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Tetrahydronaphthalene as a precursor of new series of chalcones, flavanones, and flavones

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Abstract: An efficient synthetic route for a novel series of chalcones **2a–2d** as well as for the corresponding flavanones **3a–3d** and flavones **4a–4d**, using functionalized tetrahydronaphthalene (THN), is described herein. The Claisen–Schmidt condensation of such THN and aromatic aldehydes, in the presence of an aqueous solution of KOH (40%), selectively gives the expected chalcones **2a–2d**, which may further undergo an intramolecular oxa-Michael addition using piperidine, affording the corresponding flavanones **3a–3d** in high yields. Alternatively, treatment of such chalcones **2a–2d** with I_2/DMSO provides rapidly, in a one-pot oxidative cyclization, a series of flavones **4a–4d** in excellent yields ranging from 85% to 90%.

Key words: Morita–Baylis–Hillman, tetrahydronaphthalene, chalcone, flavanone, flavone

1. Introduction

Chalcones and flavanoids such as flavones and flavanones are natural products that have been isolated from a wide range of vascular plants.[1] Their extensive spectrum of biological activities has attracted considerable interest in medicinal chemistry and in organic synthesis. Indeed, chalcones have been shown to exhibit anticancer,[1−3] antiinflammatory,[4] antioxidant,[5] antifungal,[6] and antibacterial[7] activities. Therefore, a number of synthetic methods have been reported for the synthesis of these valuable derivatives, among which aldol and Claisen–Schmidt condensations are currently the common and simple protocols toward chalcones. On the other hand, the common synthetic methods for flavanones and flavones involve chalcones as substrates. Indeed, their oxidative cyclization or intramolecular oxa-Michael addition with various bases,[8−10] acids,[11,12] and others[13] provides the corresponding flavones.

Other methods are also available for the synthesis of flavanones in a one-pot procedure including condensation between 2-hydroxyacetophenone and benzaldehyde derivatives in the presence of acids[14] or bases,[15,16] Mannich-type reactions,[17] Mitsunobu reactions,[18] Julia–Kocienski olefination,[19] and others.[20] Recently, Chen[18] and co-workers described an environmentally friendly method using tertiary amines as bases in water or ethanol as solvents, directly affording the desired flavanones.

Numerous methods have been developed for flavones synthesis, including Baker–Venkataraman rearrangement,[21,22] the Allan–Robinson protocol,[23] and the reaction of oxidative cyclization of chalcones using numerous oxidizing agents such as DDQ,[24] Ph-S-S-Ph,[25,26] I_2-DMSO,[27] I_2-SiO_2,[28] I_2-Al_2O_3,[29] NH_4I,[30] and $InBr_3$.[31]

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In our previous reports on the chemistry of Morita–Baylis–Hillman, we described the synthesis of a series of functionalized THN,[32] and currently we are interested in their further synthetic applications. In this paper, we wish to report our results dealing with the conversion of theses derivatives into new chalcones that may further undergo an intramolecular oxa-Michael addition, yielding the corresponding flavanones. Alternatively, a one-pot oxidative cyclization of these chalcones may afford the corresponding flavones.

2. Results and discussion

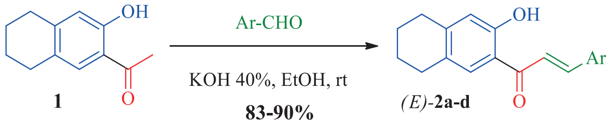
In our first attempt, we observed that, on treatment of a mixture of THN **1** (1 equiv.) and benzaldehyde (1 equiv.) with DABCO (3 equiv.) in water at reflux for 24 h, no reaction occurred and the starting materials were recovered. Under the same conditions but in refluxing ethanol, the conversion of the starting materials still remained incomplete even after a longer reaction time (48 h) and unfortunately gave a mixture of chalcone **2a** and the corresponding flavanone **3a**.

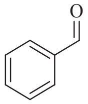
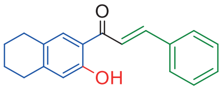
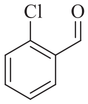
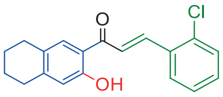
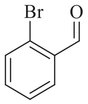
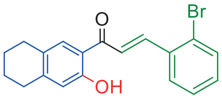
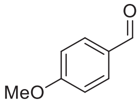
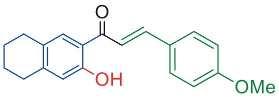
Therefore, we decided to first establish the suitable conditions for a total and selective conversion of THN **1** into chalcones **2**, and then their further cyclization into flavanones **3** or, alternatively, their tandem cyclization-oxidation into flavones **4**.

In order to first synthesize chalcone **2a**, a mixture of THN **1** (1 equiv.) and benzaldehyde (1 equiv.) in ethanol was treated with a 40% KOH aqueous solution (1 equiv.) at room temperature.[33]

Interestingly, the conversion of the starting materials was complete within 24 h and chalcone **2a** was selectively obtained and isolated in 90% yield (Table 1, entry 1).

Table 1. Synthesis of (*E*)− chalcones **2a**–**2d** from THN **1**.



Entry	ArCHO	Chalcone **2**	t (h)	Yield **2** (%)
1		(*E*)-**2a** : 	24	90
2		(*E*)-**2b** : 	24	83
3		(*E*)-**2c** : 	24	83
4		(*E*)-**2d** : 	24	90

Encouraged by this clean Claisen–Schmidt condensation of THN **1** with benzaldehyde, we attempted to further investigate this aldol reaction with various aromatic aldehydes. Under the previous conditions, the desired chalcones **2b**–**2d** were therefore obtained in 83%–90% yields (Table 1, entries 2–4).

Below, we present the whole ^{1}H NMR spectrum of chalcone $(E)-$**2d** (Figure 1), the structure of chalcone (E)-**2d** (Figure 2a), and only the region of the eight ethylenic and aromatic protons (Figure 2b). The analysis of the latter shows one singlet for 1.00 H(d), an A_2B_2 system for 2.00 H (proton h) coupled with 2.00 H (proton g), another AB system for 1.00 H (proton e) coupled with 1.00 H (proton f), and, finally, one singlet for 1.00 H (proton c) (Figure 2b).

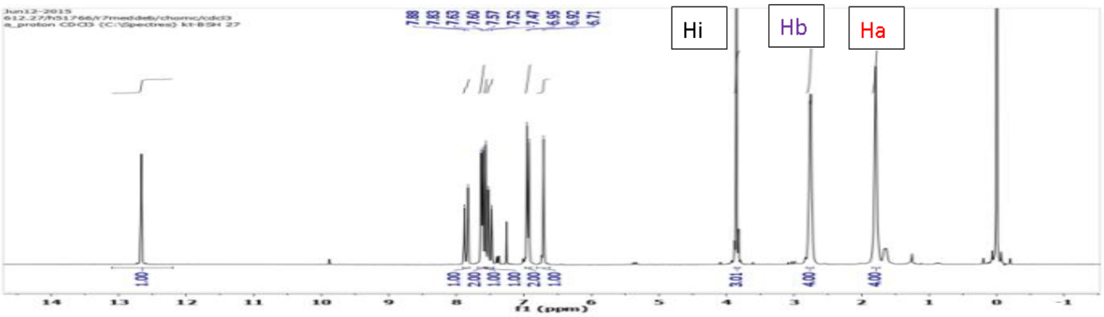


Figure 1. ^{1}H NMR spectrum of chalcone $(E)-$**2d**.

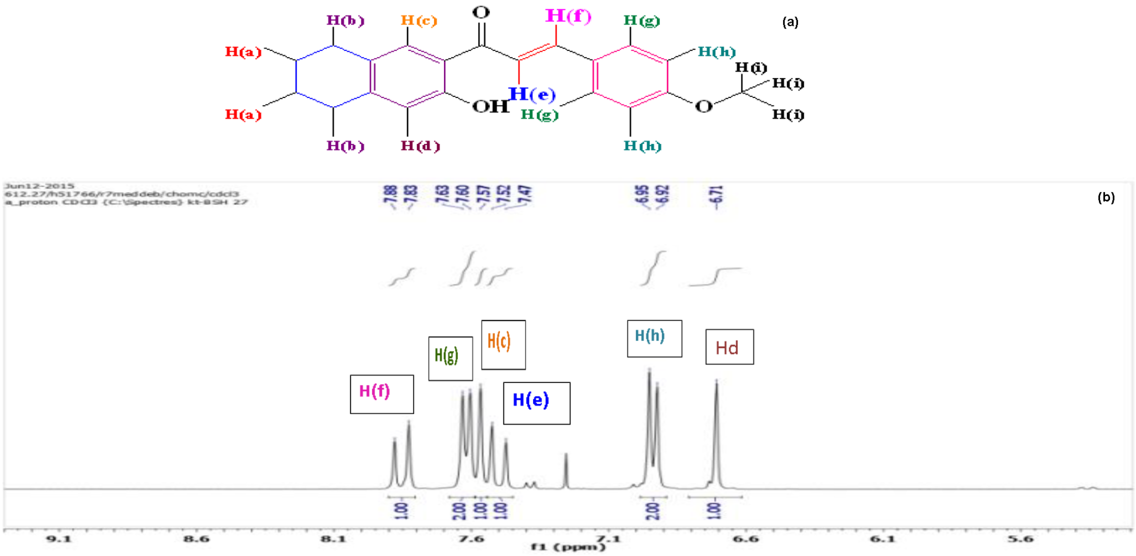


Figure 2. a) Structure of chalcone (E)**-2d**. b) Region 6–8 ppm of ^{1}H NMR spectrum of chalcone $(E)-$**2d**.

In addition, we did not observe any resonance signal in the region ranging from 6 to 8 ppm, corresponding to ethylenic protons of chalcone $(Z)-$**2d.** Moreover, the higher value of the coupling constants ($^{3}J_{H(e)-H(f)}$ = 15.6 Hz) between the ethylenic protons is in favor of $(E)-$**2d** (Figure 2b).

It is noteworthy that the chemical shifts of vinylic protons of all chalcones **2b–2d** ranged from 7.45 to 7.54 ppm and the values of the coupling constants between them are still higher ($^{3}J_{H(e)-H(f)}$ = 15.4–15.6 Hz), suggesting again the stereoselective formation of (E))**-2b–2d** (Table 2).

All these $^{3}J_{H(e)-H(f)}$ values are in agreement with those of other $(E)-$chalcones previously described in the literature.[34]

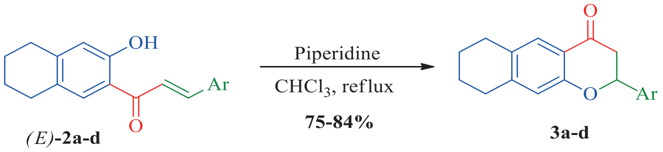
Next, we focused our attention on the cyclization of chalcones **2a–2d** into flavanones **3a–2d** by an intramolecular oxa-Michael addition, using common tertiary amines as bases[18] including 1,4-diazabicyclo[2.2.2]

Table 2. Chemical shifts and $^{3}J_{H(e)-H(f)}$ for chalcones (E)-**2a**–**2d**.

Entry	Chalcones **2**	$\delta_{\mathbf{H(e)}}$ **(ppm)**	$\delta_{\mathbf{H(f)}}$ **(ppm)**	$^{3}\boldsymbol{J}_{\mathbf{H(e)-H(f)}}$ **(Hz)**
1	$(E)-$**2a**	7.52	7.85	15.6
2	$(E)-$**2b**	7.54	8.23	15.6
3	$(E)-$**2c**	7.49	8.16	15.6
4	$(E)-$**2d**	7.45	7.83	15.4

octane (DABCO), 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), 4-dimethylaminopyridine (DMAP), and imidazole in water or ethanol as solvents (Table 3, entries 1–5).

Table 3. Optimization of the reaction conditions for the conversion of **2a** into **3a**.



Entry	Chalcone **2a**	Solvent	Amine	t (h)	Flavanone **3**	Yield **3** (%)
1	**2a**	H_2O	DABCO (3 equiv.)	48	N.R.	N.R.
2	**2a**	EtOH	DABCO (3 equiv.)	48	-	-
3	**2a**	EtOH	DBU (3 equiv.)	48	-	-
4	**2a**	EtOH	DMAP (3 equiv.)	48	-	-
5	**2a**	EtOH	Imidazole (3 equiv.)	48	-	-
6	**2a**	H_2O	Piperidine (6 mL)	48	-	-
7	**2a**	EtOH	Piperidine (6 mL)	48	**3a**	40
8	**2a**	Et_2O	Piperidine (6 mL)	48	**3a**	40
9	**2a**	CH_2Cl_2	Piperidine (6 mL)	48	**3a**	40
10	**2a**	$CHCl_3$	Piperidine (6 mL)	48	3a	75

In all these cases, heating at reflux a mixture of chalcone **2a** and 3 equiv. of each of these bases, in water or ethanol as solvents, was unsuccessful and the starting materials were completely recovered after 48 h (Table 3, entries 1–5).

After that, we followed a previous report on the cyclization of a variety chalcones into the corresponding flavanones,[35] using a piperidine excess in water, but unfortunately the conversion of **2a** into **3a** did not occur, presumably because we had observed that chalcone **2a** was not soluble in such a solvent (Table 2, entry 6). Therefore, we investigated the cyclization of compound **2a** into flavanone **3a** in the presence of an excess of piperidine in various organic solvents (EtOH, Et_2O, CH_2Cl_2, and $CHCl_3$) (Table 2, entries 7–10).

Interestingly, the reaction worked in all these solvents, affording **2a**, and the best yield (75%) was obtained when the title reaction was carried out in refluxing chloroform for 48 h (Table 3, entry 10).

Following the same protocol and involving piperidine in refluxing chloroform, a new series of flavanones **3b**–**3d** were successfully synthesized in 82%–84% yields (Table 4, entries 2–4).

Below are listed the chemical shifts of protons H-2 and H-3 of flavanones **3a**–**3d** as well as the values of the coupling constants, either ^{3}J between protons H-2 and H-3 or ^{2}J between the diastereotopic protons H-3a and H-3b (Table 5).

We summarized the ^{1}H NMR data for H-2, H-3a, and H-3b in the following triangle. Indeed, the vertices of the triangle represent these protons and their chemical shifts, and the three sides give all the coupling

Table 4. Piperidine-promoted cyclization reaction of chalcones **2a–2d** into flavanones **3a–3d** in refluxing chloroform.

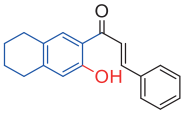
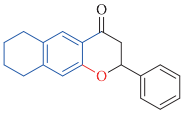
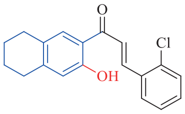
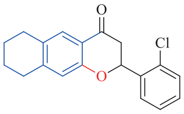
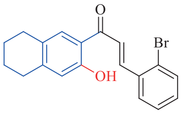
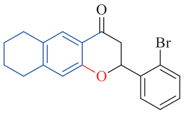
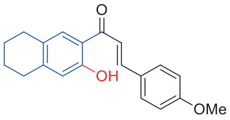
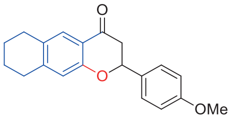
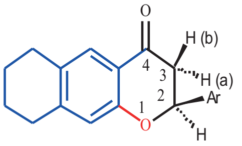
Entry	Chalcone **2**	Flavanone **3**	t (h)	Yield **3** (%)
1	*(E)*-**2a :** 	**3a :** 	48	75
2	*(E)*-**2b :** 	**3b :** 	48	82
3	*(E)*-**2c :** 	**3c :** 	48	82
4	*(E)*-**2d :** 	**3d :** 	48	84

Table 5. ^{1}H NMR data for protons H-2 and H-3 of flavanones **3a–3d.**



3

a. Ar = C_6H_5; b. Ar = 2-ClC_6H_4;
c. Ar = 2-BrC_6H_4; d. Ar = 4-$OMeC_6H_4$

Flavanone **3**	H-2: δ ppm ($^3J_{anti}$, $^3J_{syn}$Hz)	H$_a$-3: δ ppm (^2J, ^3JHz)	H$_b$-3: δ ppm (^2J, ^3JHz)
3a	5.39 (13.1, 3.1)	2.82 (16.9, 3.1)	3.01 (16.9, 13.1)
3b	5.80 (13.2, 2.6)	2.84 (16.9, 2.6)	2.98 (16.9, 13.2)
3c	5.76 (13.3, 2.8)	2.83 (16.9, 2.8)	3.01 (16.9, 13.3)
3d	5.36 (13.0, 2.9)	2.82 (16.9, 2.9)	3.03 (16.9, 13.0)

constants values of ^3Jsyn, ^3Janti, and ^2Jgem (Figure 3). It is noteworthy that all these data are in agreement with those of the literature (Figure 3).[34]

Alternatively, we next attempted the direct conversion of chalcones **2a–2d** into the corresponding flavones **4a–4d**, using a tandem oxidative cyclization approach. Successfully, upon treatment of chalcones **2a–2d** with iodine (10 mol%) as the catalyst in DMSO at 80 °C, a novel series of flavones **4a–4d** were prepared within 5 min, in 85%–90% yields (Scheme 3; Table 6). The possible mechanism is in agreement with the literature.[36]

In conclusion, we have developed an efficient synthetic route for the preparation of a series of chalcones, using a Claisen–Schmidt condensation at room temperature, between THN and aromatic aldehydes in an aqueous solution of KOH (40%) in ethanol.

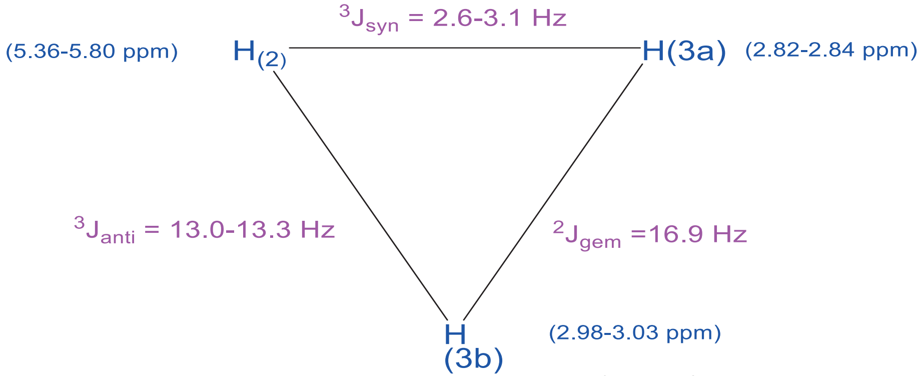
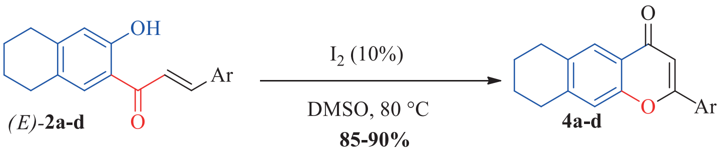
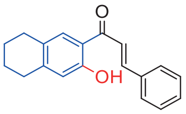
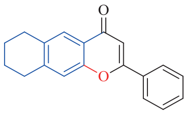
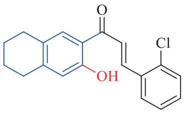
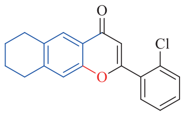
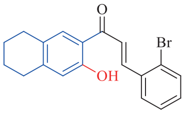
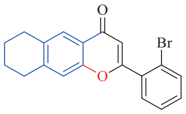
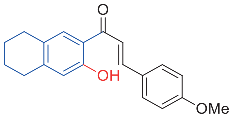
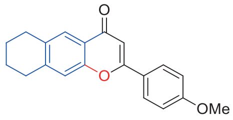


Figure 3. Chemicals shifts and coupling constants values ^2J and ^3J between H-2 and H-3.

Table 6. Straightforward conversion of chalcones **2a–2d** into flavones **4a–4d**.



Entry	Chalcone **2**	Flavone **4**	t (min)	Yield **4** (%)
1	(*E*)-**2a** : 	**4a** : 	5	90
2	(*E*)-**2d** : 	**4b** : 	5	85
3	(*E*)-**2c** : 	**4c** : 	5	85
4	(*E*)-**2d** : 	**4d** : 	5	85

Their further intramolecular cyclization into flavanones was performed in high yields, in refluxing chloroform, using piperidine. Alternatively, a tandem cyclization-oxidation of these chalcones using I_2/DMSO afforded the corresponding flavones.

All the newly synthesized chalcones, flavanones, and flavones were isolated in high yields of 80%–90% and their antimicrobial,[33] antioxidant, and antiinflammatory activities[34] as well as their modulatory properties of enzymes[37] are being evaluated.

3. Experimental

3.1. General

^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker AC-300 spectrometer (300 MHz for ^{1}H and 75 MHz for ^{13}C) in $CDCl_3$, using TMS as an internal standard (chemical shifts in δ values, J in Hz). Resolution mass spectra (MS) were recorded on a mass spectrometer. High resolution mass spectra (HRMS) were recorded as ESI-MS. Analytical thin-layer chromatography (TLC) was performed using Fluka Kieselgel 60 F_{254} precoated silica gel plates. Visualization was achieved by UV light (254 nm). Flash chromatography was performed using Merck silica gel 60 and a gradient solvent system (pet-ether/ether as eluents). Please see the Supplementary material for full experimental details, ^{1}H and ^{13}C NMR spectra, and MS.

3.1.1. General procedure for the synthesis of chalcones (2a–2d)

A mixture of tetrahydronaphthalene **1** (0.01 mol) and aromatic aldehyde (0.01 mol) was stirred in ethanol (5 mL) and then an aqueous solution of KOH (40%, 1 mL) was added. The mixture was kept overnight at room temperature, and then was acidified with an aqueous solution of 2 M HCl. The separated solid was filtered and crystallized from ethanol, affording the pure chalcone **2a**.

***(E)*-1-(3-Hydroxy-5,6,7,8-tetrahydronaphthale-2-yl)-3-phenylprop-2-en-1-one (2a).** Yellow solid; yield: 90%; mp 138–140 C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.81–1.74 (m, 4H), 2.78–2.72 (m, 4H), 6.71 (s, 1H, ArH), 7.45–7.39 (m, 4H, ArH), 7.58 (d, J_α = 15.6 Hz, 1H), 7.55–7.39 (m, 2H, ArH), 7.85 (d, J_β = 15.6 Hz, 1H), 12.37 (s, 1H, ArOH). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 22.8, 23.4, 28.8, 30.0, 118.0, 118.6, 121.0, 127.9, 128.6, 129.1, 129.7, 130.6, 135.2, 144.7, 147.6, 161.4, 193.3. MS (m/z) (rel intensity, %) 278 (M$^+$, 78), 261 (9), 201 (99), 174 (100), 77 (64). HRMS (ES+): m/z calcd for $C_{19}H_{19}O_2$ [M+H]$^+$ 279.1385, found 279.1385.

***(E)*-3-(2-Chlorophenyl)-1-(3-hydroxy-5,6,7,8-tetrahy-dronaphthalen-2-yl)prop-2-en-1-one (2b).**Yellow solid, yield: 83%; mp 134–136 C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.81–1.74 (m, 4H), 2.78–2.72 (m, 4H), 6.71(s, 1H, ArH), 7.52–7.28 (m, 4H, ArH), 7.54 (d, J_α = 15.6 Hz, 1H), 7.73–7.70 (m, 1H, ArH), 8.23 (d, J_β = 15.6 Hz, 1H), 12.28 (s, 1H, ArOH). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 22.6, 23.2, 28.6, 30.0, 117.90–118.3, 123.6, 127.0, 127.9, 127.99, 129.7, 130.3, 131.1, 133.4, 135.5, 140.3, 147.7, 161.3, 193.0. MS (m/z) (rel intensity, %) 312 (M$^+$, 35), 277 (98), 201 (34), 174 (100), 117 (1), 77 (21). HRMS (ES+): m/z calcd for $C_{19}H_{18}ClO_2$ [M+H]$^+$ 313.0995, found. 313.1007.

(*E)*-3-(2-Bromophenyl)-1-(3-hydroxy-5,6,7,8-tetray-dronaphthalen-2-yl)prop-2-en-1-one (2c). Yellow solid, yield: 83%; mp 140–142 C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.82–1.76 (m, 4H), 2.79–2.71 (m, 4H), 6.71 (s, 1H), 7.36–7.19 (m, 2H, ArH), 7.49 (d, J_α = 15.6 Hz, 1H), 7.52 (s, 1H, ArH), 7.72–7.60 (m, 2H, ArH); 8.16 (d, J_β = 15.6, 1H), 12.27 (s, 1H, ArOH). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 22.6, 23.2, 29.9, 30.5, 117.8, 118.3, 123.8, 125.8, 127.6, 127.9, 128.0, 129.7, 131.2, 133.5, 135.2, 142.8, 147.7, 161.3, 192.9. MS (m/z) (rel intensity, %) 356 (M$^+$, 11), 277 (100), 201 (47), 174 (23), 77 (12). HRMS (ES$^+$): m/z calcd for $C_{19}H_{18}^{79}BrO_2$ [M+H]$^+$ 357.0490, found 357.0482, calcd for $C_{19}H_{18}^{81}BrO_2$ [M+H]$^+$ 359.0470, found 359.0475.

(*E)*-1-(3-Hydroxy-5,6,7,8-tetrahydronaphthalen-2-yl)-3-(4-methoxyphenyl)prop-2-en-1-one (2d). Yellow solid, yield: 90%; mp 100–102 C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.82–1.76 (m, 4H), 2.79–2.73 (m, 4H), 3.84 (s, 3H), 6.71 (s, 1H) 6.94–6.91 (m, 2H, ArH),7.45 (d, J_α = 15.4 Hz, 1H), 7.6–7.54 (m, 3H, ArH), 7.83 (d, J_β = 15.4 Hz, 1H), 12.50 (s, 1H, ArOH). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 22.8, 23.2, 28.6, 30.0, 55.5, 114.7, 117.5, 117.9, 118.5, 127.6, 127.9, 129.6, 130.4, 144.6, 147.2, 161.3, 162.1, 193.3. MS (m/z) (rel intensity, %) 308 (M^+, 37), 277 (8), 174 (41), 134 (100), 77 (19). HRMS (ES^+): m/z calcd for $C_{20}H_{21}O_3$ $[M+H]^+$ 309.1491, found 309.1492.

3.1.2. General procedure for the synthesis of flavanones (3a–3d)

A mixture of 2'-hydroxychalcone (0.01 mol) **2a** and piperidine (6 mL) was stirred for 48 h in chloroform (5 mL) at reflux. Then the reaction mixture was acidified with an aqueous solution of 2 M HCl and was extracted with CH_2Cl_2 (3 × 5 mL). The resulting extracts were combined, washed with brine, and dried over anhydrous $MgSO_4$. The residue, obtained after solvent evaporation, was purified by silica-gel column chromatography (5% ether/petroleum ether), affording the pure flavanone **3a**.

2-Phenyl-6,7,8,9-tetrahydro-2H-benzo[g]chromen-4(3H)-one (3a). Pale yellow solid, yield: 75%; mp 90–92 C. ^1H NMR ($CDCl_3$, 300 MHz) δ 1.79–1.74 (m, 4H), 2.75–2.73 (m, 4H), 2.82 (dd, J = 16.9, 3.1 Hz, 1H), 3.01 (dd, J = 16.9, 13.1 Hz, 1H), 5.39 (dd, J = 13.1, 3.1 Hz, 1H), 6.74 (s, 1H), 7.47–7.35 (m, 5H, ArH), 7.62 (s, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 22.6, 23.1, 28.5, 29.7, 44.7, 79.4, 117.4, 118.8, 126.1, 126.8, 128.6, 128.7, 130.9, 139.1, 147.2, 159.1, 192. MS (m/z) (rel intensity, %) 278 (M^+, 57), 201 (49), 174 (100), 77 (22). HRMS (EI^+): m/z calcd for $C_{19}H_{18}O_2$ 278.13068, found 278.13029.

2-(2-Chlorophenyl)-6,7,8,9-tetrahydro-2H-benozo[g]chromen-4(3H)-one (3b). Pale yellow solid, yield: 82%; mp 124–126 C. ^1H NMR ($CDCl_3$, 300 MHz) δ 1.81–1.74 (m, 4H), 2.81–2.74 (m, 4H), 2.84 (dd, J = 13.2, 16.9 Hz, 1H), 2.98 (dd, J = 16.9, 2.6 Hz, 1H), 5.80 (dd, J = 13.2, 2.6 Hz, 1H), 6.77 (s, 1H), 7.42–7.23 (m, 3H, ArH), 7.65 (s, 1H), 7.74–7.72 (m, 1H, ArH). ^{13}C NMR ($CDCl_3$, 75 MHz) δ22.6, 23.05, 28.5, 30.1, 43.6, 76.3, 118.9, 126.9, 127.2, 127.4, 129.5, 129.7, 131.2, 131.6, 137.0, 147.2, 159.2, 191.6. MS (m/z) (rel intensity, %) 312 (M^+, 31), 277 (90), 201 (32), 174 (100), 117(47), 77 (23). HRMS (ES^+): m/z calcd for $C_{19}H_{18}^{35}ClO_2$ $[M+H]^+$ 313.0989, found 313.0995.

2-(2-Bromophenyl)-6,7,8,9-tetrahydro-2H-benzo[g]chromen-4(3H)-one (3c). Pale yellow solid, yield: 82%; mp 139–141 C. ^1H NMR ($CDCl_3$, 300 MHz) δ 1.82–1.75 (m, 4H), 2.81–2.73 (m, 4H), 2.83 (dd, J = 13.3, 16.9 Hz, 1H), 3.01 (dd, J = 16.9, 2.8 Hz, 1H), 5.76 (dd, J = 13.3, 2.8 Hz, 1H), 6.78 (s, 1H), 7.26–7.20 (m, 1H, ArH), 7.45–7.38 (m, 1H, ArH), 7.59–7.57 (m, 1H, ArH), 7.65 (s, 1H), 7.74–7.70 (m, 1H, ArH). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 22.7, 23.06, 28.5, 30.1, 43.7, 78.6, 117.4 118,9, 121.5, 126.9, 127.5, 128.01, 129.8, 131.2, 132.9, 138.6, 147.3, 159.2, 191.6. MS (m/z) (rel intensity, %) 356 (M^+, 7), 277 (100), 201 (45), 174 (25), 77 (18). HRMS (ES^+): m/z calcd for $C_{19}H_{18}^{79}BrO_2$ $[M+H]^+$ 357.0490, found 357.0496, calcd for $C_{19}H_{18}^{81}BrO_2$ $[M+H]^+$ 359.0470, found 359.0474.

2-(4-Methoxyphenyl)-6,7,8,9-tetrahydro-2H-benzo[g]chromen-4(3H)-one (3d). Pale yellow solid, yield: 84%; mp 100–102 C. ^1H NMR ($CDCl_3$, 300 MHz) δ 1.82–1.74 (m, 4H), 2.78–2.70 (m, 4H), 2.80 (dd, J = 16.9, 2.9 Hz, 1H), 3.03 (dd, J = 16.9, 13.0 Hz, 1H), 3.82 (s, 3H), 5.36 (dd, J = 13.0, 2.9 Hz, 1H), 6.73 (s, 1H, ArH), 6.96–6.91 (m, 2H, ArH), 7.40–7.37 (m, 2H, ArH), 7.62 (s, 1H, ArH). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 22.7, 23.08, 28.5, 30.09, 44.6, 55.3, 79.2, 114.1, 117.5, 118.8, 126.8, 127.7, 131, 131.1, 147.1, 159.3, 160, 192.2. MS (m/z) (rel intensity, %) 308 (M^+, 1), 201 (6), 174 (37), 134 (100), 117 (20), 77 (9). HRMS (ES^+): m/z calcd for $C_{20}H_{21}O_3$ $[M+H]^+$ 309.1491, found 309.1491.

3.1.3. General procedure for the synthesis of flavones (4a–4d)

To a solution of 2'-hydroxychalcone **2a** (0.01 mol) in DMSO (5 mL) was added iodine (10%) and the reaction mixture was heated at 80 °C for 5 min. After cooling, the reaction mixture was diluted with water and the iodine was removed by washing with a saturated solution of sodium thiosulfate. The product **4a** was then extracted with CH_2Cl_2 (3 × 5 mL). The resulting extracts were combined, washed with brine, and dried over anhydrous $MgSO_4$, and the residue was purified by silica-gel column chromatography (20% ether/petroleum ether), affording pure flavone **4a**.

2-Phenyl-6,7,8,9-tetrahydro-4H-benzo[g]chromen-4-one (4a). Pale yellow solid, yield: 90%; mp 147–149 C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.87–1.81 (m, 4H), 2.85–2.94 (m, 4H), 6.77 (s, 1H), 7.27 (s, 1H), 7.68–7.53 (m, 3H, ArH), 7.94–7.94 (m, 3H, ArH). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 22.6, 2.9, 28.9, 30.0, 107.2, 117.4, 121.7, 125.07, 126.2, 129.0, 131.4, 132.1, 135.1, 144.7, 154.4, 163.1, 178.6. MS (m/z) (rel intensity, %) 276 (M^+, 100), 261 (2), 174 (18), 117 (24), 77 (14). HRMS (ES^+): m/z calcd for $C_{19}H_{17}O_2$ $[M+H]^+$ 277.1229, found 277.1237.

2-(2-Chlorophenyl)-6,7,8,9-tetrahydro-4H-benzo[g]chromen-4-one (4b). Pale yellow solid, yield: 85%; mp 90–92 C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.85–1.80 (m, 4H), 2.92–2.83 (m, 4H), 6.60 (s, 1H), 7.19 (s, 1H), 7.63–7.46 (m, 3H, ArH), 7.62–7.60 (m, 1H, ArH), 7.92 (s, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 22.57, 22.8, 28.9, 29.9, 112.5, 117.4–112.5, 121.5, 127.03, 130.6, 130.7, 131.6, 132.9, 132.8, 135.2, 144.9, 154.6, 162.3, 178.2. MS (m/z) (rel intensity, %) 310 (M^+, 7), 174 (24), 117 (26). HRMS (ES^+): m/z calcd for $C_{19}H_{16}ClO_2$ $[M+H]^+$ 311.0839, found 311.0844.

2-(2-Bromophenyl)-6,7,8,9-tetrahydro-4H-benozo[g]chromen-4-one (4c). Pale yellow solid, yield: 85%; mp 99–101 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.87–1.81 (m, 4H), 2.92–2.88 (m, 4H), 6.51 (s, 1H), 7.21 (s, 1H), 7.73–7.33 (m, 2H, ArH), 7.54–7.58 (m, 1H, ArH), 7.69–7.73 (m, 1H, ArH), 7.94 (s, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 22.6, 22.9, 28.9, 30.0, 112.3, 117.4, 121.6, 121.8, 125.1, 127.6, 130.8, 131.7, 133.9, 134.3, 135.3, 145.0, 154.6, 163.8, 178.3. MS (m/z) (rel intensity, %) 354 (M^+, 100), 207 (48), 174 (44), 117 (49); HRMS (ES^+): m/z calcd for $C_{19}H^{79}_{16}BrO_2$ $[M+H]^+$ 355.0334, found 355.0331; calcd for $C_{19}H^{81}_{16}BrO_2$ $[M+H]^+$ 357.0313, found 357.0314.

