Supplementary Information

Biguanide-based synthesis of 1,3,5-triazine derivatives with anticancer activity and 1,3,5-triazine incorporated calcium citrate nanoparticles

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**Co-corresponding authors*

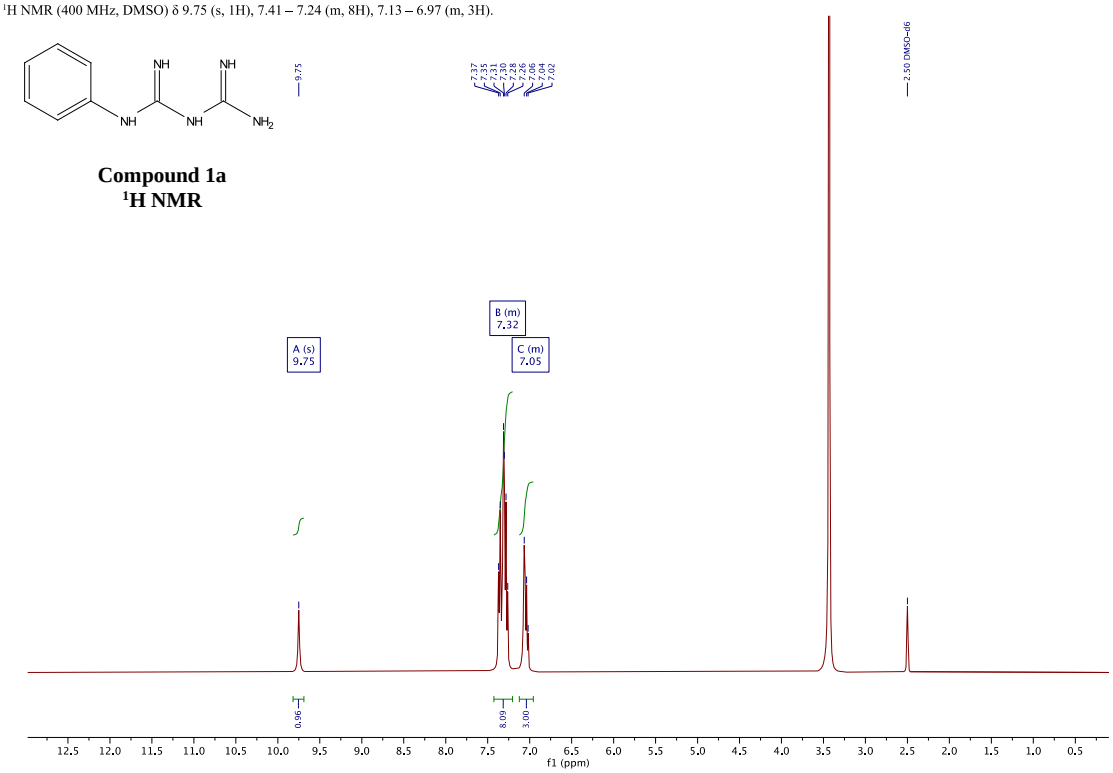

Figure 1. ^{1}H NMR of Phenylbiguanide hydrochloride (**1a**)

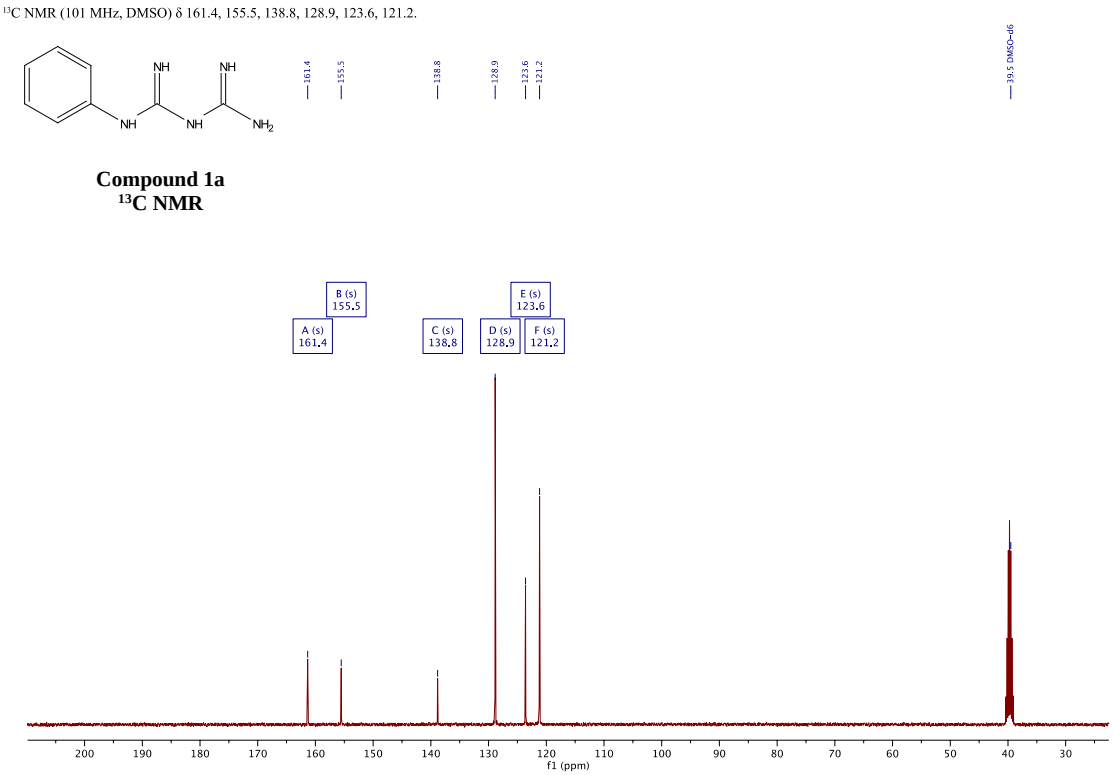

Figure 2. ^{13}C NMR of Phenylbiguanide hydrochloride (**1a**)

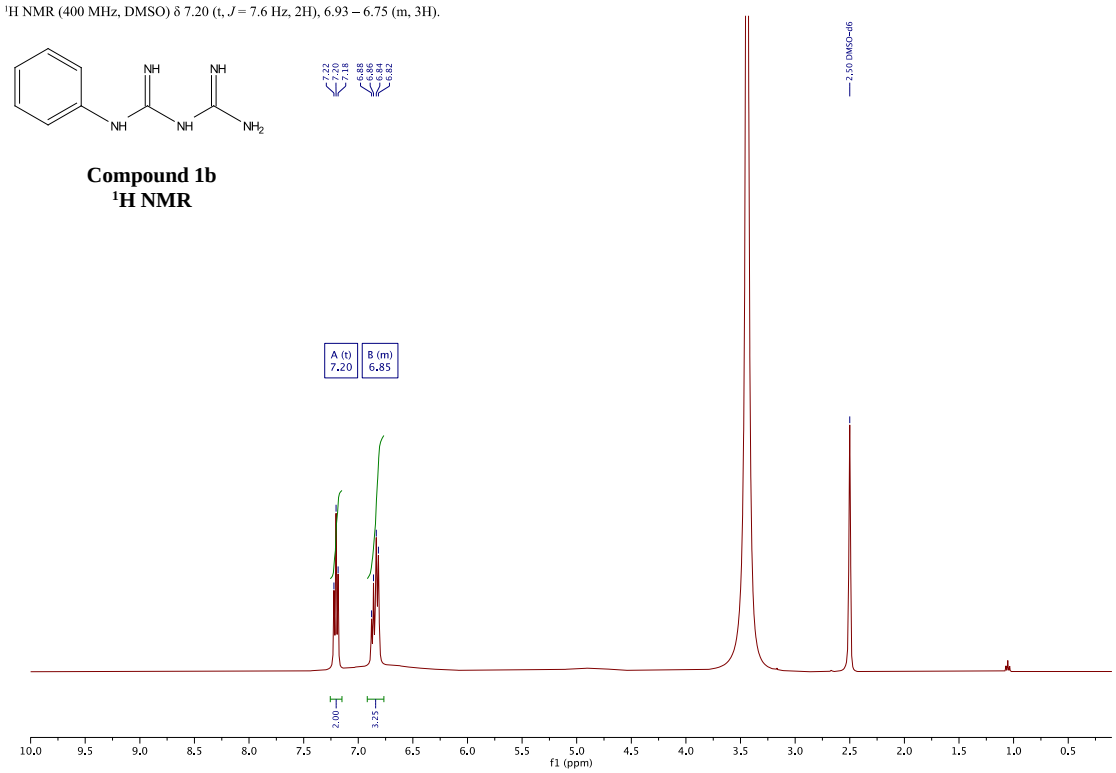

Figure 3. ^{1}H NMR of Phenylbiguanide (**1b**)

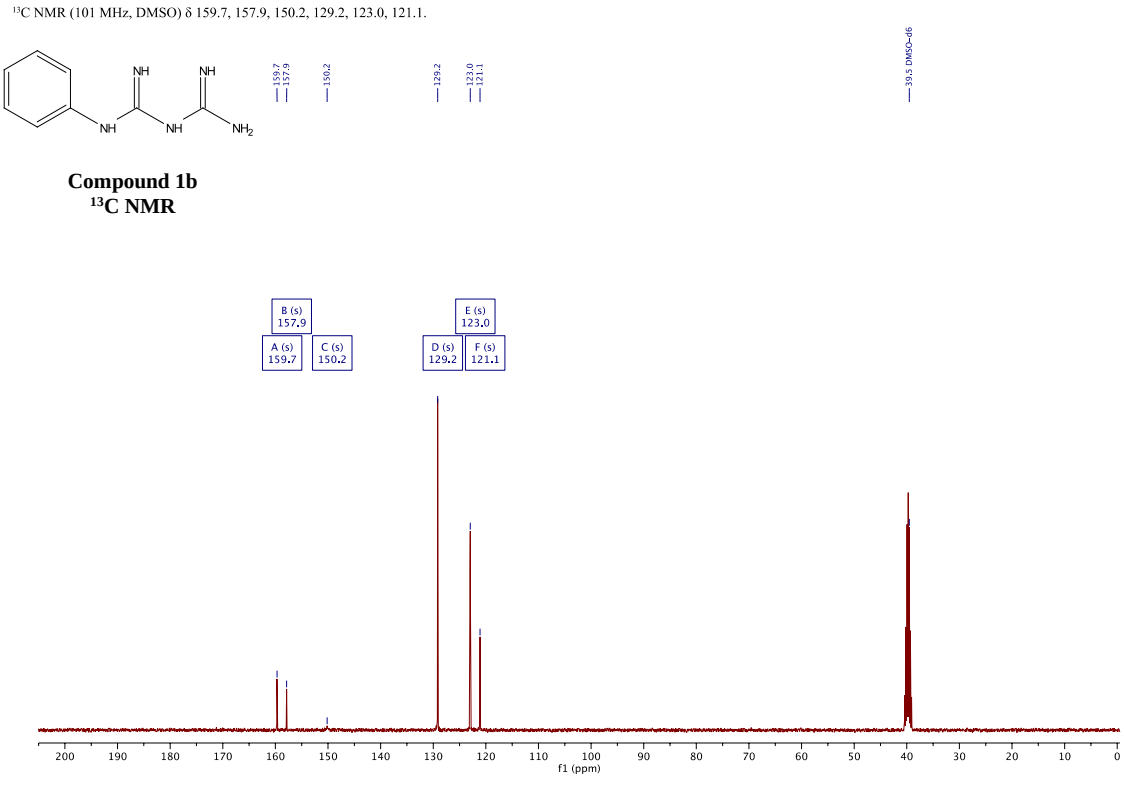

Figure 4. ^{13}C NMR of Phenylbiguanide (**1b**)

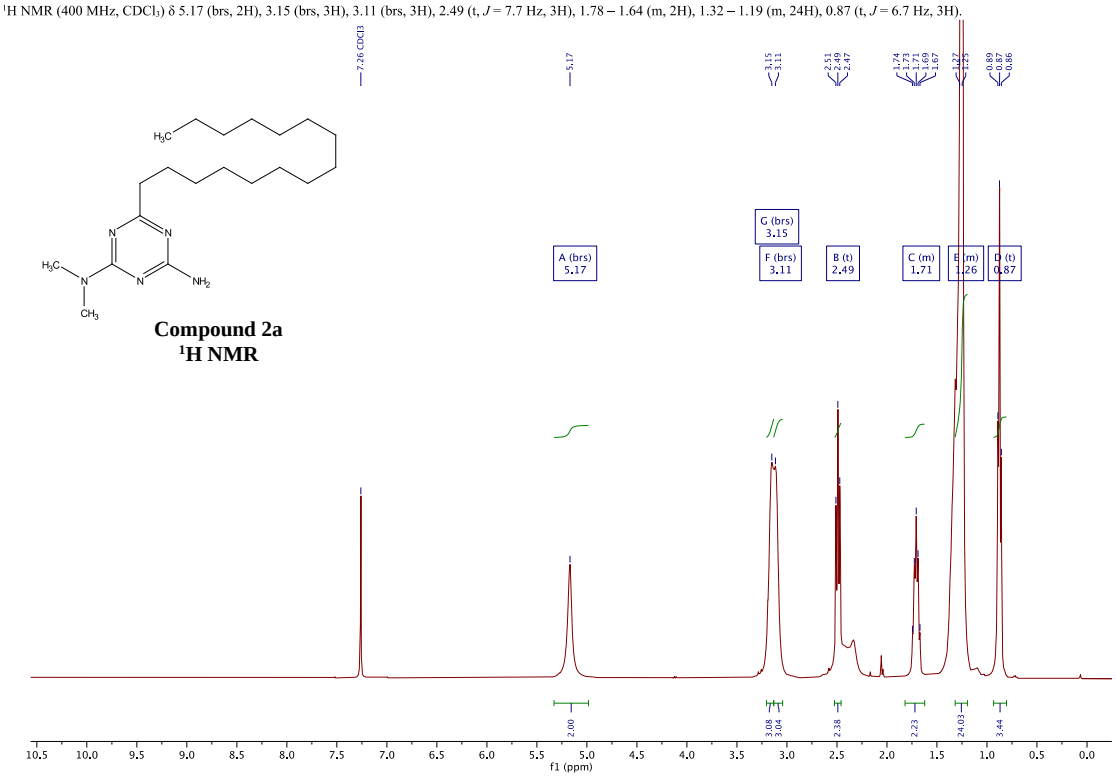

Figure 5. ^{1}H NMR of N^2,N^2-dimethyl-6-pentadecyl-1,3,5-triazine-2,4-diamine (**2a**)

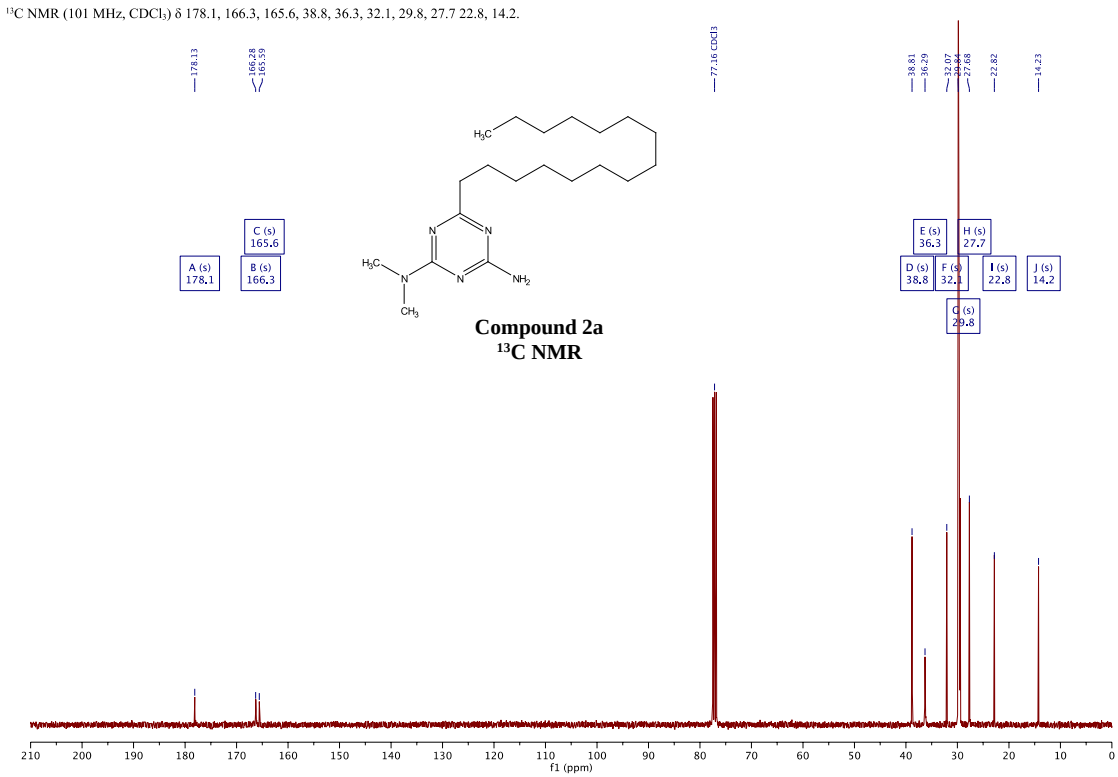

Figure 6. ^{13}C NMR of N^2,N^2-dimethyl-6-pentadecyl-1,3,5-triazine-2,4-diamine (**2a**)

