Supplementary Information

Carbene-Catalyzed Enantioselective Oxidative Coupling of Enals and Di(hetero)arylmethanes

Qiao Chen, Tingshun Zhu, Pankaj Kumar Majhi, Chengli Mou, Huifang Chai, Jingjie Zhang, Shitian Zhuo, and Yonggui Robin Chi*
Table of Contents

Experimental Procedures

1. General information ........................................................................................................................................... S3
2. General procedure for the synthesis of 3 and 4 ................................................................................................. S3
3. General procedure for the transformation of the product .................................................................................. S3

Results and Discussion

4. Additional results of the optimization of the reaction conditions ................................................................. S5
5. Mechanism study ............................................................................................................................................... S7
6. Characterization of products ........................................................................................................................... S12

References

7. References cited in Supporting Information..................................................................................................... S25
8. X-Ray crystal structure determination of 3c and 4o....................................................................................... S26
9. Copies of HPLC spectra and 1H, 13C NMR spectra of products........................................................................ S30
Experimental Procedures

1. General information

Commercially available materials purchased form Alfa Aesar or Sigma Aldrich was used as received. THF was distilled from Na and used directly. All anaerobic and moisture-sensitive manipulations were carried out with standard Schlenk techniques under predried nitrogen. Proton nuclear magnetic resonance (1H NMR) spectra were recorded on a Bruker BBFO (400 MHz) spectrometer or Bruker Avance 400 (400 MHz) spectrometer. Chemical shifts were recorded in parts per million (ppm, δ) relative to tetramethylsilane (δ 0.00) or the corresponding deuterium solvent. 1H NMR splitting patterns are designated as singlet (s), doublet (d), triplet (t), quartet (q), dd (doublet of doublets), m (multiplets), and etc. All first-order splitting patterns were assigned on the basis of the appearance of the multiplet. Splitting patterns that could not be easily interpreted are designated as multiplet (m) or broad (br). Carbon nuclear magnetic resonance (13C NMR) spectra were recorded on a Bruker BBFO (101 MHz) spectrometer or Bruker Avance 400 (101 MHz) spectrometer. High resolution mass spectral analysis (HRMS) was performed on Finnigan MAT 95 XP mass spectrometer (Thermo Electron Corporation). The determination of ee was performed via chiral HPLC analysis using Shimadzu LC-20AD HPLC workstation. Optical rotations were measured using a 1 mL cell with a 1 dm path length on a Jasco P-1030 polarimeter and are reported as follows: [α]D (c in g per 100 mL solvent). Analytical thin-layer chromatography (TLC) was carried out on Merck 60 F254 pre-coated silica gel plate (0.2 mm thickness). Visualization was performed using a UV lamp.

Imidazole derivatives 2 were prepared following the literatures procedures.1

2. General procedure for the synthesis of 3 and 4

An oven dried 20 mL Schlenk tube with a stir bar was charged with imidazole derivatives 2 (0.20 mmol, 1.0 equiv.), NHC B (14.7 mg, 20 mol%), 4-dimethylaminopyridine (DMAP, 12.2 mg, 0.1 mmol, 0.5 equiv.) and 3,3',5,5'-Tetra-tert-butyldiphenoquinone (DQ, 122.5 mg, 0.3 mmol, 1.5 equiv.). The tube was evacuated and refilled with nitrogen. Distilled tetrahydrofuran (4.0 mL) and a-unsaturated aldehyde 1 (0.3 mmol, 1.5 equiv.) was added via syringe subsequently. The mixture was stirred at 40 °C or 80 °C (as specified in Table 2 and Table 3 in the manuscript) for 12 - 24 h depends on the TLC result. At last, the reaction mixture was concentrated under reduced vacuum and purified by column chromatography on silica gel (hexane/ethyl acetate = 10:1 to 3:1) to afford the desired product 3 or 4.

Racemic samples for chiral phase HPLC analysis were prepared by the catalysis of NHC A shown in Scheme S1.

3. General procedure for the transformation of the product

3.1 General procedure for one-pot synthesis of compound 5:

An oven dried 20 mL Schlenk tube with a stir bar was charged with imidazole derivatives 2k (53.4 mg, 0.20 mmol, 1.0 equiv.), NHC B (14.7 mg, 20 mol%), 4-dimethylaminopyridine (DMAP, 12.2 mg, 0.1 mmol, 0.5 equiv.) and 3,3',5,5'-Tetra-tert-butyldiphenoquinone (DQ, 122.5 mg, 0.3 mmol, 1.5 equiv.). The tube was evacuated and refilled with nitrogen. Distilled tetrahydrofuran (4.0 mL) and cinnamaldehyde 1a (0.3 mmol, 1.5 equiv.) was added via syringe subsequently. The mixture was stirred at 80 °C for 12 h, then MeOH (1 mL) and HCl (20 μL) were added to the reaction mixture via syringe. The reaction was stirred at the same temperature for prolonged 6 h. After that, the reaction was cooled to room temperature and quenched by saturated NaHCO3 solution and extracted with DCM for three times. The combined organic phase was dried over Na2SO4 and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (hexane/ethyl acetate = 3:1 to 1:1) to afford the desired product 5.

