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Uracil derivatives as HIV-1 capsid protein inhibitors: Design, *in silico*, *in vitro* and cytotoxicity studies

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A. **Table S1:** Physicochemical properties of bis(pyrimidine-2,4(1*H*,3*H*)-diones.

Code	Lipinski's Rule of 5					Veber's Rule	
	Log P	**Mol. Wt (g/mol)**	**HD***	**HA#**	**No. of violations**	**TPSA (Å²)**	**No. of rotatable bonds**
1a	-0.61	312.28	4	8	0	131.45	3
2a	-0.45	330.27	4	8	0	131.45	3
3a	-0.47	330.27	4	8	0	131.45	3
4a	-0.49	330.27	4	8	0	131.45	3
5a	-0.35	348.26	4	8	0	131.45	3
6a	0.28	380.28	4	8	0	131.45	4
7a	0.26	380.28	4	8	0	131.45	4
8a	0.07	346.73	4	8	0	131.45	3
9a	0.04	346.73	4	8	0	131.45	3
10a	0.02	346.73	4	8	0	131.45	3
11a	0.67	381.18	4	8	0	131.45	3
12a	0.20	391.18	4	8	0	131.45	3
13a	0.15	391.18	4	8	0	131.45	3
14a	-0.65	357.28	4	11	1	177.27	4
15a	-0.68	357.28	4	11	1	177.27	4
16a	-0.85	337.30	4	9	0	155.24	3
17a	-0.88	337.30	4	9	0	155.24	3
18a	-0.16	326.31	4	8	0	131.45	3
19a	-0.21	326.31	4	8	0	131.45	3
20a	-0.51	355.35	4	9	0	134.69	4
21a	-0.55	342.31	4	9	0	140.68	4
22a	-0.96	372.34	4	10	0	149.92	5
23a	-0.98	402.36	4	11	1	159.15	6
24a	1.14	404.38	4	9	0	140.68	5
25a	-0.70	356.29	5	10	0	168.75	4

26a	-0.82	340.30	4	9	0	148.52	4
27a	-3.18	546.46	8	16	3	262.90	6
28a	0.55	362.35	4	8	0	131.45	3
Azidothymidine	-0.10	267.25	2	9	0	134.08	3
CAP-1	4.10	367.90	2	5	0	57.50	7
C1	5.95	525.01	2	8	2	99.41	8
PF74	4.43	425.53	2	5	0	65.20	7

HD: hydrogen donor; HA: hydrogen acceptor.

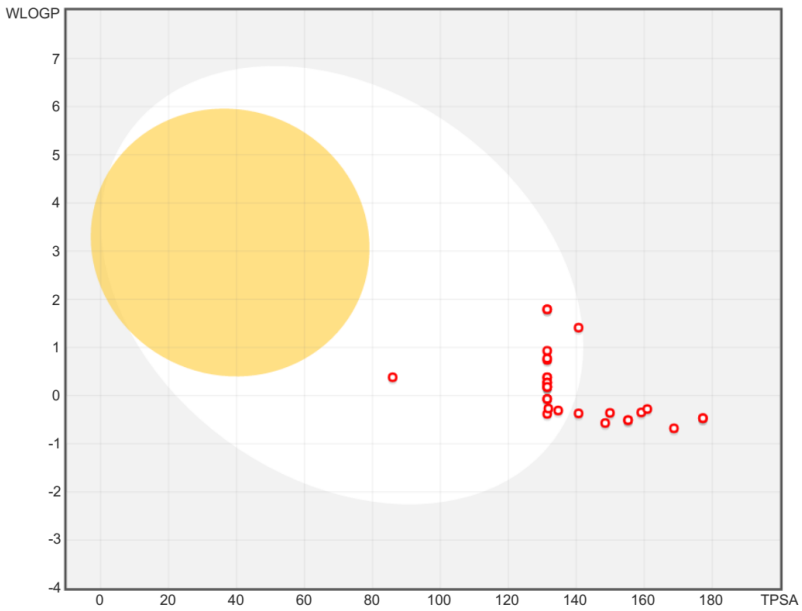
Note: Data obtained from the Molinspiration server (http://www.molinspiration.com

B. **Table S2**: ADMET properties of bis(pyrimidine-2,4(1*H*,3*H*)-diones

Code	Absorption			Distribution			Metabolism	Excretion	Toxicity	
	Log S (log mol/L)	**Caco-2 perm. (log Papp in 10^{-6} cm/s)**	**Int. abs. (% Abs.)**	**V_D (log L/kg)**	**Fract. Unb (Fu)**	**BBB perm (log BB)**		**Total clearance(log ml/min/kg)**	**Oral Rat Acute Toxicity (LD50) mol/kg**	**Hepato toxicity**
1a	-3.153	-0.487	69.75	-0.086	0.294	-1.134	CYP3A4 substrate, CYP1A2 inhibitor	0.848	2.959	No
2a	-3.047	-0.465	70.167	0.106	0.229	-1.34	CYP3A4 substrate	0.702	2.883	No
3a	-3.038	-0.46	76.187	0.141	0.209	-1.30	CYP3A4 substrate	0.717	2.851	No
4a	-3.119	-0.441	78.79	-0.08	0.22	-1.31	CYP3A4 substrate	0.701	2.913	No
5a	-3.028	-0.448	80.32	0.157	0.191	-1.473	CYP3A4 substrate	0.692	2.772	Yes
6a	-3.184	-0.497	72.06	-0.019	0.252	-1.445	CYP3A4 substrate	0.52	2.94	Yes
7a	-3.19	-0.466	72.07	-0.024	0.242	-1.426	CYP3A4 substrate	0.531	2.92	Yes
8a	-3.185	-0.513	70.929	-0.033	0.272	-1.316	CYP3A4 substrate	-0.478	2.96	No
9a	-3.18	-0.516	70.941	-0.016	0.269	-1.294	CYP3A4 substrate	-0.473	2.95	No
10a	-3.187	-0.472	70.78	-0.123	0.245	-1.309	CYP3A4 substrate, CYP1A2 inhibitor	-0.41	2.95	No
11a	-3.218	-0.508	71.957	-0.081	0.268	-1.482	CYP3A4 substrate, CYP1A2 inhibitor	-0.485	2.95	No

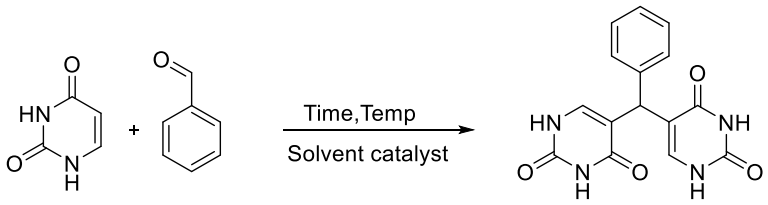
12a	-3.191	-0.507	70.665	-0.023	0.269	-1.336	CYP3A4 substrate, CYP1A2 inhibitor	0.499	2.97	No
13a	-3.193	-0.466	70.516	-0.113	0.242	-1.33	CYP3A4 substrate, CYP1A2 inhibitor	0.433	2.955	No
14a	-3.171	-0.163	66.595	-0.305	0.176	1.338	CYP3A4 substrate	0.811	3.08	Yes
15a	-3.171	0.163	66.576	-0.319	0.171	-1.322	CYP3A4 substrate	0.821	3.076	Yes
16a	-3.125	0.064	67.403	0.009	0.283	-1.198	CYP3A4 substrate	0.891	2.909	No
17a	-3.13	0.034	67.38	0.043	0.283	-1.174	CYP3A4 substrate	0.9	2.9	No
18a	-3.177	-0.511	70.221	0.011	0.285	-1.162	CYP3A4 substrate, CYP1A2 inhibitor	0.85	2.97	No
19a	-3.178	-0.469	70.072	-0.078	0.257	-1.156	CYP3A4 substrate, CYP1A2 inhibitor	0.865	2.96	No
20a	-3.159	-0.471	67.338	0.12	0.287	-1.189	CYP3A4 substrate	0.932	2.96	Yes
21a	-3.032	0.078	68.263	0.234	0.248	-1.327	CYP3A4 substrate	0.831	2.86	No
22a	-2.979	0.106	70.597	0.433	0.225	-1.464	CYP3A4 substrate	0.819	2.66	No
23a	-2.972	0.03	70.668	0.364	0.213	-1.609	CYP3A4 substrate	0.901	2.52	Yes
24a	-3.246	-0.073	77.440	-0.756	0.05	-1.379	CYP3A4 substrate, CYP1A2 inhibitor	0.788	3.22	Yes
25a	-2.954	-0.883	42.063	-0.546	0.198	-1.538	-	0.842	2.917	Yes
26a	-3.036	0.074	67.461	0.148	0.25	-1.311	CYP3A4 substrate	0.787	1.45	Yes
27a	-2.89	0.279	46.5	-0.514	0.189	-2.235	CYP3A4 substrate	0.885	2.536	No

28a	-3.199	-0.488	76.828	0.823	0.1	1.177	CYP3A4 substrate, CYP1A2 inhibitor	0.807	3.31	No
AZT	-3.204	-0.11	69.077	-0.423	0.738	-1.21	-	0.048	0.048	Yes
CAP-1	-5.442	1.093	89.96	-0.061	0.225	-0.085	CYP1A2, CYP2C9 inhibitor	0.157	2.796	No
C1	-2.896	0.473	76.399	0.065	0.269	-1.397	CYP3A4 substrate, CYP1A2 and CYP2C9 inhibitor	0.368	2.478	Yes
PF74	-3.701	0.676	93.597	0.014	0.105	-0.24	CYP2D6, CYP3A4 substrate, CYP1A2, CYP2C19, CYP2C9, CYP3A4 inhibitor	0.618	2.24	Yes



C. **Fig. S1** Human intestinal absorption (HIA) model and blood-brain barrier permeation (BBB) method (boiled-egg plot) of the 28 compounds. The Boiled-egg model works by computing the lipophilicity and polarity of small molecules. Here, all the compounds are highly absorbable in the gastrointestinal tract and is BBB impermeable. (Calculated from http://www.swissadme.ch/)

D. **Table S2. Optimization of reaction conditions**



Run No.	Catalyst	Solvent	Temp (°C)	Time (h)	Yield (%)
1.	Glacial acetic acid	H_2O	RT to 100	24	NR
2.		MeOH	RT to 70	24	
3.		EtOH	RT to 70	24	
4.		DCM	RT	24	
5.		Acetonitrile	RT to 80	24	

6.		DMSO	RT to 180	24	
7.	H_2SO_4	H_2O	RT to 100	24	NR
8.		MeOH	RT to 70	24	
9.		EtOH	RT to 70	24	
10.		DCM	RT	24	
11.		Acetonitrile	RT to 80	24	
12.		DMSO	RT to 180	24	
13.	HCl	H_2O	RT	18	80
14.			70	6	90
15.		MeOH	RT to 70	24	NR
16.		EtOH	RT to 70	24	
17.		DCM	RT	24	
18.		Acetonitrile	RT to 80	24	
19.		DMSO	RT to 180	24	

NR denotes no reaction

E. Yield and Spectroscopic data (Mass, ^{1}H and ^{13}C NMR, and FT-IR) of compounds

5,5'-(Phenylmethylene)bis(pyrimidine-2,4(1H,3H)-dione) (**1a**), White powder, Yield: 85 %, ^{1}H NMR (400 MHz, DMSO-d6) δ: 11.13 (s, 2H), 10.74 (d, *J* = 5.3 Hz, 2H), 7.31 (t, *J* = 7.4 Hz, 2H), 7.22 (t, *J* = 7.2 Hz, 1H), 7.14 (d, *J* = 7.3 Hz, 2H), 6.76 (d, *J* = 5.7 Hz, 2H), 5.01 (s, 1H). ^{13}C NMR (101 MHz, DMSO-d6) δ 163.80 (s), 151.42 (s), 140.42 (s), 139.68 (s), 128.66 (d, *J* = 6.5 Hz), 127.77 – 126.92 (m), 113.47 (s). FT-IR (KBr, cm^{-1}): 3480.67 (-NH stretching), 3119.10 (C-H stretching), 1716.53 (C=O stretching), 1640.36 (C=C stretching). ESI-HRMS calculated for $C_{15}H_{12}N_4O_4$ $[M+H]^+$: 313.0937, obtained value: 313.0928.

5,5'-((4-Fluorophenyl)methylene)bis(pyrimidine-2,4(1H,3H)-dione) **(2a)**, White powder, Yield: 90 %, ^{1}H NMR (400 MHz, DMSO-d6) δ: 11.12 (s, 2H), 10.72 (s, 2H), 7.15 (d, *J* = 28.0 Hz, 4H), 6.80 (s, 2H), 5.01 (s, 1H). ^{13}C NMR (101 MHz, DMSO-d6) δ: 163.69 (s), 160.03 (s),

151.35 (s), 139.68 (s), 136.56 (s), 130.42 (s), 115.05 (s), 113.26 (s), 40.23 – 38.74 (m), 38.39 (s). FT-IR (KBr, cm^{-1}): 3501.28 (N-H stretching), 3237.76 (CH stretching), 1715.59 (C=O stretching), 1635.73 (C=C stretching), 1431.40 (C-F stretching). ESI-HRMS calculated for $C_{15}H_{11}FN_4O_4$ $[M+H]^+$: 331.0842, obtained value: 331.0852.

5,5'-((3-Fluorophenyl)methylene)bis(pyrimidine-2,4(1H,3H)-dione) **(3a)**, White powder, Yield: 90 %, ^{1}H NMR (400 MHz, DMSO-d6) δ: 11.14 (s, 2H), 10.75 (d, *J* = 4.5 Hz, 2H), 7.34 (d, *J* = 6.6 Hz, 1H), 7.02 (t, *J* = 11.1 Hz, 3H), 6.83 (d, *J* = 5.5 Hz, 2H), 5.03 (s, 1H). ^{13}C NMR (101 MHz, DMSO-d6) δ: 163.67 (s), 161.08 (s), 150.92 (s), 143.61 (s), 139.87 (s), 130.62 (s), 124.90 (s), 112.74 (s), 40.1 (s), 40.13 (s), 39.93 (s), 39.61 (d, *J* = 21.0 Hz), 39.20 (d, *J* = 21.0 Hz), 38.89 (s), 38.24 (s). FT-IR (KBr, cm^{-1}): 3467.40 (N-H stretching), 3111.20 (CH stretching), 1711.90 (C=O stretching), 1656.20 (C=C stretching), 1436.70 (CF stretching). ESI-HRMS calculated for $C_{15}H_{11}FN_4O_4[M+H]^+$: 331.0842, obtained value: 331.0852.

5,5'-((2-Fluorophenyl)methylene)bis(pyrimidine-2,4(1H,3H)-dione) **(4a)**, Light yellow powder, Yield: 85 %, ^{1}H NMR (400 MHz, DMSO-d6) δ: 11.18 (s, 2H), 10.77 (s, 2H), 7.30 (s, 1H), 7.14 (s, 3H), 6.80 (s, 2H), 5.26 (s, 1H). ^{13}C NMR (101 MHz, DMSO-d6) δ: 163.68 (s), 161.25 (s), 158.82 (s), 151.44 (s), 139.76 (s), 129.69 (s), 129.10 (s), 127.62 – 127.54 (m), 127.48 (s), 124.54 (s), 115.68 (d, *J* = 22.2 Hz), 111.88 (s), 40.25 (s), 40.24 – 39.58 (m), 39.74 (s), 39.85 – 39.21 (m), 39.32 (s), 39.32 (s), 39.01 (d, *J* = 21.1 Hz), 32.02 (s). FT-IR (KBr, cm^{-1}): 3467.40 (N-H stretching), 3120.80 (CH stretching), 1722.80 (C=O stretching), 1645.0 (C=C stretching), 1488.70 (CF stretching). ESI-HRMS calculated for $C_{15}H_{11}FN_4O_4$ $[M+H]^+$: 331.0842, obtained value: 331.0821.

6,6'-((3,5-Difluorophenyl)methylene)bis(pyrimidine-2,4(1H,3H)-dione) **(5a),** White powder, Yield: 85 %, ^{1}H NMR (400 MHz, DMSO-d6) δ: 11.16 (s, 1H), 11.02 (s, 1H), 10.88 (d, *J* = 19.0 Hz, 2H), 7.38 (dd, *J* = 7.4, 5.9 Hz, 1H), 7.31 (t, *J* = 5.5 Hz, 1H), 7.05 (s, 2H), 6.93 – 6.87 (m, 1H), 5.48 (s, 1H). ^{13}C NMR (101 MHz, DMSO-d6) δ: 164.71 (s), 163.58 (d, *J* = 33.6 Hz),

151.74 (s), 151.34 (d, *J* = 8.1 Hz), 142.48 (s), 140.25 (s), 138.81 (s), 115.26 (s), 112.19 (s), 109.68 (s), 100.45 (s), 56.80 (s), 40.20 (s), 40.19 – 39.53 (m), 39.54 (s), 39.64 – 39.10 (m), 39.10 – 38.99 (m), 38.90 (s). FT-IR (KBr, cm^{-1}): 3422.60 (N-H stretching), 3108.60 (CH stretching), 1716.70 (C=O stretching), 1669.30 (C=C stretching), 1447.40 (C-F stretching). ESI-HRMS calculated for $C_{15}H_{10}F_2N_4O_4$ $[M+H]^+$: 349.0748, obtained value: 349.0720.

5,5'-((4-(Trifluoromethyl)phenyl)methylene)bis(pyrimidine-2,4(1H,3H)-dione) **(6a)**, Pale yellow powder, Yield: 88 %, ^{1}H NMR (400 MHz, DMSO-d6) δ: 11.11 (d, *J* = 59.5 Hz, 2H), 10.80 (s, 2H), 7.65 (d, *J* = 8.0 Hz, 2H), 7.39 (d, *J* = 7.6 Hz, 2H), 6.86 (s, 1H), 5.45 (d, *J* = 7.6 Hz, 1H), 5.09 (s, 1H).^{13}C NMR (101 MHz, DMSO-d6) δ: 164.58 (s), 163.72 (s), 151.70 (s), 151.34 (s), 145.69 (s), 142.39 (s), 129.38 (s), 125.34 (s), 112.46 (s), 100.39 (s). FT-IR (KBr, cm^{-1}): 3432.4 (N-H stretching), 3179.6 (CH stretching), 1716.50 (C=O stretching), 1660.90 (C=C stretching), 1327.60 (CF stretching). ESI-HRMS calculated for $C_{16}H_{11}F_3N_4O_4$ $[M+H]^+$: 381.0810, obtained value: 381.0792.

5,5'-((3-(Trifluoromethyl)phenyl)methylene)bis(pyrimidine-2,4(1H,3H)-dione) (**7a)**, Yellow powder, Yield: 80 %, ^{1}H NMR (400 MHz, DMSO-d6) δ: 11.12 (s, 2H), 10.94 (s, 2H), 7.67 (s, 1H), 7.58 (d, *J* = 22.6 Hz, 4H), 7.31 (s, 1H), 5.21 (s, 1H).). ^{13}C NMR (101 MHz, DMSO-d6) δ: 162.86 (s), 150.88 (s), 142.02 (s), 138.85 (s), 130.72 (s), 129.18 (s), 124.11 (s), 112.11 (s), 76.67 (s), 56.46 (s), 39.53 (s). FT-IR (KBr, cm^{-1}): 3229.0 (N-H stretching), 2828.8 (CH stretching), 1715.50 (C=O stretching), 1673.70 (C=C stretching), 1331.60 (CF stretching). ESI-HRMS calculated for $C_{16}H_{11}F_3N_4O_4$ $[M+H]^+$: 380.0732, obtained value: 380.0782.

5,5'-((4-Chlorophenyl)methylene)bis(pyrimidine-2,4(1H,3H)-dione) **(8a),** White powder, Yield: 85 %, ^{1}H NMR (400 MHz, DMSO-d6) δ: 11.13 (s, 2H), 10.73 (s, 2H), 7.27 (d, 4H), 6.82 (s, 2H), 5.00 (s, 1H). ^{13}C NMR (101 MHz, DMSO-d6) δ: 163.59 (s), 151.24 (s), 139.69 (d, *J* = 13.6 Hz), 131.22 (s), 130.36 (s), 128.34 (s), 112.78 (s), 40.15 (s), 39.94 (s), 39.63 (d, *J* = 21.0 Hz), 39.31 (s), 39.10 (s), 38.90 (s), 38.48 (s). FT-IR (KBr, cm^{-1}): 3433.30 (N-H

stretching), 3179.30 (CH stretching), 1725.20 (C=O stretching), 1640.60 (C=C stretching), 822.40 (C-Cl stretching). ESI-HRMS calculated for $C_{15}H_{11}ClN_4O_4$ $[M+H]^+$: 347.0547, obtained value: 347.0526.

5,5'-((3-Chlorophenyl)methylene)bis(pyrimidine-2,4(1H,3H)-dione) **(9a),** White powder, Yield: 82%, ^{1}H NMR (400 MHz, DMSO-d6) δ 11.15 (s, 2H), 10.75 (d, *J* = 5.0 Hz, 2H), 7.30 (dd, *J* = 14.8, 7.7 Hz, 2H), 7.21 (s, 1H), 7.13 (d, *J* = 7.2 Hz, 1H), 6.85 (d, *J* = 5.7 Hz, 2H), 5.01 (s, 1H).^{13}C NMR (101 MHz, DMSO-d6) δ: 163.60 (s), 151.25 (s), 143.25 (s), 139.92 (s), 133.13 (s), 130.29 (s), 128.20 (s), 127.29 (s), 126.72 (s), 112.52 (s), 39.52 (dp, *J* = 42.0, 21.0 Hz), 38.81 (s). FT-IR (KBr, cm^{-1}): 3548.86 (N-H stretching), 3118.08 (CH stretching), 1718.09 (C=O stretching), 1664.30 (C=C stretching), 878.62 (C-Cl stretching). ESI-HRMS calculated for $C_{15}H_{11}ClN_4O_4$ $[M+H]^+$: 347.0547, obtained value: 347.0534.

5,5'-((2-Chlorophenyl)methylene)bis(pyrimidine-2,4(1H,3H)-dione) **(10a),** White powder, Yield: 79%, ^{1}H NMR (400 MHz, DMSO-d6) δ: 11.18 (d, *J* = 1.5 Hz, 2H), 10.76 (dd, *J* = 5.8, 1.5 Hz, 2H), 7.47 – 7.43 (m, 1H), 7.31 – 7.26 (m, 2H), 7.16 (dd, *J* = 5.2, 4.2 Hz, 1H), 6.72 (d, *J* = 5.7 Hz, 2H), 5.32 (s, 1H). ^{13}C NMR (101 MHz, DMSO-d6) δ: 163.57 (s), 151.35 (s), 139.78 (s), 138.22 (s), 133.26 (s), 129.89 (s), 129.36 (s), 128.69 (s), 127.27 (s), 111.78 (s), 40.15 (s), 39.94 (s), 39.73 (s), 39.52 (s), 39.31 (s), 39.11 (s), 38.90 (s), 36.12 (s). FT-IR (KBr, cm^{-1}): 3227.69 (N-H stretching), 3060.06 (CH stretching), 1711.75 (C=O stretching), 1664.56 (C=C stretching), 895.15 (C-Cl stretching). ESI-HRMS calculated for $C_{15}H_{11}ClN_4O_4$ $[M+H]^+$: 347.0547, obtained value: 347.0537.

5,5'-((2,4-Dichlorophenyl)methylene)bis(pyrimidine-2,4(1H,3H)-dione) **(11a),** Pink powder, Yield: 75%, ^{1}H NMR (400 MHz, DMSO-d6) δ: 11.12 (s, 2H), 10.86 (s, 2H), 7.60 – 7.48 (m, 2H), 7.45 – 7.33 (m, 2H), 7.00 (d, *J* = 5.4 Hz, 1H), 5.74 (s, 1H), 5.51 – 5.22 (m, 1H). ^{13}C NMR (101 MHz, DMSO-d6) δ: 164.60 (s), 163.26 (s), 151.67 (s), 151.26 (s), 142.41 (s), 139.80 (s), 139.10 (s), 132.72 (d, *J* = 38.6 Hz), 129.99 (s), 128.72 (s), 127.31 (s), 114.35 (s), 100.39 (s),

64.13 (s), 40.04 (d, *J* = 21.0 Hz), 39.88 – 39.29 (m), 39.29 – 39.26 (m), 39.10 (s), 38.92 (s), 38.90 (s). FT-IR (KBr, cm^{-1}): 3224.39 (N-H stretching), 3085.80 (CH stretching), 1710.40 (C=O stretching), 1669.30 (C=C stretching), 862.70 (C-Cl stretching). ESI-HRMS calculated for $C_{15}H_{10}Cl_2N_4O_4$ $[M+H]^+$: 381.0157, obtained value: 381.0172.

5,5'-((4-Bromophenyl)methylene)bis(pyrimidine-2,4(1H,3H)-dione) **(12a)**, White powder, Yield: 90 %, ^{1}H NMR (400 MHz, DMSO-d6) δ: 11.15 (s, 2H), 10.75 (d, *J* = 4.9 Hz, 2H), 7.48 (d, *J* = 8.3 Hz, 2H), 7.11 (d, *J* = 8.3 Hz, 2H), 6.81 (d, *J* = 5.8 Hz, 2H), 4.97 (s, 1H).^{13}C NMR (101 MHz, DMSO-d6) δ: 163.72 (s), 151.37 (s), 139.99 (d, *J* = 21.3 Hz), 131.42 (s), 130.86 (s), 119.87 (s), 112.85 (s), 39.52 (dp, *J* = 42.0, 21.0 Hz), 38.66 (s). FT-IR (KBr, cm^{-1}): 3544.32 (N-H stretching), 3107.78 (CH stretching), 1722.18 (C=O stretching), 1663.19 (C=C stretching), 556.33 (C-Br stretching). ESI-HRMS calculated for $C_{15}H_{11}BrN_4O_4$ $[M+H]^+$: 391.0042, obtained value: 391.0014.

5,5'-((2-Bromophenyl)methylene)bis(pyrimidine-2,4(1H,3H)-dione) **(13a)**, White powder, Yield: 85 %, ^{1}H NMR (400 MHz, DMSO-d6) δ: 11.19 (d, *J* = 15.3 Hz, 2H), 10.74 (d, *J* = 3.0 Hz, 2H), 7.72 – 7.48 (m, 2H), 7.35 (t, *J* = 17.0 Hz, 1H), 7.24 – 7.12 (m, 2H), 6.68 (d, *J* = 4.6 Hz, 1H), 5.27 (s, 1H).^{13}C NMR (101 MHz, DMSO-d6) δ: 163.40 (s), 151.21 (s), 139.67 (s), 133.12 (s), 129.78 – 129.27 (m), 128.76 – 128.37 (m), 127.62 – 127.11 (m), 124.43 (s), 111.77 – 111.14 (m), 40.20 – 38.80 (m), 38.71 (s). FT-IR (KBr, cm^{-1}): 3222.59 (N-H stretching), 3029.96 (CH stretching), 1712.69 (C=O stretching), 1680.18 (C=C stretching), 587.90 (C-Br stretching). ESI-HRMS calculated for $C_{15}H_{11}BrN_4O_4$ $[M+H]^+$: 391.0042, obtained value: 391.0033.

5,5'-((4-Nitrophenyl)methylene)bis(pyrimidine-2,4(1H,3H)-dione) **(14a)**, Yellow powder, Yield: 85 %, ^{1}H NMR (400 MHz, DMSO-d6) δ: 11.41 (s, 1H), 11.27 (d, *J* = 4.4 Hz, 1H), 9.56 (s, 1H), 9.28 (s, 1H), 8.21 (d, *J* = 8.3 Hz, 3H), 7.80 (d, *J* = 8.2 Hz, 2H), 7.76 (d, *J* = 5.4 Hz, 1H), 6.57 (s, 1H).^{13}C NMR (101 MHz, DMSO-d6) δ: 163.36 (s), 151.93 (s), 151.28 (s), 146.64

(s), 138.83 (s), 127.84 (s), 123.40 (s), 115.30 (s), 67.12 (s), 40.15 (s). FT-IR (KBr, cm^{-1}): 3328.47 (NH stretching), 3110.31 (C-H stretching), 1812.70 (C=O stretching), 1630.10 (C=C stretching), 1516.84 (N-O stretching), 1230.29 (C-N stretching). ESI-HRMS calculated for $C_{15}H_{11}N_5O_6$ [M+H]+: 358.0787, obtained value: 358.0795.

5,5'-((3-Nitrophenyl)methylene)bis(pyrimidine-2,4(1H,3H)-dione) **(15a)** White powder, Yield: 80 %, ^{1}H NMR (400 MHz, DMSO-d6) δ: 11.45 (s, 1H), 11.27 (s, 1H), 9.54 (s, 1H), 9.26 (s, 1H), 8.42 (s, 1H), 8.18 (s, 1H), 8.04 (d, *J* = 40.6 Hz, 1H), 7.83 – 7.61 (m, 3H), 6.57 (s, 1H). ^{13}C NMR (101 MHz, DMSO-d6) δ: 168.04 (s), 164.80 – 163.59 (m), 150.82 (s), 147.83 (s), 140.61 (s), 134.56 (s), 130.30 (s), 122.86 (d, *J* = 39.2 Hz), 109.22 (s), 45.27 (s), 40.04 (d, *J* = 21.0 Hz), 41.56 – 39.62 (m), 39.83 (dd, *J* = 42.0, 20.9 Hz), 41.56 – 37.79 (m). FT-IR (KBr, cm^{-1}): 3439.00 (NH stretching), 2916.92 (C-H stretching), 1717.97 (C=O stretching), 1582.21 (N-O stretching), 1246.48 (C-N stretching). ESI-HRMS calculated for $C_{15}H_{11}N_5O_6$ $[M+H]^+$: 358.0787, obtained value: 358.0790.

4-(Bis(2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl)methyl)benzonitrile **(16a)** White powder, Yield: 86 %, ^{1}H NMR (400 MHz, DMSO-d6) δ: 11.14 (s, 2H), 10.77 (d, *J* = 4.9 Hz, 2H), 7.87 (d, *J* = 8.1 Hz, 2H), 7.28 (d, *J* = 8.1 Hz, 2H), 6.83 (d, *J* = 5.8 Hz, 2H), 5.08 (s, 1H). ^{13}C NMR (101 MHz, DMSO-d6) δ: 167.22 (s), 163.62 (s), 151.23 (s), 145.90 (s), 139.90 (s), 129.50 (s), 129.18 (s), 128.67 (s), 112.59 (s), 40.44 – 39.70 (m), 39.53 (s), 39.53 (s), 39.42 (d, *J* = 21.0 Hz), 39.11 (s), 38.99 – 38.84 (m). FT-IR (KBr, cm^{-1}): 3567.94 (N-H stretching), 3114.96 (CH stretching), 2350.94 (nitrile stretching), 1730.61 (C=O stretching), 1665.20 (C=C stretching). ESI-HRMS calculated for $C_{16}H_{11}N_5O_4.H_2O$ $[M+H]^+$: 355.0917, obtained value: 355.0702.

3-(Bis(2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl)methyl)benzonitrile **(17a)** White powder, Yield: 82 %, ^{1}H NMR (400 MHz, DMSO-d6) δ: 11.16 (d, *J* = 1.4 Hz, 2H), 10.76 (dd, *J* = 5.7, 1.4 Hz, 2H), 7.84 – 7.78 (m, 1H), 7.67 (s, 1H), 7.47 – 7.41 (m, 2H), 6.85 (d, *J* = 5.7 Hz, 2H), 5.07 (s, 1H). ^{13}C NMR (101 MHz, DMSO-d6) δ: 167.41 (s), 163.69 (s), 151.31 (s), 141.15 (s),

139.95 (s), 133.21 (s), 130.94 (s), 128.95 (d, *J* = 9.7 Hz), 127.79 (s), 112.82 (s), 40.15 (s), 39.94 (s), 39.73 (s), 39.52 (s), 39.31 (s), 39.10 (s), 39.21 – 38.66 (m), 38.89 (s). FT-IR (KBr, cm^{-1}): 3556.89 (N-H stretching), 3251.532 (CH stretching), 2560.14 (nitrile stretching), 1735.49 (C=O stretching), 1425.97 (C=C stretching). ESI-HRMS calculated for $C_{16}H_{11}N_5O_4.H_2O$ $[M+H]^+$: 355.0917, obtained value: 355.0702

5,5'-(P-tolylmethylene)bis(pyrimidine-2,4(1H,3H)-dione) **(18a)**, White powder, Yield: 80 %, ^{1}H NMR (400 MHz, DMSO-d6) δ: 11.11 (s, 2H), 10.69 (s, 2H), 7.07 (d, *J* = 31.9 Hz, 4H), 6.75 (s, 2H), 4.96 (s, 1H), 2.26 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d6) δ: 163.48 (s), 151.14 (s), 139.24 (s), 137.18 (s), 135.59 (s), 128.94 (s), 128.28 (s), 113.32 (s), 40.67 – 40.23 (m), 39.92 (d, *J* = 21.2 Hz), 39.73 – 39.05 (m), 39.19 (s), 39.39 – 38.61 (m), 38.39 (s), 20.52 (s). FT-IR (KBr, cm^{-1}): 3412.70 (N-H stretching), 3181.50 (CH stretching), 2915.7 (C-CH_3 stretching), 1722.40 (C=O stretching), 1640.80 (C=C stretching), 1485.50 (-CH_3 stretching). ESI-HRMS calculated for $C_{16}H_{14}N_4O_4$ [M+H]+: 327.1093, obtained value: 327.1100.

5,5'-(*O*-tolylmethylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione) **(19a)**, White powder, Yield: 72 %, ^{1}H NMR (400 MHz, DMSd6) δ: 11.14 (s, 2H), 10.71 (d, *J* = 3.5 Hz, 2H), 7.16 (d, *J* = 13.3 Hz, 3H), 6.98 (s, 1H), 6.69 (d, *J* = 5.0 Hz, 2H), 5.14 (s, 1H), 2.17 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d6) δ: 163.55 (s), 151.18 (s), 139.24 (s), 138.62 (s), 135.72 (s), 130.50 (s), 126.96 (s), 126.60 (s), 125.78 (s), 112.45 (s), 39.85 (d, *J* = 21.0 Hz), 39.74 – 39.64 (m), 39.57 (s), 39.43 (d, *J* = 21.0 Hz), 39.28 – 39.22 (m), 39.12 (s), 38.81 (d, *J* = 21.1 Hz), 34.89 (s), 18.79 (s). FT-IR (KBr, cm^{-1}): 3505.20 (N-H stretching), 3181.40 (CH stretching), 2913.20 (C-CH_3 stretching), 1720.30 (C=O stretching), 1643.90 (C=C stretching), 1489.70 (-CH_3 stretching). ESI-HRMS calculated for $C_{16}H_{14}N_4O_4$ $[M+H]^+$: 327.1093, obtained value: 327.1064.

5,5'-((4-(Dimethylamino)phenyl)methylene)bis(pyrimidine-2,4(1H,3H)-dione) **(20a)**, Light brown powder, Yield: 85 %, ^{1}H NMR (400 MHz, DMSO-d6) δ: 11.13 (s, 2H), 10.71 (s, 2H), 6.99 (s, 2H), 6.76 (d, *J* = 22.1 Hz, 4H), 4.95 (s, 1H), 2.91 (s, 6H). ^{13}C NMR (101 MHz, DMSO-

d6) δ: 163.66 (s), 151.34 (s), 149.32 (s), 139.03 (s), 129.07 (s), 127.39 (s), 114.08 (s), 112.61 (s), 40.32 (s), 40.32 – 39.92 (m), 39.94 (s), 39.73 (s), 39.92 – 39.31 (m), 39.32 (s), 39.21 (d, *J* = 21.0 Hz), 38.90 (s), 37.99 (s). FT-IR (KBr, cm^{-1}): 3416.30 (N-H stretching), 3237.70 (CH stretching), 3114.80 (N-CH_3 stretching), 1707.10 (C=O stretching), 1669.70 (C=C stretching), 1485.30 (methyl stretching). ESI-HRMS calculated for $C_{17}H_{17}N_5O_4$ $[M+H]^+$: 356.1359, obtained value: 356.1366.

6,6'-((4-Methoxyphenyl)methylene)bis(pyrimidine-2,4(1H,3H)-dione) **(21a),** Light brown powder, Yield: 90 %, ^{1}H NMR (400 MHz, DMSO-d6) δ: 11.09 (s, 3H), 9.86 (s, 1H), 7.09 (dd, *J* = 27.0, 8.5 Hz, 1H), 6.93 (d, *J* = 8.6 Hz, 1H), 6.85 (dd, *J* = 19.1, 8.6 Hz, 2H), 6.75 (s, 1H), 6.65 (d, *J* = 19.5 Hz, 1H), 4.95 (s, 1H), 3.73 – 3.67 (m, 3H). ^{13}C NMR (101 MHz, DMSO-d6) δ: 163.74 (s), 151.46 (s), 139.45 (s), 132.07 (s), 129.81 (s), 114.72 (s), 113.81 (s), 55.51 (d, *J* = 74.1 Hz), 40.15 (s), 39.94 (s), 39.80 – 39.23 (m), 39.23 – 39.17 (m), 39.00 (d, *J* = 20.9 Hz), 38.84 – 38.56 (m). FT-IR (KBr, cm^{-1}): 3459.50 (N-H stretching), 3174.90 (CH stretching), 2831.30 (OCH_3 stretching), 1711.90 (C=O stretching), 1666.50 (C=C stretching). ESI-HRMS calculated for $C_{16}H_{14}N_4O_5$ $[M+H]^+$: 343.1042, obtained value: 343.1039.

5,5'-((3,4-Dimethoxyphenyl)methylene)bis(pyrimidine-2,4(1H,3H)-dione) **(22a)**, Brown powder, Yield: 88 %, ^{1}H NMR (400 MHz, DMSO-d6) δ: 11.11 (s, 2H), 10.72 (s, 2H), 6.87 (d, *J* = 8.3 Hz, 1H), 6.78 – 6.71 (m, 3H), 6.60 (d, *J* = 8.2 Hz, 1H), 4.94 (s, 1H), 3.70 (d, *J* = 5.1 Hz, 6H). ^{13}C NMR (101 MHz, DMSO-d6) δ: 163.71 (s), 151.37 (s), 148.84 (s), 147.67 (s), 139.36 (s), 132.65 (s), 120.19 – 118.33 (m), 113.67 (s), 112.61 (s), 111.65 (s), 55.60 (s), 40.15 (s), 39.83 (d, *J* = 21.0 Hz), 39.55 (s), 39.42 (d, *J* = 21.0 Hz), 39.10 (s), 38.90 (s), 38.51 (s). FT-IR (KBr, cm^{-1}): 3418.30 (N-H stretching), 3223.60 (CH stretching), 2834.60 (OCH_3 stretching), 1712.70 (C=O stretching), 1656.20 (C=C stretching). ESI-HRMS calculated for $C_{17}H_{16}N_4O_6$ $[M+H]^+$: 373.1148, obtained value: 373.1126.

5,5'-((3,4,5-Trimethoxyphenyl)methylene)bis(pyrimidine-2,4(1H,3H)-dione) **(23a)**, Black powder, Yield: 82 %, ^{1}H NMR (400 MHz, DMSO-d6) δ: 11.10 (s, 2H), 10.71 (s, 2H), 6.75 (dd, *J* = 35.1, 20.1 Hz, 2H), 6.39 (d, *J* = 22.9 Hz, 2H), 4.91 (s, *J* = 17.5 Hz, 1H), 3.71 (s, *J* = 7.7 Hz, 3H), 3.69 (s, 3H), 3.63 (s, 3H). ^{13}C NMR (101 MHz, DMSO) δ: 163.53 (s), 152.74 (s), 151.18 (s), 139.36 (s), 126.09 (s), 113.13 (s), 105.73 (s), 60.03 (d, *J* = 24.1 Hz), 55.84 (s), 39.93 (s), 39.76 (s), 39.75 – 39.28 (m), 39.28 – 39.23 (m), 38.99 (d, *J* = 21.0 Hz), 38.82 – 38.76 (m), 38.68 (s). FT-IR (KBr, cm^{-1}): 3421.20 (N-H stretching), 3226.10 (CH stretching), 2835.70 (OCH_3 stretching), 1710.40 (C=O stretching), 1668.0 (C=C stretching). ESI-HRMS calculated for $C_{18}H_{18}N_4O_7$ $[M+H]^+$: 403.1254, obtained value: 403.1268.

5,5'-((4-Phenoxyphenyl)methylene)bis(pyrimidine-2,4(1H,3H)-dione) **(24a)**, Pale yellow powder, Yield: 70 %, ^{1}H NMR (400 MHz, DMSO-d6) δ: 11.03 (s, 2H), 10.80 (d, *J* = 36.2 Hz, 1H), 9.96 (s, 1H), 7.68 (d, *J* = 7.1 Hz, 1H), 7.62 (d, *J* = 7.8 Hz, 1H), 7.46 – 7.30 (m, 5H), 7.21 (d, *J* = 7.1 Hz, 1H), 7.09 (t, *J* = 9.5 Hz, 2H), 6.95 (dd, *J* = 16.9, 7.8 Hz, 1H), 6.82 (dd, *J* = 14.3, 7.4 Hz, 1H), 5.45 (d, *J* = 7.3 Hz, 1H). ^{13}C NMR (101 MHz, DMSO-d6) δ: 164.56 (s), 163.68 (s), 157.82 (s), 156.71 – 155.92 (m), 151.67 (s), 151.35 – 150.69 (m), 143.12 – 142.43 (m), 140.11 – 138.97 (m), 138.04 (s), 131.20 (s), 130.45 (s), 130.17 (s), 124.95 (s), 124.51 (d, *J* = 12.0 Hz), 119.48 (s), 118.66 (s), 117.38 (s), 112.94 (s), 100.37 (s), 40.15 (s), 40.00 (s), 40.00 – 39.44 (m), 39.36 (s), 39.31 (s), 39.11 (s), 38.90 (s). FT-IR (KBr, cm^{-1}): 3384.45 (N-H stretching), 3219.50 (CH stretching), 1712.30 (C=O stretching), 1670.05 (C=C stretching), 1241.50 (C-O-C stretching). ESI-HRMS calculated for $C_{21}H_{16}N_4O_5$ $[M+H]^+$: 405.1199, obtained value: 405.1188.

4-(Bis(2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl)methyl)benzoic acid **(25a)**, Pale violet powder, Yield: 74 %, ^{1}H NMR (400 MHz, DMSO-d6) δ: 11.15 (s, 2H), 10.76 (s, 2H), 7.87 (s, 2H), 7.28 (s, 2H), 6.83 (s, 2H), 5.07 (s, 1H). ^{13}C NMR (101 MHz, DMSO-d6) δ: 167.72 (d, *J* = 6.4 Hz), 164.03 (s), 163.65 (s), 151.62 (d, *J* = 7.1 Hz), 149.27 (s), 140.29 (s), 138.65 (s),

129.89 (d, *J* = 9.1 Hz), 129.59 (s), 129.07 (s), 127.06 (s), 116.12 (s), 113.02 (s), 67.58 (s), 40.32 (s), 40.11 (s), 40.11 (s), 39.90 (s), 39.58 (d, *J* = 21.0 Hz), 39.27 (s), 39.06 (s). FT-IR (KBr, cm^{-1}): 3462.70 (N-H stretching), 3116.0 (CH stretching), 3026.10 (O-H stretching), 1713.50 (C=O stretching), 1655.90 (C=C stretching), 1427.40 (OH bending), 1234.10 (C-OH stretching). ESI-HRMS calculated for $C_{16}H_{12}N_4O_6$ $[M+H]^+$: 357.0835, obtained value: 357.0818.

3-(Bis(2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl)methyl)benzaldehyde **(26a)**, White powder, Yield: 85 %, ^{1}H NMR (400 MHz, DMSO-d6) δ: 11.09 (s, 2H), 10.74 (d, *J* = 4.6 Hz, 2H), 9.98 (s, 1H), 7.78 (d, *J* = 4.8 Hz, 1H), 7.68 (s, 1H), 7.53 (s, 1H), 7.18 -7.0 (s, 1H), 6.87 (d, *J* = 5.7 Hz, 1H), 6.76 (d, *J* = 5.6 Hz, 1H), 4.98 (s, 1H). ^{13}C NMR (101 MHz, DMSO-d6) δ: 193.79 (s), 164.02 (d, *J* = 4.5 Hz), 151.61 (d, *J* = 6.0 Hz), 142.27 (s), 140.15 (d, *J* = 50.3 Hz), 136.75 (s), 129.58 (s), 113.64 (s), 112.96 (s), 40.50 (s), 40.18 (d, *J* = 21.0 Hz), 39.94 (s), 39.87 (s), 39.56 (d, *J* = 21.0 Hz), 39.25 (s). FT-IR (KBr, cm^{-1}): 3451.70 (N-H stretching), 3026.3 (CH stretching), 2844.2 (CH aldehyde) 1715.70 (C=O stretching), 1661.0 (C=C stretching). ESI-HRMS calculated for $C_{16}H_{12}N_4O_5$ $[M+H]^+$: 341.0886, obtained value: 341.0877.

6,6'-((3-(Bis(2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl)methyl)phenyl)methylene)bis(pyrimidine-2,4(1H,3H)-dione) **(27a)** White powder, Yield: 85 %, ^{1}H NMR (400 MHz, DMSO-d6) δ: 11.16 (s, 1H), 11.10 (d, *J* = 8.3 Hz, 2H), 10.75 (dd, *J* = 35.7, 5.3 Hz, 4H), 9.98 (s, 1H), 7.77 (d, *J* = 6.4 Hz, 1H), 7.67 (s, 1H), 7.57 – 7.50 (m, 1H), 7.21 (ddd, *J* = 18.4, 13.9, 6.2 Hz, 1H), 7.02 – 6.96 (m, 2H), 6.86 (d, *J* = 5.8 Hz, 1H), 6.76 (d, *J* = 5.8 Hz, 2H), 5.11 (s, 1H), 4.97 (s, 1H). ^{13}C NMR (101 MHz, DMSO-d6) δ: 163.66 (s), 151.30 (d, *J* = 3.8 Hz), 139.80 (d, *J* = 50.9 Hz), 139.54 (s), 136.43 (s), 130.41 – 125.61 (m), 113.32 (s), 112.99 (d, *J* = 66.1 Hz), 65.60 (s), 65.83 (s), 40.15 (s), 39.94 (s), 39.73 (s), 39.52 (s), 39.34 – 38.65 (m). FT-IR (KBr, cm^{-1}): 3458.1 (N-H stretching), 3103.1, 3024.8 (CH stretching), 1718.60 (C=O stretching), 1657.50 (C=C stretching). ESI-HRMS calculated for $C_{24}H_{18}N_8O_8$ $[M+H]^+$: 547.1326, obtained value: 547.1320.

6,6'-(Naphthalen-1-ylmethylene)bis(pyrimidine-2,4(1H,3H)-dione) **(28a)** Brown powder, Yield: 80 %, ^{1}H NMR (400 MHz, DMSO-d6) δ: 11.24 (s, 1H), 11.04 (s, 1H), 10.83 (s, 1H), 10.73 (d, *J* = 5.0 Hz, 1H), 8.31 – 8.05 (m, 1H), 7.84 – 7.70 (m, 1H), 7.65 (t, *J* = 7.4 Hz, 1H), 7.53 (t, *J* = 7.9 Hz, 1H), 7.47 – 7.36 (m, 2H), 7.23 (d, *J* = 7.0 Hz, 1H), 6.76 (d, *J* = 5.5 Hz, 1H), 5.46 (d, *J* = 7.5 Hz, 1H). ^{13}C NMR (101 MHz, DMSO-d6) δ: 164.55 (s), 163.74 (s), 151.67 (s), 151.36 (s), 142.34 (s), 140.01 (s), 136.96 (s), 135.41 (s), 134.11 – 133.70 (m), 133.43 (s), 129.18 (s), 128.86 (s), 127.08 (s), 125.53 (s), 124.23 (s), 100.37 (s), 40.18 (s), 40.18 – 39.71 (m), 39.52 (s), 39.31 (s), 39.10 (s), 38.90 (s), 34.42 (s). FT-IR (KBr, cm^{-1}): 3480.88 (N-H stretching), 3111.40 (CH stretching), 1715.90 (C=O stretching), 1668.30 (C=C stretching). ESI-HRMS calculated for $C_{19}H_{14}N_4O_4$ $[M+H]^+$: 363.1093, obtained value: 363.1077.

Spectroscopic data of isolated intermediate

5-(Hydroxy(4-nitrophenyl)methyl)pyrimidine-2,4(1H,3H)-dione **(1)**, Yellow powder, Yield: 16 %, ^{1}H NMR (400 MHz, DMSO-d6) δ: 11.12 (s, 1H), 10.96 (d, *J* = 5.0 Hz, 1H), 8.15 (d, *J* = 8.4 Hz, 2H), 7.62 (d, *J* = 8.6 Hz, 2H), 7.36 (d, *J* = 5.8 Hz, 1H), 5.59 (s, 1H), 4.51 (s, 1H). ^{13}C NMR (101 MHz, DMSO-d6) δ: 163.36 (s), 151.93 (s), 151.28 (s), 146.64 (s), 138.83 (s), 127.84 (s), 123.40 (s), 115.30 (s), 67.12 (s), 40.15 (s), 39.83 (d, *J* = 21.1 Hz), 39.57 (s), 39.41 (d, *J* = 21.0 Hz), 38.99 (d, *J* = 21.5 Hz), 38.86 – 38.45 (m). FT-IR (KBr, cm^{-1}): 3729.80 (OH stretching), 3464.20 (-NH stretching), 3225.47 (C-H stretching), 1712.13 (C=O stretching), 1658.55 (C=C stretching), 1348.96 (OH bend). ESI-HRMS for $C_{11}H_9N_3O_5$ $[M+H]^+$: 264.0620, obtained value: 264.0631.

