

Supplementary Materials

Design, Synthesis, and Biological Evaluation of 1,3,5-Triazine Derivatives Targeting hA₁ and hA₃ Adenosine Receptor

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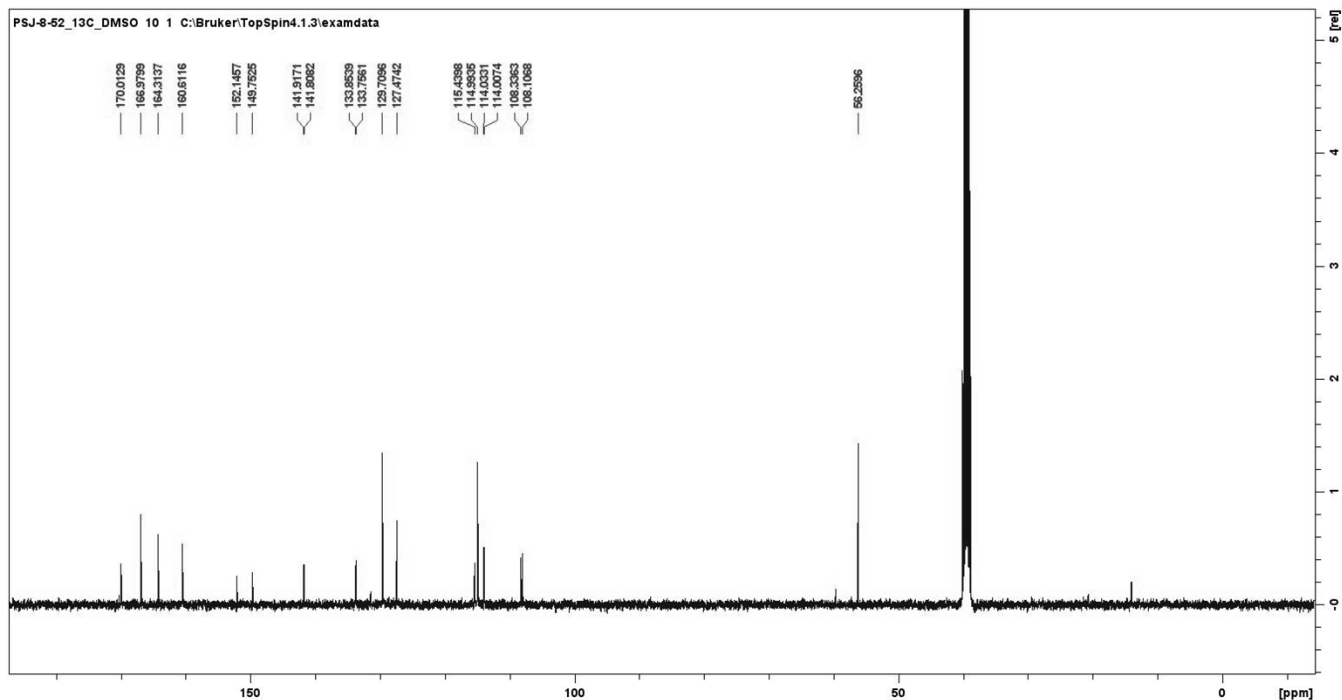
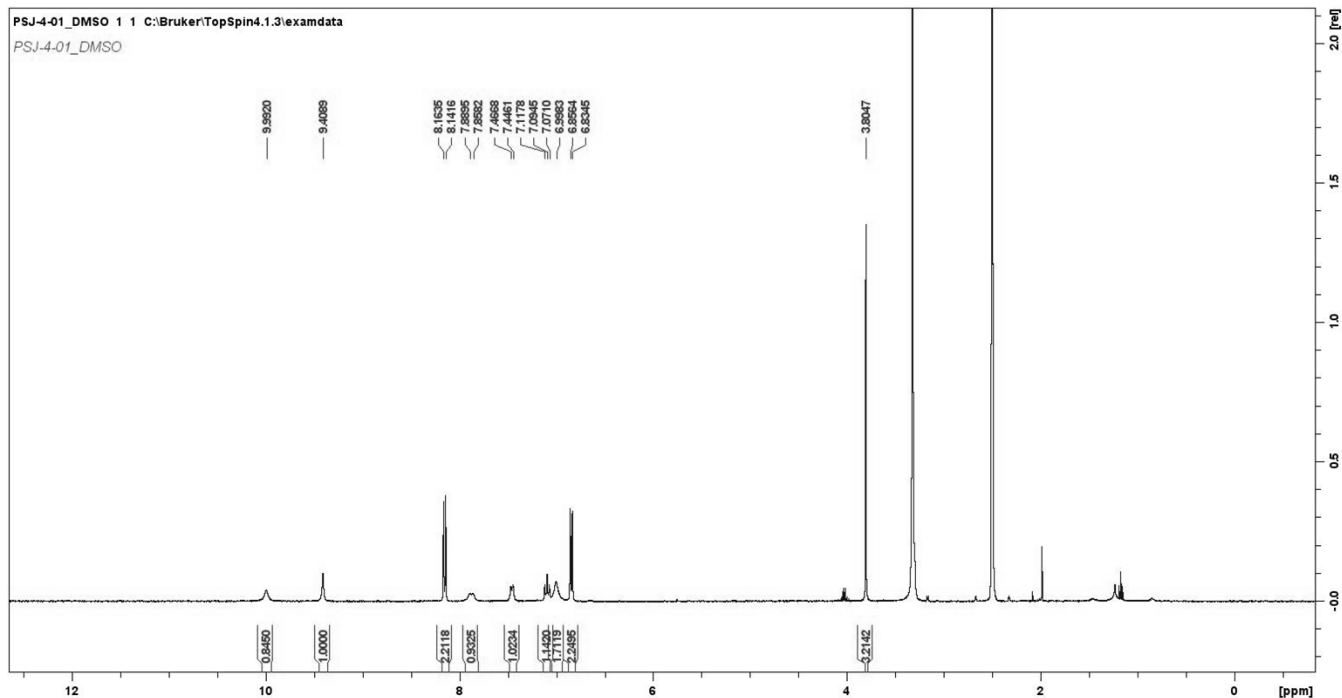
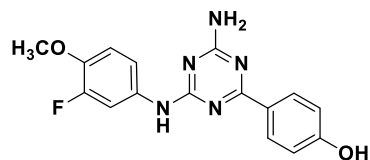
Figure S1. ¹H and ¹³C NMR Copies of Compound **9a-g**, and **11a-i**

Figure S2. HR-MS Copies of Compound **9a-g**, and **11a-i**

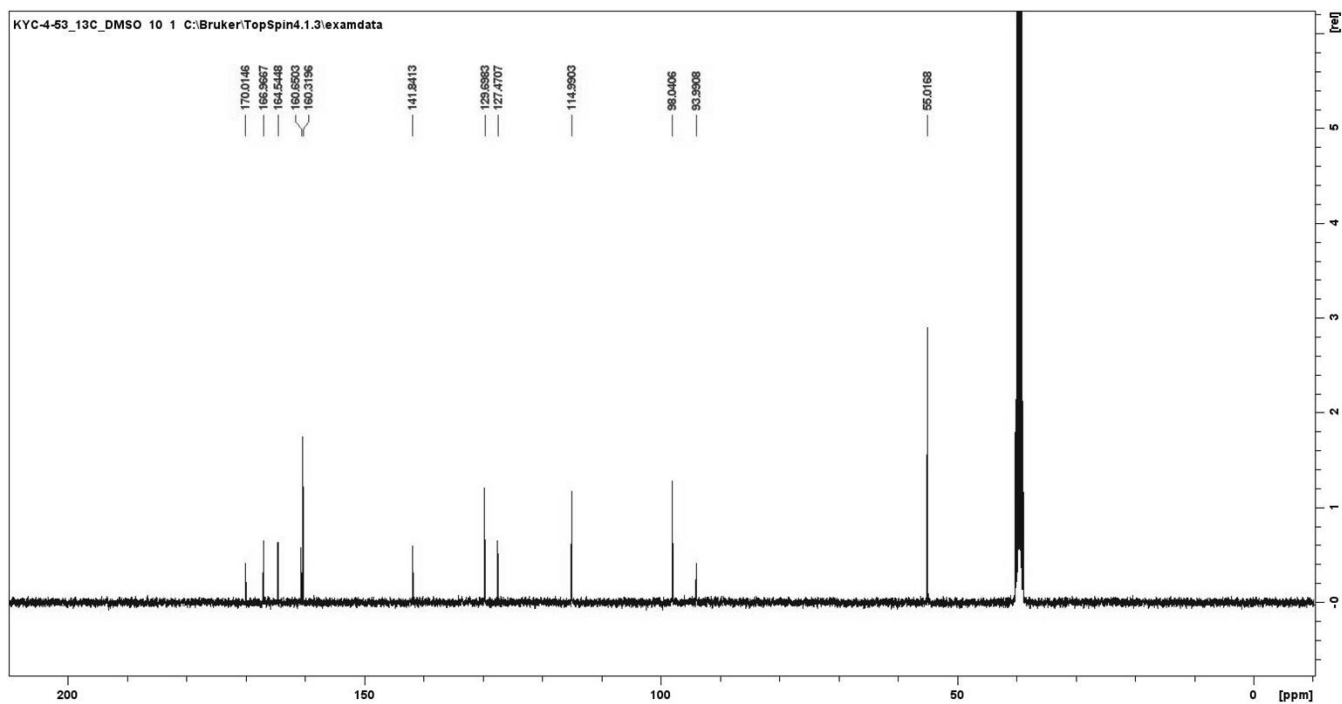
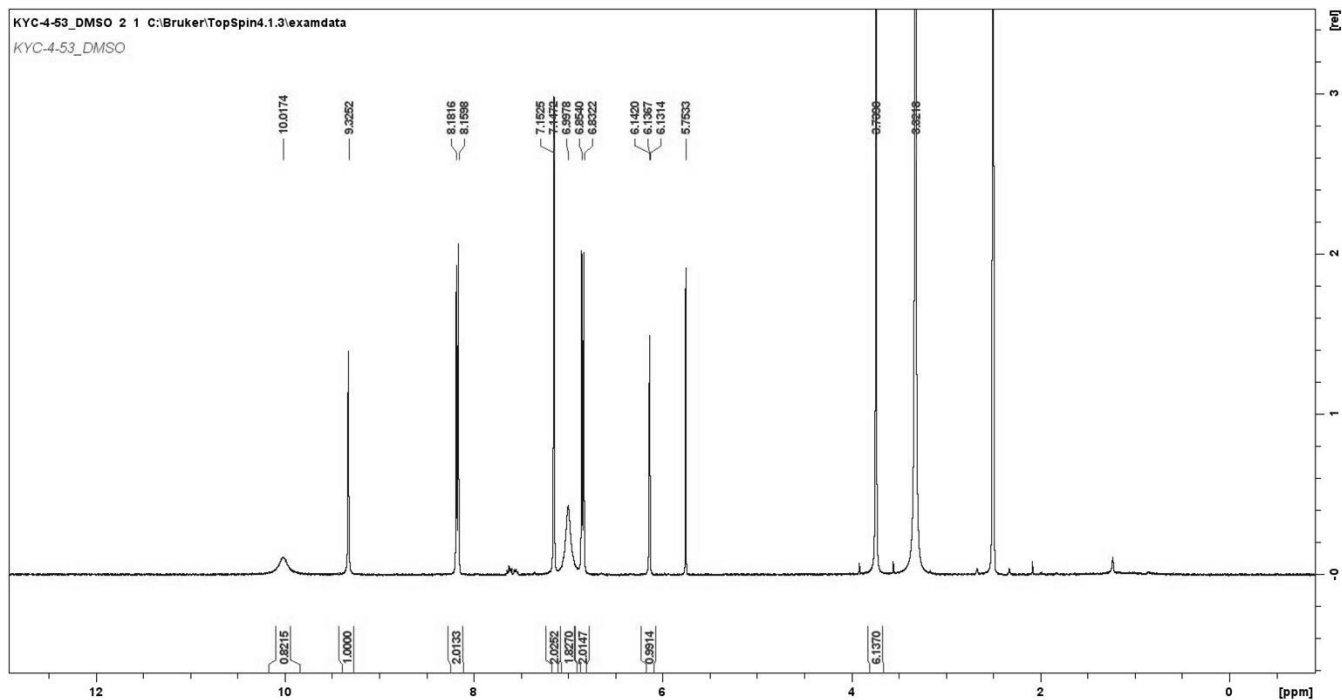
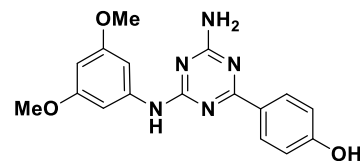
Figure S3. Molecular Docking of Compound **9a**, **11a**, and **11b**

Figure S1. ^1H and ^{13}C NMR Copies of compound **9a-g and **11a-i****

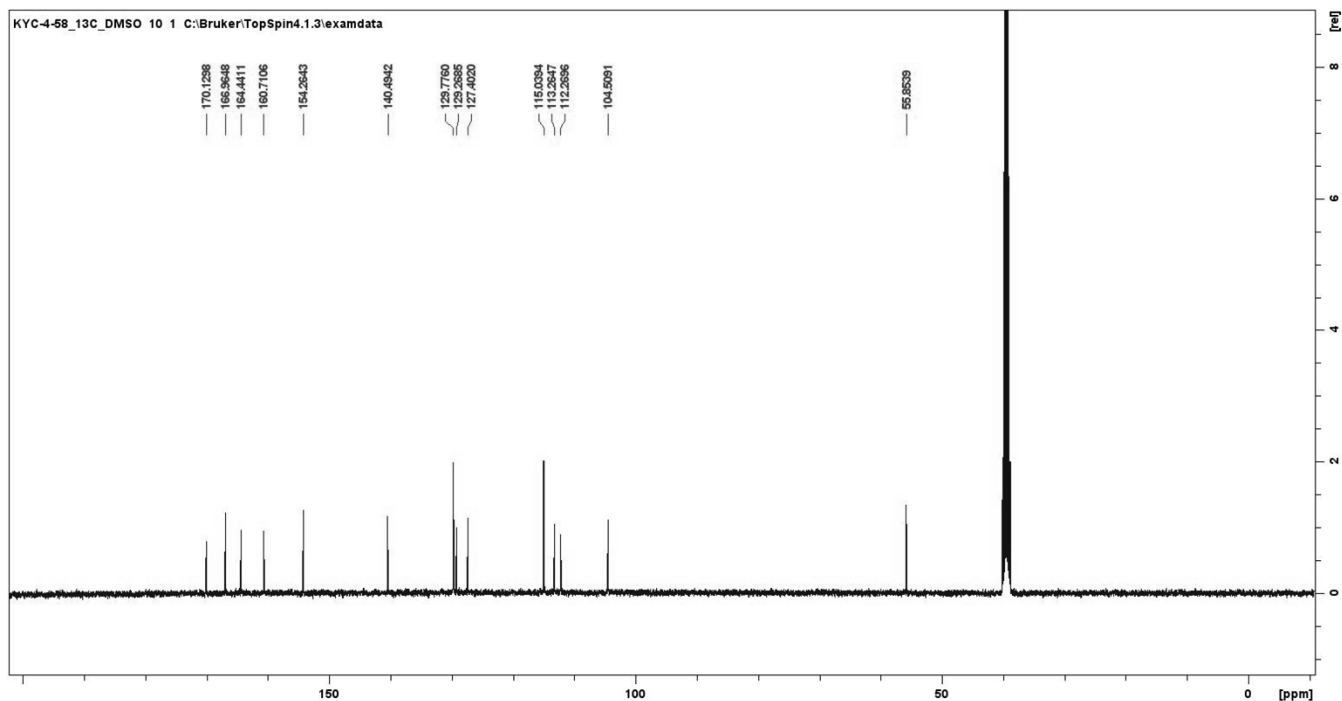
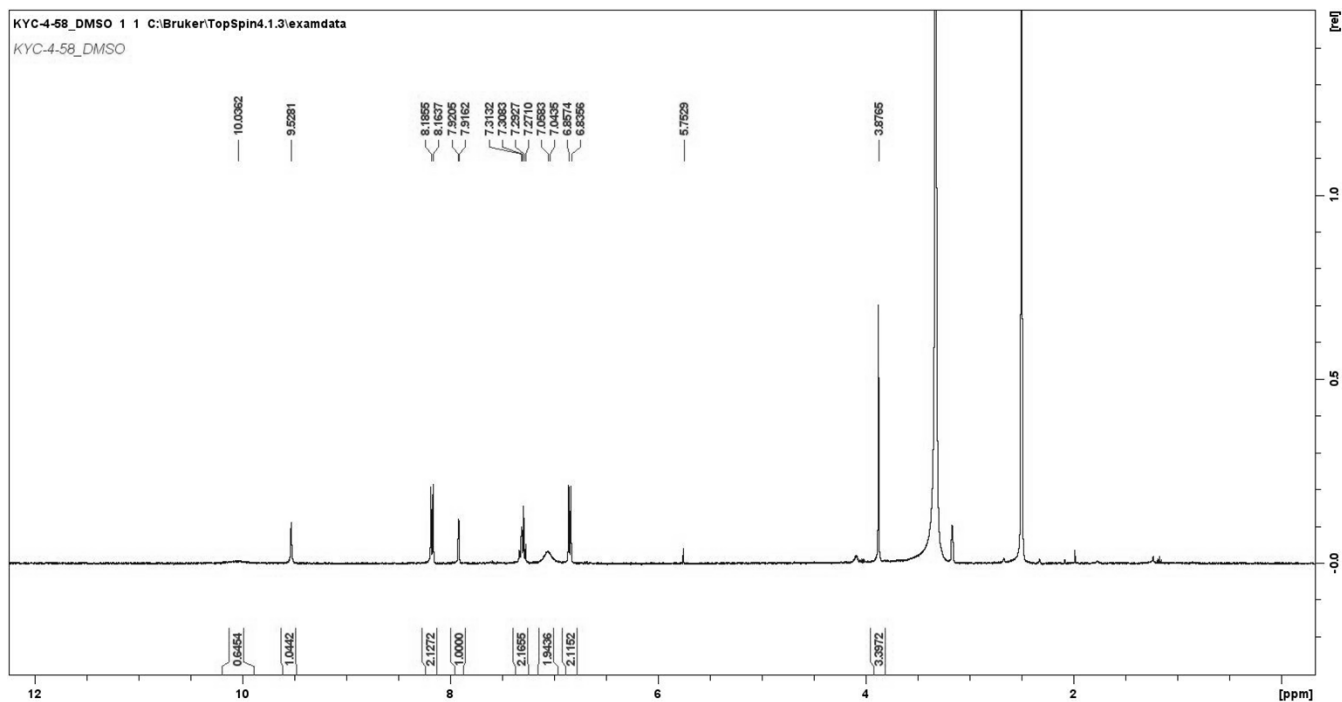
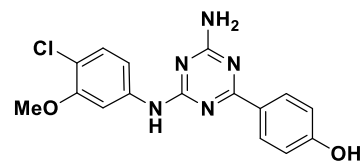
4-(4-Amino-6-((3-fluoro-4-methoxyphenyl)amino)-1,3,5-triazin-2-yl)phenol (**9a**)



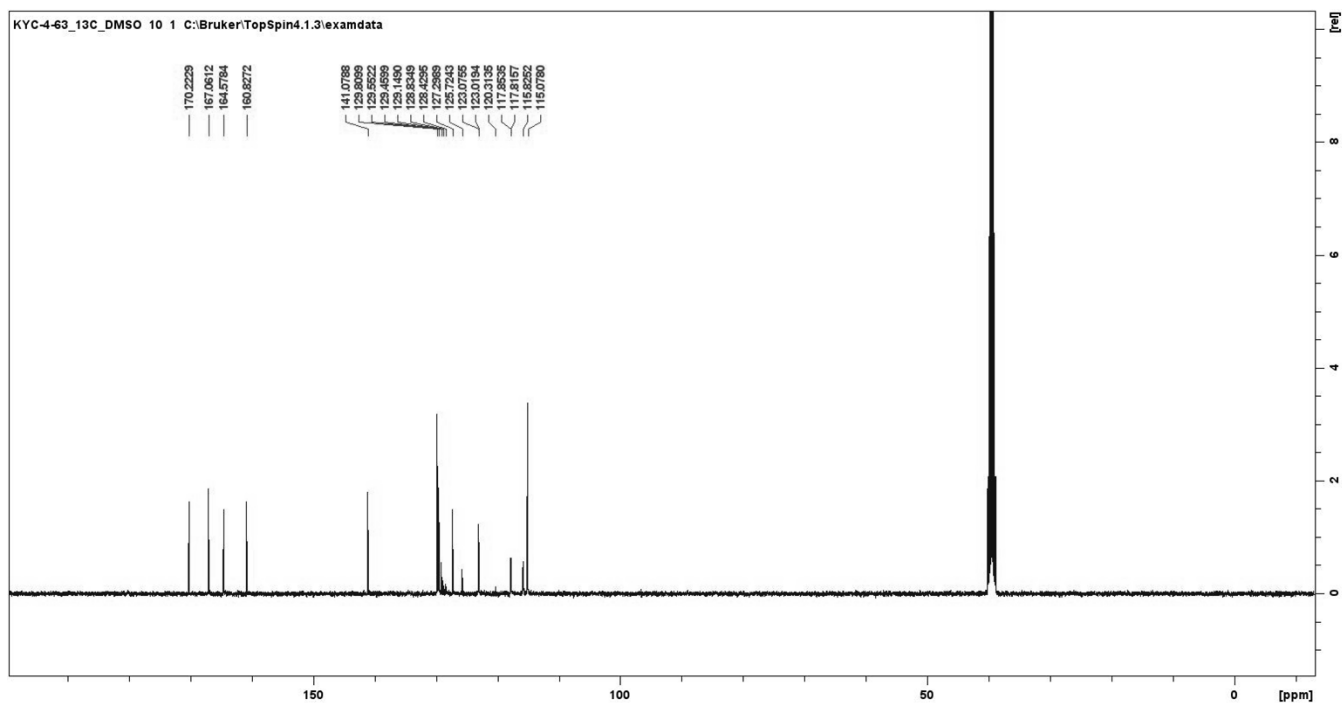
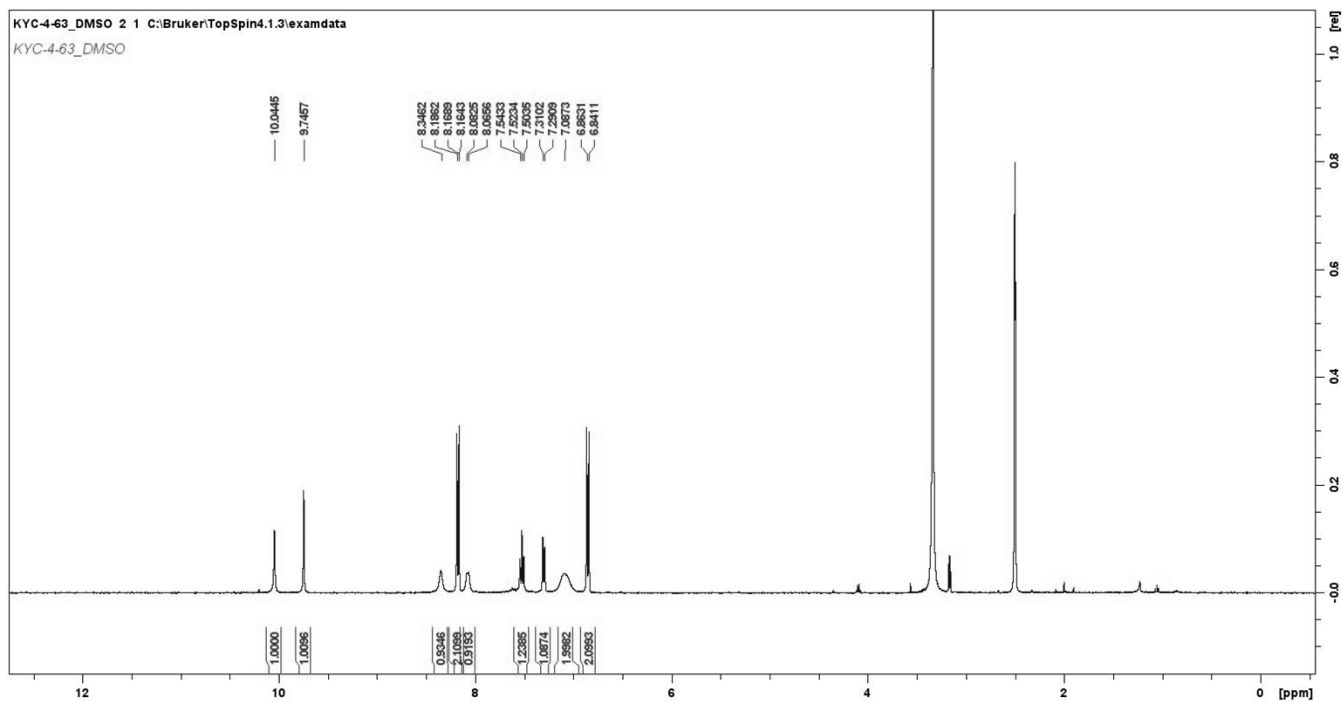
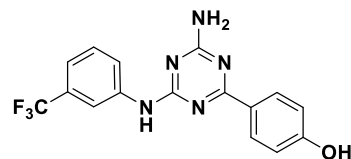
4-(4-Amino-6-((3,5-dimethoxyphenyl)amino)-1,3,5-triazin-2-yl)phenol (**9b**)



