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Enantioselective synthesis of chiral oxazolines from unactivated ketones and isocyanoacetate esters by synergistic silver/organocatalysis

Pablo Martínez-Pardo,[a] Gonzalo Blay,*[,a] M. Carmen Muñoz,[b] José R. Pedro,*[,a] Amparo Sanz-Marco,[a] and Carlos Vila

[a] Departament de Química Orgànica, Facultat de Química, Universitat de València, 46100-Burjassot, València, Spain.

[b] Departament de Física Aplicada, Universitat Politècnica de València, 46022-València 46022.

SUPPORTING INFORMATION

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General Experimental Methods

Formal [3+2] cycloaddition reactions were carried out in round bottom flasks closed with a stopper. Starting materials, including ketones and *t*-butyl isocyanoacetate were obtained from commercial sources. Methyl *tert*-Butyl ether (MTBE) was stored over 4 Å MS. Reactions were monitored by TLC analysis using Merck Silica Gel 60 F-254 thin layer plates. Flash column chromatography was performed on Merck silica gel 60, 0.040-0.063 mm. Melting points were determined in capillary tubes. NMR spectra were run at 300 MHz for ^{1}H and at 75 MHz for ^{13}C NMR using residual non-deuterated solvent ($CHCl_3$) as internal standard (δ 7.26 and 77.0 ppm, respectively). Chemical shifts are given in ppm. The carbon type was determined by DEPT experiments. High resolution mass spectra (ESI) were recorded on a Q-TOF spectrometer equipped with an electrospray source with a capillary voltage of 3.3 kV (ESI). Specific optical rotations were measured using sodium light (D line 589 nm). Chiral HPLC analyses were performed in a chromatograph equipped with a UV diode-array detector using chiral stationary phase columns from Daicel or Phenomenex.

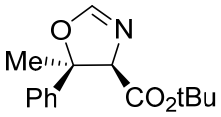
Typical procedures and characterization data for compounds 3

General procedure for the enantioselective formal [3+2] cycloaddition reaction

Squaramide **SQ4** (6.6 mg, 0.0125 mmol) and silver oxide (1.5 mg, 0.0063 mmol) were introduced in 25 mL round bottom flask followed by MTBE (8 mL) and ketone **1** (0.25 mmol). The flask was closed with a stopper and introduced in an ice bath. After 5 min, *tert*-butyl isocyanoacetate **2** (48 μL, 0.330 mmol) was added and the mixture was stirred at 0 °C until consumption of the ketone **1** (TLC). After this time, the reaction mixture was filtered through a short pad of silica gel and concentrated under reduced pressure. A small aliquot was analyzed by ^{1}H NMR to determine the diastereomer ratio and by HPLC to determine the enantiomeric excess of products **3**. The remaining crude was chromatographed on silica gel eluting with hexane:EtOAc mixtures (9:1 to 8:2) to obtain the separated diastereomers *cis*-**3** and *trans*-**3**.

The racemic products were obtained by a similar procedure using *N*-[3,5-bis(trifluoromethyl)phenyl]-*N*'-(3-dimethylaminopropyl)squaramide as a substitutive for **SQ4**.

***tert*-Butyl 5-methyl-5-phenyl-4,5-dihydrooxazole-4-carboxylate (3a)**

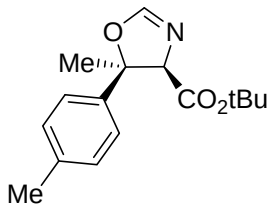


Obtained 61.8 mg (95%). The enantiomeric excess (minor isomer: 91%, major isomer: 99%) was determined by HPLC (Lux Cellulose 4), hexane:*i*PrOH 95:5, 1 mL/min, ***trans*-(4*R*,5*S*)-3a (minor diastereomer)**: minor enantiomer, t_r = 15.5 min, major enantiomer, t_r = 22.1 min; ***cis*-(4*R*,5*R*)-3a (major diastereomer)**: minor enantiomer, t_r = 20.4 min, major enantiomer, t_r = 30.5 min.

***cis*-(4*R*,5*R*)-3a (major diastereomer)**: R_f = 0.18 (7:3 hexane/EtOAc); colorless oil; $[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\mathbf{25}}$ –174.3 (*c* 0.65, $CHCl_3$, 99% *ee*); **^{1}H NMR** ($CDCl_3$, 300 MHz) δ 7.32-7.27 (5H, m, Ar), 7.15 (1H, d, *J* = 2.1 Hz, N=CHO), 4.49 (1H, d, *J* = 2.1 Hz, CH), 1.80 (3H, s, CH_3), 0.97 (9H, s, CH_3); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 167.5 (C), 156.0 (CH), 139.6 (C), 128.0 (CH), 127.9 (CH), 125.8 (CH), 88.3 (C), 81.4 (C), 78.7 (CH), 28.6 (CH_3), 27.1 (CH_3); HRMS (ESI) *m/z*: 262.1434 $[M+H]^+$, $C_{15}H_{20}NO_3^+$ requires 262.1438.

***trans*-(4*R*,5*S*)-3a (minor diastereomer)**: R_f = 0.28 (7:3 hexane/EtOAc); colorless oil; $[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\mathbf{25}}$ –98.4 (*c* 0.72, $CHCl_3$, 91% *ee*), Lit.[1] $[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\mathbf{25}}$ –72.6 (*c* 1.0, $CHCl_3$, 88% *ee*); **^{1}H NMR** ($CDCl_3$, 300 MHz) δ 7.48-7.46 (2H, m, Ar), 7.41-7.32 (2H, m, Ar), 7.30-7.27 (1H, m, Ar), 7.08 (1H, d, *J* = 2.1 Hz, N=CHO), 4.70 (1H, d, *J* = 2.1 Hz, CH), 1.66 (3H, s, CH_3), 1.56 (9H, s, CH_3); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 168.5 (C), 155.3 (CH), 145.3 (C), 128.6 (CH), 127.7 (CH), 124.0 (CH), 87.8 (C), 82.5 (C), 77.9 (CH), 28.0 (CH_3), 24.7 (CH_3).

***tert*-Butyl 5-methyl-5-(*p*-tolyl)-4,5-dihydrooxazole-4-carboxylate (3b)**

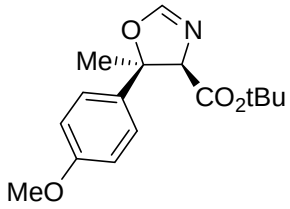


Obtained 54.6 mg (79%) The enantiomeric excess (minor isomer: 90%, *major* isomer 99%) was determined by HPLC (Chiracel IC), hexane:*i*PrOH 90:10, 1 mL/min, ***trans*-(4*R*,5*S*)-3b (minor diastereomer)**: minor enantiomer, t_r = 20.5 min, major enantiomer, t_r = 26.0 min. ***cis*-(4*R*,5*R*)-3b (major diastereomer)**: minor enantiomer, t_r = 24.7 min, major enantiomer, t_r = 28.2 min.

***cis*-(4*R*,5*R*)-3b (major diastereomer)**: R_f = 0.18 (7:3 hexane/EtOAc); white solid, m.p. 57-59 °C; $[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\mathbf{25}}$ –100.8 (*c* 1.86, $CHCl_3$, 99% *ee*); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.21 (2H, d, *J* = 8.4 Hz, Ar), 7.15 (1H, d, *J* = 1.8 Hz, N=CHO), 7.11 (2H, d, *J* = 8.1 Hz, Ar), 4.47 (1H, d, *J* = 1.8 Hz, CH), 2.3 (3H, s, CH_3), 1.78 (3H, s, CH_3), 0.98 (9H, s, CH_3); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 167.6 (C), 156.1 (CH), 137.6 (C), 136.6 (C), 128.6 (CH), 125.8 (CH), 88.3 (C), 81.4 (C), 78.7 (CH), 28.5 (CH_3), 27.1 (CH_3), 20.9 (CH_3); HRMS (ESI) *m/z*: 276.1593 $[M+H]^+$, $C_{16}H_{22}NO_3^+$ requires 276.1594.

***trans*-(4*R*,5*S*)-3b (minor diastereomer)**: R_f = 0.25 (7:3 hexane/EtOAc); colorless oil; $[\alpha]_D^{25}$ –194.5 (*c* 0.37, $CHCl_3$, 90% *ee*); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.35 (2H, d, *J* = 8.1 Hz, Ar), 7.18 (2H, d, *J* = 8.1 Hz, Ar), 7.07 (1H, d, *J* = 2.1 Hz, N=CHO), 4.68 (1H, d, *J* = 2.1 Hz, CH), 2.35 (3H, s, CH_3), 1.64 (3H, s, CH_3), 1.55 (9H, s, CH_3); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 168.6 (C), 155.4 (CH), 142.4 (C), 137.5 (C), 129.3 (CH), 124.0 (CH), 87.8 (C), 82.4 (C), 77.9 (CH), 28.0 (CH_3), 24.6 (CH_3), 21.0 (CH_3); HRMS (ESI) *m/z*: 276.1593 $[M+H]^+$, $C_{16}H_{22}NO_3^+$ requires 276.1594.

***tert*-Butyl 5-(4-methoxyphenyl)-5-methyl-4,5-dihydrooxazole-4-carboxylate (3c)**

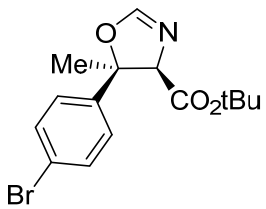


Obtained 51.1 mg (70%). The enantiomeric excess (minor isomer: 90%, major isomer: 98%) was determined by HPLC using a chiral column (Lux Cellulose 4), hexane:*i*PrOH 90:10, 1 mL/min, ***trans*-(4*R*,5*S*)-3c (minor diastereomer)**: minor enantiomer, t_r = 18.3 min, major enantiomer, t_r = 21.8 min. ***cis*-(4*R*,5*R*)-3c (major diastereomer)**: minor enantiomer, t_r = 19.9 min, major enantiomer, t_r = 22.8 min.

***cis*-(4*R*,5*R*)-3c (major diastereomer)**: R_f = 0.18 (7:3 hexane/EtOAc); white solid, m.p. 68-69 °C; $[\alpha]_D^{25}$ –146.9 (*c* 1.3, $CHCl_3$, 98% *ee*); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.27 (2H, d, *J* = 9 Hz, Ar), 7.18 (1H, d, *J* = 1.8 Hz, N=CHO), 6.88 (2H, d, *J* = 9 Hz, Ar), 4.50 (1H, d, *J* = 1.8 Hz, CH), 3.80 (3H, s, CH_3), 1.82 (3H, s, CH_3), 1.04 (9H, s, CH_3); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 167.6 (C), 159.3 (C), 156.0 (CH), 131.7 (C), 127.2 (CH), 113.4 (CH), 88.1 (C), 81.4 (C), 78.6 (CH), 55.3 (CH_3), 28.6 (CH_3), 27.3 (CH_3); HRMS (ESI) *m/z*: 292.1547 $[M+H]^+$, $C_{16}H_{22}NO_4^+$ requires 292.1543.

***trans*-(4*R*,5*S*)-3c (minor diastereomer)**: R_f = 0.25 (7:3 hexane/EtOAc); Colorless oil; $[\alpha]_D^{25}$ -159.9 (*c* 0.47, $CHCl_3$, 90% *ee*), Lit.[1] $[\alpha]_D^{25}$ -61.9 (*c* 0.8, $CHCl_3$, 88% *ee*); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.38 (2H, d, *J* = 9.0 Hz, Ar), 7.06 (1H, d, *J* = 1.8 Hz, N=CHO), 6.90 (2H, d, *J* = 9.0 Hz, Ar), 4.68 (1H, d, *J* = 2.1 Hz, CH), 3.81 (3H, s, CH_3), 1.64 (3H, s, CH_3), 1.55 (9H, s, CH_3); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 168.6 (C), 159.0 (C), 155.6 (CH), 137.4 (C), 125.4 (CH), 113.9 (CH), 87.7 (C), 82.4 (C), 80.0 (CH), 55.3 (CH_3), 28.0 (CH_3), 24.6 (CH_3).

***tert*-Butyl 5-(4-bromophenyl)-5-methyl-4,5-dihydrooxazole-4-carboxylate (3d)**



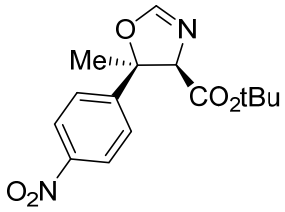
Obtained 89.7 mg (99%). The enantiomeric excess (major isomer: 98%, minor isomer: 93%) was determined by HPLC using a chiral column (Lux Cellulose 4), hexane:*i*PrOH 90:10, 1 mL/min, ***cis*-(4*R*,5*R*)-3d (major diastereomer)**: minor enantiomer, t_r = 10.8 min, major enantiomer, t_r = 11.5 min; ***trans*-**

(4*R*,5*S*)-3d (minor diastereomer): major enantiomer, t_r = 13.4 min, minor enantiomer, t_r = 16.9 min.

***cis*-(4*R*,5*R*)-3d (major diastereomer)**: R_f = 0.18 (7:3 hexane/EtOAc); white solid, m.p. 73-74 °C; $[\alpha]_D^{25}$ –98.9 (*c* 1.5, $CHCl_3$, 98% *ee*); **^{1}H NMR** (300 MHz, C_6D_6) δ 7.24 (2H, d, *J* = 9 Hz, Ar), 6.99 (2H, d, *J* = 9 Hz, Ar), 6.65 (1H, d, *J* = 1.8 Hz, N=CHO), 4.41 (1H, d, *J* = 1.8 Hz, CH), 1.26 (3H, s, CH_3), 0.93 (9H, s, CH_3); **^{13}C NMR** (75 MHz, C_6D_6) δ 167.4 (C), 155.5 (CH), 139.8 (C), 131.3 (CH), 128.2 (CH), 122.0 (C), 87.8 (C), 81.0 (C), 79.5 (CH), 28.5 (CH_3), 27.3 (CH_3). HRMS (ESI) *m/z*: 340.0542 $[M+H]^+$, $C_{15}H_{19}BrNO_3^+$ requires 340.0543.

***trans*-(4*R*,5*S*)-3d (minor diastereomer)**: R_f = 0.28 (7:3 hexane/EtOAc); Colorless oil; $[\alpha]_D^{25}$ –93.8 (*c* 0.89, $CHCl_3$, 93% *ee*), Lit.[1] $[\alpha]_D^{25}$ –102.0 (*c* 1.0, $CHCl_3$, 90% *ee*); **^{1}H NMR** (300 MHz, C_6D_6) δ 7.22 (2H, d, *J* = 9.0 Hz, Ar), 7.09 (2H, d, *J* = 9.0 Hz, Ar), 6.51 (1H, d, *J* = 2.1 Hz, N=CHO), 4.65 (1H, d, *J* = 2.1 Hz, CH), 1.50 (3H, s, CH_3), 1.30 (9H, s, CH_3); **^{13}C NMR** (75 MHz, C_6D_6) δ 168.3 (C), 154.7 (CH), 145.2 (C), 132.0 (CH), 126.3 (CH), 122.0 (C), 87.2 (C), 81.8 (C), 78.8 (CH), 27.9 (CH_3), 24.7 (CH_3).

***tert*-Butyl 5-methyl-5-(4-nitrophenyl)-4,5-dihydrooxazole-4-carboxylate (3e)**

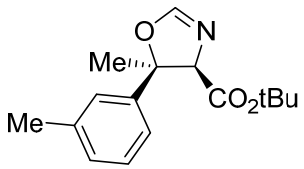


Obtained 76.4 mg (95%). The enantiomeric excess (minor isomer: 95%, *major* isomer 96%) was determined by HPLC (Chiracel IC), hexane:*i*PrOH 90:10, 1 mL/min, ***cis*-(4*R*,5*R*)-3e (major diastereomer)**: major enantiomer, t_r = 23.4 min, minor enantiomer, t_r = 26.9 min. ***trans*-(4*R*,5*S*)-3e (minor diastereomer)**: major enantiomer, t_r = 58.6 min, minor enantiomer, t_r = 83.3 min.

***cis*-(4*R*,5*R*)-3e (major diastereomer)**: R_f = 0.10 (7:3 hexane/EtOAc); white solid, m.p. 102-103 °C; $[\alpha]_D^{25}$ –257.1 (*c* 0.5, $CHCl_3$, 96% *ee*); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.20 (2H, d, *J* = 9.0 Hz, Ar), 7.54 (2H, d, *J* = 9.0 Hz, Ar), 7.18 (1H, d, *J* = 1.8 Hz, N=CHO), 4.57 (1H, d, *J* = 1.8 Hz, CH), 1.82 (3H, s, CH_3), 1.00 (9H, s, CH_3); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 167.0 (C), 155.8 (CH), 147.4 (C), 146.9 (C), 127.0 (CH), 123.2 (CH), 87.2 (C), 82.2 (C), 78.9 (CH), 28.7 (CH_3), 27.3 (CH_3); HRMS (ESI) *m/z*: 307.1285 $[M+H]^+$, $C_{15}H_{19}N_2O_5^+$ requires 307.1288.

***trans*-(4*R*,5*S*)-3e (minor diastereomer)**: R_f = 0.20 (7:3 hexane/EtOAc); colorless oil; $[\alpha]_D^{25}$ –60.3 (*c* 1.3, $CHCl_3$, 95% *ee*), Lit.[1] $[\alpha]_D^{25}$ –86.5 (*c* 1.0, $CHCl_3$, 90% *ee*); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.23 (2H, d, *J* = 9.0 Hz, Ar), 7.67 (2H, d, *J* = 9.0 Hz, Ar), 7.09 (1H, d, *J* = 2.1 Hz, N=CHO), 4.65 (1H, d, *J* = 2.1 Hz, CH), 1.67 (3H, s, CH_3), 1.57 (9H, s, CH_3); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 167.8 (C), 155.0 (CH), 152.1 (C), 147.4 (C), 125.3 (CH), 124.0 (CH), 87.2 (C), 83.2 (C), 77.7 (CH), 28.0 (CH_3), 24.7 (CH_3).

***tert*-Butyl 5-methyl-5-(*m*-tolyl)-4,5-dihydrooxazole-4-carboxylate (3f)**

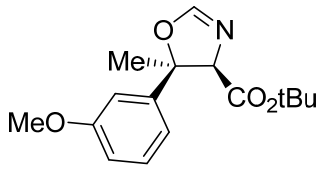


Obtained 60.8 mg (88%). The enantiomeric excess (minor isomer: 97%, *major* isomer 99%) was determined by HPLC (Lux Cellulose 4), hexane:*i*PrOH 90:10, 1 mL/min, ***trans*-(4*R*,5*S*)-3f (minor diastereomer)**: minor enantiomer, t_r = 8.9 min, major enantiomer, t_r = 12.4 min. ***cis*-(4*R*,5*R*)-3f (major diastereomer)**: minor enantiomer, t_r = 10.5 min, minor enantiomer, t_r = 14.2 min.

***cis*-(4*R*,5*R*)-3f (major diastereomer)**: R_f = 0.18 (7:3 hexane/EtOAc); white solid, m.p. 75-76 °C; $[\alpha]_D^{25}$ –155.9 (*c* 1.0, $CHCl_3$, 99% *ee*); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.26-7.14 (4H, m, Ar), 7.08-7.06 (1H, m, Ar), 4.48 (1H, d, *J* = 2.1 Hz, N=CHO), 2.33 (3H, s, CH_3), 1.79 (3H, s, CH_3), 0.99 (9H, s, CH_3); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 167.5 (C), 156.1 (CH), 139.5 (C), 137.5 (C), 128.5 (CH), 128.0 (CH), 126.5 (CH), 122.8 (CH), 88.3 (C), 81.3 (C), 78.7 (CH), 28.6 (CH_3), 27.1 (CH_3), 21.4 (CH_3); HRMS (ESI) *m/z*: 276.1594 $[M+H]^+$, $C_{16}H_{22}NO_3^+$ requires 276.1594.

***trans*-(4*R*,5*S*)-3f (minor diastereomer)**: R_f = 0.30 (7:3 hexane/EtOAc); colorless oil; $[\alpha]_D^{25}$ –92.5 (*c* 1.0, $CHCl_3$, 97% *ee*); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.28-7.26 (3H, m, Ar), 7.13-7.10 (1H, m, Ar), 7.07 (1H, d, *J* = 1.8 Hz, N=CHO), 4.69 (1H, d, *J* = 1.8 Hz, CH), 2.38 (3H, s, CH_3), 1.65 (3H, s, CH_3), 1.56 (9H, s, CH_3); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 168.6 (C), 155.3 (CH), 145.3 (C), 138.3 (C), 128.5 (CH), 128.4 (CH), 124.7 (CH), 121.0 (CH), 87.8 (C), 82.4 (C), 77.9 (CH), 28.0 (CH_3), 24.7 (CH_3), 21.2 (CH_3); HRMS (ESI) *m/z*: 276.1597 $[M+H]^+$, $C_{16}H_{22}NO_3^+$ requires 276.1594.

***tert*-Butyl 5-(3-methoxyphenyl)-5-methyl-4,5-dihydrooxazole-4-carboxylate (3g)**

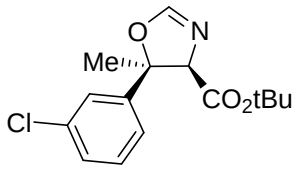


Obtained 43.3 mg (60%). The enantiomeric excess (minor isomer: 93%, *major* isomer 98%) was determined by HPLC (Lux Cellulose 4), hexane:*i*PrOH 90:10, 1 mL/min, ***trans*-(4*R*,5*S*)-3g (minor diastereomer)**: minor enantiomer, t_r = 13.2 min, major enantiomer, t_r = 19.1 min. ***cis*-(4*R*,5*R*)-3g (major diastereomer)**: minor enantiomer, t_r = 15.4 min, major enantiomer, t_r = 20.2 min.

***cis*-(4*R*,5*R*)-3g (major diastereomer)**: R_f = 0.18 (7:3 hexane/EtOAc); colorless oil; $[\alpha]_D^{25}$ –149.1 (*c* 1.0, $CHCl_3$, 99% *ee*); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.23 (1H, t, *J* = 8.1 Hz, Ar), 7.16 (1H, d, *J* = 1.8 Hz, CH), 6.91 (1H, d, *J* = 7.8 Hz, Ar), 6.88 (1H, m, Ar), 6.81 (1H, dd, *J* = 8.4, 2.1 Hz, Ar), 4.50 (1H, d, *J* = 1.8 Hz, N=CHO), 3.80 (3H, s, CH_3), 1.79 (3H, s, CH_3), 1.02 (9H, s, CH_3); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 167.5 (C), 159.3 (C), 156.1 (CH), 142.2 (C), 129.1 (CH), 118.2 (CH), 113.4 (CH), 111.8 (CH), 88.3 (C), 81.5 (C), 78.7 (CH), 55.3 (CH_3), 28.7 (CH_3), 27.2 (CH_3); HRMS (ESI) *m/z*: 292.1547 $[M+H]^+$, $C_{16}H_{22}NO_4^+$ requires 292.1543.

***trans*-(4*R*,5*S*)-3g (minor diastereomer)**: R_f = 0.25 (7:3 hexane/EtOAc); colorless oil; $[\alpha]_D^{25}$ –88.3 (*c* 0.63, $CHCl_3$, 91% *ee*); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.30 (1H, t, *J* = 8.1 Hz, Ar), 7.08-7.01 (3H, m, Ar), 6.83 (1H, dd, *J* = 7.8, 2.1 Hz, Ar), 4.70 (1H, d, *J* = 1.8 Hz, N=CHO), 3.82 (3H, s, CH_3), 1.65 (3H, s, CH_3), 1.56 (9H, s, CH_3); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 168.5 (C), 159.8 (C), 155.3 (CH), 147.0 (C), 129.8 (CH), 116.3 (CH), 112.9 (CH), 110.1 (CH), 87.7 (C), 82.5 (C), 77.8 (CH), 55.3 (CH_3), 28.1 (CH_3), 24.8 (CH_3); HRMS (ESI) *m/z*: 292.1546 $[M+H]^+$, $C_{16}H_{22}NO_4^+$ requires 292.1543.

***tert*-Butyl 5-(3-chlorophenyl)-5-methyl-4,5-dihydrooxazole-4-carboxylate (3h)**

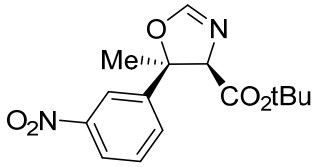


Obtained 55.8 mg (75%). The enantiomeric excess (minor isomer: 91%, *major* isomer 99%) was determined by HPLC (Chiracel IC), hexane:*i*PrOH 95:5, 1 mL/min, ***cis*-(4*R*,5*R*)-3h (major diastereomer)**: major enantiomer, t_r = 27.2 min, minor enantiomer, t_r = 29.2 min. ***trans*-(4*R*,5*S*)-3h (minor diastereomer)**: major enantiomer, t_r = 34.7 min, minor enantiomer, t_r = 39.7 min.

***cis*-(4*R*,5*R*)-3h (major diastereomer)**: R_f = 0.16 (7:3 hexane/EtOAc); white solid, m.p. 74-75 °C; $[\alpha]_D^{25}$ –160.5 (*c* 1.0, $CHCl_3$, 99% *ee*); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.34 (1H, bs, Ar), 7.27-7.23 (3H, m, Ar), 7.16 (1H, d, *J* = 1.8 Hz, N=CHO), 4.51 (1H, d, *J* = 2.1 Hz, CH), 1.79 (3H, s, CH_3), 1.05 (9H, s, CH_3). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 167.2 (C), 155.9 (CH), 141.7 (C), 134.1 (C), 129.4 (CH), 128.0 (CH), 126.3 (CH), 124.0 (CH), 87.7 (C), 81.8 (C), 78.7 (CH), 28.6 (CH_3), 27.2 (CH_3); HRMS (ESI) *m/z*: 296.1046 $[M+H]^+$, $C_{15}H_{19}ClNO_3^+$ requires 296.1048.

***trans*-(4*R*,5*S*)-3h (minor diastereomer)**: R_f = 0.28 (7:3 hexane/EtOAc); colorless oil; $[\alpha]_D^{25}$ –82.7 (*c* 0.80, $CHCl_3$, 91% *ee*); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.48 (1H, bs, Ar), 7.32-7.20 (3H, m, Ar), 7.01 (1H, d, *J* = 1.8 Hz, N=CHO), 4.60 (1H, d, *J* = 2.1 Hz, CH), 1.58 (3H, s, CH_3), 1.51 (9H, s, CH_3); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 168.2 (C), 155.2 (CH), 147.3 (C), 134.6 (C), 130.0 (CH), 127.9 (CH), 124.6 (CH), 122.3 (CH), 87.2 (C), 82.8 (C), 77.8 (CH), 28.0 (CH_3), 24.7 (CH_3); HRMS (ESI) *m/z*: 296.1043 $[M+H]^+$, $C_{15}H_{19}ClNO_3^+$ requires 296.1048.

***tert*-Butyl 5-methyl-5-(3-nitrophenyl)-4,5-dihydrooxazole-4-carboxylate (3i)**

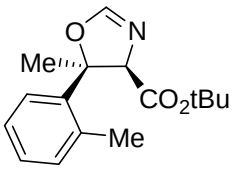


Obtained 74.6 mg (97%). The enantiomeric excess (minor isomer: 90%, *major* isomer 95%) was determined by HPLC (Lux Cellulose 4), hexane:*i*PrOH 90:10, 1 mL/min, ***cis*-(4*R*,5*R*)-3i (major diastereomer)**: major enantiomer, t_r = 17.3 min, minor enantiomer, t_r = 19.4 min. ***trans*-(4*R*,5*S*)-3i (minor diastereomer)**: minor enantiomer, t_r = 29.8 min, major enantiomer, t_r = 36.0 min.

***cis*-(4*R*,5*R*)-3i (major diastereomer)**: R_f = 0.12 (7:3 hexane/EtOAc); yellow oil; $[\alpha]_D^{25}$ –127.0 (*c* 0.65, $CHCl_3$, 95% *ee*); **NMR ^{1}H** (300 MHz, $CDCl_3$) δ 8.25 (1H, t, *J* = 1.8 Hz, Ar), 8.16 (1H, d, *J* = 9 Hz, Ar), 7.69 (1H, d, *J* = 8.1 Hz, Ar), 7.54 (1H, t, *J* = 8.1 Hz, Ar), 7.19 (1H, d, *J* =1.8 Hz, N=CHO), 4.58 (1H, d, *J* = 1.8 Hz, CH), 1.87 (3H, s, CH_3), 1.00 (9H, s, CH_3); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 167.1 (C), 155.8 (CH), 148.0 (C), 142.0 (C), 132.0 (CH), 129.3 (CH), 122.9 (CH), 121.1 (CH), 87.5 (C), 82.2 (C), 78.8 (CH), 28.7 (CH_3), 27.3 (CH_3); HRMS (ESI) *m/z*: 307.1286 $[M+H]^+$, $C_{15}H_{19}N_2O_5^+$ requires 307.1288.

***trans*-(4*R*,5*S*)-3i (minor diastereomer)**: R_f = 0.20 (7:3 hexane/EtOAc); yellow oil; $[\alpha]_D^{25}$ –37.9 (*c* 0.51, $CHCl_3$, 90% *ee*); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.41 (1H, t, *J* = 1.8 Hz, Ar), 8.19 (1H, dd, *J* = 8.4, 1.2 Hz, Ar), 7.84 (1H, d, *J* = 7.8 Hz, Ar), 7.59 (1H, t, *J* = 7.8 Hz, Ar), 7.10 (1H, d, *J* = 2.1 Hz, N=CHO), 4.68 (1H, d, *J* = 2.1 Hz, CH), 1.69 (3H, s, CH_3), 1.60 (9H, s, CH_3); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 167.8 (C), 155.05 (CH), 148.5 (C), 147.3 (C), 130.3 (CH), 129.9 (CH), 122.8 (CH), 119.7 (CH), 87.0 (C), 83.3 (C), 77.8 (CH), 28.0 (CH_3), 24.8 (CH_3); HRMS (ESI) *m/z*: 307.1286 $[M+H]^+$, $C_{15}H_{19}N_2O_5^+$ requires 307.1288.

***tert*-butyl 5-methyl-5-(o-tolyl)-4,5-dihydrooxazole-4-carboxylate (3j)**

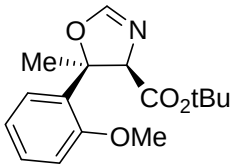


Obtained 63.2 mg (91%). The enantiomeric excess (*major* isomer: 99%, minor isomer: 89%) was determined by HPLC (Lux Cellulose 4), hexane:*i*PrOH 90:10, 1 mL/min, ***cis*-(4*R*,5*R*)-3j (major diastereomer)**: minor enantiomer, t_r = 7.6 min, major enantiomer, t_r = 10.2 min. ***trans*-(4*R*,5*S*)-3j (minor diastereomer)**: minor enantiomer, t_r = 9.3 min, major enantiomer, t_r = 11.8 min. Both diastereomers could not be separated by column chromatography.

cis-(4R,5R)-3j (major diastereomer): R_f = 0.23 (7:3 hexane/EtOAc); white solid, m.p. 53-56 °C; $[\alpha]_D^{25}$ –285.9 (*c* 1.0, $CHCl_3$, for the diastereomer mixture, dr: 91:9); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.48 (1H, m, Ar), 7.18-7.07 (4H, m, Ar, N=CHO), 4.61 (1H, d, *J* = 2.1 Hz, CH), 2.41 (3H, s, CH_3), 1.71 (3H, s, CH_3), 0.97 (9H, s, CH_3); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 167.4 (C), 155.9 (CH), 138.5 (C), 134.0 (C), 131.9 (CH), 127.8 (CH), 126.3 (CH), 125.7 (CH), 90.1 (C), 81.4 (C), 77.5 (CH), 27.8 (CH_3), 27.0 (CH_3), 22.4 (CH_3); HRMS (ESI) *m/z*: 276.1593 $[M+H]^+$, $C_{16}H_{22}NO_3^+$ requires 276.1594.

***trans*-(4*R*,5*S*)-3j (minor diastereomer)**: **^{1}H NMR** (300 MHz, $CDCl_3$), representative signals taken from the NMR spectrum of the diastereomer mixture, δ 7.50-7.00 (5H, Ar, N=CHO), 4.76 (1H, d, *J* = 1.8 Hz, CH), 2.49 (3H, s, CH_3), 2.02 (3H, s, CH_3), 1.52 (9H, s, CH_3).

***tert*-Butyl 5-(2-methoxyphenyl)-5-methyl-4,5-dihydrooxazole-4-carboxylate (3k)**

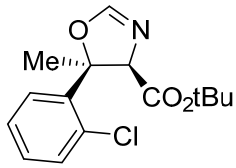


Obtained 73.2 mg (99%). The enantiomeric excess (*major* isomer: 99%, minor isomer: 95%) was determined by HPLC (Lux Cellulose 4), hexane:*i*PrOH 90:10, 1 mL/min, ***cis*-(4*R*,5*R*)-3k (major diastereomer)**: minor enantiomer, t_r = 8.2 min, major enantiomer, t_r = 10.7 min. ***trans*-(4*R*,5*S*)-3k (minor diastereomer)**: minor enantiomer, t_r = 12.5 min, major enantiomer, t_r = 21.2 min. Both diastereomers could not be separated by column chromatography.

***cis*-(4*R*,5*R*)-3k (major diastereomer)**: R_f = 0.22 (7:3 hexane/EtOAc); colorless oil; $[\alpha]_D^{25}$ –315.0 (*c* 0.85, $CHCl_3$, for the diastereomer mixture, dr: 95:5); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.46 (1H, dd, *J* = 7.8, 1.8 Hz, Ar), 7.24 (1H, m, Ar), 7.05 (1H, d, *J* = 1.8 Hz, N=CHO), 6.92 (1H, td, *J* = 7.5, 1.2 Hz, Ar), 6.80 (1H, dd, *J* = 8.1, 1.2 Hz, Ar), 4.58 (1H, d, *J* = 1.8 Hz, CH), 3.77 (3H, s, CH_3), 1.61 (3H, s, CH_3), 0.98 (9H, s, CH_3); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 167.6 (C), 155.5 (CH), 154.7 (C), 129.6 (C), 128.6 (CH), 126.0 (CH), 120.4 (CH), 110.3 (CH), 88.4 (C), 80.4 (C), 77.9 (CH), 54.8 (CH_3), 27.1 (CH_3), 27.0 (CH_3); HRMS (ESI) *m/z*: 292.1545 $[M+H]^+$, $C_{16}H_{22}NO_4^+$ requires 292.1543.

***trans*-(4*R*,5*S*)-3k (minor diastereomer)**: **^{1}H NMR** (300 MHz, $CDCl_3$), representative signals taken from the NMR spectrum of the diastereomer mixture, δ 7.7-7.20 (5H, m, Ar, N=CHO), 4.68 (1H, d, *J* = 1.8 Hz, CH), 3.85 (3H, s, CH_3), 1.52 (9H, s, CH_3), 1.47 (3H, s, CH_3).

***tert*-Butyl 5-(2-chlorophenyl)-5-methyl-4,5-dihydrooxazole-4-carboxylate (3l)**

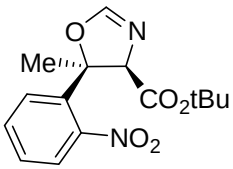


Obtained 74.2 mg (99%). The enantiomeric excess (minor isomer: 92%, *major* isomer 97%) was determined by HPLC (Lux Cellulose 4), hexane:*i*PrOH 90:10, 1 mL/min, ***cis*-(4*R*,5*R*)-3l (major diastereomer)**: minor enantiomer, t_r = 7.7 min, major enantiomer, t_r = 9.9 min. ***trans*-(4*R*,5*S*)-3l (minor diastereomer)**: minor enantiomer, t_r = 9.1 min, major enantiomer, t_r = 13.8 min. Both diastereomers could not be separated by column chromatography.

***cis*-(4*R*,5*R*)-3l (major diastereomer)**: R_f = 0.20 (7:3 hexane/EtOAc); colorless oil; $[\alpha]_D^{25}$ –275.9 (*c* 1.1, $CHCl_3$, for the diastereomer mixture, dr = 92:8); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.69 (1H, dd, *J* = 7.5, 1.5 Hz, Ar), 7.42-7.20 (3H, m, Ar), 7.12 (1H, s, N=CHO), 4.79 (1H, s, CH), 1.78 (3H, s, CH_3), 1.11 (9H, s, CH_3); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 167.4 (C), 155.4 (CH), 139.2 (C), 130.4 (CH), 130.2 (C), 129.0 (CH), 127.5 (CH), 127.0 (CH), 89.4 (C), 81.4 (C), 77.1 (CH), 27.2 (CH_3), 26.3 (CH_3); HRMS (ESI) *m/z*: 296.1046 $[M+H]^+$, $C_{15}H_{19}ClNO_3^+$ requires 296.1048.

***trans*-(4*R*,5*S*)-3l (minor diastereomer)**: **^{1}H NMR** (300 MHz, $CDCl_3$), representative signals taken from the NMR spectrum of the diastereomer mixture, δ 7.7-7.20 (5H, m, Ar, N=CHO), 4.92 (1H, s, CH), 1.87 (3H, s, CH_3), 1.53 (9H, s, CH_3).

***tert*-Butyl 5-methyl-5-(2-nitrophenyl)-4,5-dihydrooxazole-4-carboxylate (3m)**

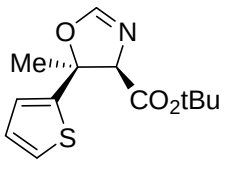


Obtained 76.9 mg (99%). The enantiomeric excess (*major* isomer: 95%, minor isomer: 30%) was determined by HPLC (Chiracel IC), hexane:*i*PrOH 90:10, 1 mL/min, ***cis*-(4*R*,5*R*)-3m (major diastereomer)**: major enantiomer, t_r = 31.5 min, minor enantiomer, t_r = 35.4 min. ***trans*-(4*R*,5*S*)-3m (minor diastereomer)**: major enantiomer, t_r = 50.5 min, minor enantiomer, t_r = 102.4 min. Both diastereomers could not be separated by column chromatography.

***cis*-(4*R*,5*R*)-3m (major diastereomer)**: R_f = 0.14 (7:3 hexane/EtOAc); yellow oil; $[\alpha]_D^{25}$ –77.2 (*c* 0.87, $CHCl_3$, for the diastereomer mixture, dr: 71:29); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.87 (1H, dd, *J* = 8.1, 1.5 Hz, Ar), 7.81 (1H, dd, *J* = 8.1, 1.5 HZ, Ar), 7.59 (1H, m, Ar), 7.43 (1H, m, Ar), 7.06 (1H, d, *J* = 1.8 Hz, N=CHO), 4.84 (1H, d, *J* = 2.1 Hz, CH), 1.64 (3H, s, CH_3), 1.10 (9H, s, CH_3); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 167.4 (C), 154.7 (CH), 147.1 (C), 135.8 (C), 133.0 (CH), 128.7 (CH), 128.6 (CH), 125.0 (CH), 88.7 (C), 81.6 (C), 78.6 (CH), 27.7 (CH_3), 27.2 (CH_3); HRMS (ESI) *m/z*: 307.1284 $[M+H]^+$, $C_{15}H_{19}N_2O_5^+$ requires 307.1288.

***trans*-(4*R*,5*S*)-3m (minor diastereomer)**: **^{1}H NMR** (300 MHz, $CDCl_3$), signals taken from the NMR spectrum of the diastereomer mixture, δ 7.68 (1H, dd, *J* = 7.8, 1.2 Hz, Ar), 7.57-7.39 (3H, m, Ar), 6.89 (1H, d, *J* = 2.1 Hz, N=CHO), 4.87 (1H, d, *J* = 2.1 Hz, CH), 1.76 (3H, s, CH_3), 1.53 (9H, s, CH_3); **^{13}C NMR** (75 MHz, $CDCl_3$), signals taken from the NMR spectrum of the diastereomer mixture, δ 167.8 (C), 154.7 (CH), 148.5 (C), 136.5 (C), 131.5 (CH), 128.9 (CH), 127.5 (CH), 123.9 (CH), 86.9 (C), 82.3 (C), 78.1 (CH), 27.9 (CH_3), 24.0 (CH_3).

***tert*-Butyl 5-methyl-5-(thiophen-2-yl)-4,5-dihydrooxazole-4-carboxylate (3n)**



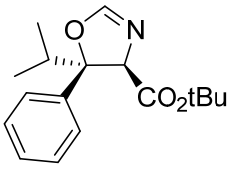
Obtained 54.4 mg (81%). The enantiomeric excess (minor isomer: 92%, *major* isomer 98%) was determined by HPLC (Lux Celullose 4) hexane:*i*PrOH 90:10, 1 mL/min, ***trans*-(4*R*,5*S*)-3n (minor diastereomer)**: minor enantiomer, t_r = 11.9 min, major enantiomer, t_r = 17.5 min, ***cis*-(4*R*,5*R*)-3n (major diastereomer)**: minor enantiomer, t_r = 16.0 min, major enantiomer, t_r = 22.4 min.

***trans*-(4*R*,5*S*)-3n (major diastereomer)**: R_f = 0.27 (7:3 hexane/EtOAc); Colourless oil; $[\alpha]_D^{25}$ –143.6 (*c* 1.22, $CHCl_3$, 98% *ee*); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.26 (1H, dd, *J* =

5.0, 1.5 Hz, Ar), 7.07 (1H, dd, *J* = 3.6, 1.2 Hz, Ar), 7.02 (1H, d, *J* = 1.8 Hz, N=CHO), 6.98 (1H, dd, *J* = 5.0, 3.6 Hz, Ar), 4.78 (1H, d, *J* = 1.8 Hz, CH), 1.74 (3H, s, CH_3), 1.52 (9H, s, CH_3); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 167.9 (C), 155.1 (CH), 148.3 (C), 127.0 (CH), 125.0 (CH), 123.4 (CH), 85.9 (C), 82.6 (C), 78.3 (CH), 28.0 (CH_3), 24.1 (CH_3); HRMS (ESI) *m/z*: 268.1003 $[M+H]^+$, $C_{13}H_{18}NO_3S^+$ requires 268.1002.

***cis*-(4*R*,5*R*)-3n (minor diastereomer)**: R_f = 0.15 (7:3 hexane/EtOAc);Colourless oil; $[\alpha]_D^{25}$ –93.8 (*c* 1.00, $CHCl_3$, 92% *ee*); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.22 (1H, dd, *J* = 3.9, 2.4 Hz, Ar), 7.11 (1H, d, *J* = 1.8 Hz, N=CHO), 6.97-6.95 (2H, m, Ar), 4.53 (1H, d, *J* = 1.8 Hz, CH), 1.91 (3H, s, CH_3), 1.12 (9H, s, CH_3); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 167.2 (C), 155.6 (CH), 142.9 (C), 126.9 (CH), 125.5 (CH), 124.9 (CH), 86.4 (C), 81.7 (C), 78.8 (CH), 29.3 (CH_3), 27.3 (CH_3); HRMS (ESI) *m/z*: 268.1003 $[M+H]^+$, $C_{13}H_{18}NO_3S^+$ requires 268.1002.

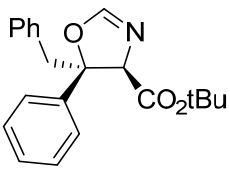
***tert*-Butyl 5-isopropyl-5-phenyl-4,5-dihydrooxazole-4-carboxylate (3o)**



Obtained 45.9 mg (63%). The enantiomeric excess (*major* isomer: 97%) was determined by HPLC (Chiracel AD-H), hexane:*i*PrOH 90:10, 1 mL/min, ***cis*-(4*R*,5*R*)-3o (major diastereomer)**: minor enantiomer, t_r = 5.6 min, major enantiomer, t_r = 6.0 min. ***trans*-(4*R*,5*S*)-3o (minor diastereomer)**: minor enantiomer, t_r = 7.1 min, major enantiomer, t_r = 4.8 min.

***cis*-(4*R*,5*R*)-3o (major diastereomer)**: R_f = 0.20 (7:3 hexane/EtOAc); Colourless oil; $[\alpha]_D^{25}$ –218.2 (*c* 0.45, $CHCl_3$, 97% *ee*, for the diastereomer mixture, dr: 98:2); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.24-7.16 (5H, m, Ar), 7.08 (1H, d, *J* = 1.5 Hz, N=CHO), 4.58 (1H, d, *J* = 1.5 Hz, CH), 2.23 (1H, sept, *J* = 6.9 Hz, CH), 0.94 (9H, s, CH_3), 0.91 (3H, d, *J* = 6.9 Hz, CH_3), 0.66 (3H, d, *J* = 6.9 Hz, CH_3); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 168.1 (C), 156.3 (CH), 139.0 (C), 127.9 (CH), 127.3 (CH), 126.0 (CH), 93.5 (C), 81.4 (C), 76.5 (CH), 38.1 (CH), 27.2 (CH_3), 17.2 (CH_3), 16.2 (CH_3); HRMS (ESI) *m/z*: 290.11754 $[M+H]^+$, $C_{17}H_{24}NO_3^+$ requires 290.1751.

***tert*-Butyl 5-benzyl-5-phenyl-4,5-dihydrooxazole-4-carboxylate (3p)**

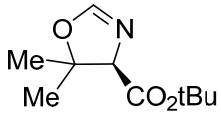


Obtained 84.7 mg (99%). The enantiomeric excess (*major* isomer: 97%, minor isomer 95%) was determined by HPLC (Chiracel IC), hexane:*i*PrOH 90:10, 1 mL/min, ***trans*-(4*R*,5*S*)-3p (minor diastereomer)**: minor enantiomer, t_r = 14.3 min, major enantiomer, t_r = 28.4 min, ***cis*-(4*R*,5*R*)-3p (major diastereomer)**: minor enantiomer, t_r = 22.9 min, major enantiomer, t_r = 23.7 min. Both diastereomers could not be separated by column chromatography.

