Efficient Enhancement of Copper-pyridineoxazoline catalysts through immobilization and process design.

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Content:

1. Synthesis of *pyox* ligands.

2-[(*S*)-4,5-dihydro-4-isopropyl-1,3-oxazol-2-yl]pyridine (*pyox*(^{i}Pr)) was synthesized according to reference 20

2-[(*S*)-4,5-didydro-4-*tert*-butyl-1,3-oxazol-2-yl]pyridine (*pyox*(^{t}Bu)). To a stirred solution of $Zn(TfO)_2$ (399 mg, 1.10 mmol) and 2-pyridincarbonitrile (104 mg, 1.0 mmol) in anhydrous toluene (20 mL), a solution of (*S*)-*tert*-leucinol (117 mg, 1.0 mmol) in anhydrous toluene (10 mL) was added *via canula*. The resulting mixture was refluxed during 72 h and then allowed to cool. AcOEt (20 mL) was added and the resulting solution was washed with brine (3x30 mL) and Na_2CO_3 5% (3x30 mL). The organic phases were collected, dried with $MgSO_4$ and the solvent was evaporated under vacuum yielding 2-[(*S*)-4,5-didydro-4-tert-butyl-1,3-oxazol-2-yl]pyridine (138 mg, 68%) as a white solid.

^{1}H-NMR: 8.70 (d, J=5.7 Hz, 1H); 8.08 (dd, J= 8.0 Hz, 1H); 7.75 (dt J= 1.4, 8.0 Hz, 1H); 7.41-7-35 (m, 1H); 4.46 (dd, J=8.8, 11.3 Hz, 1H) 4.31 (t, J=8.8 Hz, 1H); 4.11 (dd, J= 8.8, 11.3 Hz, 1H); 0.96 (s, 9H). ^{13} C NMR: 162.3, 149.6, 146.8, 136.5, 125.3, 123.9, 76.4, 69.3, 34.0, 26.0.

IR (KBr, cm^{-1}): 3051(*CH*, *py*,); 2959, 2899, 2858 (*CH*), 1642 *C=N*, *ox*; 1582 (*CH*, *C-C*). Melting point: 72ºC

6-bromo-*N*-[(*S*)-2-hydroxy-1-isopropylethyl]-2-pyridinecarboxamide (3) To a stirred suspension of 6-bromo-2-pyridincarboxylic acid **(2)** (2525 mg, 12.50 mmol) in anhydrous DCM, two drops of a solution of DMF (4% vol. in DMF) and oxalyl chloride (2.18 mL, 25.00 mmol) were added. The resulting suspension was refluxed during 6 h. and then allowed to cool. The solution was filtered through a celite pad and the filtrate was evaporated under reduced pressure to obtain a solid which corresponds with 2-bromopicolinic acid chloride. This acid chloride was dissolved in anhydrous DCM (25 mL) and added dropwise to a solution of (*S*)-valinol (1287 mg, 12.50 mmol) and triethylamine (3.46 mL, 25.0 mmol) in anhydrous DCM (25 mL) at 0ºC. The resulting solution was allowed to warm to r.t. and then stirred overnight. The subsequent solution was then washed with Na_2CO_3 sat. (3x50 mL). The organic phase was dried with $MgSO_4$ and the solution was concentrated to

obtain an oil which was purified by flash chromatography (SiO_2, Hexanes/AcOEt 1:1) to obtain 6-bromo-*N*-[(*S*)-2-hydroxy-1-isopropylethyl]-2-pyridinecarboxamide **(3)** (2859 mg, 79%)

^{1}H NMR: 8.17 (dd, *1H*, J= 1.1 ; 7.4Hz), 8.00(d, *1H*, J=8.1 Hz), 7.74 (t, *1H*, J= 7.6 Hz), 7.63 (dd, *1H*, J= 1.1 Hz, 7.9 Hz), 3.97-3.79 (m, *3H*), 2.64 (m, *1H*), 2.01 (m, *1H*), 1.05 (d, *3H*, J= 5.59Hz), 1.02 (d, *3H*, J= 4.6Hz)

6-bromo-*N*-[(*S*)-2-chloro-1-isopropylethyl]-2-pyridinecarboxamide (4) To a stirred solution of 6-bromo-*N*-[(*S*)-2-hydroxy-1-isopropylethyl]-2-pyridinecarboxamide **(3)** (2659 mg, 9.26 mmol) in anhydrous DCM (50 mL) thionyl chloride (1.34 mL, 18.53 mmol) was added and the resulting solution was refluxed during 3h. After cooling, the solvent was distilled under reduced pressure to obtain an oil which was purified by flash chromatography (SiO_2, Hexanes/AcOEt 1:1) to obtain 6-bromo-*N*-[(*S*)-2-chloro-1-isopropylethyl]-2-pyridinecarboxamide **(4)** (2340 mg, 82%) as a yellowish oil.

^{1}H NMR: 8.16 (dd, *1H*, J= 1.2 ; 7.3Hz); 7.94 (d, *1H*, J=37.1 Hz); 7.72 (t, *1H*, J=7.6 Hz); 7.65 (dd, *1H*, J=7.3, 8.90 Hz); 4.20-4.0 (m, *1H*), 3.79-3.75 (m, *2H*), 2.21-2.04 (m, *1H*); 1.04 (d, *3H*, J= 6.4 Hz), 1.01 (d, *3H*, J= 6.6 Hz)

6-bromo-2-pyridinecarbonitrile (6) To a stirred suspension of CuCN (895 mg, 10.0 mmol) in anhydrous DMF (6 mL) 2,6-dibromopyridine (7080 mg, 30 mmol) was added. The resulting suspension was stirred at 140ºC under microwave heating and then allowed to cool. The subsequent mixture was added to Na_2CO_3 sat. (40 mL) and then extracted with AcOEt (3x50 mL). The organic phases were collected and dried with $MgSO_4$ and the volatiles removed under reduced pressure obtaining a white solid which was purified by flash chromatography (SiO_2, Hexanes/AcOEt 4:1) to obtain 6-bromo-2-pyridinecarbonitrile **(6)** (902 mg, 50%). Excess 2,6-dibromopyridine was recovered and cyanide containing solutions were treated with sodium hypochlorite.

