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Thieme

Supporting Information

The reaction of 2-(acylamino)benzonitriles with primary aromatic amines: a convenient synthesis of 2-substituted 4-(arylamino)quinazolines

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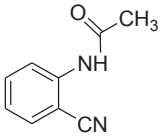
General experimental details:

All compounds were fully characterized by elemental analysis and spectroscopic data. The NMR spectra were recorded at room temperature, on a Varian Unity Plus (^{1}H: 300 MHz, ^{13}C: 75 MHz), or on a Bruker Avance III 400 (^{1}H: 400 MHz, ^{13}C: 100 MHz) including the ^{1}H-^{13}C correlation spectra (HMQC and HMBC). Deuterated DMSO was used as solvent. The chemical shifts are expressed in δ (ppm) and the coupling constants, *J*, are reported in hertz (Hz). The peak patterns are indicated as follows: s, singlet; d, doublet; t, triplet; m, multiplet; q, quartet and br, broad. IR spectra were recorded on a FT-IR Bomem MB 104 using Nujol mulls and and NaCl cells. The reactions were monitored by thin layer chromatography (TLC) using silica gel 60 F_{254} (Merck and Macherey-Nagel). The melting points were determined on a Stuart SMP3 melting point apparatus and are uncorrected. Elemental analyses were performed on a LECO CHNS-932 instrument.

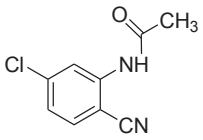
Experimental procedures for compounds **2**, **3** and **4**

Synthesis of *N*-(2-cyanophenyl)acetamide (2a)



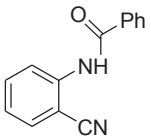
Triethylamine (40 µl) was added to a solution of anthranilonitrile **1a** (0.43 g; 3.64 mmol) in acetic anhydride (1.49 g; 14.56 mmol; 1375 µl; 4 equiv) at room temperature. After 10 min a white solid precipitated and was filtered and washed with water leading to the pure product *N*-(2-cyanophenyl)acetamide **2a** (0.51 g; 3.14 mmol; 86%).

Synthesis of *N*-(5-chloro-2-cyanophenyl)acetamide (2b)



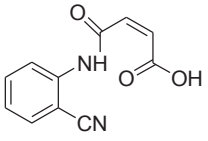
Acetic anhydride (2.72 g; 26.60 mmol; 2510 µl; 4 equiv) was added to 2-amino-4-chlorobenzonitrile **1b** (1.02 g; 6.65 mmol), followed by triethylamine (40 µl). The yellow suspension was stirred at room temperature. After 16 h, the starting materials were no longer present (evidence by TLC). The yellow solid was filtered and washed with water. The product was identified as *N*-(5-chloro-2-cyanophenyl)acetamide **2b** (1.25 g; 6.40 mmol; 96%),

Synthesis of *N*-(2-cyanophenyl)benzamide (2c)



Benzoic anhydride (0.95 g; 4.20 mmol; 2.1 equiv) and triethylamine (40 µl) were added to a solution of anthranilonitrile **1a** (0.23 g; 1.98 mmol) in acetonitrile (3 ml), at room temperature. The solution was reflux for 2 h. The solvent was evaporated in the rotary evaporator and the oil was cooled in an ice bath. After 2 h, the white solid (0.08 g) was filtered and washed with diethyl ether. Removal of the solvent from the mother liquor and addition of diethyl ether led to the isolation of a second crop of white solid (0.18 g). Both products were identical by IR spectroscopy and were combined and identified as *N*-(2-cyanophenyl)benzamide **2c** (0.26 g; 1.17 mmol; 59%).

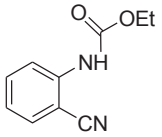
Synthesis of (2*Z*)-4-[(2-cyanophenyl)amino]-4-oxobut-2-enoic acid (2d)



Maleic anhydride (1.92 g; 19.56 mmol; 2 equiv) was added to a solution of anthranilonitrile **1a** (1.16 g; 9.78 mmol) in acetonitrile (3 ml). Triethylamine (40 µl) was also added and the yellow solution immediately evolved

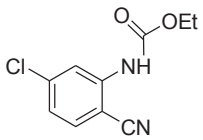
to an orange solution. The reaction mixture was stirred at room temperature. After 45 min the white precipitate was filtered and washed with water. The pure product was identified as (2*Z*)-4-[(2-cyanophenyl)amino]-4-oxobut-2-enoic acid **2d** (1.73 g; 8.02 mmol; 82%).

Synthesis of ethyl (2-cyanophenyl)carbamate (2e)



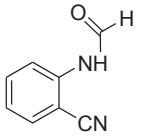
Ethyl chloroformate (0.46 g; 4.24 mmol; 404 µl; 2 equiv) was added to a yellow solution of anthranilonitrile **1a** (0.25 g; 2.12 mmol) in water (2 ml) and ethanol (2 ml). The reaction mixture was stirred at room temperature for 1.5 h. The white precipitate was filtered and washed with water. The pure product was identified as ethyl (2-cyanophenyl)carbamate **2e** (0.35 g; 1.86 mmol; 88%).

Synthesis of ethyl 5-chloro-2-cyanophenylcarbamate (2f)



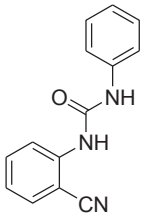
Ethyl chloroformate (0.18 g; 1.65 mmol; 160 µl; 1 equiv) was added to a yellow suspension of 2-amino-4-chlorobenzonitrile **1b** (0.25 g; 1.65 mmol) in water (2 ml) and ethanol (2 ml). The reaction mixture was heated under reflux leading immediately to a yellow solution. Ethyl chloroformate was added in 1 M equiv portions every 15 min for a total of 2 h. A solid precipitated upon addition of water and was filtered and washed with HCl 6M and water leading the pure product ethyl 5-chloro-2-cyanophenylcarbamate **2f** (0.29 g; 1.38 mmol; 79%).

Synthesis of *N*-(2-cyanophenyl)formamide (2g)



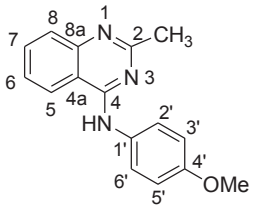
A solution of anthranilonitrile **1a** (0.20 g; 1.70 mmol) in formic acid (0.26 g; 5.10 mmol; 215 µl; 3 equiv) was stirred at room temperature. After 3.5 h a white solid precipitated and was filtered and washed with ethanol. The pure product was identified as *N*-(2-cyanophenyl)formamide **2g** (0.08 g; 0.55 mmol; 33%). The solid that precipitated from the mother liquor was a mixture of product **2g** and 2-(4-oxoquinazolin-3(4*H*)-yl)benzonitrile in a 1.3:1 molar ratio, by ^{1}H NMR.

Synthesis of 1-(2-cyanophenyl)-3-phenylurea (2h)



Phenylisocyanate (0.33 g; 2.76 mmol; 300 µl; 1.1 equiv) was added to a yellow solution of anthranilonitrile **1a** (0.30 g; 2.51 mmol) in acetonitrile (1 ml), under nitrogen atmosphere and the mixture was stirred at room temperature. After 2 h, the yellow solution was kept at -18 ºC overnight. The solid precipitate (0.03 g) was filtered and washed with acetonitrile. A second crop (0.29 g) was isolated from the mother liquor upon addition of acetonitrile. The two crops were combined as they were pure by TLC and were identified as 1-(2-cyanophenyl)-3-phenylurea **2h** (0.32 g; 1.33 mmol; 53%).

Reaction of 2a and 4-methoxyaniline leading to *N*-(4-methoxyphenyl)-2-methylquinazolin-4-amine (3a) (lit.[3])

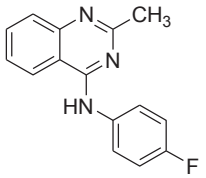


Method A: 4-Methoxyaniline (0.06 g; 0.47 mmol; 1.1 equiv) and TFA (1 equiv; 35 µl) were added to a solution of *N*-(2-cyanophenyl)acetamide **2a** (0.07 g; 0.43 mmol) in ethanol (5 ml). The brown solution was refluxed for 46 h. The solution was kept at -18 ºC and after 2.5 days the yellow solid precipitate was filtered and washed with diethyl ether. The product was identified as the trifluoroacetate salt of *N*-(4-methoxyphenyl)-2-methylquinazolin-4-amine **3a** (0.09 g; 0.24 mmol; 56%). Removal of the solvent from the mother liquor led to a mixture of the starting material **2a** and product **3a** (1.6:1, molar ratio), identified by ^{1}H NMR.

Method B: A grey suspension of *N*-(2-cyanophenyl)acetamide **2a** (0.07 g; 0.45 mmol) and 4-methoxyaniline (0.07 g; 0.50 mmol; 1.1 equiv) in acetic acid (11.6 equiv; 0.3 ml) was refluxed for 45 min. After cooling, a greenish solid precipitate was filtered and washed with diethyl ether. The product was identified as of *N*-(4-methoxyphenyl)-2-methylquinazolin-4-amine **3a** (0.06 g; 0.23 mmol; 51%).

Method C: A brown suspension of *N*-(2-cyanophenyl)acetamide **2a** (0.05 g; 0.34 mmol) and 4-methoxyaniline (0.05 g; 0.37 mmol; 1.1 equiv) in acetic acid (11.6 equiv; 230 µl) was stirred at 80 ºC, for 14 h. Diethyl ether was added to the cold reaction mixture leading to a off-white solid precipitate. The solid was filtered and washed with diethyl ether. The product was identified as of *N*-(4-methoxyphenyl)-2-methylquinazolin-4-amine **3a** (0.03 g; 0.10 mmol; 29%), by ^{1}H NMR. Removal of the solvent from the mother liquor and addition of water led to the isolation of a second crop of solid. The product was identified as 3-(4-methoxyphenyl)-2-methylquinazolin-4(3*H*)-one **4a** (0.01 g; 0.04 mmol; 10%), by ^{1}H NMR.

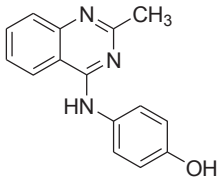
Reaction of 2a and 4-fluoroaniline leading to *N*-(4-fluorophenyl)-2-methylquinazolin-4-amine (3b)



Method A: 4-Fluoroaniline (0.08 g; 0.70 mmol; 67 µl; 1.1 equiv) and TFA (1 equiv; 35 µl) were added to a yellow solution of *N*-(2-cyanophenyl)acetamide **2a** (0.10 g; 0.64 mmol) in ethanol (2 ml). The reaction mixture was refluxed for 9 h. The solution was kept at -18 ºC overnight (16 h) and the yellow solid precipitate was filtered and washed with diethyl ether. The product was identified as the trifluoroacetate salt of *N*-(4-fluorophenyl)-2-methylquinazolin-4-amine **3b** (0.15 g; 0.41 mmol; 64%).

Method B: A yellow solution of N-(2-cyanophenyl)acetamide **2a** (0.07 g; 0.44 mmol) and 4-fluoroaniline (0.05 g; 0.48 mmol; 46 µl; 1.1 equiv) in acetic acid (11.6 equiv; 0.3 ml) was refluxed for 2 h. A saturated aqueous solution of $NaHCO_3$ was added to the reaction mixture. The emulsion was extracted with dichlorometane (3x 5 ml). The organic layer was dried and concentrated in the rotary evaporator. Addition of diethyl ether led to a yellow solid precipitate that was filtered and washed with diethyl ether. The product was identified as *N*-(4-fluorophenyl)-2-methylquinazolin-4-amine **3b** (0.02 g; 0.08 mmol; 18%). The solid that precipitated from the mother liquor was a mixture of starting material **2a** (45%), product **3b** (14%), **4c** (16%) and a compound tentatively identified as quinazoline **4** (R_3= 4-FC_6H_4, 25%) identified by ^{1}H NMR.

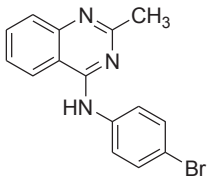
Reaction of 2a and 4-aminophenol leading to 4-(2-methylquinazolin-4-ylamino)phenol (3c)



Method A: 4-Aminophenol (0.05 g; 0.45 mmol; 1.1 equiv) and TFA (1 equiv; 25 µl) were added to a solution of *N*-(2-cyanophenyl)acetamide **2a** (0.07 g; 0.41 mmol) in ethanol (2 ml). The brown solution was refluxed for 17 h. The solution was kept at -18 ºC overnight (17 h) and the yellow solid precipitate was filtered and washed with diethyl ether. The product was identified as the trifluoroacetate salt of 4-(2-methylquinazolin-4-ylamino)phenol **3c** (0.10 g; 0.27 mmol; 66%).

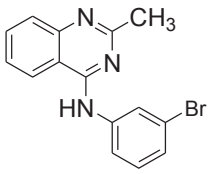
Method B: A brown solution of *N*-(2-cyanophenyl)acetamide **2a** (0.05 g; 0.32 mmol) and 4-aminophenol (0.04 g; 0.35 mmol; 1.1 equiv) in acetic acid (11.6 equiv; 220 µl) was stirred at 60 ºC for 21 h. Addition of water led to a dark solid suspension that was filtered and washed with water (0.02 g). The solid was identified by ^{1}H NMR as a mixture of **3c** and **4b**, in a 1:6.1 molar ratio, slightly contaminated with other unidentified side-products. Removal of the solvent from the mother liquor and addition of water led to the isolation of a second crop of greenish solid (0.04 g). The product was identified as 4-(2-methylquinazolin-4-ylamino)phenol **3c** (0.04 g; 0.16 mmol; 50%).

Reaction of 2a and 4-bromoaniline leading to *N*-(4-bromophenyl)-2-methylquinazolin-4-amine (3d)



4-Bromoaniline (0.13 g; 0.77 mmol; 1.1 equiv) and TFA (1 equiv; 25 µl) were added to a yellow solution of *N*-(2-cyanophenyl)acetamide **2a** (0.11 g; 0.70 mmol) in ethanol (2 ml). The solution was refluxed for 9.5 h. The solution was kept at -18 ºC overnight (16 h) and the yellow precipitate was filtered and washed with diethyl ether. The product was identified as the trifluoroacetate salt of *N*-(4-bromophenyl)-2-methylquinazolin-4-amine **3d** (0.14 g; 0.33 mmol; 47%).

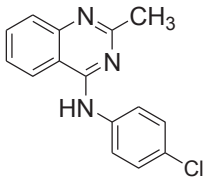
Reaction of 2a and 3-bromoaniline leading to *N*-(3-bromophenyl)-2-methylquinazolin-4-amine (3e)



Method A: 3-Bromoaniline (0.29 g; 1.70 mmol; 185 µl; 1.2 equiv) and TFA (1 equiv; 109 µl) were added to a colorless solution of *N*-(2-cyanophenyl)acetamide **2a** (0.22 g; 1.42 mmol) in ethanol (3 ml). The reaction mixture was refluxed and after 22 h, the yellow solid that precipitated was filtered and washed with diethyl ether. The product was identified as the trifluoroacetate salt of *N*-(3-bromophenyl)-2-methylquinazolin-4-amine **3e** (0.07 g; 0.16 mmol; 11%). The solid that precipitated from the mother liquor was identified as the starting material **2a** (13%), by IR.

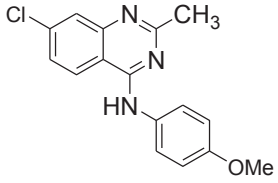
Method B: A yellow solution of *N*-(2-cyanophenyl)acetamide **2a** (0.18 g; 1.17 mmol) and 3-bromoaniline (0.24 g; 1.40 mmol; 152 µl; 1.2 equiv) in acetic acid (11.6 equiv; 0.8 ml) was refluxed for 2.5 h. Addition of water led to a yellow precipitate that was filtered and washed with water. The product was identified as *N*-(3-bromophenyl)-2-methylquinazolin-4-amine **3e** (0.07g; 0.24 mmol; 21%).

Reaction of 2a and 4-chloroaniline leading to *N*-(4-chlorophenyl)-2-methylquinazolin-4-amine (3f)



A grey solution of *N*-(2-cyanophenyl)acetamide **2a** (0.11 g; 0.67 mmol) and 4-chloroaniline (0.09 g; 0.74 mmol; 1.1 equiv) in acetic acid (11.6 equiv; 0.5 ml) was refluxed for 2 h. Addition of water led to a yellow solid that was filtered and washed with water. The solid (0.09 g) was identified as a complex mixture, by ^{1}H NMR. A second crop (0.05 g) was isolated from the mother liquor upon addition of $NaHCO_3$ (0.36 g) and was filtered and washed with water. The product was identified as *N*-(4-chlorophenyl)-2-methylquinazolin-4-amine **3f** (0.05g; 0.19 mmol; 28%).

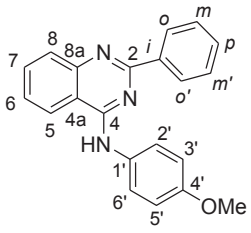
Reaction of 2b and 4-methoxyaniline leading to 7-chloro-*N*-(4-methoxyphenyl)-2-methylquinazolin-4-amine (3g)



Method A: 4-Methoxyaniline (0.18 g; 1.46 mmol; 2 equiv) was added to a white suspension of *N*-(5-chloro-2-cyanophenyl)acetamide **2b** (0.14 g; 0.73 mmol) in ethanol (5 ml), leading to a brown suspension. TFA (1 equiv; 56 µl) was added and the suspension was refluxed leading immediately to a brown solution. After 72 h, the yellow solid precipitate was filtered and washed with diethyl ether and dichloromethane, leading to a pure product identified as the trifluoroacetate salt of 7-chloro-*N*-(4-methoxyphenyl)-2-methylquinazolin-4-amine **3g** (0.07 g; 0.17 mmol; 23%).

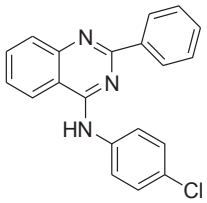
Method B: A beige suspension of *N*-(5-chloro-2-cyanophenyl)acetamide **2b** (0.07 g; 0.37 mmol) and 4-methoxyaniline (0.05 g; 0.41 mmol; 1.1 equiv) in acetic acid (11.6 equiv; 0.3 ml) was refluxed for 2 h. Addition of water led to a beige precipitate that was filtered and washed with water and ethanol (1:1). The product was identified as 7-chloro-*N*-(4-methoxyphenyl)-2-methylquinazolin-4-amine **3g** (0.02 g; 0.07 mmol; 19%). The solid that precipitated from the mother liquor was identified as a mixture of product **3g** and a compound tentatively identified as **4** (R_3= 4-OMeC_6H_4) in a 1.7:1 molar ratio, by ^{1}H NMR.

Reaction of 2c and 4-methoxyaniline leading to *N*-(4-methoxyphenyl)-2-phenylquinazolin-4-amine (3h)



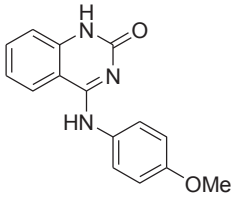
4-Methoxyaniline (0.04 g; 0.35 mmol; 1.1 equiv) was added to a suspension of *N*-(2-cyanophenyl)benzamide **2c** (0.07 g; 0.31 mmol) in ethanol (2 ml) leading to an orange solution. TFA (1 equiv; 25 µl) was added and the solution was refluxed for 13.5 h. The yellow precipitate was filtered and washed with ethanol. The product was identified as the trifluoroacetate salt of *N*-(4-methoxyphenyl)-2-phenylquinazolin-4-amine **3h** (0.06 g; 0.14 mmol; 45%).

Reaction of 2c and 4-chloroaniline leading to *N*-(4-chlorophenyl)-2-phenylquinazolin-4-amine (3i)



4-Chloroaniline (0.05 g; 0.41 mmol; 1.2 equiv) was added to a yellow solution of *N*-(2-cyanophenyl)benzamide **2c** (0.08 g; 0.34 mmol) in ethanol (10 ml). TFA (1 equiv; 30 µl) was added and the solution was refluxed for 50 h. The solvent was removed in the rotary evaporator and diethyl ether was added to the oil leading to a solid precipitate. The yellow solid was filtered and washed with petroleum ether. The product was identified as the trifluoroacetate salt of *N*-(4-chlorophenyl)-2-phenylquinazolin-4-amine **3i** (0.02g; 0.06 mmol; 18%). The green solid (0.12 g) that precipitated from the mother liquor was mainly the amine contaminated with traces of starting material **2c** and other unidentified by-products.

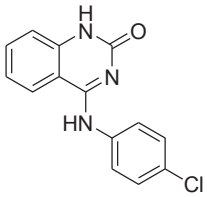
Reaction of 2h and 4-methoxyaniline leading to 4-(4-methoxyphenylamino)quinazolin-2(1*H*)-one (3j)



Method A: 4-Methoxyaniline (0.07 g; 0.51 mmol; 1.2 equiv) was added a solution of 1-(2-cyanophenyl)-3-phenylurea **2h** (0.11 g; 0.46 mmol) in ethanol (10 ml), leading to an orange solution. TFA (1 equiv; 36 µl) was added and the solution was refluxed for 72 h. After 18 h a deep-red solution was obtained. The solution was kept at -18 ºC for 1 day and the white solid precipitate was filtered and washed with *n*-hexane. The product was identified as 4-(4-methoxyphenylamino)quinazolin-2(1*H*)-one **3j** (0.05 g; 0.19 mmol; 41%).

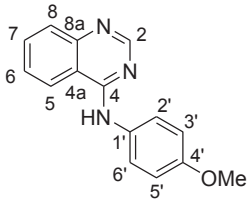
Method B: 4-Methoxyaniline (0.08 g; 0.68 mmol; 1.1 equiv) was added to a solution of ethyl (2-cyanophenyl)carbamate **2e** (0.12 g; 0.62 mmol) in ethanol (5 ml), leading to an orange solution. TFA (1 equiv; 48 µl) was added and the solution was refluxed for 97 h. The solution was kept at -18 ºC for 1 day and the white solid precipitate was filtered and washed with diethyl ether. The product was identified as the trifluoroacetate salt of 4-(4-methoxyphenylamino)quinazolin-2(1*H*)-one **3j** (0.01 g; 0.04 mmol; 7%). The solid that precipitated from the mother liquor was the starting material **2e** (13%). The aromatic amine was recovered as the third crop (7%). The fourth crop was a mixture of starting material **2e** and amine (1.5:1), by ^{1}H NMR.

Reaction of 2h and 4-chloroaniline leading to 4-(4-chlorophenylamino)quinazolin-2(1*H*)-one (3k)



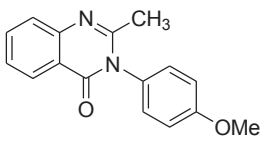
4-Chloroaniline (0.06 g; 0.45 mmol; 1.1 equiv) was added to a solution of 1-(2-cyanophenyl)-3-phenylurea **2h** (0.10 g; 0.41 mmol) in ethanol (10 ml), leading to a yellow solution. TFA (1 equiv; 32 µl) was added and the solution was refluxed for 96 h. The solution was kept at -18 ºC for 5 h and the white solid precipitate was filtered and washed with *n*-hexane. The product was identified as 4-(4-chlorophenylamino)quinazolin-2(1*H*)-one **3k** (0.02g; 0.07 mmol; 17%).

