1*H*-Benzimidazole-5-Carboxamidines Derivatives: Design, Synthesis, Molecular Docking, DFT and Antimicrobial Studies

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SUPPORTING INFORMATION

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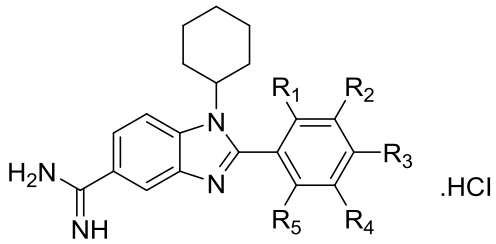
Table S1. List of synthesized compounds



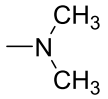
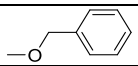
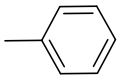
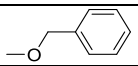
Compound	R_1	R_2	R_3	R_4	R_5
M1	-H	-H	$-CH_3$	-H	-H
M2	-H	-H	C_2H_5	-H	-H
M3	-H	-H	$-OCH_3$	-H	-H
M4	-H	-H	-Br	-H	-H
M5	-H	-H	-Cl	-H	-H
M6	-H	-H		-H	-H
M7	-H	-H		-H	-H
M8	-H	-H		-H	-H
M9	-H	-H	-COOH	-H	-H
M10	-H	-COOH	-H	-H	-H
M11	$-CH_3$	-H	-H	-H	-H
M12		-H	-H	-H	-H
M13	$-OCH_3$	-H	-H	-H	-H
M14	-F	-H	-H	-H	-H
M15	-H	-F	-H	-H	-H

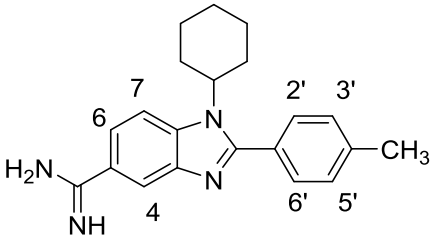
Table S2. Calculated electronic properties **(M1-M15)**

Compound	IP (-HOMO)	EA (-LUMO)	Χ (*I*P+E*A*)/ 2	ή (*I*P−E*A*/)2	S (1 /2ή)	μ −(IP+EA)/2	ω (μ2 /2η)
M1	0.2091	0.04849	0.128795	0.080305	6.226262	-0.1288	0.103282
M2	0.20827	0.04766	0.127965	0.080305	6.226262	-0.12797	0.101955
M3	0.20508	0.0426	0.12384	0.08124	6.154604	-0.12384	0.094389
M4	0.21955	0.05577	0.13766	0.08189	6.105752	-0.13766	0.115706
M5	0.21066	0.05722	0.13394	0.07672	6.517205	-0.13394	0.116918
M6	0.18287	0.02934	0.106105	0.076765	6.513385	-0.10611	0.073329
M7	0.21133	0.0362	0.123765	0.087565	5.710044	-0.12377	0.087465
M8	0.20563	0.06337	0.1345	0.07113	7.029383	-0.1345	0.127163
M9	0.2133	0.07899	0.146145	0.067155	7.445462	-0.14615	0.159023
M10	0.21256	0.0687	0.14063	0.07193	6.951203	-0.14063	0.137473
M11	0.20803	0.04758	0.127805	0.080225	6.232471	-0.12781	0.101802
M12	0.19774	0.04087	0.119305	0.078435	6.374705	-0.11931	0.090736
M13	0.2022	0.04392	0.12306	0.07914	6.317918	-0.12306	0.095677
M14	0.20696	0.05216	0.12956	0.0774	6.459948	-0.12956	0.108435
M15	0.21853	0.05794	0.138235	0.080295	6.227038	-0.13824	0.118992

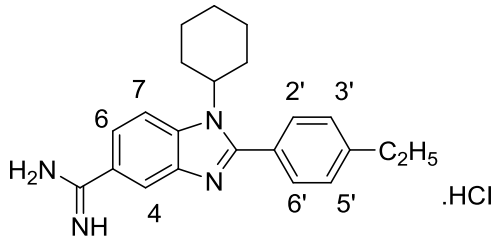
Table S3. Calculated ADME parameters **(M1-M15)**

Comp.	MW	Donor HB	Accpt HB	QPlogPo/w	QPlogS	% HumanOralAbsorption	PSA	Rule Of Five	Rule Of Three
M1	332.447	3.000	3.000	4.017	-5.839	100.000	63.566	0	1
M2	346.474	3.000	3.000	4.360	-6.202	100.000	63.538	0	1
M3	348.447	3.000	3.750	3.836	-5.566	100.000	71.867	0	0
M4	397.317	3.000	3.000	4.288	-6.149	100.000	63.591	0	1
M5	397.317	3.000	3.000	4.288	-6.149	100.000	63.591	0	1
M6	352.866	3.000	3.000	4.213	-6.036	100.000	63.591	0	1
M7	361.489	3.000	4.000	4.178	-6.220	100.000	67.002	0	1
M8	424.544	3.000	3.750	5.668	-7.730	96.800	71.169	1	1
M9	394.518	3.000	3.000	5.319	-7.259	94.828	63.494	1	1
M10	362.430	4.000	5.000	2.986	-5.166	65.270	113.935	0	1
M11	362.430	4.000	5.000	3.031	-5.013	67.140	113.834	0	1
M12	332.447	3.000	3.000	3.968	-5.536	100.000	63.521	0	0
M13	424.544	3.000	3.750	5.810	-7.561	100.000	68.675	1	1
M14	348.447	3.000	3.750	3.831	-5.366	100.000	70.359	0	0
M15	336.411	3.000	3.000	3.897	-5.478	100.000	63.730	0	0

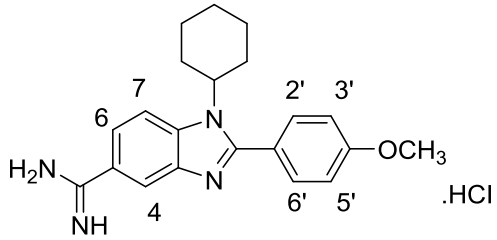
DonorHB: Estimated number of hydrogen bonds that would be donated by the solute to water molecules in an aqueous solution (recommended value:0-6); Acceptor HB: Estimated number of hydrogen bonds that would be accepted by the solute from water molecules in an aqueous solution (recommended value:2-20); QPlogPo/w: Predicted octanol/water partition coefficient (recommended value:-2-6.5); PSA: Van der Waals surface area of polar nitrogen and oxygen atoms and carbonyl carbon atoms (recommended value:7-200); Rule of Five: Number of violations of Lipinski's rule of five [41]. The rules are: mol MW < 500, QPlogPo/w < 5, donorHB ≤ 5, accptHB≤ 10.Compounds that satisfy these rules are considered druglike. (The "five" refers to the limits, RuleOfThree Number of violations of Jorgensen's rule of three. The three rules are: , QPlogS > -5.7, QP PCaco > 22 nm/s, # Primary Metabolites < 7.



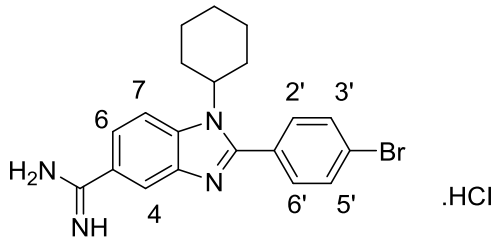
1-cyclohexyl-2-(4-methylphenyl)-1*H*-benzimidazole-5-carboxamidine HCl (M1): Yield 35%, Mp: 264-266^{0}C. ^{1}H-NMR δ ppm (DMSO-d_6): 1.20-1.61 (m, 4H, cyclohexyl -CH_2), 1.80-1.89 (m, 4H, cyclohexyl -2CH_2), 2.21-2.30 (m, 2H, cyclohexyl -CH_2), 2.40 (s, 3H, -CH_3), 4.24-4.30 (m, H, cyclohexyl -CH), 7.39 (d, 2H, Jo=7.6 Hz, H-3',5'), 7.53 (d, 2H, Jo= 8.4 Hz, H-2',6'), 7.68 (dd, H, Jo= 8.4 Hz, Jm= 2 Hz, H-6), 8.01 (d, H, Jo=8.4 Hz, H-7), 8.19 (d, H, Jm=1.6 Hz, H-4). ^{13}C-NMR δ ppm (DMSO-d_6): 20,91, 24,89, 25,43, 30,38, 56,80, 113.27, 119.24, 121.00, 122.68, 127.14, 129.32, 136.66, 139.79, 142.76, 155.49, 166.04, 176.58. MS (ESI+) *m*/*z*: 333.4 (M+H, 80%), 251.3 (100%). Anal. Calcd for $C_{21}H_{24}N_4$.1,5 HCl . 0,5 C_2H_6O; C: 65.89, H: 7.10, N:13.97 Found; C: 65.55, H:7.23, N: 14.01.



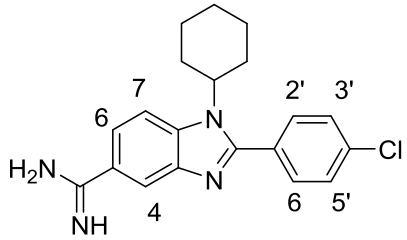
1-cyclohexyl-2-(4-ethylphenyl)-1*H*-benzimidazole-5-carboxamidine HCl (M2): Yield 40%, Mp: 300^{0}C. ^{1}H-NMR δ ppm (DMSO-d_6): 1.24.1.38 (t, 3H, -CH_2-$\underline{CH_3}$), 1.39-1.64 (m, 4H, -2CH_2), 1.85 (d, 2H, -CH_2), 1.94 (d, 2H, -CH_2), 2.26-2.34 (m, 2H, -CH_2), 2.71-2.77 (q, 2H, -$\underline{CH_2}$-CH_3), 4.31- 4.37 (m, H, -CH), 7.47 (d, 2H, Jo=8.0 Hz, H-3',5'), 7.63 (d, 2H, Jo=8.0 Hz, H-2',6'), 7.79 (dd, H, Jo= 8.8 Hz, Jm= 1.6 Hz, H-6), 8.17 (d, H, Jo= 8.8 Hz, H-7), 8.30 (d, H, Jm=1.6 Hz, H-4), 9.26 (s, 2H), 9.48 (s, 2H). ^{13}C-NMR δ ppm (DMSO-d_6) : 15.20, 24.16, 25.45, 28.01, 30.35, 57.18, 113.81, 119.46, 121.43, 121.93, 126.47, 128.29, 129.48, 136.86, 141.39, 146.46, 155.48, 165.71. MS (ESI+) *m*/*z*: 347.5 (M+H, 90%), 265.4 (100%). Anal. Calcd for $C_{22}H_{26}N_4$.1,25 HCl.0,5 C_2H_6O.0,75 H_2O C:68.22, H:7.45, N: 14.14 Found; C: 68.50, H: 7.51, N:14.40.



1-cyclohexyl-2-(4-methoxyphenyl)-1*H*-benzimidazole-5-carboxamidine HCl (M3): Yield 70%, M.p. 118-120^{0}C. ^{1}H-NMR δ ppm (DMSO-d_6): 1.22-1.63 (m, 4H, -2CH_2, 1.81-1.89 (t, 4H, -2CH_2), 2.22-2.31 (m, 2H, -CH_2), 3.84 (s, 3H, -OCH_3), 4.23-4.26 (t, H, -CH), 7.12 (d, 2H, Jo=8.8 Hz, H-3',5'), 7.58 (d, 2H, Jo= 8.8 Hz, H-2'-6'), 7.68 (d, H, Jo=8.4 Hz, H-6), 7.87 (d, H, Jo=8.4 Hz, H-7), 8.09 (d, H, Jm=1.2 Hz, H-4) ^{13}C-NMR δ ppm (DMSO-d_6) : 24.82, 25.45, 32.95, 57.09, 62,25, 113.69, 120.21, 121.15, 121.81, 123.92, 129.17, 131.49, 131.91, 137.26, 142.69, 154.69, 165.78. MS (ESI+) *m/z*: 349.37 (M+H, 50%), 267.27 (100%). Anal. Calcd for $C_{21}H_{24}N_4O$.1,25 HCl . 0,25 C_2H_6O. 3 H_2O; C:56.19, H:7.18, N:12.19, Found; C: 56.35, H: 7.01, N:12.50.

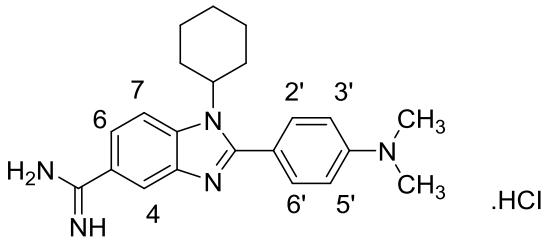


1-cyclohexyl-2-(4-bromophenyl)-1*H*-benzimidazole-5-carboxamidine HCl (M4): Yield 48%, M.p. 344-347^{0}C. ^{1}H-NMR δ ppm (DMSO-d_6): 1.23-1.63 (m, 4H, -2CH_2), 1.84 (d, 2H, -CH_2), 1.93 (d, 2H, -CH_2), 2.24-2.32 (q, 2H, -CH_2), 4.24- 4.30(m, H, -CH), 7.65 (d, 2H, Jo=8.0 Hz, H-3', 5'), 7.77 (dd, H, Jo=8.4 Hz, Jm=1.6 Hz, H-6), 7.82 (d, 2H, Jo= 8.4 Hz, H-2',6'), 8.13 (d, H, Jo=8.8 Hz, H-7), 8.30 (d, H, Jm=1.2 Hz, H-4), 9.34 (br, s, 4H, $NH_{amidine}$).^{13}C-NMR δ ppm (DMSO-d_6) : 24.19, 25.39, 30.44, 57.08, 113.68, 120.20, 121.14, 121.79, 123.90, 129.16, 131.48, 131.90, 137.25, 142.68, 154.68, 165.76. MS (ESI+) *m/z*: 397.29 (M+H, 100%), 399.25 (M+H+2, 95%). Anal. Calcd for $C_{20}H_{21}BrN_4$ .3 HCl.1,25 H_2O. 0,65 C_2H_6O C: 45.75, H 5.48, N: 10.02, Found; C: 45.53, H: 5.45, N:10.38**.**



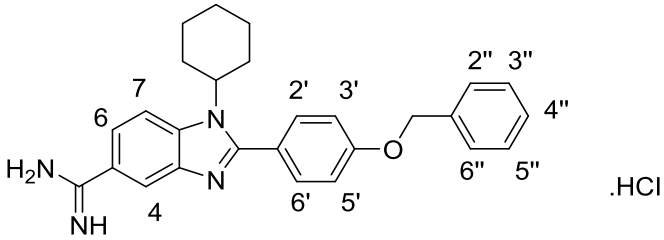
.HCl

1-cyclohexyl-2-(4-chlorophenyl)-1*H*-benzimidazole-5-carboxamidine HCl (M5): Yield 25%, M.p. 210-212^{0}C. ^{1}H-NMR δ ppm (DMSO-d_6): 1.26-1.65 (m, 4H, -2CH_2), 1.70 (d, 2H, -CH_2), 1.93 (d, 2H, -CH_2), 2.24-2.37 (m, 2H, -CH_2), 4.23-4.30 (m, H, -CH), 7.64 (d, 2H, Jo=8.4 Hz, H-3',5'), 7.78 (dd, H, Jo=8.4 Hz, Jm=1.6 Hz, H-6), 7.82 (d, 2H, Jo=8.4 Hz, H-2', 6'), 8.13 (d, H, Jo=8.4 Hz, H-7), 8.30 (d, H, Jm=1.2 Hz, H-4), 9.36 (br, s, 4H, $NH_{amidine}$).^{13}C-NMR δ ppm (DMSO-d_6) : 24.21, 25.41, 30.46, 57.09, 113.69, 120.21, 121.15, 121.81, 123.92, 129.17, 131.91, 137.26, 142.26, 142.69, 154.69, 165.78. MS (ESI+) *m/z*: 353.4 (M+H, 95%), 355.4 (%M+H+2, 40%), 271.3 (%100). Anal. Calcd for $C_{22}H_{27}N_5$. 1,55 HCl.C_2H_6O. 0,25 H_2O. C: 57.45, 4:6.37, N:12.18, Found; C: 57.72, H: 6.15, N: 11.87.

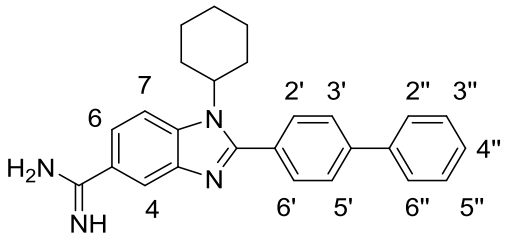


.HCl

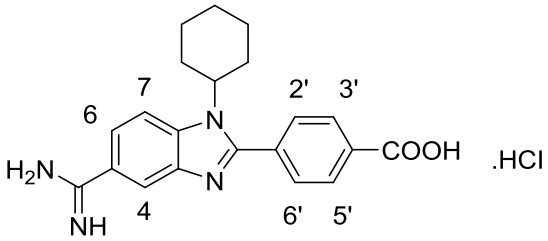
1-cyclohexyl-2-(4-dimethylaminophenyl)-1*H*-benzimidazole-5-carboxamidine HCl (M6): Yield: 17%, M.p. 210-212^{0}C. ^{1}H-NMR δ ppm (DMSO-d_6): 1.14-1.63 (m, 4H, -2CH_2), 1.85 (t, 4H, -2CH_2), 2.24-2.32 (q, 2H, -CH_2), 2.99 (s, 6H, -N(CH_3)$_2$), 4.37 (t, H, -CH), 6.85 (d, 2H, Jo= 8.4 Hz, H-3',5'), 7.48 (d, 2H, Jo=8.4 Hz, H-2', 6'), 7.67 (d, H, Jo=8.4 Hz, H-6), 8.02 (d, H, Jo=8.8 Hz, H-7), 8.18 (s, H, H-4), 9.20 (br, s, 4H, $NH_{amidine}$).^{13}C-NMR δ ppm (DMSO-d_6) : 24.19, 25.49, 30.35, 56.79, 111.58, 113.16, 116.24, 119.31, 120.64, 120.90, 130.18, 137.38, 142.91, 151.09, 156.55, 165.83. MS (ESI+) *m/z*: 362.5 (M+H, 40%), 280.4 (100%). Anal. Calcd for $C_{22}H_{27}N_5$. 3 HCl . 1.5 C_2H_6O C: 55.61, H:7.28, N: 12.97, Found; C:56.05, H:7.33, N:12.80.



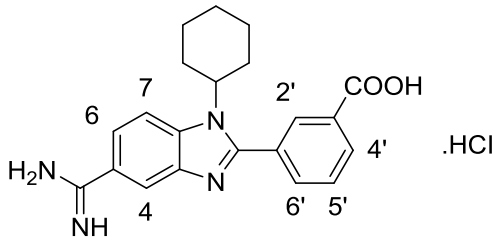
1-cyclohexyl-2-(4-benzyloxyphenyl)-1*H*-benzimidazole-5-carboxamidine HCl (M7): Yield 10%, M.p. 192-195^{0}C. ^{1}H-NMR δ ppm (DMSO-d_6): 1.1-1.51 (m, 4H, -2CH_2), 1.55-1.8 (m, 4H, -2CH_2), 2.08 (d, 2H, -CH_2), 3.88-3.94 (t, H, -CH), 5.18 (s, 2H, -OCH_2), 7.15 (dd, H, H, Jo=7.2, Jo'=7.6, H-4''), 7.23-7.33 (m, 5H), 7.44 (dd, H, Jo=7.2 Hz Jm=1.6 Hz), 7.58 (m, H), 7.69 (dd, H, Jo=8.4 Hz, Jm=1.6 Hz, Jo=8.4, H-6), 8.00 (d, H, Jo= 8.0 Hz, H-7), 8.24 (d, H, Jm=2 Hz, H-4), 9.08 (br, s, 4H, $NH_{amidine}$). ^{13}C-NMR δ ppm (DMSO-d_6) : 24.73, 26.00, 27.33, 57.06, 70.28, 113.23, 119.85, 120.43, 121.30, 121.37, 121.88, 128.15, 128.45, 128.81, 132.45, 136.80, 137.15, 143.43, 154.18, 156.79, 166.23 MS (ESI+) *m/z*: 425.28 (M+H, 70%), 343.4 (100%). Anal. Calcd for $C_{27}H_{28}N_4O$. 2HCl . 0,75 H_2O C: 63.47, H: 6.21, N:10.96, Found; C: 63.78, H: 5.89, N: 11.05.



