Electronic Supplementary Material (ESI) for ChemComm.

A Multicomponent Tetrazolo Indole Synthesis

Xiaofang Lei, Panagiota Lampiri, Pravin Patil, Giasemi Angeli, Constantinos G. Neochoritis, Alexander Dömling

Supporting information

Table of contents

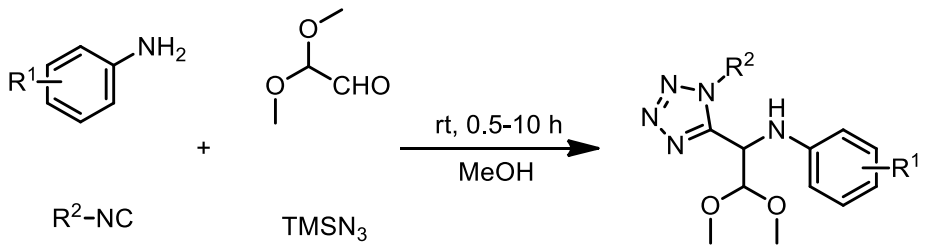
1. General methods and materials 2
2. Synthetic procedures and analytical data 3
3. Exemplary copies of NMR and MS data of novel compounds 38
4. Single crystal x-ray structure determination 151

1. General methods and materials

All the reagents and solvents were purchased from Sigma-Aldrich, AK Scientific, Fluorochem, Abcr GmbH, Acros and were used without further purification. Isocyanides were synthesized as previously described by us.[1] All microwave irradiation reactions were carried out in a Biotage Initiator™ Microwave Synthesizer. Thin layer chromatography was performed on Millipore precoated silica gel plates (0.20 mm thick, particle size 25 µm). Nuclear magnetic resonance spectra were recorded on Bruker Avance 500 spectrometers {^{1}H NMR (500 MHz), ^{13}C NMR (126 MHz)}. Chemical shifts for ^{1}H NMR were reported as δ values and coupling constants were in hertz (Hz). The following abbreviations were used for spin multiplicity: s = singlet, br s = broad singlet, d = doublet, t = triplet, q = quartet, quin = quintet, dd = double of doublets, ddd = double doublet of doublets, m = multiplet. Chemical shifts for ^{13}C NMR were reported in ppm relative to the solvent peak. Flash chromatography was performed on a Reveleris® X2 Flash Chromatography, using Grace® Reveleris Silica flash cartridges (12 grams). Mass spectra were measured on a Waters Investigator Supercritical Fluid Chromatograph with a 3100 MS Detector (ESI) using a solvent system of methanol and CO_2 on a Viridis silica gel column (4.6 x 250 mm, 5 µm particle size) or Viridis 2-ethyl pyridine column (4.6 x 250 mm, 5 µm particle size). High resolution mass spectra were recorded using a LTQ-Orbitrap-XL (Thermo) at a resolution of 60000@m/z400.

2. Synthetic procedures and analytical data

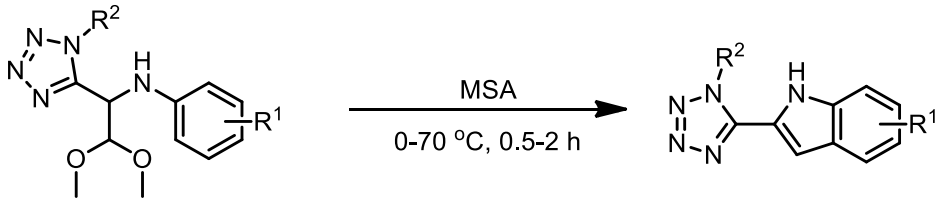
General Procedure for the Ugi tetrazole reaction (UT-4CR)



1a-y

To a stirred solution of 2,2-dimethoxyacetaldehyde (2.0 mmol) in MeOH (2.0 mL), the corresponding aniline (2.0 mmol), isocyanide (2.0 mmol) and trimethylsilyl azide (2.0 mmol) were added. The reaction mixture was stirred vigorously for 2 h. Then, if solid appears, half of the solvent is removed under reduced pressure. The resulting solid was filtered and washed with Et_2O. Alternatively, the solvent is removed under reduced pressure and the residue is purified by column chromatography (PE-EA, 2:1-1:1) to give the compounds **1a-y**.

General Procedure for the Pictet-Spengler cyclization

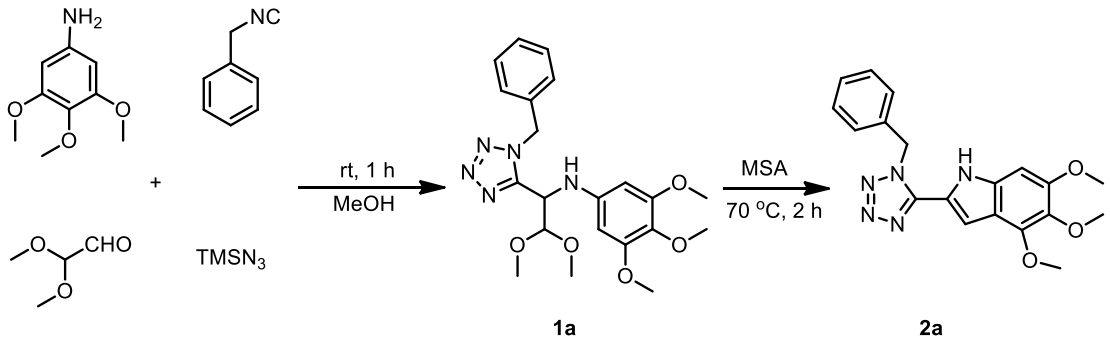


2a-z

The corresponding tetrazole derivatives (1.0 mmol) are dissolved into methanesulfonic acid (MSA) (1.0 mL) at 0 ºC and then heated up to 70 ºC for 0.5 - 2.0 h. Then, the reaction mixture was cooled to room temperature and neutralized with an aqueous solution of $NaHCO_3$, followed by extractions with ethyl acetate. The organic layer was dried with $MgSO_4$ and the solvent was removed under reduced pressure. If solid appears, the resulting solid was filtered and washed with Et_2O. Alternatively, the solvent is removed under reduced pressure and the residue is purified by column chromatography (PE-EA, 3:1-1:1) to give the compounds **2a-z**.

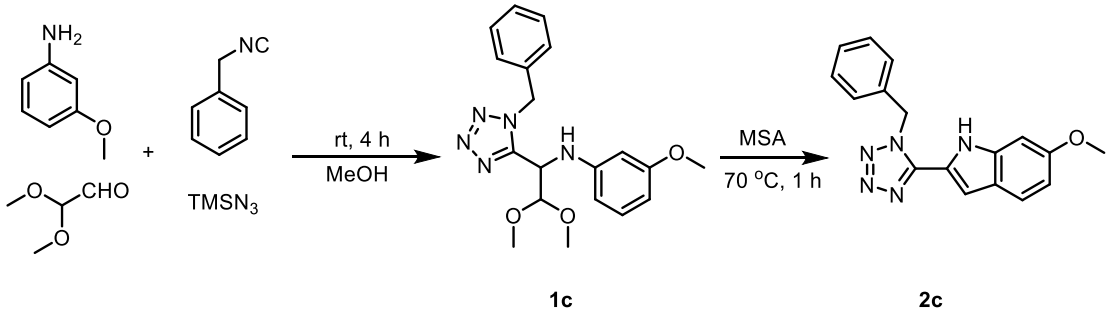
In case of meta-substituted anilines, mixture of isomers was obtained (see analytical data)

The gram-scale synthesis of 1a and 2a



To a stirred solution of 2,2-dimethoxyacetaldehyde (10.0 mmol, 1.04 g) in MeOH (10.0 mL), the 3,4,5-trimethoxyaniline (10.0 mmol, 1.83 g), benzyl isocyanide (10.0 mmol, 1.17 g) and trimethylsilyl azide (10.0 mmol, 1.15 g) were added in a 50 mL flask. The reaction mixture was stirred vigorously for 2 h. Then, half of the solvent was removed under reduced pressure, the resulting solid was filtered and washed with Et_2O to give the compound **1a** (4.15 g, 97%) as gray solid. Afterwards, the *N*-(1-(1-benzyl-1*H*-tetrazol-5-yl)-2,2-dimethoxyethyl)-3,4,5-trimethoxyaniline (**1a**, 5.0 mmol, 2.15 g) was dissolved into methanesulfonic acid (5.0 mL) at 0 °C and then heated up to 70 °C for 2 h. Then, the reaction mixture was cooled to room temperature neutralized with an aqueous solution of $NaHCO_3$ to pH 7, followed by extractions with ethyl acetate (3 x 30 mL). The organic layer was dried with $MgSO_4$ and the solvent was removed under reduced pressure. The resulting solid was filtered and washed with Et_2O to give the compound **2a** (1.67 g, 91%) as brown solid.

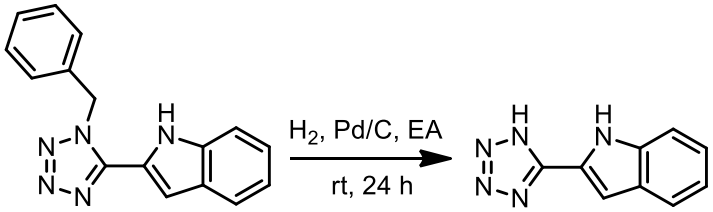
One-pot approach of 2-(1-benzyl-1*H*-tetrazol-5-yl)-6-methoxy-1*H*-indole (2c)



To a stirred solution of 2,2-dimethoxyacetaldehyde (1.0 mmol) in MeOH (1.0 mL), the 3-methoxyaniline (1.0 mmol), benzyl isocyanide (1.0 mmol) and trimethylsilyl azide (1.0 mmol) were added in a 5.0 mL vial. The reaction mixture was stirred vigorously for 4 h. Then, the solvent was removed under reduced pressure and the compound **1c**,

obtained as brown solid, was directly used in the next step without further purification. Afterwards, the methanesulfonic acid (1.0 mL) was added at 0 ^{o}C and heated up to 70 ^{o}C for 1 h. The reaction mixture was neutralized with an aqueous solution of $NaHCO_3$, followed by extractions with ethyl acetate. The organic layer was dried with $MgSO_4$ and the solvent was removed under reduced pressure. The resulting solid was purified by column chromatography (PE-EA, 3:1) to give compound **2c** (149 mg, 49% in 2-steps) as white solid, as mixture of isomers as indicated above.

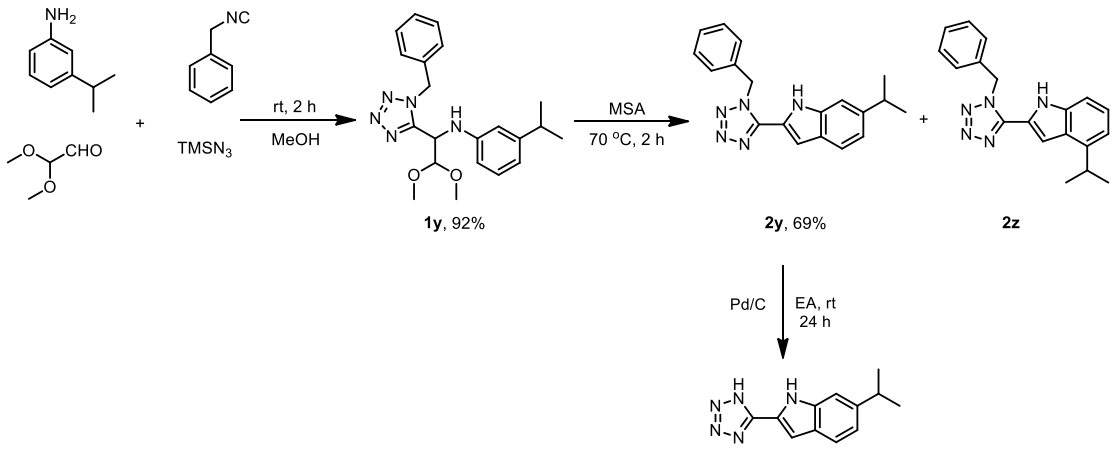
Synthesis of the 2-(1*H*-tetrazol-5-yl)-1*H*-indole



2f **3a**

To a stirred solution of 2-(1-benzyl-1*H*-tetrazol-5-yl)-1*H*-indole (**2f**, 1.0 mmol) in ethyl acetate (15.0 mL), Pd/C (10% w/w, 0.2 mmol) was added at room temperature under H_2 atmosphere at 1 atm. The reaction mixture was stirred for 24 h. Then, filtration via celite followed by purification with column chromatography (PE-EA, 1:7) gave the compound **3a** (175 mg, 95%) as yellow solid.

Synthesis of the 6-isopropyl-2-(1*H*-tetrazol-5-yl)-1*H*-indole (ATP-competitive eIF$_4$A$_3$ inhibitor 3b)



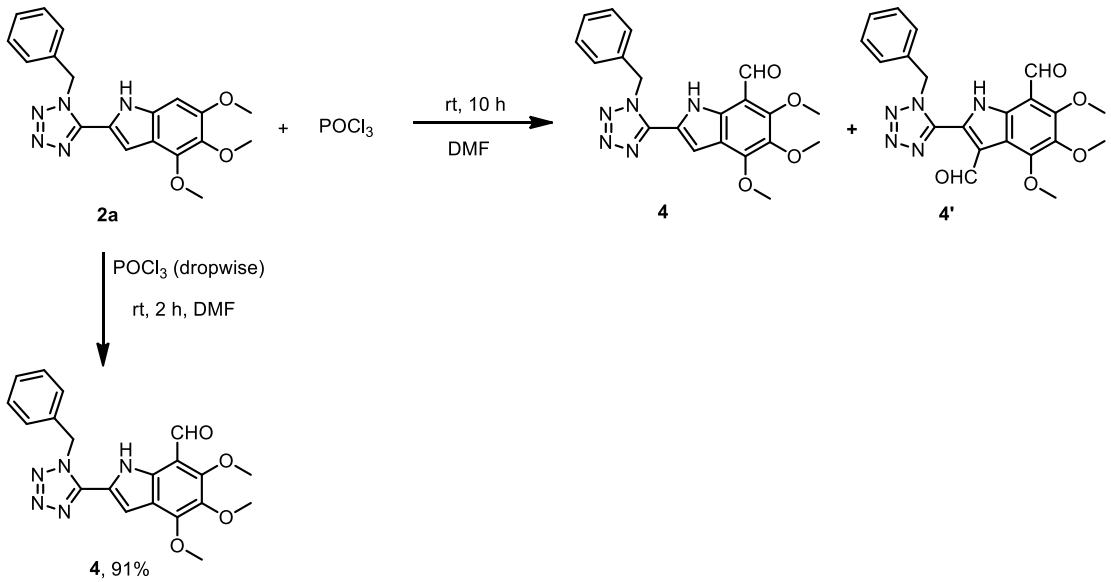
1y, 92% **2y**, 69% **2z**

1y was synthesized according to the general procedure of UT-4CR; 3-isopropylaniline (2.0 mmol), (isocyanomethyl)benzene (2.0 mmol), 2,2-dimethoxyacetaldehyde (2.0 mmol) and trimethylsilyl azide (2.0 mmol) as starting materials, isolated in 92% yield as a yellow solid.

2y and **2z** were synthesized according to the general procedure for the Pictet-Spengler cyclization; **1y** (1.0 mmol), **2y** and **2z** were obtained as mixture of isomers in 4:1 ratio (86% yield, yellow solid), pure **2y** was obtained (69% yield, white solid) after washing with ether.

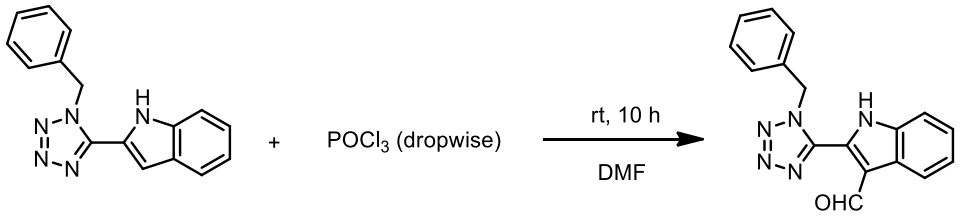
To a stirred solution of 2-(1-benzyl-1*H*-tetrazol-5-yl)-6-isopropyl-1*H*-indole (**2y**, 0.2 mmol) in ethyl acetate (2.0 mL), Pd/C (10% w/w, 0.04 mmol) was added at room temperature under H_2 atmosphere at 1 atm. The reaction mixture was stirred for 24 h. Then, filtration with celite and remove the solvent to give the compound **3b** (44 mg, 98%) as white solid.

Procedure for the formylation reactions



To a stirred solution of **2a** (1.0 mmol) in DMF (1.0 mL), phosphorus oxychloride (1.2 mmol) was added at room temperature and the reaction mixture was stirred for 10 h. Then, the reaction was quenched with $NaHCO_3$ solution to pH 7 and extracted with ethyl acetate (3 x 10 mL). The organic layer was dried with $MgSO_4$ and the solvent was removed under reduced pressure. The resulting solid was purified by column chromatography (PE-EA, 1:1) to give the compound mixture **4** and **4'** as a brown solid in a ratio 1:1.[2]

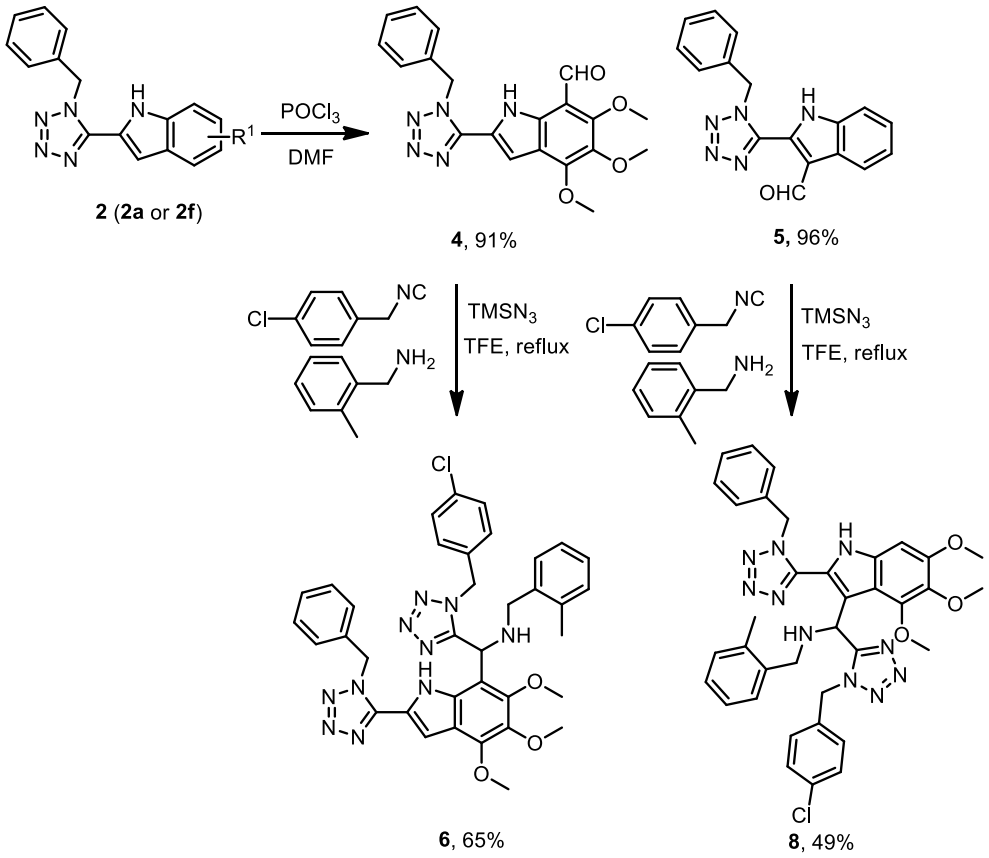
To a stirred solution of **2a** (1.0 mmol) in DMF (1.0 mL), the phosphorus oxychloride (1.2 mmol in 0.4 mL DMF) was added dropwise. The reaction mixture was stirred vigorously for 2 h at room temperature, then the reaction was quenched with $NaHCO_3$ solution to pH 7 and extracted with ethyl acetate (3 x 10 mL). The organic layer was dried with $MgSO_4$ and the solvent was removed under reduced pressure. The resulting solid was washed with ethyl acetate to give compound **4** (358 mg, 91%) as a green solid.[1]



2f **5**, 96%

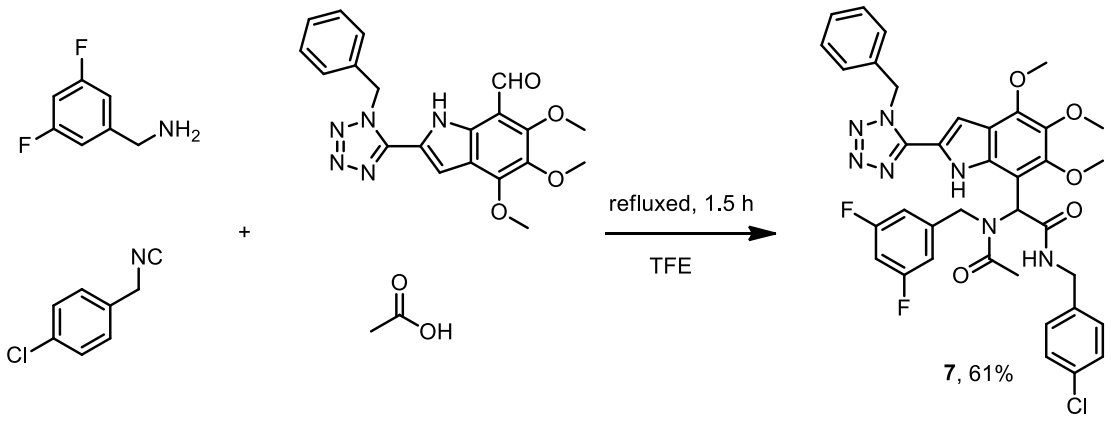
To a stirred solution of **2f** (1.0 mmol) in DMF (1.0 mL), the phosphorus oxychloride (1.2 mmol in 0.4 mL DMF) was added dropwise and the reaction mixture was stirred vigorously for 10 h at room temperature. Then, the reaction was quenched with $NaHCO_3$ solution to pH 7 and extracted with ethyl acetate (3 x 10 mL). The compound **5** (291 mg, 96%) was obtained as brown oil and used directly in the next step without further purification.

General procedure for the UT-4CR post-modification



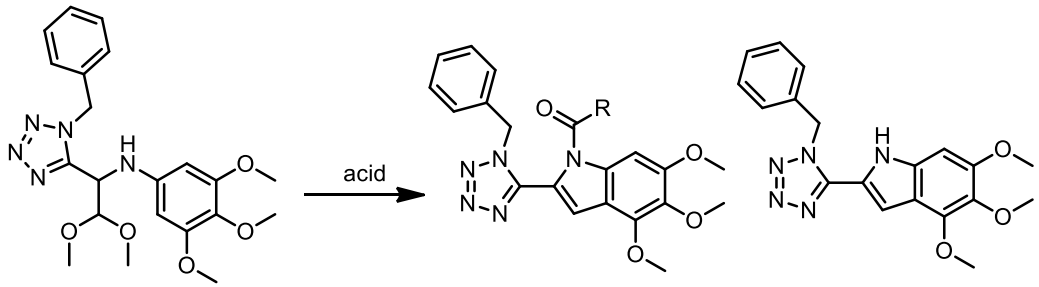
To a stirred solution of corresponding aldehyde (1.0 mmol) in TFE (1.0 mL), the *o*-tolylmethanamine (1.0 mmol), 1-chloro-4-(isocyanomethyl)benzene (1.0 mmol) and trimethylsilyl azide (1.0 mmol) were added at room temperature. Then the reaction mixture was warmed up to 80 ^{o}C and stirred vigorously for 2 h. Afterwards, the solvent was removed under reduced pressure and the resulting solid was purified by column chromatography (PE-EA, 2:1) to give compounds **6** and **8** in 65% and 49% yield, respectively.

General procedure for the U-4CR post-modification



To a stirred solution of 2-(1-benzyl-1*H*-tetrazol-5-yl)-4,5,6-trimethoxy-1*H*-indole-7-carbaldehyde (1.0 mmol) in TFE (1.0 mL), the (3,5-difluorophenyl)methanamine (1.0 mmol), 1-chloro-4-(isocyanomethyl)benzene (1.0 mmol) and acetic acid (1.0 mmol) were added at room temperature. Then, the reaction mixture was warmed up to 80 ^{o}C and stirred vigorously for 1.5 h. Afterwards, the solvent was removed under reduced pressure and the resulting solid was purified by column chromatography (PE-EA, 4:1) to give the compound **7** (445 mg, 61%) as a brown solid.

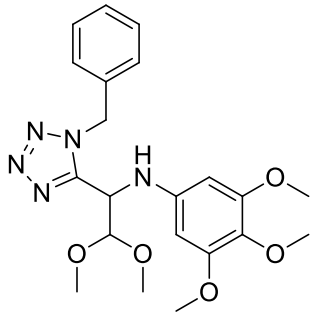
Pictet-Spengler reaction – optimization



1a **2a'** **2a**

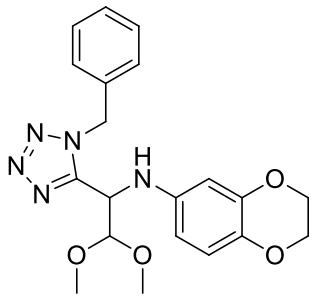
Entry	Acid	Catalyst	Temperature (°C)	Time	Solvent	Yield
1	formic acid	none	80	overnight	-	**2a'**:**2a** (65%: 22%)
2	acetic acid	$ZnCl_2$	120	48 h	-	**2a'**:**2a** (30%:30%)
3	acetic acid	$ZnCl_2$	rt	48 h	-	-
4	HCl	none	50	24 h	dioxane	**2a**: 30%
5	HCl	none	50	24 h	water	**2a**: 41%
6	HCl	none	50	24 h	isopropanol	**2a**: 45%
7	$TiCl_4$	none	rt	48 h	DCM	traces
8	methanesulfonic acid	none	45	15 h	-	**2a**: 90%
9	methanesulfonic acid	none	70	2 h	-	**2a**: 91%

***N*-(1-(1-benzyl-1*H*-tetrazol-5-yl)-2,2-dimethoxyethyl)-3,4,5-trimethoxyaniline (1a)**



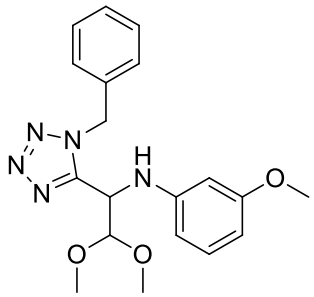
832 mg, 97% yield, gray solid. mp 131 - 134 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28 - 7.25 (m, 3H), 7.08 (dd, *J* = 6.4, 3.0 Hz, 2H), 5.76, 5.61 (ABq, *J* = 15.5 Hz, 2H), 5.68 (s, 2H), 4.95 (d, *J* = 5.1 Hz, 1H), 4.55 (d, *J* = 5.1 Hz, 1H), 3.72 (s, 3H), 3.66 (s, 6H), 3.41(s, 3H), 3.39 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 154.0, 153.7, 142.3, 134.1, 131.7, 129.0, 128.7, 127.6, 105.3, 92.1, 61.1, 56.9, 56.1, 55.8, 53.9, 51.6. HRMS (ESI) m/z calcd for $C_{21}H_{28}N_5O_5$ $[M + H]^+$ = 430.2085, found 430.2081.

***N*-(1-(1-benzyl-1*H*-tetrazol-5-yl)-2,2-dimethoxyethyl)-2,3-dihydrobenzo[*b*][1,4] dioxin-6-amine (1b)**



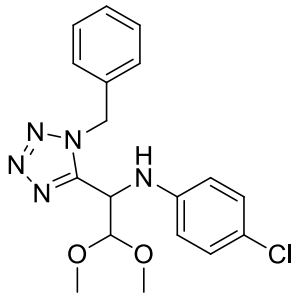
644 mg, 81% yield, white solid. mp 134 - 135 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.38 - 7.32 (m, 3H), 7.24 - 7.23 (m, 2H), 6.48 (d, *J* = 8.5 Hz, 1H), 6.18 (d, *J* = 2.7 Hz, 1H), 6.01 (dd, *J* = 8.5, 2.7 Hz, 1H), 5.89 (d, *J* = 8.9 Hz, 1H), 5.79, 5.71 (ABq, *J* = 15.4 Hz, 2H), 5.11 (dd, *J* = 8.9, 5.9 Hz, 1H), 4.70 (d, *J* = 5.9 Hz, 1H), 4.14 - 4.12 (m, 2H), 4.08 - 4.07 (m, 2H), 3.39 (s, 3H), 3.23 (s, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 154.5, 143.6, 141.2, 135.4, 134.8, 128.6, 128.1, 117.0, 106.5, 106.3, 104.4, 104.3, 102.3, 101.7, 64.3, 63.7, 56.0, 55.8, 51.2, 50.2. HRMS (ESI) m/z calcd for $C_{20}H_{24}N_5O_4$ $[M + H]^+$ = 398.1823, found 398.1820.

_N_-(1-(1-benzyl-1_H_-tetrazol-5-yl)-2,2-dimethoxyethyl)-3-methoxyaniline (1c)



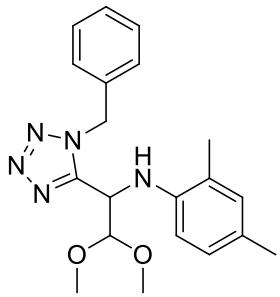
694 mg, 94% yield, brown oil. mp 110 - 113 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 - 7.30 (m, 3H), 7.17 - 7.15 (m, 2H), 6.89 (t, *J* = 8.2 Hz, 1H), 6.27 (ddd, *J* = 8.2, 2.4, 0.5 Hz, 1H), 6.00 (t, *J* = 2.4 Hz, 1H), 5.84 (dd, *J* = 8.2, 2.4 Hz, 1H), 5.76, 5.57 (ABq, *J* = 15.2 Hz, 2H), 4.93 (dd, *J* = 6.8, 5.1 Hz, 1H), 4.53 (d, *J* = 5.1 Hz, 1H), 4.52 (d, *J* = 6.8 Hz, 1H), 3.67 (s, 3H), 3.38 (s, 3H), 3.37 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 160.8, 153.8, 147.1, 133.9, 130.3, 129.1, 128.7, 127.9, 106.2, 105.3, 104.9, 100.2, 57.0, 55.3, 55.2, 52.8, 51.6. HRMS (ESI) m/z calcd for $C_{19}H_{24}N_5O_3$ $[M + H]^+$ = 370.1874, found 370.1872.

_N_-(1-(1-benzyl-1_H_-tetrazol-5-yl)-2,2-dimethoxyethyl)-4-chloroaniline (1d)



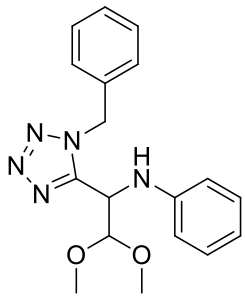
678 mg, 91% yield, gray solid. mp 98 - 100 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 - 7.31 (m, 3H), 7.17 - 7.15 (m, 2H), 6.91 - 6.88 (m, 2H), 6.12 - 6.10 (m, 2H), 5.81,5.54 (ABq, *J* = 15.2 Hz, 2H), 4.81 (dd, *J* = 7.5, 5.3 Hz, 1H), 4.57 (d, *J* = 5.3 Hz, 1H), 4.52 (d, *J* = 7.5 Hz, 1H), 3.42 (s, 3H), 3.39 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 153.7, 144.3, 133.7, 129.3, 129.2, 129.0, 128.02, 127.97, 124.1, 115.0, 105.6, 57.2, 55.5, 52.8, 51.6. HRMS (ESI) m/z calcd for $C_{18}H_{21}ClN_5O_2$ $[M + H]^+$ = 374.1378, found 374.1378.

***N*-(1-(1-benzyl-1*H*-tetrazol-5-yl)-2,2-dimethoxyethyl)-2,4-dimethylaniline (1e)**



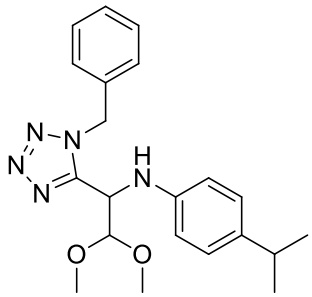
704 mg, 96% yield, white solid. mp 105 - 110 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34 - 7.29 (m, 3H), 7.16 - 7.14 (m, 2H), 6.83 (s, 1H), 6.61 - 6.60 (m, 1H), 5.84 (d, *J* = 7.6 Hz, 1H), 5.77, 5.57 (ABq, *J* = 15.2 Hz, 2H), 4.93 (t, *J* = 5.7 Hz, 1H), 4.57 (d, *J* = 5.3 Hz, 1H), 4.27 (d, *J* = 6.1 Hz, 1H), 3.38 (s, 3H), 3.37 (s, 3H), 2.16 (s, 3H), 2.15 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 154.1, 141.5, 133.9, 131.4, 129.1, 128.7, 128.4, 128.0, 127.4, 123.7, 111.4, 105.4, 56.9, 55.0, 53.1, 51.5, 20.4, 17.5. HRMS (ESI) m/z calcd for $C_{20}H_{26}N_5O_2$ $[M + H]^+$ = 368.2081, found 368.2079.

***N*-(1-(1-benzyl-1*H*-tetrazol-5-yl)-2,2-dimethoxyethyl)aniline (1f)**



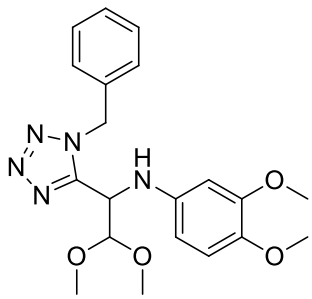
556 mg, 82% yield, white solid. mp 112 - 115 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36 - 7.32 (m, 3H), 7.21 - 7.18 (m, 2H), 7.03 - 6.99 (m, 2H), 6.73 - 6.70 (m, 1H), 6.30 - 6.29 (m, 2H), 5.81, 5.59 (ABq, *J* = 15.2 Hz, 2H), 4.95 (dd, *J* = 7.0, 5.2 Hz, 1H), 4.59 (d, *J* = 5.2 Hz, 1H), 4.55 (d, *J* = 7.0 Hz, 1H), 3.41 (s, 3H), 3.40 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 153.9, 145.7, 133.8, 129.4, 129.1, 128.8, 128.0, 119.3, 113.9, 105.4, 57.0, 55.2, 52.7, 51.6. HRMS (ESI) m/z calcd for $C_{18}H_{22}N_5O_2$ $[M + H]^+$ = 340.1768, found 340.1767.

***N*-(1-(1-benzyl-1*H*-tetrazol-5-yl)-2,2-dimethoxyethyl)-4-isopropylaniline (1g)**



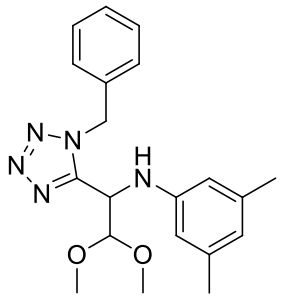
648 mg, 85% yield, colorless solid. mp 123 - 126 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 - 7.28 (m, 3H), 7.16 - 7.14 (m, 2H), 6.87 - 6.86 (m, 2H), 6.26 - 6.23 (m, 2H), 5.77, 5.57 (ABq, *J* = 15.2 Hz, 2H), 4.92 (t, *J* = 5.8 Hz, 1H), 4.54 (d, *J* = 5.2 Hz, 1H), 4.41 (d, *J* = 6.4 Hz, 1H), 3.37 (s, 3H), 3.36 (s, 3H), 2.77 - 2.71 (m, 1H), 1.15 (d, *J* = 6.9 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 154.0, 143.6, 140.0, 133.9, 129.1, 128.7, 128.0, 127.3, 114.0, 105.3, 56.9, 55.1, 53.1, 51.6, 33.2, 24.2. HRMS (ESI) m/z calcd for $C_{21}H_{28}N_5O_2$ $[M + H]^+$ = 382.2238, found 382.2237.

***N*-(1-(1-benzyl-1*H*-tetrazol-5-yl)-2,2-dimethoxyethyl)-3,4-dimethoxyaniline (1h)**



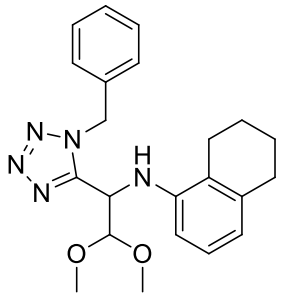
750 mg, 94% yield, gray solid. mp 120 - 125 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 - 7.27 (m, 3H), 7.13 - 7.11 (m, 2H), 6.49 (d, *J* = 8.6 Hz, 1H), 6.12 (d, *J* = 2.7 Hz, 1H), 5.76, 5.58 (ABq, *J* = 15.3 Hz, 2H), 5.71 (dd, *J* = 8.6, 2.7 Hz, 1H), 4.86 (t, *J* = 5.1 Hz, 1H), 4.54 (d, *J* = 5.2 Hz, 1H), 4.26 (d, *J* = 5.0 Hz, 1H), 3.75 (s, 3H), 3.71 (s, 3H), 3.40 (s, 3H), 3.38 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 154.0, 150.0, 143.1, 140.3, 134.0, 129.1, 128.7, 127.9, 112.8, 105.4, 104.9, 100.7, 57.0, 56.6, 55.8, 55.4, 54.0, 51.5. HRMS (ESI) m/z calcd for $C_{20}H_{26}N_5O_4$ $[M + H]^+$ = 400.1979, found 400.1978.

***N*-(1-(1-benzyl-1*H*-tetrazol-5-yl)-2,2-dimethoxyethyl)-3,5-dimethylaniline (1i)**



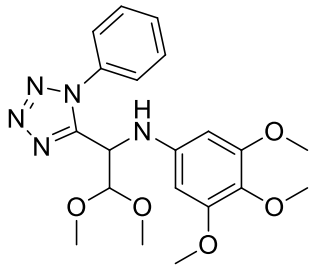
698 mg, 95% yield, white solid. mp 127 - 129 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33 - 7.29 (m, 3H), 7.18 - 7.17 (m, 2H), 6.37 (s, 1H), 6.00 (s, 2H), 5.75, 5.60 (ABq, *J* = 15.2 Hz, 2H), 4.94 (dd, *J* = 6.7, 5.2 Hz, 1H), 4.53 (d, *J* = 5.1 Hz, 1H), 4.39 (d, *J* = 6.8 Hz, 1H), 3.37 (s, 3H), 3.37 (s, 3H), 2.10 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 153.9, 145.8, 139.2, 134.0, 129.1, 128.7, 128.0, 121.5, 111.8, 105.4, 56.9, 55.2, 52.8, 51.5, 21.5. HRMS (ESI) m/z calcd for $C_{20}H_{26}N_5O_2$ $[M + H]^+$ = 368.2081, found 368.2079.

***N*-(1-(1-benzyl-1*H*-tetrazol-5-yl)-2,2-dimethoxyethyl)-5,6,7,8-tetrahydro naphthalen-1-amine (1j)**



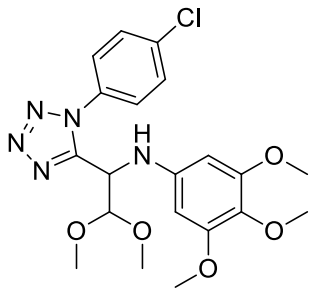
636 mg, 81% yield, yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 - 7.26 (m, 3H), 7.13 - 7.11 (m, 2H), 6.71 (t, *J* = 7.8 Hz, 1H), 6.49 (d, *J* = 7.6 Hz, 1H), 5.82 - 5.76 (m, 1H), 5.79, 5.58 (ABq, *J* = 15.2 Hz, 2H), 4.99 (t, *J* = 5.5 Hz, 1H), 4.59 (d, *J* = 5.1 Hz, 1H), 4.39 (d, *J* = 5.9 Hz, 1H), 3.38 (s, 3H), 3.38 (s, 3H), 2.68 (t, *J* = 6.1 Hz, 2H), 2.43 (t, *J* = 6.5 Hz, 2H), 1.88 - 1.80 (m, 2H), 1.73 - 1.68 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 154.1, 143.5, 138.1, 133.9, 129.0, 128.6, 127.9, 126.1, 122.5, 120.3, 108.0, 105.3, 56.9, 55.1, 52.7, 51.5, 30.1, 23.9, 23.1, 22.6. HRMS (ESI) m/z calcd for $C_{22}H_{28}N_5O_2$ $[M + H]^+$ = 394.2238, found 394.2234.

_N_-(2,2-dimethoxy-1-(1-phenyl-1_H_-tetrazol-5-yl)ethyl)-3,4,5-trimethoxyaniline (1k)



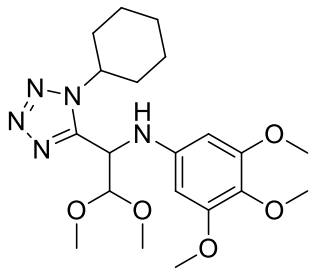
556 mg, 67% yield, gray solid. mp 133 - 135 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.59 - 7.53 (m, 3H), 7.50 - 7.48 (m, 2H), 5.62 (s, 2H), 4.94 - 4.91 (m, 1H), 4.82 (d, *J* = 6.3 Hz, 1H), 4.23 (d, *J* = 9.0 Hz, 1H), 3.70 (s, 3H), 3.60 (s, 6H), 3.47 (s, 3H), 3.43 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 154.7, 154.0, 142.1, 134.0, 131.6, 130.7, 129.7, 125.9, 105.8, 92.1, 61.1, 57.4, 56.0, 55.2, 52.5. HRMS (ESI) m/z calcd for $C_{20}H_{26}N_5O_5$ $[M + H]^+$ = 416.1928, found 416.1928.

_N_-(1-(1-(4-chlorophenyl)-1_H_-tetrazol-5-yl)-2,2-dimethoxyethyl)-3,4,5-trimethoxyaniline (1l)



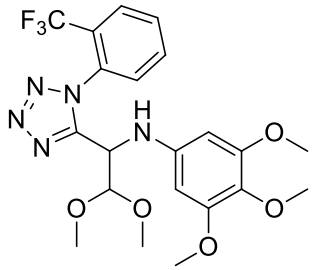
862 mg, 96% yield, gray solid. mp 162 - 166 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.49 (d, *J* = 8.7 Hz, 2H), 7.38 (d, *J* = 8.7 Hz, 2H), 5.60 (s, 2H), 4.92 (dd, *J* = 8.9, 5.9 Hz, 1H), 4.80 (d, *J* = 5.9 Hz, 1H), 4.17 (d, *J* = 8.9 Hz, 1H), 3.71 (s, 3H), 3.64 (s, 6H), 3.48 (s, 3H), 3.44 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 154.6, 154.1, 141.9, 137.0, 132.5, 131.7, 129.8, 127.4, 105.6, 92.0, 61.2, 57.3, 56.0, 55.6, 52.8. HRMS (ESI) m/z calcd for $C_{20}H_{25}ClN_5O_5$ $[M + H]^+$ = 450.1539, found 450.1538.

_N_-(1-(1-cyclohexyl-1_H_-tetrazol-5-yl)-2,2-dimethoxyethyl)-3,4,5-trimethoxyaniline (1m)



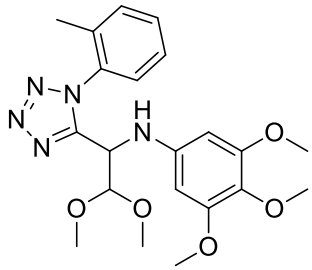
664 mg, 79% yield, gray solid. mp 133 - 135 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.83 (s, 2H), 5.00 (dd, *J* = 6.0, 4.8 Hz, 1H), 4.64 (d, *J* = 4.8 Hz, 1H), 4.58 (tt, *J* = 11.6, 3.8 Hz, 1H), 4.47 (d, *J* = 6.0 Hz, 1H), 3.72 (s, 6H), 3.70 (s, 3H), 3.48 (s, 3H), 3.43 (s, 3H), 2.02 - 1.0 (m, 5H), 1.71 - 1.64 (m, 2H), 1.30 - 1.19 (m, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 154.1, 152.6, 142.8, 131.5, 105.6, 91.8, 65.9, 61.1, 58.8, 56.9, 56.4, 56.1, 53.9, 33.3, 33.0, 25.59, 25.55, 25.0, 15.4. HRMS (ESI) m/z calcd for $C_{20}H_{32}N_5O_5$ $[M + H]^+$ = 422.2398, found 422.2396.

_N_-(2,2-dimethoxy-1-(1-(2-(trifluoromethyl)phenyl)-1_H_-tetrazol-5-yl)ethyl)-3,4,5-trimethoxyaniline (1n)



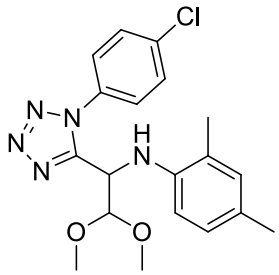
512 mg, 53% yield, yellow solid. mp 134 - 136 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82 (d, *J* = 7.8 Hz, 1H), 7.71 (t, *J* = 7.6 Hz, 1H), 7.65 (s, 1H), 7.27 (d, *J* = 14.2 Hz, 1H), 5.71 (s, 2H), 4.81 - 4.75 (m, 1H), 4.71 (s, 1H), 4.12 (s, 1H), 3.72 (s, 3H), 3.69 (s, 6H), 3.42 (s, 3H), 3.40 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 155.6, 154.0, 142.3, 132.6, 131.7, 131.5, 131.1, 127.9, 127.7, 123.5, 121.3, 105.7, 92.1, 61.1, 57.0, 56.1, 53.7. HRMS (ESI) m/z calcd for $C_{21}H_{25}F_3N_5O_5$ $[M + H]^+$ = 484.1802, found 484.1802.

_N_-(2,2-dimethoxy-1-(1-(_o_-tolyl)-1_H_-tetrazol-5-yl)ethyl)-3,4,5-trimethoxyaniline (1o)



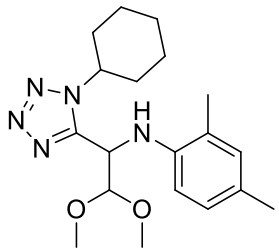
780 mg, 91% yield, gray solid. mp 149 - 151 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.46 (td, *J* = 7.6, 1.2 Hz, 1H), 7.35 - 7.29 (m, 2H), 7.13 (d, *J* = 6.3 Hz, 1H), 5.71 (s, 2H), 4.78 - 4.73 (m, 2H), 4.07 (d, *J* = 9.1 Hz, 1H), 3.72 (s, 3H), 3.66 (s, 6H), 3.44 (s, 3H), 3.42 (s, 3H), 1.84 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 155.0, 154.0, 142.2, 136.6, 132.8, 131.9, 131.5, 131.1, 127.4, 126.7, 105.6, 92.8, 61.1, 57.1, 56.0, 53.3, 17.2. HRMS (ESI) m/z calcd for $C_{21}H_{28}N_5O_5$ $[M + H]^+$ = 430.2085, found 430.2082.

***N*-(1-(1-(4-chlorophenyl)-1*H*-tetrazol-5-yl)-2,2-dimethoxyethyl)-2,4-dimethylaniline (1p)**



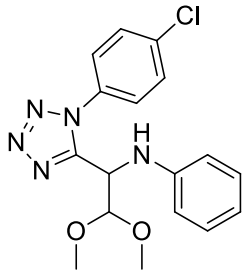
510 mg, 66% yield, colorless solid. mp 119 - 121 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.49 - 7.46 (m, 2H), 7.33 - 7.30 (m, 2H), 6.83 (s, 1H), 6.71 (d, *J* = 8.1 Hz, 1H), 6.08 (d, *J* = 8.1 Hz, 1H), 4.95 (dd, *J* = 8.4, 5.8 Hz, 1H), 4.84 (d, *J* = 5.8 Hz, 1H), 4.07 (d, *J* = 8.4 Hz, 1H), 3.44 (s, 6H), 2.17 (s, 3H), 1.99 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 155.0, 141.0, 136.9, 132.6, 131.7, 129.7, 128.7, 127.5, 127.3, 123.9, 111.4, 105.6, 57.1, 55.1, 52.1, 20.4, 17.3. HRMS (ESI) m/z calcd for $C_{19}H_{23}ClN_5O_2$ $[M + H]^+$ = 388.1535, found 388.1537.

***N*-(1-(1-cyclohexyl-1*H*-tetrazol-5-yl)-2,2-dimethoxyethyl)-2,4-dimethylaniline (1q)**



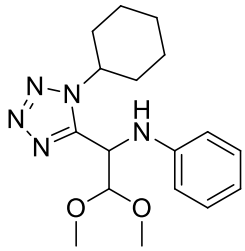
359 mg, 50% yield, white solid. mp 129 - 133 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.90 (s, 1H), 6.82 (d, *J* = 8.1 Hz, 1H), 6.38 (d, *J* = 8.1 Hz, 1H), 5.07 (t, *J* = 5.2 Hz, 1H), 4.71 (d, *J* = 4.8 Hz, 1H), 4.66 (tt, *J* = 11.6, 3.8 Hz, 1H), 4.36 (d, *J* = 5.6 Hz, 1H), 3.48 (s, 3H), 3.45 (s, 3H), 2.22 (s, 3H), 2.20 (s, 3H), 2.06 - 1.80 (m, 5H), 1.74 - 1.62 (m, 2H), 1.41 - 1.26 (m, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 152.8, 141.8, 131.5, 128.4, 127.5, 123.5, 111.3, 105.6, 58.7, 56.9, 56.1, 53.4, 33.2, 33.1, 25.64, 25.61, 25.0, 20.4, 17.5. HRMS (ESI) m/z calcd for $C_{19}H_{30}N_5O_2$ $[M + H]^+$ = 360.2394, found 360.2393.

_N_-(1-(1-(4-chlorophenyl)-1_H_-tetrazol-5-yl)-2,2-dimethoxyethyl)aniline (1r)



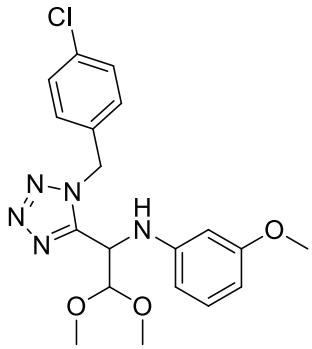
381 mg, 53% yield, white solid. mp 165 - 163 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.52 - 7.49 (m, 2H), 7.39 - 7.36 (m, 2H), 7.08 - 7.06 (m, 2H), 6.73 (t, *J* = 7.4 Hz, 1H), 6.38 (d, *J* = 7.7 Hz, 2H), 4.95 (dd, *J* = 8.9, 5.9 Hz, 1H), 4.81 (d, *J* = 5.9 Hz, 1H), 4.34 (d, *J* = 8.9 Hz, 1H), 3.43 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 154.6, 145.3, 137.0, 132.5, 129.8, 129.5, 127.4, 119.6, 113.9, 105.7, 57.2, 55.2, 51.8. HRMS (ESI) m/z calcd for $C_{17}H_{19}ClN_5O_2$ $[M + H]^+$ = 360.1222, found 360.1222.

_N_-(1-(1-cyclohexyl-1_H_-tetrazol-5-yl)-2,2-dimethoxyethyl)aniline (1s)



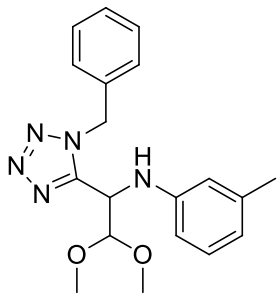
344 mg, 52% yield, white solid. mp 131 - 133 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.16 - 7.12 (m, 2H), 6.78 - 6.75 (m, 1H), 6.62 - 6.60 (m, 2H), 5.03 (dd, *J* = 6.3, 4.8 Hz, 1H), 4.67 (d, *J* = 4.8 Hz, 1H), 4.61 - 4.56 (m, 2H), 3.47 (s, 3H), 3.44 (s, 3H), 2.01 - 1.82 (m, 5H), 1.72 - 1.68 (m, 1H), 1.67-1.64 (m, 1H), 1.38 - 1.26 (m, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 152.6, 146.1, 129.6, 119.5, 113.8, 105.7, 58.7, 57.0, 56.3, 53.2, 33.3, 33.1, 25.63, 25.55, 25.0. HRMS (ESI) m/z calcd for $C_{17}H_{26}N_5O_2$ $[M + H]^+$ = 332.2081, found 332.2079.

_N_-(1-(1-(4-chlorobenzyl)-1_H_-tetrazol-5-yl)-2,2-dimethoxyethyl)-3-methoxyaniline (1t)



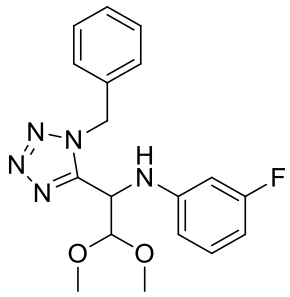
717 mg, 89% yield, yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.26 - 7.22 (m, 2H), 7.04 (d, *J* = 8.5 Hz, 2H), 6.96 - 6.92 (m, 1H), 6.31 - 6.29 (m, 1H), 5.93 - 5.91 (m, 2H), 5.72, 5.55 (ABq, *J* = 15.3 Hz, 2H), 4.95 (d, *J* = 4.7 Hz, 1H), 4.61 (d, *J* = 4.7 Hz, 1H), 3.69 (s, 3H), 3.42 (s, 3H), 3.39 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 160.9, 153.7, 146.9, 134.7, 132.4, 130.4, 129.2, 106.6, 105.4, 105.0, 100.4, 57.1, 55.8, 55.2, 53.2, 50.9. HRMS (ESI) m/z calcd for $C_{19}H_{23}ClN_5O_3$ $[M + H]^+$ = 404.1484, found 404.1483.

_N_-(1-(1-benzyl-1_H_-tetrazol-5-yl)-2,2-dimethoxyethyl)-3-methylaniline (1u)



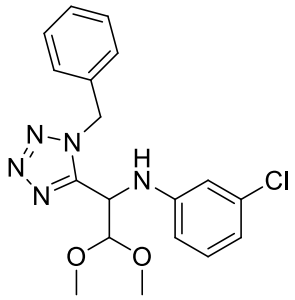
685 mg, 97% yield, white solid. mp 124 - 129 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 - 7.31 (m, 3H), 7.18 - 7.16 (m, 2H), 6.88 (t, *J* = 7.8 Hz, 1H), 6.53 (d, *J* = 7.5 Hz, 1H), 6.20 (s, 1H), 6.07 (dd, *J* = 8.0, 2.3 Hz, 1H), 5.77, 5.59 (ABq, *J* = 15.2 Hz, 2H), 4.93 (dd, *J* = 6.9, 5.2 Hz, 1H), 4.55 (d, *J* = 5.2 Hz, 1H), 4.44 (d, *J* = 6.9 Hz, 1H), 3.38 (s, 3H), 3.38 (s, 3H), 2.14 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 153.9, 145.8, 139.3, 133.93, 129.3, 129.1, 128.8, 128.0, 120.4, 114.8, 110.8, 105.4, 57.0, 55.2, 52.8, 51.6, 21.6. HRMS (ESI) m/z calcd for $C_{19}H_{24}N_5O_2$ $[M + H]^+$ = 354.1925, found 354.1922.

_N_-(1-(1-benzyl-1_H_-tetrazol-5-yl)-2,2-dimethoxyethyl)-3-fluoroaniline (1v)



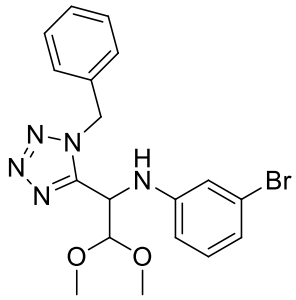
649 mg, 91% yield, yellow solid. mp 106 - 109 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34 - 7.32 (m, 3H), 7.18 - 7.16 (m, 2H), 6.93 - 6.89 (m, 1H), 6.39 - 6.35 (m, 1H), 6.01 (dd, *J* = 8.2, 2.0 Hz, 1H), 5.92 (dt, *J* = 11.1, 2.3 Hz, 1H), 5.81,5.56 (ABq, *J* = 15.2 Hz, 2H), 4.84 (dd, *J* = 7.3, 5.2 Hz, 1H), 4.60 (d, *J* = 7.3 Hz, 1H), 4.57 (d, *J* = 5.2 Hz, 1H), 3.42 (s, 3H), 3.40 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.8 (d, $^{1}J_{C\text{-}F}$ = 244.7 Hz), 153.6, 147.5 (d, $^{3}J_{C\text{-}F}$ = 10.4 Hz), 133.6, 130.6 (d, $^{3}J_{C\text{-}F}$ = 10.1 Hz), 129.3, 129.0, 127.9, 109.5 (d, $^{4}J_{C\text{-}F}$ = 2.4 Hz), 106.0 (d, $^{2}J_{C\text{-}F}$ = 21.5 Hz), 105.6, 100.9 (d, $^{2}J_{C\text{-}F}$ = 25.5 Hz), 57.2, 55.6, 52.6, 51.7.^{19}F NMR (471 MHz, $CDCl_3$) δ -112.11. HRMS (ESI) m/z calcd for $C_{18}H_{21}FN_5O_2$ $[M + H]^+$ = 358.1674, found 358.1674.

_N_-(1-(1-benzyl-1_H_-tetrazol-5-yl)-2,2-dimethoxyethyl)-3-chloroaniline (1w)



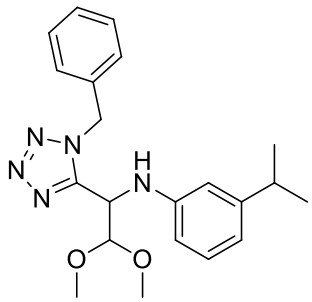
671 mg, 90% yield, yellow solid. mp 121 - 125 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33 - 7.32 (m, 3H), 7.16 - 7.14 (m, 2H), 6.88 (t, *J* = 8.1 Hz, 1H), 6.66 - 6.64 (m, 1H), 6.29 (t, *J* = 2.1 Hz, 1H), 6.08 (ddd, *J* = 8.2, 2.3, 0.6 Hz, 1H), 5.80, 5.57 (ABq, *J* = 15.2 Hz, 2H), 4.84 (dd, *J* = 7.3, 5.2 Hz, 1H), 4.57 - 4.55 (m, 2H), 3.42 (s, 3H), 3.40 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 153.6, 146.9, 135.1, 133.6, 130.4, 129.3, 129.0, 127.9, 119.4, 113.9, 111.8, 105.6, 57.2, 55.7, 52.6, 51.7. HRMS (ESI) m/z calcd for $C_{18}H_{21}ClN_5O_2$ $[M + H]^+$ = 374.1378, found 374.1378.

***N*-(1-(1-benzyl-1*H*-tetrazol-5-yl)-2,2-dimethoxyethyl)-3-bromoaniline (1x)**



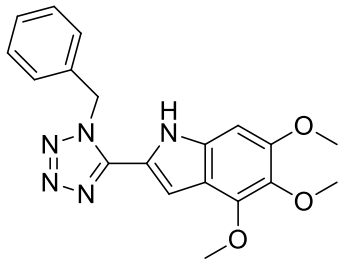
692 mg, 83% yield, yellow solid. mp 129 - 132 °C.^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33 - 7.32 (m, 3H), 7.16 - 7.14 (m, 2H), 6.83 - 6.80 (m, 2H), 6.49 - 6.48 (m, 1H), 6.12 - 6.09 (m, 1H), 5.79, 5.57 (ABq, *J* = 15.2 Hz, 2H), 4.83 (dd, *J* = 7.3, 5.1 Hz, 1H), 4.57 - 4.59 (m, 2H), 3.41 (s, 3H), 3.39 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 153.5, 147.0, 133.6, 130.7, 129.3, 129.0, 127.8, 123.3, 122.3, 116.9, 112.1, 105.6, 57.2, 55.7, 52.5, 51.7. HRMS (ESI) m/z calcd for $C_{18}H_{21}BrN_5O_2$ $[M + H]^+$ = 418.0873, found 418.0873.

***N*-(1-(1-benzyl-1*H*-tetrazol-5-yl)-2,2-dimethoxyethyl)-3-isopropylaniline (1y)**



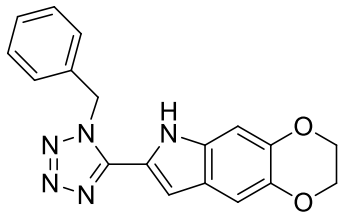
701 mg, 92% yield, yellow solid. mp 98 - 103 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 - 7.29 (m, 3H), 7.16 - 7.14 (m, 2H), 6.91 (t, *J* = 7.8 Hz, 1H), 6.60 (d, *J* = 7.6 Hz, 1H), 6.344 - 6.337 (m, 1H), 6.03 - 6.01 (m, 1H), 5.77, 5.58 (ABq, *J* = 15.2 Hz, 2H), 4.98 - 4.96 (m, 1H), 4.55 (d, *J* = 5.1 Hz, 1H), 4.47 (d, *J* = 5.0 Hz, 1H), 3.38 (s, 3H), 3.38 (s, 3H), 2.69 (dt, *J* = 13.8, 6.9 Hz, 1H), 1.14 (dd, *J* = 6.9, 3.2 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 153.9, 150.4, 145.8, 134.0, 129.4, 129.1, 128.7, 128.0, 117.7, 112.7, 110.8, 105.4, 57.0, 55.3, 52.9, 51.6, 34.2, 23.98, 23.96. HRMS (ESI) m/z calcd for $C_{21}H_{28}N_5O_2$ $[M + H]^+$ = 382.2238, found 382.2238.

2-(1-benzyl-1*H*-tetrazol-5-yl)-4,5,6-trimethoxy-1*H*-indole (2a)



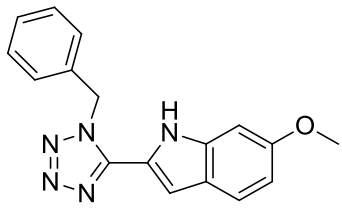
332 mg, 91% yield, white solid. mp 255 - 260 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.99 (s, 1H), 7.38 - 7.35 (m, 2H), 7.31 - 7.30 (m, 1H), 7.20 (d, *J* = 7.1 Hz, 2H), 7.04 (d, *J* = 1.4 Hz, 1H), 6.70 (s, 1H), 6.00 (s, 2H), 3.93 (s, 3H), 3.79 (s, 3H), 3.67 (s, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 152.7, 148.2, 145.5, 135.3, 134.6, 129.0, 128.2, 127.1, 117.9, 114.9, 103.2, 89.5, 60.9, 60.3, 55.8, 50.9. HRMS (ESI) m/z calcd for $C_{19}H_{20}N_5O_3$ $[M + H]^+$ = 366.1561, found 366.1558.

7-(1-benzyl-1*H*-tetrazol-5-yl)-3,6-dihydro-2*H*-[1,4]dioxino[2,3-*f*]indole (2b-1)



Mixture of isomers was formed in 5:1 ratio, but compound **2b-1** (77% yield, white solid) was obtained as only one isomer after washing with chloroform. 306 mg, 92% yield (both isomers before washing steps), yellow solid. mp 220 - 223 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.75 (s, 1H), 7.37 - 7.28 (m, 3H), 7.20 (d, *J* = 7.1 Hz, 2H), 7.01 (s, 1H), 6.95 (s, 1H), 6.88 (s, 1H), 5.96 (s, 2H), 4.23 - 4.21 (m, 2H), 4.20 - 4.19 (m, 2H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 148.4, 142.7, 139.5, 134.5, 128.9, 128.2, 127.1, 122.0, 106.6, 104.3, 98.6, 64.2, 63.8, 50.8. HRMS (ESI) m/z calcd for $C_{18}H_{16}N_5O_2$ $[M + H]^+$ = 334.1299 found 334.1299.

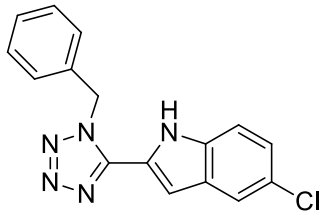
2-(1-benzyl-1*H*-tetrazol-5-yl)-6-methoxy-1*H*-indole (2c-1)



Mixture of isomers was formed in 10:1 ratio, but **2c-1** (79% yield, white solid) was obtained as only one isomer after washing with ether. 149 mg, 87% yield (both isomers before washing steps), white solid. mp 207 - 211 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.99 (s, 1H), 7.52 (d, *J* = 8.7 Hz, 1H), 7.41 - 7.33 (m, 3H), 7.25 (d, *J* = 7.8 Hz, 2H),

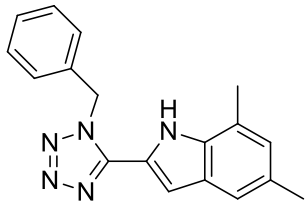
7.09 (s, 1H), 6.97 (s, 1H), 6.77 (d, *J* = 8.7 Hz, 1H), 5.99 (s, 2H), 3.80 (s, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 157.5, 148.3, 138.3, 134.4, 128.9, 128.1, 127.1, 122.1, 121.8, 118.7, 105.2, 94.0, 55.2, 50.8. HRMS (ESI) m/z calcd for $C_{17}H_{16}N_5O$ $[M + H]^+$ = 306.1349, found 306.1349.

2-(1-benzyl-1*H*-tetrazol-5-yl)-5-chloro-1*H*-indole (2d)



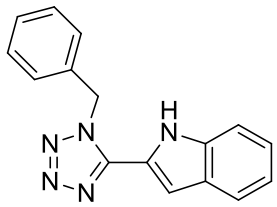
46 mg, 15% yield, colorless solid. mp 205 - 209 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.37 (s, 1H), 7.69 (d, *J* = 2.0 Hz, 1H), 7.49 (d, *J* = 8.7 Hz, 1H), 7.37 - 7.30 (m, 3H), 7.24 (dd, *J* = 8.8, 2.1 Hz, 1H), 7.22 - 7.18 (m, 2H), 7.14 (d, *J* = 1.6 Hz, 1H), 5.97 (s, 2H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 148.2, 135.8, 134.4, 129.2, 128.7, 128.5, 127.4, 124.9, 124.4, 121.7, 120.6, 114.0, 104.7, 51.2. HRMS (ESI) m/z calcd for $C_{16}H_{13}ClN_5O$ $[M + H]^+$ = 310.0854, found 310.0854.

2-(1-benzyl-1*H*-tetrazol-5-yl)-5,7-dimethyl-1*H*-indole (2e)



203 mg, 67% yield, colorless solid. mp 183 - 185 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.51 (s, 1H), 7.41 - 7.34 (m, 3H), 7.26 - 7.23 (m, 3H), 6.95 (s, 1H), 6.80 - 6.79 (m, 1H), 5.84 (s, 2H), 2.47 (s, 3H), 2.40 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 148.7, 135.3, 133.5, 130.9, 129.5, 128.9, 127.9, 127.7, 126.9, 121.0, 119.7, 118.7, 105.6, 51.7, 21.5, 16.9. HRMS (ESI) m/z calcd for $C_{18}H_{18}N_5$ $[M + H]^+$ = 304.1557, found 304.1556.

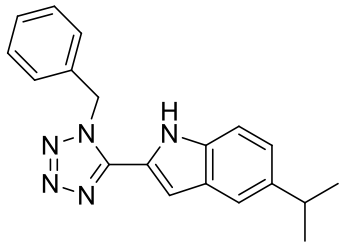
2-(1-benzyl-1*H*-tetrazol-5-yl)-1*H*-indole (2f)



140 mg, 51% yield, white solid. mp 204 - 210 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.17(s, 1H), 7.62 (d, *J* = 8.0 Hz, 1H), 7.49 - 7.48 (m, 1H), 7.37 - 7.30 (m, 3H), 7.24 - 7.21 (m, 3H), 7.14 (dd, *J* = 2.3, 0.9 Hz, 1H), 7.08 - 7.07 (m, 1H) 6.00 (s, 2H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 148.4, 137.2, 134.4, 129.0, 128.2, 127.5, 127.2, 124.1, 121.4,

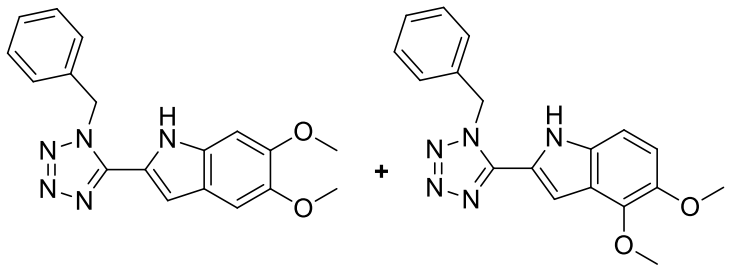
120.3, 120.0, 112.3, 105.0, 50.9. HRMS (ESI) m/z calcd for $C_{16}H_{14}N_5$ $[M + H]^+$ = 276.1244, found 276.1243.

2-(1-benzyl-1*H*-tetrazol-5-yl)-5-isopropyl-1*H*-indole (2g)



226 mg, 71% yield, white solid. mp 202 - 206 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.86 (s, 1H), 7.50 (d, *J* = 8.5 Hz, 1H), 7.46 (s, 1H), 7.42 - 7.37 (m, 3H), 7.26 - 7.23 (m, 3H), 6.83 (d, *J* = 1.4 Hz, 1H), 5.87 (s, 2H), 3.04 - 2.97 (m, 1H), 1.29 (d, *J* = 6.9 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 148.7, 142.0, 135.8, 133.5, 129.5, 128.9, 128.2, 126.9, 125.1, 120.0, 118.3, 112.0, 105.4, 51.8, 34.2, 24.6. HRMS (ESI) m/z calcd for $C_{19}H_{20}N_5$ $[M + H]^+$ = 318.1713, found 318.1712.

