## Supporting Information

# Catalytic Enantioselective Oxa-Hetero-Diels-Alder Reactions of Enones with Aryl Trifluoromethyl Ketones: Synthesis of Tetrahydropyranones 

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1. Synthesis of Amine Derivative A ..... S2
2. Oxa-Hetero-Diels-Alder Reactions (Table 2) ..... S2
3. Determination of the Absolute Configuration of 3a-1 (Scheme 2) ..... S8
4. References ..... S9
NMR Spectra ..... S10
HPLC Chromatograms ..... S67

## General

For thin layer chromatography (TLC), Merck silica gel 60 F254 aluminum sheets were used and the compounds were visualized by irradiation with UV light. Flash column chromatography was performed using Merck silica gel $60(230-400$ mesh $)$ or Yamazen flash column ( $60 \AA, 40 \mu \mathrm{~m}$ ). ${ }^{1} \mathrm{H}$ NMR and ${ }^{13} \mathrm{C}$ NMR spectra were recorded on a Bruker Avance 400 or a Bruker Avance 500. Proton chemical shifts are reported in ppm downfield from tetramethylsilane ( $\delta 0.00 \mathrm{ppm}$ ) or relative to the residual proton signal of the deuterated solvent in $\mathrm{CDCl}_{3}(\delta 7.26 \mathrm{ppm})$. Carbon chemical shifts were internally referenced to the deuterated solvent signals in $\mathrm{CDCl}_{3}$ ( $\delta 77.0$ ppm). High-resolution mass spectra were recorded on a Thermo Scientific LTQ Orbitrap ESI ion trap mass spectrometer. Optical rotations were measured on a Jasco P2200 polarimeter.

## 1. Synthesis of Amine Derivative A

Amine derivative $\mathbf{A}$ was synthesized by the reported procedure. ${ }^{1}$


A To a solution of $(1 S, 2 S)-(-)$-1,2-diphenylethylenediamine ( 1.27 g , 6.0 mmol ) and triethylamine ( $1.00 \mathrm{~mL}, 7.2 \mathrm{mmol}$ ) in dehydrated $\mathrm{CH}_{2} \mathrm{Cl}_{2}$ ( 15 mL ), (-)-10-camphorsulfonyl chloride ( $1.50 \mathrm{~g}, 6.0$ mmol ) was added at $0{ }^{\circ} \mathrm{C}$, and the mixture was stirred at same temperature for 2 h . To the mixture, saturated aqueous $\mathrm{NH}_{4} \mathrm{Cl}$ solution was added, and the mixture was extracted with $\mathrm{CH}_{2} \mathrm{Cl}_{2}$. Organic layers were combined, washed with brine, dried over $\mathrm{Na}_{2} \mathrm{SO}_{4}$, filtered, concentrated, and purified by flash column chromatography $\left(\mathrm{CHCl}_{3} / \mathrm{MeOH}=98: 2\right)$ to give $\mathbf{A}(2.40 \mathrm{~g}, 88 \%)$ as a colorless solid. ${ }^{1} \mathrm{H}$ and ${ }^{13} \mathrm{C}$ NMR data of the obtained $\mathbf{A}$ were consistent with those previously reported. ${ }^{1}$

## 2. Oxa-Hetero-Diels-Alder Reactions (Table 2)

General procedure for the synthesis of racemic standards of 3


Racemic standards of compounds $\mathbf{3}$ were synthesized by the reported procedure ${ }^{2}$ but with modified conditions.
To a solution of enone $\mathbf{1}(1.0 \mathrm{mmol})$ and aryl trifluoromethyl ketone $\mathbf{2}(3.0 \mathrm{mmol})$ in toluene (dehydrated, 2.0 mL ), pyrrolidine ( $16.5 \mu \mathrm{~L}, 0.20 \mathrm{mmol}$ ) and acetic acid ( $22.8 \mu \mathrm{~L}, 0.40 \mathrm{mmol}$ ) were added at room temperature $\left(25{ }^{\circ} \mathrm{C}\right)$, and the mixture was stirred at the same temperature until 1 was consumed (monitored by ${ }^{1} \mathrm{H}$ NMR analyses). For monitoring the reaction progress by ${ }^{1} \mathrm{H}$ NMR analyses, a portion $(50 \mu \mathrm{~L})$ of the reaction mixture was taken out and diluted with $\mathrm{CDCl}_{3}$, which was directly used for the NMR analyses. The mixture (remaining portion) was purified by flash column chromatography (hexane/EtOAc $=98: 2$ ) to give racemic product 3. For each of all cases of $\mathbf{3}$ synthesized by this method, compound 3-1 ( R and $\mathrm{CF}_{3}$, trans) ${ }^{1}$ was the major diastereomer and compound 3-2 $\left(\mathrm{R} \text { and } \mathrm{CF}_{3}, c i s\right)^{1}$ was the minor diastereomer.

General procedure for the catalytic enentioselective oxa-hetero-Diels-Alder reactions


To a solution of amine derivative $\mathbf{A}(85.6 \mathrm{mg}, 0.2 \mathrm{mmol})$ and N -Boc- O - $t$ Bu-L-threonine (B) (110 $\mathrm{mg}, 0.40 \mathrm{mmol}$ ) in toluene (dehydrated, 2.0 mL ), enone $\mathbf{1}(1.0 \mathrm{mmol})$ and aryl trifluoromethyl
ketone $2(3.0 \mathrm{mmol})$ were added at $5^{\circ} \mathrm{C}$, and the mixture was stirred at the same temperature for 9 days until 1 was completely or almost consumed (monitored by TLC and/or ${ }^{1} \mathrm{H}$ NMR analyses). Before purification, the diastereomer ratio (dr) was determined by ${ }^{1} \mathrm{H}$ NMR analysis. The mixture was purified by flash column chromatography (hexane/EtOAc $=98: 2$, this solvent system was used for the purification of each of all 3) to give 3-1 ( R and $\mathrm{CF}_{3}$, trans) ${ }^{1}$ and 3-2 ( R and $\mathrm{CF}_{3}$, cis $)^{1}$ separately. For each of all the cases of $\mathbf{3}$ synthesized by this method, compound 31 ( R and $\mathrm{CF}_{3}$, trans) ${ }^{1}$ was the major diastereomer and compound 3-2 $\left(\mathrm{R}\right.$ and $\mathrm{CF}_{3}$, cis) ${ }^{1}$ was the minor diastereomer. Formation of the aldol product was $<5 \%$ relative to the oxa-hetero-DielsAlder products (i.e., 3) for all reactions performed by this method. The enantiomer ratio (er) of 3-1 was determined by chiral-phase HPLC analysis after purification. The absolute configuration of 3a-1 obtained by this procedure was determined to be ( $R, R$ ); see Section 3 (page S 8 ).

Compound 3a-1 (minor diastereomer)


General procedure, dr 3a-1/3a-2 = 8:1 (before purification), $\mathbf{3 a - 1} 201 \mathrm{mg}$ (70\%, er 91:9), $\mathrm{R}_{\mathrm{f}} 0.39$ (hexane/EtOAc $=95: 5$ ), colorless oil. $[\alpha]^{24}{ }_{\mathrm{D}}-$ 40.7 (c 1.00, $\mathrm{CH}_{2} \mathrm{Cl}_{2}$, er $91: 9$ ). ${ }^{1} \mathrm{H}$ NMR ( $500 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ): $\delta 7.55(\mathrm{~d}, J$ $=6.7 \mathrm{~Hz}, 2 \mathrm{H}), 7.42-7.34(\mathrm{~m}, 3 \mathrm{H}), 4.45-4.37(\mathrm{~m}, 1 \mathrm{H}), 3.31(\mathrm{~d}, J=15.6$ $\mathrm{Hz}, 1 \mathrm{H}), 2.90(\mathrm{~d}, J=15.6 \mathrm{~Hz}, 1 \mathrm{H}), 2.47(\mathrm{~d}, J=16.5 \mathrm{~Hz}, 1 \mathrm{H}), 2.22(\mathrm{dd}, J$ $=16.5 \mathrm{~Hz}, 11.8 \mathrm{~Hz}, 1 \mathrm{H}), 1.85-1.76(\mathrm{~m}, 1 \mathrm{H}), 1.76-1.51(\mathrm{~m}, 3 \mathrm{H}), 1.01(\mathrm{t}, J$ $=7.0 \mathrm{~Hz}, 3 \mathrm{H}) .{ }^{13} \mathrm{C} \operatorname{NMR}\left(125 \mathrm{MHz}, \mathrm{CDCl}_{3}\right): \delta 203.4,137.7,129.0,128.3,126.2,125.1\left(\mathrm{q}, J_{\mathrm{C}, \mathrm{F}}=\right.$ $288 \mathrm{~Hz}), 78.7\left(\mathrm{q}, J_{\mathrm{C}, \mathrm{F}}=28 \mathrm{~Hz}\right), 73.0,45.7,43.9,38.4,18.4,13.7$. ESI-HRMS: $m / z$ calcd for $\mathrm{C}_{15} \mathrm{H}_{18} \mathrm{O}_{2} \mathrm{~F}_{3}\left([\mathrm{M}+\mathrm{H}]^{+}\right)$287.1253, found 287.1249. HPLC (Daicel Chiralpak AS-3, hexane/i$\operatorname{PrOH}=98: 2,0.5 \mathrm{~mL} / \mathrm{min}, \lambda=220 \mathrm{~nm}$ ): $t_{\mathrm{R}}$ (major diastereomer, major enantiomer) $=24.5 \mathrm{~min}, t_{\mathrm{R}}$ $($ major diastereomer, minor enantiomer $)=22.7 \mathrm{~min}$.