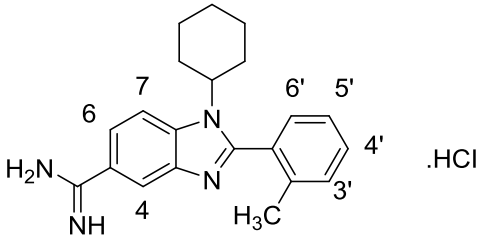
1-cyclohexyl-2-(1,1'-biphenyl-4-yl)-1*H*-benzimidazole-5-carboxamidine HCl (M8): Yield: 15%, M.p. 245^{0}C. ^{1}H-NMR δ ppm (DMSO-d_6): 1.22-1.64 (m, 4H, -2CH_2), 1.85-1.88 (t, 2H, -CH_2), 1.97 (d, 2H, -CH_2), 2.28-2.37 (q, 2H, -CH_2), 4.36-4.42 (m, H, -CH), 7.44-7.46 (d, H, Jo=8.0, H-6), 7.53 (d, 2H, Jo=7.6, H-3',5'), 7.76-7.81 (m, 5H, H-2'', 3'', 4'', 5'', 6''), 7.92 (d, 2H, Jo=8.4, H-2', 6'), 8.14 (d, H, Jo=8.4, H-7), 8.32 (d, H, Jm=0.8, H-4), 9.08 (br, s, 4H, NH_{amidin}). ^{13}C-NMR δ ppm (DMSO-d_6) : 24.22, 25.48, 30.48, 57.06, 113.63, 120.03, 121.26, 121.60, 126.84, 127.03, 128.10, 128.91, 129.10, 130.02, 137.29, 139.03, 141.68, 142.84, 155.43, 165.90 MS (ESI+) *m/z*: 395.6 (M+H, 70%), 313.2 (100%). Anal. Calcd for $C_{26}H_{26}N_4$. 0,75 HCl. 1,45 C_2H_6O. H_2O C: 70.99, H:6.59, N:12.74, Found; C: 70.80, H: 6.41, N: 12.98.



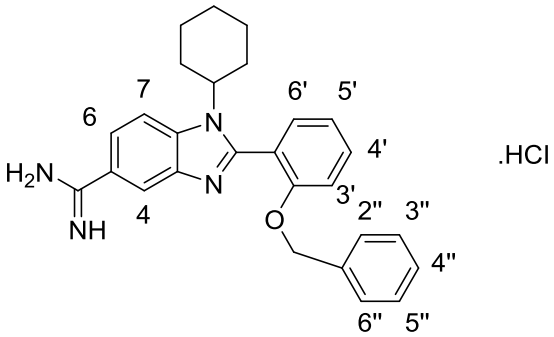
1-cyclohexyl-2- (4-carboxyphenyl)-1*H*-benzimidazole-5-carboxamidine HCl (M9): Yield: 55%, M.p. 280-282^{0}C. ^{1}H-NMR δ ppm (DMSO-d_6): 1.25-1.65 (m, 4H, -2CH_2), 1.83 (d, 2H, -CH_2), 1.92 (d, 2H, -CH_2), 2.24-2.31 (q, 2H, -CH_2), 4.24- 4.30(m, H, -CH), 7.67 (d, 2H, Jo=8 Hz, H-2',6'), 7.80 (dd, H, Jo=8.4 Hz, Jm=1.6 Hz, H-6), 7.86 (d, 2H, Jo= 8.4 Hz, H-3', 5'), 8.16 (d, H, Jo=8.8 Hz, H-7), 8.35 (d, H, Jm=1.2 Hz, H-4). ^{13}C-NMR δ ppm (DMSO-d_6): 24.18, 25.40, 30.48, 57.10, 115.67, 120.90, 121.33, 121.79, 123.98, 129.15, 131.34, 131.87, 137.25, 142.85, 154.71, 165.61, 168.85. MS (ESI+) *m*/*z*: 363.24 (M+H). Anal. Calcd for $C_{21}H_{22}N_4O_2$. 3HCl. C: 69.59, H:6.12, N:15.46, Found; C: 70.01, H: 6.15, N: 14.01.



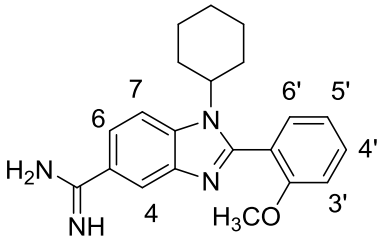
1-cyclohexyl-2-(3-carboxyphenyl)-1*H*-benzimidazole-5-carboxamidine HCl (M10): Yield: 25%, M.p. 254-256^{0}C. ^{1}H-NMR δ ppm (DMSO-d_6): 1.21-1.65 (m, 4H, -2CH_2), 1.87 (d, 2H, -CH_2), 1.90 (d, 2H, -CH_2), 2.24-2.34 (m, 2H, -CH_2), 4.24-4.28 (m, H, -CH), 7.51-7.56 (m, 3H, H-4',5', 6'), 7.66-7.71 (m, H, H-2'), 7.75 (dd, H, Jo=8.4 Hz, Jm=2 Hz, H-6), 8.15 (d, H, Jo=8.8 Hz, H-7), 8.28 (d, H, Jm=1.6 Hz, H-4). ^{13}C-NMR δ ppm (DMSO-d_6): 24.13, 25.37, 30.85, 57.08, 113.65, 116.60, 119.94, 121.41, 122.47, 125.63, 131.18, 132.14, 136.48, 143.49, 154.55, 161.72, 163.54, 165.08, 168.87. MS (ESI+) *m*/*z*: 363.5 (M+H, 70%), 281.4 (100%). Anal. Calcd for $C_{21}H_{22}N_4O_2$.1,75 HCl. 0,8 H_2O.0,5 C_2H_6O; C: 56.99, H:6.16, N:12,08 Found; C: 57.35, H: 6.01, N: 11.69.



1-cyclohexyl-2-(2-methylphenyl)-1*H*-benzimidazole-5-carboxamidine HCl (M11): Yield: 24%, M.p. 184-186^{0}C. ^{1}H-NMR δ ppm (DMSO-d_6): 1.15-1.39 (m, 4H, -2CH_2), 1.62-1.84 (m, 4H, -2CH_2), 2.19 (2H, -CH_2), 2.51 (s, 3H, -CH_3), 3.84-3.90 (t, H, -CH), 7.13-7.17 (m, H, H-3'), 7.25 (d, H, Jo= 8.4 Hz, H-4'), 7.42 (dd, H, Jo= 7.6 Hz, Jm=1.6 Hz, H-5'), 7.58-7.62 (m, H, H-6'), 7.73 (dd, H, Jo=8.8 Hz, Jm=2 Hz, H-6), 8.01 (d, H, Jo=8.8 Hz, H-7), 8.25 (s, H, H-4). ^{13}C-NMR δ ppm (DMSO-d_6): 17.25, 24.31, 25.57, 30.84, 57.05, 113.60, 116.57, 119.80, 121.53, 122.37, 125.60, 131.01, 132.19, 136.84, 142.65, 154.15, 160.71, 163.15, 166.01. MS (ESI+) *m*/*z*: 333.5 (M+H, 95%), 251.3 (100%). Anal. Calcd for $C_{21}H_{24}N_4$.HCl . 0,5 C_2H_6O. 0,25 H_2O; C :66.65, H:7.25, N:14.13, Found; C:66.81, H:6.89, N:14.45.

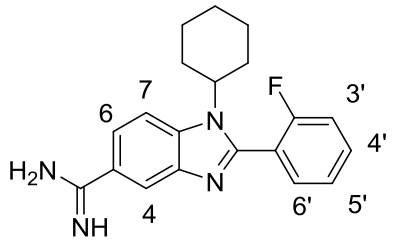


1-cyclohexyl-2-(2-benzyloxyphenyl)-1*H*-benzimidazole-5-carboxamidine HCl (M12): Yield: 20%, M.p. 192-195^{0}C. ^{1}H-NMR δ ppm (DMSO-d_6) : 1.17-1.51 (m, 4H, -2CH_2), 1.53-1.85 (m, 4H, -2CH_2), 2.18 (d, 2H, -CH_2), 3.90-3.97 (t, H, -CH), 5.25 (s, 2H, -OCH_2), 7.13-7.17 (m, H), 7.24-7.34 (m, 6H), 7.44 (dd, H, Jo=1.6 Hz, Jm=7.2 Hz), 7.56-7.61 (m, H), 7.69 (dd, H, Jo=8.4 Hz, Jm =1.6 Hz) , 8.00 (d, H, Jo= 8.0 Hz), 8.25 (d, H, Jm=2 Hz), 9.08 (br, s, 4H, $NH_{amidine}$). ^{13}C-NMR δ ppm (DMSO-d_6): 24.75, 26.04, 27.08, 57.06, 71.05, 113.65, 120.06, 121.28, 122.40, 124.80, 126.75, 127.04, 128.93, 129.16, 130.02, 132.25, 137.34, 138.03, 141.68, 144.84, 157.43, 165.80. MS (ESI+) *m*/*z*: 425.28 (M+H, 70%), 335.39 (100%). Anal. Calcd for $C_{27}H_{28}N_4O$. 1,5 HCl . 0,25 C_2H_6O . 0,5 H_2O;C: 52.65, H:5.70, N:8.93, Found; C: 52.41, H:5.88, N:9.08.



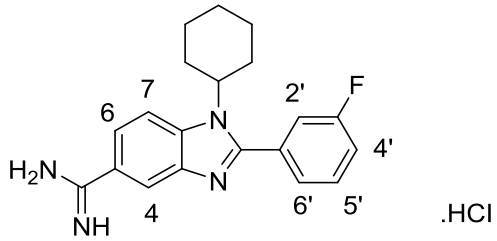
.HCl

1-cyclohexyl-2-(2-methoxyphenyl)-1*H*-benzimidazole-5-carboxamidine HCl (M13): Yield: 13%, M.p. 198-202^{0}C. ^{1}H-NMR δ ppm (DMSO-d_6): 1.14-1.39 (m, 4H, -2CH_2), 1.61-1.81 (m, 4H, -2CH_2), 2.18 (2H, -CH_2), 3.80 (s, 3H, -OCH_3), 4.04-4.10 (t, H, -CH), 7.12-7.16 (m, H, H-3'), 7.24 (d, H, Jo= 8.4 Hz, H-5'), 7.44 (dd, H, Jo= 7.6 Hz, Jm=1.6 Hz, H-4'), 7.57-7.63 (m, H, H-6'), 7.71 (dd, H, Jo=8.8 Hz, Jm=2 Hz, H-6), 8.02 (d, H, Jo=8.8 Hz, H-7), 8.30 (s, H, H-4). ^{13}C-NMR δ ppm (DMSO-d_6): 24.81, 25.23, 31.86, 57.05, 61.25, 113.68, 116.55, 118.72, 121.35, 121.89, 125.61, 132.01, 132.19, 137.47, 143.15, 154.57, 160.72, 163.51, 165.18. MS (ESI+) *m*/*z*: 349.2 (M+H, 100%), 267.1 (100%). Anal. Calcd for $C_{21}H_{24}N_4O$. 3 HCl. C: 55.09, H:5.94, N:12.24, Found; C: 55.18, H:6.05, N:12.60.



.HCl

1-cyclohexyl-2-(2-fluorophenyl)-1*H*-benzimidazole-5-carboxamidine HCl (M14): Yield: 9%, M.p. 242-244^{0}C. ^{1}H-NMR δ ppm (DMSO-d_6): 1.20-1.62 (m, 4H, -2CH_2), 1.81-1.87 (q, 4H, -2CH_2), 2.17-2.25 (m, 2H, -CH_2), 3.98-4.04 (t, H, -CH), 7.43-7.51 (m, 2H, H-3',5'), 7.64-7.74 (m, 2H, H-4', 6'), 7.76 (dd, H, Jo=8.0, Jm=1.6, H-6), 8.13 (d, H,, Jo=8.8, H-7), 8.29 (d, H, Jm=1.2, H-4). ^{13}C-NMR δ ppm (DMSO-d_6): 24.85, 25.52, 31.58, 57.08, 112.58, 115.77, 119.88, 122.53, 123.74, 126.87, 132.21, 133.87, 136.83, 142.47, 154.18, 161.58, 163.21, 167.01. MS (ESI+) *m*/*z*: 337.2 (M+H, 100%), 255.1 (100%). Anal. Calcd for $C_{20}H_{21}FN_4$.1,25 HCl . 0,5 C_2H_6O C: 62.89, H:5.87, N:14.67 Found; C: 63.05, H:5.87, N:14.67.



1-cyclohexyl-2-(3-fluorophenyl)-1*H*-benzimidazole-5-carboxamidine HCl (M15): Yield 10%, M.p. 224-226^{0}C. ^{1}H-NMR δ ppm (DMSO-d_6): 1.17-1.63 (m, 4H, -2CH_2), 1.84 (d, 2H, -CH_2), 1.95 (d, 2H, -CH_2), 2.22-2.31 (m, 2H, -CH_2), 4.23-4.29 (m, H, -CH), 7.44-7.53 (m, 3H, H-4', 5', 6'), 7.64-7.69 (m, H, H-2'), 7.72 (dd, H, Jo=8.4 Hz, Jm=2 Hz, H-6), 8.09 (d, H, Jo=8.8 Hz, H-7), 8.25 (d, H, Jm=1.6 Hz, H-4). ^{13}C-NMR δ ppm (DMSO-d_6): 24.21, 25.44, 30.43, 57.05, 113.60, 116.34, 119.80, 121.53, 122.37, 125.58, 132.01, 132.21, 136.84, 142.65, 154.15, 160.71, 163.15, 166.01. MS (ESI+) *m*/*z*: 337.5 (M+H, 100%), 255.0 (50%). Anal. Calcd for $C_{20}H_{21}FN_4$.2,25HCl.C_2H_6O. 0,5 H_2O; C:55.80, H:6.44, N:11.83 Found; C:55.47, H: 6.87, N:12.01.