2-(1-benzyl-1*H*-tetrazol-5-yl)-5,6-dimethoxy-1*H*-indole (2h-1) and **2-(1-benzyl-1*H*-tetrazol-5-yl)-4,5-dimethoxy-1*H*-indole (2h-2)**

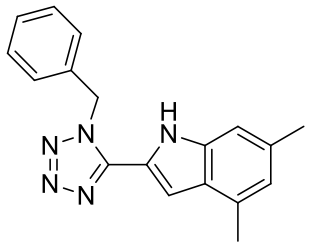


2h-1 **2h-2**

(**2h-1** : **2h-2** = 9 : 1)

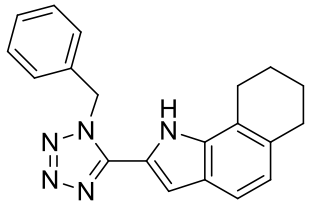
Mixture of isomers was formed in 5:1 ratio, but **2h** was obtained as the mixture of **2h-1** and **2h-2** in 9:1 ratio, after washing steps with chloroform. **2h-1** + **2h-2**: 324 mg, 97% yield (both isomers before washing steps), cream white solid. ^{1}H NMR (500 MHz, $(CD_3)_2CO$) δ 10.89 (s, 0.82H), 10.81 (s, 0.10H), 7.42 - 7.37 (m, 2H), 7.35 - 7.32 (m, 1H), 7.30 - 7.29 (m, 2H), 7.12 (s, 1H), 7.08 (s, 0.92H), 6.99 (s, 0.11H), 6.969 - 6.965 (m, 0.84H), 6.942 - 6.938 (m, 0.11H), 5.99 (s, 2H), 3.89 (d, *J* = 5.2 Hz, 0.43H), 3.84 (s, 2.74H), 3.80 (s, 3H). ^{13}C NMR (126 MHz, $(CD_3)_2CO$) δ150.8, 149.5, 147.4, 135.7, 133.4, 129.94, 129.91, 129.2, 128.0, 127.9, 122.1, 119.4, 105.9, 103.5, 95.5, 56.4, 56.2, 51.9. HRMS (ESI) m/z calcd for $C_{18}H_{18}N_5O_2$ $[M + H]^+$ = 336.1455, found 336.1455.

2-(1-benzyl-1*H*-tetrazol-5-yl)-5,7-dimethyl-1*H*-indole (2i)



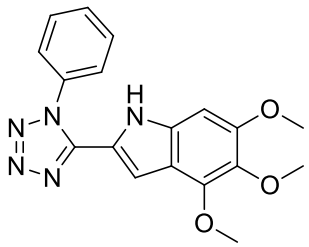
261 mg, 86% yield, white solid. mp 203 - 206 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.98 (s, 1H), 7.37 - 7.35 (m, 2H), 7.32 - 7.29 (m, 1H), 7.24 (d, *J* = 7.3 Hz, 2H), 7.11 - 7.10 (m, 1H), 7.08 (s, 1H), 6.70 (s, 1H), 6.01 (s, 2H), 2.41 (s, 3H), 2.34 (s, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 148.5, 137.6, 134.6, 133.7, 130.0, 128.9, 128.3, 127.4, 127.3, 125.8, 122.3, 118.7, 109.4, 103.9, 51.0, 21.5, 18.3. HRMS (ESI) m/z calcd for $C_{18}H_{18}N_5$ $[M + H]^+$ = 304.1557, found 304.1556.

2-(1-benzyl-1*H*-tetrazol-5-yl)-6,7,8,9-tetrahydro-1*H*-benzo[*g*]indole (2j)



322 mg, 98% yield, white solid. mp 173 - 177 °C. ^{1}H NMR (500 MHz, $(CD_3)_2CO$) δ 10.58 (s, 1H), 7.40 - 7.31 (m, 4H), 7.29 - 7.27 (m, 2H), 7.04 (d, *J* = 2.1 Hz, 1H), 6.84 (d, *J* = 8.2 Hz, 1H), 5.99 (s, 2H), 3.03 (t, *J* = 6.3 Hz, 2H), 2.83 (t, *J* = 6.1 Hz, 2H), 1.91 - 1.88 (m, 2H), 1.85 - 1.83 (m, 2H). ^{13}C NMR (126 MHz, $(CD_3)_2CO$) δ149.6, 137.9, 135.7, 133.8, 130.0, 129.3, 128.1, 126.8, 123.8, 121.5, 121.4, 120.6, 119.5, 106.8, 52.1, 25.0, 24.1, 23.6. HRMS (ESI) m/z calcd for $C_{20}H_{20}N_5$ $[M + H]^+$ = 330.1713, found 330.1713.

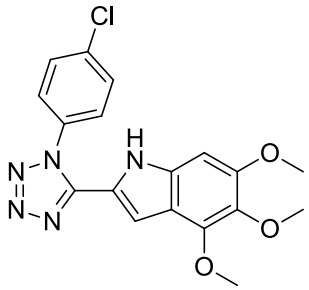
4,5,6-trimethoxy-2-(1-phenyl-1*H*-tetrazol-5-yl)-1*H*-indole (2k)



319 mg, 91% yield, yellow solid. mp 208 - 211 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.07 (d, *J* = 1.8 Hz, 1H), 7.78 - 7.70 (m, 5H), 6.71 (s, 1H), 6.00 - 5.99 (m, 1H), 3.79

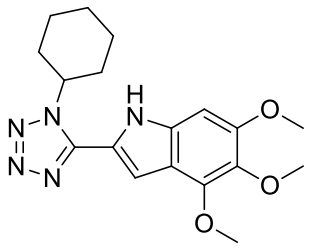
(s, 3H), 3.75 (s, 3H), 3.64 (s, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 152.8, 148.4, 145.1, 135.4, 134.5, 134.2, 131.4, 130.2, 126.7, 118.2, 114.8, 102.5, 89.6, 60.9, 60.2, 55.8. HRMS (ESI) m/z calcd for $C_{18}H_{18}N_5O_3$ $[M + H]^+$ = 352.1404, found 352.1403.

2-(1-(4-chlorophenyl)-1*H*-tetrazol-5-yl)-4,5,6-trimethoxy-1*H*-indole (2l)



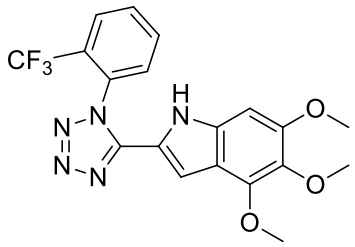
312 mg, 81% yield, yellow solid. mp 250 - 255 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.05 (s, 1H), 7.81 - 7.78 (m, 4H), 6.71 (d, *J* = 0.5 Hz, 1H), 6.10 (s, 1H), 3.80 (s, 6H), 3.65 (s, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 152.9, 148.4, 145.2, 135.9, 135.4, 134.5, 133.1, 130.2, 128.6, 118.1, 114.8, 102.6, 89.6, 60.9, 60.2, 55.8. HRMS (ESI) m/z calcd for $C_{18}H_{17}ClN_5O_3$ $[M + H]^+$ = 386.1014, found 386.1013.

2-(1-cyclohexyl-1*H*-tetrazol-5-yl)-4,5,6-trimethoxy-1*H*-indole (2m)



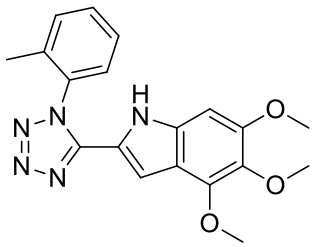
275 mg, 77% yield, white solid. mp 215 - 223 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 11.13 (s, 1H), 7.12 (s, 1H), 6.98 (d, *J* = 2.0 Hz, 1H), 4.71 (tt, *J* = 11.5, 3.7 Hz, 1H), 4.15 (s, 3H), 3.94 (s, 3H), 3.89 (s, 3H), 2.27 - 2.24 (m, 2H), 2.17 - 2.09 (m, 2H), 2.06 - 2.03 (m, 2H), 1.86 - 1.83 (m, 1H), 1.60 - 1.52 (m, 2H), 1.45 - 1.39 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 153.8, 147.7, 145.8, 136.5, 134.7, 118.5, 116.3, 102.1, 90.5, 61.6, 61.2, 59.1, 56.3, 32.7, 25.4, 25.1. HRMS (ESI) m/z calcd for $C_{18}H_{24}N_5O_3$ $[M + H]^+$ = 358.1874, found 358.1873.

4,5,6-trimethoxy-2-(1-(2-(trifluoromethyl)phenyl)-1*H*-tetrazol-5-yl)-1*H*-indole (2n)



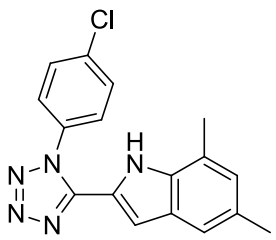
281 mg, 67% yield, yellow solid. mp 247 - 250 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.18 (d, *J* = 1.8 Hz, 1H), 8.20 (d, *J* = 7.6 Hz, 1H), 8.09 - 8.06 (m, 3H), 6.69 (s, 1H), 5.68 (d, *J* = 2.2 Hz, 1H), 3.79 (s, 3H), 3.72 (s, 3H), 3.63 (s, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 153.1, 149.5, 145.1, 135.4, 135.0, 134.6, 133.0, 131.2, 130.7, 128.4, 125.8, 123.6, 121.4, 117.8, 114.9, 102.4, 89.6, 60.9, 60.1, 55.9. ^{19}F NMR (471 MHz, DMSO-d_6) δ -58.32, -59.06. HRMS (ESI) m/z calcd for $C_{19}H_{17}F_3N_5O_3$ $[M + H]^+$ = 420.1277, found 420.1277.

4,5,6-trimethoxy-2-(1-(*o*-tolyl)-1*H*-tetrazol-5-yl)-1*H*-indole (2o)



281 mg, 84% yield, yellow solid. mp 173 - 180 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.15 (s, 1H), 7.69 (td, *J* = 7.5, 1.3 Hz, 1H), 7.62 (t, *J* = 7.4 Hz, 2H), 7.56 - 7.53 (m, 1H), 6.70 (s, 1H), 5.78 (d, *J* = 1.8 Hz, 1H), 3.79 (s, 3H), 3.72 (s, 3H), 3.63 (s, 3H), 1.92 (s, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 153.0, 148.6, 145.1, 135.4, 135.0, 134.6, 133.3, 131.8, 127.9, 127.7, 118.1, 114.9, 101.9, 89.6, 60.9, 60.1, 55.8,16.5. HRMS (ESI) m/z calcd for $C_{19}H_{20}N_5O_3$ $[M + H]^+$ = 366.1561, found 366.1557.

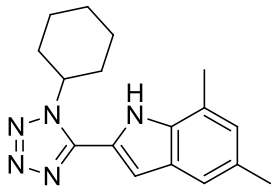
2-(1-(4-chlorophenyl)-1*H*-tetrazol-5-yl)-5,7-dimethyl-1*H*-indole (2p)



229 mg, 71% yield, cream white solid. mp 152 - 156 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.26 (s, 1H), 7.66 - 7.63 (m, 2H), 7.54 - 7.51 (m, 2H), 7.15 (s, 1H), 6.96 (s, 1H), 6.25

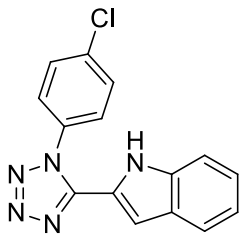
(d, *J* = 2.2 Hz, 1H), 2.51 (s, 3H), 2.38 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 148.7, 137.6, 135.2, 132.9, 131.0, 130.6, 128.0, 127.7, 120.9, 119.6, 118.8, 106.0, 21.5, 16.8. HRMS (ESI) m/z calcd for $C_{17}H_{15}ClN_5$ $[M + H]^+$ = 324.1010, found 324.1010.

2-(1-cyclohexyl-1*H*-tetrazol-5-yl)-5,7-dimethyl-1*H*-indole (2q)



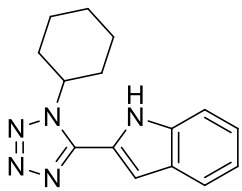
221 mg, 75% yield, colorless white solid. mp 133 - 136 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.80 (s, 1H), 7.28 (s, 1H), 7.03 (d, *J* = 2.0 Hz, 1H), 6.87 (s, 1H), 4.73 (tt, *J* = 11.4, 3.7 Hz, 1H), 2.49 (s, 3H), 2.34 (s, 3H), 2.10 (d, *J* = 11.9 Hz, 2H), 1.90 - 1.83 (m, 4H), 1.68 (d, *J* = 12.9 Hz, 1H), 1.52 - 1.44 (m, 2H), 1.31 - 1.26 (m, 1H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 147.8, 129.1, 127.8, 126.3, 121.4, 120.2, 118.1, 104.8, 57.8, 32.4, 24.61, 24.57, 21.1, 17.1. HRMS (ESI) m/z calcd for $C_{17}H_{22}N_5$ $[M + H]^+$ = 296.1870, found 296.1869.

2-(1-(4-chlorophenyl)-1*H*-tetrazol-5-yl)-1*H*-indole (2r)



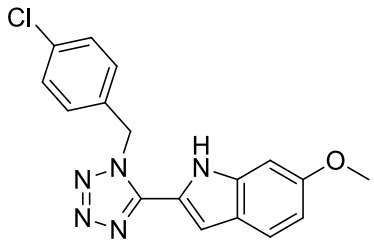
151 mg, 51% yield, brown solid. mp 244 - 248 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.23 (s, 1H), 7.82 - 7.80 (m, 4H), 7.53 (d, *J* = 8.0 Hz, 1H), 7.48 (dd, *J* = 8.3, 0.7 Hz, 1H), 7.23 - 7.20 (m, 1H), 7.03 - 7.00 (m, 1H), 6.20 (dd, *J* = 2.0, 0.7 Hz, 1H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 148.6, 137.2, 136.0, 133.0, 130.3, 128.6, 127.2, 124.2, 121.4, 120.3, 120.1, 112.2, 104.8. HRMS (ESI) m/z calcd for $C_{15}H_{11}ClN_5$ $[M + H]^+$ = 296.0697, found 296.0698.

2-(1-cyclohexyl-1*H*-tetrazol-5-yl)-1*H*-indole (2s)



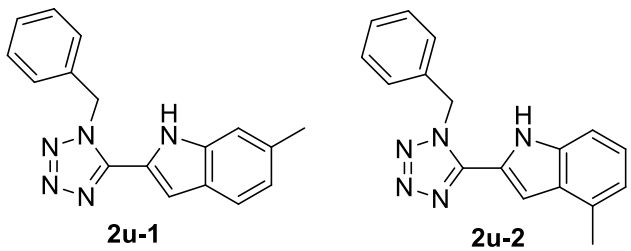
176 mg, 66% yield, colorless solid. mp 239 - 245 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.12 (s, 1H), 7.71 (d, J = 8.0 Hz, 1H), 7.51 (d, J = 8.2 Hz, 1H), 7.29 - 7.23 (m, 1H), 7.19 (s, 1H), 7.10 (t, J = 7.3 Hz, 1H), 4.85 - 4.76 (m, 1H), 2.15 (d, J = 11.5 Hz, 2H), 1.94 - 1.85 (m, 4H), 1.70 (d, J = 13.0 Hz, 1H), 1.58 - 1.50 (m, 2H), 1.31 - 1.28 (m, 1H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 147.6, 137.2, 127.6, 123.9, 121.4, 120.4, 120.2, 112.2, 104.4, 57.8, 32.3, 24.6, 24.5. HRMS (ESI) m/z calcd for $C_{15}H_{18}N_5$ $[M + H]^+$ = 268.1557, found 268.1556.

2-(1-(4-chlorobenzyl)-1*H*-tetrazol-5-yl)-6-methoxy-1*H*-indole (2t-1)



Mixture of isomers was formed in 9:1 ratio, but **2t-1** was obtained as only one isomer after washing with ether. 298 mg, 88% yield (both isomers before washing step), yellow solid. mp 207 - 211 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.99 (s, 1H), 7.50 (d, J = 8.7 Hz, 1H), 7.46 - 7.42 (m, 2H), 7.27 - 7.25 (m, 2H), 7.07 (d, J = 1.5 Hz, 1H), 6.93 (d, J = 2.2 Hz, 1H), 6.73 (dd, J = 8.7, 2.2 Hz, 1H), 5.97 (s, 2H), 3.78 (s, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 157.6, 148.3, 138.4, 133.4, 132.9, 129.2, 129.0, 122.2, 121.9, 118.6, 111.6, 105.3, 94.0, 55.2, 50.2. HRMS (ESI) m/z calcd for $C_{17}H_{15}ClN_5O$ $[M + H]^+$ = 340.0960, found 340.0958.

2-(1-benzyl-1*H*-tetrazol-5-yl)-6-methyl-1*H*-indole (2u-1) and **2-(1-benzyl-1*H*-tetrazol-5-yl)-4-methyl-1*H*-indole (2u-2)**

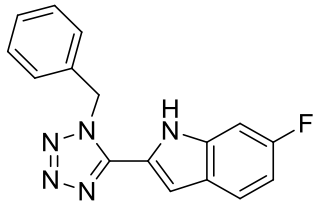


2u-1 **2u-2**

(**2u-1** : **2u-2** = 3:2)

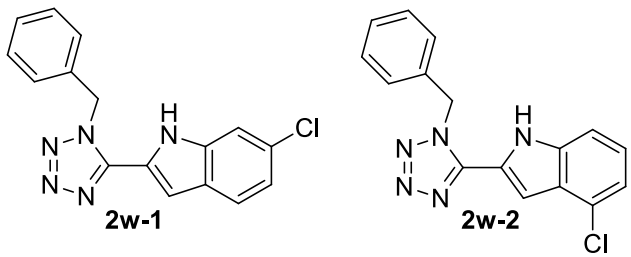
The mixture of **2u-1** + **2u-2** was formed in 3:2 ratio. 277 mg, 96% yield, white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.24 (s, 0.37H), 10.09 (s, 0.57H), 7.50 (d, *J* = 8.2 Hz, 0.60H), 7.45 (d, *J* = 8.3 Hz, 0.43H), 7.43 - 7.36 (m, 3H), 7.30 - 7.22 (m, 2H), 6.99 (d, *J* = 8.1 Hz, 0.57H), 6.95 (d, *J* = 7.0 Hz, 0.40H), 6.89 (s, 0.83H), 6.84 (s, 1.24H), 5.90 (s, 0.83H), 5.86 (s, 1.24H), 2.51 (s, 1.16H), 2.48 (s, 1.77H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 148.7, 137.7, 137.0, 135.6, 133.54, 133.47, 131.2, 129.5, 129.0, 128.9, 128.2, 127.1, 127.0, 125.9, 125.5, 123.2, 121.3, 121.1, 119.4, 119.3, 112.0, 109.9, 105.5, 104.3, 51.9, 51.8, 22.1, 18.7. HRMS (ESI) m/z calcd for $C_{17}H_{16}N_5$ $[M + H]^+$ = 290.1400, found 290.1399.

2-(1-benzyl-1*H*-tetrazol-5-yl)-6-fluoro-1*H*-indole (2v-1)



Mixture of isomers was formed in 6:5 ratio, but **2v-1** was obtained as only one isomer after washing with dichloromethane. 269 mg, 92% yield (both isomers before washing step), brown solid. mp 206 - 207 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.27 (s, 1H), 7.65 (dd, *J* = 8.8, 5.5 Hz, 1H), 7.38 - 7.35 (m, 2H), 7.32 - 7.29 (m, 1H), 7.23 - 7.19 (m, 4H), 6.97 - 6.93 (m, 1H), 5.98 (s, 2H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 160.3 (d, $^{1}J_{C\text{-}F}$ = 239.0 Hz), 148.2, 137.3 (d, $^{3}J_{C\text{-}F}$ = 13.2 Hz), 134.4, 129.0, 128.3, 127.2, 124.4, 123.0 (d, $^{3}J_{C\text{-}F}$ = 10.3 Hz), 120.8, 109.4 (d, $^{2}J_{C\text{-}F}$ = 25.0 Hz), 105.2, 99.6, 97.9 (d, $^{2}J_{C\text{-}F}$ = 25.9 Hz), 51.0. ^{19}F NMR (471 MHz, DMSO-d_6) δ -117.47. HRMS (ESI) m/z calcd for $C_{16}H_{13}FN_5$ $[M + H]^+$ = 294.1150, found 294.1149.

2-(1-benzyl-1*H*-tetrazol-5-yl)-6-chloro-1*H*-indole (2w-1) and **2-(1-benzyl-1*H*-tetrazol-5-yl)-4-chloro-1*H*-indole (2w-2)**

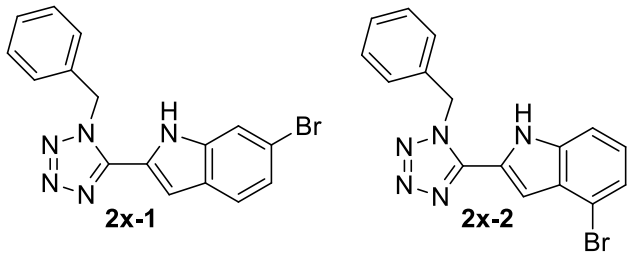


2w-1 **2w-2**

(**2w-1** : **2w-2** = 4:1)

Mixture of isomers was formed in 5:4 ratio, but **2w** was obtained as a mixture of **2w-1** and **2w-2** (4:1 ratio) after washing with dichloromethane. **2w-1** + **2w-2**: 266 mg, 86% yield (both isomers before washing steps), brown solid.^{1}H NMR (500 MHz, DMSO-d_6) δ 12.56 (s, 0.24H), 12.34 (s, 0.87H), 7.65 (d, *J* = 8.5 Hz, 0.79H), 7.50 (s, 0.79H), 7.46 (d, *J* = 8.2 Hz, 0.23H), 7.39 - 7.29 (m, 3H), 7.25 - 7.21 (m, 2H), 7.19 (d, *J* = 1.9 Hz, 0.76H), 7.15 (d, *J* = 7.5 Hz, 0.18H), 7.09 (dd, *J* = 8.5, 1.8 Hz, 1H), 6.03 (s, 0.36H), 5.99 (s, 1.58H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 148.1, 137.5, 134.3, 129.0, 128.8, 128.3, 127.23, 127.19, 126.3, 123.0, 121.1, 120.8, 111.7, 105.1, 99.6, 51.0. HRMS (ESI) m/z calcd for $C_{16}H_{13}ClN_5$ $[M + H]^+$ = 310.0854, found 310.0854.

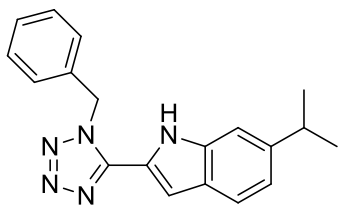
2-(1-benzyl-1*H*-tetrazol-5-yl)-6-bromo-1*H*-indole (2x-1) and **2-(1-benzyl-1*H*-tetrazol-5-yl)-4-bromo-1*H*-indole (2x-2)**



(**2x-1** : **2x-2** = 1:1)

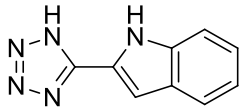
Mixture of isomers was formed in 2:1 ratio, but **2x** was obtained as a mixture of **2x-1** and **2x-2** in 1:1 ratio after washing with dichloromethane. **2x-1** + **2x-2**: 332 mg, 94% yield (both isomers before washing step), brown solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.58 (s, 0.49H), 12.34 (s, 0.50H), 7.65 (s, 0.45H), 7.60 (d, *J* = 8.5 Hz, 0.47H), 7.50 (d, *J* = 8.2 Hz, 0.51H), 7.40 - 7.30 (m, 3.43H), 7.23 - 7.16 (m, 3.42H), 6.99 (s, 0.48H), 6.03 (s, 1H), 5.99 (s, 1H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 148.1, 138.0, 137.5, 134.4, 134.3, 129.04, 129.01, 128.4, 128.3, 128.0, 127.24, 127.19, 126.5, 125.3, 123.34, 123.28, 123.0, 121.00, 120.97, 116.9, 114.7, 114.2, 111.9, 105.2, 104.7, 51.2, 51.0. HRMS (ESI) m/z calcd for $C_{16}H_{13}BrN_5$ $[M + H]^+$ = 354.0349, found 354.0348.

2-(1-benzyl-1*H*-tetrazol-5-yl)-6-isopropyl-1*H*-indole (2y)



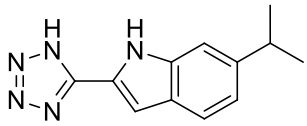
Mixture of isomers was formed in 4:1 ratio, but **2y** was obtained as only one isomer after washing with ether. 273 mg, 86% yield (both isomers before washing step), white solid. mp 169 - 174 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.72 (s, 1H), 7.55 (d, *J* = 8.3 Hz, 1H), 7.41 - 7.35 (m, 4H), 7.26 - 7.24 (m, 2H), 7.07 (dd, *J* = 8.3, 1.4 Hz, 1H), 6.84 (d, *J* = 1.4 Hz, 1H), 5.87 (s, 2H), 3.08 - 3.00 (m, 1H), 1.31 (d, *J* = 6.9 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 148.7, 147.0, 137.5, 133.5, 129.5, 128.9, 127.0, 126.3, 121.5, 120.9, 119.6, 109.1, 105.4, 51.8, 34.7, 24.4. HRMS (ESI) m/z calcd for $C_{19}H_{20}N_5$ $[M + H]^+$ = 318.1713, found 318.1714.

2-(1*H*-tetrazol-5-yl)-1*H*-indole (3a)



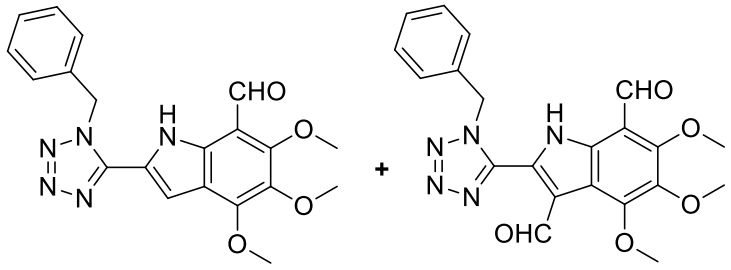
175 mg, 95% yield, yellow solid. Spectral data are in accordance to reported data. [3] ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.10 (s, 1H), 7.65 (d, *J* = 8.0 Hz, 1H), 7.47 (d, *J* = 8.2 Hz, 1H), 7.21 (t, *J* = 7.6 Hz, 1H), 7.14 - 7.13 (m, 1H), 7.07 (t, *J* = 7.5 Hz, 1H).

6-isopropyl-2-(1*H*-tetrazol-5-yl)-1*H*-indole (3b)



44 mg, 98% yield, white solid. Spectral data are in accordance to reported data. [4] ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.94 (s, 1H), 7.55 (d, *J* = 8.2 Hz, 1H), 7.29 (s, 1H), 7.07 (d, *J* = 1.5 Hz, 1H), 6.99 (dd, *J* = 8.2, 1.5 Hz, 1H), 2.97 (dt, *J* = 13.8, 6.9 Hz, 1H), 1.24 (d, *J* = 6.9 Hz, 6H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 144.2, 137.8, 125.8, 121.8, 120.9, 119.6, 109.0, 103.3, 33.8, 24.3.

2-(1-benzyl-1*H*-tetrazol-5-yl)-4,5,6-trimethoxy-1*H*-indole-7-carbaldehyde (4) and **2-(1-benzyl-1*H*-tetrazol-5-yl)-4,5,6-trimethoxy-1*H*-indole-3,7-dicarbaldehyde (4')**

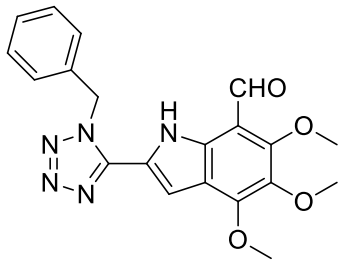


4 **4'**

4 : **4'** = 1:1

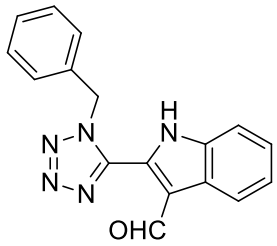
The mixture of **4** and **4'** was formed in 1:1 ratio. 374 mg, 94% yield, brown solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 13.00 (s, 1H), 11.46 (s, 1H), 10.32 (s, 1H), 10.29 (s, 1H), 10.24 (s, 1H), 7.34 - 7.26 (m, 4H), 7.24 - 7.22 (m, 3H), 7.19 - 7.17 (m, 2H), 7.14 - 7.12 (m, 2H), 5.95 (s, 2H), 5.43 (s, 2H), 4.22 (s, 3H), 4.18 (s, 3H), 4.06 (s, 3H), 4.01 (s, 3H), 3.89 (s, 3H), 3.78 (s, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 188.5, 188.4, 186.1, 157.6, 153.7, 153.3, 148.0, 147.8, 140.1, 136.8, 134.3, 133.9, 132.5, 128.9, 128.4, 128.3, 128.3, 128.1, 127.4, 120.5, 118.3, 116.3, 115.6, 111.0, 108.3, 104.8, 63.3, 63.2, 61.5, 61.2, 61.2, 60.4, 51.1, 50.9.

2-(1-benzyl-1*H*-tetrazol-5-yl)-4,5,6-trimethoxy-1*H*-indole-7-carbaldehyde (4)



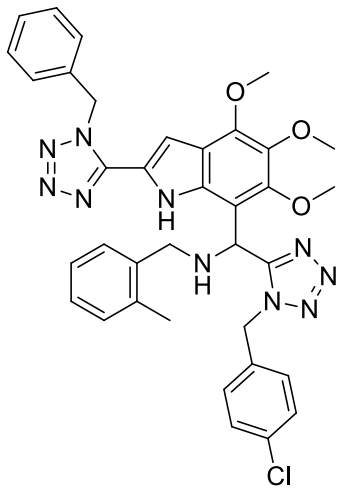
369 mg, 92% yield, brown solid. mp 198 - 199 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.47 (s, 1H), 10.25 (s, 1H), 7.34 - 7.29 (m, 4H), 7.19 - 7.17 (m, 2H), 5.95 (s, 2H), 4.22 (s, 3H), 4.02 (s, 3H), 3.78 (s, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 188.4, 157.6, 153.7, 147.8, 136.8, 134.3, 132.5, 128.9, 128.3, 127.4, 120.5, 115.6, 108.4, 104.8, 63.2, 61.2, 60.4, 51.1. HRMS (ESI) m/z calcd for $C_{20}H_{20}N_5O_4$ $[M + H]^+$ = 394.1510, found 394.1505.

2-(1-benzyl-1*H*-tetrazol-5-yl)-1*H*-indole-3-carbaldehyde (5)



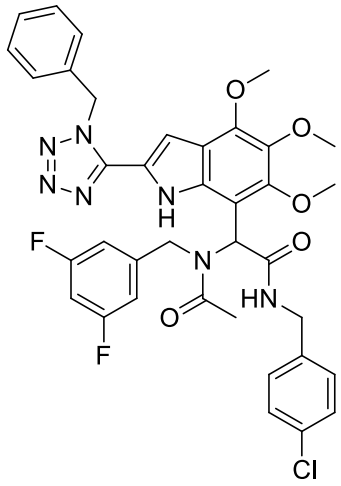
291 mg, 96% yield, brown oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.92 (s, 1H), 10.10 (s, 1H), 8.23 - 8.21 (m, 1H), 7.50 - 7.48 (m, 1H), 7.41 - 7.35 (m, 2H), 7.27 - 7.21 (m, 3H), 7.06 - 7.04 (m, 2H), 5.64 (s, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 184.8, 147.6, 136.9, 133.0, 129.4, 129.3, 128.1, 126.1, 125.9, 125.2, 124.1, 120.9, 118.4, 112.8, 52.8. HRMS (ESI) m/z calcd for $C_{17}H_{14}N_5O$ $[M + H]^+$ = 304.1193, found 304.1192.

1-(2-(1-benzyl-1*H*-tetrazol-5-yl)-4,5,6-trimethoxy-1*H*-indol-7-yl)-1-(1-(4-chlorobenzyl)-1*H*-tetrazol-5-yl)-*N*-(2-methylbenzyl)methanamine (6)



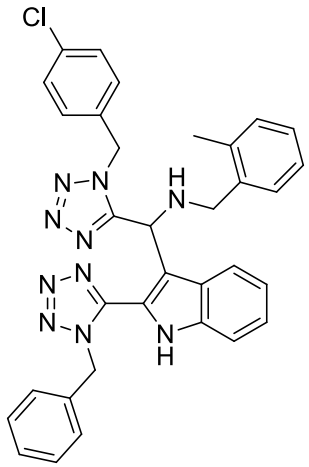
449 mg, 65% yield, white solid. mp 102 - 105 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.76 (s, 1H), 7.37 - 7.30 (m, 3H), 7.22 - 7.21 (m, 2H), 7.17 - 7.15 (m, 3H), 7.10 - 7.09 (m, 2H), 7.01 (d, *J* = 7.3 Hz, 1H), 6.90 (d, *J* = 2.3 Hz, 1H), 6.86 (d, *J* = 8.3 Hz, 2H), 5.90 - 5.80 (m, 3H), 5.50, 5.40 (ABq, *J* = 15.5 Hz, 2H), 4.01 (s, 3H), 3.79 (s, 3H), 3.78(s, 3H), 3.69, 3.58 (ABq, *J* = 13.6 Hz, 2H), 2.32 (s, 1H), 2.10 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 155.4, 150.1, 148.2, 147.2, 138.9, 136.7, 134.7, 133.6, 132.4, 132.2, 130.8, 129.3, 129.2, 128.8, 128.6, 128.5, 127.7, 126.9, 126.1, 120.3, 119.0, 103.5, 62.0, 61.4, 60.9, 51.6, 50.0, 49.2, 48.7, 18.9. HRMS (ESI) m/z calcd for $C_{36}H_{35}ClN_{10}NaO_3$ $[M + Na]^+$ = 713.2474, found 713.2477.

2-(2-(1-benzyl-1*H*-tetrazol-5-yl)-4,5,6-trimethoxy-1*H*-indol-7-yl)-*N*-(4-chlorobenzyl)-2-(*N*-(3,5-difluorobenzyl)acetamido)acetamide (7)



445 mg, 61% yield, brown solid. mp 154 - 158 °C. *Mixture of rotamers observed*.^{1}H NMR (500 MHz, DMSO-d_6) δ 11.38 (s, 0.35H), 11.04 (s, 0.64H), 9.04 (s, 0.37H), 8.77 (s, 0.64H), 7.38 - 7.30 (m, 3.46H), 7.28 - 7.26 (m, 4H), 7.21 - 7.19 (m, 2H), 7.06 (s, 0.65H), 7.00 (s, 0.33H), 6.74 (t, *J* = 9.0 Hz, 0.58H), 6.54 (s, 0.38H), 6.34 (d, *J* = 6.3 Hz, 1.2H), 6.10 (d, *J* = 7.2 Hz, 0.79H), 5.99 - 5.97 (m, 2.35H), 5.04 (d, *J* = 16.4 Hz, 0.33H), 4.75, 4.57 (ABq, *J* = 18.5 Hz, 1.24H), 4.49 - 4.37 (m, 1H), 4.30 - 4.24 (m, 1.4H), 4.04 - 4.01 (m, 0.5H), 3.87 - 3.84 (m, 3H), 3.77 - 3.74 (m, 3H), 3.63 (s, 1.18H), 3.51 (s, 2H), 2.27 (s, 1H), 2.00 (s, 2H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 171.8, 162.9, 161.2, 160.9, 151.3, 147.8, 146.4, 143.1, 138.6, 138.3, 138.1, 134.5, 131.5, 131.2, 129.5, 129.2, 129.1, 129.0, 128.3, 128.2, 128.0, 127.2, 119.7, 117.6, 108.3, 103.5, 101.6, 60.8, 60.6, 60.5, 59.8, 57.3, 54.5, 51.0, 49.3, 46.4, 42.1, 41.9, 22.1, 22.0, 20.8, 14.1. ^{19}F NMR (471 MHz, DMSO-d_6) δ -110.29, -111.51. HRMS (ESI) m/z calcd for $C_{37}H_{35}ClF_2N_7O_5$ $[M + H]^+$ = 730.2351, found 730.2352.

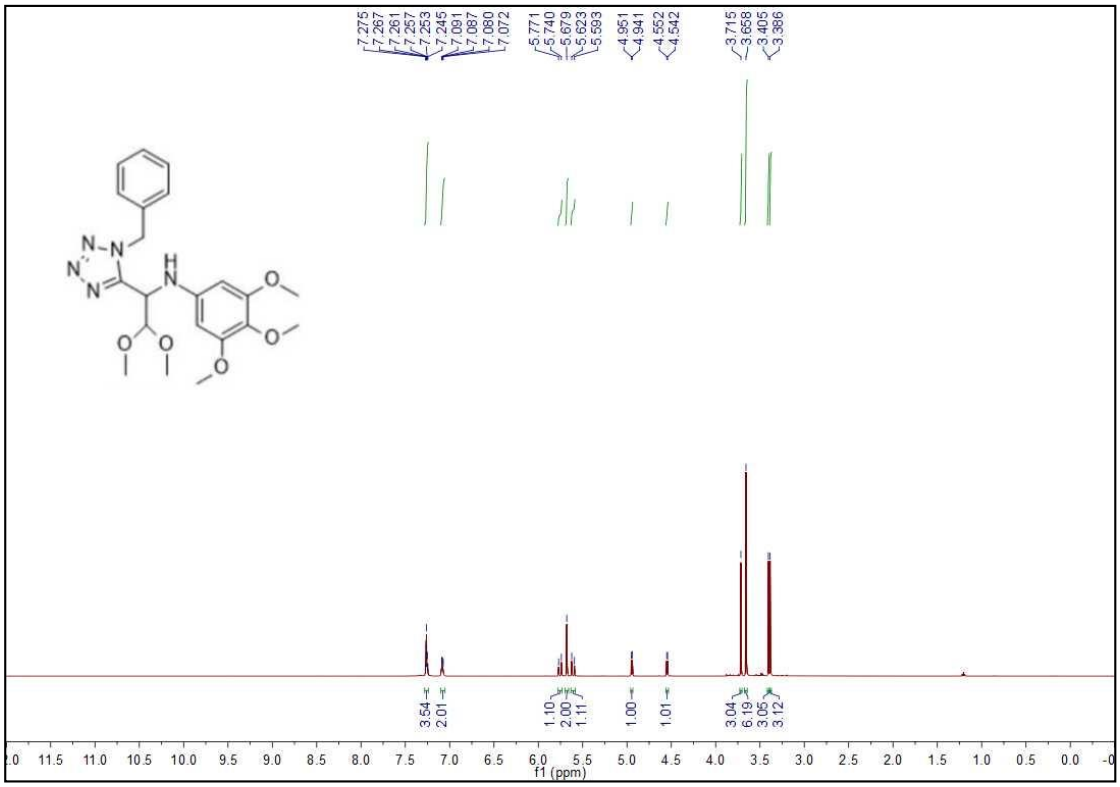
1-(2-(1-benzyl-1*H*-tetrazol-5-yl)-1*H*-indol-3-yl)-1-(1-(4-chlorobenzyl)-1*H*-tetrazol-5-yl)-*N*-(2-methylbenzyl)methanamine (8)

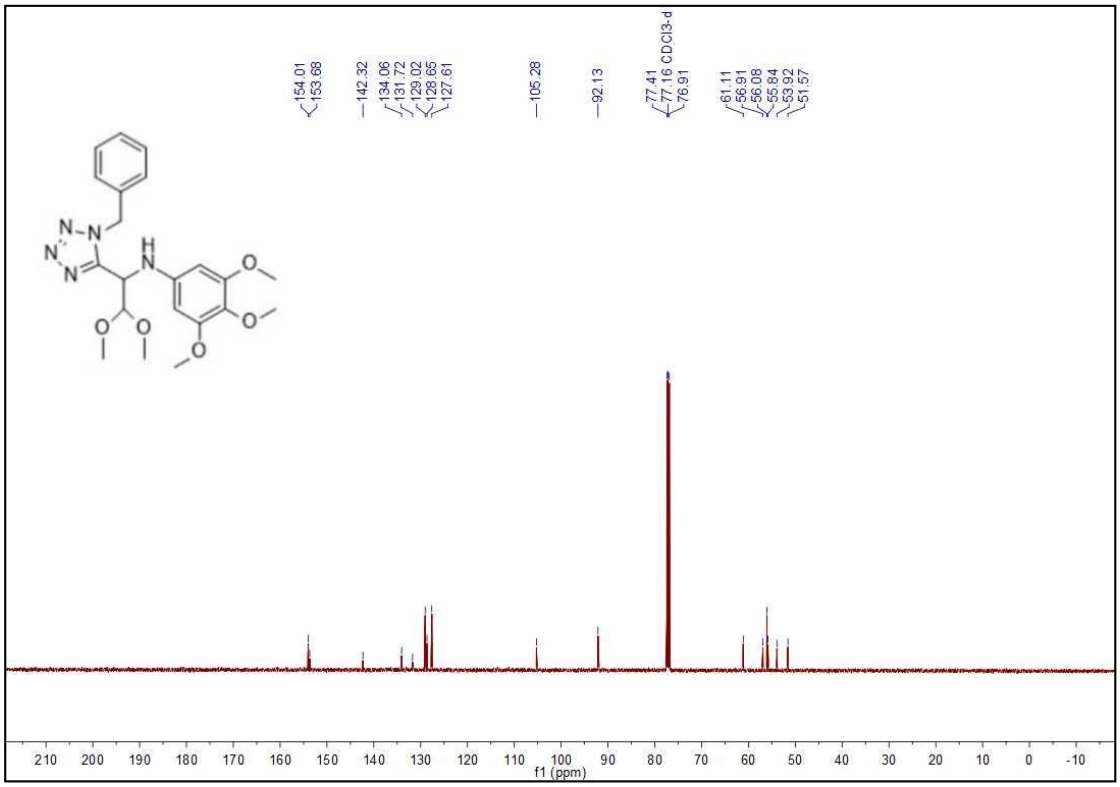


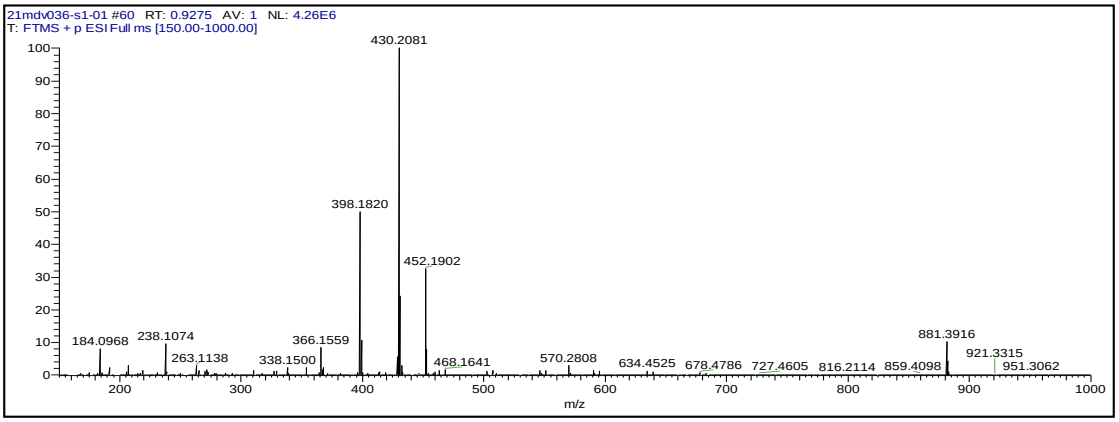
294 mg, 49% yield, white solid. mp 93 - 94 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 (s, 1H), 7.57 (d, *J* = 8.1 Hz, 1H), 7.42 - 7.39 (m, 2H), 7.23 - 7.18 (m, 3H), 7.17 - 7.14 (m, 1H), 7.10 (t, *J* = 7.1 Hz, 2H), 7.06 (d, *J* = 8.2 Hz, 1H), 7.02 - 6.99 (m, 3H), 6.84 - 6.80 (m, 2H), 6.67 (d, *J* = 8.4 Hz, 2H), 5.79 - 5.76 (m, 1H), 5.69 - 5.60 (m, 3H), 5.47 - 5.44 (m, 1H), 3.61 - 3.55 (m, 2H), 2.97 (s, 1H), 2.13 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 155.9, 148.1, 137.2, 134.3, 134.0, 132.2, 130.7, 129.9, 129.8, 129.6, 129.2, 128.9, 128.6, 128.4, 127.7, 127.6, 126.0, 125.4, 121.8, 120.3, 117.8, 112.0, 51.9, 50.1, 49.0, 48.3, 19.0. HRMS (ESI) m/z calcd for $C_{33}H_{30}ClN_{10}$ $[M + H]^+$ = 601.2338, found 601.2337.

3. Exemplary copies of NMR and MS data of novel compounds

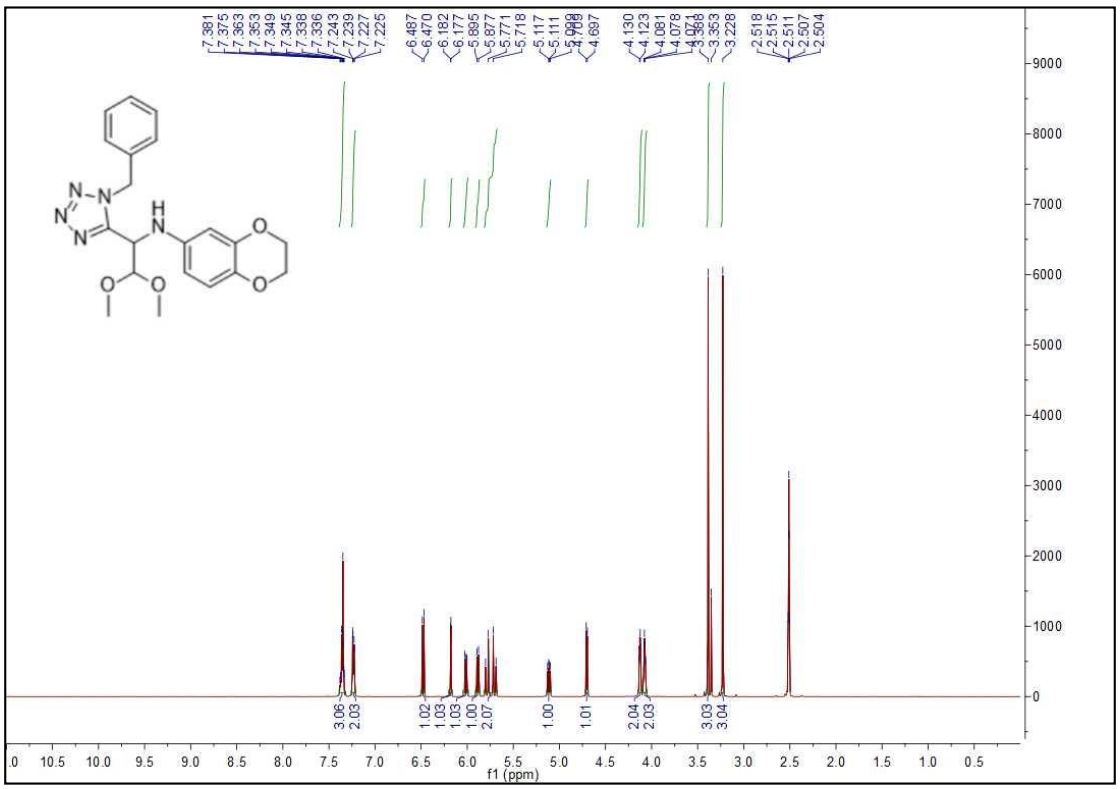
N-(1-(1-benzyl-1*H*-tetrazol-5-yl)-2,2-dimethoxyethyl)-3,4,5-trimethoxyaniline (1a)

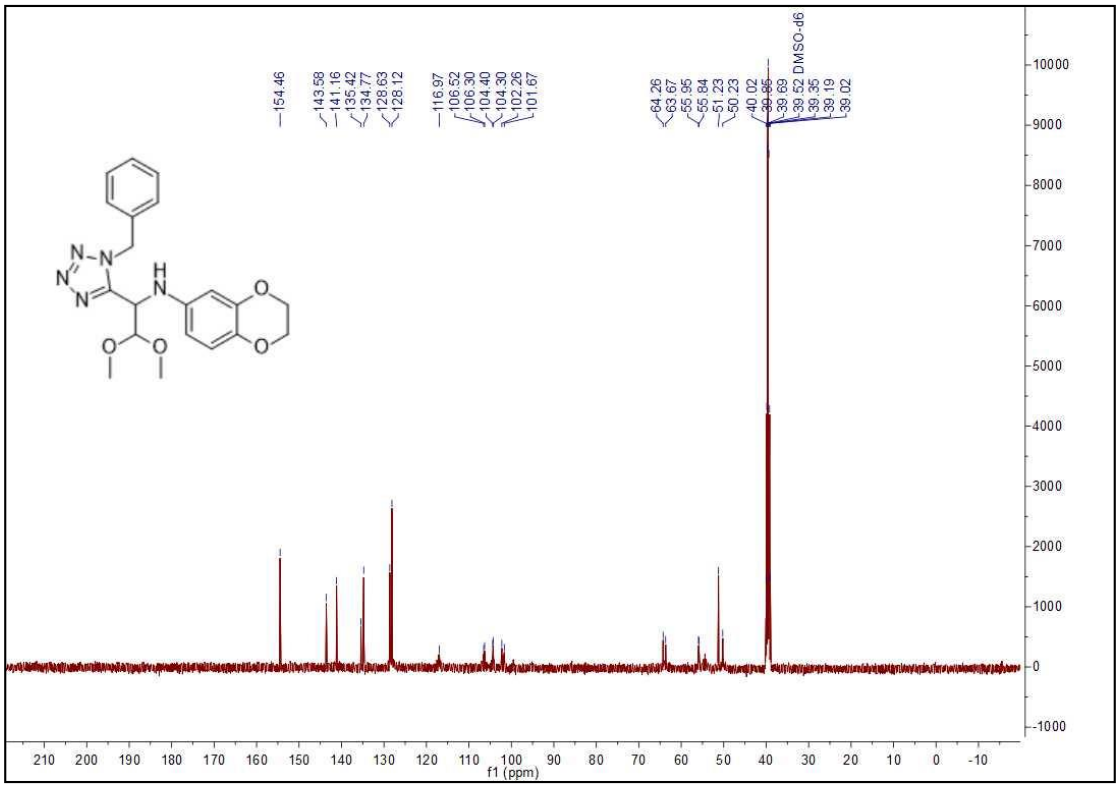


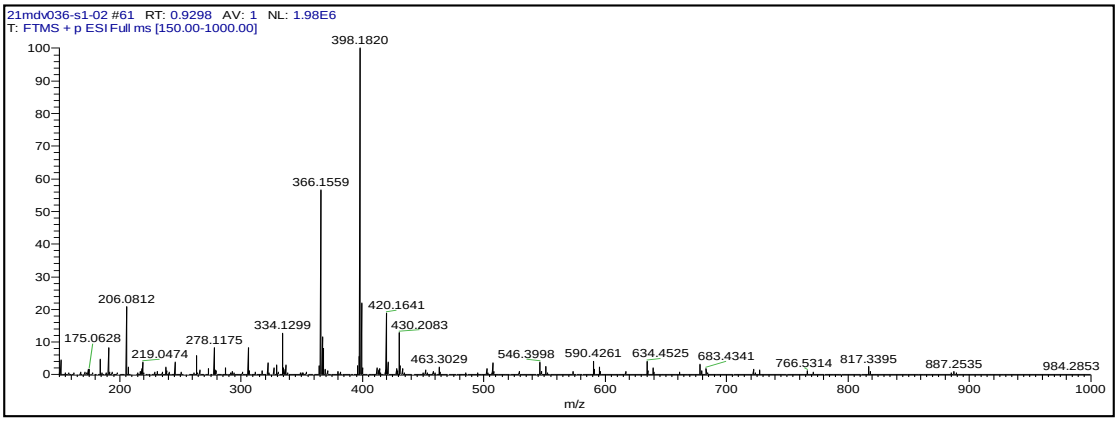



21mdv036-s1-01 #60 RT: 0.9275 AV: 1 NL: 4.26E6
T: FTMS + p ESI Full ms [150.00-1000.00]
430.2081
398.1820
452.1902
184.0968
238.1074
263.1138
338.1500
366.1559
468.1641
570.2808
634.4525
678.4786
727.4605
816.2114
859.4098
881.3916
921.3315
951.3062
m/z

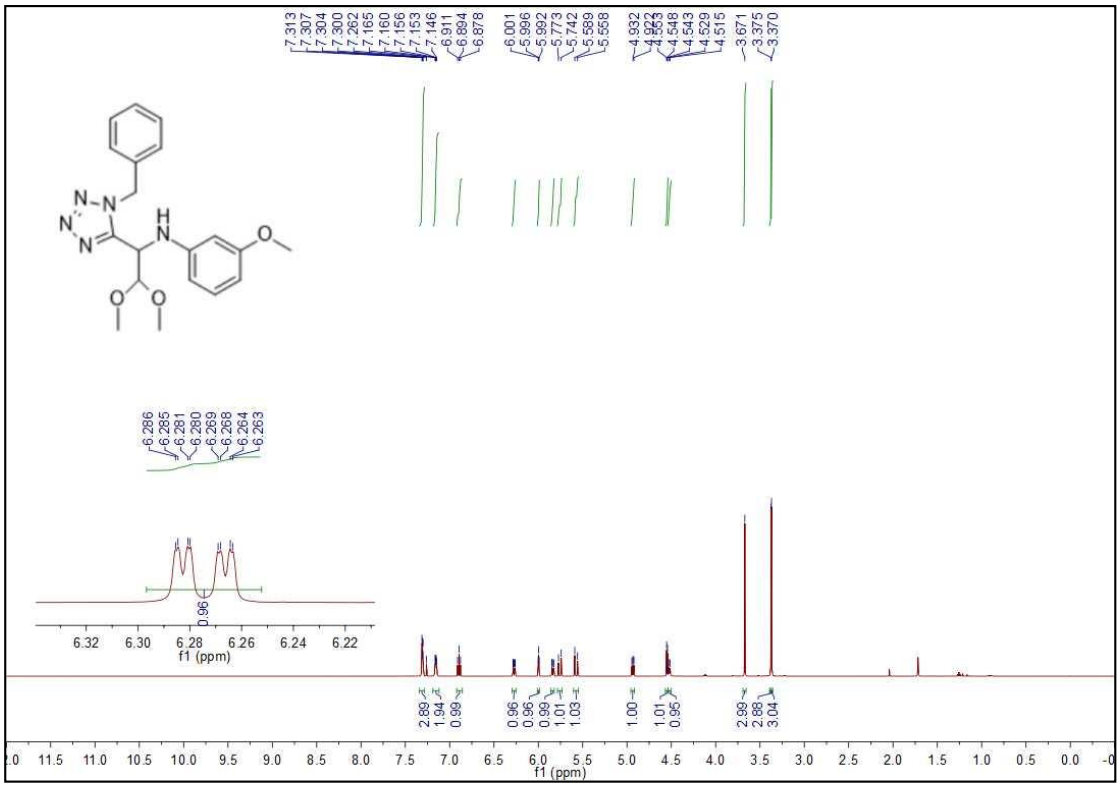
***N*-(1-(1-benzyl-1*H*-tetrazol-5-yl)-2,2-dimethoxyethyl)-2,3-dihydrobenzo [*b*][1,4]dioxin-6-amine (1b)**

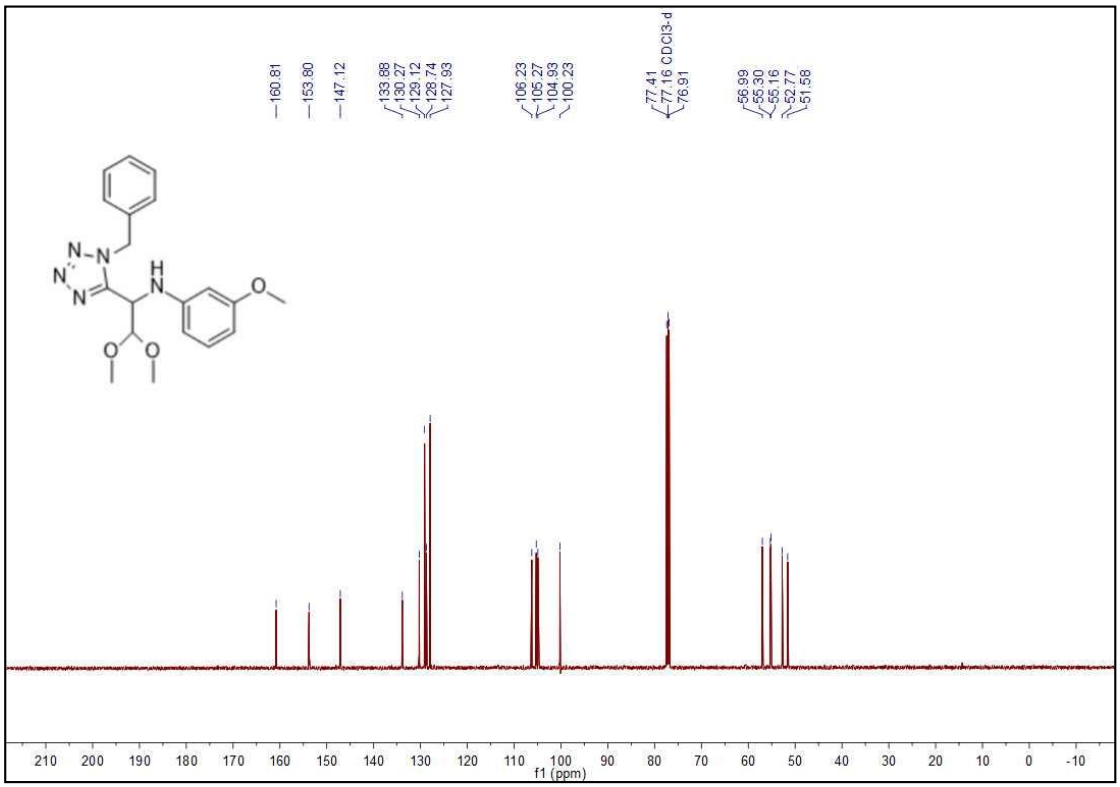


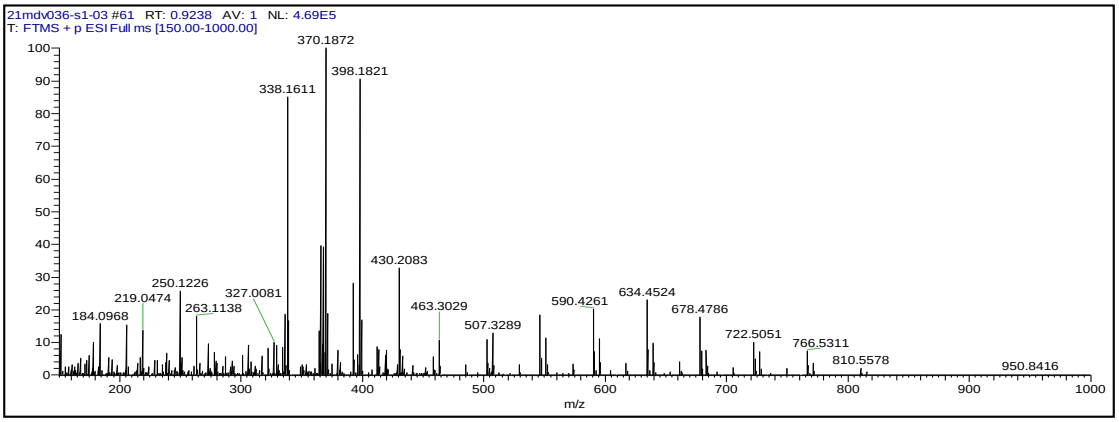



21mdv036-s1-02 #61 RT: 0.9298 AV: 1 NL: 1.98E6
T: FTMS + p ESI Full ms [150.00-1000.00]
398.1820
366.1559
206.0812
420.1641
430.2083
334.1299
175.0628
278.1175
219.0474
463.3029
546.3998
590.4261
634.4525
683.4341
766.5314
817.3395
887.2535
984.2853
100
90
80
70
60
50
40
30
20
10
0
200
300
400
500
600
700
800
900
1000
m/z

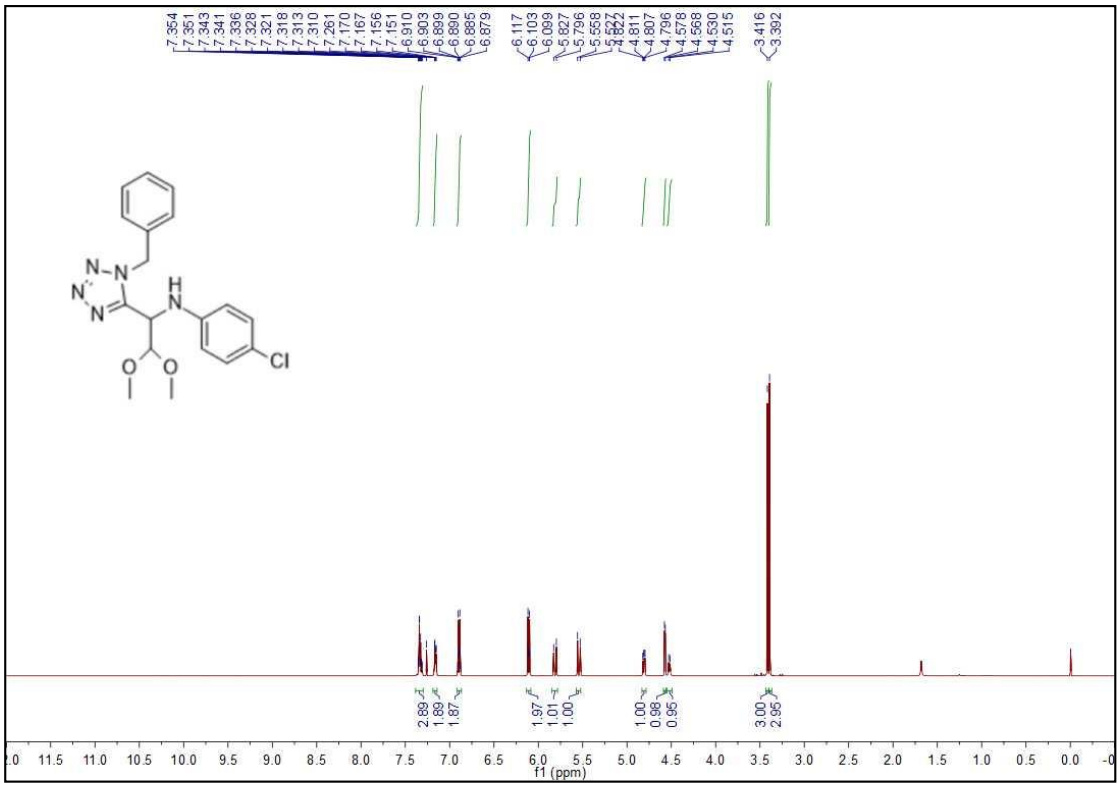
***N*-(1-(1-benzyl-1*H*-tetrazol-5-yl)-2,2-dimethoxyethyl)-3-methoxyaniline (1c)**

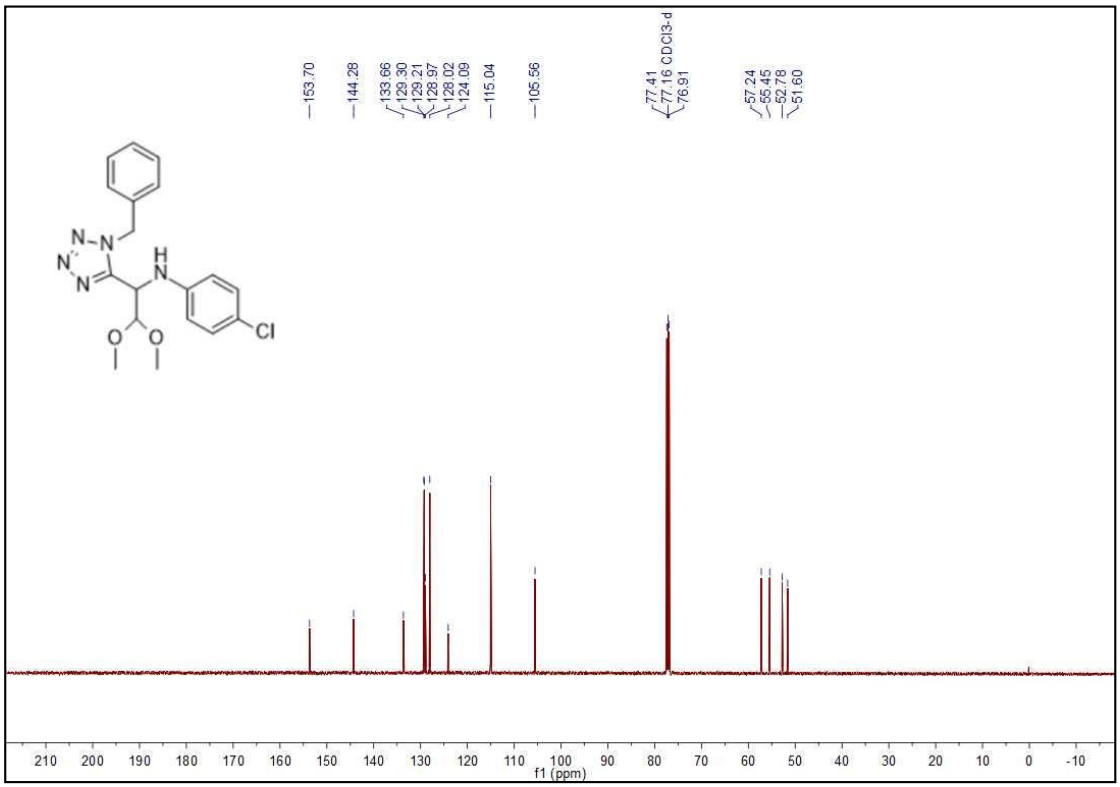


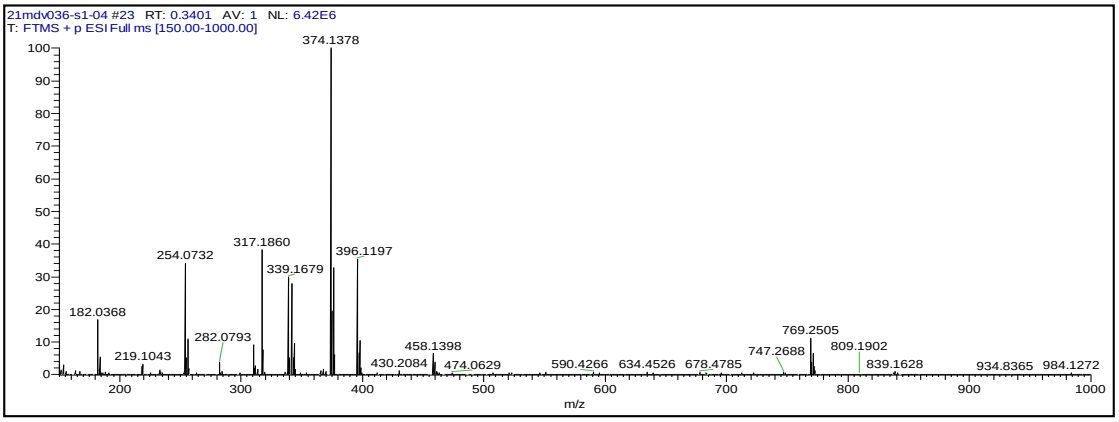



21mdv036-s1-03 #61 RT: 0.9238 AV: 1 NL: 4.69E5
T: FTMS + p ESI Full ms [150.00-1000.00]
370.1872
398.1821
338.1611
430.2083
250.1226
219.0474
327.0081
263.1138
184.0968
463.3029
507.3289
590.4261
634.4524
678.4786
722.5051
766.5311
810.5578
950.8416
m/z

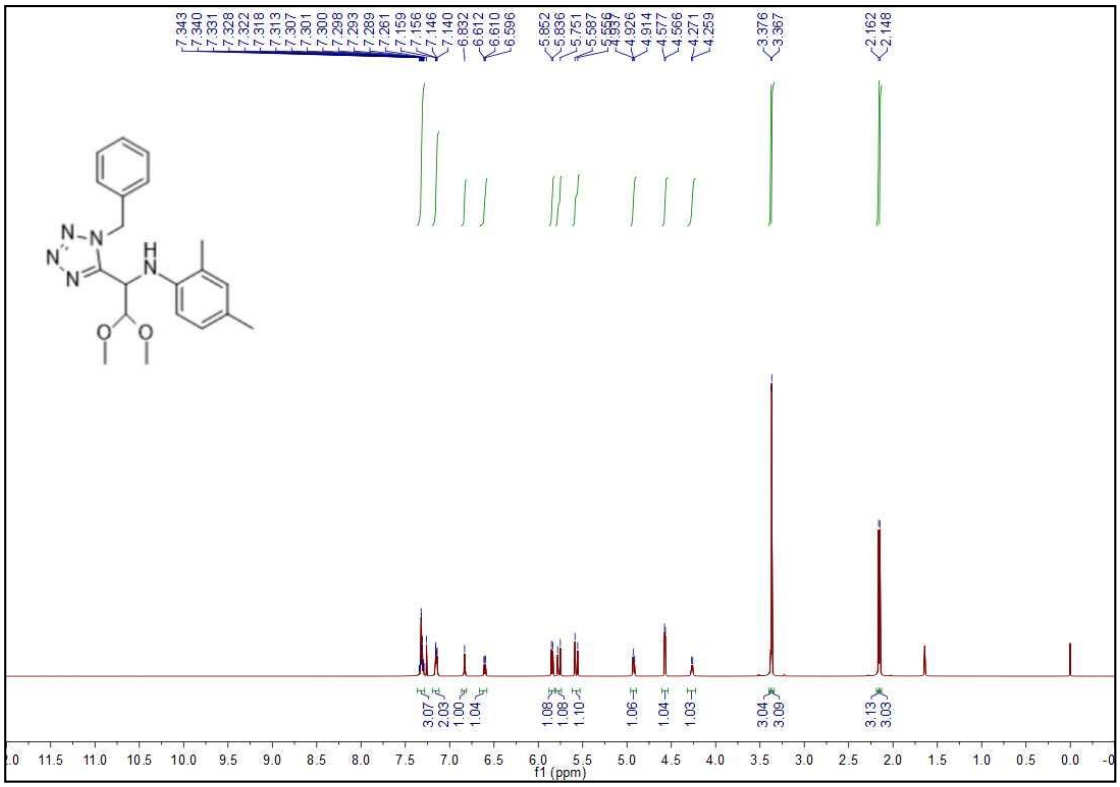
***N*-(1-(1-benzyl-1*H*-tetrazol-5-yl)-2,2-dimethoxyethyl)-4-chloroaniline (1d)**