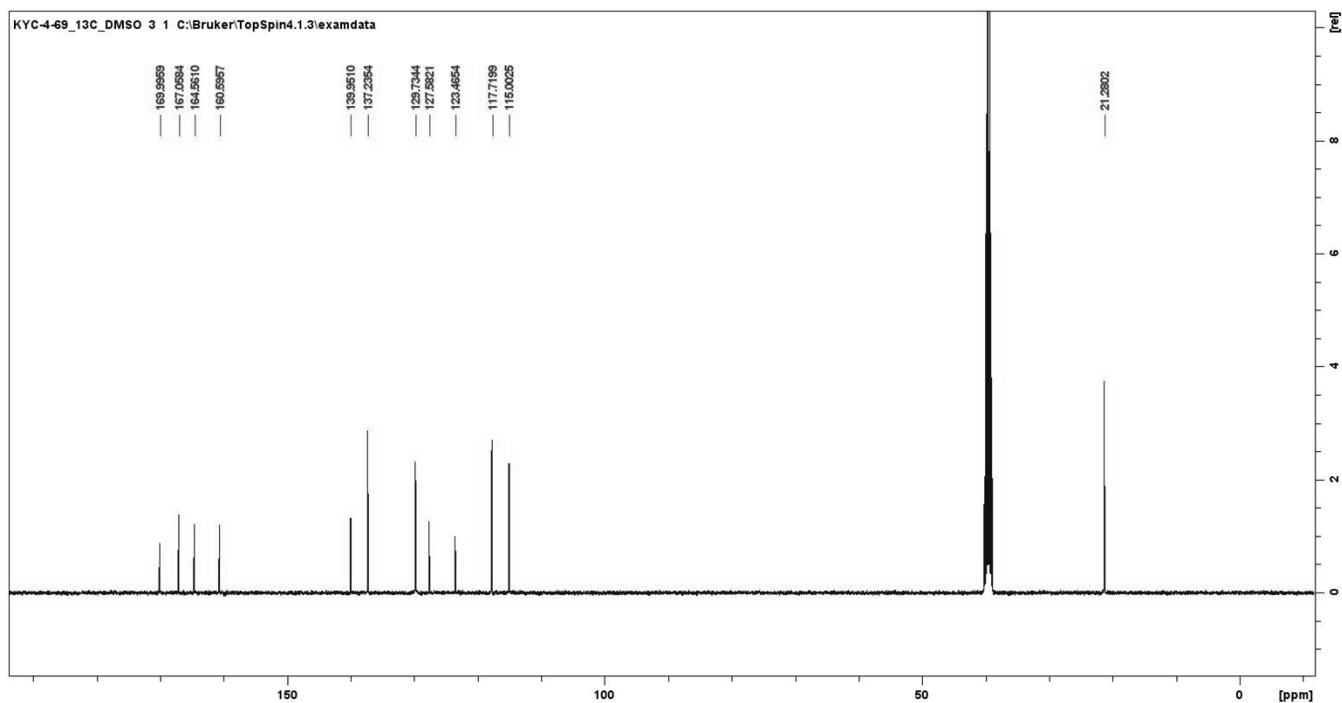
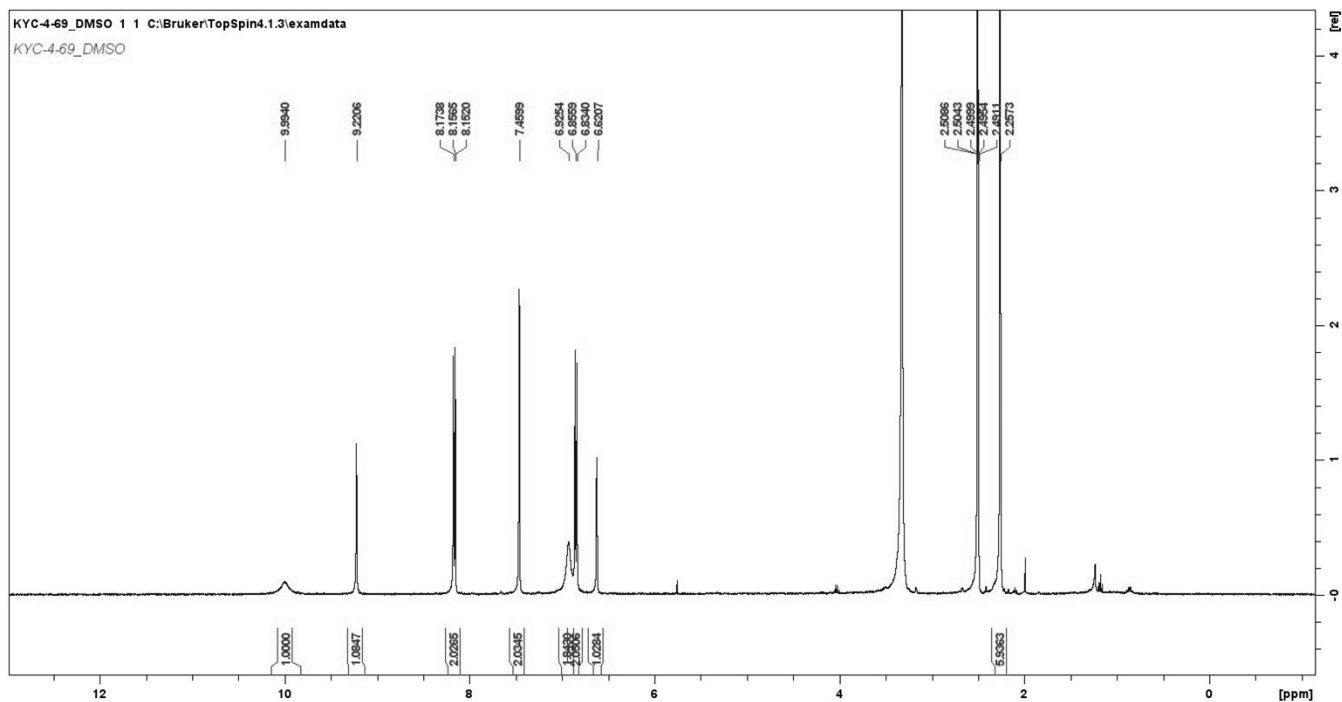
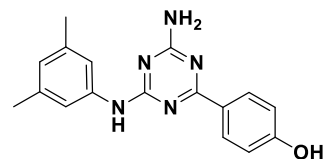
4-(4-Amino-6-((4-chloro-3-methoxyphenyl)amino)-1,3,5-triazin-2-yl)phenol (**9c**)



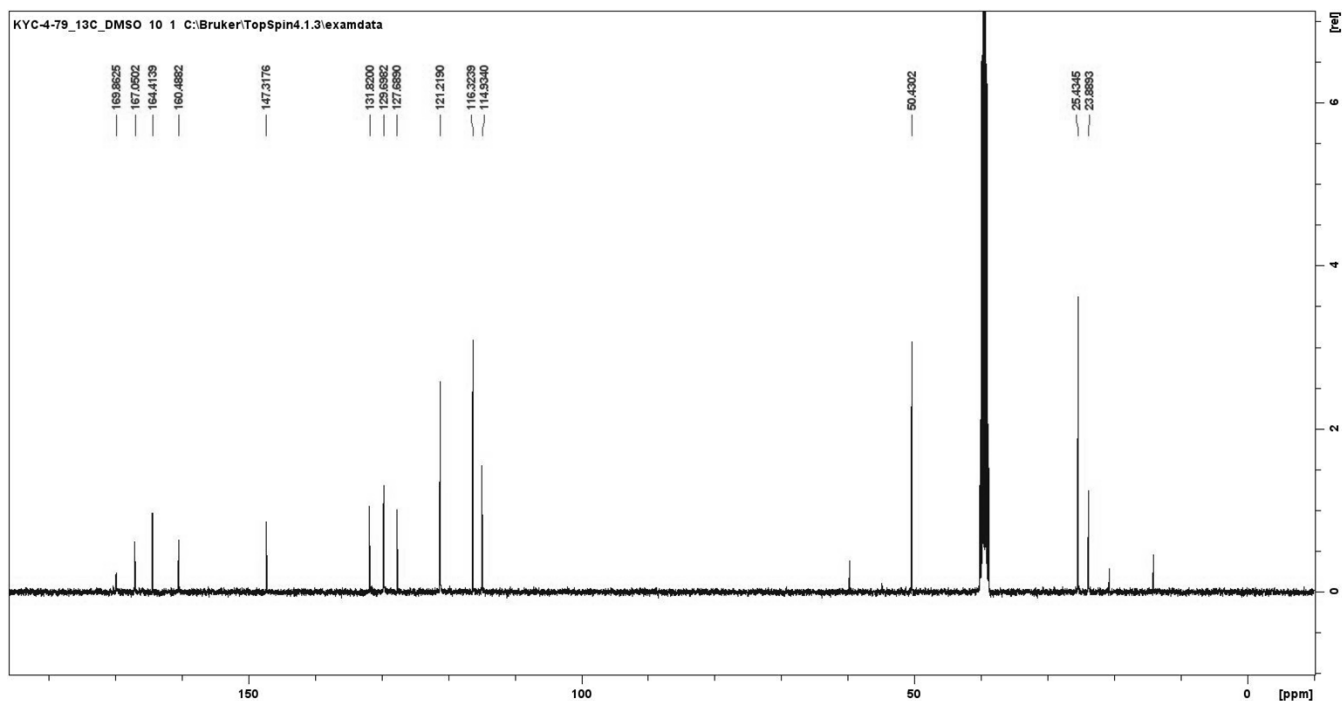
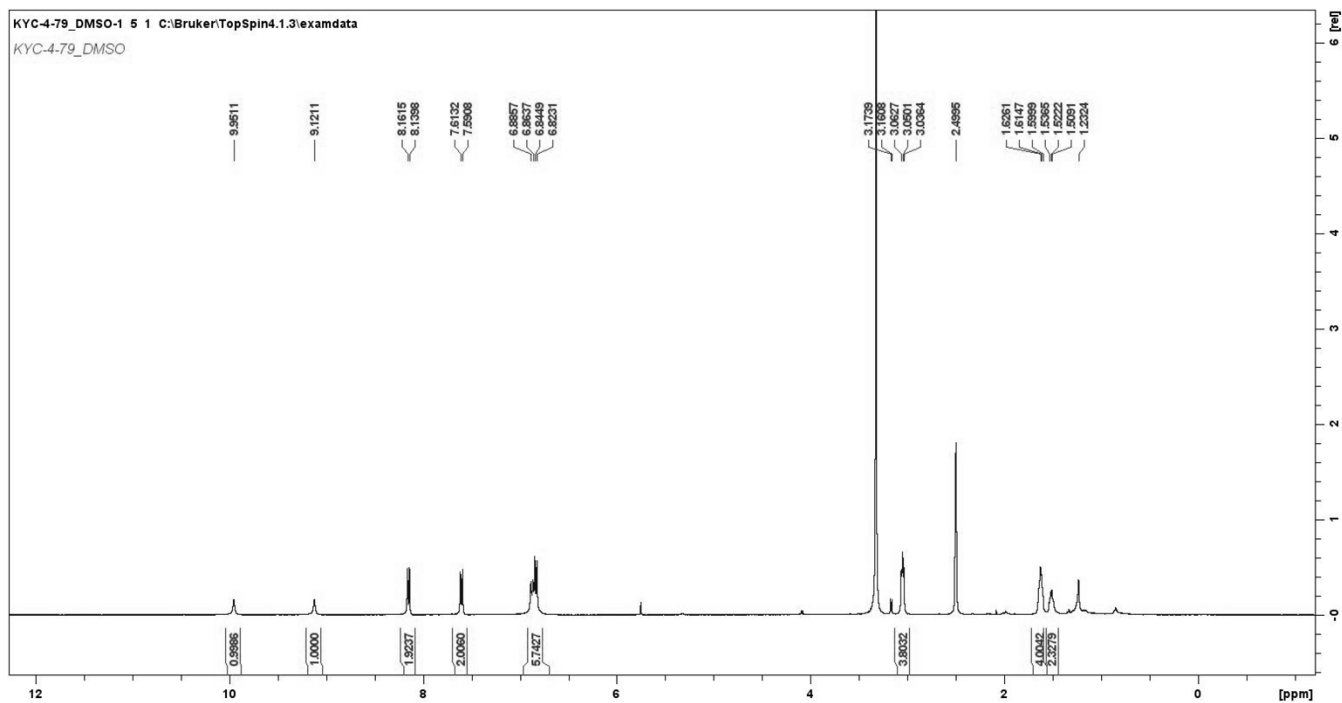
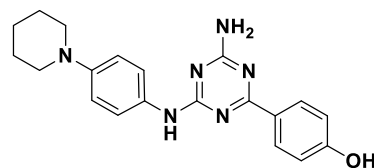
4-(4-Amino-6-((3-(trifluoromethyl)phenyl)amino)-1,3,5-triazin-2-yl)phenol (**9d**)



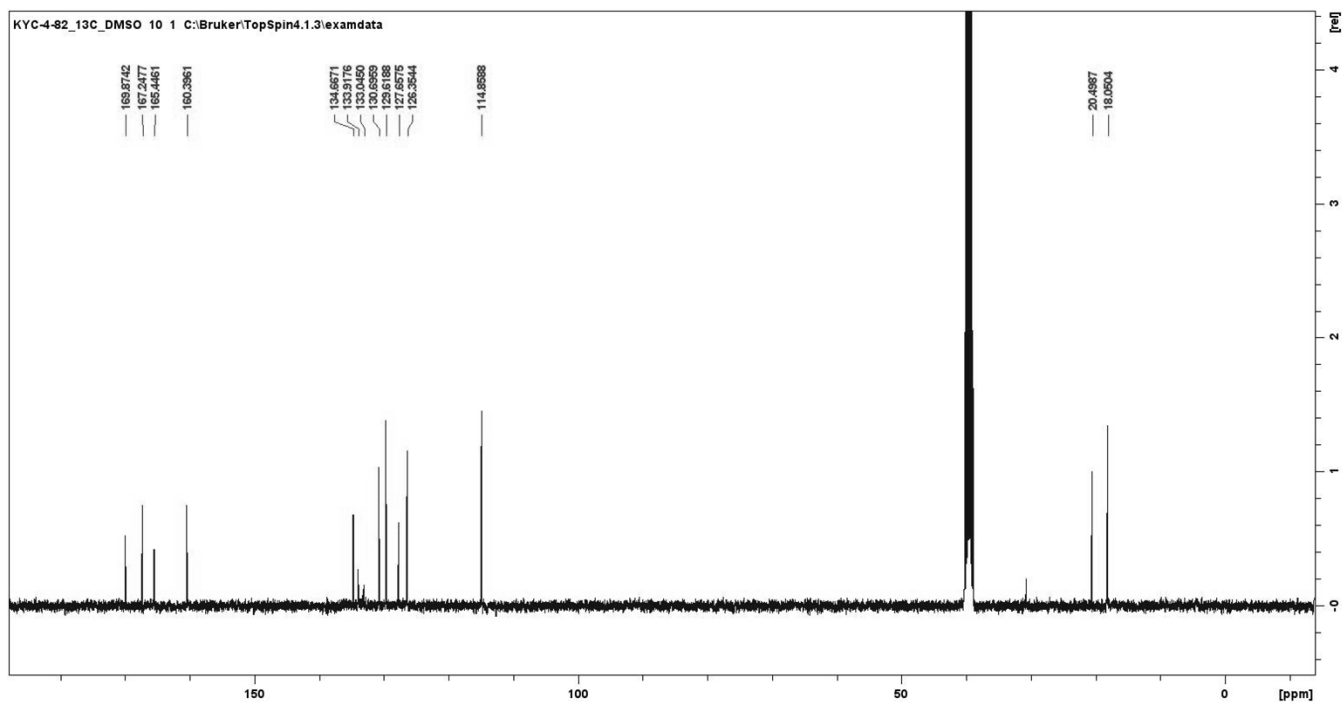
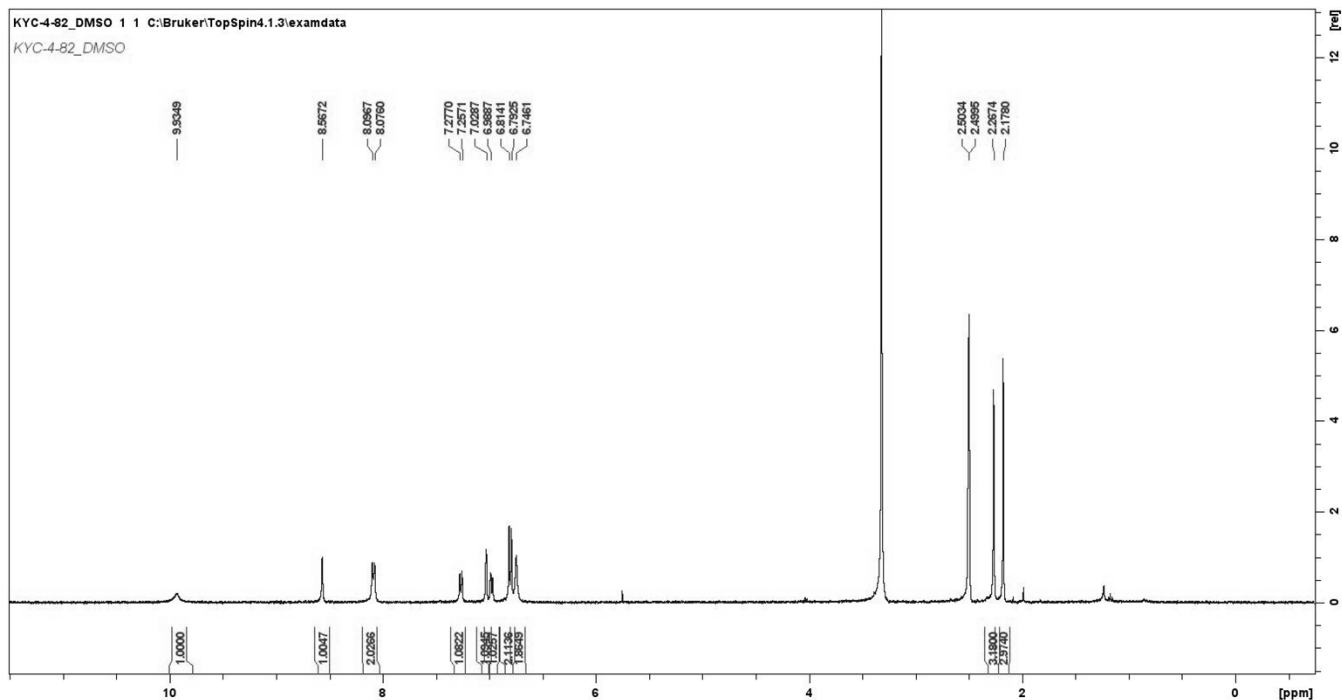
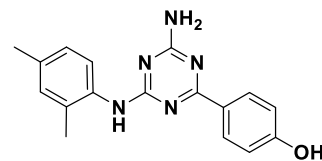
4-(4-Amino-6-((3,5-dimethylphenyl)amino)-1,3,5-triazin-2-yl)phenol (**9e**)