^{1}H NMR: 7.75-7.67 (m, *4H*); ^{13}C NMR: 142.95, 139.00, 133.72, 132.06, 127.43, 115.76

6-bromo-2-[(*S*)-4,5-dihydro-4-isopropyl-1,3-oxazol-2-yl]pyridine (5)

Method A: cyclization of **(4)**

To a stirred suspension of NaH (946 mg, 39.40 mmol), Bu_4NI (290 mg, 0.78 mmol) and 18C6 (catalytic amount) in anhydrous THF (50 mL) at r.t., a solution of 6-bromo-*N*-[(*S*)-2-chloro-1-isopropylethyl]-2-pyridinecarboxamide **(4)** (2413 mg, 7.88 mmol) in THF (10 mL) was added *via* canula. Once **(4)** was consumed (SiO_2, Hexanes/AcOEt 1:1) the resulting suspension was filtered and the filtrate was concentrated to obtain an oil which was dissolved in AcOEt (50 mL). This solution was washed with brine (3x50 mL) and dried with $MgSO_4$. The solvent was distilled under vacuum to obtain 6-bromo-2-[(*S*)-4,5-dihydro-4-isopropyl-1,3-oxazol-2-yl]pyridine **(5)** (2000 mg, 90%).

Method B: "one-pot" method using $Zn(TfO)_2$

To a stirred suspension of $Zn(TfO)_2$ (795 mg, 2.19 mmol) in anhydrous toluene (20 mL), 6-bromo-2-pyridinecarbonitrile **(6)** (365 mg, 1.99 mmol) was added and the stirring continued at r.t. for 10 min. Then, a solution of (*S*)-valinol (233 mg, 2.19 mmol) in anhydrous toluene (10 mL) was added and the resulting solution was refluxed during 48h. After that, the solution was allowed to cool and AcOEt (30 mL) was added. The resulting solution was washed with brine (3x30 mL) and Na_2CO_3 5% (3x30 mL). The organic phase was dried with $MgSO_4$ and the solvent distilled under vacuum yielding 6-bromo-2-[(*S*)-4,5-dihydro-4-isopropyl-1,3-oxazol-2-yl]pyridine **(5)** (413 mg, 77%)

^{1}H NMR: 8.04 (dd, 1*H*, J= 2.1Hz, 6.7 Hz), 7.68-7.52 (m, *2H*), 4.51 (dt, *1H*, J=1.6 Hz, 7.6 Hz), 4.27-4.13 (m, *2H*), 1.88 (sp, *1H*, J=6.7 Hz), 1.04 (d, *3H*, J=6.7 Hz), 0.94 (d, *3H*, J=6.7 Hz); ^{13}C NMR: 162.2, 147.2, 146.3, 133.5, 122.6, 120.5, 72.8, 70.9, 32.9, 19.1, 18.3

6-vinyl-2-pyridinecarbonitrile (7)

To a stirred solution of 6-bromo-2-pyridinecarbonitrile **(6)** (444 mg, 2.44 mmol) and palladiumdichlorobis(triphenylphosphine) (85.5 mg, 0.12 mmol) in anhydrous toluene, tributyvinyltin (0.86 mL, 2.93 mmol) was added and then it was refluxed during 70 min when it became black. The resulting mixture was then allowed to cool, filtered through a Celite pad and the volatiles were removed under vacuum. The resulting oil was redisolved in acetonitrile (25 mL) and washed with hexanes

(9x12 mL). The acetonitrile phase was evaporated to obtain an oil which was purified by column chromatography (SiO_2, Hexanes/AcOEt 2:1) to obtain 6-vinyl-2-pyridinecarbonitrile **(7)** (248 mg, 78%) as a yellow oil.

^{1}H NMR: 7.79 (t, *1H*, J= 7.9 Hz), 7.57-7.51 (m, *2H*), 6.81 (dd, *1H*, J=10.8 Hz, 17.5 Hz), 6.33 (d, *1H*, J= 17.5 Hz), 5.63 (d, *1H*, J= 11.0 Hz); ^{13}C NMR: 156.9, 137.0, 134.8, 133.3, 126.6, 126.5, 123.9, 120.9

2-(4-bromophenoxy)-6-pyridinecarbonitrile (10)

To a stirred solution of *p*-bromophenol (584 mg, 3.38 mmol) and potassium carbonate (466 mg, 3.38 mmol) in anhydrous DMF (1.0 mL) at r.t., 6-bromo-2-pyridinecarbonitrile **(7)** (455 mg, 2.50 mmol) was added. The solution was stirred at 100ºC during 20h and then allowed to cool. The resulting oily solid was dissolved with AcOEt (20 mL) and washed with brine (20 mL) and KOH 2% vol (4x25 mL). The organic phase was dried with $MgSO_4$ and the solvent was distilled under reduced pressure to obtain a solid which was purified by column chromatography (SiO_2, DCM) to obtain 2-(4-bromophenoxy)-6-pyridinecarbonitrile **(10)** as a solid (575 mg, 83%)

^{1}H NMR: 7.81 (dd, *1H*, J= 7.3 Hz, 8.4 Hz), 7.52 (d, *2H*, J= 9.0), 7.42 (dd, *1H*, J= 0.8 Hz, 7.3 Hz), 7.16 (dd, *1H*, J= 0.8 Hz, 8.4 Hz), 7.04 (d, *2H*, J=9.0Hz); ^{13}C NMR: 151.9, 140.5, 140.0, 133.0, 132.5, 124.1, 123.6, 123.4, 122.9, 118.1, 116.5, 116.0

6-(4-vinylphenoxy)-2-pyridinecarbonitrile (11)

To a stirred solution of 2-(4-bromophenoxy)-6-pyridinecarbonitrile **(10)** (257 mg, 0.93 mmol) and palladiumdichlorobis(triphenylphosphine) (32.7 mg, 0.05 mmol) in anhydrous toluene (20 mL), tributylvinyltin (0.41 mL, 1.40 mmol) was added. The resulting mixture was refluxed during 5 h. The subsequent solution was allowed to cool, then filtered through a Celite pad and the volatiles were removed under vacuum. The resulting oil was redisolved in acetronitrile (20 mL) and washed with hexanes (9x10 mL). The acetonitrile phase was evaporated to obtain 6-(4-vinylphenoxy)-2-pyridinecarbonitrile **(11)** (182 mg, 88%).

