Divergent Reactions on a Racemic Mixture: Catalytic Enantioselective Regiodivergent Nitroso Diels-Alder Reaction

Chandan Kumar Jana,†‡ and Armido Studer*‡

Fachbereich Chemie, Organisch-Chemisches Institut, Westfälische Wilhelms-Universität, Corrensstrasse 40, 48149 Münster, and NRW Graduate School of Chemistry, Westfälische Wilhelms-Universität, Corrensstrasse 36, 48149 Münster.

studer@uni-muenster.de

‡Organisch-Chemisches Institut, †NRW Graduate School of Chemistry.

Experimental Section:

General: All reactions involving air- or moisture-sensitive reagents or intermediates were carried out in heat-gun-dried glassware under an argon atmosphere. THF was freshly distilled from potassium under argon. Diethylether (Et₂O) was freshly distilled from K/Na under argon. Dichloromethane (CH₂Cl₂) was freshly distilled from phosphorus(V)oxide (P₂O₅). Triethylamine (Et₃N) was distilled from CaH₂ and stored under argon. All other solvents and reagents were purified according to standard procedures or were used as received from Aldrich, Acros or Fluka. 2-Nitrosopyridine was synthesized according to the known procedure¹. ¹H, ¹³C, GCOSY, GHSQC and 1D-NOE NMR spectroscopy: Bruker Unity plus 600, AMX 400, dpx 300 spectrometer; chemical shifts, δ, were measured in ppm relative to CHCl₃ (7.26 ppm), which was used as an
Syntheses of 1,3-cyclohexadiene derivatives from 1,4-cyclohexadiene

General procedure 1 (GP1): Preparation of cyclohexadienyllithium

The solution of 1,4-cyclohexadiene (1.00 eq.) and tetramethylethylendiamine (TMEDA) (1.08 eq.) in THF (~ 0.2 M) was cooled to -78 °C. Then sec-BuLi (1.08 eq.) was added to the mixture, stirred for 60-90 min at that temperature and the yellowish solution was then used for transmetalation reactions.

\[ \text{tert-Butyl-}((R)-(S))-\text{cyclohexa-2,4-dienyl-phenyl-methoxy)-diphenylsilane (1a):} \]

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\text{tert-Butyldiphenylsilyl chloride (0.34 mL, 1.3 mmol) and imidazole (0.11 g, 1.61 mmol) were added to a solution of (R)-(S)-cyclohexa-2,4-dienyl-phenyl-methanol}^1 \text{ (0.20 g, 1.6 mmol) in DMF (0.5 mL) and the solution was stirred at rt for 24 h. The reaction mixture was then diluted with methyl tert-butyl ether (MTBE), washed with brine, dried over MgSO}_4 \text{, concentrated in vacuum and the residue was purified by flash column chromatography (pentane:MTBE, 50:1) to afford 1a as a colorless oil (445 mg, 98 %). TLC: } R_f = 0.4 \text{ (pentane:MTBE, 50:1). FTIR (neat): } \nu = 3037, 2931, 2857, 1492, 1471, 1427, 1390, 1110, 1062, 821, 738, 700 \text{ cm}^{-1}. \]
2.73-2.62 (m, 1H), 2.32-2.14 (m, 1H), 1.03 ppm (s, 9H). $^{13}$C-NMR (75 MHz, CDCl$_3$): $\delta = 143.1, 136.1, 134.2, 133.7, 129.5, 129.3, 127.7, 127.5, 127.4, 127.2, 127.1, 125.6, 124.7, 123.7, 77.04, 41.7, 27.1, 25.2, 19.5 ppm. HRMS (ESI) Exact mass calculated for C$_{20}$H$_{32}$O$_{1}$Si Na ([M + Na$^+$]): 447.2115. Found: 447.2105.

(1-Cyclohexa-2,4-dienyl-1-methyl-ethoxy)-trimethyl-silane (1b):

Titanium(IV) iso-propoxide (0.66 mL, 2.2 mmol) was added to a solution of cyclohexadienyllithium (2.0 mmol, prepared according to GP 1) at -78 °C and the resulting brown mixture was stirred for 10 min. Acetone (0.12 mL, 1.6 mmol) was then added slowly at -78 °C and stirred for 6 h at that temperature. To the reaction mixture, water and MTBE were then added (white precipitate formed), warmed to rt, phases were separated and the aqueous phase was extracted with MTBE. The organic phase was washed (brine), dried (MgSO$_4$), concentrated in vacuum and the residue was purified by flash column chromatography (pentane:MTBE, 5:1) to afford 2-cyclohexa-2,4-dienyl-propan-2-ol as a colorless oil (0.20 g, 91%). TLC: $R_f = 0.2$ (pentane:MTBE, 5:1). FTIR (neat): $\nu = 3383, 3036, 2974, 2938, 2360, 1673, 1379, 1142, 1030, 953, 764, 700$ cm$^{-1}$. $^1$H-NMR (300 MHz, CDCl$_3$): $\delta = 6.13$- 6.07 (m, 1H), 6.03-5.97 (m, 1H), 5.95-5.89 (m, 2H), 2.55-2.24 (m, 3H), 1.58 (br. s, 1H), 1.35 (s, 3H), 1.34 ppm (s, 3H). $^{13}$C-NMR (101 MHz): $\delta = 126.7, 126.3, 125.3, 123.7, 73.2, 44.5, 27.3, 26.9, 24.1$ ppm. MS (EI): 138.2 ([M$^+$]), 120.2, 105.2, 91.2, 80.2.

Trimethylsilyl chloride (0.17 mL, 1.3 mmol) and imidazole (111 mg, 1.63 mmol) were added to a solution of 2-cyclohexa-2,4-dienyl-propan-2-ol (150 mg, 1.08 mmol) in DMF (0.2 mL). The solution was stirred at rt for 8 h. The reaction mixture was then diluted with MTBE, washed with brine, dried over MgSO$_4$, concentrated in vacuum and the residue was purified by flash column chromatography (pentane:MTBE, 40:1) to afford 1b as a colorless oil (220 mg, 97 %). TLC: $R_f = 0.7$ (pentane:MTBE, 20:1). FTIR (neat): $\nu = 2974, 2939, 1681, 1382, 1158, 1031, 756$ cm$^{-1}$. $^1$H-NMR (400 MHz, CDCl$_3$): $\delta = 5.93$-5.89 (m, 1H), 5.87-5.83 (m, 1H), 5.80-5.75 (m, 2H), 2.42-2.35 (m, 1H), 2.26-2.06 (m, 2H), 1.21 (s, 3H), 1.20 (s, 3H), 0.12 ppm (s, 9H). $^{13}$C-NMR (101 MHz, CDCl$_3$): $\delta = 128.1, 126.3, 124.3, 123.7, 76.1, 45.6, 27.4, 24.2, 2.6$ ppm. HRMS (ESI) Exact mass calculated for C$_{12}$H$_{22}$OSiNa ([M + Na$^+$]): 233.1332. Found: 233.1325.
tert-Butyl-(cyclohexa-2,4-dienylmethoxy)-diphenyl-silane (1c)