***cis*-(4*R*,5*R*)-3p (major diastereomer)**: R_f = 0.22 (7:3 hexane/EtOAc); Colorless oil; $[\alpha]_D^{25}$ –133.7 (*c* 0.86, $CHCl_3$, for the diastereomer mixture, dr: 61:39); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.42-7.12 (10H, m, Ar), 6.83 (1H, d, *J* = 1.8 Hz, N=CHO), 4.75 (1H, d, *J* = 1.8 Hz, CH), 3.40 (2H, d, *J* = 2.4 Hz, CH_2), 1.08 (9H, s, CH_3); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 167.5 (C), 155.8 (CH), 138.5 (C), 134.5 (C), 130.5 (CH), 127.92 (CH), 127.90 (CH), 127.4 (CH), 126.9 (CH), 126.1 (CH), 90.6 (C), 81.5 (C), 77.4 (CH), 46.9 (CH_2), 28.0 (CH_3), 27.2 (CH_3); HRMS (ESI) *m/z*: 338.1749 $[M+H]^+$, $C_{21}H_{24}NO_3^+$ requires 338.1751.

***trans*-(4*R*,5*S*)-3p (minor diastereomer)**: **^{1}H NMR**(300 MHz, $CDCl_3$), signals taken from the NMR spectrum of the diastereomer mixture, δ 7.42-7.12 (10H, m, Ar), 6.81 (1H, d, *J* = 1.8 Hz, N=CHO), 4.95 (1H, d, *J* = 1.8 Hz, CH), 3.34 (1H, d, *J* = 13.2 Hz, CH), 3.23 (1H, d, *J* = 13.2 Hz, CH), 1.70 (9H, s, CH_3); **^{13}C NMR** (75 MHz, $CDCl_3$), signals taken from the NMR spectrum of the diastereomer mixture, δ 168.5 (C), 155.2 (CH), 142.9 (C), 134.8 (C), 130.4 (CH), 128.1 (CH), 127.9 (CH), 127.7 (CH), 127.5 (CH), 126.5 (CH), 124.8 (CH), 89.8 (C), 82.8 (C), 78.8 (CH), 43.4 (CH_2), 28.1 (CH_3), 27.2 (CH_3).

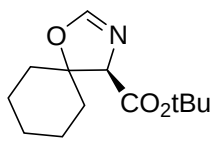
***tert*-Butyl (*R*)-5,5-dimethyl-4,5-dihydrooxazole-4-carboxylate (3q)**



Obtained 48.0 mg (85%). The enantiomeric excess (96%) was determined by HPLC (Chiracel OD-H), hexane:*i*PrOH 90:10, 1 mL/min, minor enantiomer, t_r = 4.7 min, major enantiomer, t_r = 5.9 min.

R_f = 0.25 (7:3 hexane/EtOAc); colorless oil; $[\alpha]_D^{25}$ –91.9 (*c* 0.65, $CHCl_3$, 96% *ee*); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 6.87 (1H, d, *J* = 1.8 Hz, CH), 4.23 (1H, d, *J* = 1.8 Hz, N=CHO), 1.50 (3H, s, CH_3), 1.47 (9H, s, CH_3), 1.34 (3H, s, CH_3); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 168.7 (C), 155.8 (CH), 85.1 (C), 82.0 (C), 76.2 (CH), 28.7 (CH_3), 27.9 (CH_3), 22.5 (CH_3); HRMS (ESI) *m/z*: 200.1283 $[M+H]^+$, $C_{10}H_{18}NO_3^+$ requires 200.1281.

***tert*-Butyl (*R*)-1-oxa-3-azaspiro[4.5]dec-2-ene-4-carboxylate (3r)**

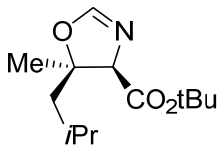


Obtained 59.0 mg (96%). The enantiomeric excess (95%) was determined by HPLC using a chiral column (Chiracel IC), hexane:*i*PrOH 90:10, 1mL/min, minor enantiomer, t_r : 20.4 min, major enantiomer, t_r : 21.4 min.

R_f = 0.25 (7:3 hexane/EtOAc); Colorless oil; $[\alpha]_D^{25}$ –72.6 (*c* 0.46, $CHCl_3$, 95% *ee*); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 6.91 (1H, d, *J* = 1.8 Hz, N=CHO), 4.13 (1H, d, *J* = 1.8 Hz, CH), 1.84-1.74 (2H, m), 1.68-1.52 (7H, m), 1.47 (9H, s, CH_3), 1.34-1.24 (1H, m); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 168.7 (C), 155.9 (CH), 86.8 (C), 81.9 (C), 76.3 (CH), 37.6

(CH_2), 31.2 (CH_2), 27.9 (CH_3), 24.8 (CH_2), 22.4 (CH_2); HRMS (ESI) *m/z*: 240.1593 $[M+H]^+$, $C_{13}H_{22}NO_3^+$ requires 240.1594.

***tert*-Butyl 5-isobutyl-5-methyl-4,5-dihydrooxazole-4-carboxylate (3s)**

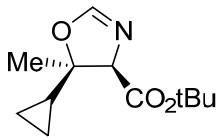


Obtained 35.3 mg (71%). The enantiomeric excess (*major* isomer: 97%, minor isomer: 56%) was determined by HPLC (Chiracel IC), hexane:*i*PrOH 90:10, 1 mL/min, ***cis*-(4*R*,5*R*)-3s (major diastereomer)**: major enantiomer, t_r = 12.2 min, minor enantiomer, t_r = 14.6 min, ***trans*-(4*R*,5*S*)-3s (minor diastereomer)**: major enantiomer, t_r = 21.7 min, minor enantiomer, t_r = 24.1 min.

***cis*-(4*R*,5*R*)-3s (major diastereomer)**: R_f = 0.18 (7:3 hexane/EtOAc); Colourless oil; $[\alpha]_D^{25}$ –45.4 (*c* 1.09, $CHCl_3$, 97% *ee*); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 6.89 (1H, d, *J* = 1.8 Hz, N=CHO), 4.22 (1H, d, *J* = 1.8 Hz, CH), 1.87 (1H, sept, *J* = 6.6 Hz, CH), 1.53-1.50 (2H, m), 1.47 (9H, s, CH_3), 1.45 (3H, s, CH_3), 0.94 (3H, d, *J* = 6.6 Hz, CH_3), 0.93 (3H, d, *J* = 6.6 Hz, CH_3); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 168.7 (C), 156.1 (CH), 87.6 (C), 82.0 (C), 78.0 (CH), 43.2 (CH), 28.0 (CH_3), 25.6 (CH_2), 24.8 (CH_3), 24.3 (CH_3), 23.0 (CH_3); HRMS (ESI) *m/z*: 242.1755 $[M+H]^+$, $C_{13}H_{24}NO_3^+$ requires 242.1751.

***trans*-(4*R*,5*S*)-3s (minor diastereomer)**: R_f = 0.27 (7:3 hexane/EtOAc);Colourless oil; $[\alpha]_D^{25}$ –67.7 (*c* 0.18, $CHCl_3$, 56% *ee*); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 6.89 (1H, d, *J* = 1.8 Hz, N=CHO), 4.29 (1H, d, *J* = 1.8 Hz, CH), 1.85 (1H, sept, *J* = 6.6 Hz, CH), 1.73 (1H, dd, *J* = 14.4, 5.1 Hz, CH), 1.63 (1H, m, CH), 1.49 (9H, s, CH_3), 1.33 (3H, s, CH_3), 0.98 (3H, d, *J* = 6.6 Hz, CH_3), 0.97 (3H, d, *J* = 6.6 Hz, CH_3); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 168.9 (C), 155.9 (CH), 88.8 (C), 82.0 (C), 75.9 (CH), 49.9 (CH), 28.0 (CH_3), 24.3 (CH_2), 24.2 (CH_3), 23.7 (CH_3), 20.7 (CH_3); HRMS (ESI) *m/z*: 242.1747 $[M+H]^+$, $C_{13}H_{24}NO_3^+$ requires 242.1751.

***tert*-Butyl -5-cyclopropyl-5-methyl-4,5-dihydrooxazole-4-carboxylate (3t)**



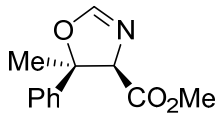
Obtained 37.3 mg (81%). The enantiomeric excess (*major* isomer: 97%, minor isomer 87%) was determined by HPLC (Lux Celullose 4), hexane:*i*PrOH 90:10, 1 mL/min, ***trans*-(4*R*,5*S*)-3t (minor diastereomer)**: minor enantiomer, t_r = 9.2 min, major enantiomer, t_r = 12.5 min, ***cis*-(4*R*,5*R*)-3t (major diastereomer)**: minor enantiomer, t_r = 11.3 min, major enantiomer, t_r = 13.2 min.

***cis*-(4*R*,5*R*)-3t (major diastereomer)**: R_f = 0.15 (7:3 hexane/EtOAc); Colourless oil; $[\alpha]_D^{25}$ –35.2 (*c* 0.62, $CHCl_3$, 97% *ee*); **^{1}H NMR**(300 MHz, $CDCl_3$) δ 6.84 (1H, d, *J* = 1.8 Hz, N=CHO), 4.32 (1H, d, *J* = 1.8 Hz, CH), 1.47 (9H, s, CH_3), 1.46 (3H, s, CH_3), 1.10-1.05 (1H, m, CH), 0.45-0.38 (4H, m, CH_2); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 168.5

(C), 155.5 (CH), 86.0 (C), 81.7 (C), 76.9 (CH), 28.0 (CH_3), 26.7 (CH_3), 15.5 (CH), 1.8 (CH_2), 1.3 (CH_2); HRMS (ESI) *m/z*: 226.1437 $[M+H]^+$, $C_{12}H_{20}NO_3^+$ requires 226.1438.

***trans*-(4*R*,5*S*)-3t (minor diastereomer)**: R_f = 0.25 (7:3 hexane/EtOAc); Colourless oil; $[\alpha]_D^{25}$ –88.8 (*c* 0.75, $CHCl_3$, 87% *ee*); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 6.83 (1H, d, *J* = 1.8 Hz, N=CHO), 4.35 (1H, d, *J* = 1.8 Hz, CH), 1.49 (9H, s, CH_3), 1.34 (3H, s, CH_3), 1.22-1.17 (1H, m, CH), 0.55-0.42 (4H, m, CH_2); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 168.8 (C), 155.6 (CH), 86.6 (C), 82.0 (C), 75.1 (CH), 28.0 (CH_3), 21.0 (CH), 21.0 (CH_3), 1.4 (CH_2), 0.73 (CH_2); HRMS (ESI) *m/z*: 226.1438 $[M+H]^+$, $C_{12}H_{20}NO_3^+$ requires 226.1438.

Methyl 5-methyl-5-phenyl-4,5-dihydrooxazole-4-carboxylate (3u)

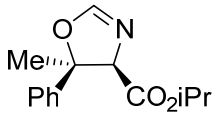


Obtained 45.2 mg (82%). The enantiomeric excess (minor isomer: 84%, major isomer: 96%) was determined by HPLC (Chiralpak AS-H) hexane:*i*PrOH 95:5, 1mL/min, ***trans*-(4*R*,5*S*)-3u (minor diastereomer)**: minor enantiomer, t_r = 12.8 min, major enantiomer, t_r = 14.2 min; ***cis*-(4*R*,5*R*)-3u (major diastereomer)**: minor enantiomer, t_r = 10.8 min, major enantiomer, t_r = 28.6 min. Both diastereomers could not be separated by column chromatography.

***cis*-(4R,5R)-3u (major diastereomer)**: R_f = 0.20 (6:4 hexane/EtOAc); colorless oil; $[\alpha]_D^{25}$ –166.0 (*c* 0.50, $CHCl_3$, 96% *ee*, for the diastereomer mixture, dr = 80:20); **^{1}H NMR** ($CDCl_3$, 300 MHz) δ 7.48-7.26 (5H, m, Ar), 7.20 (1H, d, *J* = 1.8 Hz, N=CHO), 4.64 (1H, d, *J* = 1.8 Hz, CH), 3.15 (3H, s, CH_3), 1.86 (3H, s, CH_3); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 169.0 (C), 156.6 (CH), 139.2 (C), 127.9 (CH), 125.2 (CH), 88.4 (C), 78.6 (CH), 51.6 (CH_3), 28.2 (CH_3); HRMS (ESI) *m/z*: 220.0970 $[M+H]^+$, $C_{12}H_{14}NO_3^+$ requires 220.0968.

***trans*-(4*R*,5*S*)-3u (minor diastereomer)**: R_f = 0.22 (6:4 hexane/EtOAc); colorless oil; **^{1}H NMR** ($CDCl_3$, 300 MHz), signals taken from the NMR spectrum of the diastereomer mixture, δ 7.48-7.26 (5H, m, Ar), 7.11 (1H, d, *J* = 1.8 Hz, N=CHO), 4.83 (1H, d, *J* = 1.8 Hz, CH), 3.85 (3H, s, CH_3), 1.61 (3H, s, CH_3); **^{13}C NMR** (75 MHz, $CDCl_3$), signals taken from the NMR spectrum of the diastereomer mixture, δ 170.0 (C), 155.8 (CH), 144.8 (C), 128.7 (CH), 127.8 (CH), 124.0 (CH), 87.9 (C), 77.6 (CH), 52.4 (CH_3), 24.5 (CH_3).

Isopropyl 5-methyl-5-phenyl-4,5-dihydrooxazole-4-carboxylate (3v)



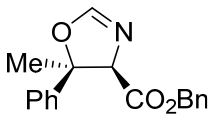
Obtained 48.4 mg (78%). The enantiomeric excess (minor isomer: 90%, major isomer: 97%) was determined by HPLC (Lux Cellulose 4) hexane:*i*PrOH 90:10, 1mL/min, ***trans*-(4*R*,5*S*)-3v (minor diastereomer)**: minor enantiomer, t_r = 11.7 min, major enantiomer, t_r = 15.5 min; ***cis*-**

(4*R*,5*R*)-3v (major diastereomer): minor enantiomer, t_r = 14.0 min, major enantiomer, t_r = 17.9 min.

***cis*-(4R,5R)-3v (major diastereomer)**: R_f = 0.22 (6:4 hexane/EtOAc); colorless oil; $[\alpha]_D^{25}$ –173.9 (*c* 0.57, $CHCl_3$, 97% *ee*); **^{1}H NMR** ($CDCl_3$, 300 MHz) δ 7.35-7.26 (5, m, Ar), 7.20 (1H, d, *J* = 1.8 Hz, N=CHO), 4.59 (1H, d, *J* = 1.8 Hz, CH), 4.47 (1H, sept, *J* = 6.3 Hz, CH), 1.84 (3H, s, CH_3), 0.86 (3H, d, *J* = 6.3 Hz, CH_3), 0.77 (3H, d, *J* = 6.3 Hz, CH_3). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 168.2 (C), 156.4 (CH), 139.3 (C), 128.0 (CH), 127.9 (CH), 125.6 (CH), 88.4 (C), 78.3 (CH), 68.8 (CH), 28.5 (CH_3), 21.2 (CH_3), 21.0 (CH_3); HRMS (ESI) *m/z*: 248.1282 $[M+H]^+$, $C_{14}H_{18}NO_3^+$ requires 248.1281.

***trans*-(4*R*,5*S*)-3v (minor diastereomer)**: R_f = 0.26 (6:4 hexane/EtOAc); colorless oil; $[\alpha]_D^{25}$ -79.5 (*c* 0.73, $CHCl_3$, 90% *ee*); **^{1}H NMR** ($CDCl_3$, 300 MHz) δ 7.49-7.29 (5H, m, Ar), 7.10 (1H, d, *J* = 1.8 Hz, N=CHO), 5.20 (1H, sept, *J* = 6.3 Hz, CH), 4.76 (1H, d, *J* = 2.1 Hz, CH), 1.63 (3H, s, CH_3), 1.35 (3H, d, *J* = 6.3 Hz, CH_3), 1.33 (3H, d, *J* = 6.3 Hz, CH_3). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 169.0 (C), 155.6 (CH), 145.0 (C), 128.7 (CH), 127.8 (CH), 124.0 (CH), 87.8 (C), 77.5 (CH), 69.3 (CH), 24.5 (CH_3), 21.9 (CH_3), 21.8 (CH_3); HRMS (ESI) *m/z*: 248.1282 $[M+H]^+$, $C_{14}H_{18}NO_3^+$ requires 248.1281.

Benzyl 5-methyl-5-phenyl-4,5-dihydrooxazole-4-carboxylate (3w)



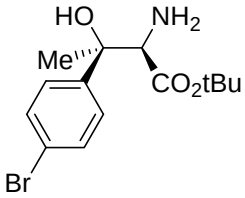
Obtained 56.1 mg (76%). The enantiomeric excess (minor isomer: 82%, major isomer: 96%) was determined by HPLC (Lux Cellulose 4) hexane:*i*PrOH 90:10, 1mL/min, ***trans*-(4*R*,5*S*)-3w (minor diastereomer)**: minor enantiomer, t_r = 21.9 min, major enantiomer, t_r = 33.2 min; ***cis*-(4*R*,5*R*)-3w (major diastereomer)**: minor enantiomer, t_r = 25.2 min, major enantiomer, t_r = 34.6 min.

***cis*-(4*R*,5*R*)-3w (major diastereomer)**: R_f = 0.26 (6:4 hexane/EtOAc); colorless oil; $[\alpha]_D^{25}$ –118.0 (*c* 0.72, $CHCl_3$, 96% *ee*); **^{1}H NMR** ($CDCl_3$, 300 MHz) δ 7.29-7.26 (8H, m, Ar), 7.20 (1H, d, *J* = 1.8 Hz, N=CHO), 7.08-7.04 (2H, m, Ar), 4.67 (1H, d, *J* = 1.8 Hz, CH), 4.65 (1H, d, *J* = 12.0 Hz, CH), 4.36 (1H, d, *J* = 12.0 Hz, CH), 1.83 (3H, s, CH_3). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 168.6 (C), 156.6 (CH), 139.1 (C), 134.8 (C), 128.5 (CH), 128.4 (CH), 128.2 (CH), 128.04 (CH), 128.01 (CH), 125.3 (CH), 88.4 (C), 78.4 (CH), 66.8 (CH_2), 28.3 (CH_3); HRMS (ESI) *m/z*: 296.1283 $[M+H]^+$, $C_{18}H_{18}NO_3^+$ requires 296.1281.

***trans*-(4*R*,5*S*)-3w (minor diastereomer)**: R_f = 0.30 (6:4 hexane/EtOAc); colorless oil; $[\alpha]_D^{25}$ -91.4 (*c* 0.56, $CHCl_3$, 82% *ee*); **^{1}H NMR** ($CDCl_3$, 300 MHz) δ 7.45-7.29 (10H, m, Ar), 7.11 (1H, d, *J* = 2.1 Hz, N=CHO), 5.30 (2H, s, CH_2), 4.84 (1H, d, *J* = 2.1 Hz, CH), 1.51 (3H, s, CH_3). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 169.4 (C), 155.9 (CH), 144.8 (C), 135.1 (C), 128.8 (CH), 128.7 (CH), 128.64 (CH), 128.62 (CH), 127.8 (CH), 124.0 (CH),

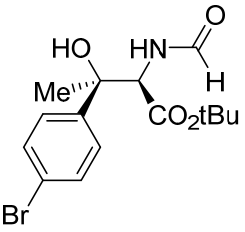
88.0 (C), 77.6 (CH), 67.3 (CH_2), 24.4 (CH_3); HRMS (ESI) *m/z*: 296.1283 $[M+H]^+$, $C_{18}H_{18}NO_3^+$ requires 296.1281.

***tert*-Butyl (2*R*,3*R*)-2-amino-3-(4-bromophenyl)-3-hydroxybutanoate (4)**



6 M Aqueous HCl (6 drops) was added to a solution of compound **3d** (25.0 mg, 0.073 mmol) in MeOH (1 mL). The reaction mixture was stirred at rt for 24 h. The mixture was basified with saturated aqueous $NaHCO_3$ (1 mL), water was added (10 mL), extracted with EtOAc (3×20 mL), washed with brine (20 mL) and dried over $MgSO_4$. Removal of the solvent under reduced pressure aforded 22.3 mg (93%) of compound **4**. The enantiomeric excess (81%) was determined by HPLC (Lux Cellulose 4), hexane:*i*PrOH 90:10, 1 mL/min, minor enantiomer, t_r = 11.8 min, major enantiomer, t_r = 10.0 min. Colorless oil; $[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\mathbf{25}}$ -23.9 (*c* 1.1, $CHCl_3$, 81% *ee*); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.43 (2H, d, *J* = 8.7 Hz, Ar), 7.28 (2H, d, *J* = 8.7 Hz, Ar), 3.55 (1H, s, CHN), 2.62 (3H, bs, NH_2, OH), 1.59 (3H, s, CH_3), 1.25 (9H, s, CH_3); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 173.0 (C), 143.8 (C), 130.9 (CH), 127.4 (CH), 121.1 (C), 82.3 (C), 62.6 (CH), 27.7 (CH_3), 26.4 (CH_3); HRMS (ESI) *m/z*: 352.0516 $[M+Na]^+$, $C_{14}H_{20}BrNNaO_3^+$ requires 352.0518.

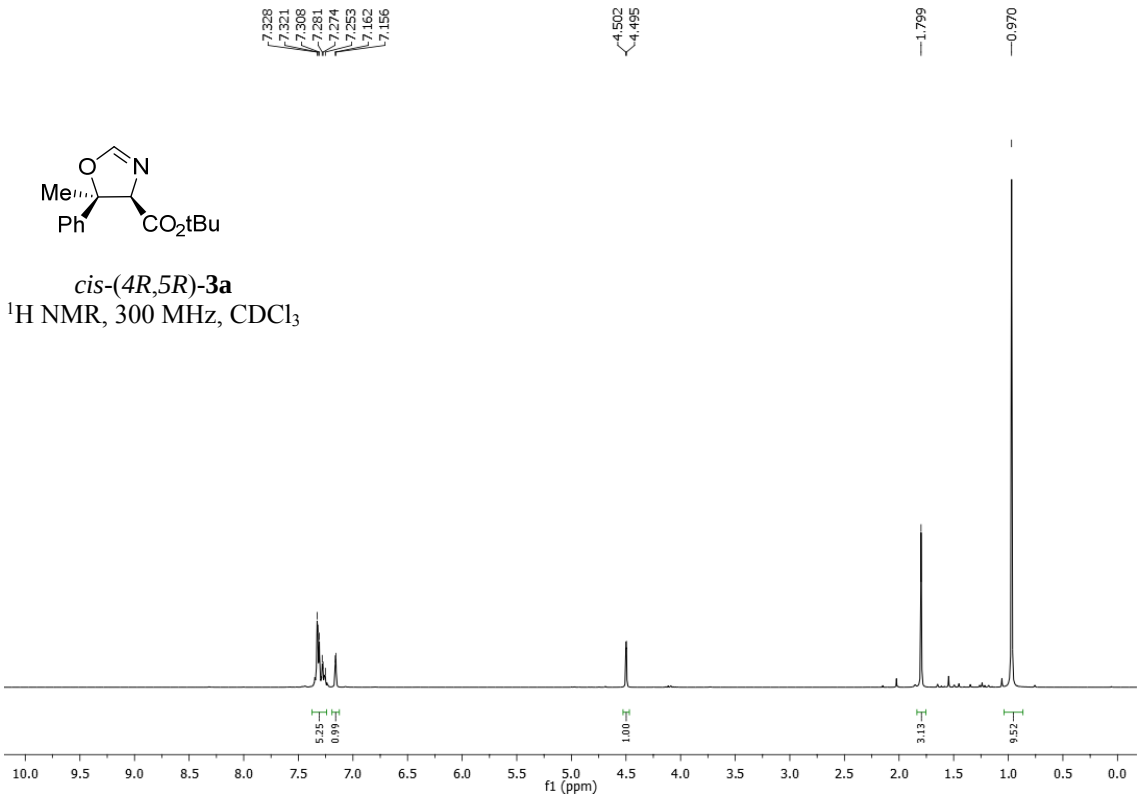
***tert*-butyl (2*R*,3*R*)-3-(4-bromophenyl)-2-formamido-3-hydroxybutanoate (5)**



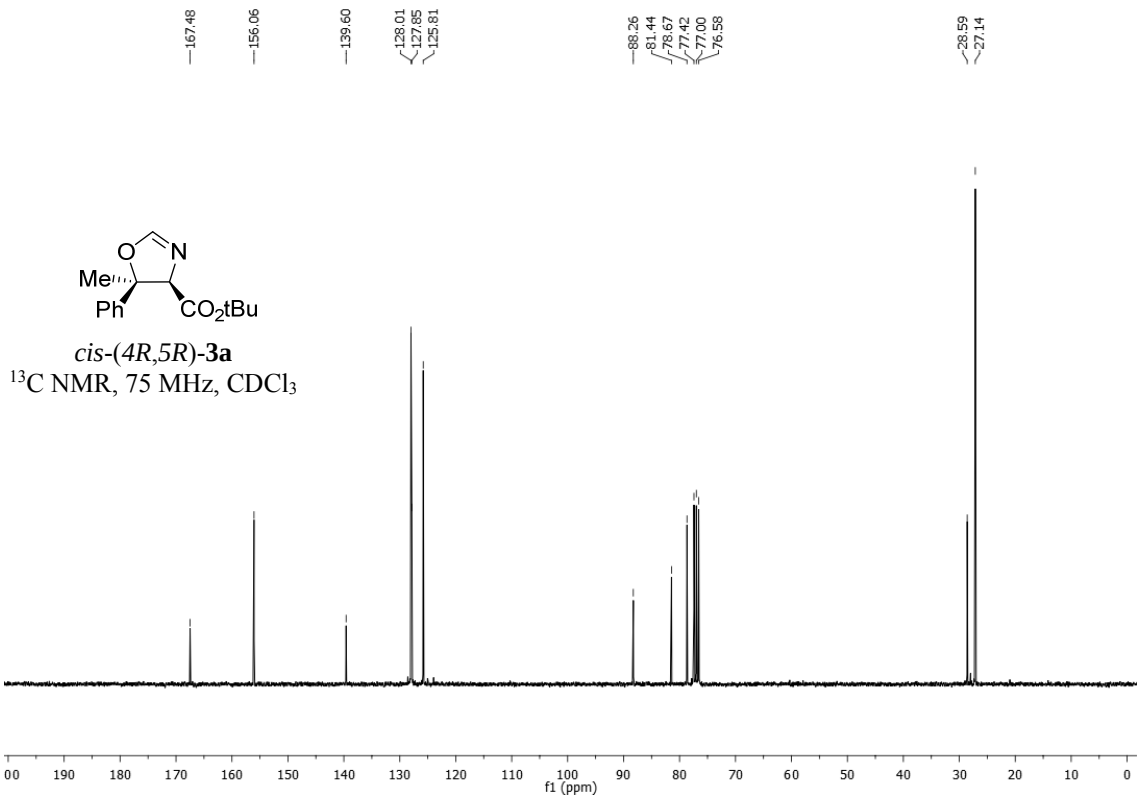
6 M Aqueous HCl (6 drops) was added to a solution of compound **3d** (33.0 mg, 0.096 mmol) in THF (1 mL). The reaction mixture was stirred at rt for 24 h. Work up as described in the previous procedure afforded 34.6 mg (99%) of compound **5**. The enantiomeric excess (98%) was determined by HPLC (Chiracel IC), hexane:*i*PrOH 90:10, 1 mL/min, major enantiomer, t_r = 5.0 min, minor enantiomer, t_r = 9.0 min. White solid; m.p. 130-131 ºC; $[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\mathbf{25}}$ +22.8 (*c* 0.37, $CHCl_3$, 98% *ee*); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.33 (1H, s, CHO), 7.49 (2H, d, *J* = 8.7 Hz, Ar), 7.33 (2H, d, *J* = 8.7 Hz, Ar), 6.53 (1H, d, *J* = 9.3 Hz, OH), 4.96 (1H, dd, *J* = 9.0, 0.6 Hz, CHN), 3.41 (1H, bs, NH), 1.49 (3H, s, CH_3), 1.14 (9H, s, CH_3); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 170.2 (C), 161.0 (C), 142.9 (C), 131.2 (CH), 127.0 (CH), 121.5 (CH), 83.4 (C), 76.0 (C), 57.7 (CH_3), 27.4 (CH_3); HRMS (ESI) *m/z*: 380.0461 $[M+Na]^+$, $C_{15}H_{20}BrNNaO_4^+$ requires 380.0468.

References

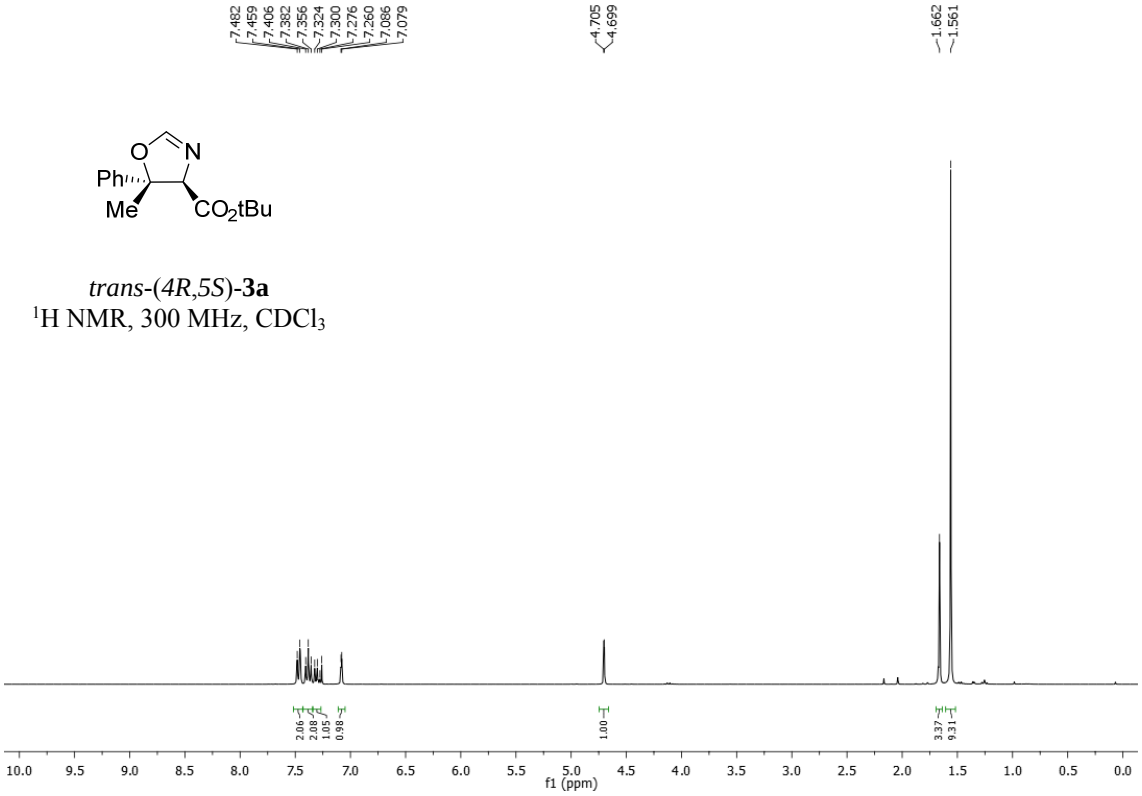
R. De La Campa, I. Ortín, D. J. Dixon, *Angew. Chem. Int. Ed.*, 2015, **54**, 4895



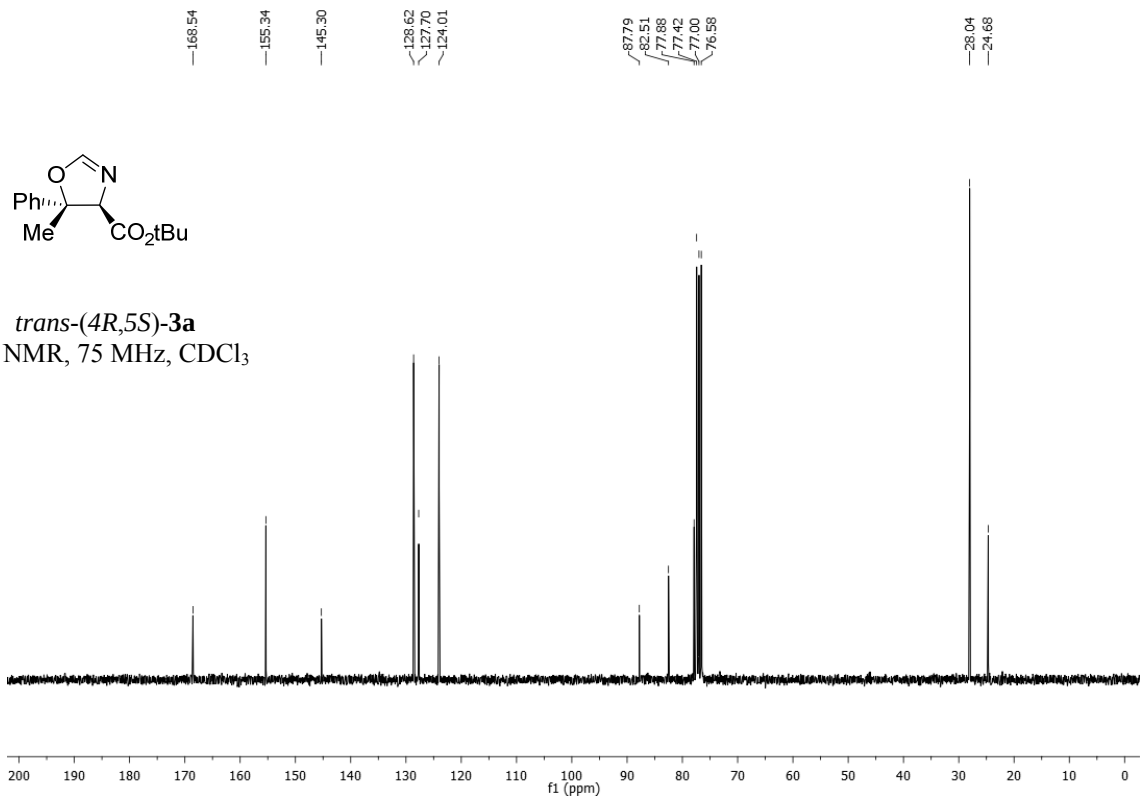
cis-(*4R*,*5R*)-**3a**
^{1}H NMR, 300 MHz, $CDCl_3$



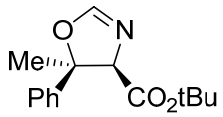
cis-(*4R*,*5R*)-**3a**
^{13}C NMR, 75 MHz, $CDCl_3$



trans-(*4R*,*5S*)-**3a**
^{1}H NMR, 300 MHz, $CDCl_3$

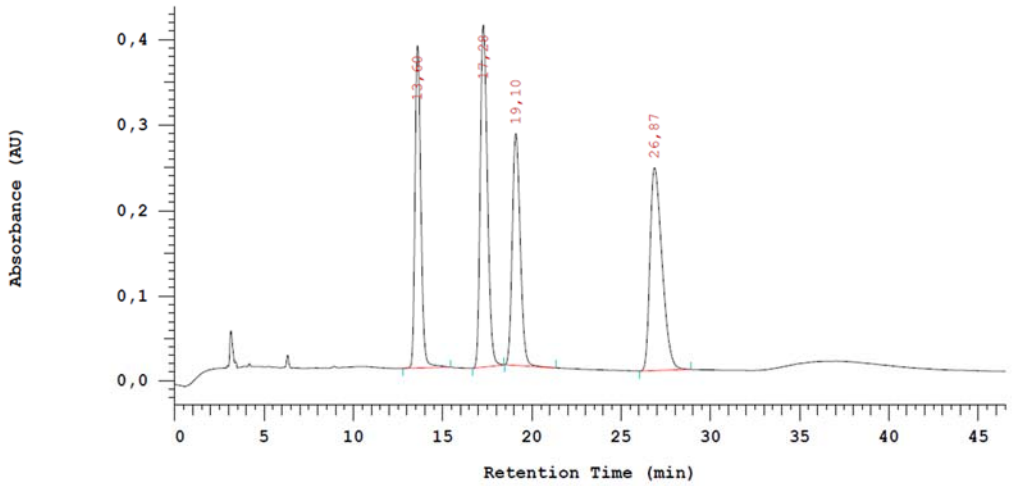


trans-(*4R*,*5S*)-**3a**
^{13}C NMR, 75 MHz, $CDCl_3$



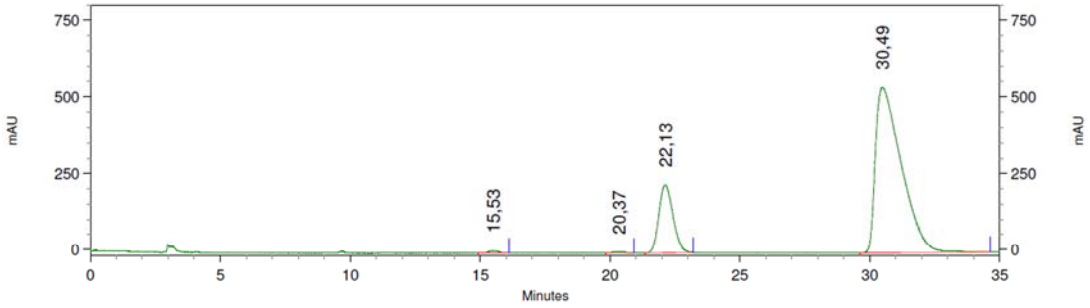
3a

Racemic product:



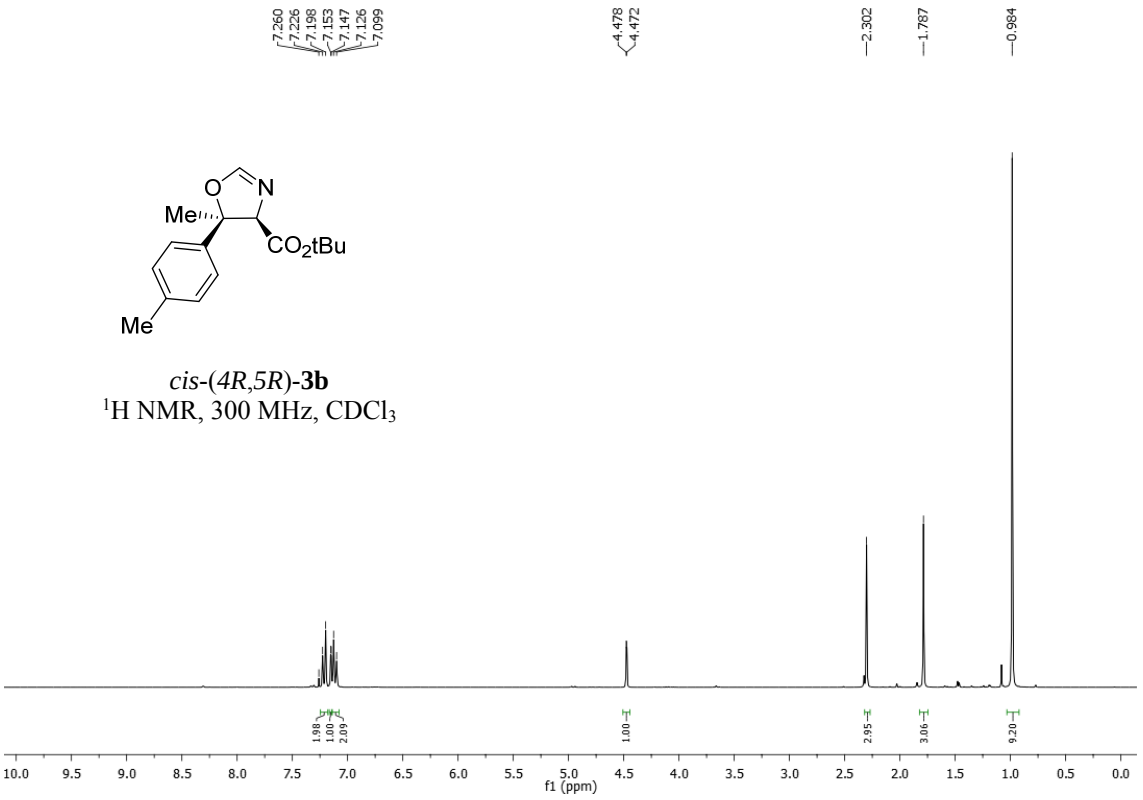
No.	RT	Area	Area %	Name
1	13,60	4232370	21,777	
2	17,28	5491370	28,256	
3	19,10	4159184	21,401	
4	26,87	5551750	28,566	enanti (-)

Enantioselective reaction:

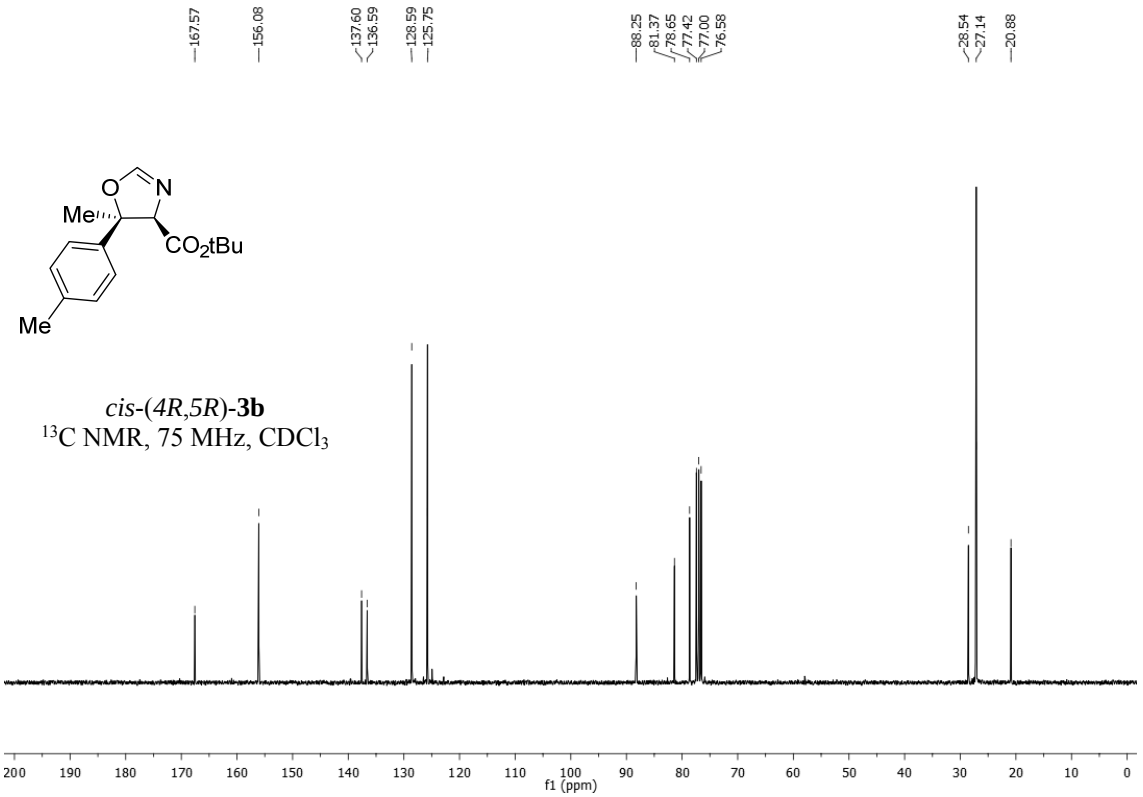


6: 214 nm, 4 nm Results

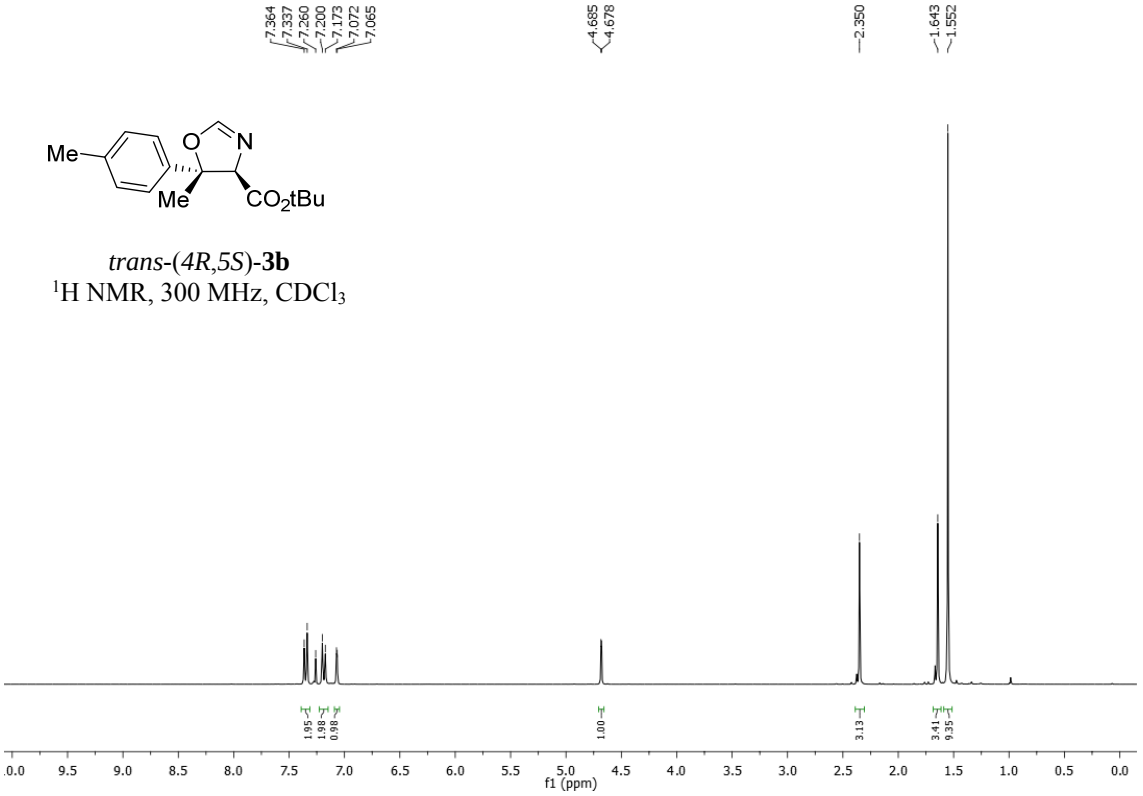
Retention Time	Area	Area Percent
15,53	1037624	0,557
20,37	671112	0,360
22,13	34163347	18,325
30,49	150559706	80,759



