Electronic Supplementary Material (ESI) for RSC Advances.

Supporting Information

Diastereoselective One Pot Five-Component Reaction toward 4-(Tetrazole)-1,3-Oxazinane

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General Information

Reagents were available from commercial suppliers (Sigma Aldrich, ABCR, Acros and AK Scientific) and used without any purification unless otherwise noted. Isocyanides are purchased from commercial suppliers or synthesized by the previously reported methods. Thin layer chromatography was performed on Fluka precoated silica gel plates (0.20 mm thick, particle size 25 μm). Flash chromatography was performed on a Teledyne ISCO Combiflash Rf, using RediSep Rf Normal-phase Silica Flash Columns (Silica Gel 60 Å, 230 - 400 mesh) and on a Reveleris® X2 Flash Chromatography, using Grace® Reveleris Silica flash cartridges (12 grams). All ultrasonic irradiation reactions were carried out in a Sonicor "SC" Ultrasonic Table Top Cleaner with 220/240V, frequency of 50/60 Hz and 25 Amps. Nuclear magnetic resonance spectra were recorded on a Bruker Avance 500 spectrometer. Chemical shifts for ^{1}H NMR were reported relative to TMS (δ 0 ppm) and coupling constants were in hertz (Hz). The following abbreviations were used for spin multiplicity: s = singlet, d = doublet, t = triplet, dt = double triplet, ddd = doublet of double doublet, and m = multiplet. Chemical shifts for ^{13}C NMR reported in ppm relative to the solvent peak ($CDCl_3$ δ 77.23 ppm). 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 × 250 mm, 5 μm particle size) and reported as (m/z). High resolution mass spectra were recorded using a LTQ-Orbitrap-XL (Thermo Fisher Scientific; ESI pos. mode) at a resolution of 60000@m/z400.

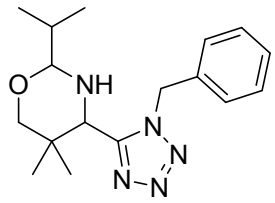
Experimental Procedures and Spectral Data

General procedure for the synthesis of 4-(tetrazole)-1,3-oxazinane:

A 10 mL tube was loaded with an aldehyde (1 mmol) and amonium hydroxyde 30% (1.5 mmol) in toluene (0.5 ml) and the mixture was sonicated for one hour in the water bath of an ultrasonic cleaner (220/240V, 25 Amps and frequency of 50/60 Hz). 3-hydroxy-2,2-dimethylpropanal (1 mmol) was added dropwise over 15 minutes and sonicated for 30 minutes. Isocyanide (1.2 mmol) and TMS-N_3 (1.2 mmol) was added to the reaction. The resulting reaction mixture was sonicated till the completion of the reaction (monitored by TLC). The solvent was removed under reduced pressure and the residue was purified by silica gel flash chromatography using EtOAc–hexane as eluent.

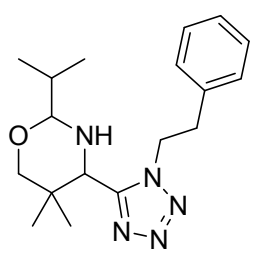
Spectral Data

5,5-dimethyl-2-phenethyl-4-(1-phenethyl-1*H*-tetrazol-5-yl)-1,3-oxazinane (1a)



Obtained from 0.5 mmol reaction as a white crystal, yield: 190 mg (60%); as 78:22 diastereomeric mixture: ^{1}H NMR (major+minor diastereomer, 500 MHz, $CDCl_3$) δ 7.40 – 7.31 (m, 5H), 7.22 – 7.15 (m, 3H), 5.82 (d, *J* = 15.4, 1H), 5.70 (d, *J* = 3.6, 2H), 5.52 (d, *J* = 15.4, 1H), 3.80 (d, *J* = 14.2, 2H), 3.62 (d, *J* = 11.3, 1H), 3.34 (d, *J* = 11.3, 1H), 3.23 (d, *J* = 8.5, 1H), 1.98 – 1.77 (m, 2H), 1.77 – 1.68 (m, 1H), 1.35 (s, 3H), 0.98 (dd, *J* = 6.8, 4.1, 6H), 0.85 (d, *J* = 6.6, 2H), 0.70 (s, 3H), 0.34 (d, *J* = 6.7, 2H). ^{13}C NMR (major+minor diastereomer, 126 MHz, $CDCl_3$) δ 153.2, 133.7, 129.1, 129.1, 128.9, 128.8, 127.7, 127.5, 92.9, 79.2, 58.5, 57.8, 51.4, 51.3, 32.7, 32.0, 22.5, 19.3, 19.0, 18.3, 17.8, 17.6. MS (ESI) m/z calculated $[M+H]^+$: 316.42; found $[M+H]^+$: 316.32. HRMS (ESI) m/z calculated $[M+H]^+$: 316.21319; found $[M+H]^+$: 316.21384.

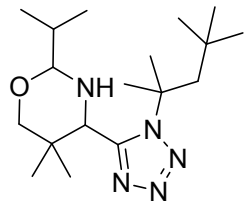
2-isopropyl-4-(1-phenethyl-1*H*-tetrazol-5-yl)-1,3-oxazinane (1b)



Obtained from 1 mmol reaction as a yellow liquid, yield: 168 mg (51%); as 91:09 diastereomeric mixture: ^{1}H NMR (major diastereomer, 500 MHz, $CDCl_3$) δ 7.33 – 7.25 (m, 3H), 7.04 (d, *J* = 6.7, 2H), 4.89 – 4.75 (m, 1H), 4.68 – 4.55 (m, 1H), 3.71 (dd, *J* = 12.0,

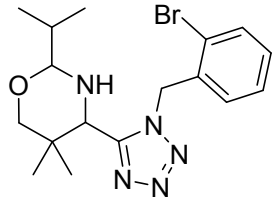
5.1, 1H), 3.57 (d, *J* = 11.3, 1H), 3.28 – 3.19 (m, 4H), 1.85 – 1.71 (m, 2H), 1.24 (s, 3H), 0.97 (dd, *J* = 6.8, 4.6, 6H), 0.67 (s, 3H). ^{13}C NMR (major diastereomer, 126 MHz, $CDCl_3$) δ 153.3, 137.0, 129.1, 128.8, 127.3, 92.8, 79.0, 58.0, 49.4, 36.3, 32.7, 22.4, 18.1, 17.9, 17.6. MS (ESI) m/z calculated $[M+H]^+$: 330.45; found $[M+H]^+$: 330.18. HRMS (ESI) m/z calculated $[M+H]^+$: 330.22884; found $[M+H]^+$: 330.22867.

2-isopropyl-5,5-dimethyl-4-(1-(2,4,4-trimethylpentan-2-yl)-1*H*-tetrazol-5-yl)-1,3-oxazinane (1c)



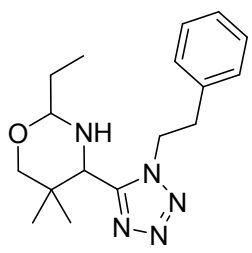
Obtained from 0.5 mmol reaction as a colorless crystal, yield: 95 mg (56%); as 90:10 diastereomeric mixture: ^{1}H NMR (major diastereomer, 500 MHz, $CDCl_3$) δ 4.30 (d, *J* = 12.8, 1H), 3.88 (dd, *J* = 12.8, 5.4, 1H), 3.72 (d, *J* = 11.2, 1H), 3.48 (d, *J* = 11.2, 1H), 1.95 – 1.80 (m, 9H), 1.53 (s, 3H), 0.96 (dd, *J* = 8.2, 6.9, 6H), 0.80 (s, 9H), 0.73 (s, 3H). ^{13}C NMR (major diastereomer, 126 MHz, $CDCl_3$) δ 153.4, 93.2, 80.3, 65.5, 59.1, 53.7, 33.9, 32.8, 31.7, 31.5, 30.5, 29.9, 23.0, 19.7, 18.1, 17.7. MS (ESI) m/z calculated $[M+H]^+$: 338.51; found $[M+H]^+$: 338.37. HRMS (ESI) m/z calculated $[M+H]^+$: 338.29144; found $[M+H]^+$: 338.29129.

4-(1-(2-bromobenzyl)-1*H*-tetrazol-5-yl)-2-isopropyl-5,5-dimethyl-1,3-oxazinane (1d)



Obtained from 1 mmol reaction as a colorless liquid, yield: 185 mg (47%); as 88:12 diastereomeric mixture: ^{1}H NMR (major diastereomer, 500 MHz, $CDCl_3$) δ 7.63 (d, *J* = 7.9, 1H), 7.32 – 7.26 (m, 1H), 7.25 – 7.18 (m, 1H), 6.84 (d, *J* = 7.6, 1H), 5.89 (d, *J* = 16.1, 1H), 5.67 (d, *J* = 16.1, 1H), 3.94 (d, *J* = 12.2, 1H), 3.84 (dd, *J* = 12.0, 5.1, 1H), 3.64 (d, *J* = 11.3, 1H), 3.41 (d, *J* = 11.3, 1H), 1.87 (t, *J* = 12.3, 1H), 1.81 – 1.73 (m, 1H), 1.36 (s, 3H), 0.94 – 0.88 (m, 6H), 0.74 (s, 3H). ^{13}C NMR (major diastereomer, 126 MHz, $CDCl_3$) δ 153.7, 133.5, 133.1, 130.2, 128.7, 128.2, 122.5, 92.9, 79.0, 58.4, 50.9, 32.8, 32.6, 22.5, 18.4, 17.7, 17.5. MS (ESI) m/z calculated $[M+H]^+$: 394.12; found $[M+H]^+$: 394.25. HRMS (ESI) m/z calculated $[M+H]^+$: 394.1237; found $[M+H]^+$: 394.12332.

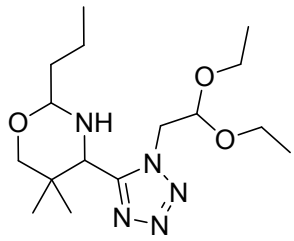
2-ethyl-5,5-dimethyl-4-(1-phenethyl-1*H*-tetrazol-5-yl)-1,3-oxazinane (1e)



Obtained from 1 mmol reaction as a pale yellow solid, yield: 120 mg 38%); as 90:10 diastereomeric mixture: ^{1}H NMR (major diastereomer,

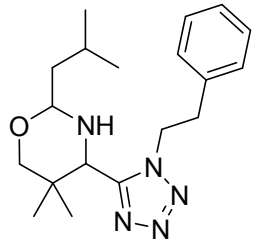
500 MHz, $CDCl_3$) δ 7.33 – 7.27 (m, 3H), 7.10 – 7.02 (m, 2H), 4.83 – 4.71 (m, 1H), 4.65 – 4.56 (m, 1H), 3.94 – 3.86 (m, 1H), 3.57 (d, *J* = 11.3, 1H), 3.34 (d, *J* = 12.5, 1H), 3.30 – 3.21 (m, 3H), 1.77 (t, *J* = 12.4, 1H), 1.69 – 1.57 (m, 2H), 1.24 (s, 3H), 0.98 (t, *J* = 7.5, 3H), 0.67 (s, 3H). ^{13}C NMR (major diastereomer, 126 MHz, $CDCl_3$) δ 154.4, 129.1, 129.0, 128.8, 127.4, 89.7, 78.9, 58.0, 49.4, 36.4, 28.4, 22.5, 18.2, 9.3. MS (ESI) m/z calculated $[M+H]^+$: 316.42; found $[M+H]^+$: 316.07. HRMS (ESI) m/z calculated $[M+H]^+$: 316.21319; found $[M+H]^+$: 316.21283.

4-(1-(2,2-diethoxyethyl)-1*H*-tetrazol-5-yl)-5,5-dimethyl-2-propyl-1,3-oxazinane (1f)



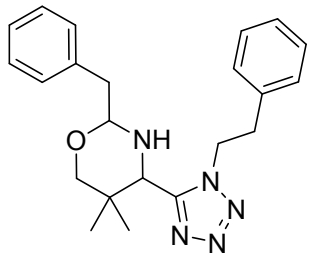
Obtained from 1 mmol reaction as a colorless solid, yield: 187 mg (55%); as 91:09 diastereomeric mixture: ^1H NMR (major diastereomer, 500 MHz, $CDCl_3$) δ 4.83 (t, *J* = 5.6, 1H), 4.70 (dd, *J* = 14.1, 5.7, 1H), 4.41 (dd, *J* = 14.1, 5.5, 1H), 4.27 (s, 1H), 4.21 – 4.11 (m, 1H), 3.82 – 3.70 (m, 2H), 3.66 (d, *J* = 11.3, 1H), 3.53 – 3.41 (m, 3H), 2.06 (s, 1H), 1.70 – 1.51 (m, 2H), 1.49 – 1.40 (m, 2H), 1.27 (s, 3H), 1.19 – 1.12 (m, 6H), 0.92 (t, *J* = 7.4, 3H), 0.84 (s, 3H). ^{13}C NMR (major diastereomer, 126 MHz, $CDCl_3$) δ 154.3, 101.3, 88.4, 78.9, 64.7, 64.6, 57.7, 50.3, 37.5, 33.0, 22.7, 18.5, 18.1, 15.2, 15.1, 13.9. MS (ESI) m/z calculated $[M+H]^+$: 342.46; found $[M+H]^+$: 342.22. HRMS (ESI) m/z calculated $[M+H]^+$: 342.24997; found $[M+H]^+$: 342.24976.

2-isobutyl-5,5-dimethyl-4-(1-phenethyl-1*H*-tetrazol-5-yl)-1,3-oxazinane (1g)



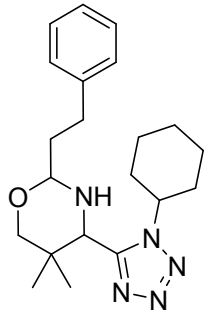
Obtained from 0.5 mmol reaction as a white solid, yield: 43 mg (25%); as 90:10 diastereomeric mixture: ^1H NMR (major diastereomer, 500 MHz, $CDCl_3$) δ 7.32 – 7.27 (m, 3H), 7.10 – 6.99 (m, 2H), 4.76 (dt, *J* = 13.8, 7.7, 1H), 4.66 – 4.56 (m, 1H), 4.01 (brs, 1H), 3.56 (d, *J* = 11.3, 1H), 3.33 (d, *J* = 8.6, 1H), 3.30 – 3.18 (m, 3H), 1.85 – 1.73 (m, 2H), 1.70 – 1.59 (m, 1H), 1.56 – 1.47 (m, 1H), 1.44 – 1.34 (m, 1H), 1.24 (s, 3H), 0.93 (dd, *J* = 6.6, 4.2, 6H), 0.67 (s, 3H). ^{13}C NMR (major diastereomer, 126 MHz, $CDCl_3$) δ 153.2, 136.9, 129.1, 128.8, 127.4, 87.3, 78.9, 58.0, 49.4, 44.4, 36.3, 32.7, 24.3, 22.8, 22.6, 22.6, 18.3. MS (ESI) m/z calculated $[M+H]^+$: 344.48; found $[M+H]^+$: 344.30. HRMS (ESI) m/z calculated $[M+H]^+$: 344.24449; found $[M+H]^+$: 344.24417.

2-benzyl-5,5-dimethyl-4-(1-phenethyl-1*H*-tetrazol-5-yl)-1,3-oxazinane (1h)



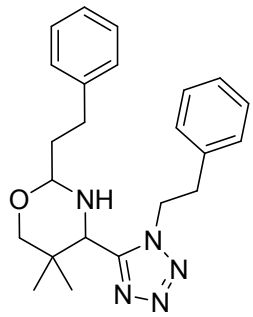
Obtained from 1 mmol reaction as a yellow liquid, yield: 128 mg (34%); as 96:04 diastereomeric mixture: ^{1}H NMR (major diastereomer, 500 MHz, $CDCl_3$) δ 7.34 – 7.29 (m, 2H), 7.26 – 7.19 (m, 6H), 6.89 (dd, *J* = 7.0, 2.3, 2H), 4.71 – 4.59 (m, 1H), 4.53 – 4.44 (m, 1H), 4.21 – 4.09 (m, 1H), 3.56 (d, *J* = 11.4, 1H), 3.22 (d, *J* = 11.4, 1H), 3.17 – 3.07 (m, 3H), 2.94 (dd, *J* = 13.9, 5.0, 1H), 2.84 (dd, *J* = 13.9, 5.8, 1H), 1.75 (t, *J* = 12.4, 1H), 1.19 (s, 3H), 0.66 (s, 3H). ^{13}C NMR (major diastereomer, 126 MHz, $CDCl_3$) δ 153.1, 137.0, 136.6, 129.7, 129.0, 128.8, 128.4, 127.5, 126.8, 89.0, 79.0, 58.0, 49.4, 41.8, 36.3, 22.5, 18.1. MS (ESI) m/z calculated $[M+H]^+$: 378.49; found $[M+H]^+$: 378.32. HRMS (ESI) m/z calculated $[M+H]^+$: 378.22884; found $[M+H]^+$: 378.22894.

(*E*)-4-(1-cyclohexyl-1*H*-tetrazol-5-yl)-5,5-dimethyl-2-styryl-1,3-oxazinane (1i)



Obtained from 0.5 mmol reaction as a white solid, yield: 89 mg (48%); as 94:06 diastereomeric mixture: ^{1}H NMR (major diastereomer, 500 MHz, $CDCl_3$) δ 7.34 – 7.27 (m, 2H), 7.22 – 7.15 (m, 3H), 4.35 – 4.23 (m, 1H), 4.19 – 4.07 (m, 1H), 3.95 (d, *J* = 12.5, 1H), 3.73 (d, *J* = 11.4, 1H), 3.52 (d, *J* = 11.4, 1H), 2.76 (t, *J* = 7.8, 2H), 2.30 – 2.11 (m, 2H), 2.03 – 1.89 (m, 7H), 1.44 – 1.33 (m, 3H), 1.29 (s, 3H), 0.77 (s, 3H). ^{13}C NMR (major diastereomer, 126 MHz, $CDCl_3$) δ 152.10, 141.37, 128.48, 128.42, 125.96, 87.79, 87.64, 78.75, 58.14, 36.72, 33.14, 30.99, 25.38, 24.85, 22.78, 18.77, 18.64. MS (ESI) m/z calculated $[M+H]^+$: 370.50; found $[M+H]^+$: 370.45. HRMS (ESI) m/z calculated $[M+H]^+$: 370.26014; found $[M+H]^+$: 370.26004.