Compound 3a-2 (minor diastereomer)

$\mathrm{R}_{\mathrm{f}} 0.27$ (hexane/EtOAc $=95: 5$ ), colorless oil. ${ }^{1} \mathrm{H}$ NMR $(500 \mathrm{MHz}$, $\left.\mathrm{CDCl}_{3}\right): \delta 7.49(\mathrm{~d}, J=6.7 \mathrm{~Hz}, 2 \mathrm{H}), 7.44-7.37(\mathrm{~m}, 3 \mathrm{H}), 3.75-3.67(\mathrm{~m}, 1 \mathrm{H})$, 3.26 (d, $J=14.8 \mathrm{~Hz}, 1 \mathrm{H}), 3.01$ (d, $J=14.8 \mathrm{~Hz}, 1 \mathrm{H}), 2.37$ (dd, $J=14.8$ $\mathrm{Hz}, 11.5 \mathrm{~Hz}, 1 \mathrm{H}), 2.25(\mathrm{~d}, J=14.8 \mathrm{~Hz}, 1 \mathrm{H}), 1.85-1.74(\mathrm{~m}, 1 \mathrm{H}), 1.69-1.38$ $(\mathrm{m}, 3 \mathrm{H}), 0.94(\mathrm{t}, J=7.2 \mathrm{~Hz}, 3 \mathrm{H}) .{ }^{13} \mathrm{C}$ NMR ( $125 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ): $\delta 203.6$, $133.3,129.5,128.7,128.3,123.8\left(\mathrm{q}, J_{\mathrm{C}, \mathrm{F}}=282 \mathrm{~Hz}\right), 80.7\left(\mathrm{q}, J_{\mathrm{C}, \mathrm{F}}=29\right.$ $\mathrm{Hz}), 71.8,46.8,42.8,38.1,18.4,13.9$. ESI-HRMS: $m / z$ calcd for $\mathrm{C}_{15} \mathrm{H}_{18} \mathrm{O}_{2} \mathrm{~F}_{3}\left([\mathrm{M}+\mathrm{H}]^{+}\right)$287.1253, found 287.1248.

Compound 3b-1 (major diastereomer)


General procedure, dr $\mathbf{3 b - 1 / 3 b - 2}=7: 1$ (before purification), $\mathbf{3 b - 1}$ $220 \mathrm{mg}\left(69 \%\right.$, er 95:5), $\mathrm{R}_{\mathrm{f}} 0.23$ (hexane/EtOAc $=95: 5$ ), colorless oil. $[\alpha]^{24}{ }_{\mathrm{D}}-31.9$ (c 1.00, $\mathrm{CH}_{2} \mathrm{Cl}_{2}$, er 95:5). ${ }^{1} \mathrm{H}$ NMR ( $500 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ): $\delta 7.48$ (d, $J=8.6 \mathrm{~Hz}, 2 \mathrm{H}$ ), 7.36 (d, $J=8.6 \mathrm{~Hz}, 2 \mathrm{H}), 4.44-4.38$ (m, $1 \mathrm{H}), 3.28(\mathrm{~d}, J=15.5 \mathrm{~Hz}, 1 \mathrm{H}), 2.84(\mathrm{~d}, J=15.5 \mathrm{~Hz}, 1 \mathrm{H}), 2.48(\mathrm{dd}, J$ $=16.6 \mathrm{~Hz}, 2.5 \mathrm{~Hz}, 1 \mathrm{H}), 2.21(\mathrm{dd}, J=16.6 \mathrm{~Hz}, 11.7 \mathrm{~Hz}, 1 \mathrm{H}), 1.81-$
$1.73(\mathrm{~m}, 1 \mathrm{H}), 1.69-1.49(\mathrm{~m}, 3 \mathrm{H}), 1.0(\mathrm{t}, J=7.1 \mathrm{~Hz}, 3 \mathrm{H}) .{ }^{13} \mathrm{C}$ NMR ( $125 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ): $\delta 202.9$,
136.1, 135.2, 128.5, 127.7, $124.9\left(\mathrm{q}, J_{\mathrm{C}, \mathrm{F}}=288 \mathrm{~Hz}\right), 78.4\left(\mathrm{q}, J_{\mathrm{C}, \mathrm{F}}=29 \mathrm{~Hz}\right), 73.2,45.7,43.8,38.3$, 18.4, 13.7. ESI-HRMS: $m / z$ calcd for $\mathrm{C}_{15} \mathrm{H}_{17} \mathrm{O}_{2} \mathrm{ClF}_{3}\left([\mathrm{M}+\mathrm{H}]^{+}\right) 321.0864$, found 321.0858. HPLC (Daicel Chiralpak AS-3, hexane $/ i-\mathrm{PrOH}=98: 2,0.5 \mathrm{~mL} / \mathrm{min}, \lambda=220 \mathrm{~nm}$ ): $t_{\mathrm{R}}$ (major diastereomer, major enantiomer $)=23.5 \mathrm{~min}, t_{\mathrm{R}}($ major diastereomer, minor enantiomer $)=27.0$ min.

Compound 3b-2 (minor diastereomer)

$\mathrm{R}_{\mathrm{f}} 0.20$ (hexane/EtOAc $=95: 5$ ), colorless oil. ${ }^{1} \mathrm{H}$ NMR $(500 \mathrm{MHz}$, $\left.\mathrm{CDCl}_{3}\right): \delta 7.44-7.38(\mathrm{~m}, 4 \mathrm{H}), 3.70-3.65(\mathrm{~m}, 1 \mathrm{H}), 3.19(\mathrm{~d}, J=14.6 \mathrm{~Hz}$, $1 \mathrm{H}), 3.01(\mathrm{~d}, J=14.6 \mathrm{~Hz}, 1 \mathrm{H}), 2.38(\mathrm{dd}, J=14.8 \mathrm{~Hz}, 11.6 \mathrm{~Hz}, 1 \mathrm{H})$, 2.26 (ddd, $J=14.8 \mathrm{~Hz}, 2.6 \mathrm{~Hz}, 1.6 \mathrm{~Hz}, 1 \mathrm{H}$ ), $1.80-1.73(\mathrm{~m}, 1 \mathrm{H}), 1.64-$ $1.47(\mathrm{~m}, 2 \mathrm{H}), 1.45-1.33(\mathrm{~m}, 1 \mathrm{H}), 0.94(\mathrm{t}, J=7.3 \mathrm{~Hz}, 3 \mathrm{H}) .{ }^{13} \mathrm{C}$ NMR $\left(125 \mathrm{MHz}, \mathrm{CDCl}_{3}\right): \delta 203.1,135.9,131.9,129.7,129.1,123.6\left(\mathrm{q}, J_{\mathrm{C}, \mathrm{F}}\right.$ $=282 \mathrm{~Hz}), 80.5\left(\mathrm{q}, J_{\mathrm{C}, \mathrm{F}}=30 \mathrm{~Hz}\right), 72.1,46.7,42.7,38.1,18.4,13.9$. ESI-HRMS: $m / z$ calcd for $\mathrm{C}_{15} \mathrm{H}_{17} \mathrm{O}_{2} \mathrm{ClF}_{3}\left([\mathrm{M}+\mathrm{H}]^{+}\right) 321.0864$, found 321.0857 .

Compound 3c-1 (major diastereomer)


General procedure, dr $\mathbf{3 c - 1} \mathbf{3 c} \mathbf{c} \mathbf{2}=5: 1$ (before purification), $\mathbf{3 c - 1} 182$ $\mathrm{mg}\left(60 \%\right.$, er $93: 7$ ), $\mathrm{R}_{\mathrm{f}} 0.34$ (hexane/EtOAc $=95: 5$ ), colorless oil. $[\alpha]^{24}{ }_{\mathrm{D}}-34.3$ (c 1.00, $\mathrm{CH}_{2} \mathrm{Cl}_{2}$, er 93:7). ${ }^{1} \mathrm{H}$ NMR ( $500 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ): $\delta 7.37-7.23(\mathrm{~m}, 3 \mathrm{H}), 7.05(\mathrm{td}, J=7.9 \mathrm{~Hz}, 1.9 \mathrm{~Hz}, 1 \mathrm{H}), 4.43-4.37(\mathrm{~m}$, 1 H ), 3.26 (d, $J=15.6 \mathrm{~Hz}, 1 \mathrm{H}), 2.84$ (d, $J=15.6 \mathrm{~Hz}, 1 \mathrm{H}), 2.47$ (dd, $J$ $=16.6 \mathrm{~Hz}, 2.2 \mathrm{~Hz}, 1 \mathrm{H}), 2.20(\mathrm{dd}, J=16.6 \mathrm{~Hz}, 11.7 \mathrm{~Hz}, 1 \mathrm{H}), 1.81-$ $1.71(\mathrm{~m}, 1 \mathrm{H}), 1.67-1.44(\mathrm{~m}, 3 \mathrm{H}), 0.99(\mathrm{t}, J=7.0 \mathrm{~Hz}, 3 \mathrm{H}) .{ }^{13} \mathrm{C} \operatorname{NMR}\left(125 \mathrm{MHz}, \mathrm{CDCl}_{3}\right): \delta 202.9$, $162.6\left(\mathrm{~d}, J_{\mathrm{C}, \mathrm{F}}=245 \mathrm{~Hz}\right), 140.2\left(\mathrm{~d}, J_{\mathrm{C}, \mathrm{F}}=8 \mathrm{~Hz}\right), 129.9\left(\mathrm{~d}, J_{\mathrm{C}, \mathrm{F}}=9 \mathrm{~Hz}\right), 124.9\left(\mathrm{q}, J_{\mathrm{C}, \mathrm{F}}=288 \mathrm{~Hz}\right)$, $121.8,116.0\left(\mathrm{~d}, J_{\mathrm{C}, \mathrm{F}}=20 \mathrm{~Hz}\right), 114.0\left(\mathrm{~d}, J_{\mathrm{C}, \mathrm{F}}=24 \mathrm{~Hz}\right), 78.3\left(\mathrm{qd}, J_{\mathrm{C}, \mathrm{F}}=29 \mathrm{~Hz}, 2 \mathrm{~Hz}\right), 73.2,45.7$, 43.9, 38.3, 18.4, 13.7. ESI-HRMS: $m / z$ calcd for $\mathrm{C}_{15} \mathrm{H}_{17} \mathrm{O}_{2} \mathrm{~F}_{4}\left([\mathrm{M}+\mathrm{H}]^{+}\right) 305.1159$, found 305.1157. HPLC (Daicel Chiralpak AS-3, hexane $/ i-\mathrm{PrOH}=98: 2,0.5 \mathrm{~mL} / \mathrm{min}, \lambda=220 \mathrm{~nm}$ ): $t_{\mathrm{R}}$ $($ major diastereomer, major enantiomer $)=18.9 \mathrm{~min}, t_{\mathrm{R}}($ major diastereomer, minor enantiomer $)=$ 23.2 min .