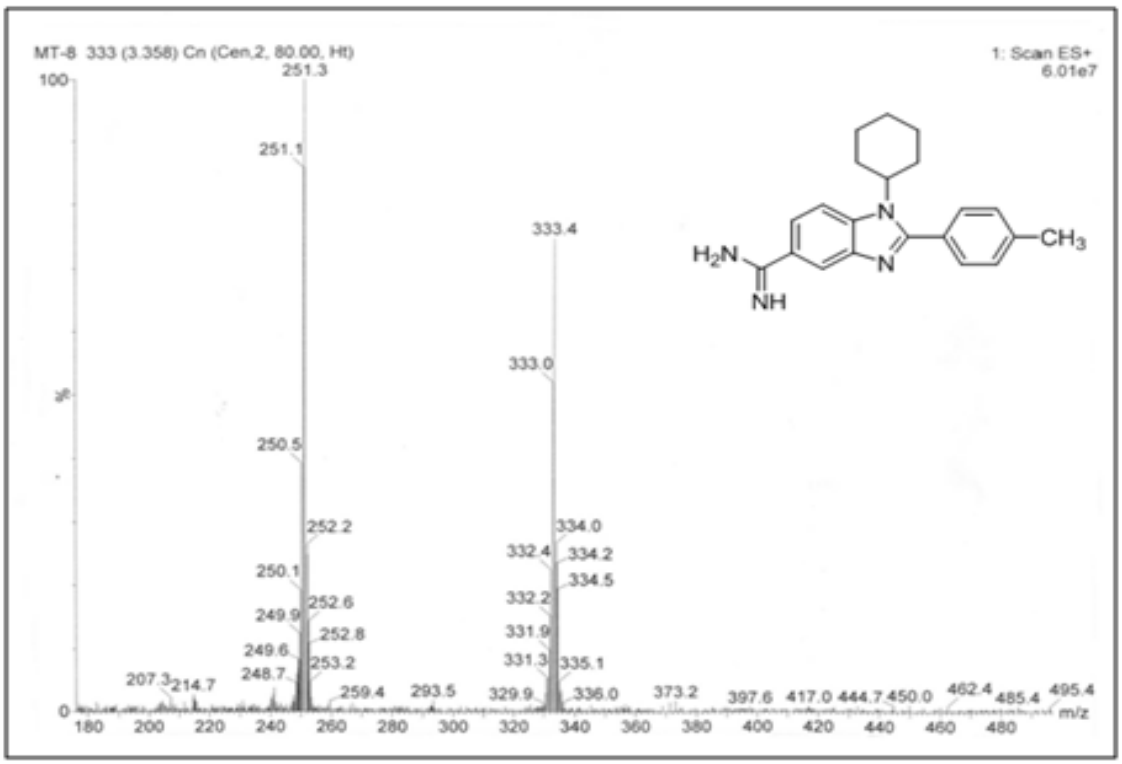


Figure 1. MASS spectra of M1

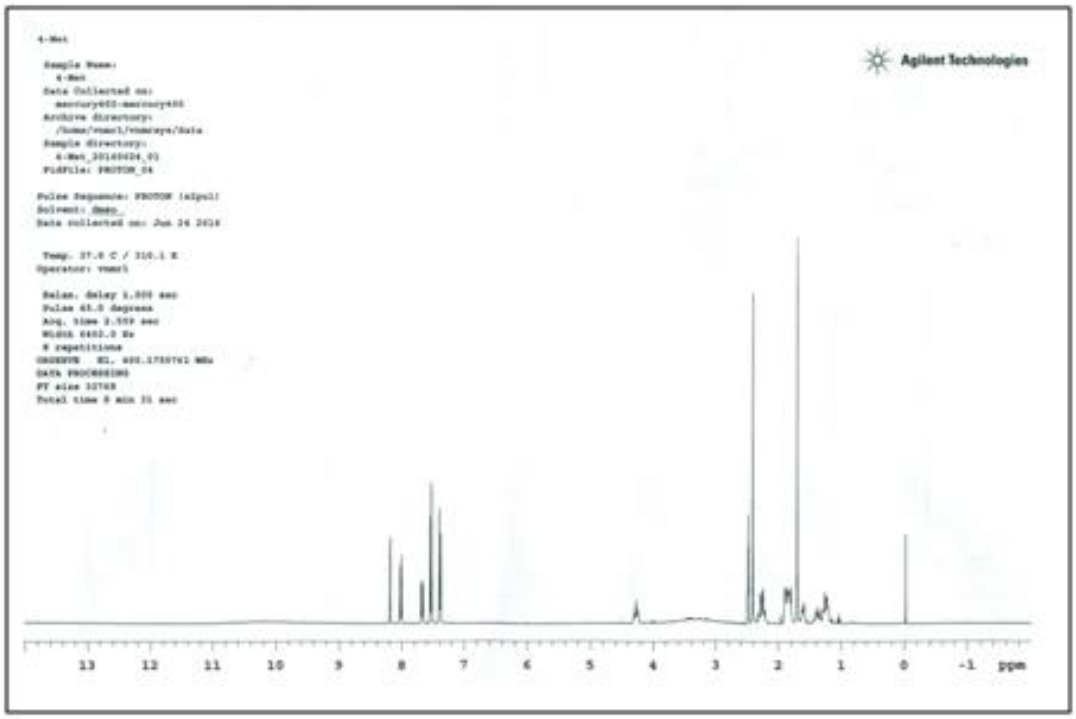


Figure 2. ^{1}H-NMR spectra of M1

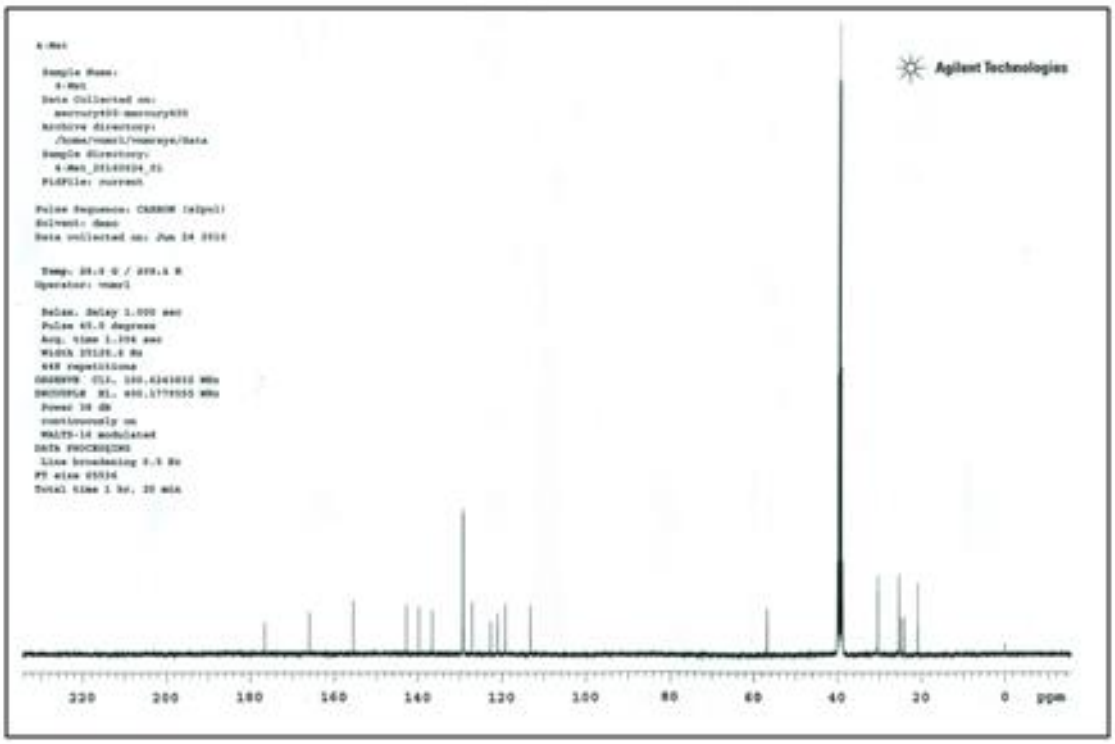


Figure 3. ^{13}C-NMR spectra of M1

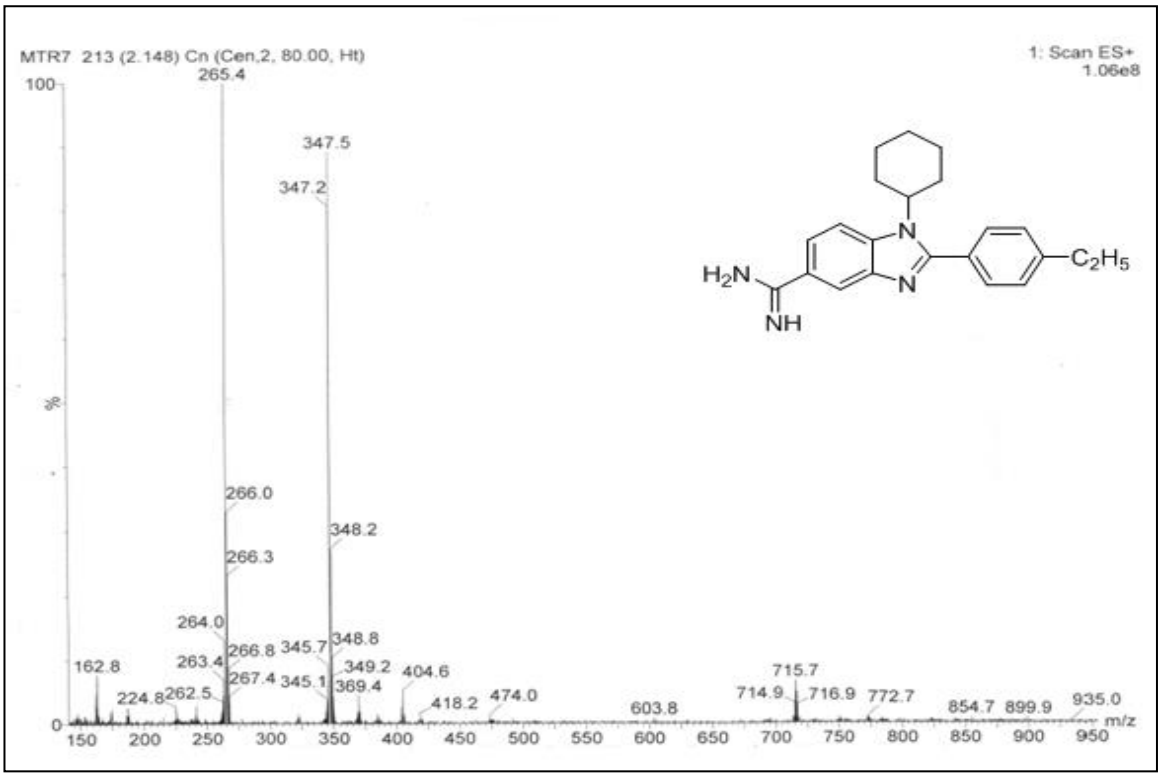


Figure 4. MASS spectra of M2

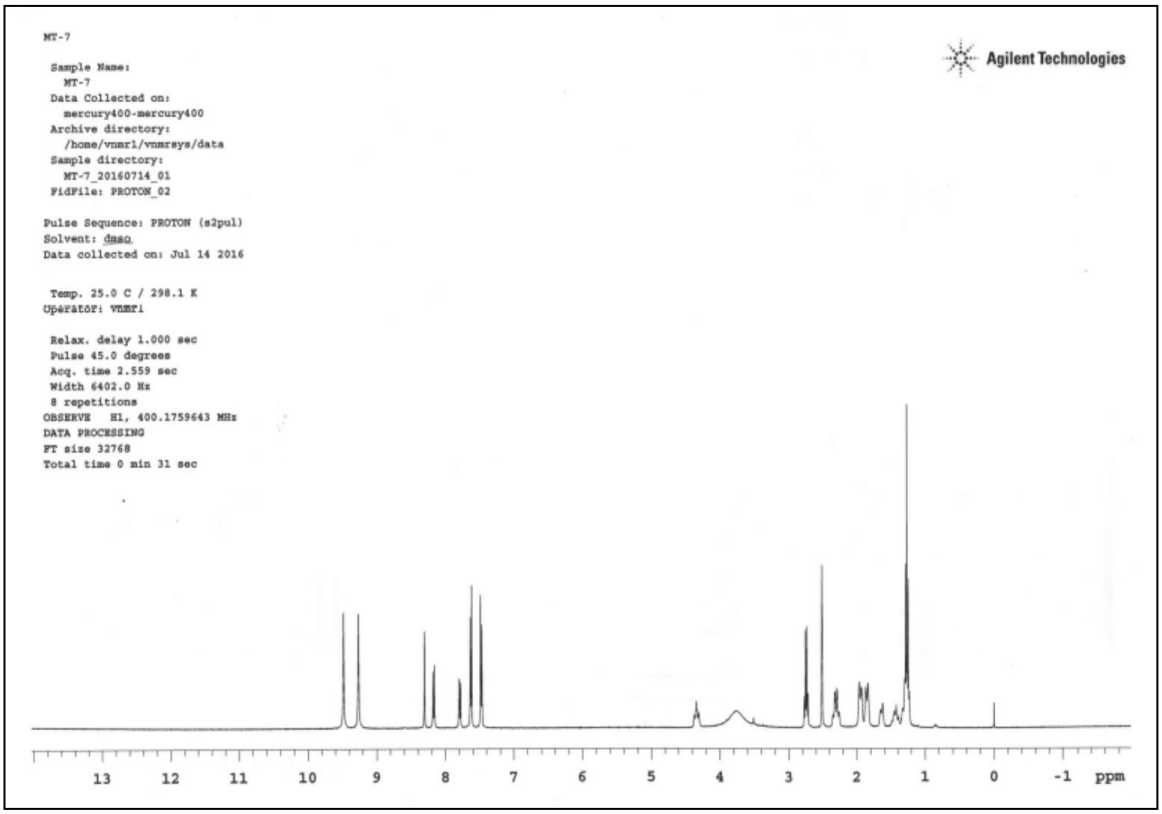


Figure 5. ^{1}H-NMR spectra of M2

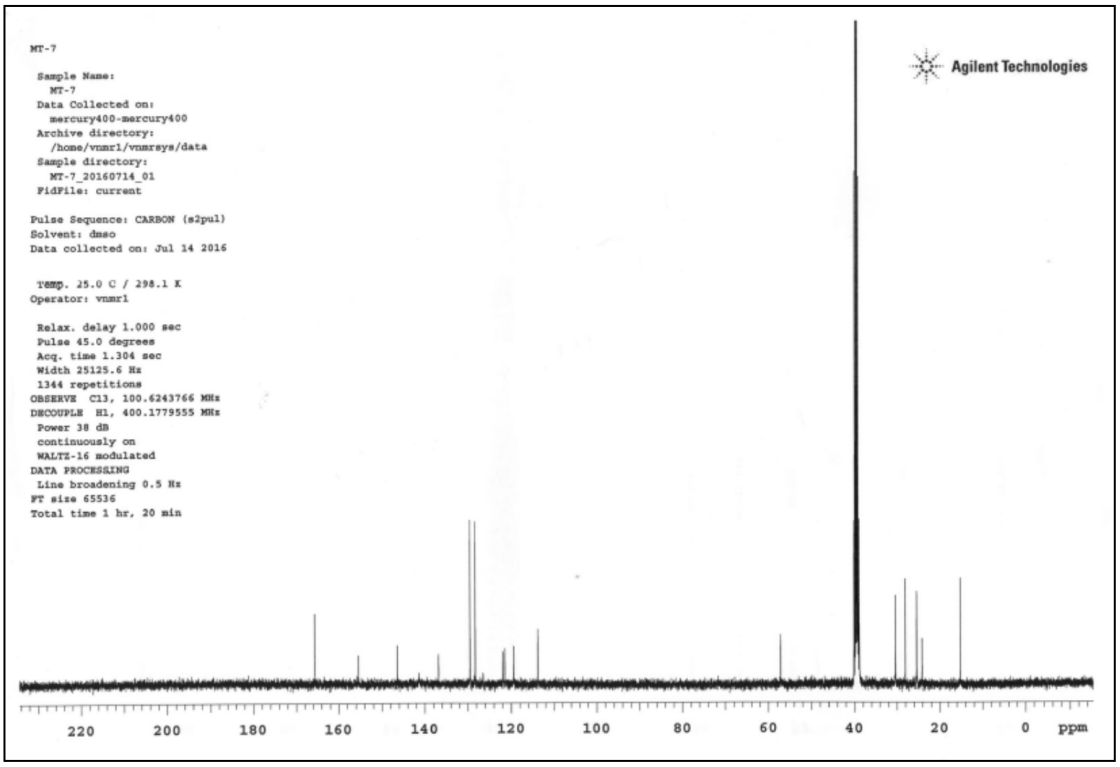


Figure 6. ^{13}C-NMR spectra spectrum of M2

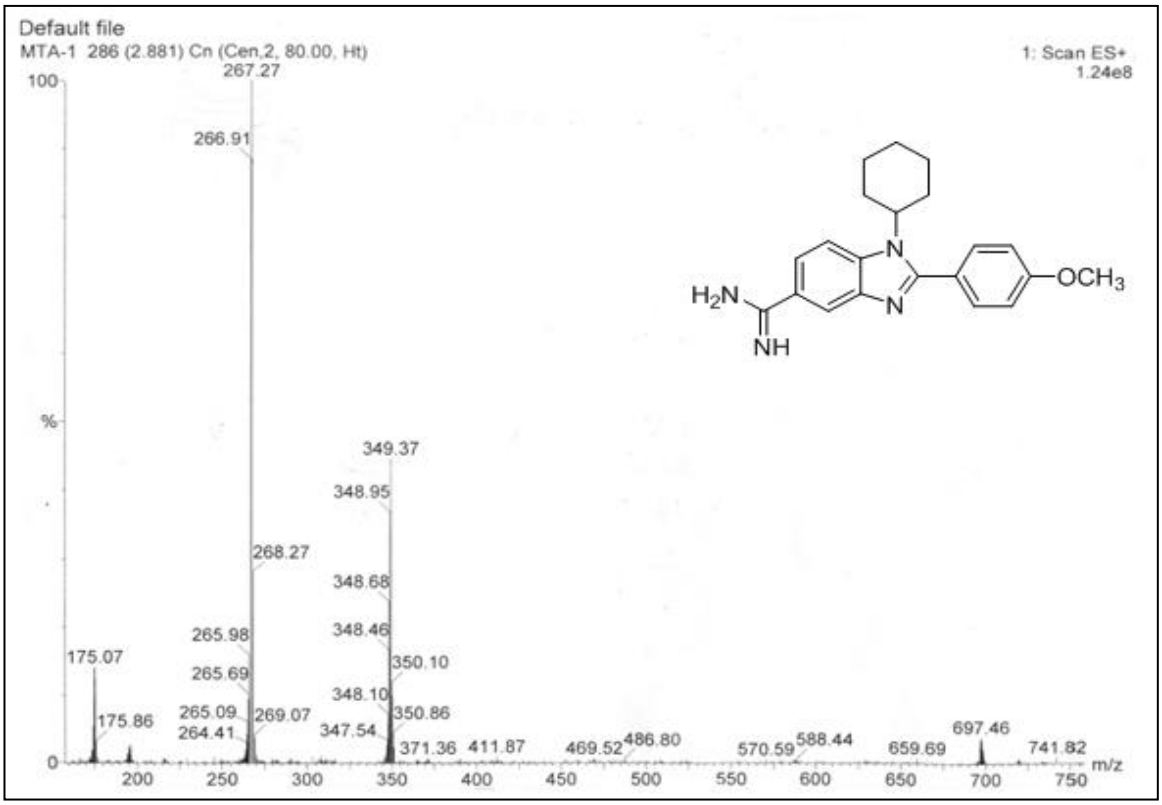


Figure 7. MASS spectra of M3

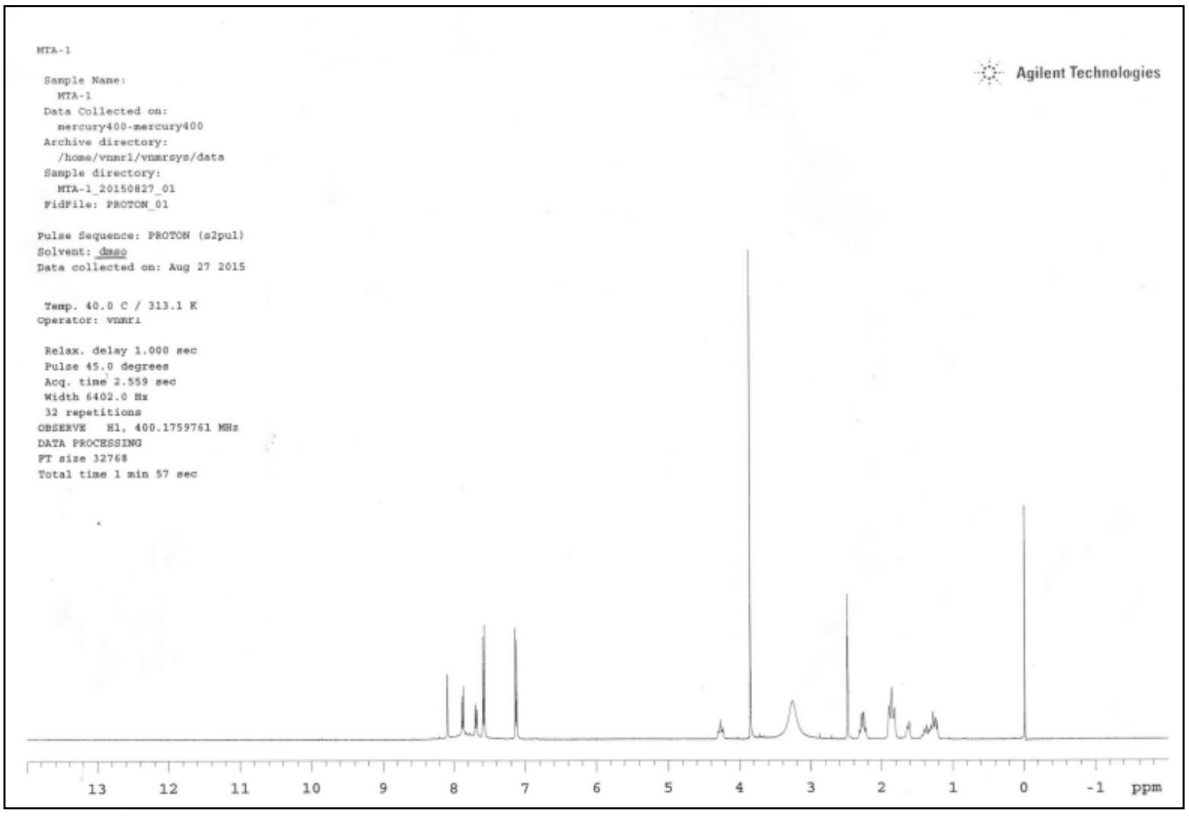


Figure 8. ^{1}H-NMR spectra of M3