Reaction of 2g and 4-methoxyaniline leading to *N*-(4-methoxyphenyl)quinazolin-4-amine (3l)



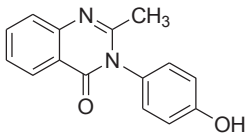
4-Methoxyaniline (0.11 g; 0.86 mmol; 1.1 equiv) and concentrated HCl (0.4 equiv; 25 µl) were added to a white suspension of *N*-(2-cyanophenyl)formamide **2g** (0.11 g; 0.78 mmol) in ethanol (3 ml), leading to a yellow solution. The reaction mixture was refluxed and after 12 h, the yellow solid that precipitated was filtered and washed with diethyl ether. The product was identified as *N*-(4-methoxyphenyl)quinazolin-4-amine **3l** (0.09 g; 0.35 mmol; 41%).

Reaction of 2a and 4-methoxyaniline leading to 3-(4-methoxyphenyl)-2-methylquinazolin-4(3*H*)-one (4a)



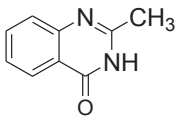
A brown solution of *N*-(2-cyanophenyl)acetamide **2a** (0.07 g; 0.46 mmol) and 4-methoxyaniline (0.06 g; 0.51 mmol; 1.1 equiv) in acetic acid (11.6 equiv; 0.3 ml) was refluxed for 2 h. After cooling, water was added to the reaction mixture and the yellow solid precipitate was filtered and washed with water. The product was identified as 3-(4-methoxyphenyl)-2-methylquinazolin-4(3*H*)-one **4a** (0.01 g; 0.04 mmol; 9 %). The mother liquor was mainly a mixture of compound **3a** and acetate salt of 4-methoxyaniline (1:1 M ratio), by ^{1}H NMR.

Reaction of 2a and 4-aminophenol leading to 3-(4-hidroxyphenyl)-2-methylquinazolin-4(3*H*)-one (4b)



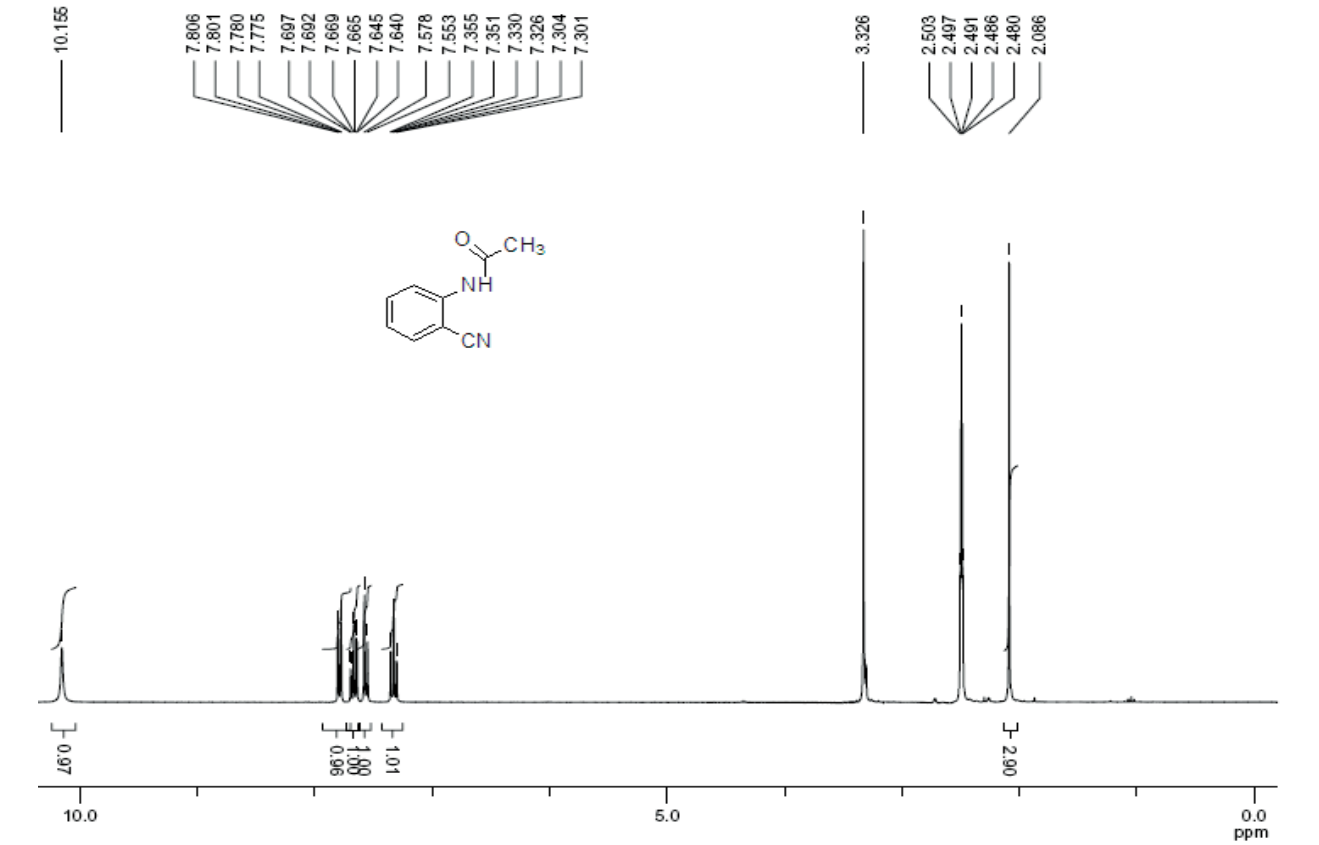
A yellow solution of *N*-(2-cyanophenyl)acetamide **2a** (0.07 g; 0.46 mmol) and 4-aminophenol (0.06 g; 0.51 mmol; 1.1 equiv) in acetic acid (11.6 equiv; 0.3 ml) was refluxed for 2 h. A saturated aqueous solution of $NaHCO_3$ was added to the reaction mixture. The emulsion was extracted with dichlorometane (3x 5 ml). The organic layer was dried and concentrated in the rotary evaporator. Addition of diethyl ether led to a greenish precipitate that was filtered and washed with diethyl ether. The product was identified as 3-(4-hydroxyphenyl)-2-methylquinazolin-4(3H)-one **4b** (0.01 g; 0.04 mmol; 9%).

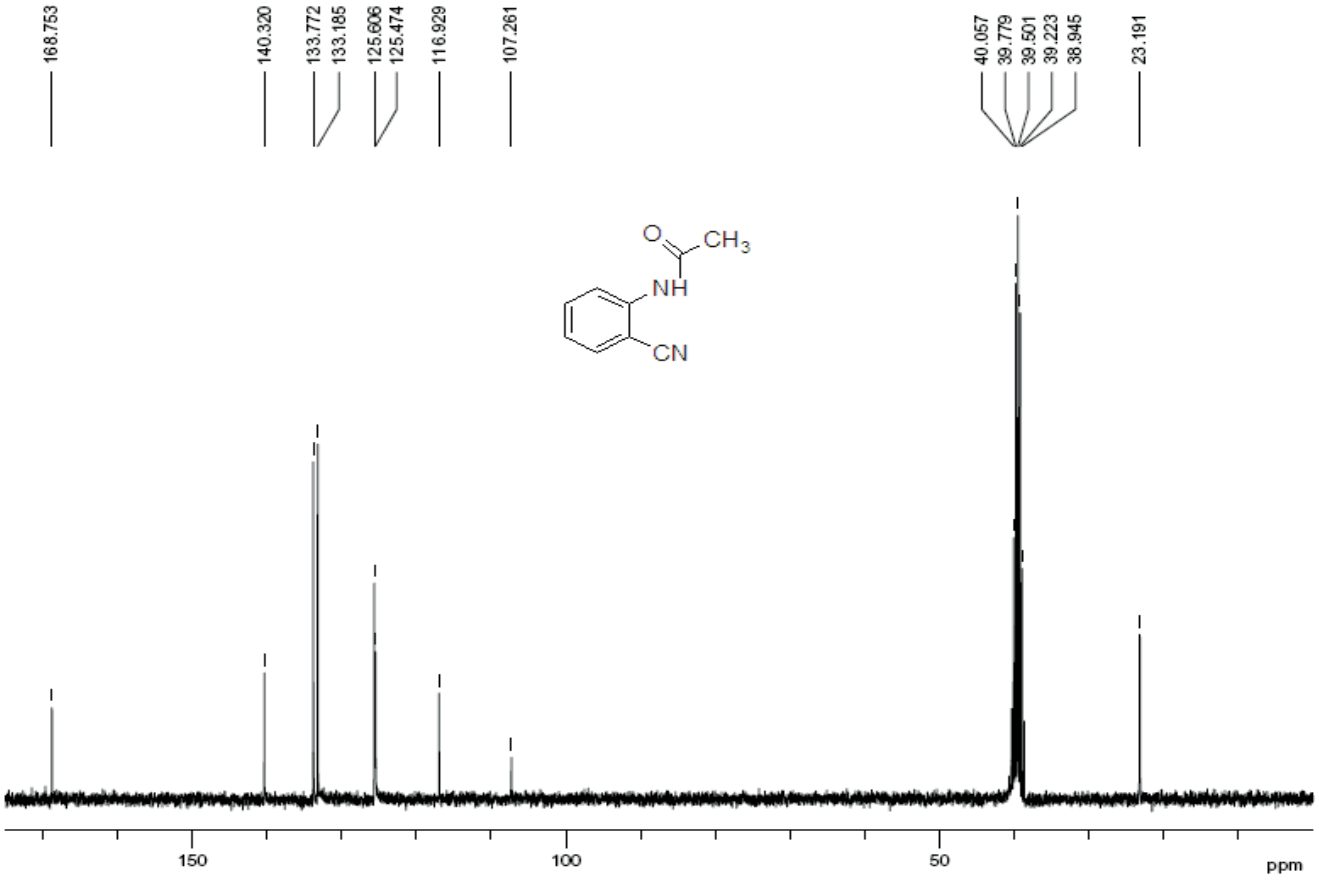
Reaction of 2a and 3-chloroaniline leading to 2-methylquinazolin-4(3*H*)-one (4c)

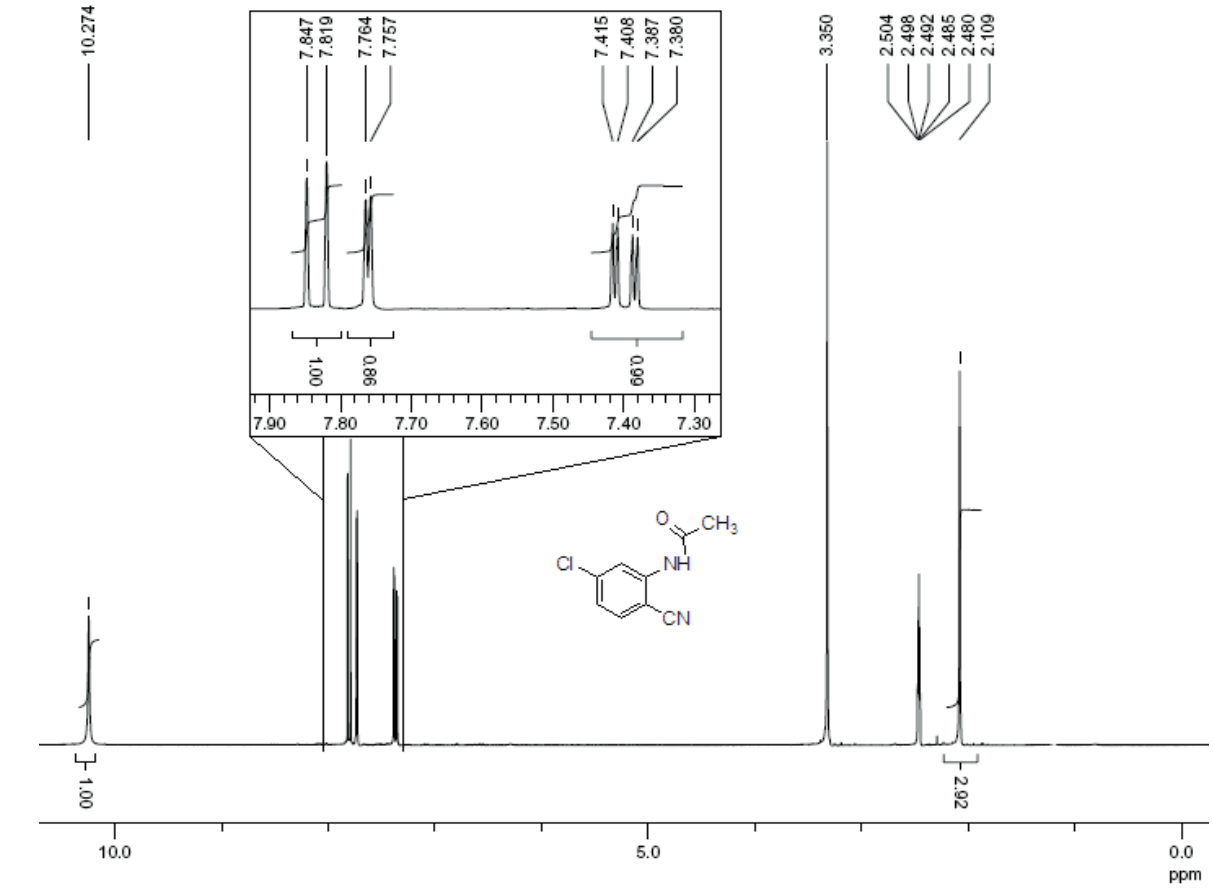


A yellow solution of *N*-(2-cyanophenyl)acetamide **2a** (0.11 g; 0.71 mmol) and 3-chloroaniline (0.10 g; 0.78 mmol; 82 µl; 1.1 equiv) in acetic acid (11.6 equiv; 0.5 ml) was refluxed for 3.5 h. After cooling, water was added to the reaction mixture and the white solid precipitate was filtered and washed with water. The product was identified as 2-methylquinazolin-4(3*H*)-one **4c** (0.06 g; 0.37 mmol; 52 %).