Compound 3c-2 (minor diastereomer)

$\mathrm{R}_{\mathrm{f}} 0.31$ (hexane/EtOAc $=95: 5$ ), colorless oil. ${ }^{1} \mathrm{H}$ NMR $(500 \mathrm{MHz}$, $\left.\mathrm{CDCl}_{3}\right): \delta 7.39(\mathrm{dt}, J=8.0 \mathrm{~Hz}, 6.0 \mathrm{~Hz}, 1 \mathrm{H}), 7.27-7.21(\mathrm{~m}, 2 \mathrm{H}), 7.13-$ $7.08(\mathrm{~m}, 1 \mathrm{H}), 3.75-3.69(\mathrm{~m}, 1 \mathrm{H}), 3.18(\mathrm{~d}, J=14.7 \mathrm{~Hz}, 1 \mathrm{H}), 3.02(\mathrm{~d}, J$ $=14.7 \mathrm{~Hz}, 1 \mathrm{H}), 2.39(\mathrm{dd}, J=14.9 \mathrm{~Hz}, 11.6 \mathrm{~Hz}, 1 \mathrm{H}), 2.27$ (ddd, $J=$ $14.9 \mathrm{~Hz}, 2.7 \mathrm{~Hz}, 1.5 \mathrm{~Hz}, 1 \mathrm{H}), 1.84-1.74(\mathrm{~m}, 1 \mathrm{H}), 1.67-1.48$ (m, 2H), 1.48-1.38 (m, 1H) $0.94(\mathrm{t}, J=7.2 \mathrm{~Hz}, 3 \mathrm{H}) .{ }^{13} \mathrm{C}$ NMR ( 125 MHz , $\left.\mathrm{CDCl}_{3}\right): \delta 203.0,162.9\left(\mathrm{~d}, J_{\mathrm{C}, \mathrm{F}}=246 \mathrm{~Hz}\right), 136.1\left(\mathrm{~d}, J_{\mathrm{C}, \mathrm{F}}=6 \mathrm{~Hz}\right), 130.4\left(\mathrm{~d}, J_{\mathrm{C}, \mathrm{F}}=9 \mathrm{~Hz}\right), 124.0$, $123.6\left(\mathrm{q}, J_{\mathrm{C}, \mathrm{F}}=285 \mathrm{~Hz}\right), 116.7\left(\mathrm{~d}, J_{\mathrm{C}, \mathrm{F}}=21 \mathrm{~Hz}\right), 115.5\left(\mathrm{~d}, J_{\mathrm{C}, \mathrm{F}}=22 \mathrm{~Hz}\right), 80.4\left(\mathrm{q}, J_{\mathrm{C}, \mathrm{F}}=30 \mathrm{~Hz}\right)$, 72.1, 46.6, 43.9, 38.1, 18.3, 13.8. ESI-HRMS: $m / z$ calcd for $\mathrm{C}_{15} \mathrm{H}_{17} \mathrm{O}_{2} \mathrm{~F}_{4}\left([\mathrm{M}+\mathrm{H}]^{+}\right)$305.1159, found 305.1154.

Compound 3d-1 (major diastereomer)


General procedure, dr $\mathbf{3 d - 1} \mathbf{3 d - 2}=8: 1$ (before purification), 3d-1 $194.2 \mathrm{mg}(64 \%$, er $94: 6), \mathrm{R}_{\mathrm{f}} 0.33$ (hexane/EtOAc $=95: 5$ ), colorless oil. $[\alpha]^{24}{ }_{\mathrm{D}}-41.2$ (c 1.00, $\mathrm{CH}_{2} \mathrm{Cl}_{2}$, er 94:6). ${ }^{1} \mathrm{H} \operatorname{NMR}(500 \mathrm{MHz}$, $\mathrm{CDCl}_{3}$ ): $\delta 7.52$ (dd, $\left.J=8.7 \mathrm{~Hz}, 5.3 \mathrm{~Hz}, 2 \mathrm{H}\right), 7.09-7.05(\mathrm{~m}, 2 \mathrm{H}), 4.44-$ $4.37(\mathrm{~m}, 1 \mathrm{H}), 3.29(\mathrm{~d}, J=15.5 \mathrm{~Hz}, 1 \mathrm{H}), 2.86(\mathrm{~d}, J=15.5 \mathrm{~Hz}, 1 \mathrm{H})$, 2.48 (dd, $J=16.6 \mathrm{~Hz}, 2.6 \mathrm{~Hz}, 1 \mathrm{H}), 2.21(\mathrm{dd}, J=16.6 \mathrm{~Hz}, 11.7 \mathrm{~Hz}$, $1 \mathrm{H}), 1.81-1.74(\mathrm{~m}, 1 \mathrm{H}), 1.67-1.48(\mathrm{~m}, 3 \mathrm{H}), 1.01(\mathrm{t}, J=7.1 \mathrm{~Hz}, 3 \mathrm{H}) .{ }^{13} \mathrm{C}$ NMR ( 125 MHz , $\left.\mathrm{CDCl}_{3}\right): \delta 203.1,163.0\left(\mathrm{~d}, J_{\mathrm{C}, \mathrm{F}}=248 \mathrm{~Hz}\right), 133.5\left(\mathrm{~d}, J_{\mathrm{C}, \mathrm{F}}=2 \mathrm{~Hz}\right), 128.3\left(\mathrm{~d}, J_{\mathrm{C}, \mathrm{F}}=8 \mathrm{~Hz}\right), 125.0(\mathrm{q}$, $\left.J_{\mathrm{C}, \mathrm{F}}=287 \mathrm{~Hz}\right), 115.3\left(\mathrm{~d}, J_{\mathrm{C}, \mathrm{F}}=21 \mathrm{~Hz}\right), 78.4\left(\mathrm{q}, J_{\mathrm{C}, \mathrm{F}}=28 \mathrm{~Hz}\right), 73.2,45.7,43.9,38.4,18.4,13.7$. ESI-HRMS: $m / z$ calcd for $\mathrm{C}_{15} \mathrm{H}_{17} \mathrm{O}_{2} \mathrm{~F}_{4}\left([\mathrm{M}+\mathrm{H}]^{+}\right) 305.1159$, found 305.1153. HPLC (Daicel Chiralpak AS-3, hexane $/ i-\mathrm{PrOH}=98: 2,0.5 \mathrm{~mL} / \mathrm{min}, \lambda=220 \mathrm{~nm}$ ): $t_{\mathrm{R}}$ (major diastereomer, major enantiomer) $=26.0 \mathrm{~min}, t_{\mathrm{R}}($ major diastereomer, minor enantiomer $)=30.9 \mathrm{~min}$.

Compound 3d-2 (minor diastereomer)

$\mathrm{R}_{\mathrm{f}} 0.31$ (hexane/EtOAc $=95: 5$ ), colorless oil. ${ }^{1} \mathrm{H}$ NMR $(500 \mathrm{MHz}$, $\mathrm{CDCl}_{3}$ ): $\delta 7.47(\mathrm{dd}, J=8.6 \mathrm{~Hz}, 5.2 \mathrm{~Hz}, 2 \mathrm{H}), 7.13-7.08(\mathrm{~m}, 2 \mathrm{H}), 3.71-$ $3.65(\mathrm{~m}, 1 \mathrm{H}), 3.20(\mathrm{~d}, J=15.0 \mathrm{~Hz}, 1 \mathrm{H}), 3.01(\mathrm{dd}, J=15.0 \mathrm{~Hz}, 0.5 \mathrm{~Hz}$, 1H), 2.38 (dd, $J=14.8 \mathrm{~Hz}, 11.7 \mathrm{~Hz}, 1 \mathrm{H}$ ), 2.26 (ddd, $J=14.8 \mathrm{~Hz}, 2.7$ $\mathrm{Hz}, 1.7 \mathrm{~Hz}, 1 \mathrm{H}), 1.83-1.73(\mathrm{~m}, 1 \mathrm{H}), 1.65-1.46(\mathrm{~m}, 2 \mathrm{H}), 1.46-1.35(\mathrm{~m}$, $1 \mathrm{H}), 0.93(\mathrm{t}, J=7.3 \mathrm{~Hz}, 3 \mathrm{H}) .{ }^{13} \mathrm{C}$ NMR ( $125 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ): $\delta 203.3$, $163.3\left(\mathrm{~d}, J_{\mathrm{C}, \mathrm{F}}=248 \mathrm{~Hz}\right), 130.4\left(\mathrm{~d}, J_{\mathrm{C}, \mathrm{F}}=9 \mathrm{~Hz}\right), 129.1\left(\mathrm{~d}, J_{\mathrm{C}, \mathrm{F}}=4 \mathrm{~Hz}\right), 123.7\left(\mathrm{q}, J_{\mathrm{C}, \mathrm{F}}=282 \mathrm{~Hz}\right)$, $115.9\left(\mathrm{~d}, J_{\mathrm{C}, \mathrm{F}}=21 \mathrm{~Hz}\right), 80.4\left(\mathrm{q}, J_{\mathrm{C}, \mathrm{F}}=30 \mathrm{~Hz}\right), 72.0,46.8,42.8,38.1,18.4,13.8$. ESI-HRMS: $m / z$ calcd for $\mathrm{C}_{15} \mathrm{H}_{17} \mathrm{O}_{2} \mathrm{~F}_{4}\left([\mathrm{M}+\mathrm{H}]^{+}\right) 305.1159$, found 305.1155 .

Compound 3e-1 (major diastereomer)


General procedure, dr 3e-1/3e-2 = 7:1 (before purification), 3e-1 158 $\mathrm{mg}(72 \%$, er $96: 4), \mathrm{R}_{\mathrm{f}} 0.36$ (hexane/EtOAc $=95: 5$ ), colorless oil. $[\alpha]^{24}{ }_{\mathrm{D}}-20.2$ (c $0.50, \mathrm{CH}_{2} \mathrm{Cl}_{2}$, er 96:4). ${ }^{1} \mathrm{H}$ NMR ( $500 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ): $\delta 7.52(\mathrm{~d}, J=8.3 \mathrm{~Hz}, 2 \mathrm{H}), 7.41(\mathrm{~d}, J=8.3 \mathrm{~Hz}, 2 \mathrm{H}), 4.44-4.38(\mathrm{~m}$, $1 \mathrm{H}), 3.28(\mathrm{~d}, J=15.5 \mathrm{~Hz}, 1 \mathrm{H}), 2.84(\mathrm{~d}, J=15.5 \mathrm{~Hz}, 1 \mathrm{H}), 2.48(\mathrm{~d}, J$ $=16.5 \mathrm{~Hz}, 1 \mathrm{H}), 2.20(\mathrm{dd}, J=16.5 \mathrm{~Hz}, 11.8 \mathrm{~Hz}, 1 \mathrm{H}), 1.81-1.73(\mathrm{~m}$, $1 \mathrm{H}), 1.60-1.47(\mathrm{~m}, 3 \mathrm{H}), 1.00(\mathrm{t}, J=7.0 \mathrm{~Hz}, 3 \mathrm{H}) .{ }^{13} \mathrm{C}$ NMR ( $125 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ): $\delta 202.8,136.7$, $131.5,128.0,124.8\left(\mathrm{q}, J_{\mathrm{C}, \mathrm{F}}=287 \mathrm{~Hz}\right), 123.5,78.5\left(\mathrm{q}, J_{\mathrm{C}, \mathrm{F}}=29 \mathrm{~Hz}\right), 73.2,45.7,43.7,38.3,18.4$, 13.7. ESI-HRMS: $m / z$ calcd for $\mathrm{C}_{15} \mathrm{H}_{17} \mathrm{O}_{2} \mathrm{BrF}_{3}\left([\mathrm{M}+\mathrm{H}]^{+}\right) 365.0359$, found 365.0349. HPLC (Daicel Chiralpak AS-3, hexane $/ i-\mathrm{PrOH}=98: 2,0.5 \mathrm{~mL} / \mathrm{min}, \lambda=220 \mathrm{~nm}$ ): $t_{\mathrm{R}}$ (major diastereomer, major enantiomer $)=24.5 \mathrm{~min}, t_{\mathrm{R}}($ major diastereomer, minor enantiomer $)=30.5 \mathrm{~min}$.