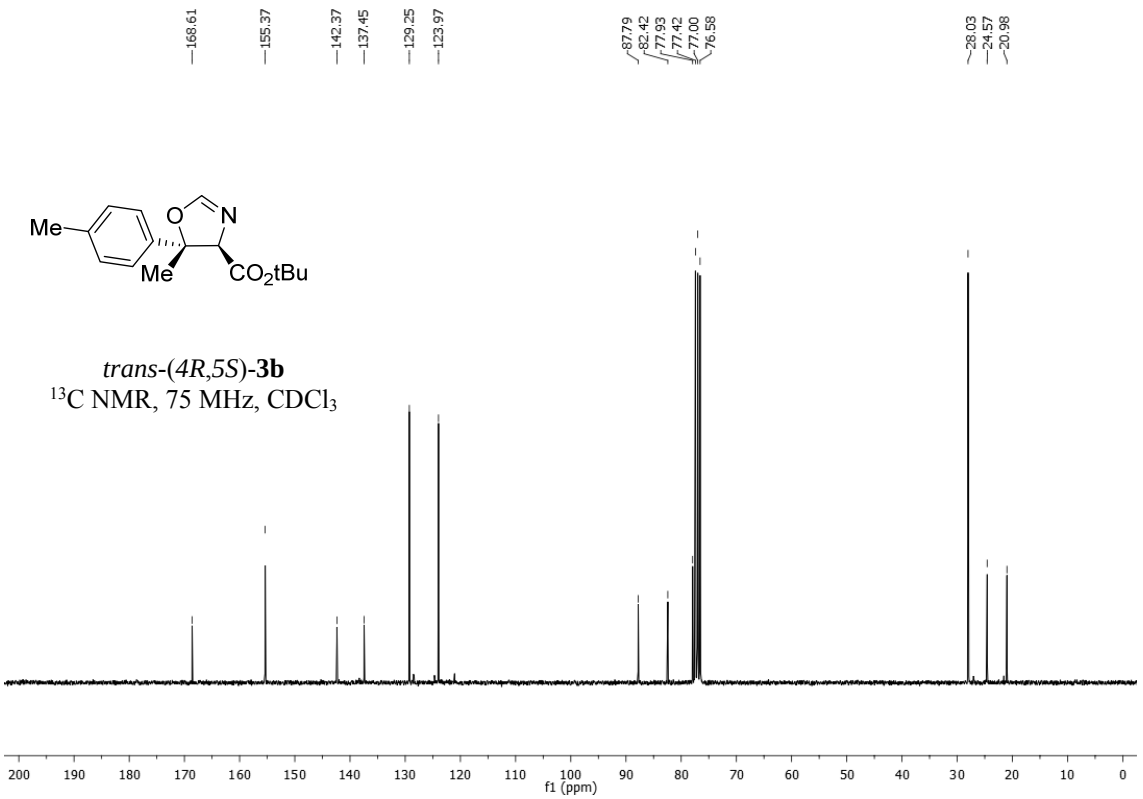
cis-(*4R*,*5R*)-**3b**
^{1}H NMR, 300 MHz, $CDCl_3$



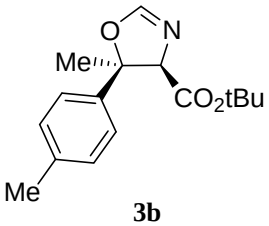
cis-(*4R*,*5R*)-**3b**
^{13}C NMR, 75 MHz, $CDCl_3$



trans-(*4R,5S*)-**3b**
^{1}H NMR, 300 MHz, $CDCl_3$

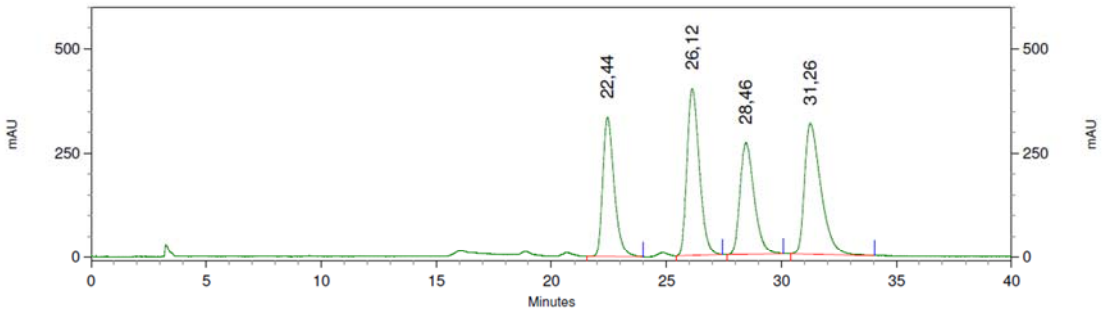


trans-(*4R,5S*)-**3b**
^{13}C NMR, 75 MHz, $CDCl_3$



3b

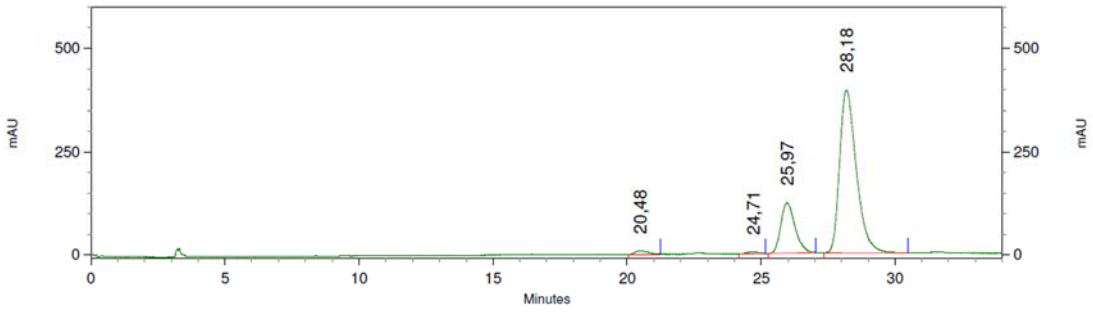
Racemic reaction:



9: 222 nm, 4 nm Results

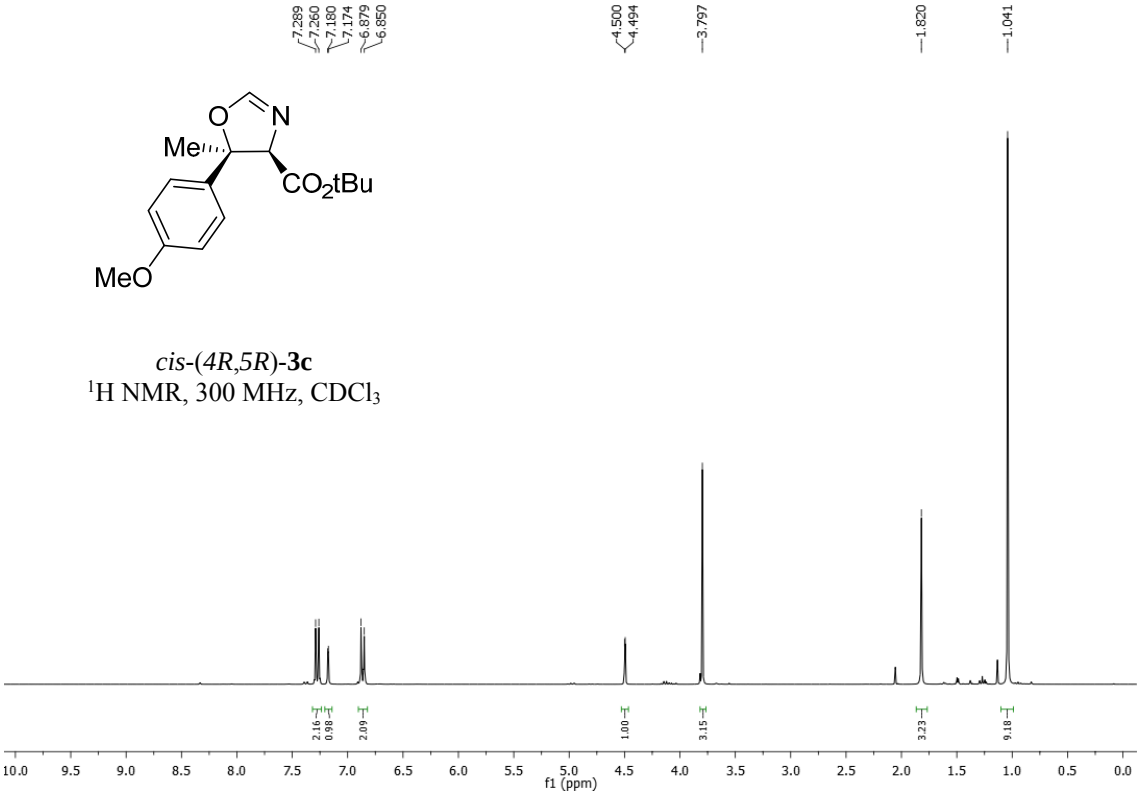
Retention Time	Area	Area Percent
22,44	46754086	21,639
26,12	60127786	27,829
28,46	46467289	21,507
31,26	62712062	29,025

Enantioselective reaction:

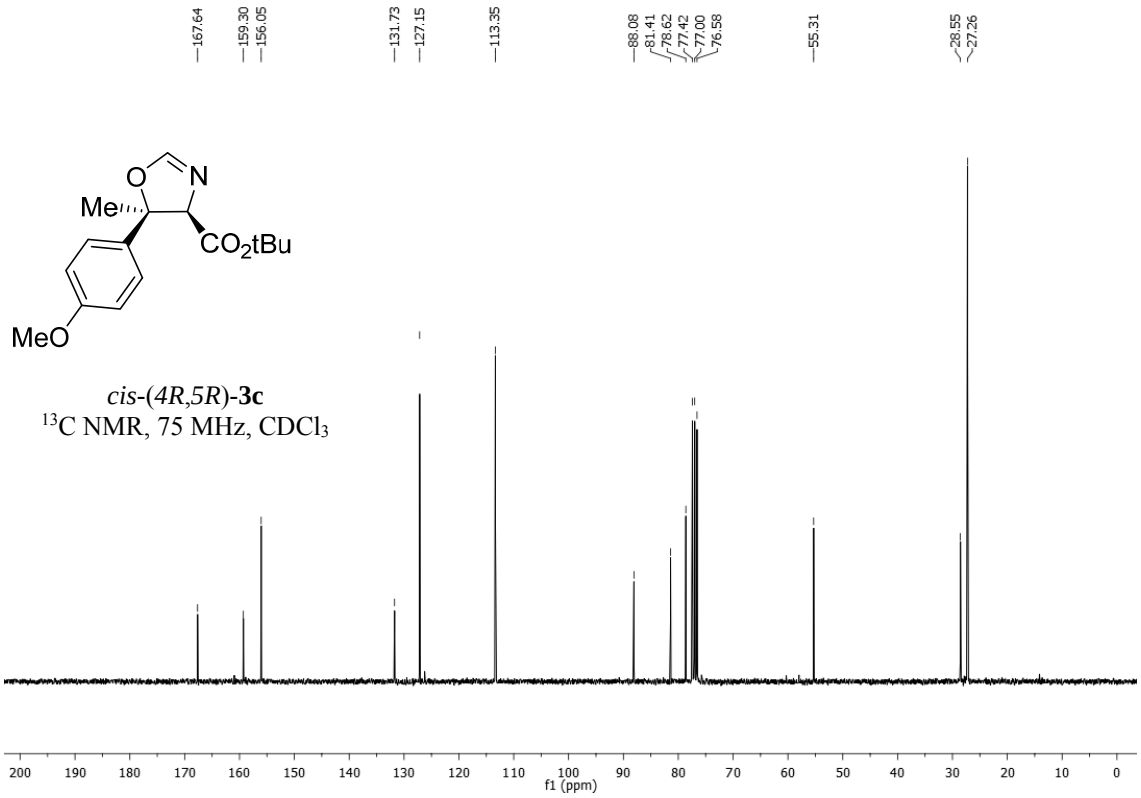


9: 222 nm, 4 nm Results

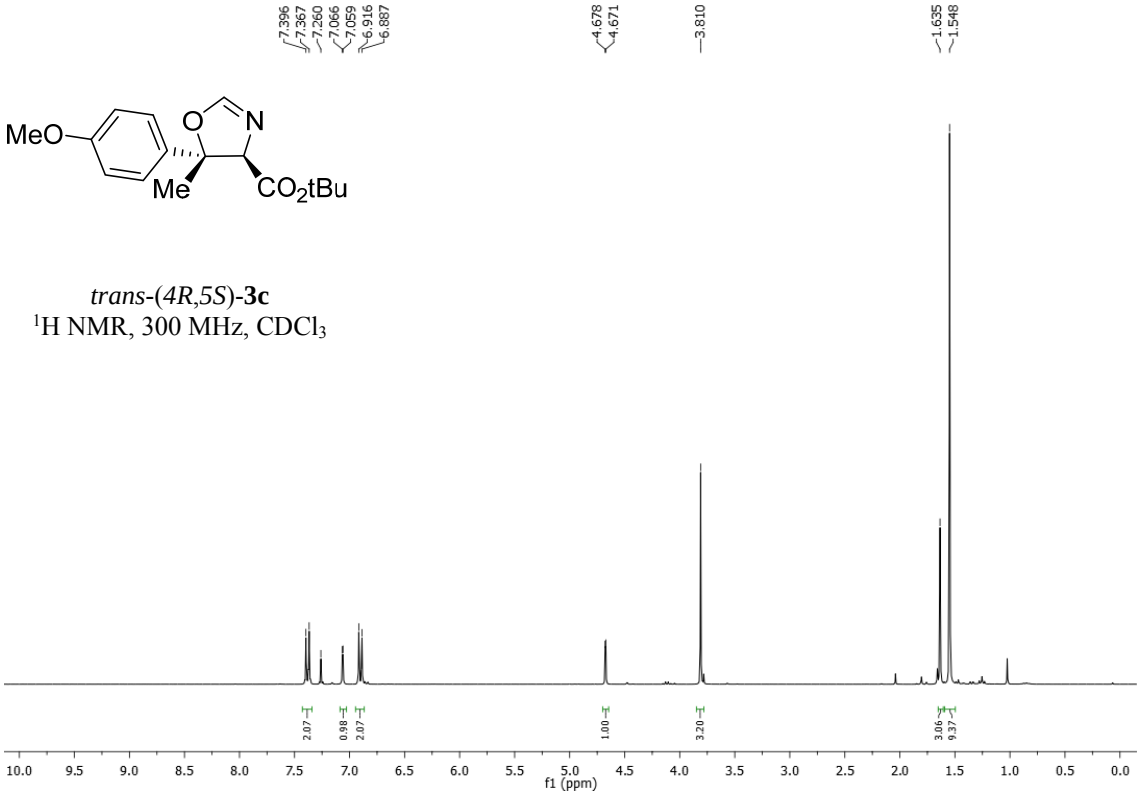
Retention Time	Area	Area Percent
20,48	1098444	1,228
24,71	493667	0,552
25,97	18455779	20,633
28,18	69399119	77,587



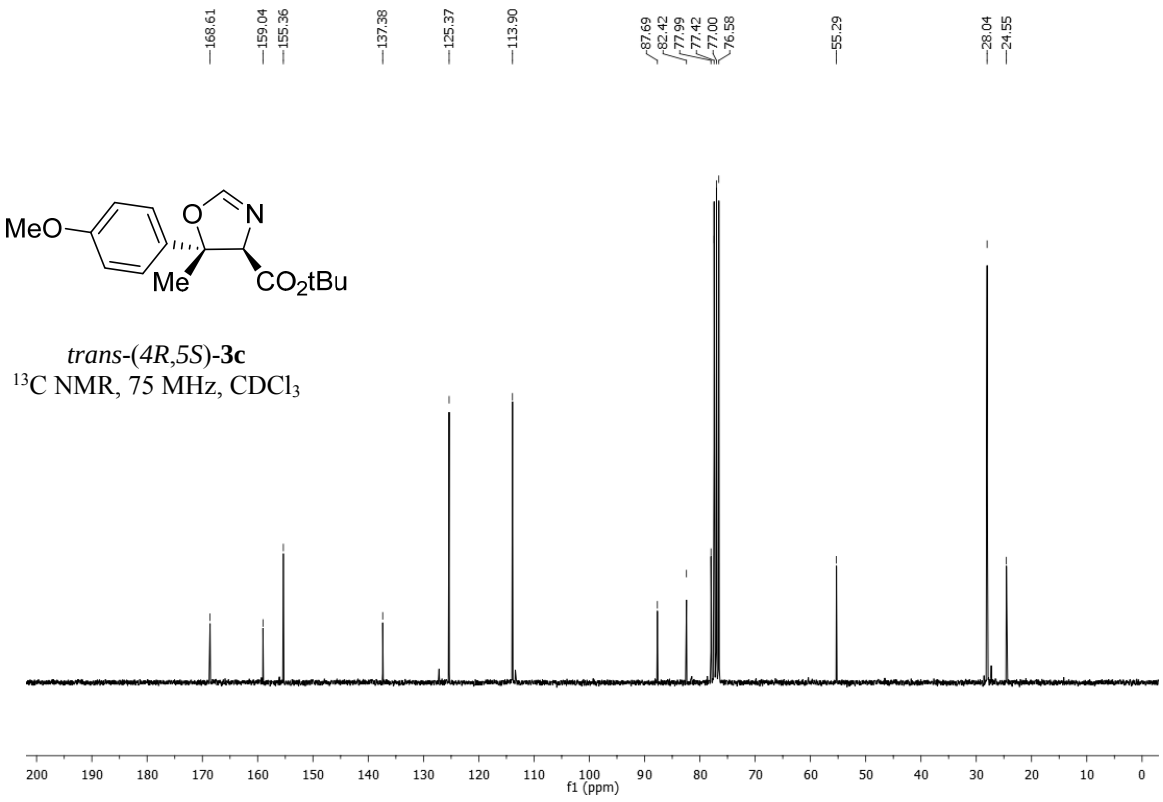
cis-(*4R*,*5R*)-**3c**
^{1}H NMR, 300 MHz, $CDCl_3$



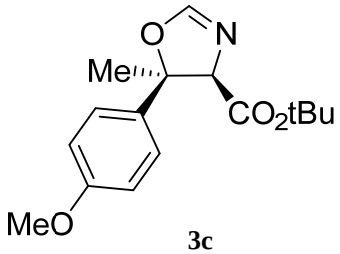
cis-(*4R*,*5R*)-**3c**
^{13}C NMR, 75 MHz, $CDCl_3$



trans-(*4R,5S*)-**3c**
^{1}H NMR, 300 MHz, $CDCl_3$

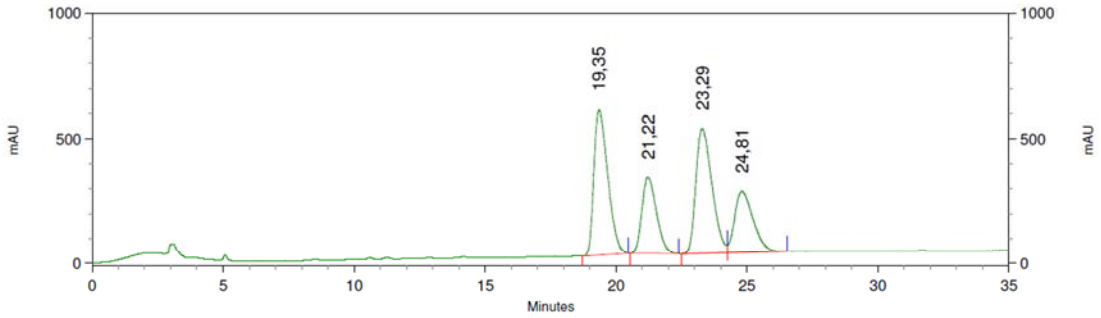


trans-(*4R,5S*)-**3c**
^{13}C NMR, 75 MHz, $CDCl_3$



3c

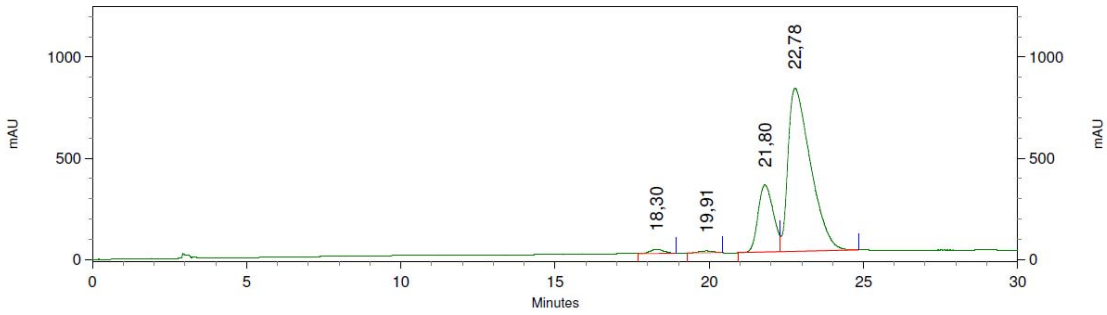
Racemic reaction:



8: 212 nm, 4 nm Results

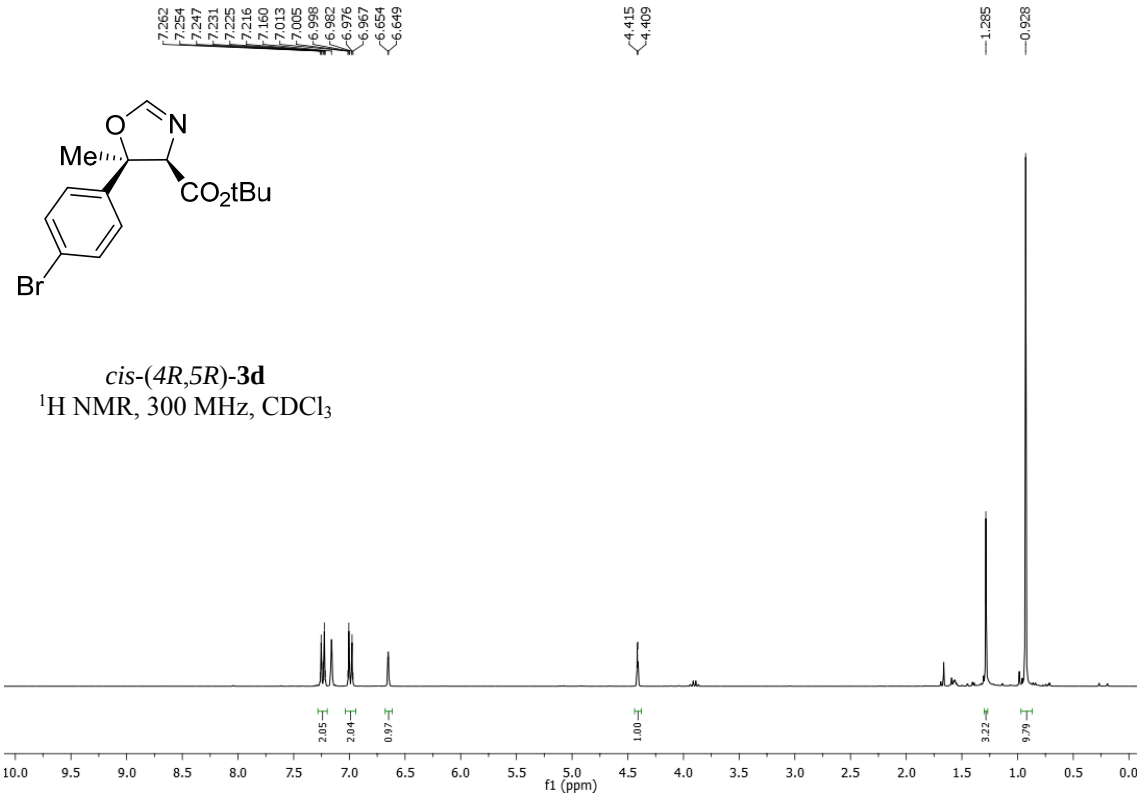
Retention Time	Area	Area Percent
19,35	85940035	32,073
21,22	47532591	17,739
23,29	85933267	32,070
24,81	48546824	18,118

Enantioselective reaction:

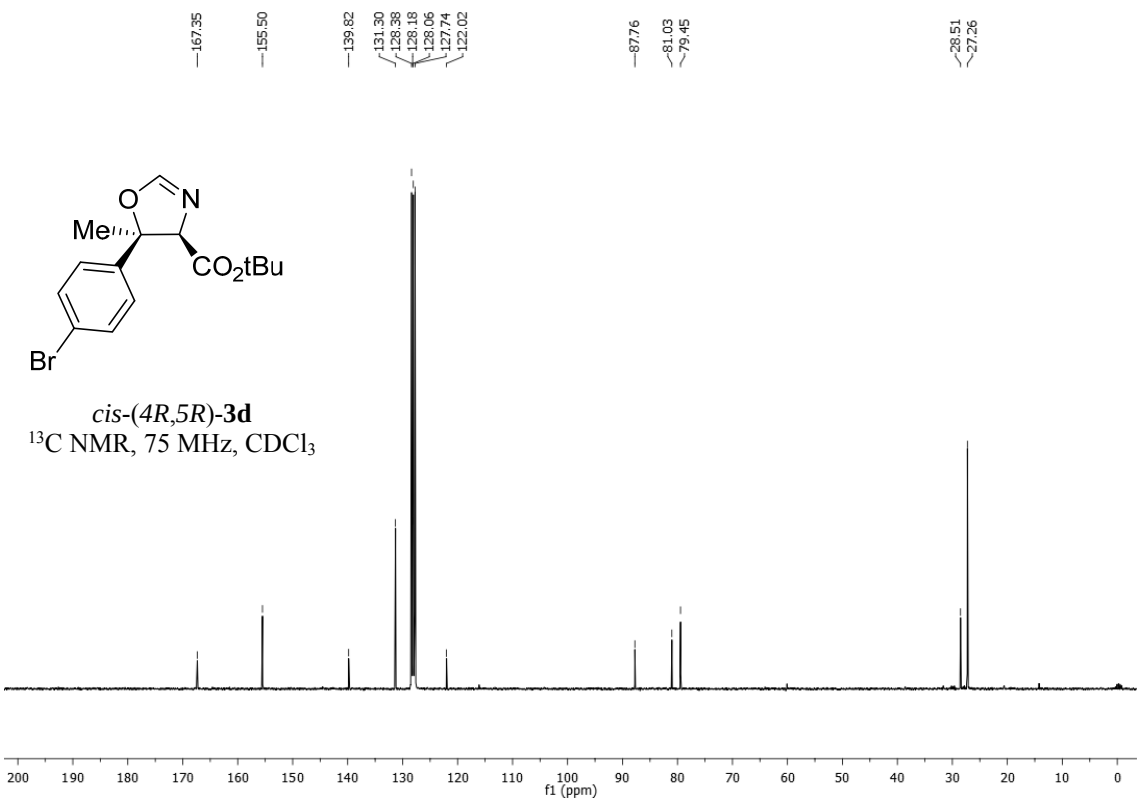


8: 212 nm, 4 nm Results

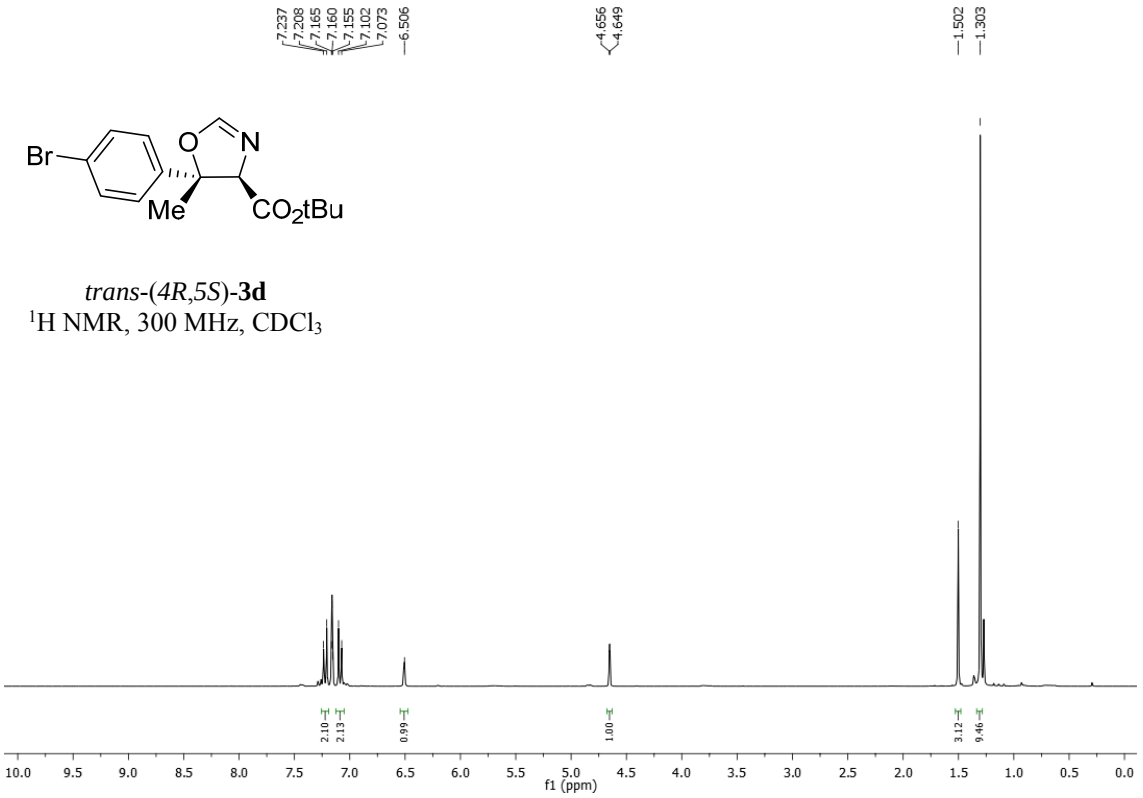
Retention Time	Area	Area Percent
18,30	2439418	1,145
19,91	1250170	0,587
21,80	45507464	21,366
22,78	163794066	76,902



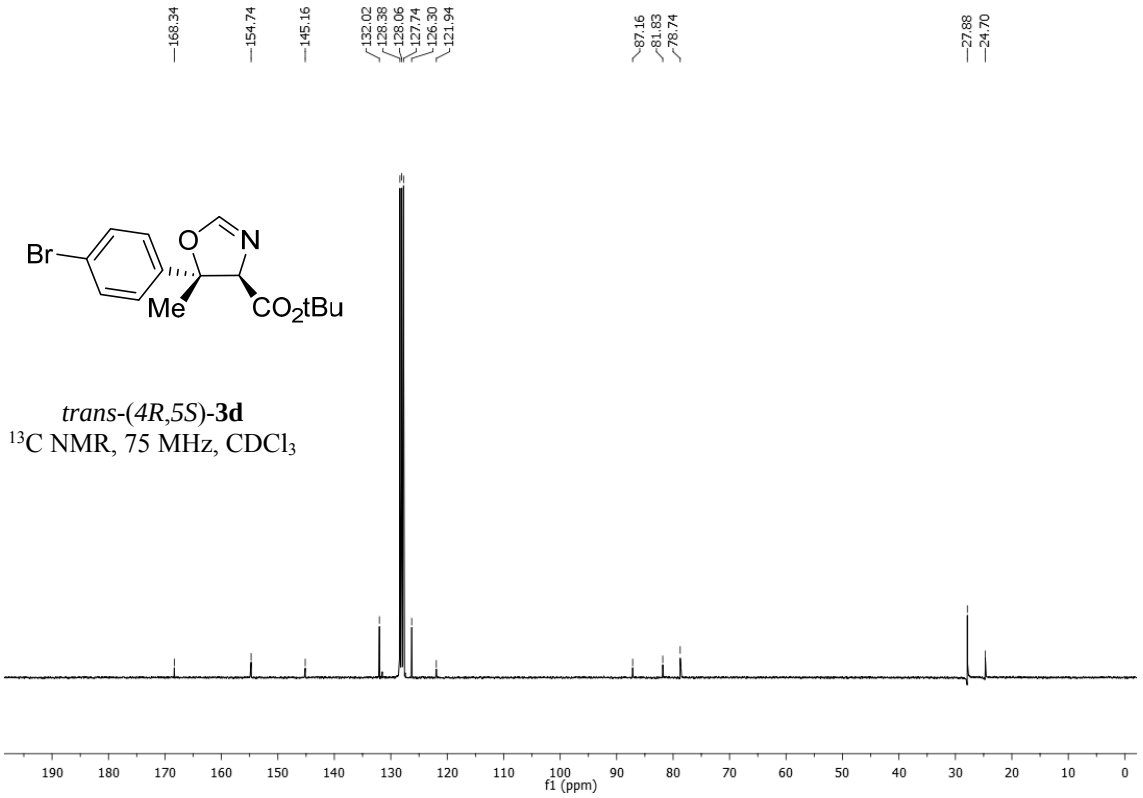
cis-(*4R,5R*)-**3d**
^{1}H NMR, 300 MHz, $CDCl_3$



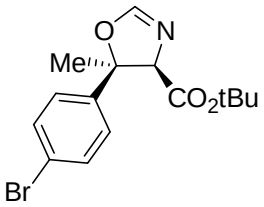
cis-(*4R,5R*)-**3d**
^{13}C NMR, 75 MHz, $CDCl_3$



trans-(*4R*,*5S*)-**3d**
^{1}H NMR, 300 MHz, $CDCl_3$

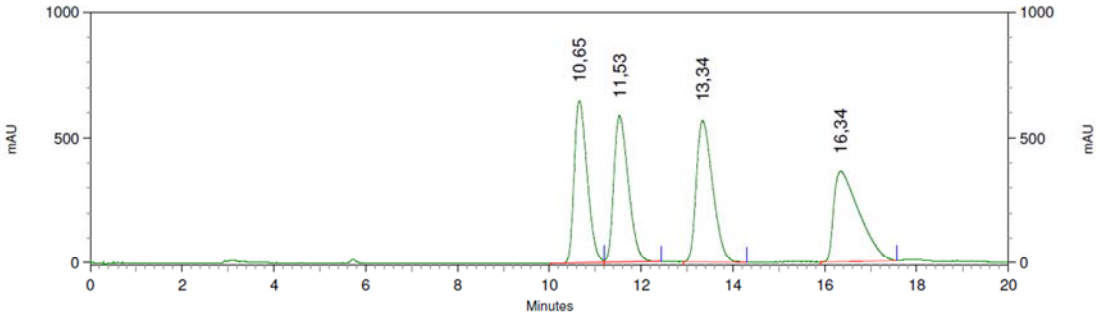


trans-(*4R*,*5S*)-**3d**
^{13}C NMR, 75 MHz, $CDCl_3$



3d

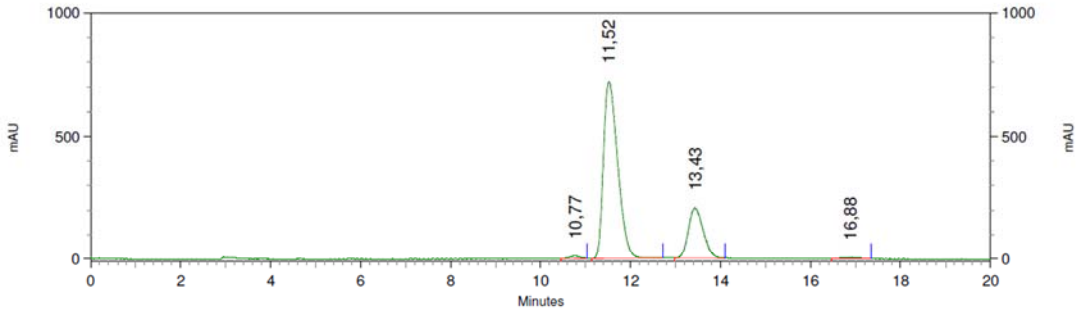
Racemic reaction:



14: 237 nm, 4 nm
Results

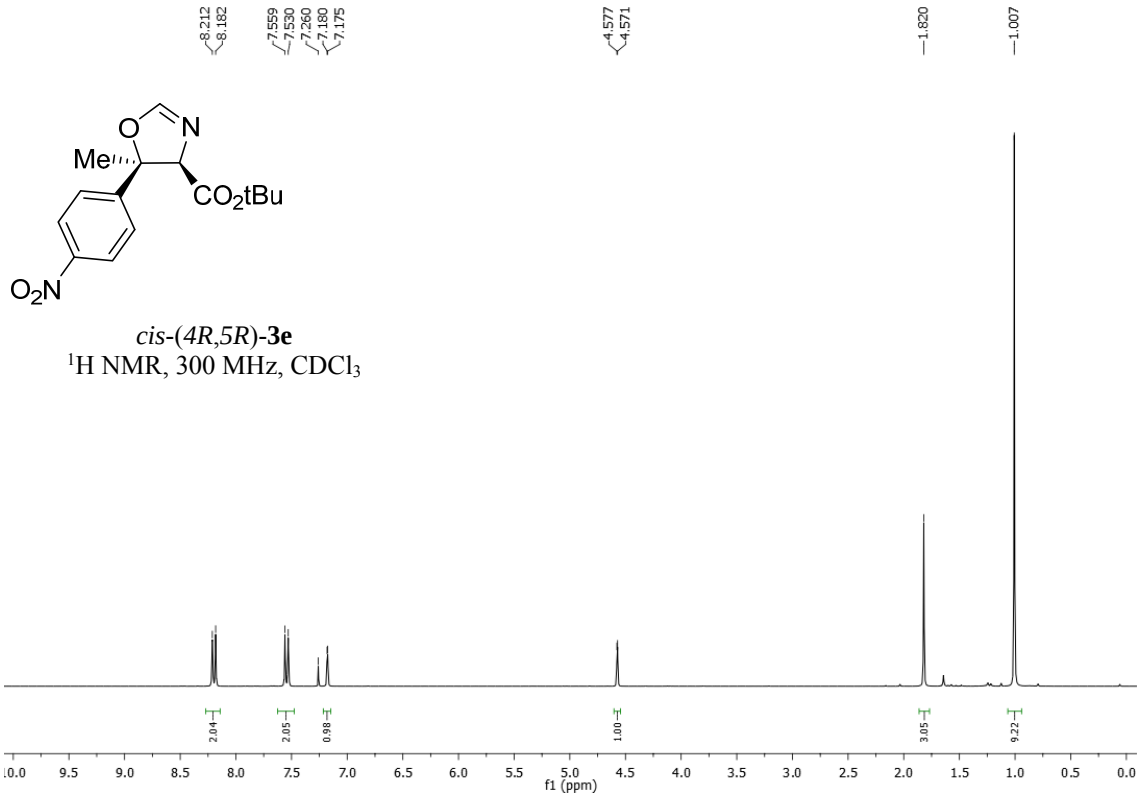
Retention Time	Area	Area Percent
10,65	51045681	23,684
11,53	51834264	24,049
13,34	56489693	26,209
16,34	56162232	26,058

Enantioselective reaction:

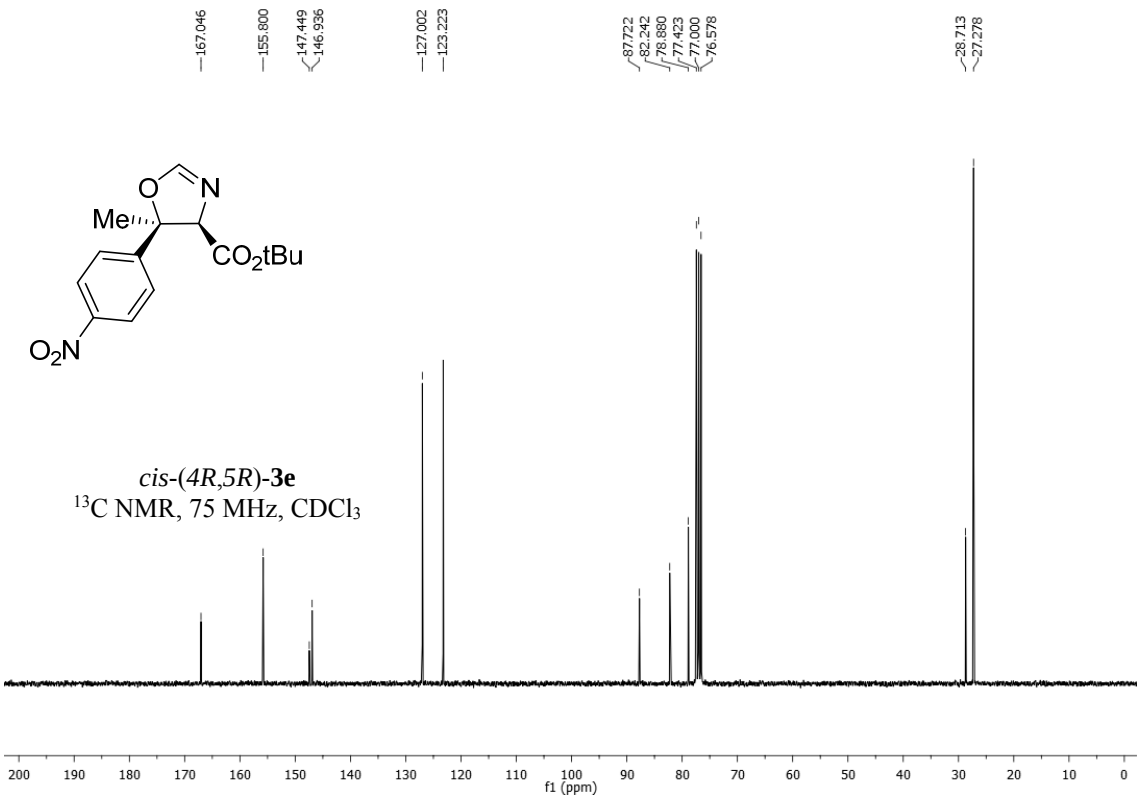


14: 237 nm, 4 nm
Results

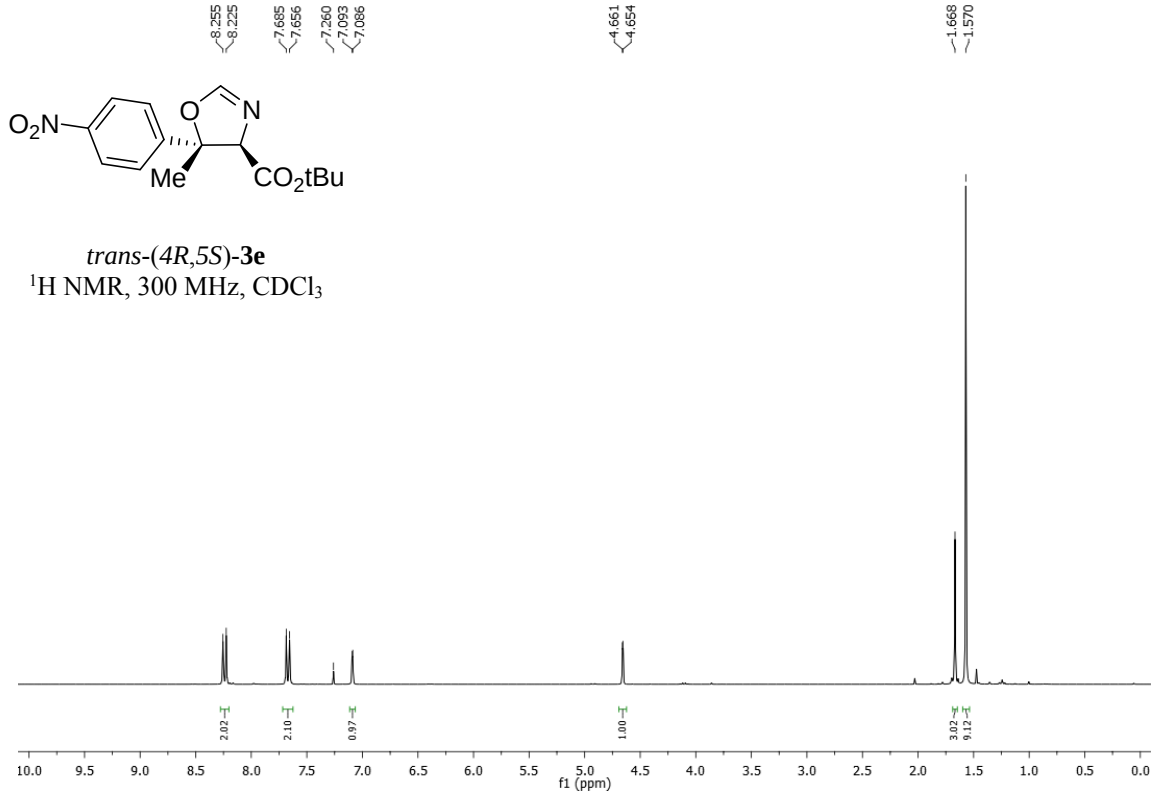
Retention Time	Area	Area Percent
10,77	731799	0,869
11,52	63730897	75,665
13,43	19066000	22,636
16,88	698788	0,830



