Enantiodivergent [4+2] Cycloaddition of Dienolates by Polyfunctional Lewis Acid/Zwitterion Catalysis
Vukoslava Miskov-Pajic, Felix Willig, Daniel M. Wanner, Wolfgang Frey, and René Peters*
anie_202009093_sm_m miscellaneous_information.pdf
Table of Contents

General Remarks .............................................................................................................. 6

General Procedures (GP) .................................................................................................. 7

General Procedure for the Imine-Synthesis (GP1) .......................................................... 7

General Procedure for the Metal Complexation (GP2) ...................................................... 7

General Procedure for the Activation of the Complexes (GP3) ........................................ 8

General Procedure for Catalytic Diels–Alder Reactions of 3-Hydroxypyrones (GP4) .......... 8

General Procedure for Catalytic Diels–Alder Reactions of 3-Hydroxypyrones in Control Experiments (GP5) ............................................................................................................. 9

General Procedure for the Catalytic Diels–Alder Reactions of 3-Hydroxypyridones (GP6) .... 9

General Procedure for the Cycloaddition Reaction with Enone (8) (GP7) ......................... 10

General Procedure for the Determination of ee values with (R)-BINOL (GP8) ................. 10

Substrate Synthesis .......................................................................................................... 11

4-Chloro-3-hydroxy-2-pyrene (1c) .................................................................................... 11

N-2-Nitrobenzenesulfonyl-4-allyl-3-hydroxy-2-pyridone (4b) .......................................... 11

N-2-Nitrobenzenesulfonyl-4-chloro-3-hydroxy-2-pyridone (4c) ........................................ 12

Ligand Synthesis ................................................................................................................ 12

(R)-2-(Imidazol-1-yl)-2′-hydroxy-1,1′-binaphthyl (K1) ......................................................... 12

(R)-3-(5-(tert-Butyl)-3-formyl-2-hydroxybenzyl)-1-(2′-hydroxy-[1,1′-binaphthalen]-2-yl)-1H-imidazol-3-ium chloride (K2) ............................................................................................................... 13

3-(5-(tert-Butyl)-2-hydroxy-3-(((E)-(((1S,2S)-2-(naphthalene-1-sulfonamido)-1,2-diphenylethylimino)methyl)benzyl)-1-((R)-2′-hydroxy-[1,1′-binaphthalen]-2-yl)-1H-imidazol-3-ium chloride (L1b-(S,S)) ........................................................................................................... 13

3-(5-(tert-Butyl)-2-hydroxy-3-(((1R,2R)-2-(naphthalene-1-sulfonamido)-1,2-diphenylethylimino)methyl)benzyl)-1-((R)-2′-hydroxy-[1,1′-binaphthalen]-2-yl)-1H-imidazol-3-ium chloride (L1b-(R,R)) ........................................................................................................... 14

3-(5-(tert-Butyl)-2-hydroxy-3-(((1S,2S)-2-(anthracene-9-sulfonamido)-1,2-diphenylethylimino)methyl)benzyl)-1-((R)-2′-hydroxy-[1,1′-binaphthalen]-2-yl)-1H-imidazol-3-ium chloride (L1c-(S,S)) ........................................................................................................... 15

3-(5-(tert-Butyl)-2-hydroxy-3-(((1S,2S)-2-(naphthalene-2-sulfonamido)-1,2-diphenylethylimino)methyl)benzyl)-1-((R)-2′-hydroxy-[1,1′-binaphthalen]-2-yl)-1H-imidazol-3-ium chloride (L1d-(S,S)) ........................................................................................................... 16

3-(5-(tert-Butyl)-2-hydroxy-3-(((1R,2R)-2-(naphthalene-2-sulfonamido)-1,2-diphenylethylimino)methyl)benzyl)-1-((R)-2′-hydroxy-[1,1′-binaphthalen]-2-yl)-1H-imidazol-3-ium chloride (L1d-(R,R)) ........................................................................................................... 16

3-(5-(tert-Butyl)-2-hydroxy-3-(((1S,2S)-2-(2-nitrobenzenesulfonylamido)-1,2-diphenylethylimino)methyl)benzyl)-1-((R)-2′-hydroxy-[1,1′-binaphthalen]-2-yl)-1H-imidazol-3-ium chloride (L1e-(S,S)) ........................................................................................................... 17
3-(5-(tert-Butyl)-2-hydroxy-3-((E)-(((1R,2R)-2-(2-nitrobenzenesulfonylamido)-1,2-diphenylethyl)limino)methyl)benzyl)-1-((R)-2'-hydroxy-[1,1',binaphthalen]-2-yl)-1H-imidazol-3-ium chloride (L1e-(R,R)) ................................................................. 18

3-(5-(tert-Butyl)-2-hydroxy-3-((E)-(((1S,2S)-2-(4-nitrobenzenesulfonylamido)-1,2-diphenylethyl)limino)methyl)benzyl)-1-((R)-2'-hydroxy-[1,1',binaphthalen]-2-yl)-1H-imidazol-3-ium chloride (L1f-(S,S)) ................................................................. 18

3-(5-(tert-Butyl)-2-hydroxy-3-((E)-(((1R,2R)-2-(2-nitrobenzenesulfonylamido)-1,2-diphenylethyl)limino)methyl)benzyl)-1-((R)-2'-hydroxy-[1,1',binaphthalen]-2-yl)-1H-imidazol-3-ium chloride (L1f-(R,R)) ................................................................. 19

3-(5-(tert-Butyl)-2-hydroxybenzyl)-1-((R)-2'-hydroxy-[1,1',binaphthalen]-2-yl)-1H-imidazol-3-ium chloride (L1g-(S,S)). ................................................................. 20

3-(5-(tert-Butyl)-2-hydroxybenzyl)-1-((R)-2'-hydroxy-[1,1',binaphthalen]-2-yl)-1H-imidazol-3-ium chloride (L1g-(R,R)) ................................................................. 20

3-(5-(tert-Butyl)-((E)-(((1S,2S)-2-(2-(p-tolylsulfonylamido)ethyl)limino)methyl)-2-hydroxybenzyl)-1-((R)-2'-hydroxy-[1,1',binaphthalen]-2-yl)-1H-imidazol-3-ium chloride (L1h-(S,S)). ................................................................. 21

3-(5-(tert-Butyl)-((E)-(((1S,2S)-2-(2-(pentfluorobenzylsulfonylamido)ethyl)limino)methyl)-2-hydroxybenzyl)-1-((R)-2'-hydroxy-[1,1',binaphthalen]-2-yl)-1H-imidazol-3-ium chloride (L1i-(S,S)) ................................................................. 22

3-(5-(tert-Butyl)-((E)-(((1S,2S)-2-(2-(pentfluorobenzylsulfonylamido)ethyl)limino)methyl)-2-hydroxybenzyl)-1-((R)-2'-hydroxy-[1,1',binaphthalen]-2-yl)-1H-imidazol-3-ium chloride (L1i-(R,R)) ................................................................. 23

Synthesis of the Complexes........................................................................................................... 24

3-(5-(tert-Butyl)-((E)-(((1S,2S)-2-((1-naphthalene)sulfonylamido)ethyl)limino)methyl)-2-hydroxybenzyl)-1-((R)-2'-hydroxy-[1,1',binaphthalen]-2-yl)-1H-imidazol-3-ium copper (II)-chloride (C1b-(S,S)) ........................................................................................................... 24

3-(5-(tert-Butyl)-((E)-(((1S,2S)-2-((1-naphthalene)sulfonylamido)ethyl)limino)methyl)-2-hydroxybenzyl)-1-((R)-2'-hydroxy-[1,1',binaphthalen]-2-yl)-1H-imidazol-3-ium copper (II)-chloride (C1b-(R,R)) ........................................................................................................... 24

3-(5-(tert-Butyl)-((E)-(((1S,2S)-2-((2-anthracene-9-sulfonylamido)ethyl)limino)methyl)-2-hydroxybenzyl)-1-((R)-2'-hydroxy-[1,1',binaphthalen]-2-yl)-1H-imidazol-3-ium copper (II)-chloride (C1c-(S,S)) ........................................................................................................... 25

3-(5-(tert-Butyl)-((E)-(((1S,2S)-2-((2-naphthalene)sulfonylamido)ethyl)limino)methyl)-2-hydroxybenzyl)-1-((R)-2'-hydroxy-[1,1',binaphthalen]-2-yl)-1H-imidazol-3-ium copper (II)-chloride (C1d-(S,S)) ........................................................................................................... 26

3-(5-(tert-Butyl)-((E)-(((1R,2R)-2-((2-naphthalene)sulfonylamido)ethyl)limino)methyl)-2-hydroxybenzyl)-1-((R)-2'-hydroxy-[1,1',binaphthalen]-2-yl)-1H-imidazol-3-ium copper (II)-chloride (C1d-(R,R)) ........................................................................................................... 27

3-(5-(tert-Butyl)-((E)-(((1S,2S)-2-((2-nitrophenyl)sulfonylamido)ethyl)limino)methyl)-2-hydroxybenzyl)-1-((R)-2'-hydroxy-[1,1',binaphthalen]-2-yl)-1H-imidazol-3-ium copper (II)-chloride (C1e-(S,S)) ........................................................................................................... 27
3-[(tert-Butyl)-3-((E)-(((1R,2R)-1,2-diphenyl-2-((2-nitrophenyl)sulfonamido)ethyl)limino)methyl)-2-hydroxybenzyl]-1-(2'-hydroxy-[1,1'-binaphthalen]-2-yl)-1H-imidazol-3-ium copper (II)-chloride (C1e(R,R)) ........................................... 28

3-[(tert-Butyl)-3-((E)-(((1S,2S)-1,2-diphenyl-2-((4-nitrophenyl)sulfonamido)ethyl)limino)methyl)-2-hydroxybenzyl]-1-(2'-hydroxy-[1,1'-binaphthalen]-2-yl)-1H-imidazol-3-ium copper (II)-chloride (C1f(S,S)) .................................................. 29

3-[(tert-Butyl)-3-((E)-(((1R,2R)-1,2-diphenyl-2-((4-nitrophenyl)sulfonamido)ethyl)limino)methyl)-2-hydroxybenzyl]-1-(2'-hydroxy-[1,1'-binaphthalen]-2-yl)-1H-imidazol-3-ium copper (II)-chloride (C1f(R,R)) .................................................. 30

3-[(tert-Butyl)-2-hydroxy-3-((E)-(((1S,2S)-2-(methylsulfonamido)-1,2-diphenylethyl)limino)methyl)benzyl]-1-((R)-2'-hydroxy-[1,1'-binaphthalen]-2-yl)-1H-imidazol-3-ium copper (II) chloride (C1g(S,S)) ...................................................................... 30

3-[(tert-Butyl)-3-((E)-(((1R,2R)-1,2-diphenyl-2-(methylsulfonamido)ethyl)limino)methyl)-2-hydroxybenzyl]-1-(2'-hydroxy-[1,1'-binaphthalen]-2-yl)-1H-imidazol-3-ium-copper(II)chloride (C1g(R,R)) ...................................................................... 31

3-[(tert-Butyl)-3-((E)-(((1S,2S)-1,2-diphenyl-2-((4-methylbenzene)sulfonamido)ethyl)limino)methyl)-2-hydroxybenzyl]-1-(2'-hydroxy-[1,1'-binaphthalen]-2-yl)-1H-imidazol-3-ium copper (II)-chloride (C1h(S,S)) .................................................. 32

3-[(tert-Butyl)-3-((E)-(((1R,2R)-1,2-diphenyl-2-((4-methylbenzene)sulfonamido)ethyl)limino)methyl)-2-hydroxybenzyl]-1-(2'-hydroxy-[1,1'-binaphthalen]-2-yl)-1H-imidazol-3-ium copper (II)-chloride (C1h(R,R)) .................................................. 33

3-[(tert-Butyl)-3-((E)-(((1S,2S)-1,2-diphenyl-2-((4-perfluorophenyl)sulfonamido)ethyl)limino)methyl)-2-hydroxybenzyl]-1-(2'-hydroxy-[1,1'-binaphthalen]-2-yl)-1H-imidazol-3-ium copper (II)-chloride (C1i(S,S)) ...................................................................... 33

3-[(tert-Butyl)-3-((E)-(((1R,2R)-1,2-diphenyl-2-((4-perfluorophenyl)sulfonamido)ethyl)limino)methyl)-2-hydroxybenzyl]-1-(2'-hydroxy-[1,1'-binaphthalen]-2-yl)-1H-imidazol-3-ium copper (II)-chloride (C1i(R,R)) ...................................................................... 34

Screening of the Sulfonyle Residues of Catalyst C1 ................................................................................................................................. 36

Investigation of Maleimide Dienophiles (2) and Maleic Anhydride (6) in the Diels-Alder Reaction with 3-Hydroxypyrrone (1a). ........................................................................................................................................... 37

Catalytic Diels−Alder Reactions of 3-Hydroxypyrrone in Control Experiments ................................................................. 38

Catalytic Diels−Alder Reactions of 3-Hydroxypyrrone in Control Experiments ................................................................. 39

Characterization of Diels-Alder Adducts ................................................................................................................................. 40

(3aR,4S,7S,7aR)-4,7-Ethenopyranol [3,4-c] pyrrole-1,3,6(2H)-trione-3a,4,7,7a-tetrahydro-7-hydroxy-2-methyl (ent-3aA) .......................................................................................................................... 40

(3aS,4S,7S,7aR)-4,7-Ethenopyranol [3,4-c] pyrrole-1,3,6(2H)-trione-3a,4,7,7a-tetrahydro-7-hydroxy-2-(phenylmethyl) (ent-3aB) .......................................................................................................................... 40

(3aS,4S,7S,7aR)-4,7-Ethenopyranol [3,4-c] pyrrole-1,3,6(2H)-trione-3a,4,7,7a-tetrahydro-7-hydroxy-2-(4-nitrophenyl) (ent-3aC) .......................................................................................................................... 41

(3aS,4S,7S,7aR)-4,7-Ethenopyranol [3,4-c] pyrrole-1,3,6(2H)-trione-3a,4,7,7a-tetrahydro-7-hydroxy-2-cyclohexyl (ent-3aD) .......................................................................................................................... 41

(3aR,4R,7S,7aS)-4,7-Ethenopyranol [3,4-c] pyrrole-1,3,6(2H)-trione-3a,4,7,7a-tetrahydro-7-hydroxy-2-tert-Butyloxycarbonyl (3aE) .......................................................................................................................... 42
Derivatisation of the Catalytic Product

Confirming the Configurational Outcome with 2D-NMR Experiments of Compound 11.

Derivatisation of the Catalytic Product 11.
General Remarks

All reactions were performed in oven-dried glassware (stored in an oven, at 150 °C) and under a positive pressure of nitrogen, unless otherwise indicated. Technical grade solvents (dichloromethane (DCM), petroleum ether (PE), ethyl acetate (EE), diethylether (Et₂O), tetrahydrofuran (THF) and toluene) were distilled before use. Dry solvents like DCM, Et₂O, toluene, THF and acetonitrile were taken from solvent purification systems (MBraun MB SPS-800). Purchased chemicals were used without further purification. Analytical thin layer chromatography (TLC) was performed on silica gel 60F-254 TLC plates and compound spots were visualized by fluorescence quenching under UV light (254 nm) or by staining with KMnO₄/NaOH. Purification by flash-chromatography was performed on silica gel 60 (40-63 μm particle size), using a forced flow of eluent. All catalytic reactions were performed in oven dried Schlenk vials under a positive pressure of nitrogen unless otherwise indicated. In reactions where low temperatures were necessary a cryostatic temperature regulator was used. n-Heptane and i-propanol for HPLC were purchased in HPLC-quality and used without further purification.

N-Methyl maleimide 2A, maleimide 2F, N-Phenyl maleimide 2G, maleic anhydride 6 and trans-β-nitrostyrene 10 were purchased from commercial supplier (Sigma-Aldrich) and were used without further purification. All other maleimides were synthesized according to literature known procedures.1 2-Pyrones 1a², 1b³, 1d⁴ and pyridone 4a⁵ were prepared according to literature methods.

NMR data were recorded on Bruker Avance spectrometers operating at Larmor frequencies of 700, 500, 400 or 300 MHz (¹H), 176, 125, 100 or 75 MHz (¹³C) and 376 MHz (¹⁹F). Chemical shifts δ are referred in terms of ppm. J-Coupling constants are given in Hz. The following abbreviations classify the multiplicity: s (singlet), d (doublet), t (triplet), q (quartet), quint (quintet), sept (septet), m (multiplet), dd (doublet of doublets), dt (doublet of triplets), td (triplet of doublets) and br (broad signal). Infrared spectra were recorded by the IR service of the University of Stuttgart on an FT-IR spectrometer (Bruker Alpha FT-IR) with an ATR unit and the signals are given by wavenumbers (cm⁻¹). Optical rotation was measured on a Perkin Elmer 241 Polarimeter operating at the sodium D line (λ₁ = 589 nm) and mercury lines (λ₁ = 578 nm and λ₂ = 546 nm) with a 100 mm path cell length. Melting points were measured using a melting point apparatus (Büchi 535) in open glass capillaries. Mass spectra were measured on a Finnigan MAT 95 for CI and EI and a Bruker MicroTOFQ for ESI and obtained from the MS service of the University of Stuttgart. The UV-Vis spectra were recorded with a Lambda 365-Spectrometer (PerkinElmer). Single crystal X-ray analysis was performed by Dr. Wolfgang Frey, University of Stuttgart, on a Bruker Kappa APEXII Duo (Cu Kα 1.54178Å and Mo Kα 0.71073 Å). Enantiomeric excesses (ee) were determined by high performance liquid chromatography (HPLC) or NMR spectroscopy using the (R)-BINOL. The applied method is given in the description of the corresponding product.

The catalysts C1a, C2, C3, C4, C5 and C6 were synthesized according to our previously described protocols.⁶
General Procedures (GP)

General Procedure for the Imine-Synthesis (GP1)

The corresponding ligands were synthesized following the literature procedure. The corresponding aldehyde (1.0 equiv.) and the corresponding amine (1.0 equiv.) were dissolved in dry DCM (5 mL/mmol) in the presence of molecular sieves (4 Å) under nitrogen atmosphere and the reaction mixture was stirred for 18 h. After that, the reaction mixture was filtered through celite, the filter cake washed with dry DCM (5 mL/1 mmol) and the solvent removed under reduced pressure. The resulting yellow solid was dissolved in a small amount of dry DCM (0.2 mL/mmol) and added to n-pentane (2 mL/mmol). The formed precipitate was filtered to afford the pure ligand as a yellow solid.

General Procedure for the Metal Complexation (GP2)

Based on a literature protocol, the corresponding ligand (1.0 equiv.) was dissolved in dry acetonitrile (5 mL/0.01 mmol) and the corresponding metal source (Cu(acac)$_2$, 1.0 equiv.) was added and the mixture was stirred at 60 °C for 16 h. The solution was filtered over celite and the filter cake washed with DCM. Subsequently, the solvent was removed under reduced pressure. The residue was dissolved in a small amount of DCM and the product was precipitated by adding n-pentane to the solution. The suspension was centrifuged, the supernatant solution was decanted off and the residue was then dried under high vacuum to afford the corresponding pre-catalyst.
General Procedure for the Activation of the Complexes (GP3)

Based on a literature protocol, the complexes were dissolved in a solvent mixture of DCM/THF/Et₃N (66/33/1) and the solution was filtered over a small silica pad in a glass frit and eluted with the same mixture. The volatiles were removed under reduced pressure and the product (activated catalyst) was dissolved in a small amount of DCM (0.1 mL), precipitated in n-pentane (5 mL), filtered and dried under high vacuum for 2 h. The activated catalyst could be used without further purification in the catalytic DA reactions.

General Procedure for Catalytic Diels–Alder Reactions of 3-Hydroxypyrones (GP4)

To an oven-dried Schlenk vial containing activated catalyst C1 (0.005 mmol, 5 mol%) and N-substituted maleimide 2 (0.105 mmol, 1.05 equiv.) dry THF (0.1 mL) was added. The solution was placed in a cryobath at −40 °C and allowed to stir for 10 min under nitrogen atmosphere. The corresponding diene 1 (0.1 mmol, 1.0 equiv.) was then added using a syringe pump over a period of 12 h as a stock solution (in 0.1 mL THF) followed by additional solvent (0.05 mL) to avoid a loss of the material on the glass wall. After the addition period was completed the reaction mixture was stirred for six hours. Afterwards the reaction mixture was filtered through a short pad of silica to remove the catalyst using a mixture of petroleum ether/ethyl acetate 1:1 as eluent. The crude product was purified by flash column chromatography (PE : EE = 2:1) to yield the pure product.
General Procedure for Catalytic Diels–Alder Reactions of 3-Hydroxypyrones in Control Experiments (GP5)

To an oven-dried Schlenk vial containing the corresponding catalyst (C2–C5) (0.05 mmol, 5 mol%), the corresponding base (0.0025 mmol, 2.5 mol%) and maleimide 2B (0.105 mmol, 1.05 equiv.) THF (0.1 mL) was added. The reaction mixture was placed in a cryobath at −40 °C and allowed to stir for 10 min under nitrogen atmosphere. The diene 1a (0.1 mmol, 1.0 equiv.) was then added using a syringe pump over the period of 12 h as a stock solution (in 0.1 mL THF, plus additional solvent 0.05 mL to avoid loss of the material on the glass wall. After the addition period was completed the reaction mixture was stirred for addition al10 hours. Afterwards the reaction mixture was filtered through a short pad of silica to remove the catalyst using a mixture of petroleum ether/ethyl acetate (1:1) as eluent. The crude product was purified by flash column chromatography (PE : EE = 2:1) to yield the pure product.

General Procedure for the Catalytic Diels–Alder Reactions of 3-Hydroxypyridones (GP6)
To an oven-dried Schlenk vial containing activated catalyst C1 (0.005 mmol, 5.0 mol%), and maleimide 2B (0.105 mmol, 1.05 equiv.) 0.1 mL of dried THF was added at room temperature. The solution was allowed to stir for 10 min under nitrogen atmosphere. The corresponding diene 4 (0.1 mmol, 1.0 equiv.) was then added using a syringe pump over the period of 12 h as a stock solution (in 0.1 mL THF) followed by additional solvent (0.05 mL) to avoid a loss of the material on the glass wall. After the addition period was completed the reaction mixture was stirred for additional six hours. Afterwards the reaction mixture was filtered through a short pad of silica to remove the catalyst using a mixture of petroleum ether/ethyl acetate 1:1 as eluent. The crude product was purified by flash column chromatography (PE : EE = 2:1) to yield the pure product.

**General Procedure for the Cycloaddition Reaction with Enone (8) (GP7)**

The activated catalyst C1a-(S,S) was added as a stock solution (0.05 mL) in anhydrous THF to a catalysis tube containing N-benzylmaleimide 2B (18.7 mg, 0.10 mmol, 1.0 equiv.) or nitroolefin 10 (14.9 mg, 0.1 mmol, 1.0 equiv.) and enone 8 (18.4 mg, 0.12 mmol, 1.2 equiv.) under nitrogen atmosphere. The reaction mixture was stirred for 20 h. Afterwards the reaction mixture was diluted with a solvent mixture of petroleum ether/ethyl acetate (1/1, 2 mL), filtered through a small pad of silica to remove the catalyst from the reaction mixture and the crude product was eluted with additional petroleum ether/ethyl acetate (1/1, 10 mL). After removal of solvent under reduced pressure, the crude product was purified via column chromatography with petroleum ether/ethyl acetate as eluent (4/1) to yield the pure product.