Compound 3e-2 (minor diastereomer)

$\mathrm{R}_{\mathrm{f}} 0.34$ (hexane/EtOAc $=95: 5$ ), colorless oil. ${ }^{1} \mathrm{H}$ NMR ( 500 MHz , $\left.\mathrm{CDCl}_{3}\right): \delta 7.55(\mathrm{~d}, J=8.3 \mathrm{~Hz}, 2 \mathrm{H}), 7.35(\mathrm{~d}, J=8.3 \mathrm{~Hz}, 2 \mathrm{H}), 3.71-$ $3.64(\mathrm{~m}, 1 \mathrm{H}), 3.18(\mathrm{~d}, J=14.6 \mathrm{~Hz}, 1 \mathrm{H}), 3.00(\mathrm{~d}, J=14.6 \mathrm{~Hz}, 1 \mathrm{H})$, $2.38(\mathrm{dd}, J=14.8 \mathrm{~Hz}, 11.6 \mathrm{~Hz}, 1 \mathrm{H}), 2.26(\mathrm{~d}, J=14.8 \mathrm{~Hz}, 1 \mathrm{H}), 1.80-$
$1.70(\mathrm{~m}, 1 \mathrm{H}), 1.60-1.46(\mathrm{~m}, 2 \mathrm{H}), 1.46-1.33(\mathrm{~m}, 1 \mathrm{H}), 0.93(\mathrm{t}, J=7.2 \mathrm{~Hz}, 3 \mathrm{H}) .{ }^{13} \mathrm{C}$ NMR (125 $\mathrm{MHz}, \mathrm{CDCl}_{3}$ ): $\delta 203.1,132.4,132.0,130.0,124.2,123.5\left(\mathrm{q}, J_{\mathrm{C}, \mathrm{F}}=282 \mathrm{~Hz}\right), 80.5\left(\mathrm{q}, J_{\mathrm{C}, \mathrm{F}}=30 \mathrm{~Hz}\right)$, 72.1, 46.7, 42.6, 38.1, 18.4, 13.9. ESI-HRMS: $m / z$ calcd for $\mathrm{C}_{15} \mathrm{H}_{17} \mathrm{O}_{2} \mathrm{BrF}_{3}\left([\mathrm{M}+\mathrm{H}]^{+}\right) 365.0359$, found 365.0348 .

Compound 3f-1 (major diastereomer)


General procedure, dr $\mathbf{3 f - 1 / 3 f - 2}=4: 1$ (before purification), $\mathbf{3 f - 1}$ $157.8 \mathrm{mg}(53 \%$, er $90: 10), \mathrm{R}_{\mathrm{f}} 0.37$ (hexane $/ \mathrm{EtOAc}=95: 5$ ), colorless oil. $[\alpha]^{24}{ }_{\mathrm{D}}-11.7$ (c $0.20, \mathrm{CH}_{2} \mathrm{Cl}_{2}$, er 90:10). ${ }^{1} \mathrm{H}$ NMR ( $500 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ): $\delta 7.43(\mathrm{~d}, J=7.8 \mathrm{~Hz}, 2 \mathrm{H}), 7.20(\mathrm{~d}, J=7.8 \mathrm{~Hz}$, $2 \mathrm{H}), 4.43-4.37(\mathrm{~m}, 1 \mathrm{H}), 3.28(\mathrm{~d}, J=15.6 \mathrm{~Hz}, 1 \mathrm{H}), 2.89(\mathrm{~d}, J=15.6$ $\mathrm{Hz}, 1 \mathrm{H}), 2.46(\mathrm{~d}, J=16.4 \mathrm{~Hz}, 1 \mathrm{H}), 2.35(\mathrm{~s}, 3 \mathrm{H}), 2.21(\mathrm{dd}, J=16.4$ $\mathrm{Hz}, 11.8 \mathrm{~Hz}, 1 \mathrm{H}), 1.83-1.75(\mathrm{~m}, 1 \mathrm{H}), 1.70-1.50(\mathrm{~m}, 3 \mathrm{H}), 1.01(\mathrm{t}, J=7.0 \mathrm{~Hz}, 3 \mathrm{H}) .{ }^{13} \mathrm{C}$ NMR ( 125 $\mathrm{MHz}, \mathrm{CDCl}_{3}$ ): $\delta 203.6,138.9,134.8,129.0,126.3,126.1,125.1\left(\mathrm{q}, J_{\mathrm{C}, \mathrm{F}}=287 \mathrm{~Hz}\right), 124.0,78.6(\mathrm{q}$, $J_{\mathrm{C}, \mathrm{F}}=33.7 \mathrm{~Hz}$ ), $73.0,45.7,43.9,38.4,21.0,18.4,13.8$. ESI-HRMS: $m / z$ calcd for $\mathrm{C}_{16} \mathrm{H}_{20} \mathrm{O}_{2} \mathrm{~F}_{3}$ $\left([\mathrm{M}+\mathrm{H}]^{+}\right)$301.1410, found 301.1408. HPLC (Daicel Chiralpak IB, hexane $/ i-\mathrm{PrOH}=98: 2,0.5$ $\mathrm{mL} / \mathrm{min}, \lambda=220 \mathrm{~nm}$ ): $t_{\mathrm{R}}$ (major diastereomer, major enantiomer) $=11.6 \mathrm{~min}, t_{\mathrm{R}}$ (major diastereomer, minor enantiomer) $=13.3 \mathrm{~min}$.

Compound 3f-2 (minor diastereomer)

$\mathrm{R}_{\mathrm{f}} 0.35$ (hexane/EtOAc $=95: 5$ ), colorless oil. ${ }^{1} \mathrm{H}$ NMR ( 500 MHz , $\left.\mathrm{CDCl}_{3}\right): \delta 7.36(\mathrm{~d}, J=7.8 \mathrm{~Hz}, 2 \mathrm{H}), 7.22(\mathrm{~d}, J=7.8 \mathrm{~Hz}, 2 \mathrm{H}), 3.73-$ $3.67(\mathrm{~m}, 1 \mathrm{H}), 3.24(\mathrm{~d}, J=14.6 \mathrm{~Hz}, 1 \mathrm{H}), 2.97(\mathrm{~d}, J=14.6 \mathrm{~Hz}, 1 \mathrm{H})$, 2.39-2.32 (m, 4H), $2.23(\mathrm{~d}, J=14.6 \mathrm{~Hz}, 1 \mathrm{H}), 1.81-1.72(\mathrm{~m}, 1 \mathrm{H})$, $1.65-1.55(\mathrm{~m}, 1 \mathrm{H}), 1.53-1.35(\mathrm{~m}, 2 \mathrm{H}), 0.93(\mathrm{t}, J=7.2 \mathrm{~Hz}, 3 \mathrm{H}) .{ }^{13} \mathrm{C}$ NMR ( $125 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ): $\delta 203.7,139.6,130.2,129.5,128.3$, $123.9\left(\mathrm{q}, J_{\mathrm{C}, \mathrm{F}}=282 \mathrm{~Hz}\right), 80.7\left(\mathrm{q}, J_{\mathrm{C}, \mathrm{F}}=29 \mathrm{~Hz}\right), 71.7,46.9,42.8,38.2,21.0,18.4$, 13.9. ESIHRMS: $m / z$ calcd for $\mathrm{C}_{16} \mathrm{H}_{20} \mathrm{O}_{2} \mathrm{~F}_{3}\left([\mathrm{M}+\mathrm{H}]^{+}\right) 301.1410$, found 301.1406.

Compound 3g-1 (major diastereomer)


General procedure, dr $\mathbf{3 g - 1} / \mathbf{3 g}-\mathbf{2}=6: 1$ (before purification), $\mathbf{3 g} \mathbf{- 1}$ $196 \mathrm{mg}\left(56 \%\right.$, er 95:5), $\mathrm{R}_{\mathrm{f}} 0.35$ (hexane/EtOAc $=95: 5$ ), colorless oil. $[\alpha]^{24}{ }_{\mathrm{D}}-36.3$ (c 1.00, $\mathrm{CH}_{2} \mathrm{Cl}_{2}$, er $95: 5$ ). ${ }^{1} \mathrm{H}$ NMR ( 500 MHz , $\left.\mathrm{CDCl}_{3}\right): \delta 7.69(\mathrm{~d}, J=9.0 \mathrm{~Hz}, 2 \mathrm{H}), 7.66(\mathrm{~d}, J=9.0 \mathrm{~Hz}, 2 \mathrm{H}), 4.48-$ $4.40(\mathrm{~m}, 1 \mathrm{H}), 3.33(\mathrm{~d}, J=15.5 \mathrm{~Hz}, 1 \mathrm{H}), 2.87(\mathrm{~d}, J=15.5 \mathrm{~Hz}, 1 \mathrm{H})$, $2.51(\mathrm{dd}, J=16.6 \mathrm{~Hz}, 2.5 \mathrm{~Hz}, 1 \mathrm{H}), 2.22(\mathrm{dd}, J=16.6 \mathrm{~Hz}, 11.7 \mathrm{~Hz}$, $1 \mathrm{H})$, 1.84-1.76 (m, 1H), 1.68-1.47 (m, 3H), $1.02(\mathrm{t}, J=7.1 \mathrm{~Hz}, 3 \mathrm{H}) .{ }^{13} \mathrm{C}$ NMR ( 125 MHz , $\left.\mathrm{CDCl}_{3}\right): \delta 202.6,141.5,131.3\left(\mathrm{q}, J_{\mathrm{C}, \mathrm{F}}=32 \mathrm{~Hz}\right), 126.9,125.3\left(\mathrm{q}, J_{\mathrm{C}, \mathrm{F}}=4 \mathrm{~Hz}\right), 124.8\left(\mathrm{q}, J_{\mathrm{C}, \mathrm{F}}=287\right.$ $\mathrm{Hz}), 123.8\left(\mathrm{q}, J_{\mathrm{C}, \mathrm{F}}=271 \mathrm{~Hz}\right), 78.6\left(\mathrm{q}, J_{\mathrm{C}, \mathrm{F}}=29 \mathrm{~Hz}\right), 73.4,45.7,43.8,38.4,18.4,13.7$. ESIHRMS: $m / z$ calcd for $\mathrm{C}_{16} \mathrm{H}_{17} \mathrm{O}_{2} \mathrm{~F}_{6}\left([\mathrm{M}+\mathrm{H}]^{+}\right)$355.1127, found 355.1119. HPLC (Daicel Chiralpak IB , hexane $/ i-\mathrm{PrOH}=98: 2,0.5 \mathrm{~mL} / \mathrm{min}, \lambda=220 \mathrm{~nm}$ ): $t_{\mathrm{R}}$ (major diastereomer, major enantiomer) $=14.5 \mathrm{~min}, t_{\mathrm{R}}$ (major diastereomer, minor enantiomer) $=18.9 \mathrm{~min}$.

