Electronic Supplementary Material (ESI) for Chemical Science

Asymmetric Michael Additions of α-Cyanoacetates by Soft Lewis Acid / Hard Brønsted Acid Catalysis: Stereodivergency with Bi- *vs* Monometallic Catalysts

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Experimental

All reactions were performed in oven dried (150 °C) glassware and were magnetically stirred. A positive pressure of nitrogen (ca. 0.2 bar) was used as protective atmosphere. For all reactions liquids and solutions were added *via* syringe and septa. Solvents were removed by rotary evaporation at 40 °C bath temperature and 600 – 10 mbar pressure or by a constant stream of nitrogen. Non-volatile compounds were dried *in vacuo* at 0.1 mbar.

Diethyl ether, tetrahydrofuran (THF) and dichloromethane were distilled and further purified by a solvent purification system. Diglyme and acetonitrile (anhydrous, >99.5%) were stored over 4Å molecular sieves in crown capped bottles under nitrogen atmosphere. Methanol (super gradient grade), absolute ethanol, *iso*-propanol, chloroform (>99%), *n*-hexane (HPLC grade) and *n*-pentane (UV quality) were used as purchased. For work-up procedures and column chromatography distilled technical grade solvents (diethyl ether, petrol ether and ethyl acetate) were used. 2-Cyclohexen-1-one (**2a**) was distilled in vacuum prior to use and stored at –30 °C under inert atmosphere. **[FBIP-Cl]$_2$**,[1] **[FIP-Cl]$_2$**,[2] α-aryl-α-cyanoacetates **1a-j**,[3] 5,5-dimethyl-cyclohexen-1-one (**2d**),[4] 1*H*-inden-1-one (**2e**)[5] and silver salts[6] were prepared according to literature procedures. All other chemicals were purchased and used without further purification.

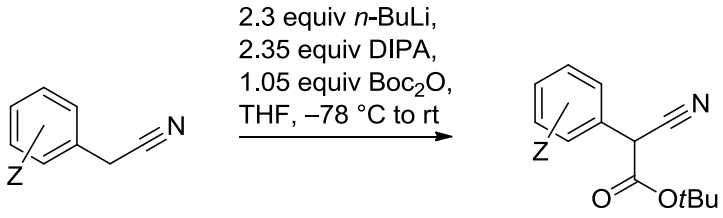
Reactions were either monitored by HPLC (reverse phase, acetonitrile/water as eluent) or by thin layer chromatography (TLC) with silica-plates (*silica gel 60 F_{254}*). Visualization was achieved by fluorescence quenching under UV light (λ = 254 nm) and/or by staining with $KMnO_4$/NaOH-solution (0.5 g $KMnO_4$ in 100 mL 0.1M NaOH). Preparative column chromatography for compound purification was performed on silica (0.040–0.063 mm), using a positive pressure of nitrogen (ca. 0.2 bar). Yields refer to pure isolated products and are calculated in mol% of the used starting material. Conversions refer to unconsumed cyanoacetate **2** and were either determined by ^{1}H-NMR using an internal standard or by RP-HPLC with a corresponding calibration curve.

^{1}H and ^{13}C NMR spectra were recorded at 21 °C on spectrometers operating at 250, 300 or 500 MHz for ^{1}H and 63, 75 or 125 MHz for ^{13}C. ^{19}F NMR spectra were recorded at 21 °C on a spectrometer operating at 235 MHz. Deuterated solvents were used as purchased and are stated after the corresponding frequency. Chemical shifts in ppm refer to tetramethylsilane (δ = 0) as internal standard. Coupling constants *J* are given in Hz and the following abbreviations are used for multiplicities: *s* (singulet), *d* (doublet), *t* (triplet), *q* (quartet), *p* (pentet), *m* (multiplet), *b* (broad signal). IR spectra were recorded by the analytical service of the Universität Stuttgart on a spectrometer with an ATR-unit. The aggregation state of the sample is stated in parentheses,

signals are given by wavenumbers (cm^{-1}). The *dr*- and *ee*-values of the Michael-Addition products **3** were determined by chiral stationary phase HPLC if not other mentioned. Optical rotation was measured at 20 °C on a polarimeter operating at the sodium-D line (λ = 589 nm). Path length of the quartz cell was 100 mm, solvent and concentration in $g\ mL^{-1}$ are stated in parentheses. Melting points were measured in open glass capillaries and are uncorrected. Mass spectra were performed by the analytical service of the Universität Stuttgart. The ionization method is stated in parentheses. Microanalyses were performed by the analytical service of the Universität Stuttgart. Single crystal X-ray analysis was performed by Dr. Wolfgang Frey.

General Procedures (GP)

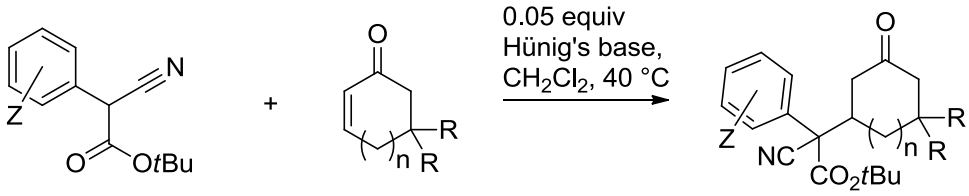
General Procedure for the Formation of α-Aryl-α-cyanoacetates 1 (GP1)



1

n-Butyllithium (39.3 mmol, 2.3 equiv) was added at –78 °C to *N*,*N*-di-*iso*-propylamine (40.1 mmol, 2.35 equiv) in THF (40 mL) under protective atmosphere. The solution was warmed to room temperature and cooled to –78 °C after 5 min. A solution of the corresponding 2-arylacetonitrile (17.1 mmol, 1 equiv) in THF (15 mL) was added slowly. The reaction mixture was then warmed to room temperature and stirred for additional 10 min before it was cooled to –78 °C. Then di-*tert*-butyldicarbonate (17.9 mmol, 1.05 equiv) in THF (10 mL) was added and the reaction mixture was stirred for 18 h at room temperature. The reaction was quenched by adding saturated aqueous ammonium chloride (10 mL). Water and diethyl ether were added for a clear phase separation. The separated organic layer was dried over Na_2SO_4, filtrated and the solvent was removed *in vacuo*. Pure α-aryl-α-cyanoacetate **1** was obtained after vacuum distillation or column chromatography.[3]

General Procedure for the Formation of Racemic Michael-Addition Products 3 (GP2)

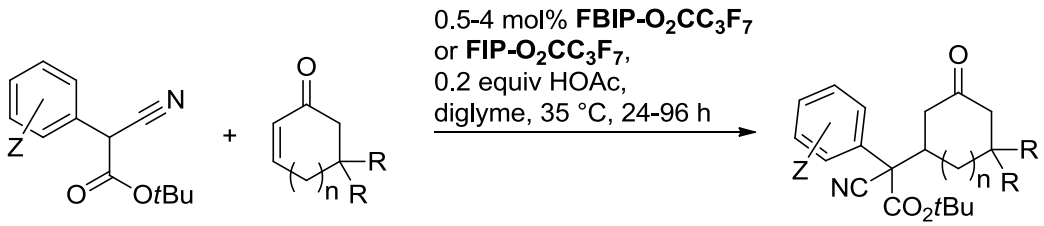


1 **2** ***rac*-3**

The α-aryl-α-cyanoacetate **1** (1 equiv) was dissolved in CH_2Cl_2 (~3 mL per mmol **1**) and the enone **2** (1 equiv) and *N*,*N*-di-*iso*-propyl-*N*-ethylamine (0.05 equiv) were added. The reaction mixture was stirred overnight at 40 °C. Solvent was removed *in vacuo* and the residue was

subjected to column chromatography to give the pure, racemic product ***rac*-3**.[6] The reaction is not optimized.

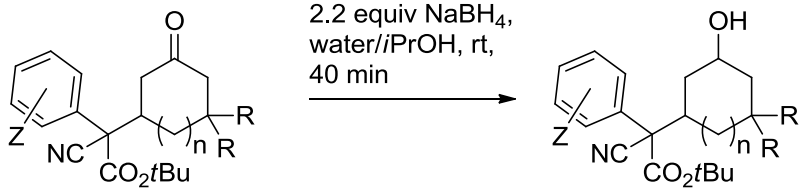
General Procedure for the Catalytic Asymmetric Michael-Addition (GP3)



1 **2** **(*R*,*R*)- or (*S*,*R*)-3**

To the corresponding α-aryl-α-cyanoacetate **1** (0.09 mmol, 1 equiv) in diglyme (in total 170 µL diglyme per 0.09 mmol α-aryl-α-cyanoacetate) were added acetic acid as a stock solution in diglyme (c = 0.87 mol L^{-1}, 0.2 equiv), the activated catalyst **FBIP-$O_2CC_3F_7$** or **FIP-$O_2CC_3F_7$** (stock solution in diglyme, see "Activation of the Precatalyst **[FBIP-Cl]$_2$** and **[FIP-Cl]$_2$** with AgO2CC3F7 / Acetonitrile", S-17) and finally the corresponding enone **2** (0.18 mmol, 2.0 equiv). The reaction mixture was stirred for the indicated time at 35 °C. Afterwards *n*-pentane was added to precipitate the catalyst and the resulting suspension was filtrated through silica. The filter cake was further washed with petrol ether: ethyl acetate (4:1). Removal of the solvent and an excess of enone **2** resulted in the pure Michael-Addition products **3**.[6]

General Procedure for the Reduction of the Keto Group in the Michael-Addition Product 3 (GP4)

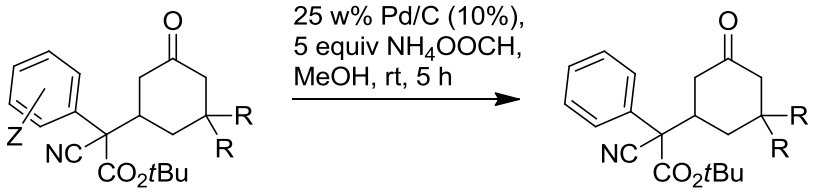


(*R*,*R*)- or (*S*,*R*)-3 **(*R*,*R*,*S*)- or (*S*,*R*,*S*)-6**

The Michael-addition product **3** (1 equiv) was dissolved in *i*-PrOH (1 mL per 60.0 mg) and a solution of $NaBH_4$ (2.2 equiv) in water (1 mL per 50 mg) was added dropwise to the ketone at room temperature. The reaction was stirred for an additional 40 min and was quenched and acidified with conc. HCl. The aqueous phase was extracted three times with ethylacetate. The

combined organic phase was dried over Na_2SO_4, filtrated and the solvent removed *in vacuo*. The residue was subjected to column chromatography (PE:EtOAc = 4:1) to give the pure secondary alcohol **6**.

General Procedure for the Reductive Dehalogenation of Michael-Addition Product 3 (GP5)

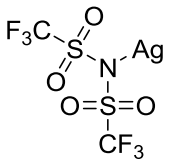


(*R*,*R*)- or (*S*,*R*)-3 **(*R*,*R*)/(*S*,*R*)-3aa or 3ad**

The Michael-addition product **3** (1 equiv) was dissolved in MeOH (1 mL per 10.0 mg) and ammonium formate (5 equiv) was added. Pd/C (10%, 25w% of the starting material **3**) was added under oxygen free atmosphere and the reaction was stirred for 5 h at room temperature. Afterwards the solvent was removed *in vacuo* and CH_2Cl_2 was added to the residue. The suspension was filtered over a short pad of celite/silica (1:1) and the solvent removed *in vacuo* to gain the crude product. The residue was subjected to column chromatography (PE:EtOAc = 9:1) to give the pure dehalogenated product **3aa** or **3ad**.[7] The reaction is not optimized.

Synthesis of Silver Salts

Silver(I)(bistrifluoromethane)sulfonimide

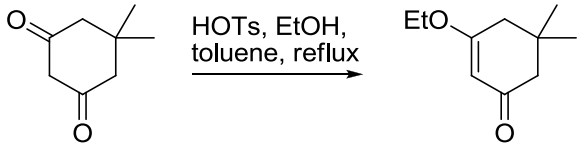


Lithium(bistrifluoromethane)sulfonimide (2.00 g, 7.00 mmol) was dissolved in demin. water and treated with conc. HCl (10M). The resulting imide polyhydrate was obtained by extraction with diethyl ether and solvent removal. The oily residue was dissolved in diethyl ether, stirred for a few min and solvent removed. This was repeated three times to give the monohydrate of the imide. Afterwards it was dissolved in acetonitrile to form a 1M solution and silver carbonate (528.3 mg, 1.92 mmol, 0.55 equiv) was added. The suspension was stirred for 2 h at room temperature, then it was filtrated and the solvent removed *in vacuo*. Recrystallization from CH_2Cl_2 resulted in solid, colorless **$AgN(Tf)_2$** (1.11 g, 2.87 mmol, 41%).

$C_2AgF_6NO_4S_2$, MW: 388.01 g mol^{-1}. **Mp:** decomposition > 250°C. **^{13}C NMR (75 MHz, CD_3CN, 21 °C):** δ = 119.5 (*q*, *J* = 321, *C*F_3). **^{19}F NMR (235 MHz, CD_3CN, 21 °C):** δ = –80.17. **Microanalysis:** Calculated for $C_2AgF_6NO_4S_2$: C: 6.19; N: 3.61; S: 16.53. Found: C: 6.50; N: 3.67; S: 16.17.

Synthesis of Cyclic Enones

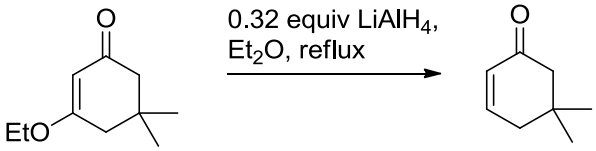
3-Ethoxy-5,5-dimethyl-2-cyclohexen-1-one[4]



Dimedone (5 g, 35.7 mmol, 1 equiv), absolute ethanol (6.7 mL, 3.2 equiv) and *p*-toluenesulfonic acid (142 mg, 2.1 mol%) in toluene (40 mL) were heated with azeotropic removal of water until dimedone had completely reacted (usually after 5 h). Removal of the solvent and vacuum distillation (95 °C at 1.6 mbar) of the residual resulted in pure liquid, colorless 3-ethoxy-5,5-dimethyl-2-cyclohexen-1-one (3.88 g, 23.1 mmol, 65%).

$C_{10}H_{16}O_2$, MW: 168.23 g mol^{-1}. **^{1}H NMR (300 MHz, $CDCl_3$, 21 °C):** δ = 5.35 (*s*, 1H, C*H*), 3.91 (*q*, *J* = 7.0, 2H, OC*H*$_2$CH$_3$), 2.28 (*s*, 2H, CH$_2$), 2.21 (*s*, 2H, CH$_2$), 1.37 (*t*, *J* = 7.0, 3H, OCH$_2$C*H*$_3$), 1.07 (*s*, 6H, CH$_3$). . **^{13}C NMR (75 MHz, $CDCl_3$, 21 °C):** δ = 199.7, 176.3, 101.5, 64.3, 50.7, 42.9, 32.5, 28.3, 14.1. The other analytical data are in accordance with the literature.[4]

5,5-dimethyl-2-cyclohexen-1-one (2d)[4]

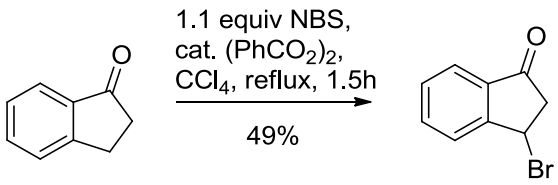


2d

3-Ethoxy-5,5-dimethyl-2-cyclohexen-1-one (2.00 g, 12 mmol, 1 equiv) in dry diethyl ether (10 mL) was dropwise added to a suspension of $LiAlH_4$ (144.4 mg, 3.8 mmol, 0.32 equiv) in dry diethyl ether (20 mL) so that the ether was slightly boiling. Subsequently the reaction mixture was heated to reflux and stirred for an additional hour. Afterwards the flask was cooled with ice and ice water was added very carefully until the formation of hydrogen ended. The formed precipitate was dissolved with aq. H_2SO_4 (9 mL, 10%). The layers were separated and the aqueous phase was extracted two times with diethyl ether. The combined organic layer was dried over $MgSO_4$, filtrated and the solvent was removed *in vacuo*. Vacuum distillation of the residue gave 5,5-dimethyl-2-cyclohexen-1-one as pale yellow liquid (0.94 g ,7.6 mmol, 63%).

$C_8H_{12}O$, **MW:** 124.18 g mol^{-1}. **^{1}H NMR (300 MHz, $CDCl_3$, 21 °C):** δ = 6.87 (*dt*, *J* = 10.1, 4.1, 1H, C*H*), 6.03 (*dt*, *J* = 10.1, 2.0, 1H, C*H*), 2.28 (*s*, 2H, CH_2), 2.25 (*dd*, *J* = 2.0, 2.0, 2H, CH_2), 1.06 (*s*, 6H, CH_3). **^{13}C NMR (75 MHz, $CDCl_3$, 21 °C):** δ = 200.0, 148.4, 128.9, 51.8, 39.9, 33.9, 28.3. The other analytical data are in accordance with the literature.[4]

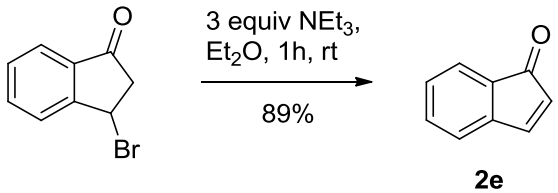
3-Bromo-2,3-dihydro-1*H*-inden-1-one[8]



To 1*H*-indan-1-one (2.64 g, 20.0 mmol, powder) in CCl_4 (150 mL) was added N-bromosuccinimide (3.91 g, 22.0 mmol, 1.1 equiv) and dibenzoylperoxide (48.4 mg, 0.20 mmol, 0.01 equiv). The mixture was stirred under reflux for 1.5h. Afterwards the reaction mixture was cooled, filtered and concentrated *in vacuo*. The oily crude product was recrystallized from EtOAc/heptanes (1:4, 10 mL) to give 3-bromo-2,3-dihydro-1*H*-inden-1-one (2.08 g, 9.88 mmol, 49%) as orange solid.

C_9H_7BrO, **MW:** 211.06 g mol^{-1}. ***Mp*:** 54.0–54.5 °C. **^{1}H NMR (300 MHz, $CDCl_3$, 21 °C):** δ = 7.77–7.70 (*m*, 3H, arom. *H*), 7.53–7.45 (*m*, 1H, arom. *H*), 5.61 (*dd*, *J* = 7.1, 2.7, 1H, C*H*), 3.39 (*dd*, *J* = 20.0, 7.2, 1H, CH_2), 3.06 (*dd*, *J* = 19.8, 2.8, 1H, CH_2). **^{13}C NMR (75 MHz, $CDCl_3$, 21 °C):** δ = 201.5, 154.3, 136.0, 135.6, 129.7, 127.5, 123.4, 48.1, 40.6. The other analytical data are in accordance with the literature.[8]

1*H*-Inden-1-one (2e)[5]



2e

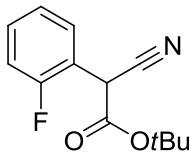
To a solution of 3-bromo-2,3-dihydro-1*H*-inden-1-one (501.0 mg, 2.37 mmol) in Et_2O (5 mL) was added triethylamine (990 µL, 7.12 mmol, 3 equiv) dropwise over 10 min at room temperature. The reaction was stirred for 1h. Then water was added and the organic phase was several times well washed with water, brine and dried over Na_2SO_4. After filtration and

concentration in vacuo, the crude product was purified by vacuum distillation (0.54 mbar, 47 °C) to give 1*H*-inden-1-one **2e** (275.0 mg, 2.11 mmol, 89%) as pale yellow, viskous oil.

C_9H_6O, **MW:** 130.14 g mol^{-1}. **^{1}H NMR (300 MHz, $CDCl_3$, 21 °C):** δ = 7.56 (*d*, *J* = 5.8, 1H, C*H*), 7.42 (*d*, *J* = 6.6, 1H, arom. *H*), 7.34 (*t*, *J* = 7.5, 1H, arom. *H*), 7.22 (*t*, *J* = 7.5, 1H, arom. *H*), 7.05 (*d*, *J* = 7.0, 1H, arom. *H*), 5.88 (*d*, *J* = 5.8, 1H, C*H*). **^{13}C NMR (75 MHz, $CDCl_3$, 21 °C):** δ = 198.5, 149.8, 144.6, 133.7, 130.4, 129.1, 127.2, 122.6, 122.3. The other analytical data are in accordance with the literature.[5]

Synthesis of α-Aryl-α-Cyanoacetates

tert-Butyl-2-cyano-(*o*-fluorophenyl)acetate (1k)

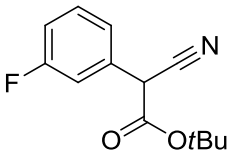


1k

According to GP1 2-(*o*-fluorophenyl)acetonitrile (2.00 g, 14.8 mmol, 1 equiv) was treated with di-*tert*-butyldicarbonate (3.39 g, 15.5 mmol, 1.05 equiv). Column chromatography (petrol ether: EtOAc = 18:1) of the crude product resulted in liquid, pale yellow *tert*-butyl-2-cyano-(*o*-fluorophenyl)acetate (**1k**, 2.33 g, 9.92 mmol, 67%).

$C_{13}H_{14}FNO_2$, MW: 235.25 g mol^{-1}. **^{1}H NMR (300 MHz, $CDCl_3$, 21 °C):** δ = 7.50 (*td*, *J* = 7.5, 1.7, 1H, arom. *H*), 7.43-7.36 (*m*, 1H, arom. *H*), 7.22 (*td*, *J* = 7.6, 1.1, 1H, arom. *H*), 7.16-7.10 (*m*, 1H, arom. *H*), 4.92 (*s*, 1H, C*H*), 1.47 (*s*, 9H, CH_3). **^{13}C NMR (75 MHz, $CDCl_3$, 21 °C):** δ = 162.9, 160.0 (*d*, *J* = 250.2, *C*F), 131.2 (*d*, *J* = 8.3, *C*CCF), 129.6 (*d*, *J* = 2.4, *C*CCCF), 124.9 (*d*, *J* = 3.8, *C*CCF), 118.4 (*d*, *J* = 14.8, *C*CF), 115.9 (*d*, *J* = 20.9, *C*CF), 115.2, 84.9, 38.3, 27.6. **^{19}F NMR (235 MHz, $CDCl_3$, 21 °C):** δ = –116.73 (*m*, 1F). **IR (film):** ν = 2984, 2938, 1747, 1619, 1592, 1496, 1396, 1372, 1280, 1243, 1151, 1106, 1094, 1035, 950. **HRMS (EI) *m/z*:** Calc. for $[M - CH_3]^+$: 220.0769. Found: 220.0770. **Microanalysis:** Calc. for $C_{13}H_{14}NO_2F$: C: 66.37; H: 6.00; N: 5.95. Found: C: 66.45; H: 6.17; N: 6.16.

tert-Butyl-2-cyano-(*m*-fluorophenyl)acetate (1l)

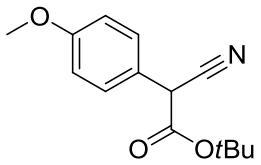


1l

According to GP1 2-(*m*-fluorophenyl)acetonitrile (2.45 g, 18.1 mmol, 1 equiv) was treated with di-*tert*-butyldicarbonate (4.15 g, 19.0 mmol, 1.05 equiv). Column chromatography (petrol ether: EtOAc = 9:1) of the crude product resulted in liquid, pale yellow *tert*-butyl-2-cyano-(*m*-fluorophenyl)acetate (**1l**, 2.68 g, 11.4 mmol, 63%).

$C_{13}H_{14}FNO_2$, MW: 235.25 g mol^{-1}. **^{1}H NMR (300 MHz, $CDCl_3$, 21 °C):** δ = 7.44-7.36 (*m*, 1H, arom. *H*), 7.26-7.16 (*m*, 2H, arom. *H*), 7.13-7.07 (*m*, 1H, arom. *H*), 4.62 (*s*, 1H, C*H*), 1.46 (*s*, 9H, CH_3). **^{13}C NMR (75 MHz, $CDCl_3$, 21 °C):** δ = 163.3, 162.9 (*d*, *J* = 248.8, *C*F), 132.5 (*d*, *J* = 7.9, *C*CCF), 130.9 (*d*, *J* = 8.4, *C*CCF), 123.6 (*d*, *J* = 3.3, *C*CCCF), 116.2 (*d*, *J* = 21.1, *C*CF), 115.5, 115.2 (*d*, *J* = 23.4, *C*CF), 85.0, 44.5, 44.4, 27.6. **^{19}F NMR (235 MHz, $CDCl_3$, 21 °C):** δ = –111.07 (*m*, 1F). **IR (film):** ν = 2984, 2939, 2252, 1744, 1606, 1510, 1480, 1459, 1420, 1396, 1372, 1282, 1259, 1238, 1150, 1101, 949. **HRMS (EI) *m/z*:** Calc. for $[M - CH_3]^+$: 220.0769. Found: 220.0767. **Microanalysis:** Calc. for $C_{13}H_{14}NO_2F$: C: 66.37; H: 6.00; N: 5.95. Found: C: 66.26; H: 5.88; N: 5.98.

tert-Butyl-2-cyano-(4-methoxyphenyl)acetate (1m)



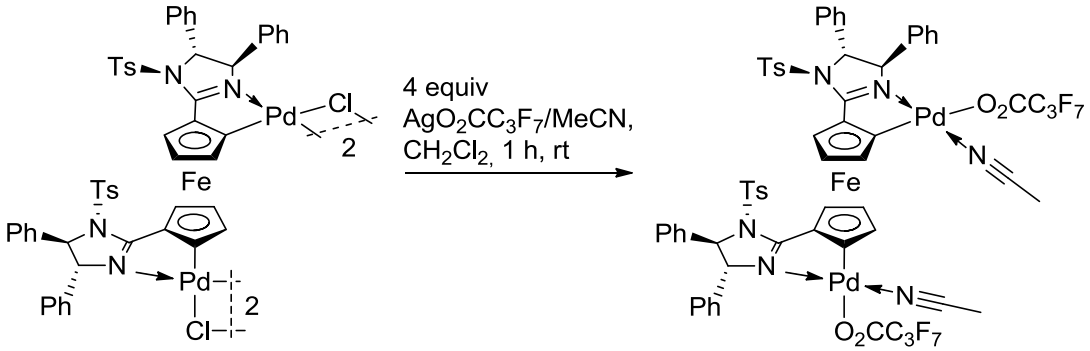
1m

According to GP1 2-(4-methoxyphenyl)acetonitrile (2.25 g, 15.3 mmol, 1 equiv) was treated with di-*tert*-butyldicarbonate (3.51 g, 16.1 mmol, 1.05 equiv). Column chromatography (petrol ether: EtOAc = 9:1) of the crude product resulted in liquid, pale yellow *tert*-butyl-2-cyano-(4-methoxyphenyl)acetate (**1l**, 3.14 g, 12.7 mmol, 83%).

$C_{14}H_{17}NO_3$, MW: 247.29 g mol^{-1}. **^{1}H NMR (300 MHz, $CDCl_3$, 21 °C):** δ = 7.35 (*d*, *J* = 8.8, 2H, *o*-C*H*), 6.92 (*d*, *J* = 8.8, 2H, *m*-C*H*), 4.55 (*s*, 1H, C*H*), 3.82 (*s*, 3H, OCH_3), 1.44 (*s*, 9H, CH_3). **^{13}C NMR (75 MHz, $CDCl_3$, 21 °C):** δ = 164.2, 160.0, 129.0, 122.4, 116.2, 114.6, 84.4, 55.4, 44.0, 27.7. **IR (film):** ν = 2981, 2938, 2840, 1742, 1612, 1587, 1514, 1461, 1396, 1371, 1306, 1255, 1181, 1150, 1034, 948. **HRMS (EI) *m/z*:** Calc. for $[C_{14}H_{17}NO_3]^+$: 247.1203. Found: 247.1203. **Microanalysis:** Calc. for $C_{14}H_{17}NO_3$: C: 68.00; H: 6.93; N: 5.66. Found: C: 68.08; H: 6.90; N: 5.92.

Activation of the Precatalyst [FBIP-Cl]$_2$ and [FIP-Cl]$_2$ with $AgO_2CC_3F_7$ / Acetonitrile

Bis(acetonitrile)[μ-[(*1S*$_p$,*1'S*$_p$)-2,2'-bis[(*4R*,*5R*)-4,5-dihydro-1-[(4-methylphenyl)sulfonyl]-4,5-diphenyl-1*H*-imidazol-2-yl-κ*N*3]-1,1'-ferrocendiyl-κ*C*1: κ*C*1']]bis(heptafluorobutyrato-κ*O*)di-palladium(II) (FBIP-$O_2CC_3F_7$)



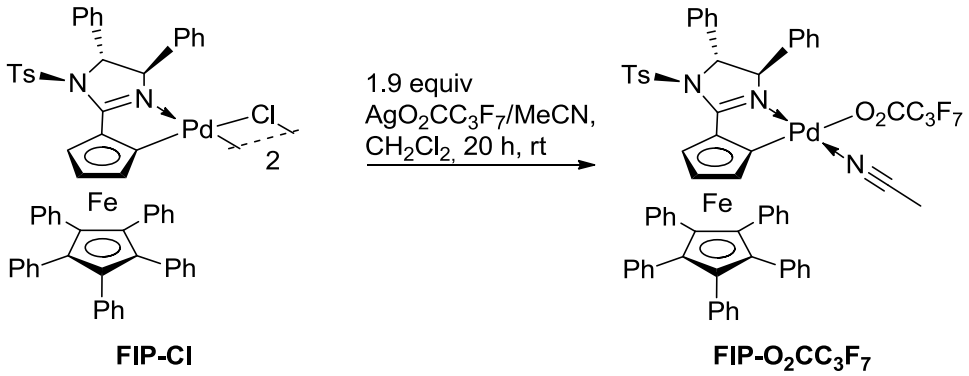
[FBIP-Cl]$_2$ **FBIP-$O_2CC_3F_7$**

$AgO_2CC_3F_7$ (77.2 mg, 0.25 mmol, 4 equiv) was dissolved in acetonitrile (~2 mL) and the solution was stirred for a few min. The solvent was then removed by a constant stream of nitrogen. A solution of the precatalyst **[FBIP-Cl]$_2$** (150.0 mg, 62 μmol, 1 equiv) in CH_2Cl_2 (1 mL per 5 mg silver salt) was added and the suspension was stirred for 1 h at room temperature. Afterwards the suspension was filtrated over celite, followed by filtration over silica, to completely remove silver traces, and the solvent was removed *in vacuo* at room temperature to give pure **FBIP-$O_2CC_3F_7$** as an orange-red solid (205.9 mg, 62 μmol, quant.).

$C_{66}H_{50}F_{14}FeN_6O_8Pd_2S_2$, MW: 1653.93 g mol^{-1}. **Mp:** decomposition > 200°C. **$[\alpha]_D^{20}$:** +15.2 (c = 0.09, CH_2Cl_2). **^{1}H NMR (300 MHz, $CDCl_3$, 21 °C):** δ = 7.60-7.42 (*m*, 16H, arom. *H*), 7.23-7.07 (*m*, 8H, arom. *H*), 6.66 (*d*, *J* = 7.8, 4H, arom. *H*), 5.33 (*d*, *J* = 2.1, 2H, Cp-*H*), 5.15 (*t*, *J* = 2.5, 2H, Cp-*H*), 5.11 (*d*, *J* = 3.3, 2H, C*H*Ph), 4.45 (*d*, *J* = 3.3, 2H, C*H*Ph), 4.35 (*d*, *J* = 1.9, 2H, Cp-*H*), 2.46 (*s*, 6H, $C_6H_4CH_3$), 1.25 (s, 6H, Pd←NCCH_3). **^{13}C NMR (125 MHz, $CDCl_3$, 21 °C):** δ = 170.9, 146.0, 139.7, 138.9, 133.6, 130.3, 129.4, 128.9, 128.1, 125.4, 125.3, 97.0, 85.7, 75.4, 73.9, 73.1, 70.6, 70.3, 29.7, 21.7. **^{19}F NMR (235 MHz, $CDCl_3$, 21 °C):** δ = –80.83 (*t*, *J* = 8.9, 3F, CF_3), –115.74 (*q*, *J* = 8.7, 1F, CF_2), –116.19 (*q*, *J* = 9.1, 1F, CF_2), –126.44 (*s*, 1F, CF_2COO), –126.50 (*s*, 1F, CF_2COO). **IR (solid):** *v* = 3003, 2944, 2925, 2253, 1679, 1645, 1596, 1555, 1467, 1362, 1334, 1210, 1168, 117, 1083, 965. **MS (ESI) *m*/*z*:** 1441.05 ([M – $O_2C_4F_7$]$^+$,

3%); 1400.02 ([M – $O_2C_4F_7$ – MeCN]$^+$, 1%); 1359.00 ([M – $O_2C_4F_7$ – 2 MeCN]$^+$, 10%), 573.01 ([M – 2 $O_2C_4F_7$ – 2 MeCN]$^{2+}$, 100%). **HRMS (ESI)** ***m/z*:** Calc. for $C_{54}H_{44}FeN_4O_4Pd_2S_2$: 573.0119. Found: 573.0114. **Microanalysis:** Calc. for $C_{66}H_{50}F_{14}FeN_6O_8Pd_2S_2$: C: 47.93; H: 3.05; N: 5.08. Found: C: 47.90; H: 3.00; N: 5.33.

(Acetonitrile-κ*N*)-(heptafluorobutyrate-κ*O*)[(1*S*$_p$)-2-[(4*R*,5*R*)-4,5-dihydro-1-[(4-methylphenyl)sulfonyl]-4,5-diphenyl-1*H*-imidazol-2-yl-κ*N*3]-1',2',3',4',5'-pentaphenylferrocenyl-κ*C*]-palladium(II) (FIP-$O_2CC_3F_7$)



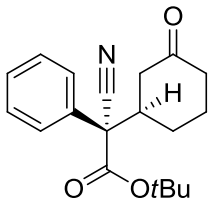
$AgO_2CC_3F_7$ (22.5 mg, 71 µmol, 2.0 equiv) was dissolved in acetonitrile (~2 mL) and the solution was stirred for a few min. The solvent was then removed by a constant stream of nitrogen. A solution of the precatalyst **[FIP-Cl]$_2$** (75.8 mg, 35 µmol, 1 equiv) in CH_2Cl_2 (1 mL per 5 mg silver salt) was added and the suspension was stirred for 20 h at room temperature. Afterwards the suspension was filtrated over celite, followed by filtration over silica, to completely remove silver traces, and the solvent was removed *in vacuo* at room temperature to give pure **FIP-$O_2CC_3F_7$** as an orange-red solid (91.0 mg, 35 µmol, quant.).

$C_{68}H_{50}F_7FeN_3O_4PdS$, **MW:** 1300.46 g mol^{-1}. **Mp:** decompostition > 200 °C. **[α]$_D^{20}$:** +24.9 (c = 0.10, CH_2Cl_2). **^{1}H NMR (500 MHz, $CDCl_3$, 21 °C) mixture of monomeric and dimeric form (ratio ~ 3.8:1):** δ = 7.52 (*d*, *J* = 7.8, 2H, arom. *H*), 7.36-7.18 (*m*, 12H, arom. *H*), 7.12-7.03 (*m*, 18H, arom. *H*), 6.98 (*t*, *J* = 7.8, 3H, arom. *H*), 6.52-6.42 (*m*, 3H, arom. *H*), 6.27 (*d*, *J* = 7.8, 1H, arom. *H*), 5.78-5.69 (*m*, 1H, Cp-*H*), 4.74-4.43 (*m*, 4H, Cp-*H* and C*H*Ph), 2.48 (*s*, 3H, $C_6H_4CH_3$), 2.17 (*s*, 3H, Pd←NCCH_3), 1.91 (*s*, free NCCH_3). For pure ^{1}H NMR of the monomeric catalyst in presence of 100 equiv MeCN see "Spectroscopic Investigation of the Nature of **FIP-O2CC3F7**", S-123. **^{13}C NMR (125 MHz, $CDCl_3$, 21 °C):** δ = 169.2, 144.0, 138.4, 137.2, 133.0, 132.7, 130.7, 130.4, 128.7, 128.5, 127.2, 126.5, 126.2, 126.1, 126.0, 125.8,

125.3, 124.8, 123.8, 118.4, 114.6, 97.3, 87.3, 78.6, 77.5, 74.1, 73.8, 72.5, 70.8, 27.8, 19.8, 1.5, –1.9. **^{19}F NMR (235 MHz, CDCl$_3$, 21 °C):** δ = –80.87 (*t*, *J* = 8.3, 3F, C*F*$_3$), –116.45 (*m*, 1F, C*F*$_2$), –117.59 (*m*, 1F, C*F*$_2$), –126.34 (*s*, 1F, C*F*$_2$COO), –127.56 (*m*, 1F, C*F*$_2$COO). **IR (film):** *v* = 3056, 2323, 1667, 1599, 1545, 1503, 1445, 1332, 1225, 1209, 1169, 1117, 1078, 964. **MS (EI) *m*/*z*:** 1045.17 ([M – $O_2CC_3F_7$ – MeCN]$^+$, 100%), 819.16 ([M – $O_2CC_3F_7$ – MeCN – Ts]$^+$, 25%). **Microanalysis:** Calc. for $C_{68}H_{50}F_7FeN_3O_4PdS$: C: 62.80; H: 3.88; N: 3.23. Found: C: 62.75; H: 3.81; N: 3.54.

Synthesis of Enantioenriched Michael-Addition Products by Asymmetric Catalysis (3)[i]

tert-Butyl-2-cyano-2-(3-oxocyclohexyl)-2-phenylacetate (3aa)

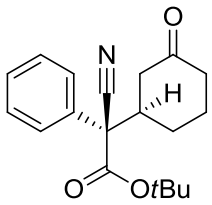


(*R*,*R*)-3aa

According to GP3 *tert*-butyl-2-cyano-2-phenylacetate (**1a**, 400.2 mg, 1.84 mmol, 1 equiv) was treated with 2-cyclohexen-1-one (**2a**, 354.1 mg, 3.68 mmol, 2 equiv) in the presence of **FBIP-O$_2$CC$_3$F$_7$** (30.4 mg, 18.0 µmol, 1 mol%) to yield **(*R*,*R*)-3aa** (577.3 mg, 1.84 mmol, 99%, $ee_{(R,R)}$ = 94%, $ee_{(S,R)}$ = 65%, $dr_{(R,R+S,S):(S,R+R,S)}$ = 89:11) as a colorless oil. The *dr* and *ee* values were determined by chiral column HPLC: Chiracel OD-H, *n*-hexane/*i*-PrOH (99/1), 0.9 mL min^{-1}, detection at 210 nm, $t_{(R,R)}$ = 13.3 min, $t_{(S,S)}$ = 41.3 min. The major diastereomer was isolated by column chromatography (CH_2Cl_2 + 1% Et_2O).

C$_{19}$H$_{23}$NO$_3$, MW: 313.39 g mol^{-1}. **[α]$_D^{20}$:** +44.5 (c = 0.01, CH_2Cl_2). **^{1}H NMR (300 MHz, CDCl$_3$, 21 °C) of the (*R*,*R*)/(*S*,*S*)-diastereomer:** δ = 7.54-7.51 (*m*, 2H, arom. *H*), 7.43-7.36 (*m*, 3H, arom. *H*), 2.86-2.75 (*m*, 1H, C*H*), 2.45-2.39 (*m*, 1H, CH_2), 2.37-2.26 (*m*, 1H, CH_2), 2.22-2.07 (*m*, 3H, CH_2), 1.92-1.64 (*m*, 3H, CH_2), 1.43 (*s*, 9H, CH_3). **^{13}C NMR (75 MHz, CDCl$_3$, 21 °C) of the (*R*,*R*)/(*S*,*S*)-diastereomer:** δ = 208.6, 165.2, 133.0, 129.2, 129.0, 126.3, 116.9, 85.0, 60.6, 45.2, 44.6, 40.8, 27.9, 25.8, 24.0. **IR (solid) of the (*R*,*R*)/(*S*,*S*)-diastereomer:** ν = 3001, 2987, 2957, 2906, 2857, 2246, 1730, 1716, 1491, 1451, 1425, 1395, 1365, 1251, 1227, 1146, 1060, 1035.

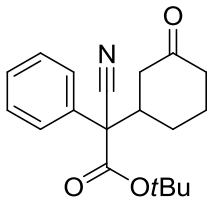
[i] The notation of the Michael-addition products, *e.g.* **3ab** implicates the use of Michael-donor **1a** and of the Michael-acceptor **2b**.



(*S,R*)-3aa

According to GP3 *tert*-butyl-2-cyano-2-phenylacetate **1a** (470.0 mg, 2.16 mmol, 1 equiv) was treated with 2-cyclohexen-1-one **2a** (415.9 mg, 4.33 mmol, 2 equiv) in the presence of **FIP-$O_2CC_3F_7$** (28.1 mg, 22.0 µmol, 1 mol%) to yield **(*S,R*)-3aa** (609.0 mg, 1.94 mmol, 90%, $ee_{(S,R)}$ = 89%, $ee_{(R,R)}$ = 33%, $dr_{(S,R+R,S):(R,R+S,S)}$ = 71:29) as a colorless oil. The *dr* and *ee* values were determined by chiral column HPLC: Chiracel OD-H, *n*-hexane/*i*-PrOH (99/1), 0.9 mL min^{-1}, detection at 210 nm, $t_{(S,R)}$ = 17.8 min, $t_{(R,S)}$ = 12.1 min. The major diastereomer was isolated by column chromatography (CH_2Cl_2 + 1% Et_2O).

$C_{19}H_{23}NO_3$, MW: 313.39 g mol^{-1}. **$[\alpha]_D^{20}$:** +9.4 (c = 0.01, CH_2Cl_2). **^{1}H NMR (300 MHz, $CDCl_3$, 21 °C) of the (*S,R*)/(*R,S*)-diastereomer:** δ = 7.60-7.57 (*m*, 2H, arom. *H*), 7.46-7.36 (*m*, 3H, arom. *H*), 2.86-2.75 (*m*, 1H, C*H*), 2.65-2.49 (*m*, 2H, CH_2), 2.45-2.25 (*m*, 2H, CH_2), 2.07-1.98 (*m*, 1H, CH_2), 1.63-1.45 (*m*, 3H, CH_2), 1.42 (*s*, 9H, CH_3). **^{13}C NMR (75 MHz, $CDCl_3$, 21 °C) of the (*S,R*)/(*R,S*)-diastereomer:** δ = 208.9, 165.6, 132.3, 129.3, 129.1, 126.2, 116.8, 84.9, 60.5, 45.2, 42.5, 41.0, 28.2, 27.6, 24.3. **IR (solid) of the (*S,R*)/(*R,S*)-diastereomer:** ν = 2982, 2964, 2942, 2876, 2247, 1729, 1708, 1494, 1449, 1392, 1369, 1251, 1233, 1145, 119, 1077, 1034.



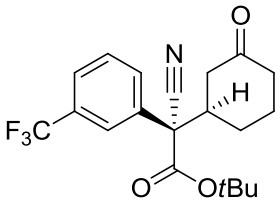
***rac*-3aa**

According to GP2 *tert*-butyl-2-cyano-2-phenylacetate **1a** (47.0 mg, 0.22 mmol, 1 equiv) was treated with 2-cyclohexen-1-one **2a** (21.3 µL, 0.22 mmol, 1 equiv). Column chromatography (petrol ether:EtOAc = 9:1 → 4:1) of the crude product yielded ***rac*-3aa** (58.0 mg, 0.19 mmol, 86%) as a colorless oil with a $dr_{(R,R+S,S):(S,R+R,S)}$ of 43:57.

$C_{19}H_{23}NO_3$, MW: 313.39 g mol^{-1}. **MS (ESI) *m/z*:** 336.16 ($[M+Na]^+$, 100%), 259.12 ($[M+Na - C_6H_5]^+$, 44%). **HRMS (ESI) *m/z*:** Calc. for $[M+Na]^+$: 336.1570. Found: 336.1581.

Microanalysis: Calc. for $C_{19}H_{23}NO_3$: C: 71.56; H: 6.71; N: 4.91. Found: C: 71.38; H: 6.65; N: 4.86.

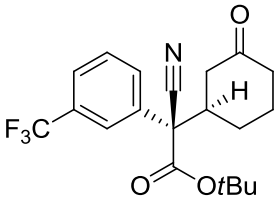
tert-Butyl-2-cyano-2-(3-oxocyclohexyl)-2-(3-(trifluoromethyl)phenyl)-acetate (3ba)



(*R*,*R*)-3ba

According to GP3 *tert*-butyl-2-cyano-2-(3-(trifluoromethyl)phenyl)acetate **1b** (40.1 mg, 0.14 mmol, 1 equiv) was treated with 2-cyclohexen-1-one **2a** (27.0 mg, 0.28 mmol, 2 equiv) in the presence of **FBIP-O$_2$CC$_3$F$_7$** (1.16 mg, 0.70 µmol, 0.5 mol%) to yield **(*R*,*R*)-3ba** (52.9 mg, 0.14 mmol, 99%, $ee_{(R,R)}$ = 85%, $ee_{(S,R)}$ = 52%, $dr_{(R,R+S,S):(S,R+R,S)}$ = 76:24) as a colorless solid. The *dr* and *ee* values were determined by chiral column HPLC: Chiracel AS-H, *n*-hexane/*i*-PrOH (97:3), 1 mL min^{-1}, detection at 210 nm, $t_{(R,R)}$ = 8.4 min, $t_{(S,S)}$ = 30.4 min. The major diastereomer was isolated by column chromatography (CH_2Cl_2 + 1% Et_2O).

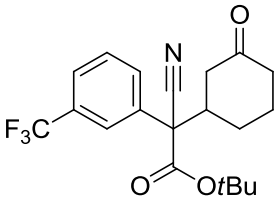
$C_{20}H_{22}NO_3F_3$, MW: 381.39 g mol^{-1}. ***Mp*:** 106.3-107.2 °C. **$[\alpha]_D^{20}$:** +21.6 (c = 0.005, CH_2Cl_2). **^{1}H NMR (300 MHz, $CDCl_3$, 21 °C) of the (*R*,*R*)/(*S*,*S*)-diastereomer:** δ = 7.81 (*s*, 1H, arom. *H*), 7.76 (*d*, *J* = 8.1, 1H, arom. *H*) 7.67 (*d*, *J* = 8.6, 1H, arom. *H*), 7.56 (*t*, *J* = 7.7, 1H, arom. *H*), 2.86-2.75 (*m*, 1H, C*H*), 2.47-2.29 (*m*, 2H, CH_2), 2.27-2.09 (*m*, 3H, CH_2), 1.94-1.66 (*m*, 3H, CH_2), 1.45 (*s*, 9H, CH_3). **^{13}C NMR (75 MHz, $CDCl_3$, 21 °C) of the (*R*,*R*)/(*S*,*S*)-diastereomer:** δ = 208.3, 165.1, 133.5, 132.1, 131.7, 130.0, 129.6, 126.2 (*m*, *C*CCF$_3$), 123.0 (*m*, *C*CCF$_3$), 116.2, 85.7, 60.4, 45.2, 42.5, 40.9, 28.1, 27.6, 24.1. **^{19}F NMR (235 MHz, $CDCl_3$, 21 °C) of the (*R*,*R*)/(*S*,*S*)-diastereomer:** δ = –62.70 (*s*, 3F). **IR (solid) of the (*R*,*R*)/(*S*,*S*)-diastereomer:** ν = 2958, 2244, 1732, 1716, 1444, 1367, 1326, 1253, 1228, 1163, 1149, 1126, 1078.



(*S,R*)-3ba

According to GP3 *tert*-butyl-2-cyano-2-(3-(trifluoromethyl)phenyl)acetate **1b** (19.7 mg, 69 µmol, 1 equiv) was treated with 2-cyclohexen-1-one **2a** (13.3 mg, 13.8 mmol, 2 equiv) in the presence of **FIP-$O_2CC_3F_7$** (0.90 mg, 0.70 µmol, 1 mol%) to yield **(*S,R*)-3ba** (24.6 mg, 0.06 mmol, 92%, $ee_{(S,R)}$ = 74%, $ee_{(R,R)}$ = 12%, $dr_{(S,R+R,S):(R,R+S,S)}$ = 63:37) as a colorless oil. The *dr* and *ee* values were determined by chiral column HPLC: Chiracel AS-H, *n*-hexane/*i*-PrOH (97:3), 1 mL min^{-1}, detection at 210 nm, $t_{(S,R)}$ = 9.7 min, $t_{(R,S)}$ = 13.5 min. The major diastereomer was isolated by column chromatography (CH_2Cl_2 + 1% Et_2O).

$C_{20}H_{22}NO_3F_3$, MW: 381.39 g mol^{-1}. **$[\alpha]_D^{20}$:** +5.7 (c = 0.26, CH_2Cl_2). **^{1}H NMR (300 MHz, $CDCl_3$, 21 °C) of the (*S,R*)/(*R,S*)-diastereomer:** δ = 7.86 (*s*, 1H, arom. *H*), 7.83 (*d*, *J* = 8.4, 1H, arom. *H*) 7.69 (*d*, *J* = 7.7, 1H, arom. *H*), 7.58 (*t*, *J* = 7.7, 1H, arom. *H*), 2.85-2.75 (*m*, 1H, C*H*), 2.65-2.50 (*m*, 2H, CH_2), 2.46-2.26 (*m*, 2H, CH_2), 2.11-2.00 (*m*, 1H, CH_2), 1.62-1.49 (*m*, 2H, CH_2), 1.44 (*s*, 9H, CH_3), 1.38-1.35 (*m*, 1H, CH_2). **^{13}C NMR (75 MHz, $CDCl_3$, 21 °C) of the (*S,R*)/(*R,S*)-diastereomer:** δ = 208.0, 164.6, 134.2, 132.0, 131.6, 129.9, 126.0 (*m*, *C*CCF_3), 123.2 (*m*, *C*CCF_3), 116.3, 85.8, 60.6, 45.5, 44.4, 40.7, 27.6, 25.8, 23.9. **^{19}F NMR (235 MHz, $CDCl_3$, 21 °C) of the (*S,R*)/(*R,S*)-diastereomer:** δ = –62.69 (*s*, 3F). **IR (solid) of the (*S,R*)/(*R,S*)-diastereomer:** ν = 2958, 1727, 1713, 1446, 1437, 1371, 1326, 1259, 1231, 1166, 1150, 1077.

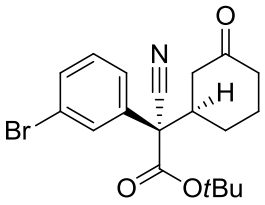


***rac*-3ba**

According to GP2 *tert*-butyl-2-cyano-2-(3-(trifluoromethyl)phenyl)acetate **1b** (146.4 mg, 0.51 mmol, 1 equiv) was treated with 2-cyclohexen-1-one **2a** (49.3 mg, 0.51 mmol, 1 equiv). Column chromatography (petrol ether:EtOAc = 9:1 → 4:1) of the crude product yielded ***rac*-3ba** (170.7 mg, 0.45 mmol, 87%) as a colorless solid with a $dr_{(R,R+S,S):(S,R+R,S)}$ of 45:55.

$C_{20}H_{22}NO_3F_3$, MW: 381.39 g mol^{-1}. **Mp:** 69.1-69.3 °C. **HRMS (ESI) *m/z*:** Calc. for $[C_{14}H_{14}F_3NO_2]^-$: 284.0898. Found: 284.0895. **Microanalysis:** Calc. for $C_{20}H_{22}NO_3F_3$: C: 62.98; H: 5.81; N: 3.67. Found: C: 63.06; H: 5.85; N: 3.71.

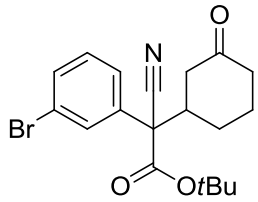
tert-Butyl-2-cyano-2-(3-bromophenyl)-2-(3-oxocyclohexyl)acetate (3ca)



(*R,R*)-3ca

According to GP3 *tert*-butyl-2-cyano-2-(3-bromophenyl)acetate **1c** (11.8 mg, 40 µmol, 1 equiv) was treated with 2-cyclohexen-1-one **2a** (7.7 mg, 80 µmol, 2 equiv) in the presence of **FBIP-$O_2CC_3F_7$** (1.32 mg, 0.80 µmol, 1 mol%) to yield **(*R,R*)-3ca** (14.8 mg, 38 µmol, 94%, $ee_{(R,R)}$ = 78%, $ee_{(S,R)}$ = 54%, $dr_{(R,R+S,S):(S,R+R,S)}$ = 77:23) as a colorless solid. The *dr* and *ee* values were determined by chiral column HPLC: Chiracel AS-H, *n*-hexane/*i*-PrOH (97:3), 1 mL min^{-1}, detection at 210 nm, $t_{(R,R)}$ = 12.7 min, $t_{(S,S)}$ = 50.0 min. The major diastereomer was isolated by column chromatography (CH_2Cl_2 + 1% Et_2O).

$C_{19}H_{22}NO_3Br$, MW: 392.29 g mol^{-1}. **Mp:** 134.7-135.2 °C. **$[\alpha]_D^{20}$:** +20.9 (c = 0.01, CH_2Cl_2). **^{1}H NMR (300 MHz, $CDCl_3$, 21 °C) of the (*R,R*)/(*S,S*)-diastereomer:** δ = 7.70 (*t*, *J* = 1.9, 1H, arom. *H*), 7.54-7.46 (*m*, 2H, arom. *H*), 7.28-7.26 (*m*, 1H, arom. H), 2.81-2.70 (*m*, 1H, C*H*), 2.46-2.26 (*m*, 2H, CH_2), 2.22-2.06 (*m*, 3H, CH_2), 1.91-1.64 (*m*, 3H, CH_2), 1.45 (*s*, 9H, CH_3). **^{13}C NMR (75 MHz, $CDCl_3$, 21 °C) of the (*R,R*)/(*S,S*)-diastereomer:** δ = 208.6, 165.1, 134.5, 132.4, 130.8, 129.2, 124.8, 123.5, 116.3, 85.5, 60.1, 45.1, 42.5, 40.9, 28.1, 27.6, 24.2. **IR (solid) of the (*R,R*)/(*S,S*)-diastereomer:** ν = 3080, 3057, 2979, 2941, 2873, 2245, 1736, 1712, 1568, 1476, 1419, 1392, 1369, 1253, 1229, 1149, 1079, 1060.

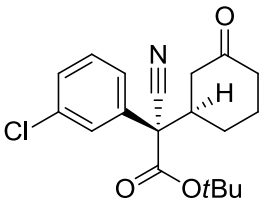


***rac*-3ca**

According to GP2 *tert*-butyl-2-cyano-2-(3-bromophenyl)acetate **1c** (246.5 mg, 0.83 mmol, 1 equiv) was treated with 2-cyclohexen-1-one **2a** (80.0 mg, 0.83 mmol, 1 equiv). Column chromatography (petrol ether:EtOAc = 9:1 → 4:1) of the crude product yielded ***rac*-3ca** (276.2 mg, 0.70 mmol, 85%) as a colorless solid with a $dr_{(R,R+S,S):(S,R+R,S)}$ of 45:55. The diastereomers were separated by column chromatography (CH_2Cl_2 + 1% Et_2O).

$C_{19}H_{22}NO_3Br$, **MW:** 392.29 g mol^{-1}. **Mp:** 120.9-121.1 °C. **^{1}H NMR (300 MHz, $CDCl_3$, 21 °C) of the (*S*,*R*)/(*R*,*S*)-diastereomer:** δ = 7.76 (*t*, *J* = 1.9, 1H, arom. *H*), 7.54 (*dd*, *J* = 7.9, 1.9, 2H, arom. *H*), 7.33-7.28 (*m*, 1H, arom. H), 2.81-2.70 (*m*, 1H, C*H*), 2.64-2.56 (*m*, 2H, CH_2), 2.51-2.41 (*m*, 2H, CH_2), 2.36-2.25 (*m*, 1H, CH_2), 2.10-2.01 (*m*, 1H, CH_2), 1.56-1.47 (*m*, 2H, CH_2), 1.44 (*s*, 9H, CH_3). **^{13}C NMR (75 MHz, $CDCl_3$, 21 °C) of the (*S*,*R*)/(*R*,*S*)-diastereomer:** δ = 208.2, 164.7, 135.2, 132.3, 130.7, 129.4, 125.0, 123.3, 116.4, 85.6, 60.2, 45.4, 44.4, 40.7, 27.6, 25.8, 23.9. **IR (solid) of the (*S*,*R*)/(*R*,*S*)-diastereomer:** ν = 3065, 2978, 2946, 2873, 2248, 1726, 1709, 1595, 1567, 1475, 1419, 1370, 1279, 1255, 1226, 1144, 1069. **MS (EI) *m*/*z*:** Found: 393.1 ($[M]^+$, 1%), 376.1 ($[M - CH_3]^+$, 17%), 290.0 ($[M - CO_2t\text{-Bu}]^+$, 8%), 97.1 ([oxo-Cyclohexyl]$^+$, 9%), 57.1 ($[C(CH_3)_3]^+$, 100%). **Microanalysis:** Calc. for $C_{19}H_{22}NO_3Br$: C: 58.17; H: 5.65; N: 3.57; Br: 20.37. Found: C: 58.10; H: 5.68; N: 3.52; Br: 20.15.

tert-Butyl-2-cyano-2-(3-chlorophenyl)-2-(3-oxocyclohexyl)acetate (3da)

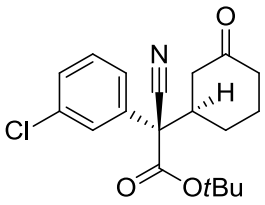


(*R*,*R*)-3da

According to GP3 *tert*-butyl-2-cyano-2-(3-chlorophenyl)acetate **1d** (41.1 mg, 0.16 mmol, 1 equiv) was treated with 2-cyclohexen-1-one **2a** (30.7 mg, 0.32 mmol, 2 equiv) in the presence of **FBIP-$O_2CC_3F_7$** (1.35 mg, 0.32 µmol, 0.5 mol%) to yield **(*R*,*R*)-3da** (54.0 mg, 0.16 mmol, 97%, $ee_{(R,R)}$ = 87%, $ee_{(S,R)}$ = 78%, $dr_{(R,R+S,S):(S,R+R,S)}$ = 83:17) as a colorless solid. The

dr and *ee* values were determined by chiral column HPLC: Chiracel AS-H, *n*-hexane/*i*-PrOH (97:3), 1 mL min^{-1}, detection at 210 nm, $t_{(R,R)}$ = 11.5 min, $t_{(S,S)}$ = 45.3 min. The major diastereomer was isolated by column chromatography (CH_2Cl_2 + 1% Et_2O).

$C_{19}H_{22}NO_3Cl$, MW: 347.84 g mol^{-1}. **Mp:** 124.5-125.8 °C. **$[\alpha]_D^{20}$:** +32.4 (c = 0.26, CH_2Cl_2). **^{1}H NMR (300 MHz, $CDCl_3$, 21 °C) of the (*R*,*R*)/(*S*,*S*)-diastereomer:** δ = 7.54 (*b*, 1H, *o*-*H*), 7.44 (*dt*, *J* = 6.8, 2.1, 1H, arom. *H*), 7.39–7.34 (*m*, 2H, arom. *H*), 2.82–2.71 (*m*, 1H, C*H*), 2.47-2.40 (*m*, 1H, CH_2), 2.37-2.26 (*m*, 1H, CH_2), 2.23-2.06 (*m*, 3H, CH_2), 1.91-1.64 (*m*, 3H, CH_2), 1.45 (*s*, 9H, CH_3). **^{13}C NMR (75 MHz, $CDCl_3$, 21 °C) of the (*R*,*R*)/(*S*,*S*)-diastereomer:** δ = 208.6, 165.1, 135.4, 134.3, 130.5, 129.5, 126.4, 124.3, 116.3, 85.4, 60.2, 45.1, 42.5, 40.9, 28.1, 27.6, 24.2. **IR (solid) of the (*R*,*R*)/(*S*,*S*)-diastereomer:** ν = 2982, 2958, 2934, 2869, 2245, 1740, 1714, 1596, 1574, 1476, 1423, 1372, 1251, 1229, 1150, 1085, 1061, 1038.

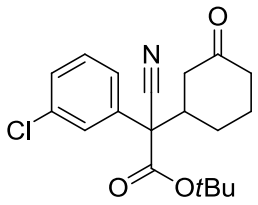


(*S*,*R*)-3da

According to GP3 *tert*-butyl-2-cyano-2-(3-chlorophenyl)acetate **1d** (10.2 mg, 41 µmol, 1 equiv) was treated with 2-cyclohexen-1-one **2a** (7.8 mg, 81 µmol, 2 equiv) in the presence of **FIP-$O_2CC_3F_7$** (0.26 mg, 0.20 µmol, 0.5 mol%) to yield **(*S*,*R*)-3da** (14.1 mg, 41 µmol, 99%, $ee_{(S,R)}$ = 77%, $ee_{(R,R)}$ = 7%, $dr_{(S,R+R,S):(R,R+S,S)}$ = 50:50) as a colorless solid. The *dr* and *ee* values were determined by chiral column HPLC: Chiracel AS-H, *n*-hexane/*i*-PrOH (97:3), 1 mL min^{-1}, detection at 210 nm, $t_{(S,R)}$ = 14.0 min, $t_{(R,S)}$ = 18.9 min. The major diastereomer was isolated by column chromatography (CH_2Cl_2 + 1% Et_2O).

$C_{19}H_{22}NO_3Cl$, MW: 347.84 g mol^{-1}. **Mp:** 103.1-103.5 °C. **$[\alpha]_D^{20}$:** +7.3 (c = 0.22, CH_2Cl_2). **^{1}H NMR (300 MHz, $CDCl_3$, 21 °C) of the (*S*,*R*)/(*R*,*S*)-diastereomer:** δ = 7.61 (*m*, 1H, *o*-*H*), 7.53-7.48 (*m*, 1H, arom. *H*), 7.40-7.34 (*m*, 2H, arom. *H*), 2.82-2.71 (*m*, 1H, C*H*), 2.64-2.56 (*m*, 2H, CH_2), 2.48-2.41 (*m*, 1H, CH_2), 2.37-2.26 (*m*, 1H, CH_2), 2.10-2.00 (*m*, 1H, CH_2), 1.65-1.47 (*m*, 3H, CH_2), 1.44 (*s*, 9H, CH_3). **^{13}C NMR (75 MHz, $CDCl_3$, 21 °C) of the (*S*,*R*)/(*R*,*S*)-diastereomer:** δ = 208.2, 164.7, 135.3, 135.0, 130.4, 129.4, 126.6, 124.5, 116.4, 85.6, 60.3, 45.4,

44.4, 40.7, 27.6, 25.8, 23.9. **IR (solid) of the (*S*,*R*)/(*R*,*S*)-diastereomer:** ν = 3070, 2980, 2934, 2874, 2250, 1725, 1710, 1594, 1574, 1478, 1422, 1371, 1279, 1256, 1226, 1145, 1069.

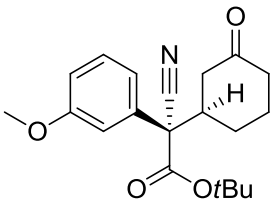


***rac*-3da**

According to GP2 *tert*-butyl-2-cyano-2-(3-chlorophenyl)acetate **1d** (141.0 mg, 0.56 mmol, 1 equiv) was treated with 2-cyclohexen-1-one **2a** (53.8 mg, 0.56 mmol, 1 equiv). Column chromatography (petrol ether:EtOAc = 9:1 → 4:1) of the crude product yielded ***rac*-3da** (157.1 mg, 0.45 mmol, 81%) as a colorless solid with a $dr_{(R,R+S,S):(S,R+R,S)}$ of 42:58.

$C_{19}H_{22}NO_3Cl$, **MW:** 347.84 g mol^{-1}. **Mp:** 109.7-110.1 °C. **MS (ESI) *m*/*z*:** Found: 370.12 ([M + Na]$^+$, 100%), 314.05 ([M − C(CH)$_3$ + Na]$^+$, 53%). **Microanalysis:** Calc. for $C_{19}H_{22}NO_3Cl$: C: 65.61; H: 6.38; N: 4.03; Cl: 10.19. Found: C: 65.32; H: 6.34; N: 3.97; Cl: 10.49.

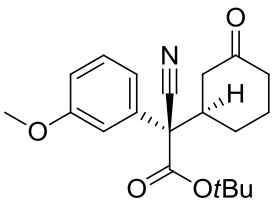
tert-Butyl-2-cyano-2-(3-methoxyphenyl)-2-(3-oxocyclohexyl)-acetate (3ea)



(*R*,*R*)-3ea

According to GP3 *tert*-butyl-2-cyano-2-(3-methoxyphenyl)acetate **1e** (40.7 mg, 0.16 mmol, 1 equiv) was treated with 2-cyclohexen-1-one **2a** (31.6 mg, 0.33 mmol, 2 equiv) in the presence of **FBIP-$O_2CC_3F_7$** (2.72 mg, 1.65 µmol, 1 mol%) to yield **(*R*,*R*)-3ea** (54.4 mg, 0.16 mmol, 99%, $ee_{(R,R)}$ = 93%, $ee_{(S,R)}$ = 72%, $dr_{(R,R+S,S):(S,R+R,S)}$ = 89:11) as a colorless solid. The *dr* and *ee* values were determined by chiral column HPLC: Chiracel AS-H, *n*-hexane/*i*-PrOH (97:3), 1 mL min^{-1}, detection at 210 nm, $t_{(R,R)}$ = 16.8 min, $t_{(S,S)}$ = 48.3 min. The major diastereomer was isolated by column chromatography (CH_2Cl_2 + 1% Et_2O).

$C_{20}H_{25}NO_4$, MW: 343.42 g mol^{-1}. **Mp:** 118.3-118.7 °C. **$[\alpha]_D^{20}$:** +25.8 (c = 0.01, CH_2Cl_2). **^{1}H NMR (300 MHz, $CDCl_3$, 21 °C) of the (*R*,*R*)/(*S*,*S*)-diastereomer:** δ = 7.30 (*t*, *J* = 8.0, 1H, *o*-*H*), 7.09 (*ddd*, *J* = 7.9, 1.8, 0.6, 1H, arom. *H*), 7.06 (*t*, *J* = 2.3, 2H, arom. *H*), 6.89 (*ddd*, *J* = 8.3, 2.3, 0.6, 1H, arom. *H*), 3.81 (*s*, 3H, OCH_3), 2.82-2.71 (*m*, 1H, C*H*), 2.45-2.39 (*m*, 1H, CH_2), 2.36-2.25 (*m*, 1H, CH_2), 2.21-2.07 (*m*, 3H, CH_2), 1.98-1.64 (*m*, 3H, CH_2), 1.44 (*s*, 9H, CH_3). **^{13}C NMR (75 MHz, $CDCl_3$, 21 °C) of the (*R*,*R*)/(*S*,*S*)-diastereomer:** δ = 209.1, 165.5, 160.2, 133.7, 130.3, 118.2, 116.8, 114.3, 112.1, 84.9, 60.4, 55.3, 45.0, 42.5, 41.0, 28.2, 27.6, 24.3. **IR (solid) of the (*R*,*R*)/(*S*,*S*)-diastereomer:** ν = 2981, 2951, 2244, 1733, 1712, 1600, 1497, 1448, 1369, 1296, 1250, 1230, 1149, 1036.

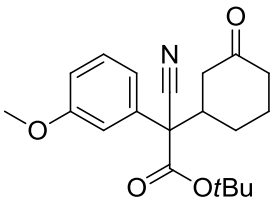


(*S*,*R*)-3ea

According to GP3 *tert*-butyl-2-cyano-2-(3-methoxyphenyl)acetate **1e** (19.8 mg, 80 µmol, 1 equiv) was treated with 2-cyclohexen-1-one **2a** (15.4 mg, 0.16 mmol, 2 equiv) in the presence of **FIP-$O_2CC_3F_7$** (0.52 mg, 0.40 µmol, 0.5 mol%) to yield **(*S*,*R*)-3ea** (20.3 mg, 59 µmol, 74%, $ee_{(S,R)}$ = 90%, $ee_{(R,R)}$ = 46%, $dr_{(S,R+R,S):(R,R+S,S)}$ = 68:32) as a colorless oil. The *dr* and *ee* values were determined by chiral column HPLC: Chiracel AS-H, *n*-hexane/*i*-PrOH (97:3), 1 mL min^{-1}, detection at 210 nm, $t_{(S,R)}$ = 24.6 min, $t_{(R,S)}$ = 19.6 min. The minor diastereomer was partially removed by column chromatography (CH_2Cl_2 + 1% Et_2O).

$C_{20}H_{25}NO_4$, MW: 343.42 g mol^{-1}. **$[\alpha]_D^{20}$:** +5.8 (c = 0.21, CH_2Cl_2). **^{1}H NMR (300 MHz, $CDCl_3$, 21 °C) of the (*S*,*R*)/(*R*,*S*)-diastereomer [(*R*,*R*)/(*S*,*S*)-diastereomer]:** δ = 7.32 (*q*, *J* = 7.8, 1H, *o*-*H*), 7.18-7.05 (*m*, 2H, arom. *H*), 6.90 (*tdd*, *J* = 7.9, 2.3, 0.6, 1H, arom. *H*), 3.83 (*s*, 3H, OCH_3), [3.82 (*s*, 3H, OCH_3)], 2.82-2.72 (*m*, 1H, C*H*), 2.64-2.52 (*m*, 2H, CH_2), 2.48-2.39 (*m*, 1H, CH_2), 2.36-2.25 (*m*, 1H, CH_2), 2.21-1.98 (*m*, 2H, CH_2), 1.96-1.64 (*m*, 1H, CH_2), 1.54-1.46 (*m*, 1H, CH_2), [1.44 (*s*, 9H, CH_3)], 1.43 (*s*, 9H, CH_3). **^{13}C NMR (63 MHz, $CDCl_3$, 21 °C) of the (*S*,*R*)/(*R*,*S*)-diastereomer [(*R*,*R*)/(*S*,*S*)-diastereomer]:** δ = [209.1], 208.7, [165.1], 160.3, 134.5, [130.3], 130.2, 118.5, [118.3], 116.9, [114.3], 114.2, 112.3, [112.1], 85.0, 60.6, 55.4, 45.3, [45.1], 44.6, [42.6], 40.8, [28.2], 27.6, 25.8, [24.3], 24.1. **IR (solid) of the (*S*,*R*)/(*R*,*S*)-**

diastereomer: ν = 3003, 2981, 2957, 2868, 2242, 1735, 1711, 1608, 1585, 1489, 1444, 1369, 1297, 1248, 1230, 1201, 1147, 1041.

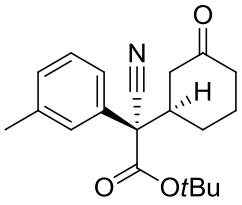


***rac*-3ea**

According to GP2 *tert*-butyl-2-cyano-2-(3-methoxyphenyl)acetate **1e** (249.3 mg, 1.01 mmol, 1 equiv) was treated with 2-cyclohexen-1-one **2a** (96.9 mg, 1.01 mmol, 1 equiv). Column chromatography (petrol ether:EtOAc = 9:1 → 4:1) of the crude product yielded ***rac*-3ea** (321.2 mg, 0.94 mmol, 93%) as a colorless oil with a $dr_{(R,R+S,S):(S,R+R,S)}$ of 38:62.

$C_{20}H_{25}NO_4$, MW: 343.42 g mol^{-1}. **HRMS (ESI) *m/z*:** Calc. for $[C_{20}H_{25}NO_4 + Na]^+$: 366.1681. Found: 366.1677. **Microanalysis:** Calc. for $C_{20}H_{25}NO_4$: C: 69.95; H: 7.34; N: 4.08. Found: C: 69.71; H: 7.31; N: 4.06.

tert-Butyl-2-cyano-2-(3-oxocyclohexyl)-2-(*m*-tolyl)-acetate (3fa)

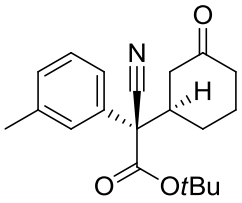


(*R,R*)-3fa

According to GP3 *tert*-butyl-2-cyano-2-(*m*-tolyl)acetate **1f** (41.0 mg, 0.18 mmol, 1 equiv) was treated with 2-cyclohexen-1-one **2a** (34.1 mg, 0.35 mmol, 2 equiv) in the presence of **FBIP-$O_2CC_3F_7$** (2.93 mg, 1.8 µmol, 1 mol%) to yield **(*R,R*)-3fa** (49.3 mg, 0.15 mmol, 85%, $ee_{(R,R)}$ = 95%, $ee_{(S,R)}$ = 71%, $dr_{(R,R+S,S):(S,R+R,S)}$ = 87:13) as a colorless solid. The *dr* and *ee* values were determined by chiral column HPLC: Chiracel OD-H, *n*-hexane/*i*-PrOH (99.5/0.5), 1 mL min^{-1}, detection at 210 nm, $t_{(R,R)}$ = 14.4 min, $t_{(S,S)}$ = 35.5 min. The major diastereomer was isolated by column chromatography (CH_2Cl_2 + 1% Et_2O).

$C_{20}H_{25}NO_3$, MW: 327.42 g mol^{-1}. **Mp:** 103.9-104.4 °C. **$[\alpha]_D^{20}$:** +31.1 (c = 0.01, CH_2Cl_2). **^{1}H NMR (300 MHz, $CDCl_3$, 21 °C) of the (*R,R*)/(*S,S*)-diastereomer:** δ = 7.31-7.24 (*m*, 3H, arom.

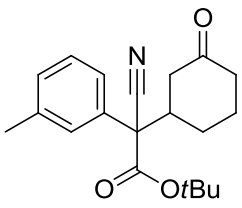
H), 7.16 (*d*, *J* = 6.6, 1H, arom. *H*), 2.84-2.73 (*m*, 1H, C*H*), 2.45-2.39 (*m*, 1H, CH_2), 2.37 (*s*, 3H, CH_3), 2.34-2.25 (*m*, 1H, CH_2), 2.22-2.06 (*m*, 3H, CH_2), 1.93-1.64 (*m*, 3H, CH_2), 1.43 (*s*, 9H, CH_3). **^{13}C NMR (75 MHz, $CDCl_3$, 21 °C) of the (*R*,*R*)/(*S*,*S*)-diastereomer:** δ = 209.2, 165.7, 139.2, 132.1, 129.9, 129.1, 126.6, 123.0, 116.9, 84.8, 60.4, 44.9, 42.6, 41.0, 28.2, 27.6, 24.3, 21.5. **IR (solid) of the (*R*,*R*)/(*S*,*S*)-diastereomer:** *v* = 2969, 2956, 2930, 2864, 2245, 1732, 1712, 1605, 1450, 1419, 1390, 1368, 1251, 1227, 1150, 1058, 1041.



(*S*,*R*)-3fa

According to GP3 *tert*-butyl-2-cyano-2-(*m*-tolyl)acetate **1f** (20.3 mg, 88 µmol, 1 equiv) was treated with 2-cyclohexen-1-one **2a** (16.9 mg, 0.18 mmol, 2 equiv) in the presence of **FIP-$O_2CC_3F_7$** (0.57 mg, 0.44 µmol, 0.5 mol%) to yield **(*S*,*R*)-3fa** (19.6 mg, 60 µmol, 68%, $ee_{(S,R)}$ = 91%, $ee_{(R,R)}$ = 60%, $dr_{(S,R+R,S):(R,R+S,S)}$ = 63:37) as a colorless oil. The *dr* and *ee* values were determined by chiral column HPLC: Chiracel OD-H, *n*-hexane/*i*-PrOH (99.5/0.5), 1 mL min^{-1}, detection at 210 nm, $t_{(S,R)}$ = 16.0 min, $t_{(R,S)}$ = 12.8 min. The major diastereomer was isolated by column chromatography (CH_2Cl_2 + 1% Et_2O).

$C_{20}H_{25}NO_3$, MW: 327.42 g mol^{-1}. **$[\alpha]_D^{20}$:** +14.7 (c = 0.27, CH_2Cl_2). **^{1}H NMR (300 MHz, $CDCl_3$, 21 °C) of the (*S*,*R*)/(*R*,*S*)-diastereomer:** δ = 7.38-7.35 (*m*, 2H, arom. *H*), 7.30 (*t*, *J* = 7.7, 1H, arom. *H*), 7.19 (*d*, *J* = 7.1, 1H, arom. *H*), 2.84-2.73 (*m*, 1H, C*H*), 2.65-2.59 (*m*, 1H, CH_2), 2.57-2.48 (*m*, 1H, CH_2), 2.39 (*s*, 3H, CH_3), 2.36-2.25 (*m*, 1H, CH_2), 2.09-1.98 (*m*, 1H, CH_2), 1.63-1.45 (*m*, 3H, CH_2), 1.42 (*s*, 9H, CH_3). **^{13}C NMR (75 MHz, $CDCl_3$, 21 °C) of the (*S*,*R*)/(*R*,*S*)-diastereomer:** δ = 208.8, 165.2, 139.1, 132.9, 129.7, 129.0, 126.9, 123.2, 117.0, 84.9, 60.5, 45.2, 44.6, 40.8, 27.6, 25.8, 24.1, 21.6. **IR (solid) of the (*S*,*R*)/(*R*,*S*)-diastereomer:** *v* = 2979, 2935, 2876, 2242, 1718, 1606, 1446, 1367, 1284, 1257, 1232, 1148, 1072.

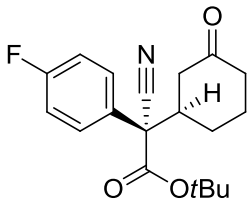


***rac*-3fa**

According to GP2 *tert*-butyl-2-cyano-2-(*m*-tolyl)acetate **1f** (260.0 mg, 1.12 mmol, 1 equiv) was treated with 2-cyclohexen-1-one **2a** (108.1 mg, 1.12 mmol, 1 equiv). Column chromatography (petrol ether:EtOAc = 9:1 → 4:1) of the crude product yielded ***rac*-3fa** (189.4 mg, 0.58 mg, 52%) as a colorless solid with a $dr_{(R,R+S,S):(S,R+R,S)}$ of 38:62.

$C_{20}H_{25}NO_3$, MW: 327.42 g mol^{-1}. **Mp:** 87.4-87.7 °C. **HRMS (ESI) *m/z*:** Calc. for $[C_{20}H_{25}NO_3 + Na]^+$: 350.1727. Found: 350.1727. **Microanalysis:** Calc. for $C_{20}H_{25}NO_3$: C: 73.37; H: 7.70; N: 4.28. Found: C: 73.31; H: 7.69; N: 4.22.

tert-Butyl-2-cyano-2-(4-fluorophenyl)-2-(3-oxocyclohexyl)-acetate (3ga)

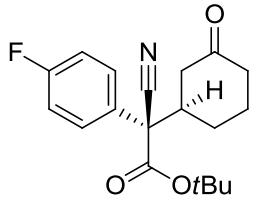


(*R*,*R*)-3ga

According to GP3 *tert*-butyl-2-cyano-2-(*m*-tolyl)acetate **1f** (39.4 mg, 0.17 mmol, 1 equiv) was treated with 2-cyclohexen-1-one **2a** (32.2 mg, 0.34 mmol, 2 equiv) in the presence of **FBIP-$O_2CC_3F_7$** (1.38 mg, 0.84 µmol, 0.5 mol%) to yield **(*R*,*R*)-3ga** (54.6 mg, 0.16 mmol, 97%, $ee_{(R,R)}$ = 92%, $ee_{(S,R)}$ = 65%, $dr_{(R,R+S,S):(S,R+R,S)}$ = 90:10) as a colorless solid. The *dr* and *ee* values were determined by chiral column HPLC: Chiracel AD-H, *n*-hexane/*i*-PrOH (99:1), 1.2 mL min^{-1}, detection at 210 nm, $t_{(R,R)}$ = 27.4 min, $t_{(S,S)}$ = 34.4 min. The major diastereomer was isolated by column chromatography (CH_2Cl_2 + 1% Et_2O).

$C_{19}H_{22}NO_3F$, MW: 331.38 g mol^{-1}. **Mp:** 143.9-144.2 °C. **$[\alpha]_D^{20}$:** +27.8 (c = 0.01, CH_2Cl_2). **^{1}H NMR (300 MHz, $CDCl_3$, 21 °C) of the (*R*,*R*)/(*S*,*S*)-diastereomer:** δ = 7.53 (*d*, *J* = 9.0, 1H, arom. *H*), δ = 7.52 (*d*, *J* = 9.0, 1H, arom. *H*), 7.11 (*d*,*J* = 8.8, 1H, arom. *H*), 7.09 (*d*,*J* = 8.8, 1H,

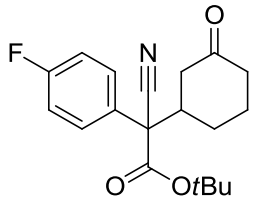
arom. *H*), 2.82-2.71 (*m*, 1H, C*H*$_2$), 2.46-2.40 (*m*, 1H, C*H*$_2$), 2.37-2.26 (*m*, 1H, C*H*$_2$), 2.23-2.14 (*m*, 1H, C*H*$_2$), 2.12-2.05 (*m*, 2H, C*H*$_2$), 1.91-1.82 (*m*, 1H, C*H*$_2$), 1.78-1.64 (*m*, 1H, C*H*$_2$), 1.44 (*s*, 9H, C*H*$_3$). **^{13}C NMR (75 MHz, CDCl$_3$, 21 °C) of the (*R*,*R*)/(*S*,*S*)-diastereomer:** δ = 208.7, 165.5, 163.0 (*d*, *J* = 251.9, *C*F), 128.11 (*m*, *C*CCCF), 128.10 (*d*, *J* = 8.3, *C*CCF), 116.7, 116.3 (*d*, *J* = 22.2, *C*CF), 85.2, 59.8, 45.1, 42.5, 40.9, 28.2, 27.6, 24.3. **^{19}F NMR (235 MHz, CDCl$_3$, 21 °C) of the (*R*,*R*)/(*S*,*S*)-diastereomer:** δ = –112.23 (*m*, 1F). **IR (solid) of the (*R*,*R*)/(*S*,*S*)-diastereomer:** *v* = 2959, 2940, 2873, 2248, 1727, 1714, 1604, 1506, 1412, 1369, 1256, 1228, 1149, 1014.



(*S*,*R*)-3ga

According to GP3 *tert*-butyl-2-cyano-2-(*m*-tolyl)acetate **1f** (20.4 mg, 87 µmol, 1 equiv) was treated with 2-cyclohexen-1-one **2a** (16.7 mg, 0.17 mmol, 2 equiv) in the presence of **FIP-O$_2$CC$_3$F$_7$** (1.13 mg, 0.87 µmol, 1 mol%) to yield **(*S*,*R*)-3ga** (26.5 mg, 80 µmol, 92%, $ee_{(S,R)}$ = 90%, $ee_{(R,R)}$ = 7%, $dr_{(S,R+R,S):(R,R+S,S)}$ = 77:23) as a colorless solid. The *dr* and *ee* values were determined by chiral column HPLC: Chiracel AD-H, *n*-hexane/*i*-PrOH (99:1), 1.2 mL min^{-1}, detection at 210 nm, $t_{(S,R)}$ = 14.4 min, $t_{(R,S)}$ = 13.2 min. The major diastereomer was isolated by column chromatography (CH_2Cl_2 + 1% Et_2O).

C$_{19}$H$_{22}$NO$_3$F, **MW:** 331.38 g mol^{-1}. **Mp:** 115.3-115.8 °C. **$[\alpha]_D^{20}$:** +11.0 (c = 0.23, CH_2Cl_2). **^{1}H NMR (300 MHz, CDCl$_3$, 21 °C) of the (*S*,*R*)/(*R*,*S*)-diastereomer:** δ = 7.59 (*d*, *J* = 9.0, 1H, arom. *H*), δ = 7.57 (*d*, *J* = 9.0, 1H, arom. *H*), 7.13 (*d*,*J* = 8.8, 1H, arom. *H*), 7.11 (*d*,*J* = 8.8, 1H, arom. *H*), 2.83-2.71 (*m*, 1H, C*H*$_2$), 2.64-2.47 (*m*, 2H, C*H*$_2$), 2.46-2.25 (*m*, 2H, C*H*$_2$), 2.16-1.99 (*m*, 1H, C*H*$_2$), 1.64-1.46 (*m*, 2H, C*H*$_2$), 1.43 (*s*, 9H, C*H*$_3$). **^{13}C NMR (75 MHz, CDCl$_3$, 21 °C) of the (*S*,*R*)/(*R*,*S*)-diastereomer:** δ = 208.4, 165.1, 162.9 (*d*, *J* = 251.9, *C*F), 128.8 (*d*, *J* = 3.3, *C*CCCF), 128.2 (*d*, *J* = 8.6, *C*CCF), 116.7, 116.2 (*d*, *J* = 21.8, *C*CF), 85.3, 59.9, 45.4, 44.5, 40.8, 30.9, 27.6, 25.7, 24.0. **^{19}F NMR (235 MHz, CDCl$_3$, 21 °C) of the (*S*,*R*)/(*R*,*S*)-diastereomer:** δ = –112.35 (*m*, 1F). **IR (solid) of the (*S*,*R*)/(*R*,*S*)-diastereomer:** *v* = 2974, 2932, 2880, 2245, 1728, 1715, 1606, 1508, 1413, 1369, 1256, 1239, 1228, 1149, 1014.

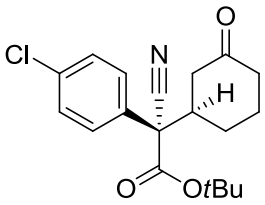


***rac*-3ga**

According to GP2 *tert*-butyl-2-cyano-2-(4-fluorophenyl)acetate **1g** (252.0 mg, 1.07 mg, 1 equiv) was treated with 2-cyclohexen-1-one **2a** (103.0 mg, 1.07 mmol, 1 equiv). Column chromatography (petrol ether:EtOAc = 9:1 → 4:1) of the crude product yielded ***rac*-3ga** (222.8 mg, 0.67 mmol, 63%) as a colorless solid with a $dr_{(R,R+S,S):(S,R+R,S)}$ of 37:63.

$C_{19}H_{22}NO_3F$, **MW:** 331.38 g mol^{-1}. **Mp:** 125.8-126.4 °C. **HRMS (ESI) *m/z*:** Calc. for $[C_{19}H_{22}NO_3F + Na]^+$: 354.1476. Found: 354.1476. **Microanalysis:** Calc. for $C_{19}H_{22}NO_3F$: C: 68.86; H: 6.69; N: 4.23. Found: C: 68.61; H: 6.62; N: 4.16.

tert-Butyl-2-cyano-2-(4-chlorophenyl)-2-(3-oxocyclohexyl)-acetate (3ha)

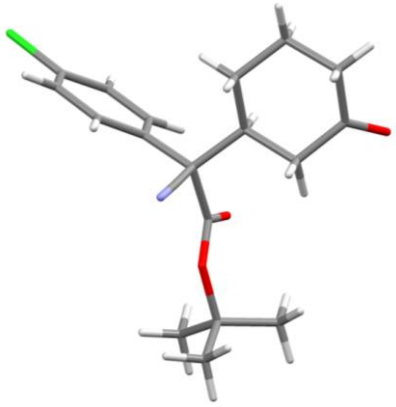


(*R*,*R*)-3ha

According to GP3 *tert*-butyl-2-cyano-2-(4-chlorophenyl)acetate **1h** (40.6 mg, 0.16 mmol, 1 equiv) was treated with 2-cyclohexen-1-one **2a** (31.0 mg, 0.32 mmol, 2 equiv) in the presence of **FBIP-$O_2CC_3F_7$** (1.33 mg, 0.81 mmol, 0.5 mol%) to yield **(*R*,*R*)-3ha** (55.1 mg, 0.16 mmol, 99%, $ee_{(R,R)}$ = 99%, $ee_{(S,R)}$ = 64%, $dr_{(R,R+S,S):(S,R+R,S)}$ = 88:12) as a colorless solid. The *dr* value was determined by ^{1}H NMR. The *ee* values were determined by chiral column HPLC: Chiracel AD-H, *n*-hexane/*i*-PrOH (99.5:0.5), 2 mL min^{-1}, detection at 210 nm, $t_{(R,R)}$ = 21.7 min, $t_{(S,S)}$ = 26.2 min. The major diastereomer was isolated by column chromatography (CH_2Cl_2 + 1% Et_2O).

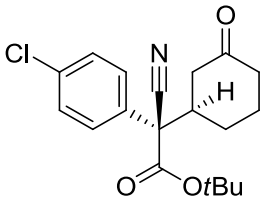
Constitution and relative configuration of **3ha** was confirmed by X-ray crystal structure analysis. The (*S*,*S*)/(*R*,*R*)-configured diastereomer **3ha** crystallized preferentially in racemic form (from a sample with $ee_{(R,R)}$ = 99%) in *n*-hexane/*i*PrOH at room temperature. CCDC 856194 contains the

supplementary crystallographic data for this compound. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.



X-ray crystal structure of **3ha** [color code: C (grey); Cl (green); N (blue); O (red); H (white)].

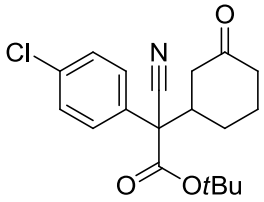
$C_{19}H_{22}NO_3Cl$, **MW:** 347.84 g mol^{-1}. **Mp:** 148.1-148.6 °C. **$[\alpha]_D^{20}$:** +36.6 (c = 0.01, CH_2Cl_2). **^{1}H NMR (500 MHz, $CDCl_3$, 21 °C) of the (*R*,*R*)/(*S*,*S*)-diastereomer:** δ = 7.48 (*d*, *J* = 8.4, 2H, *m*-*H*), 7.38 (*d*, *J* = 8.9, 2H, *o*-*H*), 2.78-2.72 (*m*, 1H, C*H*), 2.44-2.41 (*m*, 1H, CH_2), 2.34-2.28 (*m*, 1H, CH_2), 2.23-2.17 (*m*, 1H, CH_2), 2.14-2.06 (*m*, 2H, CH_2), 1.87-1.80 (*m*, 2H, CH_2), 1.72 (*qt*, *J* = 13.2, 3.7, 1H, CH_2), 1.44 (*s*, 9H, CH_3). **^{13}C NMR (125 MHz, $CDCl_3$, 21 °C) of the (*R*,*R*)/(*S*,*S*)-diastereomer:** δ = 208.6, 165.3, 135.4, 130.9, 129.5, 127.5, 116.5, 85.3, 60.0, 45.1, 42.5, 40.9, 28.2, 27.6, 24.3. **IR (solid) of the (*R*,*R*)/(*S*,*S*)-diastereomer:** ν = 2937, 2869, 2242, 1735, 1708, 1493, 1454, 1403, 1370, 1252, 1230, 1150, 1095, 1013.



(*S*,*R*)-3ha

According to GP3 *tert*-butyl-2-cyano-2-(4-chlorophenyl)acetate **1h** (10.2 mg, 41 µmol, 1 equiv) was treated with 2-cyclohexen-1-one **2a** (7.79 mg, 81 µmol, 2 equiv) in the presence of **FIP-$O_2CC_3F_7$** (0.53 mg, 0.41 µmol, 1 mol%) to yield **(*S*,*R*)-3ha** (14.1 mg, 41 mmol, 99%, $ee_{(S,R)}$ = 83%, $ee_{(R,R)}$ = 55%, $dr_{(S,R+R,S):(R,R+S,S)}$ = 84:16) as a colorless oil. The *dr* value was determined by ^{1}H NMR. The *ee* values were determined by chiral column HPLC: Chiracel AD-H, *n*-hexane/*i*-PrOH (99.5:0.5), 2 mL min^{-1}, detection at 210 nm, $t_{(S,R)}$ = 15.3 min, $t_{(R,S)}$ = 12.6 min. The major diastereomer was isolated by column chromatography (CH_2Cl_2 + 1% Et_2O).

$C_{19}H_{22}NO_3Cl$, MW: 347.84 g mol^{-1}. **$[\alpha]_D^{20}$:** +8.8 (c = 0.06, CH_2Cl_2). **^{1}H NMR (500 MHz, $CDCl_3$, 21 °C) of the (*S*,*R*)/(*R*,*S*)-diastereomer:** δ = 7.54 (*d*, *J* = 8.7, 2H, *m*-*H*), 7.41 (*d*, *J* = 8.3, 2H, *o*-*H*), 2.78-2.73 (*m*, 1H, C*H*), 2.61-2.58 (*m*, 1H, CH_2), 2.54-2.49 (*m*, 1H, CH_2), 2.44-2.41 (*m*, 1H, CH_2), 2.34-2.27 (*m*, 1H, CH_2), 2.04-2.01 (*m*, 1H, CH_2), 1.52-1.46 (*m*, 3H, CH_2), 1.43 (*s*, 9H, CH_3). **^{13}C NMR (125 MHz, $CDCl_3$, 21 °C) of the (*S*,*R*)/(*R*,*S*)-diastereomer:** δ = 208.3, 164.9, 135.3, 129.4, 127.7, 85.5, 60.1, 45.3, 44.5, 40.7, 27.6, 25.8, 24.0. **IR (solid) of the (*S*,*R*)/(*R*,*S*)-diastereomer:** *v* = 2965, 2223, 1731, 1715, 1494, 1410, 1370, 1257, 1232, 1148, 1095, 1016.

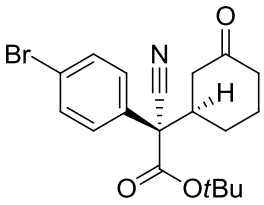


***rac*-3ha**

According to GP2 *tert*-butyl-2-cyano-2-(4-chlorophenyl)acetate **1h** (258.5 mg, 1.03 mmol, 1 equiv) was treated with 2-cyclohexen-1-one **2a** (98.7 mg, 1.03 mmol, 1 equiv). Column chromatography (petrol ether:EtOAc = 9:1 → 4:1) of the crude product yielded ***rac*-3ha** (320.3 mg, 0.93 mmol, 90%) as a colorless solid with a $dr_{(R,R+S,S):(S,R+R,S)}$ of 42:58.

$C_{19}H_{22}NO_3Cl$, MW: 347.84 g mol^{-1}. **Mp:** 140.5-141.1 °C. **HRMS (ESI) *m*/*z*:** Calc. for $[C_{19}H_{22}NO_3Cl + Na]^+$: 370.1180. Found: 370.1175. **Microanalysis:** Calc. for $C_{19}H_{22}NO_3Cl$: C: 65.61; H: 6.38; N: 4.03. Found: C: 65.27; H: 6.33; N: 3.97.

tert-Butyl-2-cyano-2-(4-bromophenyl)-2-(3-oxocyclohexyl)-acetate (3ia)

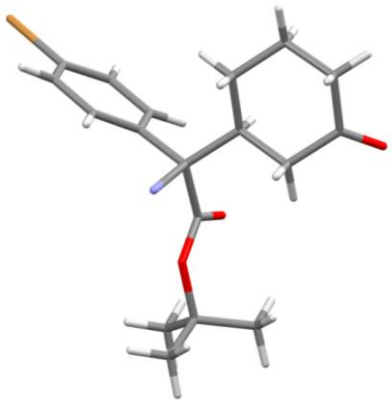


(*R*,*R*)-3ia

According to GP3 *tert*-butyl-2-cyano-2-(4-bromophenyl)acetate **1i** (40.7 mg, 0.14 mmol, 1 equiv) was treated with 2-cyclohexen-1-one **2a** (26.4 mg, 0.27 mmol, 2 equiv) in the presence

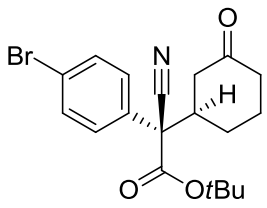
of **FBIP-$O_2CC_3F_7$** (1.14 mg, 0.69 µmol, 0.5 mol%) to yield **(*R*,*R*)-3ia** (53.8 mg, 0.14 mmol, 98%, $ee_{(R,R)}$ = 97%, $ee_{(S,R)}$ = 62%, $dr_{(R,R+S,S):(S,R+R,S)}$ = 86:14) as a colorless solid. The *dr* and *ee* values were determined by chiral column HPLC: Chiracel AD-H, *n*-hexane/*i*-PrOH (99.5/0.5), 1.2 mL min^{-1}, detection at 210 nm, $t_{(R,R)}$ = 51.3 min, $t_{(S,S)}$ = 56.9 min. The major diastereomer was isolated by column chromatography (CH_2Cl_2 + 1% Et_2O).

Constitution and relative configuration of **3ia** was confirmed by X-ray crystal structure analysis. The (*S*,*S*)/(*R*,*R*)-configured diastereomer **3ia** crystallized preferentially in racemic form (from a sample with $ee_{(R,R)}$ = 90%) in diethylether at room temperature. CCDC 856190 contains the supplementary crystallographic data for this compound. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.



X-ray crystal structure of **3ia** [color code: C (grey); Br (brown); N (blue); O (red); H (white)]. One included diethylether molecule per unit cell is omitted for clarity.

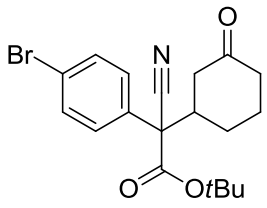
$C_{19}H_{22}NO_3Br$, **MW:** 392.29 g mol^{-1}. **Mp:** 155.6-156.2 °C. **$[\alpha]_D^{20}$:** +29.5 (c = 0.01, CH_2Cl_2). **^{1}H NMR (500 MHz, $CDCl_3$, 21 °C) of the (*R*,*R*)/(*S*,*S*)-diastereomer:** δ = 7.54 (*d*, *J* = 7.9, 2H, *m*-*H*), 7.41(*d*, *J* = 8.5, 2H, *o*-*H*), 2.78-2.72 (*m*, 1H, C*H*), 2.44-2.41 (*m*, 1H, CH_2), 2.35-2.28 (*m*, 1H, CH_2), 2.20-2.17 (*m*, 1H, CH_2), 2.14-2.06 (*m*, 2H, CH_2), 1.87-1.80 (*m*, 2H, CH_2), 1.72 (*qt*, *J* = 13.4, 3.8, 1H, CH_2), 1.44 (*s*, 9H, CH_3). **^{13}C NMR (125 MHz, $CDCl_3$, 21 °C) of the (*R*,*R*)/(*S*,*S*)-diastereomer:** δ = 208.6, 165.3, 132.5, 131.4, 127.8, 123.5, 116.4, 85.4, 60.0, 42.0, 42.5, 40.9, 28.1, 27.6, 24.3. **IR (solid) of the (*R*,*R*)/(*S*,*S*)-diastereomer:** ν = 2937, 2868, 2244, 1733, 1710, 1489, 1451, 1397, 1370, 1252, 1229, 1149, 1078, 1009.



(*S*,*R*)-3ia

According to GP3 *tert*-butyl-2-cyano-2-(4-bromophenyl)acetate **1i** (9.86 mg, 33 µmol, 1 equiv) was treated with 2-cyclohexen-1-one **2a** (6.40 mg, 67 µmol, 2 equiv) in the presence of **FIP-$O_2CC_3F_7$** (0.22 mg, 0.17 µmol, 0.5 mol%) to yield **(*S*,*R*)-3ia** (12.8 mg, 33 mmol, 99%, $ee_{(S,R)}$ = 87%, $ee_{(R,R)}$ = 23%, $dr_{(S,R+R,S):(R,R+S,S)}$ = 63:37) as a colorless oil. The *dr* and *ee* values were determined by chiral column HPLC: Chiracel AD-H, *n*-hexane/*i*-PrOH (99.5/0.5), 1.2 mL min^{-1}, detection at 210 nm, $t_{(S,R)}$ = 36.8 min, $t_{(R,S)}$ = 27.8 min. The major diastereomer was isolated by column chromatography (CH_2Cl_2 + 1% Et_2O).

$C_{19}H_{22}NO_3Br$, **MW:** 392.29 g mol^{-1}. **$[\alpha]_D^{20}$:** –2.4 (c = 0.21, CH_2Cl_2). **^{1}H NMR (500 MHz, $CDCl_3$, 21 °C) of the (*S*,*R*)/(*S*,*S*)-diastereomer:** δ = 7.56 (*d*, *J* = 8.7, 2H, *m*-*H*), 7.47 (*d*, *J* = 8.7, 2H, *o*-*H*), 2.78-2.72 (*m*, 1H, C*H*), 2.61-2.58 (*m*, 1H, CH_2), 2.55-2.49 (*m*, 1H, CH_2), 2.44-2.41 (*m*, 1H, CH_2), 2.35-2.27 (*m*, 1H, CH_2), 2.21-2.08 (*m*, 1H, CH_2), 2.05-2.01 (*m*, 1H, CH_2), 1.90-1.68 (*m*, 1H, CH_2), 1.52-1.46 (*m*, 1H, CH_2), 1.43 (*s*, 9H, CH_3). **^{13}C NMR (125 MHz, $CDCl_3$, 21 °C) of the (*S*,*R*)/(*S*,*S*)-diastereomer:** δ = 208.3, 164.8, 132.5, 132.4, 129.3, 128.0, 116.5, 85.5, 60.2, 45.3, 44.5, 40.7, 27.6, 25.8, 24.0. **IR (solid) of the (*S*,*R*)/(*R*,*S*)-diastereomer:** *v* = 3074, 3004, 2968, 2928, 2867, 2244, 1728, 1715, 1491, 1450, 1405, 1370, 1255, 1232, 1149, 1076, 1012.

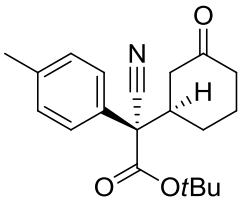


***rac*-3ia**

According to GP2 *tert*-butyl-2-cyano-2-(4-bromophenyl)acetate **1i** (255.1 mg, 0.86 mmol, 1 equiv) was treated with 2-cyclohexen-1-one **2a** (82.8 mg, 0.86 mmol, 1 equiv). Column chromatography (petrol ether:EtOAc = 9:1 → 4:1) of the crude product yielded ***rac*-3ia** (283.3 mg, 0.72 mmol, 84%) as a colorless oil with a $dr_{(R,R+S,S):(S,R+R,S)}$ of 40:60.

$C_{19}H_{22}NO_3Br$, **MW:** 392.29 g mol^{-1}. **Mp:** 143.0-143.4 °C. **HRMS (ESI) *m/z*:** Calc. for $[C_{13}H_{14}BrNO_2]^-$: 264.0130. Found: 294.0129. **Microanalysis:** Calc. for $C_{19}H_{22}NO_3Br$: C: 58.17; H: 5.65; N: 3.57. Found: C: 58.44; H: 5.65; N: 3.57.

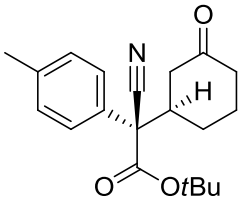
tert-Butyl-2-cyano-2-(3-oxocyclohexyl)-2-(*p*-tolyl)-acetate (3ja)



(*R,R*)-3ja

According to GP3 *tert*-butyl-2-cyano-2-(*p*-tolyl)acetate **1j** (41.0 mg, 0.18 mmol, 1 equiv) was treated with 2-cyclohexen-1-one **2a** (34.1 mg, 0.35 mmol, 2 equiv) in the presence of **FBIP-$O_2CC_3F_7$** (2.93 mg, 1.8 µmol, 1 mol%) to yield **(*R,R*)-3ja** (44.2 mg, 0.14 mmol, 75%, $ee_{(R,R)}$ = 94%, $ee_{(S,R)}$ = 76%, $dr_{(R,R+S,S):(S,R+R,S)}$ = 92:08) as a colorless solid. The *dr* and *ee* values were determined by chiral column HPLC: Chiracel AS-H, *n*-hexane/*i*-PrOH (99:1), 1.5 mL min^{-1}, detection at 210 nm, $t_{(R,R)}$ = 10.8 min, $t_{(S,S)}$ = 43.2 min. The major diastereomer was isolated by column chromatography (CH_2Cl_2 + 1% Et_2O).

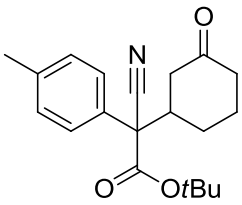
$C_{20}H_{25}NO_3$, MW: 327.42 g mol^{-1}. **Mp:** 114.4-115.4 °C. **$[\alpha]_D^{20}$:** +35.3 (c = 0.01, CH_2Cl_2). **^{1}H NMR (300 MHz, $CDCl_3$, 21 °C) of the (*R,R*)/(*S,S*)-diastereomer:** δ = 7.39 (*d*, *J* = 8.3, 2H, arom. *H*), 7.19 (*d*, *J* = 8.0, 2H, arom. *H*), 2.82-2.72 (*m*, 1H, C*H*), 2.44-2.38 (*m*, 1H, CH_2), 2.35 (*s*, 3H, CH_3), 2.32-2.25 (*m*, 1H, CH_2), 2.21-2.15 (*m*, 1H, CH_2), 2.10-2.06 (*m*, 2H, CH_2), 1.93-1.64 (*m*, 3H, CH_2), 1.43 (*s*, 9H, CH_3). **^{13}C NMR (75 MHz, $CDCl_3$, 21 °C) of the (*R,R*)/(*S,S*)-diastereomer:** δ = 209.2, 165.8, 139.1, 130.0, 129.3, 125.9, 117.0, 84.7, 60.1, 44.9, 42.6, 41.0, 28.2, 27.6, 24.3, 21.0. **IR (solid) of the (*R,R*)/(*S,S*)-diastereomer:** ν = 2958, 2924, 2863, 2248, 1718, 1511, 1447, 1369, 1316, 1258, 1227, 1148, 1059, 1043.



(*S,R*)-3ja

According to GP3 *tert*-butyl-2-cyano-2-(*p*-tolyl)acetate **1j** (20.3 mg, 88 µmol, 1 equiv) was treated with 2-cyclohexen-1-one **2a** (16.9 mg, 0.18 mmol) in the presence of **FIP-$O_2CC_3F_7$** (0.57 mg, 0.44 µmol, 0.5 mol%) to yield **(*S,R*)-3ja** (26.5 mg, 81 mmol, 92%, $ee_{(S,R)}$ = 99%, $ee_{(R,R)}$ = 32%, $dr_{(S,R+R,S):(R,R+S,S)}$ = 76:24) as a colorless solid. The *dr* and *ee* values were determined by chiral column HPLC: Chiracel AS-H, *n*-hexane/*i*-PrOH (99:1), 1.5 mL min^{-1}, detection at 210 nm, $t_{(S,R)}$ = 20.0 min, $t_{(R,S)}$ = 17.2 min. The major diastereomer was isolated by column chromatography (CH_2Cl_2 + 1% Et_2O).

$C_{20}H_{25}NO_3$, MW: 327.42 g mol^{-1}. **Mp:** 131.9-132.8 °C. **$[\alpha]_D^{20}$:** +9.7 (c = 0.20, CH_2Cl_2). **^{1}H NMR (300 MHz, $CDCl_3$, 21 °C) of the (*S,R*)/(*R,S*)-diastereomer:** δ = 7.46 (*d*, *J* = 8.3, 2H, arom. *H*), 7.22 (*d*, *J* = 8.2, 2H, arom. *H*), 2.82-2.72 (*m*, 1H, C*H*), 2.64-2.48 (*m*, 2H, CH_2), 2.44-2.39 (*m*, 1H, CH_2), 2.37 (*s*, 3H, CH_3), 2.33-2.24 (*m*, 1H, CH_2), 2.05-1.97 (*m*, 1H, CH_2), 1.55-1.45 (*m*, 3H, CH_2), 1.42 (*s*, 9H, CH_3). **^{13}C NMR (75 MHz, $CDCl_3$, 21 °C) of the (*S,R*)/(*R,S*)-diastereomer:** δ = 208.8, 165.3, 139.0, 130.0, 129.9, 126.1, 117.0, 84.9, 60.3, 45.2, 44.6, 40.8, 27.6, 25.8, 24.0, 21.0. **IR (solid) of the (*S,R*)/(*R,S*)-diastereomer:** ν = 2970, 2928, 2870, 2243, 1729, 1714, 1514, 1451,1371, 1253, 1231, 1149, 1017.

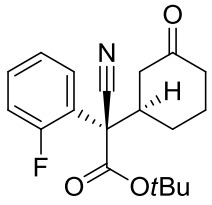


***rac*-3ja**

According to GP2 *tert*-butyl-2-cyano-2-(*p*-tolyl)acetate **1j** (260.0 mg, 1.12 mmol, 1 equiv) was treated with 2-cyclohexen-1-one **2a** (108.1 mg, 1.12 mmol, 1 equiv). Column chromatography (petrol ether:EtOAc = 9:1 → 4:1) of the crude product yielded ***rac*-3ja** (162.6 mg, 0.50 mmol, 44%) as a colorless solid with a $dr_{(R,R+S,S):(S,R+R,S)}$ of 38:62.

$C_{20}H_{25}NO_3$, MW: 327.42 g mol^{-1}. **Mp:** 102.0-102.6 °C. **HRMS (ESI) *m/z*:** Calc. for $[C_{20}H_{25}NO_3 + Na]^+$: 350.1727. Found: 350.1727. **Microanalysis:** Calc. for $C_{20}H_{25}NO_3$: C: 73.37; H: 7.70; N: 4.28. Found: C: 73.21; H: 7.61; N: 4.24.

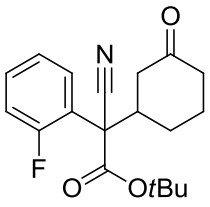
tert-Butyl-2-cyano-2-(2-fluorophenyl)-2-(3-oxocyclohexyl)-acetate (3ka)



(*S*,*R*)-3ka

According to GP3 *tert*-butyl-2-cyano-2-(2-fluorophenyl)acetate **1k** (9.93 mg, 42 µmol, 1 equiv) was treated with 2-cyclohexen-1-one **2a** (8.12 mg, 84 µmol, 2 equiv) in the presence of **FIP-$O_2CC_3F_7$** (0.55 mg, 0.42 µmol, 1 mol%) to yield **(*S*,*R*)-3ka** (6.12 mg, 18.5 mmol, 44%, $ee_{(S,R)}$ = 81%, $ee_{(R,R)}$ = 50%, $dr_{(S,R+R,S):(R,R+S,S)}$ = 57:43) as a colorless solid. The *dr* value was determined by ^{1}H NMR. The major diastereomer was isolated by column chromatography (CH_2Cl_2 + 1% Et_2O). The *ee* value of the major diastereomer was determined by chiral column HPLC: Chiracel AS-H, *n*-hexane/*i*-PrOH (97:3), 1 mL min^{-1}, detection at 210 nm, $t_{(S,R)}$ = 20.8 min, $t_{(R,S)}$ = 28.2 min.

$C_{19}H_{22}NO_3F$, MW: 331.38 g mol^{-1}. **Mp:** 72.9-73.3 °C. **$[\alpha]_D^{20}$:** +8.3 (c = 0.10, CH_2Cl_2). **^{1}H NMR (300 MHz, $CDCl_3$, 21 °C) of the (*S*,*R*)/(*R*,*S*)-diastereomer:** δ = 7.56 (*td*, *J* = 7.9, 1.6, 1H, arom. *H*), 7.44-7.37 (*m*, 1H, arom. *H*), 7.22 (*td*, *J* = 7.6, 1.1, 1H, arom. *H*), 7.16-7.07 (*m*, 1H, arom. *H*), 3.09-2.96 (*m*, 1H, C*H*), 2.75-2.68 (*m*, 1H, CH_2), 2.56-2.51 (*m*, 1H, CH_2), 2.47-2.40 (*m*, 1H, CH_2), 2.34-2.21 (*m*, 1H, CH_2), 2.10-2.04 (*m*, 1H, CH_2), 1.78-1.49 (*m*, 3H, CH_2), 1.43 (*s*, 9H, CH_3). **^{13}C NMR (63 MHz, $CDCl_3$, 21 °C) of the (*S*,*R*)/(*R*,*S*)-diastereomer:** δ = 208.7, 164.0, 159.0 (*d*, *J* = 251.7, *C*F), 131.0 (*d*, *J* = 8.7, *C*CCF), 129.6 (*d*, *J* = 2.5, *C*CCCF), 124.8 (*d*, *J* = 3.3, *C*CCF), 120.7 (*d*, *J* =11.9, *C*CF), 116.9 (*d*, *J* = 22.8, *C*CF), 116.5, 85.1, 57.3, 44.3, 42.2, 40.8, 31.0, 27.5, 26.8, 24.1. **^{19}F NMR (235 MHz, $CDCl_3$, 21 °C) of the (*S*,*R*)/(*R*,*S*)-diastereomer [(*R*,*R*)/(*S*,*S*)-diastereomer]:** δ = –110.41 (*m*, 1F), [-110.91 (*m*, 1F)]. **IR (solid) of the (*S*,*R*)/(*R*,*S*)-diastereomer:** ν = 2971, 2942, 2872, 2246, 1730, 1706, 1613, 1492, 1456, 1371, 1327, 1258, 1233, 1202, 1153, 1076.