^{1}H NMR: 7.79 (dd, *1H*, J= 7.3 Hz, 8.4 Hz), 7.48-7.38 (m, *3H*), 7.16-7.08 (m, *3H*), 6.72 (dd, *1H*, J= 10.9 Hz, 17.6 Hz), 5.72 (dd, *1H*, J= 1.0 Hz, 17.6 Hz), 5.26 (dd, *1H*, J= 1.0 Hz, 10.8 Hz);^{13}C NMR: 163.6, 152.4, 140.1, 135.8, 134.9, 131.0, 127.5, 123.6, 121.3, 116.7, 116.0, 113.9

2-[(*S*)-4,5-dihydro-4-isopropyl-1,3-oxazol-2-yl]-6-vinylpyridine (1a)

Method A: Starting from 6-bromo-2-[(S)-4,5-dihydro-4-isopropyl-1,3-oxazol-2-yl]pyridine **(5)**

To a stirred solution of 6-bromo-2-[(S)-4,5-dihydro-4-isopropyl-1,3-oxazol-2-yl]pyridine **(5)** (404 mg, 1.50 mmol) in toluene (25 mL), palladiumdichlorobis(triphenylphosphine) (52 mg, 0.075 mmol) and tributylvinyltin (0.55 mL, 1.88 mmol) were added. The solution was then refluxed during 3 h and allowed to cool. The resulting black solution was filtered through a pad of celite and concentrated by rotary distillation. The resulting oil was then dissolved in acetonitrile (20 mL) and washed with hexanes (9x10 mL). The acetonitrile phase was concentrated and the resulting oil was purified by column chromatography (Al_2O_3, Hexanes/AcOEt 4:1) obtaining 2-[(*S*)-4,5-dihydro-4-isopropyl-1,3-oxazol-2-yl]-6-vinylpyridine **(1a)** (135 mg, 41%) as a yellowish oil.

Method B: Starting from 6-vinyl-2-pyridinecarbonitrile **(7)**

To a stirred solution of $Zn(TfO)_2$ (761 mg, 2.06 mmol) and 6-vinyl-2-pyridinecarbonitrile **(7)** (248 mg, 1.91 mmol) in anhydrous toluene (20 mL), (*S*)-valinol (196 mg, 1.91 mmol) was added. The resulting mixture was refluxed during 48 h and then allowed to cool. AcOEt (20 mL) was added and the resulting solution was washed with brine (3x30 mL) and Na_2CO_3 5% (3x30 mL). The organic phases were collected, dried with $MgSO_4$ and the solvent was evaporated under vacuum. obtaining 2-[(*S*)-4,5-dihydro-4-isopropyl-1,3-oxazol-2-yl]-6-vinylpyridine **(1a)** (345 mg, 83%) as an oil

^{1}H NMR: 7.96 (dd, *1H*, J= 1.1 Hz, 7.7 Hz), 7.73 (t, *1H*, J=7.8 Hz), 7.53 (dd, *1H*, J= 1.1 Hz, 7.86 Hz), 6.94 (dd, *1H*, J= 10.9 Hz, 17.7 Hz), 6.16 (dd, *1H*, J= 0.9 Hz, 17.7 Hz), 5.54 (dd, *1H*, J= 0.9 Hz, 10.9 Hz), 4.52 (td, *1H*, J= 7.8 Hz, 1.5 Hz), 4.27-4.09 (m, *2H*), 1.98-1.92 (m, *1H*), 1.06 (d, *3H*, J= 6.7 Hz), 0.94 (d, *3H*, J= 6.7 Hz); ^{13}C NMR: 162.5, 156.1, 146.6, 136.9, 136.8, 122.7, 122.0, 119.0, 72.9, 70.8, 32.8, 19.2, 18.2

IR (cm^{-1}): 2959, 2897, 1642, 1580, , 1456, 1361

M+H: 217

2-[(*S*)-4,5-dihydro-4-*tert*-butyl-1,3-oxazol-2-yl]-6-vinylpyridine (1b)

To a stirred solution of $Zn(TfO)_2$ (635 mg, 1.75 mmol) and 6-vinyl-2-pyridinecarbonitrile **(7)** (207 mg, 1.60 mmol) in anhydrous toluene (20 mL), (*S*)-*tert*-leucinol (204 mg, 1.75 mmol) was added. The resulting mixture was refluxed during 72 h and then allowed to cool. AcOEt (20 mL) was added and the resulting solution was washed with brine (3x30 mL) and Na_2CO_3 5% (3x30 mL). The organic phases were collected, dried with $MgSO_4$ and the solvent was evaporated under vacuum. The oil obtained was purified by column chromatography (Al_2O_3) to obtain 2-[(*S*)-4,5-dihydro-4-*tert*-butyl-1,3-oxazol-2-yl]-6-vinylpyridine **(1b)** (290 mg, 78%) as an oil

^{1}H NMR: 7.99 (dd, *1H*, J= 0.9 Hz, 7.7 Hz), 7.70 (t, *1H*, J=7.8 Hz), 7.50 (dd, *1H*, J= 0.7 Hz, 7.9 Hz), 6.91 (dd, *1H*, J= 10.9 Hz, 17.7 Hz), 6.14 (d, *1H*, J=17.6 Hz, 10.9 Hz), 4.45 (dd, *1H*, J= 8.8 Hz, 10.3 Hz), 4.31 (t, *1H*, J= 8.4 Hz), 4.09 (dd, *1H*, J= 8.1 Hz, 10.4 Hz), 0.96 (s, *9H*); ^{13}C NMR: 162.7, 155.8, 146.4, 136.7, 122.6, 121.8, 119.0, 118.9, 76.1, 69.2, 33.9, 25.8

IR (cm^{-1}): 2955, 2903, 2869, 1696, 1645, 1566, 1581, 1456, 153

M+H= 231

2-[(*S*)-4,5-dihydro-4-*tert*-butyl-1,3-oxazol-2-yl]-6-(4-vinylphenoxy)pyridine (12)

To a stirred solution of $Zn(TfO)_2$ (299 mg, 0.82 mmol) and 6-cyano-2-(4-vinylphenoxy)pyridine **(11)** (166 mg, 0.74 mmol) in anhydrous toluene (20 mL), (*S*)-*tert*-leucinol (96 mg, 0.82 mmol) was added. The resulting mixture was refluxed during 72 h and then allowed to cool. AcOEt (20 mL) was added and the resulting solution was washed with brine (3x30 mL) and $NaHCO_3$ 5% (3x30 mL). The organic phases were collected, dried with $MgSO_4$ and the solvent was evaporated under vacuum. The oil obtained was purified by column chromatography (Al_2O_3,) to obtain 2-[(*S*)-4,5-dihydro-4-*tert*-butyl-1,3-oxazol-2-yl]-6-(4-vinylphenoxy)pyridine **(12)** (200 mg, 87%) as an oil.