^{1}H and ^{13}C NMR spectra for compounds **2a-h**



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7.764
7.757
7.415
7.408
7.387
7.380
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2.498
2.492
2.485
2.480
2.109
1.00
0.86
0.99
7.90
7.80
7.70
7.60
7.50
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NH
Cl
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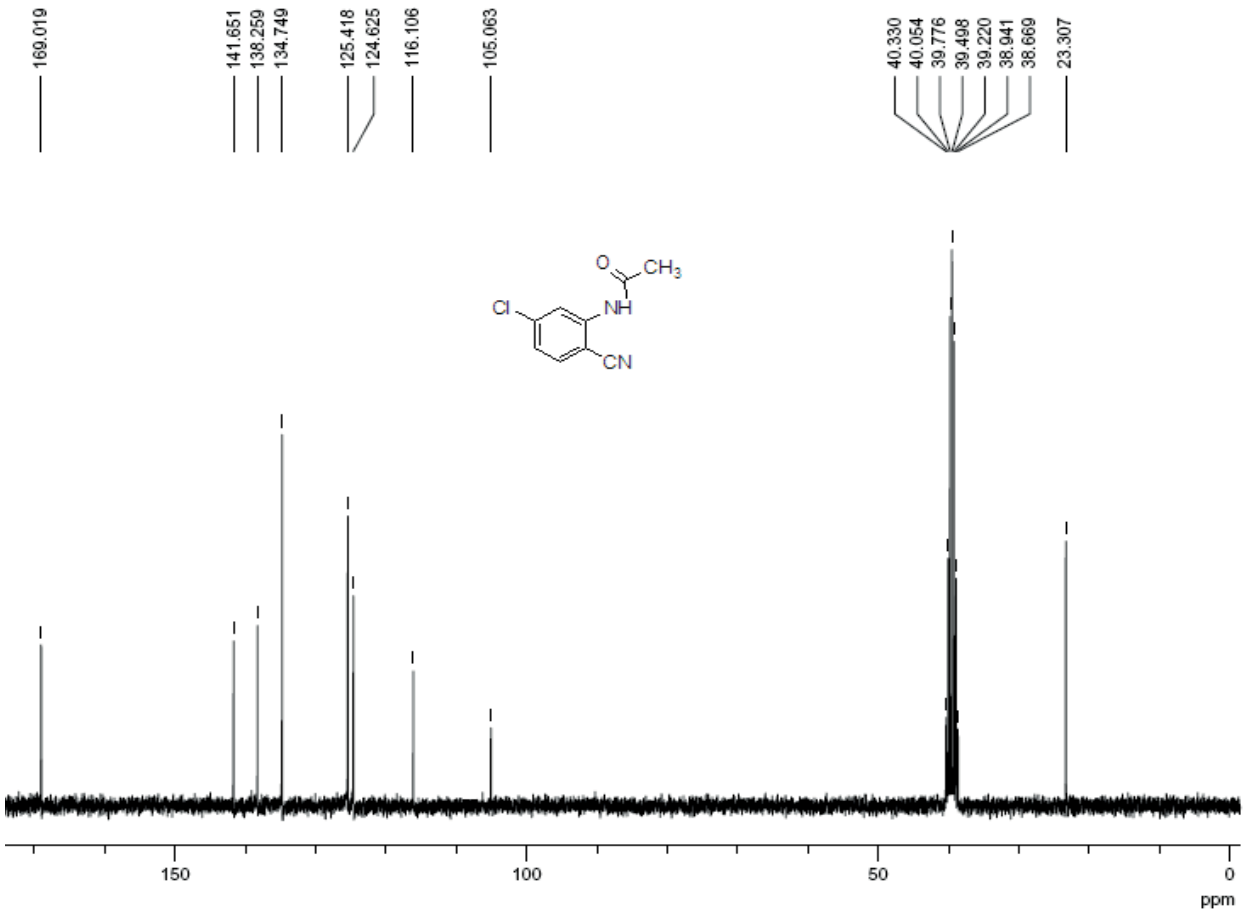
ppm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134.749
125.418
124.625
116.106
105.063
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40.054
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NH
Cl
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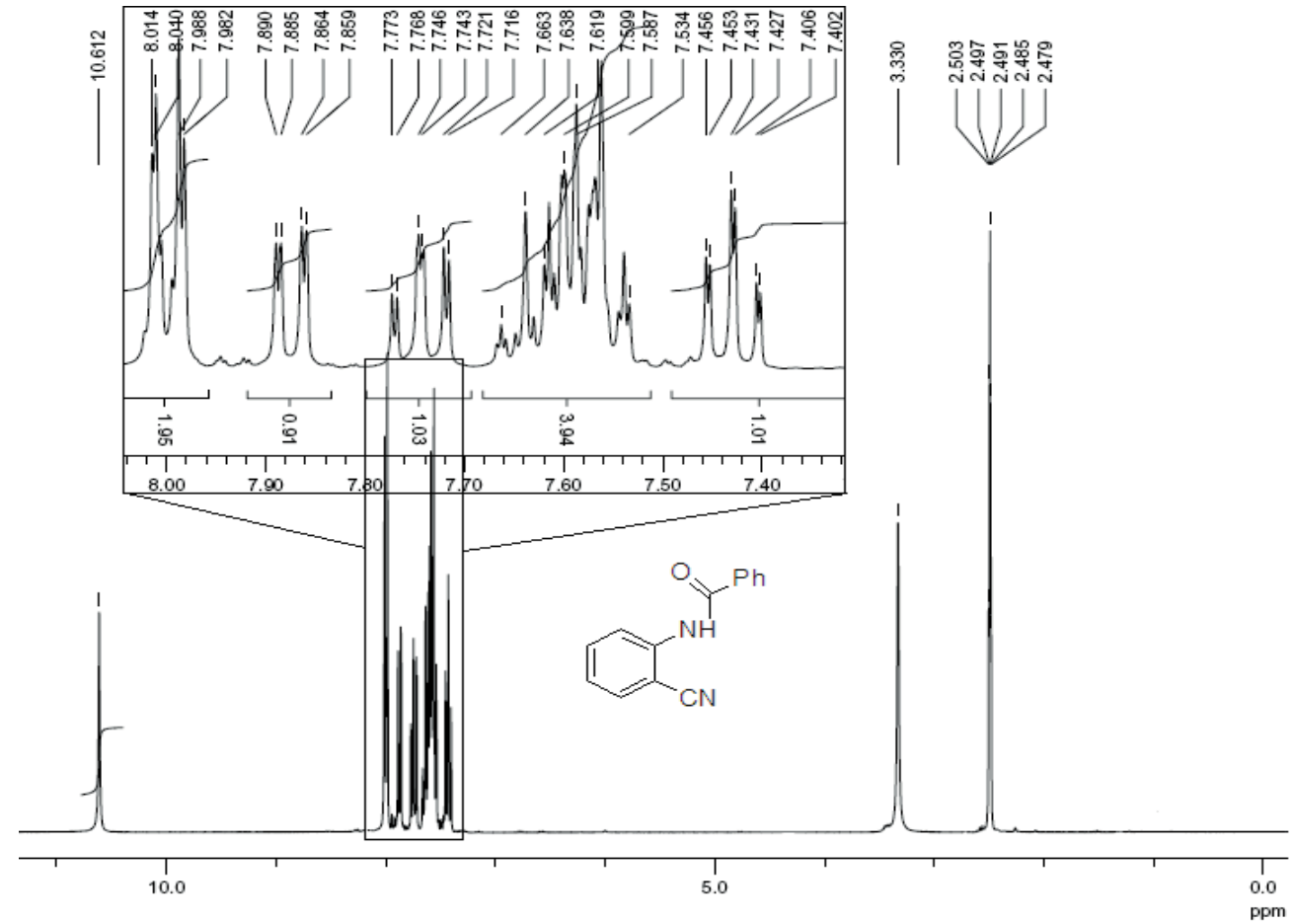
0
ppm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7.982
7.890
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7.864
7.859
7.773
7.768
7.746
7.743
7.721
7.716
7.663
7.638
7.619
7.599
7.587
7.534
7.456
7.453
7.431
7.427
7.406
7.402
3.330
2.503
2.497
2.491
2.485
2.479
1.95
0.91
1.03
3.94
1.01
8.00
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Ph
NH
CN
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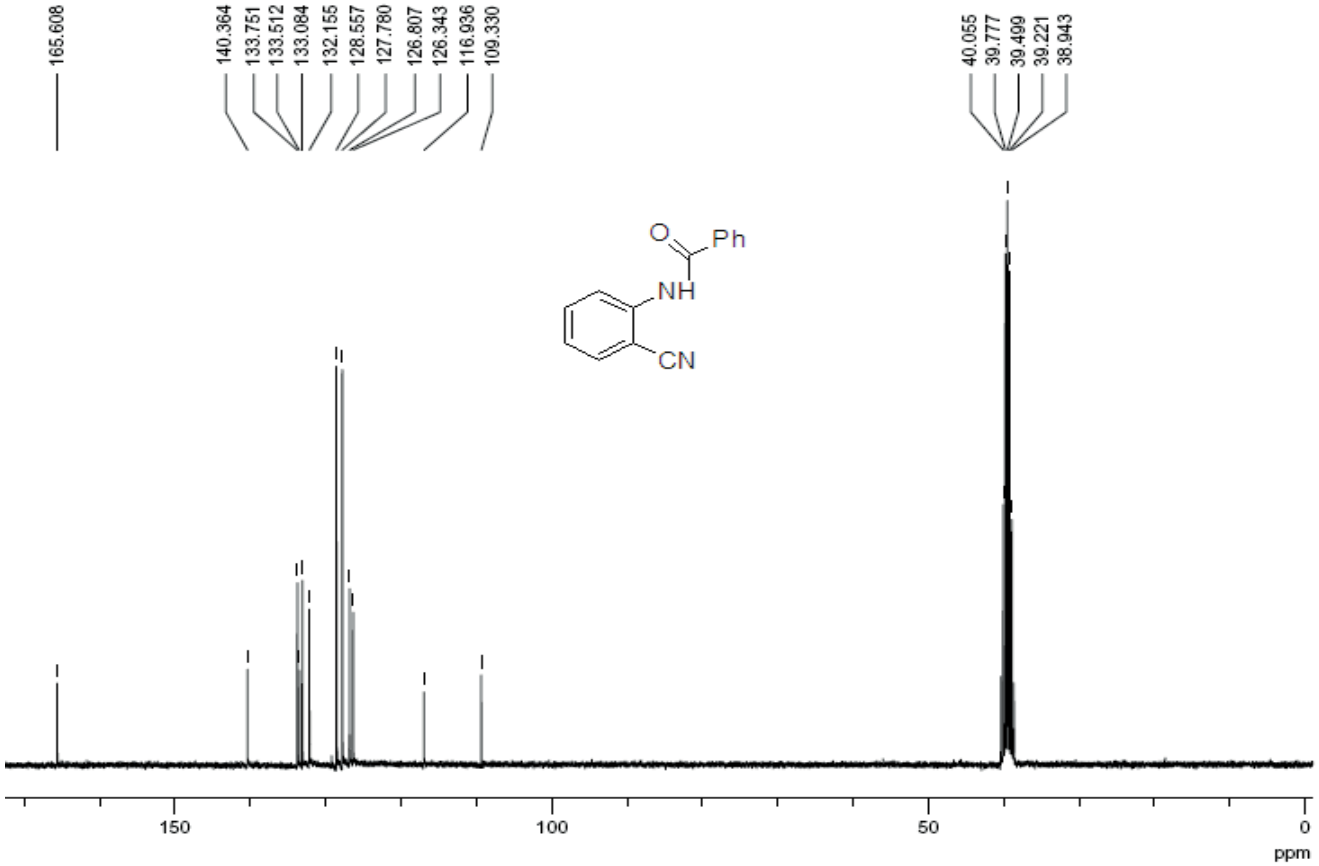
ppm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140.364
133.751
133.512
133.084
132.155
128.557
127.780
126.807
126.343
116.936
109.330
40.055
39.777
39.499
39.221
38.943
O
Ph
NH
CN
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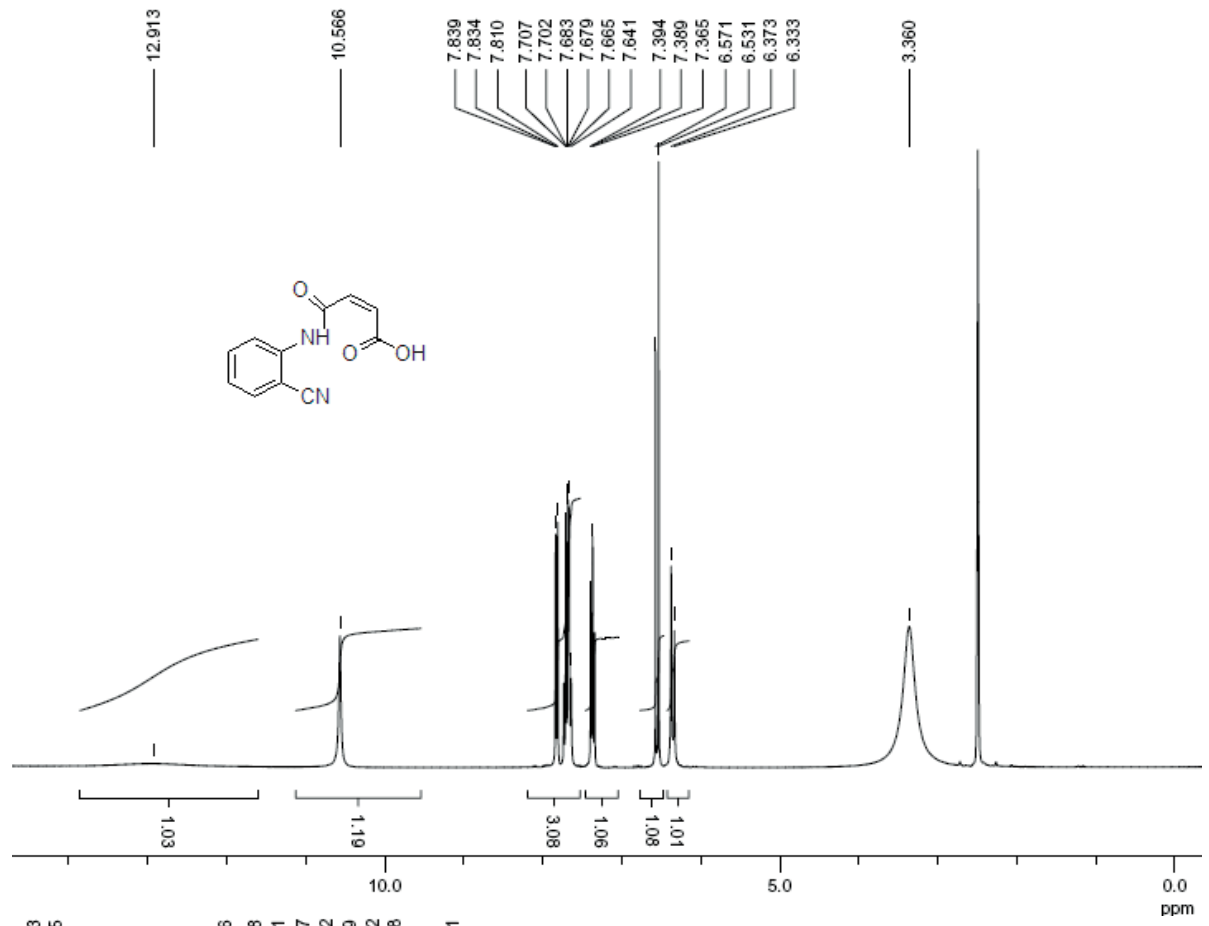
100
50
0
ppm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7.834
7.810
7.707
7.702
7.683
7.679
7.665
7.641
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7.389
7.365
6.571
6.531
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3.360
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1.01
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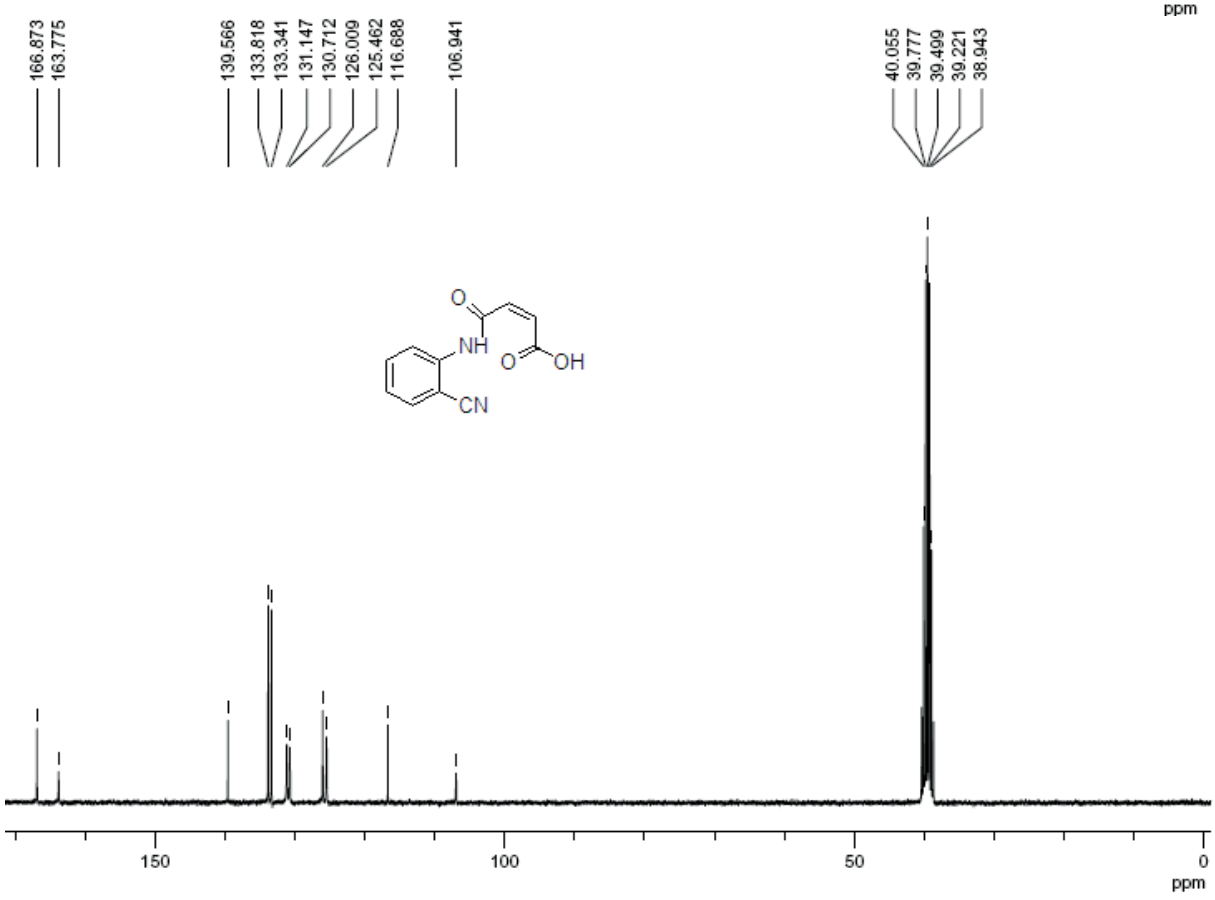
ppm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163.775
139.566
133.818
133.341
131.147
130.712
126.009
125.462
116.688
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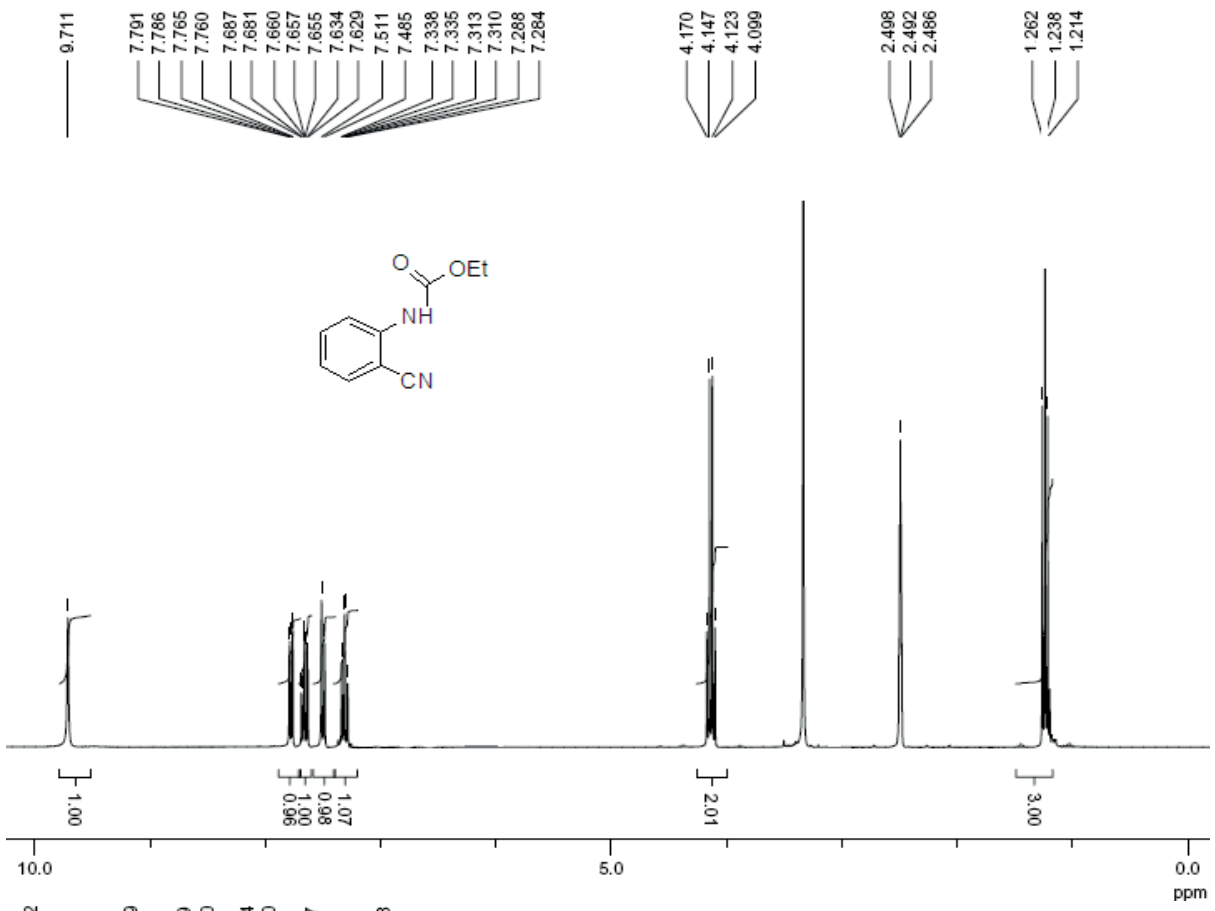
40.055
39.777
39.499
39.221
38.943
O
NH
O
OH
CN
150
100
