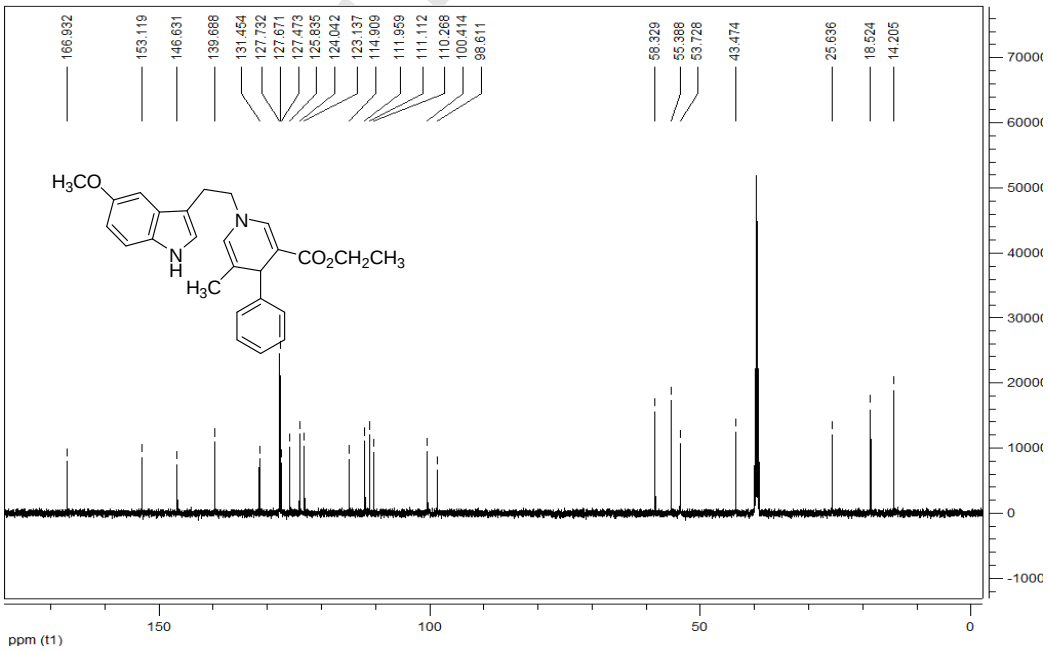




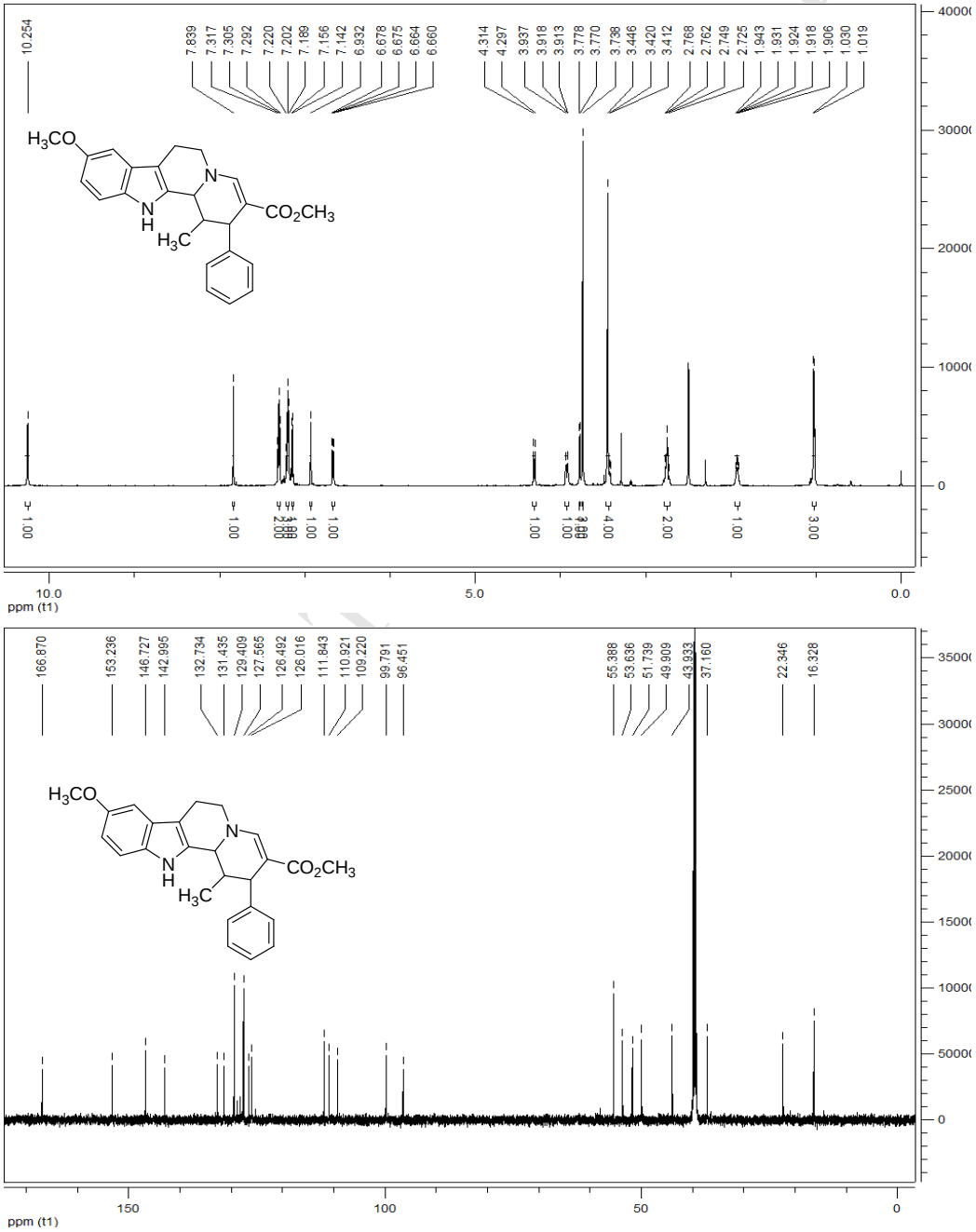
ethyl 1-[2-(5-Methoxy-1H-indol-3-yl)-ethyl]-5-methyl-4-phenyl-1,4-dihydropyridine-3-

carboxylate (2b): white solid, 89%, m.p.138~140□; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 10.74 (s, 1H, NH), 7.25~7.21 (m, 2H, CH, ArH), 7.19~7.16 (m, 3H, ArH), 7.11~7.06 (m, 4H, ArH), 6.74~6.72 (m, 1H, ArH), 6.10 (brs, 1H, CH), 4.12 (brs, 1H, CH), 3.90~3.87 (m, 1H, CH), 3.83~3.79 (m, 1H, CH), 3.77 (s, 3H, OCH_3), 3.69~3.61 (m, 2H, CH), 2.99~2.94 (m, 2H, CH), 1.42 (s, 3H, CH_3), 1.02 (t, J = 6.6Hz, 3H, CH_3); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 166.9, 153.1, 146.6, 139.7, 131.5, 127.7, 127.6, 127.5, 125.8, 124.0, 123.1, 114.9, 112.0, 111.1, 110.3, 100.4, 98.6, 58.3, 55.4, 53.7, 43.5, 25.6, 18.5, 14.2; IR (KBr) υ: 3437, 3075, 2989, 1687, 1661, 1597, 1487, 1455, 1430, 1371, 1307, 1261, 1240, 1216, 1190, 1158, 1092, 1027, 976, 922, 843, 794, 758 cm^{-1}; HRMS (ESI) Calcd. for $C_{26}H_{28}N_2NaO_3$ ([M+Na]$^+$): 439.1992. Found: 439.1993.