Anhydrous ZnCl$_2$ (327 mg, 2.40 mmol) was added to a solution of cyclohexadienyllithium (4.80 mmol, prepared according to GP 1) at -78 °C and the reaction mixture was stirred for 3 h. Paraformaldehyde (64 mg, 2.0 mmol) was then added at -78 °C and the reaction mixture was stirred for 5 h at that temperature. The mixture was slowly warmed to room temperature and was stirred for 4 h at that temperature. Water and MTBE were then added to the reaction mixture (white precipitate formed), phases were separated and the aqueous phase was extracted with MTBE. The combined organic organic layers were washed (brine), dried (MgSO$_4$), concentrated in vacuum and the residue was purified by flash column chromatography (pentane:MTBE, 2:1) to afford cyclohexa-2,4-dienyl-methanol as a colorless oil (220 mg, 95%, inseparable mixture (9:1) of two isomers). TLC: $R_f = 0.3$ (pentane:MTBE, 1:1). FTIR (neat): $\nu = 3362, 3032, 2900, 2875, 1674, 1454, 1207, 1026, 736, 701, 681$ cm$^{-1}$. $^1$H-NMR (400 MHz, CDCl$_3$): $\delta = 5.99-5.95$ (m, 1H), 5.88-5.85 (m, 1H), 5.79-5.74 (m, 1H), 5.70-5.67 (m, 1H), 3.60-3.58 (m, 2H), 2.54-2.44 (m, 1H), 2.36-2.27 (m, 1H), 2.21-2.13 ppm (m, 1H). $^{13}$C-NMR (101 MHz, CDCl$_3$): $\delta = 126.8, 125.6, 125.4, 123.8, 65.3, 35.7, 25.2$ ppm. MS (EI): 110.1 ([M]$^+\), 108.1, 79.1, 51.0.

tert-Butyldiphenylsilyl chloride (0.67 mL, 2.6 mmol) and imidazole (219 mg, 3.21 mmol) were added to a solution of cyclohexa-2,4-dienyl-methanol (237 mg, 2.15 mmol) in DMF (0.5 mL) and the solution was stirred at rt for 24 h. The reaction mixture was then diluted with MTBE, washed with brine, dried over MgSO$_4$, concentrated in vacuum and the residue was purified by flash column chromatography (pentane:MTBE, 100:1) to afford 1c as a colorless oil (0.73 g, 97 %). TLC: $R_f = 0.6$ (pentane:MTBE, 50:1). FTIR (neat): $\nu = 3071, 2901, 2931, 2880, 2858, 1472, 1427, 1390, 1361, 1112, 1007, 823, 740, 702, 613$ cm$^{-1}$. $^1$H-NMR (400 MHz, CDCl$_3$): $\delta = 7.69-7.67$ (m, 4H), 7.45-7.37 (m, 6H), 5.94-5.90 (m, 1H), 5.87-5.84 (m, 1H), 5.77-5.69 (m, 2H), 3.63-3.60 (m, 2H), 2.68-2.53 (m, 1H), 2.32-2.15 (m, 2H), 1.07 ppm (s, 9H). $^{13}$C-NMR (101 MHz, CDCl$_3$): $\delta = 135.7, 135.6, 129.5, 127.7, 127.6, 125.6, 124.8, 123.9, 65.8, 36.0, 26.9, 25.2, 19.3$ ppm. HRMS (ESI) Exact mass calculated for C$_{23}$H$_{38}$OSiNa ([M + Na]$^+$): 371.1802. Found: 371.1801.
Catalytic Enantioselective Regiodivergent Nitroso Diels-Alder Reaction

**Cyclohexa-2,4-dienylmethyl-benzene (1d):** Thiocarbonyldiimidazole (TCDI, 0.29 mg, 1.6 mmol) was added to a solution of cyclohexa-2,4-dienyl-phenyl-methanol (0.15 g, 0.81 mmol) in THF (4 mL). The mixture was refluxed at 67 °C for 6 h. Then the reaction mixture was allowed to cool to rt, concentrated under reduced pressure and passed through a short pad of silica gel (MTBE:pentane, 1:1) to afford the corresponding thiocarbonate derivative. The crude thiocarbonate was then dissolved in PhMe (5 mL). AIBN (32 mg, 0.19 mmol) and Bu$_3$SnH (0.53 mL, 2.0 mmol) were added to the solution. The reaction mixture was refluxed at 120 °C for 8 h, was then allowed to cool to rt, was concentrated under vacuum and the residue was purified by silica gel chromatography (pentane:MTBE, 200:1) to afford 1d as a colorless oil (90 mg, 65 %, over two steps). TLC: $R_f = 0.6$ (pentane/MTBE, 100:1). FTIR (neat): $\nu = 3027, 2920, 1601, 1494, 1453, 1029, 737, 699, 720$ cm$^{-1}$. $^1$H-NMR (300 MHz, CDCl$_3$): $\delta = 7.31-7.24$ (m, 2H), 7.22- 7.15 (m, 3H), 5.93-5.89 (m, 2H), 5.79-5.67 (m, 2H), 2.75-2.5 (m, 3H), 2.26-2.15 (m, 1H), 2.06-1.94 ppm (m, 1H). $^{13}$C-NMR (101 MHz, CDCl$_3$): $\delta = 140.4, 130.8, 129.1, 128.2, 125.8, 125.5, 124.1, 123.9, 40.1, 34.7, 28.1$ ppm. MS (EI): 170.2 ([M]$^+$), 91.2, 79.2.

**Acetic acid cyclohexa-2,4-dienylmethyl ester (1e):** Acetic anhydride (1.03 mL, 10.9 mmol) was added to a solution of cyclohexa-2,4-dienyl-methanol (0.60 g, 5.5 mmol) in pyridine (3.0 mL) and was stirred at rt for 24 h. The reaction mixture was then extracted with CH$_2$Cl$_2$ (3x 25 mL), washed with 10% aqueous hydrochloric acid solution and then brine, dried over MgSO$_4$, concentrated in vacuum and the residue was purified by flash column chromatography (pentane:MTBE, 10:1) to afford 1e as a colorless oil (0.76 g, 92 %). TLC: $R_f = 0.3$ (pentane:MTBE, 10:1). FTIR (neat) $\nu = 2970, 2950, 2360, 1740, 1366, 1234, 1036, 686$ cm$^{-1}$. $^1$H-NMR (300 MHz, CDCl$_3$): $\delta = 5.99-5.95$ (m, 1H), 5.91-5.87 (m, 1H), 5.78-5.74 (m, 1H), 5.67-5.63 (m, 1H), 4.03 (br.s, 1H), 4.01 (br. s, 1H), 2.69-2.58 (m, 1H), 2.33-2.25 (m, 1H), 2.16-2.10 (m, 1H), 2.06 ppm (s; 3H). $^{13}$C-NMR (101 MHz, CDCl$_3$): $\delta = 171.1, 126.1, 125.6, 125.3, 124.0, 65.9, 32.5, 25.2, 20.9$ ppm. HRMS (ESI) Exact mass calculated for C$_9$H$_{12}$O$_2$Na ([M + Na]$^+$): 175.0730. Found: 175.0732.
Regiodivergent nitroso Diels-Alder reactions