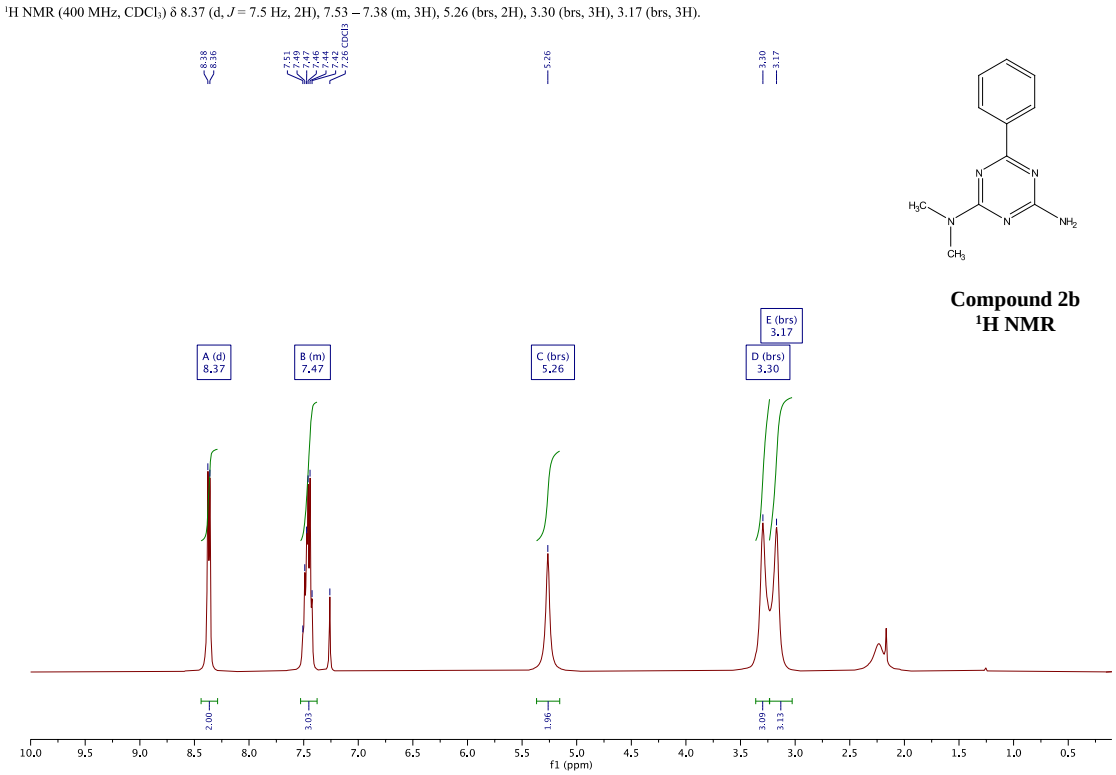

Figure 7. ^{1}H NMR of N^2,N^2-dimethyl-6-phenyl-1,3,5-triazine-2,4-diamine (**2b**)

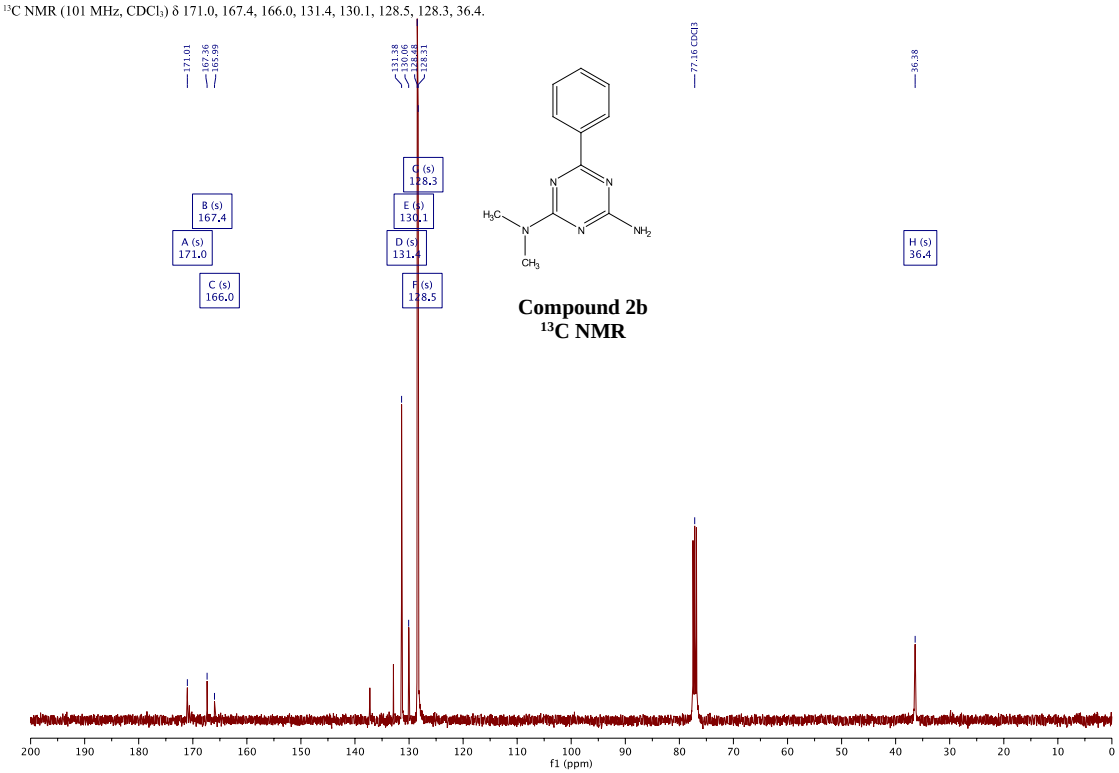

Figure 8. ^{13}C NMR of N^2,N^2-dimethyl-6-phenyl-1,3,5-triazine-2,4-diamine (**2b**)

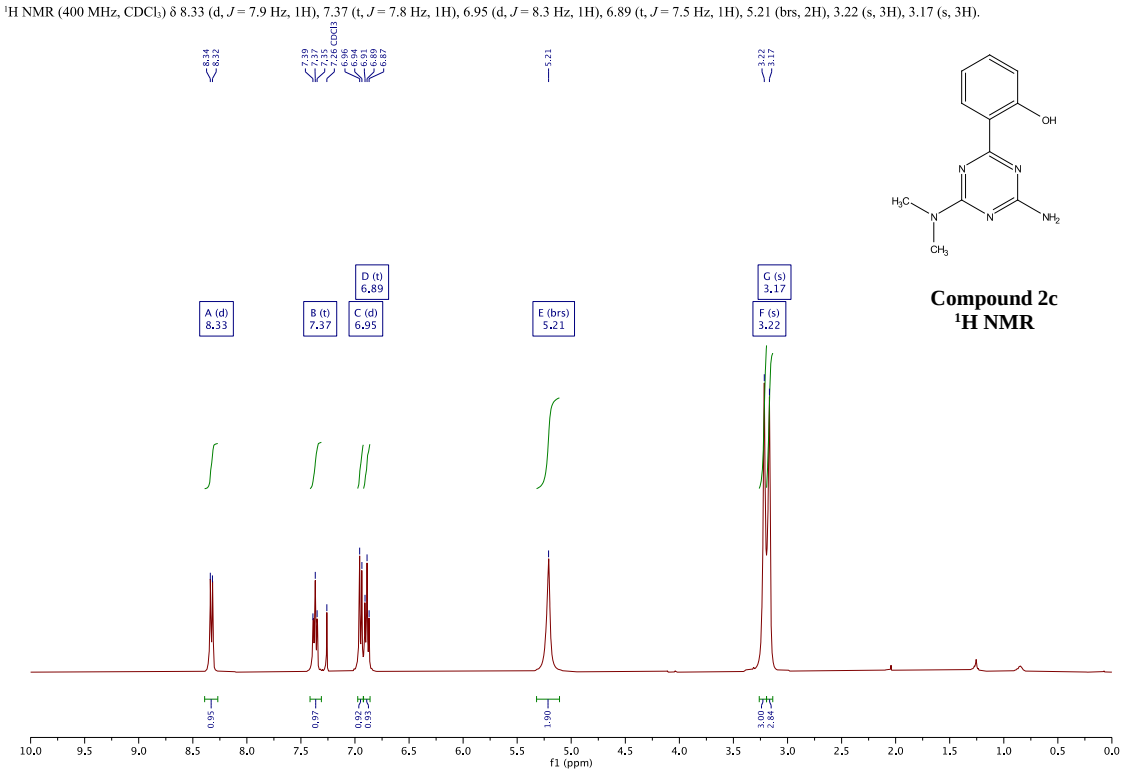

Figure 9. ^{1}H NMR of 2-(4-amino-6-(dimethylamino)-1,3,5-triazin-2-yl)phenol (**2c**)

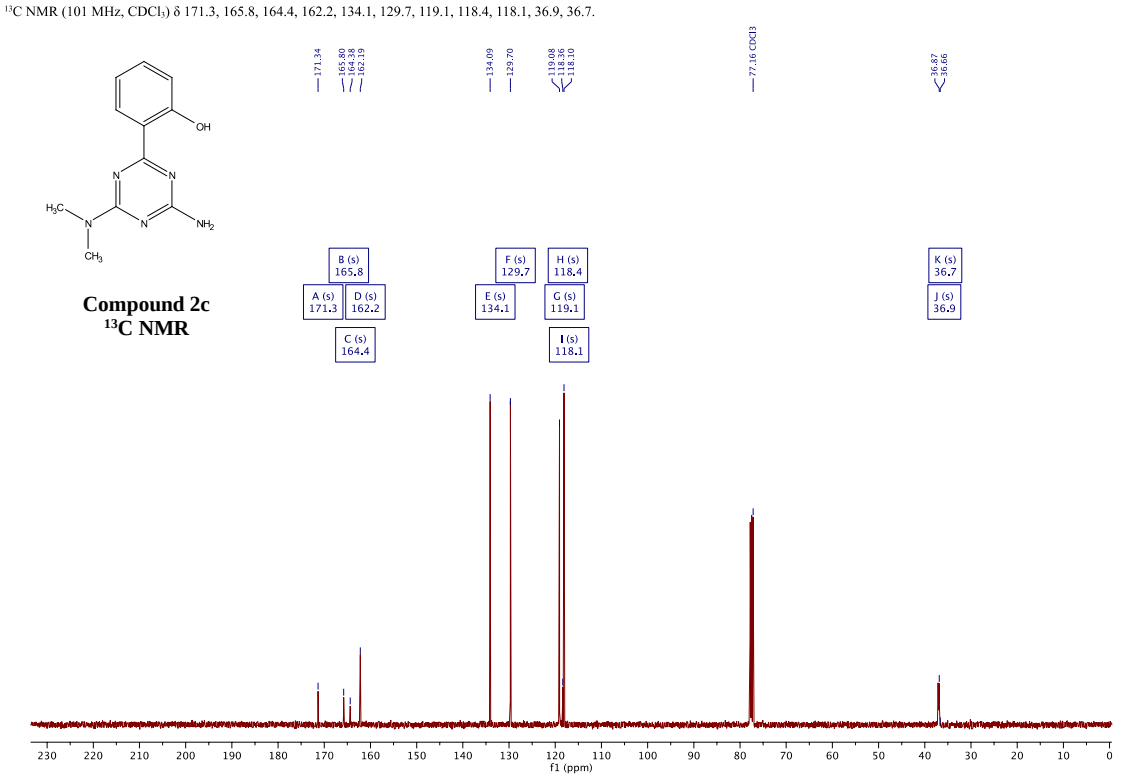

Figure 10. ^{13}C NMR of 2-(4-amino-6-(dimethylamino)-1,3,5-triazin-2-yl)phenol (**2c**)

Mass Spectrum List Report

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Comment			

Acquisition Parameter

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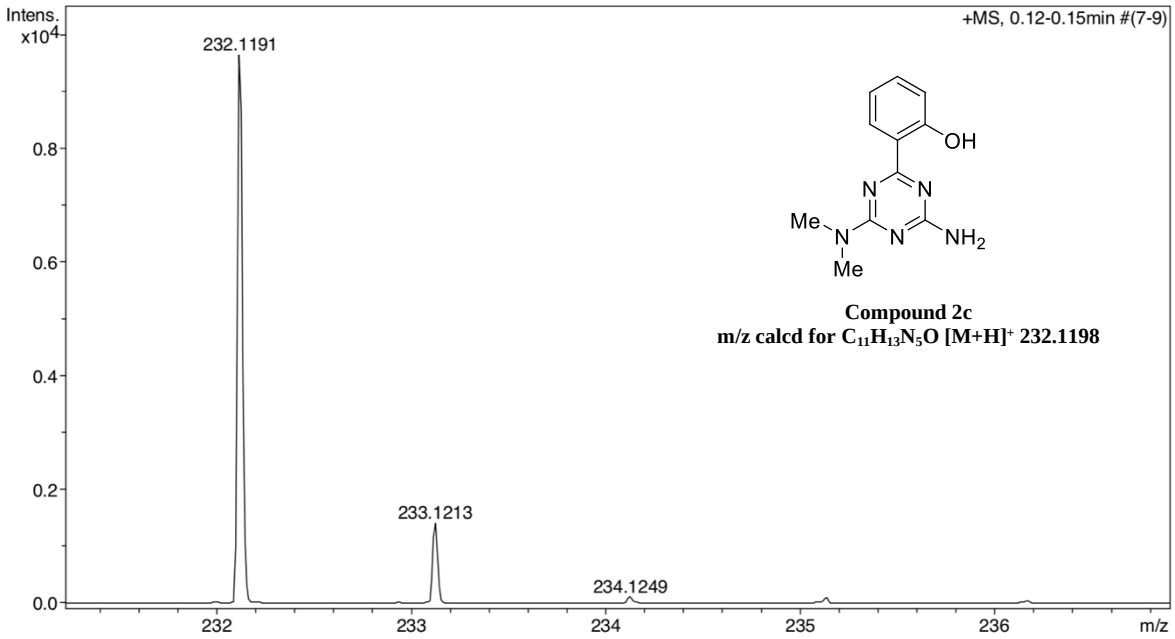

Compound 2c
m/z calcd for $C_{11}H_{13}N_5O$ $[M+H]^+$ 232.1198

Figure 11. HRMS spectrum of 2-(4-amino-6-(dimethylamino)-1,3,5-triazin-2-yl)phenol (**2c**)