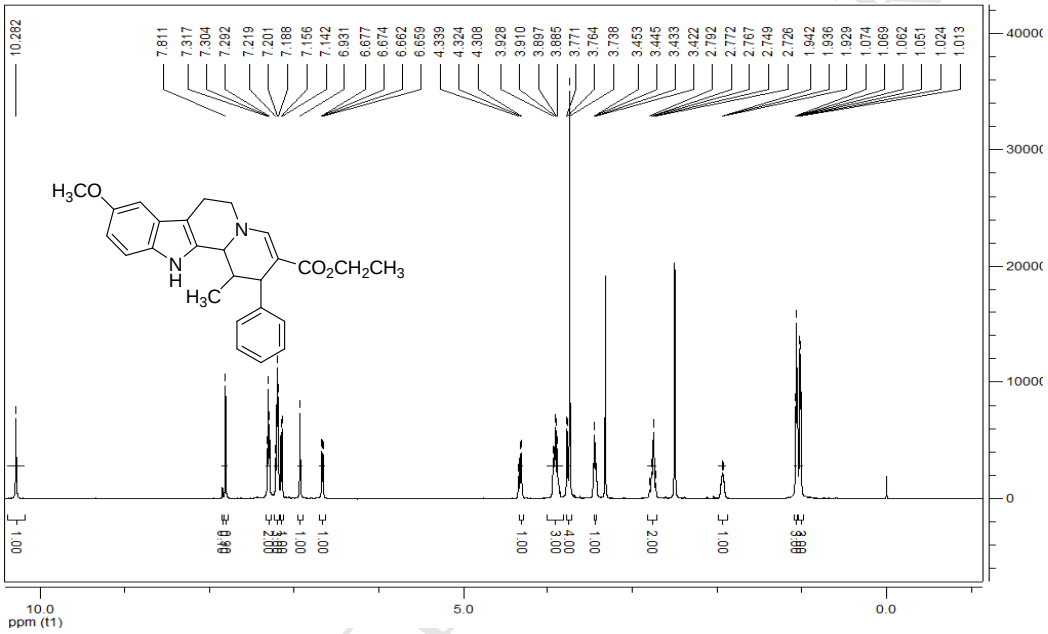


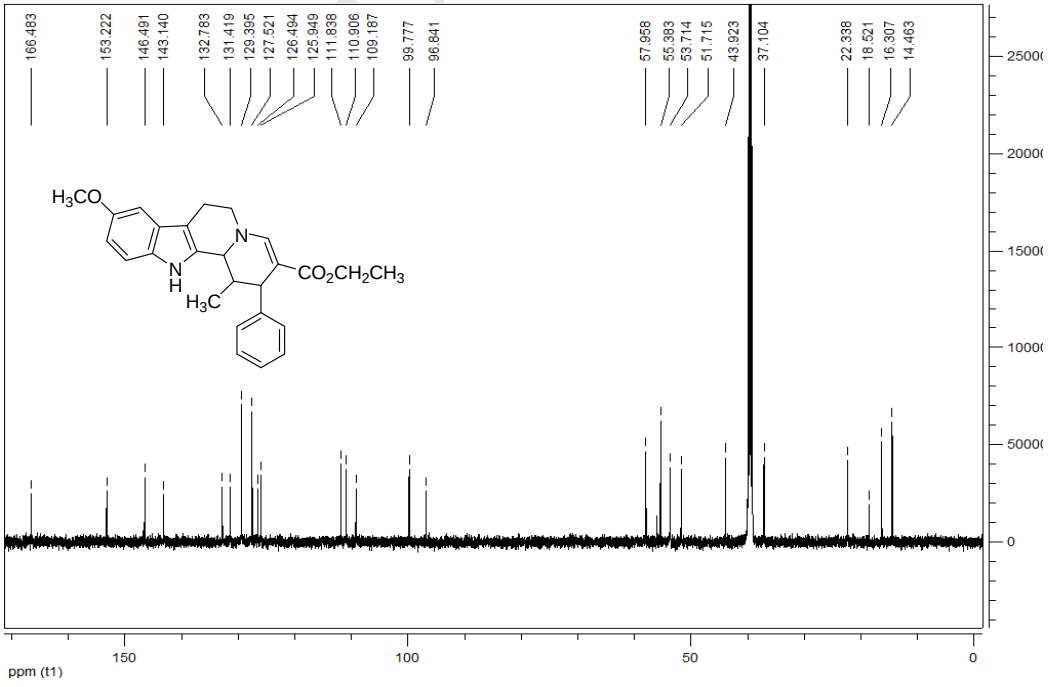


methyl 9-methoxy-1-methyl-2-p-henyl-1,2,6,7,12,12b-hexahydroindolo[2,3-a]quinolizine-3-carboxylate (3a) : white solid, 78%, m.p.264~265□; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 10.25 (s, 1H, NH), 7.27 (brs, 1H, CH), 7.32~7.29 (m, 2H, ArH), 7.22~7.19 (m, 3H, ArH), 7.15 (d, *J* = 8.4Hz, 1H, ArH), 6.93 (brs, 1H, ArH), 6.68~6.66 (m, 1H, ArH), 4.31 (d, *J* = 13.8Hz, 1H, CH), 3.94~3.91 (m, 1H, CH), 3.78~3.77 (m, 1H, CH), 3.74 (s, 3H, OCH_3), 3.45 (s, 3H, OCH_3), 3.42~3.41 (m, 1H, CH), 2.77~2.73 (m, 2H, CH), 1.94~1.91 (m, 1H, CH), 1.02 (d, *J* = 6.6Hz, 3H, CH_3); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 166.9, 153.2, 146.7, 143.0, 132.7, 131.4, 129.4, 127.6, 126.5, 126.0, 111.8, 110.9, 99.8, 96.5, 55.4, 53.6, 51.7, 49.9, 43.9, 37.2, 22.3, 16.3; IR (KBr) υ: 3313, 3029, 2999, 2956, 2918, 2824, 1657, 1624, 1485, 1459, 1415, 1335, 1245, 1214, 1178, 1154, 1122, 1095, 1033, 993, 938, 916, 879, 848, 795, 754 cm^{-1}; HRMS (ESI) Calcd. for $C_{25}H_{26}N_2NaO_3$ ([M+Na]$^{+}$): 425.1836. Found: 425.1837.