Representative experimental procedure for the regiodivergent nitroso Diels-Alder reaction using Walphos ligand 8 (GP2)

Walphos ligand 8 (5.2 mg, 5.6 µmol, 10 mol%) and [Cu^I(CH_3CN)_4]PF_6 (2.1 mg, 5.6 µmol, 10 mol%) were added to a flame dried Schlenk tube under argon atmosphere. The catalyst was dried at room temperature for 15 min under vacuum. The Schlenk tube was recharged with argon and anhydrous CH_2Cl_2 (1 mL) was added to the mixture and the resulting solution was stirred under argon for 1 h at rt. The solution was then cooled to -78 °C, a solution of 2-nitrosopyridine (6.7 mg, 62 µmol) in CH_2Cl_2 (0.4 mL) was added dropwise over 10 min and the resulting dark blue solution was stirred for 15 min. A solution of the diene (1.0 eq.) in CH_2Cl_2 (0.5 mL) was added slowly over 1 h at -78 °C. After completion of the addition stirring was continued at -78 °C for 6 h. The mixture was slowly warmed to -20 °C and was stirred for 12 h at that temperature. The solvent was removed under reduced pressure and the crude product was subjected to silica gel chromatography to afford the isomeric adducts.

(1S,4S,8S)-8-[(R)-(tert-Butyl-diphenyl-silanyloxy)-phenyl-methyl]-3-pyridin-2-yl-2-oxa-3-aza-bicyclo[2.2.2]oct-5-ene (ent-anti-2a) and (1R,4R,7R)-7-[(S)-(tert-Butyl-diphenyl-silanyloxy)-phenyl-methyl]-3-pyridin-2-yl-2-oxa-3-aza-bicyclo[2.2.2]oct-5-ene (anti-3a): According to GP2 with 8 (14.9 mg, 16.0 µmol, 10 mol%), [Cu^I(CH_3CN)_4]PF_6 (5.9 mg, 16 µmol, 10 mol%), CH_2Cl_2 (1.5 mL), 2-nitrosopyridine (19.0 mg, 176 µmol), diene 1a (68.0 mg, 160 µmol) and SiO_2-chromatography (pentane:MTBE, 10:1) to give 84 mg (99%) of ent-anti-2a and anti-3a as an inseparable mixture of isomers. The isomer ratio was determined by ^1H NMR spectroscopy (ent-anti-2a:anti-3a = 0.9:1). For analytical purposes the silyl groups were removed (TBAF). The corresponding regioisomeric alcohols ent-anti-2a-OH and anti-3a-OH were separated by SiO_2-chromatography (pentane:MTBE, 1:1).

ent-anti-2a-OH: TLC: R_f = 0.3 (pentane:MTBE, 1:1). [α]^D_{25} = +74.0° (c = 0.53, CHCl_3). FTIR (neat): ν = 3355, 3060, 2930, 1587, 1462,
1432, 1371, 1238, 1091, 953, 910, 832, 785, 764, 732, 702 cm$^{-1}$. $^1$H-NMR (600 MHz, CDCl$_3$) $\delta$ = 8.09 (ddd, $J$ = 4.8, 1.8, 1.2 Hz, 1H), 7.48 (ddd, $J$ = 8.4, 7.2, 1.8 Hz, 1H), 7.42-7.32 (m, 5H), 6.89-6.87 (m, 1H), 6.73 (ddd, $J$ = 7.2, 4.8, 1.2 Hz, 1H), 6.54-6.51 (m, 1H), 6.22-6.20 (m, 1H), 4.93-4.91 (m, 1H), 4.78-4.76 (m, 1H), 4.37 (d, $J$ = 8.4 Hz, 1H), 2.82-2.78 (m, 1H), 2.44-2.40 (m, 1H), 2.01 (br.s, 1H), 1.54 ppm (ddd, $J$ = 10.8, 3.6, 1.2 Hz, 1H). $^{13}$C-NMR (151 MHz, CDCl$_3$): $\delta$ = 163.5, 147.1, 142.6, 137.4, 131.6, 130.3, 128.8, 128.1, 126.3, 116.8, 111.7, 77.3, 69.9, 54.6, 40.8, 29.1 ppm. HRMS (ESI) Exact mass calculated for C$_{18}$H$_{19}$N$_2$O$_2$ ([M + H]$^+$): 295.1441. Found: 295.1439. Enantiomeric excess (98% ee) was determined by chiral HPLC. Column: Chiralcel OD-H; solvent: cyclohexane:2-propanol (95:5); flow: 1.0 mL/min; major enantiomer $t_r$ = 49.2 min, minor enantiomer $t_r$ = 19.8 min.

(1S,4S,8S)-8-(1-Methyl-1-trimethylsilyloxy-ethyl)-3-pyridin-2-yl-2-oxa-3-aza-bicyclo[2.2.2]oct-5-ene (ent-anti-2b) and (1R,4R,7R)-7-(1-Methyl-1-trimethylsilyloxy-ethyl)-3-pyridin-2-yl-2-oxa-3-aza-bicyclo[2.2.2]oct-5-ene (anti-3b): According to GP2 with 8 (8.8 mg, 9.4 µmol), [Cu$^\text{I}$ (CH$_3$CN)$_4$]PF$_6$ (3.5 mg, 9.4 µmol), CH$_2$Cl$_2$ (1.2 mL), 2-nitrosopyridine (11.2 mg, 103 µmol), diene 1b (19.8 mg, 94.3 µmol).
and SiO$_2$-chromatography (pentane:MTBE, 5:1) to give 29.7 mg (99%) of *ent-anti-2b* and *anti-3b* as mixture of isomers. The isomer ratio was determined by chiral HPLC (*ent-anti-2b*:anti-*3b* = 0.9:1). For analytical purposes a sample was repurified by flash chromatography (pentane:MTBE, 10:1).