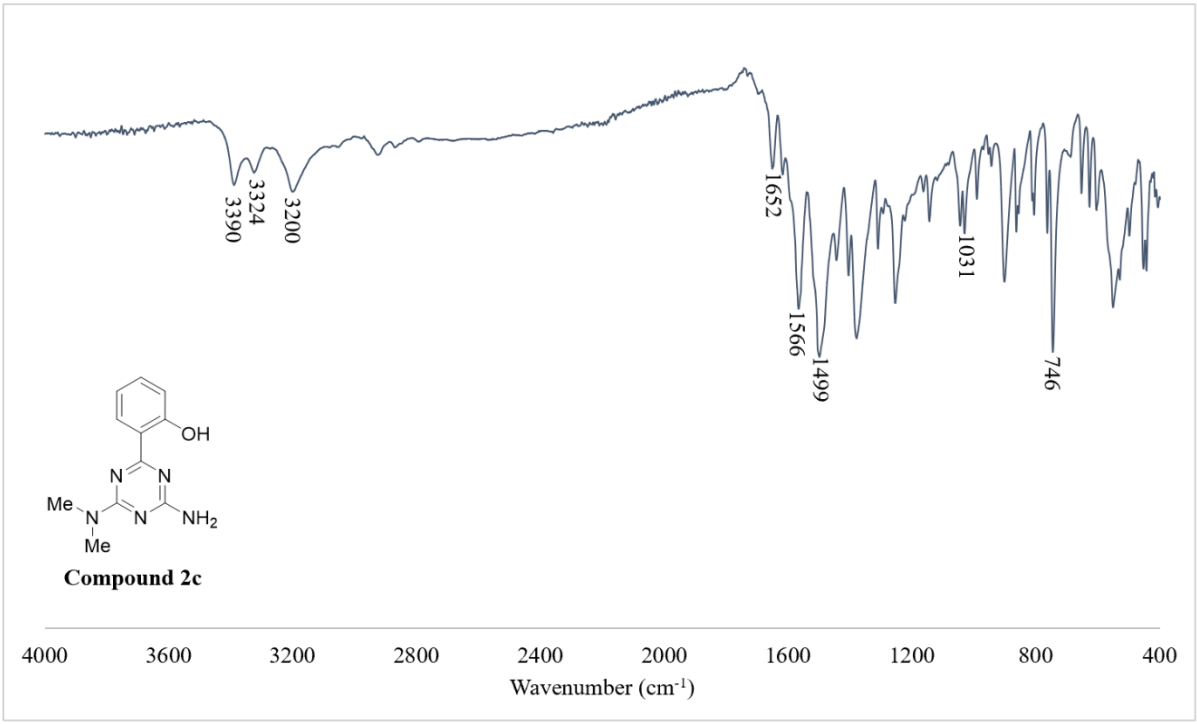

Figure 12. IR spectrum of 2-(4-amino-6-(dimethylamino)-1,3,5-triazin-2-yl)phenol (**2c**)

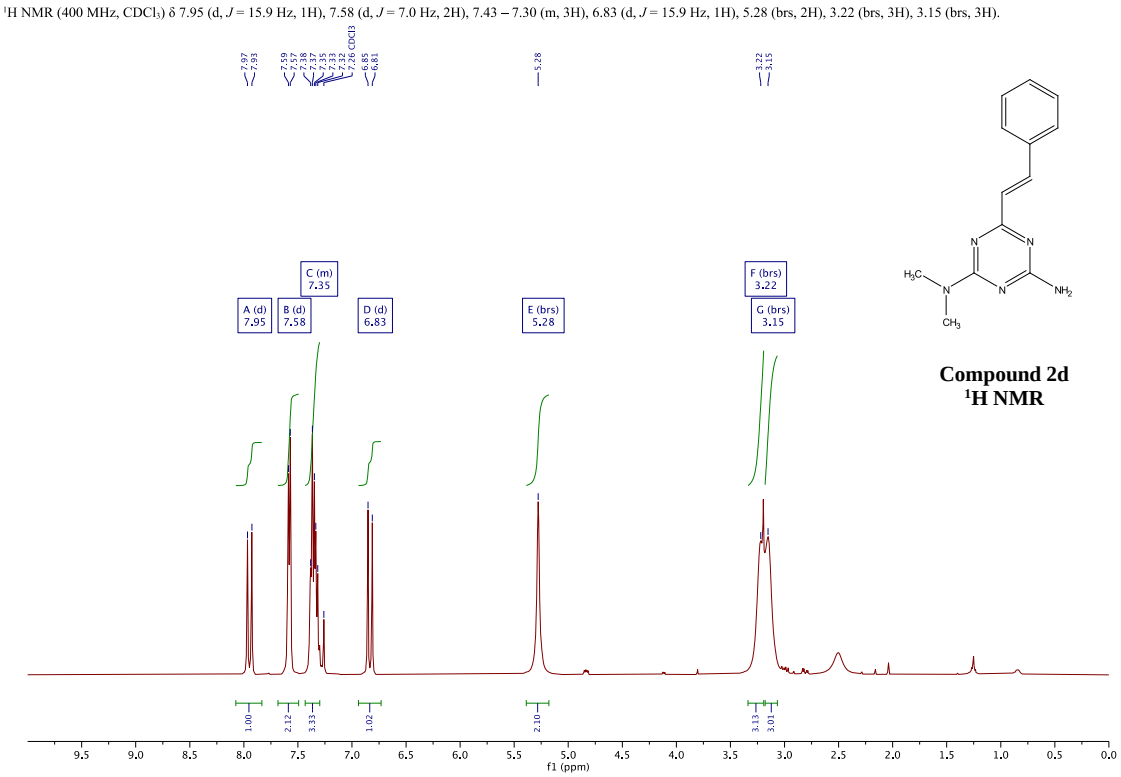

Figure 13. ^{1}H NMR of (*E*)-N^2,N^2-dimethyl-6-styryl-1,3,5-triazine-2,4-diamine (**2d**)

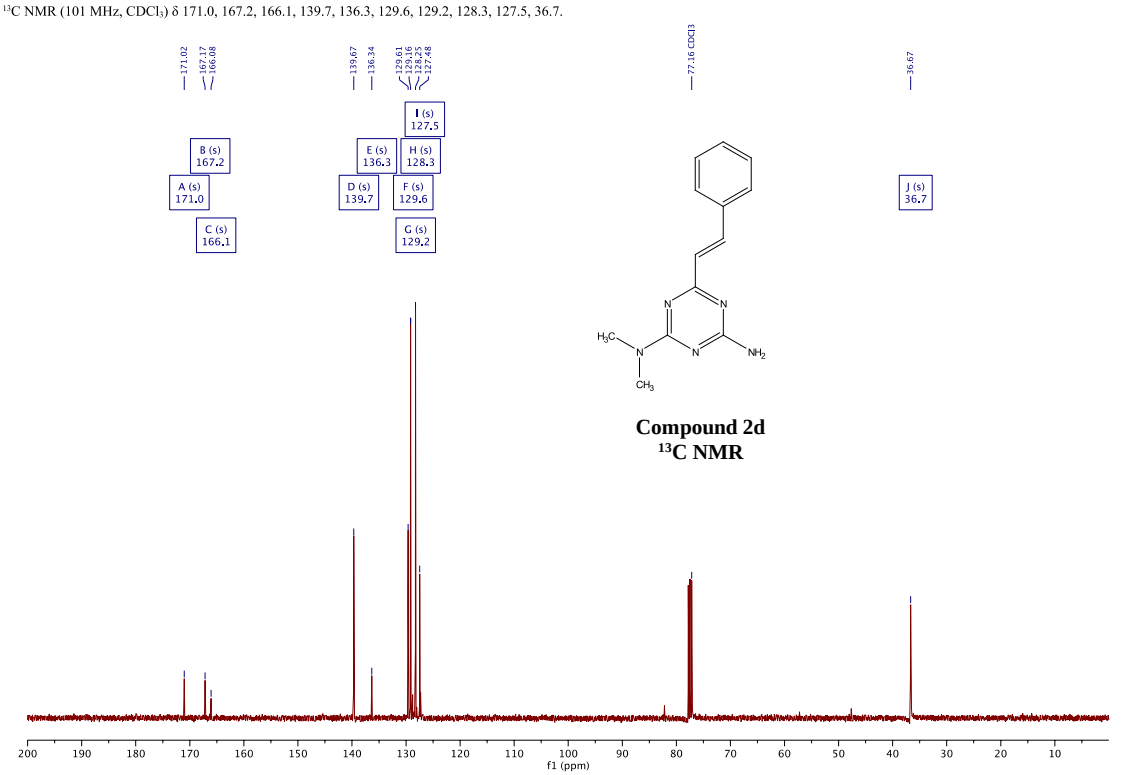

Figure 14. ^{13}C NMR of (*E*)-N^2,N^2-dimethyl-6-styryl-1,3,5-triazine-2,4-diamine (**2d**)

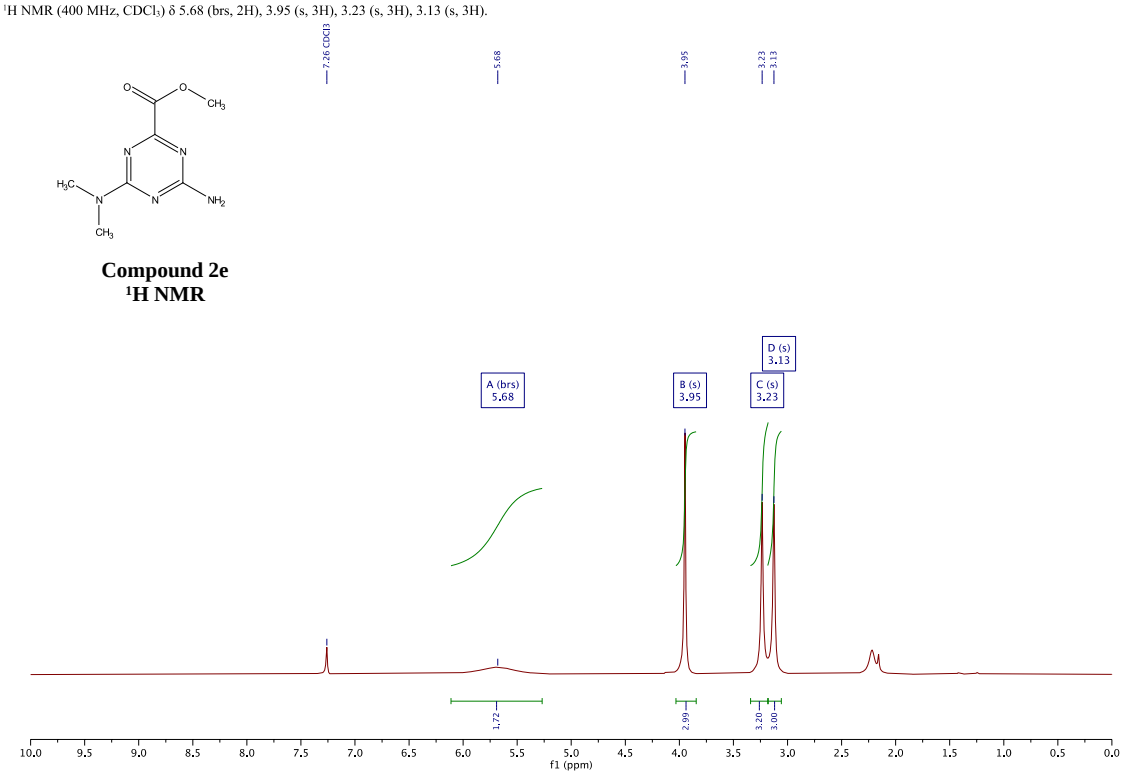

Figure 15. ^{1}H NMR of Methyl 4-amino-6-(dimethylamino)-1,3,5-triazine-2-carboxylate (**2e**)

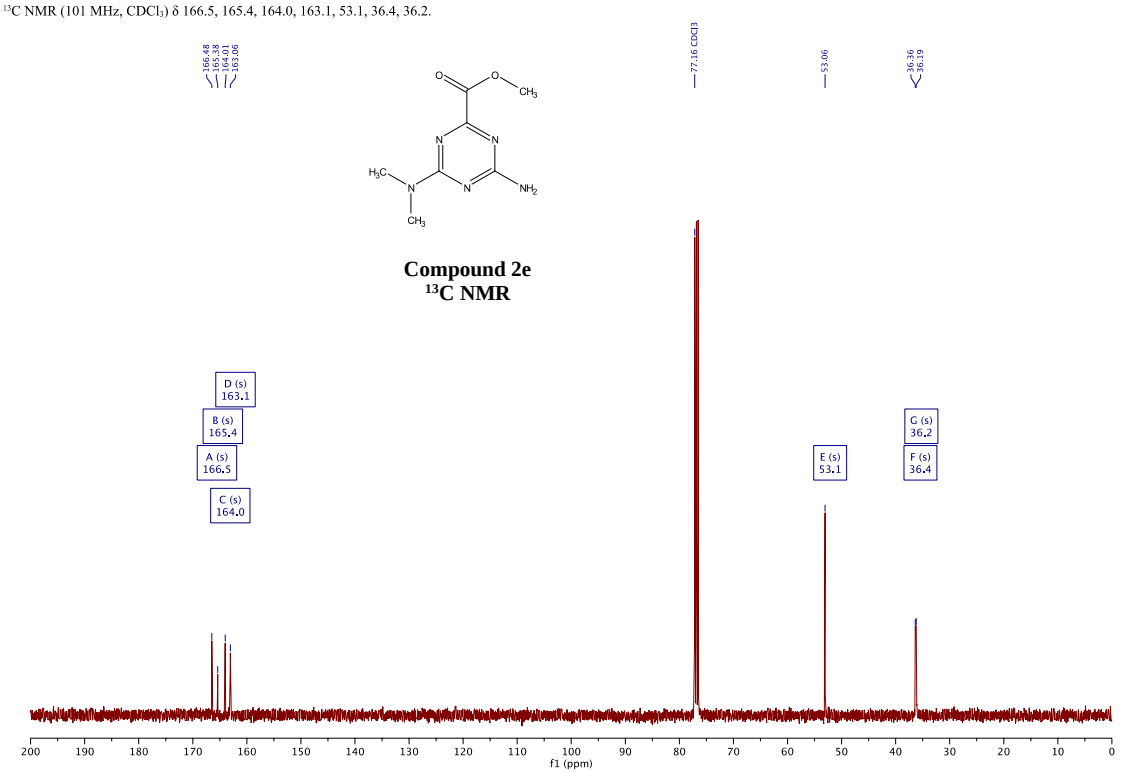

Figure 16. ^{13}C NMR of Methyl 4-amino-6-(dimethylamino)-1,3,5-triazine-2-carboxylate (**2e**)

Mass Spectrum List Report

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Comment			

Acquisition Parameter

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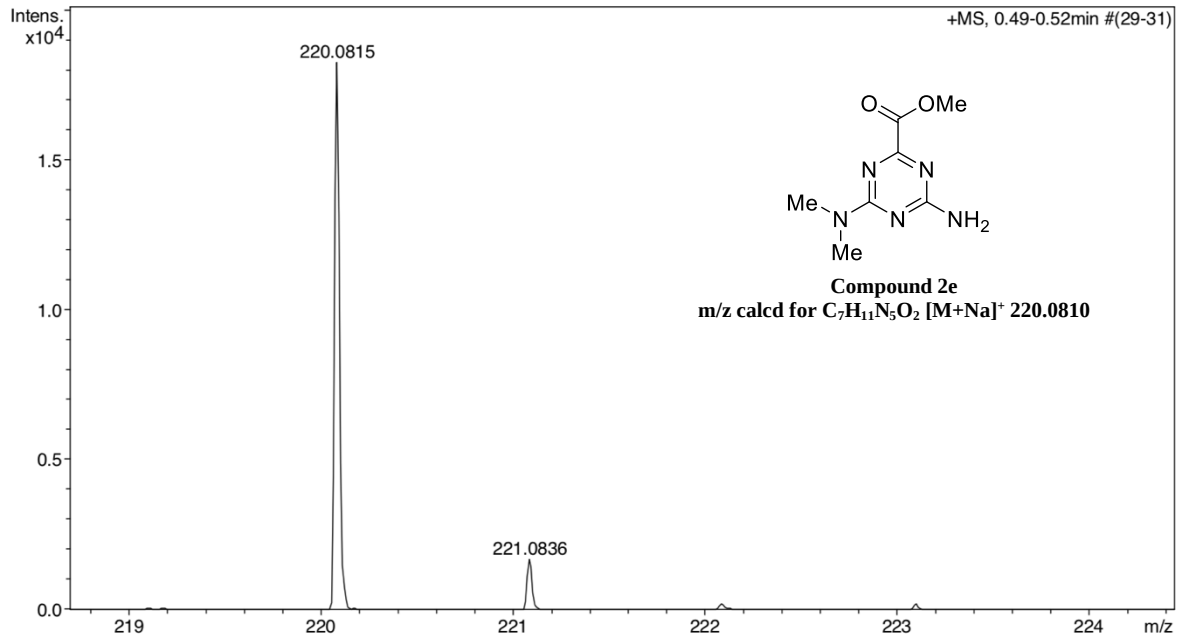

Figure 17. HRMS spectrum of Methyl 4-amino-6-(dimethylamino)-1,3,5-triazine-2-carboxylate (**2e**)