Compound 3g-2 (minor diastereomer)

$\mathrm{R}_{\mathrm{f}} 0.31$ (hexane/EtOAc $=95: 5$ ), colorless oil. ${ }^{1} \mathrm{H}$ NMR ( 500 MHz , $\mathrm{CDCl}_{3}$ ): $\delta 7.69(\mathrm{~d}, J=8.4 \mathrm{~Hz}, 2 \mathrm{H}), 7.63(\mathrm{~d}, J=8.4 \mathrm{~Hz}, 2 \mathrm{H}), 3.71-$ $3.65(\mathrm{~m}, 1 \mathrm{H}), 3.23(\mathrm{~d}, J=14.7 \mathrm{~Hz}, 1 \mathrm{H}), 3.07(\mathrm{~d}, J=14.7 \mathrm{~Hz}, 1 \mathrm{H})$, 2.42 (dd, $J=14.9 \mathrm{~Hz}, 11.6 \mathrm{~Hz}, 1 \mathrm{H}), 2.28$ (ddd, $J=14.9 \mathrm{~Hz}, 2.6 \mathrm{~Hz}$, $1.5 \mathrm{~Hz}, 1 \mathrm{H}), 1.84-1.75(\mathrm{~m}, 1 \mathrm{H}), 1.66-1.49(\mathrm{~m}, 2 \mathrm{H}), 1.49-1.36(\mathrm{~m}$, $1 \mathrm{H}), 0.95(\mathrm{t}, J=7.2 \mathrm{~Hz}, 3 \mathrm{H}) .{ }^{13} \mathrm{C}$ NMR ( $125 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ): $\delta 202.8$, $137.6,131.8\left(\mathrm{q}, J_{\mathrm{C}, \mathrm{F}}=32 \mathrm{~Hz}\right), 128.8,125.8\left(\mathrm{q}, J_{\mathrm{C}, \mathrm{F}}=4 \mathrm{~Hz}\right), 123.6\left(\mathrm{q}, J_{\mathrm{C}, \mathrm{F}}=270 \mathrm{~Hz}\right), 123.5(\mathrm{q}$, $\left.J_{\mathrm{C}, \mathrm{F}}=281 \mathrm{~Hz}\right) 80.6\left(\mathrm{q}, J_{\mathrm{C}, \mathrm{F}}=30 \mathrm{~Hz}\right), 72.4,46.7,42.7,38.1,18.4,13.9$. ESI-HRMS: $m / z$ calcd for $\mathrm{C}_{16} \mathrm{H}_{17} \mathrm{O}_{2} \mathrm{~F}_{6}\left([\mathrm{M}+\mathrm{H}]^{+}\right)$355.1127, found 355.1118.

Compound 3h-1 (major diastereomer)


General procedure, dr $\mathbf{3 h - 1 / 3 h - 2}=5: 1$ (before purification), $\mathbf{3 h} \mathbf{h} \mathbf{1}$ $206.9 \mathrm{mg}\left(63 \%\right.$, er 89:11), $\mathrm{R}_{\mathrm{f}} 0.34$ (hexane/EtOAc $=95: 5$ ), colorless oil. $[\alpha]^{24}{ }_{\mathrm{D}}-10.6$ (c $0.40, \mathrm{CH}_{2} \mathrm{Cl}_{2}$, er $89: 11$ ). ${ }^{1} \mathrm{H}$ NMR ( 500 MHz , $\left.\mathrm{CDCl}_{3}\right): \delta 7.54(\mathrm{~d}, J=6.4 \mathrm{~Hz}, 2 \mathrm{H}), 7.42-7.36(\mathrm{~m}, 3 \mathrm{H}), 4.43-4.36(\mathrm{~m}$, $1 \mathrm{H}), 3.30(\mathrm{~d}, J=15.6 \mathrm{~Hz}, 1 \mathrm{H}), 2.90(\mathrm{~d}, J=15.6 \mathrm{~Hz}, 1 \mathrm{H}), 2.48(\mathrm{~d}, J=$ $15.0 \mathrm{~Hz}, 1 \mathrm{H}), 2.21(\mathrm{dd}, J=15.0 \mathrm{~Hz}, 11.8 \mathrm{~Hz}, 1 \mathrm{H}), 1.85-1.75(\mathrm{~m}, 1 \mathrm{H})$, $1.70-1.20(\mathrm{~m}, 9 \mathrm{H}), 0.91(\mathrm{t}, J=6.4 \mathrm{~Hz}, 3 \mathrm{H}) .{ }^{13} \mathrm{C}$ NMR ( 125 MHz , $\left.\mathrm{CDCl}_{3}\right): \delta 203.5,137.7,129.0,128.3,126.3,125.1\left(\mathrm{q}, J_{\mathrm{C}, \mathrm{F}}=286 \mathrm{~Hz}\right)$, $78.7\left(\mathrm{q}, J_{\mathrm{C}, \mathrm{F}}=29 \mathrm{~Hz}\right), 73.4,45.8,44.0,36.4,31.7,29.0,25.1,22.5,14.0$. ESI-HRMS: $\mathrm{m} / \mathrm{z}$ calcd for $\mathrm{C}_{18} \mathrm{H}_{24} \mathrm{O}_{2} \mathrm{~F}_{3}\left([\mathrm{M}+\mathrm{H}]^{+}\right)$329.1723, found 329.1720. HPLC (Daicel Chiralpak IB, hexane/i$\operatorname{PrOH}=98: 2,0.5 \mathrm{~mL} / \mathrm{min}, \lambda=220 \mathrm{~nm}): t_{\mathrm{R}}\left(\right.$ major diastereomer, major enantiomer) $=12.2 \mathrm{~min}, t_{\mathrm{R}}$ $($ major diastereomer, minor enantiomer $)=14.1 \mathrm{~min}$.

Compound 3h-2 (minor diastereomer)

$\mathrm{R}_{\mathrm{f}} 0.31$ (hexane/EtOAc $=95: 5$ ), colorless oil. ${ }^{1} \mathrm{H}$ NMR ( 500 MHz , $\mathrm{CDCl}_{3}$ ): $\delta 7.49(\mathrm{~d}, J=6.4 \mathrm{~Hz}, 2 \mathrm{H}), 7.45-7.37(\mathrm{~m}, 3 \mathrm{H}), 3.74-3.67(\mathrm{~m}$, $1 \mathrm{H}), 3.25(\mathrm{~d}, J=14.6 \mathrm{~Hz}, 1 \mathrm{H}), 3.01(\mathrm{~d}, J=14.6 \mathrm{~Hz}, 1 \mathrm{H}), 2.37(\mathrm{dd}, J=$ $14.6 \mathrm{~Hz}, 11.3 \mathrm{~Hz}, 1 \mathrm{H}), 2.25(\mathrm{~d}, J=14.6 \mathrm{~Hz}, 1 \mathrm{H}), 1.82-1.74(\mathrm{~m}, 1 \mathrm{H})$, 1.63-1.49 (m, 2H), 1.35-1.25 (m, 7H), $0.90(\mathrm{t}, J=6.3 \mathrm{~Hz}, 3 \mathrm{H}) .{ }^{13} \mathrm{C}$ NMR ( $125 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ): $\delta 203.6,133.3,129.5,128.7,128.3,123.8(\mathrm{q}$, $\left.J_{\mathrm{C}, \mathrm{F}}=282 \mathrm{~Hz}\right), 80.7\left(\mathrm{q}, J_{\mathrm{C}, \mathrm{F}}=29 \mathrm{~Hz}\right) 72.0,46.8,42.8,36.0,31.6,29.1$, 25.0, 22.6, 14.0. ESI-HRMS: $m / z$ calcd for $\mathrm{C}_{18} \mathrm{H}_{24} \mathrm{O}_{2} \mathrm{~F}_{3}\left([\mathrm{M}+\mathrm{H}]^{+}\right)$ 329.1723, found 329.1717.

Compound 3i-1 (major diastereomer)


General procedure, dr $\mathbf{3 i - 1} / \mathbf{3 i} \mathbf{- 2}=3: 1$ (before purification), $\mathbf{3 i} \mathbf{i} \mathbf{1}$ $220 \mathrm{mg}\left(56 \%\right.$, er 80:20), $\mathrm{R}_{\mathrm{f}} 0.36$ (hexane/EtOAc $=95: 5$ ), colorless oil. $[\alpha]^{24}{ }_{\mathrm{D}}-12.8\left(\mathrm{c} 0.50, \mathrm{CH}_{2} \mathrm{Cl}_{2}\right.$, er 80:20). ${ }^{1} \mathrm{H}$ NMR ( 500 MHz , $\left.\mathrm{CDCl}_{3}\right): \delta 7.61-7.55(\mathrm{~m}, 4 \mathrm{H}), 7.45-7.40(\mathrm{~m}, 3 \mathrm{H}), 7.34(\mathrm{~d}, J=8.2$ $\mathrm{Hz}, 2 \mathrm{H}), 5.42(\mathrm{~d}, J=11.9 \mathrm{~Hz}, 1 \mathrm{H}), 3.44(\mathrm{~d}, J=15.7 \mathrm{~Hz}, 1 \mathrm{H}), 3.05$ (d, $J=15.8 \mathrm{~Hz}, 1 \mathrm{H}), 2.72(\mathrm{~d}, J=15.8 \mathrm{~Hz}, 1 \mathrm{H}), 2.52(\mathrm{dd}, J=15.8$
$\mathrm{Hz}, 11.9 \mathrm{~Hz}, 1 \mathrm{H}) .{ }^{13} \mathrm{C}$ NMR ( $125 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ): $\delta 201.9,138.7,137.1,132.0,129.3,128.5,127.6$, 126.3, $125.0\left(\mathrm{q}, J_{\mathrm{C}, \mathrm{F}}=286 \mathrm{~Hz}\right)$ 122.5, 74.7, 47.2, 43.8. ESI-HRMS: $m / z$ calcd for $\mathrm{C}_{18} \mathrm{H}_{15} \mathrm{O}_{2} \mathrm{BrF}_{3}$ $\left([\mathrm{M}+\mathrm{H}]^{+}\right)$399.0202, found 399.0197. HPLC (Daicel Chiralpak IB, hexane $/ i-\mathrm{PrOH}=98: 2,0.5$ $\mathrm{mL} / \mathrm{min}, \lambda=220 \mathrm{~nm}$ ): $t_{\mathrm{R}}$ (major diastereomer, major enantiomer) $=30.5 \mathrm{~min}, t_{\mathrm{R}}$ (major diastereomer, minor enantiomer) $=43.5 \mathrm{~min}$.