### ent-anti-2b:
- **TLC:** $R_f = 0.4$ (pentane:MTBE, 10:1). [α]$^D_{25} = +54.5^\circ$ (c = 0.51, CHCl$_3$).
- **FTIR (neat):** $\nu = 2969$, 2928, 1588, 1462, 1432, 1372, 1290, 1222, 1145, 1046, 1007, 953, 853, 829, 786, 767, 706 cm$^{-1}$. $^1$H-NMR (600 MHz, CDCl$_3$): $\delta = 8.20-8.19$ (m, 1H), 7.51-7.48 (m, 1H), 6.89-6.88 (m, 1H), 6.76-6.74 (m, 1H), 6.29-6.26 (m, 1H), 6.19-6.16 (m, 1H), 5.41-5.40 (m, 1H), 4.75-4.73 (m, 1H), 2.33-2.27 (m, 2H), 1.27 (s, 3H), 1.26-1.23 (m, 1H), 1.14 (s, 3H), 0.07 ppm (s, 9H). $^{13}$C-NMR (75 MHz, CDCl$_3$): $\delta = 163.7$, 146.8, 137.7, 132.2, 128.3, 116.4, 111.9, 70.9, 53.96, 44.9, 29.7, 29.3, 28.8, 28.0, 2.5 ppm. HRMS (ESI) Exact mass calculated for C$_{17}$H$_{27}$N$_2$O$_2$Si ([M + H]$^+$): 319.1836. Found: 319.1827.

Enantiomeric excess (95% ee) of the corresponding free alcohol (obtained after removal of the TMS group by treatment with TBAF in THF) was determined by chiral HPLC. Column: Chiralcel OD-H; solvent: cyclohexane:2-propanol (96:4); flow: 1.0 mL/min; major enantiomer $t_r = 19.7$ min, minor enantiomer $t_r = 26.0$ min.

### anti-3b:
- **TLC:** $R_f = 0.2$ (pentane:MTBE, 10:1). [α]$^D_{25} = +90.4^\circ$ (c = 0.41, CHCl$_3$).
- **FTIR (neat):** $\nu = 3056$, 2970, 1588, 1568, 1463, 1432, 1366, 1249, 1148, 1087, 1038, 953, 868, 839, 779, 739, 688 cm$^{-1}$. $^1$H-NMR (600 MHz, CDCl$_3$): $\delta = 8.20-8.19$ (m, 1H), 7.53-7.50 (m, 1H), 6.93-6.94 (m, 1H), 6.76 (ddd, $J = 7.2$, 4.8, 0.6 Hz, 1H), 6.42-6.40 (m, 1H), 6.25-6.22 (m, 1H), 5.33-5.31 (m, 1H), 4.84-4.82 (m, 1H), 2.43-2.40 (m, 1H), 2.32-2.27 (m, 1H), 1.34-1.31 (m, 1H), 1.20 (s, 3H), 1.05 (s, 3H), 0.09 ppm (s, 9H). $^{13}$C-NMR (151 MHz, CDCl$_3$) $\delta = 163.6$, 146.7, 137.7, 130.8, 129.9, 116.4, 111.4, 71.2, 53.3, 48.0, 29.0, 27.4, 25.8, 2.5 ppm. HRMS (ESI) Exact mass calculated for C$_{17}$H$_{27}$N$_2$O$_2$Si ([M + H]$^+$): 319.1836. Found: 319.1836. Enantiomeric excess (89% ee) of the corresponding free alcohol (obtained after removal of the TMS group by treatment with TBAF in THF) was determined by chiral HPLC. Column: Chiralcel OD-H; solvent: cyclohexane:2-propanol (96:4); flow: 1.0 mL/min; major enantiomer $t_r = 19.7$ min, minor enantiomer $t_r = 26.0$ min.
(96:4); flow: 1.0 mL/min; major enantiomer $t_r = 27.7$ min, minor enantiomer $t_r = 57.6$ min.

$(1S,4S,8S)-8-(tert-Butyl-diphenyl-silyloxy-methyl)-3-pyridin-2-yl-2-oxa-3-aza-bicyclo[2.2.2]oct-5-ene \text{ (ent-anti-2c)} \text{ and } (1R,4R,7S)-7-(tert-Butyl-diphenyl-silyloxy-methyl)-3-pyridin-2-yl-2-oxa-3-aza-bicyclo[2.2.2]oct-5-ene \text{ (anti-3c)}$: According to GP2 with $8$ (7.5 mg, 8.1 µmol), $[\text{Cu}^I(\text{CH}_3\text{CN})_4]\text{PF}_6$ (3.0 mg, 8.1 µmol), $\text{CH}_2\text{Cl}_2$ (1 mL), 2-nitrosopyridine (9.5 mg, 88 µmol), diene $1c$ (28 mg, 80 µmol) and $\text{SiO}_2$-chromatography (pentane:MTBE, 5:1) to give 36 mg (99%) of a mixture of isomers. The isomer ratio was determined by chiral HPLC (ent-anti-2c: anti-3c:syn-isomers = 3.2:3.5:1.0). For analytical purposes a sample was repurified by flash chromatography (pentane:MTBE, 10:1).

**ent-anti-2c**: TLC: $R_f = 0.3$ (pentane:MTBE, 10:1). $[\alpha]^{25}_D = +59.0^\circ$ (c = 0.53, CHCl$_3$). FTIR (neat): $\nu = 3070, 2929, 2857, 1587, 1462, 1431, 1387, 1236, 1183, 1112, 1081, 1011, 965, 910, 869, 824, 779, 738, 702$ cm$^{-1}$. $^1$H-NMR (600 MHz, CDCl$_3$): $\delta =$ 8.25-8.24 (m, 1H), 7.68-7.67 (m, 4H), 7.54-7.51 (m, 1H), 7.45-7.37 (m, 6H), 6.92-6.91 (m, 1H), 6.80-6.78 (m, 1H), 6.41-6.39 (m, 1H), 6.09-6.06 (m, 1H), 5.49-5.48 (m, 1H), 4.69-4.68 (m, 1H), 3.46 (dd, $J = 10.2, 6.0$ Hz, 1H), 3.37-3.34 (m, 1H), 2.73-2.67 (m, 1H), 2.34-2.29 (m, 1H), 1.09 (s, 9H), 0.89-0.86 ppm (m, 1H). $^{13}$C-NMR (151 MHz, CDCl$_3$): $\delta =$ 163.8, 147.2, 137.4, 135.6, 135.5, 133.6, 133.5, 130.9, 130.5, 129.63, 129.61, 127.6, 116.6, 111.5, 69.7, 66.3, 54.2, 35.4, 29.7, 28.3, 19.2 ppm. HRMS (ESI) Exact mass calculated for $\text{C}_{28}\text{H}_{33}\text{N}_2\text{O}_2\text{Si}$ ([M + H]$^+$): 457.2306. Found: 457.2293. Enantiomeric excess (99% ee) was determined by chiral HPLC. Column: Chiralcel OD-RH; solvent: acetonitrile:water (3:1); flow: 0.7 mL/min; major enantiomer $t_r = 15.4$ min, minor enantiomer $t_r = 18.8$ min.