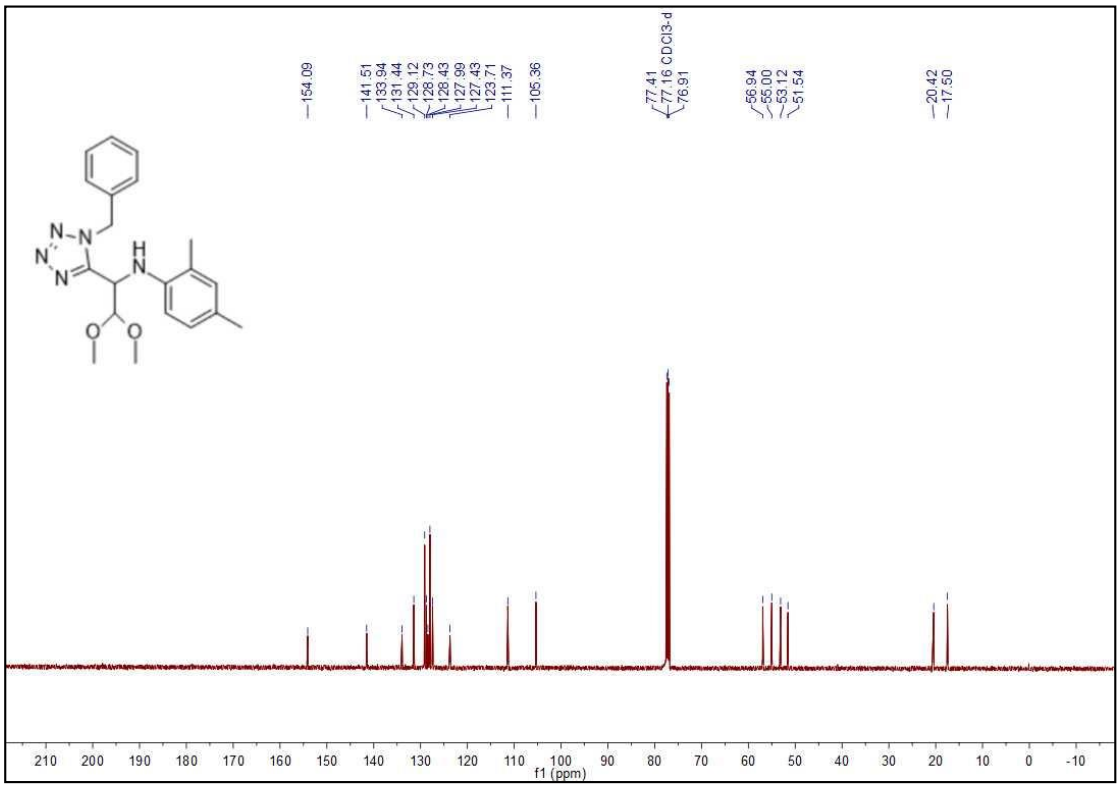


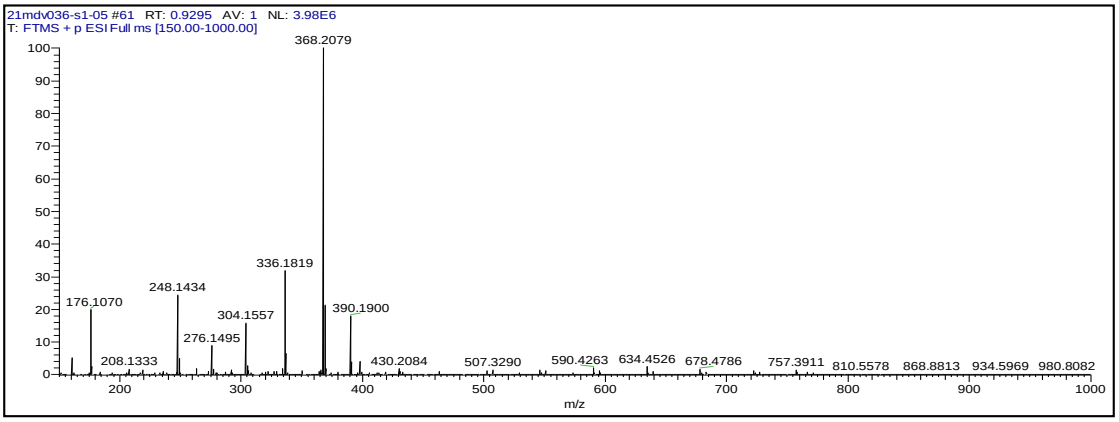



21mdv036-s1-04 #23 RT: 0.3401 AV: 1 NL: 6.42E6
T: FTMS + p ESI Full ms [150.00-1000.00]
374.1378
317.1860
396.1197
254.0732
339.1679
182.0368
282.0793
219.1043
458.1398
430.2084
474.0629
590.4266
634.4526
678.4785
769.2505
747.2688
809.1902
839.1628
934.8365
984.1272
m/z

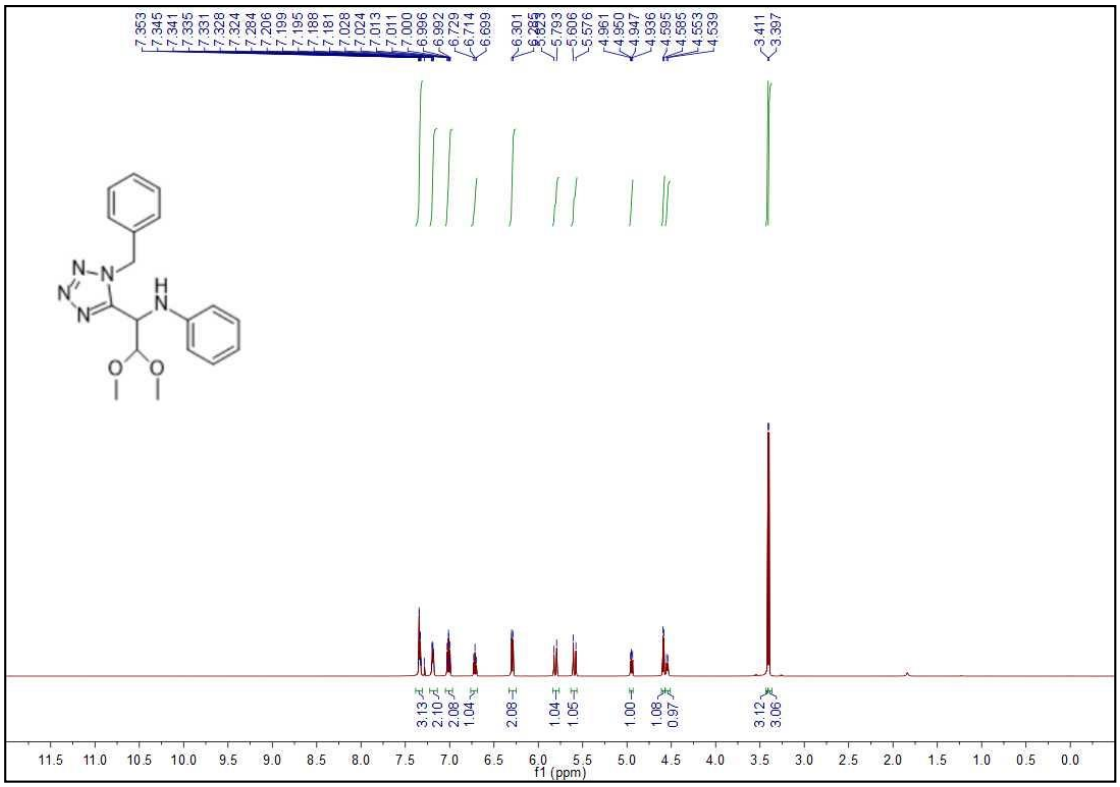
***N*-(1-(1-benzyl-1*H*-tetrazol-5-yl)-2,2-dimethoxyethyl)-2,4-dimethylaniline (1e)**

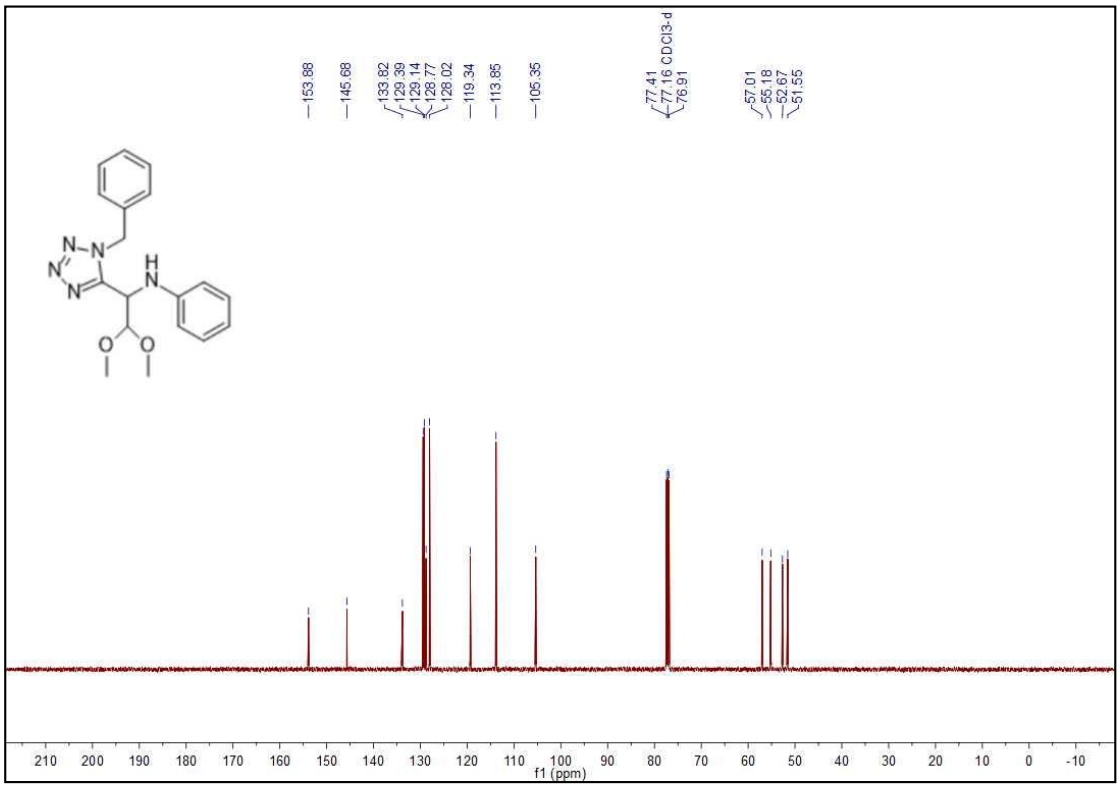


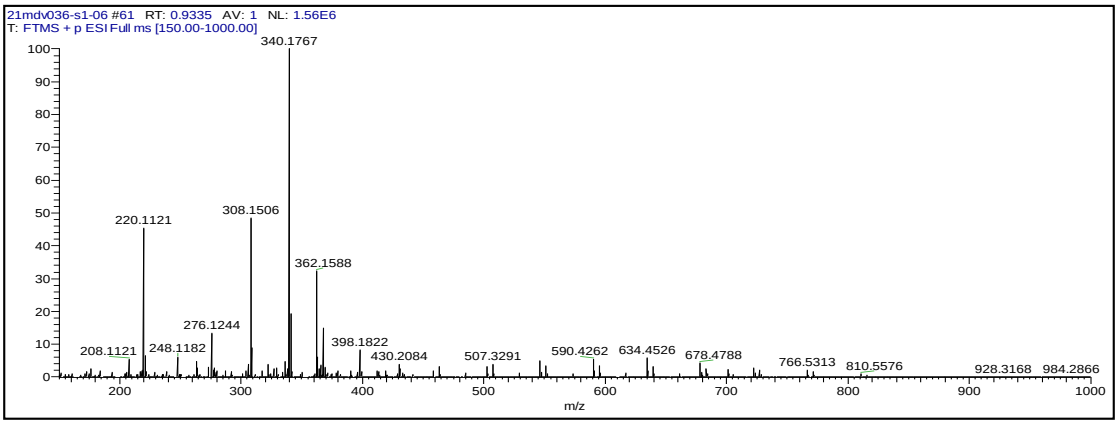



21mdv036-s1-05 #61 RT: 0.9295 AV: 1 NL: 3.98E6
T: FTMS + p ESI Full ms [150.00-1000.00]
368.2079
336.1819
248.1434
176.1070
390.1900
304.1557
276.1495
208.1333
430.2084
507.3290
590.4263
634.4526
678.4786
757.3911
810.5578
868.8813
934.5969
980.8082
m/z

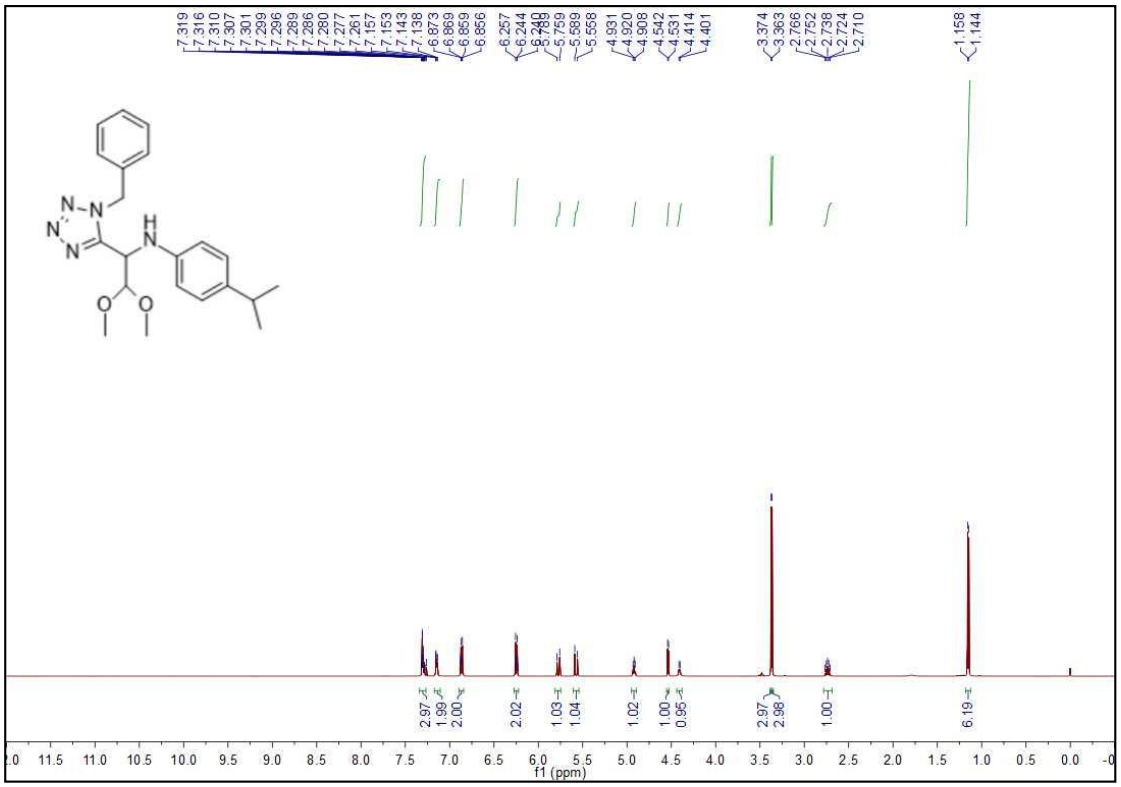
***N*-(1-(1-benzyl-1*H*-tetrazol-5-yl)-2,2-dimethoxyethyl)aniline (1f)**

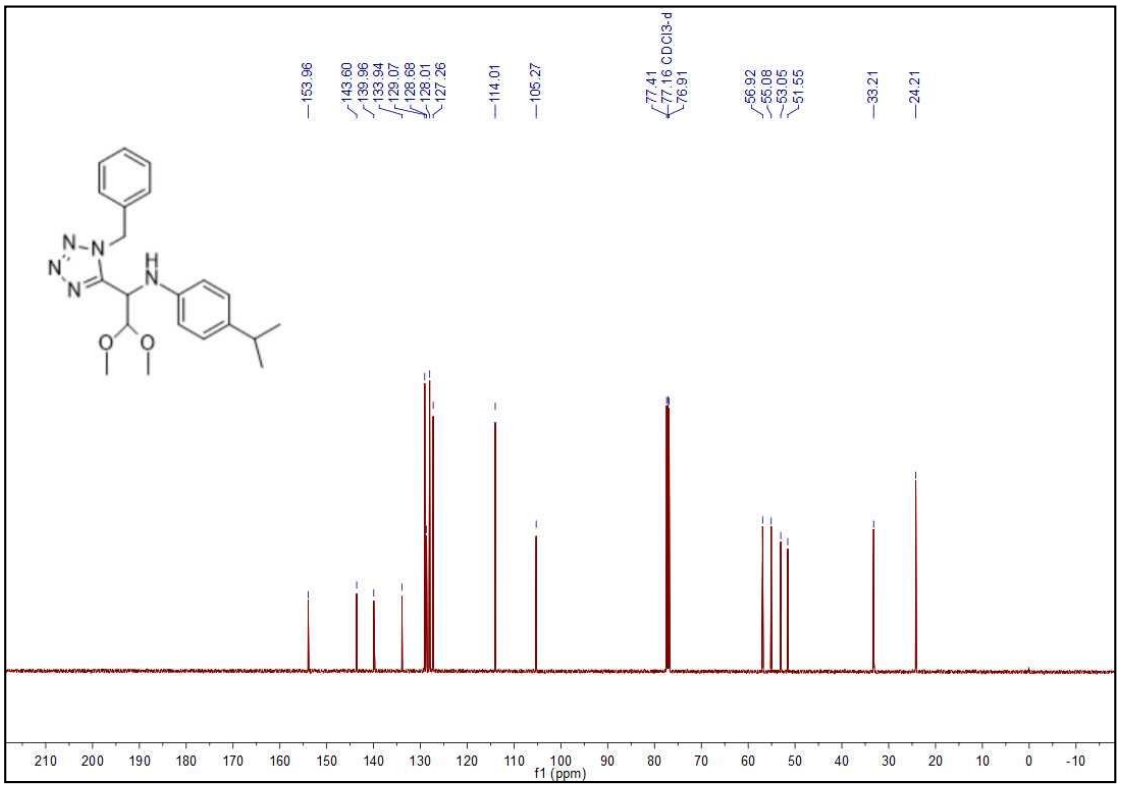


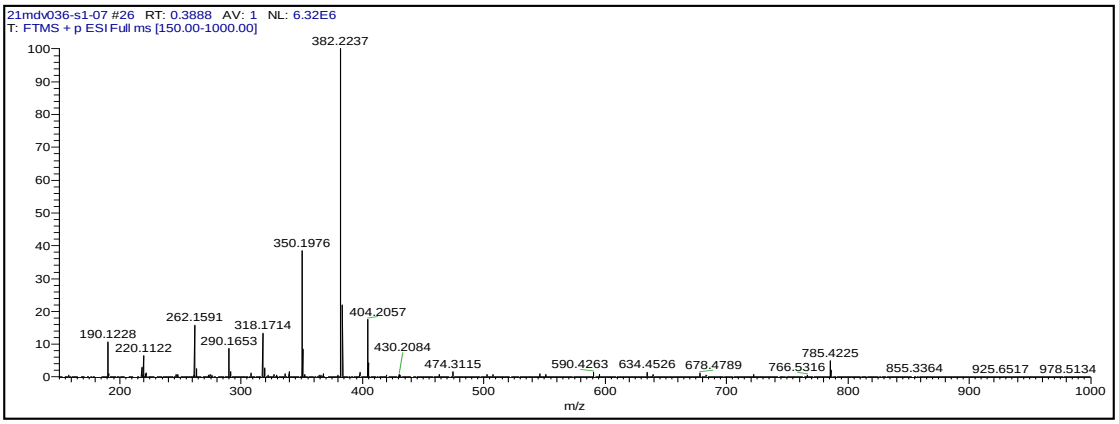



21mdv036-s1-06 #61 RT: 0.9335 AV: 1 NL: 1.56E6
T: FTMS + p ESI Full ms [150.00-1000.00]
340.1767
308.1506
220.1121
362.1588
276.1244
398.1822
208.1121
248.1182
430.2084
507.3291
590.4262
634.4526
678.4788
766.5313
810.5576
928.3168
984.2866
m/z

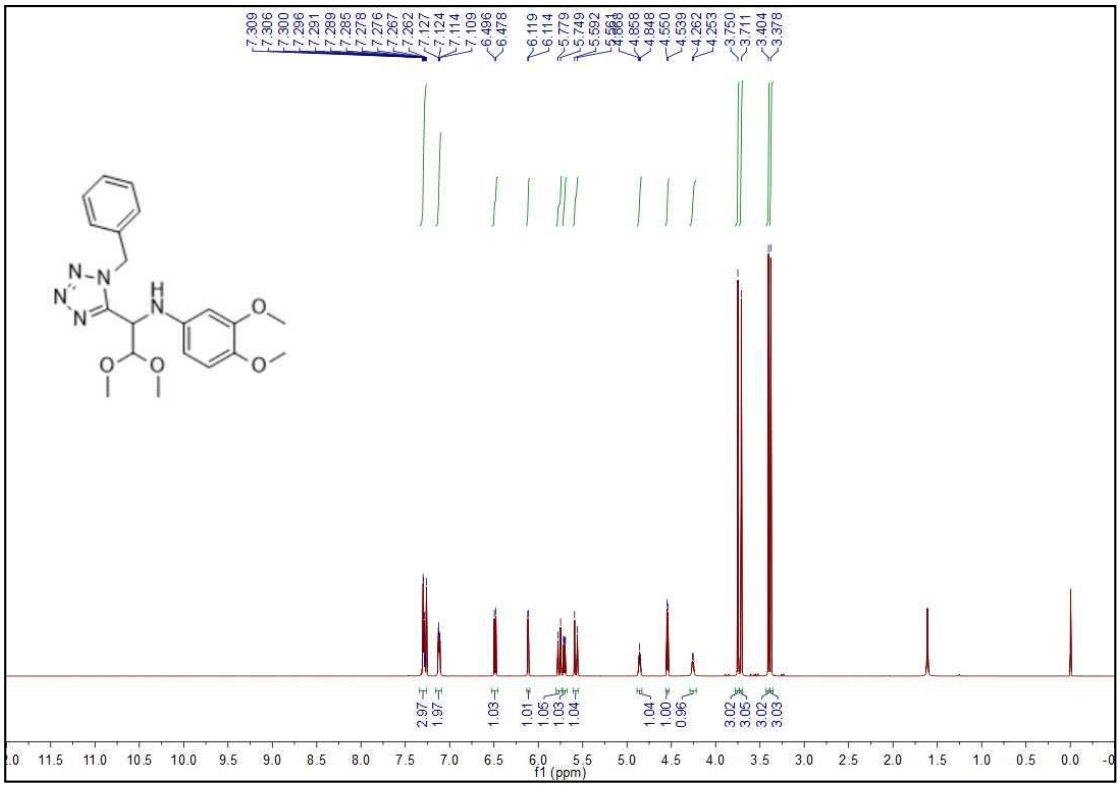
***N*-(1-(1-benzyl-1*H*-tetrazol-5-yl)-2,2-dimethoxyethyl)-4-isopropylaniline (1g)**

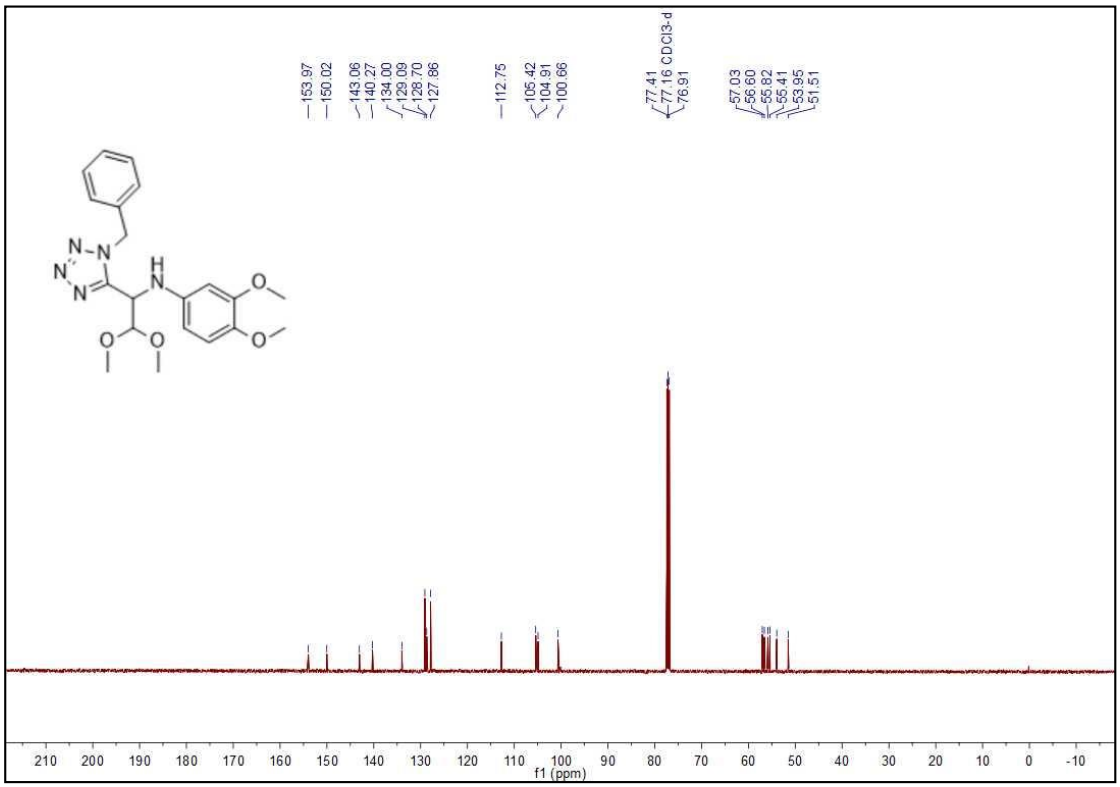


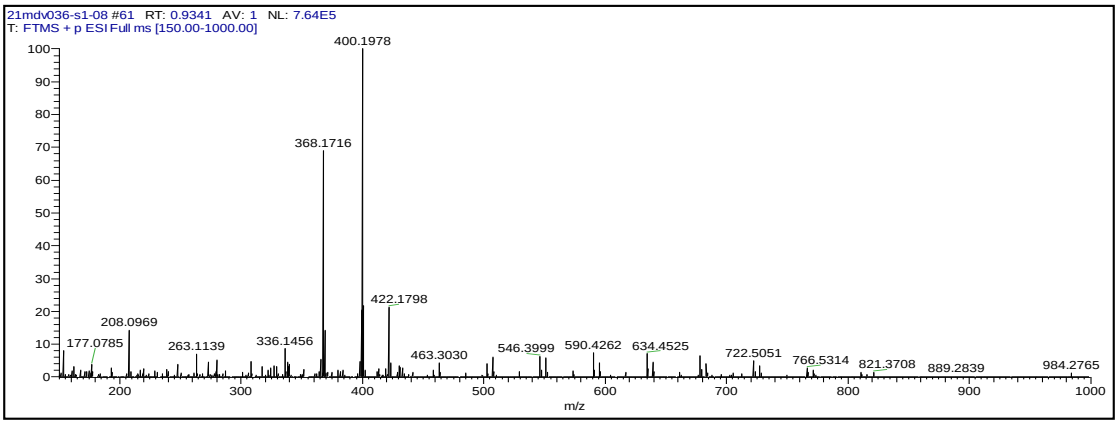



21mdv036-s1-07 #26 RT: 0.3888 AV: 1 NL: 6.32E6
T: FTMS + p ESI Full ms [150.00-1000.00]
382.2237
350.1976
404.2057
262.1591
318.1714
190.1228
220.1122
290.1653
430.2084
474.3115
590.4263
634.4526
678.4789
766.5316
785.4225
855.3364
925.6517
978.5134
m/z

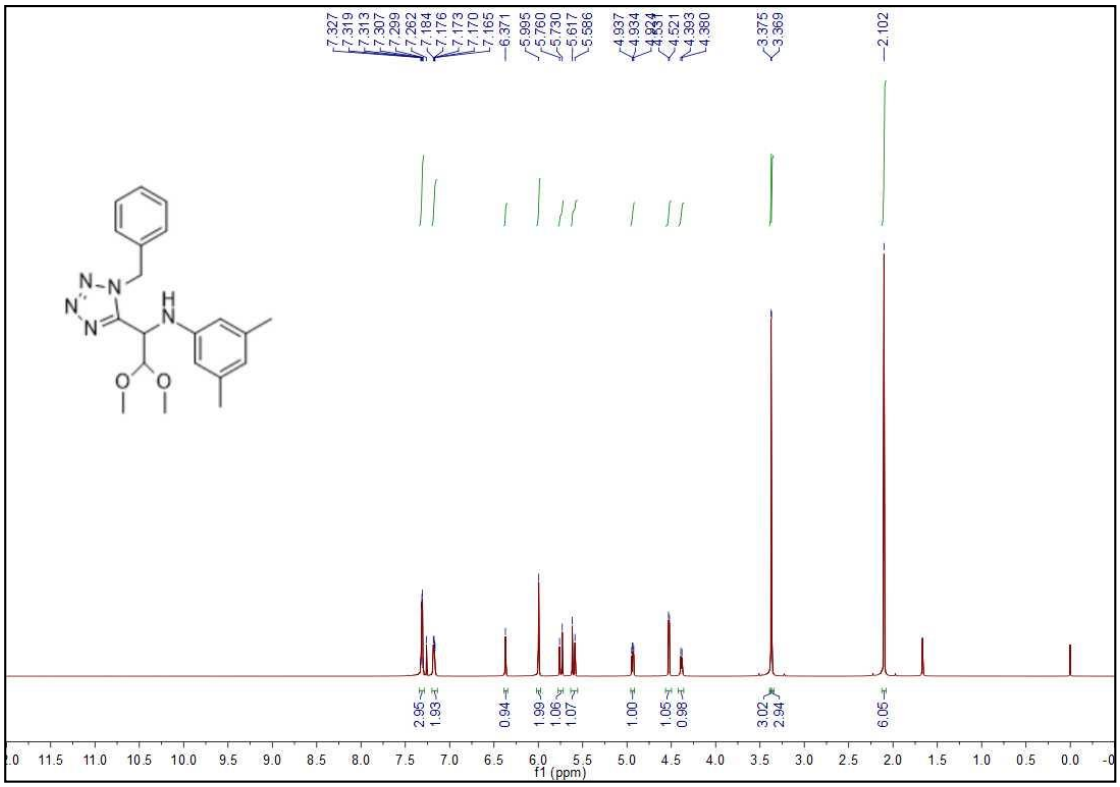
***N*-(1-(1-benzyl-1*H*-tetrazol-5-yl)-2,2-dimethoxyethyl)-3,4-dimethoxyaniline (1h)**

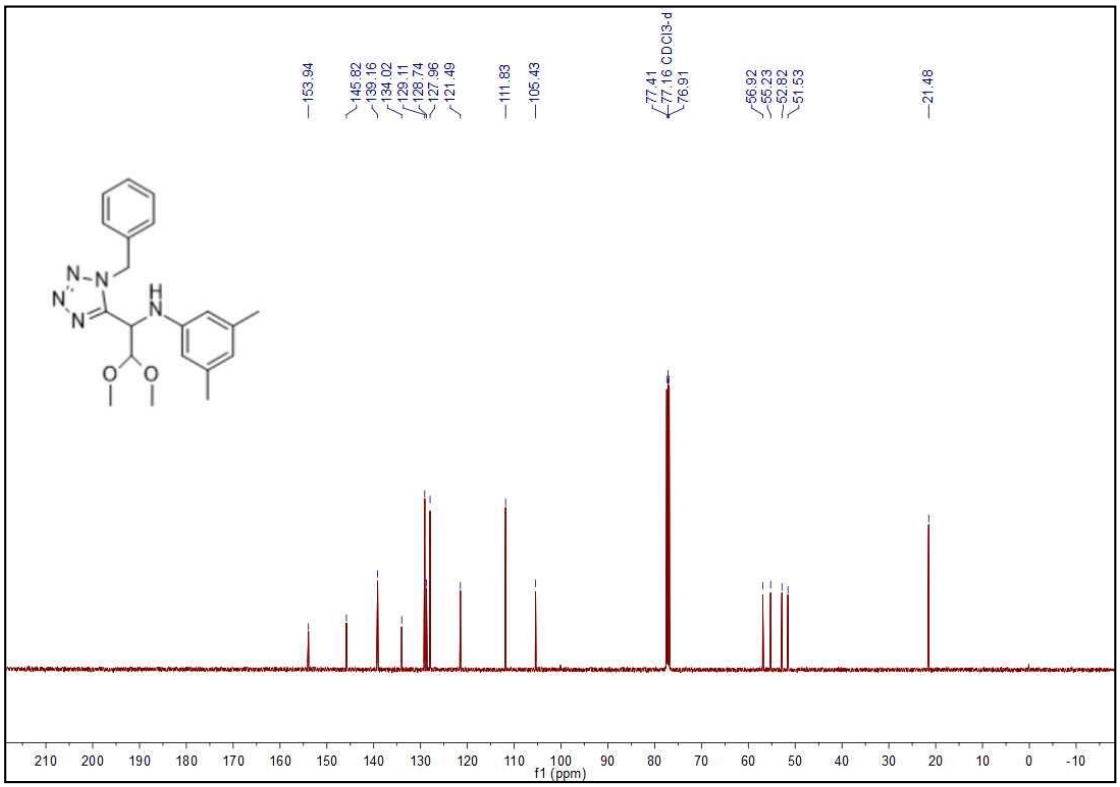


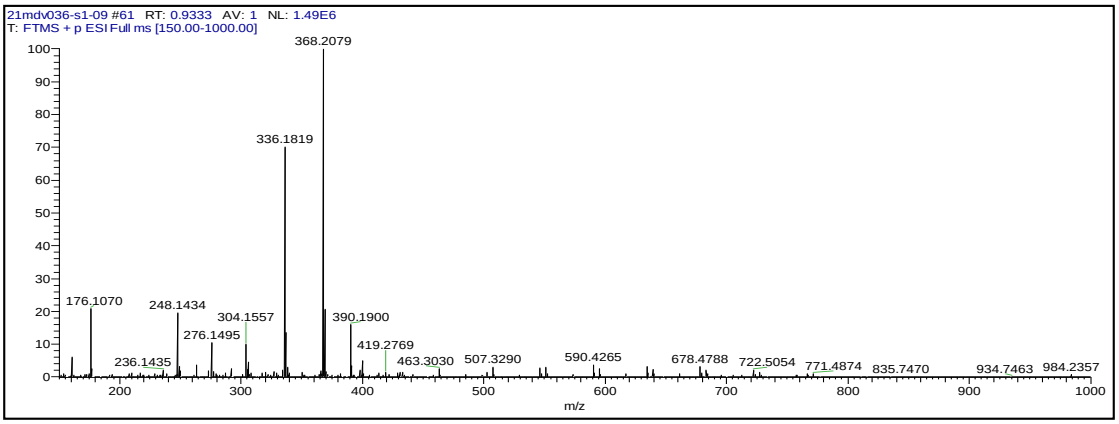



21mdv036-s1-08 #61 RT: 0.9341 AV: 1 NL: 7.64E5
T: FTMS + p ESI Full ms [150.00-1000.00]
400.1978
368.1716
422.1798
208.0969
177.0785
263.1139
336.1456
463.3030
546.3999
590.4262
634.4525
722.5051
766.5314
821.3708
889.2839
984.2765
m/z

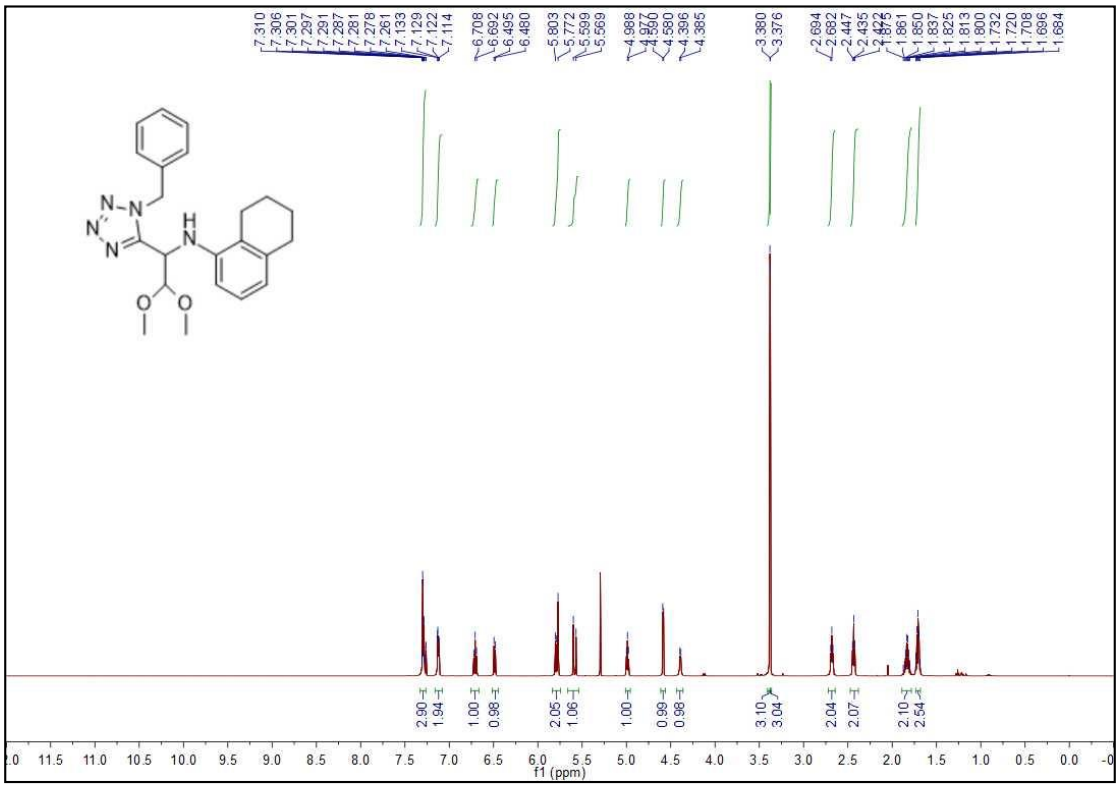
***N*-(1-(1-benzyl-1*H*-tetrazol-5-yl)-2,2-dimethoxyethyl)-3,5-dimethylaniline (1i)**

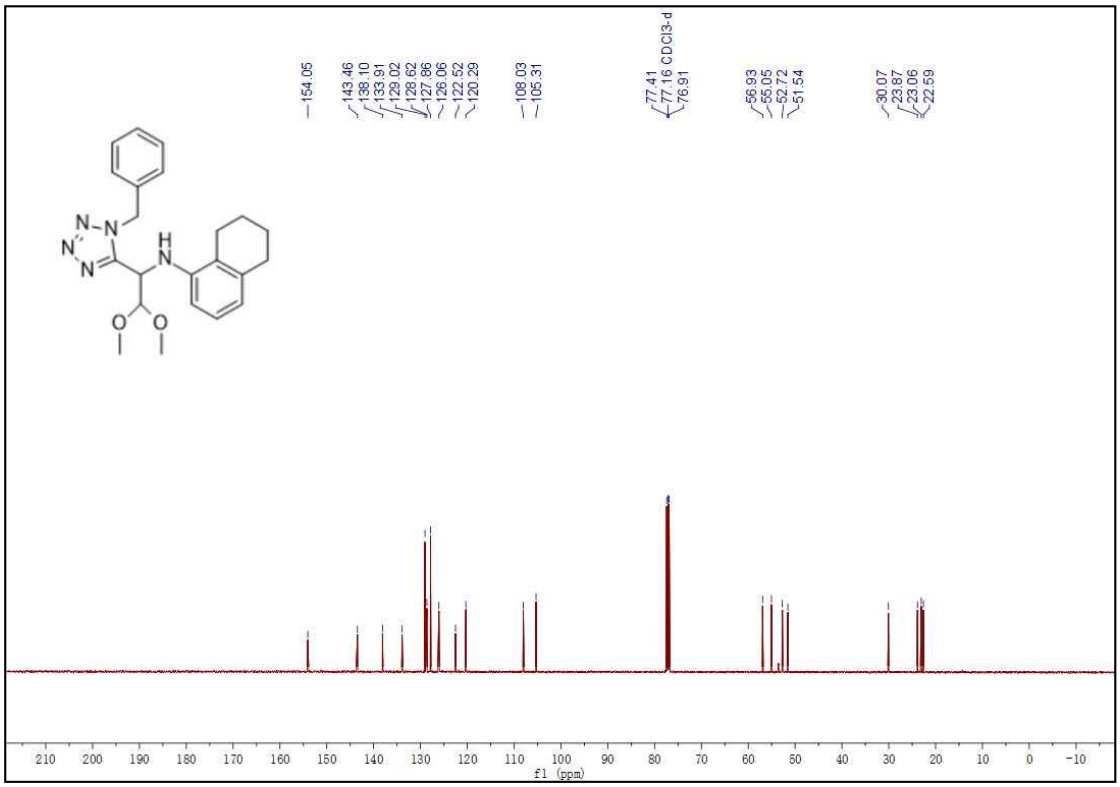


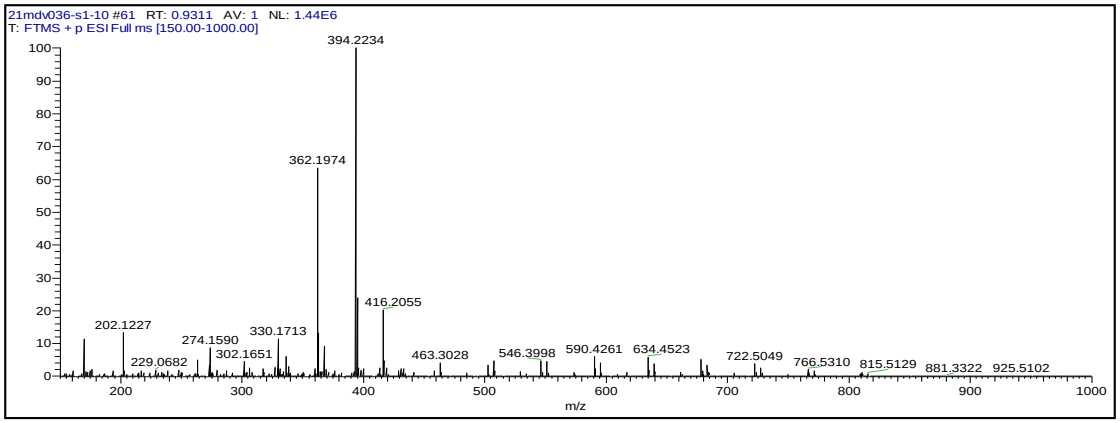



21mdv036-s1-09 #61 RT: 0.9333 AV: 1 NL: 1.49E6
T: FTMS + p ESI Full ms [150.00-1000.00]
368.2079
336.1819
176.1070
248.1434
304.1557
276.1495
390.1900
419.2769
236.1435
463.3030
507.3290
590.4265
678.4788
722.5054
771.4874
835.7470
934.7463
984.2357
m/z

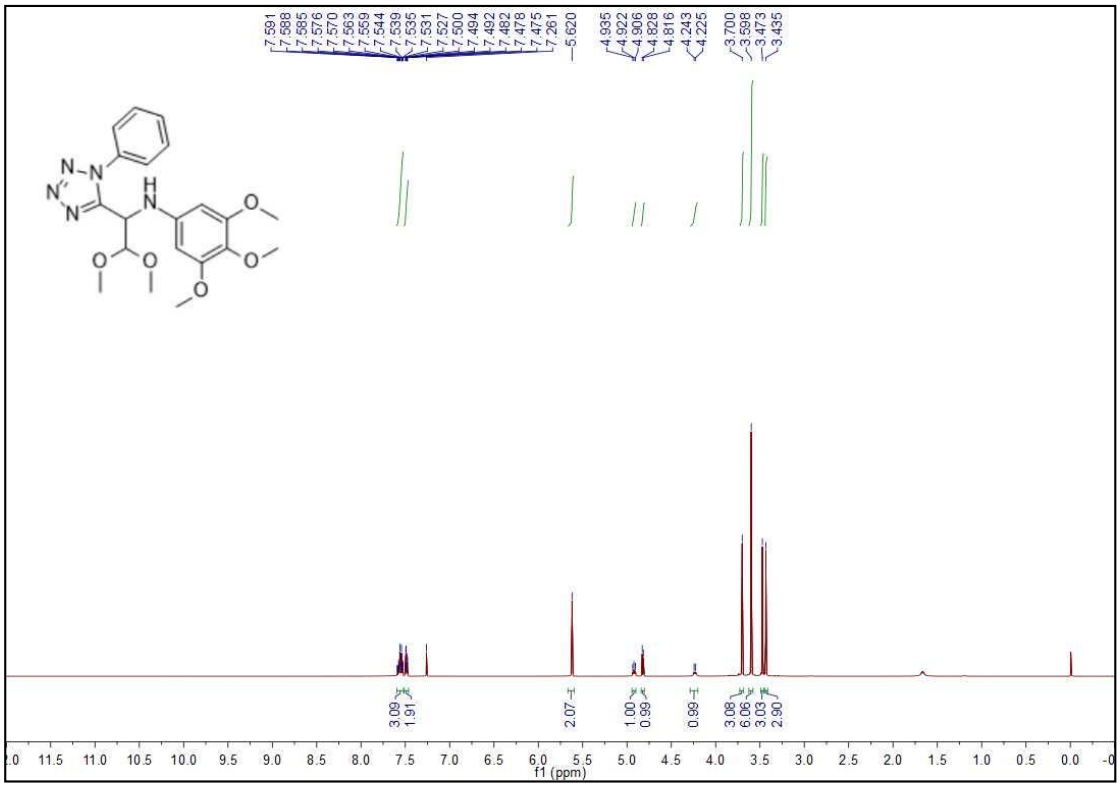
***N*-(1-(1-benzyl-1*H*-tetrazol-5-yl)-2,2-dimethoxyethyl)-5,6,7,8-tetrahydro naphthalen-1-amine (1j)**

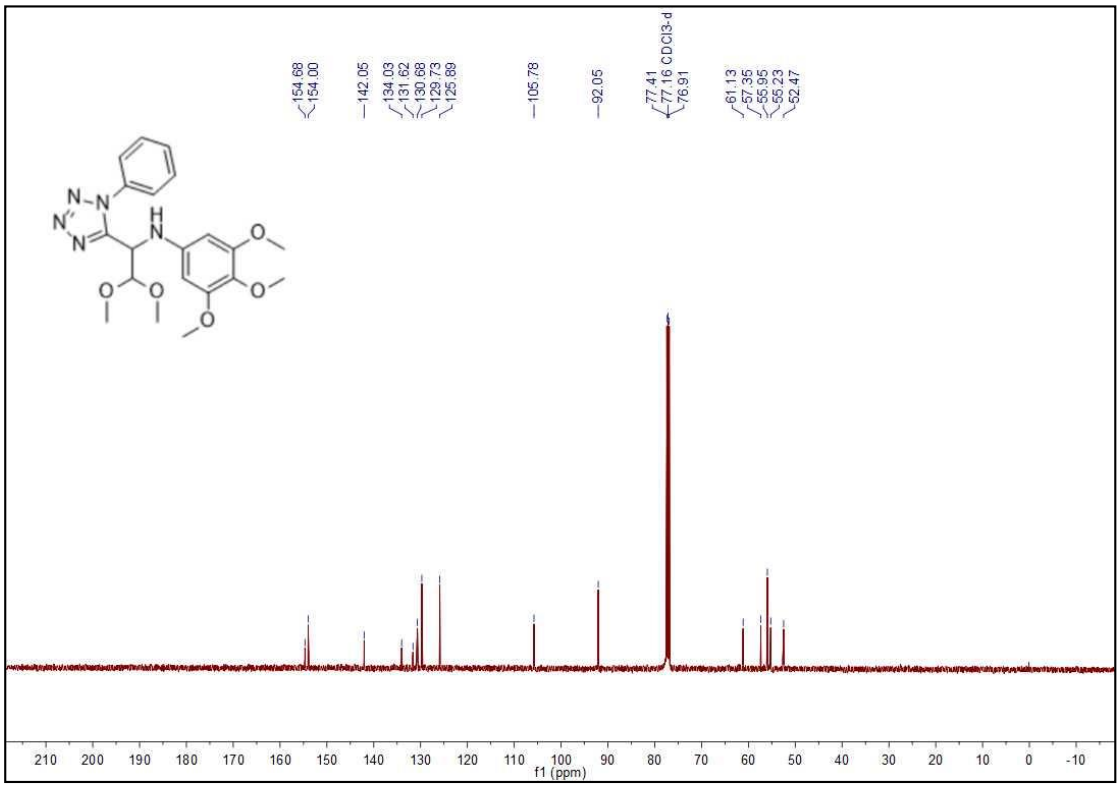


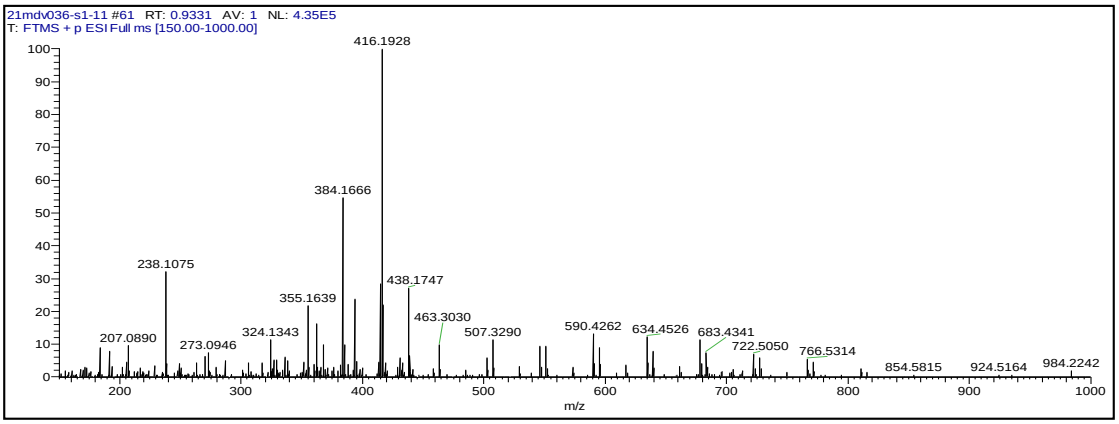



21mdv036-s1-10 #61 RT: 0.9311 AV: 1 NL: 1.44E6
T: FTMS + p ESI Full ms [150.00-1000.00]
394.2234
362.1974
416.2055
202.1227
274.1590
330.1713
302.1651
229.0682
463.3028
546.3998
590.4261
634.4523
722.5049
766.5310
815.5129
881.3322
925.5102
m/z

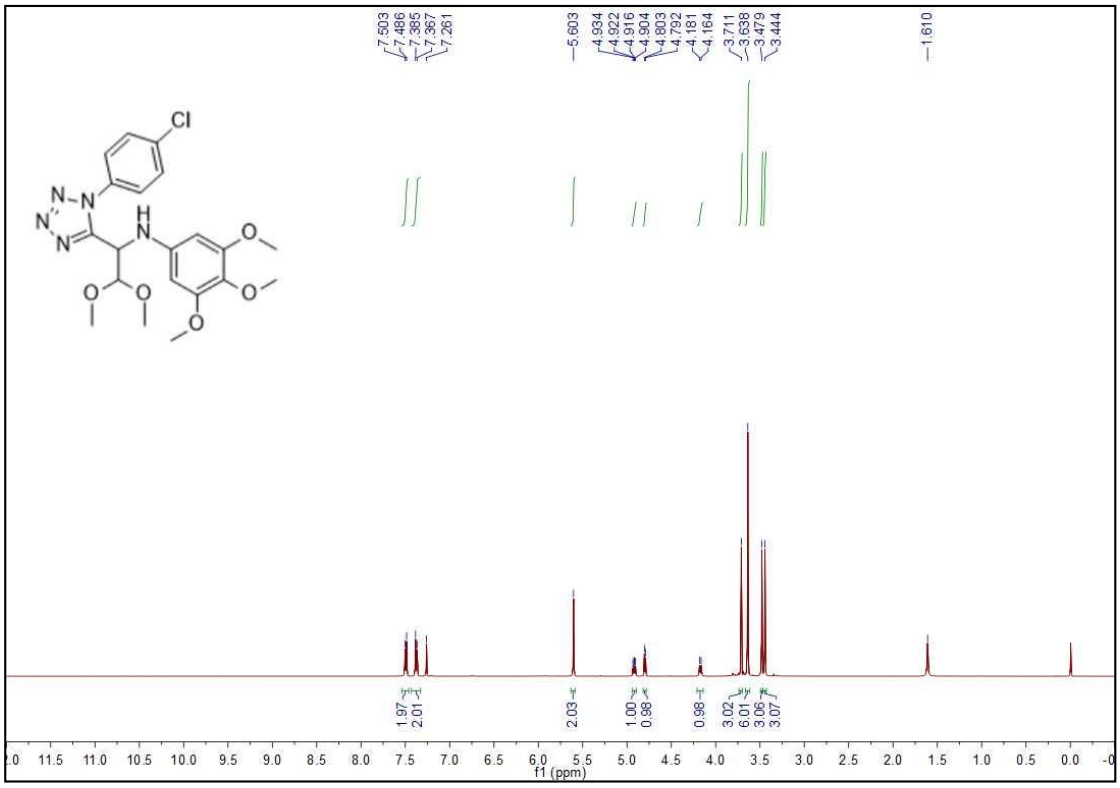
_N_-(2,2-dimethoxy-1-(1-phenyl-1_H_-tetrazol-5-yl)ethyl)-3,4,5-trimethoxyaniline (1k)

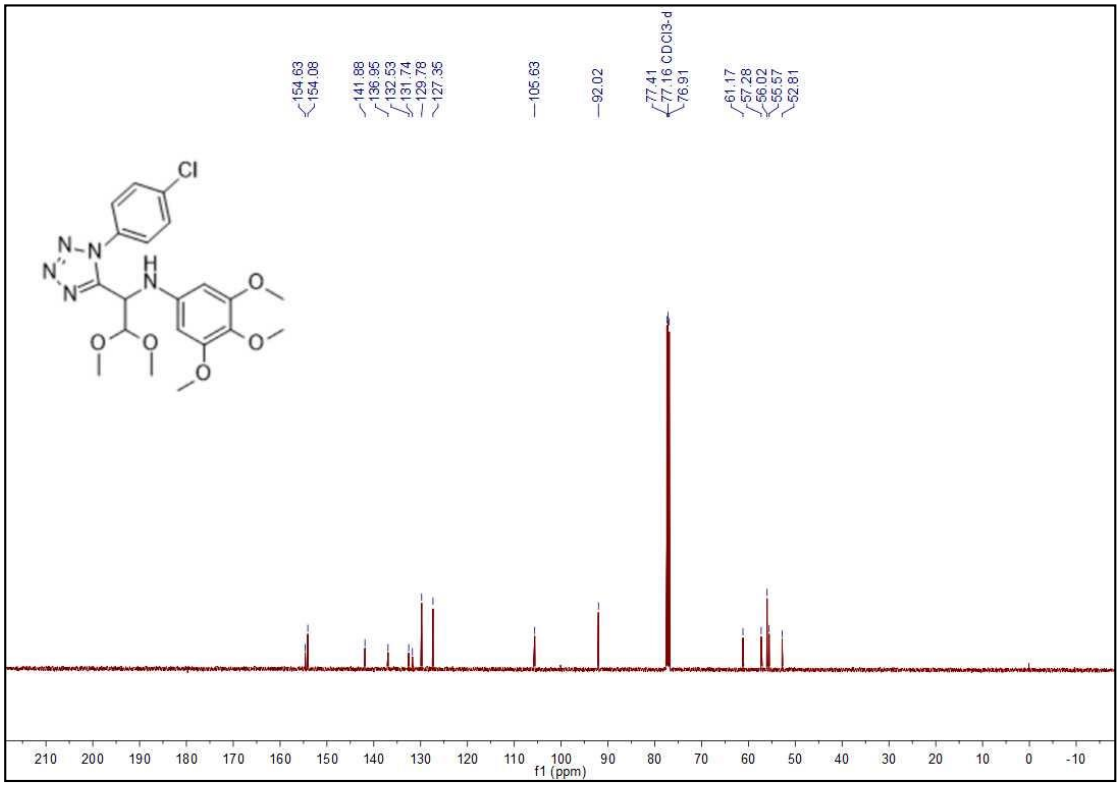


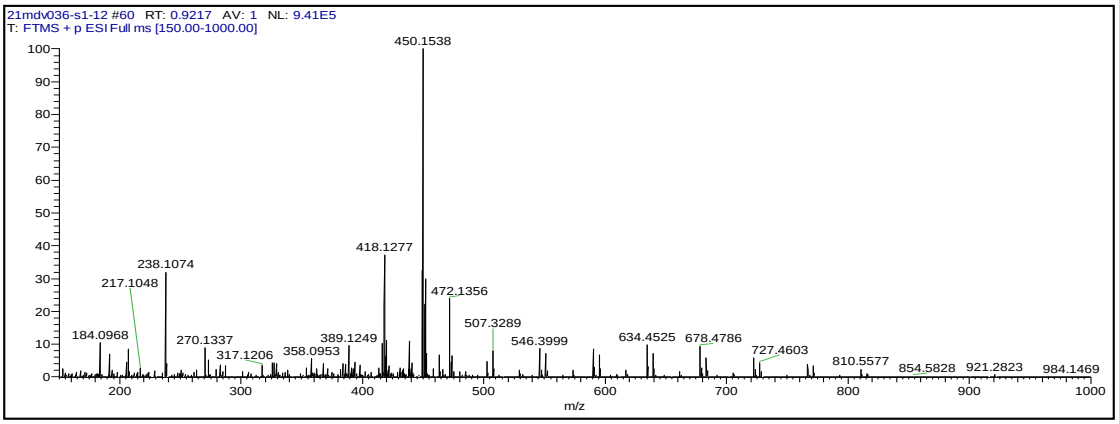



21mdv036-s1-11 #61 RT: 0.9331 AV: 1 NL: 4.35E5
T: FTMS + p ESI Full ms [150.00-1000.00]
416.1928
384.1666
238.1075
438.1747
355.1639
463.3030
207.0890
324.1343
273.0946
507.3290
590.4262
634.4526
683.4341
722.5050
766.5314
854.5815
924.5164
984.2242
m/z

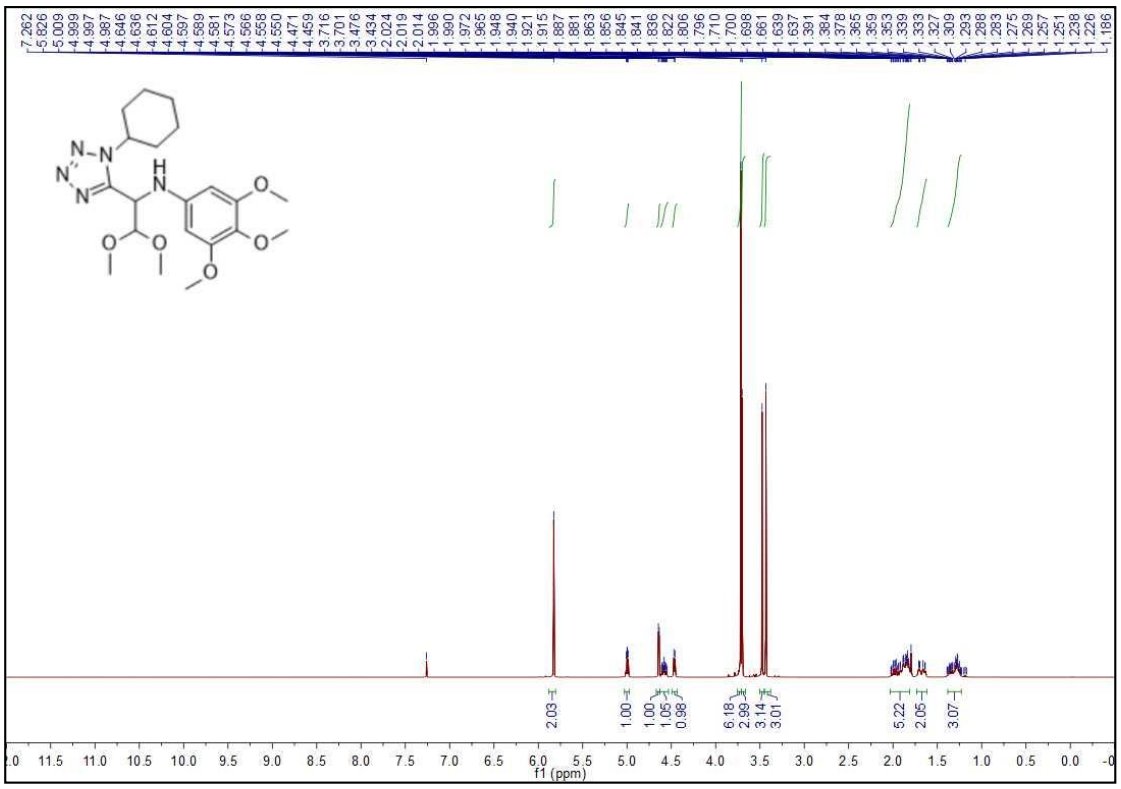
***N*-(1-(1-(4-chlorophenyl)-1*H*-tetrazol-5-yl)-2,2-dimethoxyethyl)-3,4,5-trimethoxyaniline (1l)**

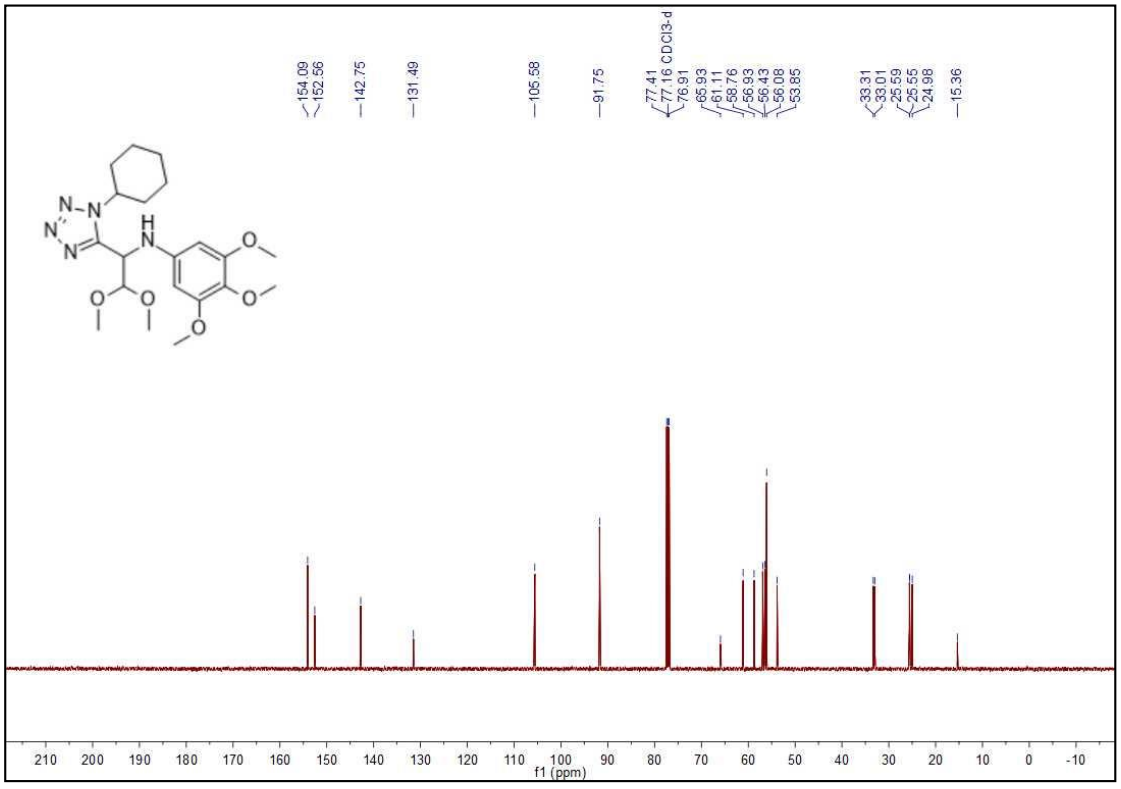


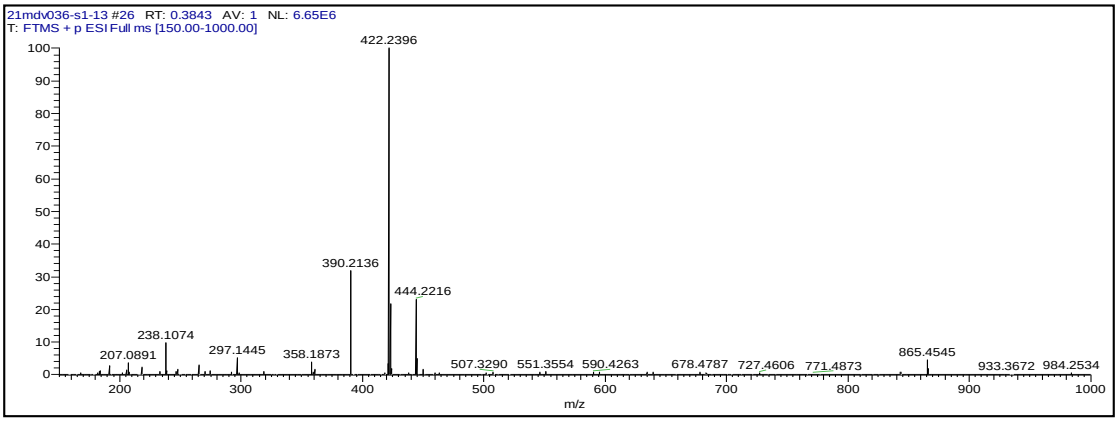



21mdv036-s1-12 #60 RT: 0.9217 AV: 1 NL: 9.41E5
T: FTMS + p ESI Full ms [150.00-1000.00]
450.1538
418.1277
238.1074
217.1048
472.1356
507.3289
184.0968
270.1337
389.1249
546.3999
634.4525
678.4786
317.1206
358.0953
727.4603
810.5577
854.5828
921.2823
984.1469
m/z

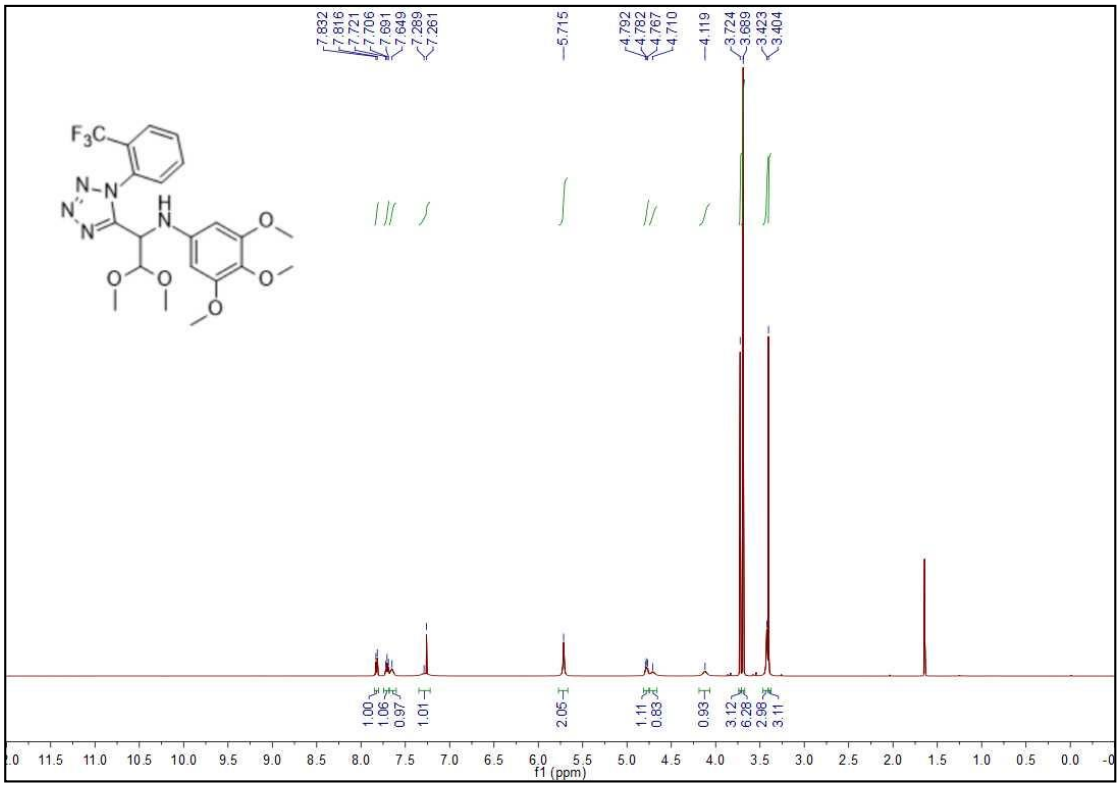
_N_-(1-(1-cyclohexyl-1_H_-tetrazol-5-yl)-2,2-dimethoxyethyl)-3,4,5-trimethoxyaniline (1m)