**General Procedure for the Determination of ee values with (R)-BINOL (GP8)**

To an NMR tube filled with 0.4 mL of saturated CDCl₃ solution of (R)-BINOL was added the corresponding cycloaddition product (1.0 mg, dissolved in 0.1 mL of CDCl₃). The ¹H NMR spectra were recorded at 500 or 700 MHz. The enantiomeric excesses were determined by integration of characteristic signals of the (+) and (−)-enantiomers.⁷
Substrate Synthesis

4-Chloro-3-hydroxy-2-pyrene (1c)

To a solution of 3-hydroxy-2-pyrene 1a (0.40 g, 3.57 mmol) in DMF (10 mL) was added NCS (0.71 g, 5.36 mmol, 1.50 equiv.) portionwise over the period of 15 min. The reaction mixture was stirred for 16 h at room temperature and diluted with 10 mL of H₂O and extracted with EtOAc (3 x 10 mL). The combined organic layers were dried over Na₂SO₄, filtrated and concentrated in vacuo. The residue was purified by column chromatography (using DCM as eluent) to afford pyrone 1c (261.5 mg, 1.78 mmol, 50%) as a yellow crystalline solid.

C₅H₃ClO₃, M: 146.53 g/mol. ¹H NMR (300 MHz, CDCl₃): δ (ppm) = 7.07 (d, J = 5.7 Hz, 1H, CH=C₆H-O), 7.05-6.76 (br, 1H, OH), 6.27 (d, J = 5.7 Hz, 1H, CH=CH-O). The NMR spectra is in agreement to the one reported in the literature.⁸

N-2-Nitrobenzenesulfonyl-4-allyl-3-hydroxy-2-pyridone (4b)

Following the literature procedure,⁹ to a mixture of 4a (592.5 mg, 2.0 mmol, 1.0 equiv.), Na₂CO₃ (212.0 mg, 2.0 mmol, 1.0 equiv.) and KI (83 mg, 1.0 mmol, 0.5 equiv.) in MeCN (5 mL) was added allyl bromide (259.6 µL, 3.0 mmol, 1.1 equiv.), and the reaction mixture was heated at reflux for two hours. After cooling to room temperature, water (10 mL) was added and the mixture was extracted with EtOAc (3 x 10 mL). The combined organic phases were dried over MgSO₄ and concentrated under reduced pressure. The obtained O-allyl pyridone was dissolved in 5 mL of mesitylene in a pressure tube and heated at 130 °C for 30 min. After cooling to room temperature the reaction mixture was directly purified by column chromatography (PE : EE = 2 : 1). 4b was isolated as a light-yellow solid (98.9 mg, 0.29 mmol, 35%, over two steps).

C₁₄H₁₂N₂O₆S, M: 336.32 g/mol. m.p. = 181 °C. ¹H NMR (400 MHz, CDCl₃): δ (ppm) = 8.70-8.50 (m, br, 2H, ArH, OH), 7.96-7.84 (m, 3H, ArH), 7.41 (d, J = 7.8 Hz, 1H, NCH=CH), 6.23 (d, J = 7.9 Hz, 1H, NCH=CH), 5.95-5.80 (m, 1H, CH=CH₂aly), 5.12 (d, J = 17.3 Hz, 1H, CH=CH₂aly), 5.05 (d, J = 10.3 Hz, 1H, CH=CH₂aly), 3.26 (d, J = 6.6 Hz, 2H, OCH₂). ¹³C NMR (176 MHz, CDCl₃): δ (ppm) = 157.0, 149.3, 144.8, 137.0, 136.9, 134.9, 132.4, 130.5, 128.7, 125.5, 121.3, 116.9, 109.3, 33.6. IR (solid) 𝜈 = 3289, 3103, 2979, 1638, 1616, 1615, 1541, 1440,
1362, 1284, 1237, 1179, 1128, 1054, 927, 852, 781, 737, 657, 593, 556 cm\(^{-1}\). **HRMS (ESI):** \(m/z\) calculated for \([C_{14}H_{12}N_2O_6SNa]^+\): 359.0308, found: 359.0308.

### N-2-Nitrobenzenesulfonyl-4-chloro-3-hydroxy-2-pyridone (4c)

![Chemical Structure](image)

To a solution of \(N\)-2-nitrobenzenesulfonyl-3-hydroxy-2-pyridone 4a (0.50 g, 1.67 mmol) in DMF (10 mL) was added NCS (247.9 mg, 1.85 mmol, 1.1 equiv.) portionwise. The reaction mixture was stirred for 18 h at 0 °C and diluted with 15 mL of H\(_2\)O and extracted with EtOAc (3 x 10 mL). The combined organic layers were dried over MgSO\(_4\), filtrated and concentrated in vacuo. The residue was purified by column chromatography (PE : EE = 2:1) to afford pyridone 4c (247.5 mg, 0.95 mmol, 56\%) as a yellow crystalline solid.

**C\(_{11}\)H\(_7\)ClN\(_2\)O\(_6\)S, \(M\):** 330.69 g/mol. **m.p. = 187 °C.** **\(^1\)H NMR (400 MHz, THF-d\(_8\)):** \(\delta\) (ppm) = 9.52 (s, 1H, O\(\text{H}\)), 8.62 (d, \(J = 6.6\) Hz, 1H, Ar\(\text{H}\)), 8.01-7.84 (m, 3H, Ar\(\text{H}\)), 7.47 (d, \(J = 8.1\) Hz, NCH=CH), 6.43 (d, \(J = 8.1\) Hz, 1H, NCH=CH). **\(^{13}\)C NMR (100 MHz, THF-d\(_8\)):** \(\delta\) (ppm) = 156.4, 149.3, 145.1, 137.2, 137.0, 132.6, 130.1, 125.7, 123.5, 121.6, 109.4. **IR (solid) \(\tilde{\nu} = 3304, 3110, 1957, 1646, 1542, 1442, 1383, 1361, 1266, 1184, 1148, 1125, 1025, 945, 896, 853, 782, 739, 657, 588, 563\) cm\(^{-1}\). **HRMS (ESI):** \(m/z\) calculated for \([C_{11}H_{7}ClN_2O_6SNa]^+\): 352.9606, found: 352.9607.

### Ligand Synthesis

**(R)-2-(Imidazol-1-yl)-2′-hydroxy-1,1′-binaphthyl (K1)**

![Chemical Structure](image)

Imidazole derivative K1 was synthesized using a modification of the procedure by Crabtree et al.\(^{10}\) To (R)-2,2-diamino-1,1'-binaphthyl ((R)-BINAM) (500 mg, 1.76 mmol, 1.0 equiv.) 10 mL of demineralized water was added, and then 478 \(\mu\)L of concentrated HBr (5.0 equiv.). The mixture was stirred for 5 min, and 40% aqueous glyoxal (1.0 mL, 8.79 mmol, 5.0 equiv.) and paraformaldehyde (264 mg, 8.79 mmol, 5.0 equiv.) were added followed by addition of 10 mL of 1,4-dioxane. The mixture was heated with stirring to 80 °C, and ammonium chloride (470.3 mg, 8.79 mmol, 5.0 equiv.) was added. The solution was refluxed for 5 h and cooled to room temperature. A saturated aqueous solution of K\(_2\)CO\(_3\) (10 mL) was added, and the mixture was extracted with dichloromethane (3 x 10 mL). The organic phases were combined, dried over Na\(_2\)SO\(_4\), and filtered. The solvent was evaporated under reduced pressure, and the crude residue was purified by column chromatography on silica gel (dried in an oven overnight, at 150 °C) using a mixture of acetone : MeOH = 20:1. Pure product was obtained in 92% yield.
(544 mg, 1.62 mmol) after additional precipitation in *n*-pentane (30 mL) from a DCM solution (5 mL).

**C$_{29}$H$_{18}$N$_2$O$_3$, M**: 336.39 g/mol. ¹H NMR (300 MHz, CDCl$_3$): δ (ppm) = 8.06 (d, J = 8.6 Hz, 1H, ArH), 7.98 (d, J = 8.6 Hz, 1H, ArH), 7.86-7.78 (m, 2H, ArH), 7.62-7.48 (m, 3H, ArH), 7.45-7.32 (m, 2H, ArH), 7.31-7.22 (m, 1H, ArH), 7.22-7.12 (m, 1H, ArH), 6.90-6.79 (m, 3H, ArH, NCH$_3$), 6.74 (d, J = 8.6 Hz, 1H, NCH$_3$).

The NMR spectra is in agreement to the one reported in the literature.¹⁰

(R)-3-(5-(**tert**-Butyl)-3-formyl-2-hydroxybenzyl)-1-(2'-hydroxy-[1,1'-binaphthalen]-2-yl)-1H-imidazol-3-ium chloride (K2)

![Diagram of the reaction between K1 and DCM, RT, 16 h, resulting in K2.](image)

According to a literature protocol,⁶ 3-(Chloromethyl)-5-(**tert**-butyl)-2-hydroxybenzaldehyde (202.2 mg, 0.89 mmol, 1.0 equiv.) was dissolved in 5 mL DCM and added to a solution of K1 (300.0 mg, 0.89 mmol, 1.0 equiv.) in DCM (5 mL). The solution was stirred at room temperature for 16 h. The solvent was removed under reduced pressure, and the residue was redissolved in a small amount of dichloromethane (2 mL) and added to a stirred solution of diethylether (20 mL) to cause precipitation. The precipitate was filtered, washed with diethylether (10 mL) and resulting solid was dried in vacuo. The imidazolium salt K2 was isolated as a beige solid (489.9 mg, 0.87 mmol, 98%).

**C$_{35}$H$_{31}$ClN$_2$O$_3$, M**: 563.09 g/mol. ¹H NMR (300 MHz, CDCl$_3$): δ (ppm) = 11.11 (s, 1H, CHO), 9.85 (s, 1H, ArOH), 9.82 (s, 1H, ArOH), 8.34 (d, J = 2.3 Hz, 1H, NCH$_3$), 8.07 (d, J = 8.7 Hz, 1H, ArH), 7.98 (d, J = 8.5 Hz, 1H, ArH), 7.76-7.34 (m, 9H, ArH), 7.22-7.02 (m, 3H, ArH), 6.85-6.70 (m, 2H, NCH$_3$), 5.80-5.56 (m, 2H, CH$_3$Nimidazole), 1.34 (s, 9H, CH$_3$).

The NMR spectra is in agreement to the one reported in the literature.⁶

3-(5-(**tert**-Butyl)-2-hydroxy-3-(((E)-(((1S,2S)-2-(naphthalene-1-sulfonamido)-1,2-diphenylethylimino)methyl)benzyl)-1-((R)-2'-hydroxy-[1,1'-binaphthalen]-2-yl)-1H-imidazol-3-ium-chloride (L1b-(S,S))

Ligand L1b-(**S**, **S**) was synthesized according to GP1 using aldehyde K2 (20.0 mg, 0.035 mmol, 1.0 equiv.) and N-((1S,2S)-(*Amino-1,2-diphenylethyl)-naphthalene-1-sulfonamide (14.3 mg, 0.035 mmol, 1.0 equiv.). The product was isolated as a yellow solid (32.7 mg, 0.034 mmol, 96%).
C₉₉H₄₅ClN₆O₄S, M: 947.59 g/mol. m.p. = 218 °C. [α]²⁰º (c = 1.00 mg/mL, DCM): −40.7. ¹H NMR (400 MHz, CDCl₃): δ (ppm) = 13.68-12.81 (br, 1H, ArOH), 10.89-9.57 (br, 1H, ArOH), 9.30 (s, 1H, CHN), 8.49 (d, J = 8.8 Hz, 1H, ArH), 8.01 (d, J = 7.6 Hz, 1H, ArH), 7.89 (d, J = 7.4 Hz, 1H, ArH), 7.87-7.65 (m, 7H, ArH), 7.65-7.29 (m, 8H, ArH), 7.22-6.87 (m, 13H, ArH), 6.83 (m, 2H, N-CH-CH-N), 6.59 (s, 1H, NCHN), 5.52 (d, J = 14.0 Hz, 1H, ArCH₂-N), 5.13 (d, J = 14.0 Hz, 1H, ArCH₂N), 4.88 (d, J = 8.1 Hz, 1H, C=N-CHPh), 4.72 (d, 1H, SO₂NH-CHPh), 1.11 (s, 9H, C(CH₃)₃). ¹³C NMR (176 MHz, CDCl₃): δ = 167.1, 157.1, 153.8, 141.8, 139.0, 138.4, 136.7, 135.5, 134.1, 133.8, 133.7, 133.6, 133.1, 132.5, 132.1, 131.7, 130.7, 129.9, 129.8, 129.0, 128.5, 128.3, 128.2, 128.1, 128.0, 127.8, 127.7, 127.7, 127.6, 127.5, 127.0, 126.8, 126.3, 124.4, 123.6, 123.5, 123.0, 122.5, 122.3, 122.1, 120.4, 120.2, 117.9, 113.5, 64.4, 48.6, 34.0, 31.4. IR (solid): ν = 3062, 2963, 1626, 1508, 1434, 1345, 1324, 1161, 1134, 1089, 1019, 771, 731, 699, 587 cm⁻¹. HRMS (ESI): m/z calculated for [C₉₉H₅₅N₆O₄S⁺]: 911.3626, found: 911.3627.

3-(5-(tert-Butyl)-2-hydroxy-3-((E)-((1R,2R)-2-(naphthalene-1-sulfonamido)-1,2-diphenylethylimino)methyl)benzyl)-1-((R)-2'-hydroxy-[1,1'-binaphthalen]-2-yl)-1H-imidazol-3-ium-chloride (L1b-(R,R))

Ligand L1b-(R,R) was synthesized according to GP1 using aldehyde K2 (20.0 mg, 0.035 mmol, 1.0 equiv.) and N-((1R,2R)-2-Amino-1,2-diphenylethyl)-naphthalene-1-sulfonamide (14.3 mg, 0.035 mmol, 1.0 equiv.). The product was isolated as a yellow solid (29.6 mg, 0.031 mmol, 88%).

C₉₉H₄₅ClN₆O₄S, M: 947.59 g/mol. m.p. = 208 °C. [α]²⁰º (c = 1.00 mg/mL, DCM): 73.4. ¹H NMR (400 MHz, CDCl₃): δ (ppm) = 14.24 (br, s, 1H, ArOH), 10.91-10.14 (br, 1H, ArOH), 9.78 (s, 1H, CHN), 9.44-9.25 (br, 1H, SO₂H), 8.62 (d, J = 8.5 Hz, 1H, ArH), 8.24 (s, 1H, ArH), 8.11 (s, 1H, ArH), 7.99 (d, J = 7.6 Hz, 1H, ArH), 7.78 (d, J = 8.8 Hz, 1H, ArH), 7.67-7.58 (m, 4H, ArH), 7.55-7.47 (m, 2H, ArH), 7.43-7.33 (m, 4H, ArH), 7.20-6.77 (m, 14H, ArH, 1H, NCHN), 6.59 (d, J = 9.0 Hz, 1H, N-CH-CH-N), 6.46 (d, J = 8.0 Hz, 1H, N-CH-CH-N), 6.40 (t, J = 6.7 Hz, 2H, ArH), 5.75 (d, J = 14.0 Hz, 1H, ArCH₂N), 5.61 (d, J = 13.0 Hz, 1H, ArCH₂N), 5.36 (d, J = 10.0 Hz, 1H, HC=N-CHPh), 4.80 (t, J = 10.0 Hz, 1H, HNCHPh), 1.27 (s, 9H, C(CH₃)₃).
**13C NMR (176 MHz, CDCl₃):** δ = 167.2, 157.4, 135.4, 141.2, 139.9, 137.1, 136.2, 133.7, 133.5, 133.4, 133.3, 133.0, 131.9, 131.4, 130.4, 130.3, 129.9, 129.7, 128.8, 128.4, 128.3, 128.2, 128.1, 128.0, 127.9, 127.6, 127.5, 127.2, 127.0, 126.9, 126.8, 126.6, 126.4, 126.2, 126.1, 126.0, 125.2, 123.9, 123.8, 123.5, 123.3, 123.0, 122.8, 122.7, 121.9, 121.3, 120.2, 118.2, 117.8, 114.6, 114.1, 72.8, 64.6, 58.5, 48.5, 34.2, 31.5, 18.5. **IR (solid):** ν = 3059, 2958, 1626, 1599, 1319, 1159, 1132, 909, 817, 771, 729, 698, 587 cm⁻¹. **HRMS (ESI):** m/z calculated for [C₉₉H₅₃N₄O₄S]⁺: 911.3626, found: 911.3630.

3-(5-(tert-Butyl)-2-hydroxy-3-((E)-(((1S,2S)-2-(anthracene-9-sulfonamido)-1,2-diphenylethyl)imino)methyl)benzyl)-1-((R)-2′-hydroxy-[1,1′-binaphthalen]-2-yl)-1H-imidazol-3-ium-chloride (L1c-(S,S))

Ligand L1c-(S,S) was synthesized according to GP1 using aldehyde K2 (17.2 mg, 0.031 mmol, 1.0 equiv.) and N-((1S,2S)-2-Amino-1,2-diphenylethyl)-anthracene-9-sulfonamide (13.86 mg, 0.031 mmol, 1.0 equiv.). The product was isolated as a yellow solid (26.3 mg, 0.026 mmol, 85%).

![Chemical structure of L1c-(S,S)](image)

**C₉₃H₅₃ClN₄O₄S, M:** 997.64 g/mol. **m.p.** = 246 °C. **[α]²⁰ₒ (c = 1.00 mg/mL, DCM):** −32.0. **¹H NMR (700 MHz, (CD₃)₂SO):** δ (ppm) = 12.99 (s, 1H, ArOH), 9.95 (s, 1H, ArOH), 9.15 (d, J = 9.4 Hz, 2H, HC=N), 8.98 (s, 1H, ArH), 8.94 (d, J = 5.8 Hz, 1H, SO₂NH), 8.63 (s, 1H, ArH), 8.56 (s, 1H, ArH), 8.28 (d, J = 9.1 Hz, 1H, ArH), 8.15 (d, J = 9.1 Hz, 1H, ArH), 7.94 (d, J = 8.5 Hz, 2H, ArH), 7.84 (d, J = 8.5 Hz, 1H, ArH), 7.66 (t, J = 8.5 Hz, 1H, ArH), 7.58-7.55 (m, 3H, ArH), 7.52-7.49 (m, 2H, ArH), 7.46-7.39 (m, 4H, ArH), 7.22 (m, 3H, ArH), 7.16-7.00 (m, 10H, ArH), 6.74-6.68 (m, 4H, ArH, NCH₆), 6.65-6.61 (m, 2H, ArH, NCH₆), 5.15 (q, J = 29.0, 14.1 Hz, 2H, NimidazoleCH₂), 4.85 (t, J = 9.8 Hz, 1H, SO₂NHCHPh), 4.61 (d, J = 9.8 Hz, 1H, C=NCHPh), 1.23 (s, 9H, C(CH₃)₃). **¹³C NMR (700 MHz, (CD₃)₂SO):** δ (ppm) = 167.8, 167.2, 156.8, 153.5, 141.0, 139.8, 138.6, 136.8, 135.9, 135.1, 135.0, 134.0, 133.5, 133.3, 132.6, 132.5, 131.20, 131.17, 131.07, 130.9, 130.6, 130.5, 130.3, 129.8, 129.6, 129.5, 128.9, 128.5, 128.25, 128.23, 128.1, 127.9, 127.8, 127.4, 127.3, 127.2, 127.0, 126.9, 125.5, 125.3, 124.0, 123.9, 123.4, 123.2, 122.8, 120.2, 118.5, 118.4, 118.0, 112.6, 77.6, 63.2, 48.0, 40.5, 34.1, 31.6. **IR (solid):** ν = 3061, 2957, 2924, 1717, 1625, 1601, 1546, 1510, 1478, 1454, 1434, 1364, 1344, 1320, 1275, 1203, 1158, 1145, 1098, 1064, 1027, 945, 908, 818, 778, 734, 698, 671, 581, 516 cm⁻¹. **HRMS (ESI):** m/z calculated for [C₉₃H₅₃N₄O₄S]⁺: 961.3782, found: 961.3780.
3-(5-(tert-Butyl)-2-hydroxy-3-((E)-(((1S,2S)-2-(naphthalene-2-sulfonamido)-1,2-diphenylethyl)limino)methyl)benzyl)-1-((R)-2'-hydroxy-[1,1'-binaphthalen]-2-yl)-1H-imidazol-3-ium-chloride (L1d-(S,S))

Ligand L1d-(S,S) was synthesized according to GP1 using aldehyde K2 (35.0 mg, 0.062 mmol, 1.0 equiv.) and N-((1S,2S)-2-Amino-1,2-diphenylethyl)-naphthalene-2-sulfonamide (25.02 mg, 0.062 mmol, 1.0 equiv.). The product was isolated as a yellow solid (55.8 mg, 0.059 mmol, 95%).

L1d-(S,S)

C_{39}H_{51}ClN_4O_s, M: 947.59 g/mol. m.p. = 190 °C. [α]_D^{20} (c = 1.00 mg/mL, DCM): −2.2. ¹H NMR (400 MHz, CDCl₃): δ (ppm) = 14.08-12.35 (br, 1H, ArOH), 10.45-9.48 (br, 1H, ArOH), 9.30 (s, 1H, H_C=N), 8.50 (s, 1H, SO₂(NH)), 7.93 (s, 1H, ArH), 7.80-7.55 (m, 6H, ArH), 7.49 (t, J = 7.5 Hz, 1H, ArH), 7.44-7.21 (m, 10H, ArH), 7.13-7.01 (m, 3H, ArH), 7.01-6.81 (m, 14H, ArH, NCH), 6.42 (s, 1H, NCH), 5.29 (d, J = 13.7 Hz, 1H, SO₂NHCHPh), 4.94-4.62 (m, 3H, C=NCHPh, NimidazolCH₂), 1.00 (s, 9H, C(CH₃)₃). ¹³C NMR (176 MHz, CDCl₃): δ (ppm) = 167.6, 157.1, 153.7, 141.9, 139.3, 138.8, 138.2, 136.9, 134.1, 134.1, 133.7, 133.2, 131.9, 131.8, 130.9, 130.0, 129.9, 129.0, 128.8, 128.6, 128.4, 128.3, 128.0, 127.9, 127.8, 127.7, 127.6, 127.3, 127.2, 127.1, 127.0, 123.6, 123.2, 122.7, 122.3, 122.2, 122.0, 120.5, 120.2, 118.1, 113.6, 76.6, 64.5, 48.7, 34.1, 31.5. IR (solid): ν = 3057, 2959, 1625, 1599, 1545, 1506, 1478, 1454, 1433, 1320, 1273, 1201, 1153, 1130, 1096, 1074, 1028, 955, 908, 858, 816, 773, 747, 728, 698, 661, 643, 626, 593, 562, 546, 480 cm⁻¹. HRMS (ESI): m/z calculated for [C₉H₅N₅O₄S]^+: 911.3626, found: 911.3627.