50
0
ppm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7.765
7.760
7.687
7.681
7.660
7.657
7.655
7.634
7.629
7.511
7.485
7.338
7.335
7.313
7.310
7.288
7.284
4.170
4.147
4.123
4.099
2.498
2.492
2.486
1.262
1.238
1.214
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1.00
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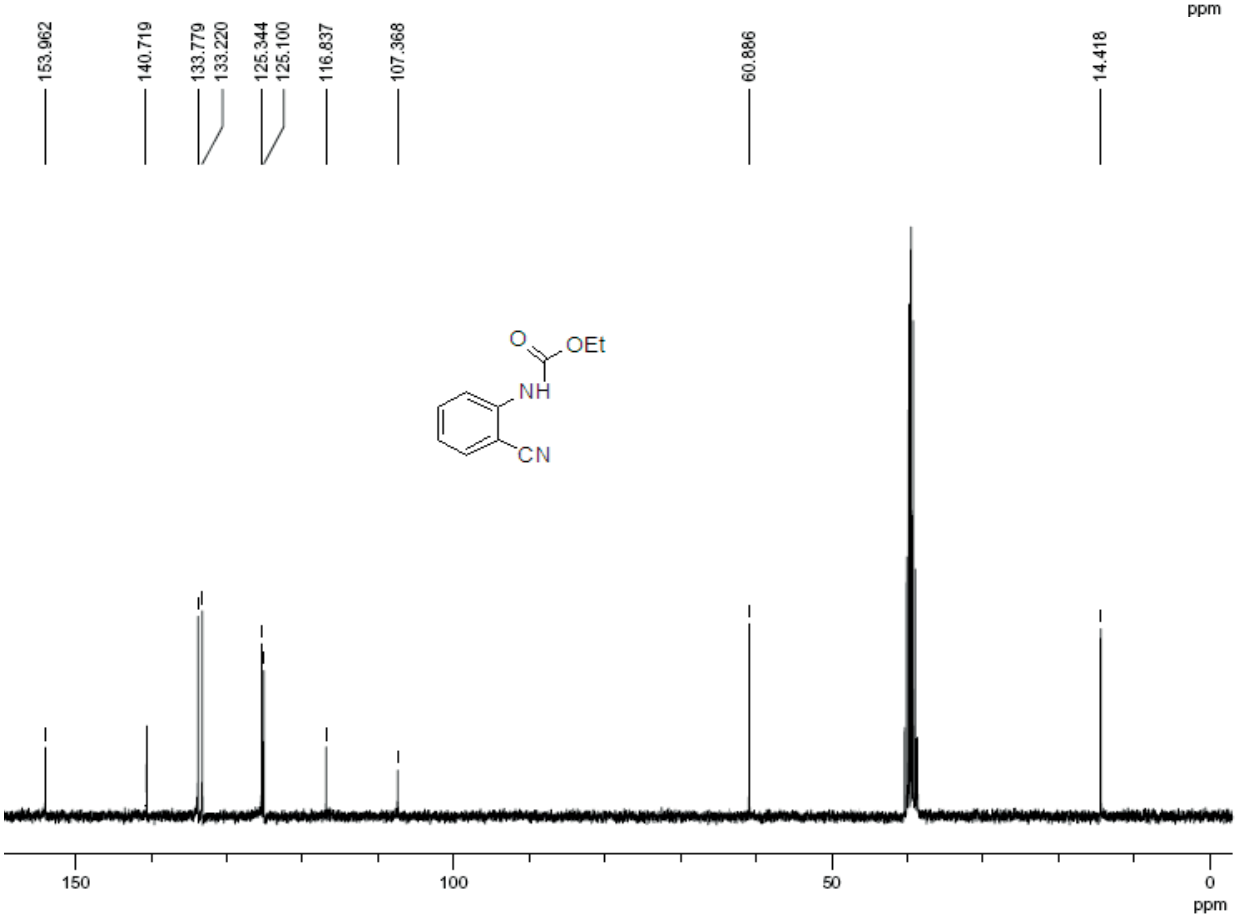
ppm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OEt
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CN
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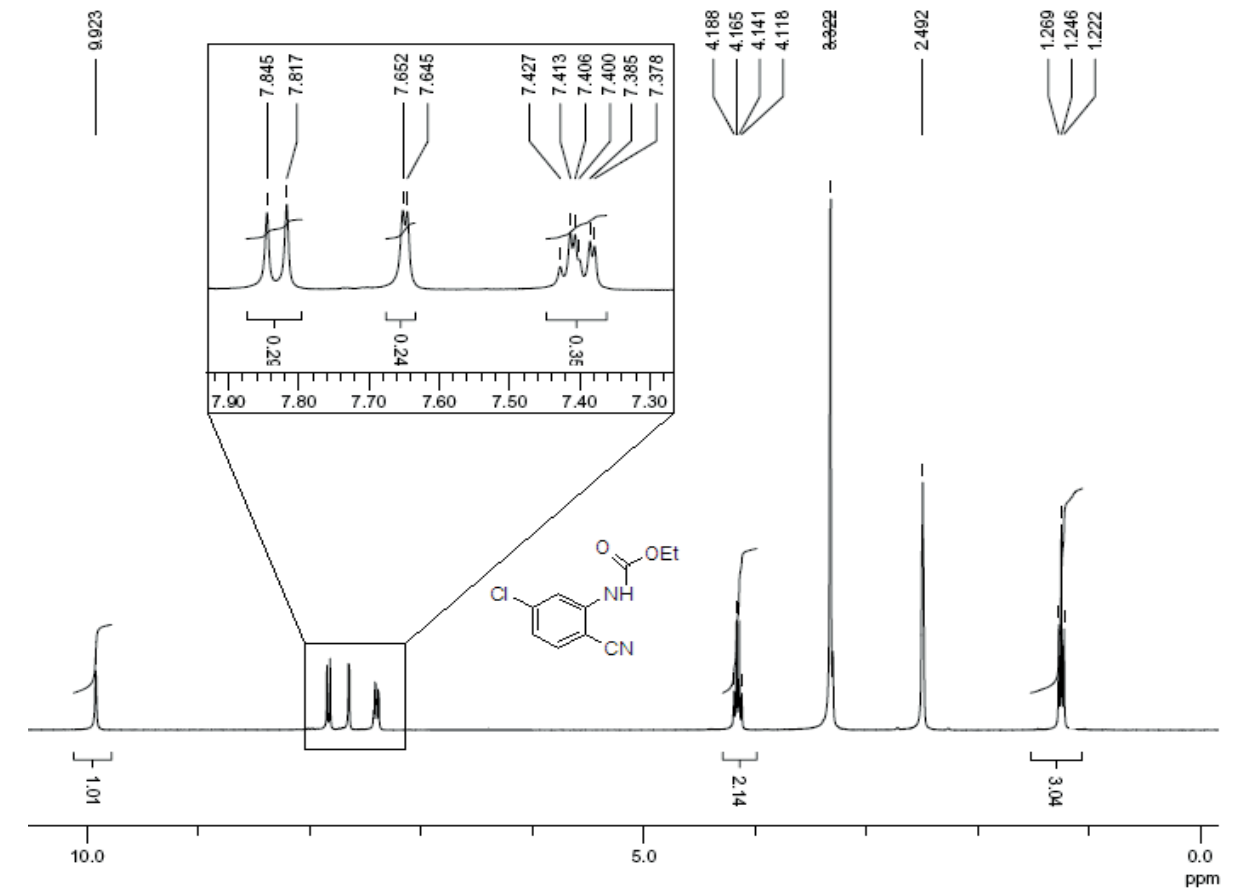
100
50
0
ppm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7.406
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4.165
4.141
4.118
2.492
1.269
1.246
1.222
0.25
0.24
0.36
7.90
7.80
7.70
7.60
7.50
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NH
Cl
CN
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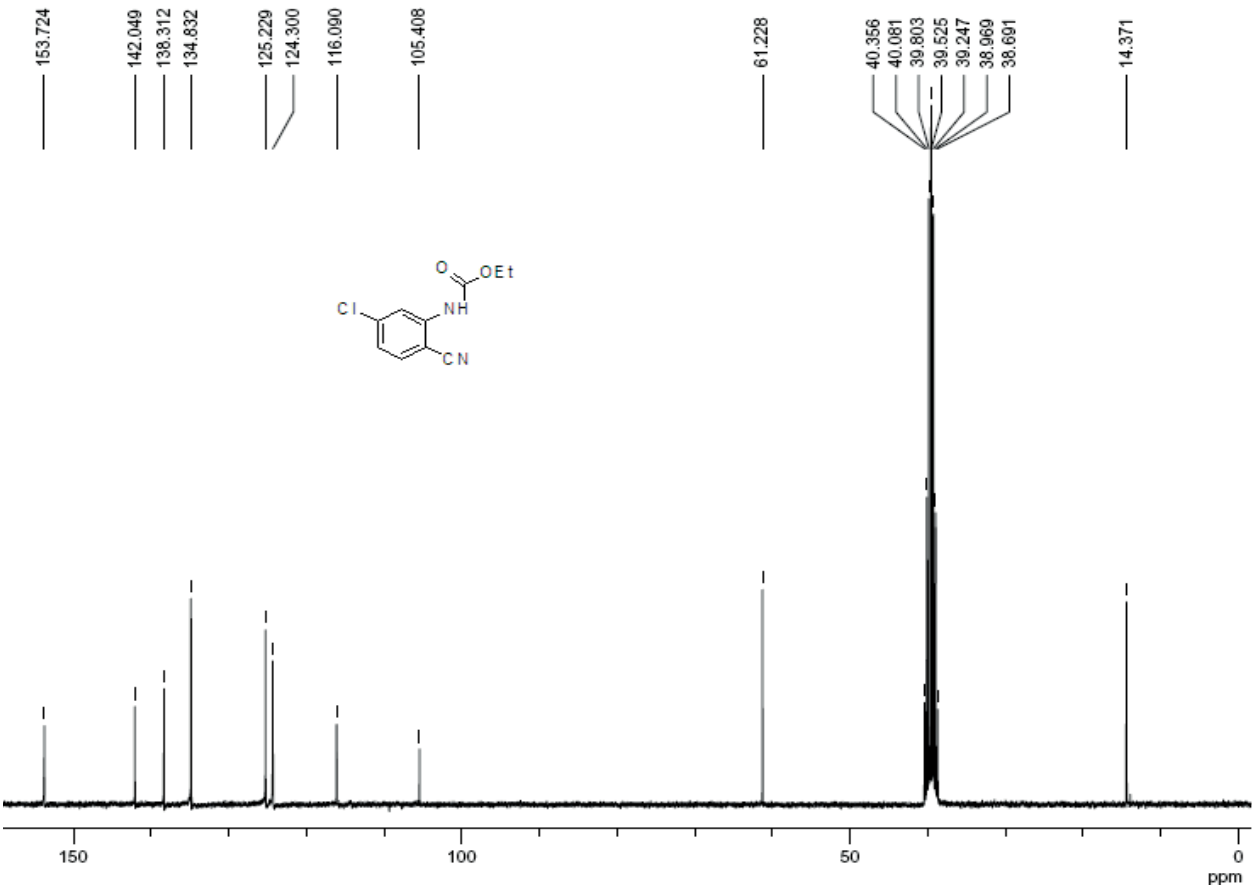
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105.408
61.228
40.356
40.081
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14.371
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Cl
CN
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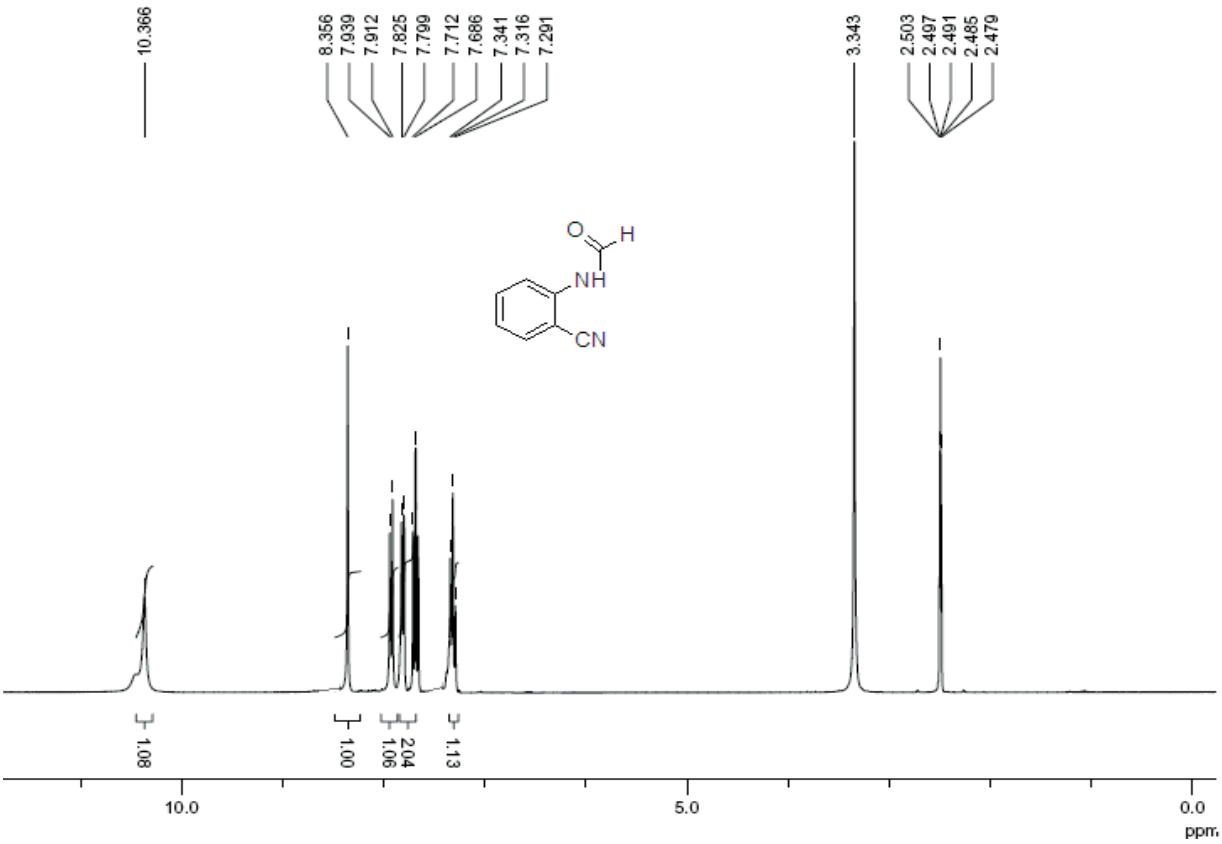
0
ppm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2.491
2.485
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CN
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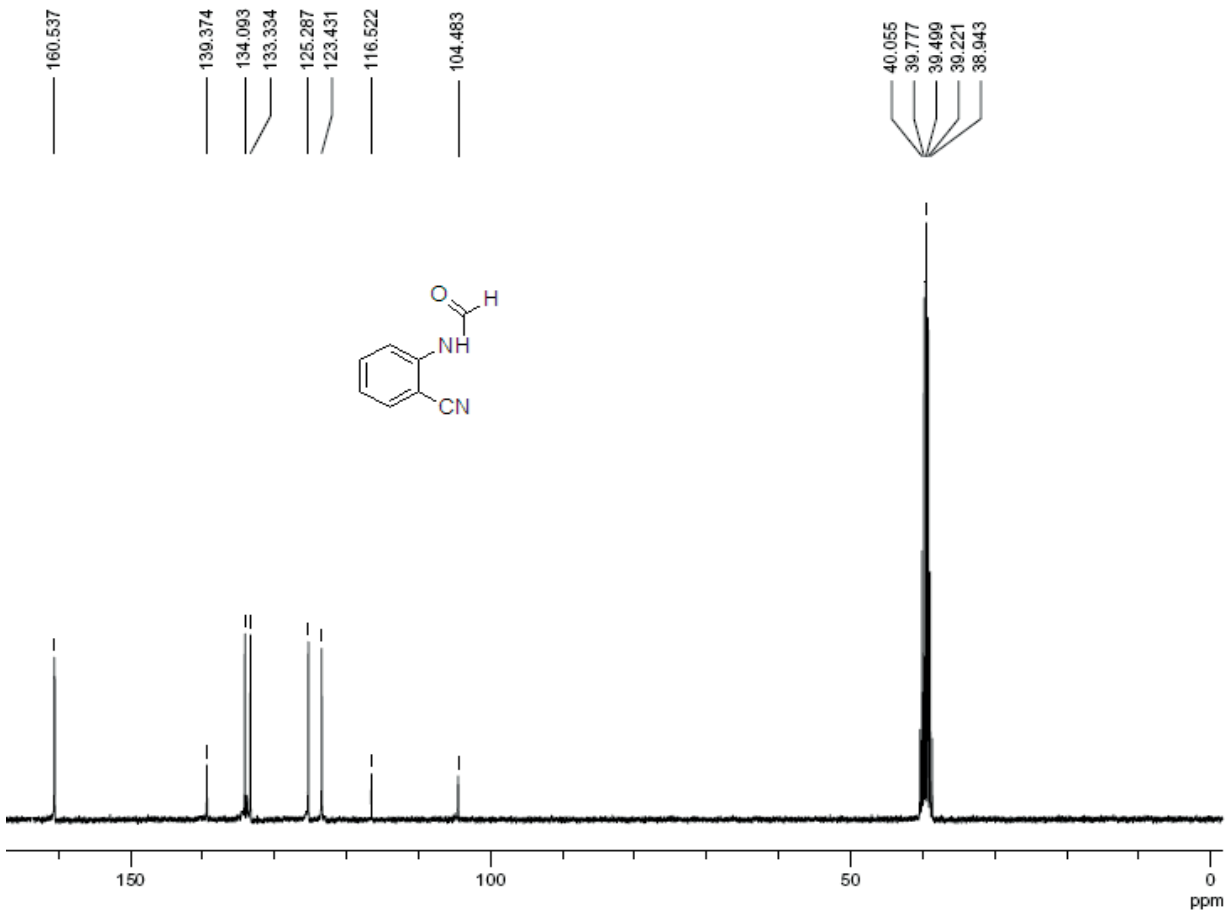
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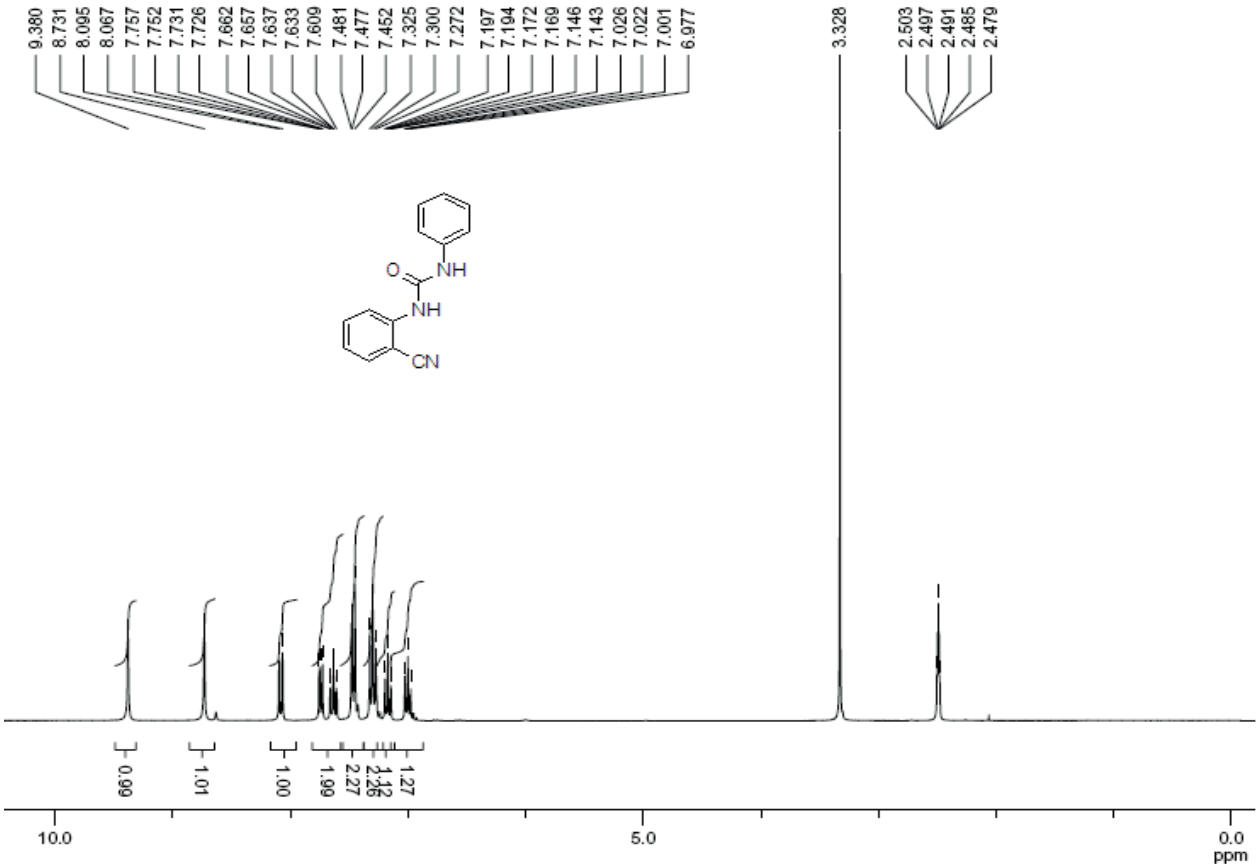
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7.633
7.609
7.481
7.477
7.452
7.325
7.300
7.272
7.197
7.194
7.172
7.169
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7.143
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7.022
7.001
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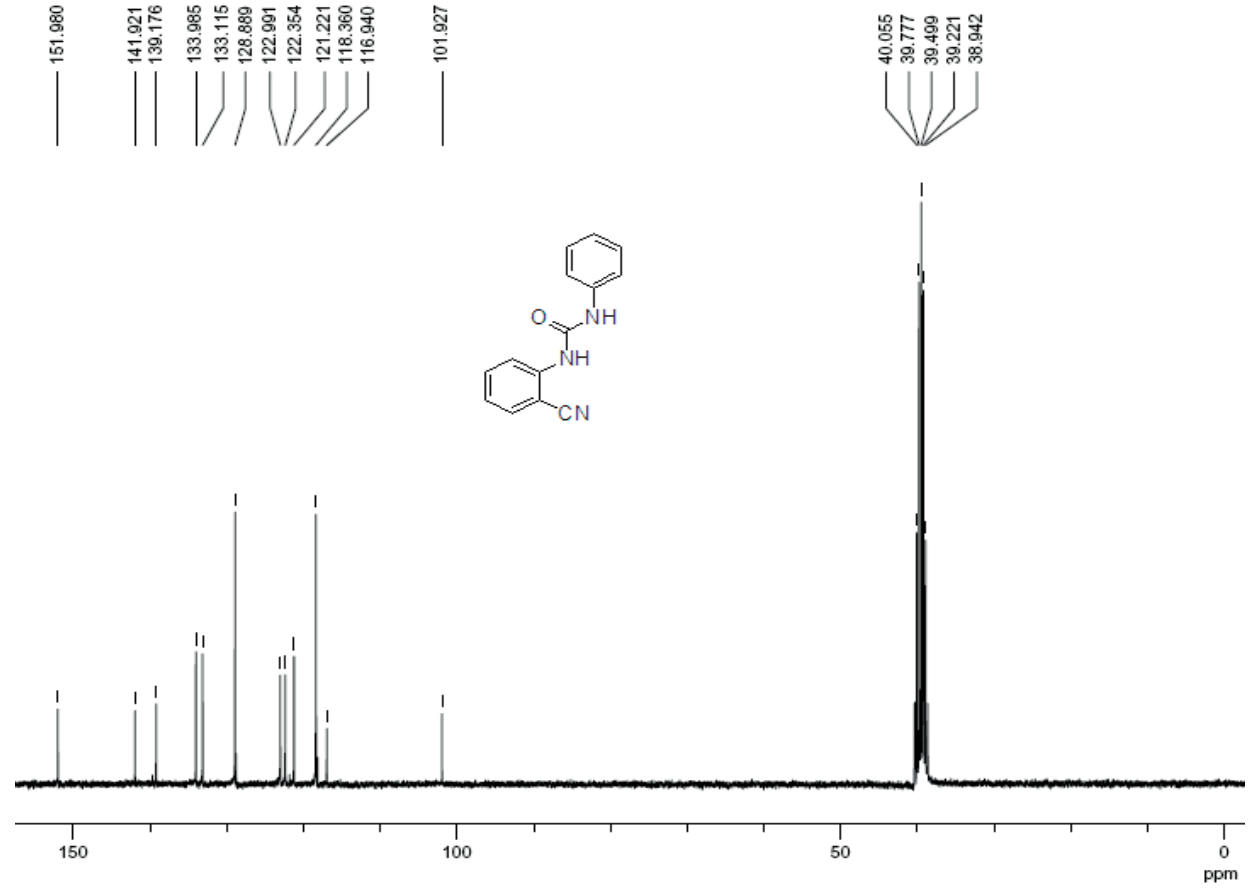
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39.777
39.499
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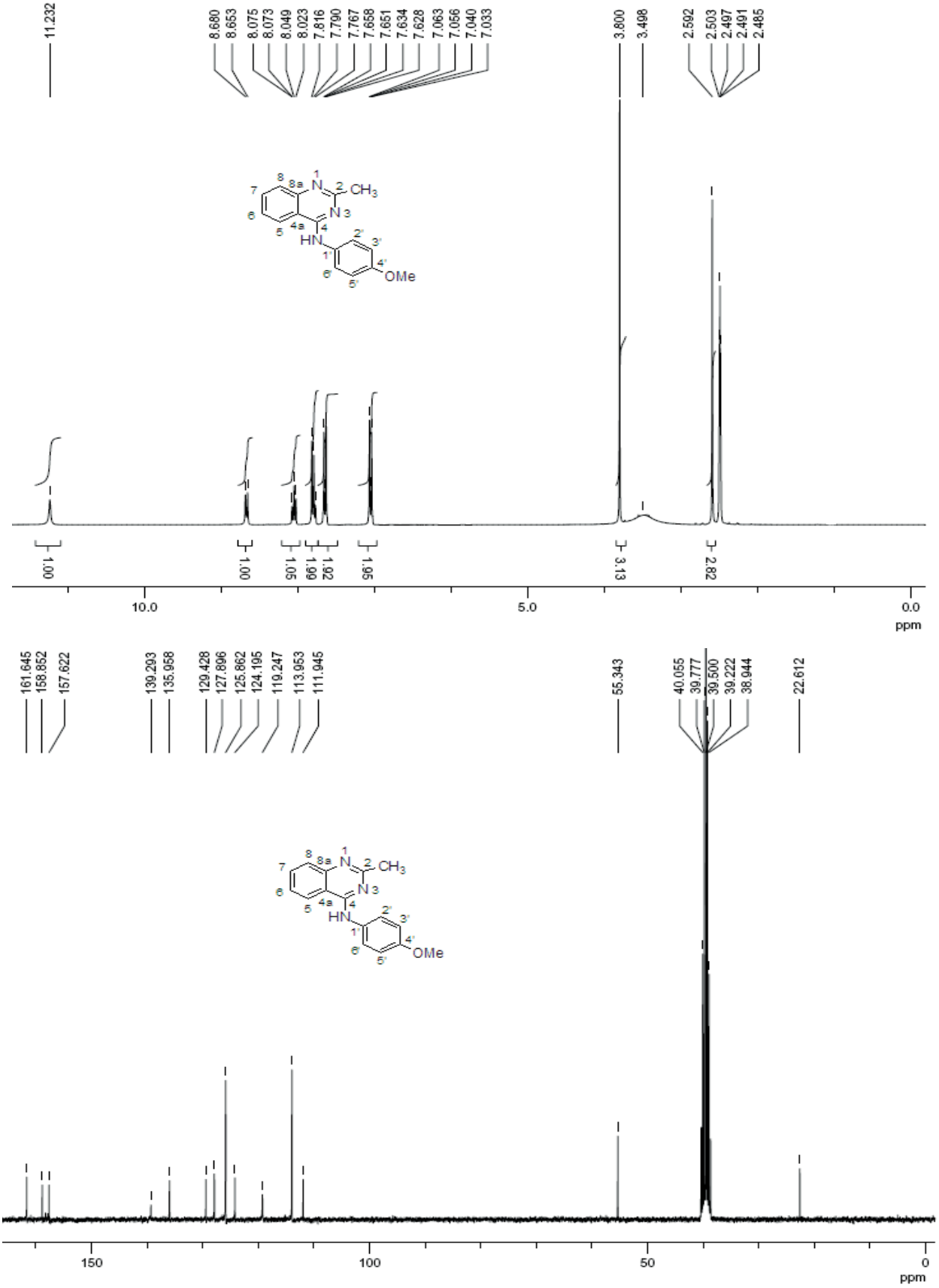
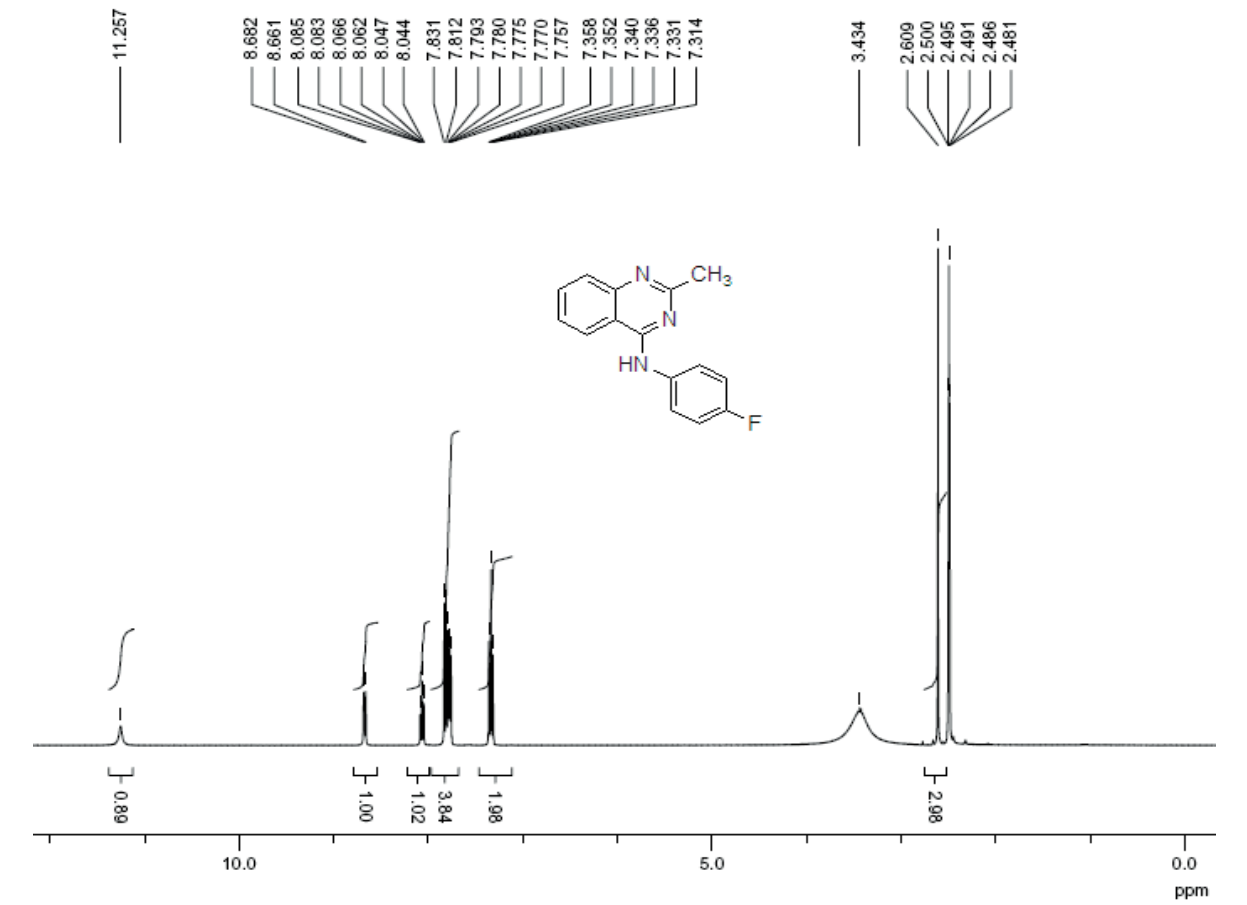
^{1}H and ^{13}C NMR spectra for compounds **3a-l**