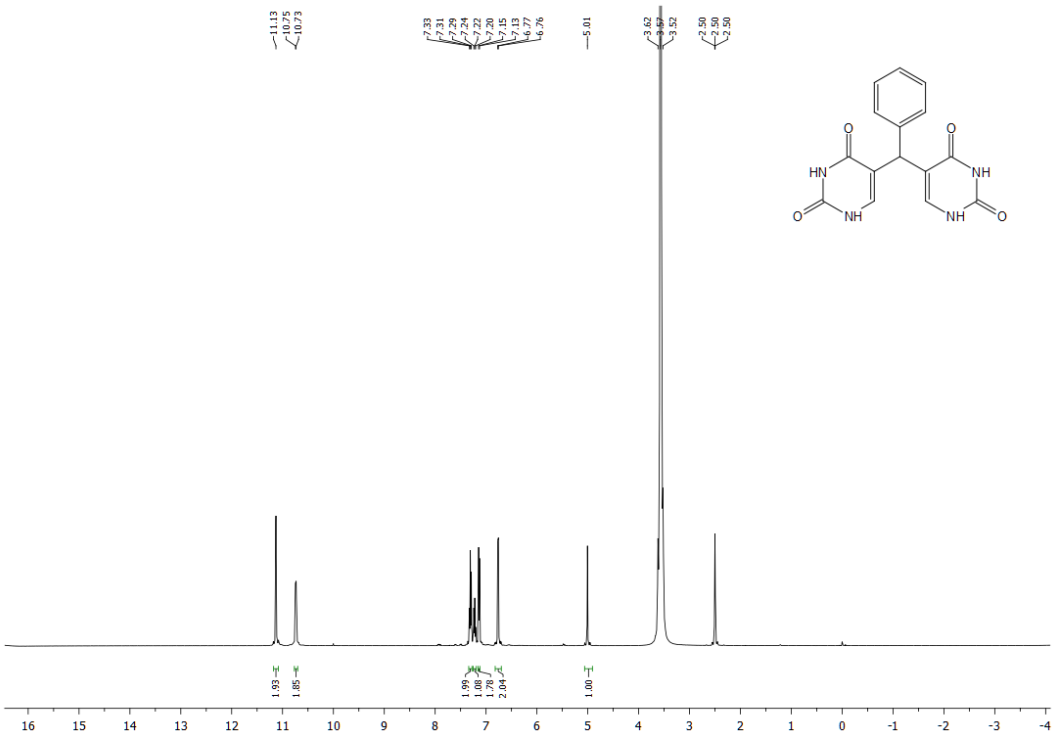
F. Table S3 Single-crystal XRD data of isolated intermediate**.**

CCDC Number	1946178

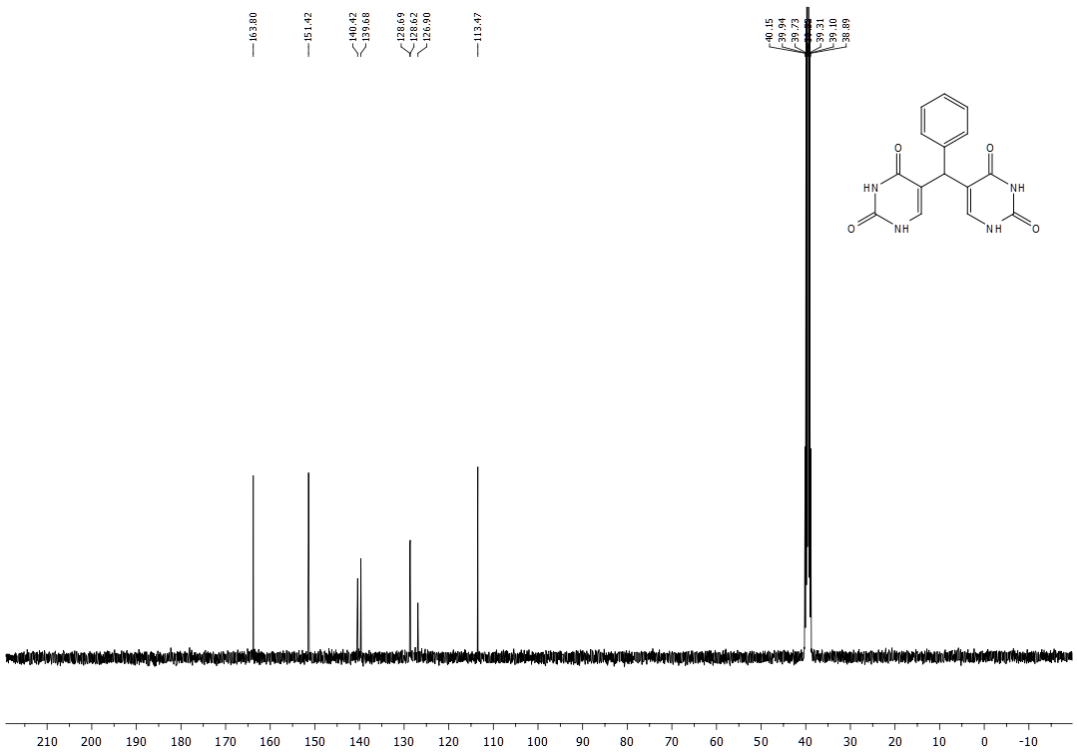
Empirical formula	$C_{20}H_{18}N_3O_5$
Formula weight	526.42
Temperature/K	298
Crystal system	monoclinic
Space group	P21/a
a/Å	12.1477(18)
b/Å	7.4576(8)
c/Å	13.8322(19)
α/°	90
β/°	114.653(18)
γ/°	90
Volume/$Å^3$	1138.9(3)
Z	2
$\rho_{calc}g/cm^3$	1.5350
μ/mm^{-1}	0.124
F(000)	544.3
Radiation	MoKa (l ¼ 0.71073)
2Θ range for data collection/°	6.48 to 58.74
Index ranges	-13 ≤ h ≤ 16, -9 ≤ k ≤ 9, -18 ≤ l ≤ 19
Reflections collected	6480
Independent reflections	2654[R(int) = 0.0196]
Goodness-of-fit on F^2	1.072

G. Spectra (Mass, ^{1}H and ^{13}C NMR, and FT-IR) of compounds from 1a to 28a

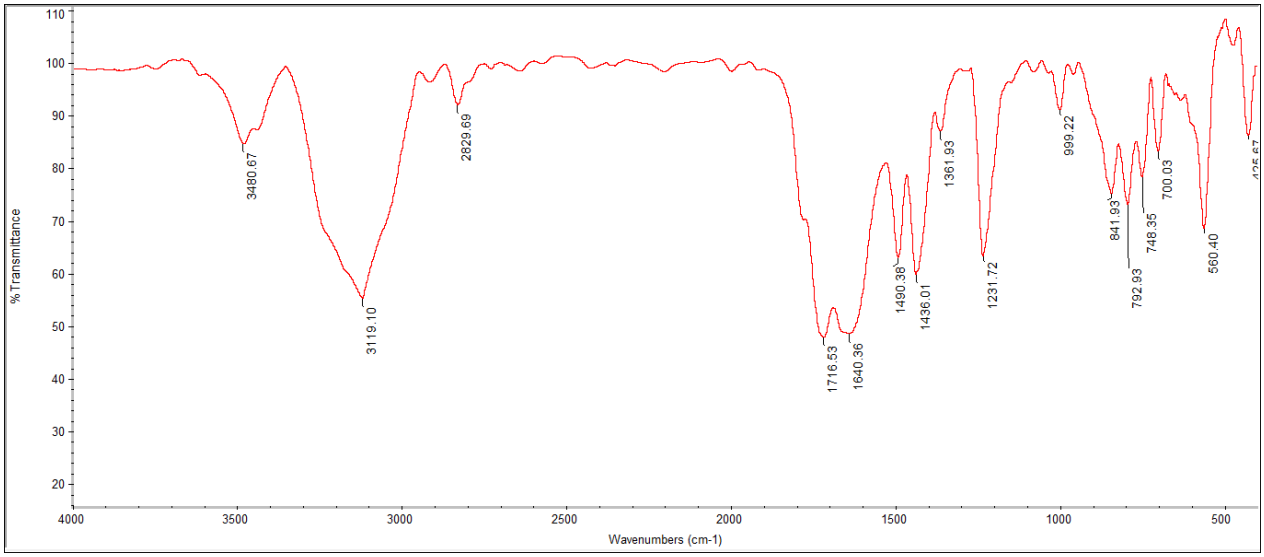
^{1}H NMR spectrum of 5,5'-(phenylmethylene)bis(pyrimidine-2,4*(*1*H*,3*H)*-dione) (**1a**)



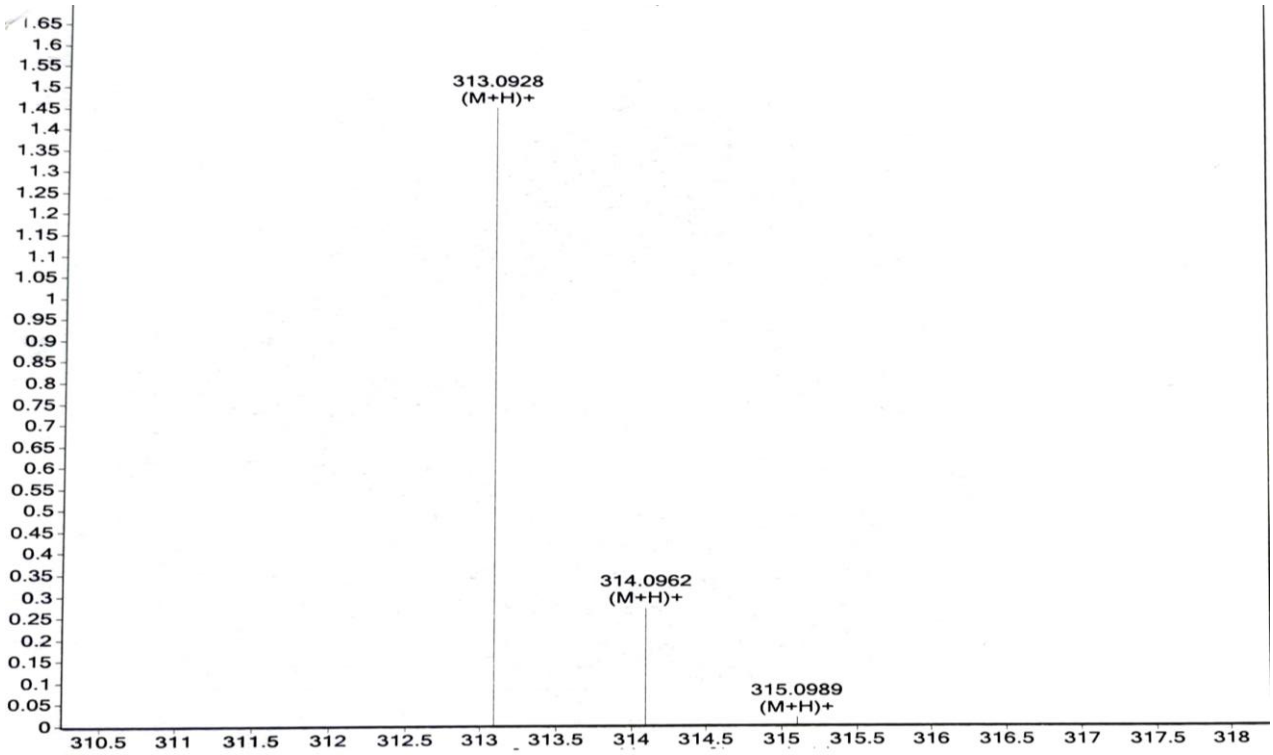
^{13}C NMR spectrum of 5,5'-(phenylmethylene)bis(pyrimidine-2,4*(*1*H*,3*H)*-dione) (**1a**)



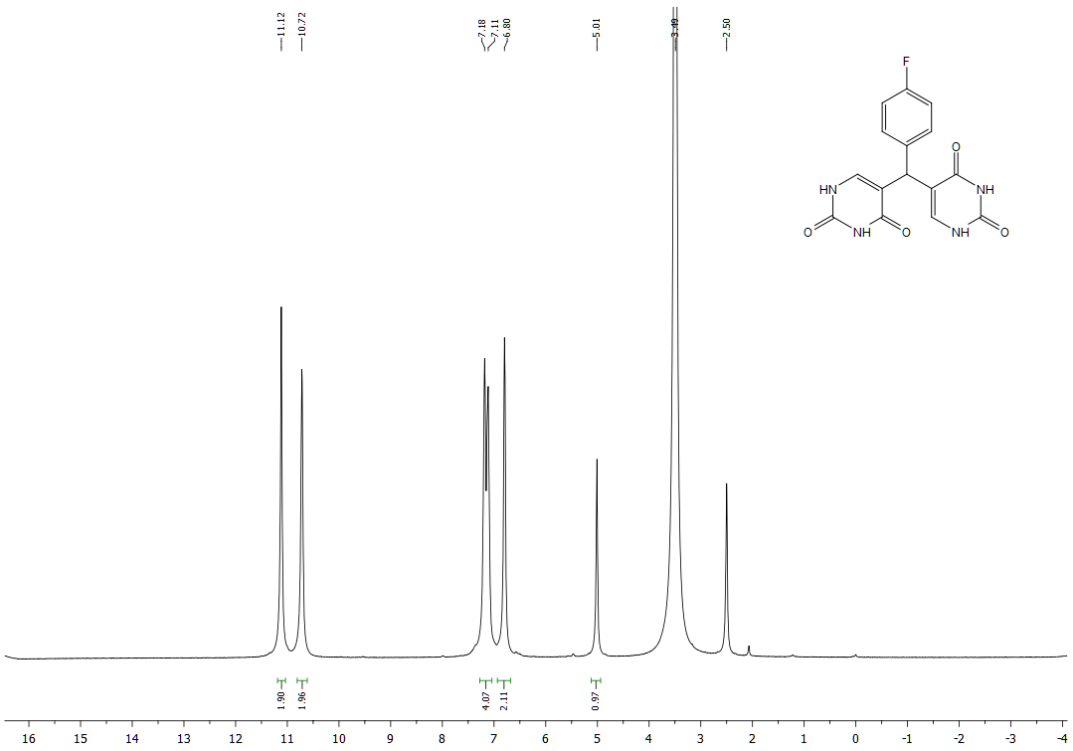
FTIR spectrum of 5,5'-(phenylmethylene)bis(pyrimidine-2,4*(*1*H*,3*H)*-dione) (**1a**)



Mass spectrum of 5,5'-(phenylmethylene)bis(pyrimidine-2,4*(*1*H*,3*H)*-dione) (**1a**)

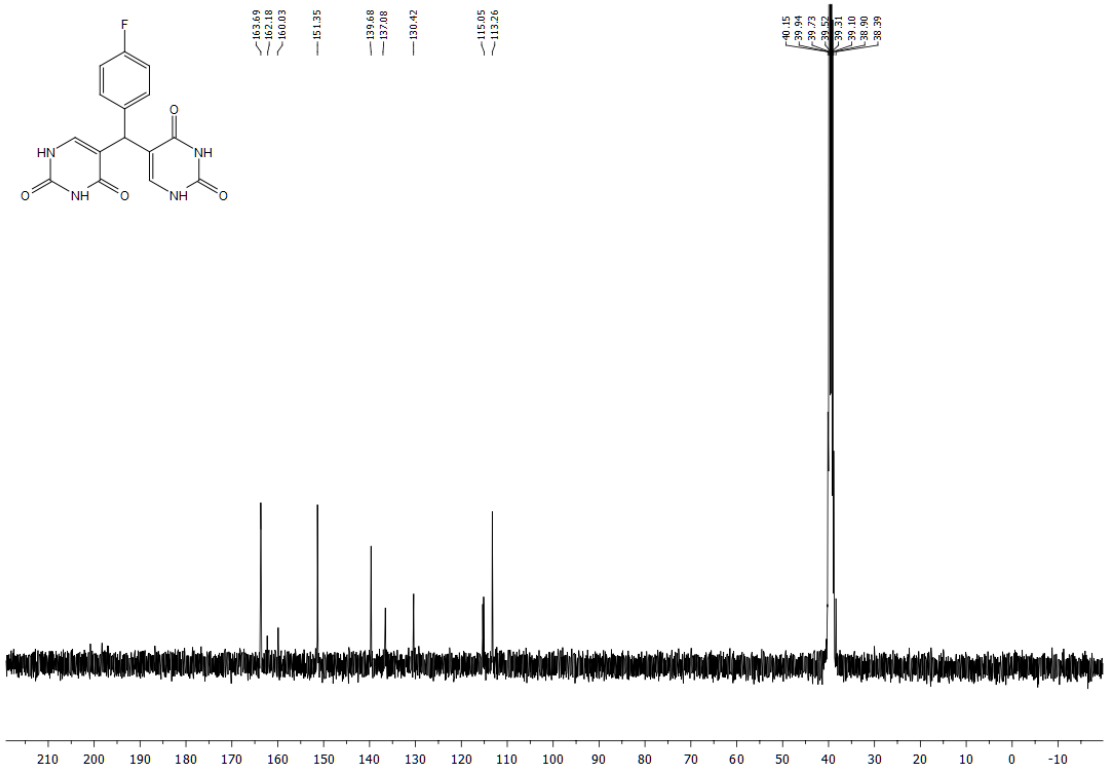


^{1}H NMR spectrum of 5,5'-((4-fluorophenyl)methylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione) **(2a)**

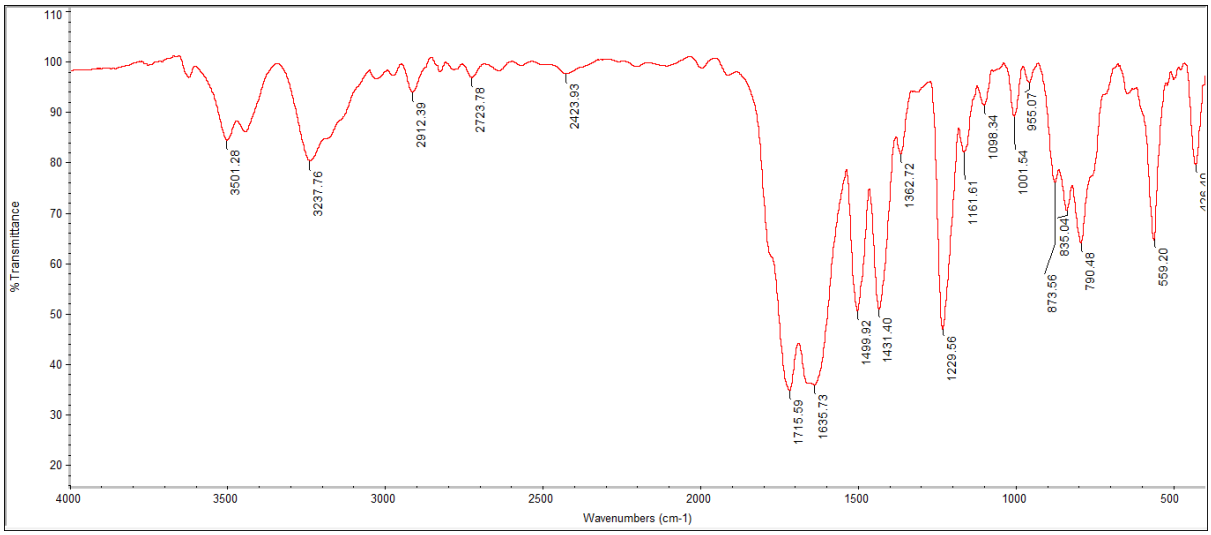


^{13}C NMR spectrum of 5,5'-((4-fluorophenyl)methylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione)

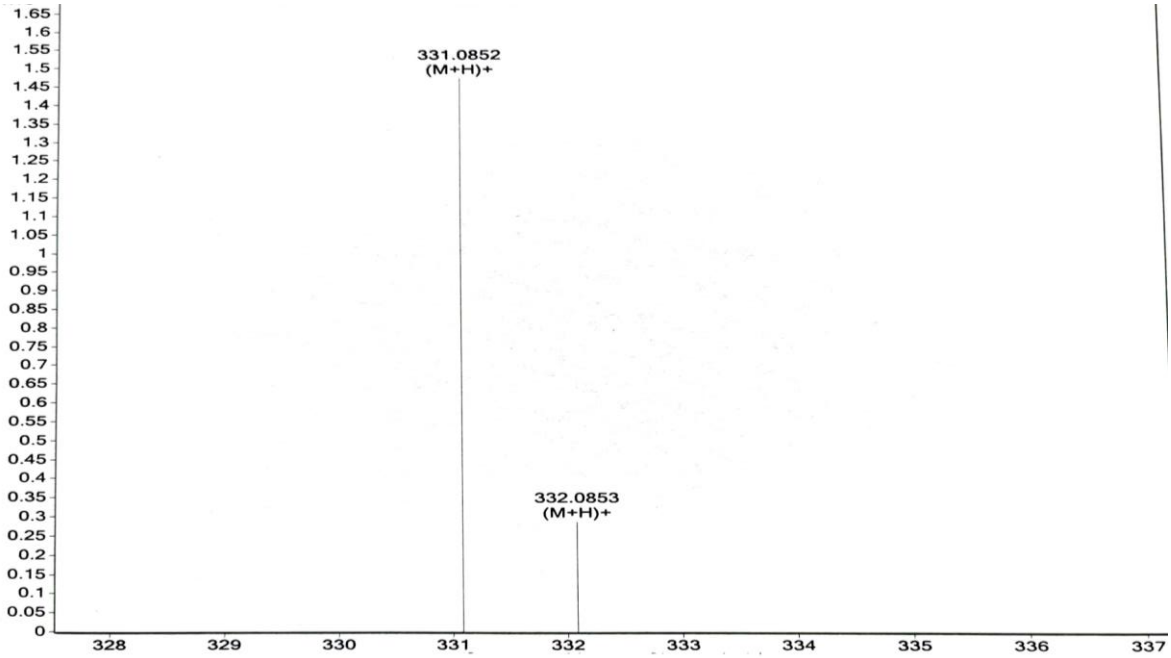
(2a)



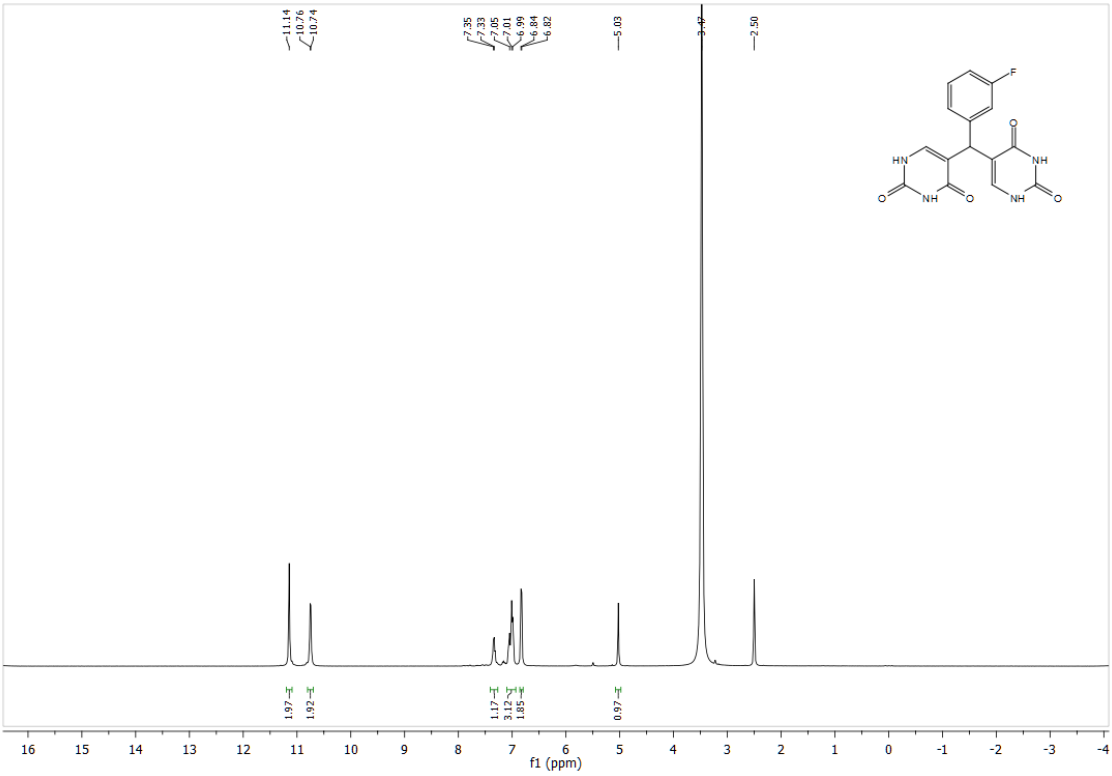
FTIR spectrum of 5,5'-((4-fluorophenyl)methylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione) **(2a)**



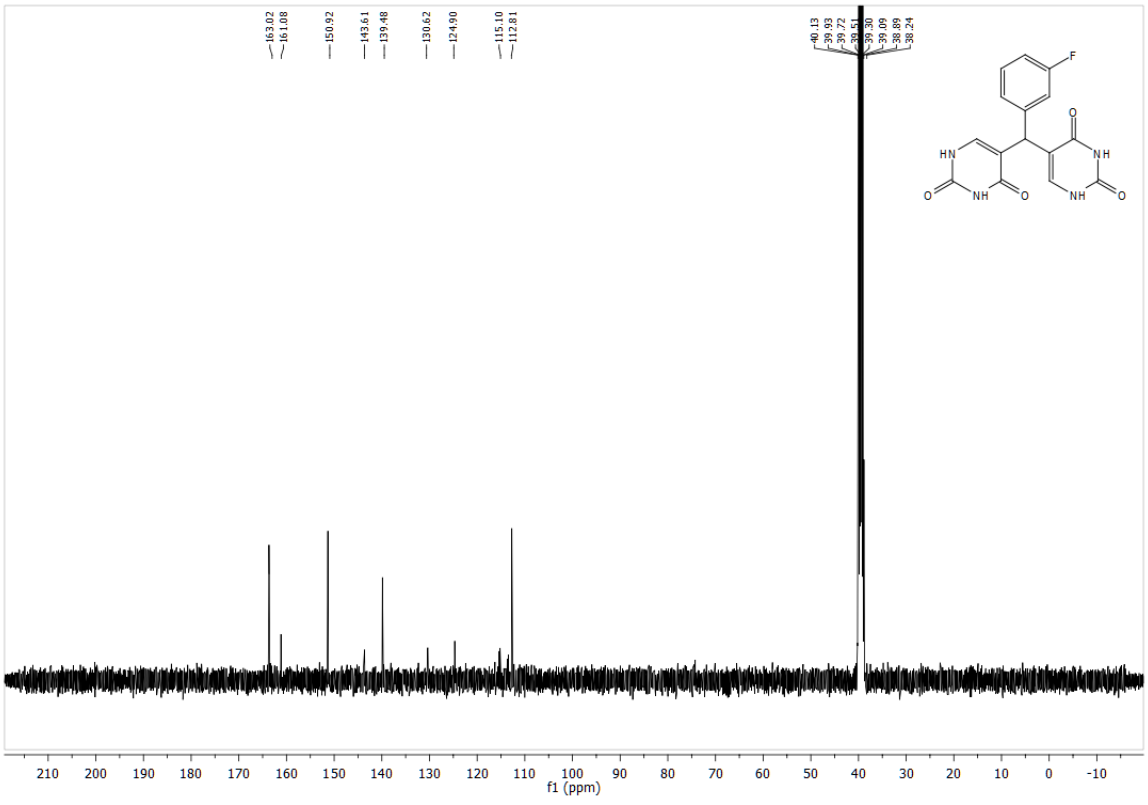
Mass spectrum of 5,5'-((4-fluorophenyl)methylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione) **(2a)**



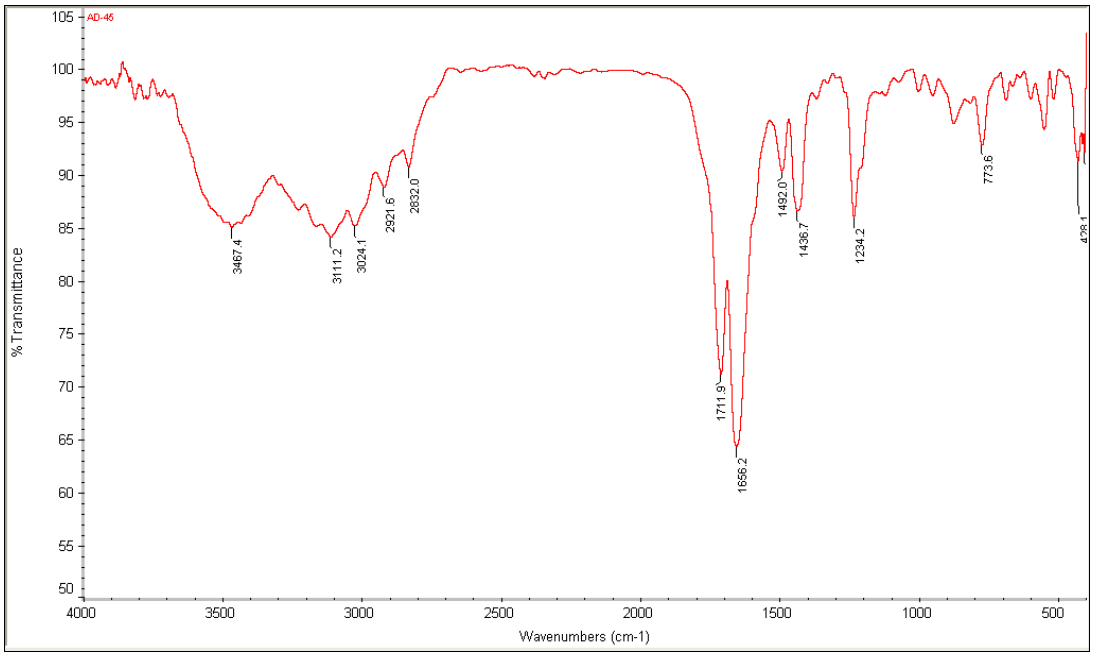
^{1}H NMR spectrum of 5,5'-((3-fluorophenyl)methylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione) **(3a)**



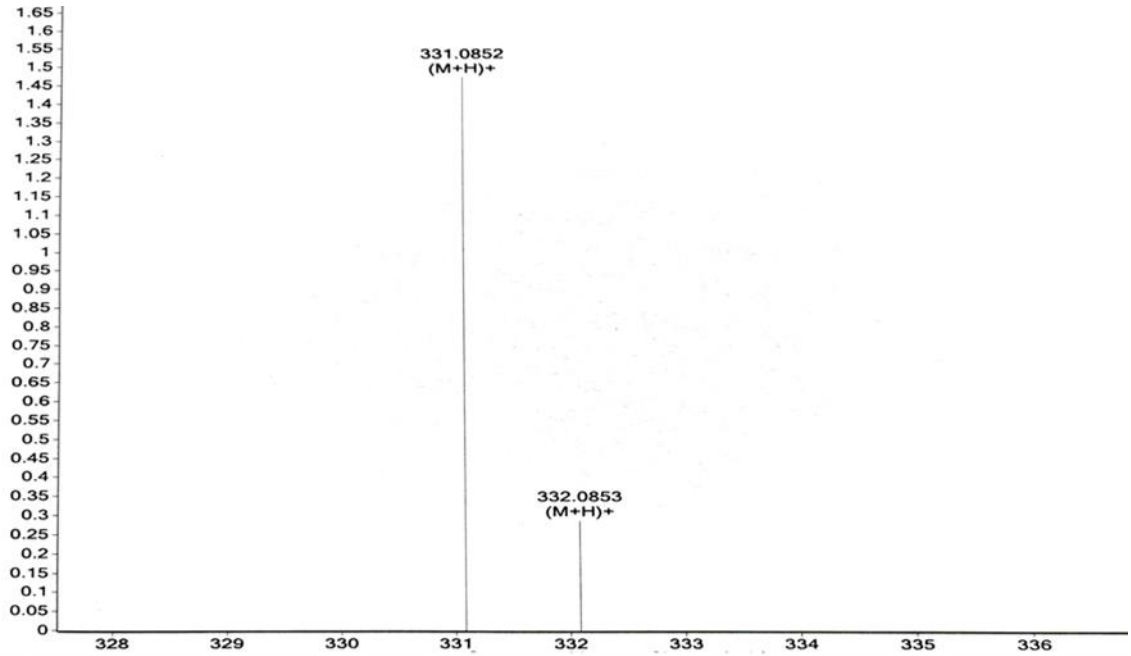
^{13}C NMR spectrum of 5,5'-((3-fluorophenyl)methylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione) **(3a)**



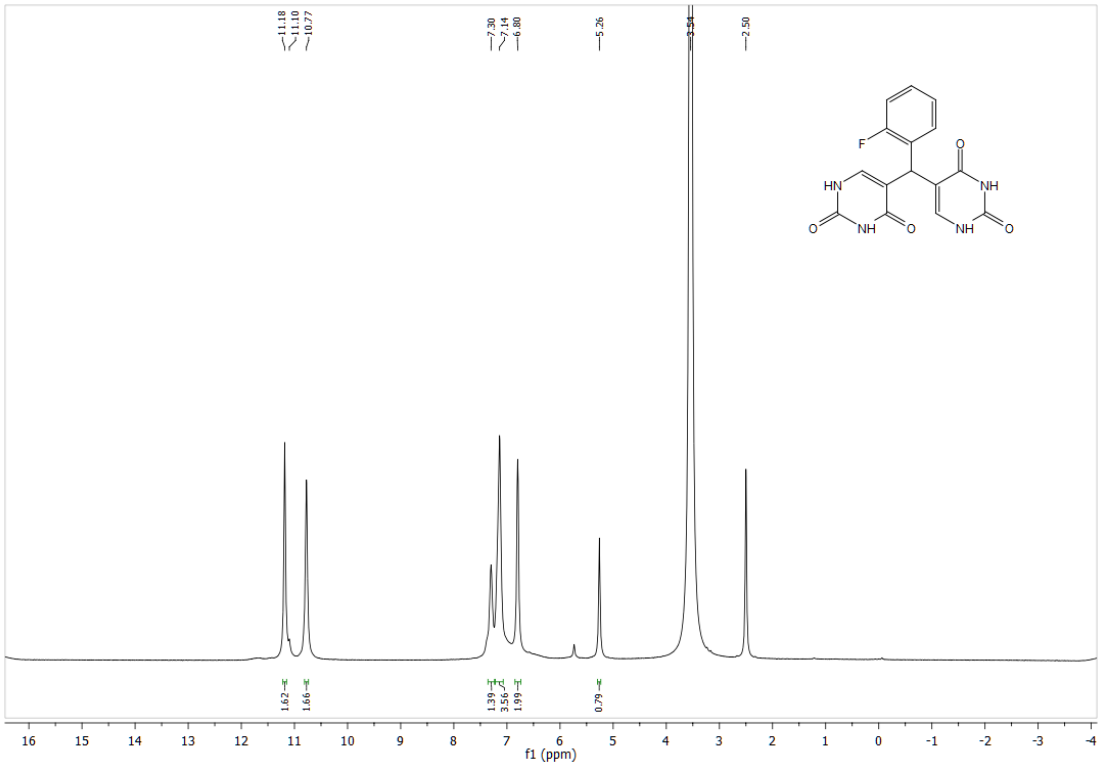
FTIR spectrum of 5,5'-((3-fluorophenyl)methylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione) **(3a)**



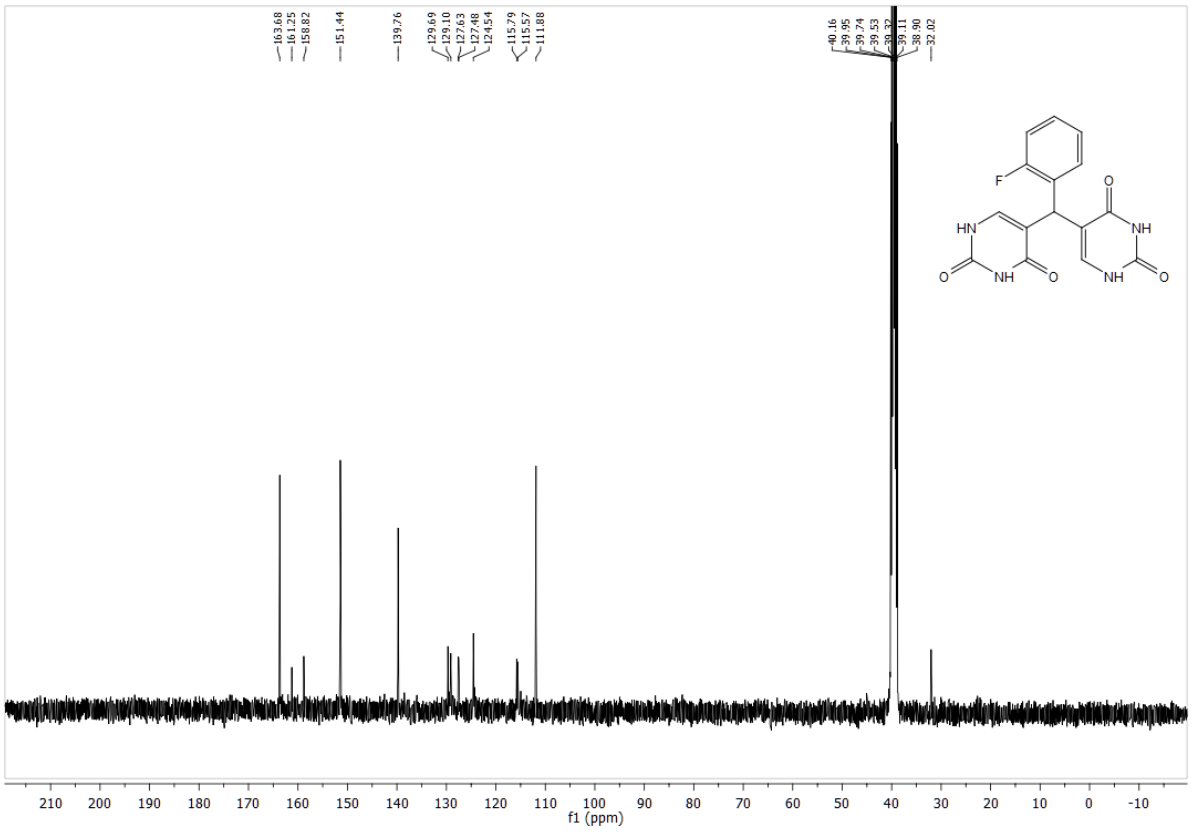
Mass spectrum of 5,5'-((3-fluorophenyl)methylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione) **(3a)**



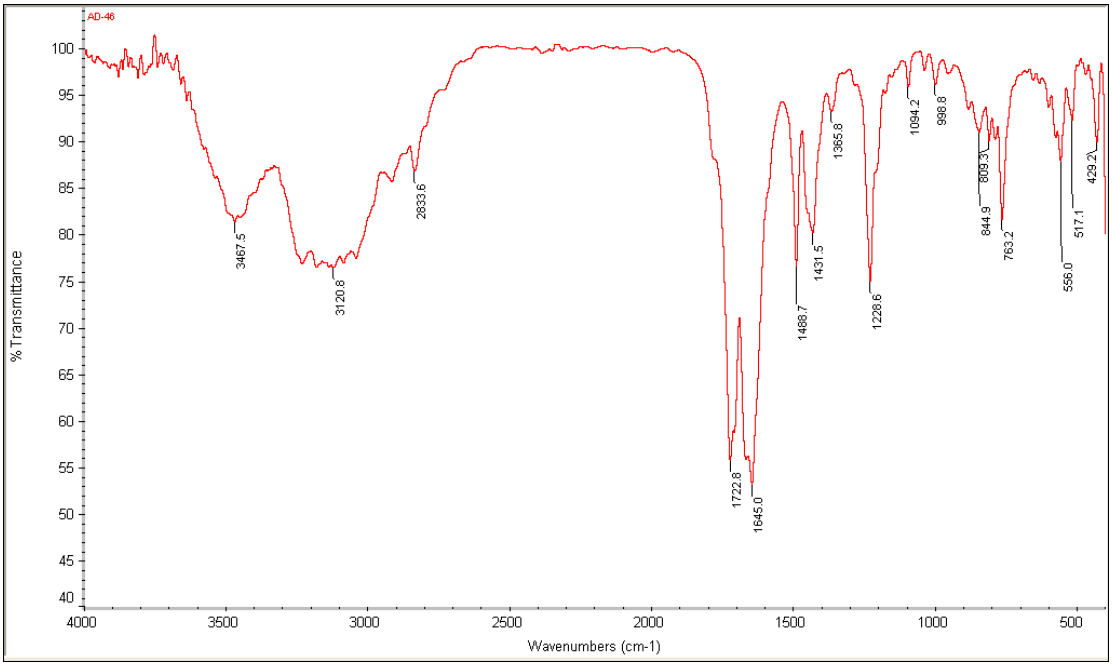
^{1}H NMR spectrum of 5,5'-((2-fluorophenyl)methylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione) **(4a)**



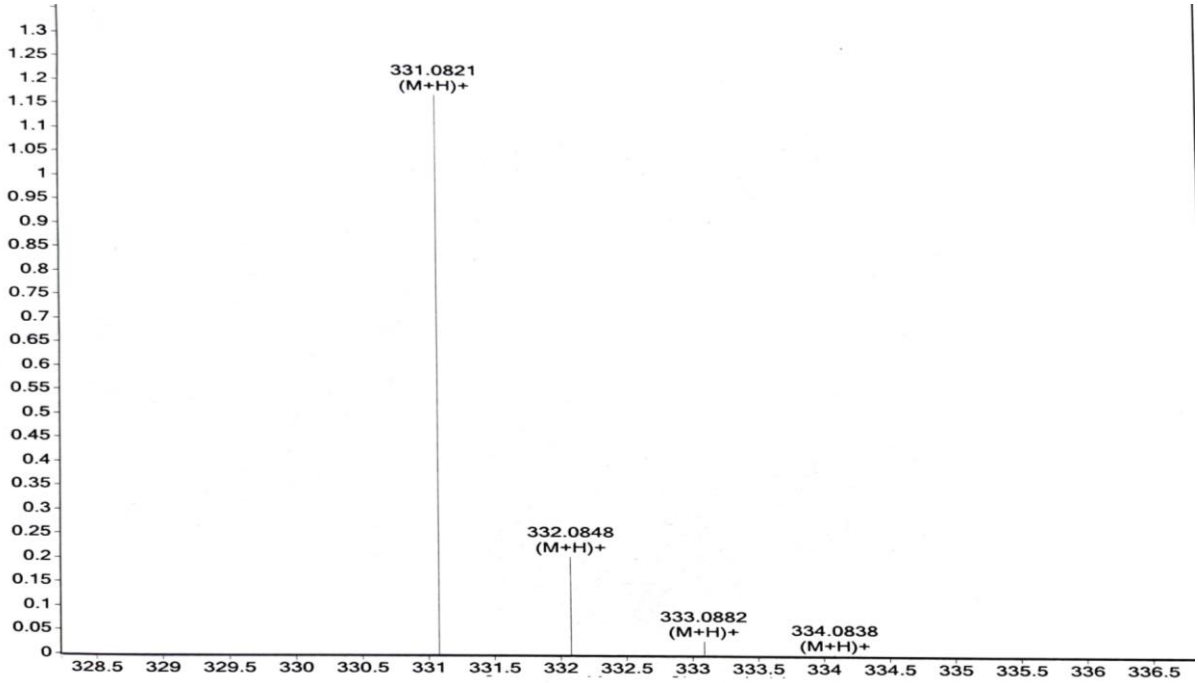
^{13}C NMR spectrum of 5,5'-((2-fluorophenyl)methylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione) **(4a)**



FTIR spectrum of 5,5'-((2-fluorophenyl)methylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione) **(4a)**

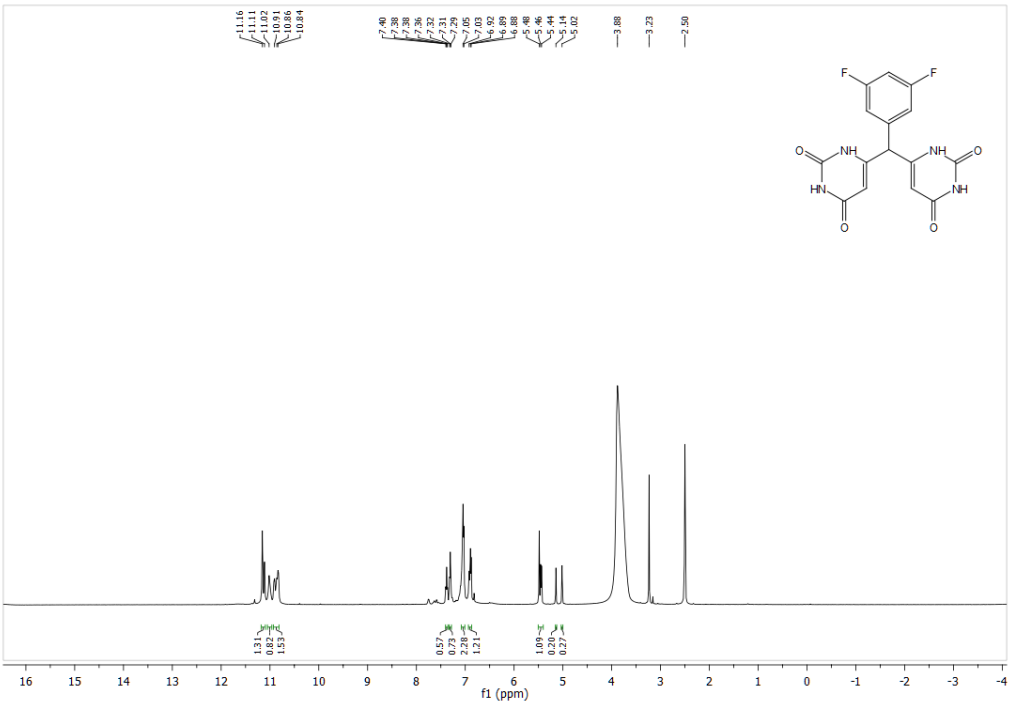


Mass spectrum of 5,5'-((2-fluorophenyl)methylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione) **(4a)**



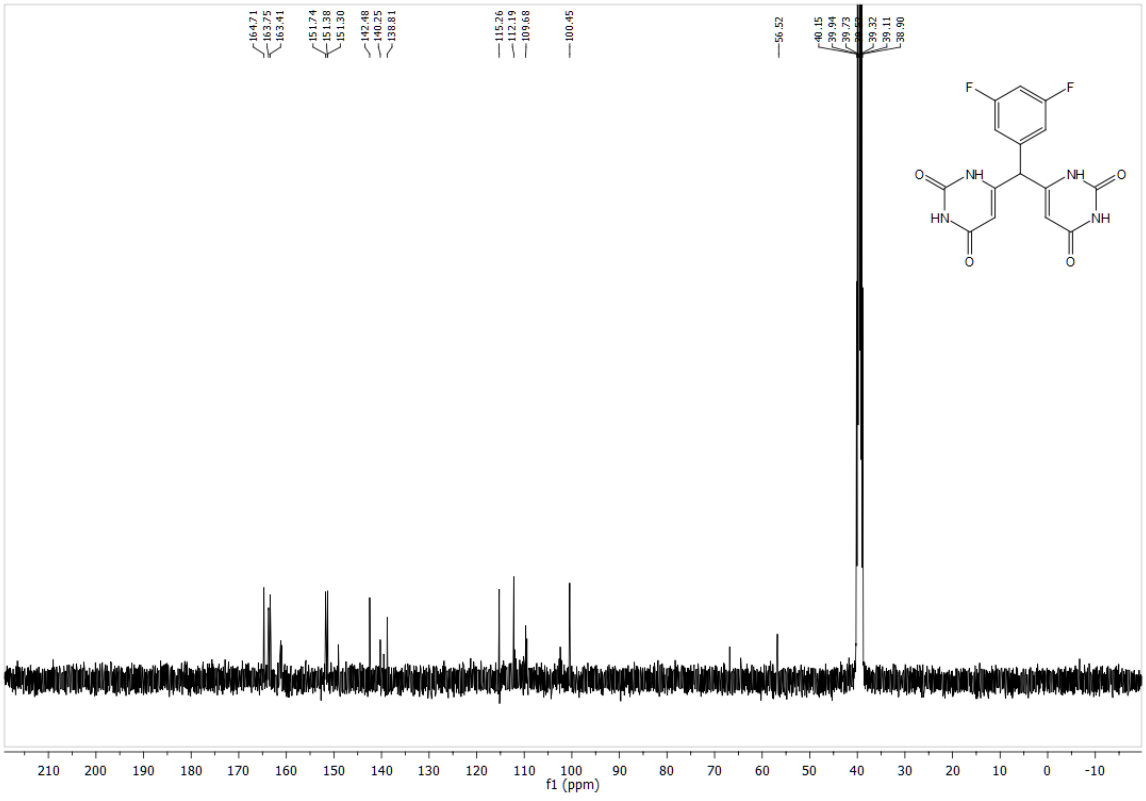
^{1}H NMR spectrum of 6,6'-((3,5-difluorophenyl)methylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione)

(5a)

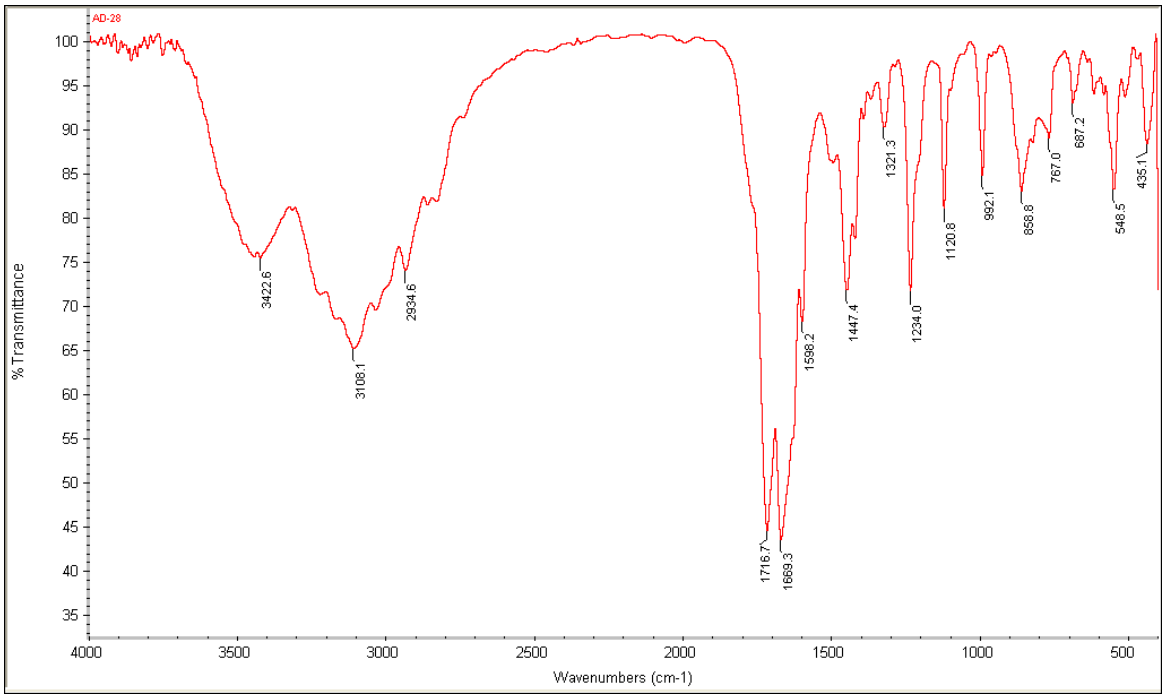


^{13}C NMR spectrum of 6,6'-((3,5-difluorophenyl)methylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione)

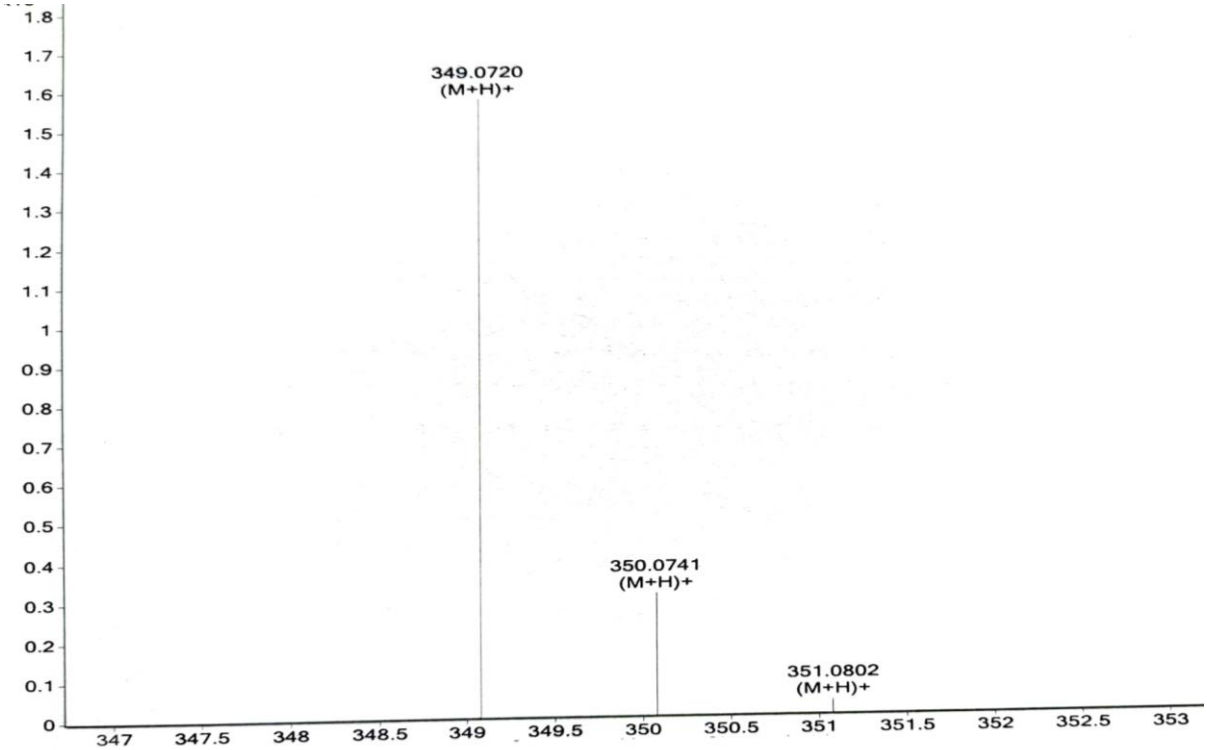
(5a)