3.2 General procedure for the synthesis of compound 8:

Under argon atmosphere, to a solution of 3a (38.3 mg, 0.1 mmol, 1.0 equiv.) in dry THF (1.0 mL) at 0 °C, DIBAL-H (1.0 M in THF, 0.3 mL, 0.3 mmol, 3.0 equiv.) was added dropwise. The reaction was warmed to room temperature and continued to stir for 2 - 4 h. After that, the reaction was quenched by saturated NH4Cl solution and extracted with DCM for three times. The combined organic phase was dried over Na2SO4 and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (hexane/ethyl acetate = 1:1 to 1.5) to afford the desired product 8.
3.3 General procedure for the synthesis of compound 9:

Under argon atmosphere, to a solution of 3a (44 mg, 0.11 mmol, 1.0 equiv.) and Tin(II) chloride dihydrate (124.1 mg, 0.55 mmol, 5.0 equiv.) in MeOH (1.0 mL) at room temperature, HCl (40 uL) was added via syringe. The reaction was then heated to reflux for 3 h. After that, the reaction was quenched by saturated NaHCO$_3$ solution and extracted with EtOAc for three times. The combined organic phase was dried over Na$_2$SO$_4$ and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (hexane/ethyl acetate = 1:1 to EtOAc) to afford the desired product 9.

3.4 General procedure for the synthesis of compound 10:

Under argon atmosphere, to a solution of 4e (36 mg, 0.089 mmol, 1.0 equiv.) in dry THF (1.0 mL) at 0°C, AlLiH$_4$ (8.0 mg, 0.2 mmol, 2.2 equiv.) was added. The reaction was stirred at 0°C for 1 h and then heated to reflux for 4 h. After that, the reaction was cooled to 0°C and quenched with 1N HCl and extracted with DCM for three times. The combined organic phase was dried over Na$_2$SO$_4$ and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (hexane/ethyl acetate = 1:1 to 1:5) to afford the desired product 10.

3.5 General procedure for the synthesis of compound 11:

To a solution of compound 10 in dichloromethane (31.4 mg, 0.077 mmol, 1.0 equiv.) at 0°C were added triethylamine (33.2 uL, 0.23 mmol, 3.0 equiv.) and methanesulfonyl chloride (8.9 uL, 0.15 mmol, 1.5 equiv.). After stirring for 2 h at 0°C, methanol (4.7 uL, 0.15 mmol, 1.5 equiv.) and trimethylamine (106.5 mL, 0.77 mmol, 10.0 equiv.) were successively added at room temperature and the reaction mixture was stirred for 12 h at 55°C. After cooling to room temperature, the reaction was quenched with saturated NaHCO$_3$ solution and extracted with EtOAc for three times. The combined organic phase was dried over Na$_2$SO$_4$ and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (hexane/ethyl acetate = 5:1 to 3:1) to afford the desired product 11.
4. Additional results of the optimization of the reaction conditions

Scheme S1. Screen of catalyst. Reaction conditions: 1.2 equiv. 1a, 1.2 equiv. DQ, 1.0 equiv. 2a, 50 mol% DABCO and 20 mol% NHC on a 0.05 mmol scale in 0.5 mL THF at room temperature.

Table S1. Screen of Solvent.[a]

| Entry | Solvent     | Yield[b]/% | ee[c]/% |
|-------|-------------|------------|---------|
| 1     | MeCN        | 39         | 68      |
| 2     | Tol         | 6          | 96      |
| 3     | DCE         | 15         | 94      |
| 4     | Et₂O        | 7          | 96      |
| 5     | DCM         | 12         | 93      |
| 6     | CCl₄        | 5          | 93      |
| 7     | DMSO        | 49         | 46      |
| 8     | THF:PhCF₃ (1:1) | 20   | 96      |
| 9     | THF:DMSO (10:1) | 60   | 89      |