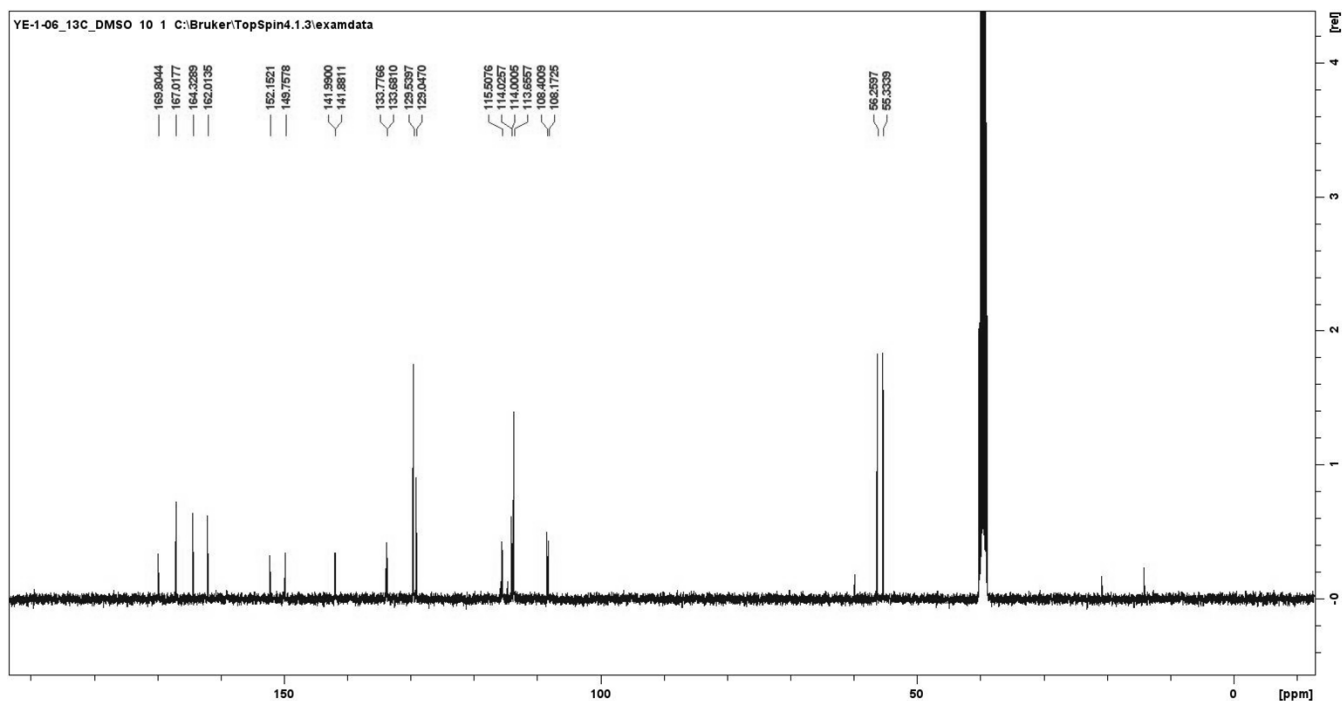
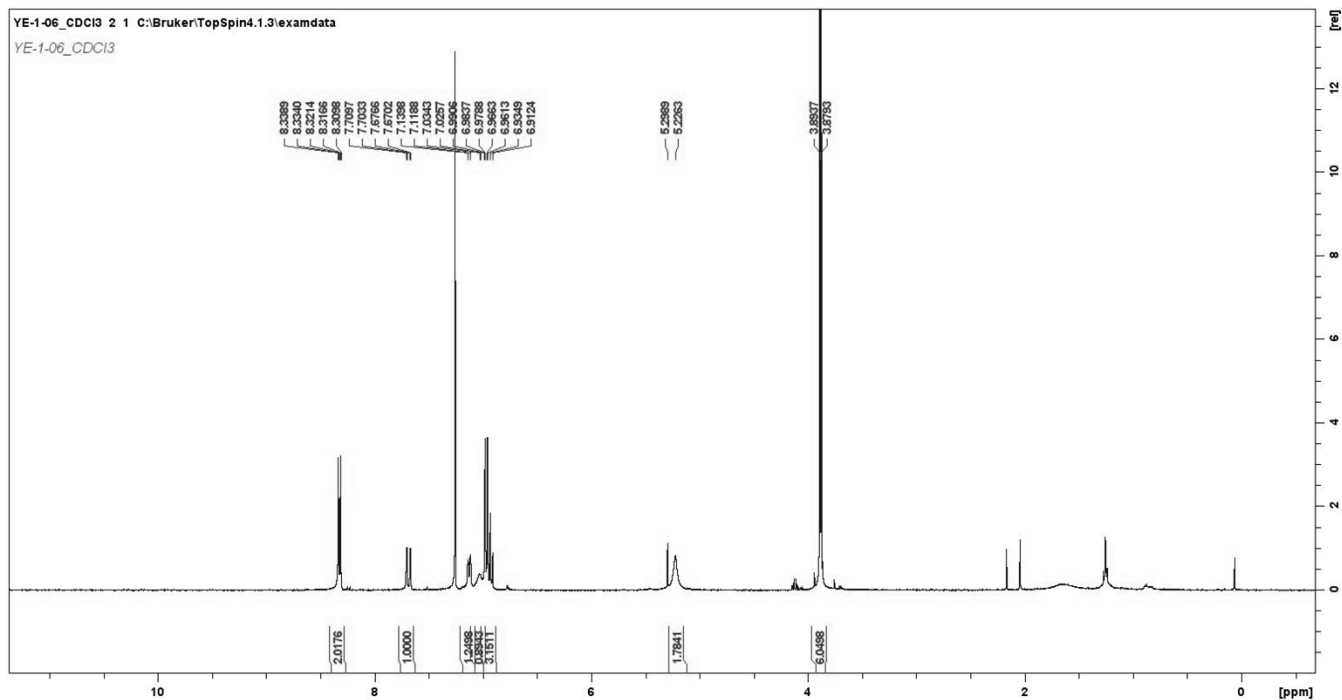
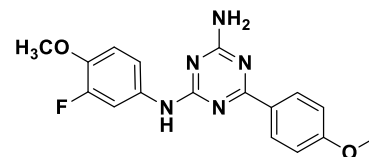
4-(4-Amino-6-((4-(piperidin-1-yl)phenyl)amino)-1,3,5-triazin-2-yl)phenol (**9f**)



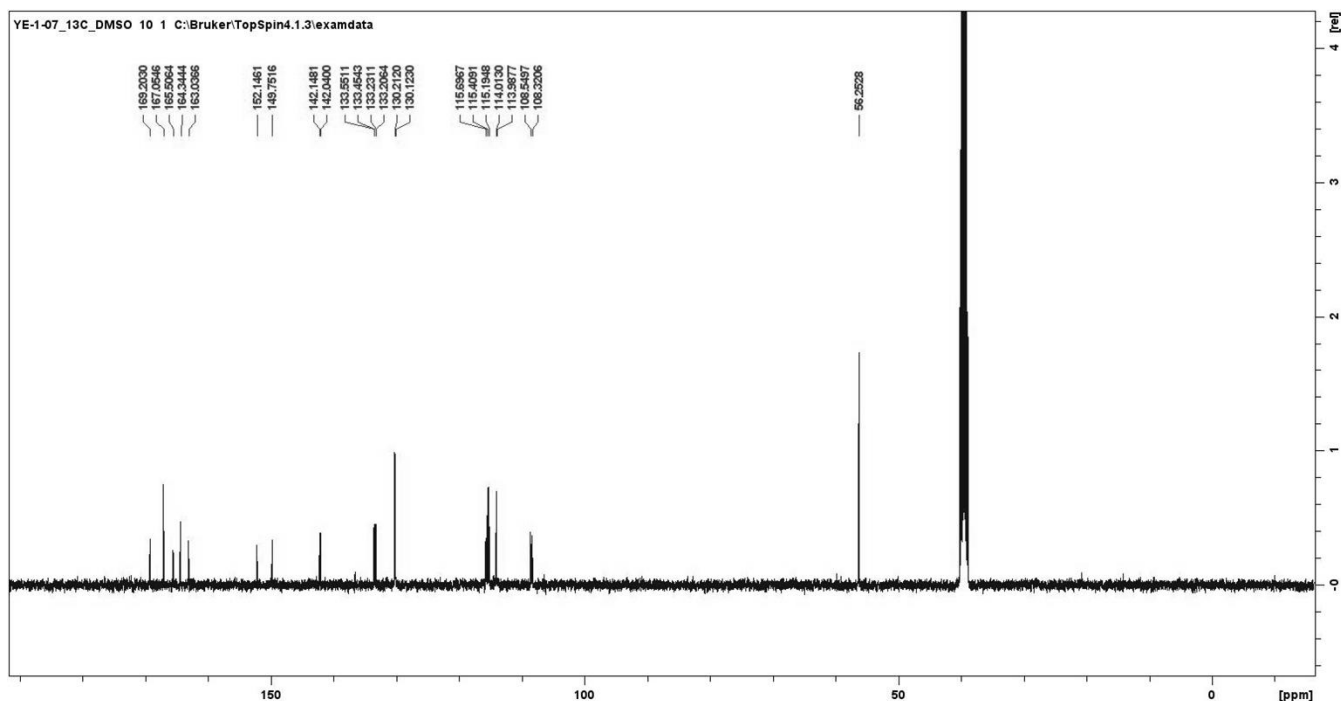
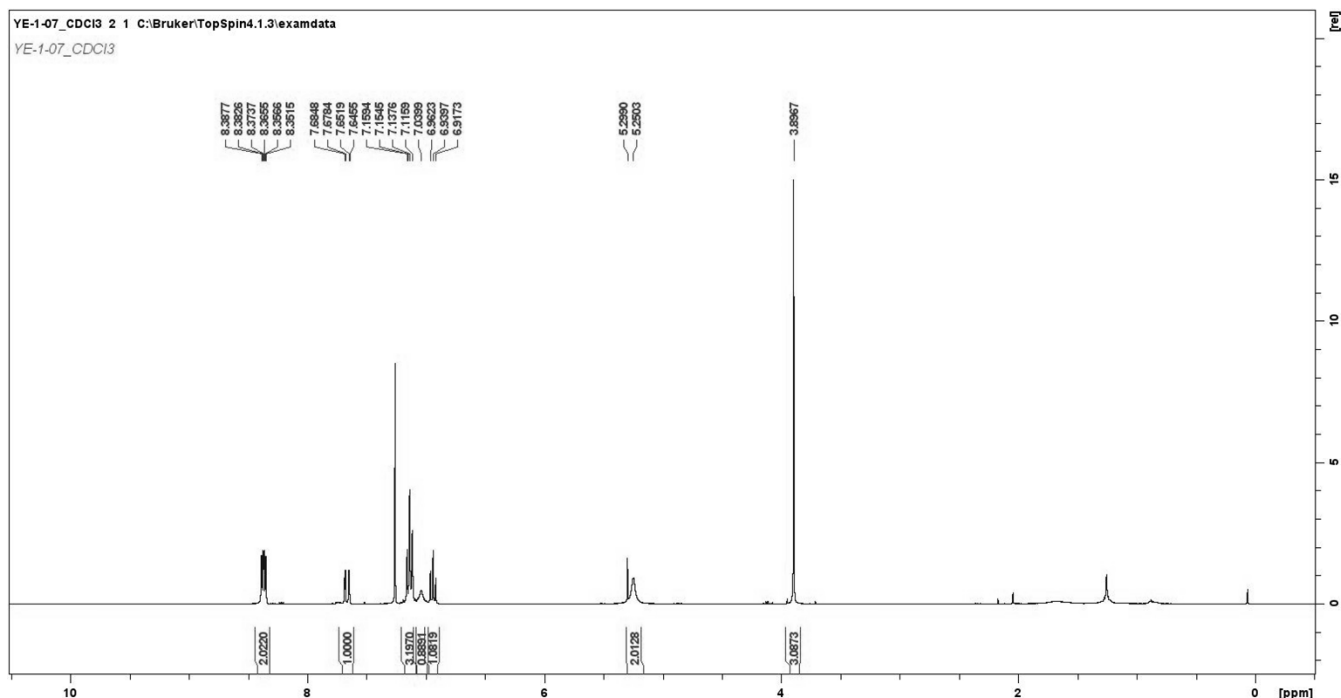
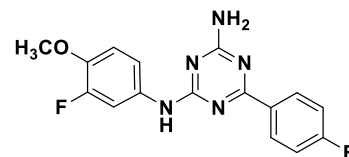
4-(4-Amino-6-((2,4-dimethylphenyl)amino)-1,3,5-triazin-2-yl)phenol (**9g**)



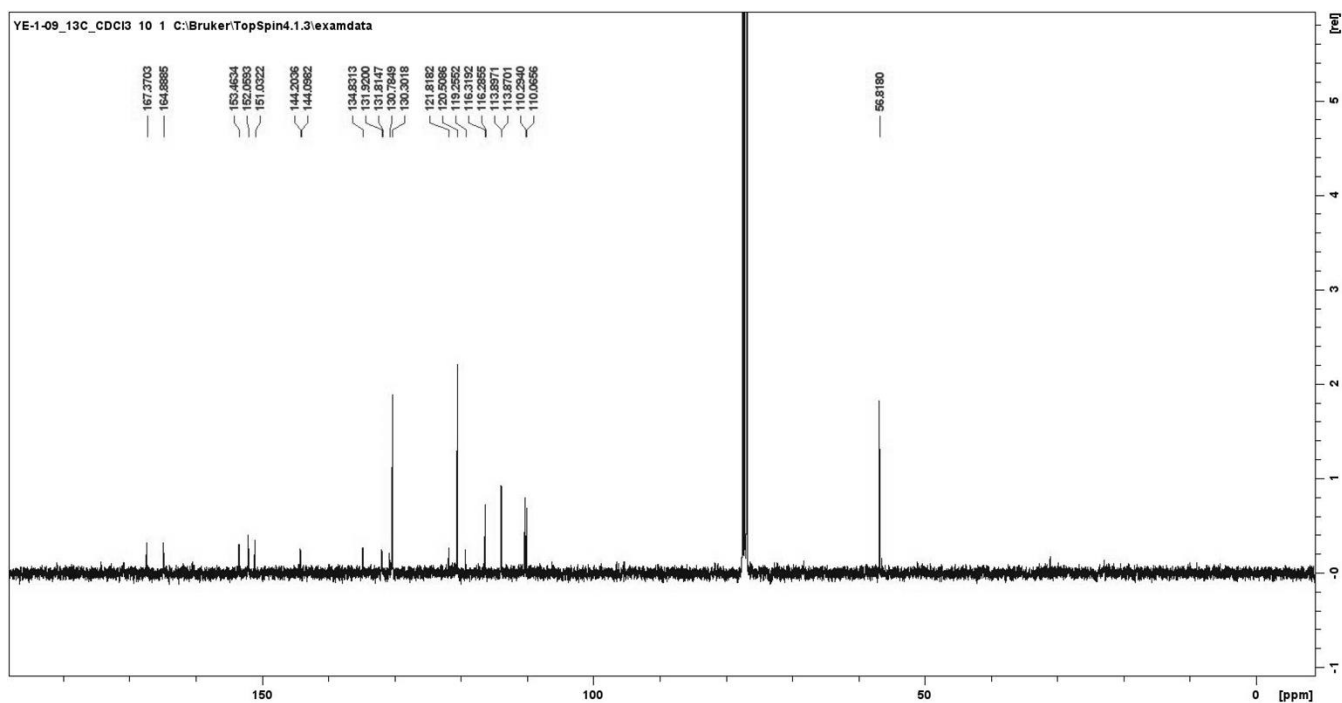
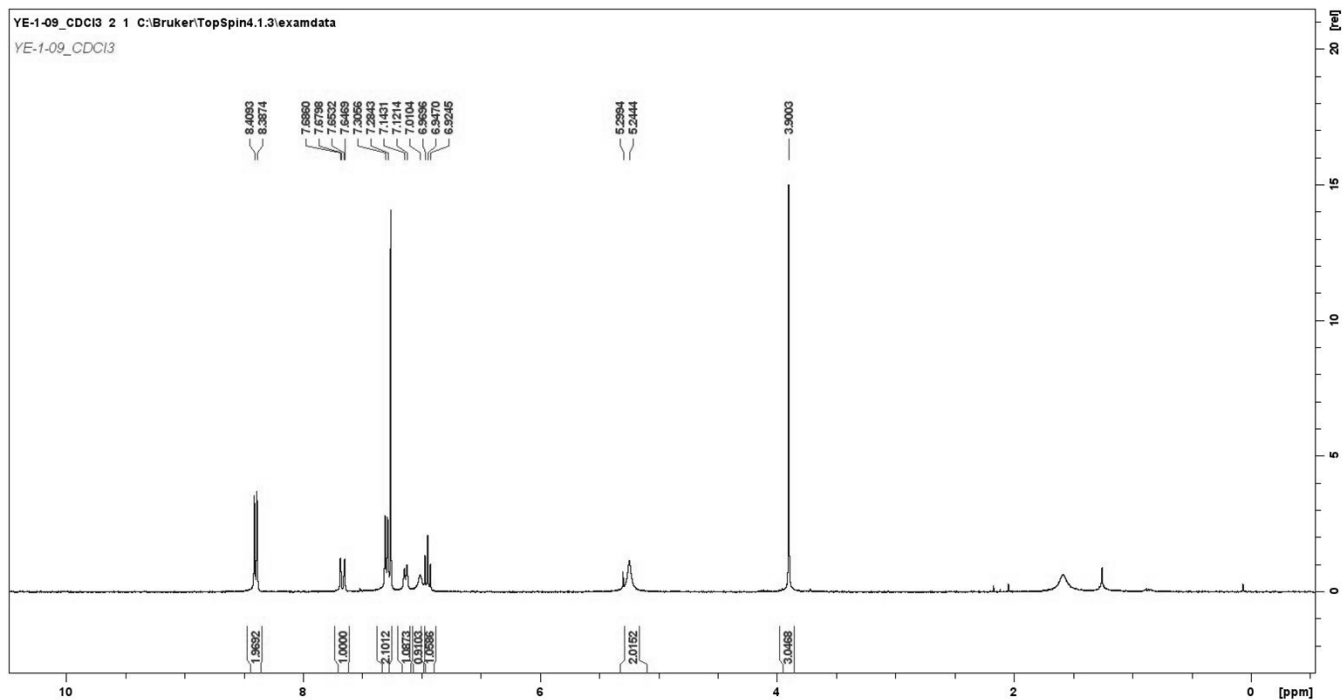
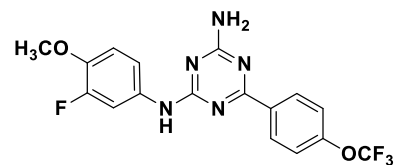
N^2 -(3-Fluoro-4-methoxyphenyl)-6-(4-methoxyphenyl)-1,3,5-triazine-2,4-diamine (**11a**)



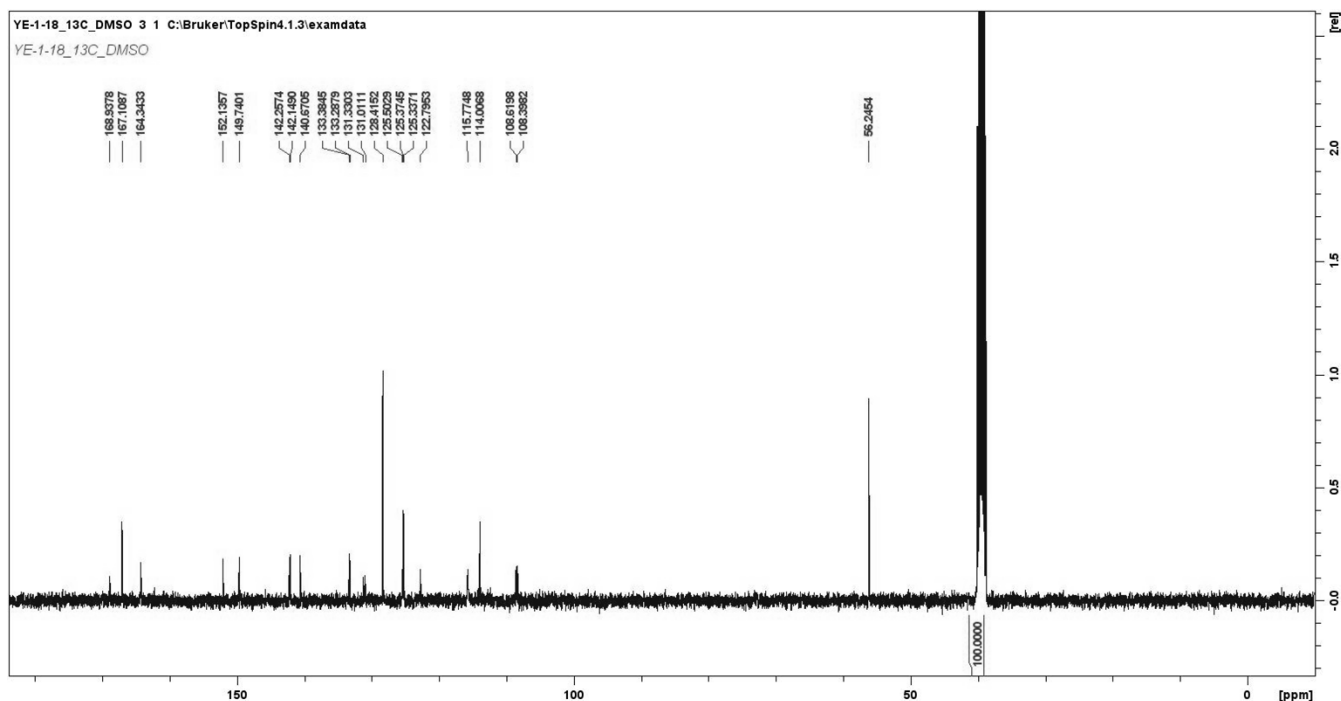
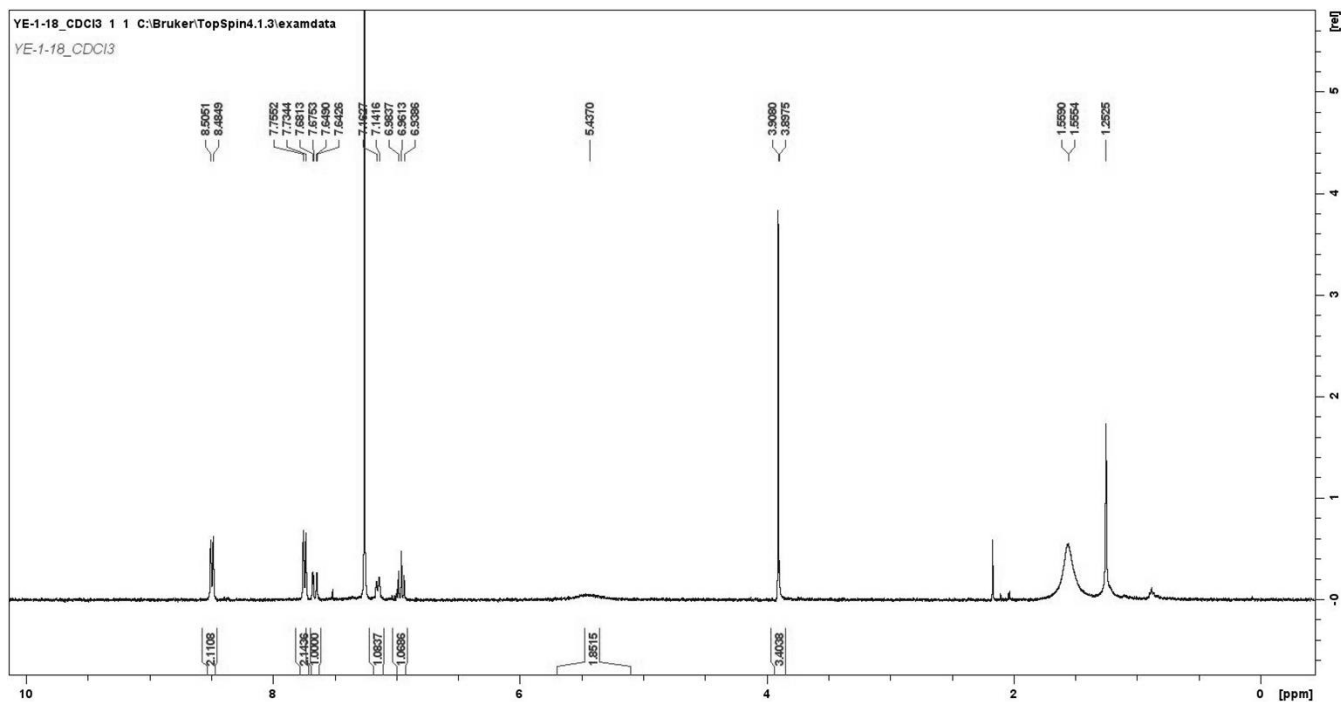
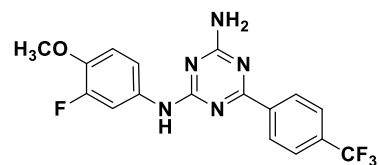
N^2 -(3-Fluoro-4-methoxyphenyl)-6-(4-fluorophenyl)-1,3,5-triazine-2,4-diamine (**11b**)



