Electronic Supporting Information

"On water" synthesis of dibenzo-[1,4]-diazepin-1-ones using L-proline as an organocatalyst, catalyst-free conditions and their evaluation as α-glucosidase inhibitors†

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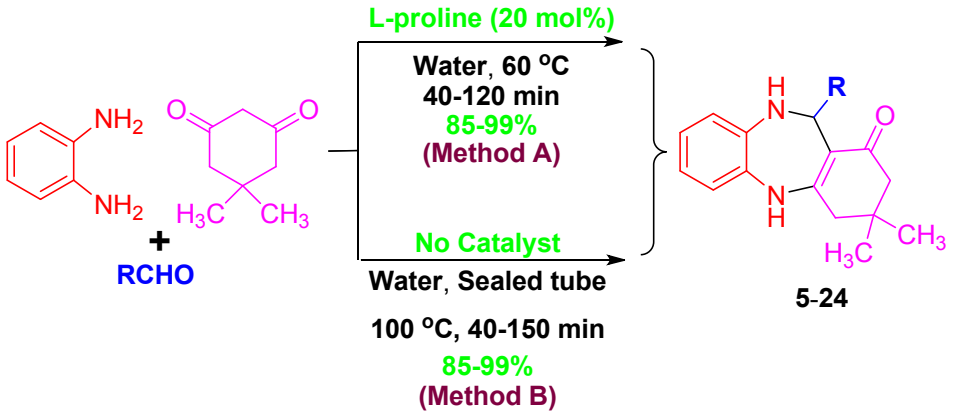
General methods: All the starting materials were purchased from Spectrochem, SD-Fine and Sigma-Aldrich and used as received. Melting points were determined in open capillaries using Stuart SMP30 melting point apparatus and uncorrected. ^{1}H and ^{13}C-NMR spectra were recorded on Bruker Avance 500 and 126 MHz spectrometer using $CDCl_3$ or CD_3OD as solvents (and reported in δ ppm). The mass spectra were recorded on Bruker-micro-TOF MS analyzer.

General procedure for the synthesis of dibenzo-[1,4]-diazepin-1-ones:

Method-A: To a mixture of *o*-phenylenediamine (1 mmol, 1 equiv), dimedone (1.1 mmol, 1.1 equiv) in water (3 mL) was added L-proline (20 mol%) and the contents were heated at 60 ^{o}C for 10 min. To this hot mixture, aldehyde (1.1 mmol, 1.1 equiv) was added and stirring continued at 60 ^{o}C for 110 min. After completion of the reaction (as monitored by TLC), the contents were cooled to room temperature. The crude compound obtained was washed with water and recrystallized using ethylacetate and petroleum ether (1:1) to give the desired compound in pure form.

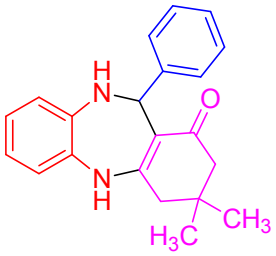
Method-B: A mixture of *o*-phenylenediamine (1 mmol, 1 equiv), dimedone (1.1 mmol, 1.1 equiv) in water (3 mL) was heated at 100 ^{o}C for 20 min in sealed tube. To this mixture aldehyde (1.1 mmol, 1.1 equiv) was added and heating continued for 130 min. After completion of the reaction (as monitored by TLC), the contents were cooled to room temperature. The crude compound obtained was washed with water and recrystallized using ethylacetate and petroleum ether (1:1) to give the desired compound in pure form. (See ESI for the ^{1}H- ^{13}C-NMR and mass spectra).



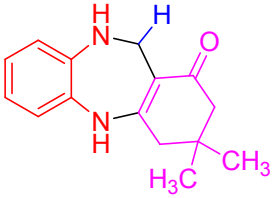
Scheme 1. Synthesis of dibenzo-[1,4]-diazepin-1-one derivatives (**5-22**) Preparation of dibenzo-[1,4]-diazepin-1-one derivatives (**5-24**); **Method A.** L-proline as catalyst, **Method B.** Sealed tube (catalyst free)

Spectral data for the compounds (4-24)

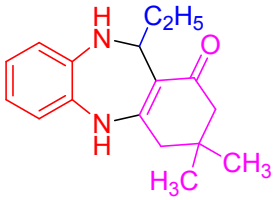
3,3-dimethyl-11-phenyl-2,3,4,5,10,11-hexahydro-1H-dibenzo[b,e][1,4]diazepin-1-one (4): Pale yellow solid; m.p.= 245-247 °C; ^{1}H-NMR (500 MHz, CD_3OD): δ 7.08–7.06 (m, 4H), 6.99 (d, *J* = 5 Hz, 1H), 6.93 (m, 1H), 6.71–6.66 (m, 2H), 6.50 (d, *J* = 5 Hz, 1H), 5.85 (s, 1H), 2.66 (s, 2H), 2.25 (dd, *J* = 25, 15 Hz, 2H), 1.20 (s, 3H), 1.14 (s, 3H); ^{13}C-NMR (126 MHz, CD_3OD): δ 194.65, 157.28, 143.59, 137.77, 131.74, 127.46, 127.23, 126.01, 123.41, 121.45, 121.02, 120.03, 110.09, 57.61, 49.25, 44.56, 31.74, 27.30, 26.83; MS (ESI): Calculated for $C_{21}H_{22}N_2O$, m/z 318; found 319 (M+1), Enantiomeric excess (ee) 80:20 Determind by HPLC analysis using chiral column (chirlpack ic) hexane and isopropanol = 80/20, flow rate 1.0 mL min^{-1}, UV 254 nm,T = 30 °C, t_R = 7.19 min (major), t_R = 19.26 min (minor).



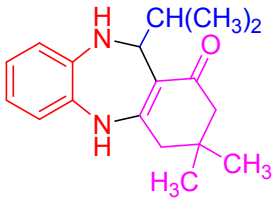
3,3-dimethyl-2,3,4,5,10,11-hexahydro-1H- dibenzo[b,e][1,4]diazepin-1-one (5): White solid; m.p.= 180-182 °C; ^{1}H NMR (500 MHz, CD_3OD): δ 7.16 – 7.05 (m, 1H), 7.05 – 6.83 (m, 3H), 4.65 (s, 1H), 4.06 (d, *J* = 58.0 Hz, 2H), 2.53 (d, *J* = 16.8 Hz, 2H), 2.25 (s, 2H), 1.12 (d, *J* = 3.5 Hz, 6H);^{13}C-NMR (126 MHz, CD_3OD): δ 194.72, 151.75, 123.58, 123.37, 122.39, 120.90, 120.36, 119.63, 52.34, 49.08, 44.04, 43.75, 26.9; MS (ESI): Calculated for $C_{15}H_{18}N_2O$ m/z 242.32; found 243 (M+1).



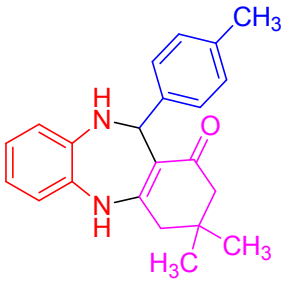
11-ethyl-3,3-dimethyl-2,3,4,5,10,11-hexahydro-1H-dibenzo[b,e][1,4]diazepin-1-one (6): White solid; m.p.= 239-240 °C; ^{1}H NMR (500 MHz, CD_3OD): δ 7.02 (d, *J* = 7.8 Hz, 1H), 6.92–6.82 (m, 3H), 4.51 (t, *J* = 15 Hz, 1H), 2.53 (dd, *J* = 20, 15Hz, 2H), 2.24 (dd, *J* = 30, 15 Hz, 2H), 1.36–1.29 (m, 2H), 1.14 (s, 3H), 1.07 (s, 3H), 0.90 (t, *J* = 5 Hz, 3H); ^{13}C-NMR (126 MHz, CD_3OD): δ 194.52, 156.26, 136.94, 131.38, 123.35, 121.11, 120.66, 120.02, 112.99, 53.94, 49.24, 44.43, 31.61, 28.43, 27.43, 26.33, 9.96; MS (ESI): Calculated for $C_{17}H_{22}N_2O$ m/z 270; Found 271 (M+1).



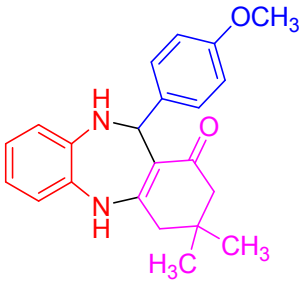
11-isopropyl-3,3-dimethyl-2,3,4,5,10,11-hexahydro-1H-dibenzo[b,e][1,4]diazepin-1-one (7): White solid; m.p.= 231-232 °C; ^{1}H-NMR (500 MHz, $CDCl_3$ + CD_3OD): δ 6.89–6.71 (m, 4H), 4.34 (t, *J* = 10 Hz, 1H), 2.58 (t, *J* = 15 Hz, 1H), 2.44 (dd, *J* = 15,15 Hz, 1H), 2.27 (dd, *J* = 15, 15 Hz, 2H), 1.11 (d, *J* = 15 Hz, 6H), 0.92 (d, *J* = 5 Hz, 3H), 0.82 (d, *J* = 5 Hz, 3H); ^{13}C-NMR (126 MHz, $CDCl_3$ + CD_3OD): δ 198.71, 140.89, 134.45, 127.3, 124.86, 124.67, 123.85, 117.19, 61.93, 49.20, 37.04, 35.65, 33.09, 31.03, 24.01, 23.46; MS (ESI): Calculated for $C_{18}H_{24}N_2O$ m/z 284; found 285 (M+1).



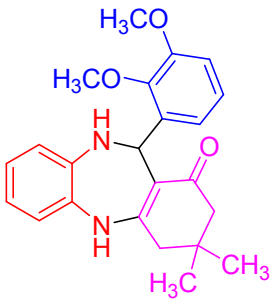
3,3-dimethyl-11-p-tolyl-2,3,4,5,10,11-hexahydro-1H-dibenzo[b,e][1,4]diazepin-1-one (8): Pale yellow solid; m.p.= 223-225 °C; ^{1}H-NMR (500 MHz, CD_3OD): δ 7.24 (dd, *J* = 6.1, 3.2 Hz, 1H), 6.99–6.95 (m, 3H), 6.91 (d, *J* = 10 Hz, 2H), 6.74–6.69 (m, 2H), 6.54 (dd, *J* = 7.5, 1.5 Hz, 1H), 5.84 (s, 1H), 2.31 (d, *J* = 15 Hz, 1H), 2.23 (d, *J* = 15 Hz, 1H), 2.21–2.14 (m, 4H), 1.99 (d, *J* = 45.9 Hz, 1H), 1.20–1.18 (m, 3H), 1.15–1.12 (m, 3H); ^{13}C-NMR (126 MHz, CD3OD): δ 194.56, 171.58, 158.16, 157.13, 137.91, 135.80, 131.78, 128.30, 123.44, 121.53, 121.04, 112.82, 110.49, 57.01, 54.13, 49.29, 44.56, 31.74, 26.86; MS (ESI): Calculated for C22H24N2O m/z 332; found 333 (M+1).



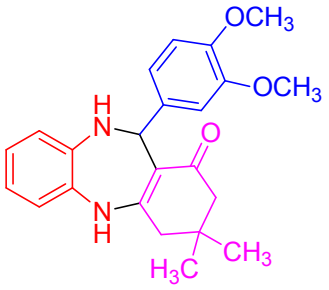
11-(4-methoxyphenyl)-3,3-dimethyl-2,3,4,5,10,11-hexahydro-1H dibenzo[b,e][1,4]diazepin-1-one (9): Pale Yellow; m.p.= 230-231 °C; ^{1}H-NMR (500 MHz, CD_3OD): δ 7.03 (d, *J* = 10 Hz, 2H), 6.96 (d, *J* = 10 Hz, 1H), 6.73 6.69 (m, 2H), 6.65 (d, *J* = 5 Hz, 2H), 6.55 (d, *J* = 10 Hz, 1H), 5.86 (s, 1H), 4.14–4.09 (m, 1H), 3.63 (s, 3H), 2.64 (s, 2H), 2.31 (d, *J* = 20 Hz, 1H), 2.23 (d, *J* = 15 Hz, 1H), 1.17 (s, 3H), 1.13 (s, 3H); ^{13}C-NMR (126 MHz, CD_3OD): δ 194.56, 171.58, 158.16, 157.13, 137.91, 135.80, 131.78, 128.30, 123.44, 121.53, 121.04, 120.05, 112.82, 110.49, 60.16, 57.01, 54.13, 49.29, 44.56, 27.40, 26.86; MS (ESI): Calculated for $C_{22}H_{24}N_2O_2$ m/z 348; found 349 (M+1). Enantiomeric excess (ee) 65:35 Determined by HPLC analysis using chiral column (chirlpack AS-H) hexane and isopropanol = 80/20, flow rate 1.0 mL min^{-1}, UV 254 nm,T = 30 °C, t_R = 9.05 min (major), t_R = 14.39 min (minor).



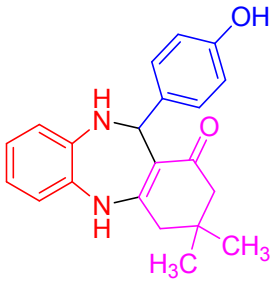
11-(2,3-dimethoxyphenyl)-3,3-dimethyl-2,3,4,5,10,11-hexahydro-1H-dibenzo[b,e]-[1,4]diazepin-1-one (10): Pale yellow solid; m.p.= 236-238 °C; ^{1}H-NMR (400 MHz, DMSO): δ 6.91 (d, *J* = 7.6 Hz, 1H), 6.85 (s, 1H), 6.68 – 6.53 (m, 4H), 6.49 (d, *J* = 8.1 Hz, 1H), 6.13 (d, *J* = 5.8 Hz, 1H), 5.64 (d, *J* = 5.7 Hz, 1H), 3.61 (s, 6H), 2.60 (t, *J* = 12.2 Hz, 2H), 2.15 (dd, *J* = 54.6, 15.9 Hz, 2H), 1.09 (s, 3H), 1.05 (s, 3H).; ^{13}C-NMR (101 MHz, DMSO): δ 192.46, 155.14, 148.55, 147.28, 139.27, 137.62, 131.62, 123.04, 121.06, 120.34, 119.90, 119.42, 112.10, 111.21, 110.95, 55.96, 55.63, 49.98, 44.57, 32.25, 29.25, 27.65.



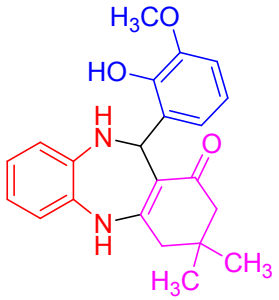
11-(3,4-dimethoxyphenyl)-3,3-dimethyl-2,3,4,5,10,11-hexahydro-1H-dibenzo[b,e]-[1,4]diazepin-1-one (11): Pale yellow solid; m.p.= 235-237 ^{o}C; ^{1}H-NMR (500 MHz, CD_3OD): δ 6.97 (d, *J* = 10 Hz, 1H), 6.77 (s, 1H), 6.73 (q, *J* = 5, Hz, 2H), 6.64 (q, *J* = 5 Hz, 2H), 6.57 (t, j = 5 1H), 5.84 (s, 1H), 3.69 (s, 3H), 3.66 (s, 3H), 2.66 (q, *J* = 15 Hz, 2H), 2.33 (d, *J* = 15 Hz, 1H), 2.24 (d, *J* = 15 Hz, 1H), 1.18 (s, 3H), 1.14 (s, 3H).; ^{13}C-NMR (126 MHz, CD_3OD): δ 194.61, 157.15, 148.46, 147.50, 137.94, 136.64, 131.78, 123.49, 121.53, 121.07, 120.02, 119.75, 111.47, 110.81, 110.45, 57.28, 54.93, 49.28, 44.56, 31.76, 27.52, 26.64.; MS (ESI): Calculated for $C_{23}H_{26}N_2O_3$ *m/z* 378; found 379 (M+1).



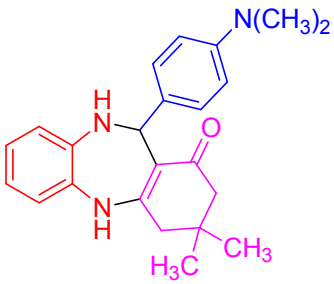
11-(4-hydroxyphenyl)-3,3-dimethyl-2,3,4,5,10,11-hexahydro-1H-dibenzo-[b,e]-[1,4]-diazepin-1-one (12): White solid; m.p.= 224-225 ^{o}C; ^{1}H-NMR (500 MHz, CD_3OD): δ 6.97-6.92 (m, 3H), 6.73 (t, *J* = 5 Hz, 2H), 6.54 (dd, *J* = 13.8, 8.0 Hz, 3H), 5.81 (s, 1H), 2.66 (s, 2H), 2.31 (d, *J* = 20 Hz, 1H), 2.23 (d, *J* = 15 Hz, 1H), 1.19 (s, 3H), 1.13 (s, 3H); ^{13}C-NMR (126 MHz, CD_3OD): δ 194.59, 157.15, 155.37, 137.87, 134.62, 131.83, 128.32, 123.40, 121.59, 121.07, 119.99, 114.14, 110.55, 57.06, 49.27, 44.56, 31.73, 27.32, 26.82; MS (ESI): Calculated for $C_{21}H_{22}N_2O_2$ m/z 334; found 335 (M+1).



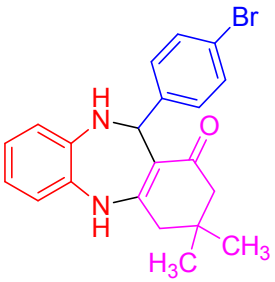
11-(2-hydroxy-3-methoxyphenyl)-3,3-dimethyl-2,3,4,5,10,11-hexahydro-1H-dibenzo[b,e][1,4]diazepin-1-one(13): White solid; m.p.= 227-228 ^{o}C; ^{1}H-NMR (500 MHz, MeOD) δ 6.97 (d, *J* = 9.2 Hz, 1H), 6.78 (d, *J* = 0.9 Hz, 1H), 6.73 (dd, *J* = 6.4, 2.7 Hz, 2H), 6.64 (dt, *J* = 8.4, 4.8 Hz, 2H), 6.60-6.55 (m, 1H), 5.83 (d, *J* = 10.3 Hz, 1H), 3.66 (s, 3H), 2.66 (q, *J* = 16.1 Hz, 2H), 2.32 (q, *J* = 16.1 Hz, 2H), 1.18 (s, 3H), 1.14 (s, 3H).; ^{13}C-NMR (126 MHz, CD_3OD): δ 194.59, 157.10, 155.37, 138.00, 134.62, 131.80, 128.32, 123.40, 122.00, 121.07, 120.00, 114.14, 110.55, 57.28, 55.00, 49.28, 44.56, 31.76, 27.52, 27.00



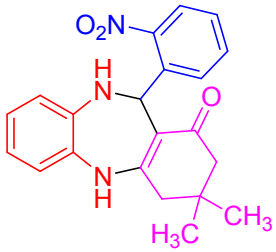
11-(4-(dimethylamino)phenyl)-3,3-dimethyl-2,3,4,5,10,11-hexahydro-1H-dibenzo[b,e][1,4]diazepin-1-one (14): White solid; m.p.= 230-232 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.93 (d, *J* = 8.1 Hz, 2H), 6.72 (s, 3H), 6.59 – 6.30 (m, 3H), 5.84 (s, 1H), 4.36 (s, 1H), 2.81 (s, 6H), 2.59 (t, *J* = 14.2 Hz, 1H), 2.33 (dd, *J* = 31.0, 15.8 Hz, 2H), 2.21 (d, *J* = 16.2 Hz, 1H), 1.13 (s, 3H), 1.07 (s, 3H); ^{13}C-NMR (126 MHz, $CDCl_3$): δ 193.76, 151.75, 149.19, 137.54, 132.23, 130.97, 127.92, 123.69, 121.70, 120.95, 119.72, 112.41, 57.47, 49.83, 40.59, 32.33, 29.00, 27.73; MS (ESI): Calculated for $C_{23}H_{27}N_3O$ m/z 361; found 362 (M+1), 384 (M+23).



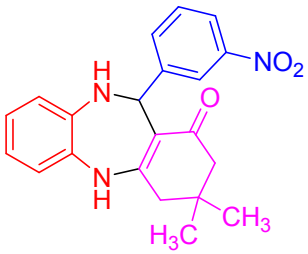
11-(4-bromophenyl)-3,3-dimethyl-2,3,4,5,10,11-hexahydro-1H-dibenzo[b,e][1,4]diazepin-1-one (15): Pale yellow solid; m.p.= 218-220 °C; ^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.27 (t, *J* = 10 Hz, 2H), 6.96 (d, *J* = 10 Hz, 2H), 6.77 (s, 3H), 6.64 (s, 1H), 6.45 (t, *J* = 5 Hz, 1H), 5.90 (s, 1H), 4.42 (s, 1H), 2.61 (d, *J* = 15 Hz, 1H), 2.44 (d, *J* = 15 Hz, 1H), 2.34 (d, *J* = 15 Hz, 1H), 2.25 (d, *J* = 8 Hz, 1H), 1.16 (s, 3H), 1.09 (s, 3H); ^{13}C-NMR (126 MHz, $CDCl_3$): δ 193.93, 153.19, 143.04, 136.83, 131.25, 130.83, 128.90, 124.12, 121.68 , 121.51, 120.45, 120.00, 111.14, 57.66, 49.75, 46.44, 32.35, 28.80, 27.77.; MS (ESI): Calculated for $C_{21}H_{21}BrN_2O$ m/z 397; found 398 (M+1).



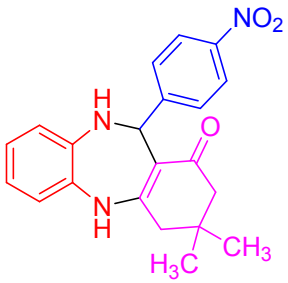
3,3-dimethyl-11-(2-nitrophenyl)-2,3,4,5,10,11-hexahydro-1H-dibenzo[b,e][1,4]diazepin-1-one (16): pale yellow solid; m.p.= 231-233 °C; ^{1}H- NMR (500 MHz, CD_3OD): δ 8.00 (d, *J* = 10 Hz, 2H), 7.34 (d, *J* = 5 Hz, 2H), 7.01 (d, *J* = 5 Hz, 1H), 6.78–6.72 (m, 2H), 6.55 (d, *J* = 5 Hz, 1H), 5.94 (s, 1H), 2.71 (dd, *J* = 15, 5, 2H), 2.30 (q, *J* = 15 Hz, 2H), 1.21 (s, 3H), 1.15 (s, 3H); ^{13}C-NMR (126 MHz, CD_3OD): δ 194.80, 171.57, 157.54, 149.59, 138.37, 136.80, 131.99, 128.22, 127.48, 124.15, 121.77, 121.42, 120.31, 108.98, 60.13, 54.58, 49.07, 44.51, 31.77, 26.97; MS (ESI): Calculated for $C_{21}H_{21}N_3O_3$ m/z 363.16; found 364 (M+1).



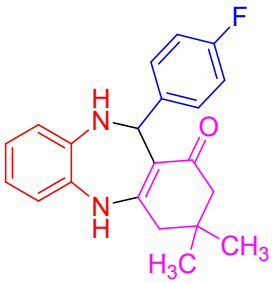
3,3-dimethyl-11-(3-nitrophenyl)-2,3,4,5,10,11-hexahydro-1H-dibenzo[b,e][1,4]diazepin-1-one (17): pale yellow solid; m.p.= 148-149 °C; ^{1}H- NMR (500 MHz, CD_3OD): δ 8.00 (s, 1H), 7.94 (d, *J* = 5 Hz, 1H), 7.55 (d, *J* = 5 Hz, 1H), 7.38 (t, *J* = 10 Hz, 1H), 7.00 (d, *J* = 10 Hz, 1H), 6.77 - 6.72 (m, 2H), 6.56 (d, *J* = 10 Hz, 1H), 5.97 (s, 1H), 2.73 (s, 2H), 2.35 (d, *J* = 15 Hz, 1H), 2.27 (d, *J* = 15 Hz, 1H), 1.22 (s, 3H), 1.17 (s, 3H); ^{13}C-NMR (126 MHz, CD_3OD): δ 194.66, 157.72, 147.97, 146.22, 137.43, 133.59, 131.57, 128.68, 123.80, 121.82, 121.31,121.27, 120.98, 120.34, 109.09, 57.10, 49.12, 44.45, 31.77, 27.24, 26.78; MS (ESI): Calculated for $C_{21}H_{21}N_3O_3$ m/z 363.16; found 364 (M+1).



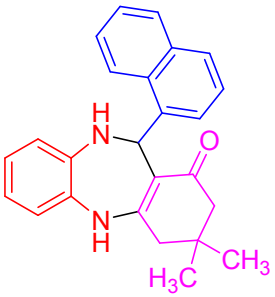
3,3-dimethyl-11-(4-nitrophenyl)-2,3,4,5,10,11-hexahydro-1H-dibenzo[b,e][1,4]diazepin-1-one (18): Pale yellow solid; m.p.= 282-283 °C; ^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.97 (d, *J* = 10 Hz, 2H), 7.30 (d, *J* = 5 Hz, 2H), 6.97 (d, *J* = 5 Hz, 1H), 6.75–6.69 (m, 2H), 6.52 (d, *J* = 5 Hz, 1H), 5.91 (s, 1H), 2.65 (dd, *J* = 20, 5, 2H), 2.27 (dd, *J* = 20, 5, Hz, 2H), 1.18 (s, 3H), 1.12 (s, 3H).; ^{13}C-NMR (126 MHz, $CDCl_3$): δ 161.45, 155.55, 151.72, 150.36, 141.35, 135.46, 132.13, 127.72, 126.56, 125.25, 125.17, 118.60, 112.90, 61.16, 48.39, 35.66, 31.03, 30.84, 2.48; MS (ESI): Calculated for $C_{21}H_{21}N_3O_3$ m/z 363.16; found 364 (M+1).



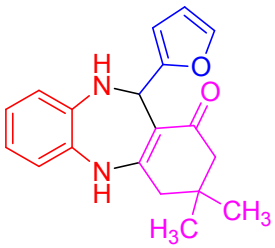
11-(4-fluorophenyl)-3,3-dimethyl-2,3,4,5,10,11-hexahydro-1H- -1-one dibenzo[b,e]-[1,4]diazepin (19): pale yellow solid; m.p.= 200-202 ^{o}C; ^{1}H- NMR (500 MHz, $CDCl_3$): δ 7.29 (s, 1H), 7.05 (t, *J* = 5.6 Hz, 2H), 6.84–6.75 (m, 5H), 6.49–6.45 (t, 2H), 5.93 (s, 1H), 4.15 (q, *J* = 10 Hz, 3H), 2.64 (d, *J* = 15, Hz, 1H), 2.45 (d, *J* = 15 Hz, 1H), 2.35 (d, *J* = 15 Hz, 1H), 2.26 (d, *J* = 15 Hz, 1H), 1.18 (s, 3H), 1.11 (s, 3H); ^{13}C-NMR (126 MHz, $CDCl_3$): δ 193.91, 171.19, 162.42, 160.48, 152.89, 139.72, 136.98, 130.92, 128.60, 124.00, 121.71, 121.44, 119.86, 114.99, 114.82, 60.41, 57.52, 49.73, 46.54, 32.36, 28.78, 27.81, 21.05, 14.20; MS (ESI): Calculated for $C_{21}H_{21}FN_2O$ m/z 336; found 337 (M+1).