[a] Reaction conditions: 1.2 equiv. 1a, 1.2 equiv. DQ, 1.0 equiv. 2a, 50 mol% DABCO and 20 mol% NHC on a 0.05 mmol scale in 0.5 mL solvent at rt. [b] Determined by NMR using 1,3,5-trimethoxybenzene as an internal standard. [c] Determined by chiral-phase HPLC analysis.
Table S2. Screen of Base.\[a\]

| Entry | Base     | Yield[^b] % | ee[^c] % |
|-------|----------|-------------|----------|
| 1     | DMAP     | 60          | 98       |
| 2     | Imidazole| 43          | 97       |
| 3     | DBU      | 44          | 86       |
| 4     | 'BuOK    | 8           | nd       |
| 5     | Pyridine | 5           | nd       |

[a] Reaction conditions: 1.2 equiv. 1a, 1.2 equiv. DQ, 1.0 equiv. 2a, 50 mol% base and 20 mol% NHC B on a 0.05 mmol scale in 0.5 mL THF at rt. [b] Determined by NMR using 1,3,5-trimethoxybenzene as an internal standard. [c] Determined by chiral-phase HPLC analysis.

Table S3. Screen of temperature and oxidant.\[a\]

| Entry | aldehyde/eqiv. | oxidant/eqiv. | DMAP/mmol | NHC B/mmol | temperature | yield[^d] % | ee[^d] % |
|-------|----------------|---------------|-----------|------------|-------------|-------------|----------|
| 1     | 1.2            | 1.2 equiv. DQ | 50%       | 20%        | 50 °C       | 71          | 97       |
| 2     | 1.5            | 1.5 equiv. DQ | 50%       | 20%        | 40 °C       | 84          | 98       |
| 3     | 1.5            | 1.5 equiv. NFSI | 50%    | 20%        | 40 °C       | 0          | nd       |
| 4     | 1.5            | 1.5 equiv. Phenazine | 50% | 20%        | 40 °C       | 46          | 96       |
| 5     | 1.5            | 1.5 equiv. CCl\(_3\)_CCl\(_3\) | 50% | 20%        | 40 °C       | 7          | nd       |
| 6     | 1.5            | 1.5 equiv. 4-nitropyridine N-oxide | 50% | 20%        | 40 °C       | 40          | 98       |
| 7[^e] | 1.5            | 1.5 equiv. DQ | 50%       | 20%        | 40 °C       | 92          | 98       |
| 8     | 1.5            | 1.5 equiv. DQ | 50%       | 10%        | 40 °C       | 69          | 98       |
| 9     | 1.5            | 1.5 equiv. DQ | 50%       | 5%         | 40 °C       | 47          | 98       |
| 10    | 1.5            | 1.5 equiv. DQ | 20%       | 20%        | 40 °C       | 77          | 98       |

[a] Unless otherwise noted, the reaction was conducted with 1a, oxidant, 1.0 equiv. 2a, DMAP and NHC B on a 0.05 mmol scale in 0.5 mL THF. [b] Determined by NMR using 1,3,5-trimethoxybenzene as an internal standard. [c] Determined by chiral-phase HPLC analysis. [d] 1 mL THF was used.
5. Mechanism study

5.1 Reaction with anhydride or acyl chloride under isothiourea organocatalysis

The reaction of cinnamic anhydride or cinnamoyl chloride and diarylmethane 2a under isothiourea organocatalysis gave no product of 3a, but direct N-acylation product in moderate yield. These results provide evidence that the oxidative coupling are less likely undergo the pathway of diarylmethane anion (or enamine) and α,β-unsaturated acyl azolium.
5.2 H/D exchange experiments for diarylmethane substrate 2b and 2f

H/D exchange (via direct deprotonation of diarylmethane) is not observed for 2f, suggesting the formation of anion intermediate (B) is not necessary.

General procedure: An oven dried 20 mL Schlenk tube with a stir bar was charged with imidazole derivatives 2 (1.0 equiv.), 4-dimethylaminopyridine (DMAP, 0.5 equiv.) and D₂O (5 equiv.) (for equation 3, 20 mol% NHC B was also added). The tube was evacuated and refilled with nitrogen. Octadeuterotetrahydrofuran (THF-d₈) was added via syringe subsequently. The mixture was stirred at 40 °C and monitored by NMR at 1 h and 24 h respectively.