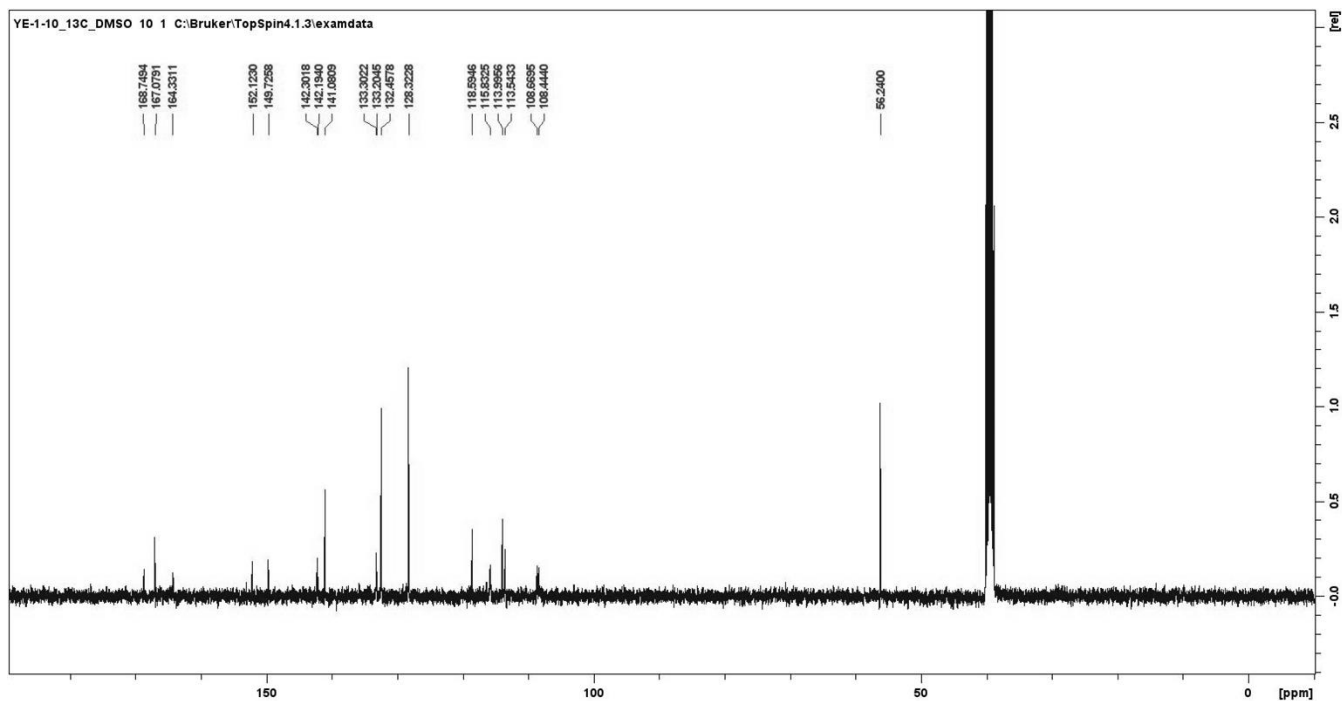
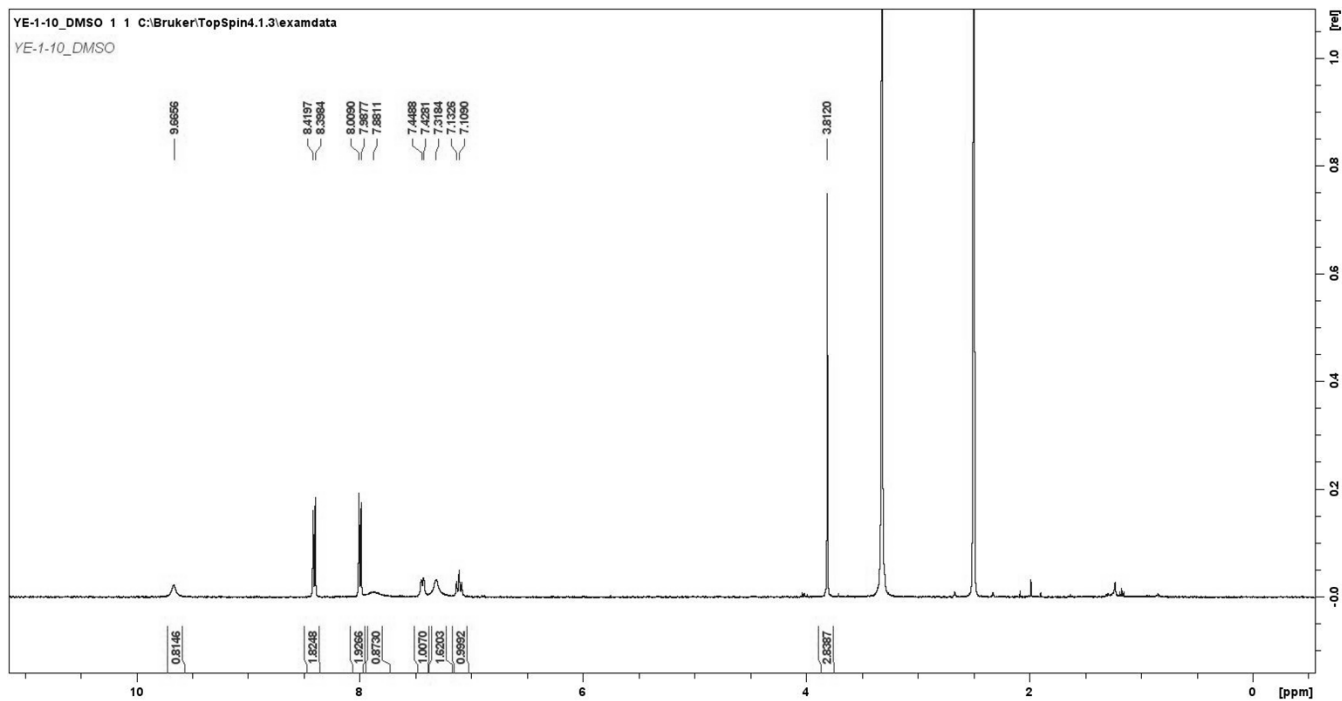
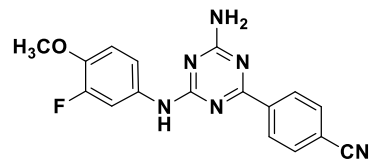
N^2 -(3-Fluoro-4-methoxyphenyl)-6-(4-(trifluoromethoxy)phenyl)-1,3,5-triazine-2,4-diamine (**11c**)



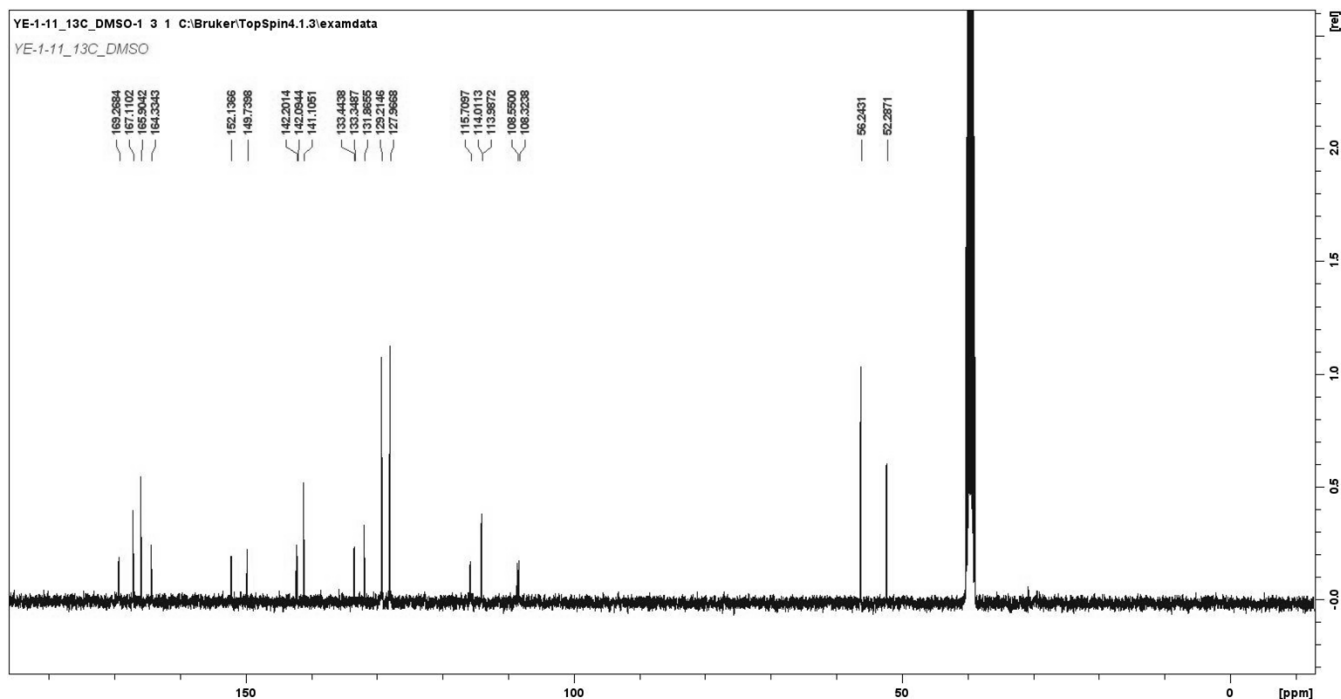
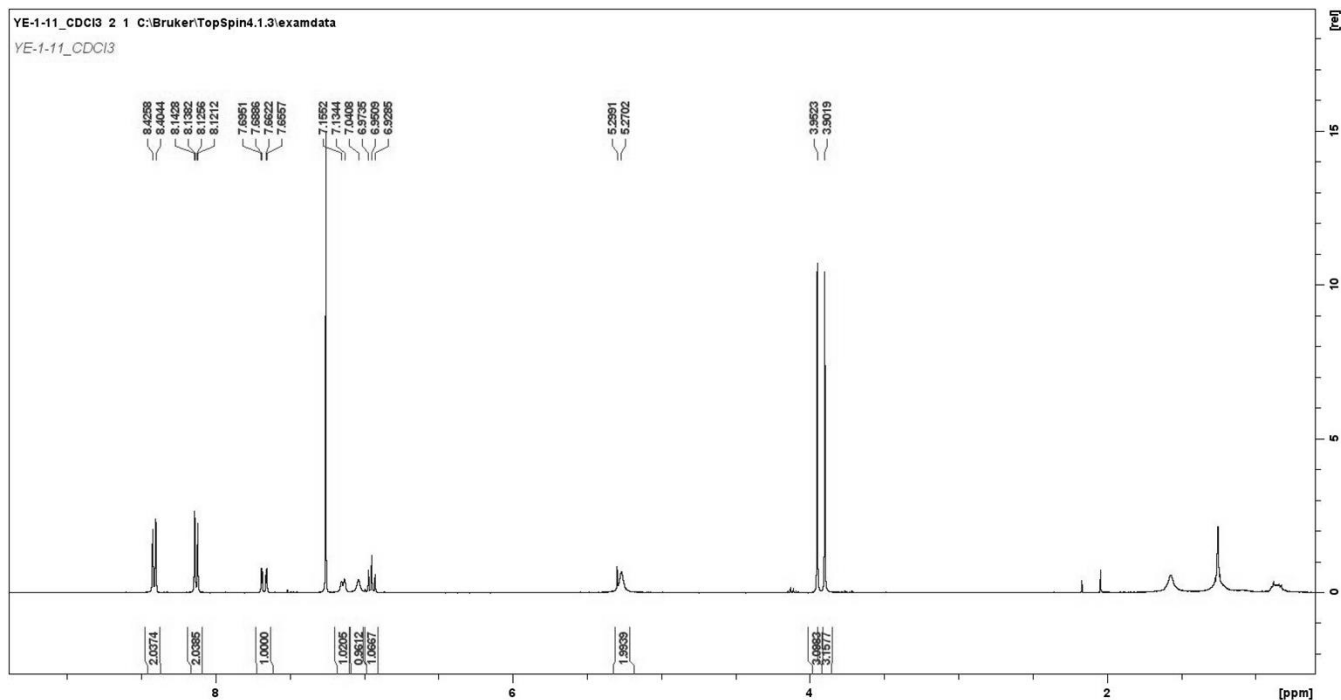
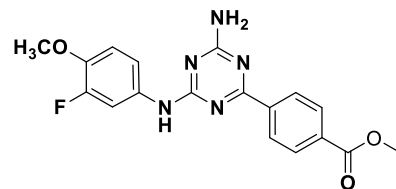
N^2 -(3-Fluoro-4-methoxyphenyl)-6-(4-(trifluoromethyl)phenyl)-1,3,5-triazine-2,4-diamine (**11d**)



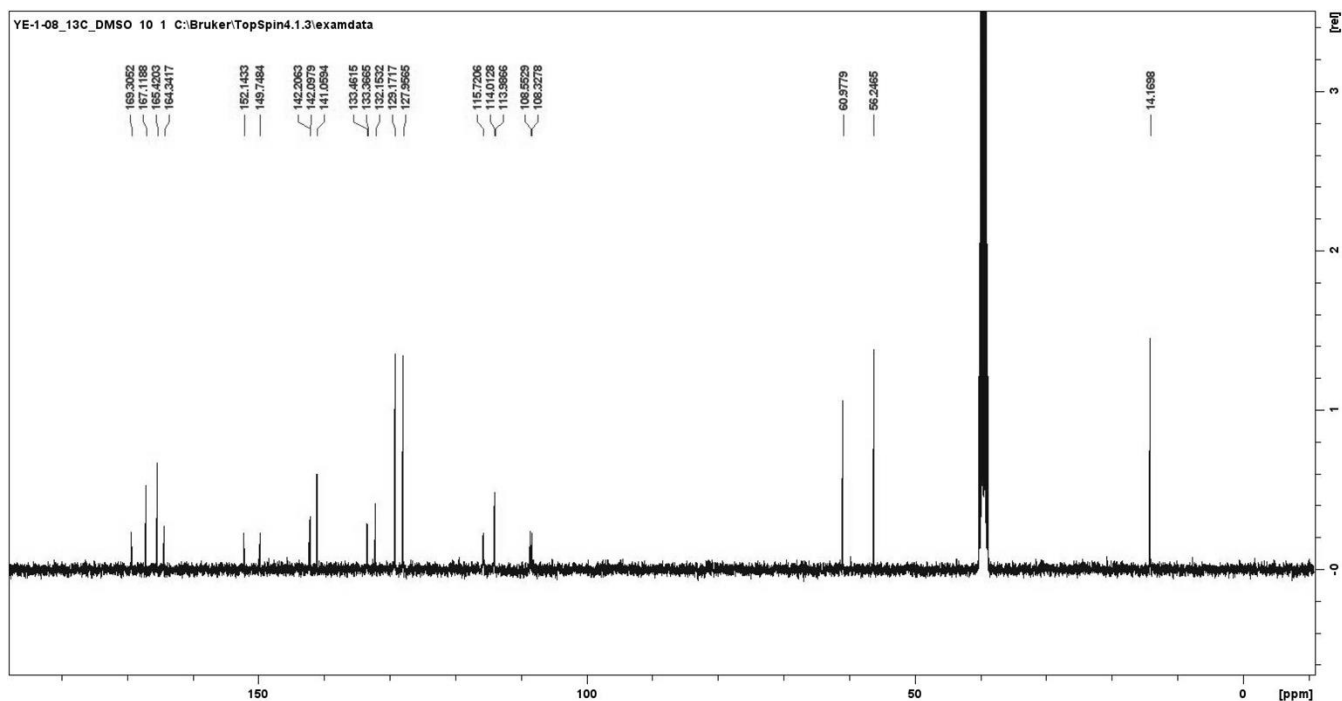
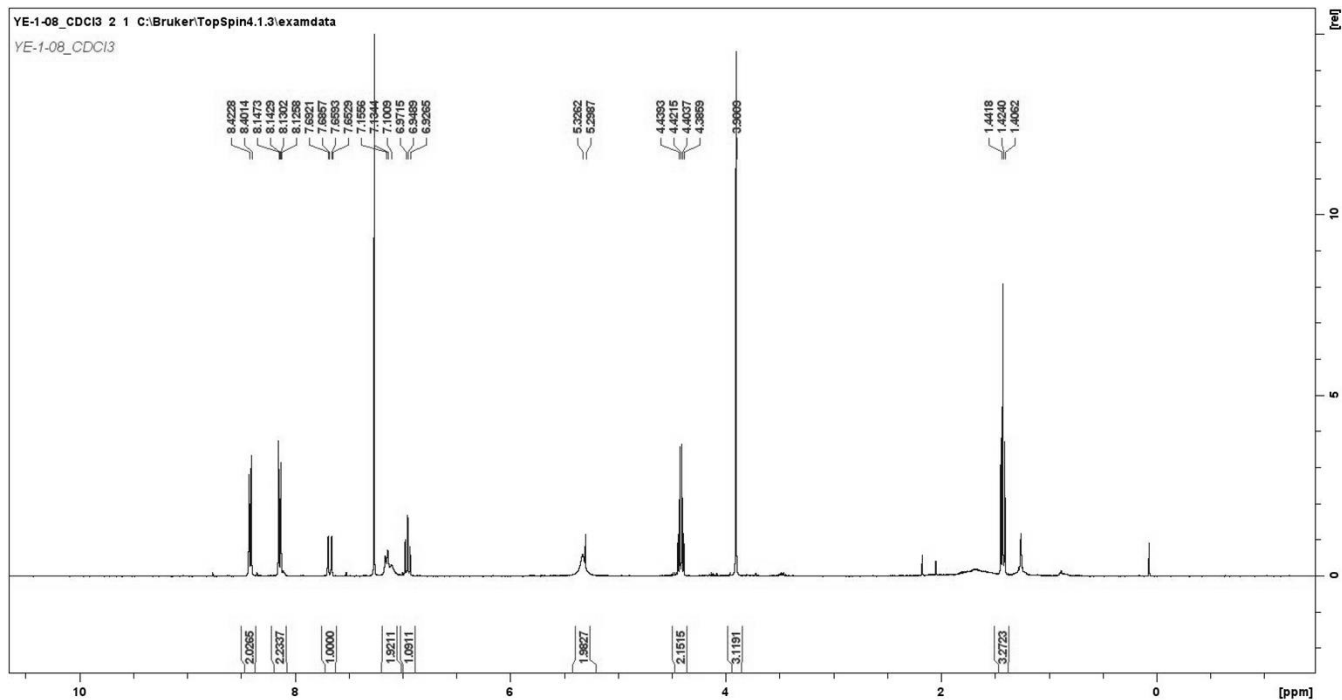
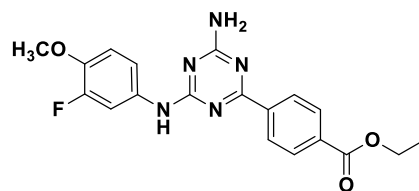
4-(4-Amino-6-((3-fluoro-4-methoxyphenyl)amino)-1,3,5-triazin-2-yl)benzonitrile (**11e**)