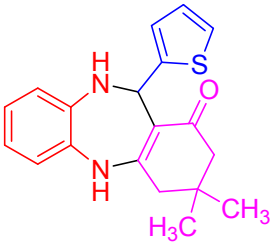
3,3-dimethyl-11-(naphthalen-1-yl)-2,3,4,5,10,11-hexahydro-1H-dibenzo[b,e]-[1,4]diazepin-1-one (20): White solid; m.p.= 220-222 ^{o}C; ^{1}H-NMR (500 MHz, $CDCl_3$): δ 8.37 (d, *J* = 10 Hz, 1H), 7.83 (d, *J* = 5 Hz, 1H), 7.65 (t, *J* = 10 Hz, 1H), 7.57 (d, *J* = 10 Hz, 1H), 7.52 (t, *J* = 5 Hz, 1H), 7.07 (t, *J* = 5 Hz, 1H), 6.86–6.84 (m, 2H), 6.76 (d, *J* = 10 Hz, 1H), 6.67 (t, *J* = 5 Hz, 2H), 6.50 (t, *J* = 5 Hz, 1H), 5.97 (d, *J* = 5 Hz, 1H), 4.56 (s, 1H), 2.68 (d, *J* = 15 Hz, 1H), 2.53 (d, *J* = 15 Hz, 1H), 2.35 (d, *J* = 15 Hz, 1H), 2.27 (d, *J* = 15 Hz, 1H), 1.19s (s, 3H), 1.15 (s, 3H); ^{13}C-NMR (126 MHz, $CDCl_3$): δ 194.09, 153.82, 138.61, 136.91, 134.13, 131.16, 129.24, 127.61, 126.56, 125.36, 124.55, 123.72, 123.21, 122.49, 121.54, 119.65, 111.11, 54.58, 49.85, 46.56, 32.42, 28.76, 27.97; MS (ESI): Calculated for $C_{25}H_{24}N_2O$ m/z 368; found 369 (M+1). Enantiomeric excess (ee) 63:37 Determined by HPLC analysis using chiral column (chiralcel oj-h) hexane and isopropanol = 80/20, flow rate 1.0 mL min^{-1}, UV 254 nm,T = 30 ^{o}C, t_R = 32.39 min (major), t_R = 9.81 min (minor).



11-(furan-2-yl)-3,3-dimethyl-2,3,4,5,10,11-hexahydro-1H-dibenzo[b,e][1,4]diazepin-1-one (21): Off white solid; m.p.= 215-217 ^{o}C; ^{1}H-NMR (500 MHz, CD_3OD): δ 7.23 (s, 1H), 6.95 (d, *J* = 10 Hz, 1H), 6.80–6.71 (m, 3H), 6.05 (s, 1H), 5.88 (s, 1H), 5.77 (d, *J* = 2.6 Hz, 1H), 2.64 (q, *J* = 16.2 Hz, 2H), 2.30 (dd, *J* = 25, 15 Hz, 2H), 1.18 (s, 3H), 1.15 (s, 3H); ^{13}C-NMR (126 MHz, CD_3OD): δ 194.33, 157.65, 155.88, 141.29, 137.98, 131.33, 123.48, 121.07 (d, *J* = 9.4 Hz), 120.03, 106.38, 51.11, 49.11, 44.45, 31.70, 27.40, 26.53.; MS (ESI): Calculated for $C_{19}H_{20}N_2O_2$ m/z 308; found 309 (M+1).

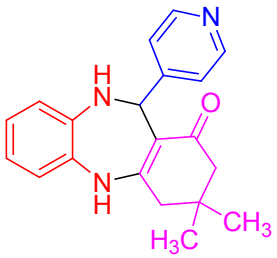


3,3-dimethyl-11-(thiophen-2-yl)-2,3,4,5,10,11-hexahydro-1H-dibenzo[b,e][1,4]diazepin-1-one (22): pale yellow solid; m.p.= 225-227 ^{o}C; ^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.0 (d, *J* = 5.0 Hz, 1H), 6.85–6.74 (m, 5H), 6.61 (d, *J* = 10 Hz, 1H), 6.49 (s, 1H), 6.24 (s, 1H), 4.47 (s, 1H), 2.64 (d, *J* = 20 Hz, 1H), 2.40–2.28 (m, 3H), 1.17 (s, 3H), 1.12 (s, 3H); ^{13}C-NMR (126 MHz, $CDCl_3$): δ 193.48, 152.96, 147.99, 137.04, 130.53, 126.31, 124.52, 123.93, 121.83, 121.51, 120.01, 112.75, 52.97, 49.65, 46.44, 32.35, 29.11, 27.51; MS (ESI): Calculated for $C_{19}H_{20}N_2OS$ *m/z* 324; found 325 (M+1). Enantiomeric excess (ee) 67/33 Determined by HPLC analysis using chiral

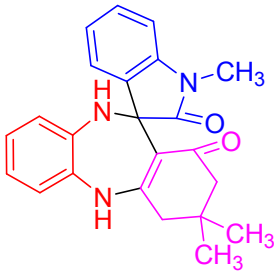


column (chirlpack ic) hexane and isopropanol = 80:20, flow rate 1.0 mL min^{-1},UV 254 nm,T = 30 °C, t_R = 7.98 min (major), t_R = 23.97 min (minor).

3,3-dimethyl-11-(pyridin-4-yl)-2,3,4,5,10,11-hexahydro-1H-dibenzo[b,e][1,4]diazepin-1-one (23): white solid; m.p.= 247-248 °C; ^{1}H-NMR (500 MHz, CD_3OD): δ 8.27 (d, *J* = 5 Hz, 2H), 7.16 (d, *J* = 5 Hz, 2H), 6.99 (q, *J* = 5 Hz, 1H), 6.75 (q, *J* = 5.9, Hz, 2H), 6.59 q, *J* = 5.8Hz, 1H), 5.89 (s, 1H), 4.93 (s, 2H), 2.68 (q, 2H), 2.33 (d, *J* = 15 Hz, 1H), 2.27 (d, *J* = 15 Hz, 1H), 1.18 (s, 3H), 1.13 (s, 3H); ^{13}C-NMR (126 MHz, CD_3OD): δ 194.70, 157.63, 154.08, 148.26, 137.44, 131.31, 123.81, 123.06, 121.23, 120.39, 108.55, 56.64, 49.11, 44.44, 31.74, 27.08.



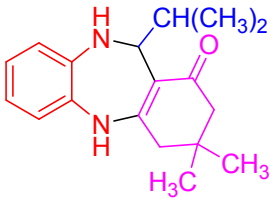
3,3-dimethyl-11-(2-oxoindolin-3-yl)-2,3,4,5,10,11-hexahydro-1H-dibenzo[b,e][1,4]diazepin-1-one (24): white solid; m.p.= 250-253 °C; ^{1}H-NMR (500 MHz, CD_3OD): δ 7.18 (t, *J* = 5 Hz, 2H), 6.98 (dd, *J* = 10, 10 Hz, 2H), 6.87 (t, *J* = 5 Hz, 1H), 6.70 (t, *J* = 5 Hz, 1H), 6.58 (d, *J* = 10 Hz, 1H), 6.31 (d, *J* = 5 Hz, 1H), 2.76 (d, *J* = 15 Hz, 1H), 2.65 (d, *J* = 15 Hz, 1H), 2.22 – 2.15 (m, 1H), 2.03 (d, *J* = 16.3 Hz, 1H), 1.22 (s, 3H), 1.06 (s, 3H); ^{13}C NMR (126 MHz, CD_3OD): δ 194.55, 176.64, 157.35, 144.13 137.14, 133.46, 133.22, 127.60, 124.11, 122.88, 1220, 121.95, 121.11, 120.15, 108.10, 107.82, 49.44, 45.23, 31.41, 26.83, 26.61, 25.36; MS (ESI): Calculated for $C_{23}H_{23}N_3O_2$ *m/z* 373; found 374 (M+1).



D_2O exchange experiment for compound (7, 10):

11-isopropyl-3,3-dimethyl-2,3,4,5,10,11-hexahydro-1H-dibenzo[b,e][1,4]diazepin-1-one (7):

^{1}H-NMR (400 MHz, DMSO): δ 8.54 (s, 1H), 6.95 (d, *J* = 7.8 Hz, 1H), 6.72 (s, 2H), 6.69 – 6.58 (m, 1H), 5.77 (d, *J* = 5.8 Hz, 1H), 4.19 – 4.00 (m, 1H), 2.48 – 2.39 (m, 2H), 2.10 (dd, *J* = 49.5, 15.9 Hz, 2H), 1.49 (dd, *J* = 15.9, 6.5 Hz, 1H), 1.04 (s, 3H), 0.99 (s, 3H), 0.81 (d, *J* = 6.3 Hz, 3H), 0.70 (d, *J* = 6.6 Hz, 3H)

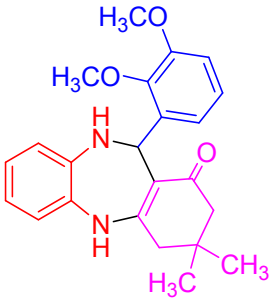


^{1}H-NMR (400 MHz, **DMSO + D_2O**): δ 8.69 (s, 1H), 6.96 (d, *J* = 7.5 Hz, 1H), 6.77 (d, *J* = 7.5 Hz, 2H), 6.68 (d, *J* = 6.6 Hz, 1H), 4.12 (d, *J* = 9.9 Hz, 1H), 2.46 (s, 2H), 2.13 (dd, *J* = 44.9, 15.9 Hz, 2H), 1.46 (s, 1H), 1.04 (s, 3H), 1.00 (s, 3H), 0.82 (d, *J* = 5.7 Hz, 3H), 0.71 (d, *J* = 6.0 Hz, 3H).

11-(2,3-dimethoxyphenyl)-3,3-dimethyl-2,3,4,5,10,11-hexahydro-1H-dibenzo[b,e]-[1,4]diazepin-1-one (10):

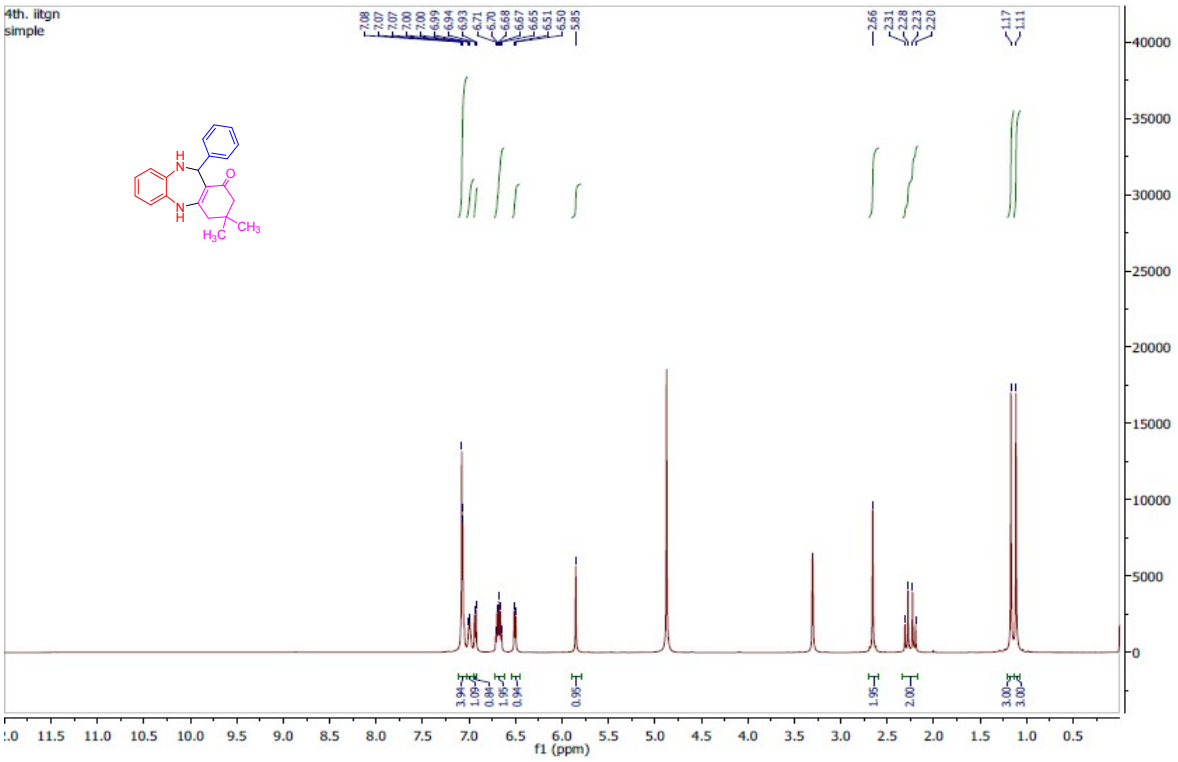
^{1}H-NMR (400 MHz, DMSO): δ 6.91 (d, *J* = 7.6 Hz, 1H), 6.85 (s, 1H), 6.68 – 6.53 (m, 4H), 6.49 (d, *J* = 8.1 Hz, 1H), 6.13 (d, *J* = 5.8 Hz, 1H), 5.64 (d, *J* = 5.7 Hz, 1H), 3.61 (s, 6H), 2.60 (t, *J* = 12.2 Hz, 2H), 2.15 (dd, *J* = 54.6, 15.9 Hz, 2H), 1.09 (s, 3H), 1.05 (s, 3H)

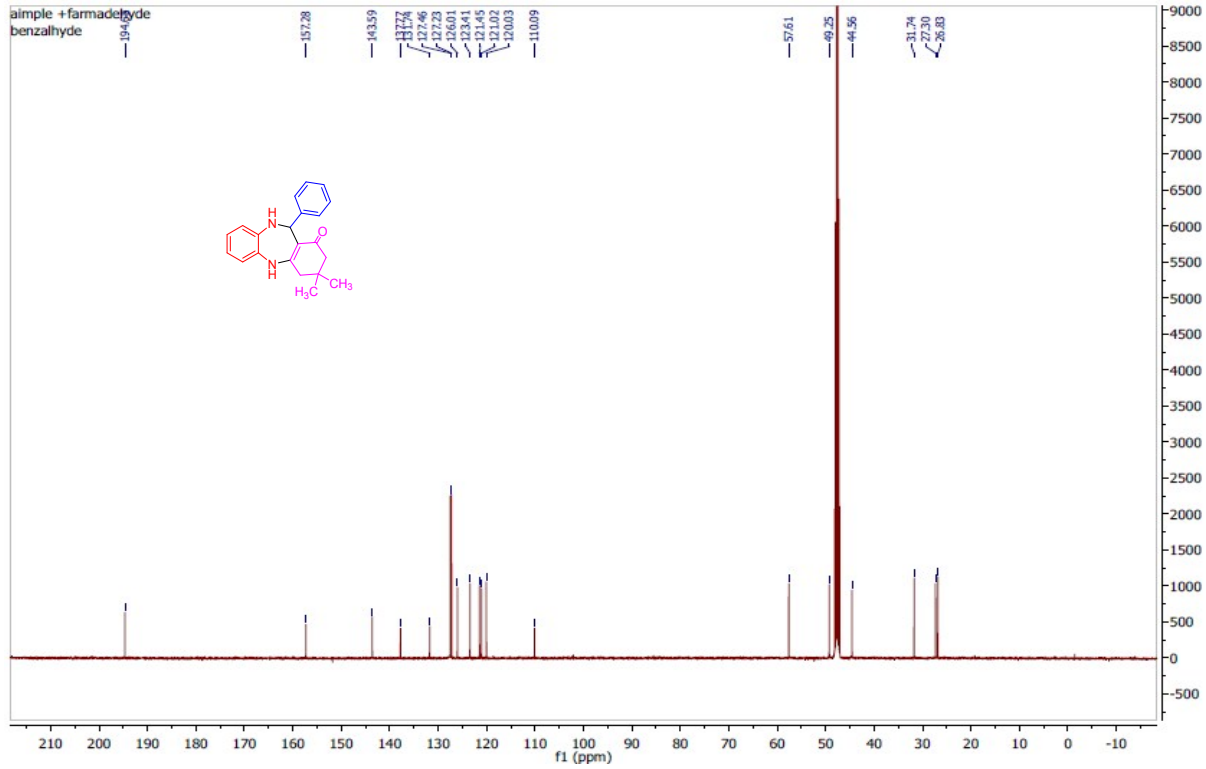
D_2O exchange: ^{1}H-NMR (400 MHz, **DMSO + D_2O**): δ 6.88 (d, *J* = 7.5 Hz, 1H), 6.78 (s, 1H), 6.66 – 6.56 (m, 3H), 6.55 (t, *J* = 7.4 Hz, 1H), 6.47 (d, *J* = 8.0 Hz, 1H), 5.61 (s, 1H), 3.96 (s, 5H), 2.56 (d, *J* = 3.2 Hz, 2H), 2.14 (dd, *J* = 49.8, 16.1 Hz, 2H), 1.06 (s, 3H), 1.02 (s, 3H).

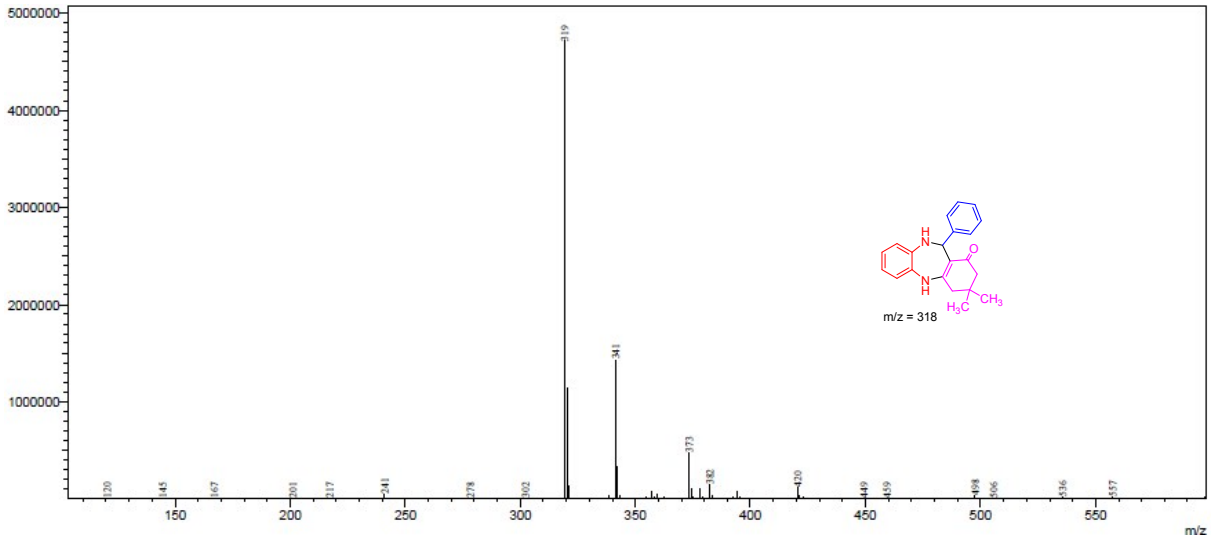


^{1}H-, ^{13}C-NMR and Mass spectra of the compounds (4-24)

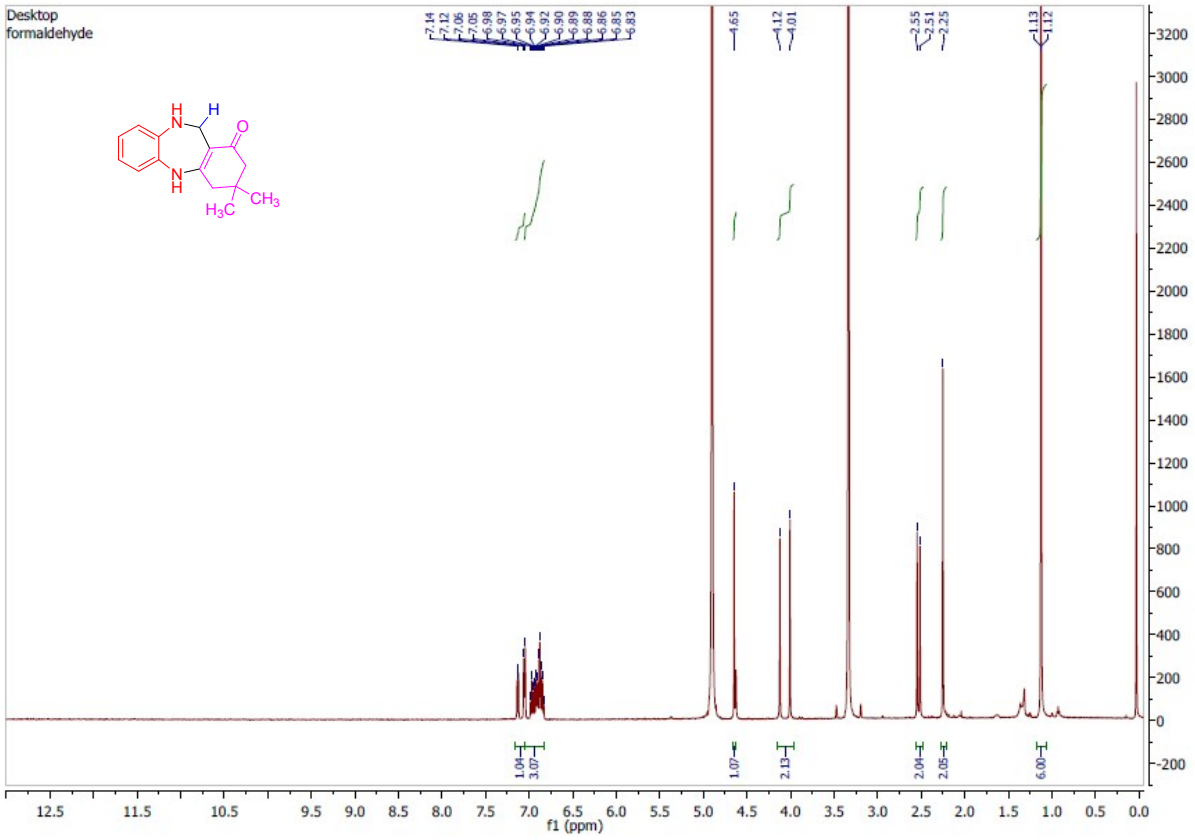
3,3-dimethyl-11-phenyl-2,3,4,5,10,11-hexahydro-1H-dibenzo[b,e][1,4]diazepin-1-one (4):

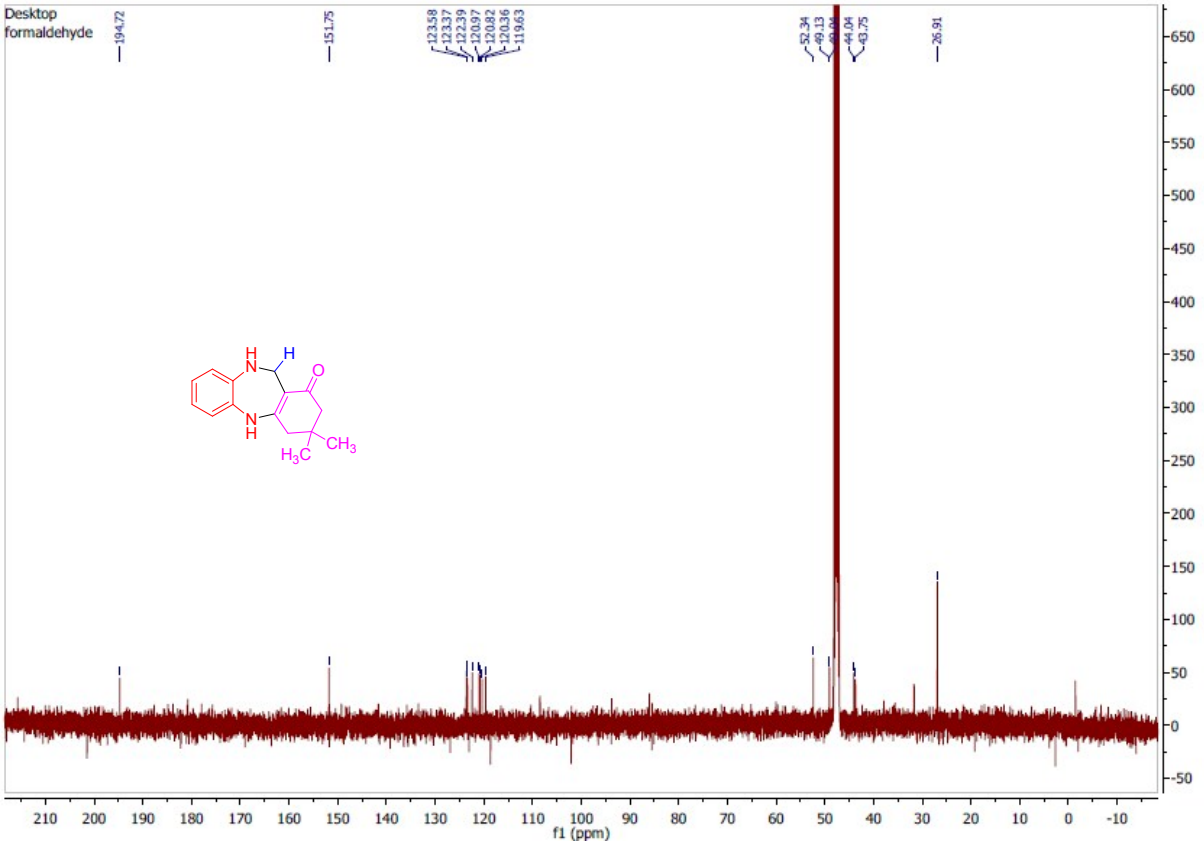


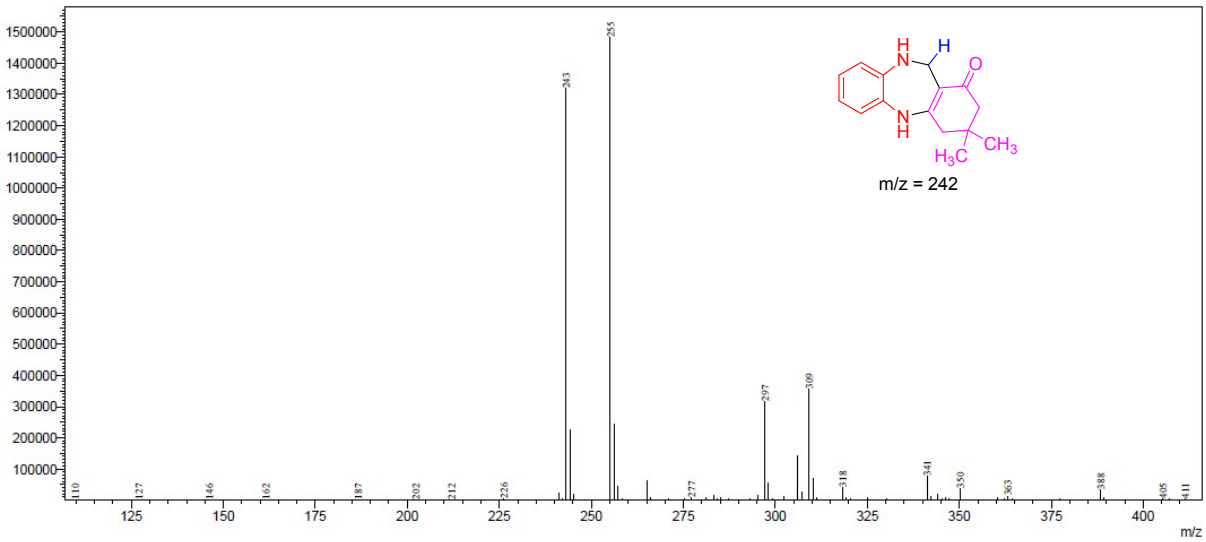




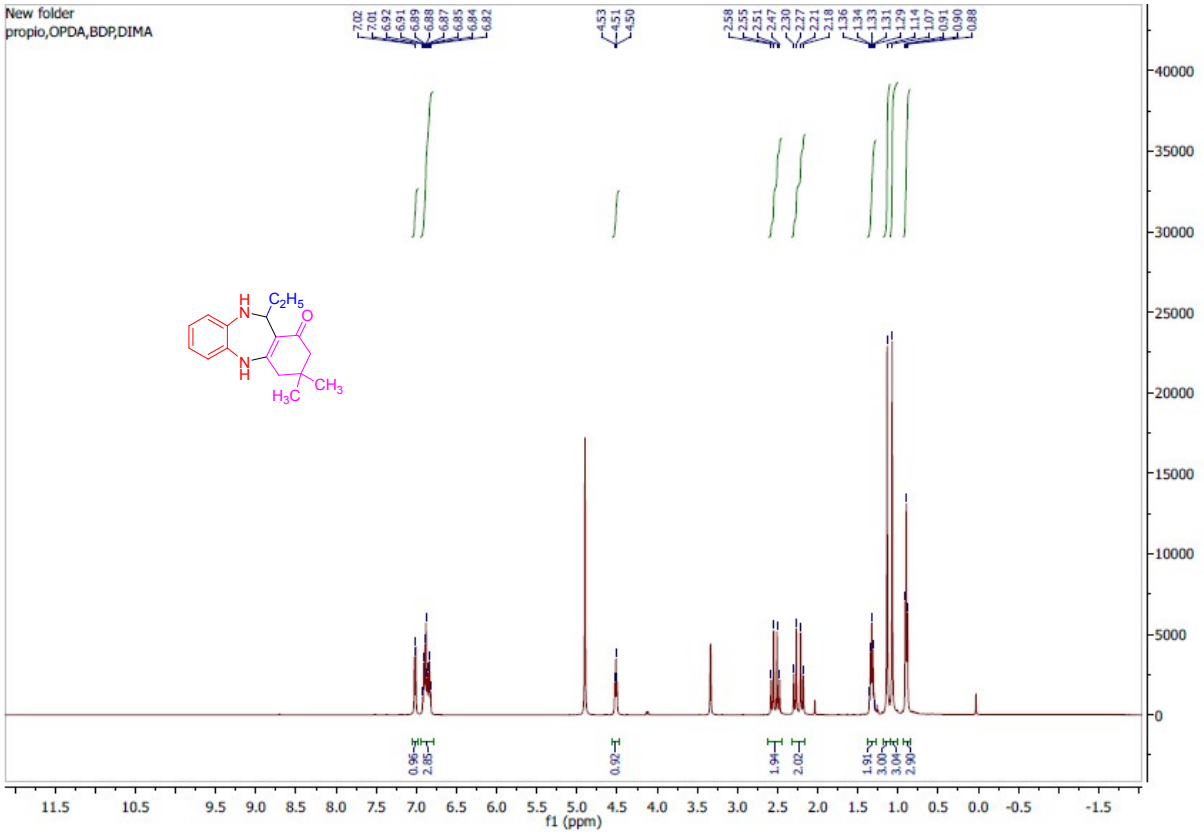
3,3-dimethyl-2,3,4,5,10,11-hexahydro-1H- dibenzo[b,e][1,4]diazepin-1-one (5):