^{1}H NMR: 7.86 (dd, *1H*, J= 0.9 Hz, 7.5 Hz), 7.73 (t, *1H*, J= 7.8Hz), 7.43 (d, *2H,* J= 8.7 Hz), 7.12 (d, *2H*, J= 8.6 Hz*), 6.*86 (dd, *1H*, J= 0.9, 8.1 Hz), 6.72 (dd, *1H,* J= 11.0 Hz, 17.4 Hz), 5.70 (dd, *1H*, J= 0.8, 17.6 Hz), 5.24 (dd, *1H*, J= 0.8, 10.9 Hz), 4.46 (dd, *1H*, J= 8.5 Hz, 10.4 Hz), 4.31 (t, *1H*, J= 8.4 Hz), 4.11 (dd, *1H*, J= 8.1 Hz, 10.3 Hz), 0.97 (s, *9H*). ^{13}C NMR: 163.2, 162.2, 153.9, 145.7, 140.0, 136.0, 134.3,

127.7, 120.7, 119.2, 113.6, 112.9, 76.5, 69.4, 34.2, 26.1.

IR (cm^{-1}): 2956, 1930, 2868, 1644, 1573, 1504, 1478, 1449, 1433, 1360, 1240, 983

M+H=323

2. Synthesis of polymeric *pyox* ligands

Poymeric materials were prepared into a glass tube. Typically, a solution of vinyl-*pyox*, styrene and divinylbenzene (80 % weight), toluene and AIBN were weighed and purged in the glass tube with N_2 during 3 min.. The glass tube was sealed and placed in a vertical position into an oil bath for 24 h at 80ºC while polymerization proceeded. The glass tube was broken and the polymer was washed with THF by soxhlet extraction during 24 h.

The composition for the different polymeric materials are given in the following table:

Supported *pyox*	ligand (mg)	VB (mg)	% DVB (mg)	Toluene (mg)	AIBN (mg)
PS-DVB-1a	**1a** (46.0)	135.4	203.6	568.5	5.4
PS-DVB-1b	**1b** (48.0)	132.8	201.4	571.5	6.4
PS-DVB-12	**12** (66.0)	134.7	204.2	601.0	6.9

3. Preparation of mini-flow reactors

Monoliths were prepared into a stainless steel column (15 cm x ¼ in.). Typically, a solution of *vinylpyox*, styrene and divinylbenzene (80 % weight), toluene, 1-dodecanol and AIBN were purged with N_2 during 3 min. and poured into the mould. The stainless steel tubular mould was sealed at the two ends and placed in a vertical position into an oil bath for 24 h at 70ºC while polymerization proceeded. The mould was properly washed and the seals removed, the tube was provided with fittings, attached to a high-pressure pump and THF first and MeOH later were pumped to remove the porogenic solvents and any other soluble impurity.

reactor	ligand (mg)[a]	VB (mg)	%DVB (mg)	toluene (mg)	1-dodecanol (mg)	AIBN (mg)
Mf-R1	**1a** (59.2)	169.2	258.9	131.3	637.4	4.7
Mf-R2	**1b** (92.0)	386.0	233.0	171.0	864.0	7.0
Mf-R3	**1b** (64.0)	207.3	281.0	124.1	281.0	5.1

4. Continuous Flow catalytic cyclopropanation.

The former monoliths were activated by passing a solution of $Cu(TfO)_2$ in MeOH. The flow of solution was dependent on the back pressure generated by the column.

reactor	Mmol $Cu(TfO)_2$	mL MeOH	Flow mL/min	Time (h)
Mf-R1	0.52	10	0.10	6
Mf-R2	0.56	10	0.10	6
Mf-R3	0.53	10	0.05	6

Yields and *ee* data were obtained by GC analyzing the out-stream of the reactor. The major enantiomer for the *cis* pair is 1*R*,2*S*. The major enantiomer for the *trans* pair was 1*R*,2*R*. Times are expressed in minutes, considering t=0 the moment in which a solution of EDA and Styrene are first pumped.

Using DCM as solvent

General

A solution of [EDA] =0.50M, [styrene] = 1.50M and [n-decane] = 0.12M in DCM was pumped through the reactor. The first measurements were taken once the observed yields were stable.

Mf-R1-Cu

Time (min)	Yield (%)	ChemSel (%)	c/t	ee cis	ee trans	Flow (mL/min)
210	49	71	49:51	41	35	0.02
242	51	69	49:51	41	35	0.02
376	51	66	49:51	39	49	0.02
454	49	64	49:51	39	44	0.02
540	48	63	49:51	38	40	0.02

Results for the single pass experiments before recirculation run.

Mf-R2-Cu

Time (min)	Yield (%)	ChemSel (%)	c/t	ee cis	ee trans	Flow (mL/min)
90	8	60	41:59	59	53	0.03
120	20	65	46:54	59	53	0.03
150	26	62	45:55	59	53	0.03
180	26	60	44:56	58	53	0.03
210	24	58	45:55	57	54	0.03
270	28	59	45:55	59	57	0.02
305	33	60	45:55	61	57	0.02
366	26	62	46:54	61	56	0.02
420	28	60	45:55	60	59	0.02
480	31	61	45:55	61	58	0.02
510	34	63	45:55	61	58	0.02
720	18	55	43:57	61	57	0.02
750	21	56	43:57	61	56	0.02
890	22	55	44:56	60	57	0.02
930	23	57	42:58	61	57	0.02
1020	23	56	43:57	60	56	0.02

Using $ScCO_2$ as solvent

General

The reaction was performed at 40°C and 8 MPa by passing through the catalytic bed an organic flow (mixture of styrene/EDA, molar ratio = 3, and n-decane as internal standard, thus [EDA] =2.05M, [styrene] = 6.15M and [n-decane] = 0.41M) mixed with a stream of CO2 accounting the organic stream for a 10% of the total flow.