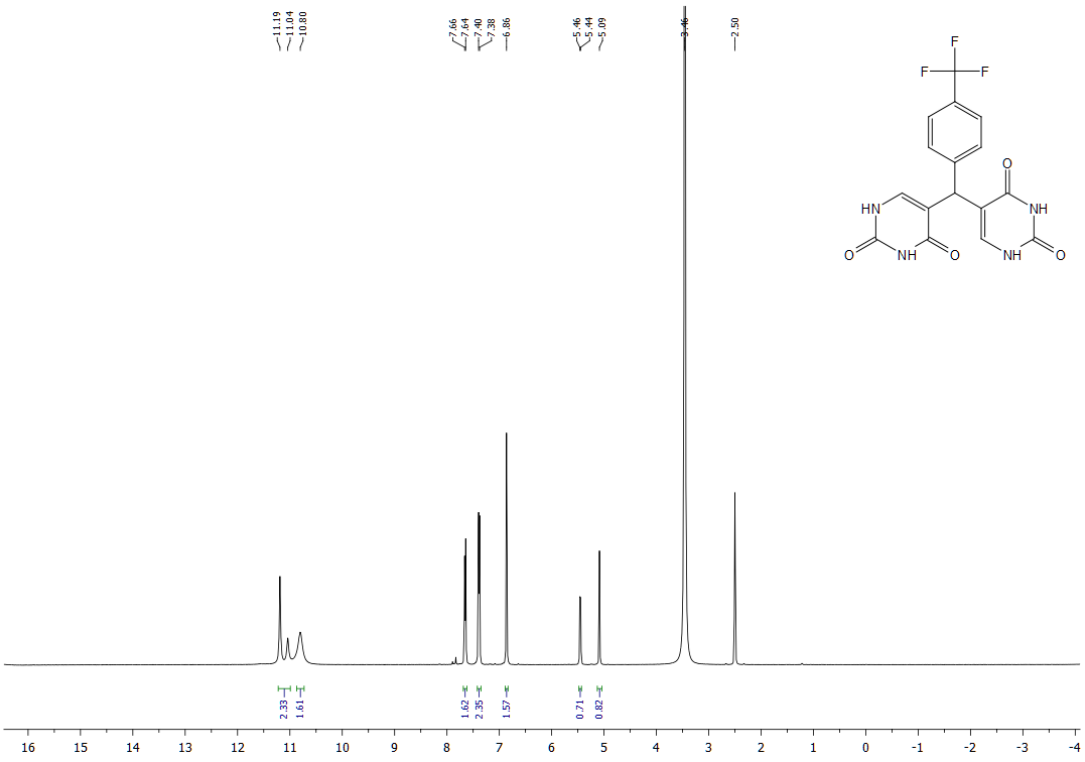
FTIR spectrum of 6,6'-((3,5-difluorophenyl)methylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione) **(5a)**



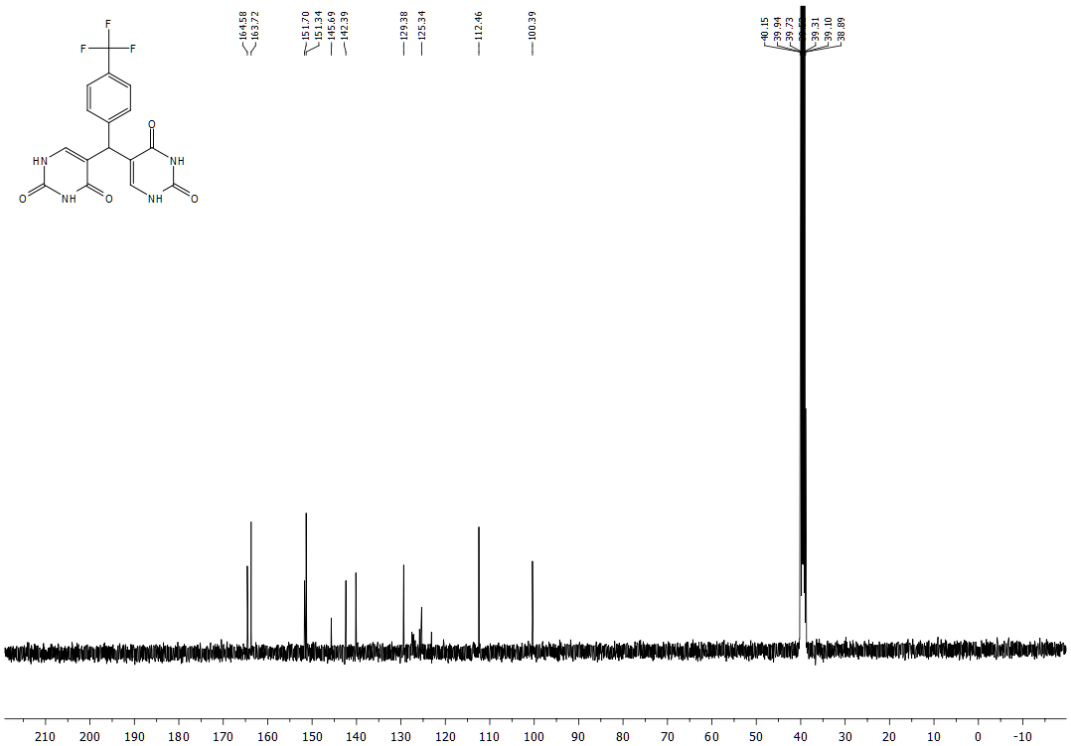
Mass spectrum of 6,6'-((3,5-difluorophenyl)methylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione) **(5a)**



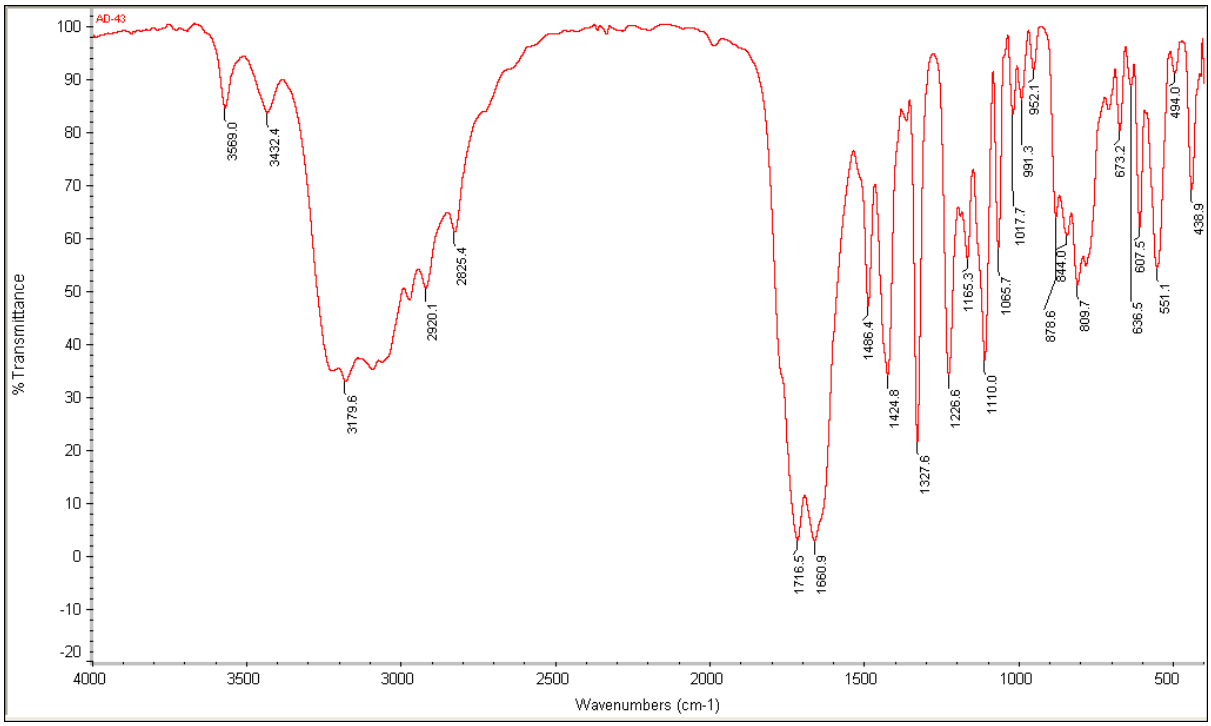
^{1}H NMR spectrum of 5,5'-((4-(trifluoromethyl)phenyl)methylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione) **(6a)**



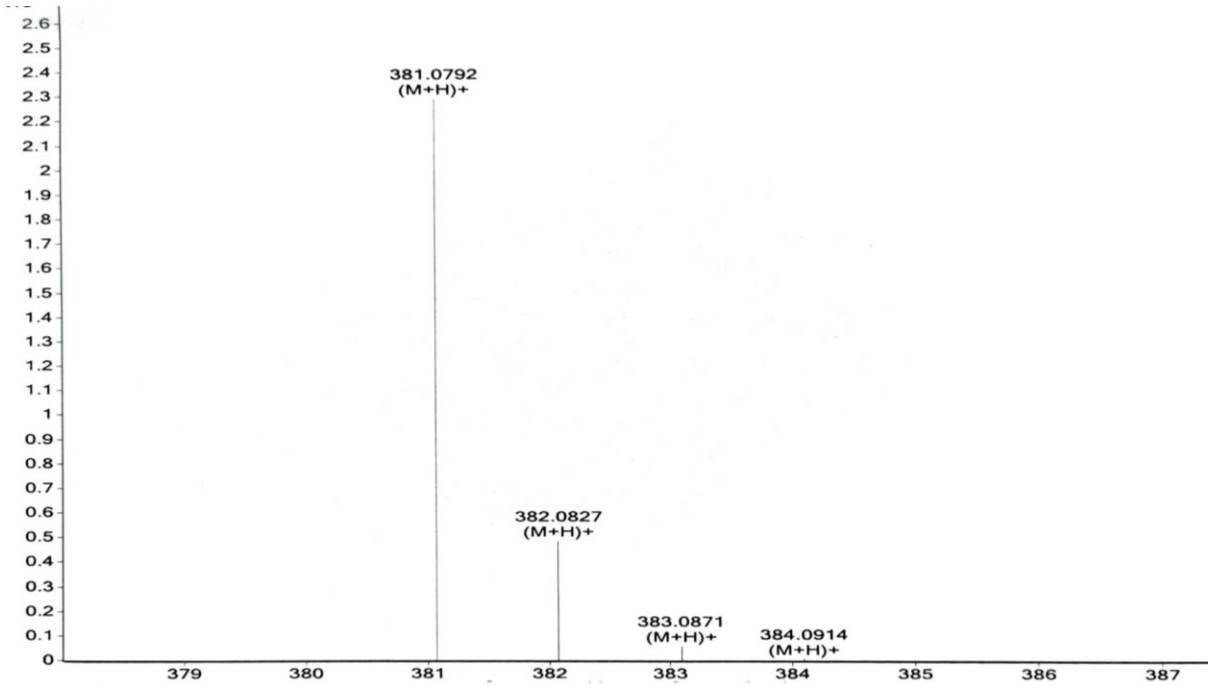
^{13}C NMR spectrum of 5,5'-((4-(trifluoromethyl)phenyl)methylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione) **(6a)**



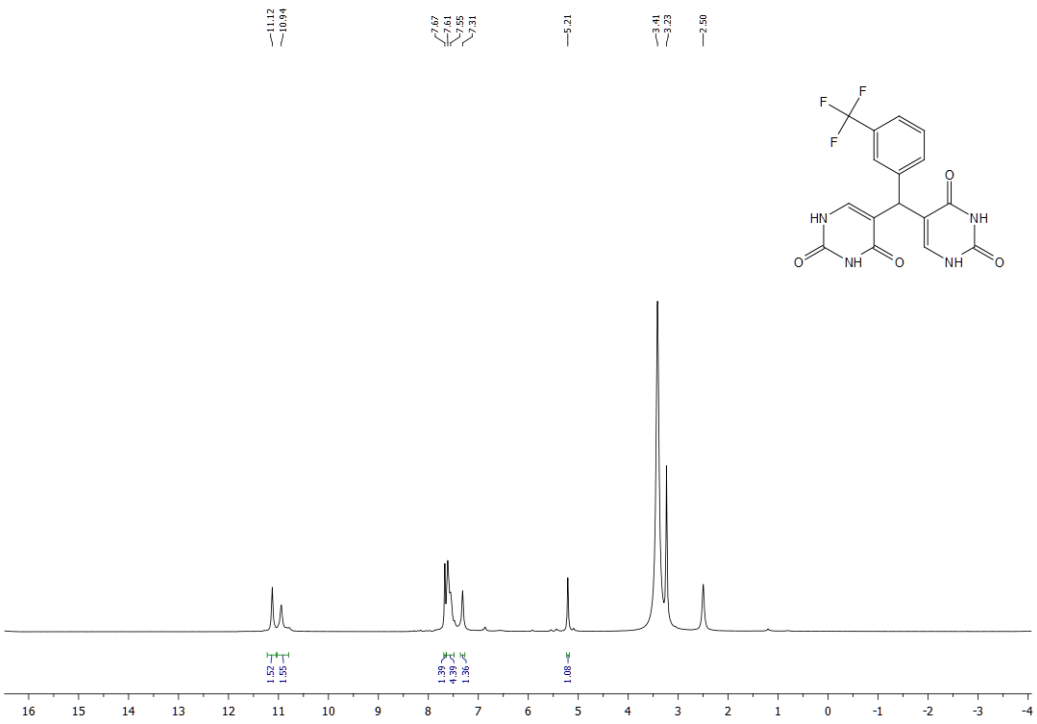
FTIR spectrum of 5,5'-((4-(trifluoromethyl)phenyl)methylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione) **(6a)**



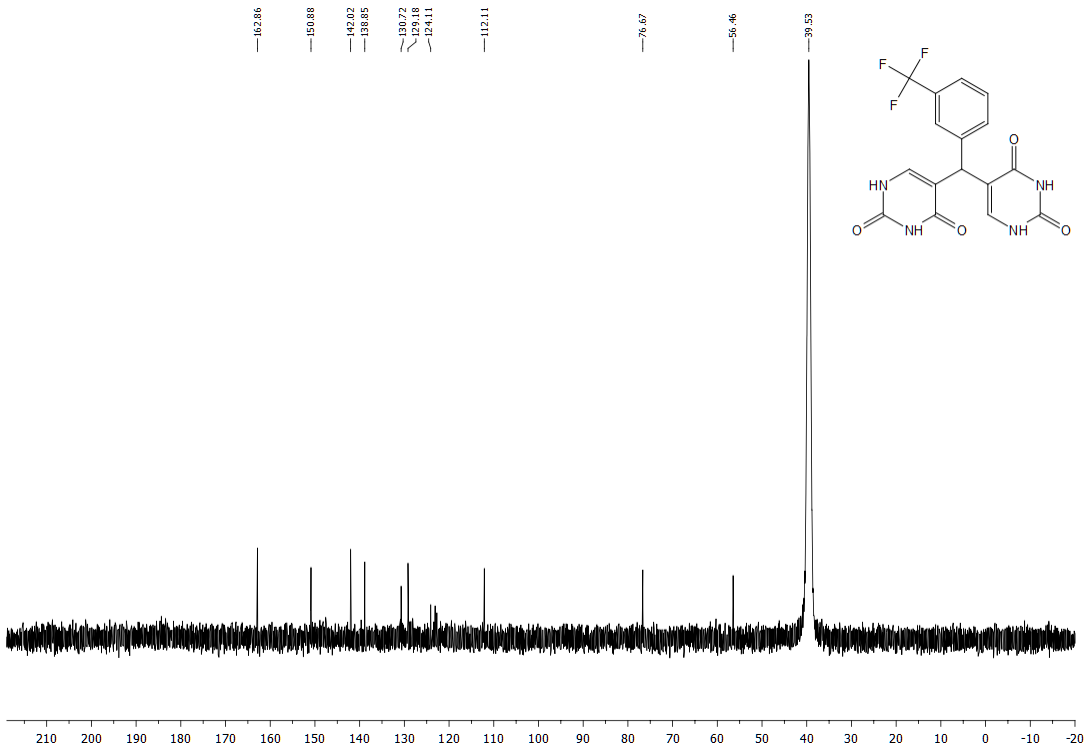
Mass spectrum of 5,5'-((4-(trifluoromethyl)phenyl)methylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione) **(6a)**



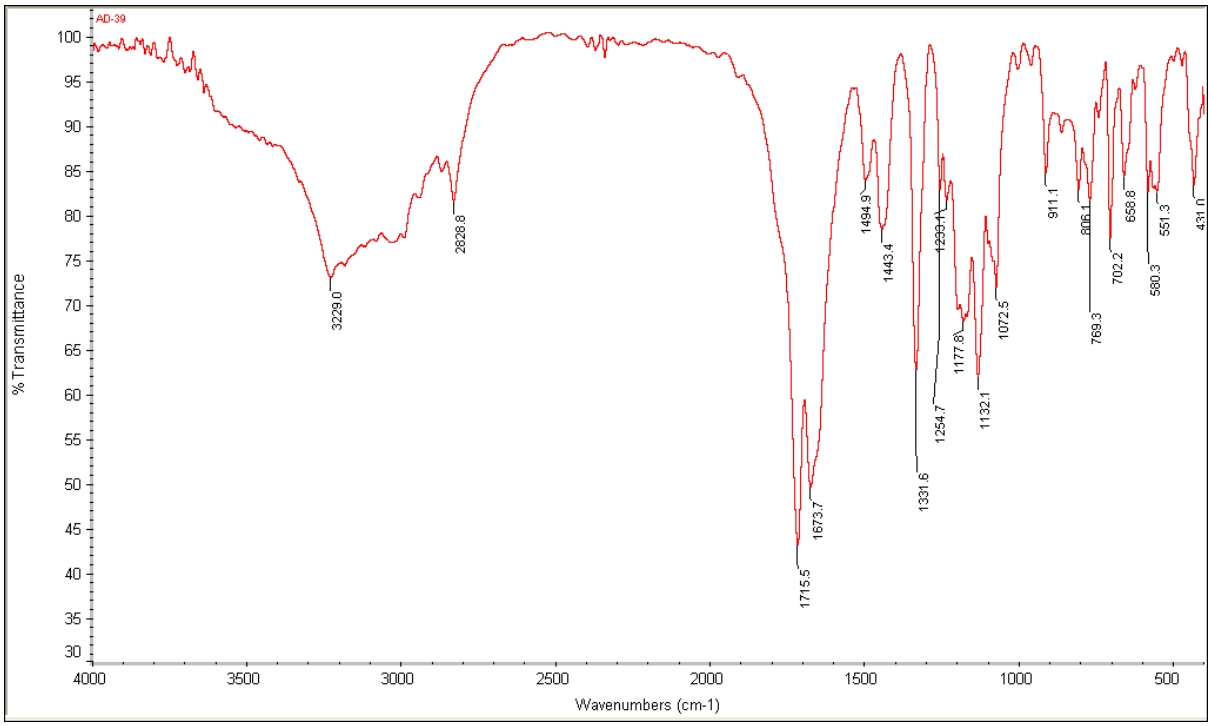
^{1}H NMR spectrum of 5,5'-((3-(trifluoromethyl)phenyl)methylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione) **(7a)**



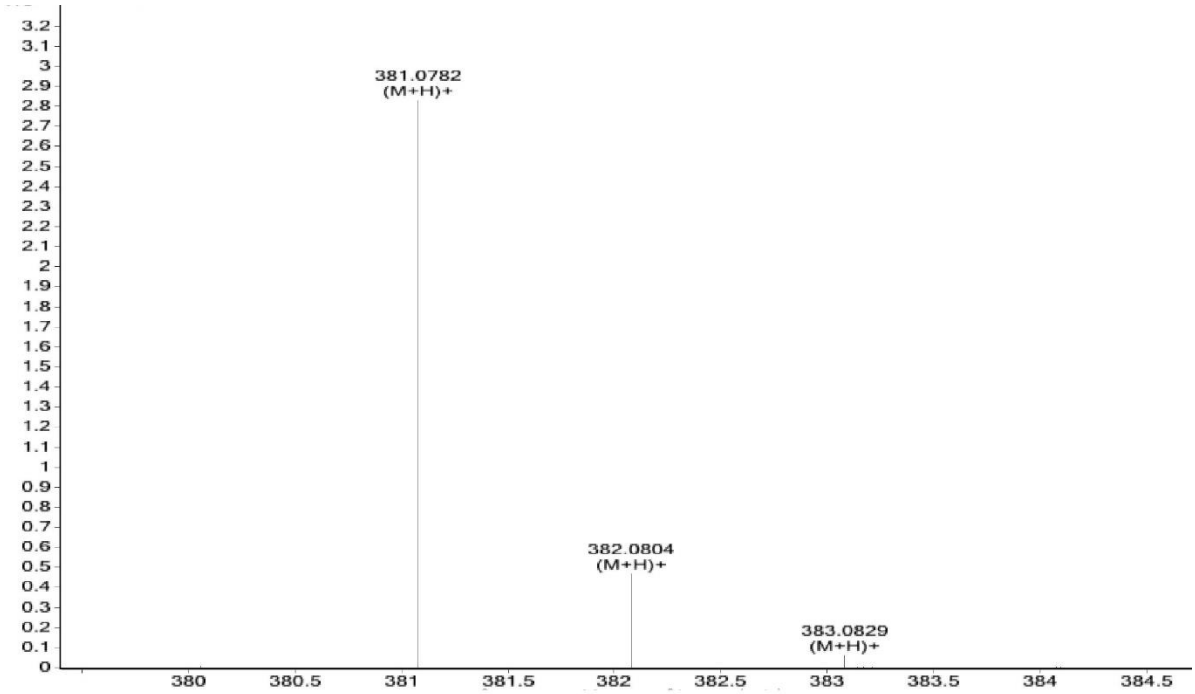
^{13}C NMR spectrum of 5,5'-((3-(trifluoromethyl)phenyl)methylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione) **(7a)**



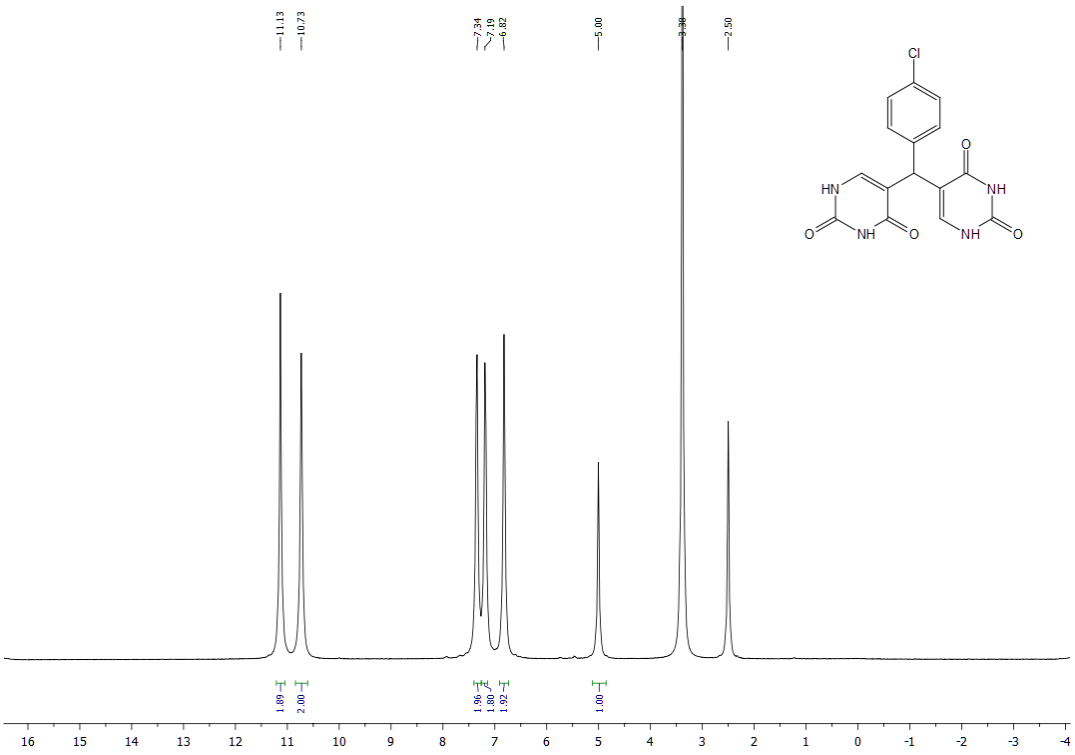
FTIR spectrum of 5,5'-((3-(trifluoromethyl)phenyl)methylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione) **(7a)**



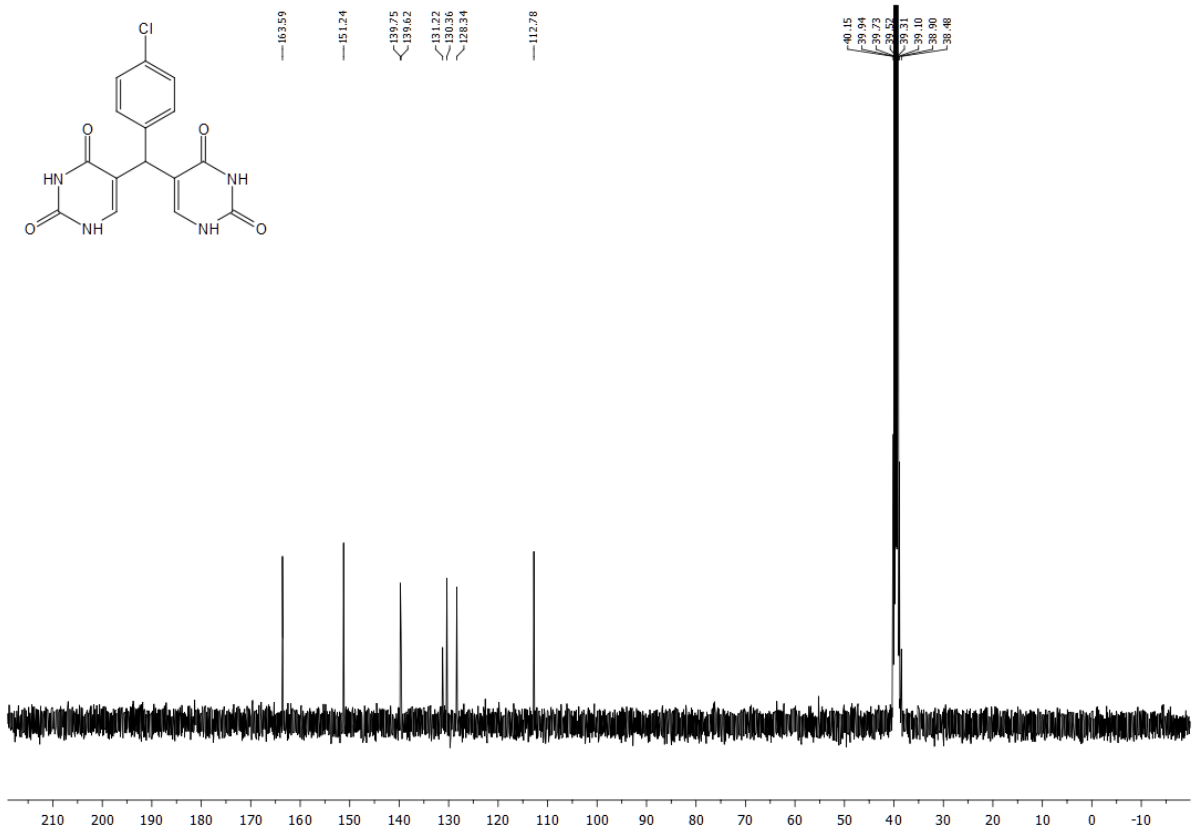
Mass spectrum of 5,5'-((3-(trifluoromethyl)phenyl)methylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione) **(7a)**



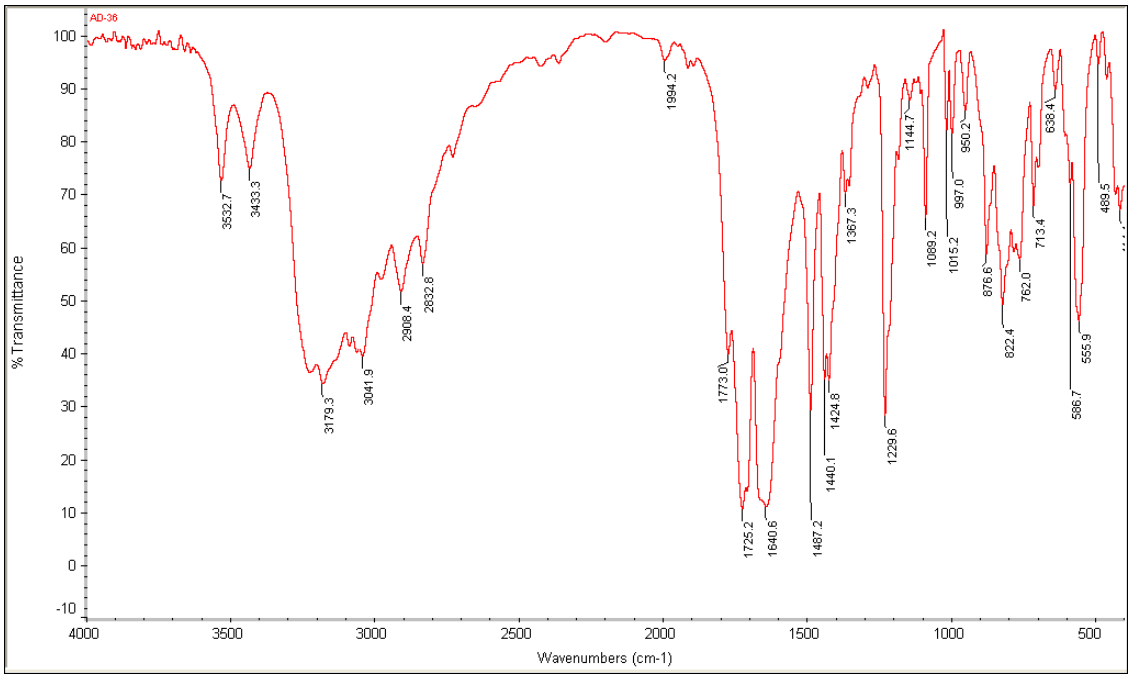
^{1}H NMR spectrum of 5,5'-((4-chlorophenyl)methylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione) **(8a)**



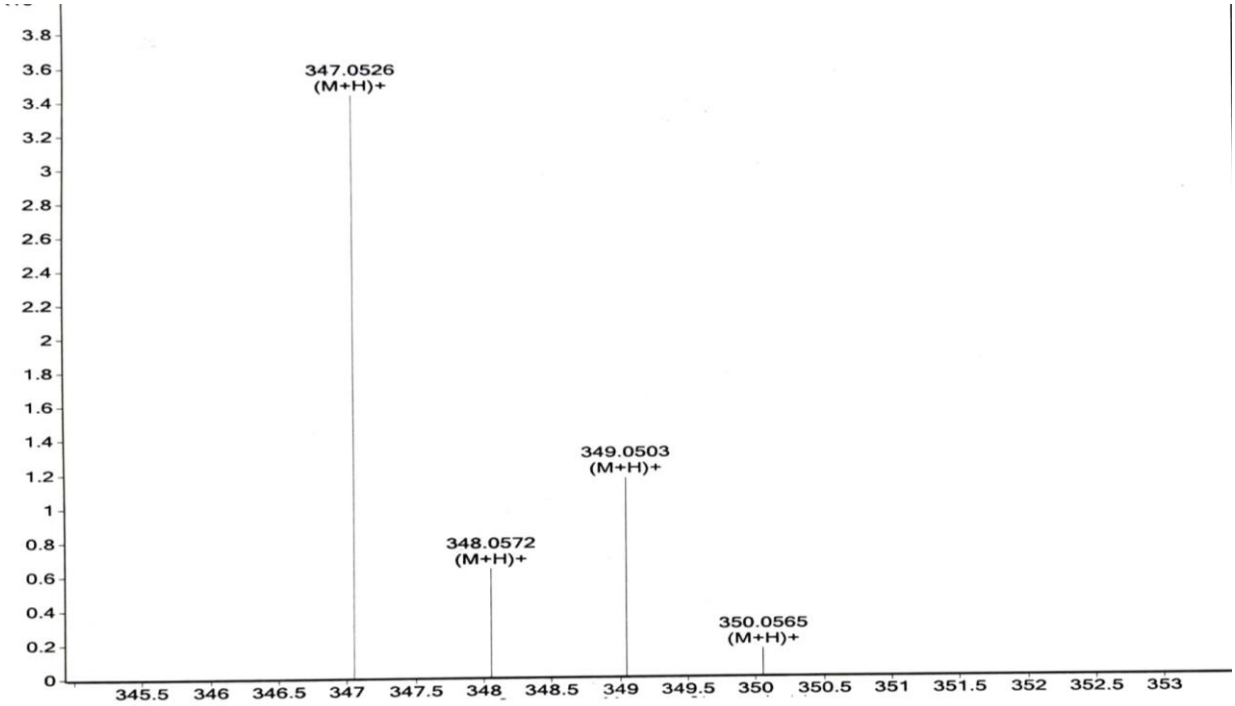
^{13}C NMR spectrum of 5,5'-((4-chlorophenyl)methylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione) **(8a)**



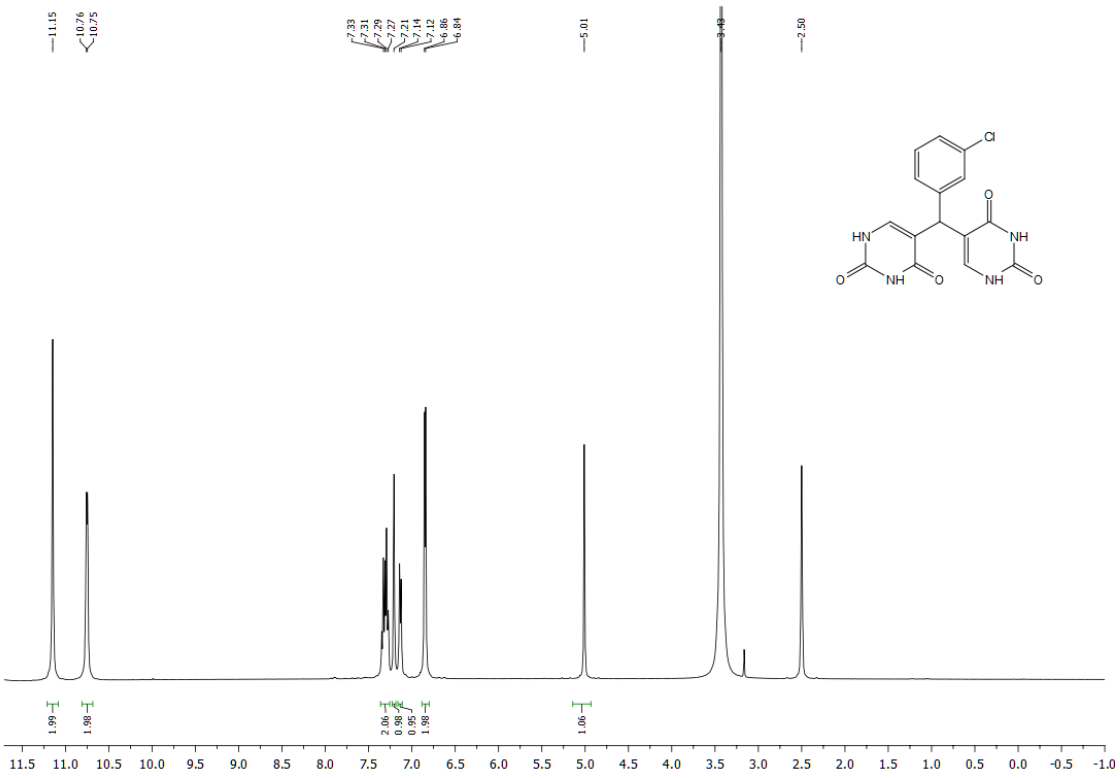
FTIR spectrum of 5,5'-((4-chlorophenyl)methylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione) **(8a)**



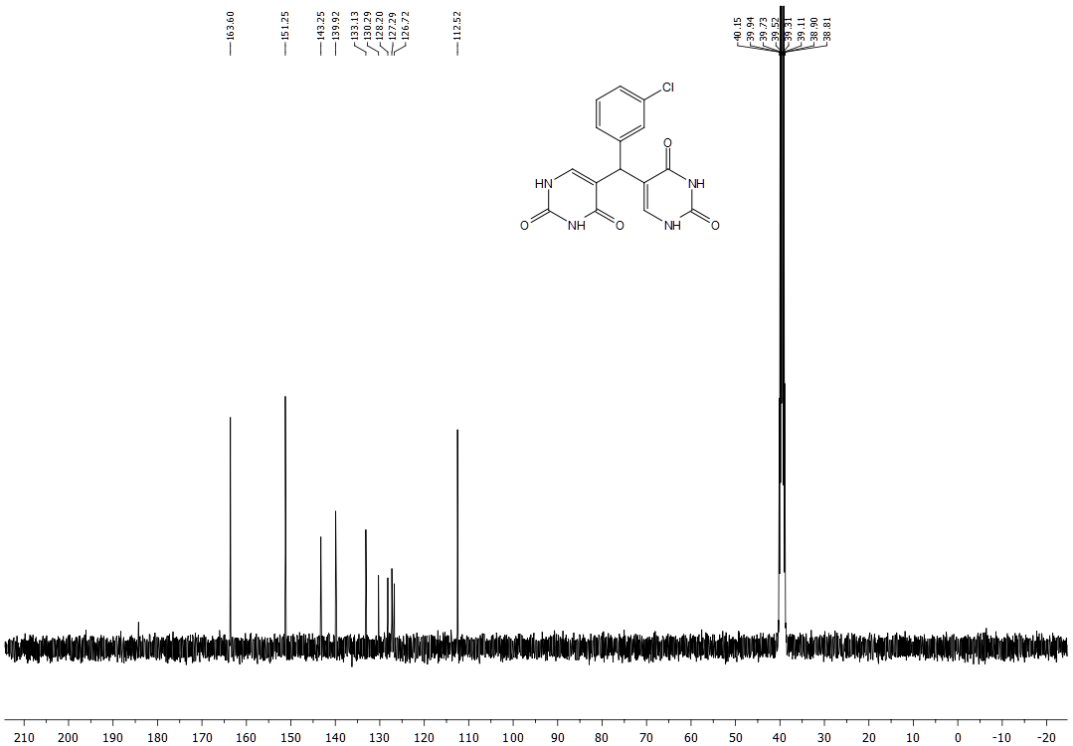
Mass spectrum of 5,5'-((4-chlorophenyl)methylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione) **(8a)**



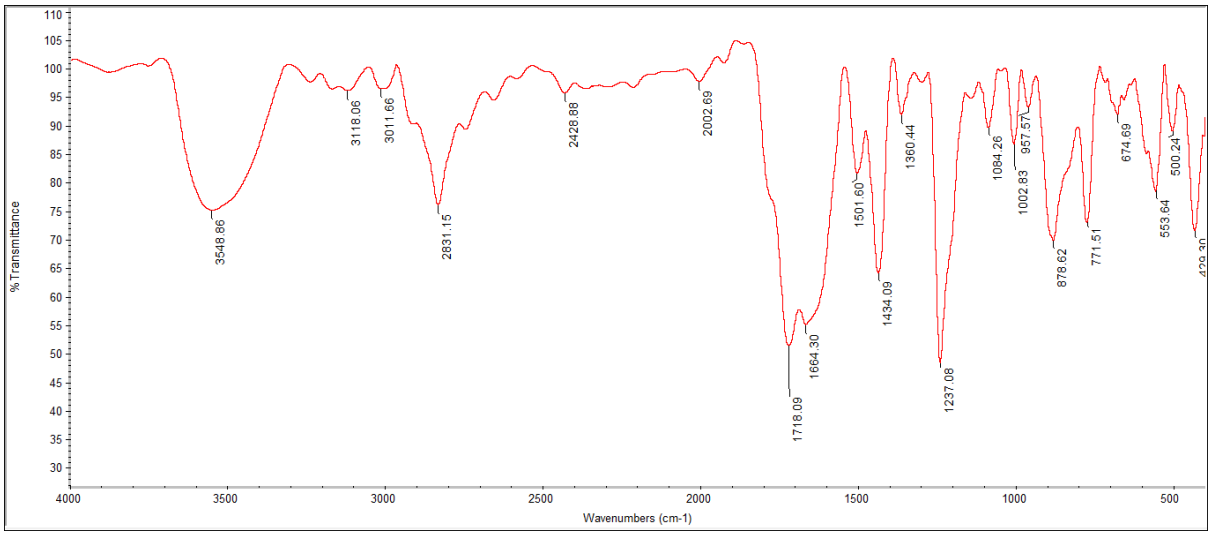
^{1}H NMR spectrum of 5,5'-((3-chlorophenyl)methylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione) **(9a)**



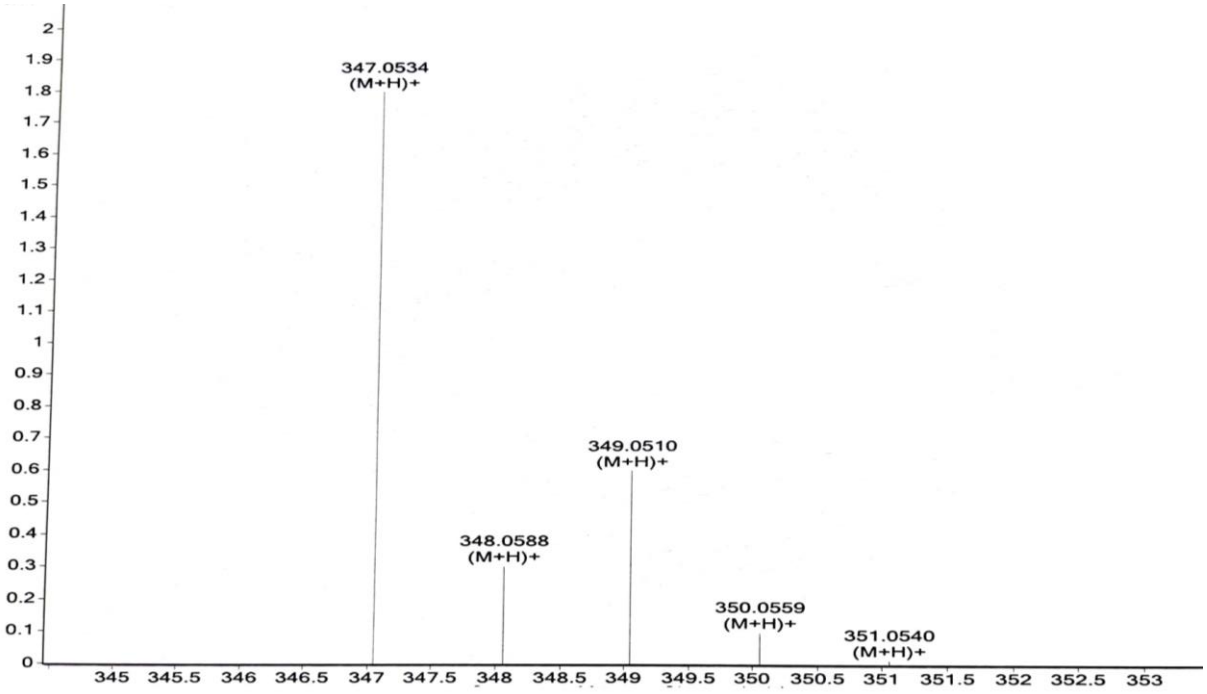
^{13}C NMR spectrum of 5,5'-((3-chlorophenyl)methylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione) **(9a)**



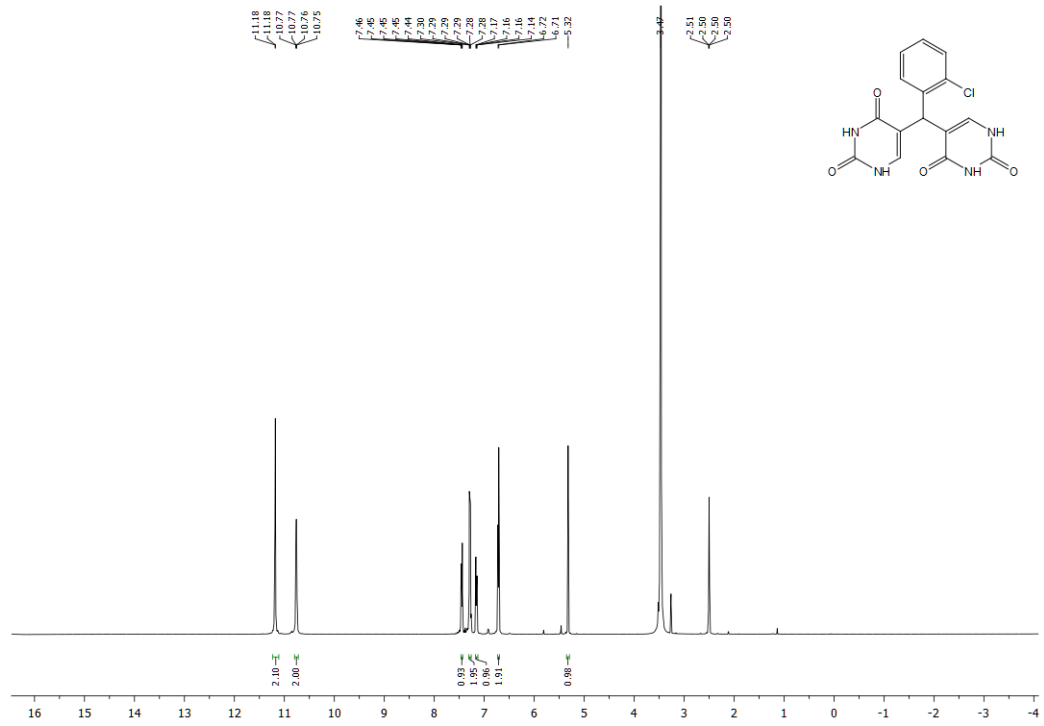
FTIR spectrum of 5,5'-((3-chlorophenyl)methylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione) **(9a)**



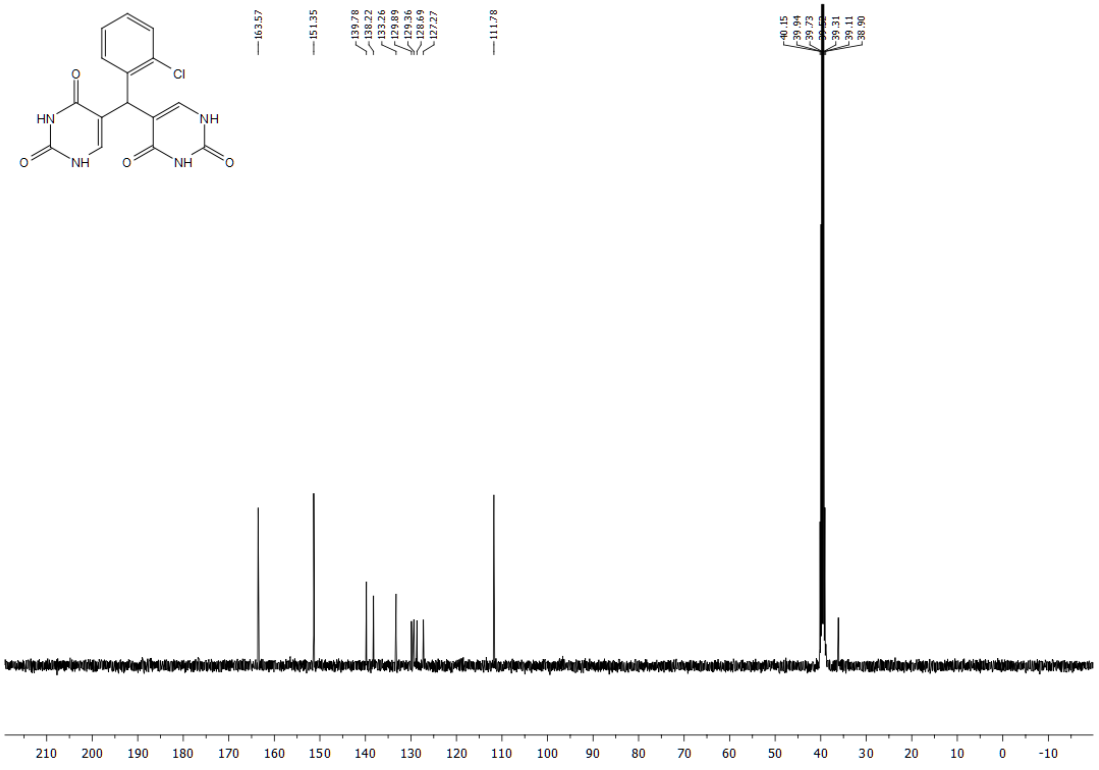
Mass spectrum of 5,5'-((3-chlorophenyl)methylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione) **(9a)**



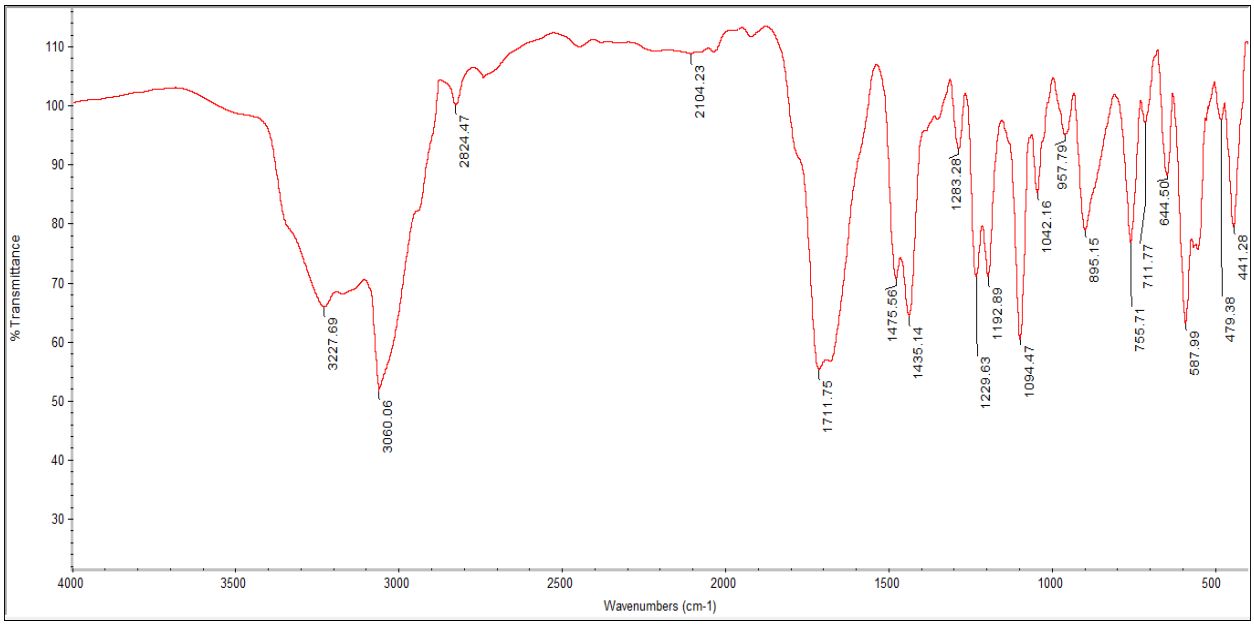
^{1}H NMR spectrum of 5,5'-((2-chlorophenyl)methylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione) **(10a)**