3-(5-(tert-Butyl)-2-hydroxy-3-((E)-(((1R,2R)-2-(naphthalene-2-sulfonamido)-1,2-diphenylethyl)limino)methyl)benzyl)-1-((R)-2'-hydroxy-[1,1'-binaphthalen]-2-yl)-1H-imidazol-3-ium-chloride (L1d-(R,R))

Ligand L1d-(R,R) was synthesized according to GP1 using aldehyde K2 (35.0 mg, 0.062 mmol, 1.0 equiv.) and N-((1R,2R)-2-Amino-1,2-diphenylethyl)-naphthalene-2-sulfonamide (25.02 mg, 0.062 mmol, 1.0 equiv.). The product was isolated as a yellow solid (54.9 mg, 0.058 mmol, 94%).
**C₈₉H₅₁Cl₃N₉O₇S, M:** 947.59 g/mol. m.p. = 195 °C. [α]²⁰ᵇ (c = 1.00 mg/mL, DCM): 0.90. ¹H NMR (400 MHz, CDCl₃): δ (ppm) = 14.93-13.58 (br, 1H, ArOH), 10.81-10.06 (br, 1H, ArOH), 9.85 (s, 1H, HCN), 9.10 (br, s, 1H, SO₂NH), 8.51 (s, 1H, ArH), 7.99 (s, 1H, ArH), 7.85-7.40 (m, 12H, ArH), 7.33 (t, J = 7.2 Hz, 1H, ArH), 7.22-6.88 (m, 14H, ArH), 6.85 (d, J = 8.3 Hz, 1H, ArH), 6.69 (s, 1H, ArH), 6.53 (m, 3H, NCH, ArH), 5.57-5.14 (m, 3H, SO₂NHCPH, NimidazoleCH₂), 5.05 (t, J = 9.1 Hz, 1H, ArH, C=NCN), 4.99 (s, 9H, C(CH₃)₃). ¹³C NMR (176 MHz, CDCl₃): δ (ppm) = 153.7, 141.7, 140.0, 138.4, 137.9, 137.2, 134.1, 133.9, 133.7, 133.4, 133.3, 132.7, 132.0, 131.8, 130.7, 129.8, 129.3, 129.1, 129.0, 128.6, 128.5, 128.4, 128.3, 128.1, 127.9, 127.8, 127.7, 127.6, 127.5, 127.4, 127.2, 126.8, 126.7, 126.1, 123.6, 123.2, 123.1, 122.3, 122.2, 121.1, 120.1, 118.1, 113.9, 73.6, 64.5, 62.8, 48.0, 34.4, 31.6. IR (solid): ν = 3057, 2959, 1626, 1599, 1545, 1506, 1478, 1454, 1433, 1336, 1273, 1162, 1096, 1047, 907, 816, 726, 697, 641, 581, 559, 528 cm⁻¹. HRMS (ESI): m/z calculated for [C₈₉H₅₁N₉O₇S]⁺: 911.3626, found: 911.3628.

3-(5-(tert-Butyl)-2-hydroxy-3-((E)-((1S,2S)-2-(2-nitrobenzenesulfonylamido)-1,2-diphenylethyl)imino)methyl)benzyl)-1-((R)-2'-hydroxy-[1,1'-binaphthalen]-2-yl)-1H-imidazol-3-ium-chloride (L₁₁e-(S,S))

Ligand L₁₁e-(S,S) was synthesized according to GP1 using aldehyde K₂ (30.0 mg, 0.053 mmol, 1.0 equiv.) and N-((1S,2S)-2-Amino-1,2-diphenylethyl)-2-nitrophenylsulfonamide (21.17 mg, 0.053 mmol, 1.0 equiv.). The product was isolated as a yellow solid (43.4 mg, 0.046 mmol, 87%).
Ligand L1e-(R,R) was synthesized according to GP1 using aldehyde K2 (30.0 mg, 0.053 mmol, 1.0 equiv.) and N-((1R,2R)-2-Amino-1,2-diphenylethyl)-2-nitrophenylsulfonamide (21.17 mg, 0.053 mmol, 1.0 equiv.). The product was isolated as a yellow solid (44.4 mg, 0.047 mmol, 89%).

\[
\text{C}_{55}\text{H}_{48}\text{ClN}_{5}\text{O}_{6}\text{S}, M: 942.52 \text{ g/mol}. \text{ m.p.} = 245 \degree \text{C.} [\alpha]^{20}_D (c = 1.00 \text{ mg/mL, DCM}): 37.2. \^1\text{H NMR (400 MHz, CDCI}_3): \delta (\text{ppm}) = 13.69-13.62 (\text{br, 1H, ArOH}), 10.27-9.99 (\text{br, 1H, ArOH}), 9.47 (\text{br s, 1H, HC=N}), 8.32 (\text{br, s, 1H, N\text{H}}), 7.96 (\text{d, J = 8.5 Hz, 1H, ArH}), 7.97 (\text{m, 2H, ArH}), 7.89-7.79 (\text{m, 2H, ArH}), 7.76-7.60 (\text{m, 4H, ArH}), 7.58-7.49 (\text{m, 2H, ArH}), 7.44-7.20 (\text{m, 6H, ArH}), 7.19-7.01 (\text{m, 11H, ArH}), 6.96-6.86 (\text{m, 3H, ArH, NCH}), 6.79 (\text{m, J = 7.7 Hz, 2H, NCH}), 5.59-5.36 (\text{m, 2H, NimidazoleCH}), 5.01 (\text{s, 2H, NsNHCH, CHN=}), 1.23 (\text{s, 9H, C(CH}_3)_3). \^13\text{C NMR (176 MHz, CDCI}_3): \delta (\text{ppm}) = 138.9, 137.6, 136.9, 134.4, 134.1, 133.5, 133.2, 132.9, 132.6, 132.5, 132.3, 131.7, 130.7, 130.4, 130.0, 129.8, 128.6, 128.4, 128.3, 128.2, 128.1, 128.0, 127.9, 127.8, 127.6, 126.8, 124.0, 123.5, 123.1, 122.8, 122.6, 122.2, 120.8, 120.3, 120.2, 118.0, 113.7, 75.8, 64.8, 48.6, 34.3, 31.5. \text{IR (solid):} \bar{\nu} = 3140, 3031, 2960, 2867, 1626, 1599, 1538, 1478, 1454, 1433, 1344, 1274, 1226, 1202, 1165, 1097, 1064, 1027, 909, 839, 817, 729, 699, 653, 627, 561, 531 \text{ cm}^{-1}. \text{HRMS (ESI):} \text{m/}z \text{ calculated for [C}_{55}\text{H}_{48}\text{N}_{5}\text{O}_{6}\text{S]}^+: 906.3320, \text{found: 906.3317.}

Ligand L1f-(S,S) was synthesized according to GP1 using aldehyde K2 (30.0 mg, 0.053 mmol, 1.0 equiv.) and N-((1S,2S)-2-Amino-1,2-diphenylethyl)-4-nitrophenylsulfonamide (21.17 mg, 0.053 mmol, 1.0 equiv.). The product was isolated as a yellow solid (44.9 mg, 0.048 mmol, 90%).
Cs₅H₄ClN₂O₅S, M: 942.52 g/mol. m.p. = 245 °C. [α]²⁰D (c = 1.00 mg/mL, DCM): 50.1. `H NMR (400 MHz, CD₂CN): δ (ppm) = 13.95-12.35 (br, 1H, ArOH), 10.08-8.85 (br, 1H, ArOHN), 9.56 (s, 1H, HC=N), 8.71 (s, 1H, NH), 8.61 (s, 1H, OH), 8.18 (d, J = 9.0 Hz, 1H, ArH), 8.06 (d, J = 8.6 Hz, 1H, ArH), 7.83-7.75 (m, 4H, ArH), 7.67 (d, J = 8.9 Hz, 1H, ArH), 7.60 (t, J = 7.2 Hz, 1H, ArH), 7.52 (d, J = 8.1 Hz, 1H, ArH), 7.42 (s, 2H, ArH), 7.37 (t, J = 8.3 Hz, 1H, ArH), 7.34-6.95 (m, 18H, ArH, NCH), 6.74 (d, J = 8.5 Hz, 1H, NCH), 5.18 (d, J = 13.9 Hz, 1H, N₃). 13C NMR (176 MHz, CD₂Cl₂): δ (ppm) = 167.8, 157.8, 154.0, 148.9, 147.9, 142.1, 139.5, 139.1, 136.8, 134.5, 133.9, 133.3, 132.6, 132.1, 130.9, 130.3, 128.8, 128.8, 128.7, 128.6, 128.5, 128.4, 128.1, 127.9, 127.7, 127.5, 127.4, 123.7, 123.6, 123.2, 122.9, 122.2, 120.1, 119.8, 118.6, 113.5, 76.24, 64.95, 49.43, 34.25, 31.40. IR (solid): ν = 3056, 2860, 1625, 1600, 1525, 1477, 1454, 1432, 1345, 1309, 1273, 1201, 1160, 1093, 1049, 1027, 952, 937, 853, 816, 774, 747, 735, 698, 684, 645, 625, 610, 557, 464 cm⁻¹. HRMS (ESI): m/z calculated for [Cs5H4ClN2O5S]+: 906.3320, found: 906.3319.

3-(5-(tert-Butyl)-2-hydroxy-3-((E)-((1R,2R)-2-(2-nitrobenzenesulfonylamido)-1,2-diphenylethyl)imino)methyl)benzyl)-1-((R)-2'-hydroxy-[1,1'-binaphthalen]-2-yl)-1H-imidazol-3-ium-chloride (L1f-(R,R))

Ligand L1f-(R,R) was synthesized according to GP1 using aldehyde K2 (30.0 mg, 0.053 mmol, 1.0 equiv.) and N-((1R,2R)-2-Amino-1,2-diphenylethyl)-4-nitrophenylsulfonamide (21.17 mg, 0.053 mmol, 1.0 equiv.). The product was isolated as a yellow solid (42.3 mg, 0.045 mmol, 85%).

Cs₅H₄ClN₂O₅S, M: 942.52 g/mol. m.p. = 242 °C. [α]²⁰D (c = 1.00 mg/mL, DCM): 44.1. `H NMR (400 MHz, CDCl₃): δ (ppm) = 14.75-13.70 (br, 1H, ArOH), 10.65-9.91 (br, 1H, ArOHN), 9.73 (s, 1H, HC=N), 9.60 (br, s, 1H, NH), 8.46 (s, 1H, OH), 7.76 (t, J = 8.2 Hz, 2H, ArH), 7.66-7.49 (m, 5H, ArH), 7.48-7.40 (m, 2H, ArH), 7.37 (d, J = 8.6 Hz, 1H, ArH), 7.28-6.77 (m, 16H, ArH), 6.76-6.57 (m, 4H, ArH, NCH), 5.39-5.13 (m, 3H, N₃imidazoleCH₂, p-NsNHCH₂). 13C NMR (100 MHz, CDCl₃): δ (ppm) = 167.7, 157.5, 153.3, 148.5, 147.3, 141.6, 139.9, 138.3, 137.5, 134.1, 133.7, 133.2, 132.9, 132.4, 131.8, 130.8, 129.5, 128.7, 128.6, 128.5, 128.3, 128.2, 128.1, 127.8, 127.6, 127.2, 127.0, 123.6, 123.2, 122.7, 122.1, 121.6, 120.5, 120.0, 118.5, 114.1, 73.7, 64.7, 48.2, 34.2, 31.6. IR (solid): ν = 3064, 2958, 2925, 2859, 1736, 1627, 1604, 1528, 1455, 1347, 1310, 1276, 1163, 1093, 1053, 1028, 937, 910, 854, 818, 736, 700, 685, 610, 557, 464 cm⁻¹. HRMS (ESI): m/z calculated for [Cs₅H₄ClN₂O₅S]+: 906.3320, found: 906.3318.
3-(5-<i>tert</i>-Butyl)-3-((<i>E</i>)-(((1S,2S)-1,2-diphenyl-2-(methylsulfonamido)ethyl)imino)<br>methyl)-2-hydroxybenzyl)-1-((<i>R</i>)-2'-hydroxy-[1,1'-binaphthalen]-2-yl)-1H-imidazol-3-iurnchlorid (L1g-(<i>S</i>,<i>S</i>))

Ligand L1g-(<i>S</i>,<i>S</i>) was synthesized according to GP1 using aldehyde K2 (17.82 mg, 0.032 mmol, 1.0 equiv.) and N-((1<i>S</i>,2<i>S</i>)-2-Amino-1,2-diphenylethyl)methanesulfonamide (9.19 mg, 0.032 mmol, 1.0 equiv.). The product was isolated as a yellow solid (26.3 mg, 0.0315 mmol, 99%).

![Structural diagram of L1g-(<i>S</i>,<i>S</i>)](image)

**C<sub>50</sub>H<sub>47</sub>ClN<sub>4</sub>O<sub>4</sub>S.** *M* : 835.46 g/mol. m.p. = 189 °C. [α]<sub>D</sub><sup>20</sup> (c = 1.00 mg/mL, DCM): 28.0. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ = 13.61 (br, 1H, ArOH), 9.57 (br, 1H, ArOH), 9.50 (s, 1H, CHN), 8.28 (s, 1H, NCHN), 8.08 (d, 1H, J = 8.8 Hz, ArH), 7.98 (d, 1H, J = 8.2 Hz, ArH), 7.68-7.51 (m, 4H, ArH), 7.93-7.90 (m, 1H, ArH), 7.76-7.64 (m, 2H, ArH), 7.63-7.54 (m, 2H, ArH), 7.45-7.37 (m, 2H, ArH), 7.34-7.28 (m, 2H, ArH), 7.25-7.12 (m, 9H, ArH, NHCCHN), 7.07 (s, 1H, ArH), 6.07 (m, 1H, NHCCCHN), 6.71 (s, 1H, ArH), 5.73 (d, 1H, J = 13.7 Hz, ArCHH), 5.44 (d, 1H, J = 13.9 Hz, ArCHH), 5.02 (m, 2H, CNCHPh, PhCHNHSO<sub>2</sub>Me), 2.40 (s, 3H, SO<sub>2</sub>CH<sub>3</sub>), 1.23 (s, 9H, C(CH<sub>3</sub>)<sub>3</sub>). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ = 167.3, 157.4, 153.3, 141.7, 139.3, 138.7, 136.7, 134.0, 133.5, 133.1, 132.6, 132.1, 131.8, 130.7, 130.0, 129.6, 128.7, 128.6, 128.5, 128.4, 128.3, 128.3, 127.9, 127.9, 127.8, 127.7, 127.6, 127.0, 123.5, 123.2, 122.7, 122.3, 122.1, 120.8, 119.6, 118.0, 113.3, 75.1, 64.3, 48.7, 41.6, 34.1, 31.4. IR (solid): ν = 3061, 2960, 1627, 1600, 1546, 1508, 1479, 1455, 1433, 1344, 1319, 1275, 1204, 1150, 1098, 1066, 975, 910, 819, 751, 731, 700 cm<sup>-1</sup>. HRMS (ESI) *m/z* calculated for [C<sub>50</sub>H<sub>47</sub>N<sub>4</sub>O<sub>4</sub>S]<sup>+</sup> 799.3313, found: 799.3312.

3-(5-<i>tert</i>-Butyl)-3-((<i>E</i>)-(((1<i>R</i>,2<i>R</i>)-1,2-diphenyl-2-(methylsulfonamido)ethyl)imino)<br>methyl)-2-hydroxybenzyl)-1-((<i>R</i>)-2'-hydroxy-[1,1'-binaphthalen]-2-yl)-1H-imidazol-3-iurnchlorid (L1g-(<i>R</i>,<i>R</i>))

Ligand L1g-(<i>R</i>,<i>R</i>) was synthesized according to GP1 using aldehyde K2 (20.2 mg, 0.036 mmol, 1.0 equiv.) and N-((1<i>R</i>,2<i>R</i>)-2-Amino-1,2-diphenylethyl)methanesulfonamide (10.4 mg, 0.036 mmol, 1.0 equiv.). The product was isolated as a yellow solid (28.1 mg, 0.032 mmol, 86%).

![Structural diagram of L1g-(<i>R</i>,<i>R</i>)](image)
C_{50}H_{45}ClN_{2}O_{5}S. M: 835.46 g/mol. m.p. = 187 °C. [α]_{D}^{20} (c = 1.8 mg/mL, DCM): 108.4. \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta = 14.06 \) (br, 1H, ArOH), 10.14 (br, 1H, ArOH), 9.42 (s, 1H, CH\(_{2}\)), 8.40 (br, 1H, NH\(_{2}\)SO\(_2\)CH\(_3\)), 8.30 (s, 1H, NCH\(_{3}\)), 8.07 (d, 1H, J = 8.8 Hz, Ar\(H\)), 8.01-7.95 (m, 2H, Ar\(H\)), 7.68-7.51 (m, 5H, Ar\(H\)), 7.43-7.37 (m, 4H, Ar\(H\)), 7.22-7.07 (m, 9H, Ar\(H\)), 7.04-6.95 (m, 3H, Ar\(H\), NHCC\(H\)), 6.82-6.78 (m, 1H, NHCC\(H\)), 6.70 (s, 1H, Ar\(H\)), 5.50 (d, 1H, J = 13.1 Hz, ArCH\(_{2}\)), 5.35 (d, 1H, J = 13.7 Hz, ArCH\(_{2}\)), 5.25 (d, 1H, J = 9.4 Hz, CNCHPh), 4.92 (t, 1H, J = 9.6 Hz, PhCH\(_{2}\)NH\(_{2}\)SO\(_2\)Me), 2.28 (s, 3H, SO\(_{2}\)CH\(_{3}\)), 1.27 (s, 9H, C(CH\(_{3}\))\(_3\)). \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta = 167.1, 157.4, 153.3, 141.4, 139.6, 138.8, 137.2, 134.1, 133.5, 133.4, 133.1, 132.7, 131.8, 130.5, 129.8, 129.0, 128.7, 128.6, 128.4, 128.3, 128.3, 127.9, 127.9, 127.7, 127.6, 127.5, 127.0, 126.7, 126.6, 123.5, 122.8, 122.8, 122.2, 122.0, 121.0, 119.8, 117.7, 113.5, 72.9, 64.3, 48.1, 41.7, 34.3, 31.5. IR (solid): \(\tilde{\nu} = 3061, 2964, 1627, 1600, 1546, 1507, 1479, 1456, 1434, 1319, 1276, 1204, 1150, 1098, 1067, 976, 912, 818, 752, 735, 702 \text{ cm}^{-1}\). HRMS (ESI) \(m/z\): calculated for [C\(_{50}H_{45}ClN_{2}O_{5}S]^+ 799.3313, found: 799.3303.

3-(5-(tert-Butyl)-3-((E)−((1S,2S)-1,2-diphenyl-2-(p-tolylsulfonamido)ethyl)imino)methyl)-2-hydroxybenzyl)-1-(\(\eta\)−2'-hydroxy-[1,1'-binaphthalen]-2-yl)-1'H-imidazol-3-iumchlorid (L1h-(S,S))

Ligand L1h-(S,S) was synthesized according to GP1 using aldehyde K2 (19.9 mg, 0.035 mmol, 1.0 equiv.) and N-((1S,2S)-2-Amino-1,2-diphenylethyl)-4-methylphenylsulfonamide (12.8 mg, 0.035 mmol, 1.0 equiv.). The product was isolated as a yellow solid (29.1 mg, 0.032 mmol, 91%).

C\(_{58}\)H\(_{51}\)ClN\(_{4}\)O\(_{5}\)S. M: 911.56 g/mol. m.p. = 149 °C. [α]_{D}^{20} (c = 0.75 mg/mL, DCM): −10.0. \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta = 13.57 \) (br, 1H, ArOH), 9.99 (br, 1H, ArOH), 9.62 (s, 1H, CH\(_{2}\)), 8.31 (s, 1H, NCH\(_{3}\)), 8.02 (d, 1H, J = 8.7 Hz, Ar\(H\)), 7.97 (d, 1H, J = 8.4 Hz, Ar\(H\)), 7.89 (d, 1H, J = 1.9 Hz, Ar\(H\)), 7.77-7.68 (m, 3H, Ar\(H\)), 7.63-7.58 (m, 1H, Ar\(H\)), 7.54 (d, 1H, J = 8.7 Hz, Ar\(H\)), 7.47-7.32 (m, 4H, Ar\(H\)), 7.29-7.21 (m, 2H, Ar\(H\)), 7.18-7.10 (m, 6H, Ar\(H\)), 7.07-6.82 (m, 10H, Ar\(H\), NHCC\(H\)), 6.75-6.72 (m, 1H, Ar\(H\)), 6.30 (br, 1H, NH\(_{2}\)) Tos), 5.81 (d, 1H, J = 13.8 Hz, ArCH\(_{2}\)), 5.48 (d, 1H, J = 13.8 Hz, ArCH\(_{2}\)), 4.82-4.76 (m, 2H, CNCHPh, PhCH\(_{2}\)Tos), 2.21 (s, 3H, ArCH\(_{2}\)), 1.24 (s, 9H, C(CH\(_{3}\))\(_3\)). \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta = 167.3, 157.4, 153.5, 142.2, 141.9, 139.0, 137.9, 136.9, 134.1, 133.6, 133.1, 132.5, 132.3, 131.8, 130.7, 129.9, 129.9, 129.1, 128.8, 128.4, 128.3, 128.3, 128.2, 128.1, 128.0, 127.9, 127.7, 127.6, 127.4, 127.3, 127.1, 126.9, 126.6, 126.6, 123.5, 123.1, 122.7, 122.2, 120.7, 120.0, 118.0, 113.5, 76.0, 64.2, 48.7, 34.1, 31.4, 21.3. IR (solid): \(\tilde{\nu} = 3060, 2960, 2868, 1626, 1599, 1546, 1508, 1479, 1455, 1433, 1364, 1344, 1324, 1275, 1204, 1156, 1094, 1066, 1028, 909, 816, 750, 729, 699 \text{ cm}^{-1}\). HRMS (ESI) \(m/z\): calculated for [C\(_{58}H_{51}ClN_{4}O_{5}S]^+ 875.3626, found: 875.3622.

S21
3-(5-(tert-Butyl)-3-(((E)-(((1R,2R)-1,2-diphenyl-2-(p-tolylsulfonamido)ethyl)imino)-methyl)-2-hydroxybenzyl)-1-(((R)-2'-hydroxy-[1,1'-binaphthen]-2-yl)-1H-imidazol-3-iumchlorid (L1h-(R,R))

Ligand L1h-(R,R) was synthesized according to GP1 using aldehyde K2 (16.4 mg, 0.029 mmol, 1.0 equiv.) and N-((1R,2R)-2-Amino-1,2-diphenylethyl)-4-methylphenylsulfonamide (10.6 mg, 0.029 mmol, 1.0 equiv.). The product was isolated as a yellow solid (24.8 mg, 0.027 mmol, 94%).