Mf-R1-Cu

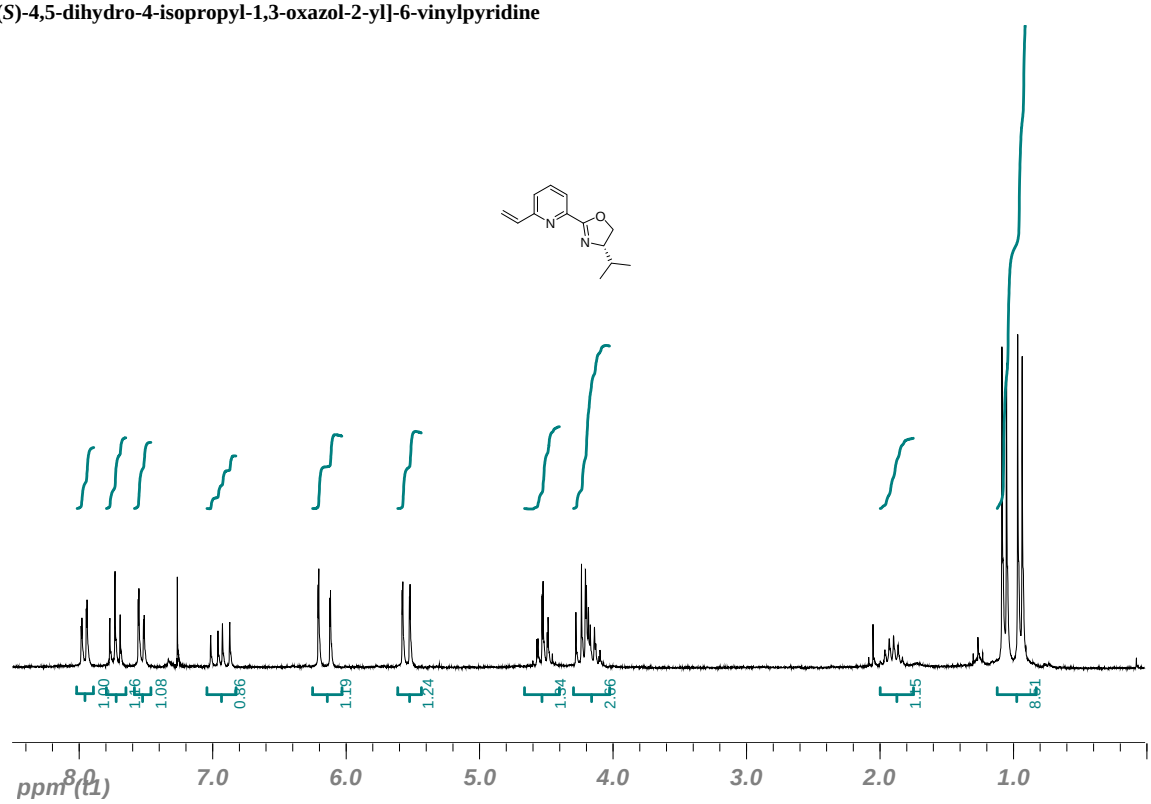
Time (min)	Yield (%)	ChemSel (%)	c/t	ee cis	ee trans	Organic Flow (mL/min)
90	34	64	47:53	39	39	0.05
120	45	59	48:52	40	39	0.05
150	45	59	48:52	39	36	0.05
165	41	56	47:53	37	36	0.05
190	41	57	47:53	37	34	0.05
220	47	59	48:52	38	34	0.02
240	46	58	48:52	37	35	0.02
270	42	58	47:53	37	30	0.02
300	33	57	45:55	32	25	0.02
330	35	57	45:55	32	25	0.02
350	36	57	45:55	33	27	0.02
410	45	59	48:52	33	30	0.02
440	25	57	47:53	39	32	0.05
470	24	52	46:54	36	36	0.05