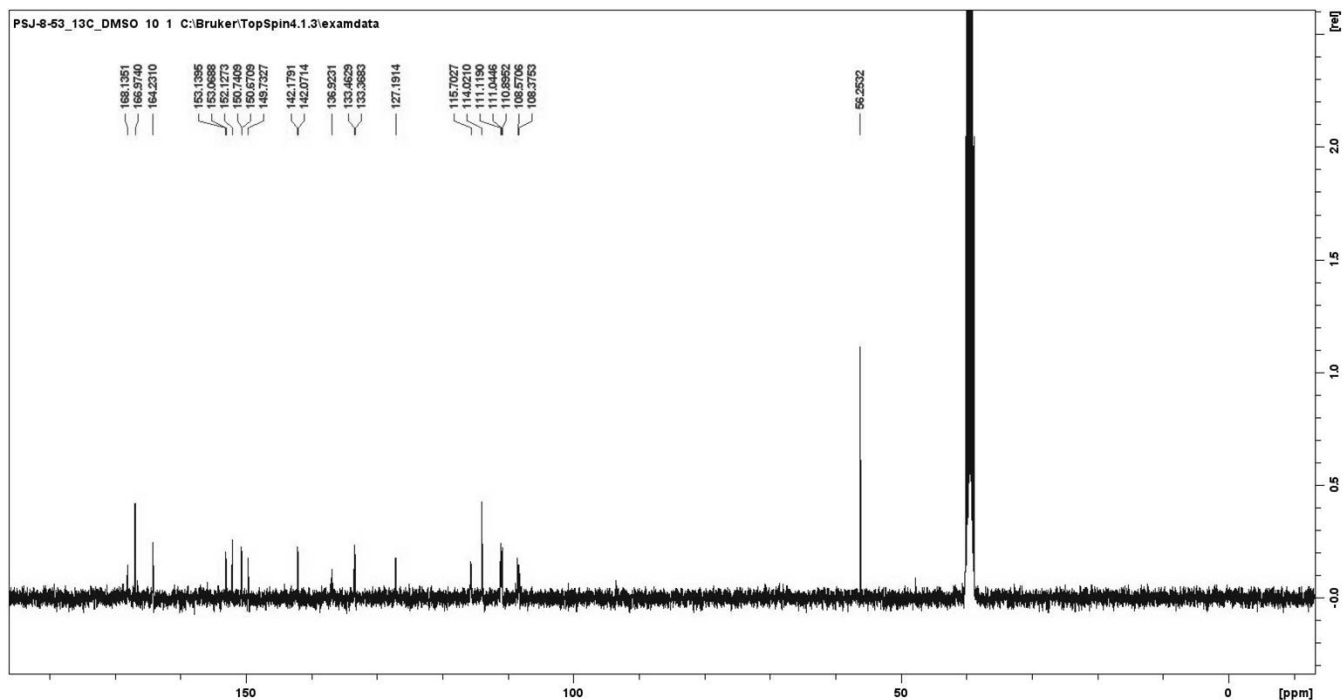
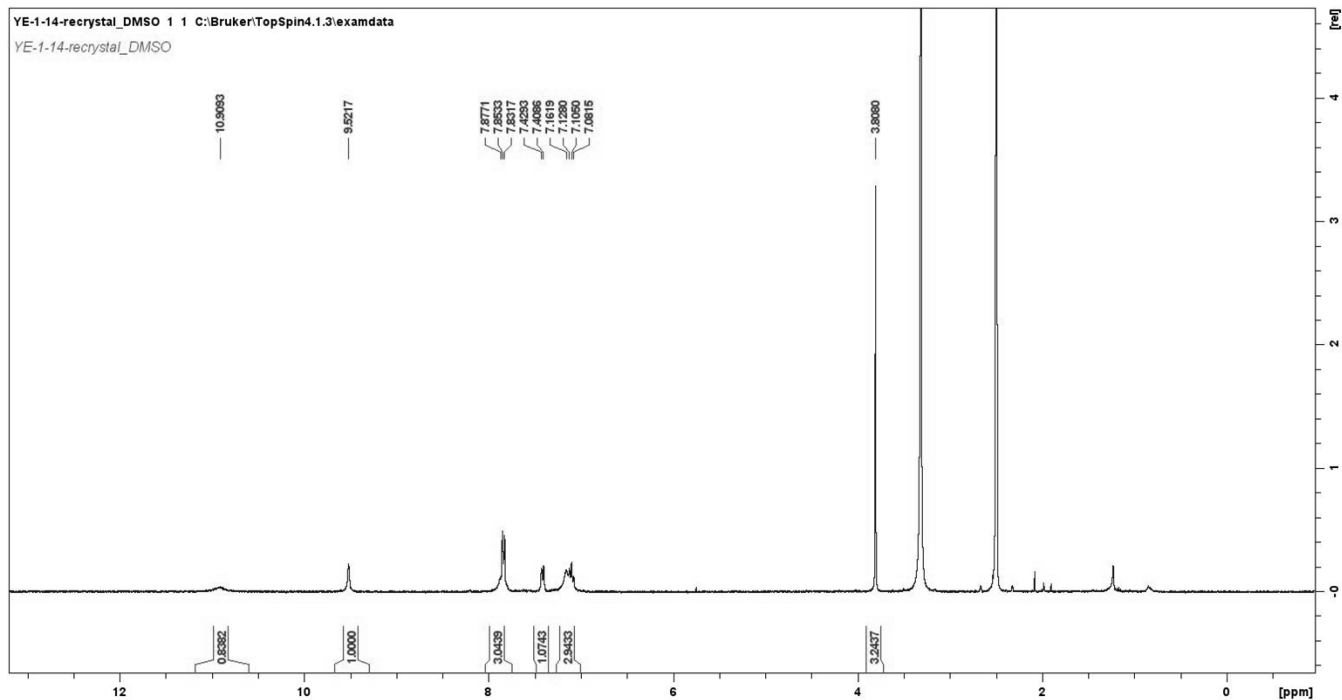
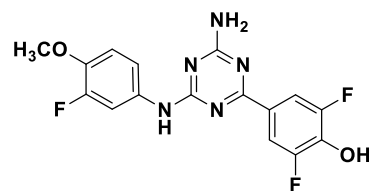
Methyl 4-(4-Amino-6-((3-fluoro-4-methoxyphenyl)amino)-1,3,5-triazin-2-yl)benzoate (**11f**)



Ethyl 4-(4-Amino-6-((3-fluoro-4-methoxyphenyl)amino)-1,3,5-triazin-2-yl)benzoate (**11g**)



4-(4-Amino-6-((3-fluoro-4-methoxyphenyl)amino)-1,3,5-triazin-2-yl)-2,6-difluorophenol (**11h**)



6-(4-Fluoro-3-nitrophenyl)-*N*²-(3-fluoro-4-methoxyphenyl)-1,3,5-triazine-2,4-diamine (**11i**)

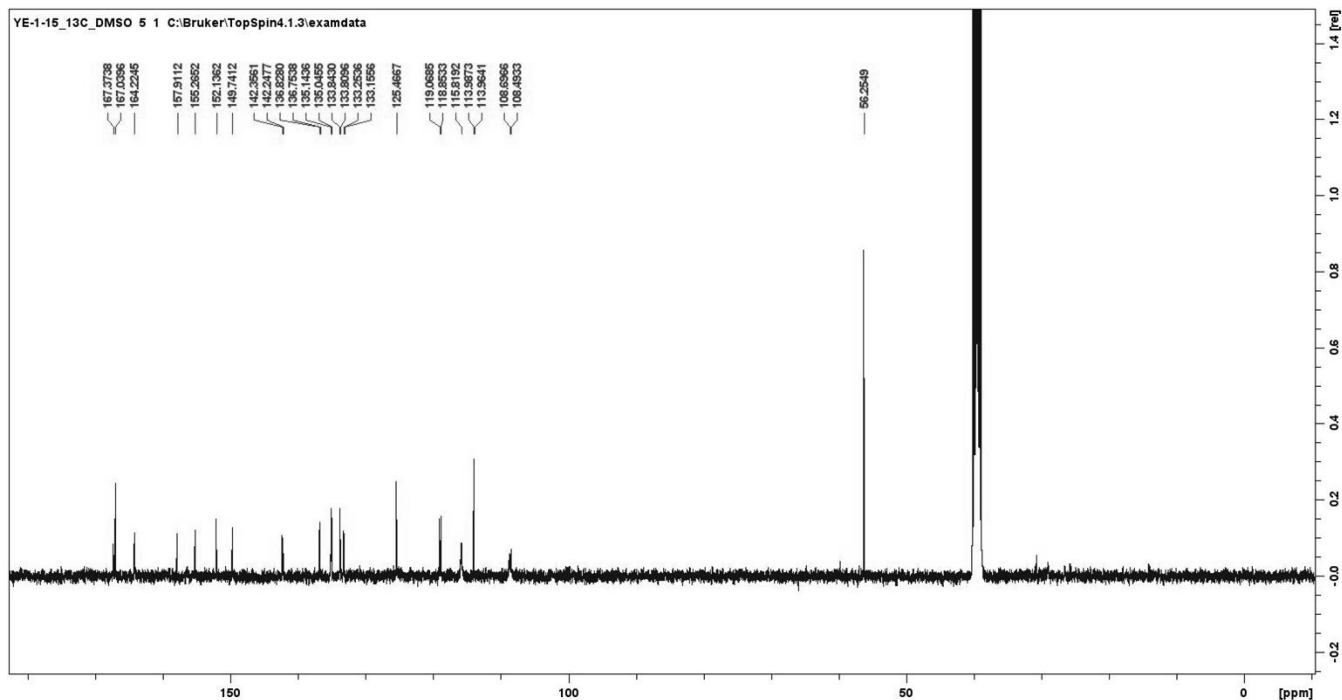
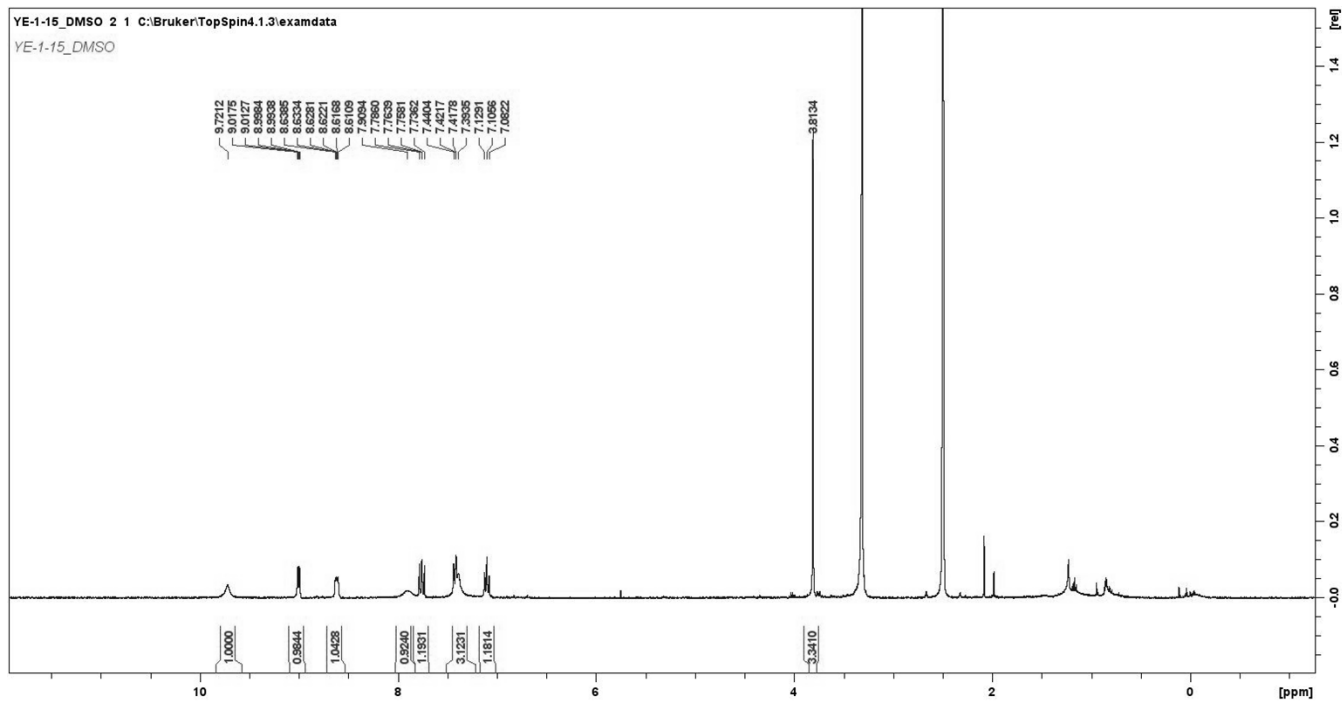
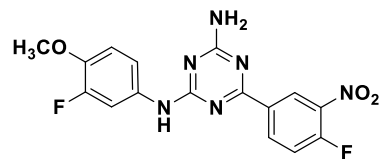
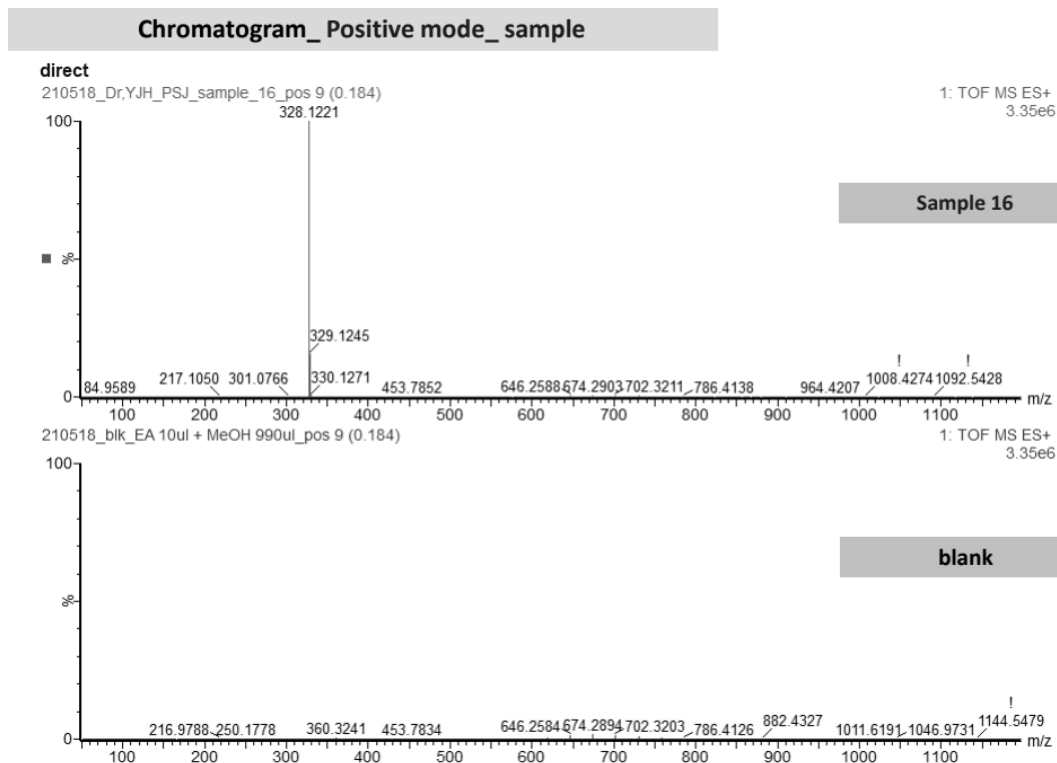
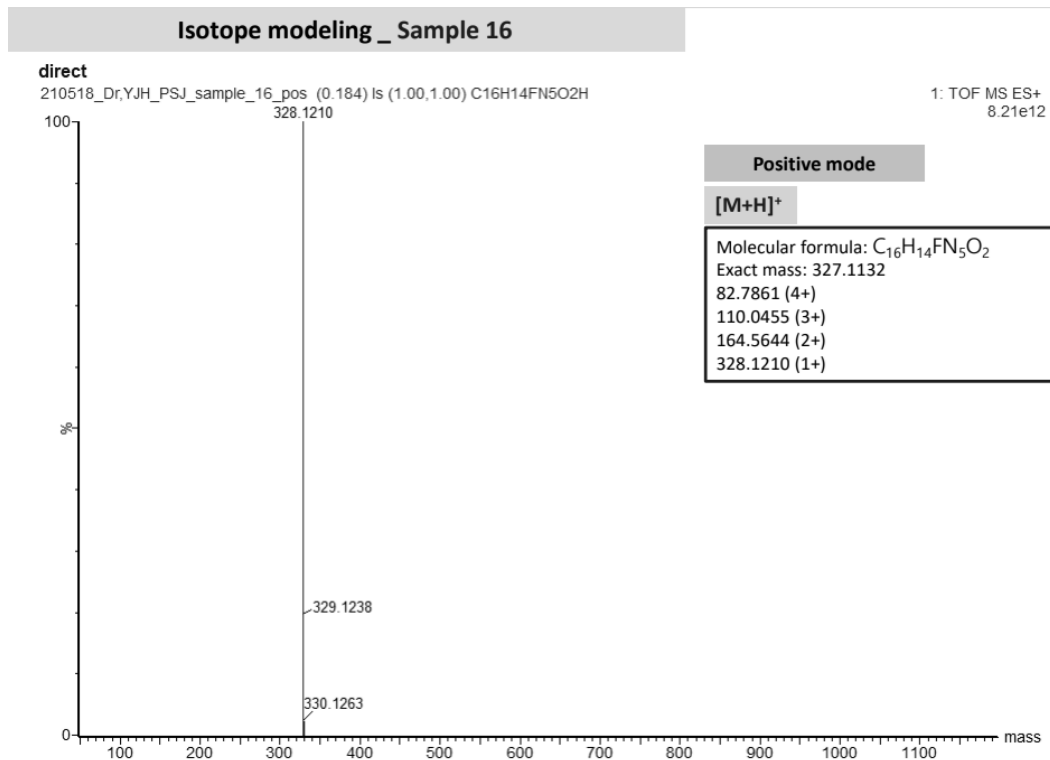
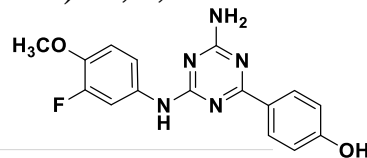
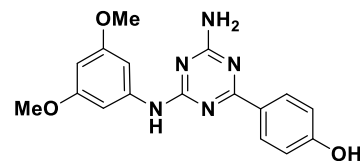


Figure S2. HR-MS Copies of Compound **9a-g** and **11a-i**

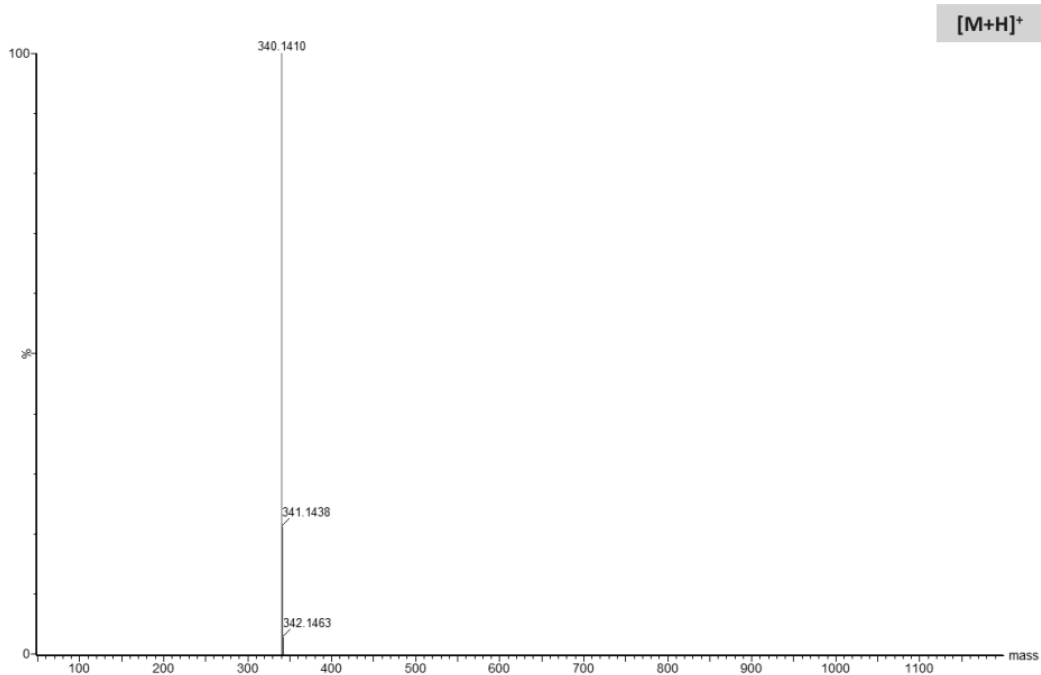
4-(4-Amino-6-((3-fluoro-4-methoxyphenyl)amino)-1,3,5-triazin-2-yl)phenol (**9a**)



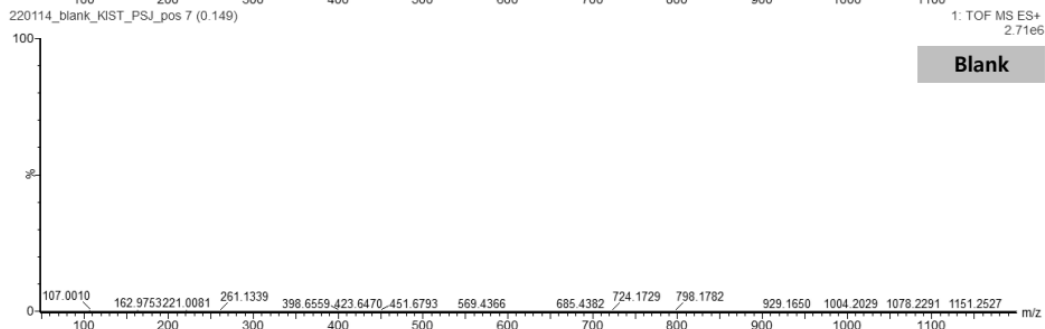
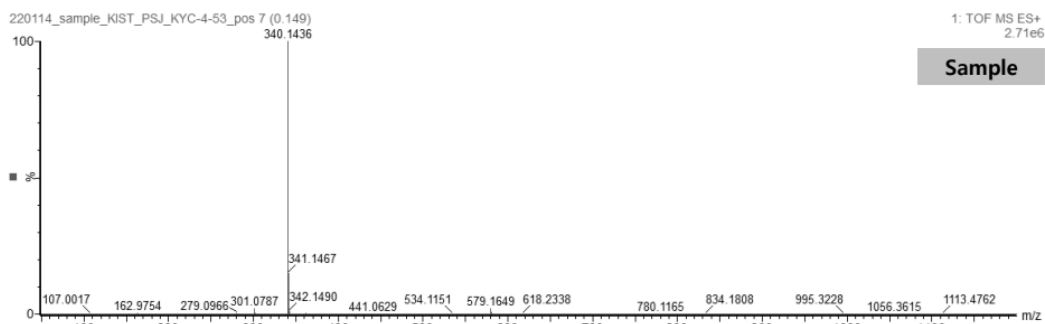
4-(4-Amino-6-((3,5-dimethoxyphenyl)amino)-1,3,5-triazin-2-yl)phenol (**9b**)