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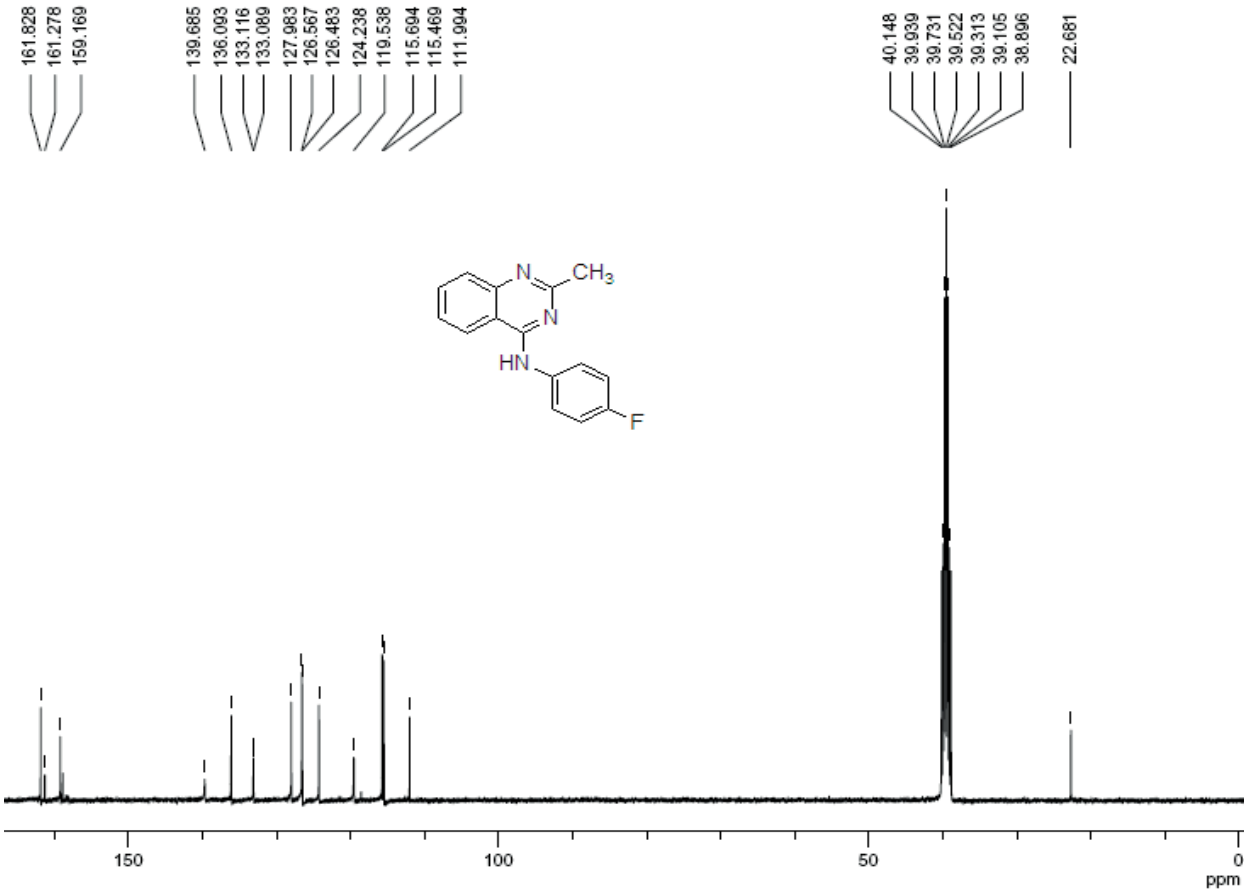
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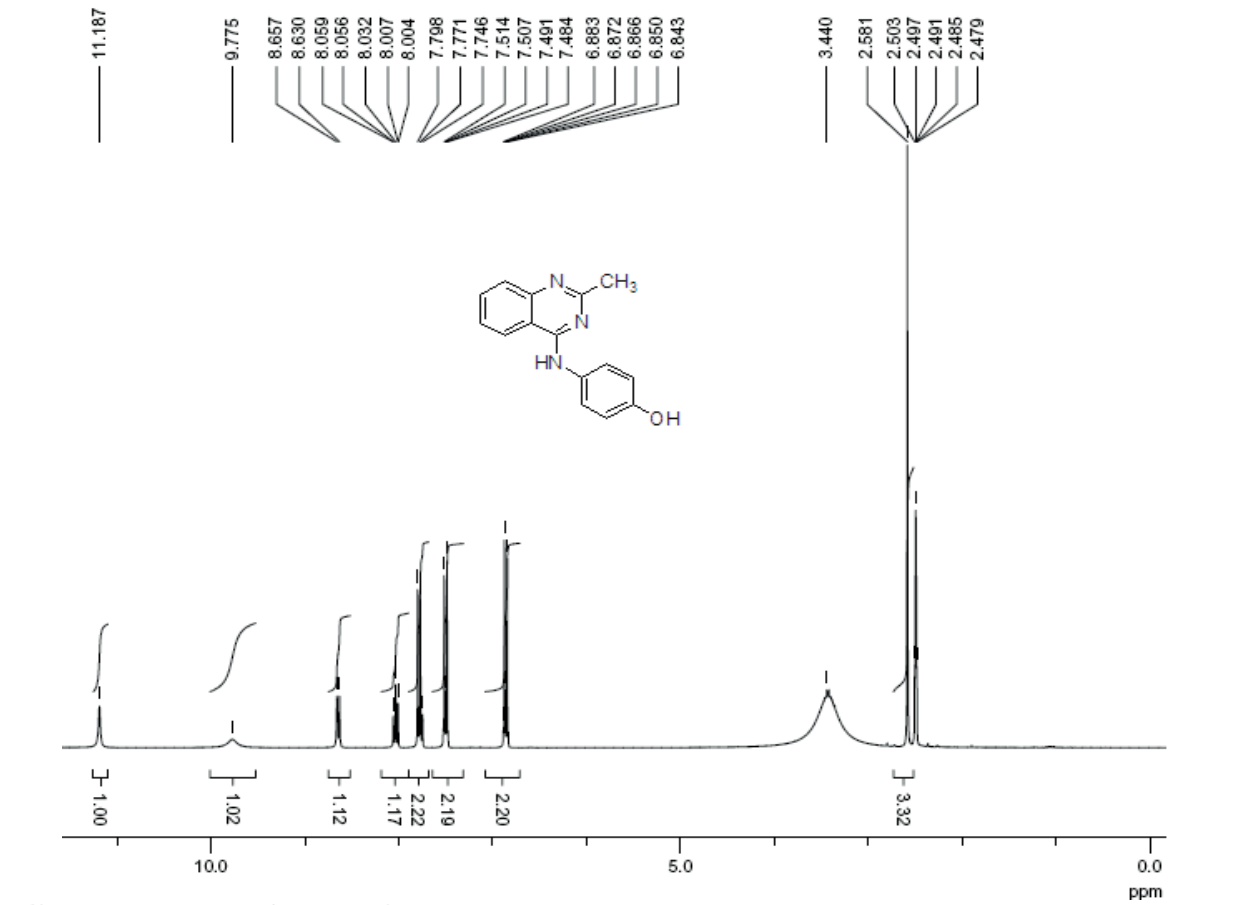
ppm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7.507
7.491
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2.491
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2.479
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HN
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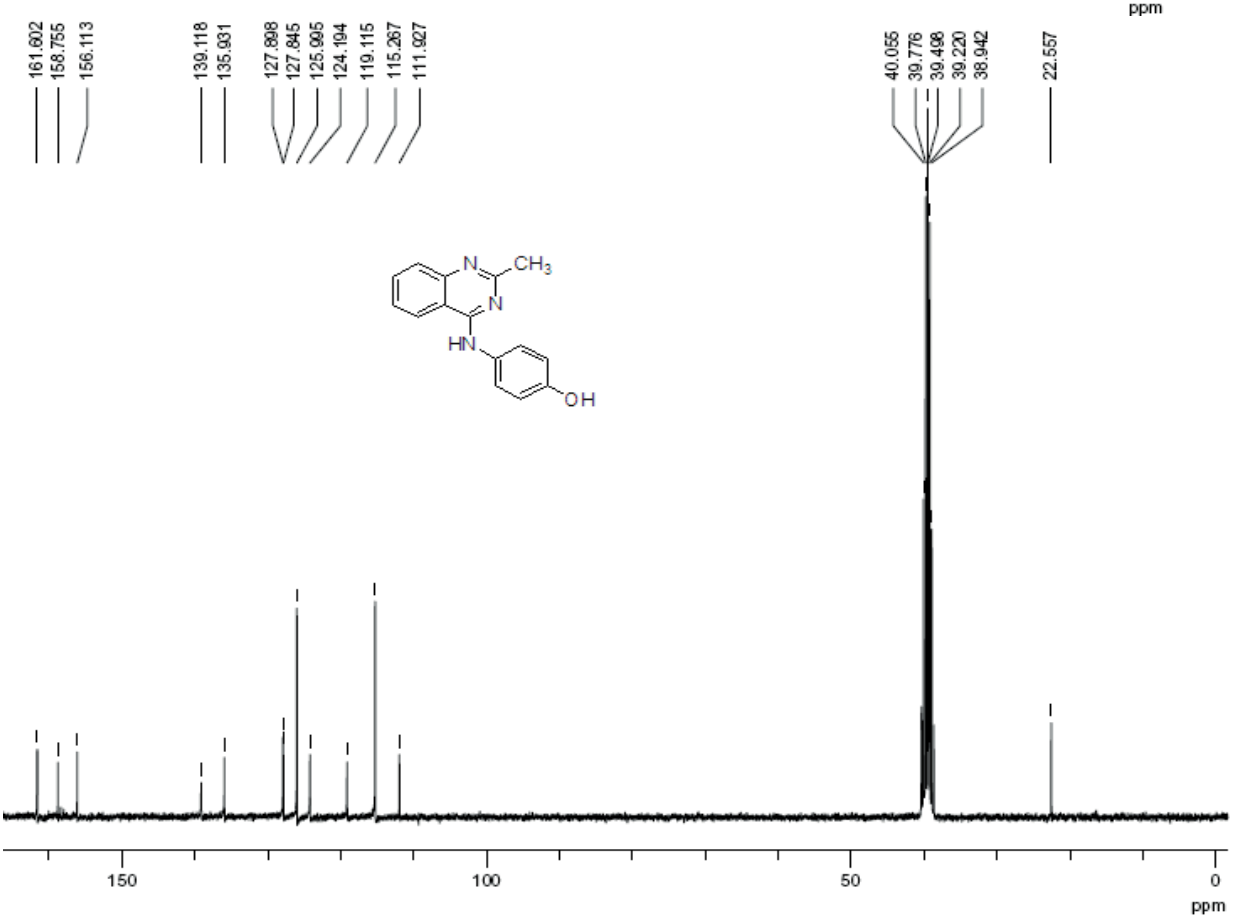
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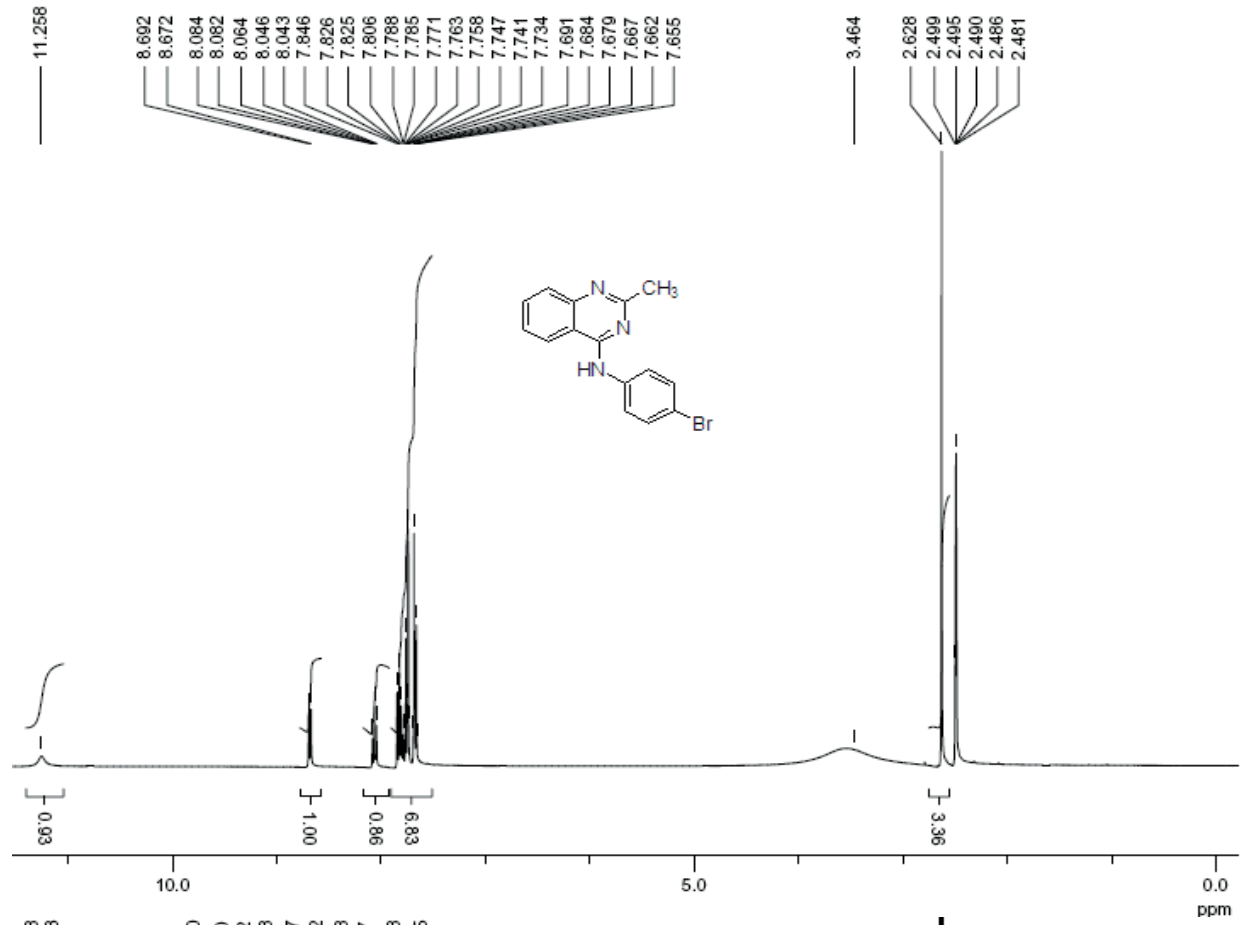
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7.771
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7.747
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7.734
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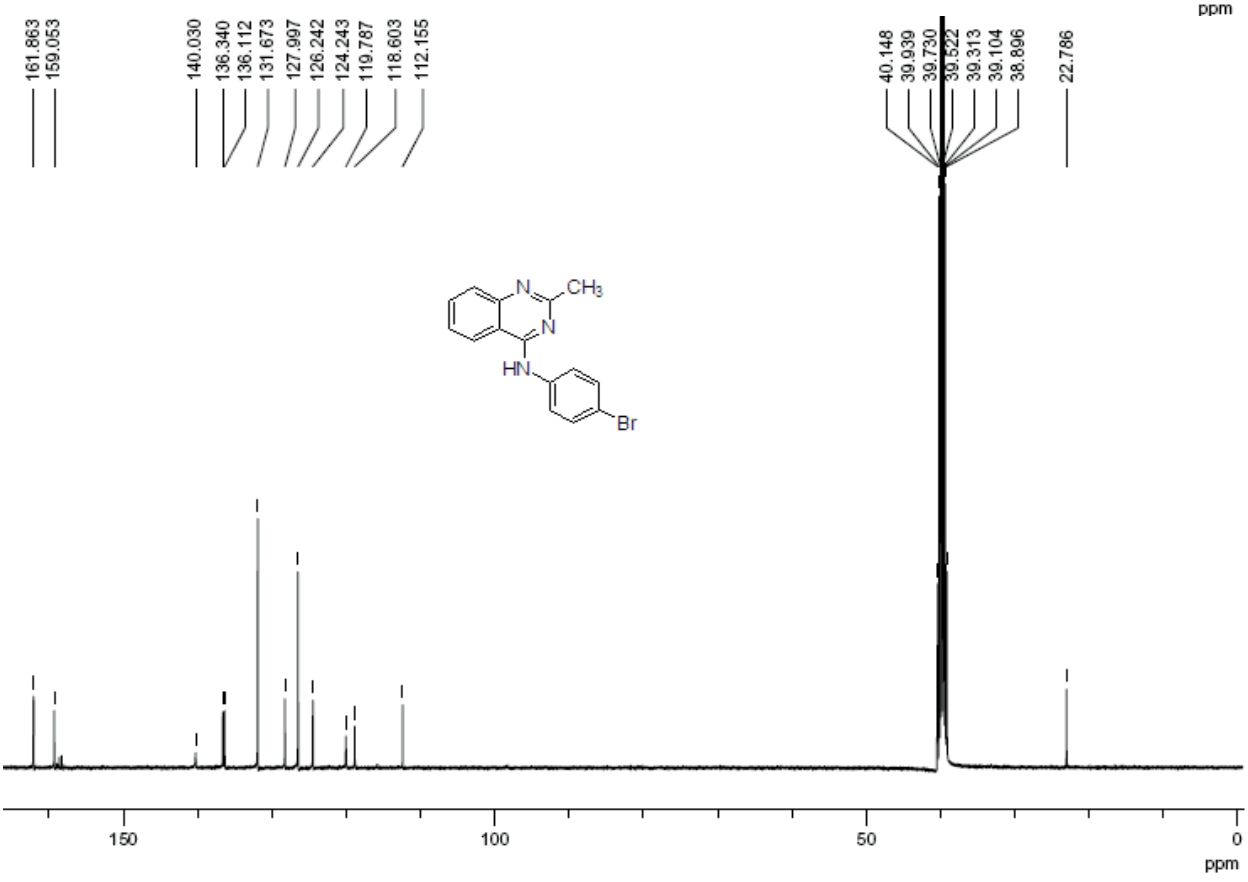
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39.939
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N
HN
Br
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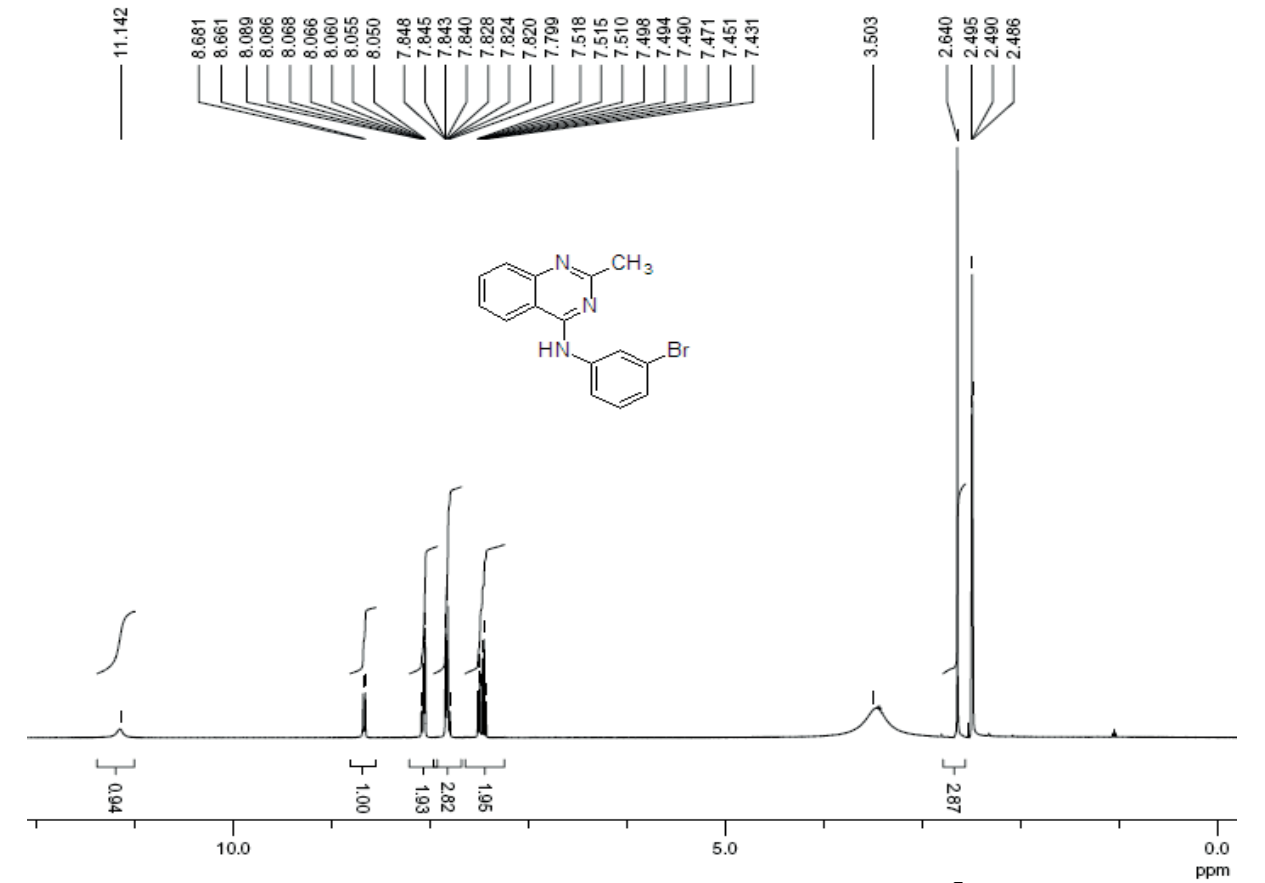
100
50
0