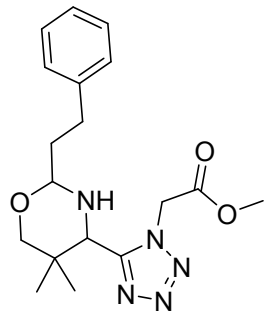
5,5-dimethyl-2-phenethyl-4-(1-phenethyl-1*H*-tetrazol-5-yl)-1,3-oxazinane (1j)



Obtained from 1 mmol reaction as a yellow solid, yield: 196 mg (50%); as 90:10 diastereomeric mixture: ^{1}H NMR (major diastereomer, 500 MHz, $CDCl_3$) δ 7.33 (t, *J* = 7.4, 2H), 7.27 – 7.19 (m, 7H), 6.99 (dd, *J* = 7.3, 1.9, 2H), 4.75 (dt, *J* = 13.8, 7.6, 1H), 4.67 – 4.53 (m, 1H), 4.01 – 3.89 (m, 1H), 3.66 – 3.55 (m, 1H), 3.31 – 3.21 (m, 4H), 2.77 (t, *J* = 7.8, 2H), 2.07 – 1.93 (m, 1H), 1.93 – 1.79 (m,

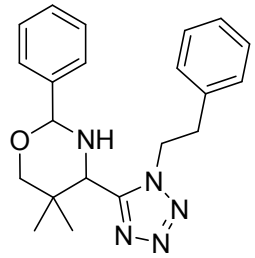
2H), 1.27 (s, 3H), 0.66 (s, 3H). ^{13}C NMR (major diastereomer, 126 MHz, $CDCl_3$) δ 153.2, 141.3, 136.9, 129.1, 128.8, 128.5, 128.5, 127.3, 126.1, 87.6, 78.9, 57.9, 49.4, 36.5, 36.3, 32.7, 31.0, 22.5, 18.3. MS (ESI) m/z calculated $[M+H]^+$: 392.52; found $[M+H]^+$: 392.24. HRMS (ESI) m/z calculated $[M+H]^+$: 392.24449; found $[M+H]^+$: 392.24426.

methyl 2-(5-(5,5-dimethyl-2-phenethyl-1,3-oxazinan-4-yl)-1*H*-tetrazol-1-yl)acetate (1k)



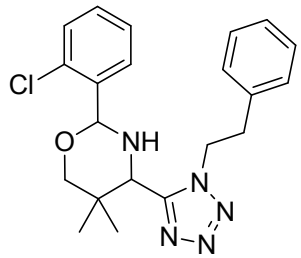
Obtained from 2 mmol reaction as a yellow liquid, yield: 598 mg (83%); as 91:09 diastereomeric mixture: ^{1}H NMR (major diastereomer, 500 MHz, $CDCl_3$) δ 7.33 – 7.28 (m, 2H), 7.23 – 7.17 (m, 3H), 5.37 (d, *J* = 17.3, 1H), 5.25 (d, *J* = 17.4, 1H), 4.09 (t, *J* = 5.6, 1H), 3.97 (s, 1H), 3.78 (s, 3H), 3.68 (d, *J* = 11.5, 1H), 3.46 (d, *J* = 11.5, 1H), 2.73 (t, *J* = 7.8, 2H), 2.17 (s, 1H), 2.02 – 1.91 (m, 1H), 1.90 – 1.79 (m, 2H), 1.38 (s, 3H), 1.03 (s, 3H). ^{13}C NMR (major diastereomer, 126 MHz, $CDCl_3$) δ 166.4, 153.6, 141.2, 128.5, 128.4, 126.1, 87.7, 79.1, 58.9, 53.4, 53.2, 49.0, 36.7, 30.9, 22.6, 18.1. MS (ESI) m/z calculated $[M+H]^+$: 360.43; found $[M+H]^+$: 360.30. HRMS (ESI) m/z calculated $[M+H]^+$: 360.20302; found $[M+H]^+$: 360.20306.

5,5-dimethyl-4-(1-phenethyl-1*H*-tetrazol-5-yl)-2-phenyl-1,3-oxazinane (1l)



Obtained from 0.5 mmol reaction as a white solid, yield: 64 mg (35%); as 94:06 diastereomeric mixture: ^{1}H NMR (major diastereomer, 500 MHz, $CDCl_3$) δ 7.50 – 7.46 (m, 2H), 7.40 – 7.34 (m, 3H), 7.30 – 7.26 (m, 3H), 7.06 – 7.01 (m, 2H), 5.02 (d, *J* = 12.0, 1H), 4.93 – 4.80 (m, 1H), 4.72 – 4.63 (m, 1H), 4.61 – 4.58 (m, 0H), 3.75 (d, *J* = 11.4, 1H), 3.52 (d, *J* = 12.1, 1H), 3.46 (d, *J* = 11.4, 1H), 3.26 (t, *J* = 7.0, 2H), 2.11 – 1.95 (m, 1H), 1.33 (s, 3H), 0.74 (s, 3H). ^{13}C NMR (major diastereomer, 126 MHz, $CDCl_3$) δ 153.1, 139.2, 136.9, 129.1, 128.9, 128.6, 128.4, 127.4, 125.8, 88.9, 79.2, 58.4, 49.5, 36.4, 32.7, 22.5, 18.3. MS (ESI) m/z calculated $[M+H]^+$: 364.47; found $[M+H]^+$: 364.33. HRMS (ESI) m/z calculated $[M+H]^+$: 364.21319; found $[M+H]^+$: 364.21304.

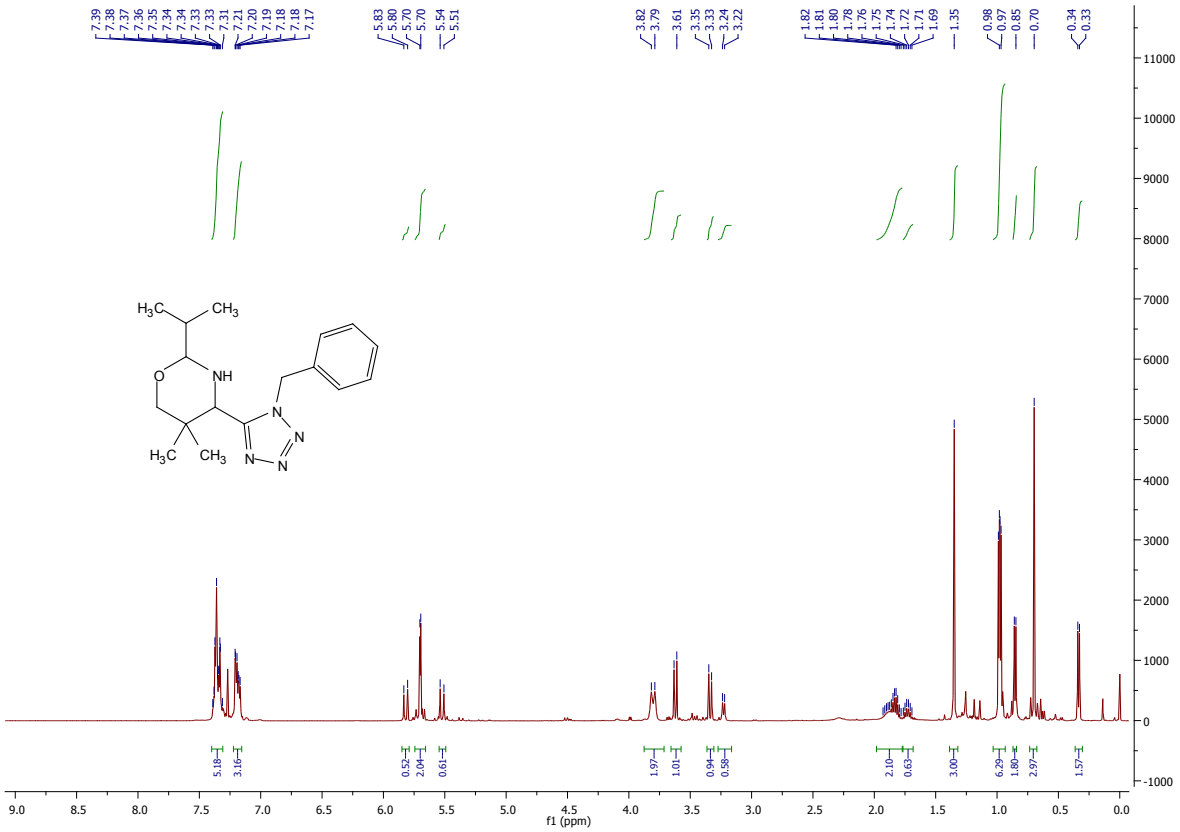
2-(2-chlorophenyl)-5,5-dimethyl-4-(1-phenethyl-1*H*-tetrazol-5-yl)-1,3-oxazinane (1m)

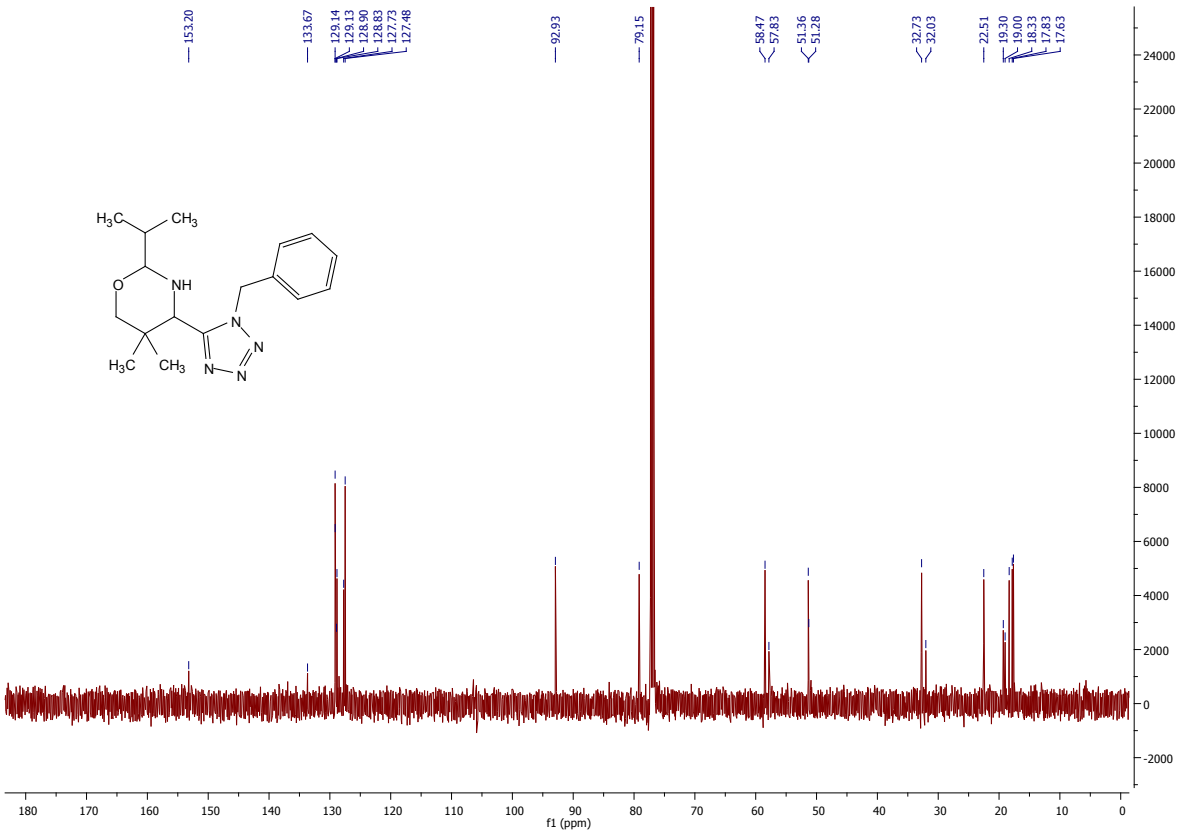


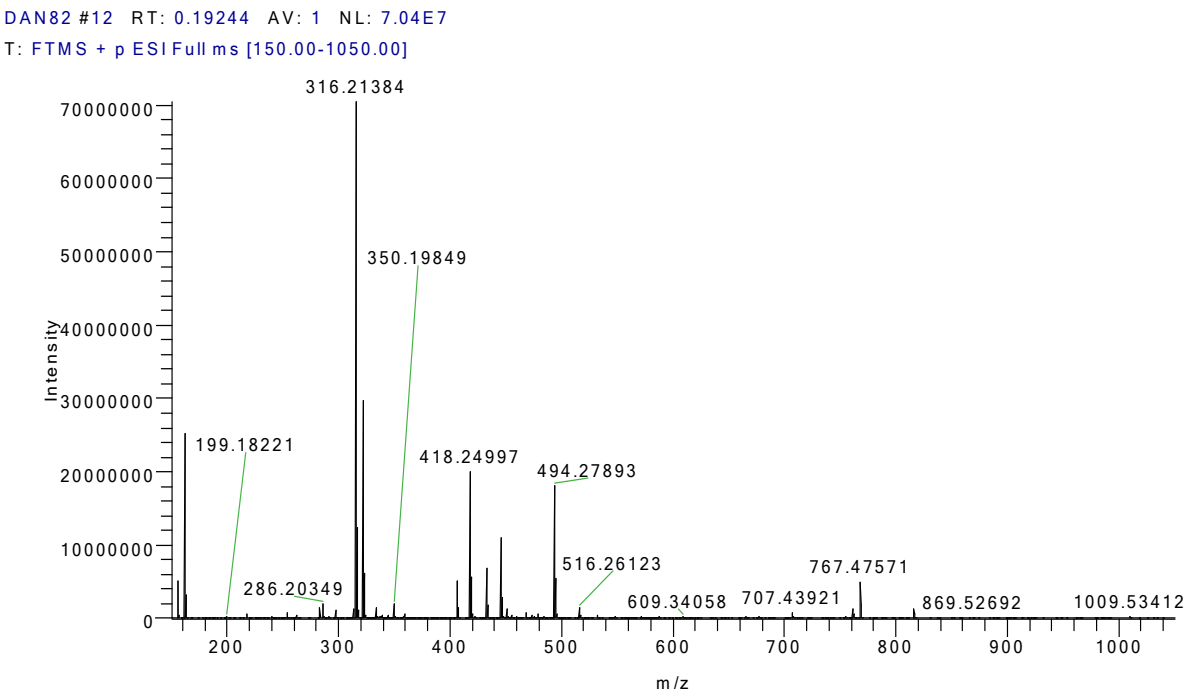
Obtained from 1 mmol reaction as a yellow liquid yield: 179 mg (45%); as 92:08 diastereomeric mixture: ^{1}H NMR (major diastereomer, 500 MHz, $CDCl_3$) δ 7.68 – 7.60 (m, 1H), 7.42 – 7.37 (m, 1H), 7.33 – 7.28 (m, 2H), 7.24 – 7.19 (m, 3H), 6.97 (dd, *J* = 7.2, 2.1, 2H), 5.33 (d, *J* = 12.0, 1H), 5.05 – 4.93 (m, 1H), 4.81 – 4.70 (m, 1H), 3.72 (d, *J* = 11.4, 1H), 3.39 (dd, *J* = 18.6, 11.9, 2H), 3.31 – 3.13 (m, 2H), 1.66 (t, *J* = 12.2, 1H), 1.41 (s, 3H), 0.78 (s, 3H). ^{13}C NMR (major diastereomer, 126 MHz, $CDCl_3$) δ 152.9, 137.1, 136.7, 132.4, 129.8, 129.6, 129.0, 127.3, 127.3, 127.0, 86.3, 79.5, 58.3, 49.5, 36.5, 32.3, 22.3, 18.2. MS (ESI) m/z calculated $[M+H]^+$: 398.91; found $[M+H]^+$: 398.04. HRMS (ESI) m/z calculated $[M+H]^+$: 398.17421; found $[M+H]^+$: 398.1741.

NMR spectra and SFC-MS Chromatograms

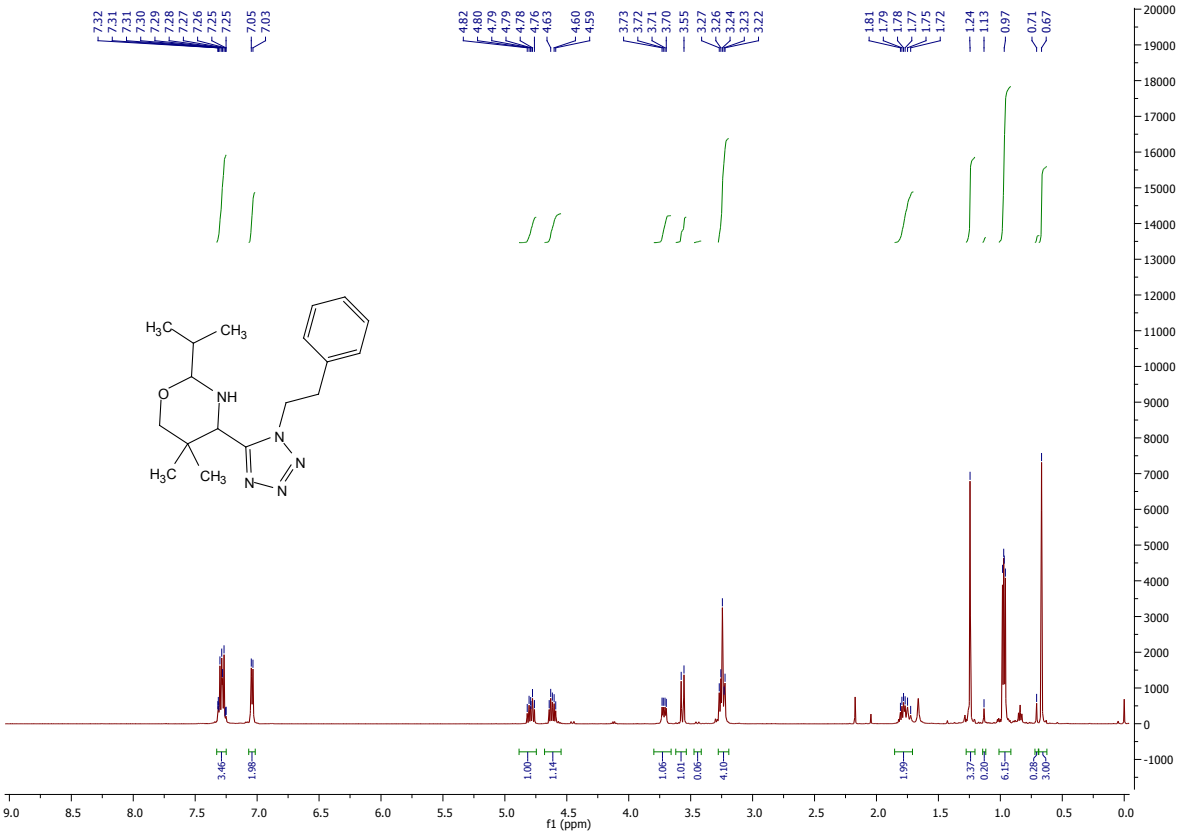
5,5-dimethyl-2-phenethyl-4-(1-phenethyl-1H-tetrazol-5-yl)-1,3-oxazinane (1a)