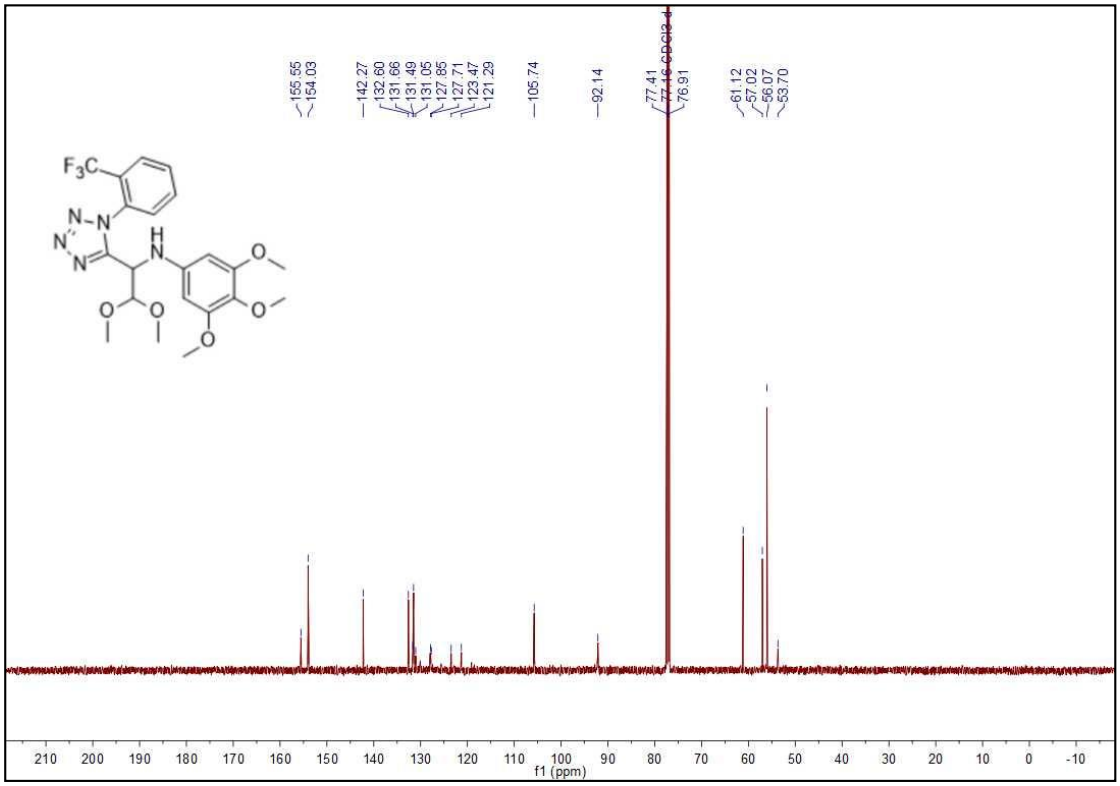


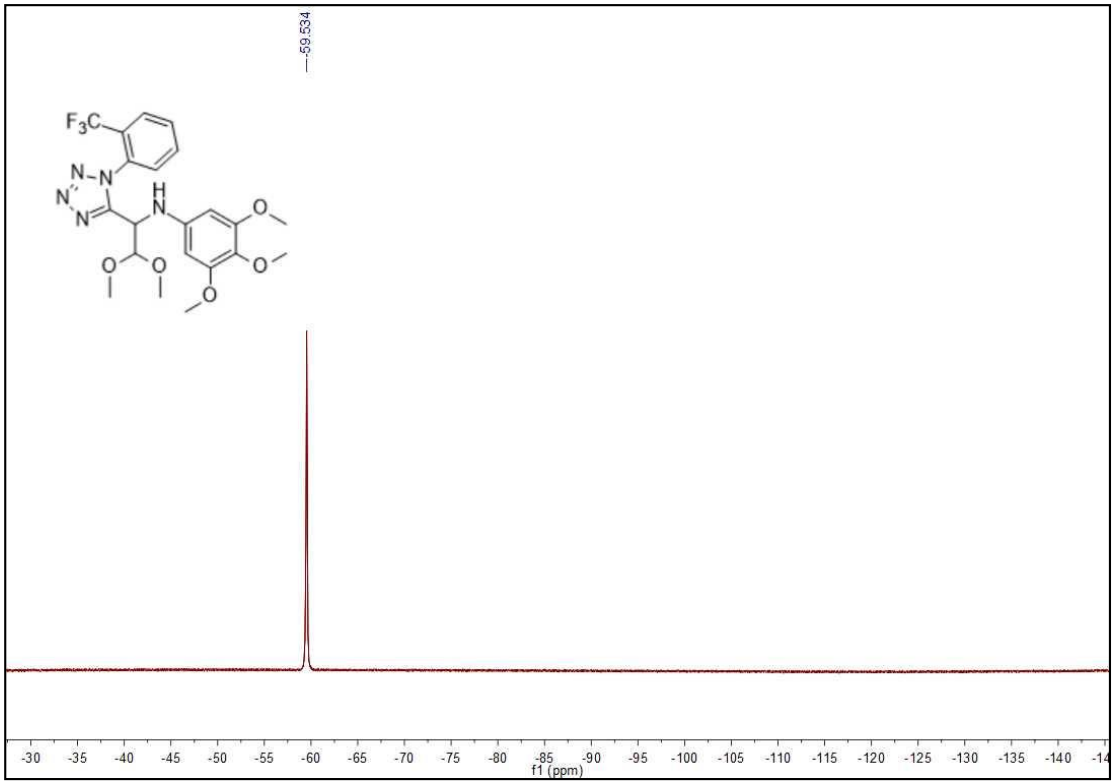


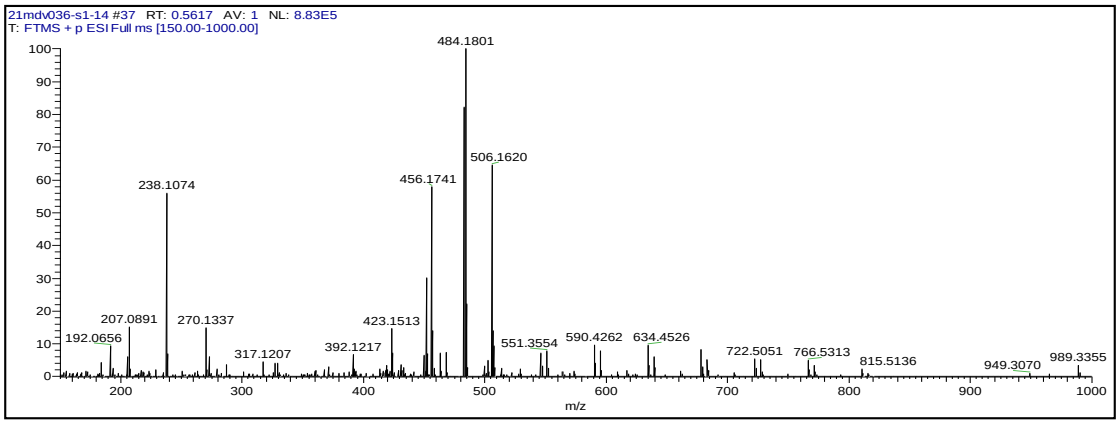

21mdv036-s1-13 #26 RT: 0.3843 AV: 1 NL: 6.65E6
T: FTMS + p ESI Full ms [150.00-1000.00]
422.2396
390.2136
444.2216
238.1074
207.0891
297.1445
358.1873
507.3290
551.3554
590.4263
678.4787
727.4606
771.4873
865.4545
933.3672
984.2534
m/z

_N_-(2,2-dimethoxy-1-(1-(2-(trifluoromethyl)phenyl)-1_H_-tetrazol-5-yl)ethyl)-3,4,5-trimethoxyaniline (1n)

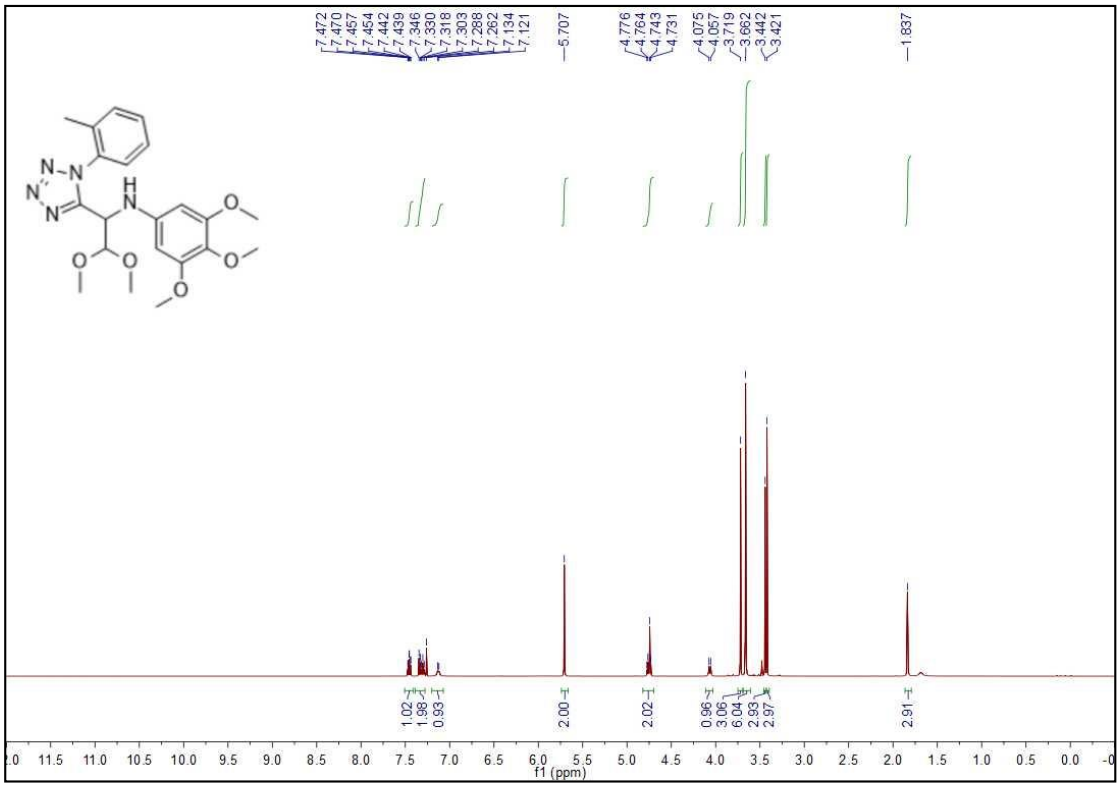


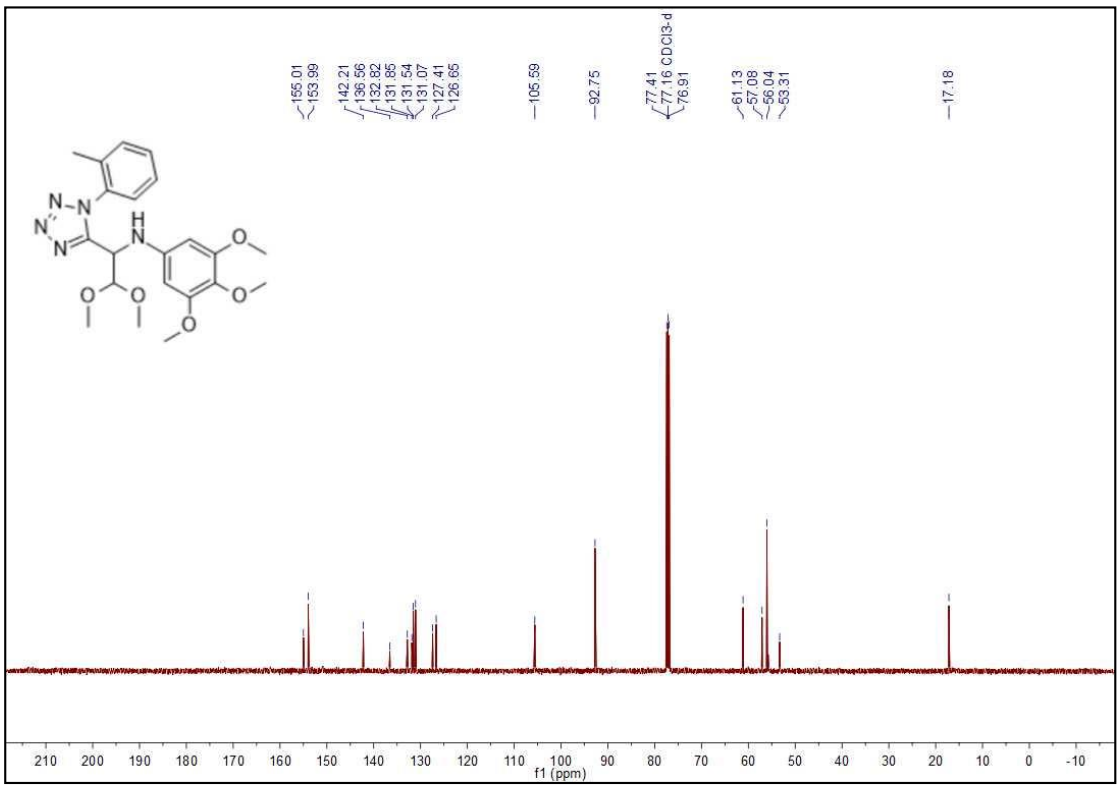


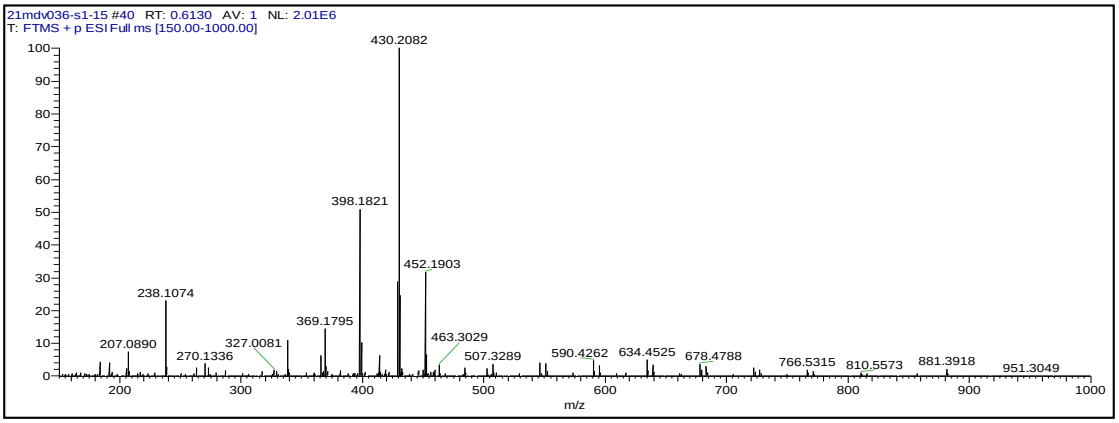

-59.534
F3C
N
N
N
H
N
O
O
O
O
O
-30 -35 -40 -45 -50 -55 -60 -65 -70 -75 -80 -85 -90 -95 -100 -105 -110 -115 -120 -125 -130 -135 -140
f1 (ppm)


21mdv036-s1-14 #37 RT: 0.5617 AV: 1 NL: 8.83E5
T: FTMS + p ESI Full ms [150.00-1000.00]
484.1801
506.1620
456.1741
238.1074
207.0891
270.1337
192.0656
423.1513
317.1207
392.1217
551.3554
590.4262
634.4526
722.5051
766.5313
815.5136
949.3070
989.3355
m/z

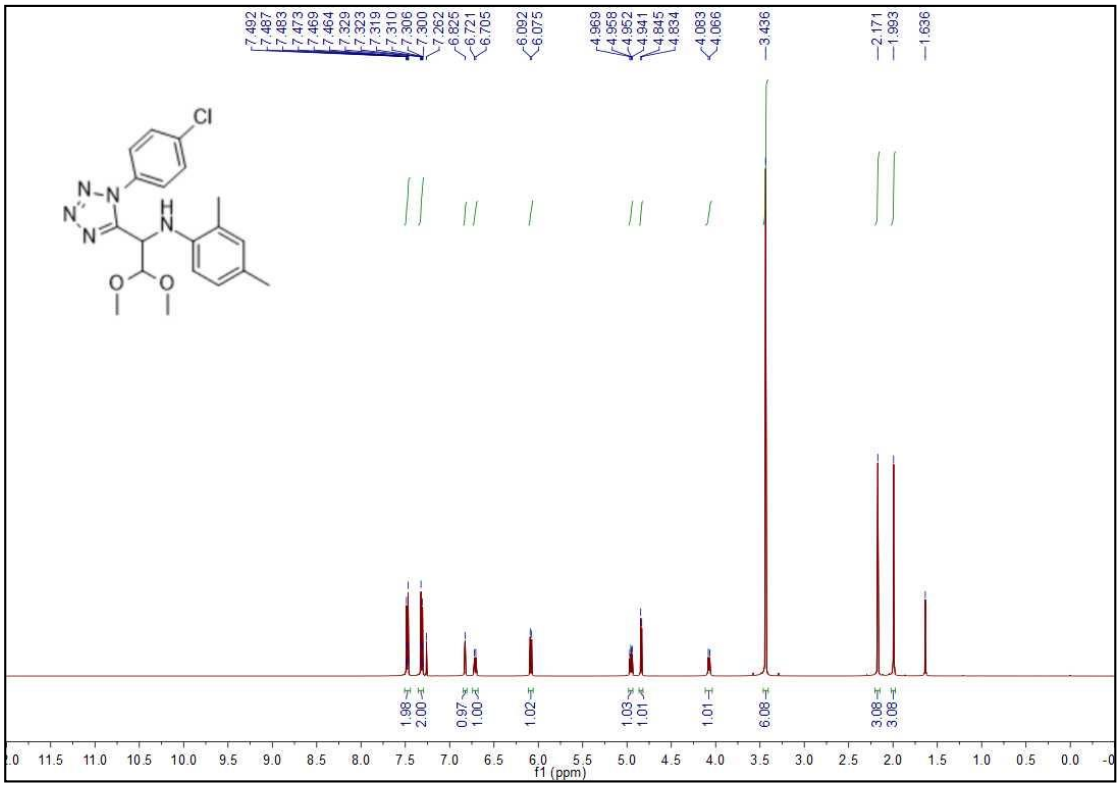
_N_-(2,2-dimethoxy-1-(1-(_o_-tolyl)-1_H_-tetrazol-5-yl)ethyl)-3,4,5-trimethoxyaniline (1o)

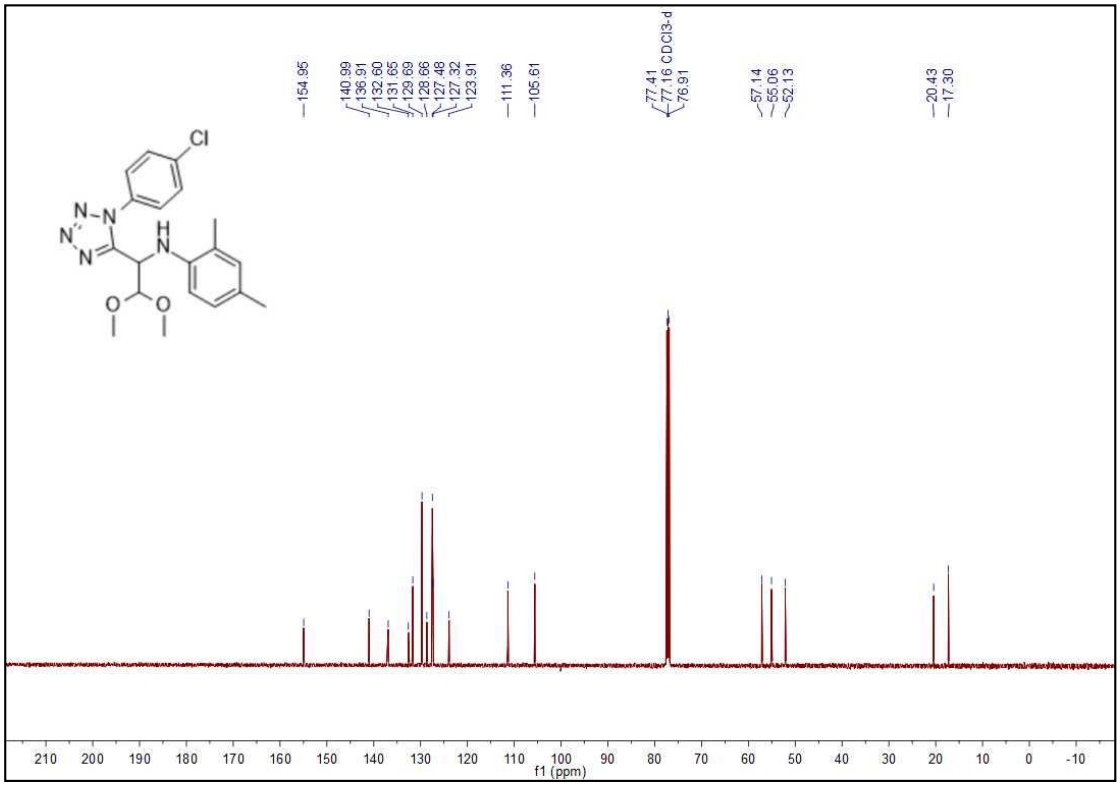


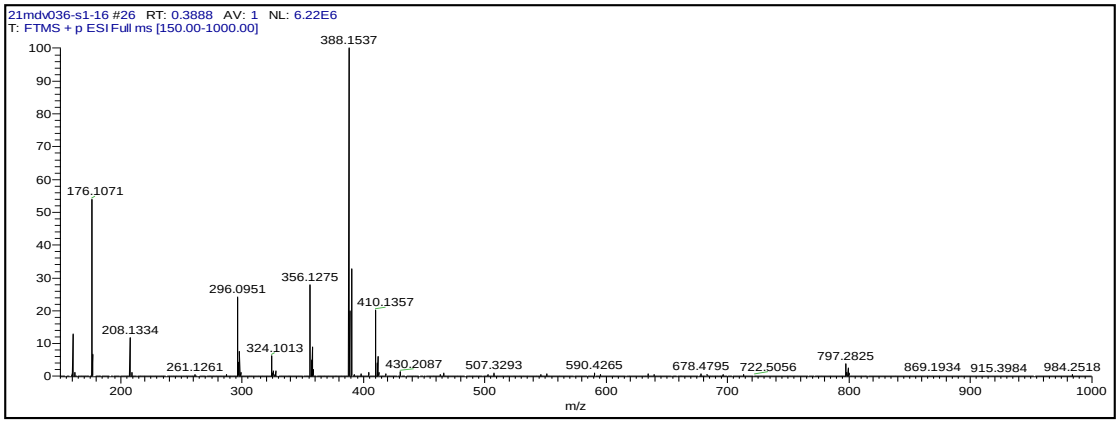



21mdv036-s1-15 #40 RT: 0.6130 AV: 1 NL: 2.01E6
T: FTMS + p ESI Full ms [150.00-1000.00]
430.2082
398.1821
452.1903
238.1074
369.1795
463.3029
207.0890
327.0081
270.1336
507.3289
590.4262
634.4525
678.4788
766.5315
810.5573
881.3918
951.3049
m/z

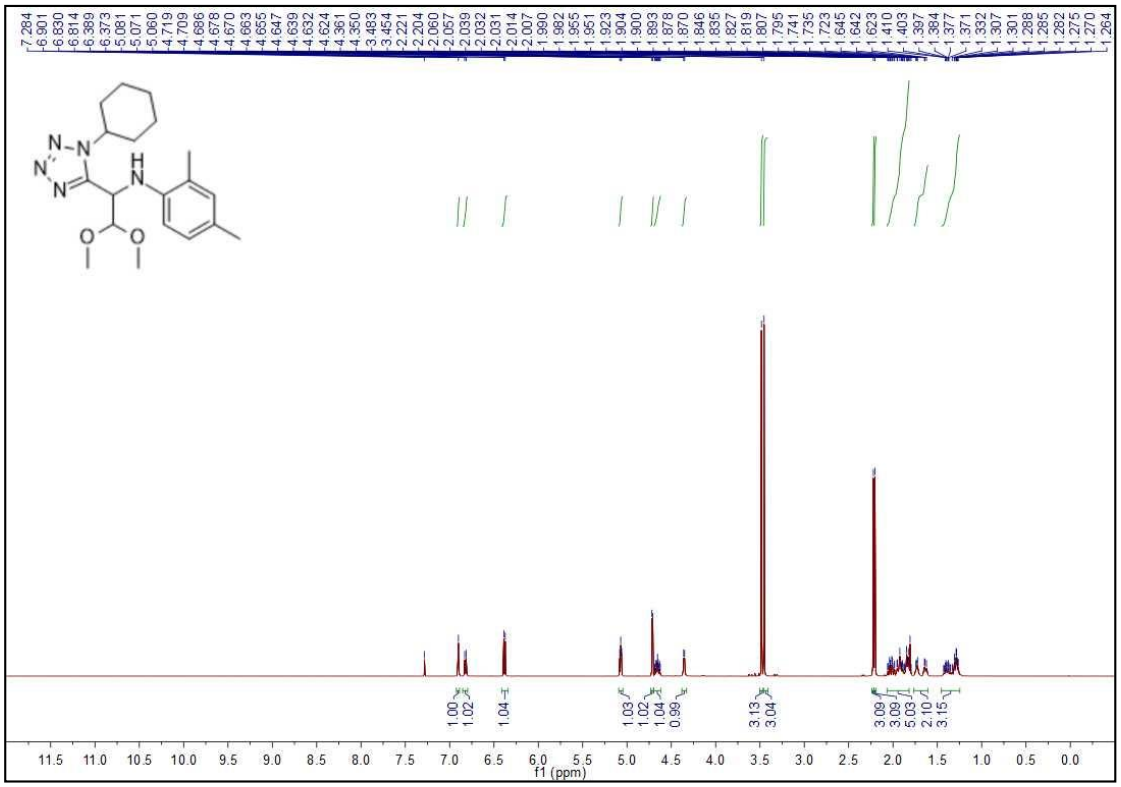
_N_-(1-(1-(4-chlorophenyl)-1_H_-tetrazol-5-yl)-2,2-dimethoxyethyl)-2,4-dimethylaniline (1p)

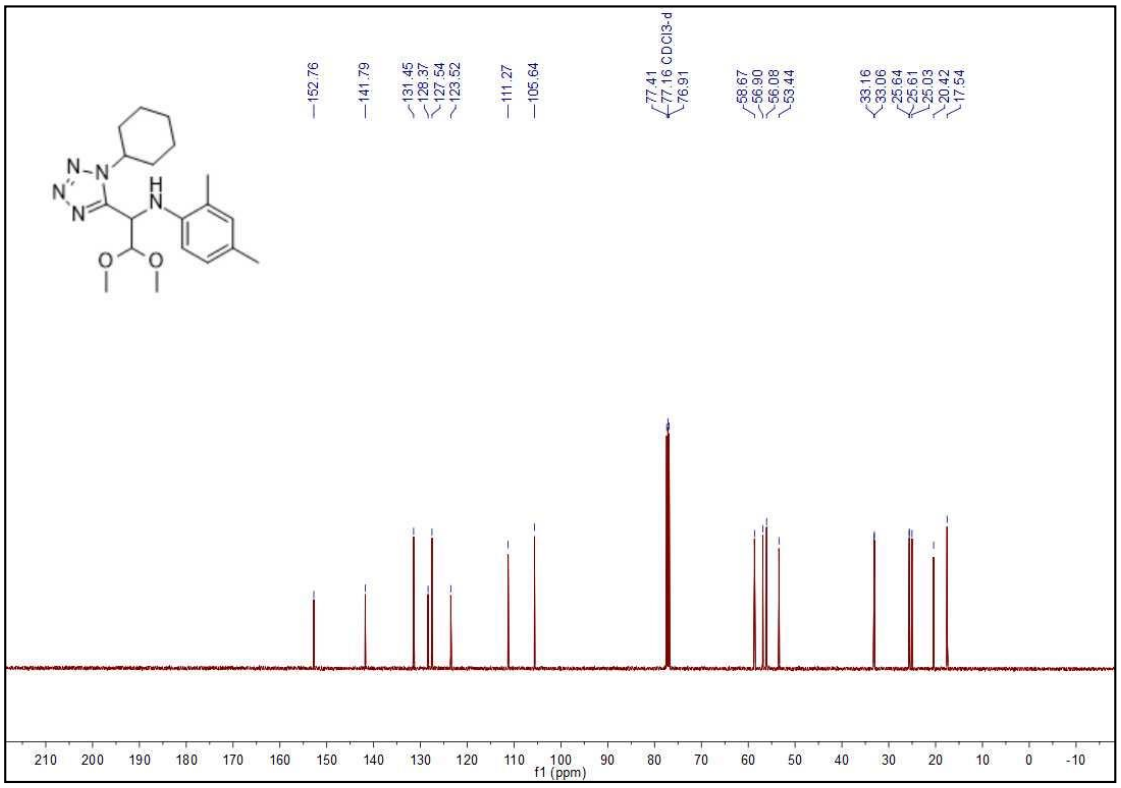


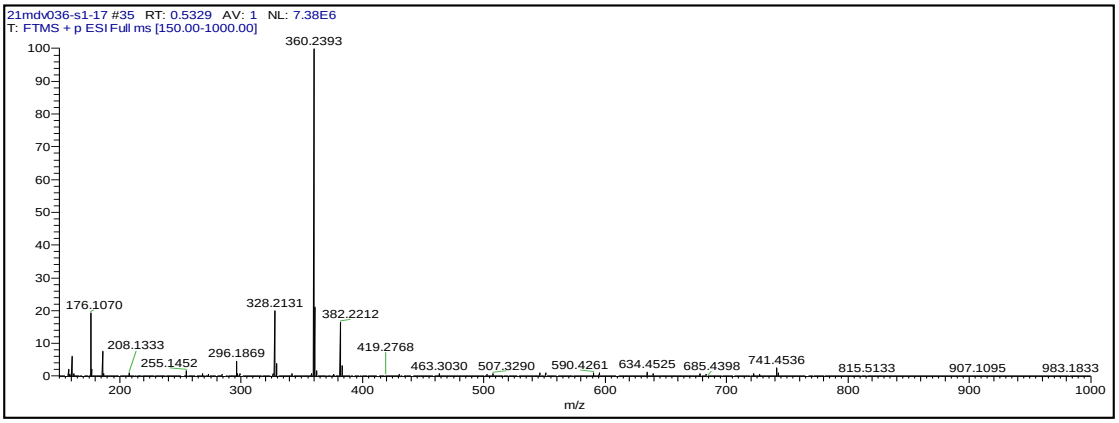



21mdv036-s1-16 #26 RT: 0.3888 AV: 1 NL: 6.22E6
T: FTMS + p ESI Full ms [150.00-1000.00]
388.1537
176.1071
296.0951
356.1275
410.1357
208.1334
324.1013
261.1261
430.2087
507.3293
590.4265
678.4795
722.5056
797.2825
869.1934
915.3984
984.2518
m/z

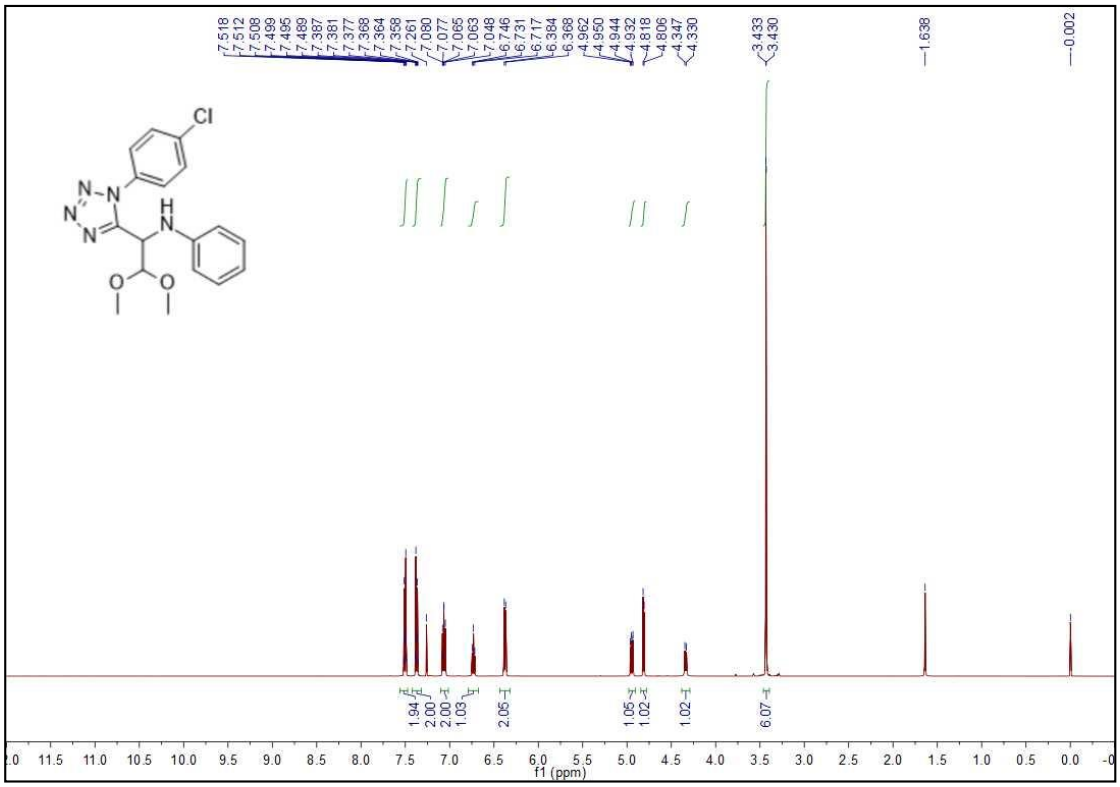
_N_-(1-(1-cyclohexyl-1_H_-tetrazol-5-yl)-2,2-dimethoxyethyl)-2,4-dimethylaniline (1q)

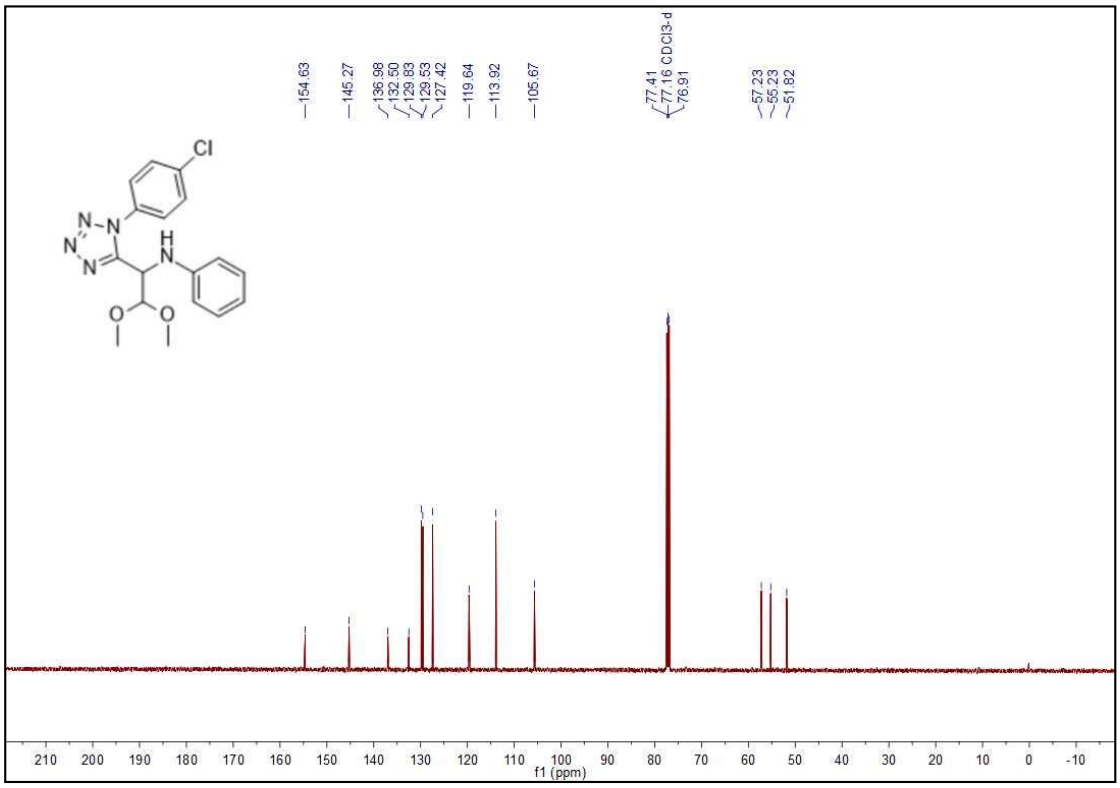


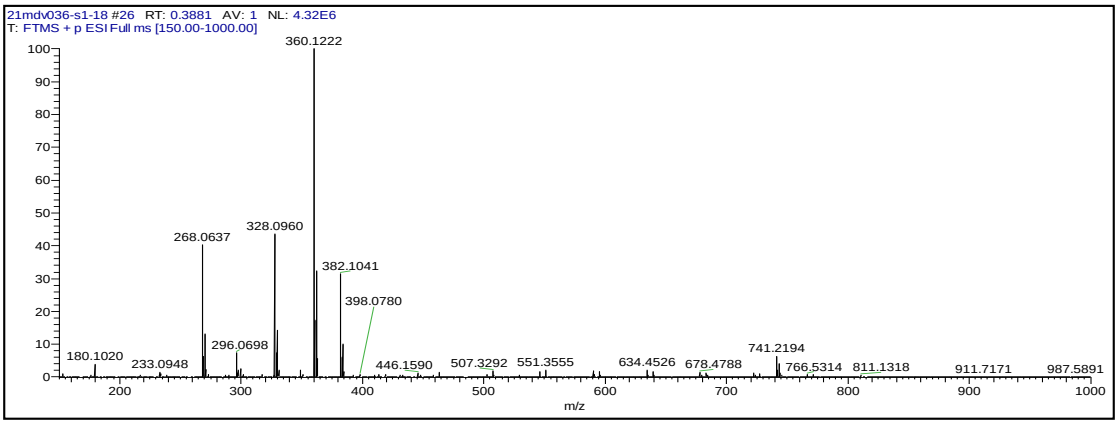



21mdv036-s1-17 #35 RT: 0.5329 AV: 1 NL: 7.38E6
T: FTMS + p ESI Full ms [150.00-1000.00]
360.2393
176.1070
328.2131
382.2212
208.1333
296.1869
419.2768
255.1452
463.3030
507.3290
590.4261
634.4525
685.4398
741.4536
815.5133
907.1095
983.1833
m/z

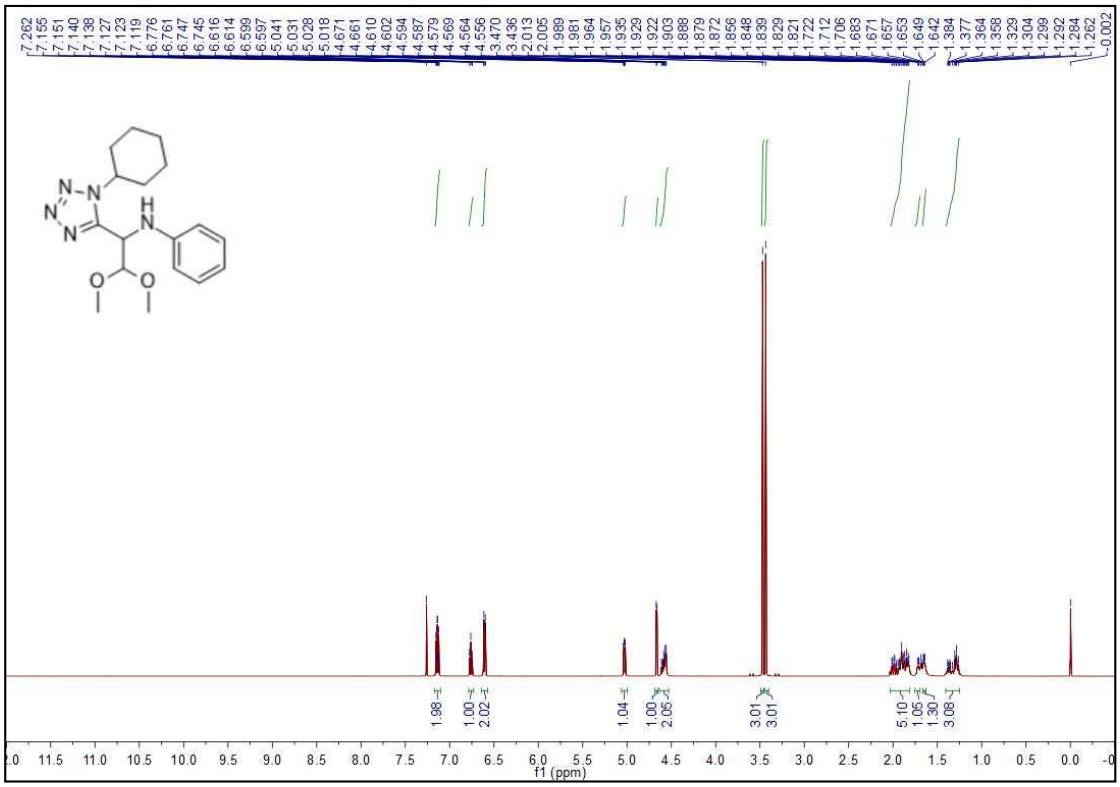
***N*-(1-(1-(4-chlorophenyl)-1*H*-tetrazol-5-yl)-2,2-dimethoxyethyl)aniline (1r)**

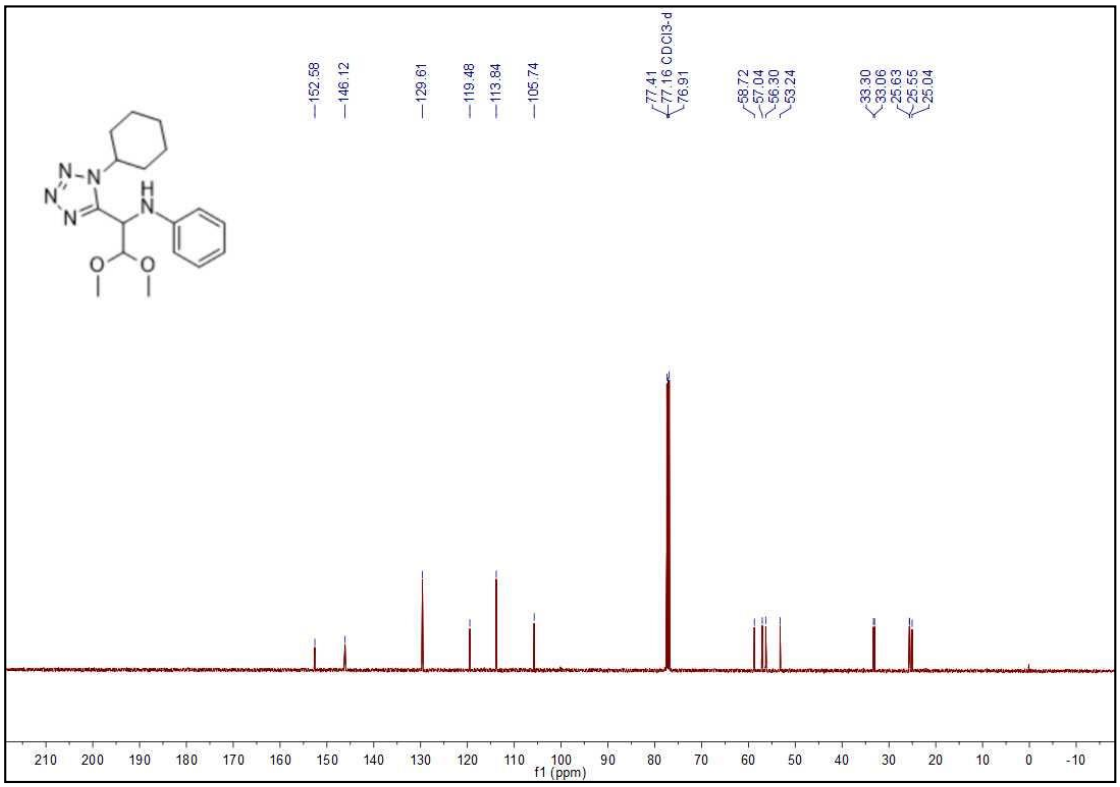


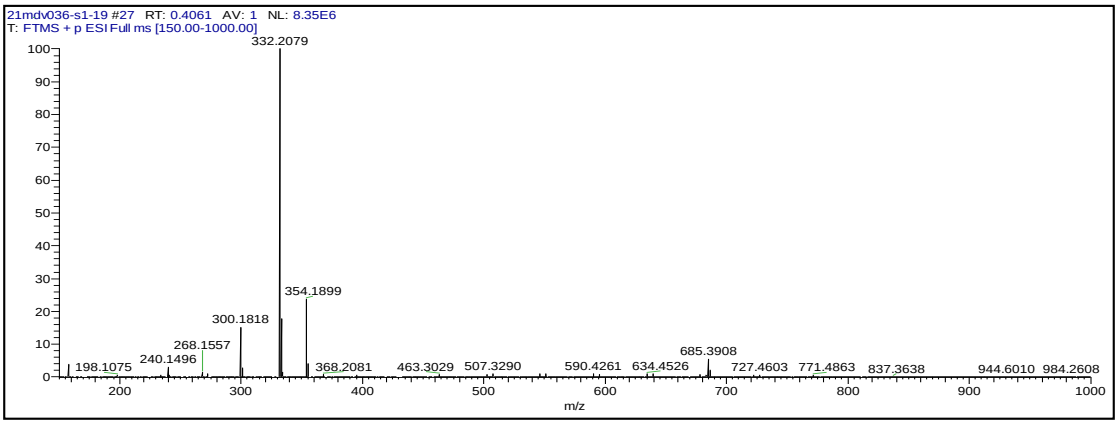



21mdv036-s1-18 #26 RT: 0.3881 AV: 1 NL: 4.32E6
T: FTMS + p ESI Full ms [150.00-1000.00]
360.1222
328.0960
268.0637
382.1041
398.0780
296.0698
180.1020
233.0948
446.1590
507.3292
551.3555
634.4526
678.4788
741.2194
766.5314
811.1318
911.7171
987.5891
m/z

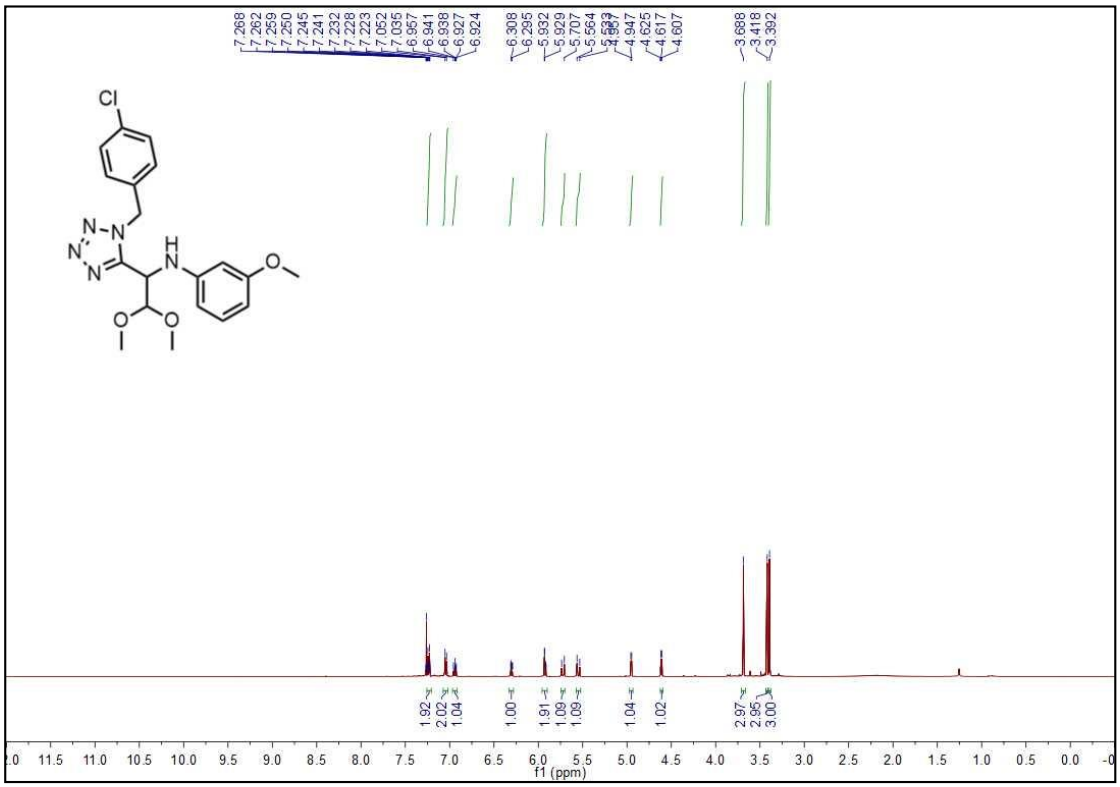
_N_-(1-(1-cyclohexyl-1_H_-tetrazol-5-yl)-2,2-dimethoxyethyl)aniline (1s)

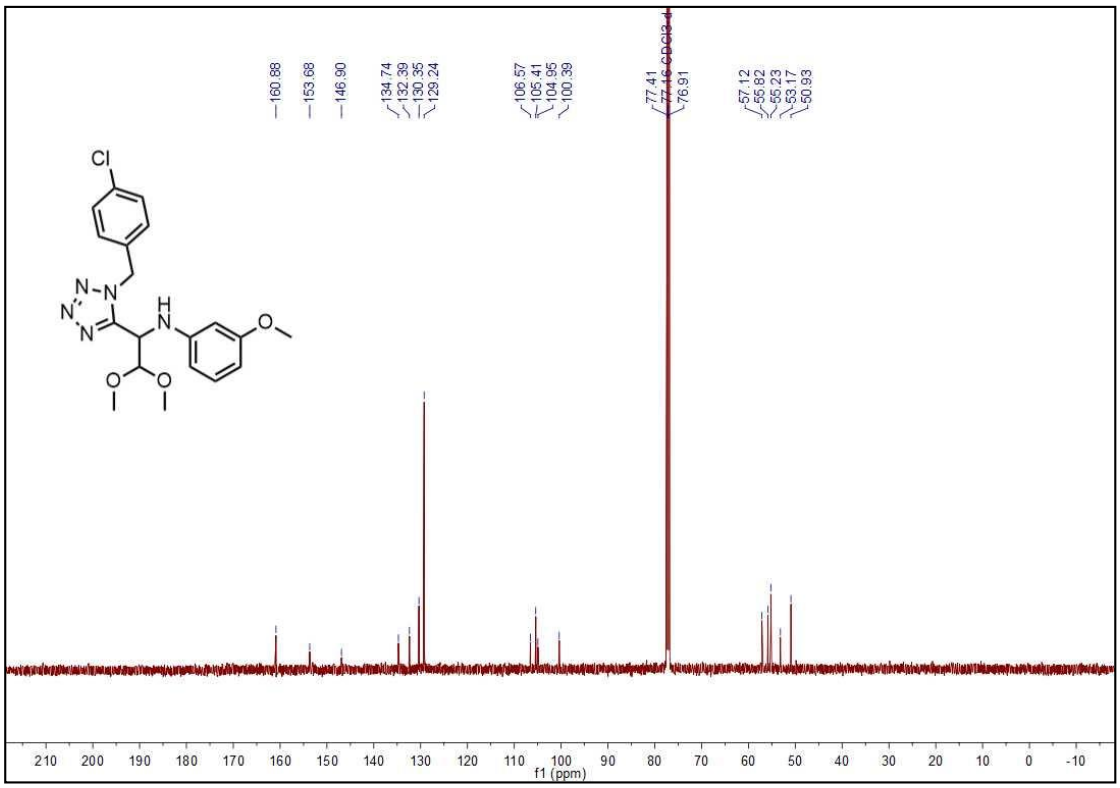


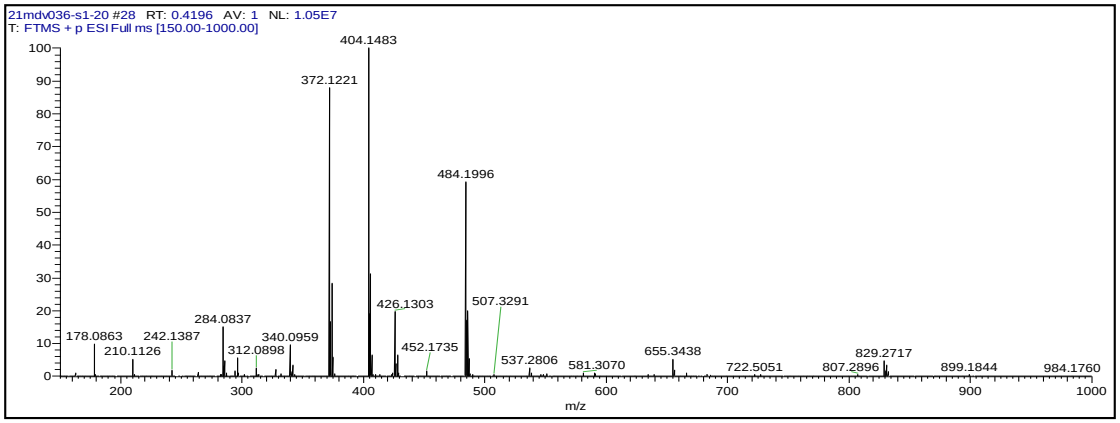



21mdv036-s1-19 #27 RT: 0.4061 AV: 1 NL: 8.35E6
T: FTMS + p ESI Full ms [150.00-1000.00]
332.2079
354.1899
300.1818
268.1557
240.1496
198.1075
368.2081
463.3029
507.3290
590.4261
634.4526
685.3908
727.4603
771.4863
837.3638
944.6010
984.2608
m/z

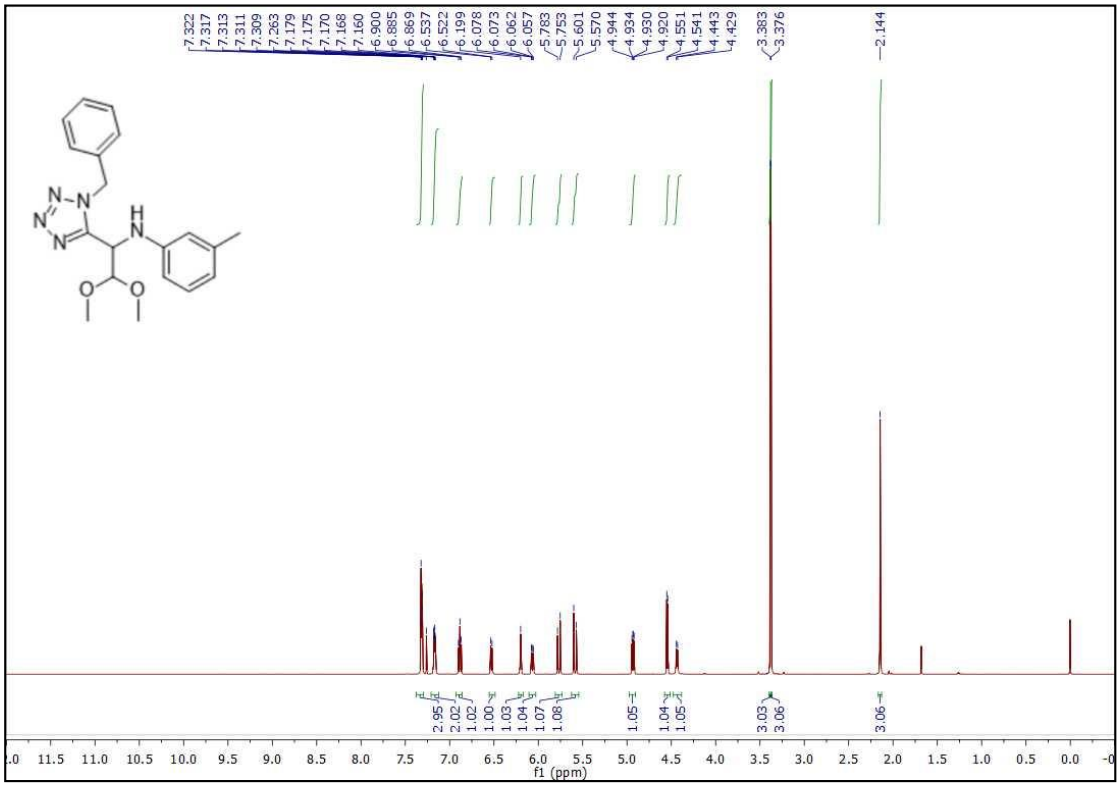
_N_-(1-(1-(4-chlorobenzyl)-1_H_-tetrazol-5-yl)-2,2-dimethoxyethyl)-3-methoxyaniline (1t)

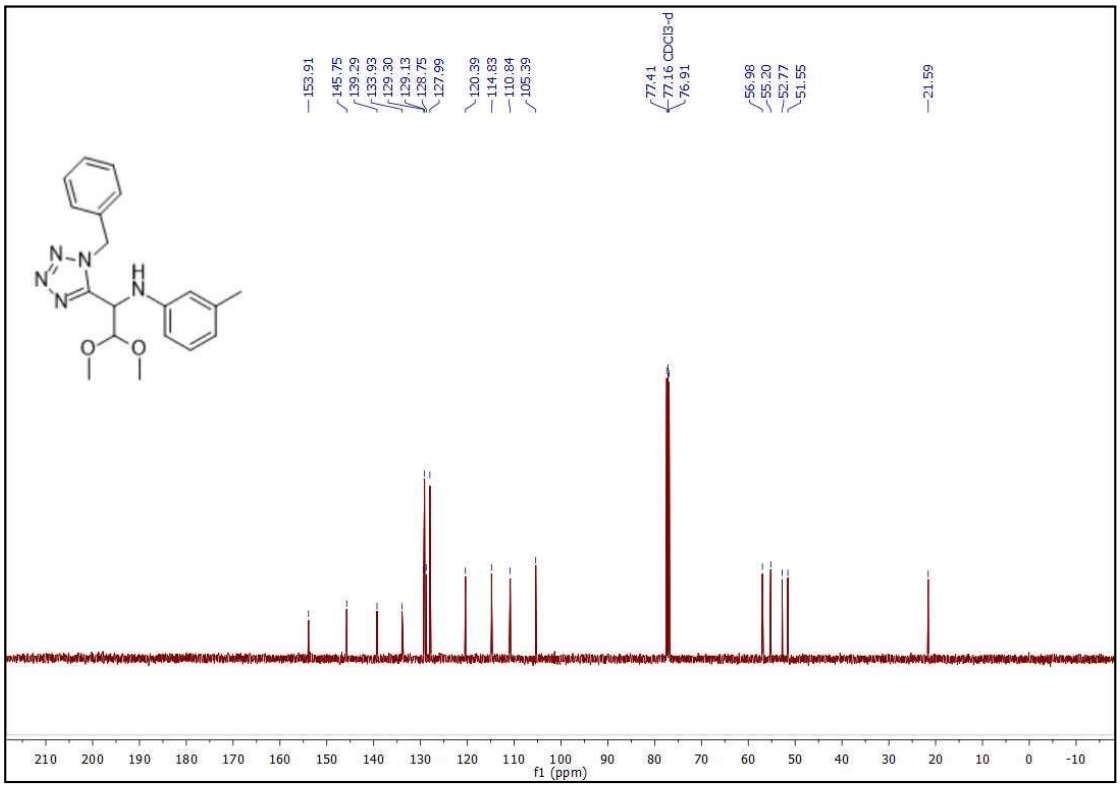


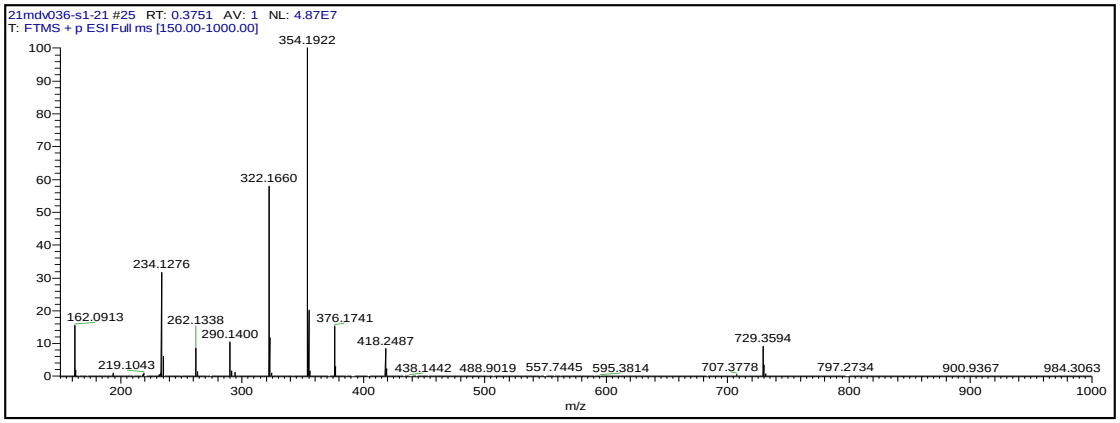



21mdv036-s1-20 #28 RT: 0.4196 AV: 1 NL: 1.05E7
T: FTMS + p ESI Full ms [150.00-1000.00]
404.1483
372.1221
484.1996
426.1303
507.3291
284.0837
178.0863
242.1387
340.0959
210.1126
312.0898
452.1735
537.2806
581.3070
655.3438
722.5051
829.2717
807.2896
899.1844
984.1760
m/z

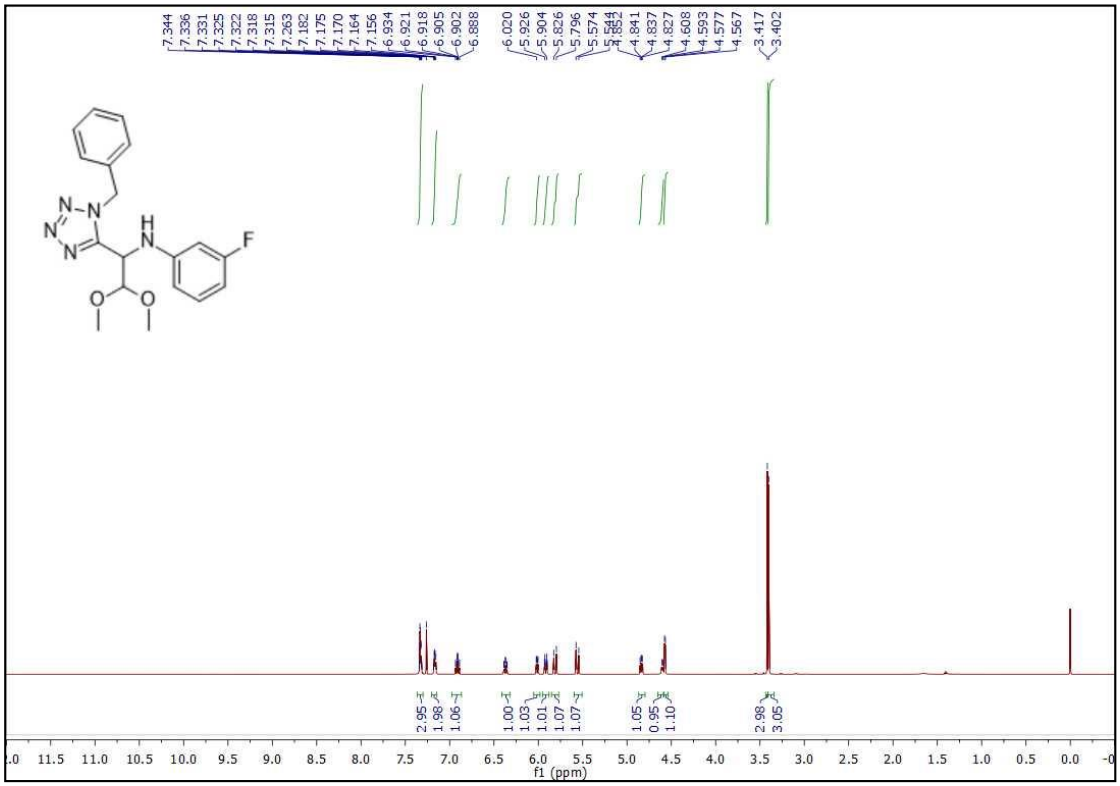
_N_-(1-(1-benzyl-1_H_-tetrazol-5-yl)-2,2-dimethoxyethyl)-3-methylaniline (1u)

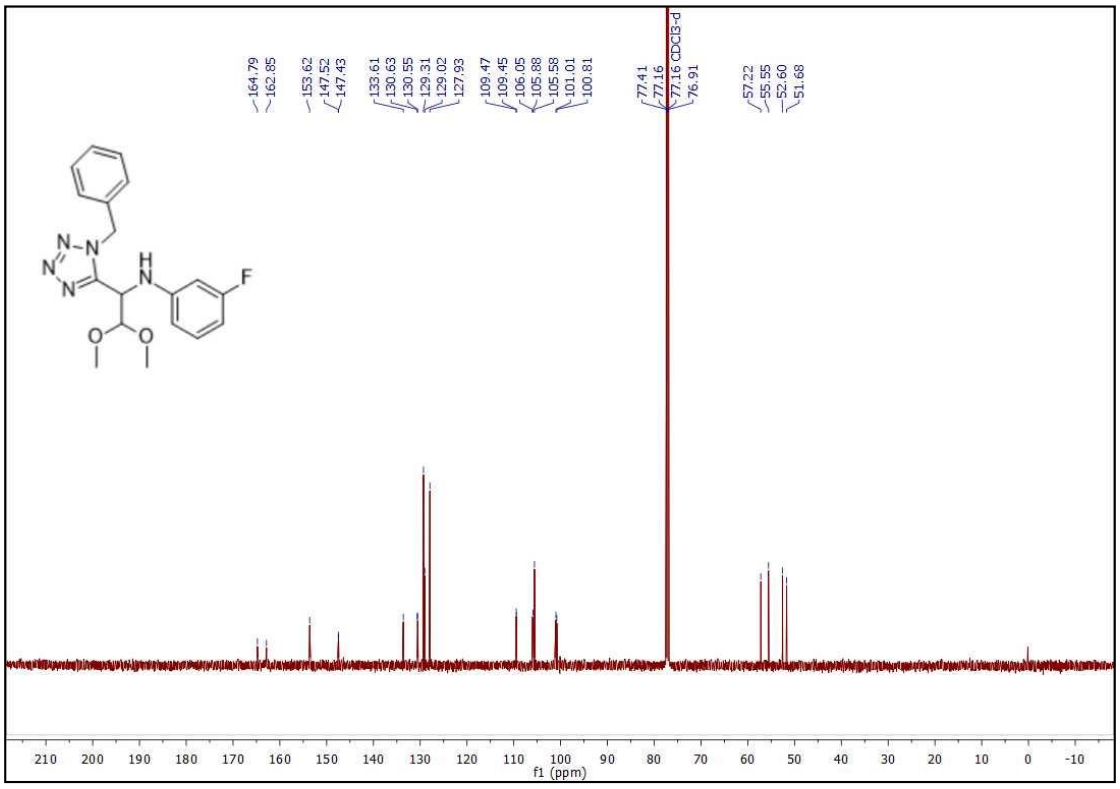


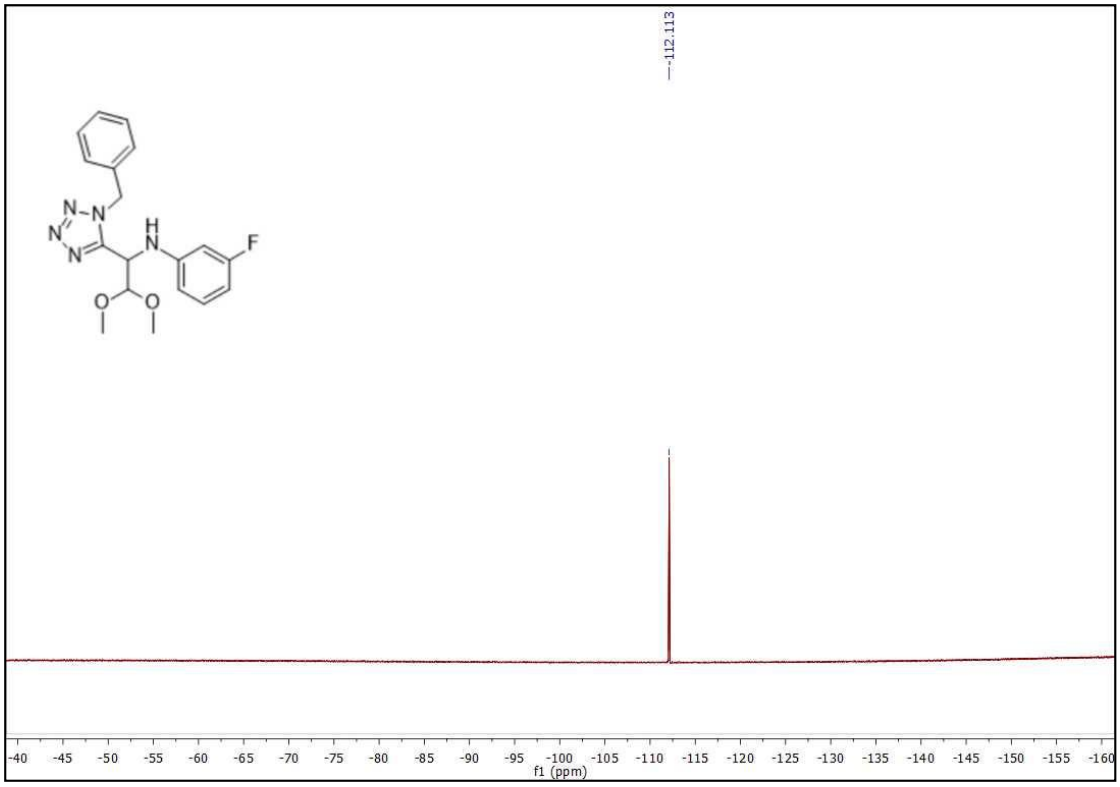


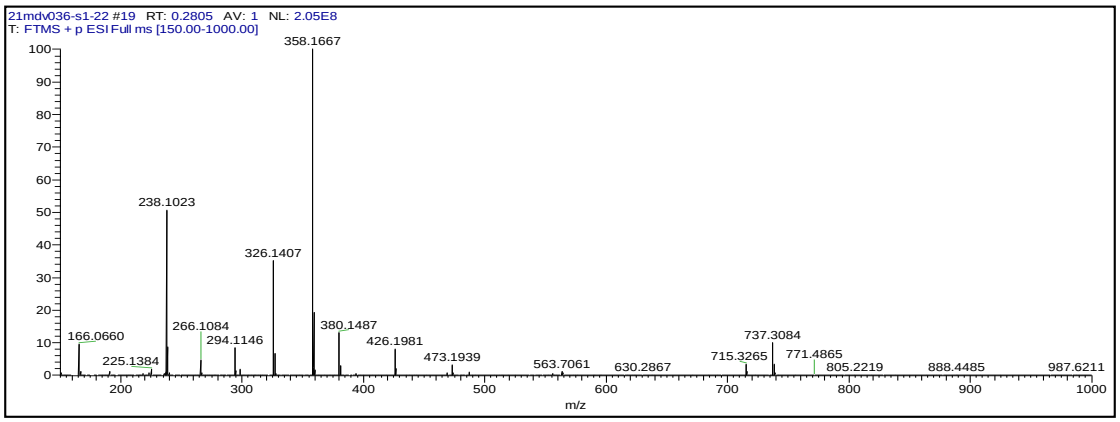

21mdv036-s1-21 #25 RT: 0.3751 AV: 1 NL: 4.87E7
T: FTMS + p ESI Full ms [150.00-1000.00]
354.1922
322.1660
234.1276
162.0913
262.1338
290.1400
376.1741
418.2487
729.3594
219.1043
438.1442
488.9019
557.7445
595.3814
707.3778
797.2734
900.9367
984.3063
m/z

_N_-(1-(1-benzyl-1_H_-tetrazol-5-yl)-2,2-dimethoxyethyl)-3-fluoroaniline (1v)