Compound 3i-2 (minor diastereomer)

$\mathrm{R}_{\mathrm{f}} 0.33$ (hexane/EtOAc $=95: 5$ ), colorless oil. ${ }^{1} \mathrm{H}$ NMR $(500 \mathrm{MHz}$, $\mathrm{CDCl}_{3}$ ): $\delta 7.54-7.48(\mathrm{~m}, 4 \mathrm{H}), 7.44-7.40(\mathrm{~m}, 3 \mathrm{H}), 7.25(\mathrm{~d}, J=8.3$ $\mathrm{Hz}, 2 \mathrm{H}), 4.70(\mathrm{~d}, J=11.8 \mathrm{~Hz}, 1 \mathrm{H}), 3.36(\mathrm{~d}, J=14.8 \mathrm{~Hz}, 1 \mathrm{H}), 3.13$ (d, $J=14.8 \mathrm{~Hz}, 1 \mathrm{H}), 2.62(\mathrm{dd}, J=14.8 \mathrm{~Hz}, 11.8 \mathrm{~Hz}, 1 \mathrm{H}), 2.50(\mathrm{~d}$, $J=14.8 \mathrm{~Hz}, 1 \mathrm{H}) .{ }^{13} \mathrm{C}$ NMR ( $125 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ): $\delta 202.1,138.4$, 132.6, 131.9, 129.8, 129.0, 128.2, 127.3, $123.7\left(\mathrm{q}, J_{\mathrm{C}, \mathrm{F}}=282 \mathrm{~Hz}\right)$, 122.3, $81.2\left(\mathrm{q}, J_{\mathrm{C}, \mathrm{F}}=30 \mathrm{~Hz}\right), 73.0,48.3$, 42.7. ESI-HRMS: $m / z$ calcd for $\mathrm{C}_{18} \mathrm{H}_{15} \mathrm{O}_{2} \mathrm{BrF}_{3}\left([\mathrm{M}+\mathrm{H}]^{+}\right)$ 399.0202, found 399.0194.

## 3. Determination of the Absolute Configuration of 3a-1 (Scheme 2)

## Synthesis of (R)-4a ${ }^{3}$

Aldol ( $R$ )-4a ${ }^{3}$ was synthesized by the previously reported procedure using cinchonidine-derived amine with benzoic acid as the catalyst. ${ }^{3}$


## Aldol (R)-4a ${ }^{3}$

$[\alpha]^{24}{ }_{\mathrm{D}}-114$ (c 1.0, $\mathrm{CH}_{2} \mathrm{Cl}_{2}$, er $95: 5$ determined by HPLC analysis). Lit. $[\alpha]^{24}{ }_{\mathrm{D}}-71.8$ (c 0.28 , $\mathrm{CH}_{2} \mathrm{Cl}_{2}, 93 \%$ ee) for ( $R$ )-4a. ${ }^{3}$ HPLC (Daicel Chiralpak AS-3, hexane $/ i-\mathrm{PrOH}=99: 1,0.5 \mathrm{~mL} / \mathrm{min}$, $\lambda=220 \mathrm{~nm}): t_{\mathrm{R}}($ major enantiomer $)=27 \mathrm{~min}, t_{\mathrm{R}}($ minor enantiomer $)=32 \mathrm{~min}$.

## Synthesis of ( $\pm$ )-4a

Racemic standard of aldol $( \pm)-\mathbf{4 a}$ was synthesized by the procedure that was used for the synthesis of $(R)$-4a but using ethylenediamine ( 0.1 equiv) with benzoic acid ( 0.1 equiv) as the catalyst instead of the cinchonidine-derived amine with benzoic acid.

Transformation of $(\boldsymbol{R})$-4a to 3a: Intramolecular oxa-Michael reaction of ( $R$ )-4
Aldol ( $R$ )-4a ${ }^{3}$ (er 95:5) was transformed to 3a in the presence of $\mathbf{T f O H} .{ }^{4}$


To a solution of $(R)-\mathbf{4 a}$ (er $95: 5,180 \mathrm{mg}, 0.62 \mathrm{mmol})$ in $\mathrm{CHCl}_{3}(5.0 \mathrm{~mL})$, $\mathrm{TfOH}(2.7 \mu \mathrm{~L}, 0.031$ mmol ) was added at room temperature $\left(25{ }^{\circ} \mathrm{C}\right)$, and the mixture was stirred at the same temperature for 3 days. A portion of the mixture was diluted with $\mathrm{CDCl}_{3}$ and analyzed by ${ }^{1} \mathrm{H}$ NMR to observe the product formation and the dr; the ratios werw $\mathbf{3 a} / \mathbf{4 a}=7: 3$ and $\mathbf{3 a - 1} / \mathbf{3 a - 2}=$ 2.5:1. The mixture (remaining portion) was purified by flash column chromatography (hexane/EtOAc $=98: 2$ ) to give $(R, R)$-3a-1 (er 96:4).

Based on the comparison of HPLC retention times of 3a-1 obtained in the presence of amine $\mathbf{A}$ and acid $\mathbf{B}$ (page S2-S3) and of $(R, R) \mathbf{- 3 a - 1}$ obtained from $(R)-\mathbf{4 a}$, the absolute configuration of 3a-1 obtained in the presence of $\mathbf{A}$ and $\mathbf{B}$ (page S2-S3) was determined to be $(R, R)$.

## 4. References

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A













3a-2




Current Data Parameters $\begin{array}{lr}\text { NAME } & \text { MH-307-MINOR } \\ \text { EXPNO } & 10\end{array}$ PROCNO
F2 - Acquisition Parameters Date_ 20200212

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\end{array}
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\text { AQ } & 3.2767999 \mathrm{sec}
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$$
\begin{array}{r}
8.00 \text { use } \\
23.68499947 \mathrm{~W}
\end{array}
$$

F2 - Frocessing parameters
SI 500.1300131
WDW EM
LB 0.30
0.30 Hz
1.00




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3b-1




| Current | Data Parameters Mh-310-minor |
| :---: | :---: |
| EXPNO | 10 |
| PROCNO | 1 |
| F2 - Acquisition Parameters |  |
| Date_ | 20200130 |
| Time | 18.18 h |
| INSTRUM | Avance |
| PROBHD | 2167889_0002 ( |
| PULPROG | zg30 |
| TD | 65536 |
| SOLVENT | CDCl3 |
| NS | 16 |
| DS | 2 |
| SWH | 10000.000 Hz |
| FIDRES | 0.305176 Hz |
| AQ | 3.2767999 sec |
| RG | 12.4562 |
| DW | 50.000 usec |
| DE | 10.45 used |
| TE | 298.1 K |
| D1 | 1.00000000 sec |
| TD0 | 1 |
| SFO1 | 500.1330883 MHz |
| NUC1 | 1H |
| P0 | 4.00 usec |
| P1 | 12.00 usec |
| PLW1 | 6.80000019 W |
| F2 - Processing parameters |  |
| SI | 65536 |
| SF | 500.1300124 MHz |
| WDW | EM |
| SSB | 0 |
| LB | 0.30 Hz |
| GB | 0 |
| PC | 1.00 |








3c-1


| Current Data Parameters |  |
| :---: | :---: |
| NAME |  |
| EXPNO | 30 |
| PROCNO | 1 |
| F2 - Acquisition Parameters |  |
| Date_ | 20200201 |
| Time | 11.57 h |
| INSTRUM | Avance |
| PROBHD | 2167889_0002 ( |
| PULPROG | zg30 |
| TD | 65536 |
| SOLVENI | CDCl3 |
| NS | 16 |
| DS | 2 |
| SWH | 10000.000 Hz |
| FIDRES | 0.305176 Hz |
| AQ | 3.2767999 sec |
| RG | 9.3756 |
| DW | 50.000 usec |
| DE | 10.45 usec |
| TE | 298.1 K |
| D1 | 1.00000000 sec |
| IDO | 1 |
| SFO1 | 500.1330883 MHz |
| NUC1 | 1H |
| PO | 4.00 usec |
| P1 | 12.00 usec |
| PLW1 | 6.80000019 W |
| F2 - Processing parameters |  |
| SI | 65536 |
| SF | 500.1300231 MHz |
| WDW | EM |
| SSB | 0 |
| IB | 0.30 Hz |
| GB | 0 |
| PC | 1.00 |





3c-1


$$
\begin{array}{lr}
\text { Current Data Parameters } \\
\text { NAME } & \text { MH-311-MAJOR } \\
\text { EXPNO } & 21 \\
\text { PROCNO } & 1
\end{array}
$$