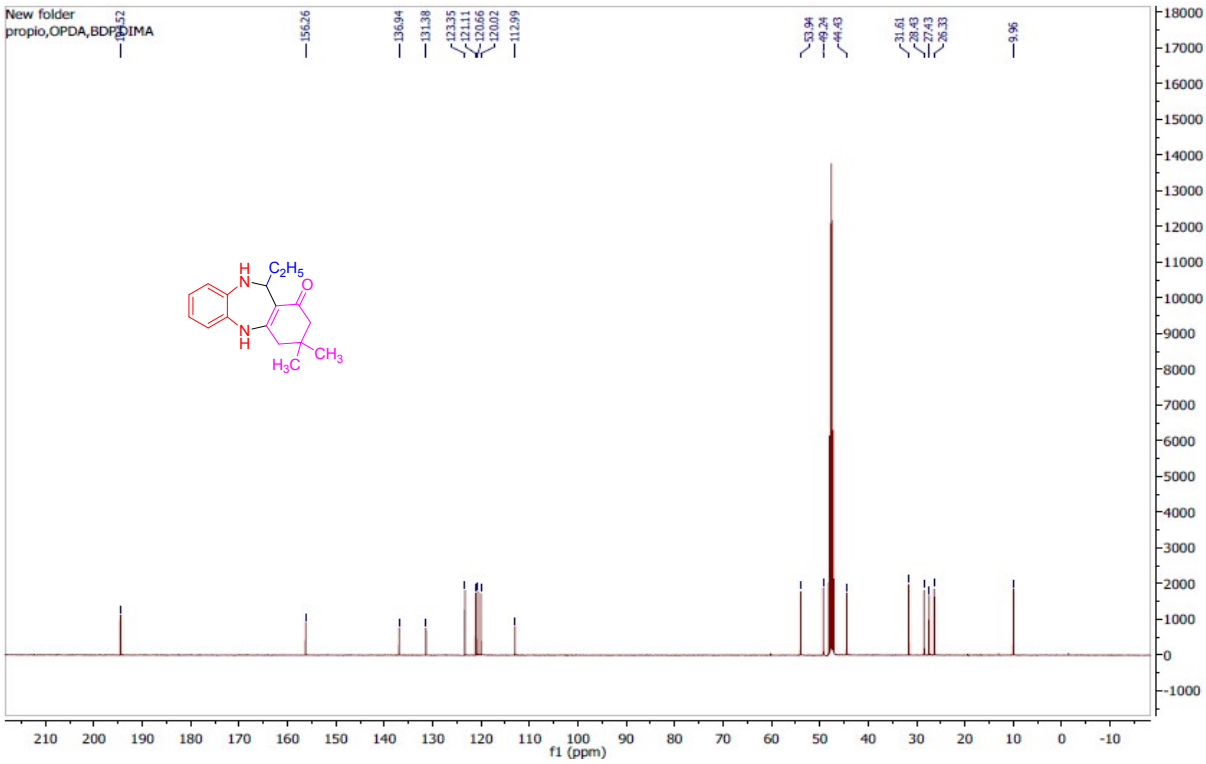


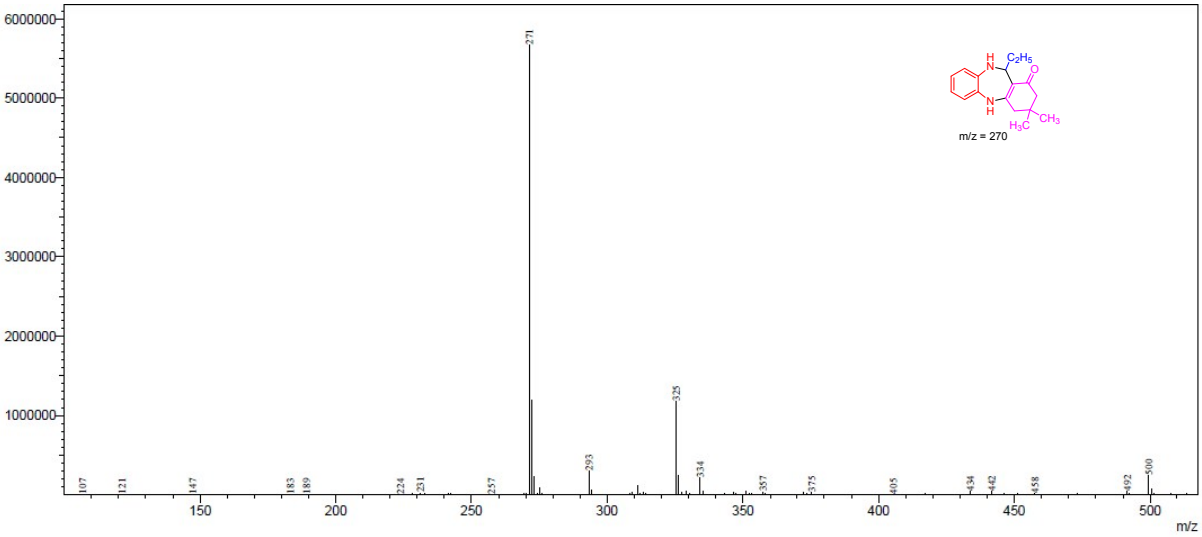

Desktop
formaldehyde
194.72
151.75
123.58
123.37
122.39
120.97
120.82
120.36
119.63
52.34
49.13
44.04
43.75
26.91
f1 (ppm)


m/z = 242
m/z

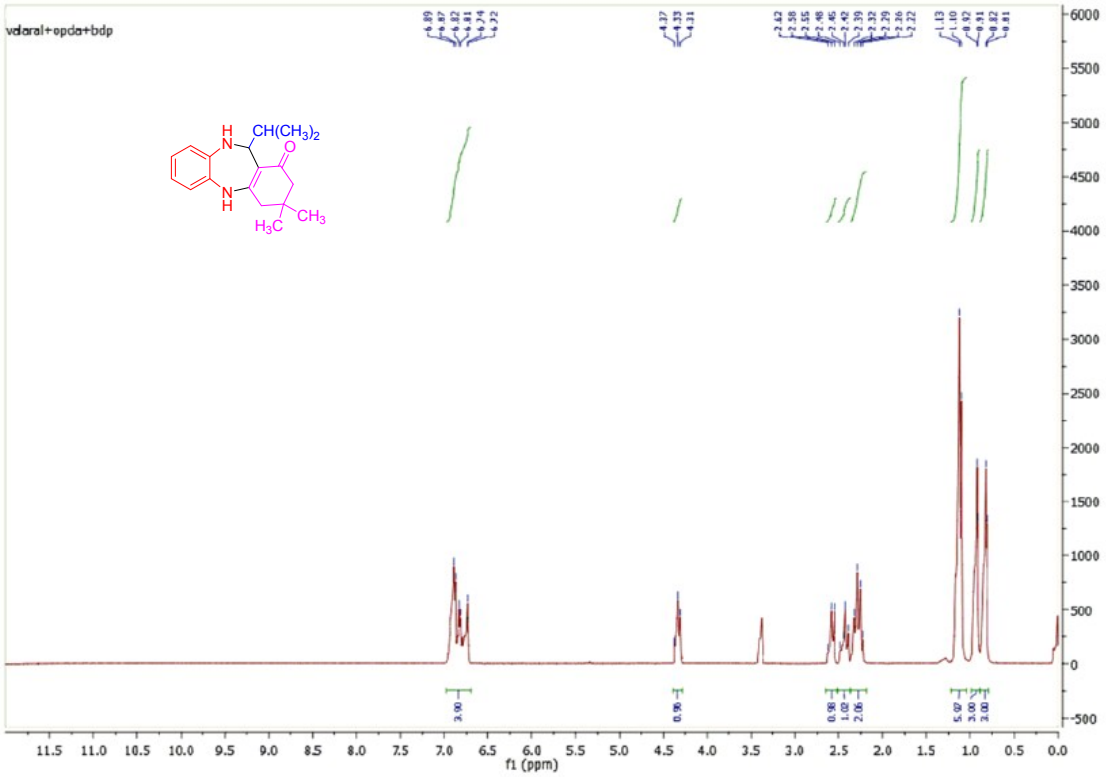
11-ethyl-3,3-dimethyl-2,3,4,5,10,11-hexahydro-1H- dibenzo[b,e][1,4]diazepin-1-one (6):

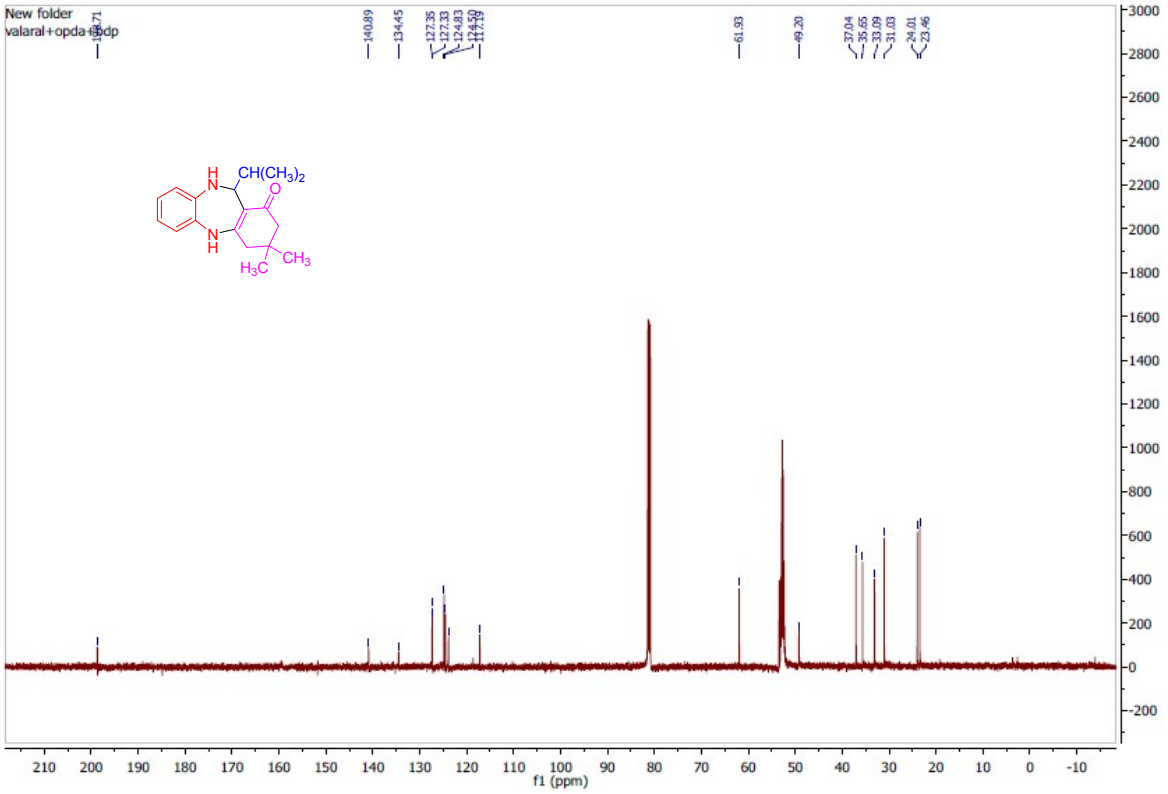






11-isopropyl-3,3-dimethyl-2,3,4,5,10,11-hexahydro-1H-dibenzo[b,e][1,4]diazepin-1-one (7):




New folder
valaral+opda+ddp
140.89
134.45
127.35
127.33
124.83
61.93
49.20
37.04
35.65
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24.01
23.46
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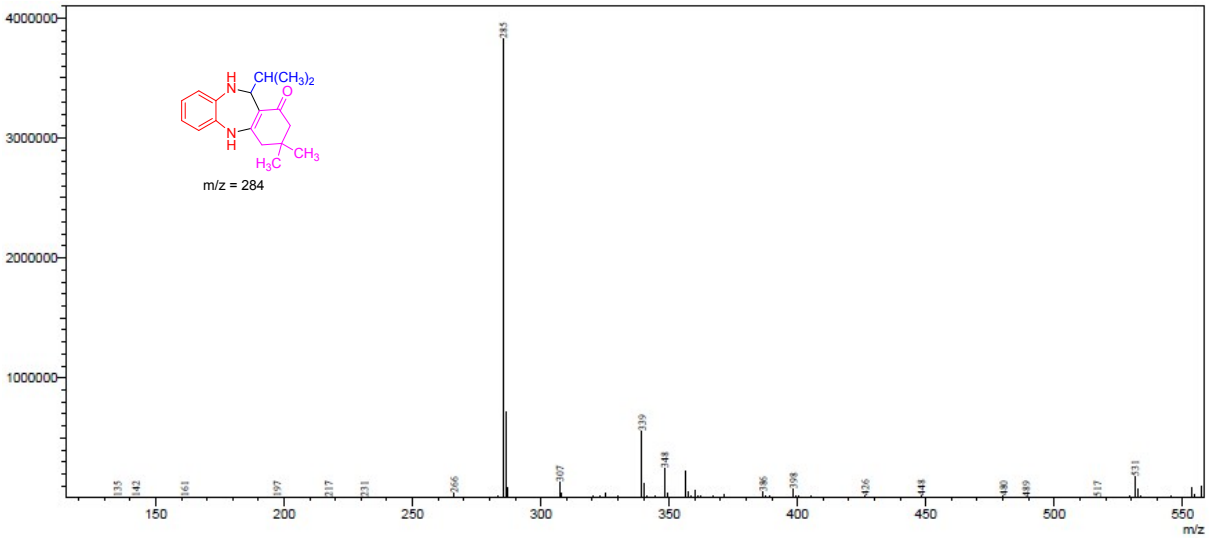
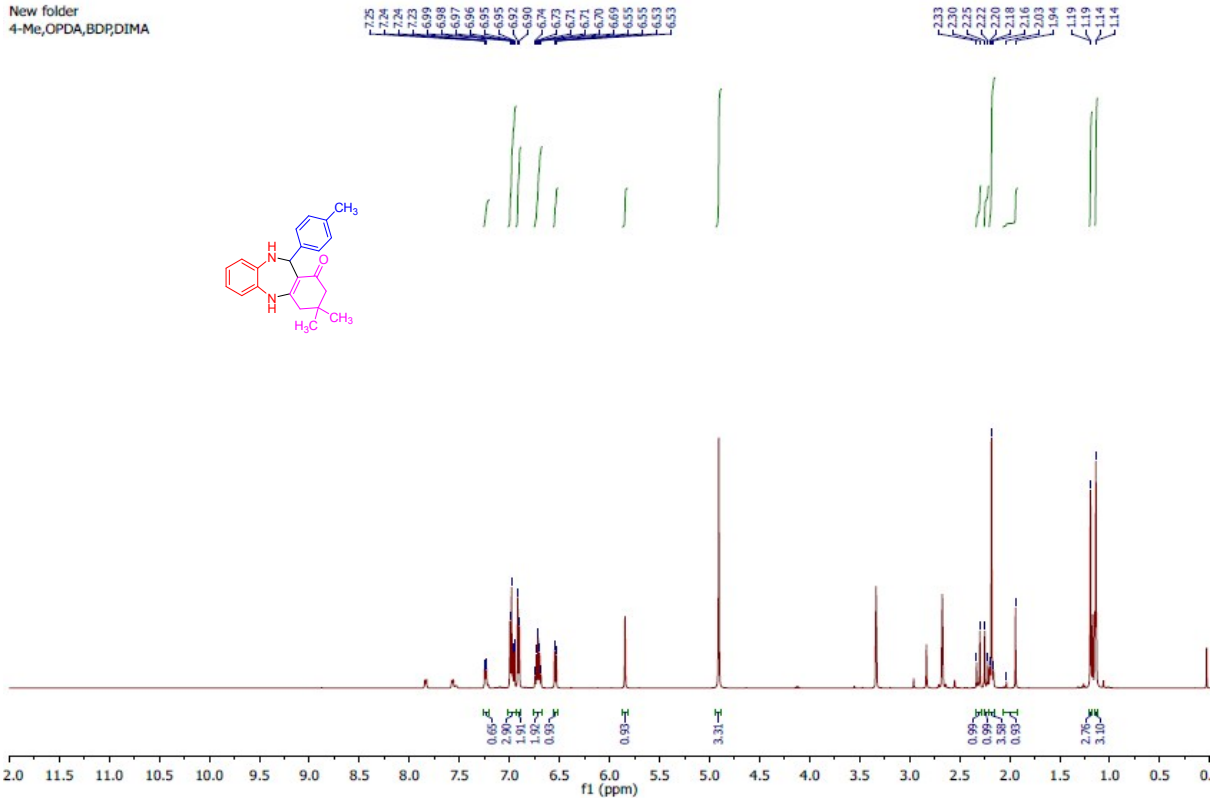
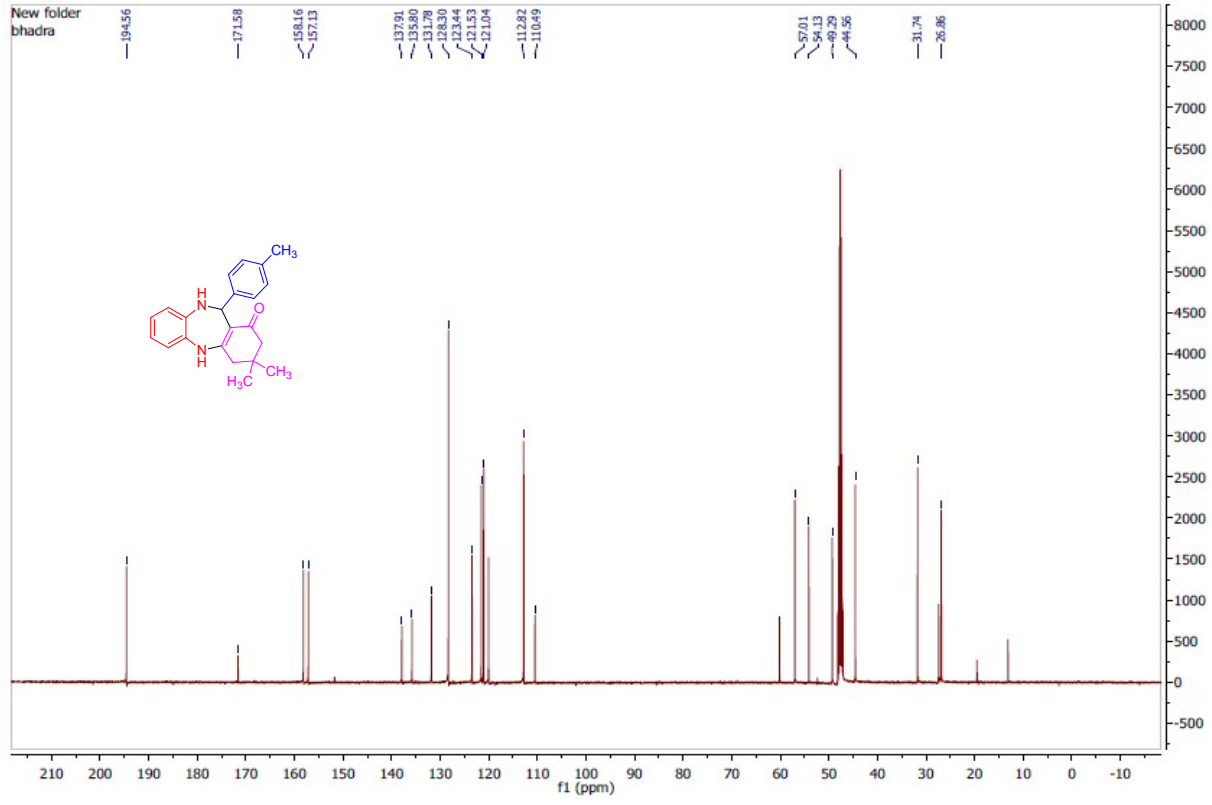
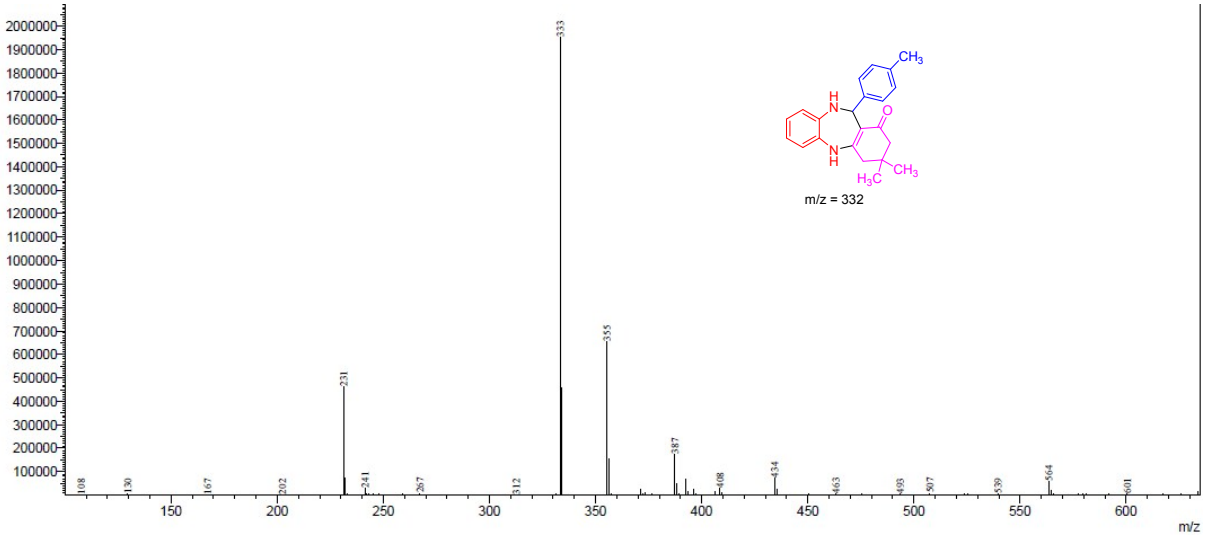
O
H
N
N
H
H3C
CH3
f1 (ppm)


CH(CH3)2
O
H
N
N
H
H3C
CH3
m/z = 284
285
339
344
307
m/z

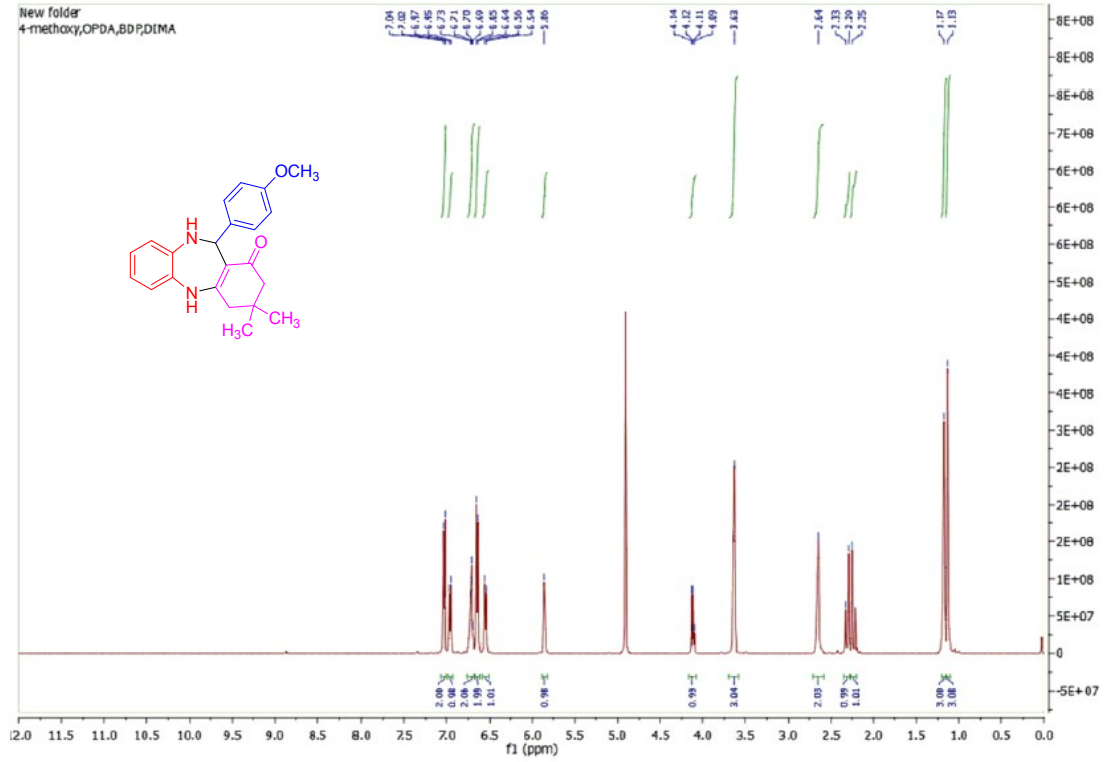
3,3-dimethyl-11-p-tolyl-2,3,4,5,10,11-hexahydro-1H-dibenzo[b,e][1,4]diazepin-1-one (8):