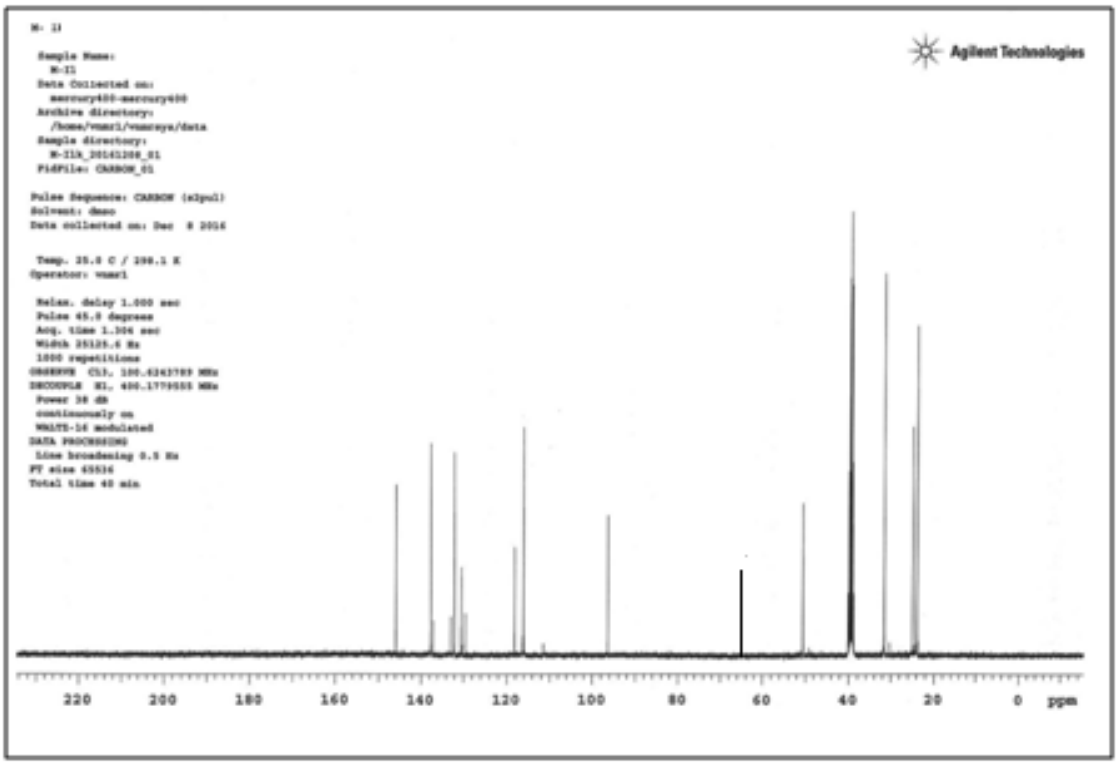


Figure 9. ^{13}C-NMR spectra of M3

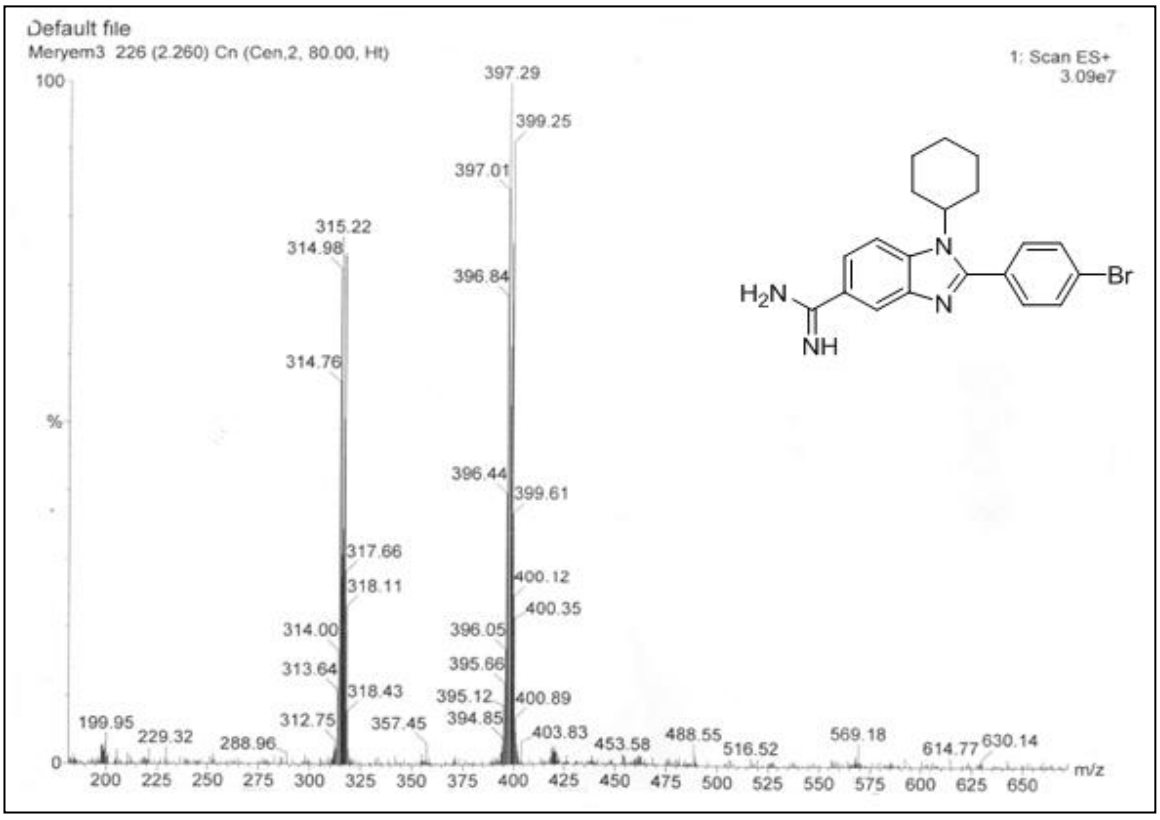


Figure 10. MASS spectra of M4

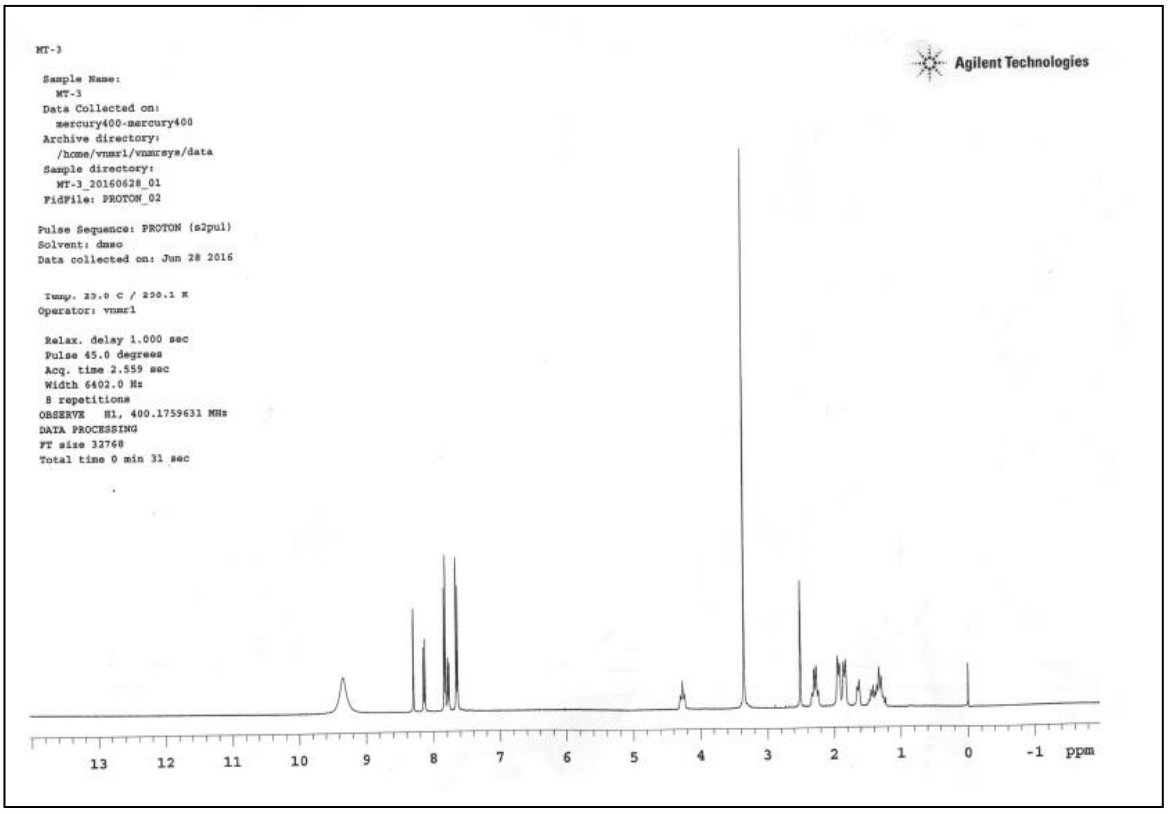


Figure 11. ^{1}H-NMR spectra of M4

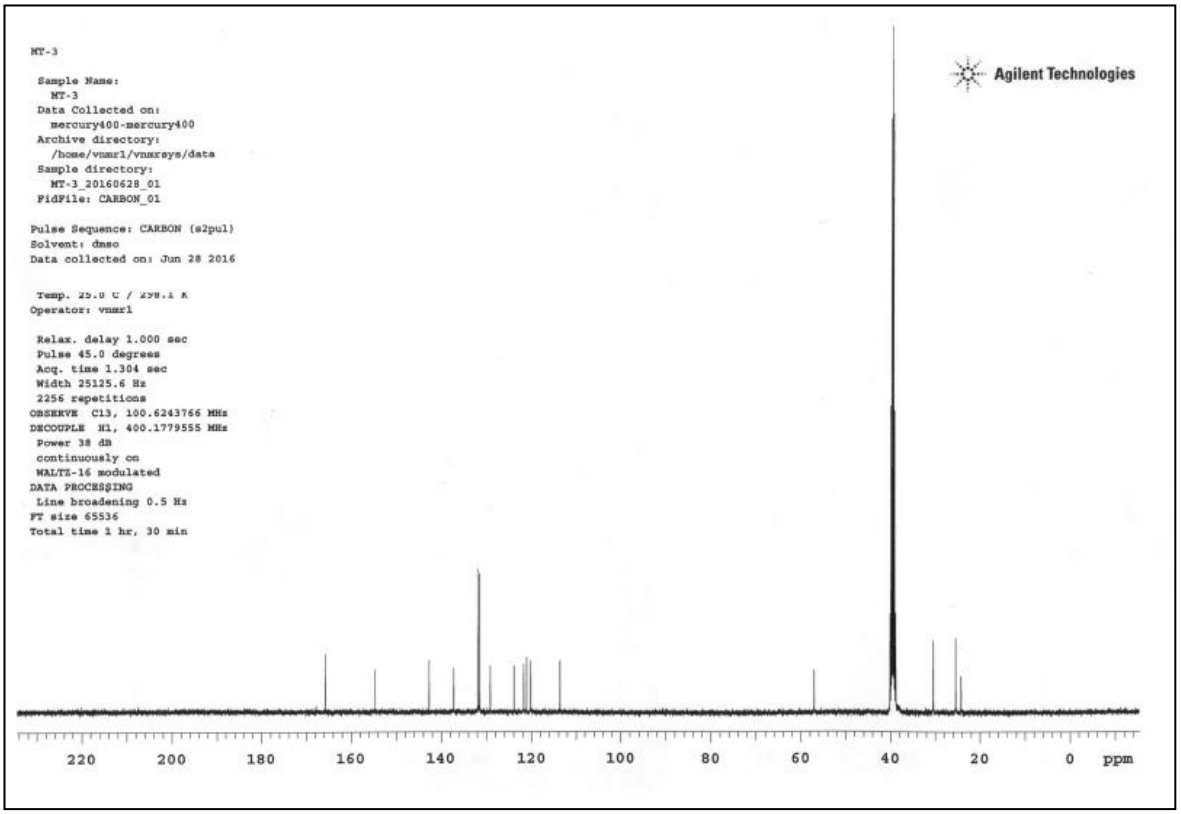


Figure 12. ^{13}C-NMR spectra of M4

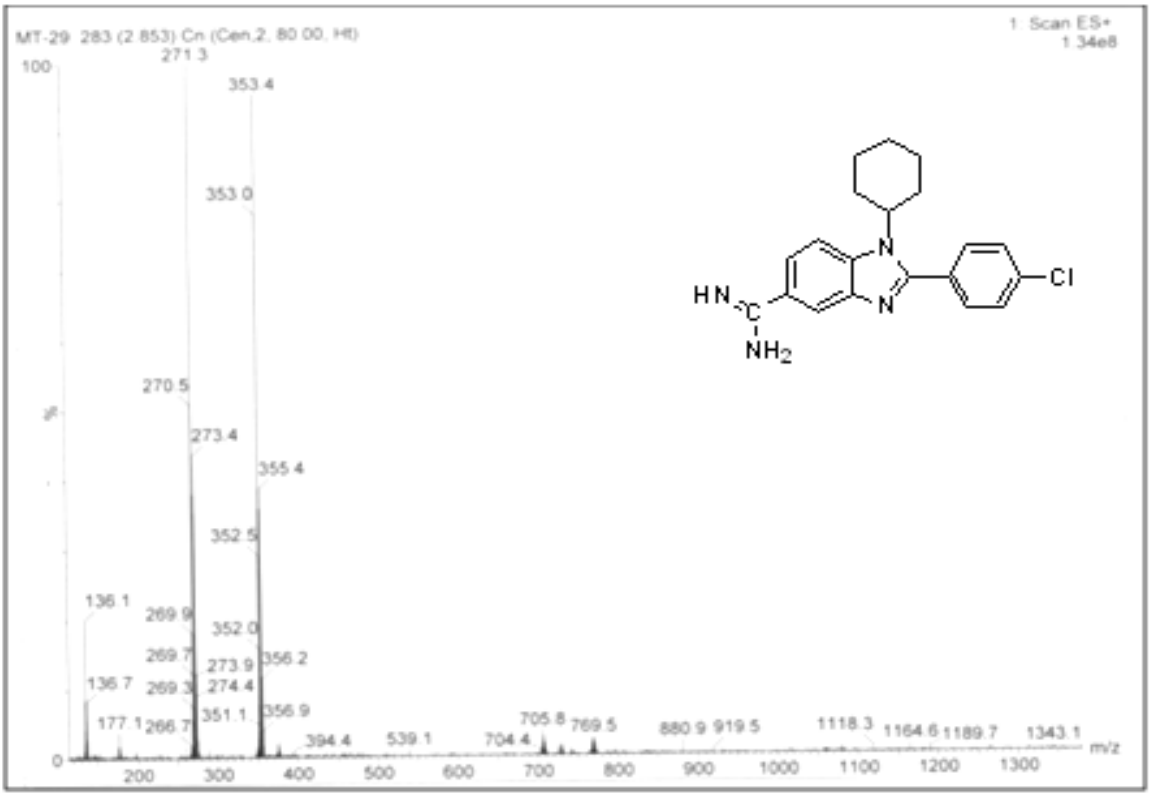


Figure 13. MASS spectra of M5

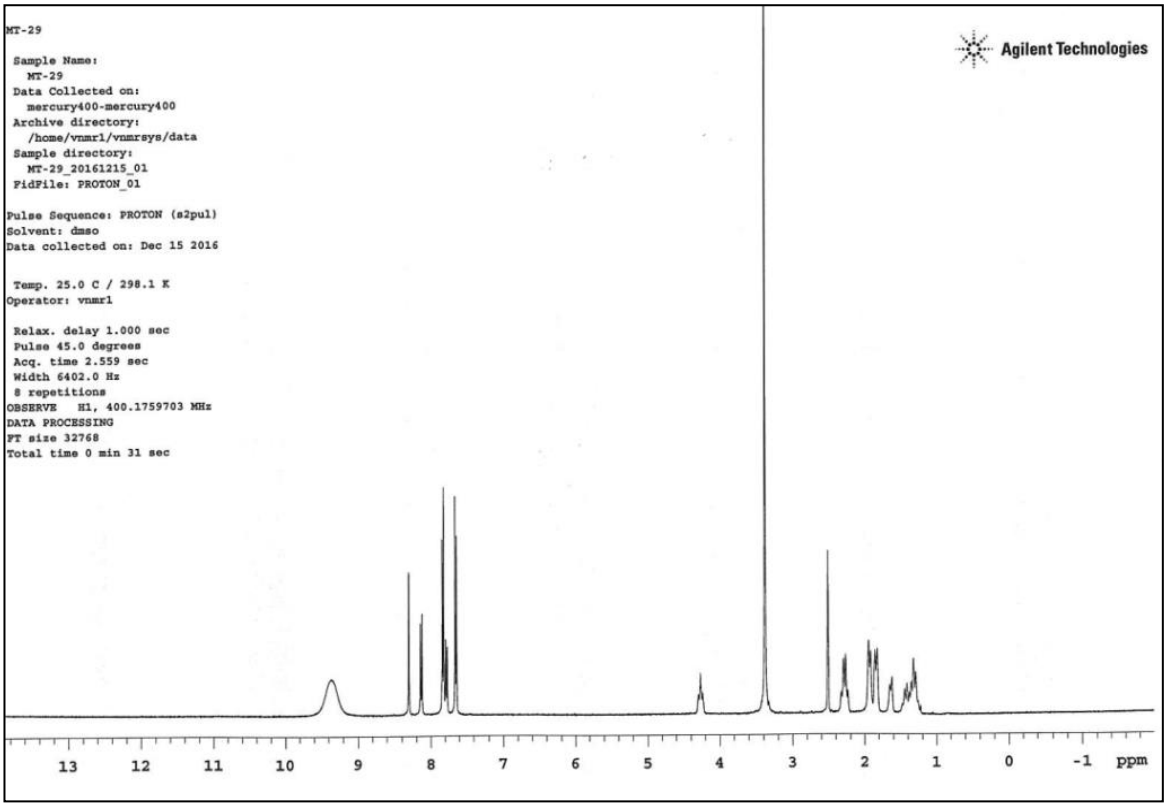


Figure 14. ^{1}H-NMR spectra of M5

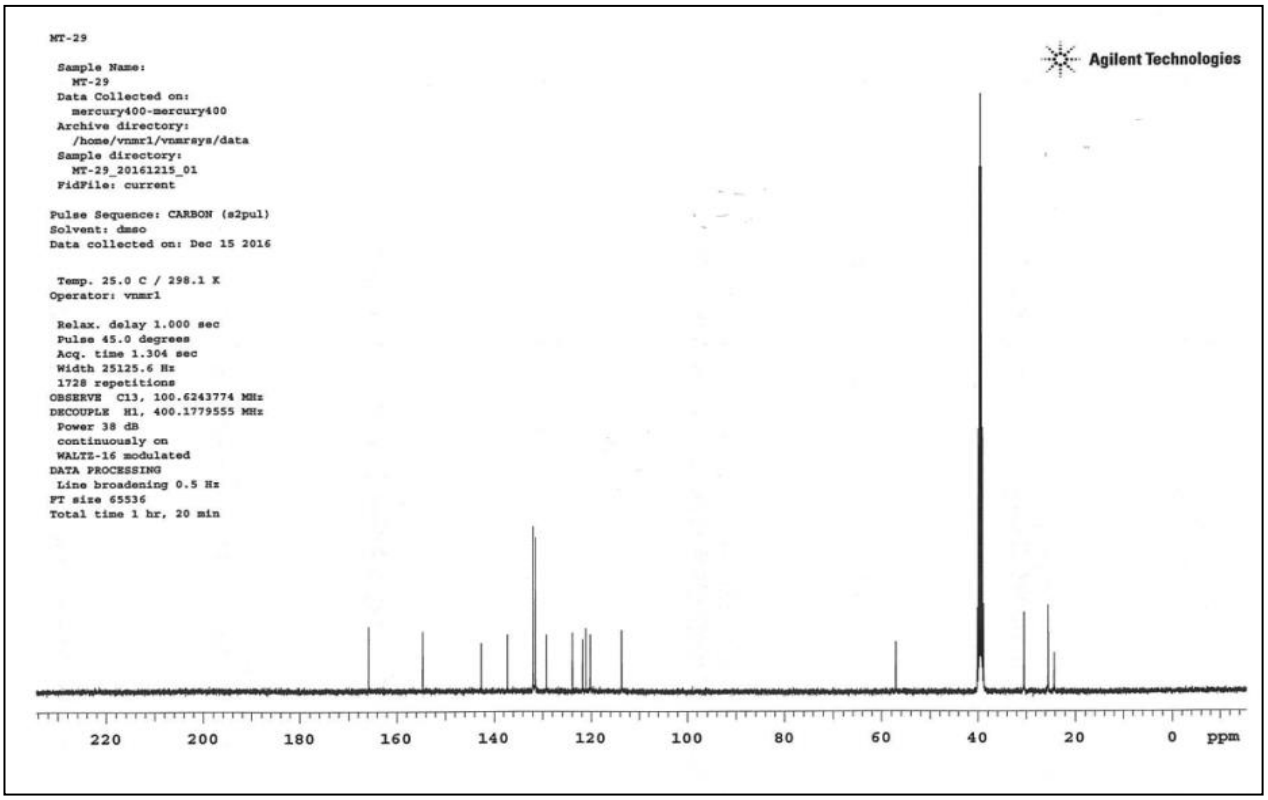


Figure 15. ^{13}C-NMR spectra of M5

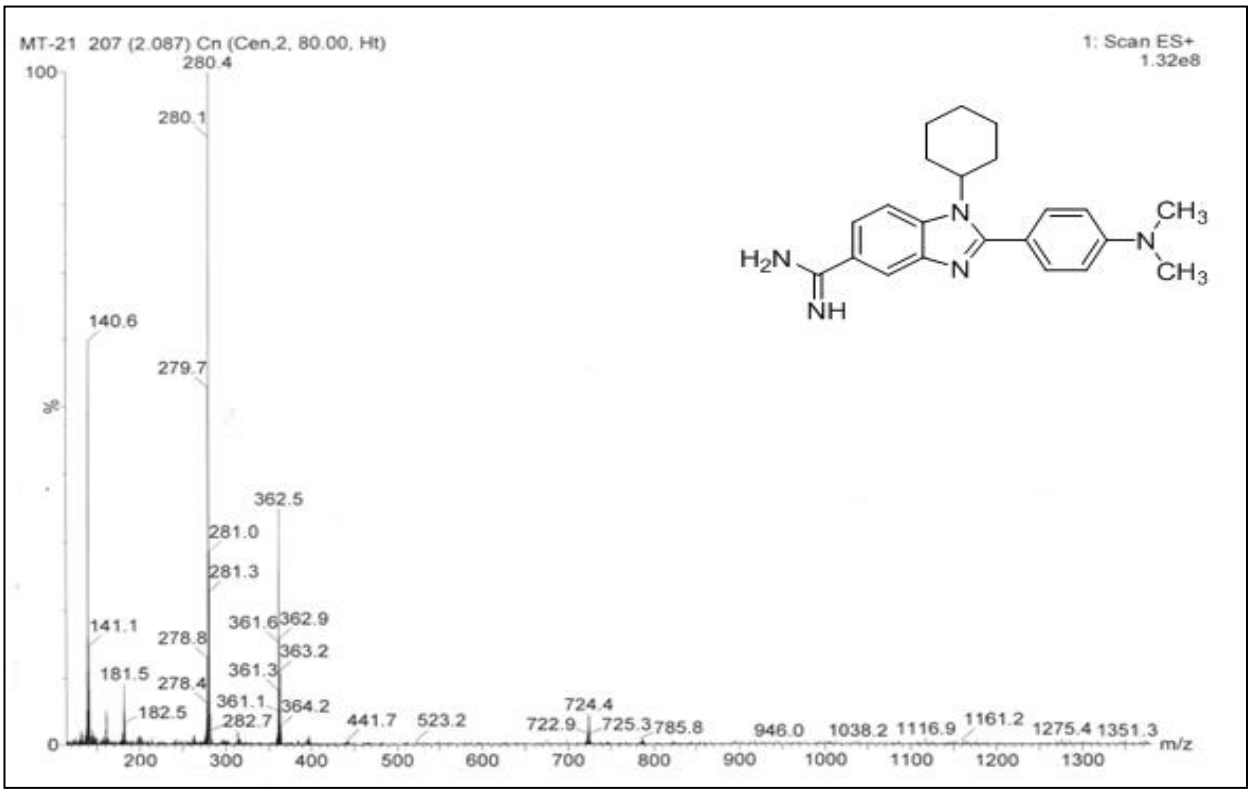