F2 - Acquisition Parameters

$$
\text { Date_ } 20200131
$$

$$
\text { Time } \quad 14.42 \mathrm{~h}
$$

INSTRUM Avance

$$
\text { PROBHD } \quad 2167889 \text { _0002 }
$$

PULPROG

$$
\begin{aligned}
& \text { EUL } \\
& \text { TD } \\
& \text { SOL }
\end{aligned}
$$

$$
\begin{array}{lr}
\text { TD } & 65536 \\
\text { SOLVENT } & \text { CDC13 }
\end{array}
$$

$$
\begin{aligned}
& \text { SOLVENT } \\
& \text { NS }
\end{aligned}
$$

$$
\begin{aligned}
& \text { ND } \\
& \text { DS }
\end{aligned}
$$

SWH
FIDRES

$$
\begin{aligned}
& A Q \\
& R G
\end{aligned}
$$

$$
\begin{aligned}
& \text { RG } \\
& \text { DW }
\end{aligned}
$$

$$
\begin{aligned}
& \text { DW } \\
& \text { DE }
\end{aligned}
$$

TE
D1

$$
\begin{aligned}
& \text { D1 } \\
& \text { D11 }
\end{aligned}
$$

TDO
SFO1
NUC1
Po

$$
\mathrm{P} 1
$$

ELW1

$$
\mathrm{SFO} 2
$$

NUC2
CPDPRG[2

$$
\text { PCPD } 2
$$

PLW2
PLW12
PLW13

$$
0.15300000 \mathrm{~W}
$$

$$
0.07683500 \mathrm{~W}
$$




 L


3c-2



NAME MH-311-MIN EXPNO
PROCNO

| F2 - Acquisition Parameters |  |
| :---: | :---: |
| Date_ | 20200131 |
| Time | 10.41 h |
| INSTRUM | Avance |
| PROBHD | 2167889_0002 ( |
| PUIPROG | zg30 |
| TD | 65536 |
| SOLVENT | CDCl3 |
| NS | 6 |
| DS | 2 |
| SWH | 10000.000 Hz |
| FIDRES | 0.305176 Hz |
| AQ | 3.2767999 sec |
| RG | 12.6367 |
| DW | 50.000 usec |
| DE | 10.45 usec |
| TE | 298.2 K |
| D1 | 1.00000000 sec |
| TDO | 1 |
| SFO1 | 500.1330883 MHz |
| NUC1 | 1H |
| PO | 4.00 usec |
| P1 | 12.00 usec |
| PLW1 | 6.80000019 W |
| F2 - Processing parameters |  |
| SI | 65536 |
| SF | 500.1300121 MHz |
| WDW | EM |
| SSB | 0 |
| LB | 0.30 Hz |
| GB | 0 |
| PC | 1.00 |










3c-2
$\begin{array}{lr}\text { Current Data } & \text { Parameters } \\ \text { NAME } & \text { MH-311-MIN } \\ \text { EXPNO } & 11 \\ \text { PROCNO } & 1\end{array}$


 -•••••••••••• $\dot{\sim}$


3d-1


$\qquad$

| NAME | MH-314-MAJOR |
| :---: | :---: |
| EXPNO | 10 |
| PROCNO |  |

PROCNO
F2 - Acquisition Parameters
Date_ 20200208
Iime $\quad 15.02 \mathrm{~h}$
-NsiRUM Avance
PULPROG TD
SOL
NS
DS
SWH
FIDRE
AQ
RG
DW
DE
TE
D1
SFOI
NUC
PO
P1
PLWI
2151574_0027 ( 2930
6536 CDCl3
10000.000 0.305176 Hz 3.2767999 sec 51.2821 50.000 usec 11.14 usec 298.0 K
1.00000000 sec
500.1330883 MHz

1 H
2.67 usec
8.00 usec
23.68499947 W

SI 65536
SF $\quad 500.1300115 \mathrm{MHz}$
EDW EM
SSB 0
$-\quad 0.30 \mathrm{~Hz}$
$\begin{array}{ll}\text { GB } & 1.00\end{array}$









3d-2


| Current | Data Parameters |
| :--- | ---: |
| NAME | MH-314-MINOR |
| EXPNO | 20 |
| PROCNO | 1 |

F2 - Acquisition Parameters Date_ 20200208 Time 16.09 h INSTRUM Avance PROBHD Z151574_0027 PULPROG $\quad$ zg30 SOLVENT NS DS DS
SWH
ETDRE ${ }_{A Q}{ }^{\text {EAD }}$ AQ
RG
DW
DE
DE $\quad 50.000$ use 11.14 usec 298.0 K

$$
1.00000000 \mathrm{sec}
$$

$$
500.1330883_{1}^{1} \mathrm{MHz}
$$

1H
$2 . \overline{67}$ usec
8.00 use
23.68499947 W
$\begin{array}{lc}\text { F2 - Processing parameters } \\ \text { SI } & 65536 \\ \text { SF } & 500.1300115 \mathrm{MHz} \\ \text { WDW } & \text { EM } \\ \text { SSB } & 0 \\ \text { LB } & 0.30 \mathrm{~Hz} \\ \text { GB } & 0 \\ \text { PC } & 1.00\end{array}$




| Current | Data Parameters |
| :--- | ---: |
| NAME | MH-315-MAJOR |
| EXPNO | 10 | EXPNO

F2 - Acquisition Parameters
Date 20200210

| Date_ | 20200210 h |
| :--- | ---: |
| Iime | 15.10 h |
| INSTRUM | Avance |

PROBHD 2151574 Avance

$$
\begin{array}{lr}
\text { PROBHD } & 2151574 \_0027 \\
\text { PULPROG } & \text { zg30 }
\end{array}
$$

$$
\begin{array}{lr}
\text { PULPROG } & \text { zg30 } \\
\text { ID } & 65536
\end{array}
$$

$$
\begin{array}{ll}
\text { TD } & 65536 \\
\text { SOLVENT } & \text { CDCl3 }
\end{array}
$$

$$
\begin{array}{lr}
\text { SOLVENT } & \text { CDCl3 } \\
\text { NS } & 16
\end{array}
$$

| DS | 16 <br> SWH$\quad 10000.000^{2}$ |
| :--- | ---: |

FIDRES $\quad 0.305176$ $\begin{array}{lr}\text { FIDRES } & 0.305176 \mathrm{~Hz} \\ \text { AQ } & 3.2767999 \mathrm{sec}\end{array}$ RG DW


$$
\begin{aligned}
& 11.14 \mathrm{usec} \\
& 298.0 \mathrm{~K}
\end{aligned}
$$

$$
00000000
$$

$$
1.00000000 \mathrm{sec}
$$

$$
500.1330883 \mathrm{MHz}
$$

$$
\begin{array}{r}
1 \mathrm{H} \\
2.67 \text { use }
\end{array}
$$

$$
\begin{aligned}
& 2.67 \text { usec } \\
& 8.00 \text { usec }
\end{aligned}
$$

$$
23.68499947 \mathrm{~W}
$$

F2 - Processing parameters

$$
\begin{array}{lr}
\text { SI } & 65536 \\
\text { SF } & 500.1300134 \mathrm{M}
\end{array}
$$

$$
\begin{array}{lc}
\mathrm{SF} & 500.1300134 \mathrm{MHz} \\
\mathrm{WDW} & \mathrm{EM}
\end{array}
$$

$$
\begin{array}{lc}
W D W & E M \\
S S B & 0
\end{array}
$$

$$
0.30 \mathrm{~Hz}
$$

$$
1.00
$$



$\begin{array}{lr}\text { Current } & \text { Data Parameters } \\ \text { NAME } & \text { MH-315-MAJOR } \\ \text { EXPNO } & 10 \\ \text { PROCNO } & 1\end{array}$
F2 - Acquisition Parameters
Date_ 20200210
20200210
$\begin{array}{lr}\text { Time- } & 15.10 \mathrm{~h} \\ \text { INSIRUM } & \text { Avance }\end{array}$
INSTRUM
PROBHD
Avance
Z151574_0027
PROBHD Z151574_0027 (
PULPROG
zg30

| PULPROG |  |
| :--- | ---: |
| ID | 6530 |
| 5536 |  |

$\begin{array}{lr}\text { SOLVENT } & 65536 \\ \text { NS } & \text { CDCl3 } \\ \text { DS } & 16 \\ \text { SWH } & 2 \\ & 10000.000 \mathrm{~Hz}\end{array}$
$\begin{array}{lr}\text { SWH } & 10000.000 \mathrm{~Hz} \\ \text { FIDRES } & 0.305176 \mathrm{~Hz}\end{array}$
$\begin{array}{ll}\text { FIDRES } & 0.305176 \mathrm{~Hz} \\ \text { AQ } & 3.2767999\end{array}$
$\begin{array}{lr}\text { AQ } & 3.2767999 \mathrm{sec} \\ \text { RG } & 42.5532\end{array}$

| DW | 42.553 |
| :--- | ---: |
| $D E$ | 50. |
| $T E$ | 11. |

50.000 usec
11.14 usec
298.0 K
1.00000000 sec
$500.1330883^{1} \mathrm{MHz}$
1H
2.67 usec
2.07 usec
8.00 usec
23.68499947 w

F2 - Processing parameters


$3 \mathrm{e}-1$





$3 \mathrm{e}-2$



| Current Data Parameters |  |
| :---: | :---: |
| NAME | MH-315-MINOR |
| EXPNO | 20 |
| PROCNO | 1 |
| F2 - Acquisition Parameters |  |
| Date_ | 20200210 |
| Time | 16.03 h |
| INSTRUM | Avance |
| PROBHD | 2151574_0027 ( |
| PULPROG | zg30 |
| TD | 65536 |
| SOLVENT | CDCl3 |
| NS | 15 |
| DS | 2 |
| SWH | 10000.000 Hz |
| FIDRES | 0.305176 Hz |
| AQ | 3.2767999 sec |
| RG | 77.6398 |
| DW | 50.000 usec |
| DE | 11.14 usec |
| TE | 298.0 K |
| D1 | 1.00000000 sec |
| TDO | 1 |
| SFO1 | 500.1330883 MHz |
| NUC1 | 1H |
| PO | 2.67 usec |
| P1 | 8.00 usec |
| PLW1 | 23.68499947 W |
| F2 - Processing parameters |  |
| SI | 65536 |
| SF | 500.1300130 MHz |
| WDW | EM |
| SSB | 0 |
| LB | 0.30 Hz |
| GB | 0 |
| PC | 1.00 |





Current Data Parameter $\begin{array}{lr}\text { NAME } & \text { MH-320-MAJOR-C } \\ \text { EXPNO } & 10 \\ \text { PROCNO } & 1\end{array}$

F2 - Acquisition Parameters

| Date_ | 20200304 |  |
| :---: | :---: | :---: |
| Time | 20.13 | h |
| INSTRUM | Avance |  |
| PROBHD | 2151574_0027 ( |  |
| PULPROG | zg30 |  |
| TD | 65536 |  |
| SOLVENT | CDCl3 |  |
| NS | 16 |  |
| DS | 2 |  |
| SWH | 10000.000 | Hz |
| FIDRES | 0.305176 | Hz |
| AQ | 3.2767999 | sec |
| RG | 60.6061 |  |
| DW | 50.000 | usec |
| DE | 11.14 | usec |
| TE | 298.1 | K |
| D1 | 1.00000000 | sec |
| TDO | 1 |  |
| SFO1 | 500.1330883 | MHz |
| NUC1 | 1H |  |
| PO | 2.67 | usec |
| P1 | 8.00 | usec |
| PLW1 | 23.68499947 | W |
| F2 - Processing parameters |  |  |
| SI | 65536 |  |
| SF | 500.1300131 | MHz |
| WDW | EM |  |
| SSB | 0 |  |
| LB | 0.30 | Hz |
| GB | 0 |  |
| PC | 1.00 |  |