3-(5-(tert-Butyl)-3-(((E)-(((1S,2S)-1,2-diphenyl-2-(pentafluorobenzylsulfonamido)ethyl)imino)-methyl)-2-hydroxybenzyl)-1-(((R)-2'-hydroxy-[1,1'-binaphthen]-2-yl)-1H-imidazol-3-iumchlorid (L1i-(S,S))

Ligand L1i-(S,S) was synthesized according to GP1 using aldehyde K2 (26.5 mg, 0.047 mmol, 1.0 equiv.) and N-((1S,2S)-2-Amino-1,2-diphenylethyl)-perfluorophenylsulfonamide (20.8 mg, 0.047 mmol, 1.0 equiv.). The product was isolated as a yellow solid (32.4 mg, 0.033 mmol, 70%).
C₅₅H₄₄ClF₅N₄O₂S. *M*: 987.48 g/mol. *m.p.* = 216 °C. [α]⁰₂⁰ (c = 1.00 mg/mL, DCM): 48.4. **¹H NMR (300 MHz, CDCI₃)**: δ = 13.83 (br, 1H, ArOH), 9.34 (br, 1H, ArOH), 9.07 (s, 1H, CHN), 8.62 (s, 1H, NCHN), 8.00 (d, 1H, J = 8.7 Hz, ArH), 7.90 (d, 1H, J = 8.3 Hz, ArH), 7.73-7.49 (m, 5H, ArH), 7.40-7.03 (m, 14H, ArH), 7.00-6.92 (m, 3H, ArH), 6.83 (m, 1H, NHCCNH), 6.65 (s, 1H, NHCCNH), 5.45 (d, 1H, J = 13.9 Hz, ArCHH), 5.35 (d, 1H, J = 9.7 Hz, CNCHAr), 5.11 (d, 1H, J = 13.9 Hz, ArCHH), 4.99 (d, 1H, J = 9.7 Hz, PhCHNHSO₂Ar), 1.10 (s, 9H, C(CH₃)₃). **¹³C NMR (100 MHz, CDCI₃)**: δ = 167.5, 157.6, 153.4, 143.1 (dd, J = 12.3, 255.4 Hz, 2C, CF), 142.9 (dt, J = 13.1, 260.4 Hz, 1C, CF), 141.1, 138.7, 137.1 (dt, J = 17.2, 255.0 Hz, 2C, CF), 136.9, 136.1, 134.0, 133.5, 133.0, 132.1, 132.0, 130.0, 130.8, 128.5, 128.4, 128.3, 128.3, 128.2, 128.1, 128.0, 128.0, 127.9, 127.8, 127.7, 127.6, 126.9, 123.4, 123.2, 122.5, 122.4, 122.0, 120.3, 119.6, 118.1, 117.2 (t, J = 14.3 Hz, 1C, ArCSO₂), 113.0, 74.3, 64.8, 48.8, 34.0, 31.3. **IR (solid)**: ν = 3054, 2961, 1627, 1601, 1519, 1497, 1455, 1434, 1363, 1346, 1296, 1275, 1171, 1098, 991, 818, 749, 700, 645, 627, 604 cm⁻¹. **HRMS (ESI) m/z**: calculated for [C₅₅H₄₄F₅N₄O₂S]⁺ 951.2998, found: 951.3006.

3-(5-(tert-Butyl)-3-(((E)-(((1R,2R)-1,2-diphenyl-2-(pentafluorobenzylsulfonamido)ethyl)-imino)-methyl)-2-hydroxybenzyl)-1-(((R)-2'-hydroxy-[1,1'-binaphthalen]-2-yl)-1H-imidazol-3-iumchlorid (L11-(R,R))

Ligand L11-(R,R) was synthesized according to GP1 using aldehyde K2 (29.1 mg, 0.046 mmol, 1.0 equiv.) and N-(((1R,2R)-2-Amino-1,2-diphenylethyl)-perfluorophenylsulfonamide (20.5 mg, 0.046 mmol, 1.0 equiv.) The product was isolated as a yellow solid (25.1 mg, 0.025 mmol, 55%).

C₅₅H₄₄ClF₅N₄O₂S. *M*: 987.48 g/mol. *m.p.* = 216 °C. [α]⁰₂⁰ (c = 1.6 mg/mL, DCM): 123.0. **¹H NMR (400 MHz, CDCI₃)**: δ = 14.25 (br, 1H, ArOH), 10.20-9.80 (br, 2H, ArOH, NH₂SO₂Ar), 9.53 (s, 1H, CHN), 8.21 (s, 1H, NCHN), 8.06-7.94 (m, 2H, ArH), 7.71-7.47 (m, 5H, ArH), 7.43-7.33 (m, 3H, ArH), 7.24-6.97 (m, 10H, ArH), 6.95-6.78 (m, 5H, ArH, NHCCNH), 6.75 (s, 1H, ArH), 5.71 (d, 1H, J = 13.9 Hz, ArCHH), 5.58 (d, 1H, J = 16.4 Hz, CNCHAr), 5.46 (d, 1H, J = 13.3 Hz, ArCHH), 4.97 (d, 1H, J = 10.2 Hz, PhCHNHSO₂Ar), 1.20 (s, 9H, C(CH₃)₃). **¹³C NMR (376 MHz, CDCI₃)**: δ = −134.6 (m), −148.8 (m), −160.5 (m). **¹³C NMR (176 MHz, CDCI₃)**: δ = 164.9, 155.1, 150.9, 141.5 (d, J = 257.0 Hz, 2C, CF), 140.1 (dt, J = 14.3, 261.8 Hz, 1C, CF), 139.2, 136.2, 134.6 (dt, J = 13.4, 255.6 Hz, 2C, CF), 134.3, 133.6, 131.5, 130.9, 130.5, 129.6, 129.5, 129.1, 128.3, 127.5, 127.4, 126.0, 125.9, 125.8, 125.7, 125.5, 125.4, 125.3, 125.2, 125.1, 125.0, 124.4, 120.8, 120.6, 120.0, 119.9, 119.5, 117.8, 117.1, 115.6, 114.6 (t, J = 14.0 Hz, ArCSO₂), 110.5, 71.7, 62.3, 46.2, 31.5, 28.7. **IR (solid)**: ν = 3065, 2960, 1627, 1600, 1518, 1497, 1455, 1434, 1364, 1346, 1296, 1275, 1171, 1098, 991, 817, 750, 699, 645, 603 cm⁻¹. **HRMS (ESI) m/z**: calculated for [C₅₅H₄₄F₅N₄O₂S]⁺ 951.2998, found: 951.3023.
Synthesis of the Complexes

3-(5-(tert-Butyl)-3-((E)-(((1R,2R)-1,2-diphenyl-2-((1-naphthalene)sulfonamido)ethyl)imino)methyl)-2-hydroxybenzyl)-1-(2'-hydroxy-[1,1'-binaphthalen]-2-yl)-1H-imidazol-3-ium copper (II)-chloride (C1b-(R,R))

The synthesis was carried out according to GP2 using ligand L1b-(R,R) (20.0 mg, 0.021 mmol, 1.0 equiv.) and Cu(acac)\(_2\) (5.52 mg, 0.021 mmol, 1.0 equiv.). The pre-catalyst C1b-(R,R) was obtained as a pale green solid (19.8 mg, 0.019 mmol, 92%).
C₅₉H₅₁ClCuN₄O₅S, \( M \): 1027.12 g/mol. m.p. = 175 °C. [\( \alpha \)]²⁰ₒ⁺ (c = 1.00 mg/mL, DCM): 91.6. \(^1\)H NMR: paramagnetic species. IR (solid): \( \tilde{\nu} \) = 3060, 2956, 2668, 1625, 1543, 1452, 1434, 1274, 1118, 802, 769, 730 cm⁻¹. HRMS (ESI) m/z: calculated for \([\text{C}_{59}\text{H}_{49}\text{CuN}_4\text{O}_4\text{S}]^+\): 972.2765. Found: 972.2760.

3-(5-(tert-Butyl)-3-((E)-(((1S,2S)-1,2-diphenyl-2-((2-(anthracene-9-sulfonamido)ethyl)imino)methyl)-2-hydroxybenzyl)-1-(2'-hydroxy-[1,1'-binaphthalen]-2-yl)-1H-imidazol-3-ium copper (II)-chloride (C₁c-(S,S))

The synthesis was carried out according to GP2. The ligand L₁c-(S,S) (18.7 mg, 0.018 mmol, 1.0 equiv.) and Cu(acac)₂ (4.91 mg, 0.018 mmol, 1.0 equiv.). After work-up the pre-catalyst C₁c-(S,S) (18.4 mg, 0.017 mmol, 95%) was obtained as light green solid.

C₆₃H₅₃ClCuN₄O₅S, \( M \): 1077.18 g/mol. m.p. = 216 °C. [\( \alpha \)]²⁰ₒ⁺ (c = 1.00 mg/mL, DCM): -36.5. \(^1\)H NMR: paramagnetic species. \(^{13}\)C NMR: paramagnetic species. IR (solid): \( \tilde{\nu} \) = 3135, 3058, 2957, 2924, 2854, 1626, 1543, 1494, 1449, 1393, 1364, 1346, 1275, 1221, 1126, 1098, 1026, 994, 950, 909, 817, 780, 734, 699, 646, 587 cm⁻¹. HRMS (ESI) m/z: calculated for \([\text{C}_{63}\text{H}_{55}\text{CuN}_4\text{O}_5\text{S}]^+\): 1022.2922. Found: 1022.2920.
3-(5-(tert-Butyl)-3-(((E))-((1S,2S)-1,2-diphenyl-2-((2-naphthalene)sulfonamido)ethyl)imino)methyl)-2-hydroxybenzyl)-1-(2'-hydroxy-[1,1'-binaphthalen]-2-yl)-1H-imidazol-3-ium copper (II)-chloride (C1d-(S,S))

The synthesis was carried out according to GP2 using the ligand L1d-(S,S) (30.0 mg, 0.032 mmol, 1.0 equiv.) and Cu(acac)₂ (8.29 mg, 0.032 mmol, 1.0 equiv.). The pre-catalyst C1d-(S,S) was obtained as a pale green solid (29.9 mg, 0.029 mmol, 91%).

\[
\text{C}_{59}\text{H}_{51}\text{ClCuN}_4\text{O}_5\text{S, } M: 1027.12 \text{ g/mol. m.p. } = 184 \, ^\circ\text{C. } [\alpha]^{20}_D (c = 1.00 \text{ mg/mL, DCM}): -35.4. \text{ } ^1\text{H NMR: paramagnetic species. } ^{13}\text{C NMR: paramagnetic species. IR (solid): } \nu = 3057, 2957, 2925, 1626, 1543, 1451, 1435, 1393, 1365, 1345, 1274, 1221, 1122, 1097, 1079, 1027, 996, 936, 816, 748, 698, 662, 618, 550, 503, 476 \text{ cm}^{-1}. \text{ HRMS (ESI) m/z: calculated for } [\text{C}_{59}\text{H}_{49}\text{CuN}_4\text{O}_4\text{S}]^+: 972.2765. \text{ Found: 972.2795.}
\]
3-(5-(tert-Butyl)-3-(((E)-(((1R,2R)-1,2-diphenyl-2-((2-naphthalene)sulfonamido)ethyl)imino)methyl)-2-hydroxybenzyl)-1-(2'-hydroxy-[1,1'-binaphthalen]-2-yl)-1H-imidazol-3-ium copper (II)-chloride (C1d-(R,R))

The synthesis was carried out according to GP2 using ligand L1d-(R,R) (30.0 mg, 0.032 mmol, 1.0 equiv.) and Cu(acac)_2 (8.29 mg, 0.032 mmol, 1.0 equiv.). The pre-catalyst C1d-(R,R) was obtained as a pale green solid (31.2 mg, 0.03 mmol, 95%).

3-(5-(tert-Butyl)-3-(((E)-(((1S,2S)-1,2-diphenyl-2-((2-nitrophenyl)sulfonamido)ethyl)imino)methyl)-2-hydroxybenzyl)-1-(2'-hydroxy-[1,1'-binaphthalen]-2-yl)-1H-imidazol-3-ium copper (II)-chloride (C1e-(S,S))

The synthesis was carried out according to GP2 using ligand L1e-(S,S) (20.0 mg, 0.021 mmol, 1.0 equiv.) and Cu(acac)_2 (5.55 mg, 0.015 mmol, 1.0 equiv.). The pre-catalyst C1e-(S,S) was obtained as a pale green solid (14.9 mg, 0.020 mmol, 95%).

C_{59}H_{51}ClCuN_{4}O_{5}S, M: 1027.12 g/mol. m.p. = 214 °C. [α]^{20}_{D} (c = 1.00 mg/mL, DCM): 59.0. \textsuperscript{1}H NMR: paramagnetic species. \textsuperscript{13}C NMR: paramagnetic species. IR (solid): \tilde{\nu} = 3055, 2950, 2920, 1627, 1542, 1450, 1437, 1392, 1366, 1346, 1271, 1221, 1123, 1095, 1071, 1028, 997, 934, 816, 749, 699, 660, 620, 555, 510, 471 cm\textsuperscript{-1}. HRMS (ESI) m/z: calculated for \([\text{C}_{59}\text{H}_{49}\text{CuN}_{4}\text{O}_{5}\text{S}]^+\): 972.2765. Found: 972.2795.
C_{55}H_{48}ClCuN_{6}O_{7}S, M: 1022.06 g/mol. m.p. = 236 °C. [α]^{20}_D (c = 1.00 mg/mL, DCM): −37.0. \textbf{^1H NMR:} paramagnetic species. \textbf{^{13}C NMR:} paramagnetic species. \textbf{IR (solid):} \tilde{\nu} = 3139, 3059, 3026, 2958, 2926, 2868, 1721, 1625, 1538, 1497, 1452, 1424, 1369, 1293, 1221, 1150, 1126, 1096, 1062, 1027, 996, 910, 816, 735, 700, 654, 631, 602, 552 cm\(^{-1}\). \textbf{HRMS (ESI) m/z:} calculated for [C_{55}H_{48}CuN_{6}O_{7}S]^{+}: 967.2459, found: 967.2453.

3-(5-(tert-Butyl)-3-(((E)-(((1R,2R)-1,2-diphenyl-2-((2-nitrophenyl)sulfonamido)ethyl)iminomethyl)-2-hydroxybenzyl)-1-(2'-hydroxy-[1,1'-binaphthalen]-2-yl)-1H-imidazol-3-ium copper (II)-chloride (C1e-(R,R))

The synthesis was carried out according to GP2 using ligand L1e-(R,R) (20.0 mg, 0.021 mmol, 1.0 equiv.) and Cu(acac)\(_2\) (5.55 mg, 0.015 mmol, 1.0 equiv.). The pre-catalyst C1e-(R,R) was obtained as a pale green solid (14.9 mg, 0.020 mmol, 95%).
The synthesis was carried out according to GP2 using ligand L1f-(S,S) (25.0 mg, 0.026 mmol, 1.0 equiv.) and Cu(acac)$_2$ (6.94 mg, 0.026 mmol, 1.0 equiv.). The pre-catalyst C1f-(S,S) was obtained as a pale green solid (25.1 mg, 0.025 mmol, 96%).

\[
\text{C}_{55}\text{H}_{46}\text{ClCuN}_5\text{O}_7\text{S}, \; M: 1022.06 \text{ g/mol. m.p. = 180 °C. \}^{[a]}_{\text{D}} (c = 1.00 \text{ mg/mL, DCM}): -49.2.} \; ^{1}\text{H NMR: paramagnetic species.} \; ^{13}\text{C NMR: paramagnetic species. IR (solid): \} = 3057, 2929, 1721, 1625, 1590, 1542, 1522, 1500, 1452, 1424, 1391, 1367, 1346, 1288, 1247, 1221, 1181, 1143, 1097, 1063, 1027, 994, 946, 910, 837, 814, 747, 734, 692, 619, 551 \text{ cm}^{-1}.} \; \text{HRMS (ESI) m/z: calculated for [C}_{55}\text{H}_{46}\text{CuN}_5\text{O}_7\text{S}^+: 967.2459. Found: 967.2454.} 
\]
3-(5-(tert-Butyl)-3-([(E)-((1R,2R)-1,2-diphenyl-2-((4-nitrophenyl)sulfonamido)ethyl)imino)methyl]-2-hydroxybenzyl)-1-(2'-hydroxy-[1,1'-binaphthalen]-2-yl)-1H-imidazol-3-ium copper (II)-chloride (C1f-(R,R))

The synthesis was carried out according to GP2 using ligand L1f-(R,R) (25.0 mg, 0.026 mmol, 1.0 equiv.) and Cu(acac)$_2$ (6.94 mg, 0.026 mmol, 1.0 equiv.). The pre-catalyst C1f-(R,R) was obtained as a pale green solid (24.7 mg, 0.024 mmol, 93%).

C$_{55}$H$_{48}$ClCuN$_5$O$_7$S, $M$: 1022.06 g/mol. m.p. = 204 °C. [α]$^{20}_D$ (c = 1.00 mg/mL, DCM): 31.2. $^1$H NMR: paramagnetic species. $^{13}$C NMR: paramagnetic species. IR (solid): $\tilde{\nu}$ = 3063, 2909, 1731, 1622, 1587, 1542, 1522, 1510, 1450, 1426, 1390, 1366, 1345, 1290, 1248, 1222, 1190, 1147, 1099, 1020, 995, 946, 911, 839, 811, 738, 691, 618, 552 cm$^{-1}$. HRMS (ESI) m/z: calculated for [C$_{55}$H$_{46}$CuN$_5$O$_6$S]$^+$: 967.2459. Found: 967.2454.

UV-Vis

3-(5-(tert-Butyl)-2-hydroxy-3-([(E)-((1S,2S)-2-(methylsulfonamido)-1,2-diphenylethyl)imino)methyl]benzyl)-1-((R)-2'-hydroxy-[1,1'-binaphthalen]-2-yl)-1H-imidazol-3-ium copper (II) chloride (C1g-(S,S))

The synthesis was carried out according to GP2 using ligand L1g-(S,S) (25.0 mg, 0.03 mmol, 1.0 equiv.) and Cu(acac)$_2$ (7.90 mg, 0.023 mmol, 1.0 equiv.). The pre-catalyst C1g-(S,S) was obtained as a pale green solid (26.3 mg, 0.029 mmol, 96%).
\( \text{C}_{50}\text{H}_{47}\text{ClCuN}_{4}\text{O}_{5}\text{S}, \ M: 915.00 \text{ g/mol. m.p.} = 223 \, ^\circ\text{C} \). [\( \alpha \)]\( ^{20}_{\text{D}} \) (c = 1.00 mg/mL, DCM): −15.2. \( ^1\text{H} \) NMR: paramagnetic species. \( ^{13}\text{C} \) NMR: paramagnetic species. IR (solid): \( \tilde{\nu} = 3137, 3060, 2959, 1713, 1625, 1543, 1510, 1494, 1434, 1346, 1267, 1222, 1120, 998, 937, 752, 735, 701, 653 \, \text{cm}^{-1} \). HRMS (ESI) m/z: calculated for \([\text{C}_{50}\text{H}_{45}\text{CuN}_{4}\text{O}_{4}\text{S}]^{+}\): 860.2452. Found: 967.2454.

\[
\text{3-([5-(tert-Butyl)-3-[(E)-([1\text{R},2\text{R}]-1,2-diphenyl-2(methylsulfonamido)ethyl)imino)methyl]-2-hydroxybenzyl)-1-([2'-hydroxy-[1,1' binaphthalen]-2-yl]-1H-imidazol-3-ium-Cu(II)]})
\]

The synthesis was carried out according to GP2 using ligand \( \text{L}_{1g}(\text{R}, \text{R}) \) (11.0 mg, 0.013 mmol, 1.0 equiv.) and \( \text{Cu(acac)}_{2} \) (3.45 mg, 0.013 mmol, 1.0 equiv.). The pre-catalyst \( \text{C}_{1g}(\text{R}, \text{R}) \) was obtained as a pale green solid (10.8 mg, 0.012 mmol, 93%).

\[
\text{C}_{50}\text{H}_{47}\text{ClCuN}_{4}\text{O}_{5}\text{S}, \ M: 915.00 \text{ g/mol. m.p.} = 196 \, ^\circ\text{C} \). [\( \alpha \)]\( ^{20}_{\text{D}} \) (c = 1.00 mg/mL, DCM): 10.1. \( ^1\text{H} \) NMR: paramagnetic species. \( ^{13}\text{C} \) NMR: paramagnetic species. IR (solid): \( \tilde{\nu} = 3138, 3062, 2955, 1717, 1621, 1545, 1514, 1492, 1437, 1345, 1269, 1220, 1121, 998, 935, 754, 730, 704, 651 \, \text{cm}^{-1} \). HRMS (ESI) m/z: calculated for \([\text{C}_{50}\text{H}_{45}\text{CuN}_{4}\text{O}_{4}\text{S}]^{+}\): 860.2452. Found: 860.2456.
The synthesis was carried out according to GP2 using ligand L1h-(S,S) (15.4 mg, 0.017 mmol, 1.0 equiv.) and Cu(acac)$_2$ (4.42 mg, 0.017 mmol, 1.0 equiv.). The pre-catalyst C1h-(S,S) was obtained as a pale green solid (15.9 mg, 0.016 mmol, 96%).

$\text{C}_56\text{H}_{51}\text{ClCuN}_4\text{O}_5\text{S}$, $M$: 991.10 g/mol. $\text{m.p.} = 208 \degree \text{C}$. $[\alpha]^{20}_D$ (c = 1.00 mg/mL, DCM): $-50.6$. $^1\text{H}$ NMR: paramagnetic species. $^{13}\text{C}$ NMR: paramagnetic species. IR (solid): $\tilde{\nu}$ = 3058, 2919, 1624, 1542, 1510, 1451, 1433, 1344, 1271, 1221, 1131, 1095, 991, 907, 815, 750, 734, 699 cm$^{-1}$. HRMS (ESI) m/z: calculated for [C$_{56}$H$_{49}$CuN$_4$O$_5$S]$^+$: 936.2765. Found: 936.2766.
The synthesis was carried out according to GP2 using ligand L1h-(R,R) (15.0 mg, 0.016 mmol, 1.0 equiv.) and Cu(acac)2 (4.31 mg, 0.016 mmol, 1.0 equiv.). The pre-catalyst C1h-(R,R) was obtained as a pale green solid (14.8 mg, 0.015 mmol, 95%).

The synthesis was carried out according to GP2 using ligand L1i-(S,S) (15.0 mg, 0.015 mmol, 1.0 equiv.) and Cu(acac)2 (3.98 mg, 0.015 mmol, 1.0 equiv.). The pre-catalyst C1i-(S,S) was obtained as a pale green solid (14.9 mg, 0.014 mmol, 95%).
$\text{C}_5\text{H}_{14}\text{ClCuF}_5\text{N}_4\text{O}_5\text{S}, \text{M}: 1049.00 \text{ g/mol. m.p.} = 191 ^\circ \text{C. } [\alpha]^{20}_D (c = 1.00 \text{ mg/mL, DCM}): -72.3.\text{ }^1\text{H NMR: paramagnetic species. } ^{13}\text{C NMR: paramagnetic species. IR (solid): } v = 3062, 2961, 1627, 1575, 1544, 1487, 1452, 1433, 1272, 1154, 1096, 989, 938, 818, 700, 601 \text{ cm}^{-1}.\text{ HRMS (ESI) } m/z: \text{ calculated for } [\text{C}_5\text{H}_{42}\text{CuN}_4\text{O}_4\text{S}]^+: 1012.2137. \text{ Found: 1012.2131.}$

3-(5-(tert-Butyl)-3-((E)-((1R,2R)-1,2-diphenyl-2-((perfluorophenyl)sulfonamido)ethyl)imino)methyl)-2-hydroxybenzyl)-1-(2'-hydroxy-[1,1'-binaphthalen]-2-yl)-1H-imidazol-3-ium copper (II)-chloride (C1i-(R,R))

The synthesis was carried out according to GP2 using ligand L1i-(R,R) (15.0 mg, 0.015 mmol, 1.0 equiv.) and Cu(acac)$_2$ (3.98 mg, 0.015 mmol, 1.0 equiv.). The pre-catalyst C1i-(R,R) was obtained as a pale green solid (14.5 mg, 0.014 mmol, 92%).