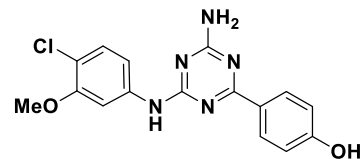
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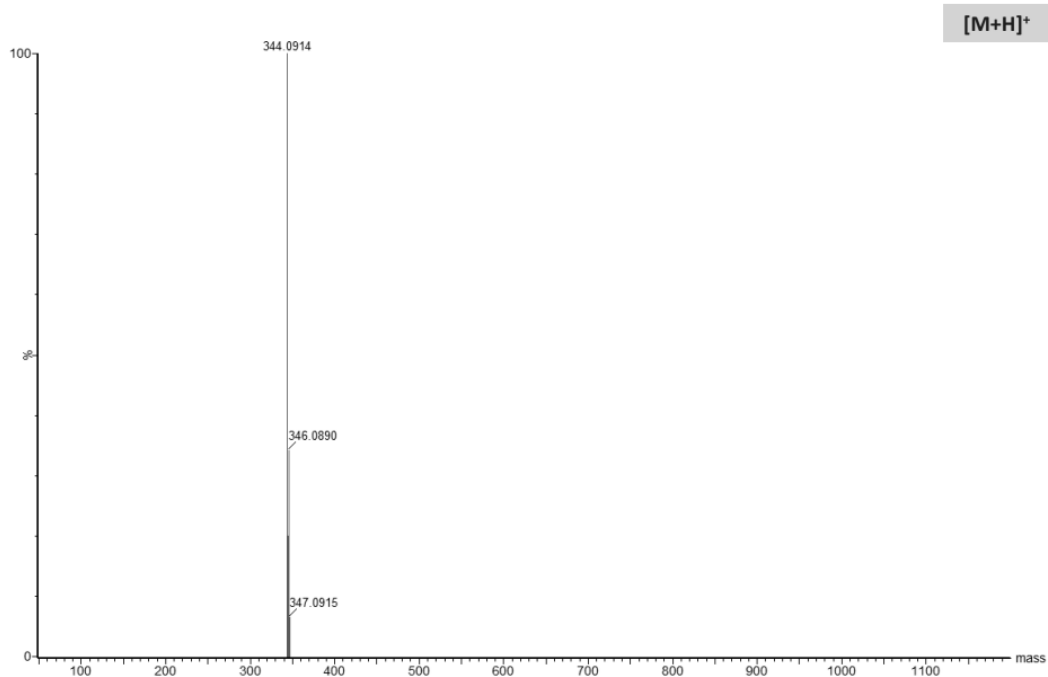
Mass Spectrum: KYC-4-53 (Positive mode)



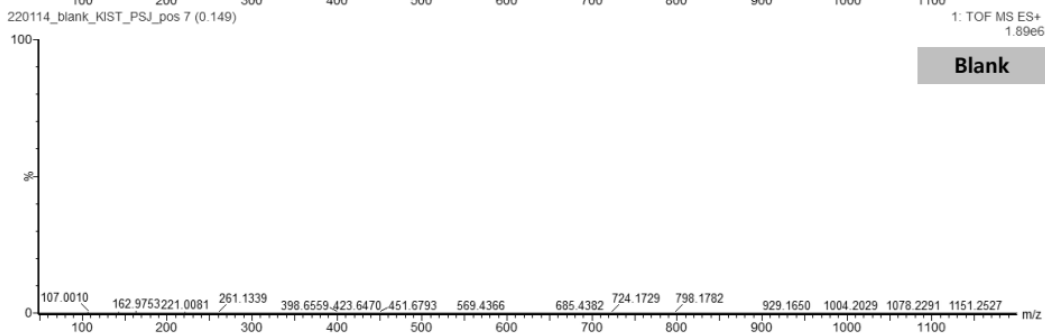
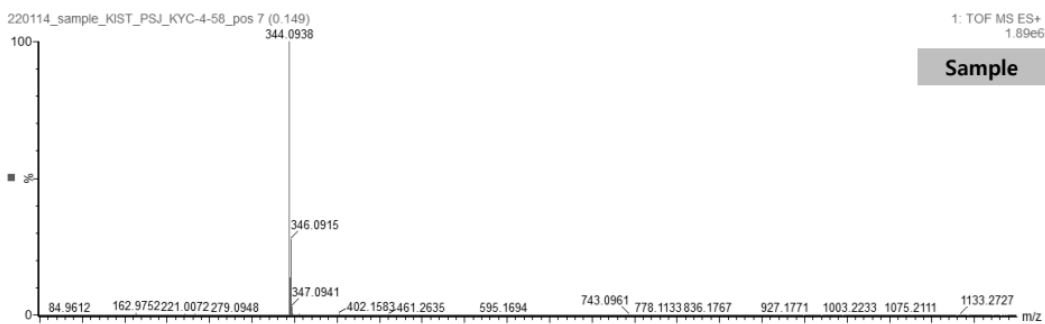
4-(4-Amino-6-((4-chloro-3-methoxyphenyl)amino)-1,3,5-triazin-2-yl)phenol (**9c**)



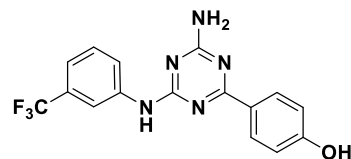
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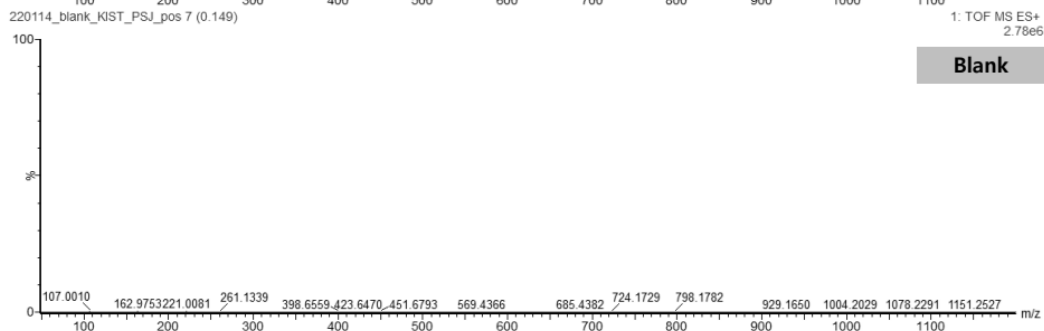
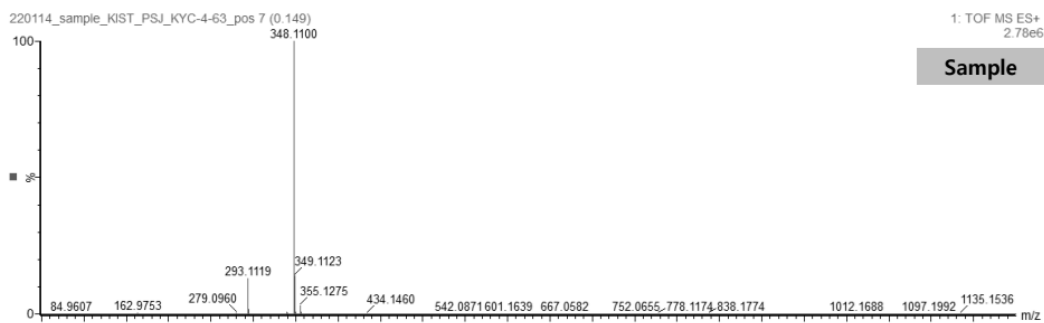
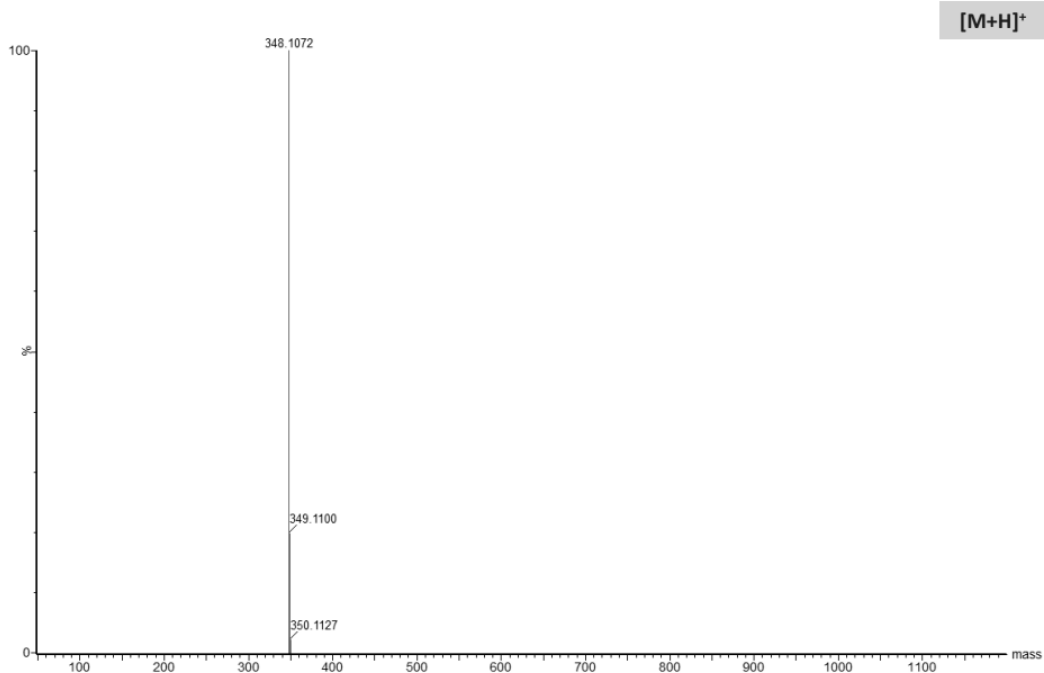
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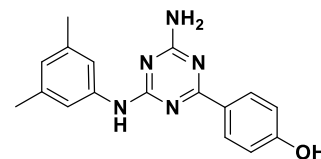
4-(4-Amino-6-((3-(trifluoromethyl)phenyl)amino)-1,3,5-triazin-2-yl)phenol (**9d**)



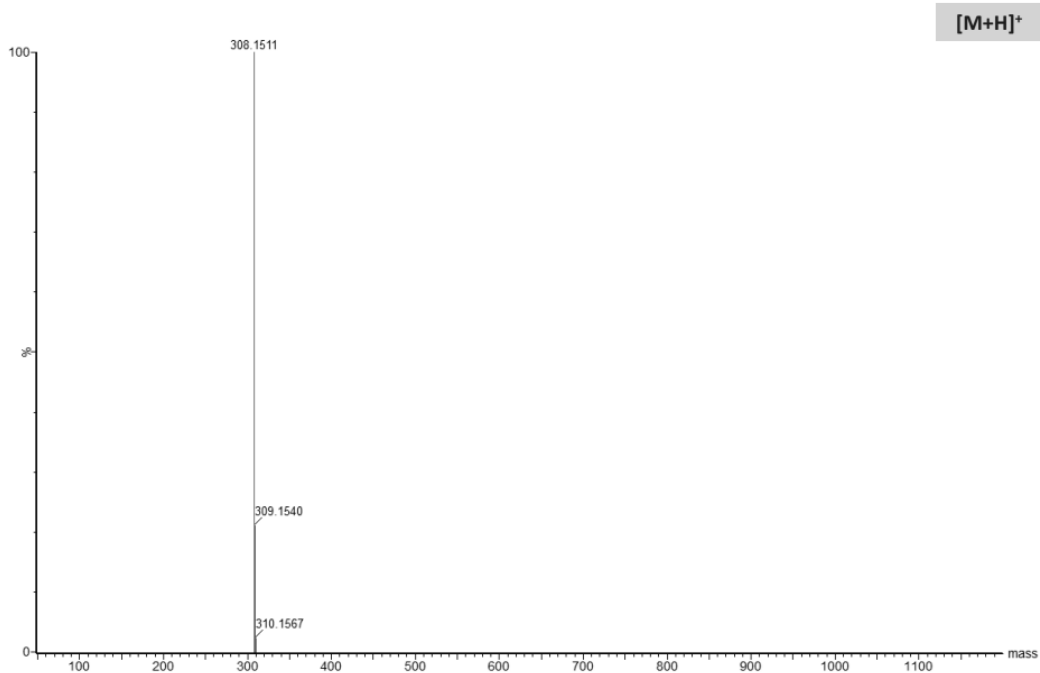
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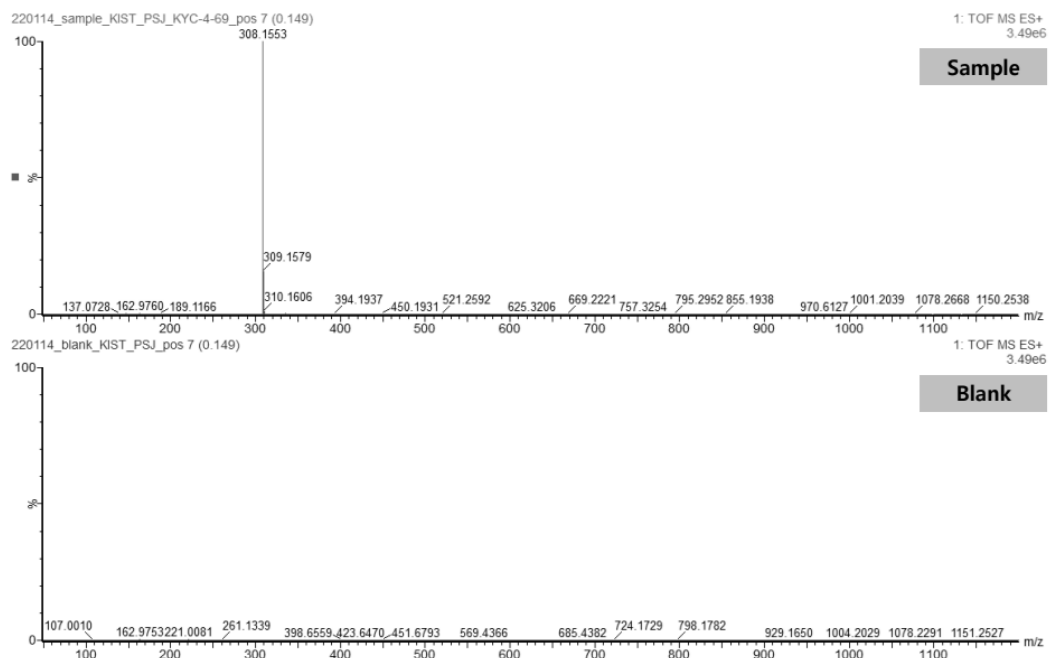
4-(4-Amino-6-((3,5-dimethylphenyl)amino)-1,3,5-triazin-2-yl)phenol (**9e**)



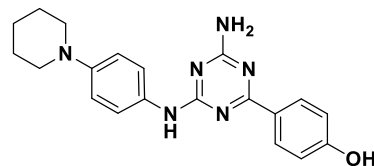
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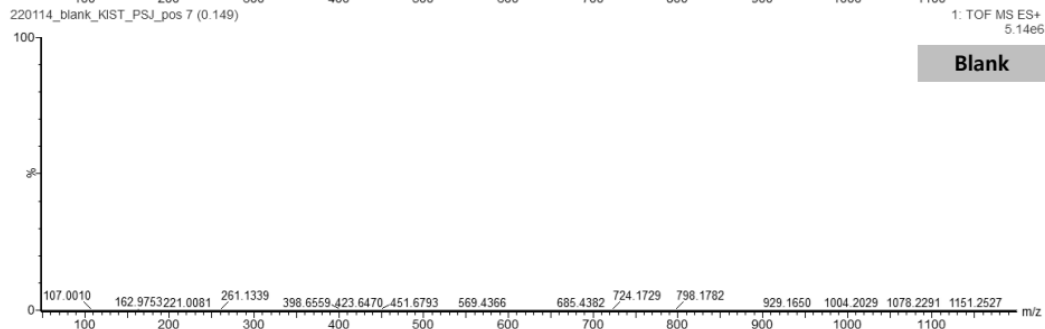
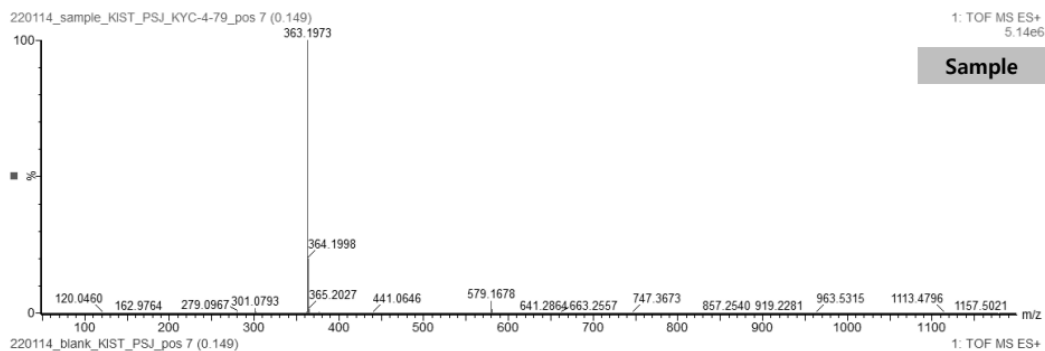
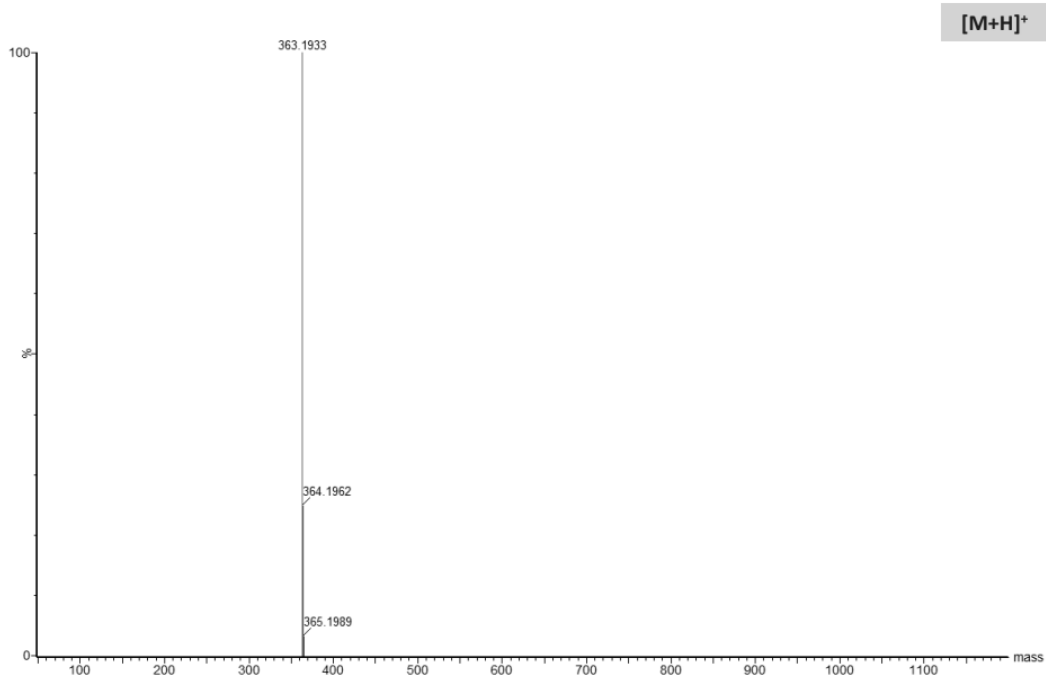
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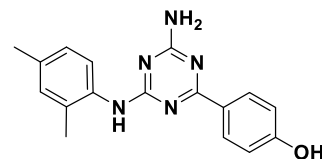
4-(4-Amino-6-((4-(piperidin-1-yl)phenyl)amino)-1,3,5-triazin-2-yl)phenol (**9f**)



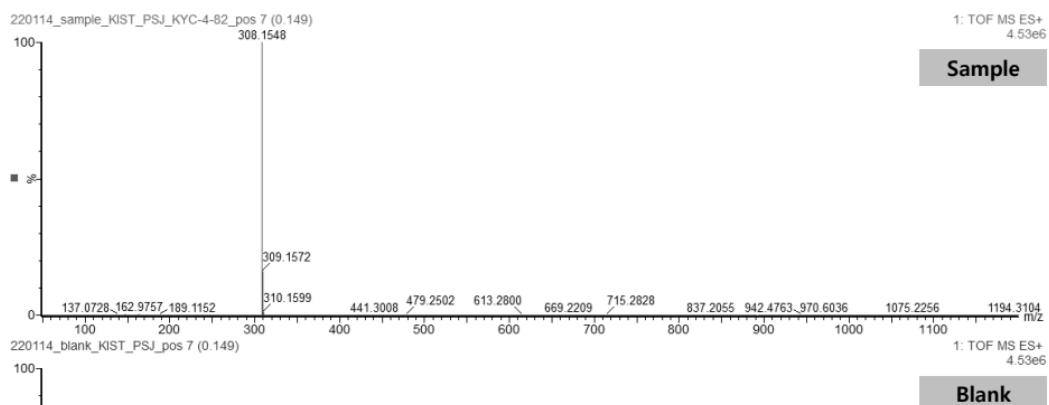
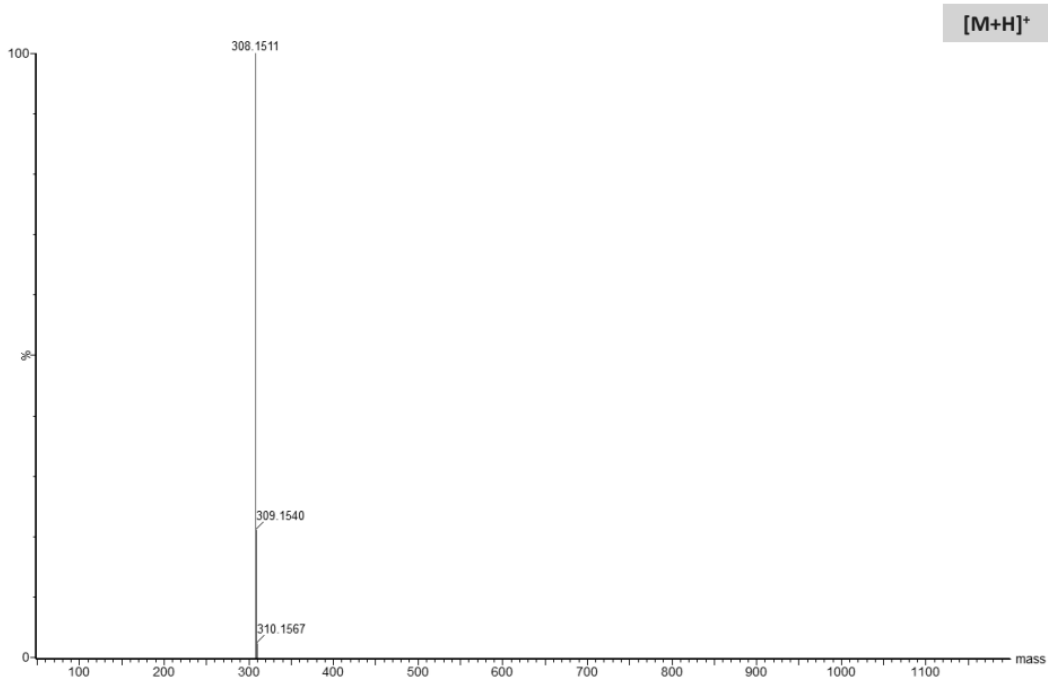
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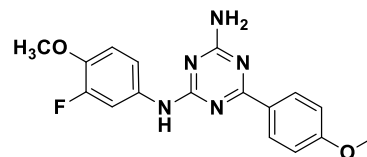
4-(4-Amino-6-((2,4-dimethylphenyl)amino)-1,3,5-triazin-2-yl)phenol (**9g**)