2-(4-Methoxyphenyl)-6,7,8,9-tetrahydro-4H benzo[g]chromen-4-one (4d). Pale yellow solid, yield: 85%; mp 135–137 C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.86–1.82 (m, 4H), 2.92–2.86 (m, 4H), 3.88 (s, 3H), 6.70 (s, 1H), 7.02 (s, 1H), 7.35–7.1 (m, 2H, ArH), 7.88–7.84 (m, 2H, ArH), 7.90 (s, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 22.6, 23.1, 28.9, 30.0, 55.5, 105.8, 114.4, 117.3, 121.6, 124.0, 125.0, 127.9, 134.9, 144.5, 154.3, 162.3, 163.1, 178.6. MS (m/z) (rel intensity, %) 306 (M^+, 100), 207 (3), 174. HRMS (ES^+): m/z calcd for $C_{20}H_{19}O_3$ $[M+H]^+$ 307.1334, found 307.1335.

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Supplementary material

1. General

^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker AC-300 spectrometer (300 MHz for ^{1}H and 75 MHz for ^{13}C) in $CDCl_3$, using TMS as an internal standard (chemical shifts in δ values, *J* in Hz). Resolution mass spectra (MS) were recorded on a mass spectrometer. High resolution mass spectra (HRMS) were recorded as ESI-MS. Analytical thin layer chromatography (TLC) was performed using Fluka Kieselgel 60 F_{254} precoated silica gel plates. Visualization was achieved by UV light (254 nm). Flash chromatography was performed using Merck silica gel 60 and a gradient solvent system (pet-ether/ether as eluents).

2. General procedure for the synthesis of chalcones (2a–2d)

A mixture of tetrahydronaphthalene **1** (0 .01 mol) and aromatic aldehyde (0.01 mol) was stirred in ethanol (5 mL) and then an aqueous solution of KOH (40%, 1 mL) was added. The mixture was kept overnight, at room temperature, and then was acidified with an aqueous solution of 2M HCl. The separated solid was filtered and crystallized from ethanol, affording the pure chalcone **2a**.

3. General procedure for the synthesis of flavanones (3a–3d)

A mixture of 2'-hydroxychalcone (0.01 mol) **2a** and piperidine (6 mL) was stirred for 48 h in chloroform (5 mL) at reflux. The reaction mixture was then acidified with an aqueous solution of 2 M HCl and was extracted with CH_2Cl_2 (3 × 5 mL). The resulting extracts were combined, washed with brine, and dried over anhydrous $MgSO_4$. The residue obtained after solvent evaporation was purified by silica-gel column chromatography (5% ether/petroleum ether), affording the pure flavanone **3a**.

4. General procedure for the synthesis of flavones (4a–4d)

To a solution of 2'-hydroxychalcone **2a** (0.01 mol) in DMSO (5 mL) was added iodine (10%)

and the reaction mixture was heated at 80 °C for 5 min. After cooling, the reaction mixture was diluted with water and the iodine was removed by washing with a saturated solution of sodium thiosulfate. The product **4a** was then extracted with CH_2Cl_2 (3 × 5 mL). The resulting extracts were combined, washed with brine, and dried over anhydrous $MgSO_4$ and the residue was purified by silica-gel column chromatography (20% ether/petroleum ether), affording the pure flavone **4a**.

5. Characterization data of chalcones (2a–2d)

(E)-1-(3-Hydroxy-5,6,7,8-tetrahydronaphthale-2-yl)-3-phenylprop-2-en-1-one (2a)

Yield (90%); yellow solid; mp = 138–140 °C; **^{1}H NMR** ($CDCl_3$, 300 MHz) δ 1.81–1.74 (m, 4H), 2.78–2.72 (m, 4H), 6.71 (s, 1H, ArH), 7.45–7.39 (m, 4H, ArH), 7.58 (d, J_α = 15.6 Hz, 1H), 7.55–7.39 (m, 2H, ArH), 7.85 (d, J_β = 15.6 Hz, 1H), 12.37 (s, 1H, ArOH); **^{13}C NMR** ($CDCl_3$, 75 MHz) δ 22.8, 23.4, 28.8, 30.0, 118.0, 118.6, 121.0, 127.9, 128.6, 129.1, 129.7, 130.6, 135.2, 144.7, 147.6, 161.4, 193.3; **MS (m/z)** (rel intensity, %) 278 (M^+, 78), 261 (9), 201 (99), 174 (100), 77 (64); HRMS (ES+): m/z calcd for $C_{19}H_{19}O_2$ $[M+H]^+$ 279.1385, found 279.1385.

(E)-3-(2-Chlorophenyl)-1-(3-hydroxy-5,6,7,8-tetrahy-dronaphthalen-2-yl)prop-2-en-1-one (2b)

Yield (83%); yellow solid; mp = 134–136 °C; **^{1}H NMR** ($CDCl_3$, 300 MHz) δ 1.81–1.74 (m, 4H), 2.78–2.72 (m, 4H), 6.71 (s, 1H, ArH), 7.52–7.28 (m, 4H, ArH), 7.54 (d, J_α = 15.6 Hz, 1H), 7.73–7.70 (m, 1H, ArH), 8.23 (d, J_β = 15.6 Hz, 1H), 12.28 (s, 1H, ArOH); **^{13}C NMR** ($CDCl_3$, 75 MHz) δ 22.6, 23.2, 28.6, 30.0, 117.90-118.3, 123.6, 127.0, 127.9, 127.99, 129.7, 130.3, 131.1, 133.4, 135.5, 140.3, 147.7, 161.3, 193.0; **MS (m/z)** (rel intensity, %) 312 (M^+, 35), 277 (98), 201 (34), 174 (100), 117 (1), 77 (21); HRMS (ES+): m/z calcd for $C_{19}H_{18}ClO_2$ $[M+H]^+$ 313.0995, found 313.1007.

(E)-3-(2-Bromophenyl)-1-(3-hydroxy-5,6,7,8-tetray-dronaphthalen-2-yl)prop-2-en-1-one (2c)

Yield (83%); yellow solid; mp = 140–142 °C; **^{1}H NMR** ($CDCl_3$, 300 MHz) δ 1.82–1.76 (m, 4H), 2.79–2.71 (m, 4H), 6.71 (s, 1H), 7.36–7.19 (m, 2H, ArH), 7.49 (d, J_α = 15.6 Hz, 1H), 7.52 (s, 1H, ArH), 7.72–7.60 (m, 2H, ArH); 8.16 (d, J_β = 15.6, 1H), 12.27 (s, 1H, ArOH); **^{13}C NMR** ($CDCl_3$, 75 MHz) δ 22.6, 23.2, 29.9, 30.5, 117.8, 118.3, 123.8, 125.8, 127.6, 127.9, 128.0, 129.7, 131.2, 133.5, 135.2, 142.8, 147.7, 161.3, 192.9; **MS (m/z)** (rel intensity, %) 356 (M^+, 11), 277 (100), 201 (47), 174 (23), 77 (12); HRMS (ES^+): m/z calcd for $C_{19}H_{18}{}^{79}BrO_2$ $[M+H]^+$ 357.0490, found 357.0482, calcd for $C_{19}H_{18}{}^{81}BrO_2$ $[M+H]^+$ 359.0470, found 359.0475.

(E)-1-(3-Hydroxy-5,6,7,8-tetrahydronaphthalen-2-yl)-3-(4-methoxyphenyl)prop-2-en-1-one (2d)

Yield (90%); yellow solid; mp = 100–102 °C; **^{1}H NMR** ($CDCl_3$, 300 MHz) δ 1.82–1.76 (m, 4H), 2.79–2.73 (m, 4H), 3.84 (s, 3H), 6.71 (s, 1H) 6.94–6.91 (m, 2H, ArH),7.45 (d, J_α = 15.4 Hz, 1H), 7.6–7.54 (m, 3H, ArH), 7.83 (d, J_β = 15.4 Hz, 1H), 12.50 (s, 1H, ArOH); **^{13}C NMR** ($CDCl_3$, 75 MHz) δ 22.8, 23.2, 28.6, 30.0, 55.5, 114.7, 117.5, 117.9, 118.5, 127.6, 127.9, 129.6, 130.4, 144.6, 147.2, 161.3, 162.1, 193.3; MS (m/z) (rel intensity, %) 308 (M^+, 37), 277 (8), 174 (41), 134 (100), 77 (19); HRMS (ES^+): m/z calcd for $C_{20}H_{21}O_3$ $[M+H]^+$ 309.1491, found 309.1492.

6. Characterization data of flavanones (3a–3d)

2-Phenyl-6,7,8,9-tetrahydro-2H-benzo[g]chromen-4 3H)-one (3a)

Yield (75%); pale yellow solid; mp = 90–92 °C; **^{1}H NMR** ($CDCl_3$, 300 MHz) δ 1.79–1.74 (m, 4H), 2.75–2.73 (m, 4H), 2.82 (dd, J = 16.9, 3.1 Hz, 1H), 3.01 (dd, J = 16.9, 13.1 Hz, 1H), 5.39 (dd, J = 13.1, 3.1 Hz, 1H), 6.74 (s, 1H), 7.47–7.35 (m, 5H, ArH), 7.62 (s, 1H); **^{13}C NMR** ($CDCl_3$, 75 MHz) δ 22.6, 23.1, 28.5, 29.7, 44.7, 79.4, 117.4, 118.8, 126.1, 126.8, 128.6, 128.7, 130.9, 139.1, 147.2, 159.1, 192. **MS (m/z)** (rel intensity, %) 278 (M^+, 57), 201 (49), 174 (100), 77 (22); HRMS (EI^+): m/z calcd for $C_{19}H_{18}O_2$ 278.13068, found 278.13029.

2-(2-Chlorophenyl)-6,7,8,9-tetrahydro 2Hbenozo[g] chromen-4(3H)-one (3b)

Yield (82%); pale yellow solid; mp = 124–126 °C; **^{1}H NMR** ($CDCl_3$, 300 MHz) δ 1.81–1.74 (m, 4H), 2.81–2.74 (m, 4H), 2.84 (dd, *J* = 13.2, 16.9 Hz, 1H), 2.98 (dd, *J* = 16.9, 2.6 Hz, 1H), 5.80 (dd, *J* = 13.2, 2.6 Hz, 1H), 6.77 (s, 1H), 7.42–7.23 (m, 3H, ArH), 7.65 (s, 1H), 7.74–7.72 (m, 1H, ArH); **^{13}C NMR** ($CDCl_3$, 75 MHz) δ22.6, 23.05, 28.5, 30.1, 43.6, 76.3, 118.9, 126.9, 127.2, 127.4, 129.5, 129.7, 131.2, 131.6, 137.0, 147.2, 159.2, 191.6; **MS (m/z)** (rel intensity, %) 312 (M^+, 31), 277 (90), 201 (32), 174 (100), 117(47), 77 (23); HRMS (ES^+): m/z calcd for $C_{19}H_{18}{}^{35}ClO_2$ $[M+H]^+$ 313.0989, found 313.0995.

2-(2-Bromophenyl)-6,7,8,9-tetrahydro-2H-benzo[g]chromen-4(3H)-one (3c)

Yield (82%); pale yellow solid; mp = 139–141 °C; **^{1}H NMR** ($CDCl_3$, 300 MHz) δ 1.82–1.75 (m, 4H), 2.81–2.73 (m, 4H), 2.83 (dd, *J* = 13.3, 16.9 Hz, 1H), 3.01 (dd, *J* = 16.9, 2.8 Hz, 1H), 5.76 (dd, *J* = 13.3, 2.8 Hz, 1H), 6.78 (s, 1H), 7.26–7.20 (m, 1H, ArH), 7.45–7.38 (m, 1H, ArH), 7.59–7.57 (m, 1H, ArH), 7.65 (s, 1H), 7.74–7.70 (m, 1H, ArH); **^{13}C NMR** ($CDCl_3$, 75 MHz) δ 22.7, 23.06, 28.5, 30.1, 43.7, 78.6, 117.4 ,118,9, 121.5, 126.9, 127.5, 128.01, 129.8, 131.2, 132.9, 138.6, 147.3, 159.2, 191.6; **MS (m/z)** (rel intensity, %) 356 (M^+, 7), 277 (100), 201 (45), 174 (25), 77 (18); HRMS (ES^+): m/z calcd for $C_{19}H_{18}{}^{79}BrO_2$ $[M+H]^+$ 357.0490, found 357.0496, calcd for $C_{19}H_{18}{}^{81}BrO_2$ $[M+H]^+$ 359.0470, found 359.0474.

2-(4-Methoxyphenyl)-6,7,8,9-tetrahydro-2Hbenzo[g]chromen-4(3H)-one (3d)

Yield (84%); pale yellow solid; mp = 100–102 °C; **^{1}H NMR** ($CDCl_3$, 300 MHz) δ 1.82–1.74 (m, 4H), 2.78–2.70 (m, 4H), 2.80 (dd, *J* = 16.9, 2.9 Hz, 1H), 3.03 (dd, *J* = 16.9, 13.0 Hz, 1H), 3.82 (s, 3H), 5.36 (dd, *J* = 13.0, 2.9 Hz, 1H), 6.73 (s, 1H, ArH), 6.96–6.91 (m, 2H, ArH), 7.40–7.37 (m, 2H, ArH), 7.62 (s, 1H, ArH); **^{13}C NMR** ($CDCl_3$, 75 MHz) δ 22.7, 23.08, 28.5, 30.09, 44.6, 55.3, 79.2, 114.1, 117.5, 118.8, 126.8, 127.7, 131, 131.1, 147.1, 159.3, 160, 192.2; **MS (m/z)** (rel intensity, %) 308 (M^+, 1), 201 (6), 174 (37), 134 (100), 117 (20), 77 (9); HRMS (ES^+): m/z calcd for $C_{20}H_{21}O_3$ $[M+H]^+$ 309.1491, found 309.1491.

7. Characterization data of flavones (4a–4d)

2-Phenyl-6,7,8,9-tetrahydro-4H-benzo[g]chromen-4-one (4a)

Yield: (90%); pale yellow solid; mp = 147–149 °C; **^{1}H NMR** ($CDCl_3$, 300 MHz) δ 1.87–1.81 (m, 4H), 2.85–2.94 (m, 4H), 6.77 (s, 1H), 7.27 (s, 1H), 7.68–7.53 (m, 3H, ArH), 7.94–7.94 (m, 3H, ArH); **^{13}C NMR** ($CDCl_3$, 75 MHz) δ 22.6, 2.9, 28.9, 30.0, 107.2, 117.4, 121.7, 125.07, 126.2, 129.0, 131.4, 132.1, 135.1, 144.7, 154.4, 163.1, 178.6; **MS (m/z)** (rel intensity, %) 276 (M^+, 100), 261 (2), 174 (18), 117 (24), 77 (14); HRMS (ES^+): m/z calcd for $C_{19}H_{17}O_2$ $[M+H]^+$ 277.1229, found 277.1237.

2-(2-Chlorophenyl)-6,7,8,9-tetrahydro-4H-benzo[g]chromen-4-one (4b)

Yield (85%); pale yellow solid; mp = 90–92 °C; **^{1}H NMR** ($CDCl_3$, 300 MHz) δ 1.85–1.80 (m, 4H), 2.92–2.83 (m, 4H), 6.60 (s, 1H), 7.19 (s, 1H), 7.63–7.46 (m, 3H, ArH), 7.62–7.60 (m, 1H, ArH), 7.92 (s, 1H); **^{13}C NMR** ($CDCl_3$, 75 MHz) δ 22.57, 22.8, 28.9, 29.9, 112.5, 117.4–112.5, 121.5, 127.03, 130.6, 130.7, 131.6, 132.9, 132.8, 135.2, 144.9, 154.6, 162.3, 178.2; **MS (m/z)** (rel intensity, %) 310 (M^+, 7), 174 (24), 117 (26); HRMS (ES^+): m/z calcd for $C_{19}H_{16}ClO_2$ $[M+H]^+$ 311.0839, found 311.0844.

2-(2-Bromophenyl)-6,7,8,9-tetrahydro-4H-benozo[g]chromen-4-one (4c)

Yield (85%); pale yellow solid; mp = 99–101 °C; **^{1}H NMR** ($CDCl_3$, 300 MHz) δ 1.87–1.81 (m, 4H), 2.92–2.88 (m, 4H), 6.51 (s, 1H), 7.21 (s, 1H), 7.73–7.33 (m, 2H, ArH), 7.54–7.58 (m, 1H, ArH), 7.69–7.73 (m, 1H, ArH), 7.94 (s, 1H); **^{13}C NMR** ($CDCl_3$, 75 MHz) δ 22.6, 22.9, 28.9, 30.0, 112.3,117.4, 121.6, 121.8, 125.1, 127.6, 130.8, 131.7, 133.9, 134.3, 135.3, 145.0, 154.6, 163.8, 178.3; **MS (m/z)** (rel intensity, %) 354 (M^+, 100), 207 (48), 174 (44), 117 (49); HRMS (ES^+): m/z calcd for $C_{19}H_{16}{}^{79}BrO_2$ $[M+H]^+$ 355.0334, found 355.0331, calcd for $C_{19}H_{16}{}^{81}BrO_2$ $[M+H]^+$ 357.0313, found 357.0314.

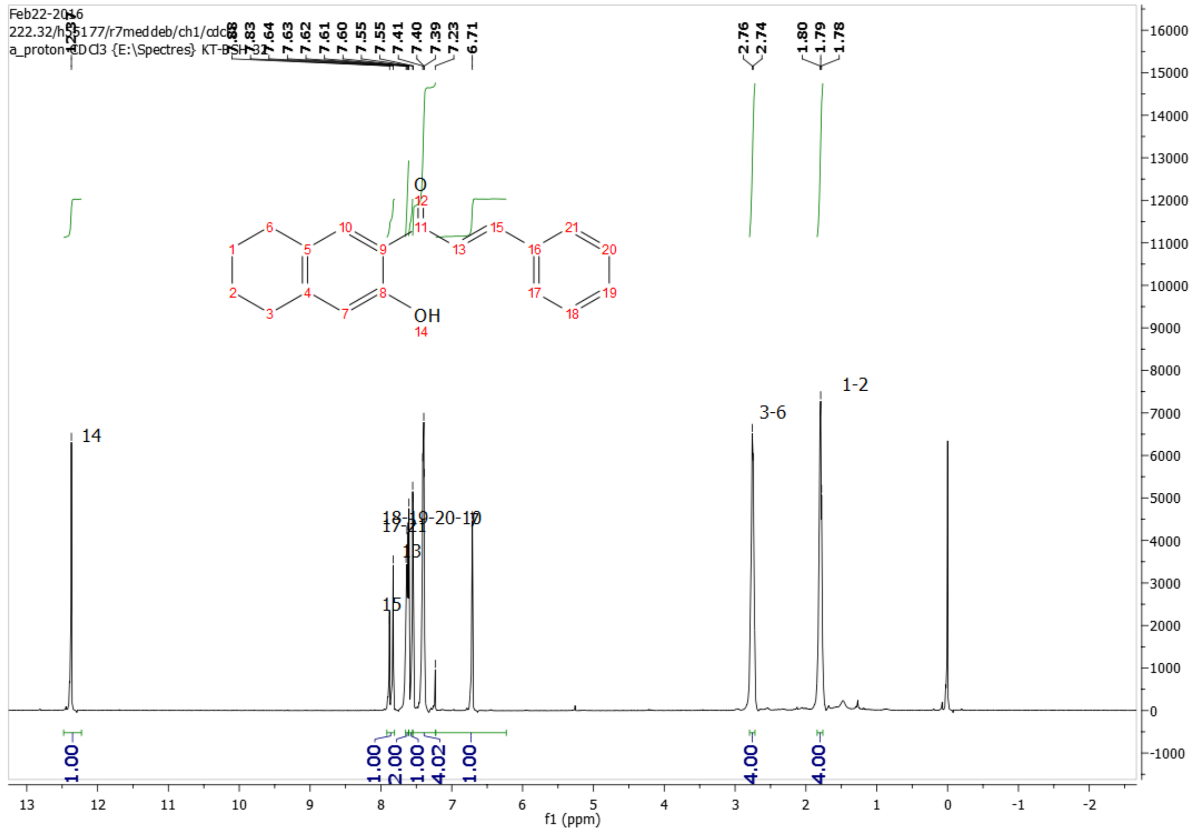
2-(4-Methoxyphenyl)-6,7,8,9-tetrahydro-4H benzo[g] chromen-4-one (4d)

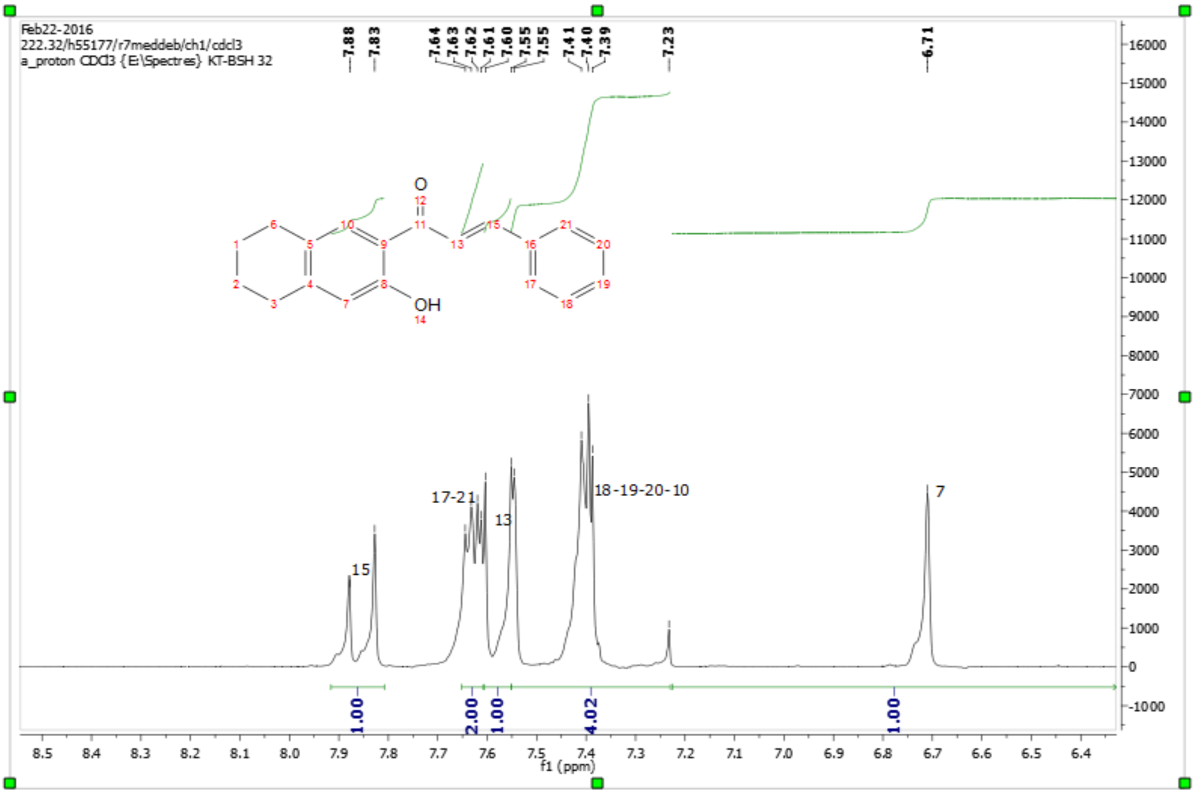
Yield (85%); pale yellow solid; mp = 135–137 °C; **^{1}H NMR** (CDCl$_3$, 300 MHz) δ 1.86–1.82 (m, 4H), 2.92–2.86 (m, 4H), 3.88 (s, 3H), 6.70 (s, 1H), 7.02 (s, 1H), 7.35–7.1 (m, 2H, ArH), 7.88–7.84 (m, 2H, ArH), 7.90 (s, 1H); **^{13}C NMR** (CDCl$_3$, 75 MHz) δ 22.6, 23.1, 28.9, 30.0, 55.5, 105.8, 114.4, 117.3, 121.6, 124.0, 125.0, 127.9, 134.9, 144.5, 154.3, 162.3, 163.1, 178.6; **MS (m/z)** (rel intensity, %) 306 (M$^+$, 100), 207 (3), 174; HRMS (ES$^+$): m/z calcd for $C_{20}H_{19}O_3$ [M+H]$^+$ 307.1334, found 307.1335.

8. ^{1}H and ^{13}C NMR spectra of chalcones (2a–2d)

(E)-1-(3-Hydroxy-5,6,7,8-tetrahydronaphthalen-2-yl)-3-phenylprop-2-en-1-one (2a)

^{1}H NMR

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7.40
7.39
7.23
6.71
O
OH
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13
18-19-20-10
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1.00
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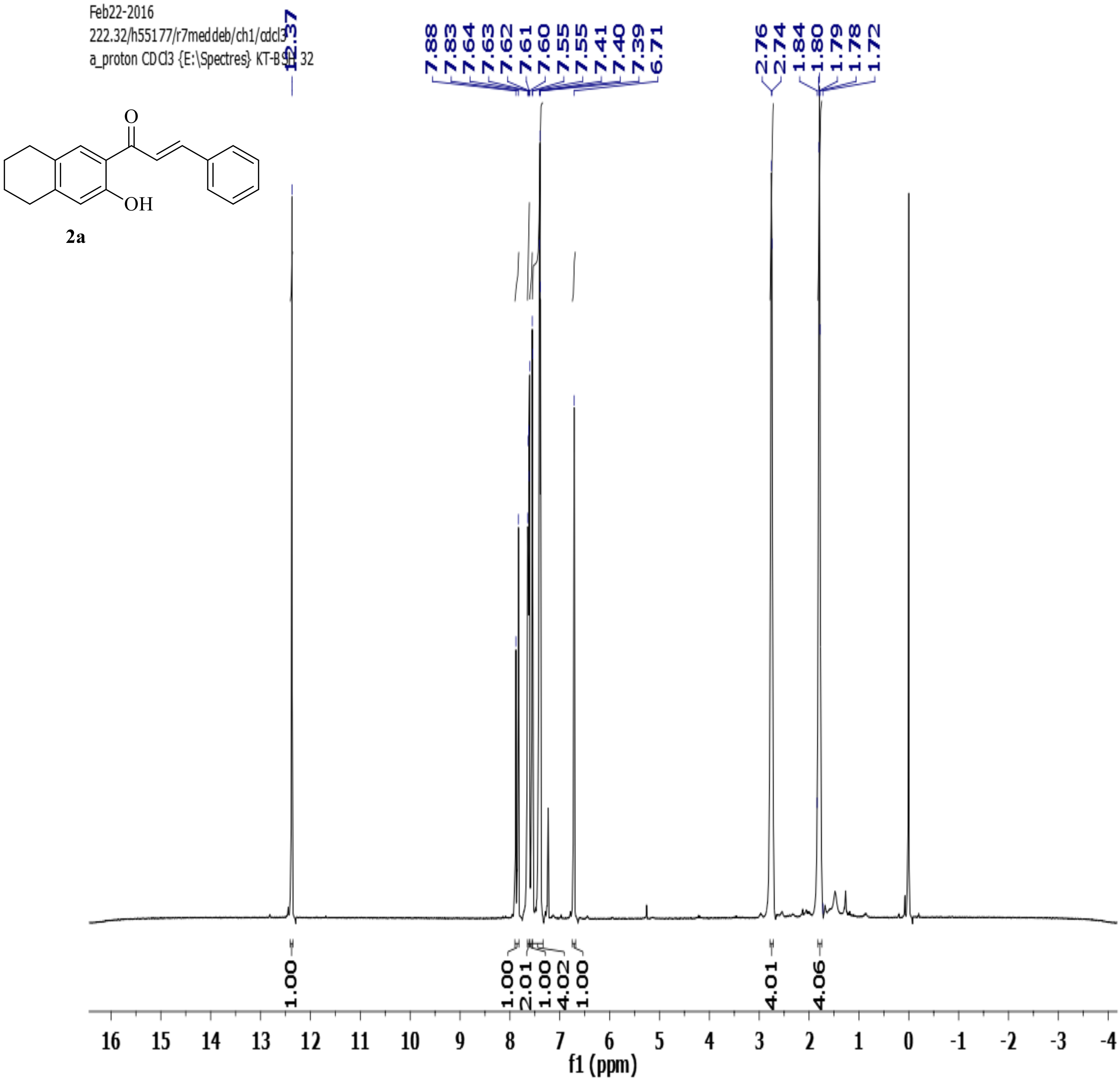
1.00
f1 (ppm)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7.55
7.41
7.40
7.39
6.71
2.76
2.74
1.84
1.80
1.79
1.78
1.72
O
OH
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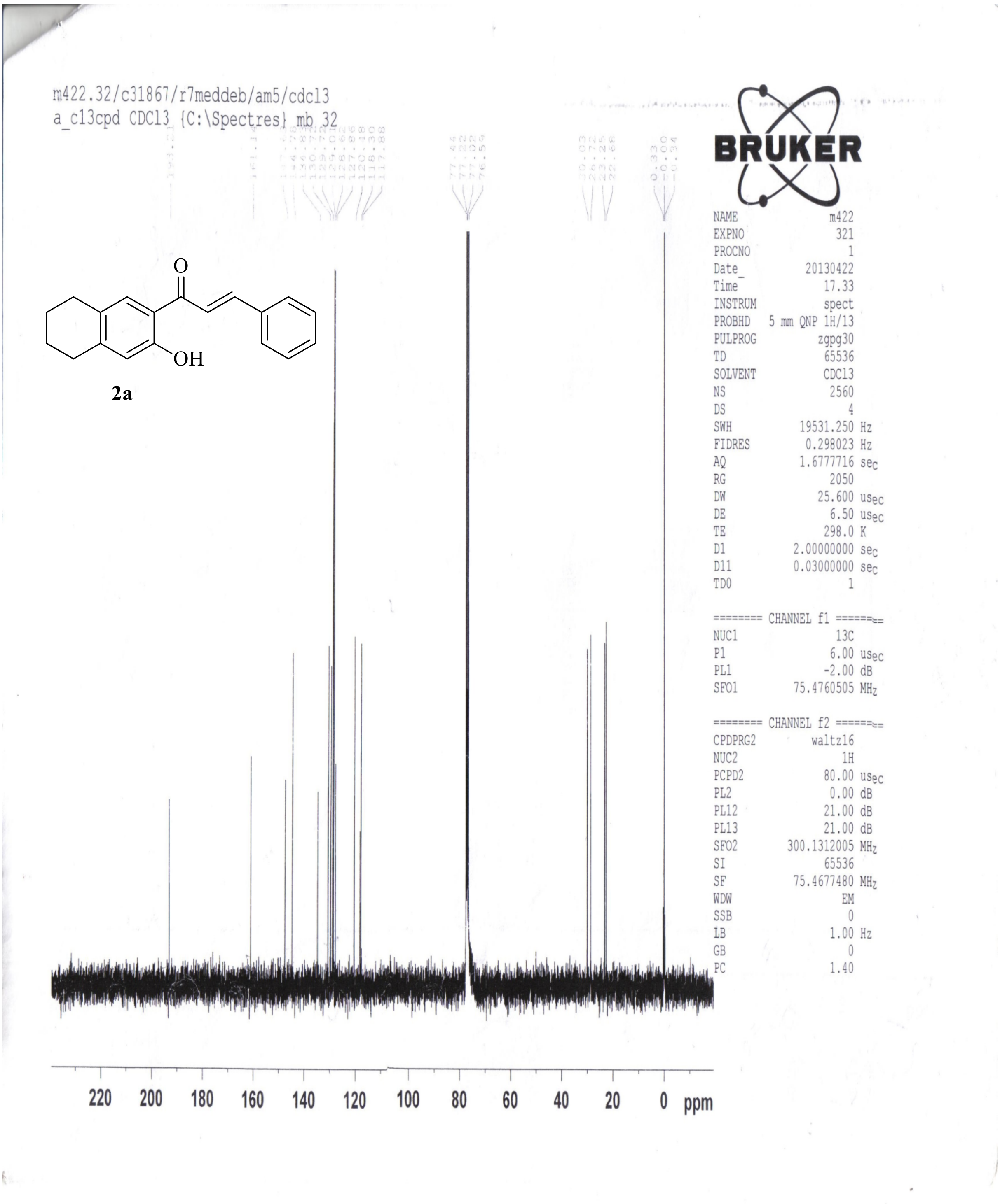
1.00
2.01
1.00
4.02
1.00
4.01
4.06
16
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
-3
-4
f1 (ppm)

2a

E)-1-(3-Hydroxy-5,6,7,8-tetrahydronaphthalen-2-yl)-3-phenylprop-2-en-1-one (2a)
^{13}C NMR



2a

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DE                   6.50 usec
TE                  298.0 K
D1             2.00000000 sec
D11            0.03000000 sec
TD0                     1

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P1                   6.00 usec
PL1                 -2.00 dB
SFO1           75.4760505 MHz