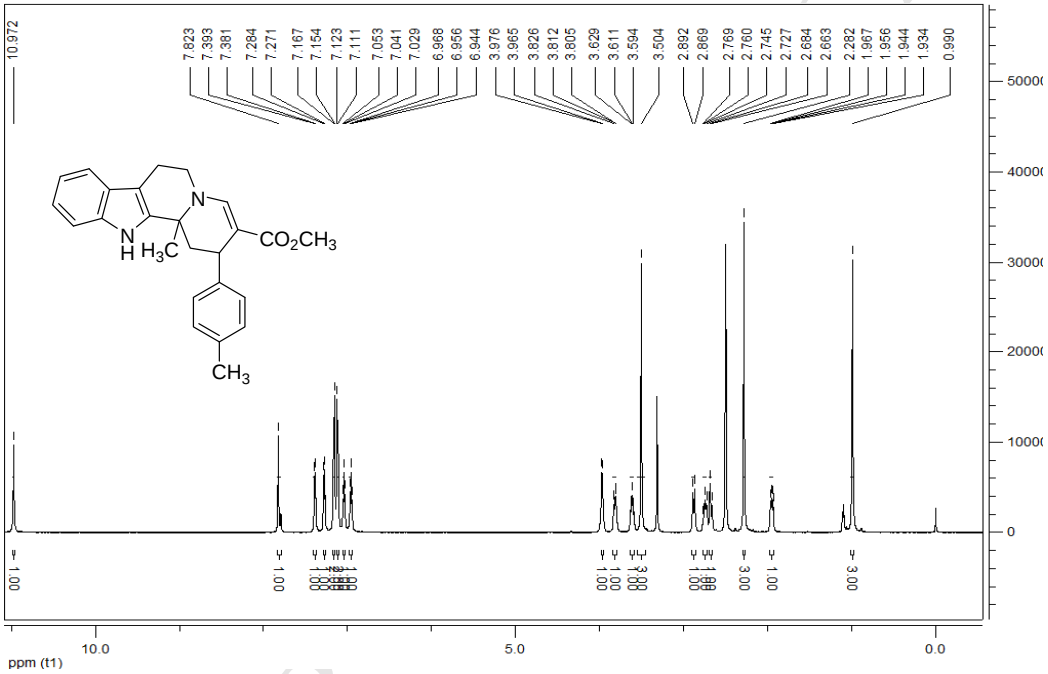


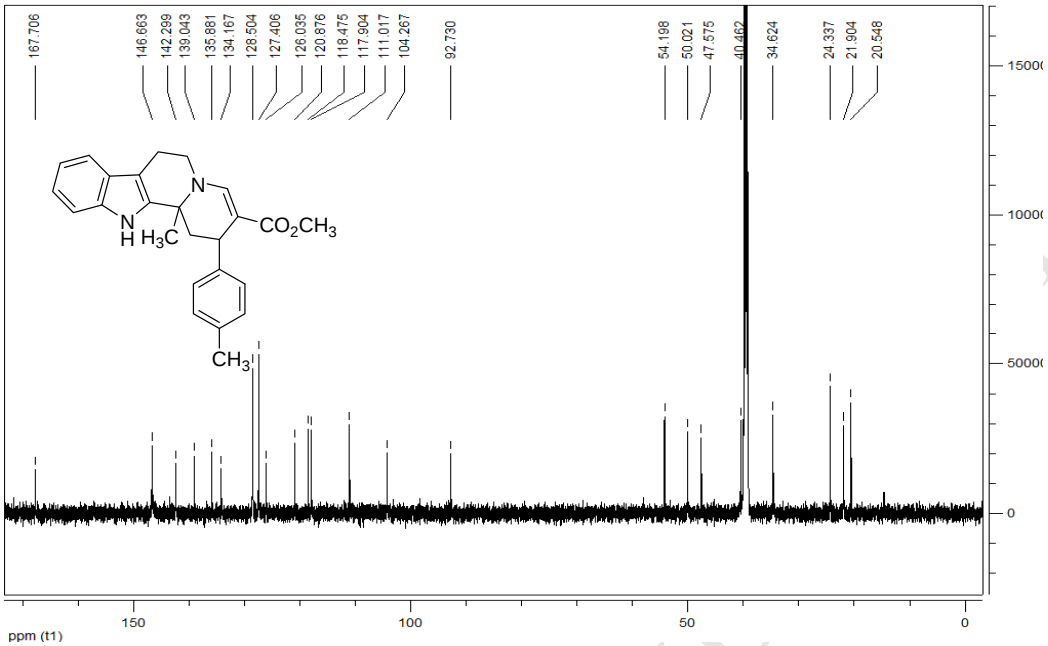
ethyl 9-methoxy-1-methyl-2-p-henyl-1,2,6,7,12,12b-hexahydroindolo[2,3-a]quinolizine-3-carboxylate (3b): white solid, 87%, m.p.226~228□; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 10.28 (s, 1H, NH), 7.81 (brs, 1H, CH), 7.32~7.29 (m, 2H, ArH), 7.22~7.19 (m, 3H, ArH), 7.15 (d, J = 8.4Hz, 1H, ArH), 6.93 (brs, 1H, ArH), 6.68~6.66 (m, 1H, ArH), 4.34~3.31 (m, 1H, CH), 3.93~3.89 (m, 3H, CH), 3.77~3.76 (m, 1H, CH), 3.74 (s, 3H, OCH_3), 3.45~3.42 (m, 1H, CH), 2.79~2.73 (m, 2H, CH), 1.94~1.93 (m, 1H, CH), 1.07~1.05 (m, 3H, CH_3), 1.02 (d, J = 6.6Hz, 3H, CH_3); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 166.5, 153.2, 146.5, 143.1, 132.8, 131.4, 129.4, 127.5, 126.5, 125.9, 111.8, 110.9, 109.2, 99.8, 96.8, 58.0, 55.4, 53.7, 51.7, 43.9, 37.1, 22.3, 18.5, 16.3, 14.5; IR (KBr) υ: 3108, 1728, 1587, 1487, 1460, 1367, 1312, 1244, 1213, 1160, 1123, 1032, 909, 843, 783, 750 cm^{-1}; HRMS (ESI) Calcd. for $C_{26}H_{28}N_2NaO_3$ ([M+Na]$^+$): 439.1992. Found: 439.1997.