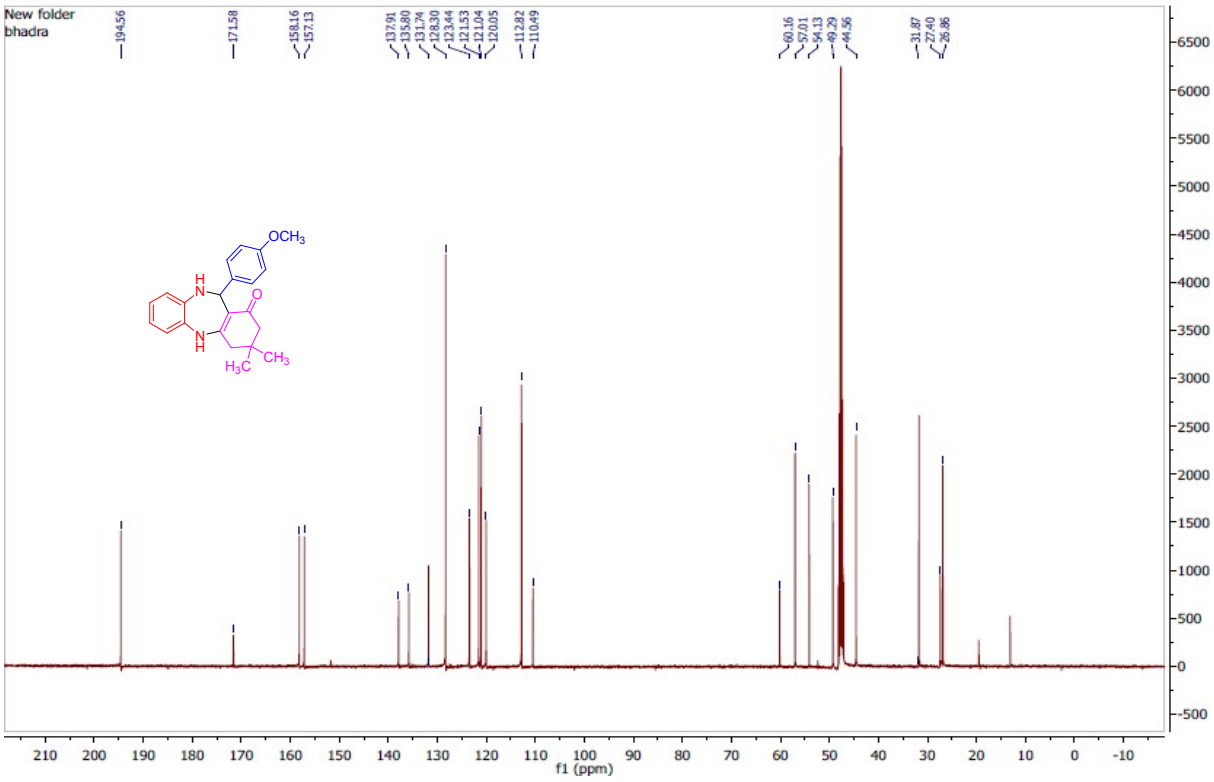


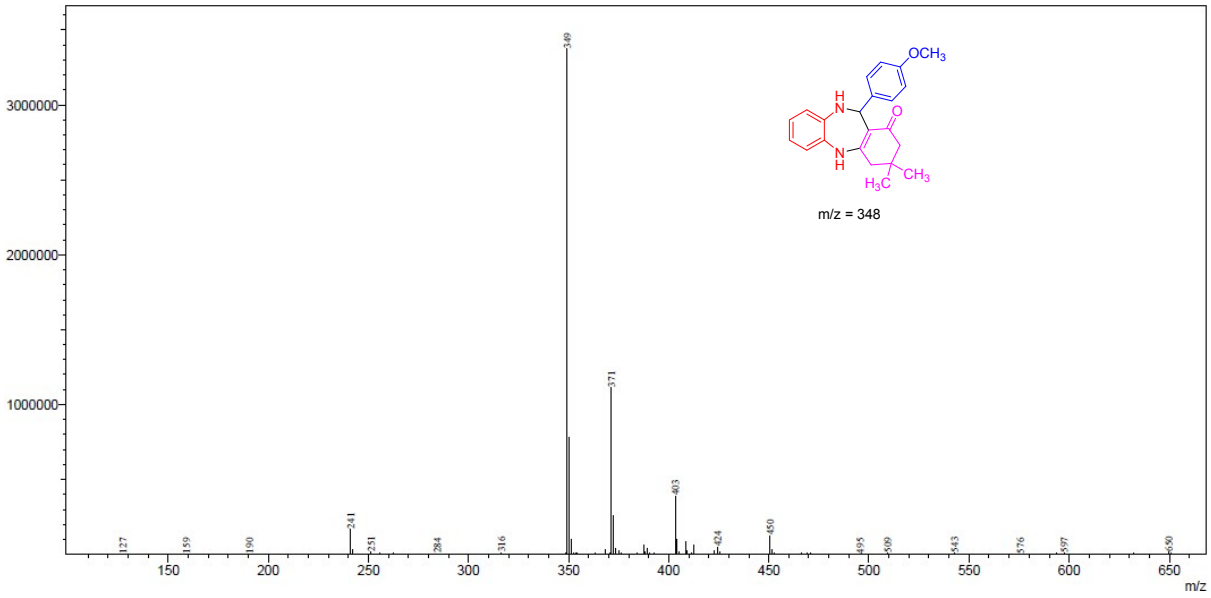




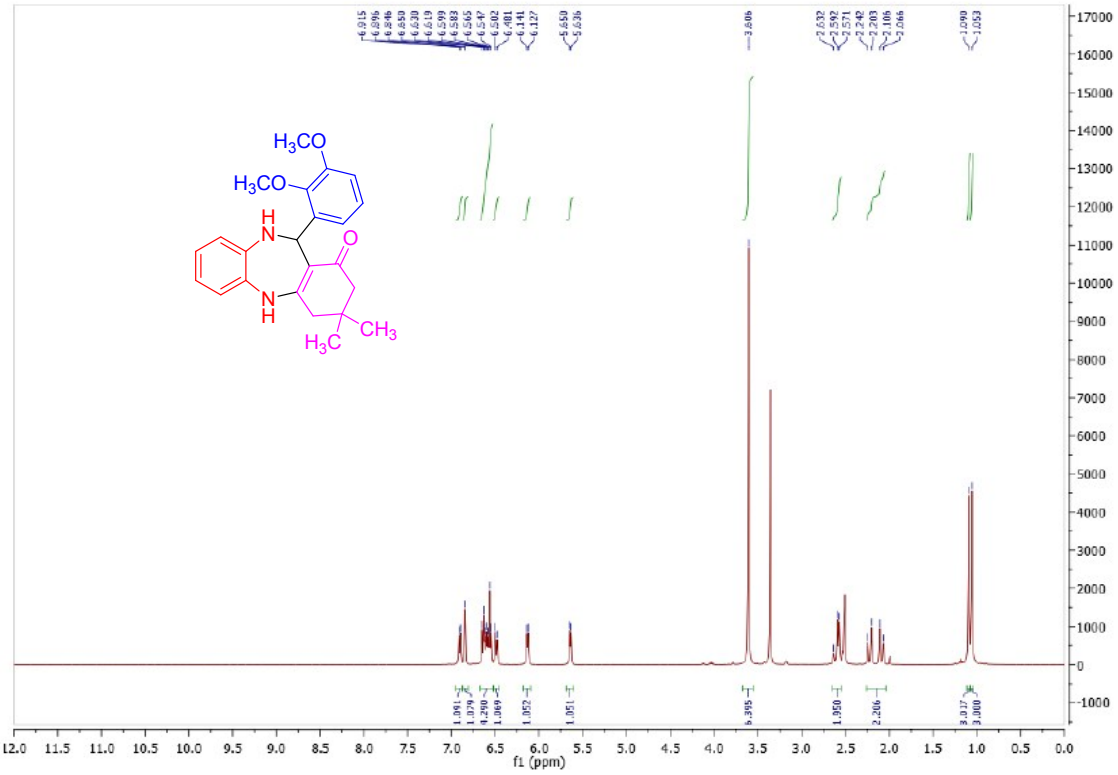
11-(4-methoxyphenyl)-3,3-dimethyl-2,3,4,5,10,11-hexahydro-1H- dibenzo[b,e] [1,4]diazepin-1-one (9):

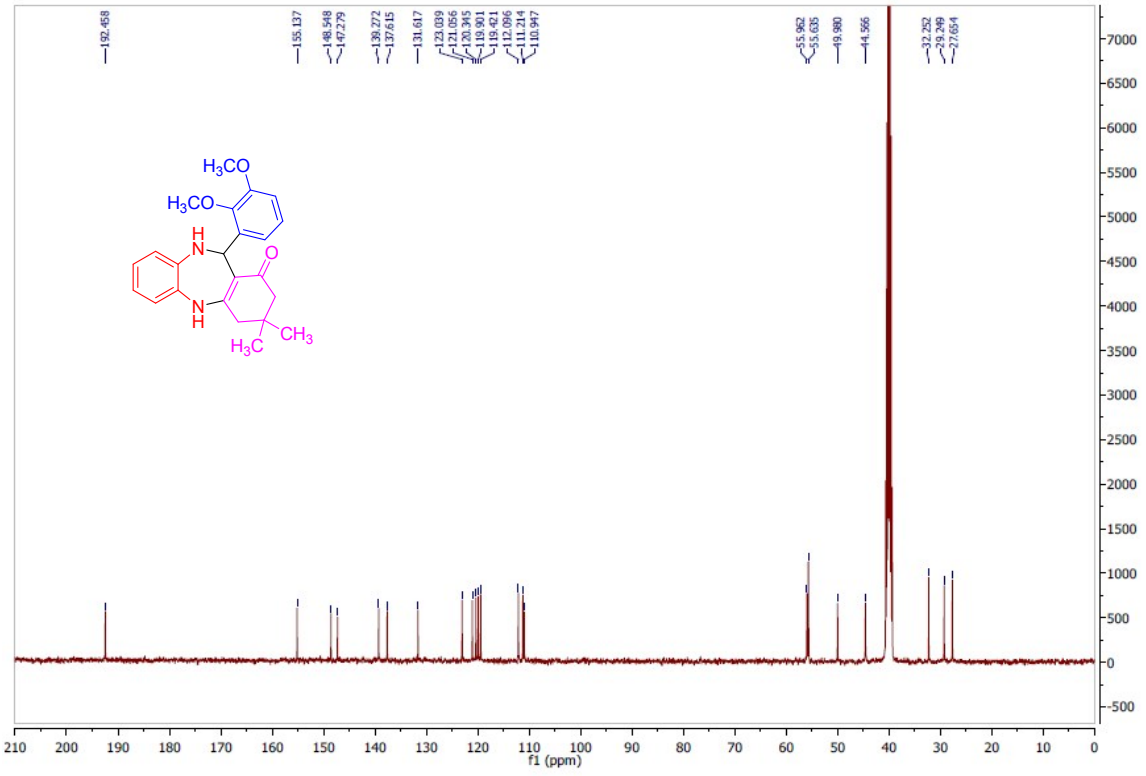



New folder
bhadra
194.56
171.58
158.16
157.13
137.91
135.80
131.74
128.30
123.44
121.53
121.04
120.05
112.82
110.49
60.16
57.01
54.13
49.29
44.56
31.87
27.40
26.86
OCH3
H
N
O
N
H
H3C
CH3
f1 (ppm)

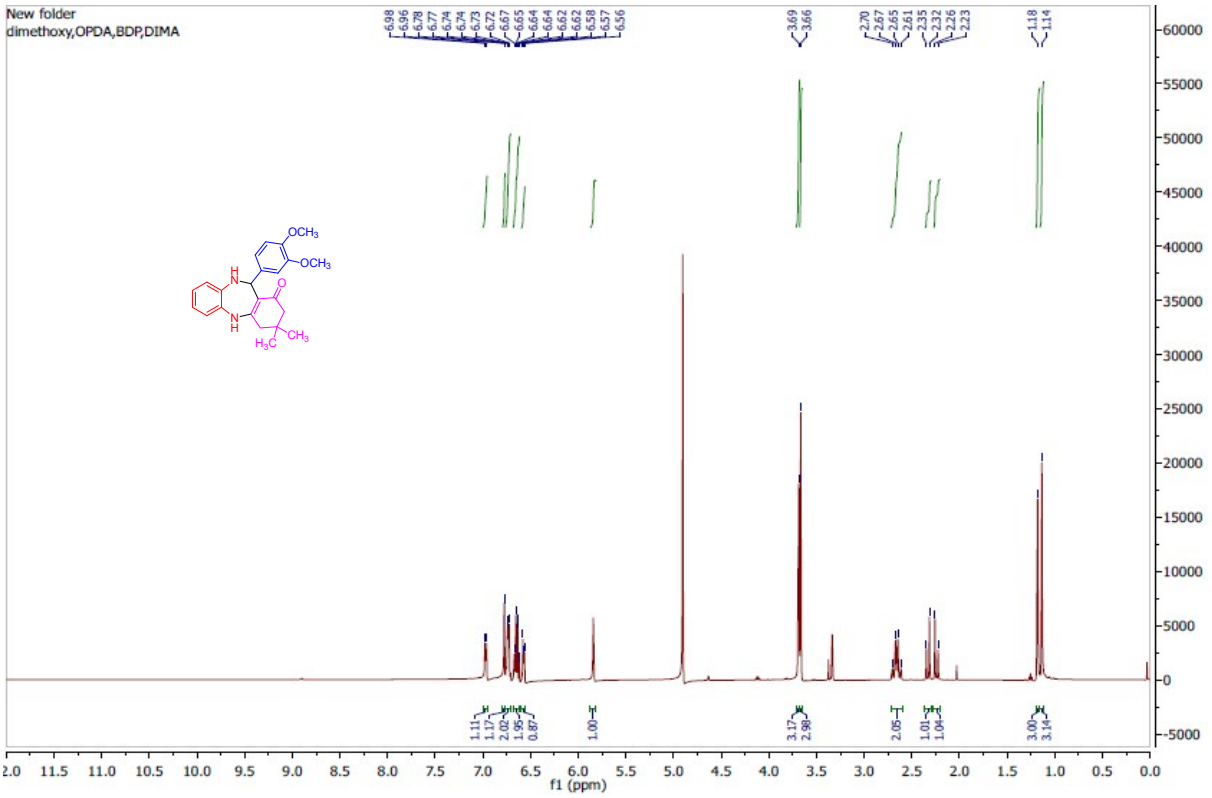

3000000
2000000
1000000
349
371
403
241
251
284
316
424
450
495
509
543
576
597
650
127
159
190
150
200
250
300
350
400
450
500
550
600
650
m/z
OCH3
H
N
O
N
H
H3C
CH3
m/z = 348

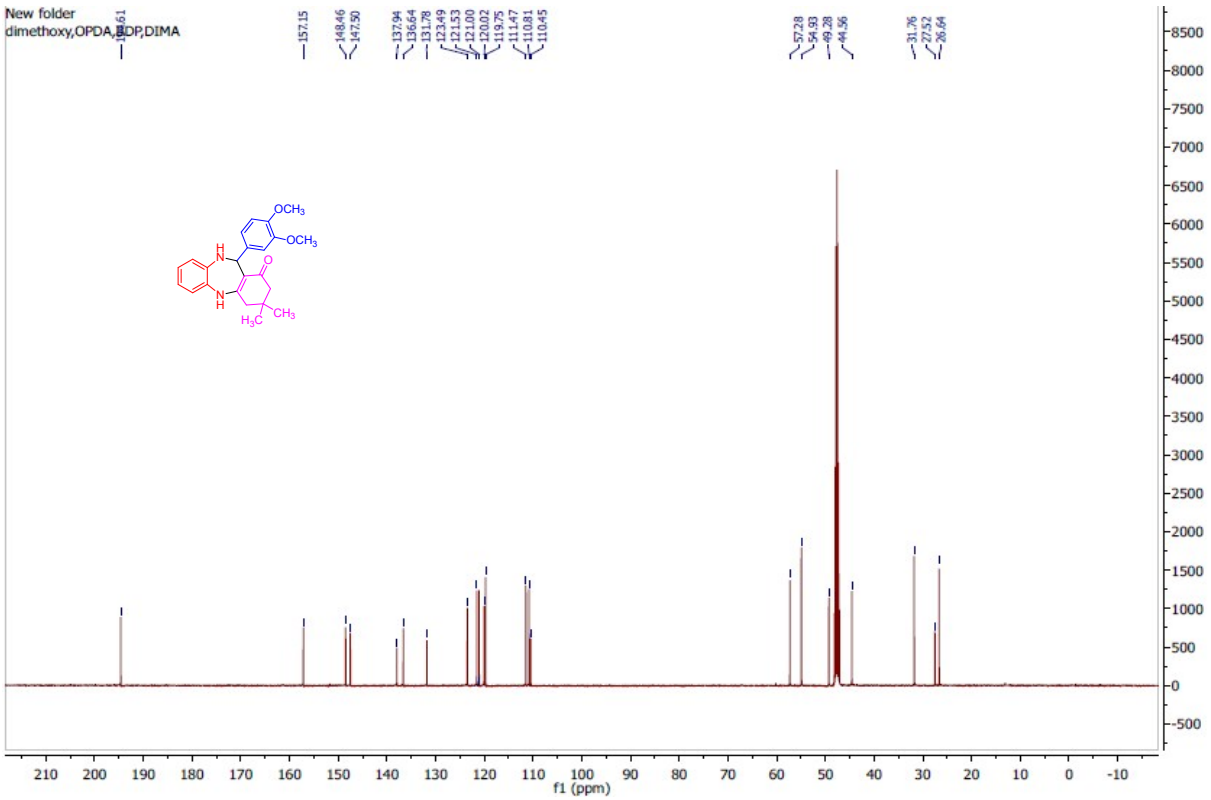
11-(2,3-dimethoxyphenyl)-3,3-dimethyl-2,3,4,5,10,11-hexahydro-1H-dibenzo[b,e][1,4]diazepin-1-one (13):

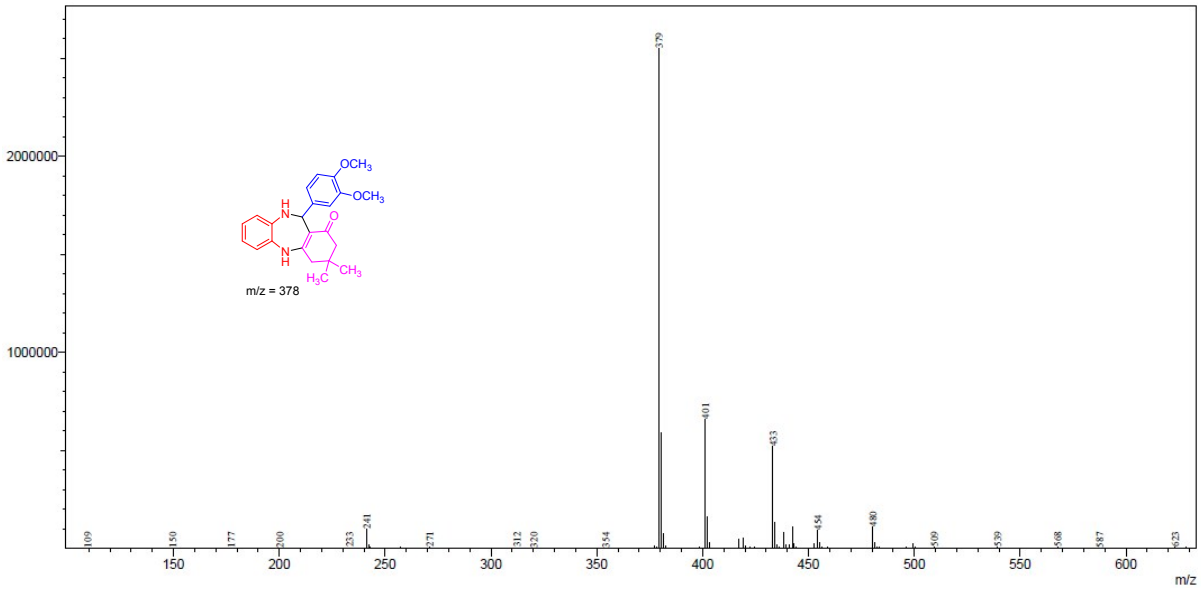




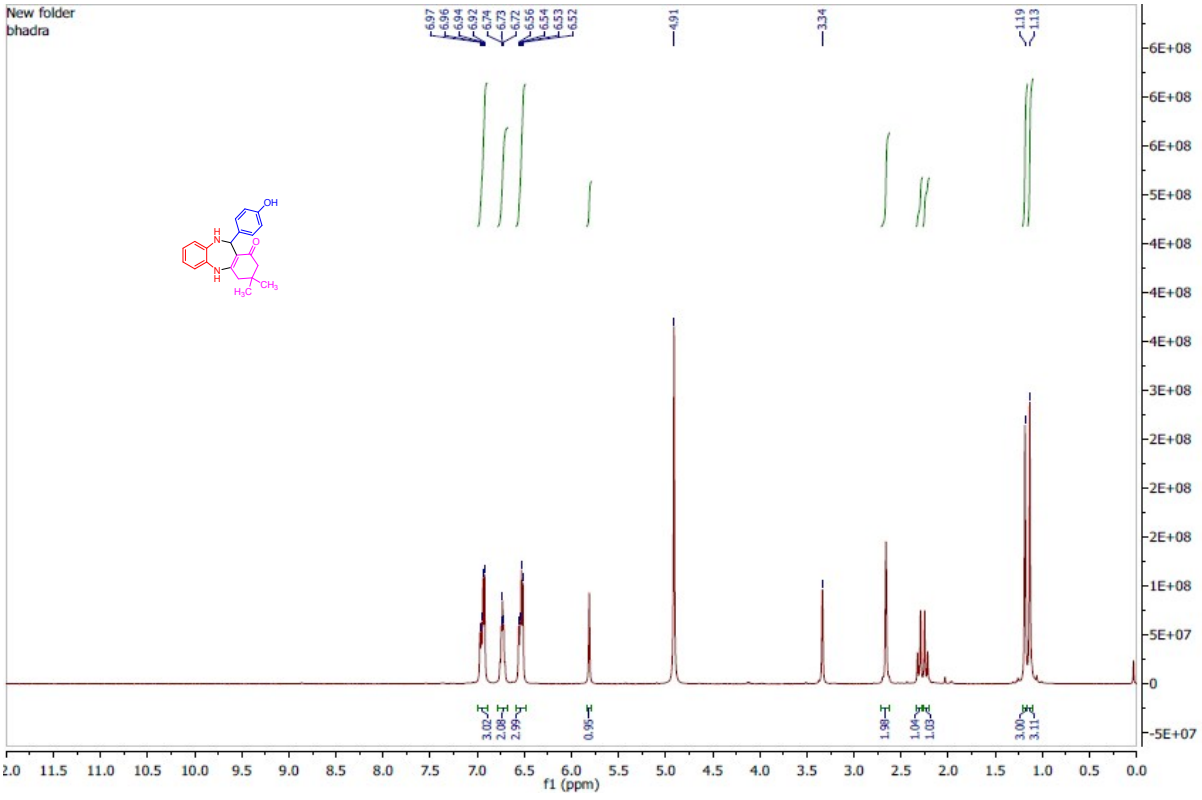
11-(3,4-dimethoxyphenyl)-3,3-dimethyl-2,3,4,5,10,11-hexahydro-1H dibenzo[b,e][1,4]diazepin-1-one (11):

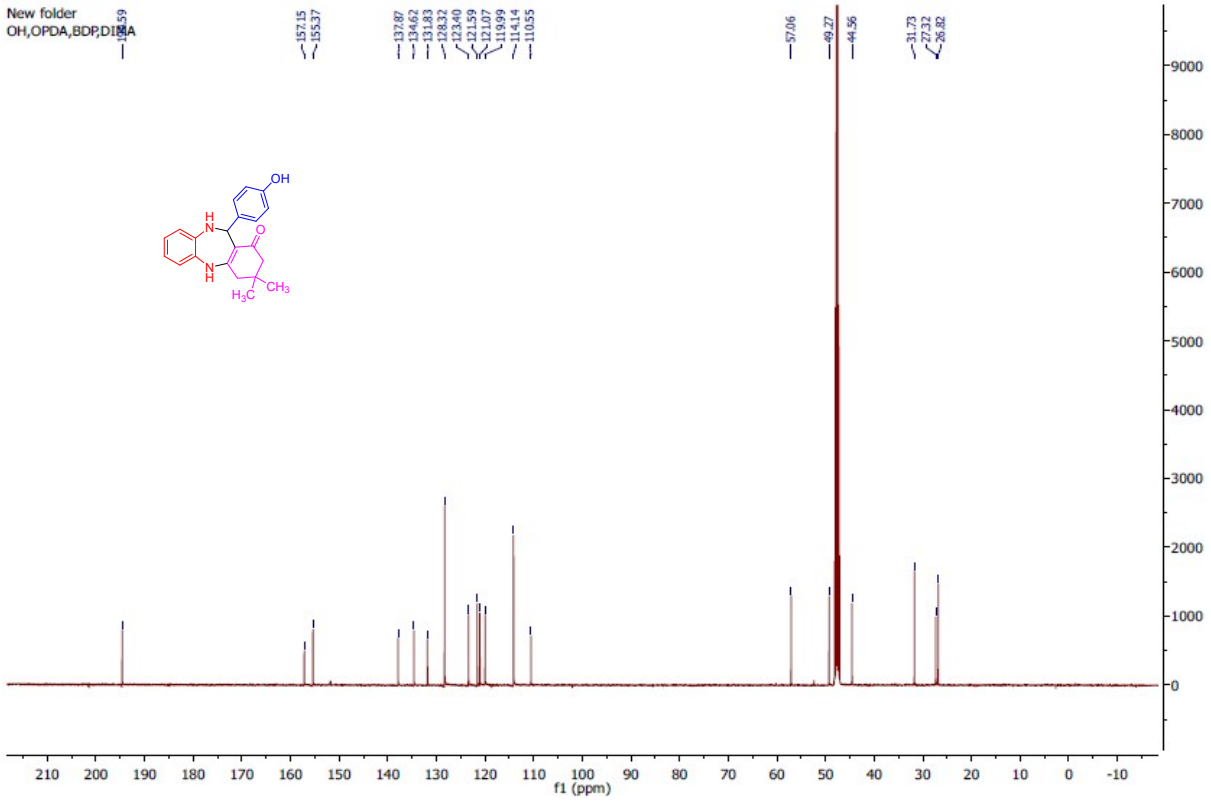


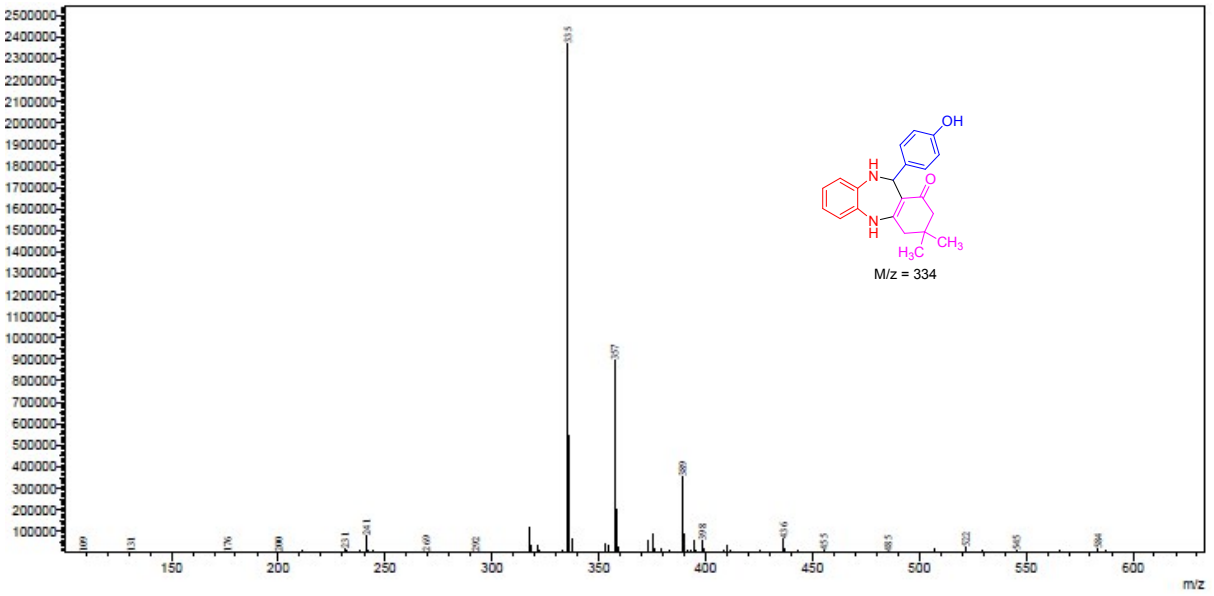




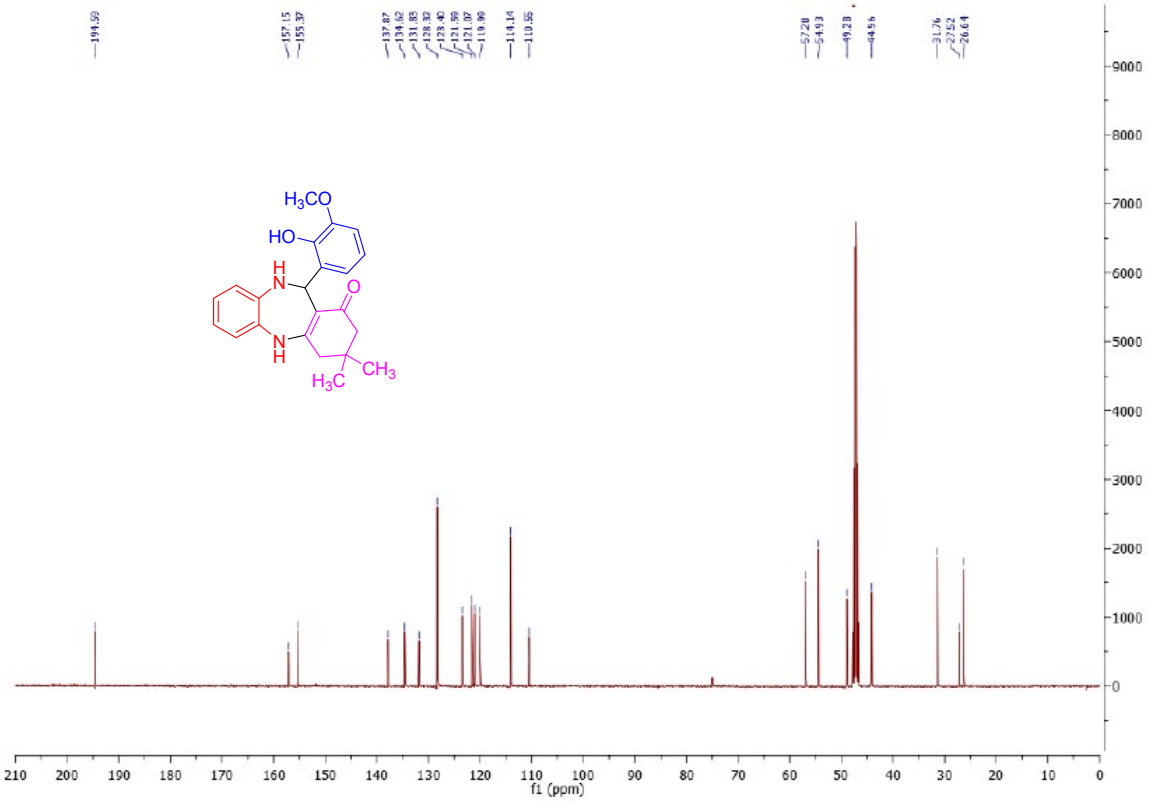
11-(4-hydroxyphenyl)-3,3-dimethyl-2,3,4,5,10,11-hexahydro-1H dibenzo[b,e][1,4]diazepin-1-one(12):