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 -••••••••••••••• •• • ••



Current Data Parameters NAME EXPNO

F2 - Acquisition Parameters

| Date_ | 20200304 |  |
| :---: | :---: | :---: |
| Time | 22.11 | h |
| INSTRUM | Avance |  |
| PROBHD | 2151574_0027 ( |  |
| PuIprog | zgpg30 |  |
| TD | 65536 |  |
| SOLVENT | CDCl3 |  |
| NS | 1024 |  |
| DS | 4 |  |
| SWH | 30120.482 | Hz |
| FIDRES | 0.919204 | Hz |
| AQ | 1.0878977 | sec |
| RG | 101 |  |
| DW | 16.600 | usec |
| DE | 6.50 | usec |
| TE | 298.2 | K |
| D1 | 2.00000000 | sec |
| D11 | 0.03000000 | sec |
| TD0 | 1 |  |
| SFO1 | 125.7703643 | MHz |
| NUC1 | 130 |  |
| PO | 3.33 | used |
| P1 | 10.00 | usec |
| PLW1 | 88.26000214 | W |
| SEO2 | 500.1320005 | MHz |
| NUC2 | 1H |  |
| CPDPRG[2 | waltz65 |  |
| PCPD2 | 80.00 | used |
| PLW2 | 23.68499947 | W |
| PLW12 | 0.23684999 | W |
| PLW13 | 0.11913000 | W |
| F2 - Processing parameters |  |  |
| SI | 32768 |  |
| SE | 125.7577928 | MHz |
| WDW | EM |  |
| SSB | 0 |  |
| LB | 1.00 | Hz |
| GB | 0 |  |
| PC | 1.40 |  |

ppm



| Current NAME | Data Parameters MH-320-MINOR-CS |
| :---: | :---: |
| EXPNO | 10 |
| PROCNO | 1 |
| F2 - Acquisition Parameters |  |
| Date_ | 20200304 |
| Time | 20.19 h |
| INSTRUM | Avance |
| PROBHD | 2151574_0027 ( |
| PULPROG | zg30 |
| TD | 65536 |
| SOLVENT | CDCl3 |
| NS | 16 |
| DS | 2 |
| SWH | 10000.000 Hz |
| FIDRES | 0.305176 Hz |
| AQ | 3.2767999 sec |
| RG | 101 |
| DW | 50.000 used |
| DE | 11.14 usec |
| TE | 298.2 K |
| D1 | 1.00000000 sec |
| TDO | 1 |
| SEO1 | 500.1330883 MHz |
| NUC1 | 1H |
| PO | 2.67 usec |
| P1 | 8.00 useo |
| PLW1 | 23.68499947 W |
| F2 - Processing parameters |  |
| SI | 65536 |
| SF | 500.1300132 MHz |
| WDW | EM |
| SSB | 0 |
| LB | 0.30 Hz |
| GB | 0 |
| PC | 1.00 |





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$3 \mathrm{~g}-1$










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3g-2

| Current D | Data Parameters |
| :---: | :---: |
| NAME | MH-324-MIN-AGAIN-C13 |
| EXPNO | 12 |
| Procno | 1 |
| F2 - Acquisition Parameters |  |
| Date_ | 20200414 |
| Time | 18.10 h |
| INSTRUM | Avance |
| PROBHD | Z151574_0027 ( |
| PULPROG | zgpg30 |
| TD | 65536 |
| SOLVENT | CDCl3 |
| NS | 1024 |
| DS | 4 |
| SWH | 30120.482 Hz |
| FIDRES | 0.919204 Hz |
| AQ | 1.0878977 sec |
| RG | 101 |
| DW | 16.600 usec |
| DE | 6.50 usec |
| IE | 298.2 K |
| D1 | 2.00000000 sec |
| D11 | 0.03000000 sec |
| TDO | 1 |
| SEO1 | 125.7703643 MHz |
| NUC1 | 13 C |
| PO | 3.33 usec |
| P1 | 10.00 usec |
| PLW1 | 88.26000214 W |
| SEO2 | 500.1320005 MHz |
| NUC2 | 1H |
| CPDPRG[2 | waltz65 |
| PCPD2 | 80.00 usec |
| PLW2 | 23.68499947 W |
| PLW12 | 0.23014790 W |
| PLW13 | 0.11535020 W |
| F2 - Processing parameters |  |
| SI | 32768 |
| SE | 125.7577911 MHz |
| WDW | EM |
| SSB | 0 |
| LB | 1.00 Hz |
| GB | 0 |
| PC | 1.40 |


| Current | Data Parameters |
| :---: | :---: |
| NAME | MH-322-MAJOR-CLEAN |
| EXPNO | 10 |
| PROCNO | 1 |
| F2 - Acquisition Parameters |  |
| Date_ | 20200310 |
| Time | 16.11 h |
| INSIRUM | Avance |
| PROBHD | 2151574_0027 ( |
| PULPROG | z930 |
| TD | 65536 |
| SOLVENT | CDCl3 |
| NS | 16 |
| DS | 2 |
| SWH | 10000.000 Hz |
| FIDRES | 0.305176 Hz |
| AQ | 3.2767999 sec |
| RG | 101 |
| DW | 50.000 usec |
| DE | 11.14 used |
| TE | 298.1 K |
| D1 | 1.00000000 sec |
| TDO | 1 |
| SFO1 | 500.1330883 MHz |
| NUC1 | 1H |
| PO | 2.67 used |
| P1 | 8.00 usec |
| PLW1 | 23.68499947 W |
| F2 - Processing parameters |  |
| SI | 65536 |
| SF | 500.1300131 MHz |
| WDW | EM |
| SSB | 0 |
| LB | 0.30 Hz |
| GB | 0 |
| PC | 1.00 |






| NAME | MH-322-MINOR-C |
| :--- | ---: |
| EXPNO | 10 |
| PROCNO | 1 |

F2 - Acquisition Parameters

$$
\text { Time } \quad 17.14 \mathrm{~h}
$$

INSTRUM Avance
PROBHD Z151574_0027

$$
\text { TD } \quad 65536
$$

$$
\begin{array}{lr}
\text { SOLVENT } & \text { CDCl3 } \\
\text { NS } & 16
\end{array}
$$

NS
SS
IDRES $\quad 10000.000 \mathrm{~Hz}$
AQ $\quad 0.305176 \mathrm{~Hz}$
RG
DW
IE $\quad \begin{aligned} & 11.14 \mathrm{us} \\ & 298.1 \mathrm{~K}\end{aligned}$
11.00000000 sec
$\begin{array}{ll}\text { TDO } & 500.1330883 \\ \text { SFO1 } & 1 \\ \text { MHz }\end{array}$
NUC1 1 H
PO
P1
PLW1
2 - Erocessing parameters
$\begin{array}{ll}\mathrm{SI} & 500.1300134 \mathrm{MHz} \\ \mathrm{SF} & 500\end{array}$
WDW EM
PC 1.00
PLW1 23.68499947 W
10000.000 Hz 3.2767999 sec 50.000 usec 11.14 usec 298.1 K 1.000 .1330883 MHz
500
2.67 usec
8.00 usec
23.68499947 W
500.1300134 MHz

EM
0
0.30 Hz
1.00












| No. | RT | Area | Area \% | BC |
| :---: | :---: | :---: | :---: | :---: |
| 1 | 23.523 | 95405742 | 95.224 | MC |
| 2 | 27.050 | 4785074 | 4.776 | MC |
|  | $1.001 \mathrm{E}+08$ | 100.000 |  |  |



| No. | RT | Area | Area \% | BC |
| :---: | :---: | :---: | :---: | :---: |
| 1 | 18.970 | 6988923 | 92.783 | MC |
| 2 | 23.280 | 543607 | 7.217 | MC |
|  | 7532530 | 100.000 |  |  |



| No. | RT | Area | Area \% | BC |
| :---: | :---: | :---: | :---: | :---: |
| 1 | 27.140 | 11102158 | 49.996 | MC |
| 2 | 31.787 | 11104156 | 50.004 | MC |
|  | 22206314 | 100.000 |  |  |

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| No. | RT | Area | Area \% | BC |
| :---: | :---: | :---: | :---: | :---: |
| 1 | 26.027 | 22810647 | 93.653 | MC |
| 2 | 30.910 | 1546000 | 6.347 | MC |
|  | 24356647 | 100.000 |  |  |




| No. | RT | Area | Area \% | BC |
| :---: | :---: | :---: | :---: | :---: |
| 1 | 24.577 | 25800875 | 95.652 | MC |
| 2 | 30.520 | 1172833 | 4.348 | MC |
|  | 26973708 | 100.000 |  |  |




| No. | RT | Area | Area \% | BC |
| :---: | :---: | :---: | :---: | :---: |
| 1 | 11.697 | 17530685 | 89.570 | MC |
| 2 | 13.377 | 2041395 | 10.430 | MC |
|  |  | 19570080 | 100.000 |  |


| No. | RT | Area | Area \% | BC |
| :---: | :---: | :---: | :---: | :---: |
| 1 | 14.533 | 8721110 | 50.534 | MC |
| 2 | 18.887 | 8536906 | 49.466 | MC |
|  |  | 17258016 | 100.000 |  |


| No. | RT | Area | Area \% | BC |
| :---: | :---: | :---: | :---: | :---: |
| 1 | 14.507 | 19393987 | 94.899 | MC |
| 2 | 18.940 | 1042496 | 5.101 | MC |
|  | 20436483 | 100.000 |  |  |



| No. | RT | Area | Area \% | BC |
| :---: | :---: | :---: | :---: | :---: |
| 1 | 12.213 | 7178251 | 49.637 | MC |
| 2 | 14.087 | 7283346 | 50.363 | MC |
|  | 14461597 | 100.000 |  |  |




| No. | RT | Area | Area \% | BC |
| :---: | :---: | :---: | :---: | :---: |
| 1 | 30.700 | 4527337 | 50.011 | MC |
| 2 | 43.457 | 4525296 | 49.989 | MC |
|  | 9052633 | 100.000 |  |  |



| No. | RT | Area | Area \% | BC |
| :---: | :---: | :---: | :---: | :---: |
| 1 | 30.580 | 17679033 | 79.620 | MC |
| 2 | 43.577 | 4525214 | 20.380 | MC |
|  | 22204247 | 100.000 |  |  |