$\text{C}_5\text{H}_{14}\text{ClCuF}_5\text{N}_4\text{O}_5\text{S}, \text{M}: 1049.00 \text{ g/mol. m.p.} = 205 ^\circ \text{C. } [\alpha]^{20}_D (c = 1.00 \text{ mg/mL, DCM}): 36.1.\text{ }^1\text{H NMR: paramagnetic species. } ^{13}\text{C NMR: paramagnetic species. IR (solid): } v = 3060, 2960,
1626, 1577, 1543, 1516, 1489, 1450, 1434, 1275, 1151, 1095, 988, 938, 817, 701, 600 cm$^{-1}$.

**HRMS (ESI)** m/z: calculated for [C$_{55}$H$_{44}$CuN$_4$O$_4$S]$^+$: 1012.2137. Found: 1012.2137.
Screening of the Sulfonyl Residues of Catalyst C1.

Table S1.

| Entry | C1 (config.) | yield[a] / [%] | dr[b]   | ee[c] / [%] |
|-------|--------------|----------------|---------|-------------|
| 1     | C1a (1S,2S)  | 97             | >98:2   | 90          |
| 2     | C1a (1R,2R)  | 96             | >98:2   | -86         |
| 3     | C1b (1S,2S)  | 98             | >98:2   | -96         |
| 4     | C1b (1R,2R)  | 96             | >98:2   | -40         |
| 5     | C1c (1S,2S)  | 98             | >98:2   | -90         |
| 6     | C1d (1S,2S)  | 97             | >98:2   | -65         |
| 7     | C1d (1R,2R)  | 98             | >98:2   | -34         |
| 8     | C1e (1S,2S)  | 95             | >98:2   | 36          |
| 9     | C1e (1R,2R)  | 97             | >98:2   | -30         |
| 10    | C1f (1S,2S)  | 94             | >98:2   | 36          |
| 11    | C1f (1R,2R)  | 96             | >98:2   | -13         |
| 12    | C1g (1S,2S)  | 98             | >98:2   | 16          |
| 13    | C1g (1R,2R)  | 95             | >98:2   | -12         |
| 14    | C1h (1S,2S)  | 97             | >98:2   | -51         |
| 15    | C1h (1R,2R)  | 96             | >98:2   | 50          |
| 16    | C1i (1S,2S)  | 98             | >98:2   | 32          |
| 17    | C1i (1R,2R)  | 96             | >98:2   | -30         |

[a] Yield of isolated product. [b] Endo/exo ratios determined by $^1$H NMR using the crude product. [c] The enantiomeric excess of the endo-isomer was determined by $^1$H NMR using saturated CDCl$_3$ solution of (R)-(+)binaphthol. A minus sign indicates that the antipode of the enantiomer depicted was generated in excess.
Investigation of Maleimide Dienophiles (2) and Maleic Anhydride (6) in the Diels-Alder Reaction with 3-Hydroxypyrone (1a).

**Table S2.**

| #  | 2 or 6 | R-N / O | (ent-3a) or 7 | yield[a] | dr[b] | ee[c] |
|----|--------|---------|---------------|----------|-------|-------|
| 1  | 2A     | Me-N    | ent-3aA       | 93       | >98:2 | 93    |
| 2  | 2B     | Bn-N    | ent-3aB       | 98       | >98:2 | 98    |
| 3  | 2C     | 4-O2N-C6H4-N | ent-3aC | 94       | >98:2 | 94    |
| 4  | 2D     | cyc-Hex-N | ent-3aD      | 92       | >98:2 | 96    |
| 5[d] | 2E   | Boc-N   | 3aE           | 90       | >98:2 | –92   |
| 6[e] | 2F  | H-N     | ent-3aF       | 89       | >98:2 | 90    |
| 7  | 2G     | Ph-N    | ent-3aG       | 94       | >98:2 | 91    |
| 8  | 2H     | 2,6-(MeO)2C6H3-N | ent-3aH | 93       | >98:2 | 91    |
| 9  | 2I     | 3-Cl-C6H4-N | ent-3aI      | 93       | >98:2 | 94    |
| 10 | 2J     | 4-F3C-C6H4-N | ent-3aJ    | 90       | >98:2 | 96    |
| 11 | 2K     | 3-O2N-C6H4-N | ent-3aK   | 94       | >98:2 | 95    |
| 12 | 2L     | 4-Cl-C6H4-N | ent-3aL     | 92       | >98:2 | 90    |
| 13 | 2M     | 2,4,6-Me3C6H2-N | ent-3aM   | 91       | >98:2 | 97    |
| 14[d][f] | 6 | O       | 7             | 92       | >98:2 | –84   |

[a] Yield of isolated product. [b] Endo/exo ratios determined by $^1$H NMR using the crude product. [c] The enantiomeric excess was determined by $^1$H NMR using saturated CDCl$_3$ solutions of (R)-(+)-binaphthol. A minus sign indicates that the antipode of the enantiomer depicted was generated in excess. [d] C1a (1S,2S) was used as catalyst. [e] The reaction was performed at –20 °C. [f] The reaction was performed at 0 °C.
Catalytic Diels–Alder Reactions of 3-Hydroxypyrone in Control Experiments

Table S3.

| #  | Base     | Catalyst | Yield[a] [%] | dr[b]     | ee[c] (endo/exo) [%] |
|----|----------|----------|--------------|-----------|----------------------|
| 1  | Cs₂CO₃   | C2       | 92           | 84/16     | -1/-2                |
| 2  | Et₃N     | C2       | 81           | 94/6      | -2/2                 |
| 3  | Cs₂CO₃   | C3       | 96           | 82/18     | -4/0                 |
| 4  | Et₃N     | C3       | 65           | 96/4      | 26/0                 |
| 5  | Cs₂CO₃   | C4       | 93           | 84/16     | 8/0                  |
| 6  | Et₃N     | C4       | 88           | 94/6      | 10/0                 |
| 7  | K₂CO₃    | C4       | 70           | 94/6      | 32/2                 |
| 8  | Cs₂CO₃   | C5       | 94           | 90/10     | 42/5                 |
| 9  | Et₃N     | C5       | 72           | 84/16     | 0/0                  |
| 10 | K₂CO₃    | C5       | 85           | 92/8      | 5/0                  |
| 11 | -        | C6       | 95           | >98/2     | 86/n.d.              |

[a] Yield of isolated product. [b] Endo/exo ratios determined by ¹H NMR using the crude product. [c] The enantiomeric excess was determined by ¹H NMR using saturated CDCl₃ solutions of (R)−(+)-binaphthol. A minus sign indicates that the antipode of the enantiomer depicted was generated in excess. [d] In the absence of additional base.
Catalytic Diels–Alder Reactions of 3-Hydroxypyrone in Control Experiments

Table S4.11

Table of Results:

| #  | Base   | CuX₂   | Ligand | T [°C] | yield[a] [%] | dr[b]   | ee[c] (endo/exo) |
|----|--------|--------|--------|--------|--------------|---------|-----------------|
| 1  | TEA    | Cu(OTf)₂ | L2     | 25     | 95           | 97/3    | 30 / n.d.       |
| 2  | DIPEA  | Cu(OTf)₂ | L2     | 25     | 93           | 98/2    | 46 / n.d.       |
| 3  | Cs₂CO₃ | Cu(OTf)₂ | L2     | 25     | 95           | 98/2    | 0 / n.d.        |
| 4  | DIPEA  | Cu(OTf)₂ | L2     | −20    | 92           | 94/6    | 24 / 1          |
| 5  |        | Cu(OAc)₂ | L2     | −20    | 85           | 96/4    | 0 / n.d.        |
| 6  | DIPEA  | Cu(OTf)₂ | L3     | 25     | 92           | 98/2    | 8 / n.d.        |
| 7  |        | Cu(OTf)₂ | L3     | −20    | 42           | 97/3    | 5 / n.d.        |
| 8  | DIPEA  | Cu(OTf)₂ | L4     | 25     | 92           | 90/10   | 0 / 0           |
| 9  |        | Cu(OTf)₂ | L4     | −20    | 55           | 92/8    | 0 / 0           |
| 10 | DIPEA  | Cu(OTf)₂ | L5     | 25     | 92           | 97/3    | 0 / 0           |
| 11 |        | Cu(OTf)₂ | L5     | −20    | 94           | 98/2    | 2 / 0           |

[a] Yield of isolated product. [b] Endo/exo ratios determined by ¹H NMR using the crude product. [c] The enantiomeric excess was determined by ¹H NMR using saturated CDCl₃ solutions of (R)-(+)-binaphthol. [d] In the absence of additional base.
Characterization of Diels-Alder Adducts

(3aS,4S,7S,7aR)-4,7-Ethenopyranol [3,4-c] pyrrole-1,3,6(2H)-trione-3a,4,7,7a-tetrahydro-7-hydroxy-2-methyl (ent-3aA)

The product 3aA was synthesized according to GP4 using 3-hydroxypyrone 1a (11.2 mg, 0.10 mmol, 1.0 equiv.), N-methylemaleimide 2A (11.6 mg, 0.105 mmol, 1.05 equiv.) and catalyst C1b (4.86 mg, 0.005 mmol, 5.0 mol%). 3aA was isolated as a white solid (20.7 mg, 0.093 mmol, 93%, ee = 93%). The enantiomeric excess was determined by 1H NMR as described in GP8.

C_{16}H_{13}NO_{5}, M: 299.28 g/mol. [α]^{20}_D = -75.4 (c = 1.0 mg/mL, acetone, sample with 93% ee). 1H NMR (CDCl_{3}, 400 MHz, 21 °C): δ (ppm) = 6.51 (d, J = 8.2 Hz, 1H, CH=CH), 6.42 (dd, J = 8.2, 2.6 Hz, 1H, CH=CH), 5.59 (dt, J = 4.7 Hz, 1.9 Hz, 1H, CH-O-C=O), 3.89 (s, 1H, O-H), 3.76 (dd, J = 7.9, 2.6 Hz, 1H, O-CH-CH-C(=O)N), 3.12 (d, J = 8.2 Hz, 1H, CH-C(OH)-C=O), 2.97 (s, 3H, CH_{3}).

The NMR spectra is in agreement to the one reported in the literature.\(^{12}\)

(3aS,4S,7S,7aR)-4,7-Ethenopyranol [3,4-c] pyrrole-1,3,6(2H)-trione-3a,4,7,7a-tetrahydro-7-hydroxy-2-(phenylmethyl) (ent-3aB)

The product 3aB was synthesized according to GP4 using 3-hydroxypyrone 1a (11.2 mg, 0.10 mmol, 1.0 equiv.), N-benzylinealeimide 2B (19.6 mg, 0.105 mmol, 1.05 equiv.) and catalyst C1b (4.86 mg, 0.005 mmol, 5.0 mol%). 3aB was isolated as a white solid (29.3 mg, 0.098 mmol, 98%, ee = 98%). The enantiomeric excess was determined by 1H NMR as described in GP8.

C_{18}H_{13}NO_{5}, M: 299.28 g/mol. [α]^{20}_D = -80.5 (c = 1.0 mg/mL, acetone, sample with 98% ee). 1H NMR (CD_{3}CN, 500 MHz, 21 °C): δ (ppm) = 7.37-7.24 (m, 3H, ArH), 7.21 (d, J = 7.6 Hz, 2H, ArH), 6.37-6.26 (m, 2H, CH=CH), 5.51 (dt, J = 4.4 Hz, 2.3 Hz, 1H, CH-O-C=O), 4.62 (s, 1H, O-H), 4.52 (s, 2H, CH_{2}Ph), 3.82 (dd, J = 8.2, 4.8 Hz, 1H, O-CH-CH-C(=O)N), 3.18 (d, J = 8.2 Hz, 1H, CH-C(OH)-C=O).

The NMR spectra is in agreement to the one reported in the literature.\(^{13}\)
(3aS,4S,7S,7aR)-4,7-Ethenopyranol [3,4-c] pyrrole-1,3,6(2H)-trione-3a,4,7,7a-tetrahydro-7-hydroxy-2-(4-nitrophenyl) (ent-3aC)

The product 3aC was synthesized according to GP4 using 3-hydroxypyrone 1a (11.2 mg, 0.10 mmol, 1.0 equiv.), N-(4-nitrophenyl)maleimide 2C (22.9 mg, 0.105 mmol, 1.05 equiv.) and catalyst C1b (4.86 mg, 0.005 mmol, 5.0 mol%). 3aC was isolated as a white solid (31.0 mg, 0.094 mmol, 94%, ee = 94%). The enantiomeric excess was determined by 1H NMR as described in GP8.

C_{15}H_{10}N_{2}O_{7}, M: 330.25 g/mol. m.p.: 185 °C. [α]^{20}_{D} = -52.2 (c = 1.0 mg/mL, acetone, sample with 94% ee). 1H NMR ((CD_{3})_{2}CO, 400 MHz, 21 °C): δ (ppm) = 8.37 (d, J = 9.1 Hz, 2H, Ar H), 7.60 (d, J = 9.1 Hz, 2H, Ar H), 6.73-6.63 (m, 2H, CH=CH), 5.75 (s, 1H, OH), 5.67 (dt, J = 4.5, 1.9 Hz, 1H, CH-O-C=O), 4.16 (dd, J = 7.9, 4.7 Hz, 1H, O-CH-CH-C(=O)N), 3.52 (d, J = 8.3 Hz, 1H, CH-C(OH)-C=O). 13C NMR ((CD_{3})_{2}CO, 100 MHz, 21 °C): δ (ppm) = 172.8, 172.3, 172.2, 147.9, 138.2, 137.5, 129.7, 128.2, 124.7, 76.2, 72.4, 47.5, 44.1. IR (solid): ν = 3463, 3082, 1768, 1718, 1596, 1525, 1497, 1379, 1348, 1309, 1249, 1183, 1141, 1054, 973, 917, 855, 747, 698 cm⁻¹. HRMS (ESI): m/z calculated for [C_{15}H_{10}N_{2}O_{7}Na]⁺: 353.0380, found: 353.0369.

CCDC 1995951 contains the supplementary crystallographic data for compound 3aC. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

(3aS,4S,7S,7aR)-4,7-Ethenopyranol [3,4-c] pyrrole-1,3,6(2H)-trione-3a,4,7,7a-tetrahydro-7-hydroxy-2-cyclohexyl (ent-3aD)

The product 3aD was synthesized according to GP4 using 3-hydroxypyrone 1a (11.2 mg, 0.10 mmol, 1.0 equiv.), N-cyclohexylmaleimide 2D (18.8 mg, 0.105 mmol, 1.05 equiv.) and catalyst C1b (4.86 mg, 0.005 mmol, 5.0 mol%). 3aD was isolated as a white solid (29.4 mg, 0.092 mmol, 92%, ee = 96%). The enantiomeric excess was determined by 1H NMR as described in GP8.
The product 3ae was synthesized according to GP4 using 3-hydroxypryrole 1a (11.2 mg, 0.10 mmol, 1.0 equiv.), N-Boc maleimide 2e (20.7 mg, 0.105 mmol, 1.05 equiv.) and catalyst C1a (4.56 mg, 0.005 mmol, 5.0 mol%). 3ae was isolated as a white solid (27.8 mg, 0.090 mmol, 90%, ee = 92%). The enantiomeric excess was determined by 1H NMR as described in GP8.

The product 3af (30.9 mg, 0.1 mmol, 1.0 equiv., sample with 92% of ee) was dissolved in DCM (3.0 mL) and TFA was added (11.5 μL, 0.15 mmol, 1.5 equiv.). The reaction mixture was stirred at room temperature until starting material was gone (3 h, monitored by TLC). The solvent was removed in vacuo and the crude product was dissolved in a small amount of DCM (0.2 mL) and n-pentane (5 mL) was added causing precipitation. The solid was filtered off and washed...
with 5 mL of pentane to provide a white solid 3aF (19.2 mg, 0.092 mmol, 92%, 92% of ee). The enantiomeric excess was determined by 1H NMR as described in GP8.

The enantiomer (ent)-3aF was synthesized according to GP4 using 3-hydroxypyrone 1a (11.2 mg, 0.10 mmol, 1.0 equiv.), the parent maleimide 2F (20.7 mg, 0.105 mmol, 1.05 equiv.) and C1b (4.86 mg, 0.005 mmol, 5.0 mol%). (ent)-3aF was isolated as a white solid after purification by column chromatography (PE : EE = 2:1 to pure EE) (18.6 mg, 0.089 mmol, 89%, ee = 90%). The enantiomeric excess was determined by 1H NMR as described in GP8.

C₉H₇NO₅S, M: 209.16 g/mol. m.p.: 135 °C. [α]D²₀ : 51.0 (c = 0.90 mg/mL, sample with 92% ee). (ent)-3aF [α]D²₀ : –62.1 (c = 0.95 mg/mL, sample with 90% ee). 1H NMR ((CD₃)₂SO, 400 MHz, 21 °C): δ (ppm) = 11.40 (s, 1H, NΗ), 6.73 (s, 1H, OΗ), 6.54-6.50 (m, 1H, CH=CH), 6.45 (d, J = 6.3 Hz, 1H, CH=CH), 5.47 (dt, J = 4.8 Hz, 1.8 Hz, 1H, CH-O-C=O), 3.79 (dd, J = 8.2, 4.7 Hz, 1H, O-CH-CH-C(=O)N), 3.12 (d, J = 8.2 Hz, 1H, CH-C(OH)-C=O). 13C NMR ((CD₃)₂SO, 100 MHz, 21 °C): δ (ppm) = 175.3, 174.6, 172.6, 136.9, 128.8, 75.2, 71.3, 47.6, 43.7. IR (solid): ν = 3257, 1763, 1712, 1359, 1188, 1142, 968, 693 cm⁻¹. HRMS (ESI): m/z calculated for [C₉H₇NO₅Na]⁺: 232.0216, found: 232.0209.

(3aS,4S,7S,7aR)-4,7-Ethenopyranol [3,4-c] pyrrole-1,3,6(2H)-trione-3a,4,7,7a-tetrahydro-7-hydroxy-2-phenyl (ent-3aG)

The product 3aG was synthesized according to GP4 using 3-hydroxypyrone 1a (11.2 mg, 0.10 mmol, 1.0 equiv.), N-phenylmaleimide 2G (18.1 mg, 0.105 mmol, 1.05 equiv.) and catalyst C1b (4.86 mg, 0.005 mmol, 5.0 mol%). 3aG was isolated as a white solid (30.0 mg, 0.094 mmol, 94%, ee = 91%). The enantiomeric excess was determined by 1H NMR as described in GP8.

C₁₅H₁₁NO₅S, M: 319.69 g/mol. m.p.: 166 °C. [α]D²₀ : –28.0 (c = 0.82 mg/mL, acetone, sample with 90% ee). 1H NMR (CD₃CN, 400 MHz, 21 °C): δ (ppm) = 7.58-7.42 (m, 3H, ArH), 7.24-7.14 (m, 2H, ArH), 6.64-6.54 (m, 2H, ArH), 5.62 (dt, J = 4.5 Hz, 1.0 Hz, 1H, CH-O-C=O), 4.74 (br. s, 1H, OH), 3.98 (dd, J = 8.0, 4.5 Hz, 1H, O-CH-CH-C(=O)N), 3.34 (d, J = 8.0 Hz, 1H, CH-C(OH)-C=O). 13C NMR (CD₃CN, 100 MHz, 21 °C): δ (ppm) = 173.8, 173.6, 173.0, 137.7, 132.9, 130.1, 130.0, 129.9, 127.8, 76.3, 73.0, 47.3, 44.0. IR (solid): ν = 3370, 3090, 2261, 2158, 1770, 1718, 1597, 1496, 1388, 1362, 1227, 1192, 1139, 1037, 972, 832, 695, 492 cm⁻¹. HRMS (ESI): m/z calculated for [C₁₅H₁₁NO₅Na]⁺: 308.0529, found: 308.0545.
(3aS,4S,7S,7aR)-4,7-Ethenopyranol [3,4-c] pyrrole-1,3,6(2H)-trione-3a,4,7,7a-tetrahydro-7-hydroxy-2-(2,6-dimethoxyphenyl) (ent-3aH)

\[
\begin{align*}
\text{C}_{17}\text{H}_{15}\text{NO}_7, \quad M: & \quad 345.30 \text{ g/mol. m.p.: } 162 ^\circ \text{C}. \quad [\alpha]^{20}_{D} : -74.9 (c = 1.0 \text{ mg/mL, acetone, sample with 91% ee}). \quad ^1\text{H} \text{ NMR (CD}\text{$_3$CN, 500 MHz, 21 °C)}: \delta (\text{ppm}) = 7.40 (t, J = 8.5 \text{ Hz, 1H, ArH}), 6.71 (t, J = 7.6 \text{ Hz, 2H, ArH}), 6.55-6.47 (m, 2H, CH=CH), 5.57 (dt, J = 4.7 \text{ Hz, 1.7 Hz, 1H, CH-O-C=O}), 4.57 (s, 1H, OH), 3.96 (dd, J = 8.2, 4.7 Hz, 1H, O-CH=CH-(=O)N), 3.75 (s, 6H, OCH$_3$), 3.32 (d, J = 8.2 Hz, 1H, CH-(OH)-(OH)=O). \quad ^{13}\text{C} \text{ NMR (CD}\text{$_3$CN, 100 MHz, 21 °C)}: \delta (\text{ppm}) = 173.2, 173.1, 173.0, 157.2, 157.1, 137.5, 132.3, 129.8, 109.9, 105.4, 105.3, 76.4, 73.2, 56.8, 56.7, 47.7, 44.3. \quad \text{IR (solid)}: \tilde{\nu} = 3453, 2947, 2844, 2259, 1765, 1710, 1599, 1503, 1482, 1446, 1385, 1363, 1306, 1262, 1196, 1139, 1111, 1054, 1030, 971, 916, 820, 791, 774, 756, 694, 481 \text{ cm}^{-1}. \quad \text{HRMS (ESI)}: m/z \text{ calculated for [C}_{17}\text{H}_{15}\text{NO}_7\text{Na}]^{+}: 368.0741, \text{ found } 368.0745.
\end{align*}
\]

(3aS,4S,7S,7aR)-4,7-Ethenopyranol [3,4-c] pyrrole-1,3,6(2H)-trione-3a,4,7,7a-tetrahydro-7-hydroxy-2-(3-chlorophenyl) (ent-3aI)

\[
\begin{align*}
\text{C}_{18}\text{H}_{10}\text{NCIO}_5, \quad M: & \quad 319.69 \text{ g/mol. m.p.: } 174 \text{ °C}. \quad [\alpha]^{20}_{D} : -80.0 (c = 1.0 \text{ mg/mL, acetone, sample with 94% ee}). \quad ^1\text{H} \text{ NMR (CD}\text{$_3$CN, 400 MHz, 21 °C)}: \delta (\text{ppm}) = 7.51-7.4 (m, 2H, ArH), 7.27-7.22 (m, 1H, ArH), 6.60-6.52 (m, 2H, CH=CH), 5.60 (dt, J = 4.6, 2.4 Hz, 1H, CH-O), 4.73-4.56 (br, 1H, OH), 3.97 (dd, J = 8.4, 4.7 Hz, 1H, O-CH=CH-(=O)N), 3.34 (d, J = 8.4 Hz, 1H, CH-C(OH)-C=O). \quad ^{13}\text{C} \text{ NMR (CD}\text{$_3$CN, 100 MHz, 21 °C)}: \delta (\text{ppm}) = 173.5, 173.3, 173.0, 137.8, 134.9, 134.1, 131.6, 130.1, 130.0, 127.7, 126.4, 76.4, 73.0, 47.4, 44.1. \quad \text{IR (solid)}:
\end{align*}
\]

The product 3aH was synthesized according to GP4 using 3-hydroxypyrene 1a (11.2 mg, 0.10 mmol, 1.0 equiv.), N-(2,6-dimethoxyphenyl)maleimide 2H (24.4 mg, 0.105 mmol, 1.05 equiv.) and catalyst C1b (4.86 mg, 0.005 mmol, 5.0 mol%). 3aH was isolated as a white solid (32.1 mg, 0.093 mmol, 93%, ee = 91%). The enantiomeric excess was determined by $^1$H NMR as described in GP8.