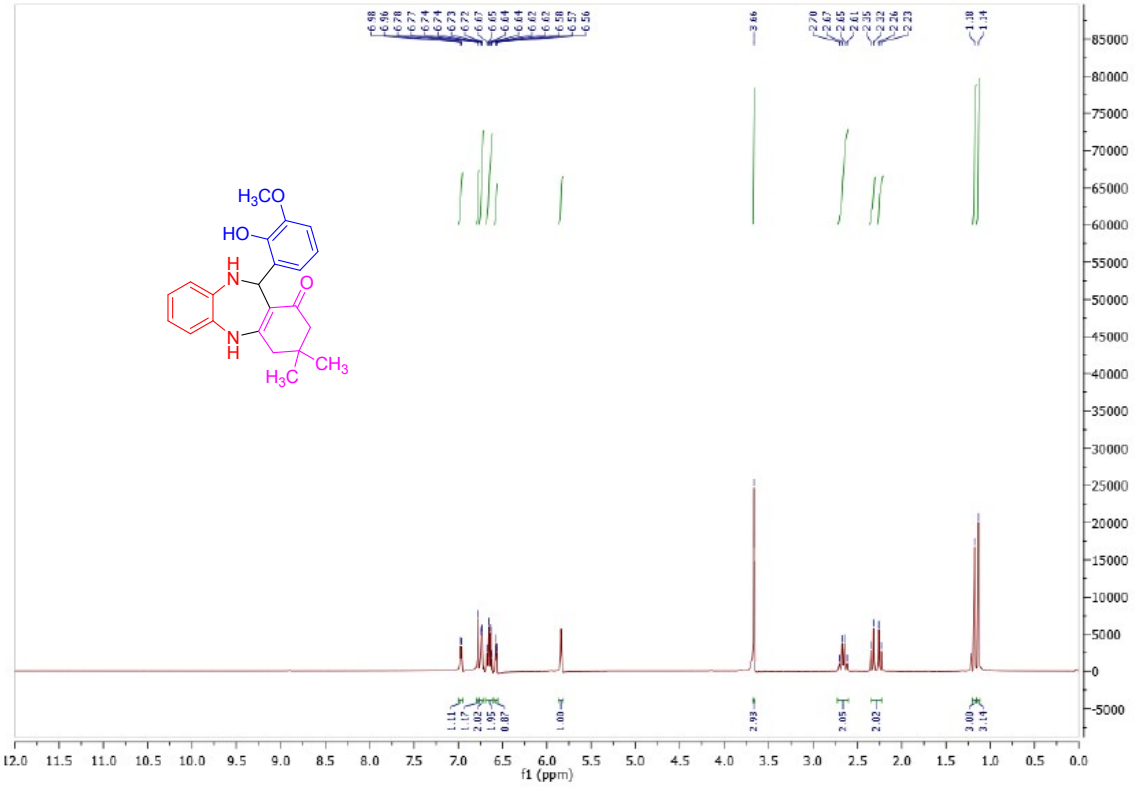



New folder
OH,OPDA,BDP;DIMA
157.15
153.37
137.87
134.62
131.83
128.32
123.40
121.59
121.07
119.99
114.14
110.55
57.06
49.27
44.56
31.73
27.32
26.82
OH
H
N
O
N
H
H3C
CH3
f1 (ppm)

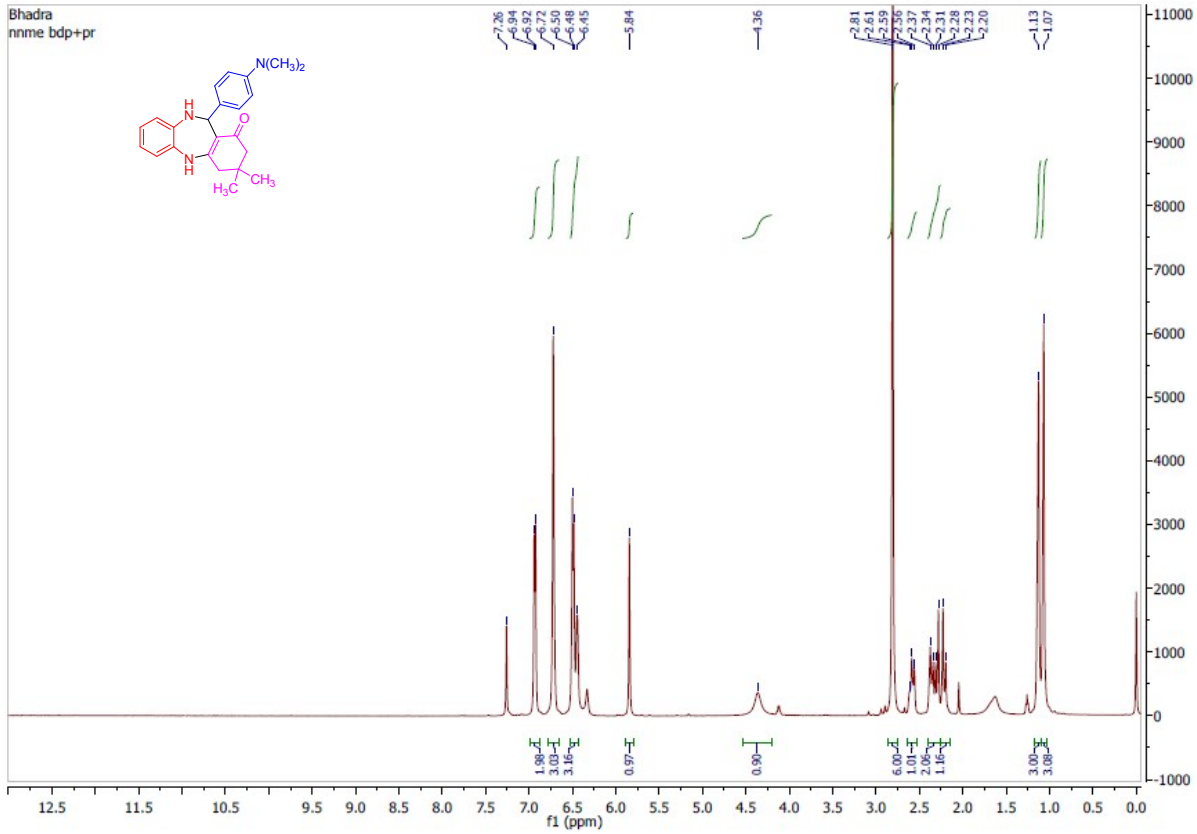

335
357
389
OH
H
N
O
N
H
H3C
CH3
M/z = 334
m/z

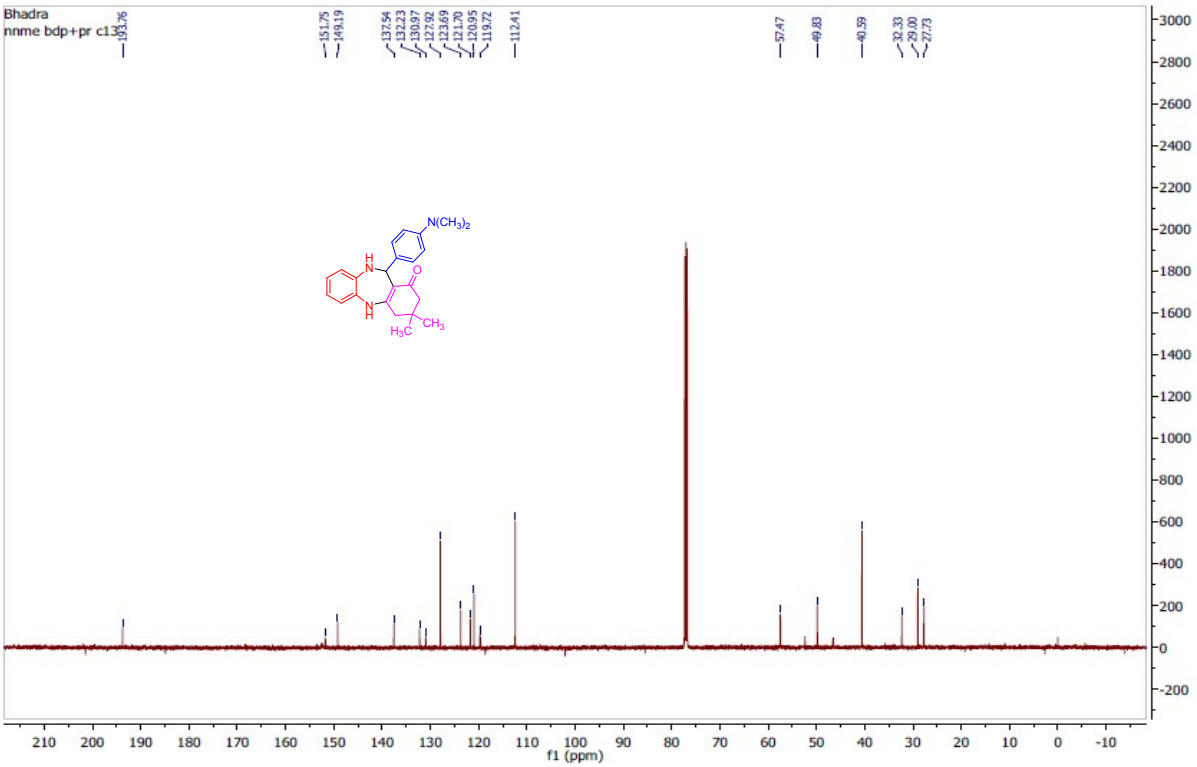
11-(2-hydroxy-3-methoxyphenyl)-3,3-dimethyl-2,3,4,5,10,11-hexahydro-1H-dibenzo[b,e][1,4]diazepin-1-one(13):

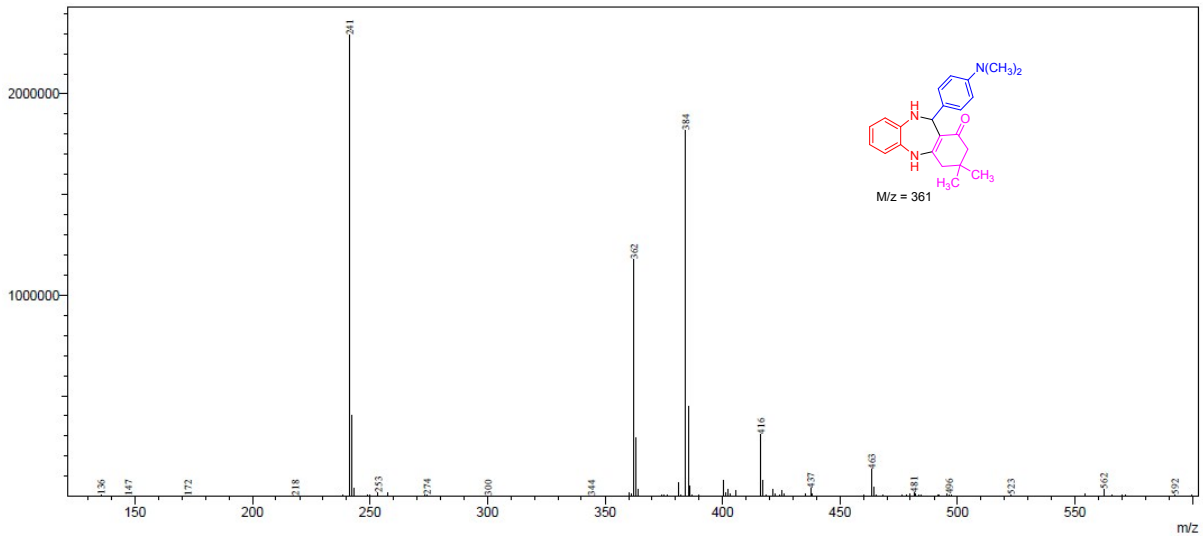




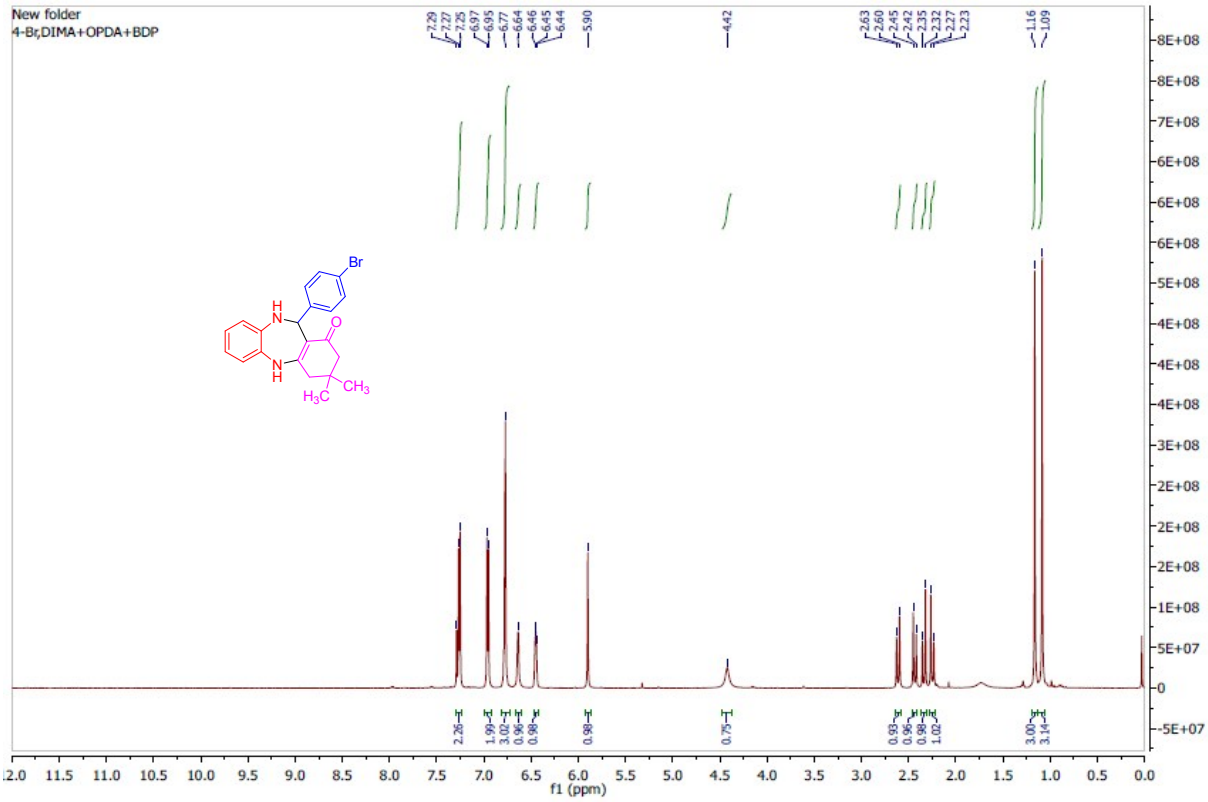
11-(4-(dimethylamino)phenyl)-3,3-dimethyl-2,3,4,5,10,11-hexahydro-1H-dibenzo[b,e][1,4]diazepin-1-one (14):

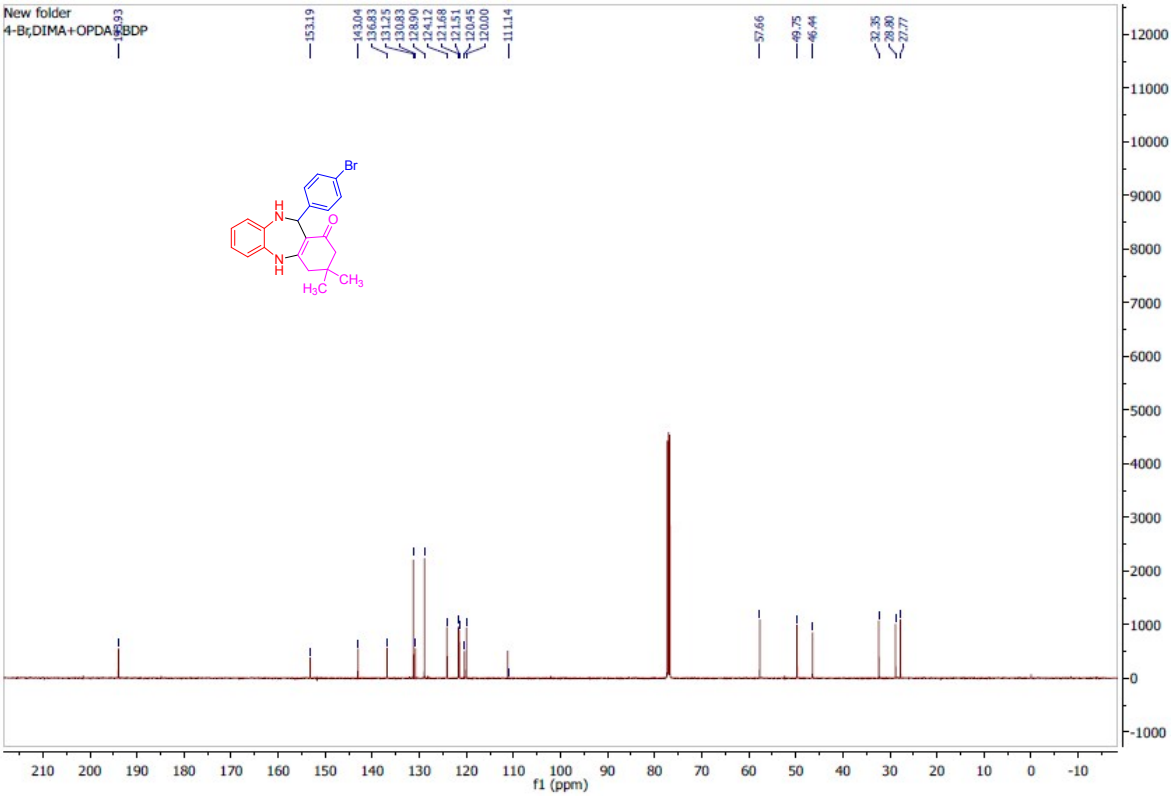


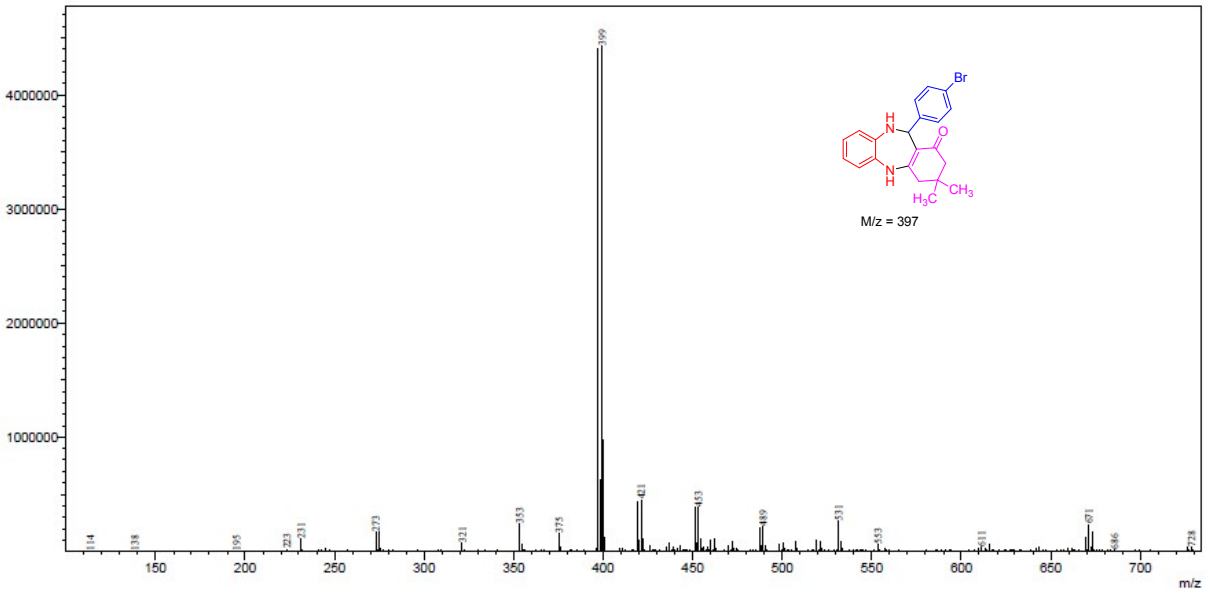




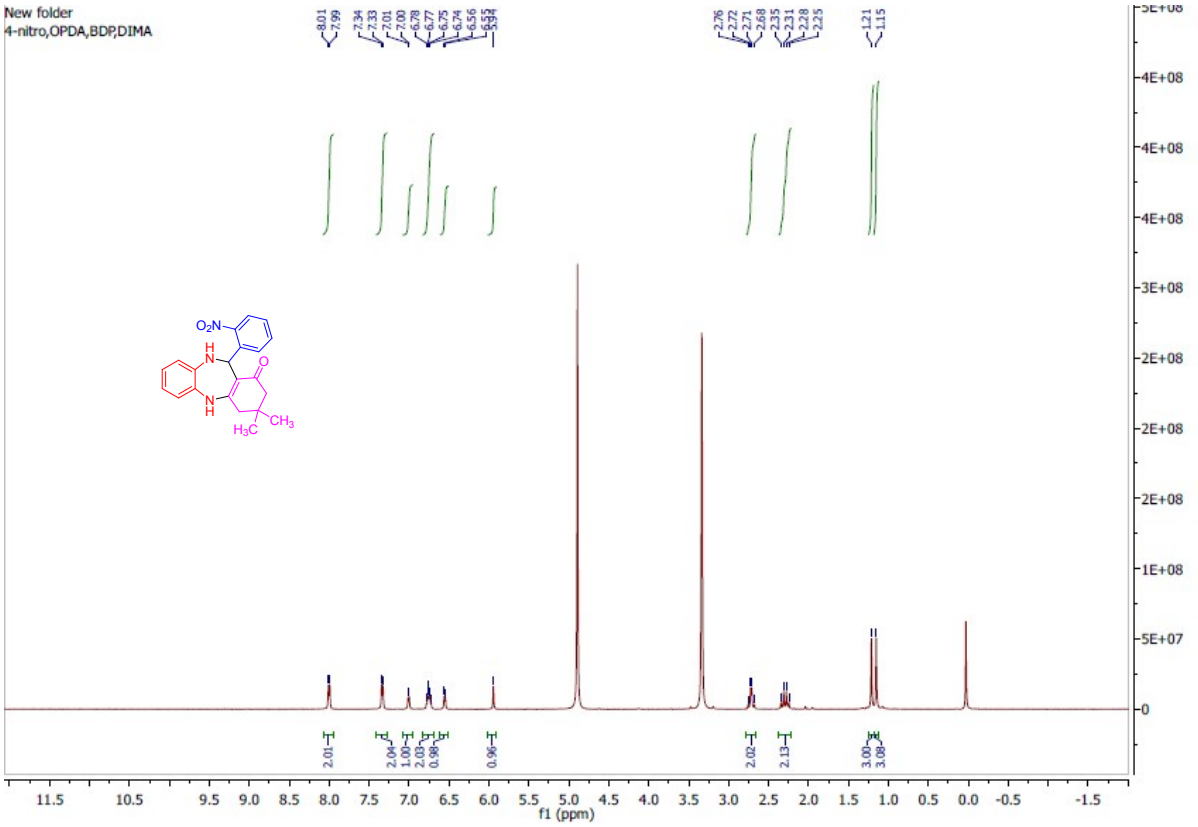
11-(4-bromophenyl)-3,3-dimethyl-2,3,4,5,10,11-hexahydro-1H-dibenzo[b,e] [1,4]diazepin-1-one (15):