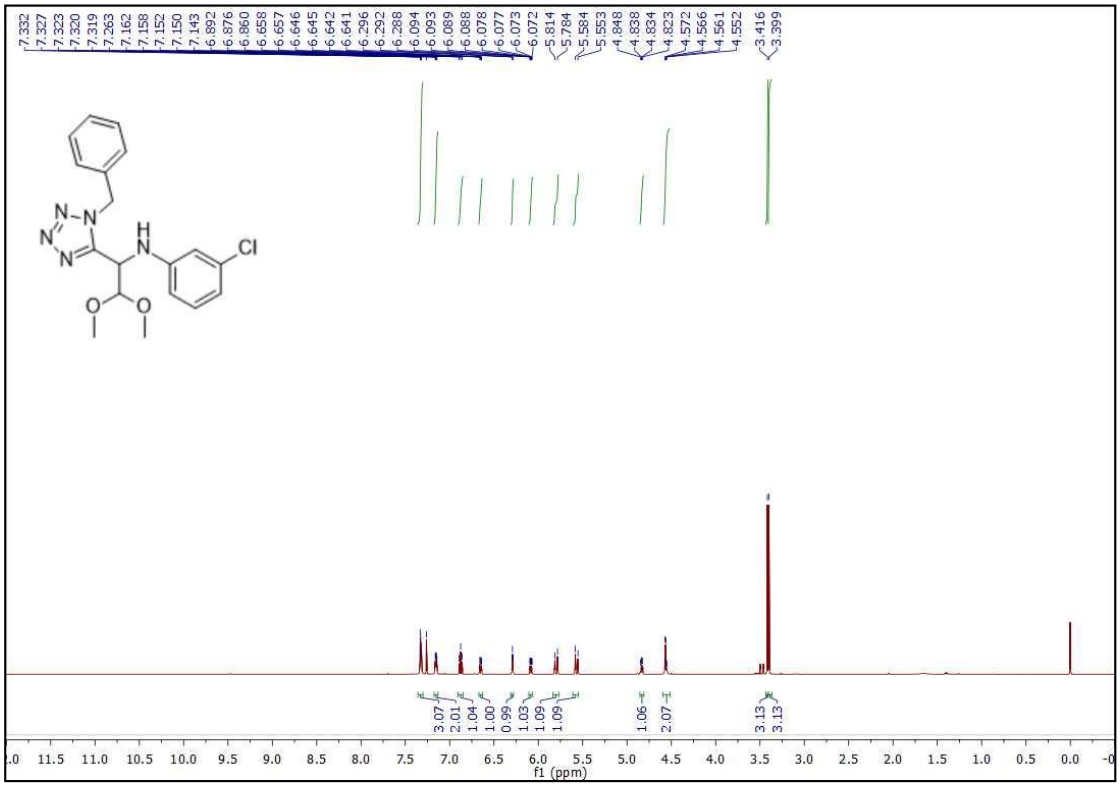


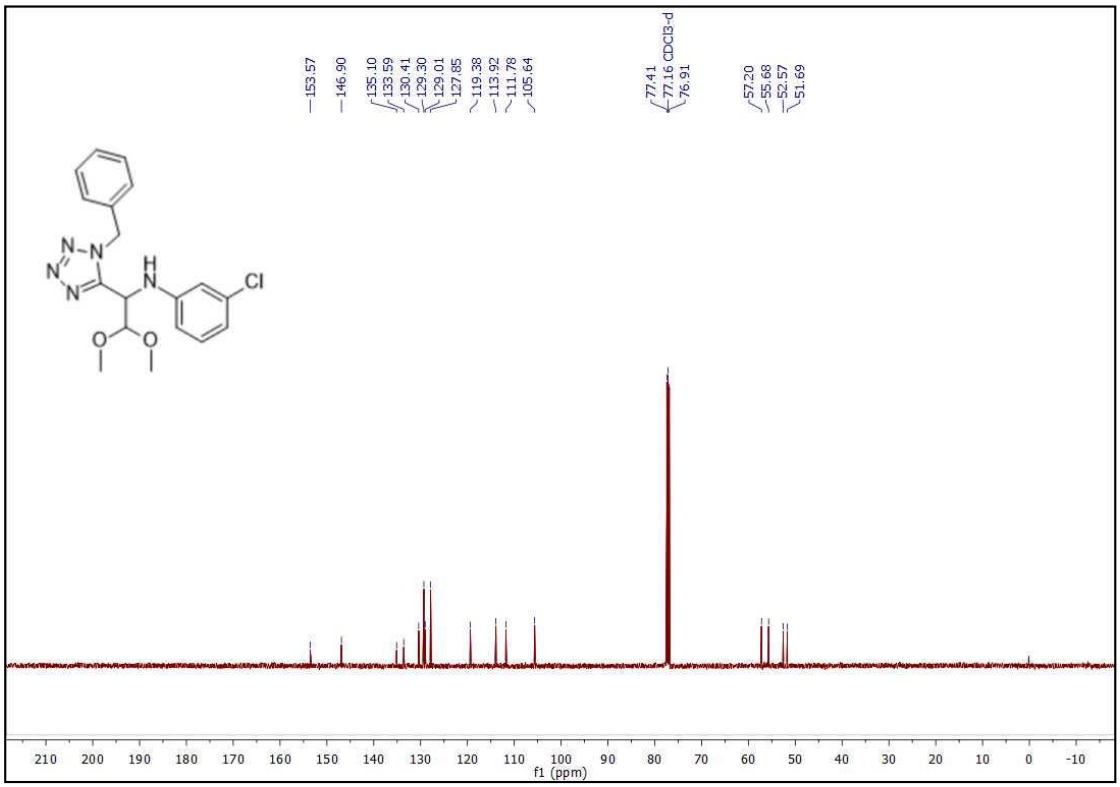


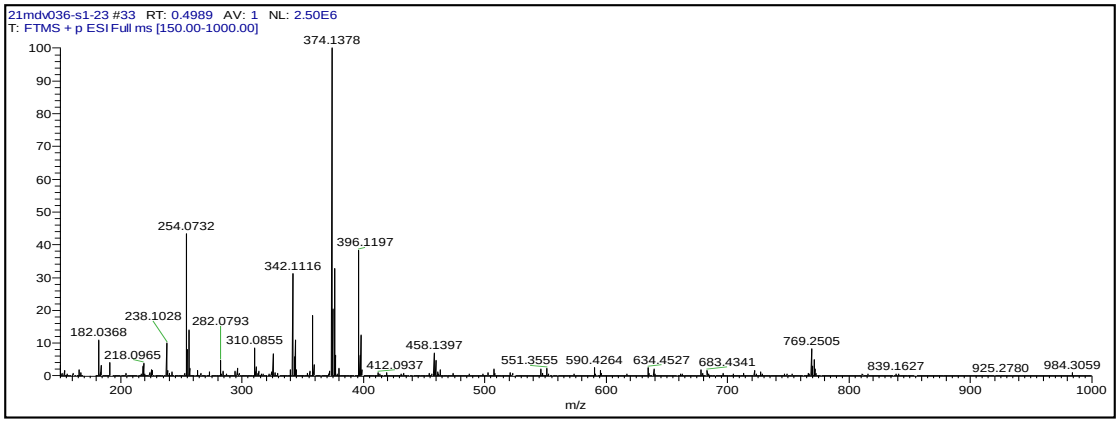

-112.113
N
N
N
H
N
F
O
O
-40 -45 -50 -55 -60 -65 -70 -75 -80 -85 -90 -95 -100 -105 -110 -115 -120 -125 -130 -135 -140 -145 -150 -155 -160
f1 (ppm)


21mdv036-s1-22 #19 RT: 0.2805 AV: 1 NL: 2.05E8
T: FTMS + p ESI Full ms [150.00-1000.00]
358.1667
238.1023
326.1407
166.0660
266.1084
294.1146
380.1487
426.1981
225.1384
473.1939
563.7061
630.2867
737.3084
715.3265
771.4865
805.2219
888.4485
987.6211
m/z

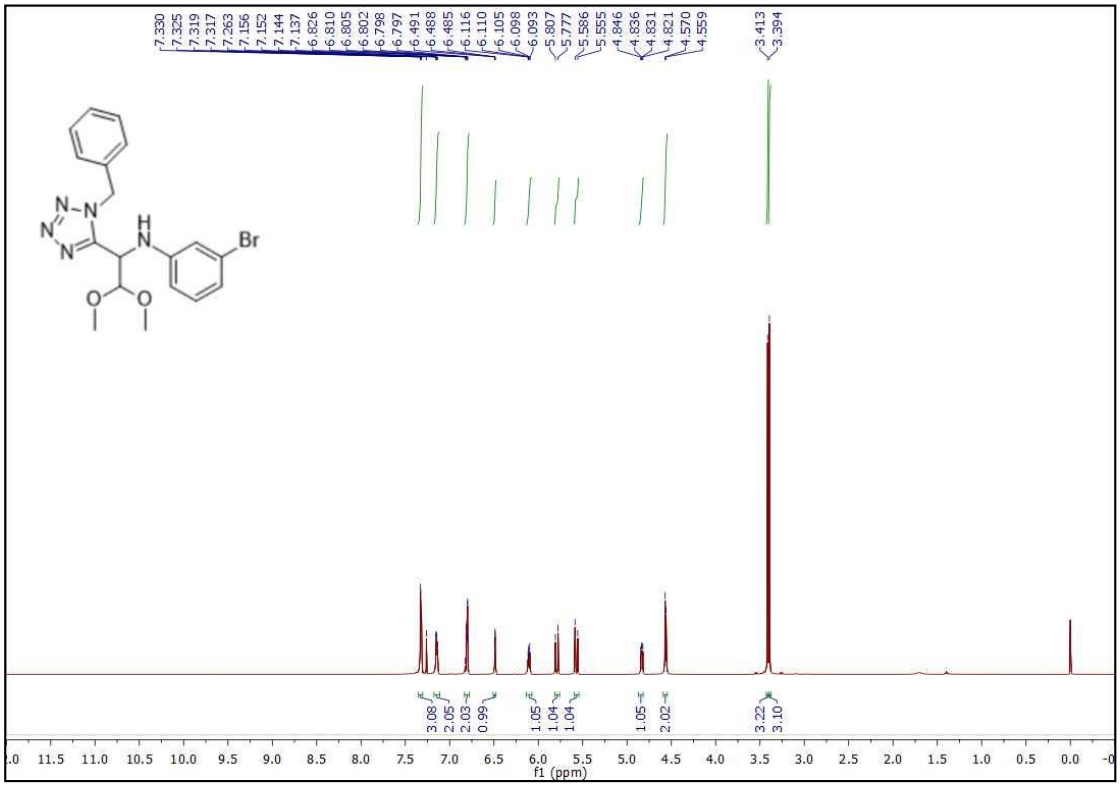
N-(1-(1-benzyl-1*H*-tetrazol-5-yl)-2,2-dimethoxyethyl)-3-chloroaniline (1w)

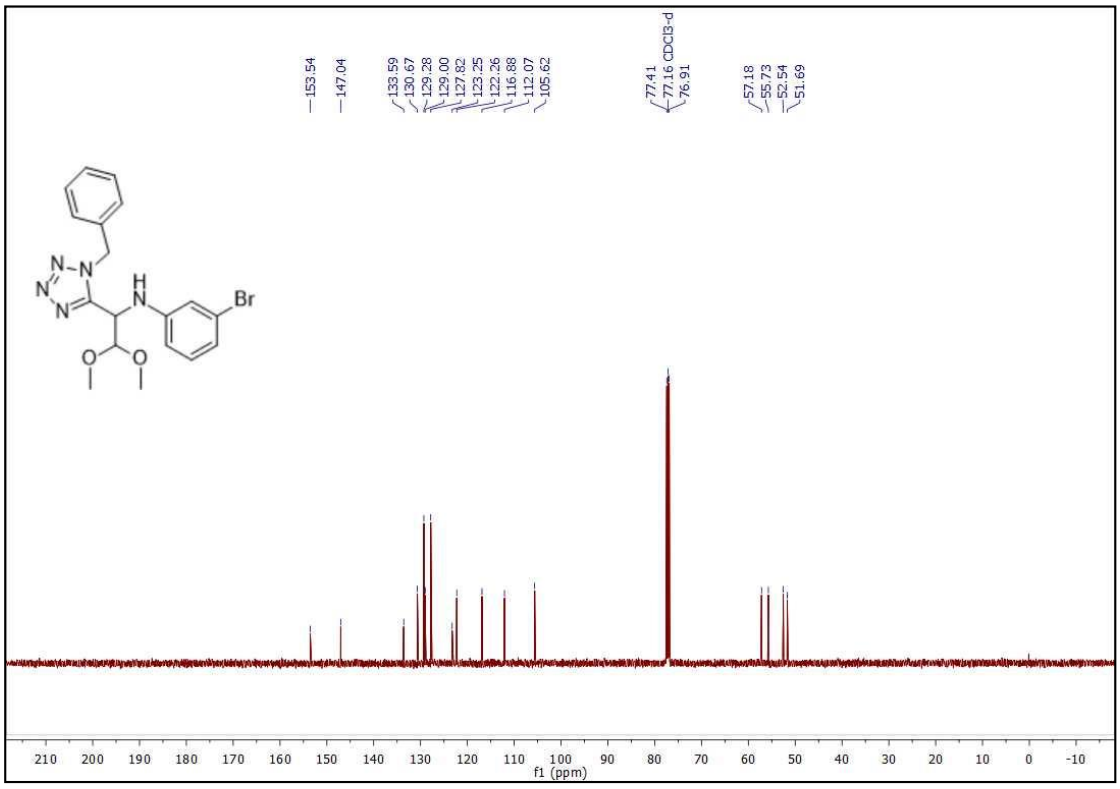


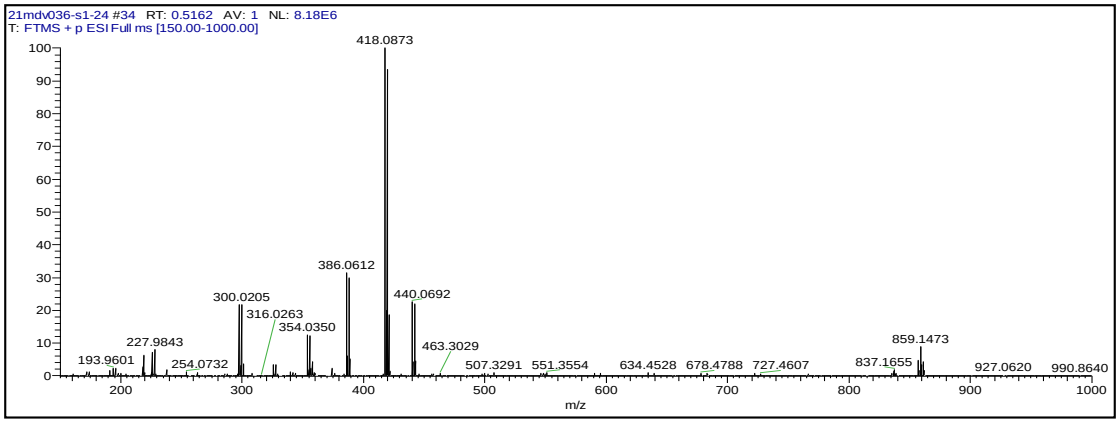



21mdv036-s1-23 #33 RT: 0.4989 AV: 1 NL: 2.50E6
T: FTMS + p ESI Full ms [150.00-1000.00]
374.1378
254.0732
396.1197
342.1116
238.1028
282.0793
182.0368
310.0855
218.0965
458.1397
412.0937
551.3555
590.4264
634.4527
683.4341
769.2505
839.1627
925.2780
984.3059
m/z

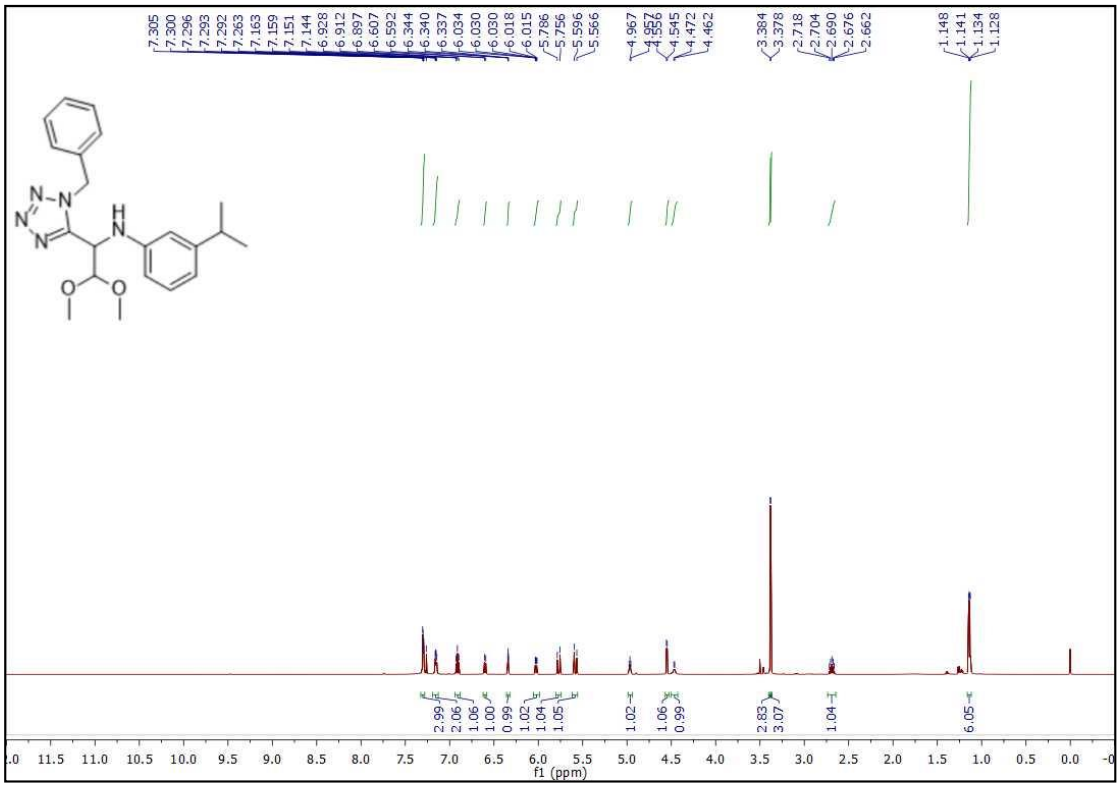
_N_-(1-(1-benzyl-1_H_-tetrazol-5-yl)-2,2-dimethoxyethyl)-3-bromoaniline (1x)

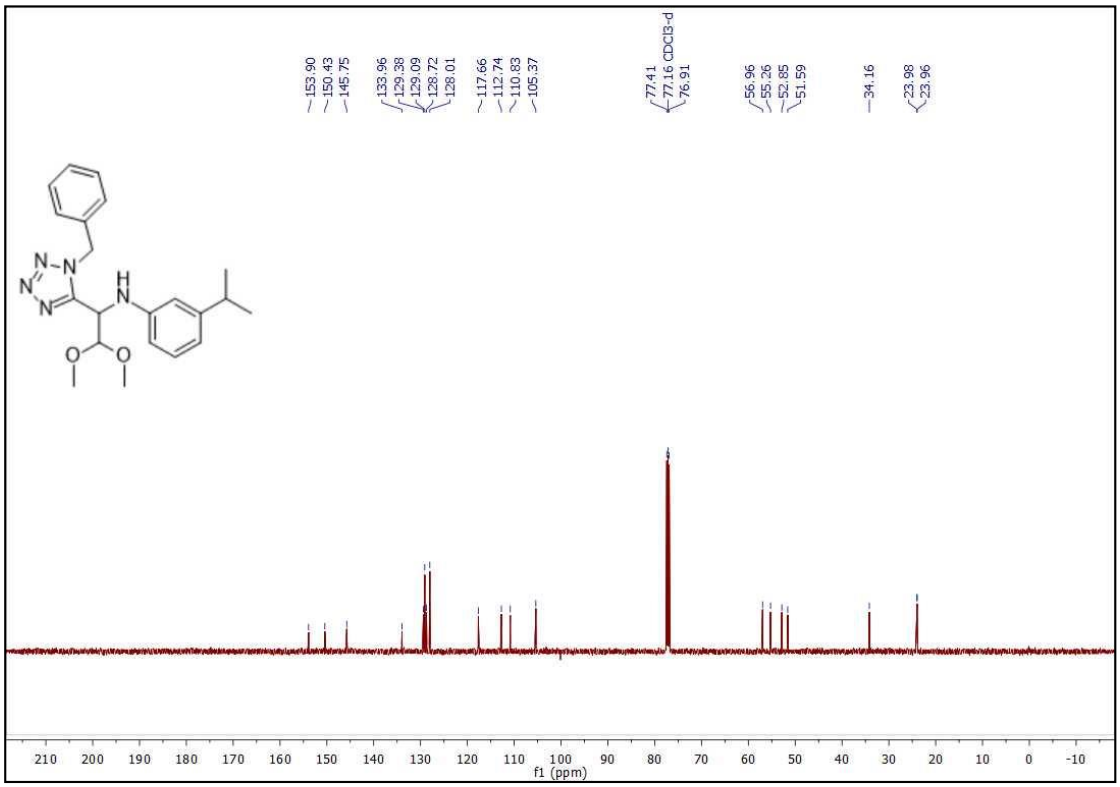


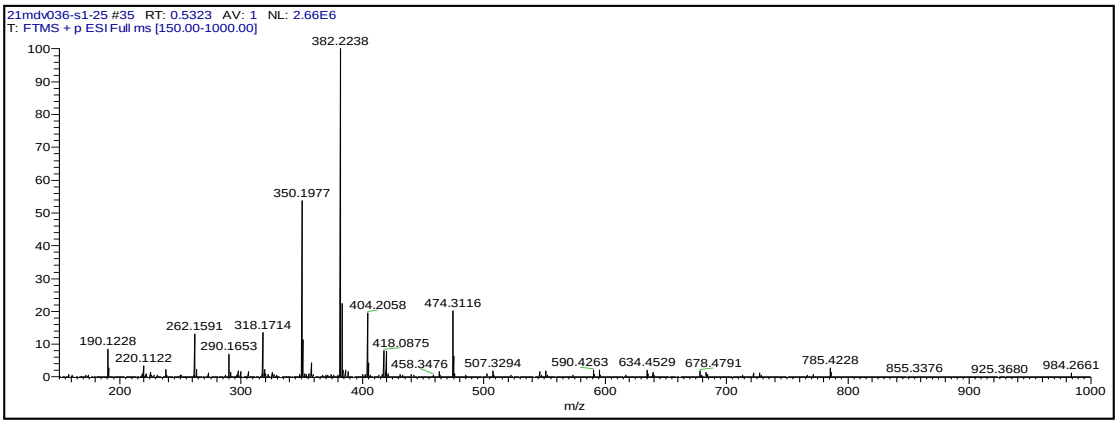



21mdv036-s1-24 #34 RT: 0.5162 AV: 1 NL: 8.18E6
T: FTMS + p ESI Full ms [150.00-1000.00]
418.0873
386.0612
300.0205
316.0263
354.0350
440.0692
227.9843
193.9601
254.0732
463.3029
507.3291
551.3554
634.4528
678.4788
727.4607
837.1655
859.1473
927.0620
990.8640
m/z

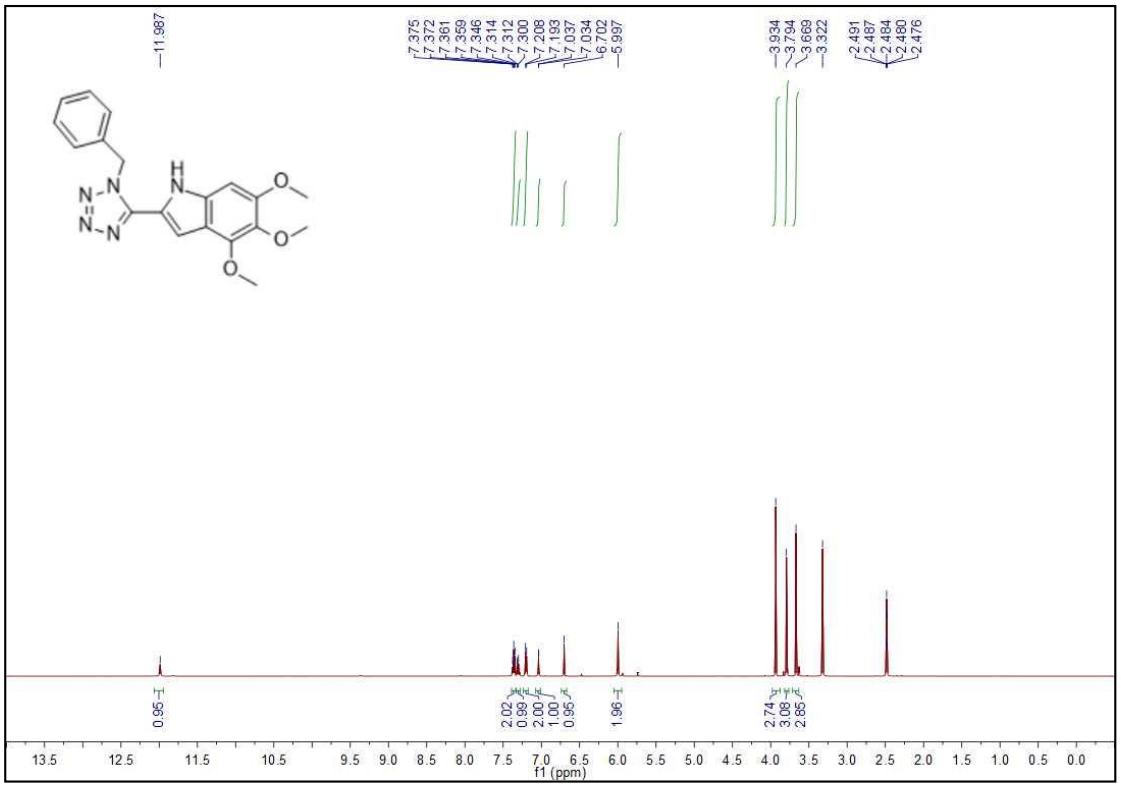
_N_-(1-(1-benzyl-1_H_-tetrazol-5-yl)-2,2-dimethoxyethyl)-3-isopropylaniline (1y)

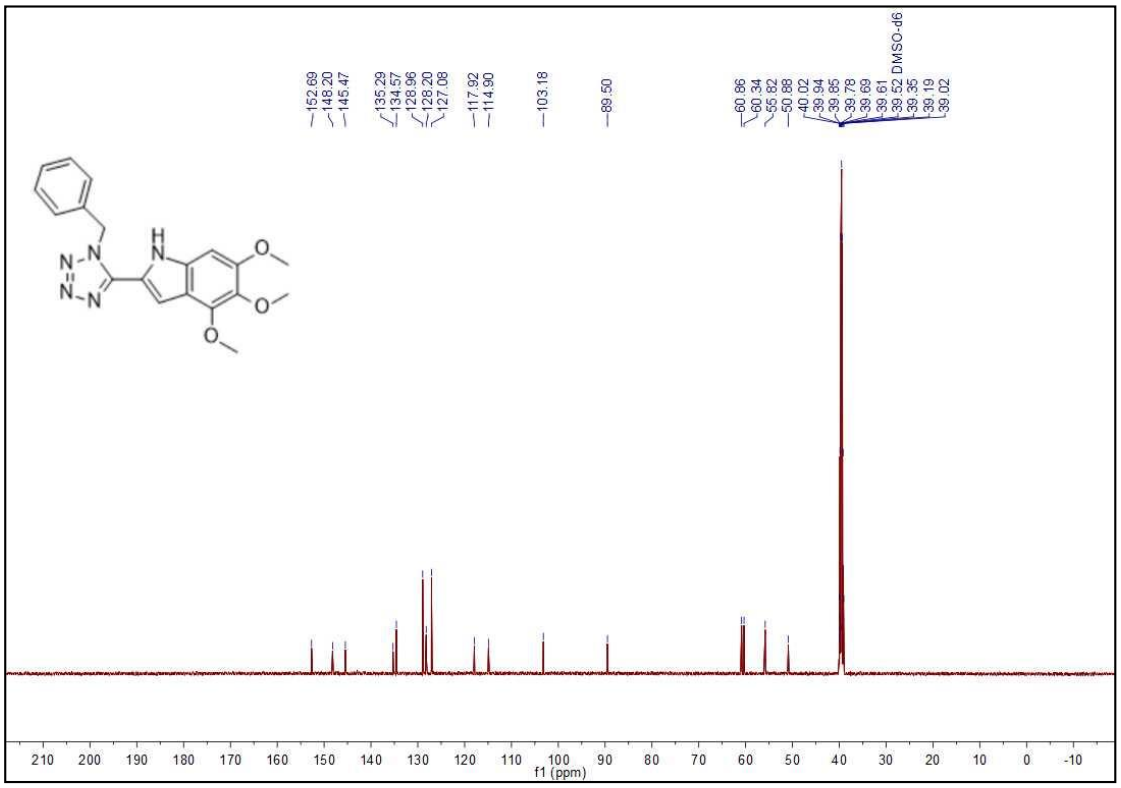


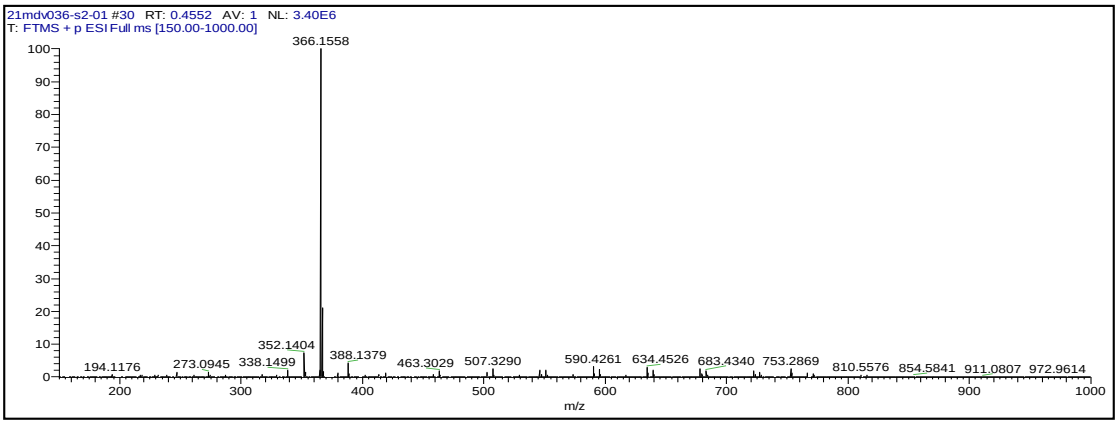



21mdv036-s1-25 #35 RT: 0.5323 AV: 1 NL: 2.66E6
T: FTMS + p ESI Full ms [150.00-1000.00]
382.2238
350.1977
404.2058
474.3116
262.1591
318.1714
190.1228
290.1653
418.0875
220.1122
458.3476
507.3294
590.4263
634.4529
678.4791
785.4228
855.3376
925.3680
984.2661
m/z

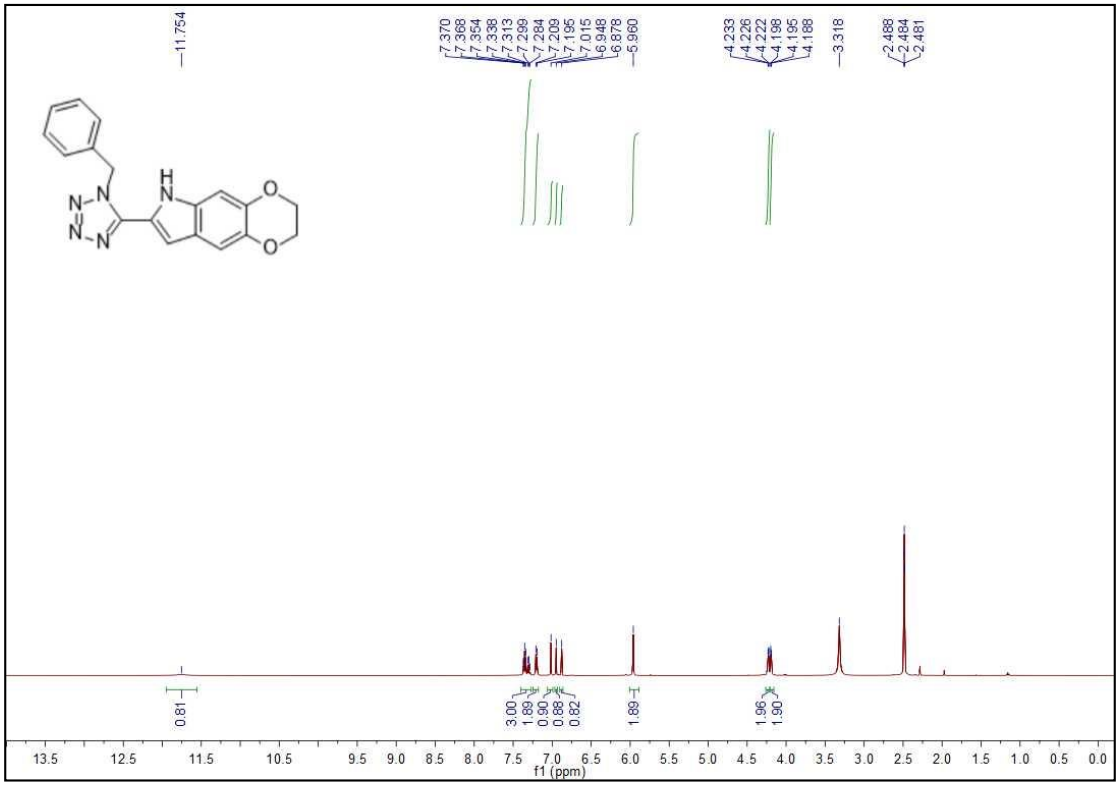
2-(1-benzyl-1*H*-tetrazol-5-yl)-4,5,6-trimethoxy-1*H*-indole (2a)

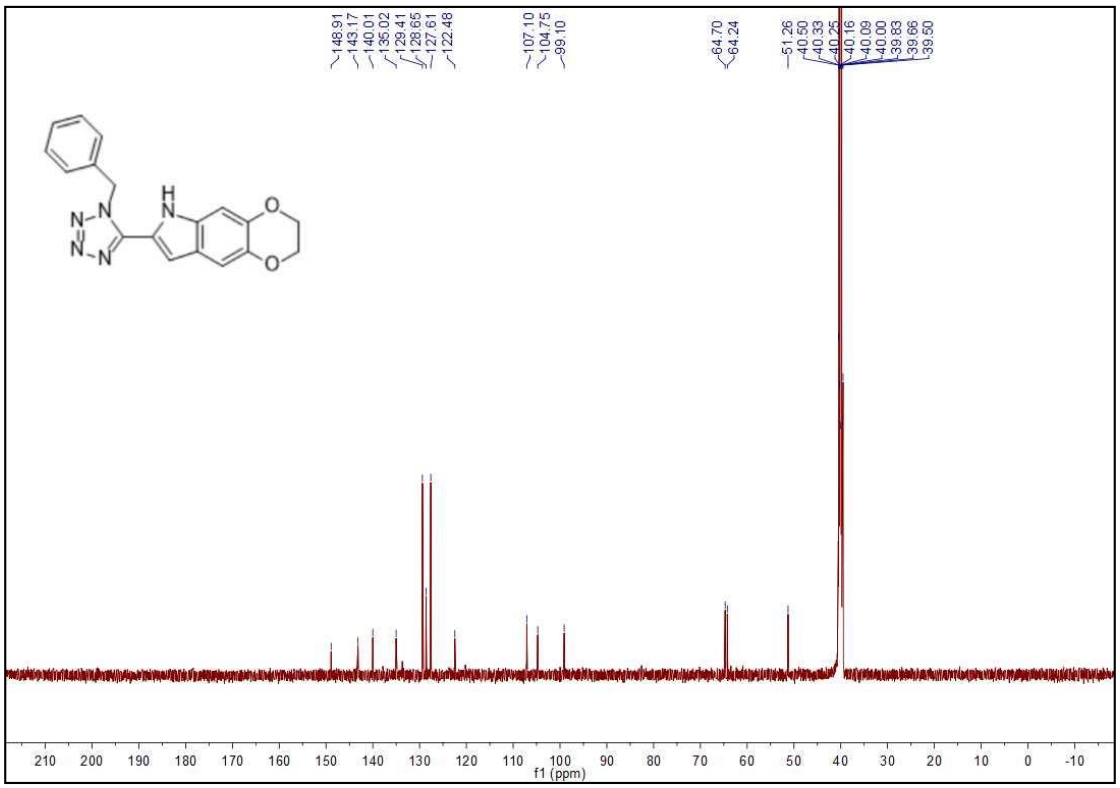


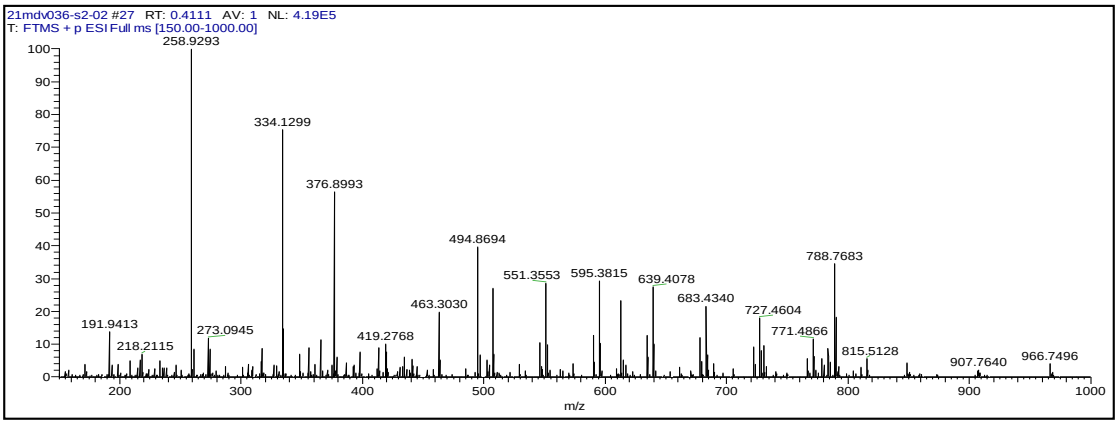



21mdv036-s2-01 #30 RT: 0.4552 AV: 1 NL: 3.40E6
T: FTMS + p ESI Full ms [150.00-1000.00]
366.1558
352.1404
388.1379
194.1176
273.0945
338.1499
463.3029
507.3290
590.4261
634.4526
683.4340
753.2869
810.5576
854.5841
911.0807
972.9614
m/z

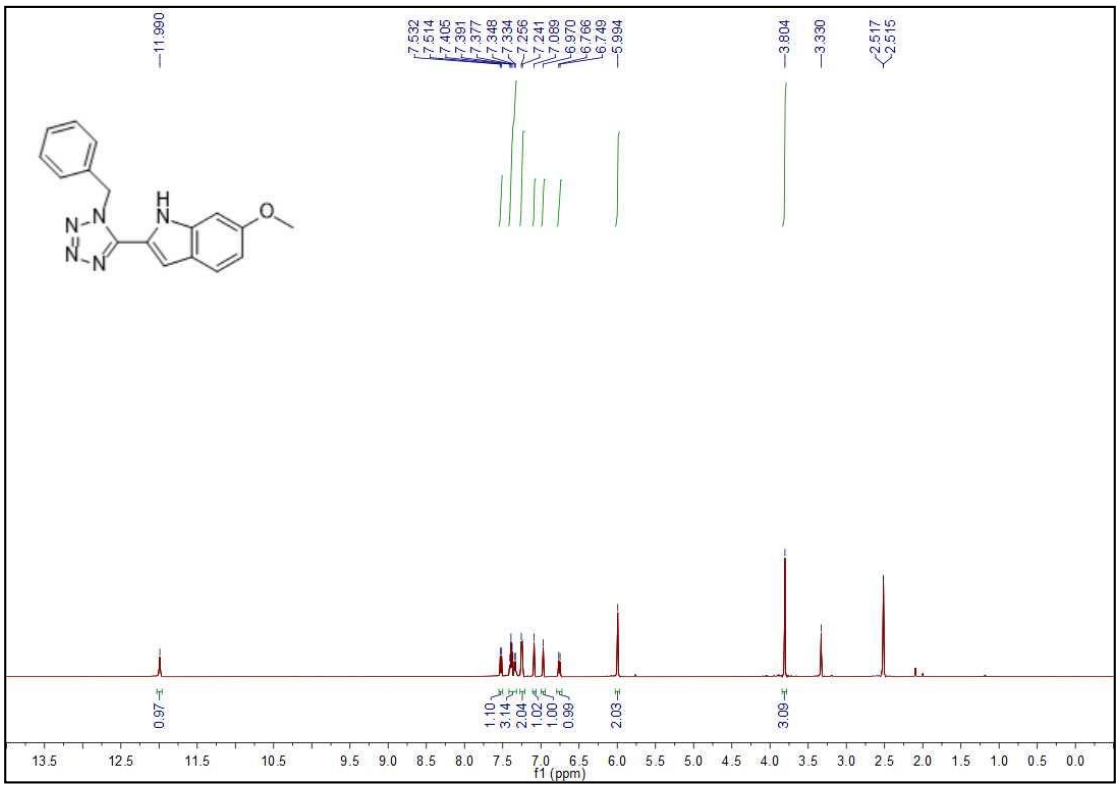
7-(1-benzyl-1*H*-tetrazol-5-yl)-3,6-dihydro-2*H*-[1,4]dioxino[2,3-*f*]indole (2b-1)

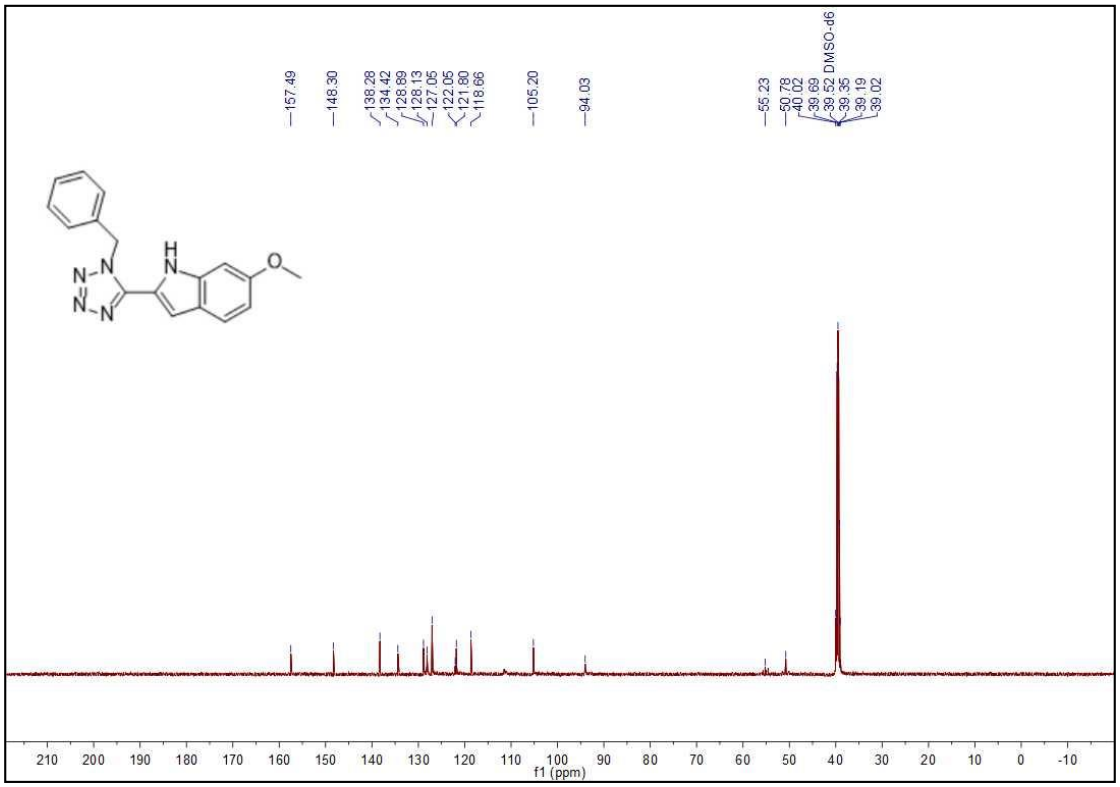


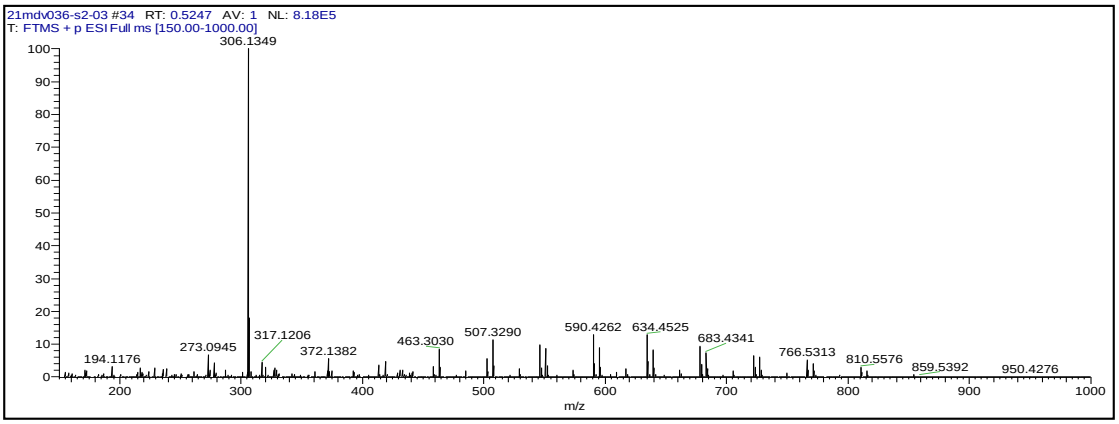



21mdv036-s2-02 #27 RT: 0.4111 AV: 1 NL: 4.19E5
T: FTMS + p ESI Full ms [150.00-1000.00]
258.9293
334.1299
376.8993
494.8694
788.7683
551.3553
595.3815
639.4078
683.4340
727.4604
463.3030
771.4866
191.9413
218.2115
273.0945
419.2768
815.5128
907.7640
966.7496
m/z

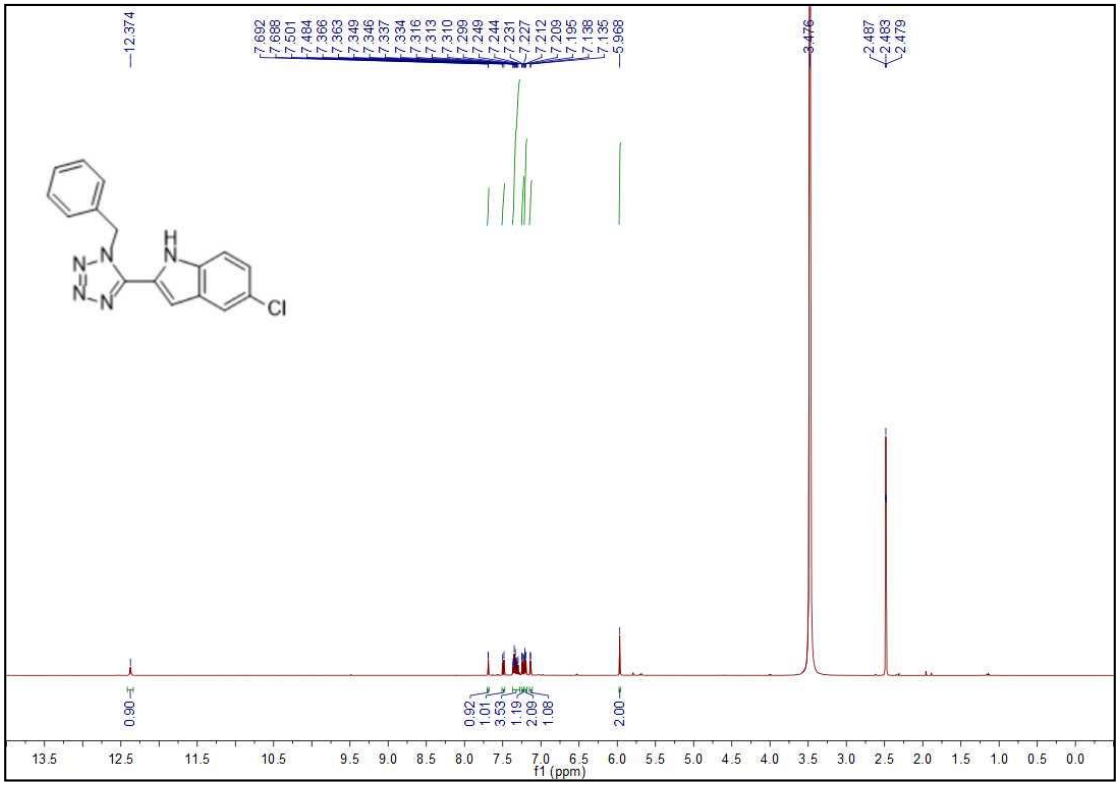
2-(1-benzyl-1*H*-tetrazol-5-yl)-6-methoxy-1*H*-indole (2c-1)

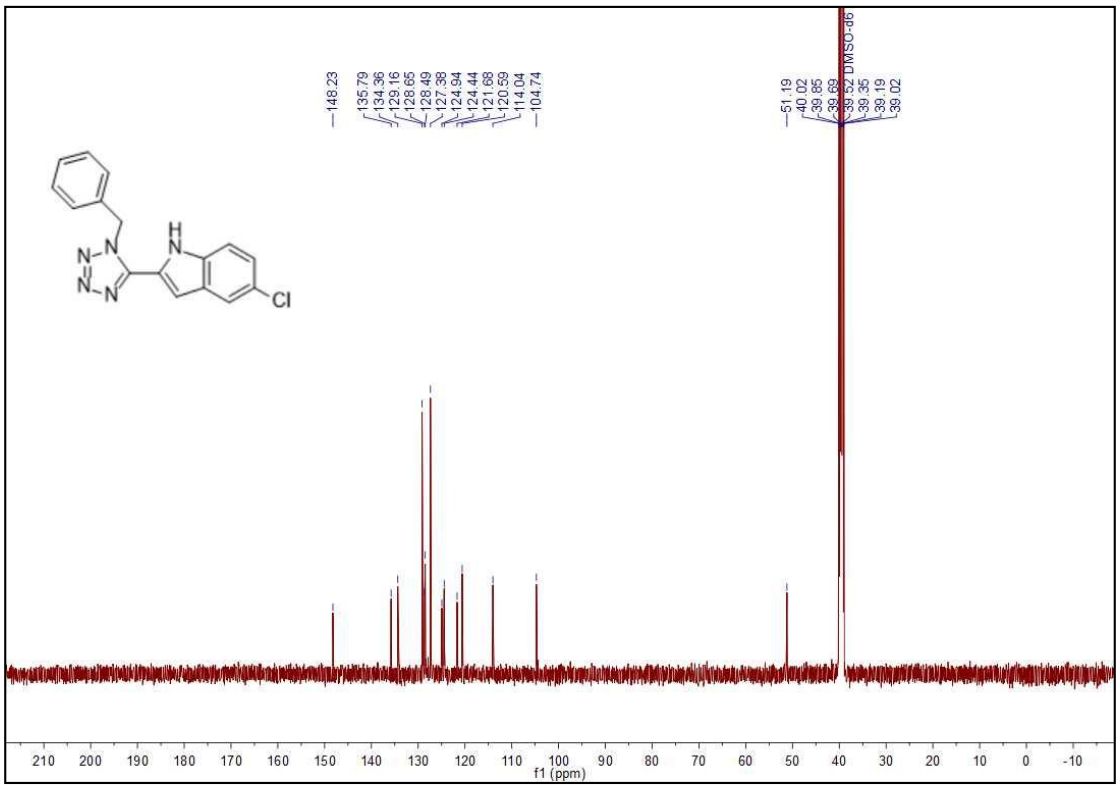


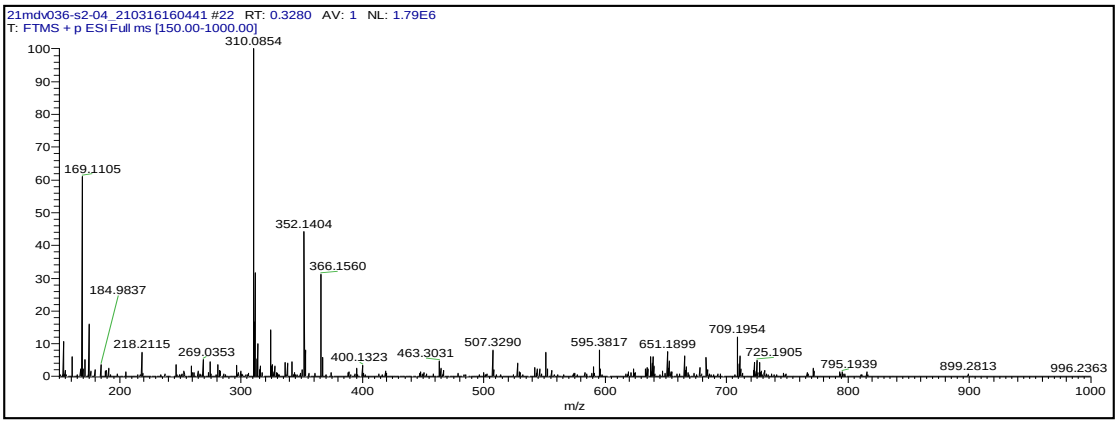



21mdv036-s2-03 #34 RT: 0.5247 AV: 1 NL: 8.18E5
T: FTMS + p ESI Full ms [150.00-1000.00]
306.1349
317.1206
273.0945
372.1382
194.1176
463.3030
507.3290
590.4262
634.4525
683.4341
766.5313
810.5576
859.5392
950.4276
m/z

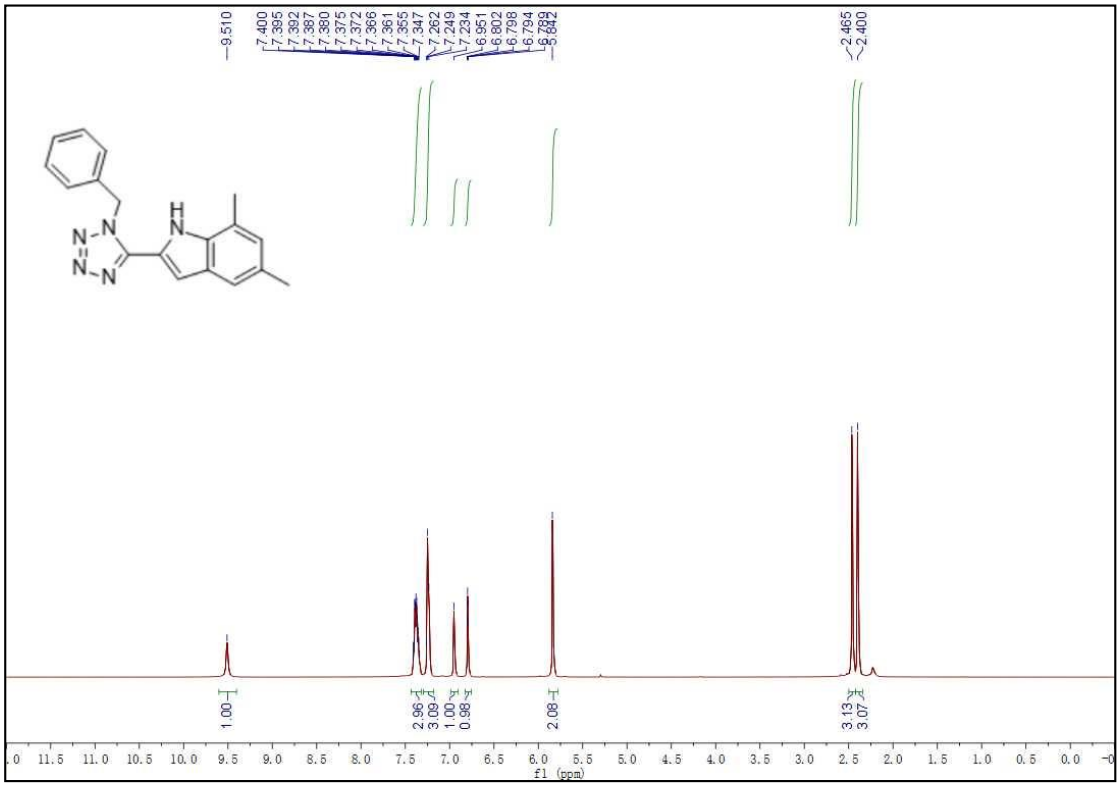
2-(1-benzyl-1*H*-tetrazol-5-yl)-5-chloro-1*H*-indole (2d)

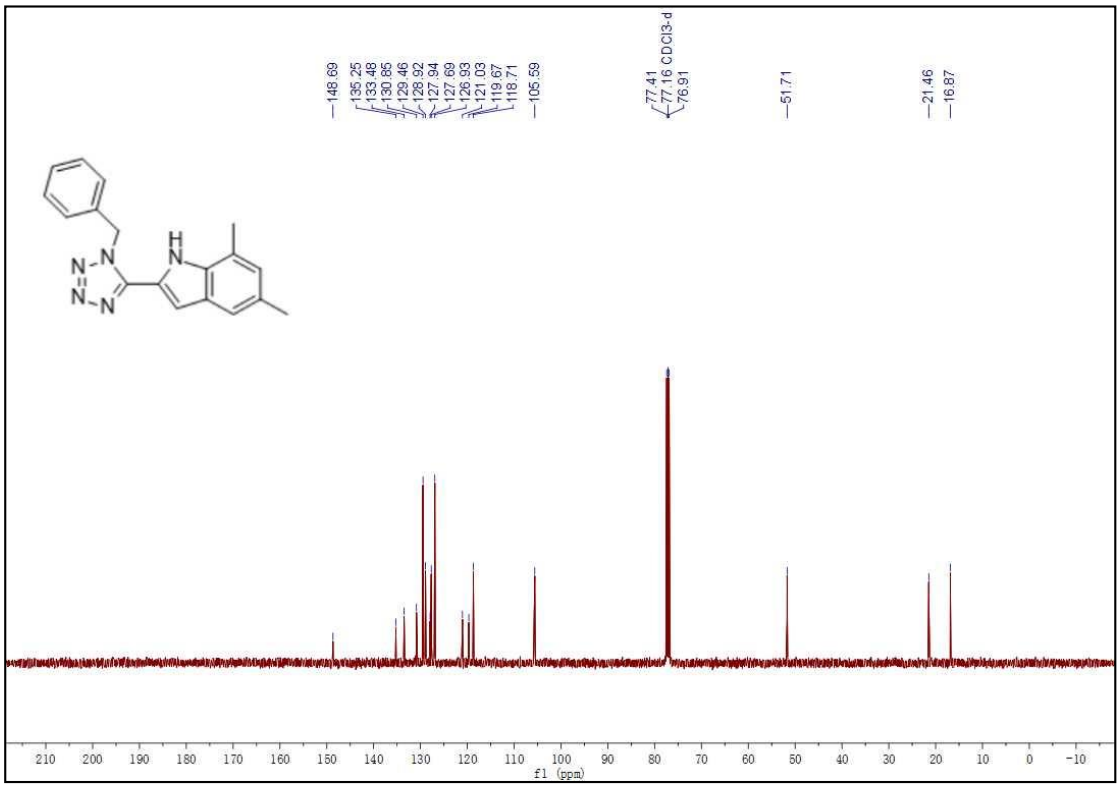


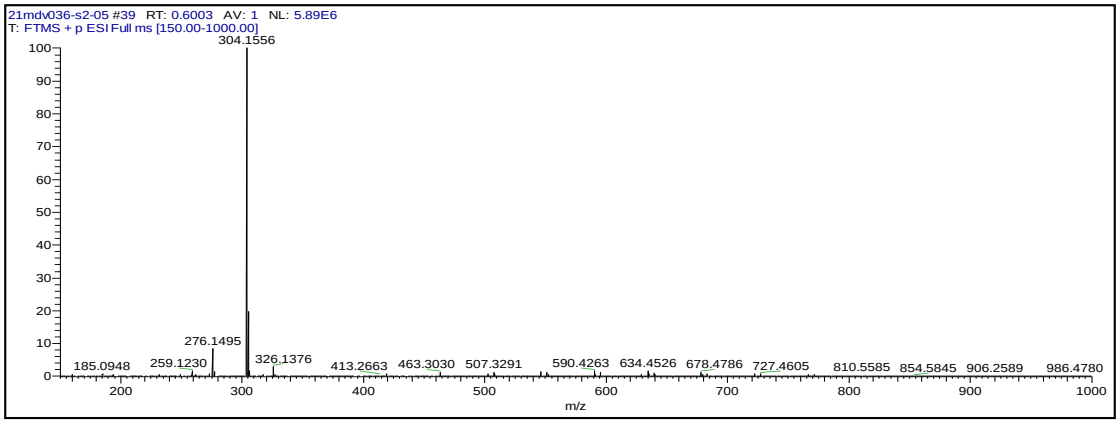



21mdv036-s2-04_210316160441 #22 RT: 0.3280 AV: 1 NL: 1.79E6
T: FTMS + p ESI Full ms [150.00-1000.00]
310.0854
169.1105
352.1404
366.1560
184.9837
218.2115
269.0353
400.1323
463.3031
507.3290
595.3817
651.1899
709.1954
725.1905
795.1939
899.2813
996.2363
m/z

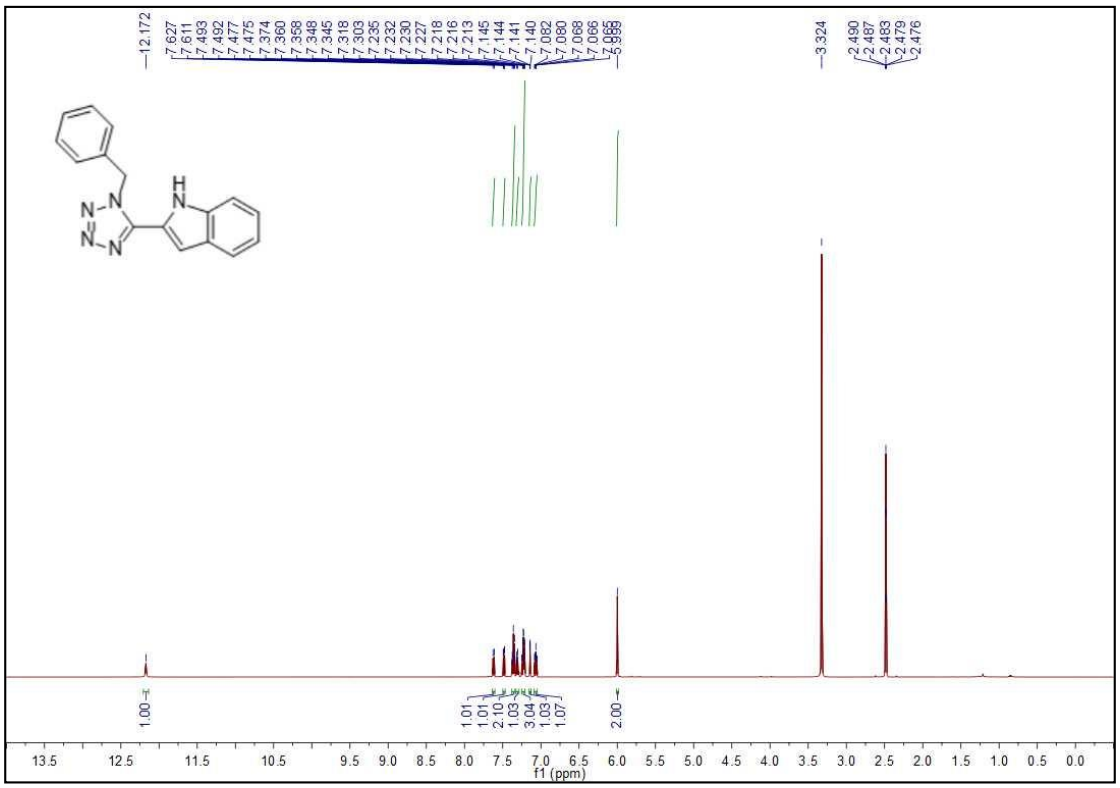
2-(1-benzyl-1*H*-tetrazol-5-yl)-5,7-dimethyl-1*H*-indole (2e)

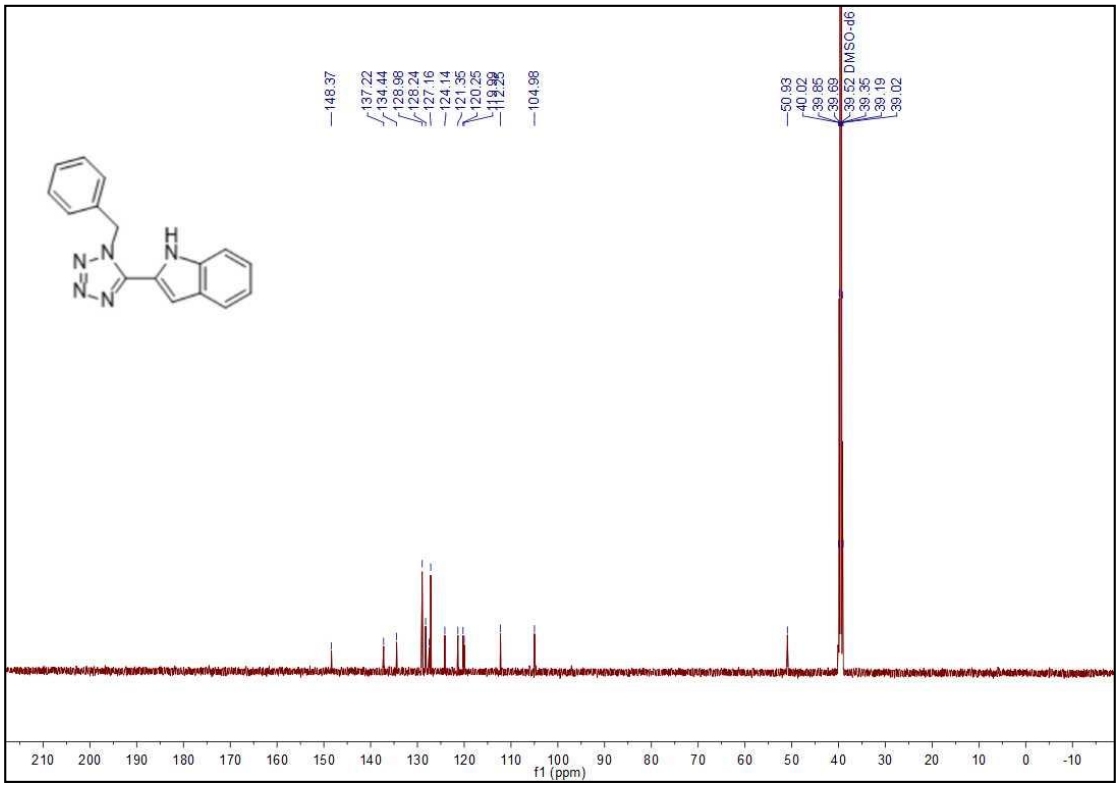


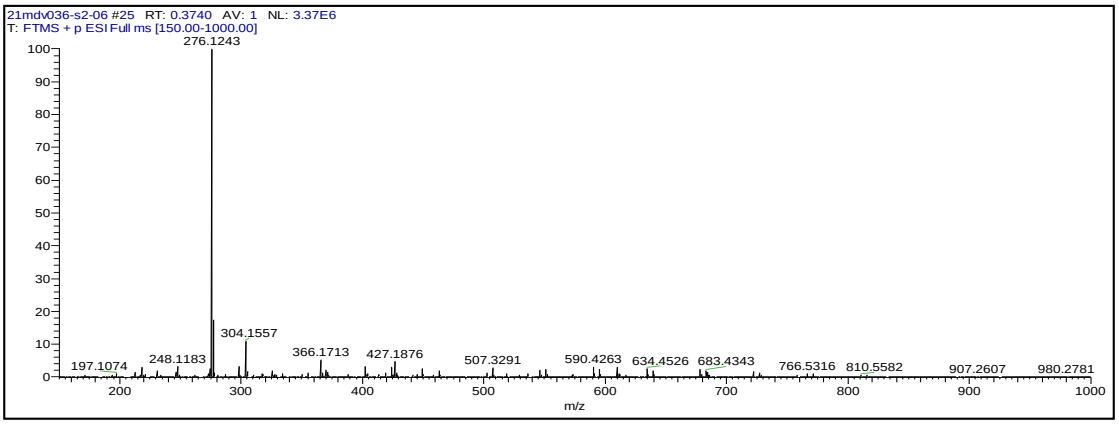



21mdv036-s2-05 #39 RT: 0.6003 AV: 1 NL: 5.89E6
T: FTMS + p ESI Full ms [150.00-1000.00]
304.1556
276.1495
326.1376
185.0948
259.1230
413.2663
463.3030
507.3291
590.4263
634.4526
678.4786
727.4605
810.5585
854.5845
906.2589
986.4780
m/z

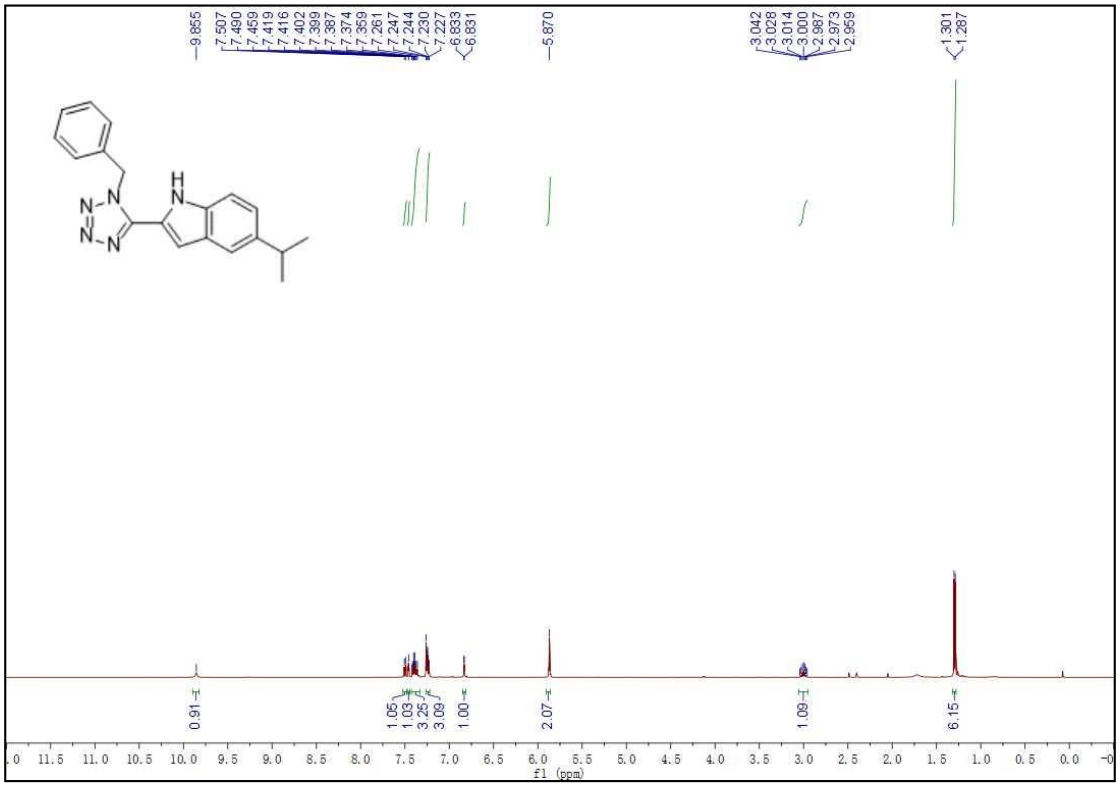
2-(1-benzyl-1*H*-tetrazol-5-yl)-1*H*-indole (2f)