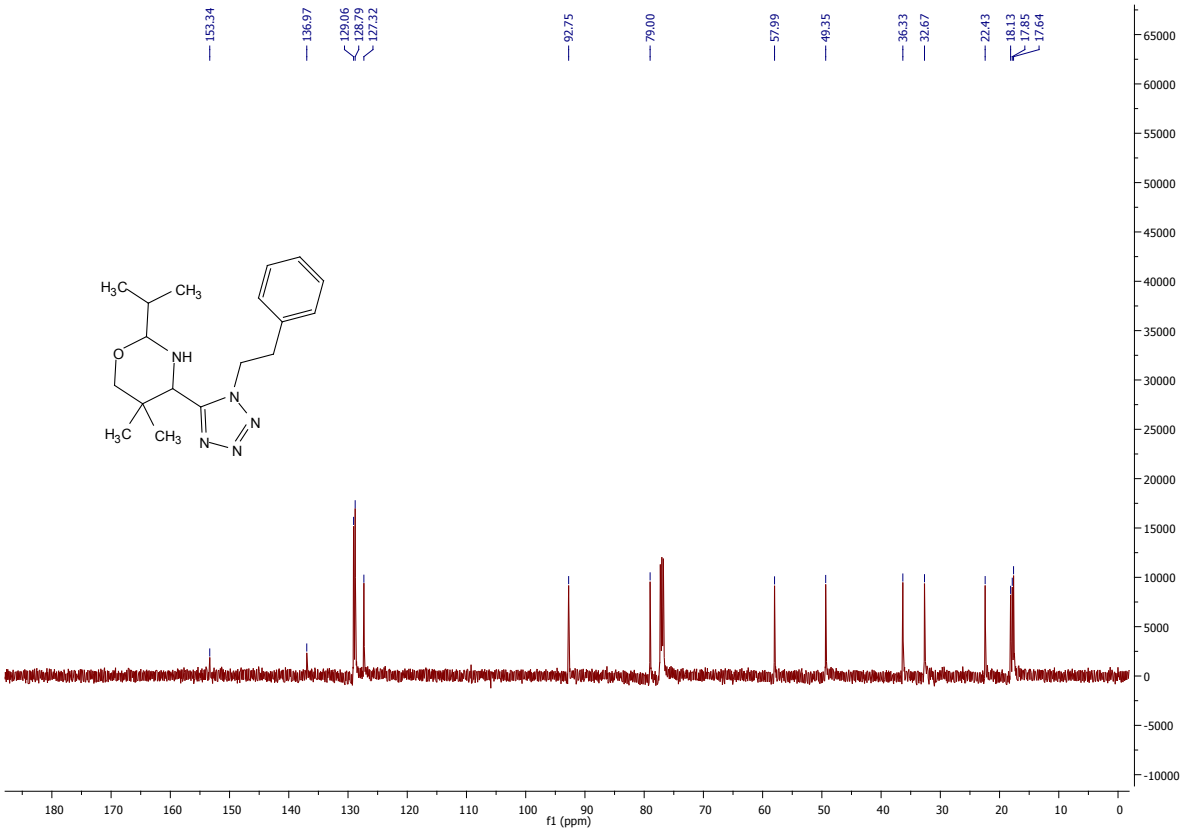




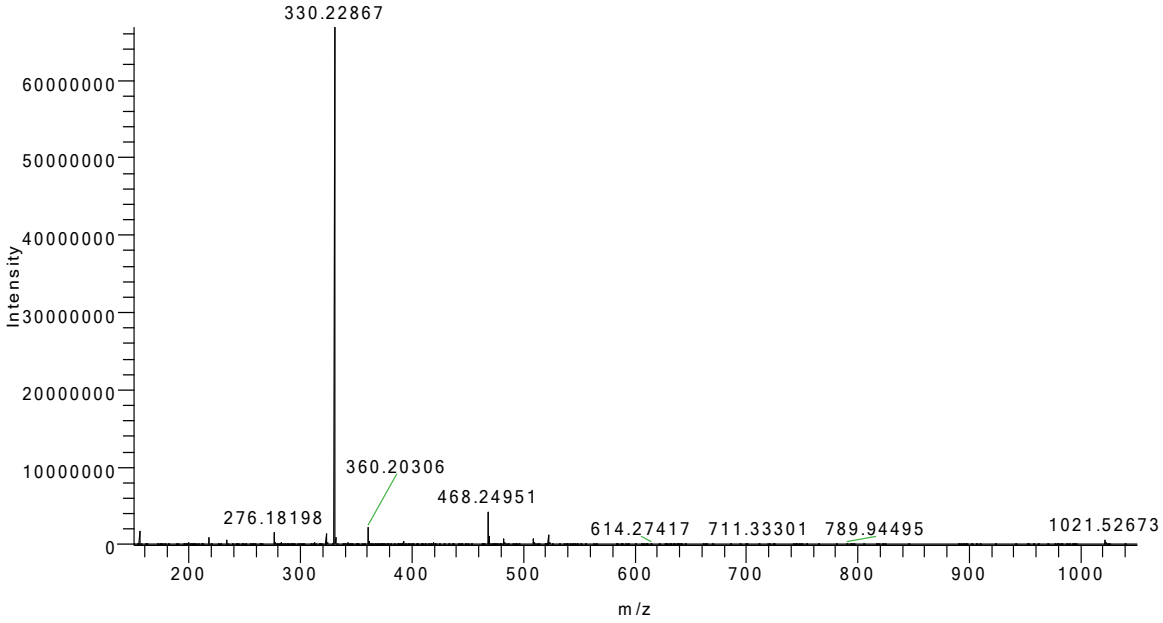


2-isopropyl-4-(1-phenethyl-1*H*-tetrazol-5-yl)-1,3-oxazinane (1b)

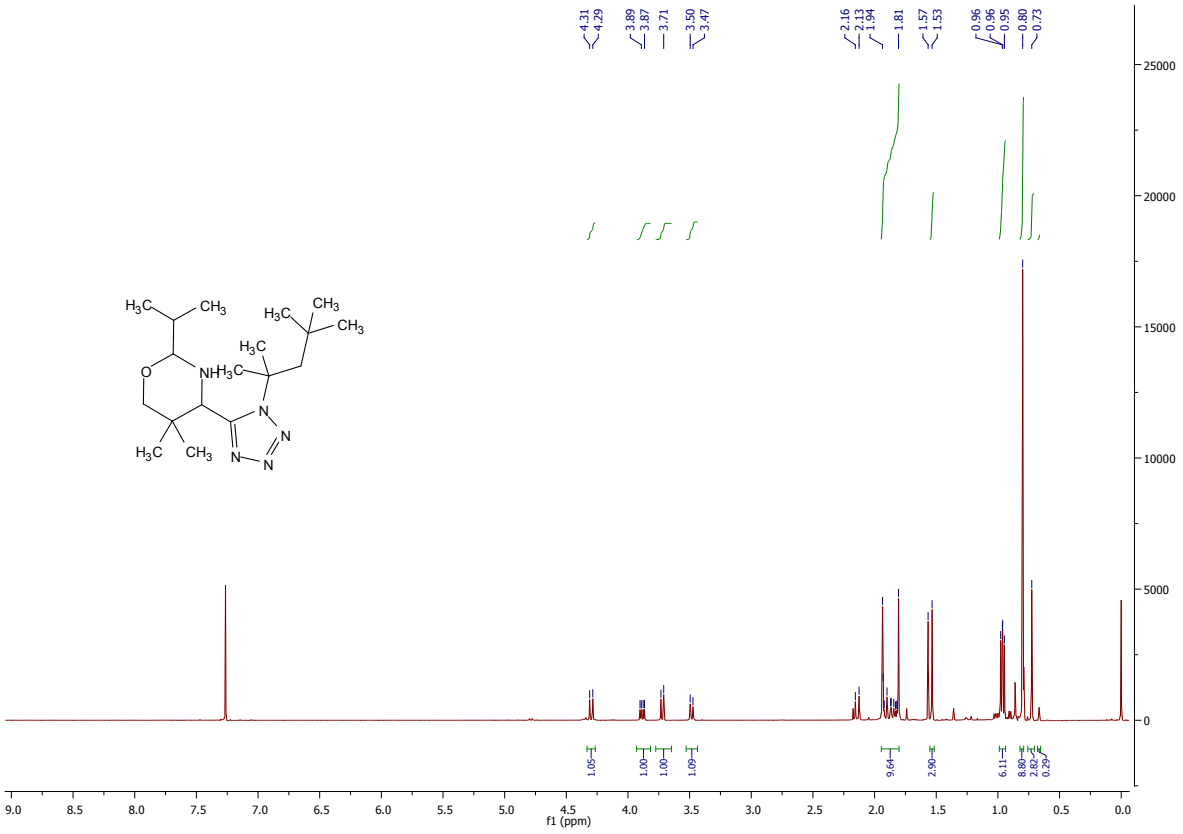


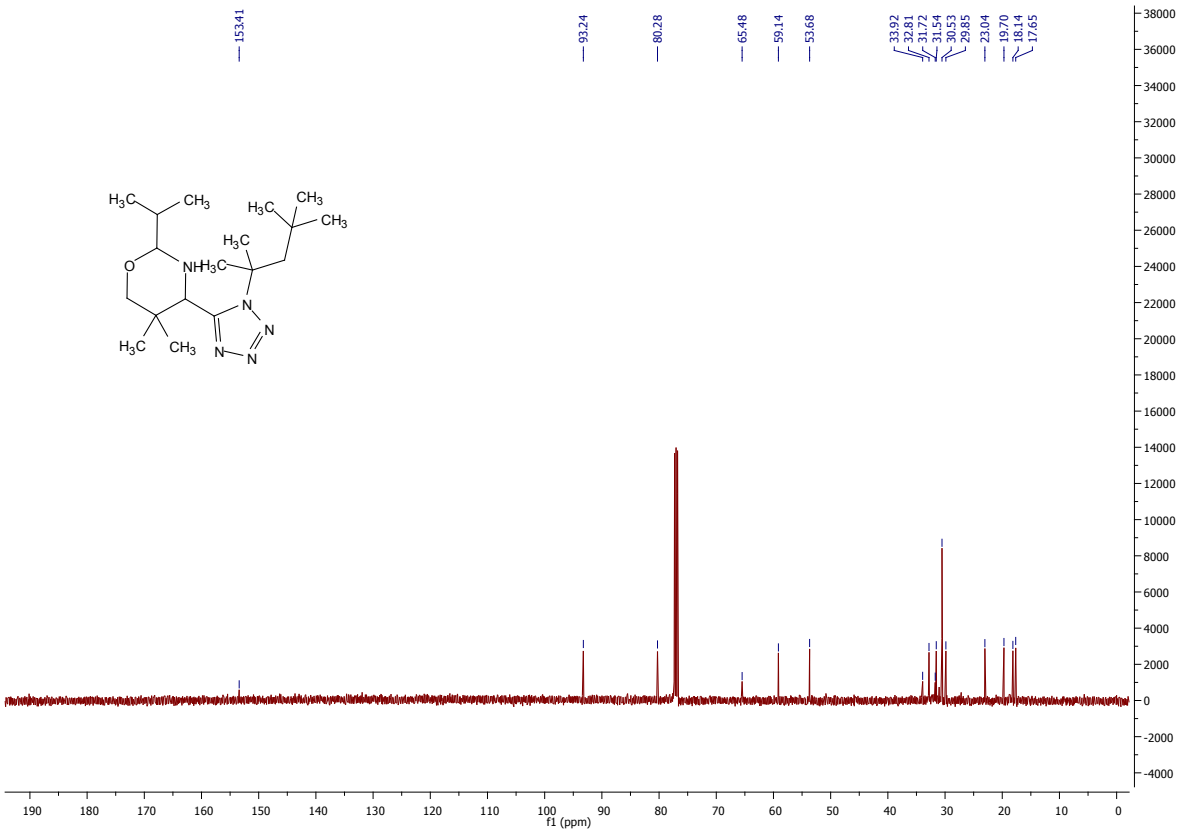


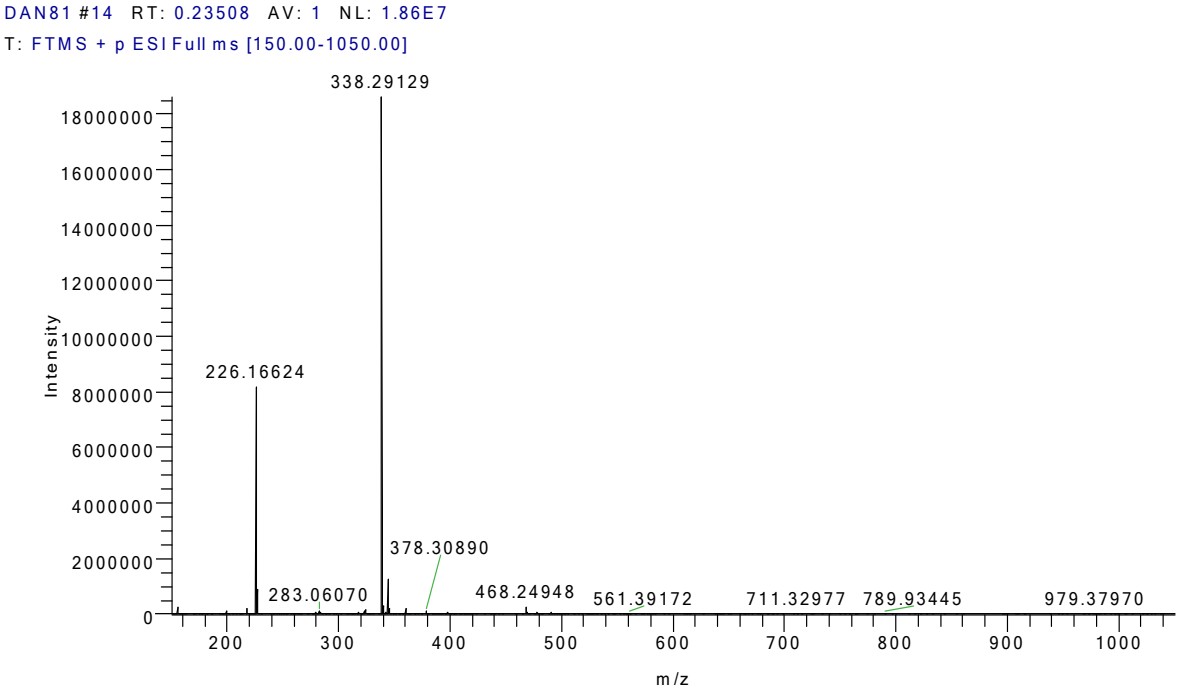
DAN79 #14 RT: 0.21848 AV: 1 NL: 6.68E7
T: FTMS + p ESI Full ms [150.00-1050.00]



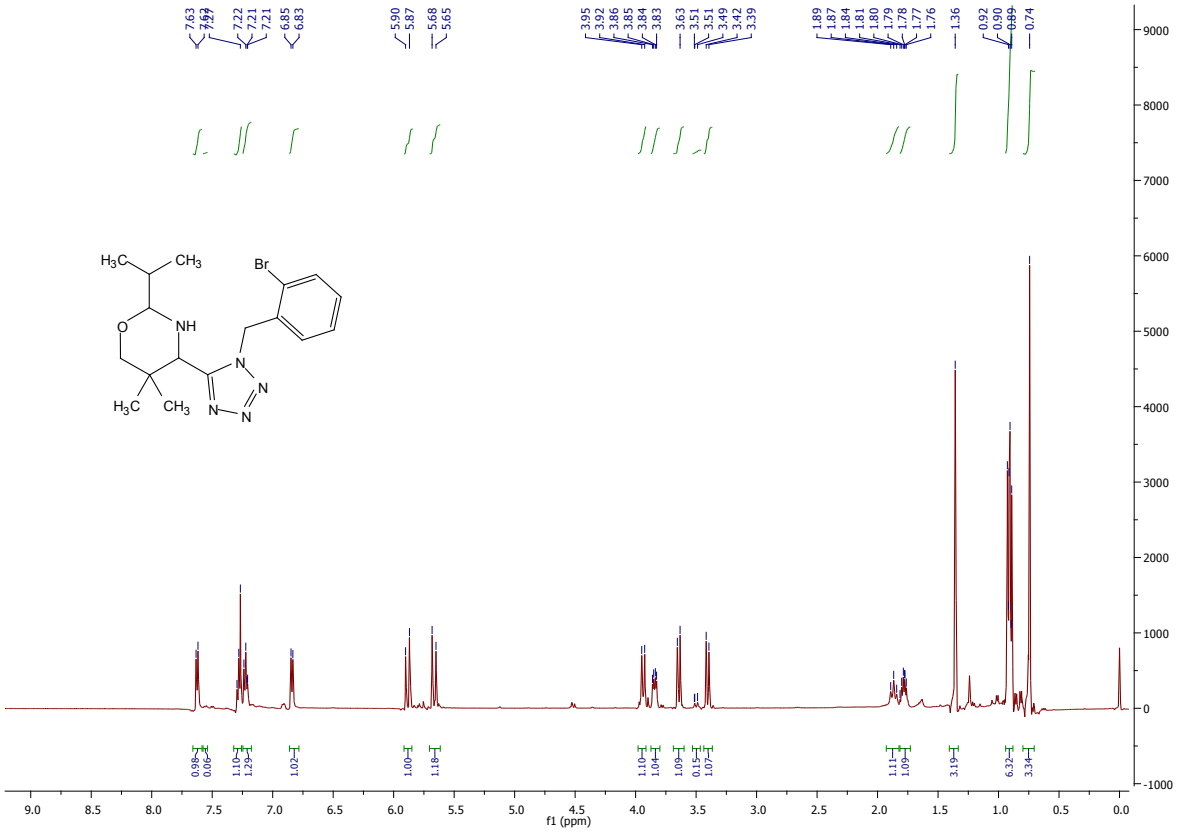
2-isopropyl-5,5-dimethyl-4-(1-(2,4,4-trimethylpentan-2-yl)-1*H*-tetrazol-5-yl)-1,3-oxazinane (1c)