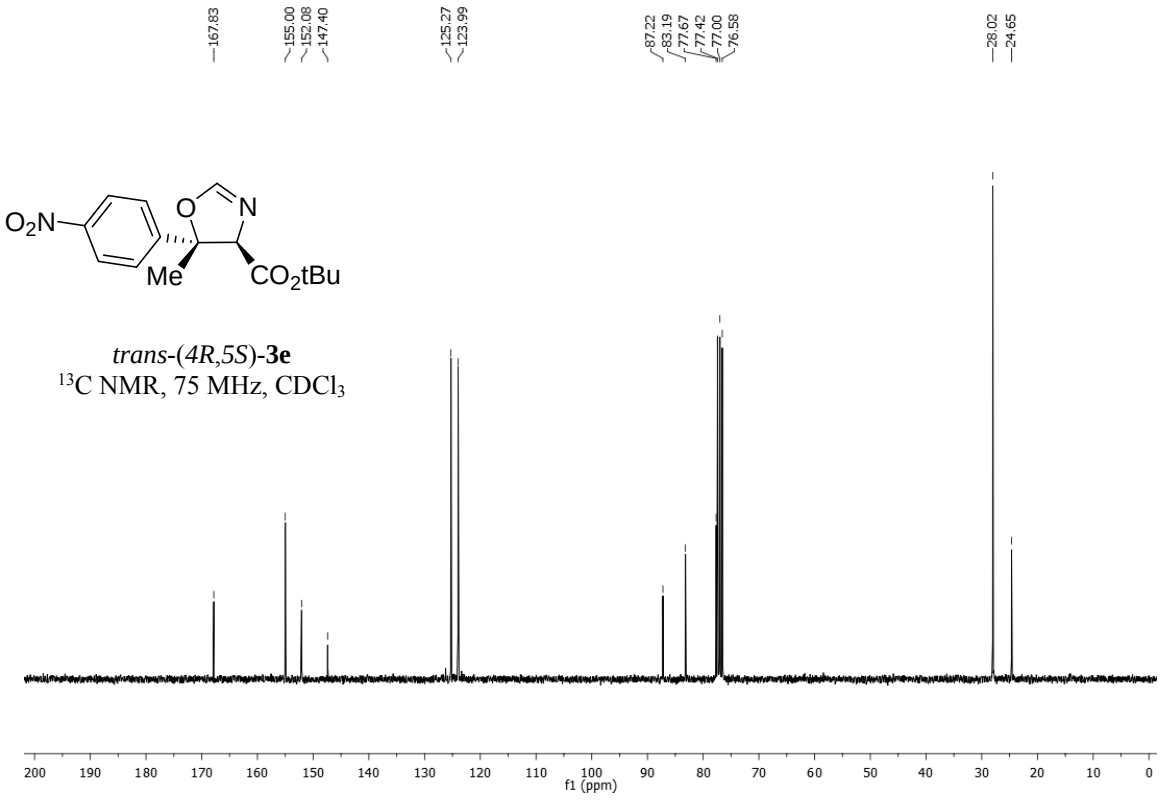
cis-(*4R*,*5R*)-**3e**
^{1}H NMR, 300 MHz, $CDCl_3$



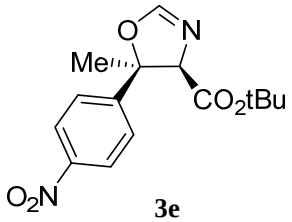
cis-(*4R*,*5R*)-**3e**
^{13}C NMR, 75 MHz, $CDCl_3$



trans-(*4R,5S*)-**3e**
^{1}H NMR, 300 MHz, $CDCl_3$

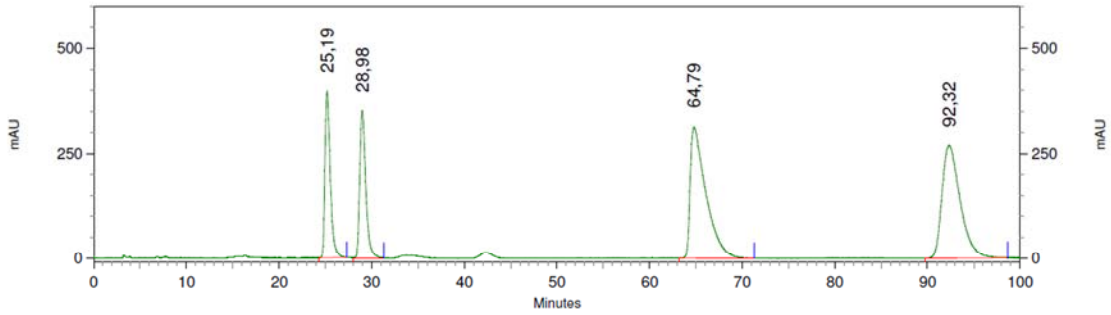


trans-(*4R,5S*)-**3e**
^{13}C NMR, 75 MHz, $CDCl_3$



3e

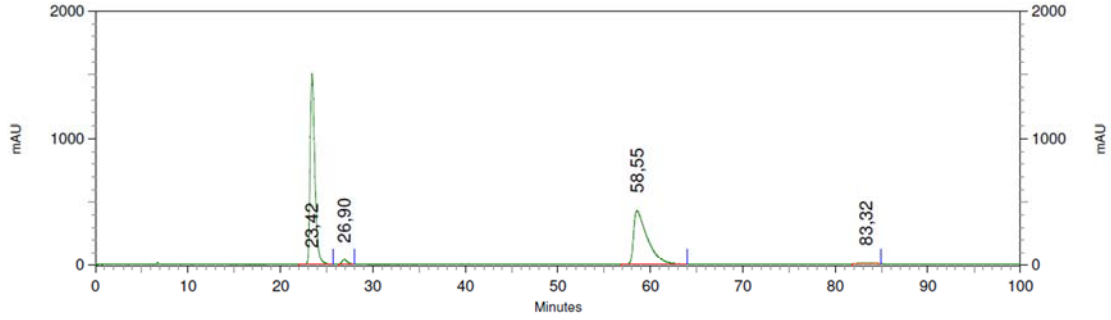
Racemic reaction:



9: 257 nm, 4 nm Results

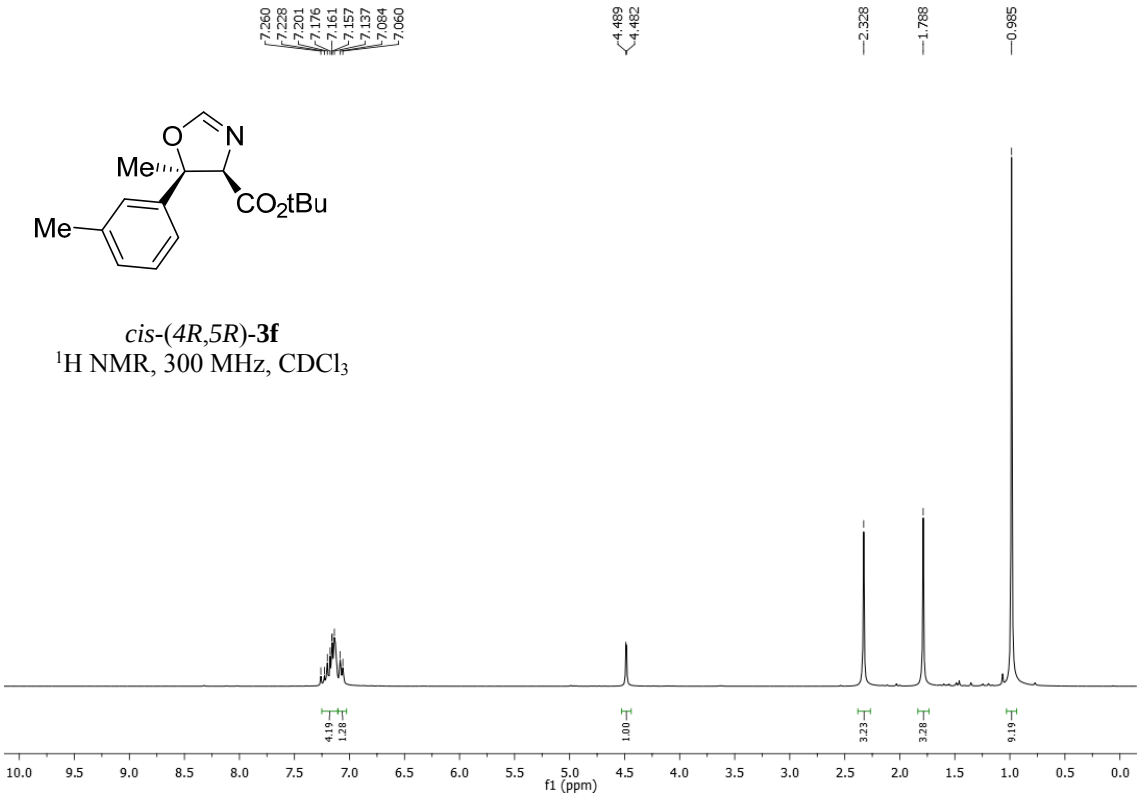
Retention Time	Area	Area Percent
25,19	63509620	14,998
28,98	63253607	14,938
64,79	148698347	35,116
92,32	147993405	34,949

Enantioselective reaction:

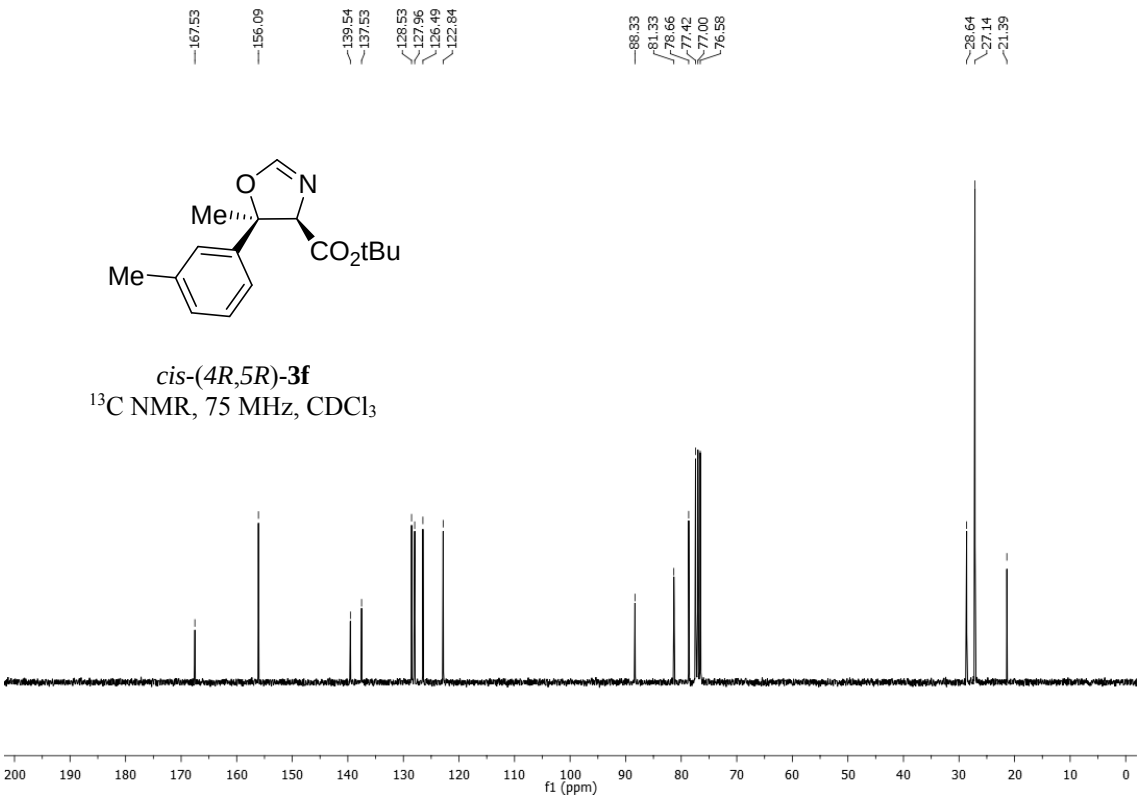


9: 257 nm, 4 nm Results

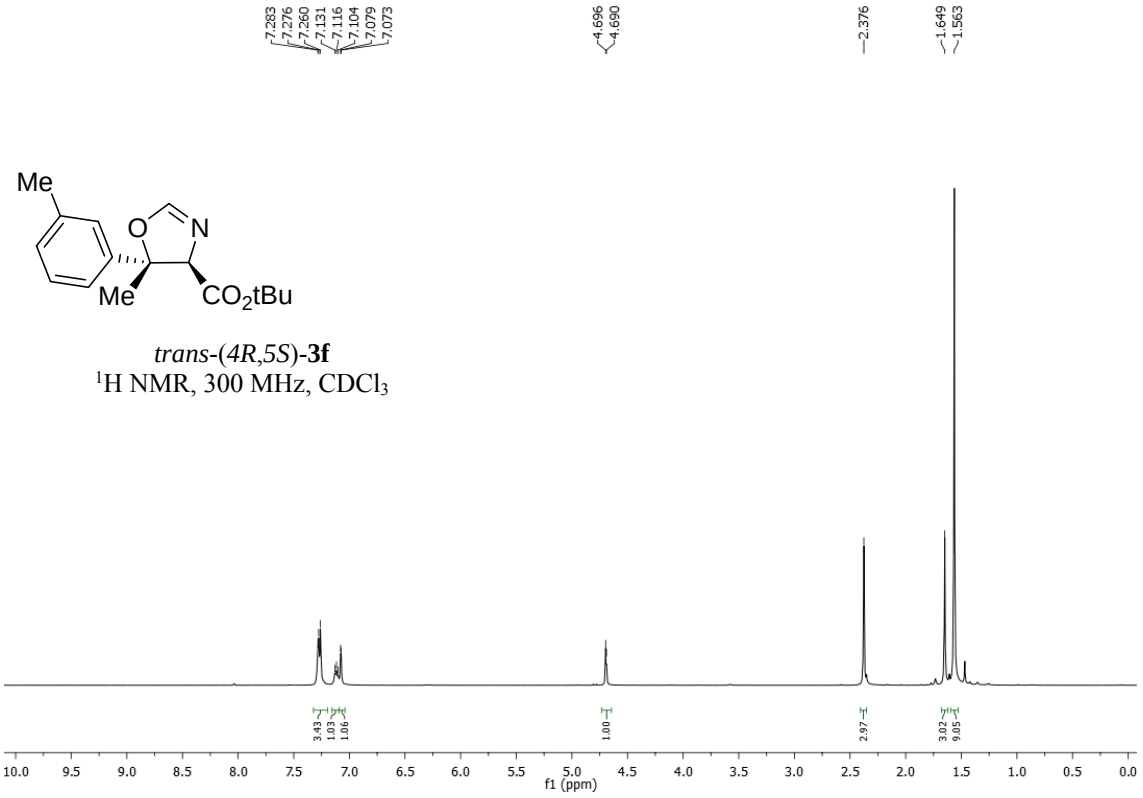
Retention Time	Area	Area Percent
23,42	212462277	53,478
26,90	5546468	1,396
58,55	175890516	44,273
83,32	3391067	0,854



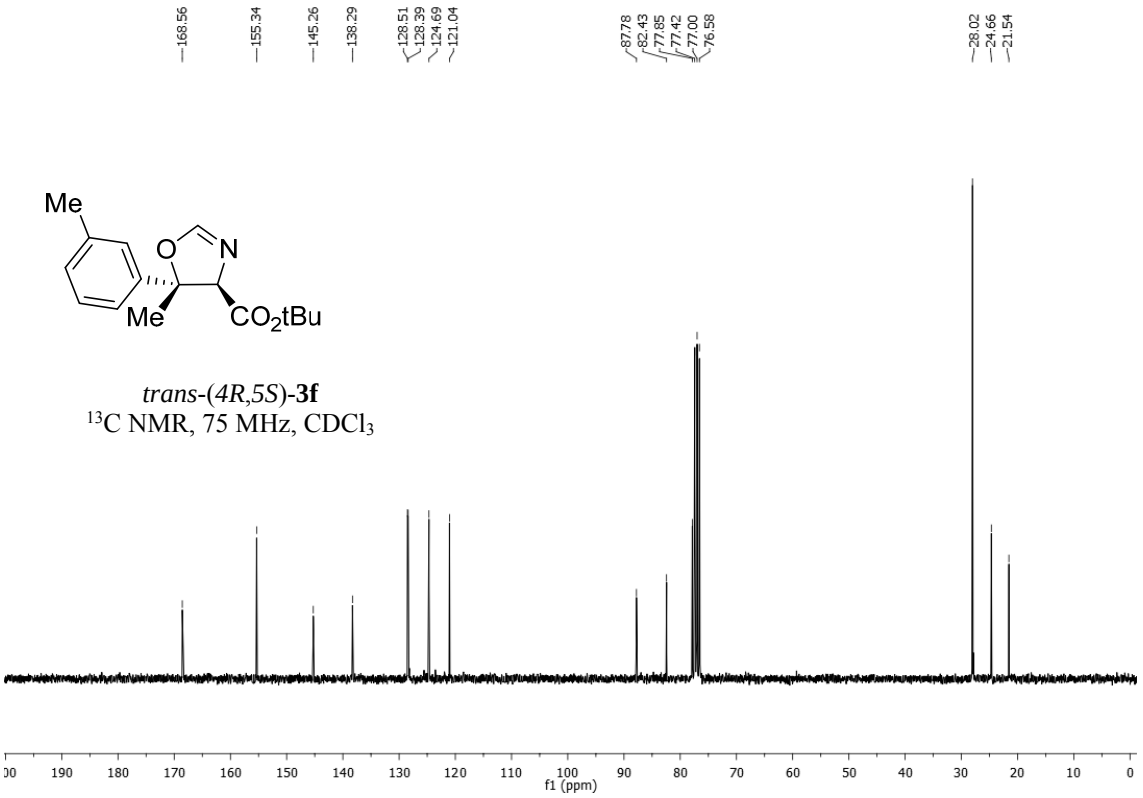
cis-(*4R,5R*)-**3f**
^{1}H NMR, 300 MHz, $CDCl_3$



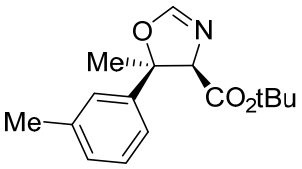
cis-(*4R,5R*)-**3f**
^{13}C NMR, 75 MHz, $CDCl_3$



trans-(*4R*,*5S*)-**3f**
^{1}H NMR, 300 MHz, $CDCl_3$

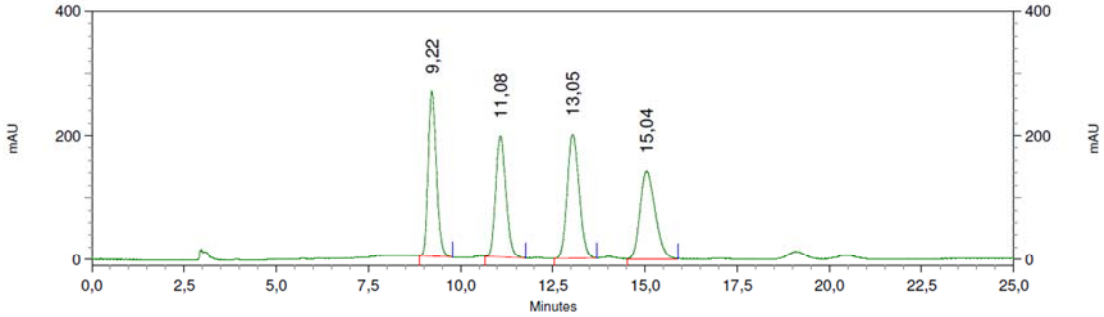


trans-(*4R*,*5S*)-**3f**
^{13}C NMR, 75 MHz, $CDCl_3$



3f

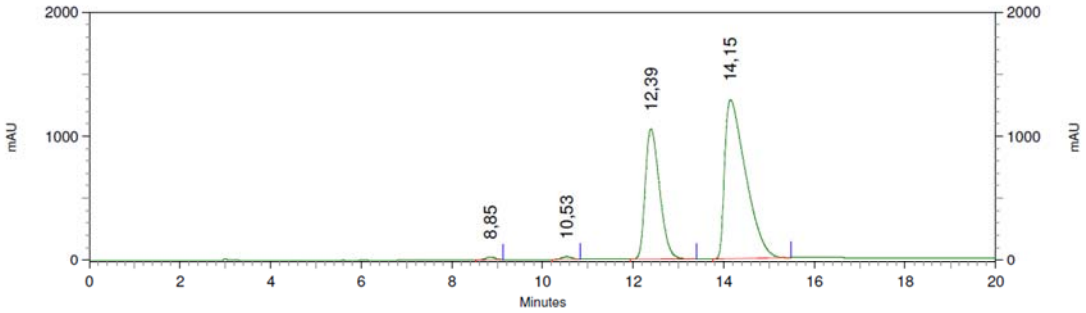
Racemic reaction:



9: 219 nm, 4 nm Results

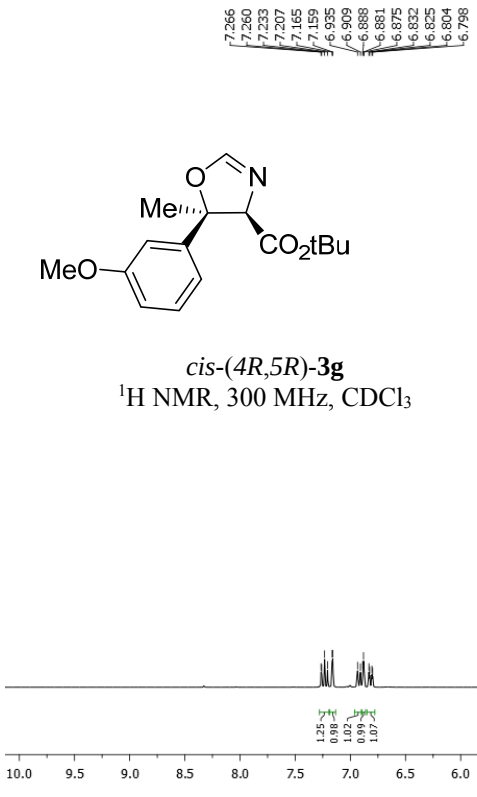
Retention Time	Area	Area Percent
9,22	16555906	25,065
11,08	15199852	23,012
13,05	18033860	27,303
15,04	16261925	24,620

Enantioselective reaction:

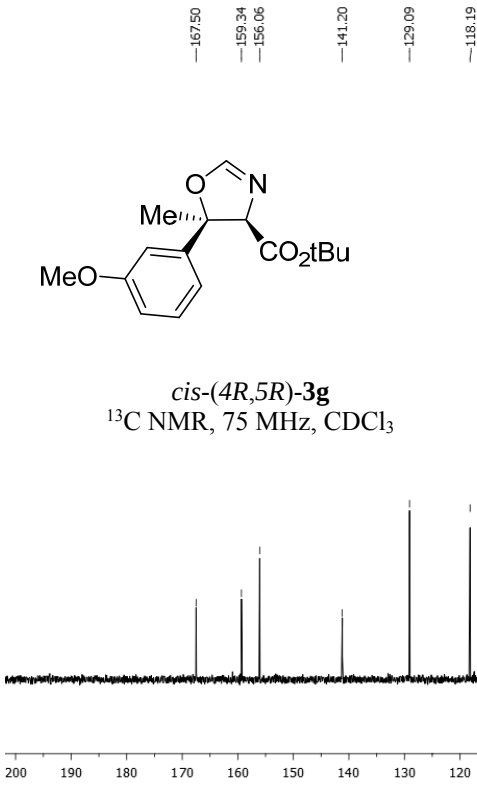


10: 219 nm, 4 nm Results

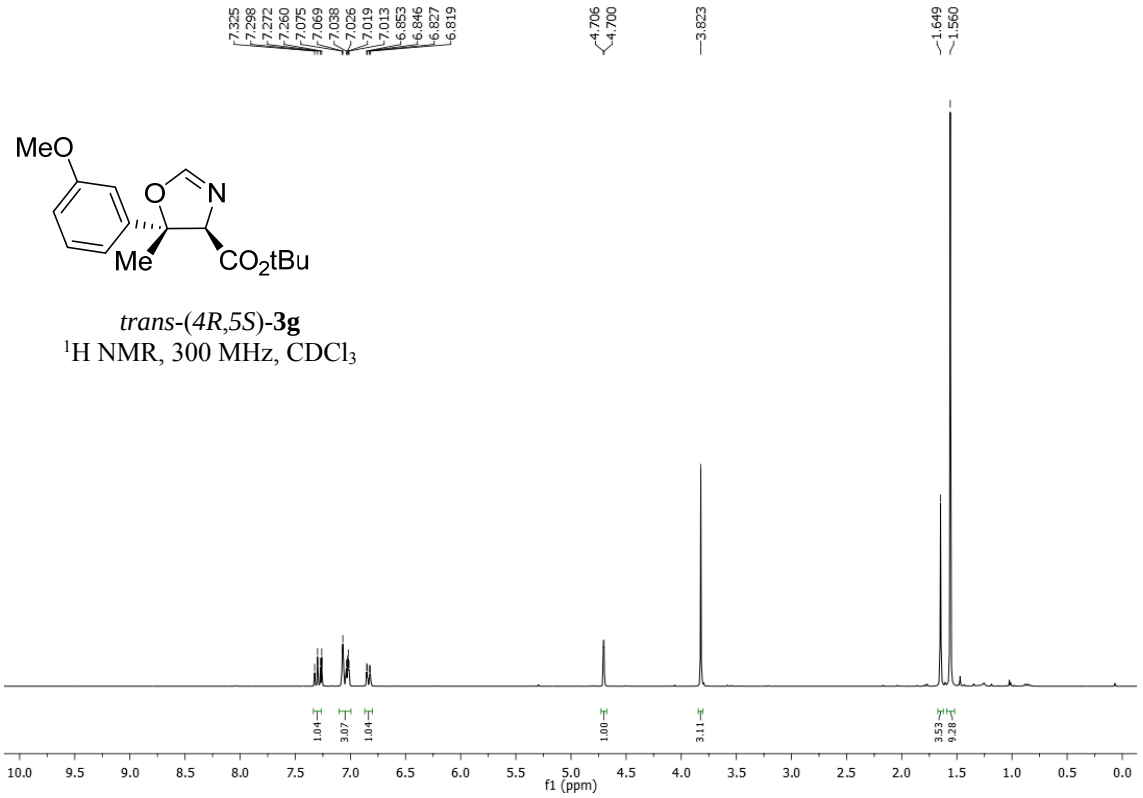
Retention Time	Area	Area Percent
8,85	1369769	0,526
10,53	1456468	0,559
12,39	92816253	35,614
14,15	164976196	63,302



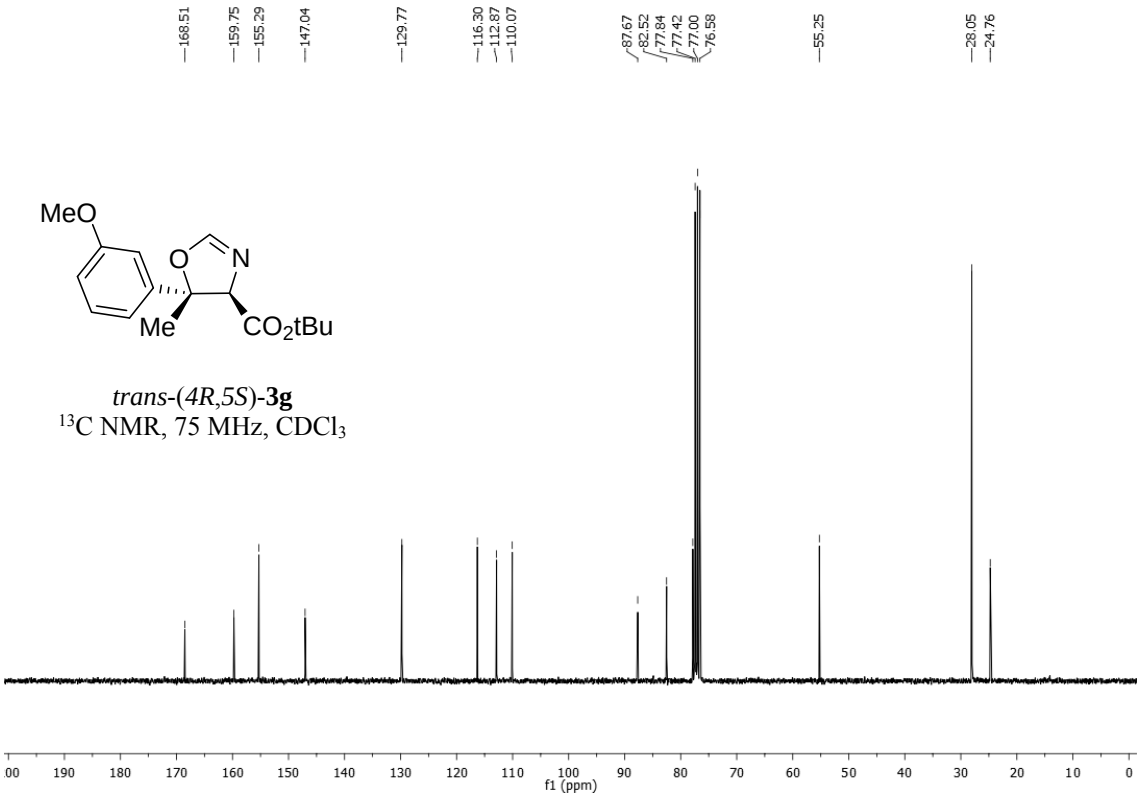
cis-(*4R*,*5R*)-**3g**
^{1}H NMR, 300 MHz, $CDCl_3$



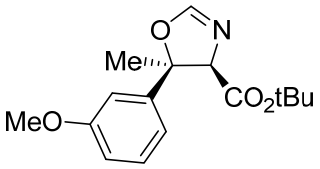
cis-(*4R*,*5R*)-**3g**
^{13}C NMR, 75 MHz, $CDCl_3$



trans-(*4R*,*5S*)-**3g**
^{1}H NMR, 300 MHz, $CDCl_3$

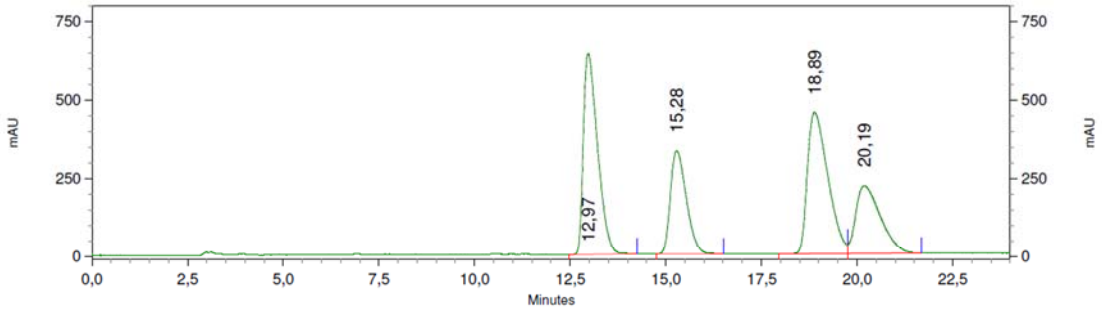


trans-(*4R*,*5S*)-**3g**
^{13}C NMR, 75 MHz, $CDCl_3$



3g

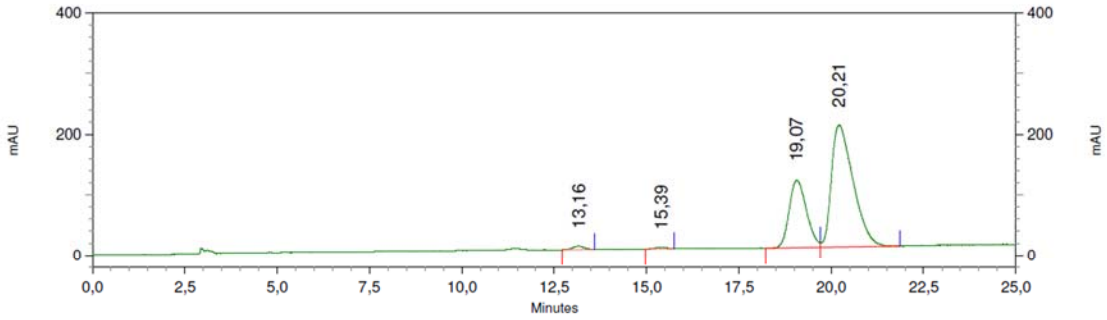
Racemic reaction:



8: 232 nm, 4 nm Results

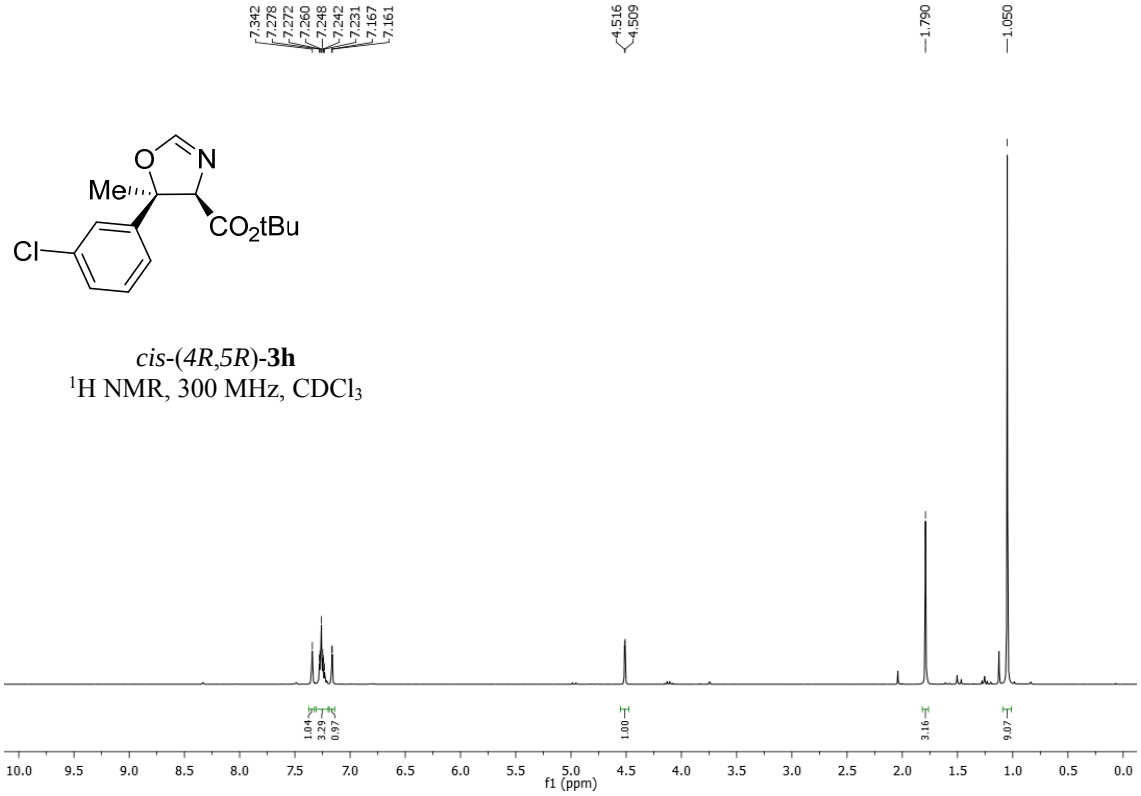
Retention Time	Area	Area Percent
12,97	66770074	31,523
15,28	38456426	18,156
18,89	67281484	31,765
20,19	39303157	18,556

Enantioselective reaction:

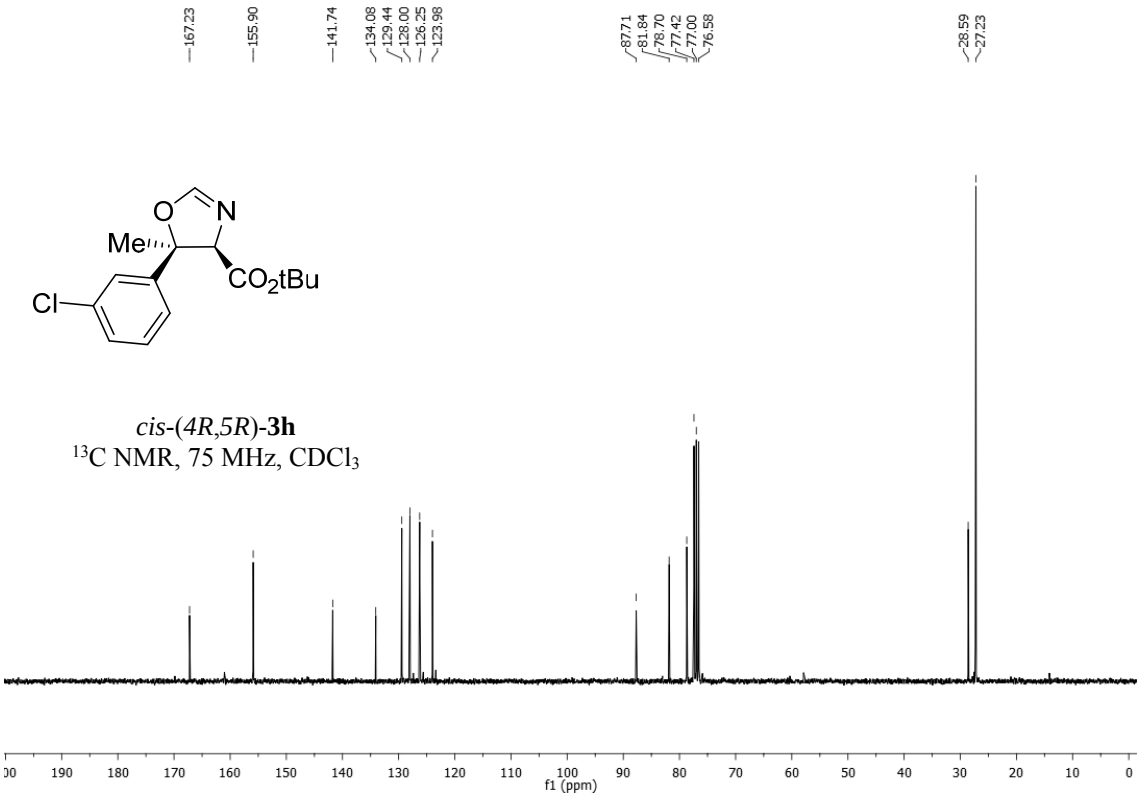


8: 232 nm, 4 nm Results

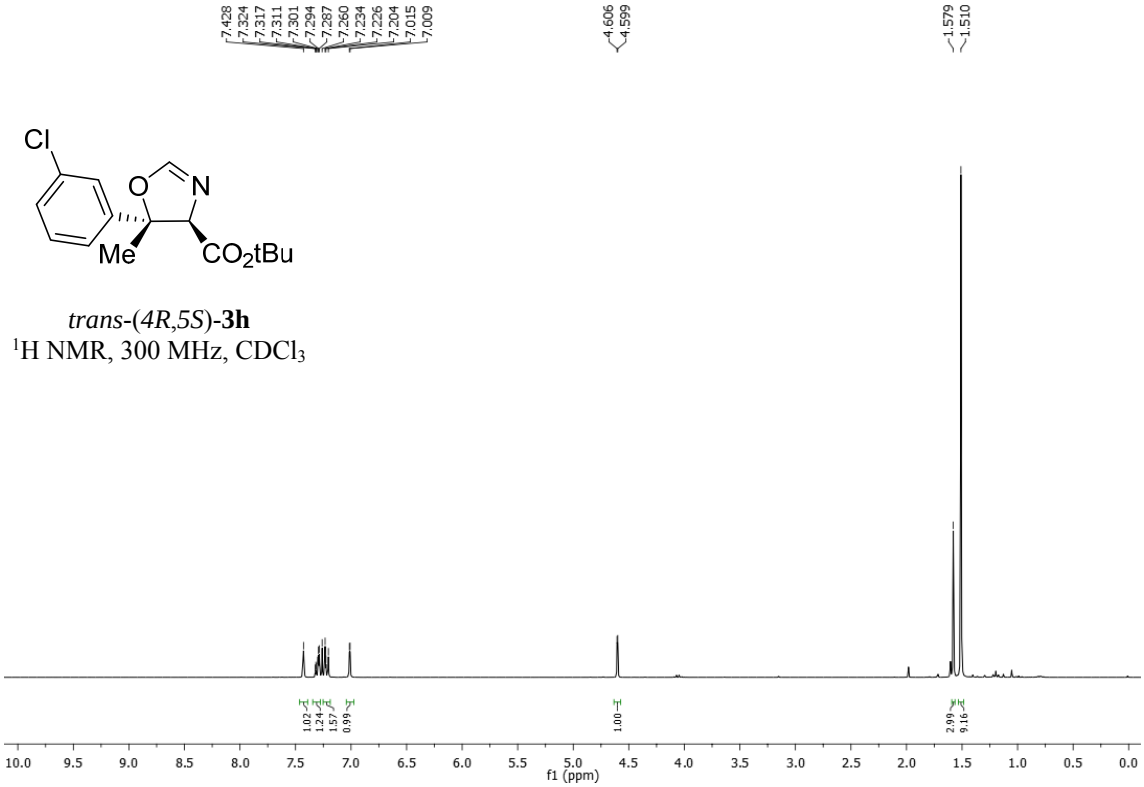
Retention Time	Area	Area Percent
13,16	512432	1,060
15,39	274666	0,568
19,07	14473743	29,944
20,21	33074828	68,427



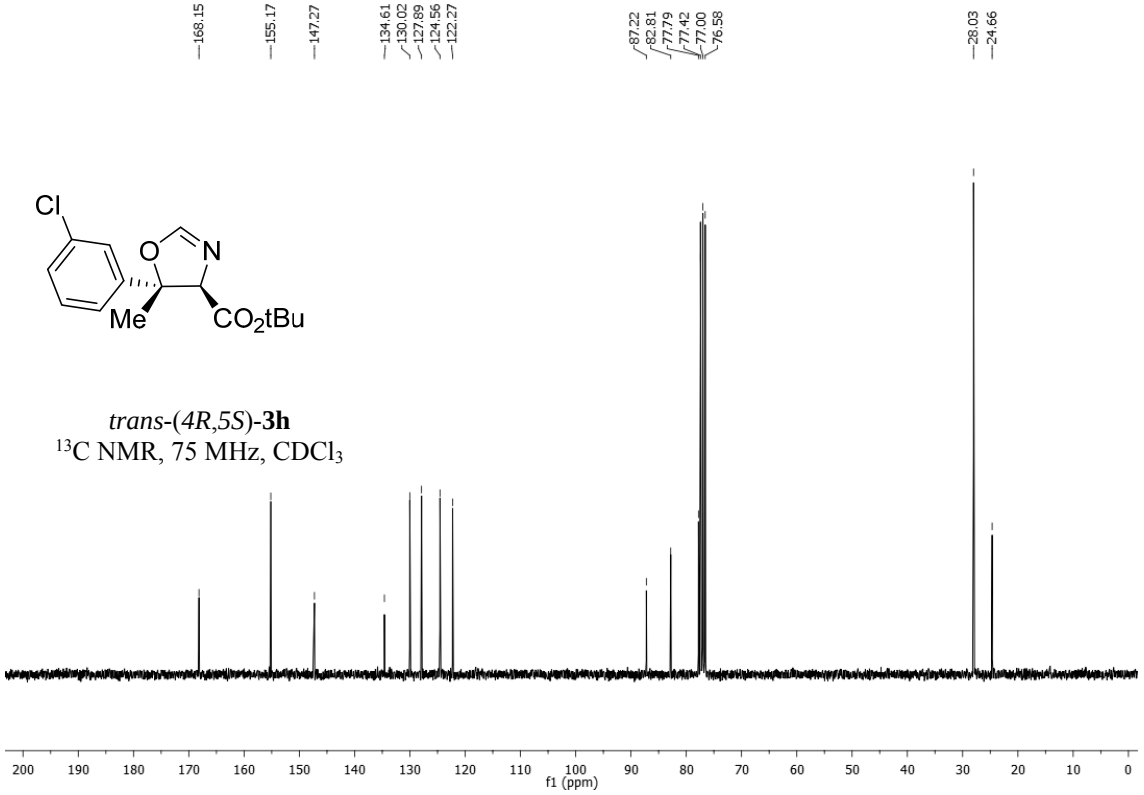
cis-(*4R*,*5R*)-**3h**
^{1}H NMR, 300 MHz, $CDCl_3$



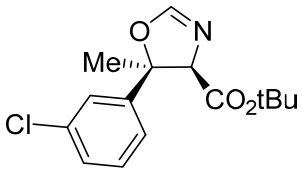
cis-(*4R*,*5R*)-**3h**
^{13}C NMR, 75 MHz, $CDCl_3$



trans-(*4R*,*5S*)-**3h**
^{1}H NMR, 300 MHz, $CDCl_3$

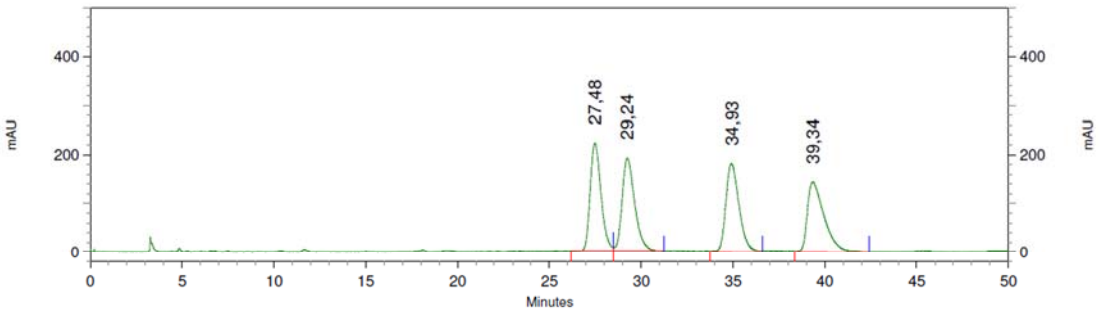


trans-(*4R*,*5S*)-**3h**
^{13}C NMR, 75 MHz, $CDCl_3$



3h

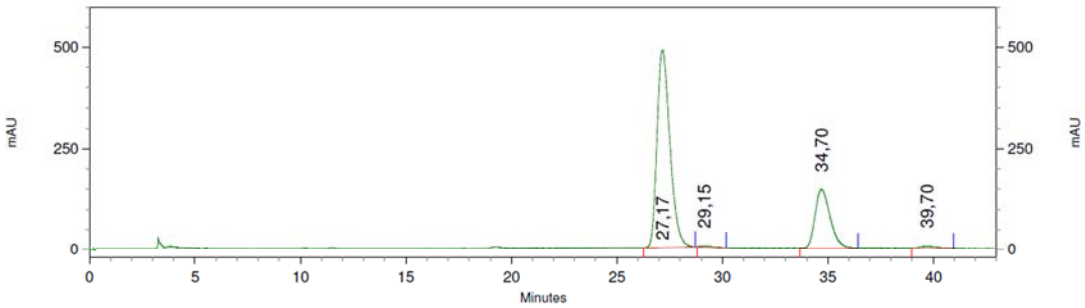
Racemic reaction:



8: 225 nm, 4 nm Results

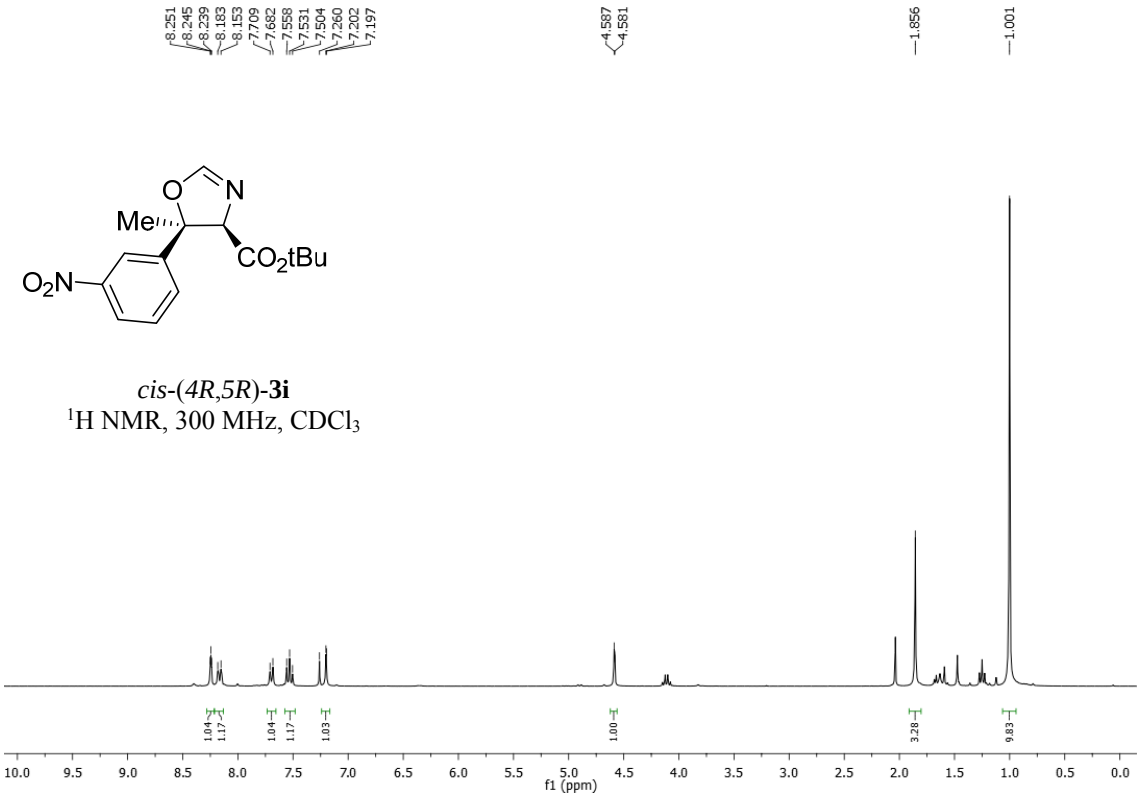
Retention Time	Area	Area Percent
27,48	36559769	25,091
29,24	36868724	25,303
34,93	35924630	24,655
39,34	36354001	24,950

Enantioselective reaction:

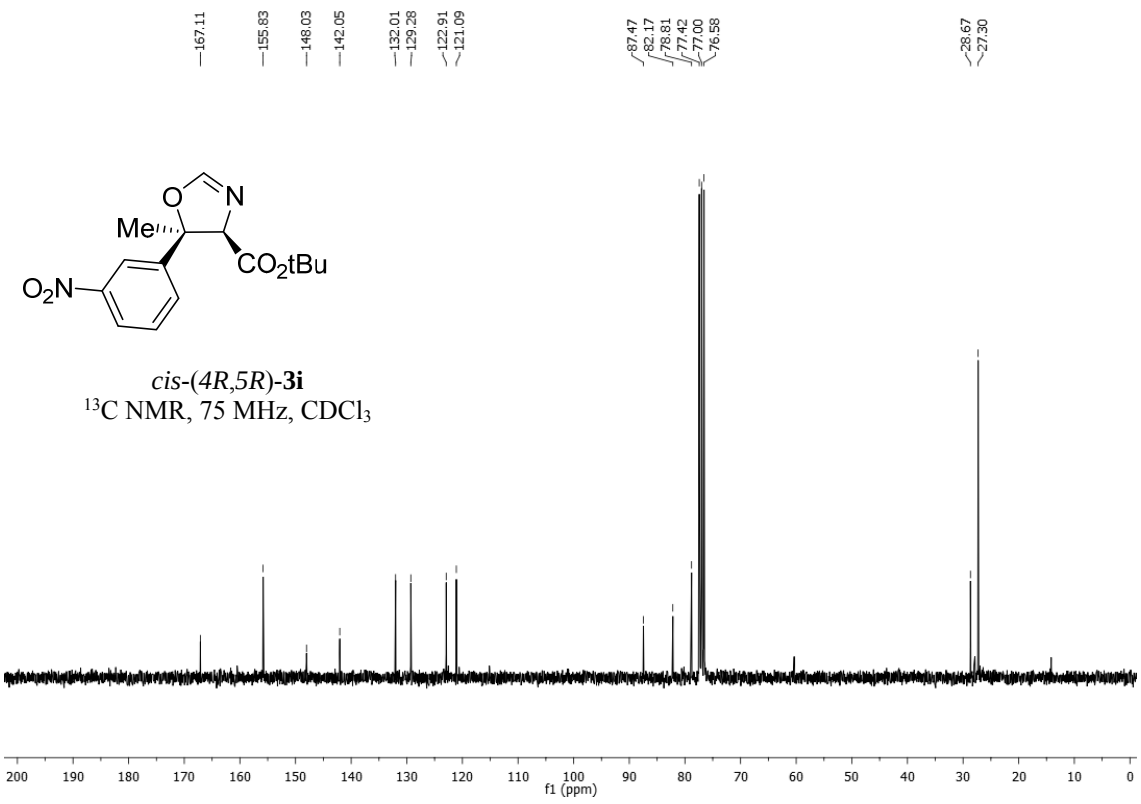


8: 225 nm, 4 nm Results

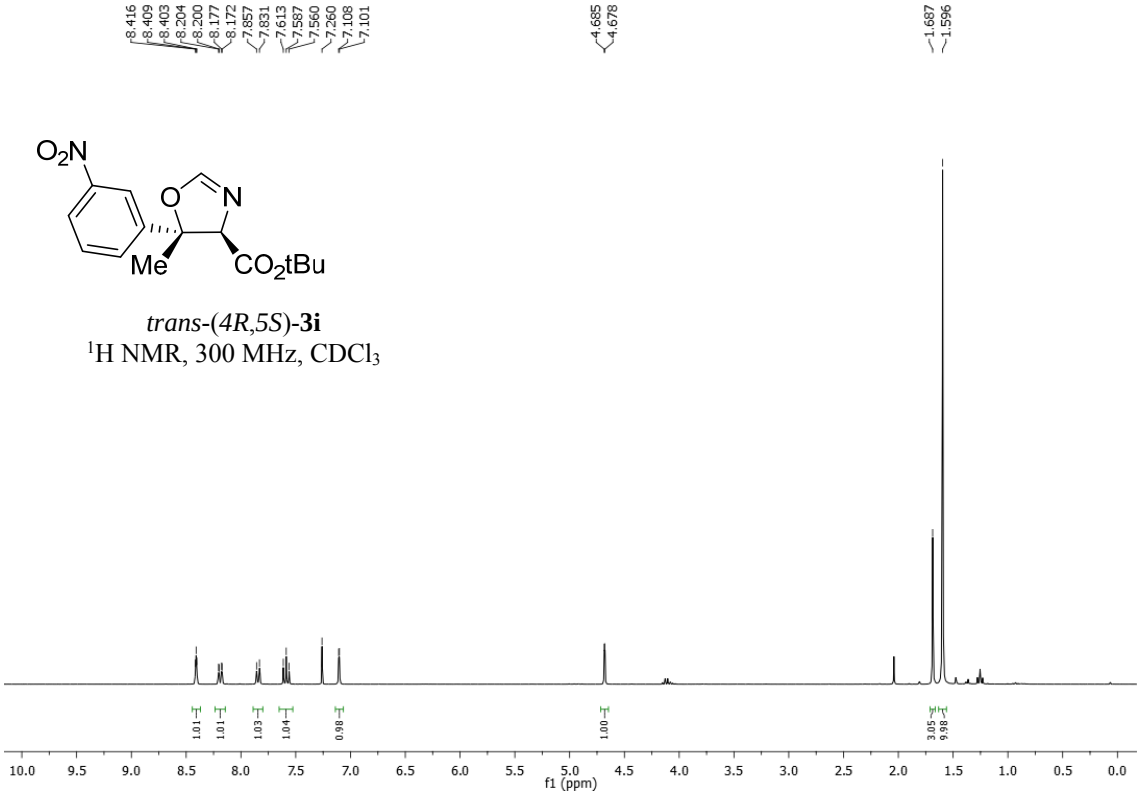
Retention Time	Area	Area Percent
27,17	83137610	72,615
29,15	583460	0,510
34,70	29405530	25,684
39,70	1364290	1,192



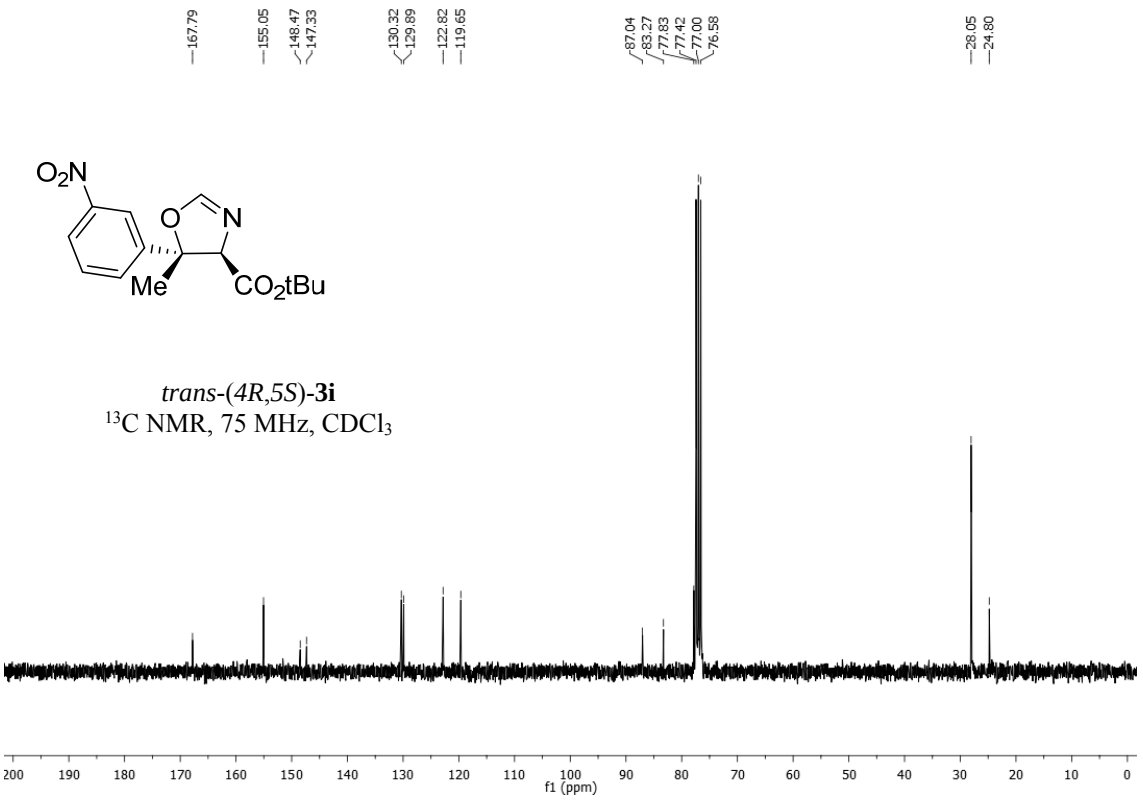
cis-(*4R,5R*)-**3i**
^{1}H NMR, 300 MHz, $CDCl_3$



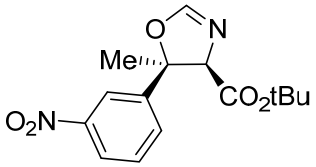
cis-(*4R,5R*)-**3i**
^{13}C NMR, 75 MHz, $CDCl_3$



trans-(*4R*,*5S*)-**3i**
^{1}H NMR, 300 MHz, $CDCl_3$

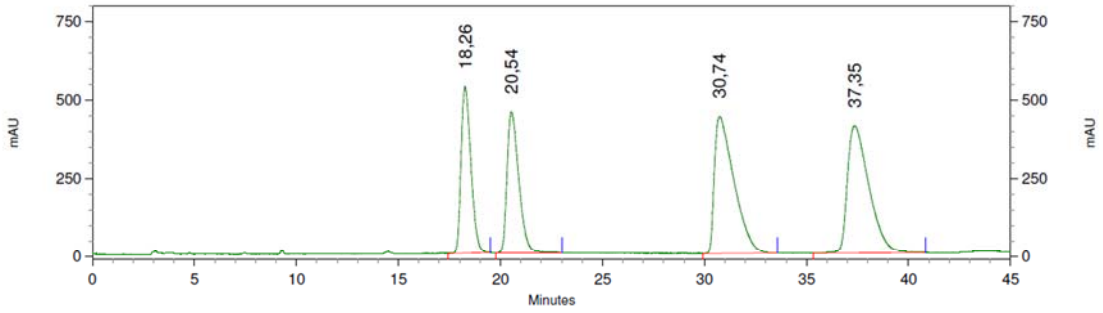


trans-(*4R*,*5S*)-**3i**
^{13}C NMR, 75 MHz, $CDCl_3$



3i

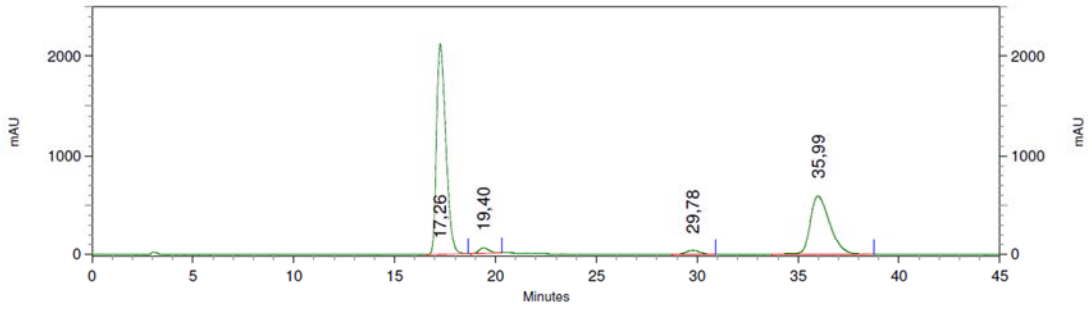
Racemic reaction:



9: 230 nm, 4 nm Results

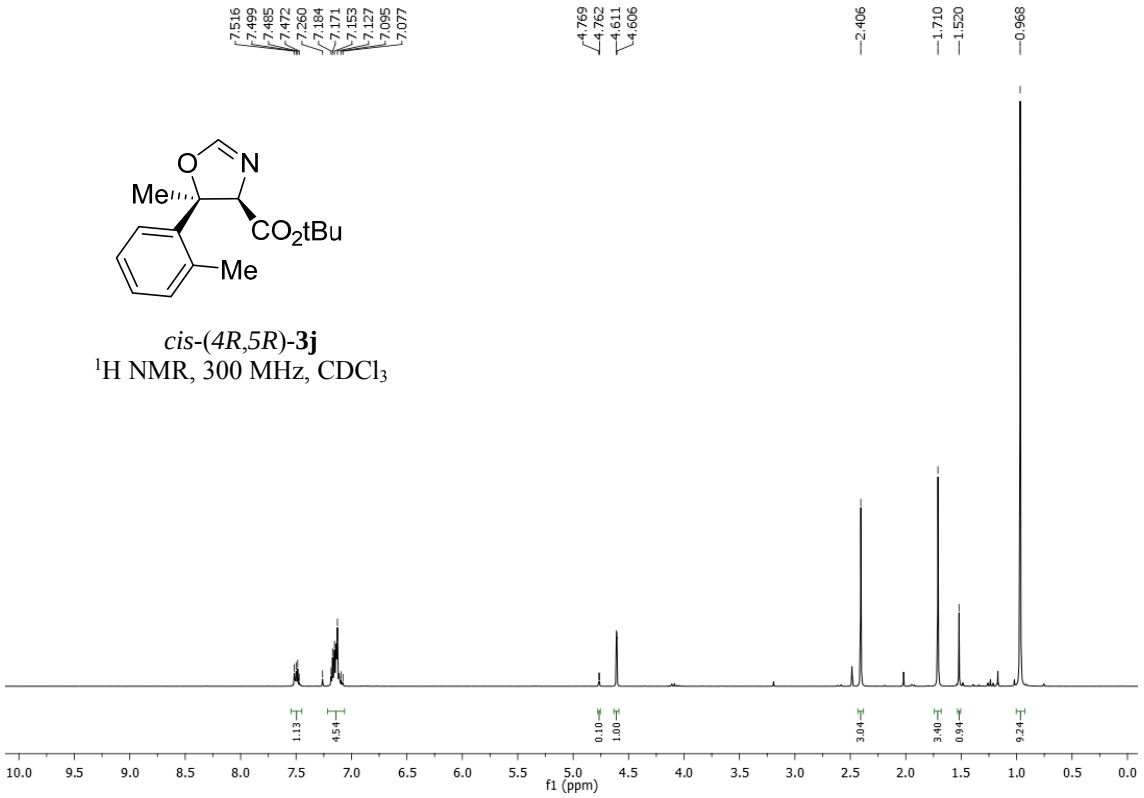
Retention Time	Area	Area Percent
18,26	71281400	18,746
20,54	72083722	18,957
30,74	116904287	30,743
37,35	119988579	31,555

Enantioselective reaction:

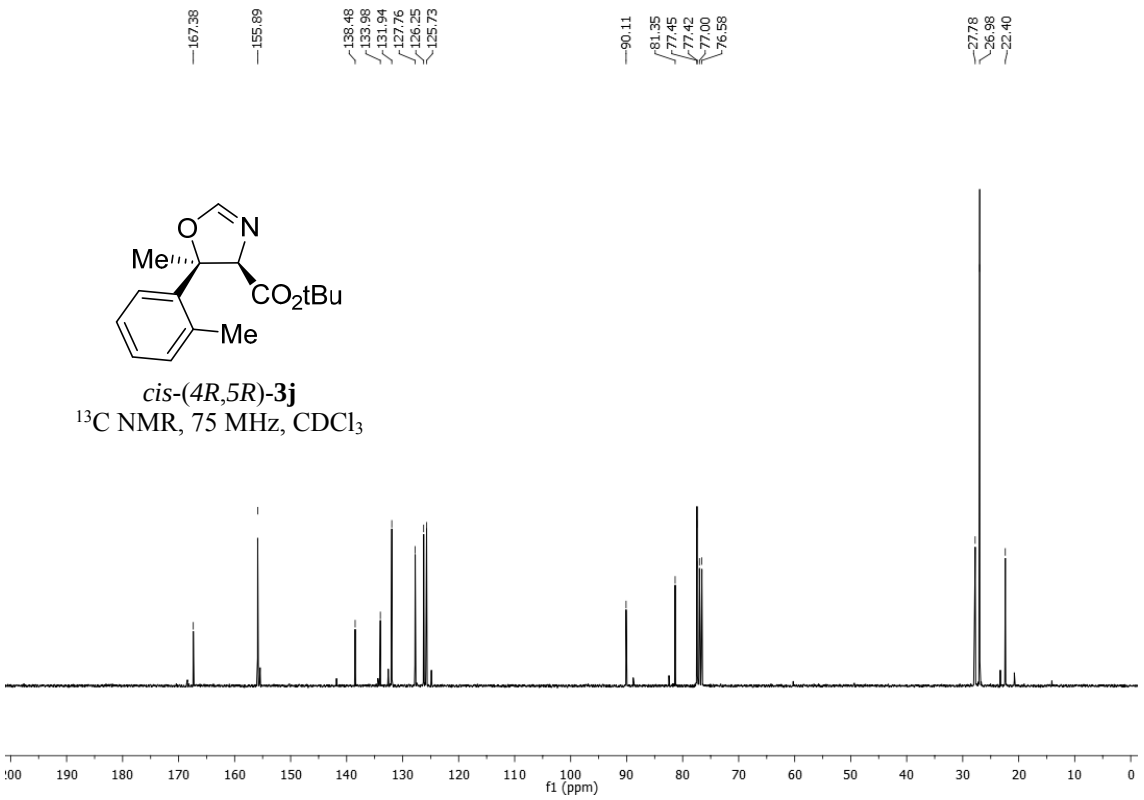


9: 212 nm, 4 nm Results

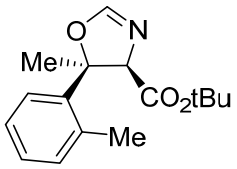
Retention Time	Area	Area Percent
17,26	273275974	60,501
19,40	7674145	1,699
29,78	8654674	1,916
35,99	162086209	35,884



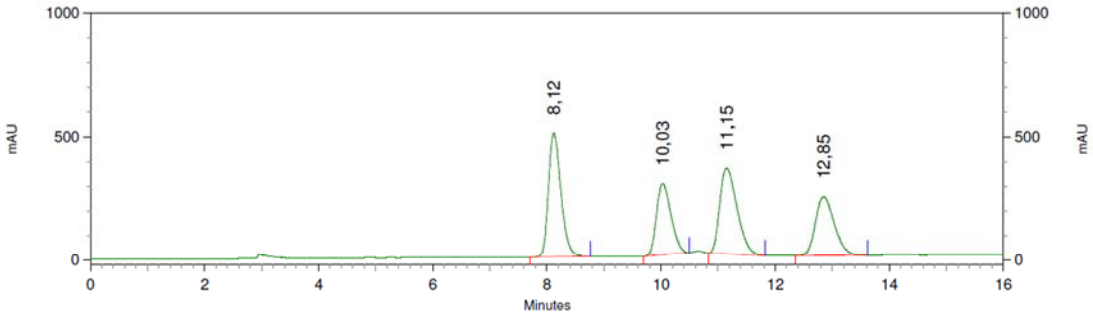
cis-(*4R*,*5R*)-**3j**
^{1}H NMR, 300 MHz, $CDCl_3$



cis-(*4R*,*5R*)-**3j**
^{13}C NMR, 75 MHz, $CDCl_3$



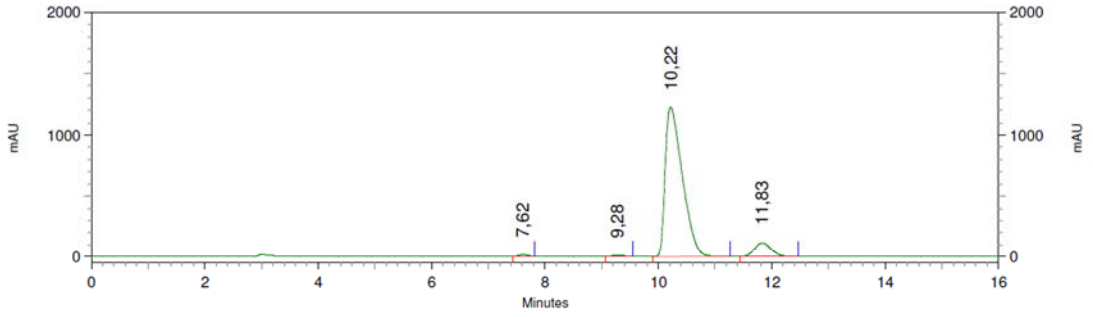
Racemic reaction: **3j**



9: 222 nm, 4 nm Results

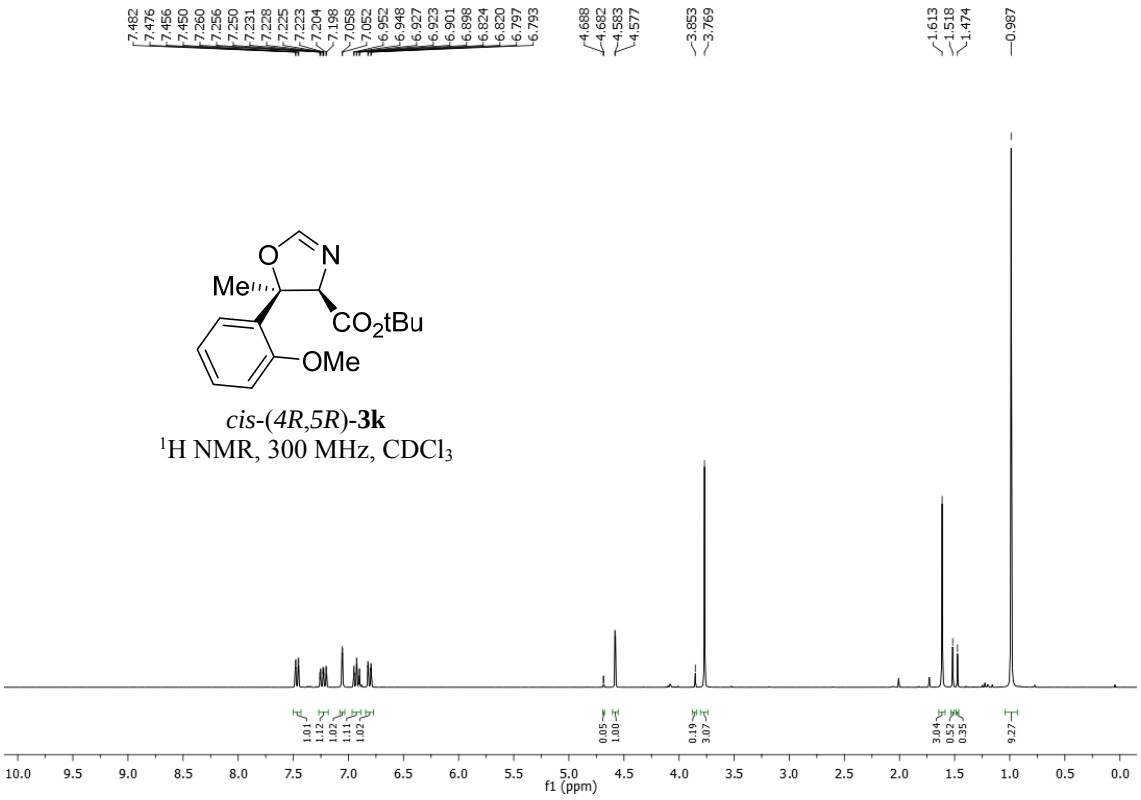
Retention Time	Area	Area Percent
8,12	30604268	29,756
10,03	20668879	20,096
11,15	29460547	28,644
12,85	22117770	21,505

Enantioselective reaction:

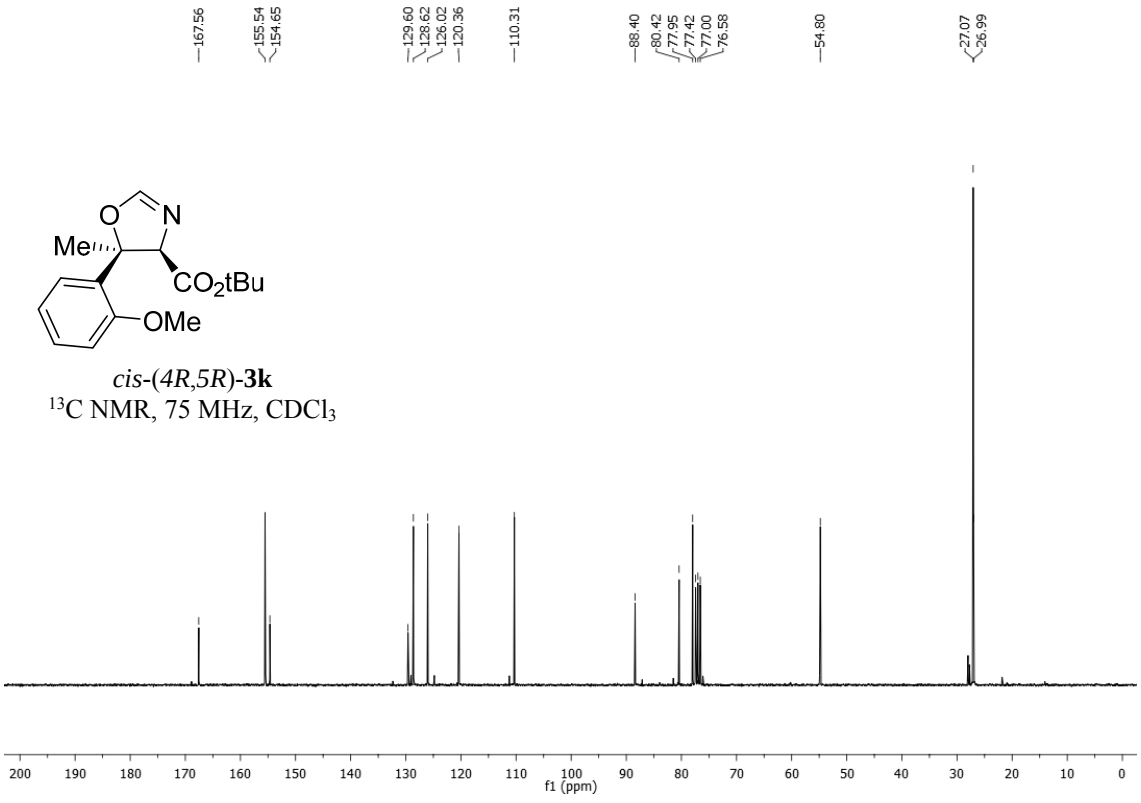


4: 222 nm, 4 nm Results

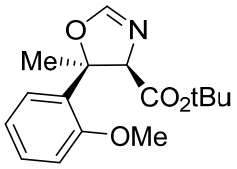
Retention Time	Area	Area Percent
7,62	709379	0,622
9,28	556974	0,489
10,22	103425288	90,712
11,83	9323700	8,178



cis-(*4R*,*5R*)-**3k**
^{1}H NMR, 300 MHz, $CDCl_3$

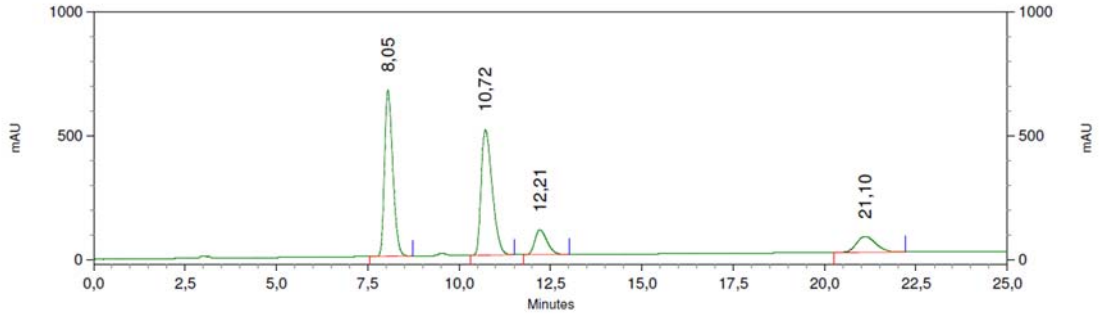


cis-(*4R*,*5R*)-**3k**
^{13}C NMR, 75 MHz, $CDCl_3$



3k

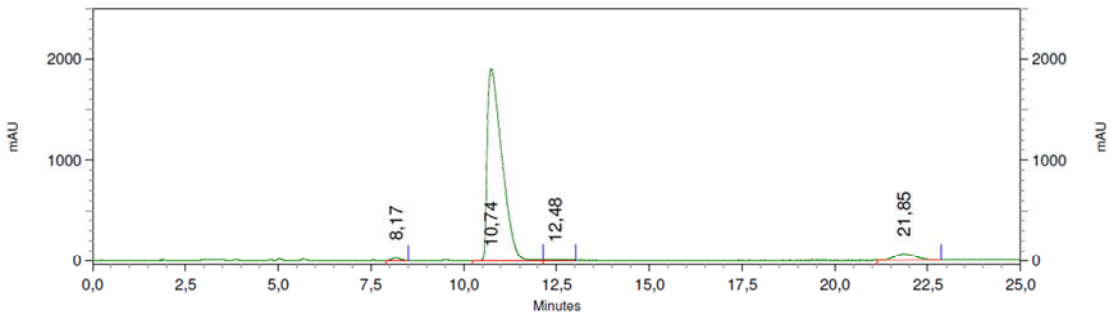
Racemic reaction:



10: 230 nm, 4 nm
Results

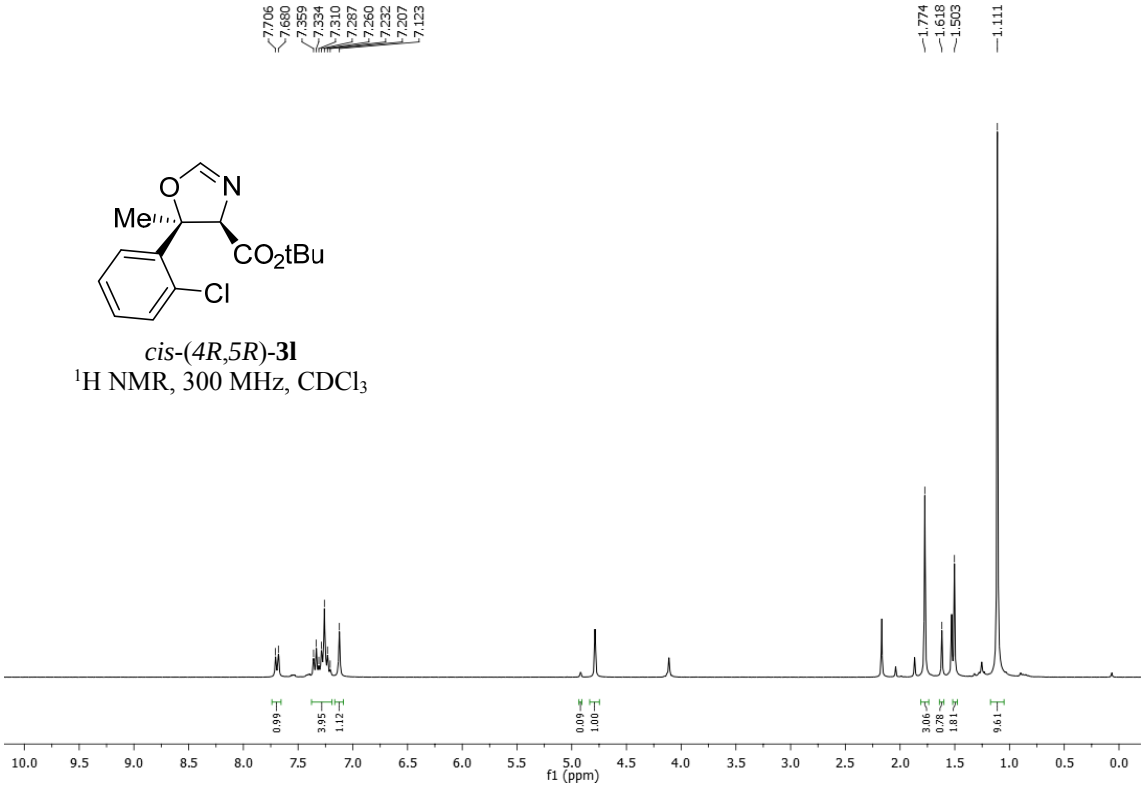
Retention Time	Area	Area Percent
8,05	42226037	40,784
10,72	42605086	41,150
12,21	9286700	8,970
21,10	9418488	9,097

Enantioselective reaction:

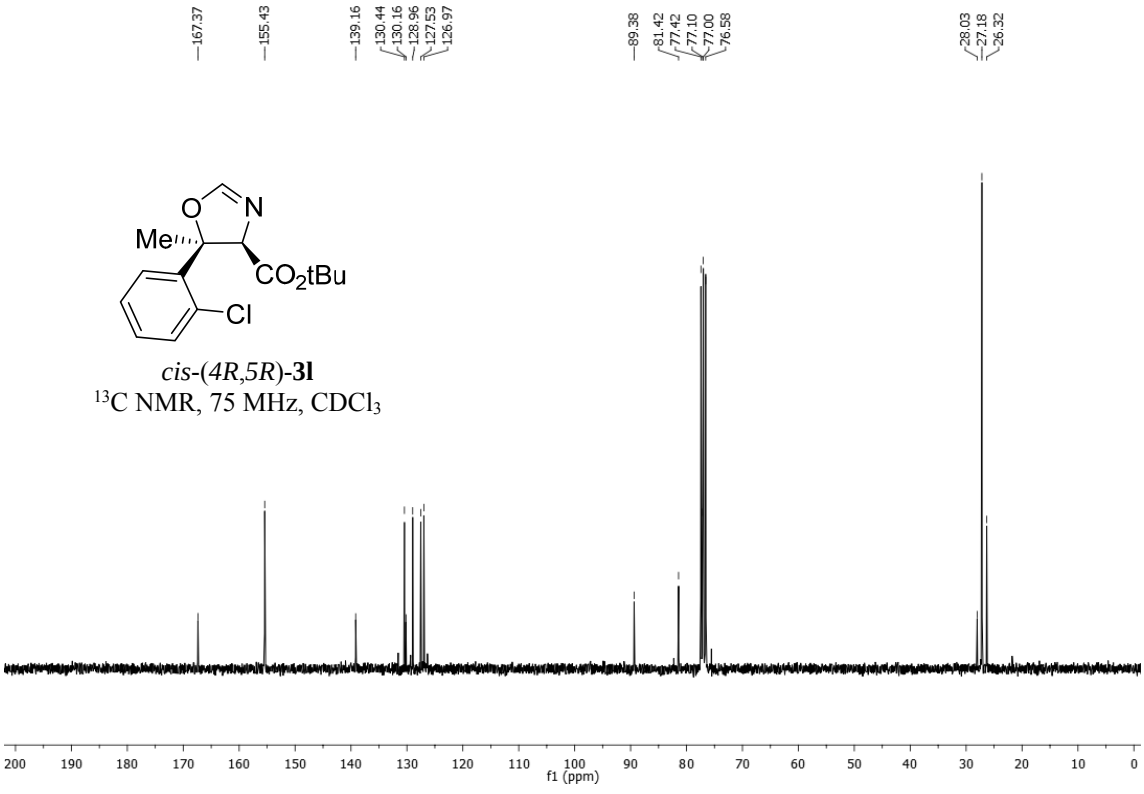


8: 229 nm, 4 nm Results

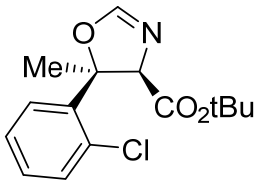
Retention Time	Area	Area Percent
8,17	1334007	0,607
10,74	207760449	94,585
12,48	280105	0,128
21,85	10280846	4,680



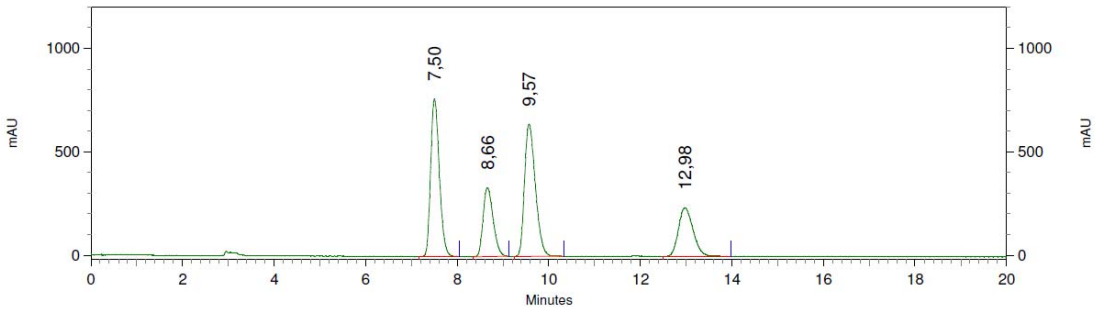
cis-(*4R*,*5R*)-**3l**
^{1}H NMR, 300 MHz, $CDCl_3$



cis-(*4R*,*5R*)-**3l**
^{13}C NMR, 75 MHz, $CDCl_3$



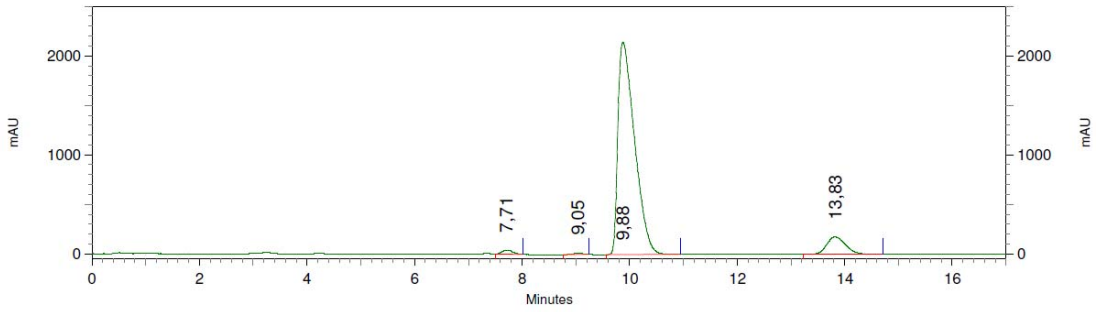
Racemic reaction: **3l**



10: 224 nm, 4 nm
Results

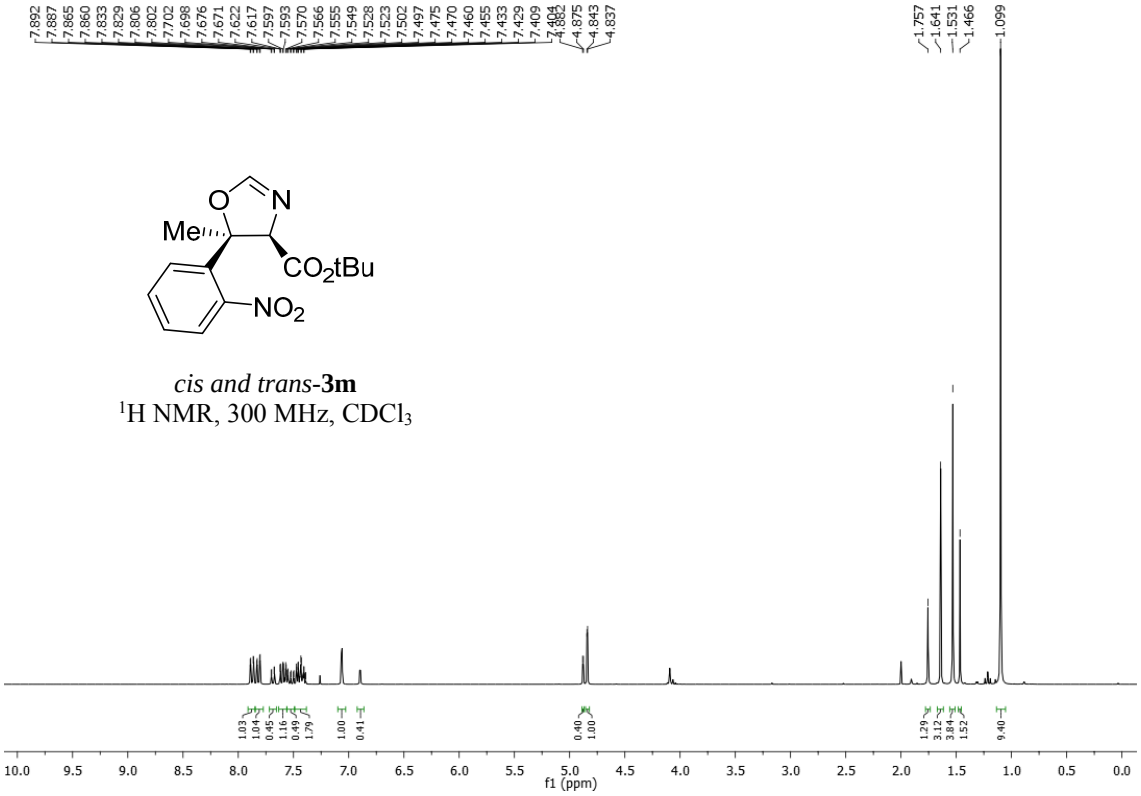
Retention Time	Area	Area Percent
7,50	40372820	32,520
8,66	20377128	16,414
9,57	42165440	33,964
12,98	21232106	17,102

Enantioselective reaction:

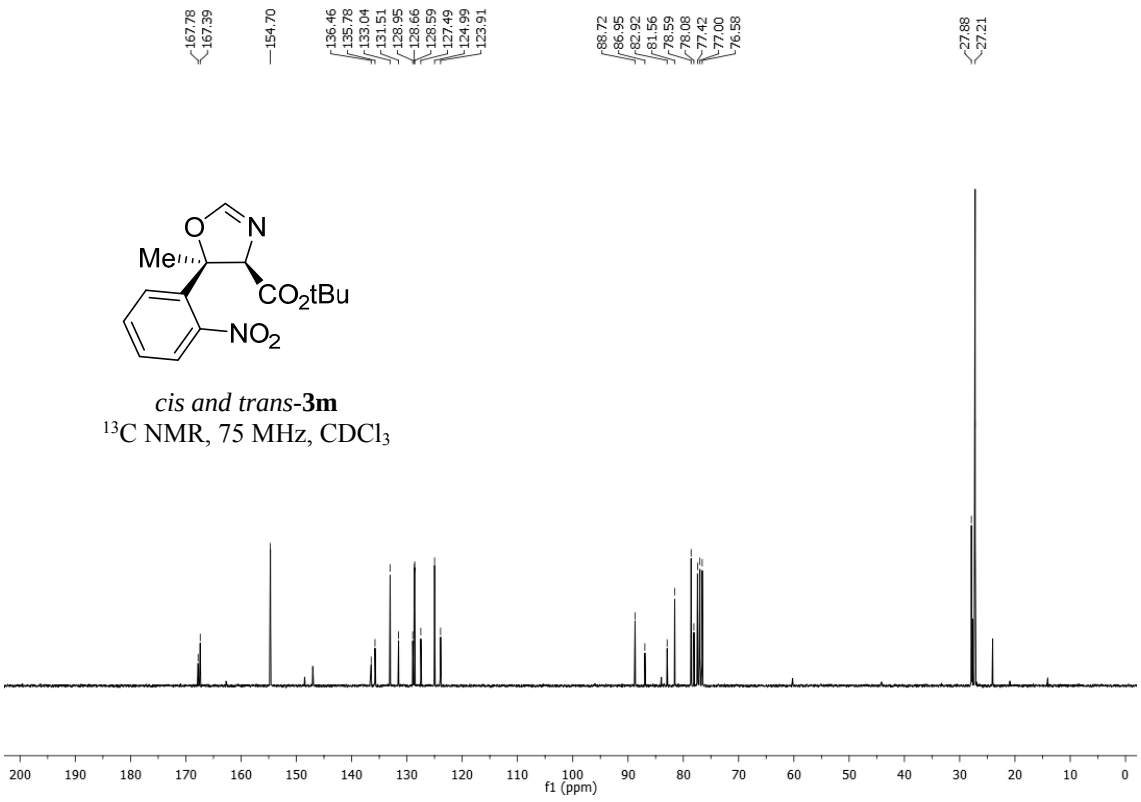


9: 224 nm, 4 nm Results

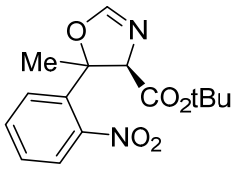
Retention Time	Area	Area Percent
7,71	2252935	1,102
9,05	546764	0,267
9,88	184424121	90,203
13,83	17231669	8,428



cis and trans-**3m**
^{1}H NMR, 300 MHz, $CDCl_3$

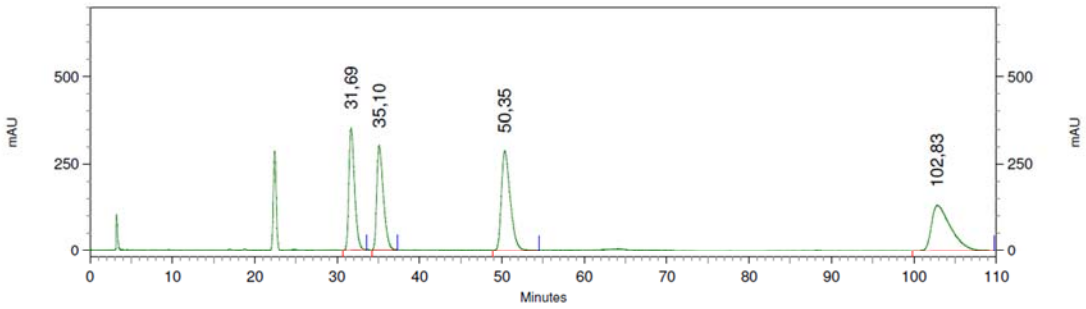


cis and trans-**3m**
^{13}C NMR, 75 MHz, $CDCl_3$



3m

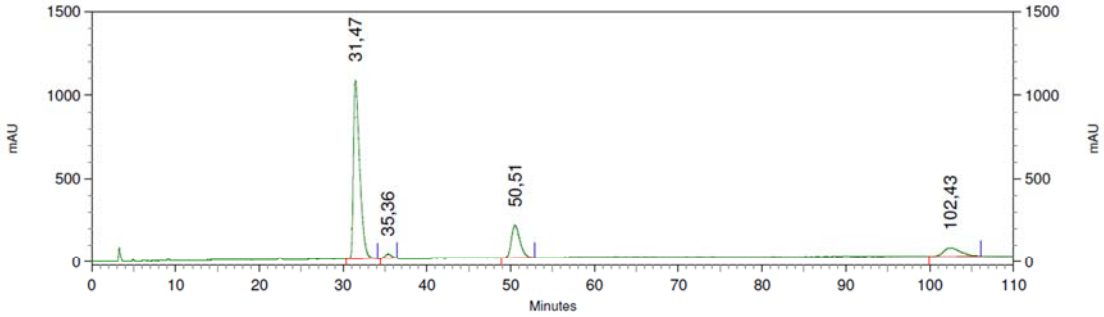
Racemic reaction:



8: 211 nm, 4 nm Results

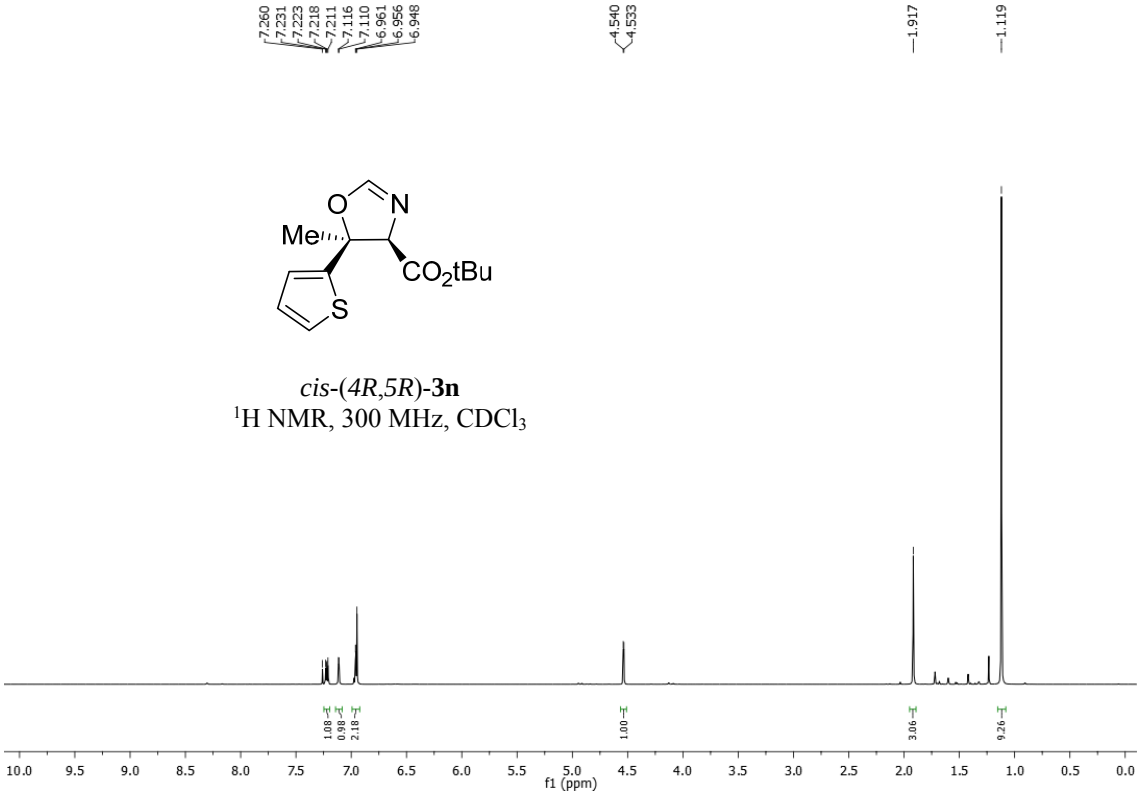
Retention Time	Area	Area Percent
31,69	68003263	21,988
35,10	67302403	21,762
50,35	86653107	28,019
102,83	87309389	28,231

Enantioselective reaction:

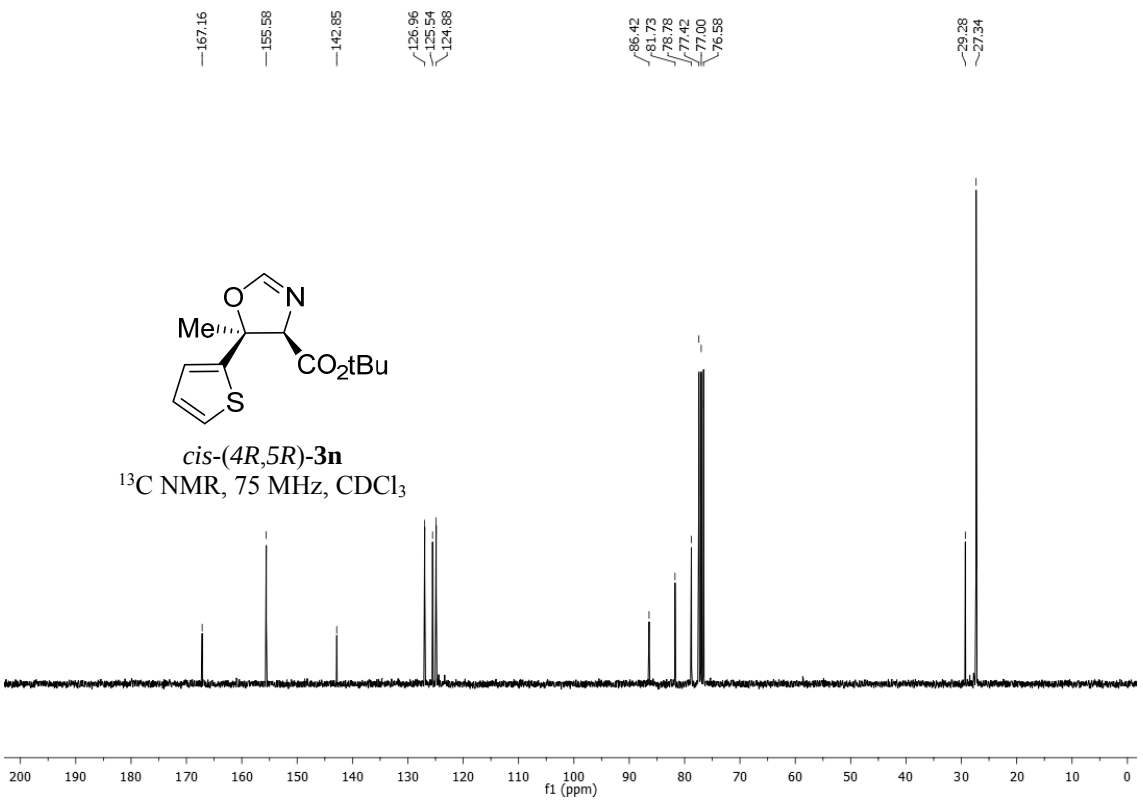


6: 211 nm, 4 nm Results

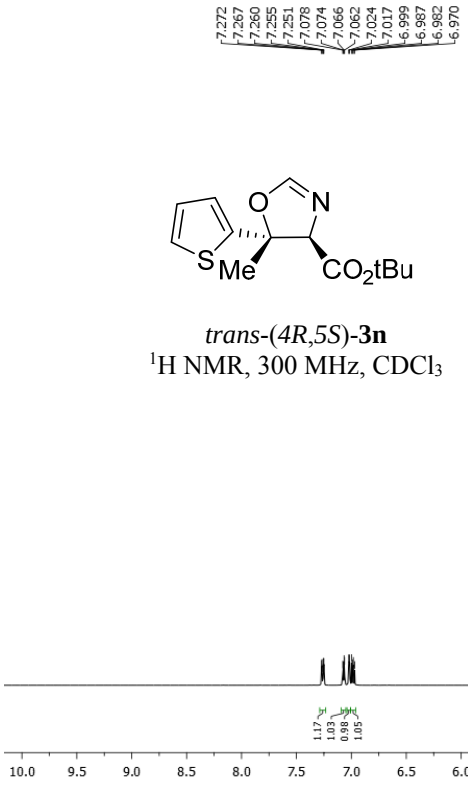
Retention Time	Area	Area Percent
31,47	222126786	70,294
35,36	5872820	1,859
50,51	57118190	18,076
102,43	30876834	9,771



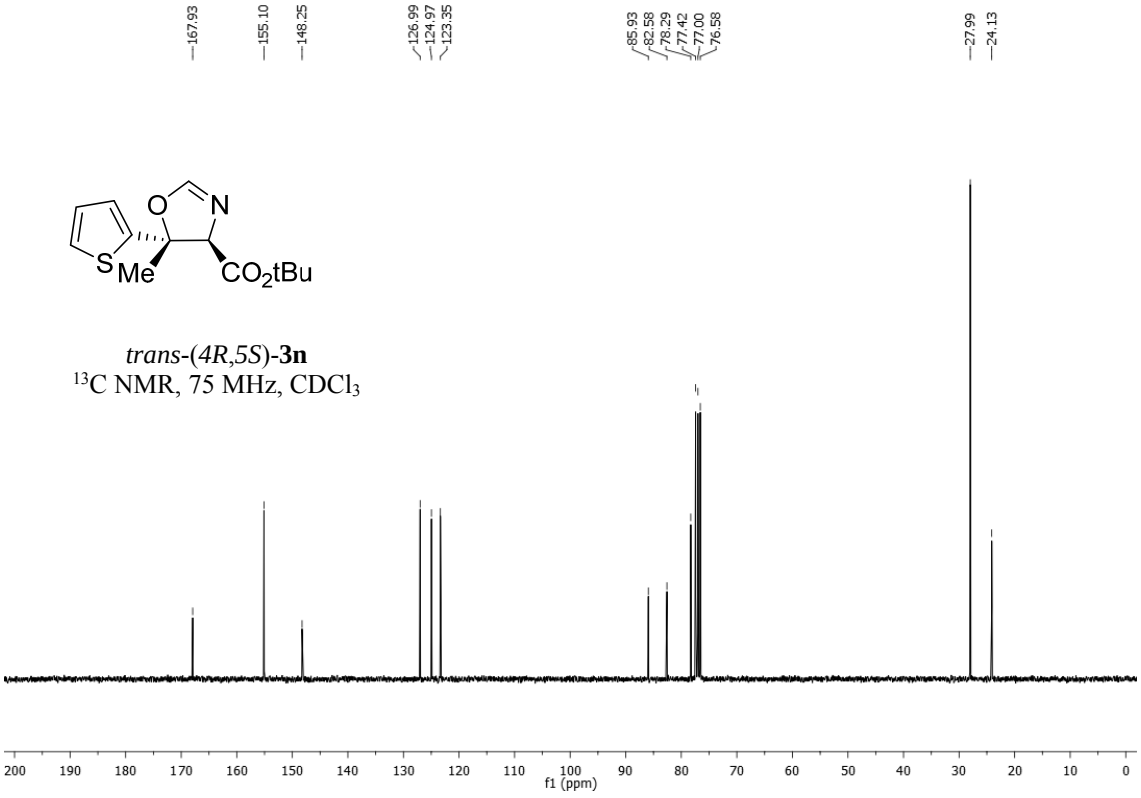
cis-(*4R*,*5R*)-**3n**
^{1}H NMR, 300 MHz, $CDCl_3$



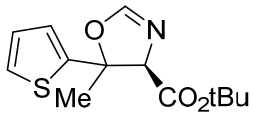
cis-(*4R*,*5R*)-**3n**
^{13}C NMR, 75 MHz, $CDCl_3$



trans-(*4R*,*5S*)-**3n**
^{1}H NMR, 300 MHz, $CDCl_3$

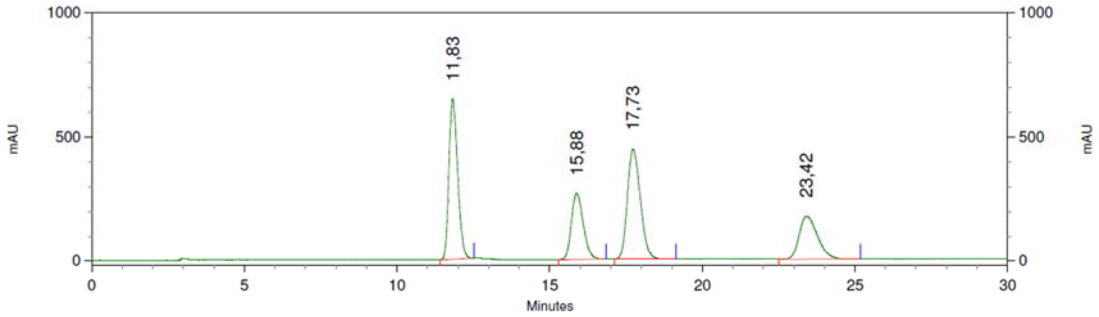


trans-(*4R*,*5S*)-**3n**
^{13}C NMR, 75 MHz, $CDCl_3$



3n

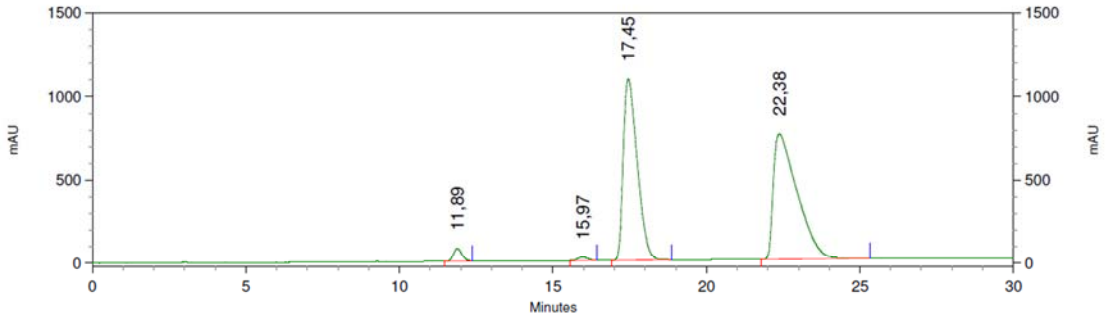
Racemic reaction:



8: 232 nm, 4 nm Results

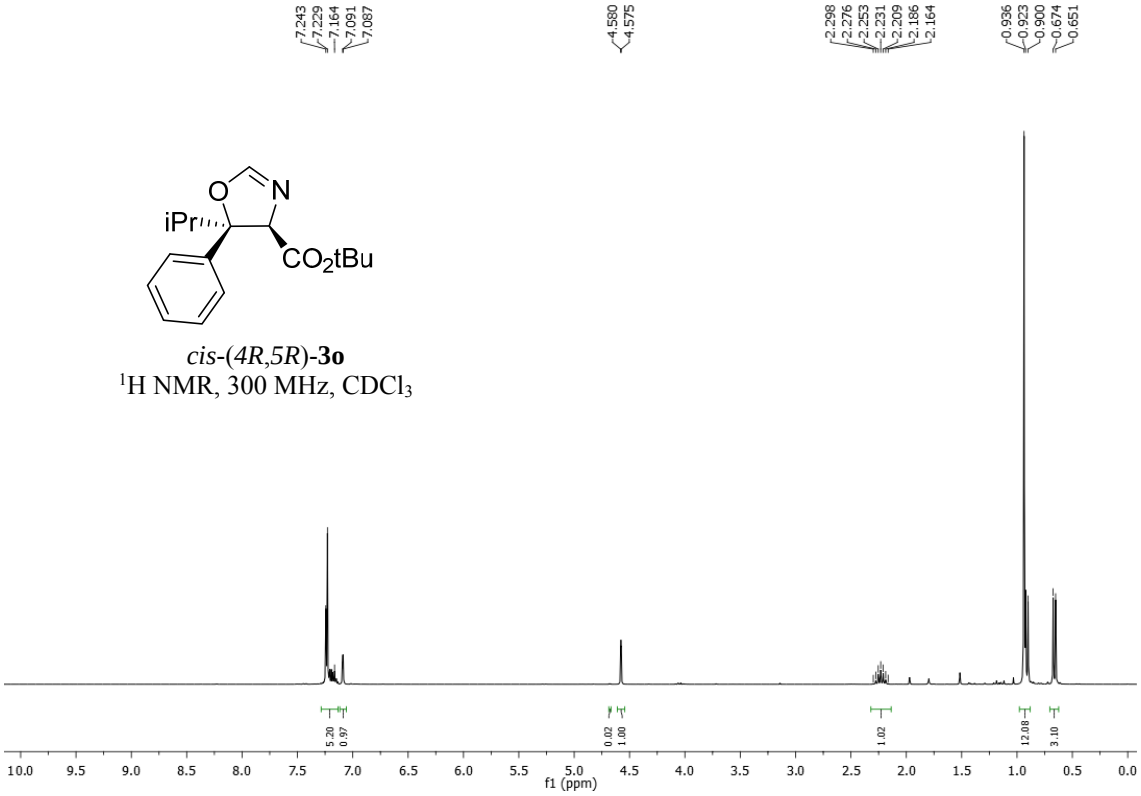
Retention Time	Area	Area Percent
11,83	51665780	31,453
15,88	29602164	18,021
17,73	52921536	32,218
23,42	30072721	18,308

Enantioselective reaction:

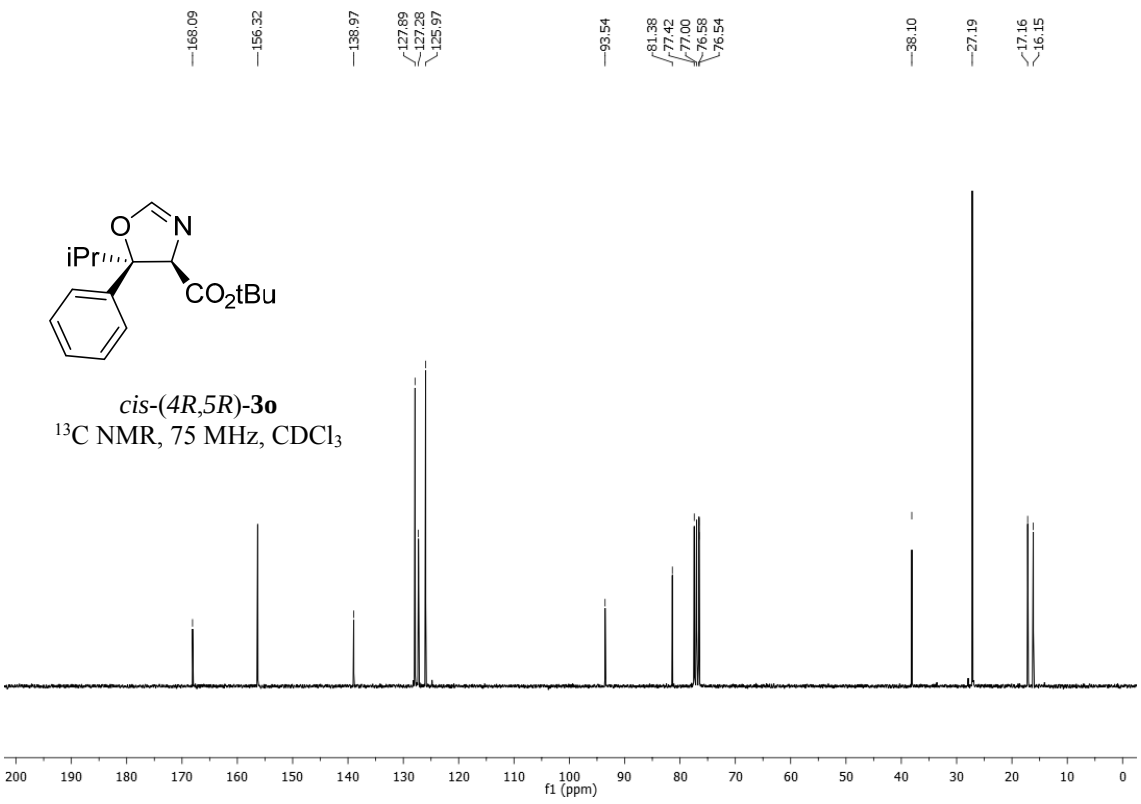


4: 246 nm, 4 nm Results

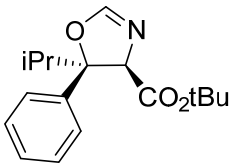
Retention Time	Area	Area Percent
11,89	6022949	1,953
15,97	1957572	0,635
17,45	137615270	44,628
22,38	162764170	52,784



cis-(*4R*,*5R*)-**3o**
^{1}H NMR, 300 MHz, $CDCl_3$

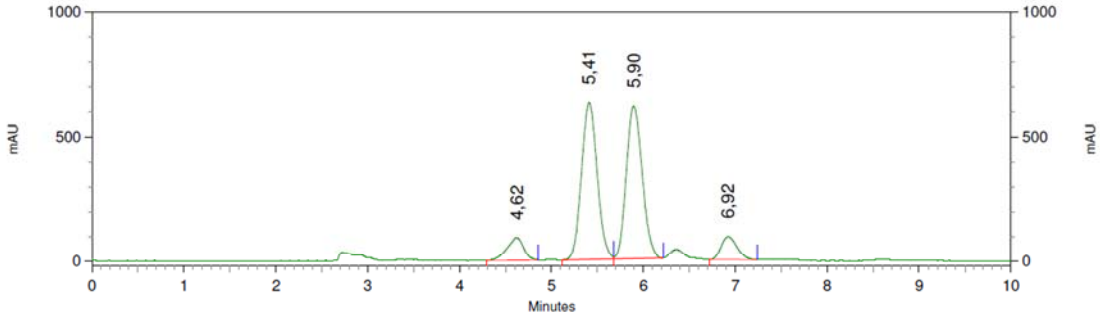


cis-(*4R*,*5R*)-**3o**
^{13}C NMR, 75 MHz, $CDCl_3$



3o

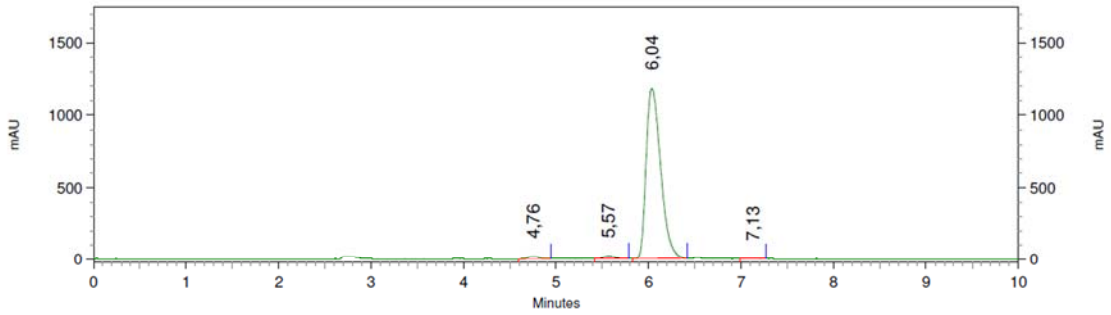
Racemic reaction:



4: 212 nm, 4 nm Results

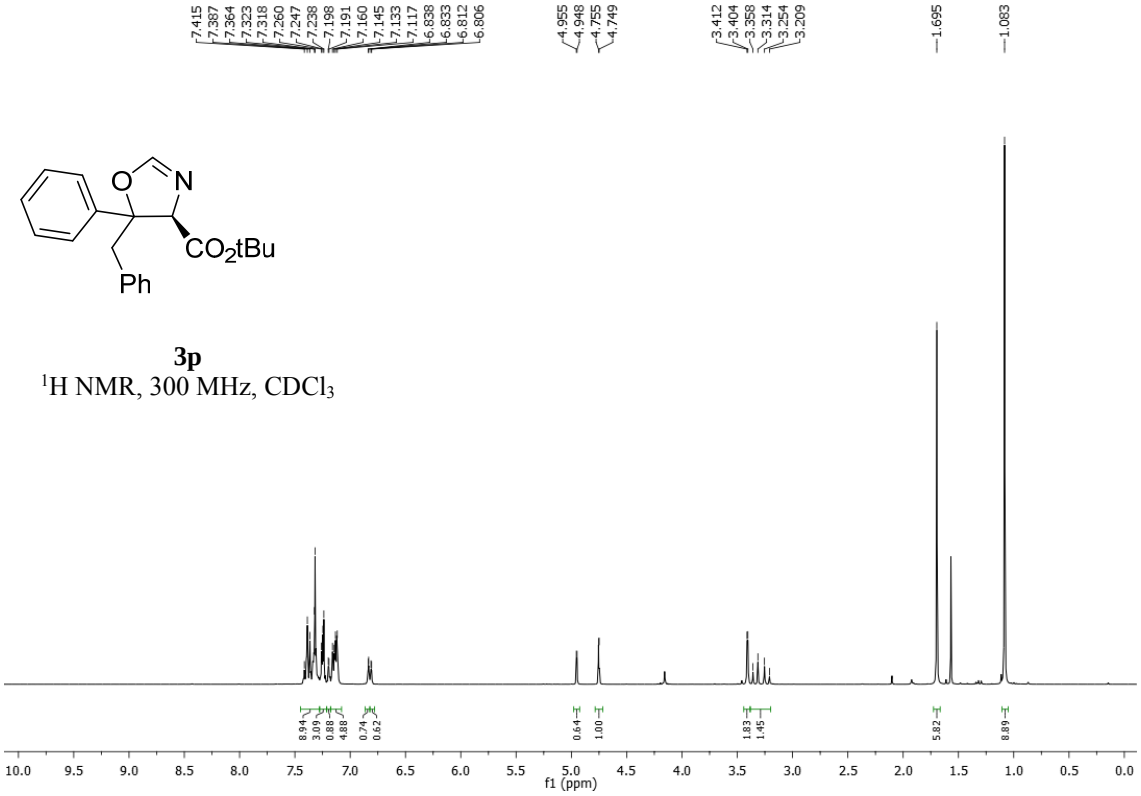
Retention Time	Area	Area Percent
4,62	4724342	6,839
5,41	30081028	43,546
5,90	29732695	43,042
6,92	4540246	6,573

Enantioselective reaction:



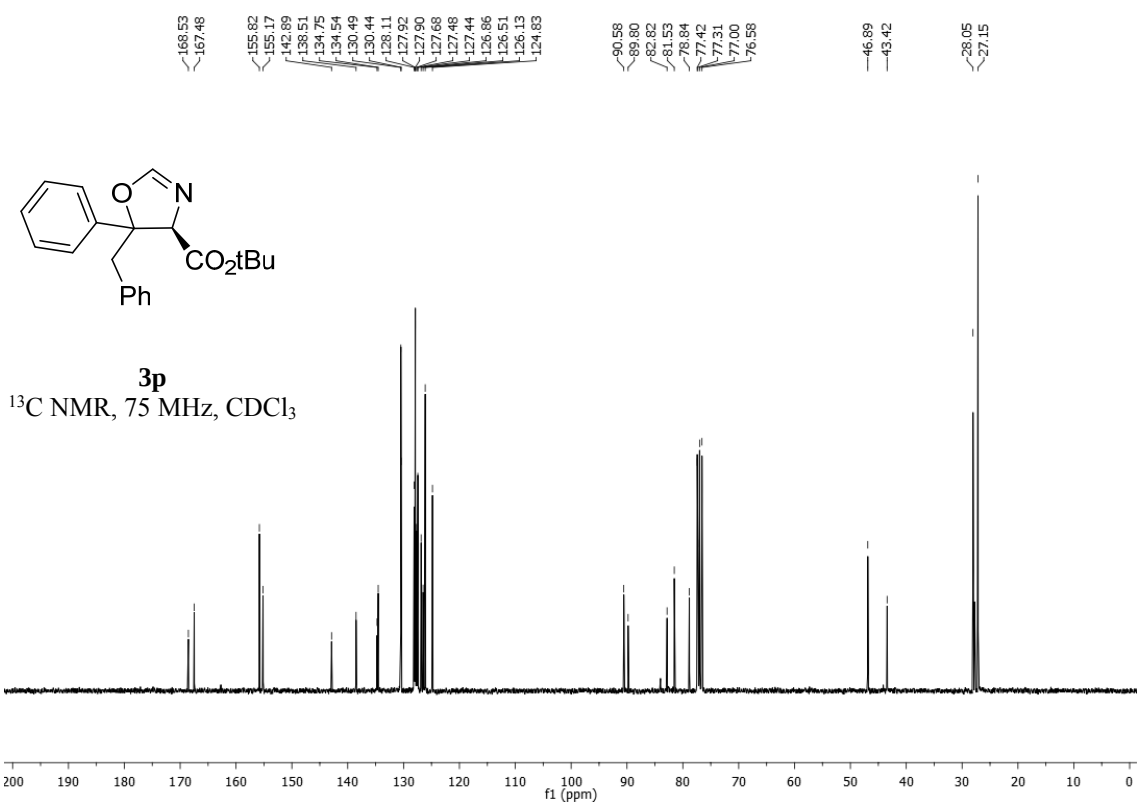
4: 222 nm, 4 nm Results

Retention Time	Area	Area Percent
4,76	628548	1,186
5,57	714494	1,348
6,04	51546207	97,226
7,13	127399	0,240



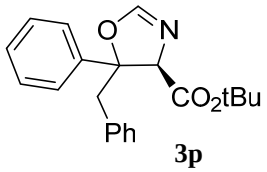
3p

^{1}H NMR, 300 MHz, $CDCl_3$



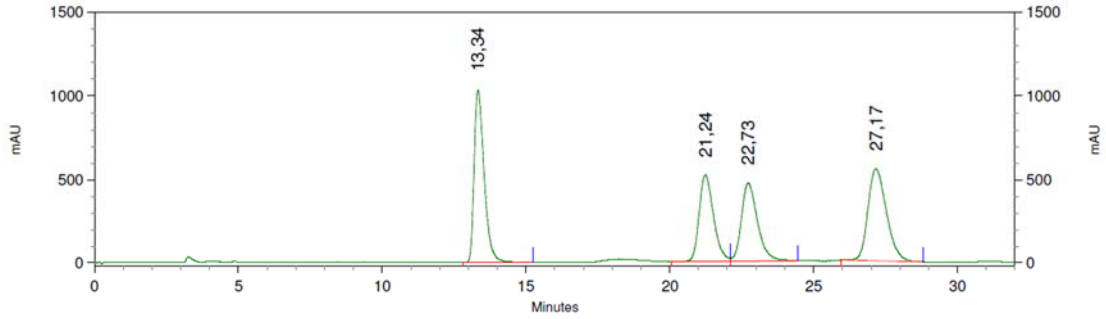
3p

^{13}C NMR, 75 MHz, $CDCl_3$



3p

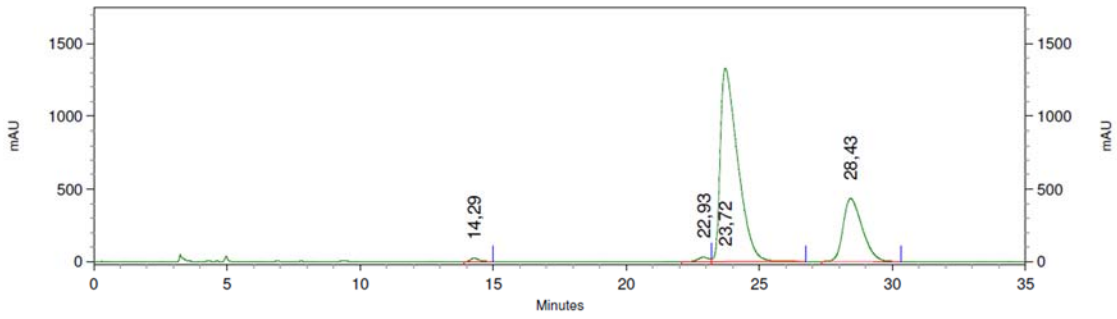
Racemic reaction:



6: 220 nm, 4 nm Results

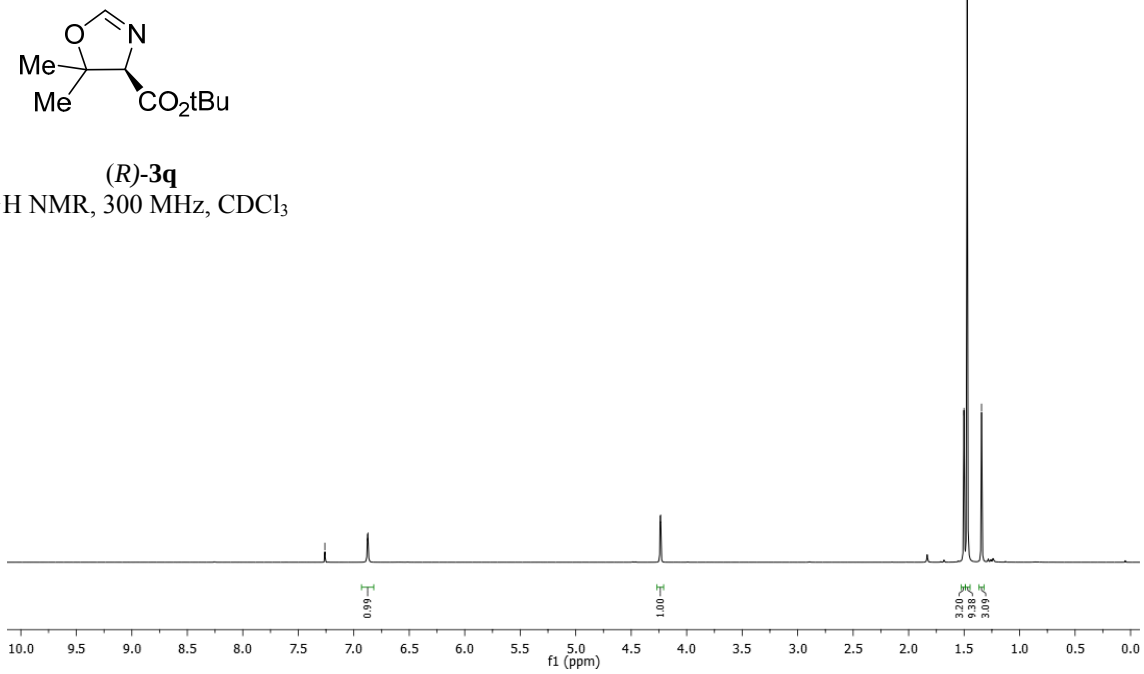
Retention Time	Area	Area Percent
13,34	99637846	28,749
21,24	72907768	21,037
22,73	73792435	21,292
27,17	100235522	28,922

Enantioselective reaction:

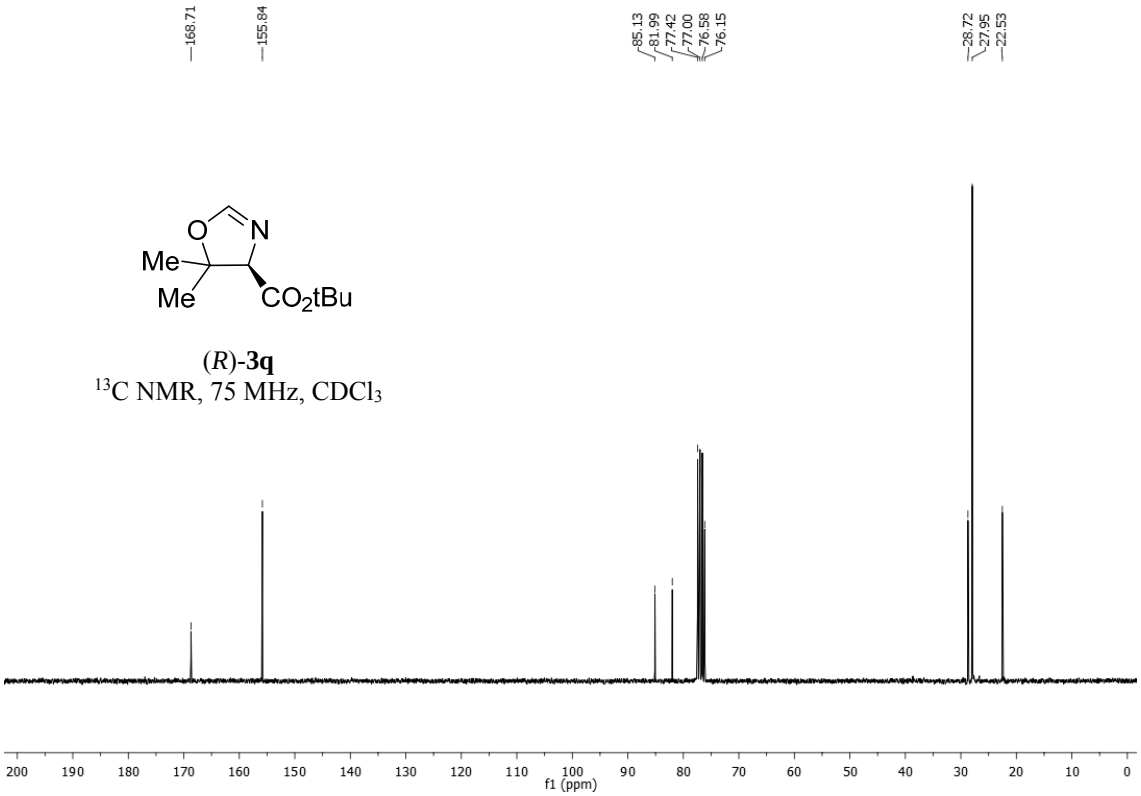


10: 223 nm, 4 nm Results

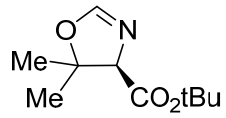
Retention Time	Area	Area Percent
14,29	2371281	0,708
22,93	3433737	1,025
23,72	242327415	72,333
28,43	86885004	25,934



(*R*)-**3q**
^{1}H NMR, 300 MHz, $CDCl_3$

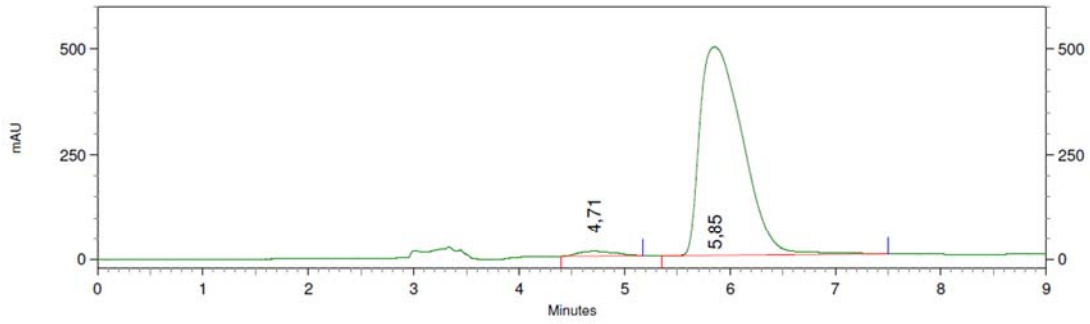


(*R*)-**3q**
^{13}C NMR, 75 MHz, $CDCl_3$



3q

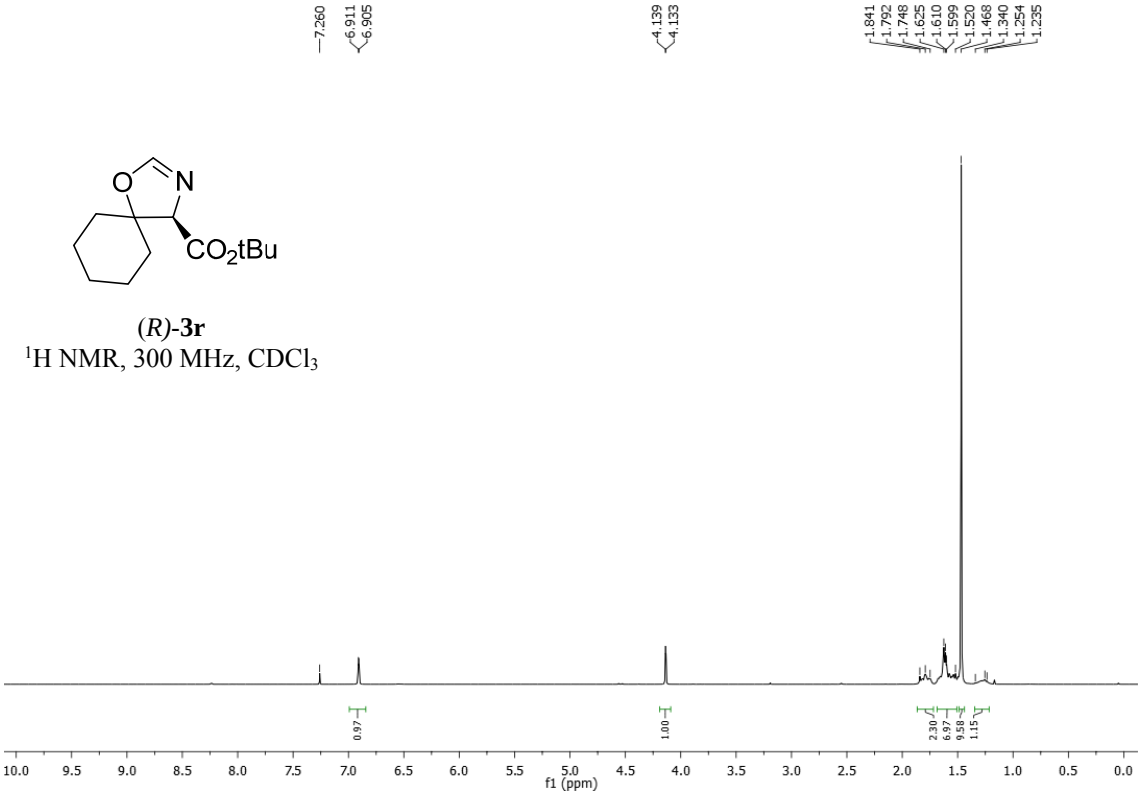
Enantioselective reaction:



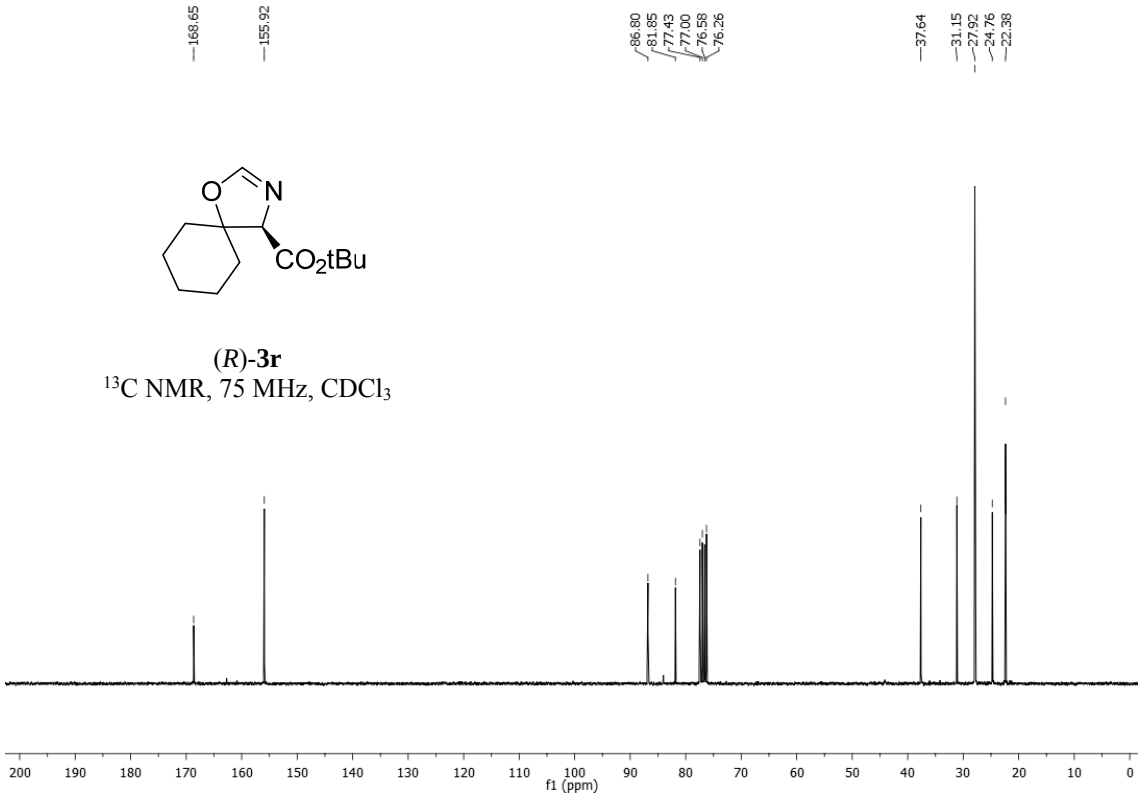
9: 210 nm, 4 nm Results

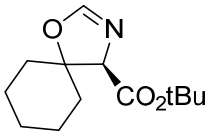
Retention Time	Area	Area Percent
4,71	1079530	1,896
5,85	55854604	98,104

(*R*)-**3r**
^{1}H NMR, 300 MHz, $CDCl_3$



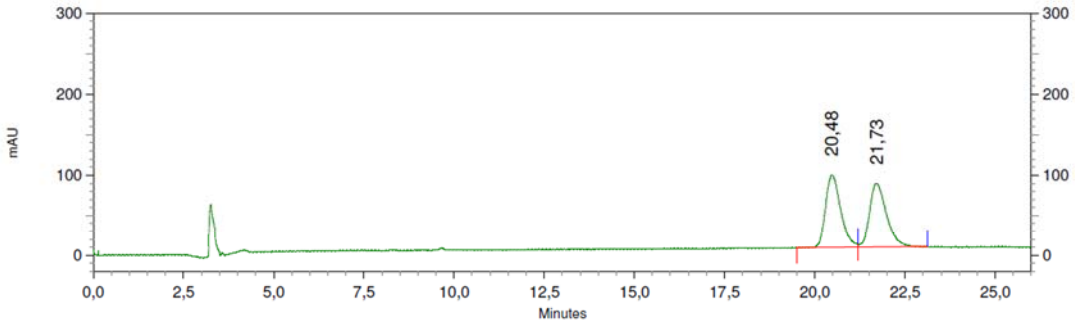
(*R*)-**3r**
^{13}C NMR, 75 MHz, $CDCl_3$





3r

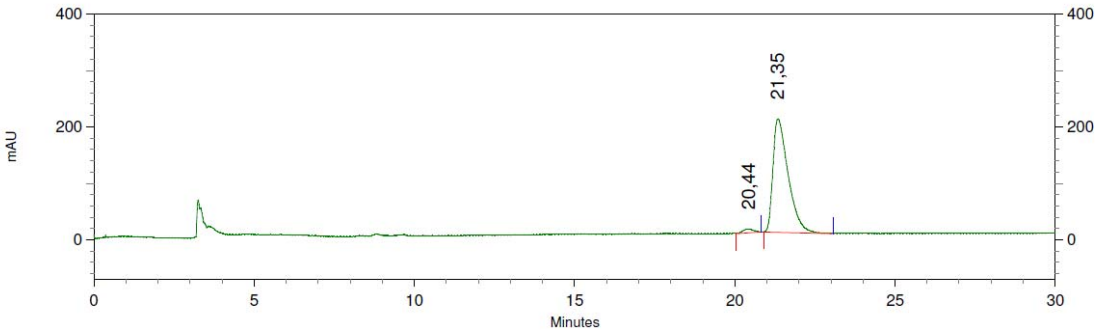
Racemic reaction:



9: 210 nm, 4 nm Results

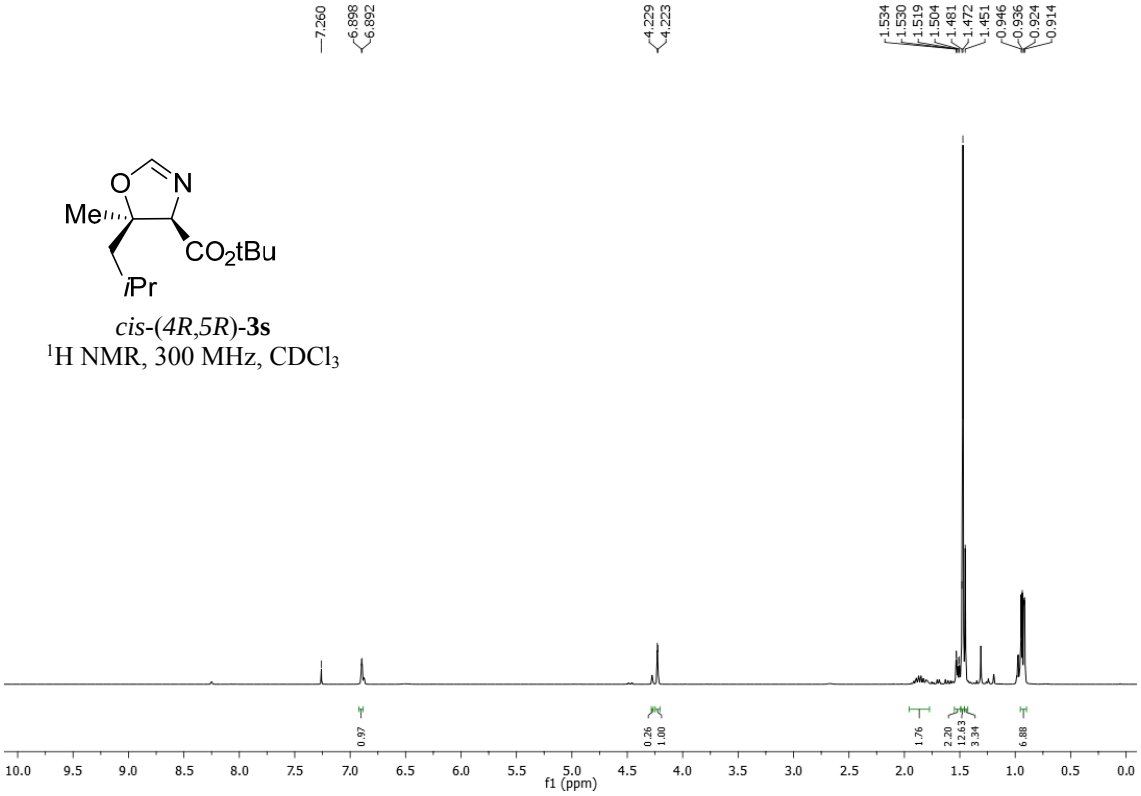
Retention Time	Area	Area Percent
20,48	10577379	50,339
21,73	10435034	49,661

Enantioselective reaction:

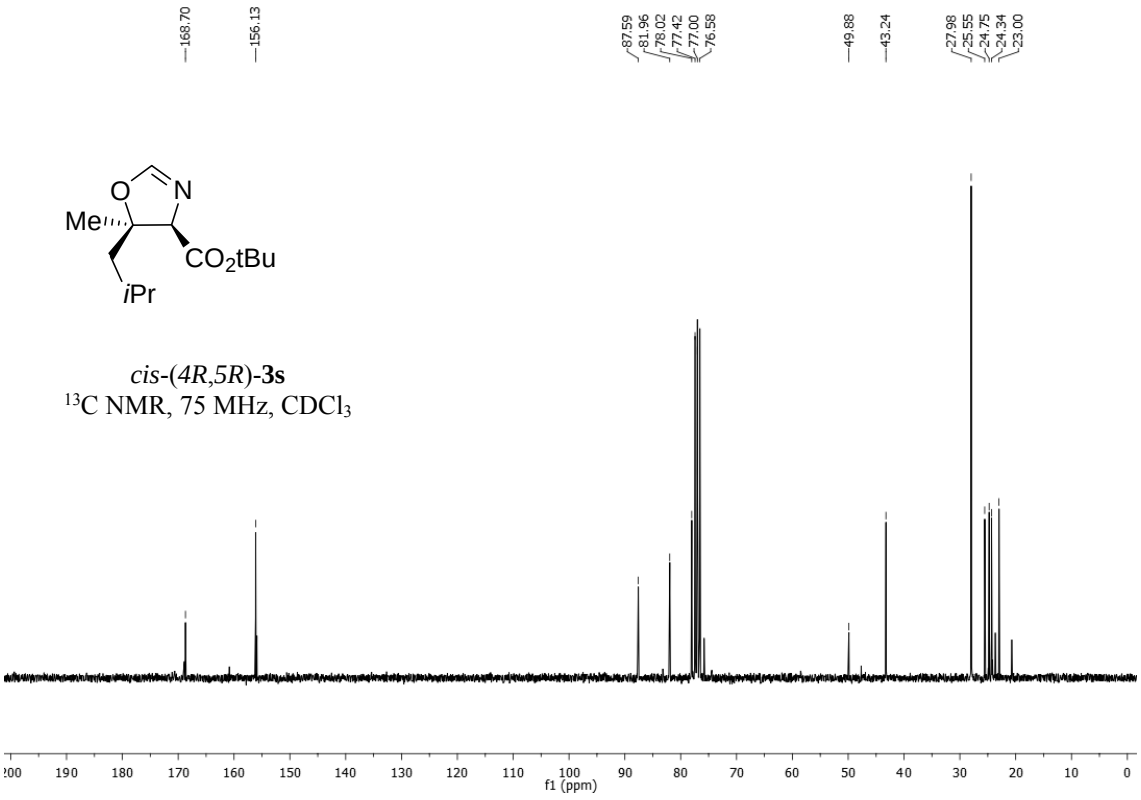


9: 210 nm, 4 nm Results

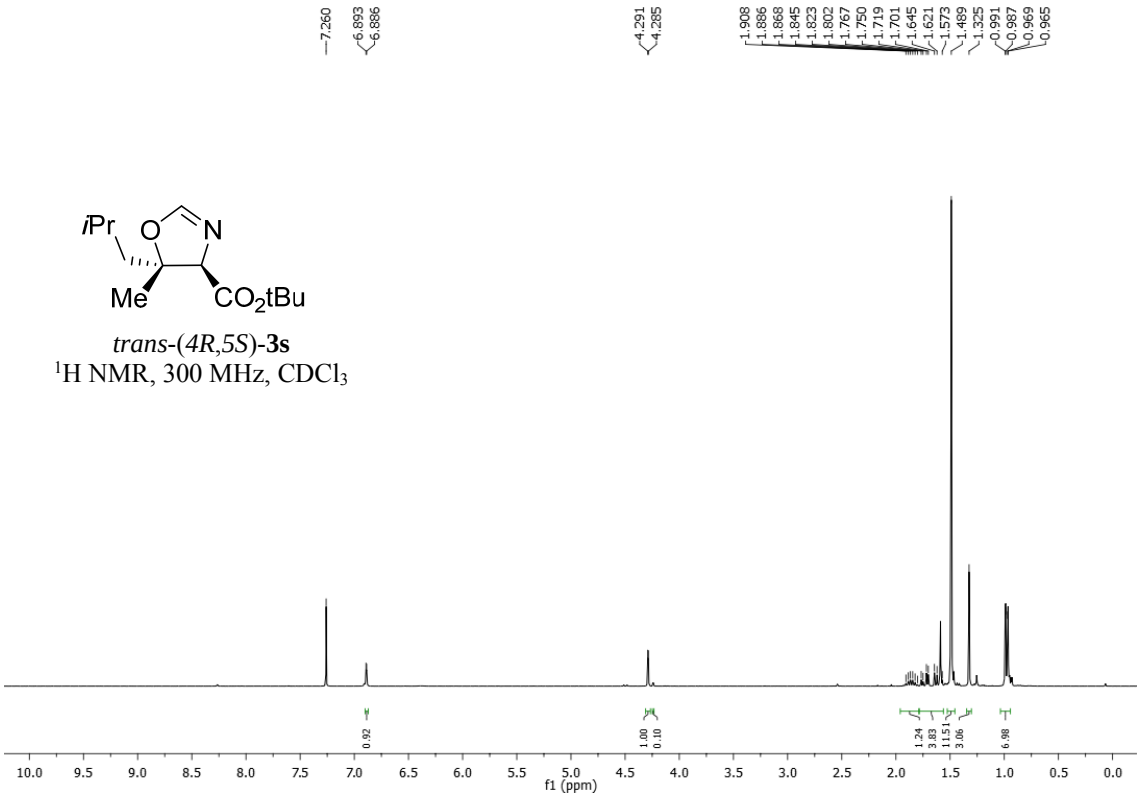
Retention Time	Area	Area Percent
20,44	649226	2,377
21,35	26660220	97,623



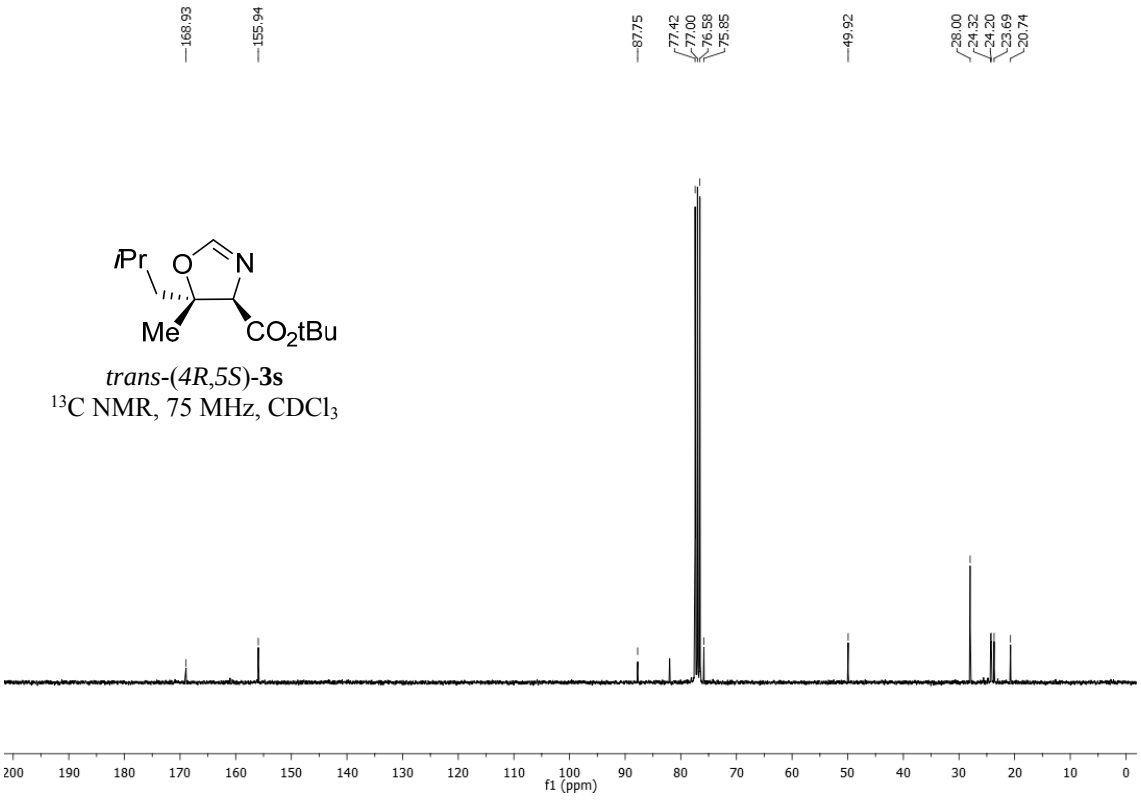
cis-(*4R*,*5R*)-**3s**
^{1}H NMR, 300 MHz, $CDCl_3$



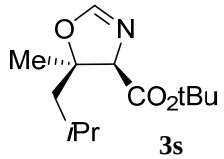
cis-(*4R*,*5R*)-**3s**
^{13}C NMR, 75 MHz, $CDCl_3$



trans-(*4R*,*5S*)-**3s**
^{1}H NMR, 300 MHz, $CDCl_3$

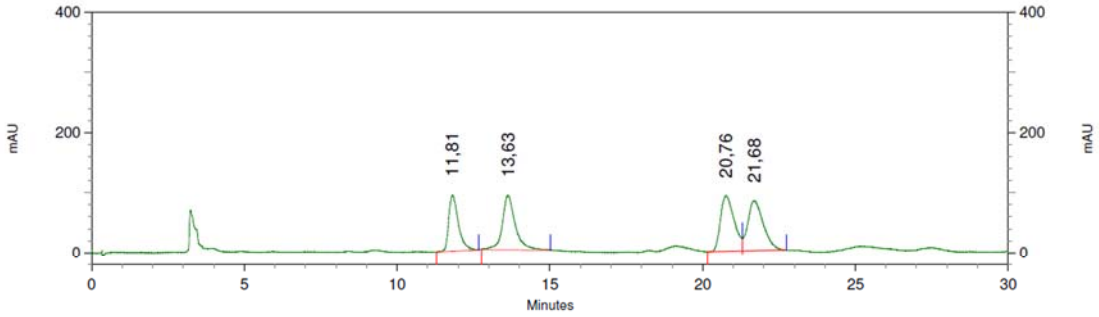


trans-(*4R*,*5S*)-**3s**
^{13}C NMR, 75 MHz, $CDCl_3$



3s

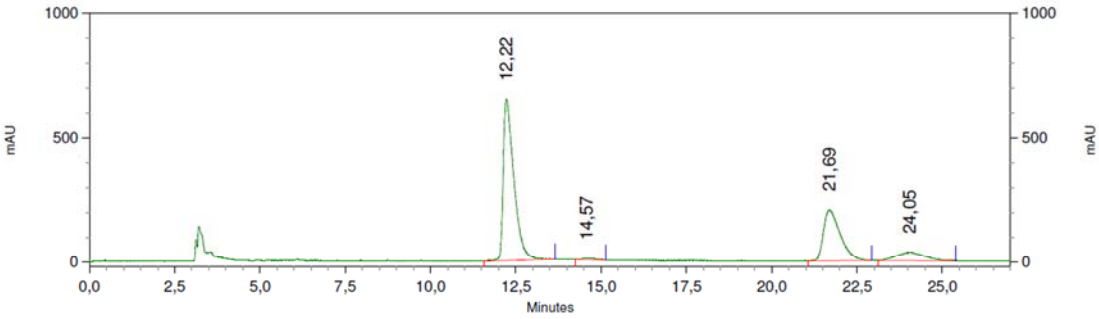
Racemic reaction:



4: 210 nm, 4 nm Results

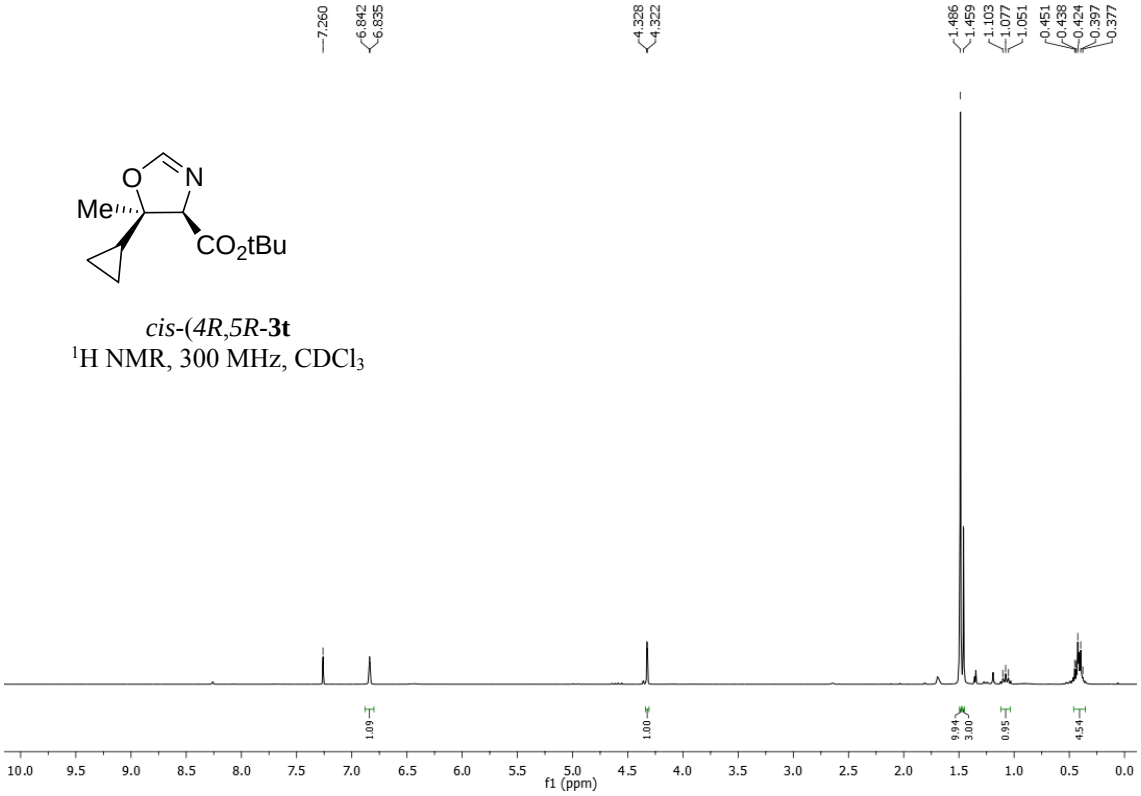
Retention Time	Area	Area Percent
11,81	8317593	19,570
13,63	10827558	25,475
20,76	11529729	27,127
21,68	11827404	27,828

Enantioselective reaction:

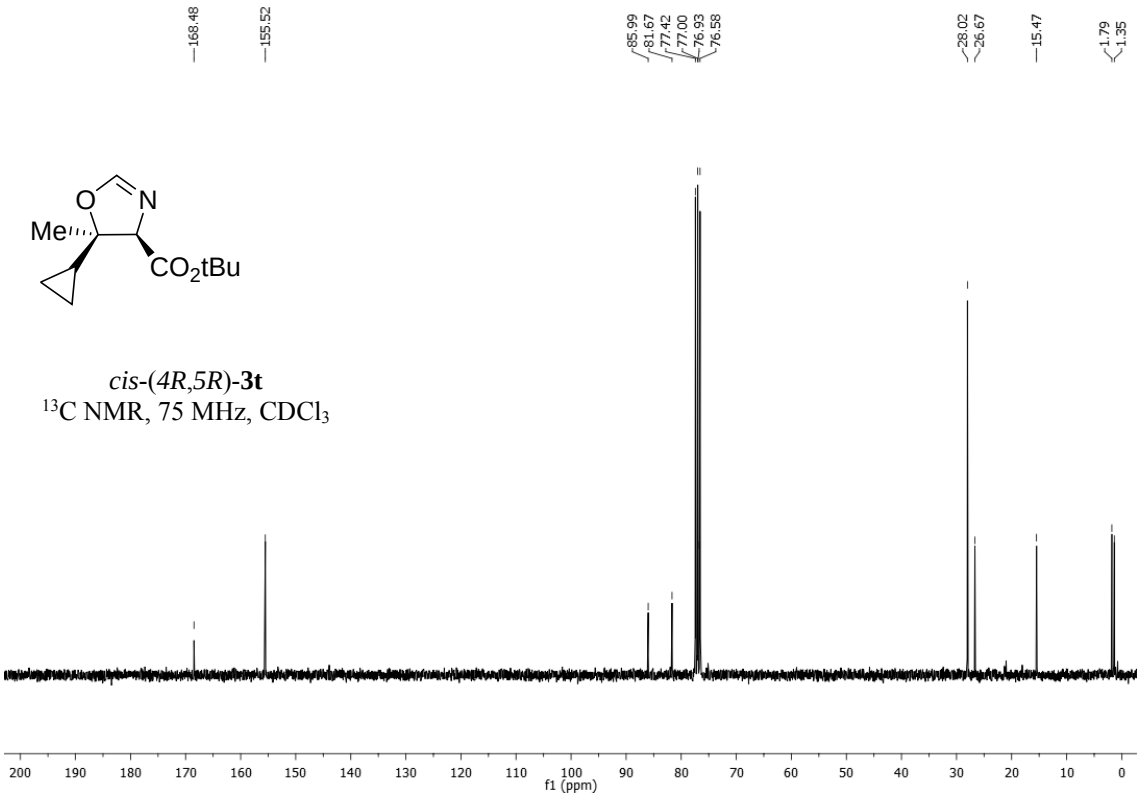


4: 208 nm, 4 nm Results

Retention Time	Area	Area Percent
12,22	56436410	60,210
14,57	681107	0,727
21,69	28513019	30,420
24,05	8101369	8,643

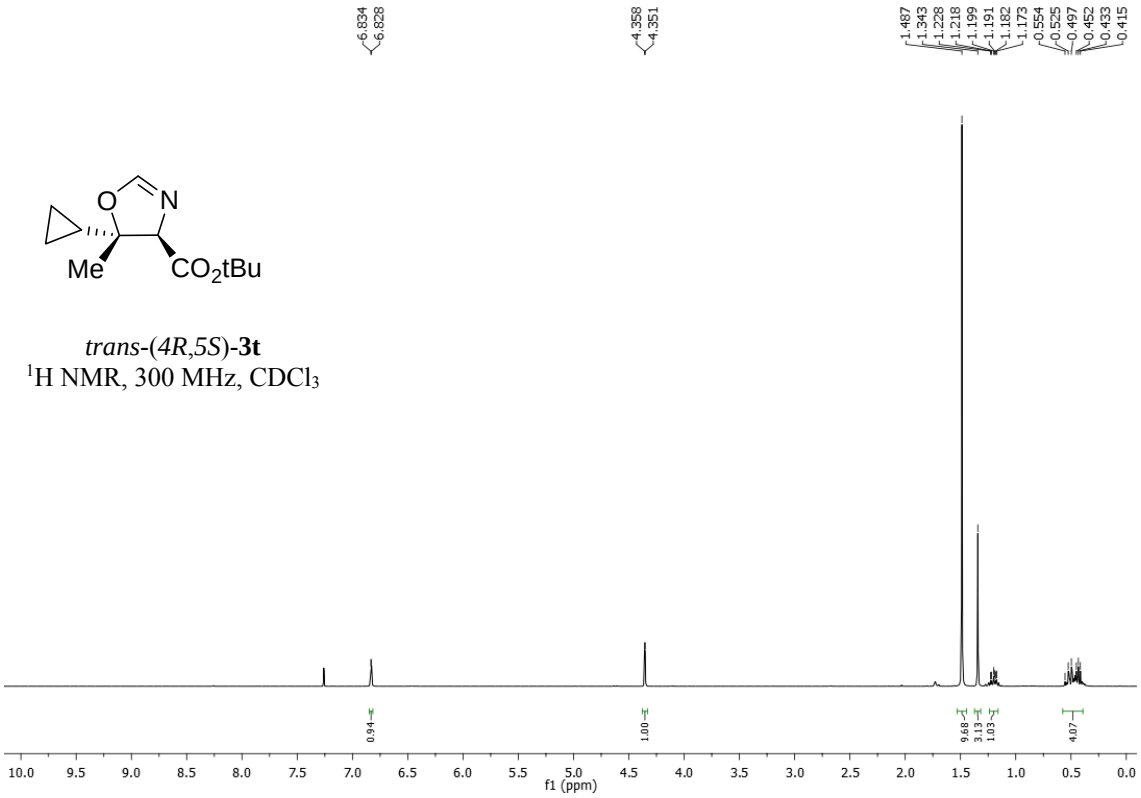


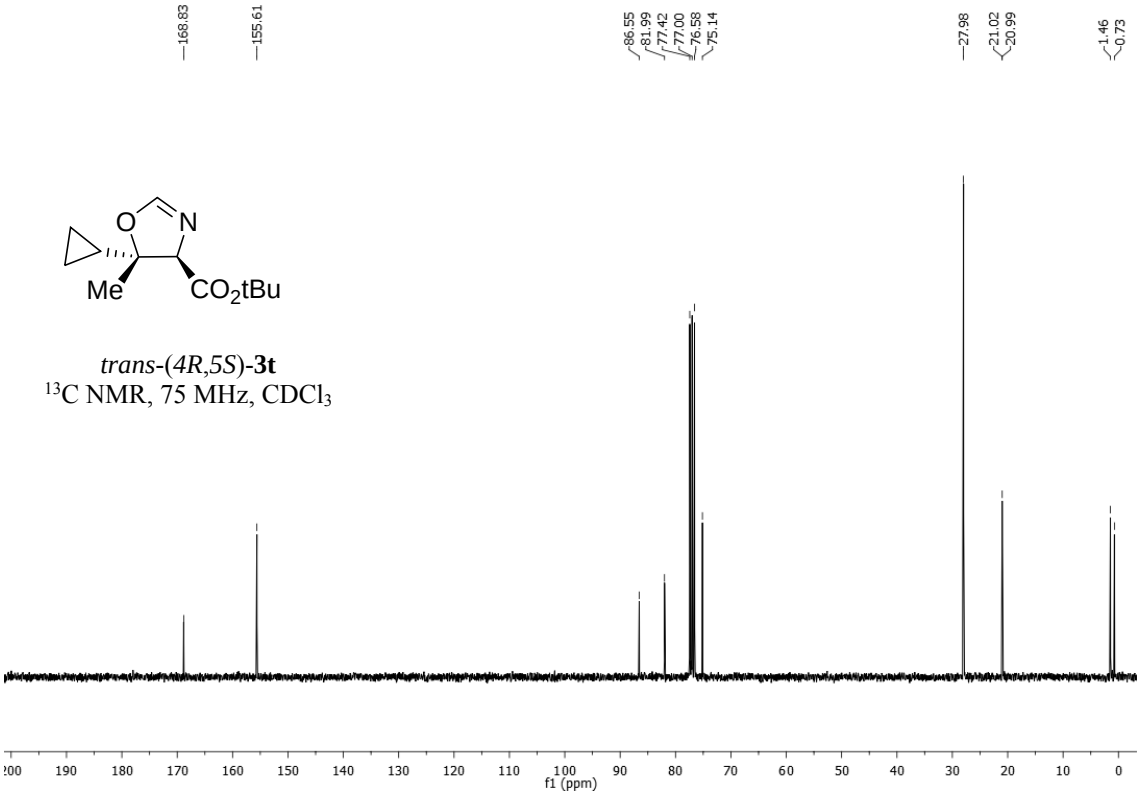
cis-(*4R*,*5R*-**3t**
^{1}H NMR, 300 MHz, $CDCl_3$



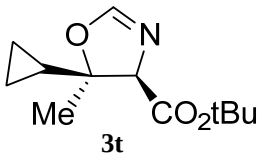
cis-(*4R*,*5R*)-**3t**
^{13}C NMR, 75 MHz, $CDCl_3$

trans-(*4R,5S*)-**3t**
^{1}H NMR, 300 MHz, $CDCl_3$



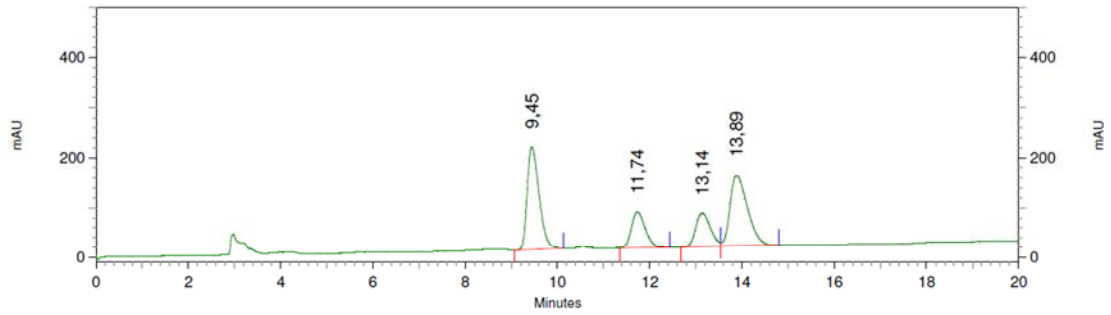


trans-(*4R,5S*)-**3t**
^{13}C NMR, 75 MHz, $CDCl_3$



3t

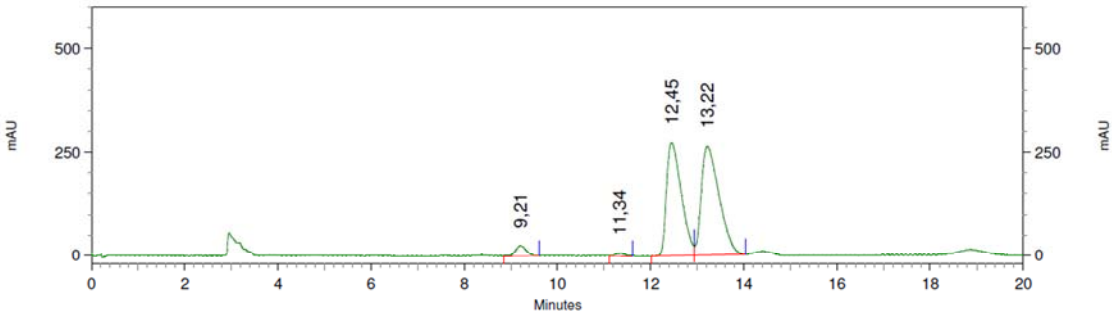
Racemic reaction:



7: 207 nm, 4 nm Results

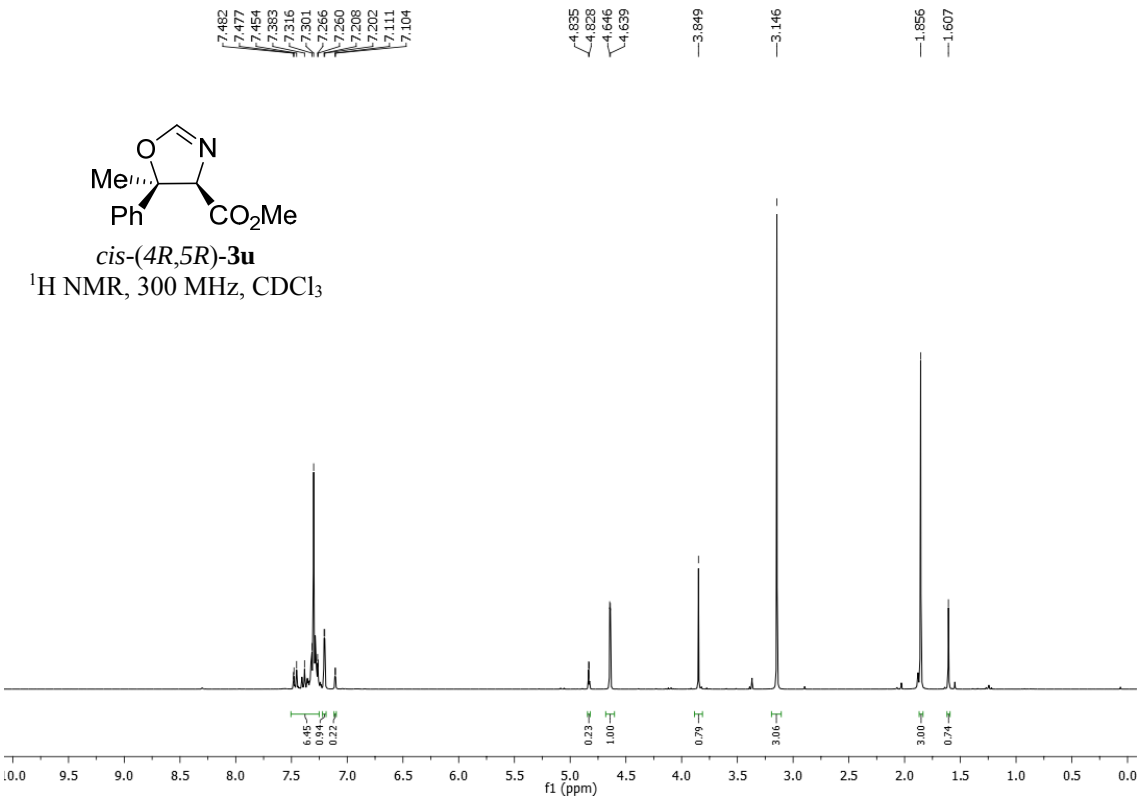
Retention Time	Area	Area Percent
9,45	14841589	35,367
11,74	6094596	14,523
13,14	6040447	14,394
13,89	14988175	35,716

Enantioselective reaction:

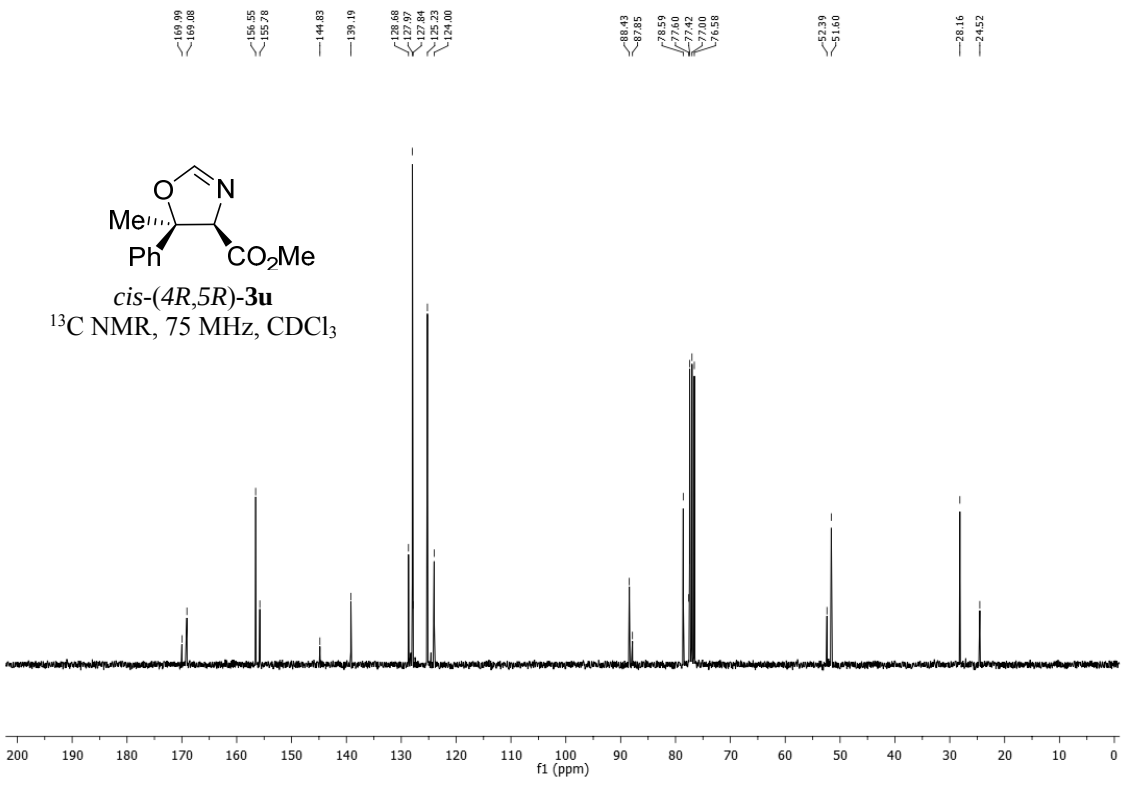


4: 207 nm, 4 nm Results

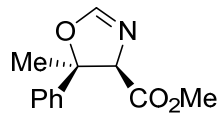
Retention Time	Area	Area Percent
9,21	1673534	3,076
11,34	425042	0,781
12,45	24166979	44,426
13,22	28132306	51,716



cis-(*4R,5R*)-**3u**
^{1}H NMR, 300 MHz, $CDCl_3$

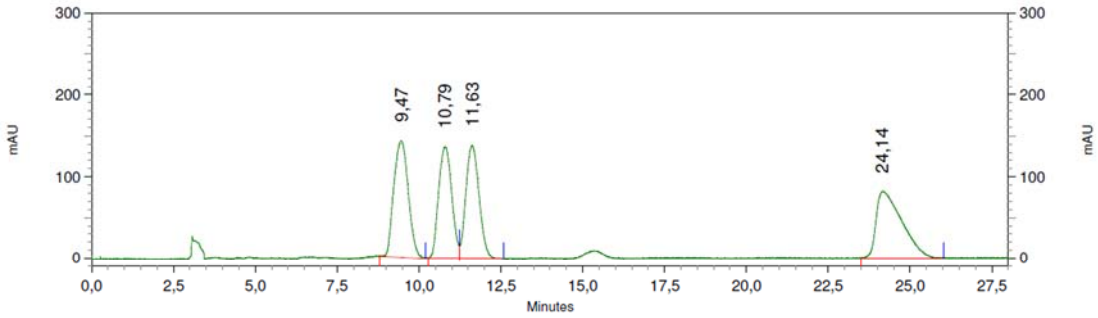


cis-(*4R,5R*)-**3u**
^{13}C NMR, 75 MHz, $CDCl_3$



3u

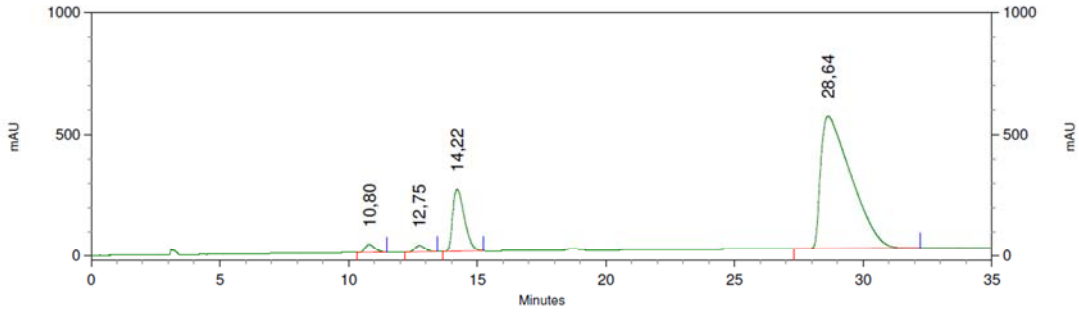
Racemic product:



3: 225 nm, 4 nm Results

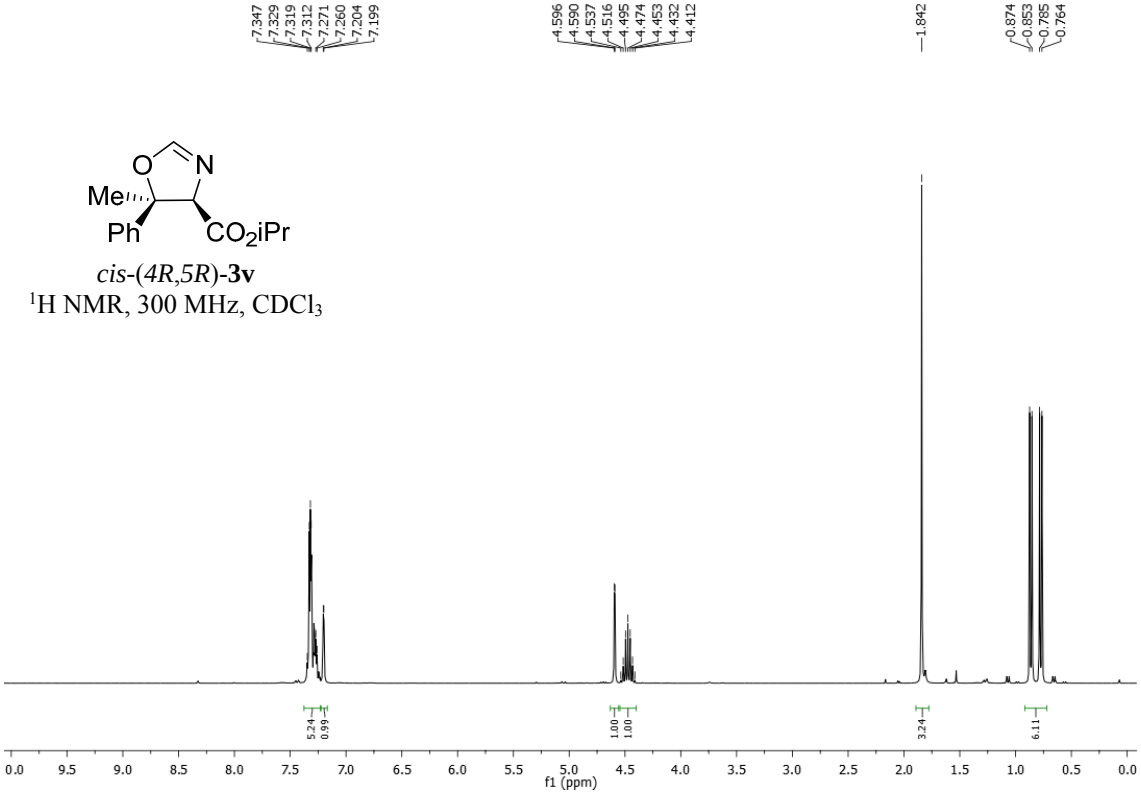
Retention Time	Area	Area Percent
9,47	17571643	26,484
10,79	15220132	22,940
11,63	15549219	23,436
24,14	18006601	27,140

Enantioselective reaction:

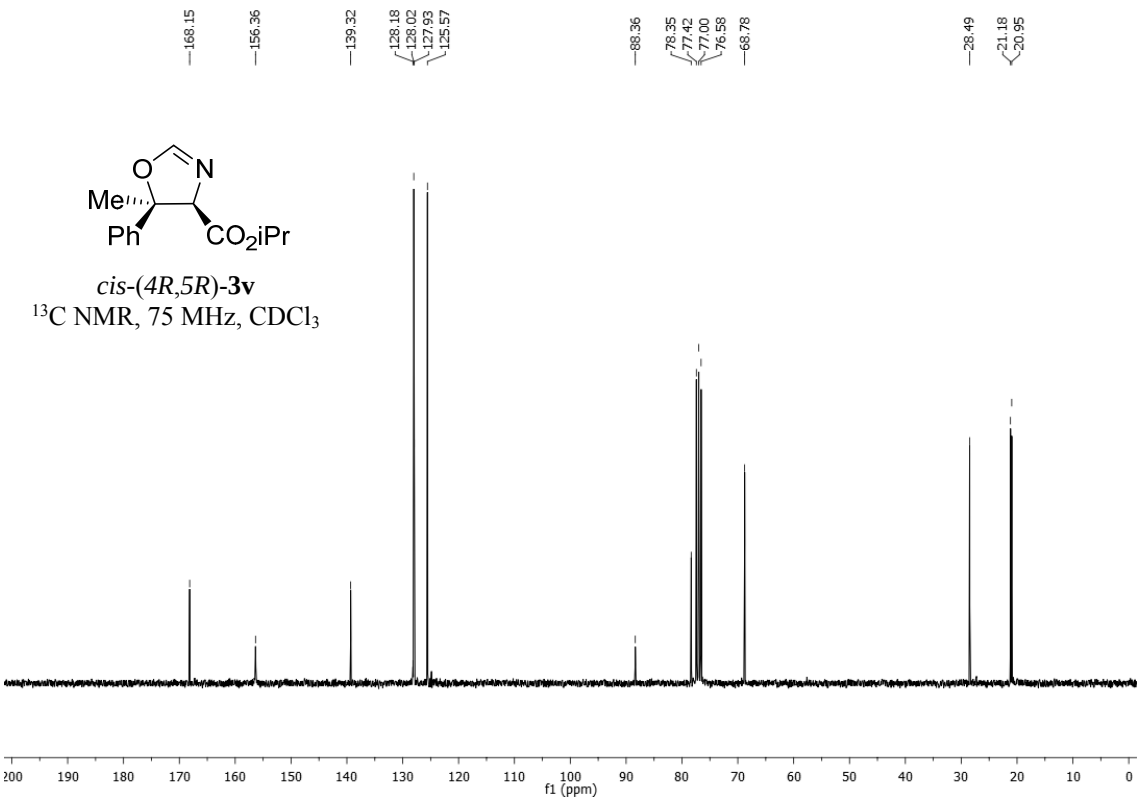


8: 219 nm, 4 nm Results

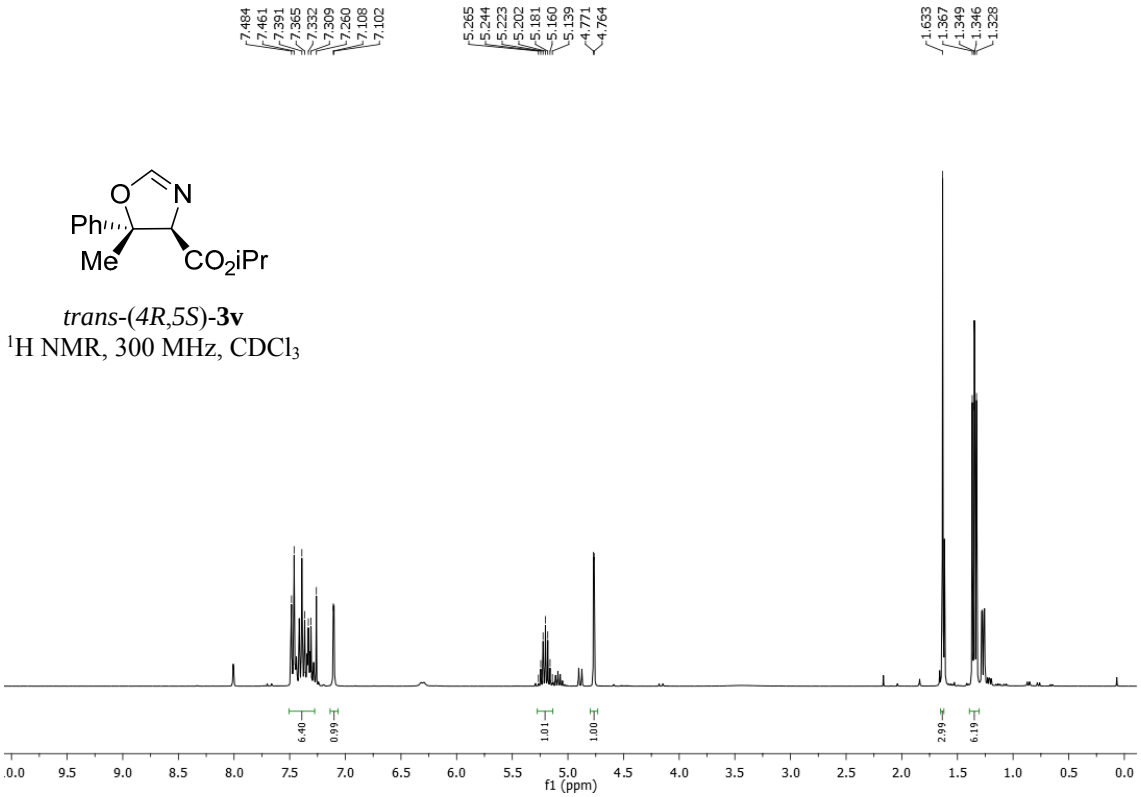
Retention Time	Area	Area Percent
10,80	3500110	1,601
12,75	2864472	1,310
14,22	32773954	14,988
28,64	179531253	82,102



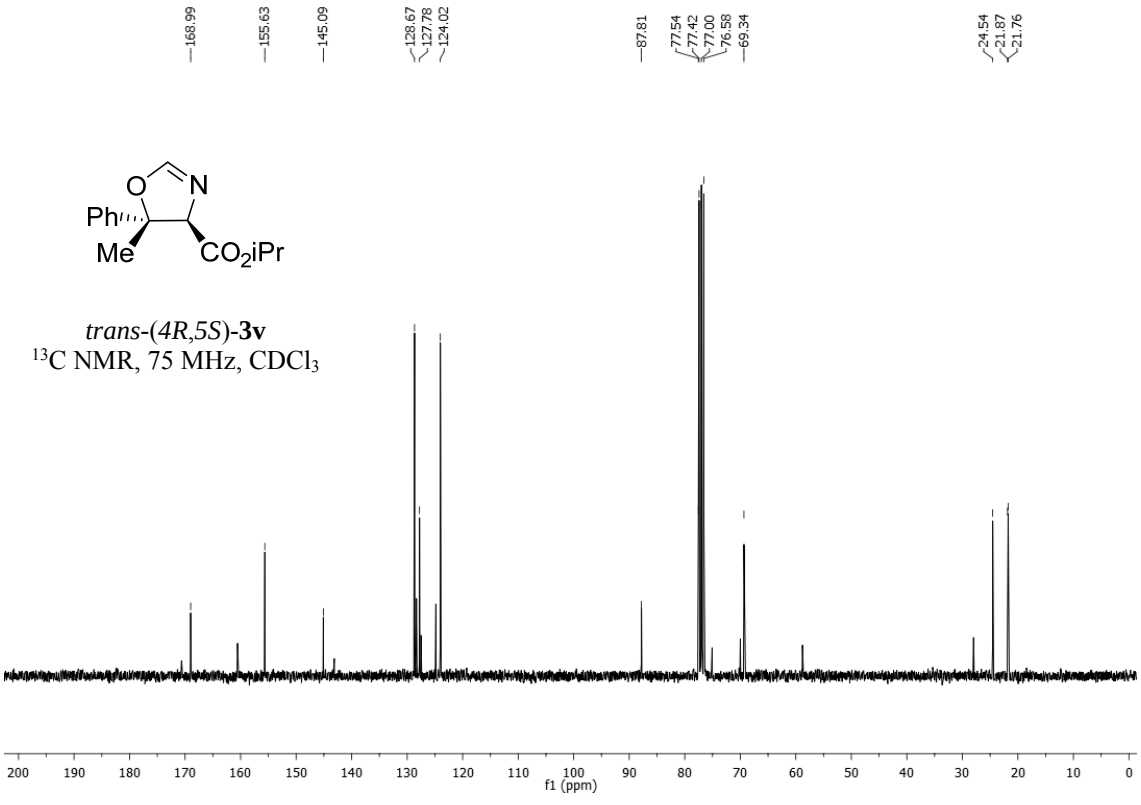
cis-(*4R*,*5R*)-**3v**
^{1}H NMR, 300 MHz, $CDCl_3$



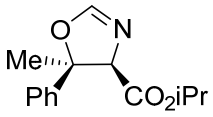
cis-(*4R*,*5R*)-**3v**
^{13}C NMR, 75 MHz, $CDCl_3$



trans-(*4R,5S*)-**3v**
^{1}H NMR, 300 MHz, $CDCl_3$

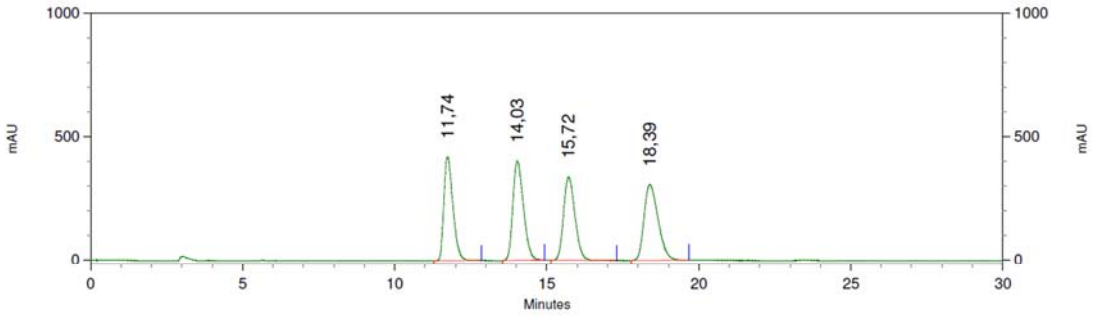


trans-(*4R,5S*)-**3v**
^{13}C NMR, 75 MHz, $CDCl_3$



3v

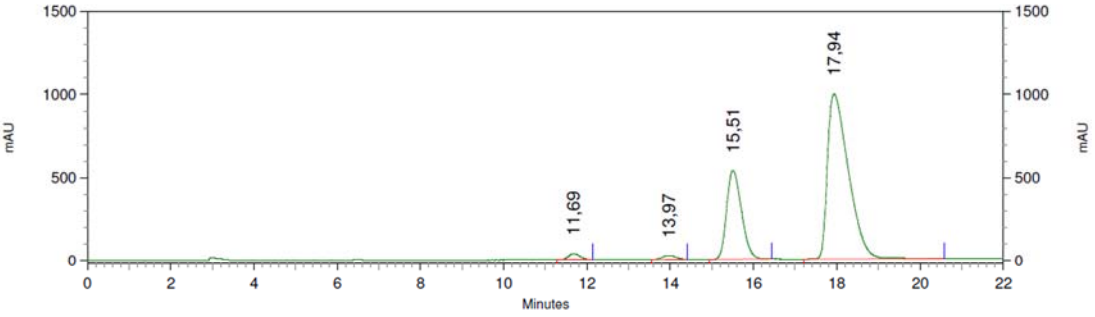
Racemic product:



12: 216 nm, 4 nm
Results

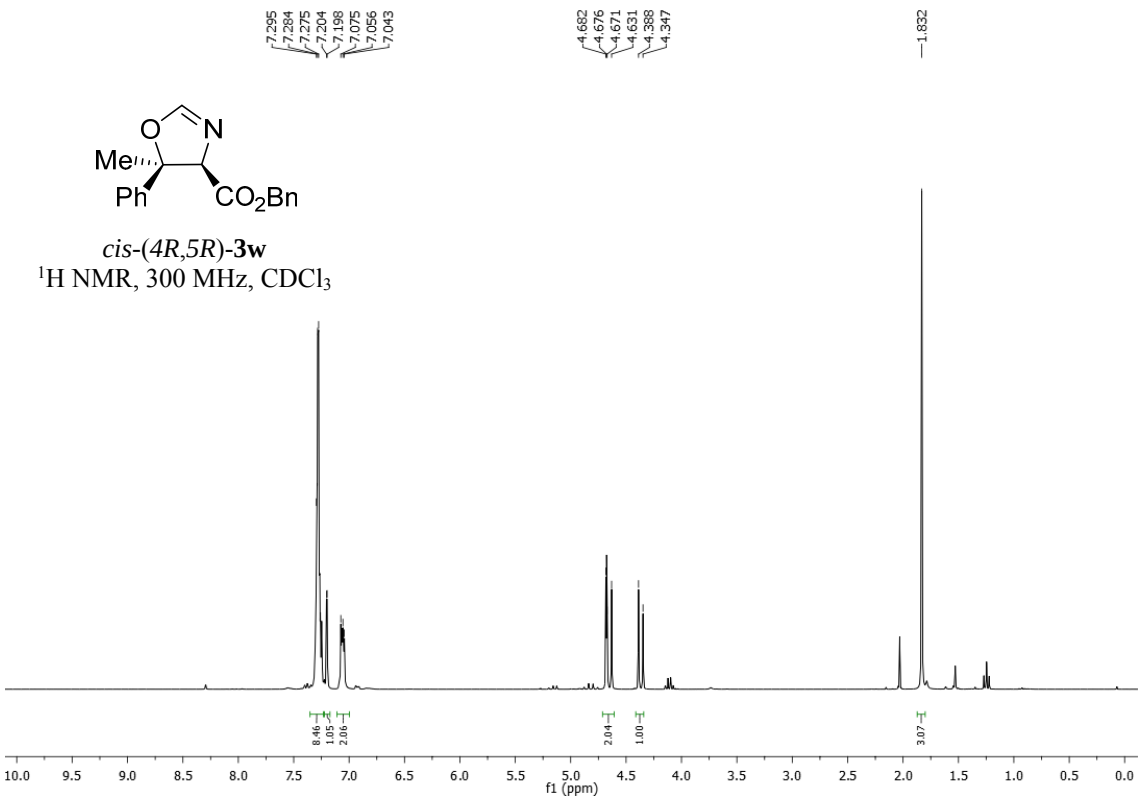
Retention Time	Area	Area Percent
11,74	35146870	23,577
14,03	39160747	26,269
15,72	35263464	23,655
18,39	39503991	26,499

Enantioselective reaction:

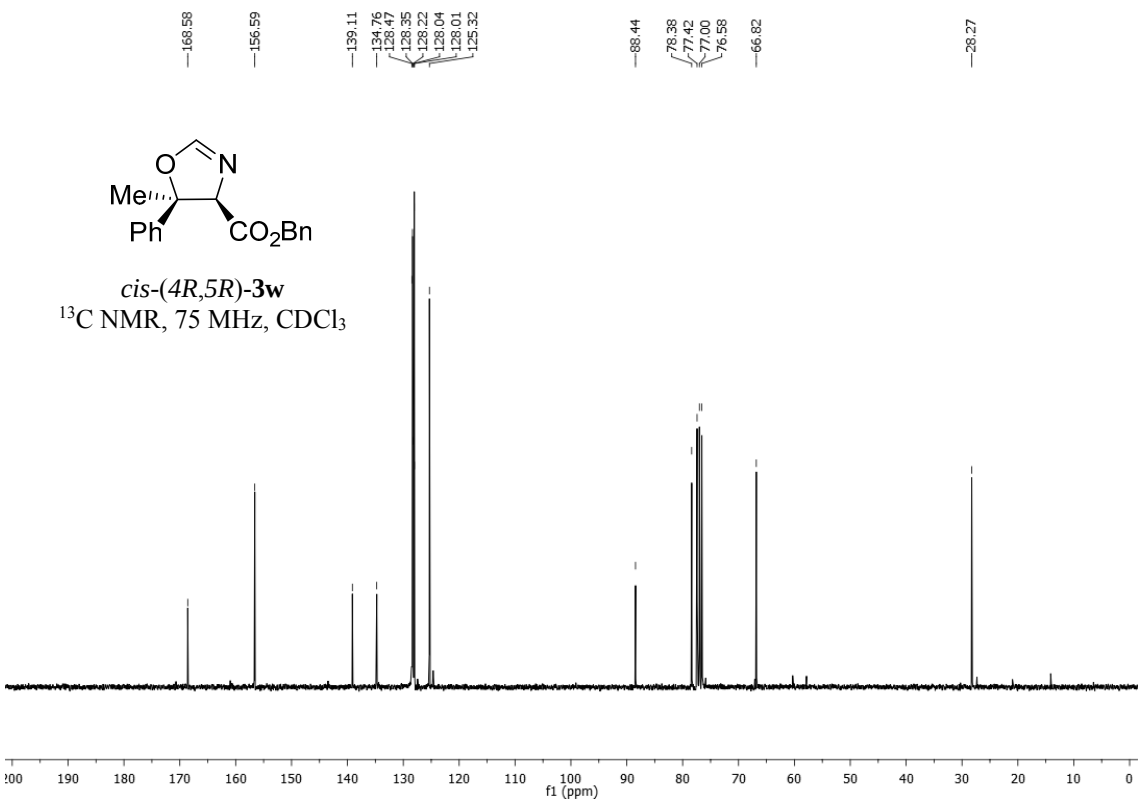


12: 216 nm, 4 nm
Results

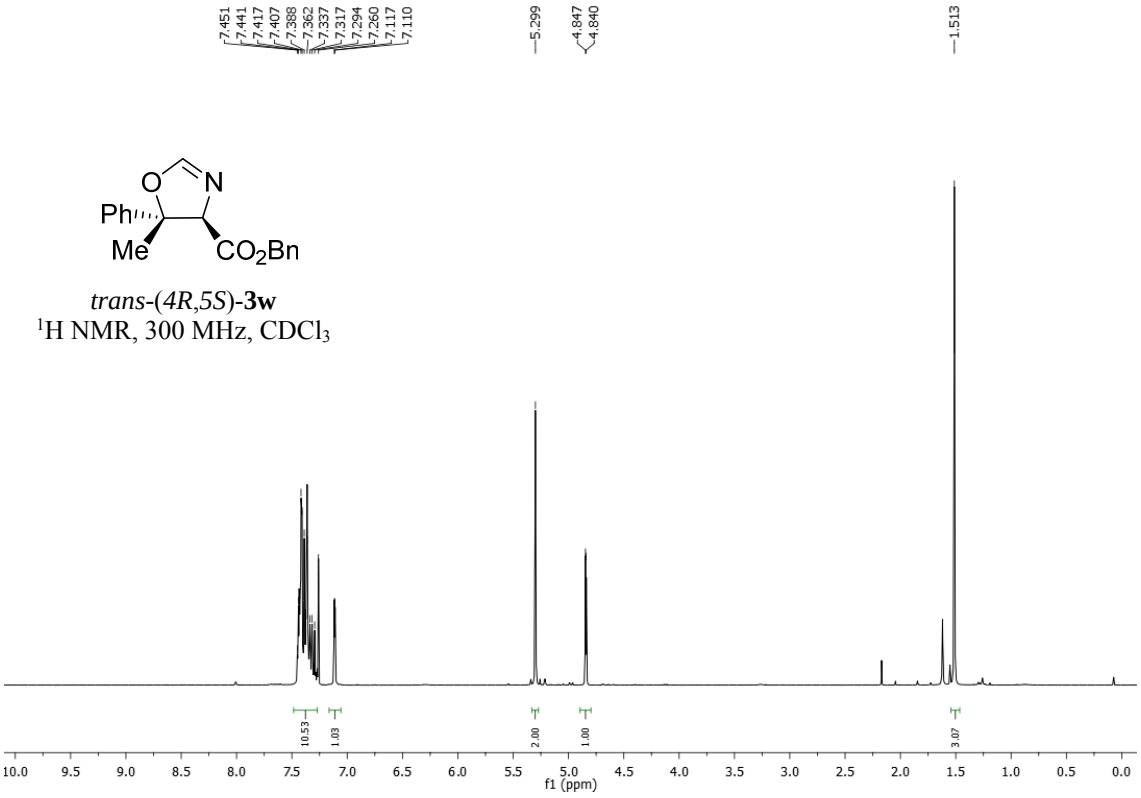
Retention Time	Area	Area Percent
11,69	2824836	1,431
13,97	2131013	1,080
15,51	53373048	27,045
17,94	139019584	70,444



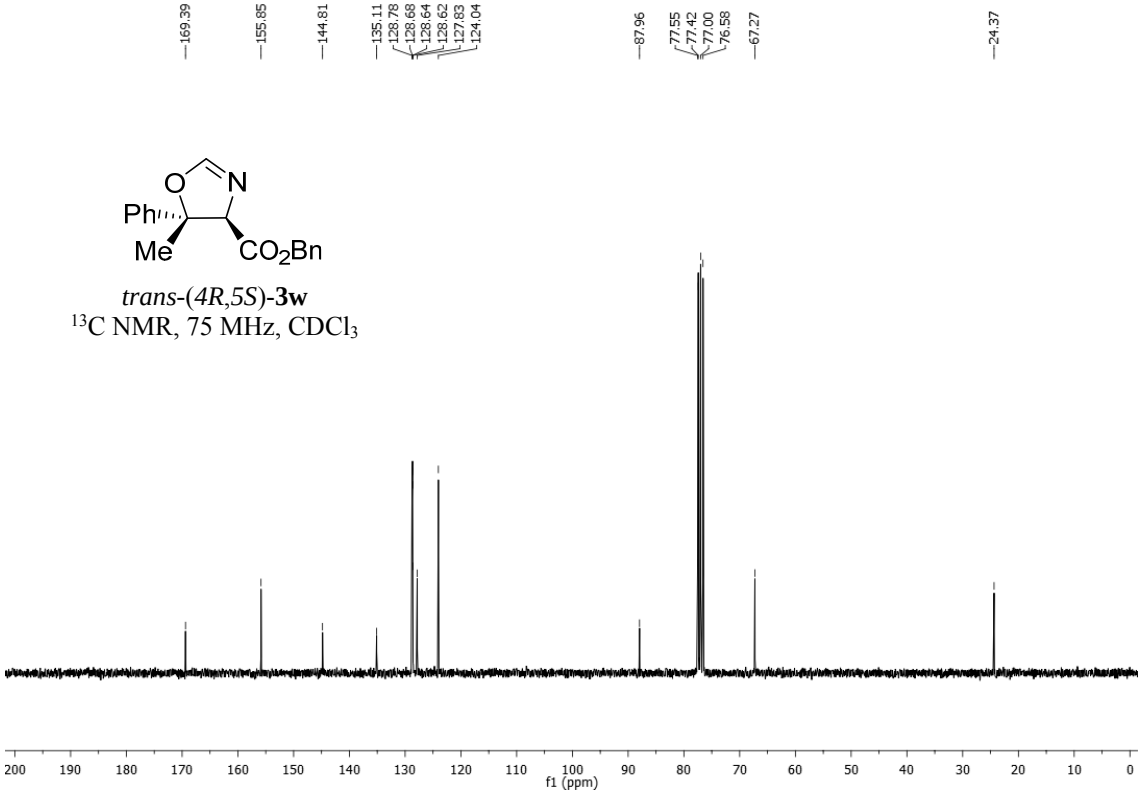
cis-(*4R*,*5R*)-**3w**
^{1}H NMR, 300 MHz, $CDCl_3$



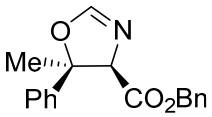
cis-(*4R*,*5R*)-**3w**
^{13}C NMR, 75 MHz, $CDCl_3$



trans-(*4R,5S*)-**3w**
^{1}H NMR, 300 MHz, $CDCl_3$

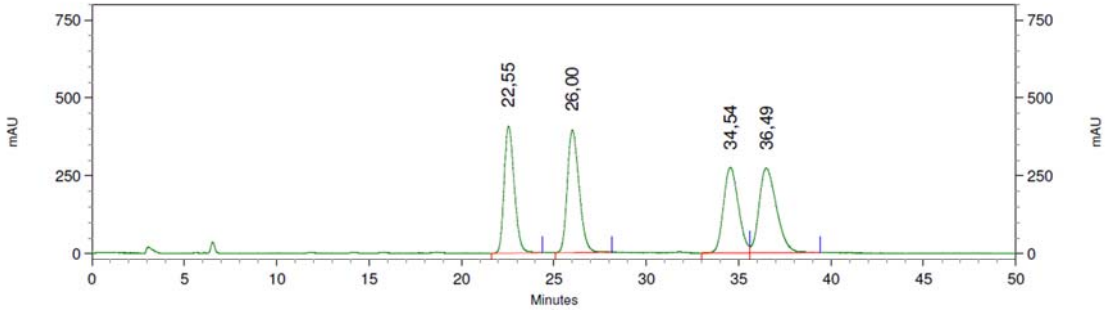


trans-(*4R,5S*)-**3w**
^{13}C NMR, 75 MHz, $CDCl_3$



3w

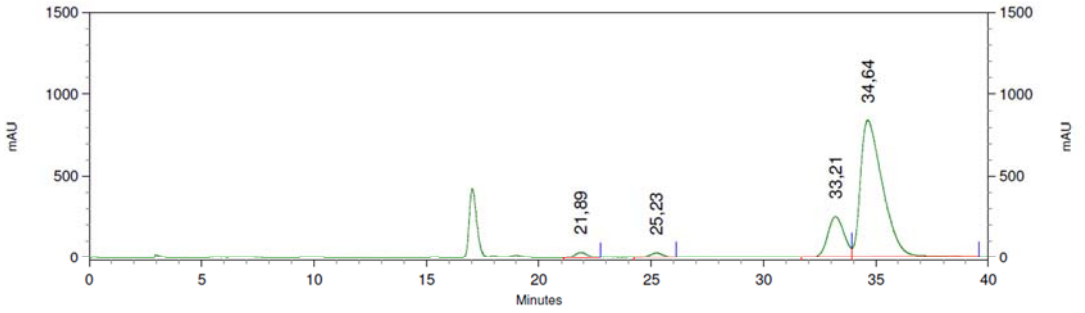
Racemic product:



12: 216 nm, 4 nm
Results

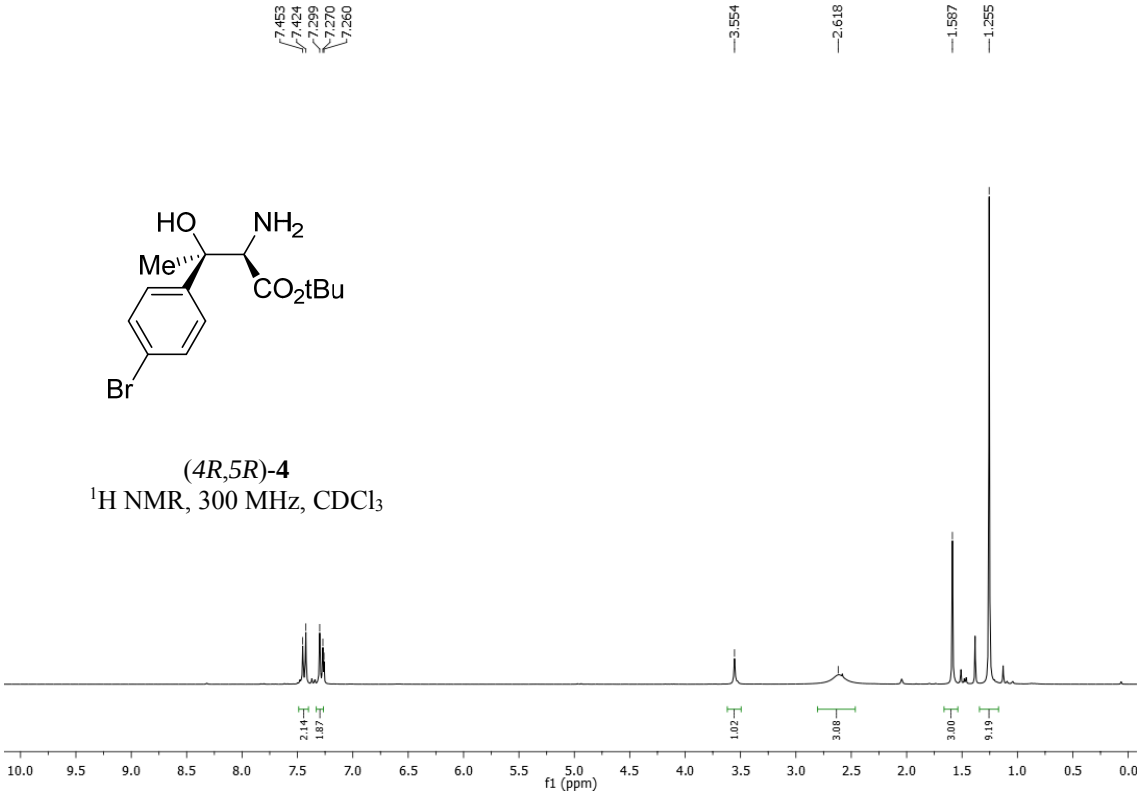
Retention Time	Area	Area Percent
22,55	62196696	23,471
26,00	70140865	26,468
34,54	61513371	23,213
36,49	71148231	26,848

Enantioselective reaction:

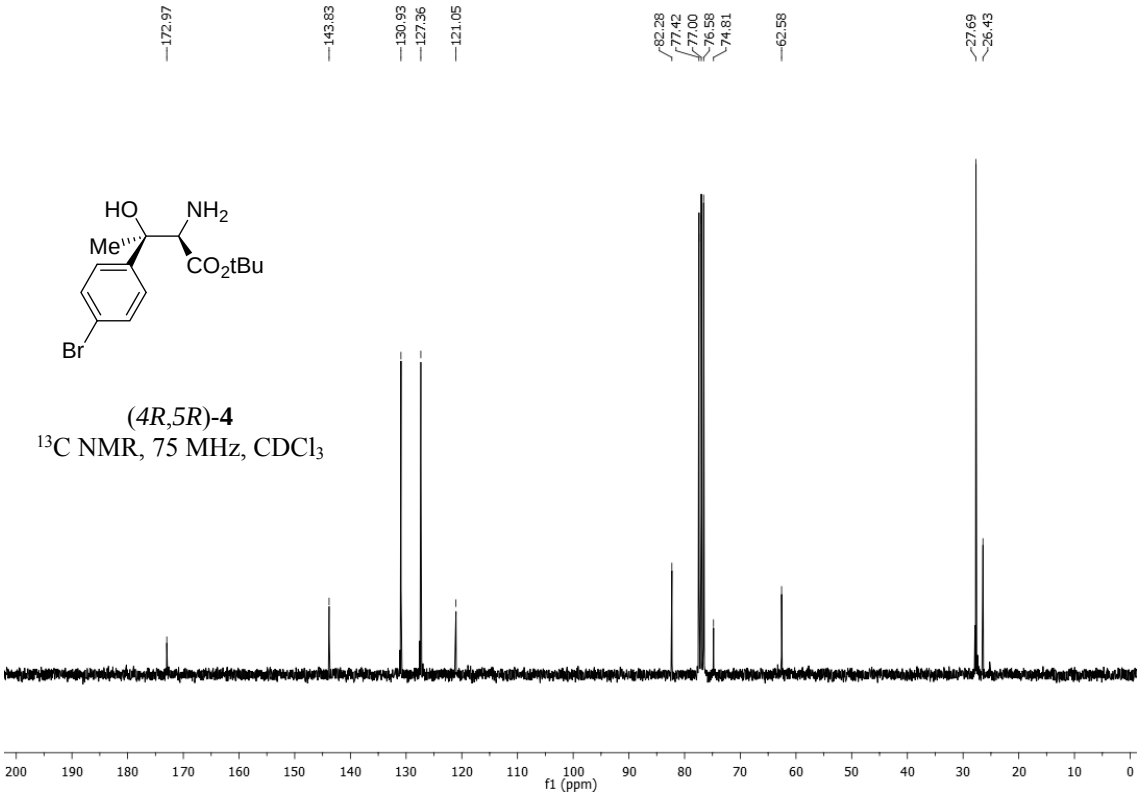


12: 216 nm, 4 nm
Results

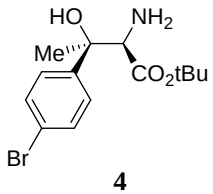
Retention Time	Area	Area Percent
21,89	4886130	1,681
25,23	4652413	1,601
33,21	50716005	17,448
34,64	230422157	79,271



(*4R*,*5R*)-**4**
^{1}H NMR, 300 MHz, $CDCl_3$

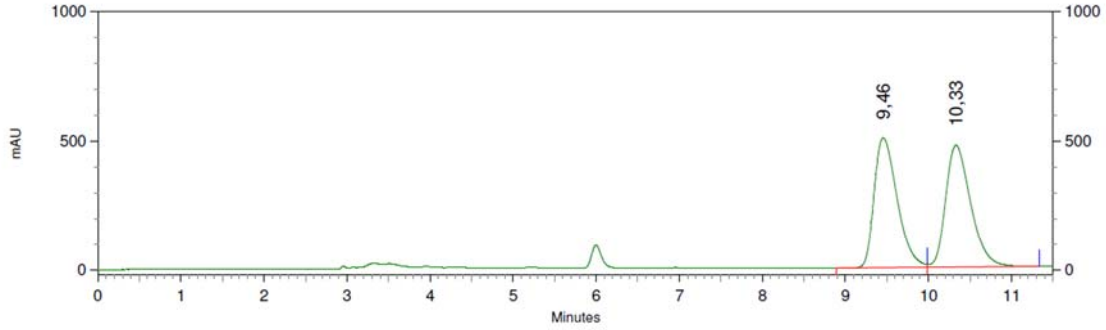


(*4R*,*5R*)-**4**
^{13}C NMR, 75 MHz, $CDCl_3$



4

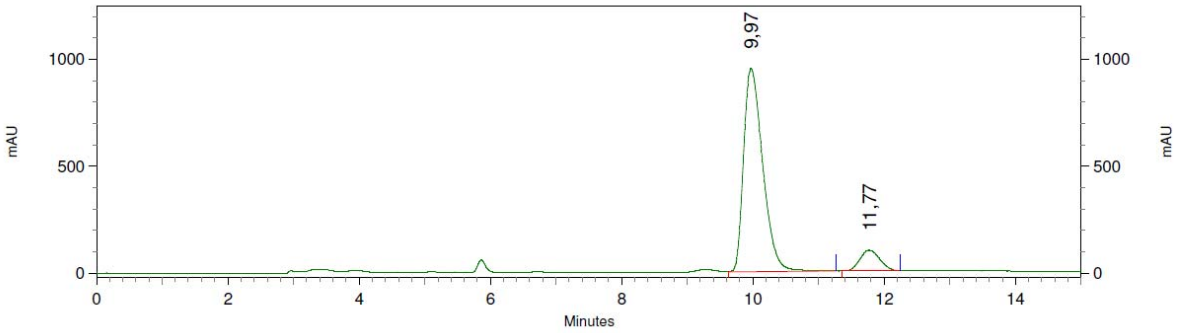
Racemic reaction:



9: 233 nm, 4 nm Results

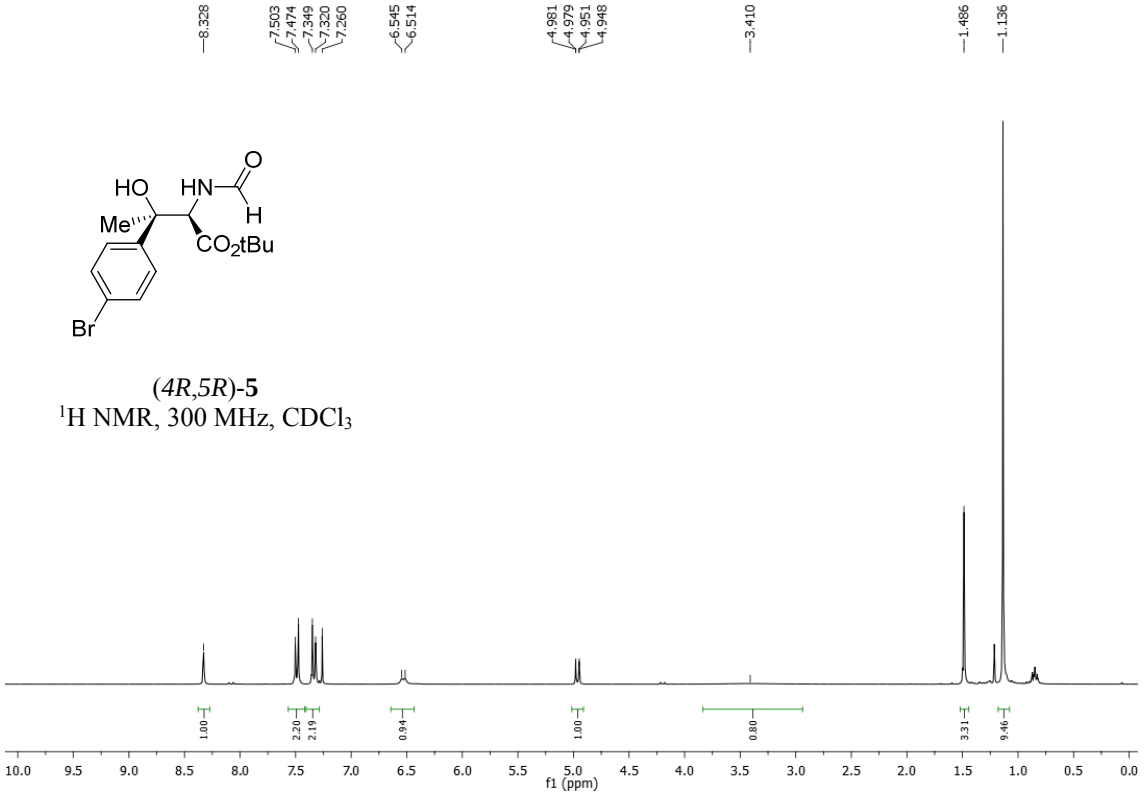
Retention Time	Area	Area Percent
9,46	38977702	49,334
10,33	40030312	50,666

Enantioselective reaction:

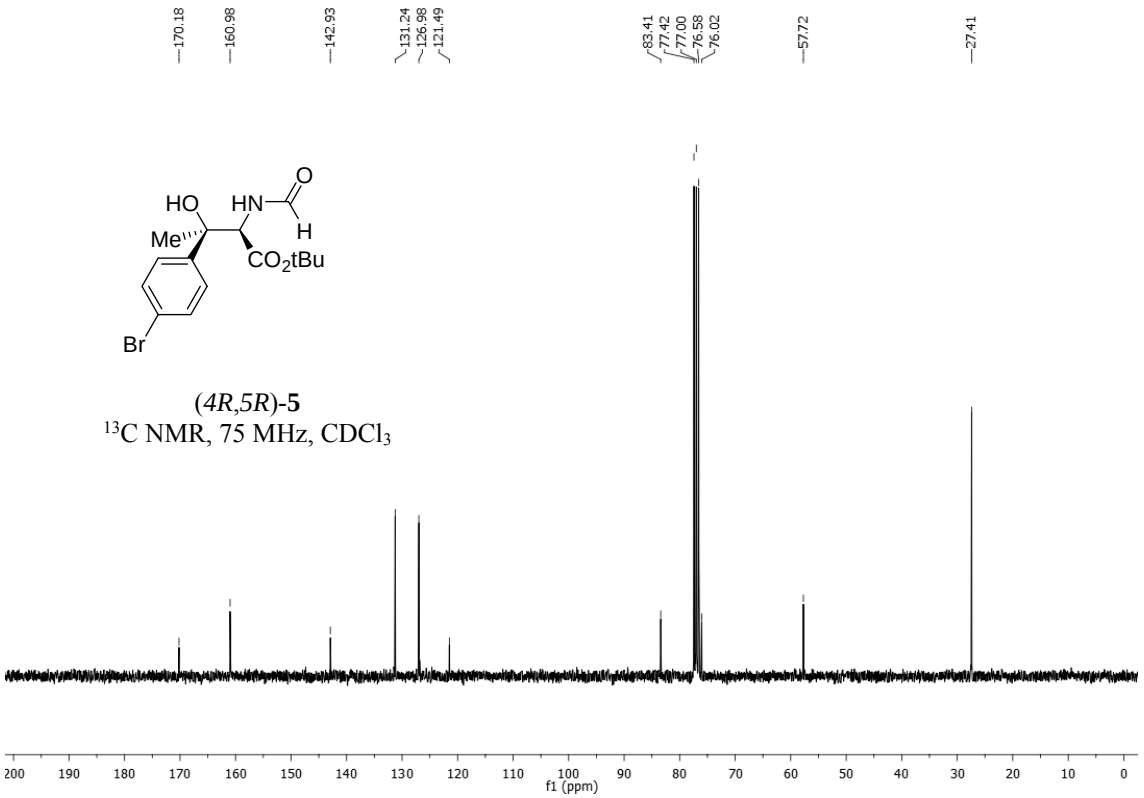


9: 233 nm, 4 nm Results

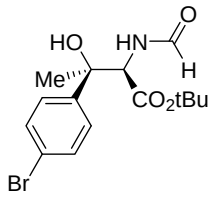
Retention Time	Area	Area Percent
9,97	77266136	90,322
11,77	8279493	9,678



(*4R*,*5R*)-**5**
^{1}H NMR, 300 MHz, $CDCl_3$

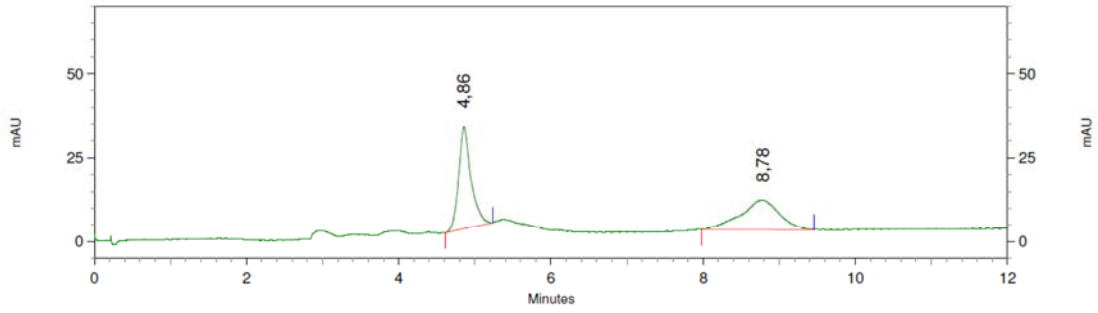


(*4R*,*5R*)-**5**
^{13}C NMR, 75 MHz, $CDCl_3$



5

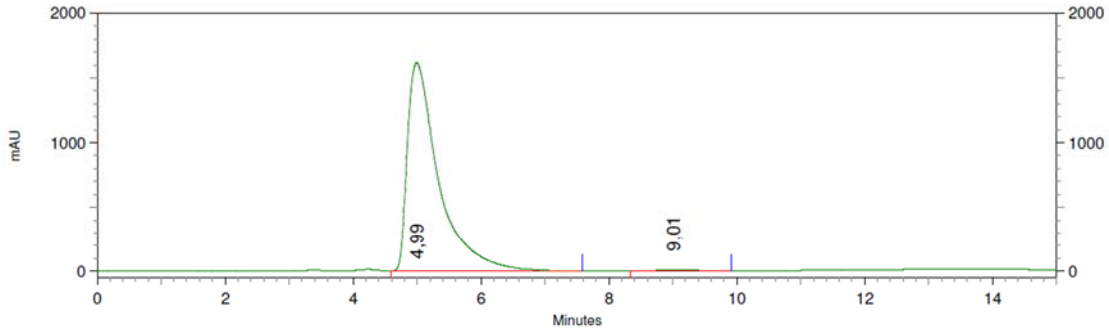
Racemic reaction:



4: 262 nm, 4 nm Results

Retention Time	Area	Area Percent
4,86	1380816	52,255
8,78	1261659	47,745

Enantioselective reaction:



1: 233 nm, 4 nm Results

Retention Time	Area	Area Percent
4,99	219996832	99,225
9,01	1717895	0,775

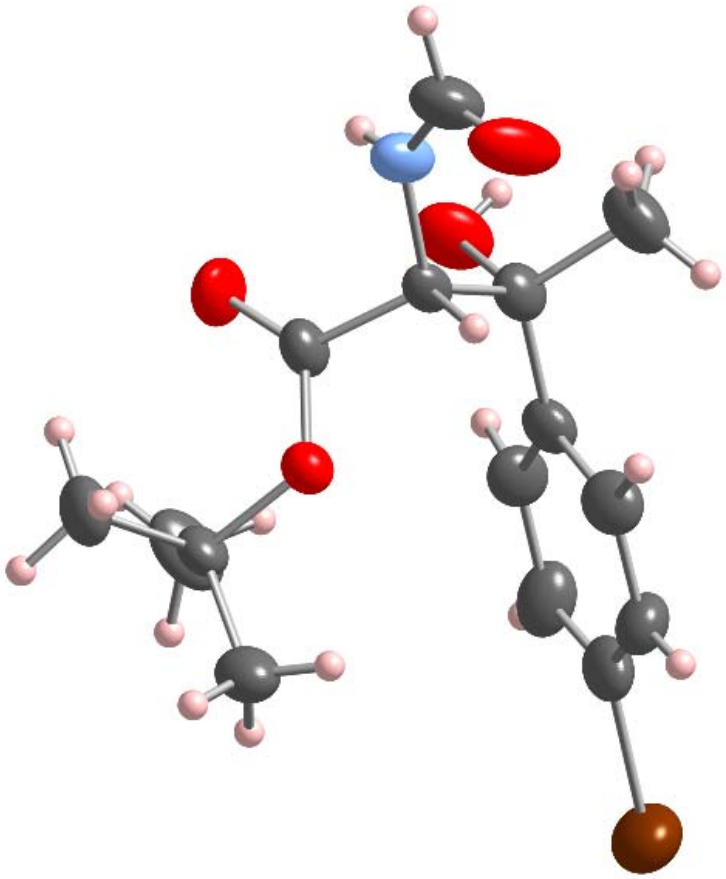


Figure S1. ORTEP plot for the X-Ray structure of compound **5**. Flack parameter = 0.019(10), Hooft parameter = 0.037(10)