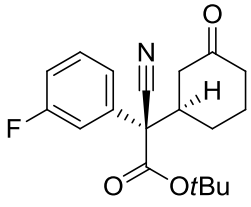


***rac*-3ka**

According to GP2 *tert*-butyl-2-cyano-2-(2-fluorophenyl)acetate **1k** (151.6 mg, 0.70 mmol, 1 equiv) was treated with 2-cyclohexen-1-one **2a** (67.1 mg, 0.70 mmol, 1 equiv). Column chromatography (petrol ether:EtOAc = 9:1 → 4:1) of the crude product yielded colorless, oily ***rac*-3ka** (106.9 mg, 0.32 mmol, 46%) as a colorless oil with a $dr_{(R,R+S,S):(S,R+R,S)}$ of 36:64. The diastereomers were separated by column chromatography (CH_2Cl_2 + 1% Et_2O).

$C_{19}H_{22}NO_3F$, MW: 331.38 g mol^{-1}. **^{1}H NMR (300 MHz, $CDCl_3$, 21 °C) of the (*R*,*R*)/(*S*,*S*)-diastereomer:** δ = 7.57 (*td*, *J* = 7.8, 1.6, 1H, arom. *H*), 7.43-7.35 (*m*, 1H, arom. *H*), 7.25-7.19 (*m*, 1H, arom. *H*), 7.14-7.07 (*m*, 1H, arom. *H*), 3.07-2.96 (*m*, 1H, C*H*), 2.46-2.41 (*m*, 1H, CH_2), 2.35-2.27 (*m*, 2H, CH_2), 2.21-2.15 (*m*, 2H, CH_2), 2.10-2.04 (*m*, 1H, CH_2), 1.87-1.56 (*m*, 2H, CH_2), 1.43 (*s*, 9H, CH_3). **^{13}C NMR (75 MHz, $CDCl_3$, 21 °C) of the (*R*,*R*)/(*S*,*S*)-diastereomer:** δ = 208.9, 164.1, 159.6 (*d*, *J* = 251.7, *C*F), 131.6 (*d*, *J* = 8.7, *C*CCF), 129.5 (*d*, *J* = 2.5, *C*CCCF) 124.9 (*d*, *J* = 3.3, *C*CCF), 120.6 (*d*, *J* =11.9, *C*CF), 116.9 (*d*, *J* = 22.8, *C*CF), 116.5, 85.0, 57.3, 57.2, 43.4, 41.8, 41.7, 41.0, 28.2, 27.5, 24.2. **^{19}F NMR (235 MHz, $CDCl_3$, 21 °C) of the (*R*,*R*)/(*S*,*S*)-diastereomer:** δ = -110.91 (*m*, 1F). **IR (solid) of the (*R*,*R*)/(*S*,*S*)-diastereomer:** ν = 2968, 2953, 2883, 2239, 1744, 1708, 1490, 1450, 1370, 1244, 1228, 1148, 1103, 1066, 1000. **MS (ESI) *m*/*z*:** 354.15 ([M+Na]$^+$, 100%). **HRMS (ESI) *m*/*z*:** Calc. for [M+Na]$^+$: 354.1476. Found: 354.1489.

tert-Butyl-2-cyano-2-(3-fluorophenyl)-2-(3-oxocyclohexyl)-acetate (3la)

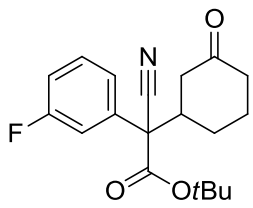


(*S*,*R*)-3la

According to GP3 *tert*-butyl-2-cyano-2-(3-fluorophenyl)acetate **1l** (10.1 mg, 43 µmol, 1 equiv) was treated with 2-cyclohexen-1-one **2a** (8.23 mg, 86 µmol, 2 equiv) in the presence of **FIP-**

$O_2CC_3F_7$ (0.56 mg, 0.43 µmol, 1 mol%) to yield **(*S*,*R*)-3la** (14.1 mg, 43 mmol, 99, $ee_{(S,R)}$ = 85%, $ee_{(R,R)}$ = 18%, $dr_{(S,R+R,S):(R,R+S,S)}$ = 69:31) as a colorless solid. The *dr* and *ee* values were determined by chiral column HPLC: Chiracel AS-H, *n*-hexane/*i*-PrOH (97:3), 1 mL min^{-1}, detection at 210 nm, $t_{(S,R)}$ = 13.7 min, $t_{(R,S)}$ = 15.6 min. The major diastereomer was isolated by column chromatography (CH_2Cl_2 + 1% Et_2O).

$C_{19}H_{22}NO_3F$, MW: 331.38 g mol^{-1}. **Mp:** 109.8-110.3 °C. **$[\alpha]_D^{20}$:** +10.1 (c = 0.10, CH_2Cl_2). **^{1}H NMR (300 MHz, $CDCl_3$, 21 °C) of the (*S*,*R*)/(*R*,*S*)-diastereomer:** δ = 7.43-7.38 (*m*, 2H, arom. *H*), 7.35-7.31 (*m*, 1H, arom. *H*), 7.14-7.07 (*m*, 1H, arom. *H*), 2.82-2.71 (*m*, 1H, C*H*), 2.64-2.52 (*m*, 2H, CH_2), 2.48-2.41 (*m*, 1H, CH_2), 2.37-2.25 (*m*, 1H, CH_2), 2.08-1.99 (*m*, 1H, CH_2), 1.65-1.47 (*m*, 3H, CH_2), 1.44 (*s*, 9H, CH_3). **^{13}C NMR (75 MHz, $CDCl_3$, 21 °C) of the (*S*,*R*)/(*R*,*S*)-diastereomer:** δ = 208.3, 164.7, 163.0 (*d*, *J* = 247.7, *C*F), 135.5 (*d*, *J* = 7.3, *C*CCF), 130.8 (*d*, *J* = 8.4, *C*CCF), 122.1 (*d*, *J* = 2.8, *C*CCCF), 116.5, 116.2 (*d*, *J* = 20.7, *C*CF), 113.7 (*d*, *J* = 24.1, *C*CF), 85.5, 60.3, 45.4, 44.5, 40.7, 27.6, 25.8, 24.0. **^{19}F NMR (235 MHz, $CDCl_3$, 21 °C) of the (*S*,*R*)/(*R*,*S*)-diastereomer:** δ = –110.54. **IR (solid) of the (*S*,*R*)/(*R*,*S*)-diastereomer:** ν = 2975, 2941, 2876, 2856, 1730, 1716, 1614, 1589, 1489, 1444, 1392, 1369, 1283, 1249, 1231, 1200, 1145, 1069.



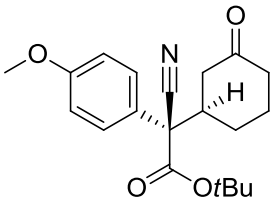
***rac*-3la**

According to GP2 *tert*-butyl-2-cyano-2-(3-fluorophenyl)acetate **1l** (249.0 mg, 1.06 mmol, 1 equiv) was treated with 2-cyclohexen-1-one **2a** (101.7 mg, 1.06 mmol, 1 equiv). Column chromatography (petrol ether:EtOAc = 9:1 → 4:1) of the crude product yielded ***rac*-3la** (199.0 mg, 0.60 mmol, 57%) as a colorless oil with a $dr_{(R,R+S,S):(S,R+R,S)}$ of 43:57. The diastereomers were separated by column chromatography (CH_2Cl_2 + 1% Et_2O).

$C_{19}H_{22}NO_3F$, MW: 331.38 g mol^{-1}.). **^{1}H NMR (300 MHz, $CDCl_3$, 21 °C) of the (*R*,*R*)/(*S*,*S*)-diastereomer:** δ = 7.43-7.25 (*m*, 3H, arom. *H*), 7.09 (*tdd*, *J* = 8.1, 2.3, 1.0, 1H, arom. *H*), 2.82-2.71 (*m*, 1H, C*H*), 2.46-2.40 (*m*, 1H, CH_2), 2.37-2.26 (*m*, 1H, CH_2), 2.22-2.06 (*m*, 3H, CH_2), 1.90-1.82 (*m*, 1H, CH_2), 1.79-1.58 (*m*, 2H, CH_2), 1.45 (*s*, 9H, CH_3). **^{13}C NMR (75 MHz, $CDCl_3$,**

21 °C) of the (*R*,*R*)/(*S*,*S*)-diastereomer: δ = 208.6, 165.2, 163.0 (*d*, *J* = 247.7, *C*F), 134.7 (*d*, *J* = 7.3, *C*CCF), 130.9 (*d*, *J* = 8.4, *C*CCF), 121.9 (*d*, *J* = 2.8, *C*CCCF), 116.4, 116.3 (*d*, *J* = 20.7, *C*CF), 113.6 (*d*, *J* = 24.1, *C*CF), 85.4, 60.20, 60.18, 45.1, 42.5, 40.9, 28.1, 27.6, 24.2. **^{19}F NMR (235 MHz, $CDCl_3$, 21 °C) of the (*R*,*R*)/(*S*,*S*)-diastereomer:** δ = –110.39. **IR (solid) of the (*R*,*R*)/(*S*,*S*)-diastereomer:** *v* = 3077, 2979, 2931, 2869, 2245, 1737, 1715, 1614, 1591, 1492, 1444, 1392, 1369, 1250, 1230, 1150, 1115, 1060. **MS (ESI) *m*/*z*:** 354.15 ($[M+Na]^+$, 100%). **HRMS (ESI) *m*/*z*:** Calc. for $[M+Na]^+$: 354.1476. Found: 354.1481.

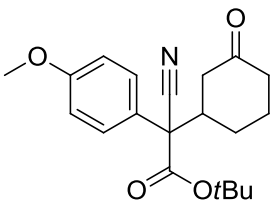
tert-Butyl-2-cyano-2-(4-methoxyphenyl)-2-(3-oxocyclohexyl)-acetate (3ma)



(*S*,*R*)-3ma

According to GP3 *tert*-butyl-2-cyano-2-(4-methoxyphenyl)acetate **1m** (40.7 mg, 0.16 mmol, 1 equiv) was treated with 2-cyclohexen-1-one **2a** (32.1 mg, 0.33 mmol, 2 equiv) in the presence of **FIP-$O_2CC_3F_7$** (1.07 mg, 0.82 µmol, 0.5 mol%) to yield **(*S*,*R*)-3ma** (49.5 mg, 0.14 mmol, 90%, $ee_{(S,R)}$ = 89%, $ee_{(R,R)}$ = 98%, $dr_{(S,R+R,S):(R,R+S,S)}$ = 80:20) as a colorless oil. The *dr* and *ee* values were determined by chiral column HPLC after reduction of the keto-group with $NaBH_4$ (see following procedure, **6ma**, S-57).

$C_{20}H_{25}NO_4$, MW: 343.42 g mol^{-1}. **$[\alpha]_D^{20}$:** +19.2 (c = 0.11, CH_2Cl_2).



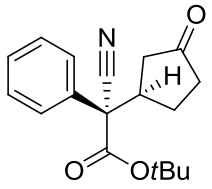
***rac*-3ma**

According to GP2 *tert*-butyl-2-cyano-2-(4-methoxyphenyl)acetate **1m** (246.6 mg, 1.00 mmol, 1 equiv) was treated with 2-cyclohexen-1-one **2a** (95.9 mg, 1.00 mmol, 1 equiv). Column chromatography (petrol ether:EtOAc = 9:1 → 4:1) of the crude product yielded ***rac*-3ma**

(105.7 mg, 0.31 mmol, 31%) as a colorless oil with a $dr_{(R,R+S,S):(S,R+R,S)}$ of 37:63. The mixture of diastereomers is inseparable by column chromatography.

$C_{20}H_{25}NO_4$, MW: 343.42 g mol^{-1}. **^{1}H NMR (300 MHz, $CDCl_3$, 21 °C) mixture of diastereomers** ((*R*,*R*)/(*S*,*S*) is marked with *, (*S*,*R*)/(*R*,*S*) with $^\#$)**:** δ = 7.49$^\#$ (*d*, *J* = 8.9, 2H, *o-H*), 7.43* (*d*, *J* = 8.9, 2H, *o-H*), 6.94-6.89 (*m*, 2H, *m-H*), 3.83$^\#$ (*s*, 3H, OCH_3), 3.82* (*s*, 3H, OCH_3), 2.81-2.70 (*m*, 1H, C*H*), 2.63-2.47 (*m*, 1H, CH_2), 2.46-2.25 (*m*, 2H, CH_2), 2.21-2.13 (*m*, 1H, CH_2), 2.11-1.99 (*m*, 2H, CH_2), 1.95-1.68 (*m*, 2H, CH_2), 1.43* (*s*, 9H, CH_3), 1.42$^\#$ (*s*, 9H, CH_3). **^{13}C NMR (75 MHz, $CDCl_3$, 21 °C) mixture of diastereomers** ((*R*,*R*)/(*S*,*S*) is marked with *, (*S*,*R*)/(*R*,*S*) with $^\#$)**:** δ = 209.2*, 208.7$^\#$, 165.9*, 165.4$^\#$, 160.0*, 159.9$^\#$, 127.5$^\#$, 127.3*, 124.9$^\#$, 124.1*, 117.1$^\#$, 117.0*, 114.6*, 114.5$^\#$, 84.9$^\#$, 84.7*, 59.9$^\#$, 59.8*, 55.4, 45.2$^\#$, 44.9*, 42.6, 41.0*, 40.8$^\#$, 28.2*, 27.6, 25.8$^\#$, 24.4*, 24.1$^\#$. **IR (film):** ν = 2939, 1732, 1713, 1608, 1510, 1459, 1370, 1249, 1148, 1031. **HRMS (ESI) *m/z*:** Calc. for [$C_{20}H_{25}NO_4$ + Na]$^+$: 366.1681. Found: 366.1677. **Microanalysis:** Calc. for $C_{20}H_{25}NO_4$: C: 69.95; H: 7.34; N: 4.08. Found: C: 69.71; H: 7.31; N: 4.06.

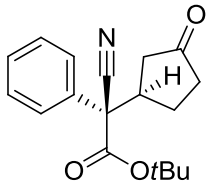
tert-Butyl-2-cyano-2-(3-oxocyclopentyl)-2-phenylacetate (3ab)



(*R*,*R*)-3ab

According to GP3 *tert*-butyl-2-cyano-2-phenylacetate **1a** (20.7 mg, 0.10 mmol) was treated with 2-cyclopenten-1-one **2b** (15.6 mg, 0.19 mmol, 2 equiv) in the presence of **FBIP-$O_2CC_3F_7$** (1.64 mg, 1.00 µmol, 1 mol%) to yield **(*R*,*R*)-3ab** (29.6 mg, 0.10 mmol, 99%, $ee_{(R,R)}$ = 90%, $ee_{(S,R)}$ = 52%, $dr_{(R,R+S,S):(S,R+R,S)}$ = 82:18) as a colorless oil. The *dr* and *ee* values were determined by chiral column HPLC: Chiracel OD-H, *n*-hexane/*i*-PrOH (99/1), 2 mL min^{-1}, detection at 210 nm, $t_{(R,R)}$ = 9.8 min, $t_{(S,S)}$ = 38.0 min.

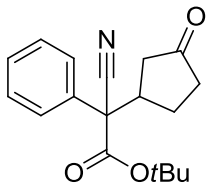
$C_{18}H_{21}NO_3$, MW: 299.36 g mol^{-1}. **$[\alpha]_D^{20}$:** +40.1 (c = 0.01, CH_2Cl_2).



(*S*,*R*)-3ab

According to GP3 *tert*-butyl-2-cyano-2-phenylacetate **1a** (20.8 mg, 96 µmol, 1 equiv) was treated with 2-cyclopenten-1-one **2b** (15.7 mg, 0.19 mmol, 2 equiv) in the presence of **FIP-$O_2CC_3F_7$** (0.62 mg, 0.48 µmol, 0.5 mol%) to yield **(*S*,*R*)-3ab** (28.5 mg, 95 mmol, 99%, $ee_{(S,R)}$ = 90%, $ee_{(R,R)}$ = 42%, $dr_{(S,R+R,S):(R,R+S,S)}$ = 80:20) as a colorless oil. The *dr* and *ee* values were determined by chiral column HPLC: Chiracel OD-H, *n*-hexane/*i*-PrOH (99/1), 2 mL min^{-1}, detection at 210 nm, $t_{(S,R)}$ = 15.5 min, $t_{(R,S)}$ = 11.6 min.

$C_{18}H_{21}NO_3$, MW: 299.36 g mol^{-1}. **$[\alpha]_D^{20}$:** +66.3 (c = 0.25, CH_2Cl_2).



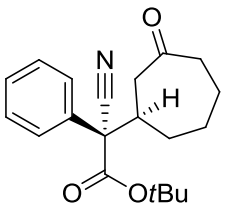
***rac*-3ab**

According to GP2 *tert*-butyl-2-cyano-2-phenylacetate **1a** (251.8 mg, 1.16 mmol, 1 equiv) was treated with 2-cyclopenten-1-one **2b** (95.2 mg, 1.16 mmol, 1 equiv). Column chromatography (petrol ether:EtOAc = 9:1 → 4:1) of the crude product yielded ***rac*-3ab** (254.5 mg, 0.85 mmol, 73%) as a colorless oil with a $dr_{(R,R+S,S):(S,R+R,S)}$ of 42:58. The mixture of diastereomers is inseparable by column chromatography.

$C_{18}H_{21}NO_3$, MW: 299.36 g mol^{-1}. **^{1}H NMR (300 MHz, $CDCl_3$, 21 °C) mixture of diastereomers** ((*R*,*R*)/(*S*,*S*) is marked with *, (*S*,*R*)/(*R*,*S*) with $^\#$)**:** δ = 7.61-7.52 (*m*, 2H, arom. *H*), 7.47-7.37 (*m*, 3H, arom. *H*), 3.32-3.13 (*m*, 1H, C*H*), 2.66-2.48 (*m*, 1H, CH_2), 2.45-2.26 (*m*, 2H, CH_2), 2.23-1.90 (*m*, 1H, CH_2), 1.79-1.64 (*m*, 2H, CH_2), 1.45$^\#$ (*s*, 9H, CH_3), 1.43* (*s*, 9H, CH_3). **^{13}C NMR (75 MHz, $CDCl_3$, 21 °C) mixture of diastereomers** ((*R*,*R*)/(*S*,*S*) is marked with *, (*S*,*R*)/(*R*,*S*) with $^\#$)**:** δ = 215.5*, 215.0$^\#$, 165.6, 133.7$^\#$, 133.2*, 129.2*, 129.1$^\#$, 126.0*, 125.8$^\#$, 116.9, 85.0, 59.5*, 59.4$^\#$, 44.0$^\#$, 43.8*, 41.9*, 40.6$^\#$, 38.4$^\#$, 38.0*, 27.6*, 27.5, 26.2$^\#$, 24.9. **IR (film):** ν = 2979, 1736, 1450, 1370, 1254, 1148, 1034. **HRMS (ESI) *m*/*z*:** Calc. for

$[C_{18}H_{21}NO_3 + Na]^+$: 322.1414. Found: 322.1423. **Microanalysis:** Calc. for $C_{18}H_{21}NO_3$: C: 72.22; H: 7.07; N: 4.68. Found: C: 71.92; H: 7.12; N: 4.51.

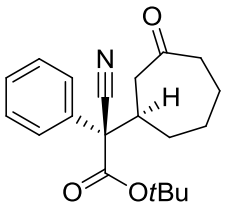
tert-Butyl-2-cyano-2-(3-oxocycloheptyl)-2-phenylacetate (3ac)



(*R*,*R*)-3ac

According to GP3 *tert*-butyl-2-cyano-2-phenylacetate **1a** (9.40 mg, 43 µmol, 1 equiv) was treated with 2-cyclohepten-1-one **2c** (9.53 mg, 87 µmol, 2 equiv) in the presence of **FBIP-$O_2CC_3F_7$** (1.43 mg, 0.87 µmol, 2 mol%) to yield **(*R*,*R*)-3ac** (10.0 mg, 31 µmol, 71%, $ee_{(R,R)}$ = 85%, $ee_{(S,R)}$ = 52%, $dr_{(R,R+S,S):(S,R+R,S)}$ = 86:14) as a colorless oil. The *dr* value was determined by ^{1}H NMR. The *ee* values were determined by chiral column HPLC: Chiracel OD-H, *n*-hexane/*i*-PrOH (99/1), 2 mL min^{-1}, detection at 210 nm, $t_{(R,R)}$ = 5.6 min, $t_{(S,S)}$ = 7.0 min. The major diastereomer was isolated by column chromatography (CH_2Cl_2 + 1% Et_2O).

$C_{20}H_{25}NO_3$, MW: 327.42 g mol^{-1}. **$[\alpha]_D^{20}$:** +42.9 (c = 0.01, CH_2Cl_2).). **^{1}H NMR (300 MHz, $CDCl_3$, 21 °C) of the (*R*,*R*)/(*S*,*S*)-diastereomer:** 7.58-7.54 (*m*, 2H, arom. *H*), 7.45-7.37 (*m*, 3H, arom. *H*), 2.88-2.79 (*m*, 1H, C*H*), 2.53-2.40 (*m*, 3H, CH_2), 2.12-1.96 (*m*, 4H, CH_2), 1.74-1.48 (*m*, 3H, CH_2), 1.41 (*s*, 9H, CH_3). **^{13}C NMR (75 MHz, $CDCl_3$, 21 °C) of the (*R*,*R*)/(*S*,*S*)-diastereomer:** δ = 211.6, 166.0, 133.0, 129.3, 129.1, 126.3, 116.8, 84.8, 61.1, 44.7, 43.6, 42.6, 34.2, 28.7, 27.6, 24.4.

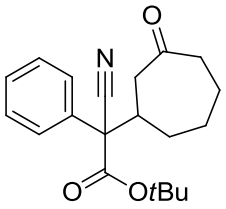


(*S*,*R*)-3ac

According to GP3 *tert*-butyl-2-cyano-2-phenylacetate **1a** (10.4 mg, 48 µmol, 1 equiv) was treated with 2-cyclohepten-1-one **2c** (10.6 mg, 96 µmol, 2 equiv) in the presence of **FIP-$O_2CC_3F_7$** (2.50 mg, 1.92 µmol, 4 mol%) to yield **(*S*,*R*)-3ac** (7.54 mg, 23 µmol, 48%, $ee_{(S,R)}$ =

72%, $ee_{(R,R)}$ = 23%, $dr_{(S,R+R,S):(R,R+S,S)}$ = 58:42) as a colorless oil. The *dr* value was determined by ^{1}H NMR. The *ee* values were determined by chiral column HPLC: Chiracel OD-H, *n*-hexane/*i*-PrOH (99/1), 2 mL min^{-1}, detection at 210 nm, $t_{(S,R)}$ = 6.3 min, $t_{(R,S)}$ = 32.2 min. The minor diastereomer could not be removed by column chromatography.

$C_{20}H_{25}NO_3$, MW: 327.42 g mol^{-1}. **$[\alpha]_D^{20}$:** +13.0 (c = 0.05, CH_2Cl_2).

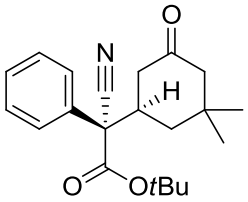


***rac*-3ac**

According to GP2 *tert*-butyl-2-cyano-2-phenylacetate **1a** (257.0 mg, 1.18 mmol, 1 equiv) was treated with 2-cyclohepten-1-one **2c** (130.3 mg, 1.18 mmol, 1 equiv). Column chromatography (petrol ether:EtOAc = 9:1 → 4:1) of the crude product yielded ***rac*-3ac** (305.9 mg, 0.93 mmol, 79%) as a colorless oil with a $dr_{(R,R+S,S):(S,R+R,S)}$ of 48:52.

$C_{20}H_{25}NO_3$, MW: 327.42 g mol^{-1}. **^{1}H NMR (300 MHz, $CDCl_3$, 21 °C) mixture of diastereomers** ((*R*,*R*)/(*S*,*S*) is marked with *, (*S*,*R*)/(*R*,*S*) with $^\#$)**:** δ = 7.61-7.55 (*m*, 2H, arom. *H*), 7.45-7.38 (*m*, 3H, arom. *H*), 2.92-2.73 (*m*, 2H, C*H*), 2.61-2.39 (*m*, 3H, CH_2), 2.06-1.85 (*m*, 2H, CH_2), 1.70-1.49 (*m*, 2H, CH_2), 1.42* (*s*, 9H, CH_3), 1.41$^\#$ (*s*, 9H, CH_3), 1.36-1.18 (*m*, 2H, CH_2). **^{13}C NMR (75 MHz, $CDCl_3$, 21 °C) mixture of diastereomers** ((*R*,*R*)/(*S*,*S*) is marked with *, (*S*,*R*)/(*R*,*S*) with $^\#$)**:** δ = 211.1, 165.8, 133.5, 129.3$^\#$, 129.2, 129.0*, 126.4*, 126.3$^\#$, 116.8, 85.0*, 84.8$^\#$, 61.1, 46.9*, 44.7$^\#$, 43.7, 42.7, 34.2$^\#$, 31.4*, 28.7$^\#$, 28.5*, 27.6, 24.4$^\#$, 24.1*. **IR (film):** ν = 2934, 1734, 1703, 1449, 1370, 1250, 1147, 1034. **HRMS (ESI) *m*/*z*:** Calc. for $[C_{20}H_{25}NO_3 + Na]^+$: 350.1727. Found: 350.1724. **Microanalysis:** Calc. for $C_{20}H_{25}NO_3$: C: 73.37; H: 7.70; N: 4.28. Found: C: 73.11; H: 7.73; N: 4.14.

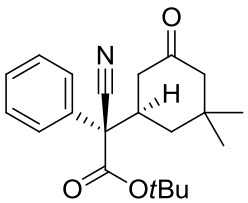
tert-Butyl-2-cyano-2-(3,3-dimethyl-5-oxocyclohexyl)-2-phenylacetate (3ad)



(*R*,*R*)-3ad

According to GP3 *tert*-butyl-2-cyano-2-phenylacetate **1a** (11.8 mg, 54 µmol, 1 equiv) was treated with 5,5-dimethyl-2-cyclohexen-1-one **2d** (13.5 mg, 0.11 mmol, 2 equiv) in the presence of **FBIP-$O_2CC_3F_7$** (1.79 mg, 1.09 mmol, 2 mol%) to yield **(*R*,*R*)-3ad** (7.56 mg, 22 µmol, 41%, $ee_{(R,R)}$ = 89%, $ee_{(S,R)}$ = 41%, $dr_{(R,R+S,S):(S,R+R,S)}$ = 84:16) as a colorless oil. The *dr* value was determined by ^{1}H NMR. The *ee* values were determined by chiral column HPLC: Chiracel OD-H, *n*-hexane/*i*-PrOH (99/1), 0.7 mL min^{-1}, detection at 210 nm, $t_{(R,R)}$ = 14.2 min, $t_{(S,S)}$ = 10.7 min. The major diastereomer was isolated by column chromatography (CH_2Cl_2 + 1% Et_2O).

$C_{21}H_{27}NO_3$, MW: 341.44 g mol^{-1}. **$[\alpha]_D^{20}$:** +8.1(c = 0.09, CH_2Cl_2). **^{1}H NMR (300 MHz, $CDCl_3$, 21 °C) of the (*R*,*R*)/(*S*,*S*)-diastereomer:** δ = 7.55-7.51 (*m*, 2H, arom. *H*), 7.44-7.36 (*m*, 3H, arom. *H*), 3.02-2.91 (*m*, 1H, arom. *H*), 2.28-2.24 (*m*, 1H, C*H*$_2$), 2.17-2.11 (*m*, 1H, C*H*$_2$), 2.08-1.99 (*m*, 1H, C*H*$_2$), 1.90-1.75 (*m*, 3H, C*H*$_2$), 1.43 (*s*, 9H, C*H*$_3$), 1.15 (*s*, 3H, C*H*$_3$), 0.99 (*s*, 3H, C*H*$_3$). **^{13}C NMR (75 MHz, $CDCl_3$, 21 °C) of the (*R*,*R*)/(*S*,*S*)-diastereomer:** δ = 208.4, 165.0, 132.4, 132.1, 127.9, 123.4, 116.6, 85.5, 60.2, 54.0, 43.5, 41.5, 38.9, 34.0, 31.7, 27.6, 25.5.

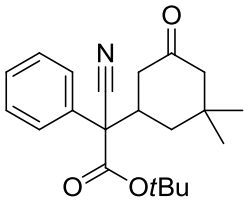


(*S*,*R*)-3ad

According to GP3 *tert*-butyl-2-cyano-2-phenylacetate **1a** (100.0 mg, 0.46 mmol, 1 equiv) was treated with 5,5-dimethyl-2-cyclohexen-1-one **2d** (114.3 mg, 0.92 mmol, 2 equiv) in the presence of **FIP-$O_2CC_3F_7$** (6.0 mg, 0.46 µmol, 1 mol%) to yield **(*S*,*R*)-3ad** (69.1 mg, 0.20 mmol, 44%, $ee_{(S,R)}$ = 96%, $ee_{(R,R)}$ = 36%, $dr_{(S,R+R,S):(R,R+S,S)}$ = 91:09) as a colorless oil. The *dr* value was determined by ^{1}H NMR. The *ee* values were determined by chiral column HPLC:

Chiracel OD-H, *n*-hexane/*i*-PrOH (99/1), 0.7 mL min^{-1}, detection at 210 nm, $t_{(S,R)}$ = 11.7 min, $t_{(R,S)}$ = 18.4 min. The minor diastereomer could not be removed by column chromatography.

$C_{21}H_{27}NO_3$, MW: 341.44 g mol^{-1}. **$[\alpha]_D^{20}$:** +11.0 (c = 0.18, CH_2Cl_2).

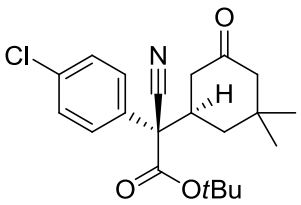


***rac*-3ad**

According to GP2 *tert*-butyl-2-cyano-2-phenylacetate **1a** (150.6 mg, 0.69 mmol, 1 equiv) was treated with 5,5-dimethyl-2-cyclohexen-1-one **2d** (86.1 mg, 0.69 mmol, 1 equiv). Column chromatography (petrol ether:EtOAc = 9:1 → 4:1) of the crude product yielded ***rac*-3ad** (89.9 mg, 0.26 mmol, 38%) as a colorless oil with a $dr_{(R,R+S,S):(S,R+R,S)}$ of 37:63.

$C_{21}H_{27}NO_3$, MW: 341.44 g mol^{-1}. **^{1}H NMR (300 MHz, $CDCl_3$, 21 °C) mixture of diastereomers** ((*R*,*R*)/(*S*,*S*) is marked with *, (*S*,*R*)/(*R*,*S*) with $^\#$)**:** δ = 7.61-7.51 (*m*, 2H, arom. *H*), 7.46-7.39 (*m*, 3H, arom. *H*), 3.05-2.94 (*m*, 1H, arom. *H*), 2.27-2.23 (*m*, 1H, C*H*$_2$), 2.77-2.72 (*m*, 1H, C*H*$_2$), 2.59-2.41 (*m*, 3H, C*H*$_2$), 2.19-2.11 (*m*, 1H, C*H*$_2$), 1.45$^\#$ (*s*, 9H, C*H*$_3$), 1.43* (*s*, 9H, C*H*$_3$), 1.29$^\#$ (*s*, 3H, C*H*$_3$), 1.15* (*s*, 3H, C*H*$_3$), 0.99* (*s*, 3H, C*H*$_3$), 0.83$^\#$ (*s*, 3H, C*H*$_3$). **^{13}C NMR (63 MHz, $CDCl_3$, 21 °C) mixture of diastereomers:** δ = 208.8, 205.1, 165.5, 165.3, 132.9, 131.4, 129.6, 129.4, 129.2, 129.0, 126.2, 126.0, 117.0, 116.8, 85.1, 84.7, 60.6, 55.1, 54.0, 52.5, 52.2, 44.4, 43.6, 41.3, 39.0, 38.8, 34.0, 31.7, 27.57, 27.50, 26.1, 25.5, 25.2. **IR (in CH_2Cl_2):** ν = 2958, 2358, 1737, 1716, 1450, 1371, 1254, 1151, 1034. **MS (ESI) *m/z*:** 364.19 ($[M+Na]^+$, 100%), 287.14 ($[M+Na - C_6H_5]^+$, 35%). **HRMS (ESI) *m/z*:** Calc. for $[M+Na]^+$: 364.1883. Found: 364.1886.

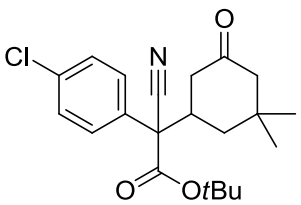
tert-Butyl-2-cyano-2-(4-chlorophenyl)-2-(3,3-dimethyl-5-oxocyclo-hexyl)acetate (3hd)



(*S*,*R*)-3hd

According to GP3 *tert*-butyl-2-cyano-2-(4-chlorophenyl)acetate **1h** (60.0 mg, 0.21 mmol, 1 equiv) was treated with 5,5-dimethyl-2-cyclohexen-1-one **2d** (51.9 mg, 0.42 mmol, 2 equiv) in the presence of **FIP-$O_2CC_3F_7$** (2.7 mg, 0.21 µmol, 1 mol%) to yield **(*S*,*R*)-3hd** (68.7 mg, 0.18 mmol, 87%, $ee_{(S,R)}$ = 92%, $ee_{(R,R)}$ = 42%, $dr_{(S,R+R,S):(R,R+S,S)}$ = 86:14) as a colorless solid. The *dr* value was determined by ^{1}H NMR. The *ee* values were determined by chiral column HPLC: Chiracel OD-H, *n*-hexane/*i*-PrOH (99/1), 0.7 mL min^{-1}, detection at 210 nm, $t_{(S,R)}$ = 15.5 min, $t_{(R,S)}$ = 10.1 min. The major diastereomer was isolated by column chromatography (CH_2Cl_2 + 1% Et_2O).

$C_{21}H_{26}NO_3Cl$, MW: 375.89 g mol^{-1}. **Mp:** 122.8-123.4 °C. **$[\alpha]_D^{20}$:** +7.7 (c = 0.10, CH_2Cl_2). **^{1}H NMR (300 MHz, $CDCl_3$, 21 °C) of the (*S*,*R*)/(*R*,*S*)-diastereomer:** δ = 7.53 (*d*, *J* = 9.0, 2H, arom. *H*), 7.42 (*d*, *J* = 9.0, 2H, arom. *H*), 2.99-2.88 (*m*, 1H, C*H*), 2.58-2.51 (*m*, 1H, CH_2), 2.47-2.39 (*m*, 1H, CH_2), 2.27-2.22 (*m*, 1H, CH_2), 2.17-2.11 (*m*, 1H, CH_2), 1.51-1.47 (*m*, 1H, CH_2), 1.42 (*s*, 9H, CH_3), 1.10-1.03 (*m*, 1H, CH_2), 0.99 (*s*, 3H, CH_3), 0.82 (*s*, 3H, CH_3). **^{13}C NMR (75 MHz, $CDCl_3$, 21 °C) of the (*S*,*R*)/(*R*,*S*)-diastereomer:** δ = 208.5, 165.0, 135.3, 131.5, 129.5, 127.7, 116.6, 85.5, 60.1, 54.0, 43.5, 41.5, 38.9, 34.0, 31.7, 27.6, 25.5. **IR (solid) of the (*S*,*R*)/(*R*,*S*)-diastereomer:** *v* = 2964, 2875, 2248, 1729, 1709, 1593, 1494, 1468, 1371, 1279, 1253, 1194, 1150, 1097, 1087, 1013.



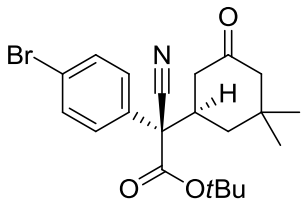
***rac*-3hd**

According to GP2 *tert*-butyl-2-cyano-2-(4-chlorophenyl)acetate **1h** (40.6 mg, 0.16 mmol, 1 equiv) was treated with 5,5-dimethyl-2-cyclohexen-1-one **2d** (20.0 mg, 0.16 mmol, 1 equiv)

for 69 h. Column chromatography (petrol ether:EtOAc = 9:1 → 4:1) of the crude product yielded ***rac*-3hd** (36.4 mg, 0.10 mmol, 60%) as a colorless solid with a $dr_{(R,R+S,S):(S,R+R,S)}$ of 40:60. The diastereomers were separated by column chromatography (CH_2Cl_2 + 1% Et_2O).

$C_{21}H_{26}NO_3Cl$, MW: 375.89 g mol^{-1}. **Mp:** 140.3-141.1 °C. **^{1}H NMR (300 MHz, $CDCl_3$, 21 °C) of the (*R*,*R*)/(*S*,*S*)-diastereomer:** δ = 7.49 (*d*, *J* = 8.9, 2H, arom. *H*), 7.39 (*d*, *J* = 8.9, 2H, arom. *H*), 2.96-2.85 (*m*, 1H, arom. *H*), 2.28-2.24 (*m*, 1H, C*H*$_2$), 2.18-2.12 (*m*, 1H, C*H*$_2$), 2.07-1.98 (*m*, 1H, C*H*$_2$), 1.88-1.72 (*m*, 3H, C*H*$_2$), 1.44 (*s*, 9H, C*H*$_3$), 1.15 (*s*, 3H, C*H*$_3$), 0.98 (*s*, 3H, C*H*$_3$). **^{13}C NMR (75 MHz, $CDCl_3$, 21 °C) of the (*R*,*R*)/(*S*,*S*)-diastereomer:** δ = 208.7, 165.1, 135.4, 131.0, 129.5, 127.5, 116.5, 85.3, 60.1, 54.1, 41.6, 41.3, 34.5, 31.9, 27.6, 25.7. **IR (solid) of the (*R*,*R*)/(*S*,*S*)-diastereomer:** ν = 2965, 2872, 2249, 1728, 1713, 1595, 1494, 1461, 1405, 1372, 1272, 1256, 1146, 1100, 1016. **MS (ESI) *m*/*z*:** 398.15 ([M+Na]$^+$, 100%). **HRMS (ESI) *m*/*z*:** Calc. for [M+Na]$^+$: 398.1493. Found: 398.1499.

tert-Butyl-2-cyano-2-(4-bromophenyl)-2-(3,3-dimethyl-5-oxocyclo-hexyl)acetate (3id)

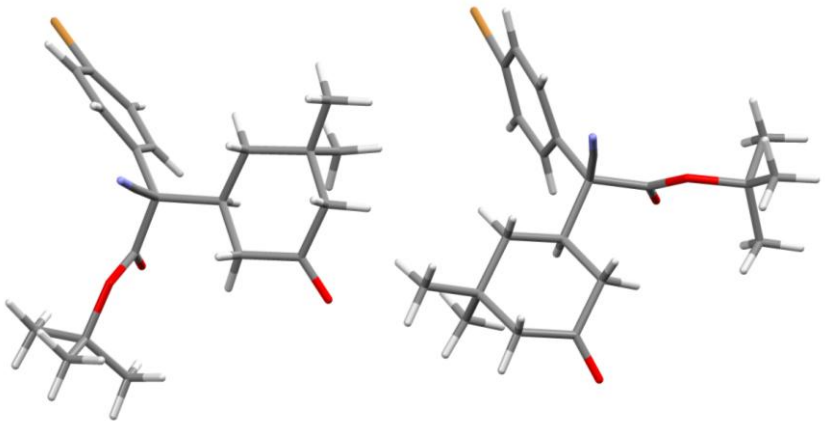


(*S*,*R*)-3id

According to GP3 *tert*-butyl-2-cyano-2-(4-bromophenyl)acetate **1i** (129.3 mg, 0.44 mmol, 1 equiv) was treated with 5,5-dimethyl-2-cyclohexen-1-one **2d** (108.4 mg, 0.87 mmol, 2 equiv) in the presence of **FIP-$O_2CC_3F_7$** (5.7 mg, 0.44 µmol, 1 mol%) to yield **(*S*,*R*)-3id** (125.8 mg, 0.30 mmol, 68%, $ee_{(S,R)}$ = 91%, $ee_{(R,R)}$ = 91%, $dr_{(S,R+R,S):(R,R+S,S)}$ = 82:18) as a colorless oil. The *dr* and *ee* values were determined by chiral column HPLC: Chiracel OD-H, *n*-hexane/*i*-PrOH (99/1), 0.7 mL min^{-1}, detection at 210 nm, $t_{(S,R)}$ = 17.2 min, $t_{(R,S)}$ = 11.1 min. The major diastereomer was isolated by column chromatography (CH_2Cl_2 + 1% Et_2O).

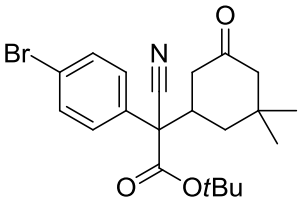
Constitution of **3id** was confirmed by X-ray crystal structure analysis. **3id** crystallized preferentially in racemic form (from a sample with both diastereomers, $ee_{(S,R)}$ = 91% and $ee_{(R,R)}$ = 91%) in *n*-hexane/*i*PrOH at room temperature. The unit cell contains both diastereomers. CCDC 856195 contains the supplementary crystallographic data for this compound. These data

can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.



X-ray crystal structure of **3id** [color code: C (grey); N (blue); Br (brown); O (red); H (white)].

$C_{21}H_{26}NO_3Br$, MW: 420.34 g mol^{-1}. **$[\alpha]_D^{20}$:** +27.4 (c = 0.10, CH_2Cl_2). **^{1}H NMR (300 MHz, $CDCl_3$, 21 °C) of the (*S*,*R*)/(*R*,*S*)-diastereomer:** δ = 7.55 (*d*, *J* = 7.9, 2H, *m*-*H*), 7.43 (*d*, *J* = 8.5, 2H, *o*-*H*), 2.99-2.89 (*m*, 1H, C*H*), 2.55-2.48 (*m*, 1H, CH_2), 2.44-2.35 (*m*, 1H, CH_2), 2.26-2.21 (*m*, 1H, CH_2), 2.19-2.13 (*m*, 1H, CH_2), 1.51-1.47 (*m*, 1H, CH_2), 1.42 (*s*, 9H, CH_3), 1.10-1.02 (*m*, 1H, CH_2), 0.95 (*s*, 3H, CH_3), 0.80 (*s*, 3H, CH_3). **^{13}C NMR (75 MHz, $CDCl_3$, 21 °C) of the (*S*,*R*)/(*R*,*S*)-diastereomer:** δ = 208.5, 165.0, 135.3, 131.5, 129.5, 127.7, 116.6, 85.5, 60.1, 54.0, 43.5, 41.5, 38.9, 34.0, 31.7, 27.6, 25.5. **IR (film) of the (*S*,*R*)/(*R*,*S*)-diastereomer:** *v* = 2958, 2247, 1736, 1714, 1494, 1450, 1370, 1250, 1148, 1035, 1006.

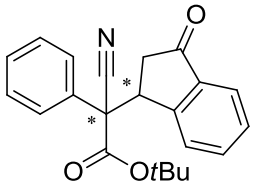


***rac*-3id**

According to GP2 *tert*-butyl-2-cyano-2-(4-bromophenyl)acetate **1i** (51.2 mg, 0.17 mmol) was treated with 5,5-dimethyl-2-cyclohexen-1-one **2d** (23.7 mg, 0.19 mmol, 1.1 equiv). Column chromatography (petrol ether:EtOAc = 9:1 → 4:1) of the crude product yielded ***rac*-3id** (53.0 mg, 0.13 mmol, 73%) as a colorless oil with a $dr_{(R,R+S,S):(S,R+R,S)}$ of 41:59. The diastereomers were separated by column chromatography (CH_2Cl_2 + 1% Et_2O).

$C_{21}H_{26}NO_3Br$, **MW:** 420.34 g mol^{-1}. **^{1}H NMR (300 MHz, $CDCl_3$, 21 °C) of the (*R*,*R*)/(*S*,*S*)-diastereomer:** δ = 7.56 (*d*, *J* = 8.7, 2H, *m-H*), 7.47 (*d*, *J* = 8.7, 2H, *o-H*), 2.96-2.85 (*m*, 1H, arom. *H*), 2.28-2.24 (*m*, 1H, CH_2), 2.18-2.12 (*m*, 1H, CH_2), 2.07-1.98 (*m*, 1H, CH_2), 1.88-1.72 (*m*, 3H, CH_2), 1.44 (*s*, 9H, CH_3), 1.15 (*s*, 3H, CH_3), 0.98 (*s*, 3H, CH_3). **^{13}C NMR (75 MHz, $CDCl_3$, 21 °C) of the (*R*,*R*)/(*S*,*S*)-diastereomer:** δ = 208.7, 165.1, 135.4, 131.0, 129.5, 127.5, 116.5, 85.3, 60.1, 54.1, 41.6, 41.3, 34.5, 31.9, 27.6, 25.7. **IR (film) of the (*R*,*R*)/(*S*,*S*)-diastereomer:** *v* = 2957, 2925, 2854, 2249, 1736, 1717, 1450, 1370, 1252, 1148, 1080, 1036, 1003. **MS (ESI) *m*/*z*:** 444.10 ([M+Na]$^+$, 100%), 387.03 ([M+Na – *t*Bu]$^+$, 14%), 364.05 ([M – *t*Bu]$^+$, 24%). **HRMS (ESI) *m*/*z*:** Calc. for [M+Na]$^+$: 444.0970. Found: 444.0976.

tert-Butyl-2-cyano-2-(3-oxo-2,3-dihydro-1*H*-inden-1-yl)-2-phenylacetate (3ae)



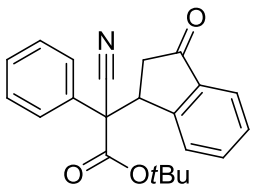
3ae

According to GP3 *tert*-butyl-2-cyano-2-phenylacetate (**1a**, 20 mg, 0.09 mmol, 1 equiv) was treated with 1*H*-inden-1-one (**2e**, 24.0 mg, 0.18 mmol, 2 equiv) in the presence of **FBIP-O_2CCF_3** (3.04 mg, 1.8 µmol, 2 mol%) to yield **3ae** (30.0 mg, 0.09 mmol, 96%, $ee_{majorisomer}$ = 62%, $ee_{minorisomer}$ = 22%, $dr_{a:b}$ = 53:47) as a colorless oil.

According to GP3 *tert*-butyl-2-cyano-2-phenylacetate (**1a**, 20.0 mg, 0.09 mmol, 1 equiv) was treated with 1*H*-inden-1-one (**2e**, 24.0 mg, 0.18 mmol, 2 equiv) in the presence of **FIP-O_2CCF_3** (0.60 mg, 0.5 µmol, 0.5 mol%) to yield **3ae** (23.5 mg, 0.07 mmol, 75%, $ee_{majorisomer}$ = 50%, $ee_{minorisomer}$ = 28%, $dr_{a:b}$ = 60:40) as a colorless oil.

Both catalysts, monopalladacycle **FIP** and bispalladacycle **FBIP**, furnish the same diastereomere (a) in excess, while the racemic reaction gave diastereomer b in excess. Therefore the reaction possibly procceds in both cases *via* a monometallic mechanism due to the different reactivity of the enone **2e**. The *dr* and *ee* values were determined by chiral column HPLC: Chiracel AD-H, *n*-hexane/*i*-PrOH (99/1), 0.9 mL min^{-1}, detection at 210 nm, t_{a1} = 21.9 min, t_{a2} = 28.3 min, t_{b1} = 32.7 min, t_{b2} = 90.5 min. The minor diastereomer (b) was only partially removed by column chromatography (CH_2Cl_2 + 1% Et_2O).

$C_{22}H_{21}NO_3$, MW: 347.41 g mol^{-1}. **^{1}H NMR (300 MHz, $CDCl_3$, 21 °C) mixture of diastereomers** (diastereomer a is marked with *, diastereomer b with $^\#$)**:** δ = 7.83$^\#$ (*d*, *J* = 7.44, 1H, arom. *H*), 7.80* (*d*, *J* = 8.19, 1H, arom. *H*), 7.69-7.37 (*m*, 8H, arom. *H*), 4.70$^\#$ (*dd*, *J* = 7.9, 3.5, 1H, C*H*), 4.50* (*dd*, *J* = 7.9, 2.8, 1H, C*H*), 3.09* (*dd*, *J* = 19.2, 7.9, 1H, CH_2), 2.71* (*dd*, *J* = 19.2, 3.1, 1H, CH_2), 2.58$^\#$ (*dd*, *J* = 19.4, 7.7, 1H, CH_2), 2.27$^\#$ (*dd*, *J* = 19.4, 3.5, 1H, CH_2), 1.47$^\#$ (*s*, 9H, CH_3), 1.43* (*s*, 9H, CH_3). **^{13}C NMR (63 MHz, $CDCl_3$, 21 °C) mixture of diastereomers** (diastereomer a is marked with *, diastereomer b with $^\#$)**:** δ = 202.9, 165.6, 150.8, 138.2, 135.1$^\#$, 134.2*, 133.5*, 129.6*, 129.4, 129.1*, 127.0*, 126.5*, 126.3$^\#$, 126.1$^\#$, 124.3$^\#$, 124.0*, 116.2, 85.4*, 85.3$^\#$, 60.5*, 60.3$^\#$, 45.6*, 44.4$^\#$, 41.7*, 40.0$^\#$. **IR (oil) mixture of diastereomers:** *v* = 2980, 2252, 1715, 1602, 1463, 1450, 1396, 1371, 1253, 1147, 1094, 1050, 1018.

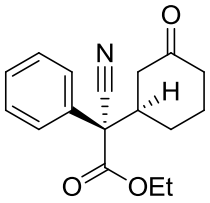


***rac*-3ae**

According to GP2 *tert*-butyl-2-cyano-2-phenylacetate **1a** (105.1 mg, 0.48 mmol, 1 equiv) was treated with1*H*-inden-1-one **2e** (70.0 mg, 0.48 mmol, 1 equiv). Column chromatography (petrol ether:EtOAc = 9:1 → 4:1) of the crude product yielded ***rac*-3ae** (30.7 mg, 0.09 mmol, 18%) as a colorless oil with a $dr_{a:b}$ of 37:63. The major diastereomer (b) was isolated by column chromatography (CH_2Cl_2 + 1% Et_2O).

$C_{22}H_{21}NO_3$, MW: 347.41 g mol^{-1}. **^{1}H NMR (300 MHz, $CDCl_3$, 21 °C) of the major diastereomer:** δ = 7.83 (*d*, *J* = 7.44, 1H, arom. *H*), 7.69-7.39 (*m*, 8H, arom. *H*), 4.70 (*dd*, *J* = 7.9, 3.5, 1H, C*H*), 2.58 (*dd*, *J* = 19.4, 7.7, 1H, CH_2), 2.27 (*dd*, *J* = 19.4, 3.5, 1H, CH_2), 1.47 (*s*, 9H, CH_3). **^{13}C NMR (63 MHz, $CDCl_3$, 21 °C) of the major diastereomer:** δ = 202.7, 166.3, 152.0, 138.0, 135.1, 133.8, 129.3, 126.3, 126.1, 124.3, 116.2, 85.3, 60.2, 44.3, 40.0, 27.6. **IR (oil) of the major diastereomer:** *v* = 2980, 2249, 1715, 1602, 1463, 1450, 1396, 1370, 1253, 1146, 1094, 1047, 1019. **MS (ESI) *m*/*z*:** 370.14 ([M+Na]$^+$, 100%), 348.16 ([M+H]$^+$, 4%). **HRMS (ESI) *m*/*z*:** Calc. for [M+Na]$^+$: 370.1414. Found: 370.1429.

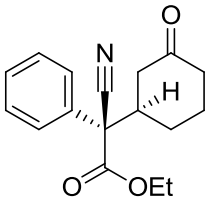
Ethyl-2-cyano-2-(3-oxocyclohexyl)-2-phenylacetate (3a'a)



(*R*,*R*)-3a'a

According to GP3 ethyl-2-cyano-2-phenylacetate (**1a'**, 20.0 mg, 0.11 mmol, 1 equiv) was treated with 2-cyclohexen-1-one **2a** (20.3 mg, 0.21 mmol, 2 equiv) in the presence of **FBIP-$O_2CC_3F_7$** (1.82 mg, 1.10 µmol, 1 mol%) to yield **(*R*,*R*)-3a'a** (31.0 mg, 0.11 mmol, 99%, $ee_{(R,R)}$ = 77%, $ee_{(S,R)}$ = 15%, $dr_{(R,R+S,S):(S,R+R,S)}$ = 62:38) as a colorless solid. The *dr* and *ee* values were determined by chiral column HPLC: Chiracel OD-H, *n*-hexane/*i*-PrOH (99/1), 2 mL min^{-1}, detection at 210 nm, $t_{(R,R)}$ = 10.7 min, $t_{(S,S)}$ = 12.8 min. The major diastereomer was isolated by column chromatography (CH_2Cl_2 + 1% Et_2O).

$C_{17}H_{19}NO_3$, MW: 285.34 g mol^{-1}. **Mp:** 74.8-75.0 °C. **$[\alpha]_D^{20}$:** +58.2 (c = 0.10, CH_2Cl_2). **^{1}H NMR (300 MHz, $CDCl_3$, 21 °C) of the (*R*,*R*)/(*S*,*S*)-diastereomer:** δ = 7.56-7.53 (*m*, 2H, arom. *H*), 7.44-7.38 (*m*, 3H, arom. *H*), 4.35-4.15 (*m*, 2H, C*H*$_2$CH$_3$), 2.92-2.81 (*m*, 1H, C*H*), 2.45-2.39 (*m*, 1H, C*H*$_2$), 2.37-2.26 (*m*, 1H, C*H*$_2$), 2.22-2.05 (*m*, 3H, C*H*$_2$), 1.93-1.65 (*m*, 3H, C*H*$_2$), 1.26 (*t*, *J* = 7.2, 3H, C*H*$_3$). **^{13}C NMR (75 MHz, $CDCl_3$, 21 °C) of the (*R*,*R*)/(*S*,*S*)-diastereomer:** δ = 208.8, 166.9, 131.9, 129.4, 129.3, 126.2, 116.5, 63.5, 59.7, 45.1, 42.4, 40.9, 28.3, 24.2, 13.8. **IR (solid) of the (*R*,*R*)/(*S*,*S*)-diastereomer:** ν = 3063, 2953, 2873, 2244, 1731, 1708, 1486, 1449, 1426, 1368, 1322, 1243, 1172, 1122, 1110, 1071, 1024, 1003.

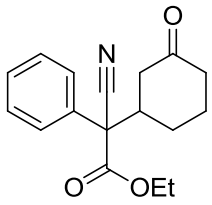


(*S*,*R*)-3a'a

According to GP3 ethyl-2-cyano-2-phenylacetate (**1a'**, 19.8 mg, 0.10 mmol, 1 equiv) was treated with 2-cyclohexen-1-one **2a** (20.1 mg, 0.21 mmol, 2 equiv) in the presence of **FIP-$O_2CC_3F_7$** (0.68 mg, 0.52 µmol, 0.5 mol%) to yield **(*S*,*R*)-3a'a** (26.3 mg, 92 mmol, 92%, $ee_{(S,R)}$ = 83%, $ee_{(R,R)}$ = 13%, $dr_{(S,R+R,S):(R,R+S,S)}$ = 67:33) as a colorless solid. The *dr* and *ee* values were determined by chiral column HPLC: Chiracel OD-H, *n*-hexane/*i*-PrOH (99/1), 2 mL min^{-1},

detection at 210 nm, $t_{(S,R)}$ = 9.0 min, $t_{(R,S)}$ = 7.6 min. The major diastereomer was isolated by column chromatography (CH_2Cl_2 + 1% Et_2O).

$C_{17}H_{19}NO_3$, MW: 285.34 g mol^{-1}. **Mp:** 71.5-71.7 °C. **$[\alpha]_D^{20}$:** +14.8 (c = 0.18, CH_2Cl_2). **^{1}H NMR (300 MHz, $CDCl_3$, 21 °C) of the (*S*,*R*)/(*R*,*S*)-diastereomer:** δ = 7.62-7.53 (*m*, 2H, arom. *H*), 7.47-7.37 (*m*, 3H, arom. *H*), 4.33-4.14 (*m*, 2H, C*H*$_2$CH$_3$), 2.92-2.81 (*m*, 1H, C*H*), 2.64-2.53 (*m*, 2H, C*H*$_2$), 2.46-2.41 (*m*, 1H, C*H*$_2$), 2.34-2.26 (*m*, 1H, C*H*$_2$), 2.07-1.99 (*m*, 1H, C*H*$_2$), 1.56-1.43 (*m*, 3H, C*H*$_2$), 1.25 (*t*, *J* = 7.2, 3H, CH$_2$C*H*$_3$). **^{13}C NMR (75 MHz, $CDCl_3$, 21 °C) of the (*S*,*R*)/(*R*,*S*)-diastereomer:** δ = 208.4, 166.5, 132.6, 129.3, 129.2, 126.4, 126.1, 116.6, 63.5, 59.9, 45.4, 44.6, 40.8, 25.7, 24.0, 13.8. **IR (solid) of the (*S*,*R*)/(*R*,*S*)-diastereomer:** ν = 2963, 2877, 2246, 1741, 1709, 1491, 1448, 1366, 1321, 1276, 1226, 1161, 1068, 1029, 1001.

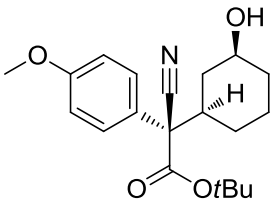


***rac*-3a'a**

According to GP2 ethyl-2-cyano-2-phenylacetate (**1a'**, 261.3 mg, 1.38 mmol, 1 equiv) was treated with 2-cyclohexen-1-one **2a** (132.8 mg, 1.38 mmol, 1 equiv). Column chromatography (petrol ether:EtOAc = 9:1 → 4:1) of the crude product yielded ***rac*-3a'a** (364.0 mg, 1.28 mmol, 92%) as a colorless oil with a $dr_{(R,R+S,S):(S,R+R,S)}$ of 36:64.

$C_{17}H_{19}NO_3$, MW: 285.34 g mol^{-1}. **HRMS (ESI) *m*/*z*:** Calc. for $[C_{17}H_{19}NO_3 + Na]^+$: 308.1257. Found: 308.1250.

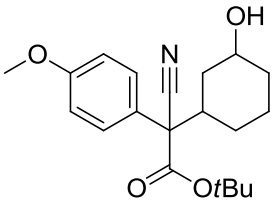
tert-Butyl-2-cyano-2-(3-hydroxycyclohexyl)-2-(4-methoxyphenyl)-acetate (6ma)



(*S*,*R*,*S*)-6ma

According to GP4 **(*S*,*R*)-3ma** (49.5 mg, 0.14 mmol, 1 equiv) was treated with $NaBH_4$ (11.5 mg, 0.31 mmol, 2.2 equiv) to yield **(*S*,*R*,*S*)-6ma** (48.4 mg, 0.31 mmol, quant., $ee_{(S,R,S)}$ = 89%, $ee_{(R,R,S)}$ = 98%, $dr_{(S,R,S+R,S,R):(R,R,S+S,S,R)}$ = 80:20) as a colorless oil. After removal of the solvent under reduced pressure, the crude oily residue could be directly used for *dr*- and *ee*-determination by chiral stationary phase HPLC: Chiracel OD-H, *n*-hexane/*i*-PrOH (97/3), 1 mL min^{-1}, detection at 210 nm, $t_{(S,R,S)}$ = 27.7 min, $t_{(R,S,R)}$ = 18.8 min. The minor diastereomer was only partially removed by column chromatography (PE : EtOAc = 4:1).

$C_{20}H_{27}NO_4$, MW: 345.43 g mol^{-1}. **$[\alpha]_D^{20}$:** –59.7 (c = 0.26, CH_2Cl_2). **^{1}H NMR (300 MHz, $CDCl_3$, 21 °C) of the (*S*,*R*,*S*)/(*R*,*S*,*R*)-diastereomer [(*R*,*R*,*S*)/(*S*,*S*,*R*)-diastereomer]:** δ = 7.48 (*d*, *J* = 8.7, 2H, arom. *H*), 6.91 (*d*, *J* = 9.2, 2H, arom. *H*), 3.82 (*s*, 3H, O*CH*$_3$), 3.72-3.63 (*m*, 1H, C*H*), [3.54-3.45 (*m*, 1H, C*H*)], 2.43-2.34 (*m*, 1H, C*H*), 2.17-1.72 (*m*, 3H, C*H*$_2$), 1.42 (*s*, 9H, C*H*$_3$), 1.35-1.00 (*m*, 5H, C*H*$_2$). **^{13}C NMR (75 MHz, $CDCl_3$, 21 °C) of the (*S*,*R*,*S*)/(*R*,*S*,*R*)-diastereomer [(*R*,*R*,*S*)/(*S*,*S*,*R*)-diastereomer]:** δ = [166.5], 166.4, [159.8], 159.7, 127.5, [125.5], 125.2, 117.5, 114.3, [114.2], [84.4], 84.3, 70.3, [70.2], 59.8, 55.3, 43.4, [38.8], 36.5, [35.2], 35.1, 28.5, 27.6, [26.1], [23.4], 23.2.

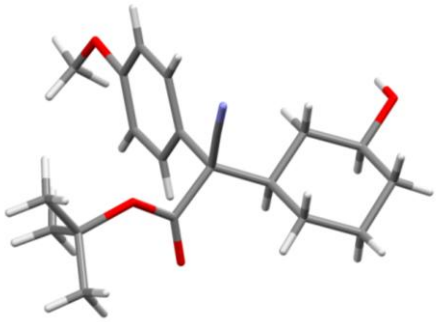


***rac*-6ma**

According to GP5 ***rac*-3ma** (22.9 mg, 67 µmol, 1 equiv) was treated with $NaBH_4$ (5.51 mg, 0.15 mmol, 2.2 equiv). Column chromatography (petrol ether:EtOAc = 4:1 → 2:1) of the crude product yielded ***rac*-6ma** (22.6 mg, 65 µmol, 98%) as a colorless solid with a

$dr_{(R,R,S+S,S,R):(S,R,S+R,S,R)}$ of 37:63. The (*R*,*R*,*S*)/(*S*,*S*,*R*)-diastereomers were isolated by column chromatography (PE : EtOAc = 4:1).

Constitution and relative configuration of the (*S*,*R*,*S*)/(*R*,*S*,*R*)-diastereomer of ***rac*-6ma** was confirmed by X-ray crystal structure analysis. The (*S*,*R*,*S*)/(*R*,*S*,*R*)-diastereomer of ***rac*-6ma** crystallized (from a racemic sample with both diastereomers) in *n*-hexane/*i*PrOH at room temperature. CCDC 856192 contains the supplementary crystallographic data for this compound. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.



X-ray crystal structure of ***rac*-6ma** [color code: C (grey); N (blue); O (red); H (white)].

$C_{20}H_{27}NO_4$, MW: 345.43 g mol^{-1}. **Mp:** 133.5-134.1 °C. **^{1}H NMR (300 MHz, $CDCl_3$, 21 °C) of the (*R*,*R*,*S*)/(*S*,*S*,*R*)-diastereomer:** δ = 7.48 (*d*, *J* = 9.2, 2H, arom. *H*), 6.92 (*d*, *J* = 9.2, 2H, arom. *H*), 3.82 (*s*, 3H, OCH_3), 3.54-3.44 (*m*, 1H, C*H*), 2.44-2.32 (*m*, 1H, C*H*), 2.01-1.78 (*m*, 3H, CH_2), 1.51-1.35 (*m*, 2H, CH_2), 1.42 (*s*, 9H, CH_3), 1.27-1.14 (*m*, 2H, CH_2), 1.12-1.00 (*m*, 1H, CH_2). **^{13}C NMR (75 MHz, $CDCl_3$, 21 °C) of the (*R*,*R*,*S*)/(*S*,*S*,*R*)-diastereomer:** δ = 166.5, 159.8, 127.6, 125.2, 117.4, 114.3, 114.2, 84.3, 70.3, 59.8, 55.3, 43.5, 36.5, 35.1, 28.5, 27.6, 23.4. **IR (in $CDCl_3$):** ν = 3368, 2936, 2859, 2251, 1733, 1608, 1582, 1510, 1456, 1394, 1297, 1251, 1185, 1153, 1033. **MS (ESI) *m*/*z*:** 368.18 ($[M+Na]^+$, 100%), 346.20 ($[M+H]^+$, 1%), 312.12 ($[M - t\text{Bu}+Na+H]^+$, 46%). **HRMS (ESI) *m*/*z*:** Calc. for $[M+Na]^+$: 368.1832. Found: 368.1837.

Recycling of the Catalyst

Experimental

The activated catalyst (3.0 mg, 0.18 µmol, 2 mol%) was dissolved in Et_2O and silica (40-63 µm, 1g silica per 25 mg catalyst, silica was washed with diglyme and Et_2O prior to use) was added. The solvent was removed by a constant stream of nitrogen to give the absorbed catalyst. This red solid was used in the catalysis as follows:

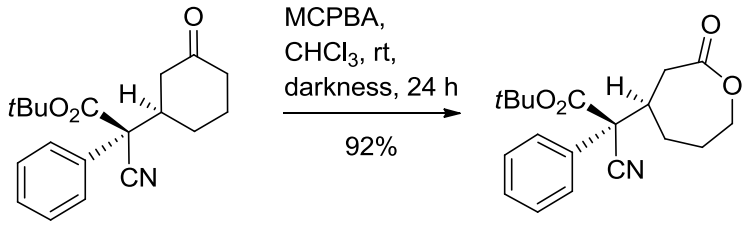
tert-Butyl-2-cyano-2-phenylacetate (**1a**, 20 mg, 0.09 mmol, 1 equiv) was dissolved in diglyme (150 µL) and HOAc in diglyme (20 µL, 0.02 mmol, 0.20 equiv, c = 47.7 mmol L^{-1}), cyclohex-2-en-1-one (**2a**, 18 µL, 0.18 mmol, 2 equiv) and the activated catalyst on silica were added. The red-wine-colored reaction mixture was stirred for 24 hours at 35 °C. The reaction was quenched with *n*-pentane (1 mL) and the catalyst precipitated on silica. The colorless solution was separated by decantation and the solid residue was additionally washed with *n*-pentane. Solvent evaporation of the combined supernatant resulted in the product (23.4-28.5 mg, 0.07-0.09 mmol, 81-99%). The absorbed catalyst was dried in vacuum and used for catalysis as described above.

Run	Conv.[a] [%]	*dr*[a] (*R*,*R*+*S*,*S*):(*S*,*R*+*R*,*S*)	*ee*[b] (*R*,*R*) [%]
1	99	89:11	94
2	95	89:11	95
3	96	89:11	95
4	94	89:11	93
5	88	87:13	93
6[c]	81	82:12	84
control experiment[d]	5	63:37	<1

[a] Determined by ^{1}H-NMR. [b] Determined by HPLC. [c] Reaction time 48 h. [d] Reaction was run with silica, without catalyst.

Derivatization of Enantioenriched Michael-Addition Products (*R*,*R*)-3 from FBIP Catalysis

(*R*)-*tert*-Butyl-2-cyano-2-((*R*)-2-oxooxepan-4-yl)-2-phenylacetate (4aa)

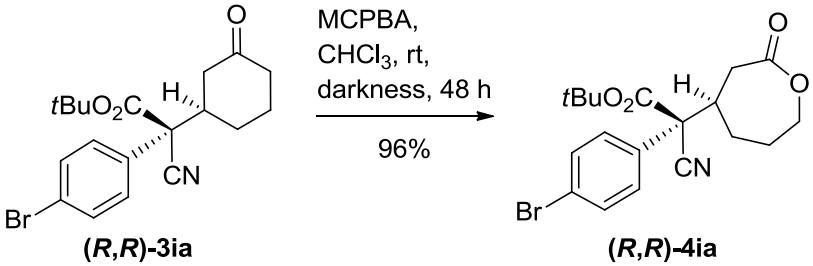


(*R*,*R*)-3aa **(*R*,*R*)-4aa**

(*R*,*R*)-3aa (208.0 mg, 0.66 mmol, $ee_{(R,R)}$ = 94%) was dissolved in chloroform (15 mL) and *m*-chloroperbenzoic acid (MCPBA, 212.5 mg, 0.86 mmol, 1.3 equiv) was added. The reaction was stirred for 24 h in the darkness. Afterwards the reaction mixture was diluted with chloroform (10 mL) and the organic layer was washed with aq. $NaHCO_3$ (~10%, 1 x 10 mL) and brine (1 x 10 mL). The organic phase was dried over Na_2SO_4, filtrated and the solvent removed. Column chromatography of the crude product (PE:EtOAc = 9:1 → 4:1) resulted in **(*R*,*R*)-4aa** (200 mg, 0.61 mmol, 92%) as a colorless solid.

$C_{19}H_{23}NO_4$, MW: 329.39 g mol^{-1}. **Mp:** 59.9-62.0 °C. **$[\alpha]_D^{20}$:** +18.3 (c = 0.07, CH_2Cl_2). **^{1}H NMR (300 MHz, $CDCl_3$, 21 °C):** δ = 7.57-7.54 (*m*, 2H, arom. *H*), 7.46-7.39 (*m*, 3H, arom. *H*), 4.35-4.18 (*m*, 2H, CH_2O), 2.99-2.91 (*m*, 1H, CH_2), 2.81-2.75 (*m*, 1H, C*H*), 2.71-2.57 (*m*, 1H, CH_2), 2.29-2.13 (*m*, 1H, CH_2), 1.99-1.90 (*m*, 1H, CH_2), 1.79-1.64 (*m*, 1H, CH_2), 1.46 (*s*, 9H, CH_3), 1.44-1.38 (*m*, 1H, CH_2). **^{13}C NMR (75 MHz, $CDCl_3$, 21 °C):** δ = 172.6, 165.2, 132.8, 129.5, 129.4, 129.2, 126.1, 116.4, 85.5, 68.7, 61.4, 41.0, 38.2, 30.0, 28.2, 27.5. **IR (solid):** ν = 2979, 2937, 2324, 1729, 1477, 1449, 1394, 1369, 1284, 1242, 1206, 1148, 1076, 1031. **MS (ESI) *m*/*z*:** 352.15 ([M+Na]$^+$, 100%), 295.09 ([M+Na – *t*Bu]$^+$, 23%), 273.11 ([M+H – *t*Bu]$^+$, 59%). **HRMS (ESI) *m*/*z*:** Calc. for [M+Na]$^+$: 352.1519. Found: 352.1525.

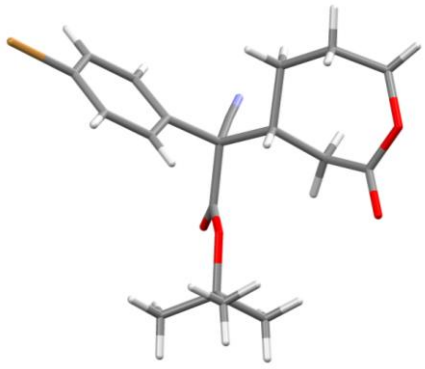
(*R*)-*tert*-Butyl-2-(4-bromophenyl)-2-cyano-2-((*R*)-2-oxooxepan-4-yl)-acetate (4ia)



(*R*,*R*)-3ia (*R*,*R*)-4ia

(*R*,*R*)-3ia (49.6 mg, 0.13 mmol, $ee_{(R,R)}$ = 90%) was dissolved in chloroform (1.5 mL) and *m*-chloroperbenzoic acid (MCPBA, 28.4 mg, 0.17 mmol, 1.3 equiv) was added. The reaction was stirred for 48 h in the darkness. Afterwards the reaction mixture was diluted with chloroform (10 mL) and the organic layer was washed with aq. $NaHCO_3$ (~10%, 1 x 10 mL) and brine (1 x 10 mL). The organic phase was dried over Na_2SO_4, filtrated and the solvent removed. Column chromatography of the crude product (PE:EtOAc = 9:1 → 4:1) resulted in **(*R*,*R*)-4ia** (94.3 mg, 0.12 mmol, 96%) as a colorless solid.

Constitution and the absolute configuration of **(*R*,*R*)-4ia** was confirmed by X-ray crystal structure analysis. **(*R*,*R*)-4ia** crystallized in enantiomerically pure form in *n*-hexane/*i*PrOH at room temperature. CCDC 856191 contains the supplementary crystallographic data for this compound. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

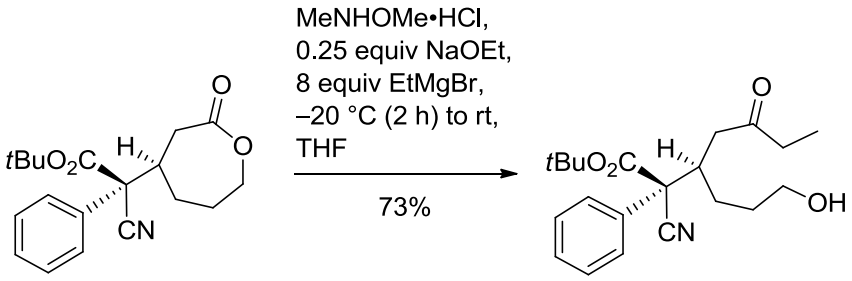


X-ray crystal structure of **(*R*,*R*)-4ia** [color code: C (grey); Br (brown); N (blue); O (red); H (white)].

$C_{19}H_{22}NO_4Br$, **MW:** 408.29 g mol^{-1}. **Mp:** 128.5-129.0 °C. **$[\alpha]_D^{20}$:** +37.9 (c = 0.25, CH_2Cl_2). **^{1}H NMR (300 MHz, $CDCl_3$, 21 °C):** δ = 7.57 (*d*, *J* = 8.8, 2H, arom. *H*), 7.45 (*d*, *J* = 8.8, 2H, arom. *H*), 4.35-4.18 (*m*, 2H, CH_2O), 2.98-2.90 (*m*, 1H, CH_2), 2.77-2.74 (*m*, 1H, C*H*), 2.68-2.64 (*m*, 1H, CH_2), 2.00-1.92 (*m*, 1H, CH_2), 1.79-1.64 (*m*, 2H, CH_2), 1.47 (*s*, 9H, CH_3), 1.30-1.22 (*m*, 1H,

CH_2). **^{13}C NMR (75 MHz, $CDCl_3$, 21 °C):** δ = 172.4, 164.8, 132.6, 131.9, 127.9, 123.6, 116.0, 86.0, 68.6, 61.0, 41.1, 38.1, 30.0, 28.2, 27.5, 26.9. **IR (solid):** ν = 2980, 2935, 1727, 1486, 1455, 1396, 1369, 1285, 1260, 1240, 1154, 1077, 1009. **MS (ESI) *m/z*:** 430.06 ($[M+Na]^+$, 100%), 425.11 ($[M+NH_4]^+$, 8%). **HRMS (ESI) *m/z*:** Calc. for $[M+Na]^+$: 430.0624. Found: 430.0631; Calc. for $[M+NH_4]^+$: 425.1070. Found: 425.1076.

(*2R*,*3R*)-*tert*-Butyl-2-cyano-3-(3-hydroxypropyl)-5-oxo-2-phenylheptanoate (5)



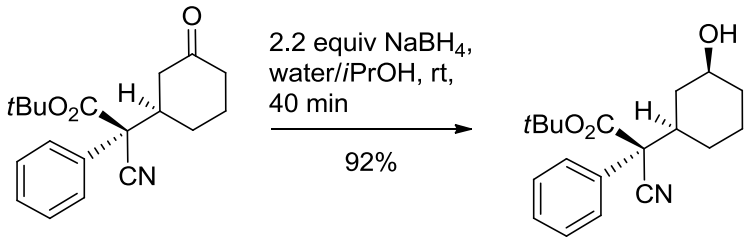
(*R*,*R*)-4aa **(*R*,*R*)-5**

(*R*,*R*)-4aa (120.7 mg, 0.37 mmol), *N*,*O*-dimethylhydroxylamine hydrochloride (42.9 mg, 0.44 mmol, 1.2 equiv), and sodium ethoxide (6.2 mg, 92 µmol, 0.25 equiv) were dissolved in dry THF (5 mL) and the solution was cooled to –20 °C. A solution of the Grignard reagent (freshly prepared from magnesium (71.3 mg, 2.93 mmol, 8 equiv), ethylbromide (218.8 µL, 2.93 mmol, 8 equiv) and THF (2.5 mL)) was added and the reaction was stirred for 2 h. Afterwards it was allowed to warm to room temperature and stirred overnight. The reaction was carefully quenched by adding water and acified with 1N HCl and stirred for additional 2 h. Water was added and the solution was extracted three times with CH_2Cl_2. The combined organic layer was dried over $MgSO_4$, filtrated and concentrated *in vacuo* to give the crude product. Column chromatography (PE:EtOAc = 9:1 → 4:1) resulted in **(*R*,*R*)-5** (95.6 mg, 0.27 mmol, 73%) as a colorless oil.

$C_{21}H_{29}NO_4$, MW: 359.46 g mol^{-1}. **$[\alpha]_D^{20}$:** –19.4 (c = 0.34, CH_2Cl_2). **^{1}H NMR (300 MHz, $CDCl_3$, 21 °C):** δ = 7.60-7.56 (*m*, 2H, arom. *H*), 7.43-7.36 (*m*, 3H, arom. *H*), 3.50-3.36 (*m*, 2H, CH_2OH), 3.34-3.24 (*m*, 1H, C*H*), 2.75-2.60 (*m*, 2H, CH_2), 2.48 (*q*, *J* = 7.5, 2H, CH_2), 1.38 (*s*, 9H, CH_3), 1.32-1.16 (*m*, 3H, CH_2), 1.09 (*t*, *J* = 7.4, 3H, CH_2). **^{13}C NMR (75 MHz, $CDCl_3$, 21 °C):** δ = 208.7, 166.1, 133.6, 129.1, 129.0, 126.4, 117.7, 84.6, 62.3, 61.0, 45.8, 38.9, 36.3, 29.8, 27.8, 27.5, 7.9. **IR (in $CDCl_3$):** ν = 3443, 2977, 2938, 1733, 1637, 1493, 1450, 1415, 1395, 1370, 1251, 1150, 1036. **MS (ESI) *m/z*:** 382.20 ($[M+Na]^+$, 100%), 360.22 ($[M+H]^+$, 5%), 326.14

([M – *t*Bu+Na+H]$^+$, 74%), 304.15 ([M – *t*Bu+2 H]$^+$, 34%), 286.14 ([M – *t*Bu – OH+H]$^+$, 17%). **HRMS (ESI) *m/z*:** Calc. for [M+Na]$^+$: 382.1989. Found: 382.1987.

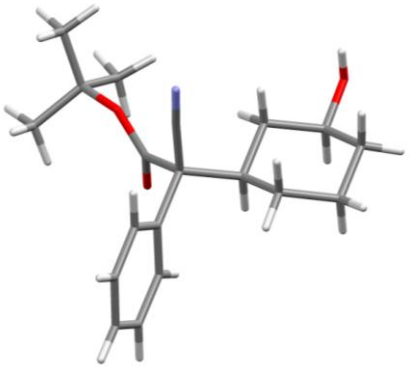
(*R*)-*tert*-Butyl-2-cyano-2-((*1R*,*3S*)-3-hydroxylcyclohexyl)-2-phenyl-acetate ((*R*,*R*,*S*)-6aa)



(*R*,*R*)-3aa **(*R*,*R*,*S*)-6aa**

According to GP5 **(*R*,*R*)-3aa** (486.5 mg, 1.55 mmol, 1 equiv, $ee_{(R,R)}$ = 94%) was treated with $NaBH_4$ (129.2 mg, 3.52 mmol, 2.2 equiv) to yield **(*R*,*R*,*S*)-6aa** (446.1 mg, 1.42 mmol, 92%) as a colorless solid.

Constitution and relative configuration of **6aa** were confirmed by X-ray crystal structure analysis. The (*R*,*R*,*S*)/(*S*,*S*,*R*)-configured diastereomer **6aa** crystallized in racemic form in *n*-hexane/*i*PrOH at room temperature. CCDC 856196 contains the supplementary crystallographic data for this compound. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

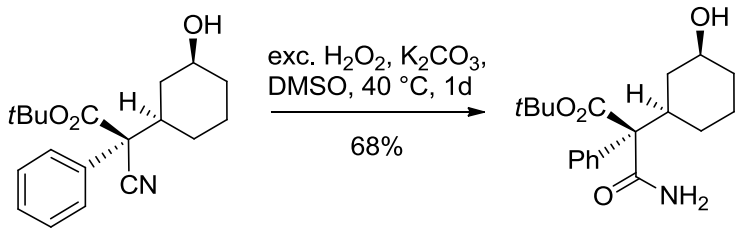


X-ray crystal structure of **6aa** [color code: C (grey); N (blue); O (red); H (white)].

$C_{19}H_{25}NO_3$, MW: 315.41 g mol^{-1}. **Mp:** 125.1-125.3 °C. **$[\alpha]_D^{20}$:** –3.7 (c = 0.47, CH_2Cl_2). **^{1}H NMR (300 MHz, $CDCl_3$, 21 °C):** δ = 7.59-7.55 (*m*, 2H, *arom. H*), 7.43-7.35 (*m*, 3H, *arom. H*), 3.75-3.65 (*m*, 1H, C*H*OH), 2.44 (*tt*, *J* = 12.0, 3.3, 1H, C*H*), 2.18-2.14 (*m*, 1H, CH_2), 2.01-1.99 (*m*, 1H, CH_2), 1.76-1.71 (*m*, 1H, CH_2), 1.42 (*s*, 9H, CH_3), 1.29-0.86 (*m*, 5H, CH_2). **^{13}C NMR (75 MHz, $CDCl_3$, 21 °C):** δ = 166.1, 133.6, 129.3, 129.0, 128.98, 128.7, 126.3, 117.3, 84.5,

70.1, 60.5, 60.4, 43.4, 38.8, 36.5, 35.2, 27.6, 26.1, 23.4, 23.2, 21.1. **IR (solid):** ν = 3346, 2937, 2860, 2246, 1734, 1449, 1370, 1250, 1149, 1047, 1032. **MS (ESI) *m*/*z*:** 338.17 ($[M+Na]^+$, 100%), 316.19 ($[M+H]^+$, 8%), 282.11 ($[m+H - t\text{Bu}]^+$, 16%), 259.17 ($[M+H - t\text{Bu}]^+$, 22%). **HRMS (ESI) *m*/*z*:** Calc. for $[M+Na]^+$: 338.1727. Found: 338.1729.

(*R*)-*tert*-Butyl-3-amino-2-((*1R*,*3S*)-3-hydroxycyclohexyl)-3-oxo-2-phenylpropanoate ((*R*,*R*,*S*)-7)

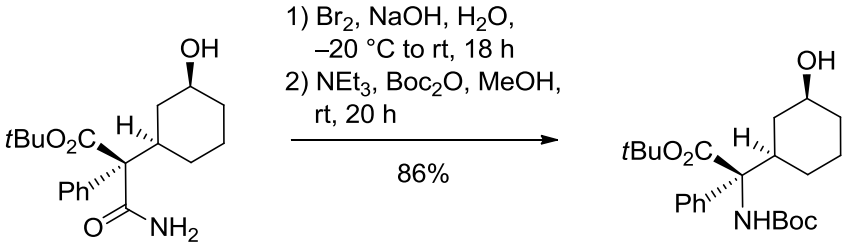


(*R*,*R*,*S*)-6aa **(*R*,*R*,*S*)-7**

(*R*,*R*,*S*)-6aa (209.4 mg, 0.66 mmol) was dissolved in DMSO (13 mL) and K_2CO_3 (45.9 mg, 0.33 mmol, 0.5 equiv) was added at RT. The mixture was heated to 45 °C under very fast stirring (fast stirring of the reaction using a large magnetic stirring bar is essential to avoid precipitation of the starting material). Aq. H_2O_2 (33.3 mL, 332.0 mmol, 500 equiv, 35%, 25 equiv/h) and aq. K_2CO_3 solution (458.8 mg, 3.32 mmol, 5 equiv, 0.25 equiv/h) were added *via* a syringe pump overnight (20 h). Afterwards the reaction mixture was cooled to RT, acidified with aq. HCl (1M), saturated with NaCl and extracted with EtOAc (4 x 25 mL). The solvent of the combined organic layer was removed and the residue dissolved in diethyl ether and extracted with brine (3 times) to remove dimethylsulfone. The combined organic phase was dried over $MgSO_4$, filtrated and concentrated *in vacuo*. Column chromatography of the crude product (CH_2Cl_2 + 2.5% MeOH → CH_2Cl_2 + 5% MeOH) resulted in **(*R*,*R*,*S*)-7** (150.3 mg, 0.45 mmol, 68 %) as a colorless solid.

$C_{19}H_{27}NO_4$, MW: 333.42 g mol^{-1}. **Mp:** 108.0-108.6 °C. **$[\alpha]_D^{20}$:** −1.8 (c = 0.11, CH_2Cl_2). **^{1}H NMR (300 MHz, $CDCl_3$, 21 °C):** δ = 7.35-7.28 (*m*, 5H, *arom. H*), 6.98 (*b*, 1H, N*H*$_2$), 5.62 (*b*, 1H, N*H*$_2$), 3.74-3.63 (*m*, 1H, C*H*OH), 2.76 (*tt*, *J* = 12.1, 2.4, 1H, C*H*), 2.06-1.94 (*m*, 1H, C*H*$_2$), 1.82-1.56 (*m*, 3H, C*H*$_2$), 1.47 (*s*, 9H, C*H*$_3$), 1.42-1.26 (*m*, 1H, C*H*$_2$), 1.11-0.86 (*m*, 3H, C*H*$_2$). **^{13}C NMR (75 MHz, $CDCl_3$, 21 °C):** δ = 172.4, 171.6, 137.3, 128.7, 128.0, 127.3, 83.0, 71.1, 67.5, 40.6, 38.4, 35.6, 27.8, 24.1. **IR (solid):** ν = 3344, 2934, 2858, 1670, 1581, 1447, 1367, 1245, 1152, 1045, 840. **MS (ESI) *m*/*z*:** 356.16 ($[M+Na]^+$, 100%), 334.20 ($[M+H]^+$, 15%), 279.14 ($[M - C_6H_5]^+$, 29%) . **HRMS (ESI) *m*/*z*:** Calc. for $[M+Na]^+$: 356.1832. Found: 356.1834.

(*S*)-*tert*-Butyl-2-((*tert*-butoxylcarbonyl)amino)-2-((*1R*,*3S*)-3-hydroxycyclohexyl)-2-phenylacetate ((*S*,*R*,*S*)-8)



(*R*,*R*,*S*)-7 **(*S*,*R*,*S*)-8**

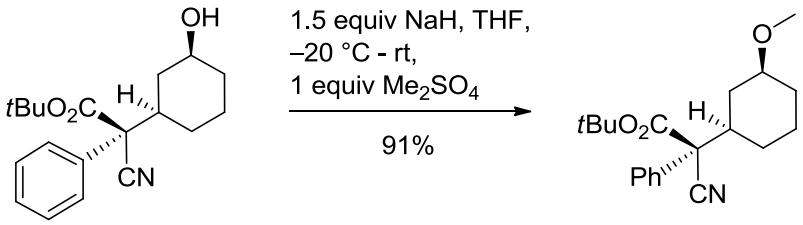
(*R*,*R*,*S*)-7 (92.1 mg, 0.28 mmol) was cooled to –20 °C and sodium hypobromite solution (freshly prepared from bromine (17.0 µL, 0.33 mmol, 1.2 equiv), NaOH (66.3 mg, 1.66 mmol, 6 equiv) and water (2 mL)) was added slowly. The reaction mixture was allowed to warm to room temperature and stirred overnight. Sodium sulfite (~45 mg) was added and the mixture was acified to pH = 2 with aq. HCl (1M) and stirred for 15 min. Afterwards the mixture was neutralized with sat. aq. $NaHCO_3$, brine was added and the mixture was extracted with CH_2Cl_2 (3 x 25 mL). The combined organic phase was dried over Na_2SO_4, filtrated and concentrated *in vacuo* to give the unprotected aminoester. **$C_{18}H_{27}NO_3$, MW:** 305.41 g mol^{-1}. **^{1}H NMR (300 MHz, $CDCl_3$, 21 °C):** δ = 7.57-7.52 (*m*, 2H, *arom. H*), 7.38-7.29 (*m*, 3H, *arom. H*), 3.73-3.62 (*m*, 1H, C*H*OH), 2.39 (*tt*, *J* = 11.8, 3.1, 1H, C*H*), 1.96-1.92 (*m*, 2H, CH_2), 1.72-1.66 (*m*, 1H, CH_2), 1.58-1.52 (*m*, 1H, CH_2), 1.45 (*s*, 9H, CH_3), 1.38-1.24 (*m*, 1H, CH_2), 1.22-1.13 (*m*, 1H, CH_2), 1.09-1.04 (*m*, 1H, CH_2), 0.98-0.84 (*m*, 1H, CH_2). **^{13}C NMR (75 MHz, $CDCl_3$, 21 °C):** δ = 170.0, 138.0, 128.4, 128.0, 127.9, 125.8, 84.2, 70.5, 44.6, 37.6, 35.5, 27.7, 25.4, 23.3.

The residue was dissolved in MeOH (1 mL), Et_3N (115 µL, 0.83 mmol, 3 equiv) and Boc_2O (301 mg, 1.38 mmol, 5 equiv) was added and the reaction was stirred overnight.[9] Solvent was removed *in vacuo*, the residue was dissolved in ethyl acetate and the solution washed once with aq. $NaHCO_3$ (5%) and twice with brine. Then it was dried over Na_2SO_4, filtrated and the solvent was removed *in vacuo* to give the crude product. Column chromatography (PE:EtOAc = 18:1 → 9:1) resulted in **(*S*,*R*,*S*)-8** (96.7 mg, 0.24 mmol, 86%) as a colorless oil.

$C_{23}H_{35}NO_5$, MW: 405.53 g mol^{-1}. **$[\alpha]_D^{20}$:** –12.3 (c = 0.17, CH_2Cl_2). **^{1}H NMR (300 MHz, $CDCl_3$, 21 °C):** δ = 7.56-7.52 (*m*, 2H, *arom. H*), 7.39-7.29 (*m*, 3H, *arom. H*), 4.56-4.45 (*m*, 1H, C*H*OH), 2.60-2.41 (*m*, 1H, C*H*), 2.10-2.06 (*m*, 1H, CH_2), 1.94-1.88 (*m*, 1H, CH_2), 1.65-1.59 (*m*, 1H, CH_2), 1.55 (*m*, 1H, CH_2), 1.43 (*s*, 9H, CH_3), 1.42 (*s*, 9H, CH_3), 1.35-1.11 (*m*, 4H, CH_2). **^{13}C**

NMR (75 MHz, $CDCl_3$, 21 °C): δ = 169.9, 152.6, 137.2, 128.5, 128.1, 125.7, 84.3, 81.9, 44.5, 32.1, 31.6, 30.7, 27.7, 26.9, 23.1. **IR (in $CDCl_3$):** ν = 2970, 2938, 2853, 2239, 1732, 1448, 1355, 1310, 1277, 1250, 1148, 1098. **MS (ESI) *m/z*:** 406.22 ($[M+H]^+$, 100%), 349.16 ($[M - t\text{Bu}+H]^+$, 20%), 272.11 ($[M - t\text{Bu} - Ph+H]^+$, 15%). **HRMS (ESI) *m/z*:** Calc. for $[M+H]^+$: 406.2588. Found: 406.2590.

(*R*)-*tert*-Butyl-2-cyano-2-((*1R*,*3S*)-3-methoxycyclohexyl)-2-phenyl-acetate



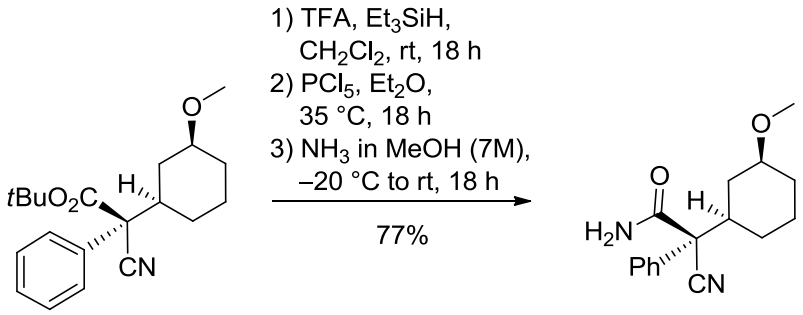
(*R*,*R*,*S*)-6aa

A solution of **(*R*,*R*,*S*)-6aa** (367.4 mg, 1.17 mmol) in dry THF (8 mL) was slowly added to a NaH (76 mg, 1.75 mmol, 1.5 equiv, 55-60% in oil) suspension in THF (2 mL) at –20 °C. The reaction was allowed to warm to room temperature and stirred for additional 30 min. Afterwards dimethylsulfate (137 µL, 1.28 mmol, 1.1 equiv) was added in one portion at –20 °C, the reaction was allowed to warm to room temperature and stirred for 30 min for complete conversion.[10] Saturated aq. NH_4Cl was added carefully, the mixture was acidified with HCl (1M) and extracted three times with Et_2O. The combined organic layer was dried over Na_2SO_4, filtrated and the solvent removed *in vacuo*. Column chromatography of the crude product (PE:EtOAc = 18:1) resulted in (*R*)-*tert*-Butyl-2-cyano-2-((*1R*,*3S*)-3-methoxycyclohexyl)-2-phenylacetate (349.2 mg, 1.06 mmol, 91%) as a colorless oil.

$C_{20}H_{27}NO_3$, MW: 329.43 g mol^{-1}. **$[\alpha]_D^{20}$:** –11.8 (c = 0.11, CH_2Cl_2). **^{1}H NMR (300 MHz, $CDCl_3$, 21 °C):** δ = 7.59-7.55 (*m*, 2H, *arom. H*), 7.43-7.35 (*m*, 3H, *arom. H*), 3.20 (*s*, 3H, $CHOCH_3$), 3.09-2.99 (*m*, 1H, $CHOCH_3$), 2.45-2.35 (*m*, 1H, C*H*), 2.12-2.07 (*m*, 1H, CH_2), 1.93-1.77 (*m*, 3H, CH_2), 1.55-0.97 (*m*, 4H, CH_2), 1.42 (*s*, 9H, CH_3). **^{13}C NMR (75 MHz, $CDCl_3$, 21 °C):** δ = 153.0, 139.7, 128.9 127.8, 125.8, 122.1, 82.1, 75.5, 46.8, 45.9, 33.6, 31.3, 27.8, 27.6, 27.4, 26.9, 24.8, 23.1. **IR (oil):** ν = 2940, 2863, 2239, 1733, 1601, 1494, 1453, 1393, 1368, 1316, 1276, 1251, 1154, 1089, 1036, 982. **MS (ESI) *m/z*:** 352.19 ($[M+Na]^+$, 100%), 338.17 ([M –

CH_3+Na+H]$^+$, 20%), 282.11 ([M – COO*t*Bu]$^+$, 9%). **HRMS (ESI) *m/z*:** Calc. for [M+Na]$^+$: 352.1883. Found: 352.1873.

(*R*)-2-cyano-2-((*1R*,*3S*)-3-methoxycyclohexyl)-2-phenylacetamide ((*R*,*R*,*S*)-9)



(*R*,*R*,*S*)-9

1) Hydrolysis of the ester:[11] To a solution of (*R*)-*tert*-Butyl-2-cyano-2-((*1R*,*3S*)-3-methoxycyclohexyl)-2-phenylacetate (105.9 mg, 0.32 mmol) in dry CH_2Cl_2 (1 mL) was added trifluoroacetic acid (476 µL, 4.18 mmol, 13 equiv) and triethylsilane (130 µL, 0.80 mmol, 2.5 equiv) at room temperature and the reaction mixture was stirred overnight. The solvent was removed *in vacuo* and *n*-pentane (~5 mL) was added to precipitate the acid, which was isolated by decantation of the residual liquid and dried in high vacuum.

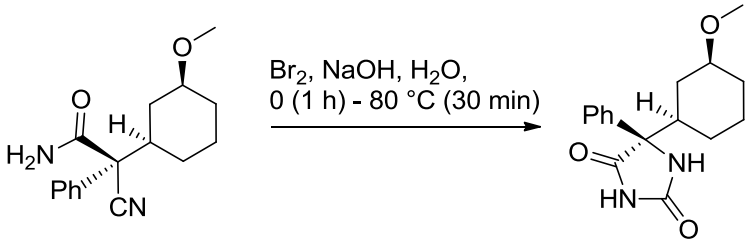
2) Formation of the acid chloride:[12] To the acid was added dry Et_2O (4 mL) and PCl_5 (72 mg, 0.34 mmol, 1.05 equiv). The mixture was stirred overnight at room temperature.

3) Formation of the amide:[12] The acid chloride solution was slowly added to a NH_3 solution in MeOH (7M, 4 mL) at –20 °C. After 1 h the reaction was warmed to room temperature and stirred overnight. The solvent was removed, water was added and the mixture was washed three times with Et_2O. The combined organic phase was dried over Na_2SO_4, filtrated and the solvent was removed *in vacuo* to give the crude product. Column chromatography (PE:EtOAc = 2:1) resulted in **(*R*,*R*,*S*)-9** (67.5 mg, 0.25 mmol, 77%) as a colorless solid.

$C_{16}H_{20}N_2O_2$, MW: 272.34 g mol^{-1}. **Mp:** 111.9-112.4 °C. **$[\alpha]_D^{20}$:** –19.2 (c = 0.05, CH_2Cl_2). **^{1}H NMR (300 MHz, $CDCl_3$, 21 °C):** δ = 7.64-7.60 (*m*, 2H, *arom. H*), 7.43-7.36 (*m*, 3H, *arom. H*), 6.32 (*b*, 1H, NH_2), 5.72 (*b*, 1H, NH_2), 3.21 (*s*, 3H, CHOCH_3), 3.09-2.99 (*m*, 1H, C*H*OCH$_3$), 2.58-2.49 (*m*, 1H, C*H*), 2.13-2.08 (*m*, 1H, CH_2), 1.92-1.88 (*m*, 2H, CH_2), 1.55-1.50 (*m*, 1H, CH_2), 1.44-1.26 (*m*, 2H, CH_2), 1.17-0.94 (*m*, 2H, CH_2). **^{13}C NMR (75 MHz, $CDCl_3$, 21 °C):** δ =

167.9, 133.4, 129.1, 128.9, 126.3, 119.0, 78.7, 59.6, 55.6, 43.0, 33.3, 31.1, 28.9, 23.2. **IR (in $CDCl_3$):** *v* =3336, 3193, 2938, 2826, 2242, 1693, 1607, 1494, 1449, 1352, 1277, 1198 1147, 1089, 1036, 992. **MS (ESI) *m/z*:** 295.14 ($[M+Na]^+$, 100%), 273.16 ($[M+H]^+$, 2%), 241.13 ($[M - OCH_3]^+$, 13%), 160.07 ([M – 3-methoxycyclohexyl+H]$^+$, 12%). **HRMS (ESI) *m/z*:** Calc. for $[M+Na]^+$: 295.1417. Found: 295.1415.

(*R*)-5-((*1R*,*3S*)-3-methoxycyclohexyl)-5-phenylimidazolidine-2,4-dione ((*R*,*R*,*S*)-10)



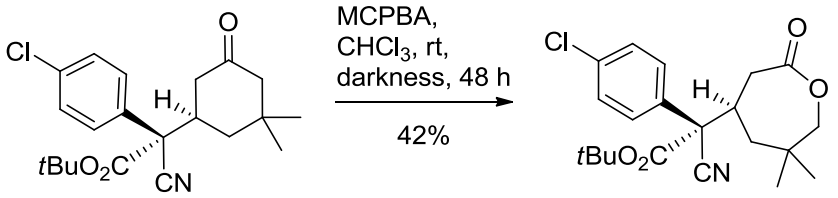
(*R*,*R*,*S*)-9 (*R*,*R*,*S*)-10

(*R*,*R*,*S*)-9 (33.3 mg, 0.12 mmol) was cooled to 0 °C and sodium hypobromite solution (freshly prepared from bromine (3.6 µL, 0.07 mmol, 0.57 equiv), NaOH (26.4 mg, 0.66 mmol, 5.4 equiv) and water (0.5 mL)) was added and the reaction mixture was stirred for 1 h. Afterwards the reaction was heated to 80 °C for 30 min.[12] Then the mixture was cooled to room temperature, water was added and the mixture was acidified with HCl (1M). The aqueous layer was extracted three times with CH_2Cl_2 (25 mL), the combined organic phase was dried over Na_2SO_4, filtrated and the solvent was removed *in vacuo*. Crystallization of the crude hydantoin from EtOAc resulted in **(*R*,*R*,*S*)-10** (30.0 mg, 0.10 mmol, 85%) as a colourless solid.

$C_{16}H_{20}N_2O_2$, **MW:** 288.34 g mol^{-1}. **Mp:** decomposition >200 °C. **$[\alpha]_D^{20}$:** +14.3 (c = 0.30, MeOH). **^{1}H NMR (300 MHz, MeOD-D_4, 21 °C):** δ = 7.59-7.55 (*m*, 2H, *arom. H*), 7.43-7.33 (*m*, 3H, *arom. H*), 3.36 (*s*, 3H, CHOCH_3), 3.29-3.22 (*m*, 1H, C*H*OCH$_3$), 2.33 (*tt*, *J* = 12.3, 3.0, 1H, C*H*), 2.11-1.98 (*m*, 2H, CH_2), 1.81-1.71 (*m*, 1H, CH_2), 1.23-1.13 (*m*, 3H, CH_2), 1.09-0.83 (*m*, 2H, CH_2). **^{13}C NMR (75 MHz, MeOD-D_4, 21 °C):** δ = 178.1, 159.4, 139.1, 129.7, 129.2, 126.6, 80.4, 73.0, 56.1, 45.1, 34.0, 32.7, 26.6, 24.4. **IR (in MeOD-D_4):** *v* = 3220, 3058, 2938, 2851, 2358, 1767, 1716, 1495, 1448, 1260, 1187, 1152, 1083. **MS (ESI) *m/z*:** 311.14 ($[M+Na]^+$, 22%), 289.15 ($[M+H]^+$, 100%), 257.13 ($[M - OCH_3]^+$, 19%), 175.05 ([M – 3-methoxycyclohexyl]$^+$, 14%). **HRMS (ESI) *m/z*:** Calc. for $[M+H]^+$: 289.1547. Found: 189.1550.

Derivatization of Enantioenriched Michael-Addition Products (*S*,*R*)-3 from FIP Catalysis

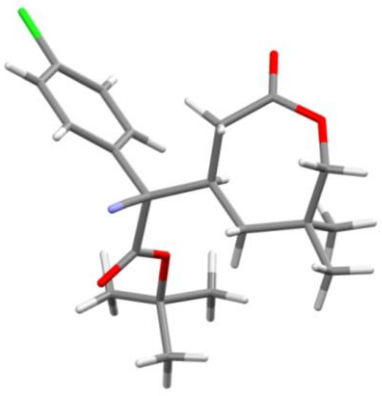
(*S*)-*tert*-Butyl-2-(4-chlorophenyl)-2-cyano-2-((*R*)-6,6-diemthyl-2-oxooxepan-4-yl)acetate (4hd)



(*S*,*R*)-3hd **(*S*,*R*)-4hd**

(*S*,*R*)-3hd (28.5 mg, 76 µmol, $ee_{(S,R)}$ = 94%) was dissolved in chloroform (1.5 mL) and *m*-chloroperbenzoic acid (MCPBA, 17.1 mg, 99 µmol, 1.3 equiv) was added. The reaction was stirred for 48 h at 45 °C in the darkness. Afterwards the reaction mixture was diluted with chloroform (10 mL) and the organic layer was washed with aq. $NaHCO_3$ (~10%, 1 x 10 mL) and brine (1 x 10 mL). The organic phase was dried over Na_2SO_4, filtrated and the solvent removed. Column chromatography of the crude product (PE:EtOAc = 9:1 → 4:1) resulted in **(*S*,*R*)-4hd** (12.6 mg, 32 µmol, 42%) as a colorless solid.

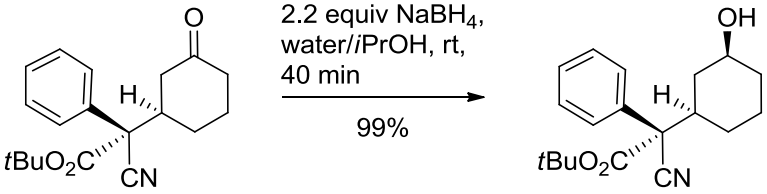
Constitution and relative configuration of **4hd** were confirmed by X-ray crystal structure analysis. The (*S*,*R*)/(*R*,*S*)-configured diastereomer **4hd** crystallized in racemic form in *n*-hexane/*i*PrOH at room temperature. CCDC 856193 contains the supplementary crystallographic data for this compound. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.



X-ray crystal structure of **4hd** [color code: C (grey); Cl (green); N (blue); O (red); H (white)].

$C_{21}H_{26}NO_4Cl$, MW: 391.89 g mol^{-1}. **Mp:** 132.0-132.6 °C. **$[\alpha]_D^{20}$:** +34.9 (c = 0.27, CH_2Cl_2). **^{1}H NMR (300 MHz, $CDCl_3$, 21 °C):** δ = 7.55 (*d*, *J* = 8.7, 2H, arom. *H*), 7.44 (*d*, *J* = 8.8, 2H, arom. *H*), 4.13 (*d*, *J* = 13.0, 1H, CH_2O), 3.83 (*d*, *J* = 13.0, 1H, CH_2O), 2.90-2.82 (*m*, 1H, C*H*), 2.56-2.48 (*m*, 1H, CH_2), 2.23-2.28 (*m*, 1H, CH_2), 1.80-1.58 (*m*, 1H, CH_2), 1.41 (*s*, 9H, CH_3), 1.28-1.16 (*m*, 1H, CH_2), 1.13 (*s*, 3H, CH_2), 1.03 (*s*, 3H, CH_2). **^{13}C NMR (75 MHz, $CDCl_3$, 21 °C):** δ = 172.5, 165.0, 135.8, 131.1, 129.8, 127.9, 116.2, 85.5, 60.4, 45.6, 37.6, 35.2, 34.4, 28.2, 27.5, 22.1. **IR (solid):** *v* = 2947, 2322, 1476, 1447, 1394, 1369, 1280, 1248, 1201, 1148, 1076, 1031. **MS (ESI) *m*/*z*:** 414.15 ([M+Na]$^+$, 100%), 357.07 ([M+Na – *t*Bu]$^+$, 15%), 335.08 ([M+H – *t*Bu]$^+$, 485). **HRMS (ESI) *m*/*z*:** Calc. for [M+Na]$^+$: 414.1448. Found: 414.1450.

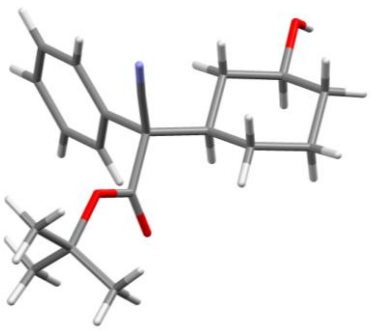
(*S*)-*tert*-Butyl-2-cyano-2-((*1R*,*3S*)-3-hydroxylcyclohexyl)-2-phenyl-acetate ((*S*,*R*,*S*)-6aa)



(*S*,*R*)-3aa **(*S*,*R*,*S*)-6aa**

According to GP5 **(*S*,*R*)-3aa** (554.3 mg, 1.77 mmol, 1 equiv, $ee_{(S,R)}$ = 89%) was treated with $NaBH_4$ (147.2 mg, 3.89 mmol, 2.2 equiv) to yield **(*S*,*R*,*S*)-6aa** (557.0 mg, 1.77 mmol, 99%) as a colorless solid.

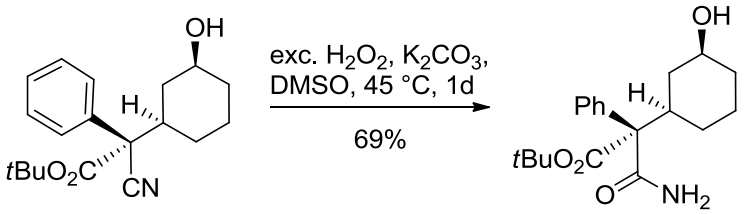
Constitution and the absolute configuration of **(*S*,*R*,*S*)-6aa** was confirmed by X-ray crystal structure analysis. **(*S*,*R*,*S*)-6aa** crystallized in enantiomerically pure form in *n*-hexane/*i*PrOH at room temperature. CCDC 856197 contains the supplementary crystallographic data for this compound. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif.



X-ray crystal structure of **(*S*,*R*,*S*)-6aa** [color code: C (grey); N (blue); O (red); H (white)].

$C_{19}H_{25}NO_3$, MW: 315.41 g mol^{-1}. **Mp:** 123.5-124.2 °C. **$[\alpha]_D^{20}$:** –104.2 (c = 0.38, CH_2Cl_2). **^{1}H NMR (300 MHz, $CDCl_3$, 21 °C):** δ = 7.62-7.55 (*m*, 2H, *arom. H*), 7.43-7.34 (*m*, 3H, *arom. H*), 3.54-3.44 (*m*, 1H, C*H*OH), 2.47-2.37 (*m*, 1H, C*H*), 2.02-1.97 (*m*, 1H, CH_2), 1.94-1.87 (*m*, 1H, CH_2), 1.85-1.82 (*m*, 1H, CH_2), 1.48-1.36 (*m*, 2H, CH_2), 1.42 (*s*, 9H, CH_3), 1.27-1.01 (*m*, 3H, CH_2). **^{13}C NMR (125 MHz, $CDCl_3$, 21 °C):** δ = 166.2, 133.3, 129.0, 128.7, 126.3, 117.2, 84.4, 70.3, 60.5, 43.5, 36.5, 35.1, 29.7, 28.5, 27.6, 23.4. **IR (solid):** ν = 3346, 2937, 2860, 2246, 1734, 1449, 1370, 1250, 1149, 1047, 1032. **MS (ESI) *m*/*z*:** 338.17 ([M+Na]$^+$, 100%), 316.19 ([M+H]$^+$, 8%), 282.11 ([m+H – *t*Bu]$^+$, 16%), 259.17 ([M+H – *t*Bu]$^+$, 22%). **HRMS (ESI) *m*/*z*:** Calc. for [M+Na]$^+$: 338.1727. Found: 338.1729.