**anti-3c**: TLC: $R_f = 0.2$ (pentane:MTBE, 10:1). $[\alpha]^{25}_D = +75.6^\circ$ (c = 0.66, CHCl$_3$). FTIR (neat): $\nu = 3070, 2929, 2857, 1587, 1568, 1463, 1431, 1382, 1246, 1186, 1112, 1004, 960, 909, 883, 823, 781, 737,
702 cm\(^{-1}\). \(^{1}\)H-NMR (600 MHz, CDCl\(_3\)): \(\delta = 8.20-8.19\) (m, 1H), 7.66-7.64 (m, 4H), 7.55-7.52 (m, 1H), 7.45-7.37 (m, 6H), 6.97-6.95 (m, 1H), 6.79-6.77 (m, 1H), 6.29-6.26 (m, 1H), 6.23-6.21 (m, 1H), 5.25-5.23 (m, 1H), 4.99-4.97 (m, 1H), 3.56 (dd, \(J = 10.2, 6.0\) Hz, 1H), 3.17-3.14 (m, 1H), 2.78-2.72 (m, 1H), 2.29-2.25 (m, 1H), 1.07 (s, 9H), 0.89-0.85 ppm (m, 1H). \(^{13}\)C-NMR (75 MHz, CDCl\(_3\)): \(\delta = 163.2, 146.4, 138.0, 135.5, 133.5, 133.4, 132.3, 129.7, 129.1, 127.7, 116.5, 111.6, 71.8, 66.2, 52.3, 38.0, 29.7, 26.9, 26.8, 24.3, 19.2 ppm. HRMS (ESI) Exact mass calculated for C\(_{28}\)H\(_{33}\)N\(_2\)O\(_2\)Si ([M + H\(^{+}\)]: 457.2306. Found: 457.2302. Enantiomeric excess (88% ee) was determined by chiral HPLC, Column: Chiralcel OD-H; solvent: cyclohexane:2-propanol (99.5:0.5); flow: 1.0 mL/min; major enantiomer \(t_r = 15.9\) min, minor enantiomer \(t_r = 7.4\) min.

\((1\text{S,4R,8S})\)-8-Benzyl-3-pyridin-2-yl-2-oxa-3-aza-bicyclo[2.2.2]oct-5-ene (\textit{ent-anti-2d}) and \((1\text{S,4R,7R})\)-7-Benzyl-3-pyridin-2-yl-2-oxa-3-aza-bicyclo[2.2.2]oct-5-ene (\textit{anti-3d}): According to GP2 with \(8\) (10.8 mg, 11.6 \(\mu\)mol), [Cu\(^{1}\)(CH\(_3\)CN)\(_4\)]PF\(_6\) (4.3 mg, 12 \(\mu\)mol), CH\(_2\)Cl\(_2\) (1.2 mL), 2-nitrosopyridine (13.9 mg, 129 \(\mu\)mol), diene \(1d\) (20 mg, 0.12 mmol) and SiO\(_2\)-chromatography (pentane:MTBE, 5:1) to give 32 mg (99%) of \textit{ent-anti-2d} and \textit{anti-3d} as mixture isomers. The isomer ratio was determined by chiral HPLC (\textit{ent-anti-2d}: \textit{anti-3d}:syn-isomers = 2.3:2.5:1.0). For analytical purposes a sample was repurified by flash chromatography (pentane:MTBE, 9:1).

\textit{ent-anti-2d}: TLC: \(R_f = 0.2\) (pentane:MTBE, 10:1). FTIR (neat): \(\nu = 3058, 2924, 2853, 1587, 1496, 1461, 1432, 1244, 1146, 1012, 955, 865, 836, 780, 739, 701\) cm\(^{-1}\). \(^{1}\)H-NMR (600 MHz, CDCl\(_3\)): \(\delta = 8.26-8.15\) (m, 1H), 7.61-7.56 (m, 1H), 7.34-7.18 (m, 5H), 6.95-6.91 (m, 1H), 6.87-6.81 (m, 1H), 6.59-6.54 (m, 1H), 6.35-6.32 (m, 1H), 5.33-5.25 (m, 1H), 4.83-4.74 (m, 1H), 2.77-2.66 (m, 1H), 2.45-2.32 (m, 2H), 1.14-1.05 (m, 1H), 0.90-0.81 ppm (m, 1H). \(^{13}\)C-NMR (151 MHz, CDCl\(_3\)): \(\delta = 139.2, 131.6, 130.2, 129.2, 128.9, 128.5, 126.3, 116.4, 111.8, 70.3, 56.3, 41.3, 34.3, 31.6 ppm. HRMS (ESI) Exact mass calculated for C\(_{18}\)H\(_{19}\)N\(_2\)O ([M + H\(^{+}\)]: 279.1492. Found: 279.1487. Enantiomeric excess (98% ee) was determined by chiral HPLC. Column: Chiralcel OD-H; solvent:
cyclohexane:2-propanol (99.5:0.5); flow: 1.0 mL/min; major enantiomer \textit{t}_r = 28.0 \text{ min}, minor enantiomer \textit{t}_r = 40.0 \text{ min}.

**anti-3d:** TLC: \textit{R}_f = 0.1 (pentane:MTBE, 10:1). \([\alpha]^{D}_{25} = +110.0^\circ \text{ (c = 0.46, CHCl}_3\)). FTIR (neat): \nu = 3058, 2925, 1587, 1567, 1494, 1462, 1431, 1373, 1287, 1258, 1147, 1085, 1061, 1001, 956, 880, 780, 743, 701 \text{ cm}^{-1}. \textsuperscript{1}H-NMR (600 MHz, CDCl\textsubscript{3}): \delta = 8.13-8.12 \text{ (m, 1H)}, 7.43 \text{ (ddd, } J = 10.2, 9.0, 2.4 \text{ Hz, 1H}), 7.24-7.09 \text{ (m, 5H)}, 6.83-6.81 \text{ (m, 1H)}, 6.70 \text{ (ddd, } J = 9.0, 6.0, 1.2 \text{ Hz, 1H}), 6.38-6.33 \text{ (m, 2H), 5.26-5.23 \text{ (m, 1H)}, 4.43-4.41 \text{ (m, 1H)}, 2.70-2.63 \text{ (m, 1H), 2.42-2.28 \text{ (m, 3H), 1.19-1.15 ppm \text{ (m, 1H).} \textsuperscript{13}C-NMR (75 MHz, CDCl\textsubscript{3}): \delta = 163.3, 146.5, 139.4, 137.9, 132.7, 129.0, 128.7, 128.5, 126.3, 116.5, 111.6, 72.8, 52.7, 40.9, 37.2, 28.4 \text{ ppm. HRMS (ESI) Exact mass calculated for C}_{18}H_{19}N_2O ([M + H]^+) : 279.1492. Found: 279.1485. Enantiomeric excess (84\% ee) was determined by chiral HPLC. Column: Chiralcel OD-H; solvent: cyclohexane:2-propanol (99.5:0.5); flow: 1.0 mL/min; major enantiomer \textit{t}_r = 29.3 \text{ min, minor enantiomer \textit{t}_r = 20.1 \text{ min.}}