======== CHANNEL f2 ========
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PCPD2               80.00 usec
PL2                  0.00 dB
PL12                21.00 dB
PL13                21.00 dB
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SI                  65536
SF             75.4677480 MHz
WDW                    EM
SSB                     0
LB                   1.00 Hz
GB                      0
PC                   1.40
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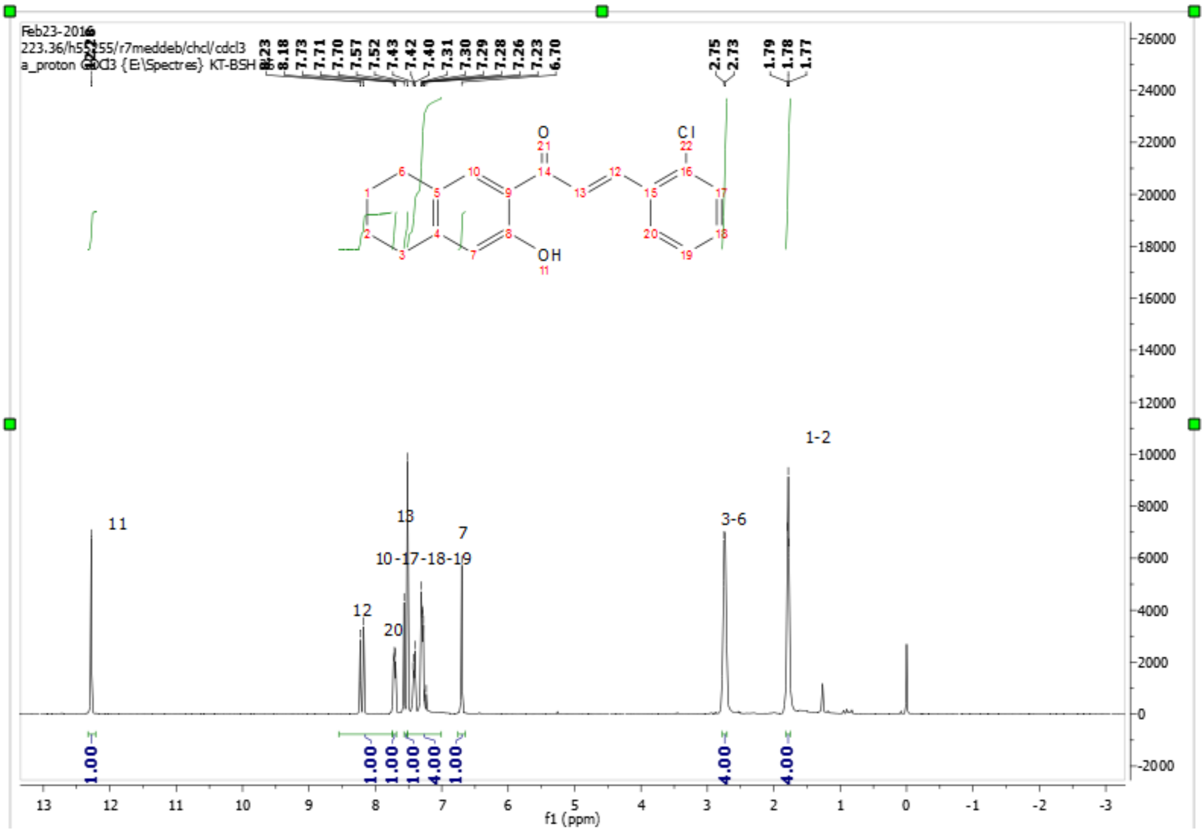
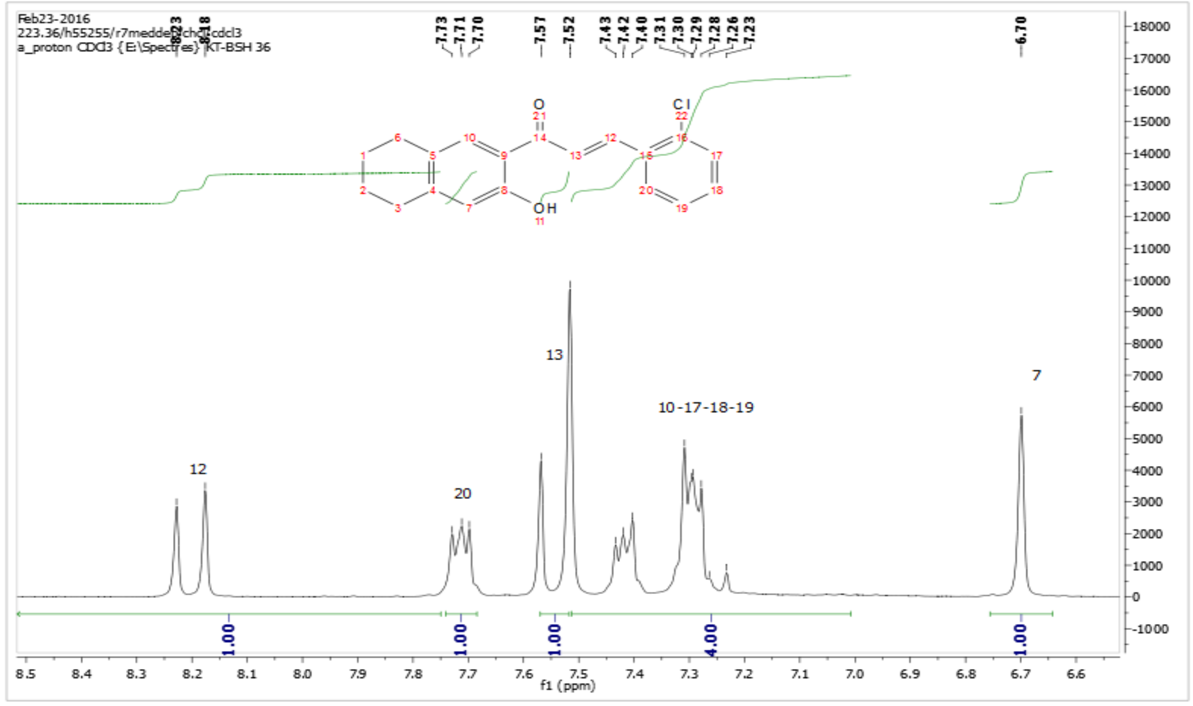
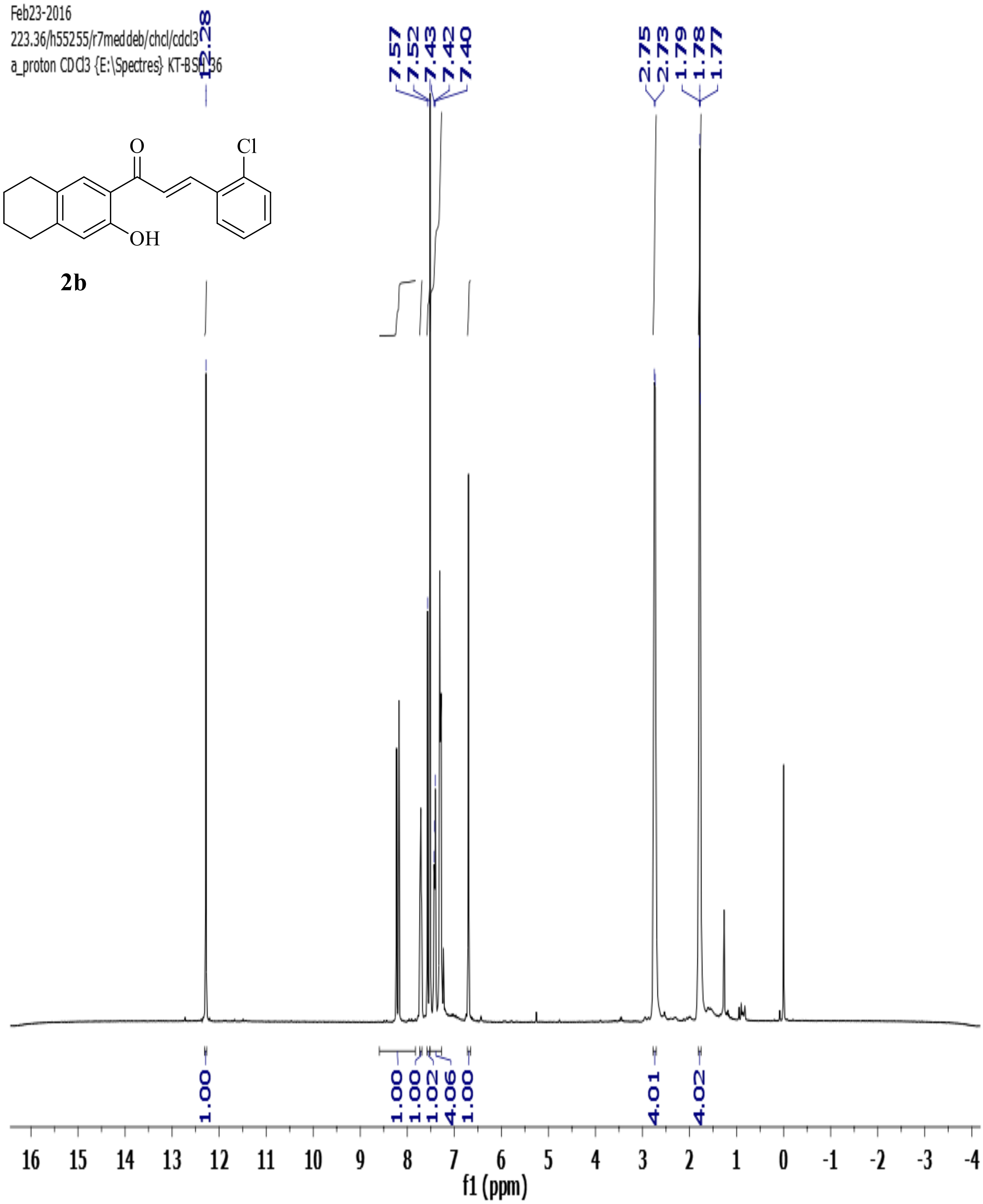
_(E)_-3-(2-Chlorophenyl)-1-(3-hydroxy-5,6,7,8-tetrahydronaphthalen-2-yl)prop-2-en-1-one (2b)

^{1}H NMR






Feb23-2016
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O
Cl
OH
2b
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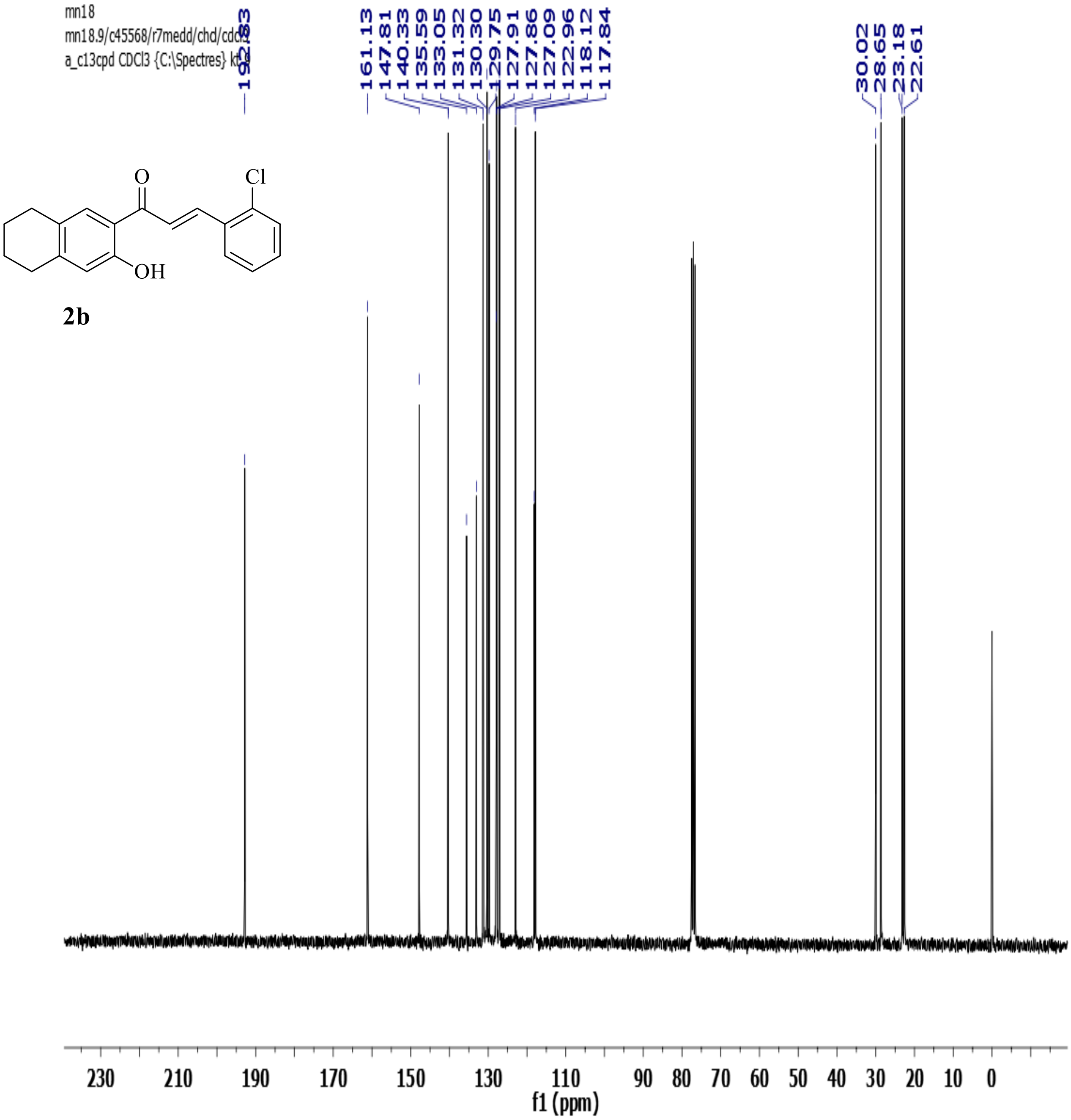
1.00
1.00
1.02
4.06
1.00
4.01
4.02
16
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
-3
-4
f1 (ppm)

(E)-3-(2-Chlorophenyl)-1-(3-hydroxy-5,6,7,8-tetrahydronaphthalen-2-yl)prop-2-en-1-one (2b)

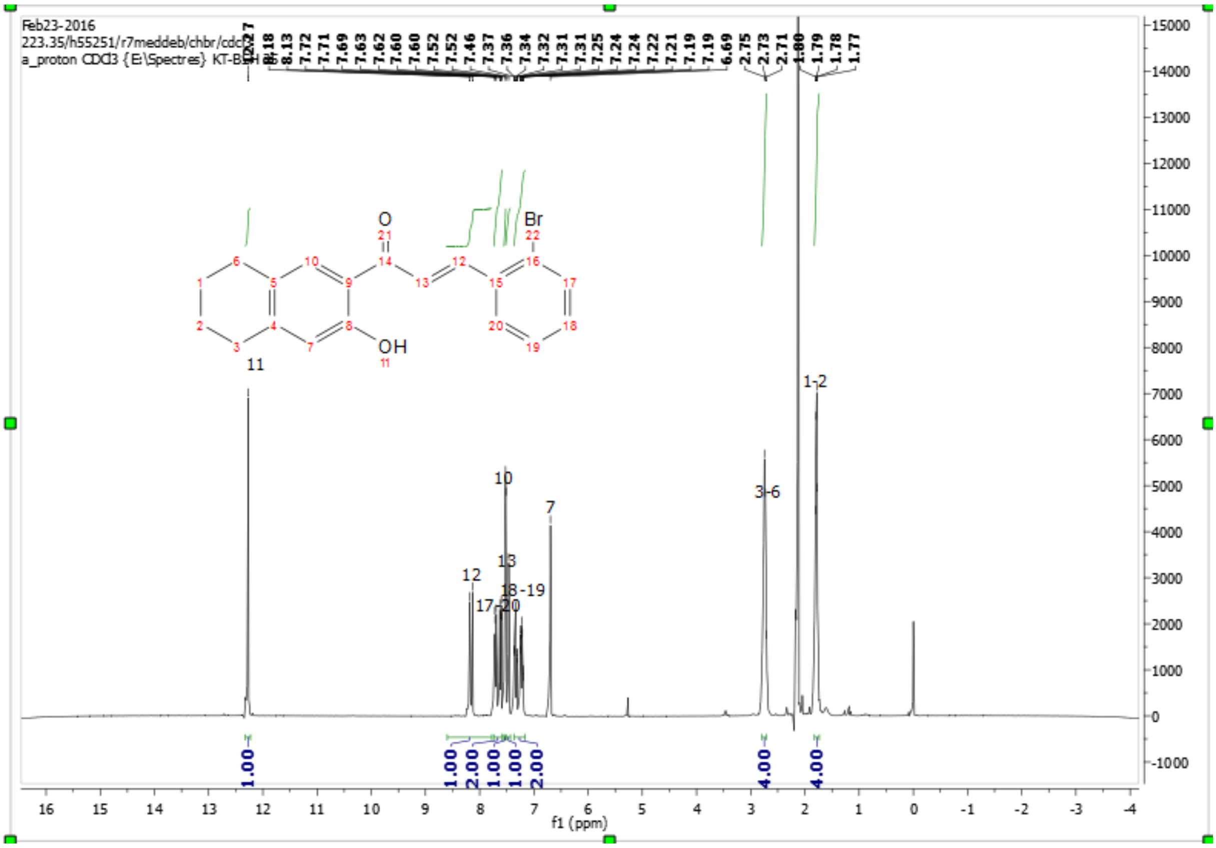
^{13}C NMR

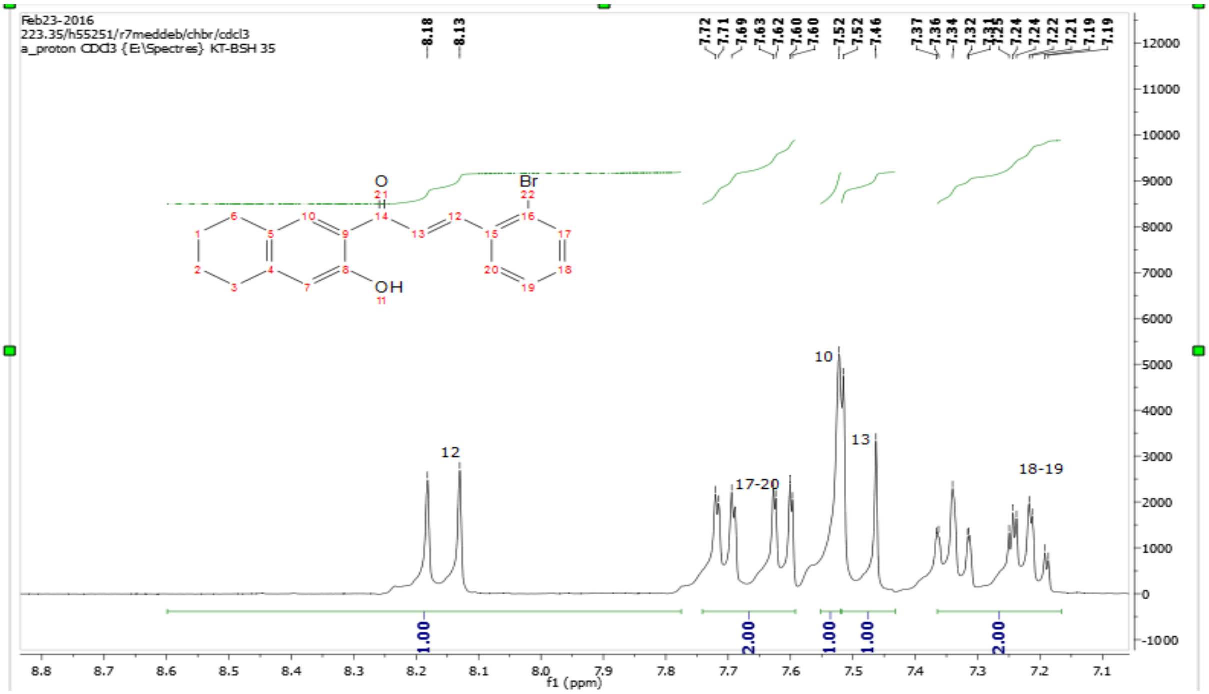


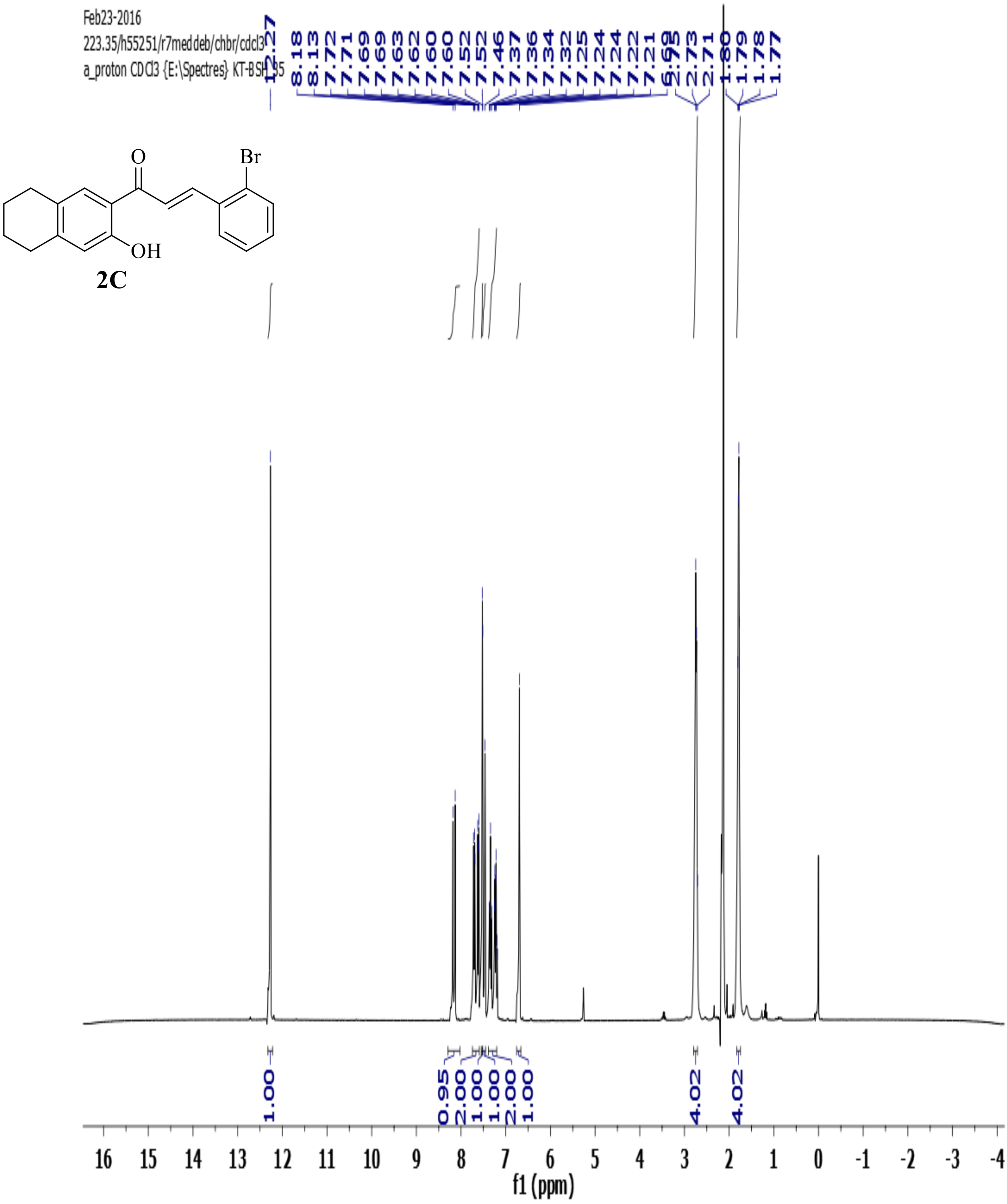
2b

(E)-3-(2-Bromophenyl)-1-(3-hydroxy-5,6,7,8-tetrahydronaphthalen-2-yl)prop-2-en-1-one (2c)

^{1}H NMR






Feb23-2016
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7.21
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2.73
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1.77
O
Br
OH
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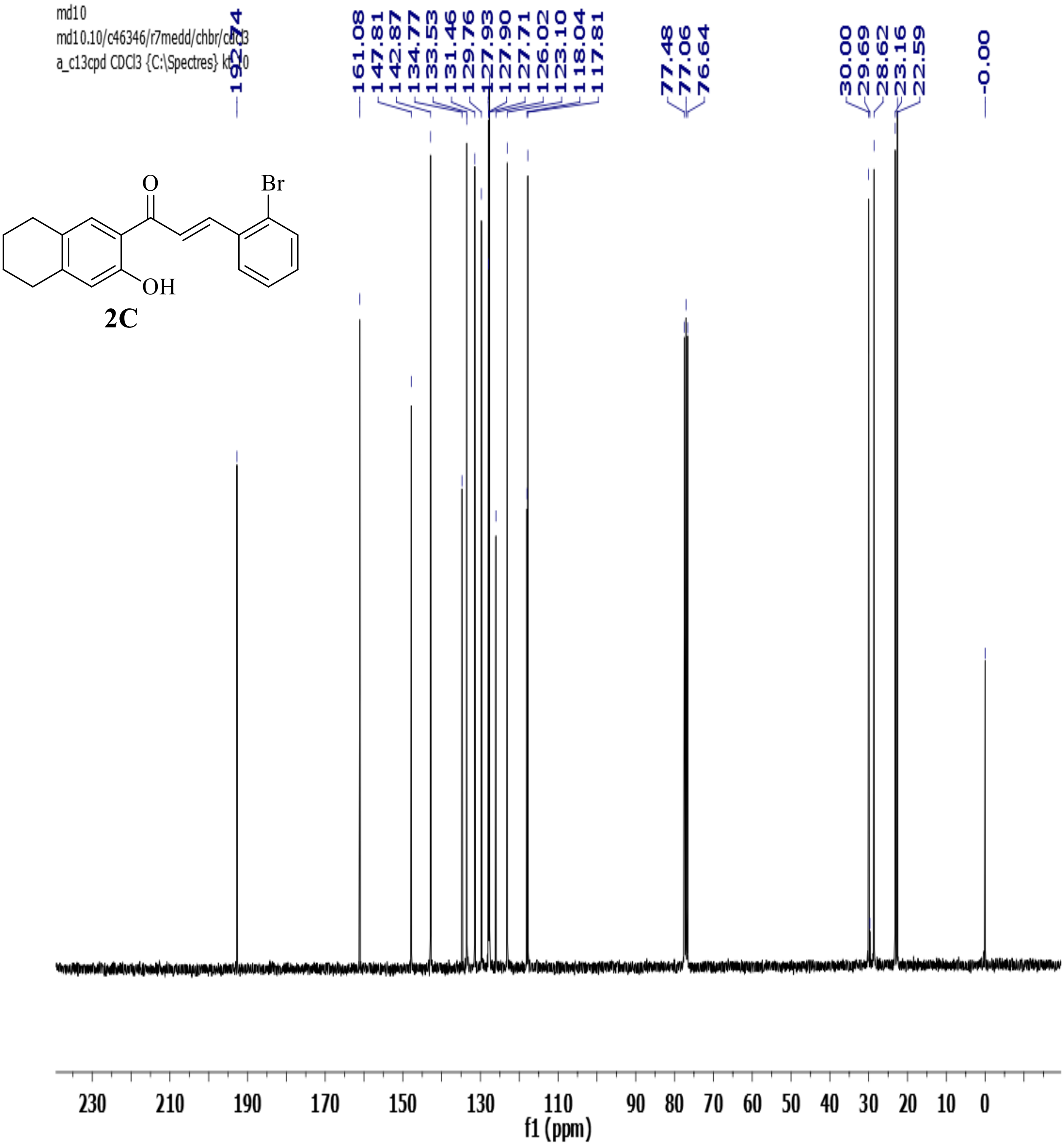
1.00
1.00
2.00
1.00
4.02
4.02
16
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
-3
-4
f1 (ppm)

2C

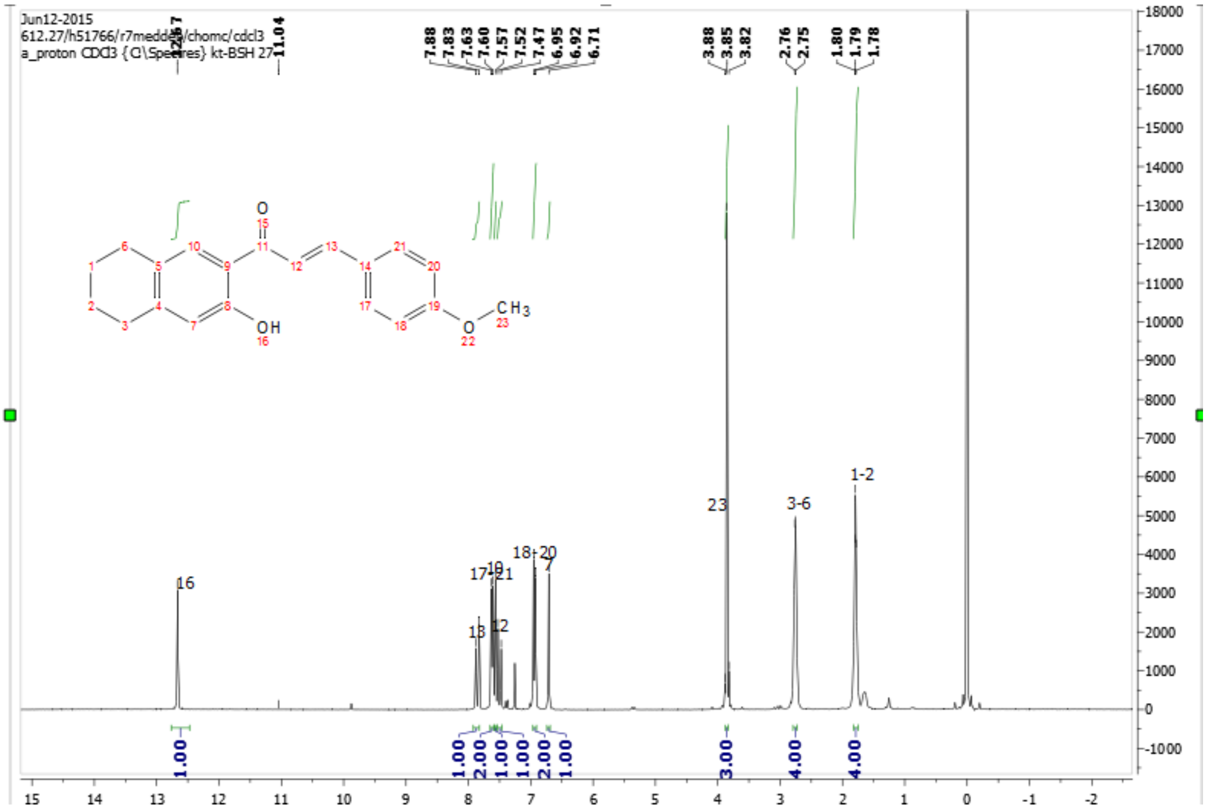
(E)-3-(2-Bromophenyl)-1-(3-hydroxy-5,6,7,8-tetrahydronaphthalen-2-yl)prop-2-en-1-one (2c)

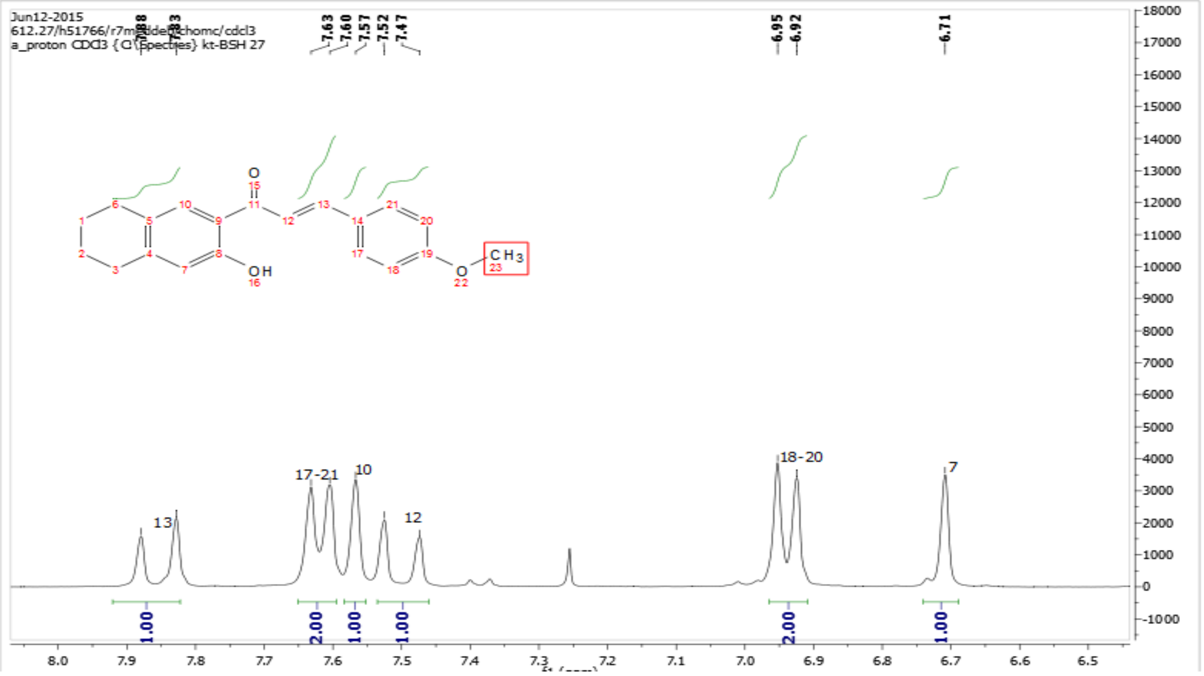
^{13}C NMR

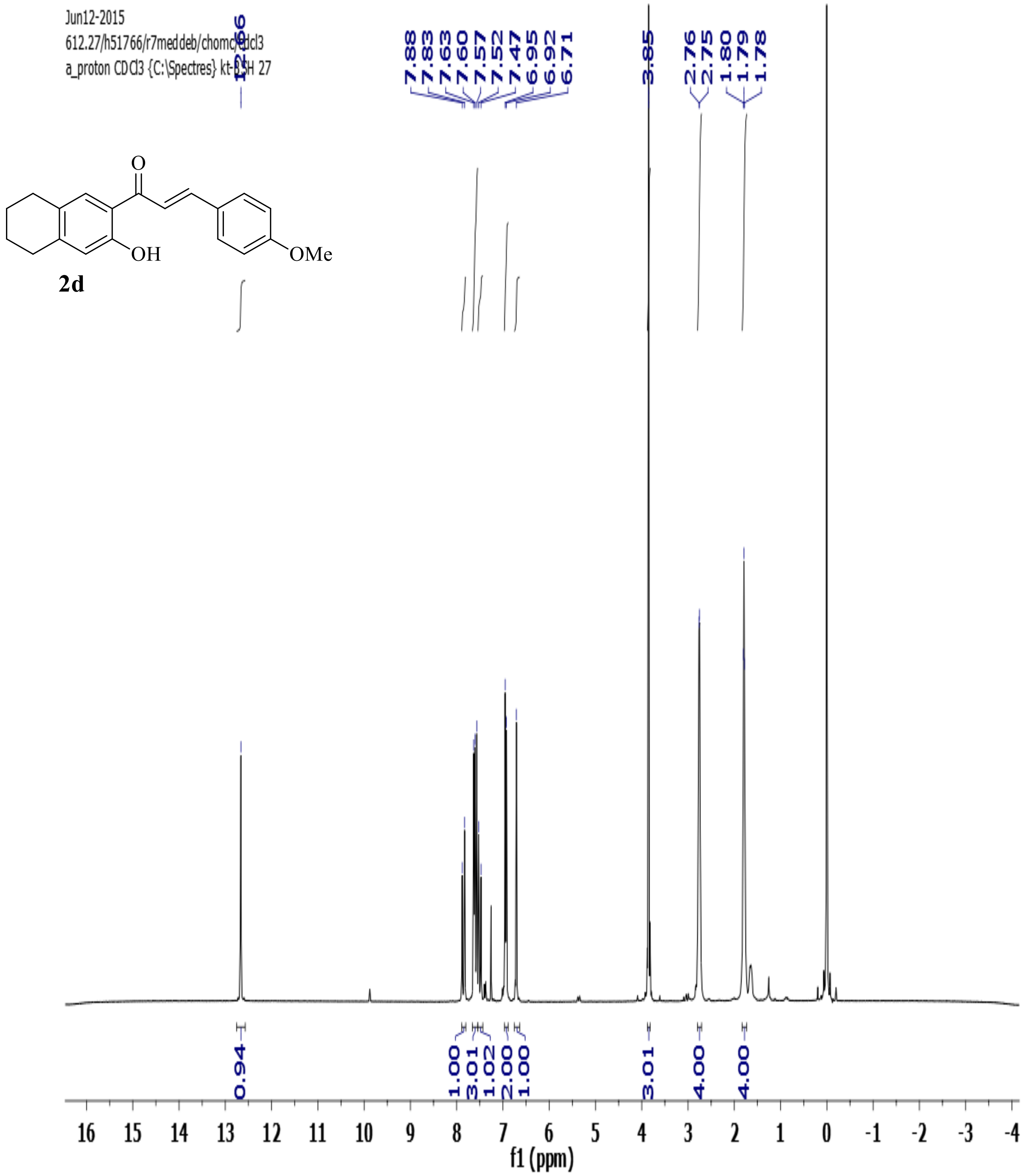


(E)-1-(3-Hydroxy-5,6,7,8-tetrahydronaphthalen-2-yl)-3-(4-methoxyphenyl)prop-2-en-1-one (2d)