(*S*)-*tert*-Butyl-3-amino-2-((*1R*,*3S*)-3-hydroxycyclohexyl)-3-oxo-2-phenylpropanoate ((*S*,*R*,*S*)-7)

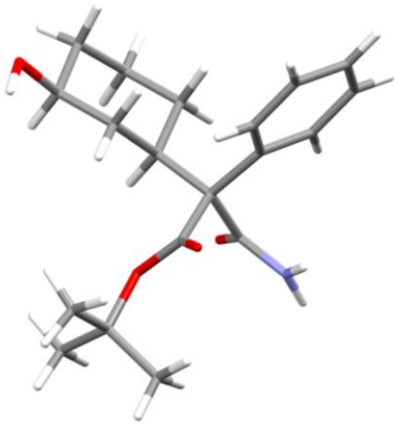


(*S*,*R*,*S*)-6aa **(*S*,*R*,*S*)-7**

(*S*,*R*,*S*)-6aa (436.1 mg, 1.38 mmol) was dissolved in DMSO (28 mL) and K_2CO_3 (95.4 mg, 0.69 mmol, 0.5 equiv) was added at RT. The mixture was heated to 45 °C under very fast stirring (fast stirring with a large magnetic stirring bar is essential to avoid precipitation of the starting material). Aq. H_2O_2 (70 mL, 691 mmol, 500 equiv, 35%, 25 equiv/h) and aq. K_2CO_3 (955.5 mg, 5 equiv, 0.25 equiv/h) were added *via* a syringe pump overnight (20 h). Afterwards the reaction mixture was cooled to RT, acidified with aq. HCl (1M), saturated with NaCl and extracted with EtOAc (4x25 mL). The solvent of the combined organic layer was removed, the residue dissolved in diethyl ether and washed with brine (3 times) to remove dimethylsulfone. The combined organic phase was dried over $MgSO_4$, filtrated and concentrated *in vacuo*. Column chromatography of the crude product (CH_2Cl_2 + 2.5% MeOH → CH_2Cl_2 + 5% MeOH) resulted in **(*S*,*R*,*S*)-7** (315.9 mg, 0.95 mmol, 69%) as a colorless solid.

Constitution and the absolute configuration of **(*S*,*R*,*S*)-7** was confirmed by X-ray crystal structure analysis. **(*S*,*R*,*S*)-7** crystallized in enantiomerically pure form in CH_2Cl_2 at –28 °C. CCDC 916148 contains the supplementary crystallographic data for this compound. These data

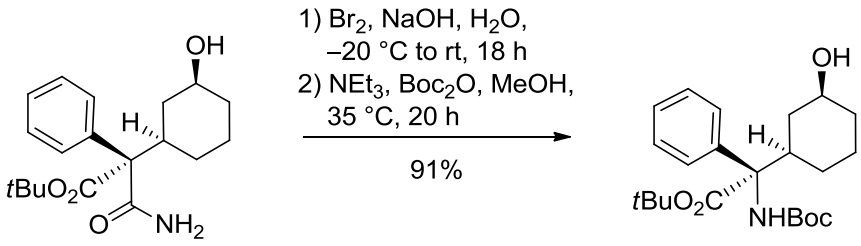
can be obtained free of charge from the Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif.



X-ray crystal structure of **(*S*,*R*,*S*)-7** [color code: C (grey); N (blue); O (red); H (white)].

$C_{19}H_{27}NO_4$, MW: 333.42 g mol^{-1}. **Mp:** 69.6-69.9 °C. **$[\alpha]_D^{20}$:** –5.7 (c = 0.12, CH_2Cl_2). **^{1}H NMR (300 MHz, $CDCl_3$, 21 °C):** δ = 7.35-7.26 (*m*, 5H, *arom. H*), 7.00 (*b*, 1H, NH_2), 5.66 (*b*, 1H, NH_2), 3.74-3.64 (*m*, 1H, C*H*OH), 2.74 (*tt*, *J* = 12.0, 2.3, 1H, C*H*), 2.07-1.95 (*m*, 2H, CH_2), 1.79-1.54 (*m*, 2H, CH_2), 1.47 (*s*, 9H, CH_3), 1.43-1.36 (*m*, 1H, CH_2), 1.11-0.98 (*m*, 2H, CH_2), 0.97-0.83 (*m*, 1H, CH_2). **^{13}C NMR (75 MHz, $CDCl_3$, 21 °C):** δ = 172.4, 171.5, 137.4, 128.7, 128.0, 127.3, 83.0, 71.0, 67.5, 40.7, 38.4, 35.6, 27.8, 24.1. **IR (solid):** ν = 3344, 2934, 2858, 1670, 1581, 1447, 1367, 1245, 1152, 1045, 840. **MS (ESI) *m*/*z*:** 356.16 ([M+Na]$^+$, 100%), 334.20 ([M+H]$^+$, 15%), 279.14 ([M – C_6H_5]$^+$, 29%) . **HRMS (ESI) *m*/*z*:** Calc. for [M+Na]$^+$: 356.1832. Found: 356.1834.

(*R*)-*tert*-Butyl-2-((*tert*-butoxylcarbonyl)amino)-2-((*1R*,*3S*)-3-hydroxycyclohexyl)-2-phenylacetate ((*R*,*R*,*S*)-8)



(*S*,*R*,*S*)-7 **(*R*,*R*,*S*)-8**

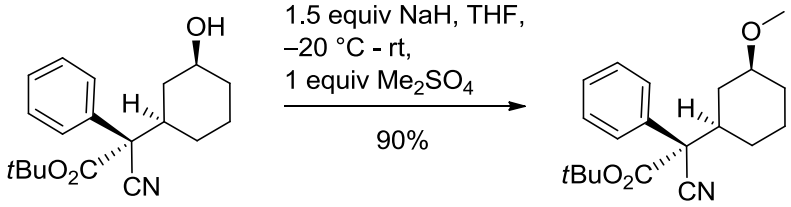
(*S*,*R*,*S*)-7 (88.3 mg, 0.27 mmol) was cooled to –20 °C and sodium hypobromite solution (freshly prepared from bromine (16.3 µL, 0.32 mmol, 1.2 equiv), NaOH (63.4 mg, 1.59 mmol, 6 equiv)

and water (2 mL)) was added slowly. The reaction mixture was allowed to warm to room temperature and stirred overnight. Sodium sulfite (~40 mg) was added and the mixture was acidified to pH = 2 with HCl (1M) and stirred for 15 min. Afterwards it was neutralized with sat. $NaHCO_3$, brine was added and the mixture was extracted with CH_2Cl_2 (3 x 25 mL). The combined organic phase was dried over Na_2SO_4, filtrated and concentrated *in vacuo* to give the unprotected aminoester. **$C_{18}H_{27}NO_3$, MW:** 305.41 g mol^{-1}. **^{1}H NMR (300 MHz, $CDCl_3$, 21 °C):** δ = 7.57-7.53 (*m*, 2H, *arom. H*), 7.39-7.30 (*m*, 3H, *arom. H*), 3.53-3.43 (*m*, 1H, C*H*OH), 2.37 (*tt*, *J* = 11.7, 2.9, 1H, C*H*), 1.99-1.85 (*m*, 2H, CH_2), 1.65-1.57 (*m*, 1H, CH_2), 1.44 (*s*, 9H, CH_3), 1.39-1.33 (*m*, 1H, CH_2), 1.31-1.08 (*m*, 3H, CH_2), 1.04-0.92 (*m*, 1H, CH_2). **^{13}C NMR (75 MHz, $CDCl_3$, 21 °C):** δ = 170.1, 137.7, 128.4, 128.1, 128.0, 125.9, 84.1, 70.5, 44.7, 35.9, 35.2, 27.7, 27.0, 26.9, 23.4.

The residue was dissolved in MeOH (1 mL), Et_3N (110 µL, 0.79 mmol, 3 equiv) and Boc_2O (289 mg, 1.32 mmol, 5 equiv) were added and the reaction was stirred overnight.[9] The solvent was removed *in vacuo*, the residue was dissolved in ethyl acetate and washed once with aq. $NaHCO_3$ (5%) and twice with brine. Then it was dried over Na_2SO_4, filtrated and the solvent was removed *in vacuo*. Column chromatography of the crude product (PE:EtOAc = 18:1 → 9:1) resulted in **(*R*,*R*,*S*)-8** (97.6 mg, 0.25 mmol) as a colorless oil.

$C_{23}H_{35}NO_5$, MW: 405.53 g mol^{-1}. **$[\alpha]_D^{20}$:** –19.6 (c = 0.23, CH_2Cl_2). **^{1}H NMR (300 MHz, $CDCl_3$, 21 °C):** δ = 7.56-7.52 (*m*, 2H, *arom. H*), 7.39-7.29 (*m*, 3H, *arom. H*), 4.44-4.34 (*m*, 1H, C*H*OH), 2.51-2.38 (*m*, 1H, C*H*), 2.10-2.06 (*m*, 1H, CH_2), 1.94-1.88 (*m*, 1H, CH_2), 1.65-1.59 (*m*, 1H, CH_2), 1.55 (*m*, 1H, CH_2), 1.44 (*s*, 9H, CH_3), 1.41 (*s*, 9H, CH_3), 1.35-1.10 (*m*, 4H, CH_2). **^{13}C NMR (75 MHz, $CDCl_3$, 21 °C):** δ = 170.0, 152.8, 137.4, 128.5, 128.1, 125.8, 84.2, 81.8, 44.5, 32.0, 31.5, 30.9, 27.73, 27.68, 26.9, 23.1. **IR (in $CDCl_3$):** ν = 2979, 2938, 2865, 2238, 1732, 1449, 1394, 1369, 1317, 1277, 1251, 1148, 1098, 984. **MS (ESI) *m/z*:** 406.20 ([M+H]$^+$, 100%), 349.15 ([M – *t*Bu+H]$^+$, 25%), 272.11 ([M – *t*Bu – Ph+H]$^+$, 19%). **HRMS (ESI) *m/z*:** Calc. for [M+H]$^+$: 406.2588. Found: 406.2585.

(*S*)-*tert*-Butyl-2-cyano-2-((*1R*,*3S*)-3-methoxycyclohexyl)-2-phenyl-acetate

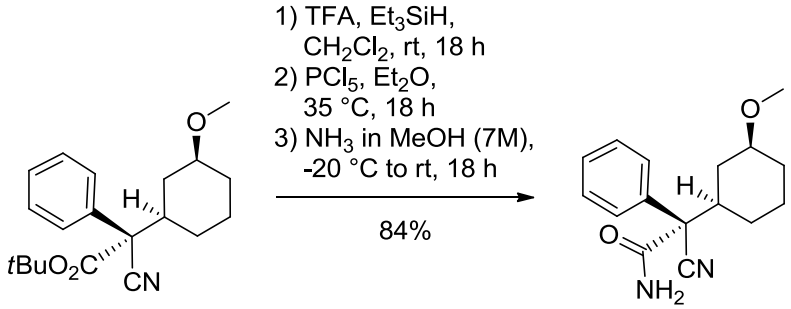


(*S*,*R*,*S*)-6aa

(*S*,*R*,*S*)-6aa (628.6 mg, 1.99 mmol) was dissolved in dry THF (15 mL) and slowly added to a NaH (130 mg, 2.99 mmol, 1.5 equiv, 55-60% in oil) suspension in THF (5 mL) at –20 °C. The reaction was allowed to warm to room temperature and stirred for additional 30 min. Afterwards dimethylsulfate (234 µL, 2.19 mmol, 1.1 equiv) was added in one portion at –20 °C, the reaction was allowed to warm to room temperature and stirred for additional 30 min for complete conversion.[10] Saturated aq. NH_4Cl was added carefully, the mixture was acidified with HCl (1M) and extracted three times with Et_2O. The combined organic layer was dried over Na_2SO_4, filtrated and the solvent removed *in vacuo* to give the crude product. Column chromatography (PE:EtOAc = 20:1) resulted in (*S*)-*tert*-butyl-2-cyano-2-((*1R*,*3S*)-3-methoxycyclohexyl)-2-phenylacetate (593.4 mg, 1.80 mmol, 90%) as a colorless solid.

$C_{20}H_{27}NO_3$, MW: 329.43 g mol^{-1}. **Mp:** 86.1-87.4 °C. **$[\alpha]_D^{20}$:** –3.8 (c = 0.40, CH_2Cl_2). **^{1}H NMR (300 MHz, $CDCl_3$, 21 °C):** δ = 7.59-7.55 (*m*, 2H, *arom. H*), 7.43-7.34 (*m*, 3H, *arom. H*), 3.20 (*s*, 3H, CHOCH_3), 3.09-2.96 (*m*, 1H, C*H*OCH$_3$), 2.45-2.35 (*m*, 1H, C*H*), 2.11-2.07 (*m*, 1H, CH_2), 1.94-1.73 (*m*, 3H, CH_2), 1.42 (*s*, 9H, CH_3), 1.38-0.98 (*m*, 4H, CH_2). **^{13}C NMR (75 MHz, $CDCl_3$, 21 °C):** δ = 166.3, 133.3, 129.0, 128.9, 126.3, 117.2, 84.4, 78.7, 60.6, 55.5, 43.5, 33.0, 31.2, 28.9, 27.6, 26.9, 23.3. **IR (in $CDCl_3$):** ν = 2978, 2938, 2863, 2823, 2237, 1736, 1493, 1450, 1394, 1370, 1252, 1153, 1093, 1037, 996. **MS (ESI) *m*/*z*:** 352.19 ([M+Na]$^+$, 14%), 338.17 ([M – CH_3+Na+H]$^+$, 100%), 282.11 ([M – COO*t*Bu]$^+$, 57%), 260.13 ([M – CH_3 – C_6H_5+Na]$^+$, 7%) . **HRMS (ESI) *m*/*z*:** Calc. for [M+Na]$^+$: 352.1883. Found: 352.1872.

(*S*)-2-Cyano-2-((1*R*,3*S*)-3-methoxycyclohexyl)-2-phenylacetamide ((*S*,*R*,*S*)-9)



(*S*,*R*,*S*)-9

1) Hydrolysis of the ester:[11] To a solution of (*S*)-*tert*-Butyl-2-cyano-2-((*1R*,*3S*)-3-methoxycyclohexyl)-2-phenylacetate (159.4 mg, 0.48 mmol) in dry CH_2Cl_2 (1 mL) was added trifluoroacetic acid (467 µL, 6.29 mmol, 13 equiv) and triethylsilane (195 µL, 1.21 mmol, 2.5 equiv) at room temperature and the reaction was stirred overnight. The solvent was removed *in vacuo* and *n*-pentane (~7 mL) was added to precipitate the acid, which was isolated by decantation of the residual liquid and dried in high vacuum.

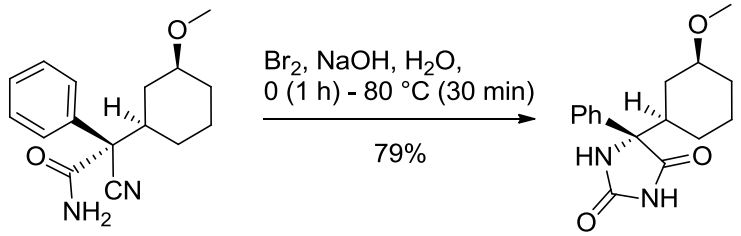
2) Formation of the acid chloride:[12] To the acid was added dry Et_2O (4 mL) and PCl_5 (108 mg, 0.51 mmol, 1.05 equiv). The mixture was stirred overnight at room temperature.

3) Formation of the amide:[12] The acid chloride solution was added slowly to a NH_3 solution in MeOH (7M, 4 mL) at –20 °C. After 1 h the reaction was warmed to room temperature and stirred overnight. The solvent was removed, water was added and the mixture was washed three times with Et_2O. The combined organic phase was dried over Na_2SO_4, filtrated and solvent removed *in vacuo* to give the crude product. Column chromatography (CH_2Cl_2 + 2.5% MeOH) resulted in **(*S*,*R*,*S*)-9** (110 mg, 0.40 mmol, 84%) as a colorless oil.

$C_{16}H_{20}N_2O_2$, MW: 272.34 g mol^{-1}. **$[\alpha]_D^{20}$:** +1.3 (c = 0.30, CH_2Cl_2). **^{1}H NMR (300 MHz, $CDCl_3$, 21 °C):** δ = 7.64-7.59 (*m*, 2H, *arom. H*), 7.44-7.34 (*m*, 3H, *arom. H*), 6.34 (*b*, 1H, NH_2), 5.88 (*b*, 1H, NH_2), 3.20 (*s*, 3H, CHOCH_3), 3.09-2.99 (*m*, 1H, C*H*OCH$_3$), 2.58-2.49 (*m*, 1H, C*H*), 2.13-2.08 (*m*, 1H, CH_2), 1.92-1.89 (*m*, 2H, CH_2), 1.55-1.51 (*m*, 1H, CH_2), 1.43-1.22 (*m*, 2H, CH_2), 1.17-0.94 (*m*, 2H, CH_2). **^{13}C NMR (75 MHz, $CDCl_3$, 21 °C):** δ = 168.0, 133.4, 129.1, 128.9, 126.3, 125.9, 119.0, 78.7, 59.6, 55.6, 43.0, 33.3, 31.1, 28.9, 23.2. **IR (in $CDCl_3$):** ν = 3331, 3192, 2937, 2861, 2826, 2241, 1692, 1607, 1493, 1449, 1350, 1278, 1198, 1147, 1088. **MS (ESI) *m*/*z*:** 295.14 ([M+Na]$^+$, 100%), 273.16 ([M+H]$^+$, 2%), 241.13 ([M – OCH$_3$]$^+$, 13%),

160.07 ([M – 3-methoxycyclohexyl+H]$^+$, 12%). **HRMS (ESI) *m/z*:** Calc. for [M+Na]$^+$: 295.1417. Found: 295.1418.

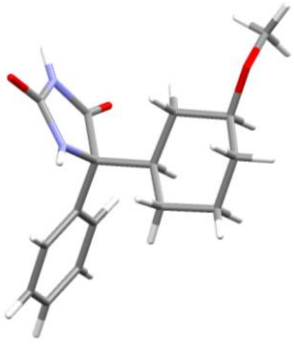
(*S*)-5-((*1R*,*3S*)-3-Methoxycyclohexyl)-5-phenylimidazolidine-2,4-dione ((*S*,*R*,*S*)-10)



(*S*,*R*,*S*)-9 **(*S*,*R*,*S*)-10**

(*S*,*R*,*S*)-9 (70.9 mg, 0.26 mmol) was cooled to 0 °C and sodium hypobromite solution (freshly prepared from bromine (7.6 µL, 0.15 mmol, 0.57 equiv), NaOH (56.2 mg, 1.40 mmol, 5.4 equiv) and water (1 mL)) were added and the reaction was stirred for 1 h. Afterwards the reaction was heated to 80 °C for 30 min.[12] Then the mixture was cooled to room temperature, water was added and the mixture was acidified with HCl (1M). The aqueous layer was extracted three times with CH_2Cl_2 (25 mL), the combined organic phase was dried over Na_2SO_4, filtrated and the solvent removed *in vacuo*. Column chromatography of the crude hydantoin (PE:EtOAc = 2:1 → 1:1) resulted in **(*S*,*R*,*S*)-10** (59.4 mg, 0.21 mmol, 79%) as a colorless solid.

Constitution and absolute configuration of **(*S*,*R*,*S*)-10** was confirmed by X-ray crystal structure analysis. **(*S*,*R*,*S*)-10** crystallized in enantiomerically pure form in MeOH/MeCN at room temperature. CCDC 884921 contains the supplementary crystallographic data for this compound. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.



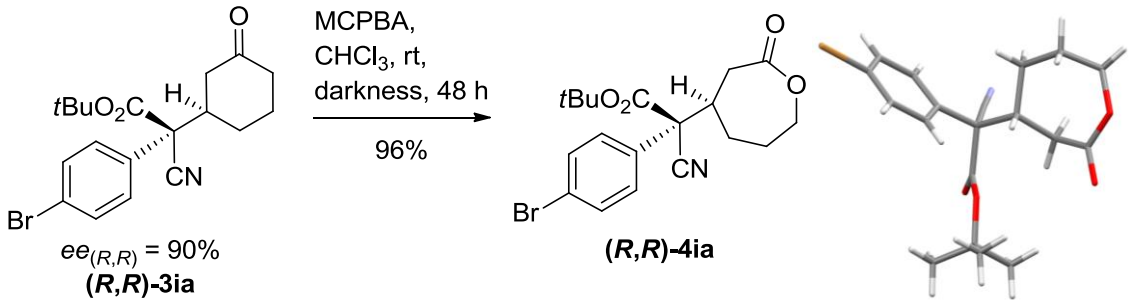
X-ray crystal structure of **(*S*,*R*,*S*)-10** [color code: C (grey); N (blue); O (red); H (white)]. Two included water molecules per unit cell are omitted for clarity.

$C_{16}H_{20}N_2O_3$, **MW:** 288.34 g mol^{-1}. **Mp:** decomposition >200 °C. **$[\alpha]_D^{20}$:** +49.3 (c = 0.28, MeOH). **^{1}H NMR (300 MHz, MeOD-D_4, 21 °C):** δ = 7.59-7.55 (*m*, 2H, *arom. H*), 7.45-7.31 (*m*, 3H, *arom. H*), 3.36 (*s*, 3H, CHOCH_3), 3.30-3.21 (*m*, 1H, C*H*OCH$_3$), 2.33 (*tt*, *J* = 12.3, 3.0, 1H, C*H*), 2.11-1.98 (*m*, 2H, CH_2), 1.78-1.72 (*m*, 1H, CH_2), 1.36-0.82 (*m*, 5H, CH_2). **^{13}C NMR (75 MHz, MeOD-D_4, 21 °C):** δ = 178.1, 159.4, 139.1, 129.7, 129.2, 126.6, 80.4, 73.0, 56.1, 45.1, 34.0, 32.7, 26.6, 24.4. **IR (in MeOD-D_4):** ν = 3227, 3065, 2938, 2860, 2357, 1769, 1716, 1495, 1448, 1398, 1359, 1262, 1187, 1152, 1084. **MS (ESI) *m/z*:** 311.14 ([M+Na]$^+$, 22%), 289.15 ([M+H]$^+$, 100%), 257.13 ([M – OCH$_3$]$^+$, 19%), 175.05 ([M – 3-methoxycyclohexyl]$^+$, 14%). **HRMS (ESI) *m/z*:** Calc. for [M+H]$^+$: 289.1547. Found: 189.1542.

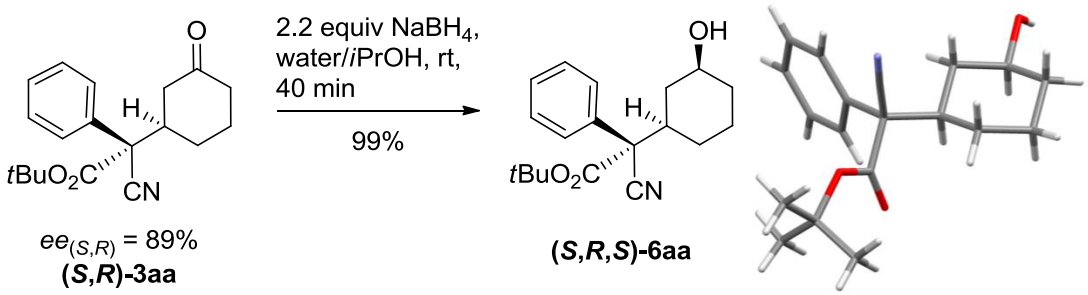
Determination of the Absolute Configuration by X-Ray Analysis and Chemical Correlation

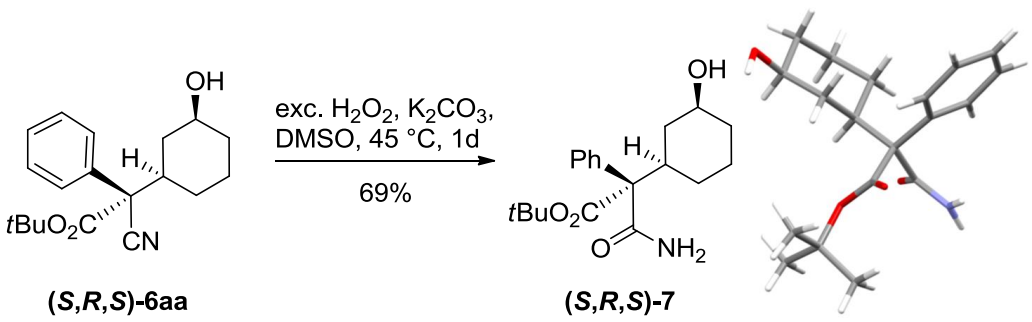
Various crystal structures could be solved by X-ray diffraction to determine the configuration of the products. The following color code is used: C (gray); N (blue); O (red); H (white), Br (brown), Cl (green). For details about the syntheses and product characterizations, see the previous chapters.

- Determination of the absolute configuration of **(*R*,*R*)-3ia** was possible from the crystal structure of **(*R*,*R*)-4ia**, which was synthesized from **(*R*,*R*)-3ia** (single diastereomer, $ee_{(R,R)}$ = 90%) and crystallized in enantiomerically pure form from *n*-hexane/*i*PrOH at room temperature.

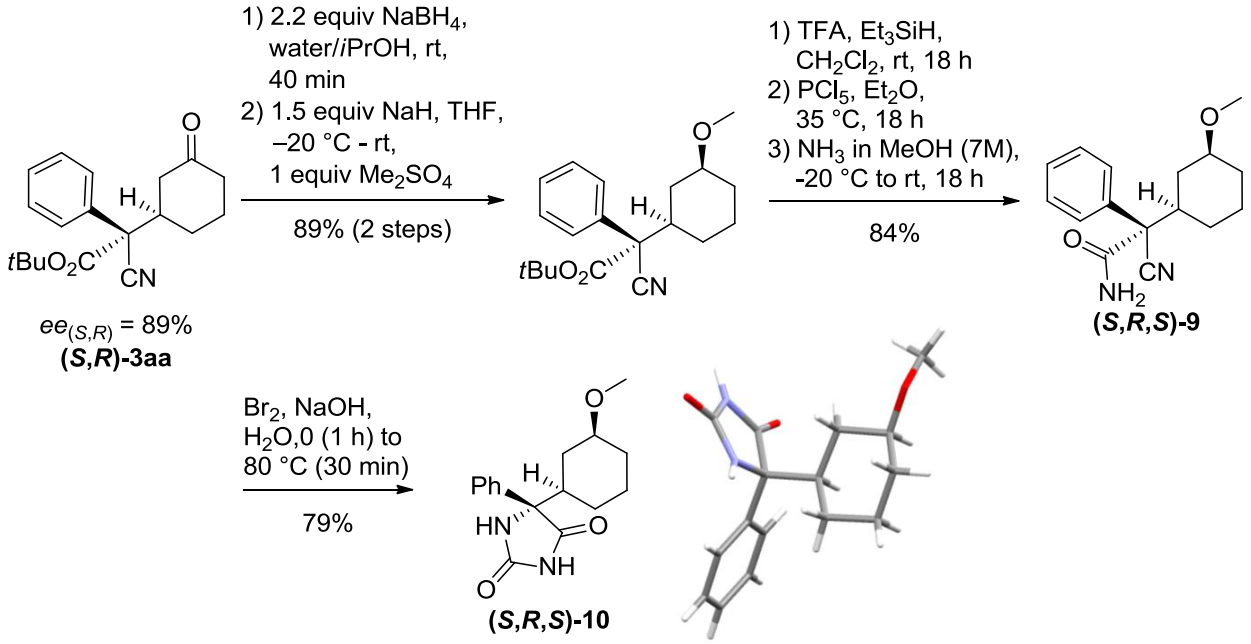


(*S*,*R*,*S*)-6aa was synthesized from **(*S*,*R*)-3aa** (single diastereomer, $ee_{(R,R)}$ = 89%) and crystallized in enantiomerically pure form in *n*-hexane/*i*PrOH at room temperature. **(*S*,*R*,*S*)-6aa** was further converted into **(*S*,*R*,*S*)-7** and crystallized in enantiomerically pure form from CH_2Cl_2 at –28 °C. For both products the absolute configuration was determined by X-ray analysis.



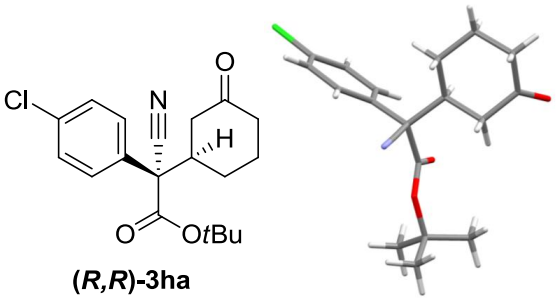


(*S*,*R*,*S*)-10 was synthesized in a six step sequence from **(*S*,*R*)-3aa** (single diastereomer, $ee_{(R,R)}$ = 89%) and crystallized in enantiomerically pure form from MeOH/MeCN at room temperature. Its absolute configuration was determined by X-ray analysis.

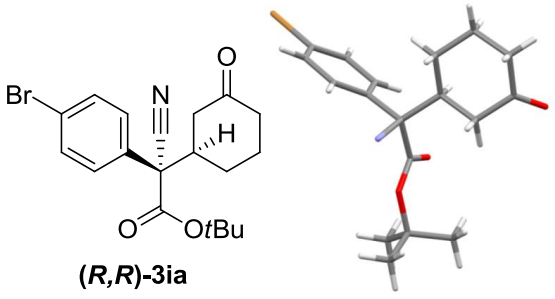


- Determination of the relative configuration was possible for the following crystal structures:

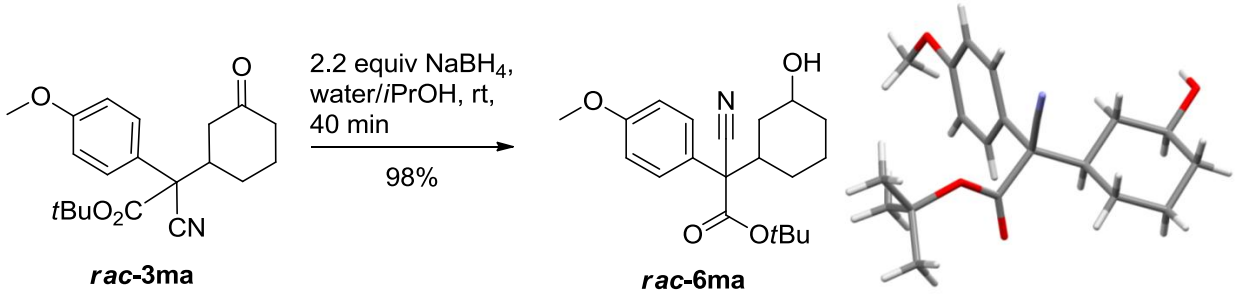
The (*R*,*R*)/(*S*,*S*)-configured diastereomer **3ha** crystallized preferentially in racemic form (from a sample with $ee_{(R,R)}$ = 99%) from *n*-hexane/*i*PrOH at room temperature.



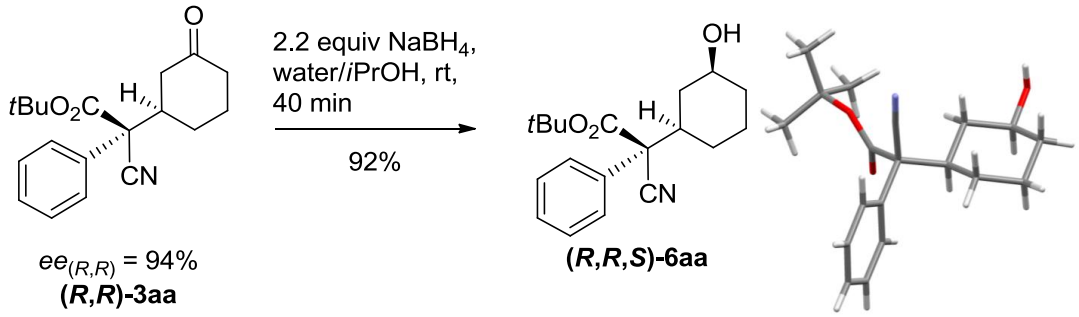
The (*R*,*R*)/(*S*,*S*)-configured diastereomer **3ia** crystallized preferentially in racemic form (from a sample with $ee_{(R,R)}$ = 90%) from diethylether at room temperature.



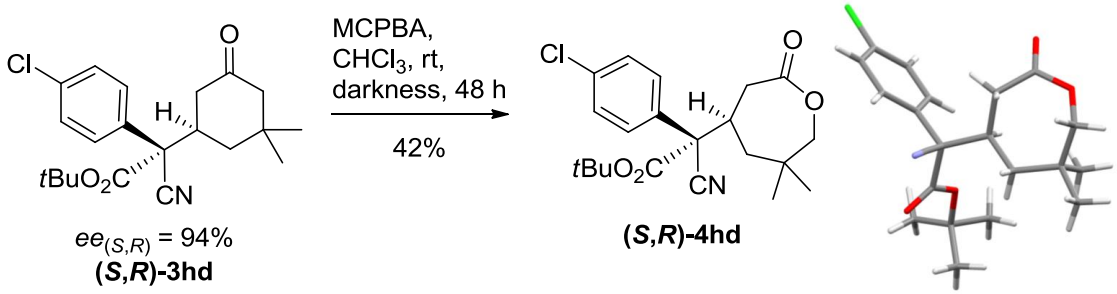
***rac*-6ma** was synthesized from ***rac*-3ma** and crystallized preferentially as the (*S*,*R*,*S*)/(*R*,*S*,*R*)-configured diastereomer (from a racemic sample with both diastereomers) from *n*-hexane/*i*PrOH at room temperature.



(*R*,*R*,*S*)-6aa was synthesized from **(*R*,*R*)-3aa** (single diastereomer, $ee_{(R,R)}$ = 94%) and crystallized preferentially in racemic form from *n*-hexane/*i*PrOH at room temperature.

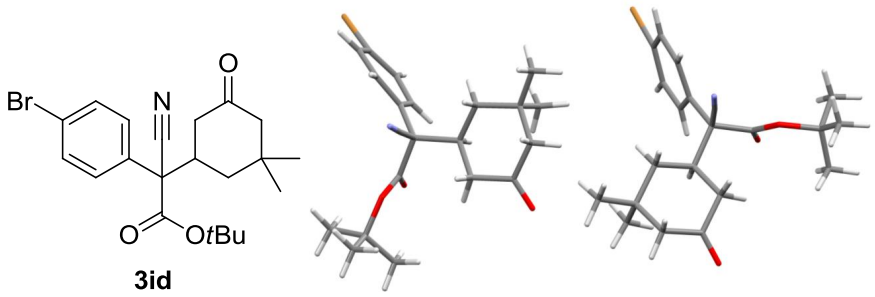


(*S*,*R*)-4hd was synthesized from **(*S*,*R*)-3hd** (single diastereomer, $ee_{(S,R)}$ = 94%) and crystallized preferentially in racemic form from *n*-hexane/*i*PrOH at room temperature.



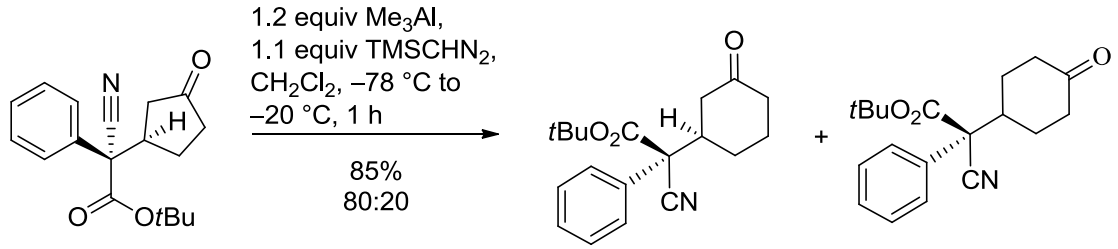
- Determination of the constitution of **3id** was possible from the following crystal structure:

3id crystallized preferentially in racemic form (from a sample with both diastereomers, $ee_{(S,R)}$ = 91% and $ee_{(R,R)}$ = 91%, $dr_{(S,R+R,S):(R,R+S,S)}$ = 82:18) in *n*-hexane/*i*PrOH at room temperature. The unit cell contains both diastereomers.



3id

Transformation of (*R*,*R*)-3ab into (*R*,*R*)-3aa and further into (*R*,*R*)-3ac by Gradual Ring Expansion



(*R*,*R*)-3ab
$ee_{(R,R)}$ = 90%
$ee_{(S,R)}$ = 52%
dr = 82:18

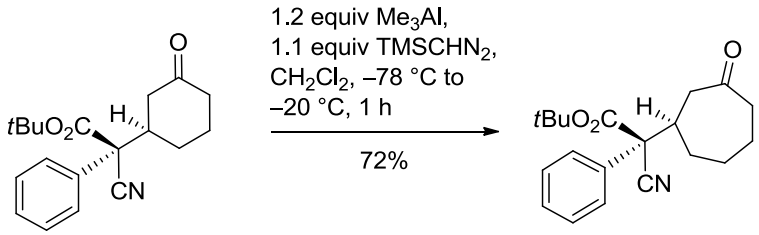
(*R*,*R*)-3aa
$ee_{(R,R)}$ = 90%
$ee_{(S,R)}$ = 56%
dr = 81:19

3aa*

To a solution of trimethylaluminum in toluene (573.2 µL, 1.15 mmol, 1.2 equiv, 2M in toluene) was added the enantioenriched ketone **(*R*,*R*)-3ab** (286.0 mg, 0.96 mmol, 1 equiv, $ee_{(R,R)}$ = 90%, $ee_{(S,R)}$ = 52%, $dr_{(R,R+S,S):(S,R+R,S)}$ = 82:18) in CH_2Cl_2 at –78 °C under nitrogen atmosphere. Trimethylsilyldiazomethane in hexane (525.5 µL, 1.05 mmol, 1.1 equiv, 2M in hexane) was added in one portion at this temperature.[13] The mixture was allowed to warm to –20 °C and stirring was continued for one hour. The reaction mixture was then poured into 1M aq. HCl solution and extracted with CH_2Cl_2. The combined organic phase was dried over Na_2SO_4, filtered and the solvent was removed in vacuo. Column chromatography of the crude product (PE:EtOAc = 9:1) resulted in **(*R*,*R*)-3aa** (204.1 mg, 0.65 mmol, 68%, $ee_{(R,R)}$ = 90%, $ee_{(S,R)}$ = 56%, $dr_{(R,R+S,S):(S,R+R,S)}$ = 81:19) as a colorless oil. As mentioned before the *ee* values of **3aa** were determined by chiral column HPLC: Chiracel OD-H, *n*-hexane/*i*-PrOH (99/1), 0.9 mL min^{-1}, detection at 210 nm, $t_{(R,R)}$ = 13.3 min, $t_{(S,S)}$ = 41.3 min, $t_{(S,R)}$ = 17.8 min, $t_{(R,S)}$ = 12.1 min.
In a second fraction the regioisomer **3aa*** (49.9 mg, 0.16 mmol, 17%) was obtained as colourless oil.

For characterization of **3aa**, see above.

Side product **3aa*: $C_{19}H_{23}NO_3$, MW:** 313.39 g mol^{-1}. **^{1}H NMR (300 MHz, $CDCl_3$, 21 °C):** δ = 7.63-7.55 (*m*, 2H, arom. *H*), 7.47-7.37 (*m*, 3H, arom. *H*), 2.83 (*tt*, *J* = 11.6, 3.7, 1H, C*H*), 2.65-2.46 (*m*, 3H, CH_2), 2.41-2.32 (*m*, 1H, CH_2), 2.30-2.17 (*m*, 2H, CH_2), 2.03-1.88 (*m*, 2H, CH_2), 1.75-1.50 (*m*, 2H, CH_2), 1.43 (*s*, 9H, CH_3). **^{13}C NMR (75 MHz, $CDCl_3$, 21 °C):** δ = 209.5, 166.0, 133.4, 129.2, 128.9, 126.1, 116.8, 84.9, 59.7, 47.8, 42.1, 40.1, 28.9, 27.6, 26.9. **IR (film):** *v* = 2978, 2939, 2247, 1733, 1716, 1449, 1370, 1250, 1148, 1073, 1035, 914. **MS (ESI) *m/z*:** 336.16 ([M+Na]$^+$, 100%). **HRMS (ESI) *m/z*:** Calc. for [M+Na]$^+$: 336.1570. Found: 336.1571.



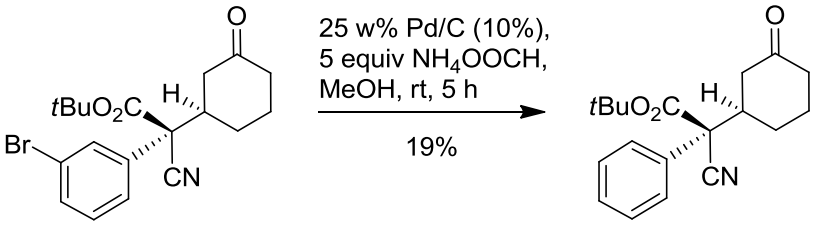
(*R*,*R*)-3aa
$ee_{(R,R)}$ = 90%
$ee_{(S,R)}$ = 56%
dr = 81:19

(*R*,*R*)-3ac
$ee_{(R,R)}$ = 88%
$ee_{(S,R)}$ = 56%
dr = 81:19

The next ring expansion to the 7-membered ring was achieved in analogy to the above described procedure. The enantioenriched ketone **(*R*,*R*)-3aa** (50.2 mg, 0.16 mmol, $ee_{(R,R)}$ = 90%, $ee_{(S,R)}$ = 56%, $dr_{(R,R+S,S):(S,R+R,S)}$ = 81:19) was treated with trimethlyaluminum (96 µL, 0.19 mmol, 1.2 equiv, 2M in toluene) and trimethylsilyldiazomethane (88 µL, 0.18 mmol, 1.1 equiv, 2M in hexane) at –78 °C. The reaction mixture was stirred again for one hour at –20 °C. Column chromatography of the crude product (PE:EtOAc = 9:1) resulted in **(*R*,*R*)-3ac** (37.6 mg, 0.11 mmol, 72%, $ee_{(R,R)}$ = 88%, $ee_{(S,R)}$ = 56%, $dr_{(R,R+S,S):(S,R+R,S)}$ = 81:19) as a colorless oil. As mentioned before the *ee* values of **3ac** were determined by chiral column HPLC: Chiracel OD-H, *n*-hexane/*i*-PrOH (99/1), 2 mL min^{-1}, detection at 210 nm, $t_{(R,R)}$ = 5.6 min, $t_{(S,S)}$ = 7.0 min, $t_{(S,R)}$ = 6.3 min, $t_{(R,S)}$ = 32.2 min.

For characterization of **3ac**, see above.

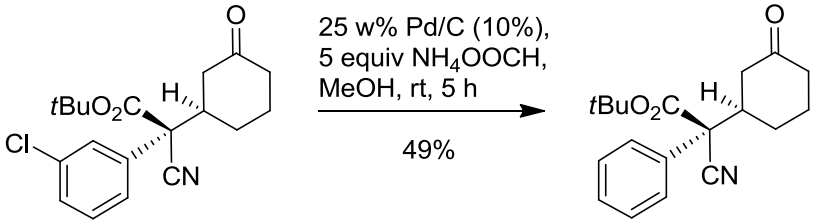
Reductive Dehalogenation of Michael-Addition Products



(*R*,*R*)-3ca
$ee_{(R,R)}$ = 78%
$ee_{(S,R)}$ = 54%
dr = 77:23

(*R*,*R*)-3aa
$ee_{(R,R)}$ = 77%
$ee_{(S,R)}$ = 54%
dr = 76:24

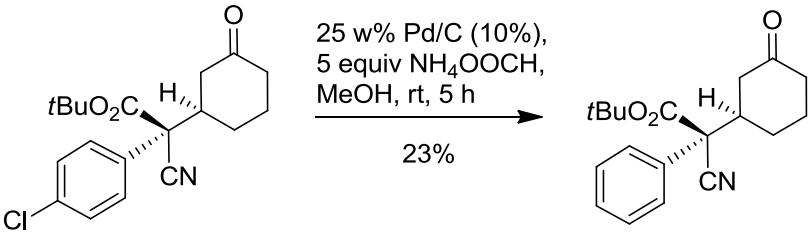
According to GP5 enantioenriched **(*R*,*R*)-3ca** (15.9 mg, 41 µmol, $ee_{(R,R)}$ = 78%, $ee_{(S,R)}$ = 54%, $dr_{(R,R+S,S):(S,R+R,S)}$ = 77:23) in MeOH was treated with ammonium formate (12.8 mg, 0.20 mmol, 5 equiv) and palladium on charcoal (10%, 4.0 mg) to yield **(*R*,*R*)-3aa** (2.4 mg, 8 µmol, 19%, $ee_{(R,R)}$ = 77%, $ee_{(S,R)}$ = 54%, $dr_{(R,R+S,S):(S,R+R,S)}$ = 76:24) as colorless oil. The *dr* and *ee* values were determined by chiral column HPLC: Chiracel OD-H, *n*-hexane/*i*-PrOH (99/1), 0.9 mL min^{-1}, detection at 210 nm. For characterization of **3aa**, see above.



(*R*,*R*)-3da
$ee_{(R,R)}$ = 87%
$ee_{(S,R)}$ = 78%
dr = 83:17

(*R*,*R*)-3aa
$ee_{(R,R)}$ = 85%
$ee_{(S,R)}$ = 75%
dr = 83:17

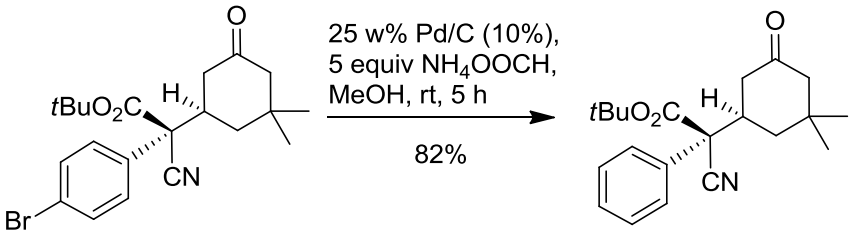
According to GP5 enantioenriched **(*R*,*R*)-3da** (20.0 mg, 57 µmol, $ee_{(R,R)}$ = 87%, $ee_{(S,R)}$ = 78%, $dr_{(R,R+S,S):(S,R+R,S)}$ = 83:17) in MeOH was treated with ammonium formate (18.1 mg, 0.29 mmol, 5 equiv) and palladium on charcoal (10%, 5.0 mg) to yield **(*R*,*R*)-3aa** (8.9 mg, 28 µmol, 49%, $ee_{(R,R)}$ = 85%, $ee_{(S,R)}$ = 75%, $dr_{(R,R+S,S):(S,R+R,S)}$ = 83:17) as colorless oil. The *dr* and *ee* values were determined by chiral column HPLC: Chiracel OD-H, *n*-hexane/*i*-PrOH (99/1), 0.9 mL min^{-1}, detection at 210 nm. For characterization of **3aa**, see above.



(*S*,*R*)-3ha
$ee_{(S,R)}$ = 85%
$ee_{(R,R)}$ = 15%
dr = 84:16

(*S*,*R*)-3aa
$ee_{(S,R)}$ = 85%
$ee_{(R,R)}$ = 11%
dr = 84:16

According to GP5 enantioenriched **(*S*,*R*)-3ha** (42.5 mg, 0.12 mmol, $ee_{(S,R)}$ = 85%, $ee_{(R,R)}$ = 15%, $dr_{(S,R+R,S):(R,R+S,S)}$ = 84:16) in MeOH was treated with ammonium formate (38.5 mg, 0.61 mmol, 5 equiv) and palladium on charcoal (10%, 10.6 mg) to yield in **(*S*,*R*)-3aa** (8.8 mg, 28 µmol, 23%, $ee_{(S,R)}$ = 85%, $ee_{(R,R)}$ = 11%, $dr_{(S,R+R,S):(R,R+S,S)}$ = 84:16) as colorless oil. The *dr* and *ee* values were determined by chiral column HPLC: Chiracel OD-H, *n*-hexane/*i*-PrOH (99/1), 0.9 mL min^{-1}, detection at 210 nm. For characterization of **3aa**, see above.



(*S*,*R*)-3id
$ee_{(S,R)}$ = 91%
$ee_{(R,R)}$ = 91%
dr = 82:18

(*S*,*R*)-3ad
$ee_{(S,R)}$ = 91%
$ee_{(R,R)}$ = 90%
dr = 80:20

According to GP5 enantioenriched **(*S*,*R*)-3id** (15.5 mg, 37 µmol, $ee_{(S,R)}$ = 91%, $ee_{(R,R)}$ = 91%, $dr_{(S,R+R,S):(R,R+S,S)}$ = 82:18) in MeOH was treated with ammonium formate (11.6 mg, 0.18 mmol, 5 equiv) and palladium on charcoal (10%, 3.9 mg) to yield in **(*S*,*R*)-3aa** (10.3 mg, 30 µmol, 82%, $ee_{(S,R)}$ = 91%, $ee_{(R,R)}$ = 90%, $dr_{(S,R+R,S):(R,R+S,S)}$ = 80:20) as colorless oil. The *dr* and *ee* values were determined by chiral column HPLC: Chiracel OD-H, *n*-hexane/*i*-PrOH (99/1), 0.7 mL min^{-1}, detection at 210 nm. For characterization of **3ad**, see above.

Kinetic Investigations of the FBIP Catalyzed Asymmetric Michael-Addition

Experimental

The catalysis reactions were performed according to GP 3 with the mentioned addition order (to the cyanoacetate **1a** is added acetic acid as stock solution, the catalyst as stock solution and finally the enone **2a** at 35 °C, except in the case of reverse substrate addition, see below) using 0.09 mmol **1a** in 170 µL solvent. For the determination of the reaction order of **1a**, 0.19 mmol enone **2a** was used in 170 µL of solvent. In all cases the time measurement was started with the addition of the enone **2a** (or **1a** in the case of reverse addition order of substrates, see below) at 35 °C. For monitoring, aliquots of 10 µL of the reaction mixture were taken and added to 200 µL of acetonitrile to stop the reaction (confirmed by HPLC analysis) and to release product and starting material from the catalyst. The samples were analyzed by RP-HPLC (RP-18 column, gradient of acetonitrile/water as eluent, detection at 210 nm, $t_{(\mathbf{1a})}$ = 2.0 min , $t_{(\mathbf{3aa})}$ = 2.3 min) and the conversion and product concentration/yield of each sample was calculated by the corresponding calibration curve (Figure 1).

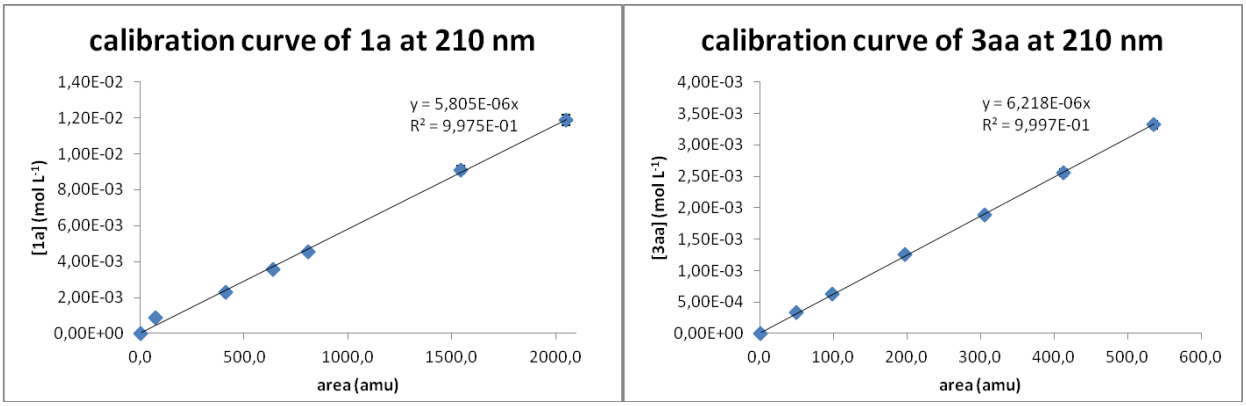


Figure 1: *Left*: Calibration curve of **1a** at 210 nm. *Right*: Calibration curve of **3aa** at 210 nm.

The initial reaction rates *r* were calculated from the [product]-time data of each reaction and the error for each value was calculated from the test series standard deviation (probability of 95%).

The partial reaction order of one compound (in this example for the catalyst, eq. 1 to 3) was determined by variation of its concentration while the other reagents were present in excess (simplification of eq. 1 to eq. 2)[14].

$$r = k \cdot c_{catalyst}^{m_1} \cdot c_{enone}^{m_2} \cdot c_{CA}^{m_3} \cdot c_{HOAc}^{m_4} \cdot c_{diglyme}^{m_5} \qquad \text{(eq. 1)}$$

$$r = k^* \cdot c_{catalyst}^{m_1} \qquad \text{with} \qquad k^* = k \cdot c_{enone,0}^{m_2} \cdot c_{CA,0}^{m_3} \cdot c_{HOAc,0}^{m_4} \cdot c_{diglyme}^{m_5} = const. \qquad \text{(eq. 2)}$$

Logarithmic transformation of the obtained initial conversion rate/concentration data results in the partial reaction order m_i of the corresponding compound (eq. 3).

$$\ln r = \ln k^* + m_1 \cdot \ln c_{catalyst} \qquad \text{(eq. 3)}$$

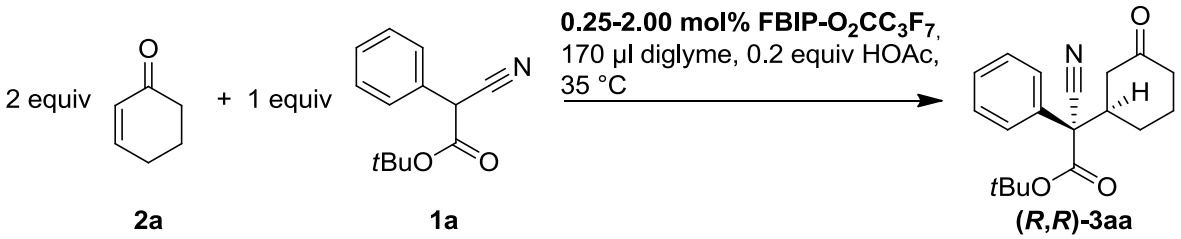
Reaction Order of the Catalyst FBIP-$O_2CC_3F_7$

The determination of the reaction order of the catalyst **FBIP-$O_2CC_3F_7$** was achieved in two slightly different series:

a) normal catalysis procedure as mentioned above with 0.25 to 2.00 mol% catalyst
b) reverse substrate addition (cyanoacetate **1a** is added as final component) using 0.25 to 1.25 mol% catalyst

The corresponding results are discussed in detail in the following section:

a) Normal Procedure with 0.25 to 2.00 mol% Catalyst



2a **1a** **(*R*,*R*)-3aa**

In the first series for the determination of the order of the catalyst **FBIP-$O_2CC_3F_7$** the catalysis was performed with catalyst amounts from 0.25 to 2.00 mol%, while all other concentrations were kept constant.

The yield-time graph (Figure 2, *left*) shows a dependency of the reaction rate from the catalyst concentration. With higher loadings higher initial reaction rates are achieved (Figure 2, *right*). The initial reaction rates (Table 1) were calculated from the slope of the yield-time data for each test series.

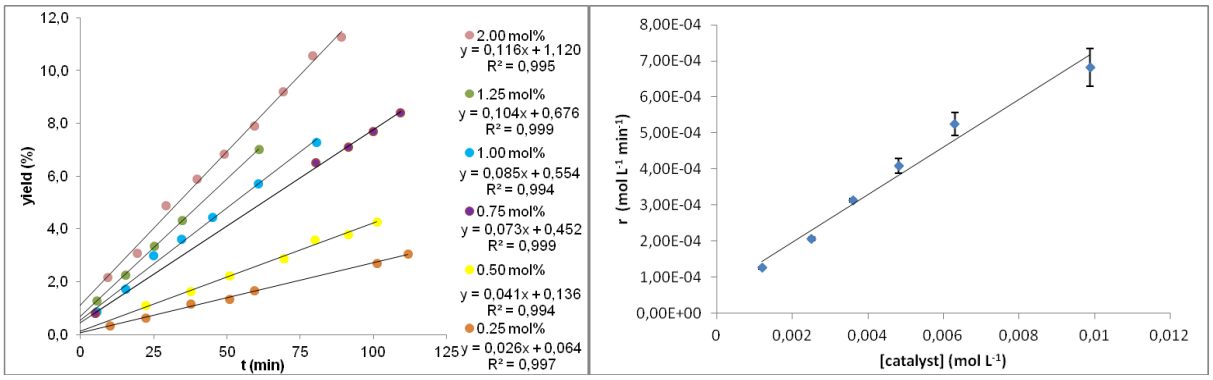


Figure 2: *Left:* Yield-time data for varying amounts of catalyst **FBIP-$O_2CC_3F_7$**. *Right:* Dependency of the initial reaction rate from the catalyst concentration.

Table 1: Initial reaction rates for varying amounts of catalyst FBIP-$O_2CC_3F_7$.

#	**FBIP-$O_2CC_3F_7$** (mol%)	[catalyst] (mmol L^{-1})	*r* (mol L^{-1} min^{-1})
1	0.25	1.19	$1.26 \cdot 10^{-4} \pm 3.78 \cdot 10^{-6}$
2	0.50	2.51	$2.05 \cdot 10^{-4} \pm 4.64 \cdot 10^{-6}$
3	0.75	3.59	$3.13 \cdot 10^{-4} \pm 4.96 \cdot 10^{-6}$
4	1.00	4.81	$4.09 \cdot 10^{-4} \pm 1.97 \cdot 10^{-5}$
5	1.25	6.30	$5.25 \cdot 10^{-4} \pm 3.13 \cdot 10^{-5}$
6	2.00	9.88	$6.82 \cdot 10^{-4} \pm 5.19 \cdot 10^{-5}$

Logarithmic transformation of the obtained reaction rate data results in a straight line with a slope of 0.84 (Figure 3, *left*) revealing a reaction order of **0.84** for the catalyst **FBIP-$O_2CC_3F_7$** according to equation 3.

Extrapolation of the yield-time data to t_0 = 0 min (y-axis intercepts in Figure 2, *left*) reveals a relationship between the extrapolated product yield at t_0 = 0 min and the corresponding catalyst loading (Figure 3, *right*). The slope of the regression line (0.615) shows that 100 catalyst molecules have statistically already generated about 60 product molecules initially after addition of all reagents and reactants. The C–C bond formation thus occurs very rapidly with the bis-palladium catalyst.

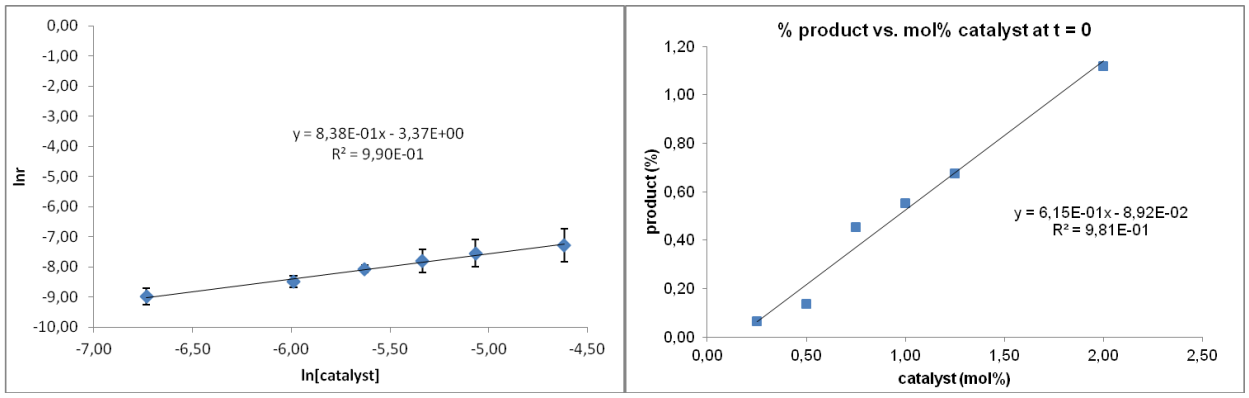
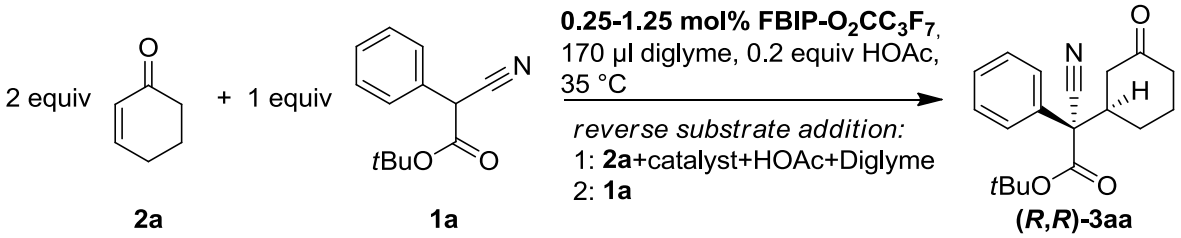


Figure 3: *Left:* Determination of the reaction order for the catalyst **FBIP-$O_2CC_3F_7$**. *Right:* Dependency of the extrapolated product-yield data at t_0 = 0 min on the catalyst loading.

b) 0.25 to 1.25 mol% Catalyst and Reverse Substrate Addition



In the second series for the determination of the reaction order of the catalyst **FBIP-$O_2CC_3F_7$** the catalysis was performed with catalyst amounts from 0.25 to 1.25 mol%, while all other concentrations were kept constant. A reverse addition order of the substrates was used. In these experiments the catalyst was first mixed with the enone **2a**, acetic acid and diglyme. The time measurement was started with the addition of the cyanoacetate **1a** in diglyme at 35 °C.

The yield-time graph (Figure 4, *left*) shows a dependency of the reaction rate from the catalyst concentration. With higher catalyst loadings higher initial reaction rates are achieved (Figure 4, *right*). The initial reaction rates (Table 2) were calculated from the slope of the yield-time data for each test series.

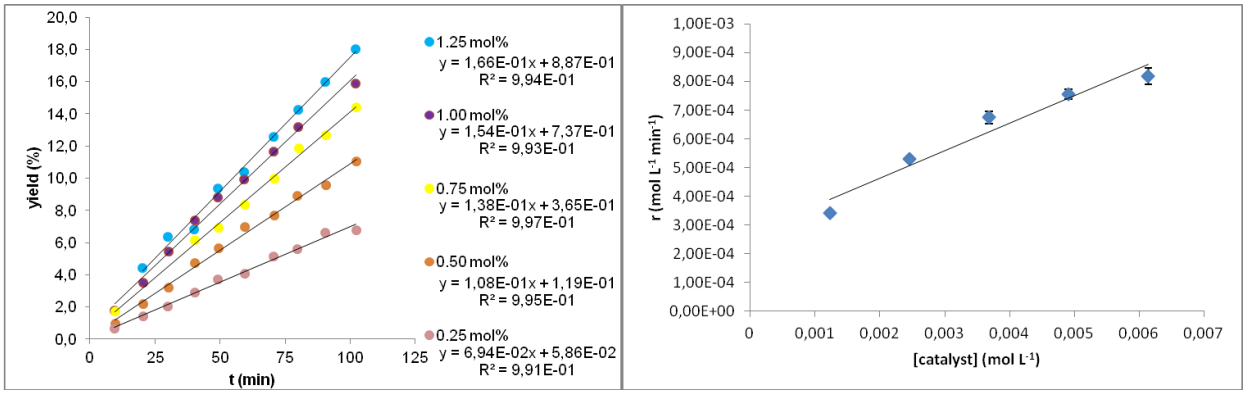


Figure 4: *Left:* Yield-time data for varying amounts of catalyst **FBIP-$O_2CC_3F_7$** with reverse substrate addition. *Right:* Dependency of the initial reaction rate from the catalyst concentration with reverse substrate addition.

Table 2: Initial reaction rates for varying amounts of catalyst FBIP-$O_2CC_3F_7$.

#	**FBIP-$O_2CC_3F_7$** (mol%)	[catalyst] (mmol L^{-1})	*r* (mol L^{-1} min^{-1})
1	0.25	1.23	$3.41 \cdot 10^{-4} \pm 4.54 \cdot 10^{-6}$
2	0.50	2.45	$5.30 \cdot 10^{-4} \pm 8.32 \cdot 10^{-6}$
3	0.75	3.68	$6.75 \cdot 10^{-4} \pm 2.14 \cdot 10^{-5}$
4	1.00	4.91	$7.55 \cdot 10^{-4} \pm 1.66 \cdot 10^{-5}$
5	1.25	6.14	$8.17 \cdot 10^{-4} \pm 2.84 \cdot 10^{-5}$

Logarithmic transformation of the obtained reaction rate data results in a straight line with a slope of 0.55 (Figure 5, *left*) revealing under the reverse order of substrate addition a reaction order of **0.55** for the catalyst **FBIP-$O_2CC_3F_7$**, corresponding to equation 3.

The graph of the extrapolated product-yield at t_0 = 0 min (y-axis intercepts in Figure 4, *left*) as function of the corresponding catalyst loadings results in a straight line with a slope of 0.91.

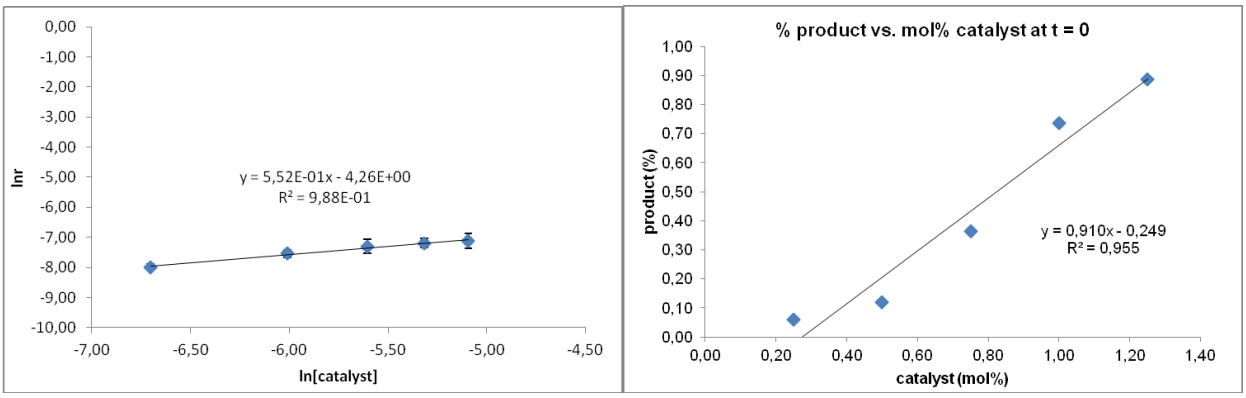
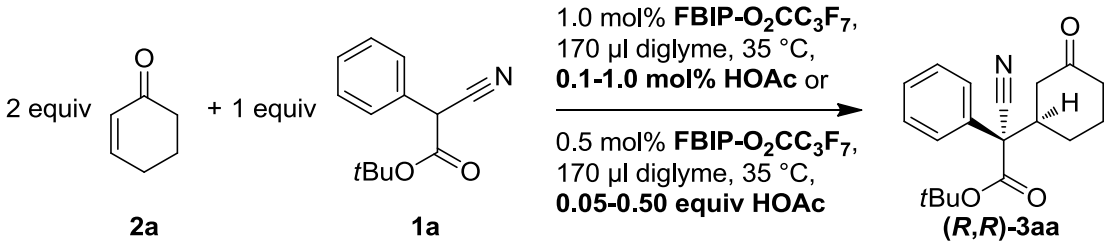


Figure 5: *Left:* Determination of the reaction order for the catalyst **FBIP-$O_2CC_3F_7$** with reverse substrate addition. *Right:* Dependency of the extrapolated product-yield data at t_0 = 0 min on the catalyst loading of the experiments with reverse substrate addition.

Reaction Order of Acetic Acid



2a **1a** **(*R*,*R*)-3aa**

For the determination of the reaction order of acetic acid the catalysis was performed with a wide range of different acetic acid amounts. In one series acid amounts (0.10 to 1.00 mol%) smaller

and equal to the concentration of palladium were used, in another series larger amounts (0.05 to 0.50 equiv) were used to analyze a possible saturation effect, while all other concentrations were constant.

In case of [HOAc] ≤ [Pd] the yield-time graph shows a very small dependency of the reaction rate from the acetic acid amount (Figure 6, *top*). Higher acid amounts resulted in slightly higher reaction rates. Nearly identical reaction rates were obtained for [HOAc] >> [Pd] (Figure 6, *bottom*).

The initial reaction rates (Table 3) were calculated from the slope of the yield-time data for each test series.

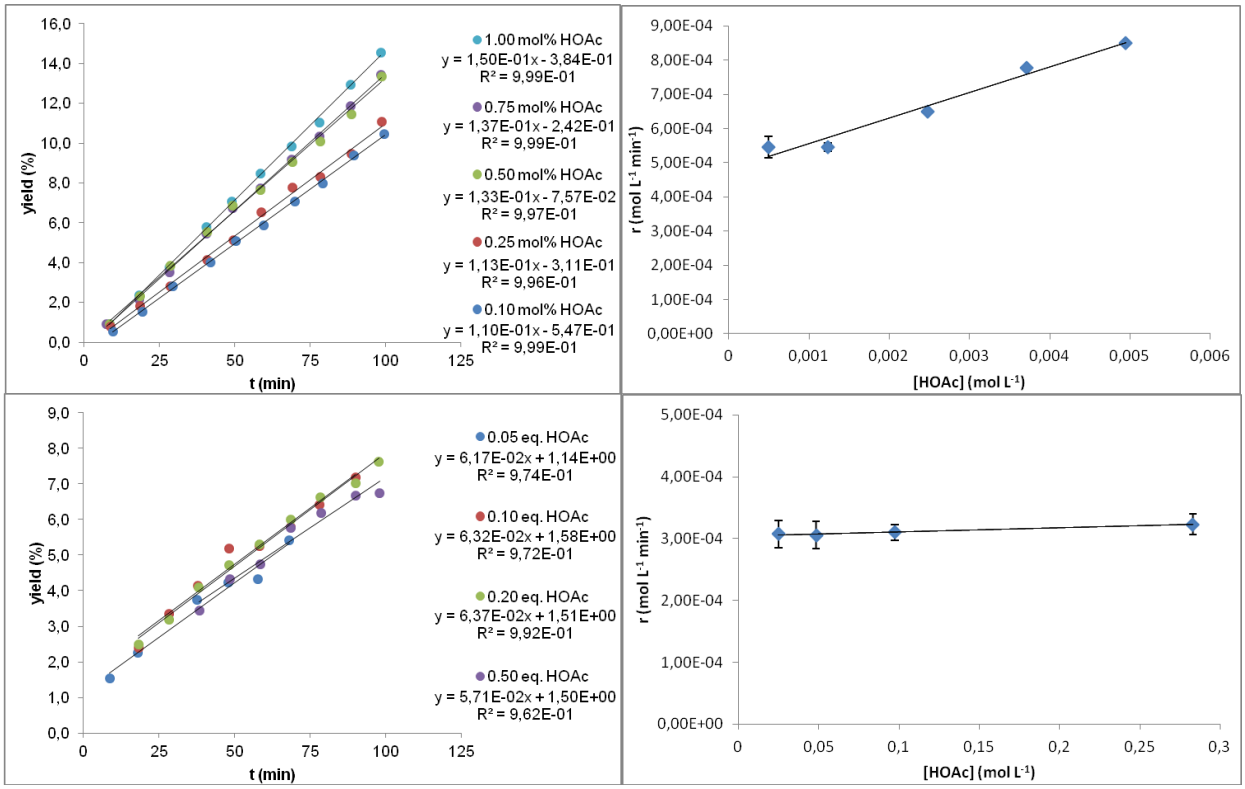


Figure 6: *Top:* Yield-time data and dependency of the initial reaction rate for varying amounts of HOAc, where [HOAc] ≤ [Pd]. *Bottom:* Yield-time data and dependency of the initial reaction rate for varying amounts of HOAc, where [HOAc] >> [Pd].

Table 3: Initial reaction rates for varying amounts of HOAc.

#	**HOAc** (mol%)	[HOAc] (mol L^{-1})	*r* (mol L^{-1} min^{-1})
1[a]	0.10	$4.94 \cdot 10^{-4}$	$5.46 \cdot 10^{-4} \pm 3.13 \cdot 10^{-5}$
2[a]	0.25	$1.24 \cdot 10^{-3}$	$5.46 \cdot 10^{-4} \pm 1.18 \cdot 10^{-5}$
3[a]	0.50	$2.47 \cdot 10^{-3}$	$6.48 \cdot 10^{-4} \pm 6.78 \cdot 10^{-6}$
4[a]	0.75	$3.71 \cdot 10^{-3}$	$7.78 \cdot 10^{-4} \pm 4.41 \cdot 10^{-6}$
5[a]	1.00	$4.95 \cdot 10^{-3}$	$8.50 \cdot 10^{-4} \pm 4.74 \cdot 10^{-6}$
6[b]	5.0	$2.49 \cdot 10^{-2}$	$3.08 \cdot 10^{-4} \pm 2.19 \cdot 10^{-5}$
7[b]	10	$4.84 \cdot 10^{-2}$	$3.06 \cdot 10^{-4} \pm 2.21 \cdot 10^{-5}$
8[b]	20	$9.74 \cdot 10^{-2}$	$3.10 \cdot 10^{-4} \pm 1.24 \cdot 10^{-5}$
9[b]	50	$2.83 \cdot 10^{-1}$	$3.23 \cdot 10^{-4} \pm 1.64 \cdot 10^{-5}$

[a] 1 mol% catalyst was used. [b] 0.5 mol% of catalyst was used.

The double reciprocal plot r^{-1} *vs* $[HOAc]^{-1}$ of both test series is shown in Figure 7.

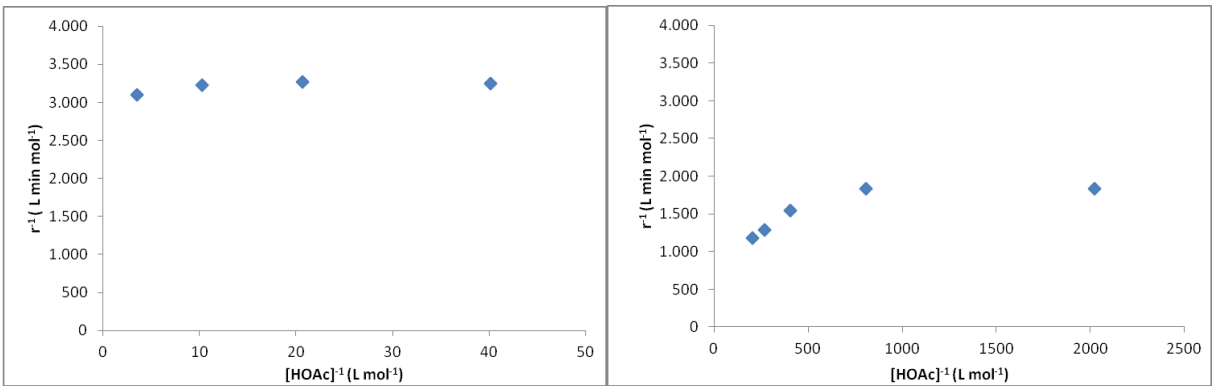


Figure 7: Double reciprocal plot r^{-1} *vs* $[HOAc]^{-1}$ of the obtained data. *Left:* [HOAc] >> [Pd]. *Right:* [HOAc] ≤ [Pd].

Logarithmic transformation of the obtained reaction rate data results in straight lines with a slope of 0.20 for [HOAc] ≤ [Pd] (Figure 8, *left*) and 0.02 for [HOAc] >> [Pd] (Figure 8, *right*). The zero order dependence only in case of [HOAc] >> [Pd] implicates saturation kinetics for these high concentrations. According to equation 3 the reaction order of acetic acid is determined to be **0.20**.

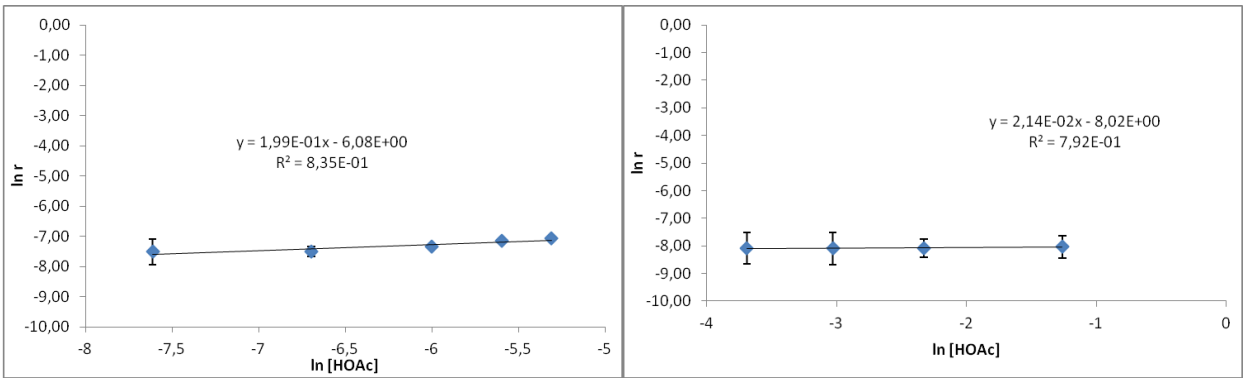
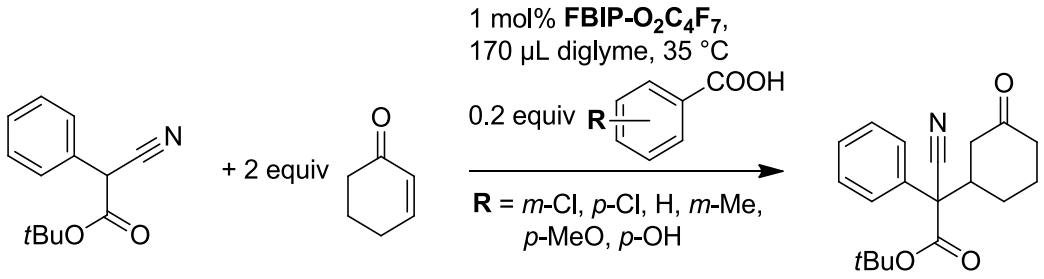


Figure 8: Determination of the reaction order for acetic acid. *Left:* [HOAc] ≤ [Pd]. *Right:* [HOAc] >> [Pd].

Influence of Substituted Benzoic Acids



Different substituted benzoic acids were used as co-catalysts to test the influence of the acids' pKa values on the reaction outcome. Stock solutions of the corresponding acid in diglyme (c = 0.435 mol L^{-1}) were prepared and used instead of HOAc.

The yield-time data using 1 mol% of **FBIP-$O_2CC_3F_7$** in diglyme at 35 °C show a dependency of the initial reaction rate on the substituent R of the benzoic acid derivative (Figure 9, *left*). The Hammett plot log k *vs* σ-constant shows a correlation with a negative value for ρ (–0.41, Figure 9, *right*). The initial reaction rates (Table 4) were calculated from the slope of the yield-time data for each test series and further converted into the rate constants k.

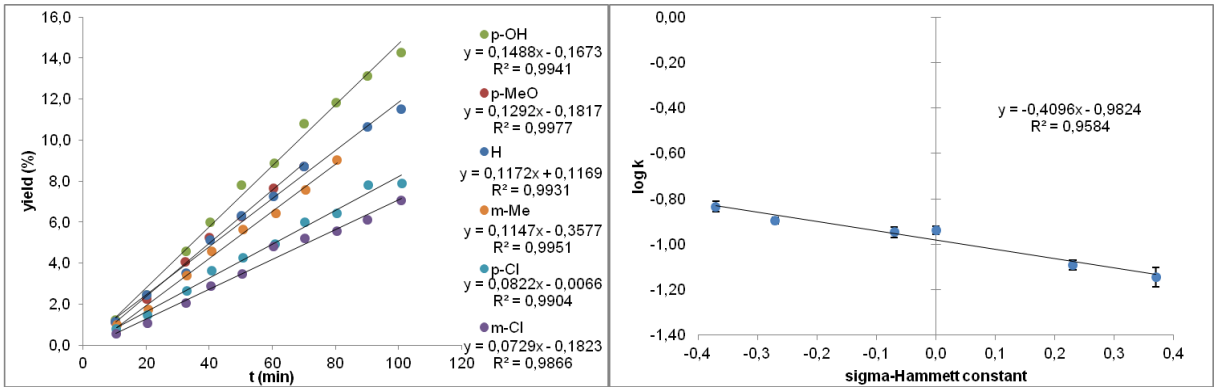


Figure 9: *Left:* Yield-time data for different substituted benzoic acid derivatives. *Right:* Hammett plot of the obtained data.

Table 4: Initial reaction rates and rate constants for different substituted benzoic acid derivatives.

#	**R**	σ-constant	*r* (mol L^{-1} min^{-1})	k ($L^{1.56}$ $mol^{-1.56}$ min^{-1})
1	*m*-Cl	0.37	$3.54 \cdot 10^{-4} \pm 1.32 \cdot 10^{-5}$	$7.18 \cdot 10^{-2}$
2	*p*-Cl	0.23	$3.99 \cdot 10^{-4} \pm 8.33 \cdot 10^{-6}$	$8.10 \cdot 10^{-2}$
3	H	0	$5.69 \cdot 10^{-4} \pm 1.06 \cdot 10^{-5}$	$1.15 \cdot 10^{-1}$
4	*m*-Me	–0.07	$5.57 \cdot 10^{-4} \pm 1.37 \cdot 10^{-5}$	$1.13 \cdot 10^{-1}$
5	*p*-MeO	–0.27	$6.27 \cdot 10^{-4} \pm 1.04 \cdot 10^{-5}$	$1.27 \cdot 10^{-1}$
6	*p*-OH	–0.37	$7.22 \cdot 10^{-4} \pm 1.94 \cdot 10^{-5}$	$1.47 \cdot 10^{-1}$

The selectivity outcome after 24 h reaction time is shown in Table 5 and Figure 10.

Table 5: Selectivity data of the catalysis reaction with various benzoic acid derivatives.

#	**R**	σ-constant	Yield (%)	$ee_{(R,R)}$ (%)	$ee_{(S,R)}$ (%)	$dr_{(R,R+S,S):(S,R+R,S)}$
1	*m*-Cl	0.37	61	92	66	87:13
2	*p*-Cl	0.23	71	93	72	88:12
3	H	0	77	94	76	90:10
4	*m*-Me	–0.07	75	81	74	90:10
5	*p*-MeO	–0.27	75	94	79	90:10
6	*p*-OH	–0.37	87	95	78	90:10

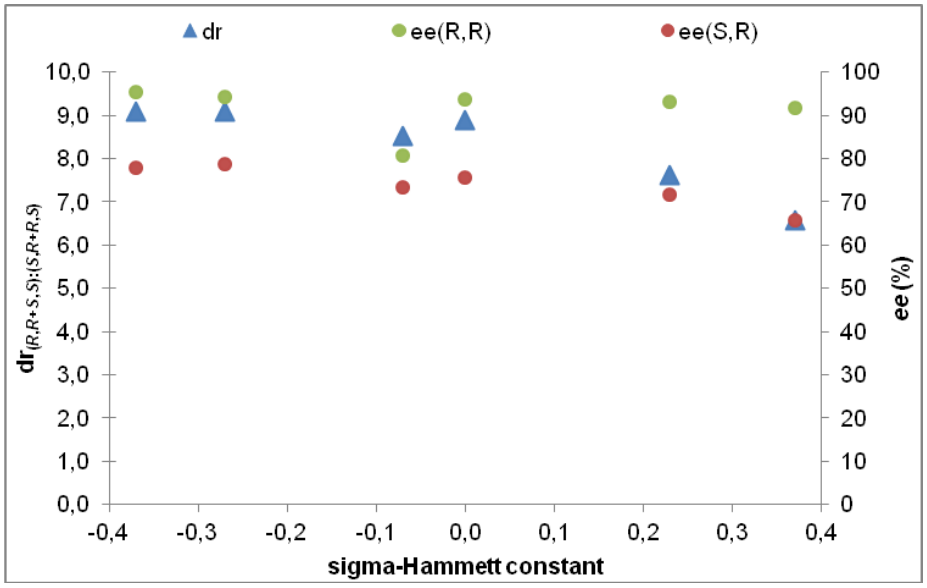
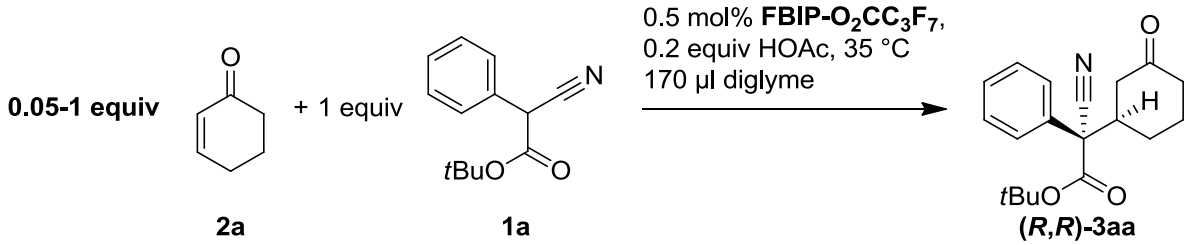


Figure 10: Effect of the electronic properties of the benzoic acid derivative on the selectivity (left axis: *dr*, right axis: *ee*).

Reaction Order of Enone 2a



For the determination of the reaction order of the enone **2a** the catalysis was performed with amounts from 0.05 to 1.00 equiv of enone **2a**, while all other concentrations were kept constant. The yield-time data show a dependency of the initial reaction rate on the enone concentration (Figure 11, *left*). With higher concentrations the initial reaction rate increases (Figure 11, *right*). The following initial reaction rates (Table 6) were calculated from the slope of the yield-time data.

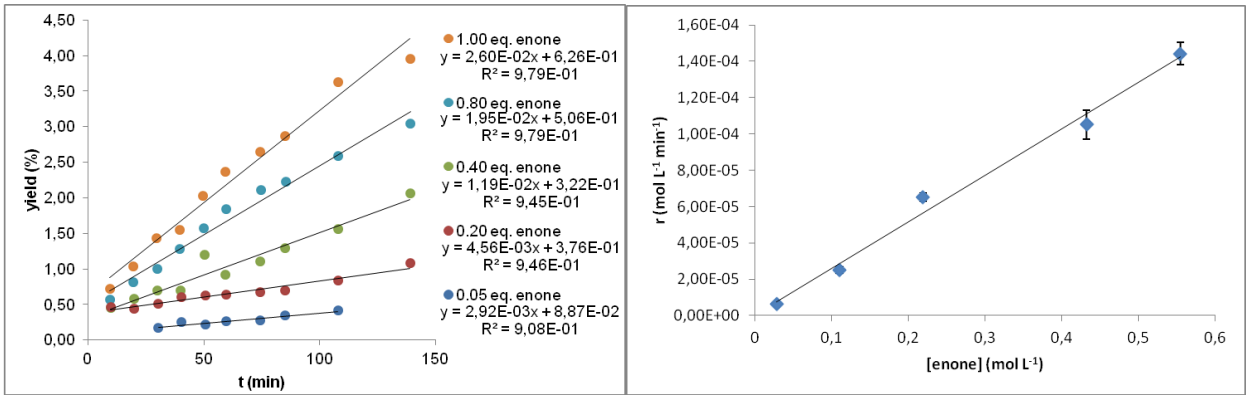


Figure 11: *Left:* Yield-time data for varying amounts of enone. *Right:* Plot of the initial reaction rates as a function of the enone concentration.

Table 6: Initial reaction rates for varying amounts of enone 2a.

#	Enone **2a** (equiv)	[**2a**] (mol L^{-1})	*r* (mol L^{-1} min^{-1})
1	0.05	0.028	$6.33 \cdot 10^{-6} \pm 6.95 \cdot 10^{-7}$
2	0.20	0.110	$2.50 \cdot 10^{-5} \pm 1.75 \cdot 10^{-6}$
3	0.40	0.219	$6.53 \cdot 10^{-5} \pm 2.28 \cdot 10^{-6}$
4	0.80	0.432	$1.05 \cdot 10^{-4} \pm 8.04 \cdot 10^{-6}$
5	1.00	0.554	$1.44 \cdot 10^{-4} \pm 6.24 \cdot 10^{-6}$

Logarithmic transformation of the initial reaction rate data provides a straight line with a slope of 1.05 (Figure 12) revealing a reaction order of **1.05** for the enone, according to equation 3.

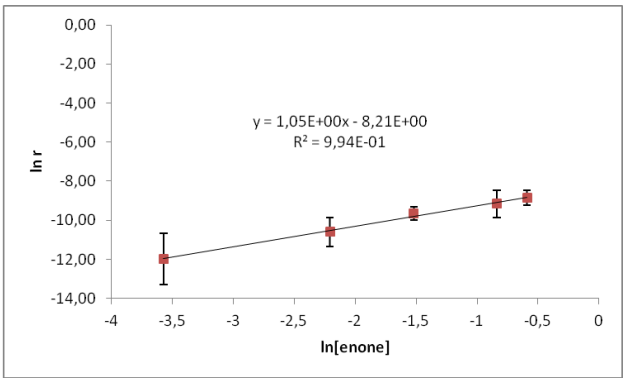
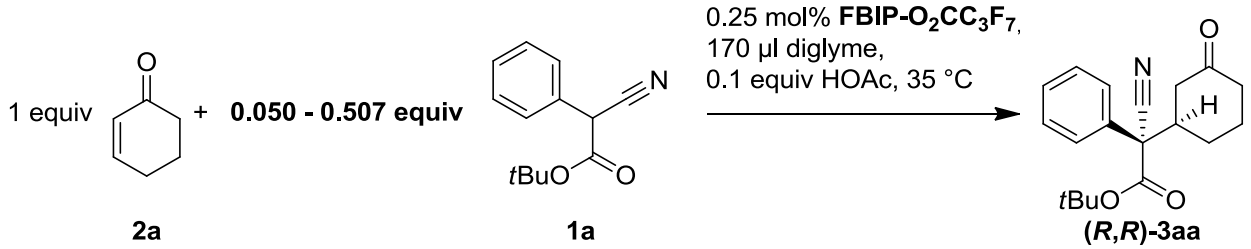


Figure 12: Determination of the reaction order for the enone.

Reaction Order of α-Phenyl-α-cyanoacetate (1a)



For the determination of the reaction order of α-phenyl-α-cyanoacetate (**1a**) the catalysis was performed with α-phenyl-α-cyanoacetate amounts from 0.050 to 0.507 equiv, while all other concentrations were kept constant. The yield-time data shows a dependency of the reaction rate from the cyanoacetate concentration (Figure 13, *left*). With higher cyanoacetate concentrations the reaction proceeds faster. The plot of the initial reaction rate against the cyanoacetate concentration shows a clear departure from a straight line implying a broken reaction order (Figure 13, *right*). The following initial reaction rates (Table 7) were calculated from the slope of the yield-time data.

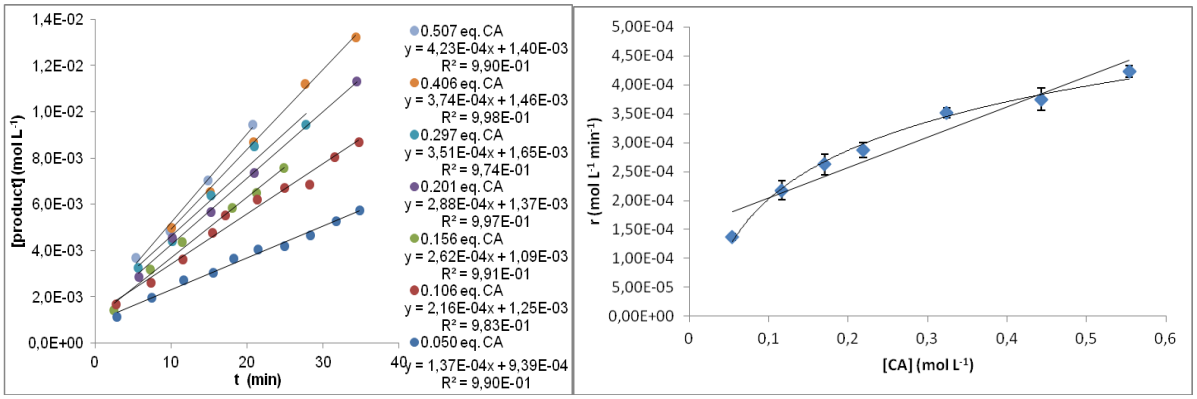


Figure 13: *Left:* Yield-time data for varying amounts of α-phenyl-α-cyanoacetate. *Right:* Initial reaction rates as a function of the cyanoacetate concentration.

Table 7: Initial reaction rates for varying amounts of α-phenyl-α-cyanoacetate.

#	CA **1a** (equiv)	[**1a**] (mol L^{-1})	*r* (mol L^{-1} min^{-1})
1	0.050	0.054	$1.37 \cdot 10^{-4} \pm 5.97 \cdot 10^{-6}$
2	0.106	0.116	$2.17 \cdot 10^{-4} \pm 1.63 \cdot 10^{-5}$
3	0.156	0.170	$2.62 \cdot 10^{-4} \pm 1.81 \cdot 10^{-5}$
4	0.201	0.219	$2.88 \cdot 10^{-4} \pm 1.29 \cdot 10^{-5}$
5	0.297	0.324	$3.50 \cdot 10^{-4} \pm 8.41 \cdot 10^{-6}$
6	0.406	0.443	$3.75 \cdot 10^{-4} \pm 1.93 \cdot 10^{-5}$
7	0.507	0.554	$4.22 \cdot 10^{-4} \pm 1.03 \cdot 10^{-5}$

Logarithmic transformation of the initial reaction rate data results in a straight line with a slope of 0.47 (Figure 14) revealing a reaction order of **0.47** for the α-phenyl-α-cyanoacetate, corresponding to equation 3.

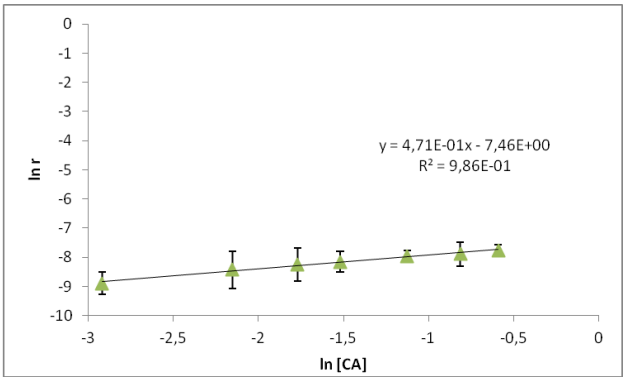
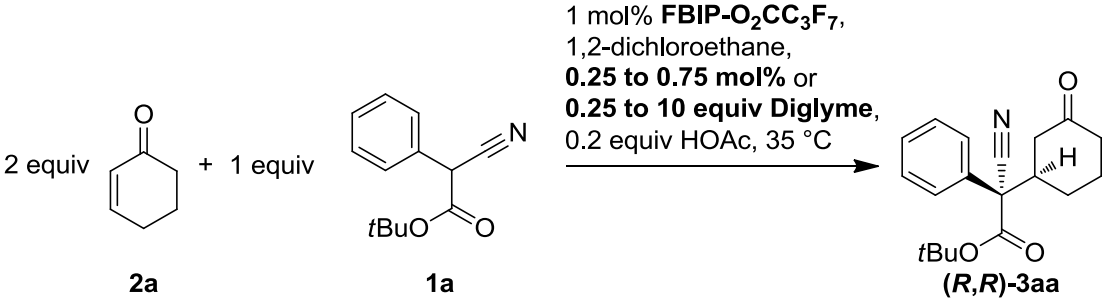


Figure 14: Determination of the reaction order for the α-phenyl-α-cyanoacetate.

Influence of Diglyme on the Reaction Rate and Stereoselectivity



To investigate the influence of diglyme to the reaction rate of the catalysis reaction the experiments were performed in 1,2-dichloroethane with varying amounts of diglyme (0.25 to

0.75 mol% and 0.25 to 10 equiv of diglyme). The total reaction volume of each experiment was 170 µL solvent mixture. For high diglyme amounts (2 to 10 equiv), the yield-time data show an accelerating effect of diglyme, while the lower concentrations have a lower influence on the reaction rate (Figure 15). The following initial reaction rates were calculated from the slope of the yield-time data (Table 8).

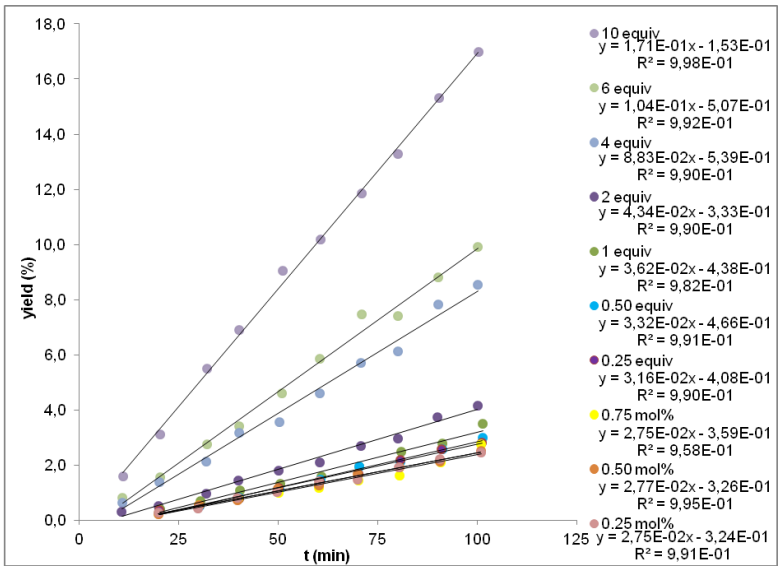


Figure 15: Yield-time data for varying amounts of diglyme.

Table 8: Initial reaction rates for varying amounts of diglyme.

#	Diglyme (equiv)	Diglyme (vol%)	[Diglyme] (mol L^{-1})	*r* (mol L^{-1} min^{-1})
1	$2.5 \cdot 10^{-3}$	0.02	$1.24 \cdot 10^{-3}$	$1.36 \cdot 10^{-4} \pm 6.61 \cdot 10^{-6}$
2	$5.0 \cdot 10^{-3}$	0.04	$2.47 \cdot 10^{-3}$	$1.37 \cdot 10^{-4} \pm 7.14 \cdot 10^{-6}$
3	$7.5 \cdot 10^{-3}$	0.06	$3.71 \cdot 10^{-3}$	$1.36 \cdot 10^{-4} \pm 6.30 \cdot 10^{-6}$
4	0.25	2.0	$1.24 \cdot 10^{-1}$	$1.56 \cdot 10^{-4} \pm 6.63 \cdot 10^{-6}$
5	0.5	3.9	$2.47 \cdot 10^{-1}$	$1.64 \cdot 10^{-4} \pm 7.65 \cdot 10^{-6}$
6	1.0	7.8	$4.95 \cdot 10^{-1}$	$1.79 \cdot 10^{-4} \pm 6.98 \cdot 10^{-6}$
7	2.0	15.6	$9.89 \cdot 10^{-1}$	$2.14 \cdot 10^{-4} \pm 7.94 \cdot 10^{-6}$
8	4.0	31.4	1.98	$4.37 \cdot 10^{-4} \pm 1.36 \cdot 10^{-5}$
9	6.0	47.0	2.97	$5.12 \cdot 10^{-4} \pm 1.55 \cdot 10^{-5}$
10	10	78.2	4.95	$8.44 \cdot 10^{-4} \pm 1.56 \cdot 10^{-5}$

The initial reaction rate as function of the diglyme concentration shows that there is a significant change of the initial reaction rate when higher amounts of diglyme are present (Figure 16). It is

most likely that diglyme facilitates the decomplexation of the product from the bis-palladium complex, also see "Derivation of the Theoretical Rate Law from the Proposed Mechanism". Determination of the reaction order for diglyme under these reaction conditions results in a broken reaction order of **0.46**.

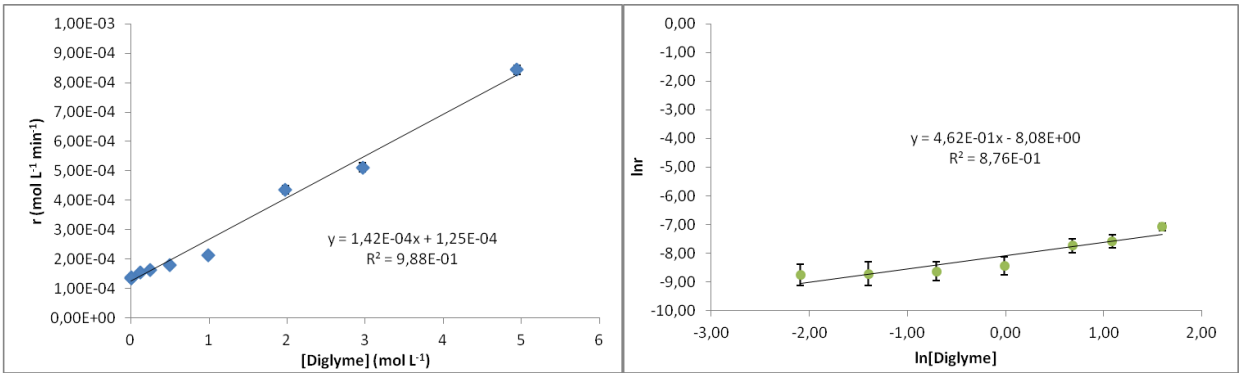


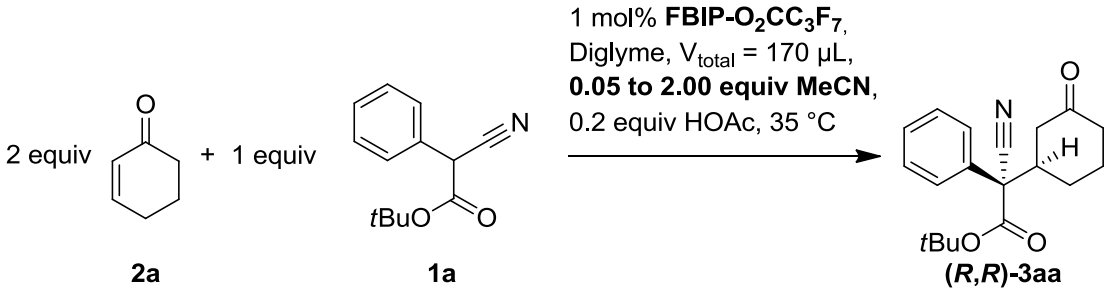
Figure 16: Initial reaction rates as a function of the diglyme concentration and the logarithmic data.

Besides the activity enhancing effect of diglyme as solvent it also has a crucial effect on the selectivity of the reaction. While the reaction in 1,2-dichloroethane proceeds only with low enantio- and diastereoselectivity, already 2 equiv of diglyme cause a drastic increase of the selectivity (Table 9).

Table 9: Influence of diglyme on the selectivity.

#	Diglyme (equiv)	Diglyme (vol%)	$ee_{(R,R)}$ (%)	$ee_{(S,R)}$ (%)	$dr_{(R,R+S,S):(S,R+R,S)}$
1	-	0	36	48	62:38
2	2.0	15.6	93	51	85:15
3	4.0	31.4	97	76	90:10
4	6.0	47.0	95	65	88:12
5	10	78.2	96	76	89:11
6	-	100	94	65	89:11

Influence of MeCN on the Reaction Rate



To investigate the influence of MeCN to the reaction rate of the catalysis reaction the experiments were performed in diglyme with varying amounts of MeCN (0.05 to 2.00 equiv of MeCN). The total reaction volume of each experiment was 170 µL of the solvent mixture. The yield-time data shows a decrease of the initial reaction rate with increased MeCN amounts (Figure 17). The following initial reaction rates were calculated from the slope of the yield-time data (Table 10).

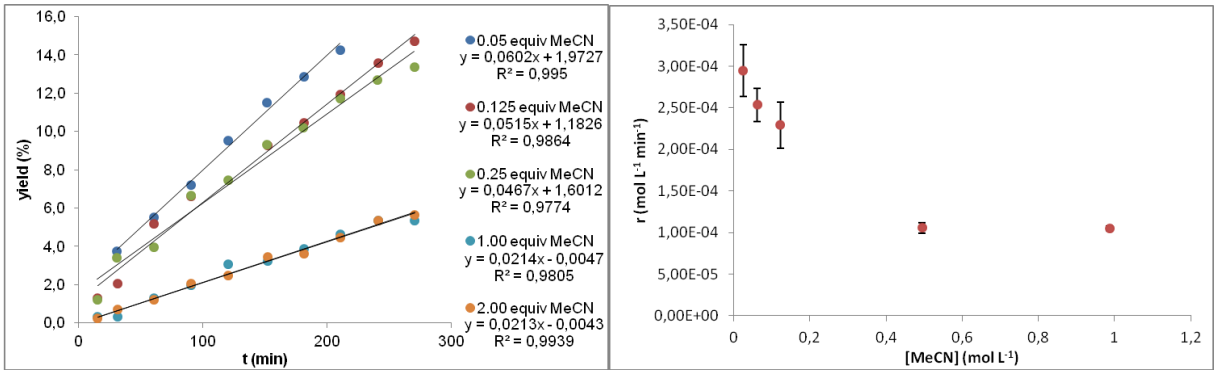


Figure 17: Yield-time data for varying amounts of MeCN and initial reaction rates as a function of the MeCN concentration.

Table 10: Initial reaction rates for varying amounts of MeCN.

#	MeCN (equiv)	[MeCN] (mol L^{-1})	*r* (mol L^{-1} min^{-1})
1	0.05	$2.44 \cdot 10^{-2}$	$2.94 \cdot 10^{-4} \pm 3.12 \cdot 10^{-5}$
2	0.125	$6.16 \cdot 10^{-2}$	$2.54 \cdot 10^{-4} \pm 1.98 \cdot 10^{-5}$
3	0.25	$1.23 \cdot 10^{-1}$	$2.29 \cdot 10^{-4} \pm 2.79 \cdot 10^{-5}$
4	1	$4.95 \cdot 10^{-1}$	$1.06 \cdot 10^{-4} \pm 6.37 \cdot 10^{-6}$
5	2	$9.87 \cdot 10^{-1}$	$1.05 \cdot 10^{-4} \pm 2.80 \cdot 10^{-6}$

Logarithmic transformation of the initial reaction rate data results in a straight line with a slope of –0.32 (Figure 18) revealing a broken, negative reaction order of **–0.32** for MeCN under these reaction conditions.

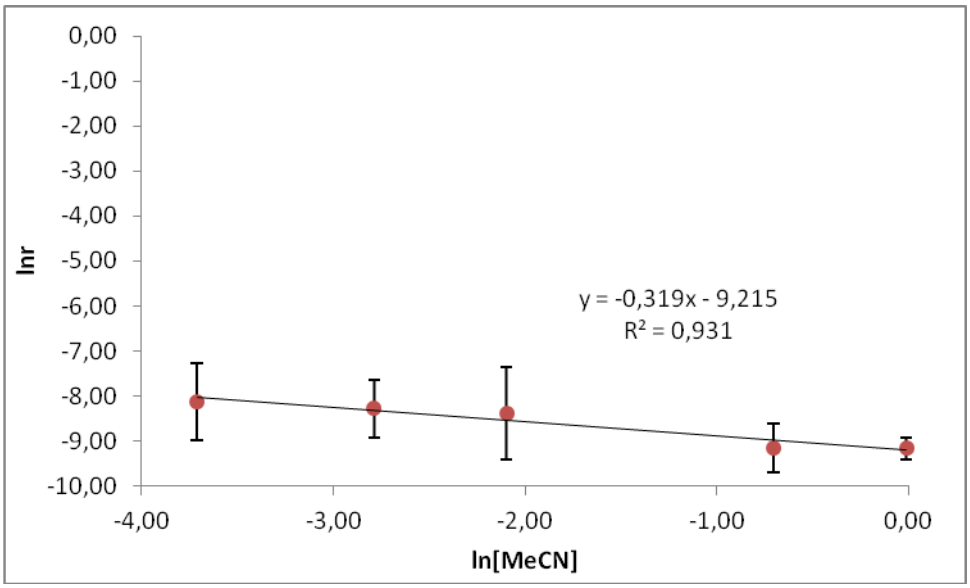
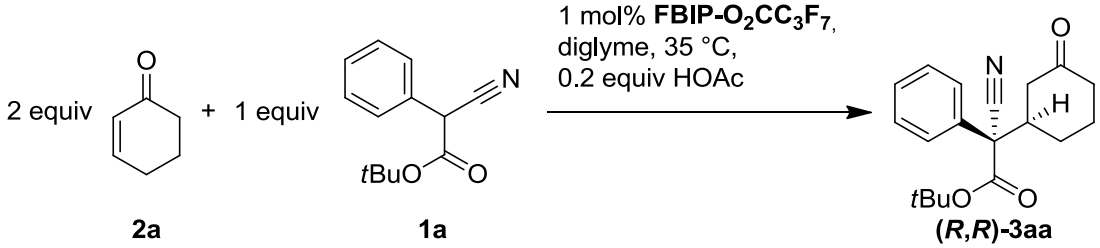


Figure 18: Determination of the reaction order of MeCN.

Course of the Reaction

The investigation of the course of the reaction was performed to gain a detailed insight into the evolution of the enantio- and diastereoselectivity of the product formation. For this purpose the reaction was carried out according to GP3, yet on a larger scale with 0.46 mmol **1a** in 850 µL of diglyme. For the analysis 25 µL of the reaction mixture were added to 500 µL acetonitrile to stop the reaction and release product and starting material from the catalyst. The sample was filtered over a short pad of silica to completely remove the catalyst. The filter cake was further washed with petrol ether: ethyl acetate (4:1). After removal of the solvent and an excess of enone **2a** the samples were analyzed by RP-HPLC and chiral stationary phase HPLC to determine yield, enantiomeric excess and diasteromeric ratio (Table 11).

Table 11: Collected data during the reaction.



#	Time (min)	Conv. (%)	$ee_{(R,R)}$ (%)	$ee_{(S,R)}$ (%)	$dr_{(R,R+S,S):(S,R+R,S)}$
1	9.77	2.02	98	54	44.87:1
2	54.62	8.94	99	61	21.37:1
3	120.03	16.44	98	78	16.30:1
4	174.32	21.83	99	73	13.34:1
5	234.17	28.68	97	86	13.01:1
6	298.17	33.68	95	83	14.90:1
7	371.43	38.12	96	90	9.11:1
8	420.88	43.42	95	79	8.31:1
9	478.23	48.39	93	77	8.17:1
10	538.8	50.37	95	75	8.35:1
11	598.33	51.49	95	75	8.28:1
12	20h	>99	94	71	8.10:1

The yield-time data shows a curve with slowly decreasing slope (Figure 19). The reaction was followed for nearly 10h to a yield of 51%.

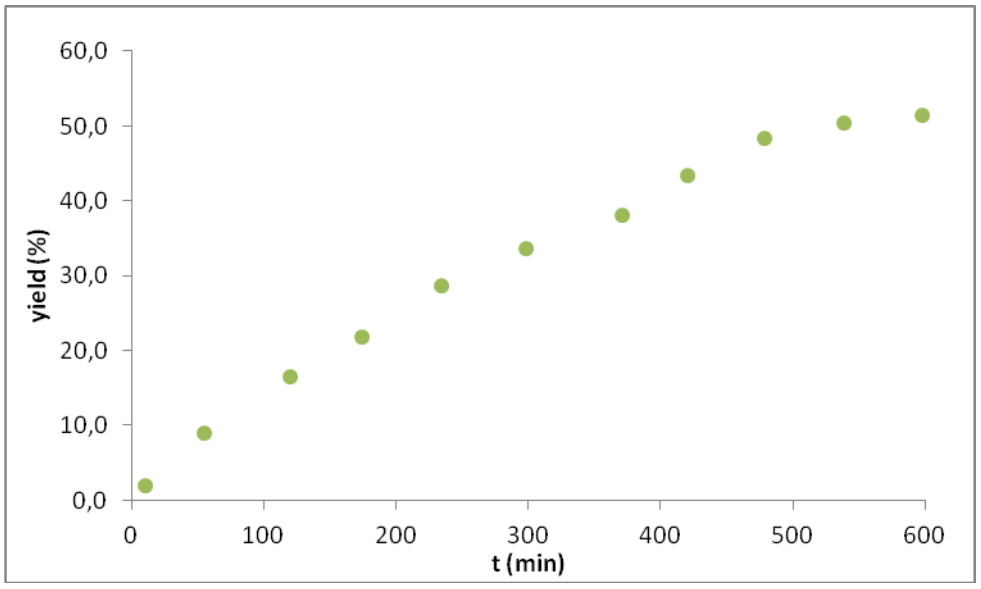


Figure 19: Time depending yields of the **FBIP-$O_2CC_3F_7$** catalyzed reaction.