**Acetic acid (1S,4S,5S)-3-pyridin-2-yl-2-oxa-3-aza-bicyclo[2.2.2]oct-7-en-5-ylmethyl ester (ent-anti-2e) and Acetic acid (1R,4R,6S)-3-pyridin-2-yl-2-oxa-3-aza-bicyclo[2.2.2]oct-7-en-6-ylmethyl ester (anti-3e):** According GP2 with 8 (6.0 mg, 6.4 \text{ µmol}), \([Cu}(\text{CH}_3\text{CN})_4 PF_6 (2.4 mg, 6.4 \text{ µmol}), \text{CH}_2\text{Cl}_2 (1 \text{ mL}), 2\text{-nitrosopyridine (7.8 mg, 72. \text{ µmol}), diene 1e (10 mg, 65 \text{ µmol) and SiO}_2\text{-chromatography (pentane:MTBE, 1:1) to give 17 mg (99\%) of ent-anti-2e, anti-3e and both syn-isomers as an inseparable mixture of isomers. The isomer ratio was determined by chiral HPLC (ent-anti-2e: anti-3e:syn-isomers = 2.0:2.2:1.0). The isomers could not be separated. Therefore, \textsuperscript{1}H-NMR and \textsuperscript{13}NMR data are not provided. HRMS (ESI) Exact mass calculated for C}_{14}H_{17}N_2O_3 ([M + H]^+) : 261.1234. Found: 261.1226 \textbf{ent-anti-2e: Enantiomeric excess (98\% ee) was determined by chiral HPLC. Column: Chiralcel OD-H; solvent: cyclohexane:2-propanol**
(99:1); flow: 1.0 mL/min; major enantiomer $t_r = 42.8$ min, minor enantiomer $t_r = 31.1$ min.

**anti-3e**: Enantiomeric excess (82% ee) was determined by chiral HPLC. Column: Chiralcel OD-H; solvent: cyclohexane:2-propanol (99:1); flow: 1.0 mL/min; major enantiomer $t_r = 37.6$ min, minor enantiomer $t_r = 20.7$ min.

(1S,4S,8R)-8-Phenyl-3-pyridin-2-yl-2-oxa-3-aza-bicyclo[2.2.2]oct-5-ene (**ent-anti-2f**) and (1R,4R,7S)-7-Phenyl-3-pyridin-2-yl-2-oxa-3-aza-bicyclo[2.2.2]oct-5-ene (**anti-3f**): According to GP2 with 8 (10.7 mg, 11.5 µmol), [Cu\textsuperscript{I}(CH\textsubscript{3}CN)\textsubscript{4}]PF\textsubscript{6} (4.3 mg, 12 µmol), CH\textsubscript{2}Cl\textsubscript{2} (1.2 mL), 2-nitrosopyridine (13.7 mg, 127 µmol), diene 1d (18 mg, 0.12 mmol) and SiO\textsubscript{2}-chromatography (pentane:MTBE, 5:1) to give 30 mg (99%) of **ent-anti-2f** and **anti-3f** as mixture isomers. The isomer ratio was determined by chiral HPLC (**ent-anti-2f**: anti-3f = 1.0:1.2). For analytical purposes a sample was repurified by flash chromatography (pentane:MTBE, 10:1).

**ent-anti-2f**: TLC: $R_f = 0.2$ (pentane:MTBE, 5:1). FTIR (neat): $\nu = 3057$, 2932, 1587, 1493, 1461, 1432, 1371, 1280, 1236, 1069, 986, 892, 830, 771, 740, 700 cm\textsuperscript{-1}. $^1$H-NMR (300 MHz, CDCl\textsubscript{3}): $\delta = 8.19-8.09$ (m, 1H), 7.52-7.47 (m, 1H), 7.25-7.12 (m, 5H), 6.92-6.89 (m, 1H), 6.76-6.72 (m, 1H), 6.59-6.54 (m, 1H), 6.19-6.17 (m, 1H), 5.35-5.33 (m, 1H), 4.86-4.83 (m, 1H), 3.66-3.60 (m, 1H), 2.74-2.65 (m, 1H), 1.65-1.59 ppm (m, 1H).

$^{13}$C-NMR (75 MHz, CDCl\textsubscript{3}): $\delta = 162.9, 146.5, 142.9, 138.1, 131.6, 130.8, 128.4, 128.1, 126.7, 116.7, 111.7, 70.5, 57.8, 38.5, 33.7 ppm. HRMS (ESI) Exact mass calculated for C\textsubscript{17}H\textsubscript{17}N\textsubscript{2}O ([M + H]\textsuperscript{+}): 265.1335. Found: 265.1339. Enantiomeric excess (98% ee) was determined by chiral HPLC. Column: Chiralcel OD-H; solvent: cyclohexane:2-propanol (99.5:0.5); flow: 1.0 mL/min; major enantiomer $t_r = 25.4$ min, minor enantiomer $t_r = 71.2$ min.
anti- 3f: TLC: \( R_f = 0.1 \) (pentane:MTBE, 5:1). \( [\alpha]^{25}_{D} = +263.4^\circ \) (c = 0.55, CHCl\(_3\)). FTIR (neat): \( \nu = 3054, 2932, 1589, 1493, 1432, 1373, 1247, 1216, 1069, 1018, 892, 873, 754, 704, 667 \) cm\(^{-1}\). \( ^1\)H-NMR (300 MHz, CDCl\(_3\)): \( \delta = 8.17-8.15 \) (m, 1H), 7.52-7.46 (m, 1H), 7.24-7.10 (m, 5H), 6.93-6.91 (m, 1H), 6.76-6.72 (m, 1H), 6.49-6.44 (m, 1H), 6.33-6.28 (m, 1H), 5.45-5.44 (m, 1H), 4.69-4.68 (m, 1H), 3.68-3.63 (m, 1H), 2.75-2.66 (m, 1H), 1.85-1.78 ppm (m, 1H). \( ^{13}\)C-NMR (75 MHz, CDCl\(_3\)): \( \delta = 163.2, 146.6, 141.8, 137.9, 132.9, 129.7, 128.4, 128.2, 126.7, 116.7, 111.6, 74.2, 52.9, 41.7, 30.3 \) ppm. HRMS (ESI) Exact mass calculated for C\(_{17}\)H\(_{17}\)N\(_2\)O ([M + H\(^+\)]: 265.1335. Found: 265.1338. Enantiomeric excess (94% ee) was determined by chiral HPLC. Column: Chiralcel OD-H; solvent: cyclohexane:2-propanol (99.5:0.5); flow: 1.0 mL/min; major enantiomer \( t_r = 19.4 \) min, minor enantiomer \( t_r = 17.3 \) min.