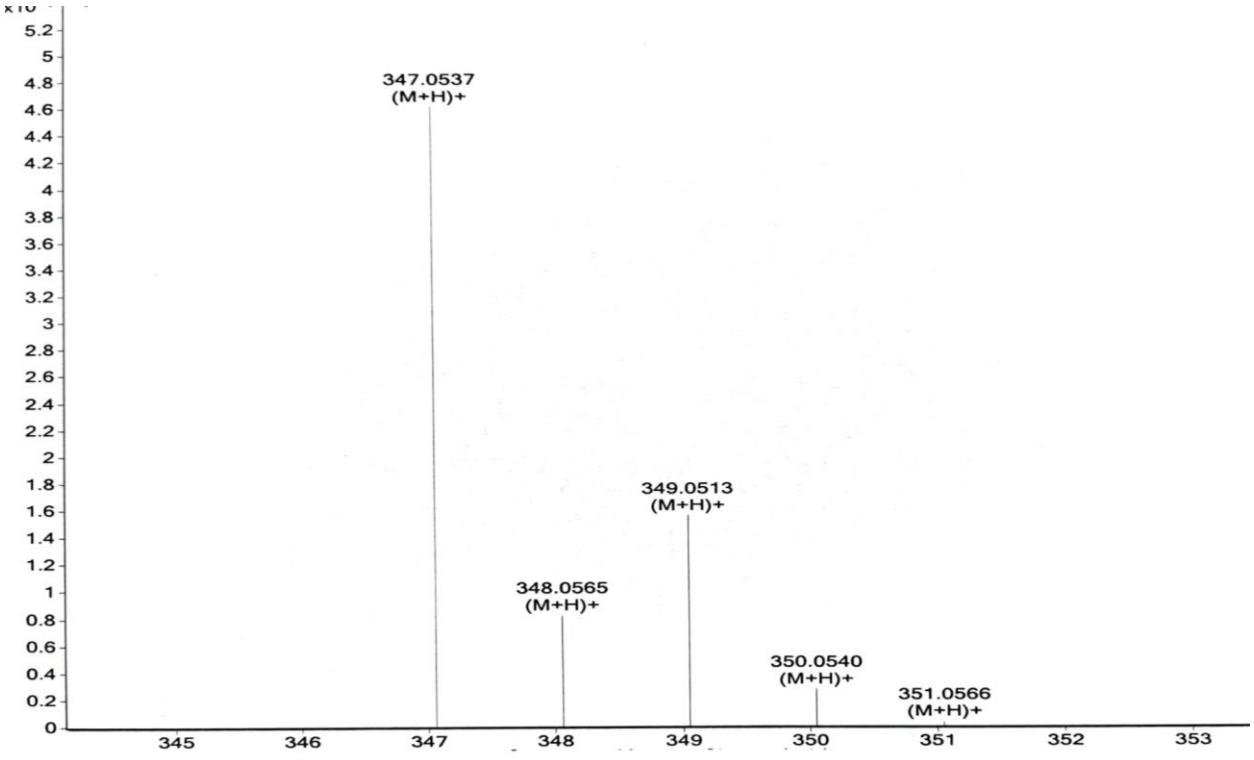
^{13}C NMR spectrum of 5,5'-((2-chlorophenyl)methylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione) **(10a)**



FTIR spectrum of 5,5'-((2-chlorophenyl)methylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione) **(10a)**

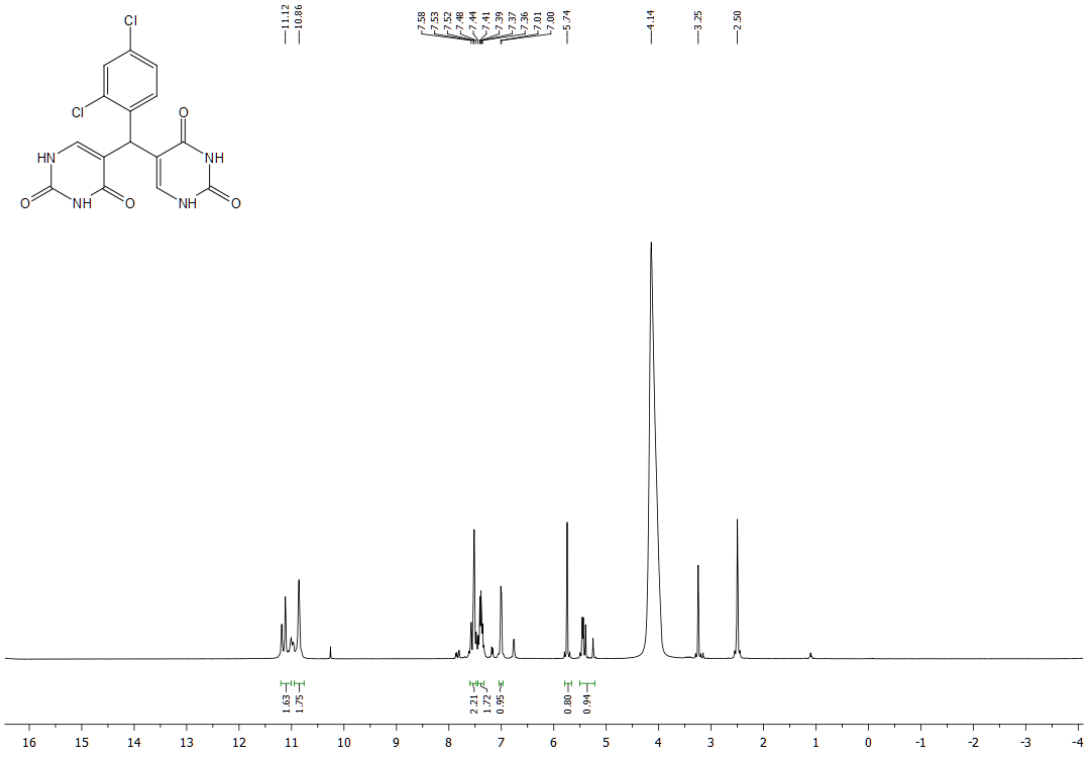


Mass spectrum of 5,5'-((2-chlorophenyl)methylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione) **(10a)**



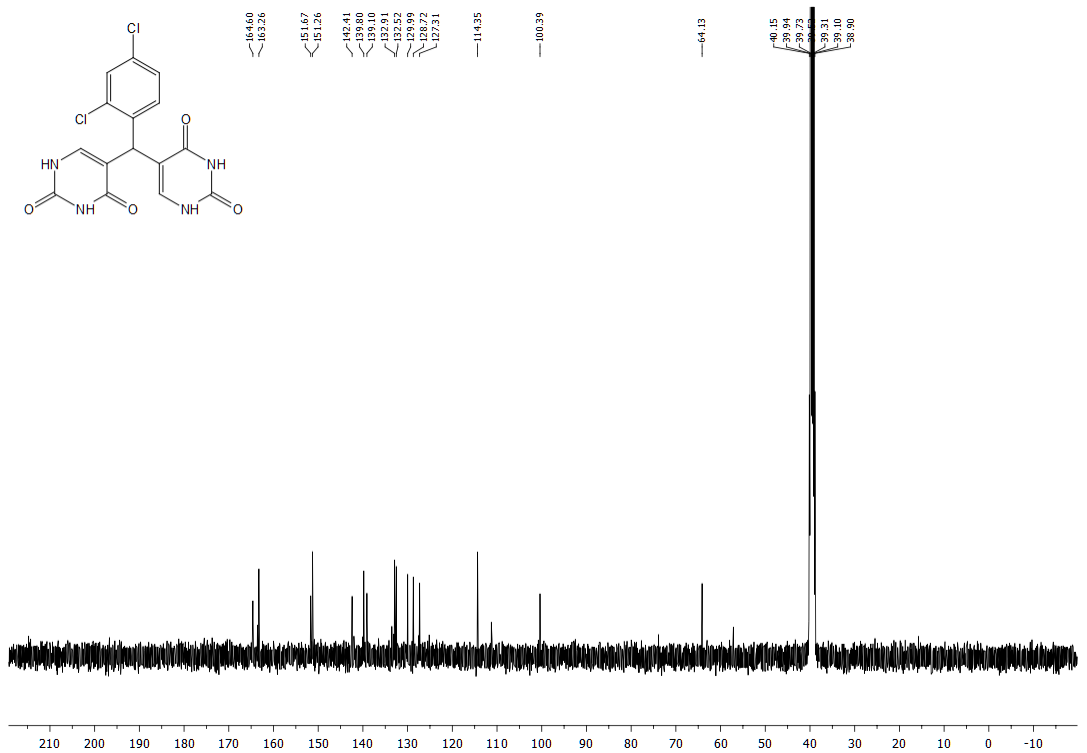
^{1}H NMR spectrum of 5,5'-((2,4-dichlorophenyl)methylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione)

(11a)



^{13}C NMR spectrum of 5,5'-((2,4-dichlorophenyl)methylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione)

(11a)

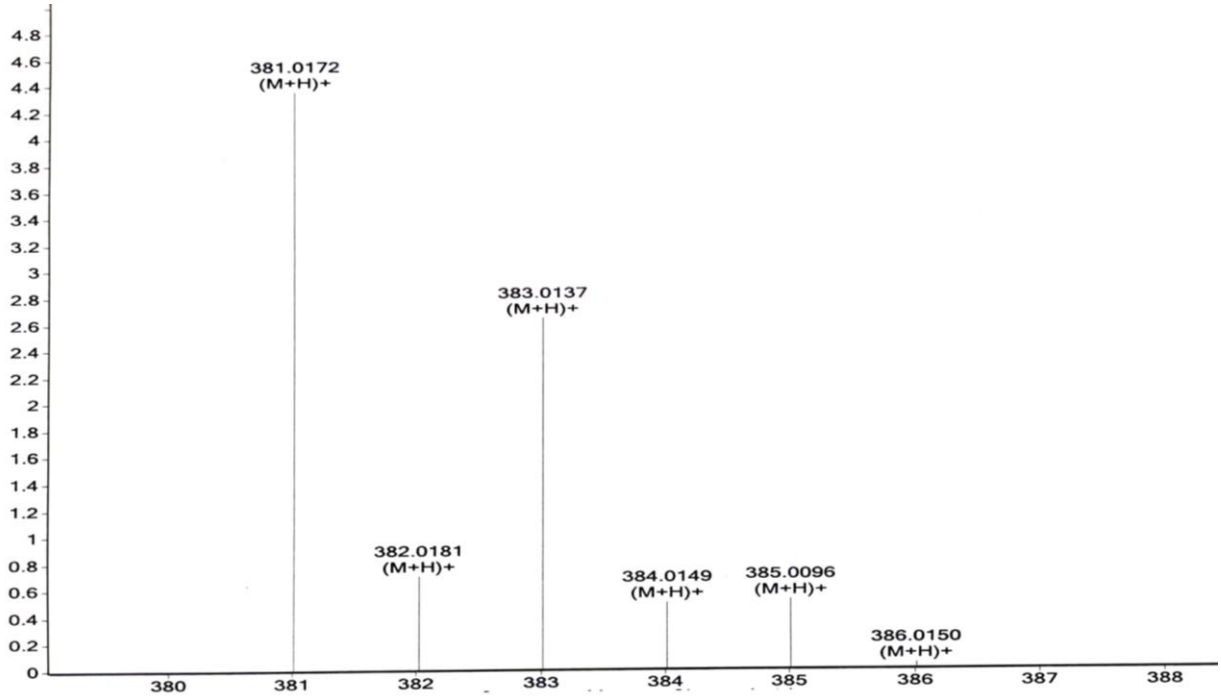


FTIR spectrum of 5,5'-((2,4-dichlorophenyl)methylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione)

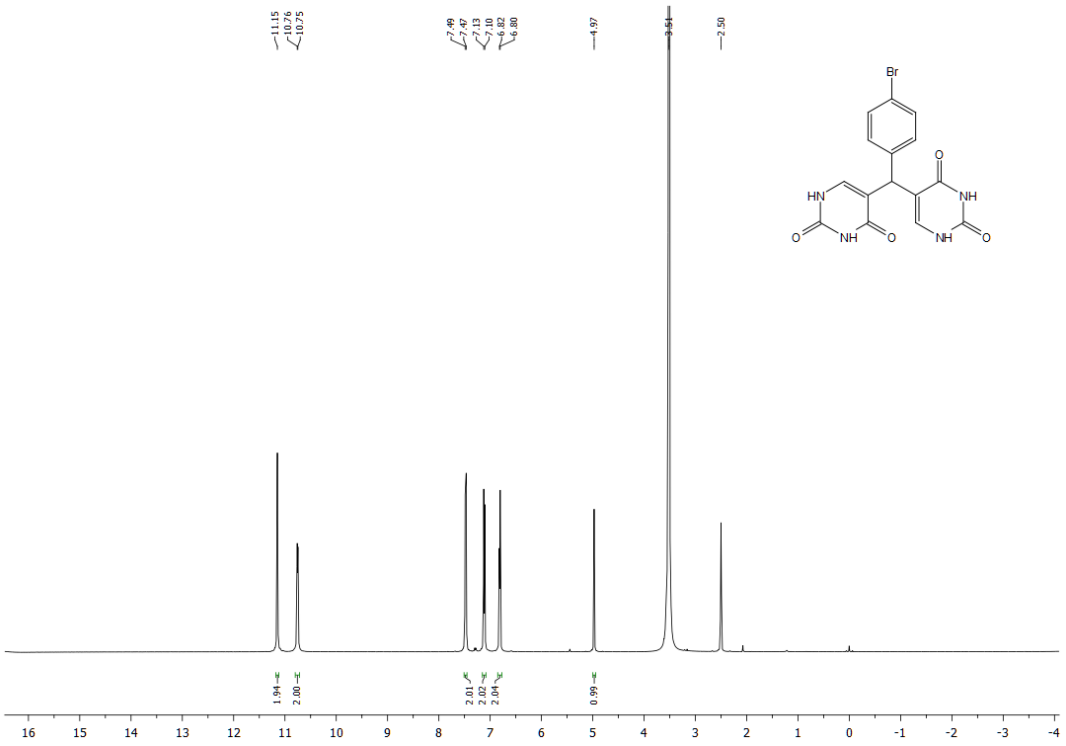
(11a)

Mass spectrum of 5,5'-((2,4-dichlorophenyl)methylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione)

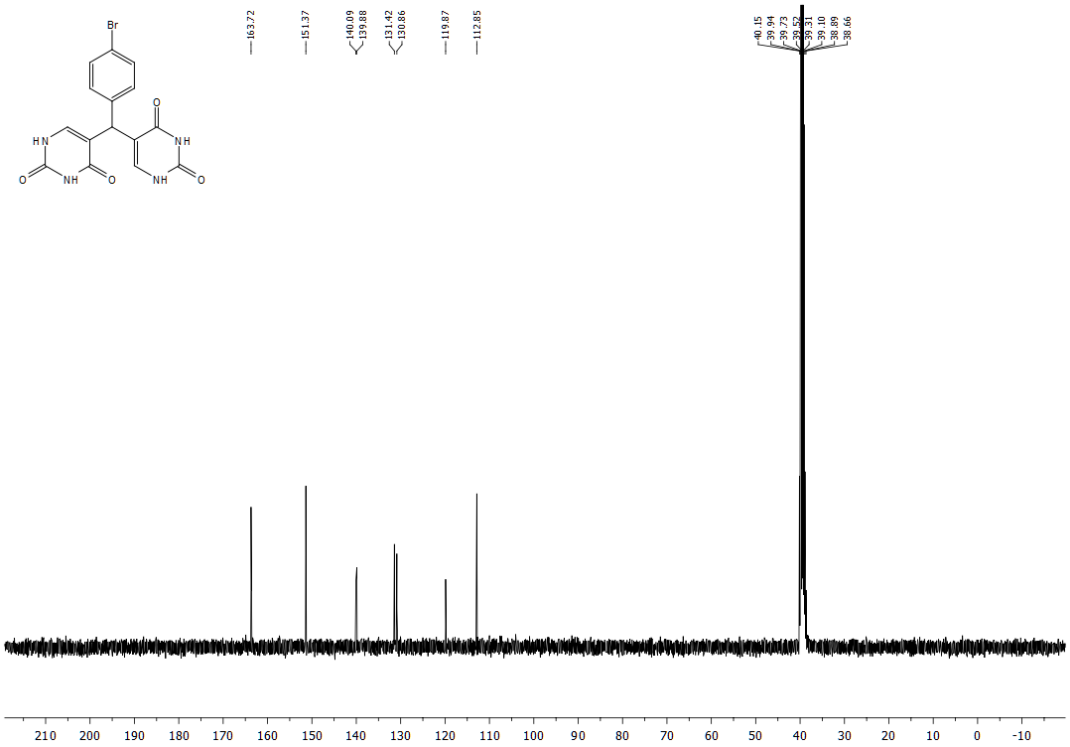
(11a)



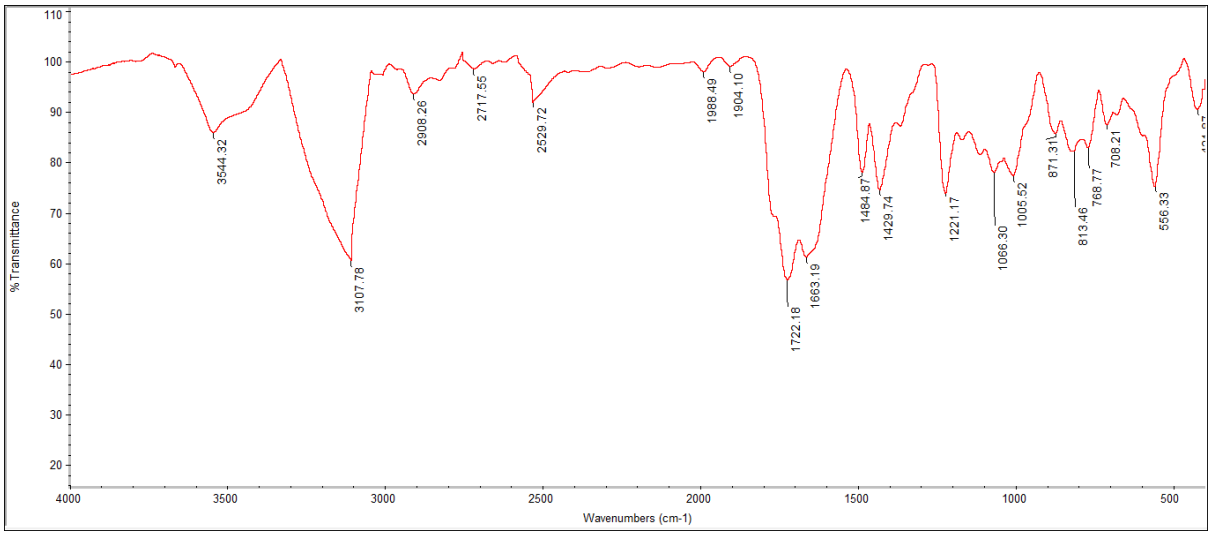
^{1}H NMR spectrum of 5,5'-((4-bromophenyl)methylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione) **(12a)**



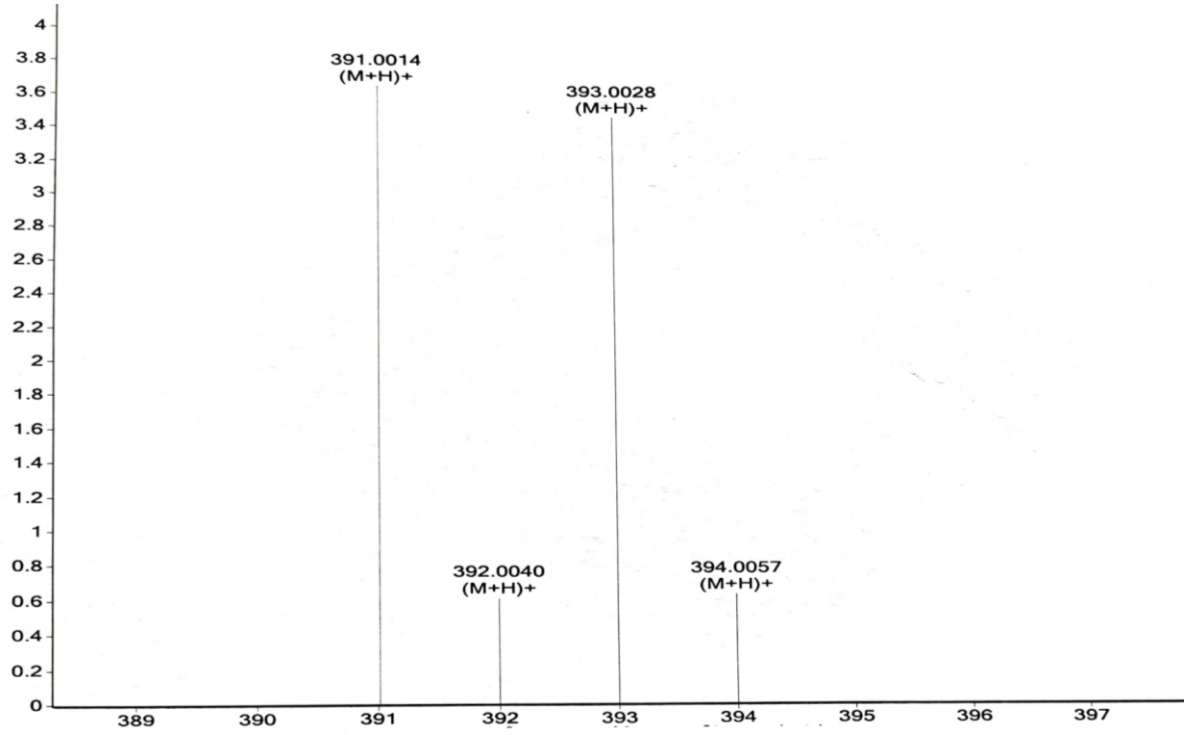
^{13}C NMR spectrum of 5,5'-((4-bromophenyl)methylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione) **(12a)**



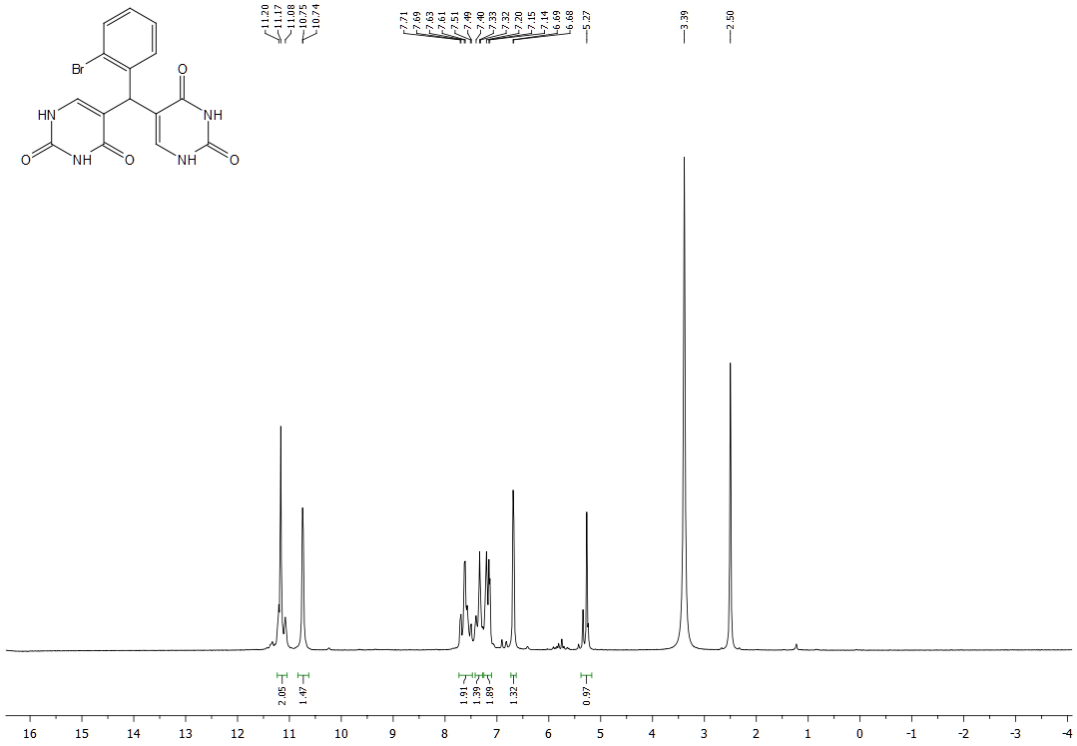
FTIR spectrum of 5,5'-((4-bromophenyl)methylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione) **(12a)**



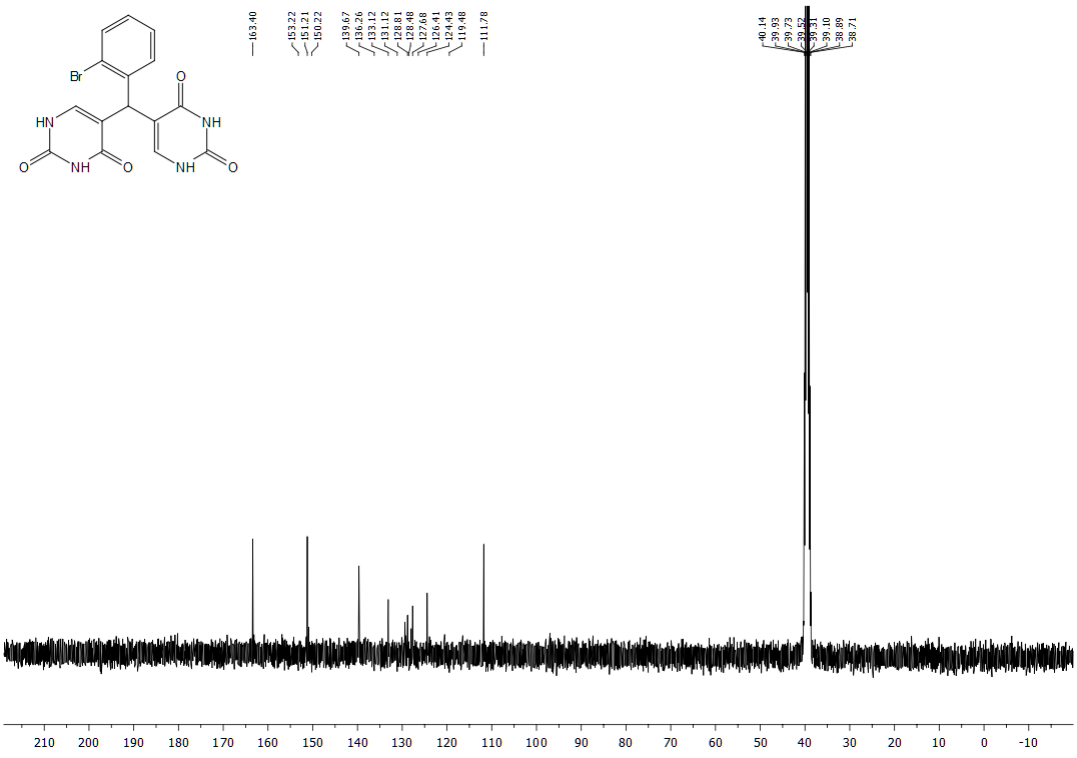
Mass spectrum of 5,5'-((4-bromophenyl)methylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione) **(12a)**



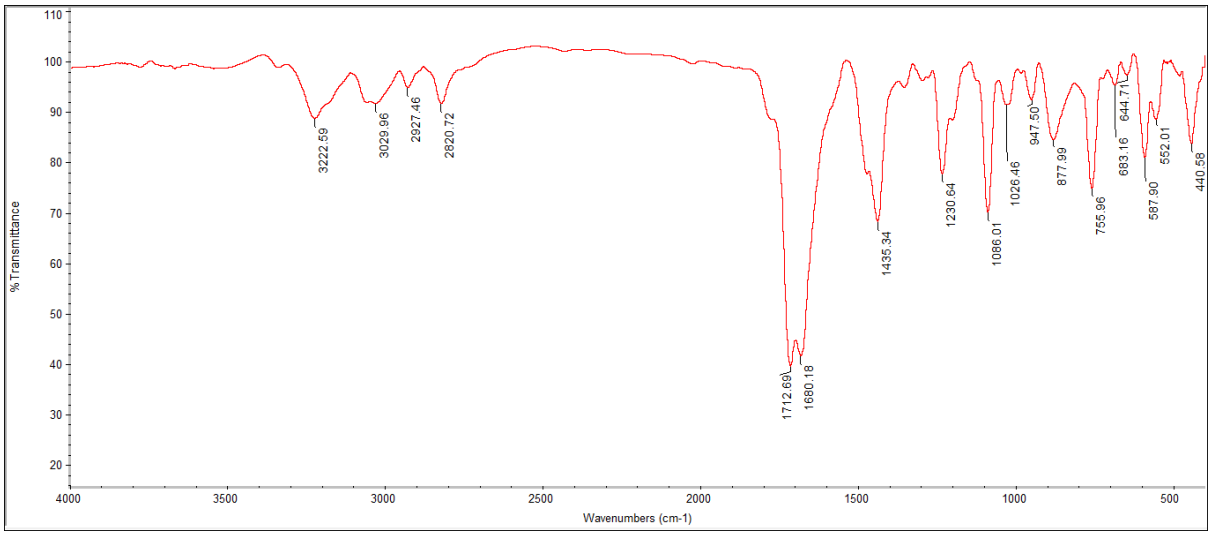
^{1}H NMR spectrum of 5,5'-((2-bromophenyl)methylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione) **(13a)**



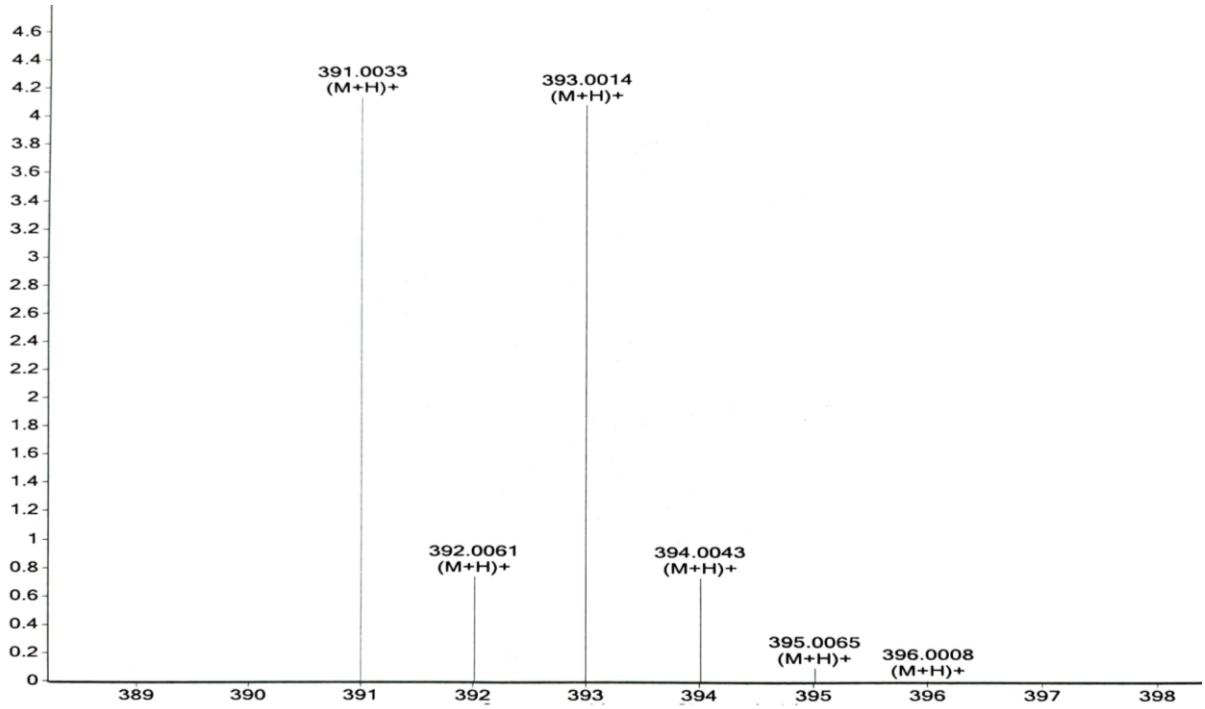
^{13}C NMR spectrum of 5,5'-((2-bromophenyl)methylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione) **(13a)**



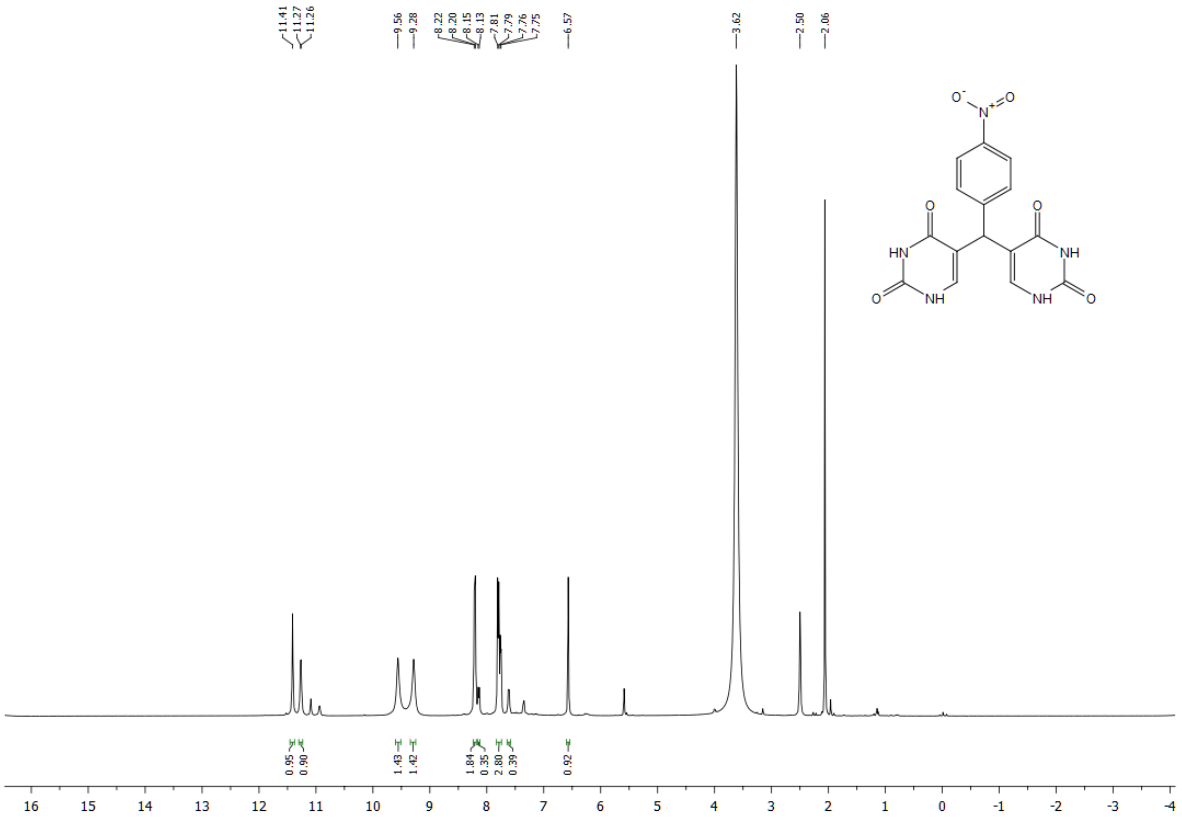
FTIR spectrum of 5,5'-((2-bromophenyl)methylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione) **(13a)**



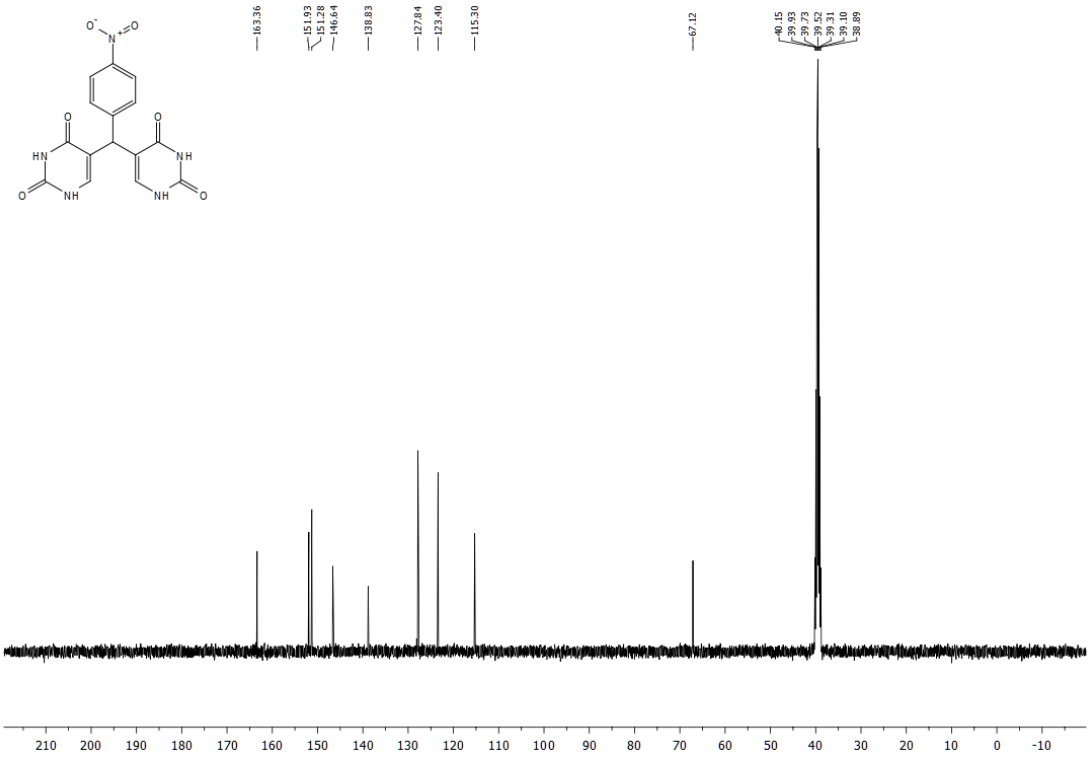
Mass spectrum of 5,5'-((2-bromophenyl)methylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione) **(13a)**



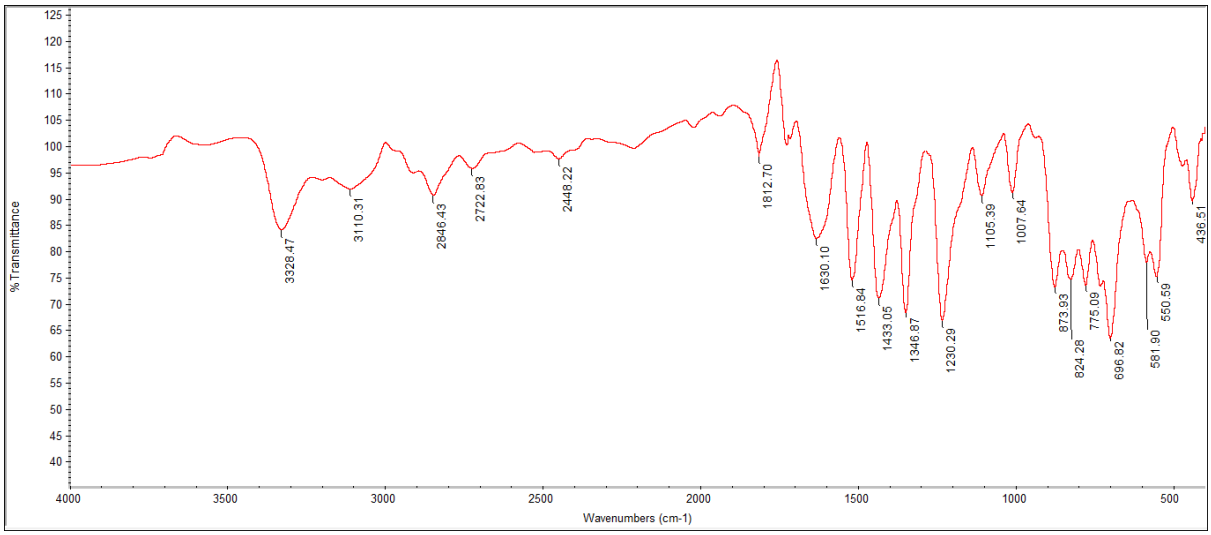
^{1}H NMR spectrum of 5,5'-((4-nitrophenyl)methylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione) **(14a)**



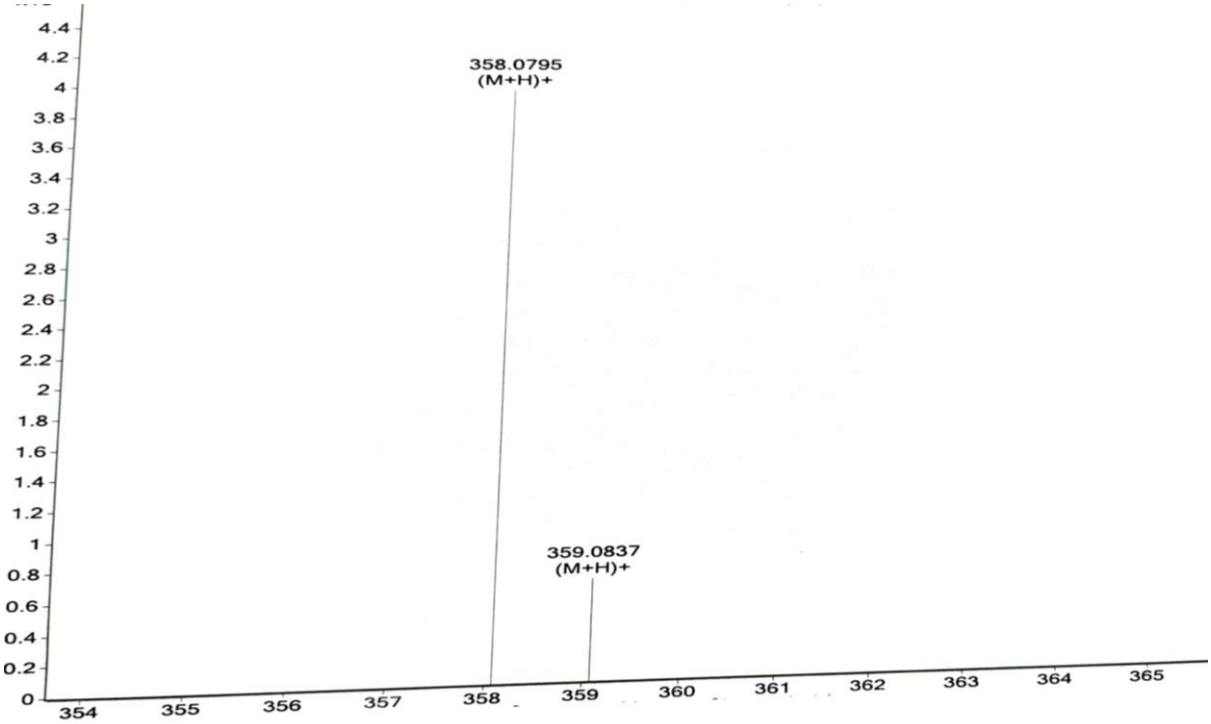
^{13}C NMR spectrum of 5,5'-((4-nitrophenyl)methylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione) **(14a)**



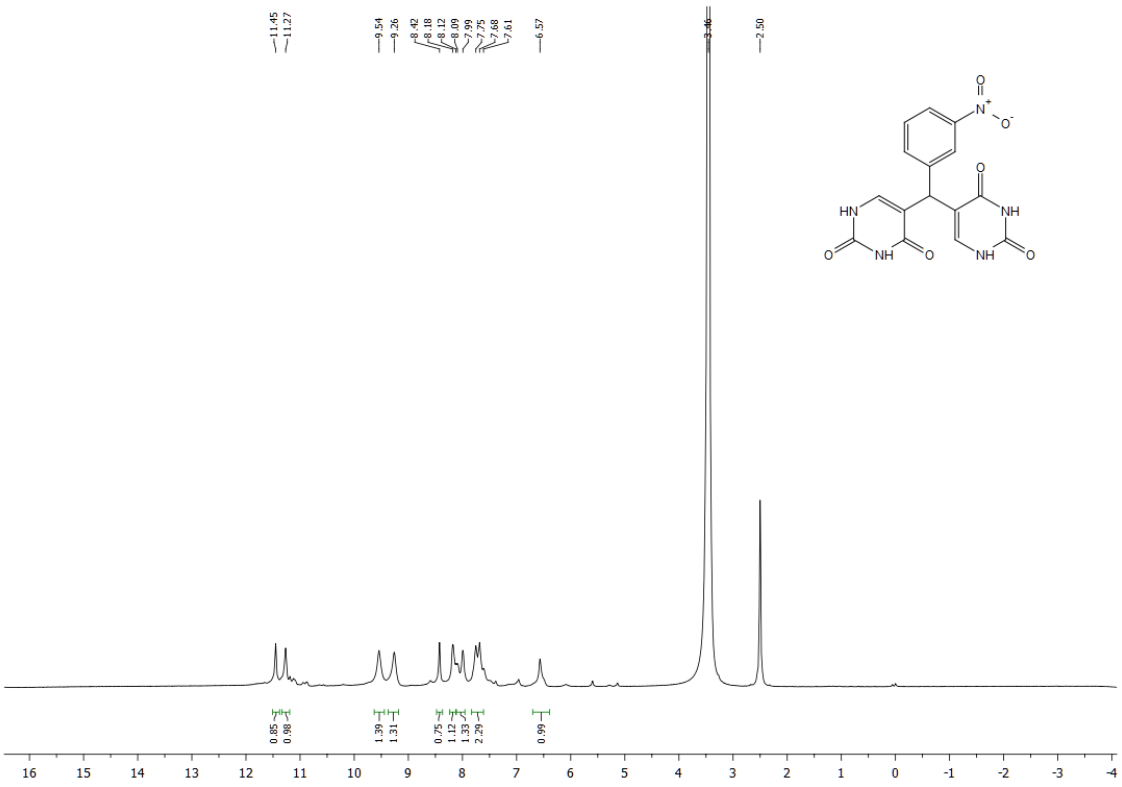
FTIR spectrum of 5,5'-((4-nitrophenyl)methylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione) **(14a)**



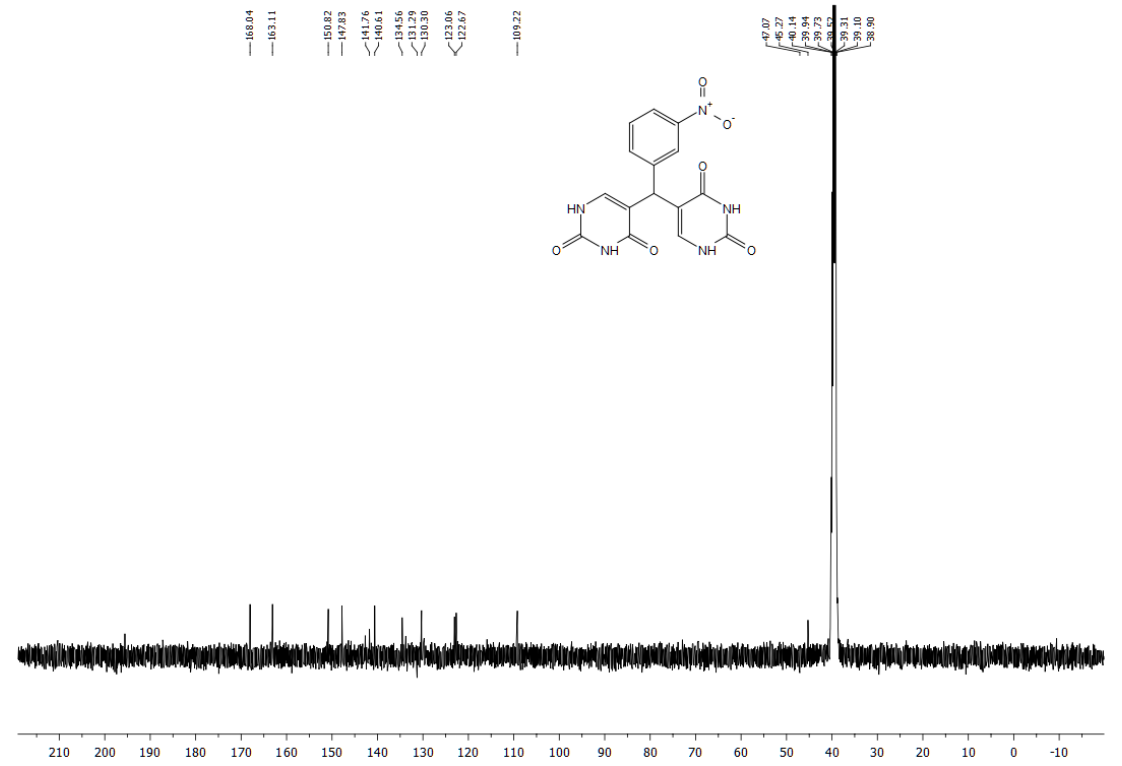
Mass spectrum of 5,5'-((4-nitrophenyl)methylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione) **(14a)**



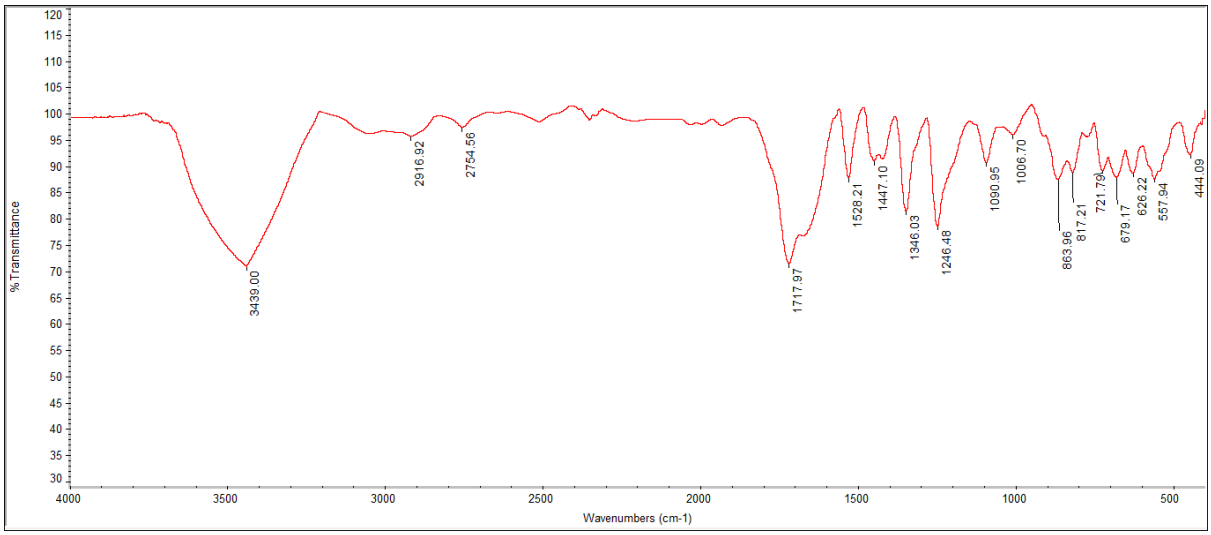
^{1}H NMR spectrum of 5,5'-((3-nitrophenyl)methylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione) **(15a)**