^{1}H NMR






Jun12-2015
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1.78
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OH
OMe
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4.00
16
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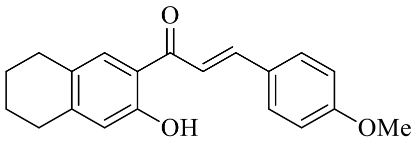
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
-3
-4
f1 (ppm)

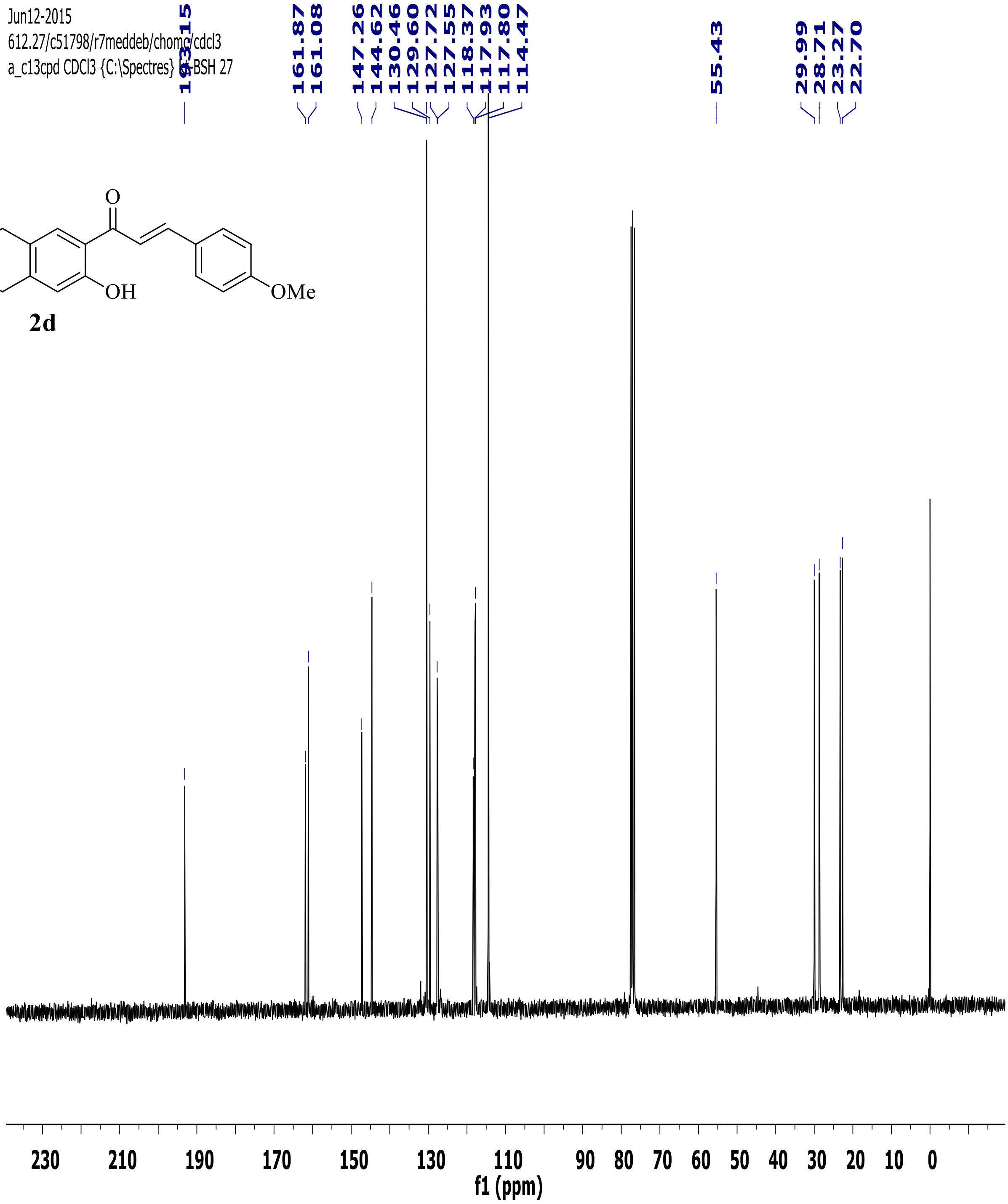
2d

(E)-1-(3-Hydroxy-5,6,7,8-tetrahydronaphthalen-2-yl)-3-(4-methoxyphenyl)prop-2-en-1-one (2d)

^{13}C NMR



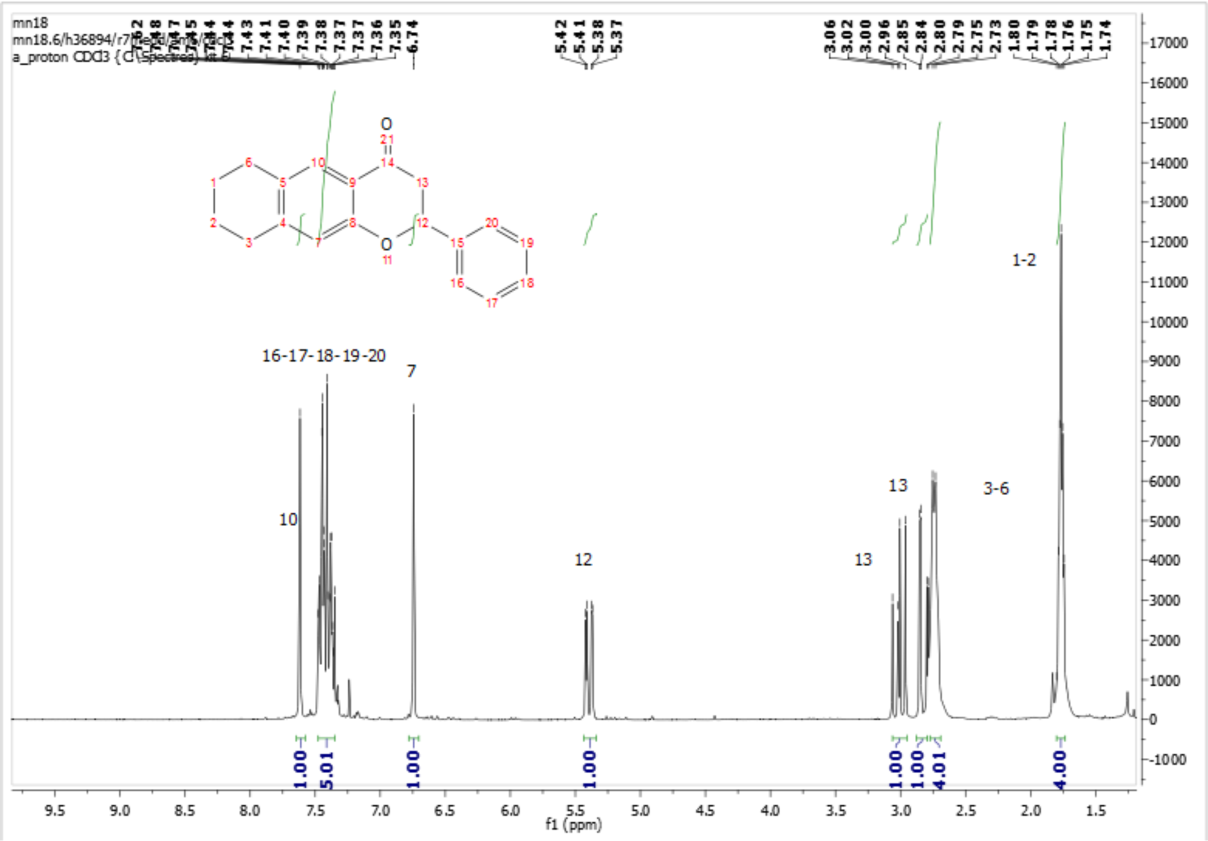
2d

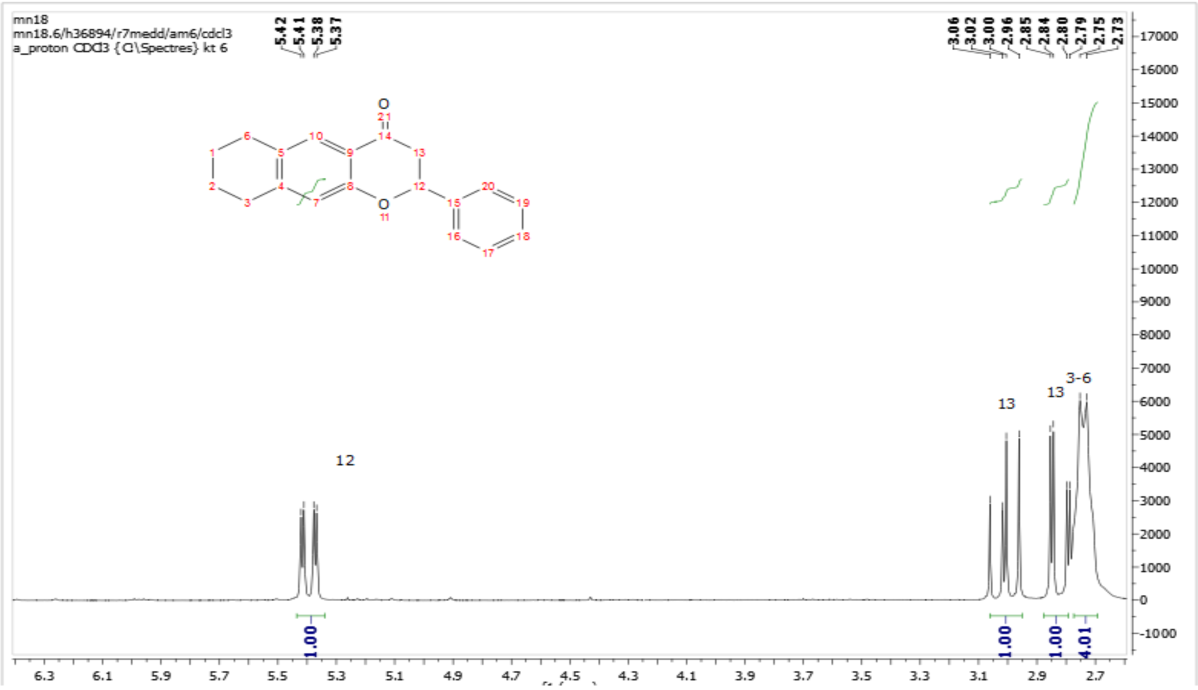


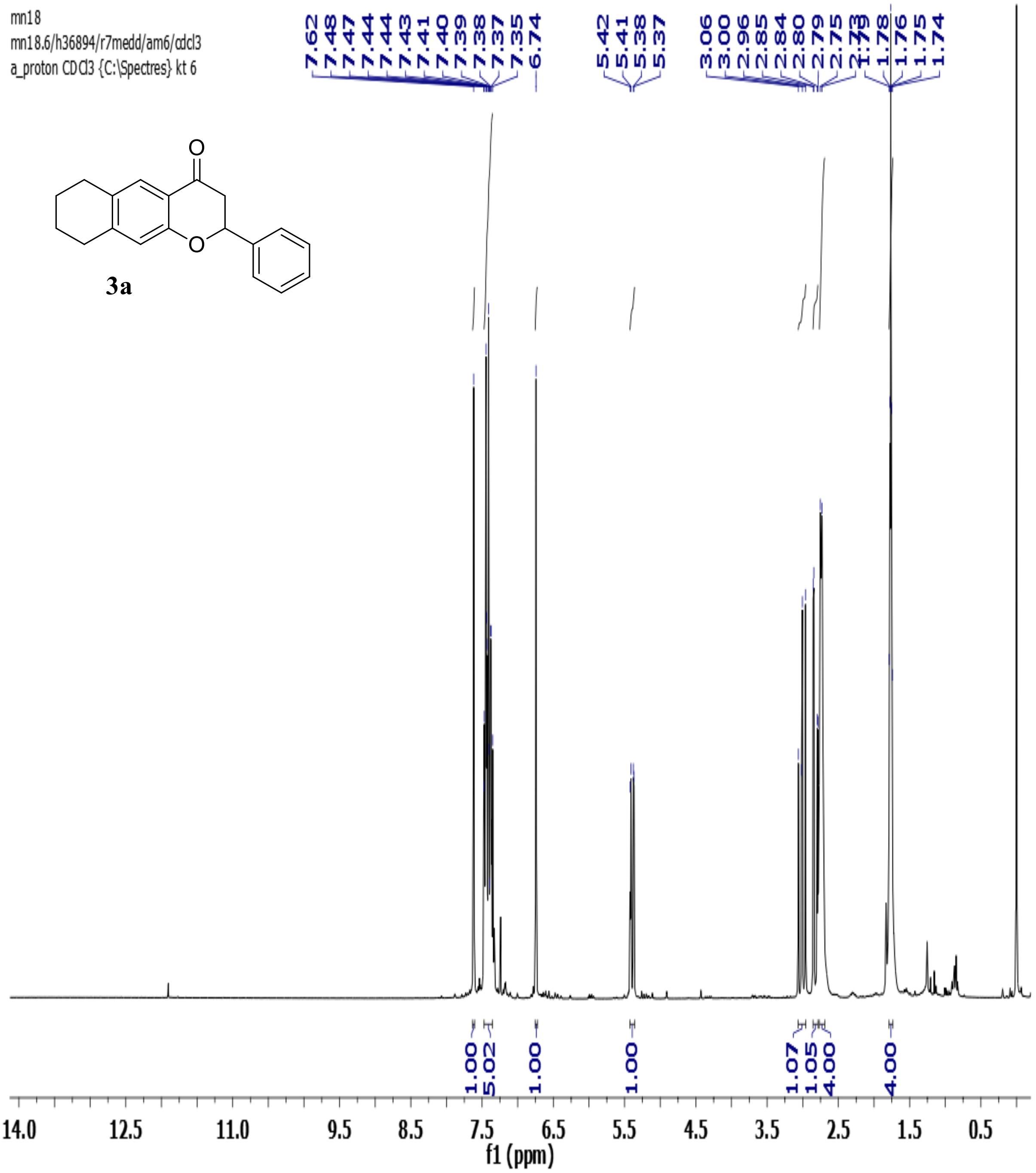
9. ^{1}H and ^{13}C NMR spectra of flavanones (3a–3d)

2-Phenyl-6,7,8,9-tetrahydro-2H-benzo[g]chromen-4(3H)-one (3a)

^{1}H NMR

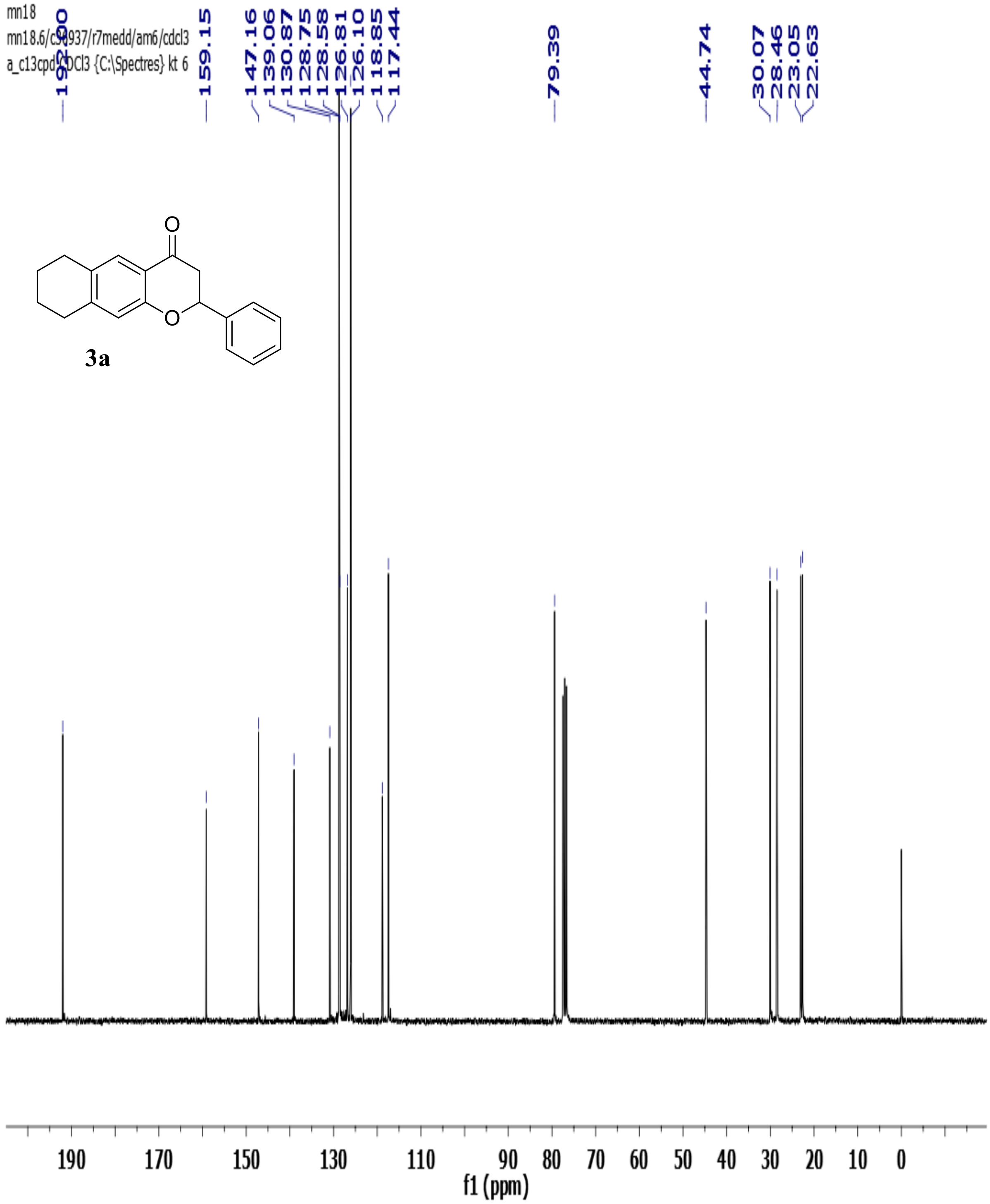




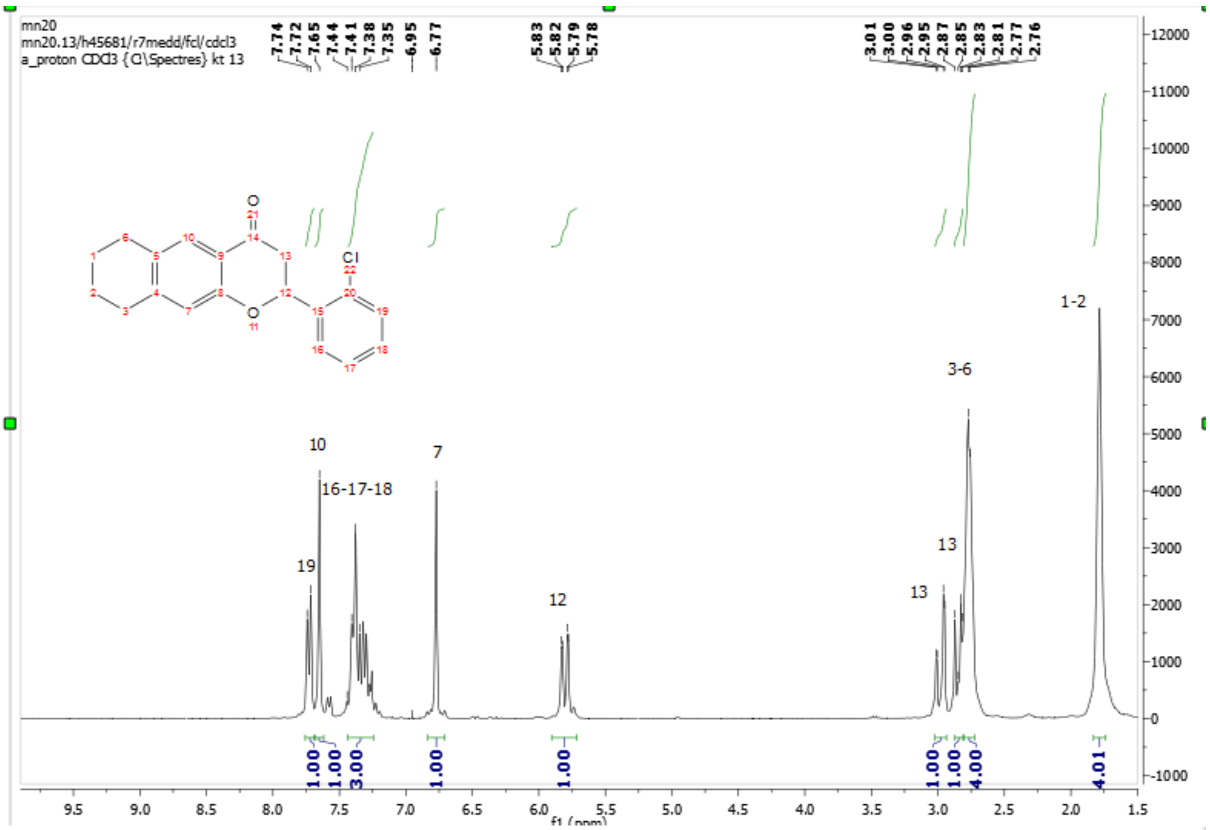

mn18
mn18.6/h36894/r7medd/am6/cdcl3
a_proton CDCl3 {C:\Spectres} kt 6
7.62
7.48
7.47
7.44
7.44
7.43
7.41
7.40
7.39
7.38
7.37
7.35
6.74
5.42
5.41
5.38
5.37
3.06
3.00
2.96
2.85
2.84
2.80
2.79
2.75
2.73
1.79
1.78
1.76
1.75
1.74
O
O
1.00
5.02
1.00
1.00
1.07
1.05
4.00
4.00
14.0
12.5
11.0
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
f1 (ppm)

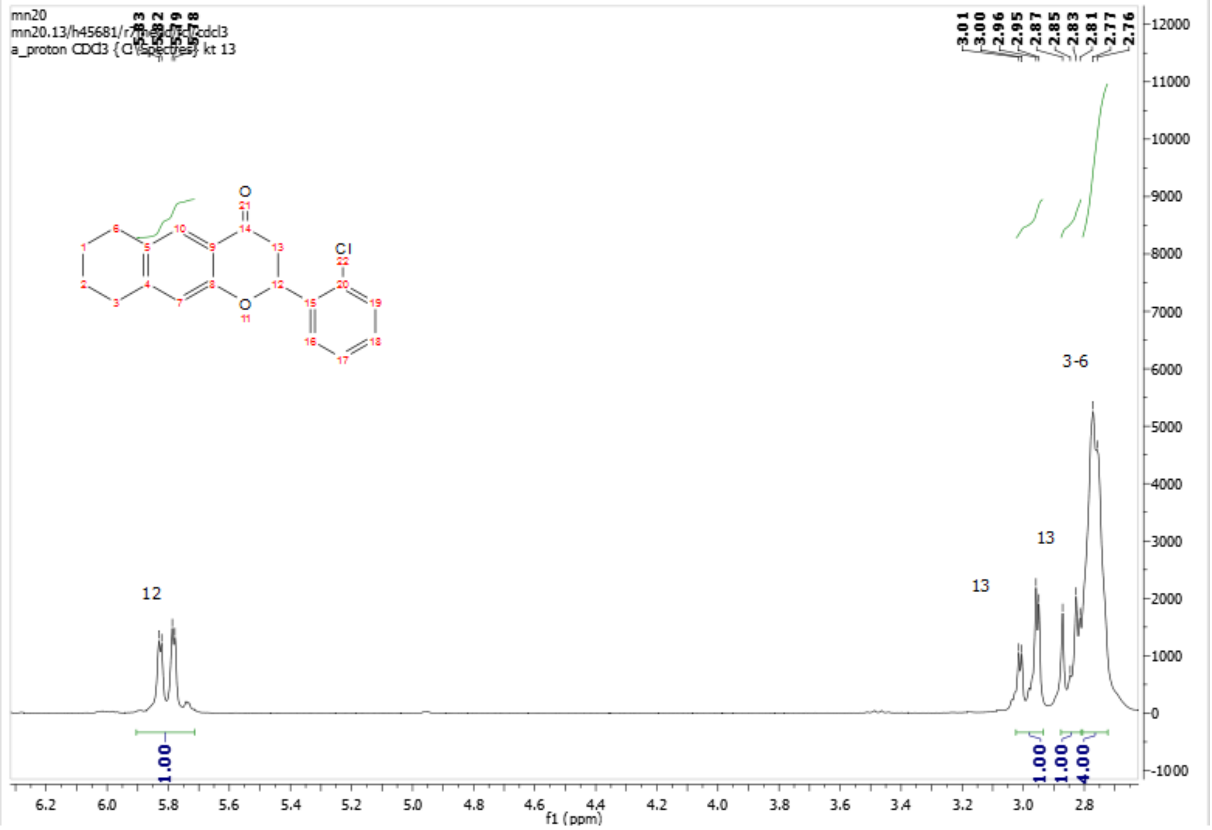
3a

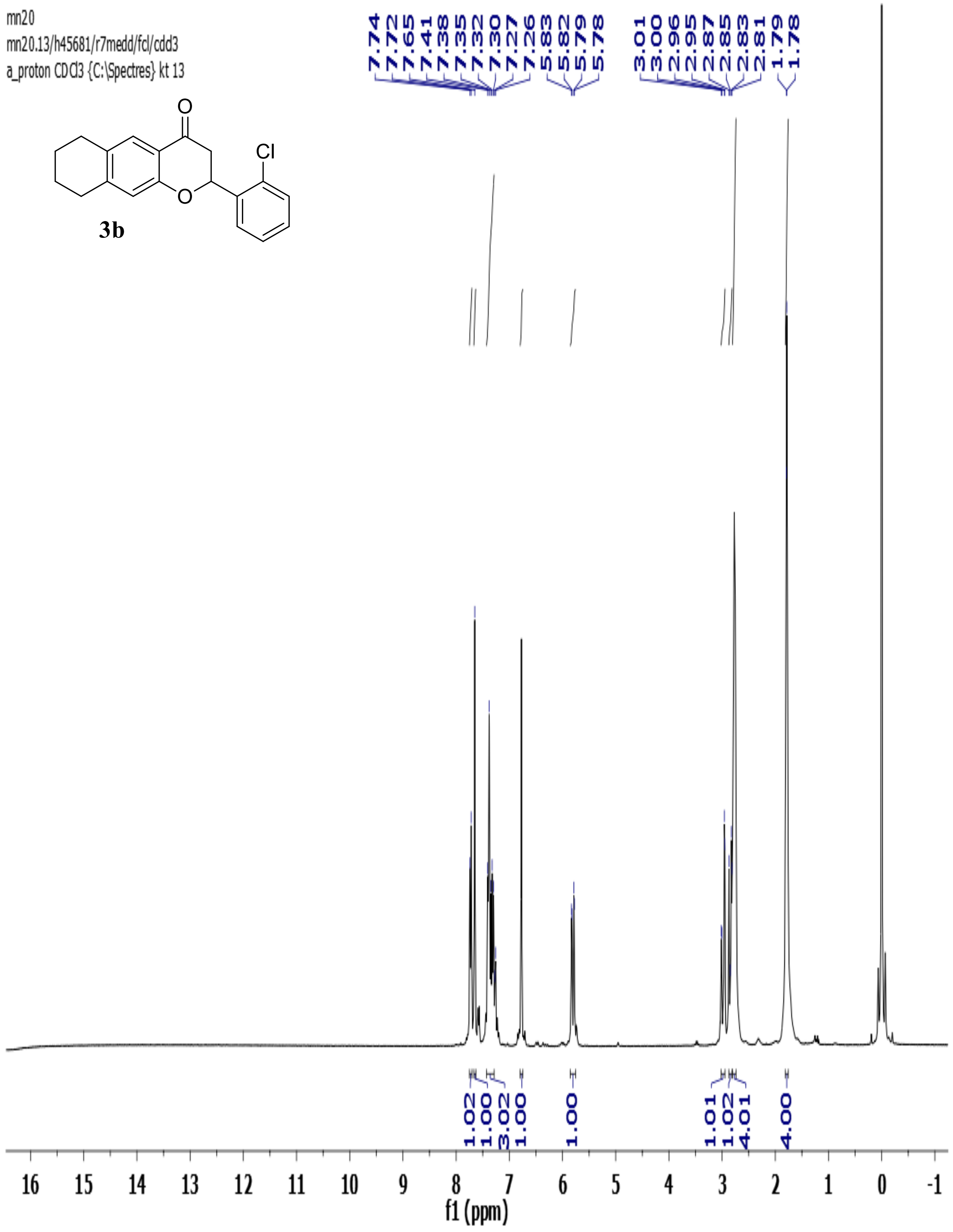
2-Phenyl-6,7,8,9-tetrahydro-2H-benzo[g]chromen-4(3H)-one (3a)
^{13}C NMR



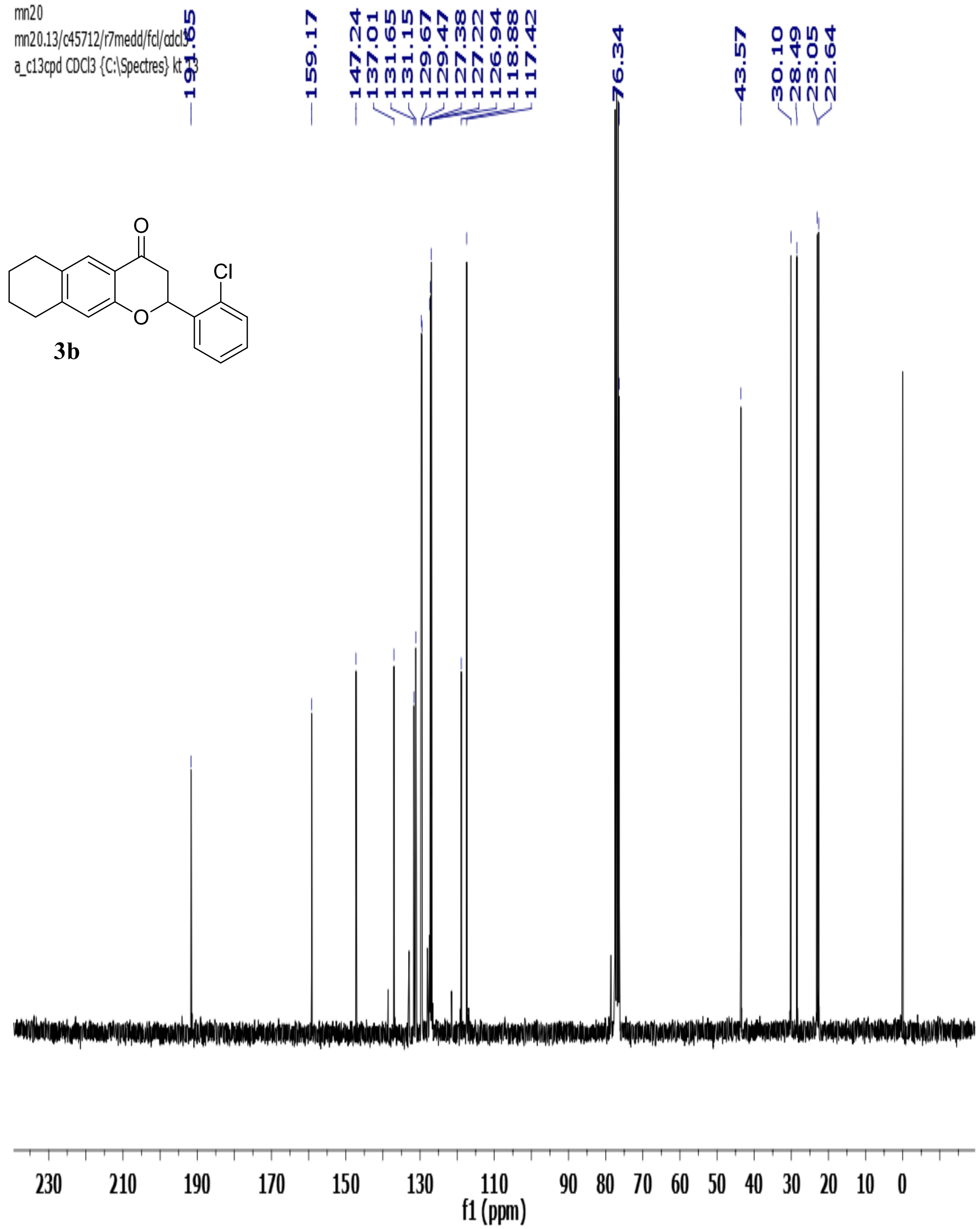
2-(2-Chlorophenyl)-6,7,8,9-tetrahydro-2H-benzo[g]chromen-4(3H)-one (3b)
^{1}H NMR