ppm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7.840
7.828
7.824
7.820
7.799
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7.515
7.510
7.498
7.494
7.490
7.471
7.451
7.431
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2.495
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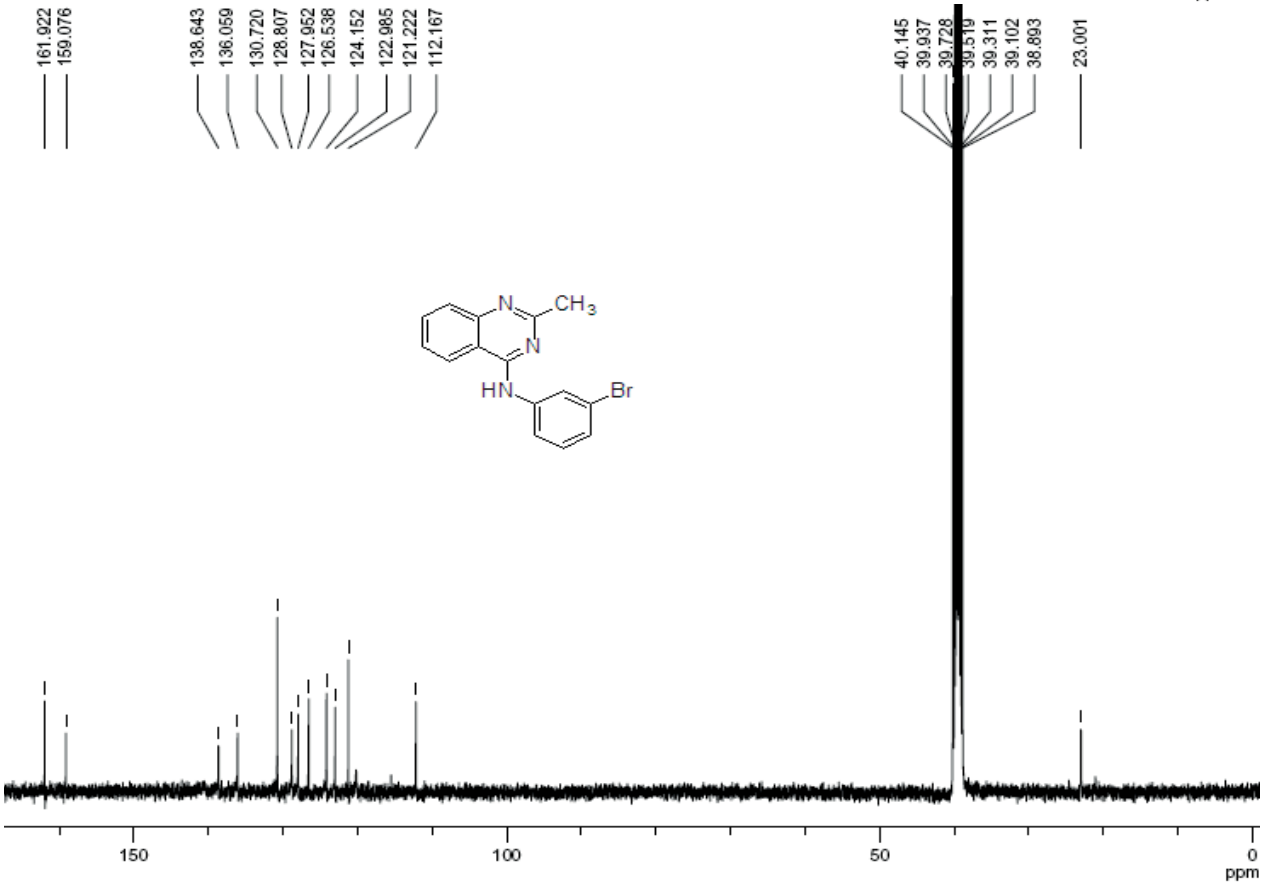
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39.937
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39.102
38.893
23.001
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CH3
N
HN
Br
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50
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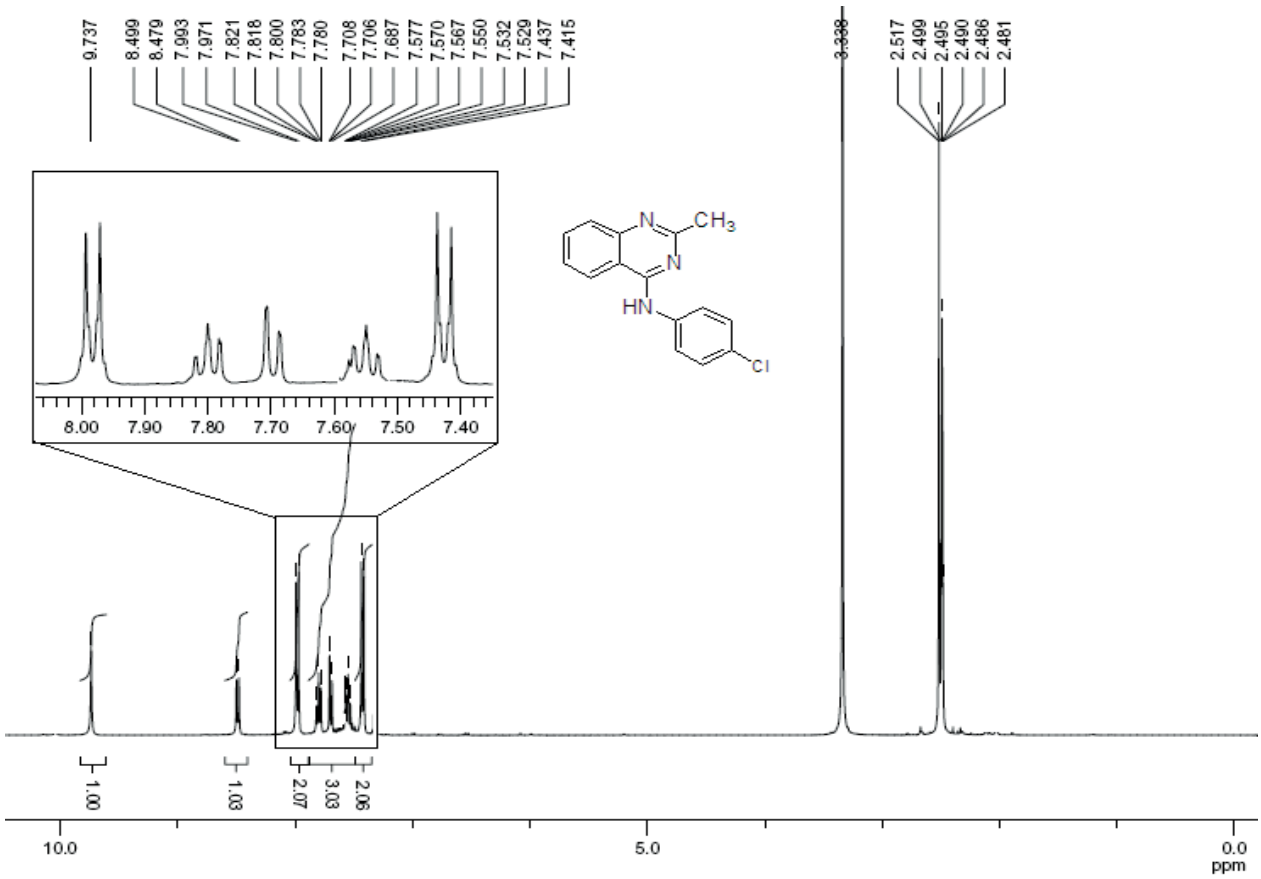
ppm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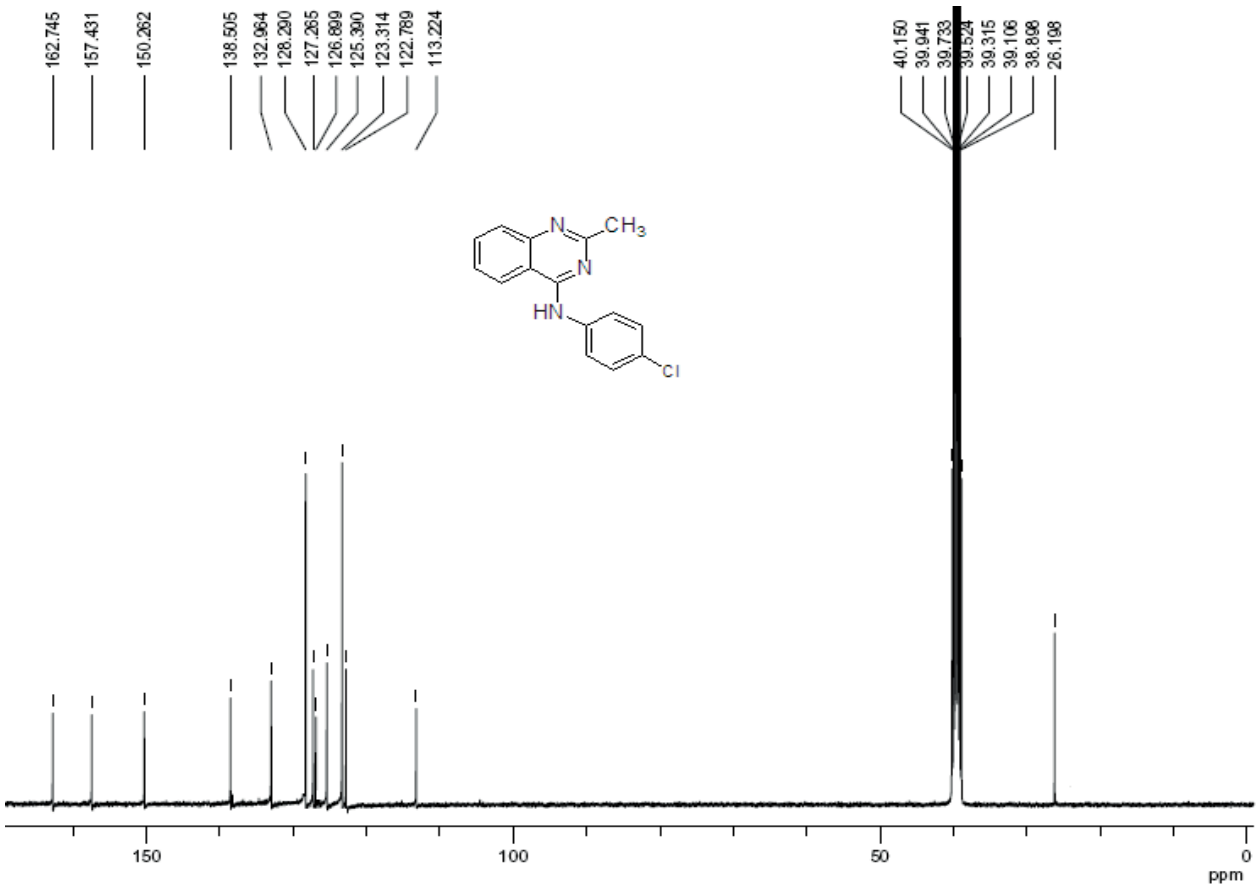
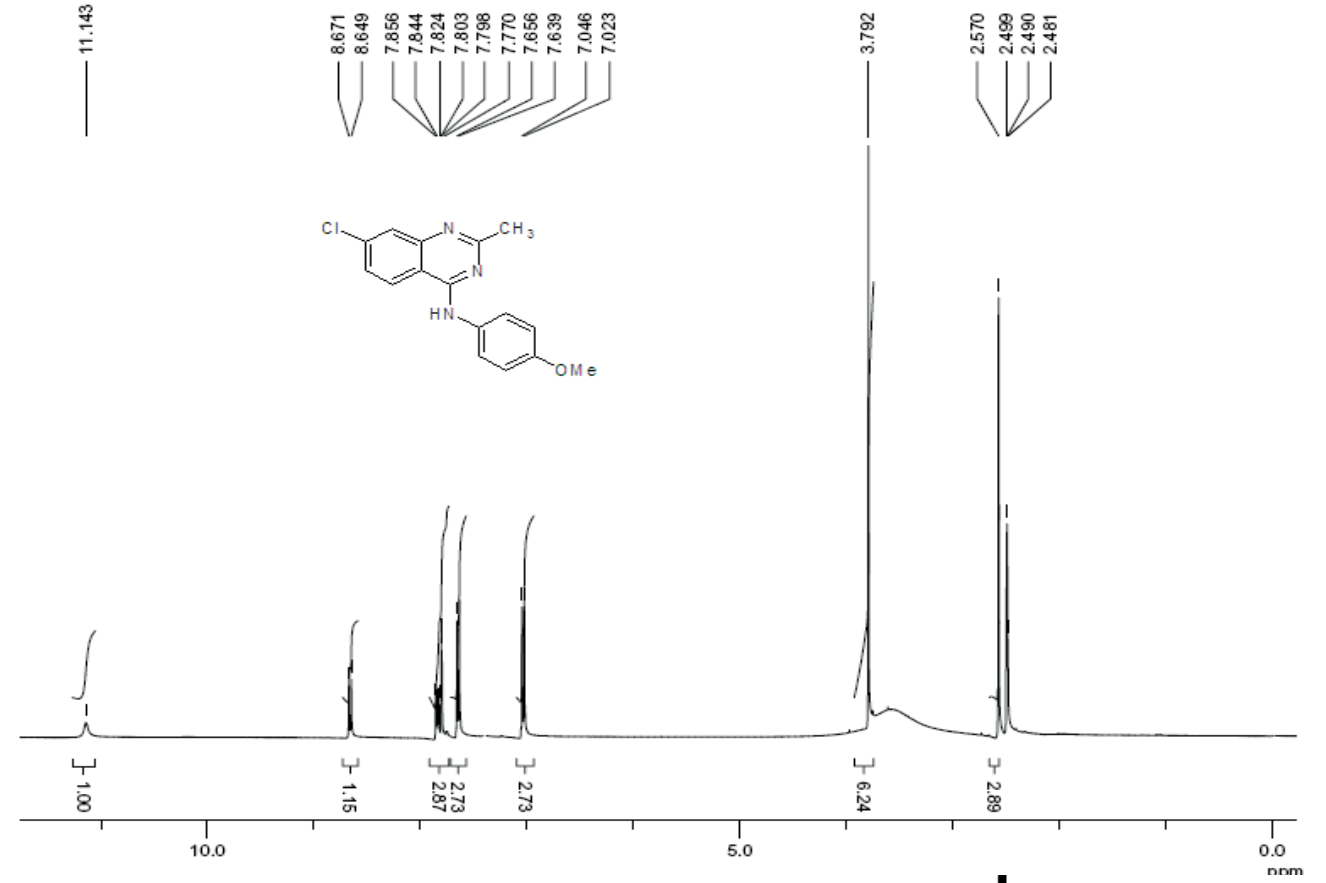
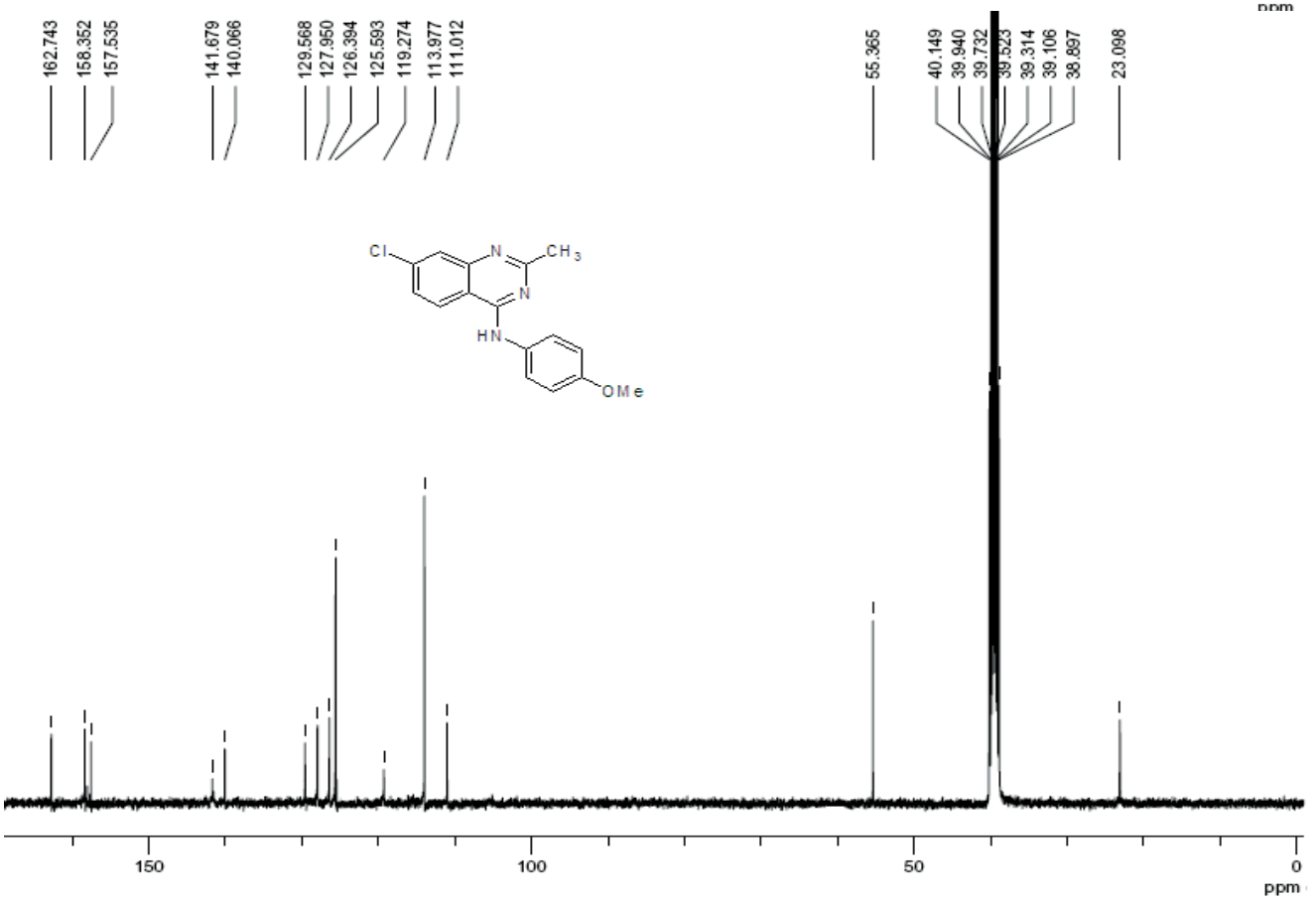
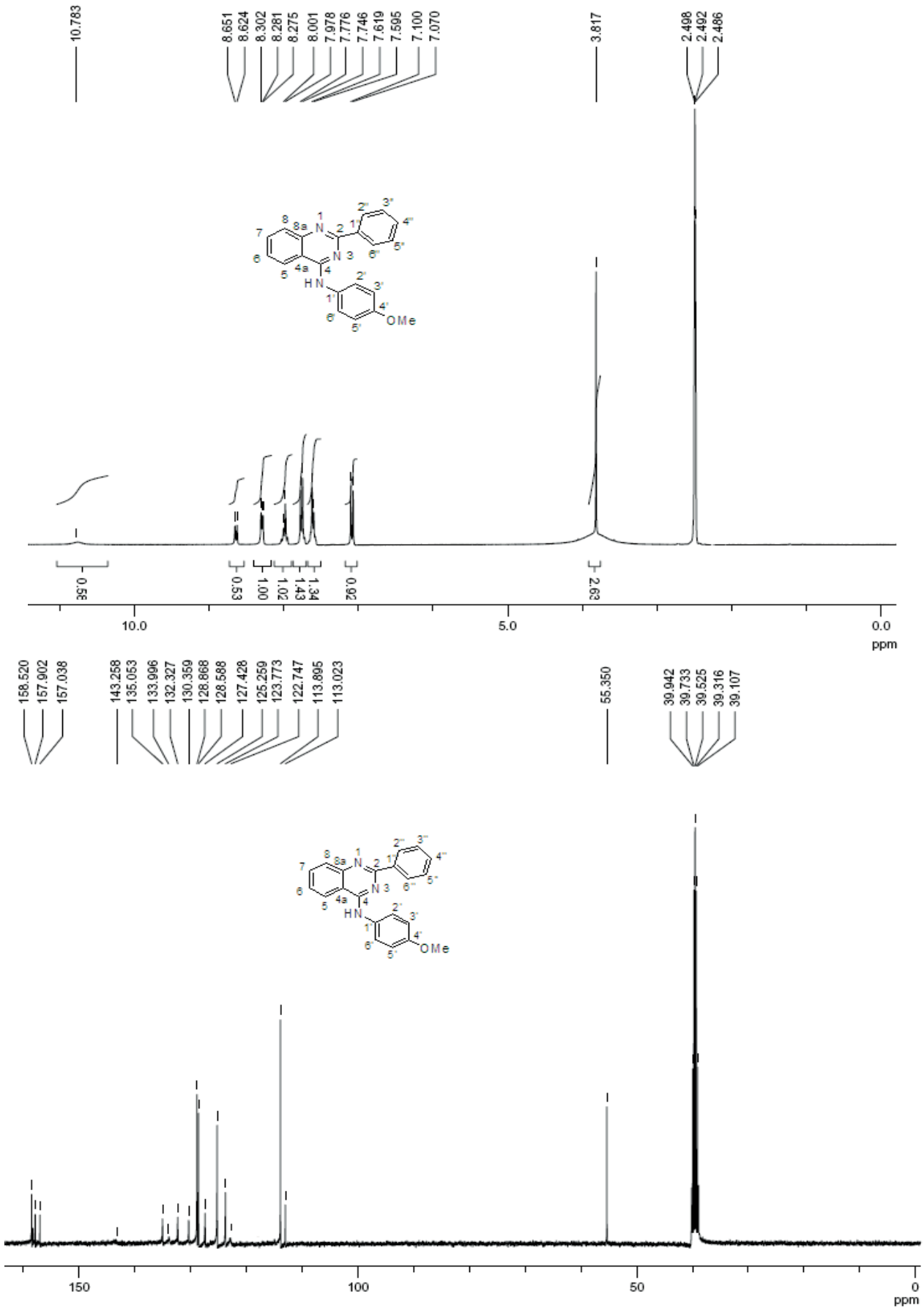
8.499
8.479
7.993
7.971
7.821
7.818
7.800
7.783
7.780
7.708
7.706
7.687
7.577
7.570
7.567
7.550
7.532
7.529
7.437
7.415
3.338
2.517
2.499
2.495
2.490
2.486
2.481
8.00
7.90
7.80
7.70
7.60
7.50
7.40
N
CH3
N
HN
Cl
1.00
1.08
2.07
3.03
2.06
10.0
5.0
0.0
ppm