**Synthesis of peracetylated 2-epi-valdamine 11**

\( (1S,4S,7R)-7-(\text{tert-Butyl-diphenyl-silanyloxymethyl})-3\text{-pyridin-2-yl-2-oxa-3-aza-bicyclo[2.2.2]oct-5-ene (ent-anti-3c):} \) According to GP2 with ent-8 (360 g, 387 \( \mu \)mol), \( [\text{Cu}(\text{CH}_3\text{CN})_4]\)PF\(_6\) (144 mg, 387 \( \mu \)mol), CH\(_2\)Cl\(_2\) (25 mL), 2-nitrosopyridine in 6 mL CH\(_2\)Cl\(_2\) (0.46 g, 4.2 mmol), diene 1c (1.35 g, 3.87 mmol) in CH\(_2\)Cl\(_2\) (20 mL) and SiO\(_2\)-chromatography (pentane:MTBE, 10:1) to give 775 mg (44%) of ent-anti-3c. Enantiomeric excess (89% ee) was determined by chiral HPLC, Column: Chiralcel OD-H; solvent: cyclohexane:2-propanol (99.5:0.5); flow: 1.0 mL/min; major enantiomer \( t_r = 7.8 \) min, minor enantiomer \( t_r = 17.3 \) min. \( [\alpha]^{25}_{D} = -74.3^\circ \) (c = 1.03, CHCl\(_3\)).

**Acetic acid (1S,4S,6R)-6-acetoxymethyl-4-(acetyl-pyridin-2-yl-amino)-cyclohex-2-enyl ester (9):** The N-O bond of the ent-anti-3c was cleaved according to the previously reported procedure\(^3\). Mo(CO)\(_6\) (0.14 mg, 0.53 mmol) and NaBH\(_4\) (24 mg, 0.65 mmol) was added to the suspension of ent-anti-3c (242 mg, 530 \( \mu \)mol) in MeOH:H\(_2\)O (10:1, 4.0 mL). Then the reaction mixture was heated to 65 \( ^\circ \)C and stirred for 10 h at that
temperature. The precipitate was removed by filtration through a short pad of celite and the filtrate was concentrated in vacuo. The residue was dissolved in CH$_2$Cl$_2$, washed (brine), dried (MgSO$_4$) and concentrated under reduced pressure. To remove the silyl group, the resulting residue was dissolved in THF (3 mL), treated with TBAF (2.4 mL, 2.4 mmol) and stirred for 24 h at room temperature. Then the volatiles were removed under reduced pressure and the residue was passed through a short pad of silica gel (MeOH:MTBE, 1:10) to remove the excess TBAF. CH$_3$MgCl (3 M in THF, 0.71 mL, 2.1 mmol) was added dropwise to the solution of the resulting mass in THF (3.0 mL) at rt and was stirred for 10 min at that temperature. Acetyl chloride (0.23 mL, 3.2 mmol) was then added and stirred at rt for 10 h. The reaction mixture was then diluted with CH$_2$Cl$_2$, washed (brine), dried (MgSO$_4$), concentrated under vacuum and subjected to flash column chromatography (MTBE:MeOH, 20:1) to give 9 as a colorless oil (142 mg, 77 %, over three steps). TLC: $R_f = 0.2$ (MTBE:MeOH, 20:1). $[\alpha]^{25}_D = -5.6^\circ$ (c = 1.16, CHCl$_3$). FTIR (neat): $\nu = 2937, 1737, 1662, 1584, 1469, 1437, 1372, 1315, 1240, 1025, 785, 752$. $^1$H-NMR (300 MHz, CDCl$_3$): $\delta = 8.58-8.56$ (m, 1H), 7.78 (dt, J = 2.0, 7.7 Hz, 1H), 7.33 (ddd, J = 1.0, 4.9, 7.5 Hz, 1H), 7.14 (td, J = 0.9, 7.9 Hz, 1H), 5.87-5.82 (m, 1H), 5.72-5.67 (m, 1H), 5.40-5.35 (m, 1H), 5.01-4.98 (m, 1H), 3.94 (d, J = 5.8 Hz, 2H), 2.11-2.00 (m, 1H), 2.03 (s, 3H), 1.94 (s, 3H), 1.92-1.84 (m, 1H), 1.81 (s, 3H), 1.75-1.64 ppm (m, 1H). $^{13}$C-NMR (75 MHz, CDCl$_3$): $\delta = 170.9, 170.4, 169.9, 153.5, 149.6, 138.3, 130.5, 128.7, 124.4, 123.5, 67.9, 64.1, 48.1, 34.7, 26.9, 23.2, 21.0, 20.8 ppm. HRMS (ESI): Exact mass calculated for C$_{18}$H$_{22}$N$_2$O$_5$Na ([M + Na]$^+$): 369.1421. Found: 369.1418.

**Acetic acid (1R,2S,3R,4S,6R)-2,3-diacetoxy-6-acetoxymethyl-4-(acetyl-pyridin-2-yl-amino)-cyclohexyl ester (10):** K$_2$OsO$_4$, 2H$_2$O (25 mg, 65 µmol) and NMO (0.18 mg, 1.5 mmol) were added to a solution of 9 (311 mg, 898 µmol) in acetone:water (9:1, 4 mL). The reaction mixture was then stirred for 24 h at rt. Then the resulting mixture was concentrated under reduced pressure and the residue was passed through a short pad of silica gel (CH$_2$Cl$_2$:MeOH, 20:1). The dihydroxylated compound was then dissolved in pyridine (2.5 mL). Acetic anhydride (0.5 mL, 5.29 mmol) was added and the solution was stirred for 24 h at rt. Then the solvent was removed under reduced pressure and the residue was purified by flash column chromatography (MTBE:MeOH, 12:1) to
obtain 10 as a colorless foam (335 mg, 80%, over two steps). TLC: \( R_f = 0.3 \) (MTBE:MeOH, 10:1). \([\alpha]^{D}_{25} = +7.5^\circ (c = 0.85, \text{CHCl}_3)\). FTIR (CDCl\(_3\)): \( \nu = 2940, 1745, 1667, 1585, 1469, 1438, 1371, 1231, 1045, 920, 731 \text{ cm}^{-1} \). \(^1\)H-NMR (300 MHz, CDCl\(_3\)): \( \delta = 860-8.58 (m, 1H), 7.85-7.79 (m, 1H), 7.37-7.32 (m ,1H), 7.17-7.15 (m, 1H), 5.23-4.98 (m, 4H), 4.32-4.26 (m, 1H), 4.21-4.15 (m, 1H), 2.14-1.97 (m, 3H), 2.08 (s, 3H), 2.06 (s, 3H), 2.00 (s, 3H), 1.99 (s, 3H), 1.81 ppm (s, 3H). \(^1^3\)C-NMR (101 MHz, CDCl\(_3\)): \( \delta = 170.6, 170.3, 169.7, 169.4, 149.8, 138.6, 124.0, 123.6, 122.8, 70.0, 69.5, 69.4, 63.6, 50.0, 37.1, 26.8, 23.4, 20.9, 20.84, 20.79, 20.7 ppm. HRMS (ESI) Exact mass calculated for \( \text{C}_{22}\text{H}_{28}\text{N}_{2}\text{O}_{9}\text{Na} \) \([\text{M + Na}^+]\): 487.1687. Found: 487.1684.