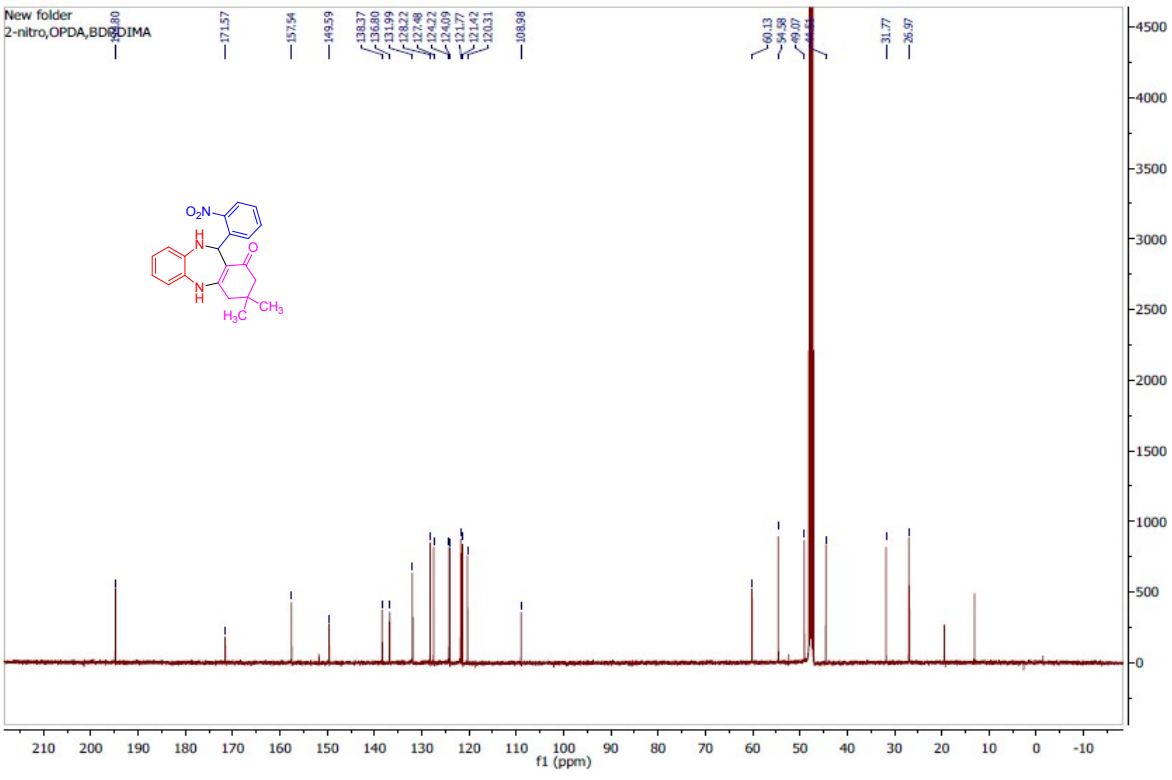


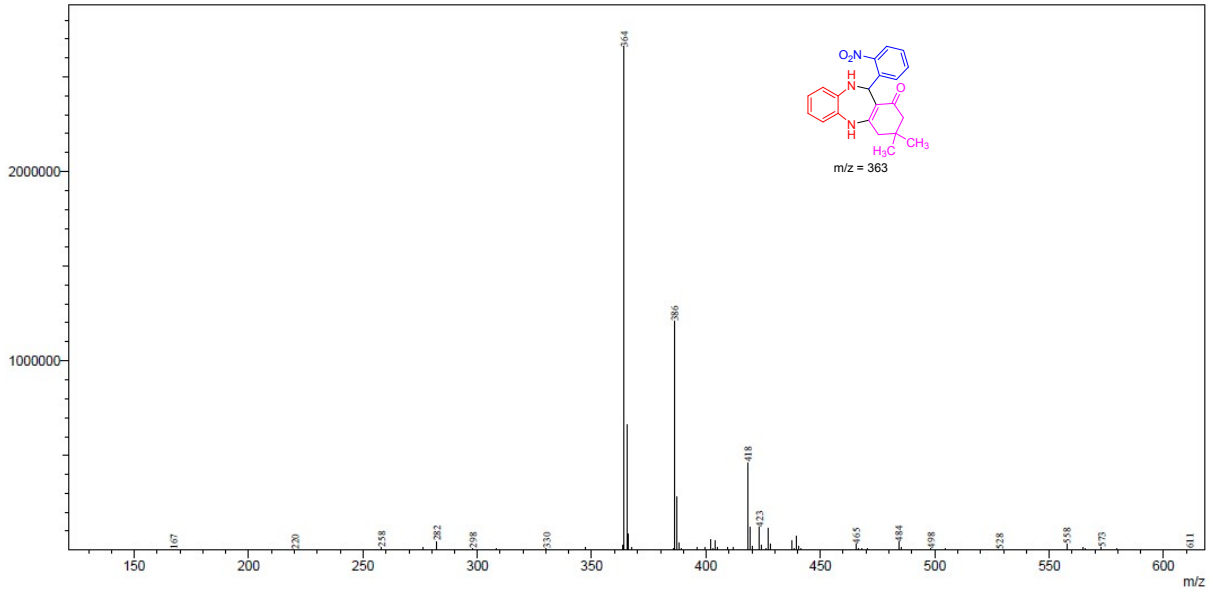

New folder
4-Br,DIMA+OPDA+BDP
153.19
143.04
136.83
131.25
130.83
128.90
124.12
121.68
121.51
120.45
120.00
111.14
57.66
49.75
46.44
32.35
28.80
27.77
Br
H
N
H
N
O
H3C
CH3
f1 (ppm)


399
421
453
Br
H
N
H
N
O
H3C
CH3
M/z = 397
m/z

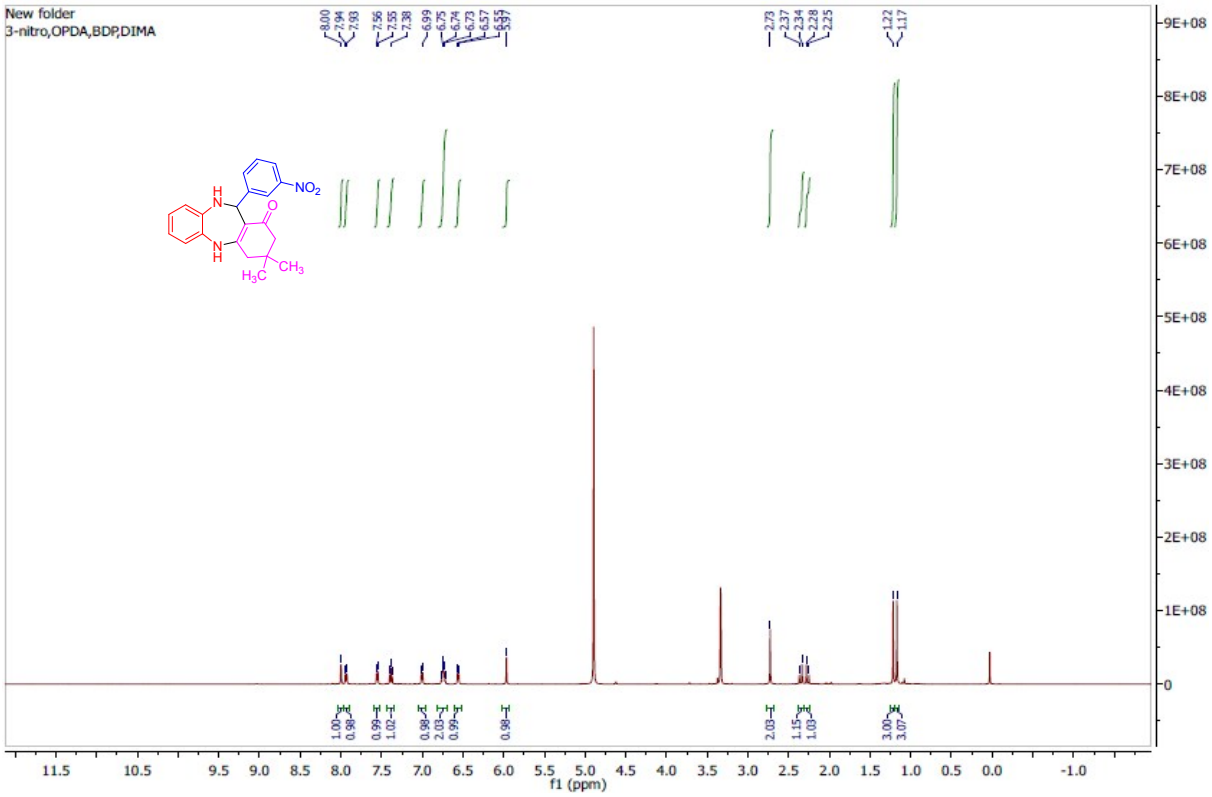
3,3-dimethyl-11-(2-nitrophenyl)-2,3,4,5,10,11-hexahydro-1H-dibenzo[b,e][1,4]diazepin-1-one (16):

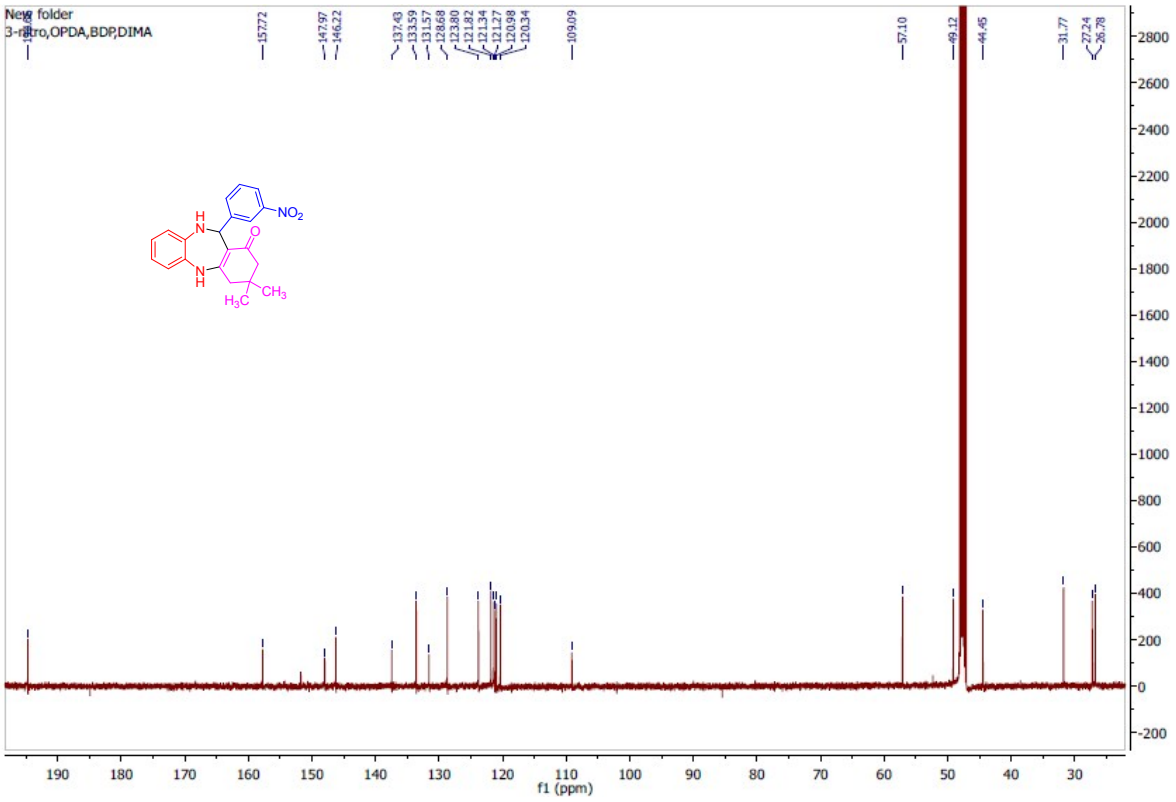


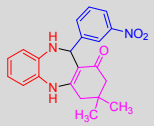




3,3-dimethyl-11-(3-nitrophenyl)-2,3,4,5,10,11-hexahydro-1H-dibenzo[b,e][1,4]diazepin-1-one (16):

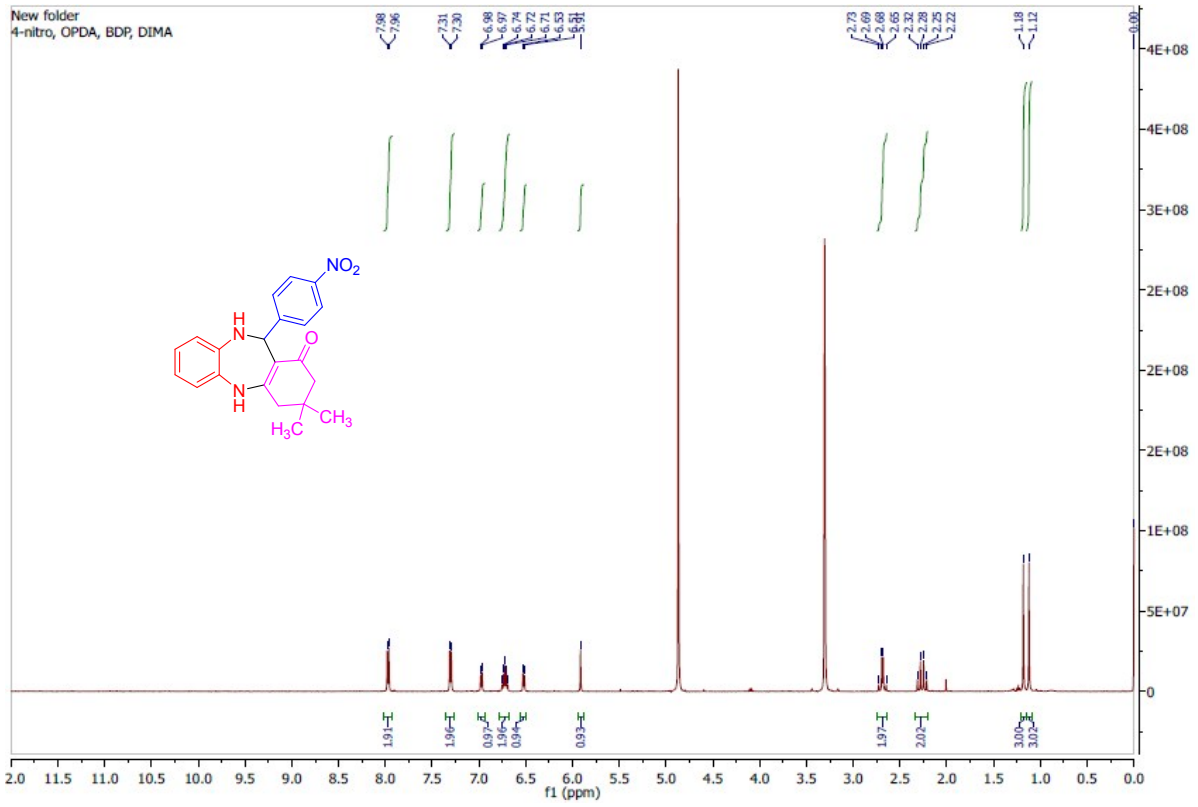


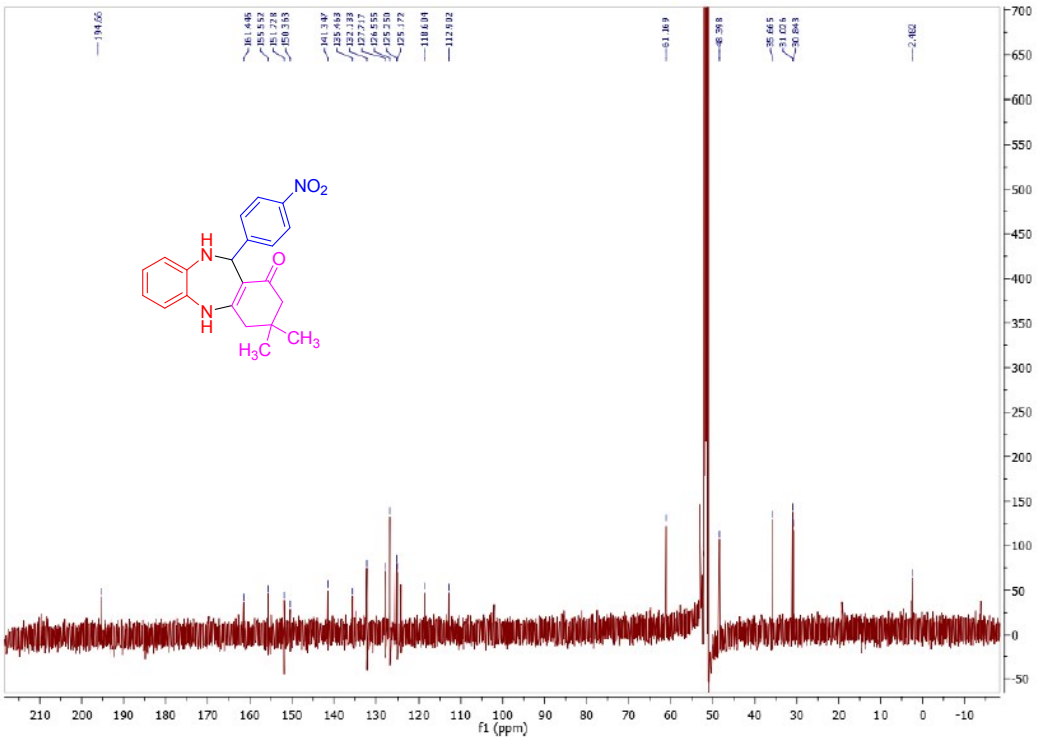

New folder
3-nitro,OPDA,BDP,DIMA
157.72
147.97
146.22
137.43
133.59
131.57
128.68
123.80
121.82
121.34
121.27
120.98
120.34
109.09
57.10
49.12
44.45
31.77
27.24
26.78
NO2
O
H
N
N
H
H3C
CH3
2800
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
-200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
f1 (ppm)

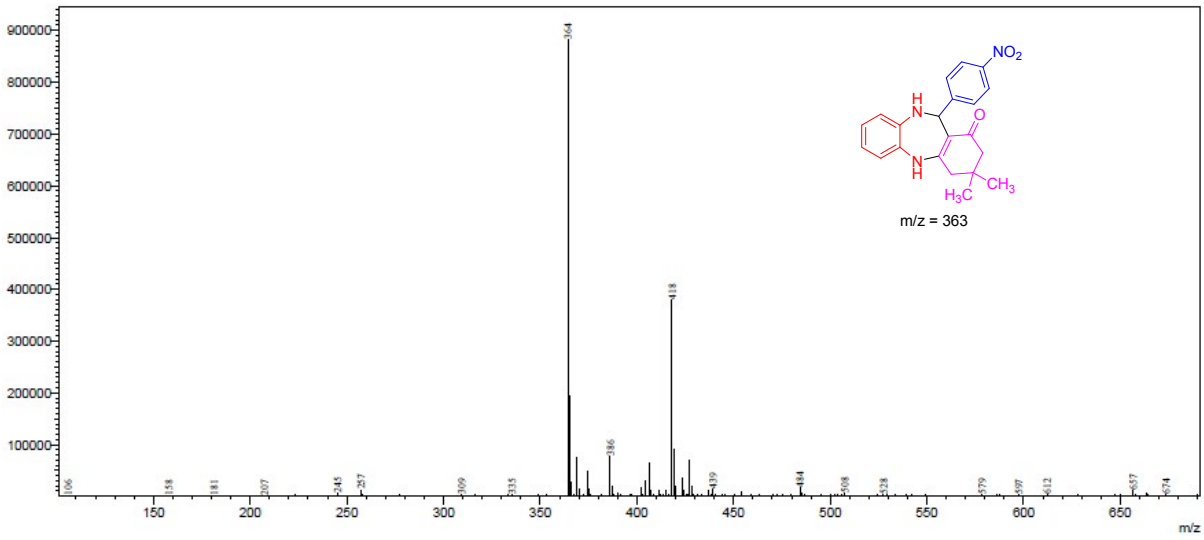

NO2
O
H
N
N
H
H3C
CH3

m/z = 363

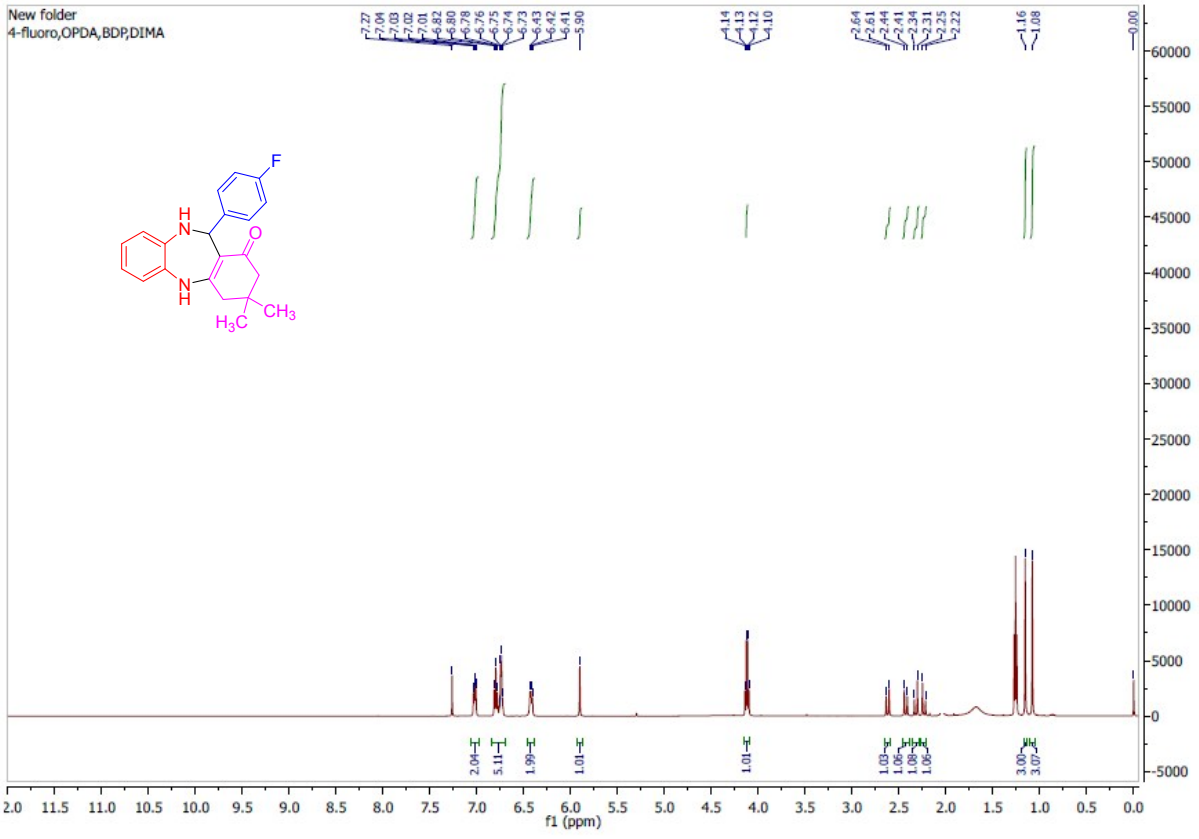
3,3-dimethyl-11-(4-nitrophenyl)-2,3,4,5,10,11-hexahydro-1H-dibenzo[b,e][1,4]diazepin-1-one (18):

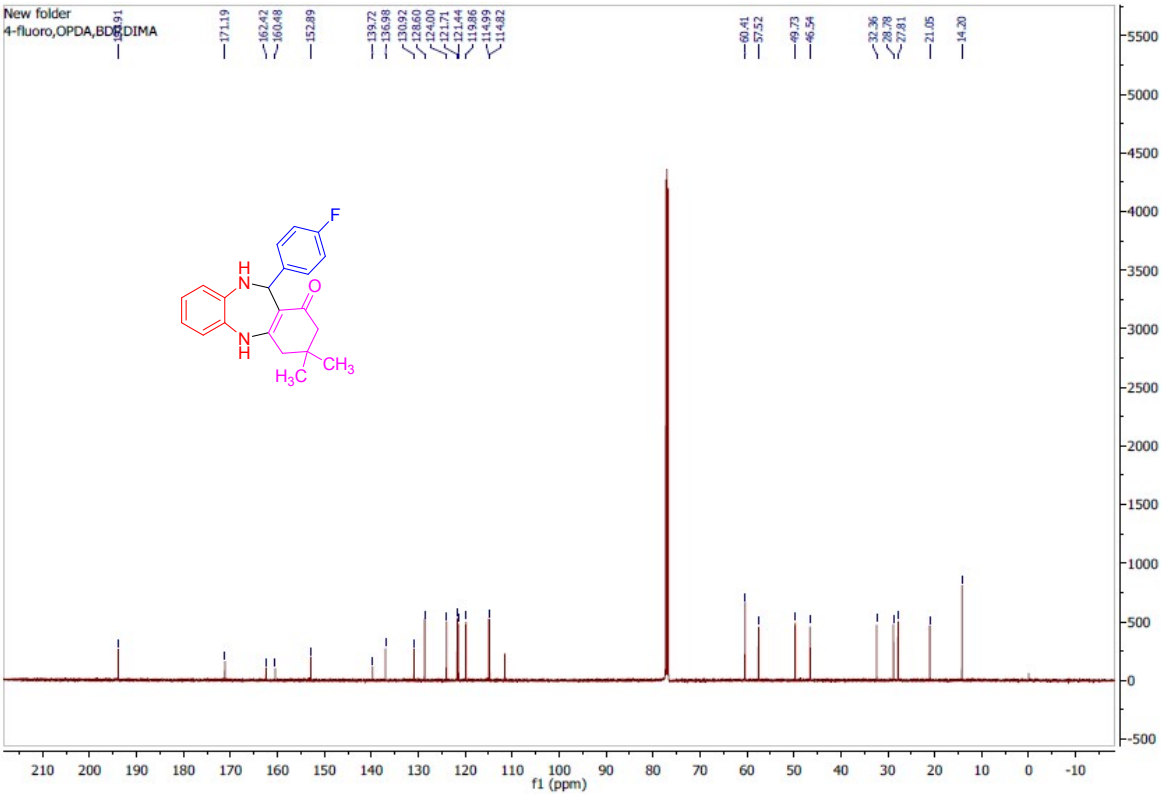


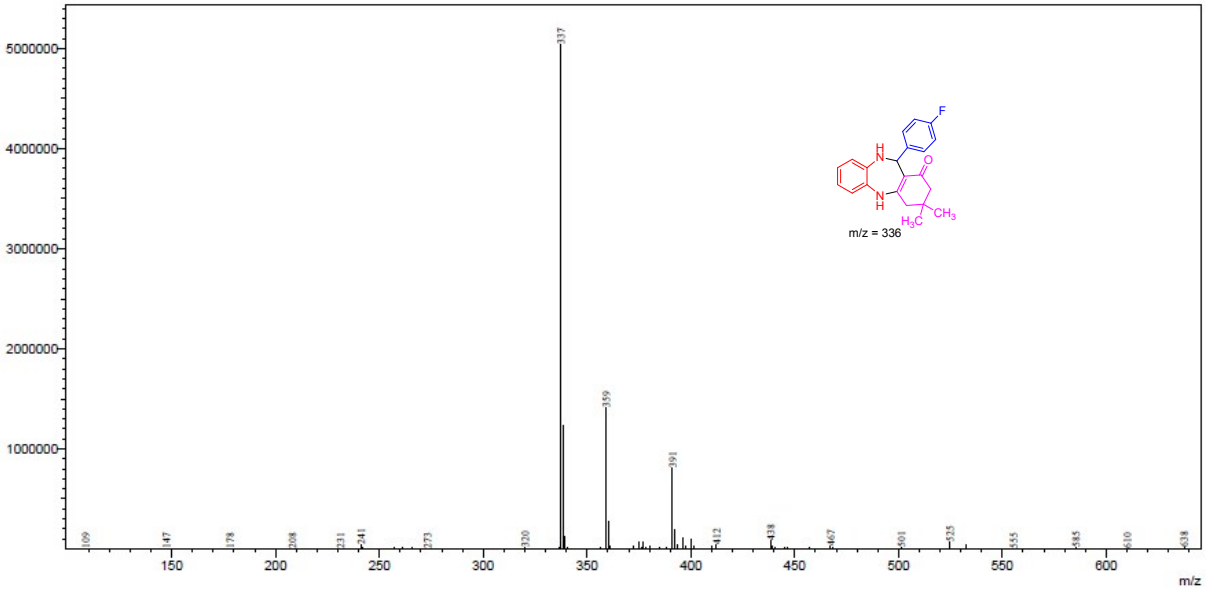




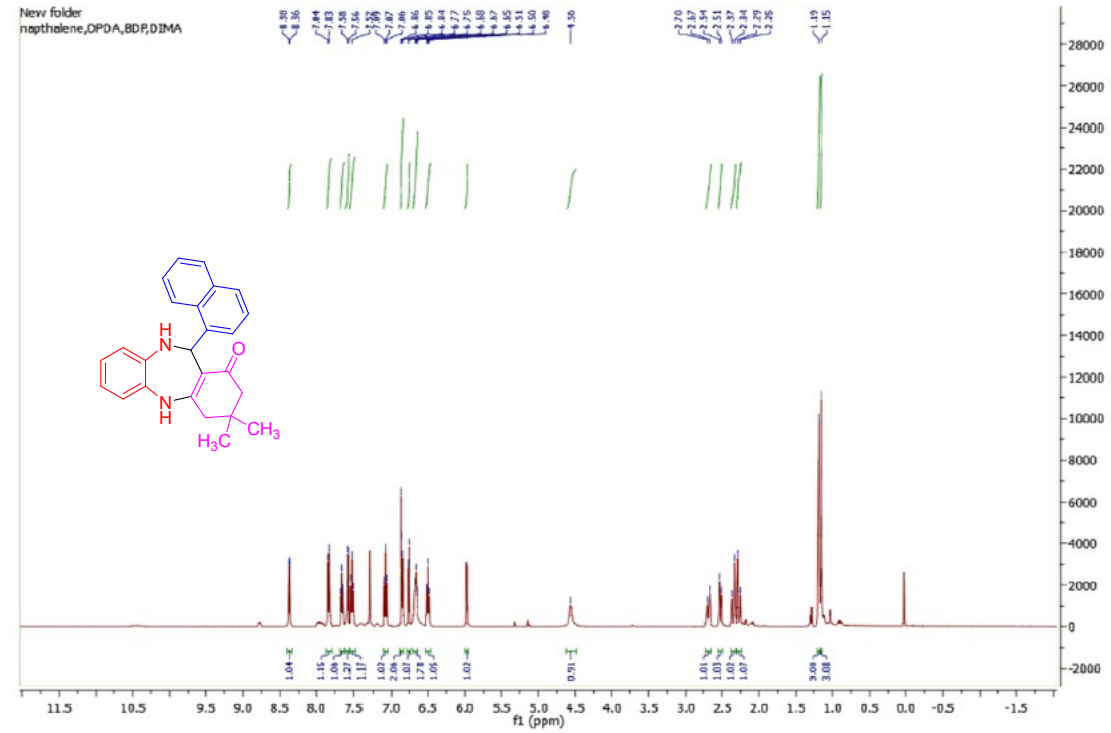
11-(4-fluorophenyl)-3,3-dimethyl-2,3,4,5,10,11-hexahydro-dibenzo[b,e][1,4]diazepin-1H-1-one (19):