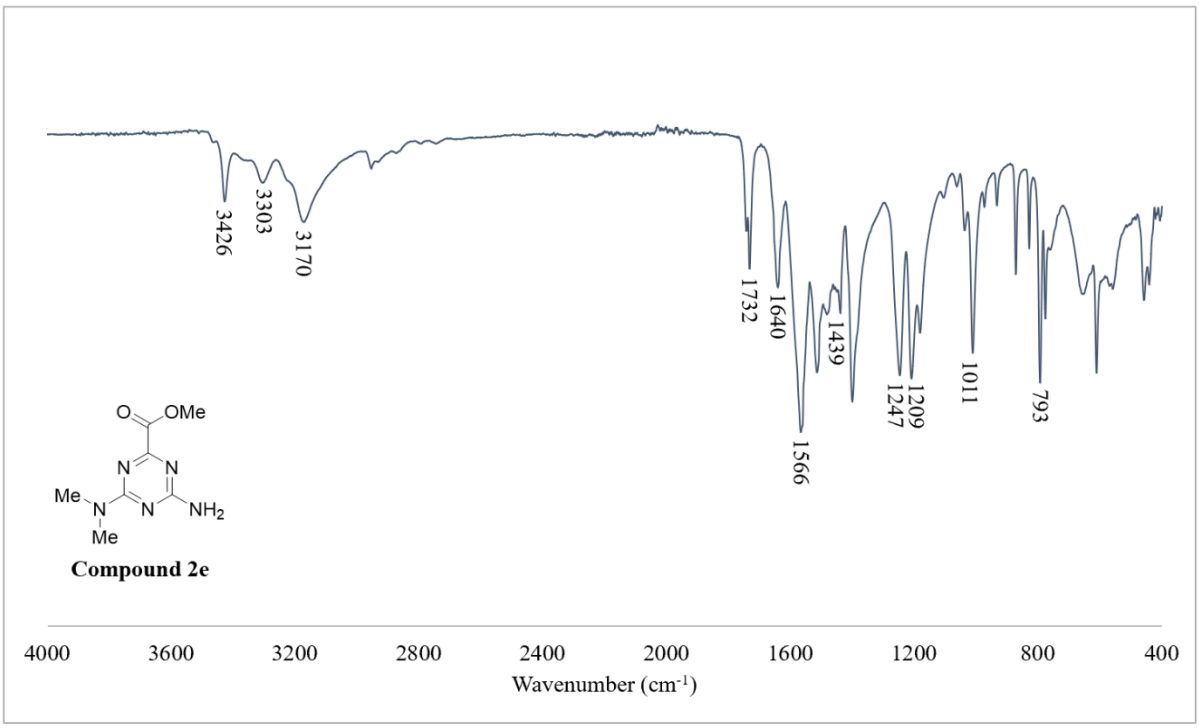

Figure 18. IR spectrum of Methyl 4-amino-6-(dimethylamino)-1,3,5-triazine-2-carboxylate (**2e**)

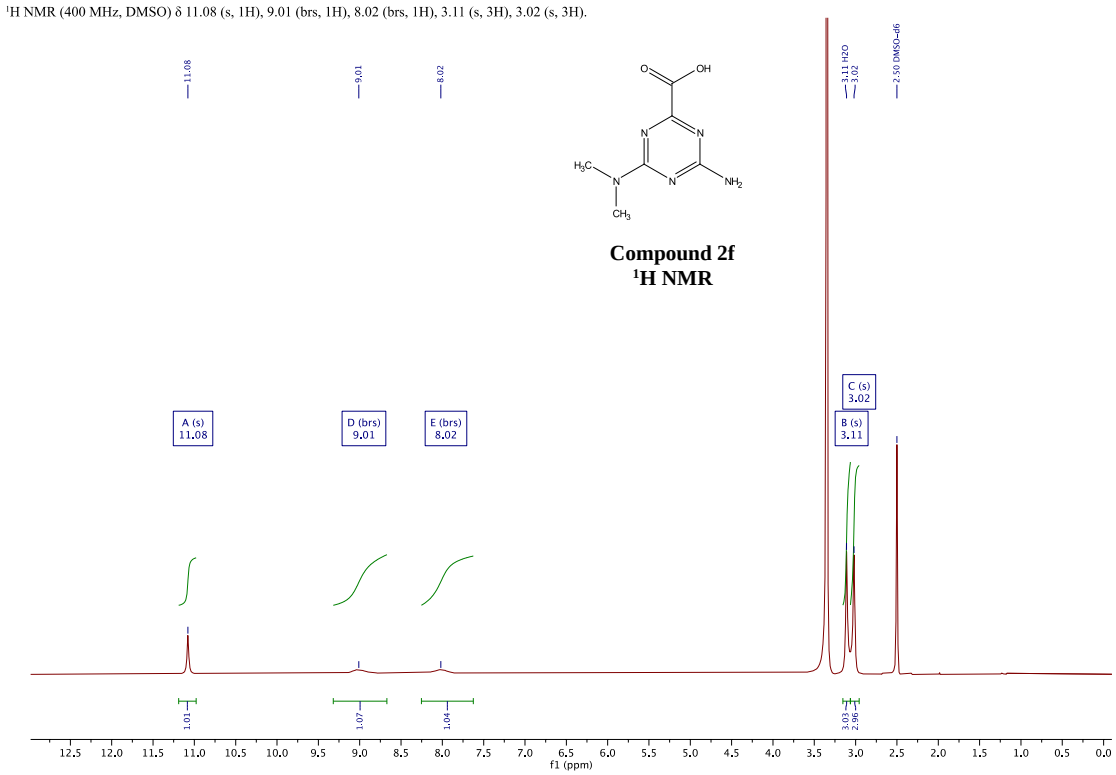

Figure 19. ^{1}H NMR of 4-amino-6-(dimethylamino)-1,3,5-triazine-2-carboxylic acid (**2f**)

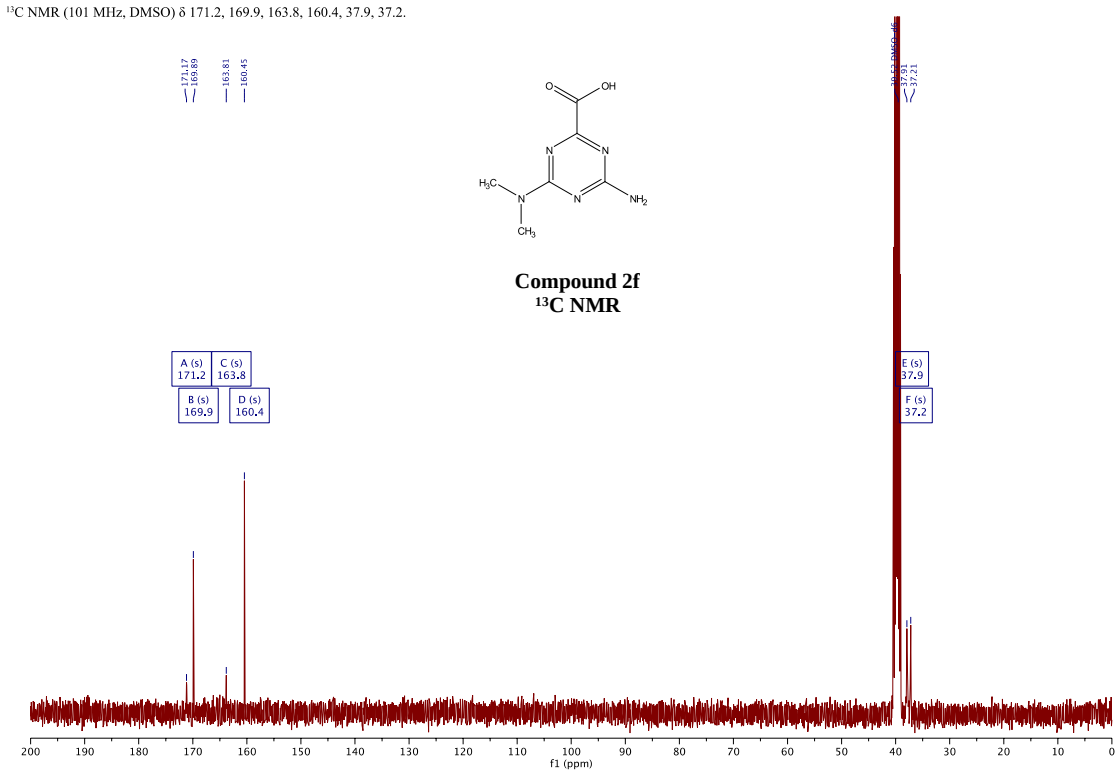

Figure 20. ^{13}C NMR of 4-amino-6-(dimethylamino)-1,3,5-triazine-2-carboxylic acid (**2f**)

Mass Spectrum List Report

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Comment			

Acquisition Parameter

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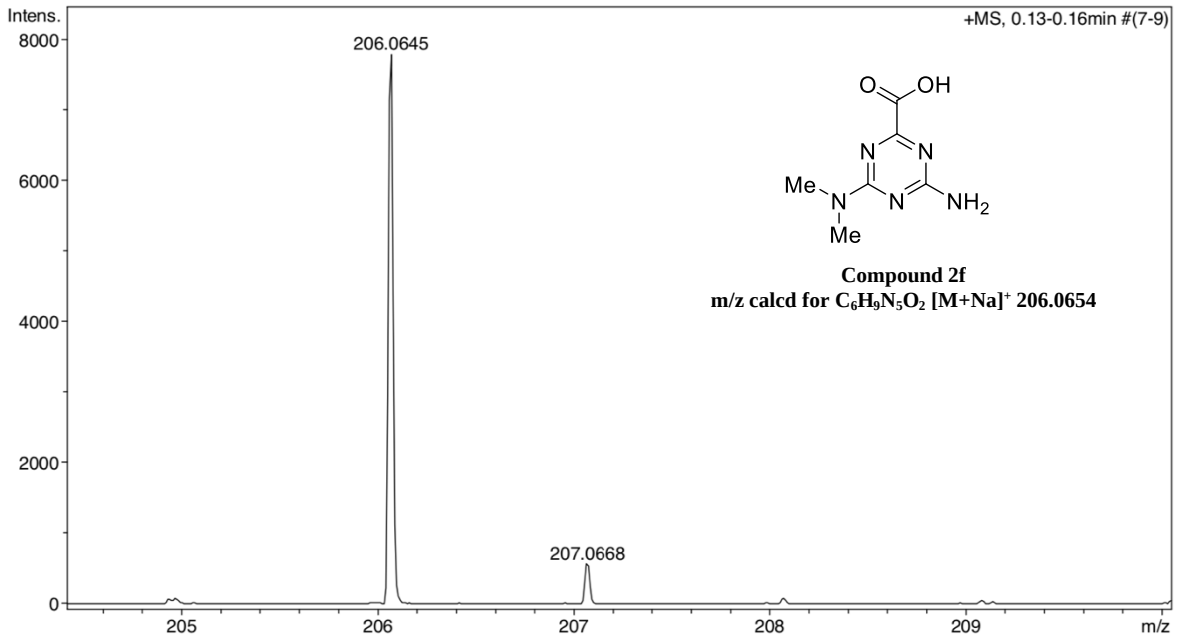

Compound 2f

m/z calcd for $C_6H_9N_5O_2$ $[M+Na]^+$ 206.0654

Figure 21. HRMS spectrum of 4-amino-6-(dimethylamino)-1,3,5-triazine-2-carboxylic acid (**2f**)

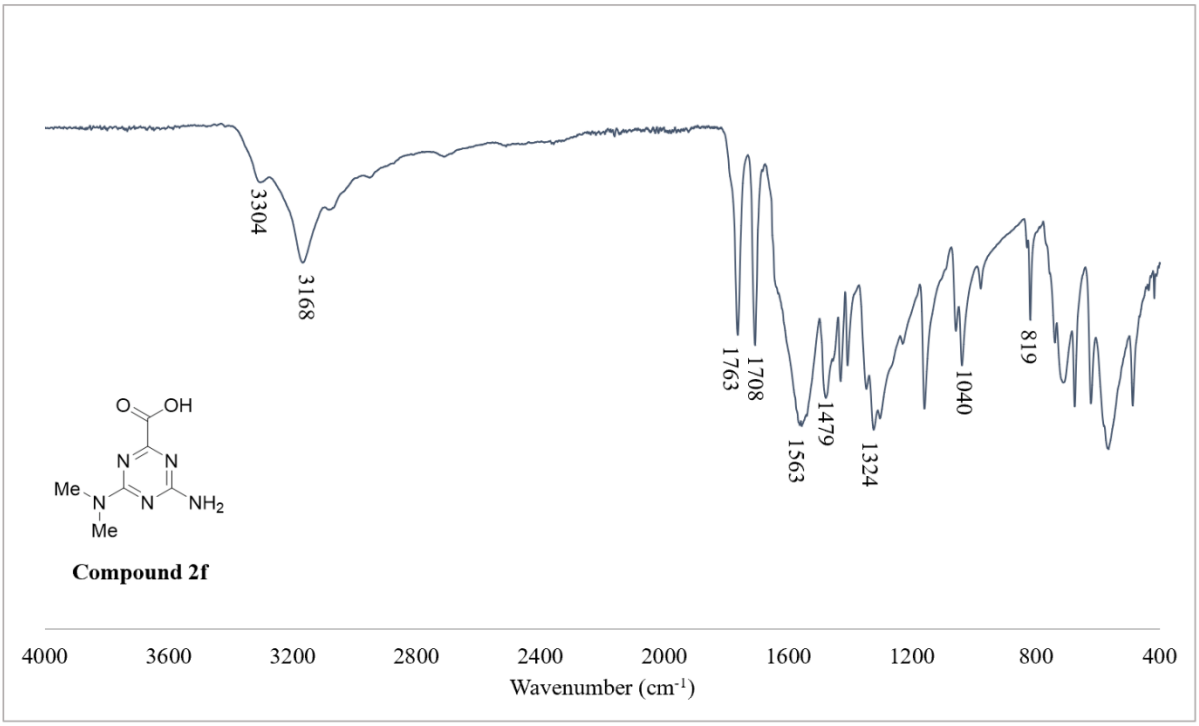

Figure 22. IR spectrum of 4-amino-6-(dimethylamino)-1,3,5-triazine-2-carboxylic acid (**2f**)

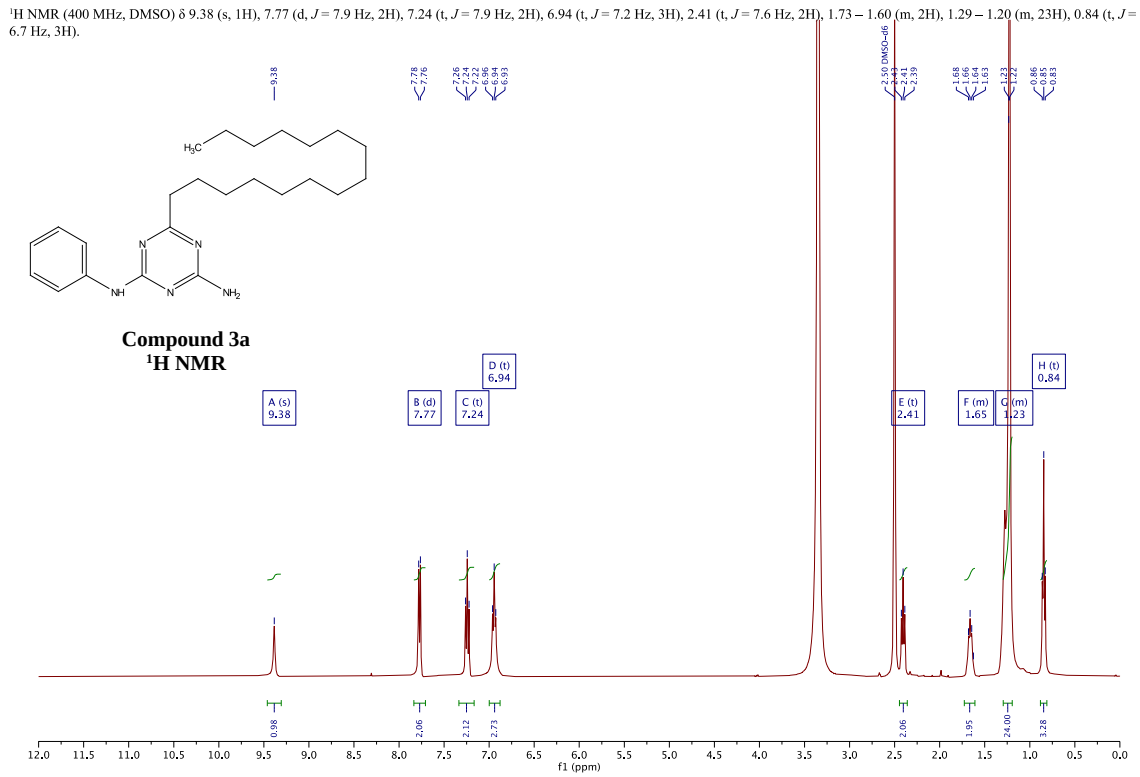

Figure 23. ^{1}H NMR of 6-pentadecyl-*N*^{2}-phenyl-1,3,5-triazine-2,4-diamine (**3a**)