Figure 16. MASS spectra of M6

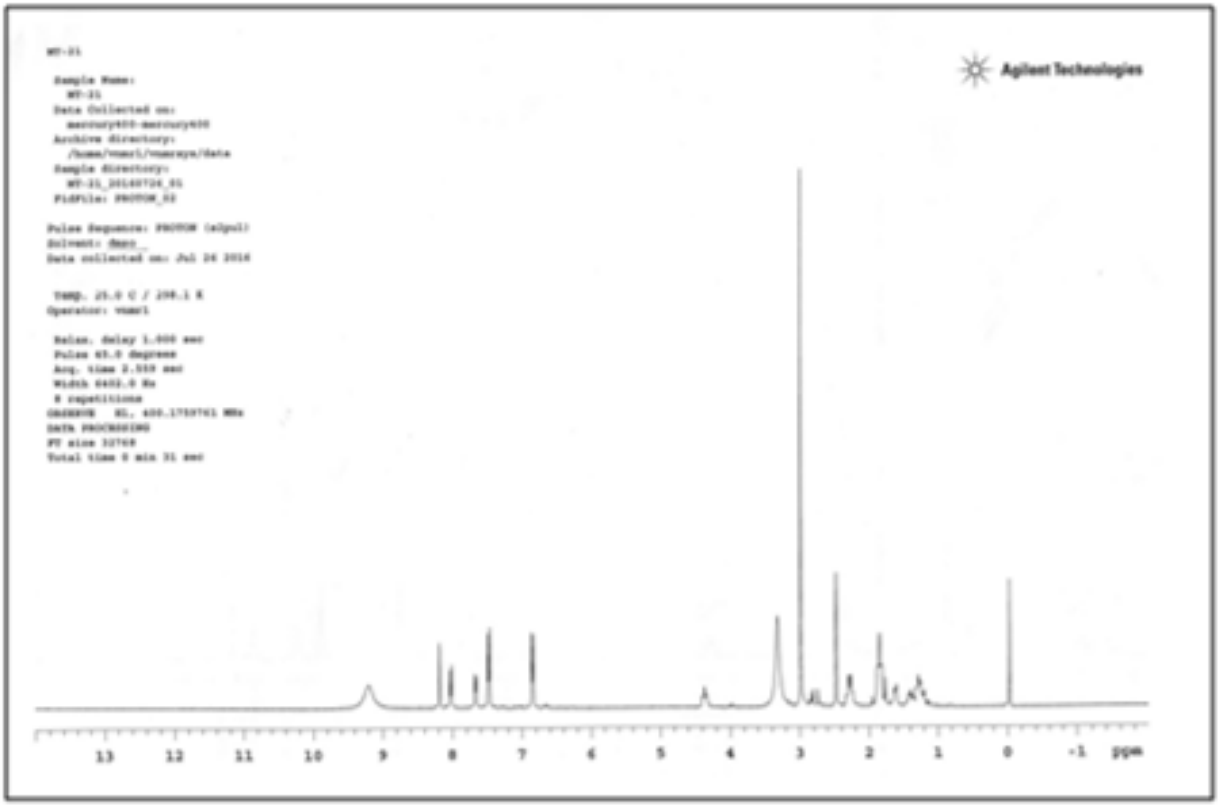


Figure 17. ^{1}H-NMR spectra of M6

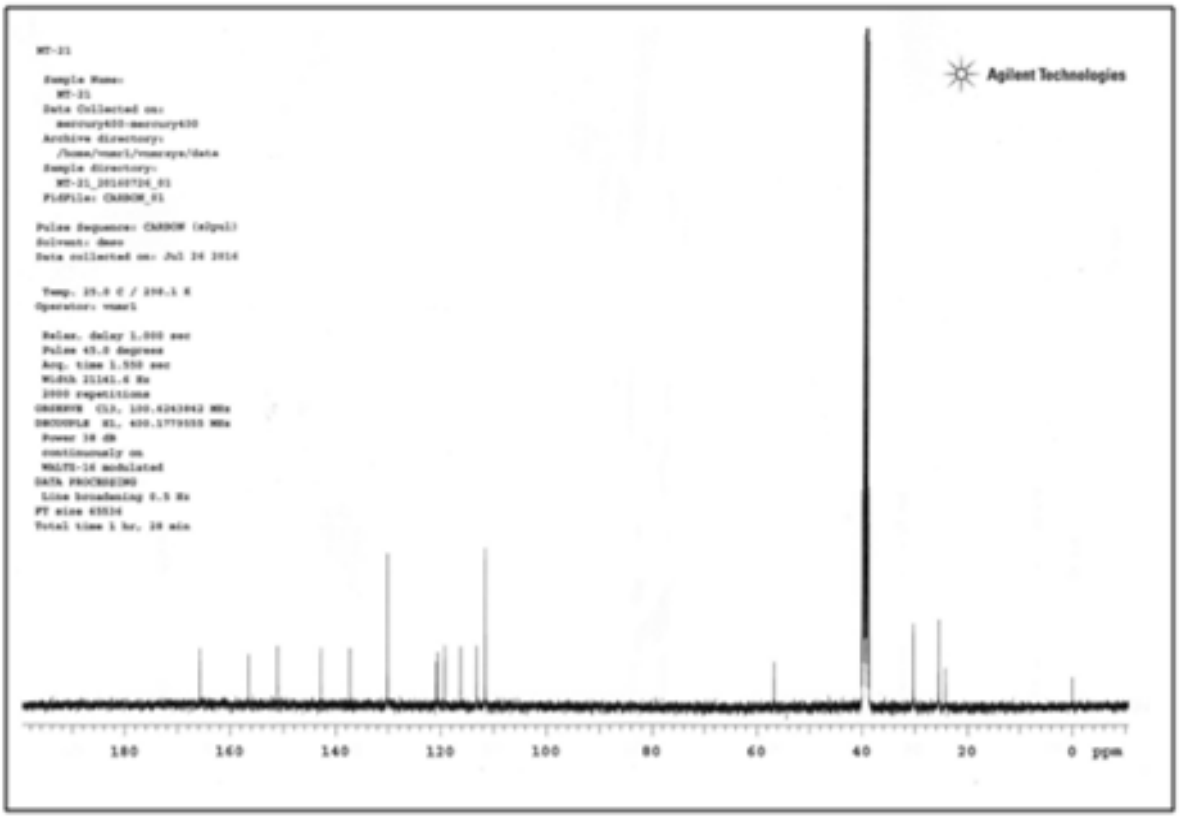


Figure 18. ^{13}C-NMR spectra of M6

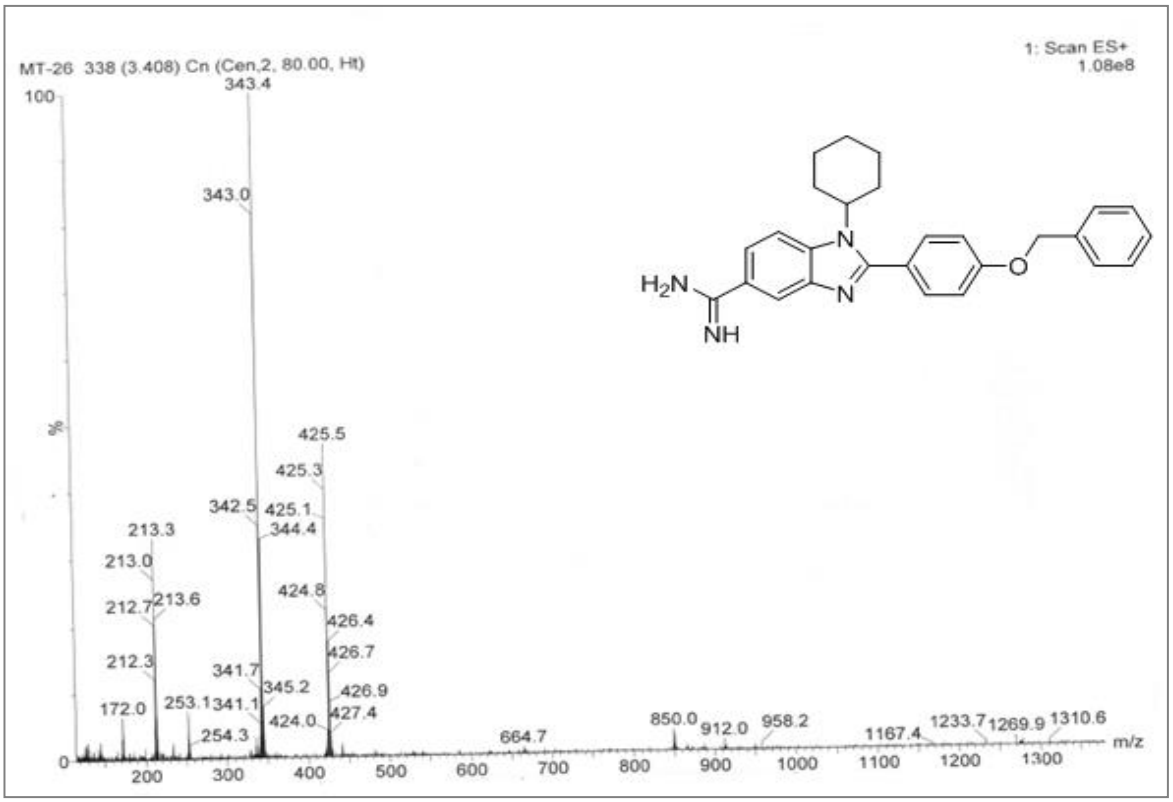


Figure 19. MASS spectra of M7

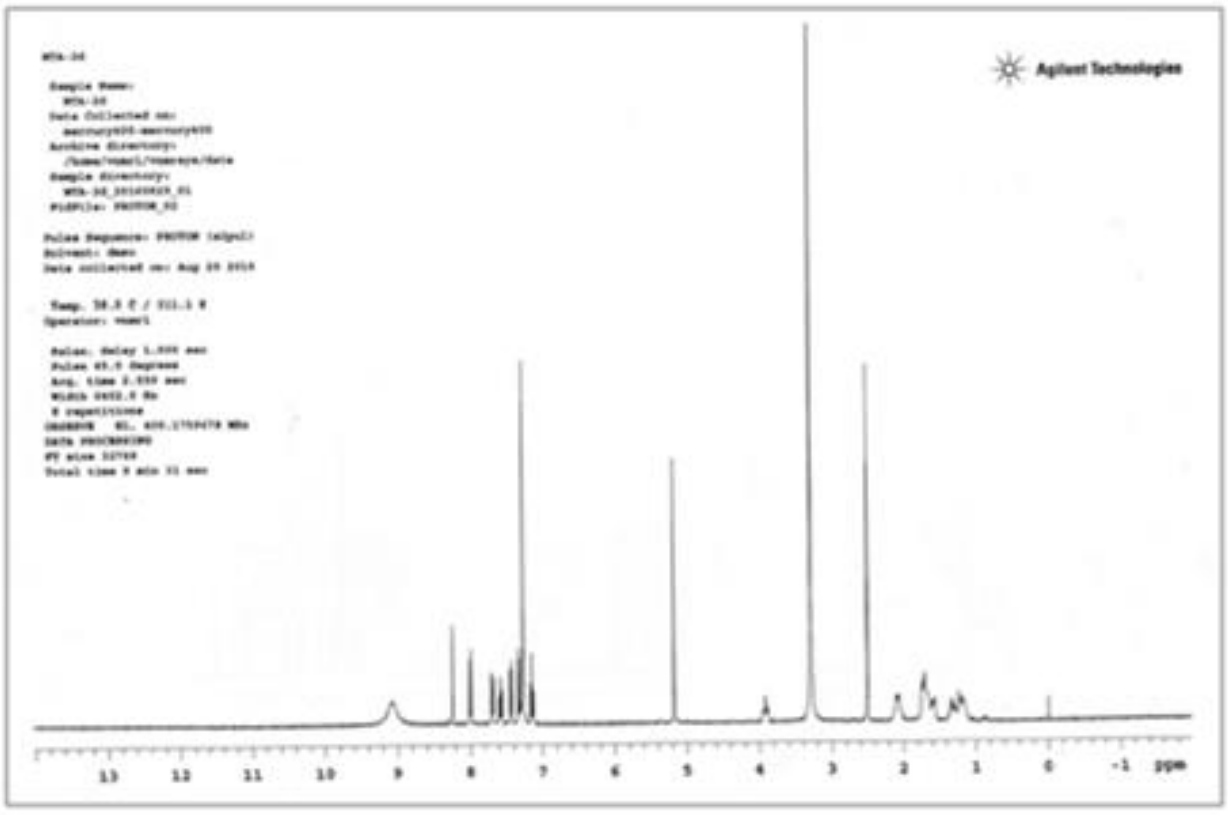


Figure 20. [1]H-NMR spectra of M7

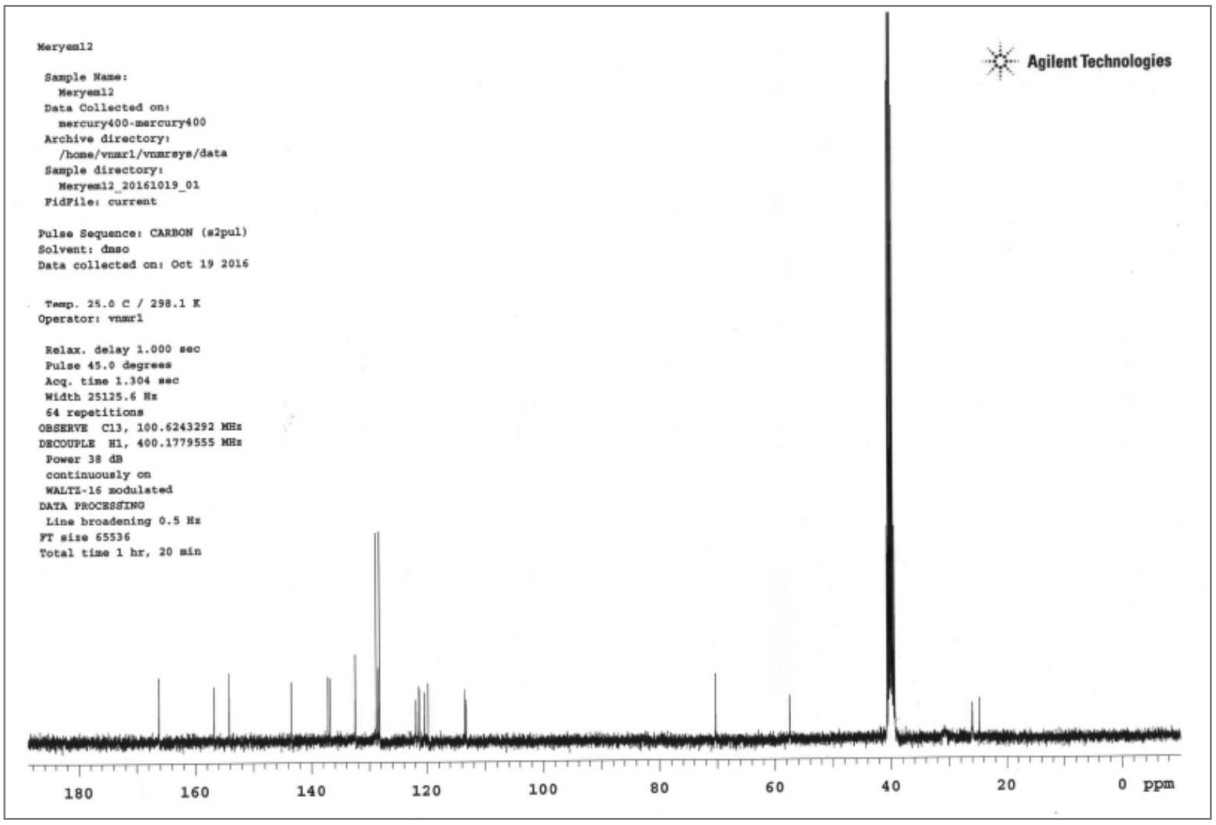


Figure 21. ^{13}C-NMR spectra of M7

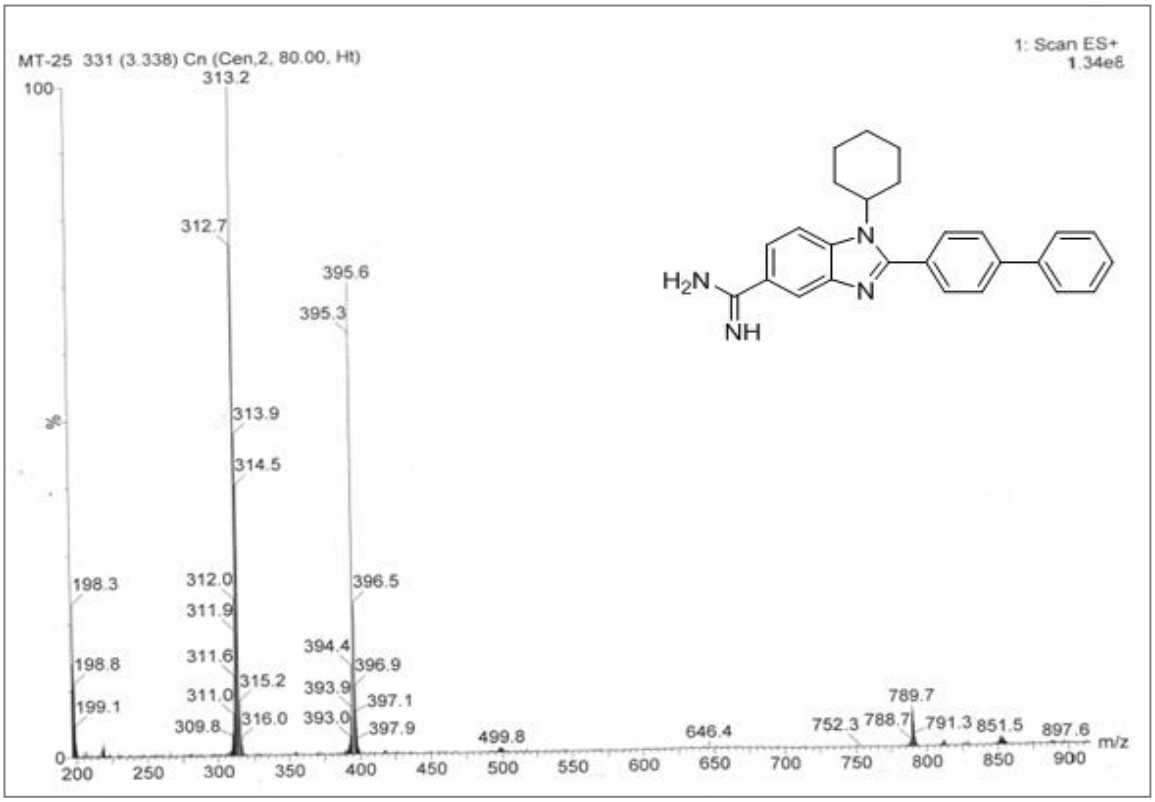


Figure 22. MASS spectra of M8

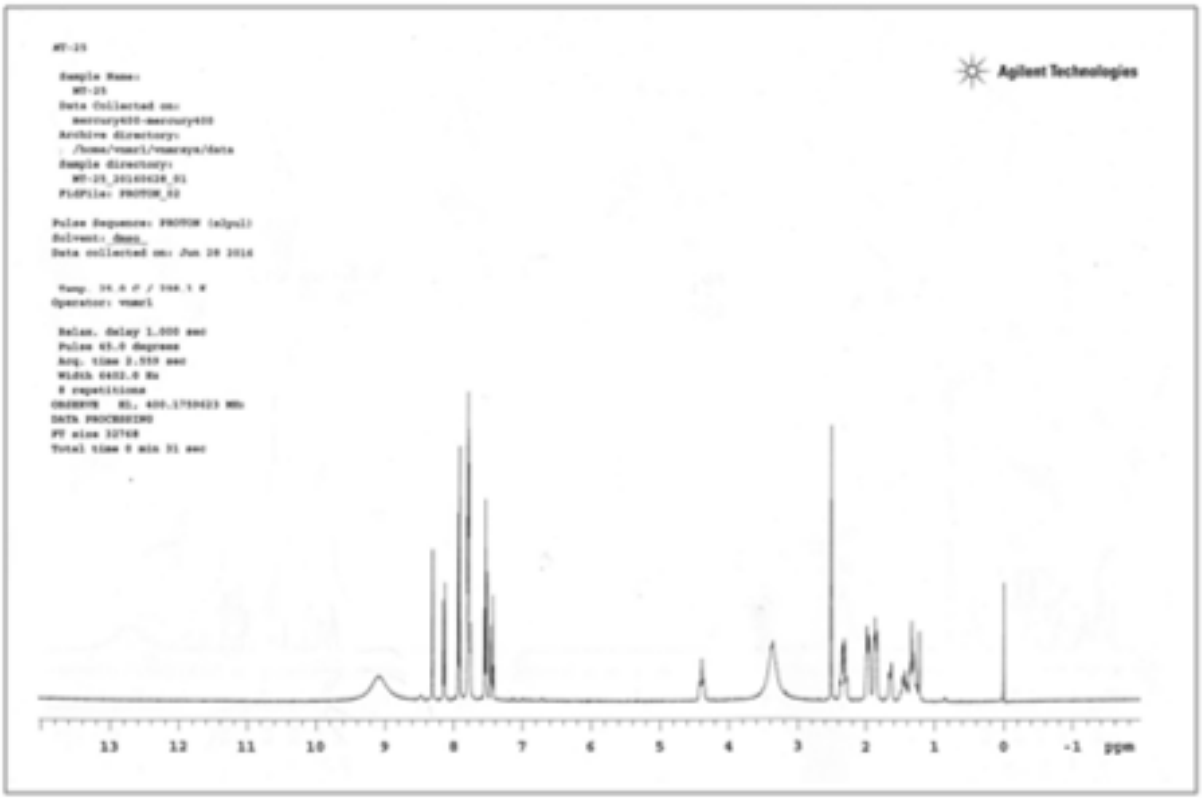


Figure 23. ^{1}H-NMR spectra of M8

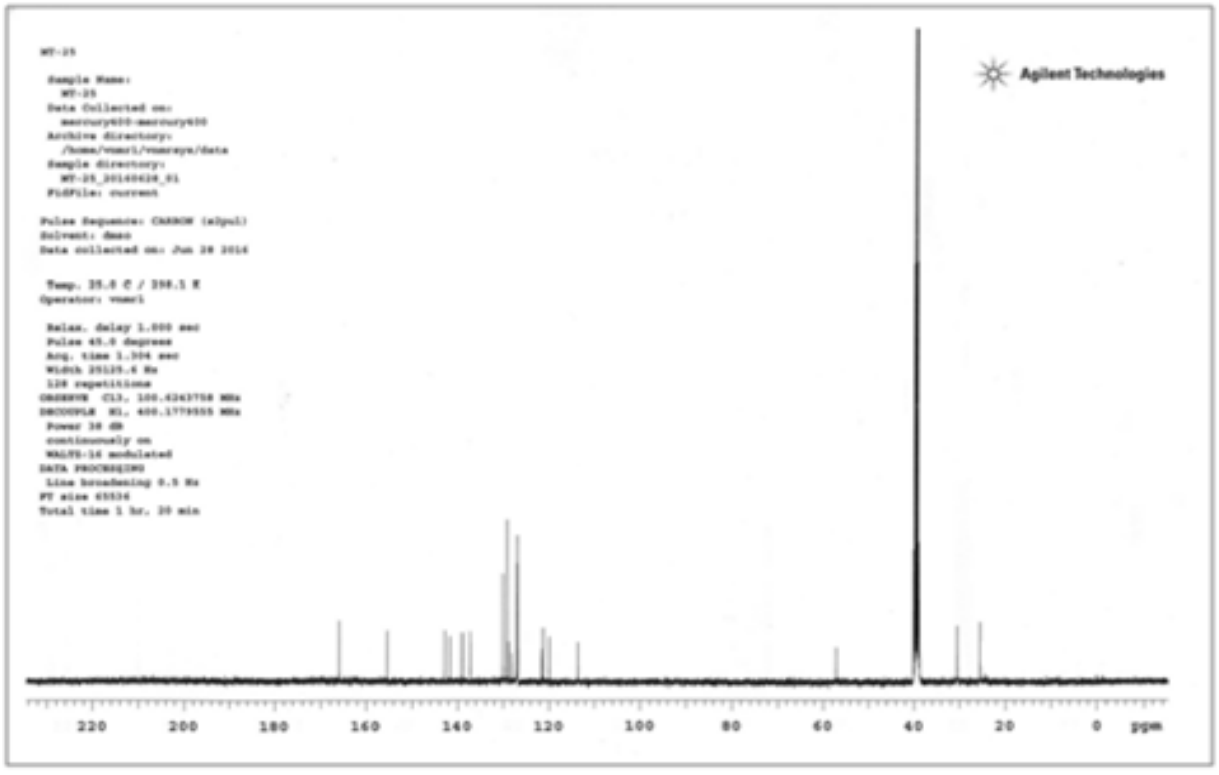