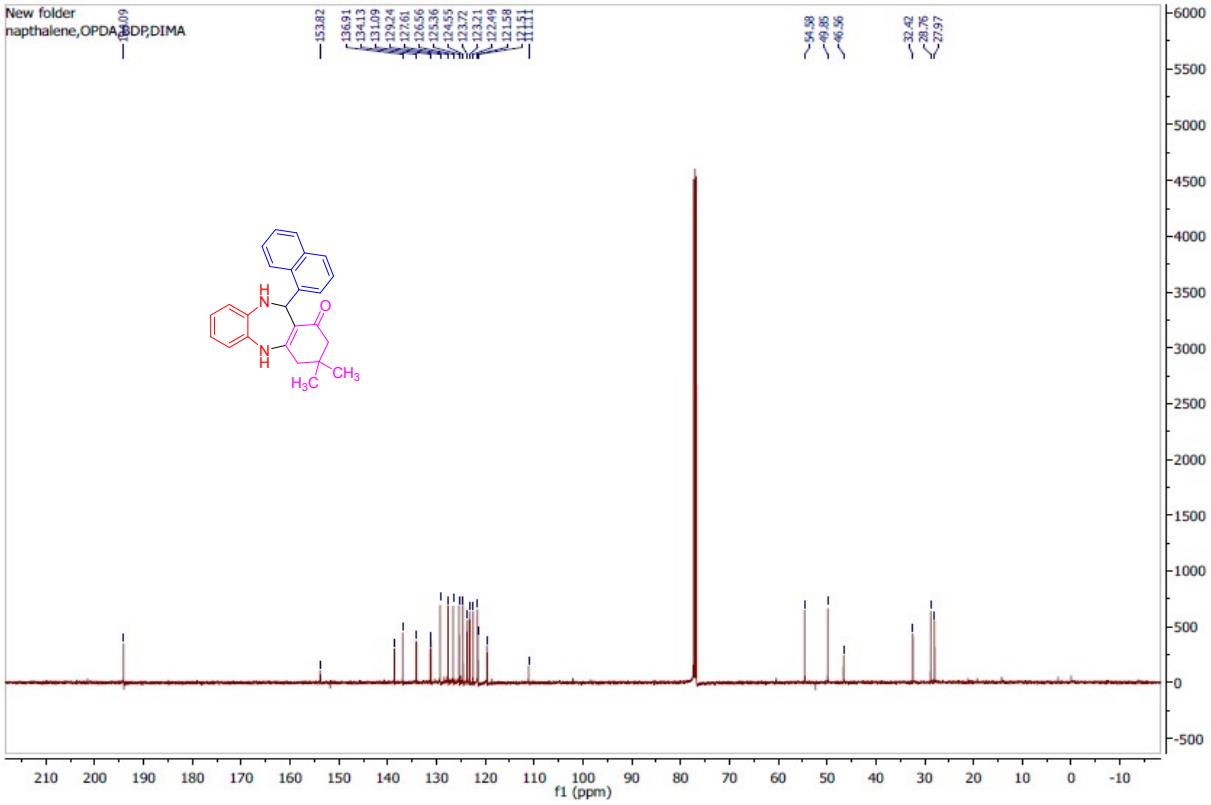


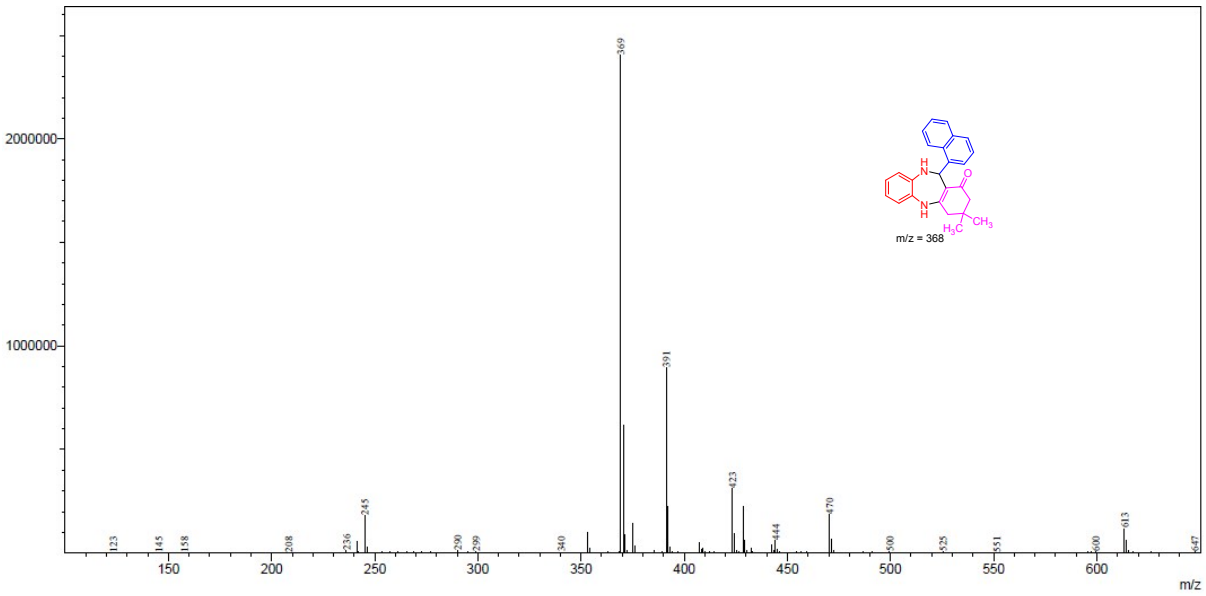

New folder
4-fluoro,OPDA,BDDIMA
195.91
171.19
162.42
160.48
152.89
139.72
136.98
130.92
128.60
124.00
121.71
121.44
119.86
114.99
114.82
60.41
57.52
49.73
46.54
32.36
28.78
27.81
21.05
14.20
F
H
N
O
N
H
H3C
CH3
f1 (ppm)


337
359
391
m/z
F
H
N
O
N
H
H3C
CH3
m/z = 336

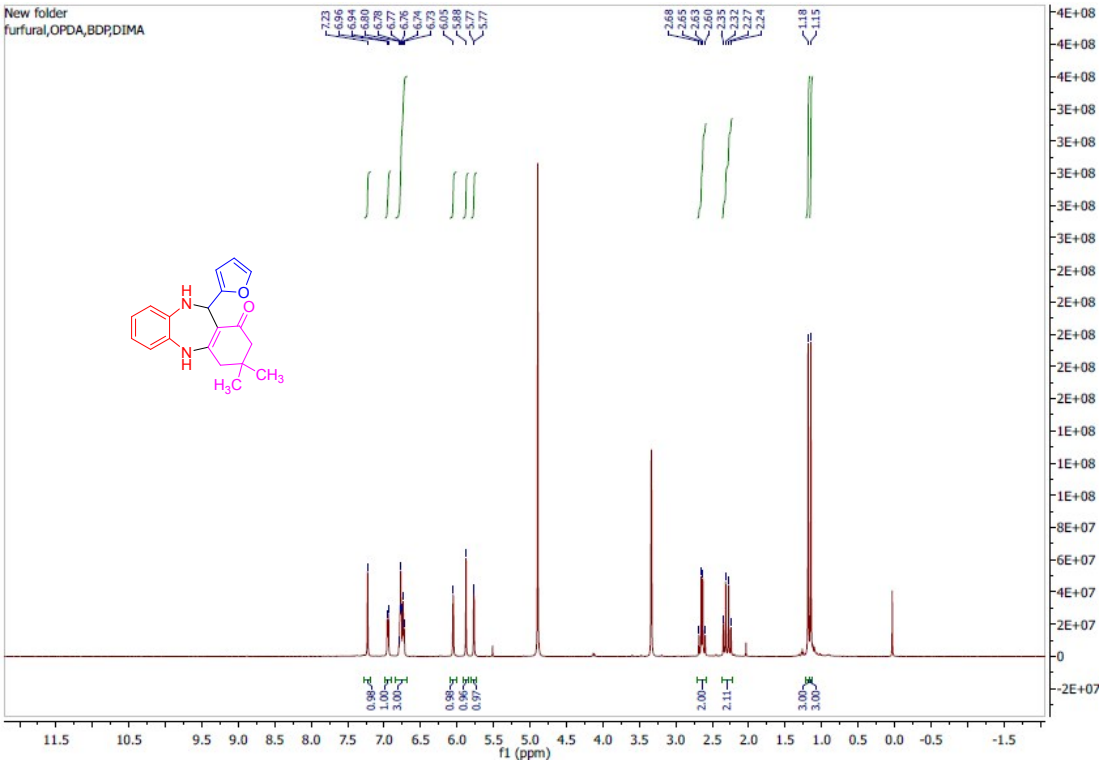
3,3-dimethyl-11-(naphthalen-1-yl)-2,3,4,5,10,11-hexahydro-1H dibenzo[b,e][1,4]diazepin-1-one(20):

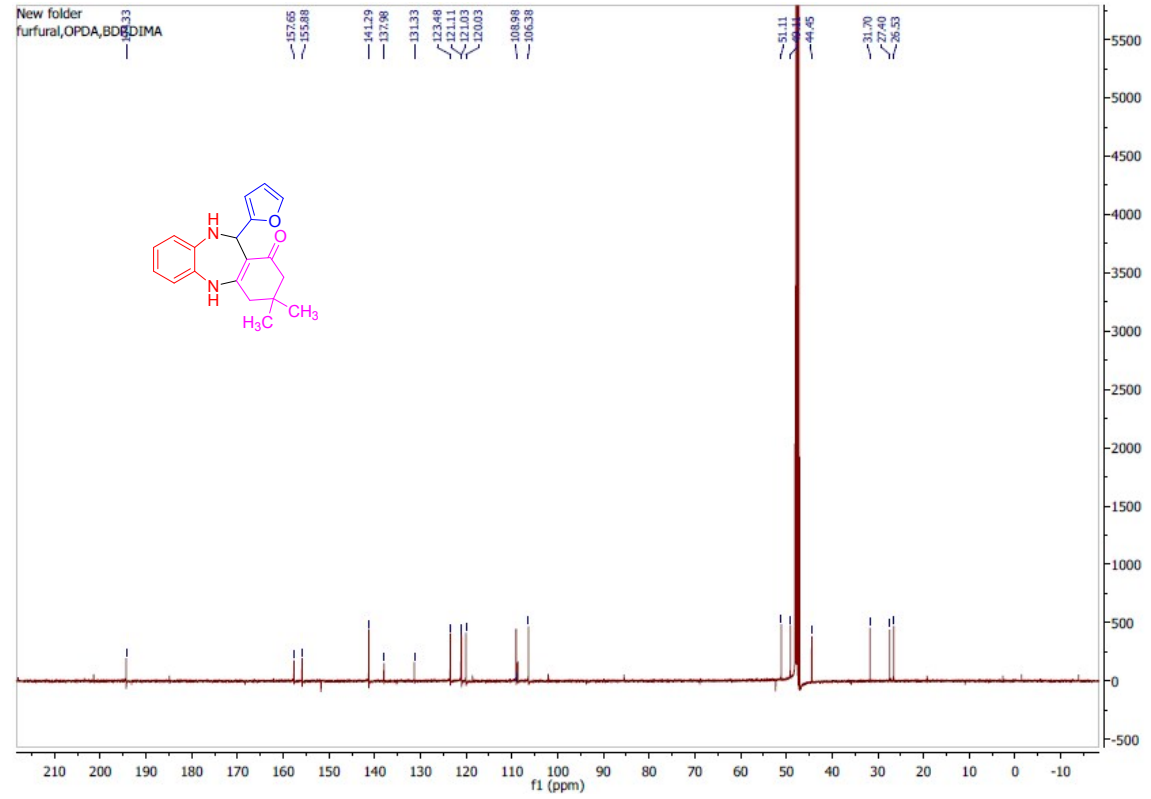


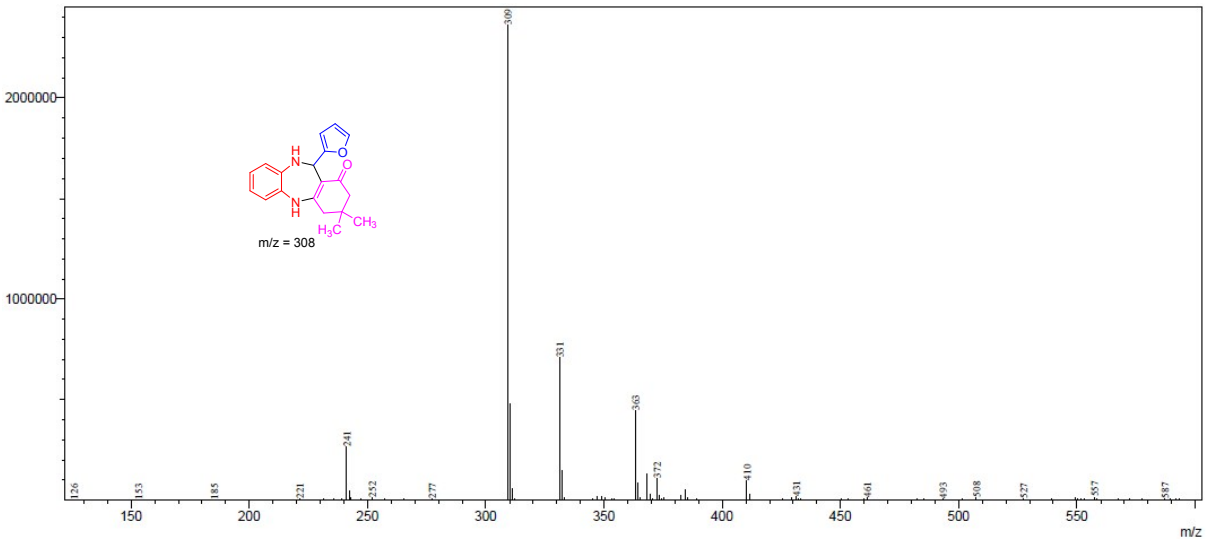




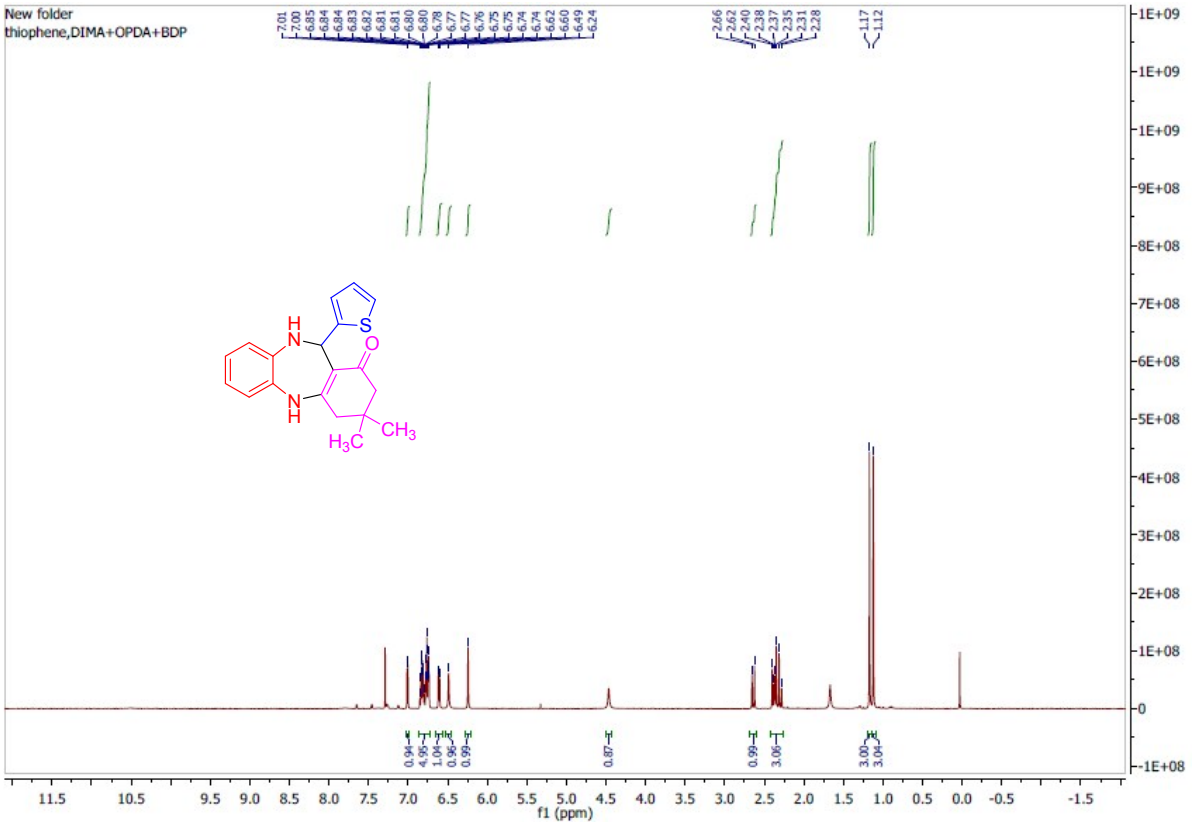
11-(furan-2-yl)-3,3-dimethyl-2,3,4,5,10,11-hexahydro-1H-dibenzo[b,e][1,4]diazepin-1-one(21):

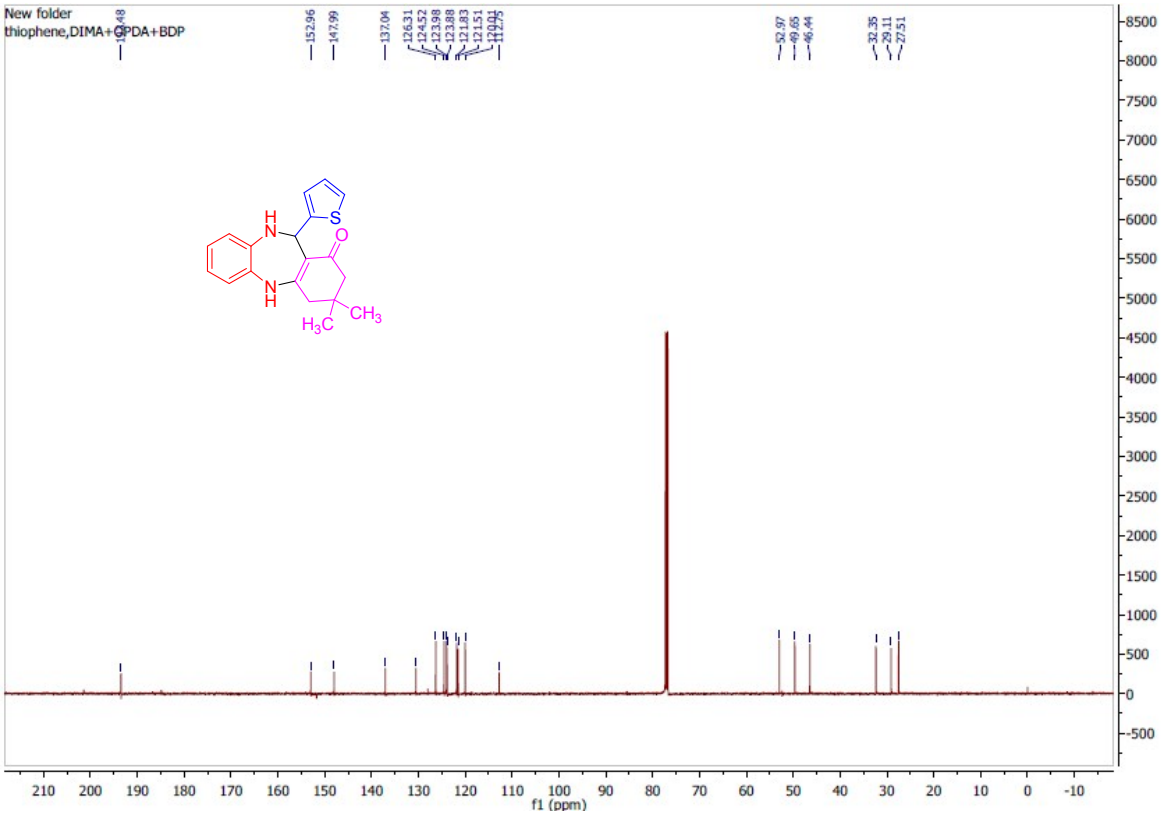


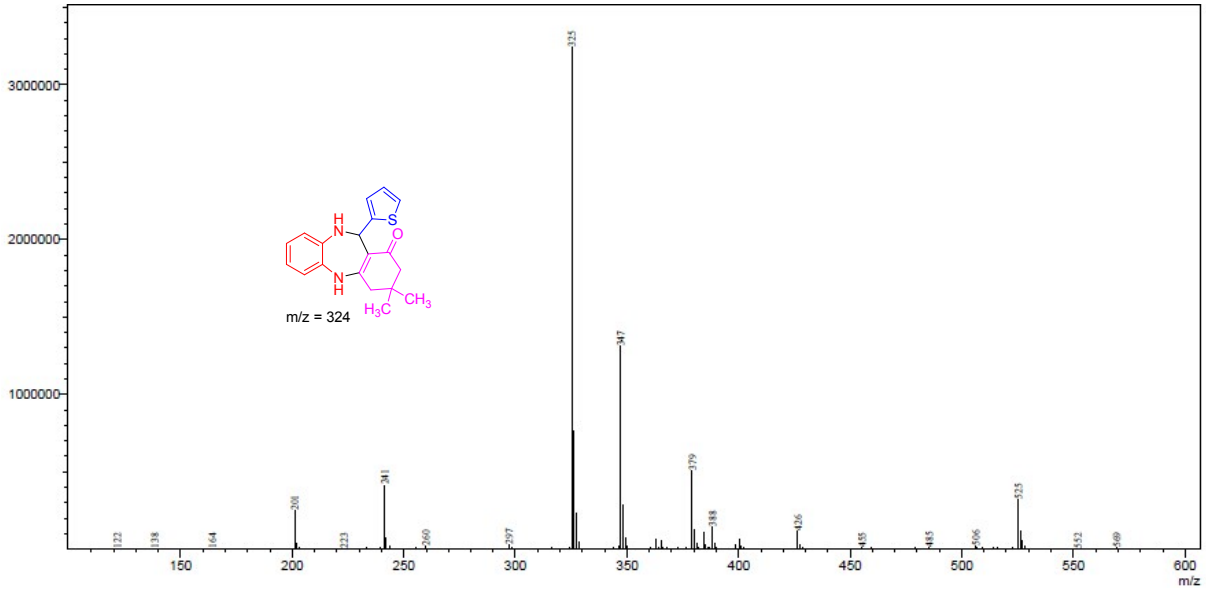

New folder
furfural,OPDA,BDBDIMA
157.65
155.88
141.29
137.98
131.33
123.48
121.11
121.03
120.03
108.98
106.38
51.11
44.45
31.70
27.40
26.53
f1 (ppm)


m/z = 308
309
331
363
241
372
410
m/z

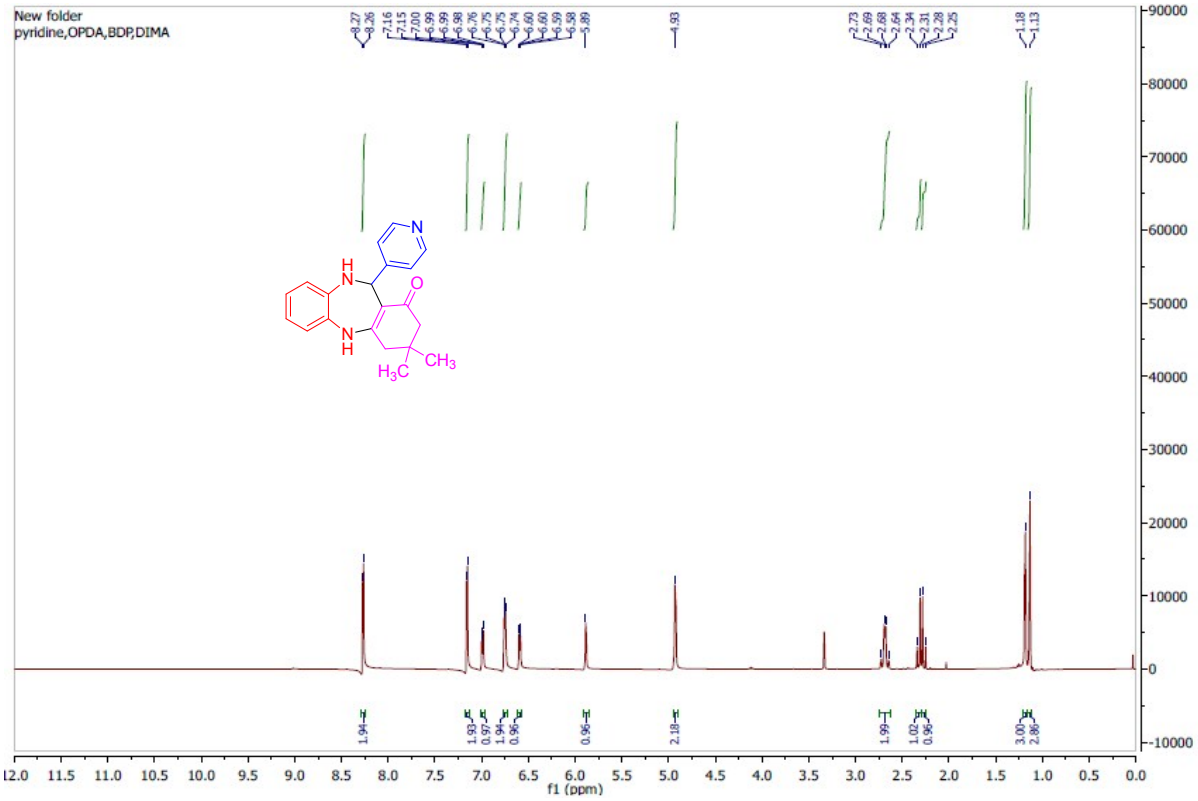
3,3-dimethyl-11-(thiophen-2-yl)-2,3,4,5,10,11-hexahydro-1H-dibenzo[b,e][1,4]diazepin-1-one(22):