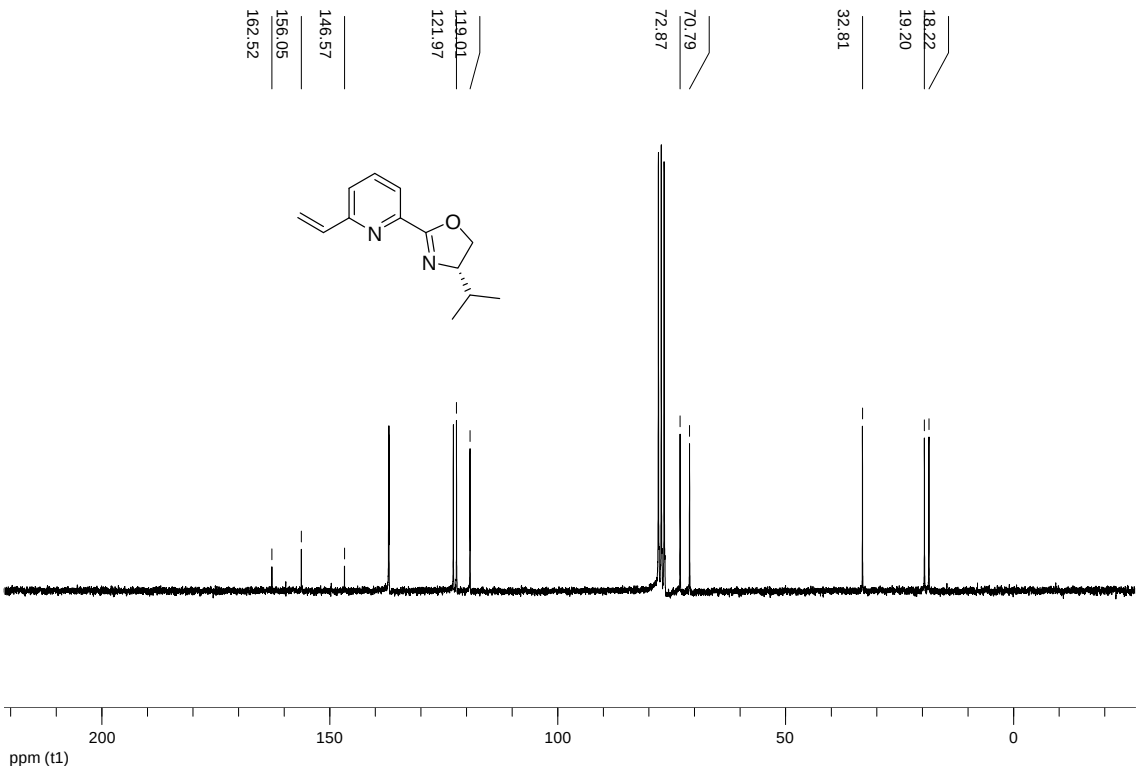
Mf-R3-Cu

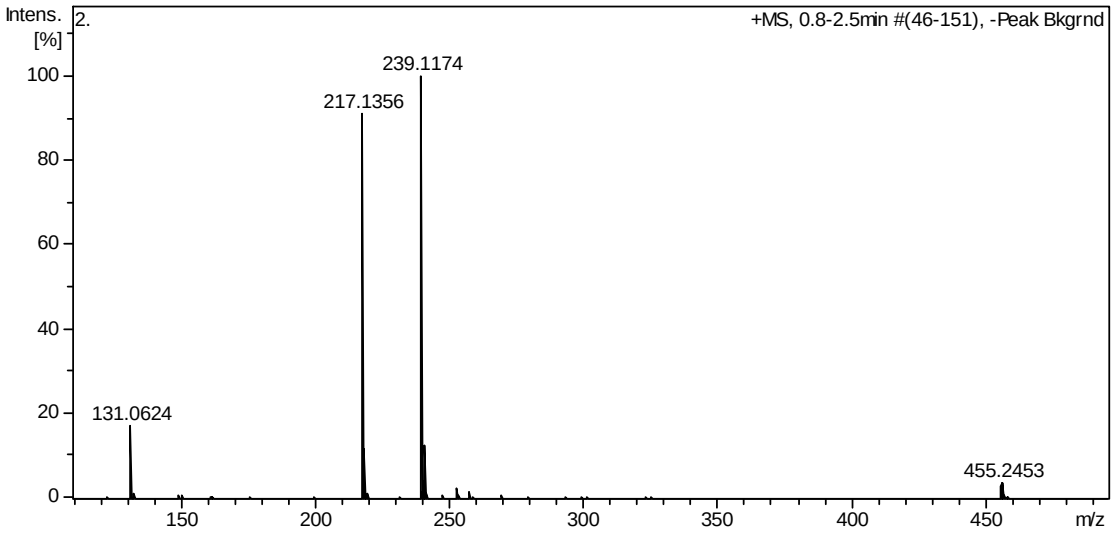
Time (min)	Yield (%)	ChemSel (%)	c/t	ee cis	ee trans	Organic Flow (mL/min)
237	39	59	44:56	nm	nm	0.02
252	47	61	46:54	57	55	0.02
272	49	61	46:54	54	54	0.02
294	49	61	47:53	54	52	0.02
317	48	61	47:53	54	49	0.02
337	49	61	47:53	54	53	0.0175
372	48	61	47:53	53	53	0.015
392	48	61	47:53	52	50	0.015
422	48	61	47:53	52	51	0.015
452	48	60	47:53	51	49	0.015
477	48	61	46:54	52	49	0.015
507	48	60	47:53	51	51	0.015
627	36	75	47:53	nm	nm	0.015
657	41	66	43:57	58	52	0.015
677	45	65	44:56	55	55	0.015
697	47	63	45:55	55	53	0.015
717	47	60	46:54	52	49	0.015
747	45	59	46:54	51	47	0.015
777	42	58	46:54	49	44	0.015
807	37	56	45:55	45	43	0.015
837	30	55	44:56	43	44	0.015
867	24	53	43:57	37	31	0.015
897	21	53	43:57	36	29	0.0125
927	20	49	43:57	nm	nm	0.01

5. NMR spectra and MS

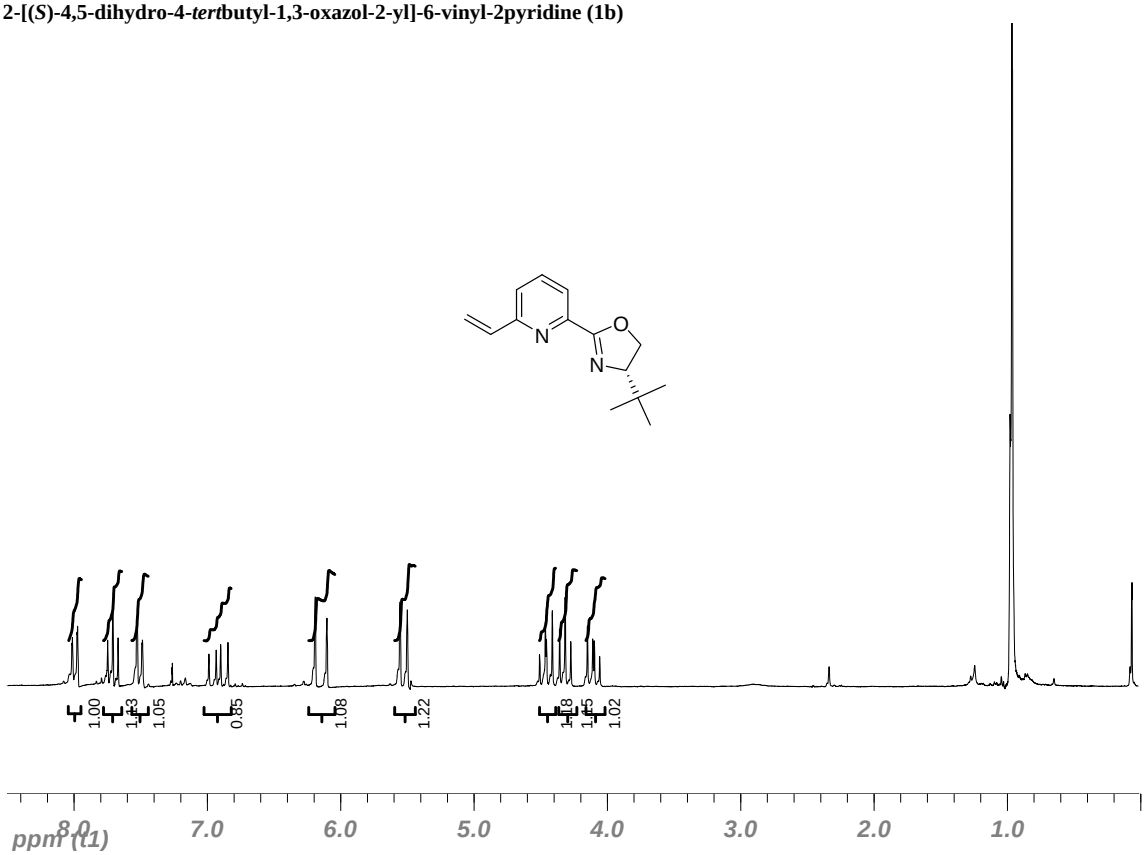
2-[(*S*)-4,5-dihydro-4-isopropyl-1,3-oxazol-2-yl]-6-vinylpyridine