Figure 24. ^{13}C-NMR spectra of M8

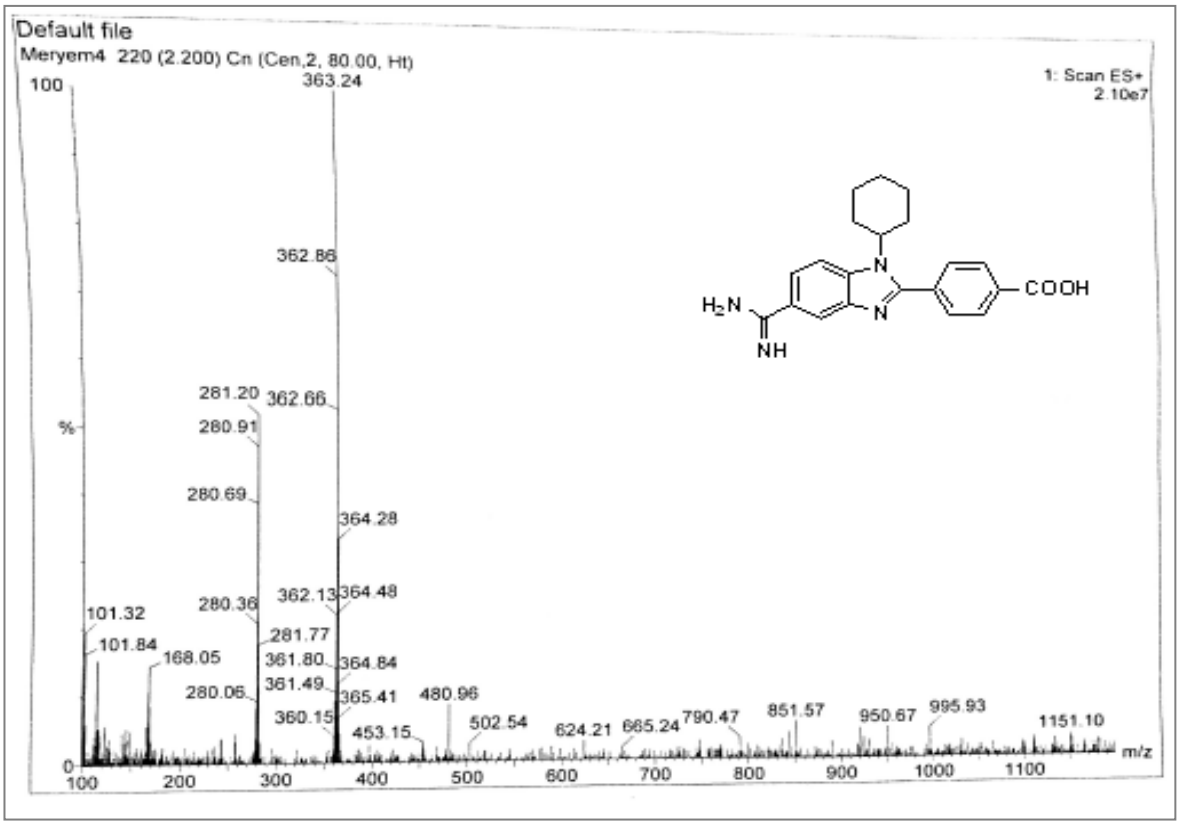


Figure 25. MASS spectra of M9

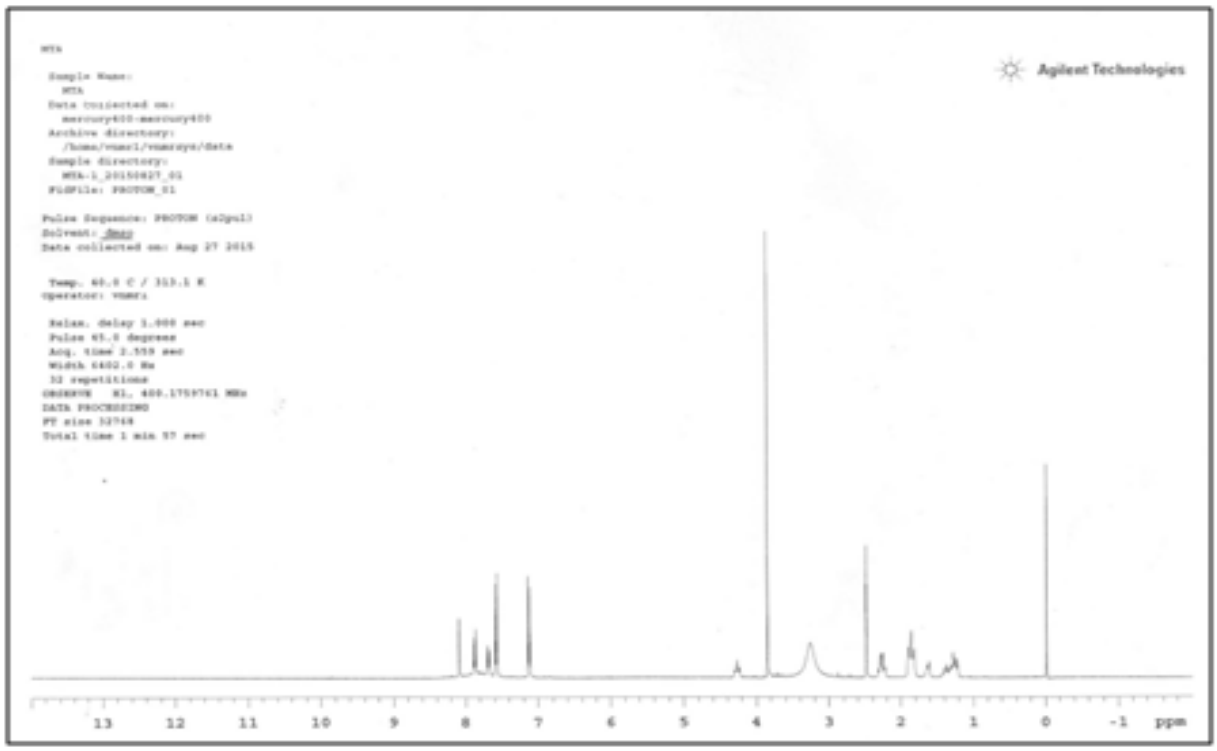


Figure 26. ^{1}H-NMR spectra of M9

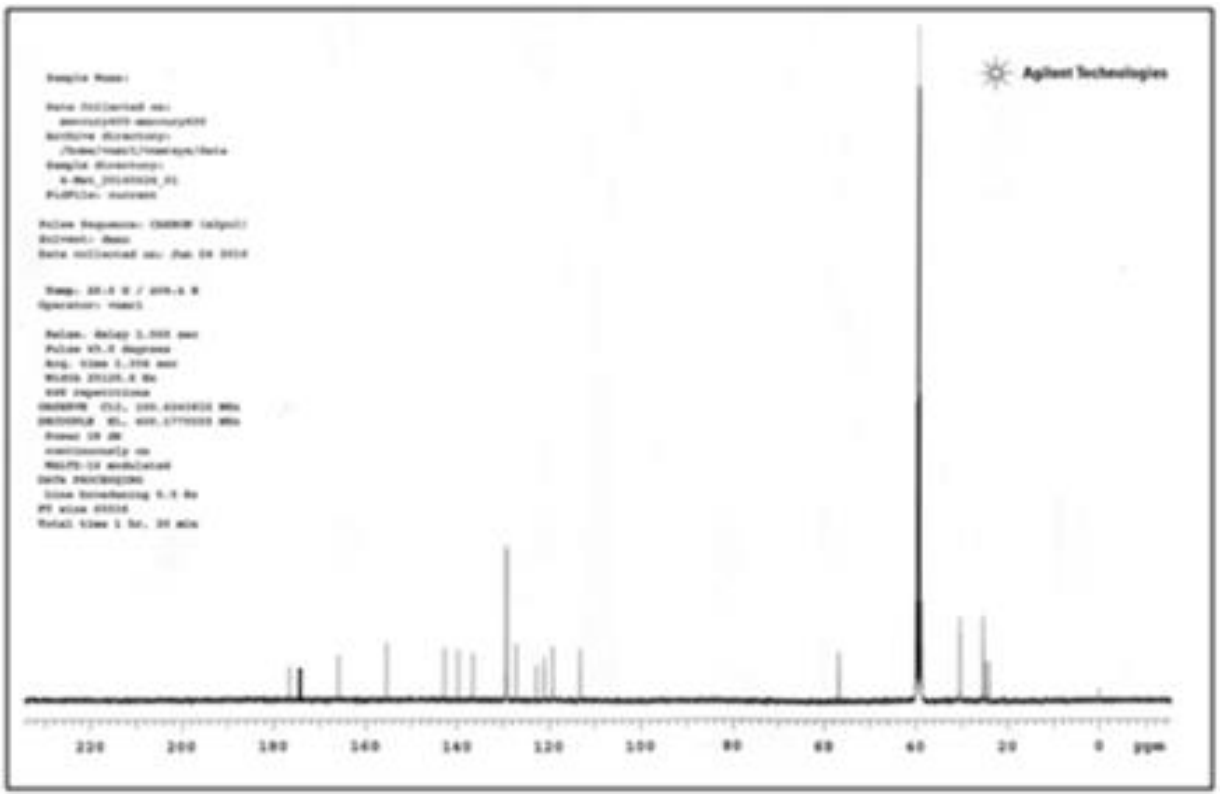


Figure 27. ^{13}C-NMR spectra of M9

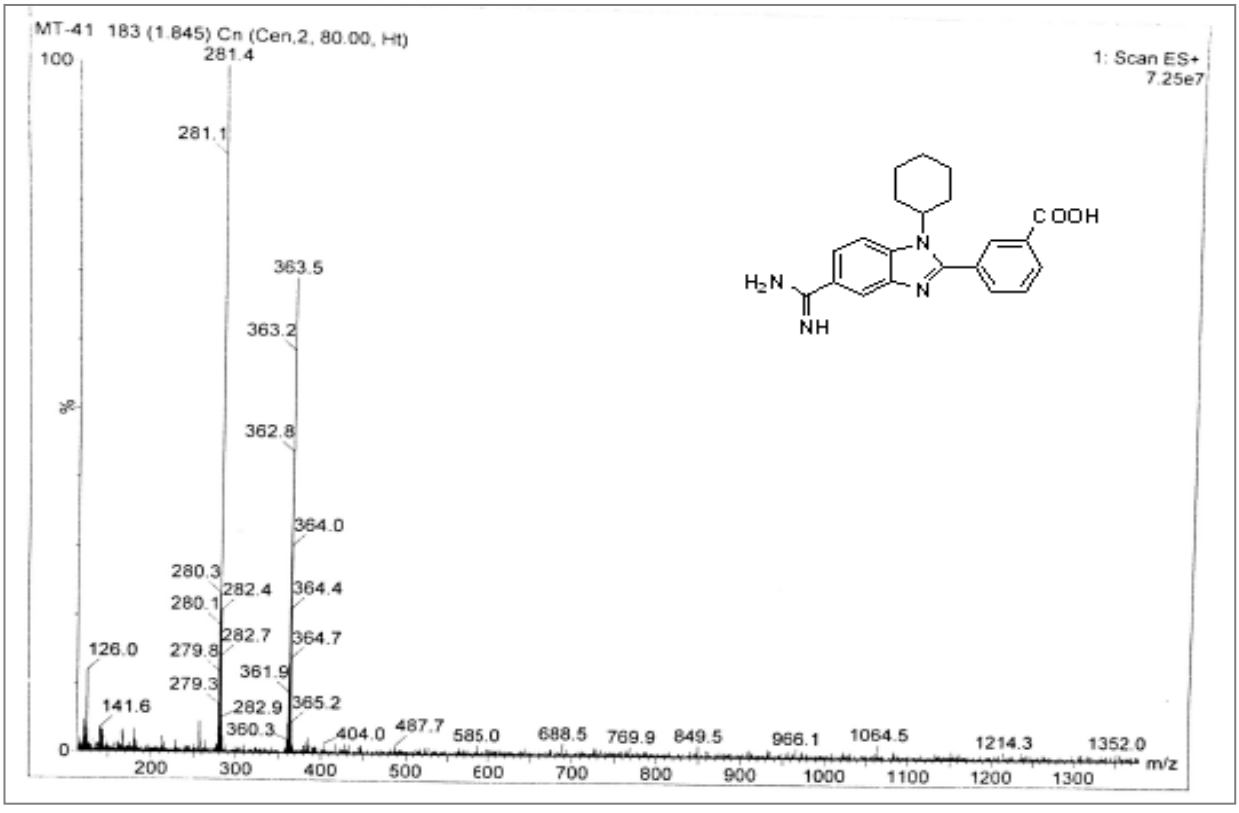


Figure 28. MASS spectra of M10

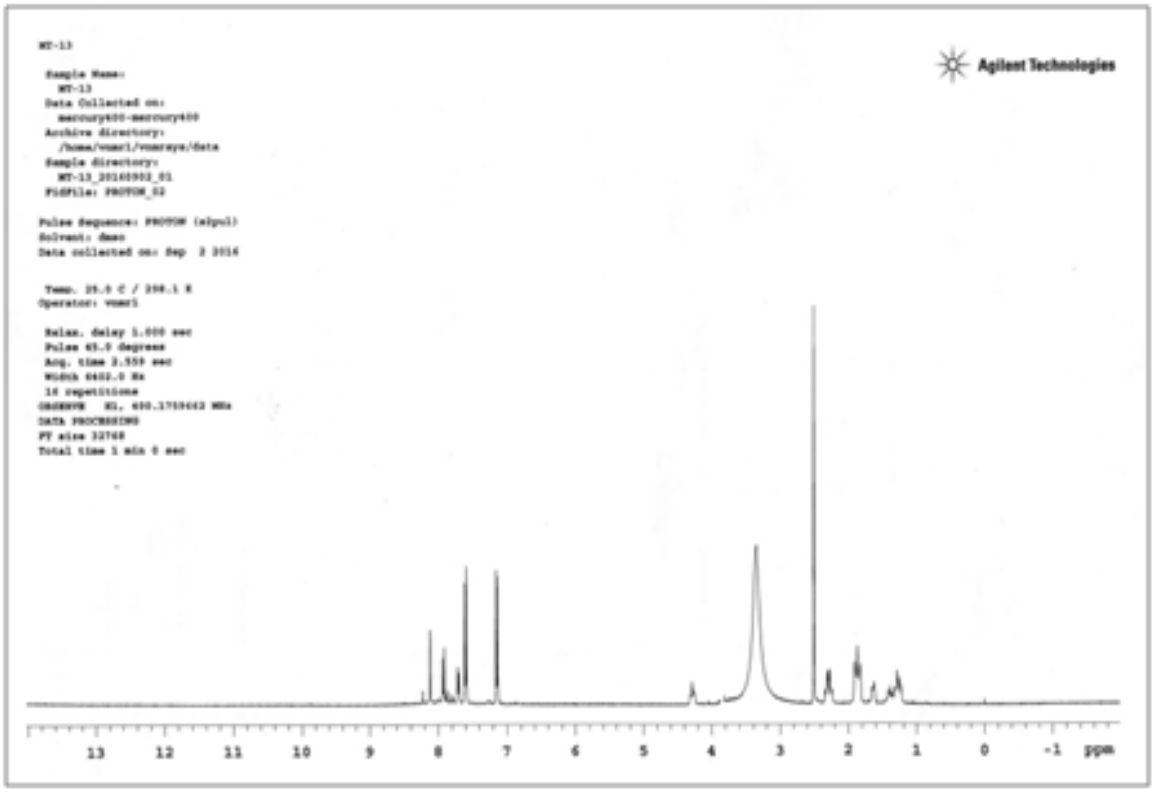


Figure 29. ^{1}H-NMR spectra of M10

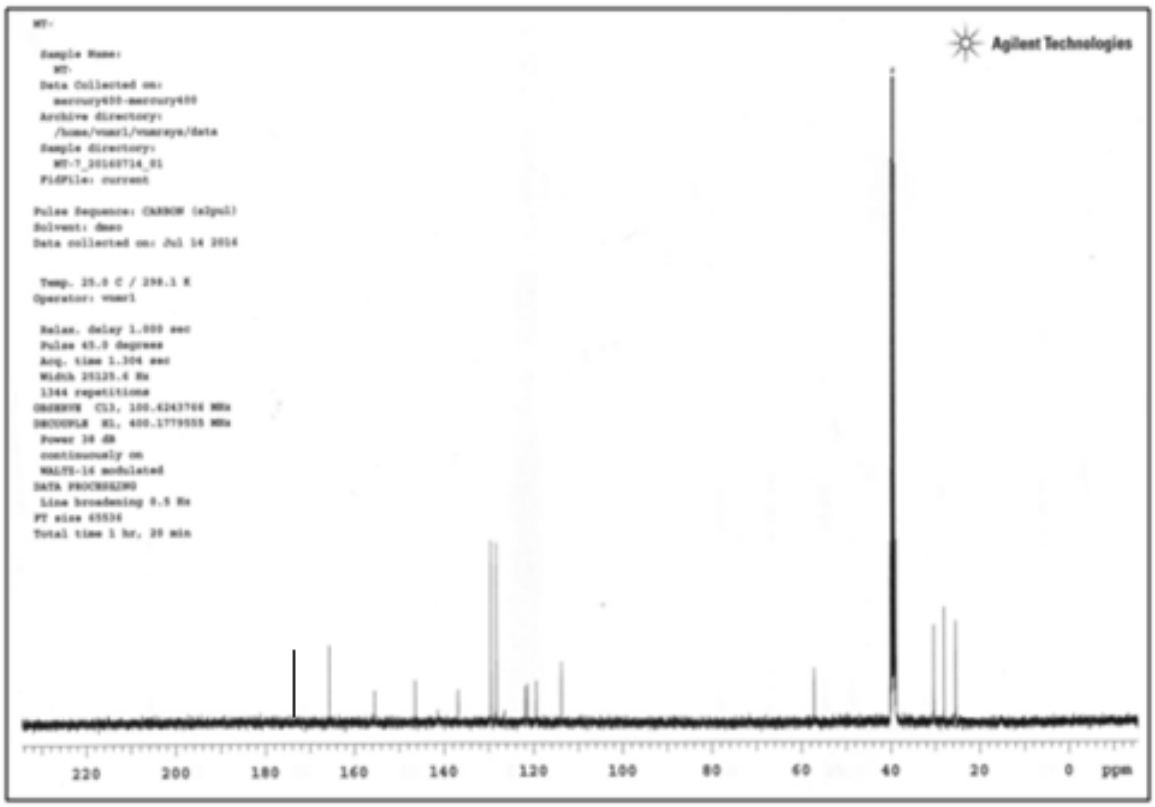


Figure 30. ^{13}C-NMR spectra of M10

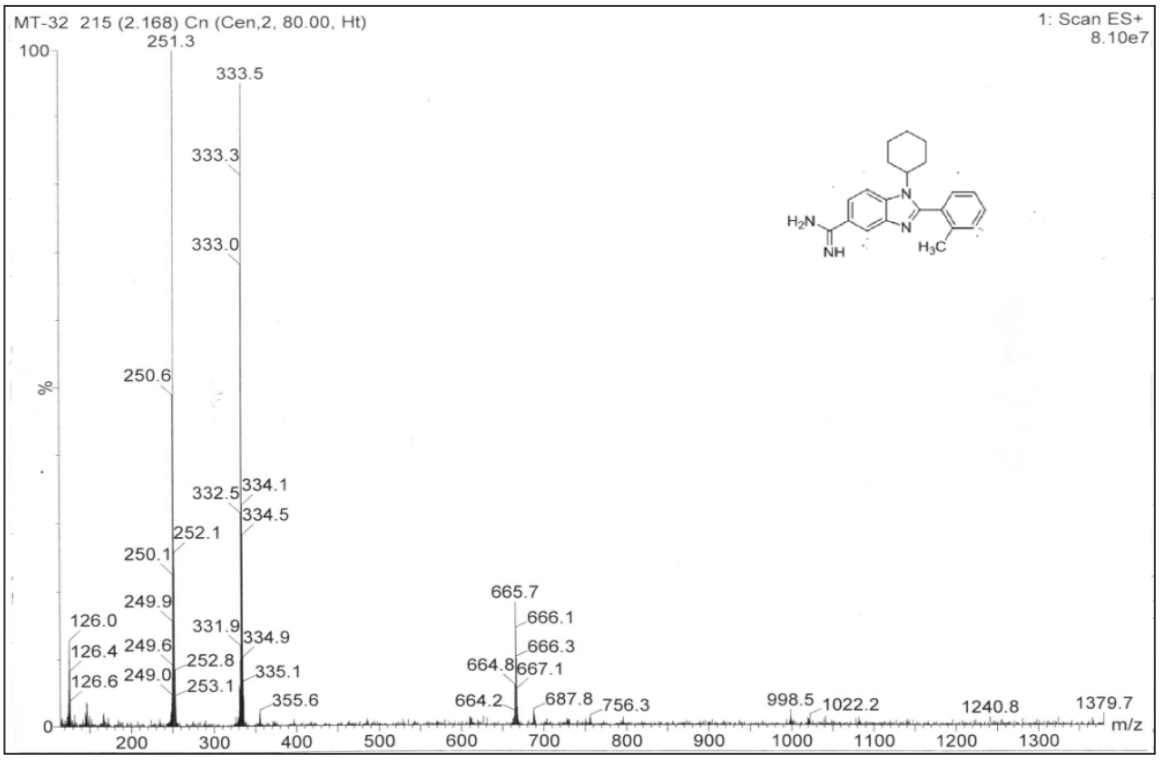


Figure 31. MASS spectra of M11

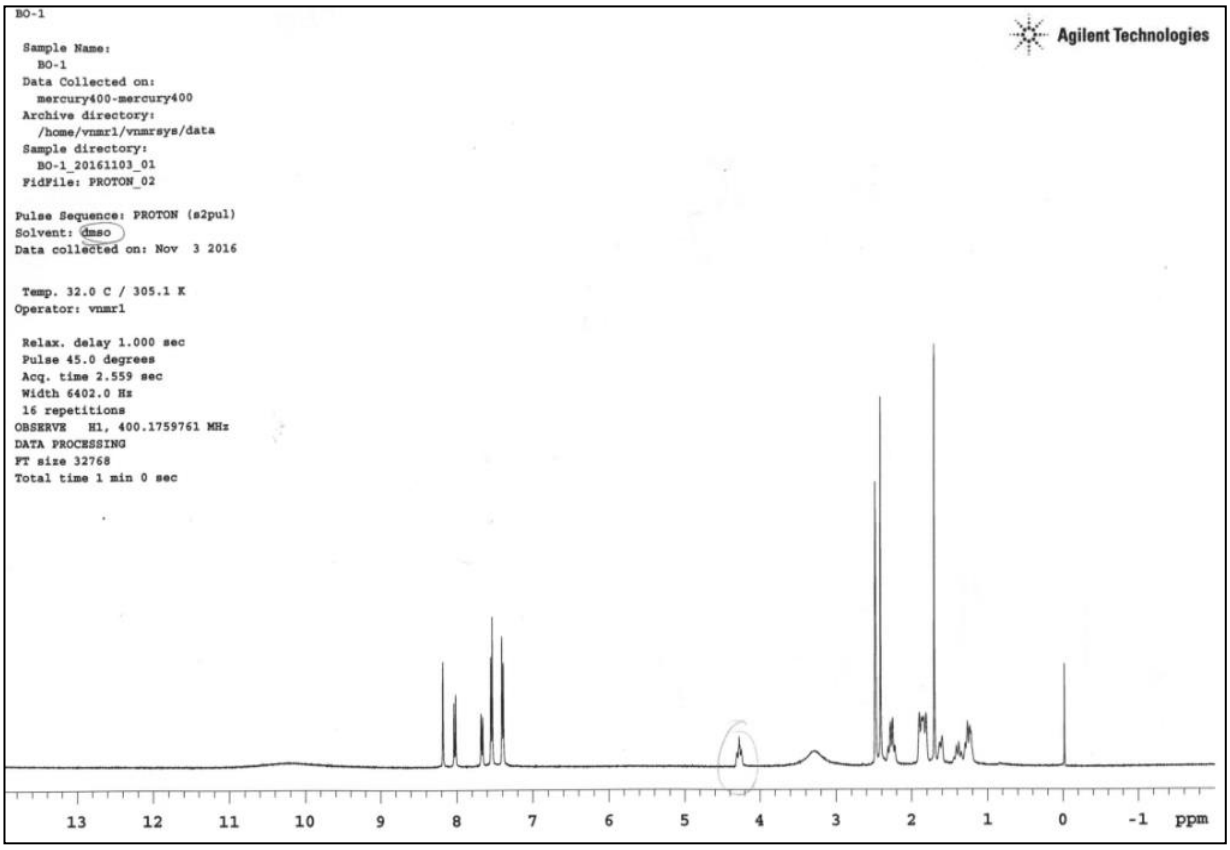