Isotope Modeling: KYC-4-82 (C₁₇H₁₇N₅O, Exact MS 307.1433)



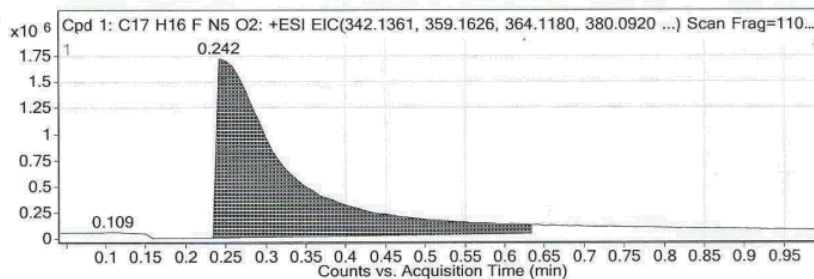
N^2 -(3-Fluoro-4-methoxyphenyl)-6-(4-methoxyphenyl)-1,3,5-triazine-2,4-diamine (**11a**)



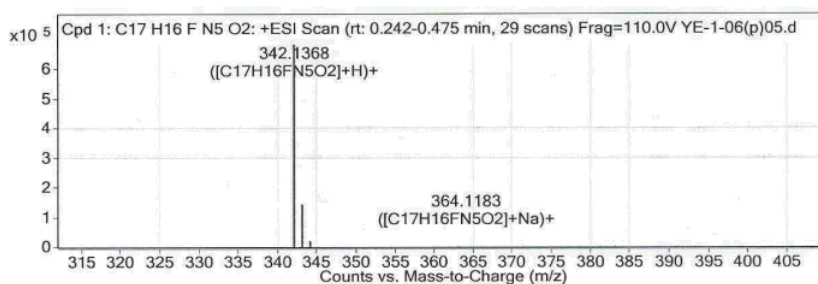
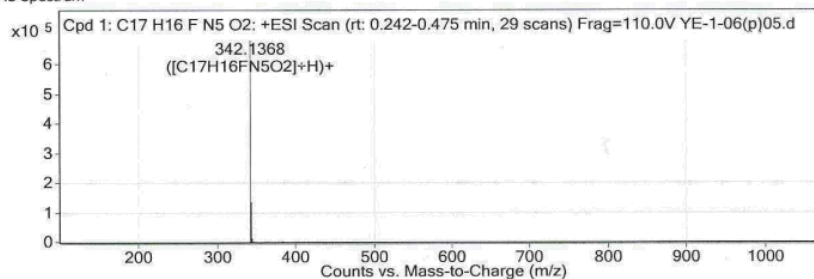
Compound Table

Compound Label	RT	Mass	Abund	Formula	Tgt Mass	Diff (ppm)
Cpd 1: C17 H16 F N5 O2	0.242	341.1295	681105	C17 H16 F N5 O2	341.1288	1.96

Compound Label	m/z	RT	Algorithm	Mass
Cpd 1: C17 H16 F N5 O2	342.1368	0.242	Find By Formula	341.1295



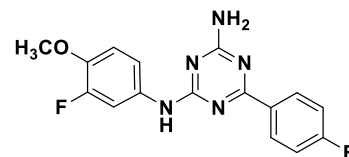
MS Spectrum



MS Spectrum Peak List

m/z	Calc m/z	Diff(ppm)	z	Abund	Formula	Ion
342.1368	342.1361	-2.13	1	681105.13	C17H16FN5O2	(M+H)+
343.1393	343.1389	-1.15	1	135914.66	C17H16FN5O2	(M+H)+
344.1418	344.1415	-0.93	1	12011.48	C17H16FN5O2	(M+H)+
345.1447	345.1439	-2.33	1	1009.78	C17H16FN5O2	(M+H)+
364.1183	364.118	-0.66	1	94.29	C17H16FN5O2	(M+Na)+
380.0932	380.092	-3.17	1	62.38	C17H16FN5O2	(M+K)+

N^2 -(3-Fluoro-4-methoxyphenyl)-6-(4-fluorophenyl)-1,3,5-triazine-2,4-diamine (**11b**)

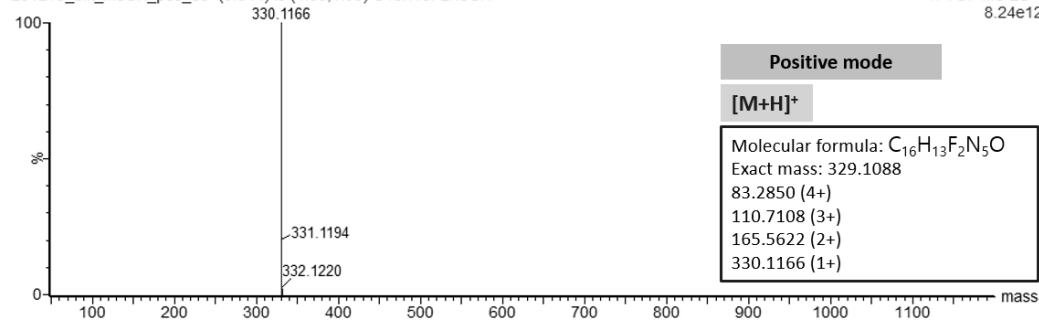


Isotope modeling _ YE-1-07

direct

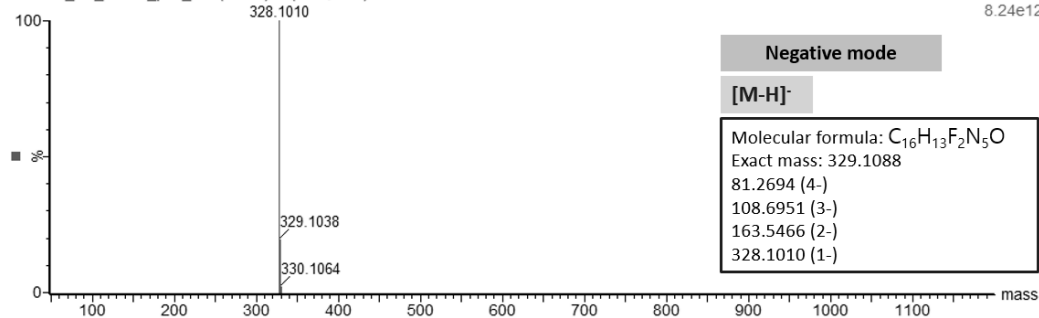
201215_blk_MeOH_pos_35 (0.044) Is (1.00,1.00) C₁₆H₁₃F₂N₅O

1: TOF MS ES+
8.24e12



201215_blk_MeOH_pos_35 (0.184) Is (1.00,1.00) C₁₆H₁₂F₂N₅O

1: TOF MS ES+
8.24e12

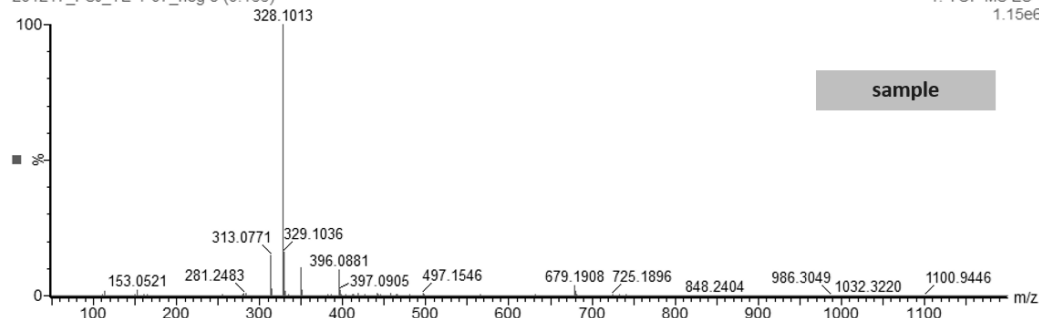


Chromatogram_ Negative mode_ YE-1-07

direct

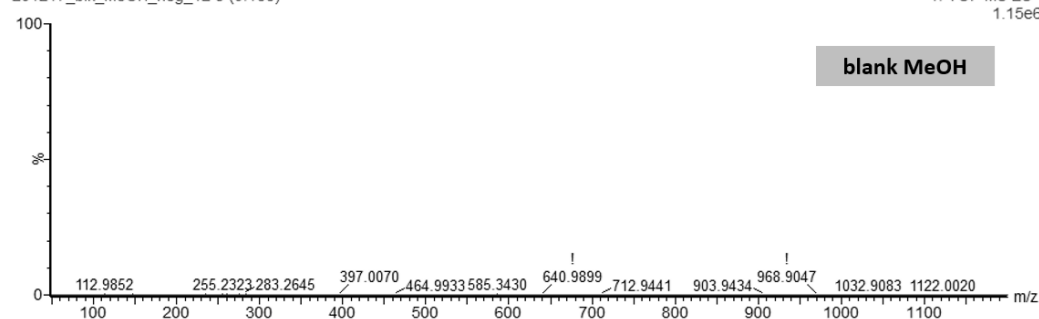
201217_PSI_YE-1-07_neg 8 (0.166)

1: TOF MS ES-
1.15e6

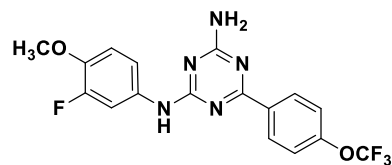


201217_blk_MeOH_neg_12 8 (0.166)

1: TOF MS ES-
1.15e6



N^2 -(3-Fluoro-4-methoxyphenyl)-6-(4-(trifluoromethoxy)phenyl)-1,3,5-triazine-2,4-diamine (**11c**)

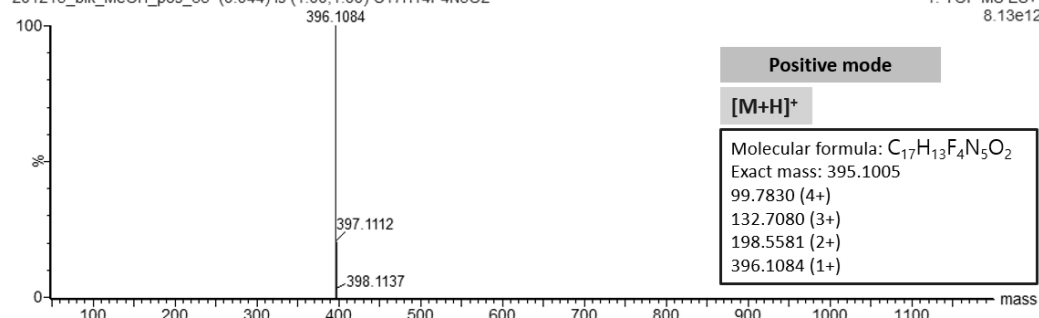


Isotope modeling _ YE-1-09

direct

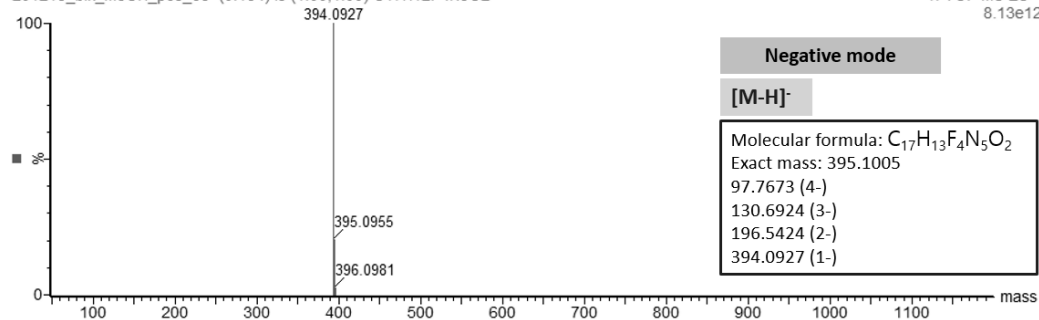
201215_blk_MeOH_pos_35 (0.044) Is (1.00,1.00) C₁₇H₁₄F₄N₅O₂

1: TOF MS ES+
8.13e12



201215_blk_MeOH_pos_35 (0.184) Is (1.00,1.00) C₁₇H₁₂F₄N₅O₂

1: TOF MS ES+
8.13e12

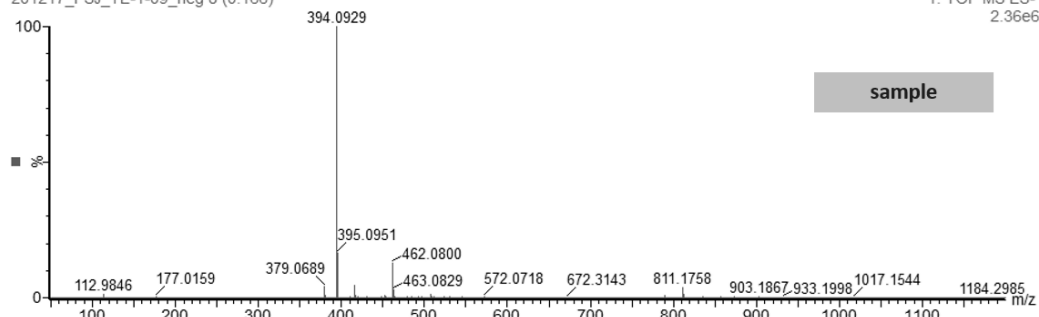


Chromatogram_ Negative mode_ YE-1-09

direct

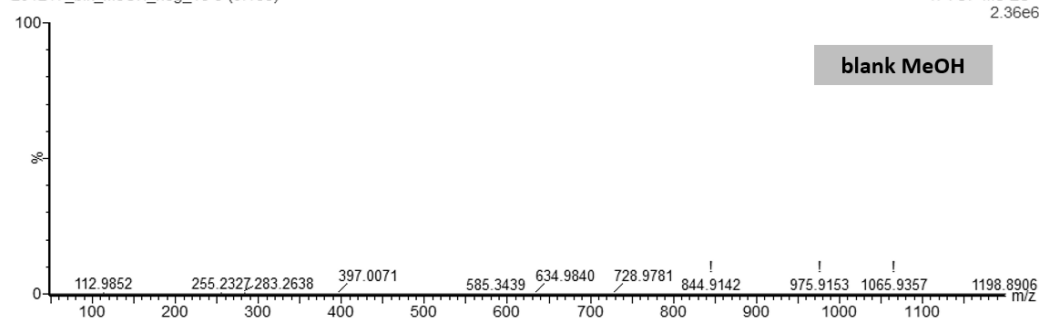
201217_PsJ_YE-1-09_neg 8 (0.166)

1: TOF MS ES-
2.36e6

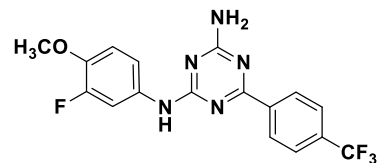


201217_blk_MeOH_neg_18 8 (0.166)

1: TOF MS ES-
2.36e6



N^2 -(3-Fluoro-4-methoxyphenyl)-6-(4-(trifluoromethyl)phenyl)-1,3,5-triazine-2,4-diamine (**11d**)

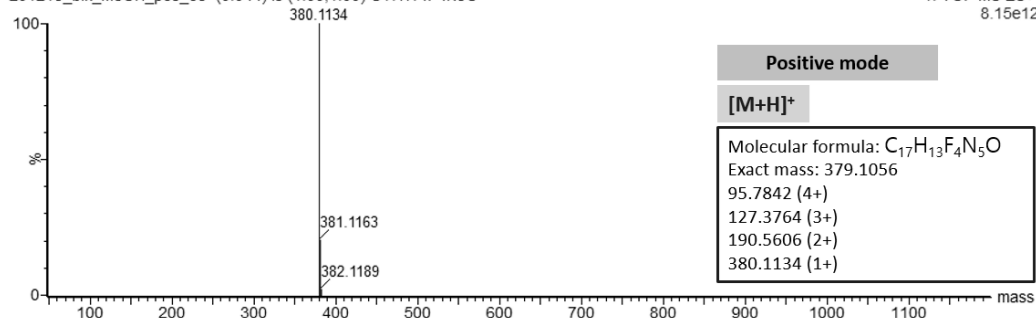


Isotope modeling _ YE-1-18

direct

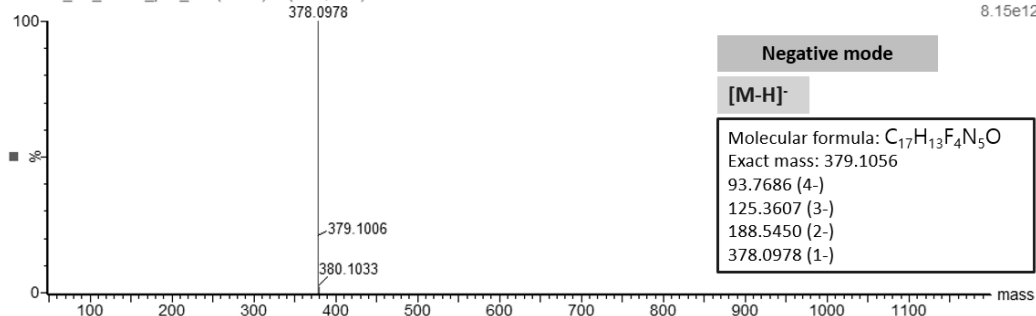
201215_blk_MeOH_pos_35 (0.044) Is (1.00,1.00) C₁₇H₁₄F₄N₅O

1: TOF MS ES+
8.15e12



201215_blk_MeOH_pos_35 (0.184) Is (1.00,1.00) C₁₇H₁₂F₄N₅O

1: TOF MS ES+
8.15e12

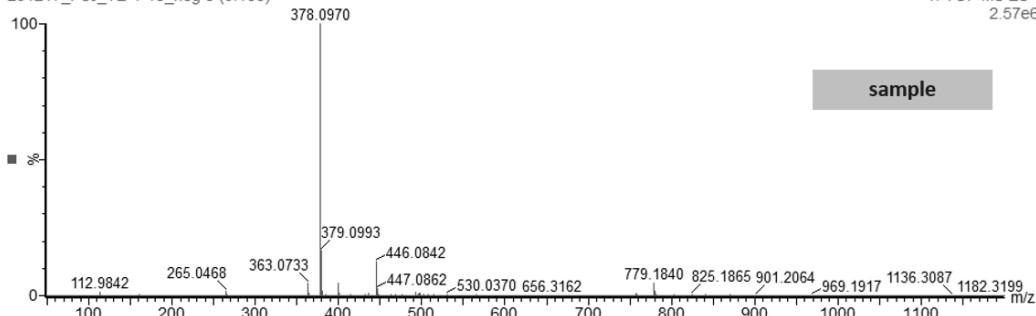


Chromatogram_ Negative mode_ YE-1-18

direct

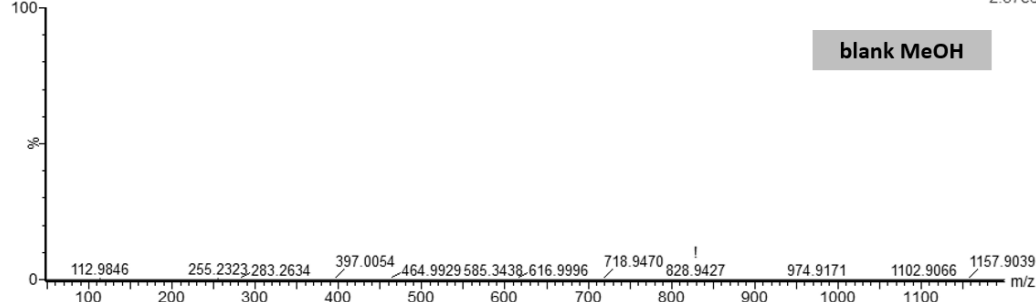
201217_PSI_YE-1-18_neg 8 (0.166)

1: TOF MS ES-
2.57e6

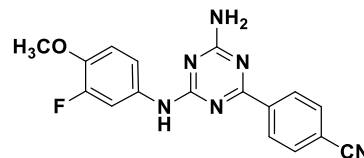


201217_blk_MeOH_neg_33 8 (0.166)

1: TOF MS ES-
2.57e6



4-(4-Amino-6-((3-fluoro-4-methoxyphenyl)amino)-1,3,5-triazin-2-yl)benzonitrile (**11e**)

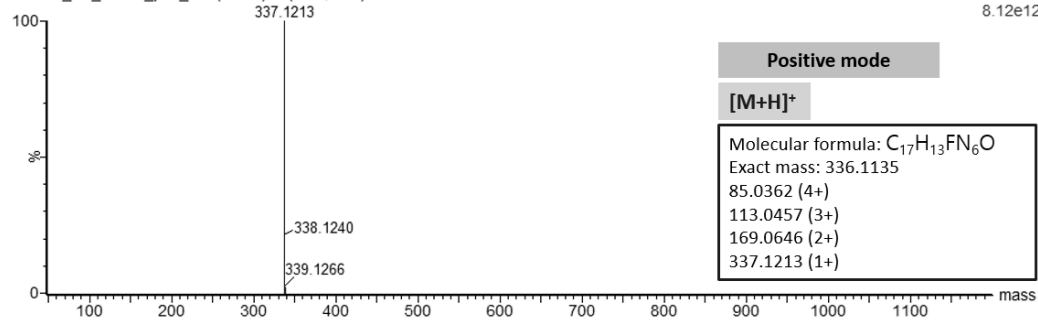


Isotope modeling _ YE-1-10

direct

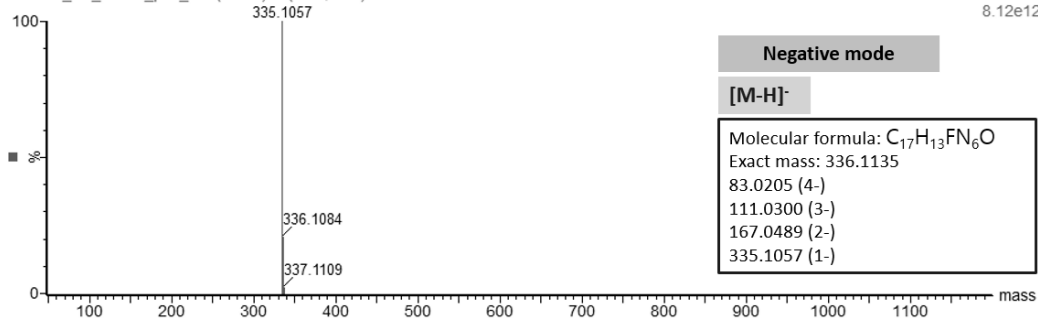
201215_blk_MeOH_pos_35 (0.044) Is (1.00,1.00) C₁₇H₁₃FN₆O