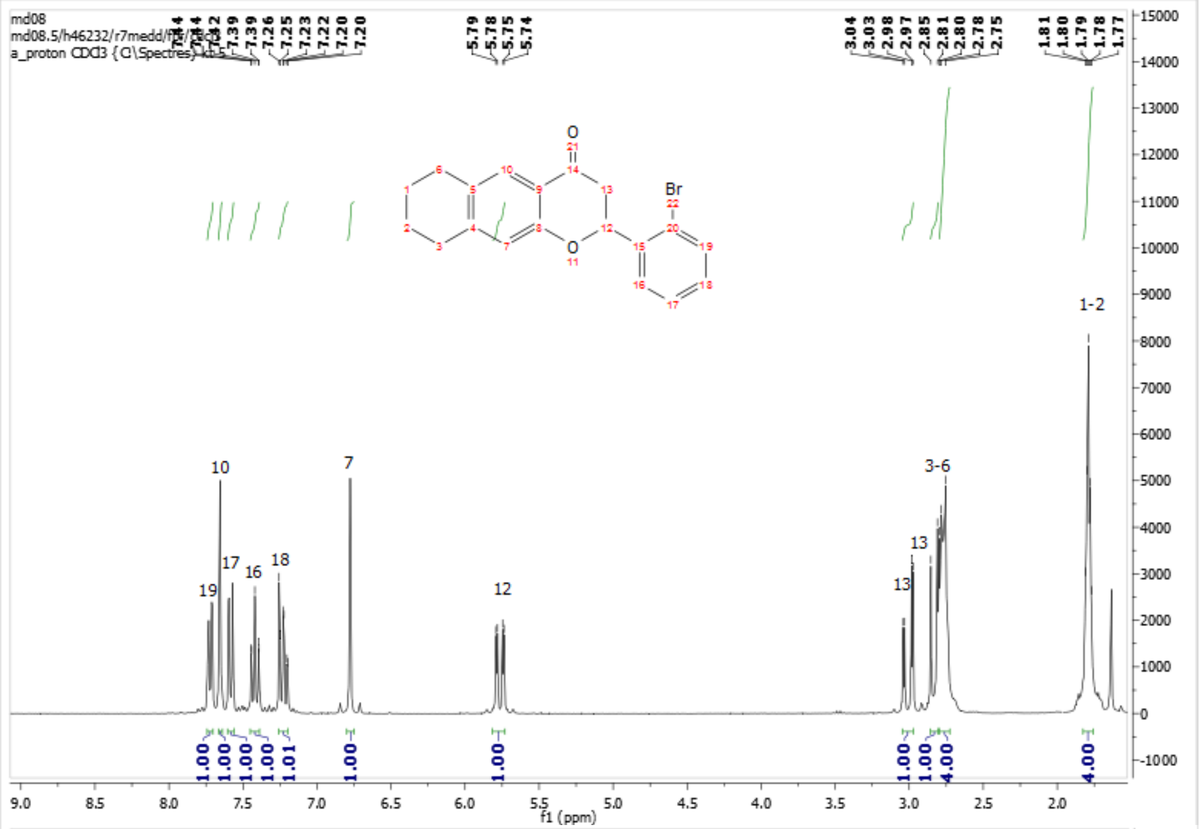


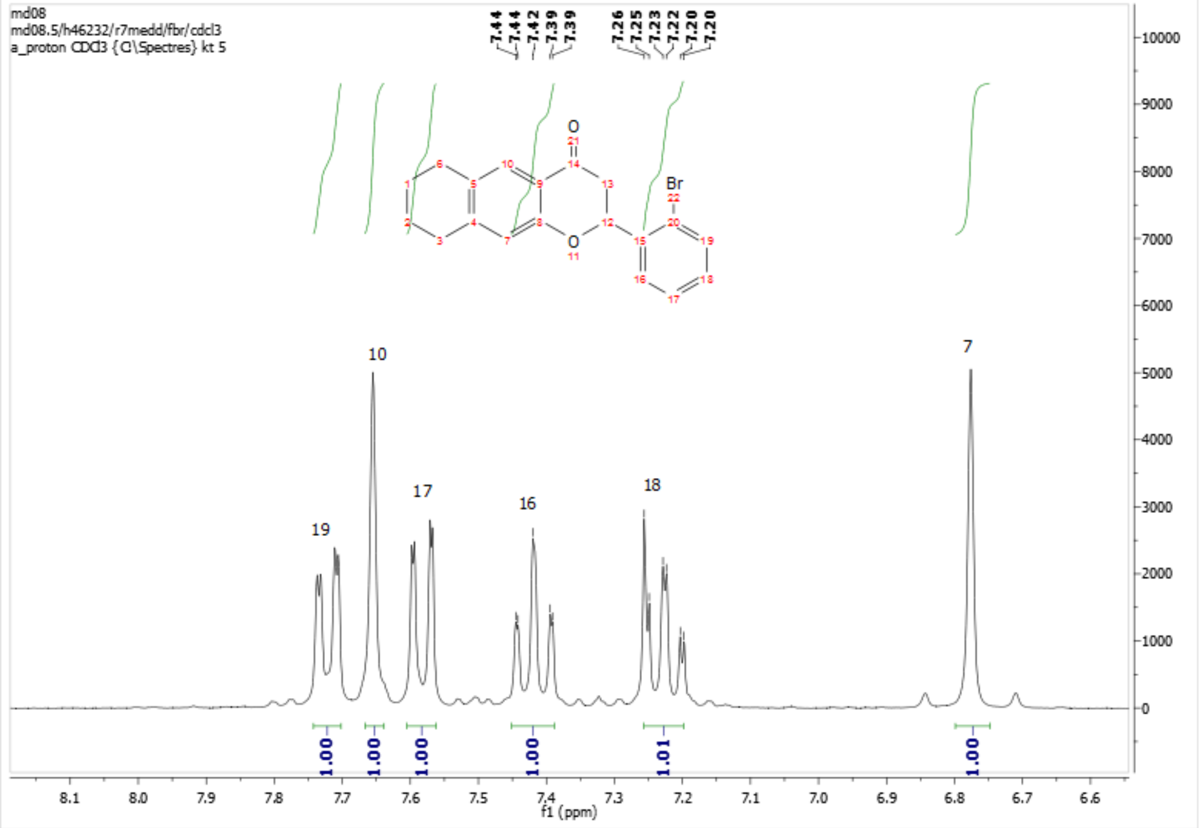

mn20
mn20.13/h45681/r7medd/fcl/cdcl3
a_proton CDCl3 {C:\Spectres} kt 13
O
Cl
O
3b
7.74
7.72
7.65
7.41
7.38
7.35
7.32
7.30
7.27
7.26
5.83
5.82
5.79
5.78
3.01
3.00
2.96
2.95
2.87
2.85
2.83
2.81
1.79
1.78
1.02
1.00
3.02
1.00
1.00
1.01
1.02
4.01
4.00
16
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)

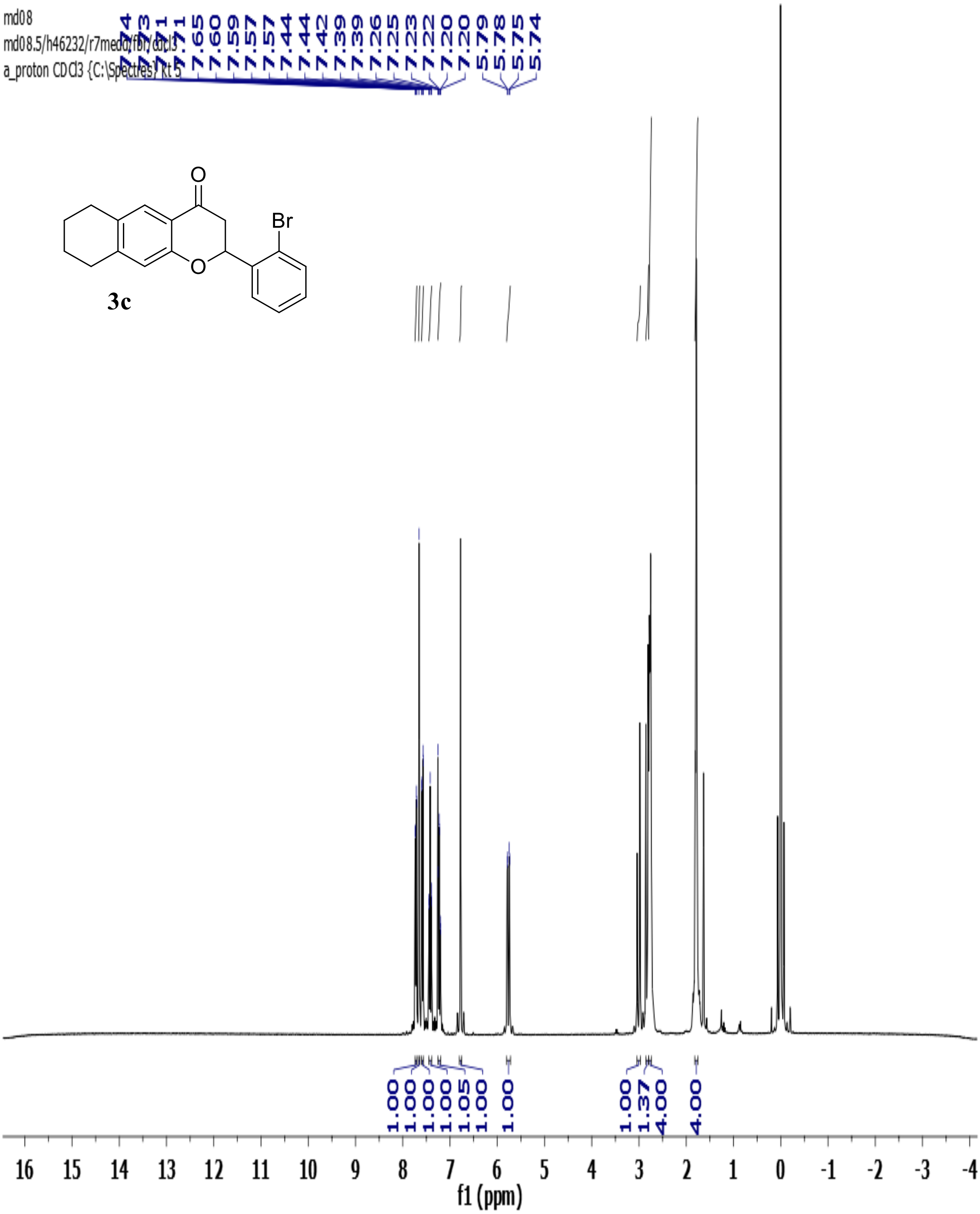
2-(2-Chlorophenyl)-6,7,8,9-tetrahydro-2H-benzo[g]chromen-4(3H)-one (3b)
^{13}C NMR



2-(2-Bromophenyl)-6,7,8,9-tetrahydro-2H-benzo[g]chromen-4(3H)-one (3c)
^{1}H NMR

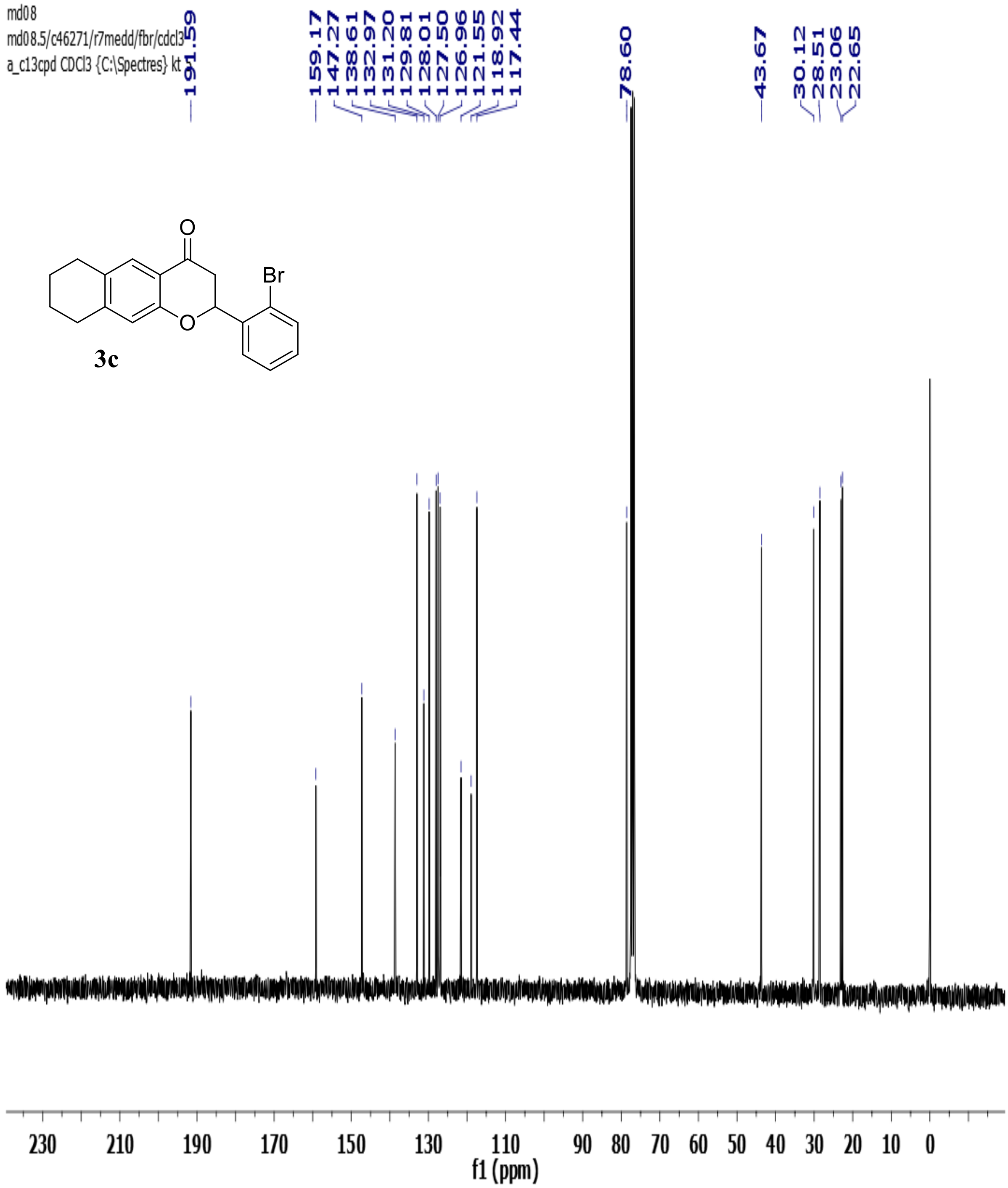





md08
md08.5/h46232/r7medq/fbr/cdcl3
a_proton CDCl3 {C:\Spectres} Rt 5
7.74
7.73
7.71
7.71
7.65
7.60
7.59
7.57
7.57
7.44
7.42
7.39
7.39
7.26
7.25
7.23
7.22
7.20
7.20
5.79
5.78
5.75
5.74
O
Br
O
3c
1.00
1.00
1.00
1.00
1.05
1.00
1.00
1.00
1.37
4.00
4.00
16
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
-3
-4
f1 (ppm)

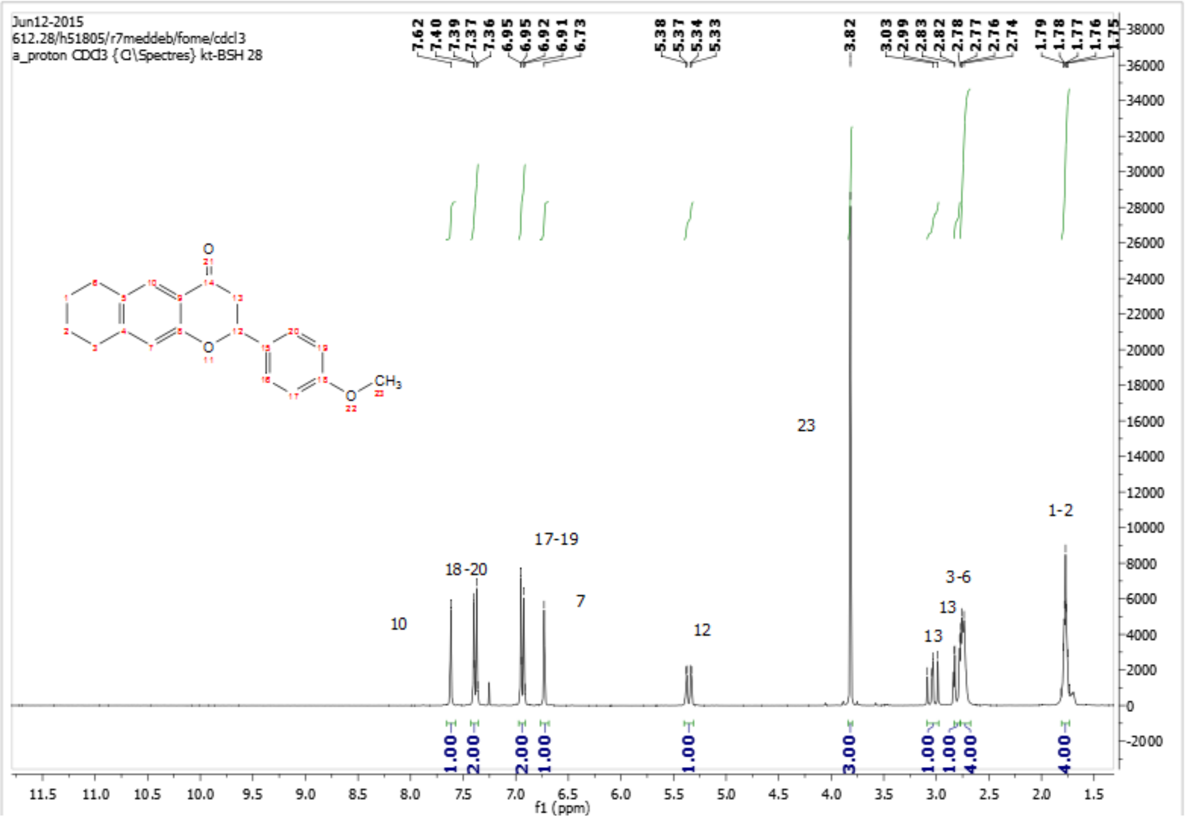
2-(2-Bromophenyl)-6,7,8,9-tetrahydro-2H-benzo[g]chromen-4(3H)-one (3c)

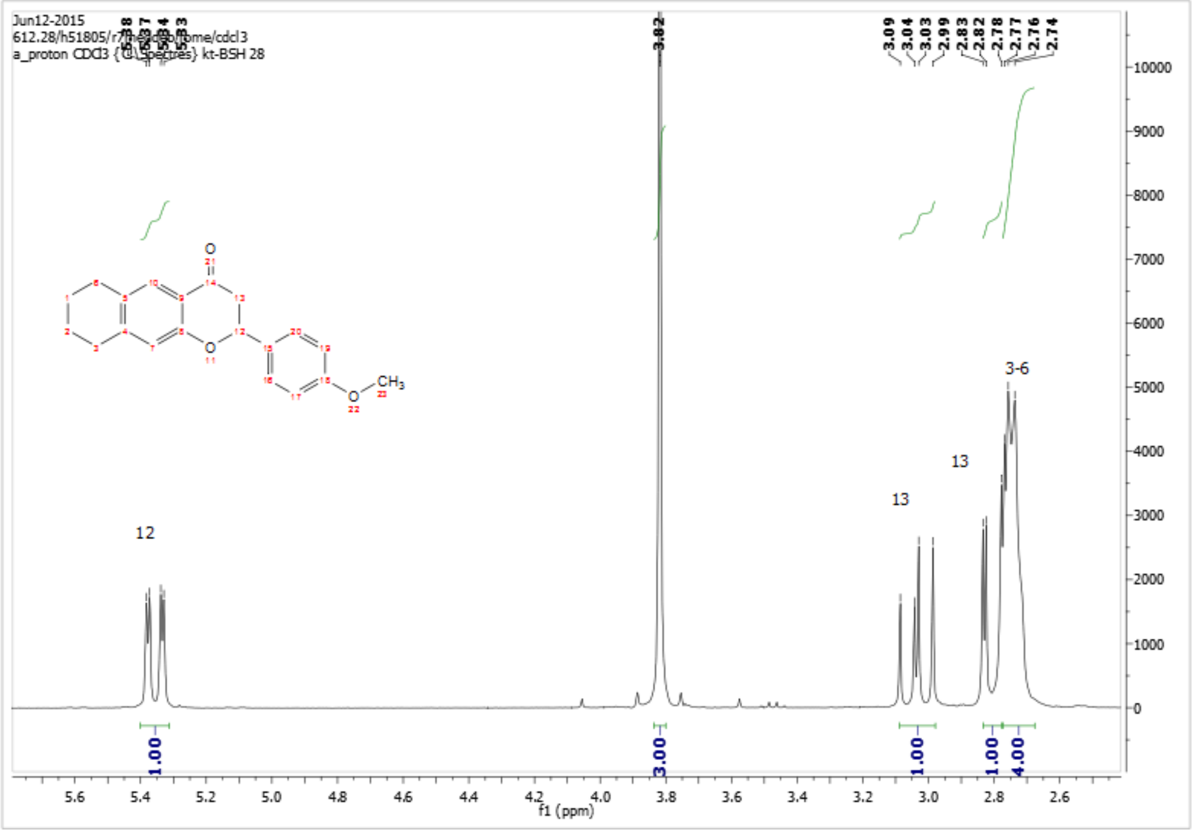
^{13}C NMR

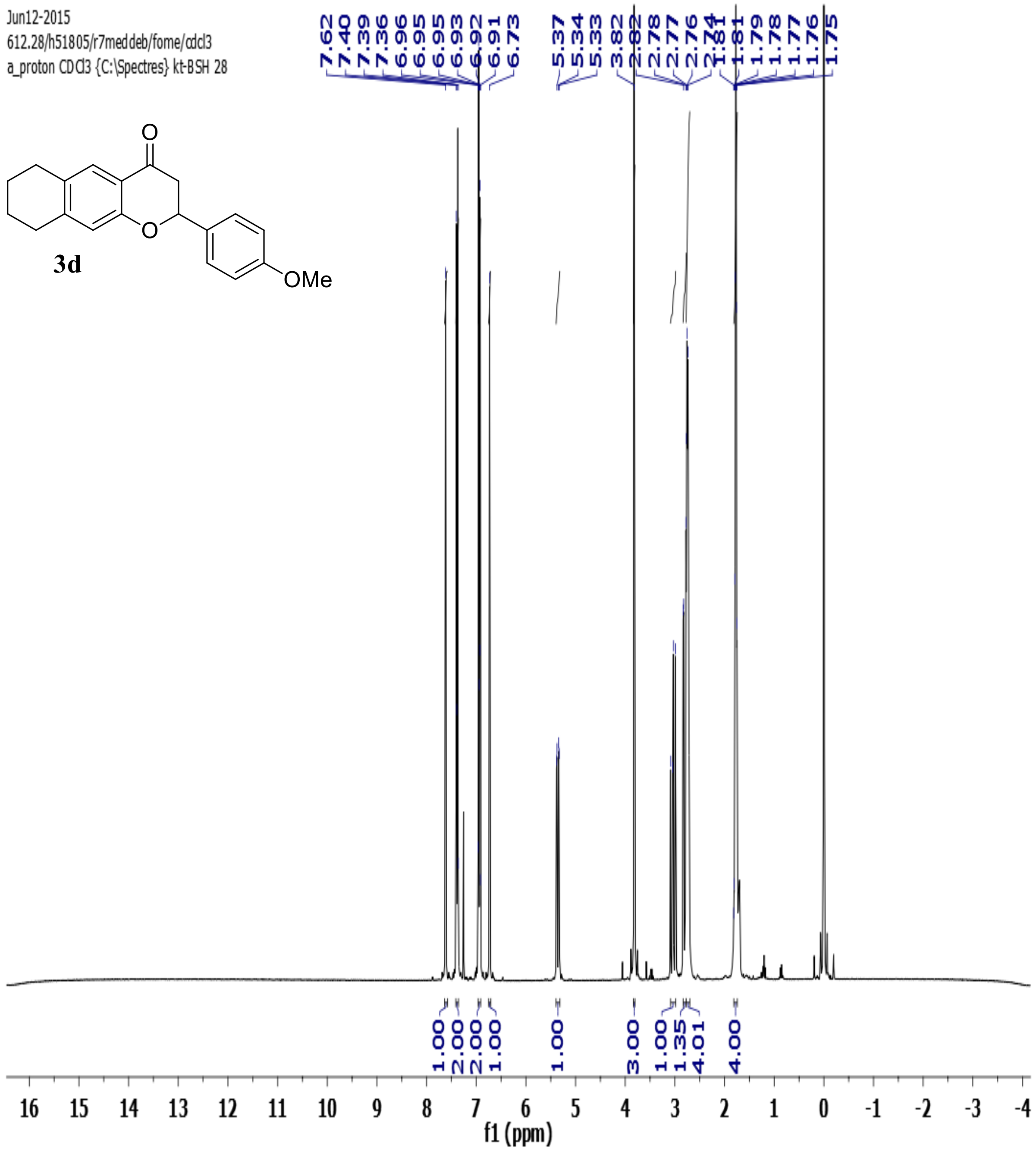


2-(4-Methoxyphenyl)-6,7,8,9-tetrahydro-2H-benzo[g]chromen-4(3H)-one (3d)

^{1}H NMR



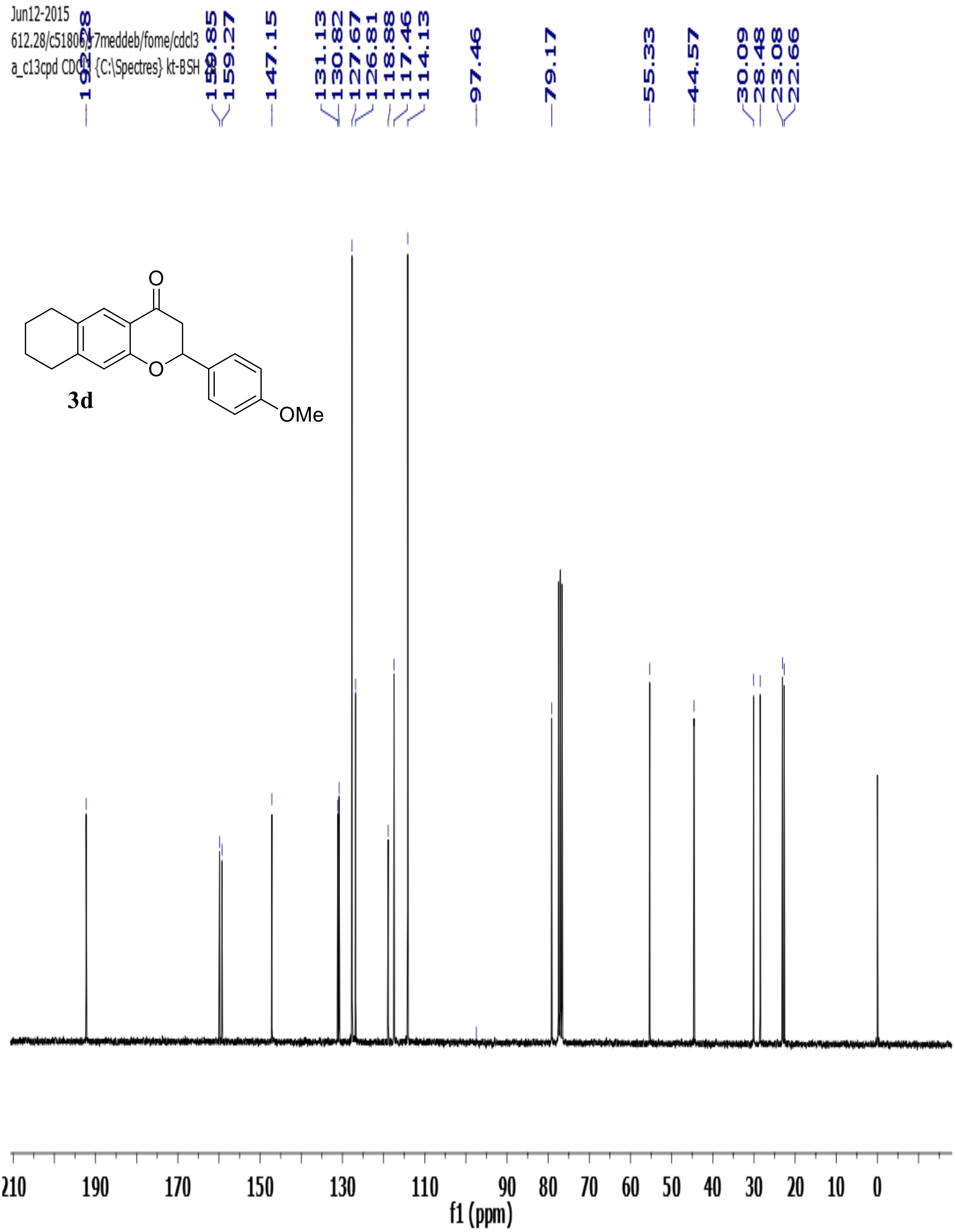




3d

Jun12-2015
612.28/h51805/r7meddeb/fome/cdcl3
a_proton CDCl3 {C:\Spectres} kt-BSH 28
O
O
OMe
7.62
7.40
7.39
7.36
6.96
6.95
6.93
6.92
6.91
6.73
5.37
5.34
5.33
3.82
2.82
2.78
2.77
2.76
2.74
1.81
1.81
1.79
1.78
1.77
1.76
1.75
1.00
2.00
2.00
1.00
1.00
3.00
1.00
1.35
4.01
4.00
16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3 -4
f1 (ppm)

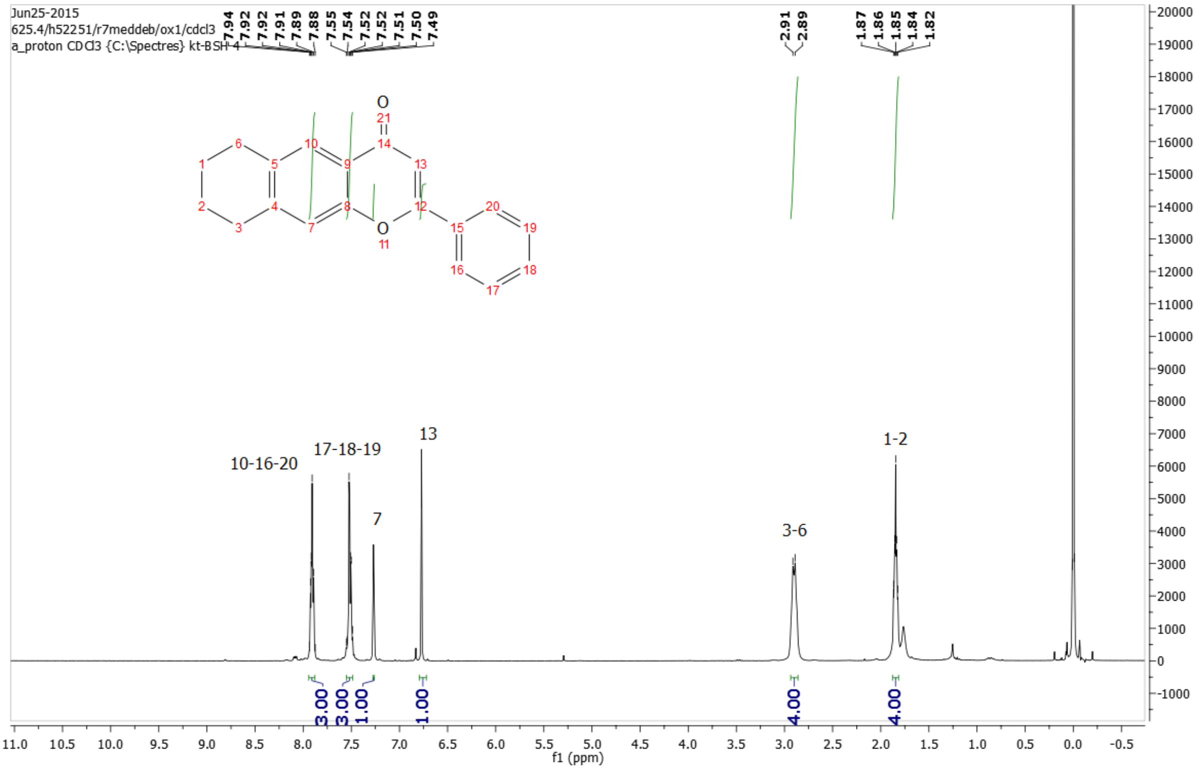
2-(4-Methoxyphenyl)-6,7,8,9-tetrahydro-2H-benzo[g]chromen-4(3H)-one (3d)
^{13}C NMR

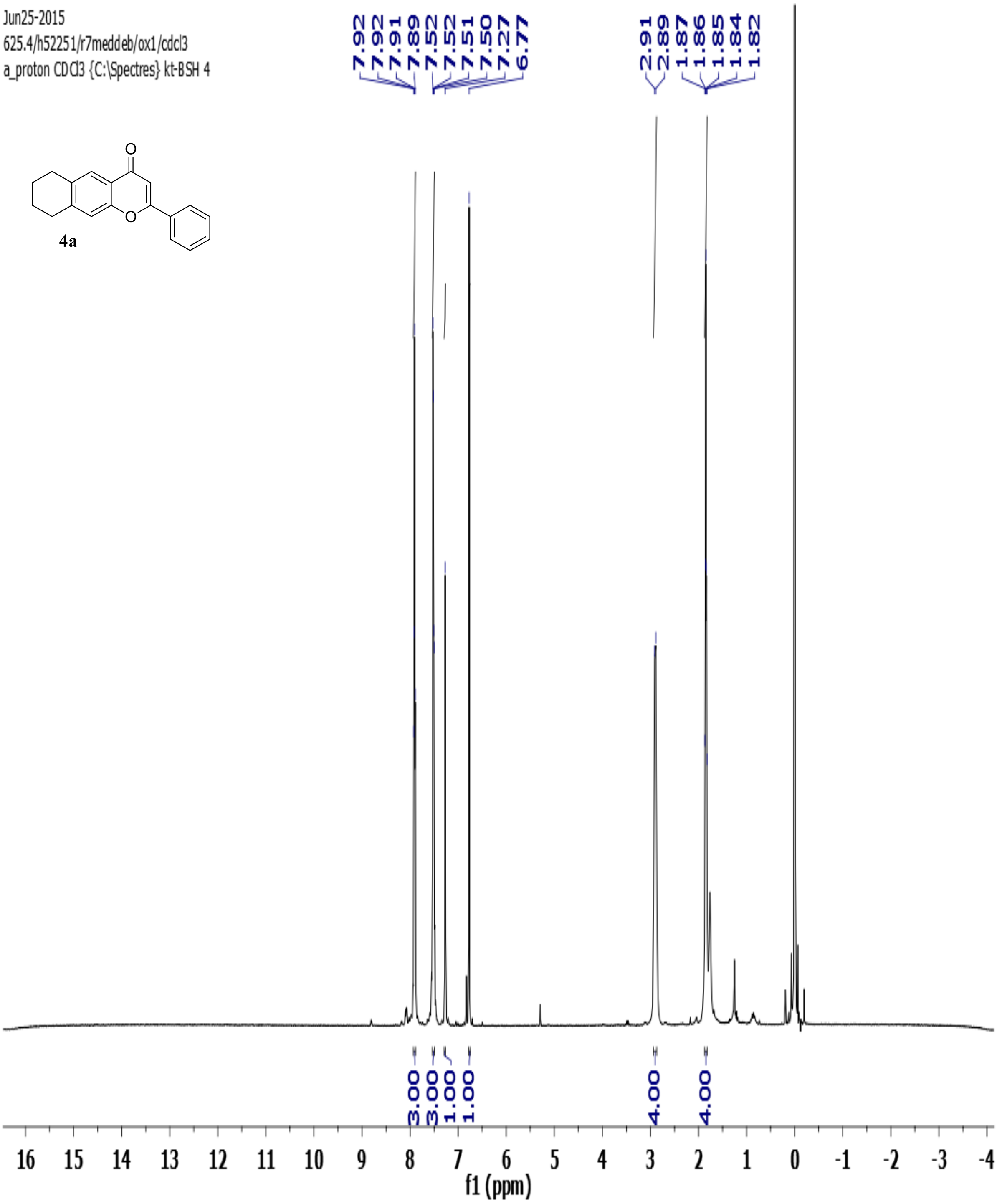


10. ^{1}H and ^{13}C NMR spectra of flavones (4a–4d)

2-Phenyl-6,7,8,9-tetrahydro-4H-benzo[g]chromen-4-one (4a)