Figure 32. ^{1}H-NMR spectra of M11

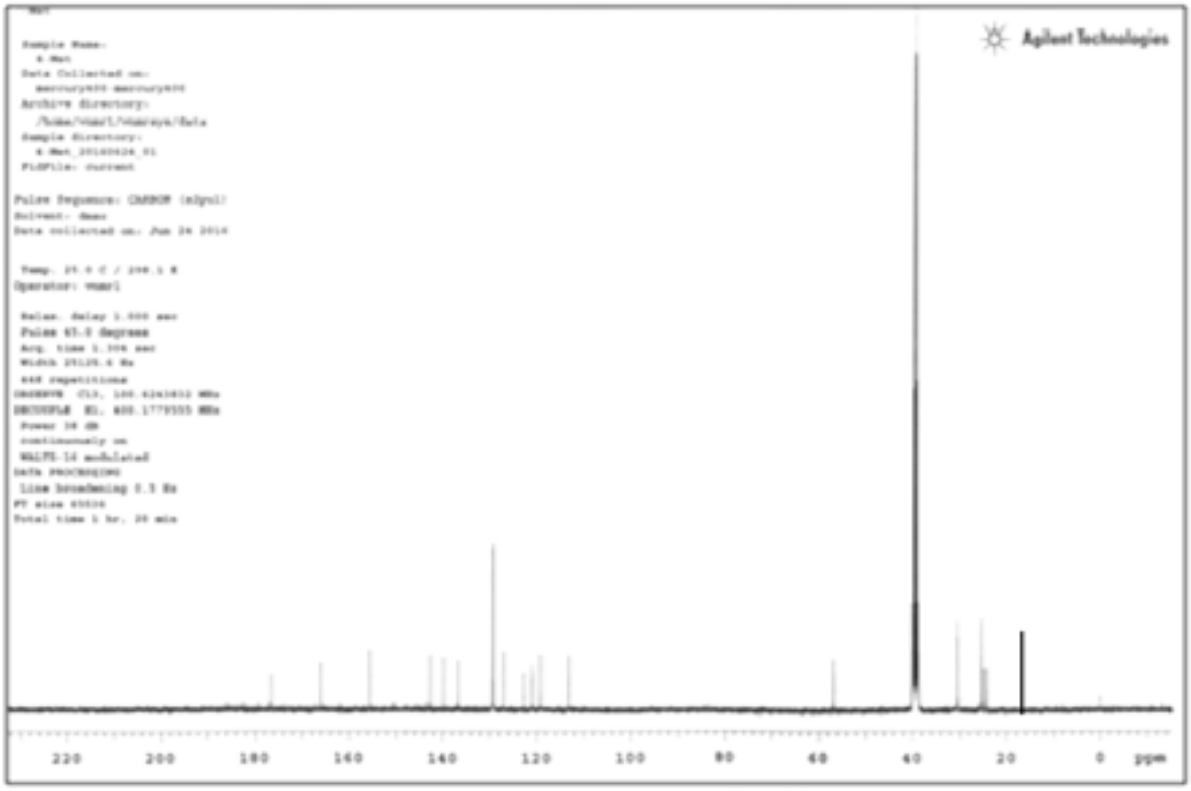


Figure 33. ^{13}C-NMR spectra of M11

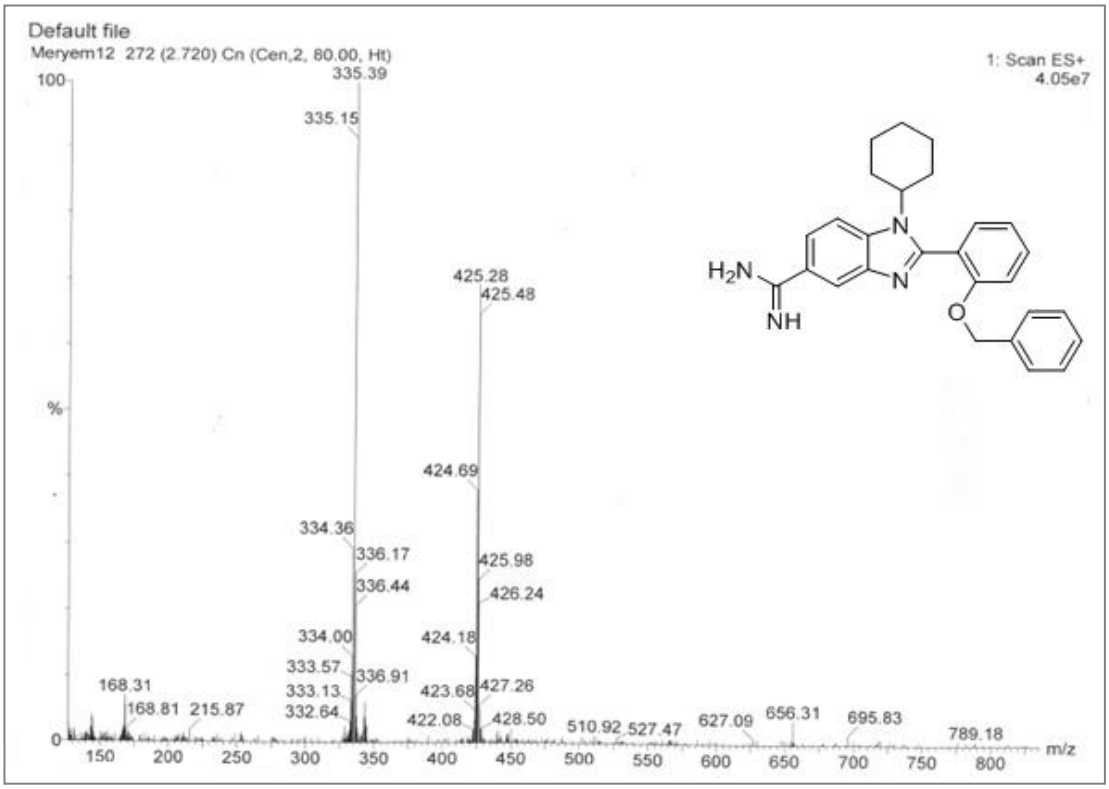


Figure 34. MASS spectra of M12

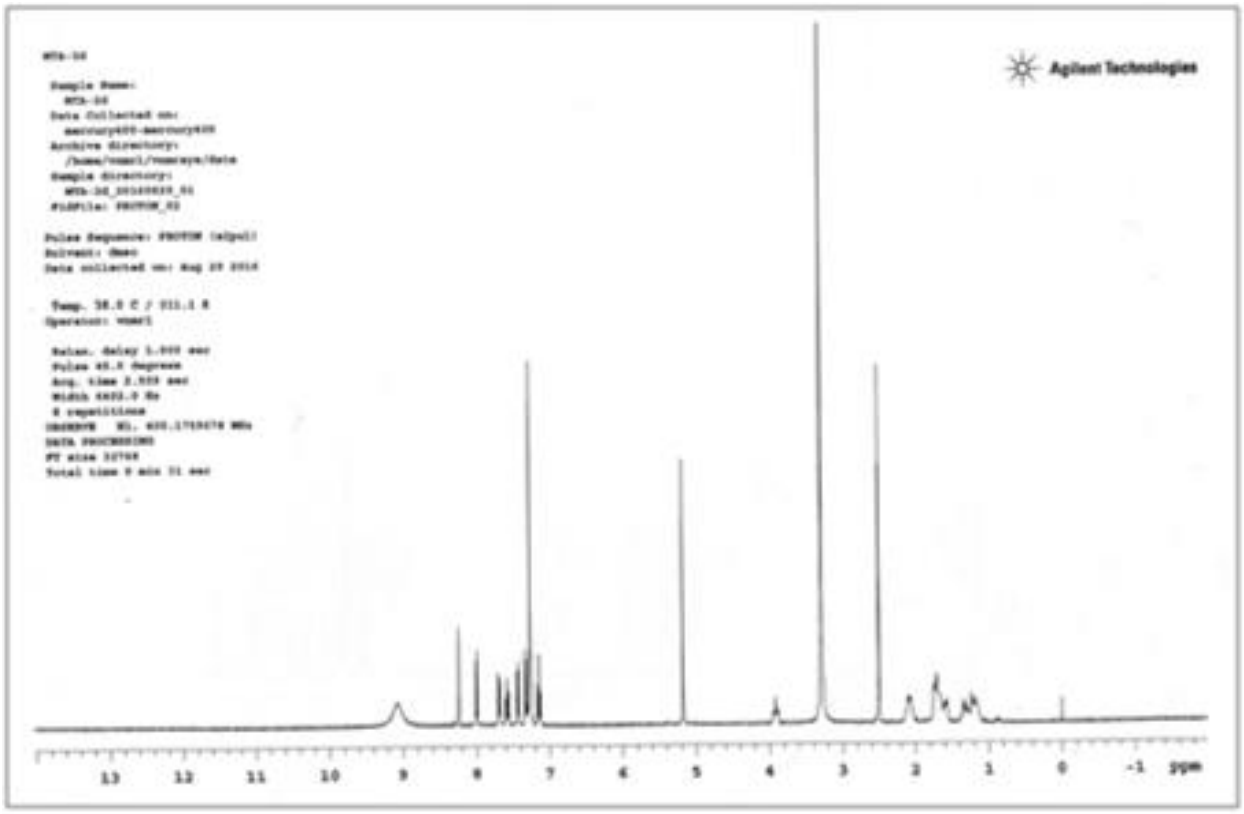


Figure 35. ^{1}H-NMR spectra of M12

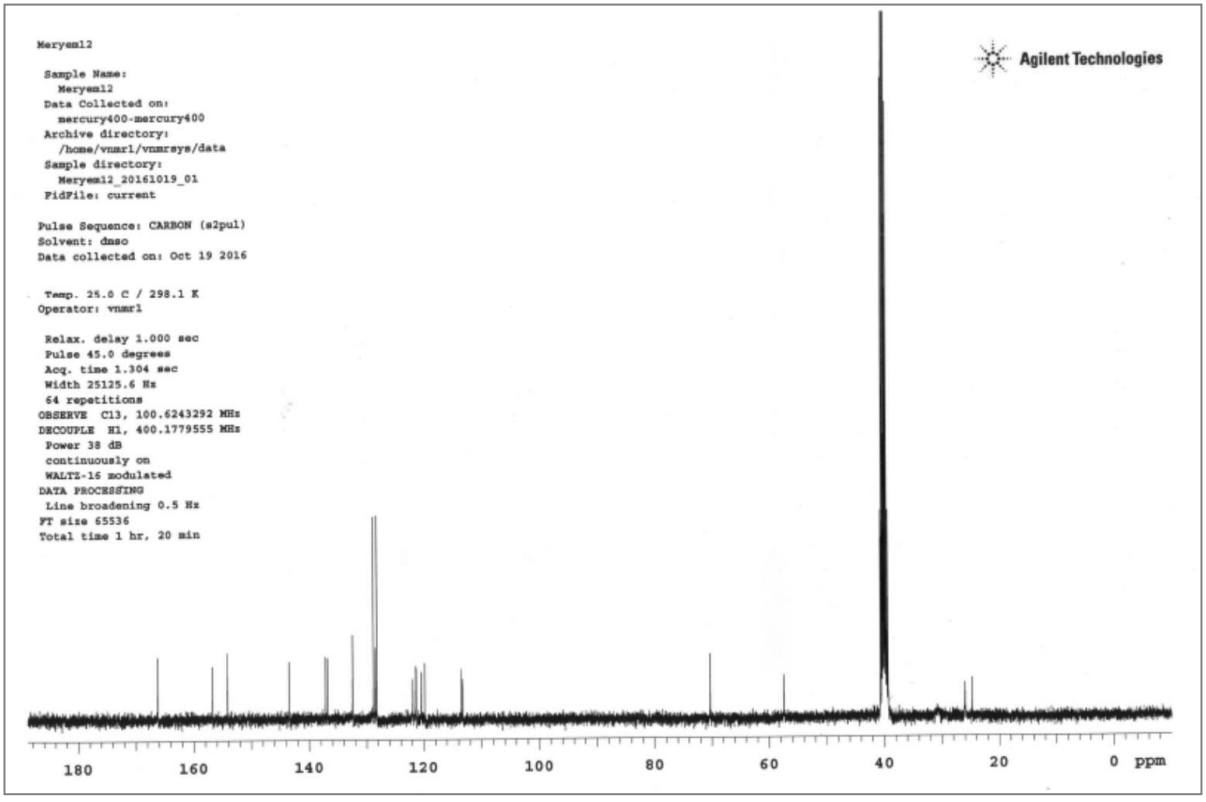


Figure 36. ^{13}C-NMR spectra of M12

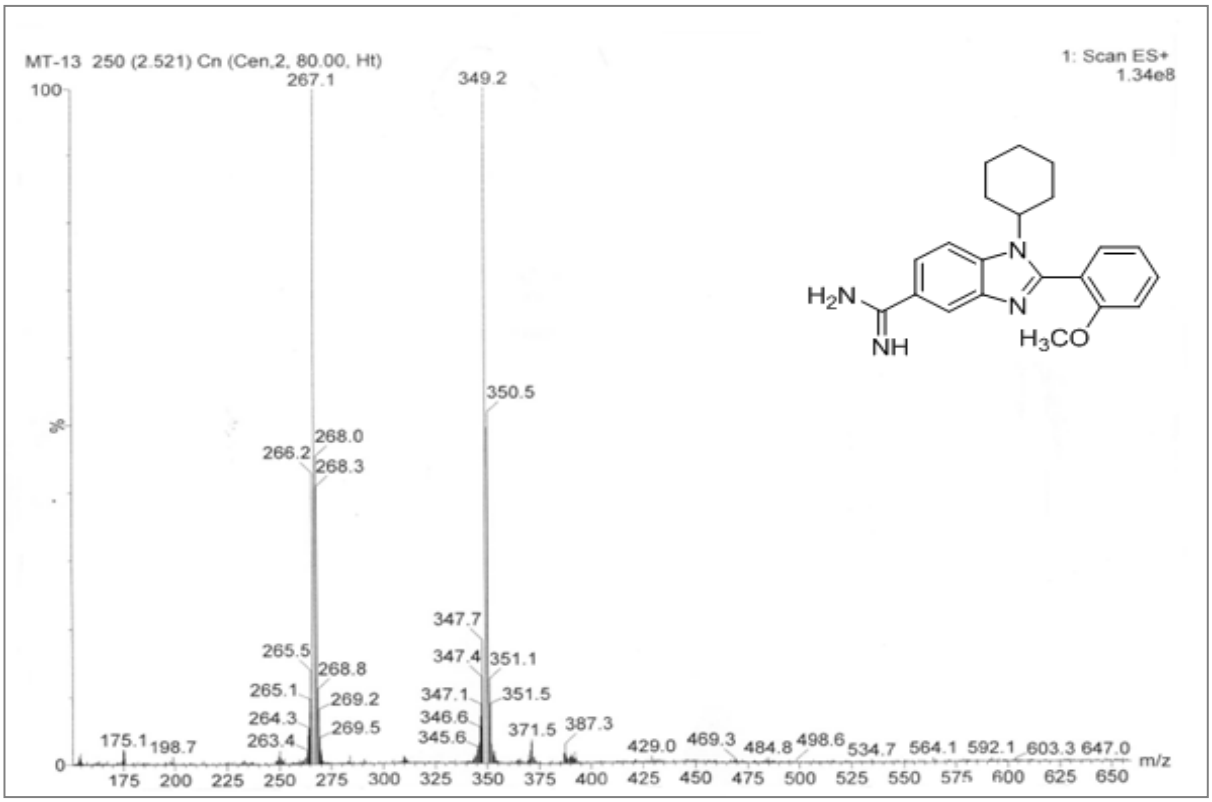


Figure 37. MASS spectra of M13

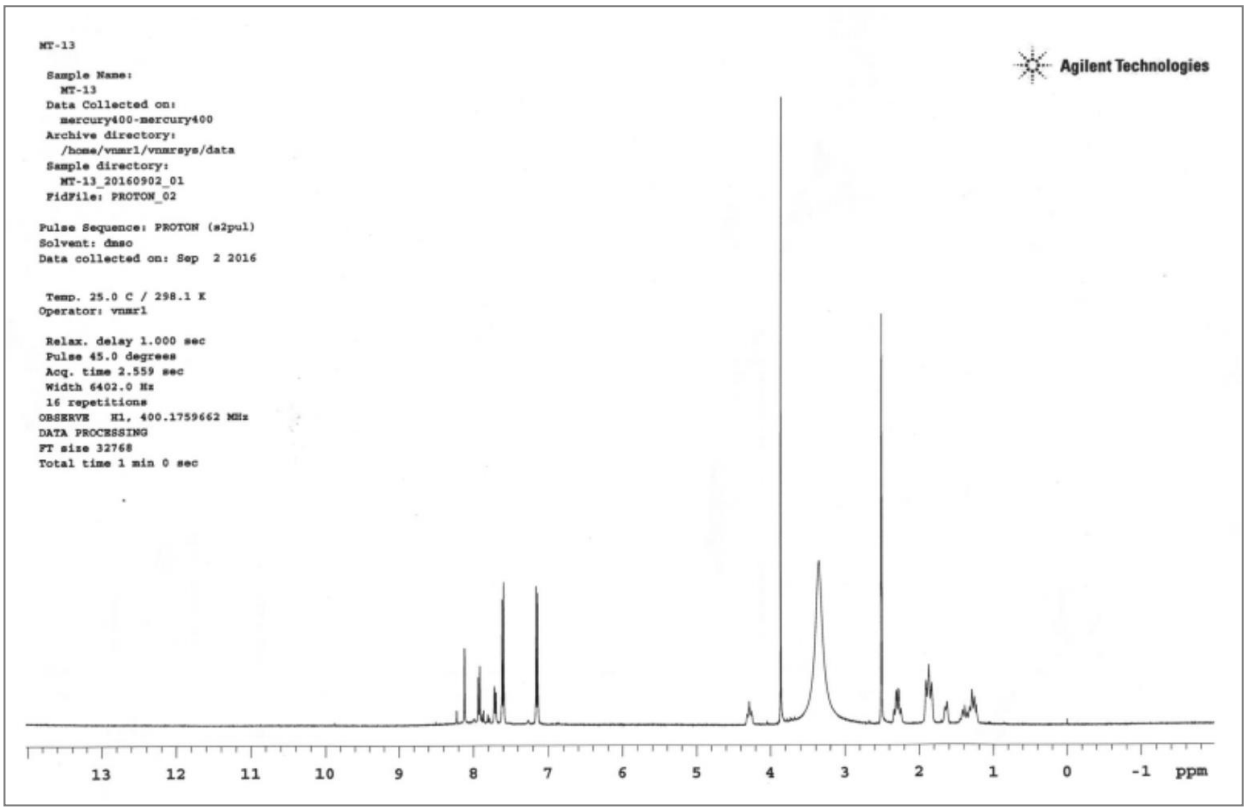


Figure 38. ^{1}H-NMR spectra of M13

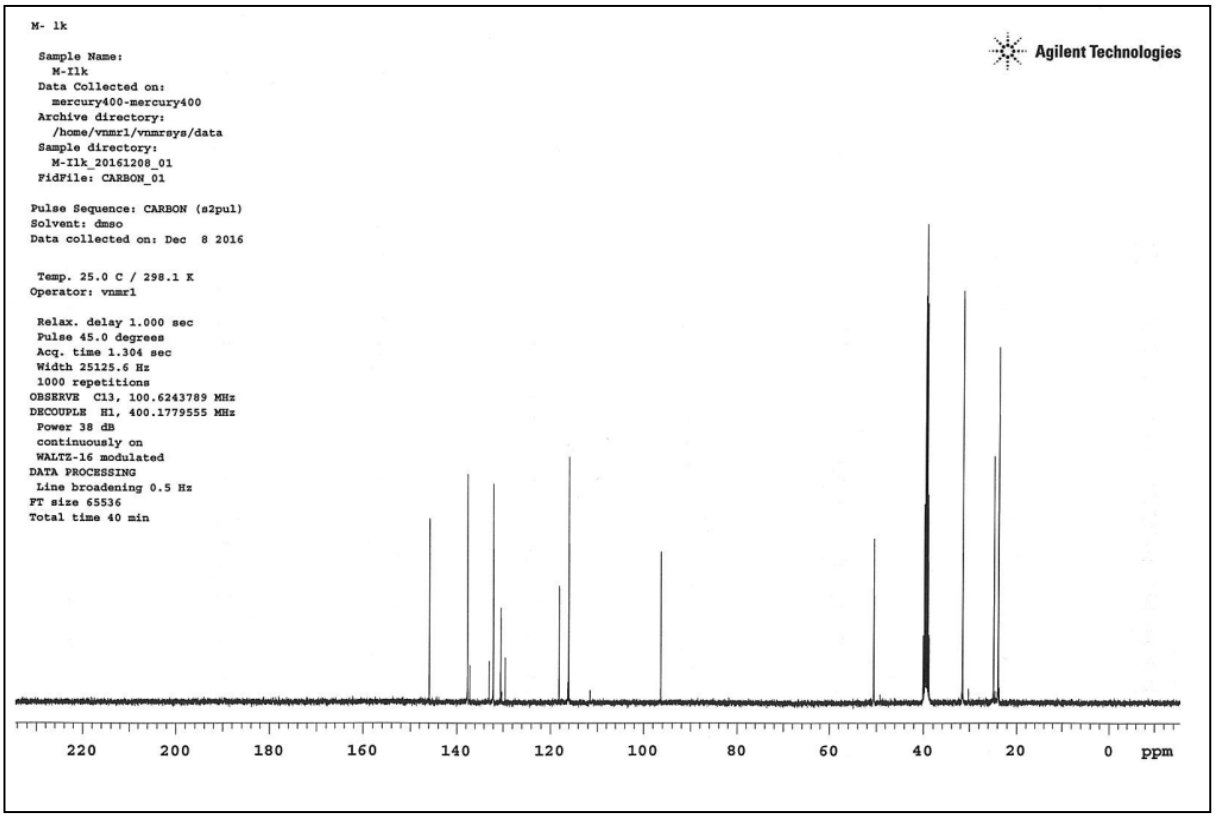


Figure 39. ^{13}C-NMR spectra of M13