The product 3al was synthesized according to GP4 using 3-hydroxypyrene 1a (11.2 mg, 0.10 mmol, 1.0 equiv.), N-(3-chlorophenyl)maleimide 2I (21.7 mg, 0.105 mmol, 1.05 equiv.) and catalyst C1b (4.86 mg, 0.005 mmol, 5.0 mol%). 3al was isolated as a white solid (29.7 mg, 0.093 mmol, 93%, ee = 94%). The enantiomeric excess was determined by $^1$H NMR as described in GP8.
\( \nu = 3434, 3077, 1765, 1709, 1647, 1593, 1480, 1380, 1185, 1138, 1078, 1054, 978, 931, 782, 695, 493 \text{ cm}^{-1} \). HRMS (ESI): \( m/z \) calculated for \([\text{C}_{15}\text{H}_{10}\text{NCIO}_{5}\text{Na}]^+\): 342.0140, found: 342.0140.

\((3aS,4S,7S,7aR)-4,7\text{-Ethenopyranol} [3,4-c] \text{ pyrrole-1,3,6(2H)-trione-3a,4,7,7a-tetrahydro-7-hydroxy-2-(4-(trifluoromethyl)phenyl) (ent-3aJ)}\)

![3aJ diagram]

The product 3aJ was synthesized according to GP4 using 3-hydroxypyrone 1a (11.2 mg, 0.10 mmol, 1.0 equiv.), \( N\)-(4-(trifluoromethyl)phenyl)maleimide 2J (25.3 mg, 0.105 mmol, 1.05 equiv.) and catalyst C1b (4.86 mg, 0.005 mmol, 5.0 mol%). 3aJ was isolated as a white solid (31.0 mg, 0.094 mmol, 94%, \( ee = 95\% \)). The enantiomeric excess was determined by \(^1\text{H} \text{NMR} \) as described in GP8.

\(: C_{16}H_{10}F_3NO_5, \text{ } M: 353.25 \text{ g/mol. } m.p.: 180 \text{ °C. } [\alpha]^{20}D_2: -42.1 \text{ (c = 1.0 mg/mL, acetone, sample with 96% ee). } ^{1}\text{H NMR (CD$_3$CN, 400 MHz, 21 °C): } \delta \text{ (ppm) = 7.82 (d, J = 8.5 Hz, 2H, ArH), 7.40 (d, J = 8.3 Hz, 2H, ArH), 6.61-6.54 (m, 2H, CH=CH), 5.61 (dt, J = 4.6 Hz, 2.6 Hz, 1H, -CH-O-C=O), 4.75 (s, 1H, O-H), 3.99 (dd, J = 8.0, 4.4 Hz, 1H, O-CH-CH-C(=O)N), 3.36 (d, J = 8.1 Hz, 1H, CH-C(OH)-C=O). }^{19}\text{F NMR (CD$_3$CN, 376 MHz, 21 °C): } \delta \text{ (ppm) = -63.3. } ^{13}\text{C NMR (CD$_3$CN, 100 MHz, 21 °C): } \delta \text{ (ppm) = 173.5, 173.3, 173.0, 137.9, 136.3, 131.3, 130.2, 128.5, 127.3, 127.2, 126.3, 123.6, 76.4, 73.1, 47.6, 44.3. IR (solid): } \nu = 3453, 3088, 2968, 1766, 1711, 1615, 1519, 1417, 1386, 1324, 1238, 1169, 1131, 1067, 1021, 972, 917, 873, 846, 815, 729, 696, 605, 506 \text{ cm}^{-1}. \) HRMS (ESI): \( m/z \) calculated for \([\text{C}_{16}H_{10}F_3NO_5\text{Na}]^+\): 376.0403, found: 376.0392.

\((3aS,4S,7S,7aR)-4,7\text{-Ethenopyranol} [3,4-c] \text{ pyrrole-1,3,6(2H)-trione-3a,4,7,7a-tetrahydro-7-hydroxy-2-(3-nitrophenyl) (ent-3aK)}\)

![3aK diagram]

The product 3aK was synthesized according to GP4 using 3-hydroxypyrone 1a (11.2 mg, 0.10 mmol, 1.0 equiv.), \( N\)-(3-nitrophenyl)maleimide 2K (22.9 mg, 0.105 mmol, 1.05 equiv.) and catalyst C1b (4.86 mg, 0.005 mmol, 5.0 mol%). 3aK was isolated as a white solid (31.0 mg, 0.094 mmol, 94%, \( ee = 95\% \)). The enantiomeric excess was determined by \(^1\text{H} \text{NMR} \) as described in GP8.
C_{15}H_{10}N_{2}O_{7}, M: 330.25 g/mol. m.p.: 179 °C. [α]^{20}_D: −65.9 (c = 1.0 mg/mL, acetone, sample with 95% ee). \(^1\)H NMR (CD_{3}CN, 400 MHz, 21 °C): δ (ppm) = 8.27 (dd, J = 8.2, 2.3, 1.1 Hz, 1H, ArH), 8.13 (t, J = 2.1 Hz, 1H, ArH), 7.66-7.60 (m, 2H, ArH), 6.66-6.53 (m, 2H, CH=CH), 5.69 (dt, J = 4.5 Hz, 2.3 Hz, 1H, CH-O-C=O), 4.10 (s, 1H, OCH), 4.00 (dd, J = 8.1, 4.8 Hz, 1H, O-CH-C(=O)N), 3.37 (d, J = 8.2 Hz, 1H, CH-C(OH)-C=O).

IR (solid): 𝜈̃ = 3465, 3092, 1767, 1716, 1532, 1484, 1384, 1352, 1309, 1238, 1187, 1141, 1095, 979, 939, 697, 483 cm\(^{-1}\). HRMS (ESI): m/z calculated for [C_{15}H_{10}N_{2}O_{7}Na]^+: 353.0380, found: 353.0369.

(3aS,4S,7S,7aR)-4,7-Ethenopyranol [3,4-c] pyrrole-1,3,6(2H)-trione-3a,4,7,7a-tetrahydro-7-hydroxy-2-(4-chlorophenyl) (ent-3aL)

3aL

The product 3aL was synthesized according to GP4 using 3-hydroxypyrone 1a (11.2 mg, 0.10 mmol, 1.0 equiv.), N-(4-chlorophenyl)maleimide 2L (22.8 mg, 0.105 mmol, 1.05 equiv.) and catalyst C1b (4.86 mg, 0.005 mmol, 5.0 mol%). 3aL was isolated as a white solid (29.4 mg, 0.092 mmol, 92%, ee = 90%). The enantiomeric excess was determined by \(^1\)H NMR as described in GP8.

C_{15}H_{10}NClO_{5}, M: 319.69 g/mol. m.p.: 180 °C. [α]^{20}_D: −69.4 (c = 1.0 mg/mL, acetone, sample with 90% ee). \(^1\)H NMR ((CD_{3})_{2}SO, 700 MHz, 21 °C): δ = 7.58-7.56 (m, 2H, ArH), 7.21-7.19 (m, 2H, ArH), 6.89 (s, 1H, OCH), 6.61 (dd, J = 8.3, 4.9 Hz, 1H, CH=CH), 6.53 (d, J = 8.3 Hz, 1H, CH=CH), 5.61 (dt, J = 4.9, 1.9 Hz, 1H, O-CH), 4.01 (dd, J = 8.3, 4.9 Hz, 1H, O-CH-C(=O)N), 3.34 (dd, J = 7.9, 0.88 Hz, 1H, CH-C(OH)-C=O). \(^1\)C NMR ((CD_{3})_{2}SO, 176 MHz, 21 °C): δ = 172.8, 172.4, 172.2, 136.9, 133.26, 130.6, 129.2, 129.0, 128.7, 75.3, 71.4, 46.4, 42.8. IR (solid): 𝜈̃ = 3437, 3078, 1766, 1711, 1493, 1386, 1307, 1188, 1140, 1091, 1055, 972, 811, 786, 756, 695, 508, 427 cm\(^{-1}\). HRMS (ESI): m/z calculated for [C_{15}H_{10}NClO_{5}Na]^+: 342.0140, found: 342.0135.
(3aS,4S,7S,7aR)-4,7-Ethenopyranol [3,4-c] pyrrole-1,3,6(2H)-trione-3a,4,7,7a-tetrahydro-7-hydroxy-2-(2,4,6-trimethylphenyl) (ent-3aM)

![Chemical structure of ent-3aM](image)

The product 3aM was synthesized according to GP4 using 3-hydroxypyrone 1a (11.2 mg, 0.10 mmol, 1.0 equiv.), N-(2,4,6-trimethylphenyl)maleimide 2M (22.6 mg, 0.105 mmol, 1.05 equiv.) and catalyst C1b (4.86 mg, 0.005 mmol, 5.0 mol%). 3aM was isolated as a white solid (29.8 mg, 0.091 mmol, 91%, ee = 97%). The enantiomeric excess was determined by 1H NMR as described in GP8.

C_{18}H_{17}NO_{5}. M: 327.34 g/mol. [α]^{20}_{D} = -34.8 (c = 1.0 mg/mL, acetone, sample with 97% ee). 1H NMR (CDCl₃, 400 MHz, 21 °C): δ (ppm) = 6.97 (s, 1H, ArH), 6.93 (s, 1H, ArH), 6.65 (s, 1H, ArH), 6.62 (m, 2H, CH=CH), 5.72 (m, 1H, CH-O-C=O), 4.05 (s, 1H, OH), 3.97 (dd, J = 4.4, 8.1 Hz, 1H, O-CH-CH-(=O)N), 3.33 (d, J = 8.2 Hz, 1H, CH-C(OH)-C=O), 2.28 (s, 3H, CH₃), 2.03 (s, 3H, CH₃), 2.00 (s, 3H, CH₃). The NMR spectra is in agreement to the one reported in the literature.

(3aR,4R,7S,7aS)-4,7-Ethenopyranol-(8-methyl) [3,4-c] pyrrole-1,3,6(2H)-trione-3a,4,7,7a-tetrahydro-7-hydroxy-2-(phenylmethyl) (3bB)

![Chemical structure of 3bB](image)

The product 3bB was synthesized according to GP4 using 4-methyl-3-hydroxypyrone 1b (12.6 mg, 0.10 mmol, 1.0 equiv.), N-benzylmaleimide 2B (19.6 mg, 0.105 mmol, 1.05 equiv.) and catalyst C1a (4.56 mg, 0.005 mmol, 5.0 mol%). 3bB was isolated as a white solid (29.1 mg, 0.093 mmol, 93%, ee = 93%). The enantiomeric excess was determined by 1H NMR as described in GP8.

C_{11}H_{15}NO_{5}. M: 313.30 g/mol. m.p.: 166 °C. [α]^{20}_{D} = 53.9 (c = 1.0 mg/mL, acetone, sample with 93% ee). 1H NMR (CD_{2}CN, 400 MHz, 21 °C): δ (ppm) = 7.37-7.25 (m, 3H, ArH), 7.24-7.18 (m, 2H, ArH), 5.94 (m, 1H, CH=CH-CH₃), 5.41 (t, J = 4.8 Hz, 1H, CH-O-C=O), 4.51 (q, J = 18.7, 14.5 Hz, 2H, CH₂Ph), 4.40 (br, 1H, OH), 3.77 (dd, J = 8.1, 4.8 Hz, 1H, O-CH-CH-(=O)N), 3.14 (d, J = 7.9 Hz, 1H, CH-C(OH)-C=O), 1.52 (d, J = 1.8 Hz, 3H, CH₃). 13C NMR (CD_{2}CN, 176 MHz, 21 °C): δ (ppm) = 174.5, 174.2, 173.4, 146.6, 136.8, 129.4, 128.9, 128.6, 122.5, 77.5, 72.9, 47.7, 43.9, 43.0, 15.4. IR (solid): ν = 3449, 2957, 1758, 1693, 1431, 1396, 1342, 1312, 1291, 1237, 1156, 1133, 1086, 1029, 1004, 949, 903, 803, 772, 750, 699, 629, 484 cm⁻¹. HRMS (ESI): m/z calculated for [C_{11}H_{15}NO_{5}Na]⁺: 336.0842, found: 336.0838.
(3aR,4S,7R,7aS)-4,7-Ethenopyranol-(8-chloro) [3,4-c] pyrrole-1,3,6(2H)-trione-3a,4,7,7a-tetrahydro-7-hydroxy-2-(phenylmethyl) (3cB)

![3cB](image)

The product 3cB was synthesized according to GP4 using 4-chloro-3-hydroxypryone 1c (14.6 mg, 0.10 mmol, 1.0 equiv.), 2-homopyridine 2B (19.6 mg, 0.105 mmol, 1.05 equiv.) and catalyst C1a (4.56 mg, 0.005 mmol, 5.0 mol%). 3cB was isolated as a white solid (30.7 mg, 0.092 mmol, 92%, ee = 95%). The enantiomeric excess was determined by 1H NMR as described in GP8.

C18H12ClNO5, M: 333.72 g/mol. m.p.: 172 °C. [α]D20 : 80.5 (c = 0.98 mg/mL, acetone, sample with 95% ee). 1H NMR (CDCl3, 400 MHz, 21 °C): δ (ppm) = 7.33-7.27 (m, 5H, ArH), 6.16 (d, J = 5.4 Hz, 1H, CH=C-Cl), 5.53 (t, J = 5.2 Hz, 1H, CH-O-C=O), 4.61 (q, J = 14.2, 13.8 Hz, 2H, CH2Ph), 4.11 (br. s, 1H, OH), 3.78 (dd, J = 7.7, 4.8 Hz, 1H, O-CH-CH-C(=O)N), 3.26 (d, J = 8.1 Hz, 1H, CH-C(OH)-C=O). 13C NMR (CDCl3, 176 MHz, 21 °C): δ (ppm) = 172.2, 172.1, 169.7, 138.9, 134.8, 129.0, 128.9, 128.5, 123.1, 75.8, 71.9, 46.7, 43.3, 43.0. IR (solid): ν = 3434, 3087, 1767, 1696, 1612, 1496, 1455, 1432, 1396, 1296, 1236, 1170, 1137, 1079, 1004, 955, 907, 815, 779, 730, 701, 662, 619, 575, 526, 491, 491 cm⁻¹. HRMS (ESI): m/z calculated for [C18H12ClNO5Na]⁺: 356.0296, found: 356.0292.

(3aR,4S,7R,7aS)-4,7-Ethenopyranol-(8-bromo) [3,4-c] pyrrole-1,3,6(2H)-trione-3a,4,7a-tetrahydro-7-hydroxy-2-(phenylmethyl) (3dB)

![3dB](image)

The product 3dB was synthesized according to GP4 using 4-bromo-3-hydroxypryone 1d (19.1 mg, 0.10 mmol, 1.0 equiv.), 2-homopyridine 2B (19.6 mg, 0.105 mmol, 1.05 equiv.) and catalyst C1a (4.56 mg, 0.005 mmol, 5.0 mol%). 3dB was isolated as a white solid (34.0 mg, 0.094 mmol, 94%, ee = 93%). The enantiomeric excess was determined by 1H NMR as described in GP8.

C18H12BrNO5, M: 362.18 g/mol. m.p.: 182 °C. [α]D20 : 82.8 (c = 1.0 mg/mL, sample with 93% ee). 1H NMR ((CD3)2SO, 500 MHz, 21 °C): δ (ppm) = 7.44 (s, 1H, OH), 7.35-7.22 (m, 3H, ArH), 7.16 (d, J = 7.5 Hz, 2H, ArH), 6.80 (d, J = 5.8 Hz, 1H, CH=C-Br), 5.59 (t, J = 5.1 Hz, 1H, CH-O-C=O), 4.50 (q, J = 15.1, 10.6 Hz, 2H, CH2Ph), 3.93 (dd, J = 7.3, 4.5 Hz, 1H, O-CH-CH=C(=O)N), 3.44 (d, J = 7.8 Hz, 1H, CH-C(OH)-C=O). 13C NMR ((CD3)2SO, 100 MHz, 21 °C): δ (ppm) = 173.1, 171.8, 170.9, 135.5, 129.2, 128.5, 128.4, 127.4, 127.3, 75.9, 72.0, 46.5, 43.0, 41.8. IR (solid): ν = 3064, 2922, 1768, 1700, 1607, 1430, 1395, 1353, 1316, 1275, 1171, 1132, 1051, 1024, 1001, 954, 943, 821, 804, 732, 700, 614, 568, 486 cm⁻¹. HRMS (ESI): m/z calculated for [C16H12BrNO5Na]⁺: 399.9791, found: 399.9800.
(3aS,4S,7S,7aR)-4,7-Etheno-1H-pyrrolo [3,4-c] pyridine-1,3,6(2H, 3aH)-trione-4,5,7,7a-tetrahydro-7-hydroxy-2-(methylphenyl)-5-[(2-nitrophenyl)sulfonyl] (ent-5aB)

5aB

The product 5aB was synthesized according to GP6 using N-nosyl-3-hydroxypyrindone 4a (29.6 mg, 0.10 mmol, 1.0 equiv.), N-benzylmaleimide 2B (19.6 mg, 0.105 mmol, 1.05 equiv.) and catalyst C1b (4.96 mg, 0.005 mmol, 5.0 mol%). 5aB was isolated as a white solid (46.9 mg, 0.097 mmol, 97%, ee = 94%). The enantiomeric excess was determined by 1H NMR as described in GP8.

C_{22}H_{17}N_3O_8S, \textit{M}: 483.45 g/mol. \textit{m.p.:} 193 °C. [\alpha]^{20}_D : –92.3 (c = 1.0 mg/mL, acetone, sample with 94% ee). 1H NMR (CD_{3}CN, 400 MHz, 21 °C): δ (ppm) = 8.37 (d, J = 7.6 Hz, 1H, ArH), 7.98-7.86 (m, 3H, ArH), 7.39-7.21 (m, 5H, ArH), 6.55 (dd, J = 8.7, 5.6 Hz, 1H, CH=CH), 6.18 (d, J = 8.0 Hz, 1H, CH=CH), 5.50 (dt, J = 4.8, 1.7 Hz, 1H, CH-O-C=O), 4.59 (br. s, 1H, OH), 4.62-4.52 (m, 2H, CH_{2}Ph), 3.90 (dd, J = 7.9, 4.1 Hz, 1H, O-CH-CH-C(=O)N), 3.25 (d, J = 8.1 Hz, 1H, CH-C(OH)=C=O). 13C NMR (CD_{3}CN, 100 MHz, 21 °C): δ (ppm) = 174.3, 173.6, 170.8, 148.3, 136.9, 136.4, 136.3, 133.9, 133.4, 131.1, 131.0, 129.1, 128.5, 128.2, 125.6, 78.8, 53.2, 47.8, 44.4, 42.9. IR (solid): ν = 3094, 2261, 1742, 1711, 1546, 1376, 1351, 1183, 1156, 1038, 960, 915, 832, 780, 594, 556 cm^{-1}. HRMS (ESI): m/z calculated for [C_{22}H_{17}N_3O_8SNa]^+: 506.0629, found: 506.0628.

(3aS,4S,7S,7aR)-4,7-Etheno-1H-pyrrolo [3,4-c] pyridine-1,3,6(2H, 3aH)-trione-4,5,7,7a-tetrahydro-7-hydroxy-2-(4-nitrophenyl)-5-[(2-nitrophenyl)sulfonyl] (ent-5aC)

5aC

The product 5aC was synthesized according to GP6 using N-nosyl-3-hydroxypyrindone 4a (29.6 mg, 0.10 mmol, 1.0 equiv.), N-(4-nitrophenyl)maleimide 2C (22.9 mg, 0.105 mmol, 1.05 equiv.) and catalyst C1b (4.96 mg, 0.005 mmol, 5.0 mol%). 5aC was isolated as a white solid (48.3 mg, 0.094 mmol, 94%, ee = 94%). The enantiomeric excess was determined by 1H NMR as described in GP8.

C_{21}H_{14}N_{4}O_{10}S, \textit{M}: 514.42 g/mol. m.p.: 215 °C. [\alpha]^{20}_D : –110.2 (c = 1.0 mg/mL, acetone, sample with 94% ee). 1H NMR ((CD_{3})_{2}SO, 400 MHz, 21 °C): δ (ppm) = 8.40 (d, J = 9.0 Hz, 2H, ArH), 8.35 (dd, J = 7.5, 1.7 Hz, 1H, ArH), 8.18 (dd, J = 7.5, 1.7 Hz, 1H, ArH), 8.11-8.00 (m, 2H, ArH),
The product 5aF was synthesized according to GP6 using N-nosyl-3-hydroxypyridone 4a (29.6 mg, 0.10 mmol, 1.0 equiv.), maleamide 2F (10.2 mg, 0.105 mmol, 1.05 equiv.) and catalyst C1b (4.96 mg, 0.005 mmol, 5.0 mol%). 5aF was isolated as a white solid (37.4 mg, 0.095 mmol, 94%, ee = 95%). The enantiomeric excess was determined by 1H NMR as described in GP8.

C15H11N3O6S, M: 393.32 g/mol. m.p.: 198 °C. [α]20D: -98.3 (c = 1.0 mg/mL, acetone, sample with 95% ee). 1H NMR (CD3CN, 400 MHz, 21 °C): δ (ppm) = 8.37 (d, J = 6.8 Hz, 1H, ArH), 8.00-7.85 (m, 3H, ArH), 6.69 (m, 1H, CH=CH2), 6.34 (d, J = 7.9 Hz, 1H, CH=CH-), 5.44 (dt, J = 4.7, 1.6 Hz, 1H, CH-O-C=O), 3.84 (dd, J = 8.2, 4.3 Hz, 1H, O-CH-CH-C(=O)N), 3.19 (d, J = 8.1 Hz, 1H, CH-C(OH)-C=O). 13C NMR (CD3CN, 176 MHz, 21 °C): δ (ppm) = 174.8, 174.0, 170.9, 136.9, 136.6, 135.7, 133.9, 133.4, 131.1, 130.9, 125.6, 78.7, 53.1, 49.0, 45.7. IR (solid): ν = 2360, 2261, 2178, 1721, 1542, 1352, 1183, 1102, 1044, 832, 779 cm⁻¹. HRMS (ESI): m/z calculated for [C15H12N3O6S]+: 394.0340, found: 394.0341.