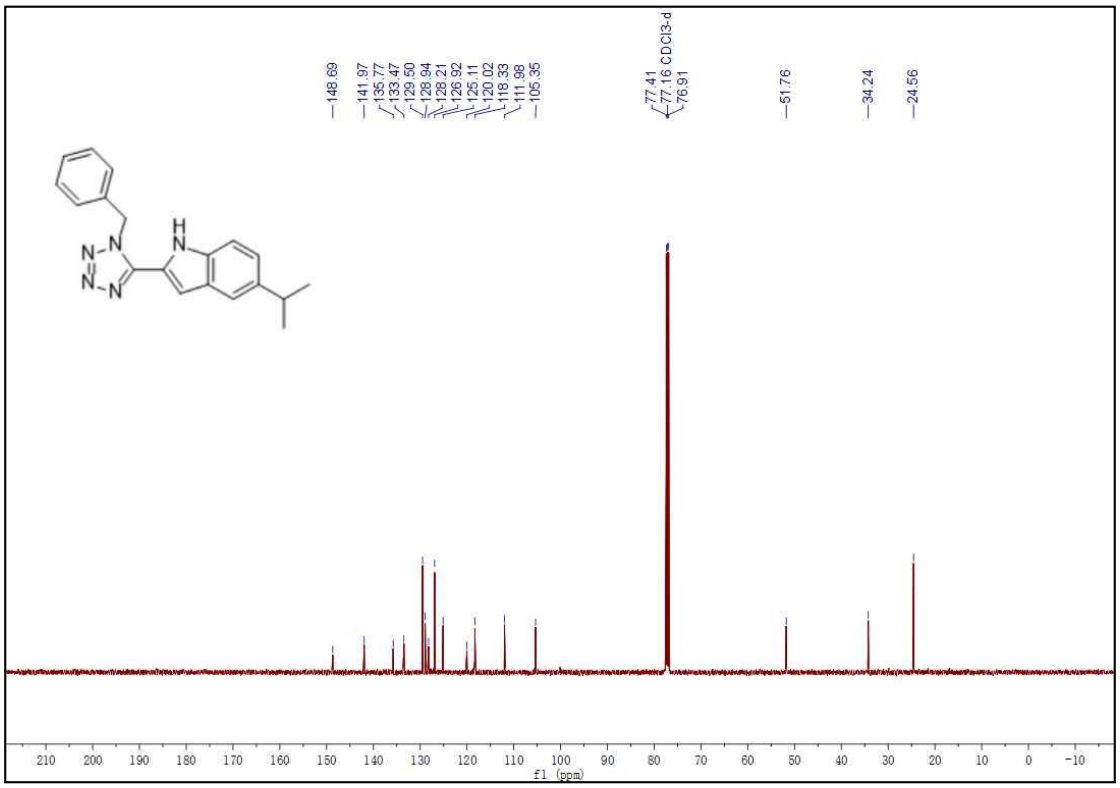


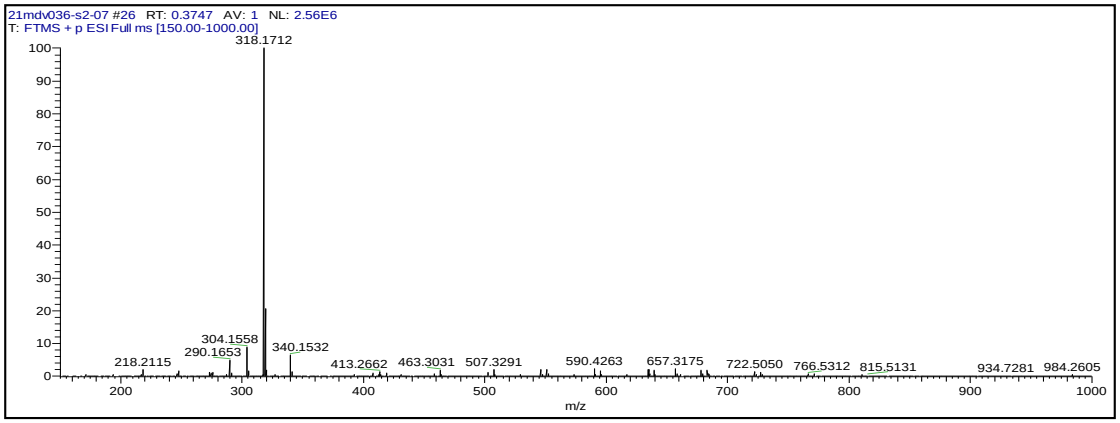



21mdv036-s2-06 #25 RT: 0.3740 AV: 1 NL: 3.37E6
T: FTMS + p ESI Full ms [150.00-1000.00]
276.1243
304.1557
366.1713
427.1876
197.1074
248.1183
507.3291
590.4263
634.4526
683.4343
766.5316
810.5582
907.2607
980.2781
m/z

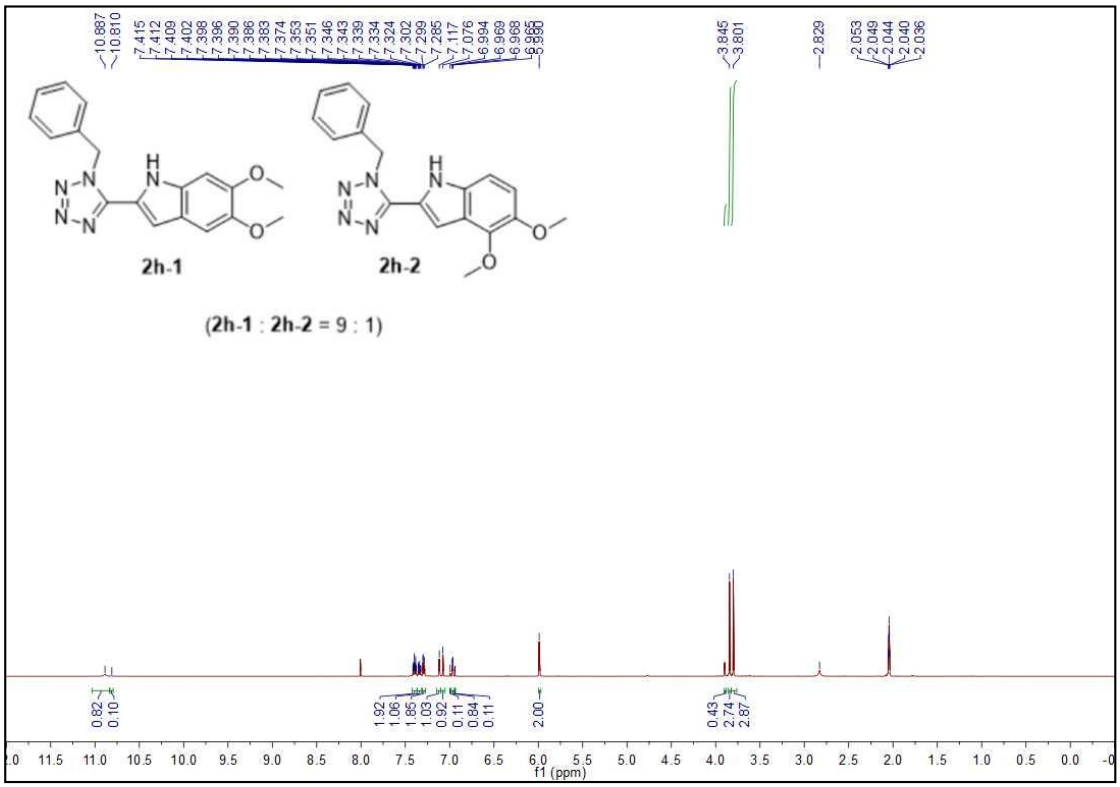
2-(1-benzyl-1*H*-tetrazol-5-yl)-5-isopropyl-1*H*-indole (2g)

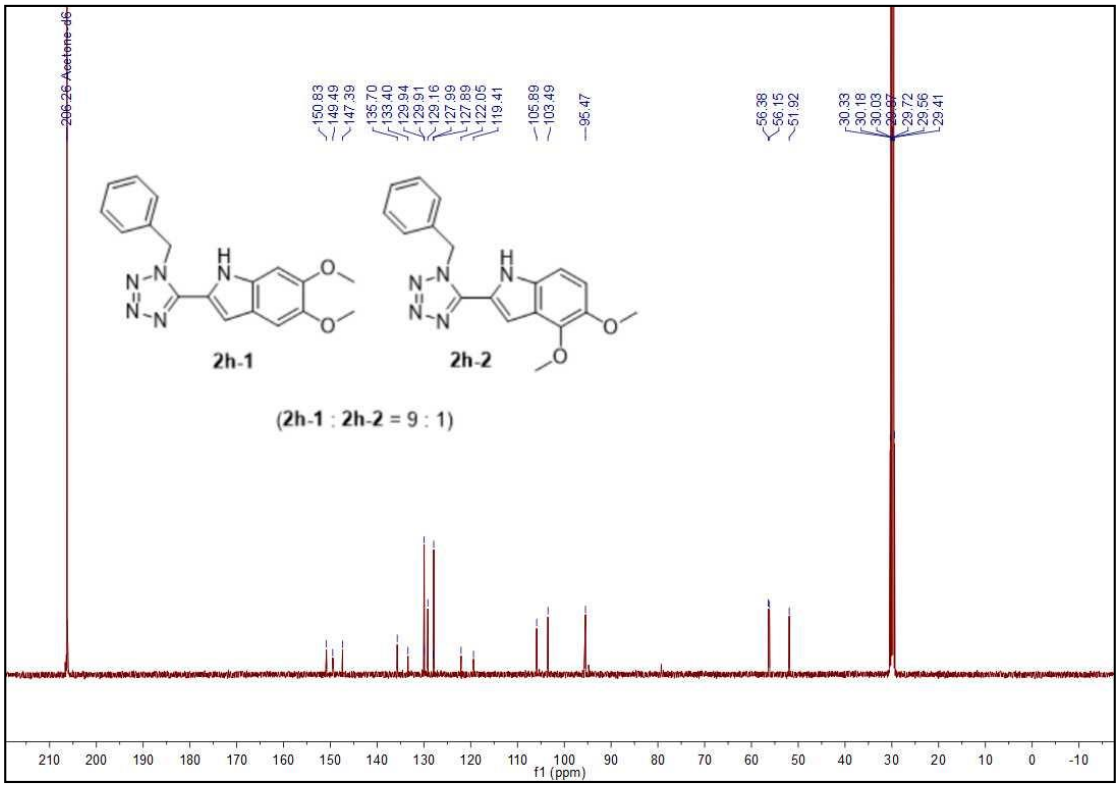


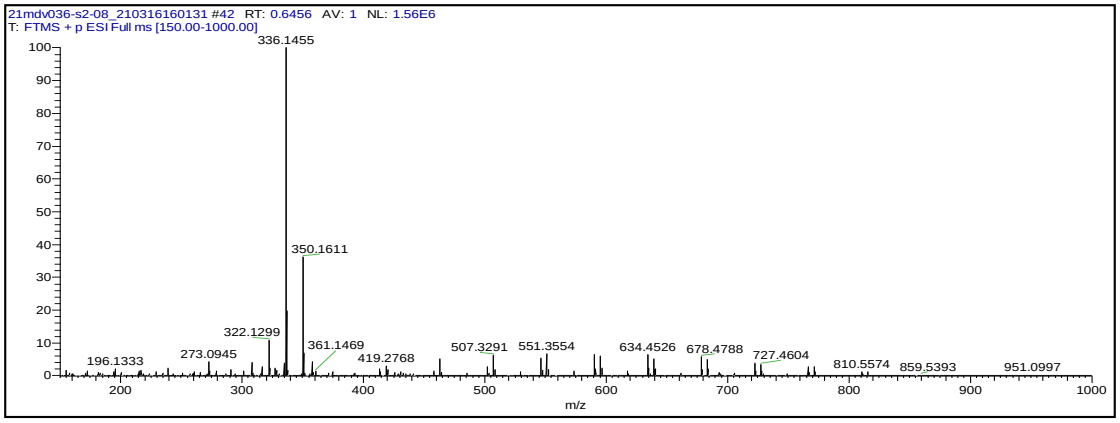



21mdv036-s2-07 #26 RT: 0.3747 AV: 1 NL: 2.56E6
T: FTMS + p ESI Full ms [150.00-1000.00]
318.1712
304.1558
290.1653
340.1532
218.2115
413.2662
463.3031
507.3291
590.4263
657.3175
722.5050
766.5312
815.5131
934.7281
984.2605
m/z

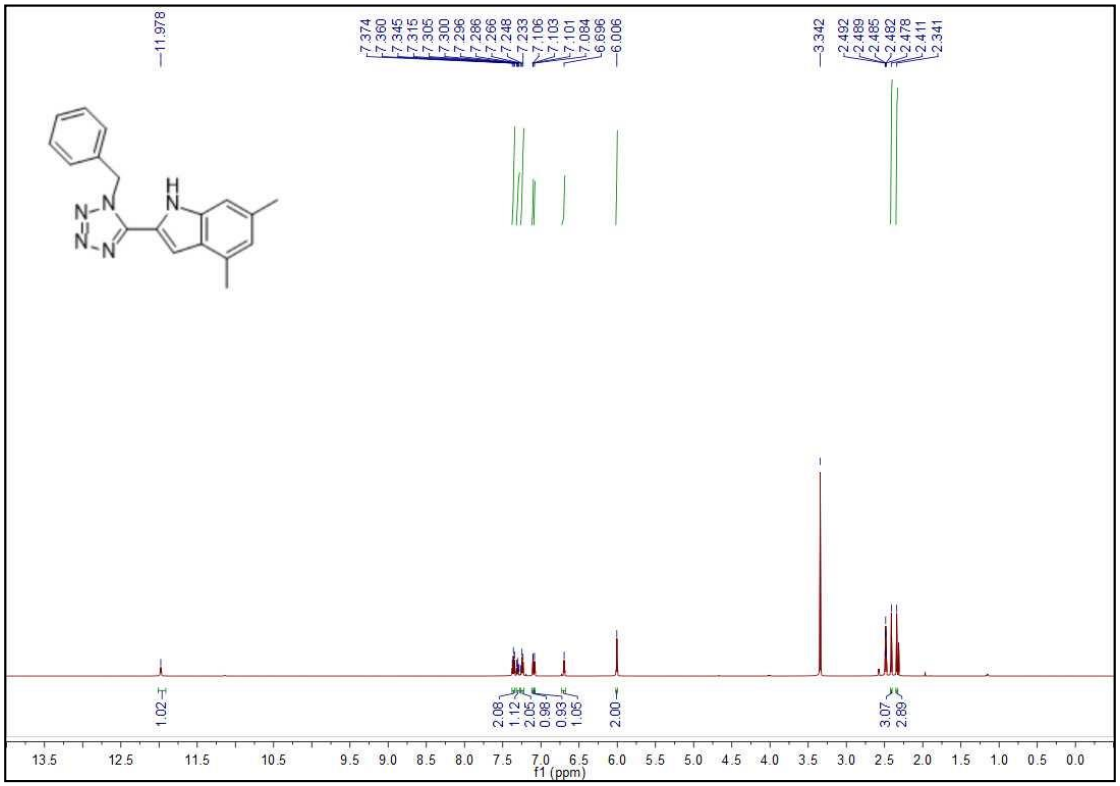
2-(1-benzyl-1*H*-tetrazol-5-yl)-5,6-dimethoxy-1*H*-indole (2h-1) and **2-(1-benzyl-1*H*-tetrazol-5-yl)-4,5-dimethoxy-1*H*-indole (2h-2) (2h-2)**

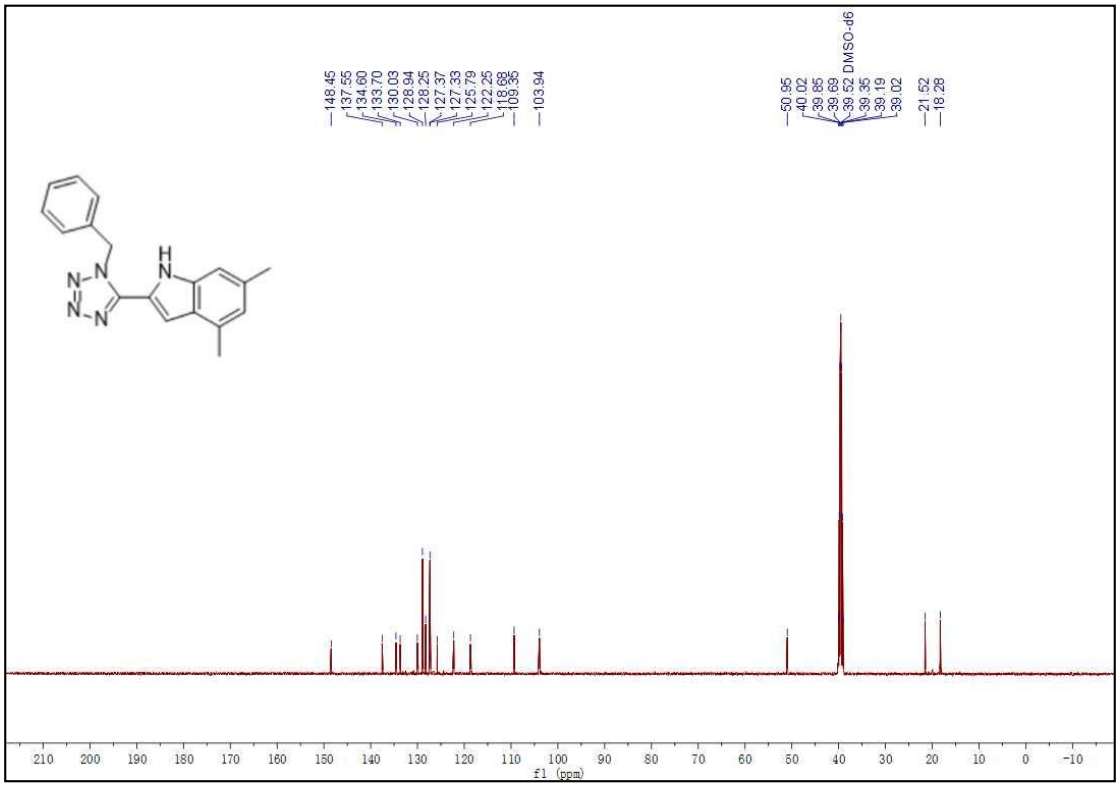


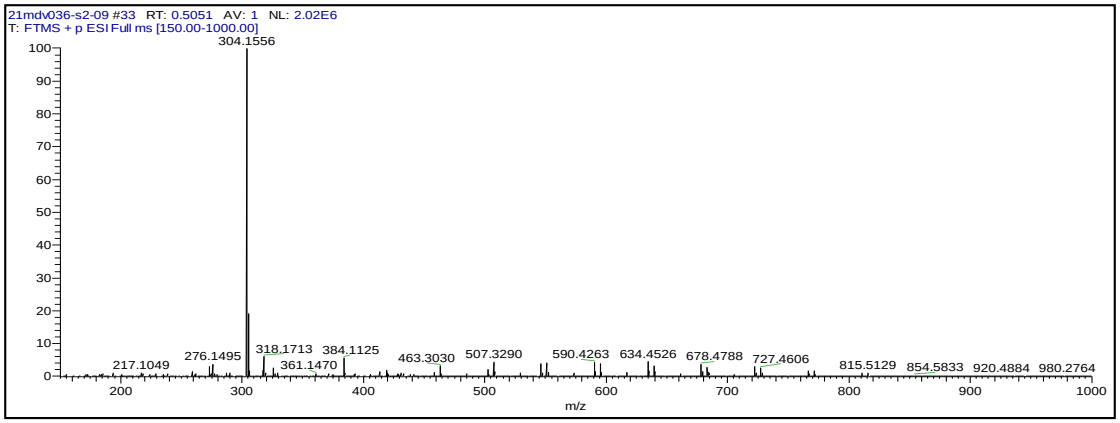



21mdv036-s2-08_210316160131 #42 RT: 0.6456 AV: 1 NL: 1.56E6
T: FTMS + p ESI Full ms [150.00-1000.00]
336.1455
350.1611
322.1299
361.1469
273.0945
196.1333
419.2768
507.3291
551.3554
634.4526
678.4788
727.4604
810.5574
859.5393
951.0997
m/z

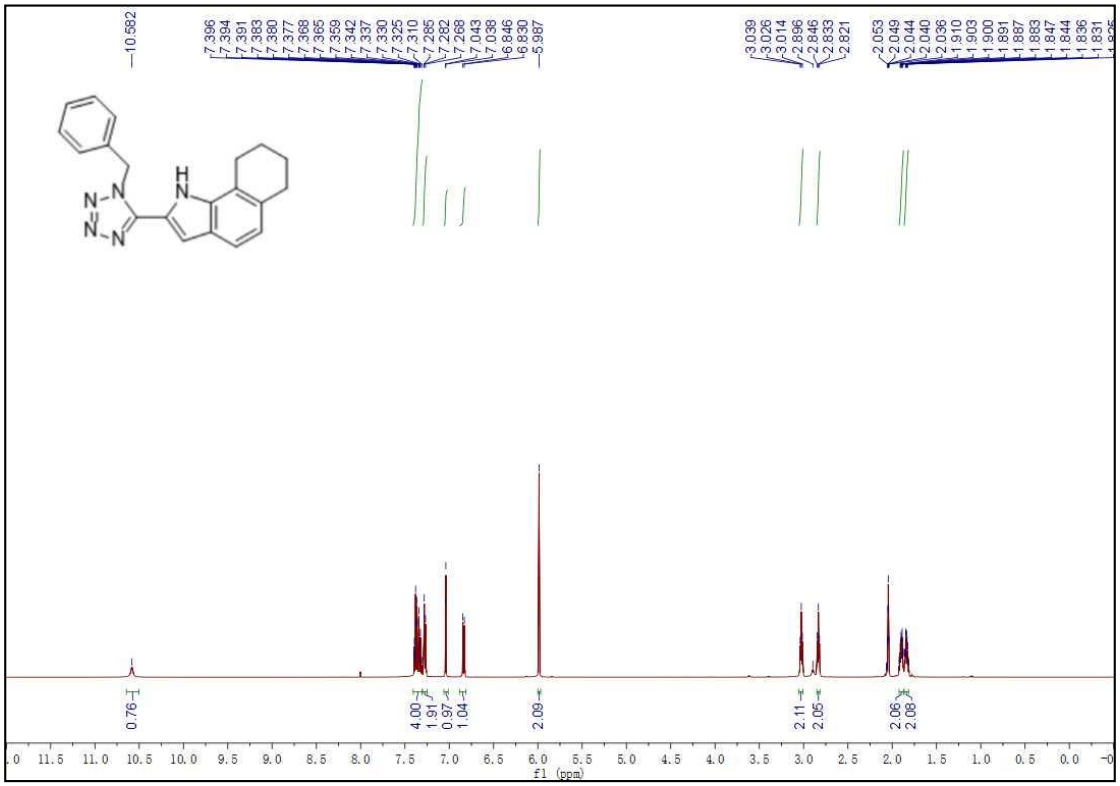
2-(1-benzyl-1*H*-tetrazol-5-yl)-5,7-dimethyl-1*H*-indole (2i)

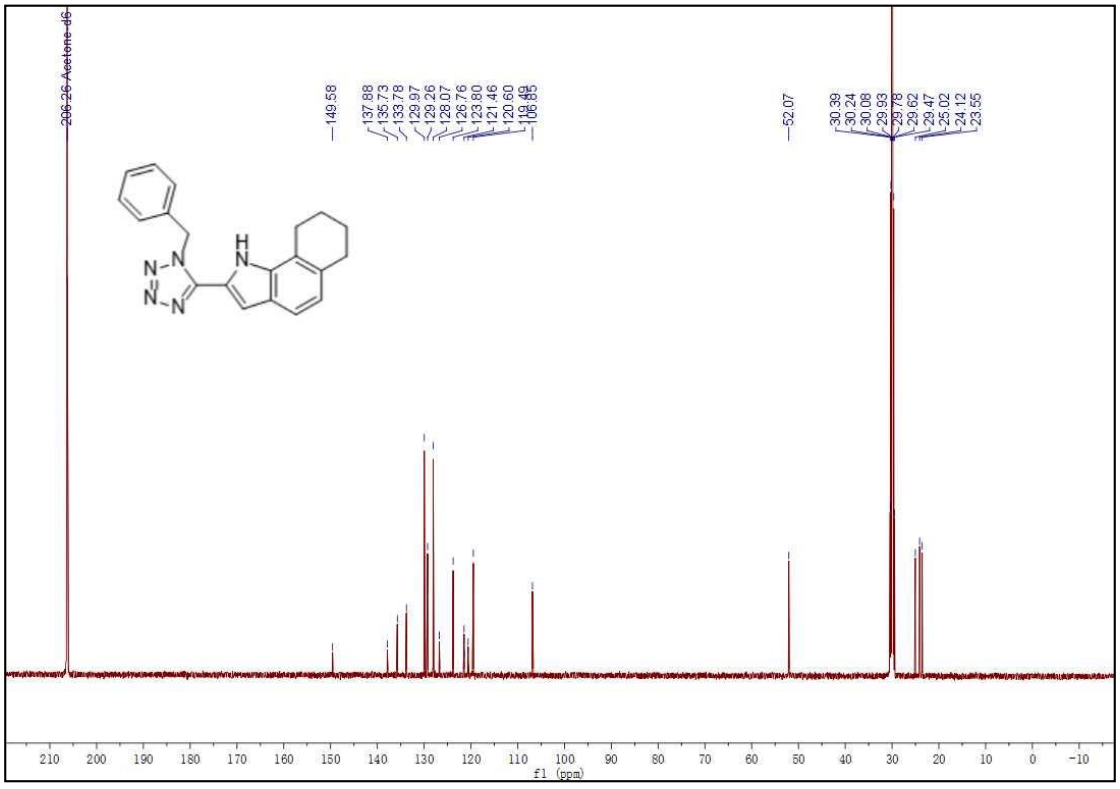


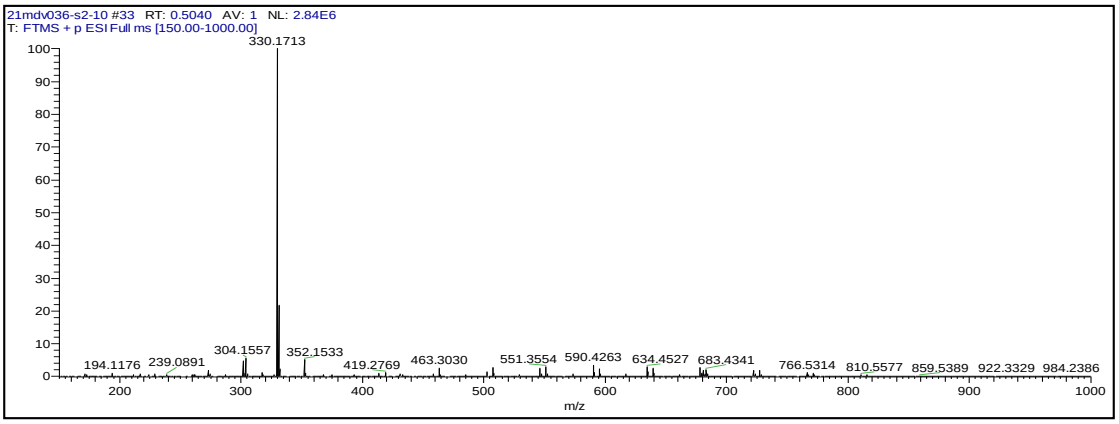



21mdv036-s2-09 #33 RT: 0.5051 AV: 1 NL: 2.02E6
T: FTMS + p ESI Full ms [150.00-1000.00]
304.1556
217.1049
276.1495
318.1713
361.1470
384.1125
463.3030
507.3290
590.4263
634.4526
678.4788
727.4606
815.5129
854.5833
920.4884
980.2764
m/z

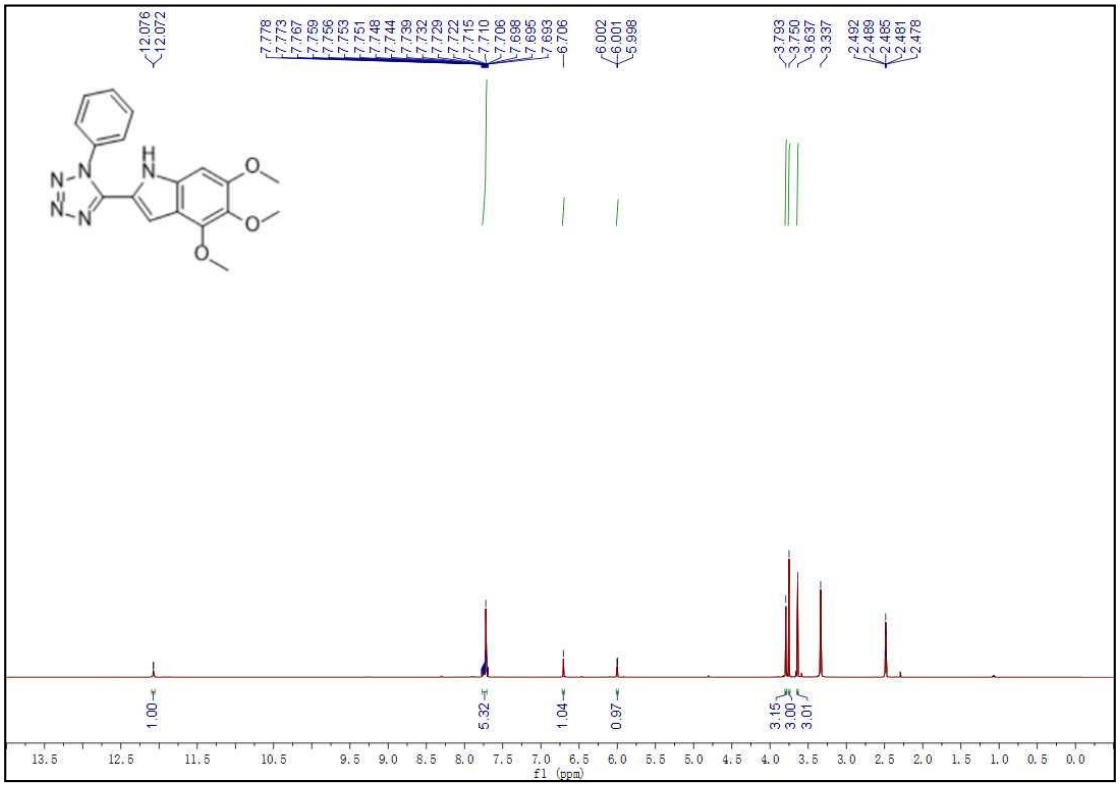
2-(1-benzyl-1*H*-tetrazol-5-yl)-6,7,8,9-tetrahydro-1*H*-benzo[*g*]indole (2j)

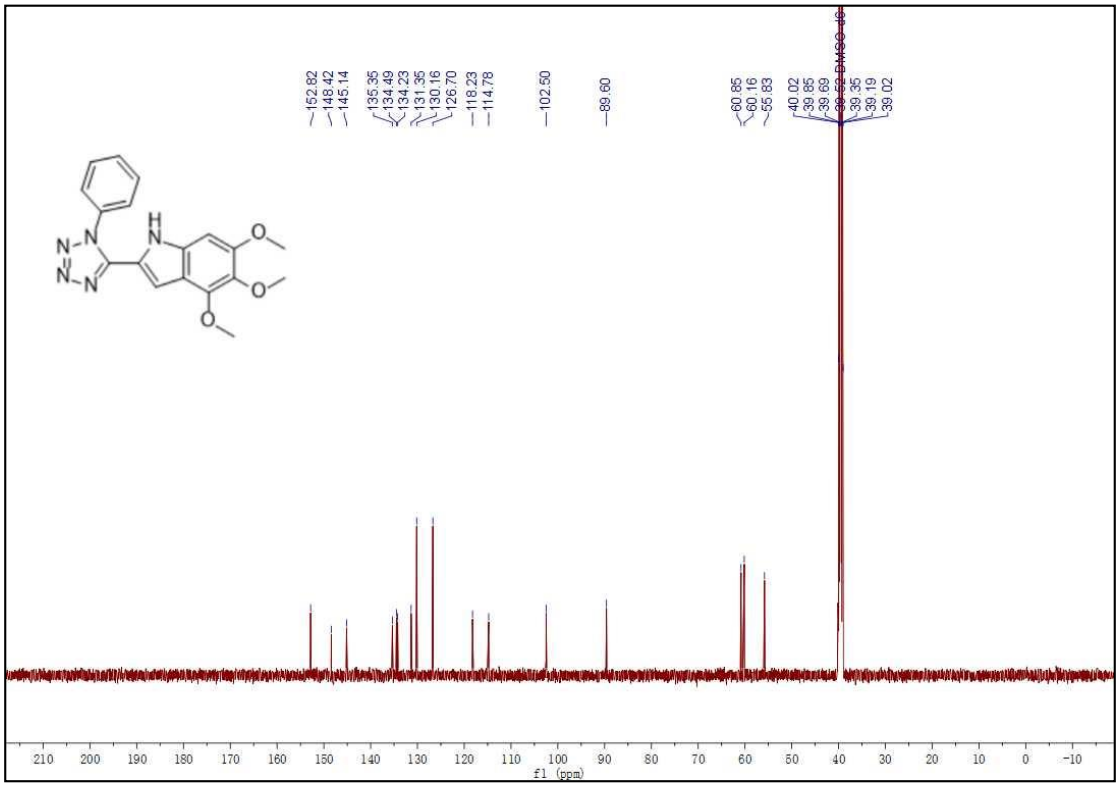


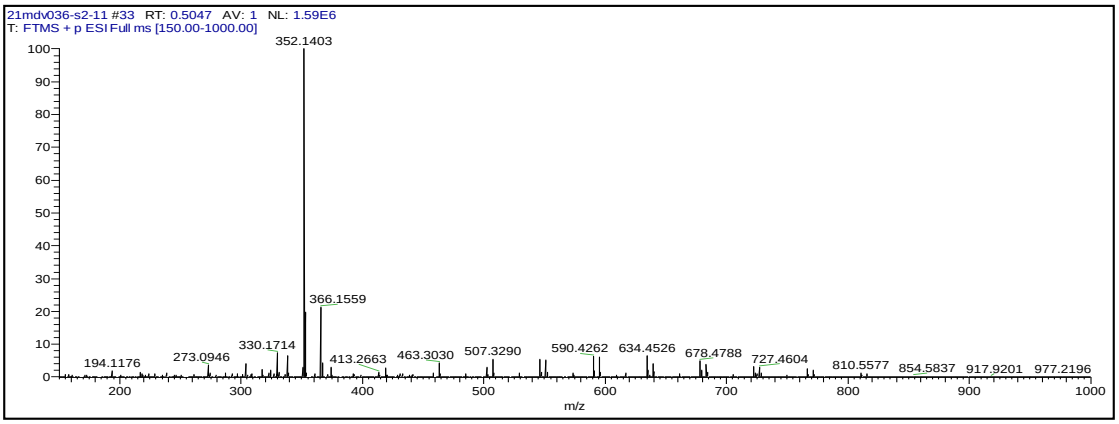



21mdv036-s2-10 #33 RT: 0.5040 AV: 1 NL: 2.84E6
T: FTMS + p ESI Full ms [150.00-1000.00]
330.1713
304.1557
352.1533
194.1176
239.0891
419.2769
463.3030
551.3554
590.4263
634.4527
683.4341
766.5314
810.5577
859.5389
922.3329
984.2386
m/z

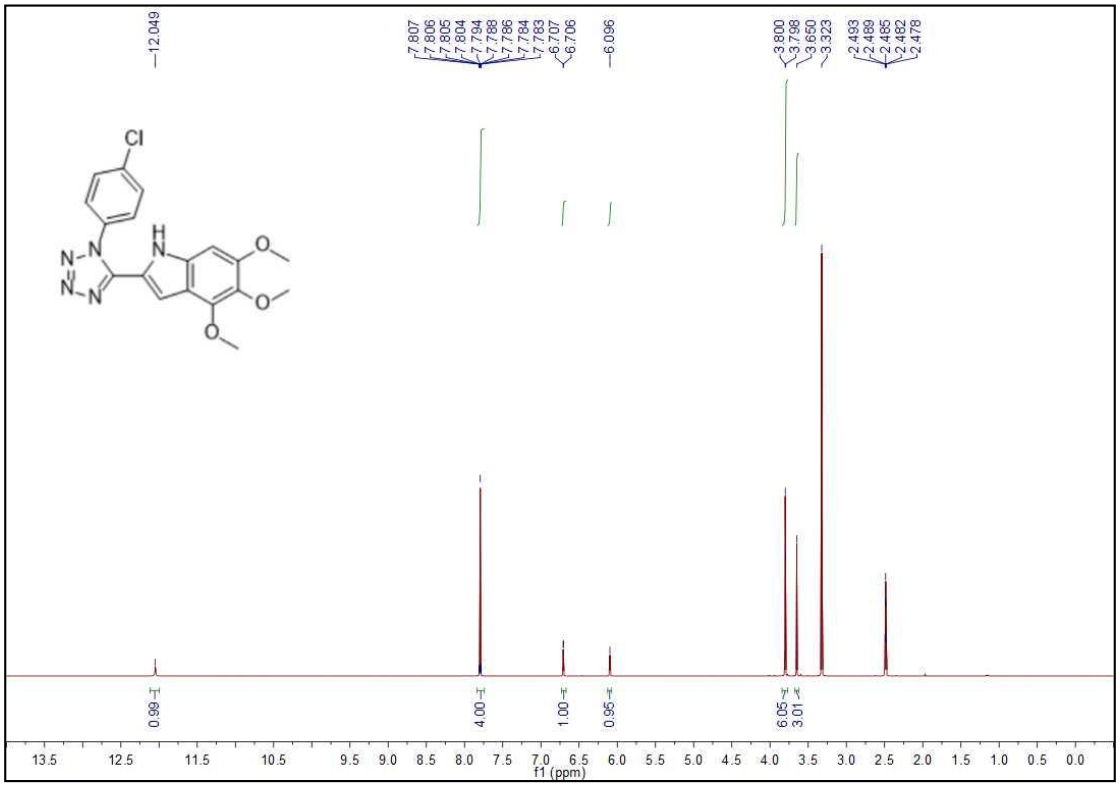
4,5,6-trimethoxy-2-(1-phenyl-1*H*-tetrazol-5-yl)-1*H*-indole (2k)

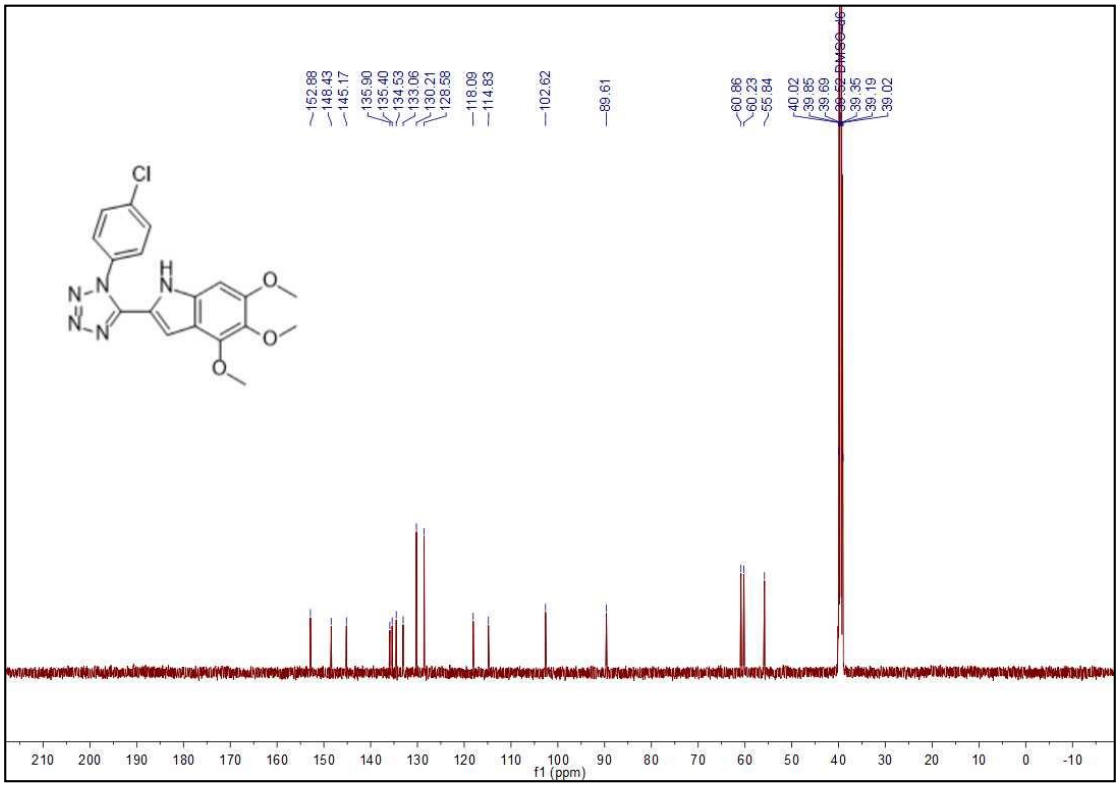


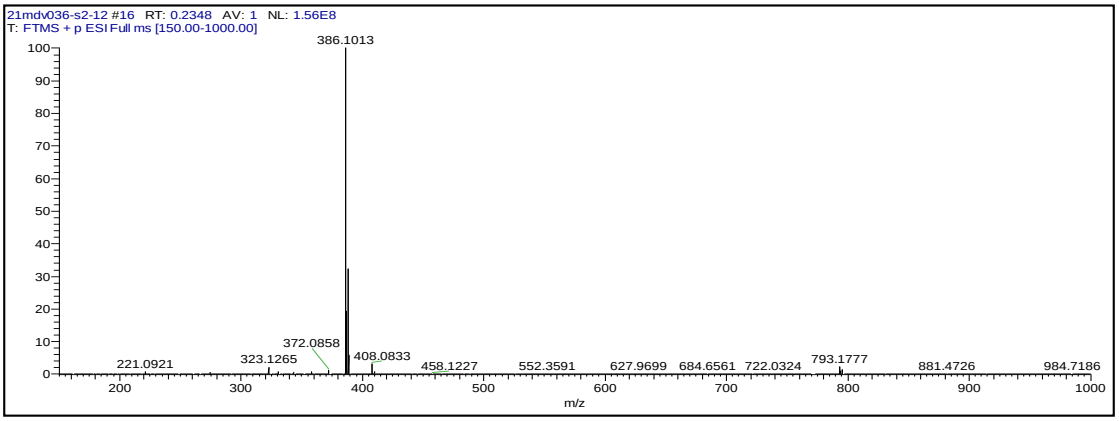



21mdv036-s2-11 #33 RT: 0.5047 AV: 1 NL: 1.59E6
T: FTMS + p ESI Full ms [150.00-1000.00]
352.1403
366.1559
330.1714
273.0946
194.1176
413.2663
463.3030
507.3290
590.4262
634.4526
678.4788
727.4604
810.5577
854.5837
917.9201
977.2196
m/z

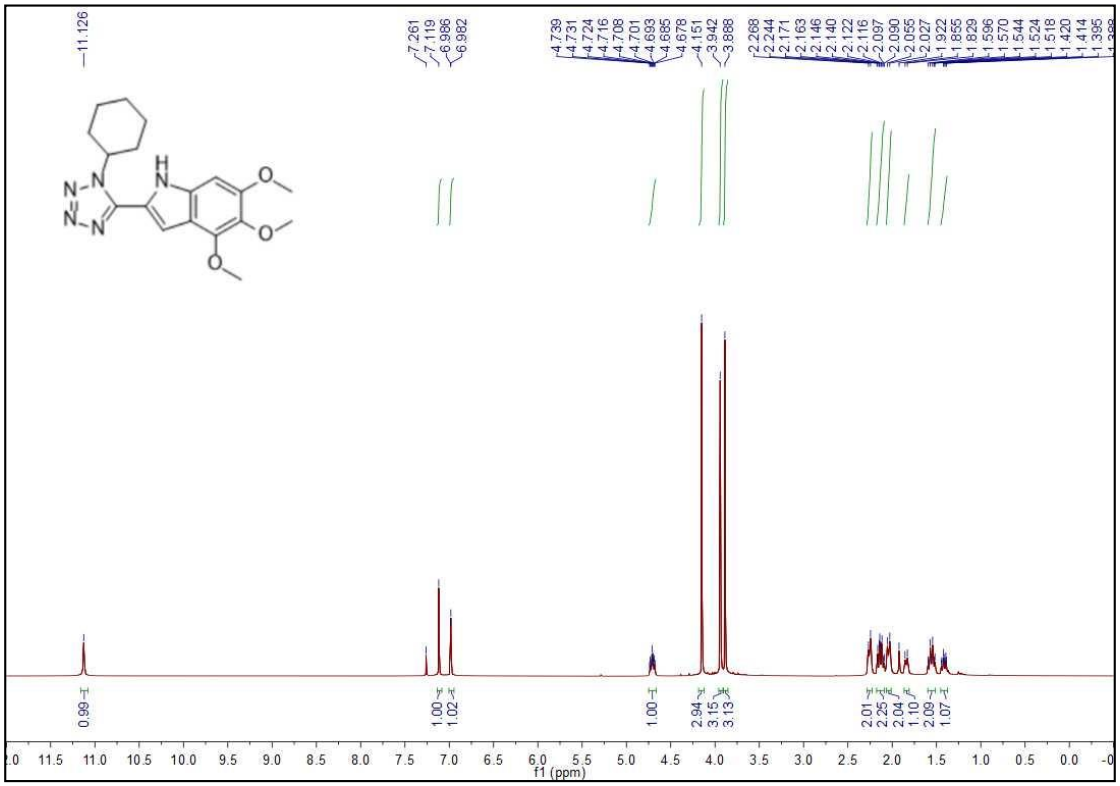
2-(1-(4-chlorophenyl)-1*H*-tetrazol-5-yl)-4,5,6-trimethoxy-1*H*-indole (2l)

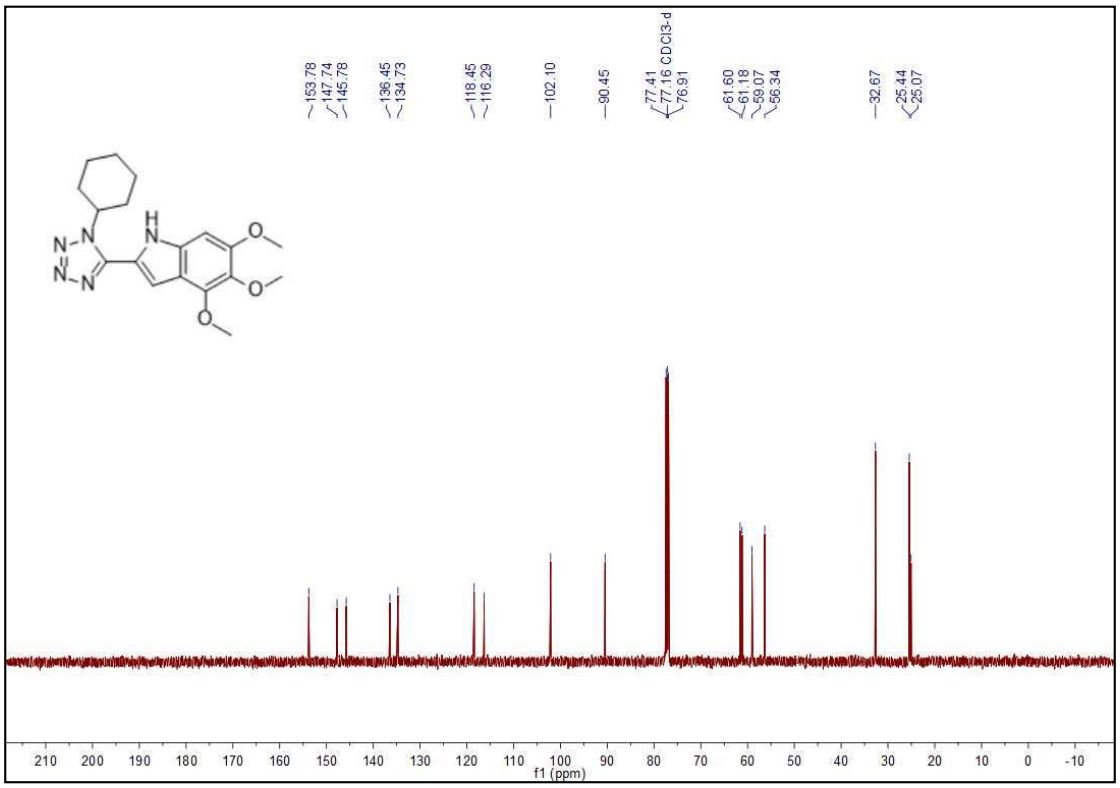


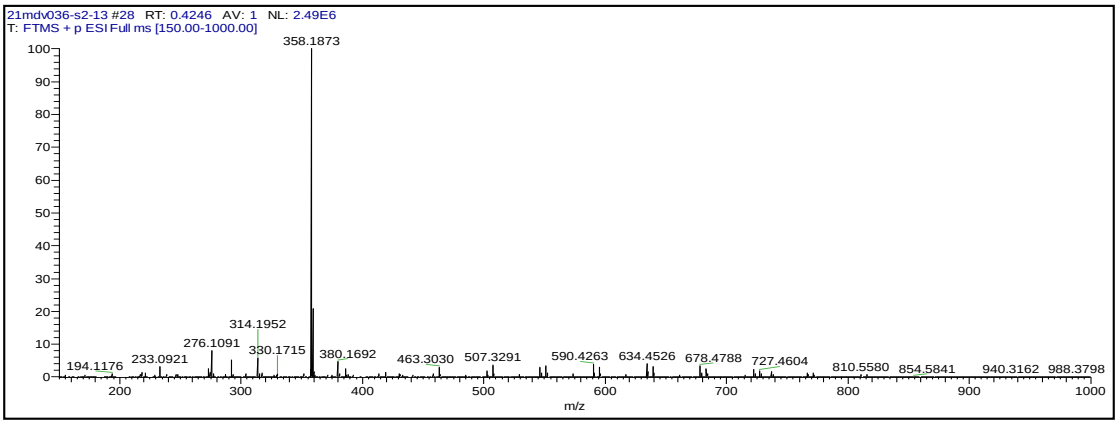



21mdv036-s2-12 #16 RT: 0.2348 AV: 1 NL: 1.56E8
T: FTMS + p ESI Full ms [150.00-1000.00]
386.1013
372.0858
408.0833
221.0921
323.1265
458.1227
552.3591
627.9699
684.6561
722.0324
793.1777
881.4726
984.7186
m/z

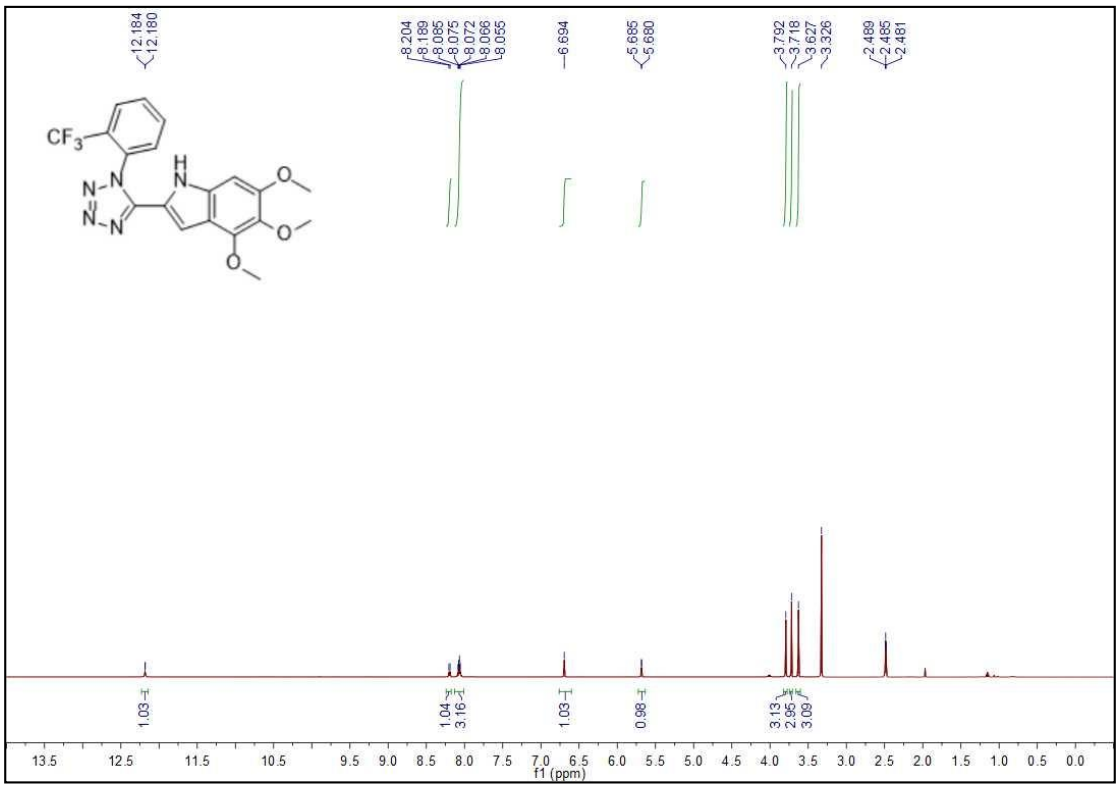
2-(1-cyclohexyl-1*H*-tetrazol-5-yl)-4,5,6-trimethoxy-1*H*-indole (2m)

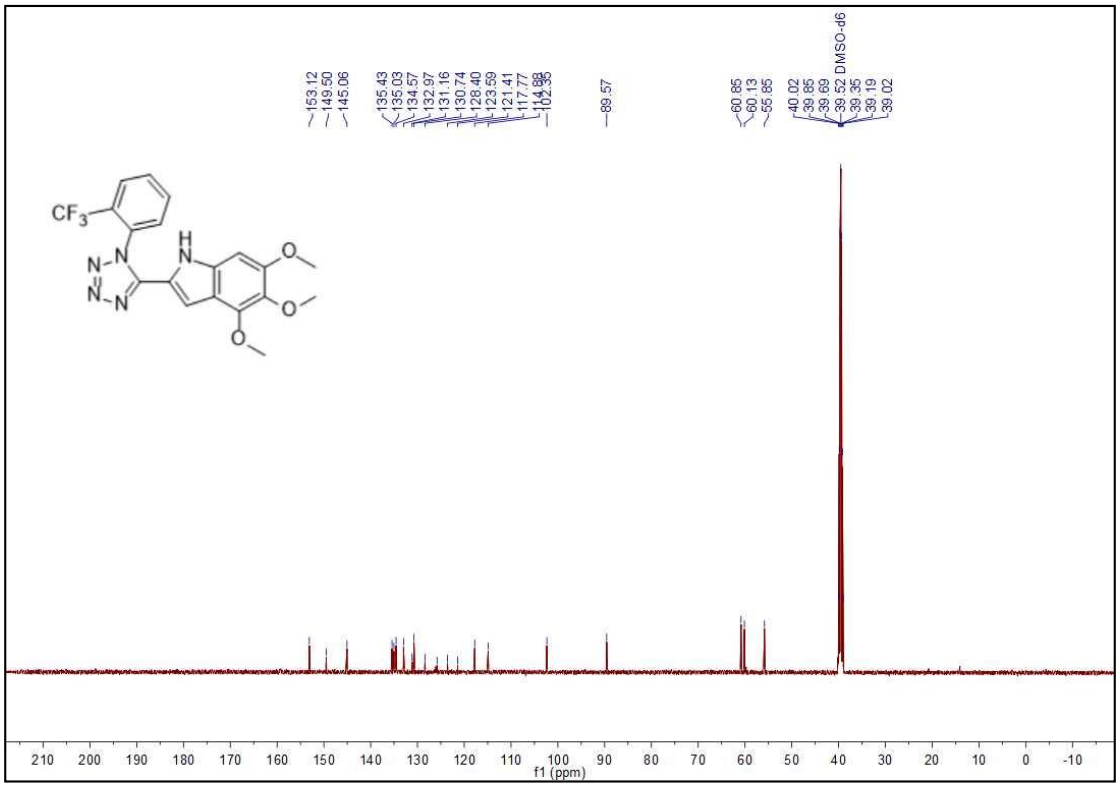


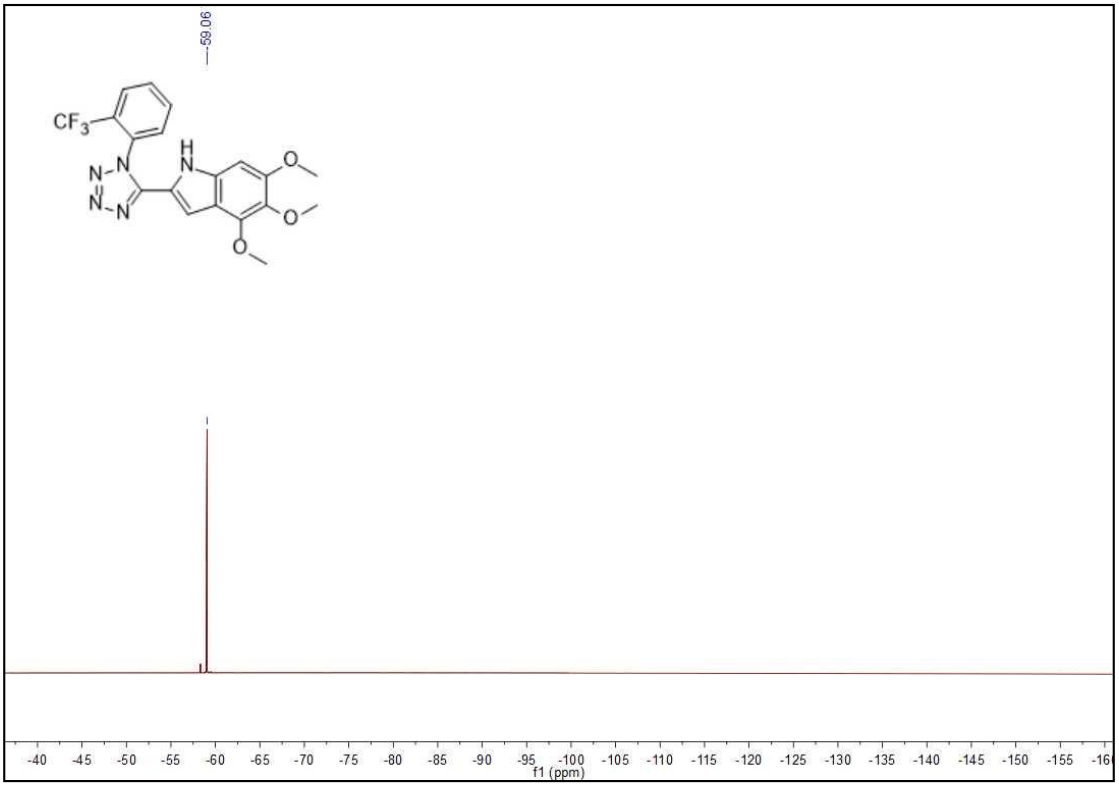


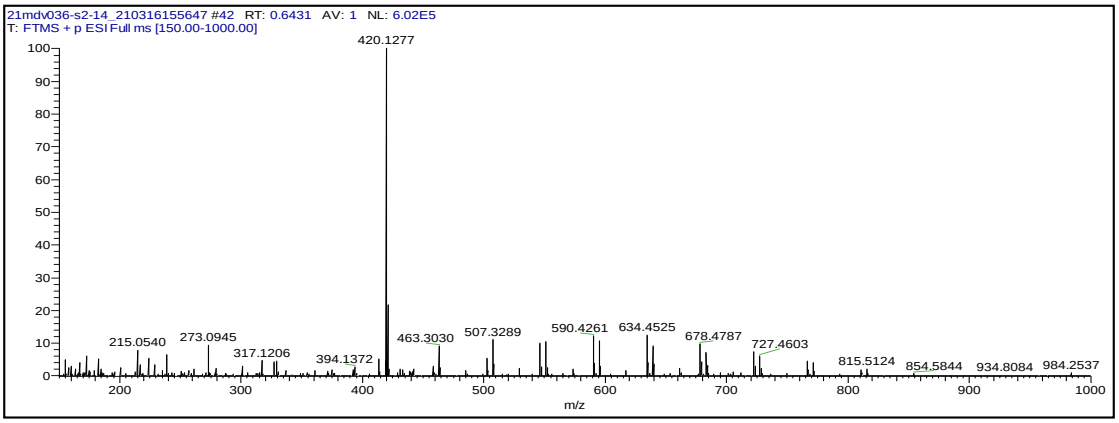

21mdv036-s2-13 #28 RT: 0.4246 AV: 1 NL: 2.49E6
T: FTMS + p ESI Full ms [150.00-1000.00]
358.1873
314.1952
276.1091
330.1715
380.1692
233.0921
194.1176
463.3030
507.3291
590.4263
634.4526
678.4788
727.4604
810.5580
854.5841
940.3162
988.3798
m/z

4,5,6-trimethoxy-2-(1-(2-(trifluoromethyl)phenyl)-1*H*-tetrazol-5-yl)-1*H*-indole (2n)

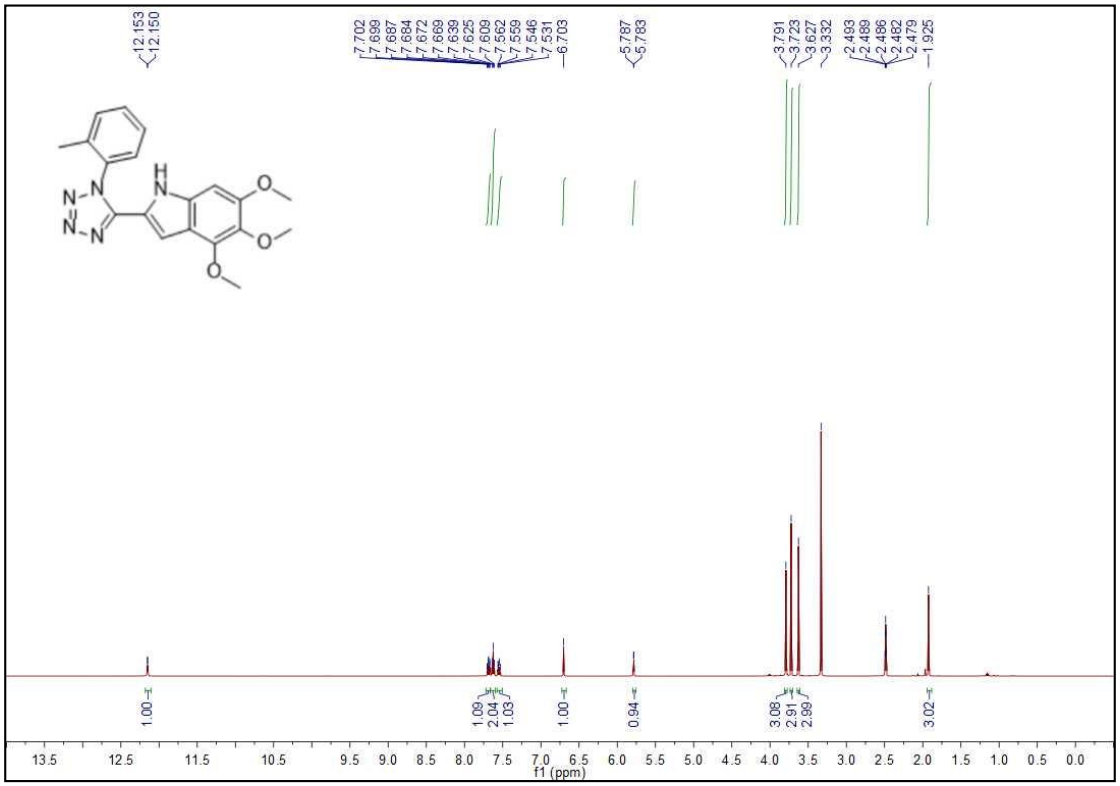


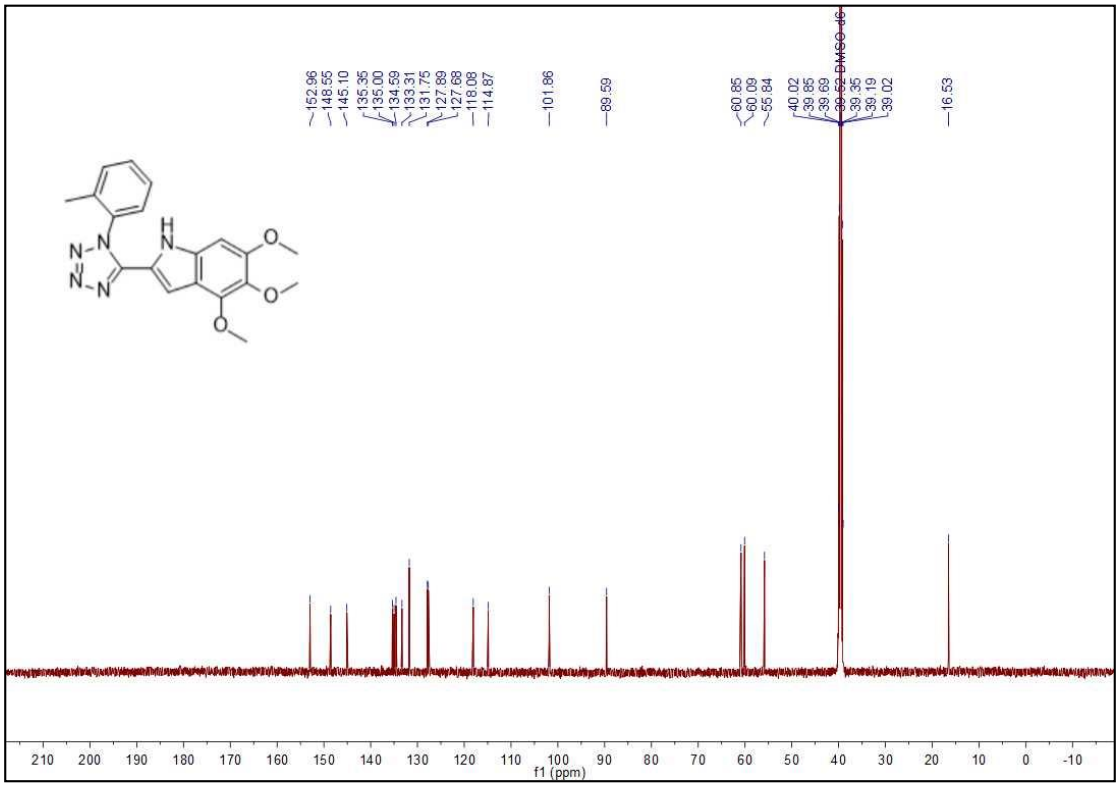


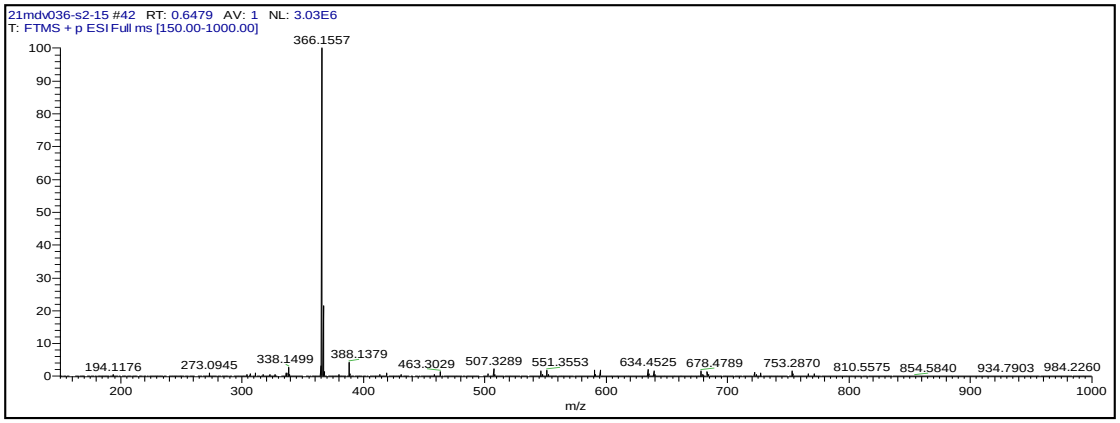

-59.06
CF3
N
N
N
H
N
O
O
O
-40 -45 -50 -55 -60 -65 -70 -75 -80 -85 -90 -95 -100 -105 -110 -115 -120 -125 -130 -135 -140 -145 -150 -155
f1 (ppm)


21mdv036-s2-14_210316155647 #42 RT: 0.6431 AV: 1 NL: 6.02E5
T: FTMS + p ESI Full ms [150.00-1000.00]
420.1277
215.0540
273.0945
317.1206
394.1372
463.3030
507.3289
590.4261
634.4525
678.4787
727.4603
815.5124
854.5844
934.8084
984.2537
m/z