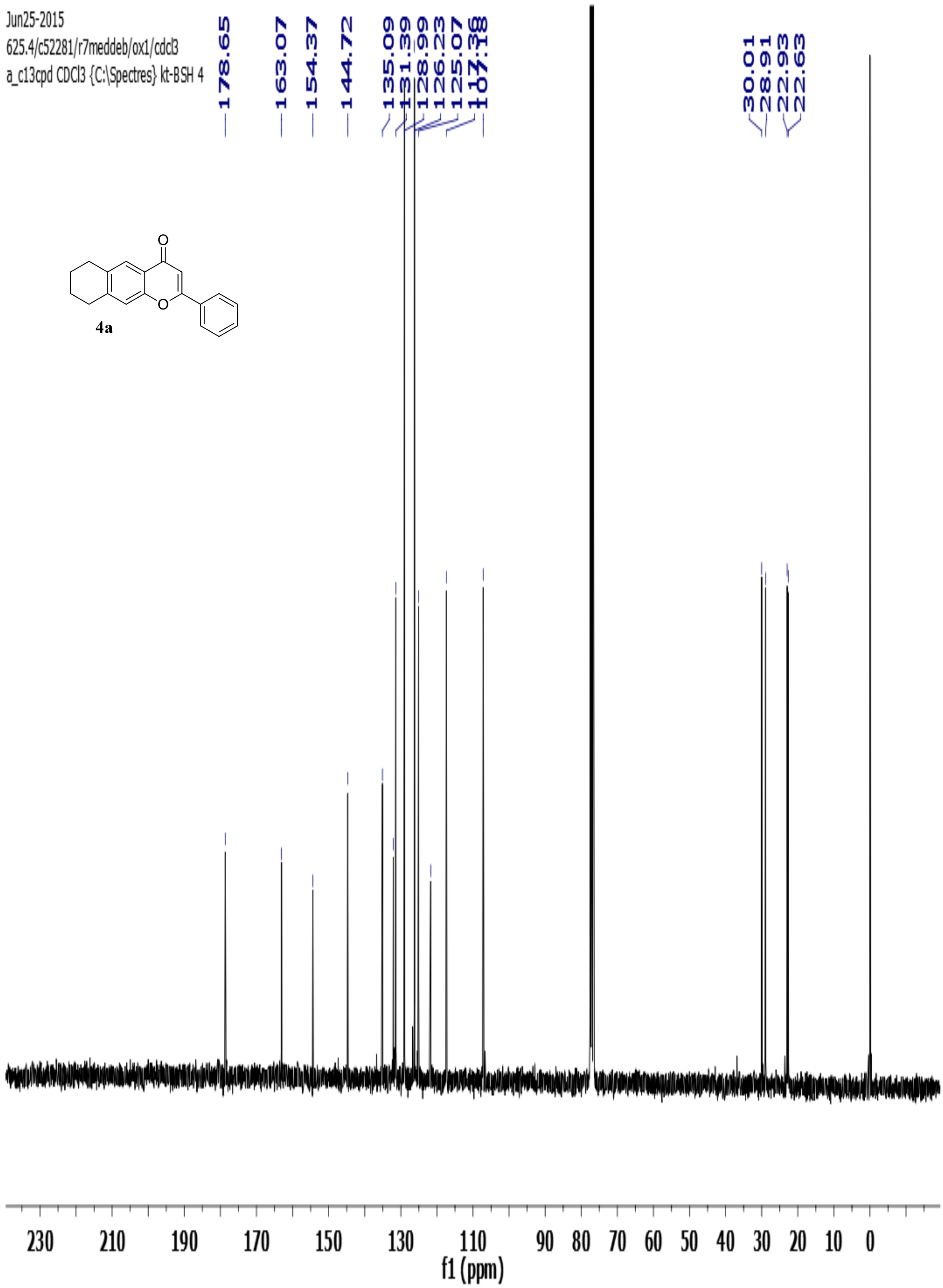
^{1}H NMR




Jun25-2015
625.4/h52251/r7meddeb/ox1/cdcl3
a_proton CDCl3 {C:\Spectres} kt-BSH 4
7.92
7.92
7.91
7.89
7.52
7.52
7.51
7.50
7.27
6.77
2.91
2.89
1.87
1.86
1.85
1.84
1.82
O
O
4a
3.00
3.00
1.00
1.00
4.00
4.00
16
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
-3
-4
f1 (ppm)

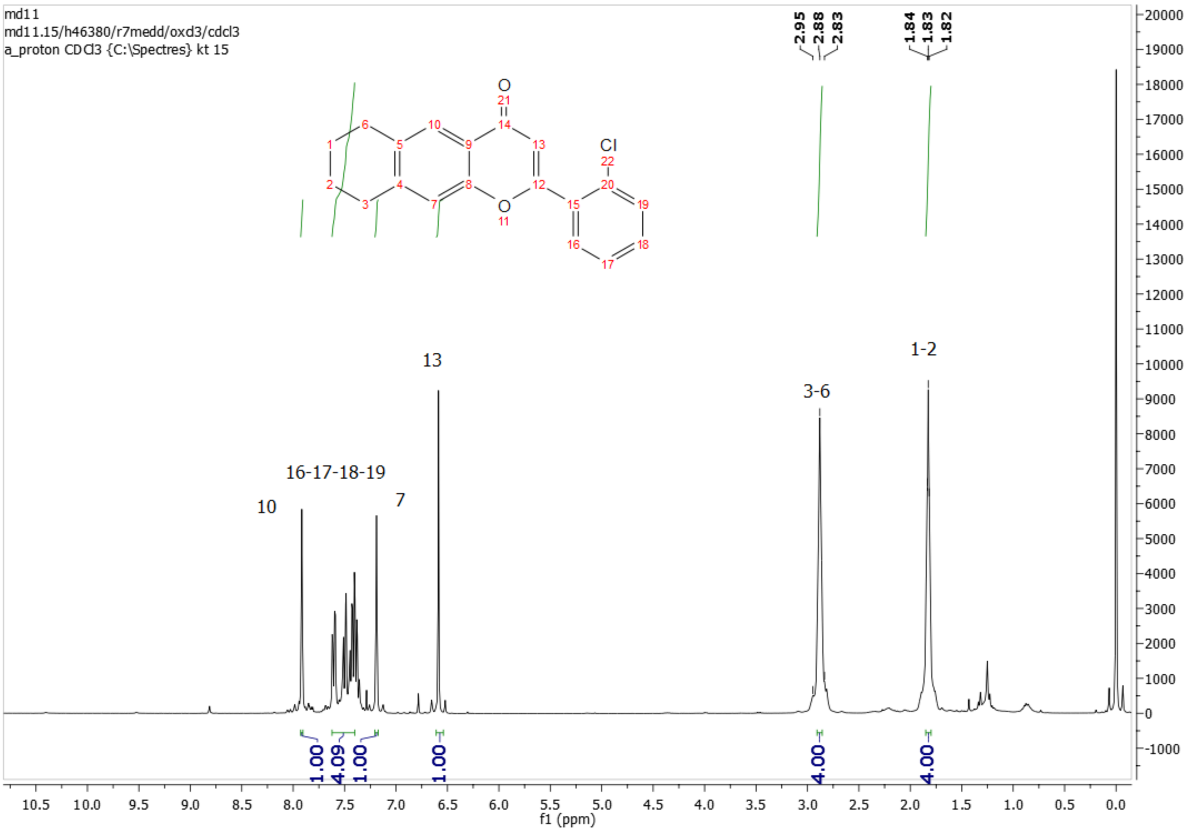
.

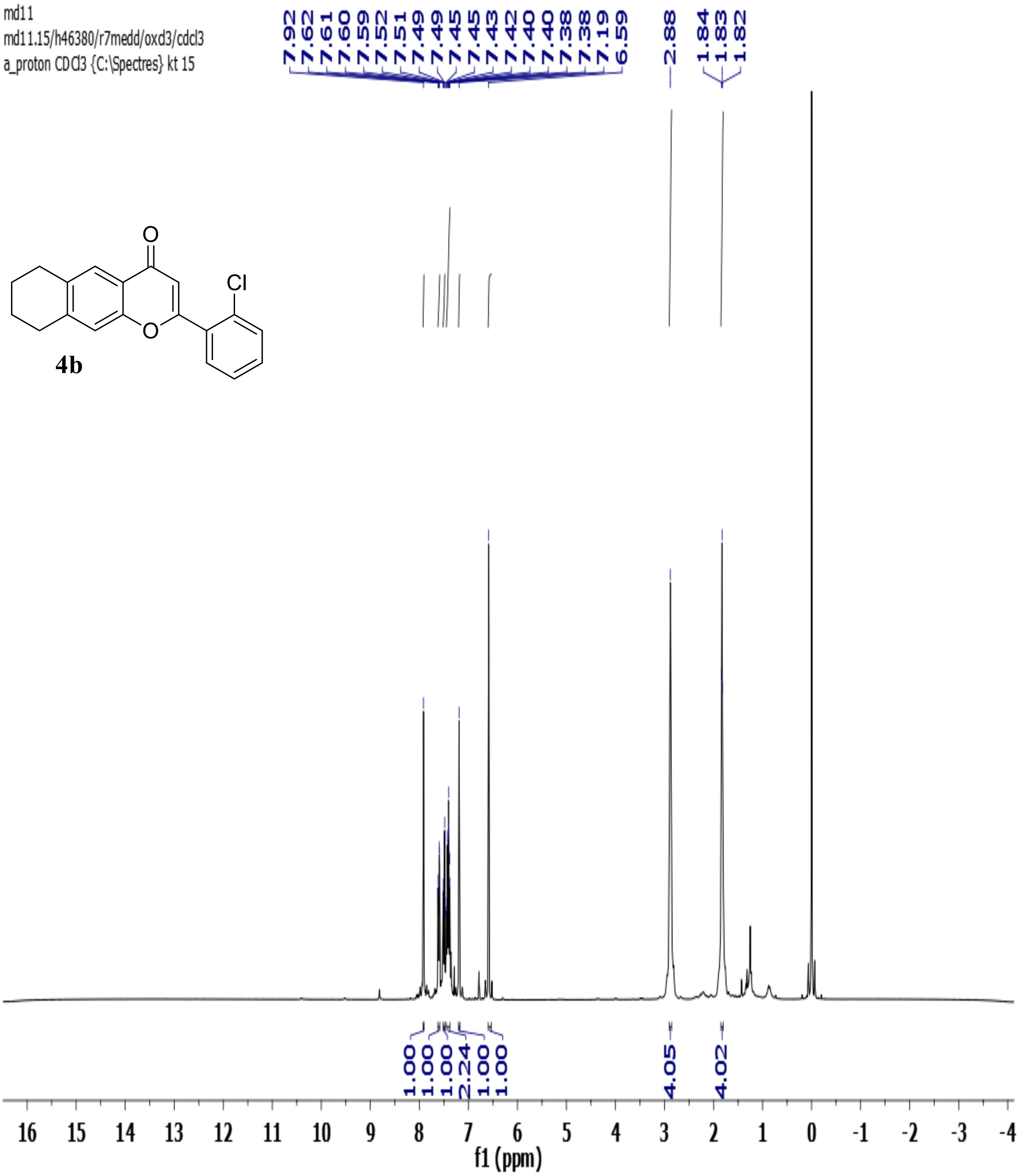
2-Phenyl-6,7,8,9-tetrahydro-4H-benzo[g]chromen-4-one (4a)
^{13}C NMR



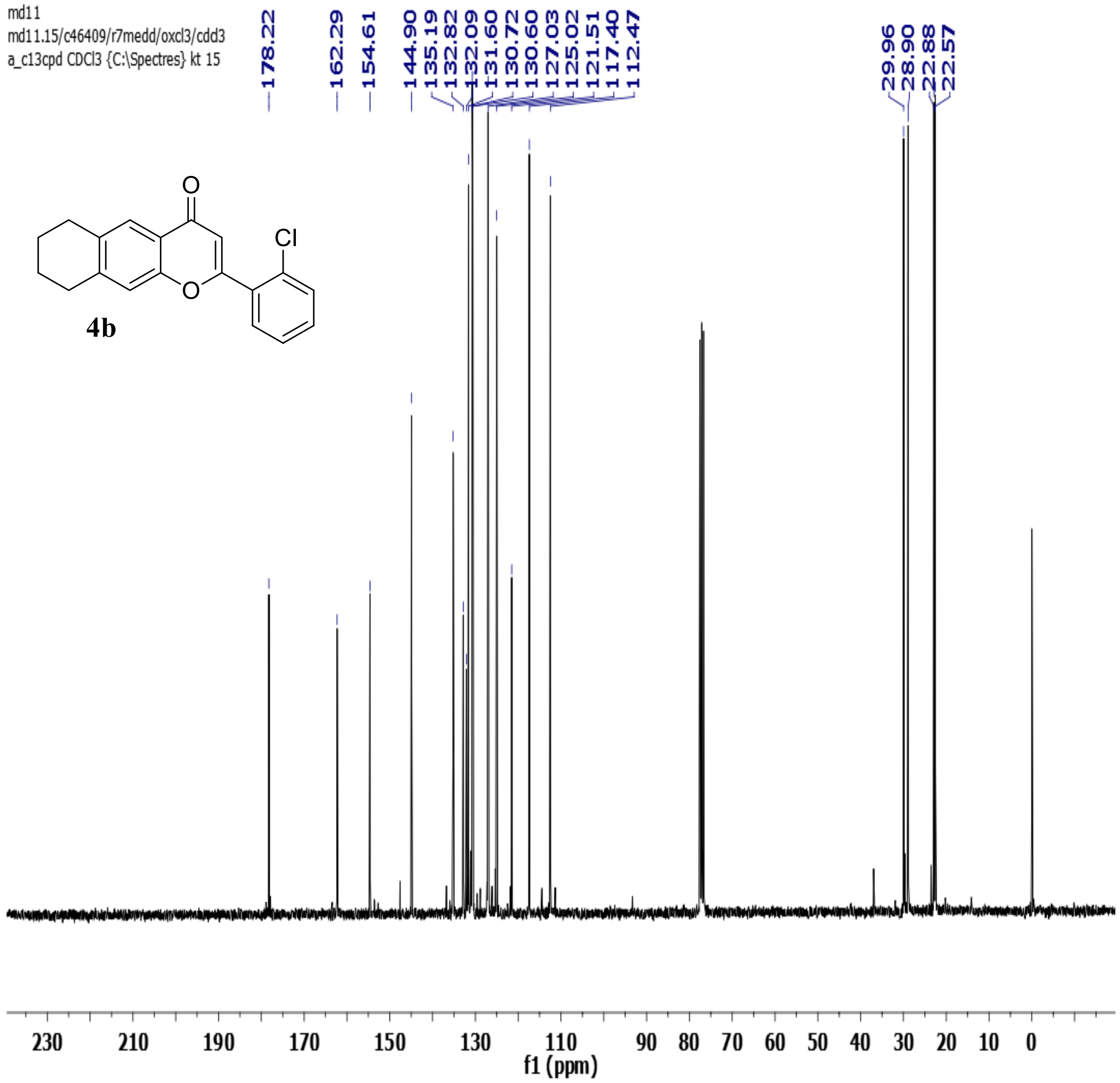
2-(2-Chlorophenyl)-6,7,8,9-tetrahydro-4H-benzo[g]chromen-4-one (4b)

^{1}H NMR

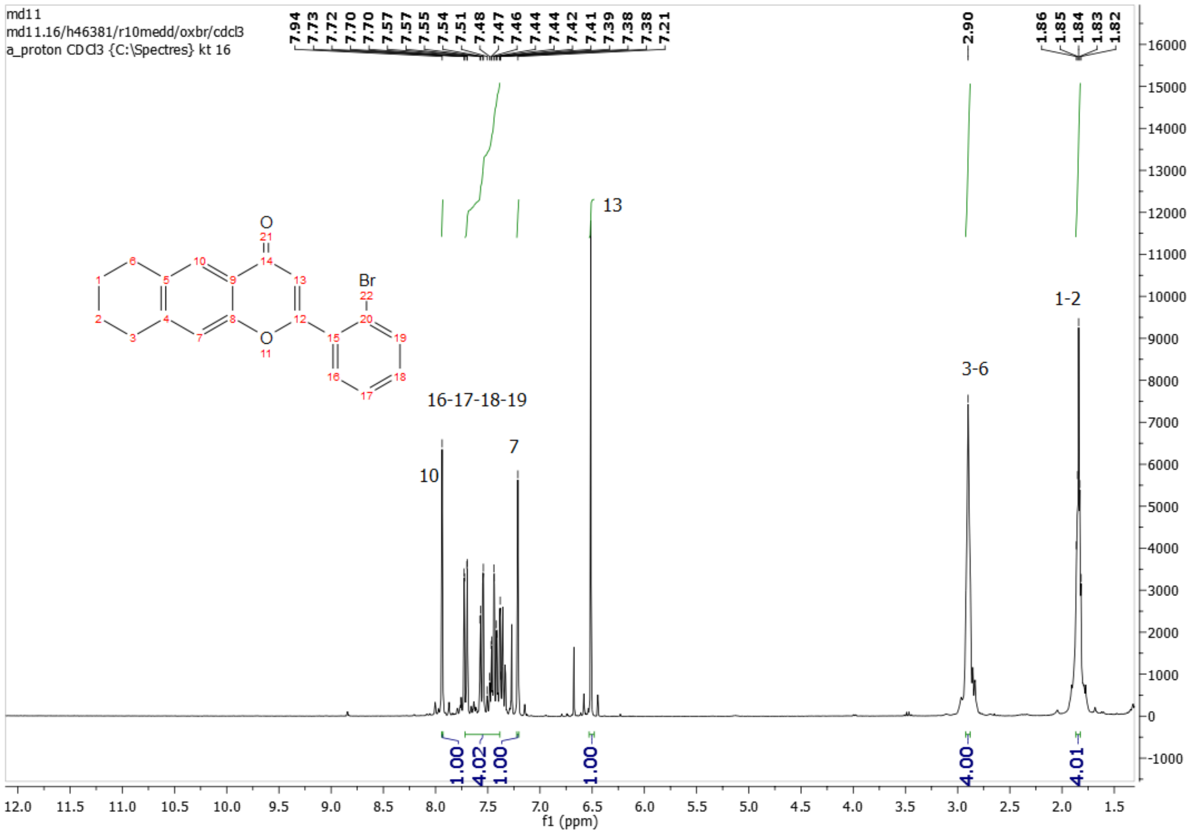


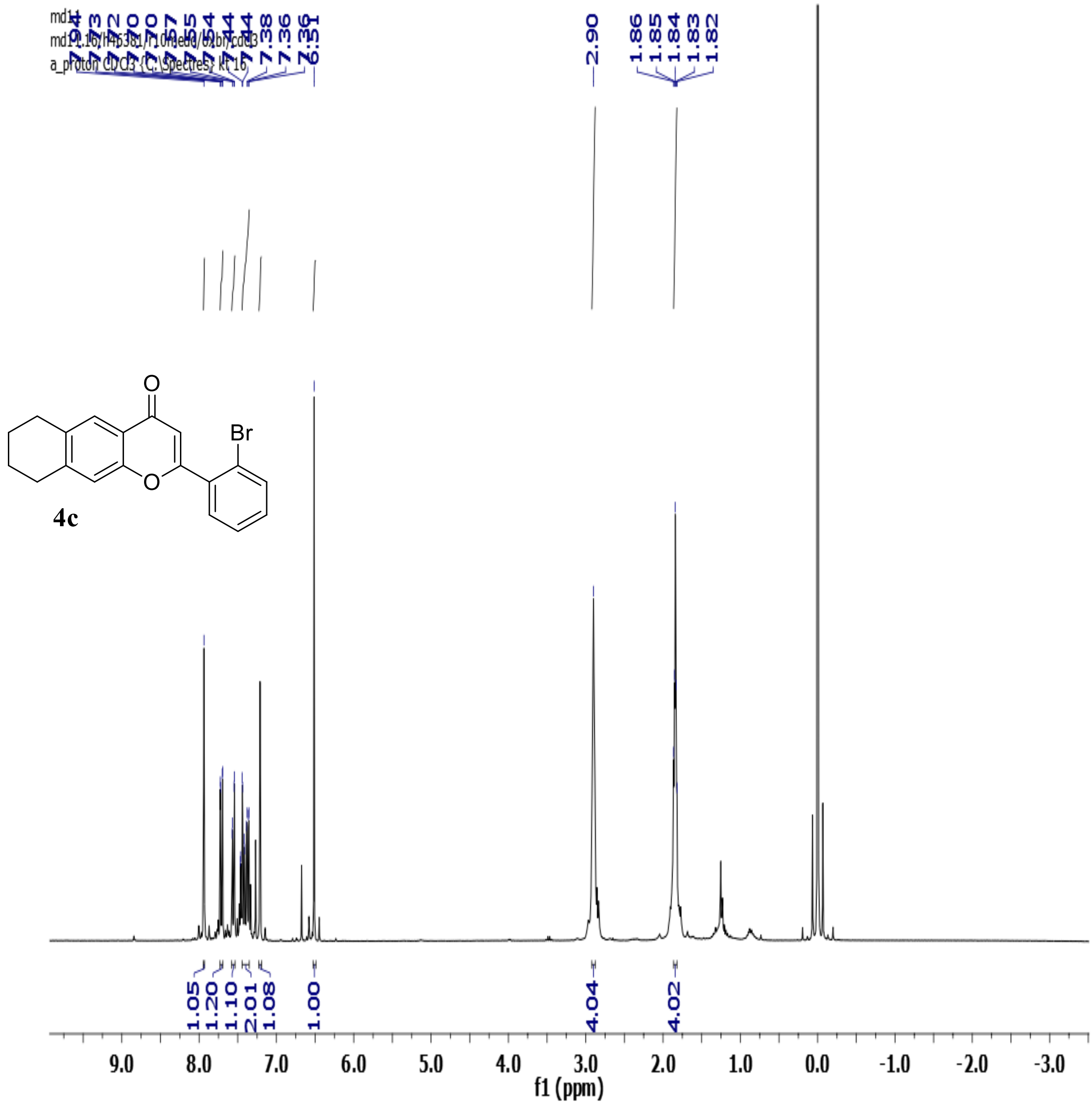

md11
md11.15/h46380/r7medd/oxd3/cdcl3
a_proton CDCl3 {C:\Spectres} kt 15
7.92
7.62
7.61
7.60
7.59
7.52
7.51
7.49
7.49
7.45
7.45
7.43
7.42
7.40
7.38
7.38
7.19
6.59
2.88
1.84
1.83
1.82
O
Cl
O
4b
1.00
1.00
1.00
2.24
1.00
1.00
4.05
4.02
16
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
-3
-4
f1 (ppm)

2-(2-Chlorophenyl)-6,7,8,9-tetrahydro-4H-benzo[g]chromen-4-one (4b)
^{13}C NMR



2-(2-Bromophenyl)-6,7,8,9-tetrahydro-4H-benzo[g]chromen-4-one (4c)
^{1}H NMR

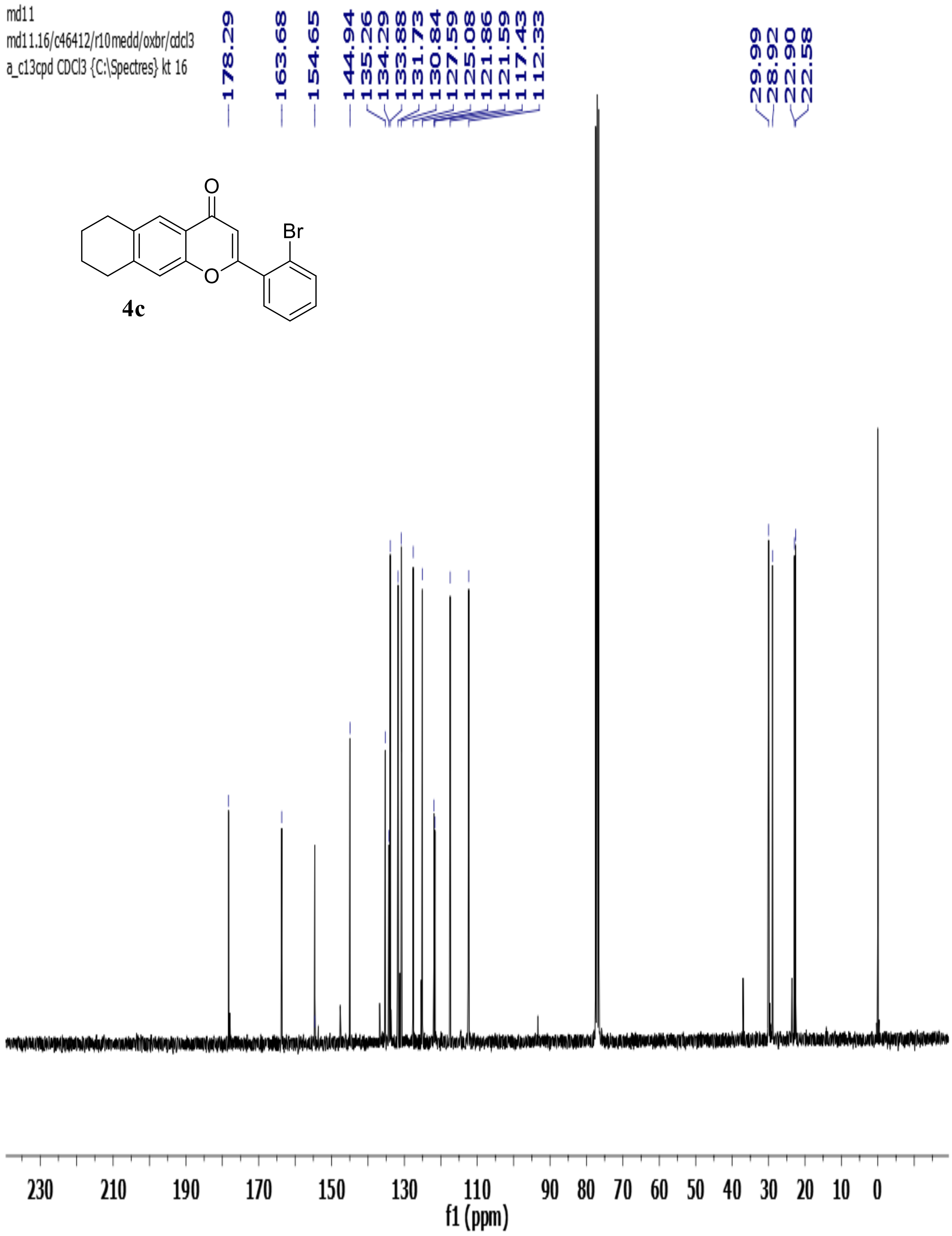




4c

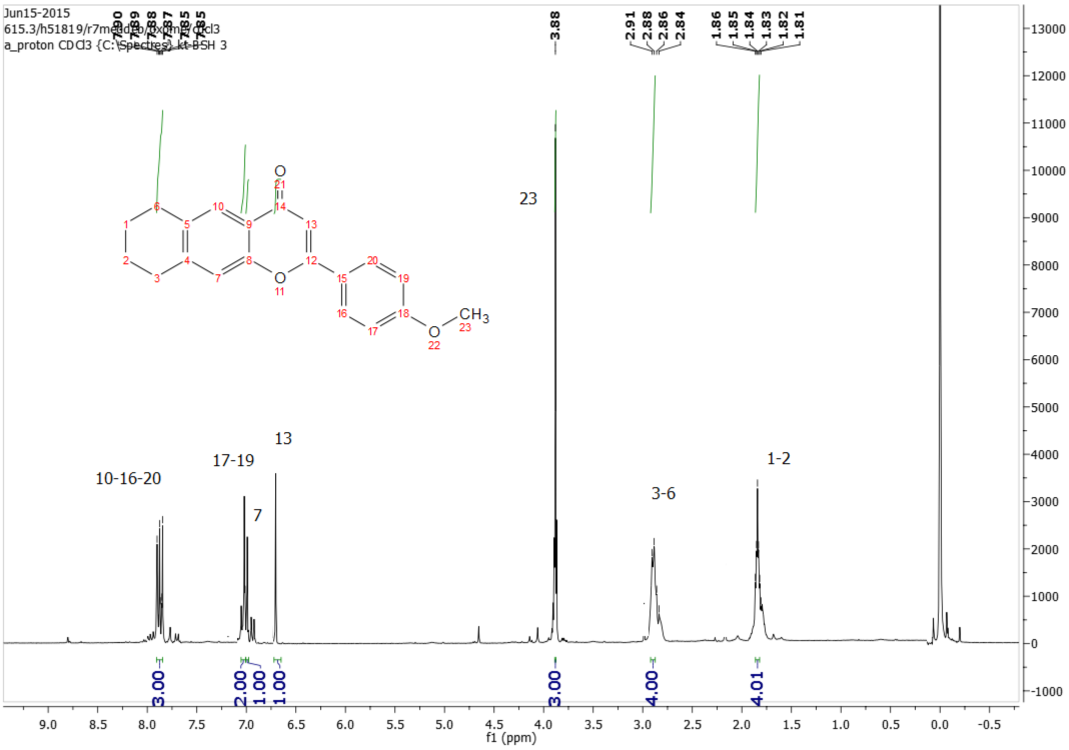
md11
md11.16/h46381/r10mjedd/0xbr/cdcl3
a_proton CDCl3 {C:\Spectres} kt 16
7.94
7.73
7.72
7.70
7.70
7.57
7.55
7.54
7.44
7.44
7.38
7.36
7.36
6.51
2.90
1.86
1.85
1.84
1.83
1.82
1.05
1.20
1.10
2.01
1.08
1.00
4.04
4.02
O
Br
O
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
-1.0
-2.0
-3.0
f1 (ppm)

2-(2-Bromophenyl)-6,7,8,9-tetrahydro-4H-benzo[g]chromen-4-one (4c)
^{13}C NMR

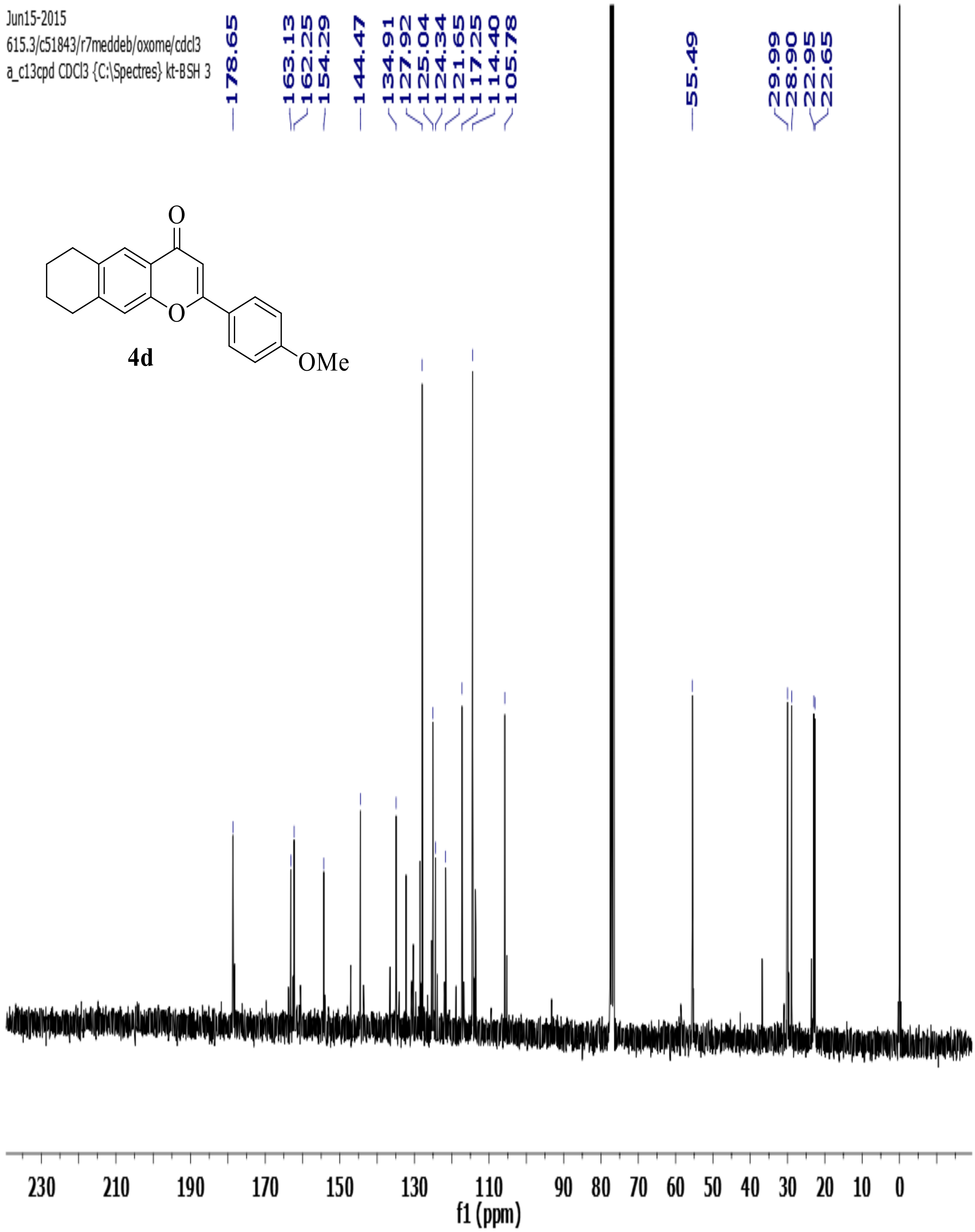


2-(4-Methoxyphenyl)-6,7,8,9-tetrahydro-4H-benzo[g]chromen-4-one (4d)