**Acetic acid (1R,2S,3R,4S,6R)-2,3-diacetoxy-6-acetoxyethyl-4-acetylamino-cyclohexyl ester (11):** Rh/C (90 mg, 44 \( \mu \)mol) was added to a solution of 10 (100 mg, 215 \( \mu \)mol) in glacial acetic acid (5 mL) and stirred in an autoclave under hydrogen pressure (74 bar) at 65 \( ^\circ \text{C} \) for 28 h. Then the reaction mixture was filtered through a short pad of celite. The celite pad was washed with CH\(_2\)Cl\(_2\):MeOH (1:1), the combined organic layer were concentrated under reduced pressure and the residue was subjected to column chromatography (cyclohexane:isopropanol, 2:1) to yield 11 as a colorless oil (53 mg, 64 %). TLC: \( R_f = 0.3 \) (cyclohexane:isopropanol, 2:1). \([\alpha]^{D}_{25} = +16.5^\circ (c = 1.26, \text{CHCl}_3)\). (lit\(^4\). \([\alpha]^{D}_{24} = +18.0^\circ (c = 1.1, \text{CHCl}_3)\)). FTIR (CDCl\(_3\)): \( \nu = 2958, 1746, 1653, 1546, 1370, 1228, 1044 \text{ cm}^{-1} \). \(^1\)H-NMR (300 MHz, CDCl\(_3\)): \( \delta = 5.97 \) (br.s, 1H), 5.26-5.23 (m, 1H), 5.18-5.09 (m, 2H), 4.31-4.24 (m, 1H), 4.15-4.03 (m, 2H), 2.22-1.90 (m, 2H), 2.09 (s, 3H), 2.05 (s, 3H), 2.03 (s, 3H), 2.00 (s, 3H), 1.99 (s, 3H), 1.87-1.78 ppm (m, 1H). \(^1^3\)C-NMR (75 MHz, CDCl\(_3\)): \( \delta = 170.7, 169.97, 169.89, 169.79, 169.6, 70.5, 70.1, 69.5, 63.8, 46.4, 36.3, 27.8, 23.3, 20.8, 20.7, 20.6 ppm. HRMS (ESI) Exact mass calculated for \( \text{C}_{17}\text{H}_{25}\text{NO}_{9}\text{Na} \) \([\text{M + Na}^+]\): 410.1422. Found: 410.1421.

**References:**


Catalytic Enantioselective Regiodivergent Nitroso Diels-Alder Reaction

$^1$H and $^{13}$C-NMR Spectra
Catalytic Enantioselective Regiodivergent Nitroso Diels-Alder Reaction
Catalytic Enantioselective Regiodivergent Nitroso Diels-Alder Reaction
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Catalytic Enantioselective Regiodivergent Nitroso Diels-Alder Reaction

[Chemical structures and spectra images are present, showing molecular structures with peak assignments and spectra graphs.]

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Determination of Relative Configurations

$^1$H-NMR (600 MHz, CDCl$_3$)

$^{13}$C-NMR (151 MHz, CDCl$_3$)
Catalytic Enantioselective Regiodivergent Nitroso Diels-Alder Reaction

NOE Experiment

![Diagram of NOE Experiment]

ppm (H)

NOE Experiment

![Diagram of NOE Experiment]

ppm (H)

NOE Experiment

![Diagram of NOE Experiment]

ppm (H)
Catalytic Enantioselective Regiodivergent Nitroso Diels-Alder Reaction

$^1$H-NMR (600 MHz, CDCl$_3$)

$^{13}$C-NMR (151 MHz, CDCl$_3$)
Catalytic Enantioselective Regiodivergent Nitroso Diels-Alder Reaction

\begin{align*}
\text{\textsuperscript{1}H-\textsuperscript{1}C-COSY (600 MHz, CDCl\textsubscript{3})} \\
\text{\textsuperscript{1}H-\textsuperscript{13}C-HSQC (600 MHz, CDCl\textsubscript{3})}
\end{align*}
Catalytic Enantioselective Regiodivergent Nitroso Diels-Alder Reaction
Catalytic Enantioselective Regiodivergent Nitroso Diels-Alder Reaction

$^1$H-NMR (600 MHz, CDCl$_3$)

$^{13}$C-NMR (151 MHz, CDCl$_3$)
Catalytic Enantioselective Regiodivergent Nitroso Diels-Alder Reaction

$^1$H-$^1$H-COSY (600 MHz, CDCl$_3$)

$^1$H-$^{13}$C-HSQC (600 MHz, CDCl$_3$)
Catalytic Enantioselective Regiodivergent Nitroso Diels-Alder Reaction

\[^{1}H\text{-NMR (600 MHz, CDCl}_3\text{)}\]

\[^{13}C\text{-NMR (151 MHz, CDCl}_3\text{)}\]

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Catalytic Enantioselective Regiodivergent Nitroso Diels-Alder Reaction

\[ ^1H-^1H-COSY (600 MHz, CDCl_3) \]

\[ ^1H-^{13}C-HSQC (600 MHz, CDCl_3) \]
Catalytic Enantioselective Regiodivergent Nitroso Diels-Alder Reaction
HPLC Traces

racemic ent-anti-2a-OH

ent-anti-2a-OH

racemic anti-3a-OH

anti-3a-OH
Catalytic Enantioselective Regiodivergent Nitroso Diels-Alder Reaction

**racemic ent-anti-2b** (after desilylation)

**racemic anti-3b** (after desilylation)

**ent-anti-2b-OH**

**anti-3b-OH**

**racemic ent-anti-2c**

**ent-anti-2c**
Catalytic Enantioselective Regiodivergent Nitroso Diels-Alder Reaction

racemic anti-3c

anti-3c

racemic syn-isomer  racemic ent-anti-2d

syn-isomer  ent-anti-2d
Catalytic Enantioselective Regiodivergent Nitroso Diels-Alder Reaction
Catalytic Enantioselective Regiodivergent Nitroso Diels-Alder Reaction

**racemic ent-anti-2f**

**racemic anti-3f**

**anti-3f**