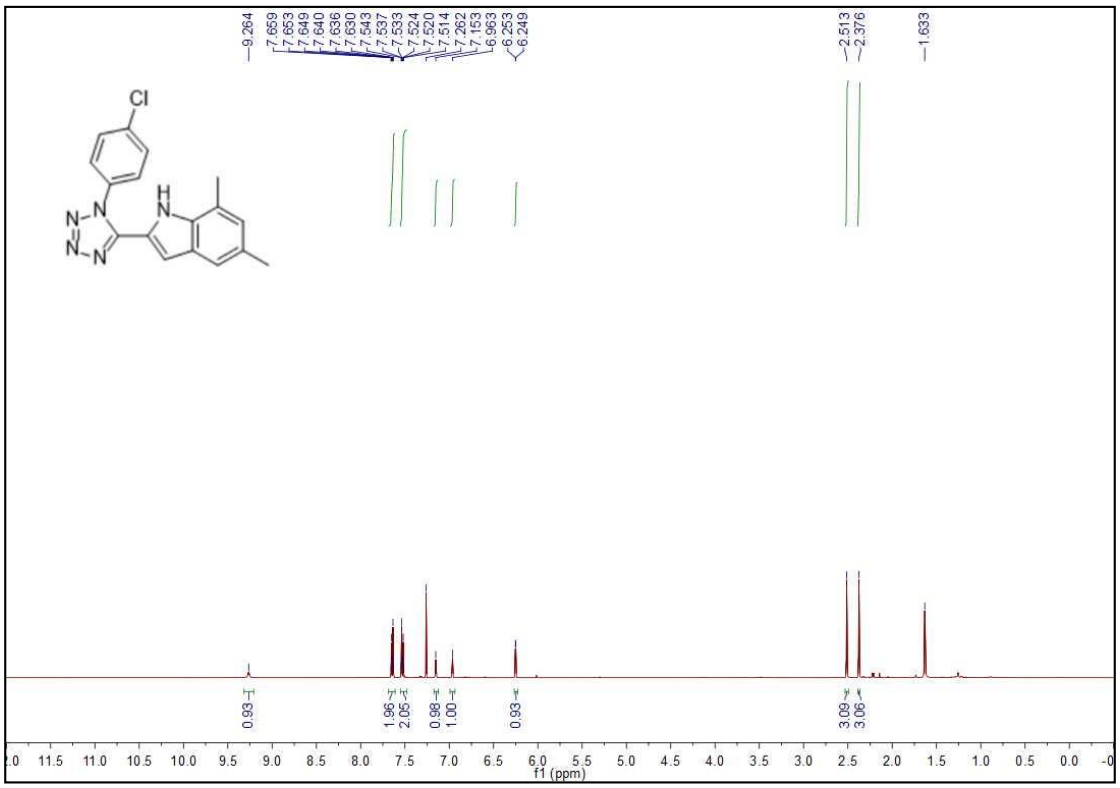
4,5,6-trimethoxy-2-(1-(*o*-tolyl)-1*H*-tetrazol-5-yl)-1*H*-indole (2o)

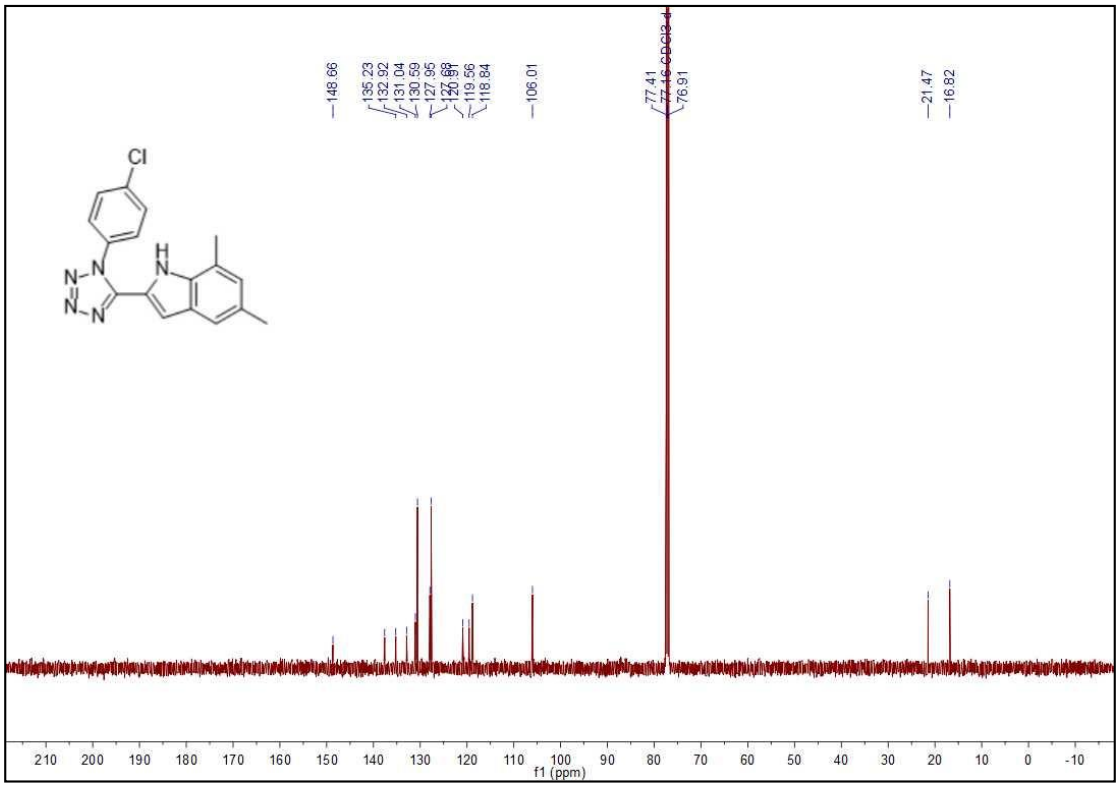


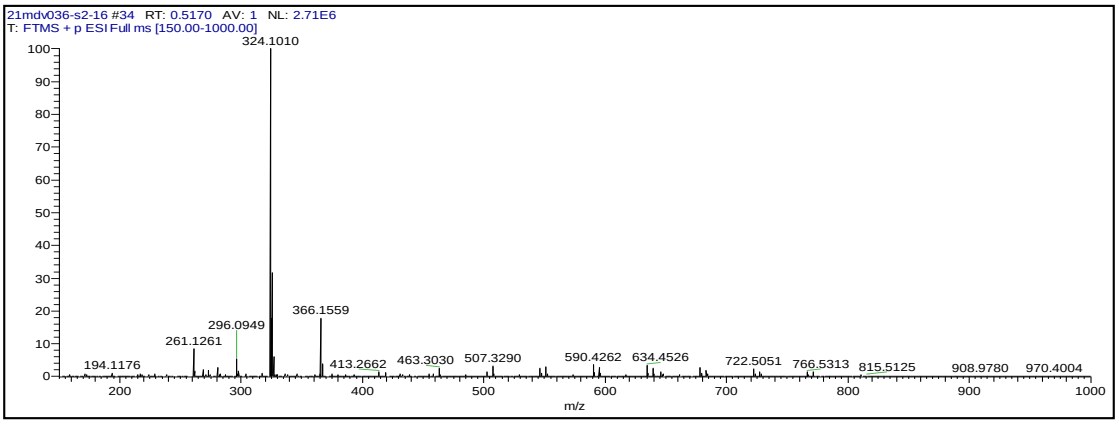



21mdv036-s2-15 #42 RT: 0.6479 AV: 1 NL: 3.03E6
T: FTMS + p ESI Full ms [150.00-1000.00]
366.1557
194.1176
273.0945
338.1499
388.1379
463.3029
507.3289
551.3553
634.4525
678.4789
753.2870
810.5575
854.5840
934.7903
984.2260
m/z

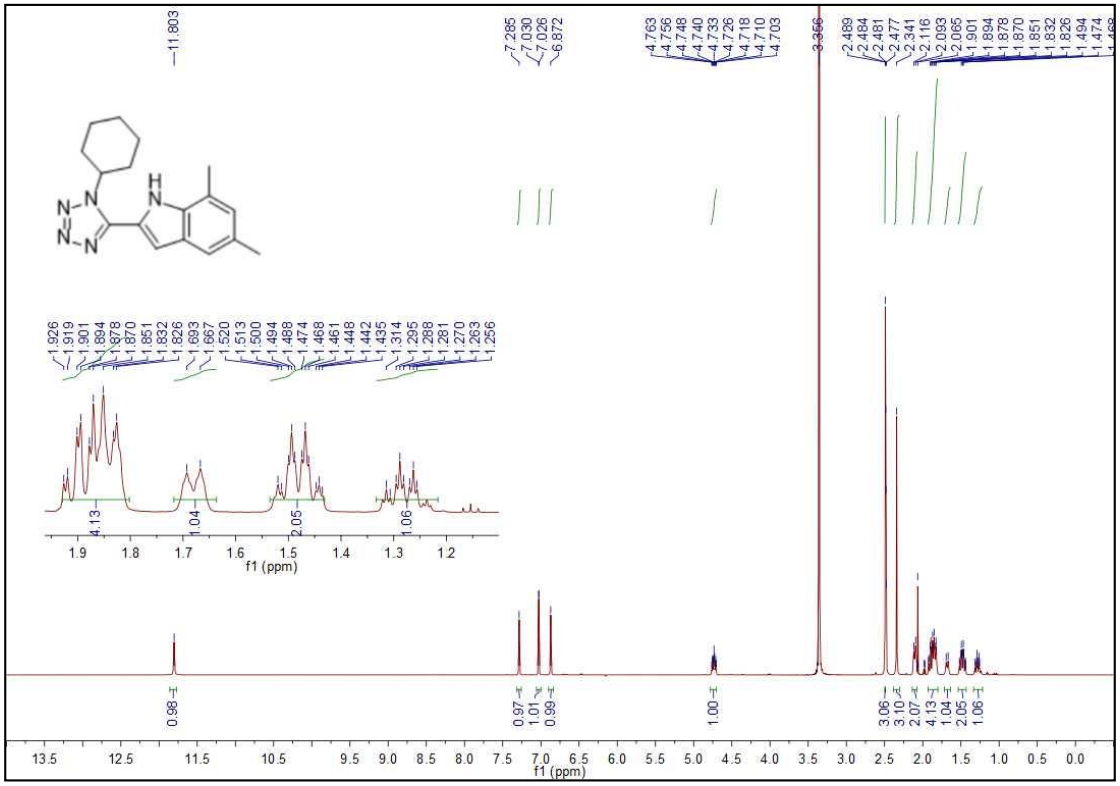
2-(1-(4-chlorophenyl)-1*H*-tetrazol-5-yl)-5,7-dimethyl-1*H*-indole (2p)

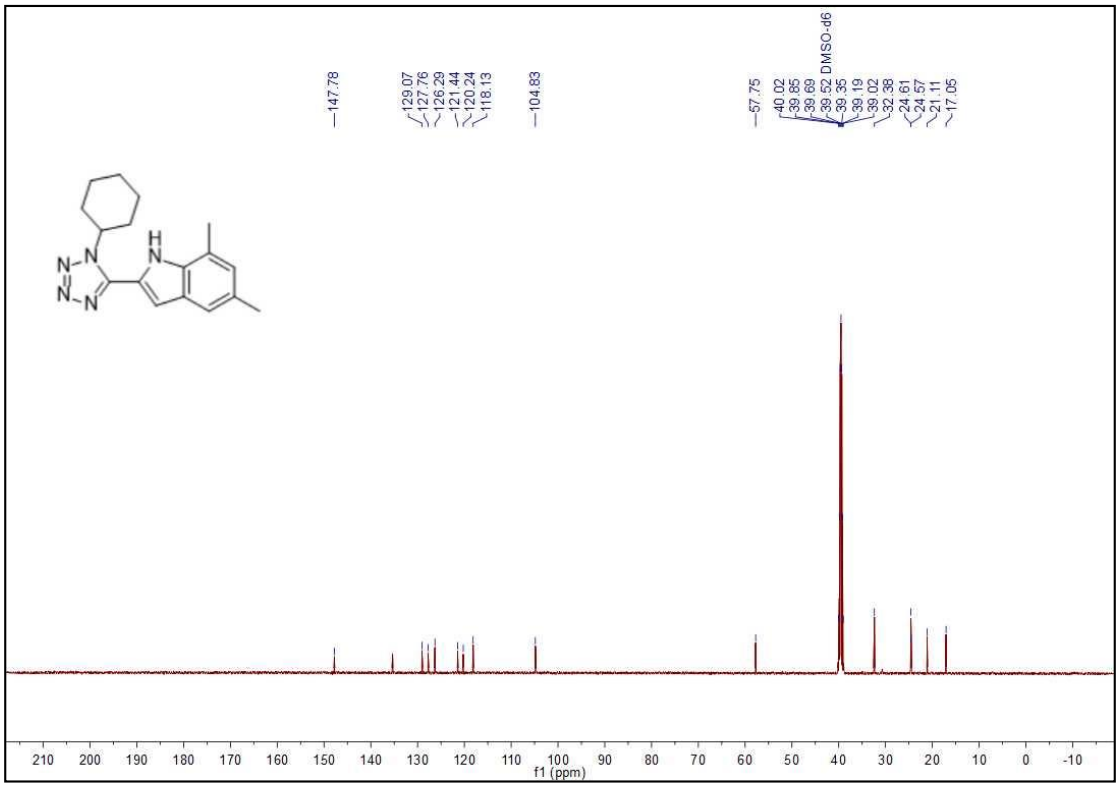


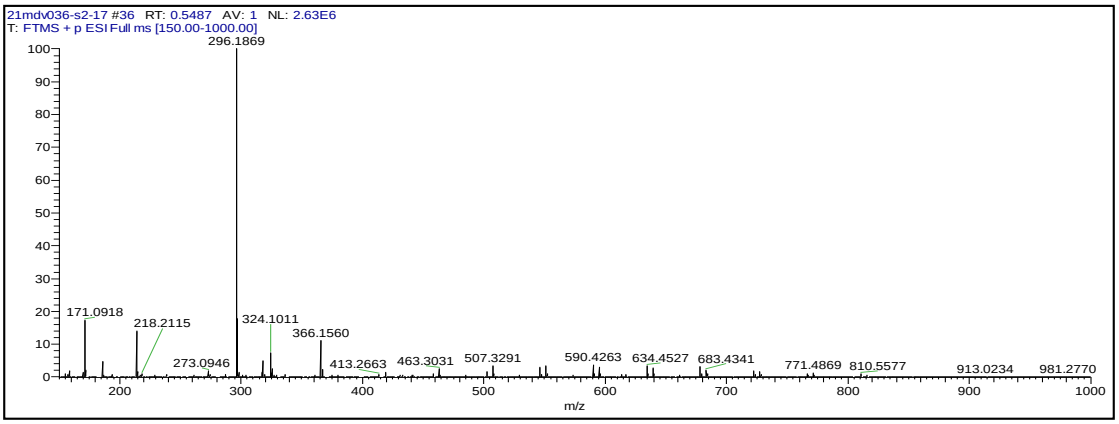



21mdv036-s2-16 #34 RT: 0.5170 AV: 1 NL: 2.71E6
T: FTMS + p ESI Full ms [150.00-1000.00]
324.1010
366.1559
296.0949
261.1261
194.1176
413.2662
463.3030
507.3290
590.4262
634.4526
722.5051
766.5313
815.5125
908.9780
970.4004
m/z

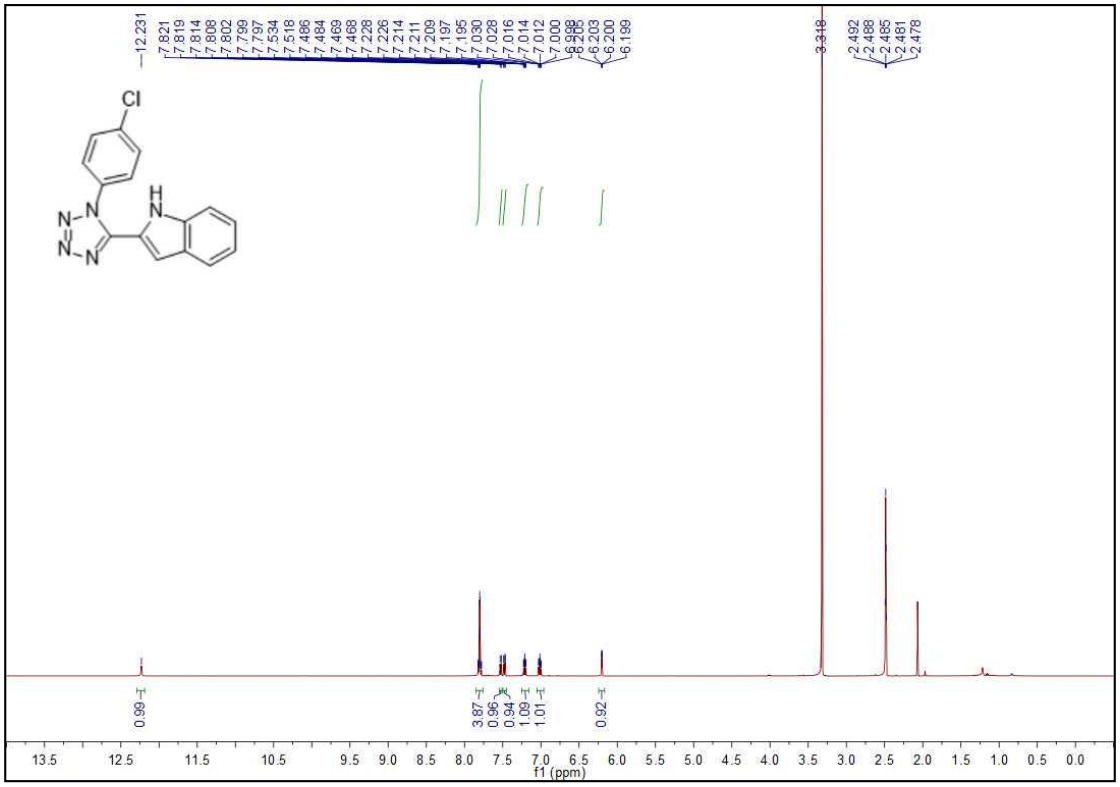
2-(1-cyclohexyl-1*H*-tetrazol-5-yl)-5,7-dimethyl-1*H*-indole (2q)

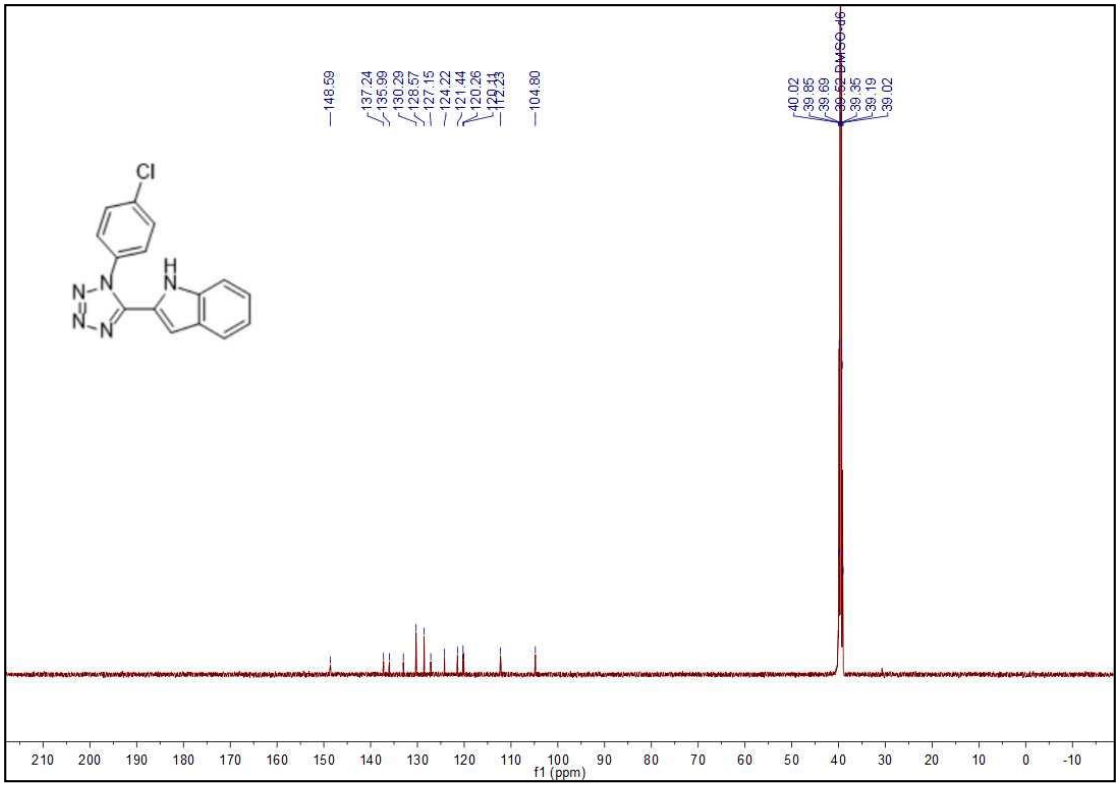


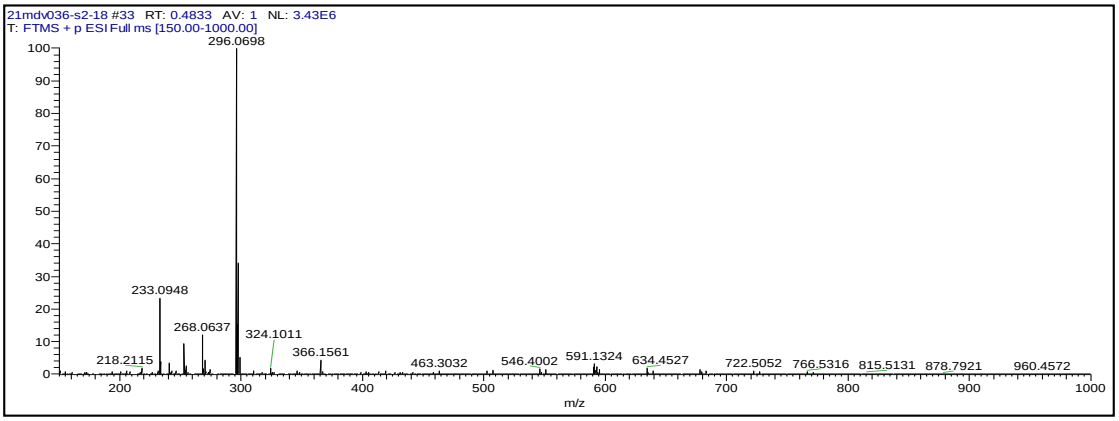



21mdv036-s2-17 #36 RT: 0.5487 AV: 1 NL: 2.63E6
T: FTMS + p ESI Full ms [150.00-1000.00]
296.1869
171.0918
218.2115
324.1011
366.1560
273.0946
413.2663
463.3031
507.3291
590.4263
634.4527
683.4341
771.4869
810.5577
913.0234
981.2770
m/z

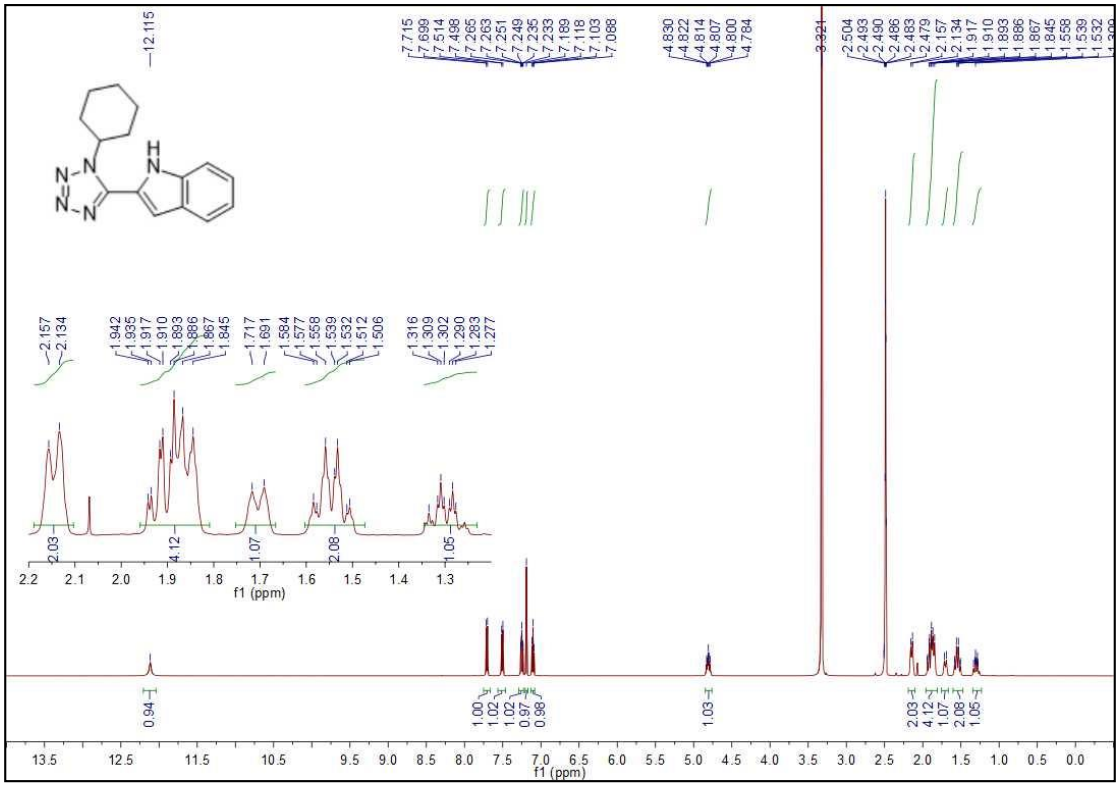
2-(1-(4-chlorophenyl)-1*H*-tetrazol-5-yl)-1*H*-indole (2r)

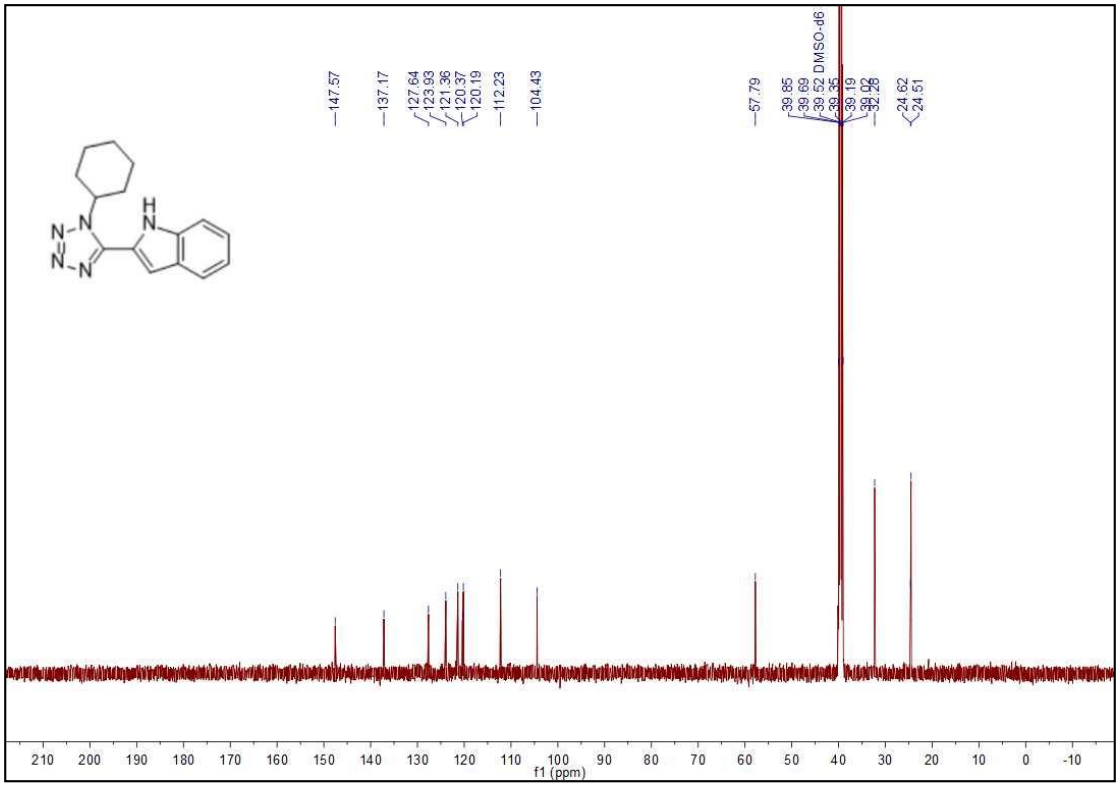


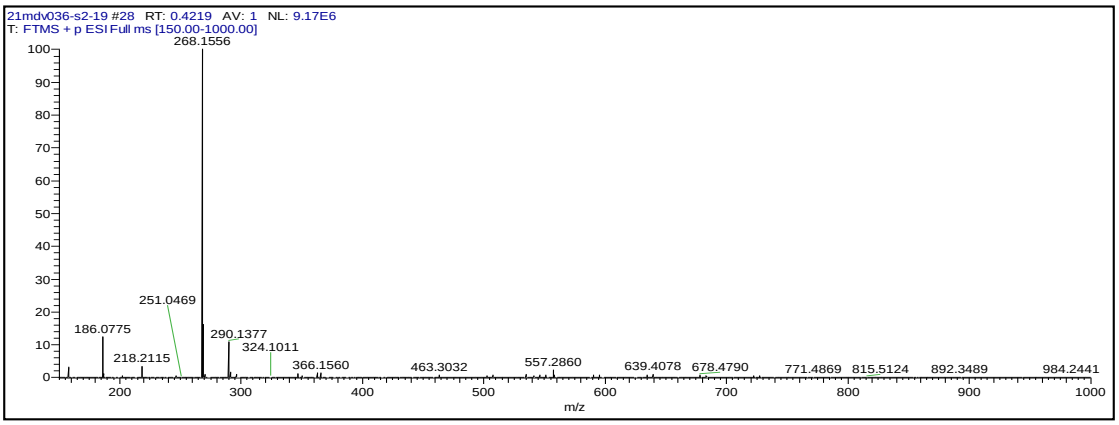



21mdv036-s2-18 #33 RT: 0.4833 AV: 1 NL: 3.43E6
T: FTMS + p ESI Full ms [150.00-1000.00]
296.0698
233.0948
268.0637
324.1011
366.1561
218.2115
463.3032
546.4002
591.1324
634.4527
722.5052
766.5316
815.5131
878.7921
960.4572
m/z

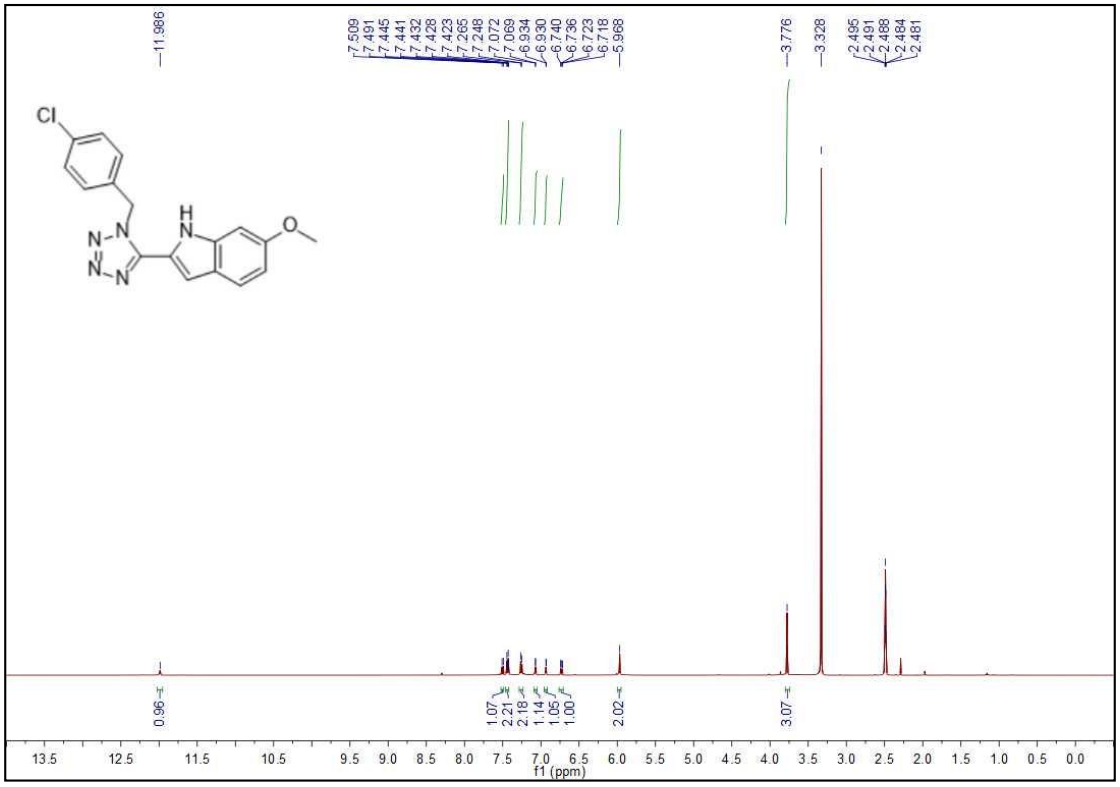
2-(1-cyclohexyl-1*H*-tetrazol-5-yl)-1*H*-indole (2s)

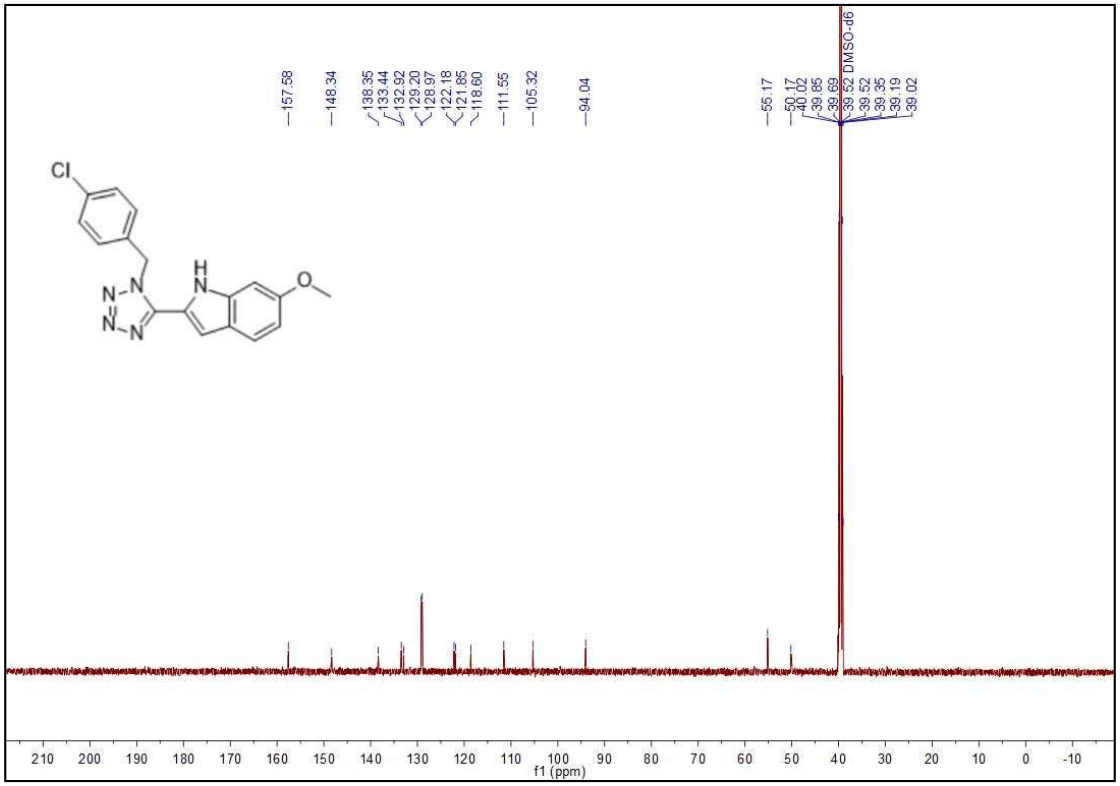


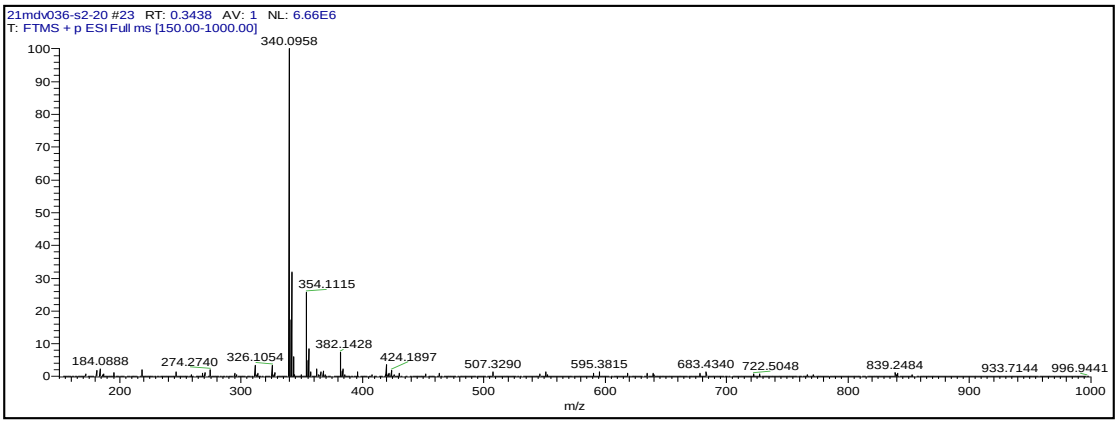



21mdv036-s2-19 #28 RT: 0.4219 AV: 1 NL: 9.17E6
T: FTMS + p ESI Full ms [150.00-1000.00]
268.1556
251.0469
186.0775
290.1377
324.1011
218.2115
366.1560
463.3032
557.2860
639.4078
678.4790
771.4869
815.5124
892.3489
984.2441
m/z

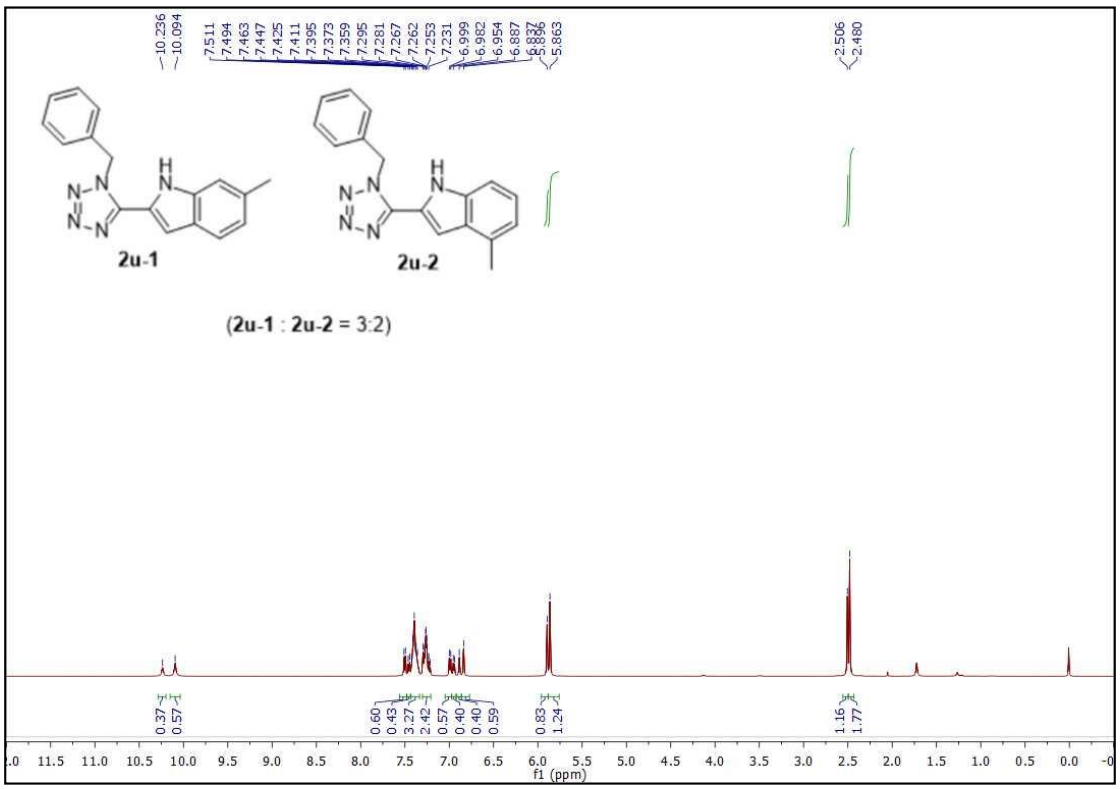
2-(1-(4-chlorobenzyl)-1*H*-tetrazol-5-yl)-6-methoxy-1*H*-indole (2t-1)

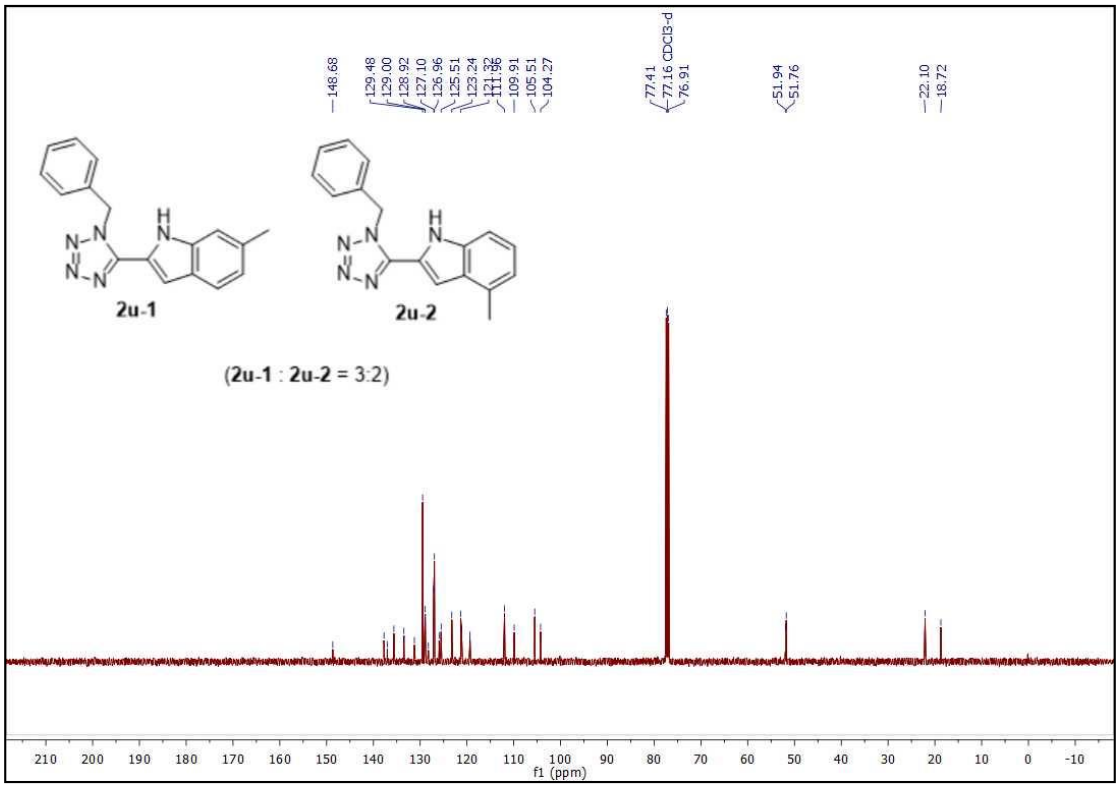


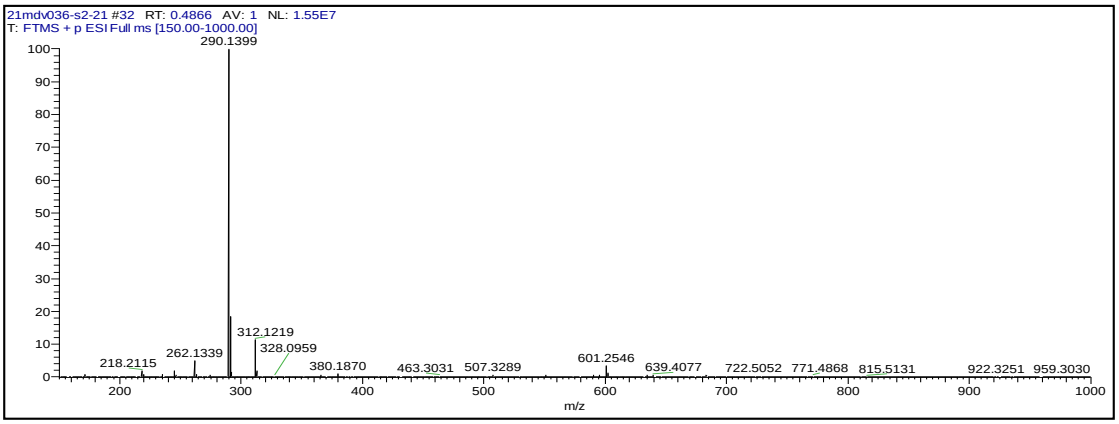



21mdv036-s2-20 #23 RT: 0.3438 AV: 1 NL: 6.66E6
T: FTMS + p ESI Full ms [150.00-1000.00]
340.0958
354.1115
382.1428
184.0888
274.2740
326.1054
424.1897
507.3290
595.3815
683.4340
722.5048
839.2484
933.7144
996.9441
m/z

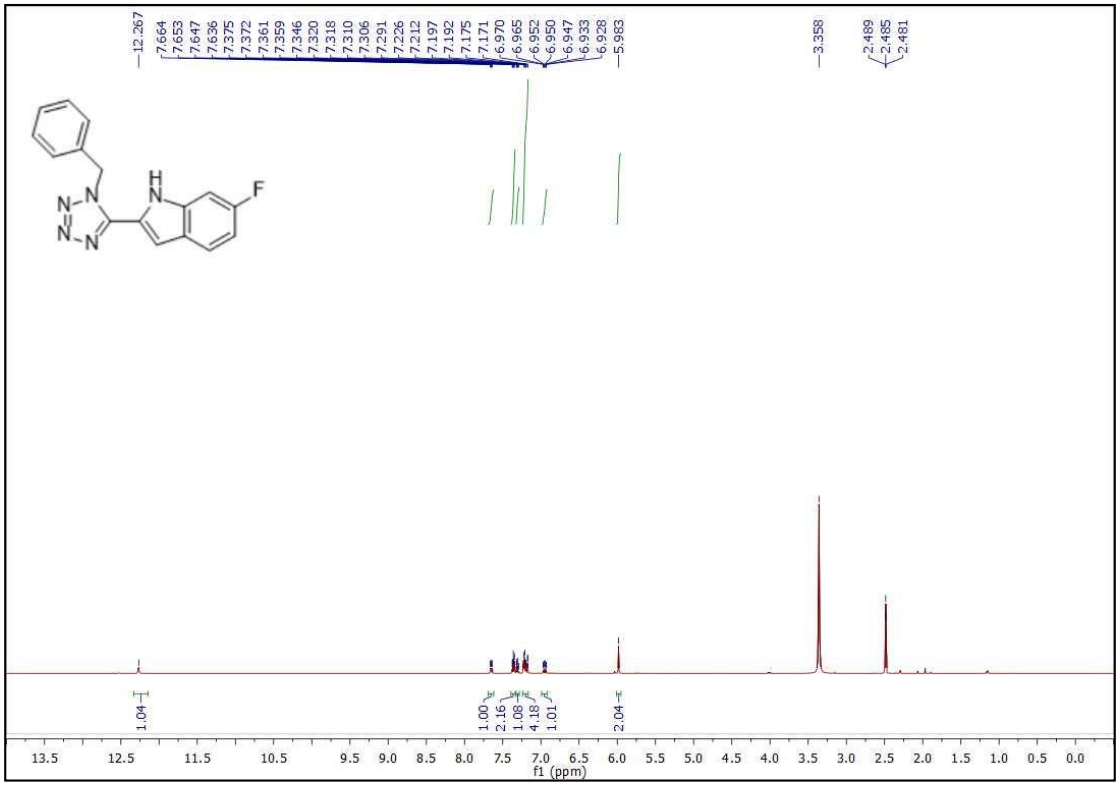
2-(1-benzyl-1*H*-tetrazol-5-yl)-6-methyl-1*H*-indole (2u-1) and **2-(1-benzyl-1*H*-tetrazol-5-yl)-4-methyl-1*H*-indole (2u-2)**

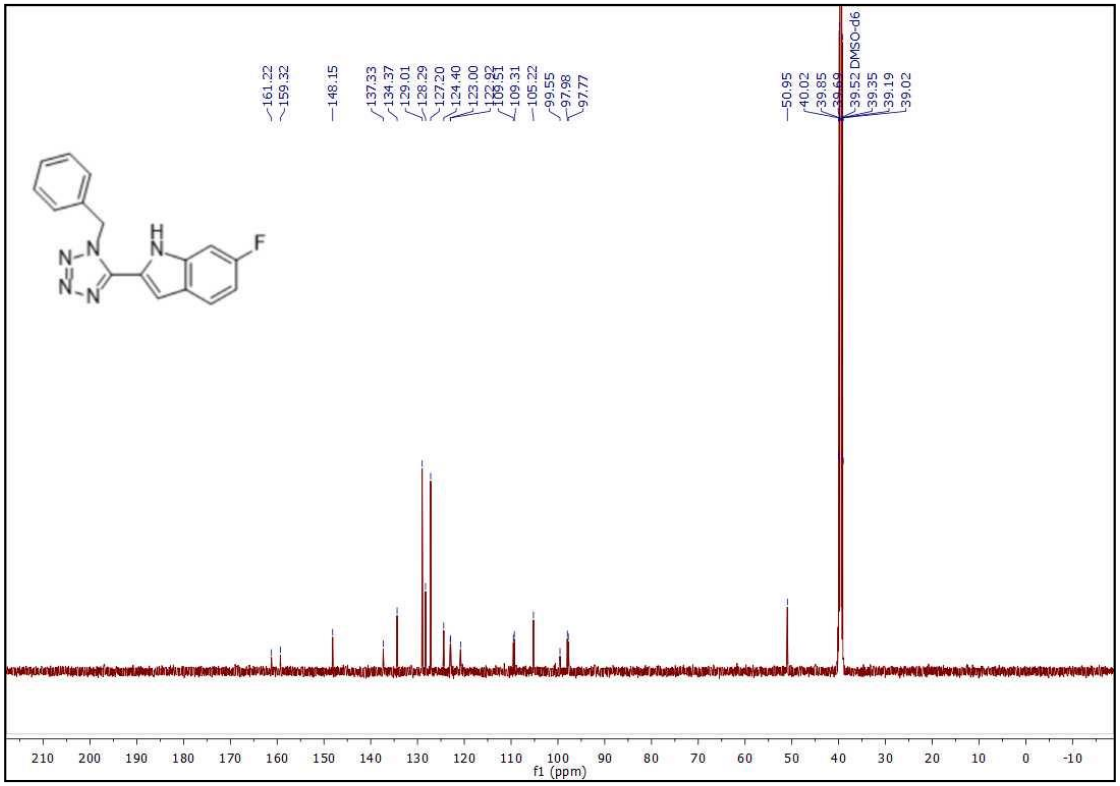


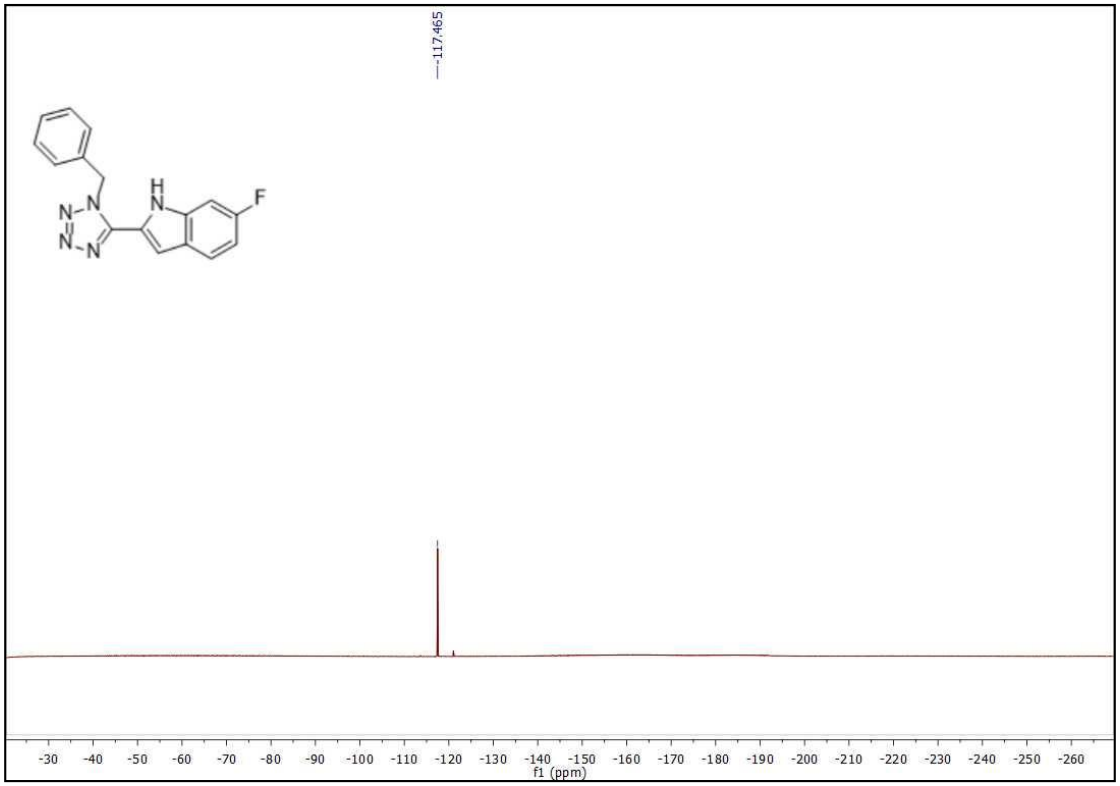


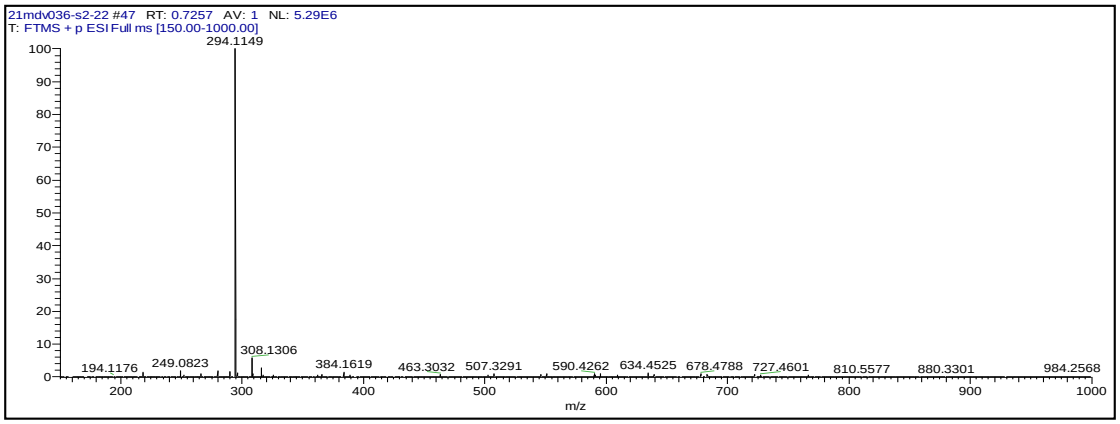

21mdv036-s2-21 #32 RT: 0.4866 AV: 1 NL: 1.55E7
T: FTMS + p ESI Full ms [150.00-1000.00]
290.1399
312.1219
328.0959
262.1339
218.2115
380.1870
463.3031
507.3289
601.2546
639.4077
722.5052
771.4868
815.5131
922.3251
959.3030
m/z

2-(1-benzyl-1*H*-tetrazol-5-yl)-6-fluoro-1*H*-indole (2v-1)

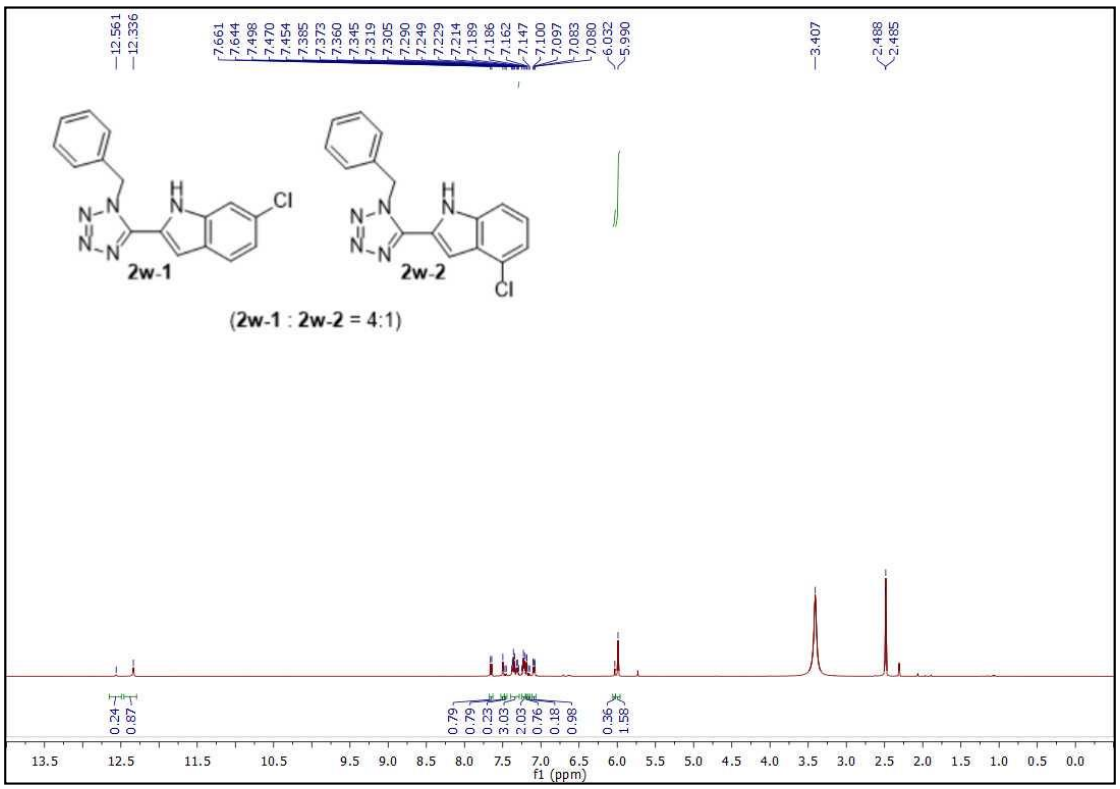


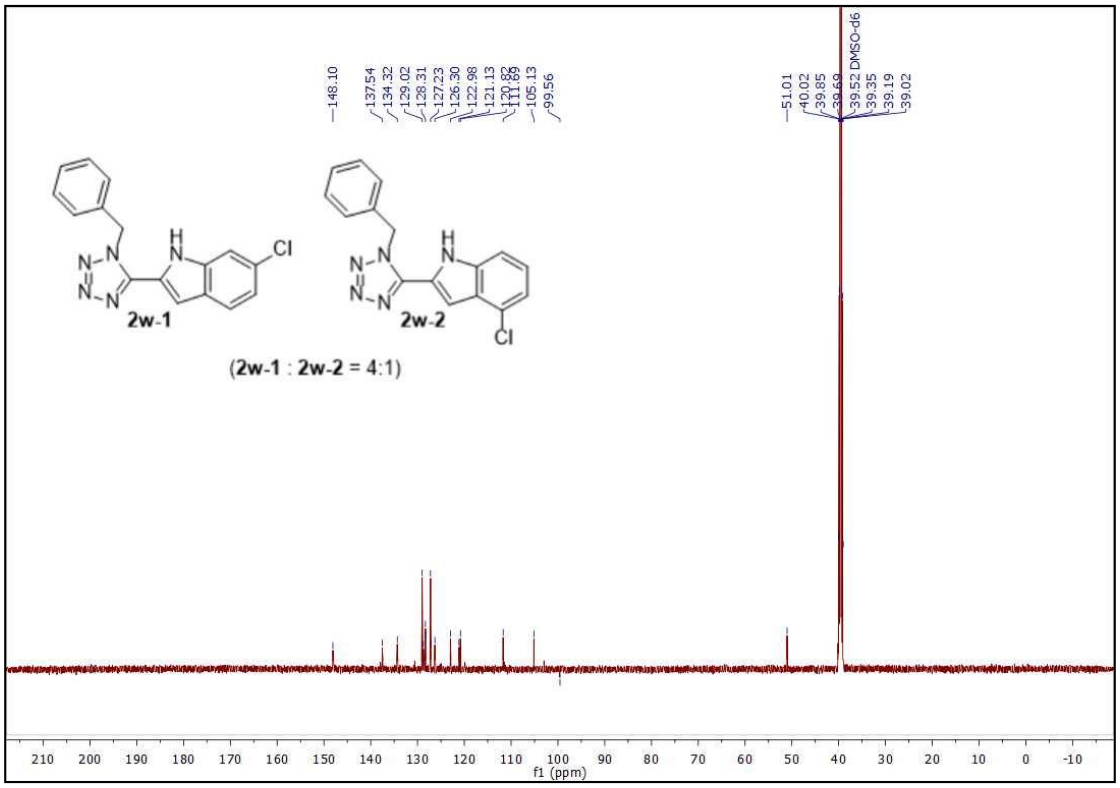


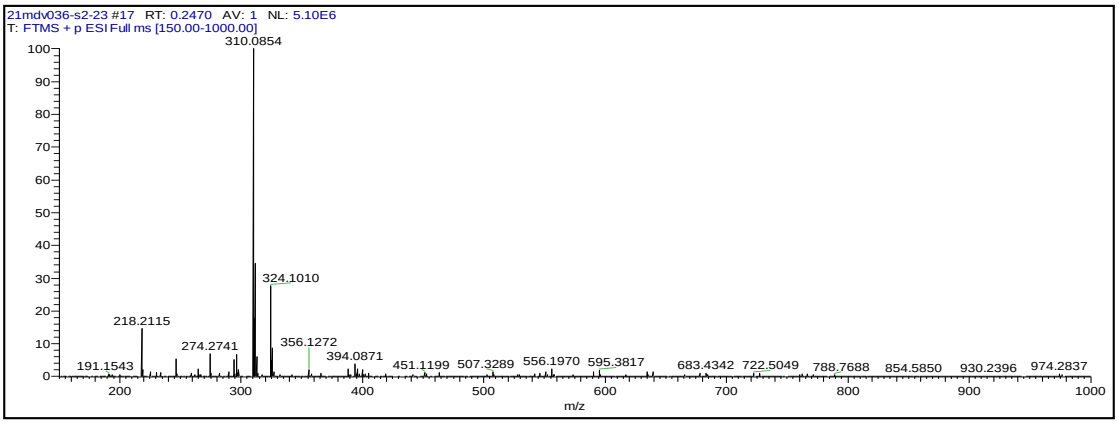

-117.465
H
N
N
N
N
F
-30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220 -230 -240 -250 -260
f1 (ppm)


21mdv036-s2-22 #47 RT: 0.7257 AV: 1 NL: 5.29E6
T: FTMS + p ESI Full ms [150.00-1000.00]
294.1149
308.1306
194.1176
249.0823
384.1619
463.3032
507.3291
590.4262
634.4525
678.4788
727.4601
810.5577
880.3301
984.2568
m/z

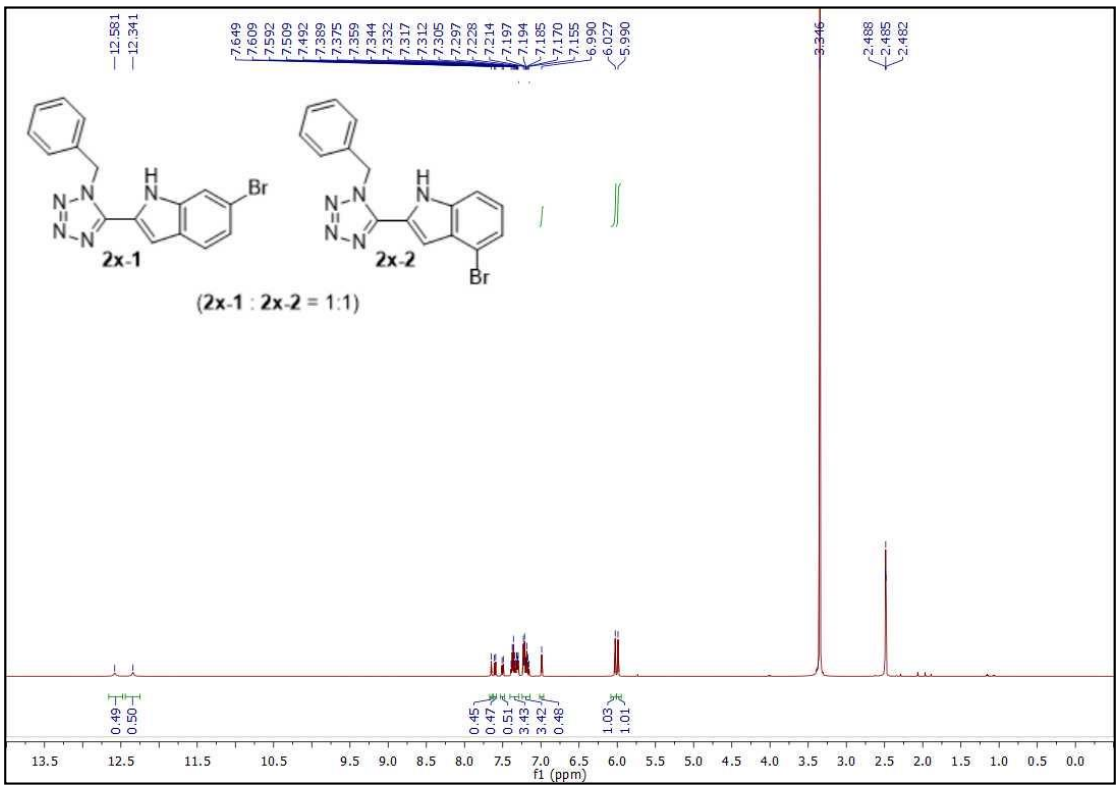
2-(1-benzyl-1*H*-tetrazol-5-yl)-6-chloro-1*H*-indole (2w-1) and **2-(1-benzyl-1*H*-tetrazol-5-yl)-4-chloro-1*H*-indole (2w-2)**

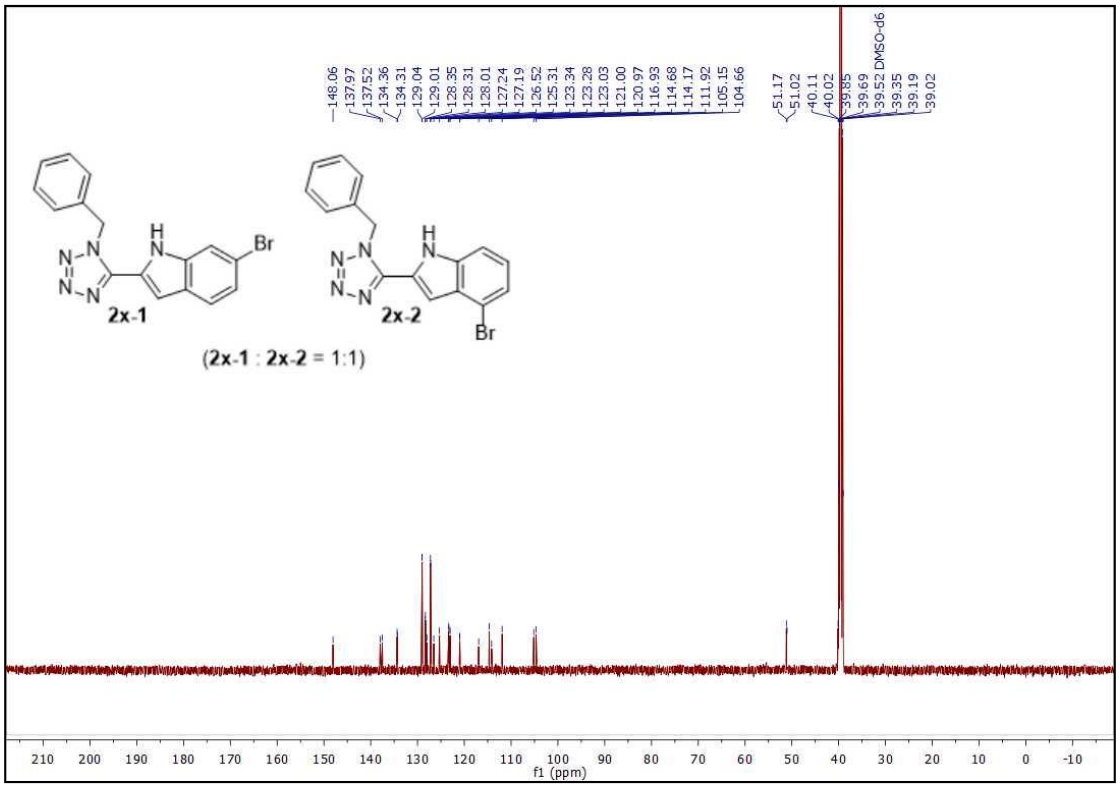


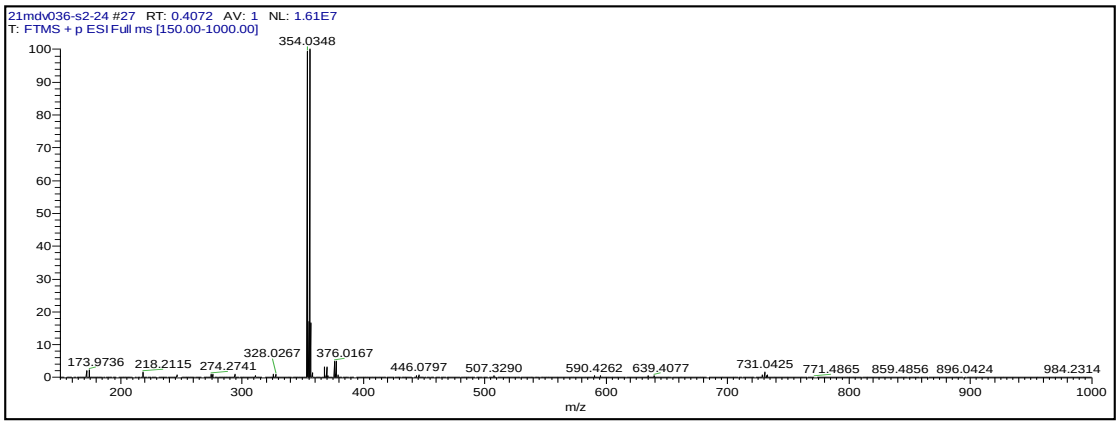



21mdv036-s2-23 #17 RT: 0.2470 AV: 1 NL: 5.10E6
T: FTMS + p ESI Full ms [150.00-1000.00]
310.0854
324.1010
218.2115
274.2741
356.1272
394.0871
191.1543
451.1199
507.3289
556.1970
595.3817
683.4342
722.5049
788.7688
854.5850
930.2396
974.2837
m/z