^{1}H NMR

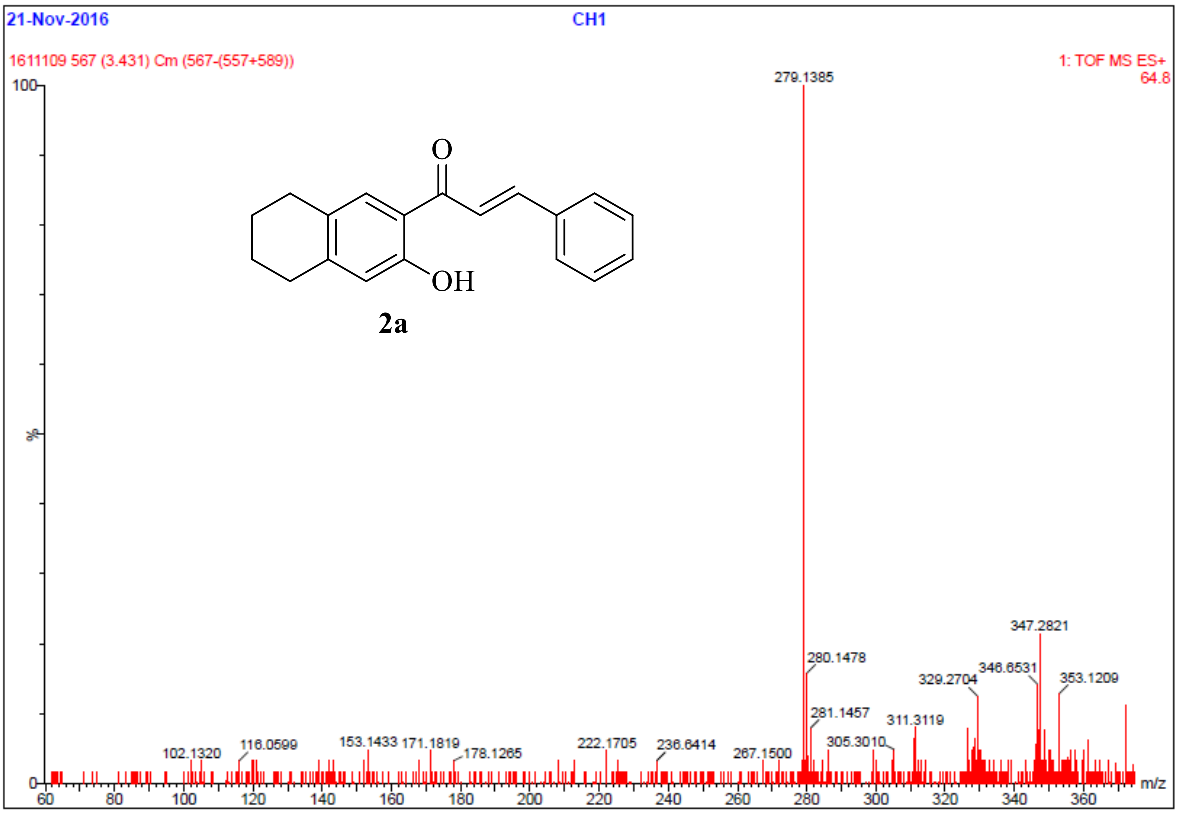


2-(4-Methoxyphenyl)-6,7,8,9-tetrahydro-4H-benzo[g]chromen-4-one (4d)
^{13}C NMR

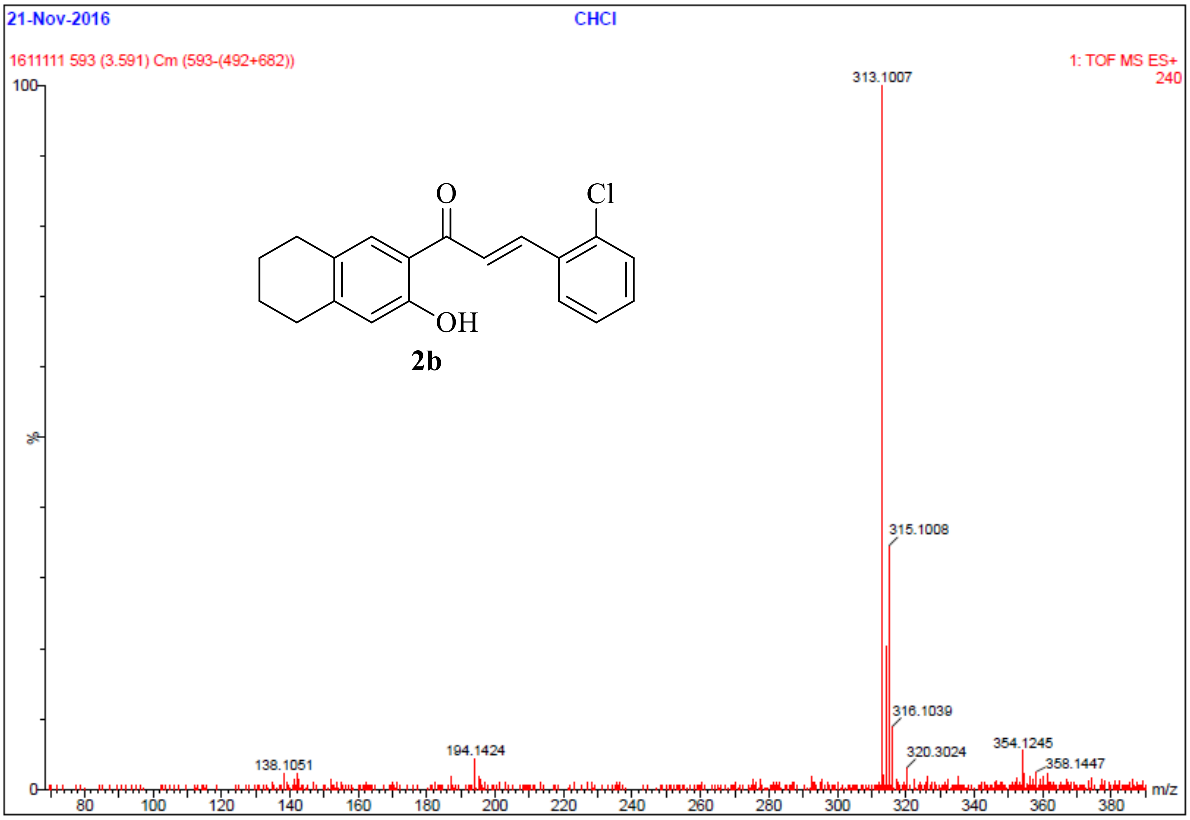


11. HRMS spectra of chalcones (2a–2d)

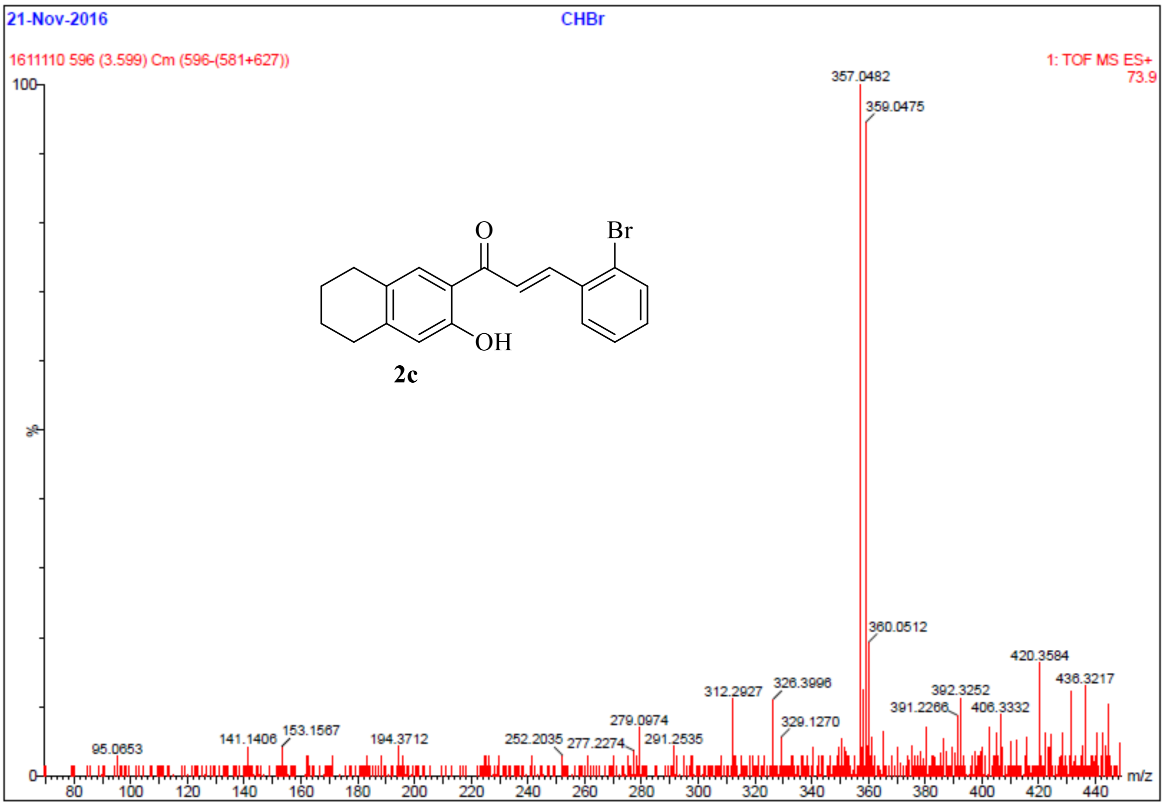
(E)-1-(3-Hydroxy-5,6,7,8-tetrahydronaphthalen-2-yl)-3-phenylprop-2-en-1-one (2a)



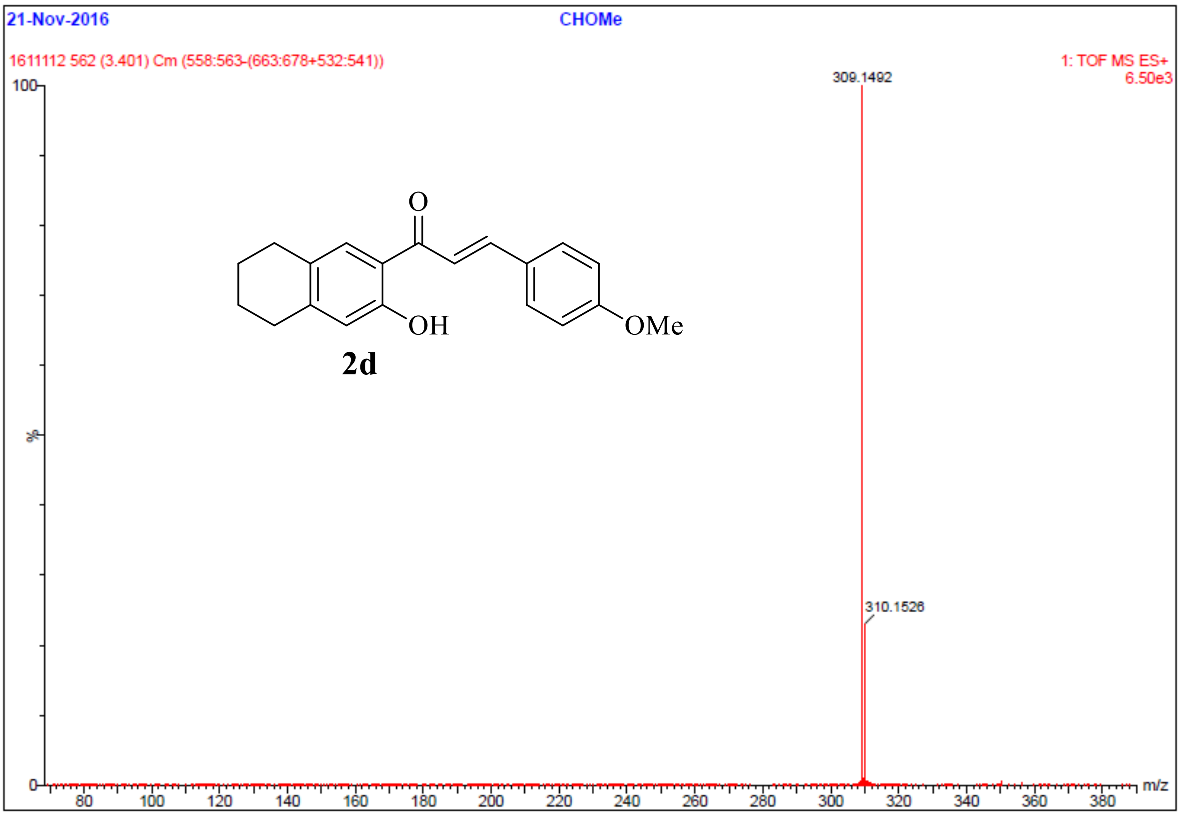
(E)-3-(2-Chlorophenyl)-1-(3-hydroxy-5,6,7,8-tetrahydronaphthalen-2-yl)prop-2-en-1-one (2b)



(E)-3-(2-Bromophenyl)-1-(3-hydroxy-5,6,7,8-tetrahydronaphthalen-2-yl)prop-2-en-1-one (2c)



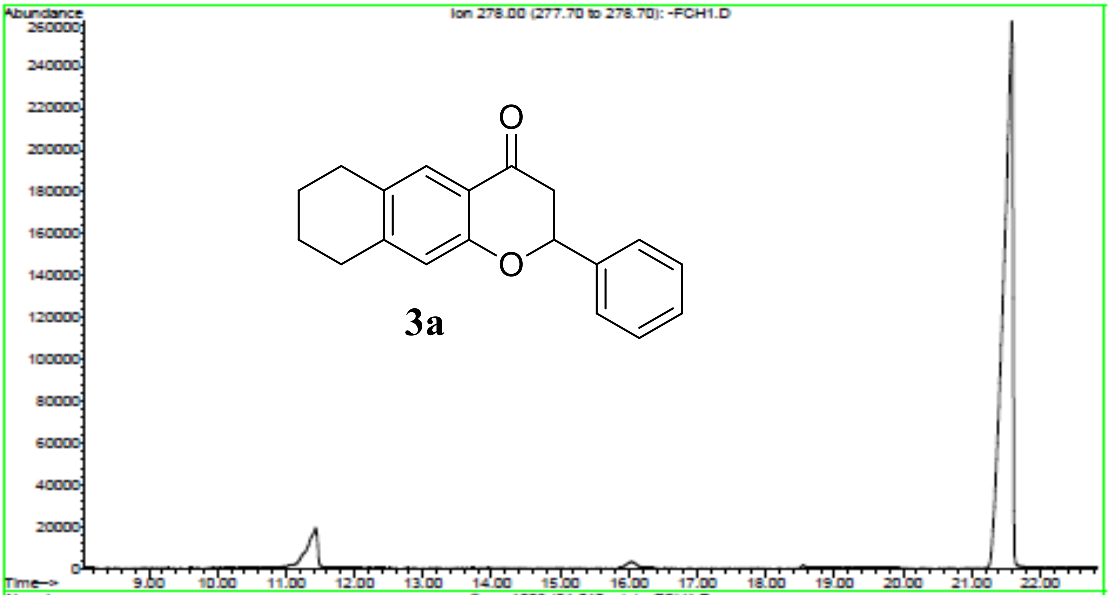
E)-1-(3-Hydroxy-5,6,7,8-tetrahydronaphthalen-2-yl)-3-(4-methoxyphenyl)prop-2-en-1-one (2d)

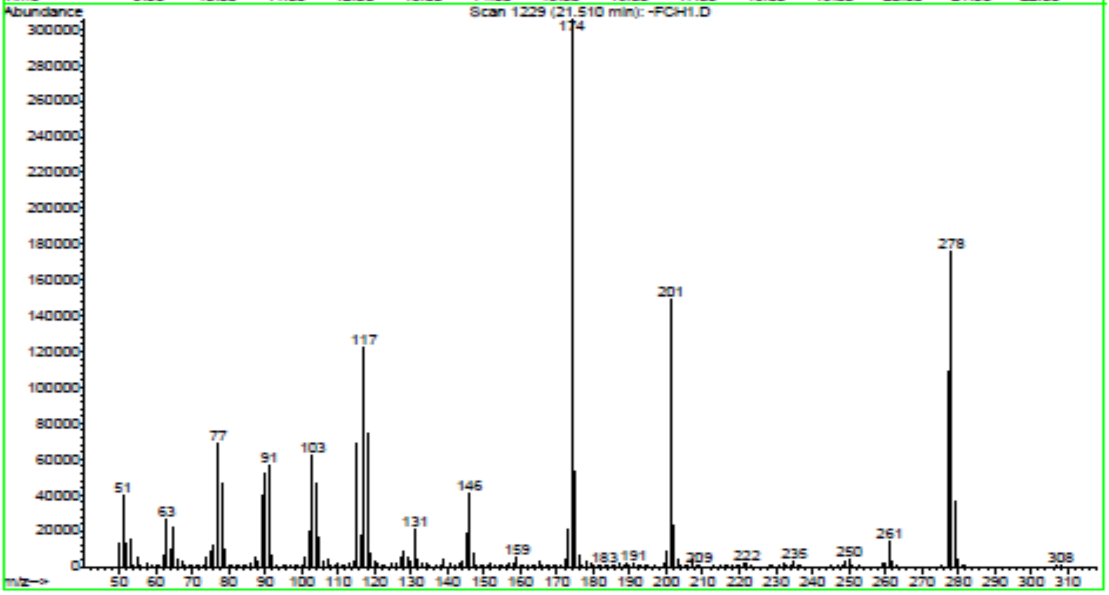


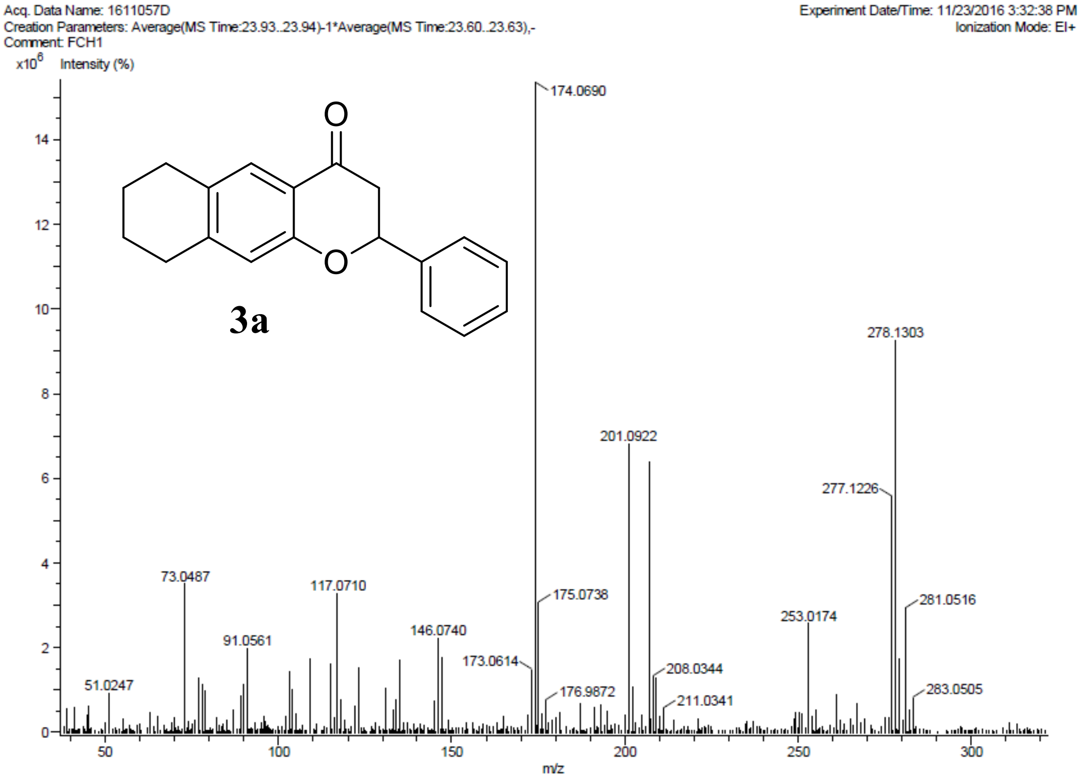
12. GC/MS and HRMS spectra of flavanones (3a–3d)

2-Phenyl-6,7,8,9-tetrahydro-2H-benzo[g]chromen-4(3H)-one (3a)

```
File        :C:\MSDChem\1\DATA\fst\-FCH1.D
Operator    :
Acquired    :  2 Dec 2015  15:42      using AcqMethod SYNT
Instrument  :     GC/MS Ins
Sample Name:
Misc Info   :
Vial Number: 1
```



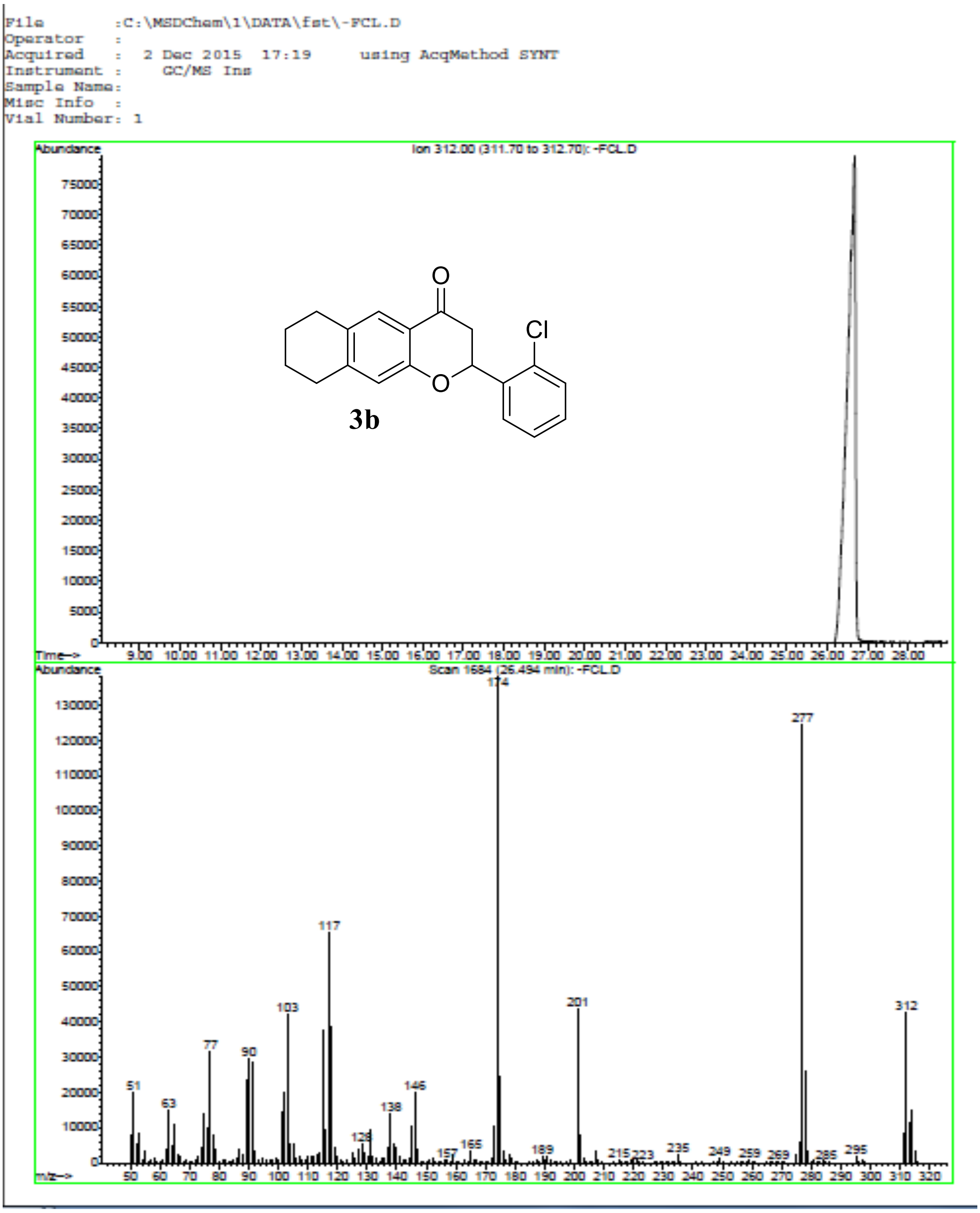




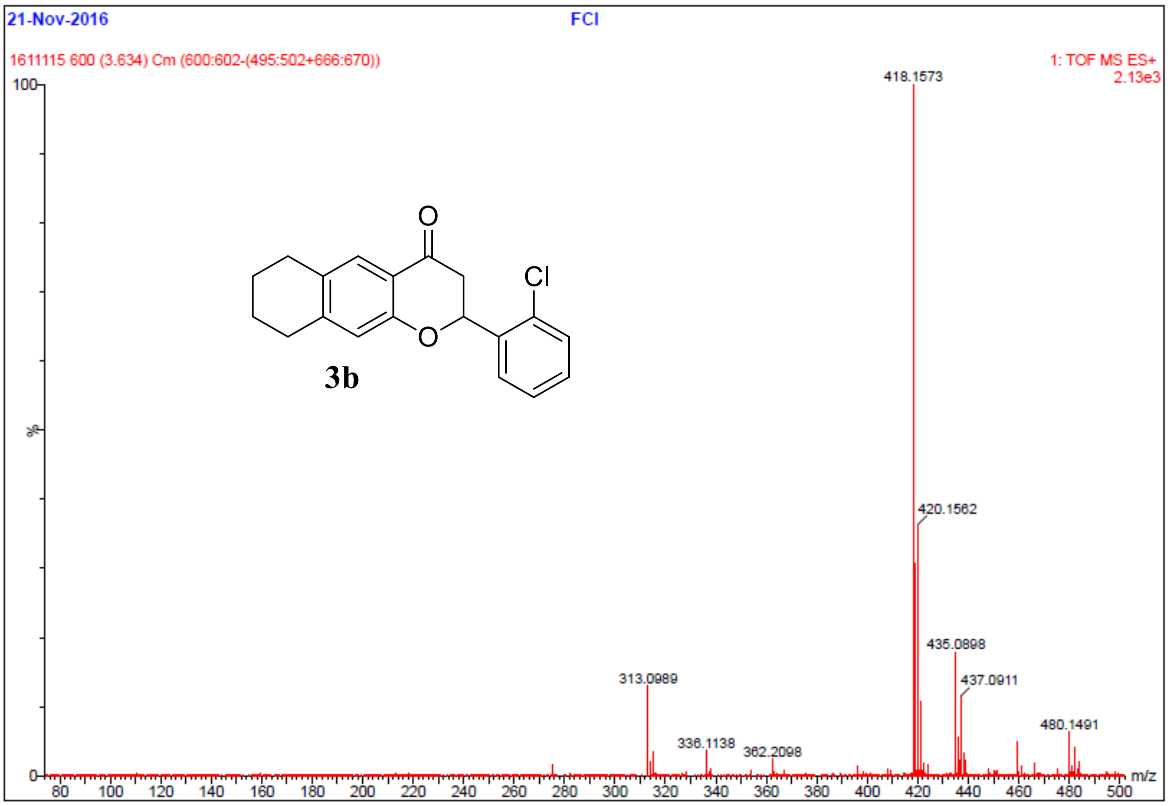
Acq. Data Name: 1611057D
Creation Parameters: Average(MS Time:23.93..23.94)-1*Average(MS Time:23.60..23.63),-
Comment: FCH1

Experiment Date/Time: 11/23/2016 3:32:38 PM
Ionization Mode: EI+

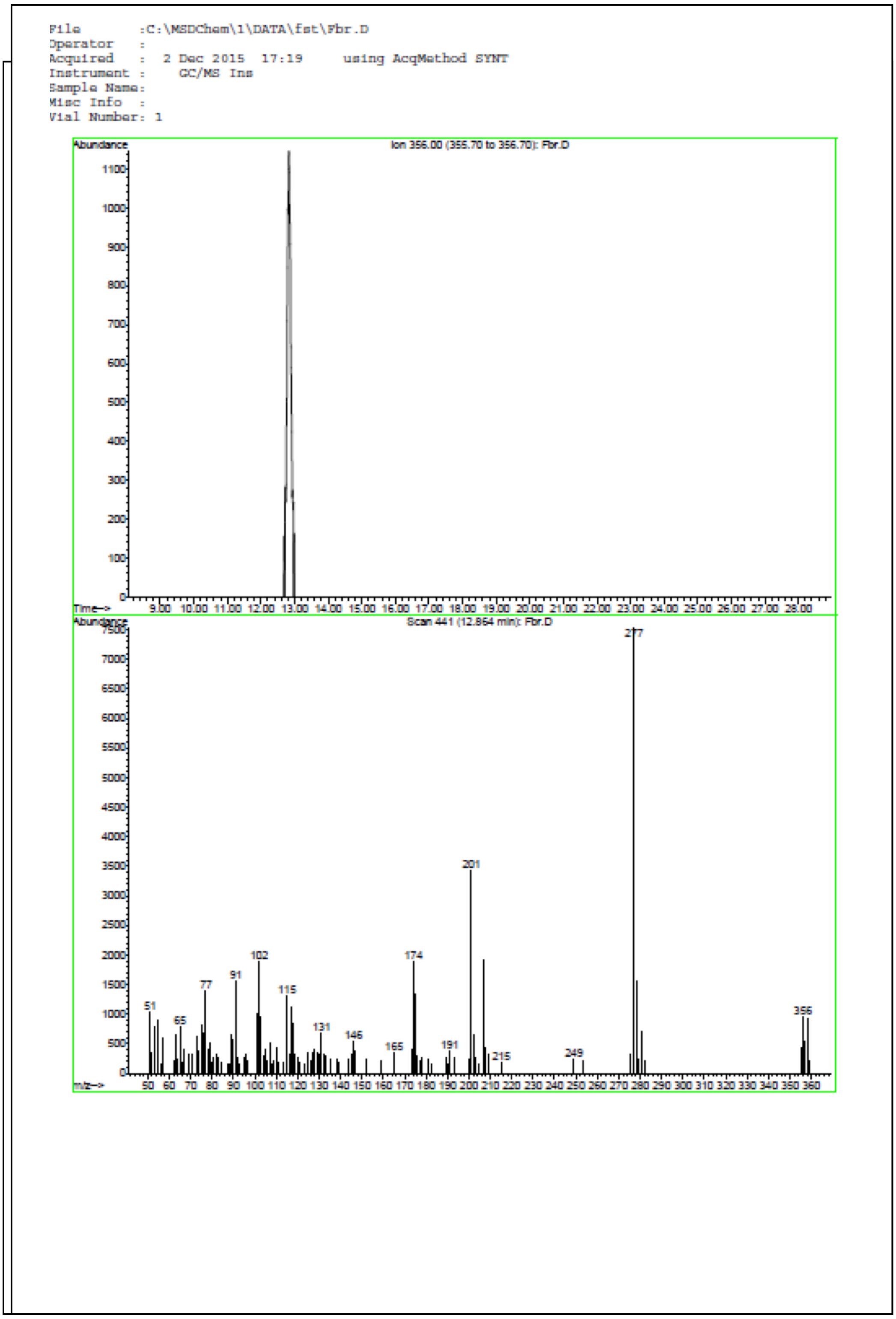
2-(2-Chlorophenyl)-6,7,8,9-tetrahydro-2H-benzo[g]chromen-4(3H)-one (3b)



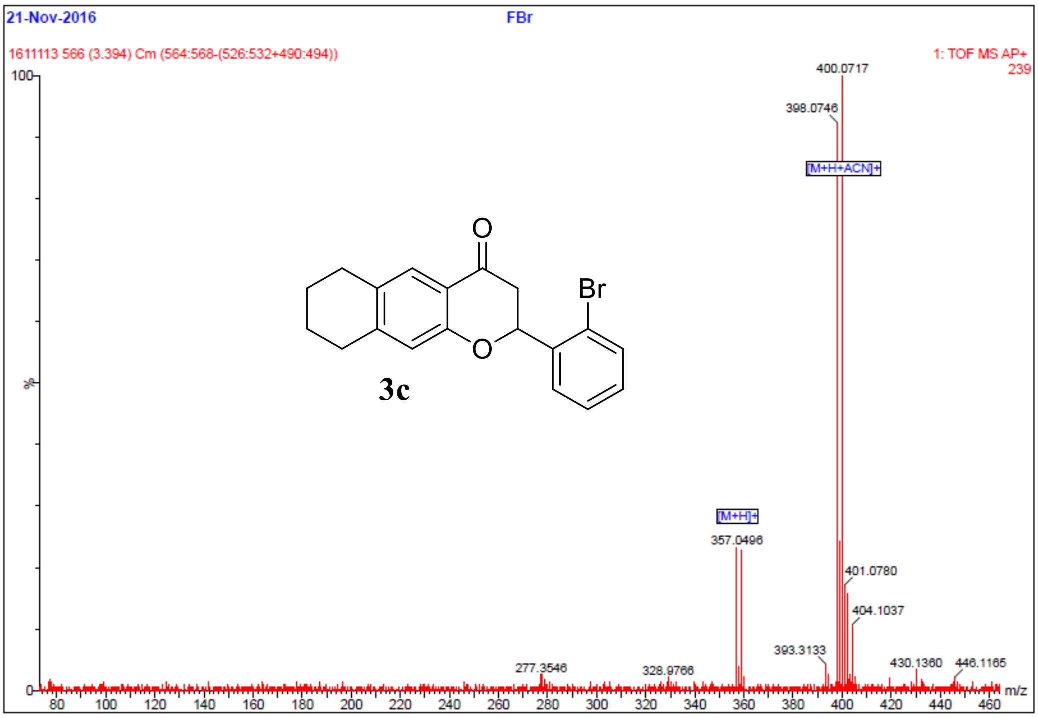
```
File        :C:\MSDChem\1\DATA\fst\-FCL.D
Operator    :
Acquired    :  2 Dec 2015  17:19     using AcqMethod SYNT
Instrument  :    GC/MS Ins
Sample Name:
Misc Info   :
Vial Number: 1
```


21-Nov-2016
FCI
1611115 600 (3.634) Cm (600:602-(495:502+666:670))
1: TOF MS ES+
2.13e3
100
%
0
418.1573
420.1562
435.0898
437.0911
313.0989
336.1138
362.2098
480.1491
O
O
Cl
3b
80
100
120
140
160
180
200
220
240
260
280
300
320
340
360
380
400
420
440
460
480
500
m/z

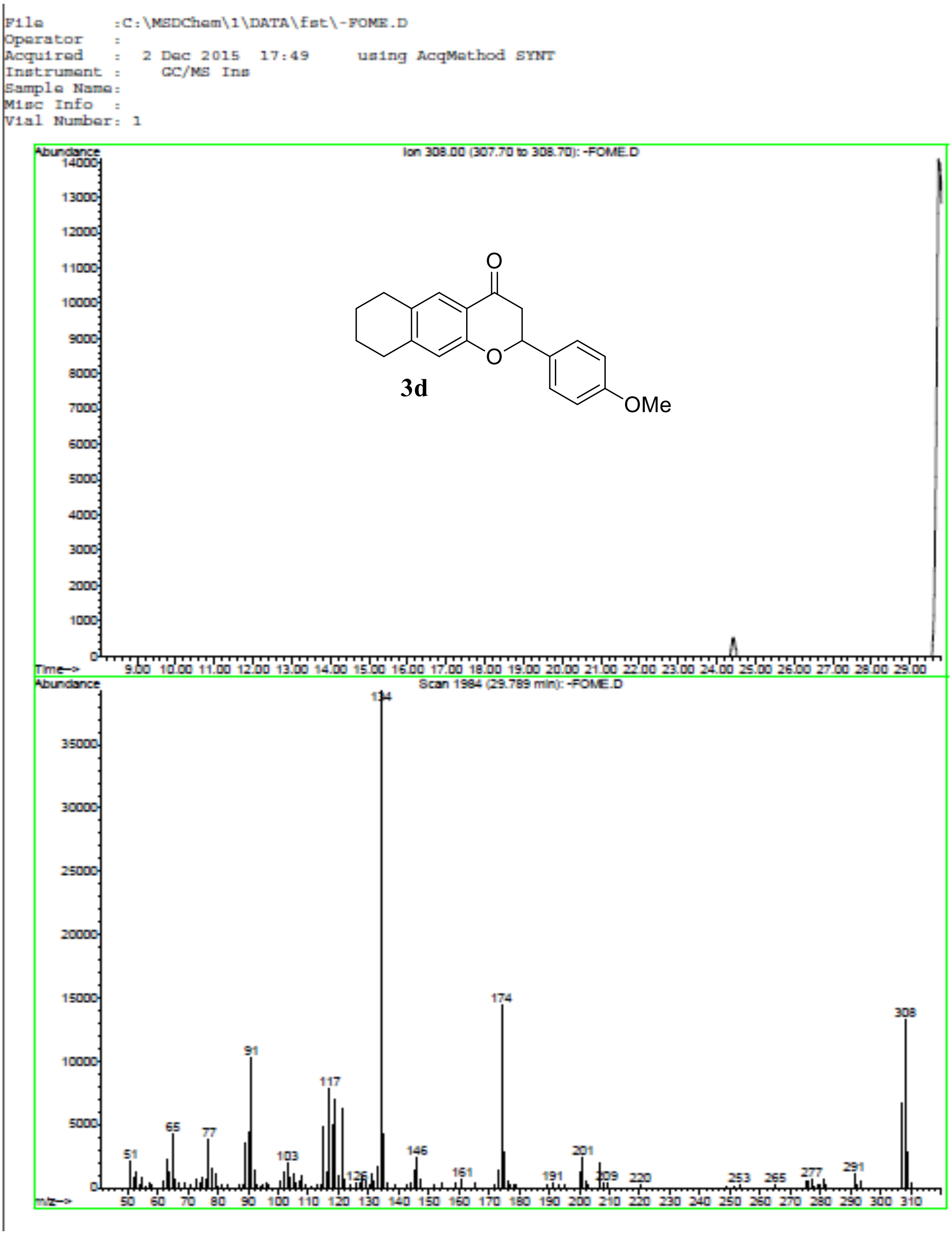
2-(2-Bromophenyl)-6,7,8,9-tetrahydro-2H-benzo[g]chromen-4(3H)-one (3c)