The development of the enantiomeric excess of the two diastereomers is shown in Figure 20. The major (*R*,*R*)-enantiomer is formed right from the beginning on with high enantioselectivity (Table 11, #1). The *ee* stays at a high value during the reaction. In contrast, the enantiomeric excess of the (*S*,*R*)-enantiomer is increasing in the first hours until it reaches its final value after around 5h.

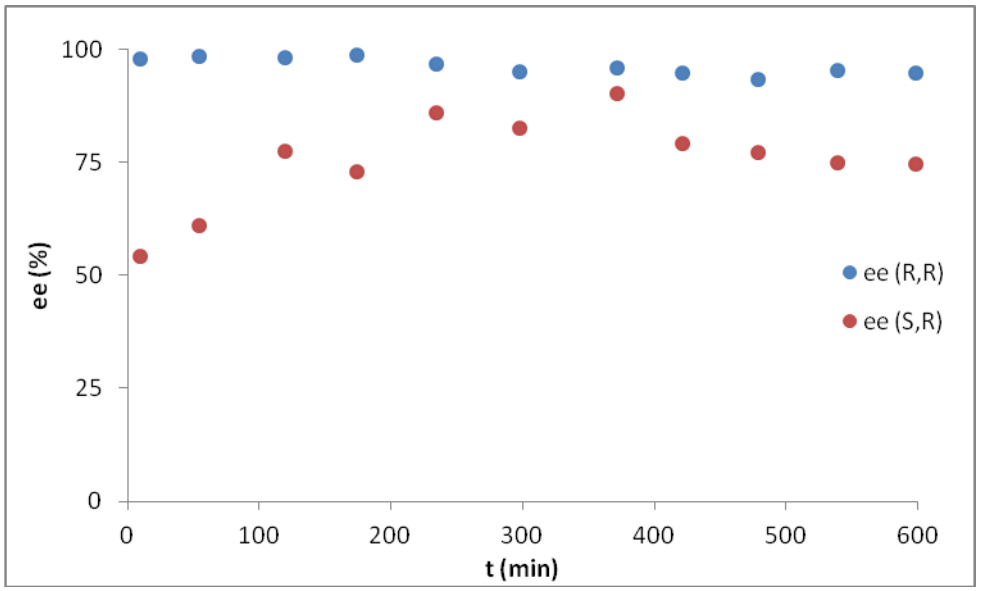


Figure 20: Development of the enantioselectivity of the **FBIP-$O_2CC_3F_7$** catalyzed reaction.

The development of the diastereomeric excess is presented in Figure 21. The reaction starts with remarkably high diastereoselectivity for the desired diastereomer (Table 11, #1 & #2). With increasing reaction time the *dr* decreases until the final value is reached after approximately 7h.

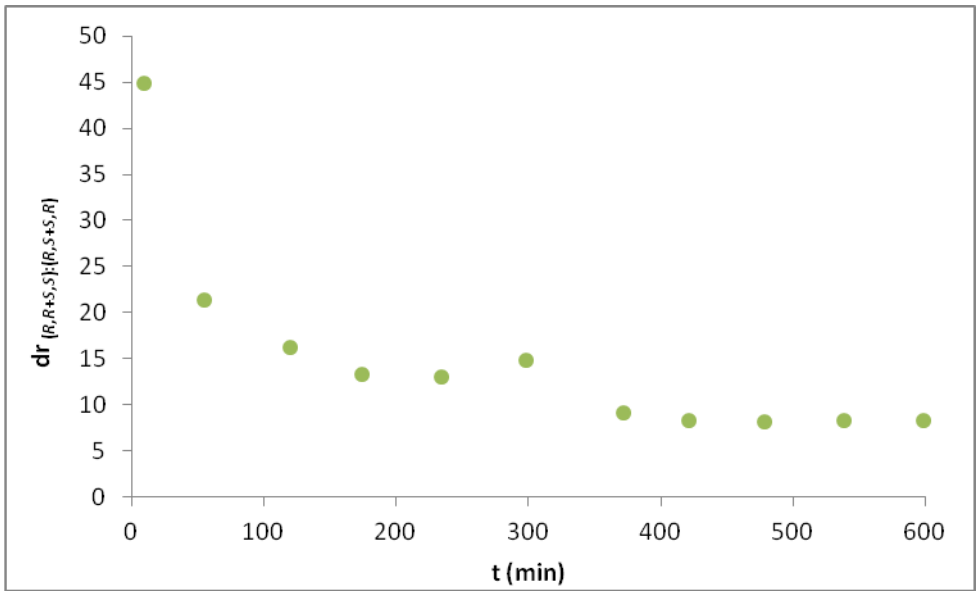
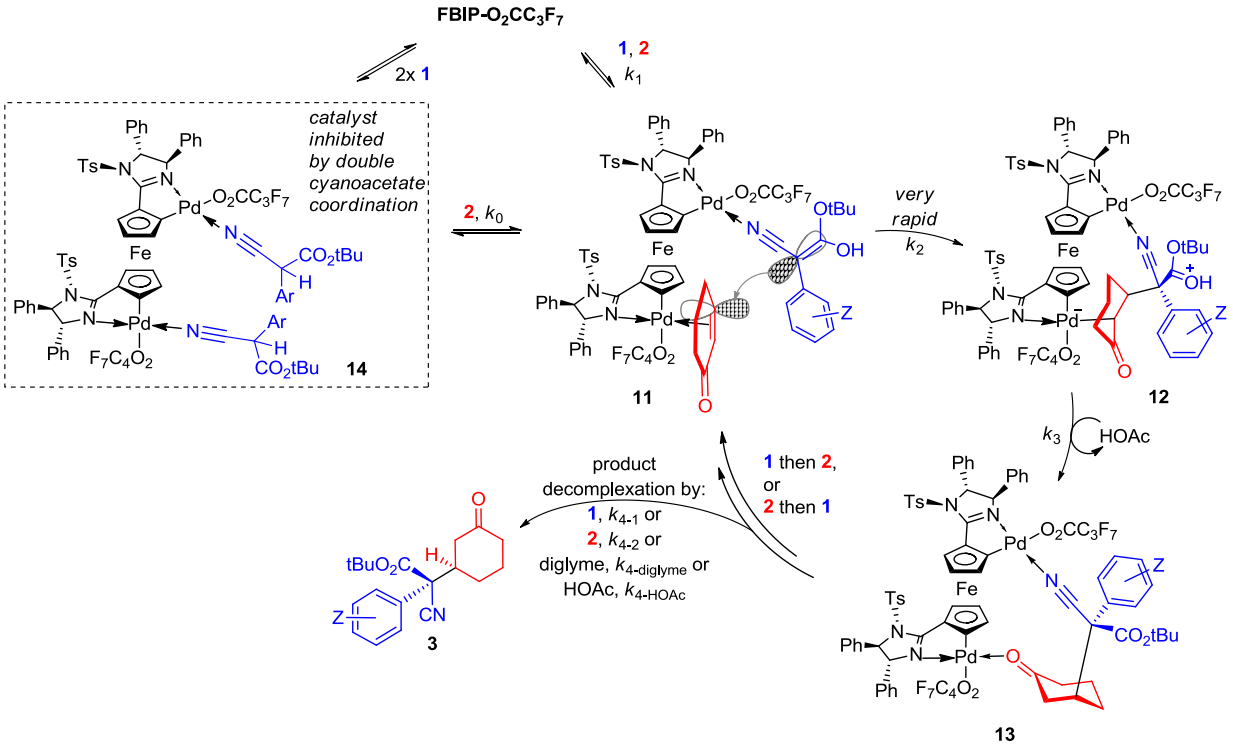


Figure 21: Development of the diastereomeric ratio of the **FBIP-$O_2CC_3F_7$** catalyzed reaction.

Derivation of the Theoretical Rate Law from the Proposed Mechanism



A theoretical rate law was derived from the proposed mechanism by application of steady state kinetics simplifications with nearly steady state concentrations of catalyst species **11-13** in the catalytic cycle, a rate limiting product decomplexation from **13** and an off-cycle catalyst reservoir **14** – that means two resting states **13** and **14**. The rate constants of each elementary

step are defined in Scheme 2. [cat_0] is the initial concentration of the activated catalyst, *i.e.* if two resting states are present, the following simplification is possible: [**13**] + [**14**] ≈ [cat_0]; and [**13**] ≈ [cat_0-**14**]}.

Assumption of a rate limiting product decomplexation from **13** via an associative ligand exchange with **1**, **2**, HOAc or diglyme:

$$\frac{d[3]}{dt} = [13]\left(k_{4\text{-}1}[1] + k_{4\text{-}2}[2] + k_{4\text{-diglyme}}[\text{diglyme}] + k_{4\text{-HOAc}}[\text{HOAc}]\right)$$

Steady state concentration of compound **13**:

$$\frac{d[13]}{dt} \approx 0 = -[13](k_{4\text{-}1}[1] + k_{4\text{-}2}[2] + k_{4\text{-diglyme}}[\text{diglyme}] + k_{4\text{-HOAc}}[\text{HOAc}]) + k_3[12][\text{HOAc}]$$

$$[13] = \frac{k_3[12][\text{HOAc}]}{k_{4\text{-}1}[1] + k_{4\text{-}2}[2] + k_{4\text{-diglyme}}[\text{diglyme}] + k_{4\text{-HOAc}}[\text{HOAc}])}$$

Steady state concentration of compound **12**:

$$\frac{d[12]}{dt} \approx 0 = -k_3[12][\text{HOAc}] + k_2[11]c]$$

$$[12] = \frac{k_2[11]}{k_3[\text{HOAc}]}$$

Steady state concentration of compound **11**:

$$\frac{d[11]}{dt} \approx 0 = k_1[\text{FBIP-O}_2\text{CC}_3\text{F}_7][1][2] - k_{-1}[11] + k_0[2][14] - k_{-0}[11][1] - k_2[11] + k_{4\text{-}1}[13][1] + k_{4\text{-}2}[13][2] + k_{4\text{-diglyme}}[13][\text{diglyme}] + k_{4\text{-HOAc}}[13][\text{HOAc}]$$

$$[11] = \frac{k_1[\text{FBIP-O}_2\text{CC}_3\text{F}_7][1][2] + k_0[2][14] + k_{4\text{-}1}[13][1] + k_{4\text{-}2}[13][2]}{k_{-1} + k_{-0}[1] + k_2} + \frac{k_{4\text{-diglyme}}[13][\text{diglyme}] + k_{4\text{-HOAc}}[13][\text{HOAc}]}{k_{-1} + k_{-0}[1] + k_2}$$

Application of the steady state concentration of **13** results in the rate law:

$$\frac{d[3]}{dt} = \frac{k_3[12][\text{HOAc}]\left(k_{4\text{-}1}[1] + k_{4\text{-}2}[2] + k_{4\text{-diglyme}}[\text{diglyme}] + k_{4\text{-HOAc}}[\text{HOAc}]\right)}{k_{4\text{-}1}[1] + k_{4\text{-}2}[2] + k_{4\text{-diglyme}}[\text{diglyme}] + k_{4\text{-HOAc}}[\text{HOAc}])} = k_3[12][\text{HOAc}]$$

Substitution of [**12**] by the steady state concentration results in:

$$\frac{d[3]}{dt} = \frac{k_3 k_2 [11][HOAc]}{k_3[HOAc]} = k_2 [11]$$

Application of the steady state concentration of **11** results in:

$$\frac{d[3]}{dt} = k_2 \frac{k_1 [FBIP\text{-}O_2CC_3F_7][1][2] + k_0 [2][14] + k_{4\text{-}1} [13][1] + k_{4\text{-}2} [13][2]}{k_{-1} + k_{-0}[1] + k_2}$$
$$+ k_2 \frac{k_{4\text{-}diglyme}[13][diglyme] + k_{4\text{-}HOAc}[13][HOAc]}{k_{-1} + k_{-0}[1] + k_2}$$

The assumption of two resting states **13** (rate limiting product-decomplexation) and **14** (off-cycle catalyst reservoir), and thus a very small concentration of **FBIP-$O_2CC_3F_7$** results in following empirical rate law:

$$\frac{d[3]}{dt} = k_2 \frac{k_0 [2][14] + k_{4\text{-}1} [13][1] + k_{4\text{-}2} [13][2] + k_{4\text{-}diglyme}[13][diglyme] + k_{4\text{-}HOAc}[13][HOAc]}{k_{-1} + k_{-0}[1] + k_2}$$

$$\frac{d[3]}{dt} = k_2 \frac{k_0 [2][14] + [cat_0 - 14]\left(k_{4\text{-}1} [1] + k_{4\text{-}2} [2] + k_{4\text{-}diglyme}[diglyme] + k_{4\text{-}HOAc}[HOAc]\right)}{k_{-1} + k_{-0}[1] + k_2}$$

The cyanoacetate **1** thus shows a broken reaction order and the reaction rate also depends on diglyme and acetic acid which might facilitate product decomplexation.

The derived reaction orders in the theoretical rate law are thus in good agreement to the empirical orders:

$$\frac{d[3]}{dt} = k \cdot [FBIP\text{-}O_2CC_3F_7]^{0.84} \cdot [1]^{1.05} \cdot [2]^{0.47} \cdot [HOAc]^{0.20} \cdot [diglyme]^{0.46}$$

Kinetic Investigations of the FIP Catalyzed Asymmetric Michael-Addition

Reaction Order of the Catalyst FIP-$O_2CC_3F_7$

The determination of the reaction order of the catalyst **FIP-$O_2CC_3F_7$** was done in four slightly different series:

a) normal procedure as mentioned above with 0.10 to 1.25 mol% catalyst,

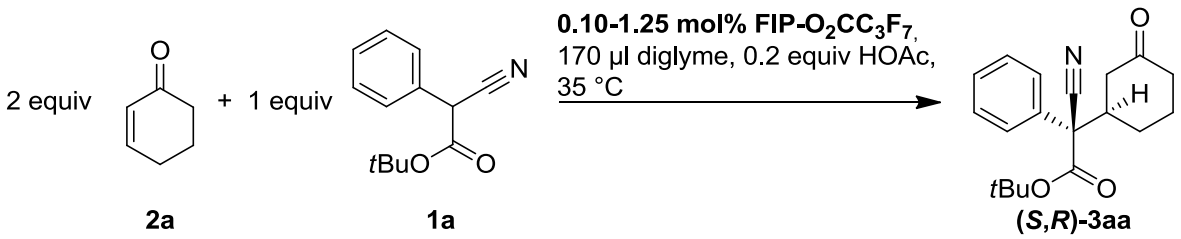
b) use of 0.10 to 1.25 mol% catalyst with additional 5 equiv MeCN per catalyst molecule,

c) 0.50 to 1.50 mol% catalyst with reverse substrate addition (cyanoacetate **1a** is added as final component),

d) use of 0.10 to 1.00 mol% of the dimeric catalyst under normal conditions.

All four series gave similar results, which are presented in detail in the following section.

a) Normal Procedure with 0.10 to 1.25 mol% Catalyst



2a **1a** **(*S*,*R*)-3aa**

In the first series the reaction order of the catalyst **FIP-$O_2CC_3F_7$** was determined with catalyst amounts from 0.10 to 1.25 mol%, while the concentrations of all other components were kept constant.

The yield-time graph (Figure 22, *left*) shows that almost identical reaction rates are observed for the tested catalyst concentrations. With higher loadings only slightly increased initial reaction rates have been noticed (Figure 22, *right*). The initial reaction rates (Table 12) were calculated from the slope of the yield-time data for each series.

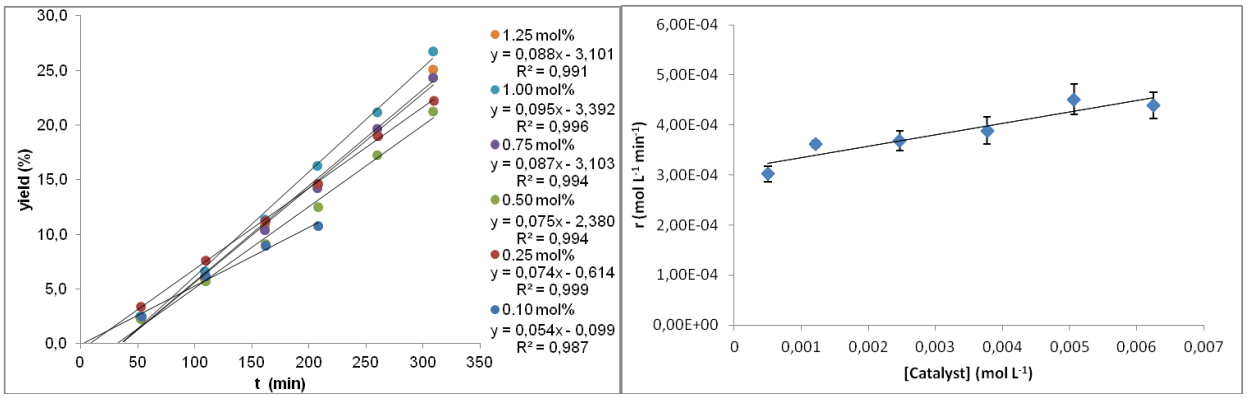


Figure 22: *Left:* Yield-time data for varying amounts of catalyst **FIP-$O_2CC_3F_7$**. *Right:* Dependency of the initial reaction rate from the catalyst concentration.

Table 12: Initial reaction rates for varying amounts of catalyst FIP-$O_2CC_3F_7$.

#	**FIP-$O_2CC_3F_7$** (mol%)	[catalyst] (mmol L^{-1})	*r* (mol L^{-1} min^{-1})
1	0.10	0.50	$3.02 \cdot 10^{-4} \pm 1.51 \cdot 10^{-5}$
2	0.25	1.22	$3.62 \cdot 10^{-4} \pm 6.66 \cdot 10^{-6}$
3	0.50	2.47	$3.68 \cdot 10^{-4} \pm 1.96 \cdot 10^{-5}$
4	0.75	3.77	$3.89 \cdot 10^{-4} \pm 2.69 \cdot 10^{-5}$
5	1.00	5.07	$4.51 \cdot 10^{-4} \pm 3.11 \cdot 10^{-5}$
6	1.25	6.25	$4.39 \cdot 10^{-4} \pm 2.65 \cdot 10^{-5}$

Logarithmic transformation of the obtained reaction rate data results in a straight line with a slope of 0.15 (Figure 23, *left*) revealing a reaction order of **0.15** for the catalyst **FIP-$O_2CC_3F_7$**, according to equation 3.

Extrapolation of the yield-time data to t_0 = 0 min (y-axis intercepts in Figure 22, *left*) results in the following plot of the product yield at t_0 = 0 min and the corresponding catalyst loading (Figure 23, *right*). The negative values indicate an induction period.

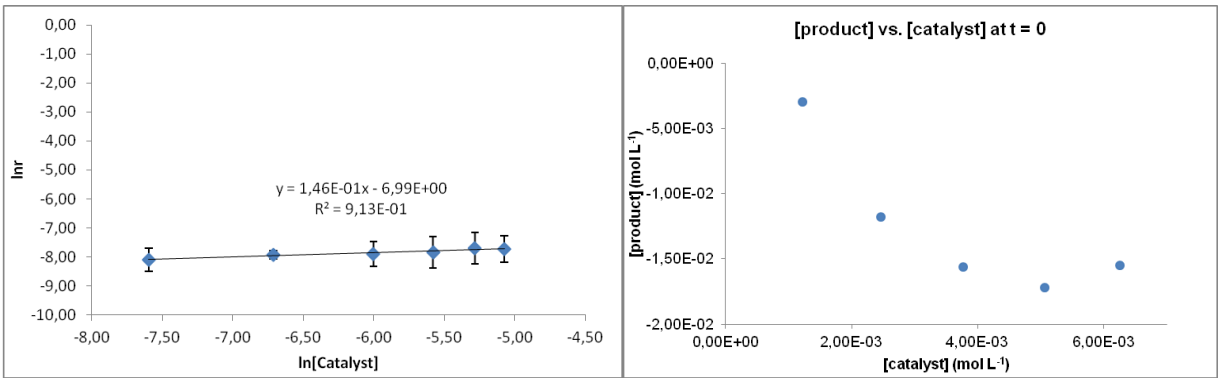
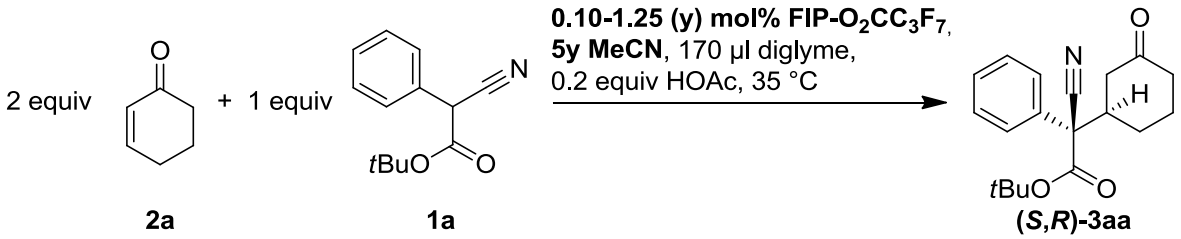


Figure 23: *Left:* Determination of the reaction order for the catalyst **FIP-$O_2CC_3F_7$**. *Right:* Dependency of the extrapolated product-yield data at t_0 = 0 min on the catalyst loading.

b) Use of 0.10 to 1.25 mol% Catalyst and Additional 5 equiv MeCN per Catalyst



The second series was performed with catalyst amounts from 0.10 to 1.25 mol% in the presence of additional 5 equiv MeCN per catalyst molecule, while all other concentrations were kept constant. MeCN was investigated as an additive to avoid dimerization of the catalyst.

The yield-time graph (Figure 24, *left*) again shows that almost identical reaction rates are observed for the tested catalyst concentrations. With higher loadings only slightly increased initial reaction rates are achieved (Figure 24, *right*). The initial reaction rates (Table 13) were calculated from the slope of the yield-time data for each test series.

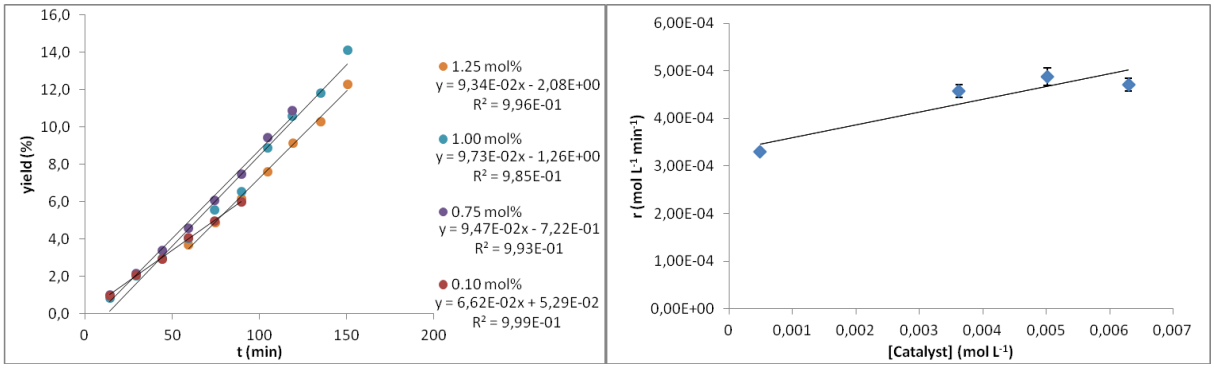


Figure 24: *Left:* Yield-time data for varying amounts of catalyst **FIP-$O_2CC_3F_7$** with additional MeCN. *Right:* Dependency of the initial reaction rate from the catalyst concentration.

Table 13: Initial reaction rates for varying amounts of catalyst FIP-$O_2CC_3F_7$.

#	**FIP-$O_2CC_3F_7$** (mol%)	[catalyst] (mmol L^{-1})	*r* (mol L^{-1} min^{-1})
1	0.10	0.48	$3.29 \cdot 10^{-4} \pm 3.56 \cdot 10^{-6}$
2	0.75	3.62	$3.62 \cdot 10^{-4} \pm 1.33 \cdot 10^{-5}$
3	1.00	5.01	$4.88 \cdot 10^{-4} \pm 1.86 \cdot 10^{-5}$
4	1.25	6.29	$4.70 \cdot 10^{-4} \pm 1.32 \cdot 10^{-5}$

Logarithmic transformation of the obtained reaction rate data results in a straight line with a slope of 0.15 (Figure 25, *left*) revealing again a reaction order of **0.15** for the catalyst **FIP-$O_2CC_3F_7$**, according to equation 3.

Extrapolation of the yield-time data to t_0 = 0 min (y-axis intercepts in Figure 24, *left*) results in the following plot of the product yield at t_0 = 0 min and the corresponding catalyst loading (Figure 25, *right*). The negative values indicate an induction period.

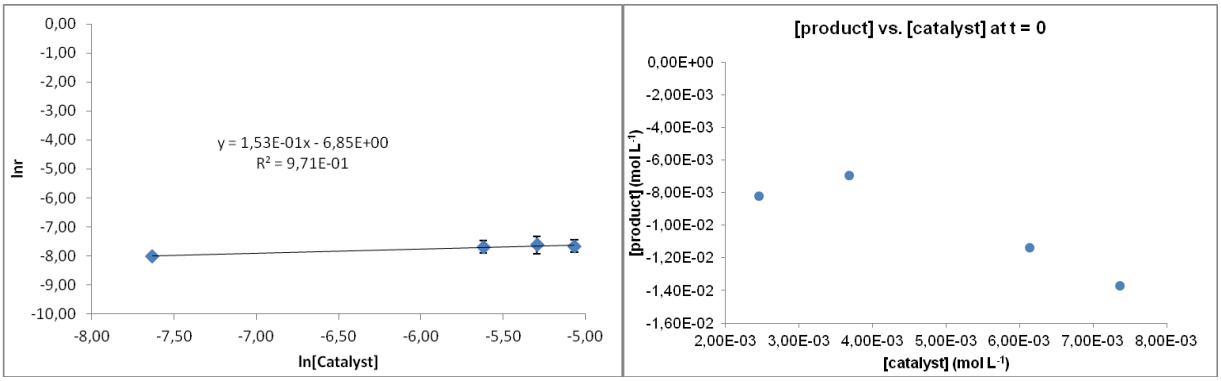
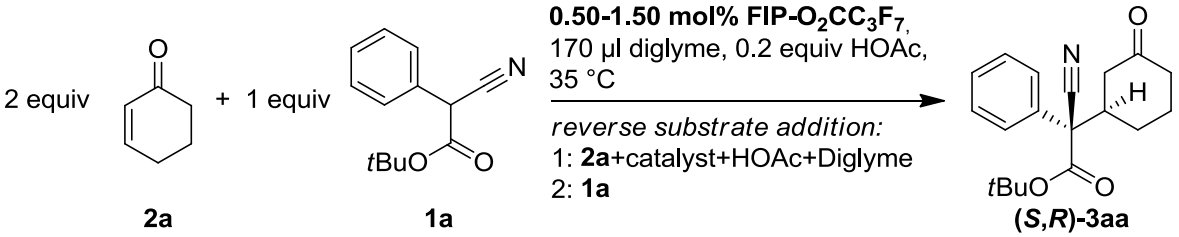


Figure 25: *Left:* Determination of the reaction order for the catalyst **FIP-$O_2CC_3F_7$** in the presence of add. MeCN. *Right:* Dependency of the extrapolated product-yield data at t_0 = 0 min on the catalyst loading.

c) Reverse Substrate Addition



2a **1a**

The third series was performed with catalyst amounts from 0.50 to 1.50 mol%, while all other concentrations were kept constant. The substrates were added in a reverse order. In these experiments the catalyst was first mixed with the enone **2a**, acetic acid and diglyme. The reaction time measurement was started with the addition of the cyanoacetate **1a** in diglyme at 35 °C.

The yield-time graph (Figure 26, *left*) shows that almost identical reaction rates are observed for the tested catalyst concentrations also with reverse order of substrate addition. With higher loadings only slightly increased initial reaction rates are achieved (Figure 26, *right*). The initial reaction rates (Table 14) were calculated from the slope of the yield-time data for each test series.

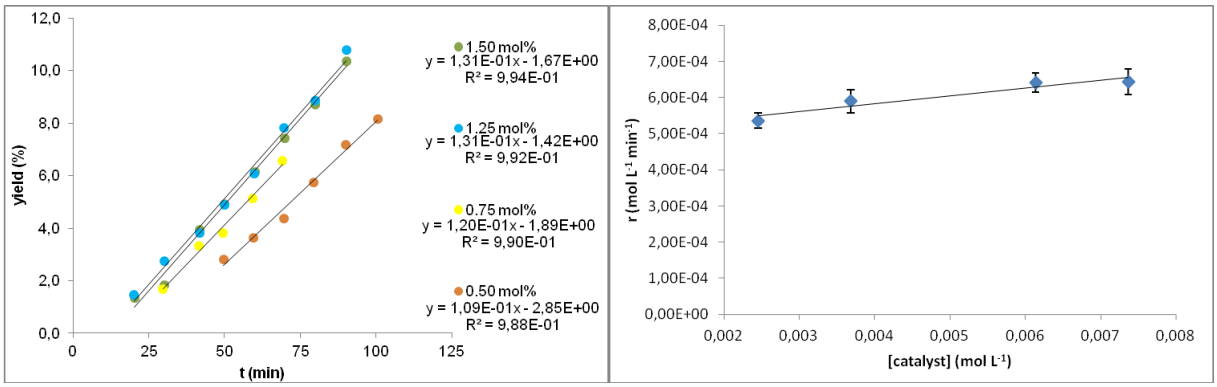


Figure 26: *Left:* Yield-time data for varying amounts of catalyst **FIP-$O_2CC_3F_7$** with reverse addition order of the substrates. *Right:* Dependency of the initial reaction rate from the catalyst concentration.

Table 14: Initial reaction rates for varying amounts of catalyst FIP-$O_2CC_3F_7$.

#	**FIP-$O_2CC_3F_7$** (mol%)	[catalyst] (mmol L^{-1})	*r* (mol L^{-1} min^{-1})
1	0.50	2.45	$5.36 \cdot 10^{-4} \pm 2.07 \cdot 10^{-5}$
2	0.75	3.68	$5.90 \cdot 10^{-4} \pm 3.12 \cdot 10^{-5}$
3	1.25	6.14	$6.42 \cdot 10^{-4} \pm 2.61 \cdot 10^{-5}$
4	1.50	7.36	$6.44 \cdot 10^{-4} \pm 3.45 \cdot 10^{-5}$

Logarithmic transformation of the obtained reaction rate data results in a straight line with a slope of 0.17 (Figure 27, *left*) revealing a reaction order of **0.17** for the catalyst **FIP-$O_2CC_3F_7$**, in agreement to equation 3.

Extrapolation of the yield-time data to t_0 = 0 min (y-axis intercepts in Figure 26, *left*) results in the following plot of the product yield at t_0 = 0 min and the corresponding catalyst loading (Figure 27, *right*). The negative values indicate an induction period.

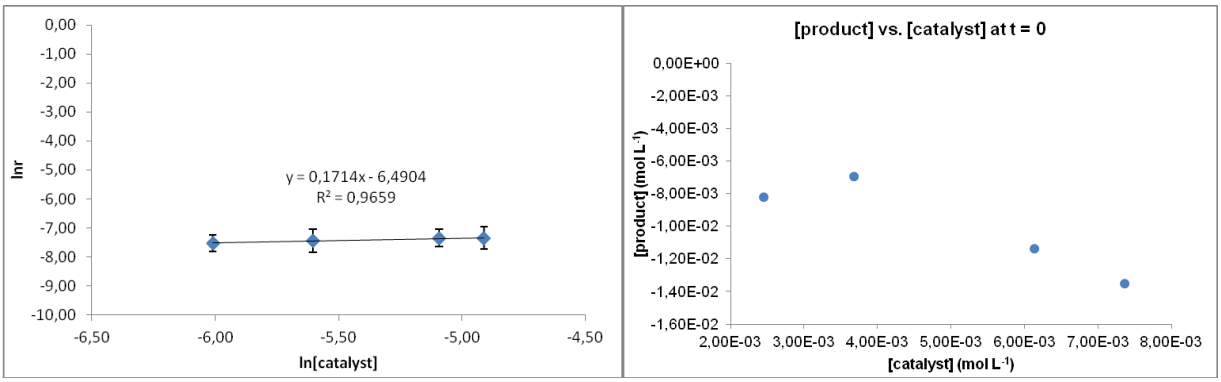
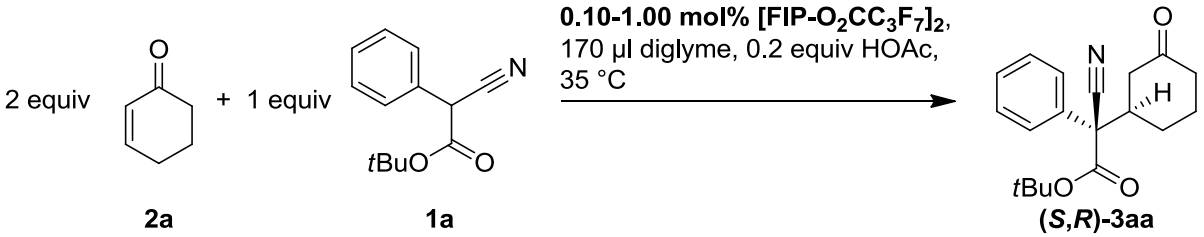


Figure 27: *Left:* Determination of the reaction order for the catalyst **FIP-$O_2CC_3F_7$** with reverse addition order of the substrates. *Right:* Dependency of the extrapolated product-yield data at t_0 = 0 min on the catalyst loading.

d) Use of 0.10 to 1.00 mol% of Dimeric Catalyst



The fourth series was performed with catalyst amounts from 0.10 to 1.00 mol%, while all other concentrations were kept constant. Activation of the catalyst was done in the absence of acetonitrile to form a dimeric catalyst species **[FIP-$O_2CC_3F_7$]$_2$**. The catalysis was performed following the general procedure.

The yield-time graph (Figure 28, *left*) shows that similar reaction rates are observed for the tested catalyst concentrations. With higher loadings only slightly increased initial reaction rates have been noticed (Figure 28, *right*). The initial reaction rates (Table 15) were calculated from the slope of the yield-time data for each test series.

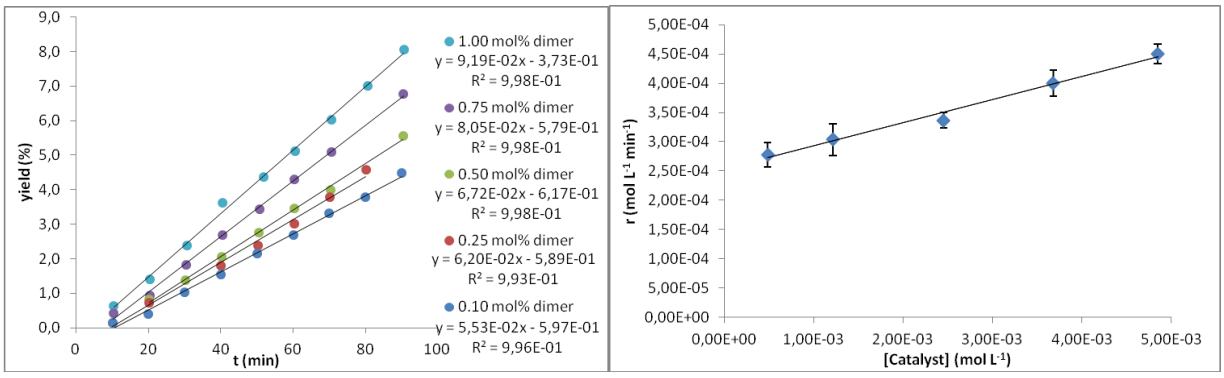


Figure 28: *Left:* Yield-time data for varying amounts of dimeric catalyst **[FIP-$O_2CC_3F_7$]$_2$**. *Right:* Dependency of the initial reaction rate from the catalyst concentration.

Table 15: Initial reaction rates for varying amounts of catalyst [FIP-$O_2CC_3F_7$]$_2$.

#	**FIP-$O_2CC_3F_7$** (mol%)	[catalyst] (mmol L^{-1})	*r* (mol L^{-1} min^{-1})
1	0.10	0.49	$2.78 \cdot 10^{-4} \pm 2.12 \cdot 10^{-5}$
2	0.25	1.22	$3.04 \cdot 10^{-4} \pm 2.69 \cdot 10^{-5}$
3	0.50	2.45	$3.37 \cdot 10^{-4} \pm 1.36 \cdot 10^{-5}$
4	0.75	3.68	$4.00 \cdot 10^{-4} \pm 2.19 \cdot 10^{-5}$
5	1.00	4.50	$4.50 \cdot 10^{-4} \pm 1.63 \cdot 10^{-5}$

Logarithmic transformation of the obtained reaction rate data results in a straight line with a slope of 0.20 (Figure 29, *left*) revealing a reaction order of **0.20** for the dimeric catalyst **[FIP-$O_2CC_3F_7$]$_2$**, according to equation 3.

Extrapolation of the yield-time data to t_0 = 0 min (y-axis intercepts in Figure 28, *left*) results in the following plot of the product yield at t_0 = 0 min and the corresponding catalyst loading (Figure 29, *right*). The negative values indicate an induction period.

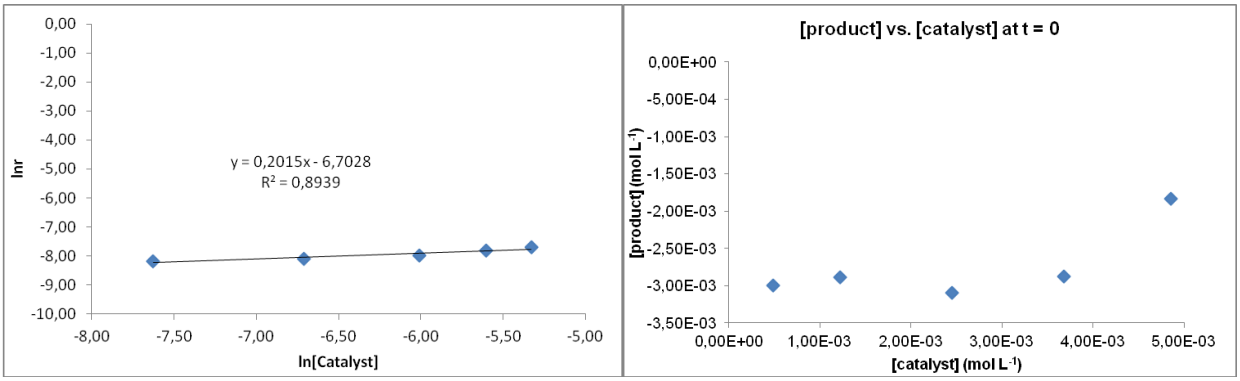


Figure 29: *Left:* Determination of the reaction order for the dimeric catalyst **[FIP-$O_2CC_3F_7$]$_2$**. *Right:* Dependency of the extrapolated product-yield data at t_0 = 0 min on the catalyst loading.

Summary of the Determination of the Reaction Order for the Catalyst FIP-$O_2CC_3F_7$

All four series have provided the same result. Under all tested reaction conditions the reaction order of the catalyst **FIP-$O_2CC_3F_7$** is broken ranging from **0.15** to **0.20**. The very similar initial reaction rates of all experiments (*Left*) and the corresponding logarithmic data (*Right*) for the determination of the reaction order are shown together in Figure 30.

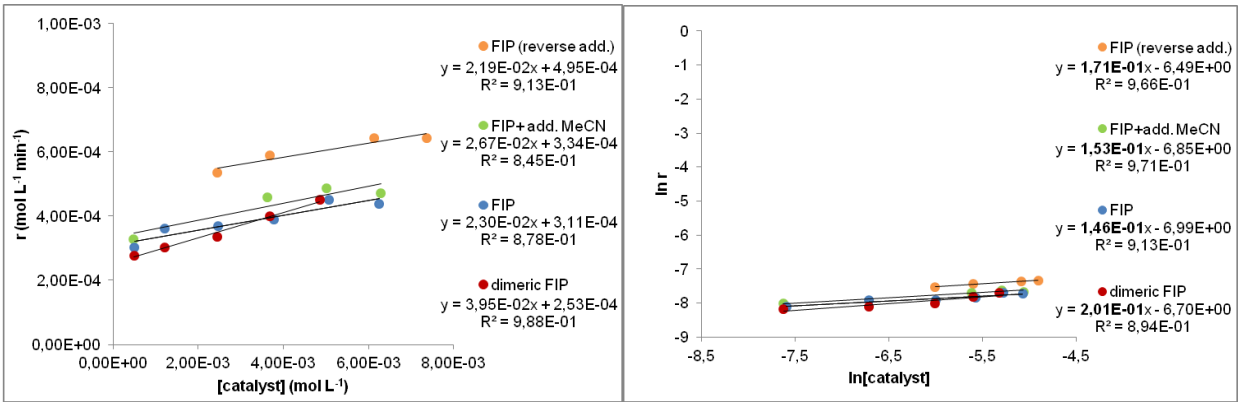
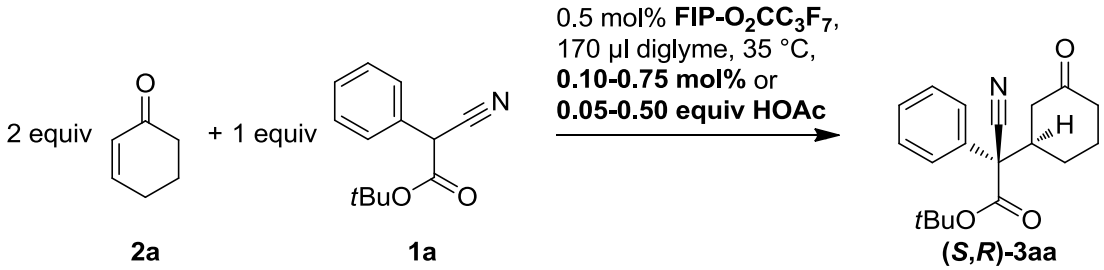


Figure 30: *Left:* Initial reaction rates of the four kinetic series with varying amounts of catalyst. *Right:* Logarithmic initial reaction rates for the determination of the reaction rate of the catalyst **FIP-$O_2CC_3F_7$**.

In all four series an induction period is observed, which could not be suppressed by changing the reaction conditions (additional MeCN, reverse addition order of the substrates or a MeCN free, dimeric catalyst). The induction period might be caused by slow generation of a reactive catalyst-substrate complex. The slow generation of the active catalyst-substrate complex might be caused by an equilibrium of a monomeric and a dimeric catalyst reservoir, where only the monomeric form is active or by slow ligand exchange (e.g. enone coordination might be necessary for a productive reaction pathway), also see chapter "Investigation of the Non-Linear Effect of FIP-$O_2CC_3F_7$".

Reaction Order of Acetic Acid



For the determination of the reaction order of acetic acid the catalysis was performed with a wide range of acetic acid amounts. Either acid amounts smaller or almost equal to the concentration of palladium were used (0.10 to 0.75 mol%), or larger amounts (0.05 to 0.50 equiv) were used.

Nearly identical reaction rates were obtained for [HOAc] ≤ [Pd] (Figure 31, *top*) pointing to a zero order kinetic. In case of [HOAc] >> [Pd] the yield-time graph shows a slight dependency of

the reaction rate from the acetic acid amount (Figure 31, *bottom*). Higher acid amounts result in slightly higher reaction rates.

The initial reaction rates (Table 16) were calculated from the slope of the yield-time data for each test series.

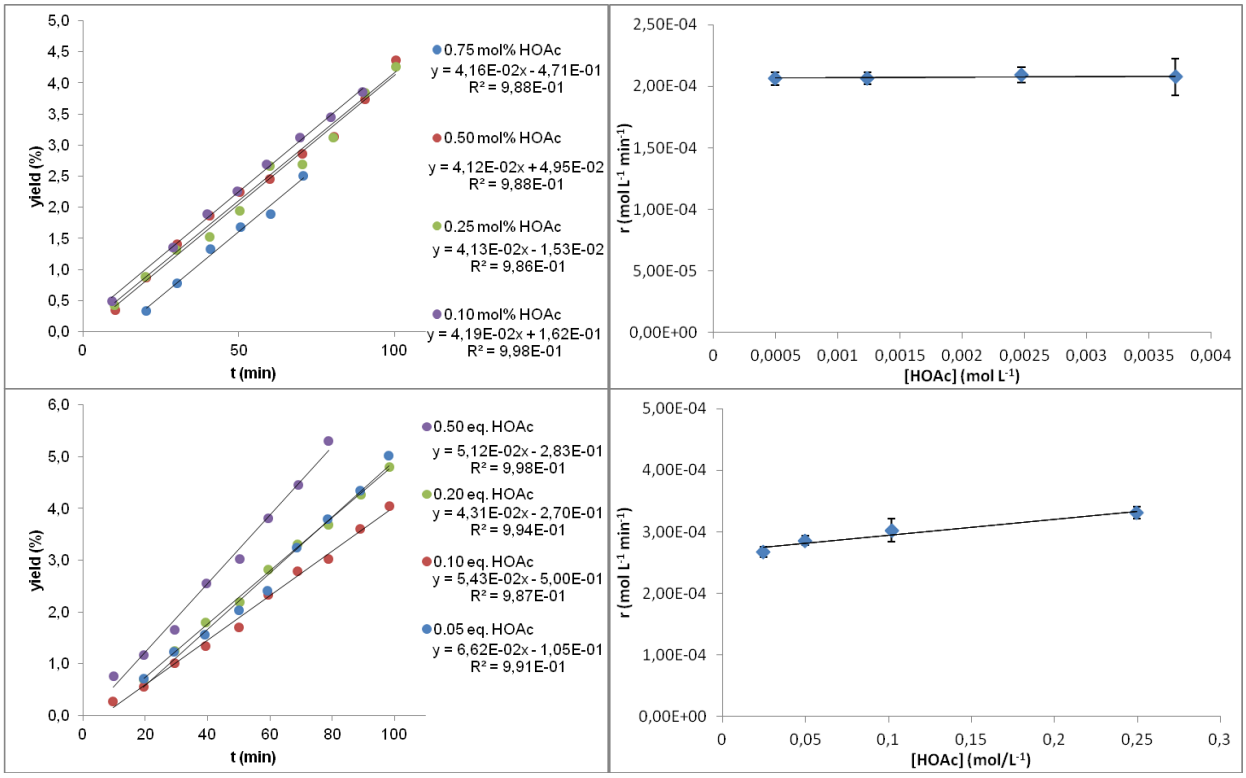


Figure 31: *Top:* Yield-time data and dependency of the initial reaction rate for varying amounts of HOAc, where [HOAc] ≤ [Pd]. *Bottom:* Yield-time data and dependency of the initial reaction rate for varying amounts of HOAc, where [HOAc] >> [Pd].

Table 16: Initial reaction rates for varying amounts of HOAc.

#	**HOAc** (mol%)	[HOAc] (mmol L^{-1})	*r* (mol L^{-1} min^{-1})
1	0.10	0.49	$2.06 \cdot 10^{-4} \pm 5.14 \cdot 10^{-6}$
2	0.25	1.24	$2.07 \cdot 10^{-4} \pm 4.73 \cdot 10^{-6}$
3	0.50	2.47	$2.09 \cdot 10^{-4} \pm 6.23 \cdot 10^{-6}$
4	0.75	3.71	$2.07 \cdot 10^{-4} \pm 1.46 \cdot 10^{-5}$
5	5	24.7	$2.68 \cdot 10^{-4} \pm 8.02 \cdot 10^{-6}$
6	10	49.7	$2.85 \cdot 10^{-4} \pm 7.61 \cdot 10^{-6}$
7	20	101.8	$3.02 \cdot 10^{-4} \pm 1.87 \cdot 10^{-4}$
8	50	249.6	$3.31 \cdot 10^{-4} \pm 9.77 \cdot 10^{-6}$

Logarithmic transformation of the obtained reaction rate data and the corresponding plots result in straight lines with a slope of 0.005 for [HOAc] ≤ [Pd] (Figure 32, *left*) and 0.09 for [HOAc] >> [Pd] (Figure 32, *right*). Corresponding to equation 3 the reaction order of acetic acid is determined to be **zero**. Both experiments lead to the same result.

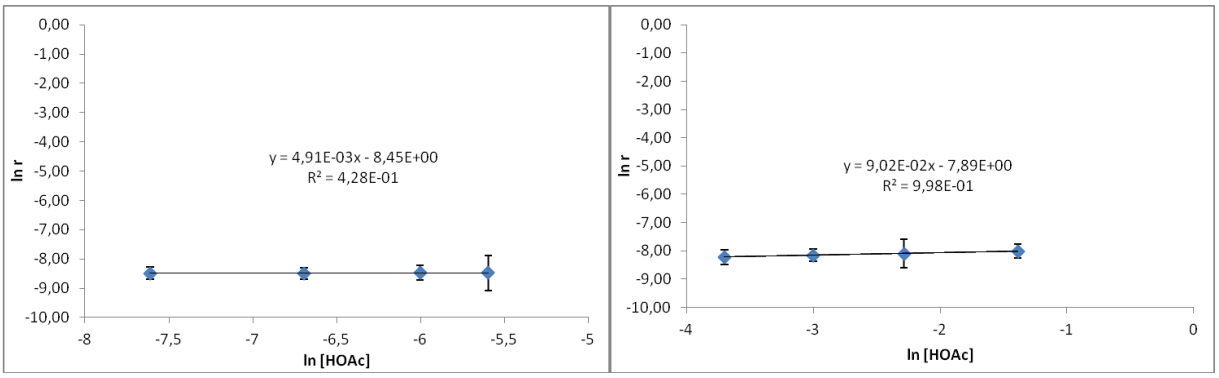
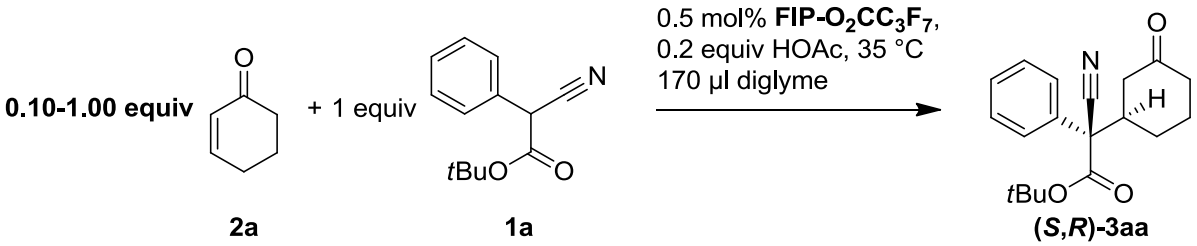


Figure 32: Determination of the reaction order for acetic acid. *Left:* [HOAc] ≤ [Pd]. *Right:* [HOAc] >> [Pd].

Reaction Order of Enone 2a



For the determination of the reaction order of the enone 2a **the catalysis was performed with enone** 2a **amounts from 0.10 to 1.00 equiv, while all other concentrations were kept constant. The yield-time data shows a dependency of the initial reaction rate on the enone concentration (Figure 33, *left*). With higher concentrations the reaction occurs faster (Figure 33, *right*). The following initial reaction rates (**

Table 17) were calculated from the slope of the yield-time data.

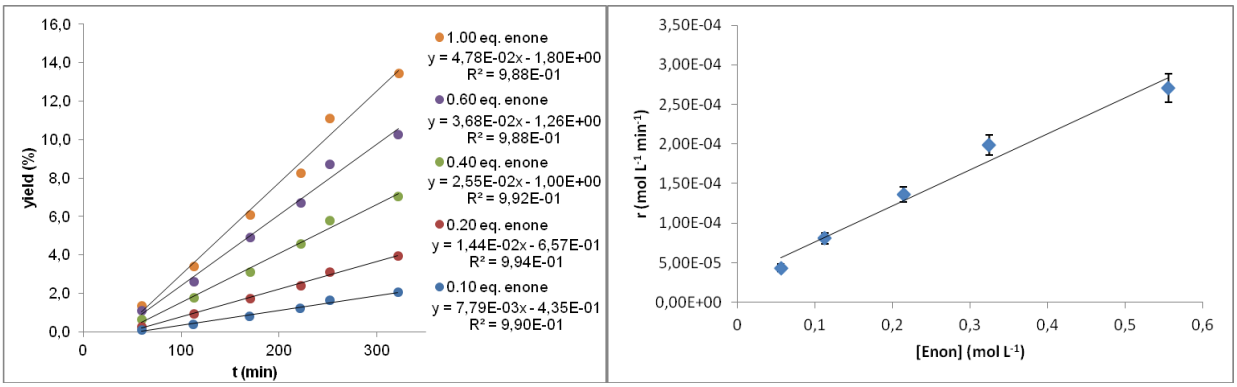


Figure 33: *Left:* Yield-time data for varying amounts of enone. *Right:* Plot of the initial reaction rates as a function of the enone concentration.

Table 17: Initial reaction rates for varying amounts of enone.

#	Amount enone (equiv)	[enone] (mol L^{-1})	*r* (mol L^{-1} min^{-1})
1	0.10	0.056	$4.35 \cdot 10^{-5} \pm 4.44 \cdot 10^{-6}$
2	0.20	0.113	$8.10 \cdot 10^{-5} \pm 6.72 \cdot 10^{-6}$
3	0.40	0.214	$1.36 \cdot 10^{-4} \pm 9.88 \cdot 10^{-6}$
4	0.60	0.324	$1.99 \cdot 10^{-4} \pm 1.31 \cdot 10^{-5}$
5	1.00	0.555	$2.71 \cdot 10^{-4} \pm 1.80 \cdot 10^{-5}$

Logarithmic transformation of the initial reaction rate data results in a straight line with a slope of 0.81 (Figure 34) revealing a reaction order of **0.81** for the enone, according to equation 3.

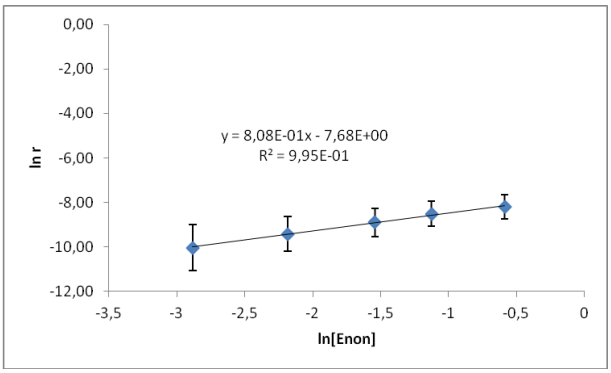
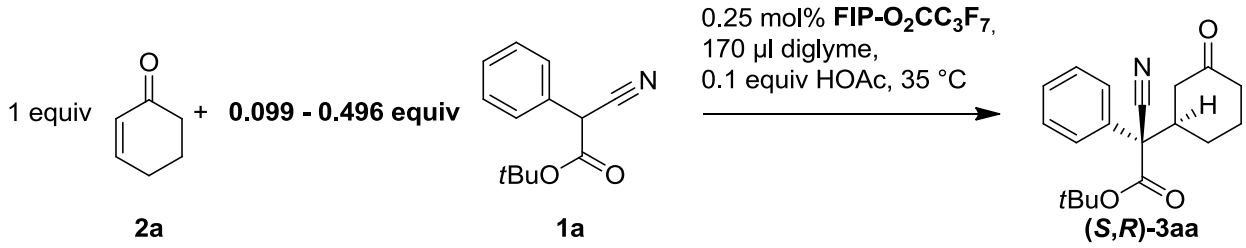


Figure 34: Determination of the reaction order for the enone.

Reaction Order of α-Phenyl-α-cyanoacetate (1a)



For the determination of the reaction order of the α-phenyl-α-cyanoacetate **1a** the catalysis was performed with α-phenyl-α-cyanoacetate amounts from 0.099 to 0.496 equiv, while all other concentrations were kept constant. The [product]-time data shows a dependency of the reaction rate from the cyanoacetate concentration (Figure 35, *left*). With higher cyanoacetate concentrations the reaction proceeds faster (Figure 35, *right*). The following initial reaction rates (Table 18) were calculated from the slope of the [product]-time data.

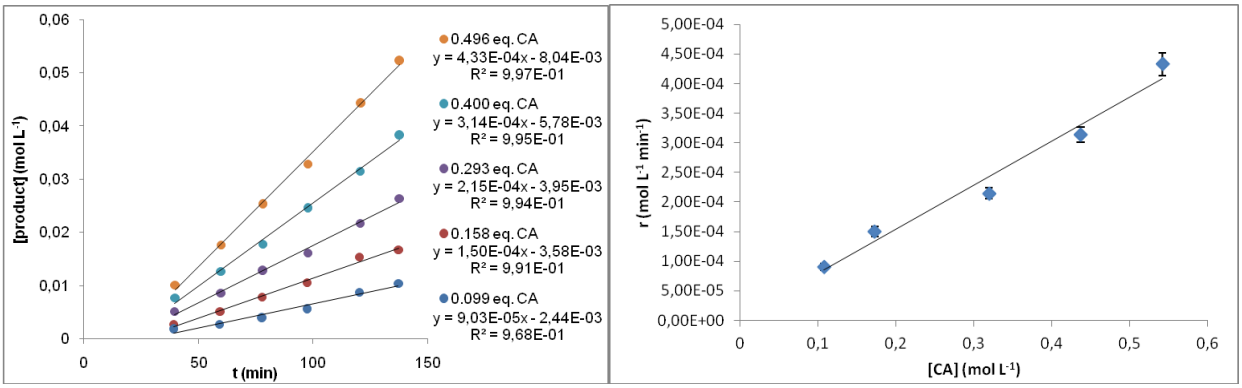


Figure 35: *Left:* [Product]-time data for varying amounts of α-phenyl-α-cyanoacetate. *Right:* Initial reaction rates as a function of the cyanoacetate concentration.

Table 18: Initial reaction rates for varying amounts of α-phenyl-α-cyanoacetate.

#	Amount CA (equiv)	[CA] (mol L^{-1})	*r* (mol L^{-1} min^{-1})
1	0.099	0.108	$9.03 \cdot 10^{-5} \pm 5.30 \cdot 10^{-6}$
2	0.158	0.173	$15.0 \cdot 10^{-5} \pm 9.03 \cdot 10^{-6}$
3	0.293	0.217	$23.1 \cdot 10^{-5} \pm 9.26 \cdot 10^{-6}$
4	0.400	0.437	$31.4 \cdot 10^{-5} \pm 1.32 \cdot 10^{-5}$
5	0.496	0.542	$43.3 \cdot 10^{-5} \pm 1.91 \cdot 10^{-5}$

Logarithmic transformation of the initial reaction rate data results in a straight line with a slope of 0.91 (Figure 36) revealing a reaction order of **0.91** for the α-phenyl-α-cyanoacetate, according to equation 3.

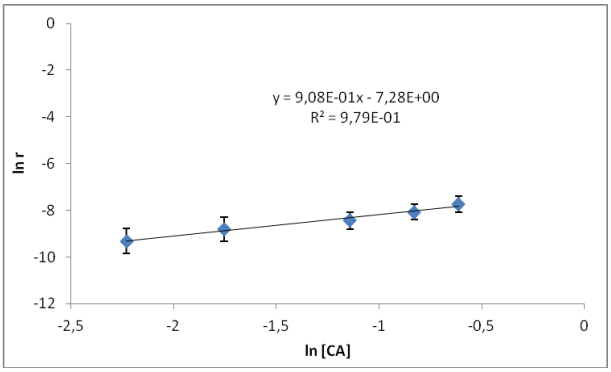
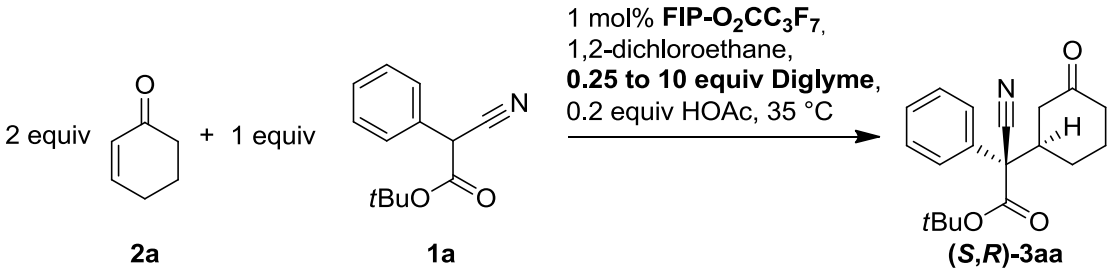


Figure 36: Determination of the reaction order for the α-phenyl-α-cyanoacetate.

Influence of Diglyme on the Reaction Rate



To investigate the influence of diglyme on the reaction rate of the catalysis reaction the experiments were performed in 1,2-dichloroethane with varying amounts of diglyme (0.25 to 10 equiv of diglyme). The total reaction volume of each experiment was 170 µL solvent mixture. The yield-time data shows a dependency for the diglyme amounts on the reaction rate (Figure 37). The following initial reaction rates were calculated from the slope of the yield-time data (Table 19).

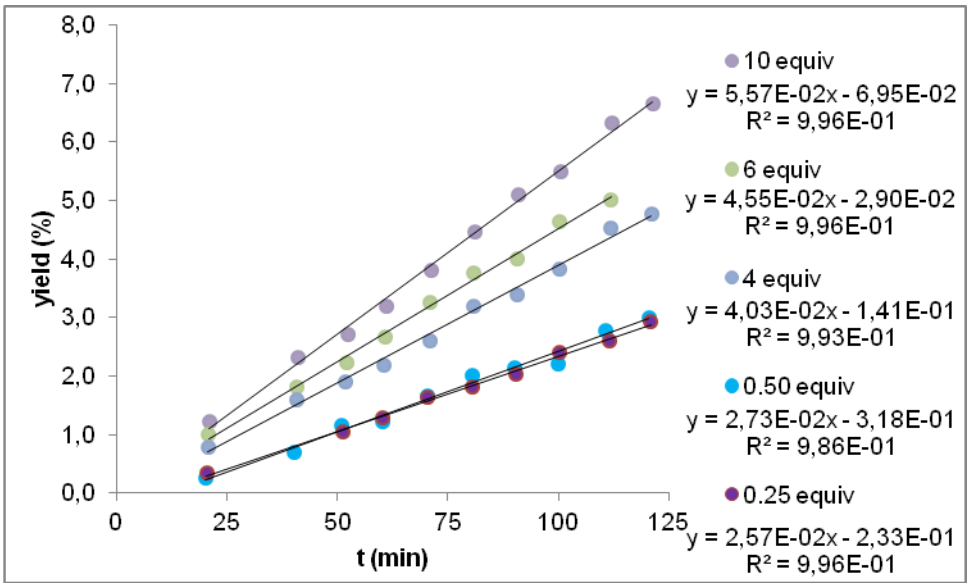


Figure 37: Yield-time data for varying amounts of diglyme.

Table 19: Initial reaction rates for varying amounts of diglyme.

#	Diglyme (equiv)	Diglyme (vol%)	[Diglyme] (mol L^{-1})	*r* (mol L^{-1} min^{-1})
1	0.25	2.0	$1.24 \cdot 10^{-1}$	$1.27 \cdot 10^{-4} \pm 4.04 \cdot 10^{-6}$
2	0.5	3.9	$2.47 \cdot 10^{-1}$	$1.35 \cdot 10^{-4} \pm 6.75 \cdot 10^{-6}$
3	4.0	31.4	1.98	$1.99 \cdot 10^{-4} \pm 2.46 \cdot 10^{-6}$
4	6.0	47.0	2.97	$2.25 \cdot 10^{-4} \pm 2.61 \cdot 10^{-6}$
5	10	78.2	4.95	$2.76 \cdot 10^{-4} \pm 3.28 \cdot 10^{-6}$

The initial reaction rate as function of the diglyme concentration shows slightly higher initial reaction rates when higher amounts of diglyme are present (Figure 38). Determination of the reaction order for diglyme under these reaction conditions results in a broken reaction order of **0.20**. The influence of diglyme is thus lower than with the bimetallic catalyst **FBIP-$O_2CC_3F_7$** (reaction order 0.46, for comparison see "Kinetic Investigations to the FBIP Catalyzed Asymmetric Michael-Addition").

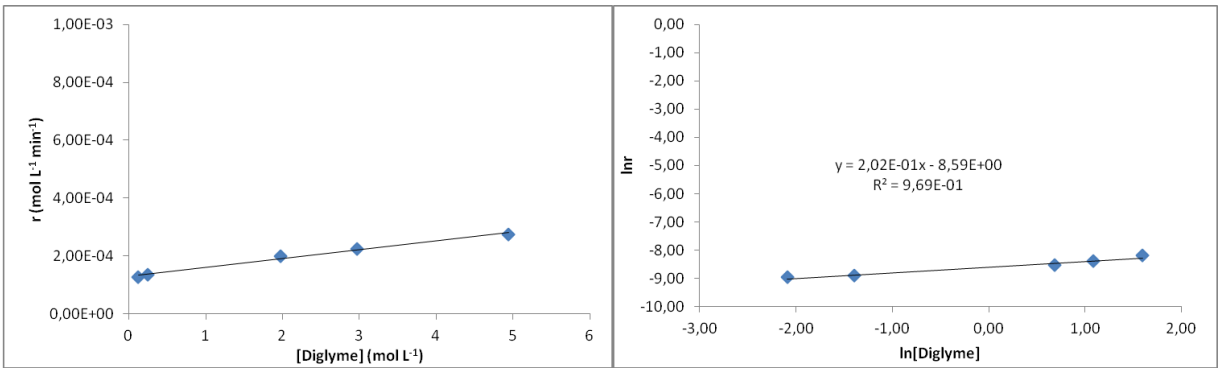


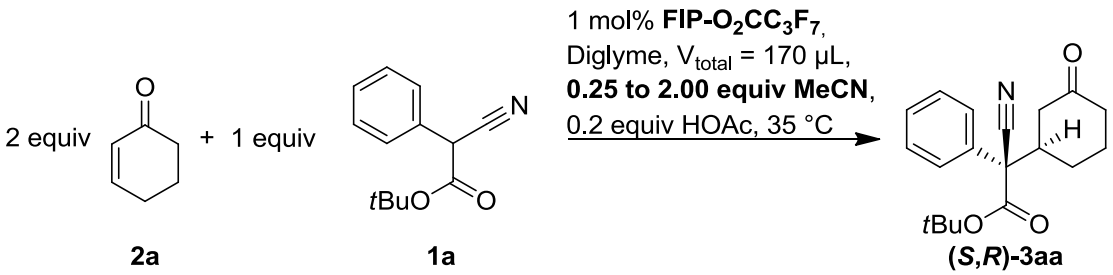
Figure 38: Initial reaction rates as a function of the diglyme concentration and the logarithmic data.

In contrast to the reaction with the bimetallic catalyst **FBIP-$O_2CC_3F_7$** the experiments with the monometallic catalyst **FIP-$O_2CC_3F_7$** in 1,2-dichloroethane have resulted in poor selectivity data, almost independent on the used amount of diglyme (Table 20). Concerning the enantioselectivity the reactions using a solvent mixture proceeded even worse than with pure 1,2-dichloroethane. However, an improved diastereoselectivity is achieved compared to experiments in pure DCE.

Table 20: Influence of diglyme on the stereoselectivity.

#	Diglyme (equiv)	Diglyme (vol%)	$ee_{(S,R)}$ (%)	$ee_{(R,R)}$ (%)	$dr_{(S,R+R,S):(R,R+S,S)}$
1	-	0	64	35	49:51
3	0.25	2.0	-15	2	67:33
4	0.50	3.9	-5	6	66:34
5	4.0	31.4	17	30	70:30
6	6.0	47.0	22	18	72:28
7	10	78.2	26	15	74:26
8	-	100	89	33	71:29

Influence of MeCN on the Reaction Rate



To investigate the influence of MeCN on the reaction rate of the catalysis reaction the experiments were performed in diglyme with varying amounts of MeCN (0.125 to 2.00 equiv of MeCN). The total reaction volume of each experiment was 170 µL solvent mixture. The yield-time data shows a decrease of the initial reaction rate with increased MeCN amounts (Figure 39). The following initial reaction rates were calculated from the slope of the yield-time data (Table 21).

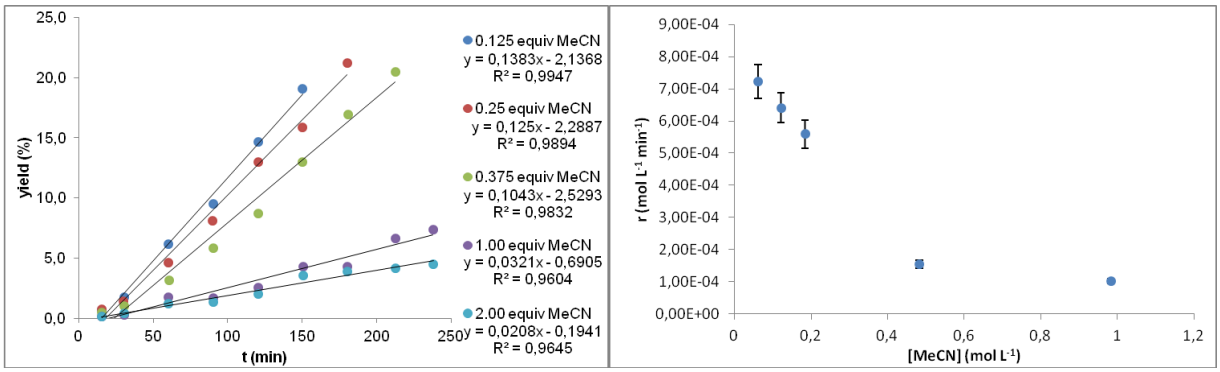


Figure 39: Yield-time data for varying amounts of MeCN and initial reaction rates as a function of the MeCN concentration.

Table 21: Initial reaction rates for varying amounts of MeCN.

#	MeCN (equiv)	[MeCN] (mol L^{-1})	*r* (mol L^{-1} min^{-1})
1	0.125	$6.14 \cdot 10^{-2}$	$7.23 \cdot 10^{-4} \pm 5.31 \cdot 10^{-5}$
2	0.25	$1.22 \cdot 10^{-1}$	$6.41 \cdot 10^{-4} \pm 4.64 \cdot 10^{-5}$
3	0.375	$1.85 \cdot 10^{-1}$	$5.59 \cdot 10^{-4} \pm 4.35 \cdot 10^{-5}$
4	1.00	$4.83 \cdot 10^{-1}$	$1.55 \cdot 10^{-4} \pm 1.27 \cdot 10^{-5}$
5	2.00	$9.83 \cdot 10^{-1}$	$1.02 \cdot 10^{-4} \pm 7.39 \cdot 10^{-6}$

Logarithmic transformation of the initial reaction rate data results in a straight line with a slope of –0.79 (Figure 40) revealing a broken, negative reaction order of **–0.79** for MeCN under these

reaction conditions. The negative reaction order can be explained by reversible coordination of MeCN to the catalyst and thereby inhibition of the active catalyst.

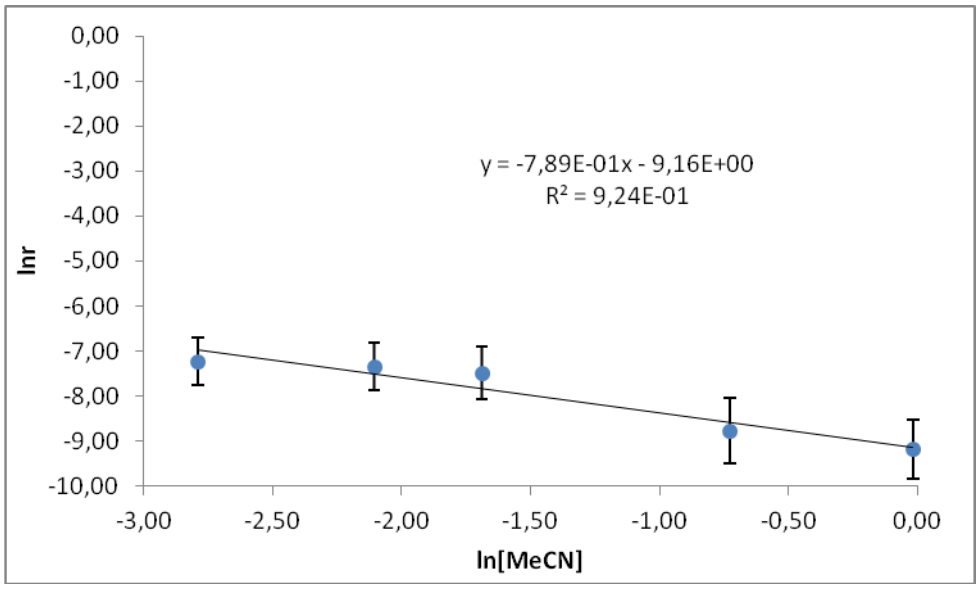


Figure 40: Determination of the reaction order of MeCN.

Investigation of the Non-Linear Effect of FIP-$O_2CC_3F_7$

For the investigation of the presence of a non-linear effect in the **FIP-$O_2CC_3F_7$** catalysis, a series of catalyst mixtures with defined enantiomeric excesses were used in the Michael-addition of **1a** to **2a** following GP3 (Table 22). Both the monomeric and the dimeric systems show a positive non-linear effect (Figure 41).

Table 22: Investigation on the non-linear effect of monomeric and dimeric FIP-$O_2CC_3F_7$.

	monomeric catalyst		*dimeric catalyst*	
#	*ee* of monomeric catalyst (%)	$ee_{product}$ (%)	*ee* of dimeric catalyst (%)	$ee_{product}$ (%)
1	0	3	0	0
2	15	15	15	18
3	30	34	30	34
4	45	50	45	53
5	60	53	60	65
6	75	75	75	83
7	>99	85	>99	89

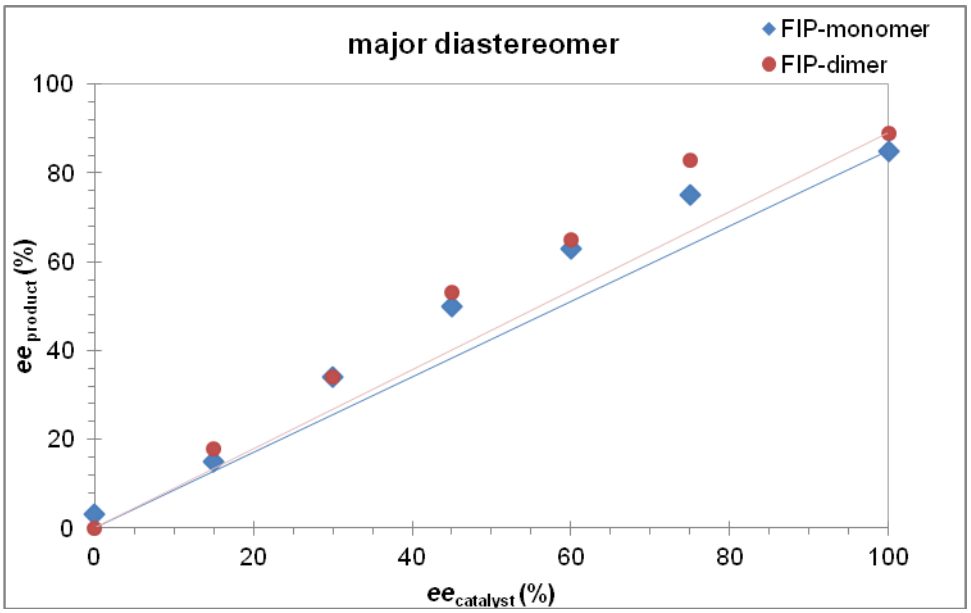


Figure 41: Investigation of the non-linear effect of monomeric and dimeric **FIP-$O_2CC_3F_7$**.

Spectroscopic Investigation of the Nature of FIP-$O_2CC_3F_7$

The presence of the above mentioned equilibrium between a monomeric and dimeric catalyst species is confirmed by ^{1}H NMR measurements. The ^{1}H NMR of **FIP-$O_2CC_3F_7$** (6.17 mg) in $CDCl_3$ (600 µL) shows a monomeric (*e.g.*: δ = 5.80 ppm, Cp-*H*) and a dimeric (*e.g.*: δ = 5.75 ppm, Cp-*H*) form with a ratio of 3.8:1 (Figure 42, spectrum a). Addition of 50 equiv of MeCN slightly pushes the equilibrium to the side of the monomeric species (ratio 6.4:1, spectrum b), while with 100 equiv MeCN only the monomeric catalyst **FIP-$O_2CC_3F_7$** is visible (spectrum c). ^{1}H-NMR of **FIP-$O_2CC_3F_7$** in MeCN-D_3 shows that the Cp-*H* and C*H*Ph signals between δ = 4.74 and 4.43 ppm are shifted (spectrum d), pointing to a new species with probably two MeCN molecules coordinating to the Pd center.

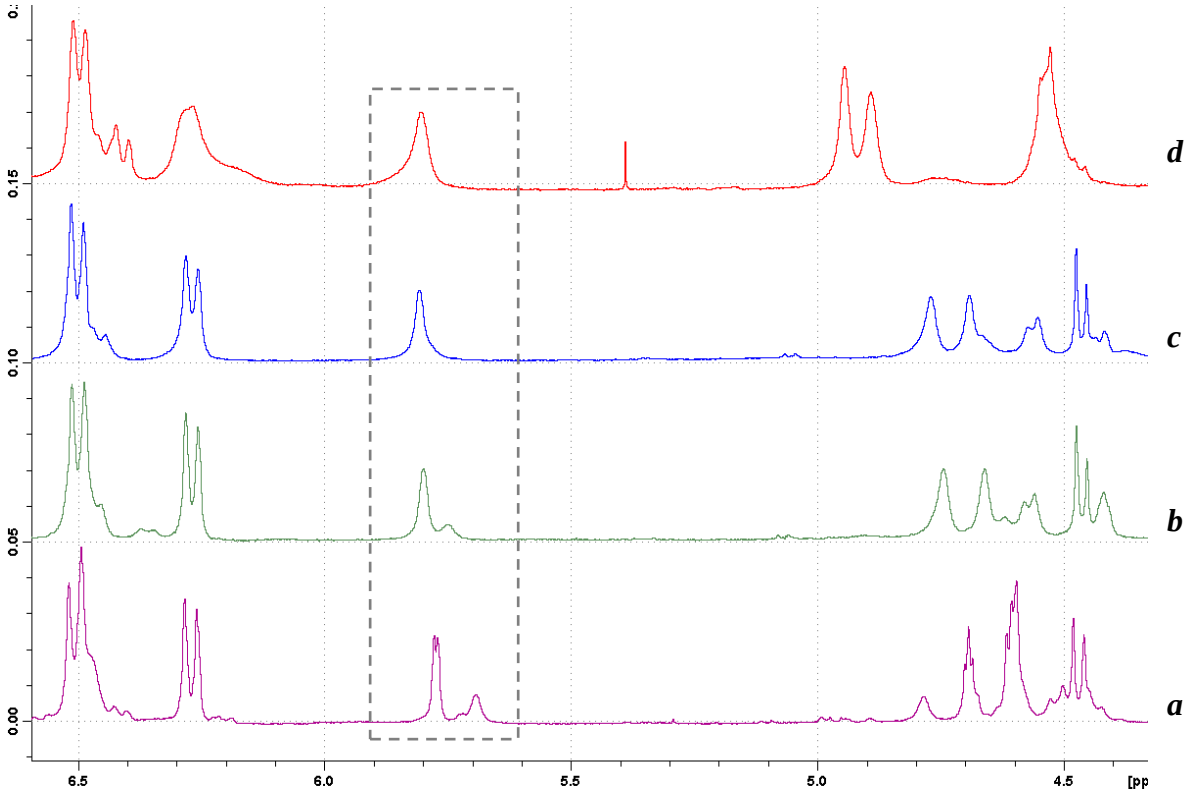


Figure 42: Detail of the ^{1}H NMR of **FIP-$O_2CC_3F_7$** in a) $CDCl_3$, b) $CDCl_3$ + 50 equiv MeCN, c) $CDCl_3$ +100 equiv MeCN and d) MeCN-D_3.

^{1}H NMR (500 MHz, $CDCl_3$, 21 °C) of the monomeric form in the presence of 100 equiv MeCN: δ = 7.55 (*d*, *J* = 7.8, 2H, arom. *H*), 7.29 (*d*, *J* = 7.8, 2H, arom. *H*), 7.24-7.19 (*m*, 12H, arom. *H*), 7.12-6.99 (*m*, 19H, arom. *H*), 6.89 (*b*, 2H, arom. *H*), 6.50 (*d*, *J* = 6.7, 2H, arom. *H*), 6.27 (*d*, *J* = 7.8, 1H, arom. *H*), 5.81 (*b*, 1H, Cp-*H*), 4.74-4.42 (*m*, 3H, Cp-*H* and C*H*Ph), 2.50 (*s*, 3H, $C_6H_4CH_3$), 2.21 (*s*, 3H, Pd←NCCH_3), 2.00 (*s*, free NCCH_3).

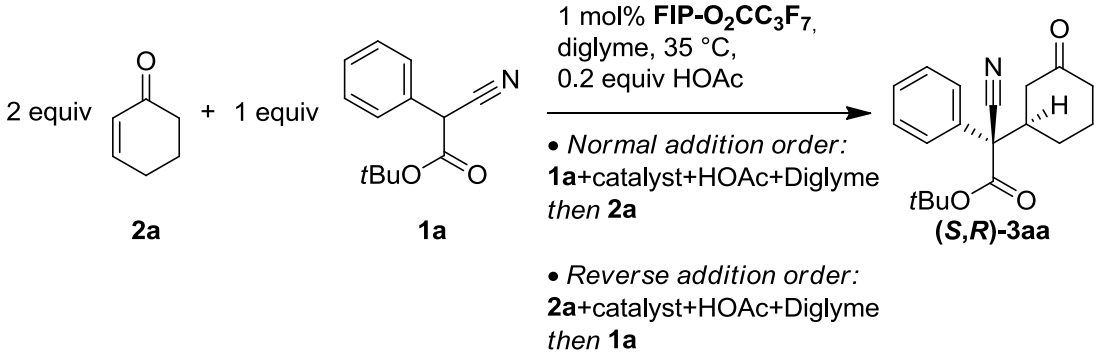
Course of the Reaction

The investigation of the course of the reaction was performed to gain a detailed insight into the evolution of the enantio- and diastereoselectivity of the reaction. For this purpose the reaction was carried out according to GP3, but on a larger scale using 0.46 mmol of **1a** in diglyme (850 µL). For the analysis 25 µL of the reaction mixture were added to 500 µL of acetonitrile to stop the reaction and release product and starting material from the catalyst. The sample was filtered over a short pad of silica to completely remove the catalyst. The filter cake was washed with petrol ether: ethyl acetate (4:1). After removal of the solvent and an excess of enone **2a** the

samples were analyzed by RP-HPLC and chiral stationary phase HPLC to determine yield, enantiomeric excess and diasteromeric ratio.

Two different experiments were performed:

- normal substrate addition order (enone **2a** is added as last component),
- and reverse substrate addition (cyanoacetate **1a** is added as last component).



The collected yield, enantioselectivity data and diastereoselectivity data of both experiments are shown in Table 23.

Table 23: Collected data during the reaction.

	normal addition order					*reverse addition order*				
#	Time (min)	Conv. (%)	$ee_{(S,R)}$ (%)	$ee_{(R,R)}$ (%)	$dr_{(S,R+R,S):(R,R+S,S)}$	Time (min)	Conv. (%)	$ee_{(S,R)}$ (%)	$ee_{(R,R)}$ (%)	$dr_{(S,R+R,S):(R,R+S,S)}$
1	9.88	1.90	15	28	49:51	5.17	0.10	-5	58	48:52
2	14.83	2.66	16	11	47:53	10.27	0.29	2	48	46:54
3	30.25	2.01	50	6	48:52	15.5	0.40	15	59	44:56
4	44.50	3.30	52	3	51:49	20.12	0.55	50	26	46:54
5	112.85	10.37	73	-5	59:41	25.33	0.82	73	23	46:54
6	171.92	15.87	76	-2	62:38	50.17	1.95	75	-10	52:48
7	236.63	25.07	81	1	65:35	60.43	2.39	76	-15	53:47
8	310.25	33.89	82	8	67:33	97.92	4.82	74	-5	57:43
9	359.58	43.90	83	11	68:32	125.92	7.04	74	-12	56:44
10	476.55	49.13	85	13	70:30	180.58	11.89	75	-5	62:38
11	536.23	55.15	85	14	70:30	240.17	17.57	84	-6	64:36
12	591.95	59.61	85	14	70:30	300.67	23.95	81	-3	65:34
13	-					362.30	30.18	85	-2	64:36
14	20h	90	89	33	71:29	20h	-	86	17	69:31

The yield-time curves of both reactions are similar (Figure 43). The reaction with normal addition order was followed for nearly 10 h. Using the reverse addition order the reaction was monitored for 6 h.

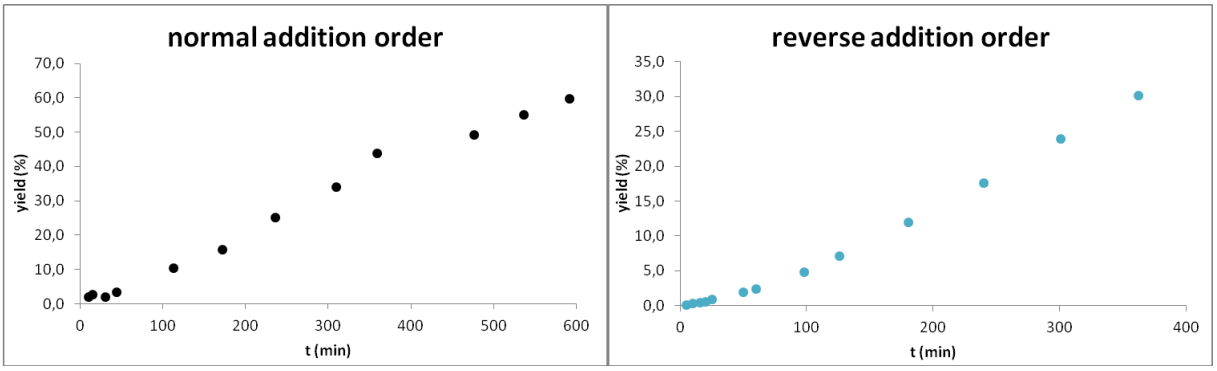


Figure 43: Time depending yields for the experiments with normal and reverse addition order of the substrates.

A slight difference for both experiments is the development of the enantiomeric excess (Figure 44). When the reaction is performed with the normal addition order of the substrates the *ee* of both diastereomers is moderate in the first minutes (Table 23, #1 to 5 *normal addition order*) until it reaches its final value after approximately six hours. When the addition order is changed and the cyanoacetate is added as last component, the *ee* of both diastereomers is in the first minutes again only moderate (Table 23, #1 to 4 *reverse addition order*) but increases faster than in the other experiment. The final value of the enantiomeric excesses is already reached after around three hours, but is in general slightly lower than the final *ee* value of the product, if the substrates are added in the normal order (Table 23, #14).

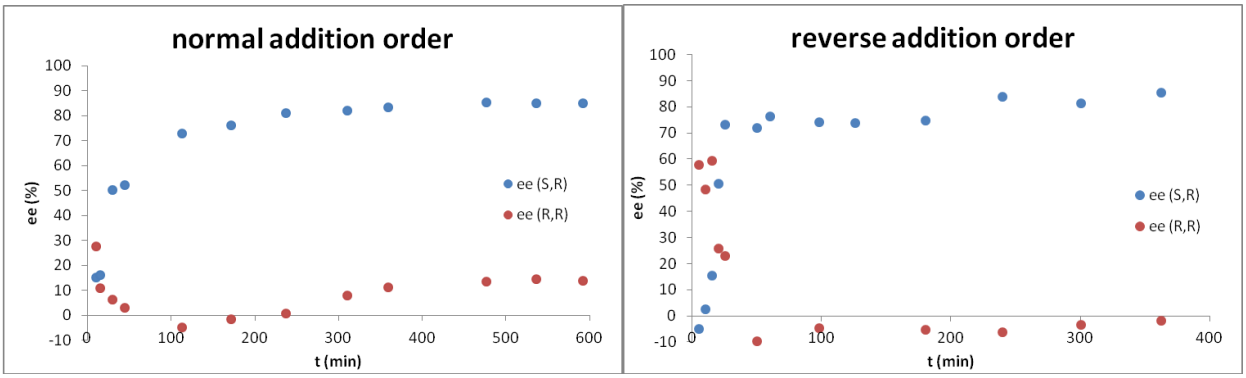


Figure 44: Development of the enantioselectivity in the experiments with normal and reverse addition order of the substrates.

A nearly identical course is observed for the development of the diastereomeric ratio for both experiments (Figure 45). Independent from the addition order of the substrates the reaction starts with poor diastereoselectivity (Table 23). With increasing reaction time the *dr* increases slowly

until the final value is reached after several hours. The final diastereomeric ratio is only little lower when the substrates are added in reverse order (Table 23, #14).

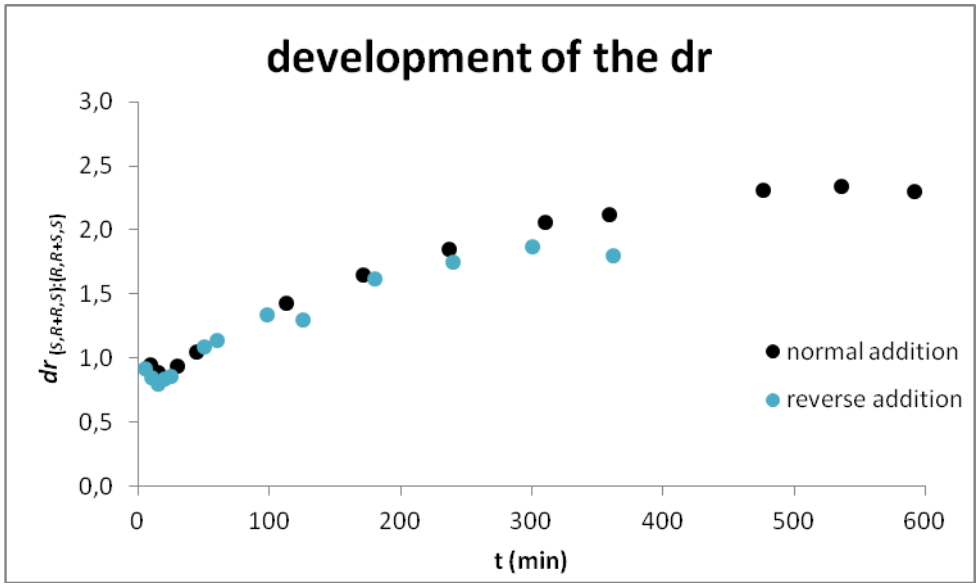


Figure 45: Development of the diastereomeric ratio in the experiments with normal and reverse addition order of the substrates.

In general the substrate addition order has only a low impact on the course of the **FIP-$O_2CC_3F_7$** catalyzed asymmetric Michael-Addition of **1a** to **2a**. Under the tested reaction conditions the catalysis with reverse addition order of the substrates results in a faster formation of the desired (*S*,*R*)-enantiomer, but proceeds with little lower enantio- and diastereoselectivity in the end.

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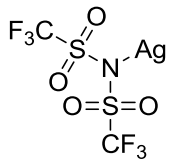
NMR Spectra

Silver(I)(bistrifluoromethane)sulfonimide



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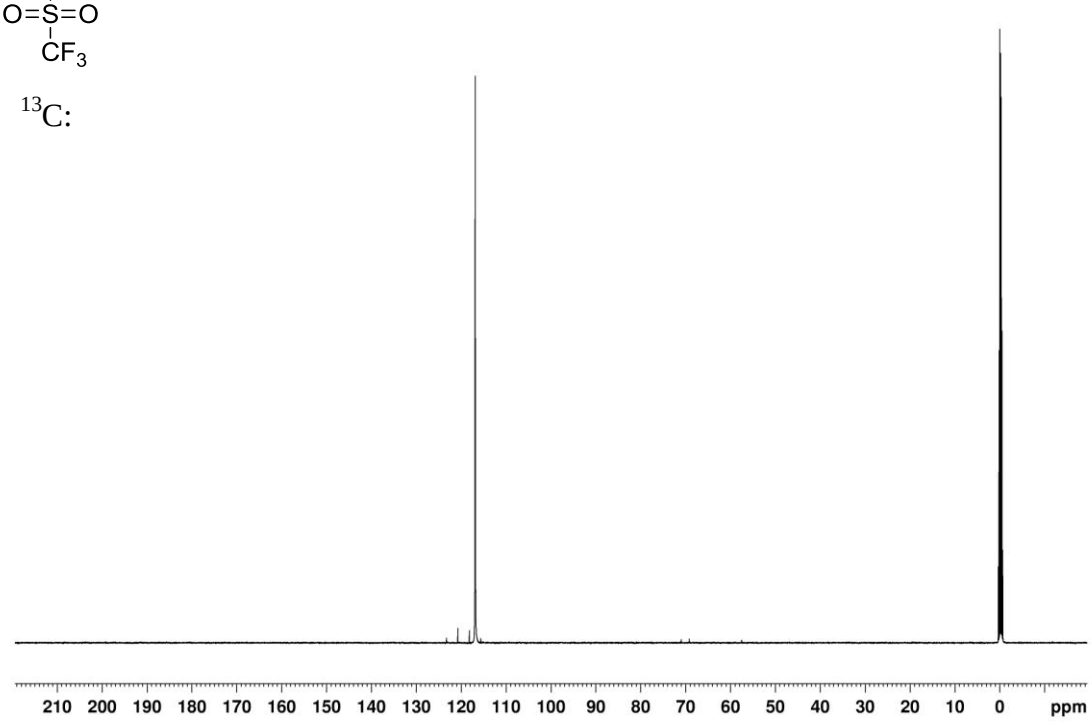

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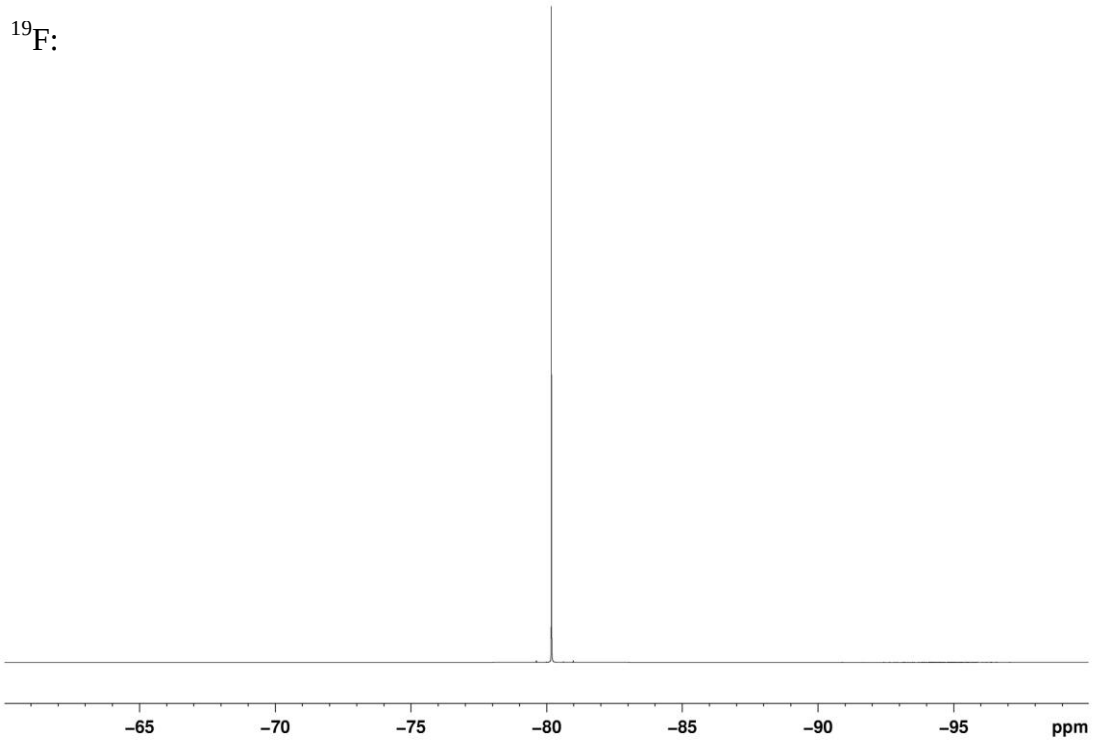
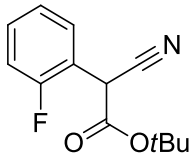


tert-Butyl-2-cyano-(*o*-fluorophenyl)acetate (**1k**)



1k

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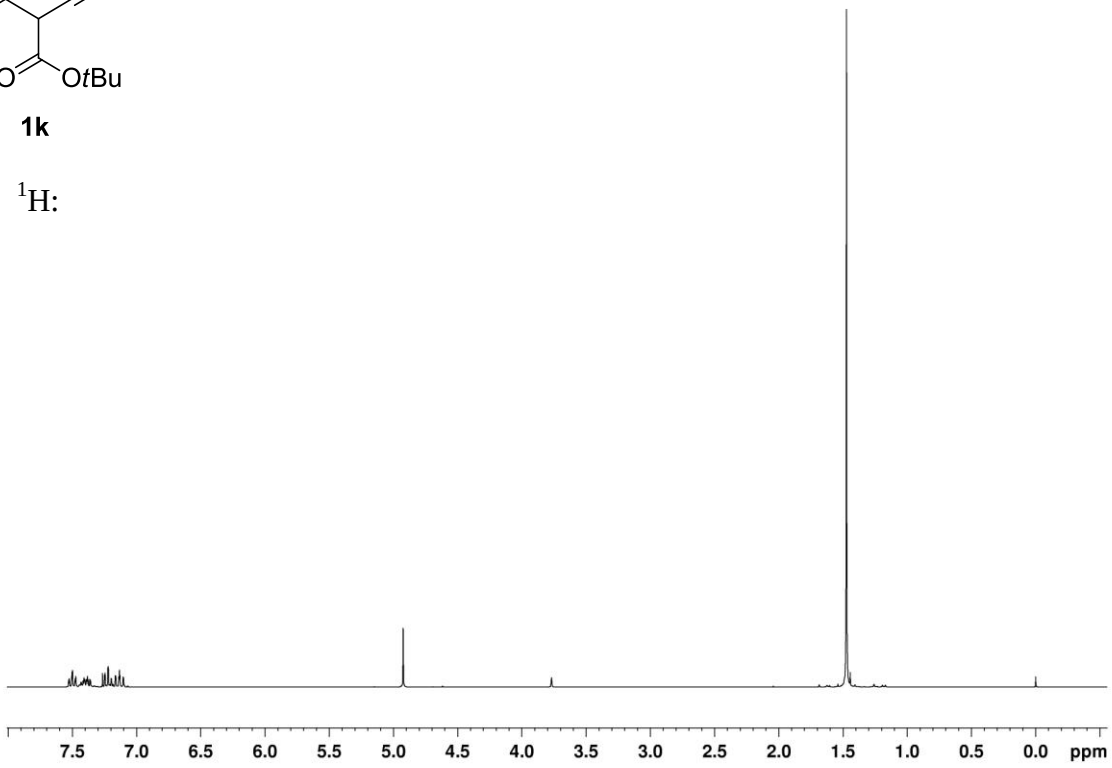

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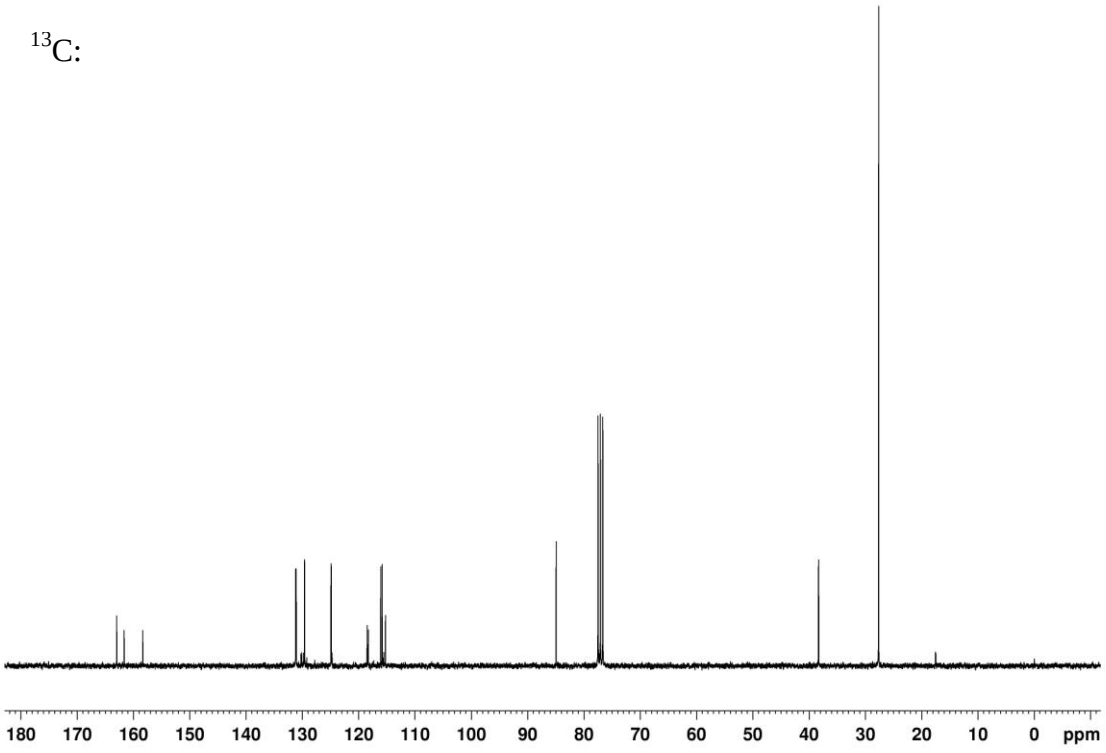

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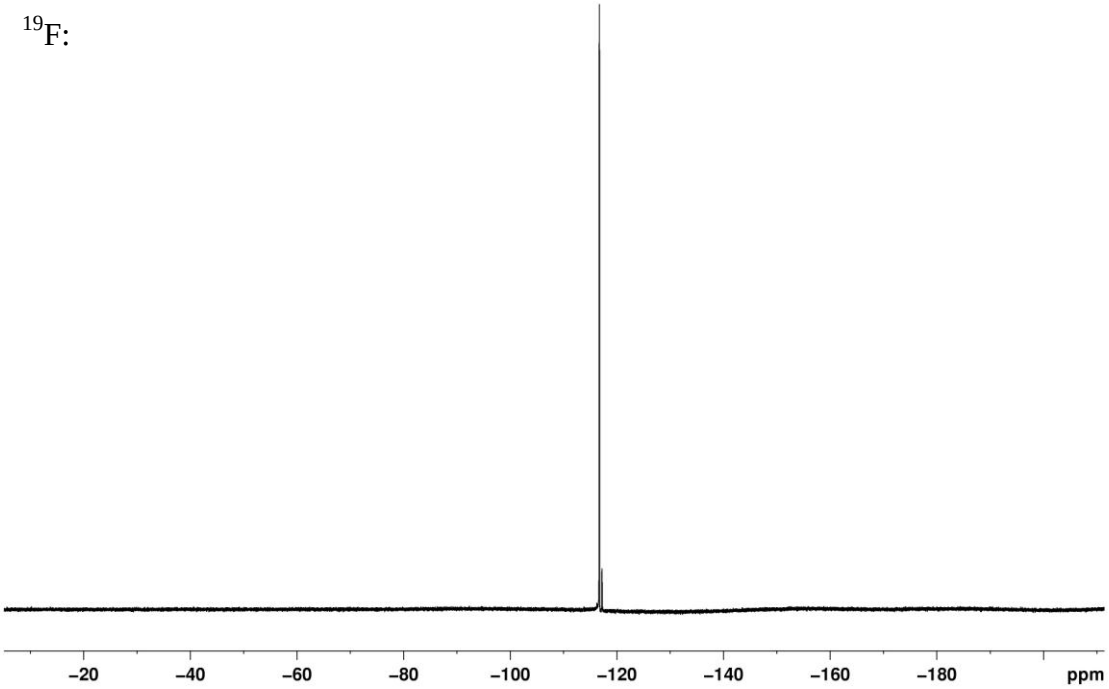
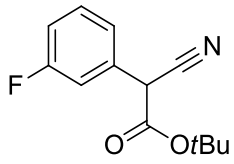
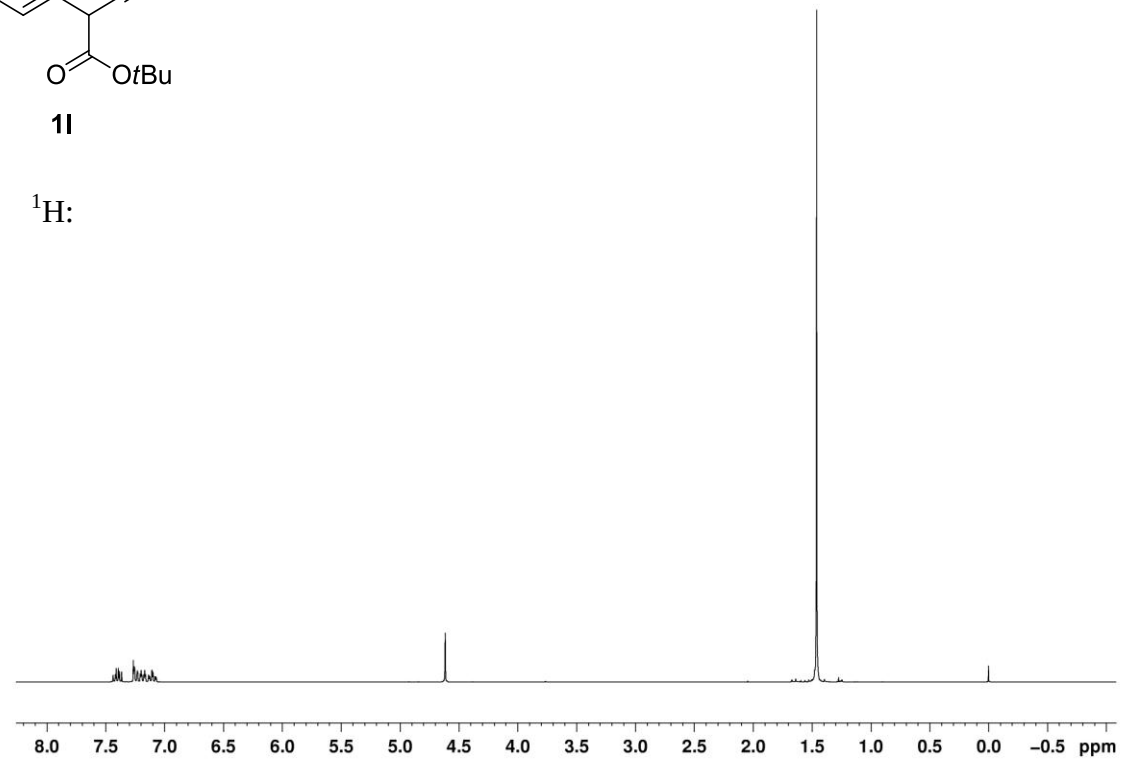


tert-Butyl-2-cyano-(*m*-fluorophenyl)acetate (**1l**)



1l

^{1}H:



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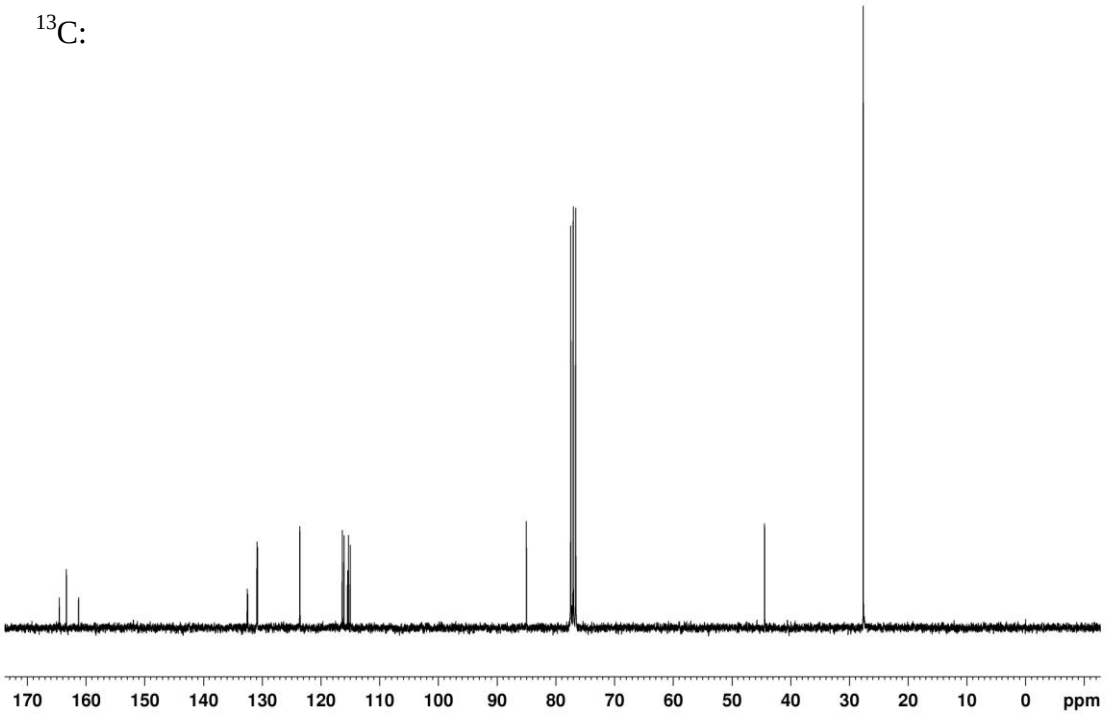