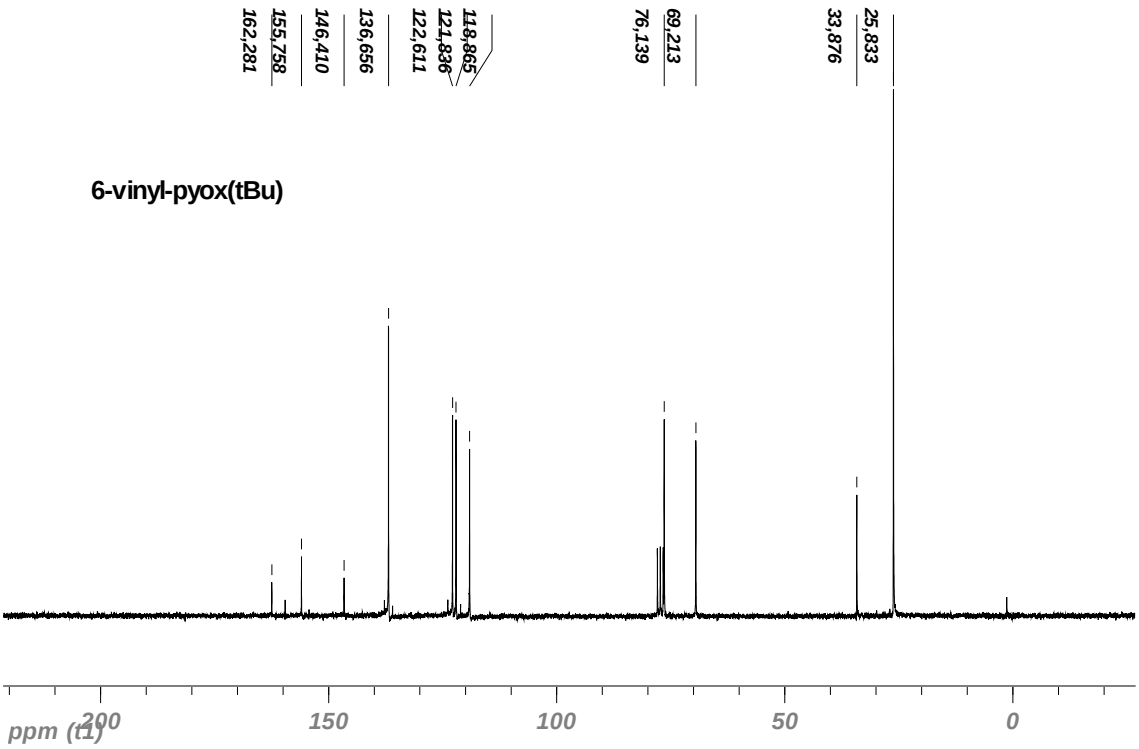


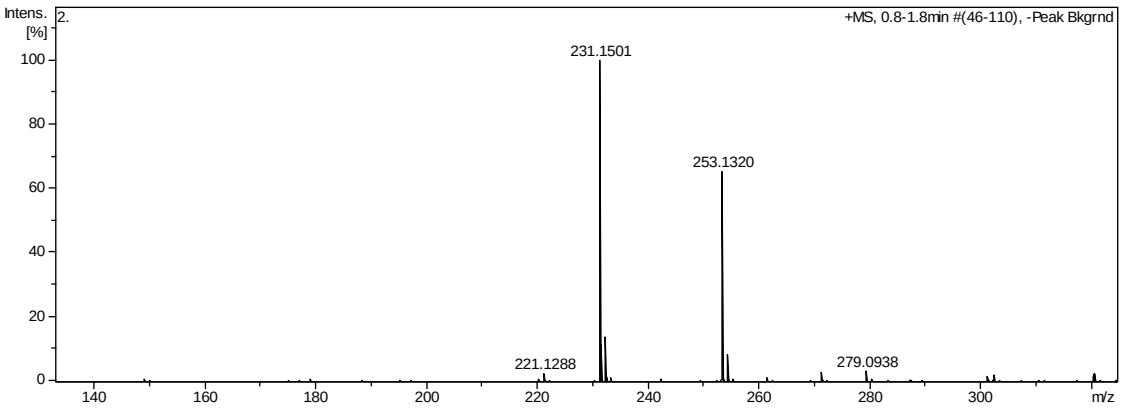




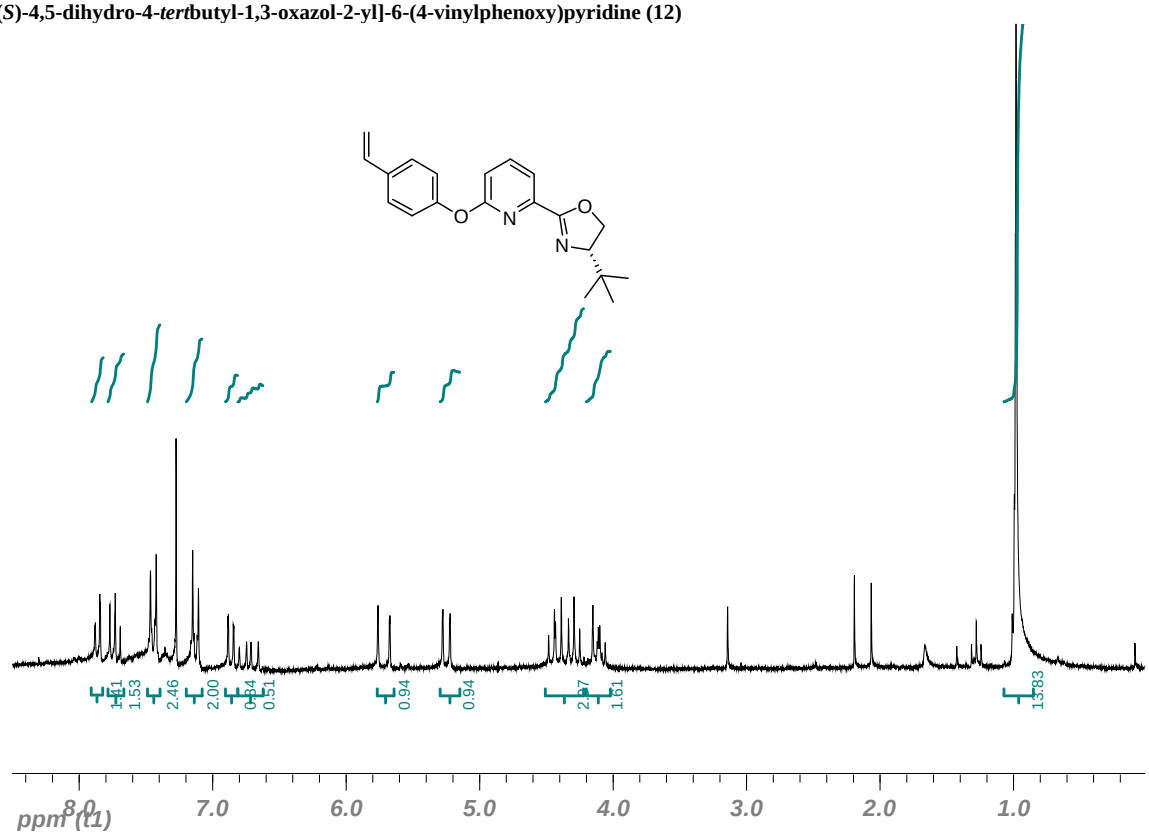
2-[(*S*)-4,5-dihydro-4-*tert*butyl-1,3-oxazol-2-yl]-6-vinyl-2pyridine (1b)