The product 5bB was synthesized according to GP6 using N-nosyl-4-allyl-3-hydroxypyridone 4b (33.6 mg, 0.10 mmol, 1.0 equiv.), N-benzylmaleimide 2B (19.6 mg, 0.105 mmol, 1.05
equiv.) and catalyst C1b (4.96 mg, 0.005 mmol, 5.0 mol%). 5bB was isolated as a white solid (49.7 mg, 0.095 mmol, 95%, ee = 95%). The enantiomeric excess was determined by 1H NMR as described in GP8.

C_{25}H_{21}N_{2}O_{5}S, M: 523.52 g/mol. m.p.: 181°C. [α]_{D}^{20} = -96.1 (c = 1.0 mg/mL, sample with 96% ee). 1H NMR (CD_{3}CN, 400 MHz, 21 °C): δ (ppm) = 8.35 (d, J = 7.7 Hz, 1H, ArH), 7.97-7.86 (m, 3H, ArH), 7.38-7.24 (m, 5H, ArH), 6.31 (dt, J = 6.0 Hz, 1H, CH=CH), 5.44 (dd, J = 6.3, 3.9 Hz, CH-O-C=O), 5.42-5.33 (m, 1H, CH=CH_{2}allyl), 4.92 (m, 1H, CH=CH_{2}allyl), 4.92 (dq, J = 17.0, 3.7, 1.6 Hz, 1H, CH=CH_{2}allyl), 4.54 (m, 2H, CH_{2}Ph), 4.48 (br. s, 1H, OCH), 3.85 (dd, J = 8.1, 4.1 Hz, 1H, O-CH=CH-C(=O)N), 3.23 (d, J = 8.1 Hz, 1H, CH-C(OH)-C=O), 2.79-2.69 (m, 1H, OCH_{2}), 2.53-2.43 (m, 1H, OCH_{2}). 13C NMR (CD_{3}CN, 176 MHz, 21 °C): δ (ppm) = 174.8, 174.0, 171.4, 148.7, 147.9, 137.3, 136.9, 134.3, 134.1, 133.5, 133.8, 129.6, 129.2, 128.8, 126.0, 123.9, 180.1, 53.4, 48.3, 45.1, 43.3, 33.6. IR (solid): ν = 3466, 1701, 1542, 1432, 1396, 1312, 1266, 1177, 1123, 1100, 980, 927, 735, 701, 558 cm⁻¹. HRMS (ESI): m/z calculated for [C_{25}H_{21}N_{2}O_{5}SNa]⁺: 546.0942, found: 546.0943.

(3aS,4R,7S,7aR)-4,7-Etheno-1H-pyrrolo[3,4-c] pyridine-1,3,6(2H, 3aH)-trione-4,5,7,7a- tetrahydro-7-hydroxy-8-chloro-2-(methylphenyl)-5-[(2-nitrophenyl)sulfonyl] (ent-5cB)

5cB

The product 5cB was synthesized according to GP6 using N-nosyl-4-chloro-3-hydroxyxypyridone 4c (33.1 mg, 0.10 mmol, 1.0 equiv.), N-benzylmaleimide 2B (19.6 mg, 0.015 mmol, 0.015 equiv.) and catalyst C1b (4.96 mg, 0.005 mmol, 5.0 mol%). 5cB was isolated as a white solid (50.2 mg, 0.097 mmol, 97%, ee = 79%). The enantiomeric excess was determined by 1H NMR as described in GP8.

C_{22}H_{16}ClN_{3}O_{5}S, M: 517.89 g/mol. m.p.: 167°C. [α]_{D}^{20} = -92.1 (c = 1.0 mg/mL, acetone, sample with 79% ee). 1H NMR (CD_{3}CN, 400 MHz, 21 °C): δ (ppm) = 8.38 (d, J = 7.1 Hz, 1H ArH), 8.00-7.87 (m, 3H, ArH), 7.41-7.20 (m, 5H, ArH), 6.60 (d, J = 6.6 Hz, 1H, CH=CH), 5.53 (dd, J = 6.6, 4.0 Hz, CH-O-C=O), 4.92 (br. s, 1H, OCH), 4.58 (m, 2H, CH_{2}Ph), 3.94 (dd, J = 7.6, 4.2 Hz, 1H, O-CH=CH-C(=O)N), 3.39 (d, J = 8.2 Hz, 1H, CH-C(OH)-C=O). 13C NMR (CD_{3}CN, 75 MHz, 21 °C): δ (ppm) = 173.8, 172.7, 168.9, 148.2, 138.1, 137.1, 136.2, 134.0, 133.5, 130.8, 129.1, 128.3, 128.2, 126.3, 125.8, 79.2, 53.1, 48.0, 44.6, 42.9. IR (solid): ν = 3467, 3093, 1779, 1737, 1702, 1591, 1541, 1434, 1395, 1352, 1289, 1177, 1102, 942, 852, 735, 583, 557, 495 cm⁻¹. HRMS (ESI): m/z calculated for [C_{22}H_{16}ClN_{3}O_{5}SNa]⁺: 540.0239, found: 540.0242.
(3aS,4S,7S,7aR)-4,7-Etheno-1H-pyrrolo[3,4-c] pyridine-1,3,6(2H, 3aH)-trione-4,5,7,7a-tetrahydro-7-hydroxy-2-(methylphenyl) (ent-5dB)

To a solution of the 5aB (48.3 mg, 0.1 mmol, 1.0 equiv., sample with 94% of ee) in THF (5.0 mL) was added DBU (16.7 mg, 0.11 mmol, 1.1 equiv.) and PhSH (11.6 mg, 0.105 mmol, 1.05 equiv.). The resulting reaction mixture was stirred for 10 min at room temperature, diluted with water (5 mL) and extracted with AcOEt (3 x 5 mL). The combined organic phases were dried over Na₂SO₄ and solvent was evaporated under reduced pressure. The crude product was dissolved in a small amount of DCM (0.2 mL) and Na water (10 equiv., 5 mL) was added. The resulting reaction mixture was stirred for 16.7 min at room temperature. The reaction mixture was precipitated with pentane causing to afford the pure product 5dB as white solid (28.0 mg, 0.094 mmol, 94%, 94% ee). The enantiomeric excess was determined by 1H NMR as described in GP8.

C₁₆H₁₄N₂O₄, M: 298.29 g/mol. m.p.: 158°C. [α]D°₂⁰: −72.0 (c = 1.0 mg/mL, sample with 94% ee). 1H NMR ((CD₃)₂CO, 400 MHz, 21°C): δ (ppm) = 7.97 (br. s, 1H, NH), 7.37-7.21 (m, 5H, ArH), 6.31 (dd, J = 8.2, 2.3 Hz, 1H, CH=CH), 6.18 (d, J = 8.2 Hz, 1H, CH=CH), 4.72 (m, 1H, CH-O-C=O), 4.67 (s, 1H, OH), 4.55 (s, 2H, CH₃Ph), 3.71 (dd, J = 8.1, 4.3 Hz, 1H, O-CH-CH-C(=O)N), 3.08 (d, J = 8.2 Hz, 1H, CH-C(OH)-C=O). 13C NMR ((CD₃)₂CO, 100 MHz, 21°C): δ (ppm) = 174.6, 174.2, 173.7, 136.3, 136.2, 130.3, 128.3, 128.1, 127.4, 77.1, 49.1, 48.2, 45.8, 41.7. IR (solid): ν = 3317, 1771, 1431, 1397, 1297, 1204, 1171, 1068, 923, 739, 699, 485 cm⁻¹. HRMS (ESI) m/z calculated for [C₁₆H₁₄N₂O₄Na]⁺: 321.0846, found: 321.0841.

(3aR,4R,7R,7aS)-4,7-Ethenopyranol [3,4-c] pyrrole-1,3,6(2H)-trione-3a,4,7,7a-tetrahydro-7-hydroxy (7)

The product 7 was synthesized according to GP4 using 3-hydroxypyrene 1a (11.2 mg, 0.10 mmol, 1.0 equiv.), maleic anhydride 6 (10.2 mg, 0.105 mmol, 1.05 equiv.) and catalyst C1a (4.56 mg, 0.005 mmol, 5.0 mol%) at 0 °C. 7 was isolated as a white solid (19.3 mg, 0.092 mmol, 92%, ee = 84%). The enantiomeric excess was determined by 1H NMR as described in GP8.

C₉H₈O₆, M: 210.14 g/mol. m.p.: 110°C. [α]D²⁰: 29.1 (c = 0.90 mg/mL, acetonitrile, sample with 84% ee). 1H NMR (CD₃CN, 400 MHz, 21°C): δ (ppm) = 6.67-6.56 (m, 2H, CH=CH), 5.62 (dt, J = 4.8 Hz, 2.2 Hz, 1H, CH-O-C=O), 4.86 (br. s, 1H, OH), 4.20 (dd, J = 8.2, 4.8 Hz, 1H, O-CH-CH-C(=O)N), 3.58 (d, J = 8.5 Hz, 1H, CH-C(OH)-C=O). 13C NMR (CD₃CN, 176 MHz, 21°C): δ (ppm) = 171.6, 168.5, 168.0, 138.1, 130.5, 75.2, 71.7, 48.1, 45.2. IR (solid): ν = 3424, 1769, 1364, 1234, 1149, 1063, 1013, 965, 926, 697 cm⁻¹. MS (ESI) m/z: 211.0 (M⁺), 166.0 (M–CO₂), 122.0 (M–CO₂–CO₂), 94.0 (M–CO₂–CO₂–CO₂).
Ethyl (3aR,4S,7R,7aR)-4,7-Methano-1H-isooindole-(2H,7H)-1,3,5-trione, tetrahydro-2-(phenylmethyl)-4-carboxylate (9)

The product 9 was synthesized according to GP7 using enone 8 (18.4 mg, 0.12 mmol, 1.2 equiv.), N-benzylmaleimide 2B (18.7 mg, 0.10 mmol, 1.0 equiv.) and catalyst C1a (0.45 mg, 0.0005 mmol, 0.50 mol%) at −20 °C. 9 was isolated as a white solid (31.7 mg, 0.093 mmol, 93%, ee = 98%). The enantiomeric excess was determined by 1H NMR as described in GP8.

C_{19}H_{19}NO_{5}, M: 341.36 g/mol. [α]^{20}_{D} : 63.7 (c = 1.0 mg/mL, acetone, sample with 98% ee). 1H NMR (CDCl$_3$, 400 MHz, 21 °C): δ (ppm) = 7.33-7.20 (m, 5H, ArH), 4.59 (q, J = 27.6 Hz, 14.0 Hz, 2H, CH$_2$Ph), 4.27 (m, 2H, OCH$_2$CH$_3$), 3.17 (d, J = 7.4 Hz, 1H, O=C-CHCH-C=O), 2.97 (m, 1H, CH(CH$_2$)), 2.86 (d, J = 7.4 Hz, 1H, O=C-CHCH-C=O), 2.35 (dd, J = 18.7, 4.7 Hz, 1H, CHHC=O), 2.10 (dd, J = 18.0, 4.0 Hz, 1H, CHHC=O), 1.93 (dd, J = 12.1, 1.2 Hz, 1H, CH$_2$), 1.60 (m, 1H CH$_2$), 1.29 (t, J = 7.4 Hz, 3H, OCH$_2$CH$_3$). $^{13}$C NMR (CDCl$_3$ 176 MHz, 21 °C): δ (ppm) = 204.9, 175.8, 173.5, 166.3, 135.4, 128.9, 128.8, 128.3, 65.2, 61.8, 48.0, 44.9, 43.8, 43.0, 36.6, 34.3, 14.2. IR (solid): ν = 2956, 2917, 1762, 1704, 1543, 1462, 1394, 1319, 1260, 1174, 1097, 1018, 800, 733, 701 cm$^{-1}$. HRMS (ESI): m/z calculated for [C$_{19}$H$_{19}$NO$_5$Na]$^+$: 364.1155, found: 364.1162.

CCDC 2002396 contains the supplementary crystallographic data for compound 9. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via [www.ccdc.cam.ac.uk/data_request/cif](http://www.ccdc.cam.ac.uk/data_request/cif).
Ethyl (1S,2S,3S,4R)-3-Nitro-6-oxo-2-phenylbicyclo[2.2.1]heptane-1-carboxylate (11)

The product 11 was synthesized according to GP7 using enone 8 (18.4 mg, 0.12 mmol, 1.2 equiv.), β-nitrostyrene 10 (14.9 mg, 0.10 mmol, 1.0 equiv.) and catalyst C1a (0.023 mg, 0.000025 mmol, 0.025 mol%). 11 was isolated as a white oily solid (27.9 mg, 0.092 mmol, 92%, ee = 98%). The enantiomeric excess was determined by HPLC with a Chiralcel OD-H column (n-heptane/i-propanol = 90/10, 0.6 mL/min, detection at 220 nm, t (minor) = 48.0 min, t (major) = 66.5 min.

C_{16}H_{17}NO_{5}, M: 303.31 g/mol. [α]^{20}_D^\circ = 56.9 (c = 1.0 mg/mL, acetone, sample with 98% ee). \[^1\]H NMR (CDCl₃, 400 MHz, 21 °C): δ (ppm) = 7.28-7.22 (m, 3H, ArH), 7.19-7.16 (m, 2H, ArH), 5.08 (dt, J = 5.1 Hz, 1.4 Hz, 1H, CHNO₂), 4.00 (dd, J = 5.2, 1.9 Hz, 1H, CHPh), 3.89 (q, J = 7.5 Hz, 2H, OCH₂CH₃), 3.36 (m, 1H, (CH₂)CHCHNO₂), 2.68 (m, 1H, COCHH), 2.45-2.26 (m, 3H, COCHH, (CH₂)), 0.82 (t, J = 7.4 Hz, 3H, OCH₂CH₃). \[^{13}\]C NMR (CD₂CN 176 MHz, 21 °C): δ (ppm) = 204.1, 166.9, 137.8, 129.1, 128.3, 127.9, 93.1, 68.4, 61.3, 47.3, 38.8, 38.4, 37.8, 13.6. IR (solid): ν = 2982, 1761, 1725, 1547, 1467, 1370, 1315, 1260, 1098, 1030, 1012, 984, 756, 701 cm⁻¹. HRMS (ESI): m/z calculated for [C_{16}H_{17}NO_{5}Na]^+: 326.0999, found: 326.0994.
Confirming the Configurational Outcome with 2D-NMR Experiments of Compound 11.

To confirm the relative configuration of compound 11, several 2D-NMR-Experiments were performed (COSY, HSQC, HMBC and NOESY).

**COSY-Experiment**

![COSY-Experiment](image1)

**HSQC-Experiment**

![HSQC-Experiment](image2)
Derivatisation of the Catalytic Product 11.

Ethyl (1S,2S,3S,4R,6R)-3-Nitro-6-hydroxy-2-phenylbicyclo[2.2.1]heptane-1-carboxylate (11a)

11 (30.3 mg, 0.10 mmol, 1.0 equiv., ee = 98%) was dissolved in ethanol/dichloromethane (2.0 mL / 1 mL) and cooled to −78 °C under nitrogen atmosphere. NaBH₄ (15.1 mg, 0.40 mmol, 4.0 equiv.) was added in portions over the five minutes at −78 °C. Reaction mixture was allowed to slowly warm to room temperature and stirred for 12 h. Saturated aqueous ammonium chloride (5 mL) was added and reaction mixture was extracted with EE (3 x 10 mL). The combined organic phases were dried over Na₂SO₄ and the solvent was removed under reduced pressure. The crude product was dissolved in a small amount of DCM (0.5 mL) and added to n-pentane solution (5 mL) causing the precipitation. The solid was filtered, dried under high pressure to yield the pure 11a (25.9 mg, 0.085 mmol, 85%).

C₁₆H₁₉NO₅, M: 305.33 g/mol. m.p.: 140-141 °C [α]²₀ D: 36.1. (c = 1.0 mg/mL, acetone). ¹H NMR (CDCl₃, 400 MHz, 21 °C): δ (ppm) = 7.34-7.26 (m, 5H, ArH), 5.05 (dt, J = 5.3 Hz, 1.8 Hz, 1H, CHNO₂), 4.63 (dd, J = 6.4, 2.3 Hz, 1H, CPh), 4.40 (dd, J = 10.5, 4.2 Hz, 1H, CHO), 3.78 (m, 2H, OCH₂CH₃), 3.00 (m, 1H, (CH₃)CHCHNO₂), 2.80 (br. s, 1H, OH), 2.36 (dd, J = 11.5, 3.4 Hz, 1H, (CH₃)COOEt), 2.19 (m, 1H, HO-CCHH), 1.93 (dt, J = 11.8, 2.0 Hz, 1H, (CH₃)COOEt), 1.35 (dt, J = 14.3, 4.1 Hz, 1H, HO-CCHH), 0.82 (t, J = 7.3 Hz, 3H, OCH₂CH₃).

¹³C NMR (CDCl₃, 176 MHz, 21 °C): δ (ppm) = 172.1, 139.0, 128.7, 128.5, 127.7, 93.3, 73.0, 61.8, 60.8, 43.0, 40.3, 36.9, 30.8, 13.6. IR (solid): ν = 3564, 2982, 1708, 1542, 1455, 1372, 1340, 1316, 1259, 1100, 1081, 1057, 756, 700, 605 cm⁻¹. HRMS (ESI): m/z calculated for [C₁₆H₁₉NO₅Na]⁺: 328.1155 found: 328.1151.

CCDC 1998669 contains the supplementary crystallographic data for compound 11a. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.
Catalyst Recycling

The catalytic reaction was done applying GP6. The reaction mixture was filtered over silica gel with PE / EE = 1:1 as eluent. The catalyst C1b turned green and was sticking on the top. After elution with 20 mL of the solvent mixture, residual solvent was then largely pressed through the silica pad (to dryness). By using a solvent mixture of DCM/THF/NEt$_3$ (66/33/1) the catalyst turned brown again and the activated catalyst was flashed down from the silica and collected using approximately 10 mL of the solvent mixture. The solvent was removed under reduced pressure, the resulting brown solid was dissolved in a small amount of DCM and precipitated by addition of $n$-pentane (app. 5 mL). The precipitate was filtered off, and the activated catalyst was used in the next catalytic reaction without further purification as described in GP6.

![Reaction Scheme]

### Run[a] yield (%)[b] dr[c] ee[d] / [%]

|  |  |  |  |  |
|---|---|---|---|---|
| 1 | 94 | >98:2 | 98 |
| 2 | 92 | >98:2 | 98 |
| 3 | 92 | >98:2 | 96 |
| 4 | 91 | >98:2 | 93 |
| 5 | 90 | >98:2 | 91 |

[a] Reactions were performed on 0.1 mmol scale. [b] Yield of isolated product. [c] Endo/exo ratios determined by $^1$H NMR using the crude product. [d] The enantiomeric excess was determined by $^1$H NMR using saturated CDCl$_3$ solution of (R)-(+)-binaphthol.
Mechanistic Study

Mass Spectrometric Experiments

The activated catalyst C1b (0.51 mg, 0.00052 mmol, 1.0 equiv.) and hydroxypyrone 1a (0.11 mg, 0.001 mmol, 2.0 equiv.) were dissolved in THF (0.5 mL). The reaction sample was measured by ESI-MS after 15 min. A Cu-dienolate species was detected as shown by the following spectra.

![Measured and Calculated Mass Spectra](image-url)
**¹H NMR Titration Experiments**

Catalyst **C1b** (0.51 mg, 0.00052 mmol, 1.0 equiv.) was dissolved in THF-d₈ (0.2 mL) and filled in the NMR-tube. The hydroxypyrone **1a** (0, 1.0, 2.0 and 10.0 equiv.) was added directly to the tube and after shaking for one minute at −20 °C the ¹H NMR spectra was recorded (**Figure S1**).

---

**Figure S1.** ¹H-NMR titration experiments. The blue curve shows the spectrum of **C1b** in THF-d₈ at −20 °C. For the red curve, 1.0 equiv. of **1a** were added. For the green and purple curve, 2.0, and 10.0 equiv. of **1a** were added, respectively. The yellow curve shows the spectra of pre-catalyst of **C1b**.

---

**UV-Vis Titration Experiments**

UV-Vis titration experiments were performed in which the betaine catalyst **C1b** was treated with 3-hydroxy-2-pyrene **1a**. Catalyst **C1b** (0.25 mg, 0.00025mmol, 1.0 equiv.) was dissolved in THF (1.0 mL) and filled in a cuvette (d = 10mm, Quartz SUPRASIL®). **1a** (0.2-10.0 equiv.) was added directly to the cuvette and after shaking, the UV-Vis spectra were measured at room temperature (**Figure S2**).

---

**Figure S2.** UV-Vis spectra of the titration experiment using **1a**.
Kinetic Experiments

Probing Catalyst Robustness and Product Influence

Blackmond’s reaction progress kinetic analysis (RPKA) was performed using $^1$H-NMR spectroscopy for monitoring the complete course of the catalytic reaction. By the so-called “same excess” protocol, the catalyst robustness and a possible product inhibition under the reaction conditions was assessed. The model reaction of 1a and 2B was examined at −20 °C in THF-d8 using 3.0 mol% of C1b. The experiments were performed starting from three different points. The different initial concentrations for the reactants 1a and 2B and the catalyst for the kinetic experiments are summarized in Table S1.

![Reaction Scheme]

**Table S1**: Different initial concentrations of hydroxypyrone 1a, maleimide 2B and product 3aB in “same-excess”-experiments and “product addition” for investigation of possible product inhibition and catalyst stability.

| Experiment | Description           | [1a] / mol/L | Equiv. of 1a | [2B] / mol/L | Equiv. of 2B | [3aB] / mol/L | Equiv. of 3aB | [C1b] / mol/L | Equiv. of C1b |
|------------|-----------------------|--------------|--------------|--------------|--------------|--------------|---------------|--------------|---------------|
| B1         | reference              | 0.04         | 1.00         | 0.042        | 1.05         | 0.00         | 0.00          | 0.0012       | 0.03          |
| B2         | same excess            | 0.02         | 0.50         | 0.022        | 0.55         | 0.00         | 0.00          | 0.0012       | 0.03          |
| B3         | product addition       | 0.02         | 0.50         | 0.022        | 0.55         | 0.02         | 0.50          | 0.0012       | 0.03          |

The reactions were performed by adding a solution of the catalyst C1b, 1,2-diphenylethane (internal standard, 0.02 mmol), hydroxypyrone 1a, maleimide 2B in tetrahydrofuran-d8 (0.5 mL) to an NMR sample tube. The reaction mixture was analysed by $^1$H NMR spectroscopy at −20 °C to monitor the conversion of 2B in dependence of time. First, the progress of a reference reaction was monitored with the indicated initial substrate concentrations (Table 1, Experiment B1). The second experiment was done with the initial substrate concentrations which were equal to those of the reference reaction when 50% conversion was reached (Experiment B2). The third measurement was done with the same initial conditions like in the second reaction, but with the addition of product 3aB (Experiment B3). These experiments could provide information of either catalyst deactivation or product inhibition. The difference between the reactions B2 and B3 compared to B1 is that when the latter reaction reached 50% of conversion, the catalyst was not fresh anymore because it has undergone a number of turnovers already, whereas in B2 and B3 the catalyst is fresh at the starting point. Figure S3 presents a comparison of kinetic profiles of these three reactions. Time adjustment was done by simple shifting the data of reactions B2 and B3 to the point where the concentrations...
are the same as for reference reaction B1. Since the reaction progress from this point onward is almost identical as the time shift of the B2 curve shows, it appears that no significant catalyst decomposition occurs during the reaction. Additionally, an overlay of the reaction profiles B3 with B1 was found demonstrating that the product 3aB does not inhibit the catalyst.