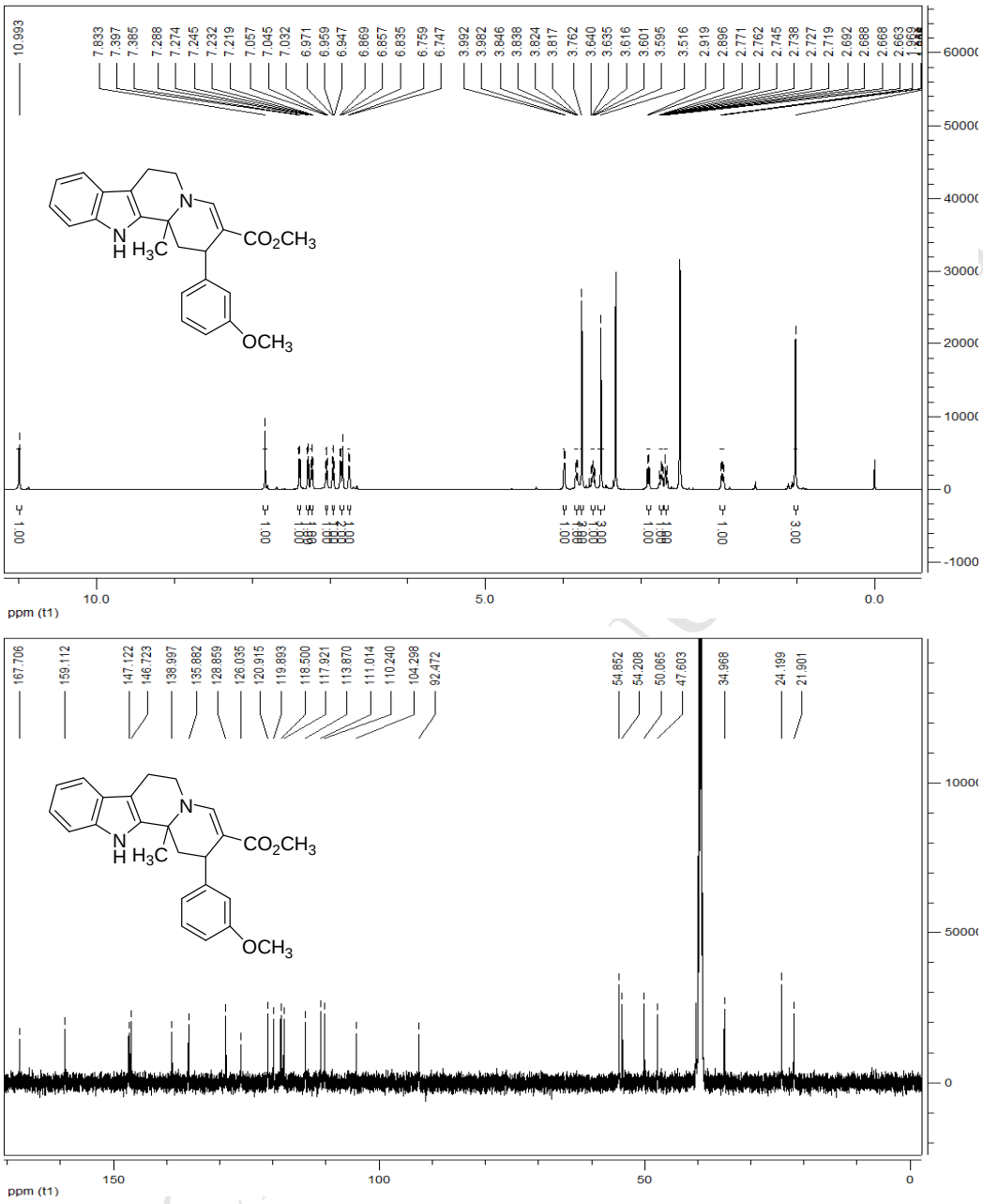


methyl 12b-methyl-2-(4-methylphenyl-1,2,6,7,12,12b-hexahydroindolo[2,3-a]quinolizine-3-carboxylate (4a): white solid, 70%, m.p.288~290℃; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 10.97 (s, 1H, NH), 7.82 (brs, 1H, CH), 7.39 (d, J = 7.2Hz, 1H, ArH), 7.28 (d, J = 7.8Hz, 1H, ArH), 7.16 (d, J = 7.8Hz, 2H, ArH), 7.12 (d, J = 7.2Hz, 2H, ArH), 7.04 (t, J = 7.2Hz, 1H, ArH), 6.96 (t, J = 7.2Hz, 1H, ArH), 3.98~3.97 (m, 1H, CH), 3.83~3.81 (m, 1H, CH), 3.63~3.59 (m, 1H, CH), 3.50 (s, 3H, OCH_3), 2.88 (d, J = 13.8Hz, 1H, CH), 2.77~2.73 (m, 1H, CH), 2.67 (d, J = 12.6Hz, 1H, CH), 2.28 (s, 3H, CH_3), 1.97~1.93 (m, 1H, CH), 0.99 (s, 3H, CH_3); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 167.7, 146.7, 142.3, 139.0, 135.9, 134.2, 128.5, 127.4, 126.0, 120.9, 118.5, 117.9, 111.0, 104.3, 92.7, 54.2, 50.0, 47.6, 40.5, 34.6, 24.3, 21.9, 20.5; IR (KBr) υ: 3446, 2916, 2849, 1664, 1582, 1425, 1353, 1311, 1217, 1183, 1142, 1093, 1039, 923, 853, 818, 795, 774 cm^{-1}; HRMS (ESI) Calcd. for $C_{25}H_{26}N_2NaO_2$ ([M+Na]$^+$): 409.1886. Found: 409.1878.