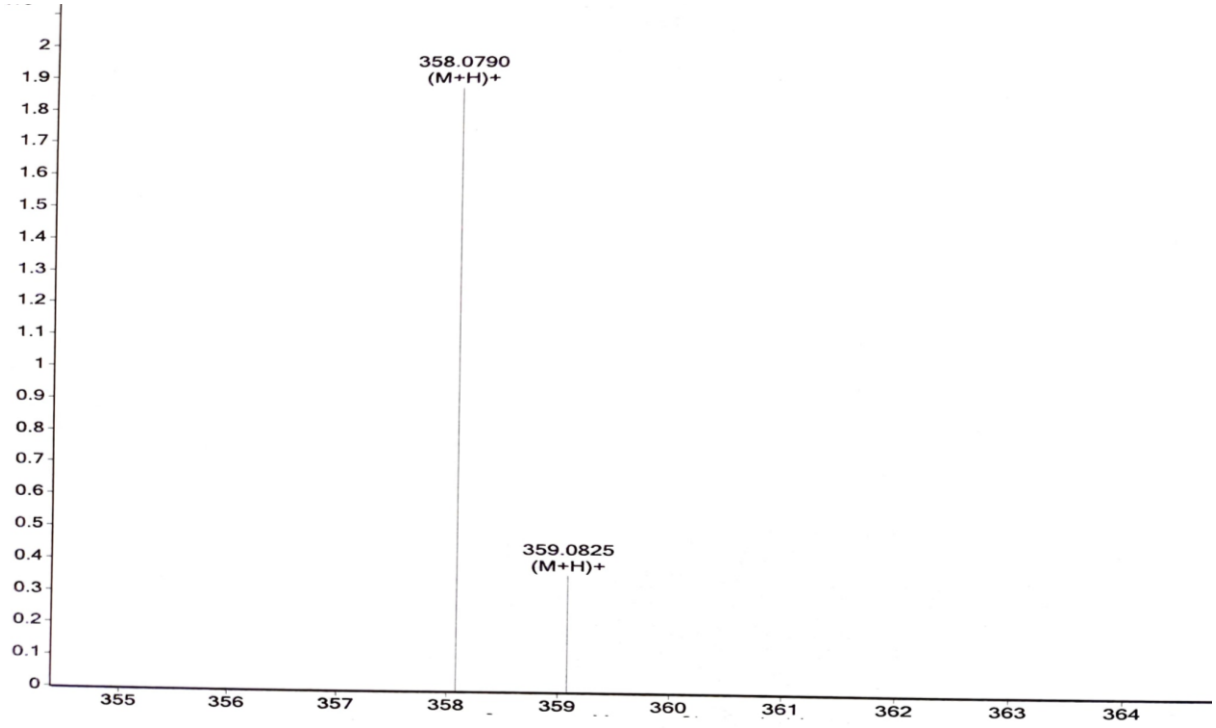
^{13}C NMR spectrum of 5,5'-((3-nitrophenyl)methylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione) **(15a)**



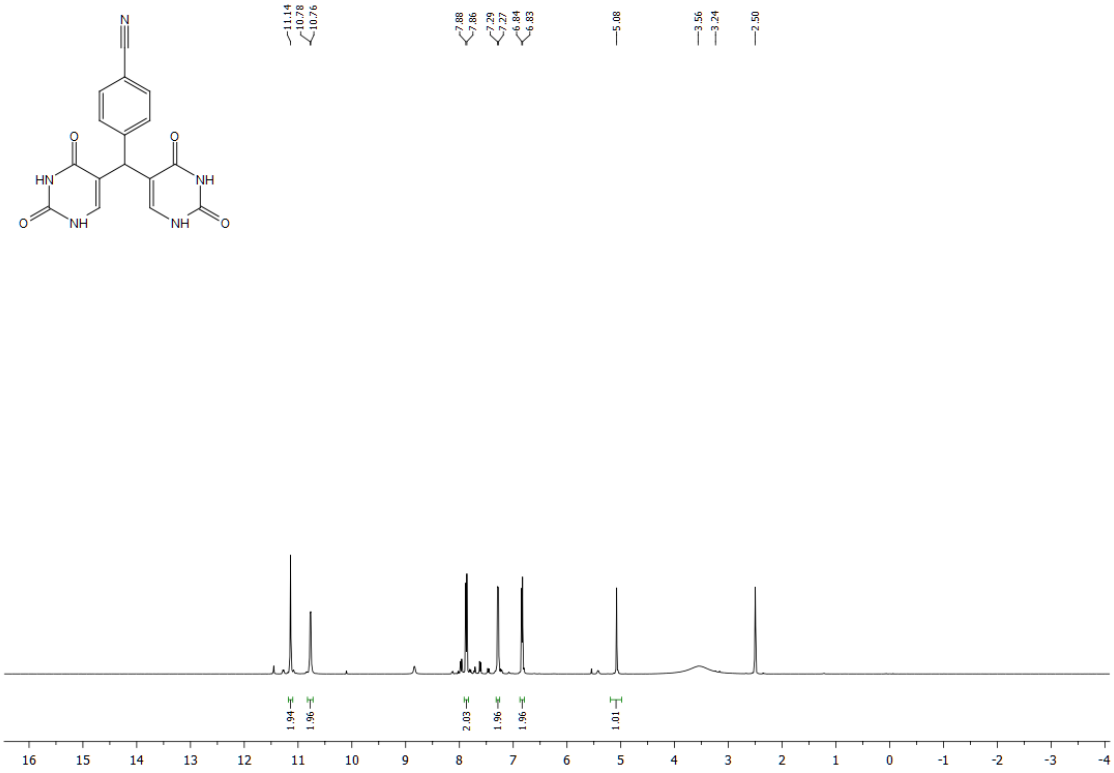
FTIR spectrum of 5,5'-((3-nitrophenyl)methylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione) **(15a)**



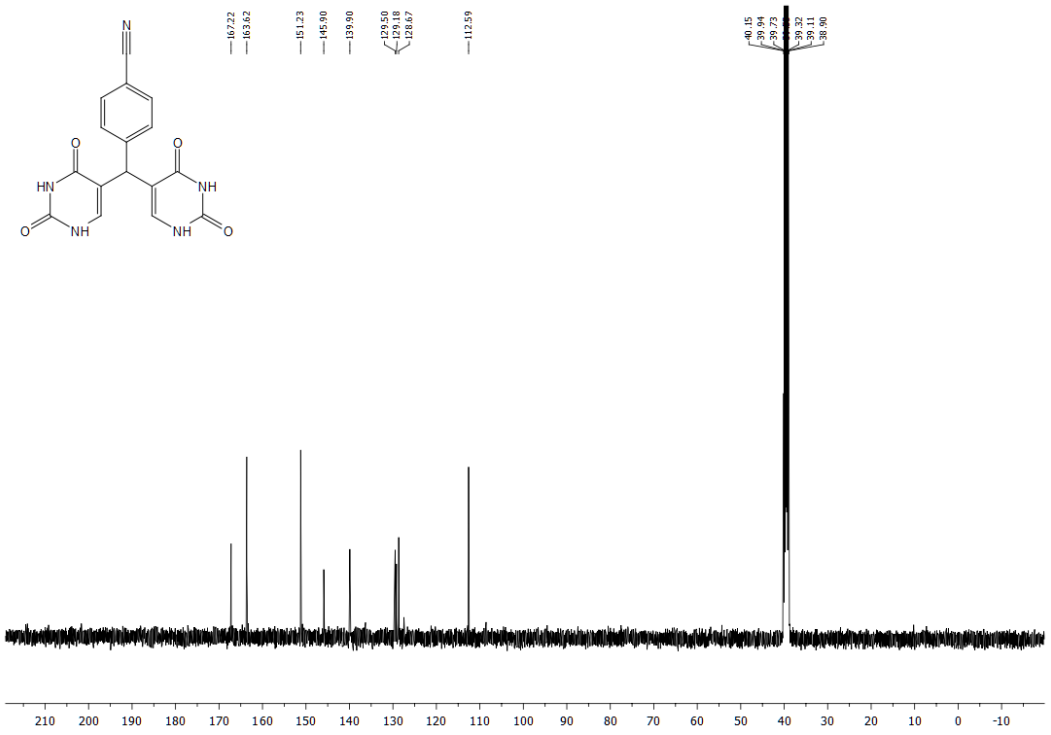
Mass spectrum of 5,5'-((3-nitrophenyl)methylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione) **(15a)**



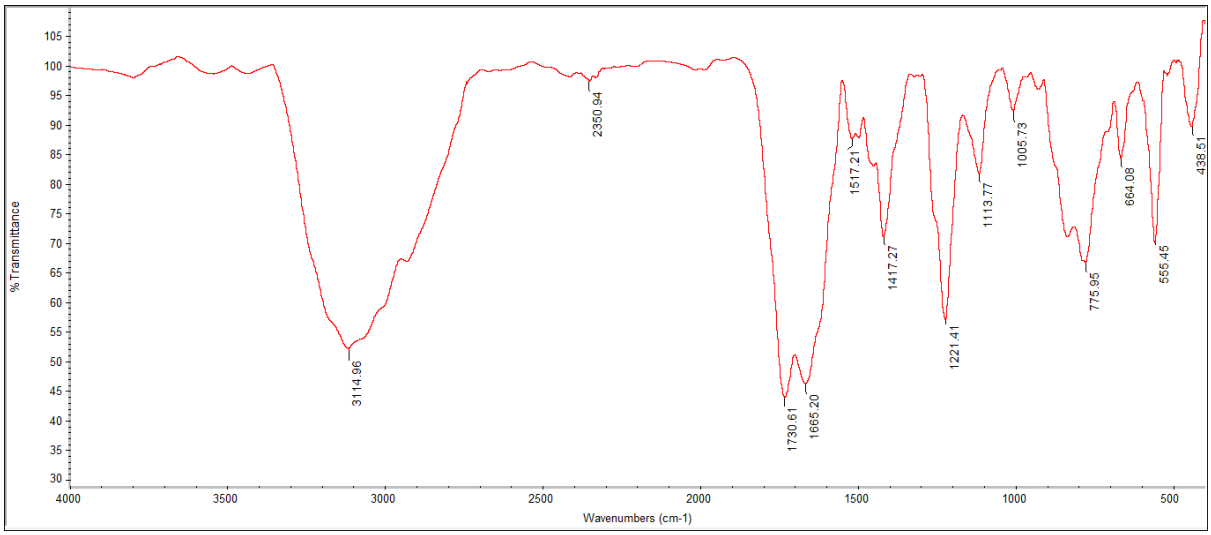
^{1}H NMR spectrum of 4-(bis(2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl)methyl)benzonitrile **(16a)**



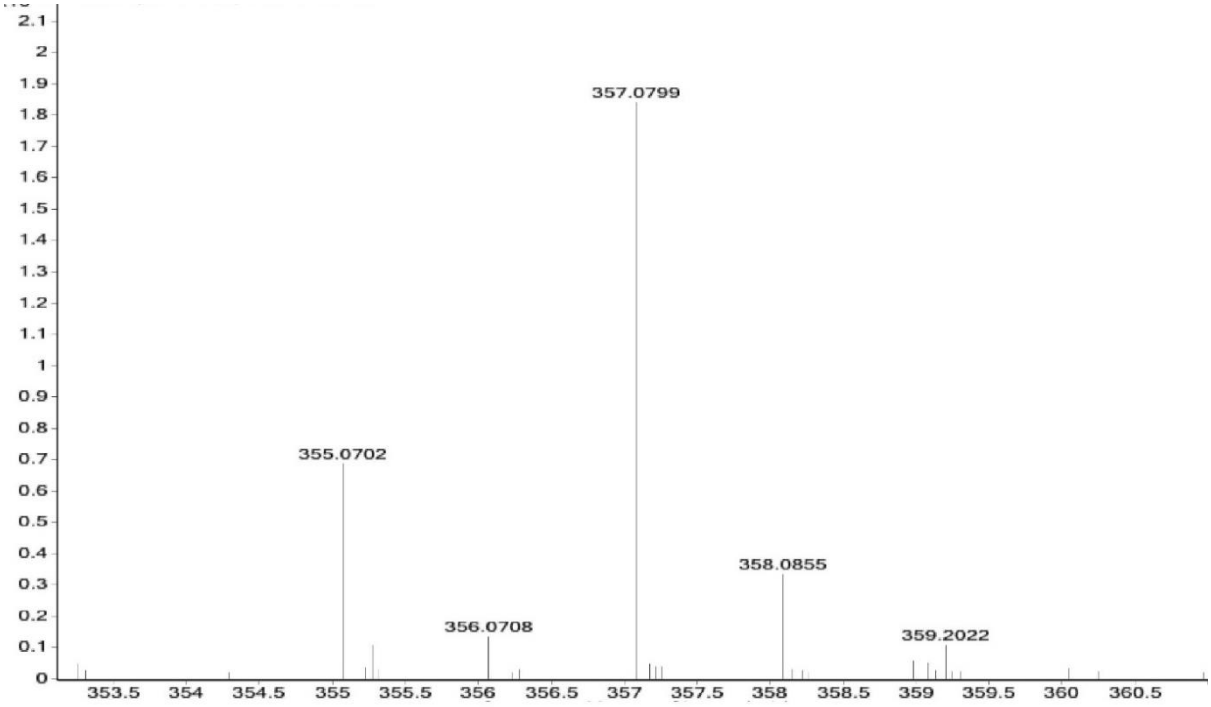
^{13}C NMR spectrum of 4-(bis(2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl)methyl)benzonitrile **(16a)**



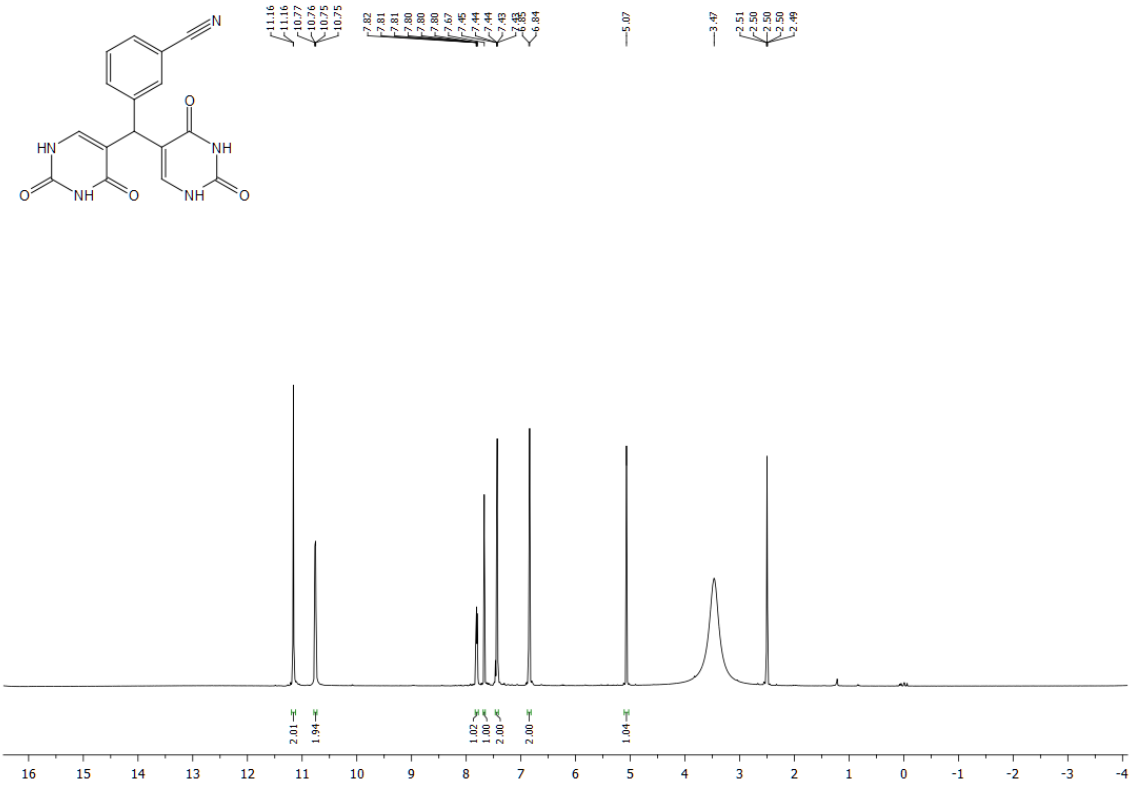
FTIR spectrum of 4-(bis(2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl)methyl)benzonitrile **(16a)**



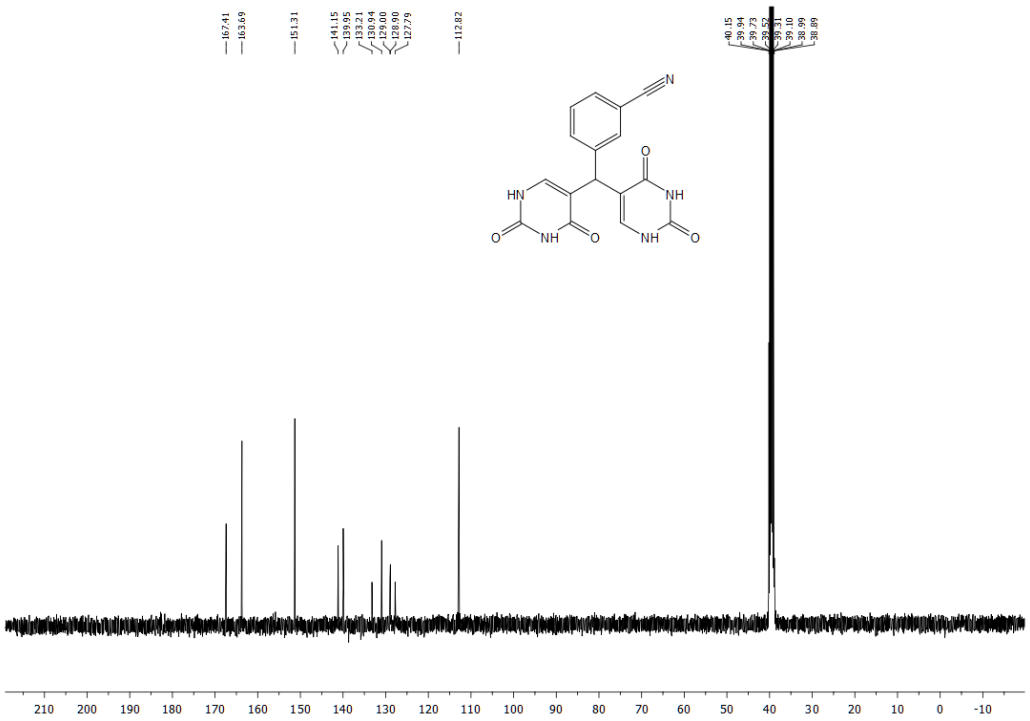
Mass spectrum of 4-(bis(2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl)methyl)benzonitrile **(16a)**



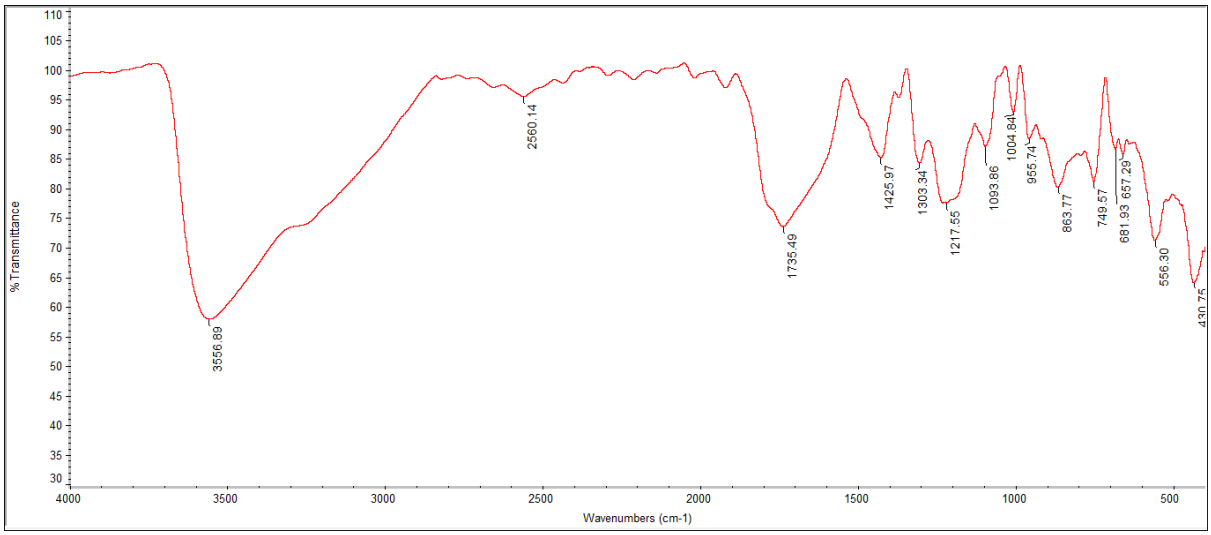
^{1}H NMR spectrum of 3-(bis(2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl)methyl)benzonitrile **(17a)**



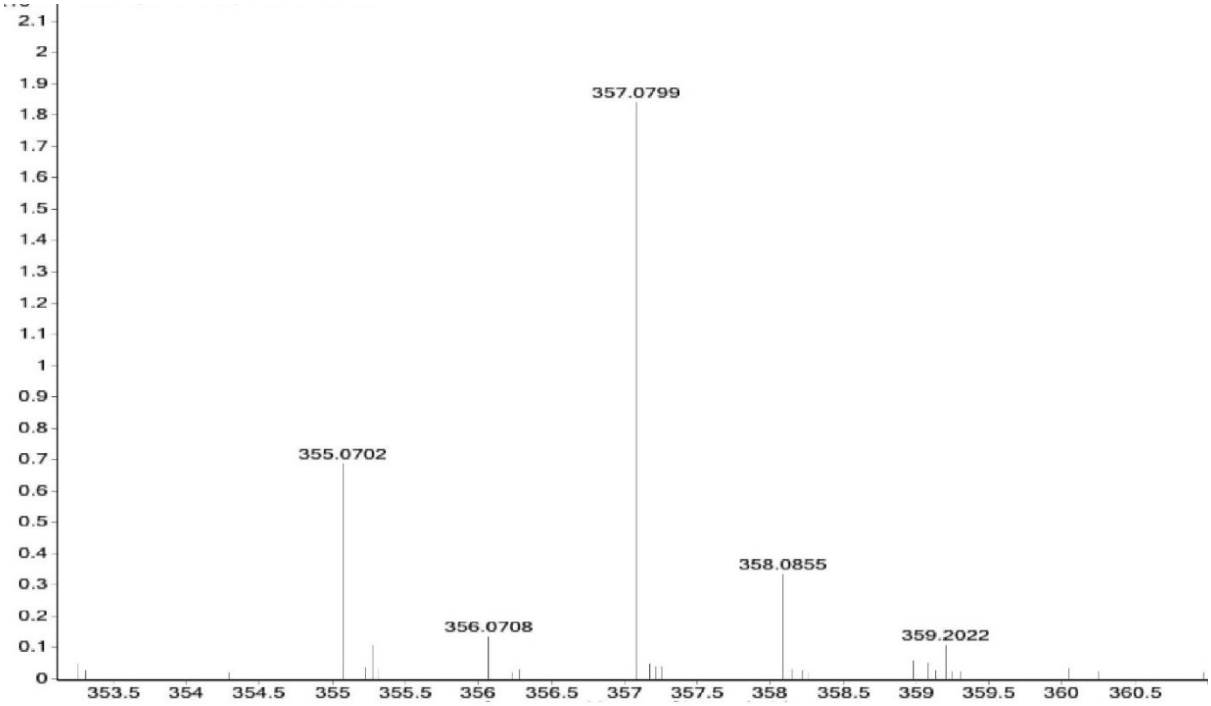
^{13}C NMR spectrum of 3-(bis(2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl)methyl)benzonitrile **(17a)**



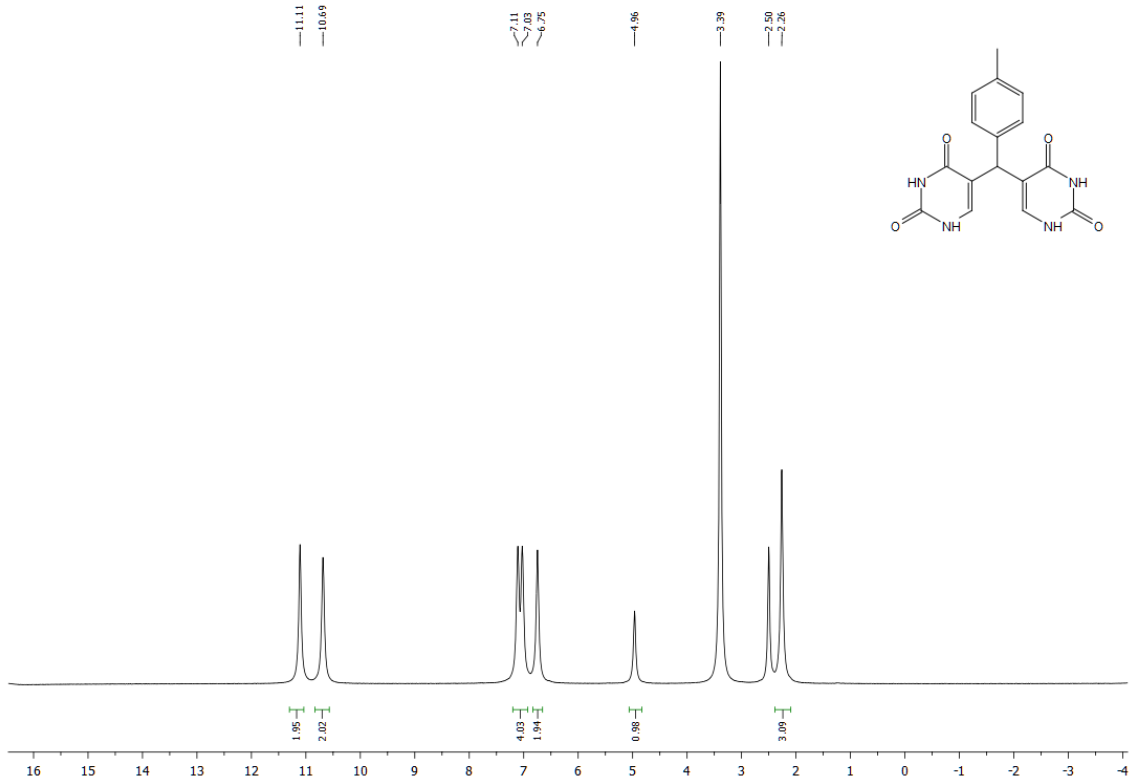
FTIR spectrum of 3-(bis(2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl)methyl)benzonitrile **(17a)**



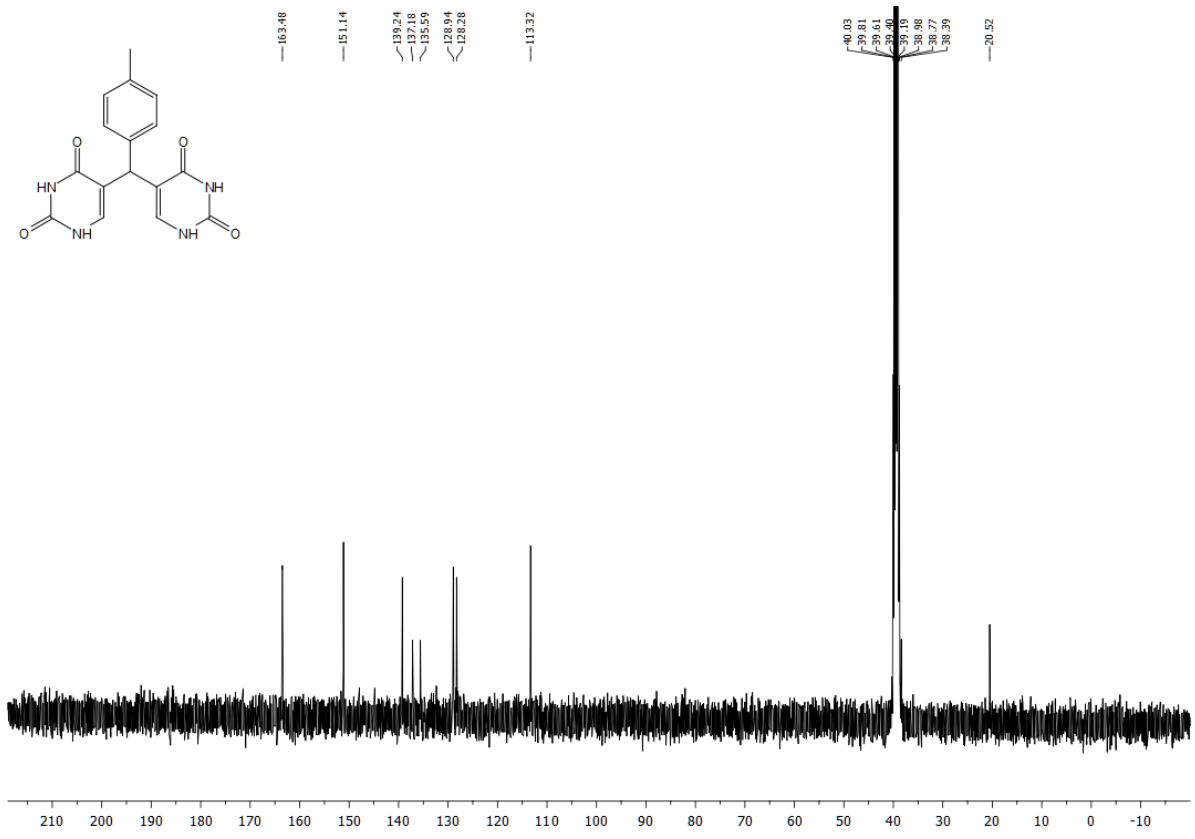
Mass spectrum of 3-(bis(2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl)methyl)benzonitrile **(17a)**



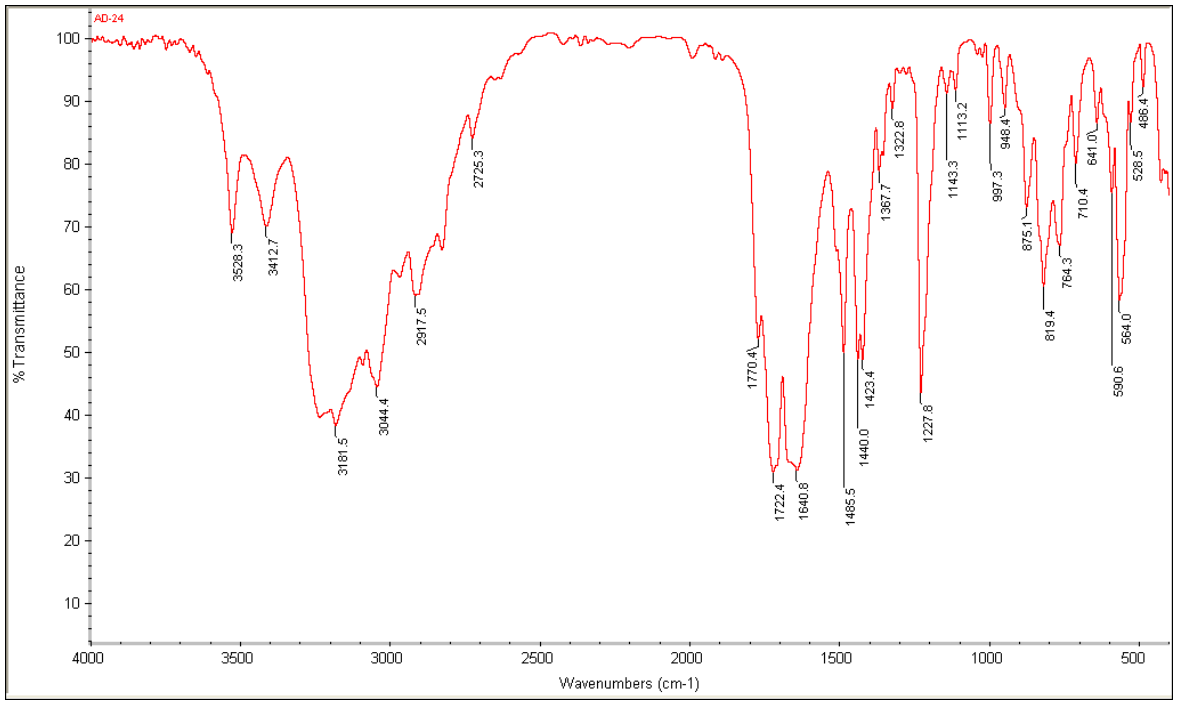
^{1}H NMR spectrum of 5,5'-(p-tolylmethylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione) **(18a)**



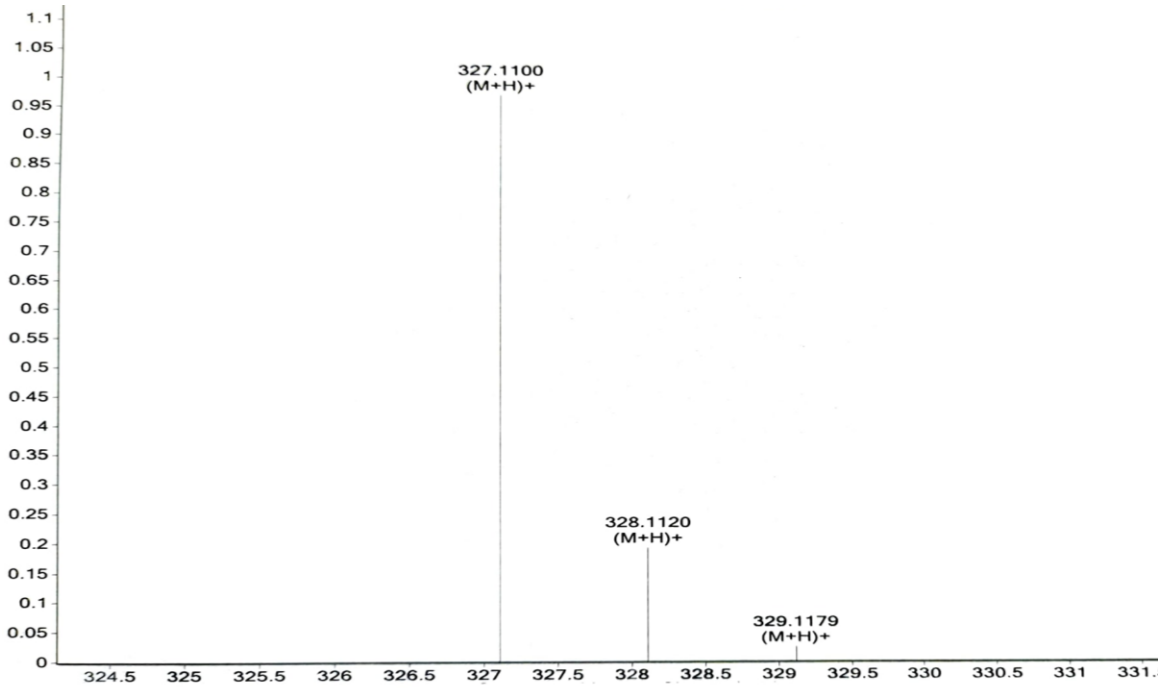
^{13}C NMR spectrum of 5,5'-(p-tolylmethylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione) **(18a)**



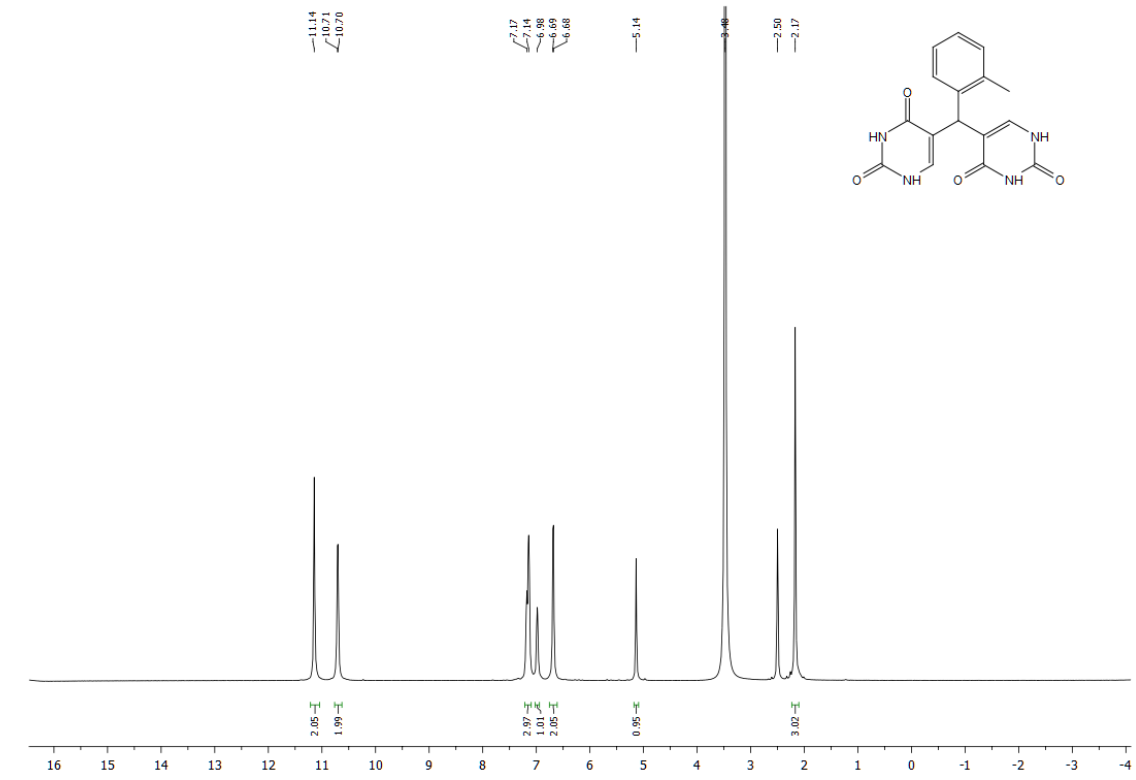
FTIR spectrum of 5,5'-(p-tolylmethylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione) **(18a)**



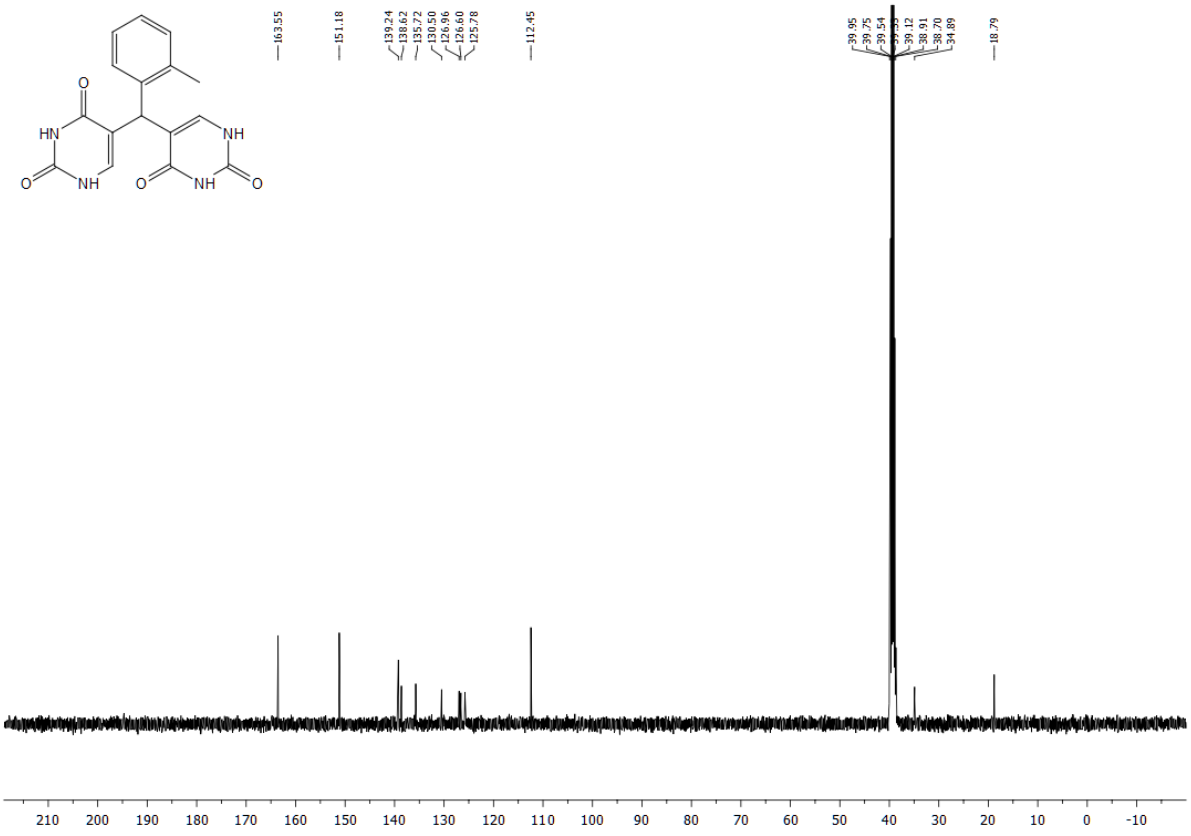
Mass spectrum of 5,5'-(p-tolylmethylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione) **(18a)**



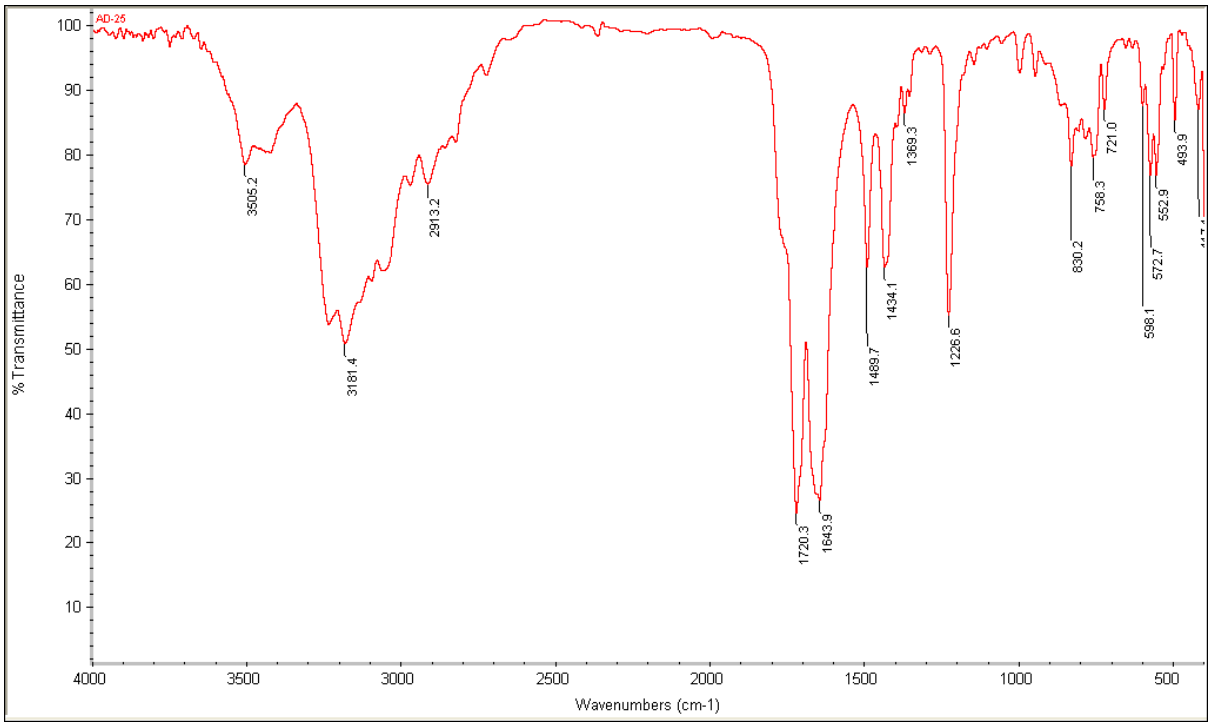
^{1}H NMR spectrum of 5,5'-(o-tolylmethylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione) **(19a)**



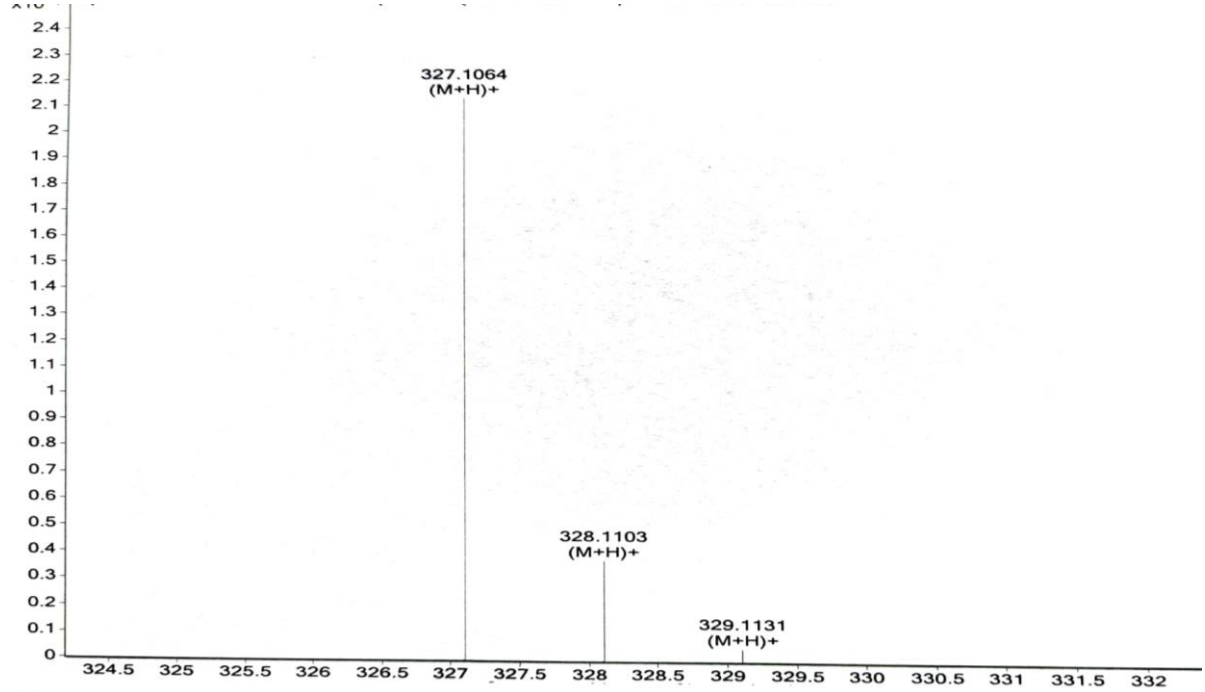
^{13}C NMR spectrum of 5,5'-(o-tolylmethylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione) **(19a)**



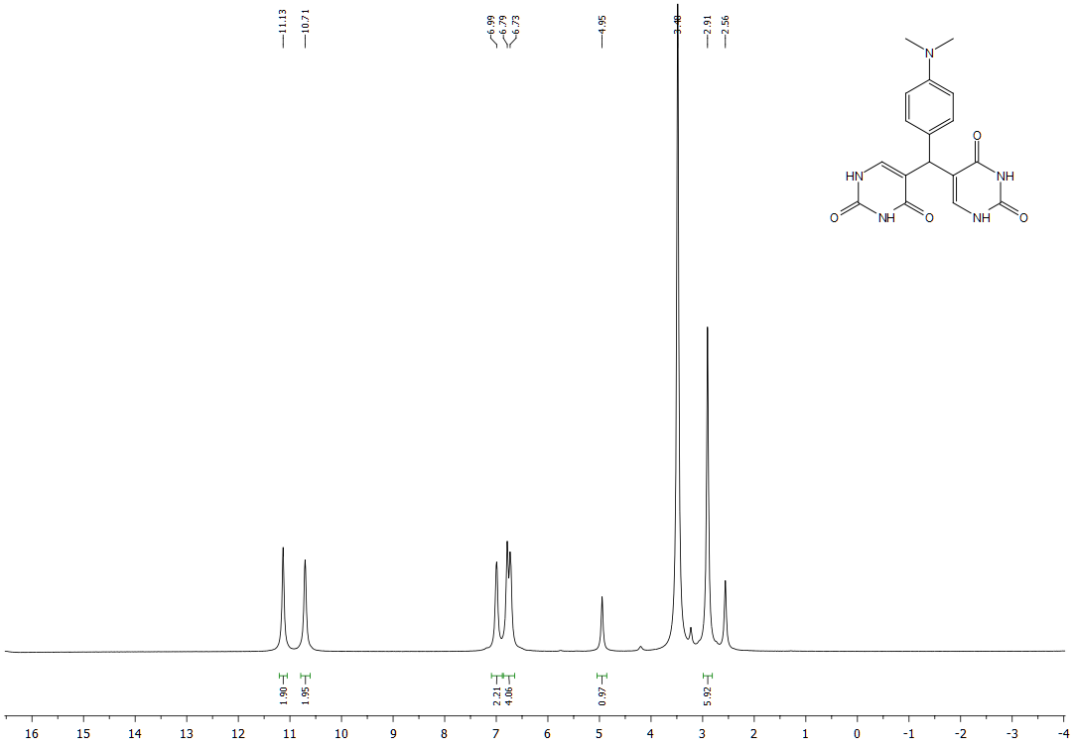
FTIR spectrum of 5,5'-(o-tolylmethylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione) **(19a)**



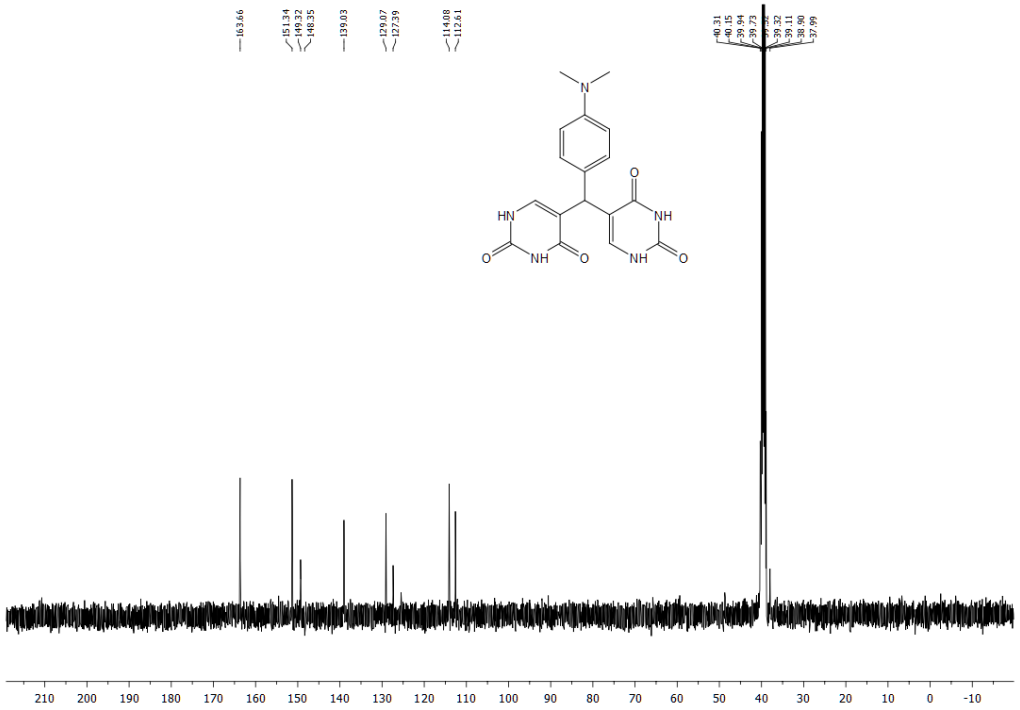
Mass spectrum of 5,5'-(o-tolylmethylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione) **(19a)**