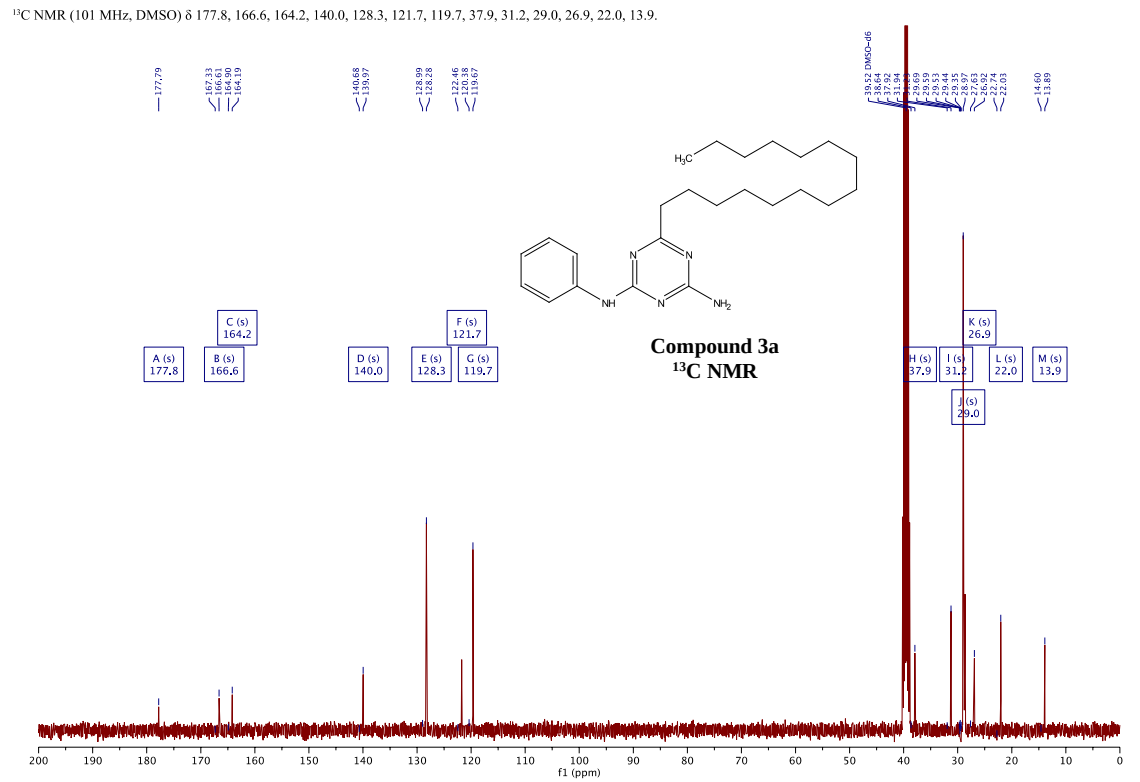

Figure 24. ^{13}C NMR of 6-pentadecyl-*N*^{2}-phenyl-1,3,5-triazine-2,4-diamine (**3a**)

Mass Spectrum List Report

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Comment			

Acquisition Parameter

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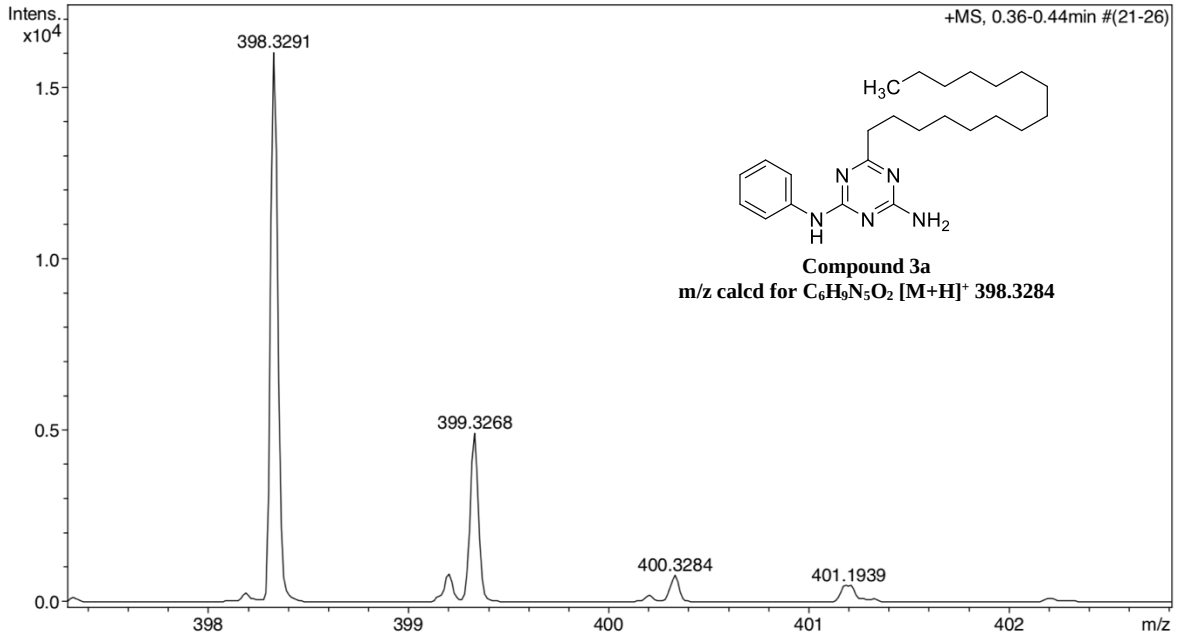

Figure 25. HRMS spectrum of 6-pentadecyl-*N*^{2}-phenyl-1,3,5-triazine-2,4-diamine (**3a**)

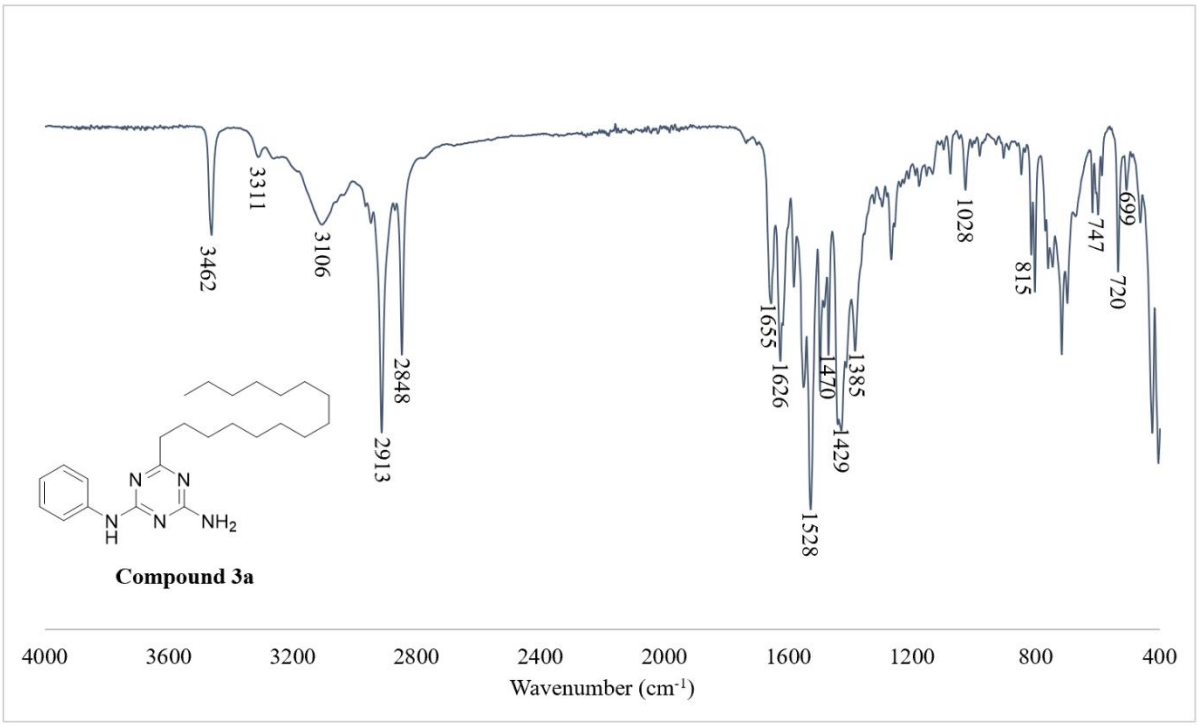

Figure 26. IR spectrum of 6-pentadecyl-N^2-phenyl-1,3,5-triazine-2,4-diamine (**3a**)

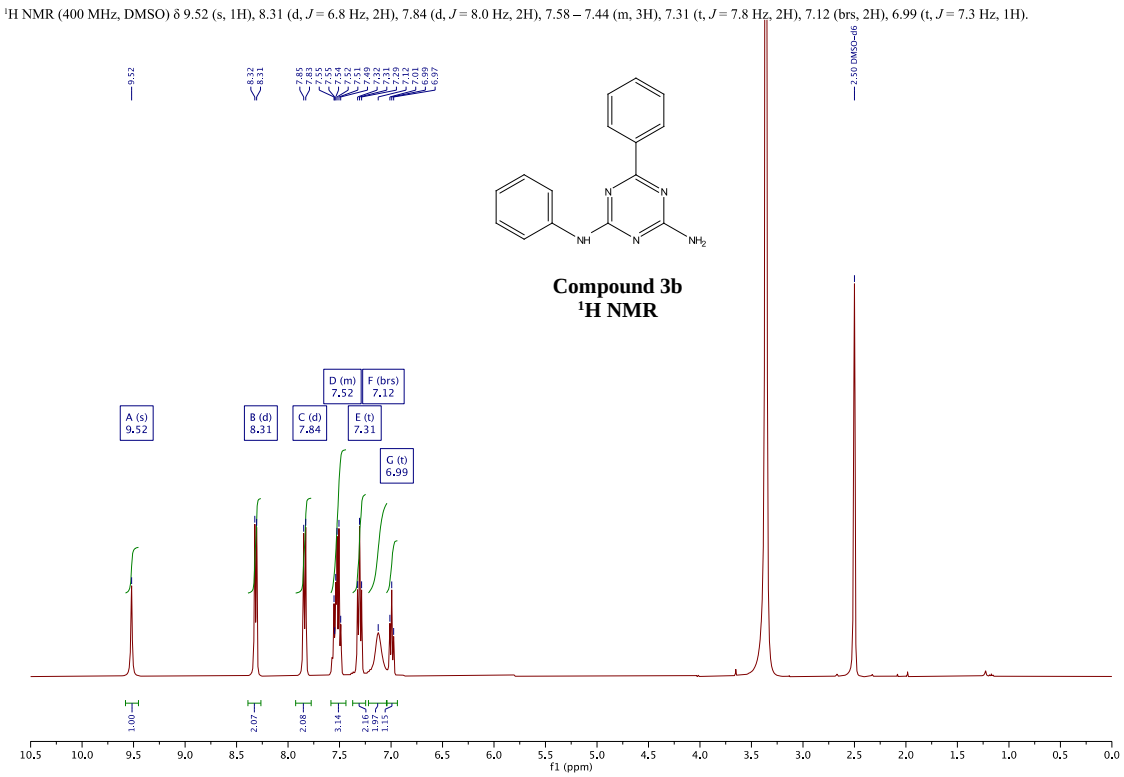

Figure 27. [1]H NMR of *N*[2],6-diphenyl-1,3,5-triazine-2,4-diamine (**3b**)

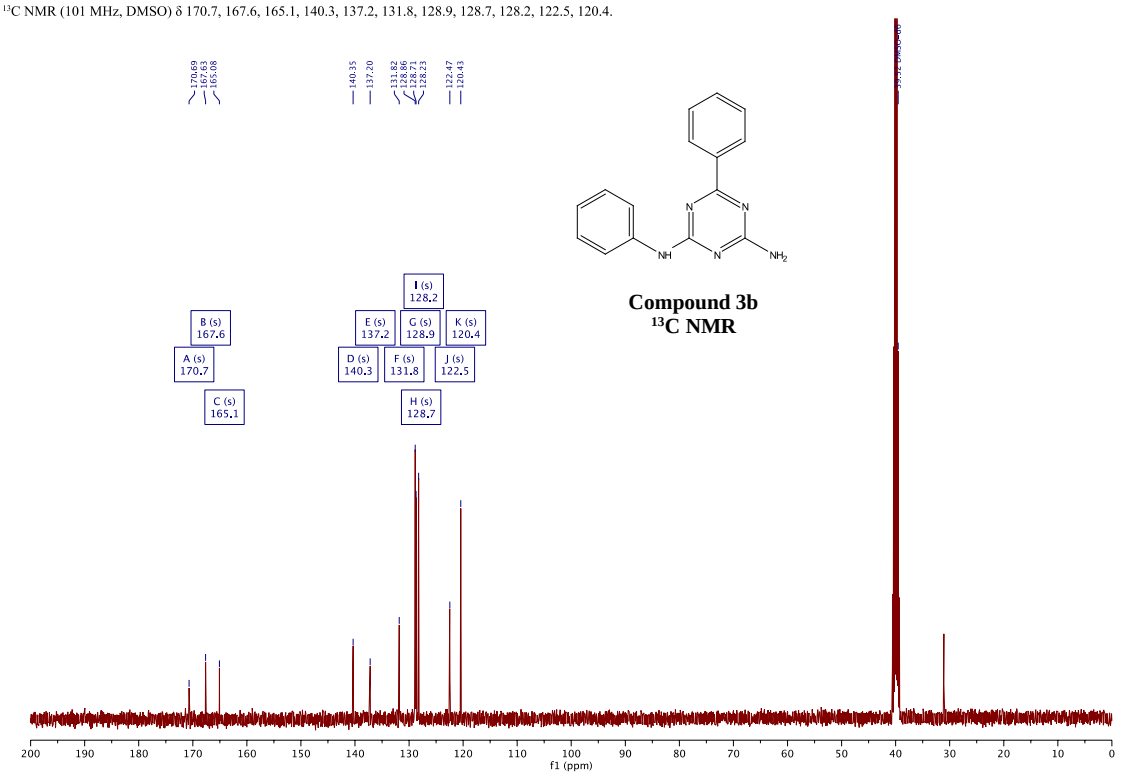

Figure 28. [13]C NMR of *N*[2],6-diphenyl-1,3,5-triazine-2,4-diamine (**3b**)