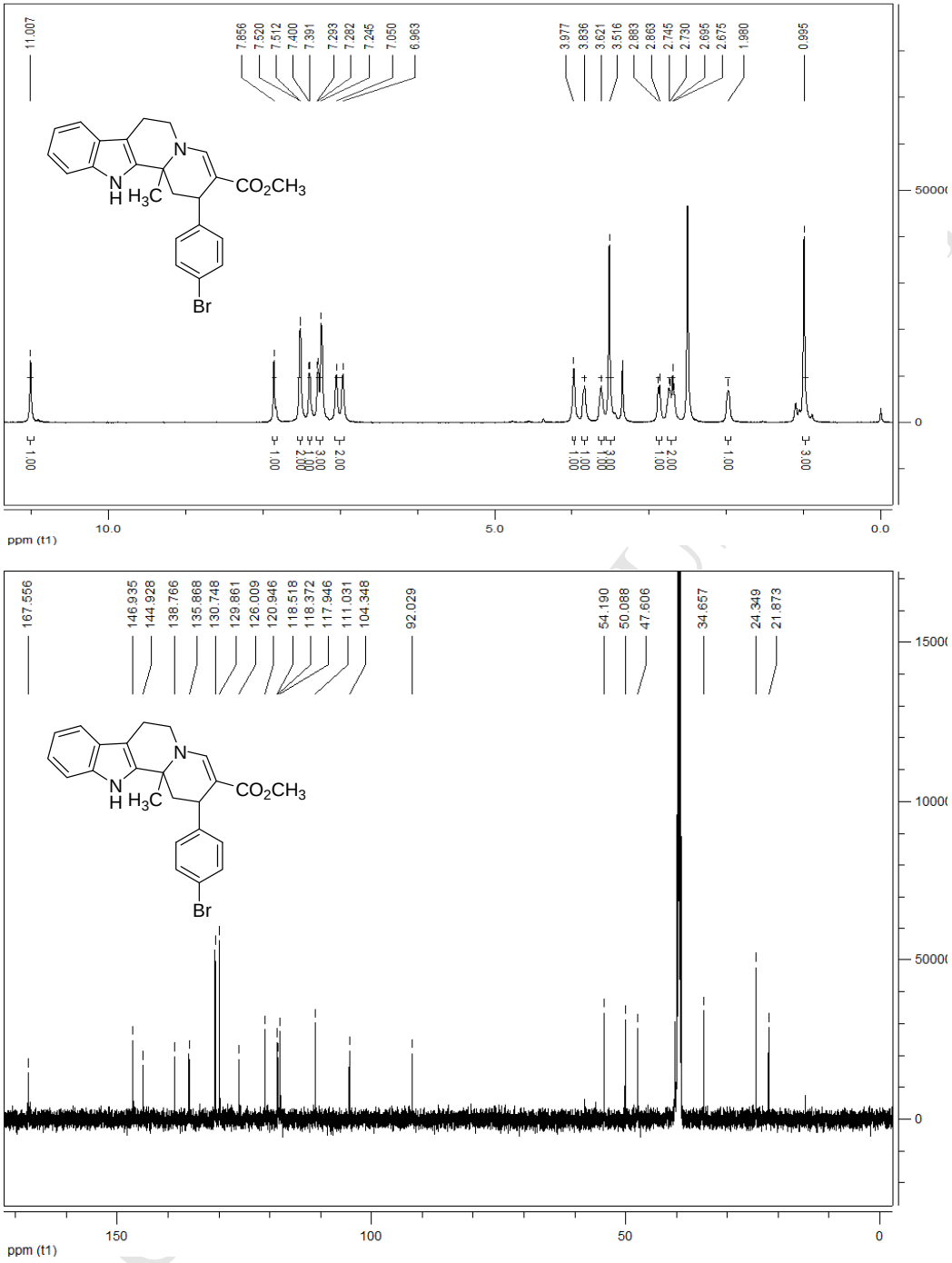




methyl 12b-methyl-2-(3-methoxyphenyl)-1,2,6,7,12,12b-hexahydroindolo[2,3-a]quinolizine-3-carboxylate (4b): white solid, 72%, m.p.272~274℃; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 10.99 (s, 1H, NH), 7.83 (brs, 1H, CH), 7.39 (d, J = 7.2Hz, 1H, ArH), 7.28 (d, J = 8.4Hz, 1H, ArH), 7.23 (t, J = 7.8Hz, 1H, ArH), 7.05 (t, J = 7.8Hz, 1H, ArH), 6.96 (t, J = 7.2Hz, 1H, ArH), 6.87~6.84 (m, 2H, ArH), 6.75 (d, J = 7.2Hz, 1H, ArH), 3.99~3.98 (m, 1H, CH), 3.85~3.82 (m, 1H, CH), 3.76 (s, 3H, OCH_3), 3.64~3.60 (m, 1H, CH), 3.52 (s, 3H, OCH_3), 2.91 (d, J = 13.8Hz, 1H, CH), 2.77~2.72 (m, 1H, CH), 2.69~2.66 (m, 1H, CH), 1.95 (dd, J_1 = 13.8Hz, J_2 = 6.6Hz, 1H, CH), 1.02 (s, 3H, CH_3); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 167.7, 159.1, 147.1, 146.7, 139.0, 135.9, 128.9, 126.0, 120.9, 119.9, 118.5, 117.9, 113.9, 111.0, 110.2, 104.3, 92.5, 54.9, 54.2, 50.1, 47.6, 35.0, 24.2, 21.9; IR (KBr) υ: 3452, 2930, 2853, 1637, 1485, 1424, 1383, 1349, 1308, 1268, 1221, 1185, 1141, 1092, 1053, 879, 776 cm^{-1}; HRMS (ESI) Calcd. for $C_{25}H_{26}N_2NaO_3$ ($[M+Na]^+$): 425.1836. Found: 425.1831.