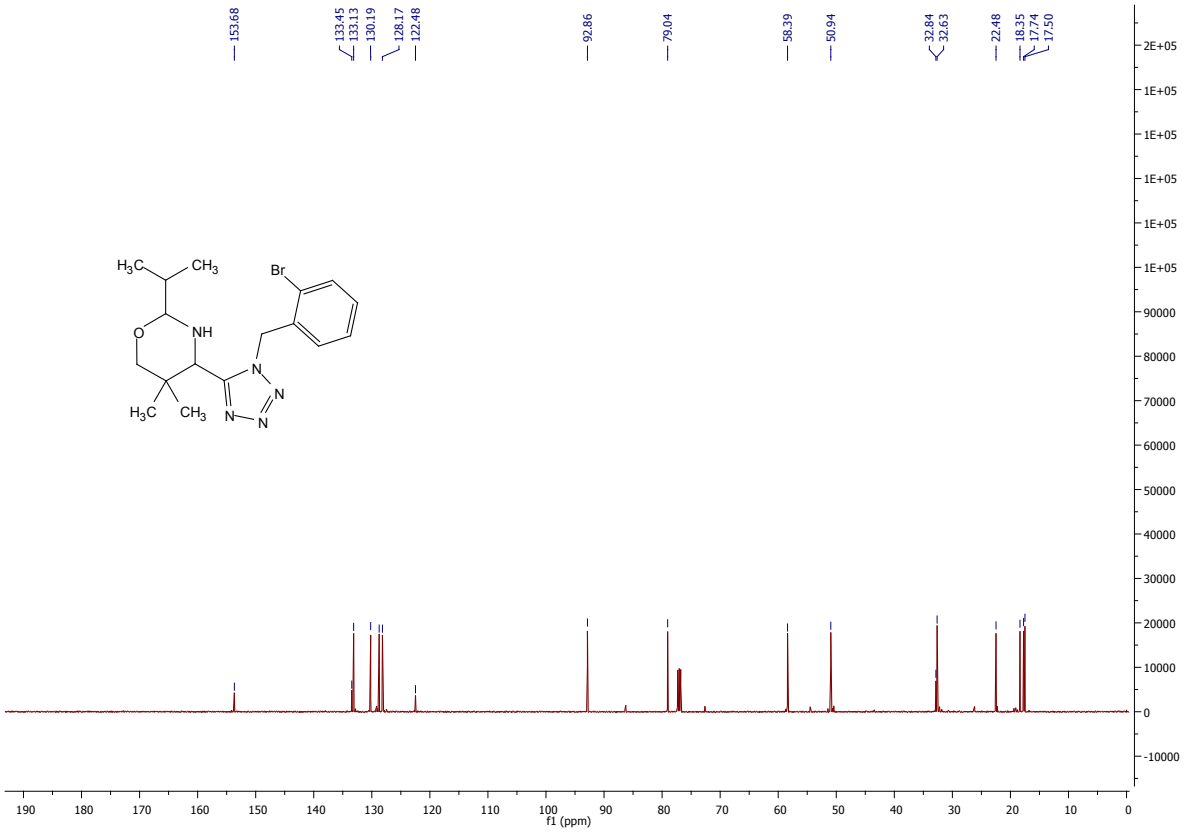






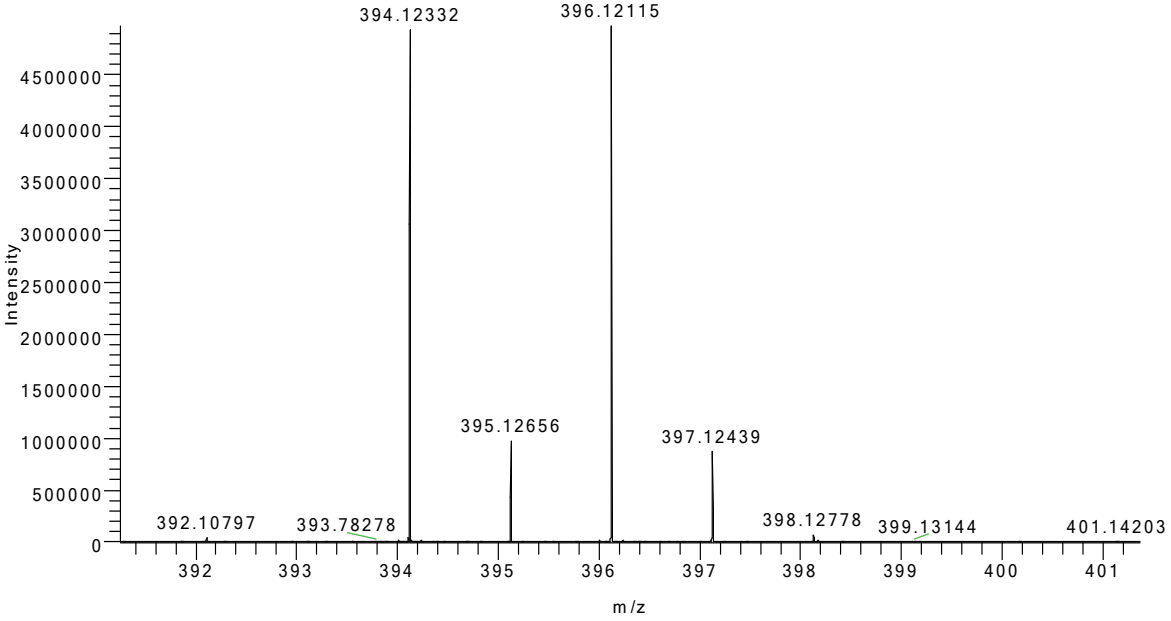
4-(1-(2-bromobenzyl)-1*H*-tetrazol-5-yl)-2-isopropyl-5,5-dimethyl-1,3-oxazinane (1d)



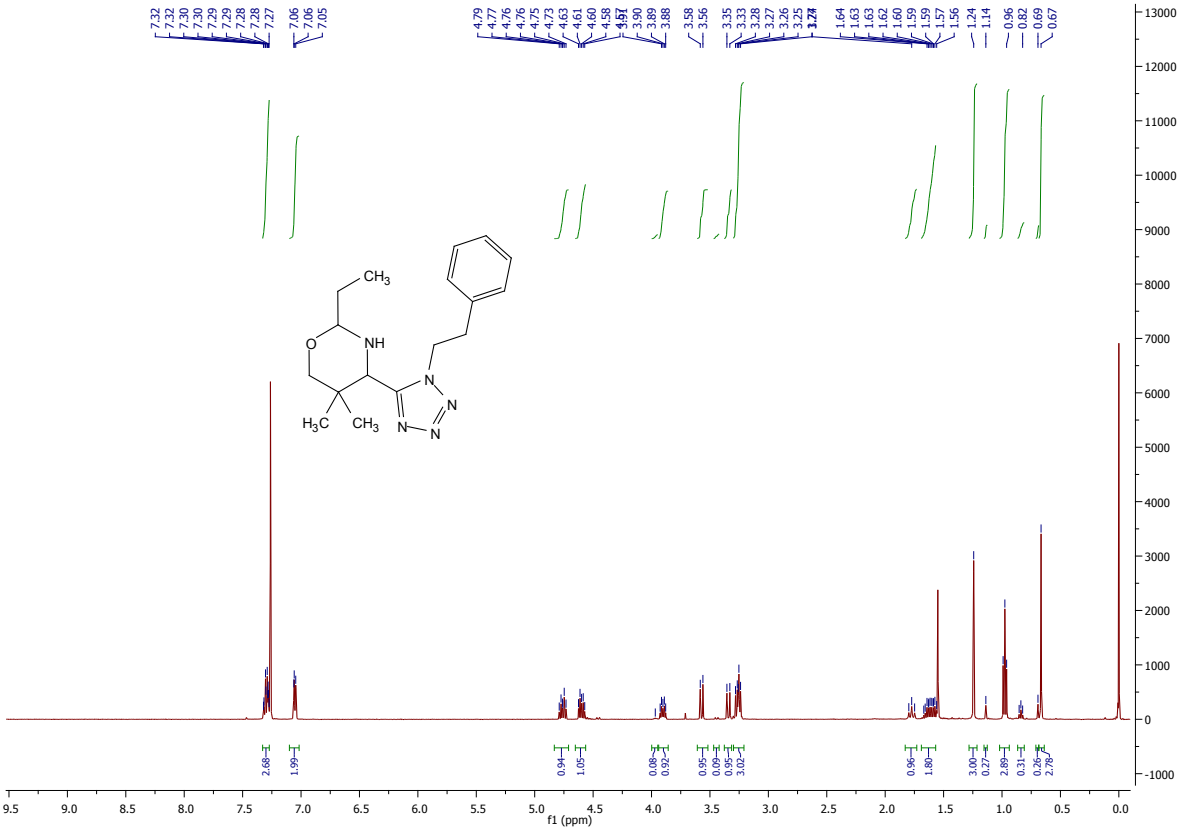


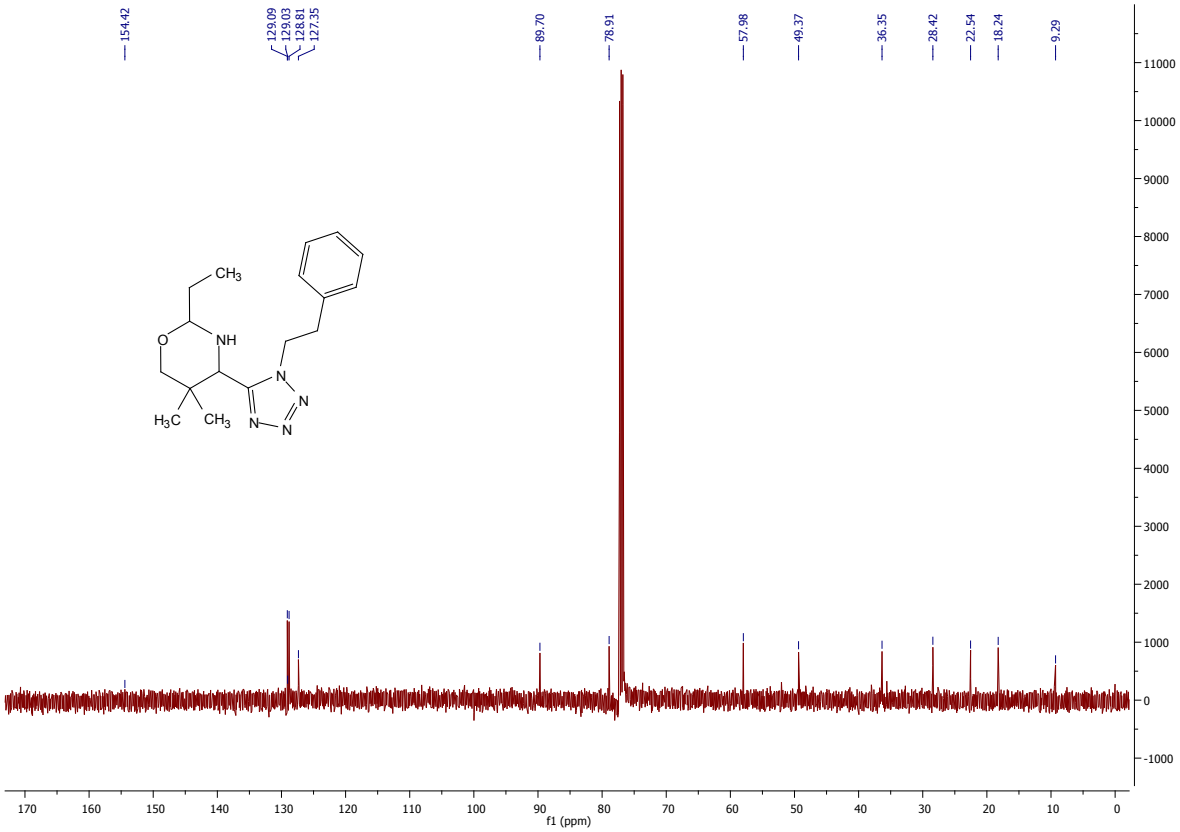
DAN84-7 #31 RT: 0.52583 AV: 1 NL: 4.96E6

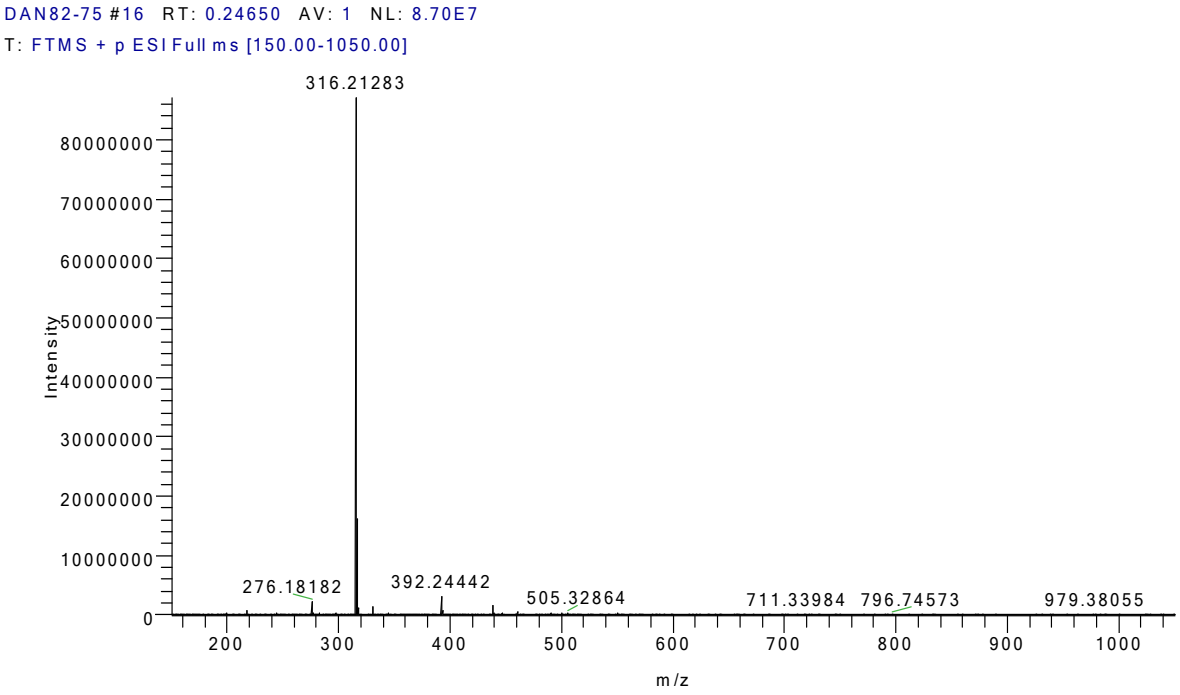
T: FTMS + p ESI Full ms [150.00-1050.00]



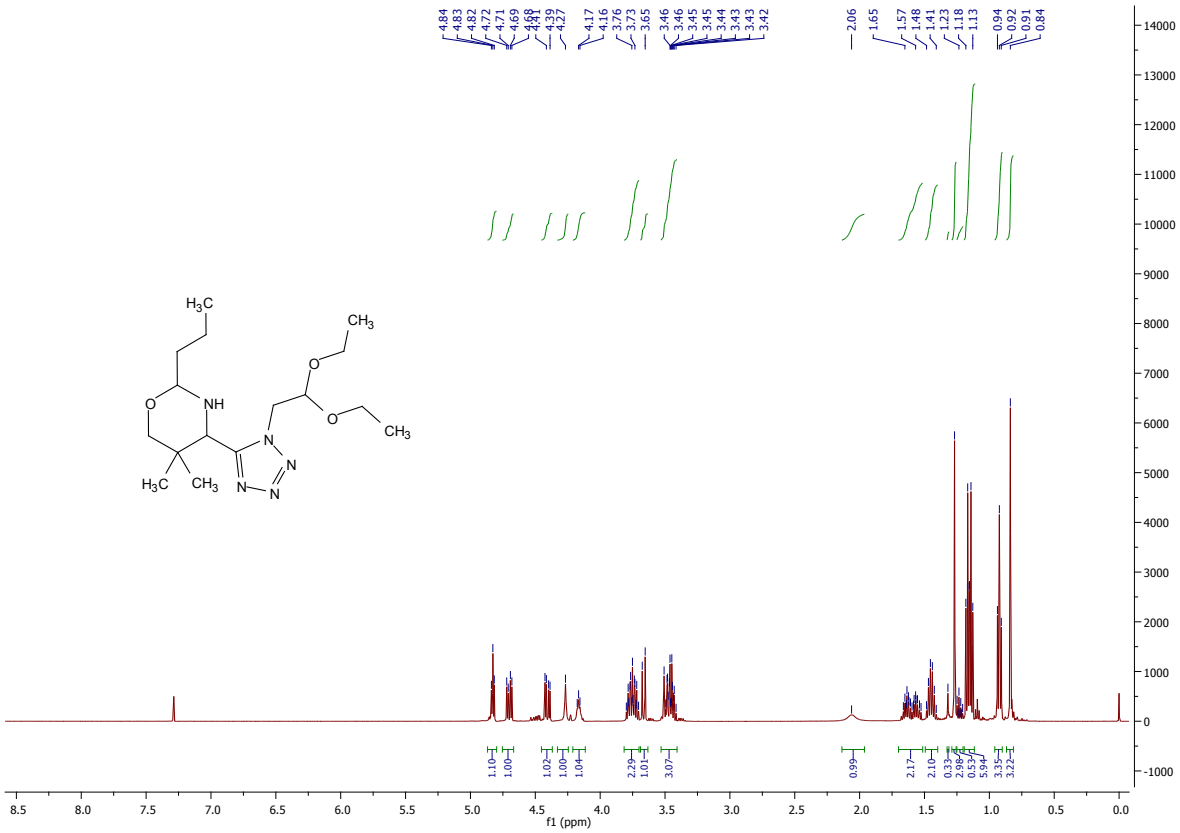
2-ethyl-5,5-dimethyl-4-(1-phenethyl-1*H*-tetrazol-5-yl)-1,3-oxazinane (1e)

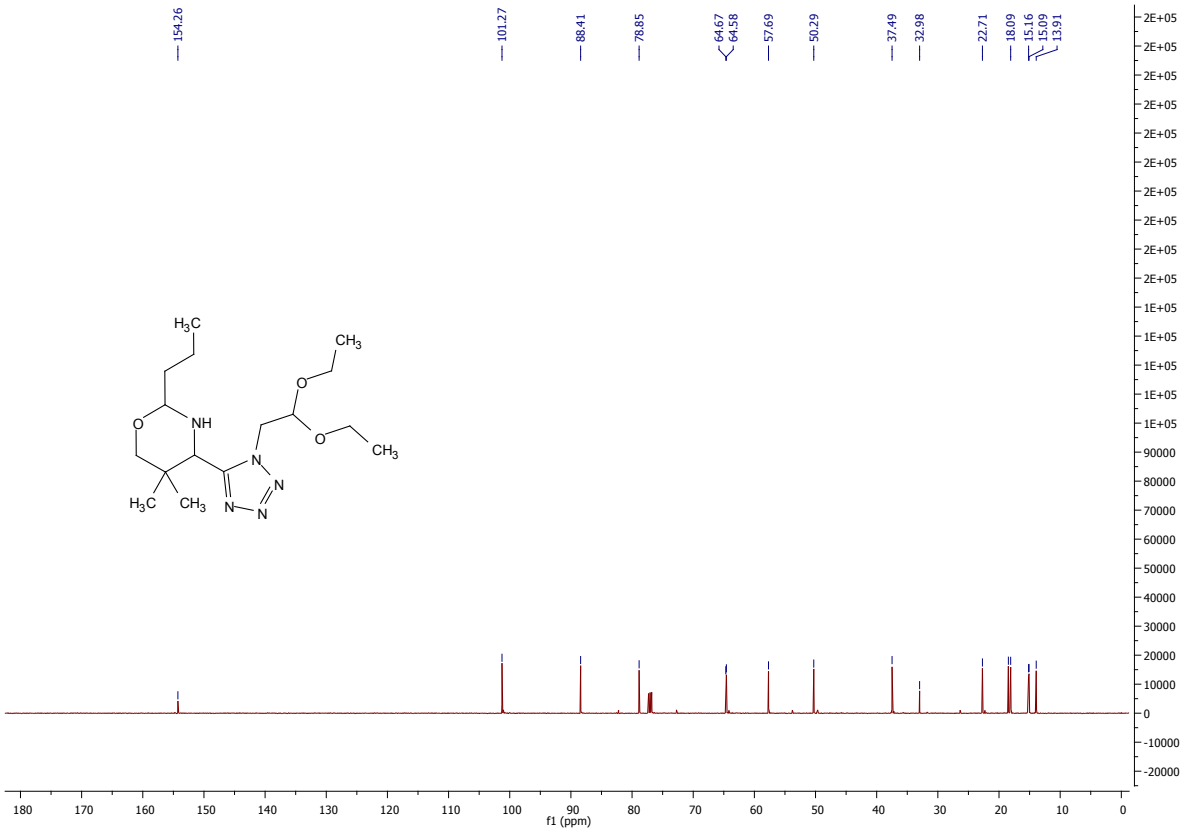






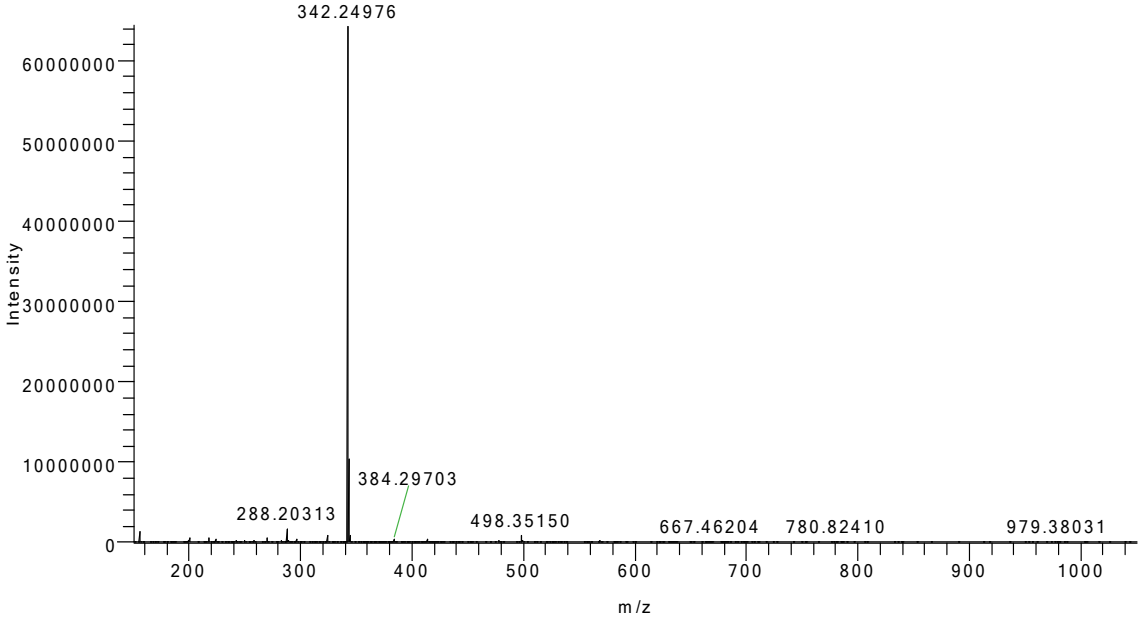
4-(1-(2,2-diethoxyethyl)-1*H*-tetrazol-5-yl)-5,5-dimethyl-2-propyl-1,3-oxazinane (1f)