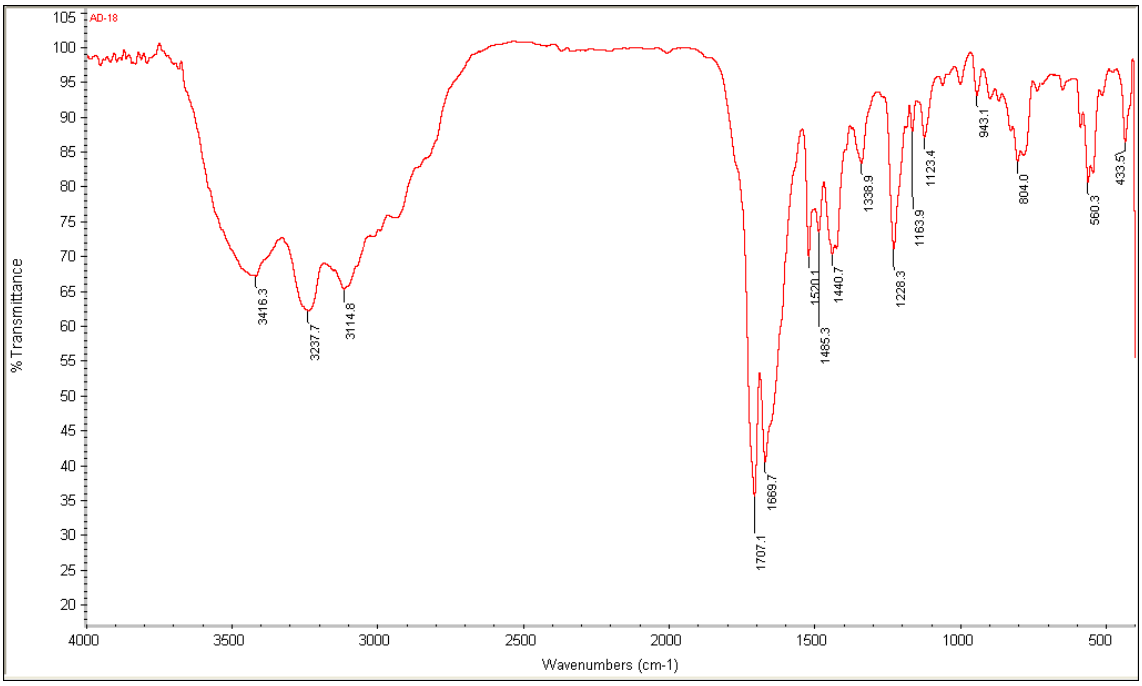
^{1}H NMR spectrum of 5,5'-((4-(dimethylamino)phenyl)methylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione) **(20a)**



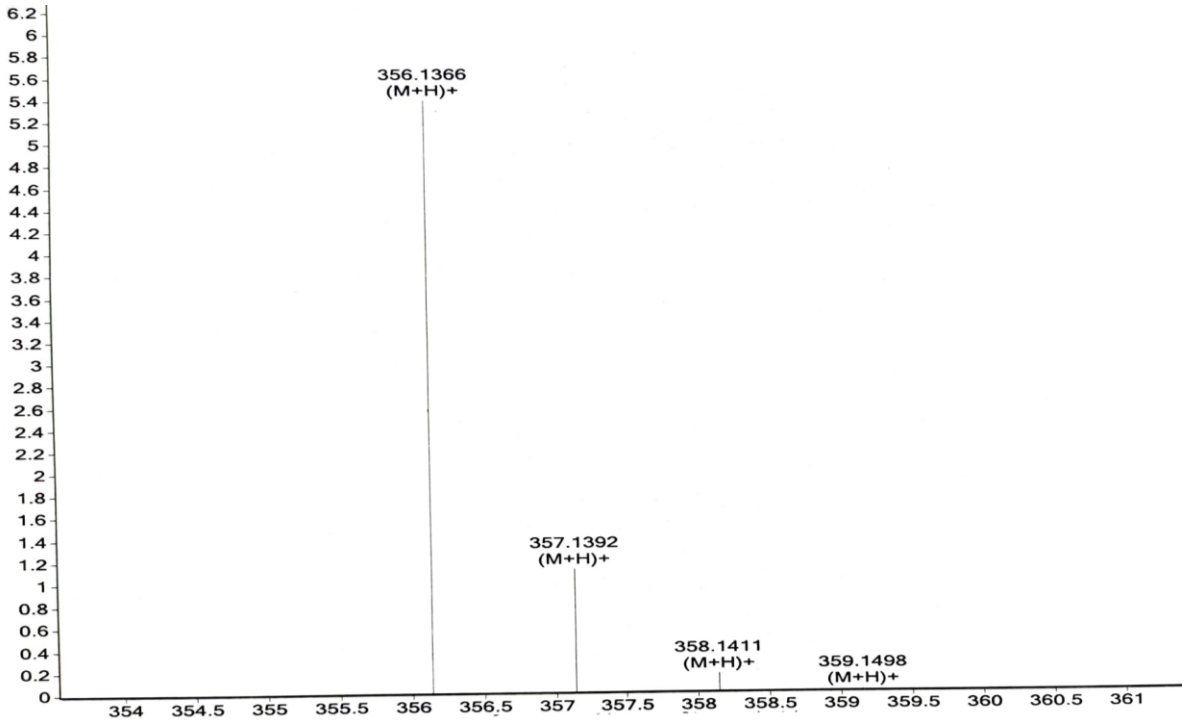
^{13}C NMR spectrum of 5,5'-((4-(dimethylamino)phenyl)methylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione) **(20a)**



FTIR spectrum of 5,5'-((4-(dimethylamino)phenyl)methylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione) **(20a)**

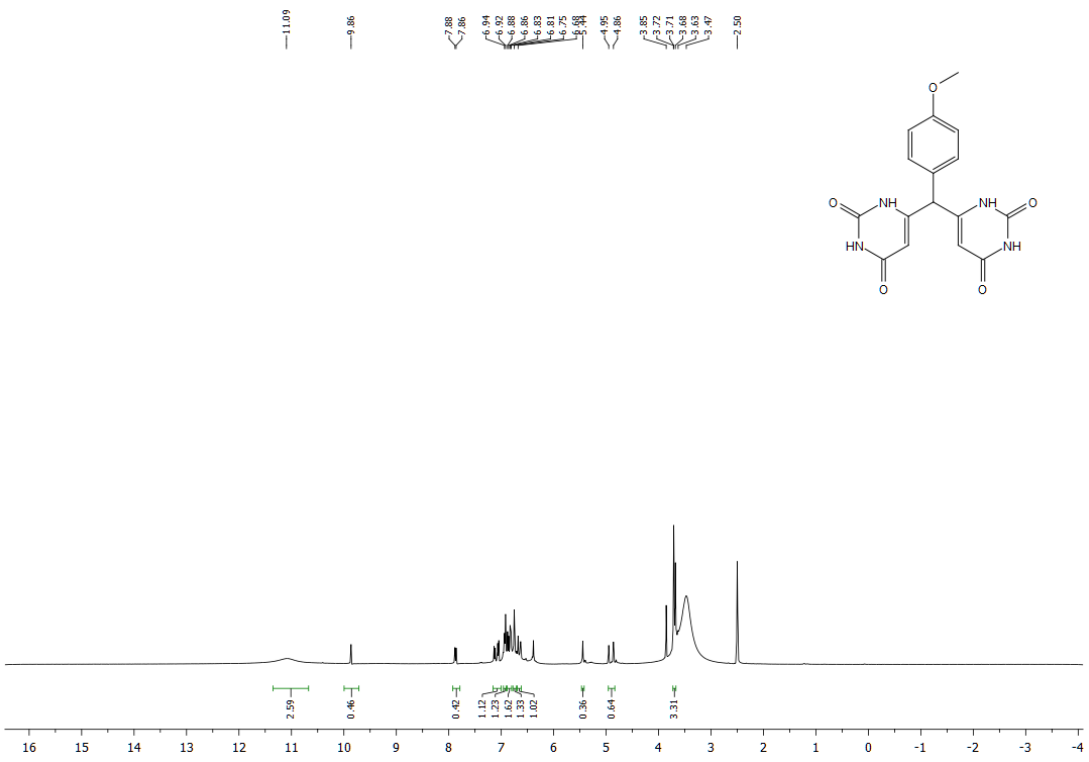


Mass spectrum of 5,5'-((4-(dimethylamino)phenyl)methylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione) **(20a)**



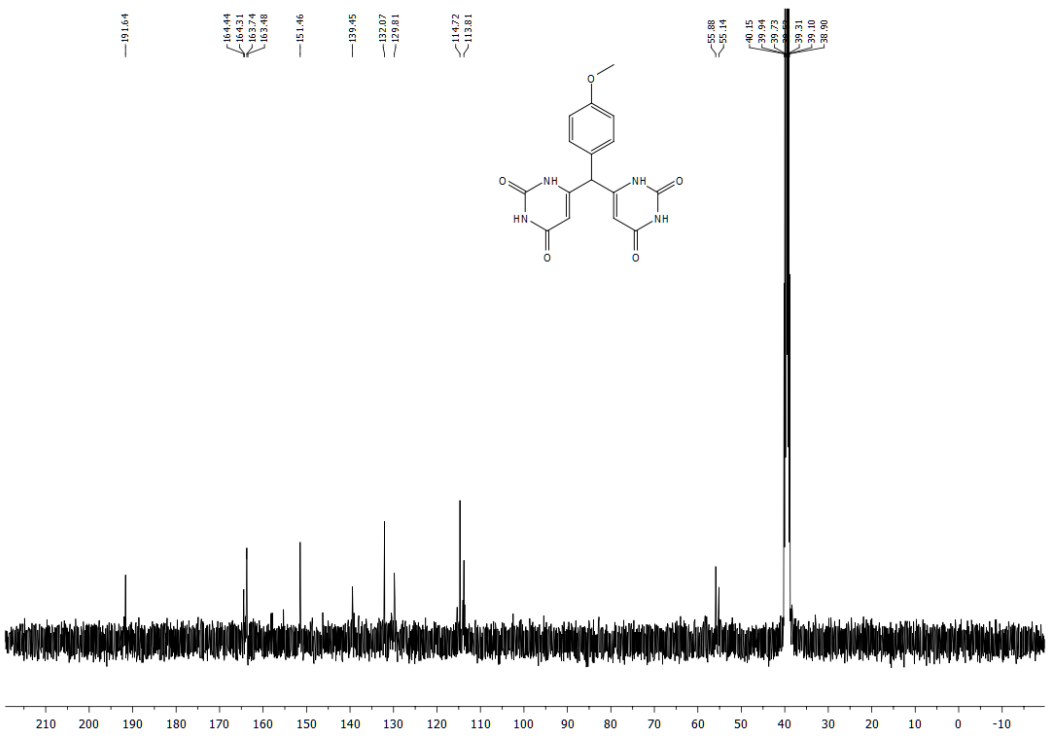
^{1}H NMR spectrum of 6,6'-((4-methoxyphenyl)methylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione)

(21a)

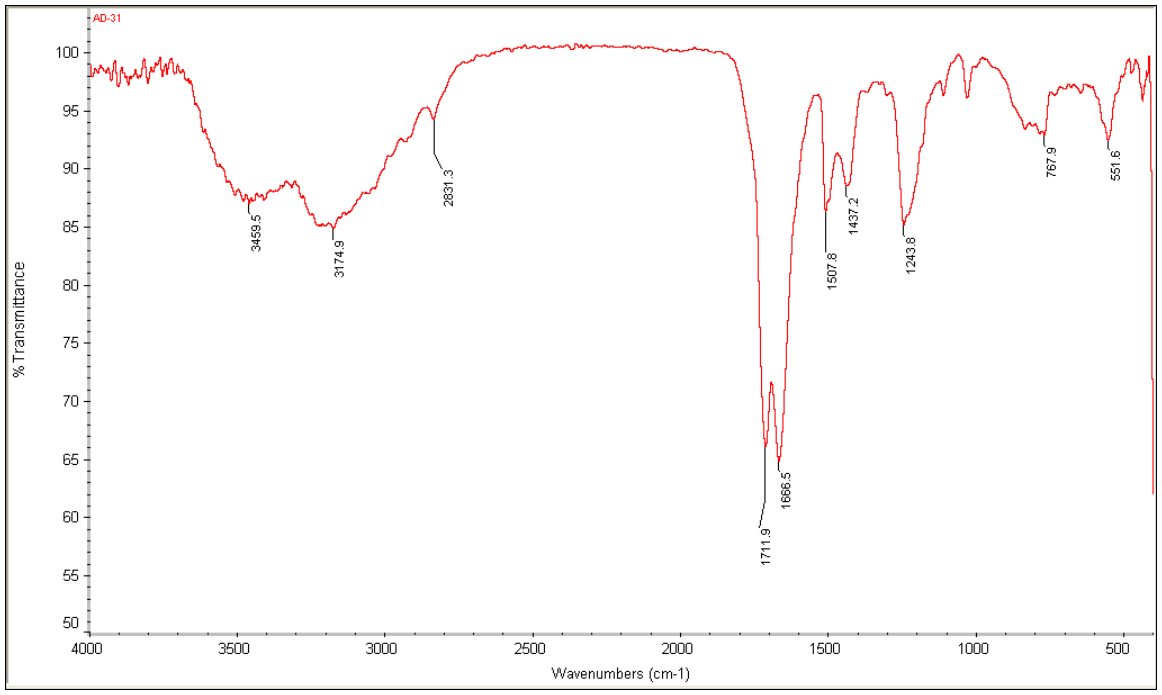


^{13}C NMR spectrum of 6,6'-((4-methoxyphenyl)methylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione)

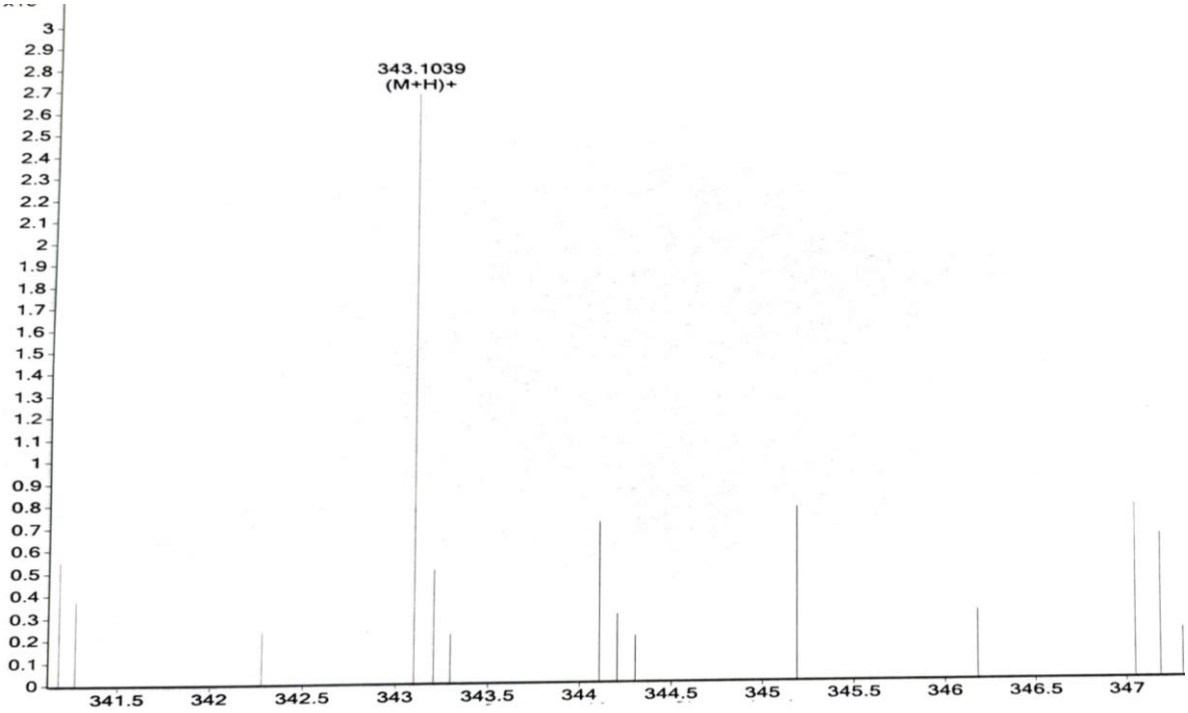
(21a)



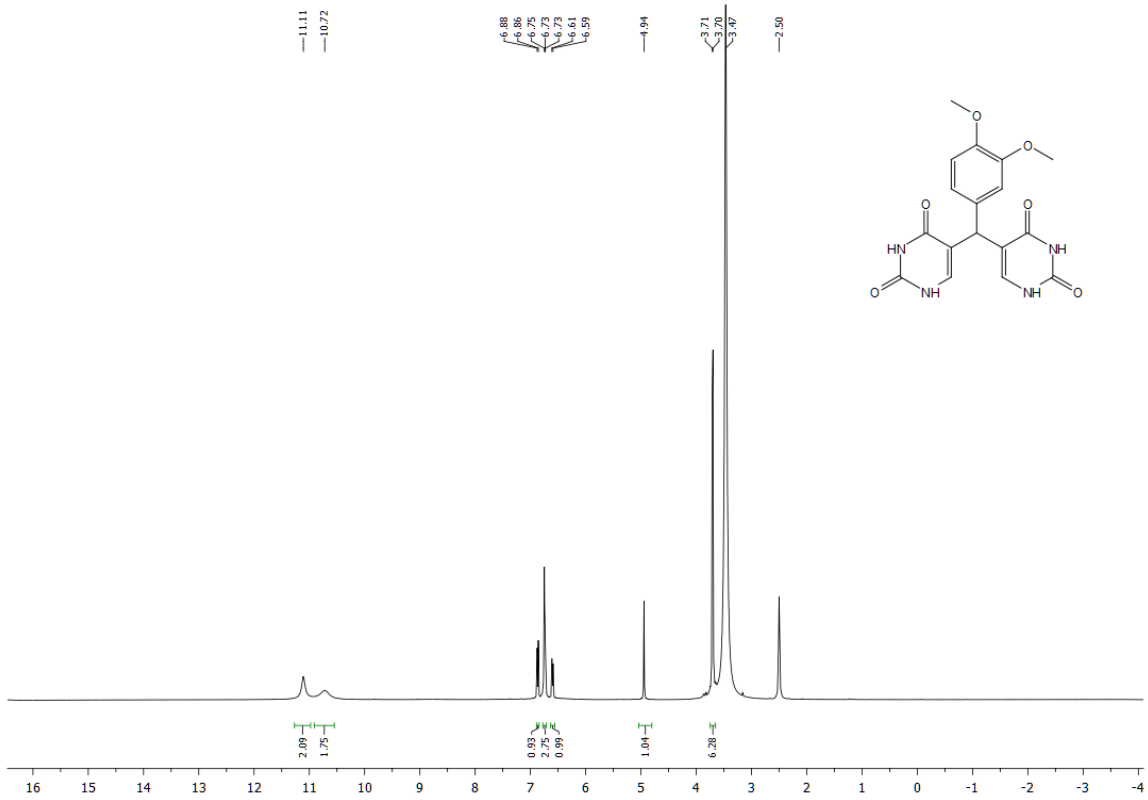
FTIR spectrum of 6,6'-((4-methoxyphenyl)methylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione) **(21a)**



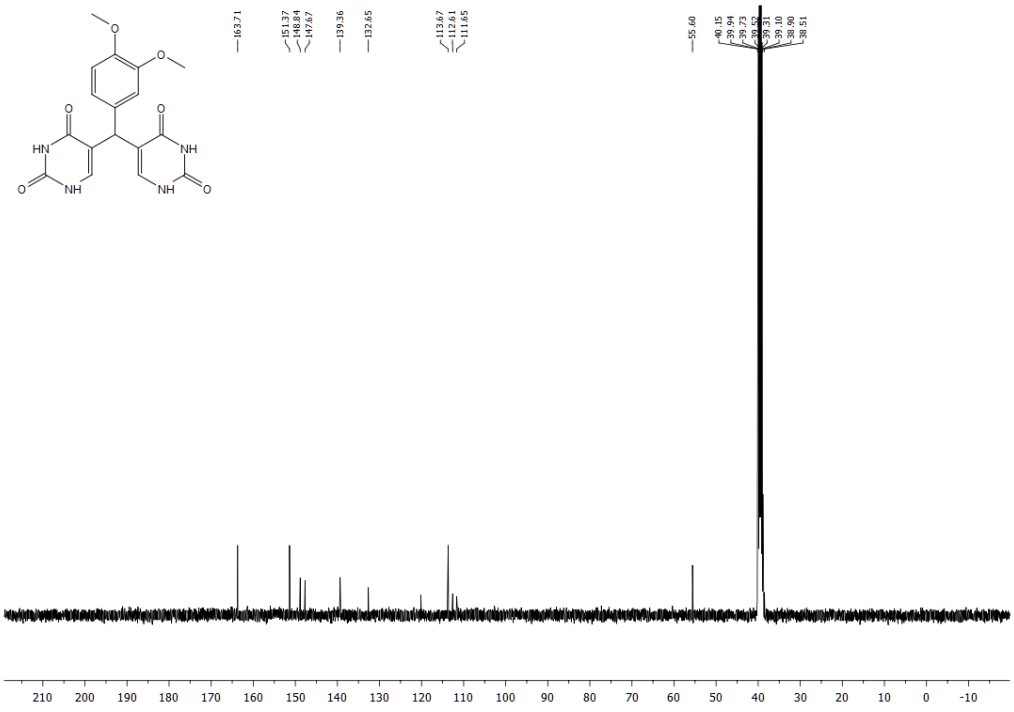
Mass spectrum of 6,6'-((4-methoxyphenyl)methylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione) **(21a)**



^{1}H NMR spectrum of 5,5'-((3,4-dimethoxyphenyl)methylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione) **(22a)**

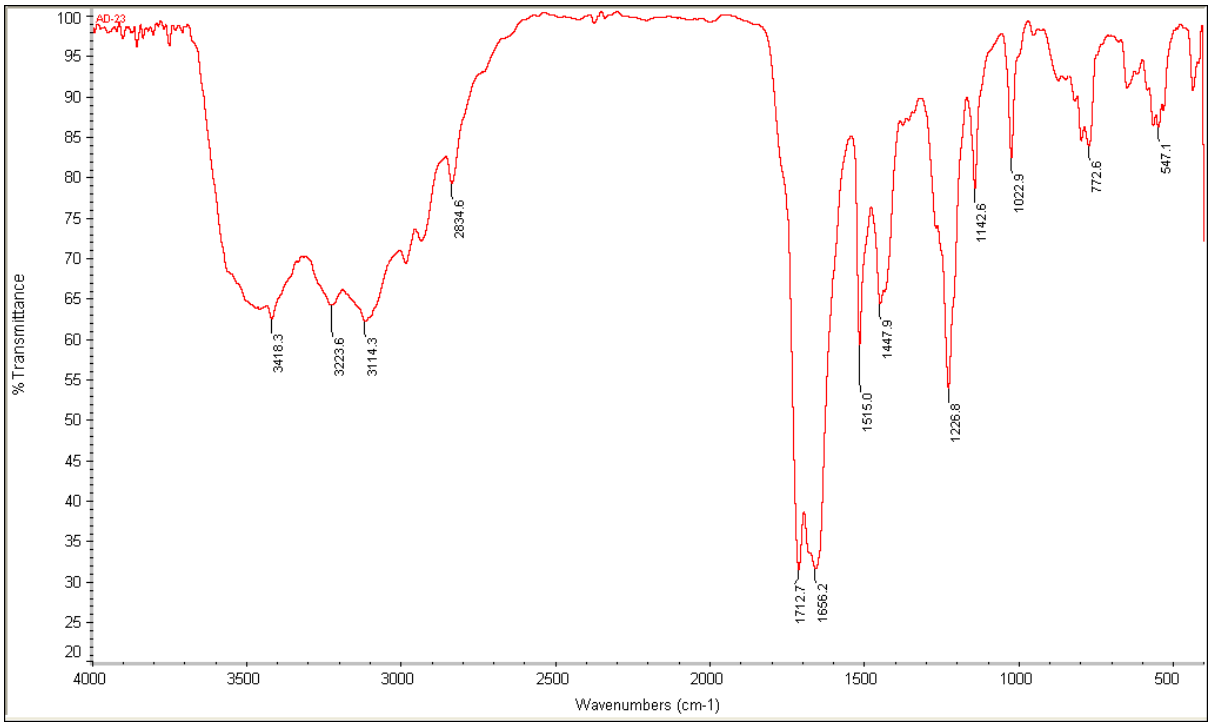


^{13}C NMR spectrum of 5,5'-((3,4-dimethoxyphenyl)methylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione) **(22a)**



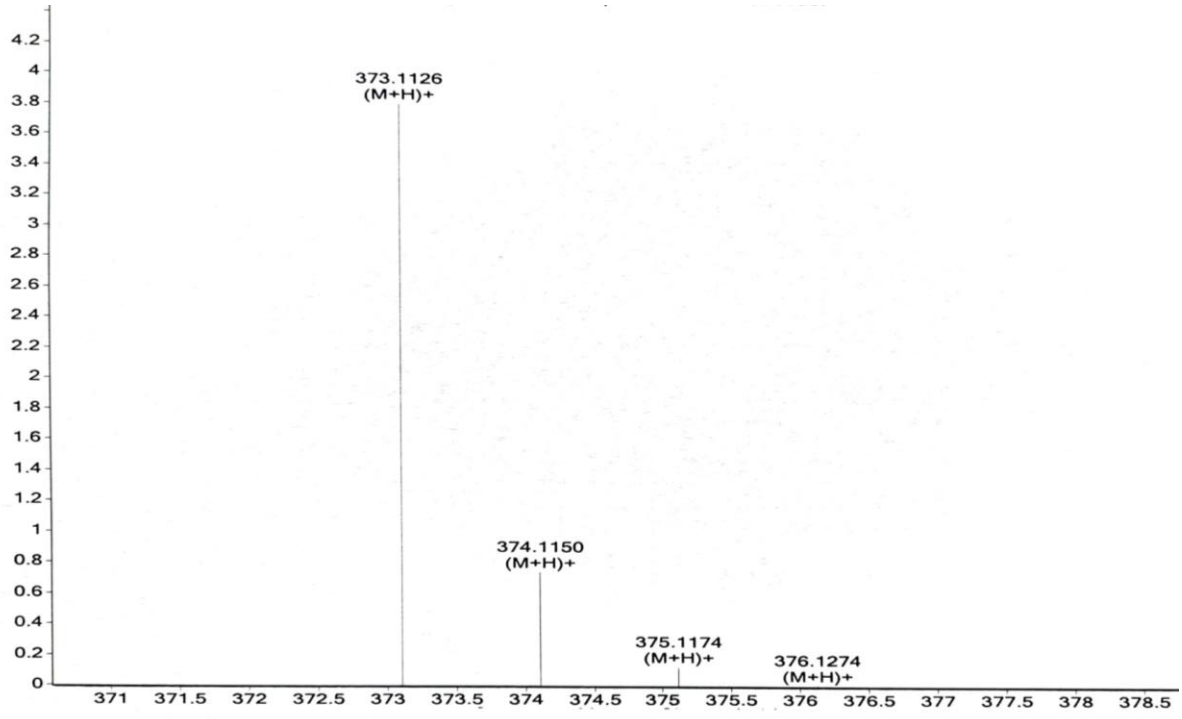
FTIR spectrum of 5,5'-((3,4-dimethoxyphenyl)methylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione)

(22a)

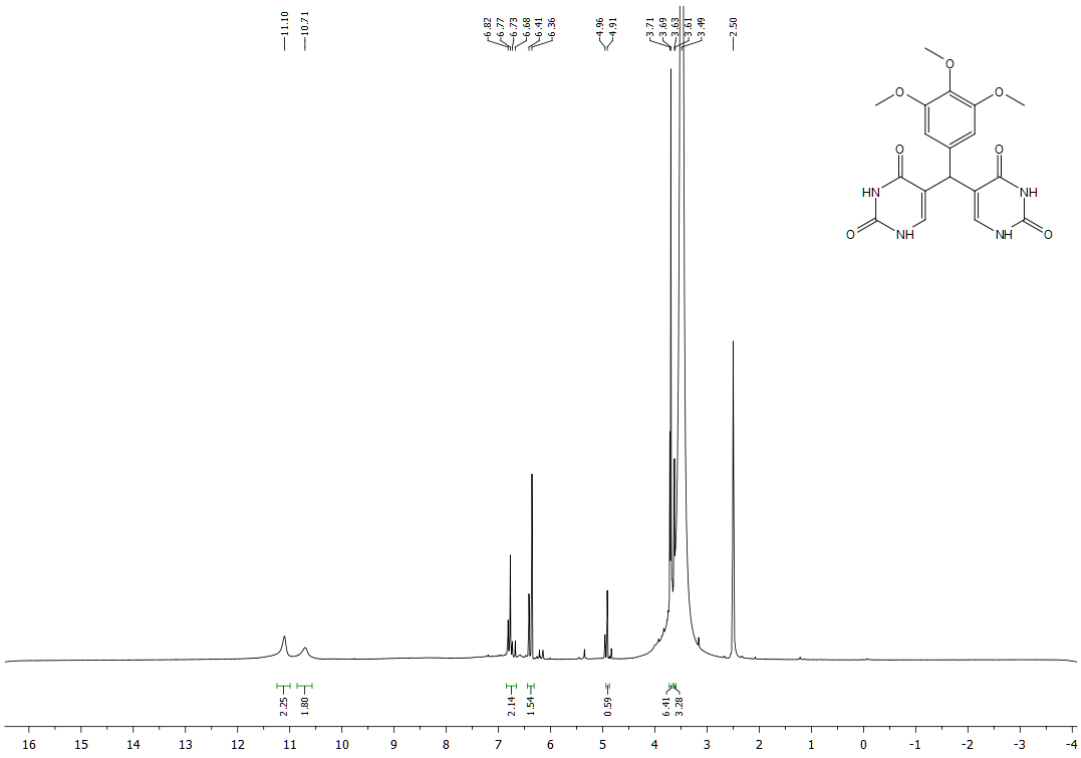


Mass spectrum of 5,5'-((3,4-dimethoxyphenyl)methylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione)

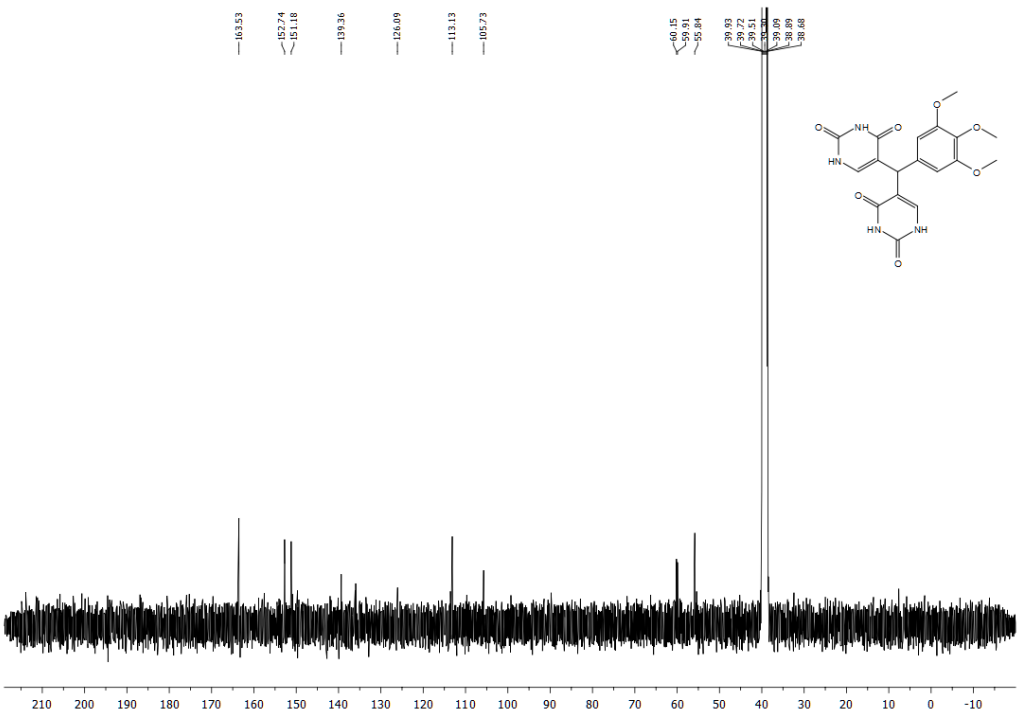
(22a)



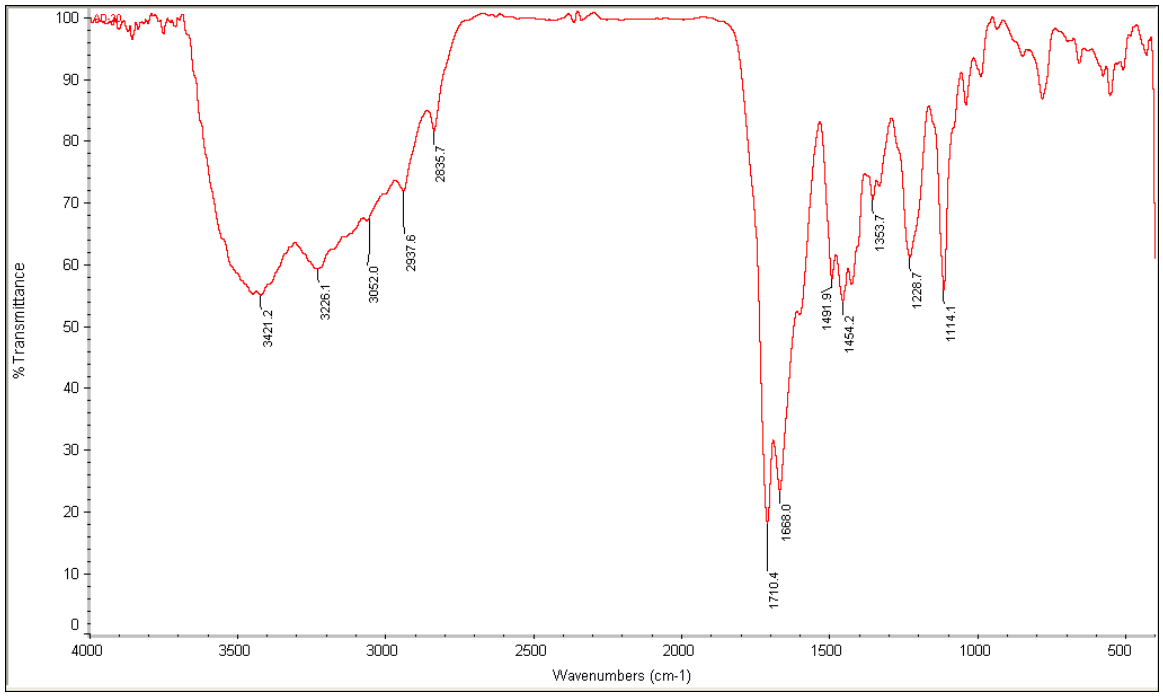
^{1}H NMR spectrum of 5,5'-((3,4,5-trimethoxyphenyl)methylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione) **(23a)**



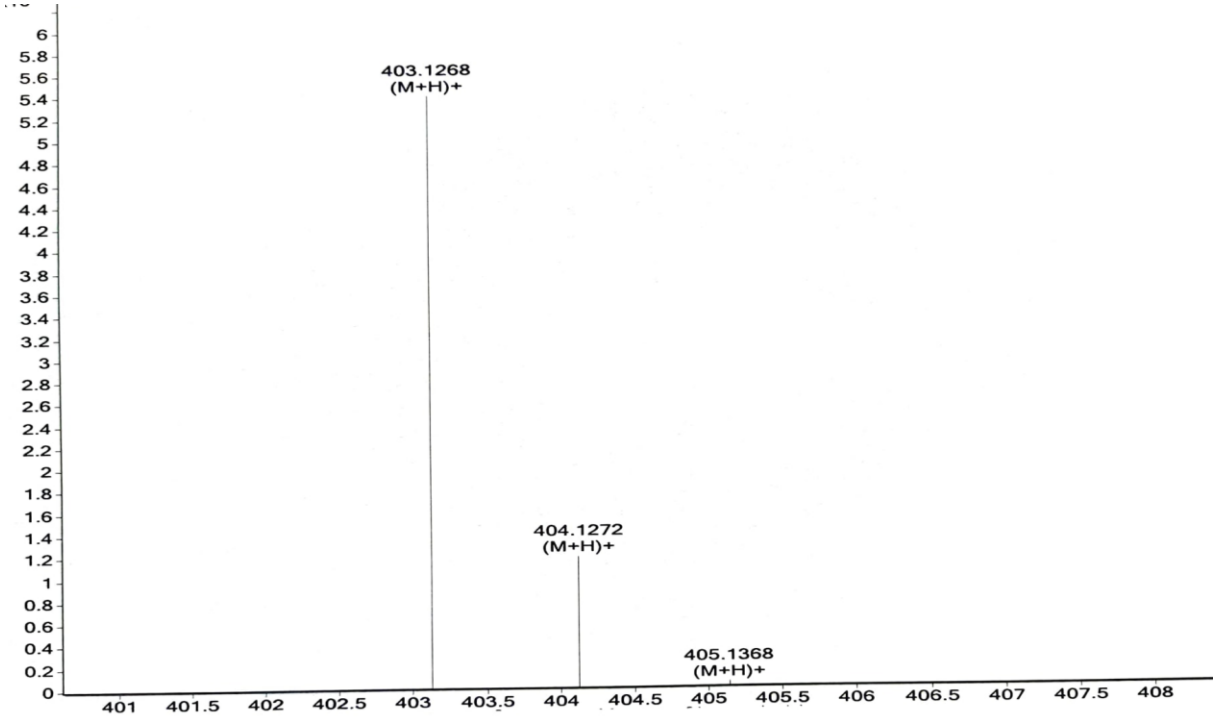
^{13}C NMR spectrum of 5,5'-((3,4,5-trimethoxyphenyl)methylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione) **(23a)**



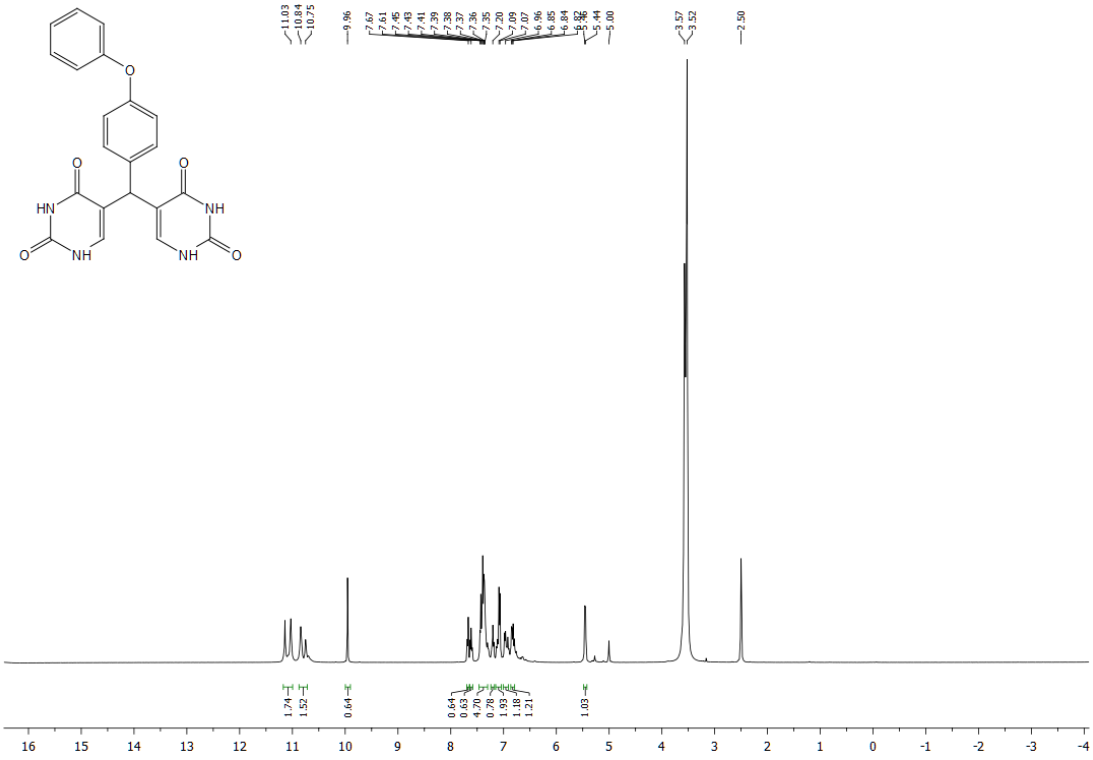
FTIR spectrum of 5,5'-((3,4,5-trimethoxyphenyl)methylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione) **(23a)**



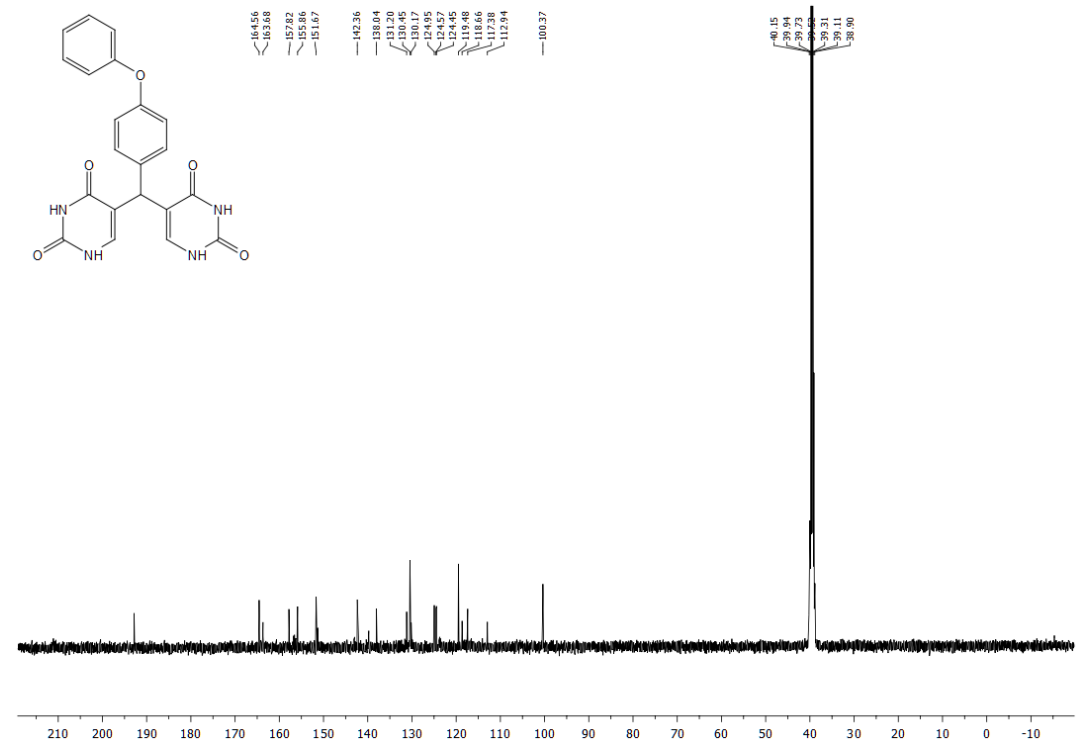
Mass spectrum of 5,5'-((3,4,5-trimethoxyphenyl)methylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione) **(23a)**



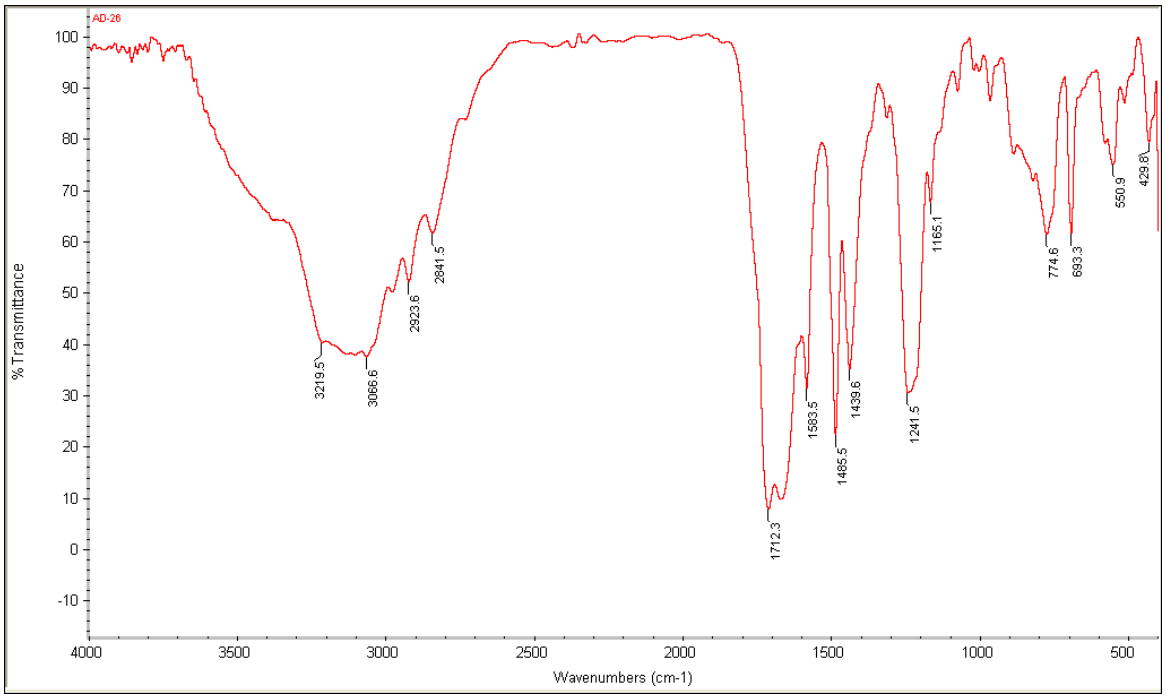
^{1}H NMR spectrum of 5,5'-((4-phenoxyphenyl)methylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione) **(24a)**



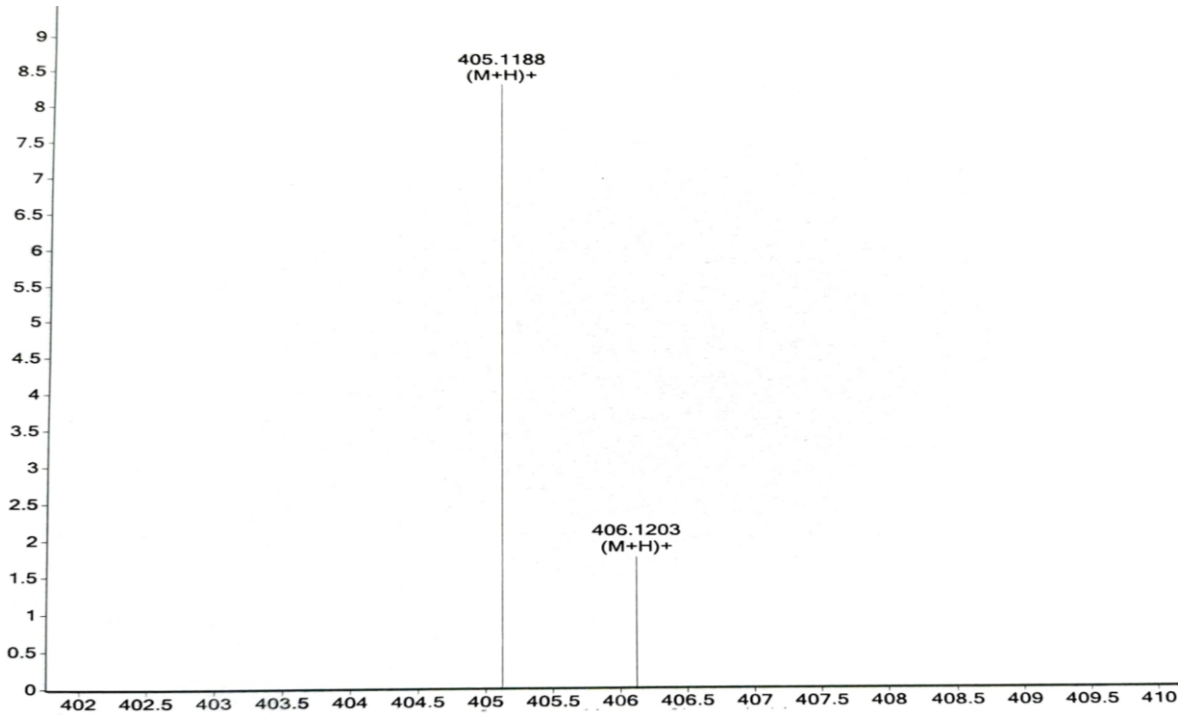
^{13}C NMR spectrum of 5,5'-((4-phenoxyphenyl)methylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione) **(24a)**



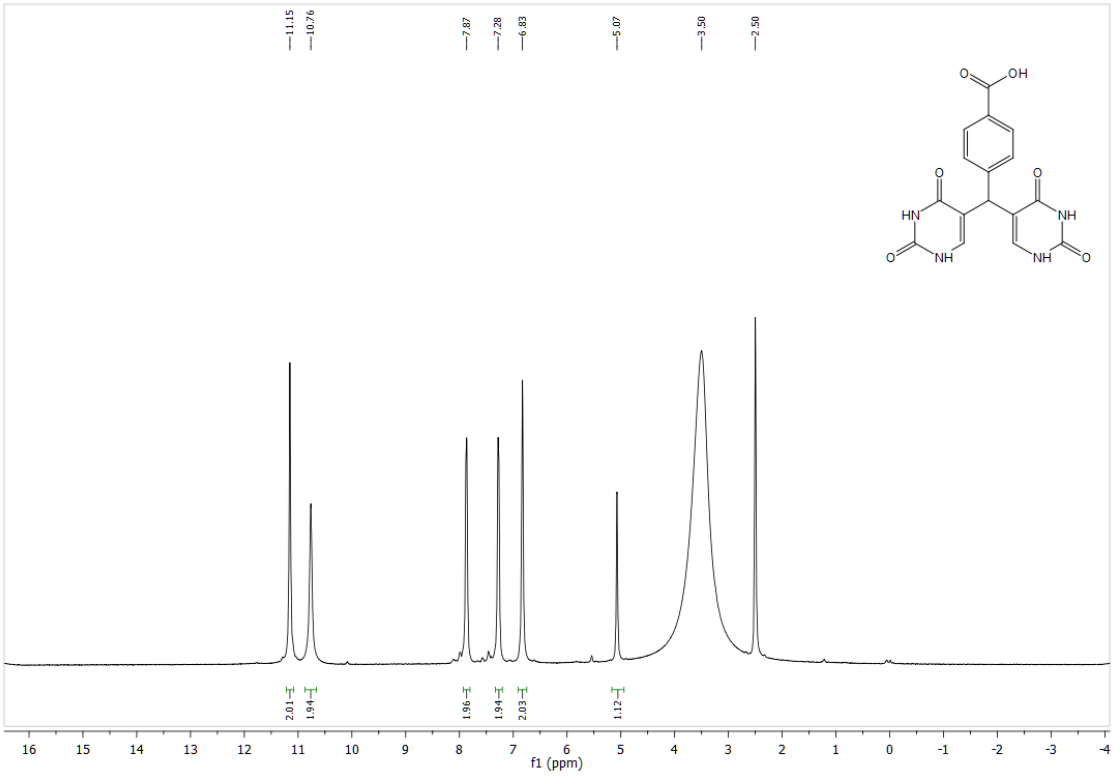
FTIR spectrum of 5,5'-((4-phenoxyphenyl)methylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione) **(24a)**