162.745
157.431
150.262
138.505
132.964
128.290
127.265
126.899
125.390
123.314
122.789
113.224
40.150
39.941
39.733
39.524
39.315
39.106
38.898
26.198
N
CH3
N
HN
Cl
150
100
50
0
ppm


11.143
8.671
8.649
7.856
7.844
7.824
7.803
7.798
7.770
7.656
7.639
7.046
7.023
3.792
2.570
2.499
2.490
2.481
Cl
N
CH3
N
HN
OMe
1.00
1.15
2.87
2.73
2.73
6.24
2.89
10.0
5.0
0.0
ppm


162.743
158.352
157.535
141.679
140.066
129.568
127.950
126.394
125.593
119.274
113.977
111.012
55.365
40.149
39.940
39.732
39.523
39.314
39.106
38.897
23.098
Cl
N
CH3
N
HN
OMe
150
100
50
0
ppm


10.783
8.651
8.624
8.302
8.281
8.275
8.001
7.978
7.776
7.746
7.619
7.595
7.100
7.070
3.817
2.498
2.492
2.486
0.56
0.53
1.00
1.02
1.43
1.34
0.92
2.62
10.0
5.0
0.0
ppm
158.520
157.902
157.038
143.258
135.053
133.996
132.327
130.359
128.868
128.588
127.428
125.259
123.773
122.747
113.895
113.023
55.350
39.942
39.733
39.525
39.316
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150
100
50
0
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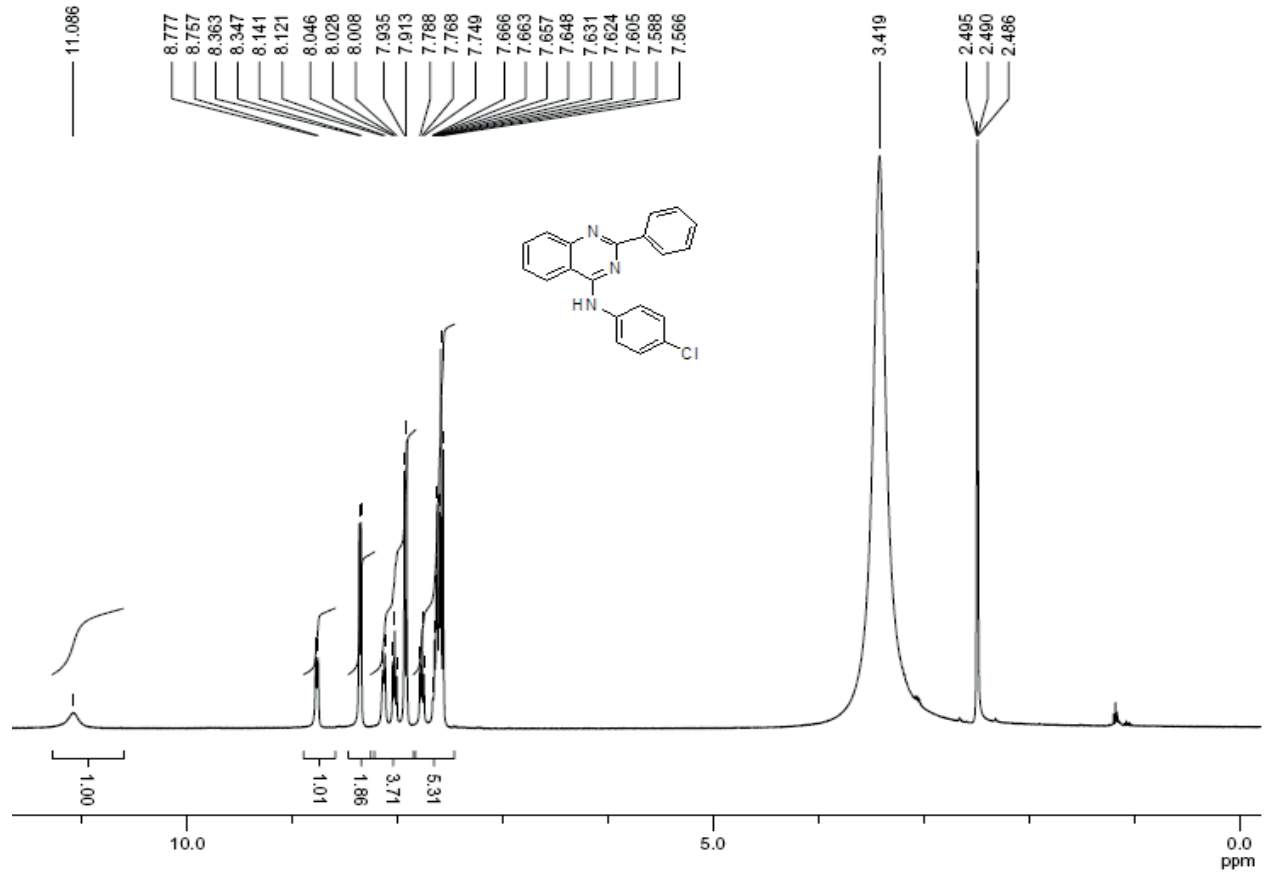
11.086
8.777
8.757
8.363
8.347
8.141
8.121
8.046
8.028
8.008
7.935
7.913
7.788
7.768
7.749
7.666
7.663
7.657
7.648
7.631
7.624
7.605
7.588
7.566
3.419
2.495
2.490
2.486
N
N
HN
Cl
1.00
1.01
1.86
3.71
5.31
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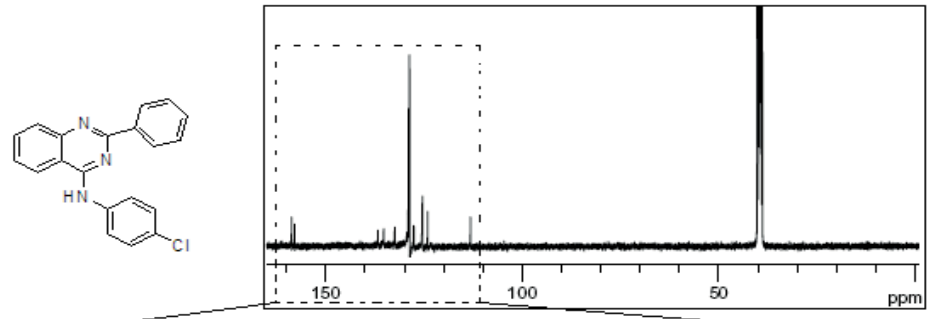
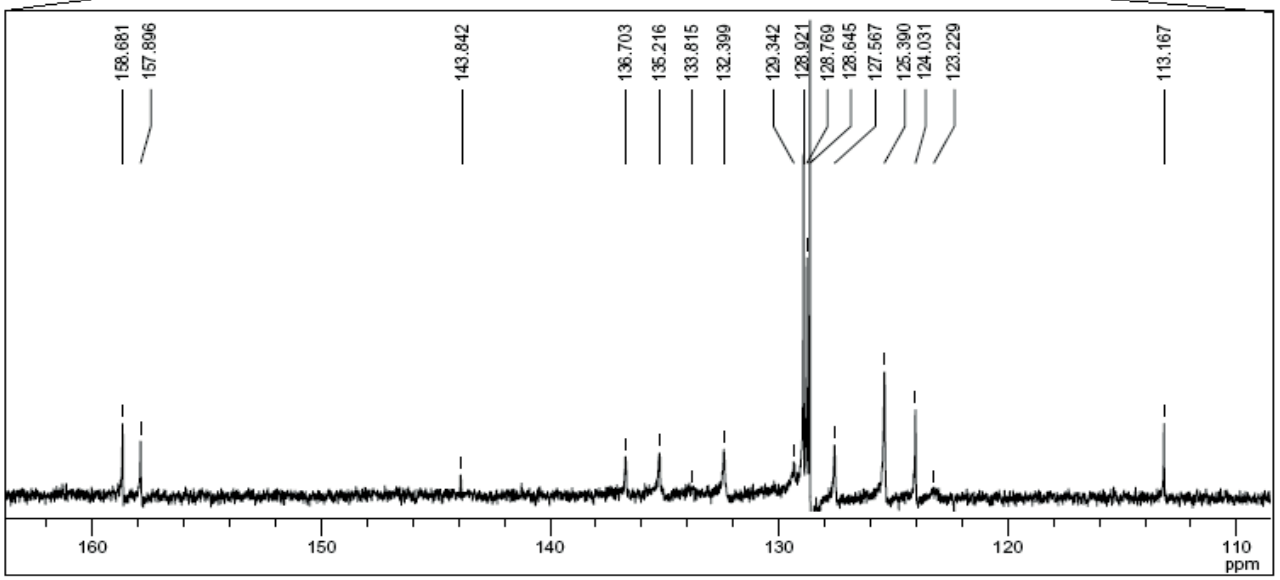
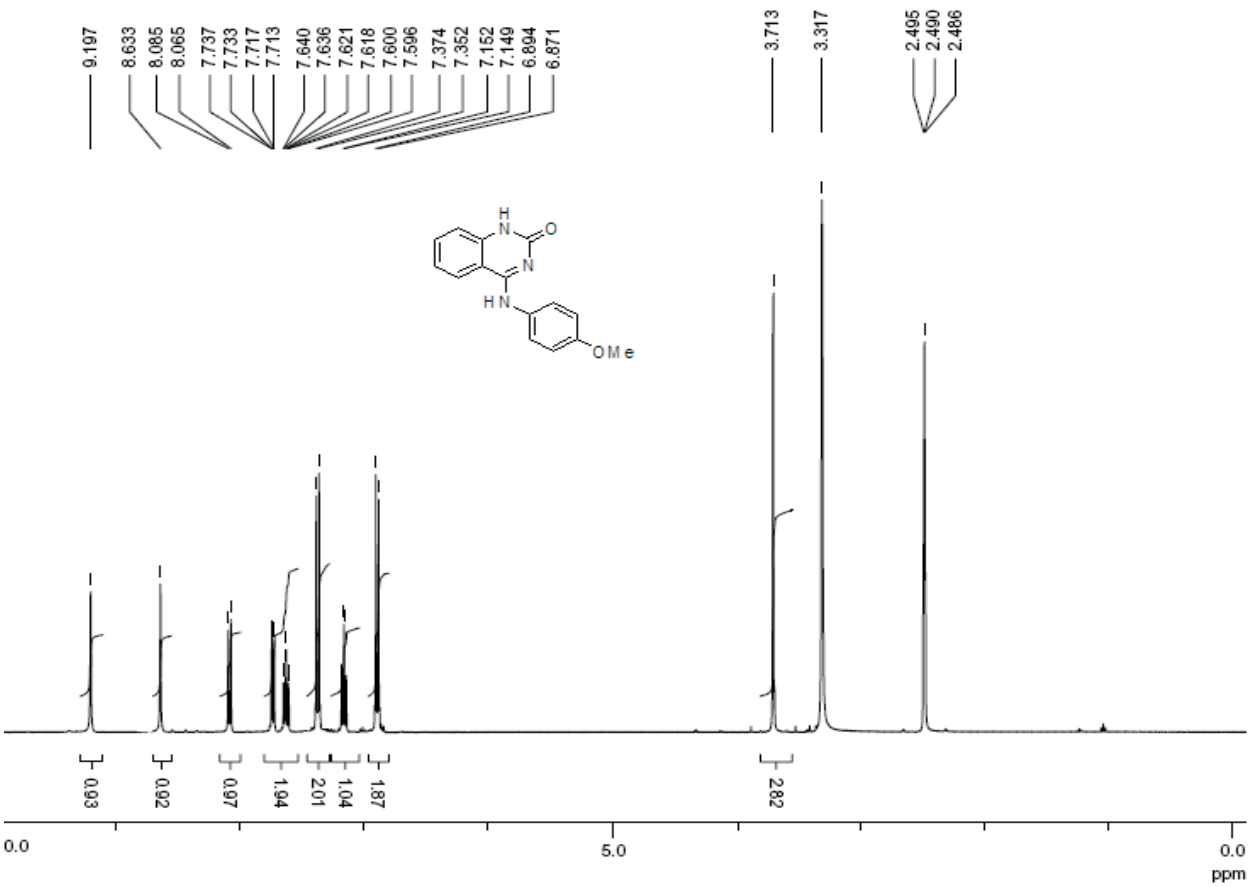
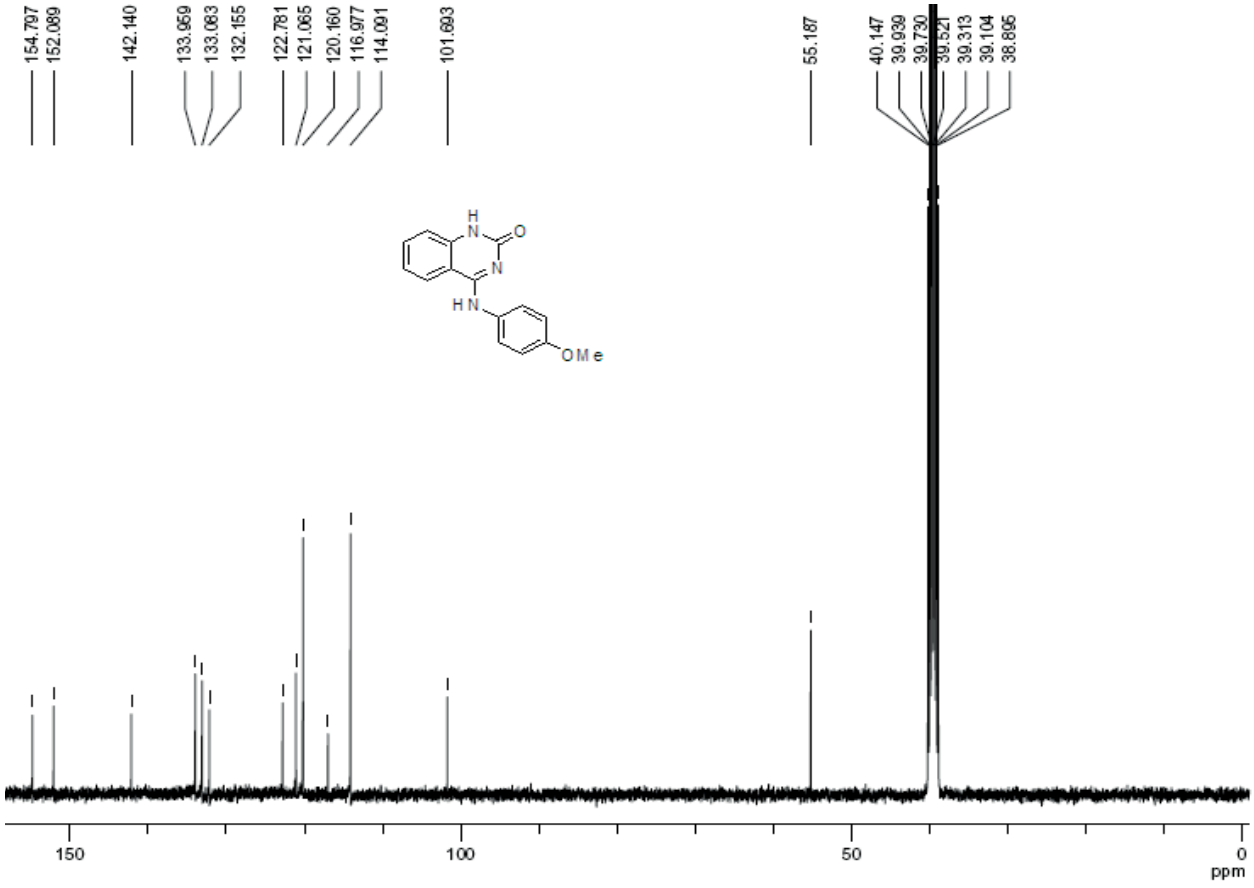
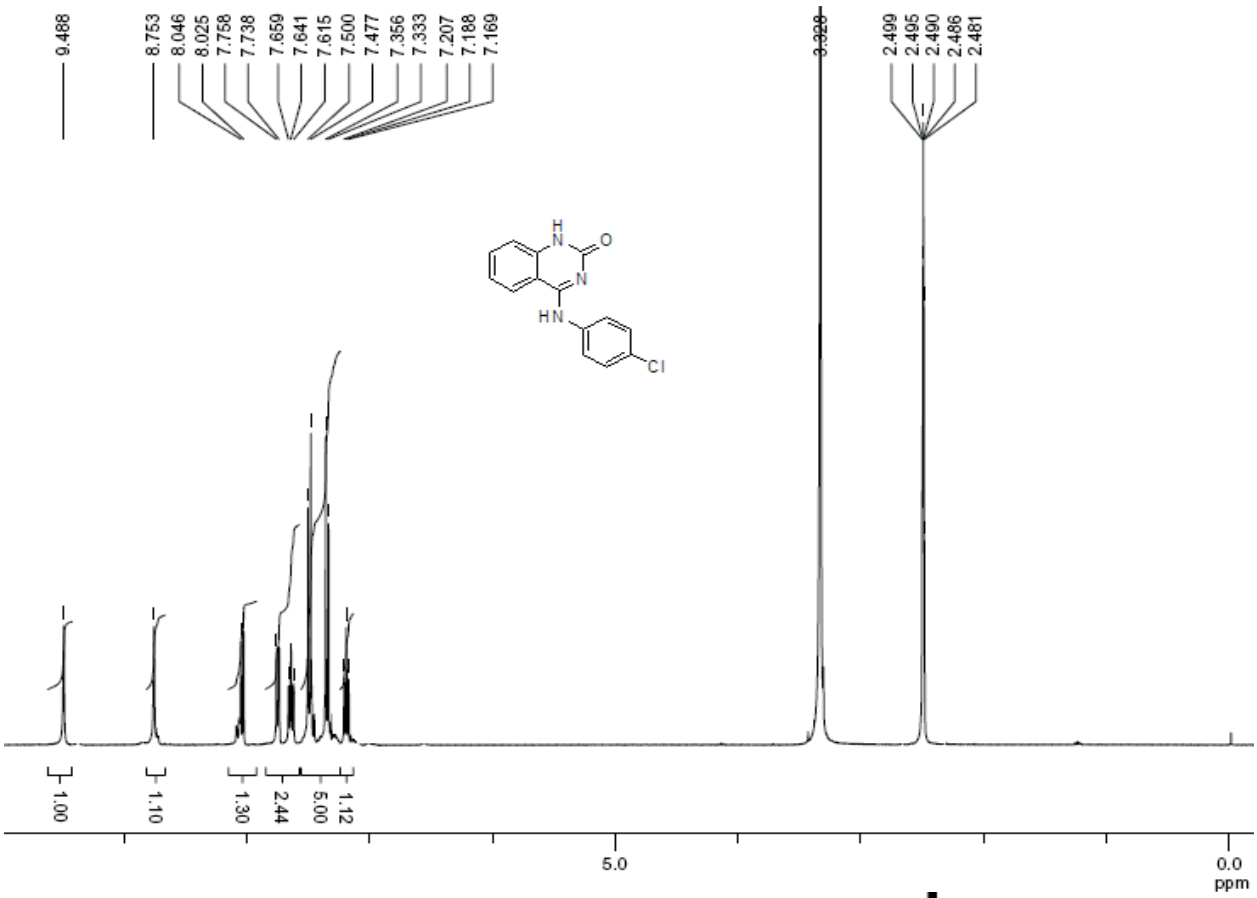
5.0
0.0
ppm

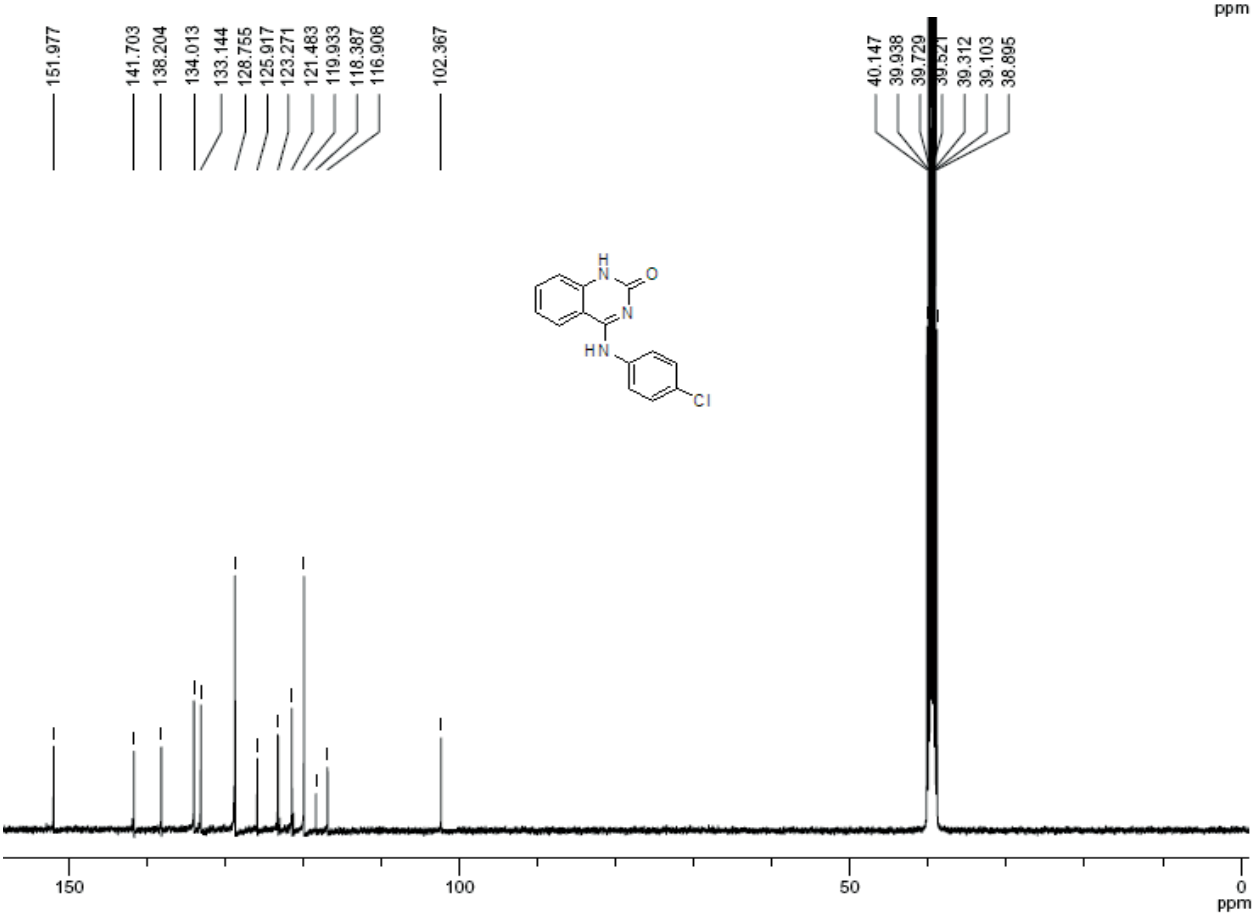

N
N
HN
Cl
150
100
50
ppm

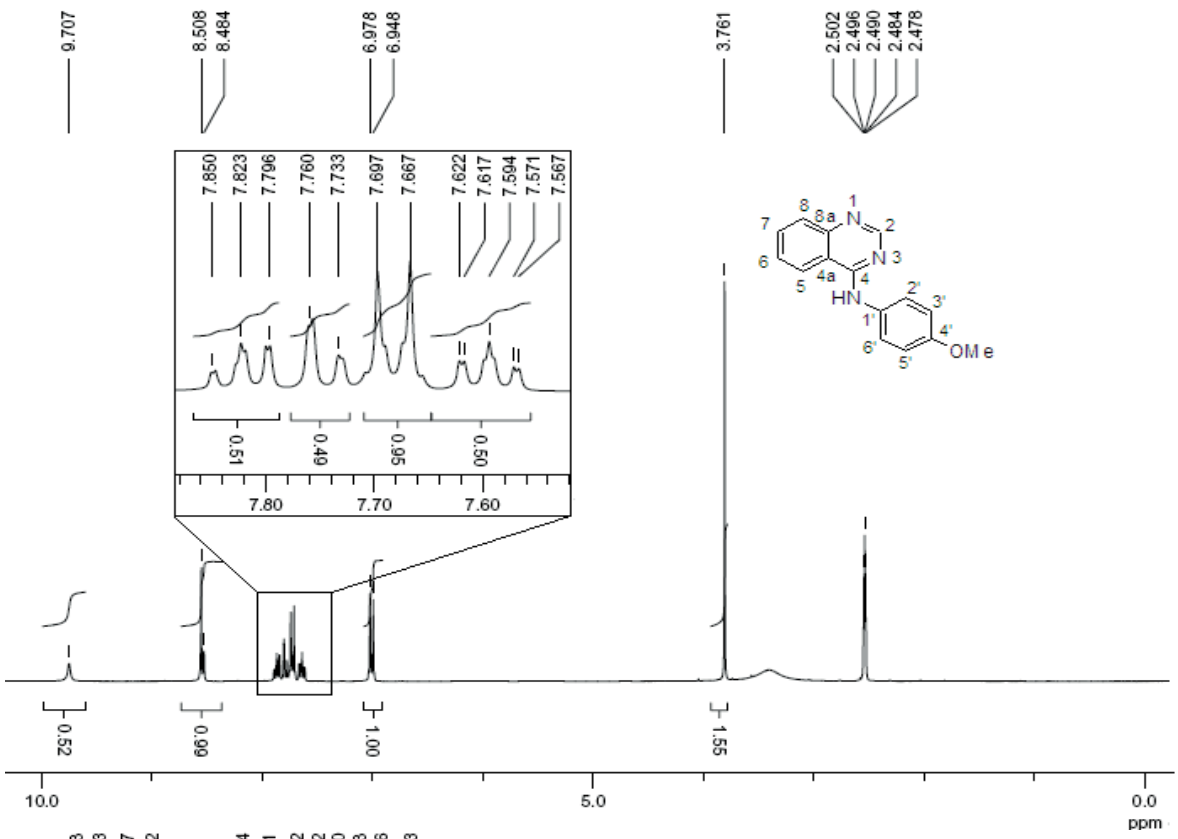

158.681
157.896
143.842
136.703
135.216
133.815
132.399
129.342
128.921
128.769
128.645
127.567
125.390
124.031
123.229
113.167
160
150
140
130
120
110
ppm