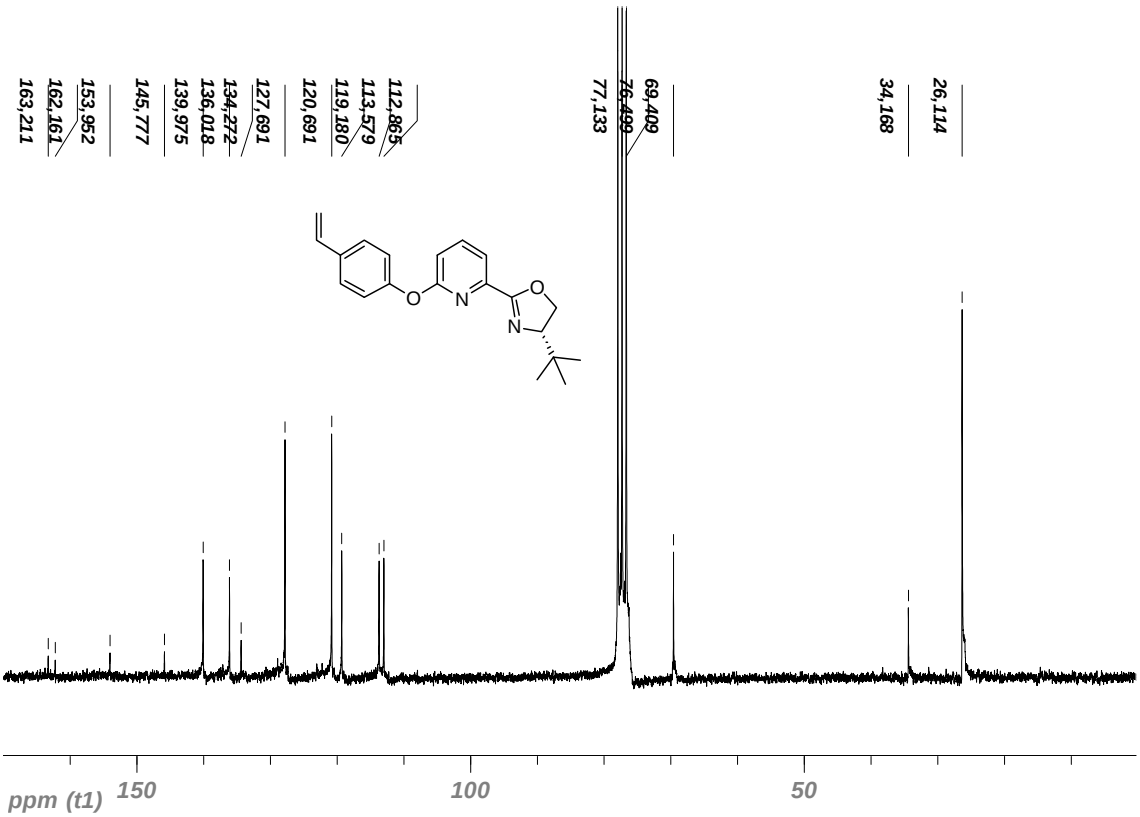


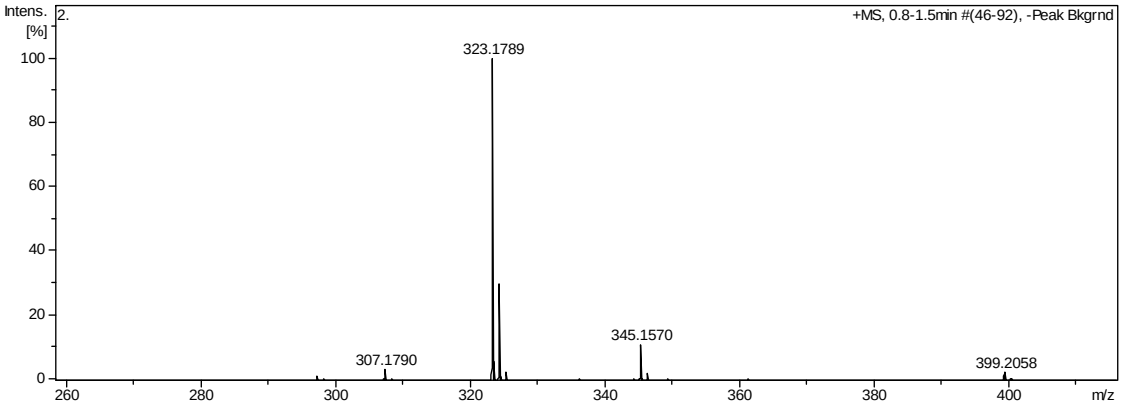

162,281
155,758
146,410
136,656
122,611
121,836
118,865
76,139
69,213
33,876
25,833
6-vinyl-pyox(tBu)
200
150
100
50
0
ppm (t1)


Intens.
[%]
2.
+MS, 0.8-1.8min #(46-110), -Peak Bkgrnd
231.1501
253.1320
221.1288
279.0938
100
80
60
40
20
0
140
160
180
200
220
240
260
280
300
m/z

2-[(*S*)-4,5-dihydro-4-*tert*butyl-1,3-oxazol-2-yl]-6-(4-vinylphenoxy)pyridine (12)






Intens.
[%]
2.
+MS, 0.8-1.5min #(46-92), -Peak Bkgrnd
323.1789
345.1570
307.1790
399.2058
100
80
60
40
20
0
260
280
300
320
340
360
380
400
m/z