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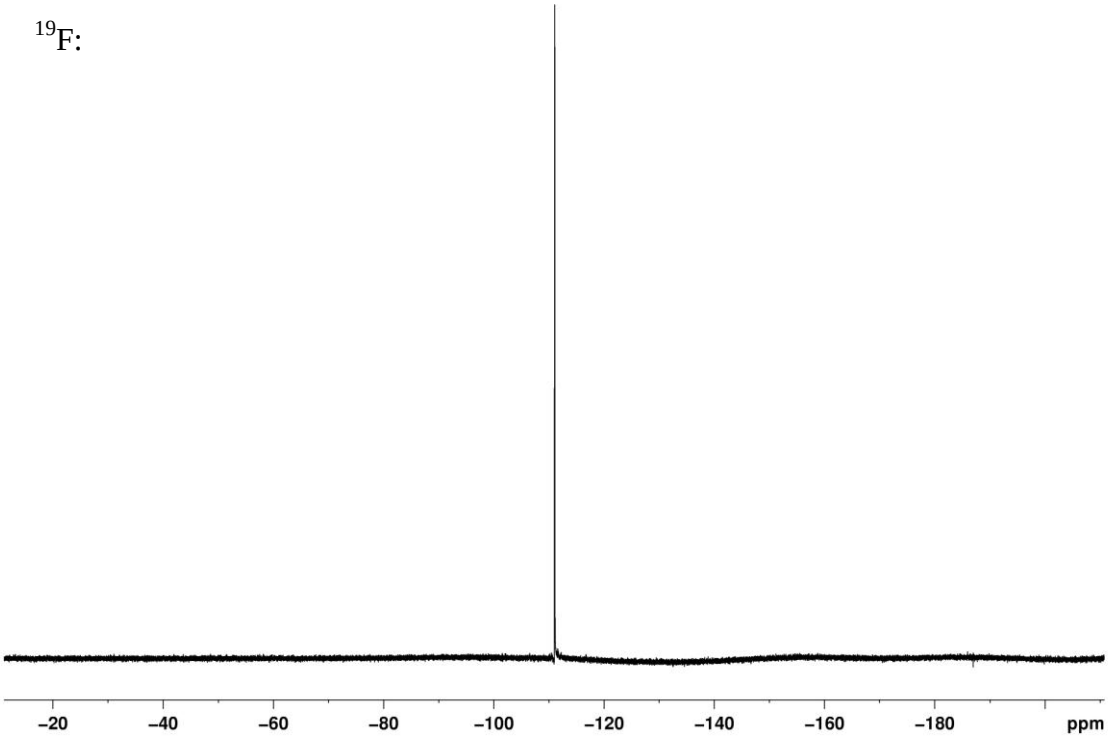
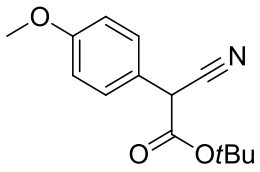
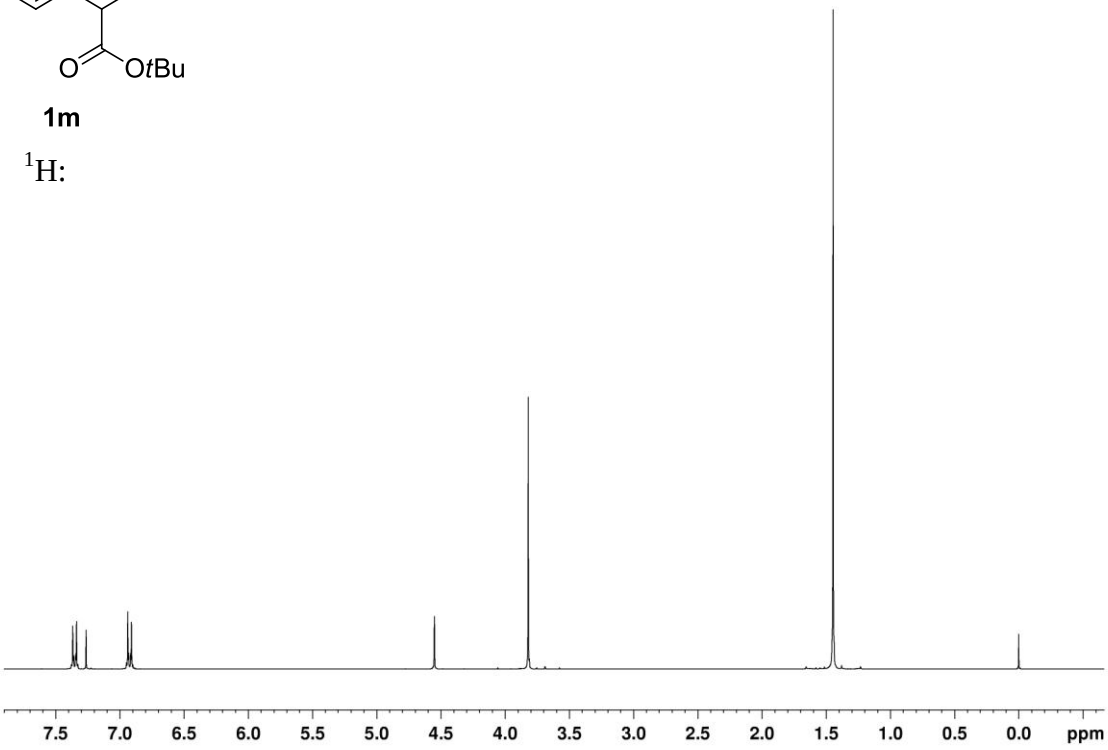


tert-Butyl-2-cyano-(4-methoxyphenyl)acetate (**1m**)

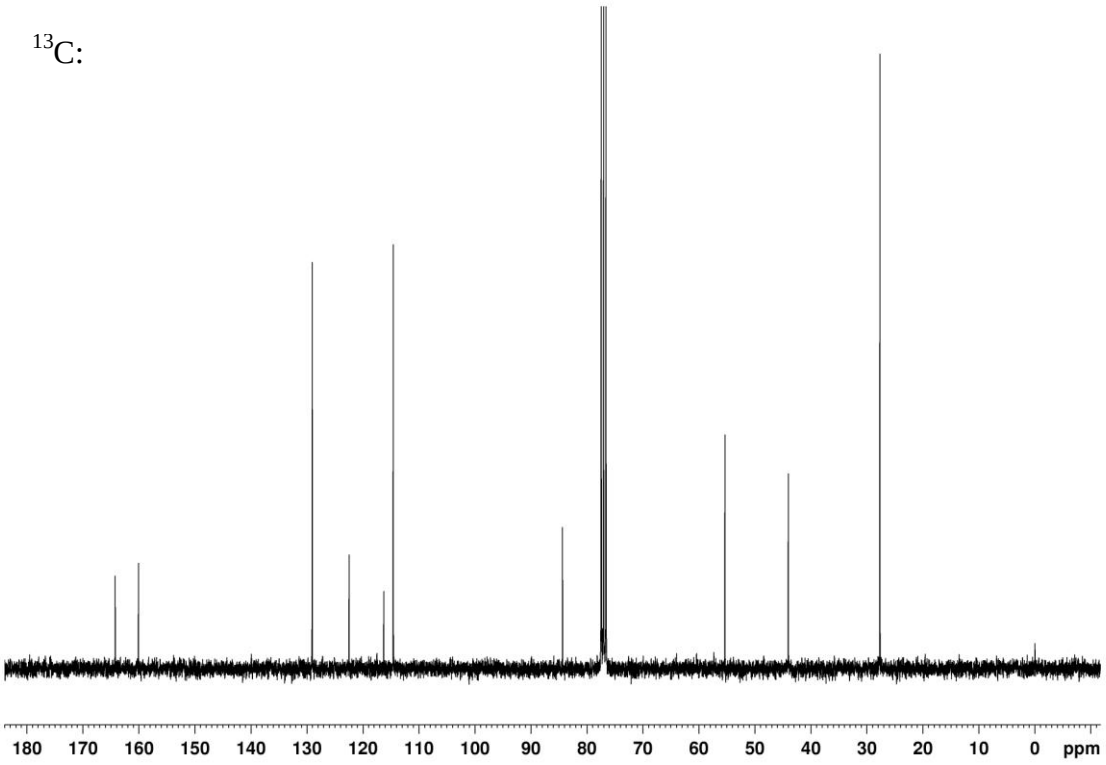


1m

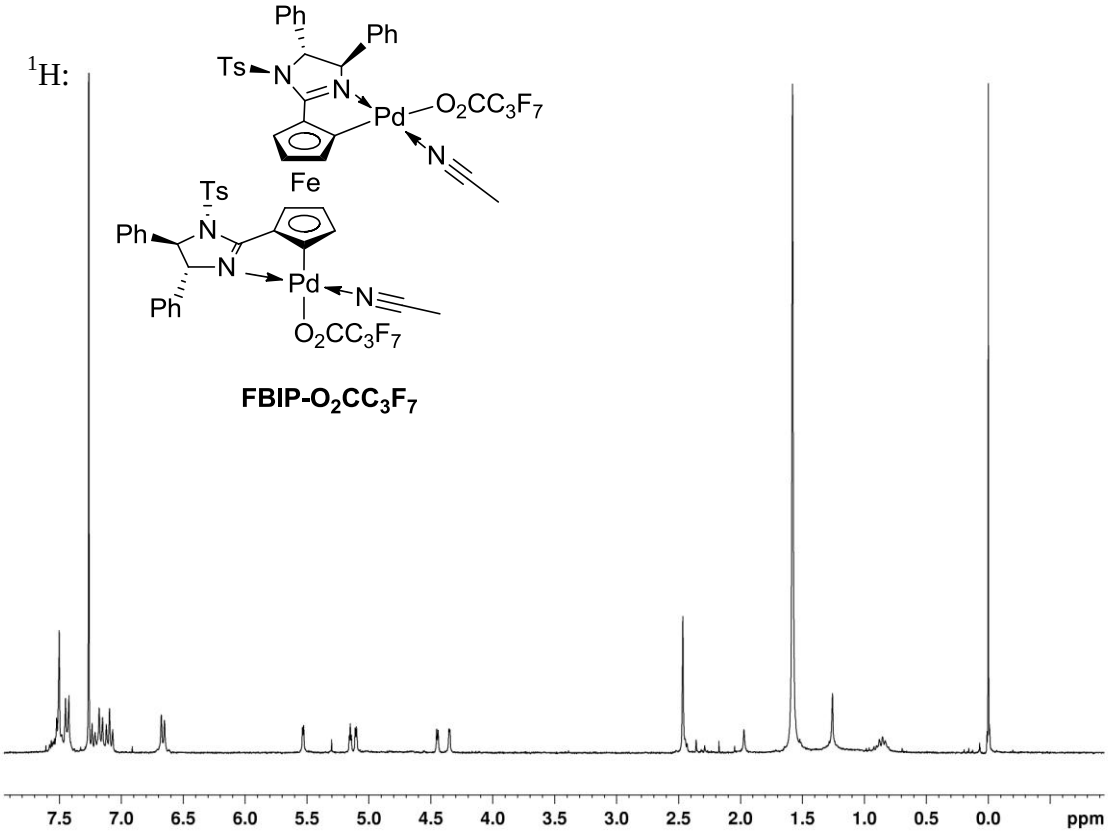
^{1}H:



^{13}C:



Bis(acetonitrile)[μ-[(*1S*$_p$,1'*S*$_p$)-2,2'-bis[(*4R*,*5R*)-4,5-dihydro-1-[(4-methylphenyl)sulfonyl]-4,5-diphenyl-1*H*-imidazol-2-yl-κ*N*3]-1,1'-ferrocendiyl-κ*C*1: κ*C*1']]bis(heptafluorobutyrato-κ*O*)di-palladium(II) (**FBIP-O$_2$CC$_3$F$_7$**)



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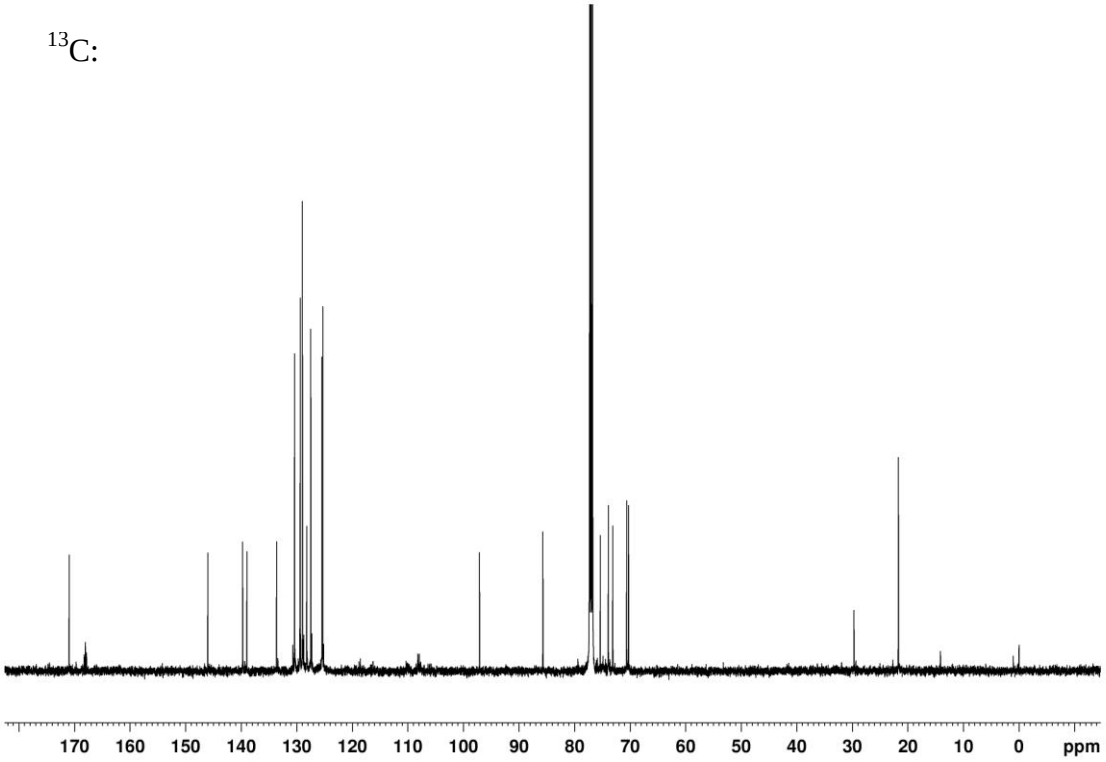
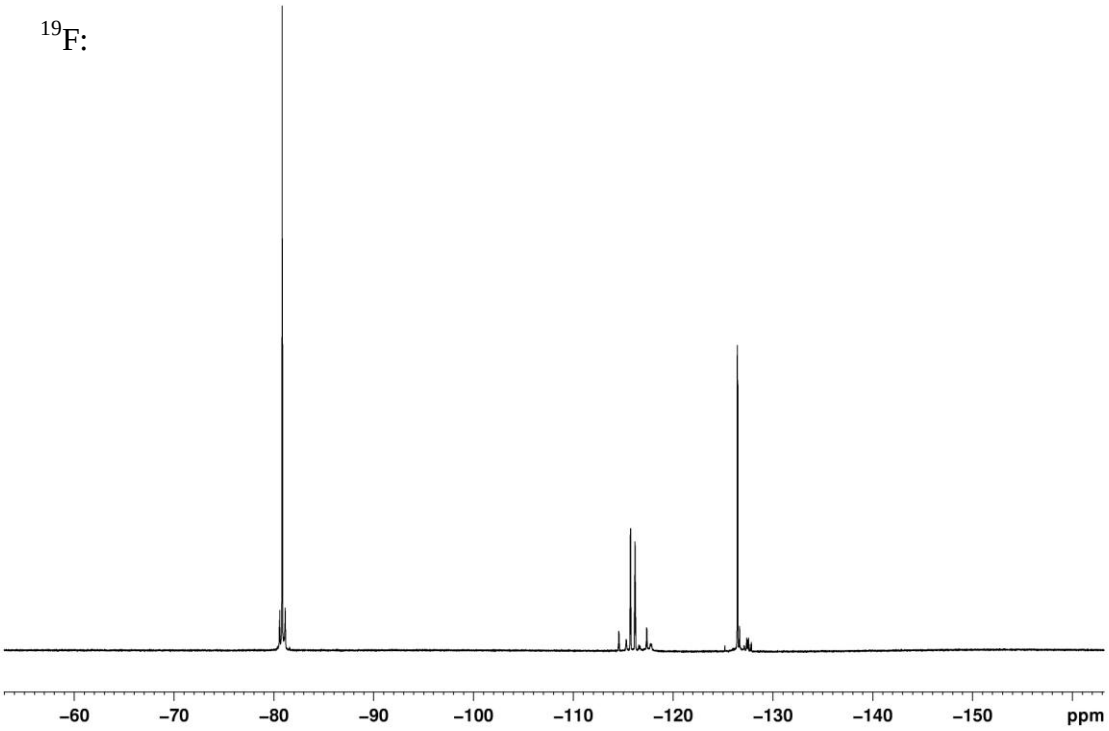
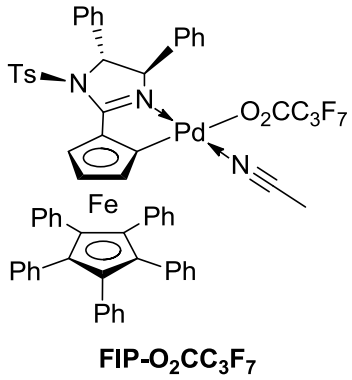


^{19}F:



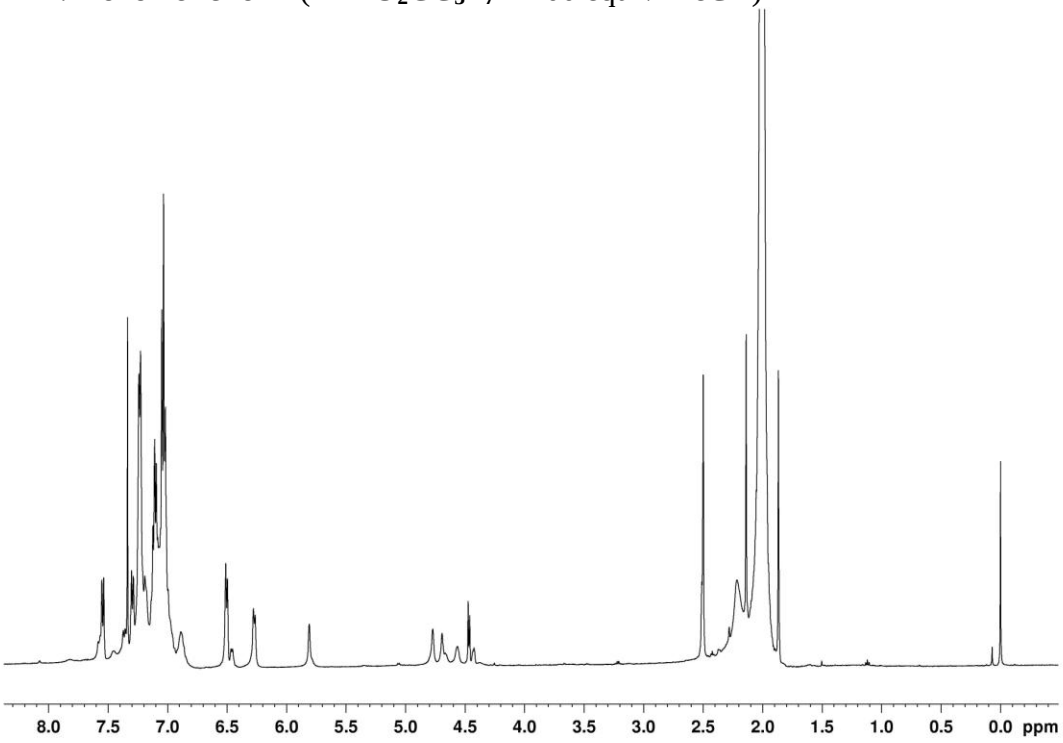
(Acetonitrile-κ*N*)-(heptafluorobutyrate-κ*O*)[(*1S*$_p$)-2-[(*4R*,*5R*)-4,5-dihydro -1-[(4-methylphenyl)sulfonyl]-4,5-diphenyl-1*H*-imidazol-2-yl-κ*N*3]-1',2',3',4',5'-pentaphenylferrocenyl-κ*C*]-palladium(II) (**FIP-$O_2CC_3F_7$**)

^{1}H: mixture of monomeric and dimeric form



FIP-$O_2CC_3F_7$

^{1}H: monomeric form (**FIP-$O_2CC_3F_7$** + 100 equiv MeCN)



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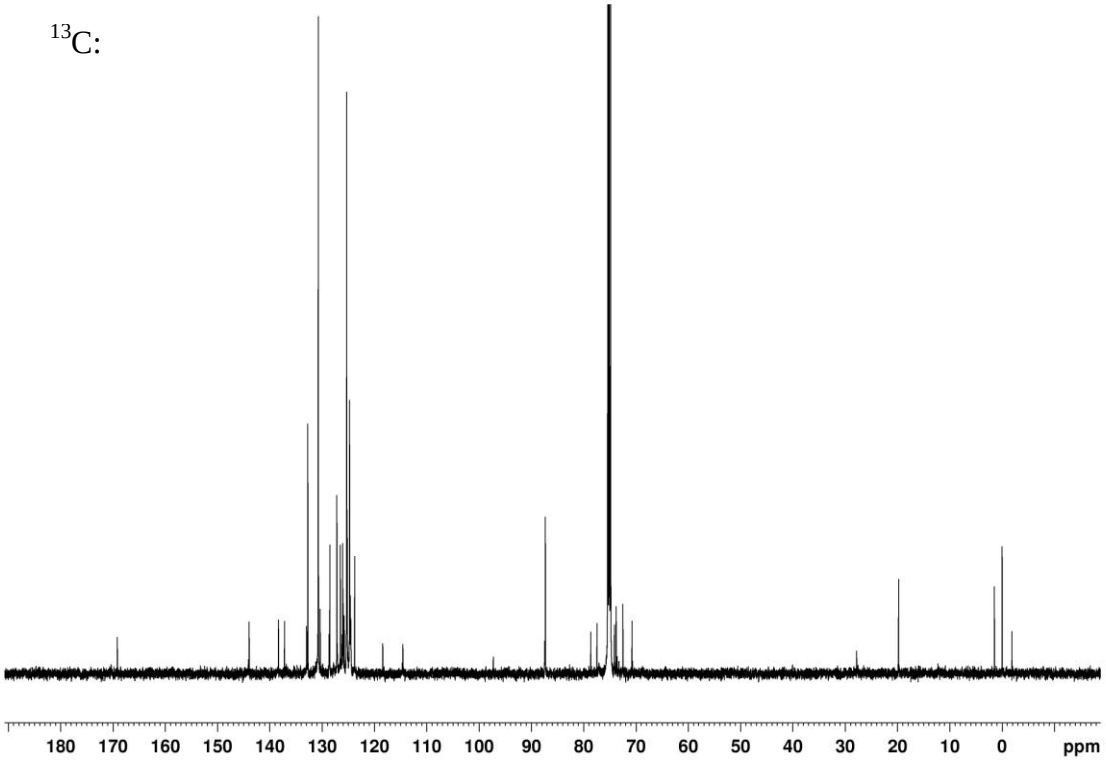

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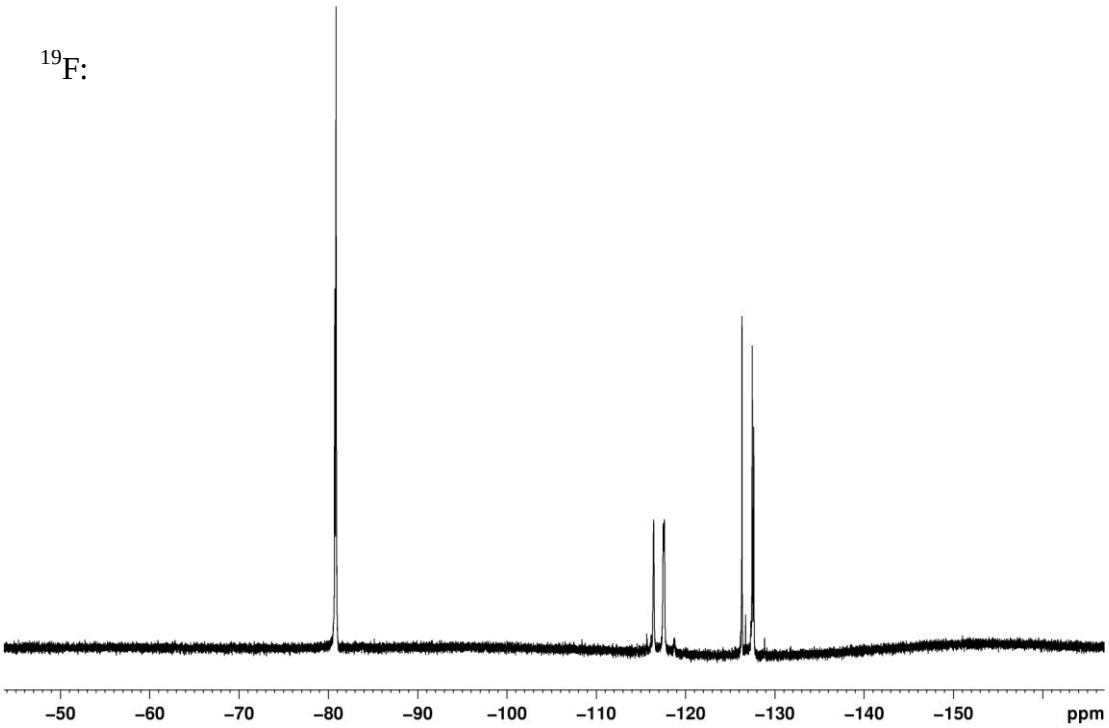
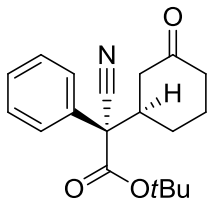
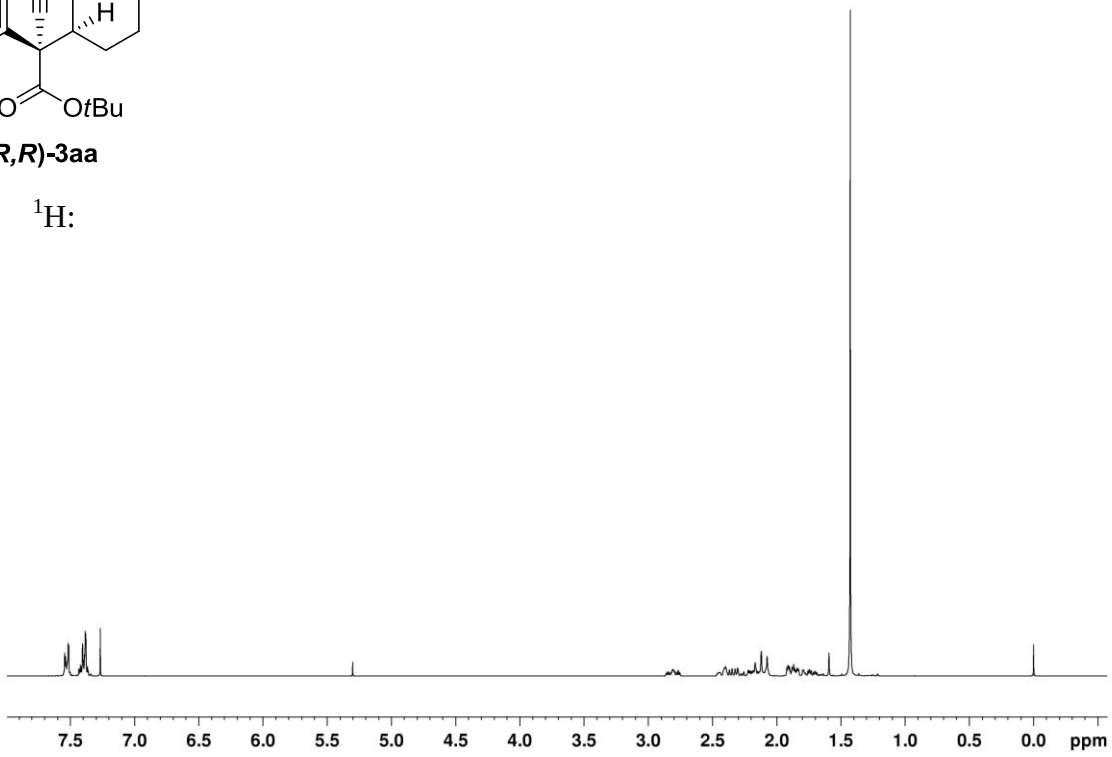


tert-Butyl-2-cyano-2-(3-oxocyclohexyl)-2-phenylacetate (**(*R*,*R*)-3aa**)



(*R*,*R*)-3aa

^{1}H:



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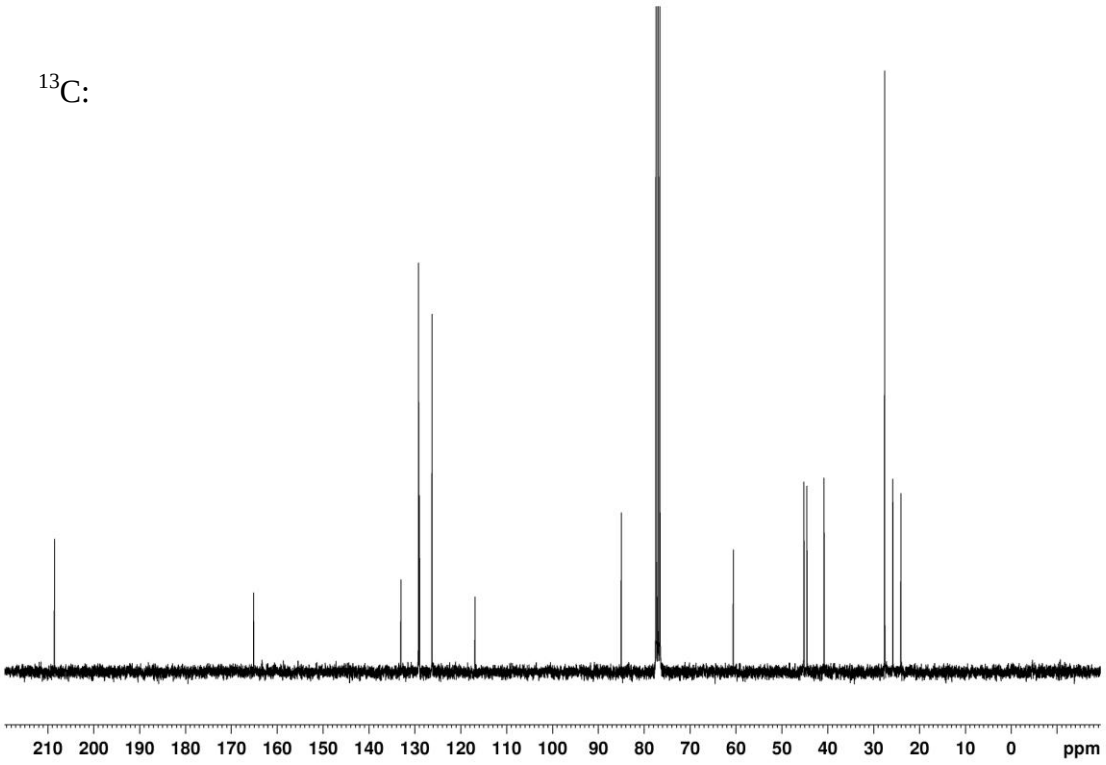
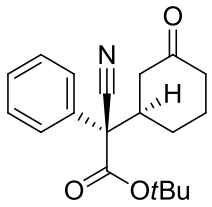
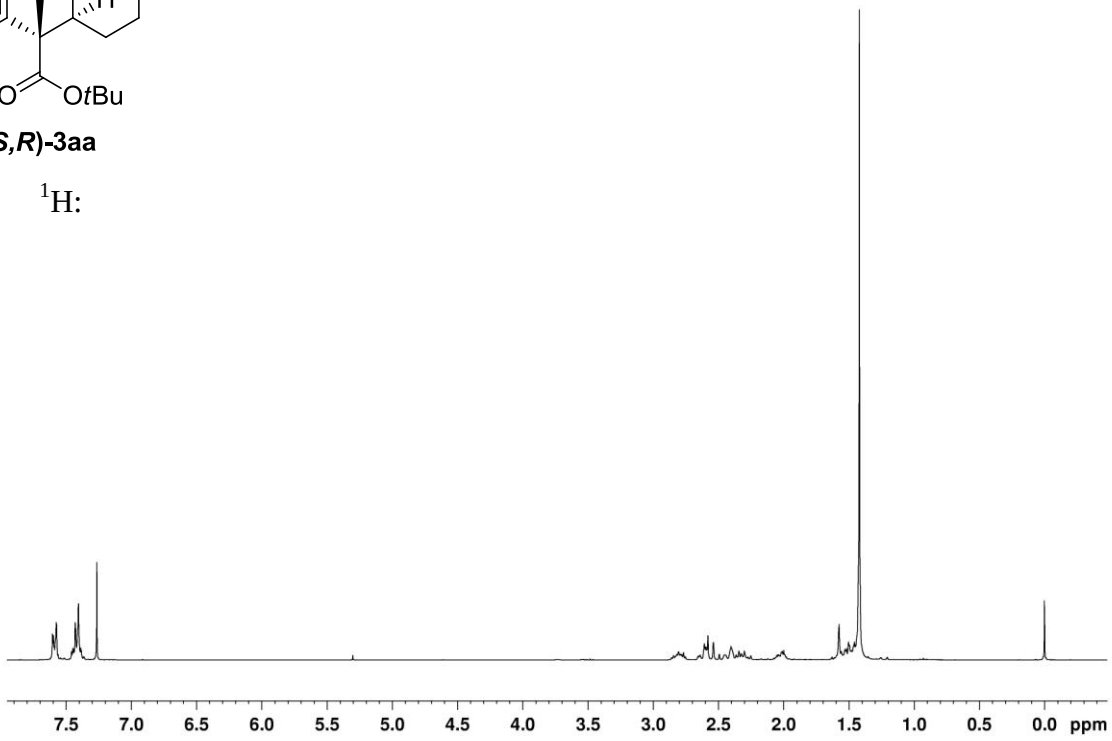


tert-Butyl-2-cyano-2-(3-oxocyclohexyl)-2-phenylacetate (**(*S*,*R*)-3aa**)

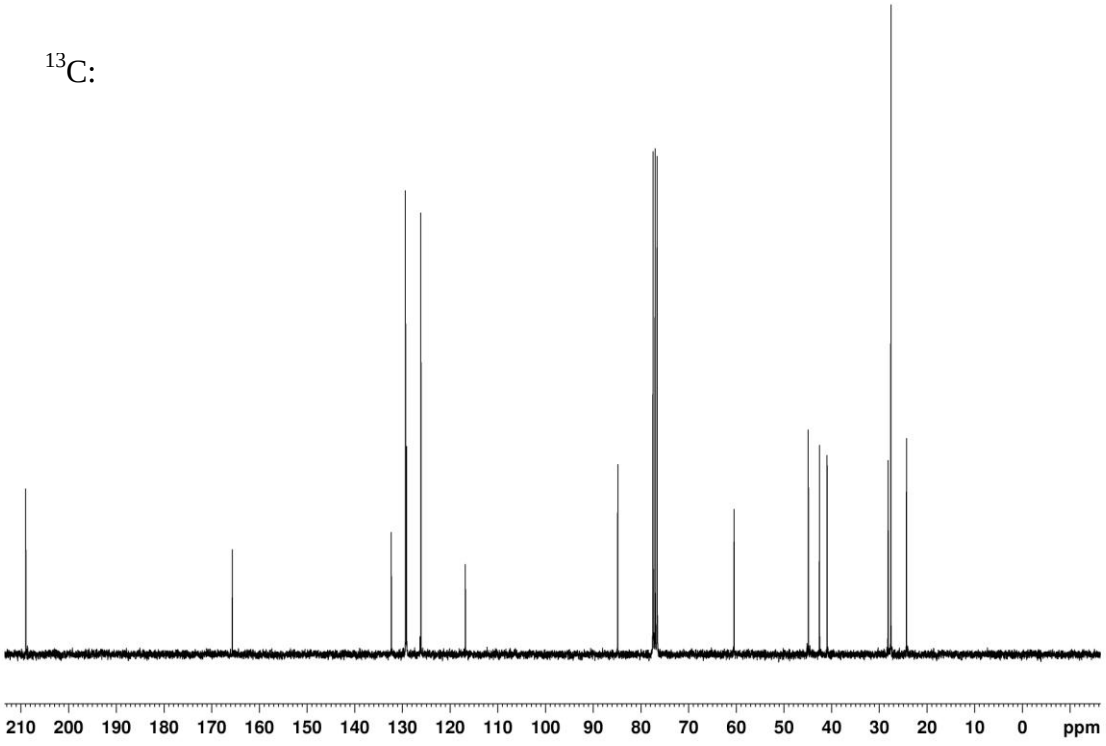


(*S*,*R*)-3aa

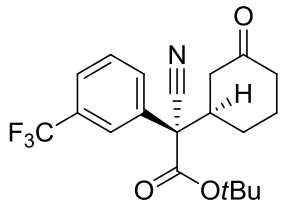
^{1}H:



^{13}C:

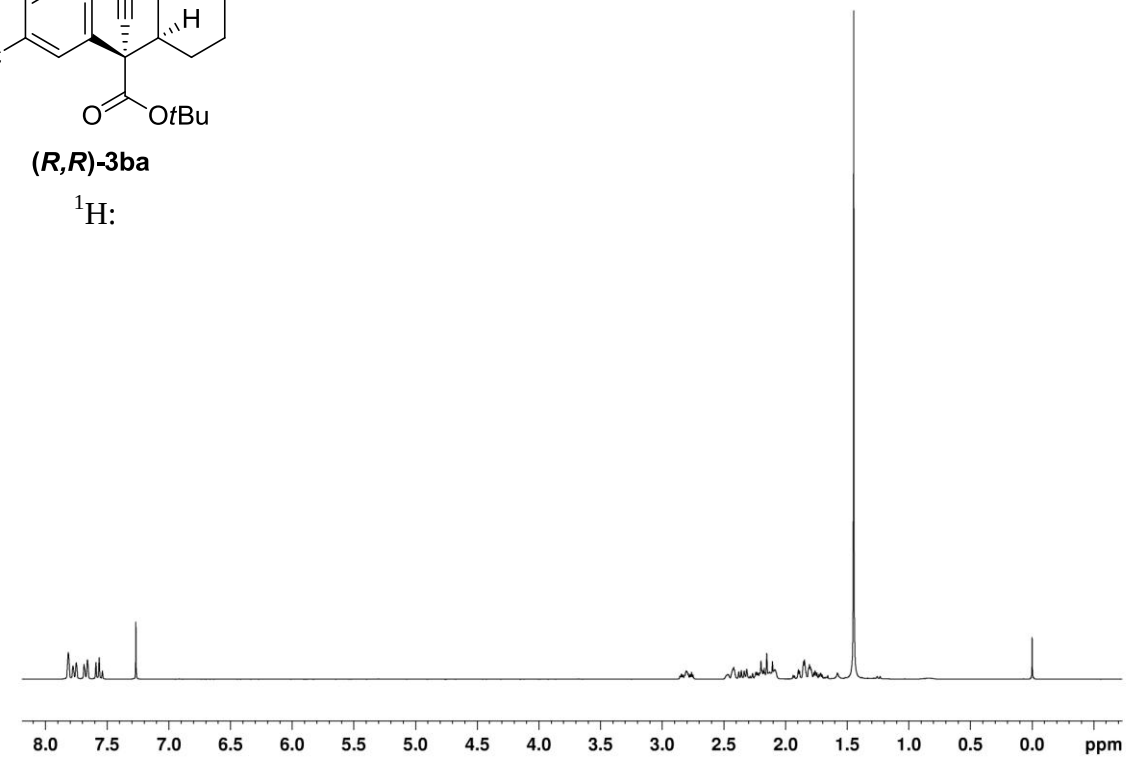


tert-Butyl-2-cyano-2-(3-oxocyclohexyl)-2-(3-(trifluoromethyl)phenyl)acetate (**(*R*,*R*)-3ba**)



(*R*,*R*)-3ba

^{1}H:



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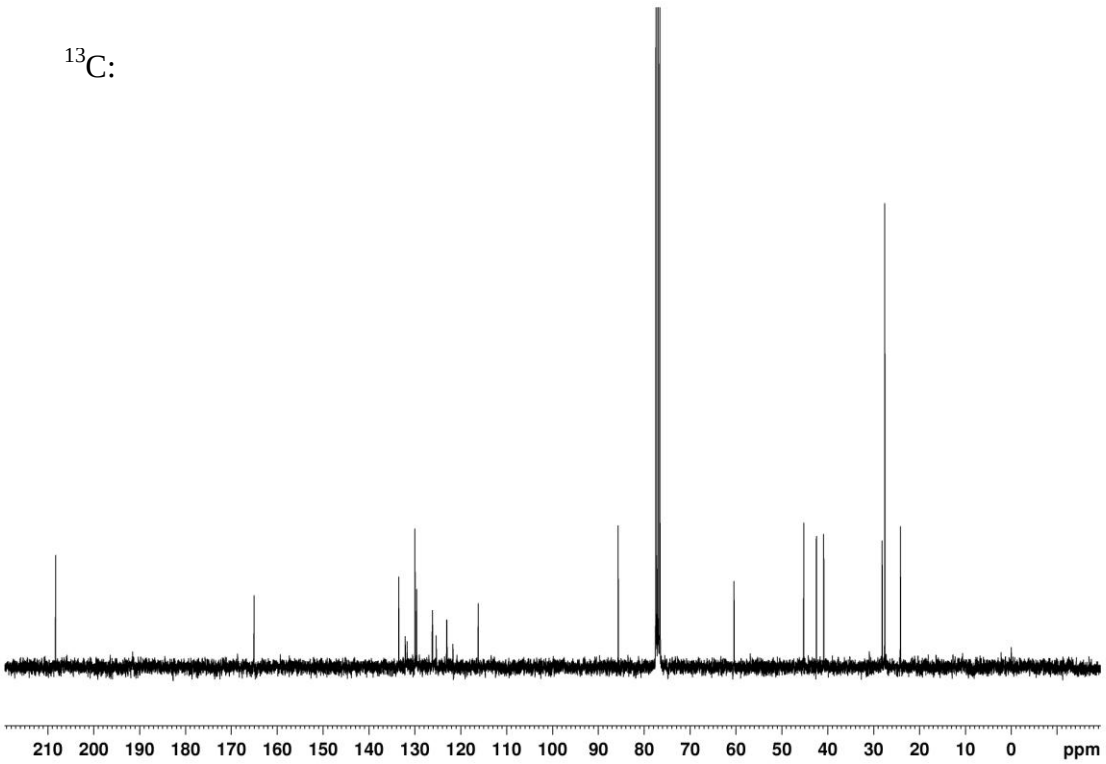
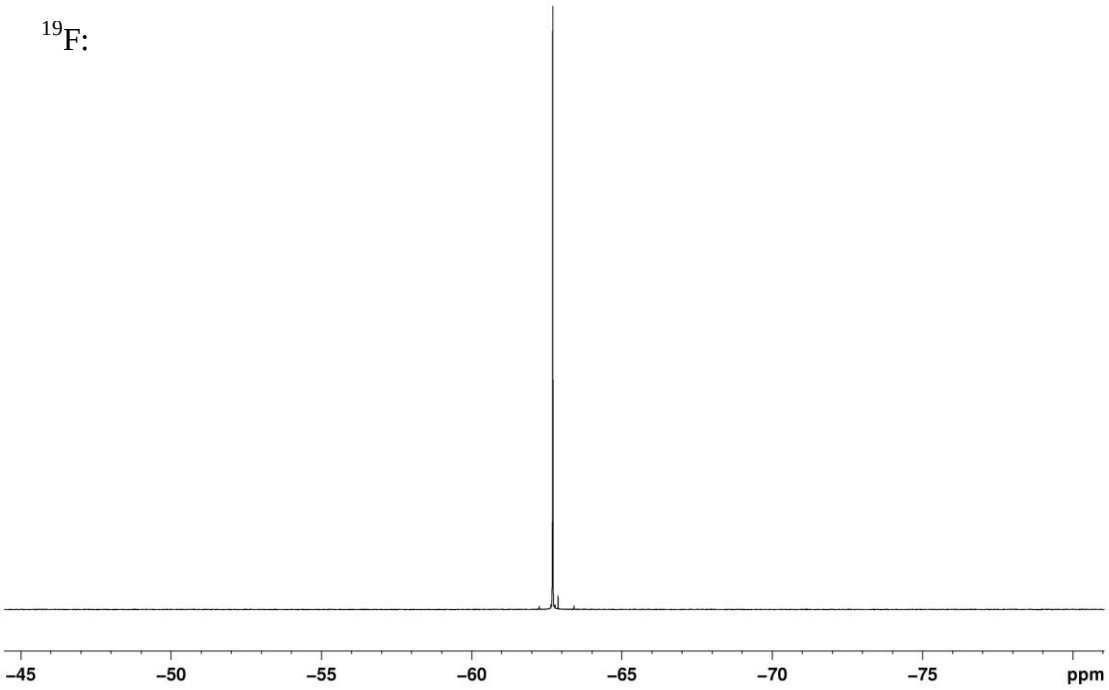
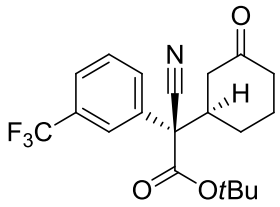


^{19}F:



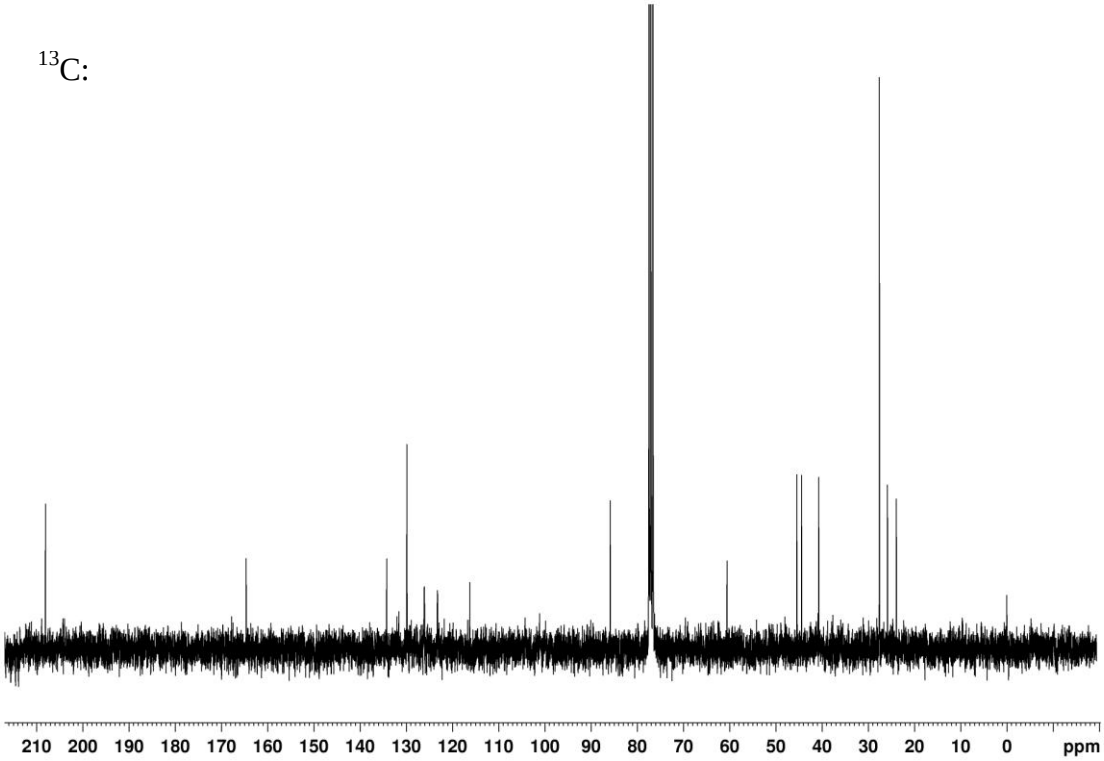
tert-Butyl-2-cyano-2-(3-oxocyclohexyl)-2-(3-(trifluoromethyl)phenyl)acetate (**(*S*,*R*)-3ba**)



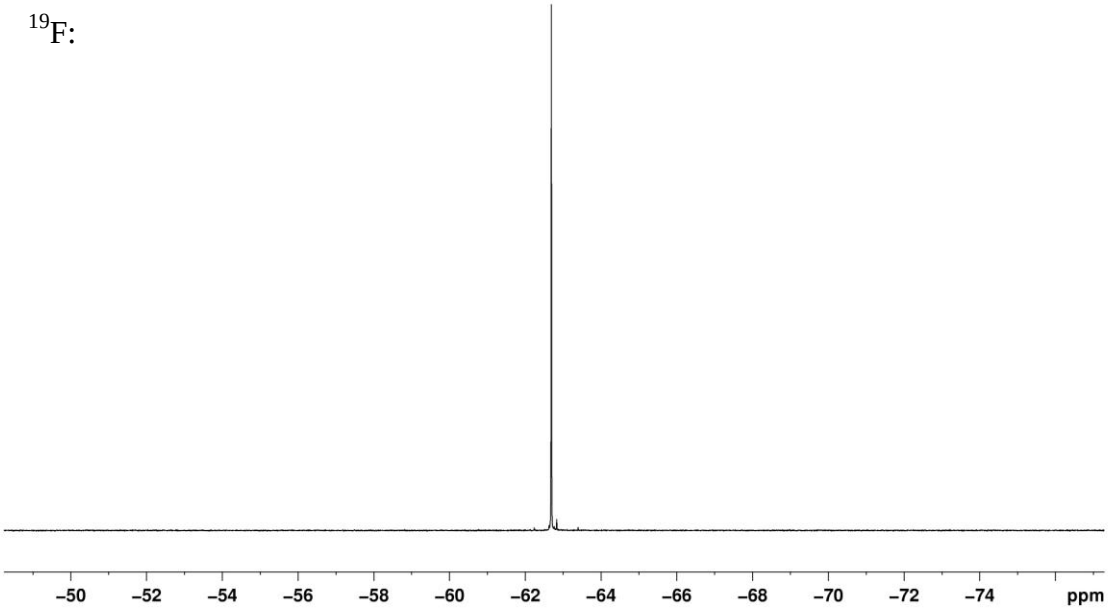
(*S*,*R*)-3ba

^{1}H:

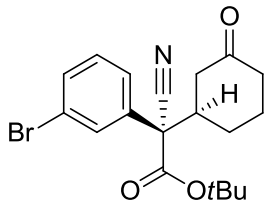
^{13}C:



^{19}F:

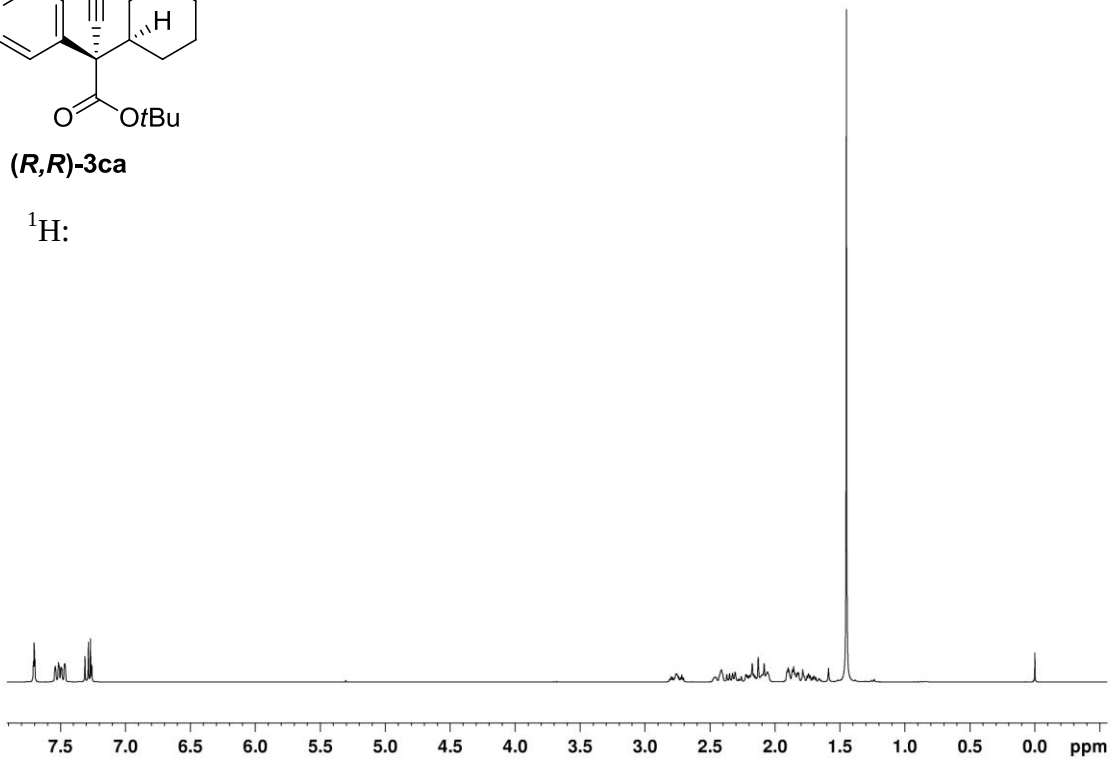


tert-Butyl-2-cyano-2-(3-bromophenyl)-2-(3-oxocyclohexyl)acetate (**(*R*,*R*)-3ca**)



(*R*,*R*)-3ca

^{1}H:



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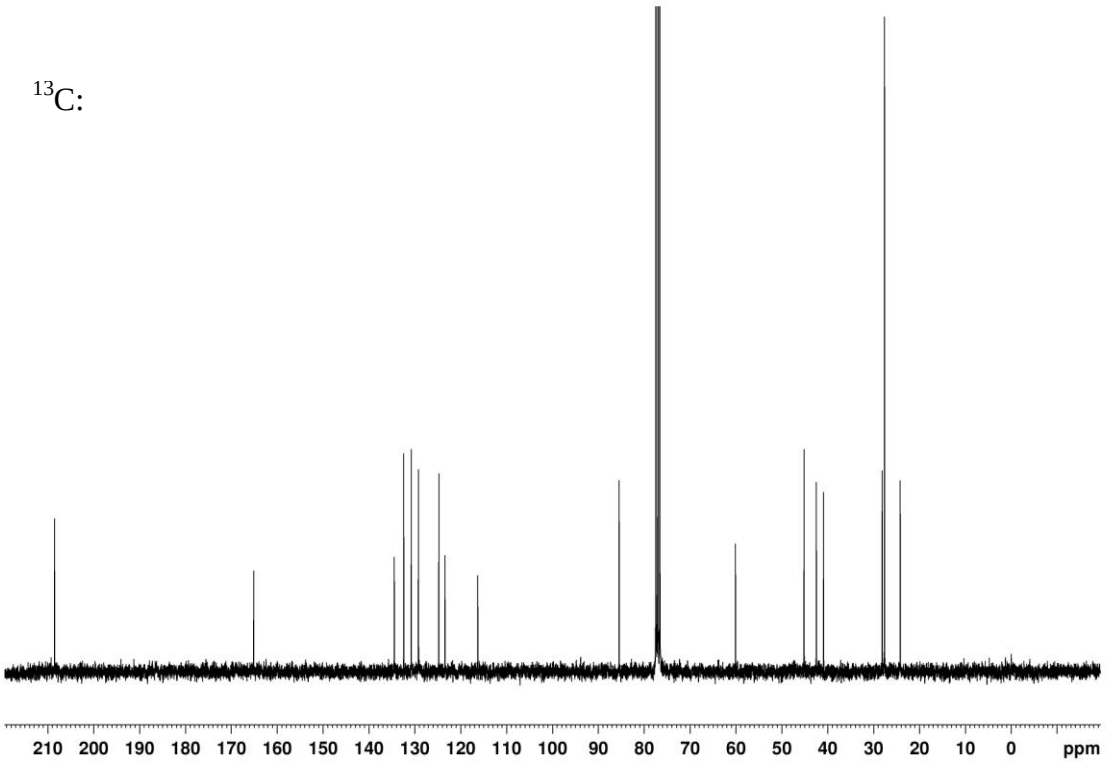
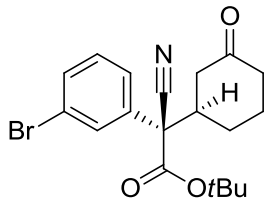
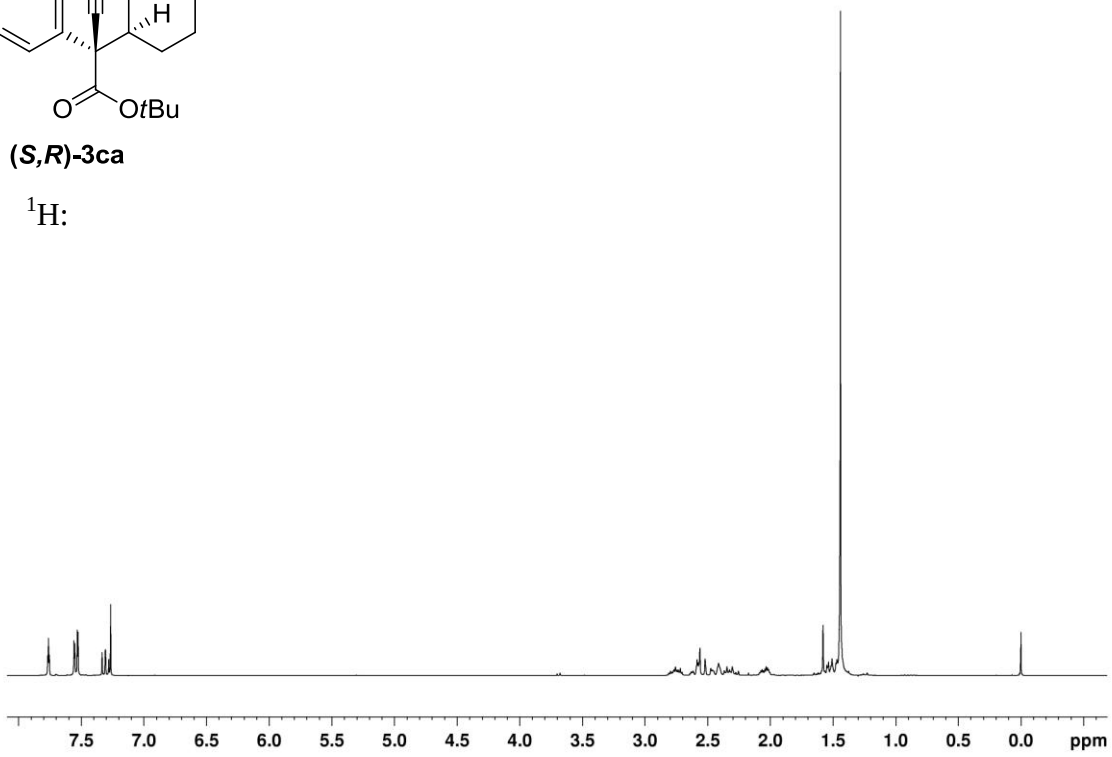


tert-Butyl-2-cyano-2-(3-bromophenyl)-2-(3-oxocyclohexyl)acetate (**(*S*,*R*)-3ca**)



(*S*,*R*)-3ca

^{1}H:



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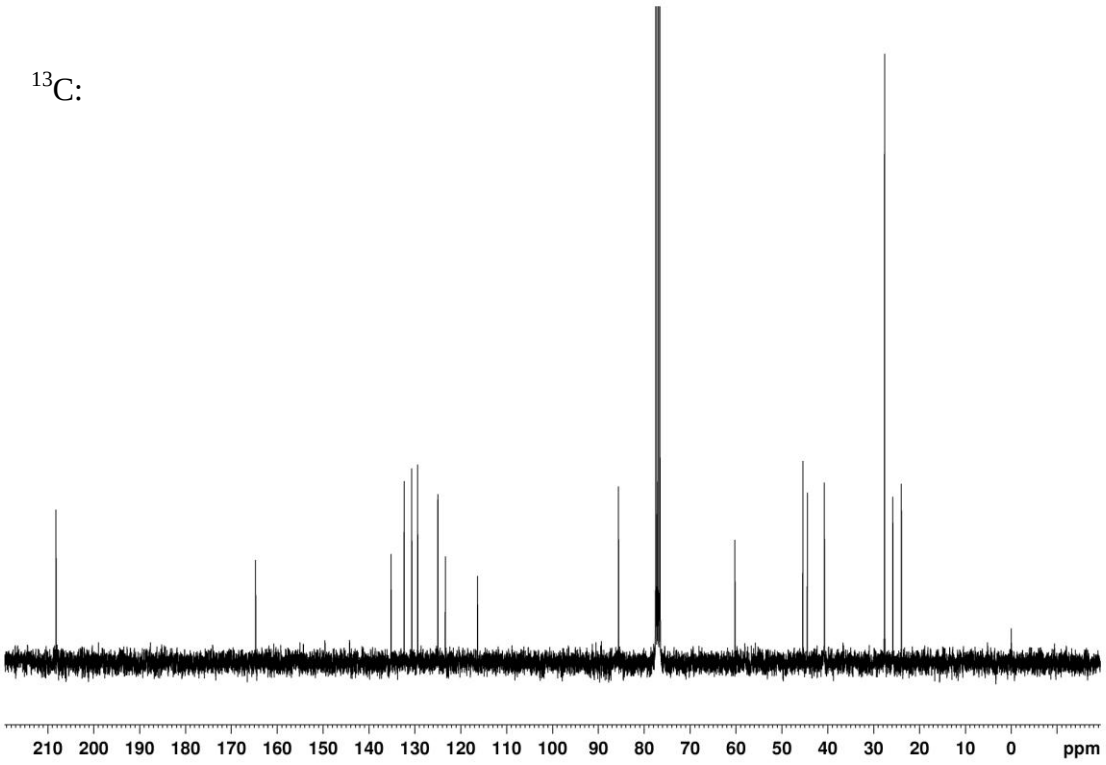
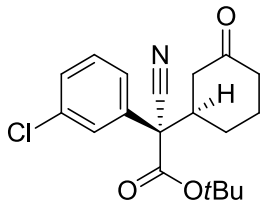
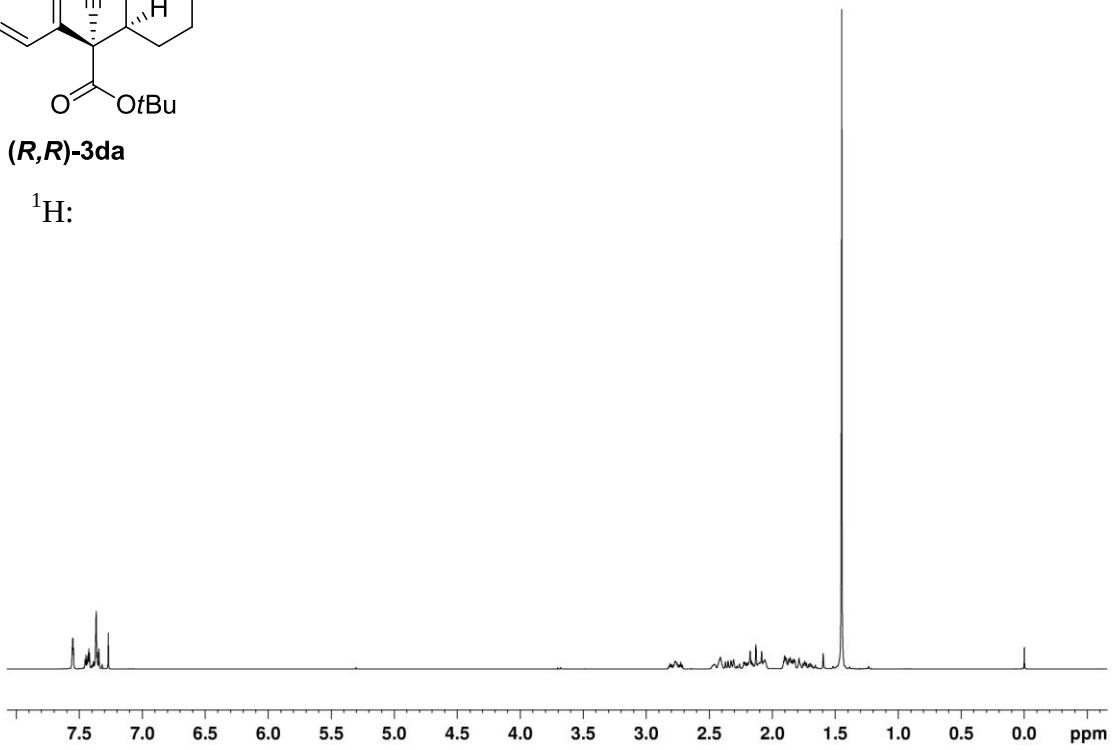


tert-Butyl-2-cyano-2-(3-chlorophenyl)-2-(3-oxocyclohexyl)acetate (**(*R*,*R*)-3da**)



(*R*,*R*)-3da

^{1}H:



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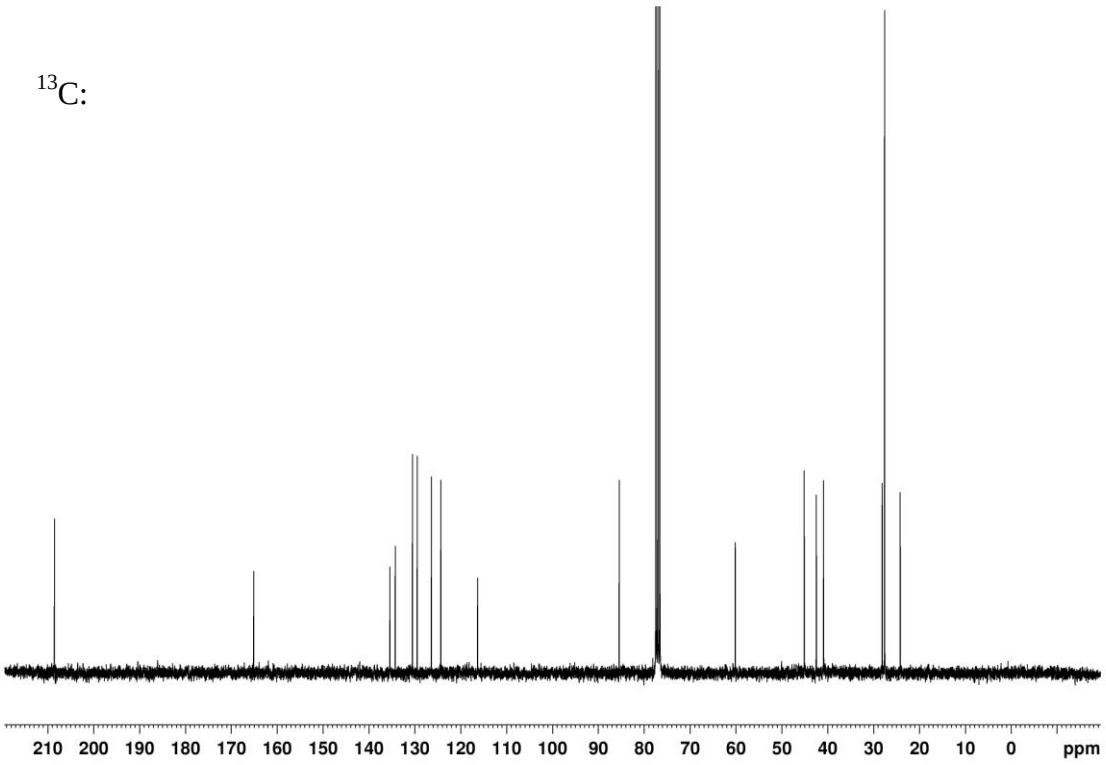
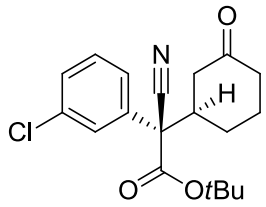
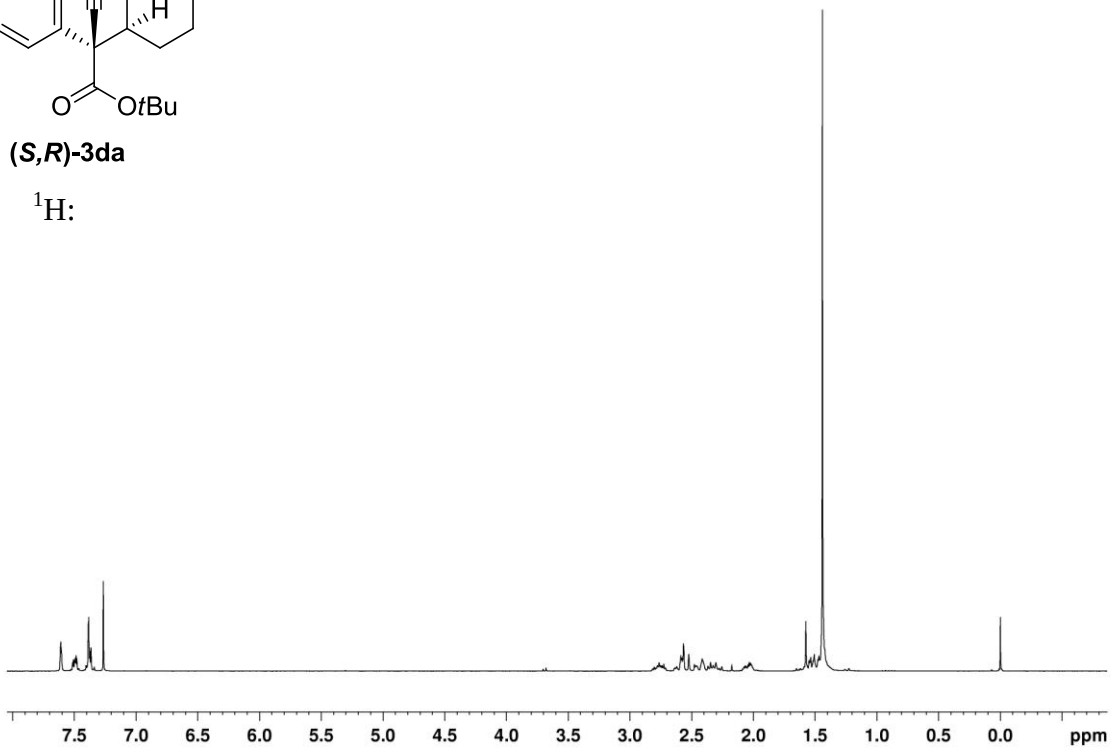


tert-Butyl-2-cyano-2-(3-chlorophenyl)-2-(3-oxocyclohexyl)acetate (**(*S*,*R*)-3da**)



(*S*,*R*)-3da

^{1}H:



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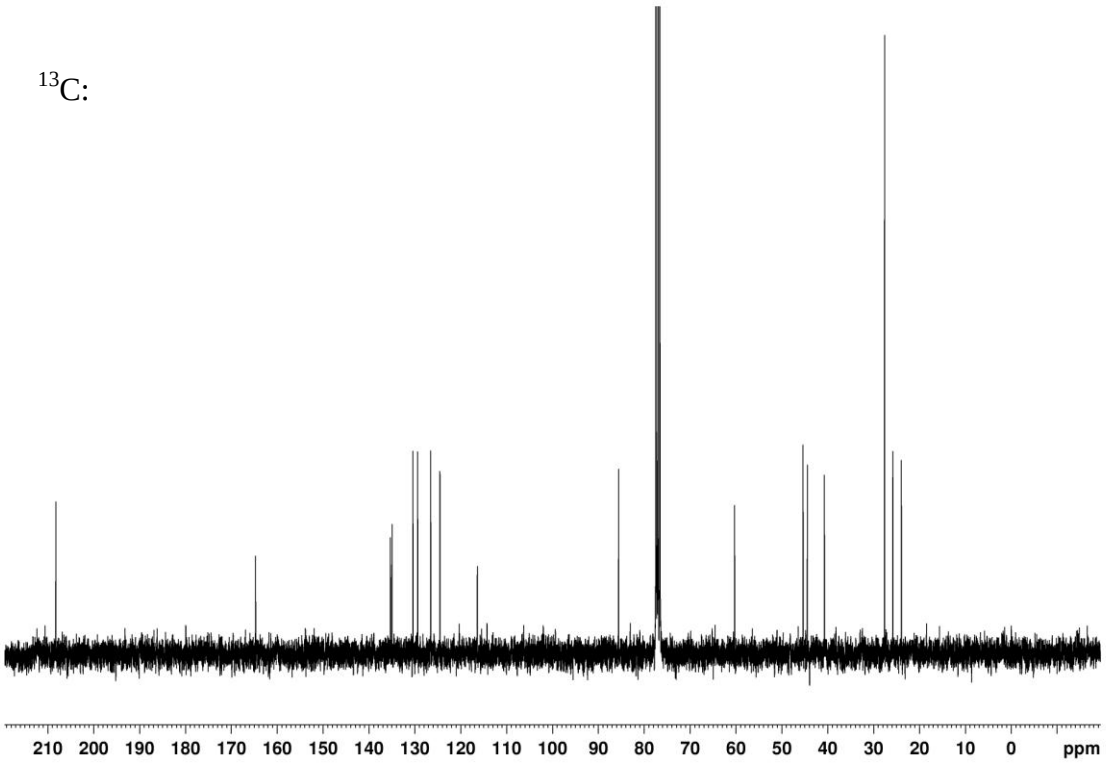
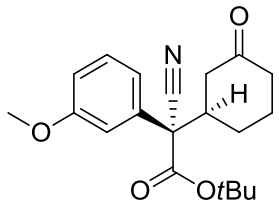
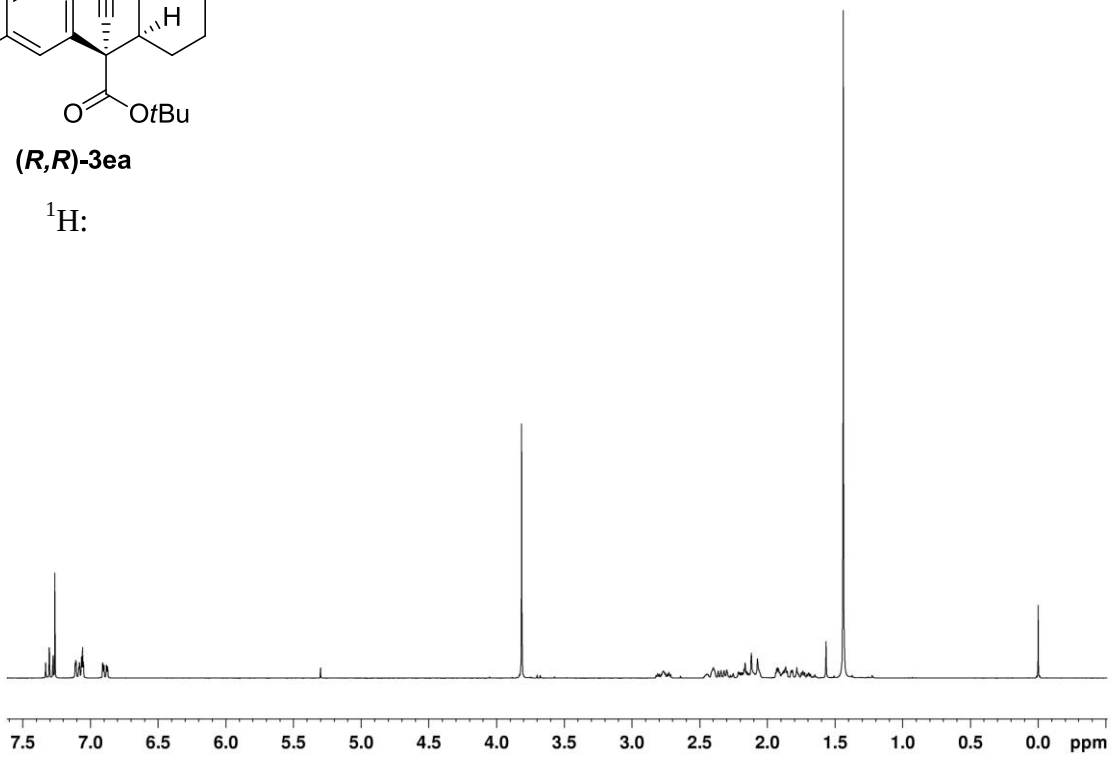


tert-Butyl-2-cyano-2-(3-methoxyphenyl)-2-(3-oxocyclohexyl)-acetate (**(*R*,*R*)-3ea**)



(*R*,*R*)-3ea

^{1}H:



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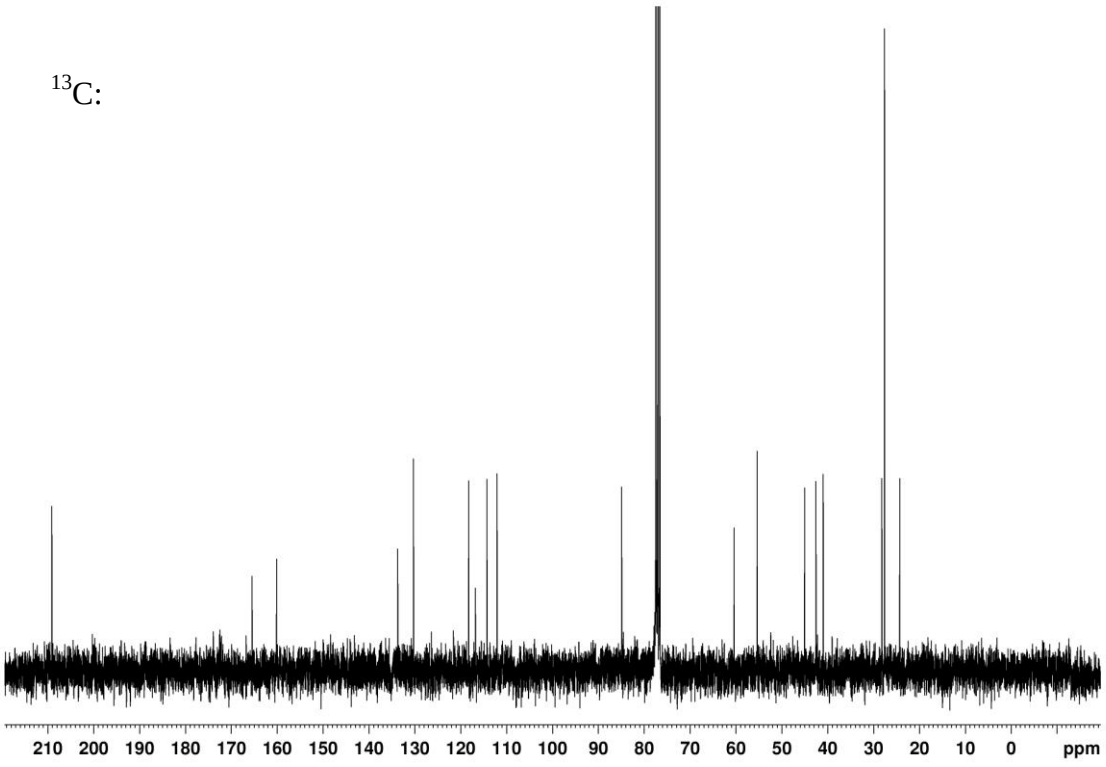
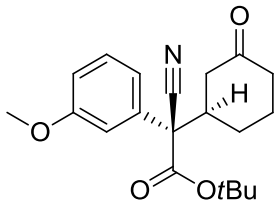
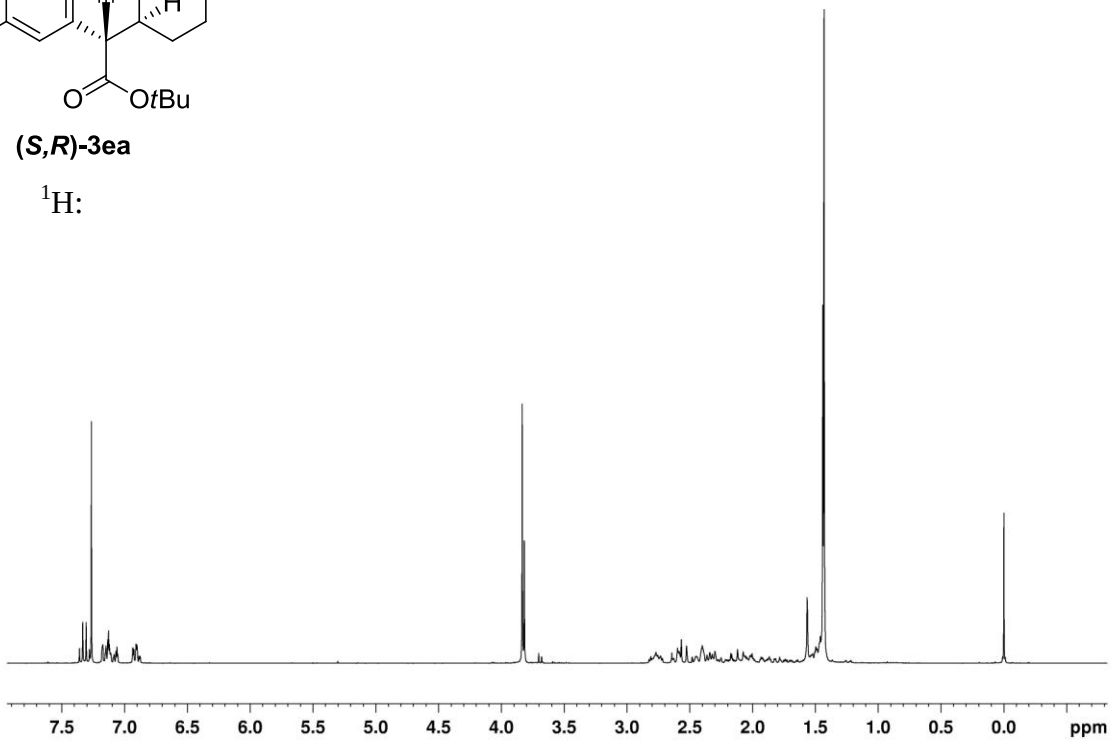


tert-Butyl-2-cyano-2-(3-methoxyphenyl)-2-(3-oxocyclohexyl)-acetate (**(*S*,*R*)-3ea**)



(*S*,*R*)-3ea

^{1}H:



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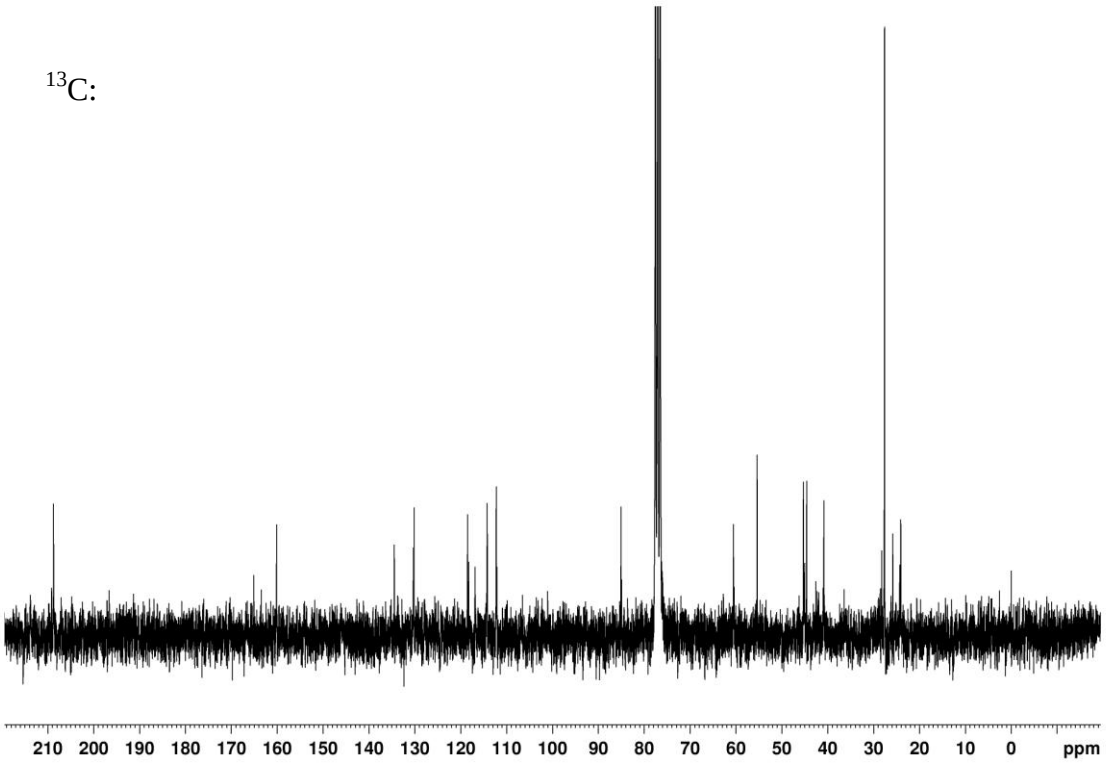
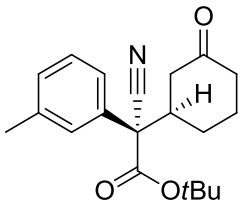
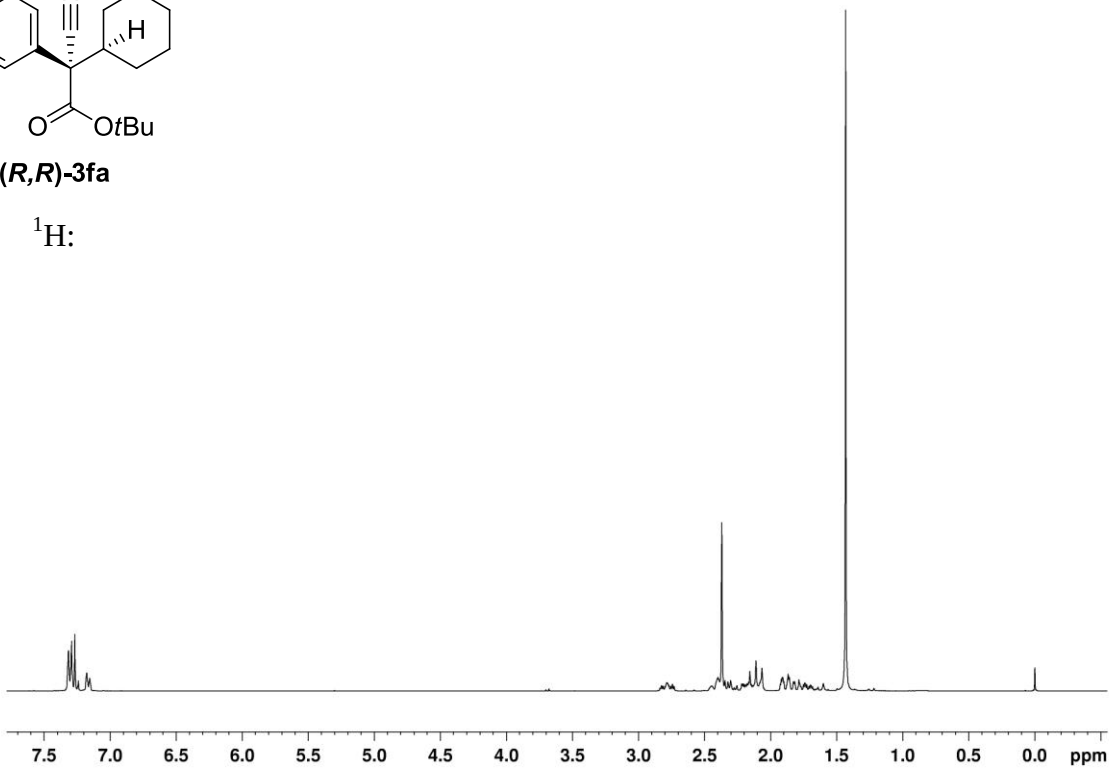


tert-Butyl-2-cyano-2-(3-oxocyclohexyl)-2-(*m*-tolyl)-acetate (**(*R*,*R*)-3fa**)



(*R*,*R*)-3fa

^{1}H:



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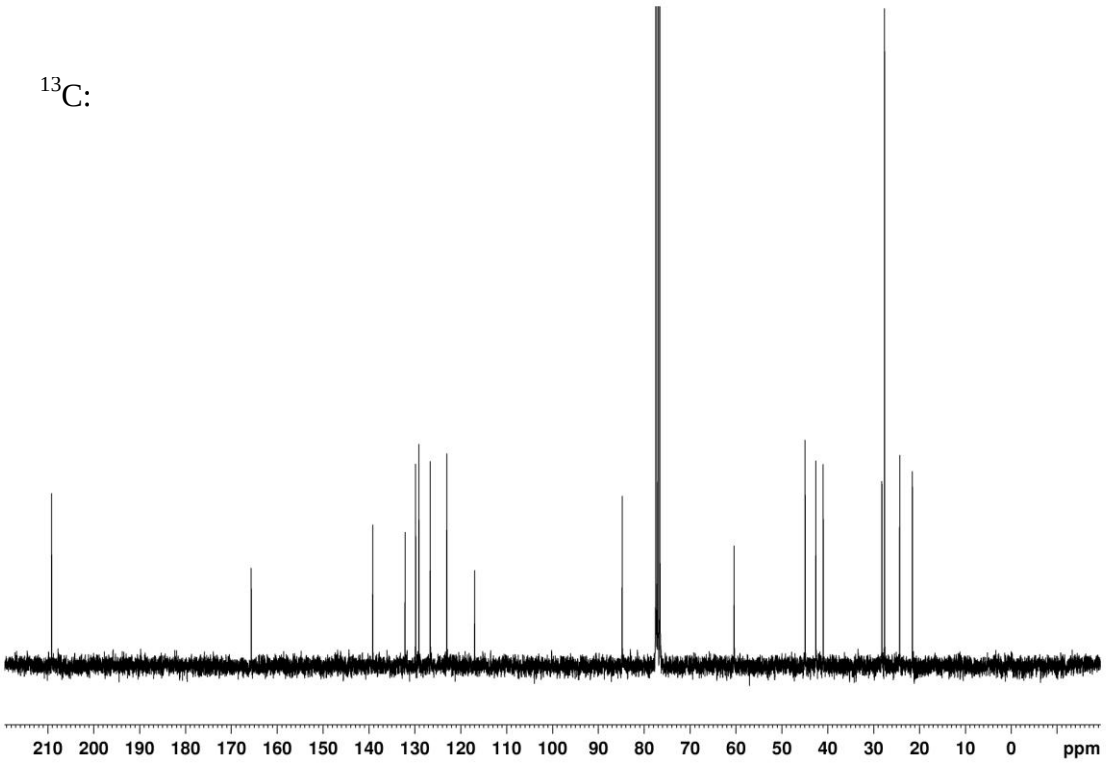
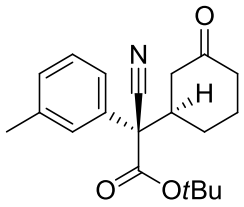
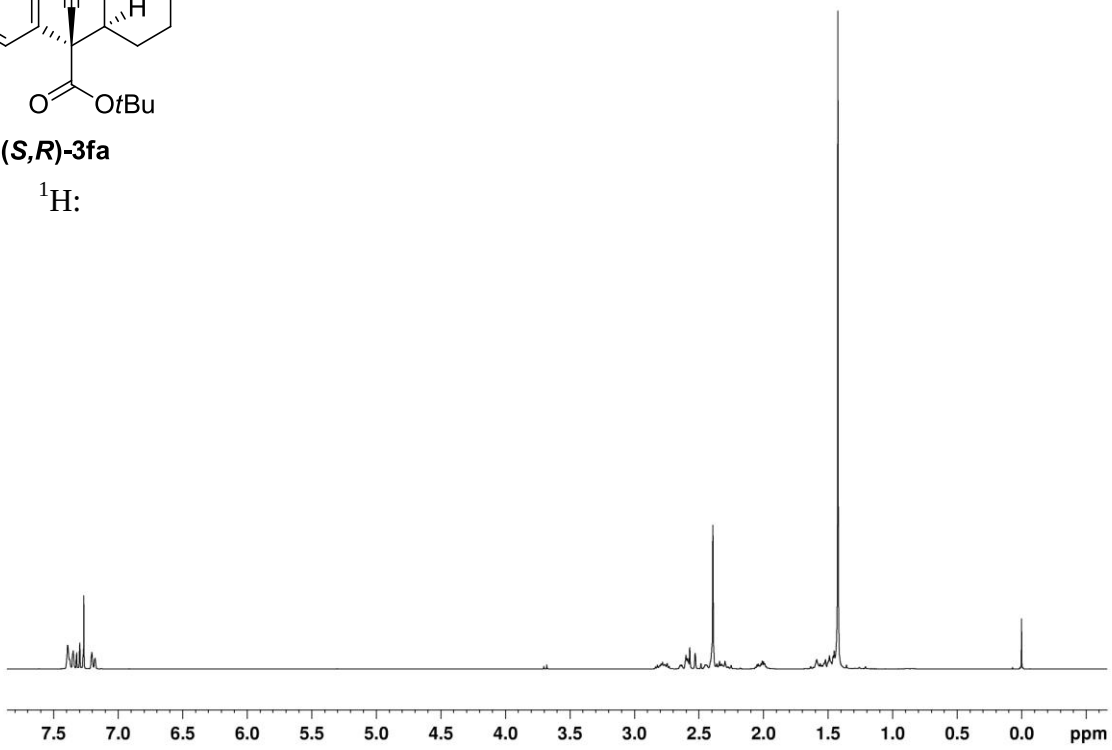


tert-Butyl-2-cyano-2-(3-oxocyclohexyl)-2-(*m*-tolyl)-acetate (**(*S*,*R*)-3fa**)

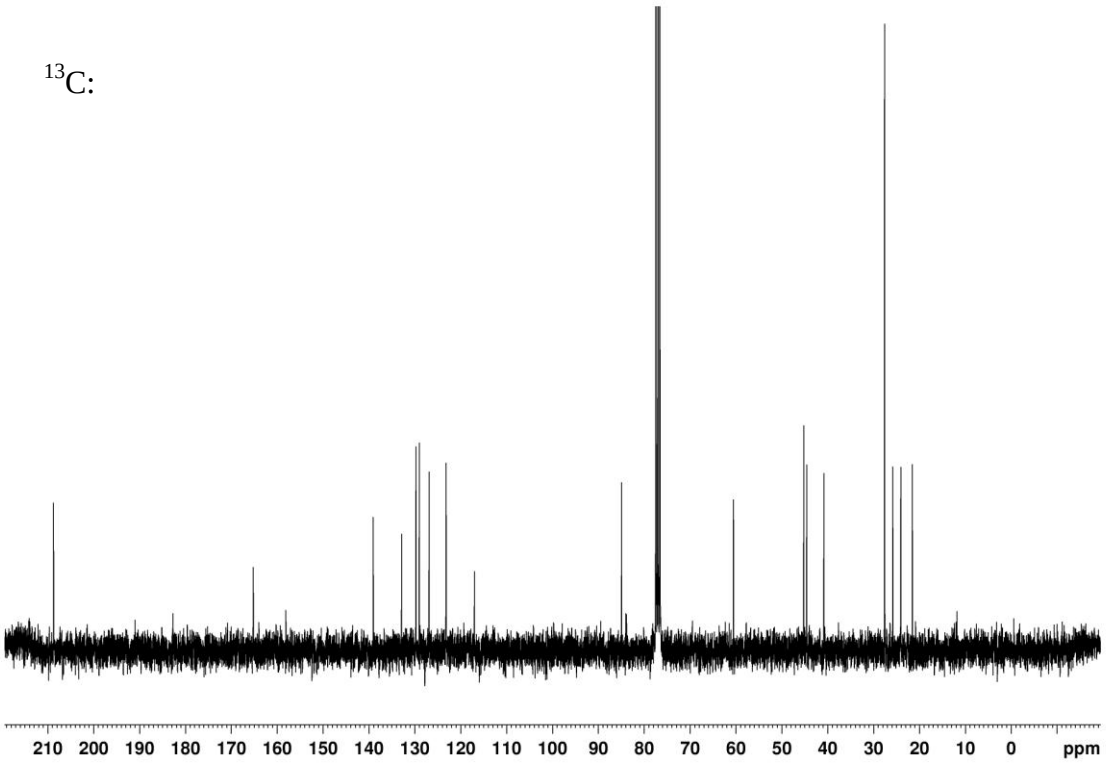


(*S*,*R*)-3fa

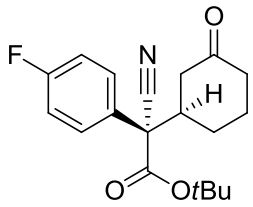
^{1}H:



^{13}C:

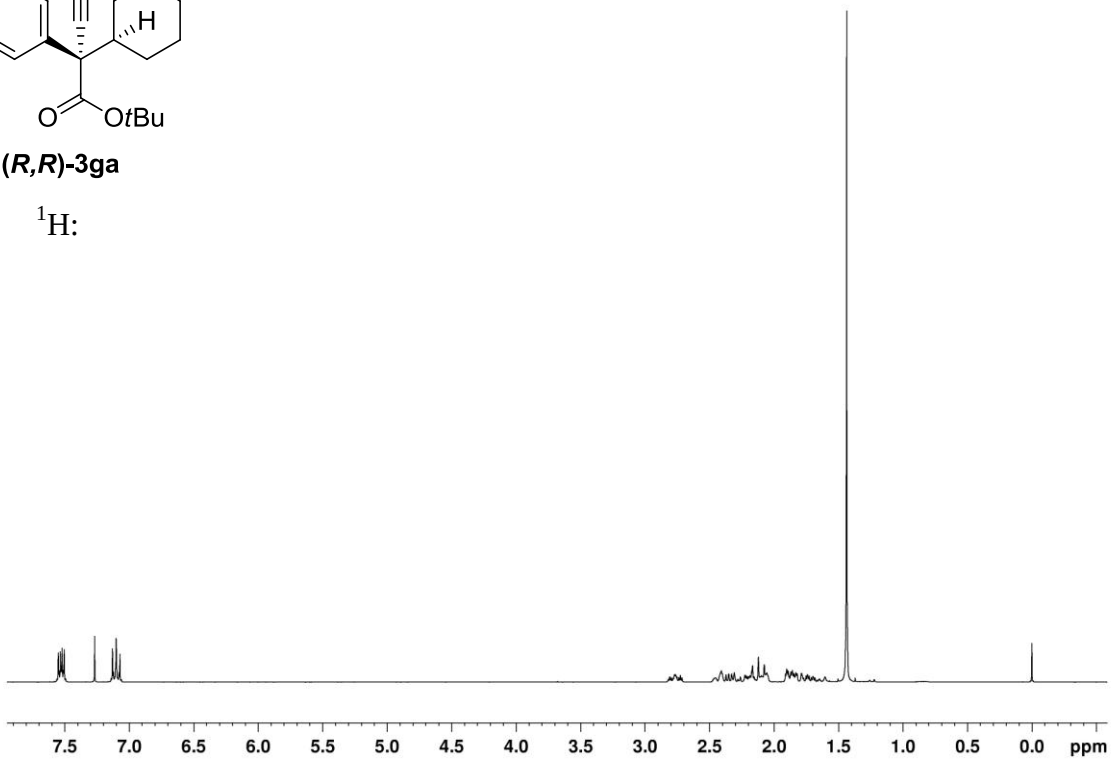


tert-Butyl-2-cyano-2-(4-fluorophenyl)-2-(3-oxocyclohexyl)-acetate (**(*R*,*R*)-3ga**)

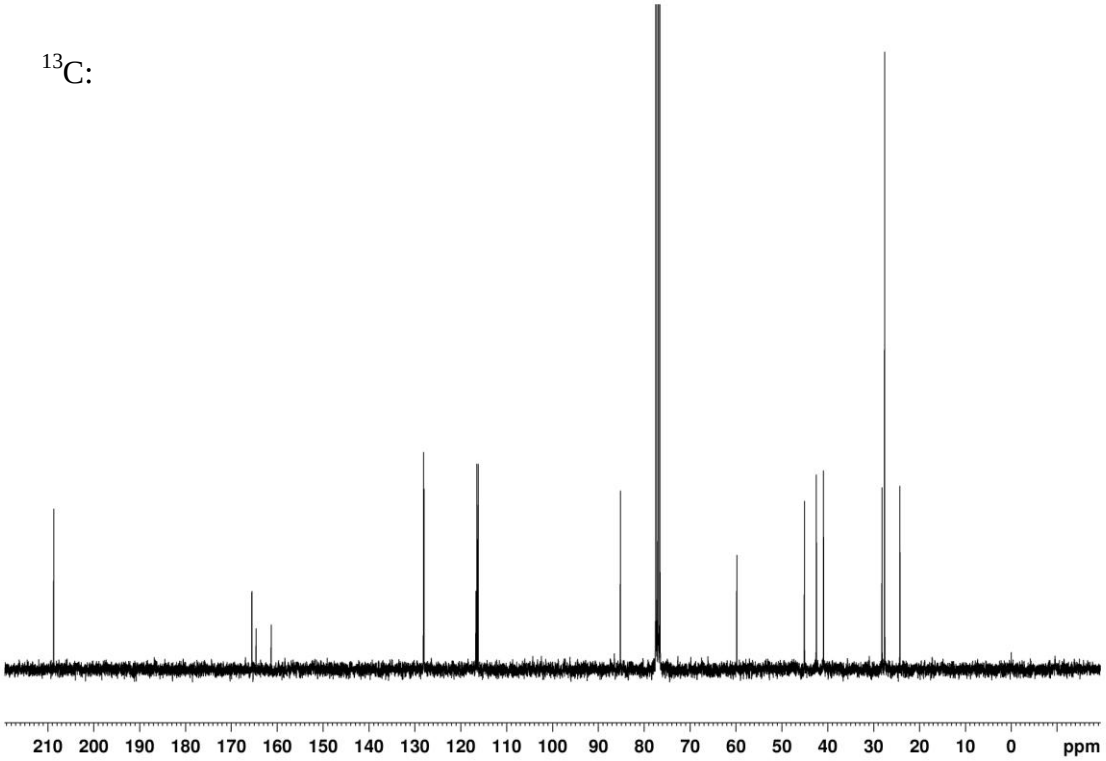


(*R*,*R*)-3ga

^{1}H:



^{13}C:



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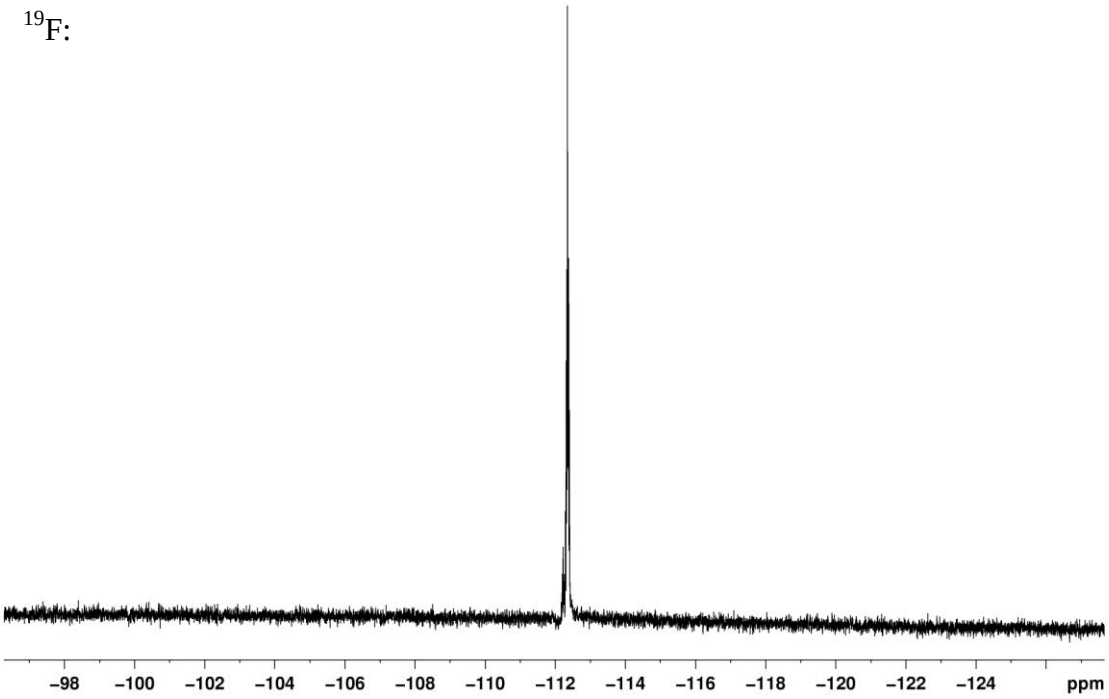
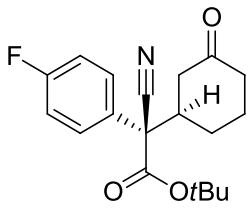


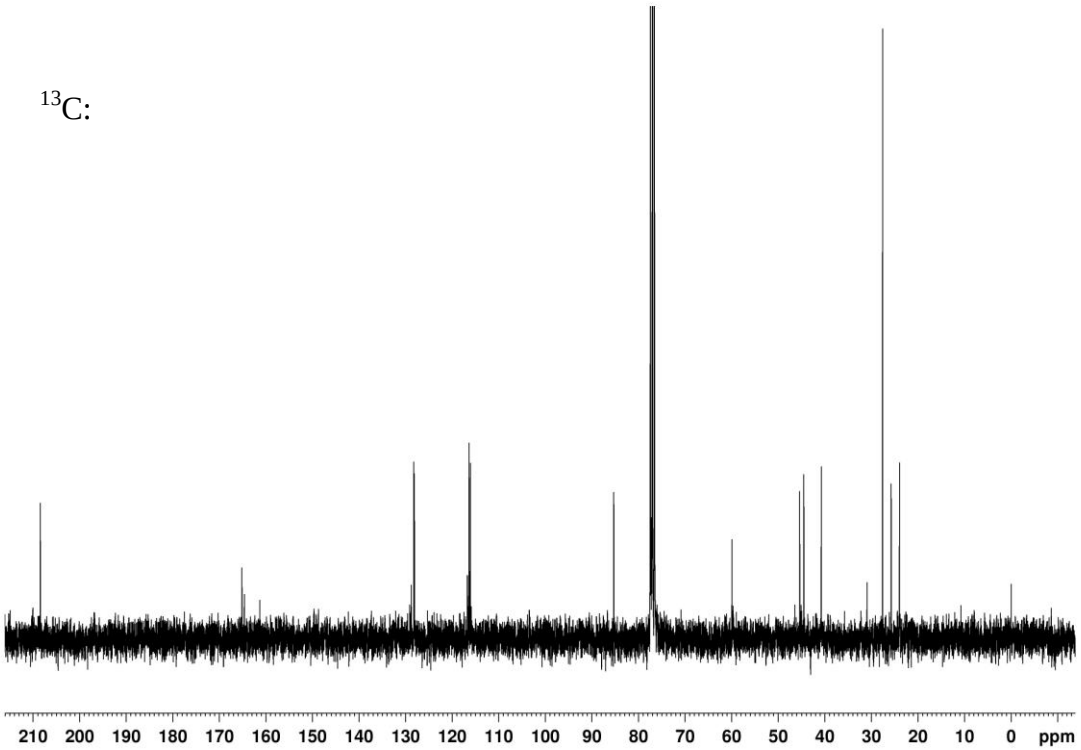
tert-Butyl-2-cyano-2-(4-fluorophenyl)-2-(3-oxocyclohexyl)-acetate (**(*S*,*R*)-3ga**)



(*S*,*R*)-3ga

^{1}H:

^{13}C:



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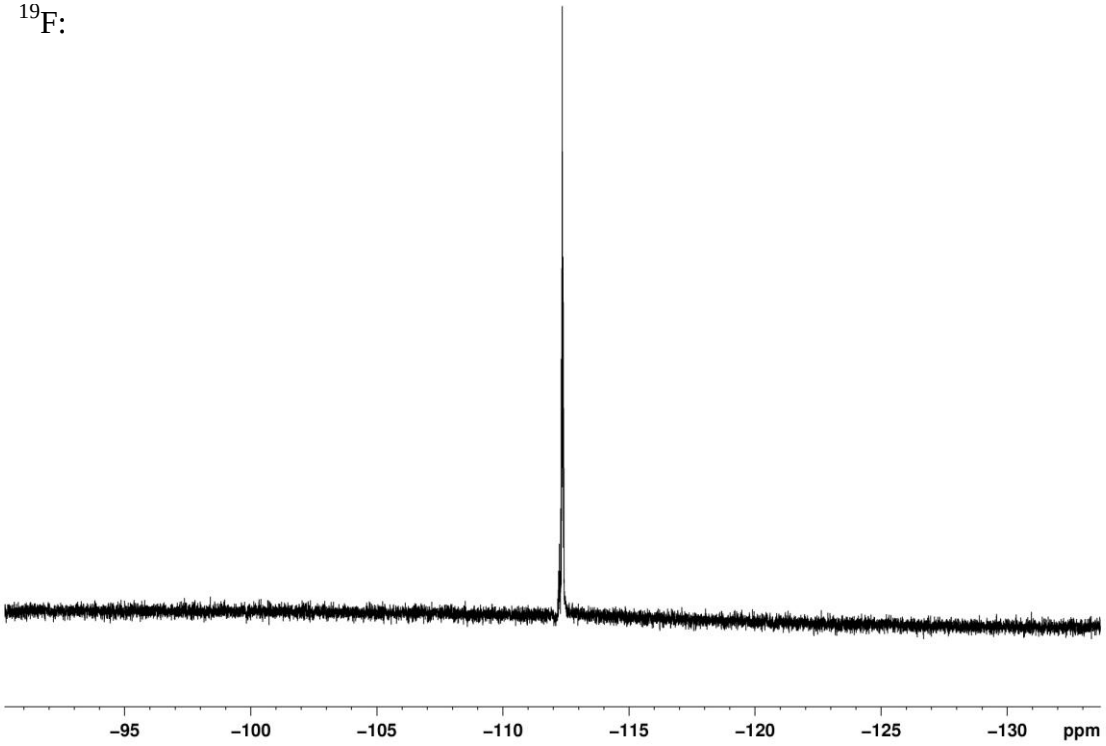
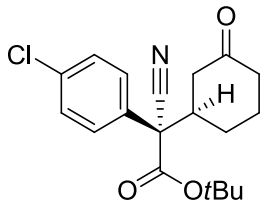
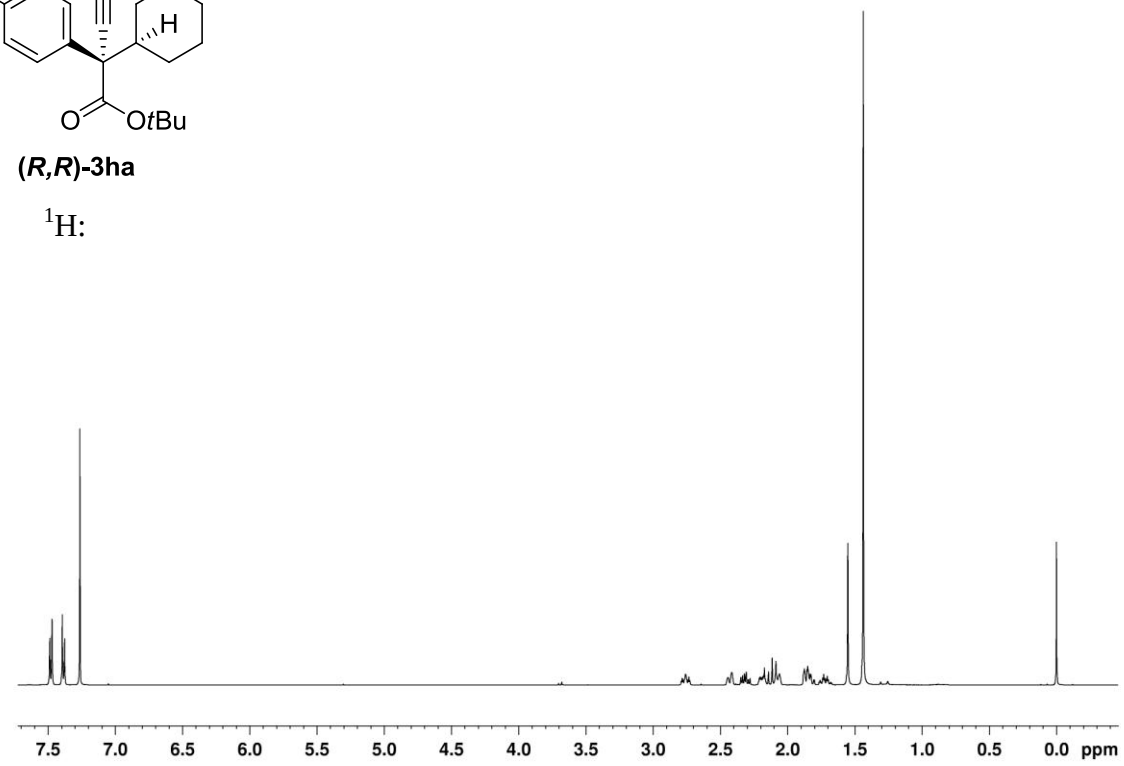


tert-Butyl-2-cyano-2-(4-chlorophenyl)-2-(3-oxocyclohexyl)-acetate (**(*R*,*R*)-3ha**)



(*R*,*R*)-3ha

^{1}H:



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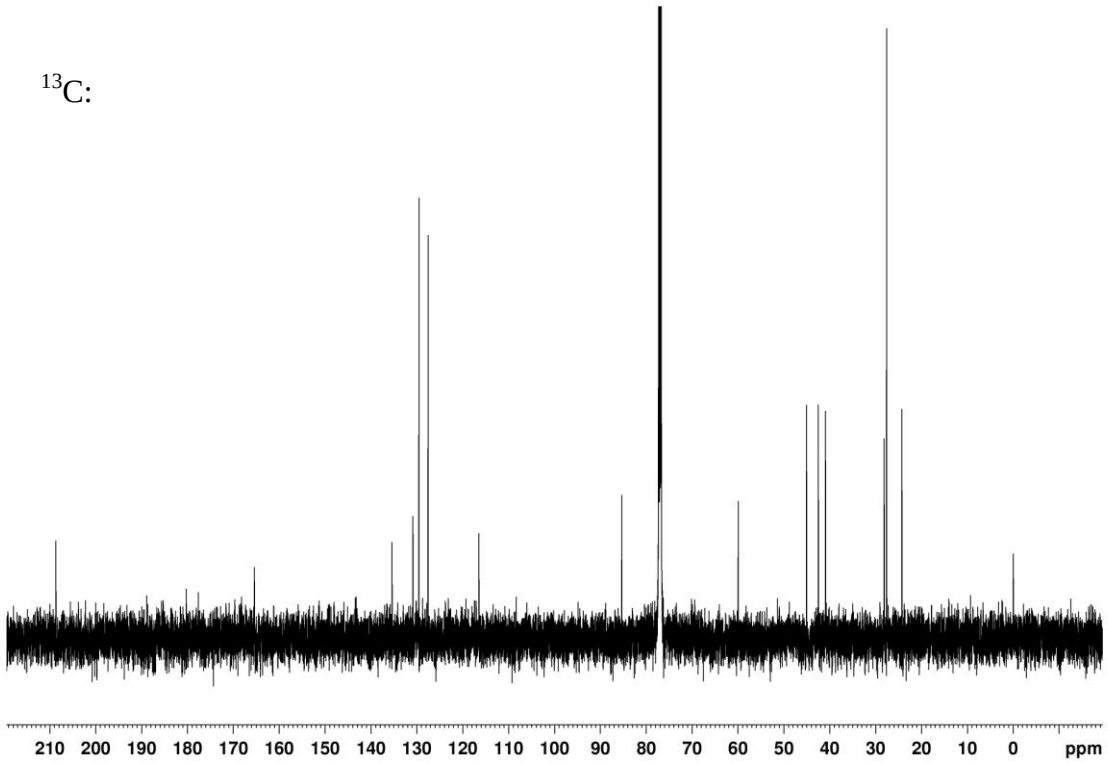
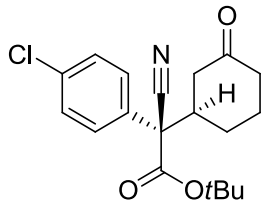
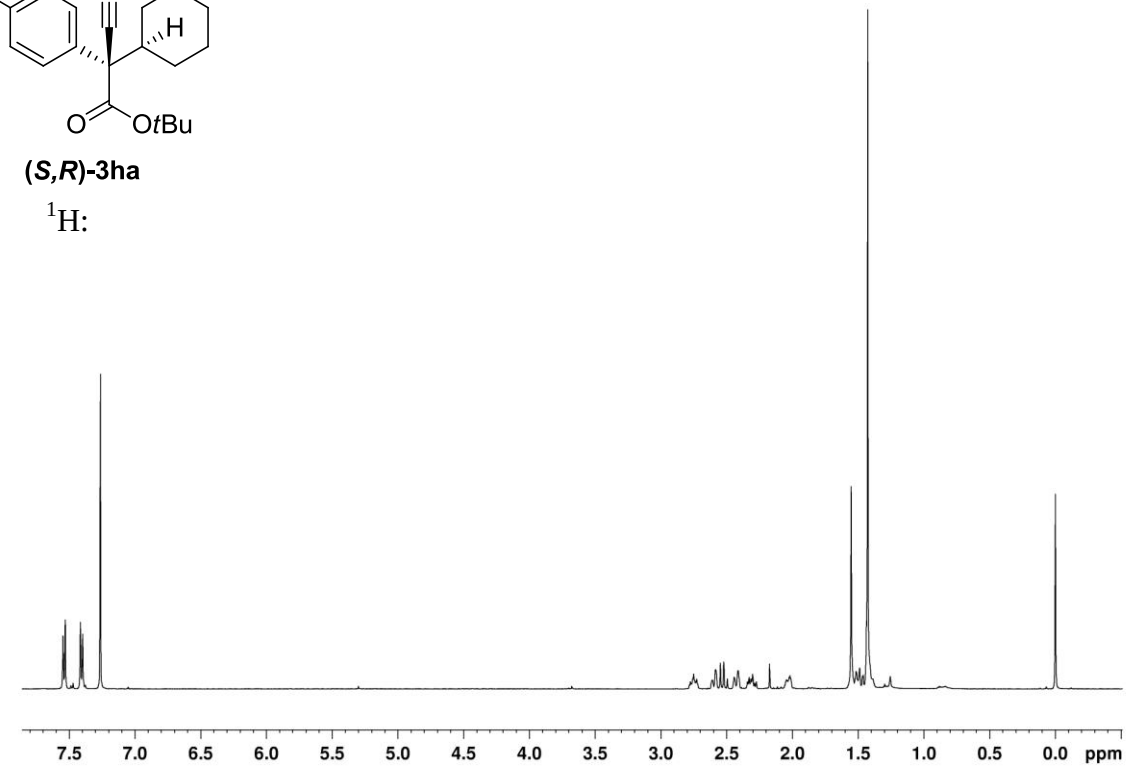


tert-Butyl-2-cyano-2-(4-chlorophenyl)-2-(3-oxocyclohexyl)-acetate (**(*S*,*R*)-3ha**)



(*S*,*R*)-3ha

^{1}H:



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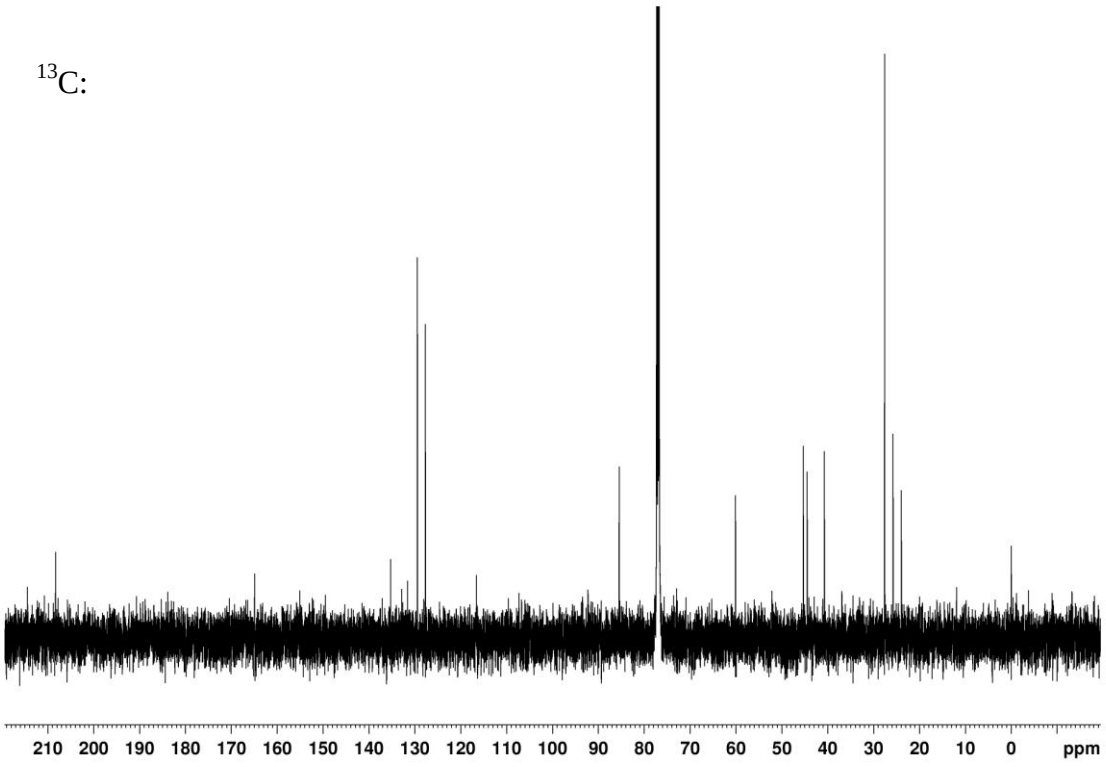
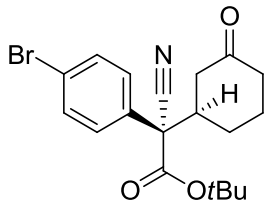


tert-Butyl-2-cyano-2-(4-bromophenyl)-2-(3-oxocyclohexyl)-acetate (**(*R*,*R*)-3ia**)



(*R*,*R*)-3ia

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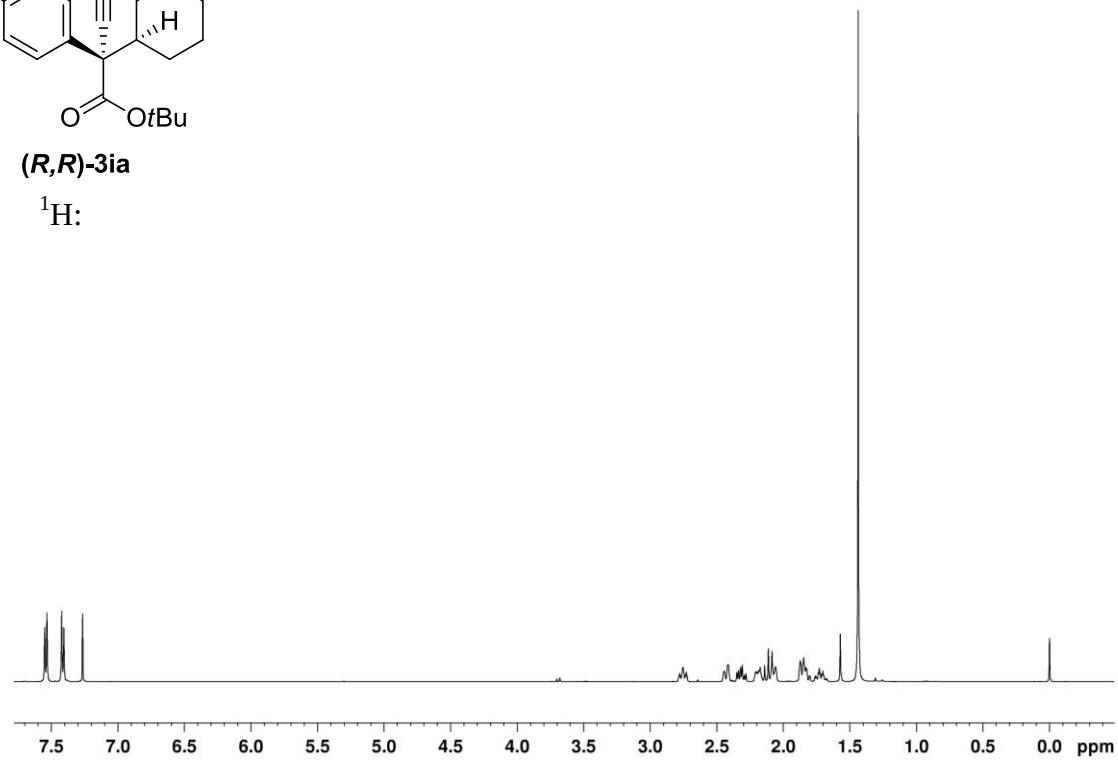

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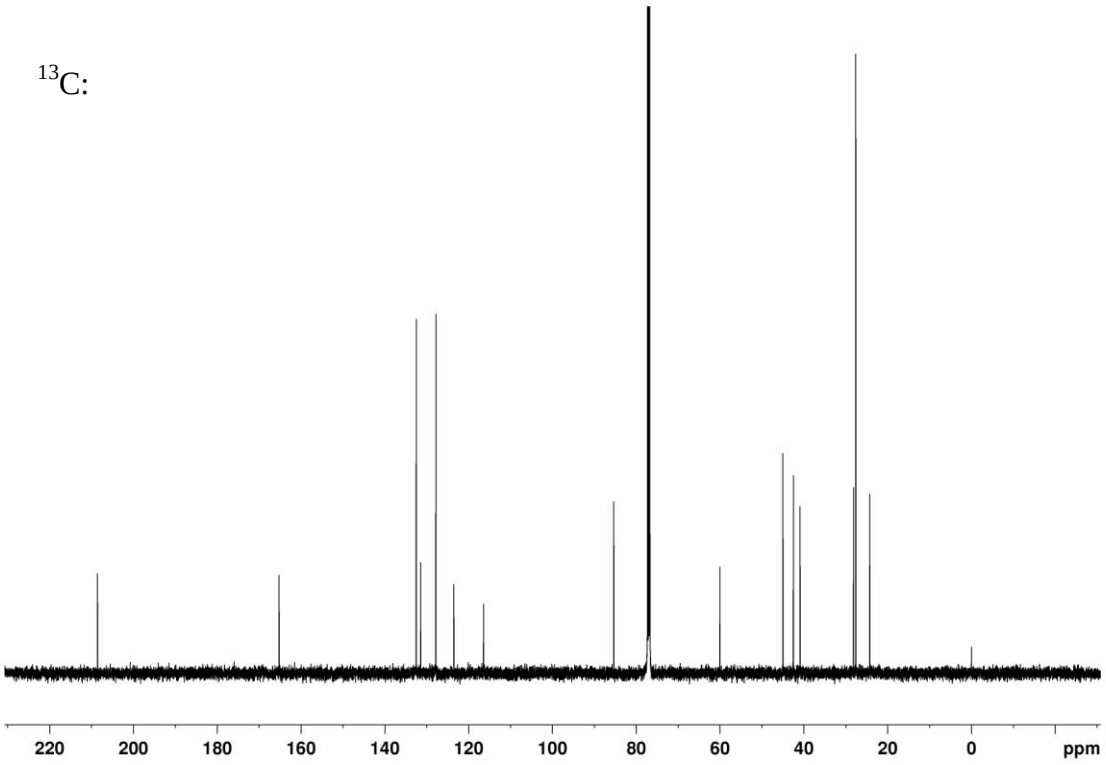
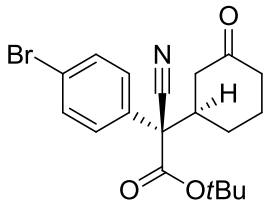
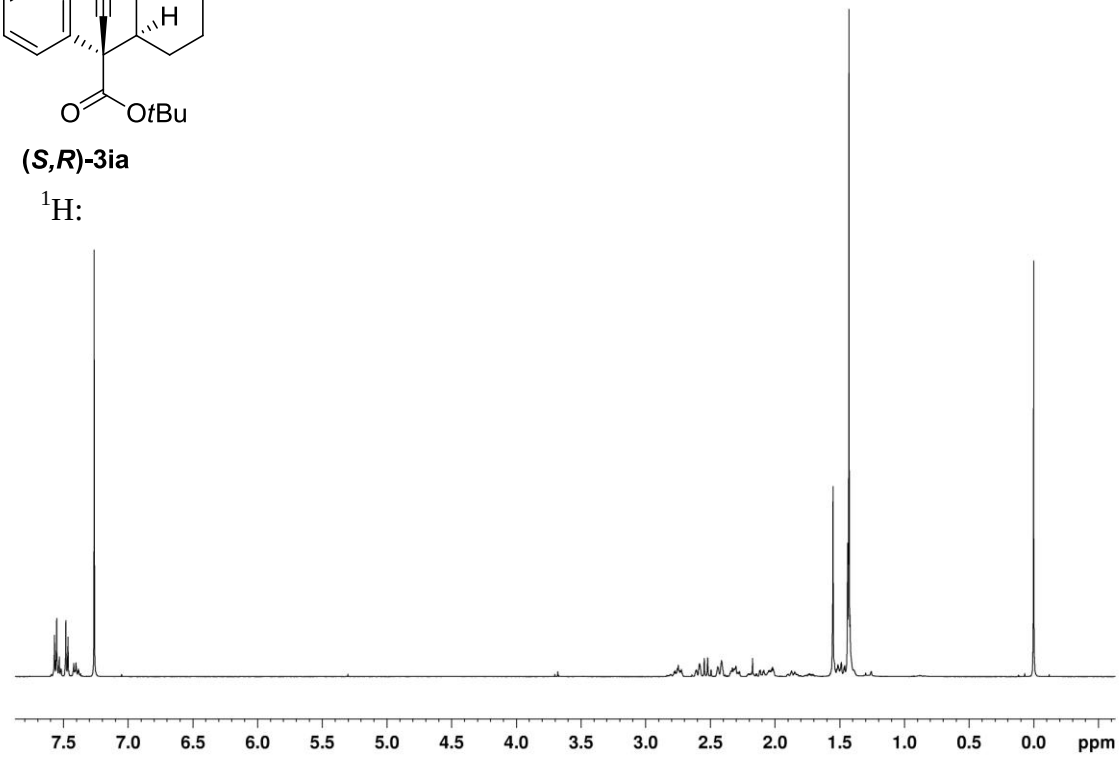


tert-Butyl-2-cyano-2-(4-bromophenyl)-2-(3-oxocyclohexyl)-acetate (**(*S*,*R*)-3ia**)



(*S*,*R*)-3ia

^{1}H:



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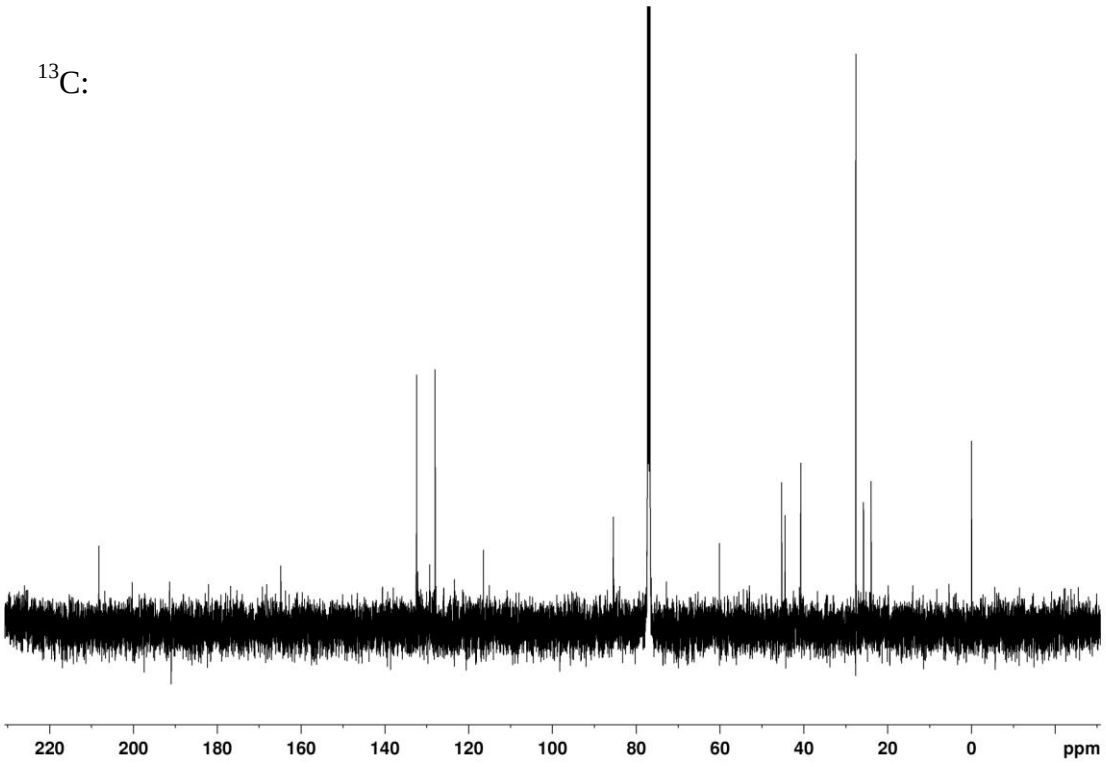
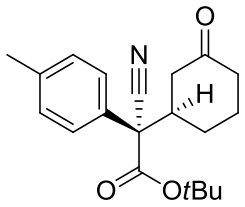
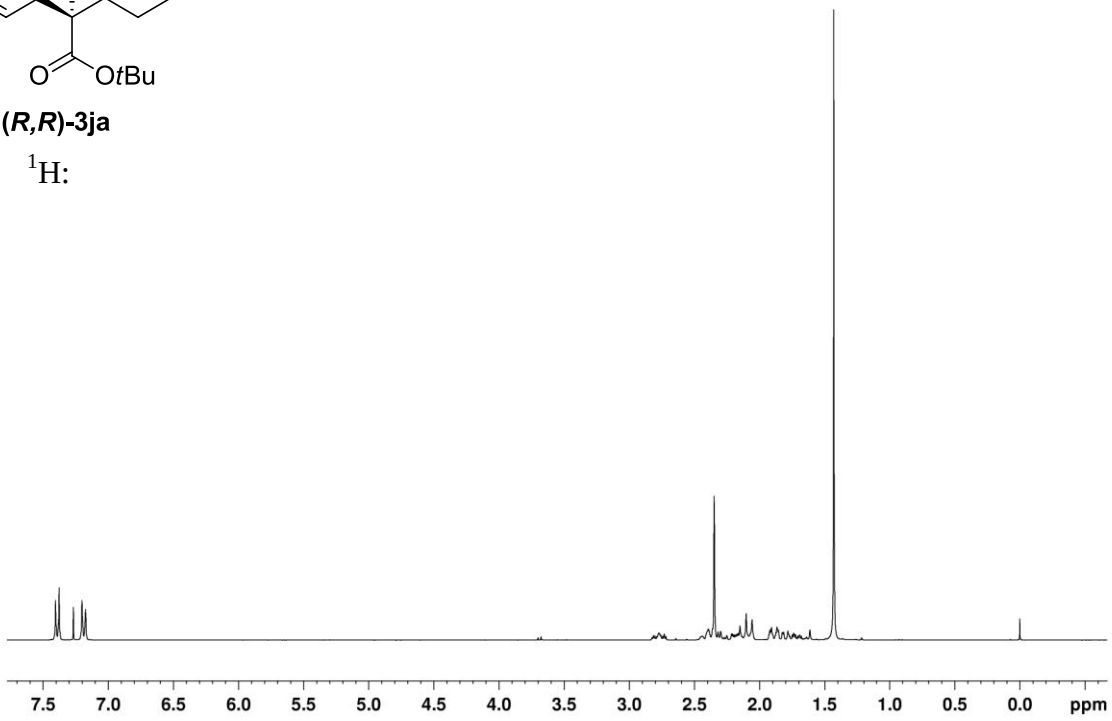


tert-Butyl-2-cyano-2-(3-oxocyclohexyl)-2-(*p*-tolyl)-acetate (**(*R*,*R*)-3ja**)



(*R*,*R*)-3ja

^{1}H:



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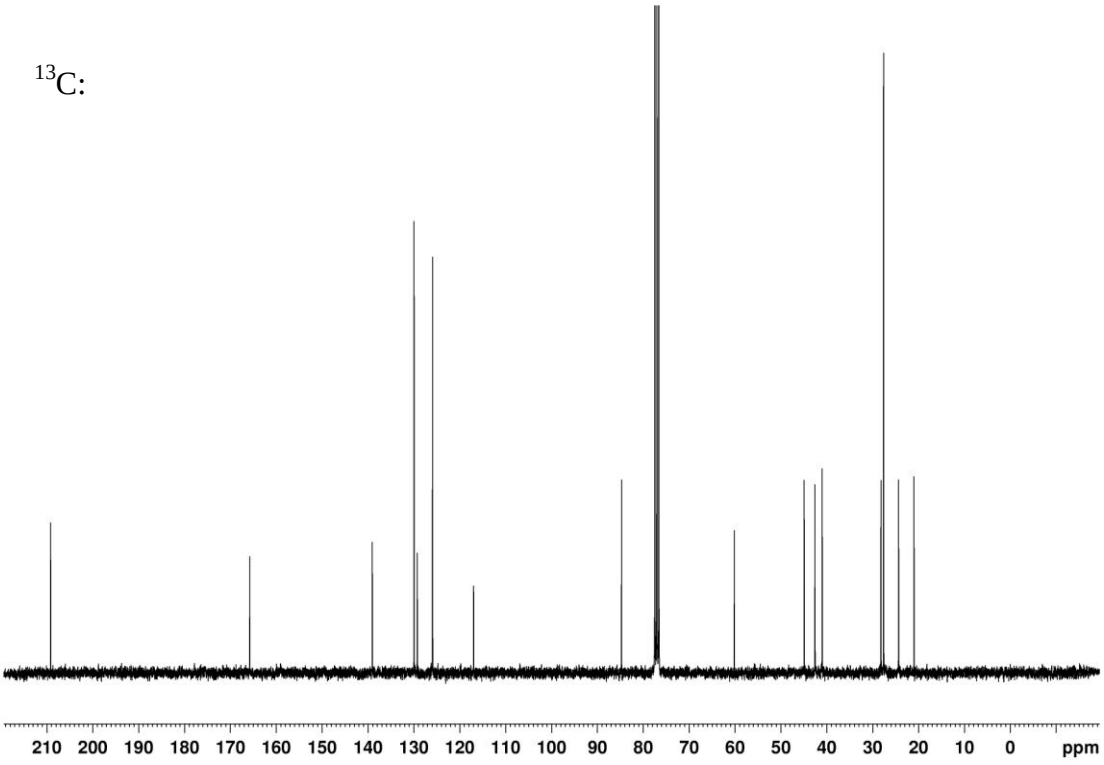
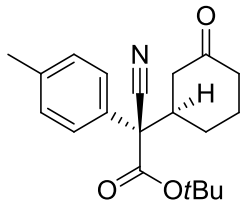
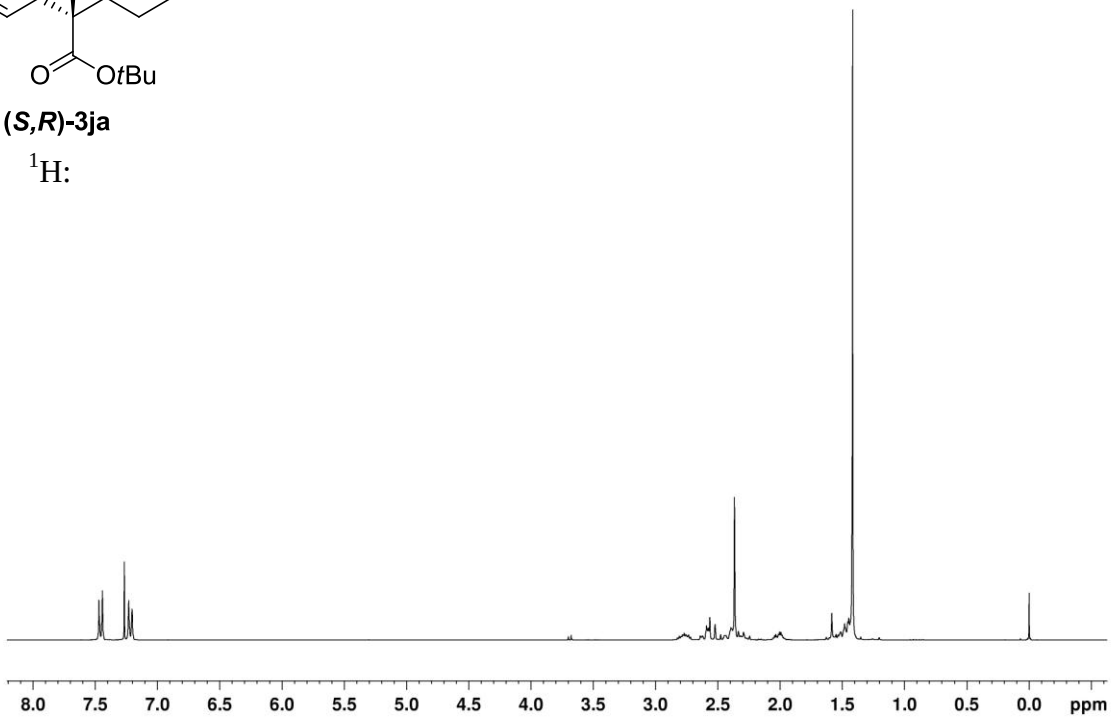


tert-Butyl-2-cyano-2-(3-oxocyclohexyl)-2-(*p*-tolyl)-acetate (**(*S*,*R*)-3ja**)



(*S*,*R*)-3ja

^{1}H:



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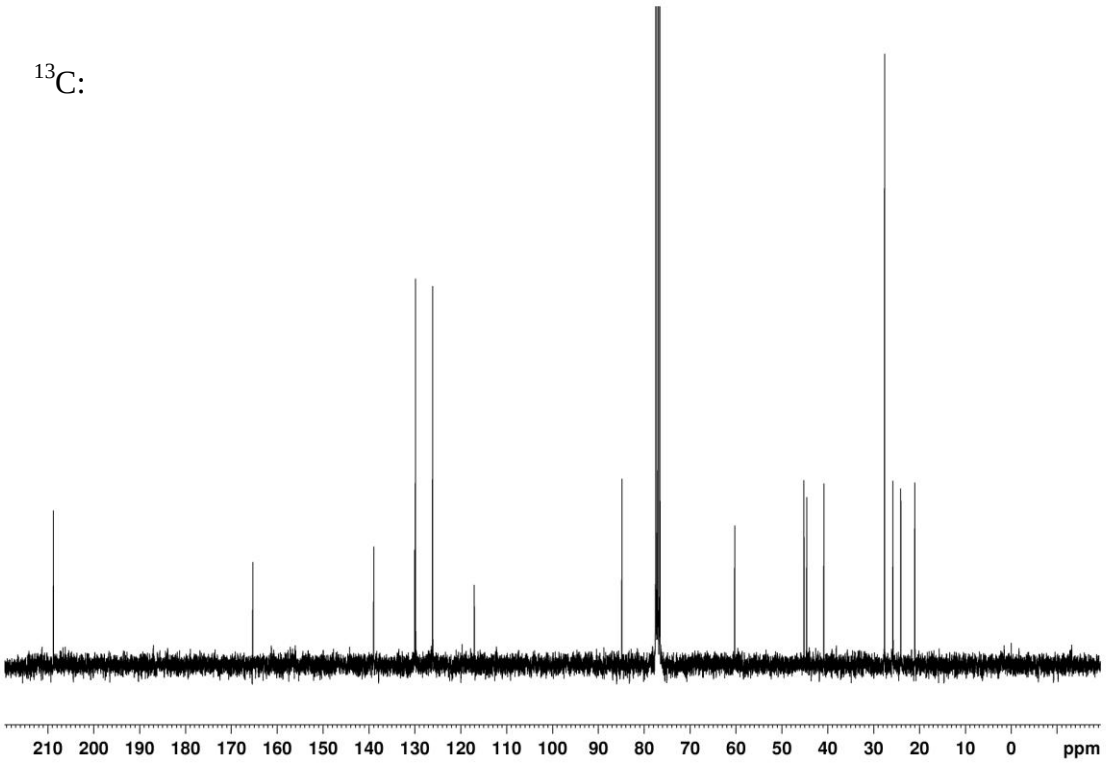
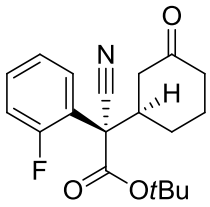
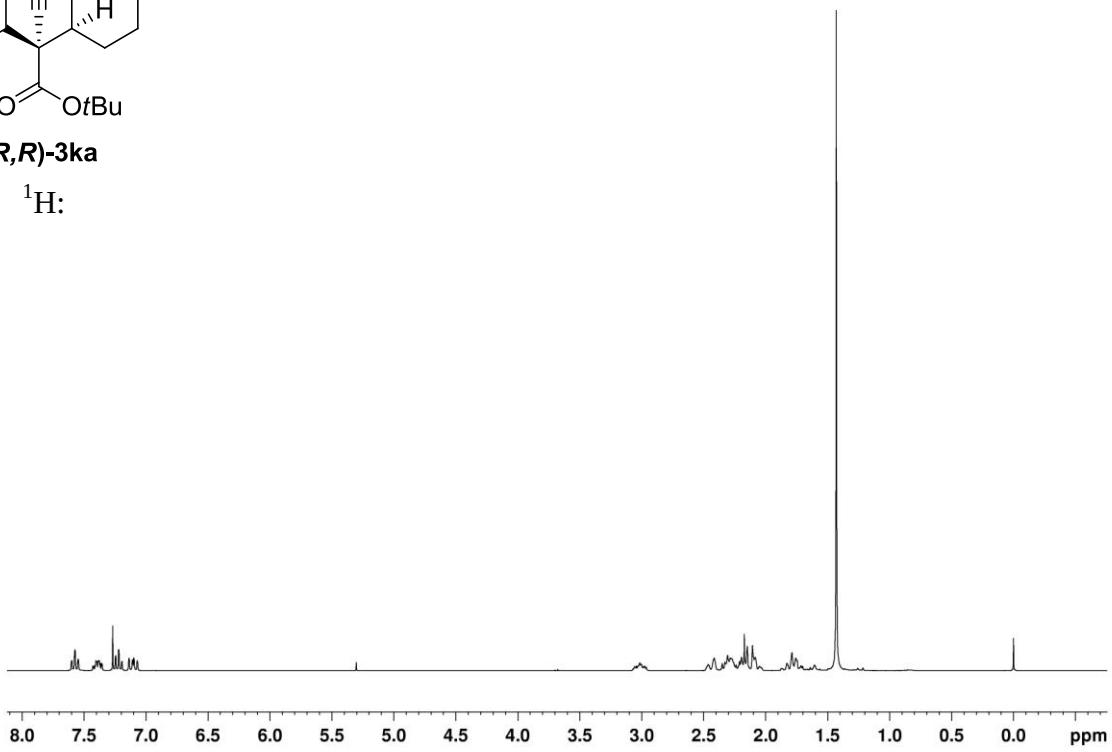


tert-Butyl-2-cyano-2-(2-fluorophenyl)-2-(3-oxocyclohexyl)-acetate (**(*R*,*R*)-3ka**)



(*R*,*R*)-3ka

^{1}H:



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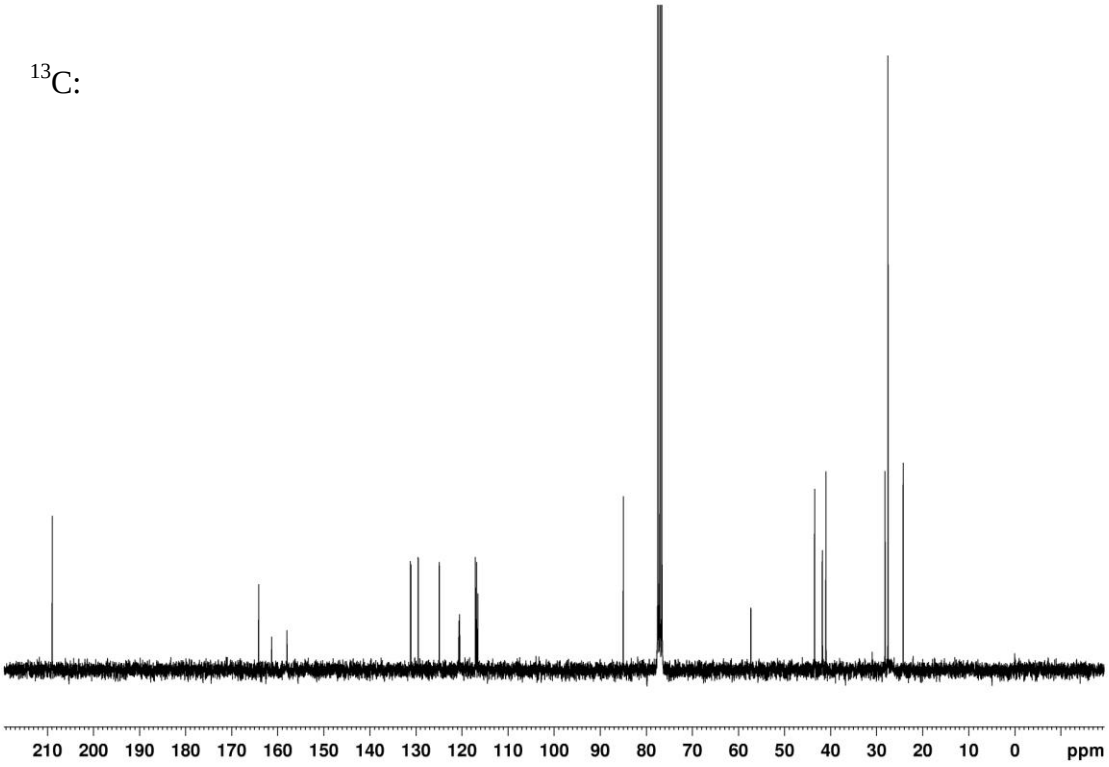

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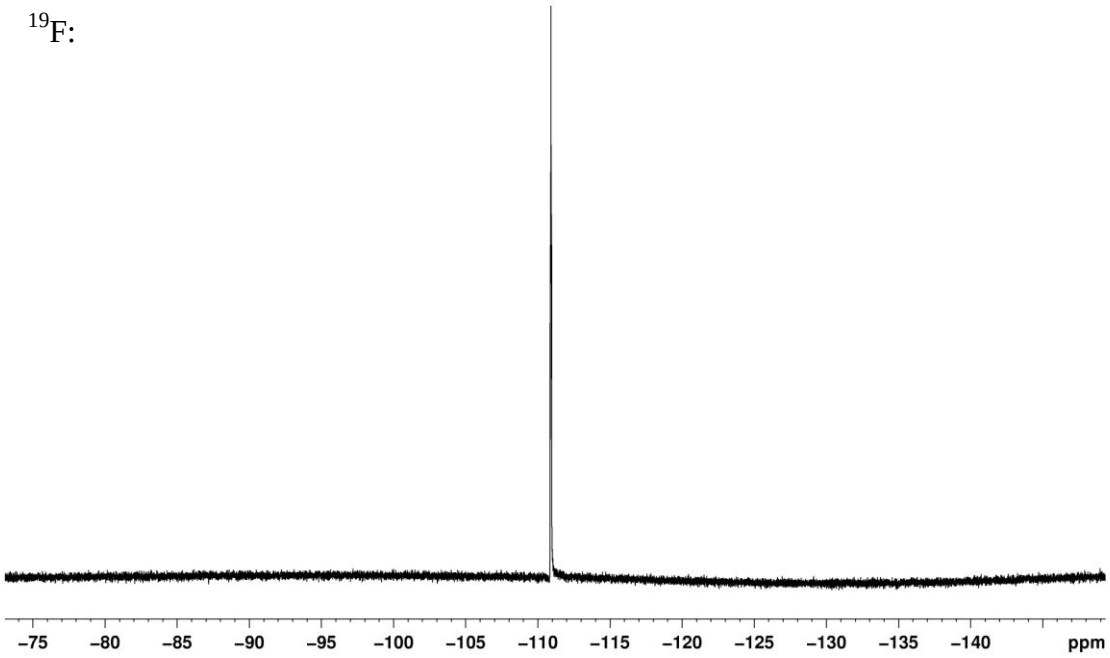
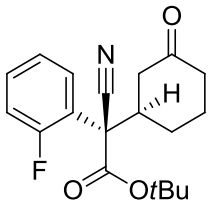
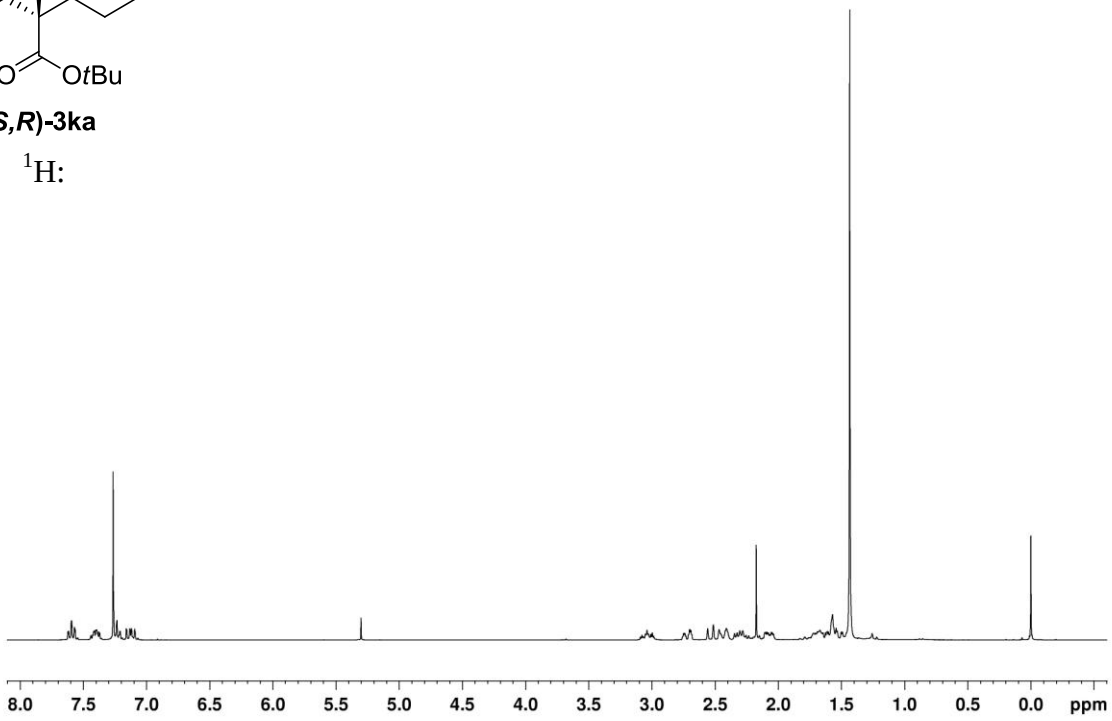


tert-Butyl-2-cyano-2-(2-fluorophenyl)-2-(3-oxocyclohexyl)-acetate (**(*S*,*R*)-3ka**)



(*S*,*R*)-3ka

^{1}H:



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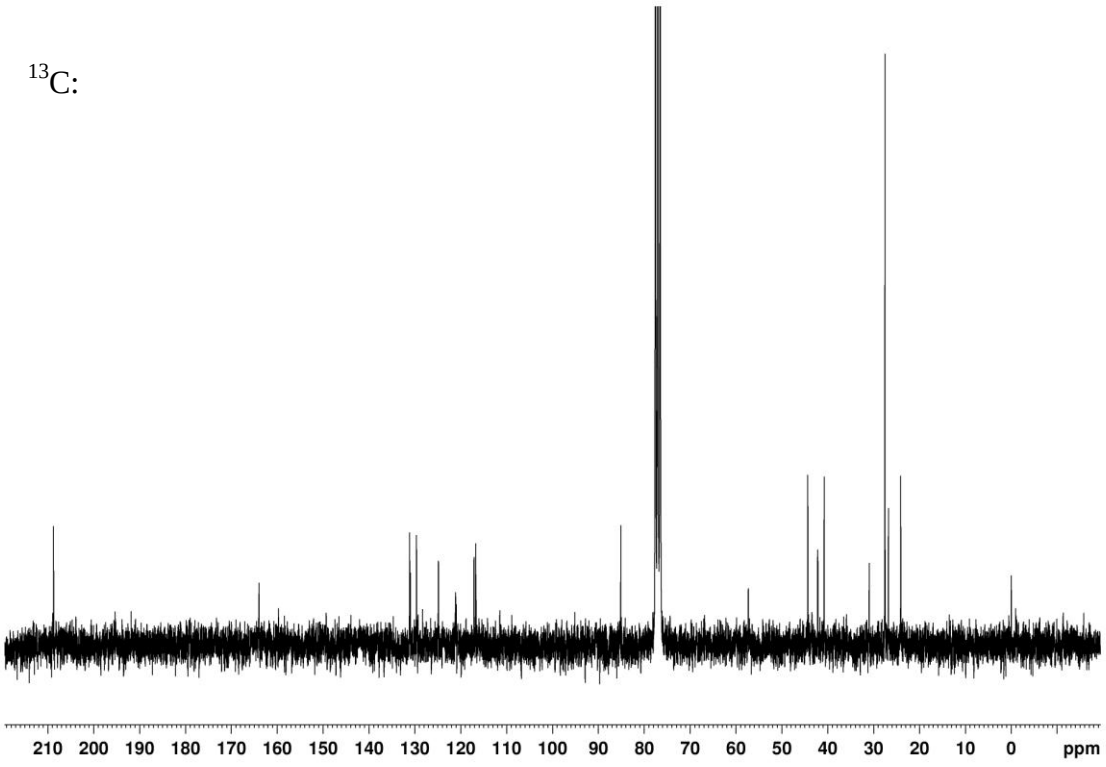

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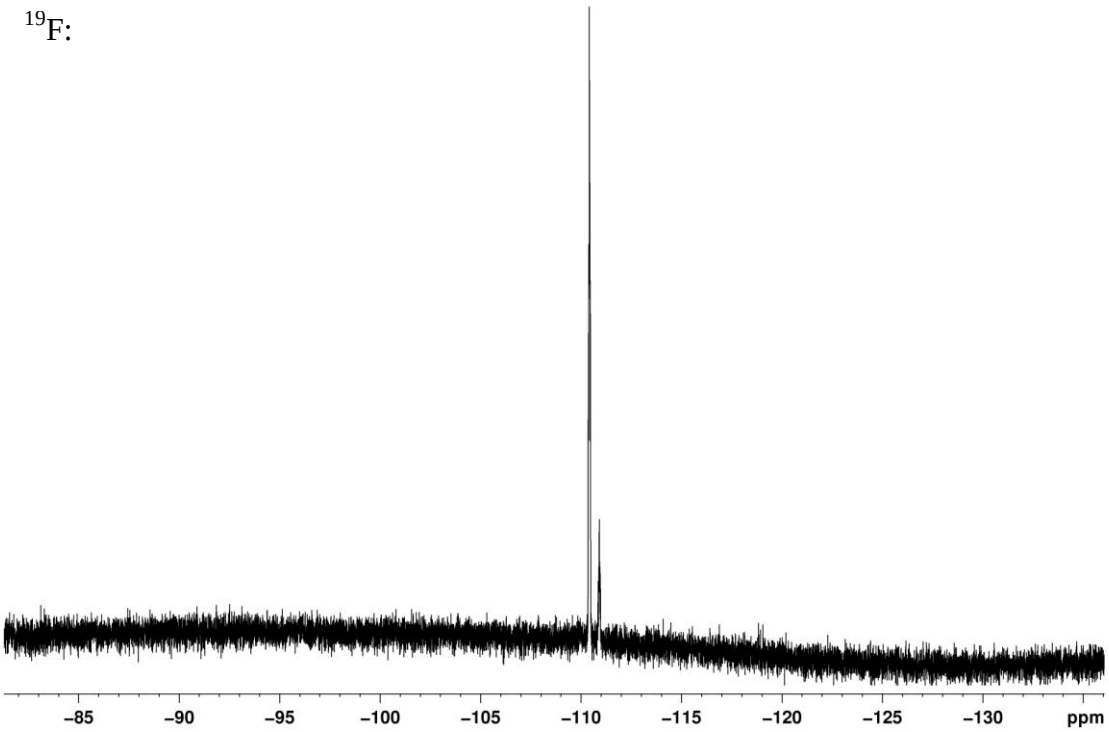
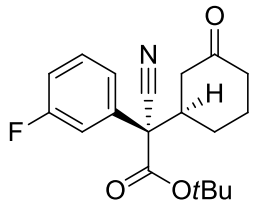
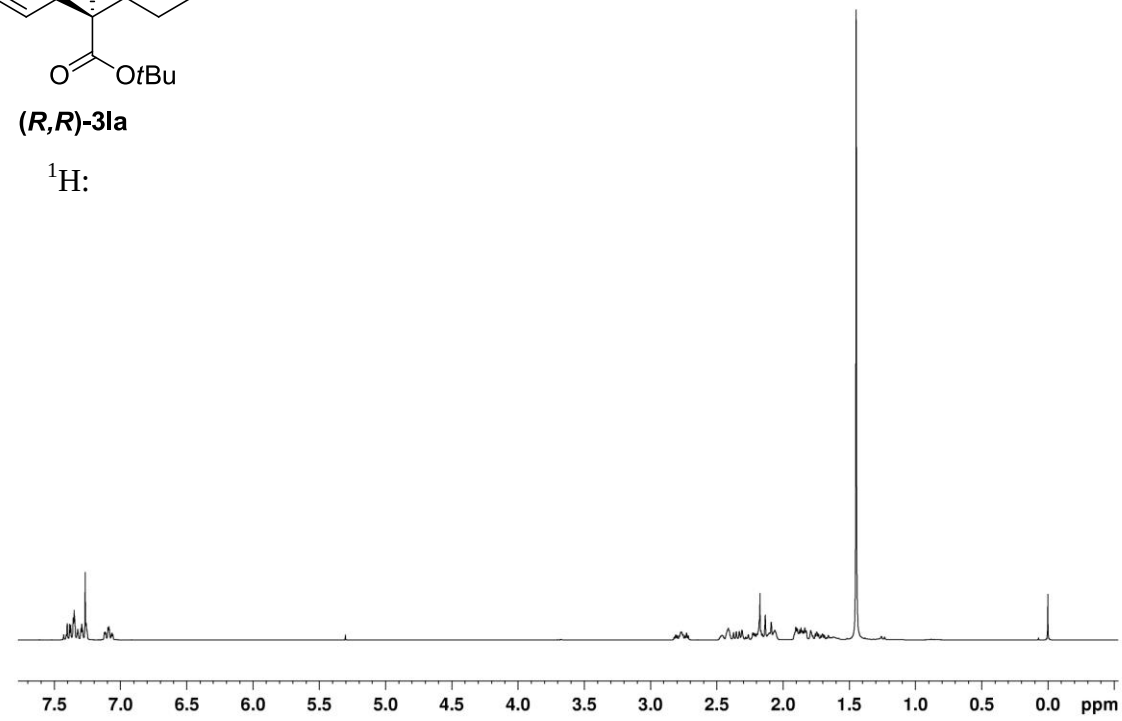


tert-Butyl-2-cyano-2-(3-fluorophenyl)-2-(3-oxocyclohexyl)-acetate (**(*R*,*R*)-3la**)



(*R*,*R*)-3la

^{1}H:



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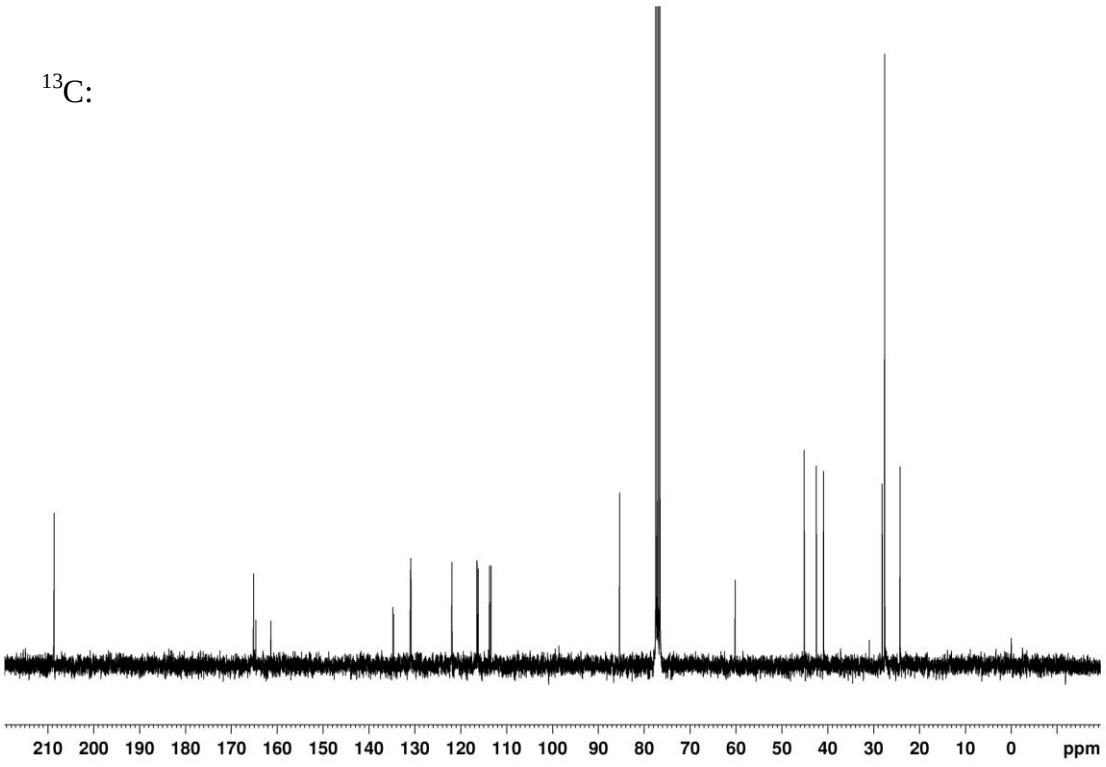

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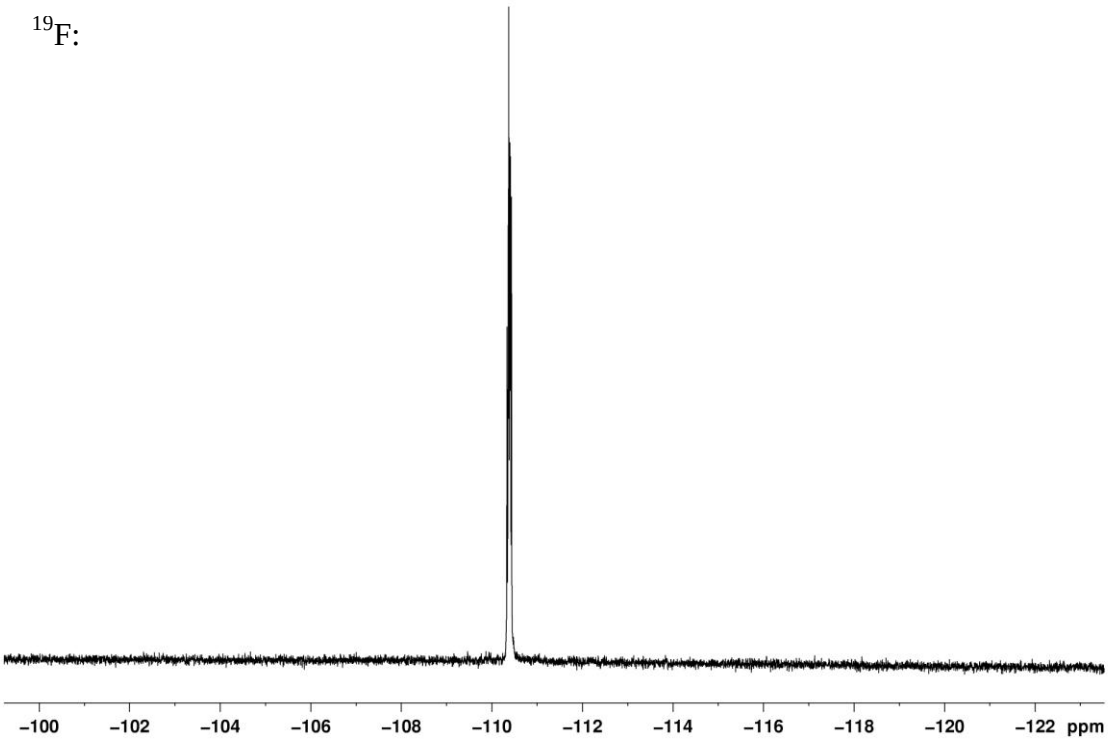
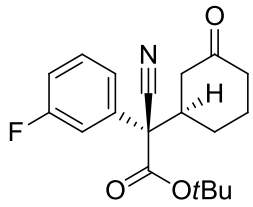
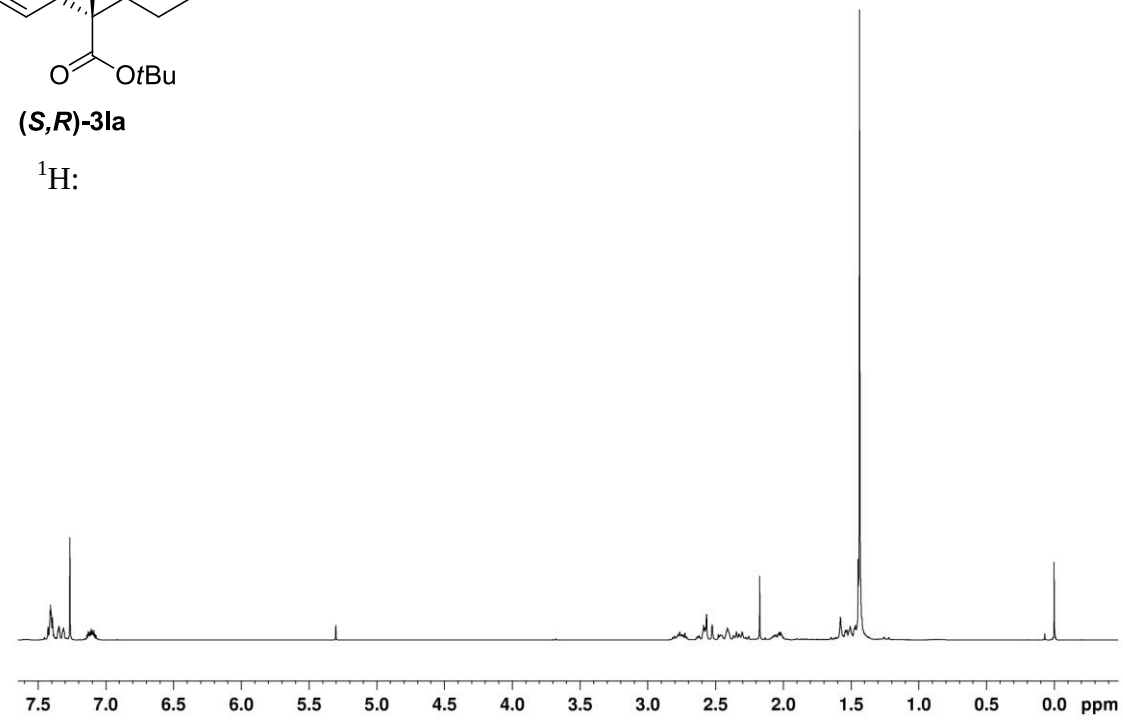


tert-Butyl-2-cyano-2-(3-fluorophenyl)-2-(3-oxocyclohexyl)-acetate (**(*S*,*R*)-3la**)



(*S*,*R*)-3la

^{1}H:



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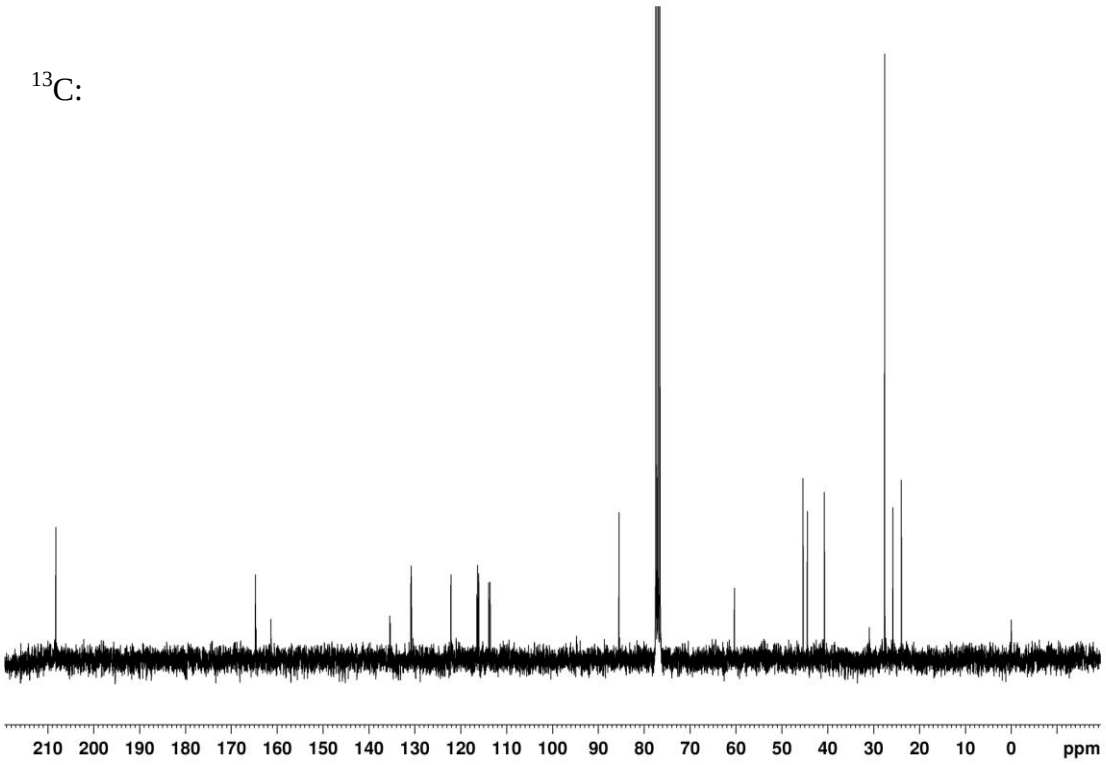

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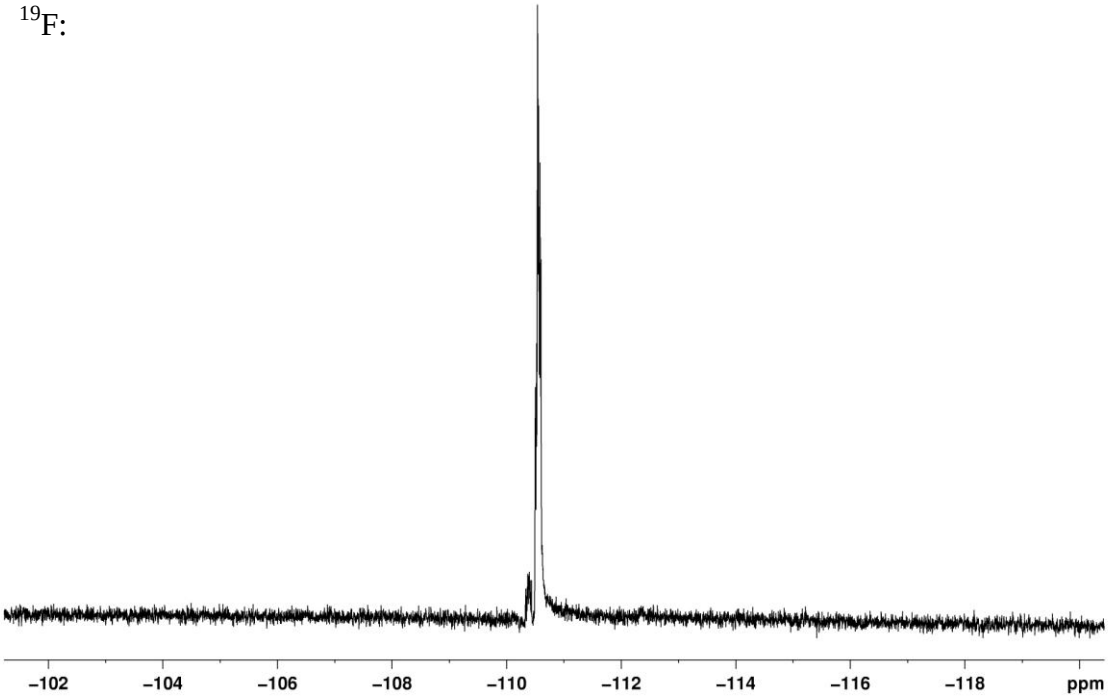
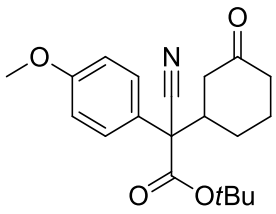
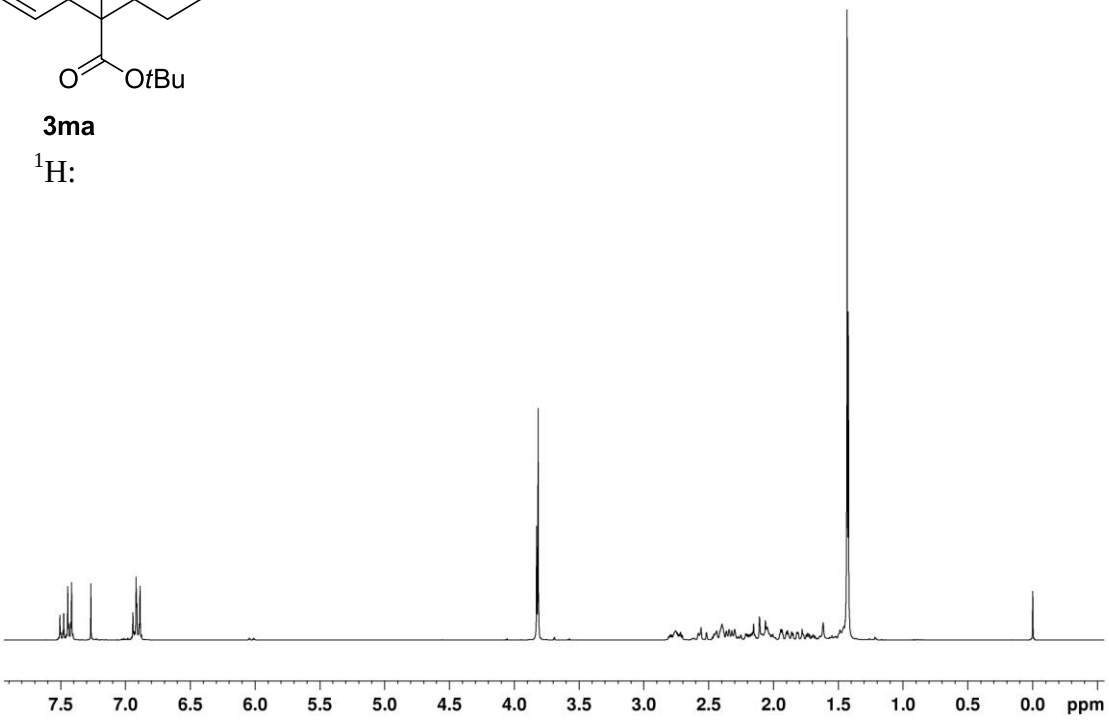


tert-Butyl-2-cyano-2-(4-methoxyphenyl)-2-(3-oxocyclohexyl)-acetate (**3ma**)



3ma

^{1}H:



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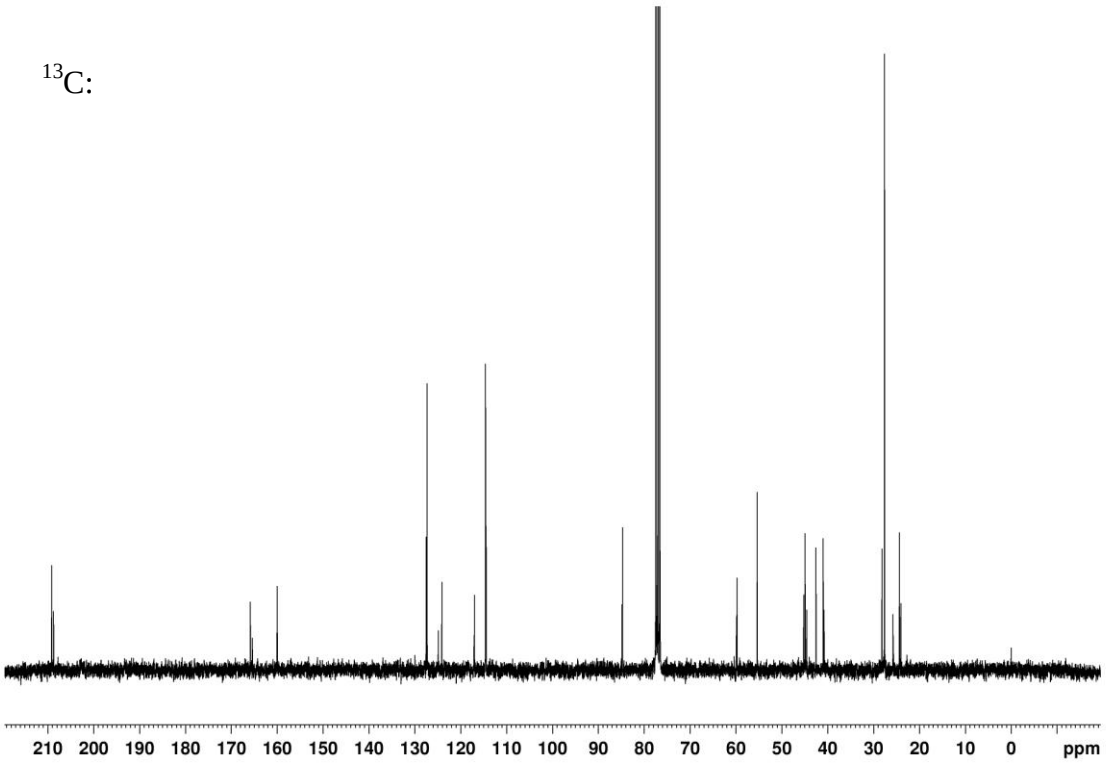
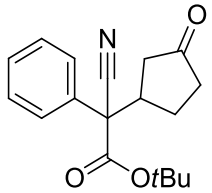
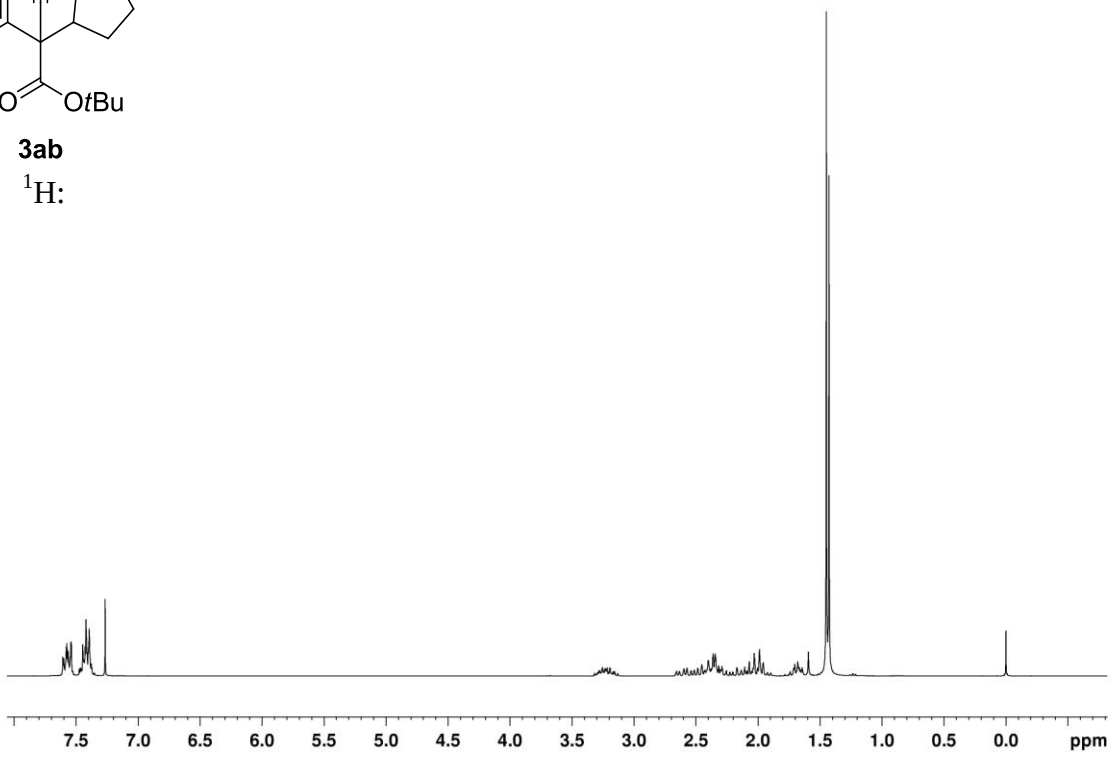


tert-Butyl-2-cyano-2-(3-oxocyclopentyl)-2-phenylacetate (**3ab**)



3ab

^{1}H:



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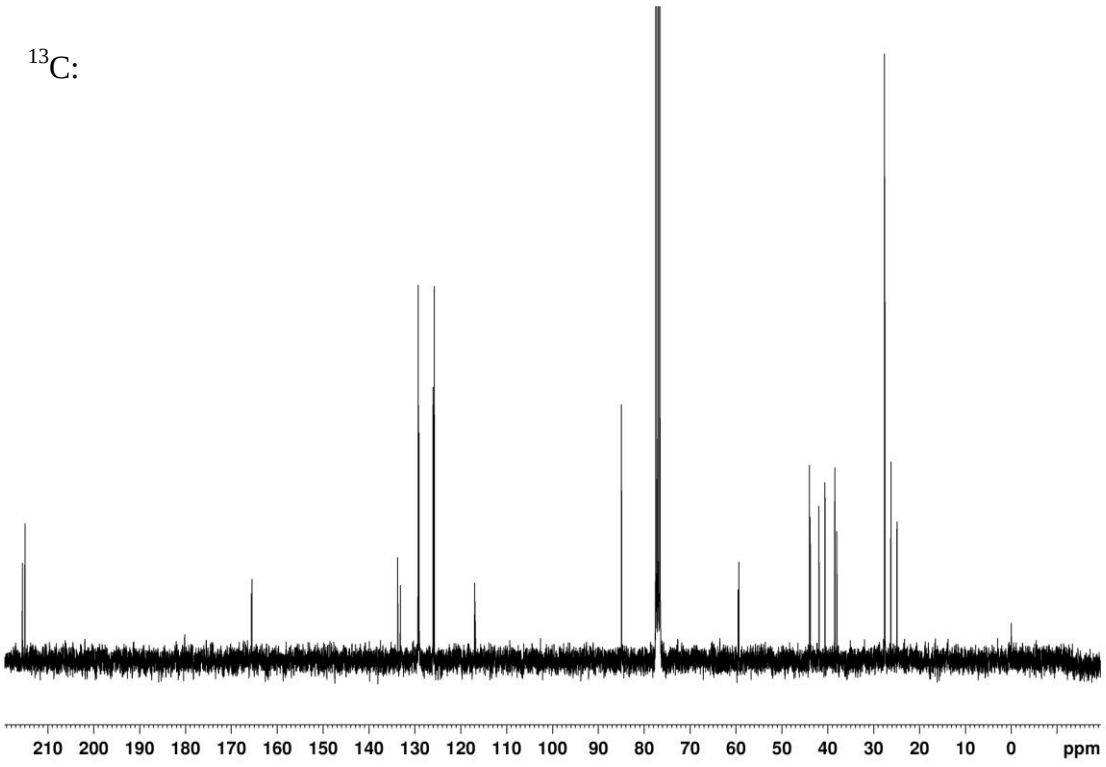
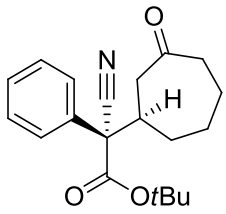
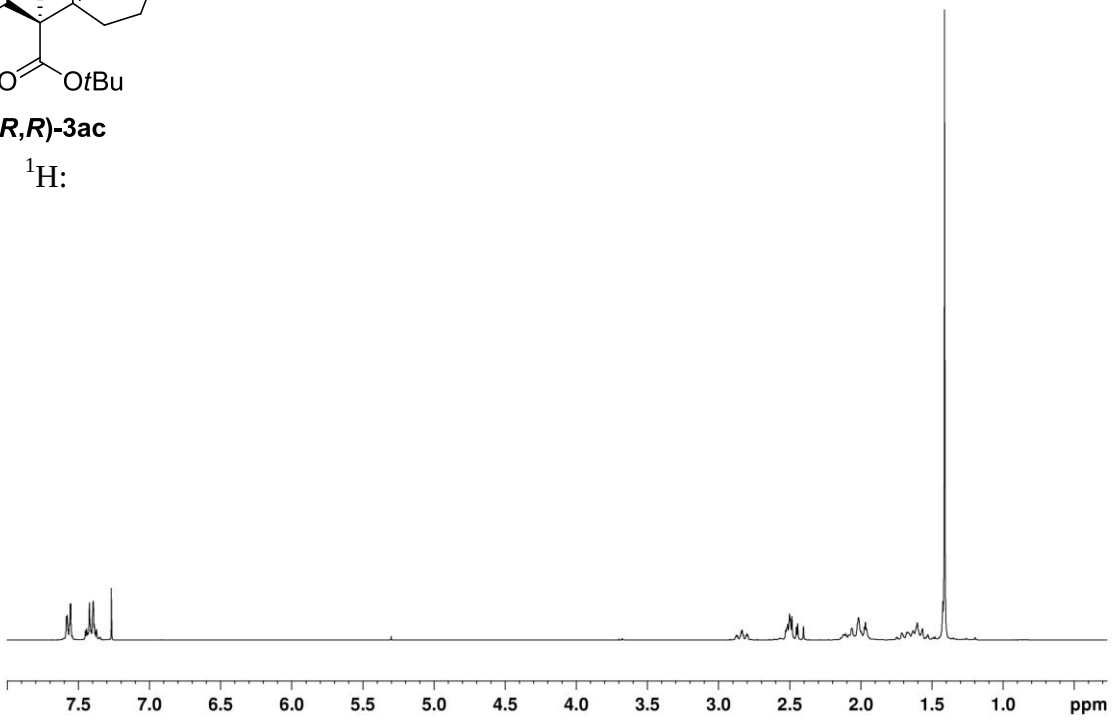


tert-Butyl-2-cyano-2-(3-oxocycloheptyl)-2-phenylacetate (**(*R*,*R*)-3ac**)



(*R*,*R*)-3ac

^{1}H:



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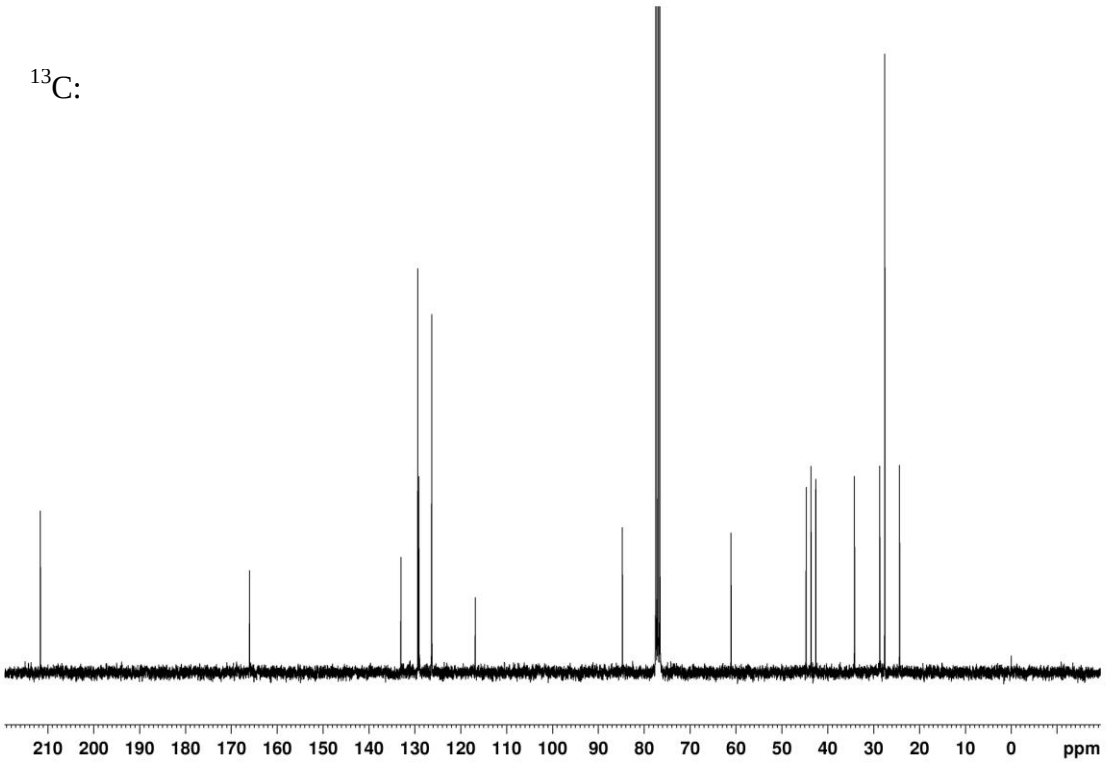
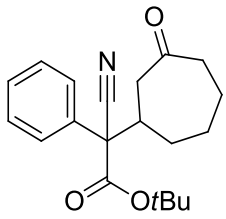
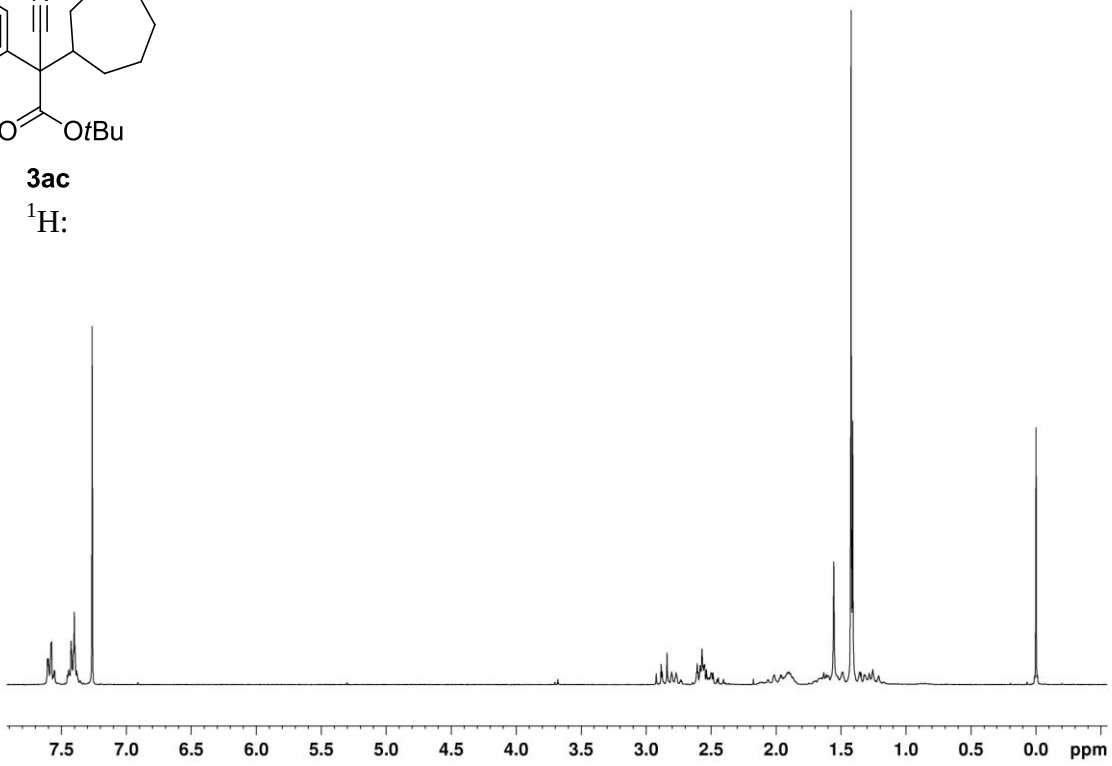


tert-Butyl-2-cyano-2-(3-oxocycloheptyl)-2-phenylacetate (**3ac**)

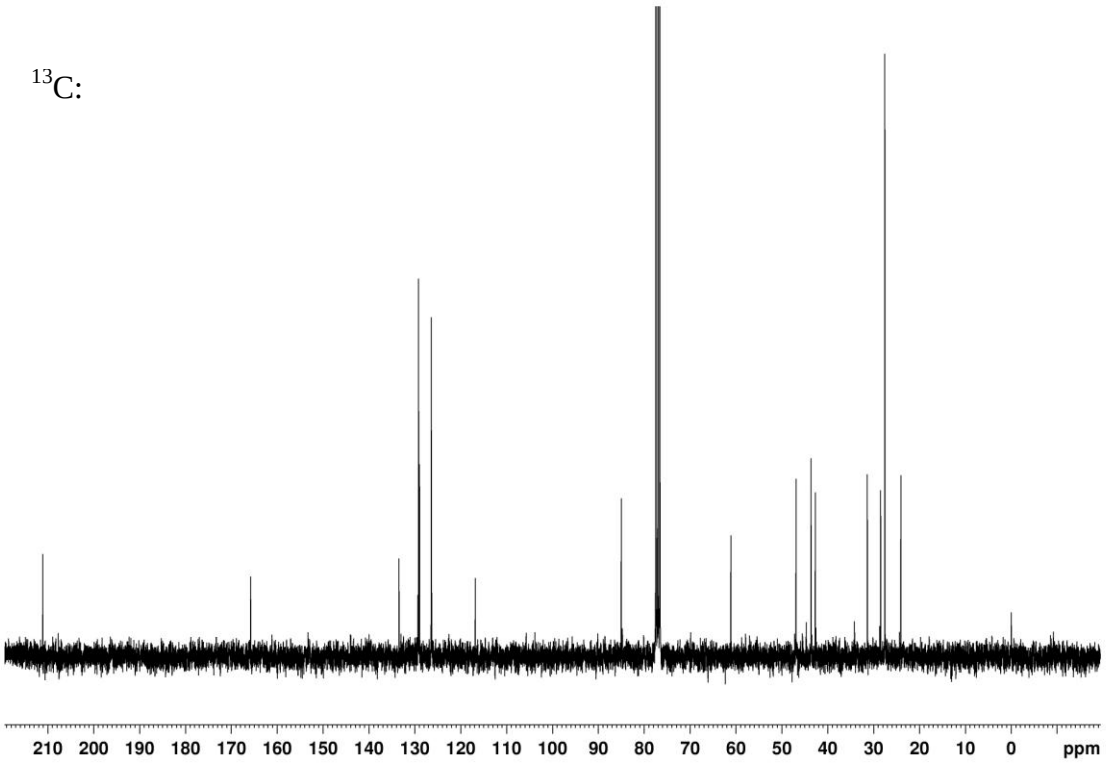


3ac

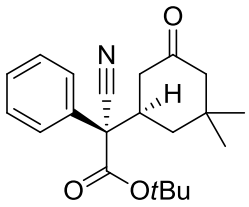
^{1}H:



^{13}C:

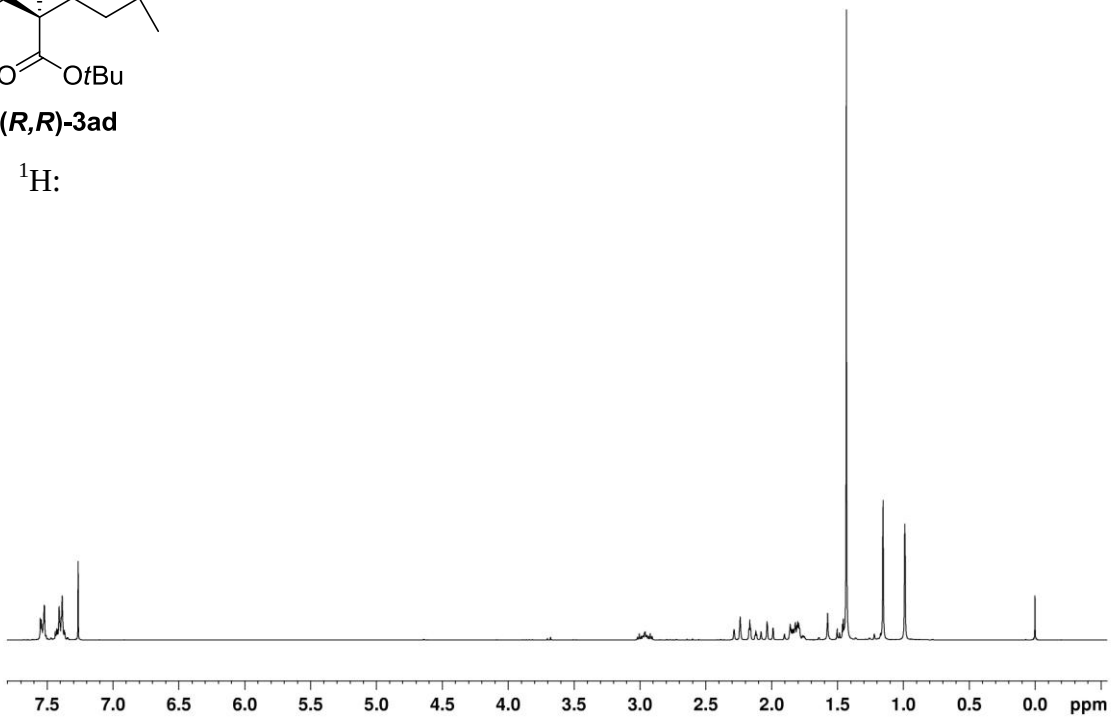


tert-Butyl-2-cyano-2-(3,3-dimethyl-5-oxocyclohexyl)-2-phenylacetate (**(*R*,*R*)-3ad**)

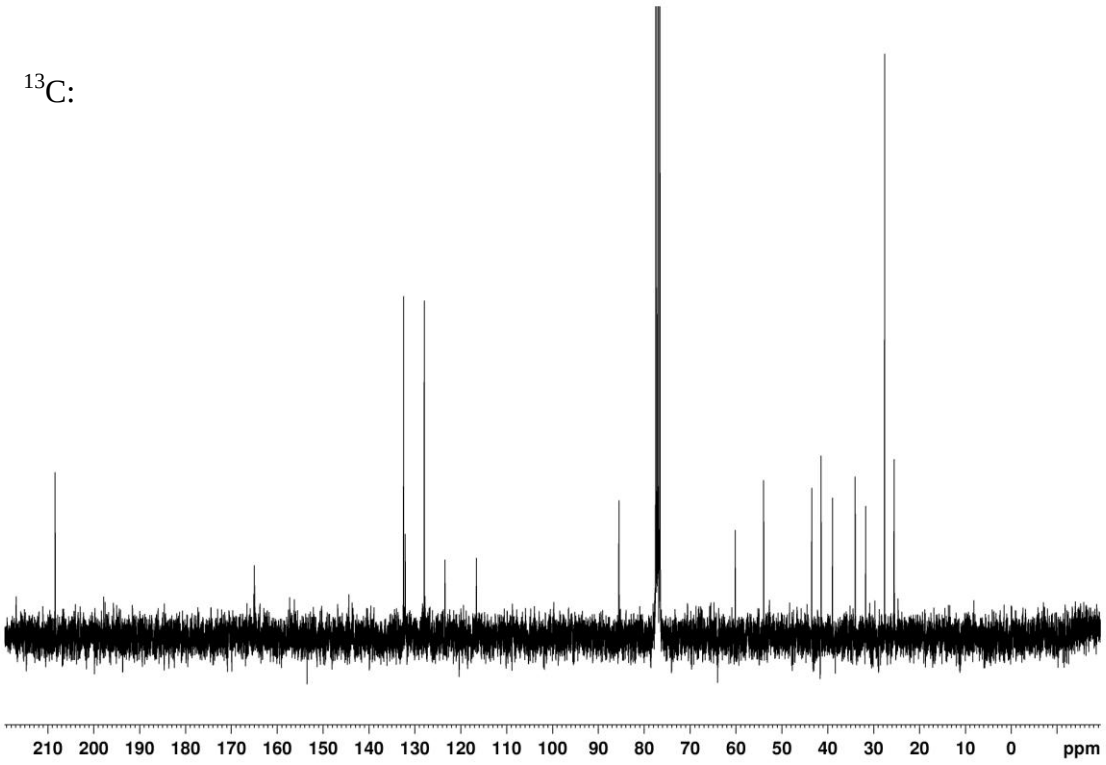


(*R*,*R*)-3ad

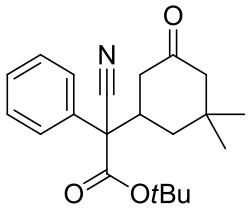
^{1}H:



^{13}C:

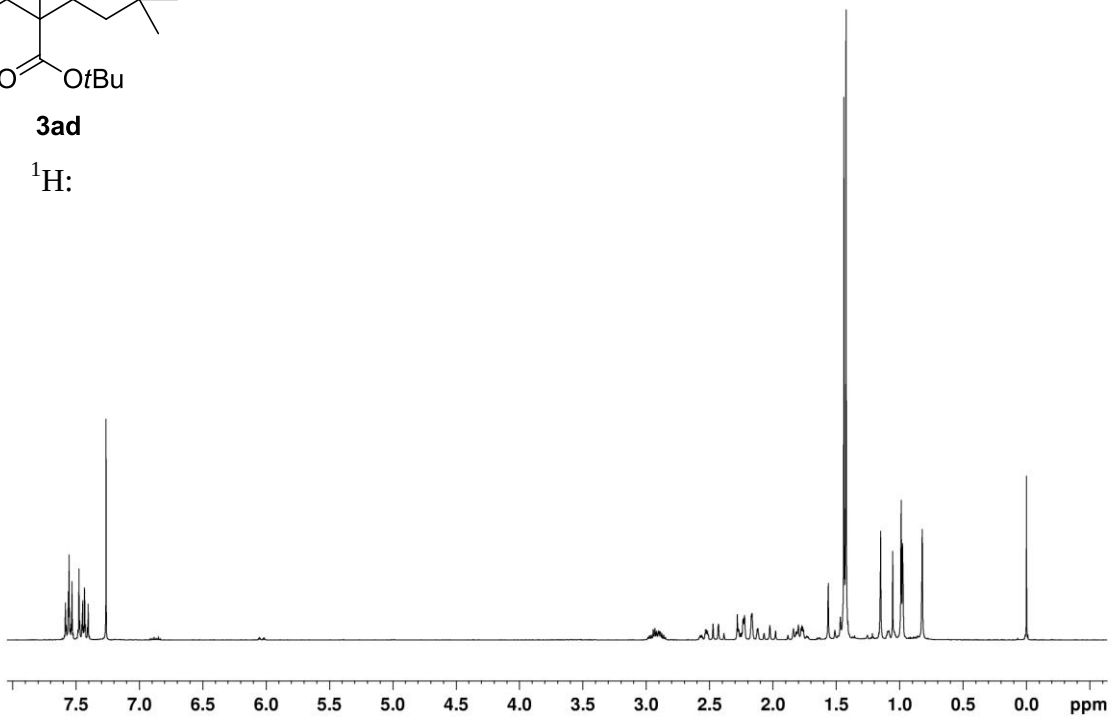


tert-Butyl-2-cyano-2-(3,3-dimethyl-5-oxocyclohexyl)-2-phenylacetate (**3ad**)

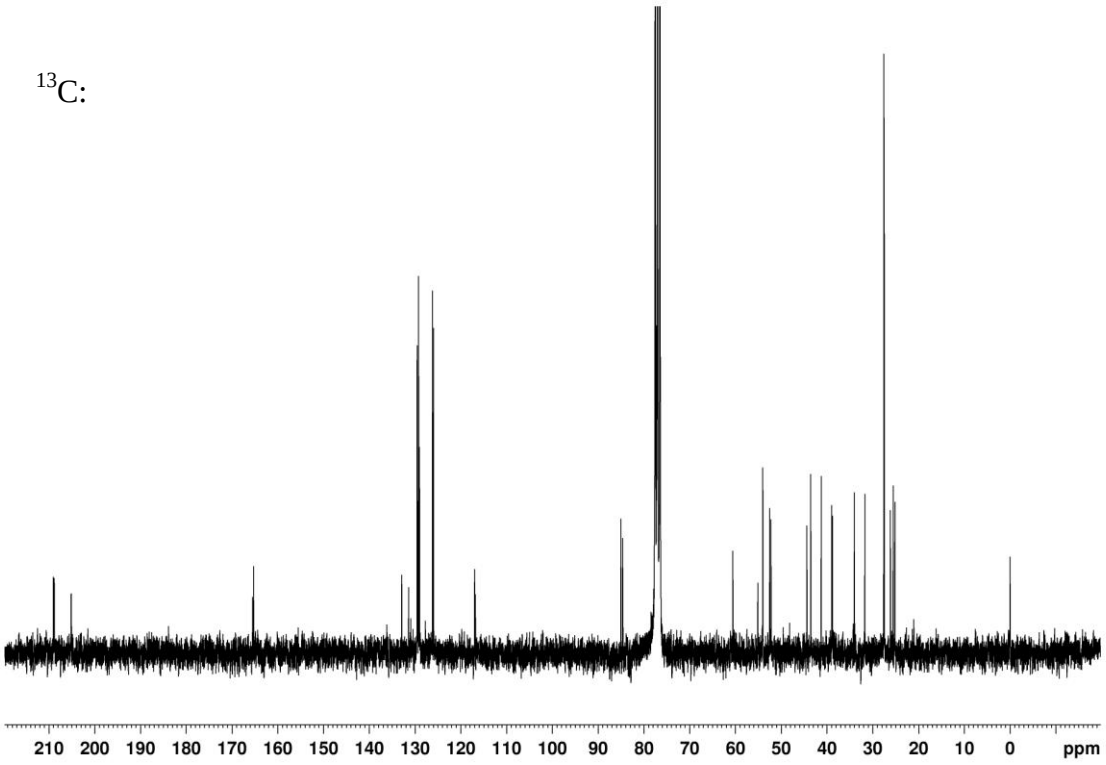


3ad

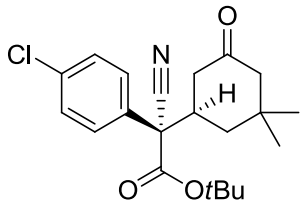
^{1}H:



^{13}C:

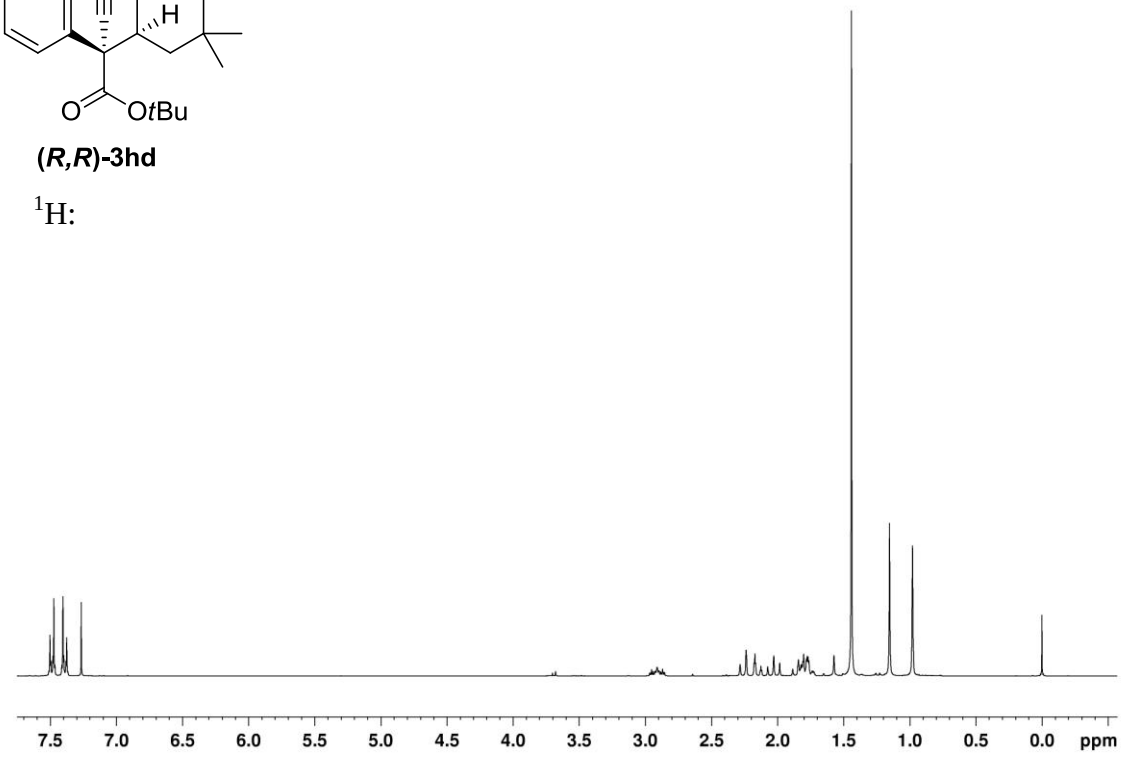


tert-Butyl-2-cyano-2-(4-chlorophenyl)-2-(3,3-dimethyl-5-oxocyclohexyl)acetate (**(*R*,*R*)-3hd**)



(*R*,*R*)-3hd

^{1}H:



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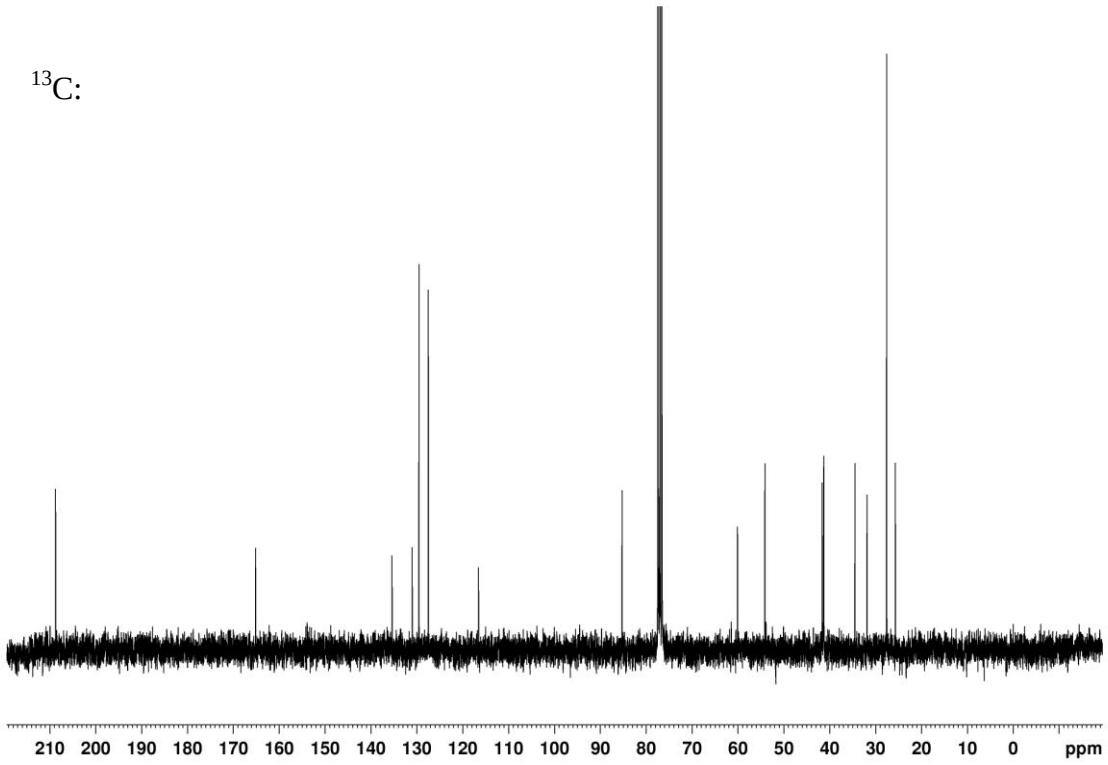
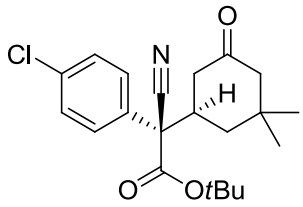
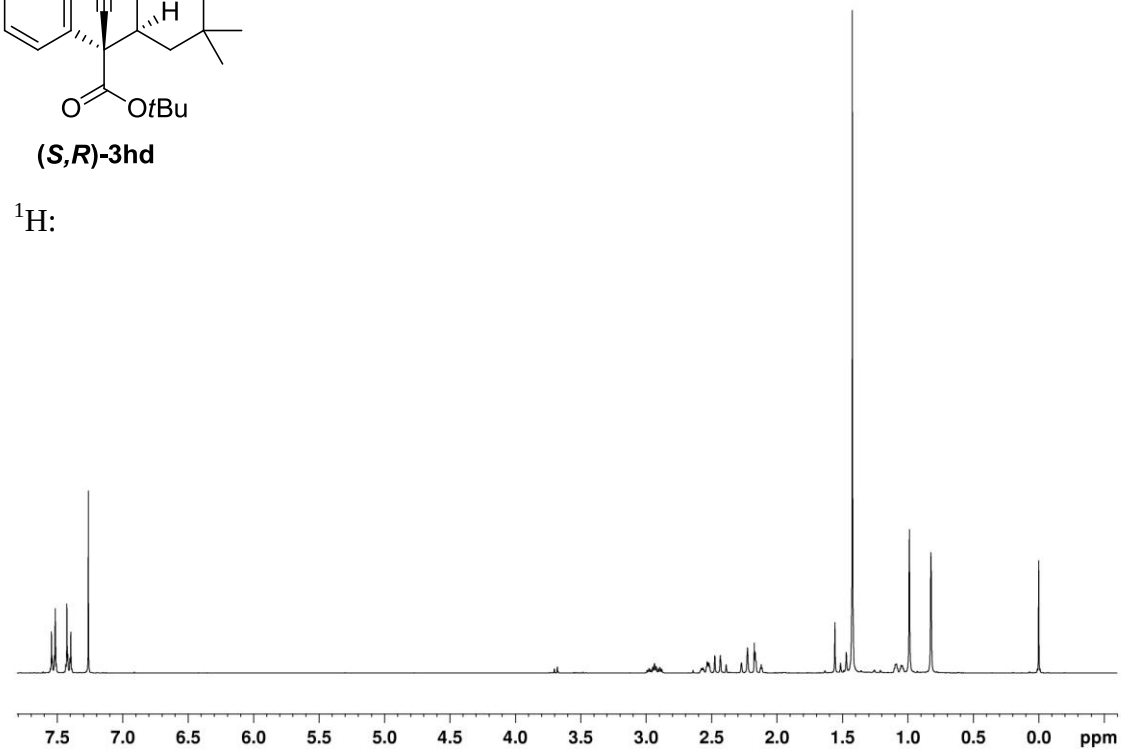


tert-Butyl-2-cyano-2-(4-chlorophenyl)-2-(3,3-dimethyl-5-oxocyclohexyl)acetate (**(*S*,*R*)-3hd**)



(*S*,*R*)-3hd

^{1}H:



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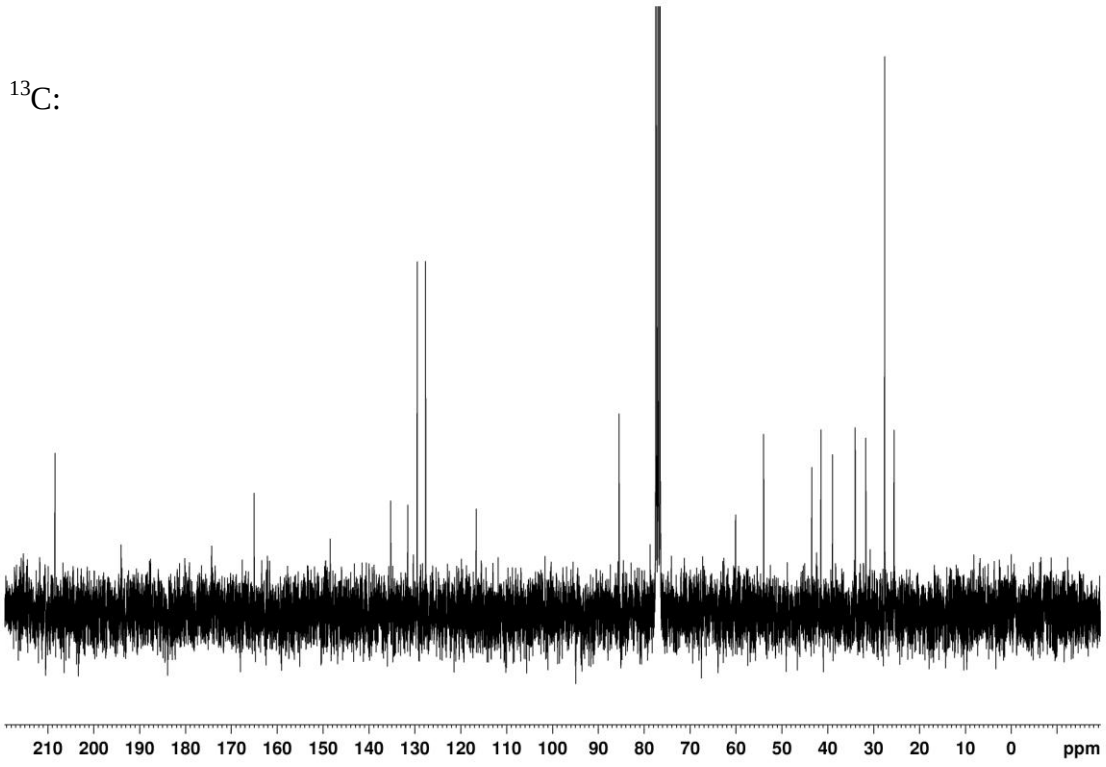
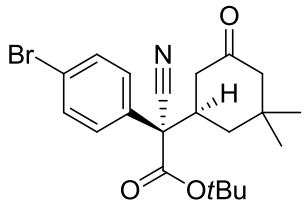
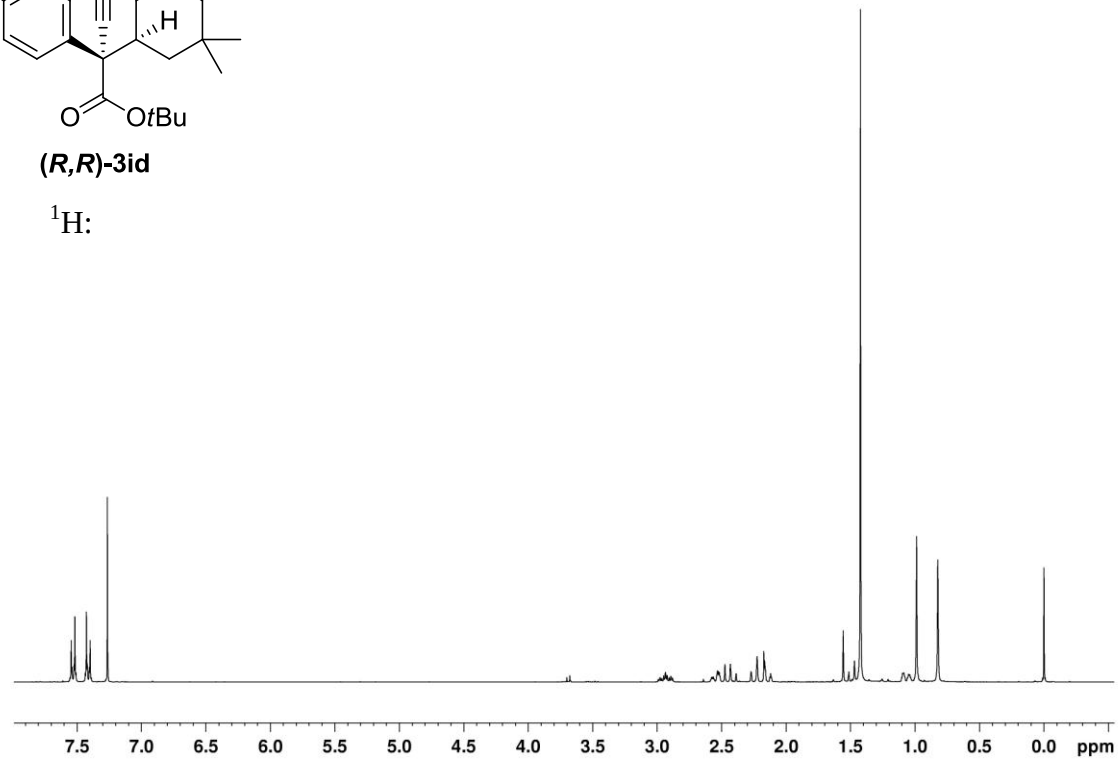


tert-Butyl-2-cyano-2-(4-bromophenyl)-2-(3,3-dimethyl-5-oxocyclohexyl)acetate (**(*R*,*R*)-3id**)



(*R*,*R*)-3id

^{1}H:



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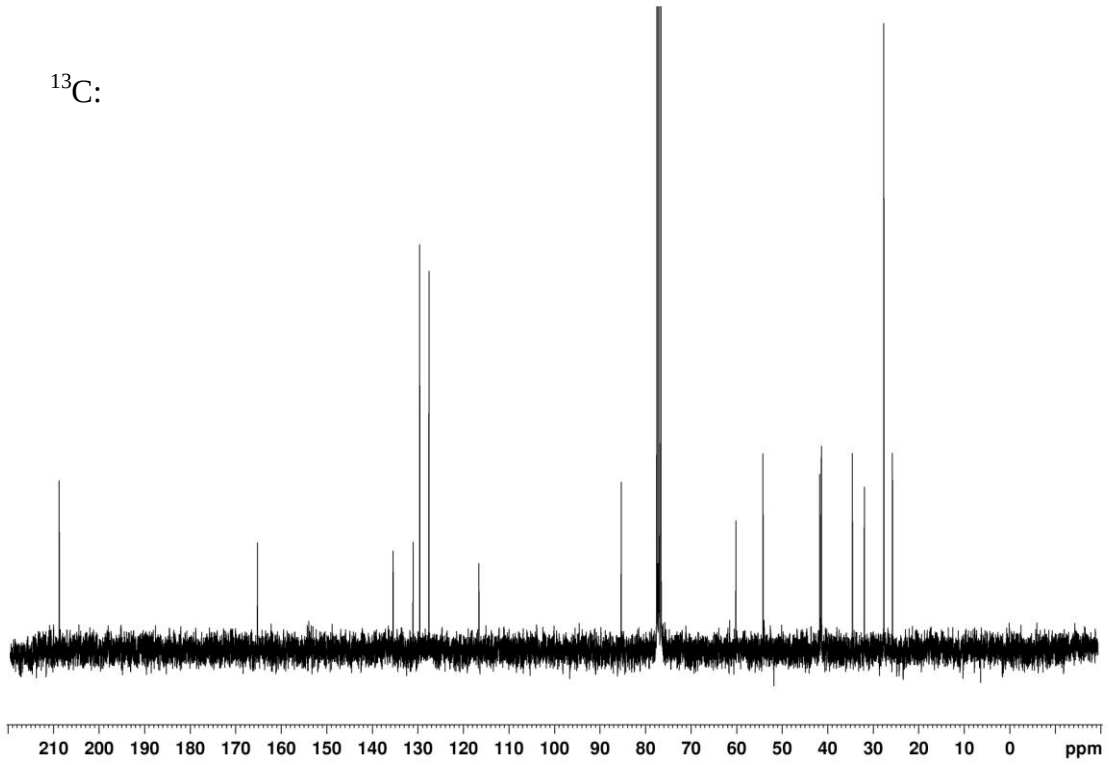
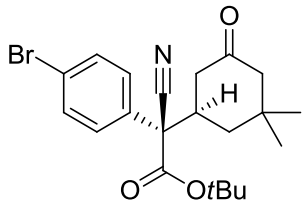
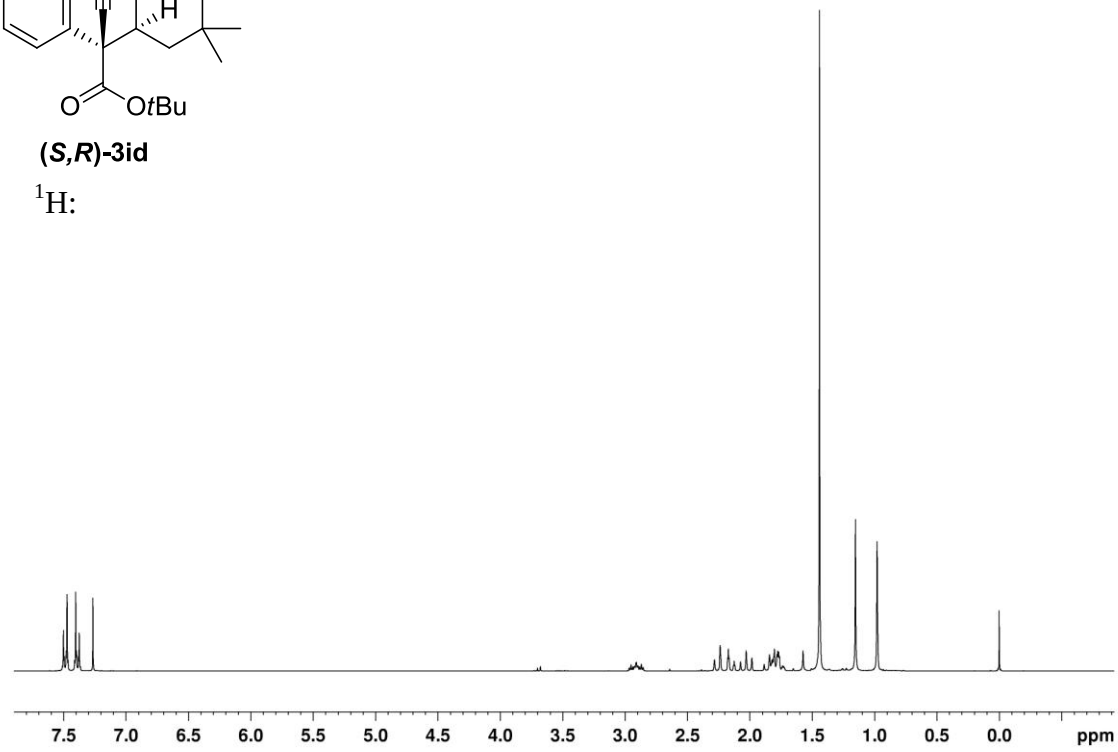


tert-Butyl-2-cyano-2-(4-bromophenyl)-2-(3,3-dimethyl-5-oxocyclohexyl)acetate (**(*S*,*R*)-3id**)



(*S*,*R*)-3id

^{1}H:



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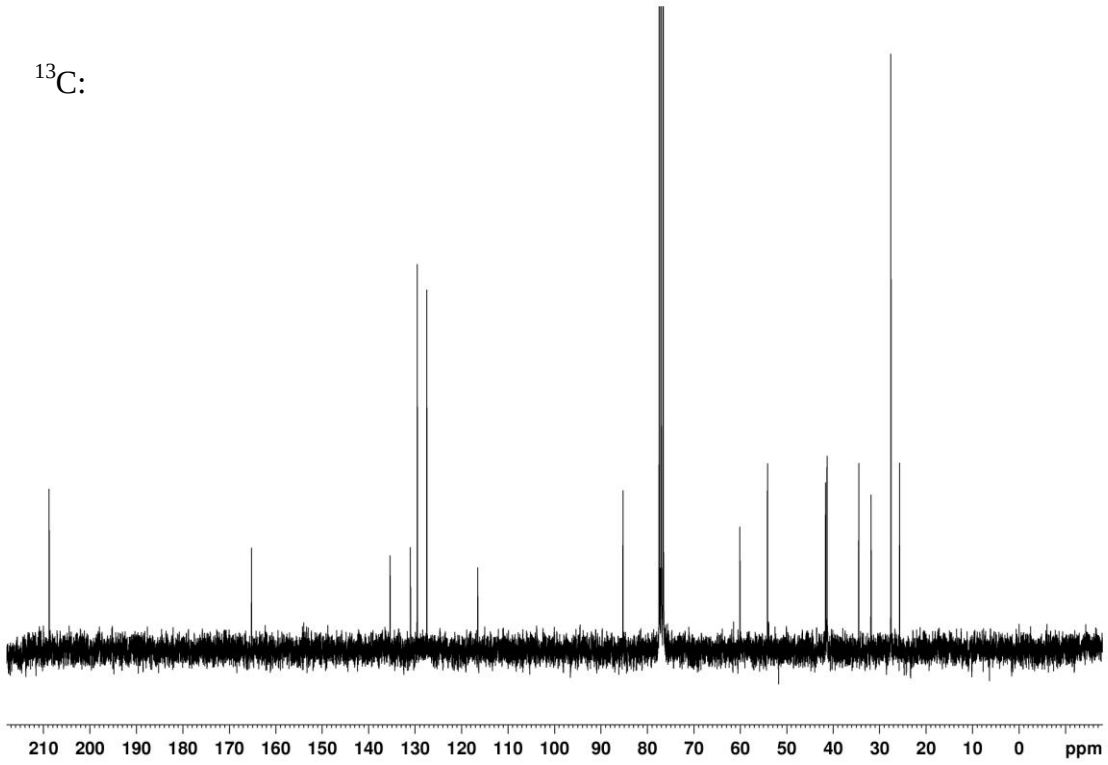
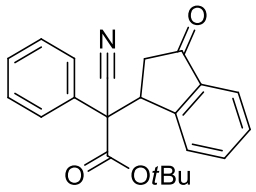
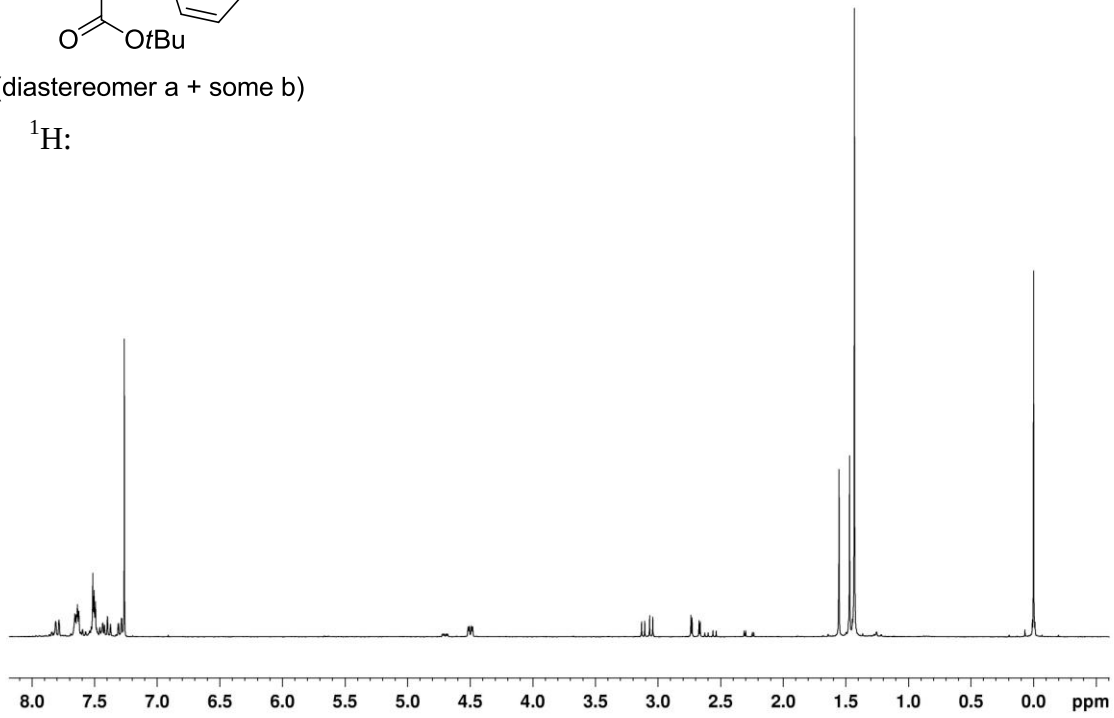


tert-Butyl-2-cyano-2-(3-oxo-2,3-dihydro-1H-inden-1-yl)-2-phenylacetate (**3ae**)



3ea (diastereomer a + some b)

^{1}H:



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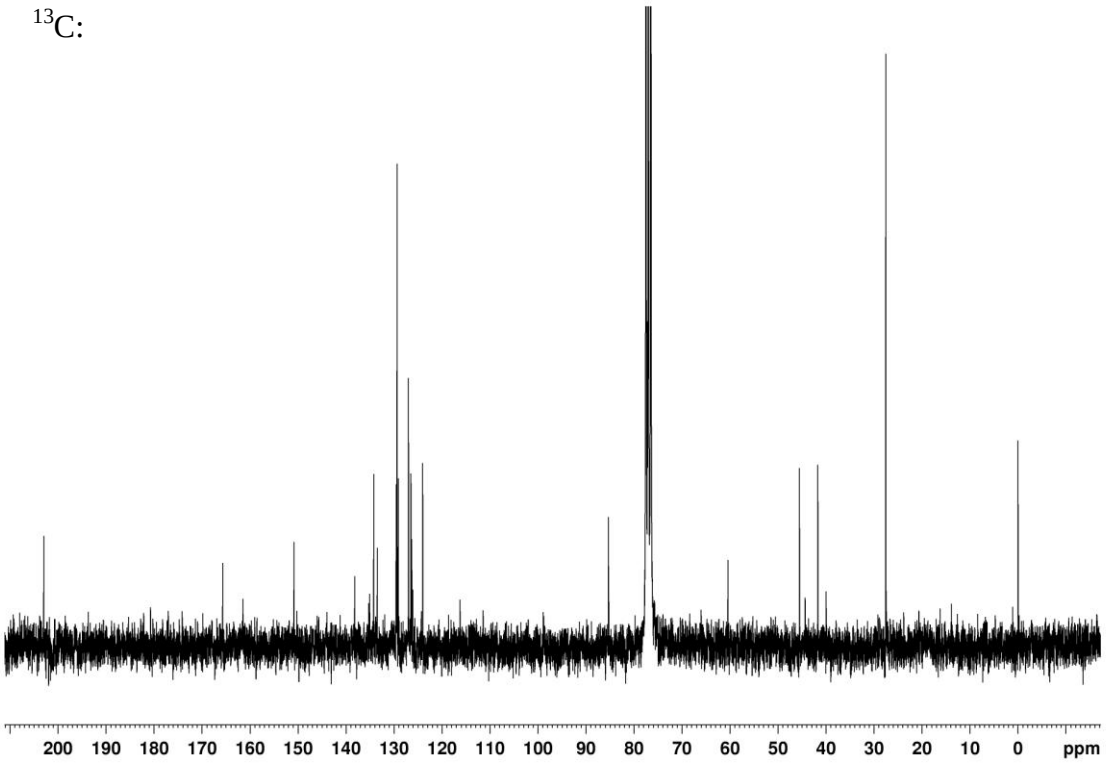
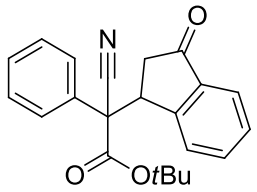
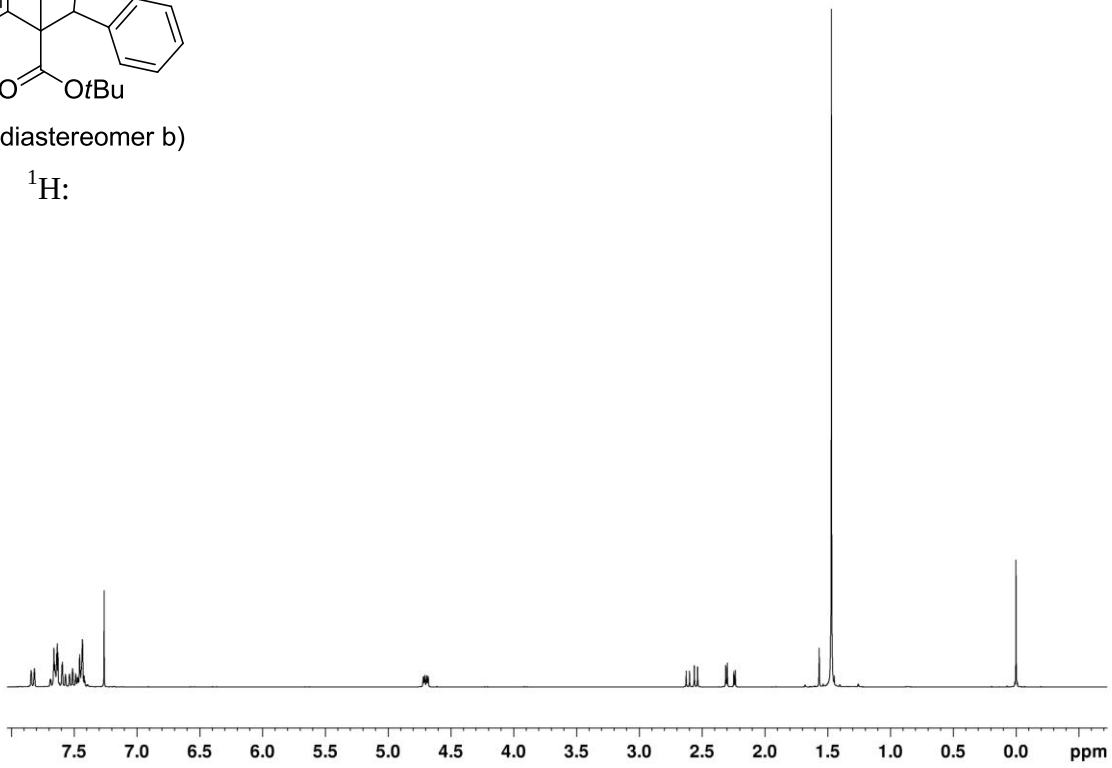


tert-Butyl-2-cyano-2-(3-oxo-2,3-dihydro-1H-inden-1-yl)-2-phenylacetate (**3ae**)

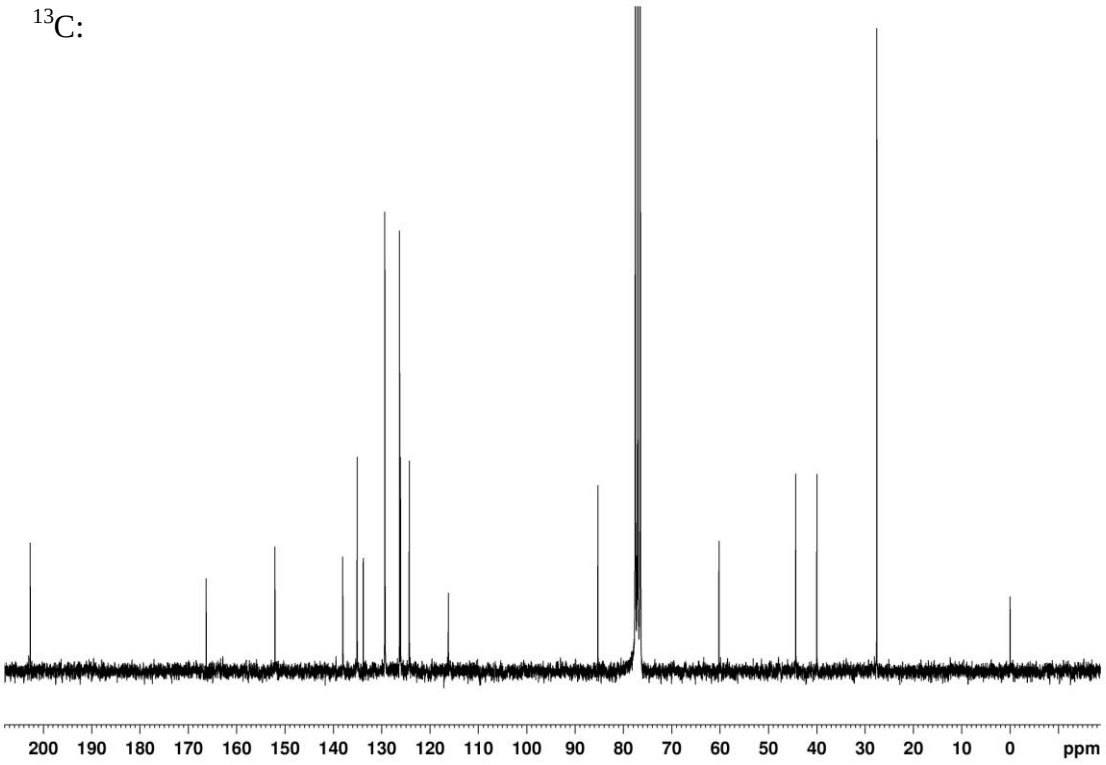


3ea (diastereomer b)

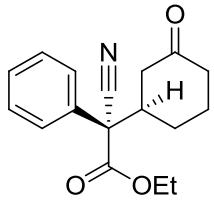
^{1}H:



^{13}C:

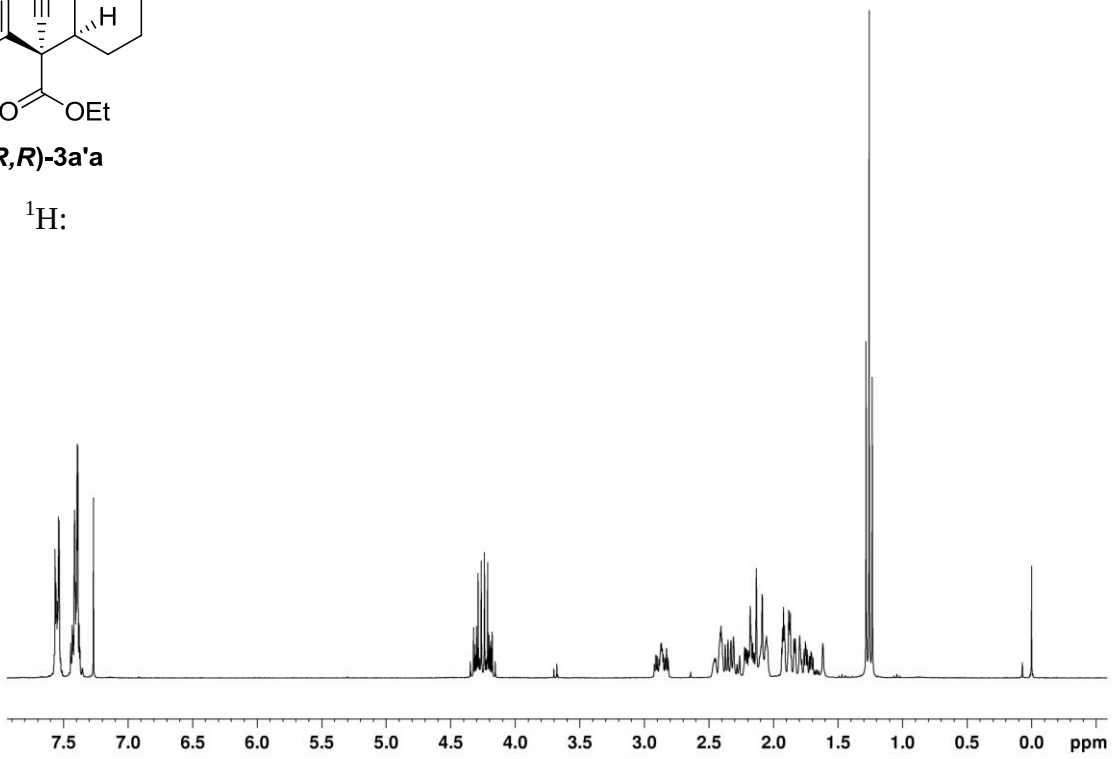


Ethyl-2-cyano-2-(3-oxocyclohexyl)-2-phenylacetate (**(*R*,*R*)-3a'a**)



(*R*,*R*)-3a'a

^{1}H:



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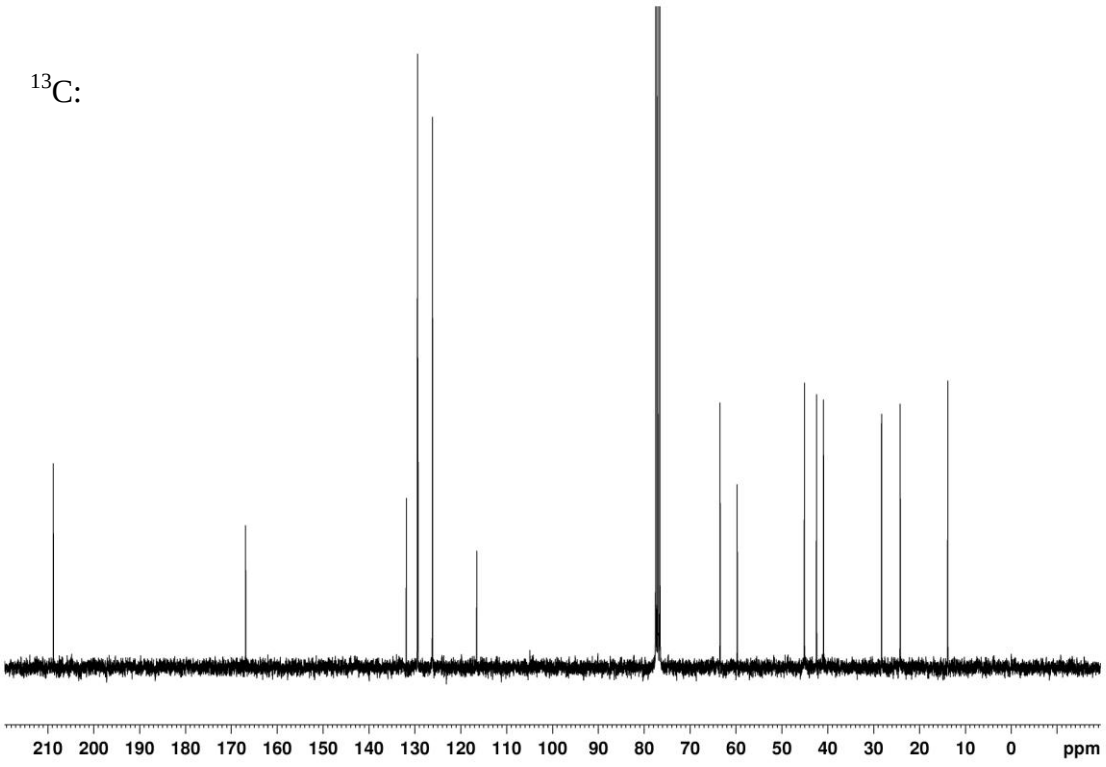
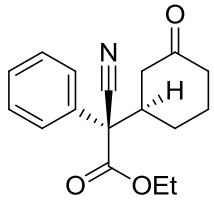
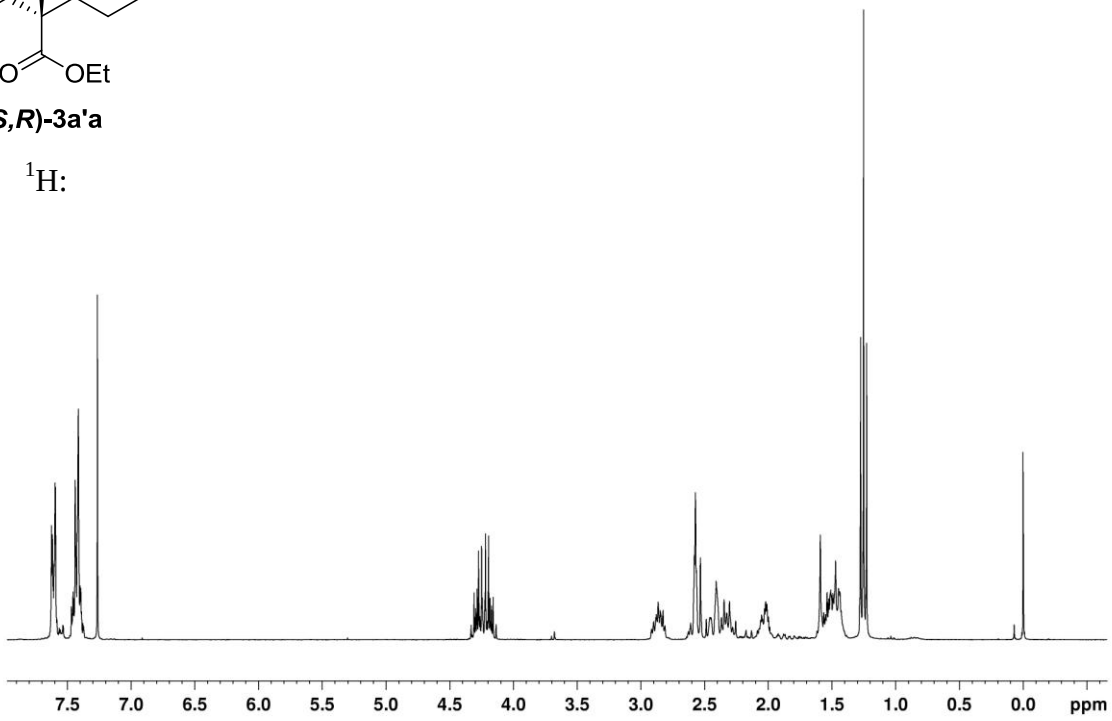


Ethyl-2-cyano-2-(3-oxocyclohexyl)-2-phenylacetate (**(*S*,*R*)-3a'a**)



(*S*,*R*)-3a'a

^{1}H:



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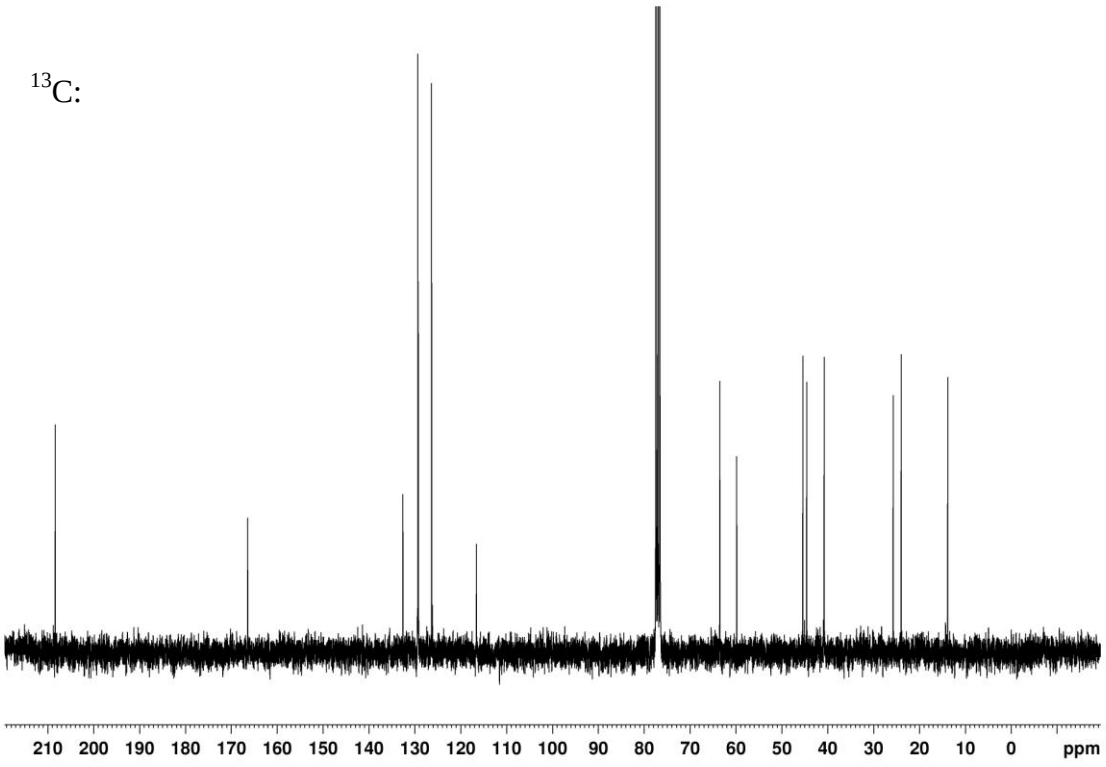
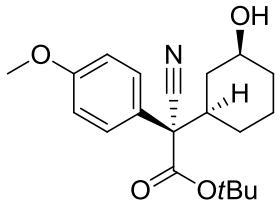
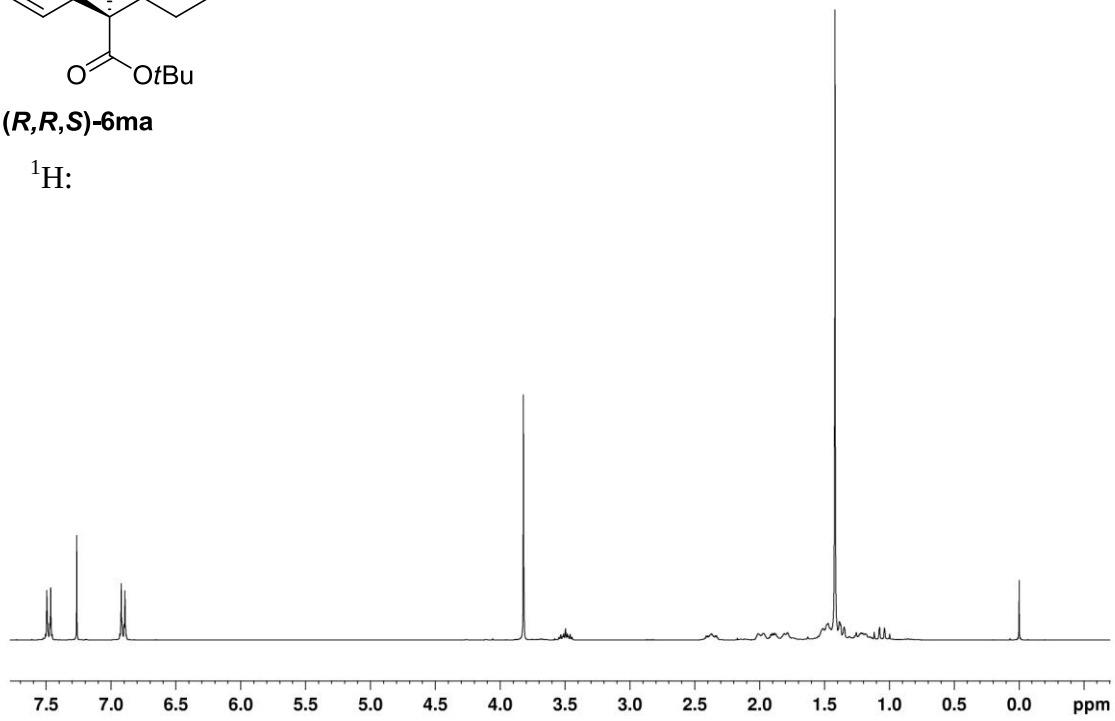


tert-Butyl-2-cyano-2-(3-hydroxycyclohexyl)-2-(4-methoxyphenyl)-acetate (**(*R*,*R*,*S*)-6ma**)



(*R*,*R*,*S*)-6ma

^{1}H:



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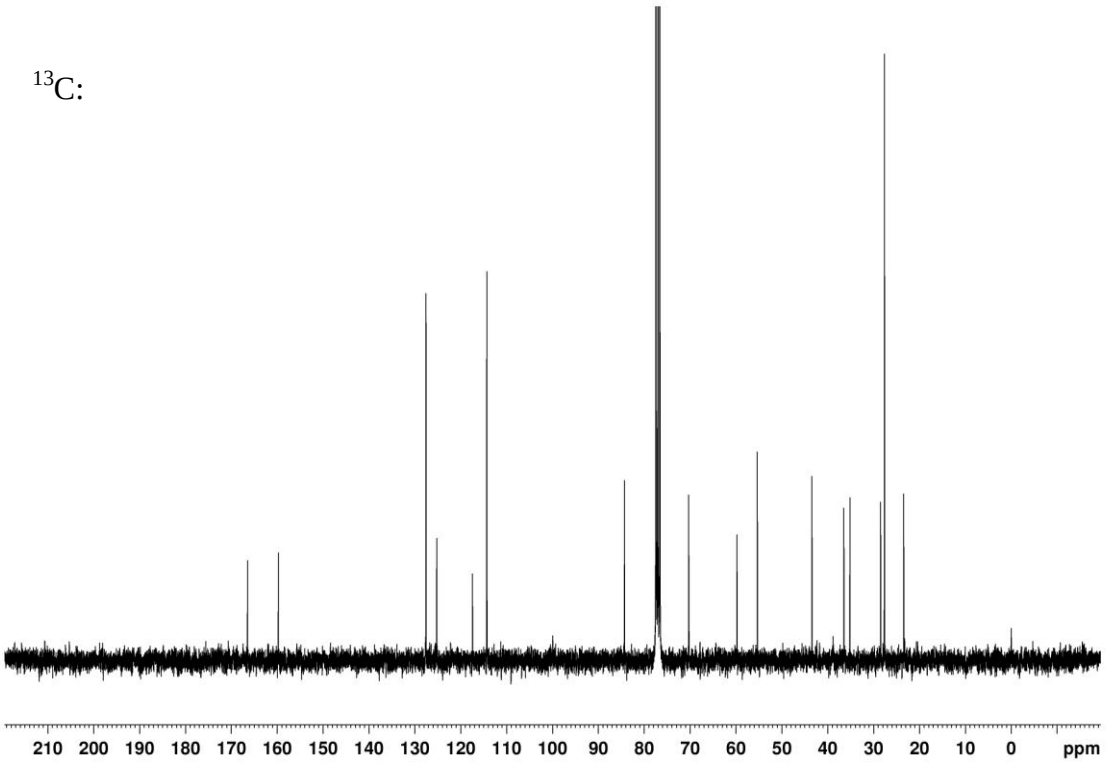
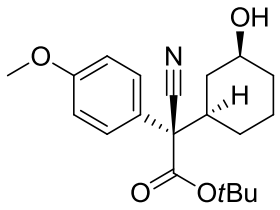
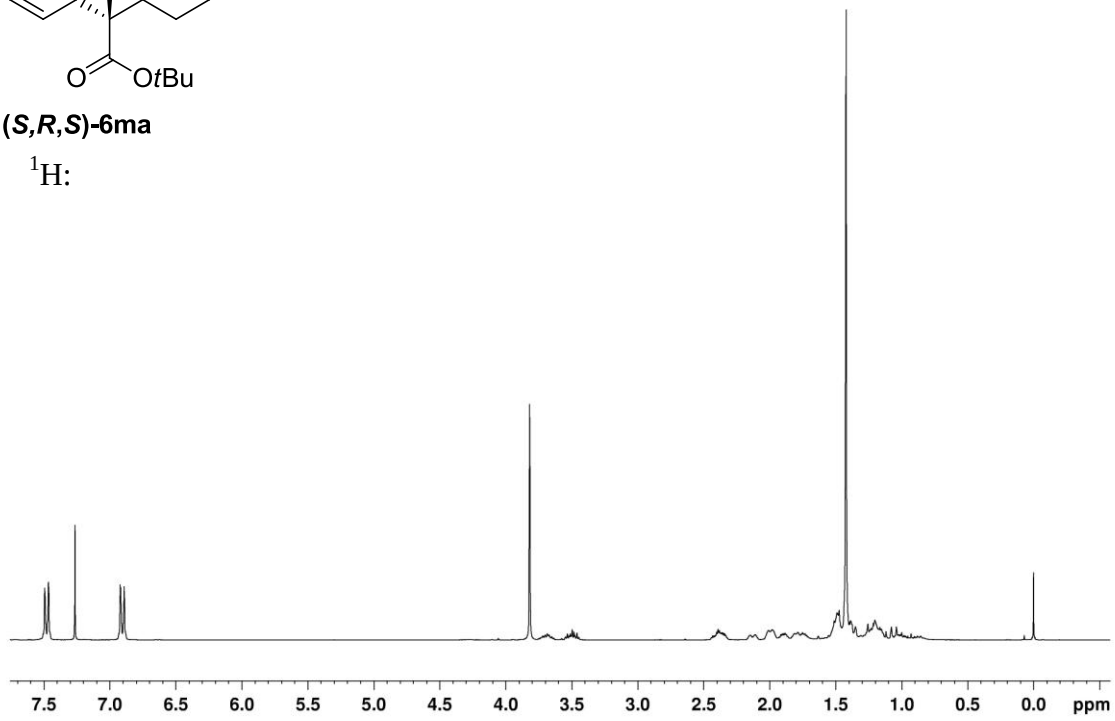


tert-Butyl-2-cyano-2-(3-hydroxycyclohexyl)-2-(4-methoxyphenyl)-acetate (**(*S*,*R*,*S*)-6ma**)



(*S*,*R*,*S*)-6ma

^{1}H:



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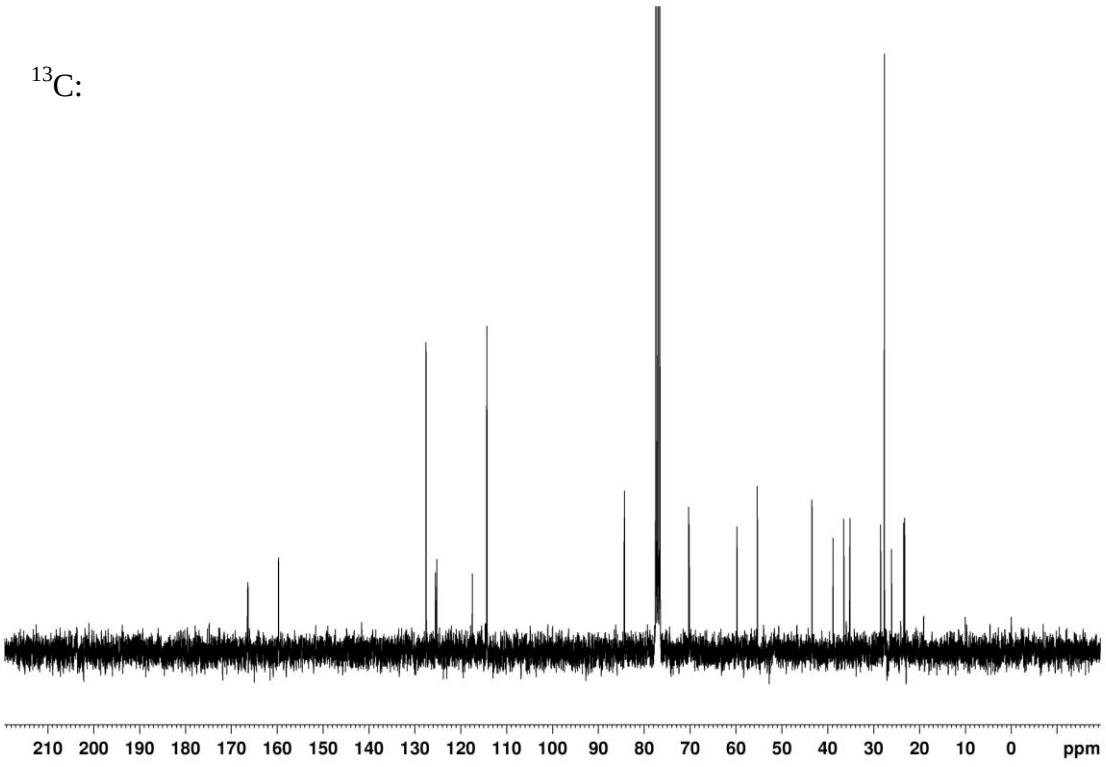
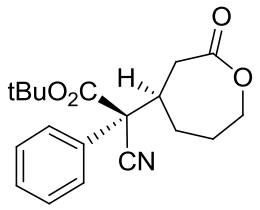
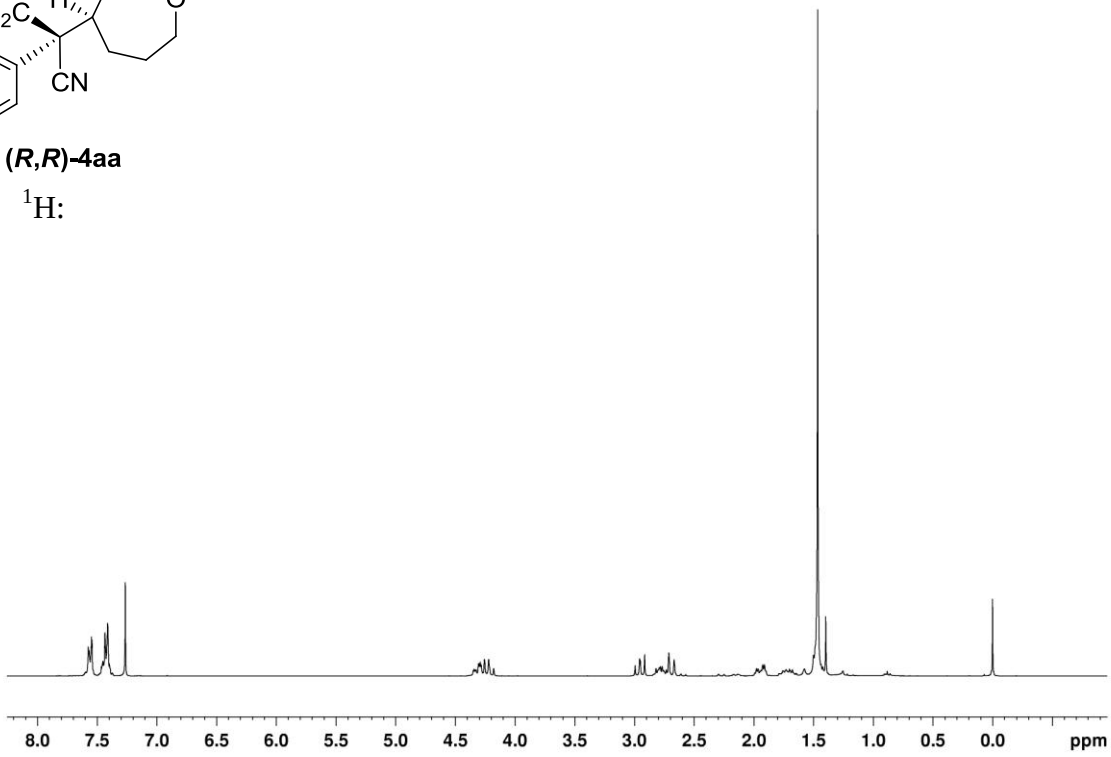


(*R*)-*tert* -Butyl-2-cyano-2-((*R*)-2-oxooxepan-4-yl)-2-phenylacetate (**(*R*,*R*)-4aa**)



(*R*,*R*)-4aa

^{1}H:



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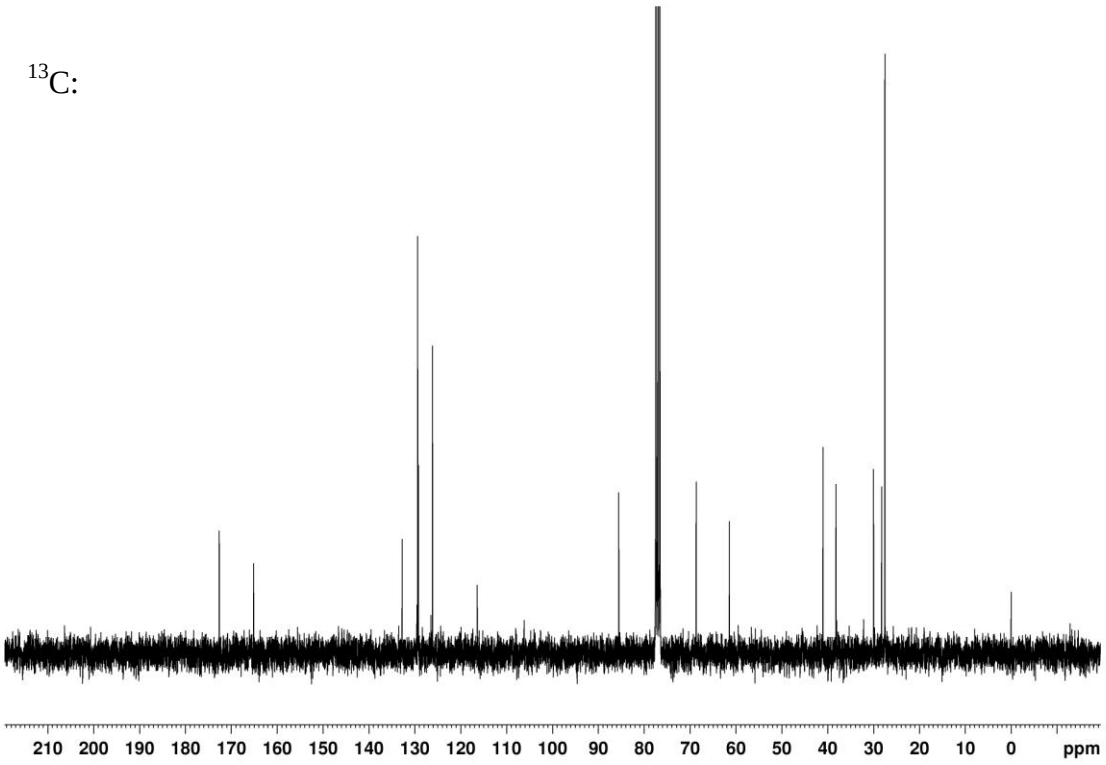
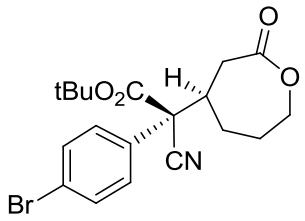
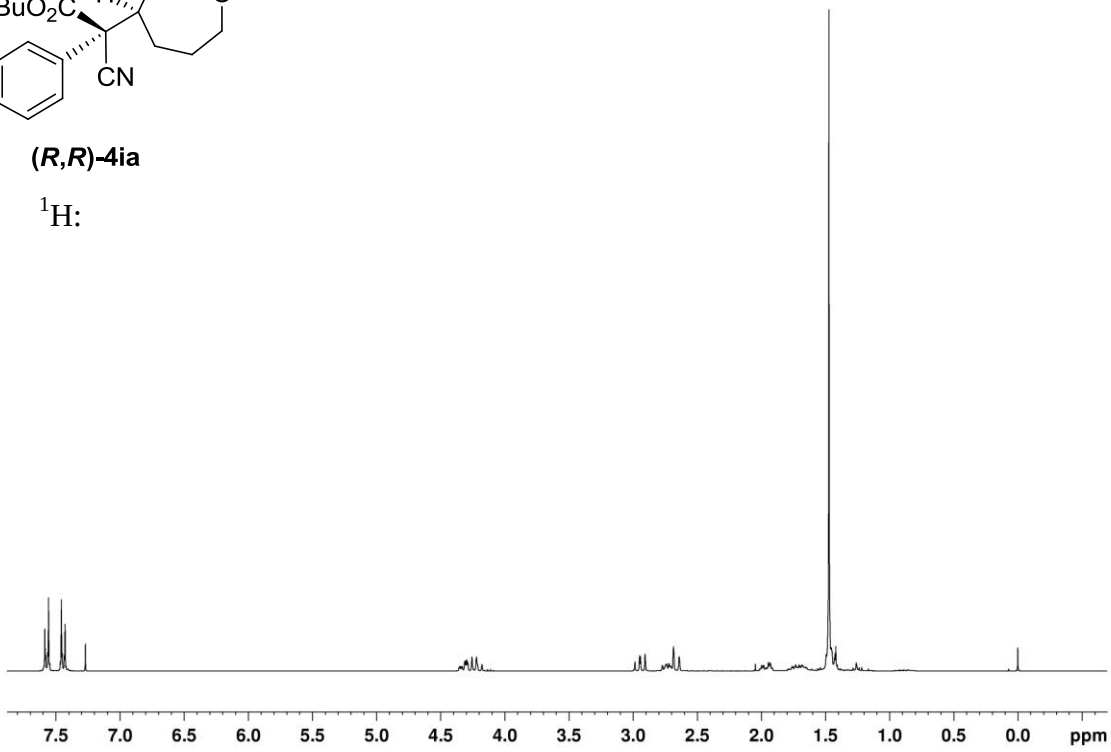


(*R*)-*tert* -Butyl-2-(4-bromophenyl)-2-cyano-2-((*R*)-2-oxooxepan-4-yl)acetate (**(*R*,*R*)-4ia**)



(*R*,*R*)-4ia

^{1}H:



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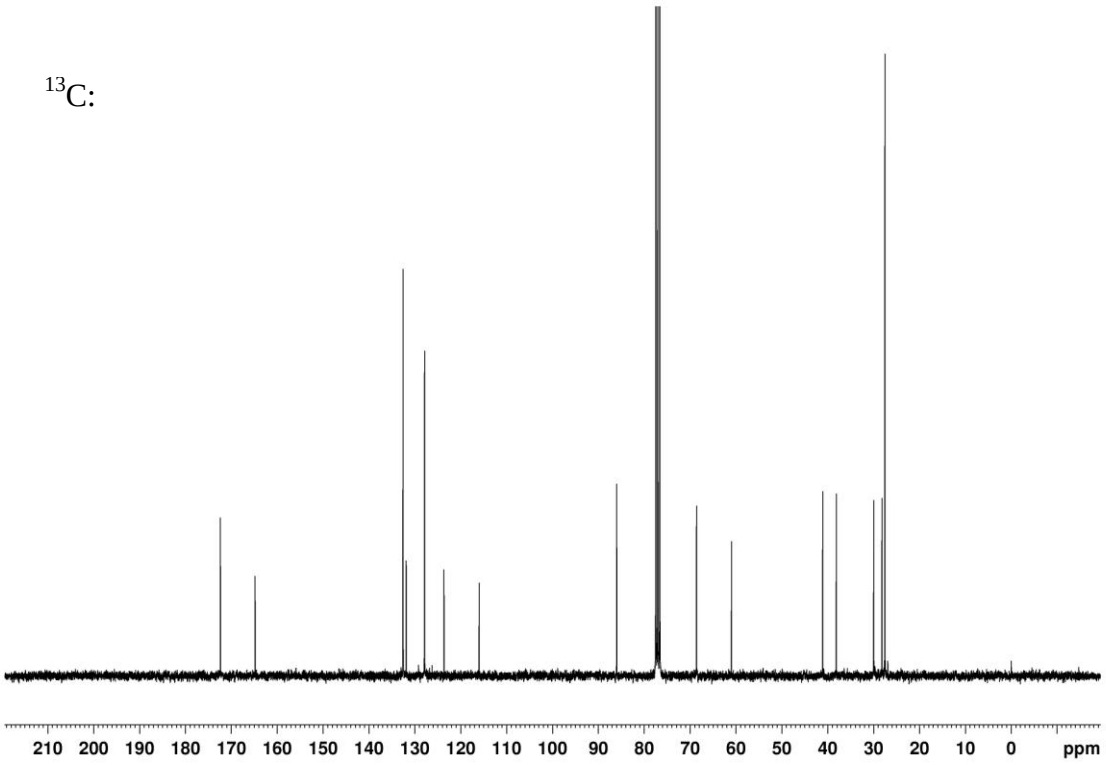
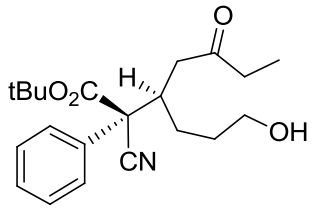


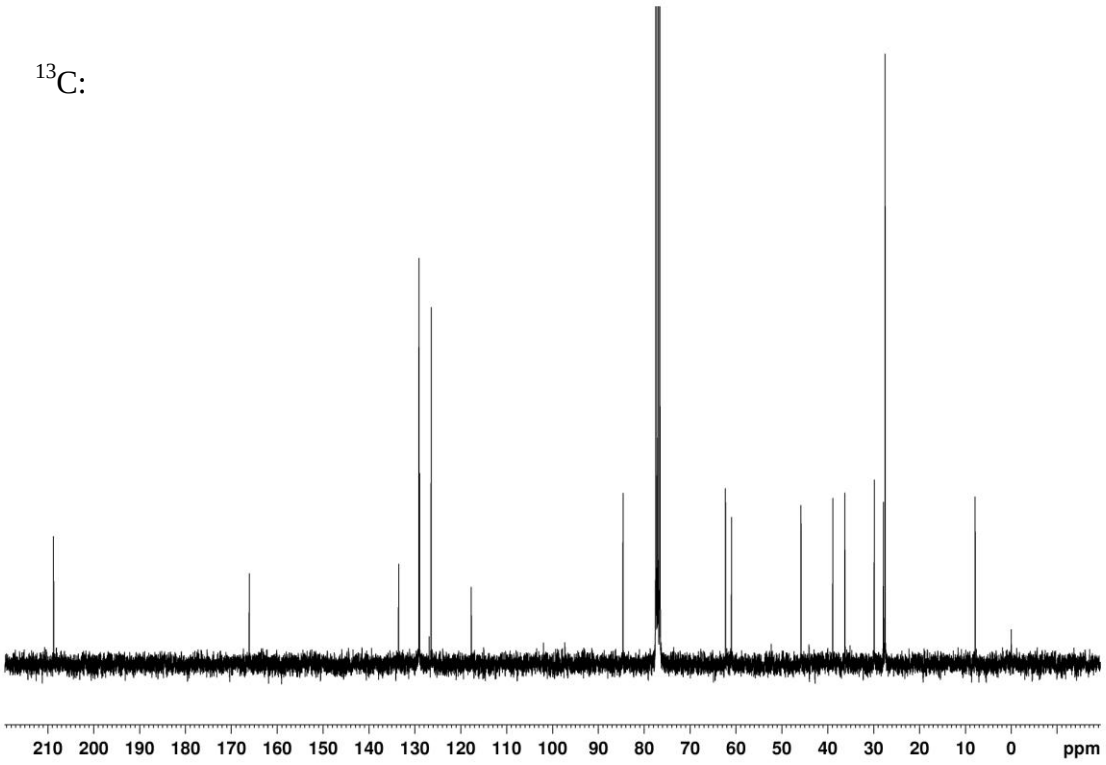
(*2R,3R*)-*tert* -butyl-2-cyano-3-(3-hydroxypropyl)-5-oxo-2-phenylheptanoate (**(*R,R*)-5**)



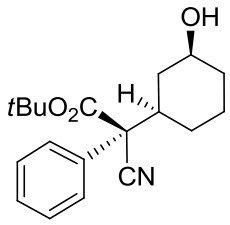
(*R,R*)-5

^{1}H:

^{13}C:

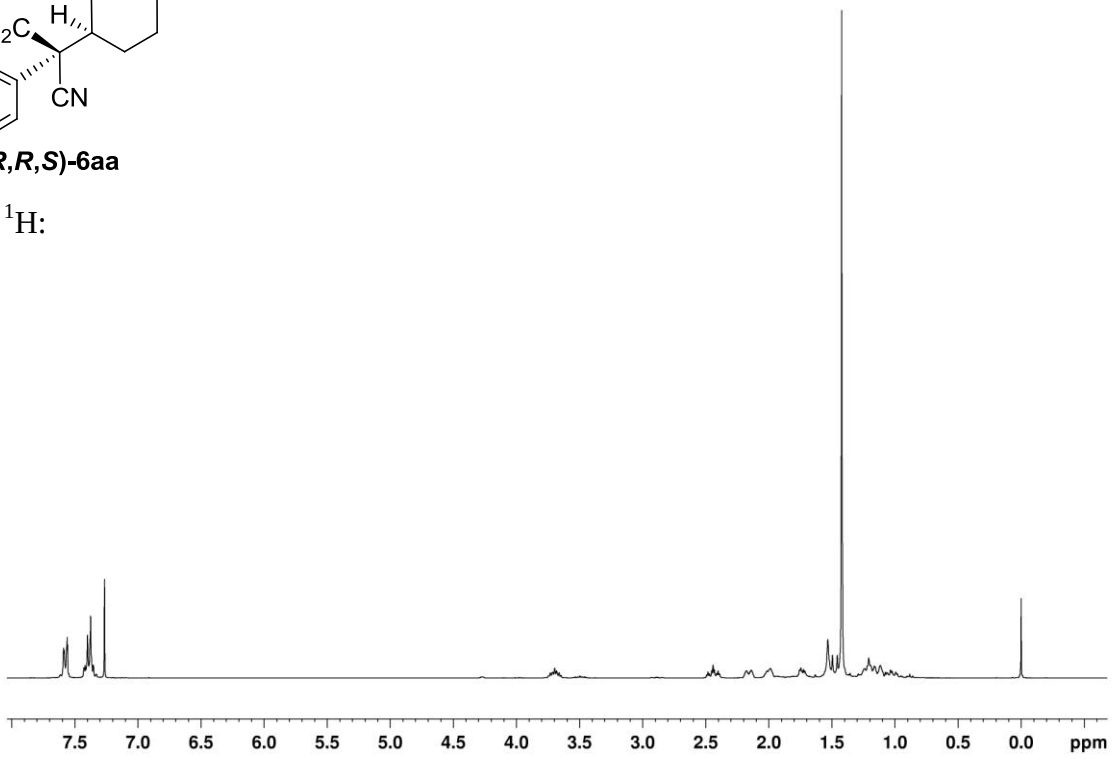


(*R*)-*tert*-Butyl-2-cyano-2-((*1R,3S*)-3-hydroxylcyclohexyl)-2-phenylacetate (**(*R,R,S*)-6aa**)



(*R,R,S*)-6aa

^{1}H:



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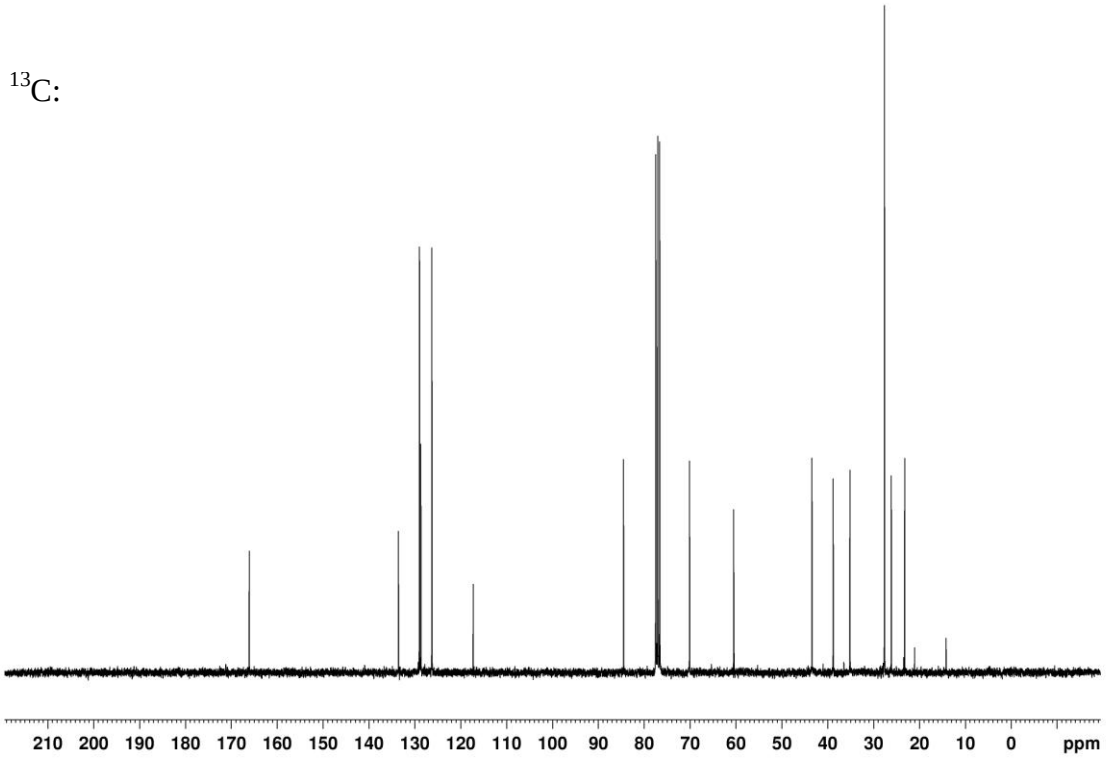
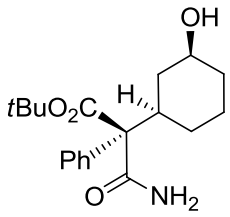


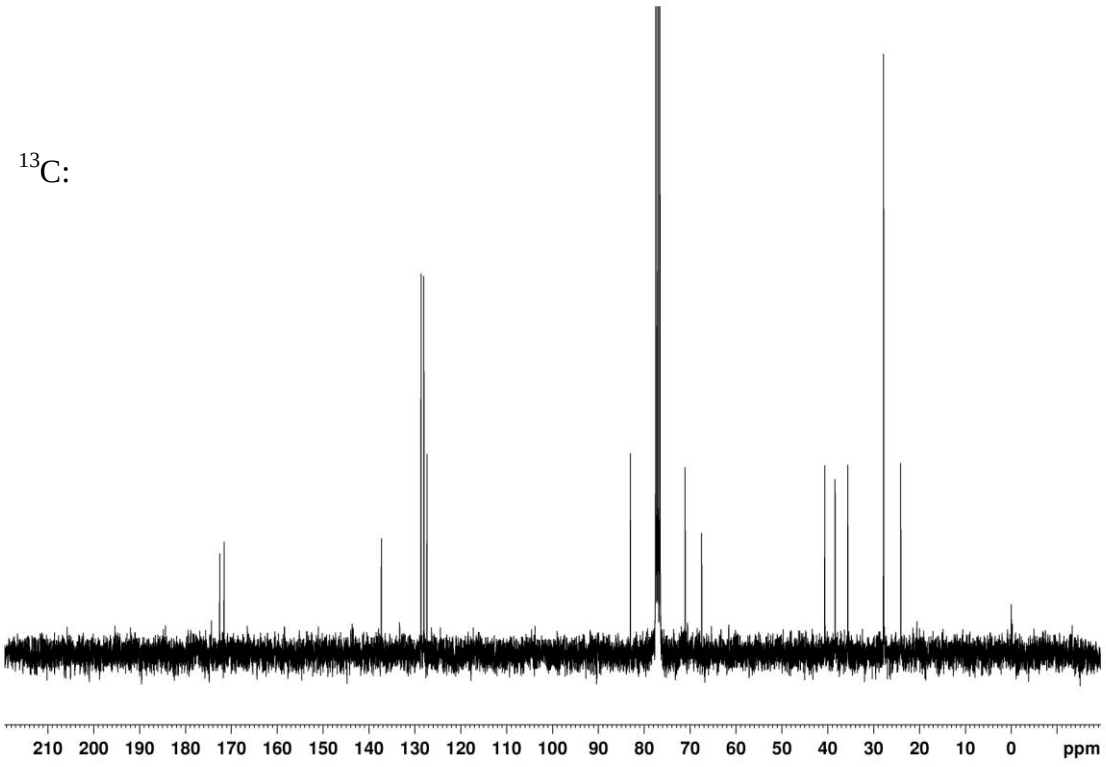
(*R*)-*tert*-Butyl-3-amino-2-((*1R,3S*)-3-hydroxycyclohexyl)-3-oxo-2-phenylpropanoate (**(*R,R,S*)-7**)



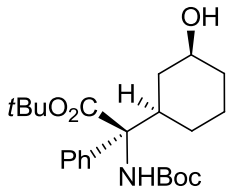
(*R,R,S*)-7

^{1}H:

^{13}C:

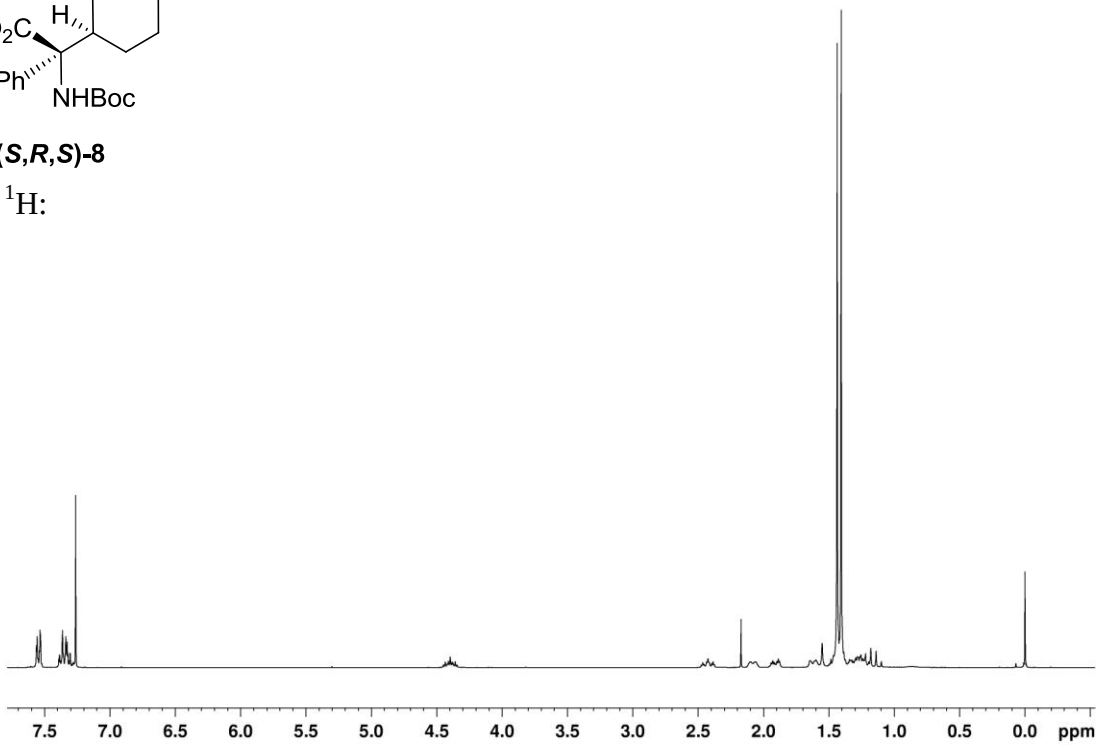


(*S*)-*tert*-Butyl-2-((*tert*-butoxylcarbonyl)amino)-2-((*1R,3S*)-3-hydroxycyclohexyl)-2-phenylacetate (**(*S,R,S*)-8**)



(*S*,*R*,*S*)-8

^{1}H:



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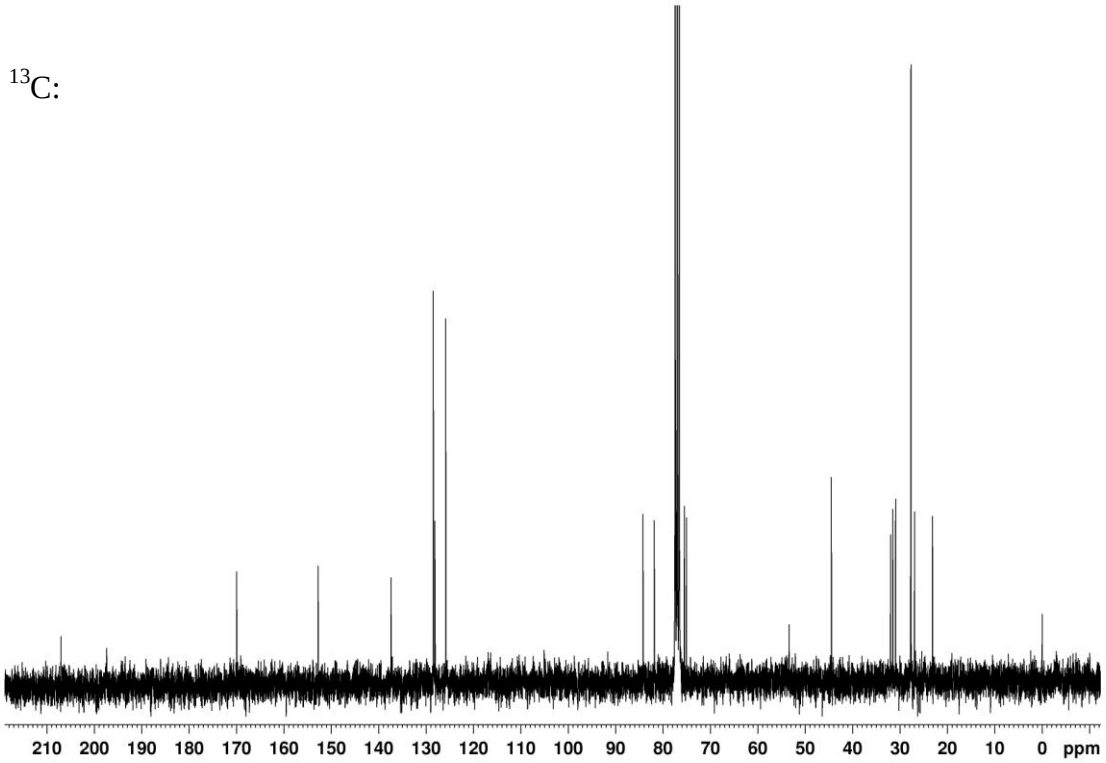
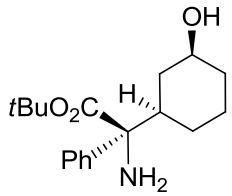


(*S*)-*tert*-Butyl-2-amino-2-((*1R*,*3S*)-3-hydroxycyclohexyl)-2-phenylacetate



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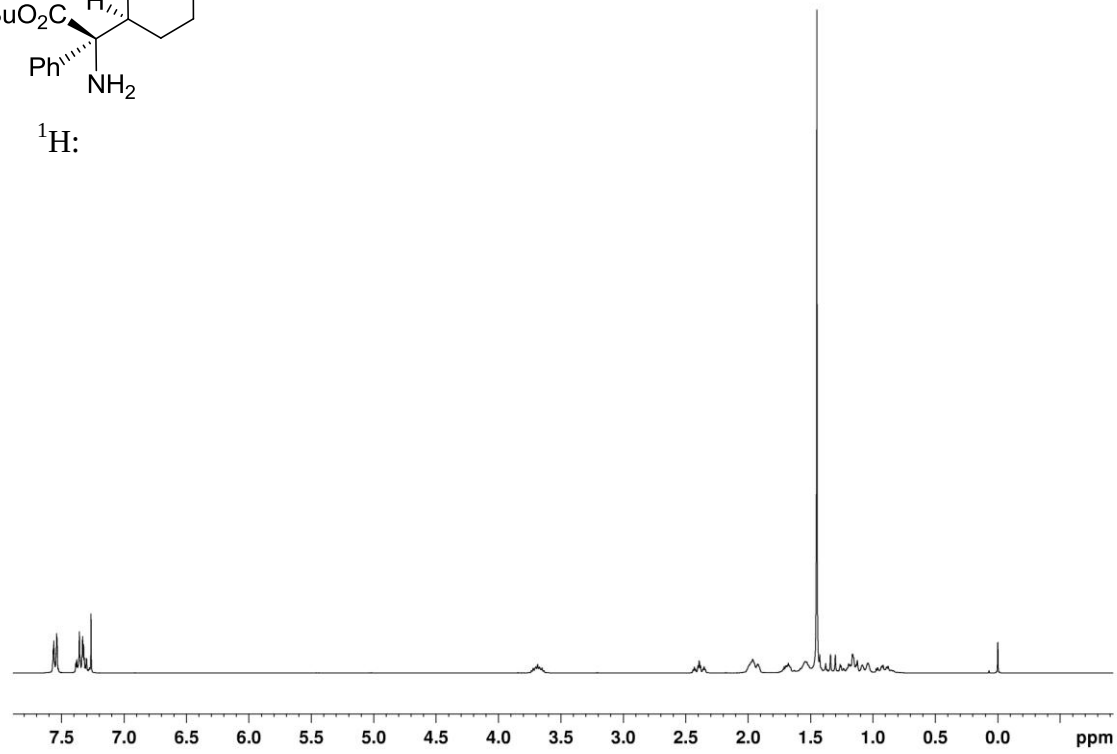

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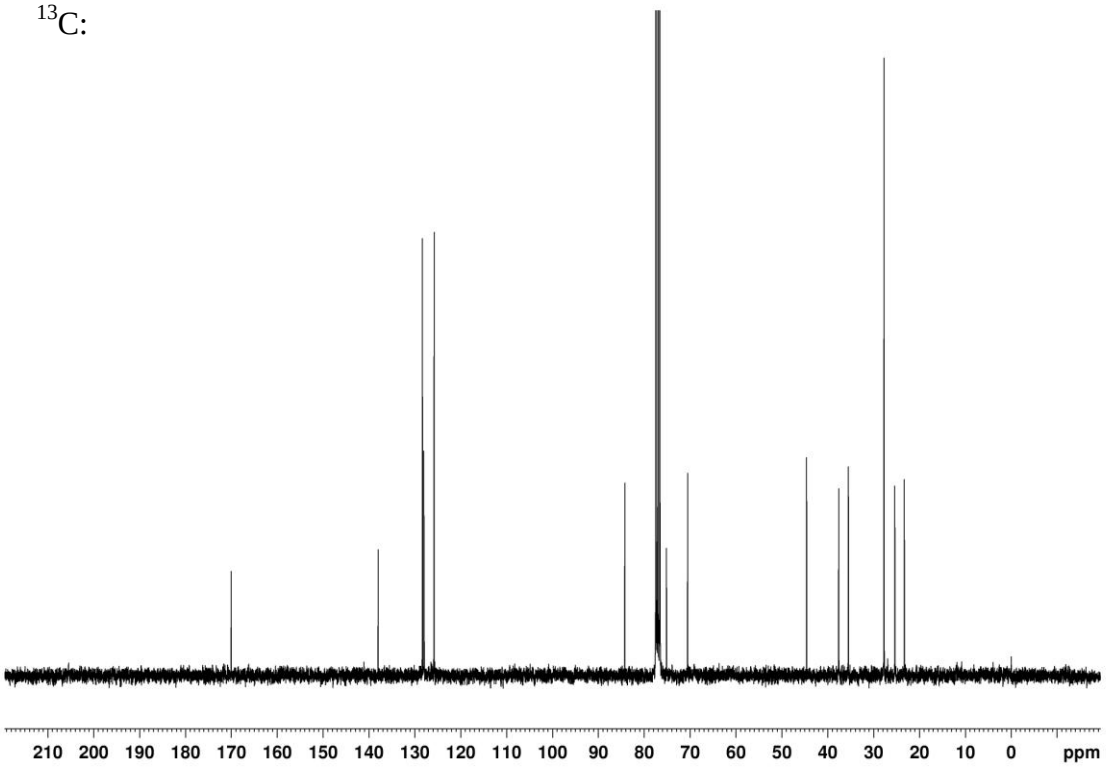
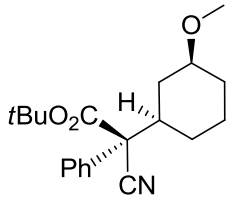


(*R*)-*tert*-Butyl-2-cyano-2-((*1R*,*3S*)-3-methoxycyclohexyl)-2-phenylacetate



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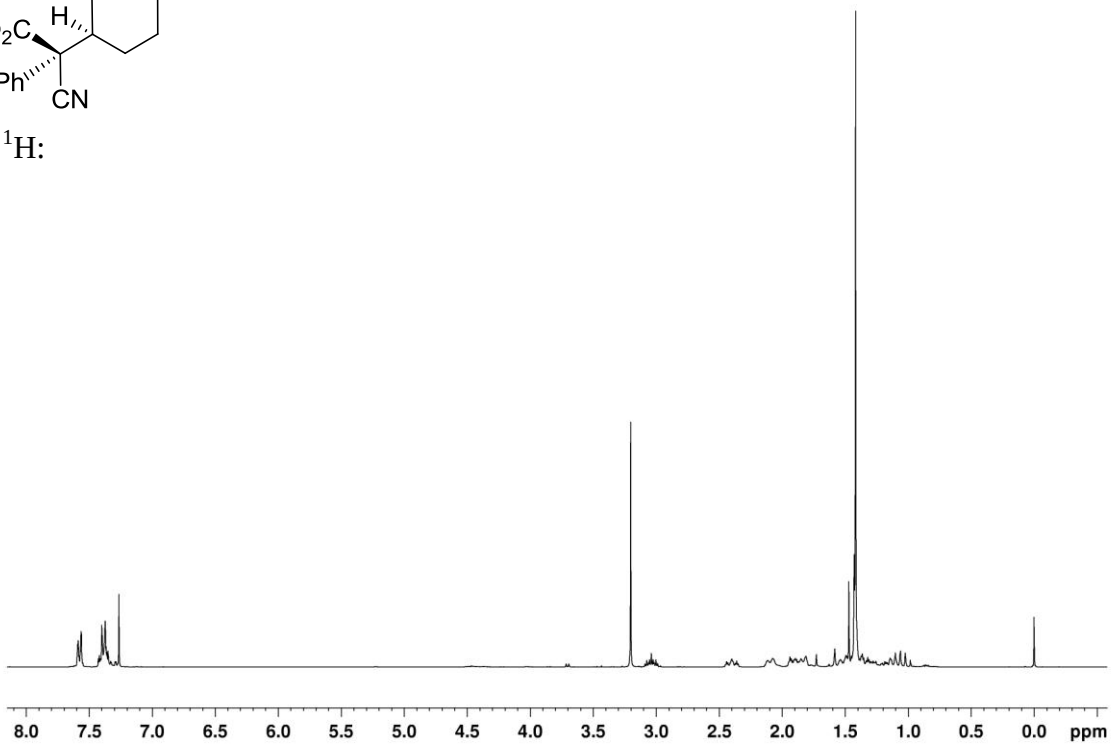

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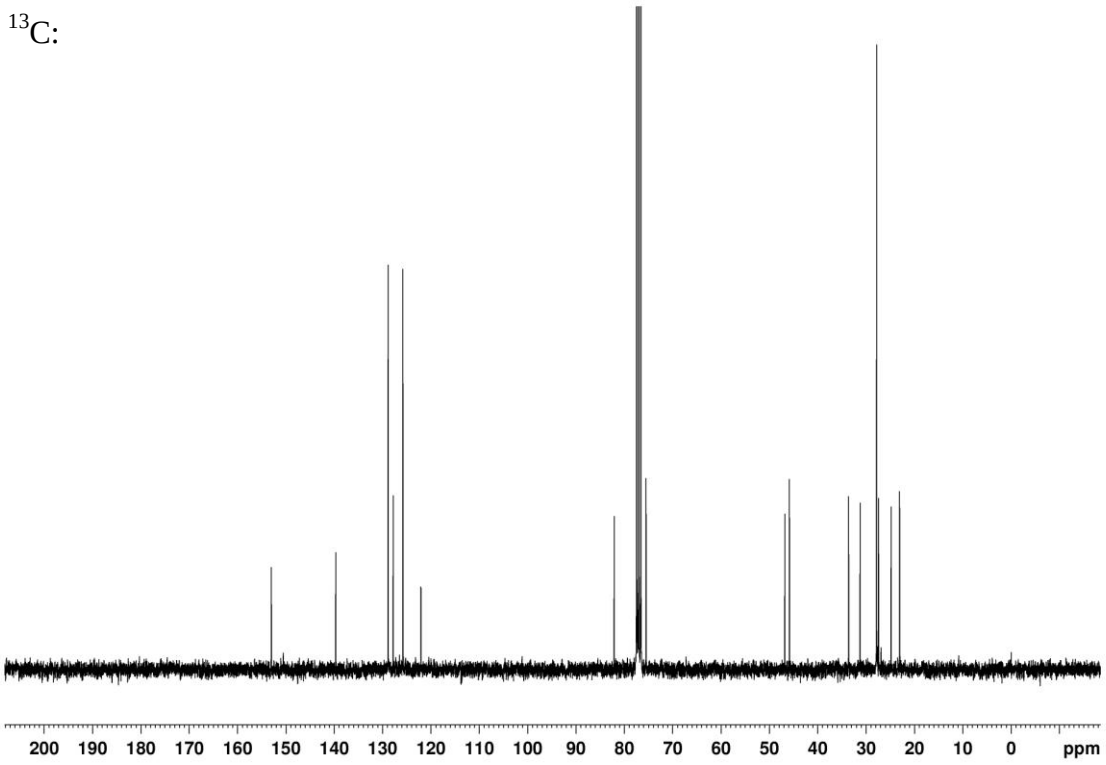
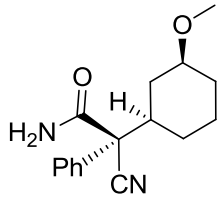


(*R*)-2-cyano-2-((*1R,3S*)-3-methoxycyclohexyl)-2-phenylacetamide (**(*R,R,S*)-9**)



(*R*,*R*,*S*)-9

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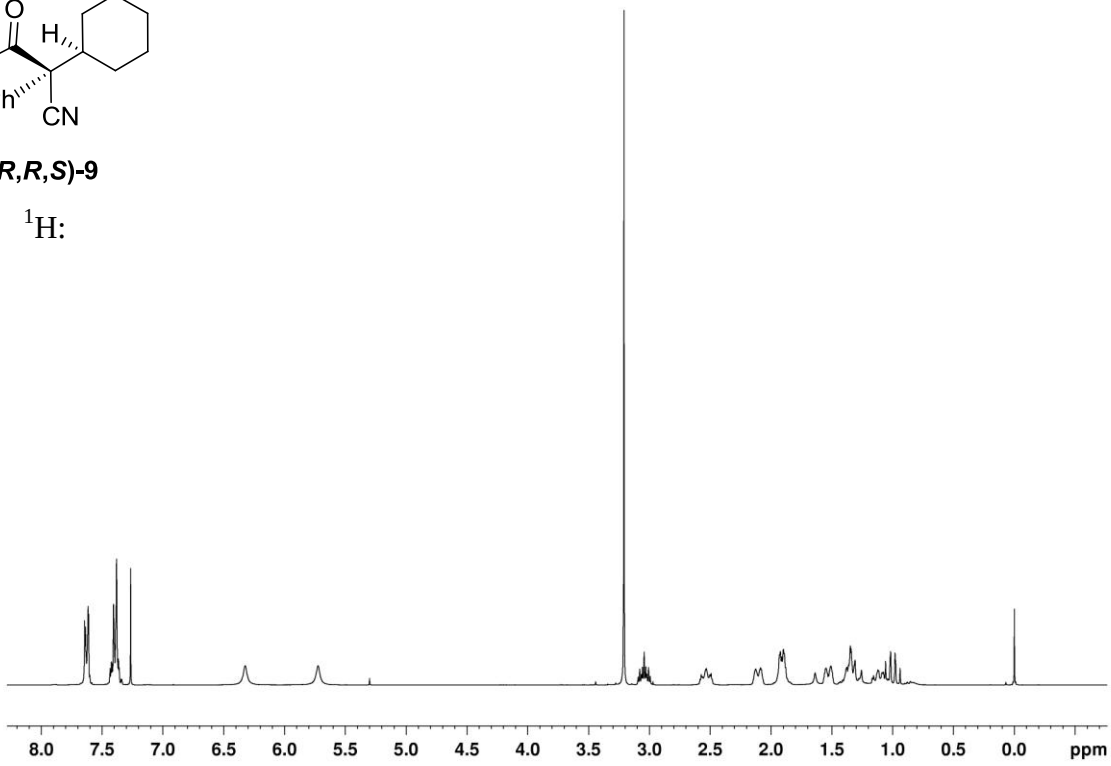

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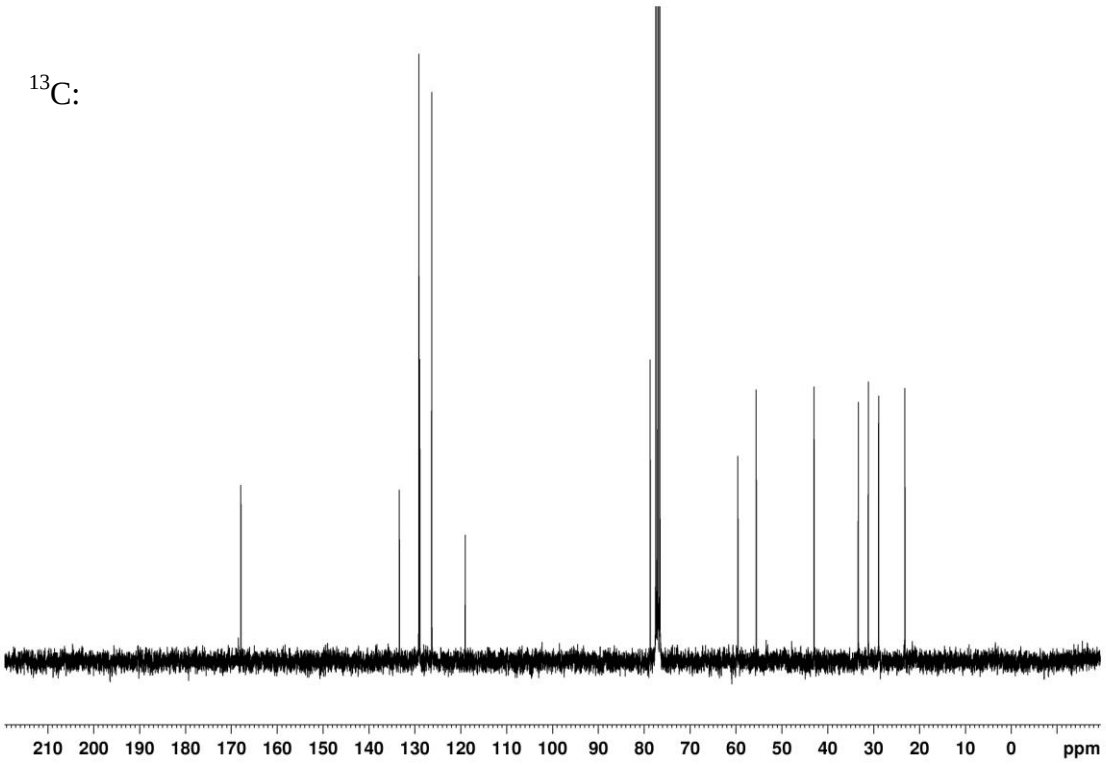
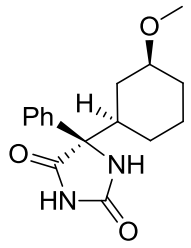


(*R*)-5-((*1R,3S*)-3-methoxycyclohexyl)-5-phenylimidazolidine-2,4-dione (**(*R,R,S*)-10**)



(*R*,*R*,*S*)-10

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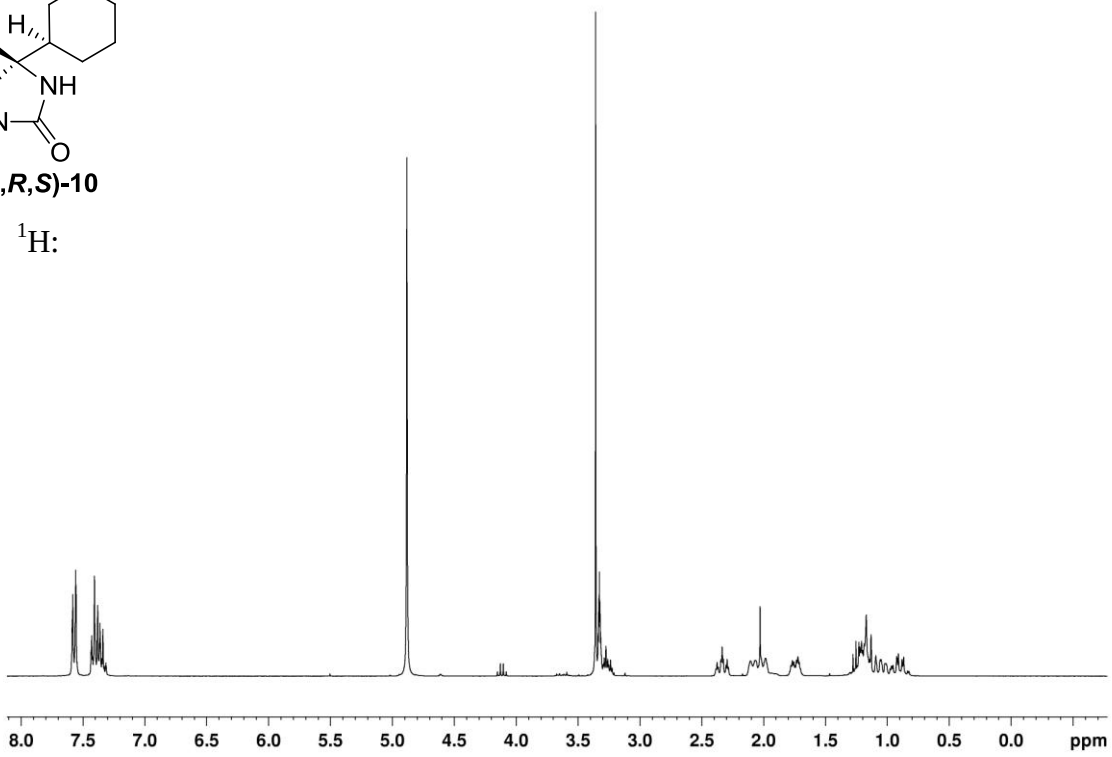

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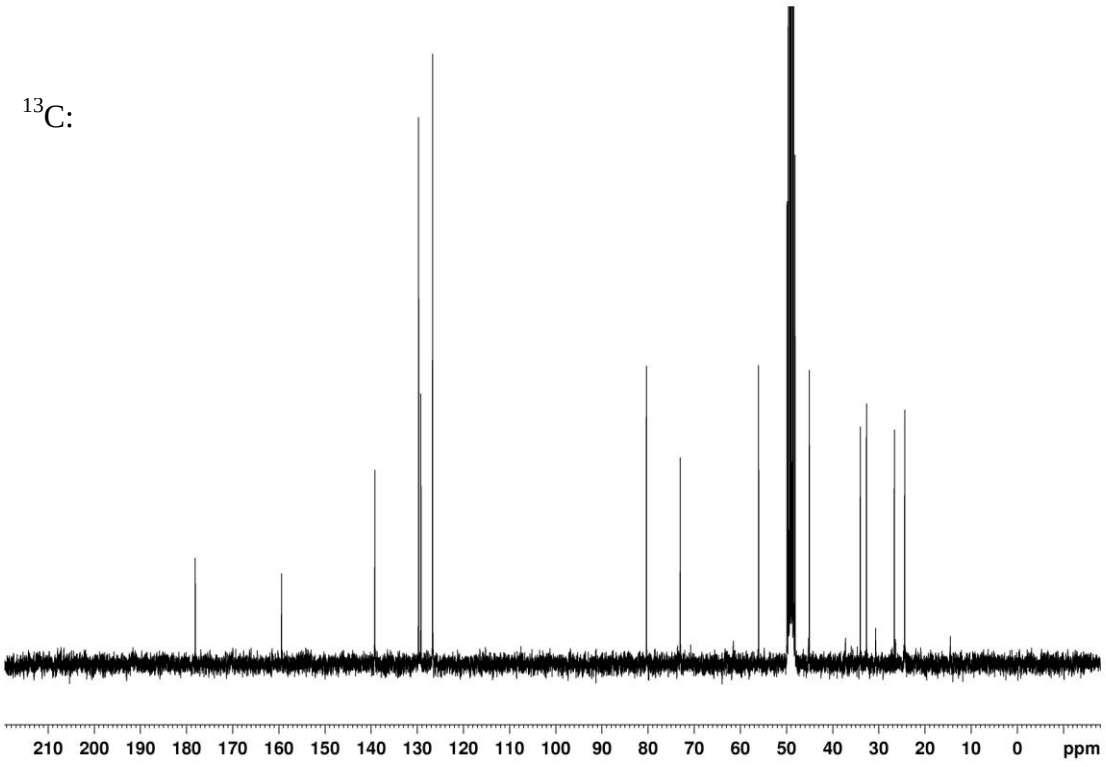
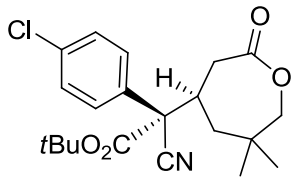
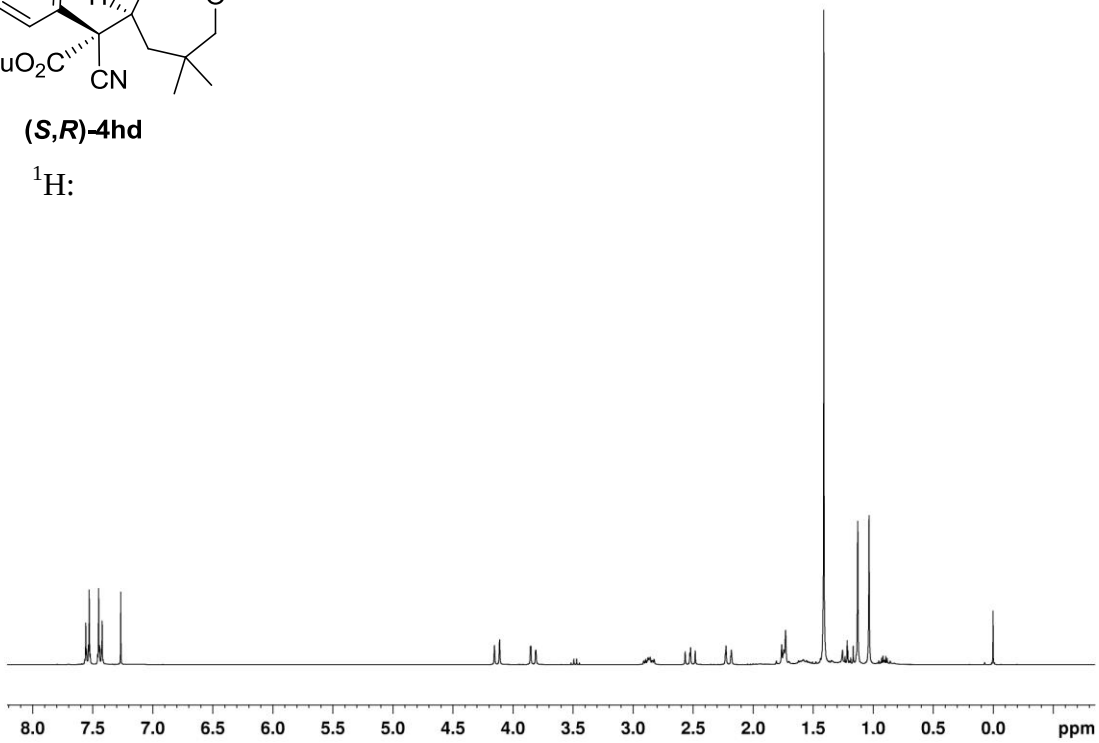


(*S*)-*tert*-Butyl-2-(4-chlorophenyl)-2-cyano-2-((*R*)-6,6-diemthyl-2-oxooxepan-4-yl)acetate (**(*S*,*R*)-4hd**)



(*S*,*R*)-4hd

^{1}H:



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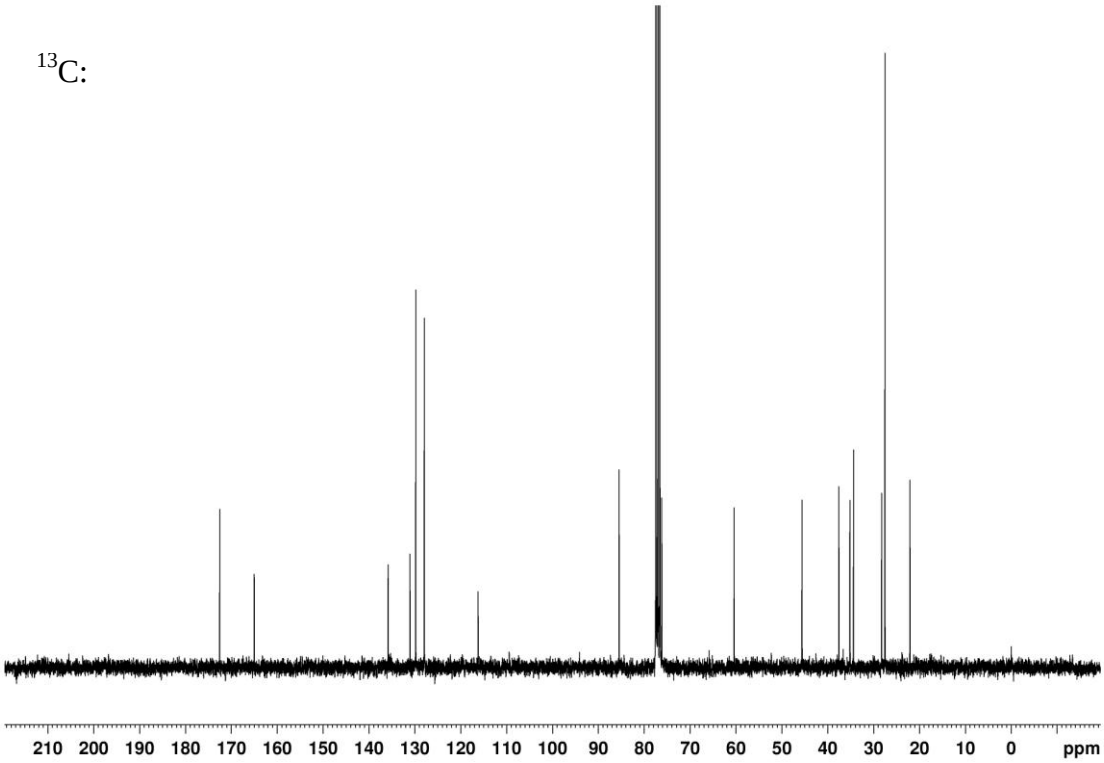
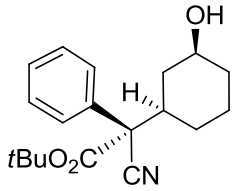


(*S*)-*tert*-Butyl-2-cyano-2-((*1R*,*3S*)-3-hydroxylcyclohexyl)-2-phenylacetate (**(*S*,*R*,*S*)-6aa**)



(*S*,*R*,*S*)-6aa

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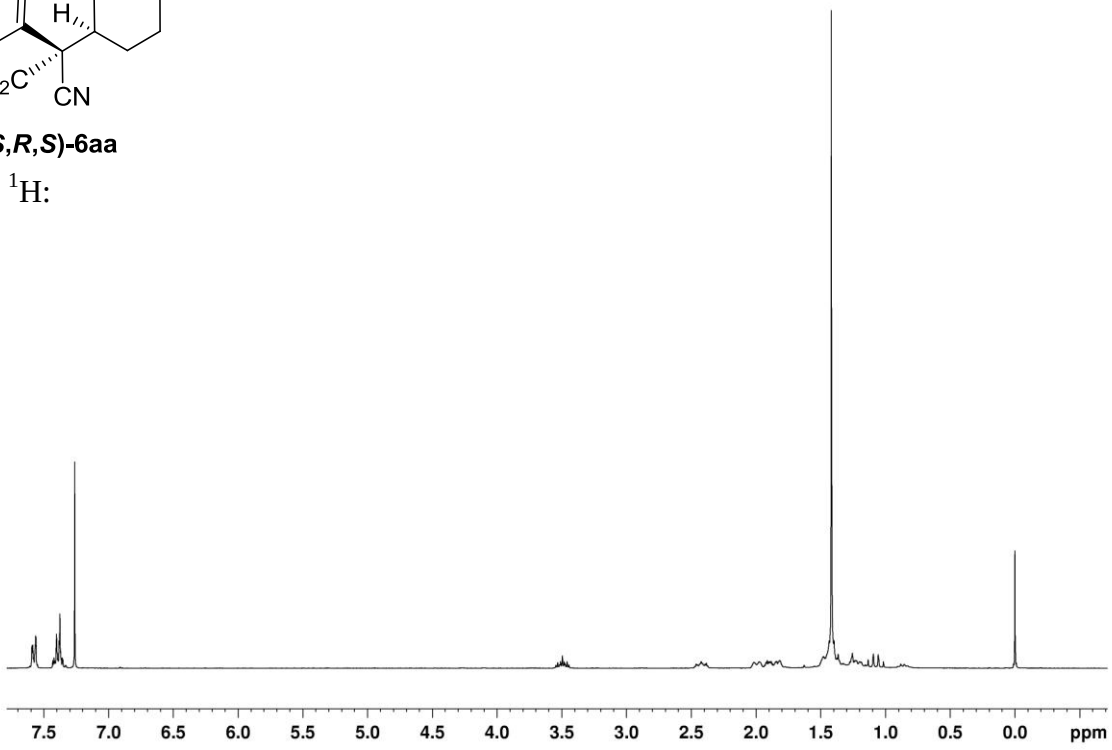

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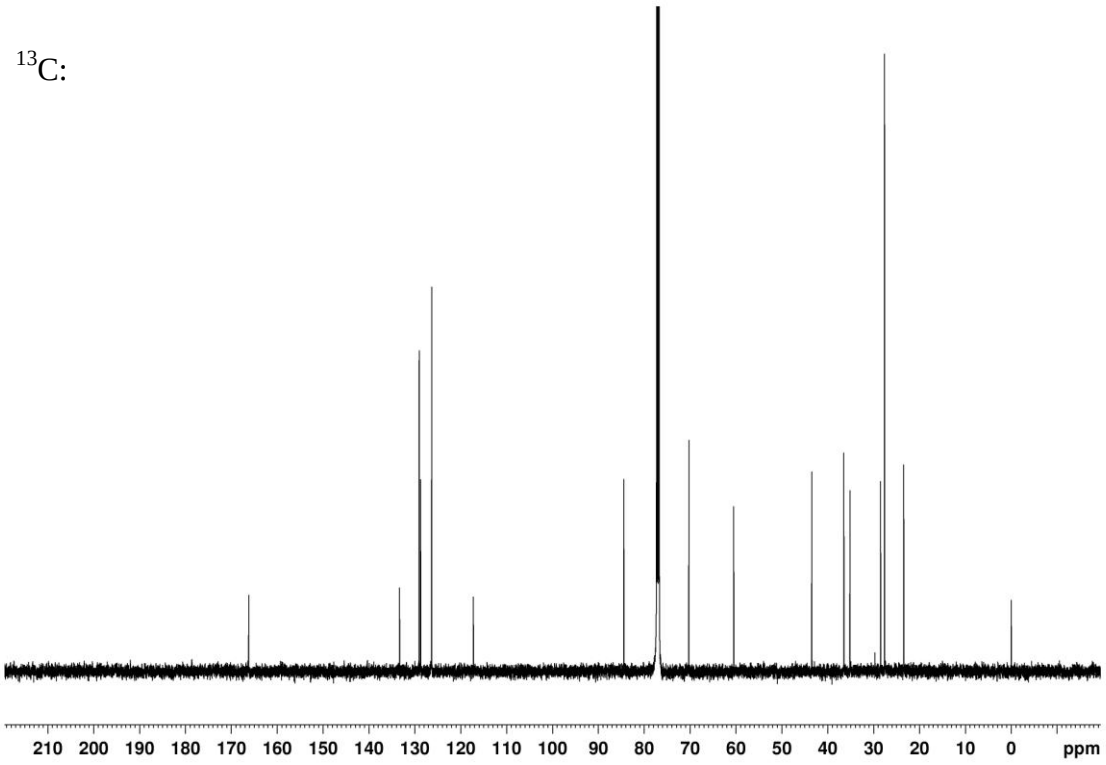
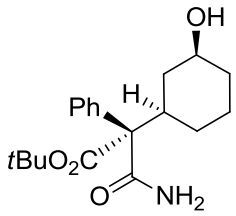
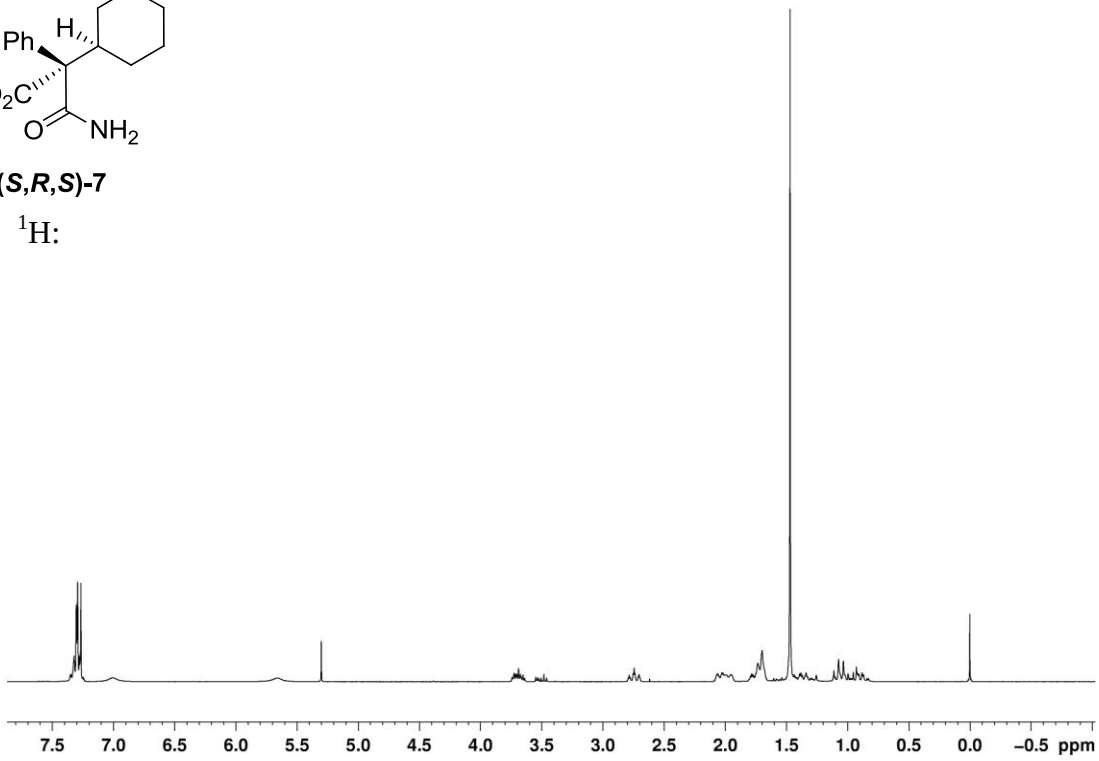


(*S*)-*tert*-Butyl-3-amino-2-((*1R*,*3S*)-3-hydroxycyclohexyl)-3-oxo-2-phenylpropanoate (**(*S*,*R*,*S*)-7**)



(*S*,*R*,*S*)-7

^{1}H:



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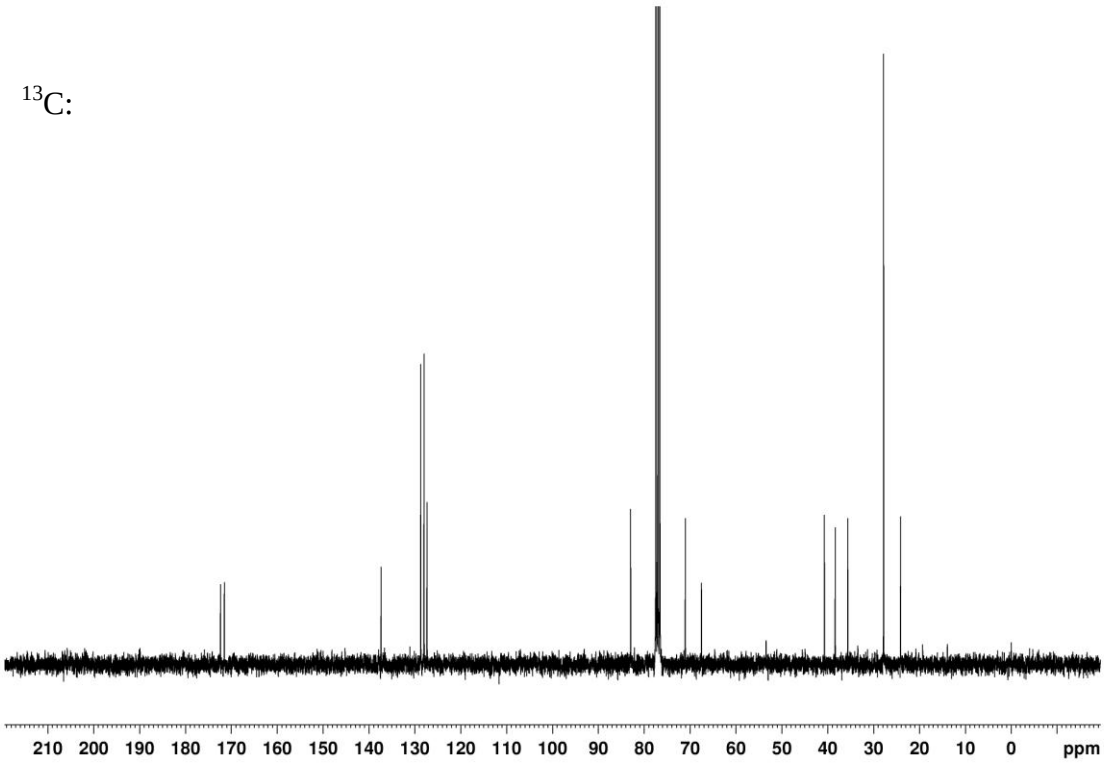
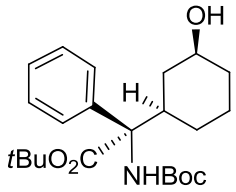


(*R*)-*tert*-Butyl-2-((*tert*-butoxylcarbonyl)amino)-2-((*1R,3S*)-3-hydroxycyclohexyl)-2-phenylacetate (**(*R,R,S*)-8**)