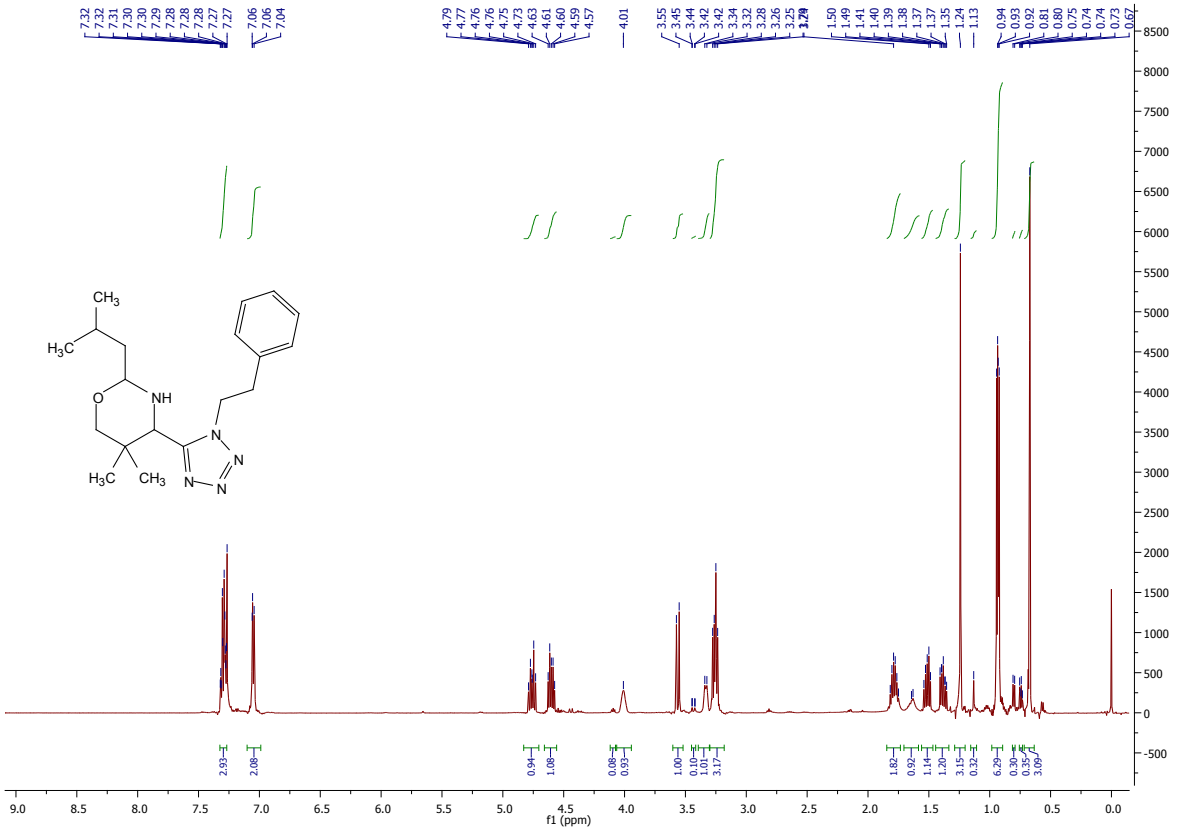


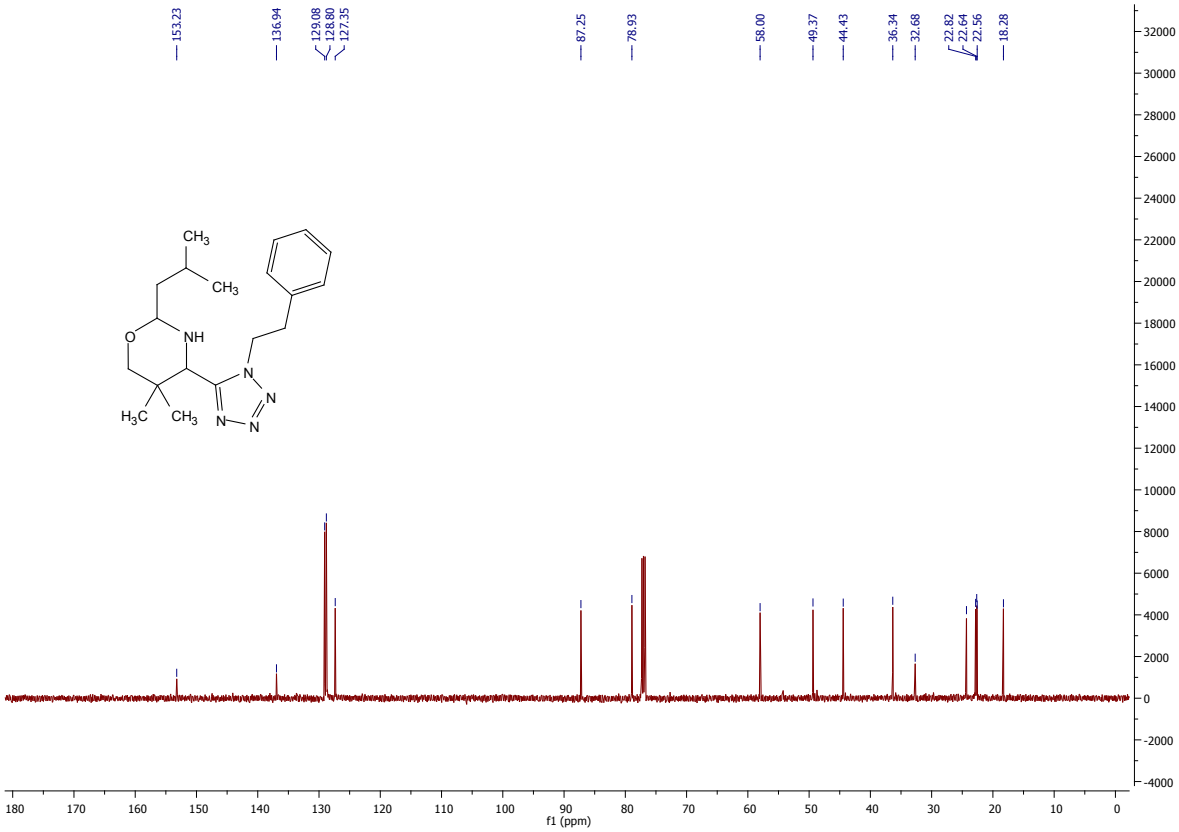
DAN0610B #22 RT: 0.36954 AV: 1 NL: 6.43E7

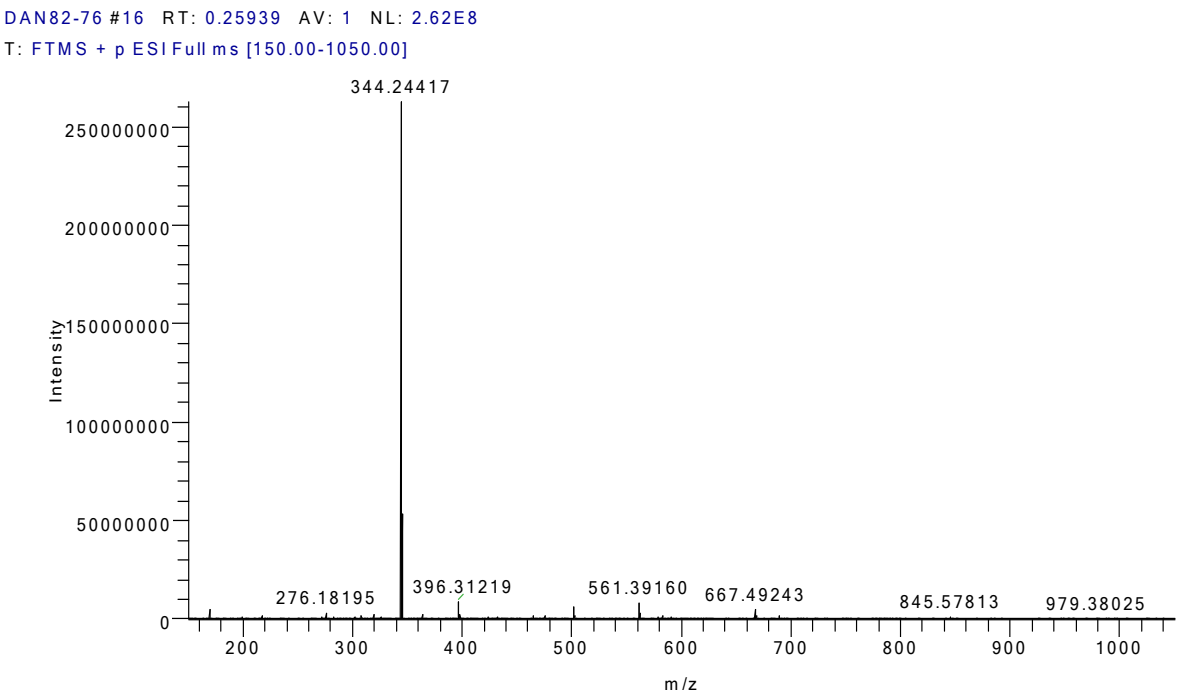
T: FTMS + p ESI Full ms [150.00-1050.00]



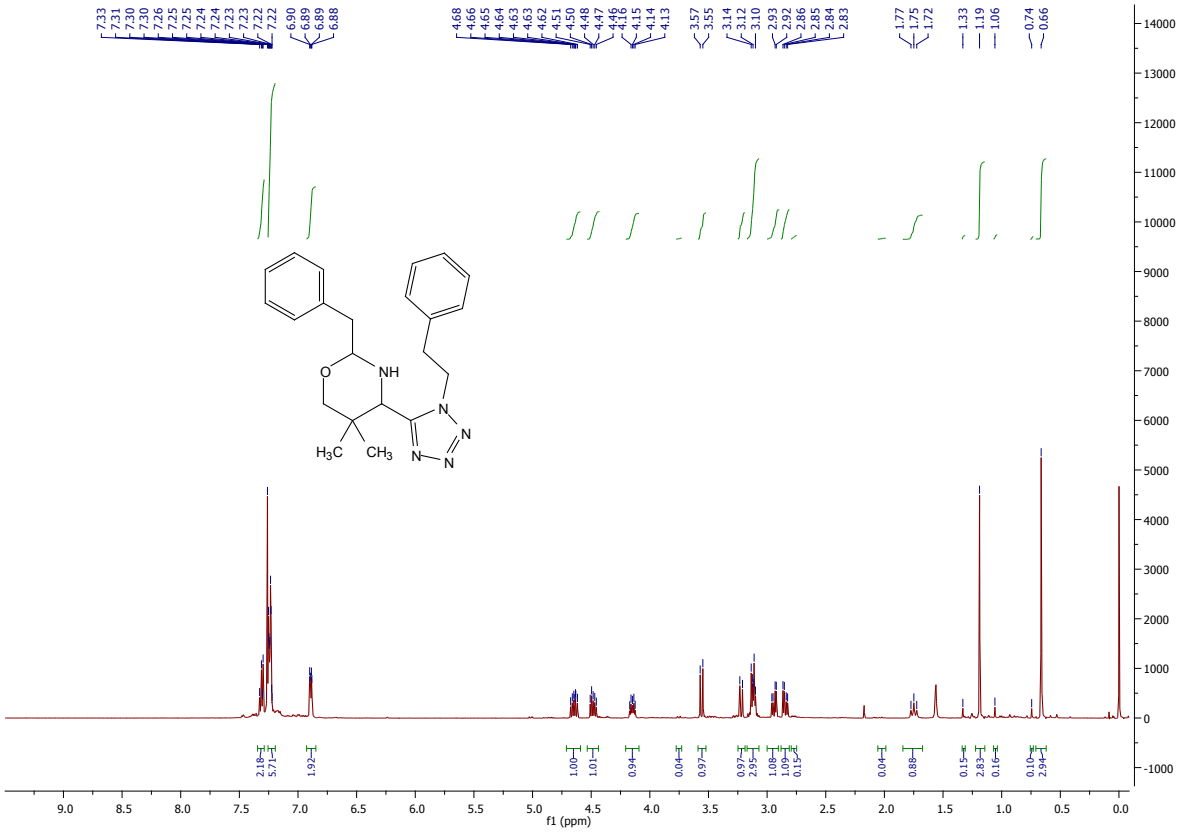
2-isobutyl-5,5-dimethyl-4-(1-phenethyl-1*H*-tetrazol-5-yl)-1,3-oxazinane (1g)

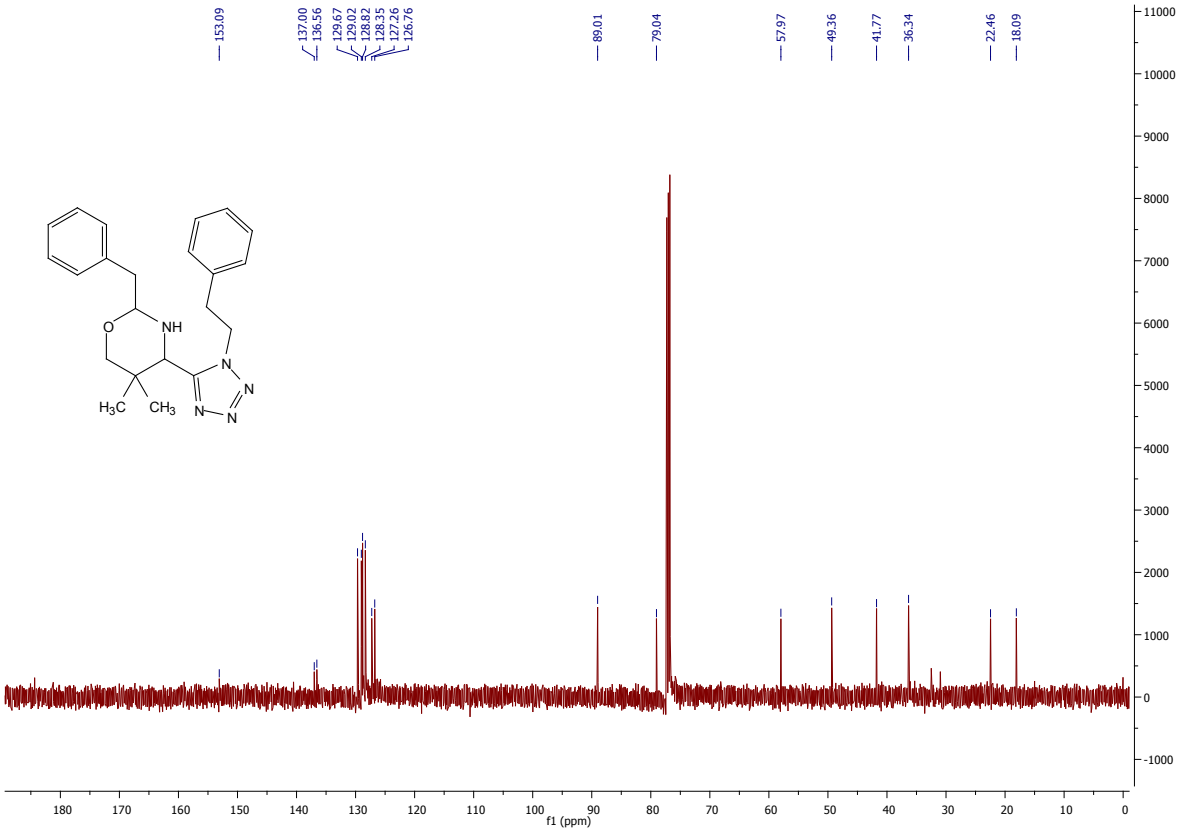






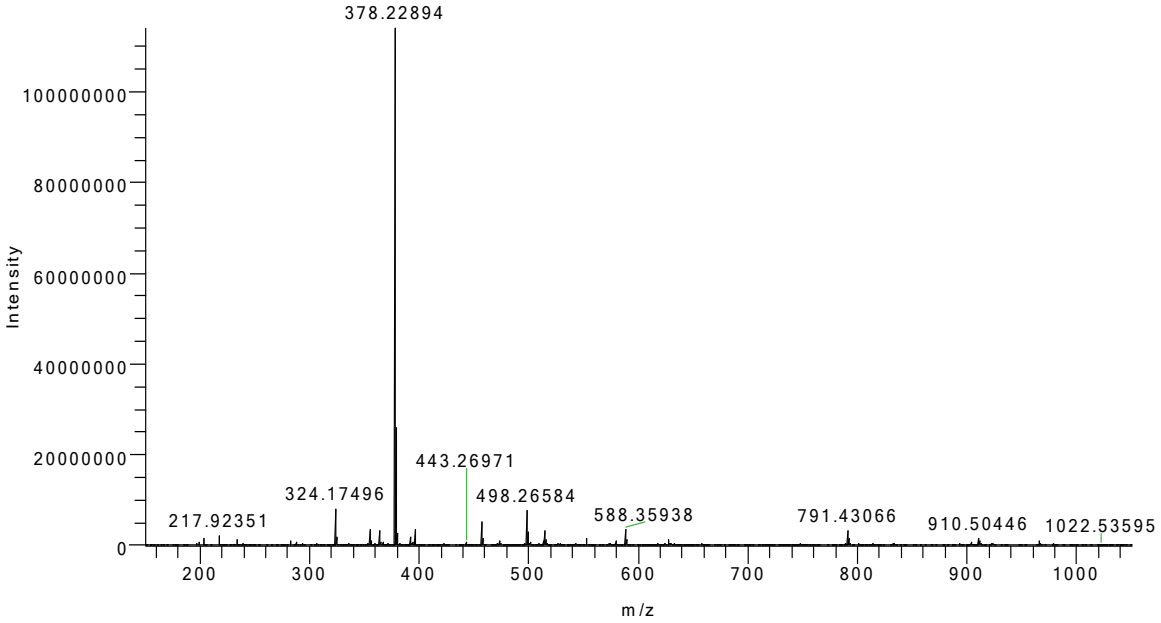
2-benzyl-5,5-dimethyl-4-(1-phenethyl-1*H*-tetrazol-5-yl)-1,3-oxazinane (1h)