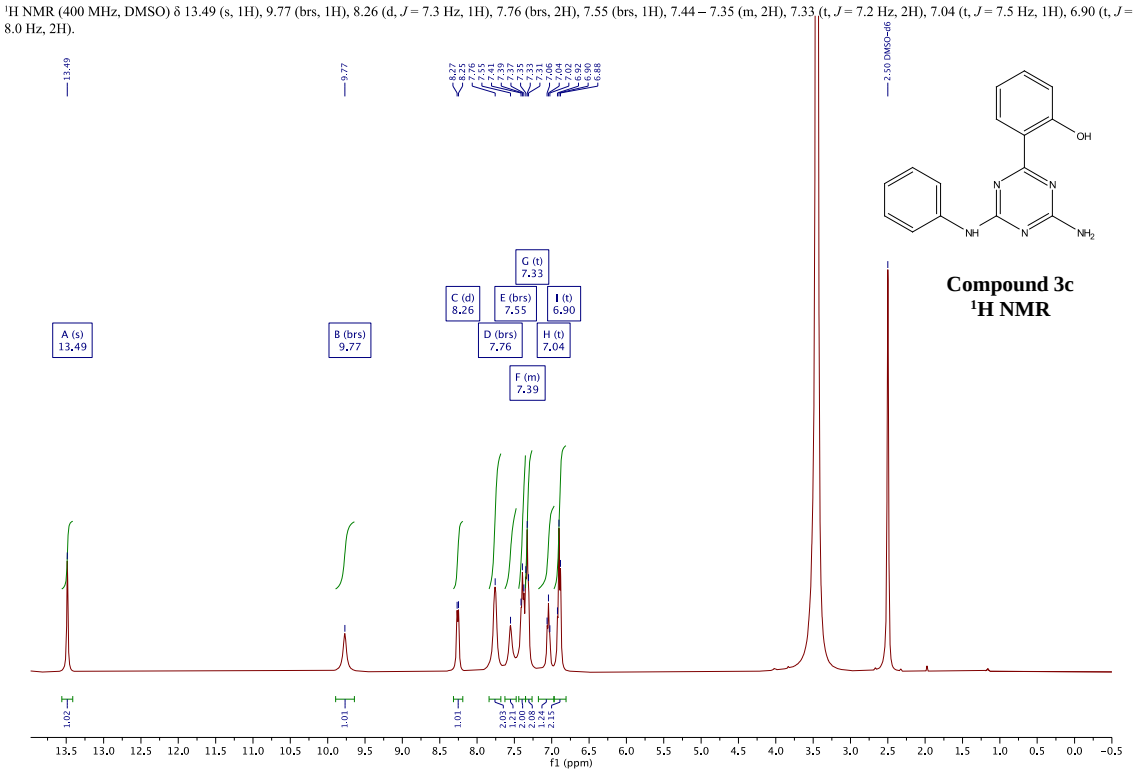

Figure 29. ^{1}H NMR of 2-(4-amino-6-(phenylamino)-1,3,5-triazin-2-yl)phenol (**3c**)

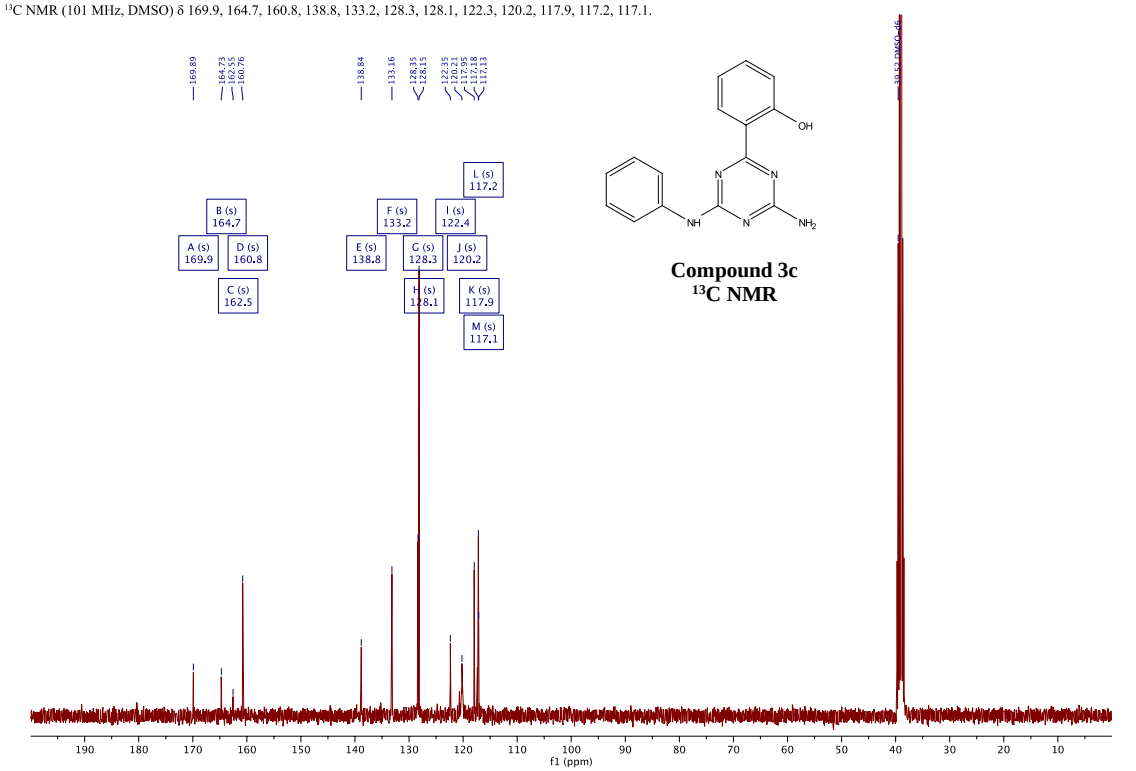

Figure 30. ^{13}C NMR of 2-(4-amino-6-(phenylamino)-1,3,5-triazin-2-yl)phenol (**3c**)

Mass Spectrum List Report

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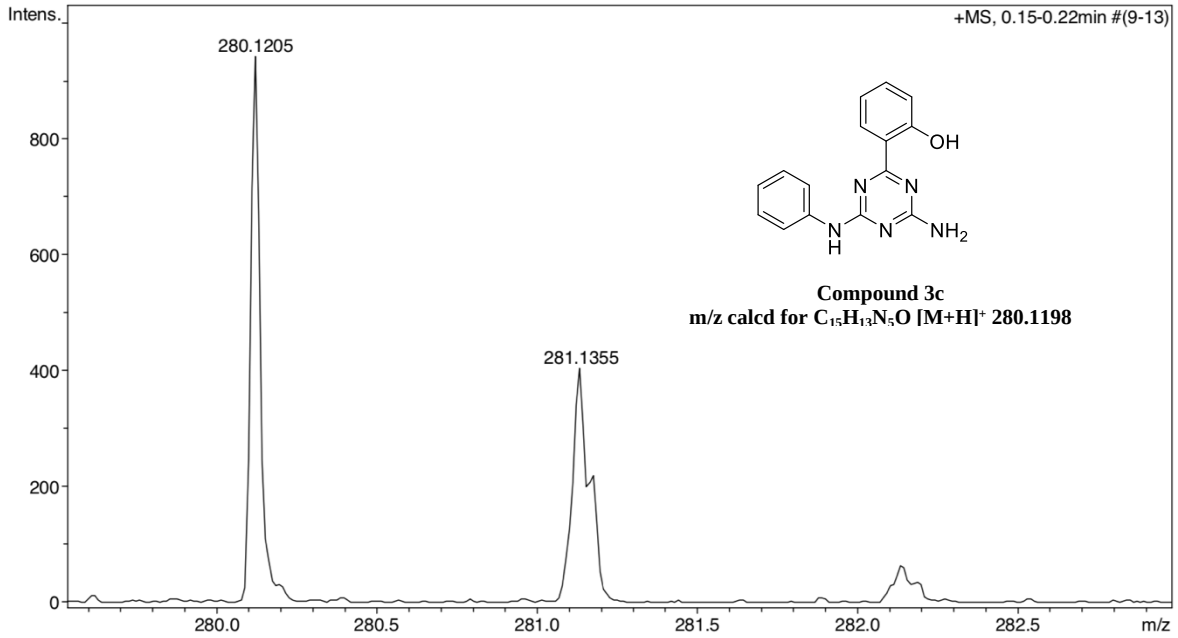

Figure 31. HRMS spectrum of 2-(4-amino-6-(phenylamino)-1,3,5-triazin-2-yl)phenol (**3c**)

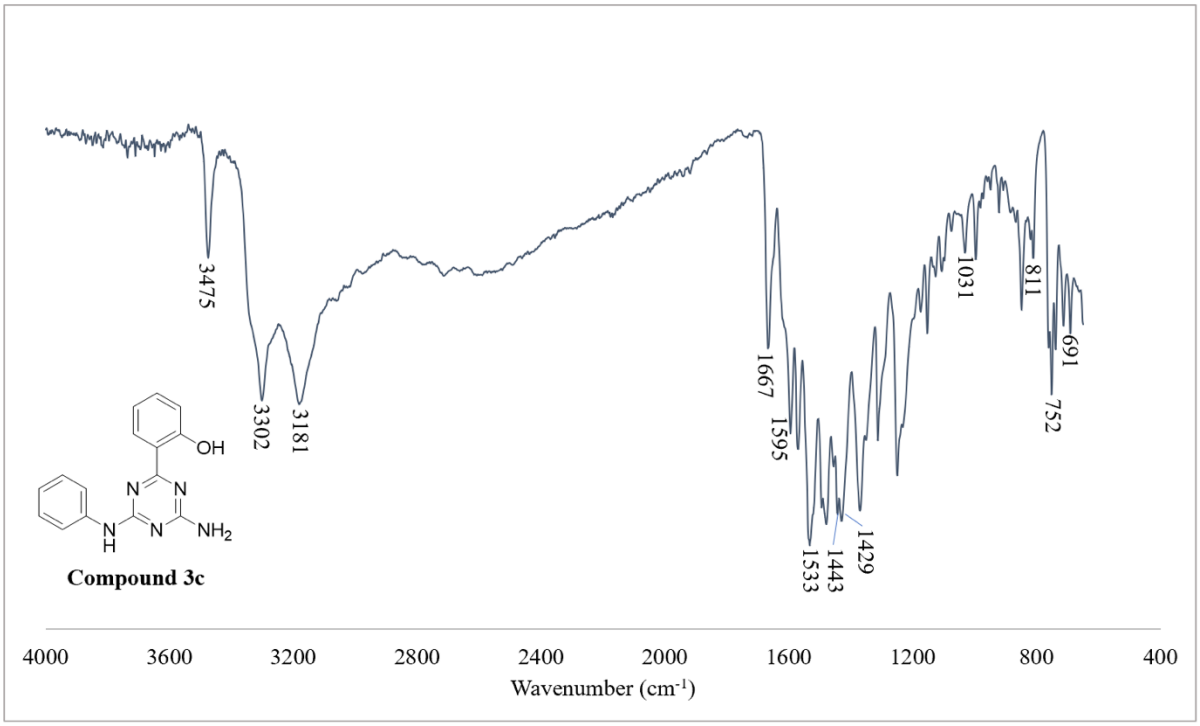

Figure 32. IR spectrum of 2-(4-amino-6-(phenylamino)-1,3,5-triazin-2-yl)phenol (**3c**)

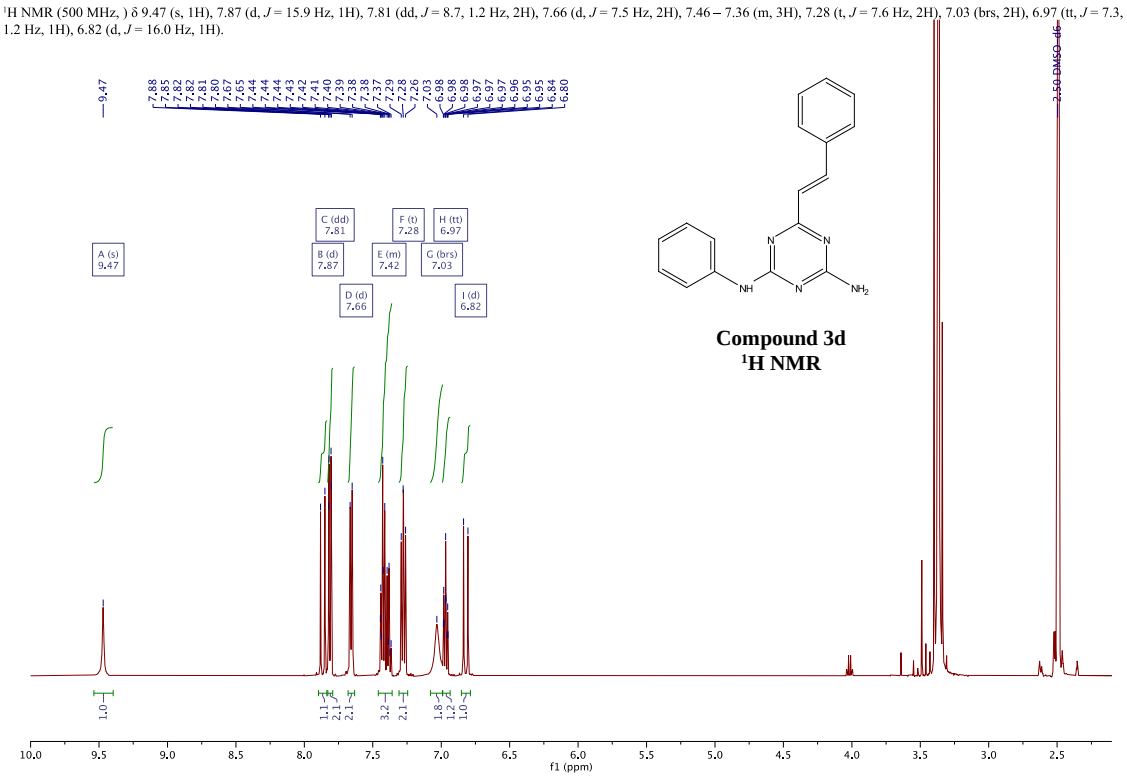

Figure 33. ^{1}H NMR of (*E*)-*N*^{2}-phenyl-6-styryl-1,3,5-triazine-2,4-diamine (**3d**)

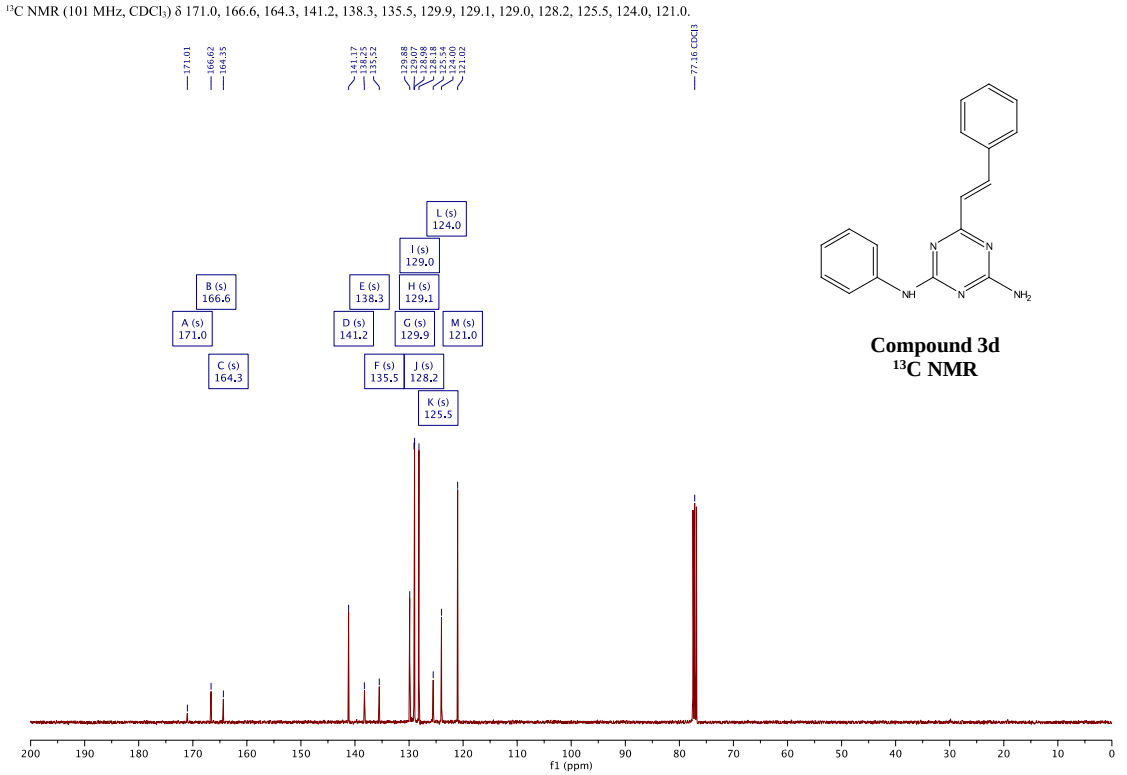

Figure 34. ^{13}C NMR of (*E*)-*N*^{2}-phenyl-6-styryl-1,3,5-triazine-2,4-diamine (**3d**)