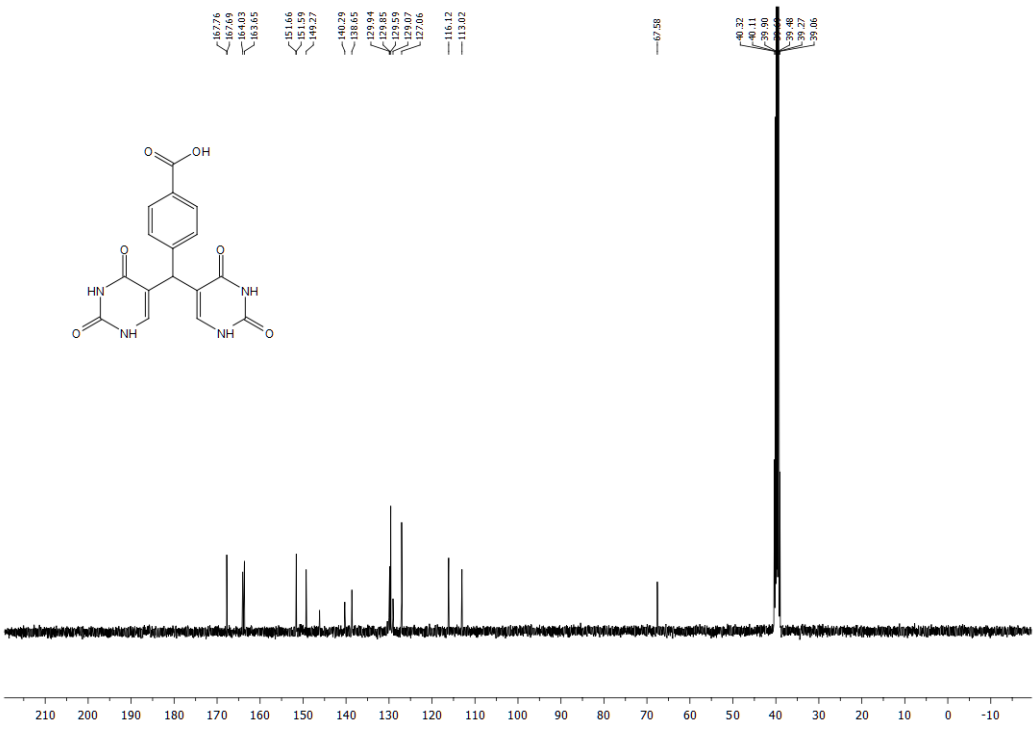
Mass spectrum of 5,5'-((4-phenoxyphenyl)methylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione) **(24a)**



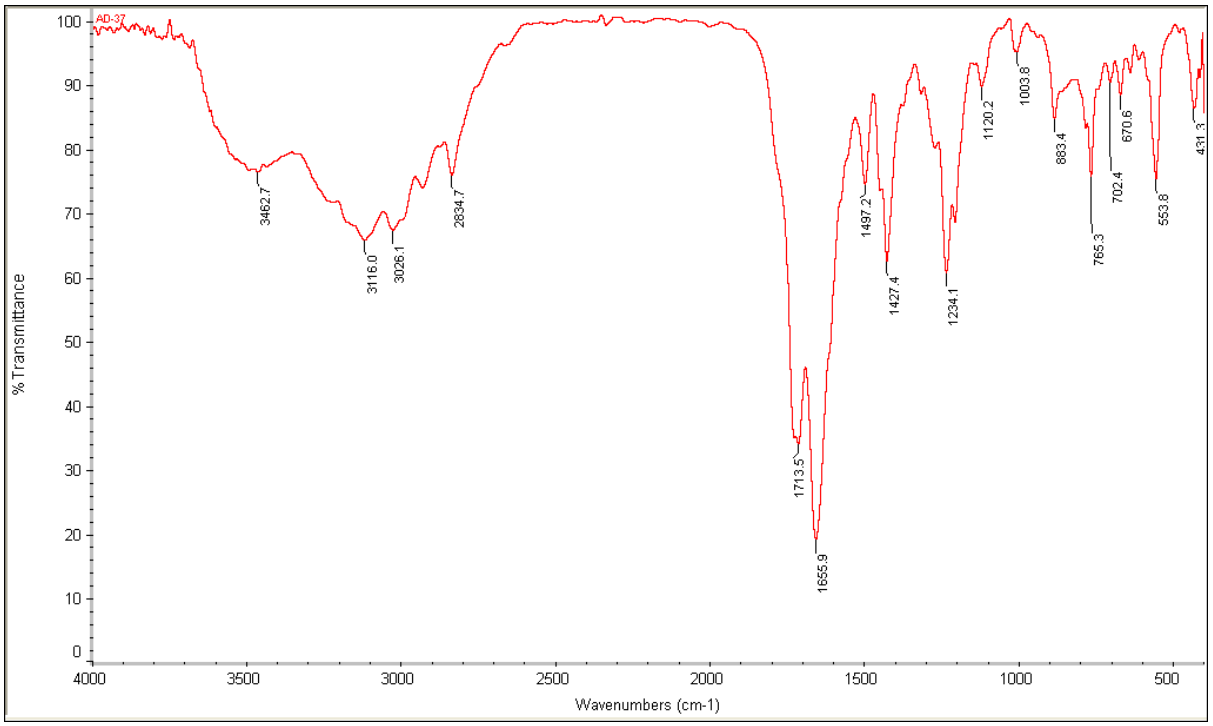
^{1}H NMR spectrum of 4-(bis(2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl)methyl)benzoic acid **(25a)**



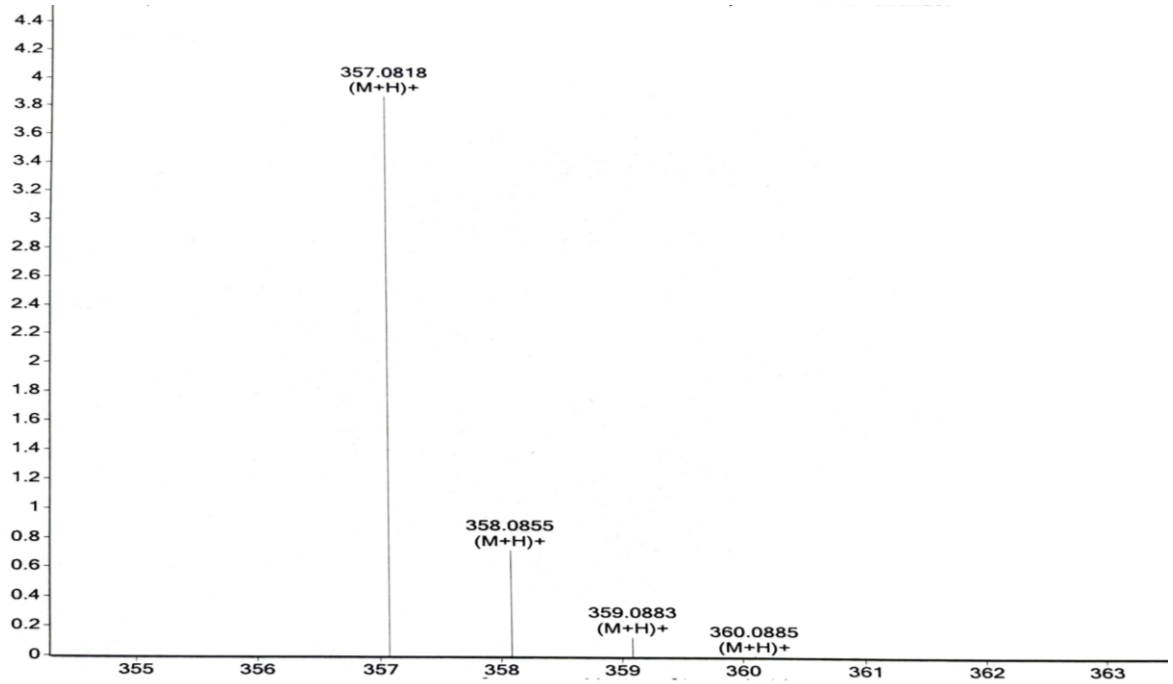
^{13}C NMR spectrum of 4-(bis(2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl)methyl)benzoic acid **(25a)**



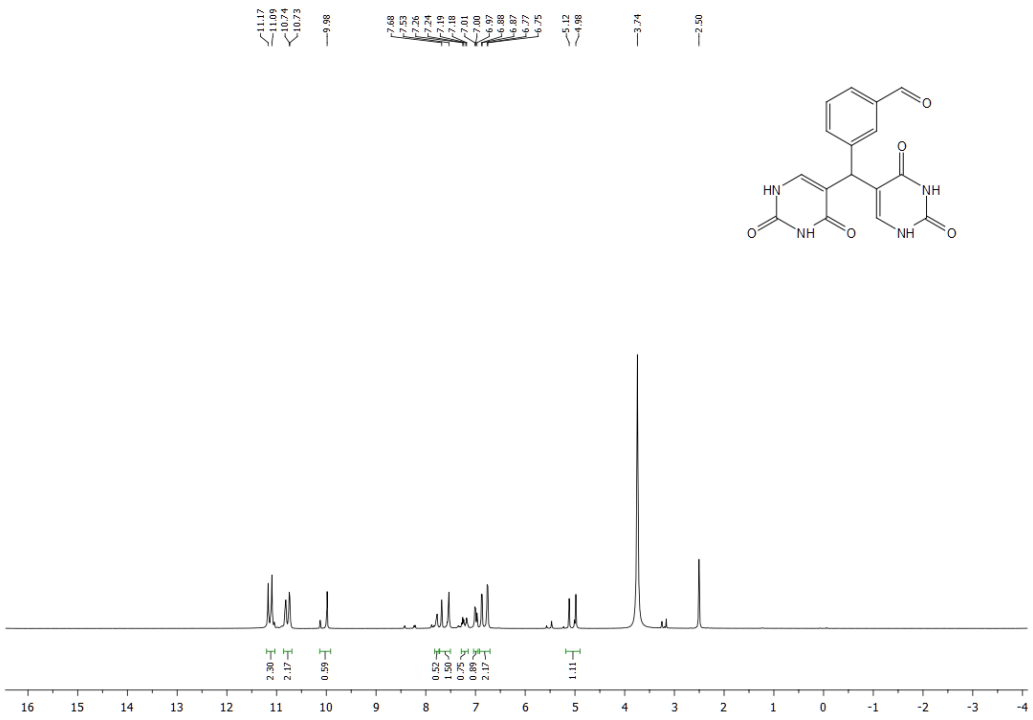
FTIR spectrum of 4-(bis(2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl)methyl)benzoic acid **(25a)**



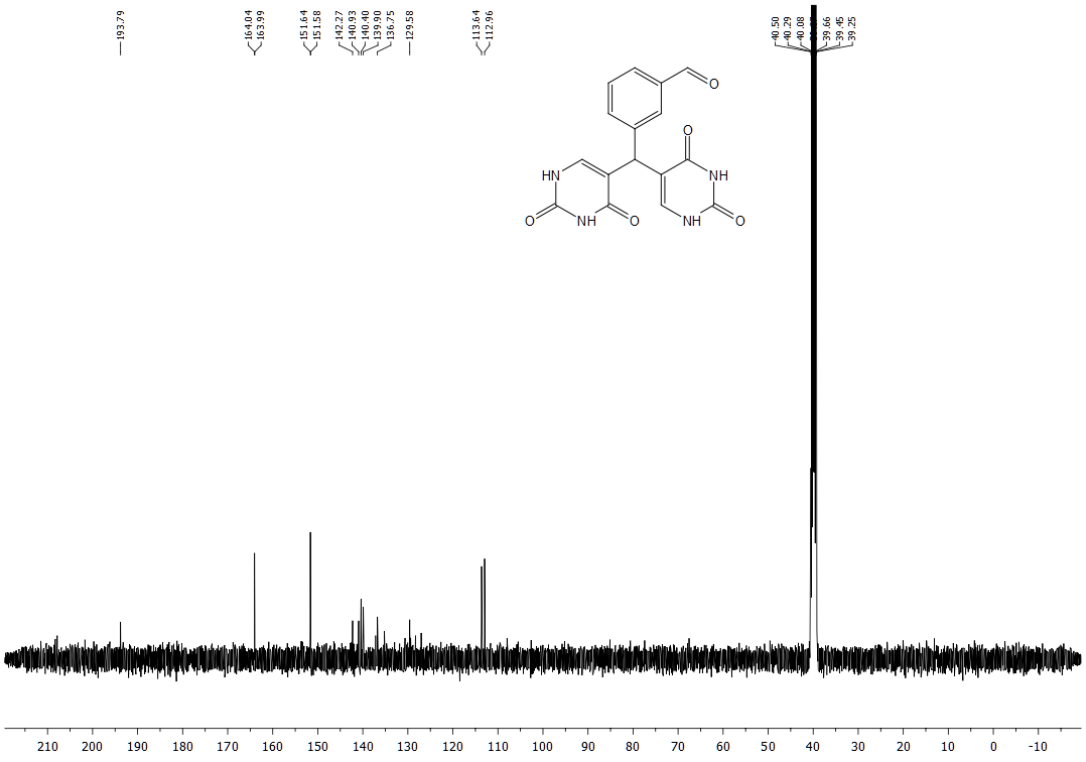
Mass spectrum of 4-(bis(2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl)methyl)benzoic acid **(25a)**



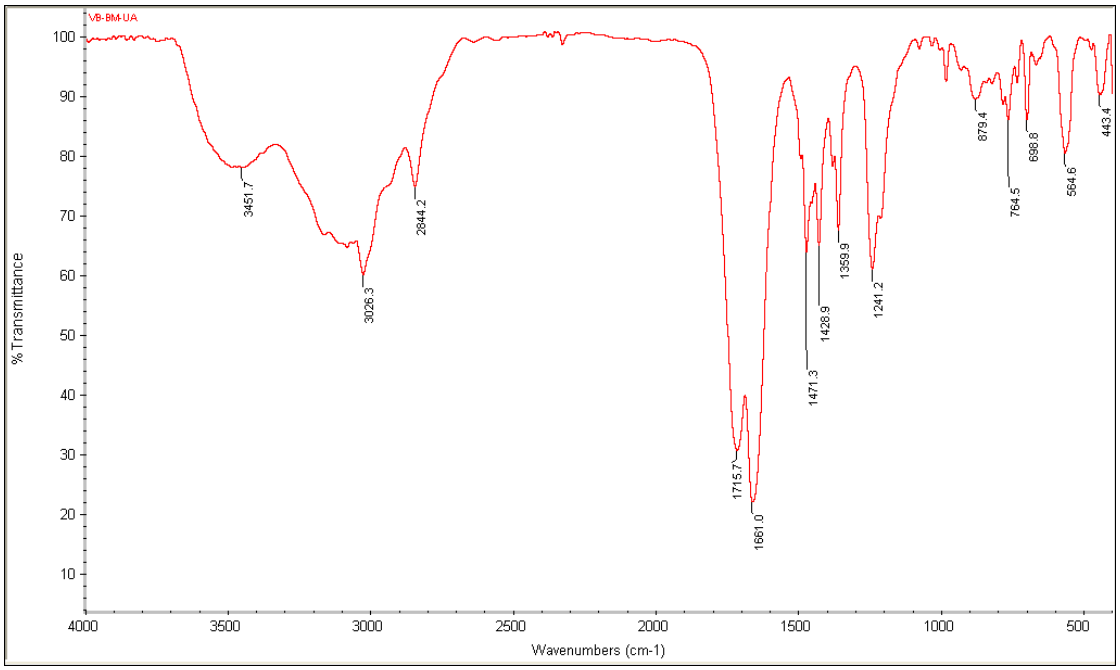
^{1}H NMR spectrum of 3-(bis(2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl)methyl)benzaldehyde **(26a)**



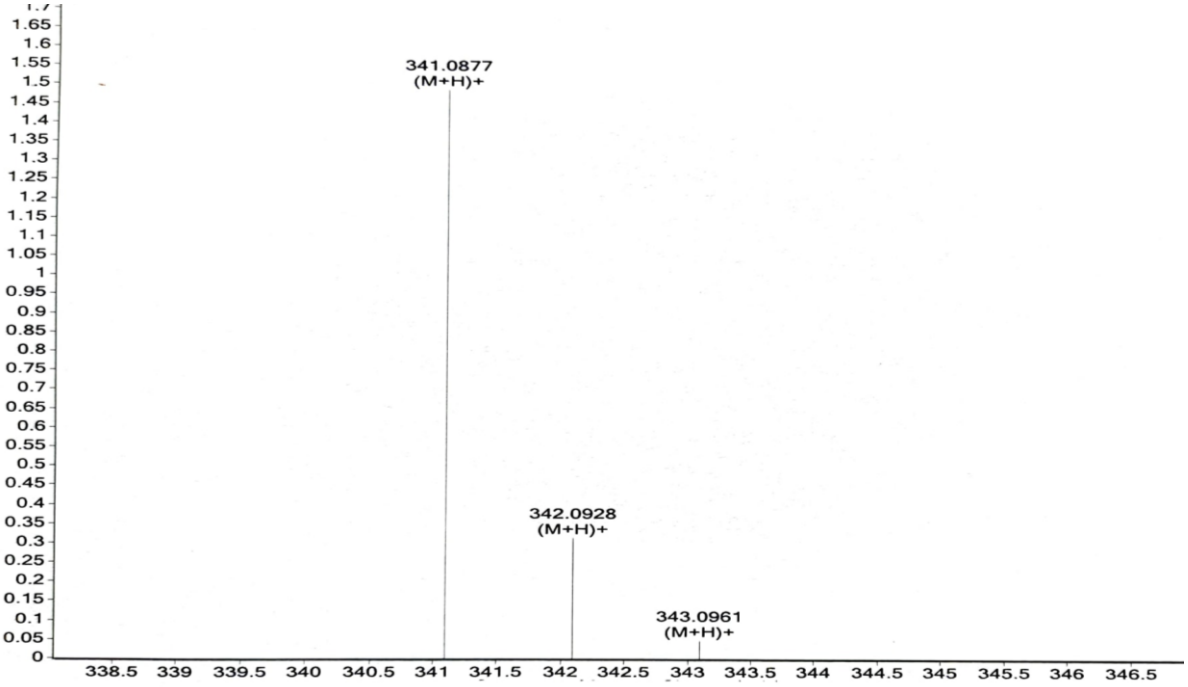
^{13}C NMR spectrum of 3-(bis(2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl)methyl)benzaldehyde **(26a)**



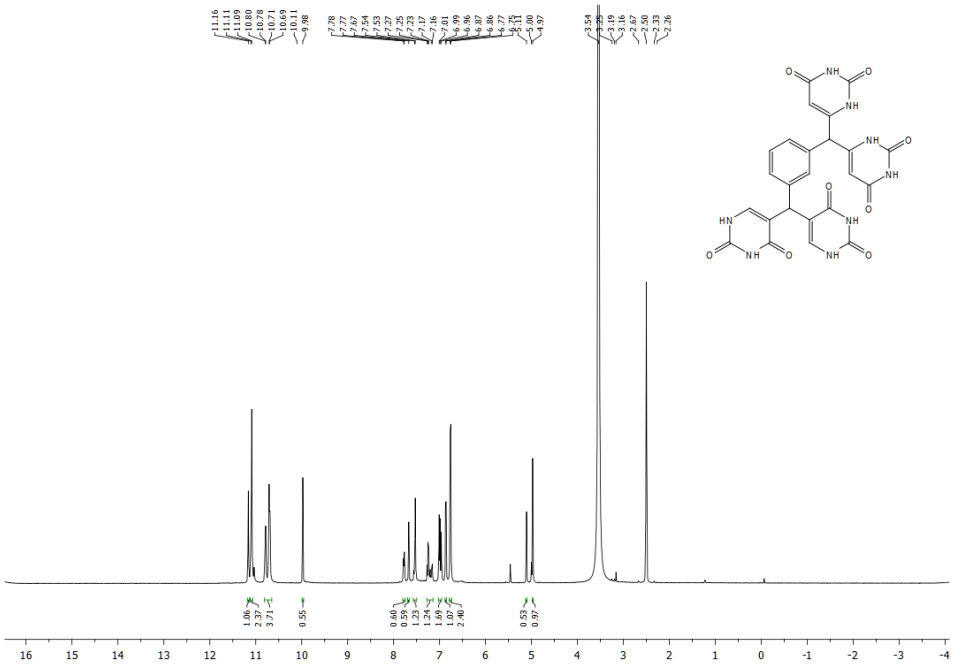
FTIR spectrum of 3-(bis(2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl)methyl)benzaldehyde **(26a)**



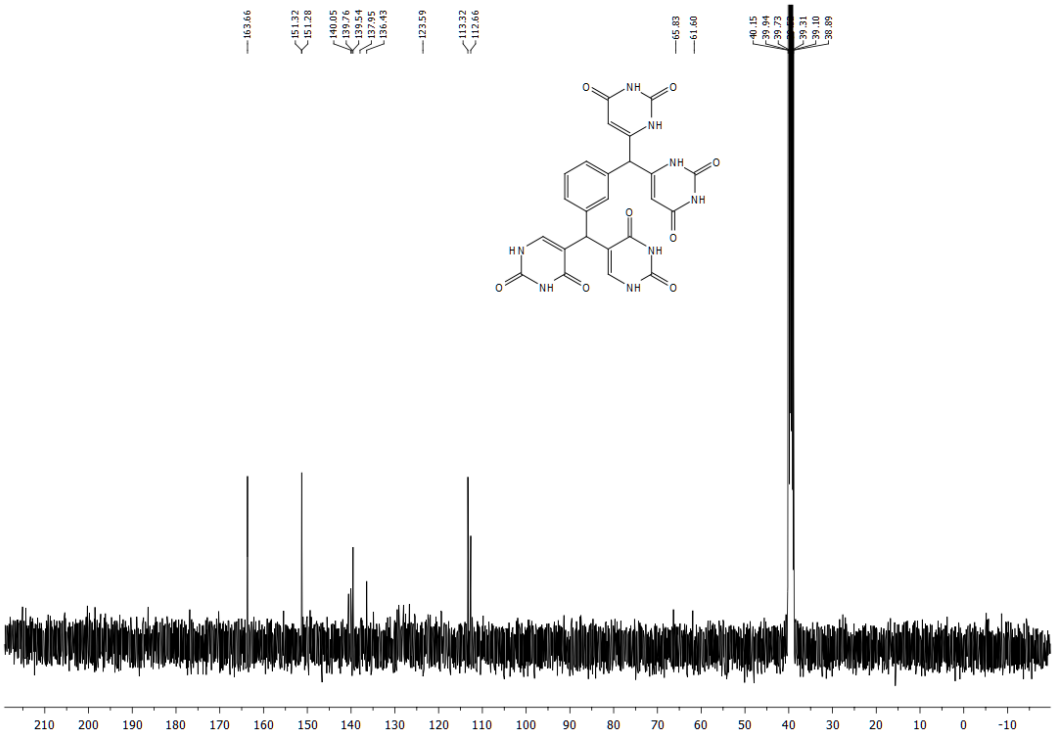
Mass spectrum of 3-(bis(2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl)methyl)benzaldehyde **(26a)**



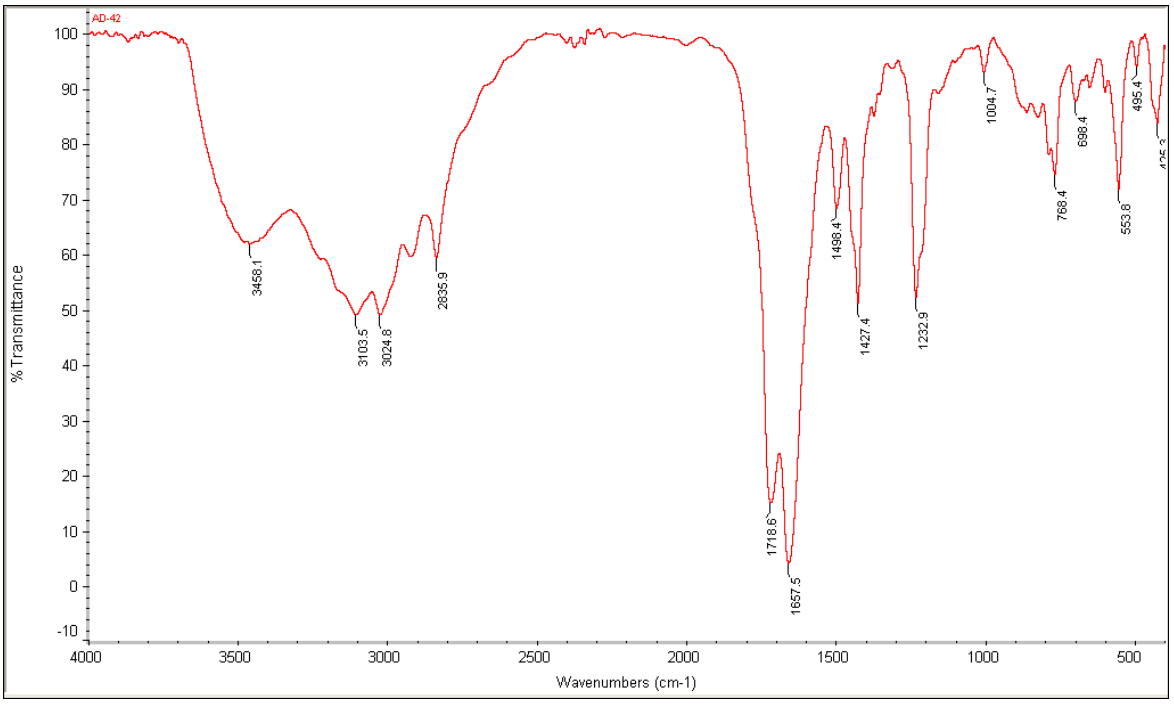
^{1}H NMR spectrum of 6,6'-((3-(bis(2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl)methyl)phenyl)methylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione) **(27a)**



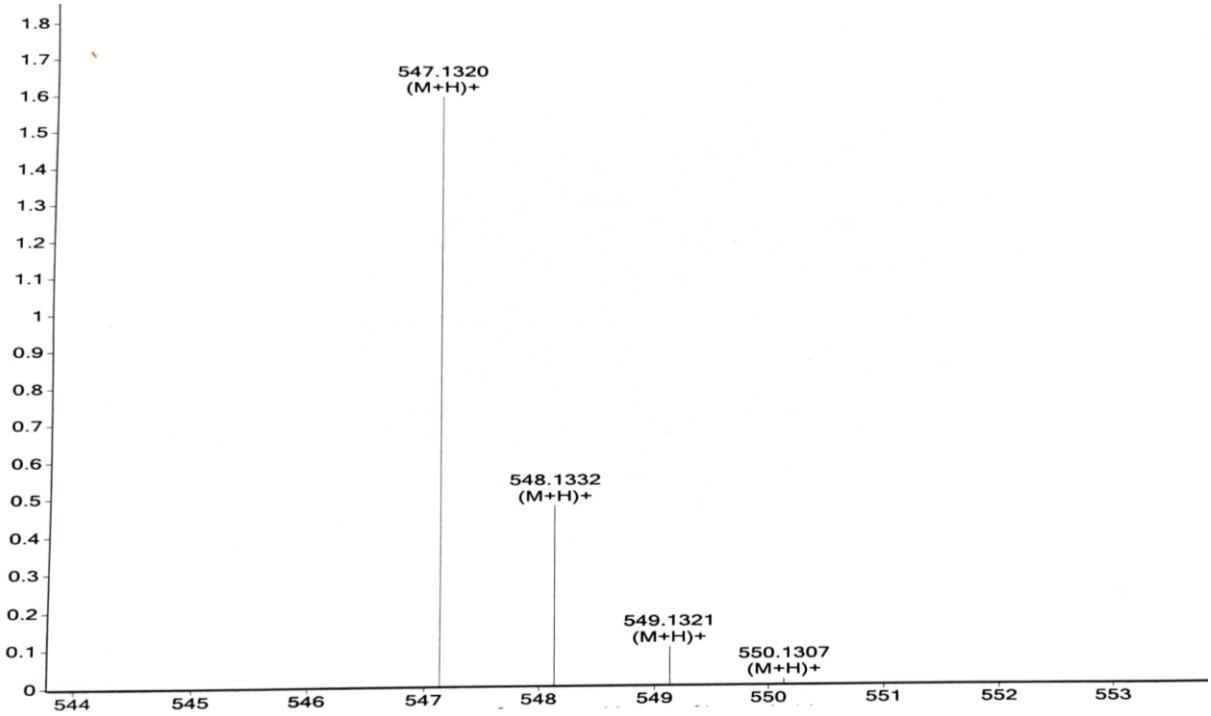
^{13}C NMR spectrum of 6,6'-((3-(bis(2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl)methyl)phenyl)methylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione) **(27a)**



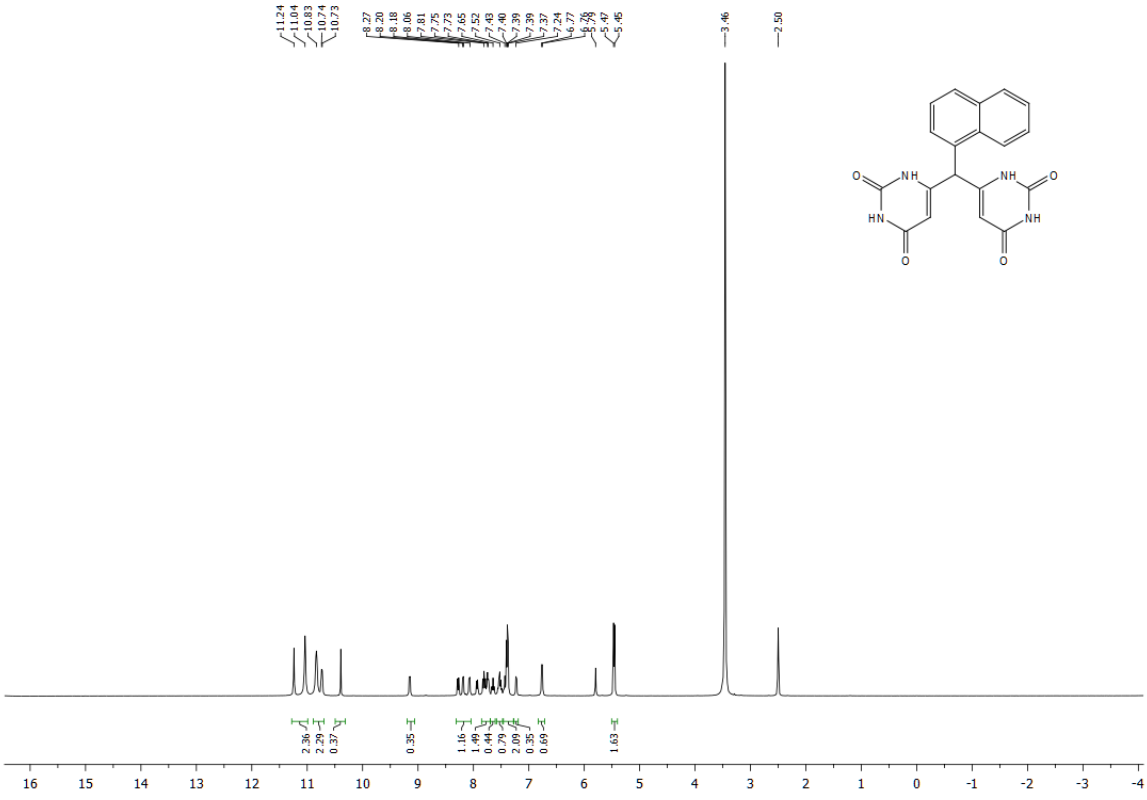
FTIR spectrum of 6,6'-((3-(bis(2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl)methyl)phenyl)methylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione) **(27a)**



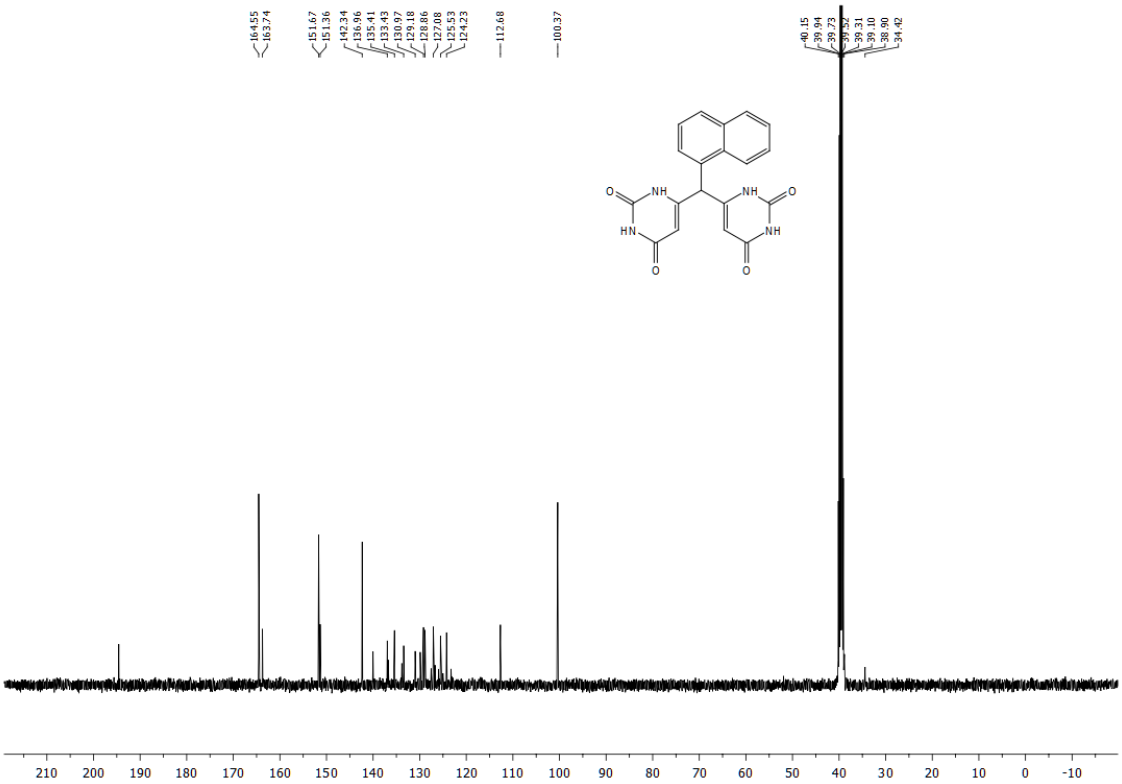
Mass spectrum of 6,6'-((3-(bis(2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl)methyl)phenyl)methylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione) **(27a)**



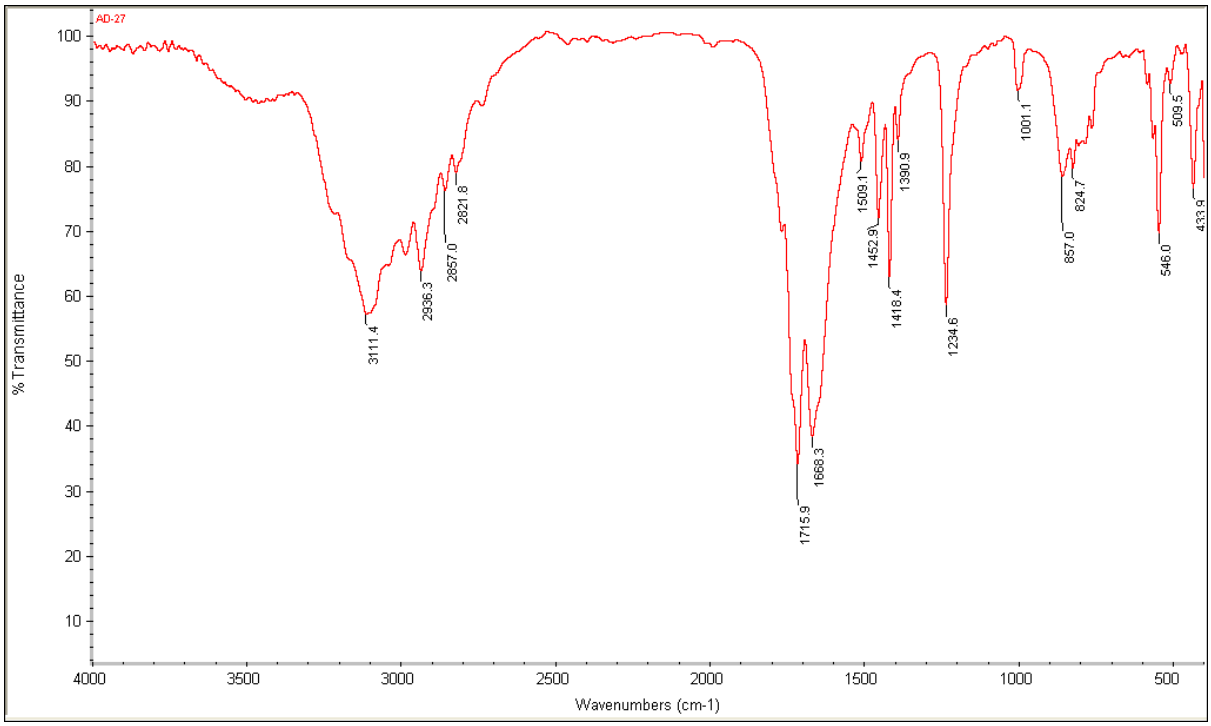
^{1}H NMR spectrum of 6,6'-(naphthalen-1-ylmethylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione) **(28a)**



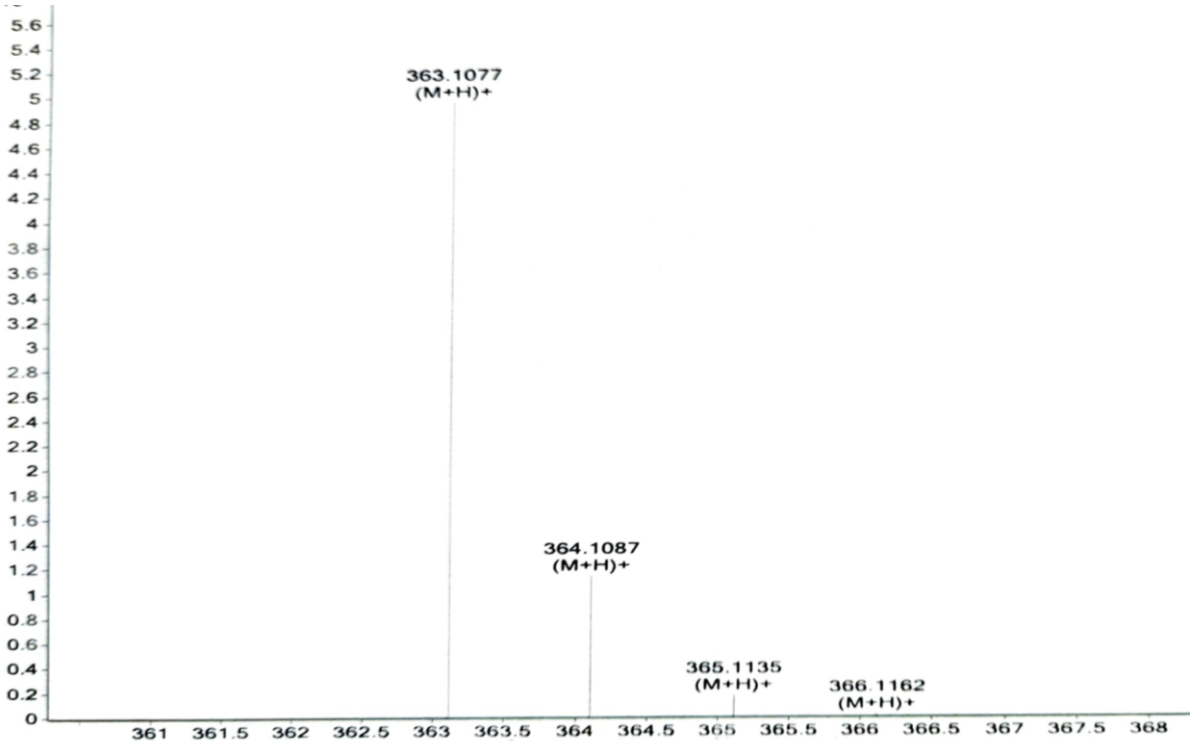
^{13}C NMR spectrum of 6,6'-(naphthalen-1-ylmethylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione) **(28a)**



FTIR spectrum of 6,6'-(naphthalen-1-ylmethylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione) **(28a)**

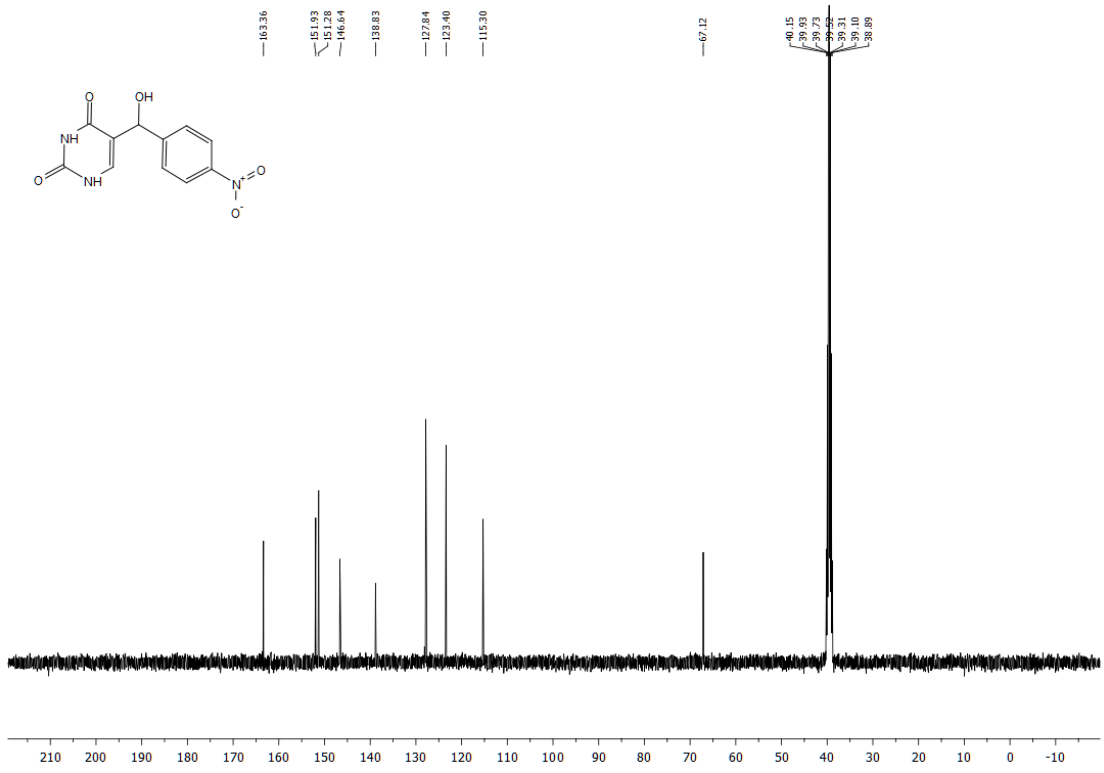


Mass spectrum of 6,6'-(naphthalen-1-ylmethylene)bis(pyrimidine-2,4(1*H*,3*H*)-dione) **(28a)**

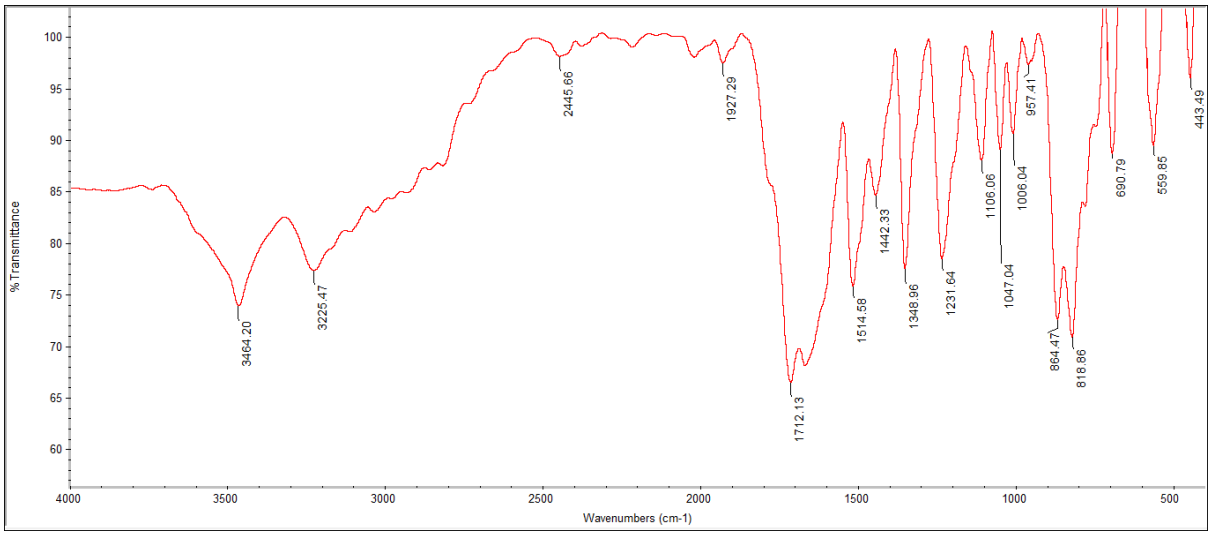


^{1}H NMR spectrum of 5-(hydroxy(4-nitrophenyl)methyl)pyrimidine-2,4*(1H,3H)*-dione **(1)**

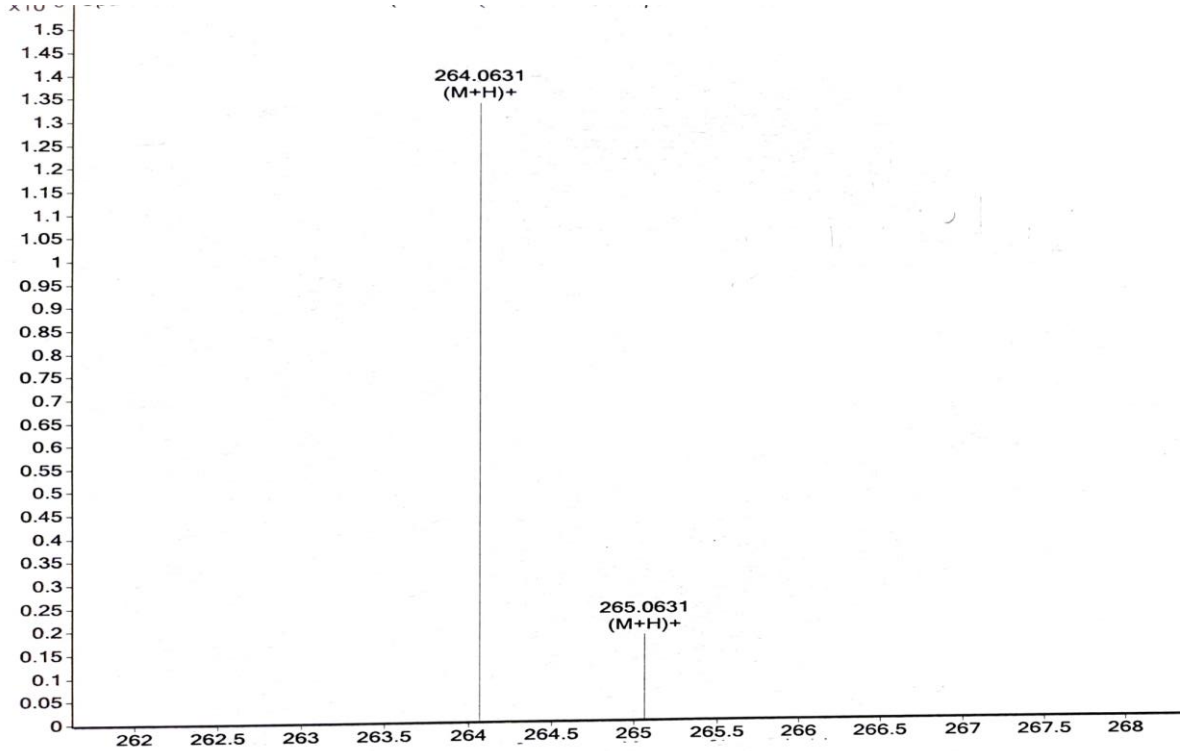
^{13}C NMR spectrum of 5-(hydroxy(4-nitrophenyl)methyl)pyrimidine-2,4*(1H,3H)*-dione **(1)**



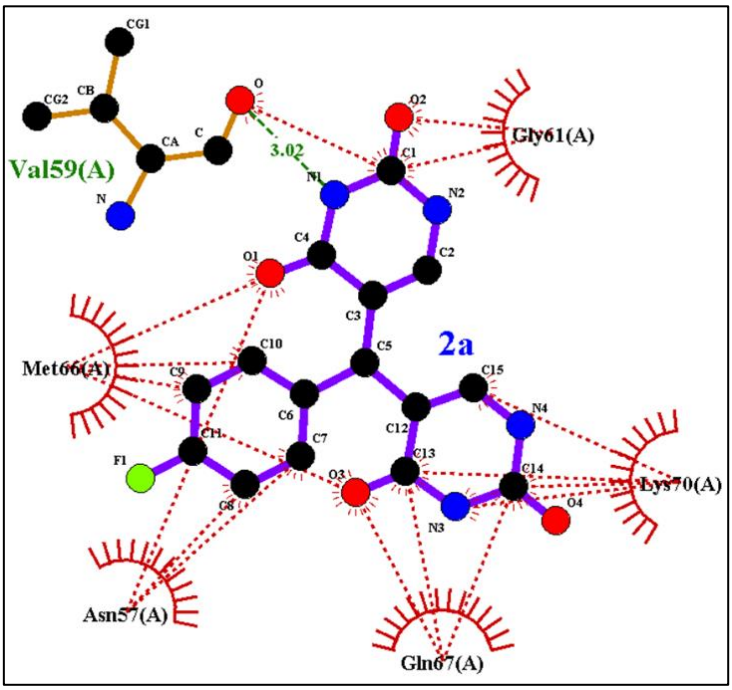
FTIR spectrum of 5-(hydroxy(4-nitrophenyl)methyl)pyrimidine-2,4(*1H*,3*H*)-dione **(1)**