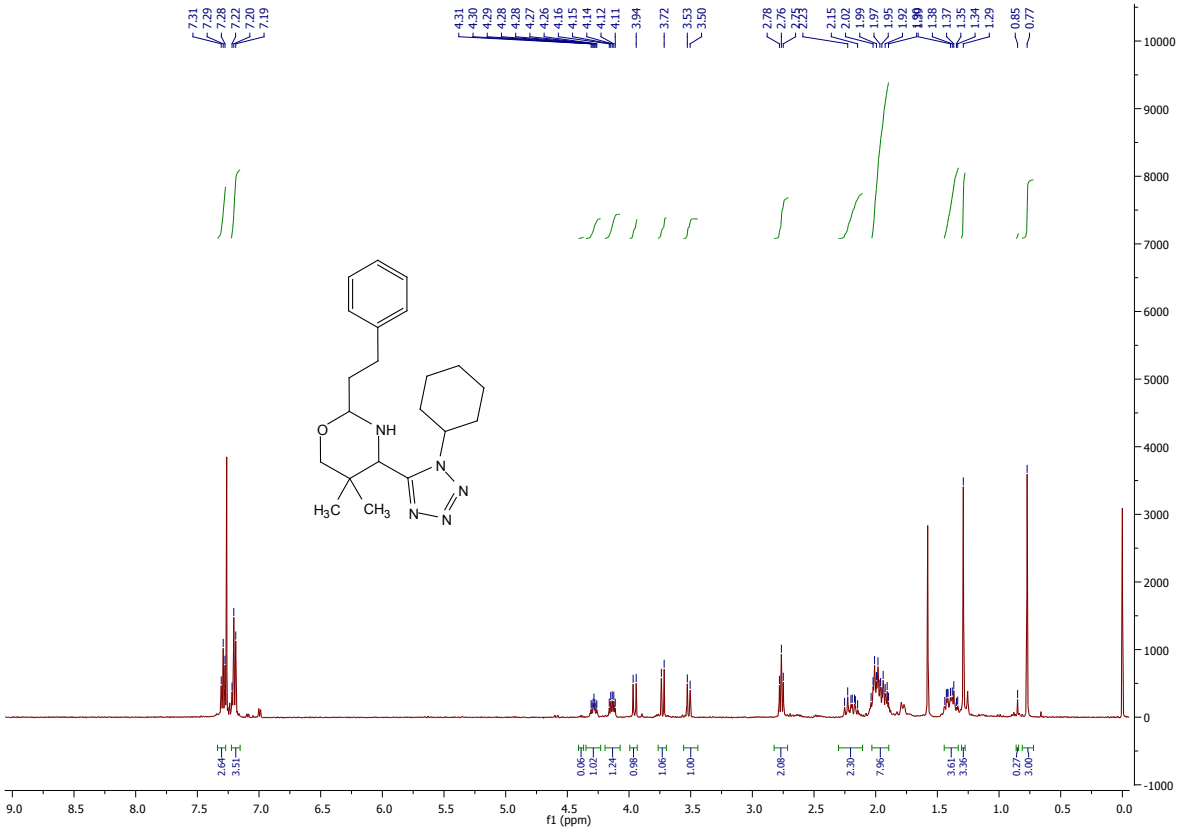


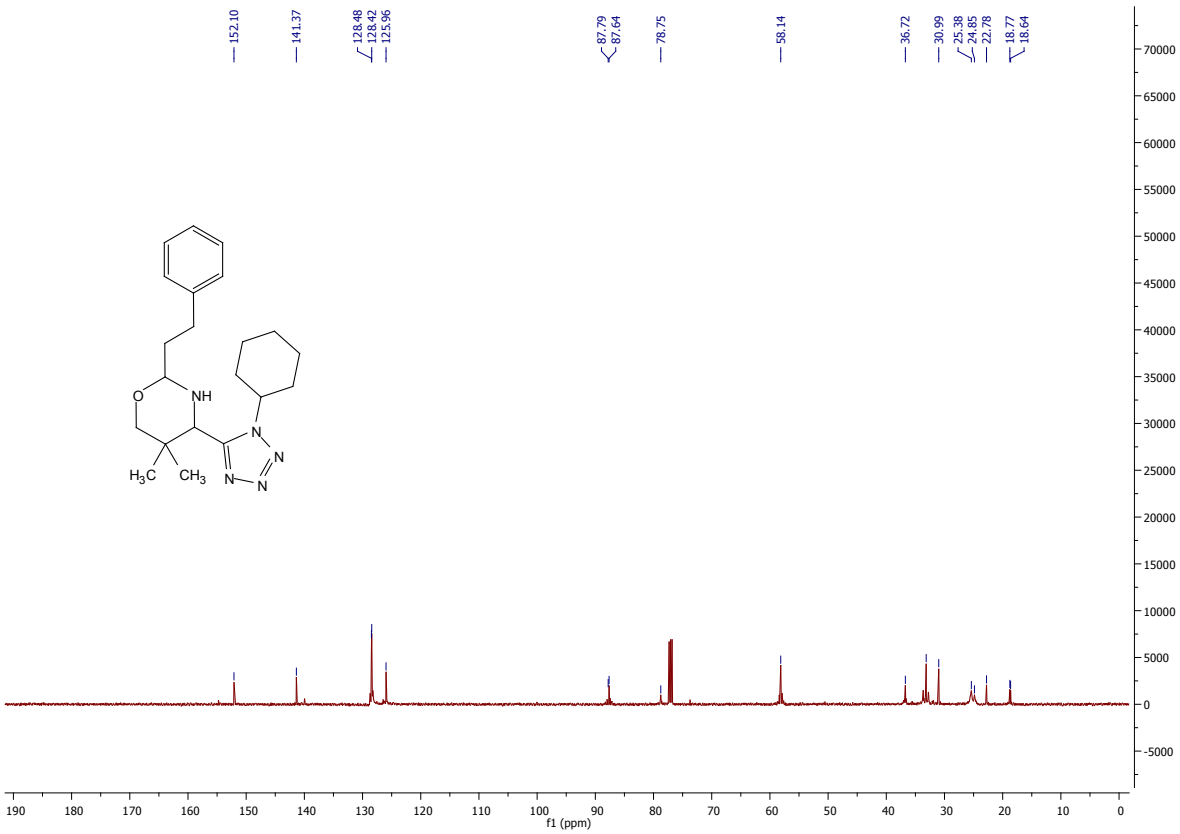
DAN82-61 #15 RT: 0.25034 AV: 1 NL: 1.14E8

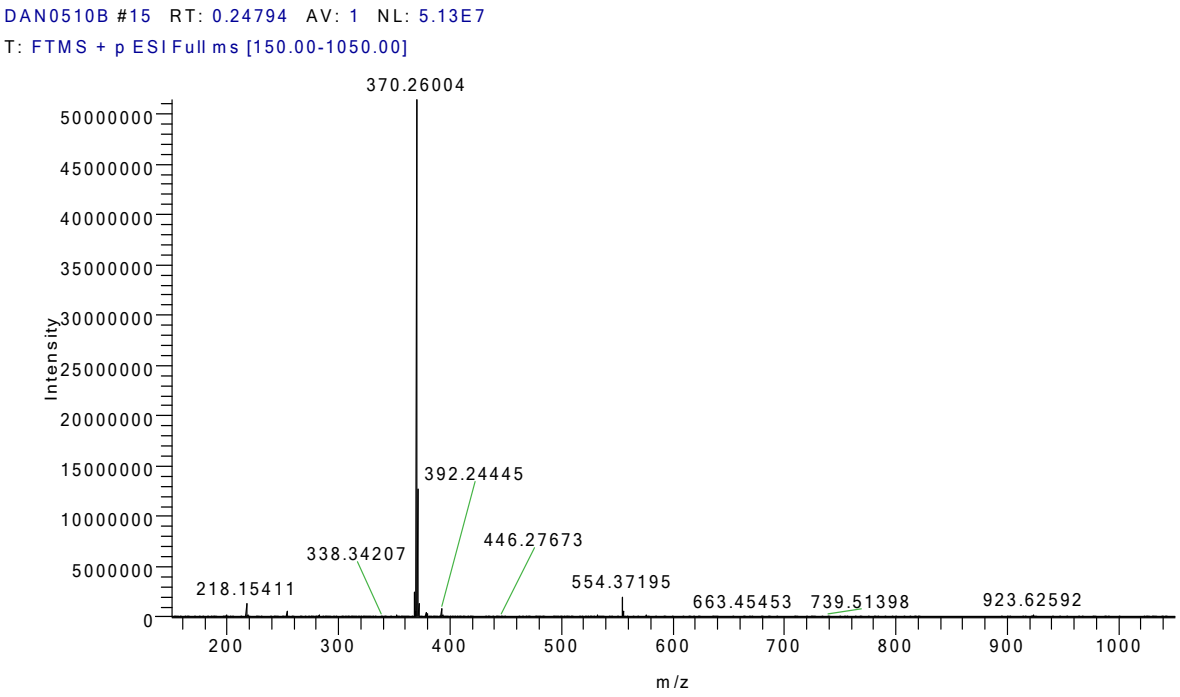
T: FTMS + p ESI Full ms [150.00-1050.00]



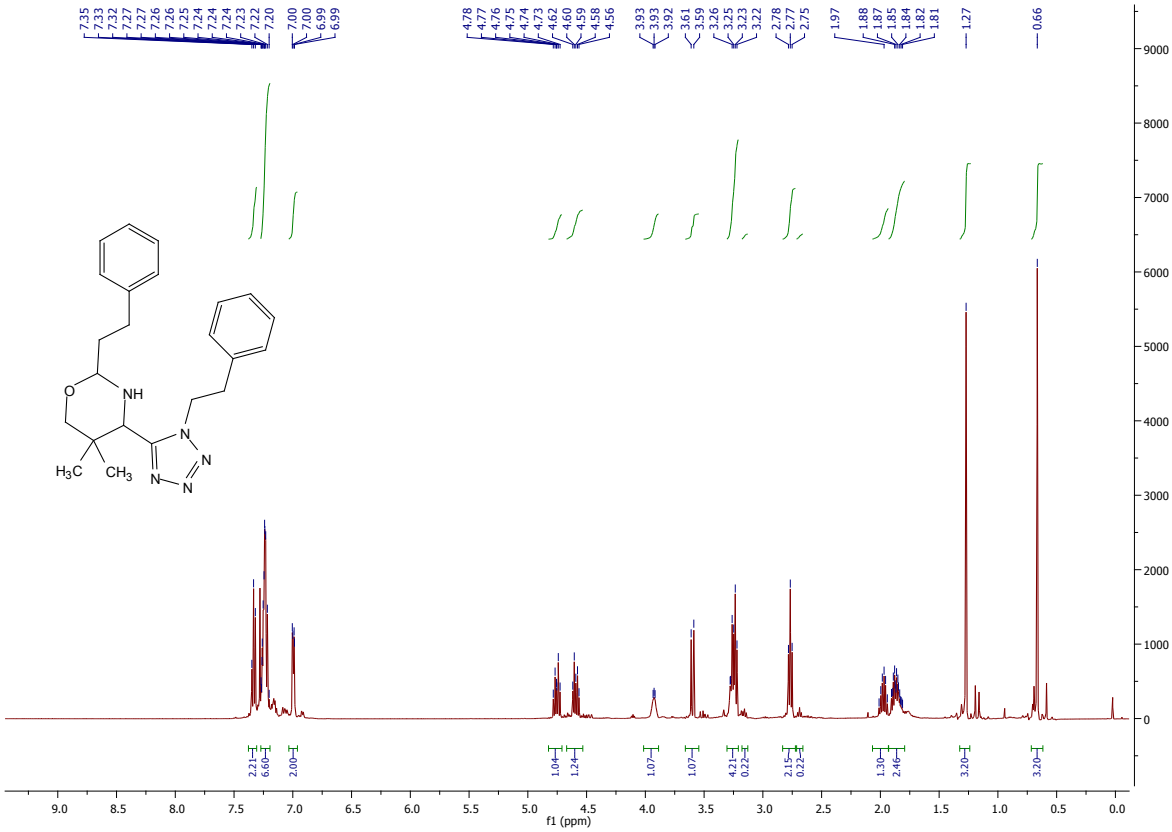
(*E*)-4-(1-cyclohexyl-1*H*-tetrazol-5-yl)-5,5-dimethyl-2-styryl-1,3-oxazinane (1i)

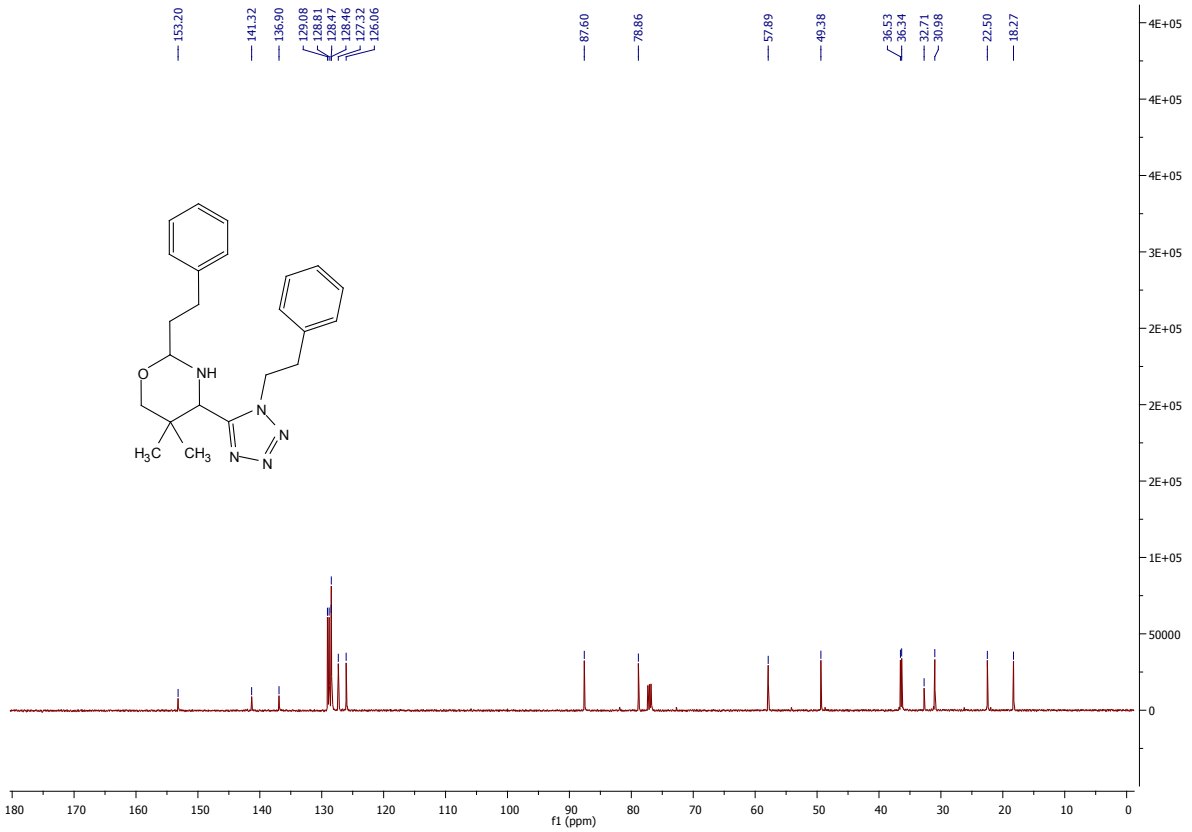






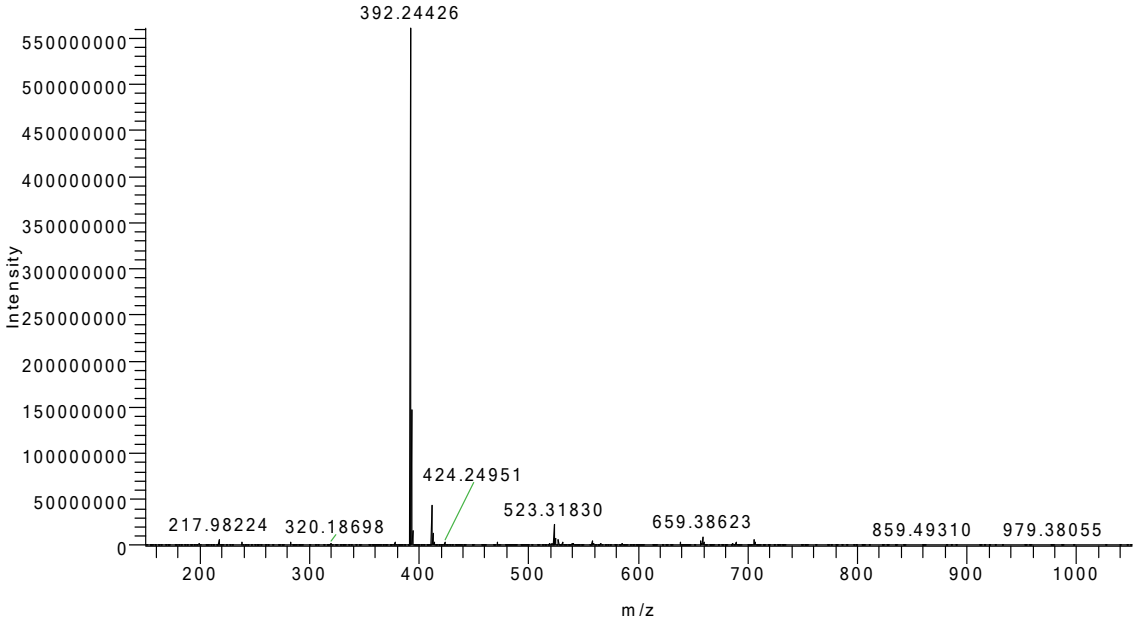
5,5-dimethyl-2-phenethyl-4-(1-phenethyl-1*H*-tetrazol-5-yl)-1,3-oxazinane (1j)