Mass Spectrum List Report

Analysis Info

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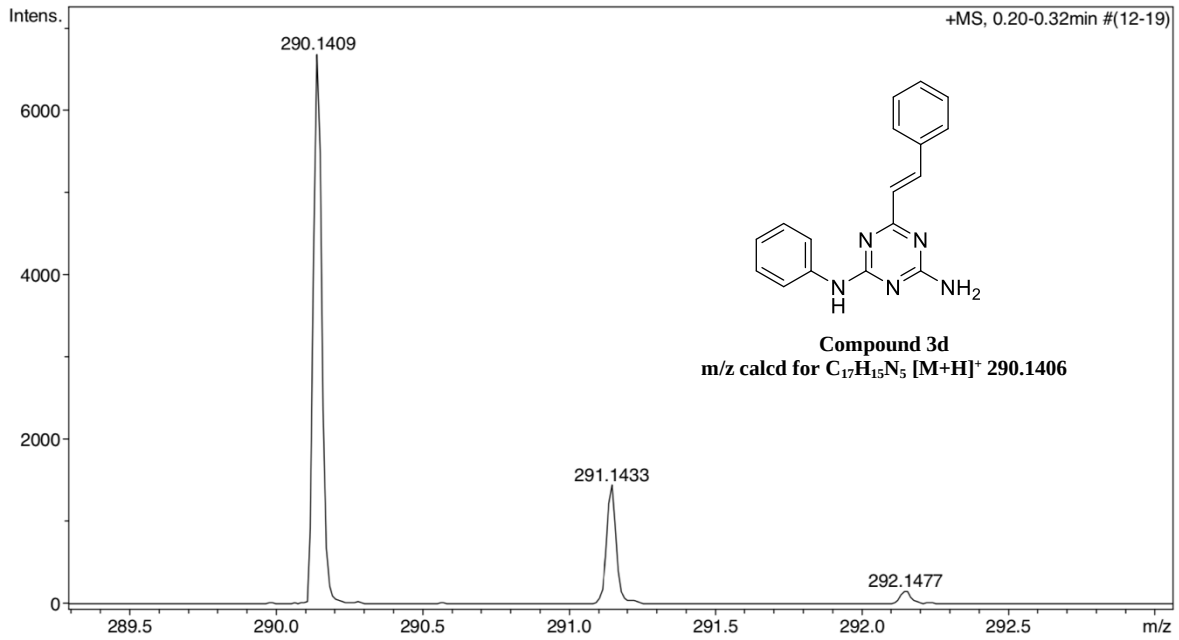

Figure 35. HRMS spectrum of (*E*)-N^2-phenyl-6-styryl-1,3,5-triazine-2,4-diamine (**3d**)

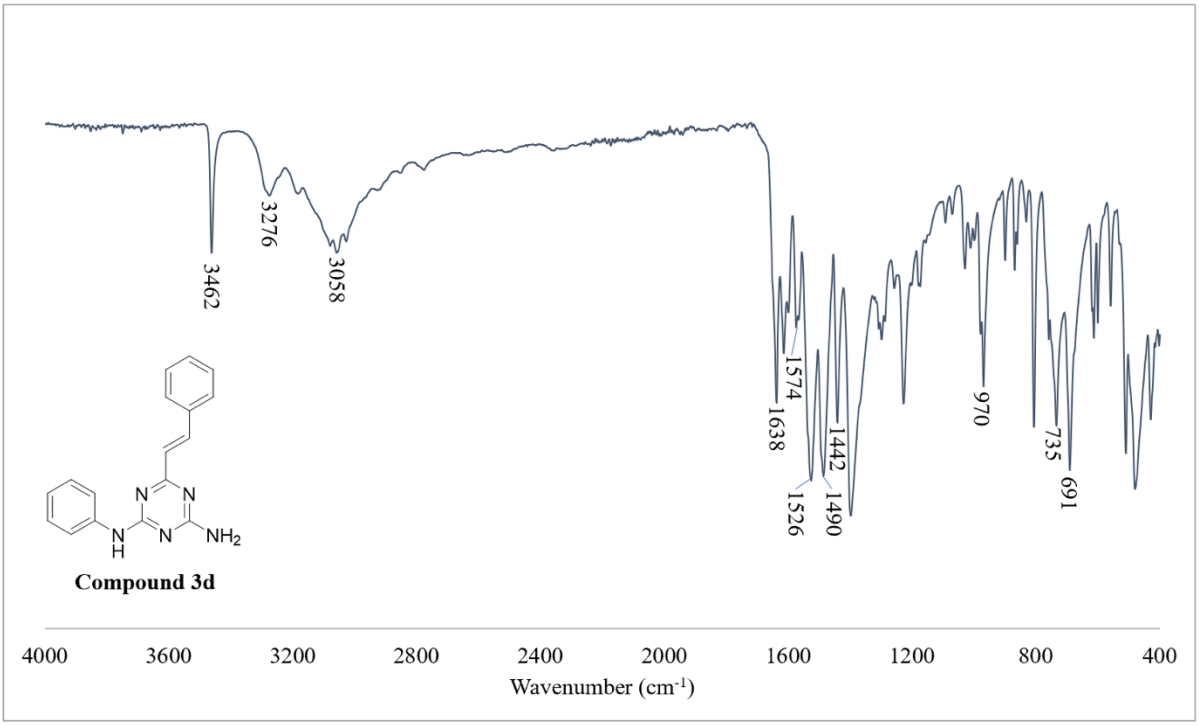

Figure 36. IR spectrum of (*E*)-N^2-phenyl-6-styryl-1,3,5-triazine-2,4-diamine (**3d**)

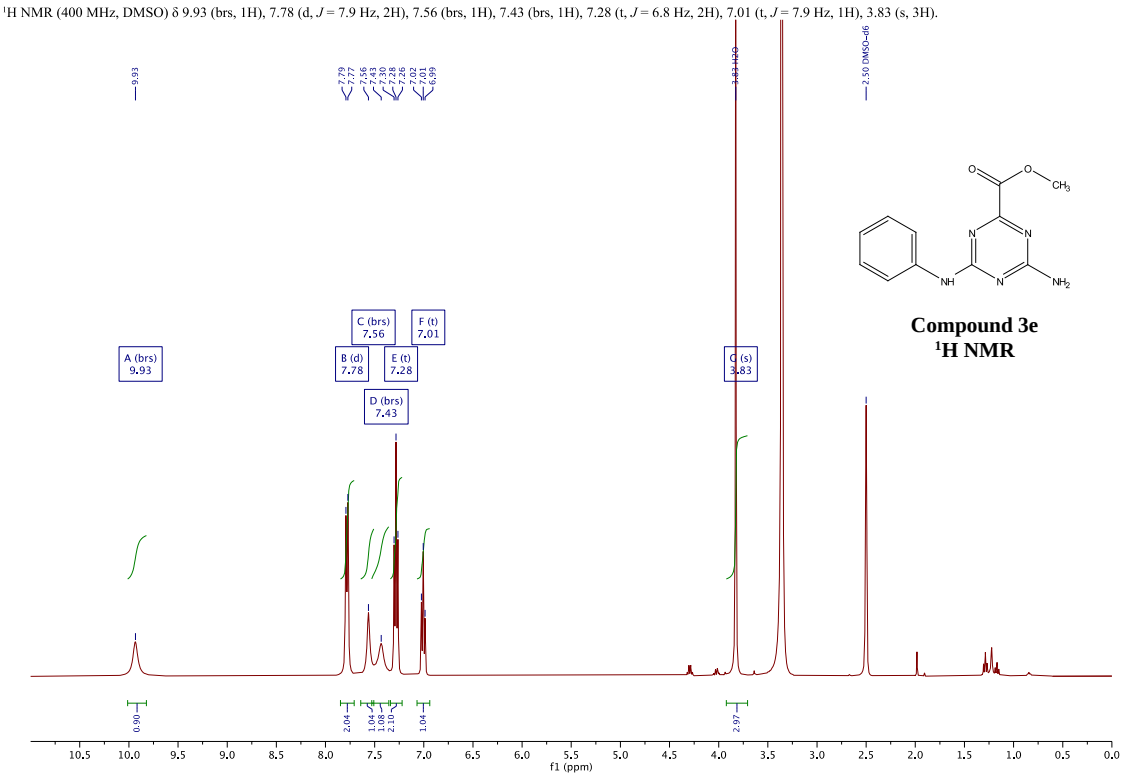

Figure 37. [1]H NMR of Methyl 4-amino-6-(phenylamino)-1,3,5-triazine-2-carboxylate (**3e**)

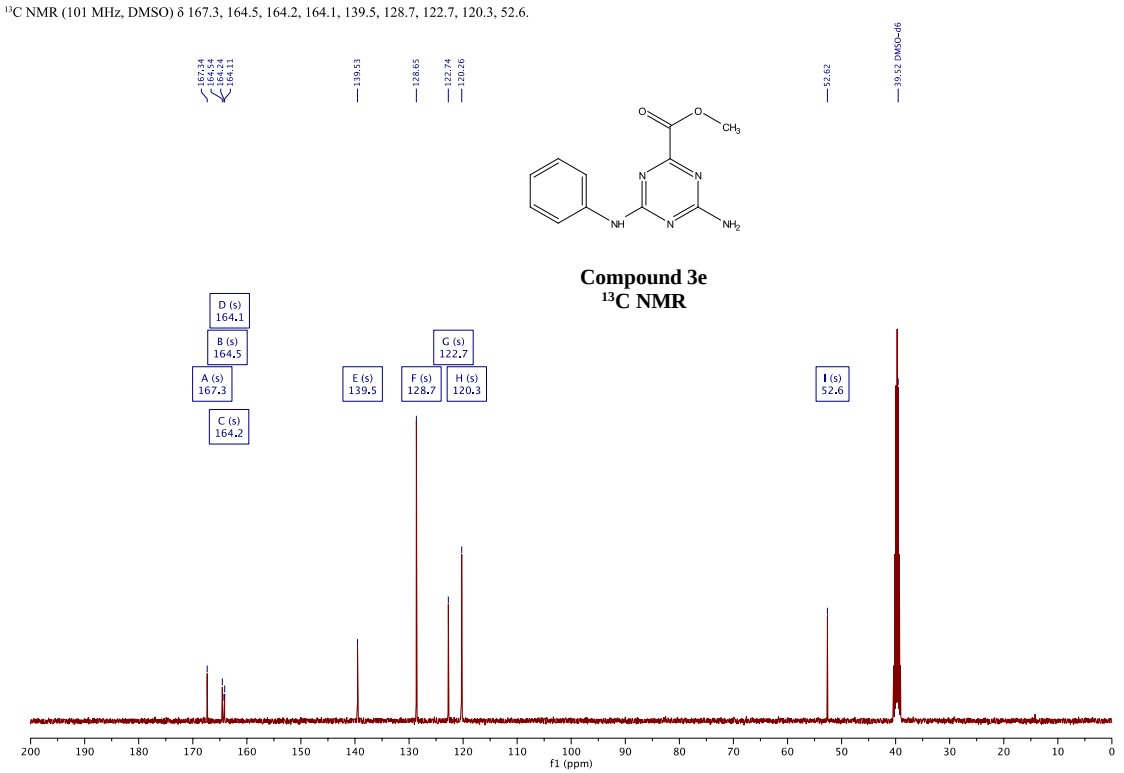

Figure 38. [13]C NMR of Methyl 4-amino-6-(phenylamino)-1,3,5-triazine-2-carboxylate (**3e**)

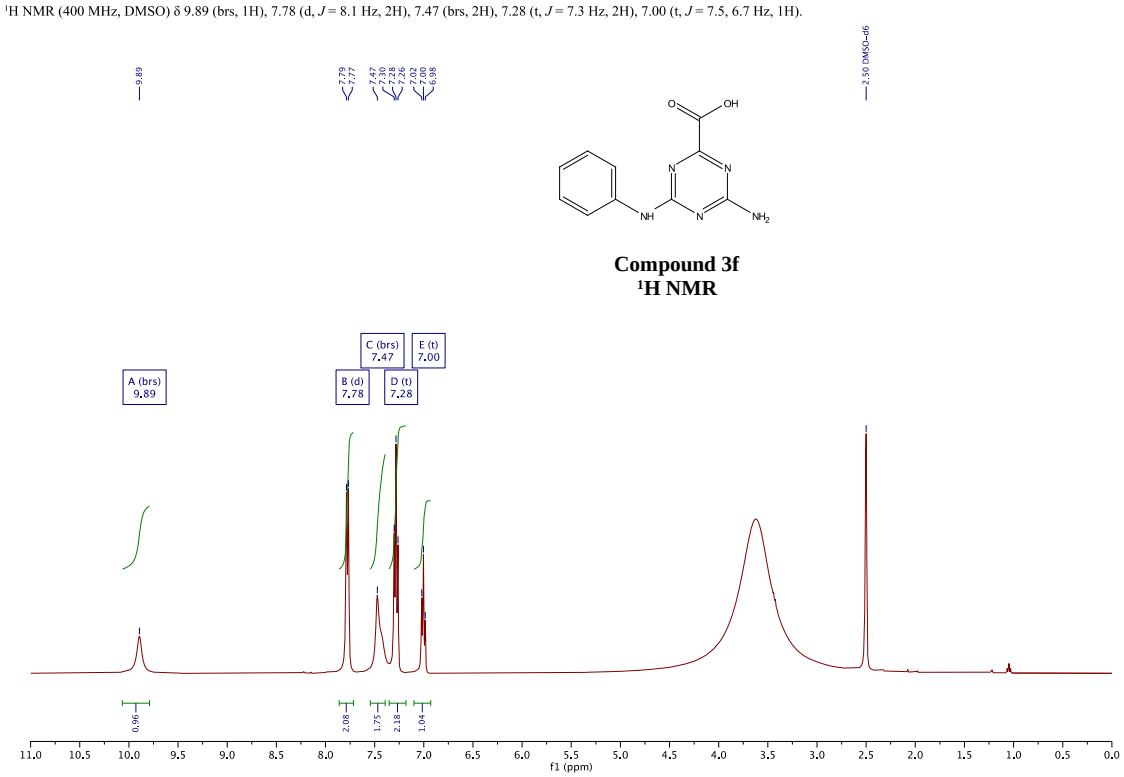

Figure 39. ^{1}H NMR of 4-amino-6-(phenylamino)-1,3,5-triazine-2-carboxylic acid (**3f**)

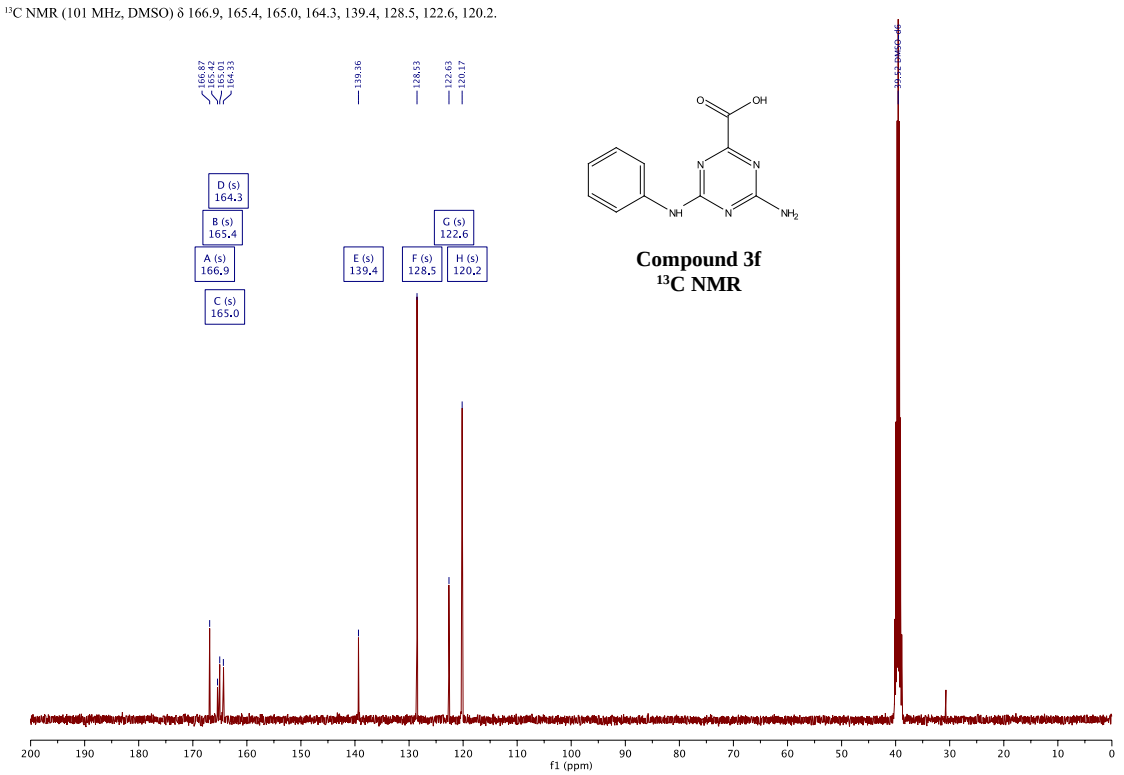

Figure 40. ^{13}C NMR of 4-amino-6-(phenylamino)-1,3,5-triazine-2-carboxylic acid (**3f**)