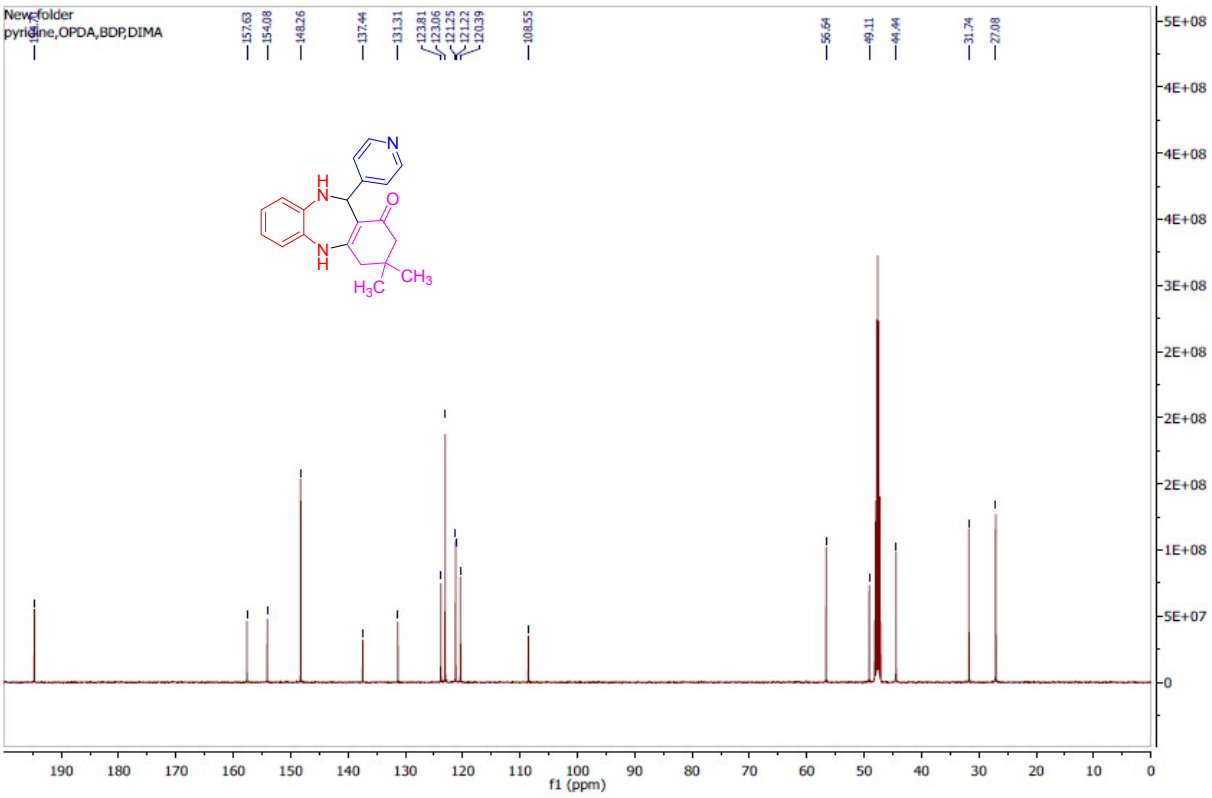




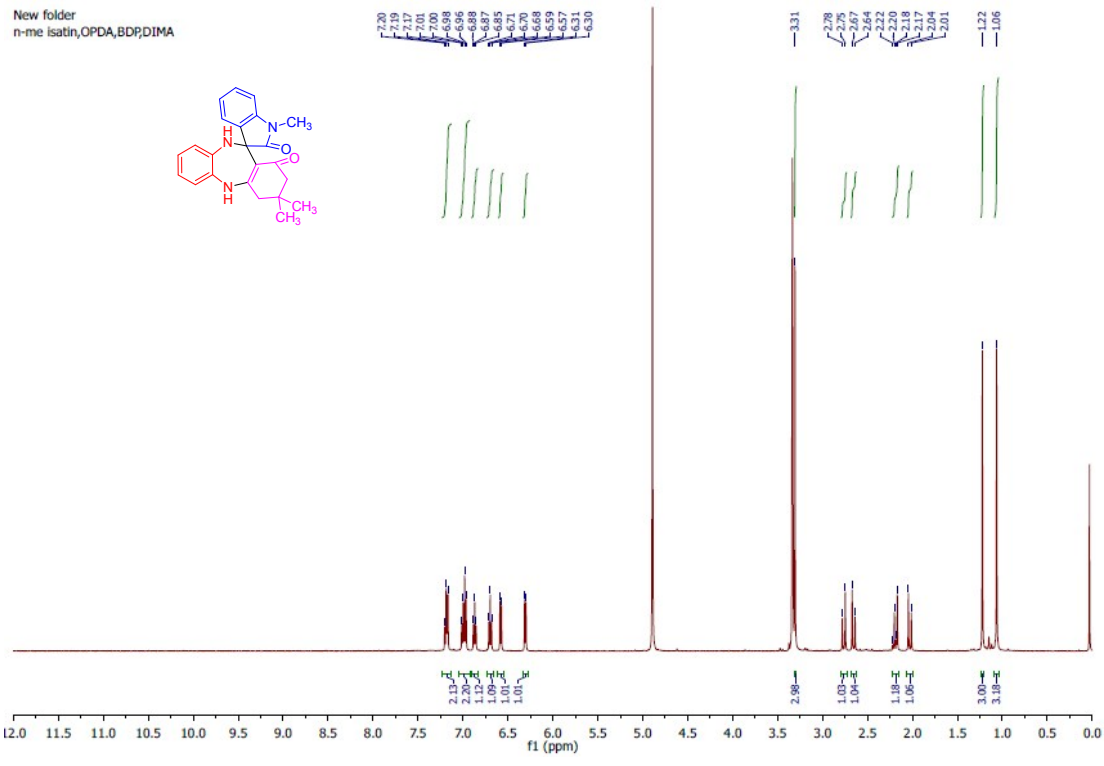


3,3-dimethyl-11-(pyridin-4-yl)-2,3,4,5,10,11-hexahydro-1H-dibenzo[b,e][1,4]diazepin-1-one (23):

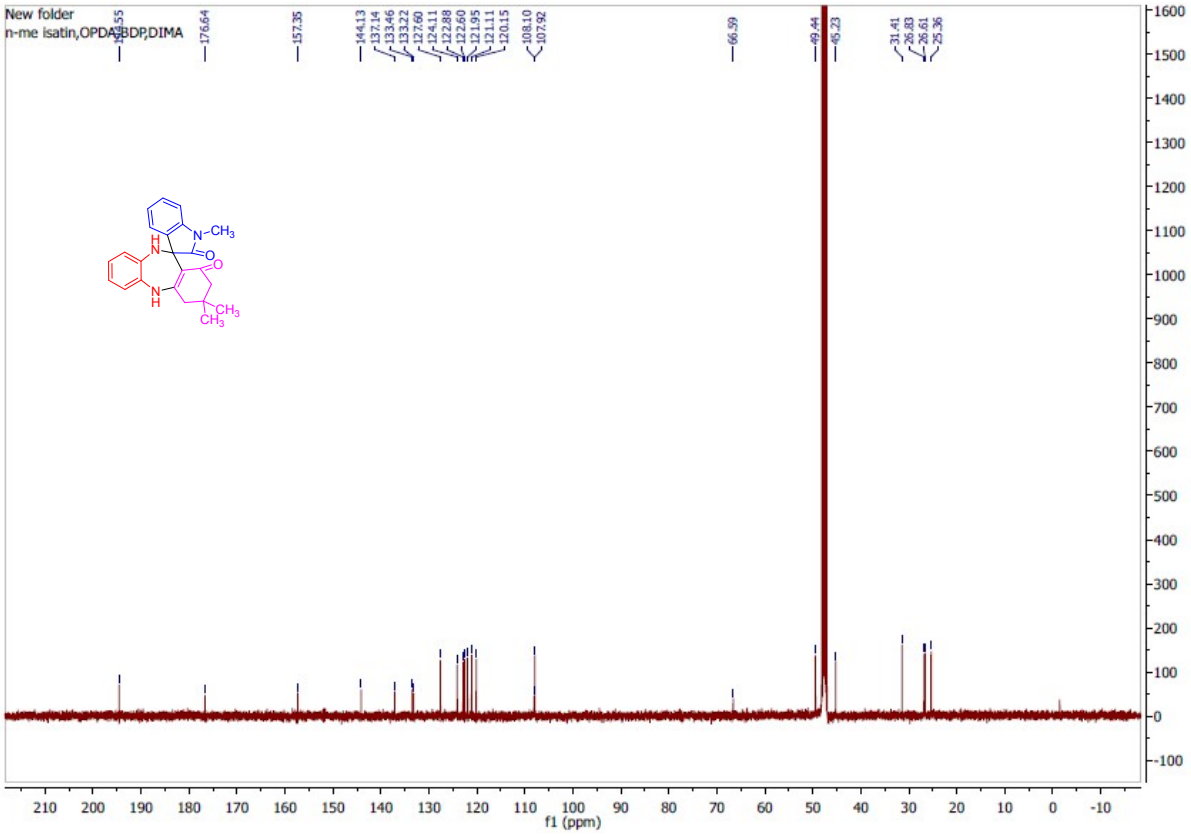


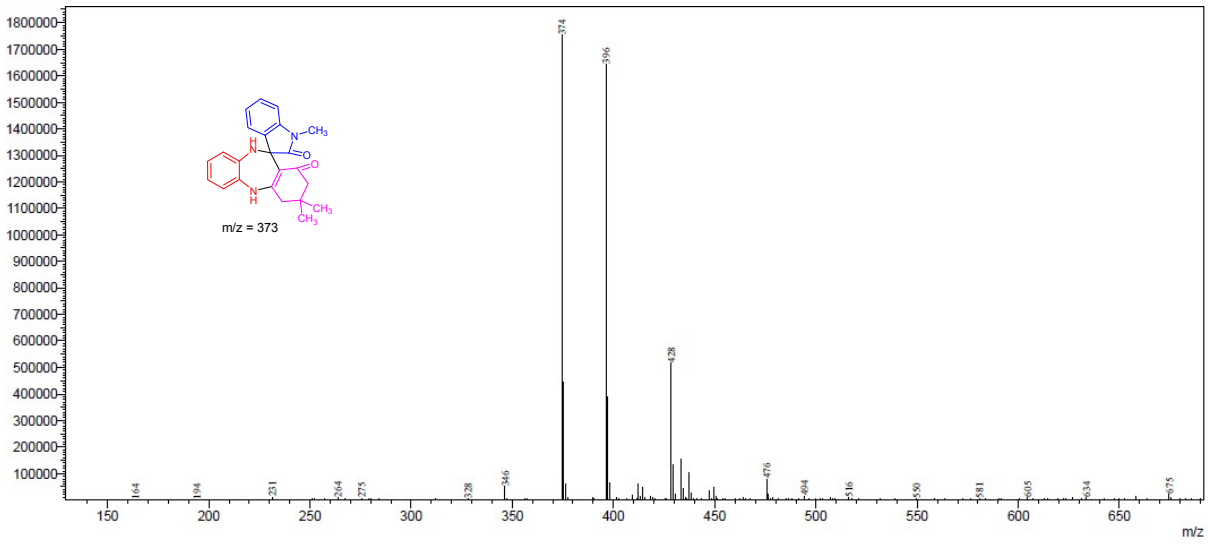


3,3-dimethyl-2,3,4,5,10,11-hexahydro-1H-dibenzo[b,e][1,4]diazepin-1-one(15) 3,3-dimethyl-11-(2-oxoindolin-3-yl)-2,3,4,5,10,11-hexahydro-1H-dibenzo[b,e][1,4]diazepin-1-one (24):



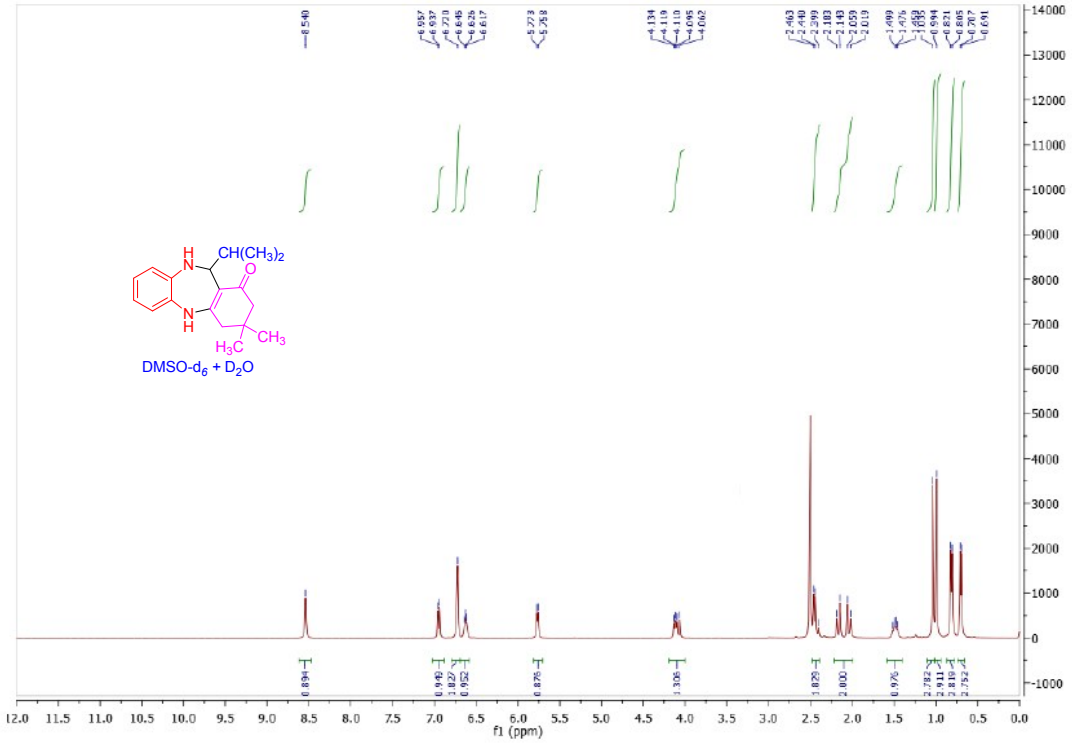
S

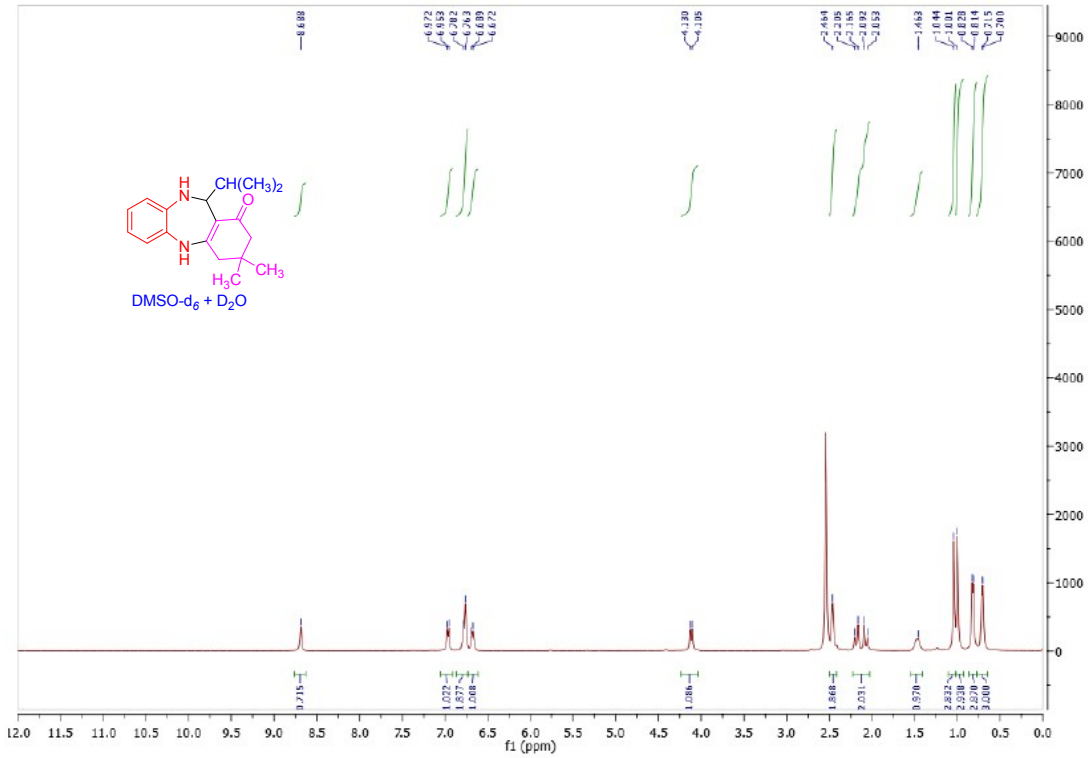

New folder
n-me isatin,OPDA,BDP,DIMA
176.64
157.35
144.13
137.14
133.46
133.22
127.60
124.11
122.88
122.60
121.95
121.11
120.15
108.10
107.92
66.59
49.44
45.23
31.41
26.83
26.61
25.36
f1 (ppm)


m/z = 373
374
396
428
m/z

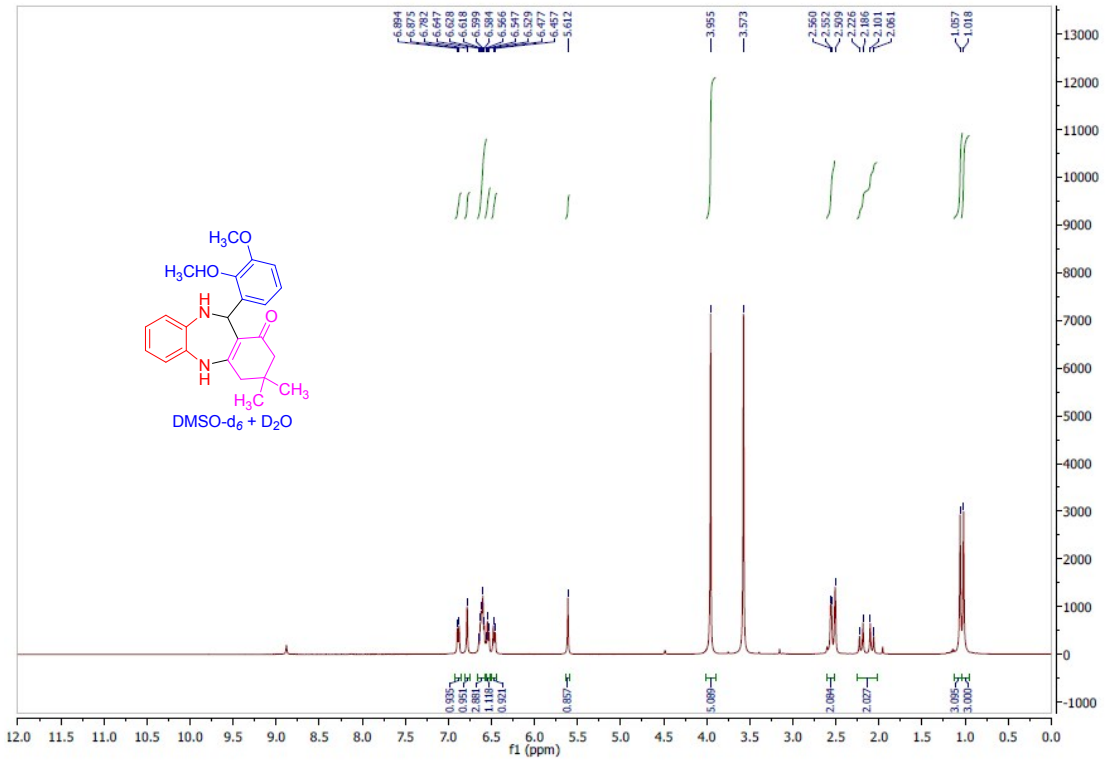
D_2O exchange studies: ^{1}H-NMR spetcrs of compounds (7, 10)

11-isopropyl-3,3-dimethyl-2,3,4,5,10,11-hexahydro-1H-dibenzo[b,e][1,4]diazepin-1-one(7):



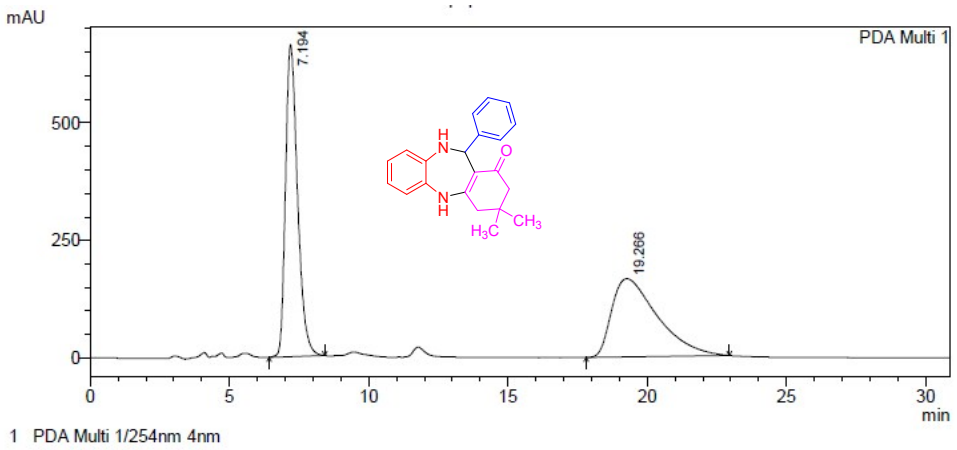


11-(2-hydroxy-3-methoxyphenyl)-3,3-dimethyl-2,3,4,5,10,11-hexahydro-1H-dibenzo[b,e][1,4]diazepin-1-one(10):



HPLC profiles of the compounds 4, 9, 21, and 20

3,3-dimethyl-11-phenyl-2,3,4,5,10,11-hexahydro-1H-dibenzo[b,e][1,4]diazepin-1-one (4):

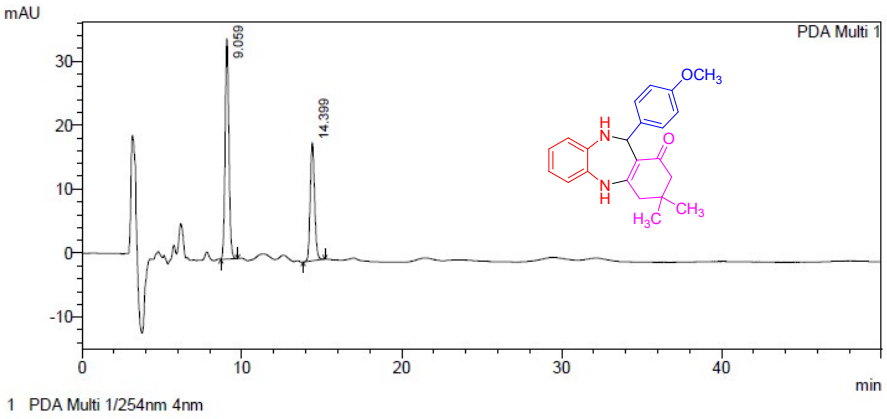


PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.194	19888693	662944	51.098	79.942
2	19.266	19033990	166335	48.902	20.058
Total		38922683	829279	100.000	100.000

11-(4-methoxyphenyl)-3,3-dimethyl-2,3,4,5,10,11-hexahydro-1H-dibenzo[b,e][1,4]diazepin-1-one (9):

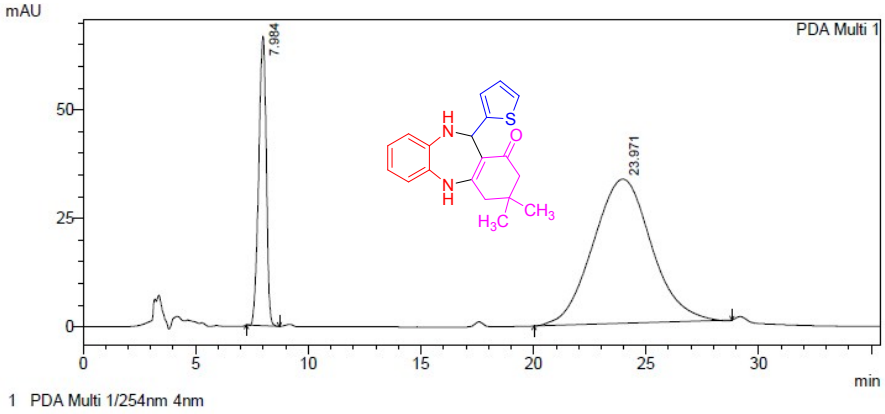


PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.059	568967	34445	61.799	65.036
2	14.399	351703	18518	38.201	34.964
Total		920670	52963	100.000	100.000

3,3-dimethyl-11-(thiophen-2-yl)-2,3,4,5,10,11-hexahydro-1H-dibenzo[b,e][1,4]diazepin-1-one (21)

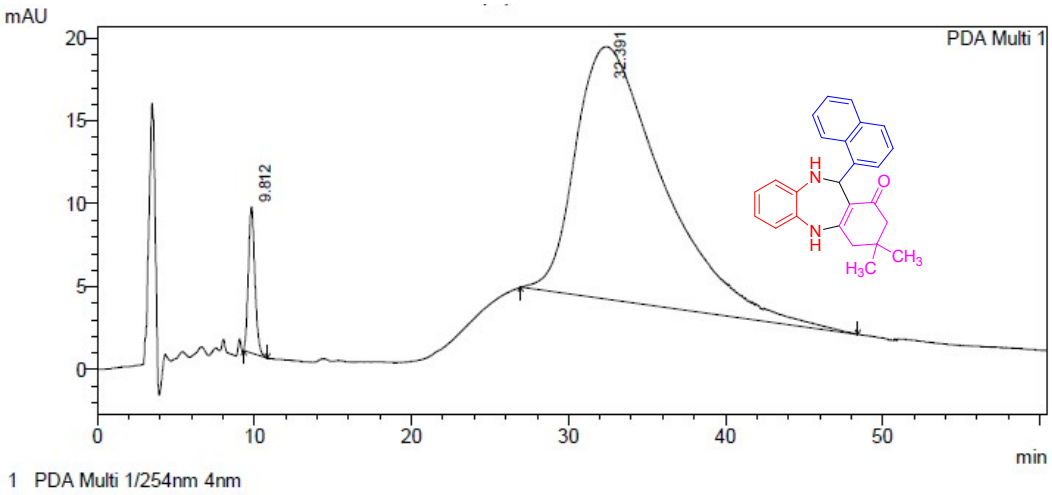


PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.984	1548414	66579	20.526	66.727
2	23.971	5995322	33199	79.474	33.273
Total		7543735	99777	100.000	100.000

3,3-dimethyl-11-(naphthalen-1-yl)-2,3,4,5,10,11-hexahydro-1H-dibenzo[b,e][1,4]diazepin-1-one (20):



PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.812	255879	8825	4.133	36.668
2	32.391	5935647	15243	95.867	63.332
Total		6191526	24068	100.000	100.000