1: TOF MS ES+
8.12e12



201215_blk_MeOH_pos_35 (0.184) Is (1.00,1.00) C₁₇H₁₂FN₆O

1: TOF MS ES+
8.12e12

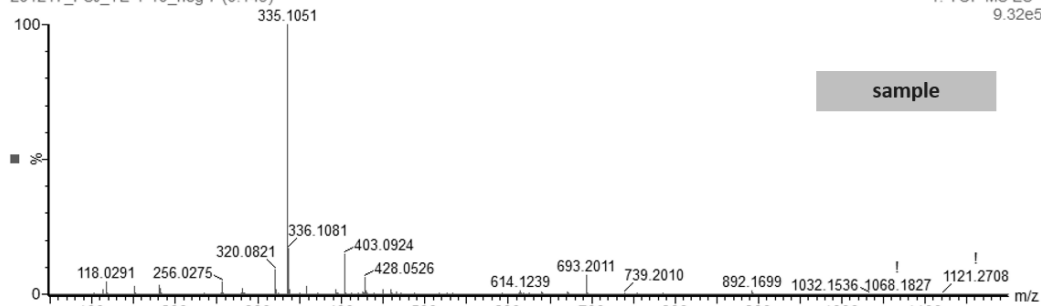


Chromatogram_ Negative mode_ YE-1-10

direct

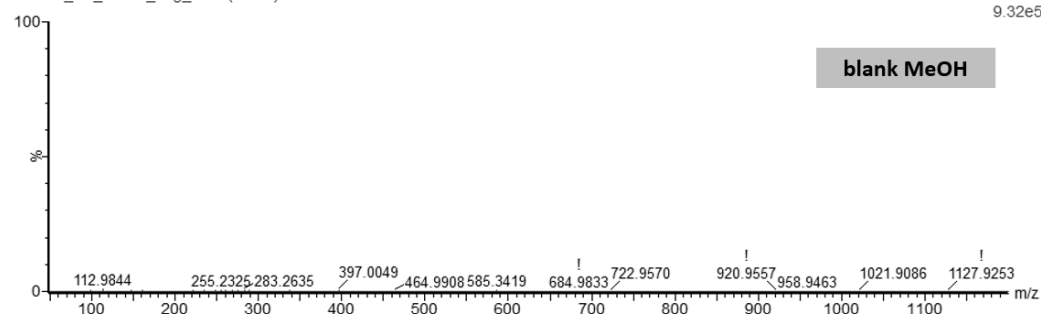
201217_PJS_YE-1-10_neg 7 (0.149)

1: TOF MS ES-
9.32e5

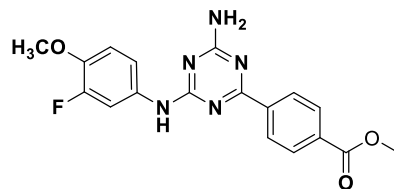


201217_blk_MeOH_neg_21 7 (0.149)

1: TOF MS ES-
9.32e5



Methyl 4-(4-Amino-6-((3-fluoro-4-methoxyphenyl)amino)-1,3,5-triazin-2-yl)benzoate (**11f**)

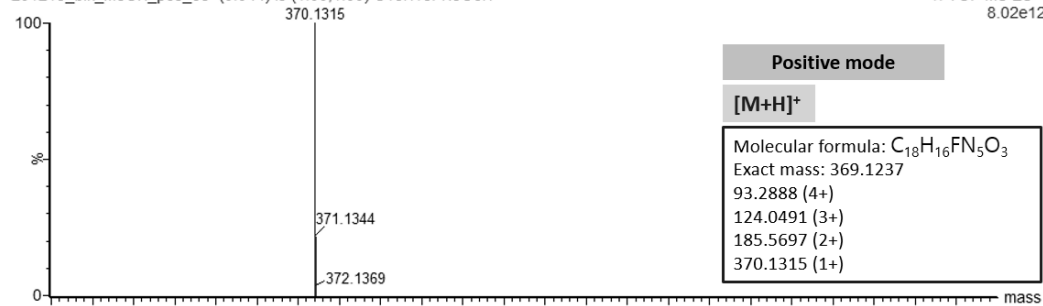


Isotope modeling _ YE-1-11

direct

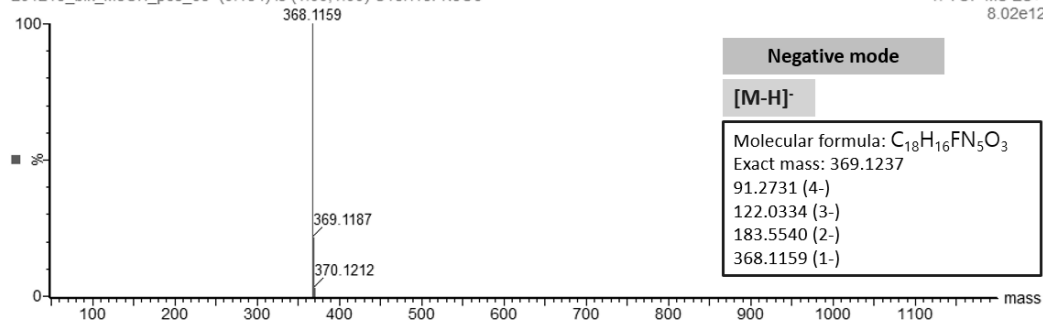
201215_blk_MeOH_pos_35 (0.044) Is (1.00,1.00) C₁₈H₁₆FN₅O₃H

1: TOF MS ES+
8.02e12



201215_blk_MeOH_pos_35 (0.184) Is (1.00,1.00) C₁₈H₁₅FN₅O₃

1: TOF MS ES+
8.02e12

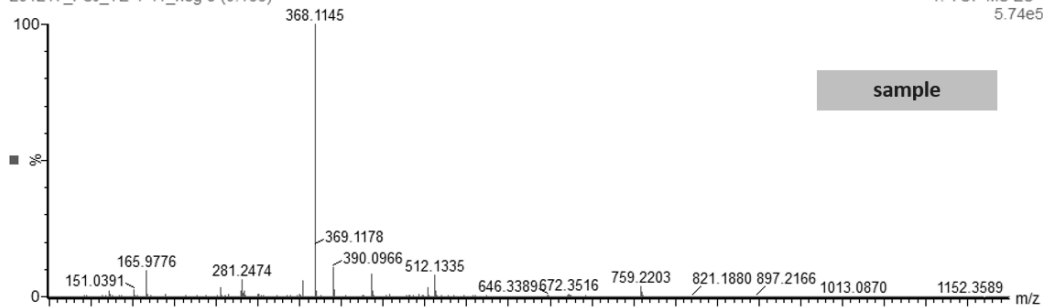


Chromatogram_ Negative mode_ YE-1-11

direct

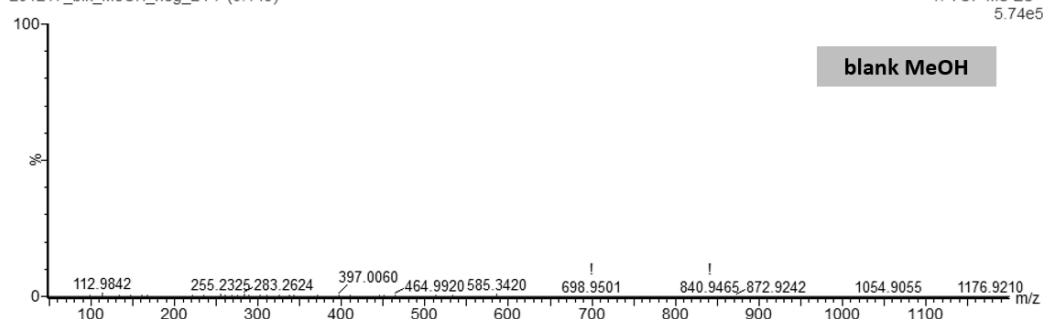
201217_PsJ_YE-1-11_neg 8 (0.166)

1: TOF MS ES-
5.74e5

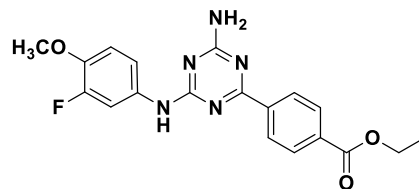


201217_blk_MeOH_neg_24 7 (0.149)

1: TOF MS ES-
5.74e5



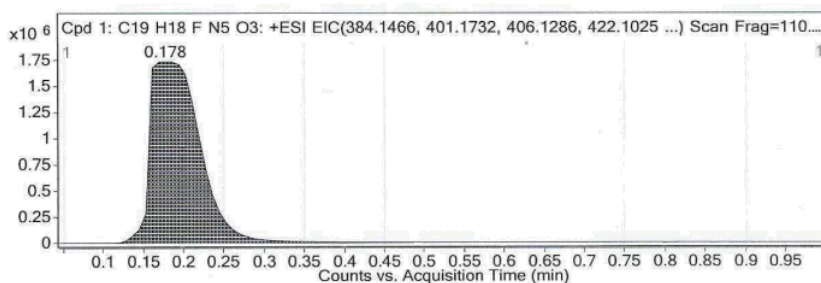
Ethyl 4-(4-Amino-6-((3-fluoro-4-methoxyphenyl)amino)-1,3,5-triazin-2-yl)benzoate (**11g**)



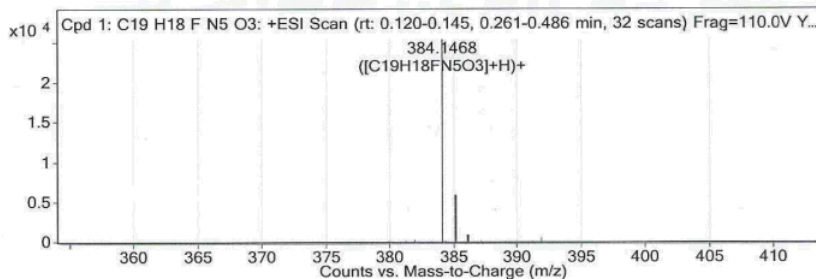
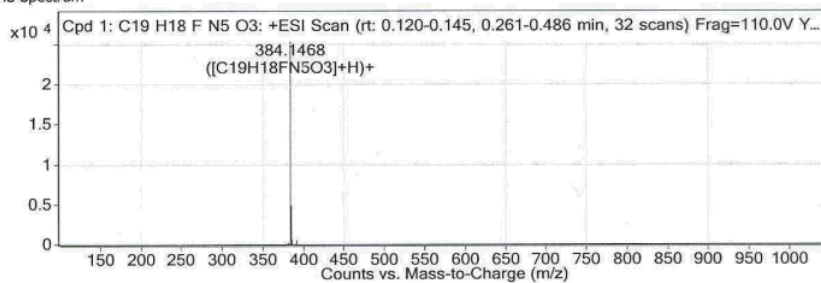
Compound Table

Compound Label	RT	Mass	Abund	Formula	Tgt Mass	Diff (ppm)
Cpd 1: C ₁₉ H ₁₈ F N ₅ O ₃	0.178	383.1395	25410	C ₁₉ H ₁₈ F N ₅ O ₃	383.1394	0.4

Compound Label	m/z	RT	Algorithm	Mass
Cpd 1: C ₁₉ H ₁₈ F N ₅ O ₃	384.1468	0.178	Find By Formula	383.1395



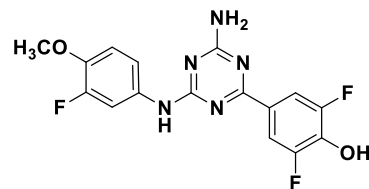
MS Spectrum



MS Spectrum Peak List

m/z	Calc m/z	Diff(ppm)	z	Abund	Formula	Ion
384.1468	384.1466	-0.43	1	25409.76	C ₁₉ H ₁₈ FN ₅ O ₃	(M+H) ⁺
385.1496	385.1495	-0.17	1	4864.49	C ₁₉ H ₁₈ FN ₅ O ₃	(M+H) ⁺
386.1523	386.1521	-0.52	1	582.88	C ₁₉ H ₁₈ FN ₅ O ₃	(M+H) ⁺
387.1566	387.1546	-5.39	1	32.66	C ₁₉ H ₁₈ FN ₅ O ₃	(M+H) ⁺

4-(4-Amino-6-((3-fluoro-4-methoxyphenyl)amino)-1,3,5-triazin-2-yl)-2,6-difluorophenol (**11h**)

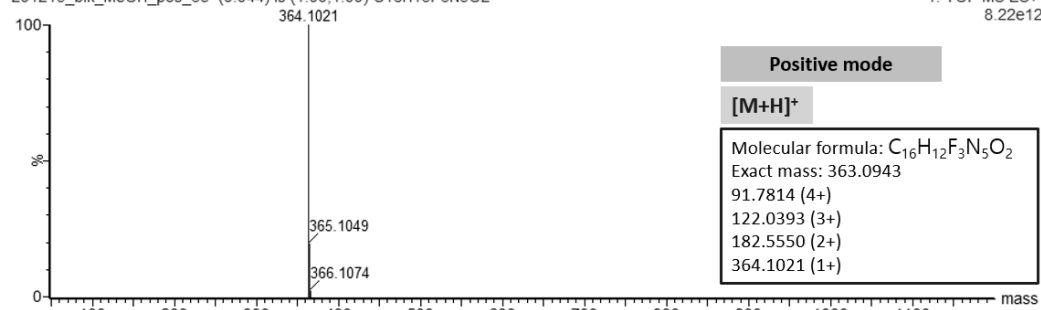


Isotope modeling _ YE-1-14

direct

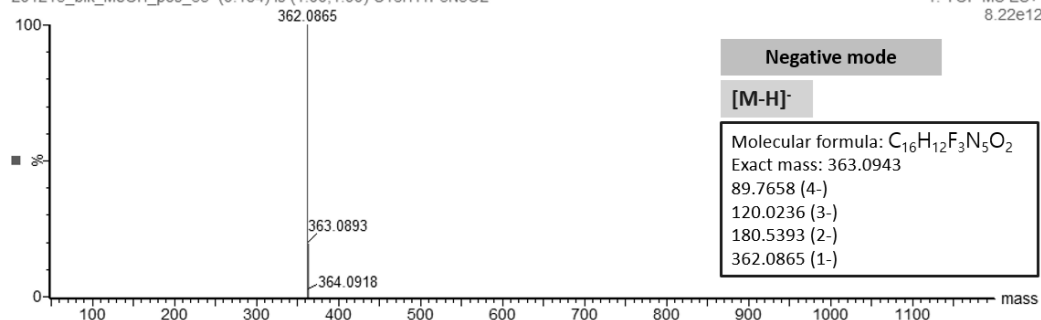
201215_blk_MeOH_pos_35 (0.044) Is (1.00,1.00) C₁₆H₁₃F₃N₅O₂

1: TOF MS ES+
8.22e12



201215_blk_MeOH_pos_35 (0.184) Is (1.00,1.00) C₁₆H₁₁F₃N₅O₂

1: TOF MS ES+
8.22e12

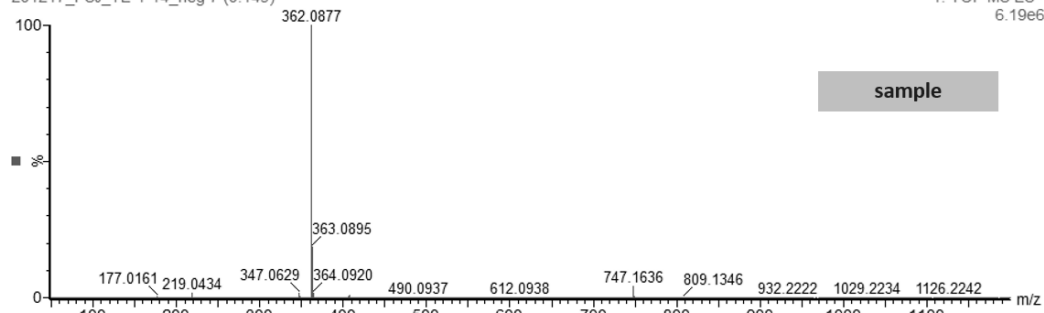


Chromatogram_ Negative mode_ YE-1-14

direct

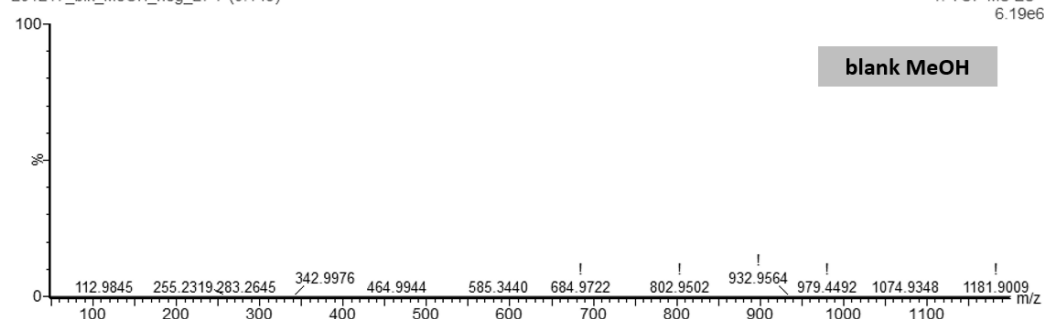
201217_PSJ_YE-1-14_neg 7 (0.149)

1: TOF MS ES-
6.19e6

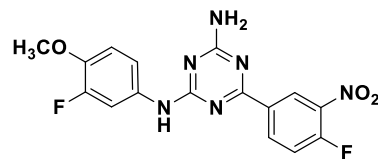


201217_blk_MeOH_neg_27 7 (0.149)

1: TOF MS ES-
6.19e6



6-(4-Fluoro-3-nitrophenyl)-*N*²-(3-fluoro-4-methoxyphenyl)-1,3,5-triazine-2,4-diamine (**11i**)

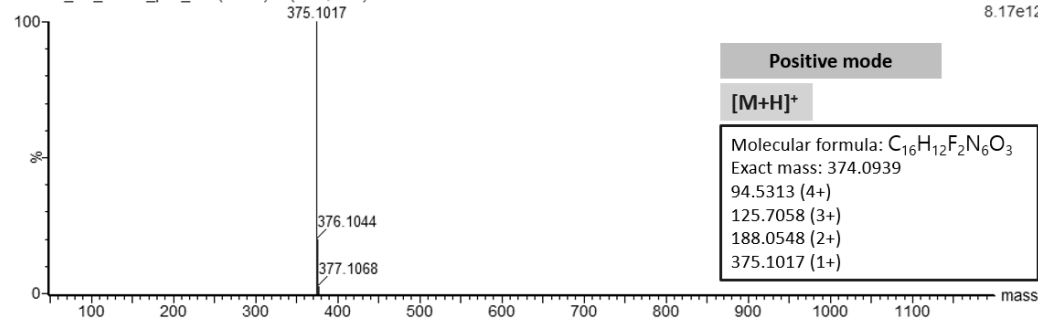


Isotope modeling _ YE-1-15

direct

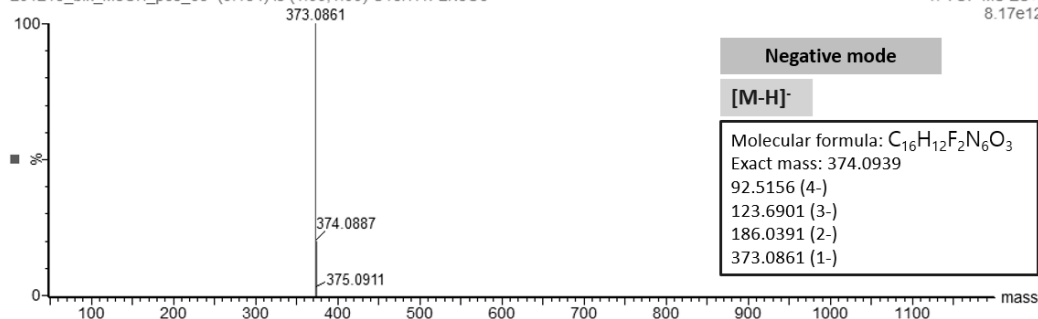
201215_blk_MeOH_pos_35 (0.044) Is (1.00,1.00) C₁₆H₁₂F₂N₆O₃H

1: TOF MS ES+
8.17e12



201215_blk_MeOH_pos_35 (0.184) Is (1.00,1.00) C₁₆H₁₁F₂N₆O₃

1: TOF MS ES+
8.17e12

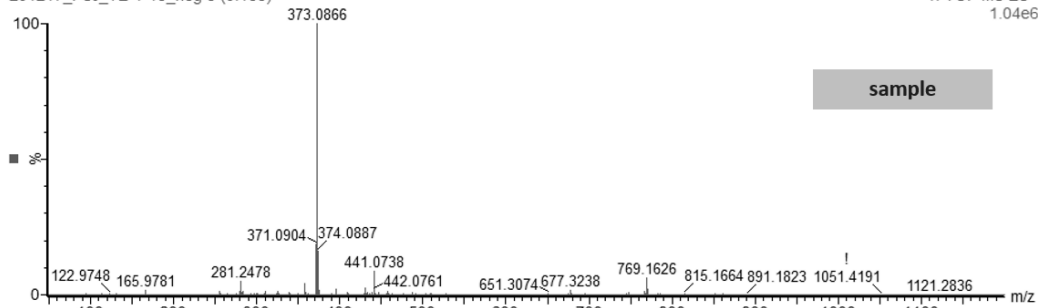


Chromatogram_ Negative mode_ YE-1-15

direct

201217_PSJ_YE-1-15_neg 8 (0.166)

1: TOF MS ES-
1.04e6



201217_blk_MeOH_neg_30 7 (0.149)

1: TOF MS ES-
1.04e6

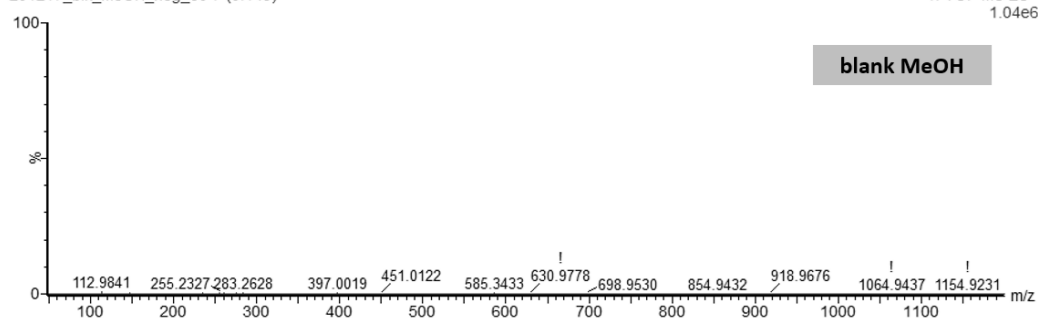


Figure S3. Molecular Docking of Compound **9a**, **11a**, and **11b**