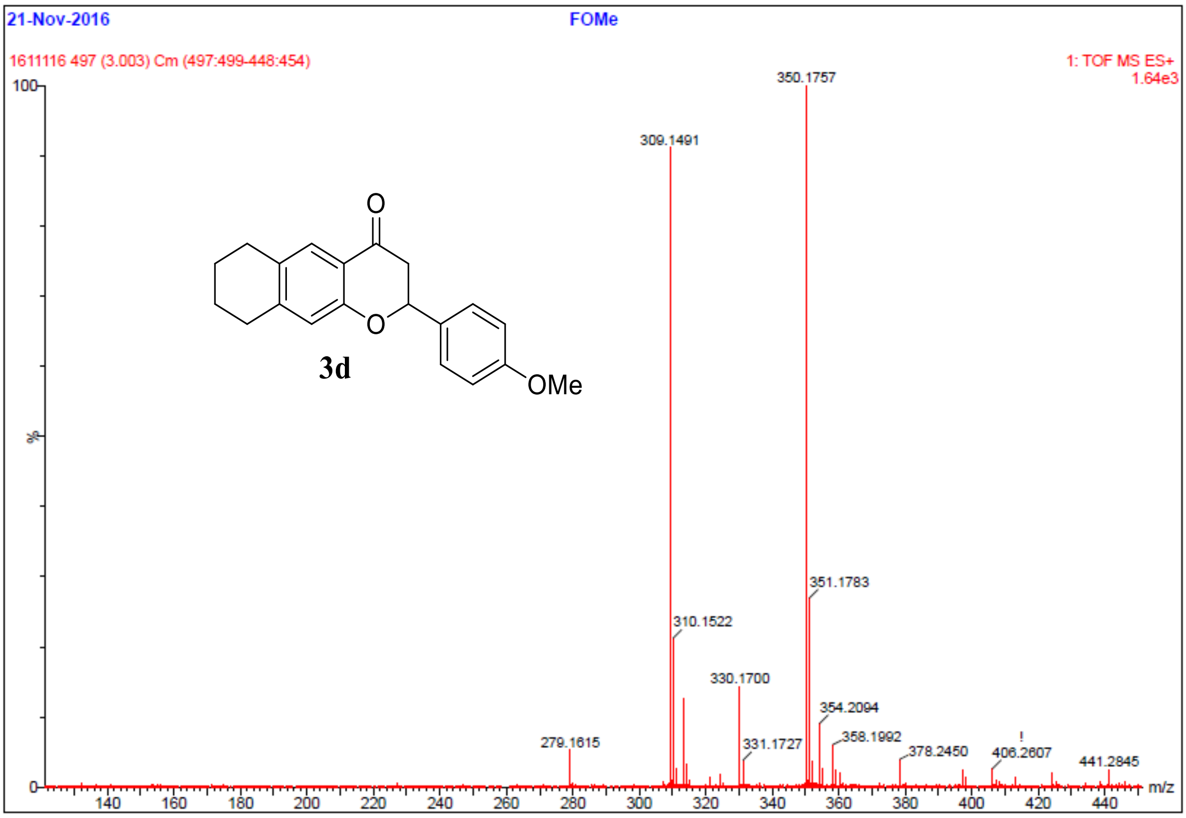
```
File       :C:\MSDChem\1\DATA\fst\Fbr.D
Operator   :
Acquired   :  2 Dec 2015  17:19     using AcqMethod SYNT
Instrument :    GC/MS Ins
Sample Name:
Misc Info  :
Vial Number: 1
```


21-Nov-2016
FBr
1611113 566 (3.394) Cm (564:568-(526:532+490:494))
1: TOF MS AP+
239
100
%
0
400.0717
398.0746
[M+H+ACN]+
[M+H]+
357.0496
401.0780
404.1037
393.3133
277.3546
328.9766
430.1360
446.1165
80
100
120
140
160
180
200
220
240
260
280
300
320
340
360
380
400
420
440
460
m/z
O
O
Br
3c

2-(4-Methoxyphenyl)-6,7,8,9-tetrahydro-2H-benzo[g]chromen-4(3H)-one (3d)



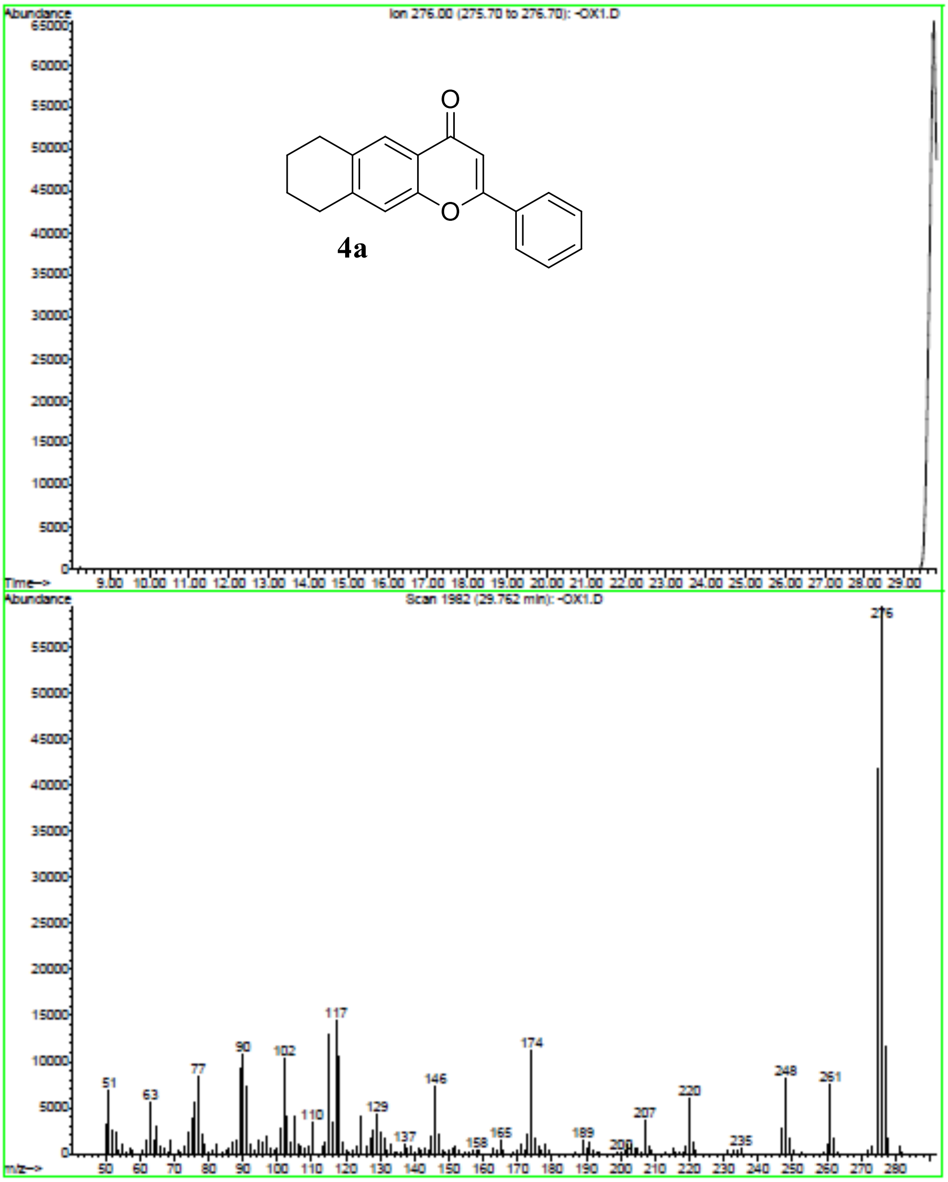
```
File        :C:\MSDChem\1\DATA\fst\-FOME.D
Operator    :
Acquired    :  2 Dec 2015  17:49     using AcqMethod SYNT
Instrument  :     GC/MS Ins
Sample Name:
Misc Info   :
Vial Number: 1
```

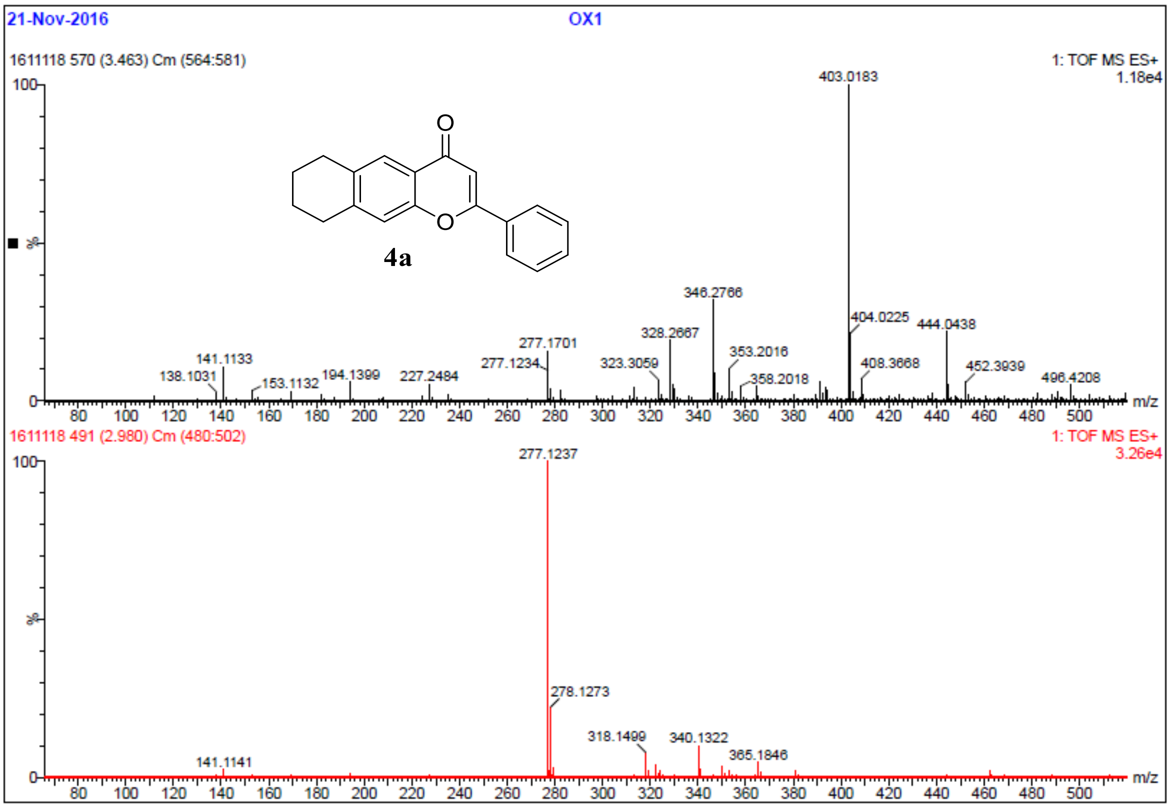

21-Nov-2016
FOMe
1611116 497 (3.003) Cm (497:499-448:454)
1: TOF MS ES+
1.64e3
100
%
0
350.1757
309.1491
351.1783
310.1522
330.1700
354.2094
331.1727
358.1992
378.2450
406.2607
441.2845
279.1615
m/z
140
160
180
200
220
240
260
280
300
320
340
360
380
400
420
440
O
O
OMe
3d

13. GC/MS and HRMS spectra of flavonees (4a–4d)

2-Phenyl-6,7,8,9-tetrahydro-4H-benzo[g]chromen-4-one (4a)

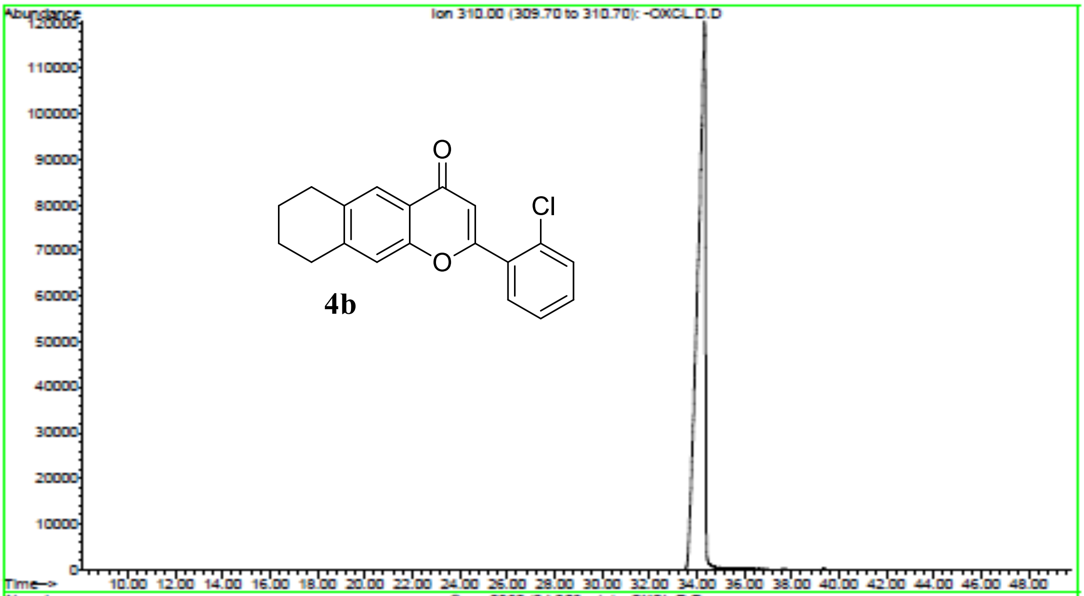
```
File       :C:\MSDChem\1\DATA\fst\-OX1.D
Operator   :
Acquired   :  2 Dec 2015  16:41     using AcqMethod SYNT
Instrument :    GC/MS Ins
Sample Name:
Misc Info  :
Vial Number: 1
```

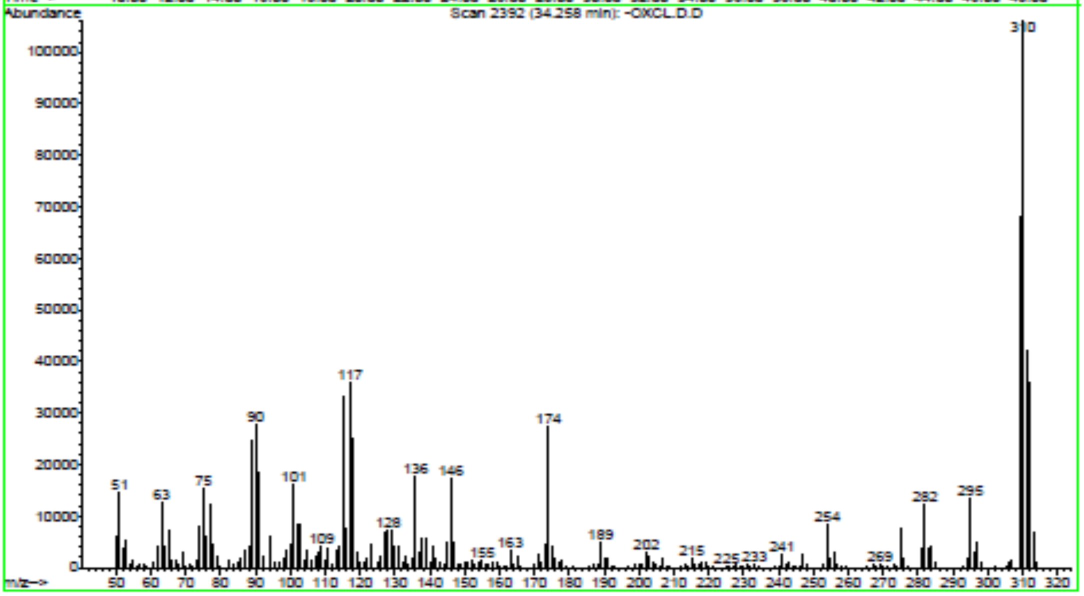


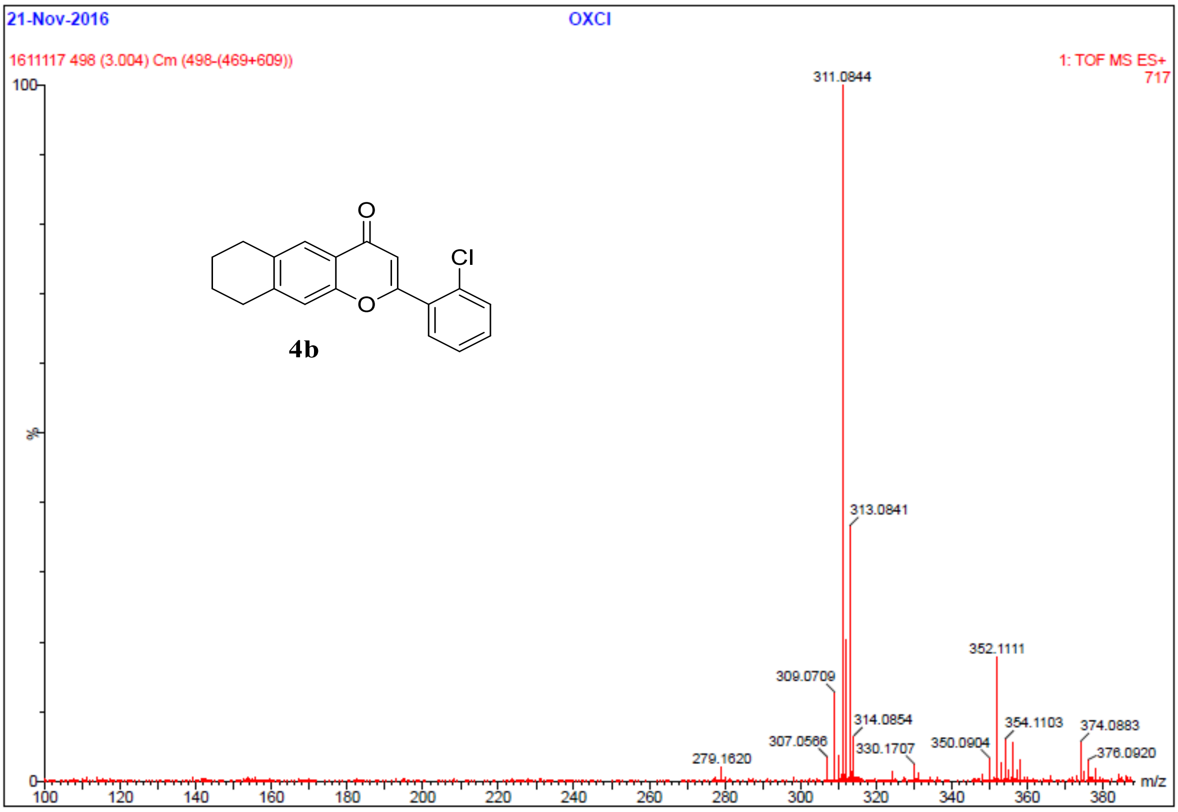

21-Nov-2016
OX1
1611118 570 (3.463) Cm (564:581)
1: TOF MS ES+
1.18e4
100
%
0
403.0183
346.2766
404.0225
444.0438
328.2667
353.2016
277.1701
323.3059
408.3668
452.3939
141.1133
277.1234
358.2018
496.4208
138.1031
194.1399
227.2484
153.1132
m/z
80
100
120
140
160
180
200
220
240
260
280
300
320
340
360
380
400
420
440
460
480
500
4a
O
O
1611118 491 (2.980) Cm (480:502)
1: TOF MS ES+
3.26e4
277.1237
278.1273
318.1499
340.1322
365.1846
141.1141

2-(2-Chlorophenyl)-6,7,8,9-tetrahydro-4H-benzo[g]chromen-4-one (4b)

```
File        :C:\MSDChem\1\DATA\-OXCL.D.D
Operator    :
Acquired    :  3 Dec 2015   8:07     using AcqMethod SYNT
Instrument  :    GC/MS Ins
Sample Name:
Misc Info   :
Vial Number: 1
```

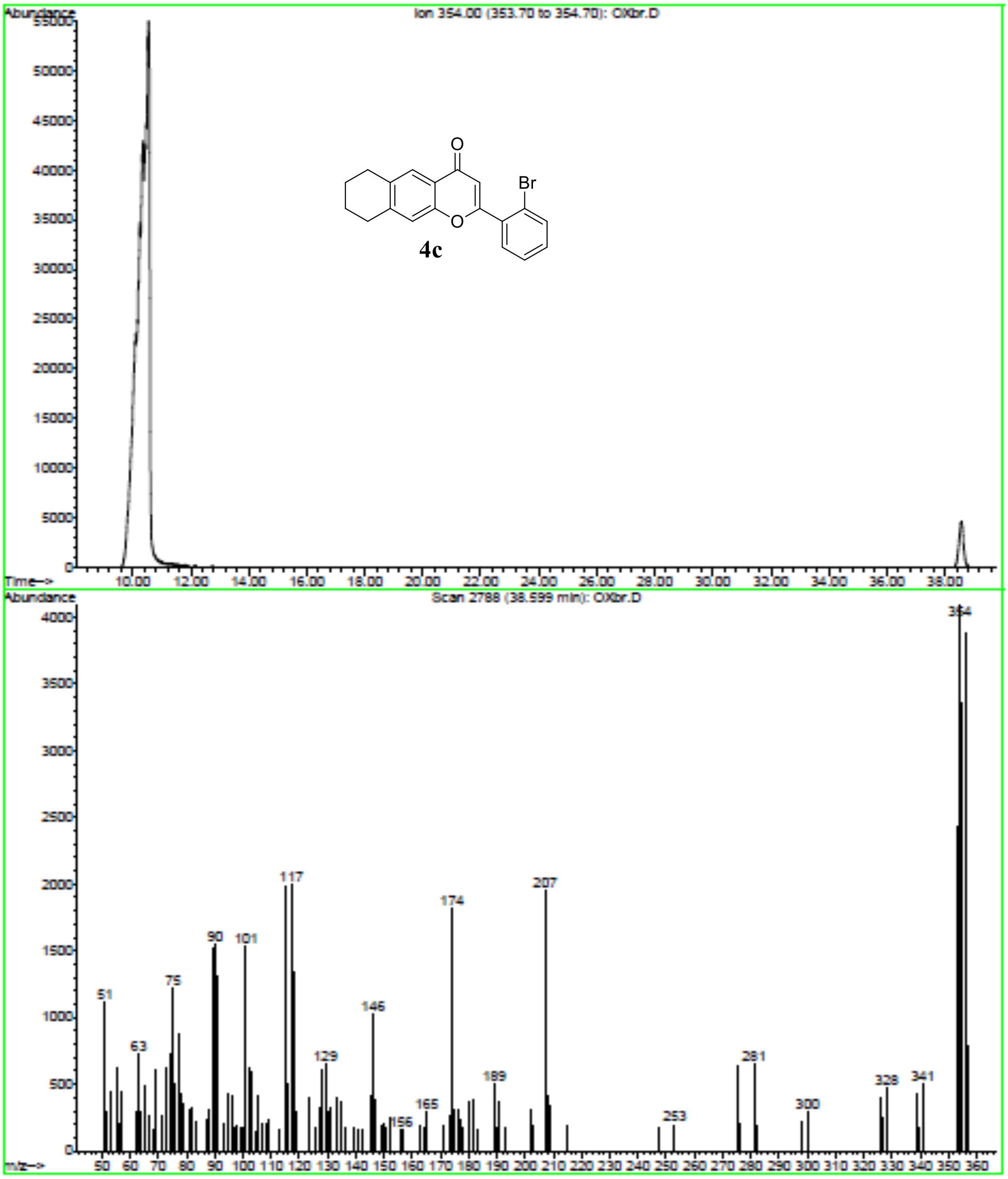


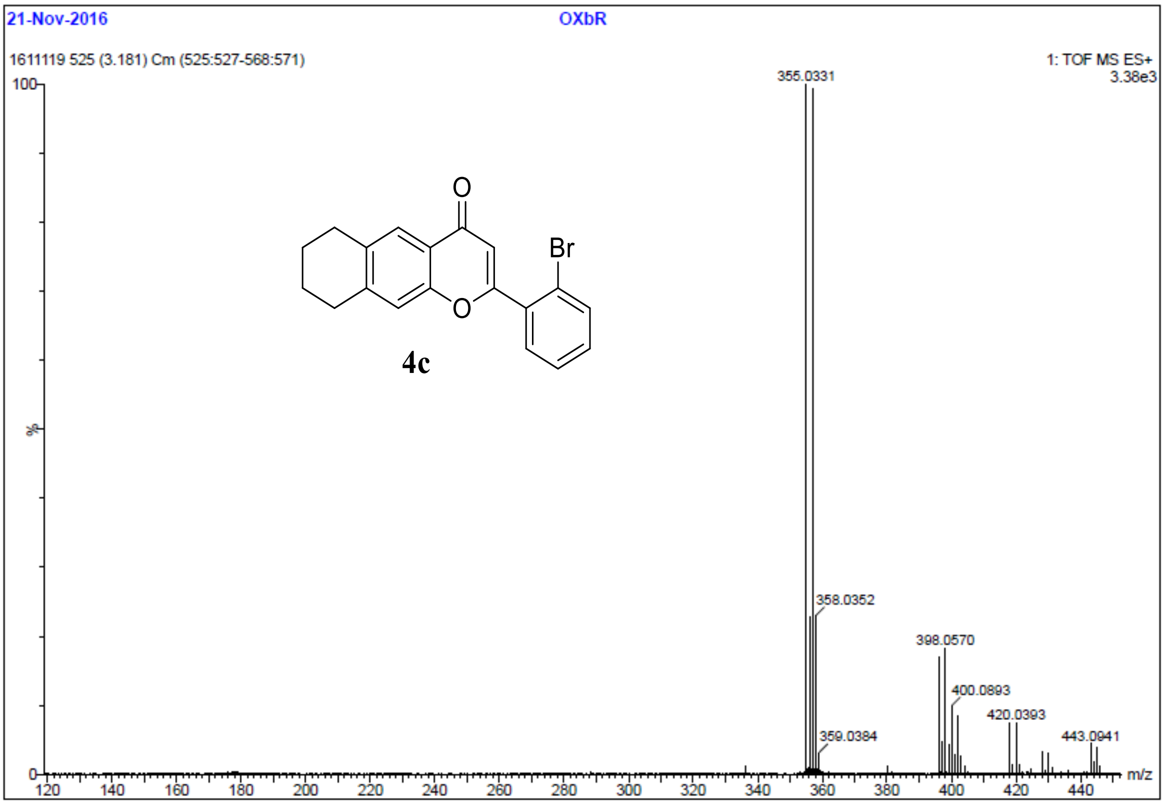



21-Nov-2016
OXCI
1611117 498 (3.004) Cm (498-(469+609))
1: TOF MS ES+
717
100
%
0
4b
Cl
O
311.0844
313.0841
352.1111
309.0709
314.0854
354.1103
374.0883
307.0566
330.1707
350.0904
376.0920
279.1620
100
120
140
160
180
200
220
240
260
280
300
320
340
360
380
m/z

2-(2-Bromophenyl)-6,7,8,9-tetrahydro-4H-benzo[g]chromen-4-one (4c)

```
File        :C:\MSDChem\1\DATA\fst\OXbr.D
Operator    :
Acquired    :  3 Dec 2015    7:22      using AcqMethod SYNT
Instrument  :    GC/MS Ins
Sample Name:
Misc Info   :
Vial Number: 1
```



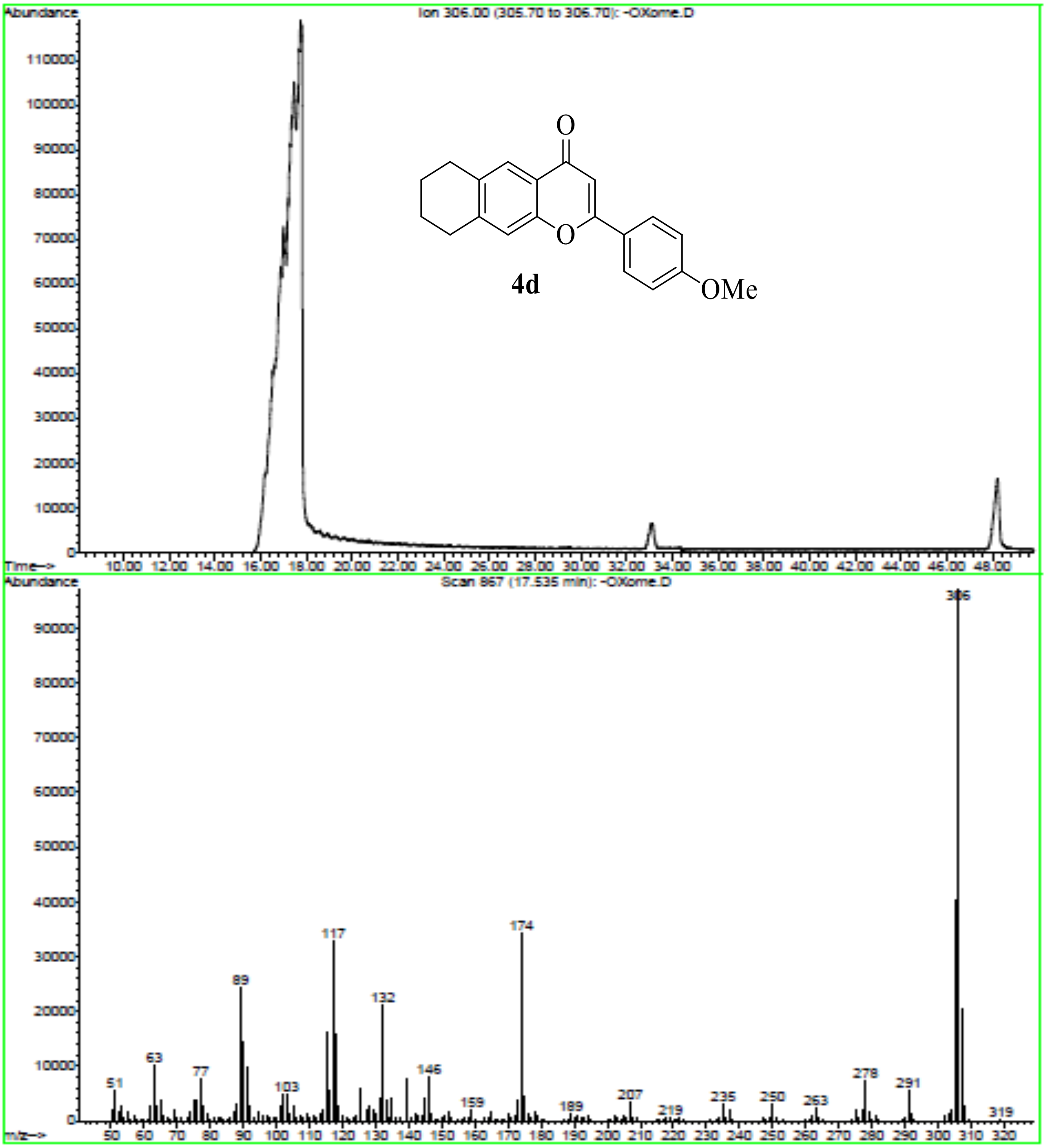


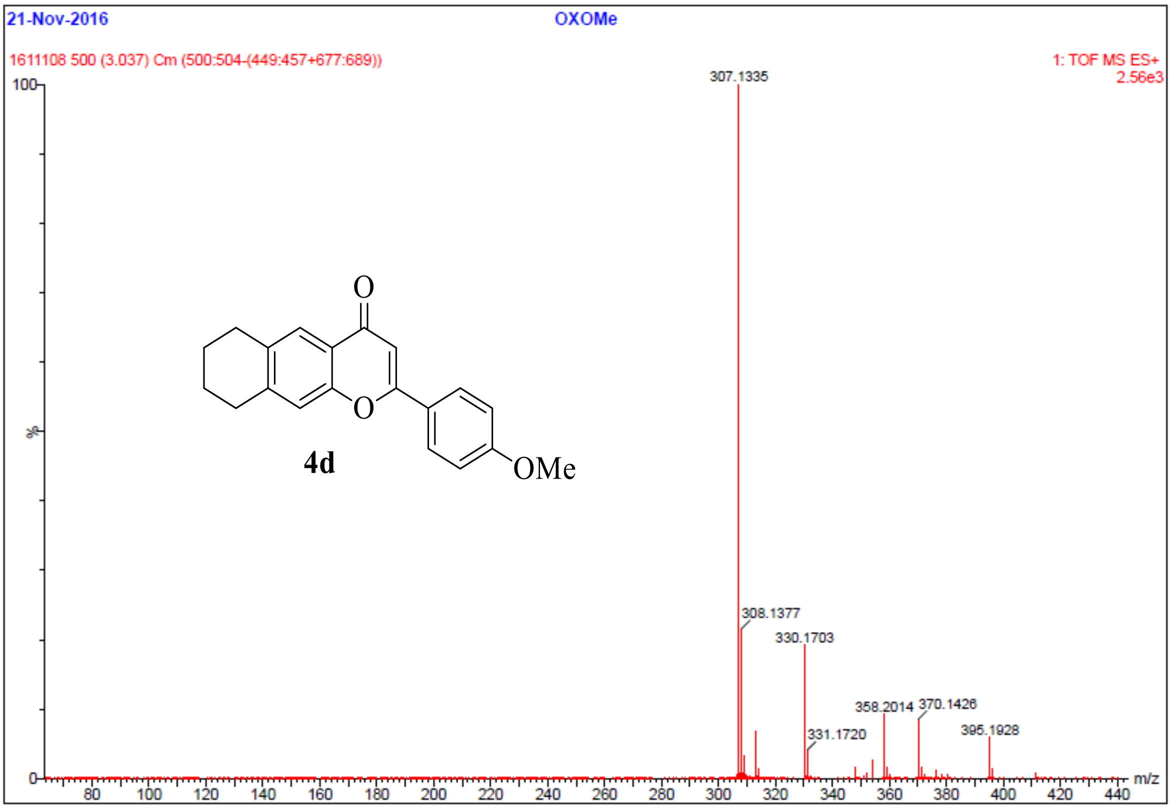
4c

21-Nov-2016
OXbR
1611119 525 (3.181) Cm (525:527-568:571)
1: TOF MS ES+
3.38e3
100
%
0
355.0331
358.0352
359.0384
398.0570
400.0893
420.0393
443.0941
120
140
160
180
200
220
240
260
280
300
320
340
360
380
400
420
440
m/z
O
O
Br

2-(4-Methoxyphenyl)-6,7,8,9-tetrahydro-4H-benzo[g]chromen-4-one (4d)

```
File        :C:\MSDChem\1\DATA\-OXome.D
Operator    :
Acquired    :  3 Dec 2015   8:07     using AcqMethod SYNT
Instrument  :     GC/MS Ins
Sample Name:
Misc Info   :
Vial Number: 1
```




21-Nov-2016
OXOMe
1611108 500 (3.037) Cm (500:504-(449:457+677:689))
1: TOF MS ES+
2.56e3
100
%
0
307.1335
308.1377
330.1703
331.1720
358.2014
370.1426
395.1928
O
O
OMe
4d
80
100
120
140
160
180
200
220
240
260
280
300
320
340
360
380
400
420
440
m/z