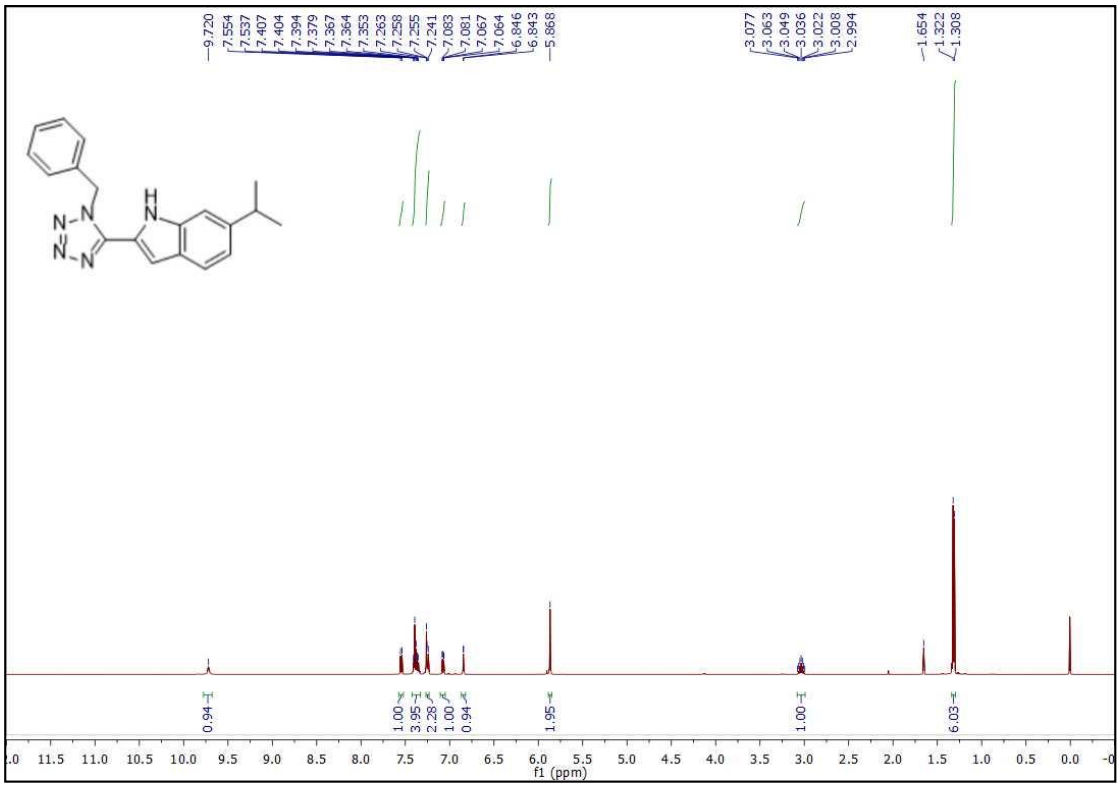
2-(1-benzyl-1*H*-tetrazol-5-yl)-6-bromo-1*H*-indole (2x-1) and **2-(1-benzyl-1*H*-tetrazol-5-yl)-4-bromo-1*H*-indole (2x-2)**

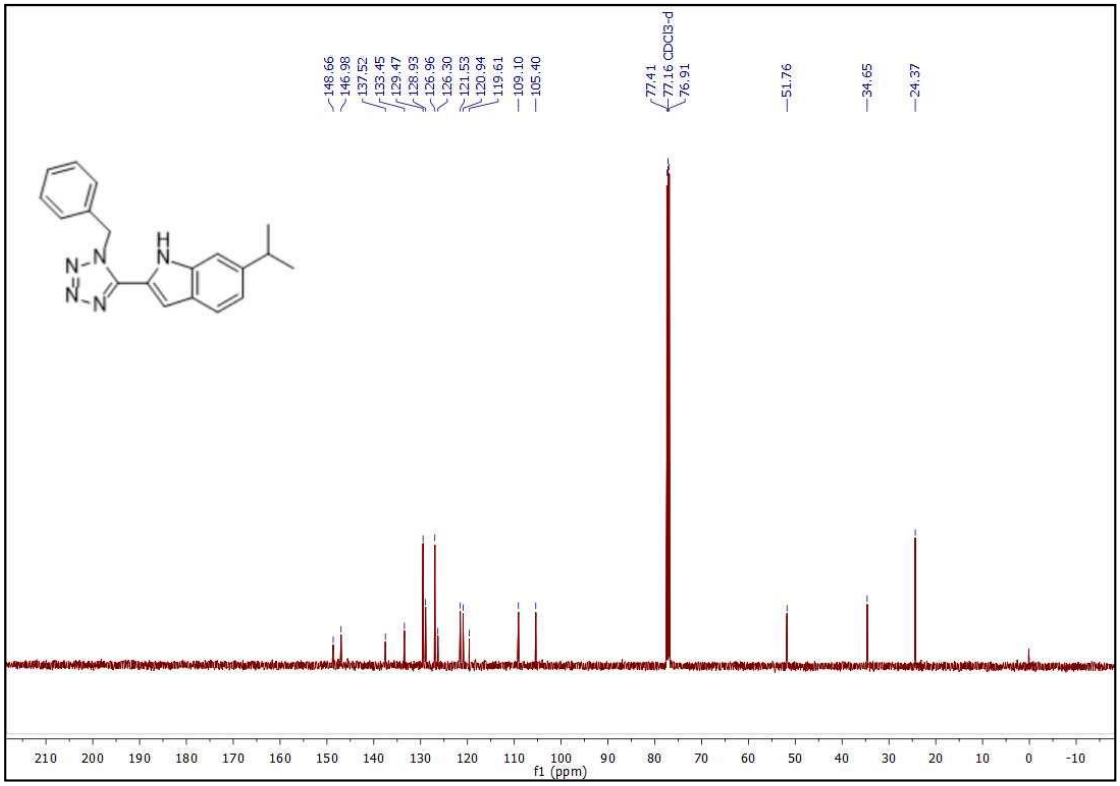


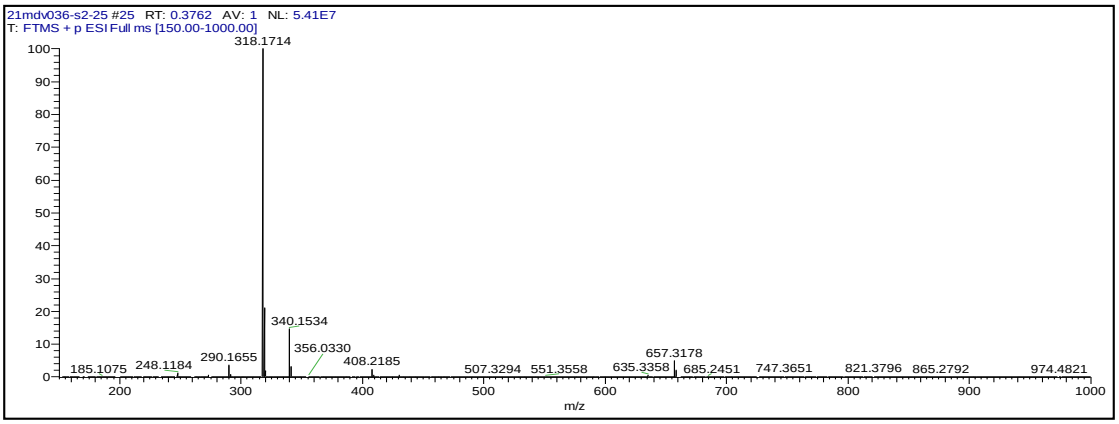



21mdv036-s2-24 #27 RT: 0.4072 AV: 1 NL: 1.61E7
T: FTMS + p ESI Full ms [150.00-1000.00]
354.0348
328.0267
376.0167
173.9736
218.2115
274.2741
446.0797
507.3290
590.4262
639.4077
731.0425
771.4865
859.4856
896.0424
984.2314
m/z

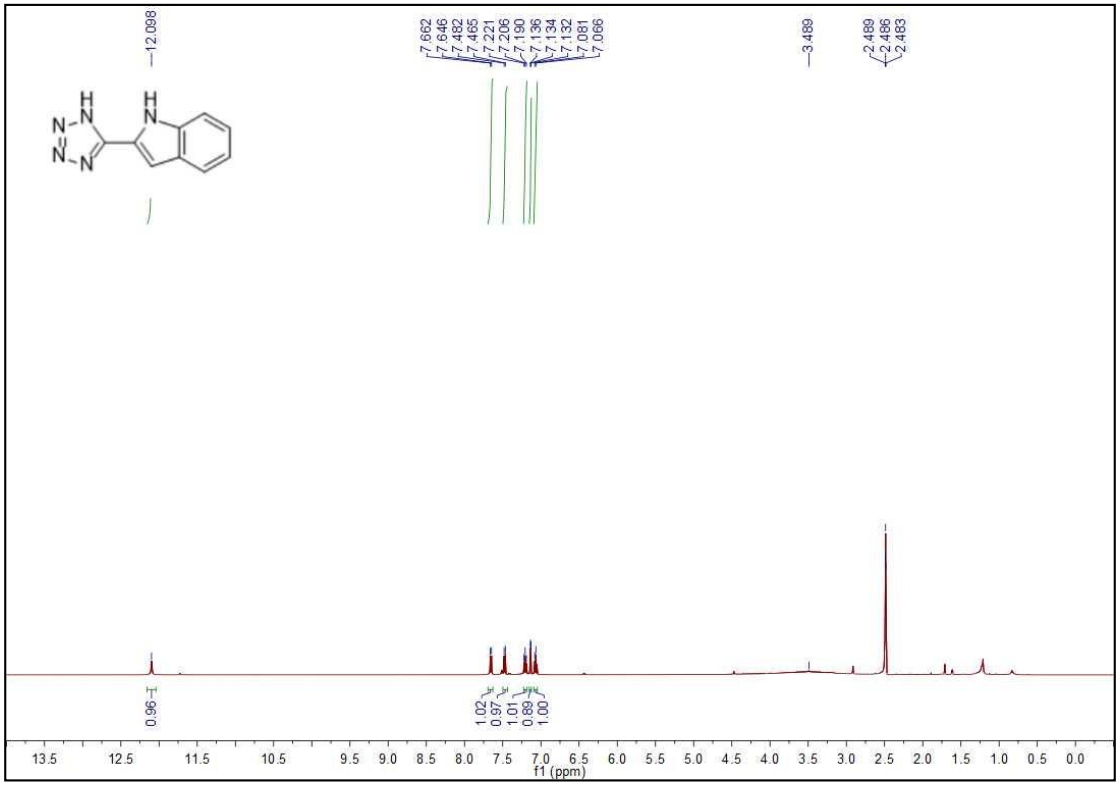
2-(1-benzyl-1*H*-tetrazol-5-yl)-6-isopropyl-1*H*-indole (2y)



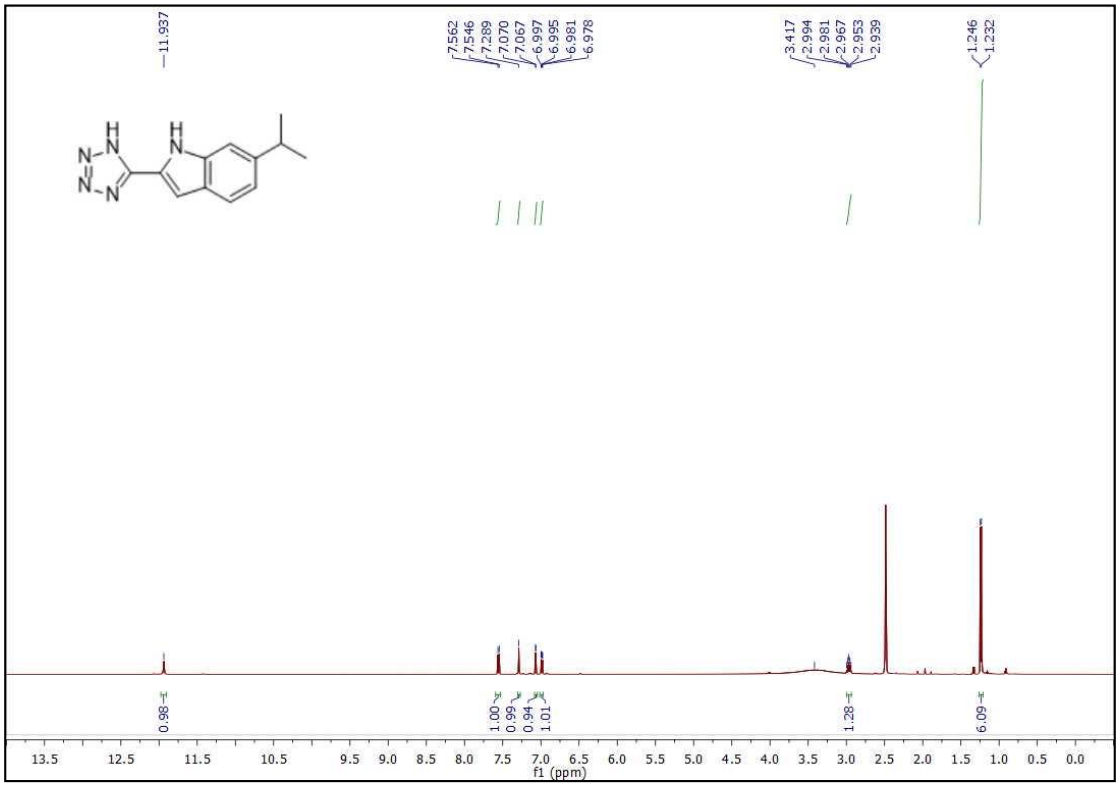


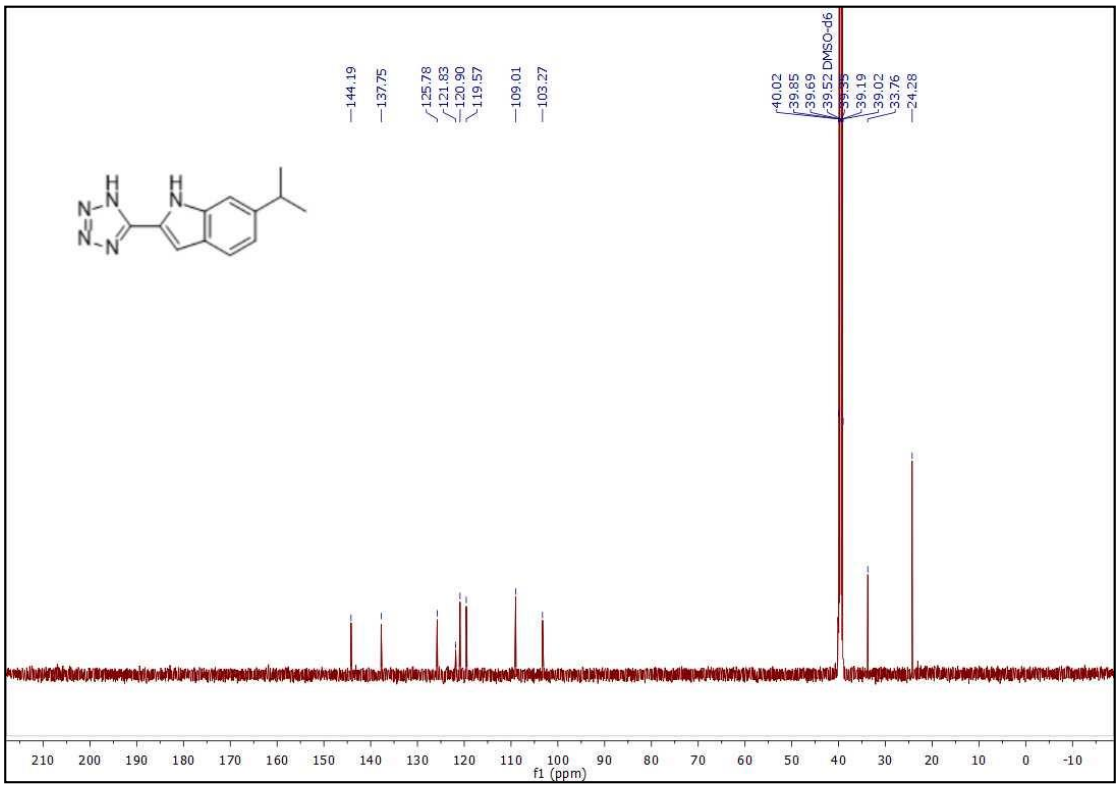

21mdv036-s2-25 #25 RT: 0.3762 AV: 1 NL: 5.41E7
T: FTMS + p ESI Full ms [150.00-1000.00]
318.1714
340.1534
356.0330
290.1655
408.2185
248.1184
185.1075
507.3294
551.3558
657.3178
635.3358
685.2451
747.3651
821.3796
865.2792
974.4821
m/z

2-(1*H*-tetrazol-5-yl)-1*H*-indole (3a)

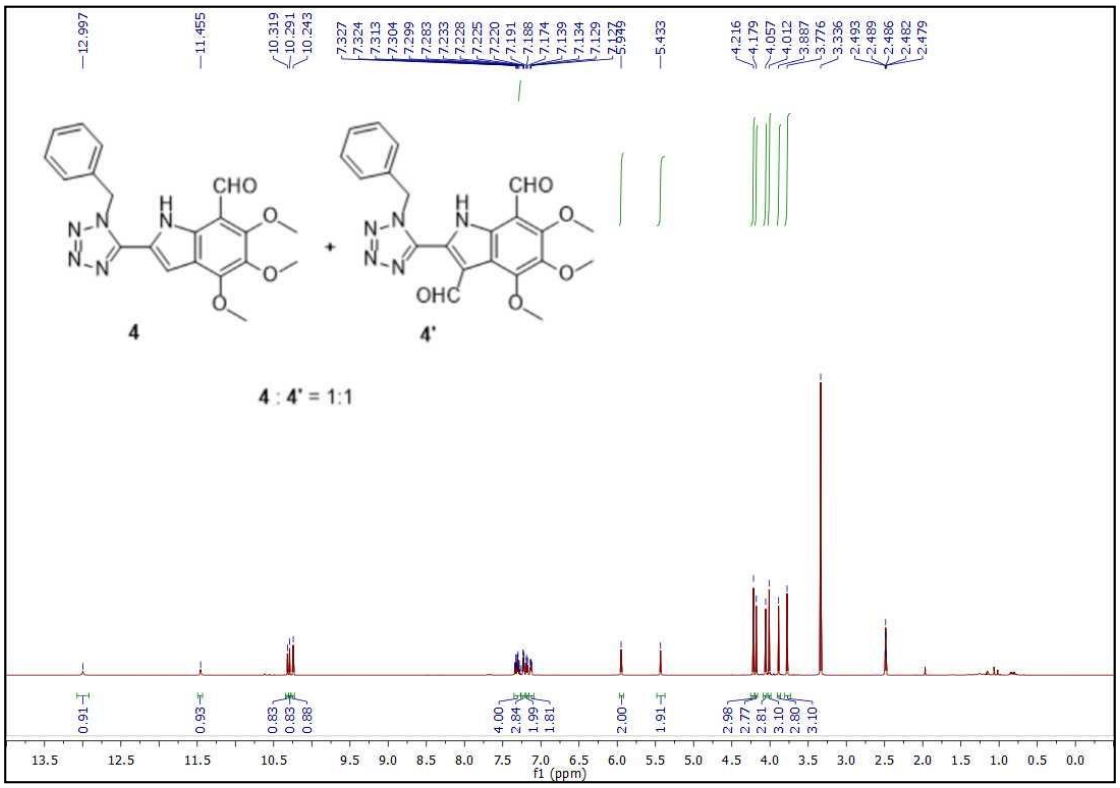


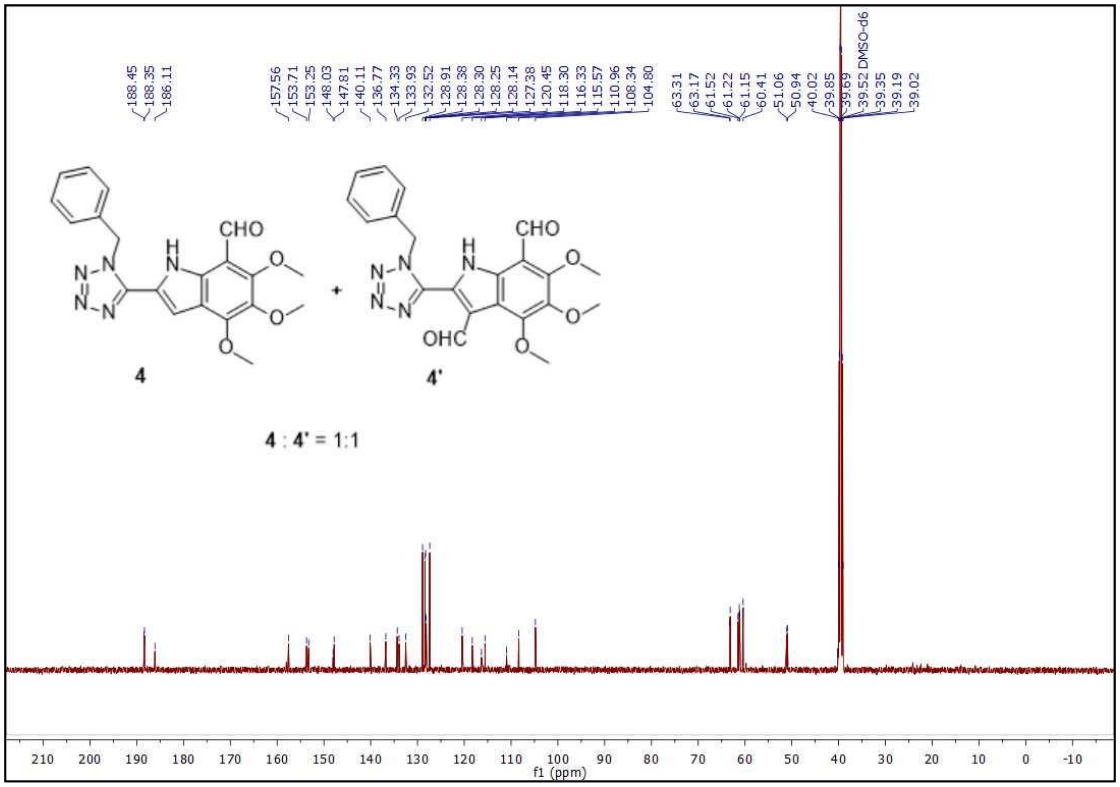
6-isopropyl-2-(1*H*-tetrazol-5-yl)-1*H*-indole (3b)



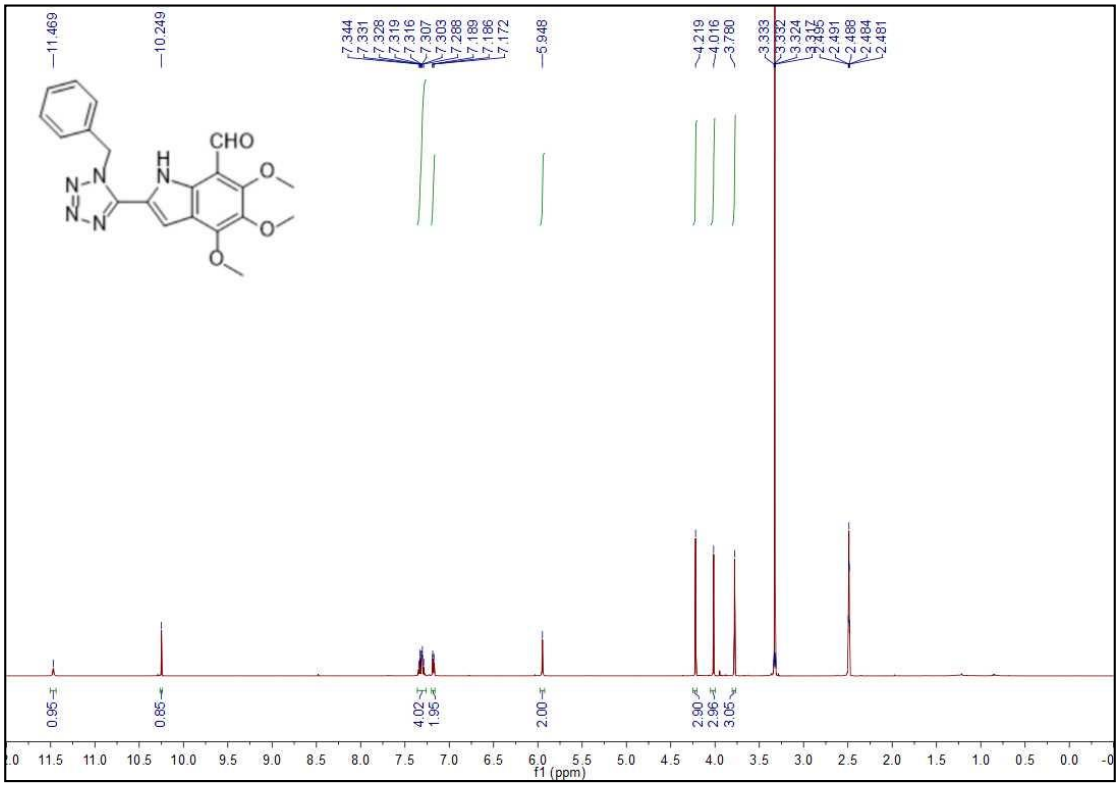


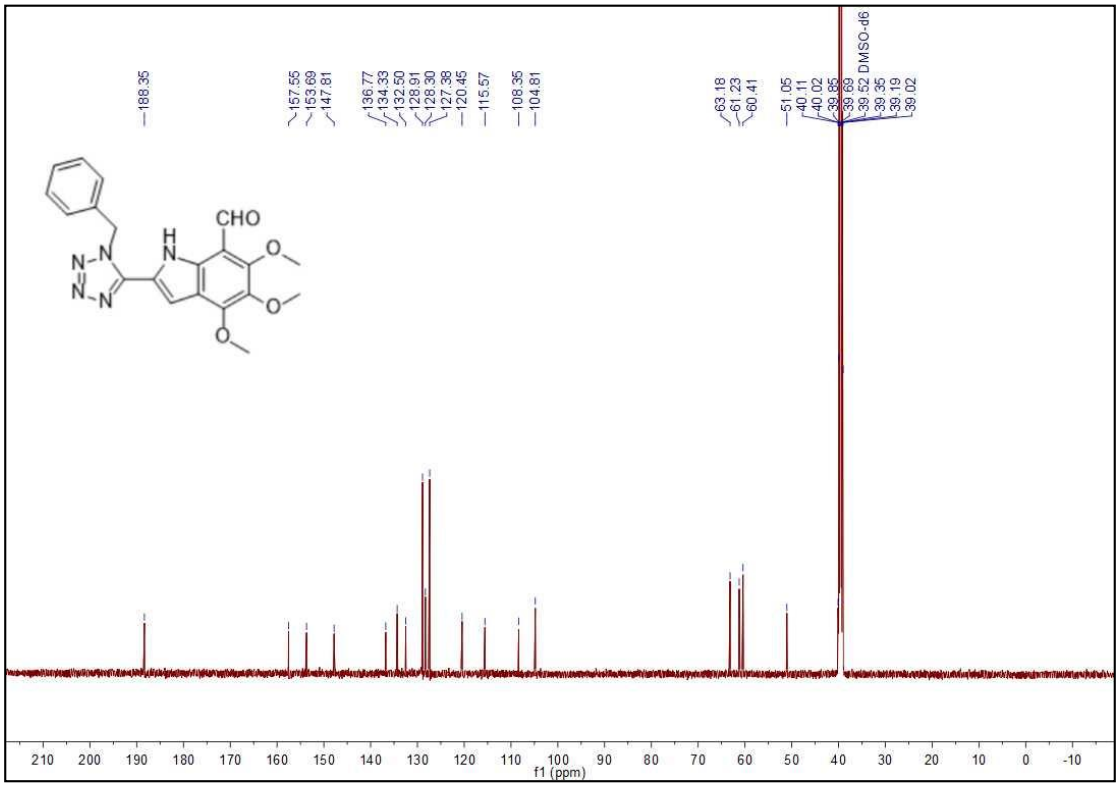
2-(1-benzyl-1*H*-tetrazol-5-yl)-4,5,6-trimethoxy-1*H*-indole-7-carbaldehyde (4) and
2-(1-benzyl-1*H*-tetrazol-5-yl)-4,5,6-trimethoxy-1*H*-indole-3,7-dicarbaldehyde (4')

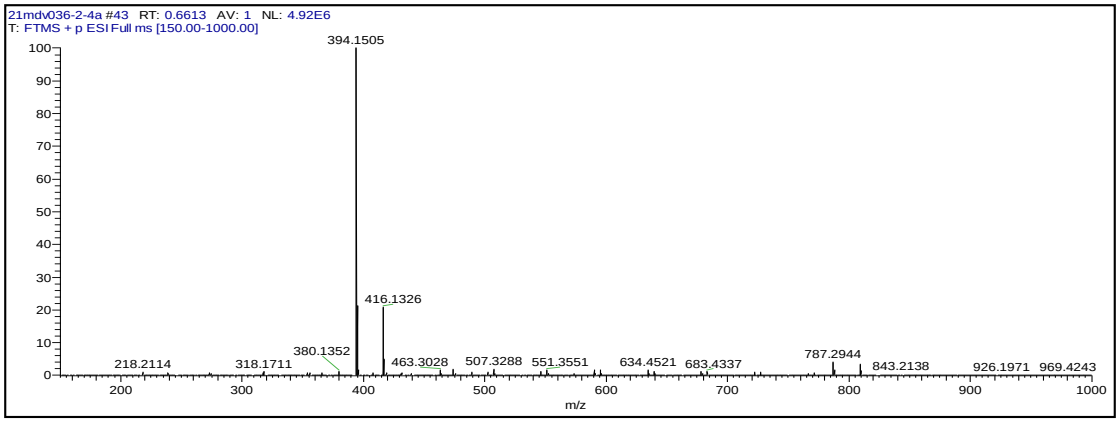




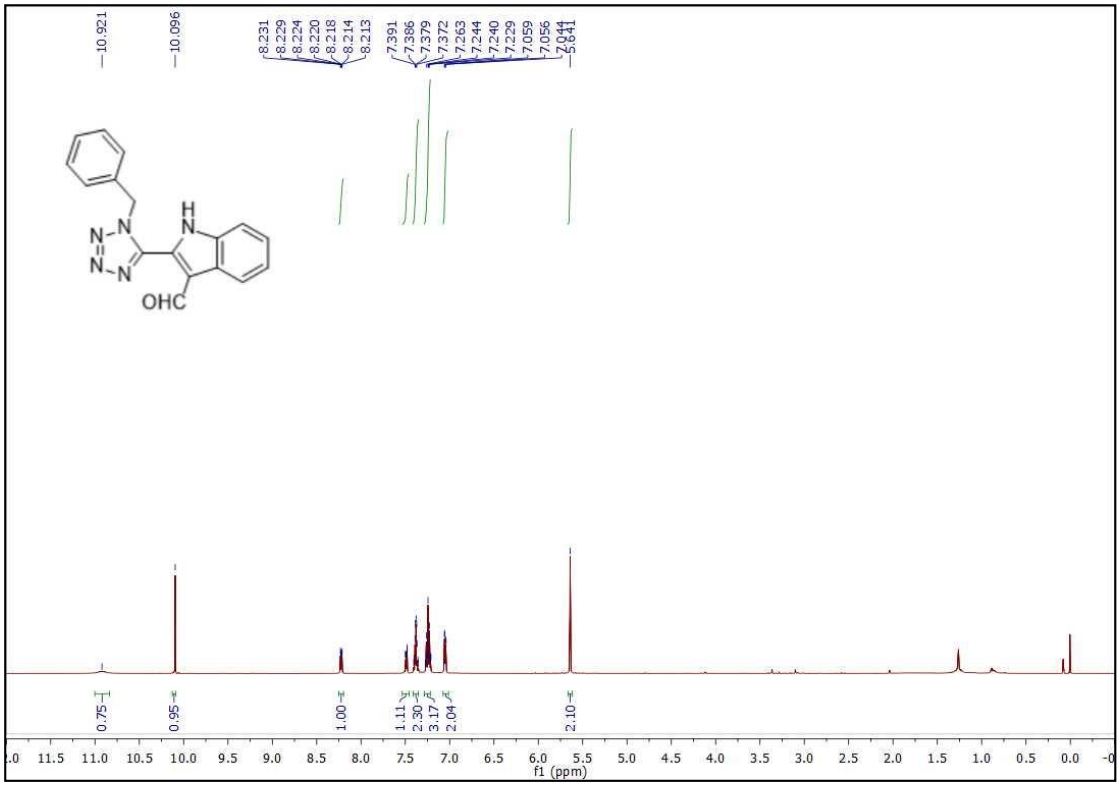
2-(1-benzyl-1*H*-tetrazol-5-yl)-4,5,6-trimethoxy-1*H*-indole-7-carbaldehyde (4)

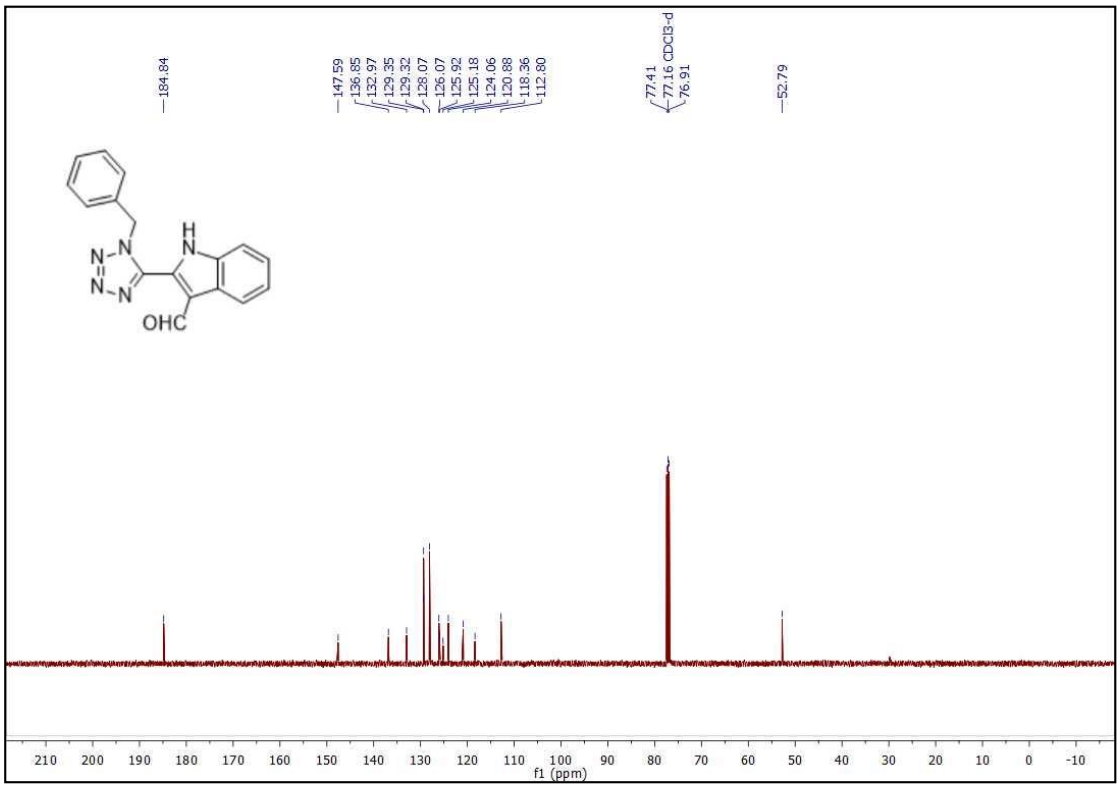


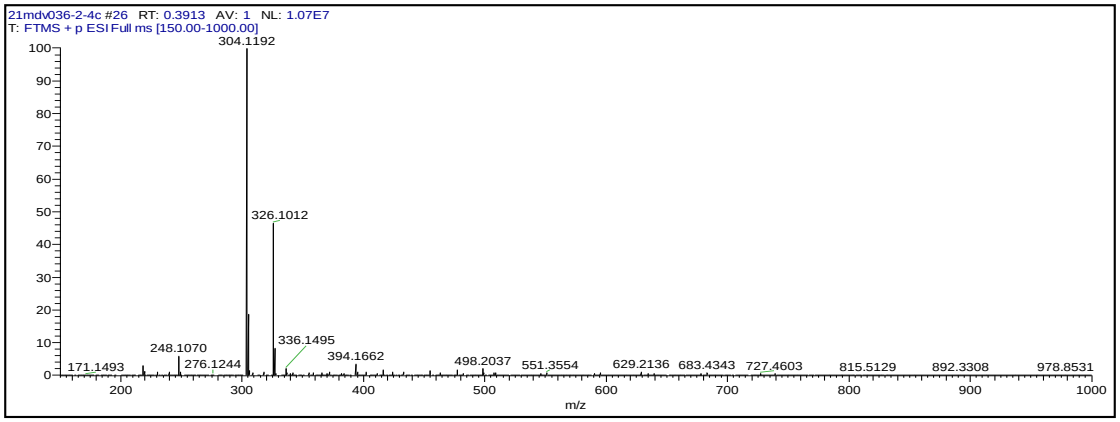



21mdv036-2-4a #43 RT: 0.6613 AV: 1 NL: 4.92E6
T: FTMS + p ESI Full ms [150.00-1000.00]
394.1505
416.1326
380.1352
218.2114
318.1711
463.3028
507.3288
551.3551
634.4521
683.4337
787.2944
843.2138
926.1971
969.4243
m/z

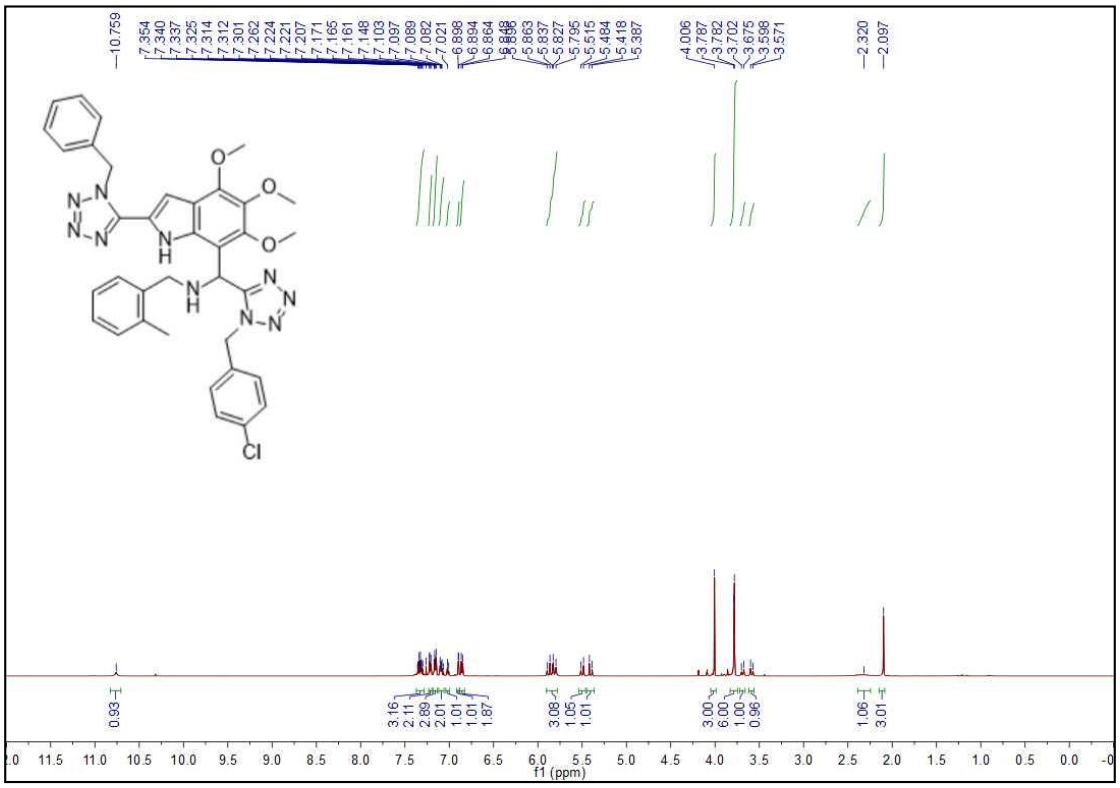
2-(1-benzyl-1*H*-tetrazol-5-yl)-1*H*-indole-3-carbaldehyde (5)

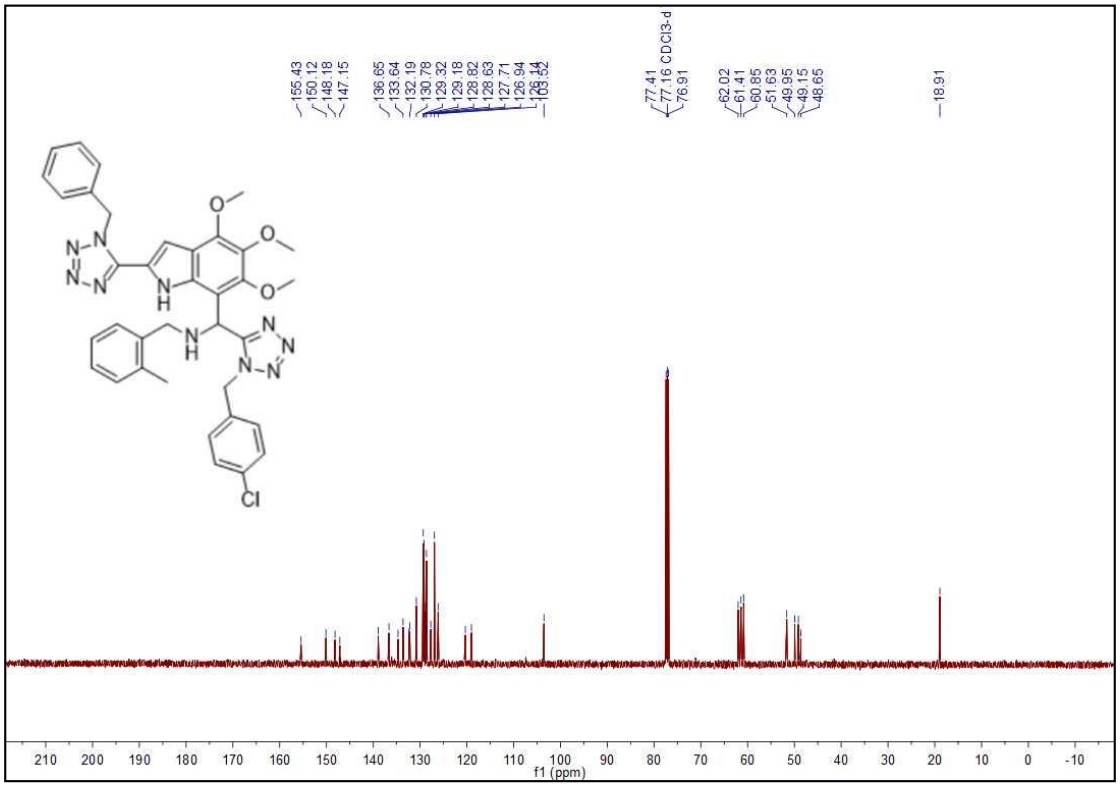


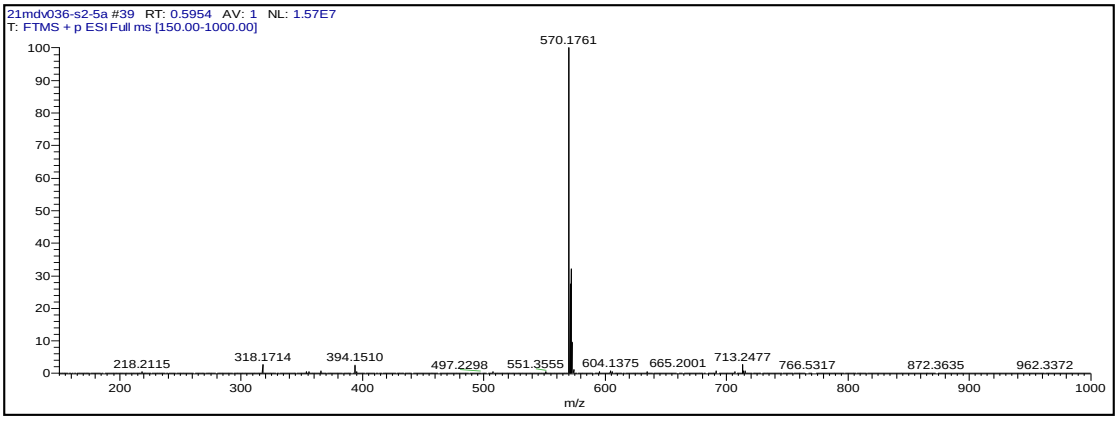



21mdv036-2-4c #26 RT: 0.3913 AV: 1 NL: 1.07E7
T: FTMS + p ESI Full ms [150.00-1000.00]
304.1192
326.1012
336.1495
248.1070
276.1244
394.1662
171.1493
498.2037
551.3554
629.2136
683.4343
727.4603
815.5129
892.3308
978.8531
m/z

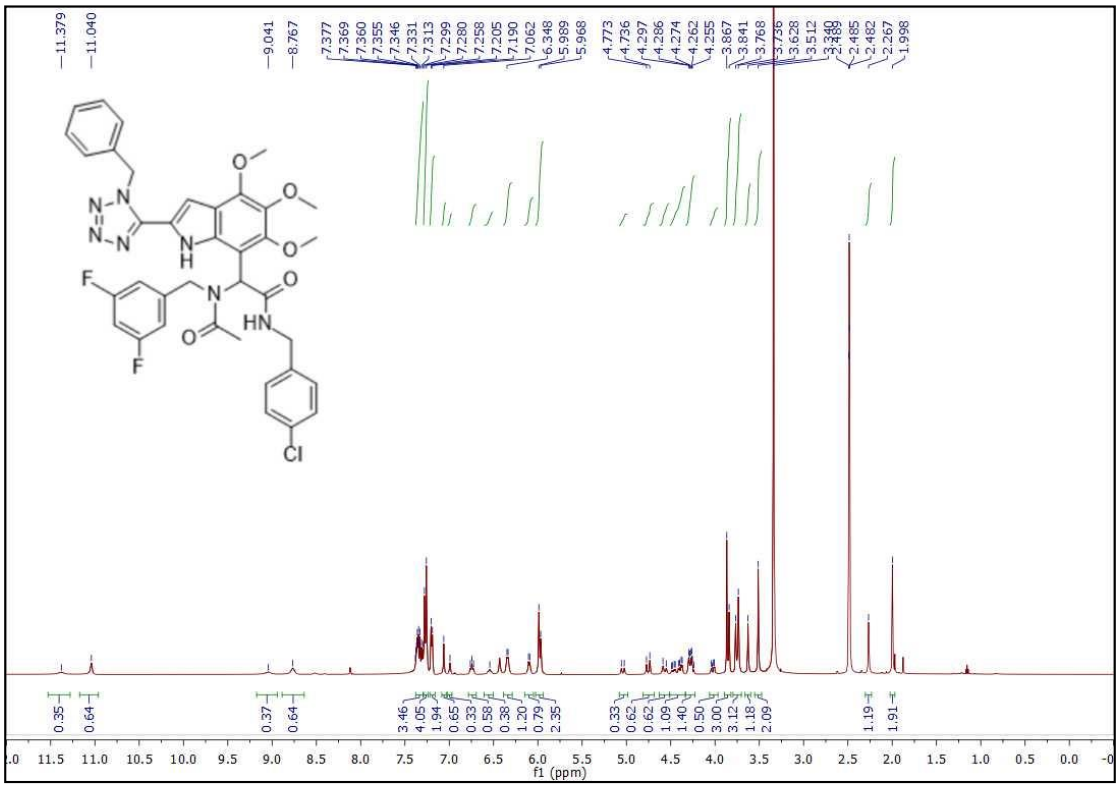
1-(2-(1-benzyl-1*H*-tetrazol-5-yl)-4,5,6-trimethoxy-1*H*-indol-7-yl)-1-(1-(4-chlorobenzyl)-1*H*-tetrazol-5-yl)-*N*-(2-methylbenzyl)methanamine (6)

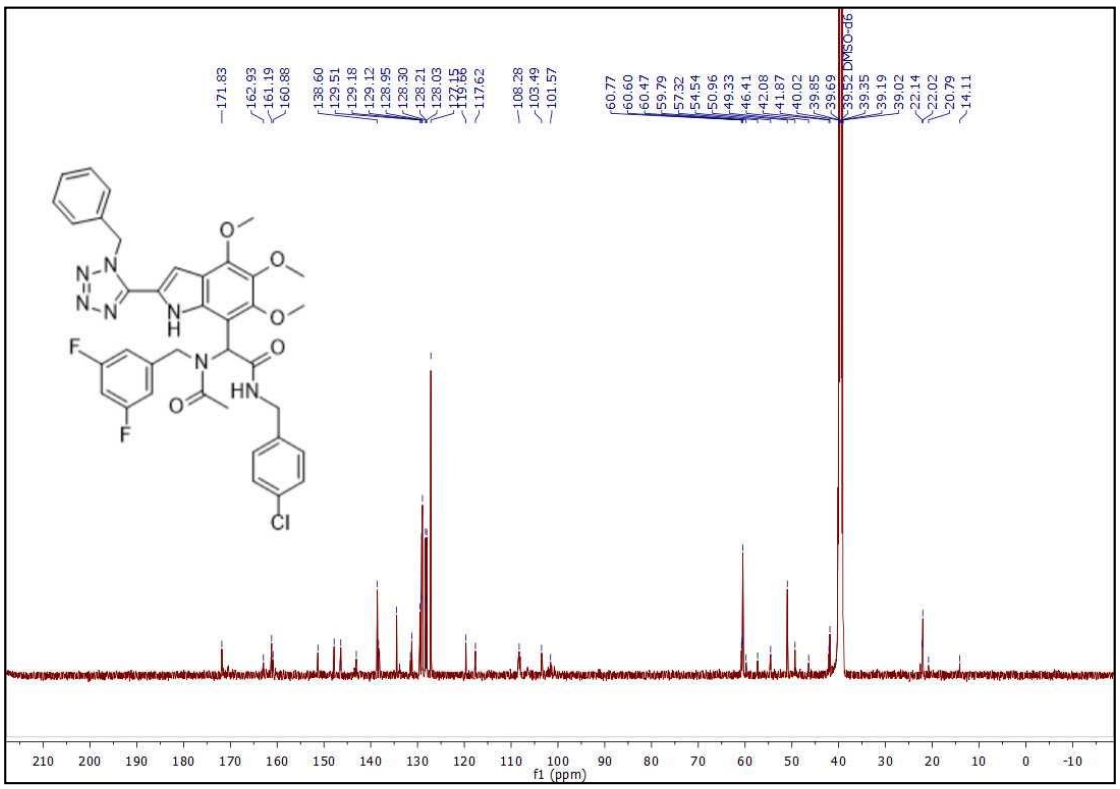


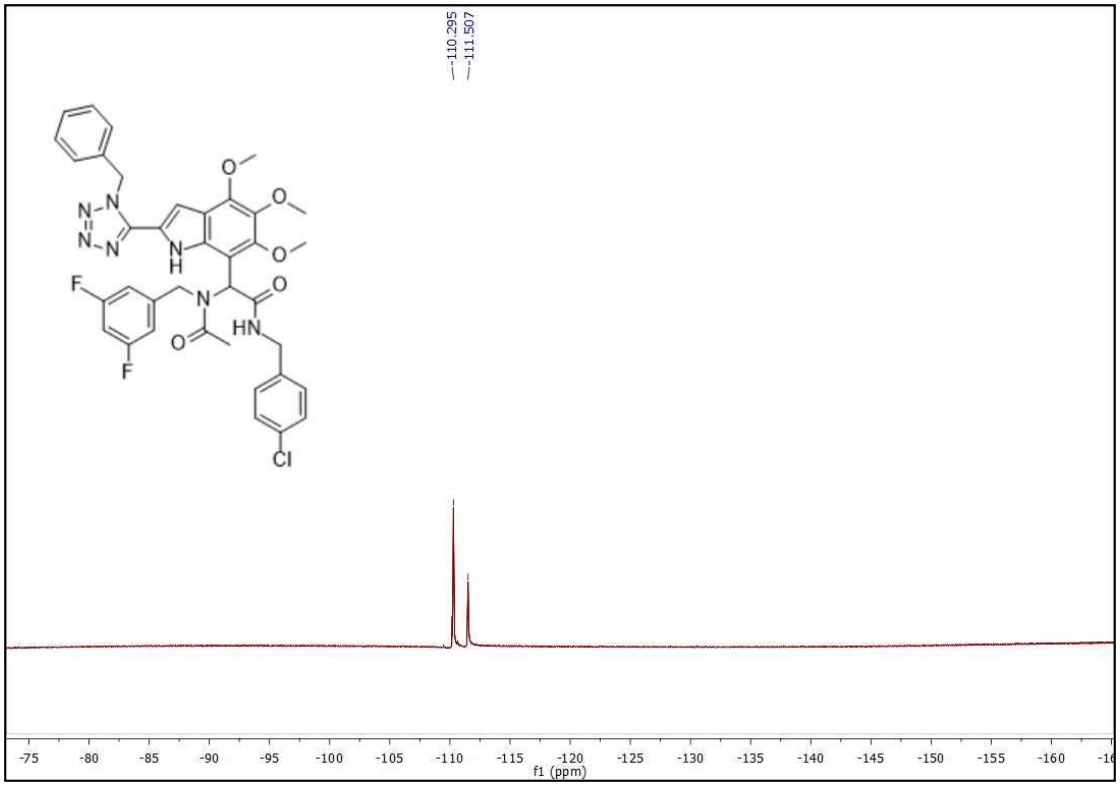


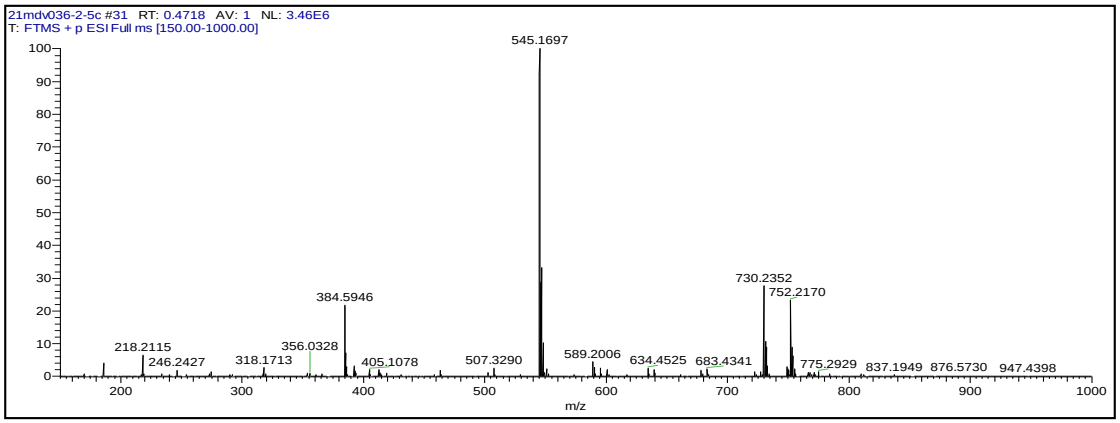

21mdv036-s2-5a #39 RT: 0.5954 AV: 1 NL: 1.57E7
T: FTMS + p ESI Full ms [150.00-1000.00]
570.1761
218.2115
318.1714
394.1510
497.2298
551.3555
604.1375
665.2001
713.2477
766.5317
872.3635
962.3372
m/z

2-(2-(1-benzyl-1*H*-tetrazol-5-yl)-4,5,6-trimethoxy-1*H*-indol-7-yl)-*N*-(4-chlorobenzyl)-2-(*N*-(3,5-difluorobenzyl)acetamido)acetamide (7)

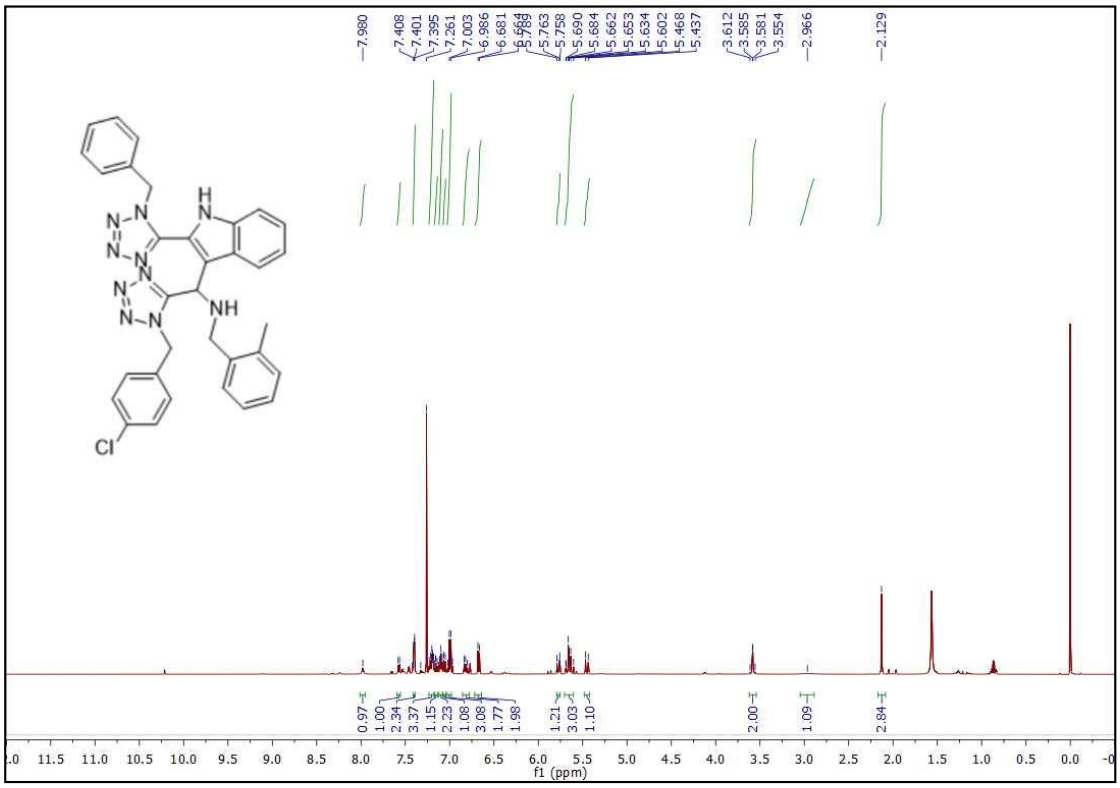


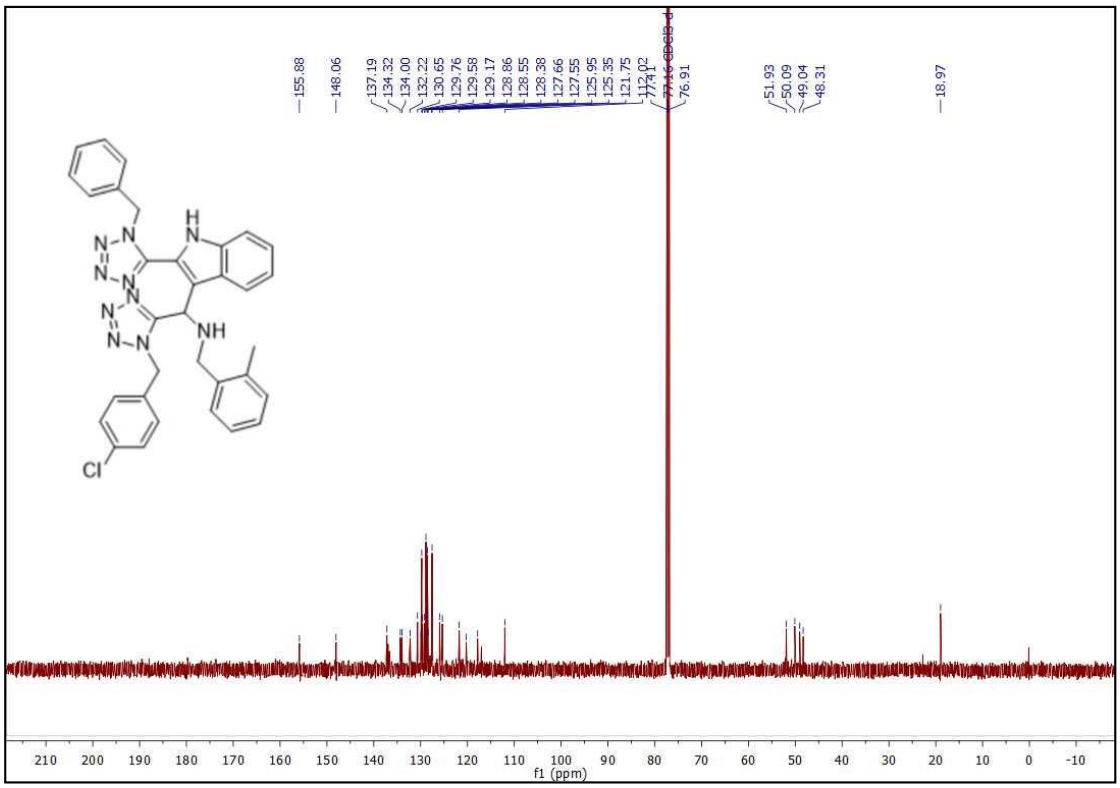


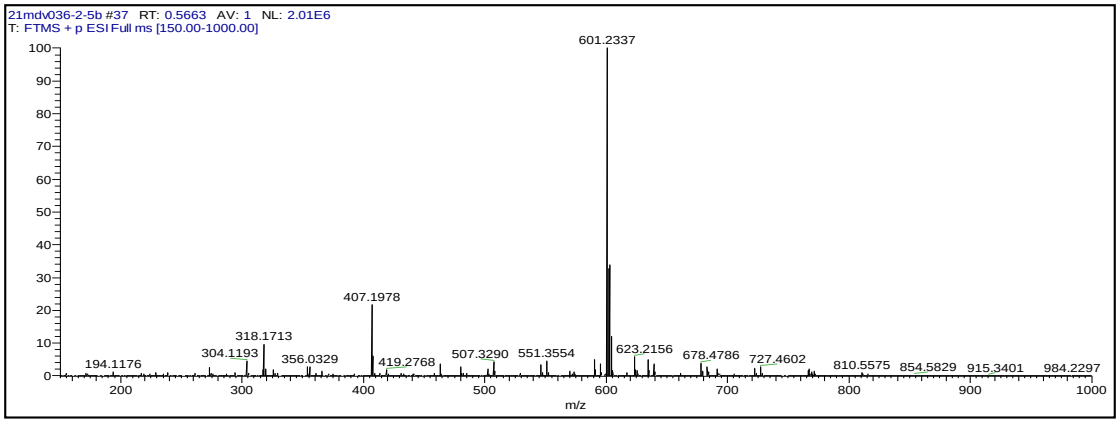

-110.295
-111.507
f1 (ppm)


21mdv036-2-5c #31 RT: 0.4718 AV: 1 NL: 3.46E6
T: FTMS + p ESI Full ms [150.00-1000.00]
545.1697
730.2352
752.2170
384.5946
218.2115
246.2427
318.1713
356.0328
405.1078
507.3290
589.2006
634.4525
683.4341
775.2929
837.1949
876.5730
947.4398
m/z

1-(2-(1-benzyl-1*H*-tetrazol-5-yl)-1*H*-indol-3-yl)-1-(1-(4-chlorobenzyl)-1*H*-tetrazol-5-yl)-*N*-(2-methylbenzyl)methanamine (8)






21mdv036-2-5b #37 RT: 0.5663 AV: 1 NL: 2.01E6
T: FTMS + p ESI Full ms [150.00-1000.00]
601.2337
407.1978
318.1713
304.1193
356.0329
194.1176
419.2768
507.3290
551.3554
623.2156
678.4786
727.4602
810.5575
854.5829
915.3401
984.2297
m/z

4. Single crystal x-ray structure determination

*Data for compound **4***

A specimen of $C_{20}H_{21}N_5O_4$ was used for the X-ray crystallographic analysis. The X-ray intensity data were measured (λ = 1.54178 Å). A total of 1692 frames were collected. The total exposure time was 2.35 hours. The frames were integrated with the Bruker SAINT software package using a narrow-frame algorithm. The integration of the data using a monoclinic unit cell yielded a total of 10266 reflections to a maximum θ angle of 50.51° (1.00 Å resolution), of which 1965 were independent (average redundancy 5.224, completeness = 99.6%, R_{int} = 4.96%, R_{sig} = 3.84%) and 1606 (81.73%) were greater than $2\sigma(F^2)$. The final cell constants of a = 9.5268(3) Å, b = 25.0880(8) Å, c = 8.4177(3) Å, β = 111.280(2)°, volume = 1874.73(11) $Å^3$, are based upon the refinement of the XYZ-centroids of 5363 reflections above 20 σ(I) with 7.047° < 2θ < 100.7°. Data were corrected for absorption effects using the Multi-Scan method (SADABS). The ratio of minimum to maximum apparent transmission was 0.808.

The structure was solved and refined using the Bruker SHELXTL Software Package, using the space group P 1 21/c 1, with Z = 4 for the formula unit, $C_{20}H_{21}N_5O_4$. The final anisotropic full-matrix least-squares refinement on F^2 with 269 variables converged at R1 = 6.56%, for the observed data and wR2 = 19.34% for all data. The goodness-of-fit was 1.435. The largest peak in the final difference electron density synthesis was 0.212 $e^-/Å^3$ and the largest hole was -0.435 $e^-/Å^3$ with an RMS deviation of 0.058 $e^-/Å^3$. On the basis of the final model, the calculated density was 1.401 g/cm^3 and F(000), 832 e^-. CCDC number: 2077271

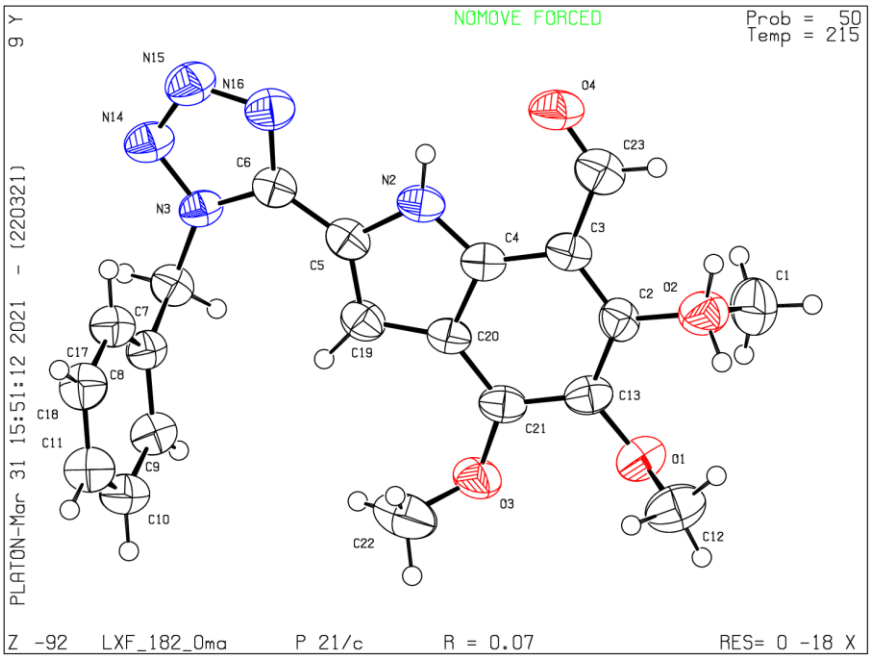


Table 1. Sample and crystal data for **4**

Identification code	**4** (LXF_182)	
Chemical formula	$C_{20}H_{21}N_5O_4$	
Formula weight	395.42 g/mol	
Temperature	215(2) K	
Wavelength	1.54178 Å	
Crystal system	monoclinic	
Space group	P 1 21/c 1	
Unit cell dimensions	a = 9.5268(3) Å	α = 90°
	b = 25.0880(8) Å	β = 111.280(2)°
	c = 8.4177(3) Å	γ = 90°
Volume	1874.73(11) $Å^3$	
Z	4	
Density (calculated)	1.401 g/cm^3	
Absorption coefficient	0.831 mm^{-1}	
F(000)	832	

Table 2. Data collection and structure refinement for **4**

Theta range for data collection	3.52 to 50.51°	
Index ranges	-9<=h<=9, -24<=k<=25, -8<=l<=8	
Reflections collected	10266	
Independent reflections	1965 [R(int) = 0.0496]	
Coverage of independent reflections	99.6%	
Absorption correction	Multi-Scan	
Structure solution technique	direct methods	
Structure solution program	SHELXT 2014/5 (Sheldrick, 2014)	
Refinement method	Full-matrix least-squares on F^2	
Refinement program	SHELXL-2018/3 (Sheldrick, 2018)	
Function minimized	$\Sigma\, w(F_o^2 - F_c^2)^2$	
Data / restraints / parameters	1965 / 0 / 269	
Goodness-of-fit on F^2	1.435	
Δ/σ_{max}	0.002	
Final R indices	1606 data; I>2σ(I)	R1 = 0.0656, wR2 = 0.1793
	all data	R1 = 0.0822, wR2 = 0.1934
Weighting scheme	$w=1/[\sigma^2(F_o^2)+(0.1000P)^2]$ where $P=(F_o^2+2F_c^2)/3$	
Largest diff. peak and hole	0.212 and -0.435 $eÅ^{-3}$	
R.M.S. deviation from mean	0.058 $eÅ^{-3}$	

References and Notes

1. Patil, P., Ahmadian-Moghaddam, M., & Dömling, A. *Green Chemistry*. **2020**, 22, 6902-6911.
2. Lanke, V., & Ramaiah Prabhu, K. *Organic Letters*, **2015**, *15(24)*, 6262-6265.
3. Kou, X.; Zhao, M.; Qiao, X.; Zhu, Y.; Tong, X.; Shen, Z. *Chemistry - A European Journal*, **2013**, *19*, 16880.
4. Ito, M., Iwatani, M., Kamada, Y., Sogabe, S., Nakao, S., Tanaka, T., Imaeda, Y. *Bioorganic & Medicinal Chemistry,* **2017**, *25(7)*, 2200-2209.