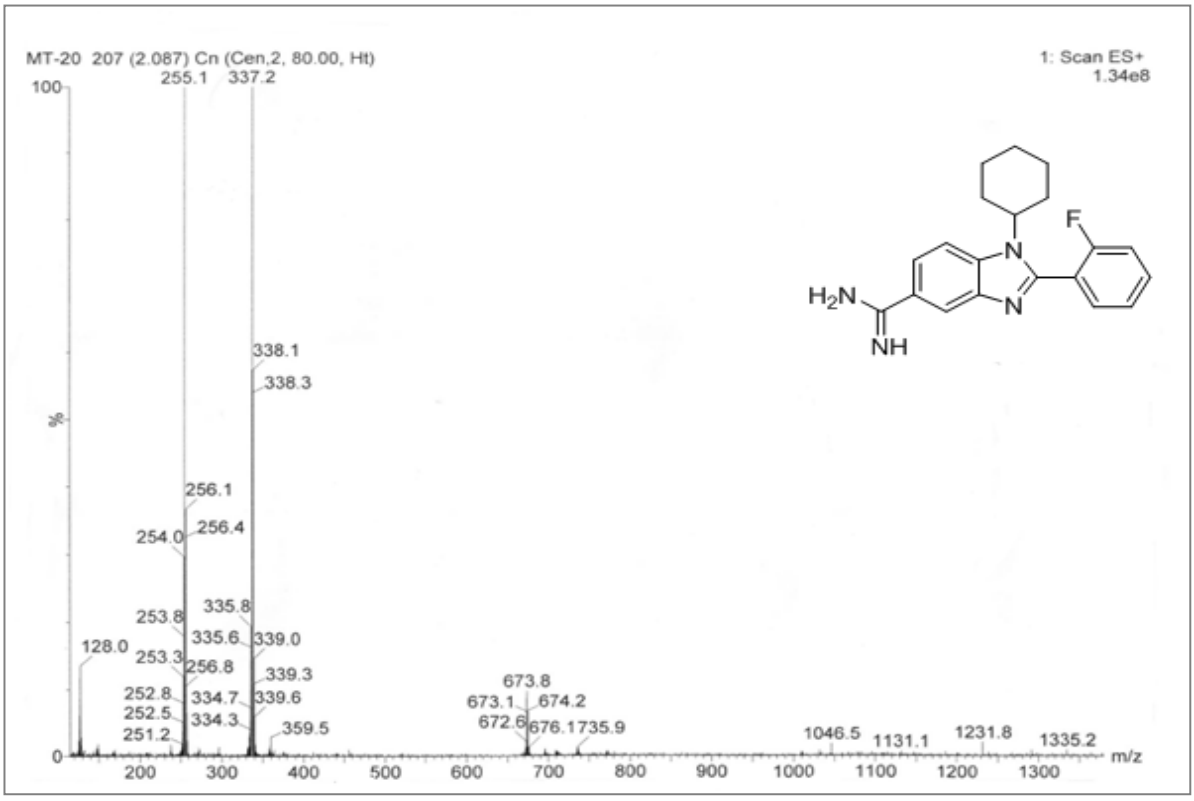


Figure 40. MASS spectra of M14

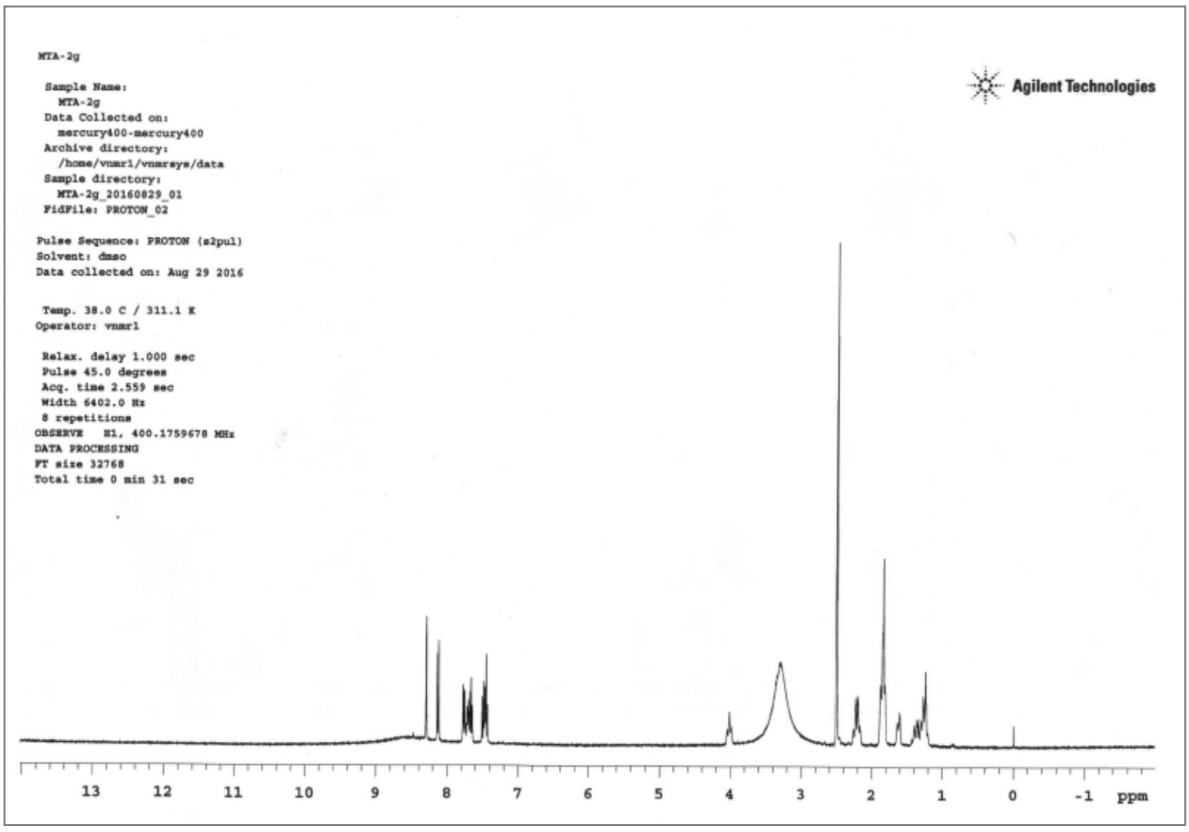


Figure 41. ^{1}H-NMR spectra of M14

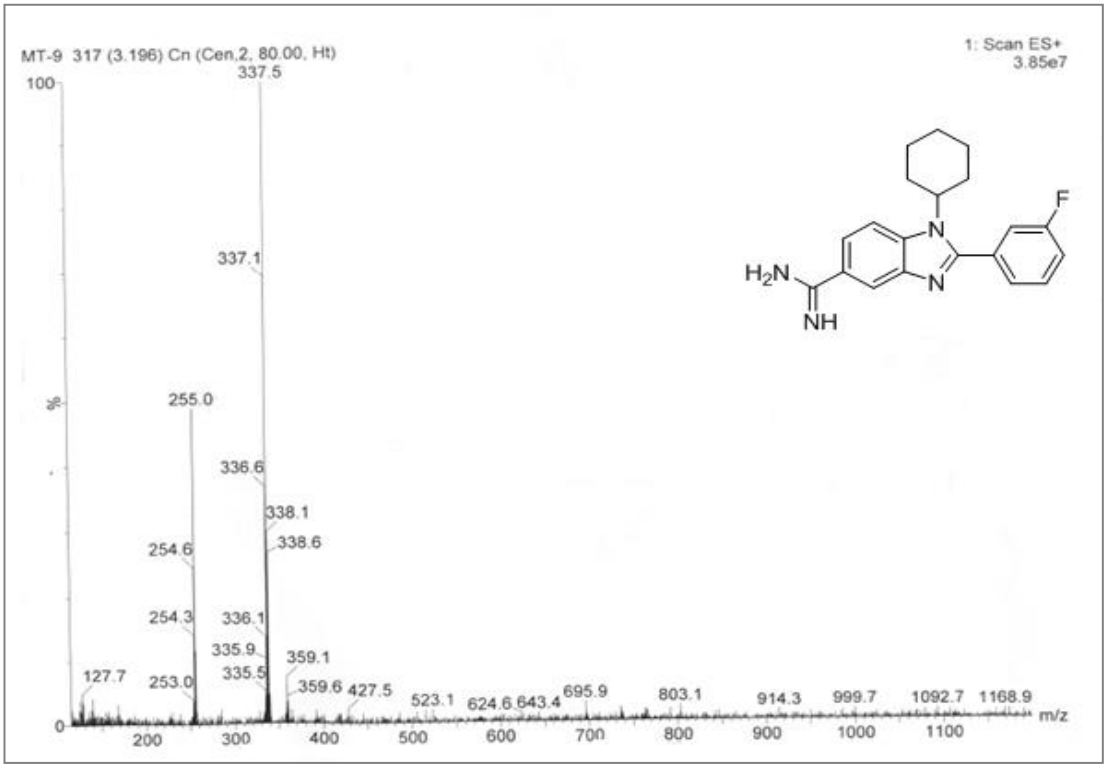


Figure 42. MASS spectra spectrum of M15

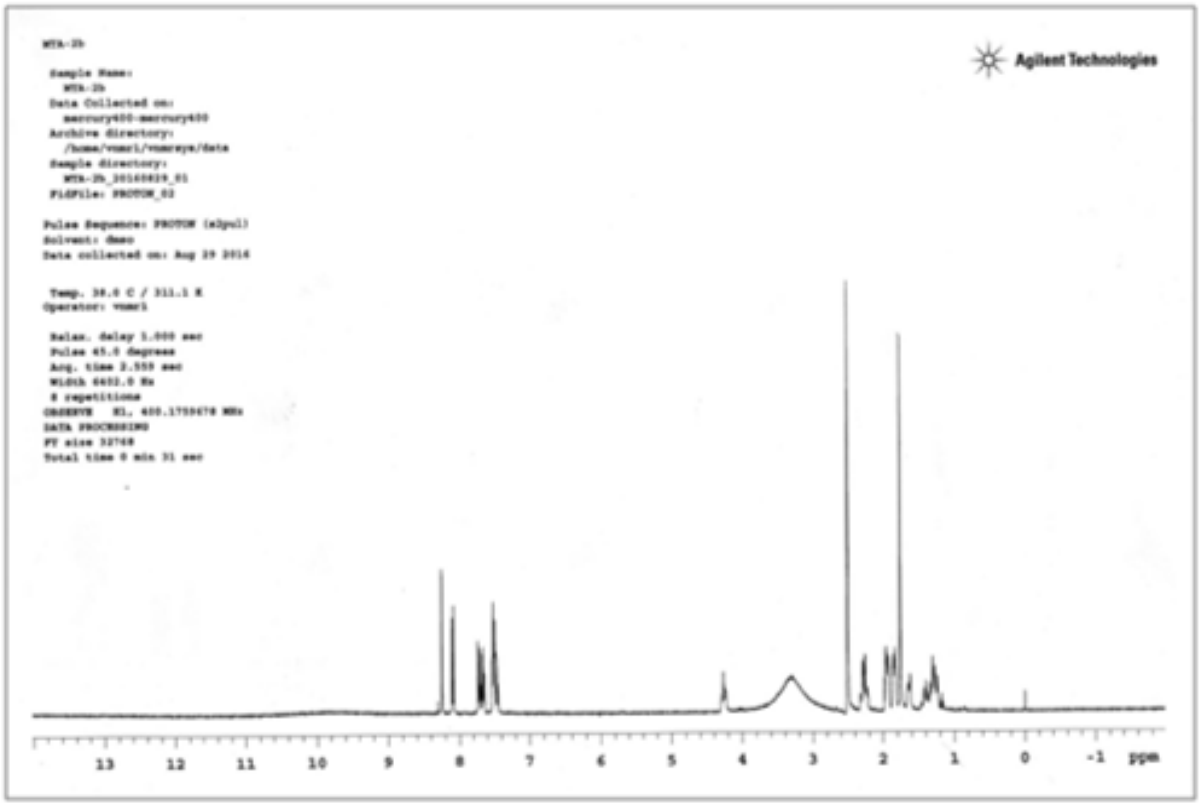


Figure 43. ^{1}H-NMR spectra of M15

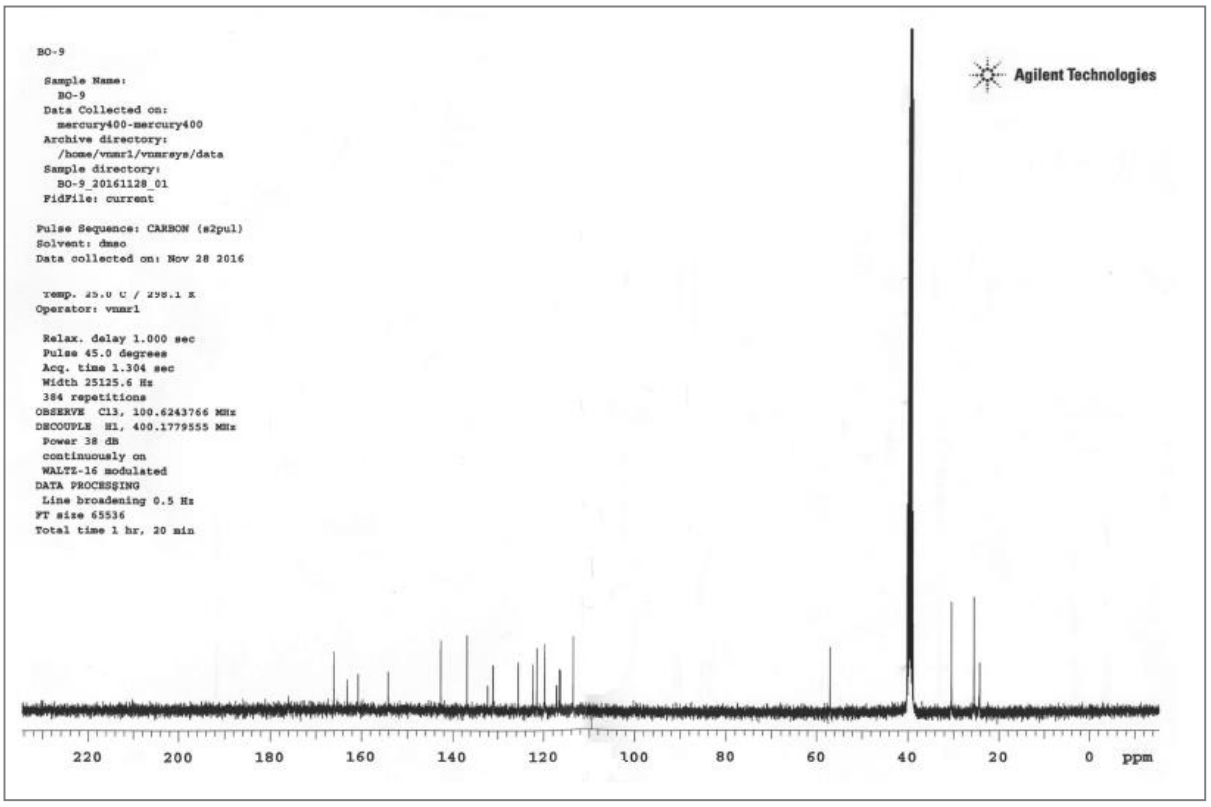


Figure 44. ^{13}C-NMR spectra of M15

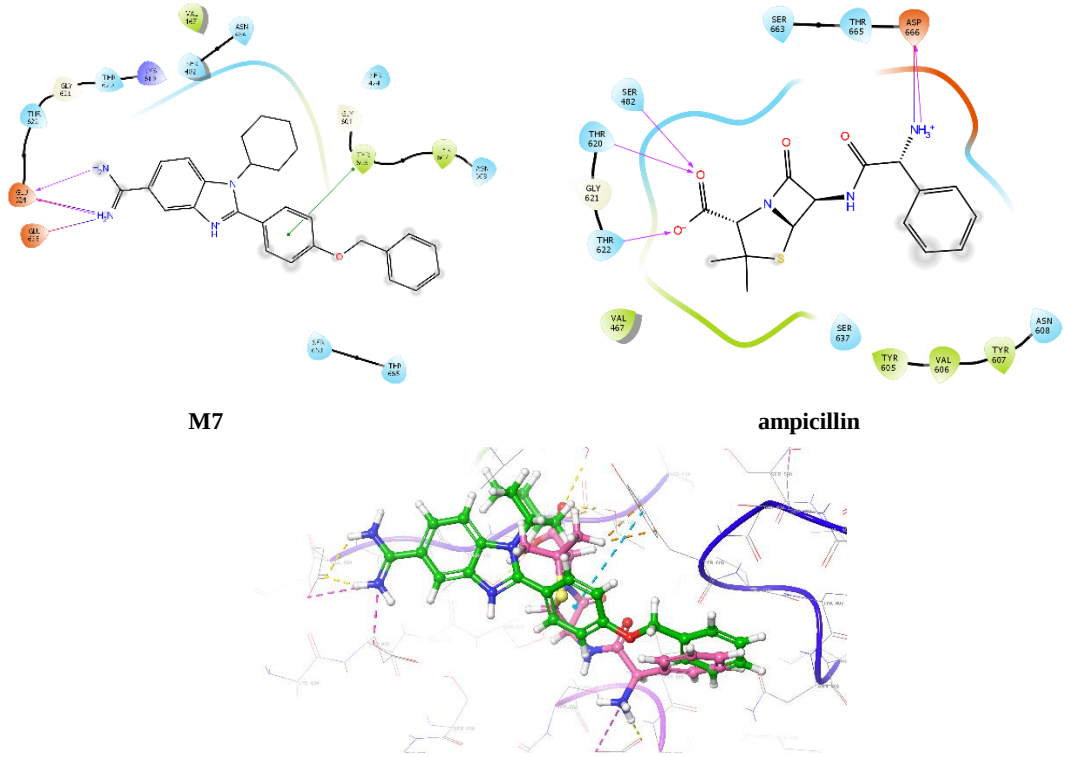


Figure 45. Ampicillin and **M7** interaction diagram on the PBP4 at the active site (PDB: 6MKI) (left) and binding poses of ampicillin (pink) and **M7** (green)