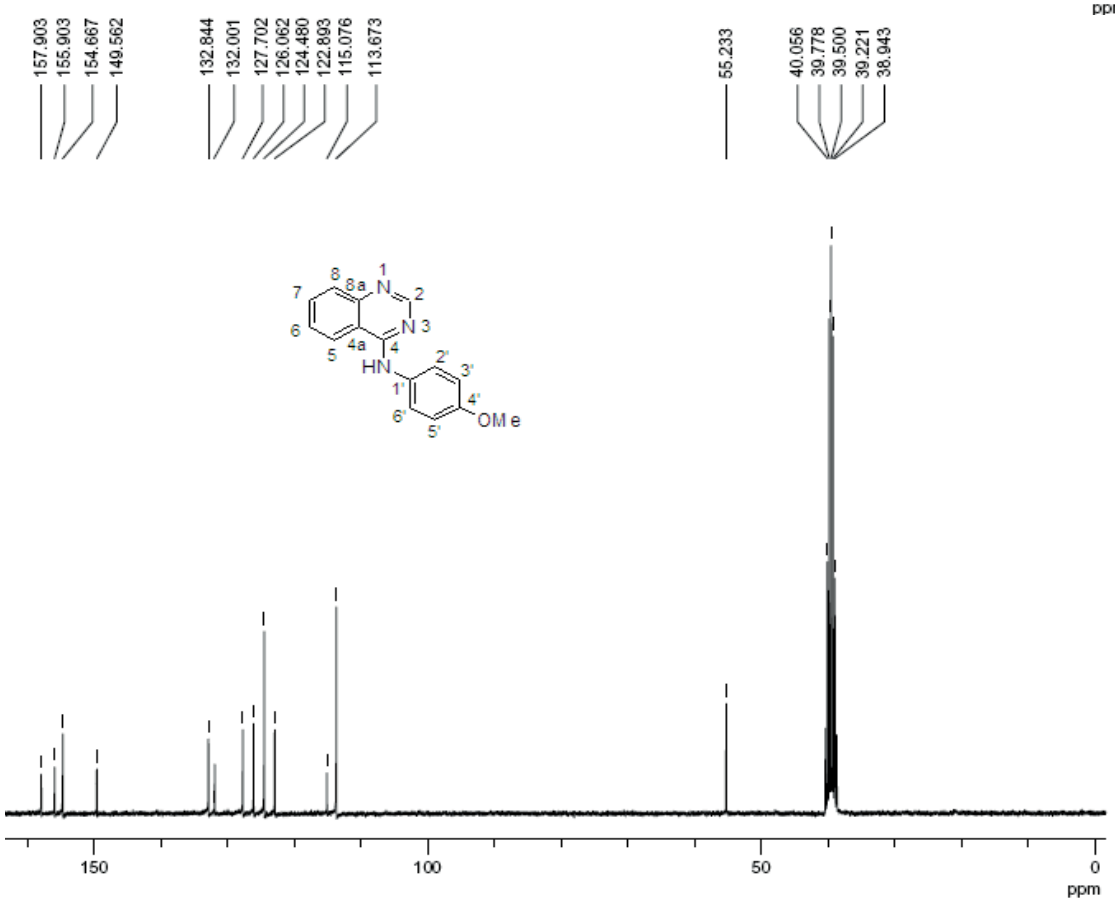

9.197
8.633
8.085
8.065
7.737
7.733
7.717
7.713
7.640
7.636
7.621
7.618
7.600
7.596
7.374
7.352
7.152
7.149
6.894
6.871
3.713
3.317
2.495
2.490
2.486
0.93
0.92
0.97
1.94
2.01
1.04
1.87
2.82
0.0
5.0
0.0
ppm


154.797
152.089
142.140
133.969
133.083
132.155
122.781
121.065
120.160
116.977
114.091
101.693
55.187
40.147
39.939
39.730
39.521
39.313
39.104
38.895
150
100
50
0
ppm

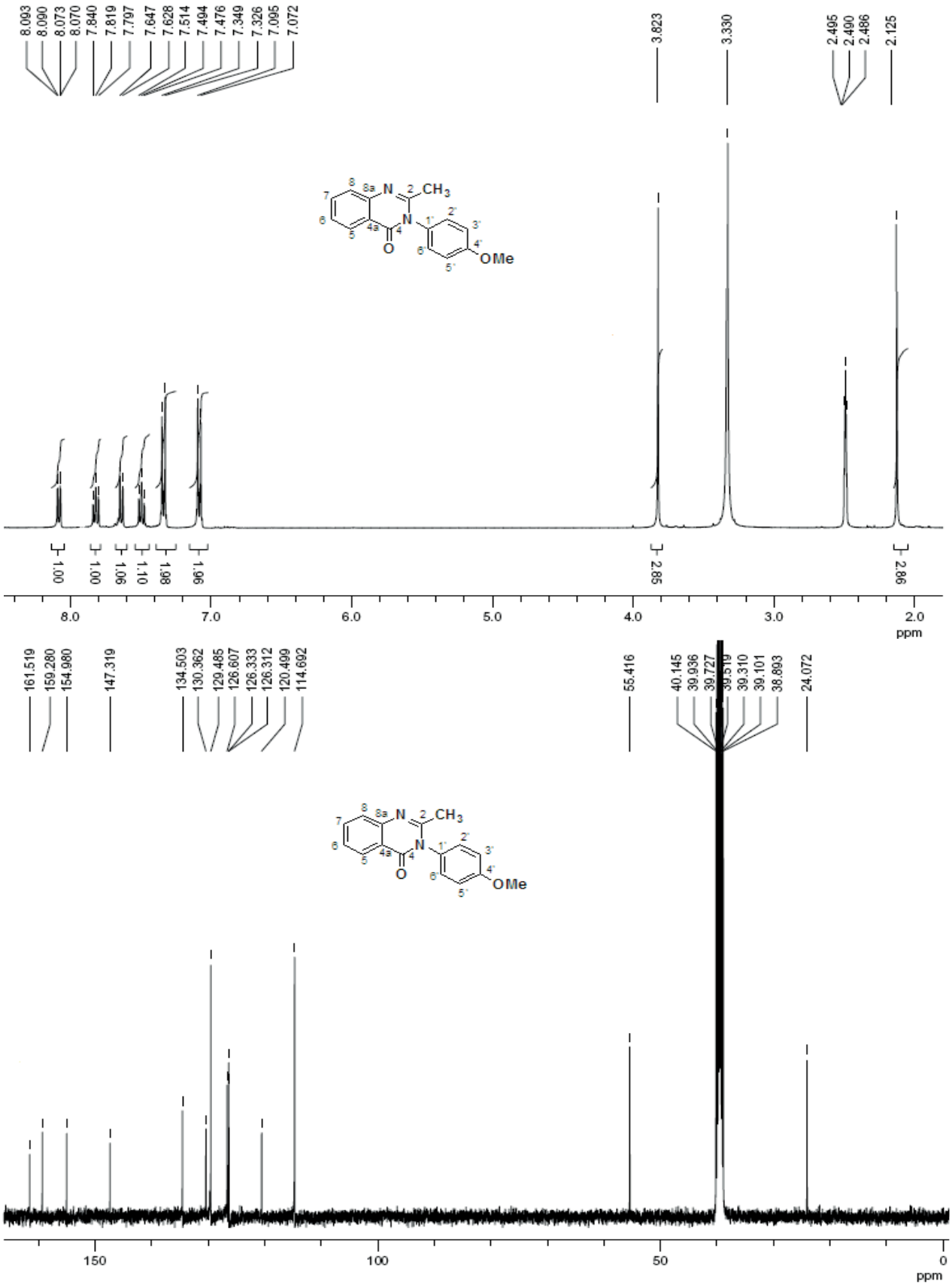

9.488
8.753
8.046
8.025
7.758
7.738
7.659
7.641
7.615
7.500
7.477
7.356
7.333
7.207
7.188
7.169
3.320
2.499
2.495
2.490
2.486
2.481
1.00
1.10
1.30
2.44
5.00
1.12
5.0
0.0
ppm

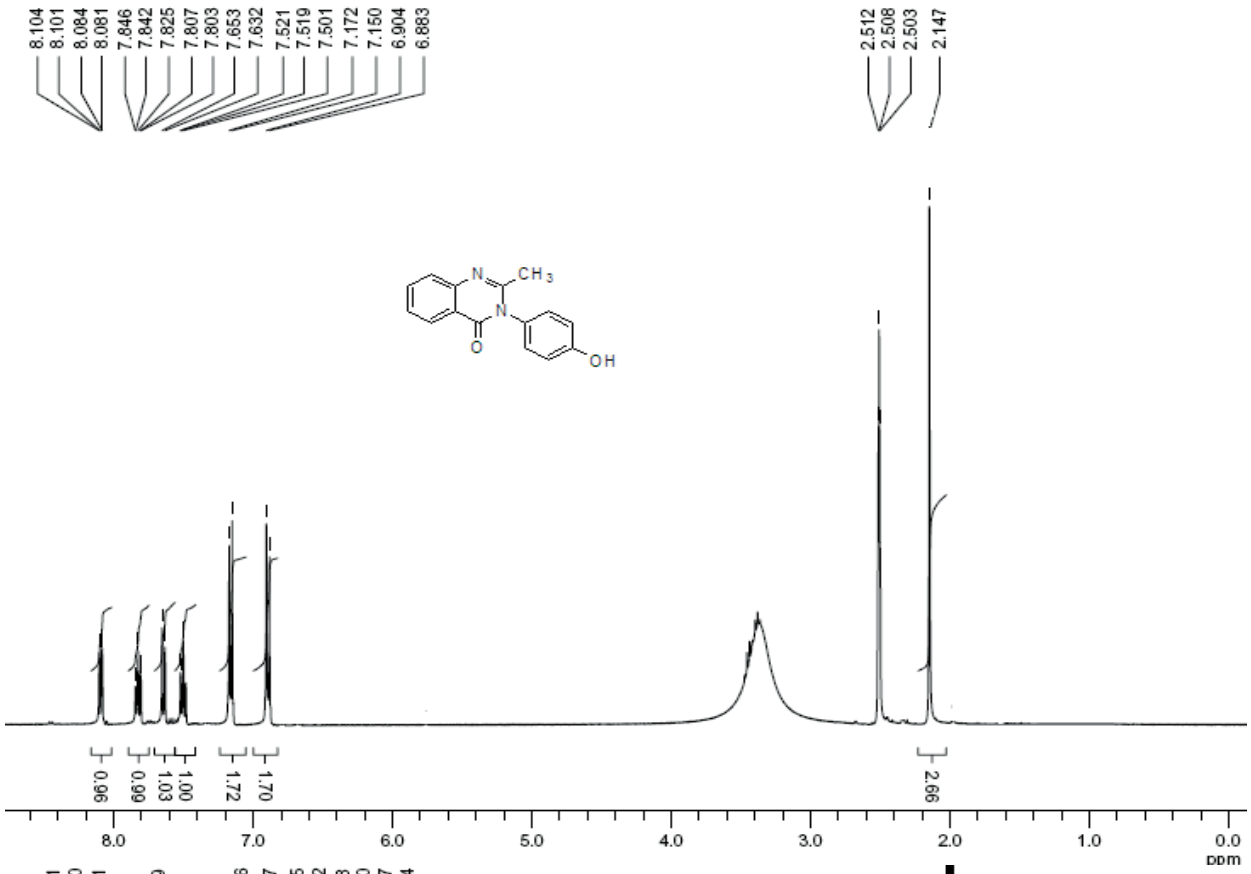

151.977
141.703
138.204
134.013
133.144
128.755
125.917
123.271
121.483
119.933
118.387
116.908
102.367
40.147
39.938
39.729
39.521
39.312
39.103
38.895
150
100
50
0
ppm

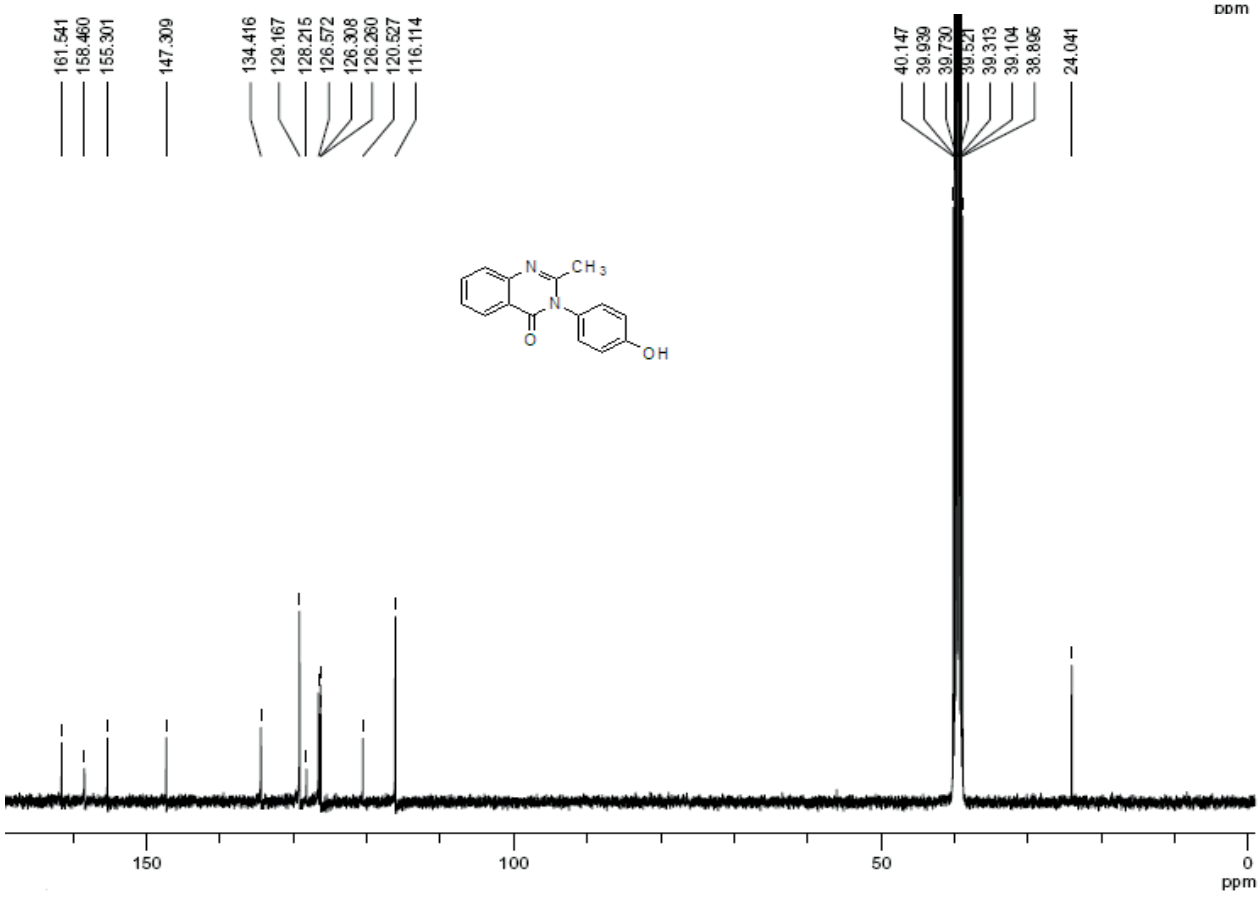

9.707
8.508
8.484
6.978
6.948
3.761
2.502
2.496
2.490
2.484
2.478
7.850
7.823
7.796
7.760
7.733
7.697
7.667
7.622
7.617
7.594
7.571
7.567
0.51
0.49
0.96
0.60
7.80
7.70
7.60
0.52
0.99
1.00
1.55
10.0
5.0
0.0
ppm
OMe


157.903
155.903
154.667
149.562
132.844
132.001
127.702
126.062
124.480
122.893
115.076
113.673
55.233
40.056
39.778
39.500
39.221
38.943
150
100
50
0
ppm
OMe

^{1}H and ^{13}C NMR spectra for compound **4a-c**




8.104
8.101
8.084
8.081
7.846
7.842
7.825
7.807
7.803
7.653
7.632
7.521
7.519
7.501
7.172
7.150
6.904
6.883
2.512
2.508
2.503
2.147
CH3
N
N
O
OH
0.96
0.99
1.03
1.00
1.72
1.70
2.66
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm


161.541
158.460
155.301
147.309
134.416
129.167
128.215
126.572
126.308
126.260
120.527
116.114
40.147
39.939
39.730
39.521
39.313
39.104
38.895
24.041
CH3
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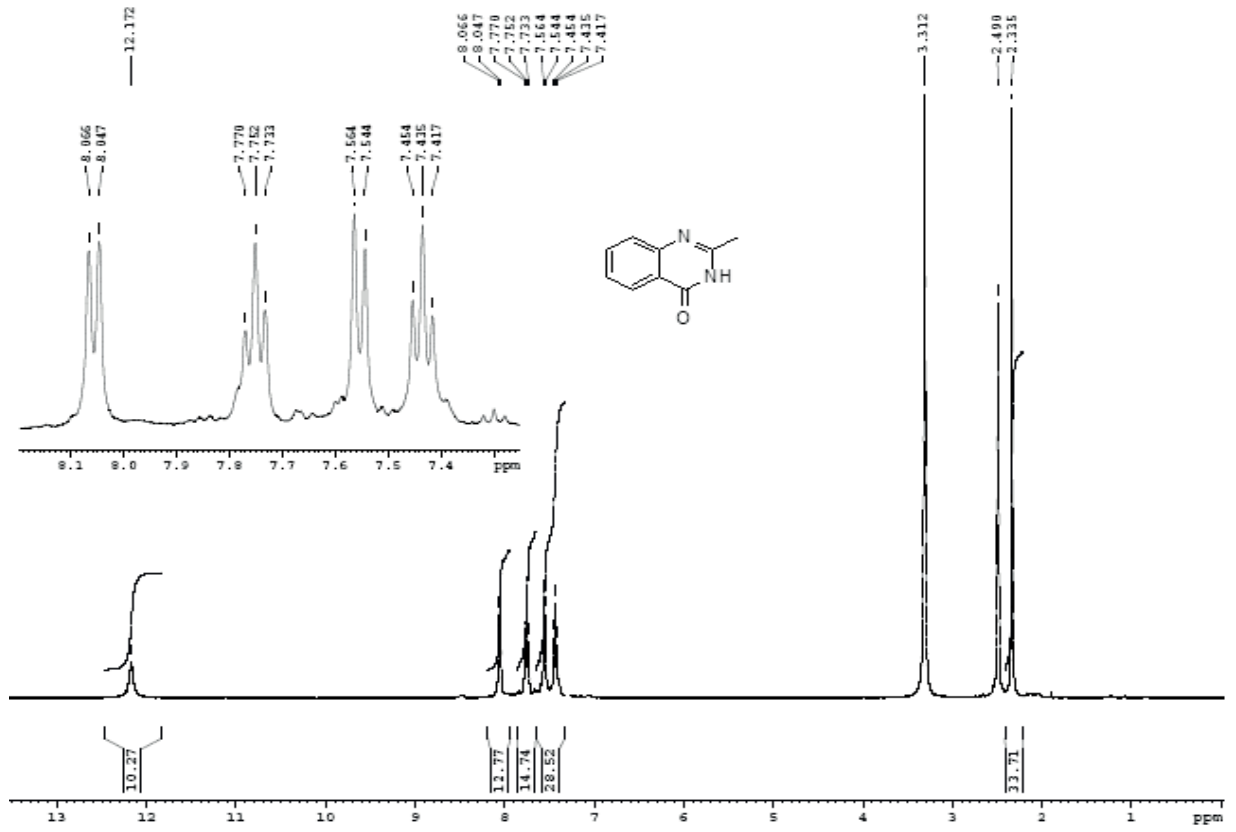
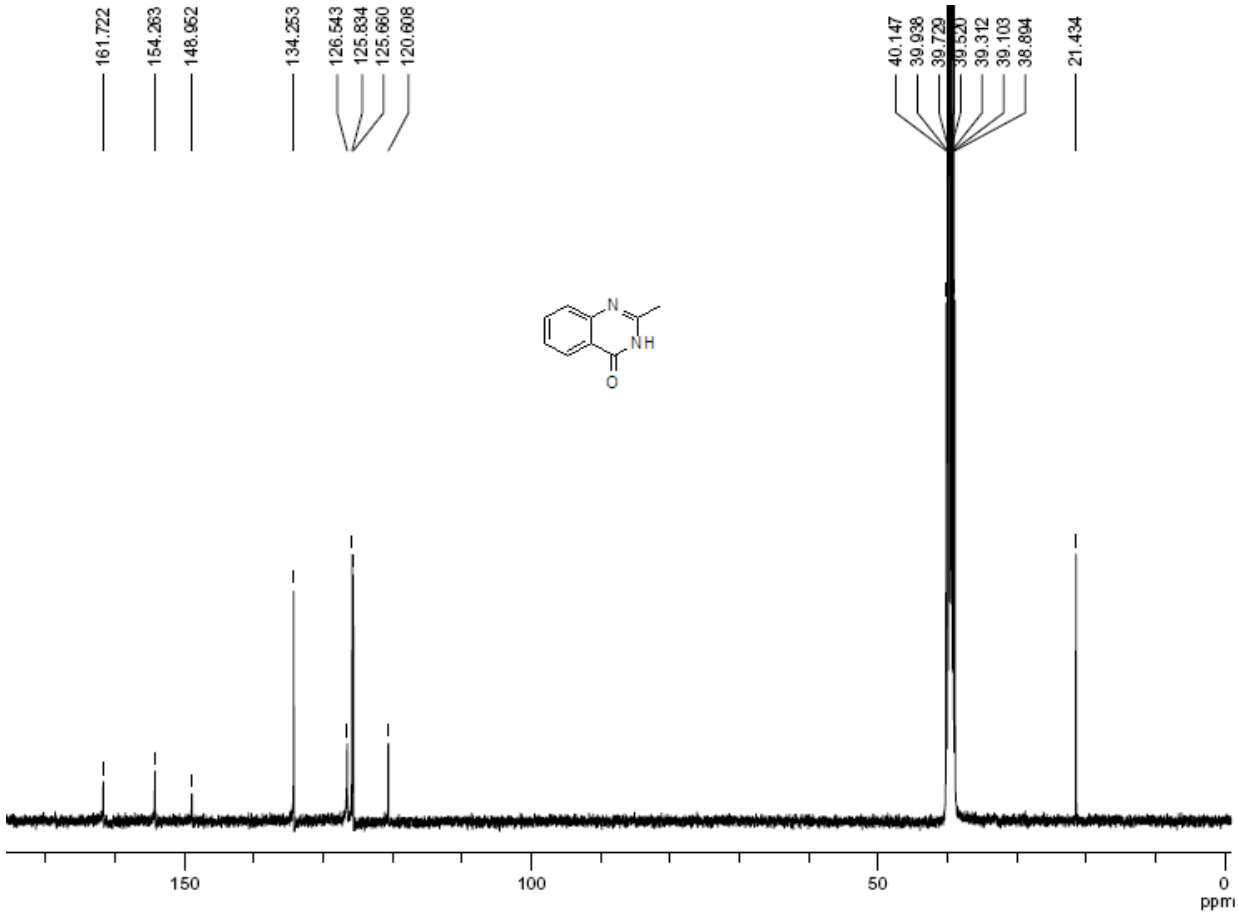
N
O
OH
150
100
50
0
ppm


12.172
8.066
8.047
7.770
7.752
7.733
7.564
7.544
7.454
7.435
7.417
3.312
2.490
2.335
10.27
12.77
14.74
28.52
33.71
ppm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134.253
126.543
125.834
125.660
120.608
40.147
39.938
39.729
39.520
39.312
39.103
38.894
21.434
150
100
50
0
ppm