Mass Spectrum List Report

Analysis Info

Analysis Name	D:\Data\Data Service\190827\A53_RB1_01_3017.d	Acquisition Date	8/27/2019 9:33:05 PM
Method	nv_pos_6min_profile_wguardcol_190624.m	Operator	CU.
Sample Name	A53	Instrument / Ser#	micrOTOF-Q II 10335
Comment			

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	3.0 Bar
Focus	Not active	Set Capillary	4000 V	Set Dry Heater	200 ℃
Scan Begin	100 m/z	Set End Plate Offset	-500 V	Set Dry Gas	8.0 l/min
Scan End	1500 m/z	Set Collision Cell RF	250.0 Vpp	Set Divert Valve	Waste

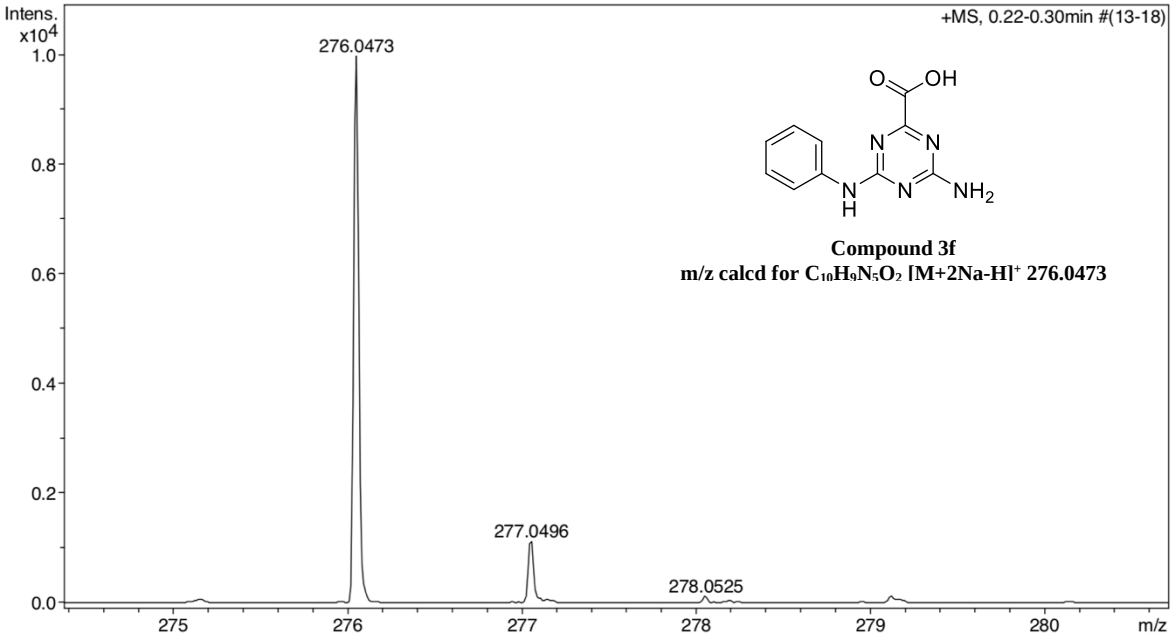

Figure 41. HRMS spectrum of 4-amino-6-(phenylamino)-1,3,5-triazine-2-carboxylic acid (**3f**)

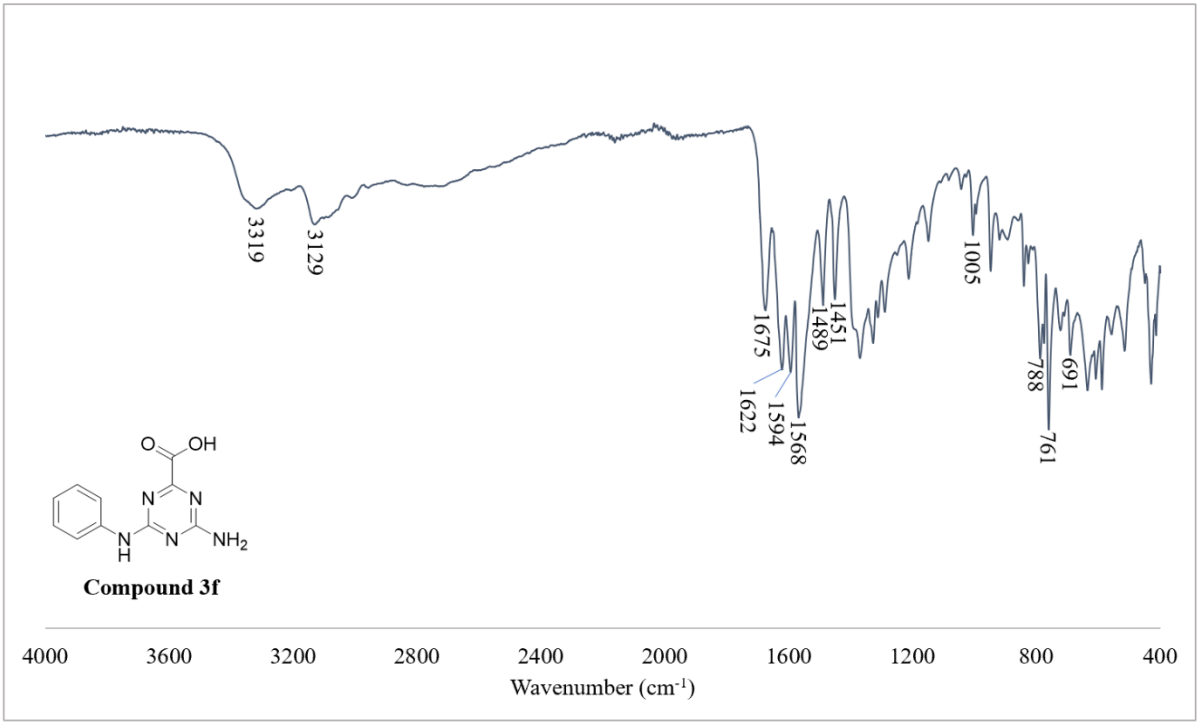

Figure 42. IR spectrum of 4-amino-6-(phenylamino)-1,3,5-triazine-2-carboxylic acid (**3f**)

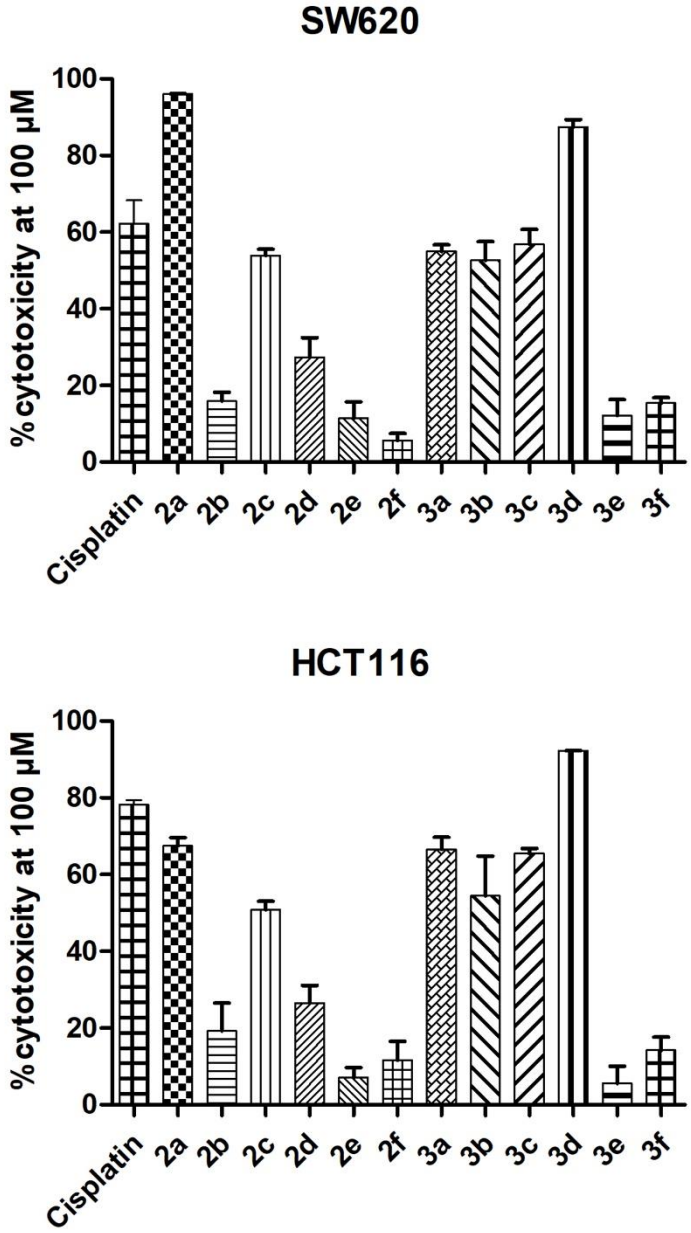

Figure 43. The cytotoxicity of twelve 1,3,5-triazine derivatives at 100 µM.

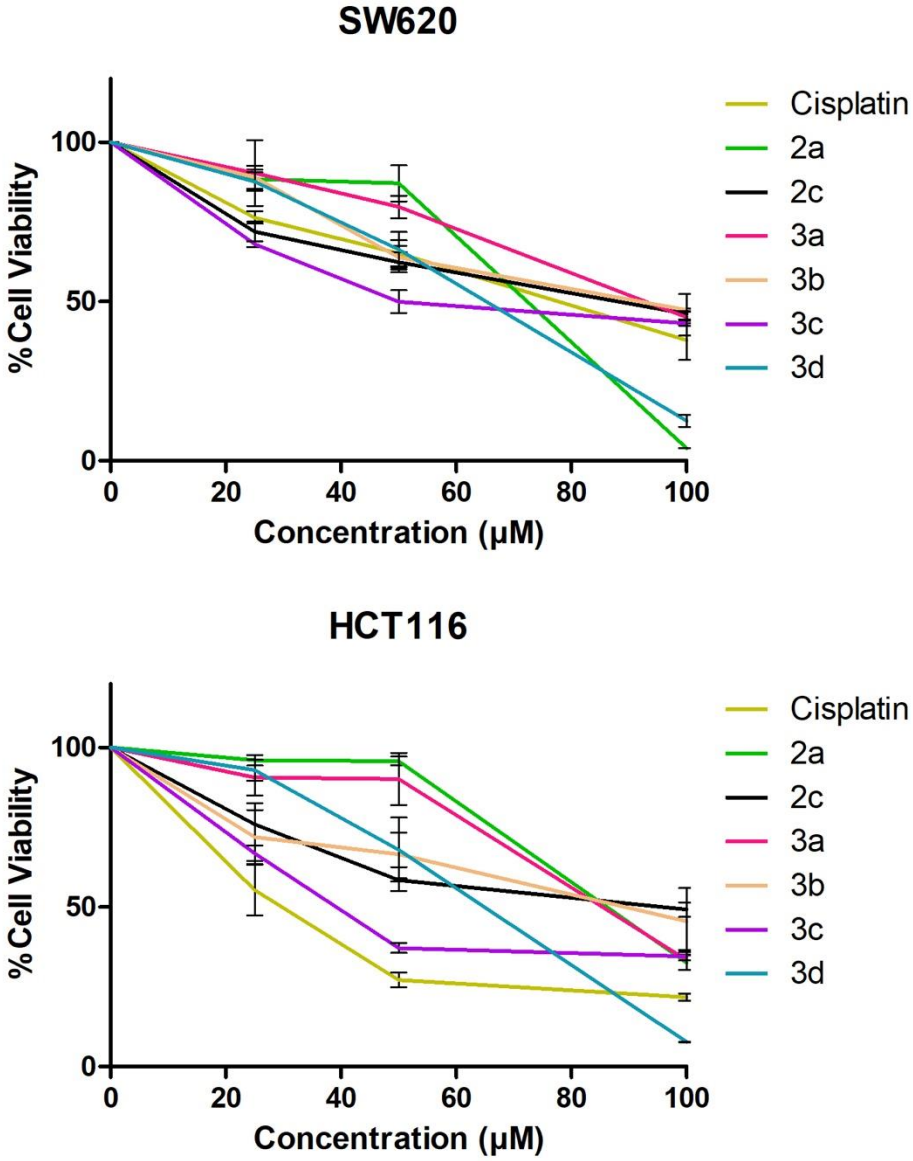

Figure 44. The concentration-response curves of the six 1,3,5-triazine derivatives at different concentrations (25, 50 and 100 μM) against SW620 and HCT116 cell lines for the calculation of IC_{50} values.

		Size (d.nm):	% Intensity:	St Dev (d.n...
Z-Average (d.nm): 369.3	Peak 1:	319.6	94.9	113.4
PdI: 0.464	Peak 2:	4908	5.1	701.4
Intercept: 1.01	Peak 3:	0.000	0.0	0.000

Result quality : Refer to quality report

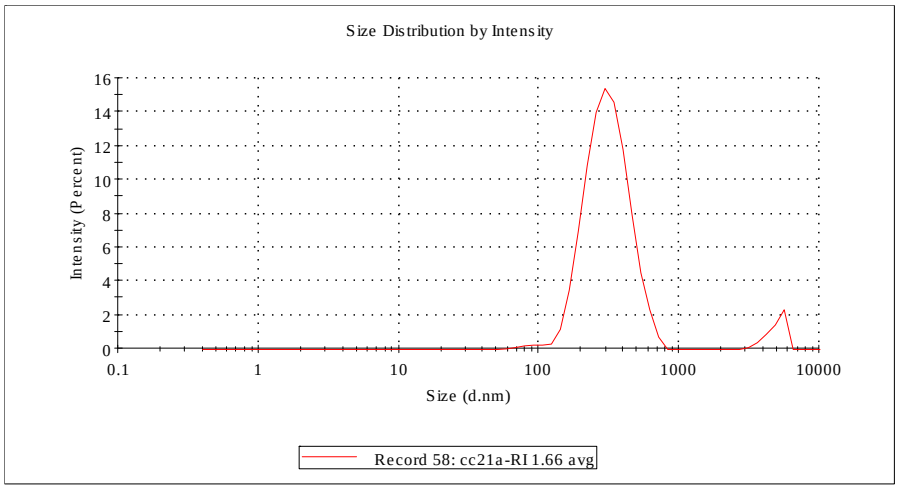

Figure 45. Particle size distribution determined by DLS – Condition A

		Size (d.nm):	% Intensity:	St Dev (d.n...
Z-Average (d.nm): 300.3	Peak 1:	326.3	94.7	140.4
PdI: 0.322	Peak 2:	4915	5.3	693.6
Intercept: 0.947	Peak 3:	0.000	0.0	0.000

Result quality : Good

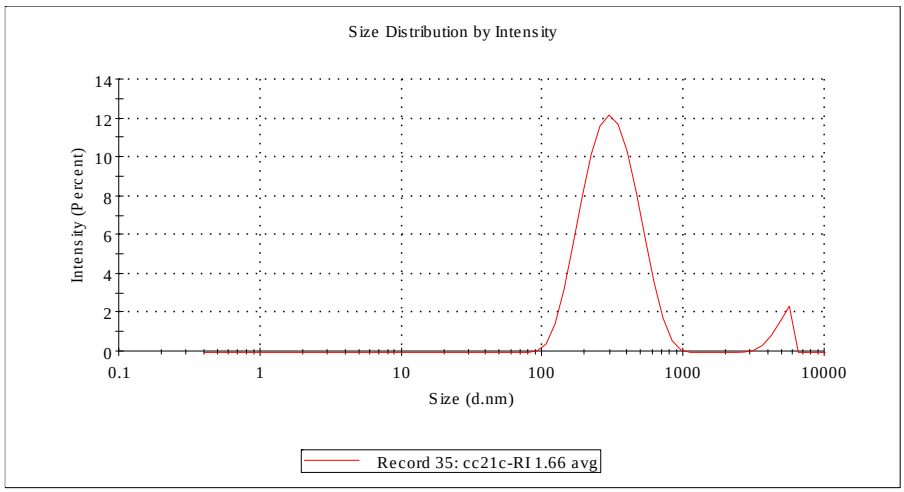

Figure 46. Particle size distribution determined by DLS – Condition C