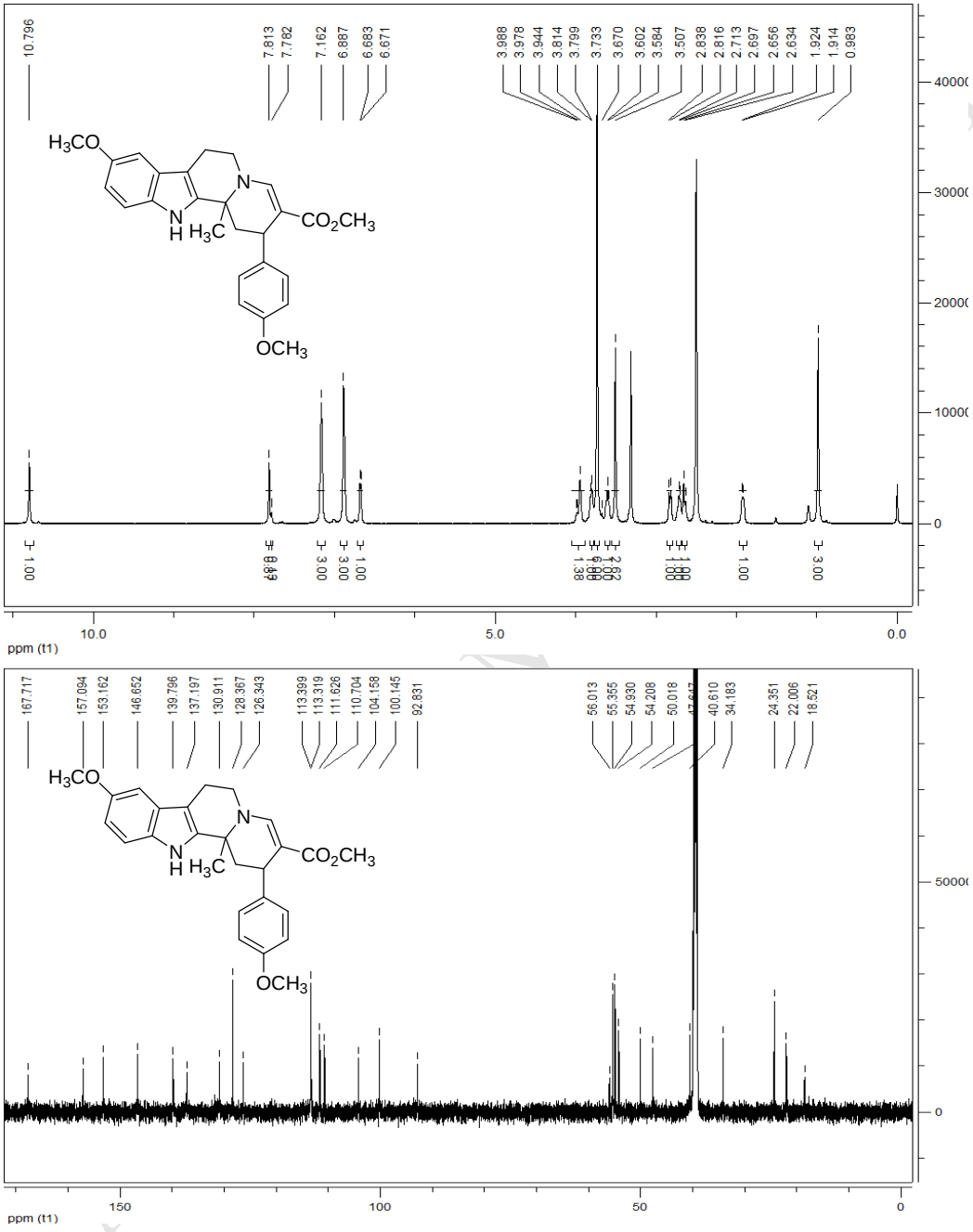


methyl 12b-methyl-2-(4-bromophenyl)-1,2,6,7,12,12b-hexahydroindolo[2,3-a]quinolizine-3-carboxylate (4c): white solid, 67%, m.p.299~300℃; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 11.00 (s, 1H, NH), 7.86 (brs, 1H, CH), 7.52~7.51 (m, 2H, ArH), 7.40~7.39 (m, 1H, ArH), 7.29~7.25 (m, 3H, ArH), 7.05~6.96 (m, 2H, ArH), 3.98 (brs, 1H, CH), 3.84 (brs, 1H, CH), 3.62 (brs, 1H, CH), 3.52 (s, 3H, OCH_3), 2.87 (d, J = 12.0Hz, 1H, CH), 2.75~2.68 (m, 2H, CH), 1.98 (brs, 1H, CH), 1.00 (s, 3H, CH_3); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 167.6, 146.9, 144.9, 138.8, 135.9, 130.7, 129.9, 126.0, 120.9, 118.5, 117.9, 111.0, 104.3, 92.0, 54.2, 50.1, 47.6, 34.7, 24.3, 21.9; IR (KBr) υ: 3448, 2926, 2854, 2025, 1663, 1582, 1485, 1426, 1353, 1309, 1219, 1185, 1143, 1094, 1039, 1011, 823, 782 cm^{-1}; HRMS (ESI) Calcd. for $C_{24}H_{23}BrN_2NaO_2$ ($[M+Na]^+$): 473.0835. Found: 473.0822.



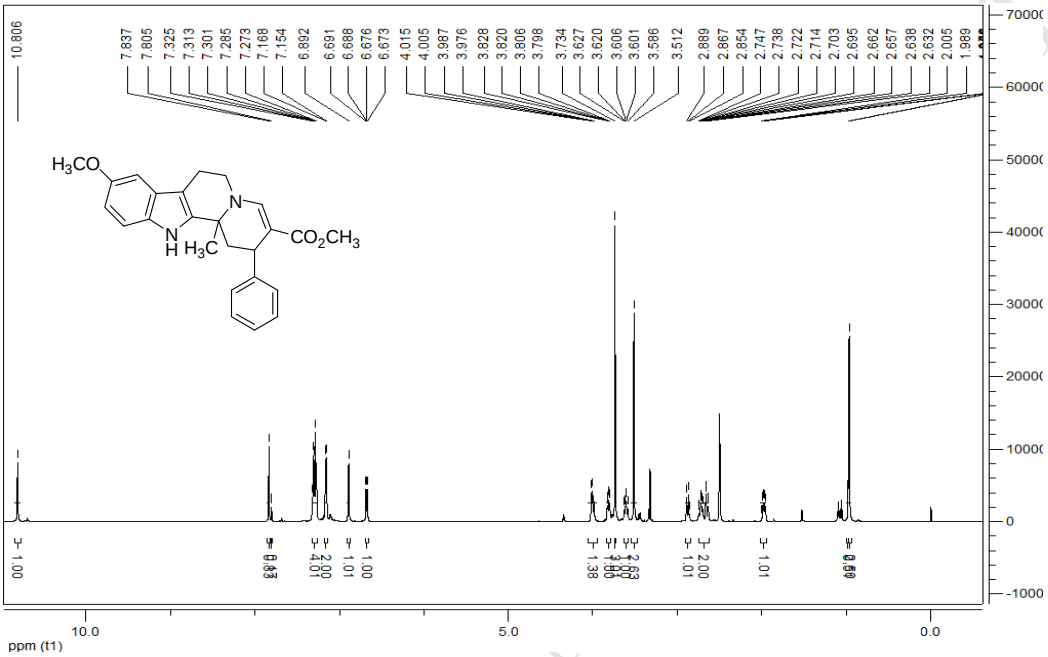
methyl 9-methoxy-12b-methyl-2-(4-methoxyphenyl)-1,2,6,7,12,12b-hexahydroindolo[2,3-a]-quinolizine-3-carboxylate (4d): white solid, 73%, m.p.266~267℃; ^{1}H NMR (600 MHz, DMSO-d_6) δ: *cis/trans* = 1:8; *trans-isomer*: 10.80 (s, 1H, NH), 7.81 (brs, 1H, CH), 7.16 (brs, 3H, ArH), 6.89 (brs, 3H, ArH), 6.68 (d, *J* = 7.2Hz, 1H, ArH), 4.18 (d, *J* = 12.0Hz, 1H, CH), 3.99~3.94 (m, 1H, CH), 3.81~3.80 (m, 1H, CH), 3.73 (s, 6H, $0CH_3$), 3.51 (s, 3H, $0CH_3$), 2.83 (d, *J* = 13.2Hz, 1H, CH), 2.71~2.70 (m, 1H, CH), 2.65 (d, *J* = 13.2Hz, 1H, CH), 1.92~1.91 (m, 1H, CH), 0.98 (s, 3H, CH_3); *cis-isomer*: 7.78 (brs, 1H, CH), 3.94 (s, 3H, OCH_3); ^{13}C NMR (150 MHz, DMSO-d_6) δ:

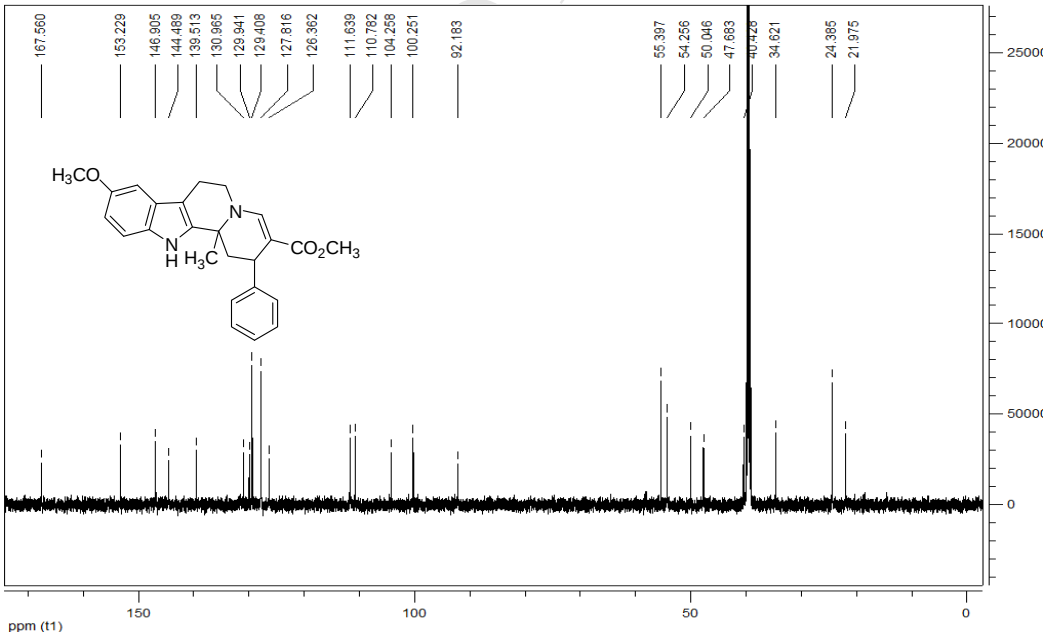
167.7, 157.1, 153.2, 146.7, 139.8, 137.2, 130.9, 128.4, 126.3, 113.4, 113.3, 111.6, 110.7, 104.2, 100.1, 92.8, 55.4, 54.9, 54.2, 50.0, 47.6, 40.6, 34.2, 24.4, 22.0; IR (KBr) υ: 3451, 3240, 2949, 2831, 1662, 1579, 1510, 1461, 1426, 1357, 1314, 1253, 1216, 1180, 1139, 1091, 1036, 984, 910, 829, 774 cm^{-1}; HRMS (ESI) Calcd. for $C_{26}H_{28}N_2NaO_4$ ($[M+Na]^+$): 455.1941. Found: 455.1937.



methyl 9-methoxy-12b-methyl-2-phenyl-1,2,6,7,12,12b-hexahydroindolo[2,3-a]quinolizine-3-carboxylate (4e): white solid, 81%, m.p. >300℃; ^{1}H NMR (600 MHz, DMSO-d_6) δ: *cis/trans* = 1:8; *trans-isomer*: 10.81 (s, 1H, NH), 7.84 (brs, 1H, CH), 7.33~7.27 (m, 4H, ArH), 7.17~7.15 (m, 2H, ArH), 6.89 (brs, 1H, ArH), 6.69~6.67 (m, 1H, ArH), 4.02~3.98 (m, 1H, CH), 3.83~3.80 (m, 1H, CH), 3.73 (s, 3H, 0CH_3), 3.63~3.59 (m, 1H, CH), 3.51 (s, 3H, 0CH_3), 2.89~2.85 (m, 1H, CH),

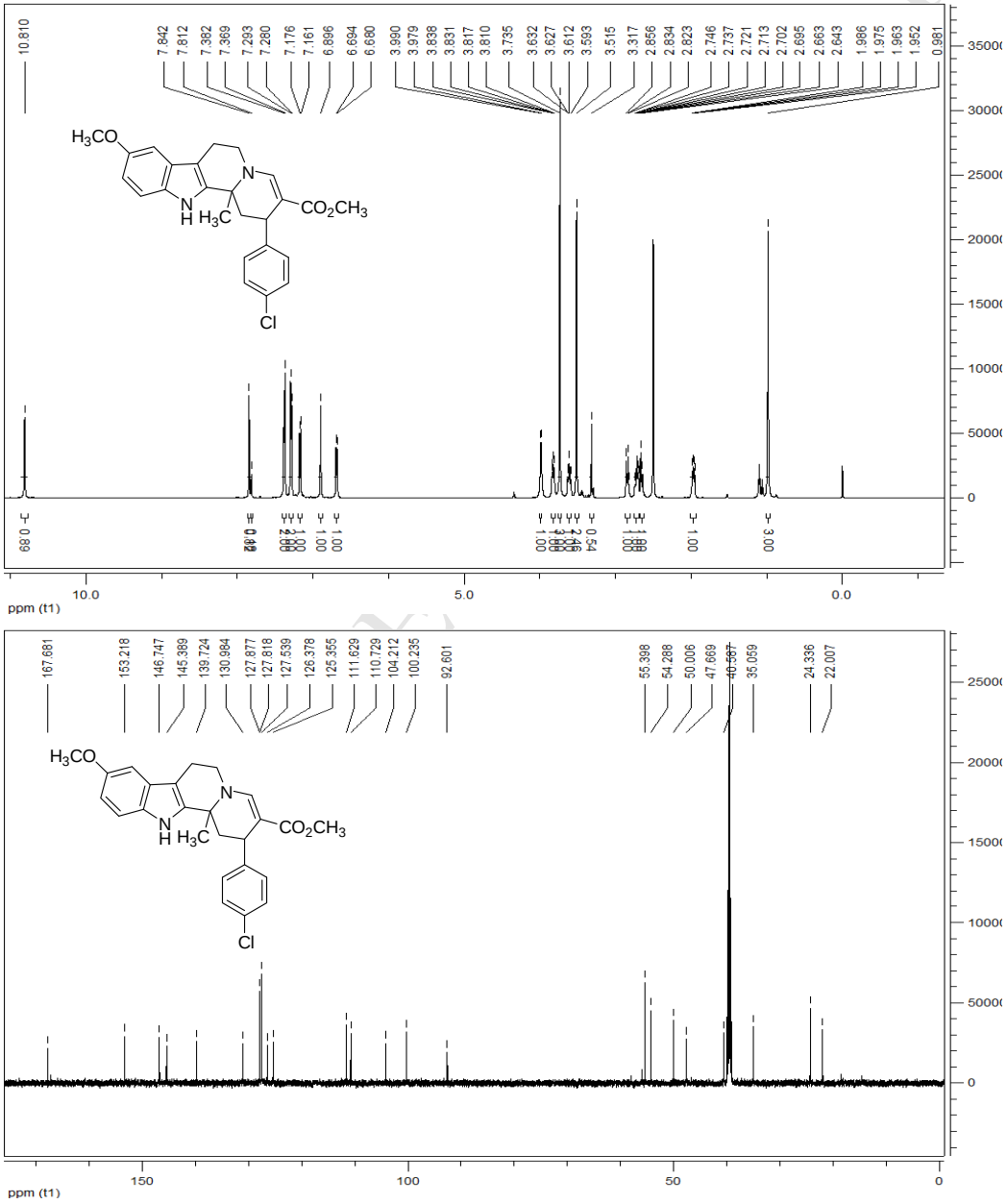
2.75~2.63 (m, 2H, CH), 2.00~1.96 (m, 1H, CH), 0.97 (s, 3H, CH_3); *cis-isomer*: 7.78 (brs, 1H, CH), 3.94 (s, 3H, OCH_3); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 167.6, 153.2, 146.9, 144.5, 139.5, 131.0, 129.9, 129.4, 127.8, 126.4, 111.6, 110.8, 104.3, 100.3, 92.2, 55.4, 54.3, 50.0, 47.7, 40.4, 34.6, 24.4, 22.0; IR (KBr) υ: 3453, 3291, 2976, 2924, 2865, 2828, 2733, 1647, 1610, 1488, 1436, 1416, 1329, 1311, 1219, 1183, 1139, 1113, 1091, 1030, 1012, 952, 913, 889, 822, 797, 783 cm^{-1}; HRMS (ESI) Calcd. for $C_{25}H_{26}N_2NaO_3$ ($[M+Na]^+$): 425.1836. Found: 425.1840.