Figure S3. Probing catalyst stability and product influence on the catalytic reaction.

Raw Data and Calculated Concentrations for the “Same-Excess”-and “Product Addition”-Experiments

Table S2. Raw data of the “same-excess”-Experiments B1-B3, calculated concentration of maleimide 2B and time adjustment

| Time (min) | [2B] mol/L | Time /min | Time adjustment /min | [2B] mol/L | Time /min | Time adjustment /min | [2B] mol/L |
|------------|------------|-----------|----------------------|------------|-----------|----------------------|------------|
| 0          | 0.0420     | 0         | 22                   | 0.0220     | 0         | 22                   | 0.0220     |
| 10         | 0.0323     | 10        | 27                   | 0.0189     | 10        | 27                   | 0.0190     |
| 15         | 0.0276     | 15        | 32                   | 0.0167     | 15        | 32                   | 0.0166     |
| 20         | 0.0245     | 20        | 37                   | 0.0145     | 20        | 37                   | 0.0147     |
| 25         | 0.0207     | 25        | 42                   | 0.0131     | 25        | 42                   | 0.0129     |
| 30         | 0.0175     | 30        | 47                   | 0.0116     | 30        | 47                   | 0.0110     |
| 35         | 0.0160     | 35        | 52                   | 0.0101     | 35        | 52                   | 0.0096     |
| 40         | 0.0136     | 40        | 57                   | 0.0088     | 40        | 57                   | 0.0085     |
| 45         | 0.0121     | 45        | 62                   | 0.0078     | 45        | 62                   | 0.0076     |
| 50         | 0.0106     | 50        | 67                   | 0.0069     | 50        | 67                   | 0.0068     |
| 55         | 0.0091     | 55        | 72                   | 0.0064     | 55        | 72                   | 0.0065     |
| 60         | 0.0078     | 60        | 77                   | 0.0058     | 60        | 77                   | 0.0054     |
| 65         | 0.0074     | 65        | 82                   | 0.0056     | 65        | 82                   | 0.0049     |
| 70         | 0.0062     | 70        | 87                   | 0.0052     | 70        | 87                   | 0.0048     |
| 75         | 0.0057     | 75        | 97                   | 0.0047     | 75        |                      |            |
| 80         | 0.0048     | 80        | 102                  | 0.0043     | 80        |                      |            |
Kinetic Experiments–Determination of Reaction Orders Using Variable Time Normalization Graphical Analysis (VTNA)

The orders of all reaction components were determined using the variable time normalization graphical analysis method (VTNA) described by Burés.\(^{15,16}\) Four reactions E1-E4 with different initial concentrations of each component, catalyst C1b, hydroxypyrone 1a and maleimide 2B, were performed and monitored via \(^1\)H NMR. The different initial concentrations for the components used in the kinetic experiments are summarized in the Table S3.

![Reaction Scheme](image)

Table S3: Variation of the initial concentrations of catalyst C1b, hydroxypyrone 1a and maleimide 2B.

| Experiment | Description | [1a] / mol/L | [2B] / mol/L | [C1b] / mol/L |
|------------|-------------|--------------|--------------|---------------|
| E1         | reference   | 0.04         | 0.042        | 0.0012        |
| E2         | diff. [C1b] | 0.04         | 0.042        | 0.0016        |
| E3         | diff. [1a]  | 0.08         | 0.042        | 0.0012        |
| E4         | diff. [2B]  | 0.04         | 0.024        | 0.0012        |

The corresponding experiments E1-E4 were performed by adding a solution of the catalyst C1b, 1,2-diphenylethane (internal standard, 0.02 mmol), hydroxypyrone 1a, maleimide 2B in THF-d\(_8\) (0.5 mL) to an NMR sample tube at –20 °C as shown in Table S3. The reaction mixture was analysed by \(^1\)H NMR spectroscopy at –20 °C to monitor the conversion of 1a and 2B and the yield of 3aB in dependence of time (Figure S4).

![Conversion](image)

Figure S4. Conversion of 1a and 2B and the yield of 3aB in dependence of time.
The reaction progress profiles of all four experiments E1-E4 are plotted in Figure S5 and were investigated using VTNA. The order in each component can be determined by systematically changing each exponent of the normalized time axis, with the intention to obtain a linear overlay of all reaction profiles in the plot.

![Figure S5. Original reaction progress profile of the formation of product 3aB for the four reactions.](image)

The best fit for the normalization of the time scale axis was achieved for partial orders of 0.07 for 3-hydroxy-2-pyrone 1a, 1.00 for N-Benzylmaleimide 2B and 1.95 for catalyst C1b. The empirical rate law under the mentioned reaction conditions is thus:

$$ r = k \times [C1b]^{1.95} \times [1a]^{0.07} \times [2B]^{1.00} $$

When the normalization is applied to all the components, the result is a plot with a straight line with a slope equal to $k_{obs}$. The slope, $k_{obs}$ of the reaction and was found to be $k_{obs} = 1.8 \cdot 10^4 \text{L}^2 \cdot \text{mol}^{-2} \cdot \text{s}^{-1}$. The plot of this time normalized reaction profiles is shown in Figure S6.

![Figure S6. Best overlay of all four reaction progress profiles with orders 1.95 in C1b, 0.07 in 1a and 1.00 in 2B. Unit of x-axis in mol/(L·s) ($k_{obs} = 1.8 \cdot 10^4 \text{L}^2 \cdot \text{mol}^{-2} \cdot \text{s}^{-1}$).](image)
Raw Data, Calculated Concentrations and Processed Data for the VTNA.

All processed data are given in $\alpha = 1.95$, $\beta = 0.07$, $\gamma = 1.00$.

### E1, reference reaction

| Time (min) | $[\text{C1b}]$ mol/L | $[\text{1a}]$ mol/L | $[\text{2B}]$ mol/L | $[\text{3aB}]$ mol/L | $\sum [\text{C1b}]-[\text{1a}]+[\text{2B}] \Delta t$ |
|------------|-----------------------|---------------------|---------------------|---------------------|---------------------------------|
| 0          | 0.0012                | 0.0400              | 0.0420              | 0.0000              | 0.0000                          |
| 10         | 0.0012                | 0.0303              | 0.0323              | 0.0104              | 5.8643E-07                      |
| 15         | 0.0012                | 0.0256              | 0.0276              | 0.0152              | 8.1902E-07                      |
| 20         | 0.0012                | 0.0227              | 0.0245              | 0.0188              | 1.0189E-06                      |
| 25         | 0.0012                | 0.0187              | 0.0207              | 0.0218              | 1.1906E-06                      |
| 30         | 0.0012                | 0.0155              | 0.0175              | 0.0242              | 1.3341E-06                      |
| 35         | 0.0012                | 0.0140              | 0.0160              | 0.0267              | 1.4585E-06                      |
| 40         | 0.0012                | 0.0116              | 0.0136              | 0.0287              | 1.5673E-06                      |
| 45         | 0.0012                | 0.0101              | 0.0121              | 0.0303              | 1.6060E-06                      |
| 50         | 0.0012                | 0.0085              | 0.0106              | 0.0320              | 1.7423E-06                      |
| 55         | 0.0012                | 0.0071              | 0.0091              | 0.0331              | 1.8121E-06                      |
| 60         | 0.0012                | 0.0058              | 0.0078              | 0.0340              | 1.8714E-06                      |
| 65         | 0.0012                | 0.0054              | 0.0074              | 0.0350              | 1.9241E-06                      |
| 70         | 0.0012                | 0.0042              | 0.0062              | 0.0356              | 1.9706E-06                      |
| 75         | 0.0012                | 0.0037              | 0.0057              | 0.0366              | 2.0109E-06                      |
| 80         | 0.0012                | 0.0028              | 0.0048              | 0.0372              | 2.0460E-06                      |

$[\text{1a}]$ was calculated using the Blackmond’s “excess” method. ($[\text{1a}] = [\text{2B}] - [\varepsilon]$). $[\varepsilon]$ is defined as the difference of concentration of the two reactants and remains constant during the reaction.

### E2, Difference in $[\text{C1b}]$

| Time (min) | $[\text{C1b}]$ mol/L | $[\text{1a}]$ mol/L | $[\text{2B}]$ mol/L | $[\text{3aB}]$ mol/L | $\sum [\text{C1b}]-[\text{1a}]+[\text{2B}] \Delta t$ |
|------------|-----------------------|---------------------|---------------------|---------------------|---------------------------------|
| 0          | 0.0016                | 0.0400              | 0.0420              | 0.0000              | 0.0000                          |
| 3          | 0.0016                | 0.0345              | 0.0359              | 0.0060              | 3.5734E-07                      |
| 5          | 0.0016                | 0.0305              | 0.0319              | 0.0102              | 5.7983E-07                      |
| 7          | 0.0016                | 0.0277              | 0.0290              | 0.0141              | 7.7805E-07                      |
| 9          | 0.0016                | 0.0242              | 0.0255              | 0.0168              | 9.5412E-07                      |
| 11         | 0.0016                | 0.0215              | 0.0227              | 0.0195              | 1.0610E-06                      |
| 13         | 0.0016                | 0.0193              | 0.0206              | 0.0221              | 1.1879E-06                      |
| 15         | 0.0016                | 0.0166              | 0.0178              | 0.0243              | 1.2994E-06                      |
| 17         | 0.0016                | 0.0154              | 0.0167              | 0.0260              | 1.3988E-06                      |
| 19         | 0.0016                | 0.0137              | 0.0149              | 0.0271              | 1.4982E-06                      |
| 21         | 0.0016                | 0.0122              | 0.0134              | 0.0294              | 1.5695E-06                      |
| 23         | 0.0016                | 0.0111              | 0.0123              | 0.0307              | 1.6417E-06                      |
| 25         | 0.0016                | 0.0099              | 0.0111              | 0.0314              | 1.7072E-06                      |
| 27         | 0.0016                | 0.0086              | 0.0097              | 0.0325              | 1.7651E-06                      |
| 29         | 0.0016                | 0.0078              | 0.0090              | 0.0333              | 1.8166E-06                      |
| 31         | 0.0016                | 0.0070              | 0.0081              | 0.0340              | 1.8633E-06                      |
| 33         | 0.0016                | 0.0059              | 0.0071              | 0.0345              | 1.9045E-06                      |
| 35         | 0.0016                | 0.0054              | 0.0065              | 0.0351              | 1.9409E-06                      |
| 37         | 0.0016                | 0.0050              | 0.0061              | 0.0359              | 1.9744E-06                      |
| 39         | 0.0016                | 0.0045              | 0.0056              | 0.0363              | 2.0055E-06                      |
| 41         | 0.0016                | 0.0041              | 0.0052              | 0.0368              | 2.0338E-06                      |

$[\text{1a}]$ was calculated using the Blackmond’s “excess” method. ($[\text{1a}] = [\text{2B}] - [\varepsilon]$). $[\varepsilon]$ is defined as the difference of concentration of the two reactants and remains constant during the reaction.
### E3, Difference in [1a]

| Time (min) | [C1b] mol/L | [1a] mol/L | [2B] mol/L | [3aB] mol/L | ∑[C1b]−[1a]−[2B]Δt |
|------------|-------------|------------|------------|-------------|-----------------|
| 0          | 0.0012      | 0.0800     | 0.0420     | 0.0000      | 0.00000         |
| 6          | 0.0012      | 0.0734     | 0.0354     | 0.0071      | 4.2526E-07      |
| 11         | 0.0012      | 0.0679     | 0.0299     | 0.0121      | 6.7043E-07      |
| 16         | 0.0012      | 0.0639     | 0.0259     | 0.0162      | 9.0055E-07      |
| 21         | 0.0012      | 0.0604     | 0.0224     | 0.0203      | 1.0976E-06      |
| 26         | 0.0012      | 0.0573     | 0.0193     | 0.0229      | 1.2658E-06      |
| 31         | 0.0012      | 0.0547     | 0.0167     | 0.0257      | 1.4094E-06      |
| 36         | 0.0012      | 0.0525     | 0.0145     | 0.0285      | 1.5325E-06      |
| 41         | 0.0012      | 0.0507     | 0.0127     | 0.0306      | 1.6387E-06      |
| 46         | 0.0012      | 0.0491     | 0.0111     | 0.0317      | 1.7304E-06      |
| 51         | 0.0012      | 0.0472     | 0.0092     | 0.0333      | 1.8074E-06      |
| 56         | 0.0012      | 0.0461     | 0.0081     | 0.0345      | 1.8721E-06      |
| 61         | 0.0012      | 0.0451     | 0.0071     | 0.0353      | 1.9283E-06      |
| 66         | 0.0012      | 0.0441     | 0.0061     | 0.0368      | 1.9762E-06      |
| 71         | 0.0012      | 0.0433     | 0.0053     | 0.0376      | 2.0170E-06      |
| 76         | 0.0012      | 0.0425     | 0.0046     | 0.0379      | 2.0517E-06      |

[1a] was calculated using the Blackmond’s “excess” method. ([1a] = [2B]−[e]). [e] is defined as the difference of concentration of the two reactants and remains constant during the reaction.

### E3, Difference in [2B]

| Time (min) | [C1b] mol/L | [1a] mol/L | [2B] mol/L | [3aB] mol/L | ∑[C1b]−[1a]−[2B]Δt |
|------------|-------------|------------|------------|-------------|-----------------|
| 0          | 0.0012      | 0.0400     | 0.0240     | 0.0000      | 0.00000         |
| 8          | 0.0012      | 0.0357     | 0.0197     | 0.0042      | 2.7933E-07      |
| 13         | 0.0012      | 0.0326     | 0.0166     | 0.0070      | 4.2351E-07      |
| 18         | 0.0012      | 0.0302     | 0.0142     | 0.0098      | 5.4506E-07      |
| 23         | 0.0012      | 0.0277     | 0.0117     | 0.0115      | 6.4694E-07      |
| 28         | 0.0012      | 0.0260     | 0.0100     | 0.0133      | 7.3212E-07      |
| 33         | 0.0012      | 0.0244     | 0.0084     | 0.0149      | 8.0393E-07      |
| 38         | 0.0012      | 0.02377    | 0.0077     | 0.0163      | 8.6636E-07      |
| 43         | 0.0012      | 0.0225     | 0.0065     | 0.0173      | 9.2115E-07      |
| 48         | 0.0012      | 0.0215     | 0.0055     | 0.0181      | 9.6747E-07      |
| 53         | 0.0012      | 0.0206     | 0.0046     | 0.0186      | 1.0063E-06      |
| 58         | 0.0012      | 0.0201     | 0.0042     | 0.0193      | 1.0398E-06      |
| 63         | 0.0012      | 0.0195     | 0.0035     | 0.0199      | 1.0690E-06      |
| 68         | 0.0012      | 0.0188     | 0.0029     | 0.0204      | 1.0933E-06      |
| 73         | 0.0012      | 0.0184     | 0.0024     | 0.0206      | 1.1138E-06      |
| 78         | 0.0012      | 0.0181     | 0.0021     | 0.0208      | 1.1309E-06      |
| 83         | 0.0012      | 0.0178     | 0.0018     | 0.0211      | 1.1457E-06      |
| 88         | 0.0012      | 0.0177     | 0.0017     | 0.0213      | 1.1590E-06      |
| 93         | 0.0012      | 0.0176     | 0.0016     | 0.0215      | 1.1717E-06      |
| 98         | 0.0012      | 0.0174     | 0.0014     | 0.0218      | 1.1832E-06      |

[1a] was calculated using the Blackmond’s “excess” method. ([1a] = [2B]−[e]). [e] is defined as the difference of concentration of the two reactants and remains constant during the reaction.
Investigation of a Possible Non-Linear-Effect

Examination of linear or non-linear effects was done under the conditions described in GP4 using 5.0 mol% of catalyst C1b with six different enantiomeric excesses (Table S4), which were prepared by mixing the corresponding amounts of pure enantiomers of the catalysts C1b. The plot of ee(3aB) as a function of ee(C1b) showed a positive non-linear effect which might be an indication of the relevance of catalyst dimers (Figure S7).

Table S4. Enantiomeric excess of the catalyst C1b and the product 3aB.

| #  | ee (C1b)/% | ee (3aB)/% |
|----|------------|------------|
| 1  | 100        | 98         |
| 2  | 80         | 86         |
| 3  | 60         | 77         |
| 4  | 40         | 54         |
| 5  | 20         | 34         |
| 6  | 0          | 0          |

Figure S7: Non-linear effect plot of the catalytic reaction with different ee-values of the catalyst C1b.
Crystallographic Data

Catalyst C6

CCDC 1995950 contains the supplementary crystallographic data for compound C6. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.
Current Data Parameters
NAME 56-L2_2PC1
EXPER 89
PROCNO 1

F3 - Acquisition Parameters
Data 29020122
Time 16.49
INSTNIR spect
PROBW 5 mm PABRO B/W
POLPNO 0x00
TE 6536
SOLVENT TSP
NS 1024
DG 4
SW 8025.425 Hz
PFIRES 0.123699 MHz
AG 4.068865 sec
DW 205.35
DE 8.20 ussec
TE 286.0 kHz
DI 1.00000000 ussec
TD0 1

----- CHANNEL 1 -----  
SF01 100.103479 MHz
NSC1 100
PFIRES 1
POLW 12.30000000 MHz

----- CHANNEL 2 -----  
SF01 100.103479 MHz
NSC1 100
PFIRES 1
POLW 12.30000000 MHz

----- CHANNEL 3 -----  
SF01 100.103479 MHz
NSC1 100
PFIRES 1
POLW 12.30000000 MHz

--- F2 - Processing parameters ---
S1 88553
SF 400.100000 MHz
WOW EM
ZDD 0
LB 0.00 Hz
GB 0
P0 1.00

Current Data Parameters
NAME 4-01
EXPER 391
PROCNO 1

F3 - Acquisition Parameters
Data 29020123
Time 16.55
INSTNIR spect
PROBW 5 mm PABRO B/W
POLPNO 0x00
TE 6536
SOLVENT TSP
NS 1024
DG 4
SW 8025.425 Hz
PFIRES 0.123699 MHz
AG 4.068865 sec
DW 205.35
DE 8.20 ussec
TE 286.0 kHz
DI 1.00000000 ussec
TD0 1

----- CHANNEL 1 -----  
SF01 100.615281 MHz
NSC1 100
PFIRES 1
POLW 48.00000000 MHz

----- CHANNEL 2 -----  
SF01 100.615281 MHz
NSC1 100
PFIRES 1
POLW 48.00000000 MHz

----- CHANNEL 3 -----  
SF01 100.615281 MHz
NSC1 100
PFIRES 1
POLW 48.00000000 MHz

--- F2 - Processing parameters ---
S1 32768
SF 100.6051472 MHz
NSC1 EM
ZDD 0
LB 1.00 Hz
GB 0
P0 1.40

S70
5bB

S105
Determination of Enantiomeric Excess

3aA

Racemic

3aB

Racemic

3aC

Racemic
3dB

Racemic

5aB

Racemic

5aC

Racemic
HPLC Data

11

Column: ODH, \( n \)-heptane/iPrOH (90/10), 0.6 mL/min, 220 nm

Racemic:

| Retention time | Area    | Area (%) |
|----------------|---------|----------|
| 45.92          | 35288703| 48.84    |
| 65.49          | 36969922| 51.16    |

| Retention time | Area    | Area (%) |
|----------------|---------|----------|
| 48.05          | 1582827 | 1.00     |
| 66.51          | 156967898| 99.00    |
References

1. (a) M. Sortino, V. Cechinel Filho, R. Corrêa, S. Zacchino *Bioorg. Med. Chem.* **2008**, *16*, 560–568; (b) Y. Lu, Y. Li, R. Zhang, K. Jin, C. Duan *Tetrahedron* **2013**, *69*, 9422-9427. (c) K. P. Haval, S. B. Mhaske, N. P. Argade, *Tetrahedron* **2006**, *62*, 937–942.

2. J. A. Profitt, T. Jones, D. S. Watt *Synth. Commun.* **1975**, *5*, 457–460.

3. T. Suzuki, S. Watanabe, S. Kobayashi, K. Tanino *Org. Lett.* **2017**, *19*, 922–925.

4. T. Ishiyama, D. Urabe, H. Fujisawa, M. Inoue *Org. Lett.* **2013**, *15*, 4488–4491.

5. N. T. Kipassa, H. Okamura, K. Kina, T. Hamada, T. Iwagawa *Org. Lett.* **2008**, *10*, 815–816.

6. F. Willig, J. Lang, A. C. Hans, M. Ringenberg, D. Pfeffer, W. Frey, R. Peters *J. Am. Chem. Soc.* **2019**, *141*, 30, 12029–12043.

7. H. Okamura, Y. Nakamura, T. Iwagawa, M. Nakatani *Chem. Lett.* **1996**, *25*, 193–194.

8. (a) T. Komiyama, Y. Takaguchi, S. Tsuboi *Tetrahedron Lett.* **2004**, *45*, 6299–6301; (b) T. Komiyama, Y. Takaguchi, A. T. Gubaidullin, V. A. Mamedov, I. A. Litvinov, S. Tsuboi *Tetrahedron* **2005**, *61*, 2541–2547.

9. J. Y.-T. Soh, C.-H. Tan *J. Am. Chem. Soc.* **2009**, *131*, 6904–6905.

10. A. R. Chianese, R. H. Crabtree *Organometallics* **2005**, *24*, 4432–4436.

11. S. Reymond, J. Cossy, *Chem. Rev.* **2008**, *108*, 5359–5406.

12. H. Okamura, T. Iwagawa, M. Nakatani *Tetrahedron Lett.* **1995**, *36*, 5939–5942.

13. H. Okamura, H. Nagaie, T. Iwagawa, M. Nakatani *Tetrahedron Lett.* **2000**, *41*, 8317–8321.

14. (a) D. G. Blackmond *J. Am. Chem. Soc.* **2015**, *137*, 10852–10866; (b) R. D. Baxter, D. Sale, K. M. Engle, J.-Q. Yu, D. G. Blackmond *J. Am. Chem. Soc.* **2012**, *134*, 10, 4600–4606.

15. J. Burés *Angew. Chem. Int. Ed.* **2016**, *55*, 16084–16087.

16. C. D.-T. Nielsen, J. Burés *Chem. Sci.* **2019**, *10*, 348–353.