(*R*,*R*,*S*)-8

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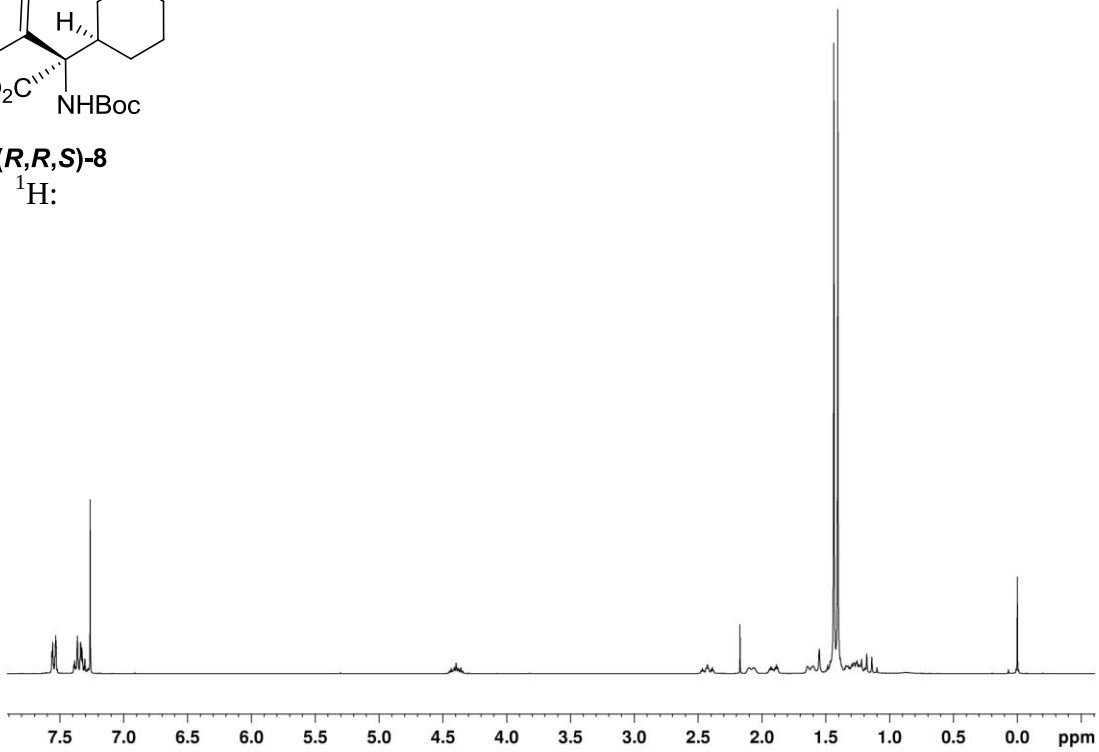

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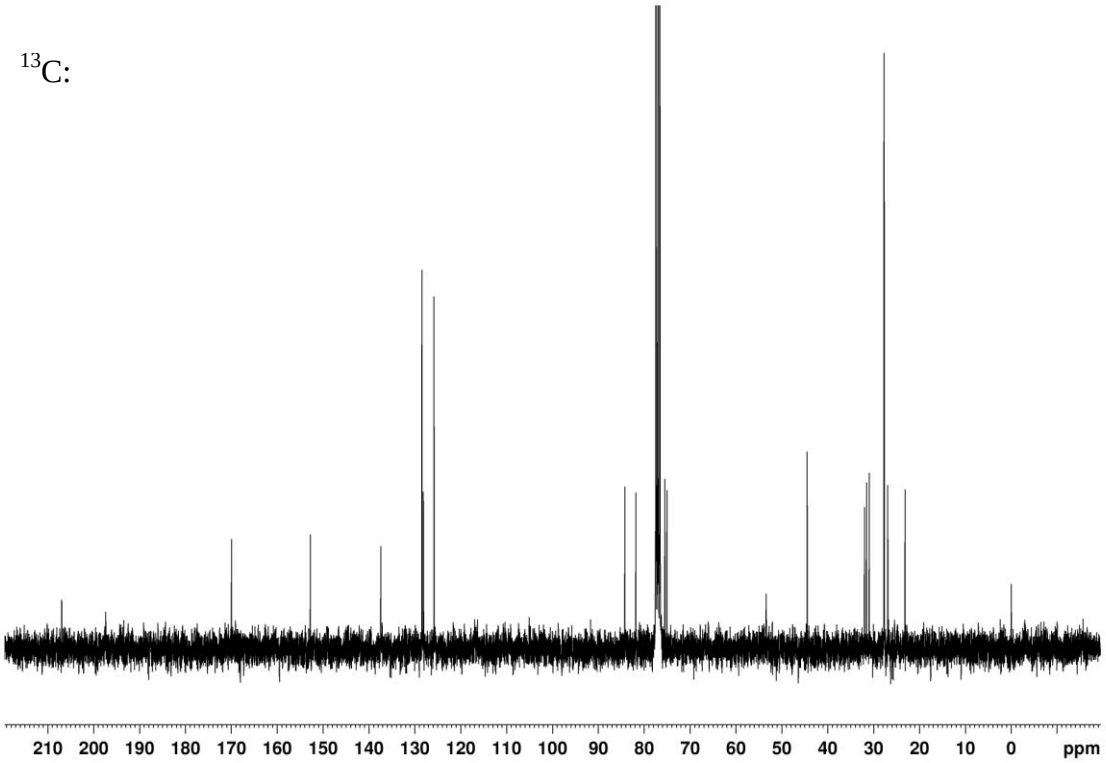
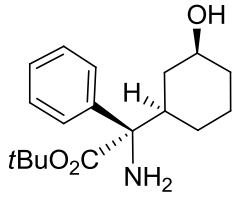


(*R*)-*tert*-Butyl-2-amino-2-((*1R*,*3S*)-3-hydroxycyclohexyl)-2-phenylacetate



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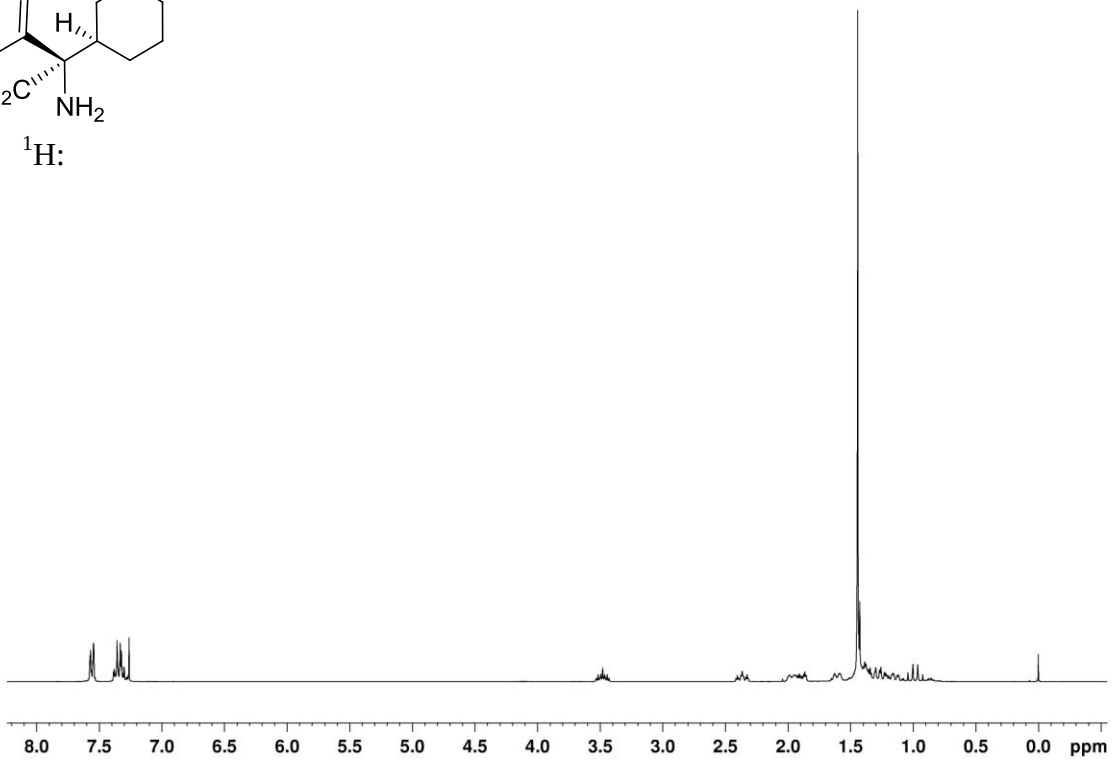

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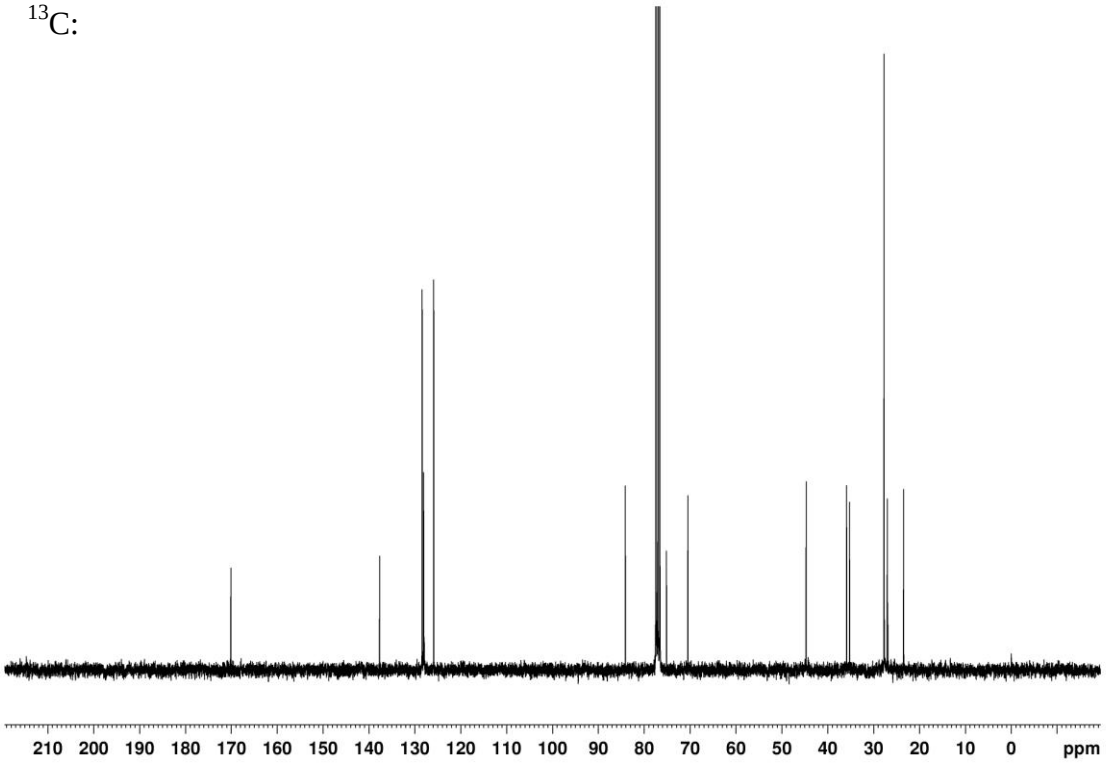
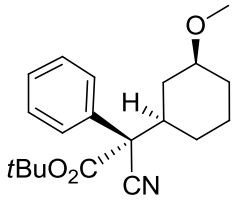


(*S*)-*tert*-Butyl-2-cyano-2-((*1R*,*3S*)-3-methoxycyclohexyl)-2-phenylacetate



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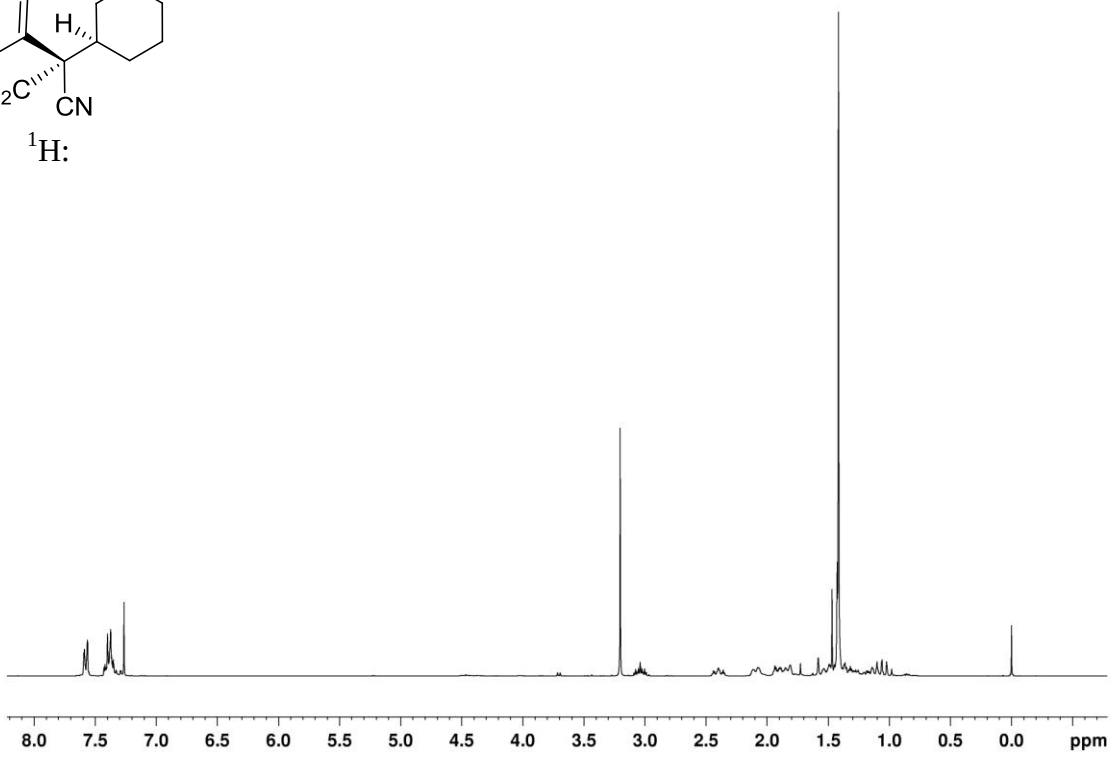

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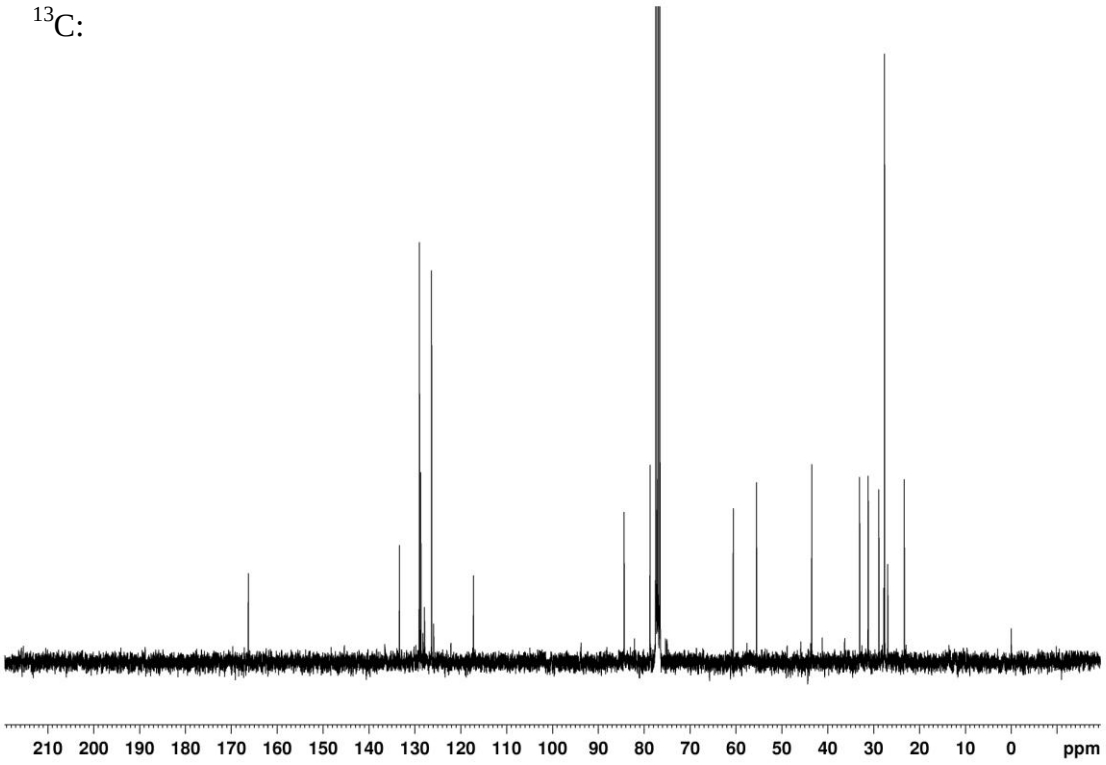
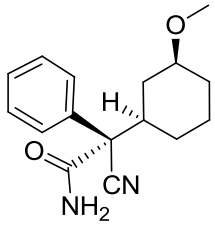


(*S*)-2-cyano-2-((*1R*,*3S*)-3-methoxycyclohexyl)-2-phenylacetamide (**(*S*,*R*,*S*)-9**)



(*S*,*R*,*S*)-9

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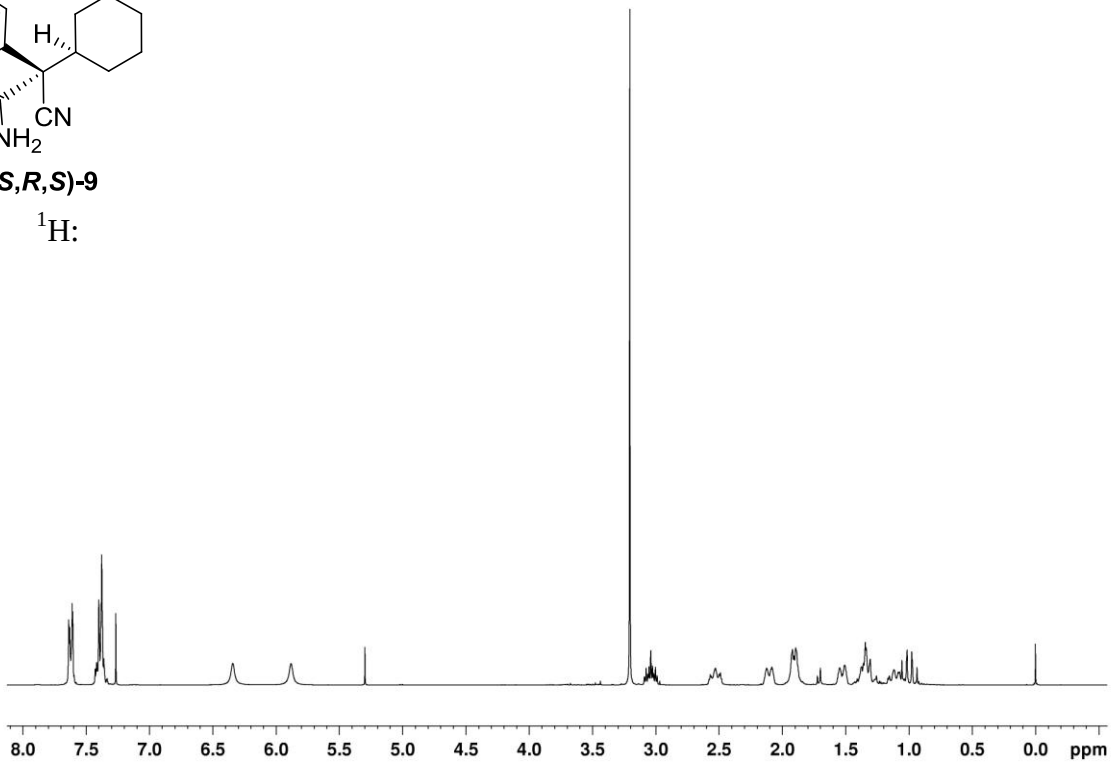

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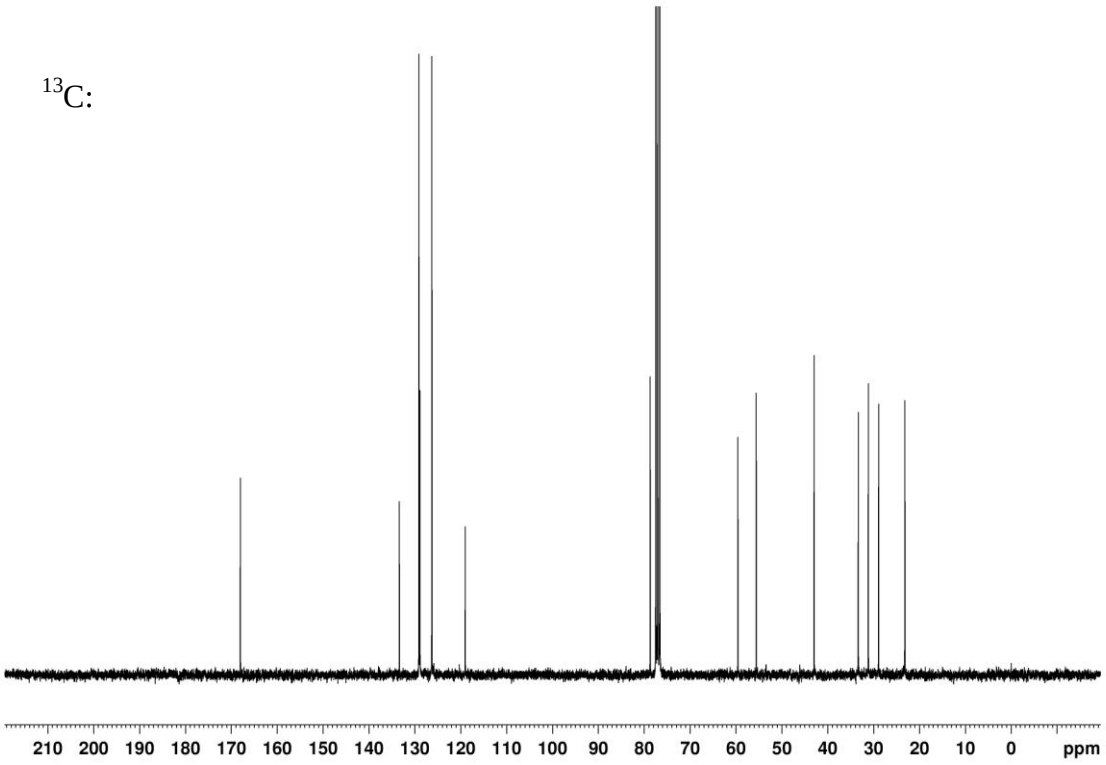
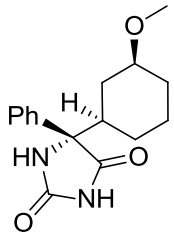


(*S*)-5-((*1R,3S*)-3-methoxycyclohexyl)-5-phenylimidazolidine-2,4-dione (**(*S,R,S*)-10**)



(*S*,*R*,*S*)-10

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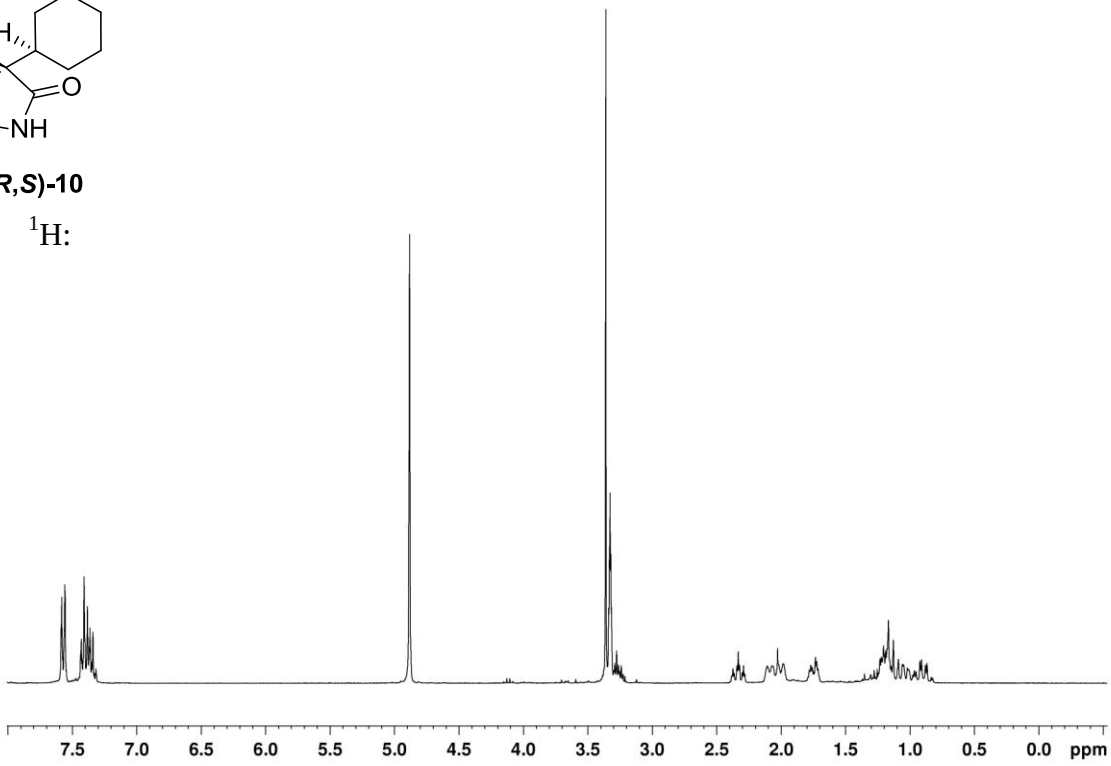

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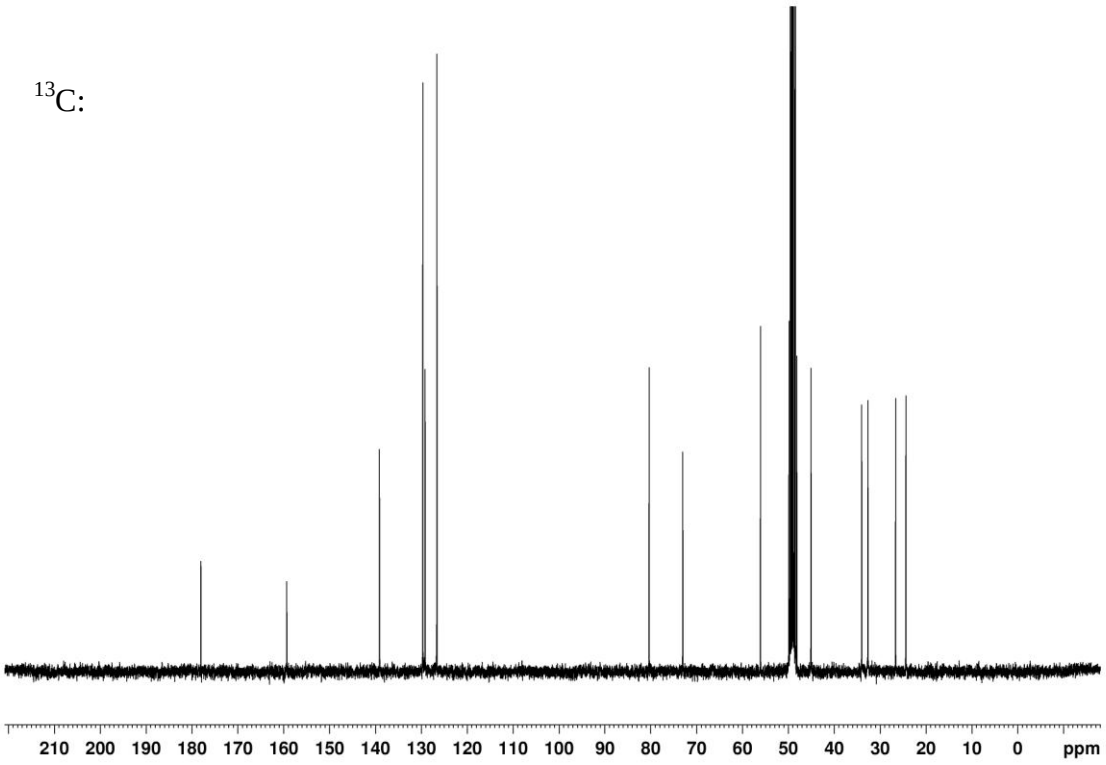
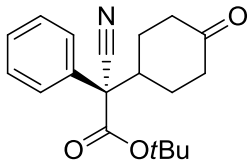


tert-Butyl-2-cyano-2-(4-oxocyclohexyl)-2-phenylacetate (**3aa***)



3aa*

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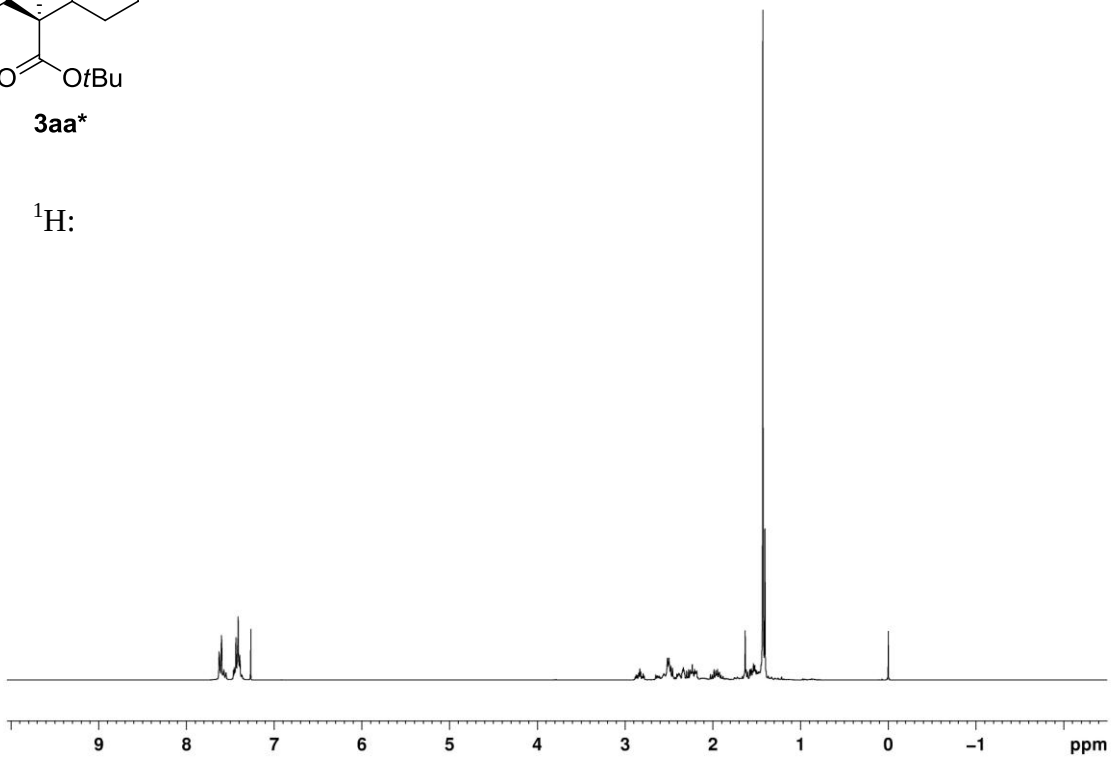

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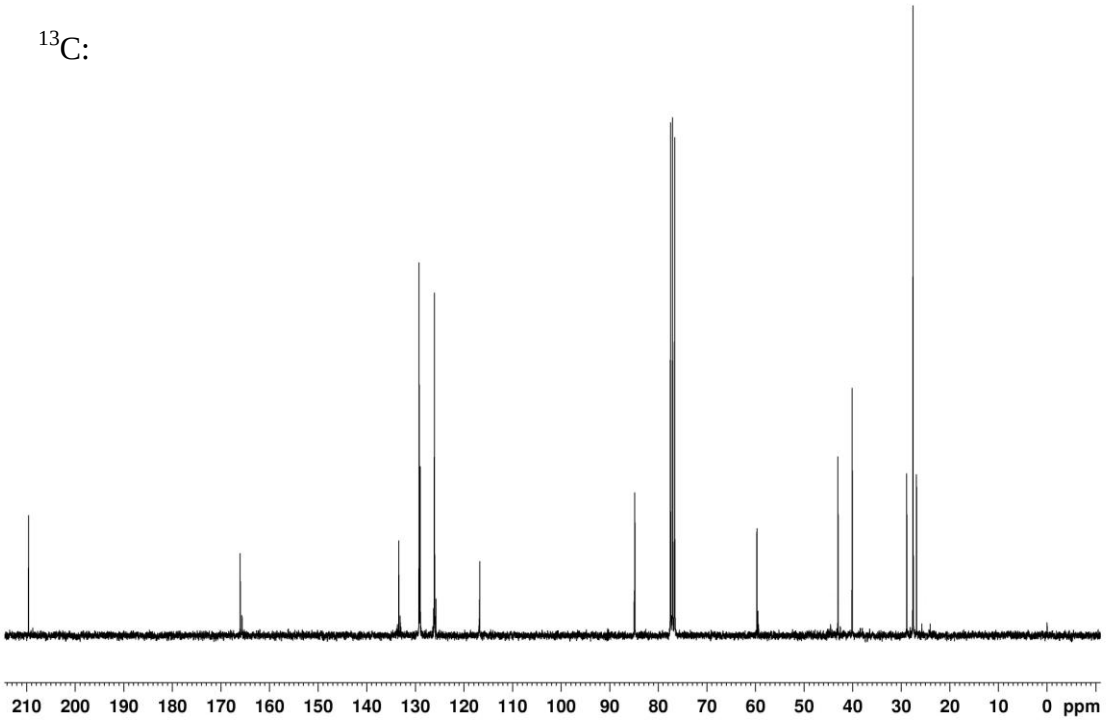
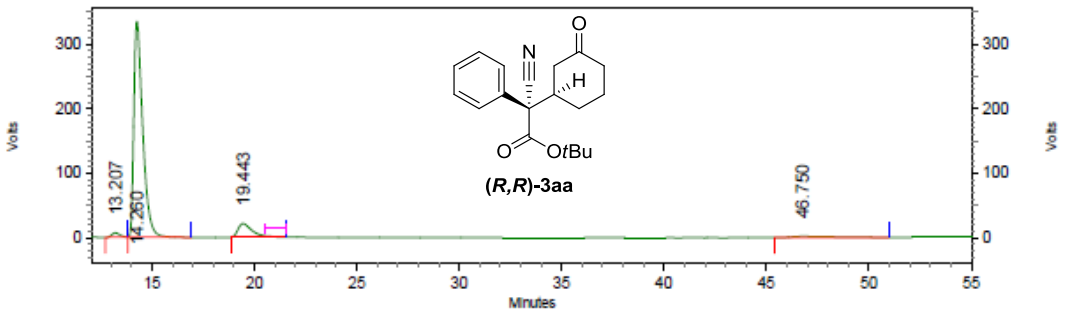


HPLC Data

tert-Butyl-2-cyano-2-(3-oxocyclohexyl)-2-phenylacetate (**3aa**)

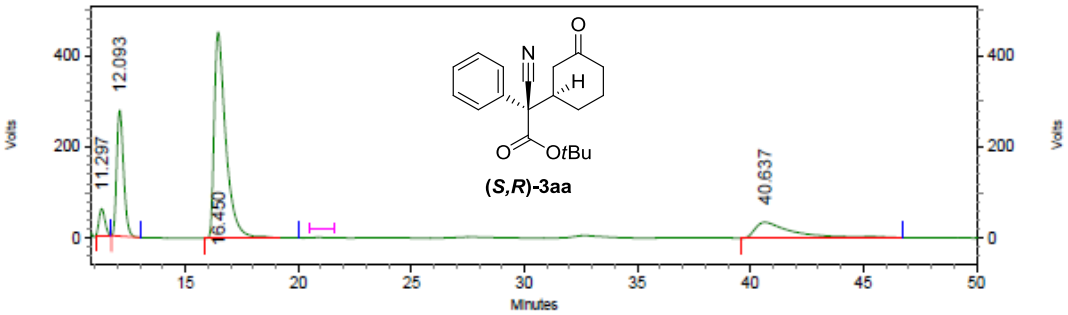
Area % Report : C:\EZChrom Elite\Enterprise\Projects\Simon Eitel\Data\MA new\10-MA340 Aa_ODH_SE-99-1-210nm-60min-0.9flow.met.dat



UV Results

Retention Time	Area	Area %
13.207	726061	1.57
14.260	40185821	87.02
19.443	4128717	8.94
46.750	1139298	2.47

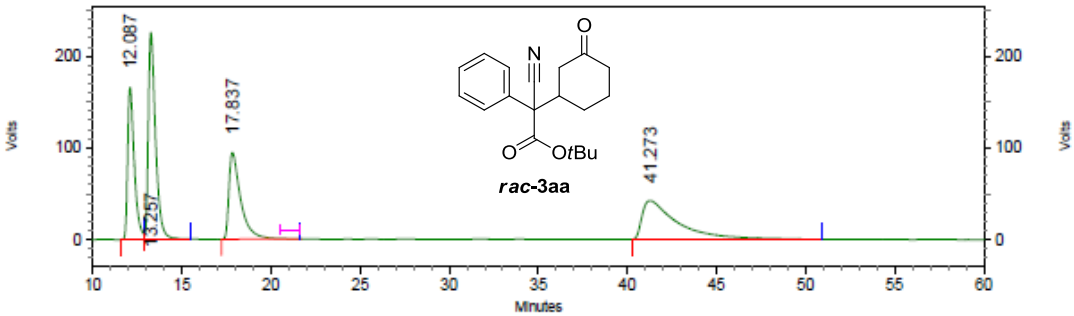
Area % Report : C:\EZChrom Elite\Enterprise\Projects\Simon Eitel\Data\10-MA250G



UV Results

Retention Time	Area	Area %
11.297	4157533	3.82
12.093	23379420	21.46
16.450	64754864	59.43
40.637	16676353	15.30

Area % Report : C:\EZChrom Elite\Enterprise\Projects\Simon Eitel\Data\MA new\SJM206

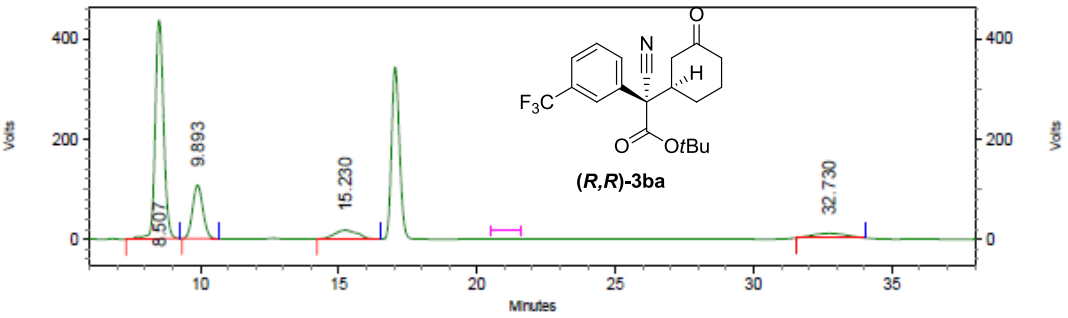


UV Results

Retention Time	Area	Area %
12.087	17283912	20.78
13.257	25240655	30.35
17.837	17347341	20.86
41.273	23302480	28.02

tert -Butyl-2-cyano-2-(3-oxocyclohexyl)-2-(3-(trifluoromethyl)phenyl)acetate (**3ba**)

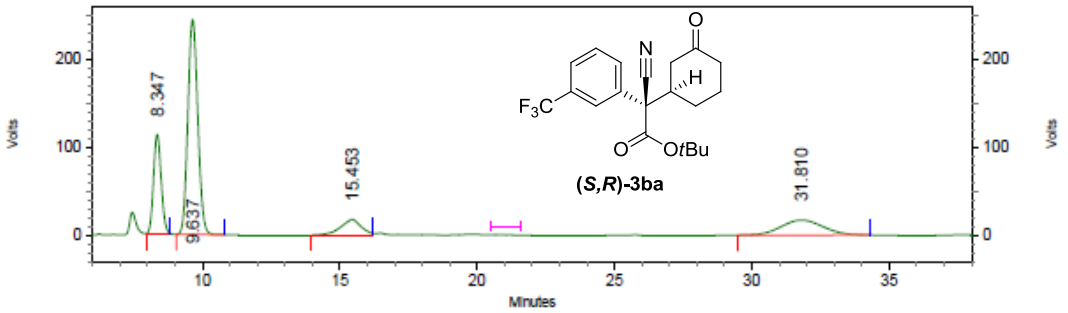
Area % Report : C:\EZChrom Elite\Enterprise\Projects\Simon Eitel\Data\Old data\SEM-104 A



UV Results

Retention Time	Area	Area %
8.507	36847344	66.91
9.893	11150871	20.25
15.230	4070129	7.39
32.730	2999234	5.45

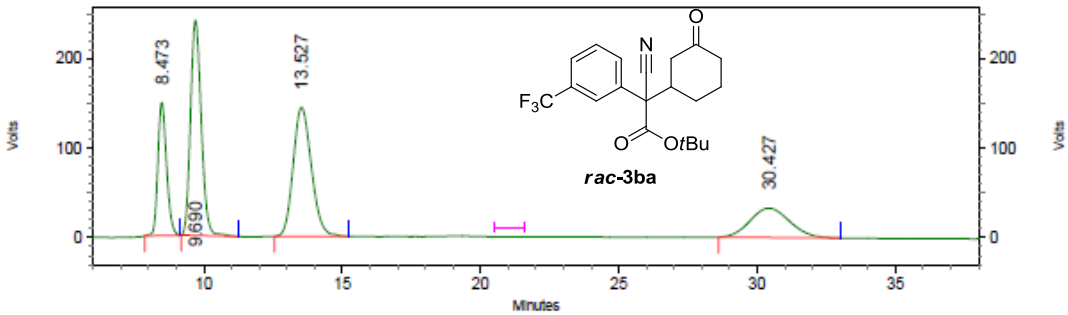
Area % Report : C:\EZChrom Elite\Enterprise\Projects\Simon Eitel\Data\10-MA089 Da



UV Results

Retention Time	Area	Area %
8.347	8750398	19.77
9.637	24618114	55.62
15.453	3613252	8.16
31.810	7277465	16.44

Area % Report : C:\EZChrom Elite\Enterprise\Projects\Simon Eitel\Data\MA new\SEM-025rac

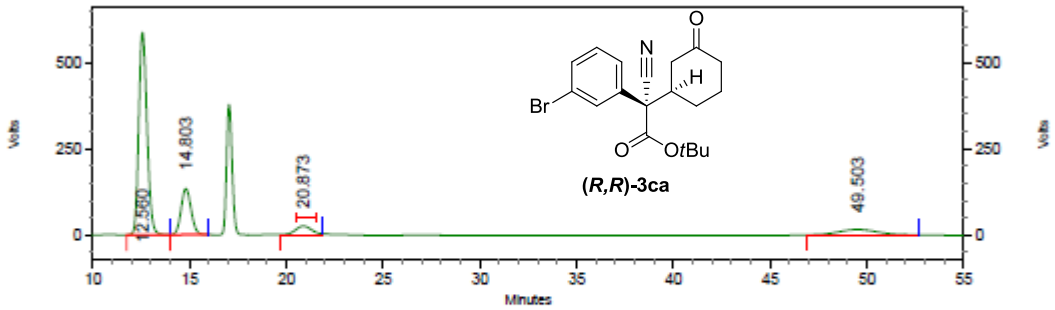


UV Results

Retention Time	Area	Area %
8.473	13016406	16.56
9.690	26002480	33.09
13.527	26471342	33.69
30.427	13093085	16.66

tert -Butyl-2-cyano-2-(3-bromophenyl)-2-(3-oxocyclohexyl)acetate (**3ca**)

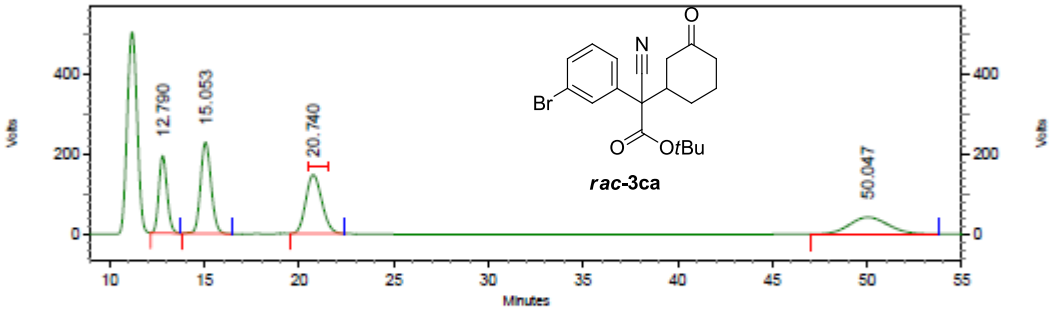
Area % Report : C:\EZChrom Elite\Enterprise\Projects\Simon Eitel\Data\Old data\SEM-105



UV Results

Retention Time	Area	Area %
12.560	69655224	67.39
14.803	19295171	18.67
20.873	5790051	5.60
49.503	8619143	8.34

Area % Report : C:\EZChrom Elite\Enterprise\Projects\Simon Eitel\Data\Old data\SEM-023 RAC+SM_ASH_se-97-3-210nm-60min-1flow.met.dat

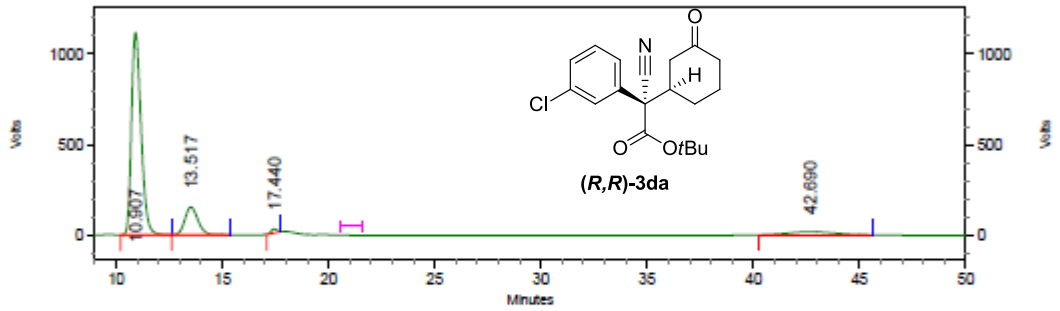


UV Results

Retention Time	Area	Area %
12.790	23507608	19.95
15.053	35612271	30.22
20.740	34764548	29.50
50.047	23954359	20.33

tert -Butyl-2-cyano-2-(3-chlorophenyl)-2-(3-oxocyclohexyl)acetate (**3da**)

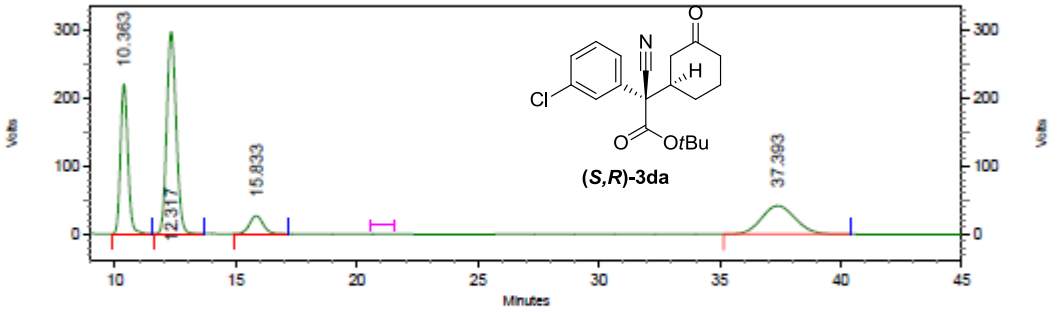
Area % Report : C:\EZChrom Elite\Enterprise\Projects\Simon Eitel\Data\10-MA032 Ib



UV Results

Retention Time	Area	Area %
10.907	140617502	78.84
13.517	26303583	14.75
17.440	1686685	0.95
42.690	9751001	5.47

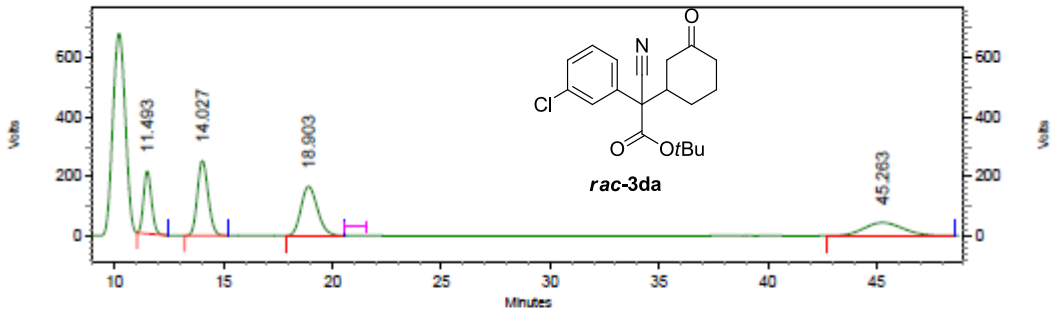
Area % Report : C:\EZChrom Elite\Enterprise\Projects\Simon Eitel\Data\10-MA101 Aa_ASH_SE-97-3-210nm-60min-1flow.met.dat



UV Results

Retention Time	Area	Area %
10.363	18819896	26.34
12.317	32137313	44.99
15.833	4138518	5.79
37.393	16341069	22.87

Area % Report : C:\EZChrom Elite\Enterprise\Projects\Simon Eitel\Data\Old data\SEM-024 RAC+SM_ASH_se-97-3-210nm-60min-1flow.met.dat

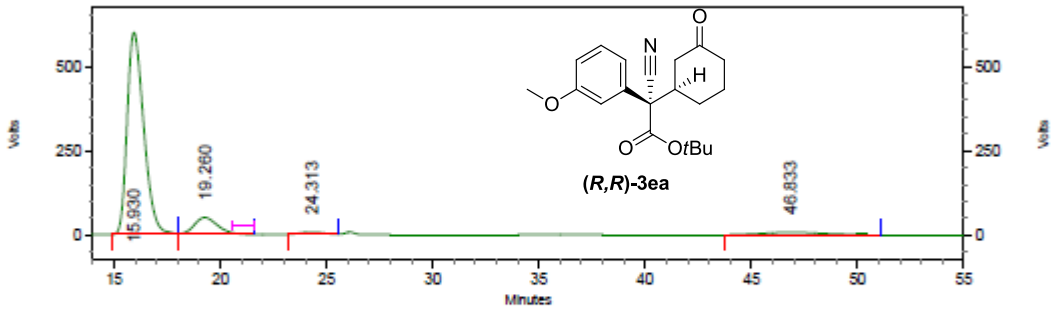


UV Results

Retention Time	Area	Area %
11.493	21521607	18.91
14.027	34919720	30.68
18.903	34930219	30.69
45.263	22444671	19.72

tert -Butyl-2-cyano-2-(3-methoxyphenyl)-2-(3-oxocyclohexyl)-acetate (**3ea**)

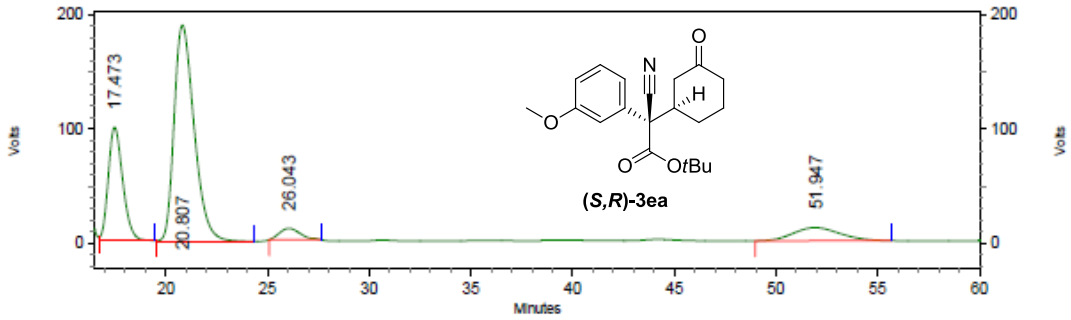
Area % Report : C:\EZChrom Elite\Enterprise\Projects\Simon Eitel\Data\10-MA032 Ea



UV Results

Retention Time	Area	Area %
15.930	130828820	85.57
19.260	15628366	10.22
24.313	1743396	1.14
46.833	4685413	3.06

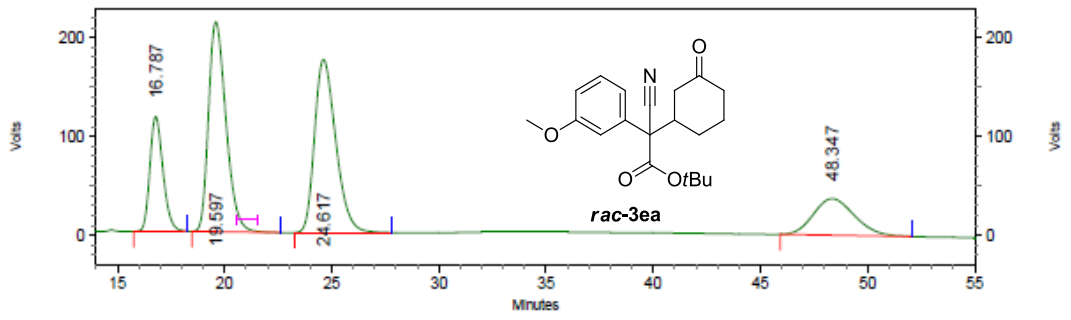
Area % Report : C:\EZChrom Elite\Enterprise\Projects\Simon Eitel\Data\MA new\10-MA089Cb_ASH_SE-97-3-210nm-60min-1flow.met.dat



UV Results

Retention Time	Area	Area %
17.473	19643030	24.03
20.807	51860715	63.45
26.043	2860361	3.50
51.947	7365790	9.01

Area % Report : C:\EZChrom Elite\Enterprise\Projects\Simon Eitel\Data\MA new\SEM-026rac

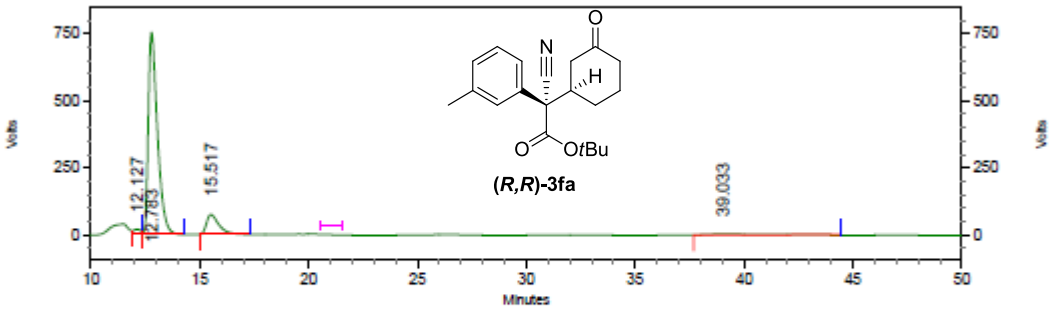


UV Results

Retention Time	Area	Area %
16.787	19765639	14.54
19.597	48133867	35.41
24.617	48264749	35.51
48.347	19767238	14.54

tert -Butyl-2-cyano-2-(3-oxocyclohexyl)-2-(*m*-tolyl)-acetate (**3fa**)

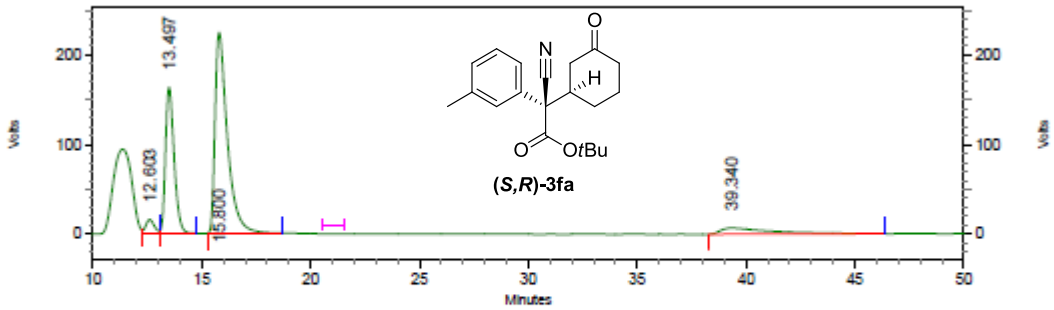
Area % Report : C:\EZChrom Elite\Enterprise\Projects\Simon Eitel\Data\10-MA032 Ga



UV Results

Retention Time	Area	Area %
12.127	1908330	1.84
12.783	87620443	84.70
15.517	11825657	11.43
39.033	2090639	2.02

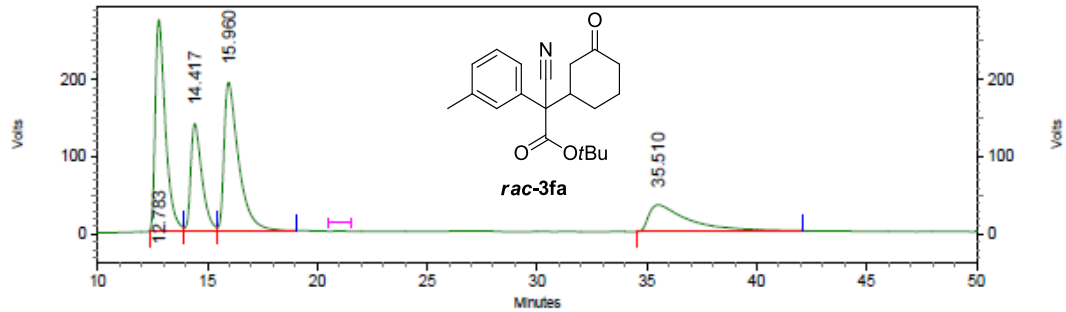
Area % Report : C:\EZChrom Elite\Enterprise\Projects\Simon Eitel\Data\10-MA089 Bb



UV Results

Retention Time	Area	Area %
12.603	1643982	2.77
13.497	17972474	30.27
15.800	35241420	59.36
39.340	4506984	7.59

Area % Report : C:\EZChrom Elite\Enterprise\Projects\Simon Eitel\Data\MA new\SEM-031rac-4

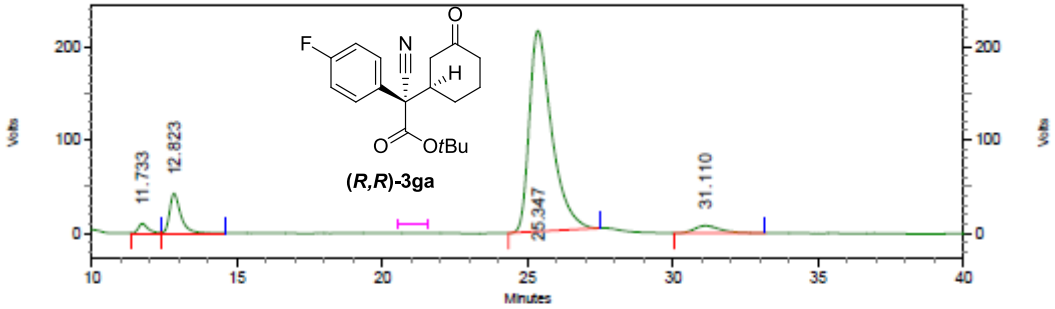


UV Results

Retention Time	Area	Area %
12.783	34928714	32.32
14.417	19500245	18.04
15.960	35290663	32.65
35.510	18355607	16.98

tert -Butyl-2-cyano-2-(4-fluorophenyl)-2-(3-oxocyclohexyl)-acetate (**3ga**)

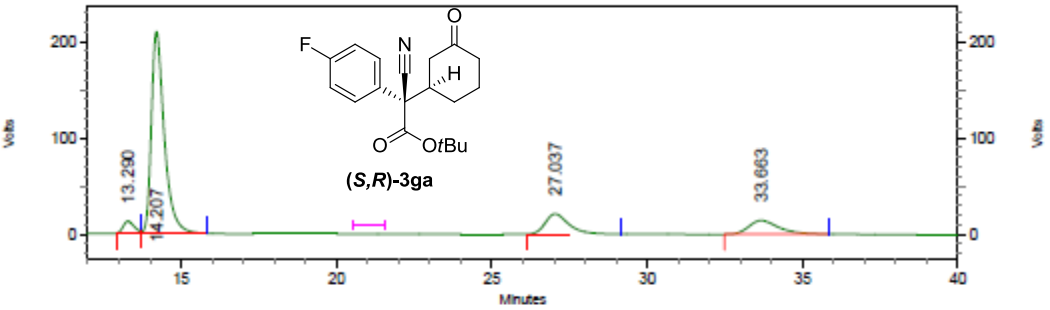
Area % Report : C:\EZChrom Elite\Enterprise\Projects\Simon Eitel\Data\10-MA032 Fb-2



UV Results

Retention Time	Area	Area %
11.733	941654	1.76
12.823	4496001	8.40
25.347	46127983	86.18
31.110	1957638	3.66

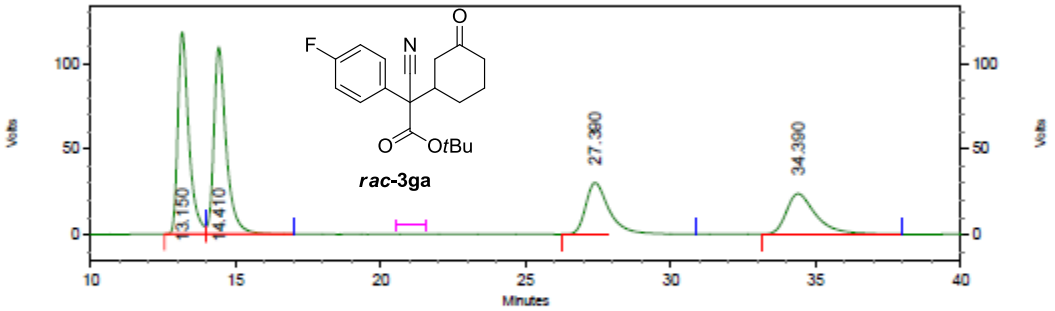
Area % Report : C:\EZChrom Elite\Enterprise\Projects\Simon Eitel\Data\10-MA089 Fa



UV Results

Retention Time	Area	Area %
13.290	1233889	3.67
14.207	24133944	71.79
27.037	4408955	13.11
33.663	3841118	11.43

Area % Report : C:\EZChrom Elite\Enterprise\Projects\Simon Eitel\Data\Old data\SEM-020 RAC_ADH_sj-99-1-210nm-60min-1.2flow.met.dat

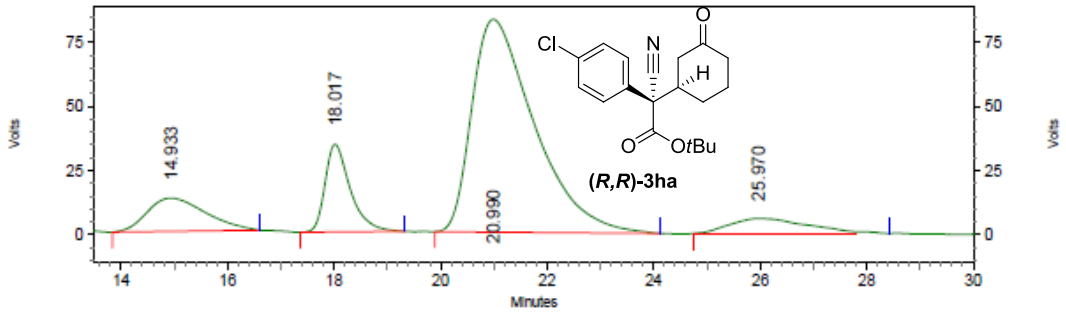


UV Results

Retention Time	Area	Area %
13.150	12452127	31.92
14.410	12995122	33.32
27.390	6845602	17.55
34.390	6713697	17.21

tert -Butyl-2-cyano-2-(4-chlorophenyl)-2-(3-oxocyclohexyl)-acetate (**3ha**)

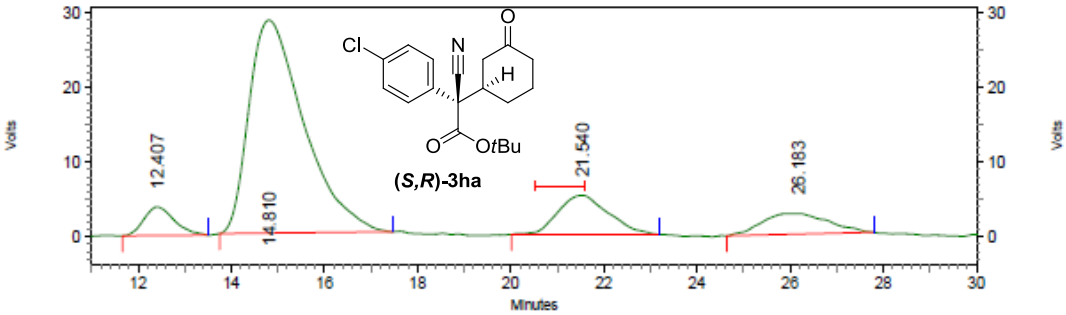
Area % Report : C:\EZChrom Elite\Enterprise\Projects\Simon Eitel\Data\MA new\10-MA340 Da2



UV Results

Retention Time	Area	Area %
14.933	3947108	10.41
18.017	4499584	11.87
20.990	27063467	71.38
25.970	2401914	6.34

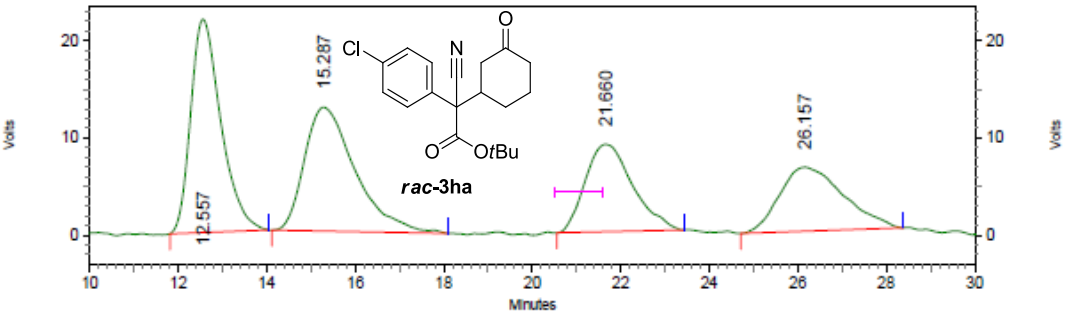
Area % Report : C:\EZChrom Elite\Enterprise\Projects\Simon Eitel\Data\MA new\10-MA094 Aa2



UV Results

Retention Time	Area	Area %
12.407	696004	5.46
14.810	9378253	73.55
21.540	1580066	12.39
26.183	1096945	8.60

Area % Report : C:\EZChrom Elite\Enterprise\Projects\Simon Eitel\Data\MA new\SEM-016rac5

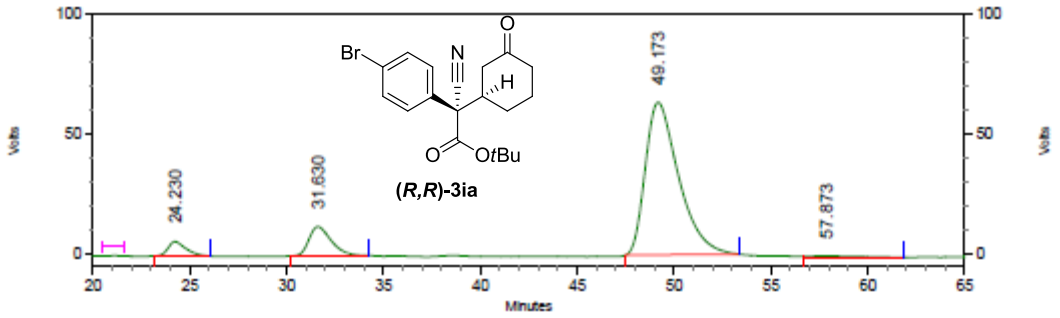


UV Results

Retention Time	Area	Area %
12.557	4167989	30.78
15.287	4054514	29.95
21.660	2675411	19.76
26.157	2641308	19.51

tert -Butyl-2-cyano-2-(4-bromophenyl)-2-(3-oxocyclohexyl)-acetate (**3ia**)

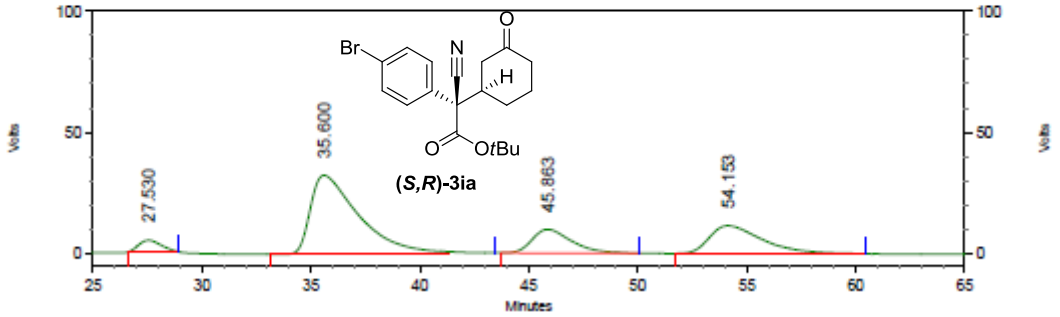
Area % Report : C:\EZChrom Elite\Enterprise\Projects\Simon Eitel\Data\10-MA032 Ca



UV Results

Retention Time	Area	Area %
24.230	1538677	4.24
31.630	3977853	10.97
49.173	30334686	83.69
57.873	397105	1.10

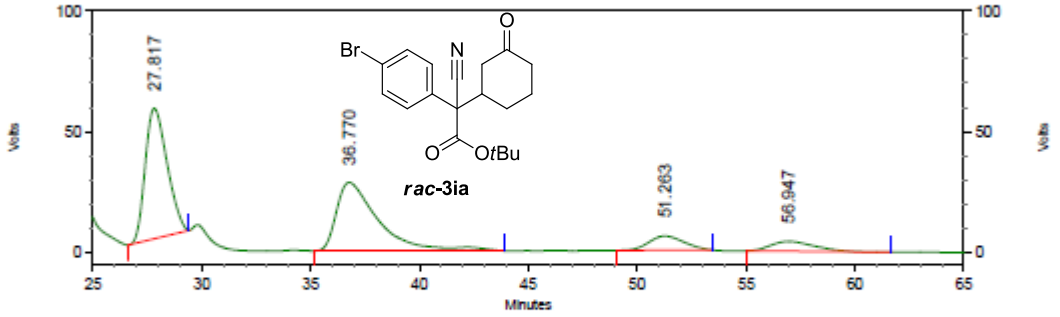
Area % Report : C:\EZChrom Elite\Enterprise\Projects\Simon Eitel\Data\10-MA101 Ba_ADH_SE-99.5-0.5-210nm-70min-1.2flow.met.dat



UV Results

Retention Time	Area	Area %
27.530	1400488	4.00
35.600	20869465	59.63
45.863	4918347	14.05
54.153	7811650	22.32

Area % Report : C:\EZChrom Elite\Enterprise\Projects\Simon Eitel\Data\Old data\SEM-041 RAC + SM_ADH_SE-99.5-0.5-210nm-70min-1.2flow.met.dat

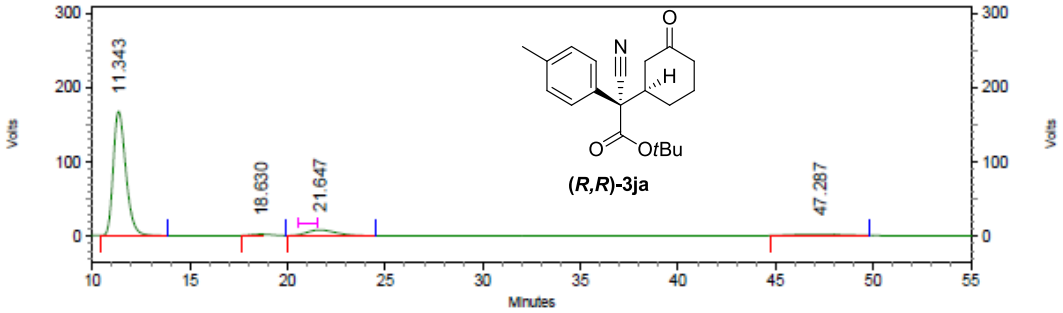


UV Results

Retention Time	Area	Area %
27.817	15104786	42.96
36.770	15172451	43.15
51.263	2628153	7.47
56.947	2256252	6.42

tert -Butyl-2-cyano-2-(3-oxocyclohexyl)-2-(*p*-tolyl)-acetate (**3ja**)

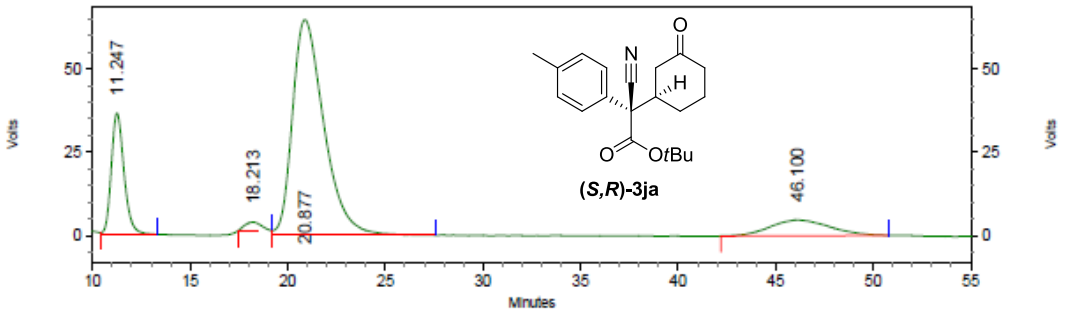
Area % Report : C:\EZChrom Elite\Enterprise\Projects\Simon Eitel\Data\MA new\10-MA340 Ca



UV Results

Retention Time	Area	Area %
11.343	30143064	86.22
18.630	528608	1.51
21.647	3288304	9.41
47.287	999844	2.86

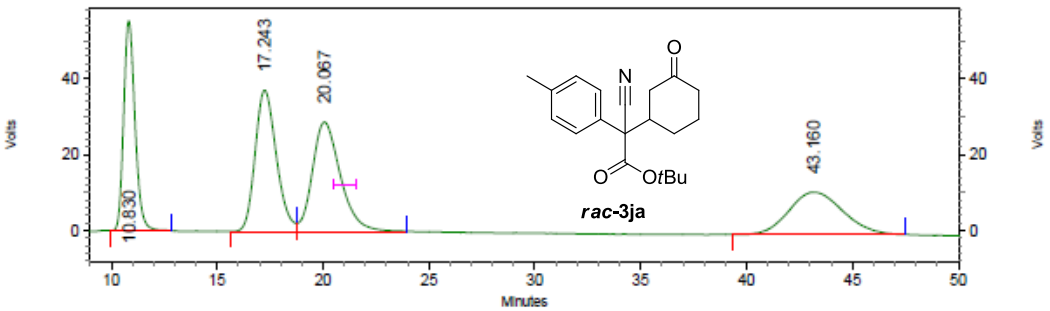
Area % Report : C:\EZChrom Elite\Enterprise\Projects\Simon Eitel\Data\MA new\10-MA089 Ab-2



UV Results

Retention Time	Area	Area %
11.247	6647742	16.46
18.213	165485	0.41
20.877	29117252	72.11
46.100	4044795	10.02

Area % Report : C:\EZChrom Elite\Enterprise\Projects\Simon Eitel\Data\MA new\SEM-021rac-3

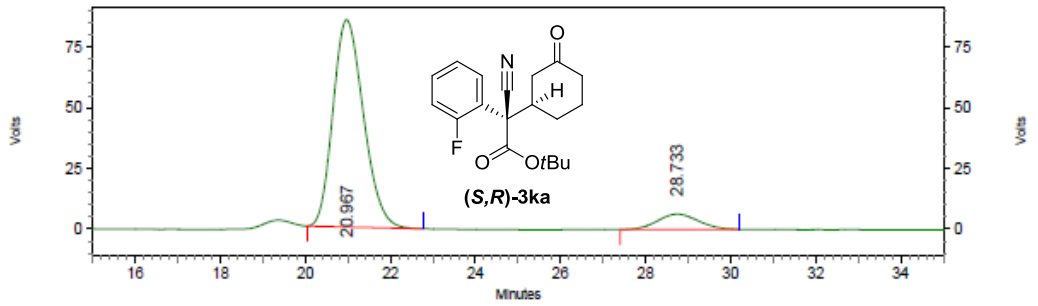


UV Results

Retention Time	Area	Area %
10.830	8254140	22.21
17.243	10369011	27.91
20.067	10601900	28.53
43.160	7932894	21.35

tert -Butyl-2-cyano-2-(2-fluorophenyl)-2-(3-oxocyclohexyl)-acetate (**3ka**)

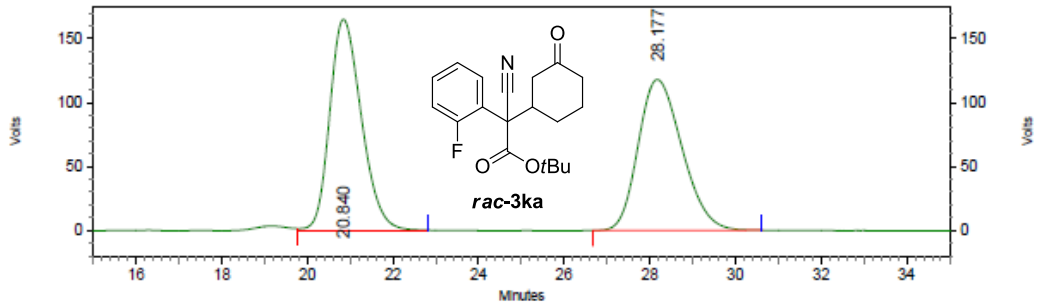
Area % Report : C:\EZChrom Elite\Enterprise\Projects\Simon Eitel\Data\MA new\10-MA101Cb 14+15



UV Results

Retention Time	Area	Area %
20.967	17060841	91.05
28.733	1676204	8.95

Area % Report : C:\EZChrom Elite\Enterprise\Projects\Simon Eitel\Data\MA new\10-MA037rac Dia1

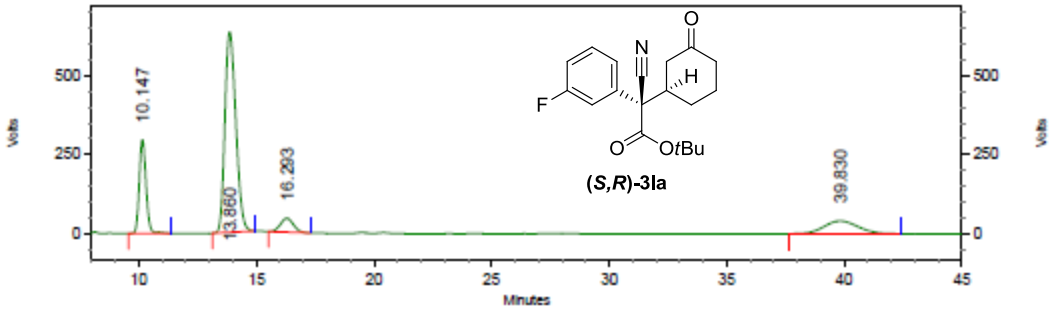


UV Results

Retention Time	Area	Area %
20.840	33877370	50.17
28.177	33650867	49.83

tert -Butyl-2-cyano-2-(3-fluorophenyl)-2-(3-oxocyclohexyl)-acetate (**3la**)

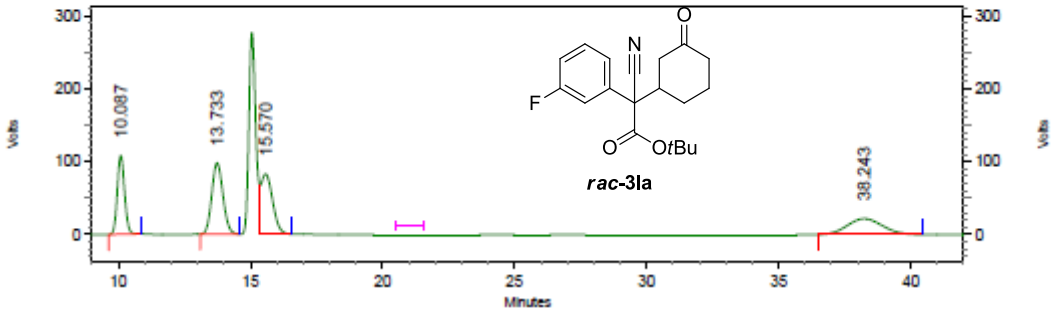
Area % Report : C:\EZChrom Elite\Enterprise\Projects\Simon Eitel\Data\10-MA114 A_ASH_SE-97-3-210nm-45min-1flow.met.dat



UV Results

Retention Time	Area	Area %
10.147	23756126	18.41
13.860	82061104	63.60
16.293	6729763	5.22
39.830	16482979	12.77

Area % Report : C:\EZChrom Elite\Enterprise\Projects\Simon Eitel\Data\racemic products\10-MA115 rac dirty_ASH_SE-97-3-210nm-45min-1flow.met.dat

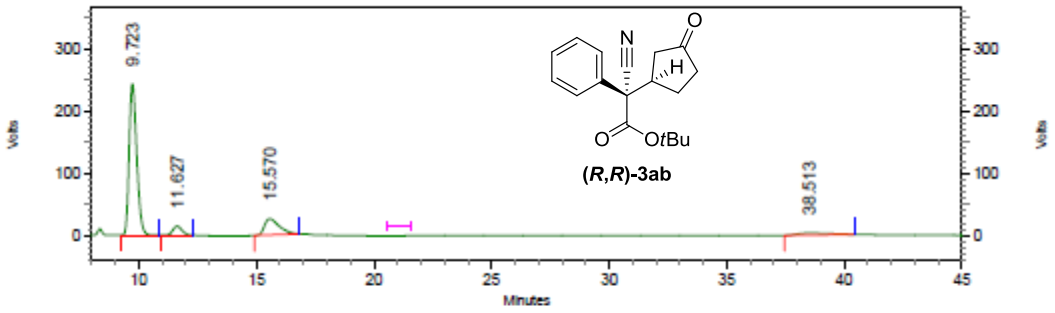


UV Results

Retention Time	Area	Area %
10.087	8205686	21.66
13.733	11472096	30.28
15.570	10071839	26.58
38.243	8142506	21.49

tert -Butyl-2-cyano-2-(3-oxocyclopentyl)-2-phenylacetate (**3ab**)

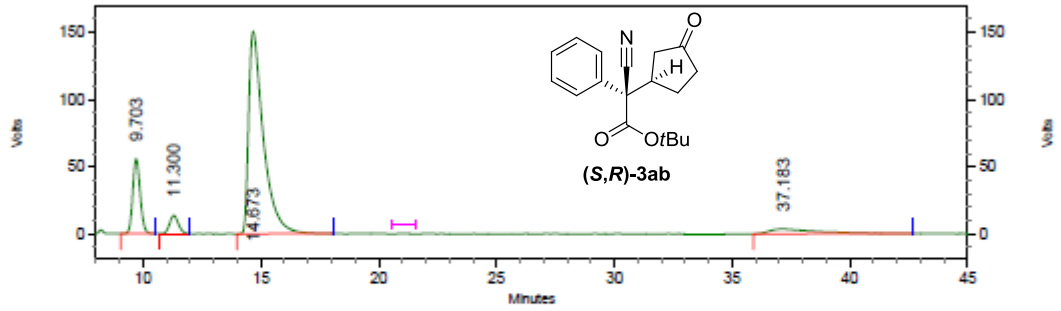
Area % Report : C:\EZChrom Elite\Enterprise\Projects\Simon Eitel\Data\Old data\SEM-094 A



UV Results

Retention Time	Area	Area %
9.723	21749926	74.95
11.627	1581847	5.45
15.570	4530841	15.61
38.513	1158345	3.99

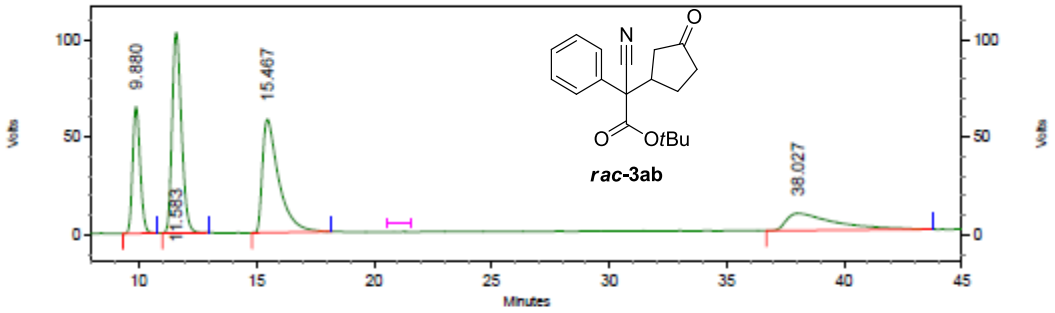
Area % Report : C:\EZChrom Elite\Enterprise\Projects\Simon Eitel\Data\10-MA090 Cb



UV Results

Retention Time	Area	Area %
9.703	4869768	14.10
11.300	1403817	4.07
14.673	26264605	76.07
37.183	1988279	5.76

Area % Report : C:\EZChrom Elite\Enterprise\Projects\Simon Eitel\Data\Old data\SEM-060 RAC_ODH_sj-99-1-210nm-60min-2ml.met.dat

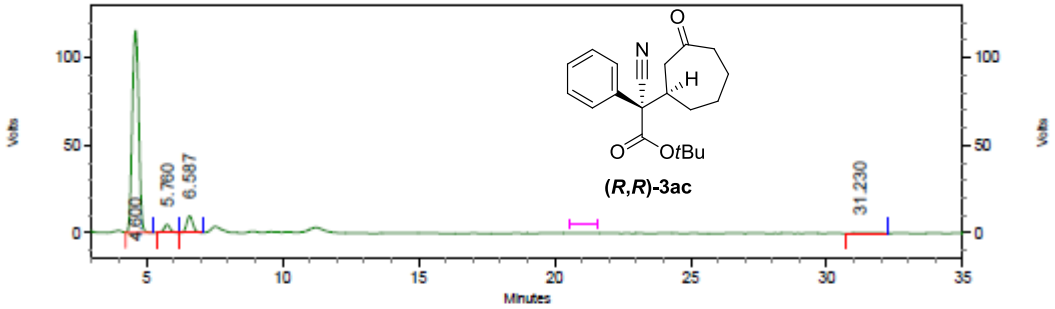


UV Results

Retention Time	Area	Area %
9.880	5763796	17.27
11.583	11358772	34.04
15.467	11214808	33.61
38.027	5032845	15.08

tert -Butyl-2-cyano-2-(3-oxocycloheptyl)-2-phenylacetate (**3ac**)

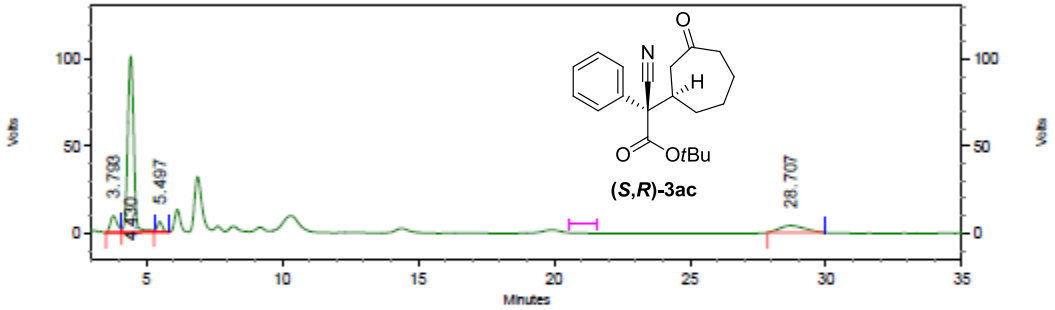
Area % Report : C:\EZChrom Elite\Enterprise\Projects\Simon Eitel\Data\10-MA096 A



UV Results

Retention Time	Area	Area %
4.600	7603170	89.22
5.760	284012	3.33
6.587	604049	7.09
31.230	30146	0.35

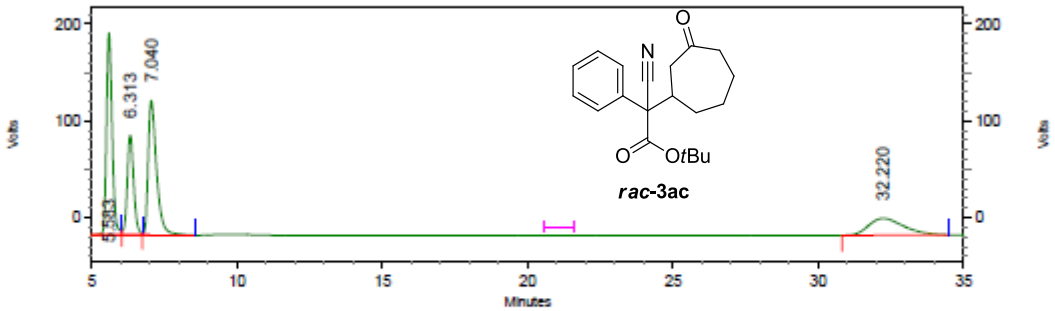
Area % Report : C:\EZChrom Elite\Enterprise\Projects\Simon Eitel\Data\10-MA102 Bb_ODH_SE-99-1-210nm-35min-2ml.met.dat



UV Results

Retention Time	Area	Area %
3.793	680814	8.24
4.430	6247257	75.59
5.497	318779	3.86
28.707	1017661	12.31

Area % Report : C:\EZChrom Elite\Enterprise\Projects\Simon Eitel\Data\Old data\SEM-059 RAC_ODH_sj-99-1-210nm-35min-2ml.met.dat

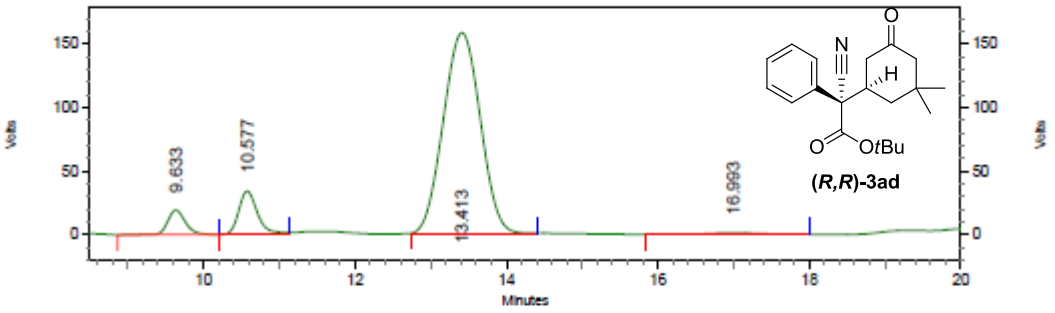


UV Results

Retention Time	Area	Area %
5.583	11319143	32.48
6.313	6395375	18.35
7.040	11229829	32.23
32.220	5902239	16.94

tert -Butyl-2-cyano-2-(3,3-dimethyl-5-oxocyclohexyl)-2-phenylacetate (**3ad**)

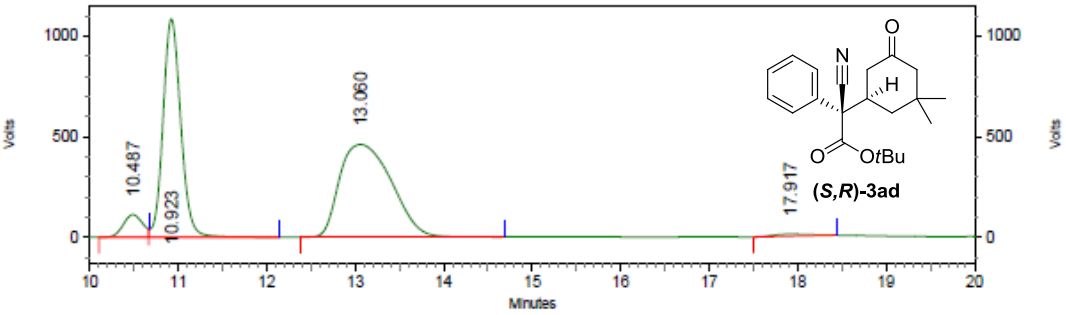
Area % Report : C:\EZChrom Elite\Enterprise\Projects\Simon Eitel\Data\10-MA097 B2



UV Results

Retention Time	Area	Area %
9.633	1259958	5.01
10.577	2388653	9.49
13.413	21332820	84.76
16.993	187743	0.75

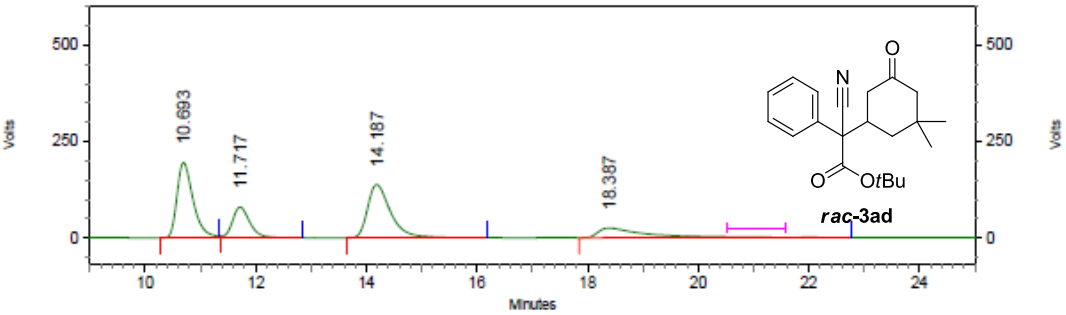
Area % Report : C:\EZChrom Elite\Enterprise\Projects\Simon Eitel\Data\10-MA090 Bb



UV Results

Retention Time	Area	Area %
10.487	6684733	4.67
10.923	60274531	42.11
13.060	75026155	52.42
17.917	1151214	0.80

Area % Report : C:\EZChrom Elite\Enterprise\Projects\Simon Eitel\Data\MA new\10-MA017rac-2

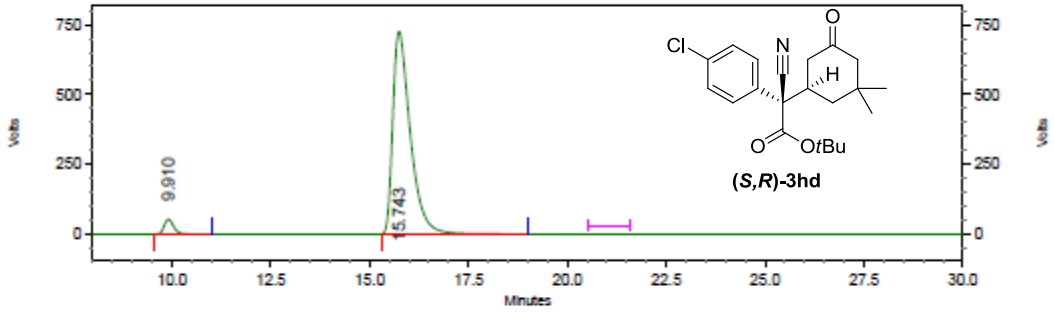


UV Results

Retention Time	Area	Area %
10.693	15859681	35.24
11.717	6895738	15.32
14.187	16031721	35.63
18.387	6211357	13.80

tert -Butyl-2-cyano-2-(4-chlorophenyl)-2-(3,3-dimethyl-5-oxocyclohexyl)acetate (**3hd**)

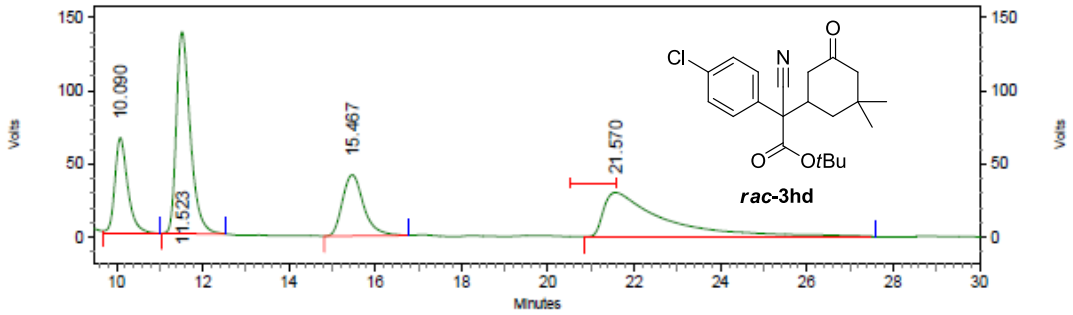
Area % Report : C:\EZChrom Elite\Enterprise\Projects\Simon Eitel\Data\10-MA121-HD_ODH_SE-99-1-210nm-60min-0.7flow.met.dat



UV Results

Retention Time	Area	Area %
9.910	3675498	3.95
15.743	89354722	96.05

Area % Report : C:\EZChrom Elite\Enterprise\Projects\Simon Eitel\Data\MA new\10-MA122rac A

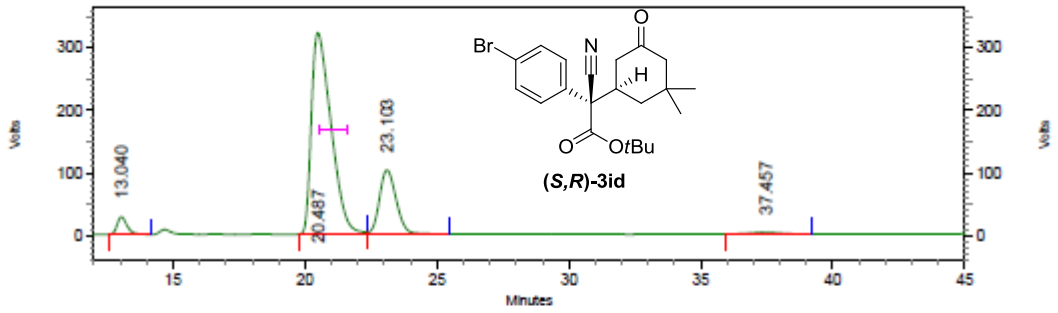


UV Results

Retention Time	Area	Area %
10.090	5466964	15.60
11.523	12351420	35.25
15.467	5707721	16.29
21.570	11514968	32.86

tert -Butyl-2-cyano-2-(4-bromophenyl)-2-(3,3-dimethyl-5-oxocyclohexyl)acetate (**3id**)

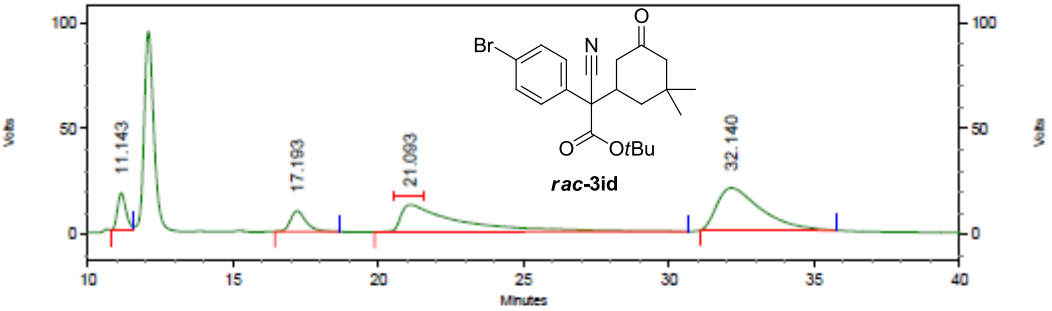
Area % Report : C:\EZChrom Elite\Enterprise\Projects\Simon Eitel\Data\10-MA169-5-10



UV Results

Retention Time	Area	Area %
13.040	2970154	3.36
20.487	66524529	75.30
23.103	18031655	20.41
37.457	815737	0.92

Area % Report : C:\EZChrom Elite\Enterprise\Projects\Simon Eitel\Data\racemic products\10-MA304rac_ODH_SE-99-1-210nm-60min-0.7flow.met.dat

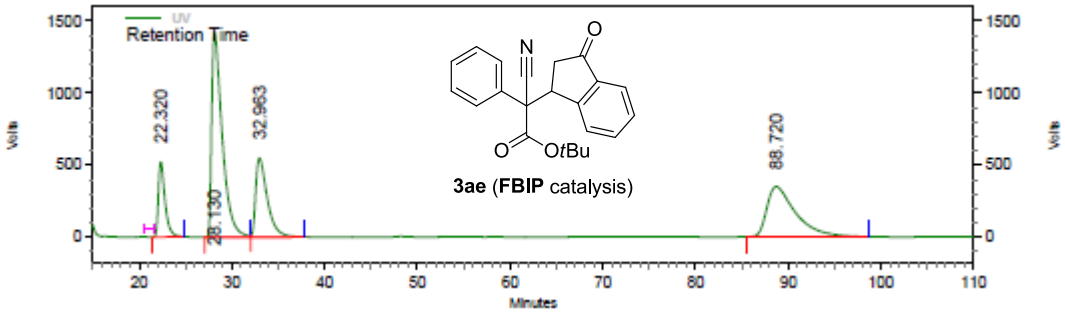


UV Results

Retention Time	Area	Area %
11.143	1440273	7.73
17.193	1456323	7.82
21.093	7277670	39.07
32.140	8451243	45.37

tert -Butyl-2-cyano-2-(3-oxo-2,3-dihydro-1*H*-inden-1-yl)-2-phenylacetate (**3ae**)

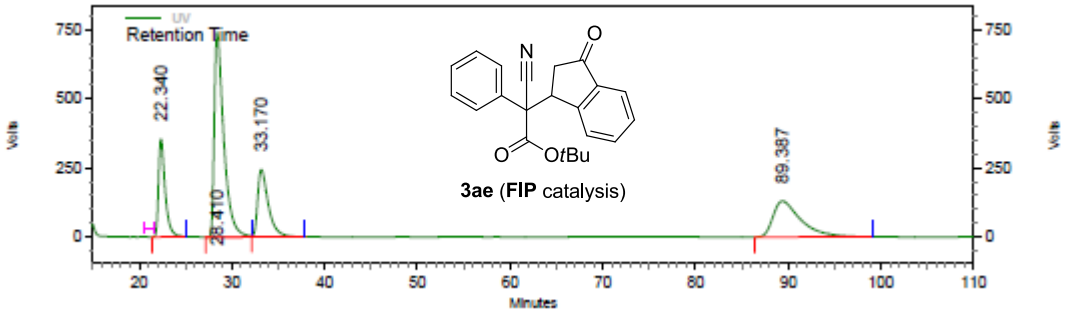
Data File: C:\EZChrom Elite\Enterprise\Projects\Simon Eitel\Data\MA new\10-MA392c



UV Results

Retention Time	Height	Area	Area %
22.320	2086262	103803905	9.95
28.130	5687697	449619745	43.08
32.963	2193092	190422925	18.24
88.720	1392940	299929136	28.74

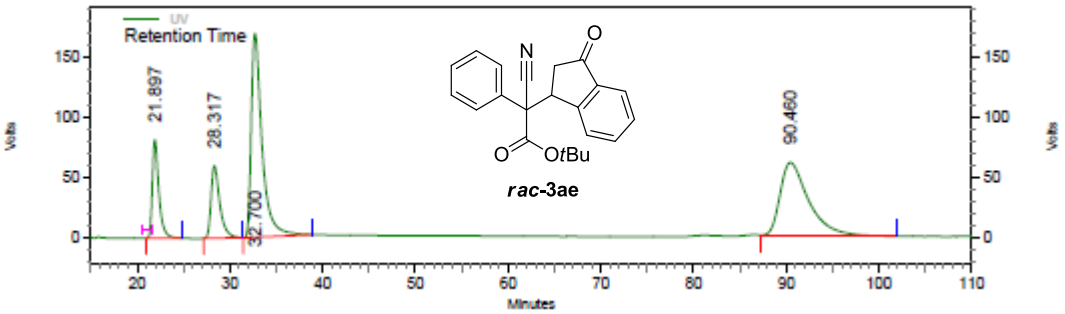
Data File: C:\EZChrom Elite\Enterprise\Projects\Simon Eitel\Data\MA new\10-MA393a



UV Results

Retention Time	Height	Area	Area %
22.340	1419474	70419618	15.03
28.410	2966712	211254865	45.09
33.170	974763	78077641	16.66
89.387	519599	108804666	23.22

Data File: C:\EZChrom Elite\Enterprise\Projects\Simon Eitel\Data\racemic products\10-MA374rac_ADH_SE-99-1-210nm-120min-1.5flow.met.dat

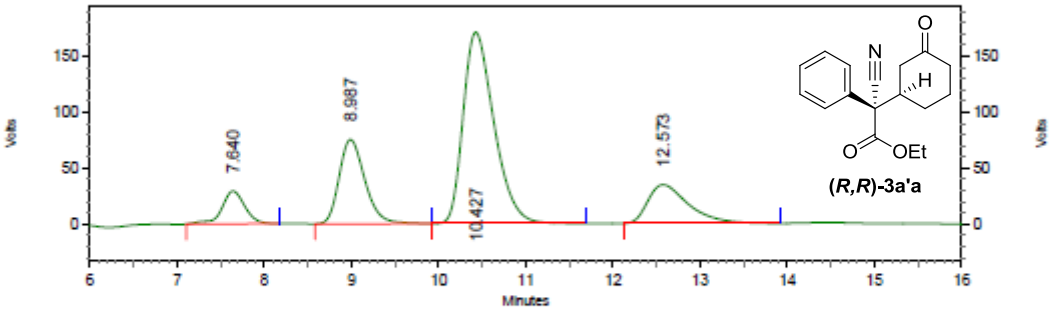


UV Results

Retention Time	Height	Area	Area %
21.897	327178	16034409	11.46
28.317	240888	15753964	11.26
32.700	677894	54813166	39.17
90.460	245289	53342303	38.12

Ethyl-2-cyano-2-(3-oxocyclohexyl)-2-phenylacetate (**3a'a**)

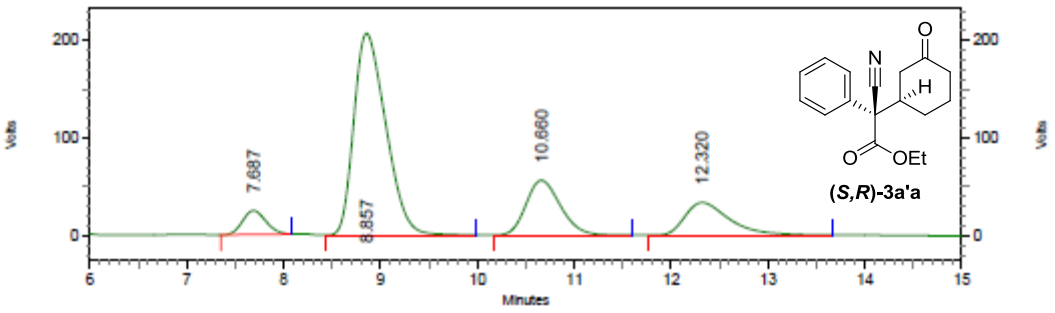
Area % Report : C:\EZChrom Elite\Enterprise\Projects\Simon Eitel\Data\Old data\SEM-057_OdH_sj-99-1-210nm-32min-2ml.met.dat



UV Results

Retention Time	Area	Area %
7.640	2146215	7.26
8.987	6166033	20.86
10.427	16798762	56.83
12.573	4449943	15.05

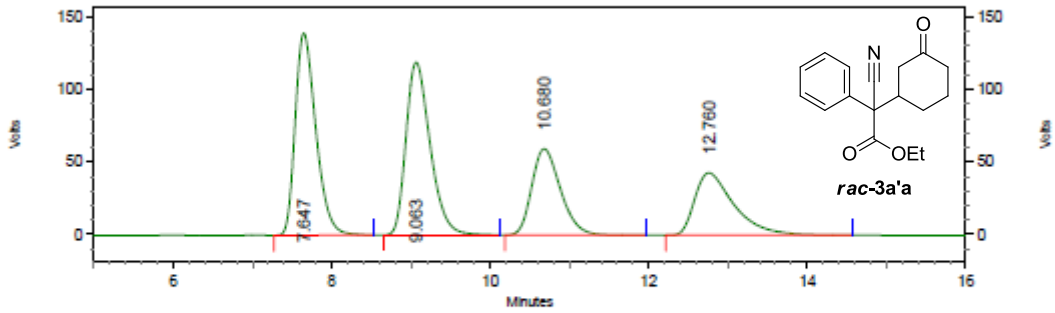
Area % Report : C:\EZChrom Elite\Enterprise\Projects\Simon Eitel\Data\10-MA089 Gb



UV Results

Retention Time	Area	Area %
7.687	1647990	5.42
8.857	18949213	62.32
10.660	5532241	18.20
12.320	4275531	14.06

Area % Report : C:\EZChrom Elite\Enterprise\Projects\Simon Eitel\Data\Old data\SEM-058 RAC_ODH_sj-99-1-210nm-35min-2ml.met.dat

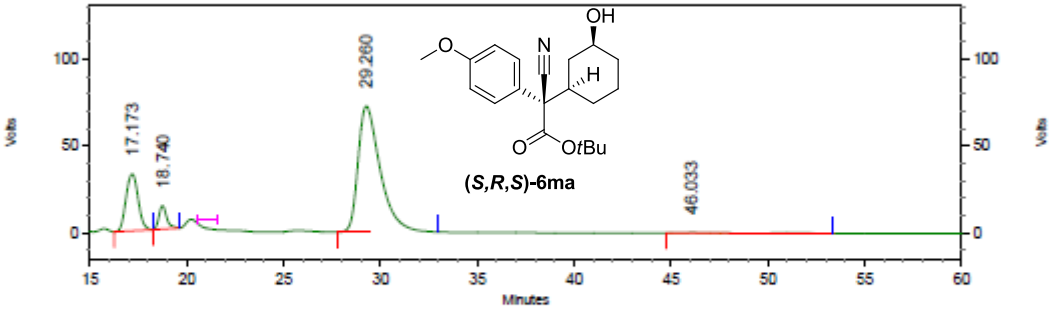


UV Results

Retention Time	Area	Area %
7.647	10112042	31.40
9.063	10115934	31.41
10.680	6011446	18.67
12.760	5966729	18.53

tert -Butyl-2-cyano-2-(3-hydroxycyclohexyl)-2-(4-methoxyphenyl)-acetate (**6ma**)

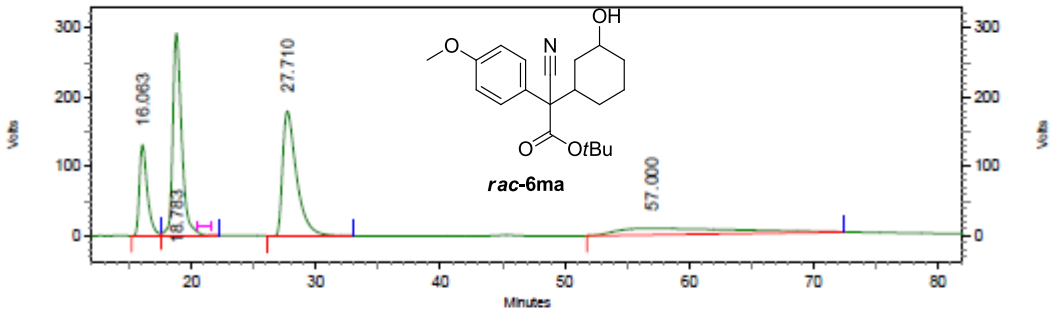
Area % Report : C:\EZChrom Elite\Enterprise\Projects\Simon Eitel\Data\10-MA131 A_ODH_SE-97-3-210nm-90min-1flow.met.dat



UV Results

Retention Time	Area	Area %
17.173	5689478	18.69
18.740	1507434	4.95
29.260	23016431	75.61
46.033	226685	0.74

Area % Report : C:\EZChrom Elite\Enterprise\Projects\Simon Eitel\Data\racemic products\10-MA068 rac-2_ODH_SE-97-3-210nm-90min-1flow.met.dat



UV Results

Retention Time	Area	Area %
16.063	23389625	14.37
18.783	58116902	35.70
27.710	56150704	34.49
57.000	25135385	15.44