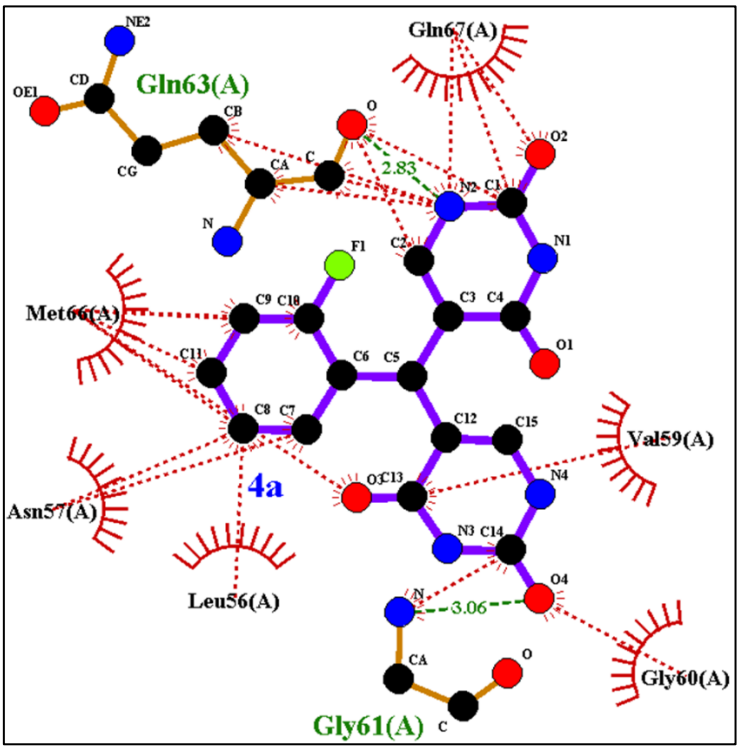


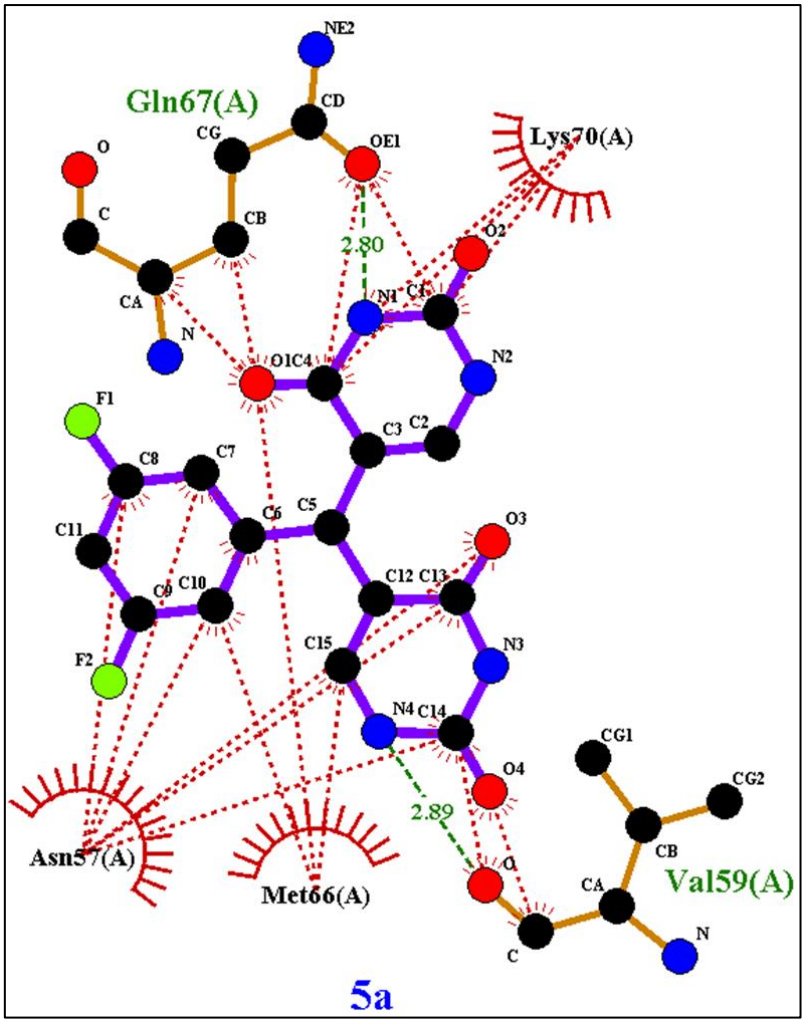
Mass spectrum of 5-(hydroxy(4-nitrophenyl)methyl)pyrimidine-2,4(*1H*,3*H*)-dione **(1)**

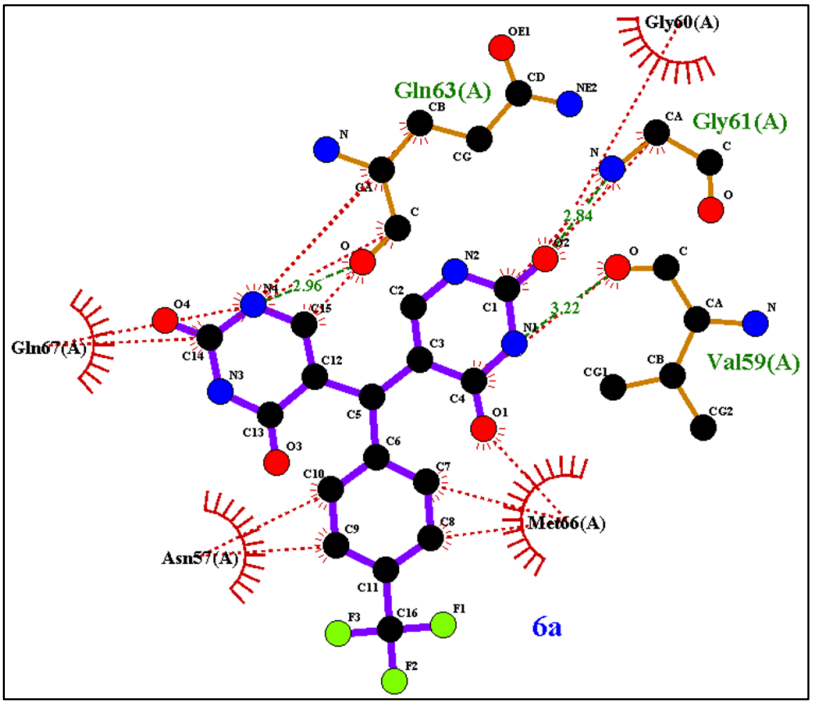


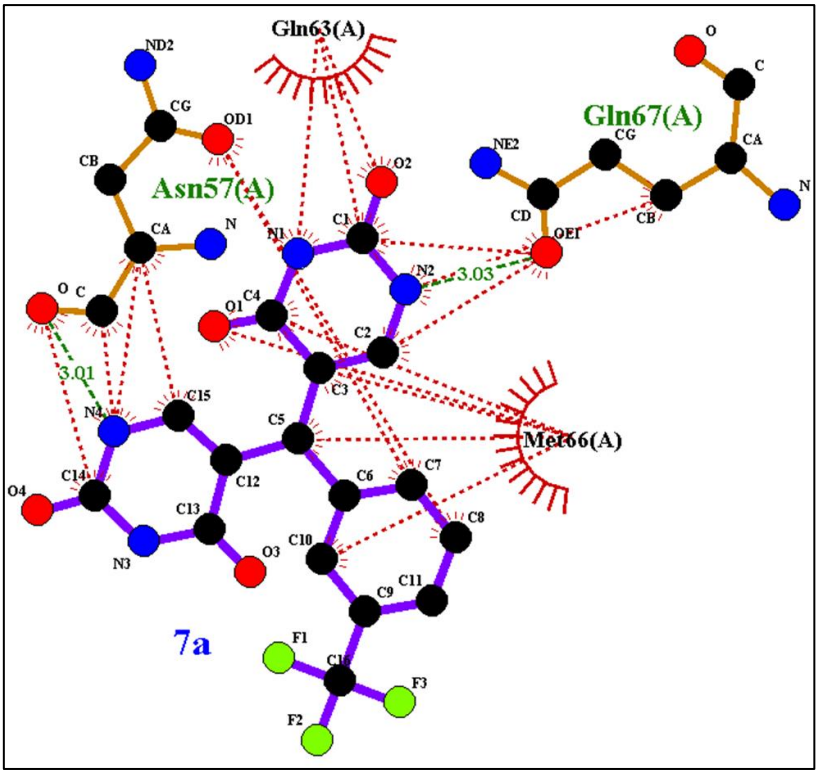
H. Fig. S2: 2D interaction diagrams of HIV CA with the compounds

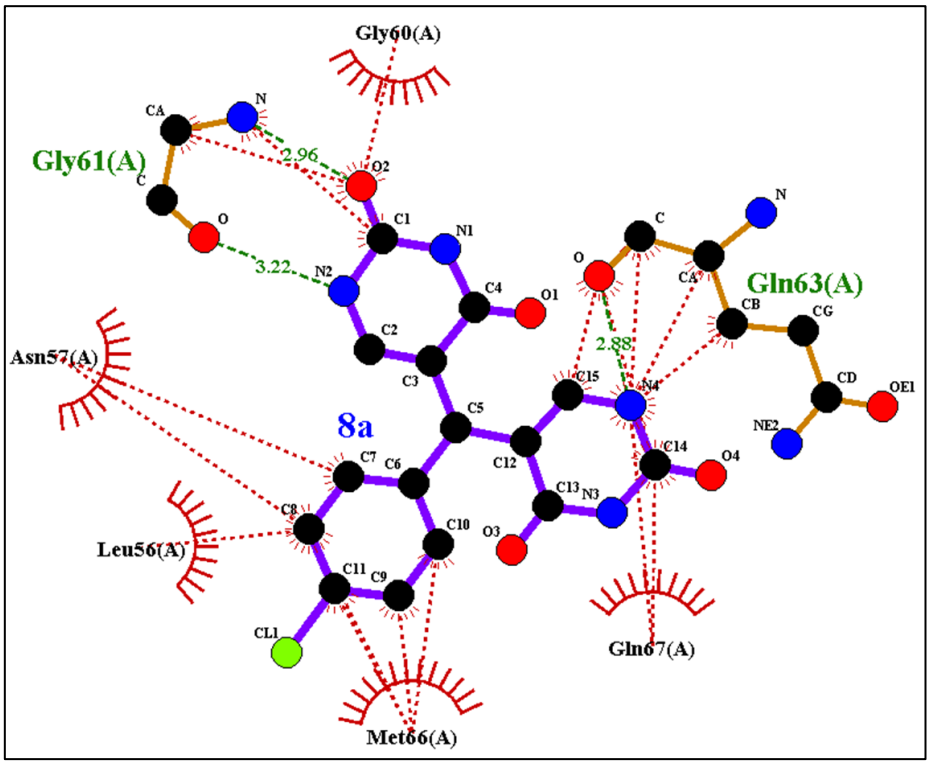


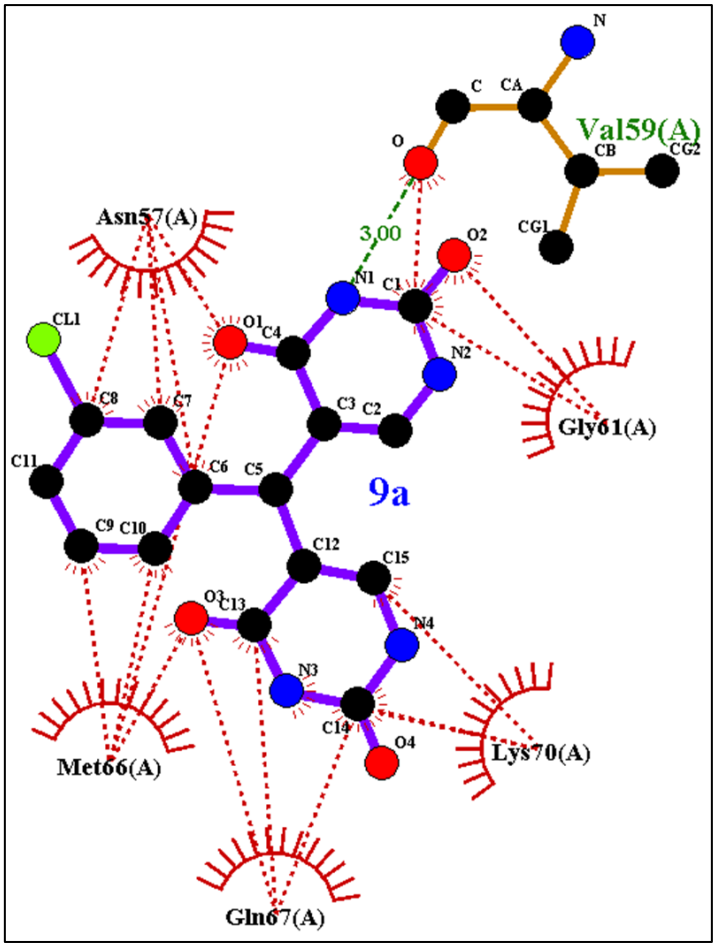


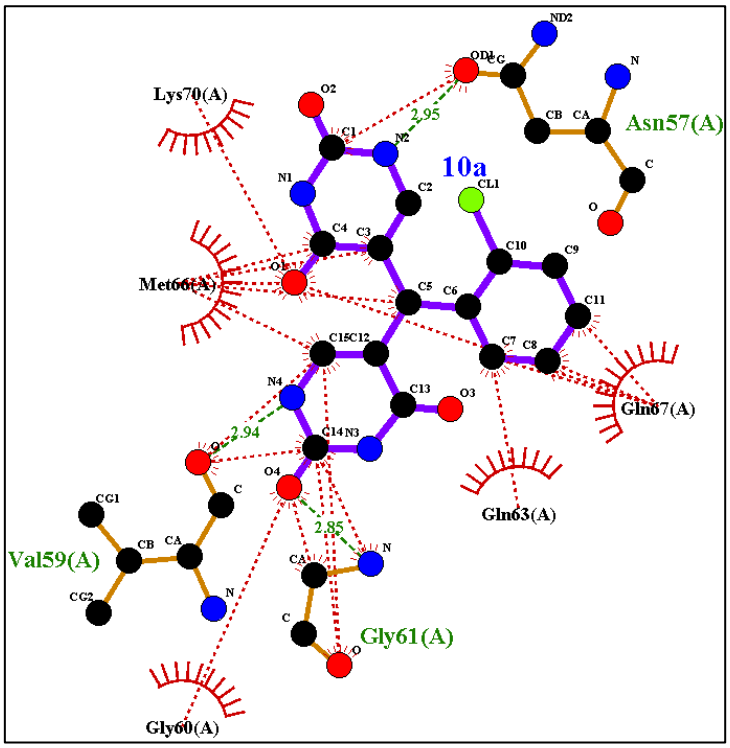

Gln67(A)
Lys70(A)
Asn57(A)
Met66(A)
Val59(A)
2.80
2.89
5a

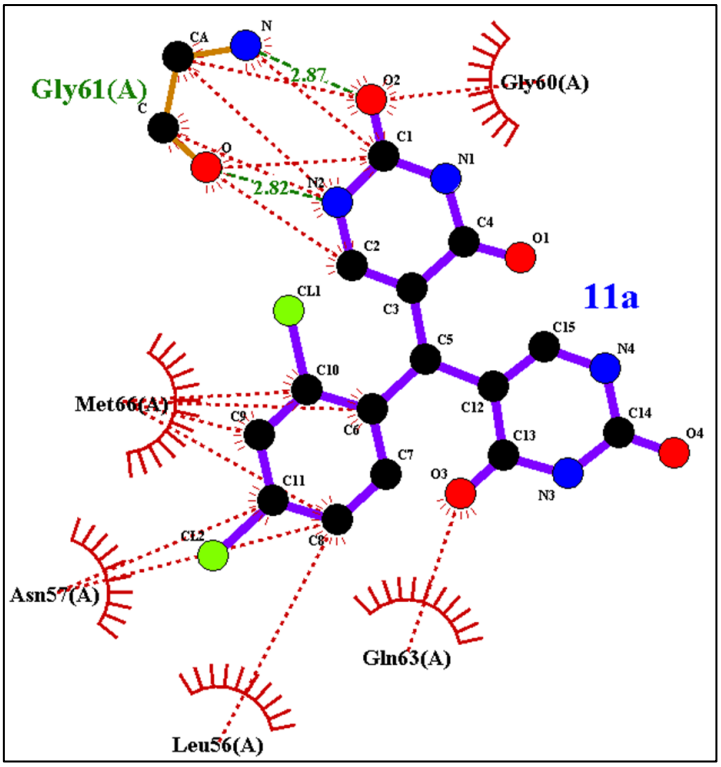

Gln63(A)
Gly60(A)
Gly61(A)
Gln67(A)
Val59(A)
Asn57(A)
Met66(A)
2.84
2.96
3.22
6a

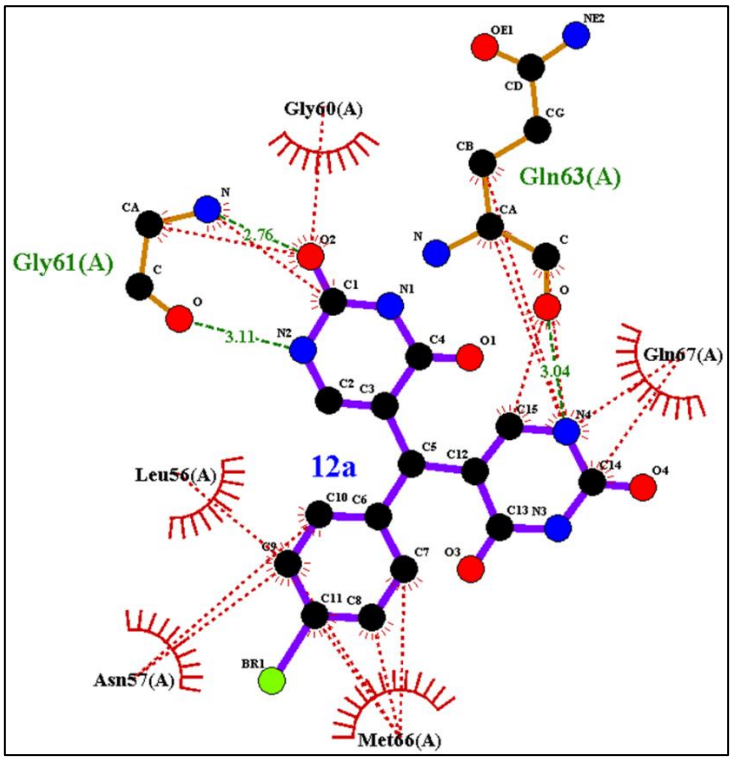

Gln63(A)
Gln67(A)
Asn57(A)
Met66(A)
7a
3.03
3.01

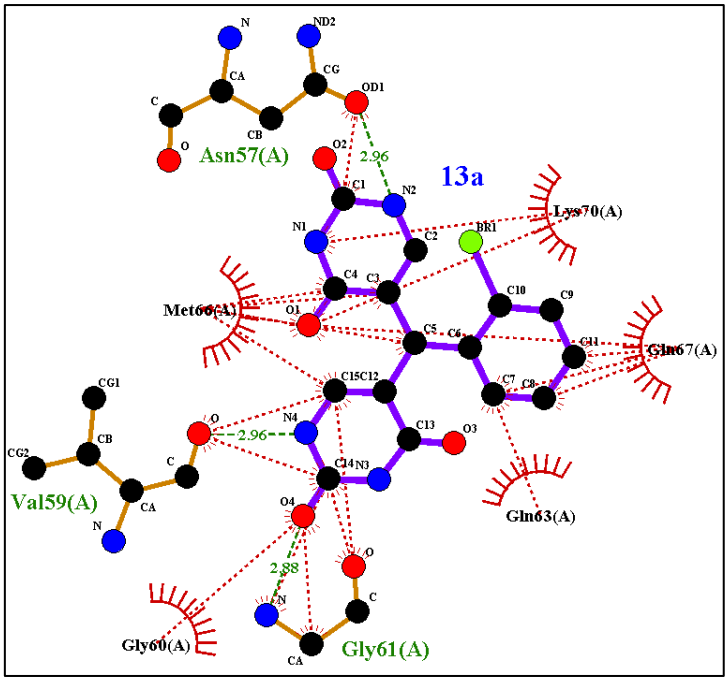

Gly60(A)
Gly61(A)
Gln63(A)
Asn57(A)
Leu56(A)
Gln67(A)
Met66(A)
8a
2.96
3.22
2.88

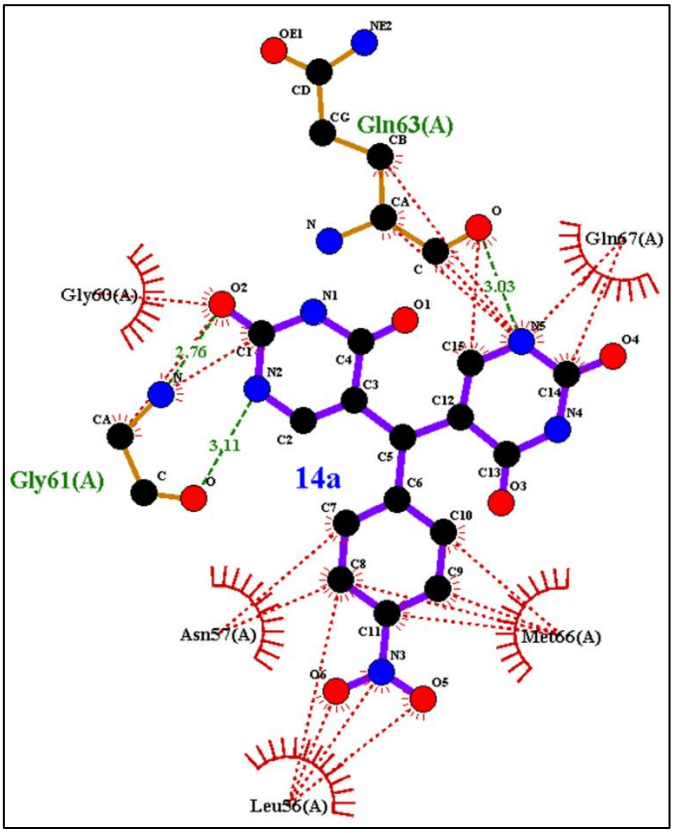

N
C
CA
Val59(A)
CB
CG2
O
CG1
Asn57(A)
3.00
O2
N1
C1
CL1
O1
C4
N2
C8
C7
C3
C2
Gly61(A)
C11
C6
C5
9a
C9
C10
C12
C15
O3
C13
N4
N3
C14
O4
Lys70(A)
Met66(A)
Gln67(A)

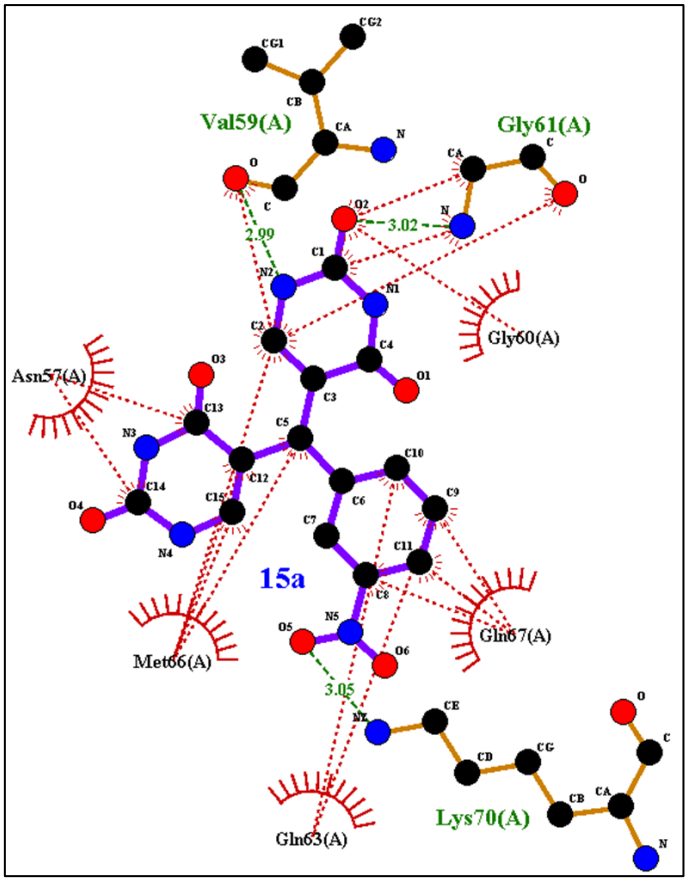

ND2
OD1
CG
N
Lys70(A)
O2
2.95
CB
CA
Asn57(A)
C1
N2
10a
C
N1
C2
CL1
O
C4
C3
C10
C9
O1
Met66(A)
C5
C6
C11
C15
C12
C7
C8
N4
C13
O3
Gln67(A)
2.94
C14
N3
O4
Gln63(A)
CG1
C
2.85
CB
CA
N
Val59(A)
CA
CG2
N
C
Gly61(A)
O
Gly60(A)

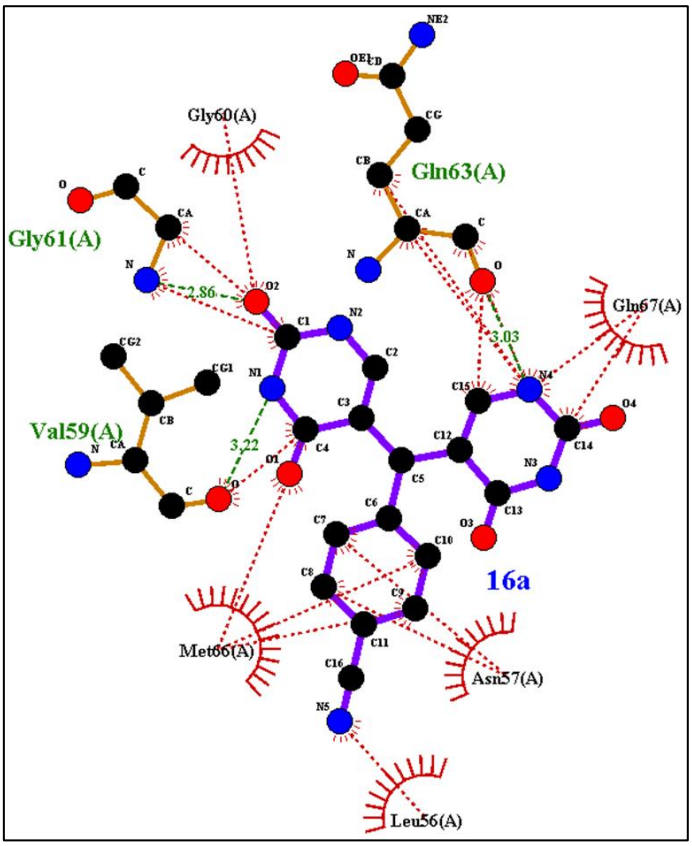

Gly61(A)
Gly60(A)
11a
Met66(A)
Asn57(A)
Gln63(A)
Leu56(A)
2.87
2.82

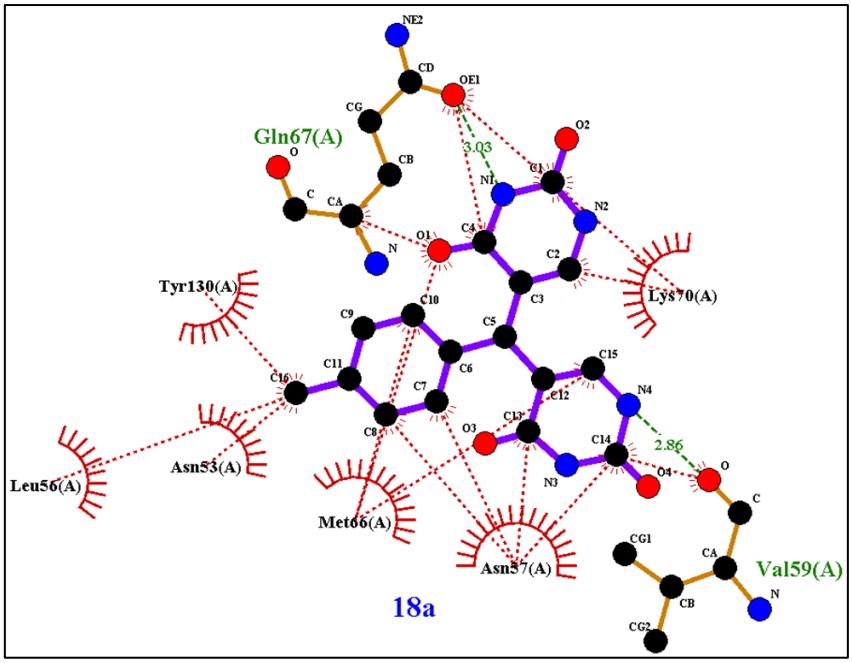

Gly60(A)
Gln63(A)
Gly61(A)
Gln67(A)
Leu56(A)
12a
Asn57(A)
Met66(A)
2.76
3.11
3.04

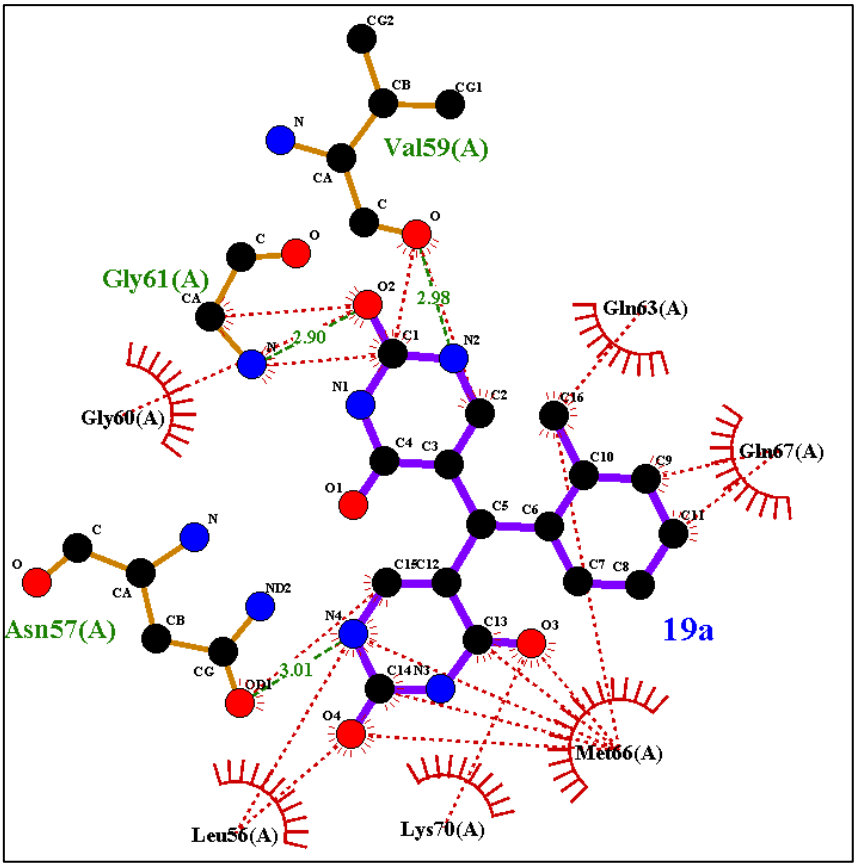

Asn57(A)
13a
Lys70(A)
Met66(A)
Gln67(A)
Val59(A)
Gln63(A)
Gly60(A)
Gly61(A)
2.96
2.88

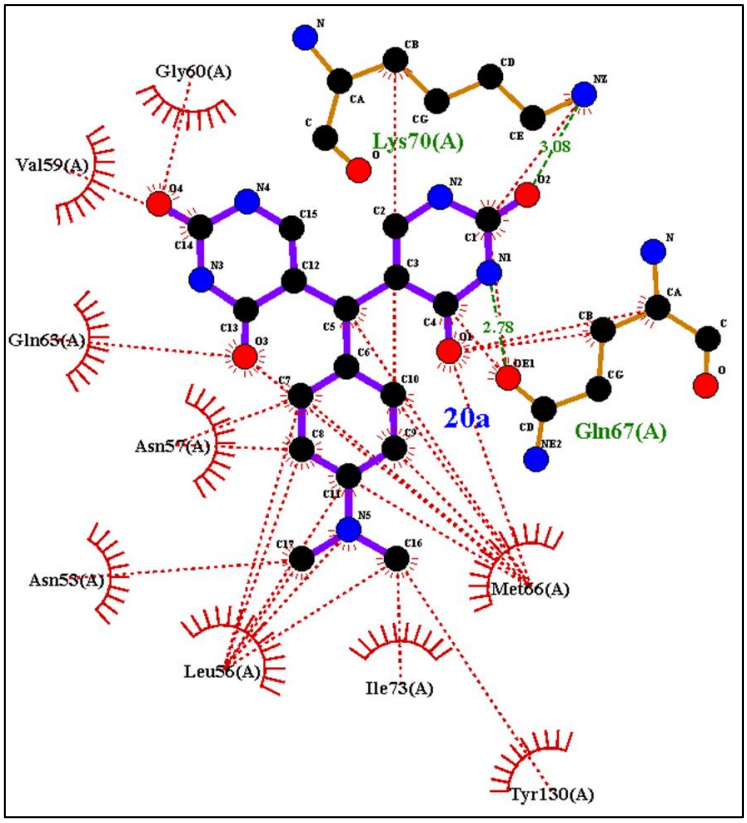

Gln63(A)
Gln67(A)
Gly60(A)
Gly61(A)
14a
Asn57(A)
Met66(A)
Leu56(A)
3.03
2.76
3.11

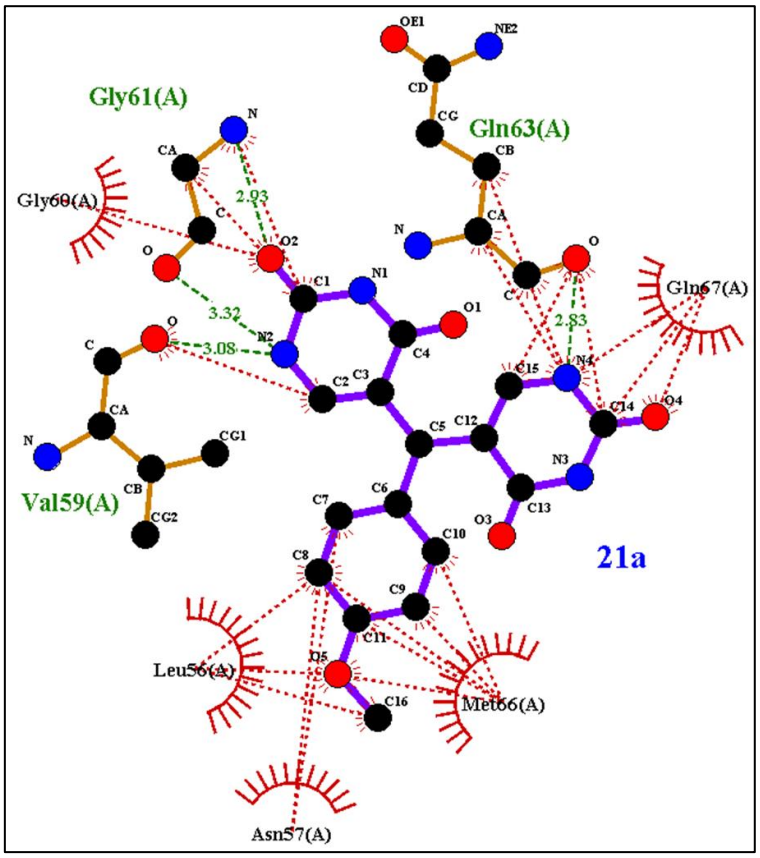

Val59(A)
Gly61(A)
Gly60(A)
Asn57(A)
15a
Met66(A)
Gln67(A)
Lys70(A)
Gln63(A)
2.99
3.02
3.05

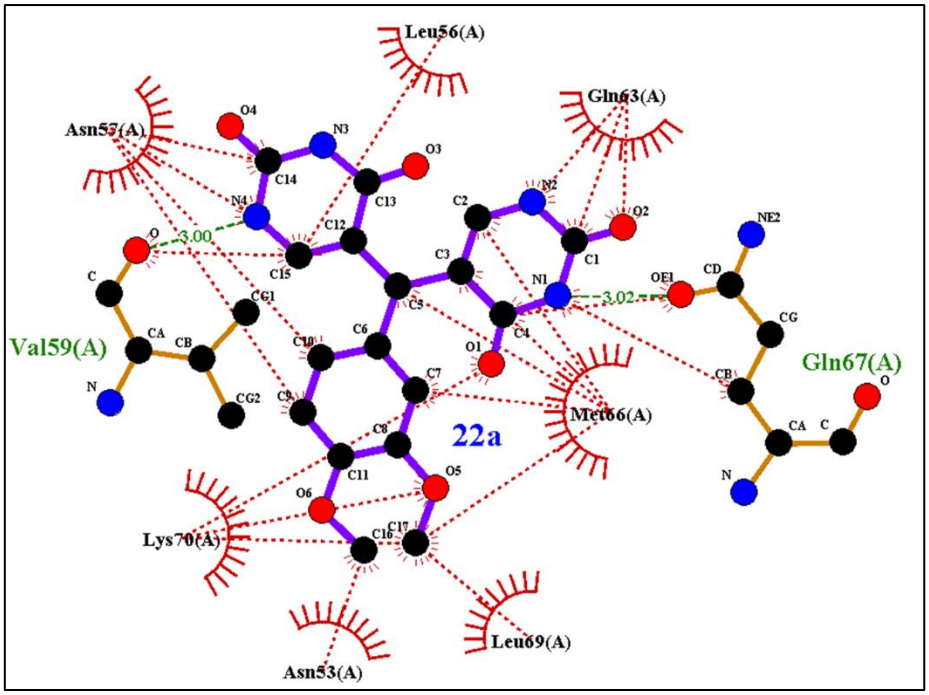

Gly60(A)
Gln63(A)
Gly61(A)
Gln67(A)
Val59(A)
16a
Met66(A)
Asn57(A)
Leu56(A)
2.86
3.03
3.22

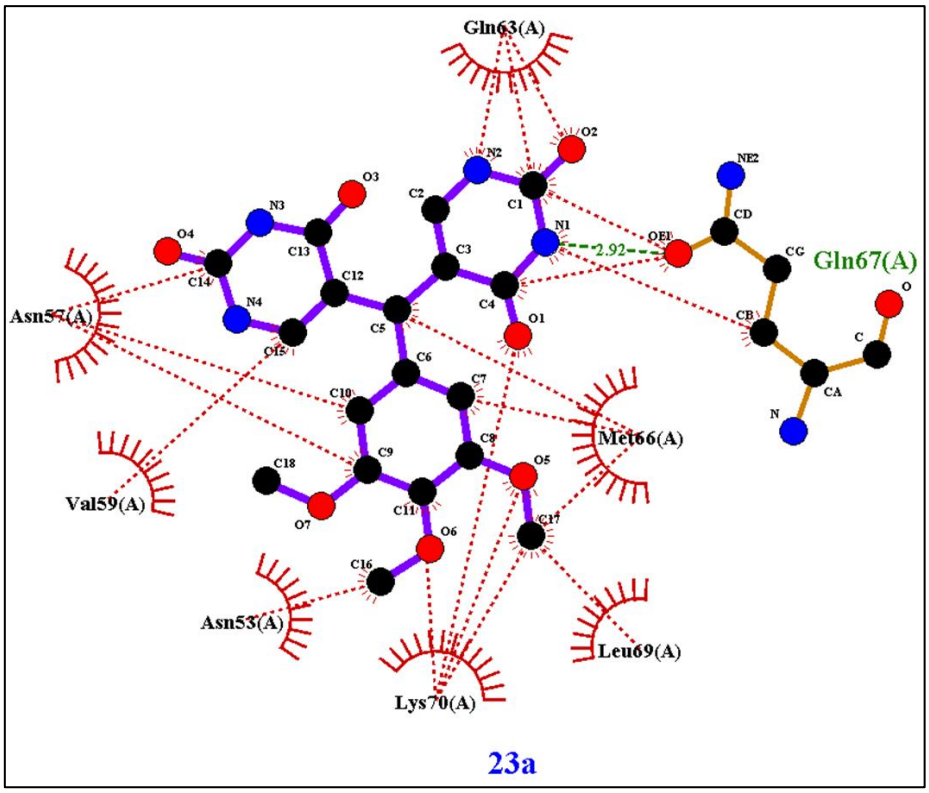

Gln67(A)
Tyr130(A)
Lys70(A)
Leu56(A)
Asn53(A)
Met66(A)
Asn57(A)
Val59(A)
18a

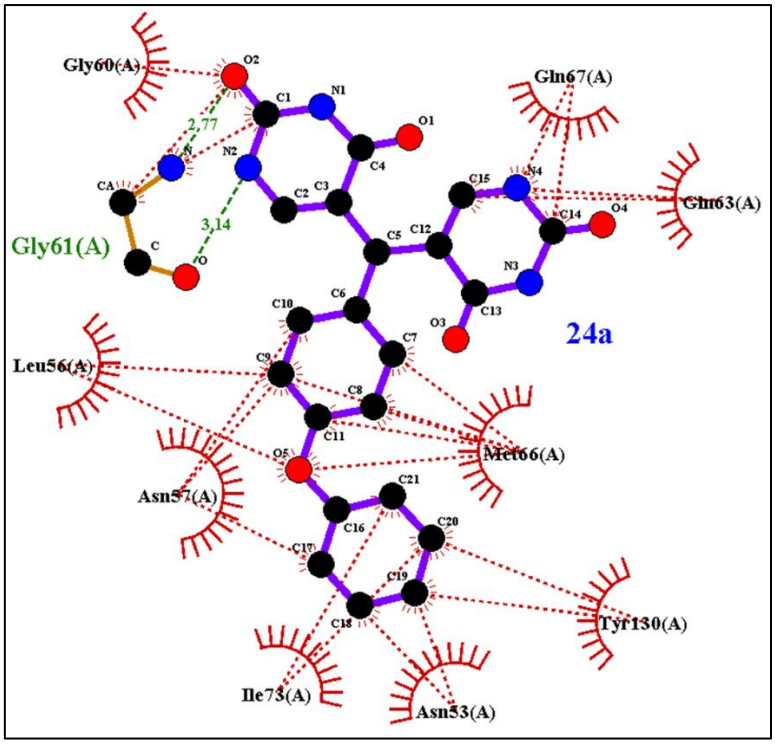

Val59(A)
Gly61(A)
Gln63(A)
Gly60(A)
Gln67(A)
Asn57(A)
19a
Met66(A)
Leu56(A)
Lys70(A)

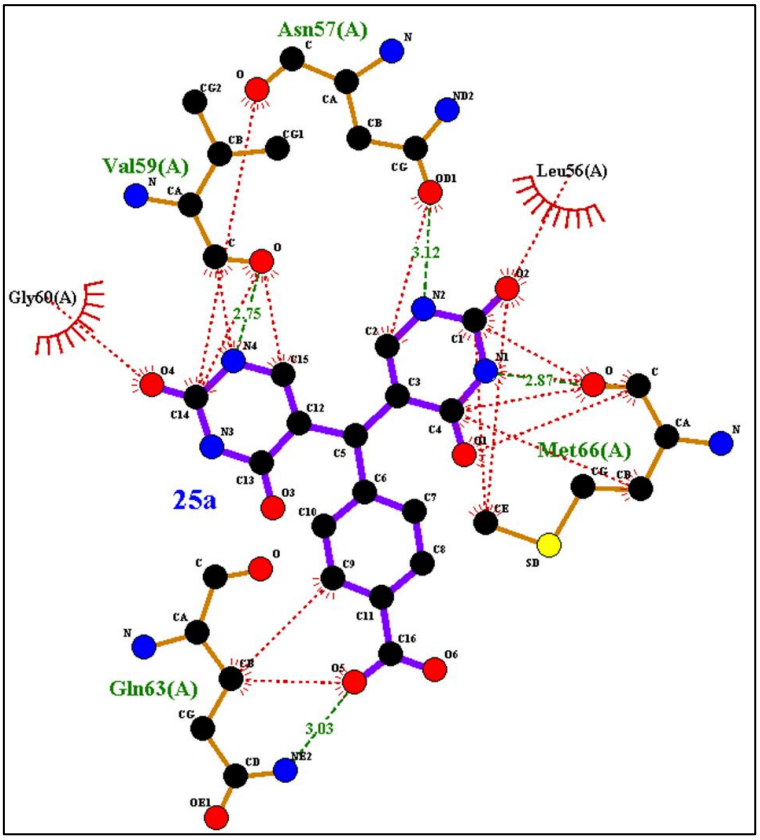

Gly60(A)
Lys70(A)
Val59(A)
3.08
2.78
Gln63(A)
20a
Gln67(A)
Asn57(A)
Asn58(A)
Met66(A)
Leu56(A)
Ile73(A)
Tyr130(A)

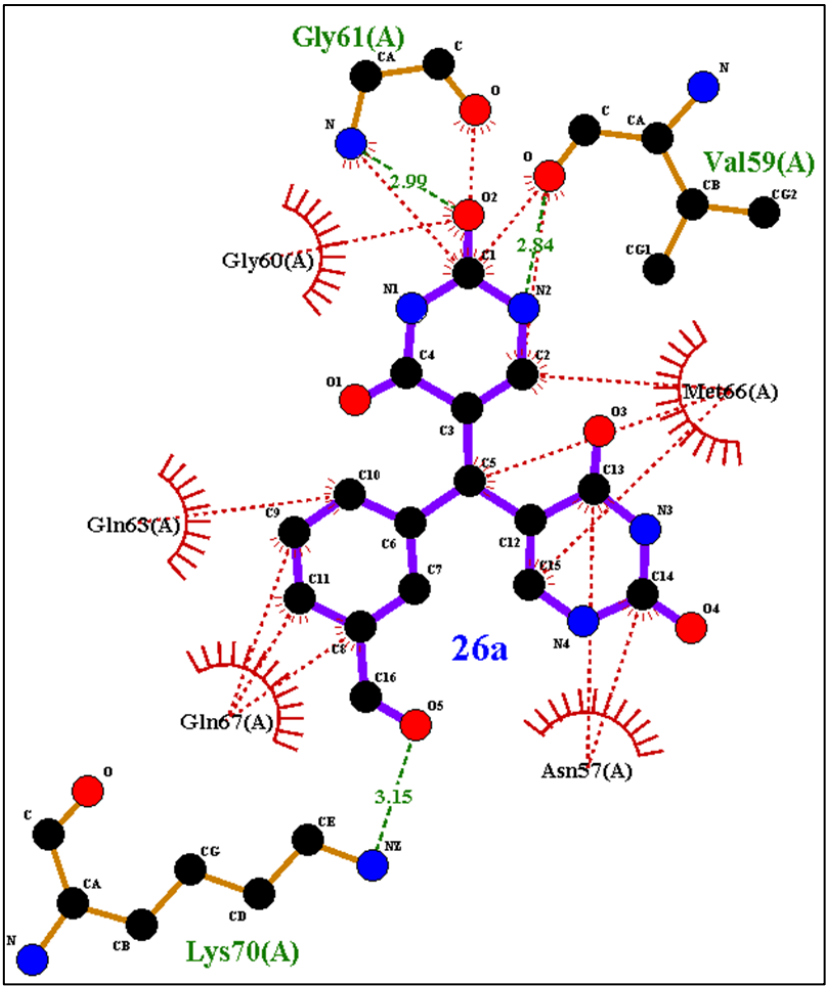

Gly61(A)
Gln63(A)
Gly60(A)
2.93
3.32
3.08
2.83
Gln67(A)
Val59(A)
21a
Leu56(A)
Met66(A)
Asn57(A)

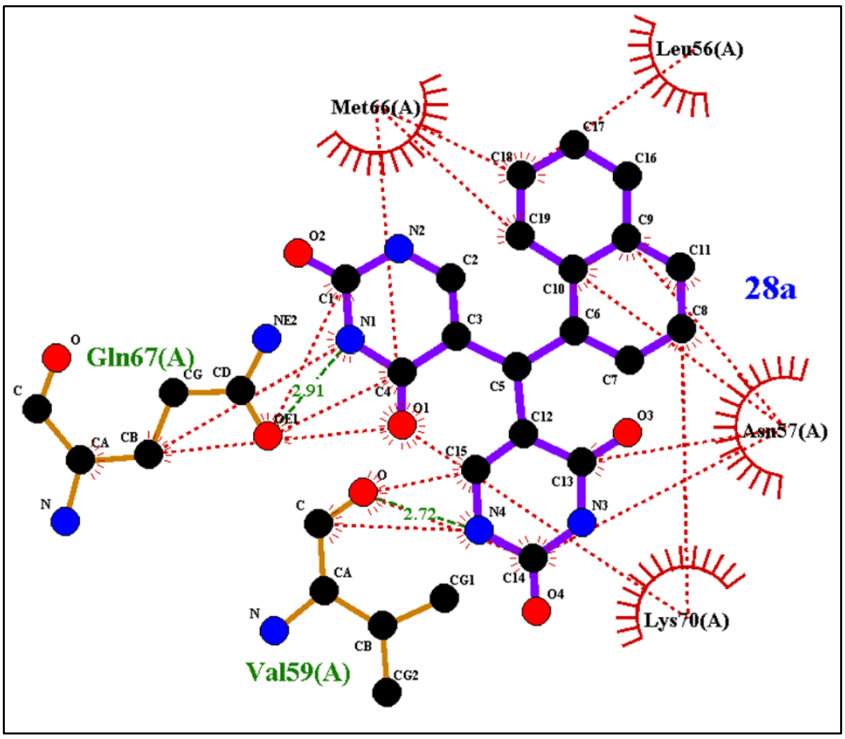

Leu56(A)
Gln63(A)
Asn57(A)
Val59(A)
Gln67(A)
Met66(A)
Lys70(A)
Leu69(A)
Asn53(A)
22a
3.00
3.02


Gln63(A)
Gln67(A)
Asn57(A)
Met66(A)
Val59(A)
Asn53(A)
Leu69(A)
Lys70(A)
23a
2.92


Gly60(A)
Gln67(A)
Gln63(A)
Gly61(A)
Leu56(A)
Met66(A)
Asn57(A)
Tyr130(A)
Ile73(A)
Asn53(A)
24a
2.77
3.14


Asn57(A)
Val59(A)
Leu56(A)
Gly60(A)
Met66(A)
Gln63(A)
25a
3.12
2.75
2.87
3.03


Gly61(A)
Val59(A)
Gly60(A)
Met66(A)
Gln65(A)
Gln67(A)
Asn57(A)
Lys70(A)
26a
2.99
2.84
3.15


Leu56(A)
Met66(A)
Gln67(A)
Asn57(A)
Lys70(A)
Val59(A)
28a
2.91
2.72

I. **Table S4** Percentage inhibition of bis(pyrimidine-2,4(1*H*,3*H)*-diones on HIV-1 p24 antigen production at 1 µg/ml

Sample Code	**% Inhibition at 1 µg/ml**
1a	4 %
2a	20 %
3a	23 %
4a	3 %
5a	28 %
6a	11 %
7a	**74 %**
8a	**69 %**
9a	**58 %**
10a	20 %
11a	7 %
12a	22 %
13a	**65 %**
14a	43 %
15a	42 %
16a	12 %
17a	10 %
18a	21 %
19a	**64 %**
20a	7 %
21a	5 %
22a	19 %
23a	32 %
24a	33 %
25a	16 %
26a	7 %
27a	20 %
28a	22 %

J. Table S5 Inhibition of p24 of HIV-1C by bis(pyrimidine-2,4(1*H*,3*H*)-diones. Azidothymidine (AZT) was used as positive control and virus control was $1x10^4$ PFU/ml.

Sr. No:	Sample concentration (µg/ml)	% Inhibition of samples				
		7a	**8a**	**9a**	**13a**	**19a**
1.	1000	90	97	93	88	89
2.	500	63	83	86	70	78
3.	250	55	70	77	61	55
4.	125	42	51	63	52	48
5.	62.5	30	32	50	39	35
6.	31.25	<25	30	33	31	31
7.	15.6	<25	<25	<25	<25	<25
8.	7.8	<25	<25	<25	<25	<25
9.	3.9	<25	<25	<25	<25	<25
10.	1.95	<25	<25	<25	<25	<25

K. Cytotoxicity studies

Cell cytotoxicity assay was performed using WST-1 (Roche, Basel, Switzerland) according to manufacturer's protocol. Mo7e and BA/F3 cells were plated in 96-well tissue culture plate at a concentration of 20,000 cells per well in 100 µL of media and stimulated with different concentrations of compounds 7a, 8a, 9a, 13a and 19a for 24 hours. Cells were also treated only with DMSO to exclude solvent induced cytotoxicity. After incubation, 10 µL of WST-1 reagent was added and absorbance was measured against a background control as blank using microplate (ELISA) reader at 440 nm. Statistical analysis was performed using GraphPad Prism v.6.0.1 (GraphPad Software, Inc., CA, US). P values of <0.05 are considered significant.