methyl 9-methoxy-12b-methyl-2-(4-chlorophenyl)-1,2,6,7,12,12b-hexahydroindolo[2,3-a]-quinolizine-3-carboxylate (4f): white solid, 73%, m.p. **>** 300℃; ^1H NMR (600 MHz, DMSO-d_6) δ: *cis/trans* = 1:5; *trans-isomer*: 10.81 (s, 1H, NH), 7.84 (brs, 1H, CH), 7.38 (d, *J* = 7.8Hz, 2H,

ArH), 7.29 (d, *J* = 7.8Hz, 2H, ArH), 7.17 (d, *J* = 9.0Hz, 1H, ArH), 6.90 (brs, 1H, ArH), 6.69 (d, *J* = 8.4Hz, 1H, ArH), 3.99~3.98 (m, 1H, CH), 3.84~3.81 (m, 1H, CH), 3.74 (s, 3H, $0CH_3$), 3.63~3.59 (m, 1H, CH), 3.52 (s, 3H, $0CH_3$), 2.86~2.82 (m, 1H, CH), 2.75~2.70 (m, 1H, CH), 2.68~2.64 (m, 1H, CH), 1.99~1.98 (m, 1H, CH), 0.98 (s, 3H, CH_3); *cis-isomer*: 7.81 (brs, 1H, CH); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 167.7, 153.2, 146.7, 145.4, 139.7, 131.0, 127.9, 127.8, 127.5, 126.4, 125.4, 111.6, 110.7, 104.2, 100.2, 92.6, 55.4, 54.3, 50.0, 47.7, 40.6, 35.1, 24.3, 22.0; IR (KBr) υ: 3446, 3273, 2950, 2926, 2864, 2826, 1642, 1611, 1489, 1418, 1335, 1315, 1219, 1185, 1139, 1093, 1033, 953, 914, 879, 829, 800, 769 cm^{-1}; HRMS (ESI) Calcd. for $C_{25}H_{25}ClN_2NaO_3$ ($[M+Na]^+$): 459.1992. Found: 459.1945.



ethyl 9-methoxy-12b-methyl-2-phenyl-1,2,6,7,12,12b-hexahydroindolo[2,3-a]quinolizine-3-carboxylate (4g): white solid, 64%, m.p.266~268℃; ^1H NMR (600 MHz, DMSO-d_6) δ: *cis/trans*

= 1:5; *trans-isomer*: 10.98 (s, 1H, NH), 7.81 (brs, 1H, CH), 7.41~7.38 (m, 1H, ArH), 7.33~7.28 (m, 5H, ArH), 7.18~7.15 (m, 1H, ArH), 7.06~7.02 (m, 1H, ArH), 6.96 (t, J = 7.2Hz, 1H, ArH), 4.01~3.98 (m, 3H, CH), 3.83~3.81 (m, 1H, CH), 3.65~3.60 (m, 1H, CH), 2.89 (d, J = 13.2Hz, 1H, CH), 2.76~2.73 (m, 1H, CH), 2.69~2.66 (m, 1H, CH), 2.00 (dd, J_1 = 13.2Hz, J_2 = 6.6Hz, 1H, CH), 1.10 (t, J = 6.6Hz, 3H, CH_3), 0.99 (s, 3H, CH_3); *cis-isomer*: 10.87 (s, 1H, NH), 7.66 (brs, 1H, CH), 7.24~7.23 (m, 1H, ArH), 7.20~7.19 (m, 1H, ArH), 7.12~7.09 (m, 3H, ArH), 3.80~3.77 (m, 2H, CH), 3.73~3.70 (m, 1H, CH), 3.69~3.67 (m, 1H, CH), 3.29 (brs, 1H, CH), 2.81~2.77 (m, 1H, CH), 2.61~2.58 (m, 1H, CH), 1.55 (s, 3H, CH_3), 0.85 (t, J = 6.6Hz, 3H, CH_3); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 167.2, 146.6, 145.5, 139.0, 135.9, 127.8, 127.5, 126.6, 126.1, 125.3, 125.2, 120.9, 118.5, 117.9, 111.0, 104.3, 93.2, 58.0, 54.2, 47.6, 40.6, 35.1, 24.3, 21.9, 14.6; IR (KBr) υ: 3417, 3241, 2978, 2911, 2856, 1664, 1585, 1445, 1363, 1308, 1221, 1187, 1142, 1090, 1038, 960, 923, 882 cm^{-1}; HRMS (ESI) Calcd. for $C_{25}H_{26}N_2NaO_2$ ([M+Na]$^+$): 409.1886. Found: 409.1893.