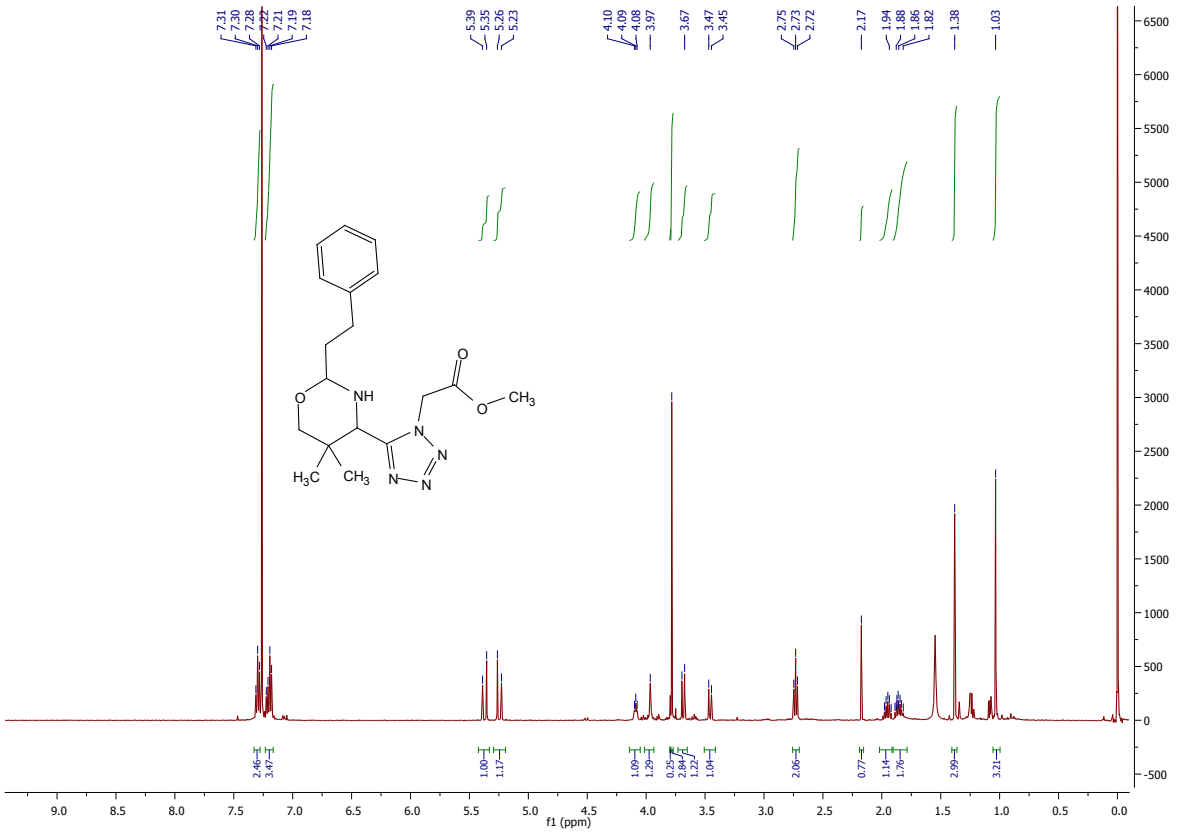


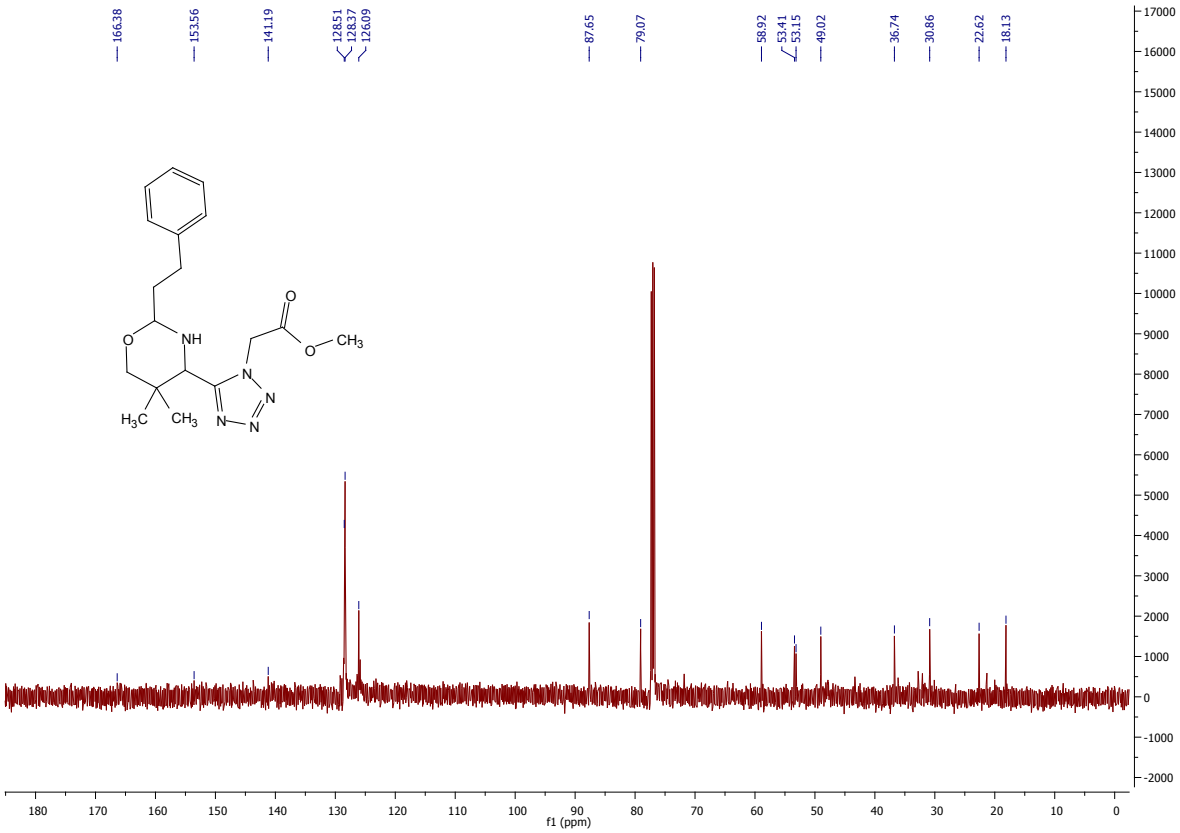
DAN84-1 #16 RT: 0.25751 AV: 1 NL: 5.60E8

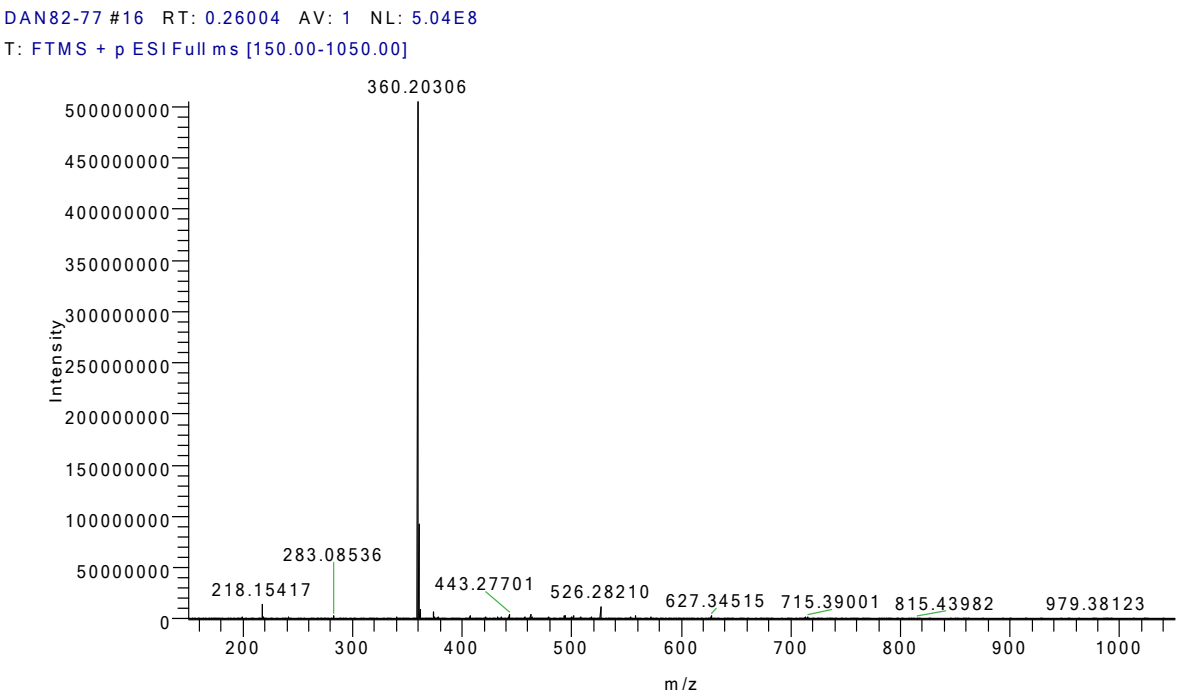
T: FTMS + p ESI Full ms [150.00-1050.00]



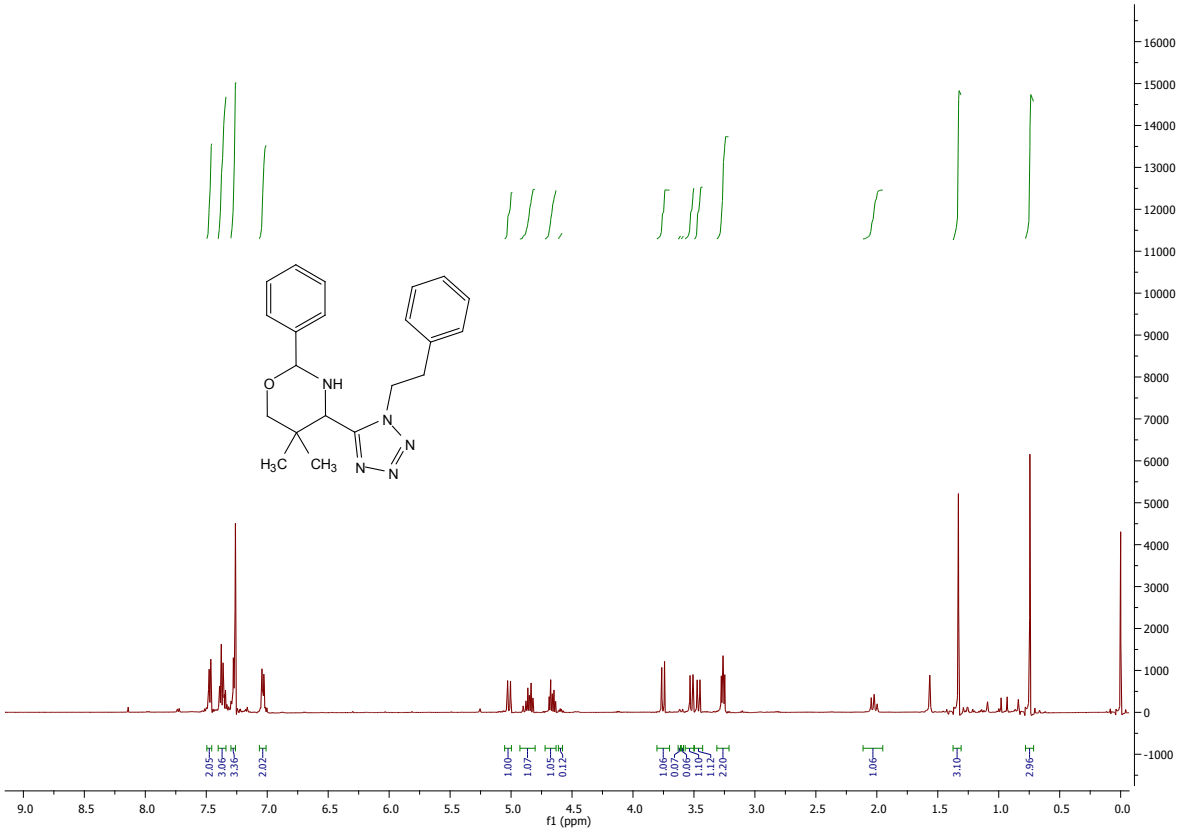
methyl 2-(5-(5,5-dimethyl-2-phenethyl-1,3-oxazinan-4-yl)-1*H*-tetrazol-1-yl)acetate (1k)

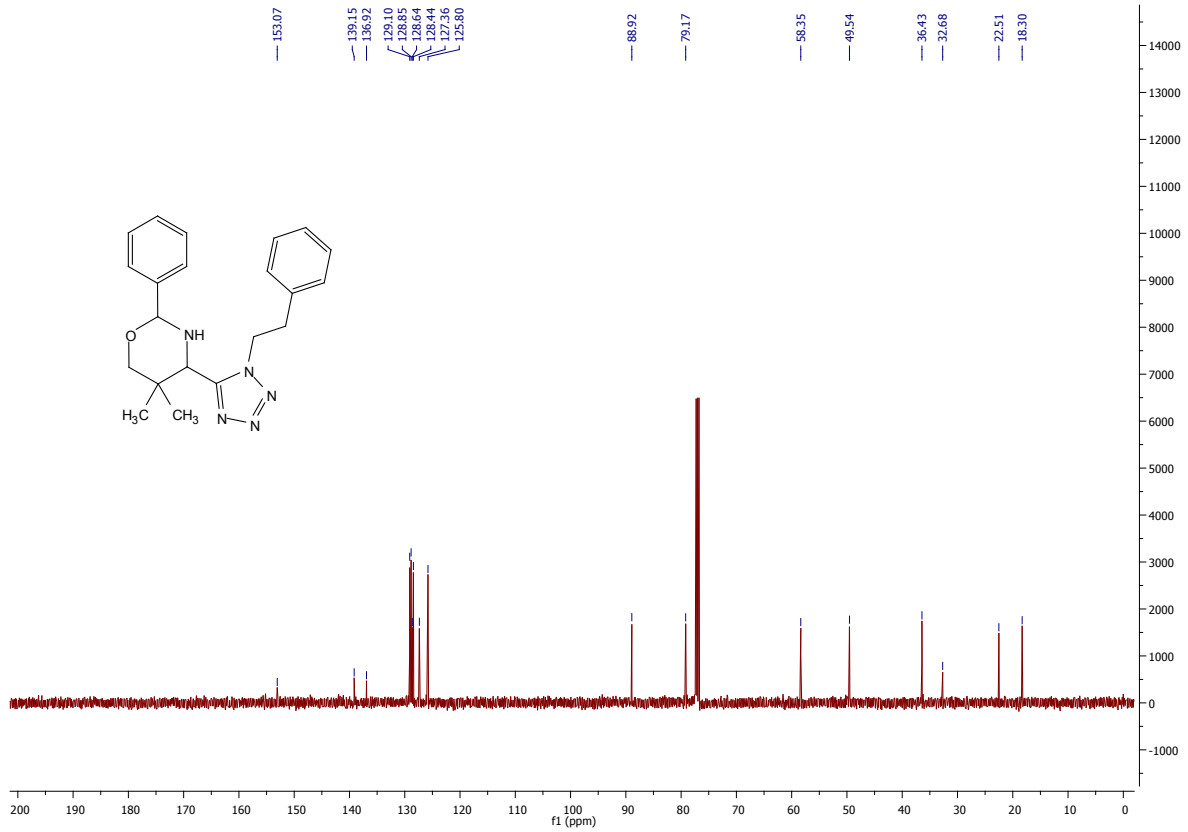






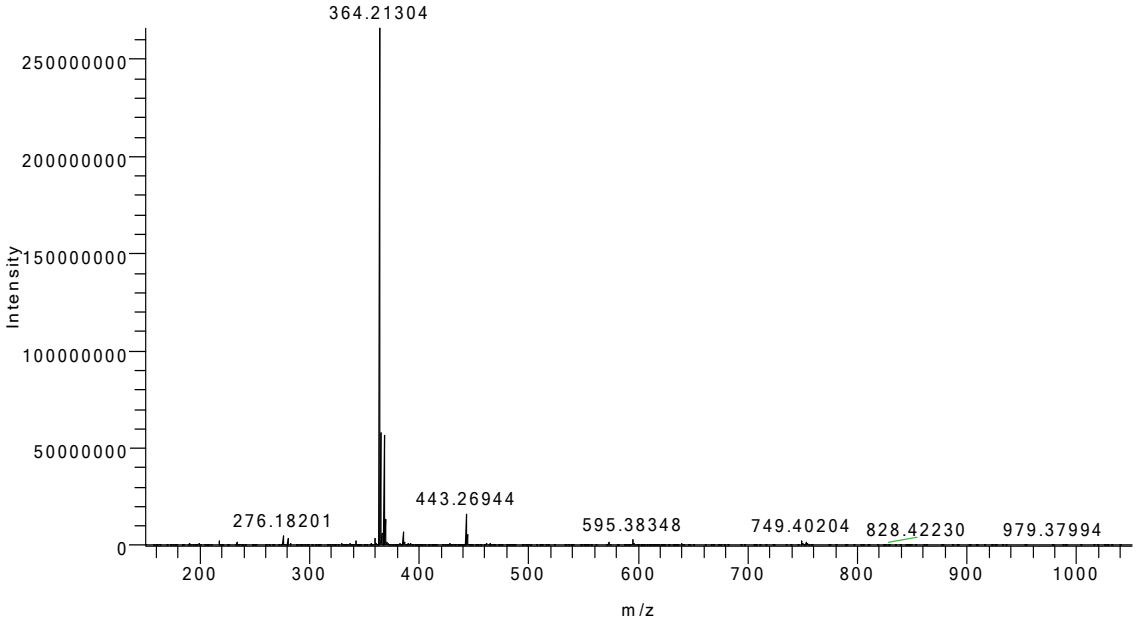
5,5-dimethyl-4-(1-phenethyl-1*H*-tetrazol-5-yl)-2-phenyl-1,3-oxazinane (1l)



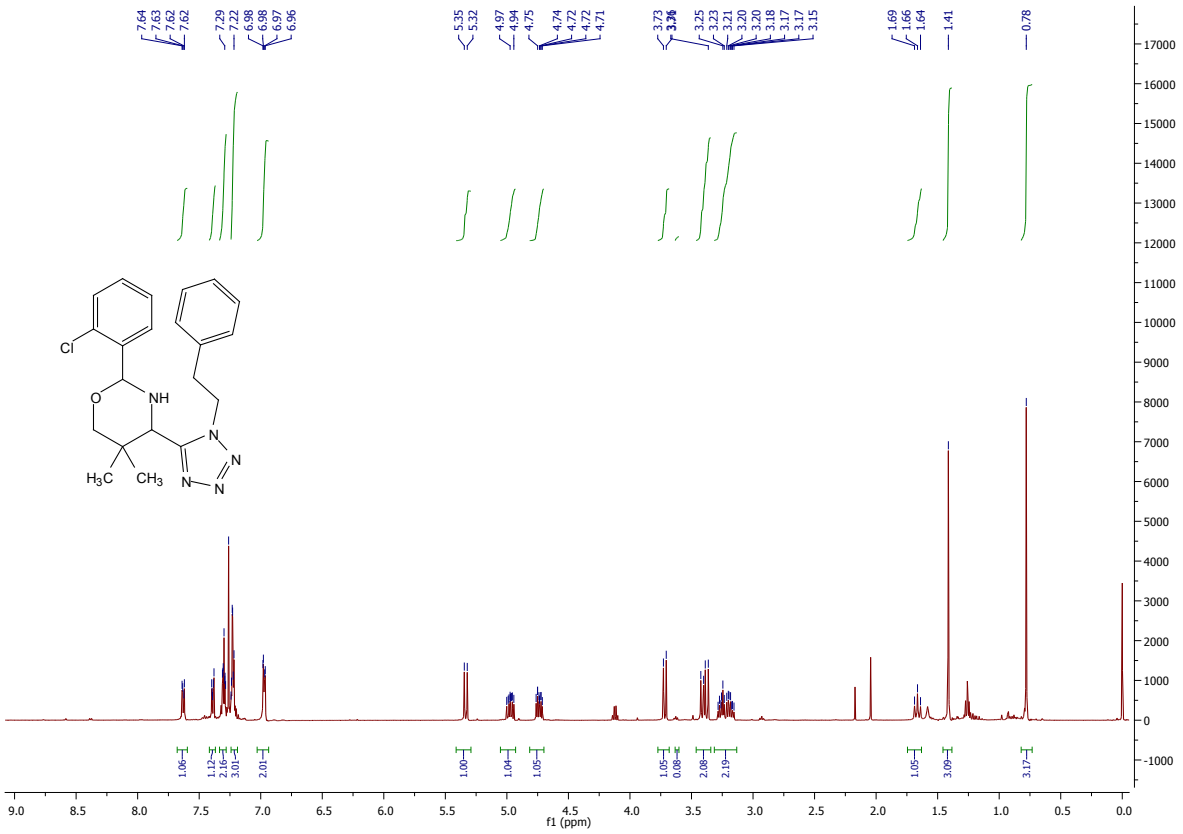


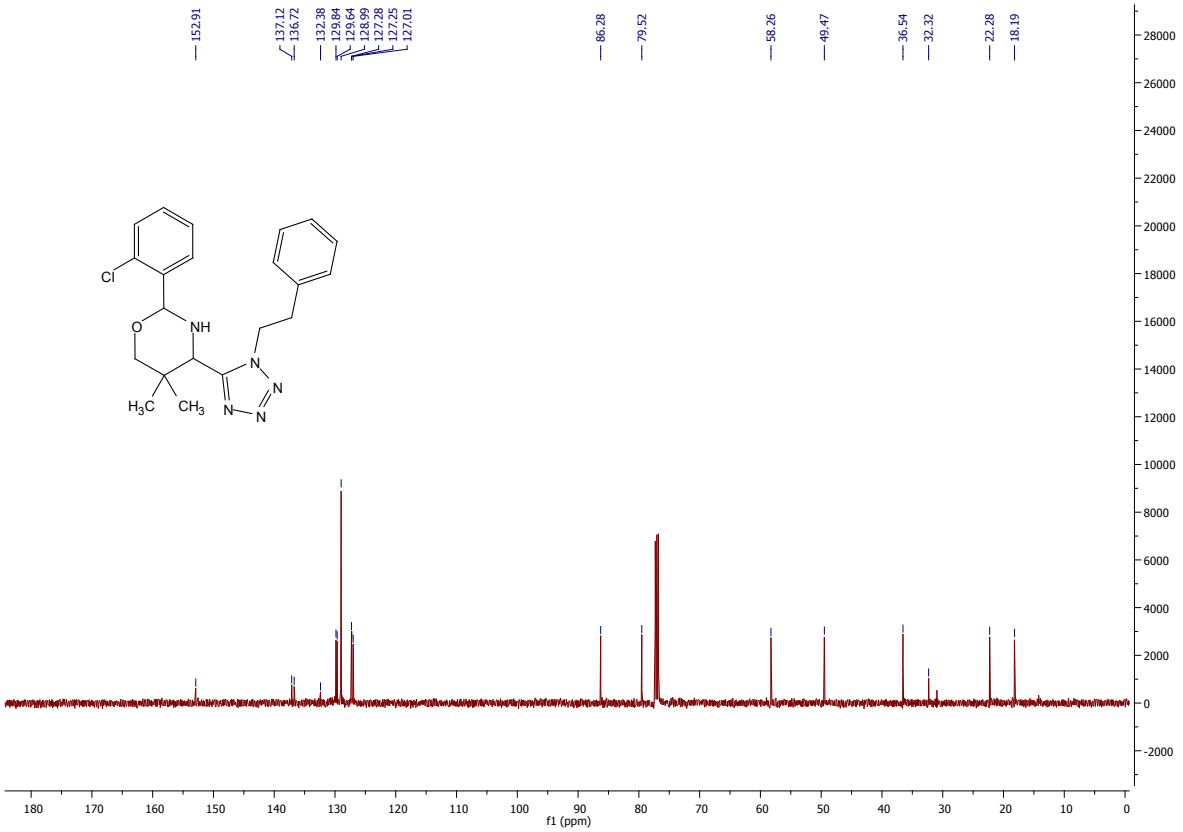
DAN82-59 #15 RT: 0.23709 AV: 1 NL: 2.66E8

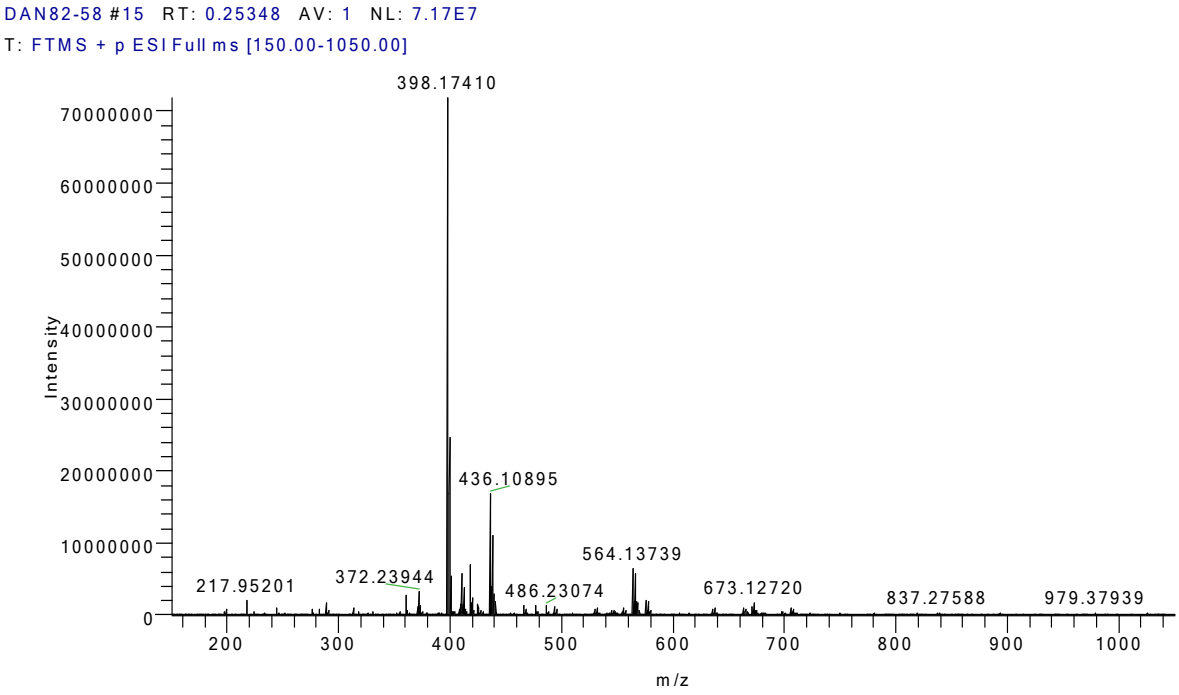
T: FTMS + p ESI Full ms [150.00-1050.00]



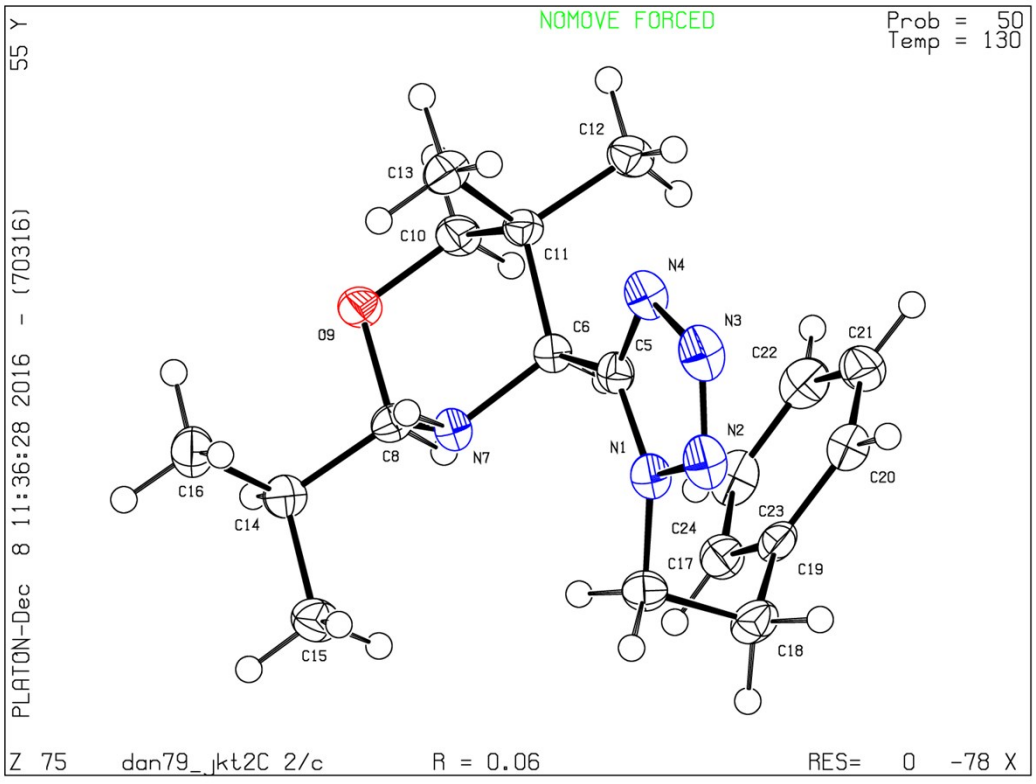
2-(2-chlorophenyl)-5,5-dimethyl-4-(1-phenethyl-1*H*-tetrazol-5-yl)-1,3-oxazinane (1m)]



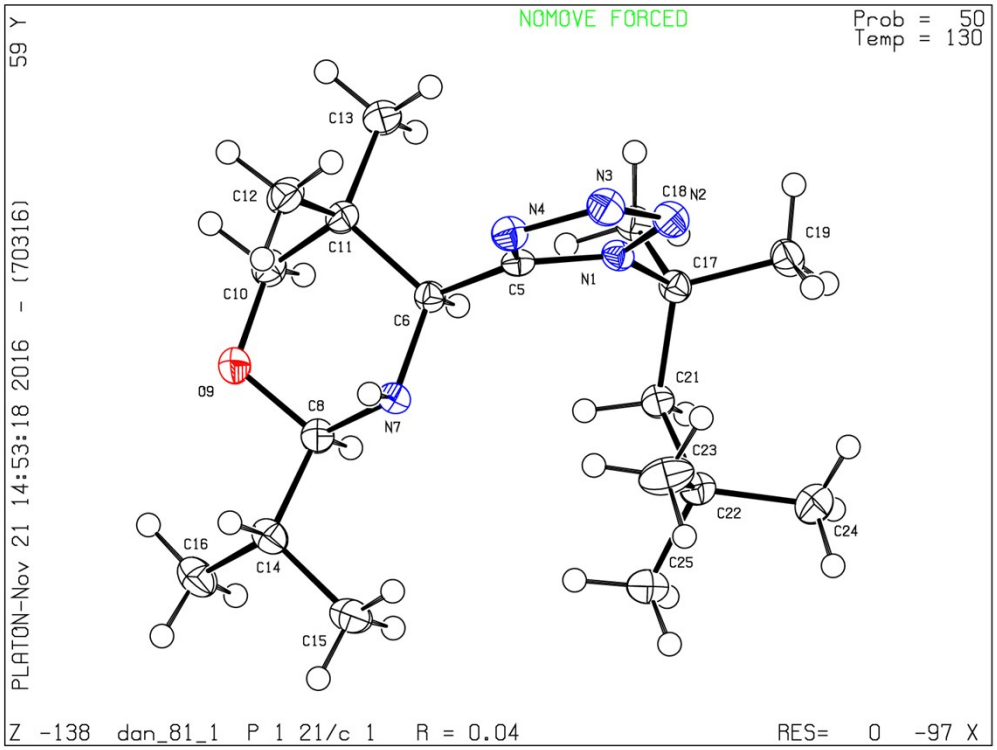




Single Crystal X-Ray Structure Determination of Compound 1b



Single Crystal X-Ray Structure Determination of Compound 1C



Crystal structure determination

X-ray diffraction data for single crystals of compounds **1b** and **1c** were collected using SuperNova (Rigaku - Oxford Diffraction) four circle diffractometer with a mirror monochromator and a microfocus MoKα radiation source (λ = 0.71073 Å). Additionally, the diffractometer was equipped with a CryoJet HT cryostat system (Oxford Instruments) allowing low temperature experiments. Single crystals X-ray experiments were performed at 130 K and 129.6 K for **1b** and **1c**, respectively. The obtained data sets were processed with CrysAlisPro software [S1]. The phase problem was solved by direct methods using SIR2004 [S2]. Parameters of obtained models were refined by full-matrix least-squares on F^2 using SHELXL-2014/6 [S3]. Calculations were performed using WinGX integrated system (ver. 2014.1) [S4]. Figures were prepared with Mercury 3.5 software [S5].

All non-hydrogen atoms were refined anisotropically. All hydrogen atoms attached to carbon atoms were positioned with the idealised geometry and refined using the riding model with the isotropic displacement parameter $U_{iso}[H] = 1.2$ (or 1.5 (methyl groups only)) $U_{eq}[C]$. The position of hydrogen atoms linked to nitrogen (amine group) were found on the difference Fourier map and refined with no restrains on the isotropic displacement parameter. Crystal data and structure refinement results for presented crystal structures are shown in Table S1. Asymmetric units are shown in Figure S1.

Crystallographic data for structures presented in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication nos. CCDC 1521456 (**1b**), CCDC 1521499 (**1c**). Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK, (fax: +44-(0)1223-336033 or e-mail: deposit@ccdc.cam.ac.uk).

References:

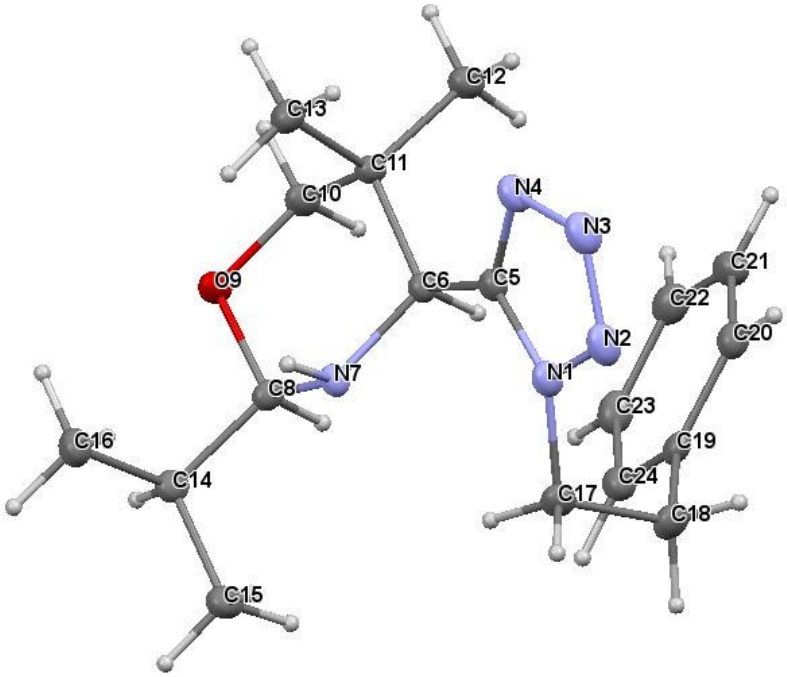
[S1] Oxford Diffraction (2006). CrysAlisPro Oxford Diffraction Ltd, Abingdon, England, Version 1.171.36.20 (release 27-06-2012 CrysAlis171.NET)

[S2] Maria C. Burla, Rocco Caliandro,Mercedes Camalli, Benedetta Carrozzini,Giovanni L. Cascarano, Liberato De Caro,Carmelo Giacovazzo, Giampiero Polidori and Riccardo Spagna J. Appl.Cryst. 2005 Vol. 38, Issue 2, pages 381–388

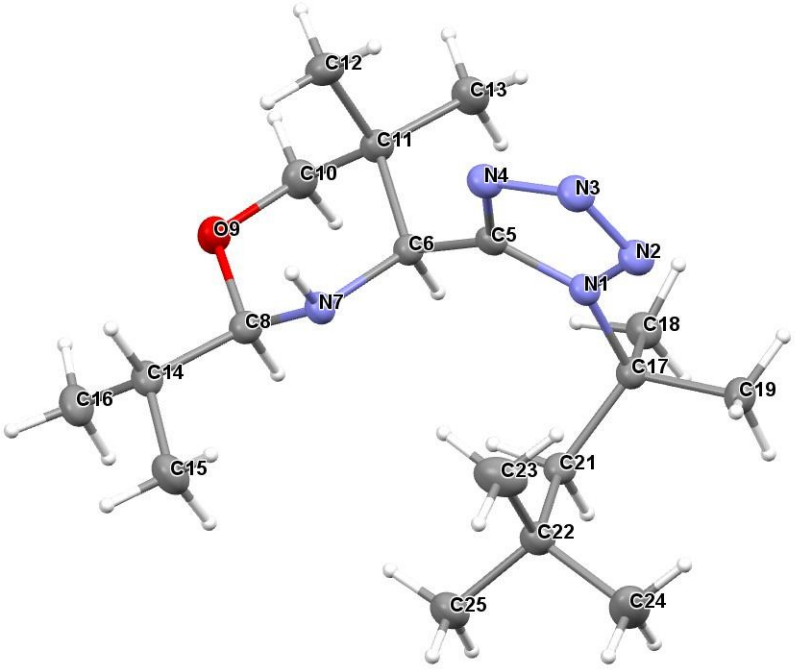
[S3] Sheldrick, G. M. ActaCryst. 2008, A64, 112-122.

[S4] Farrugia, L., J. J. Appl. Cryst. 1999, 32, 837-838.

[S5] Macrae C. F., Edgington P.R., McCabe P., Pidcock E., Shields G.P., Taylor R., Towler M., & van de Streek J., J. Appl. Cryst. 2006, 39, 453-45



1b



1c

Figure S1. Molecular geometry observed in the crystal structures of compounds **1b** and **1c** (asymmetric units here), showing the atom labelling scheme. Displacement ellipsoids of non-hydrogen atoms are drawn at the 30% probability level. H atoms are presented as small spheres with an arbitrary radius.

Table S1. Crystal data and structure refinement results for compounds **1b** and **1c**.

	1b	**1c**
Empirical moiety formula	$C_{18}\ H_{27}\ N_5\ O$	$C_{18}\ H_{35}\ N_5\ O$
Formula weight [g/mol]	329.44	337.51
Crystal system	Monoclinic	Monoclinic
Space group	C2/c	$P2_1/c$
Unite cell dimensions	a = 25.2277(15) Å b = 8.2188(4) Å c = 17.5148(9) Å α=90° β=99.025(5)° γ=90°	a = 12.4795(8) Å b = 15.9839(7) Å c = 10.6108(8) Å α=90° β=112.921(8)° γ=90°
Volume [$Å^3$]	3586.6(3)	1949.4(3)
Z	8	4
D_{calc} [Mg/m^3]	1.220	1.150
μ [mm^{-1}]	0.079	0.074
F(000)	1424	744
Crystal size [mm^3]	0.2 x 0.1 x 0.1	0.4 x 0.4 x 0.15
Θ range	2.92° to 28.62°	3.11 to 28.52°
Index ranges	$-30 \le h \le 32$, $-10 \le k \le 10$, $-20 \le l \le 23$	$-15 \le h \le 15$, $-21 \le k \le 20$, $-14 \le l \le 14$
Refl. collected	14233	15428
Independent reflections	4248 [R(int) = 0.0745]	4568 [R(int) = 0.0373]
Completeness [%] to Θ	99.8 (Θ 25.2°)	99.8 (Θ 26.3°)
Absorption correction	Multi-scan	Multi-scan
Tmin. and Tmax.	0.651 and 1.000	0.642 and 1.000
Data/restraints/parameters	4248 / 0 / 225	4568 / 0 / 231
GooF on F2	1.070	1.038
Final R indices [I>2sigma(I)]	R1= 0.0574, wR2= 0.1052	R1= 0.0424, wR2= 0.0991
R indices (all data)	R1= 0.1090, wR2= 0.1273	R1= 0.0576, wR2= 0.1108
$\Delta\rho_{max}$, $\Delta\rho_{min}$ [$e \cdot Å^{-3}$]	0.220 and -0.270	0.293 and -0.232