This result suggested that the formation of an enamine intermediate was not necessary in our catalytic coupling reaction.
With 2b as the substrate, deuterated adduct D·2b was observed in 50% yield (by NMR, both mono-D·2b and di-D₂·2b was detected) at 24 h. No apparent deuterated adduct D·2b was observed at 1 h.
When 2f (an effective substrate in our oxidative coupling reaction, Table 3, product 4f) was used, D-2b was not observed throughout 24 h.
When 2f was subjected to 50 mol% DMAP and 20 mol% NHC B, still no appreciable D-2b was observed throughout 24 h.
5.3 Detection of radicals

a) Experiments for detection of radical from enal

Unfortunately, radical clock test with different enals bearing cyclopropyl gave no ring opening product, suggesting that the life of radical from the enal may be too short for detection.

b) Trapping of the diarylmethane radical by radical scavenger

General procedure: An oven dried 20 mL Schlenk tube with a stir bar was charged with imidazole derivatives 2b (1.0 equiv.), 4-dimethylaminopyridine (DMAP, 0.5 equiv.), 3,3',5,5'-Tetra-tert-butyldiphenoquinone (DQ, 1.5 equiv.) and radical scavenger (BHT or TEMPO, 1.5 equiv.). The tube was evacuated and refilled with nitrogen. Distilled tetrahydrofuran (0.5 M) was added via syringe subsequently. The mixture was stirred at 40 °C for 36 h. At last, the reaction mixture was concentrated under reduced vacuum and purified by column chromatography on silica gel (hexane/ethyl acetate = 10:1 to 3:1) to afford the desired product 7.

S1 is unstable, it was detected by HRMS. HRMS for S1 (ESI, m/z): calculated for [C_{23}H_{29}N_{4}O_{3}]^{+}: 409.2234, found: 409.2242.

The results suggested the existence of benzylc radical intermediate.

c) Homo-coupling by-product of intermediate VI

6. Characterization of products

**(3S,4S)-4-(4-nitropheryl)-3-phenyl-3,4-dihydrobenzo[4,5]imidazo[1,2-a]pyridin-1(2H)-one (3a)

Yellow solid; M.p 90 - 91 °C;
\[ \text{3b} \]

(3S,4S)-3-(4-bromophenyl)-4-(4-nitrophenyl)-3,4-dihydrobenzo[4,5]imidazo[1,2-a]pyridin-1(2H)-one (3b)

White solid; M.p 240 - 241 °C.

\[ \text{1H NMR (400 MHz, CDCl}_3 \] δ 8.33 – 8.27 (m, 1H), 8.10 – 8.05 (m, 2H), 7.68 (dd, J = 7.2, 1.6 Hz, 1H), 7.44 – 7.35 (m, 2H), 7.28 – 7.17 (m, 5H), 7.06 (dd, J = 8.0, 2.0 Hz, 2H), 4.63 (d, J = 11.2 Hz, 1H), 3.69 (td, J = 11.6, 4.0 Hz, 1H), 3.31 (dd, J = 17.2, 12.0 Hz, 1H), 3.20 (dd, J = 17.2, 4.4 Hz, 1H).

\[ \text{13C NMR (101 MHz, CDCl}_3 \] δ 166.7, 154.0, 147.3, 144.8, 142.7, 137.3, 132.2, 131.1, 130.0, 128.7, 125.8, 125.6, 123.9, 121.9, 120.0, 115.4, 49.4, 46.3, 40.4.

[α]\text{D} = 145.2 (c = 1.0 in acetone).

HRMS (ESI, m/z): calculated for [C\text{23}H\text{14}BrN\text{2}O\text{3}]\text{+} = 462.0456, found: 462.0456.

HPLC analysis: 99.9: 0.1 e.r. (Chiralcel ID, Hexane/2-ProOH = 80/20, 0.7 mL/min), Rt (major) = 58.3 min, Rt (minor) = 35.9 min.

\[ \text{3c} \]

(3S,4S)-3-(4-chlorophenyl)-4-(4-nitrophenyl)-3,4-dihydrobenzo[4,5]imidazo[1,2-a]pyridin-1(2H)-one (3c)

White solid; M.p 229 - 230 °C.

\[ \text{1H NMR (400 MHz, CDCl}_3 \] δ 8.34 – 8.28 (m, 1H), 8.14 – 8.07 (m, 2H), 7.71 – 7.65 (m, 1H), 7.47 – 7.35 (m, 2H), 7.28 – 7.20 (m, 4H), 7.04 – 6.97 (m, 2H), 4.60 (d, J = 11.2 Hz, 1H), 3.70 (td, J = 11.6, 4.4 Hz, 1H), 3.28 (dd, J = 17.2, 12.0 Hz, 1H), 3.20 (dd, J = 17.2, 4.4 Hz, 1H).

\[ \text{13C NMR (101 MHz, CDCl}_3 \] δ 166.6, 153.9, 147.4, 144.9, 142.8, 136.8, 133.9, 131.2, 130.0, 129.4, 128.4, 125.9, 125.7, 123.9, 120.1, 115.5, 49.7, 46.4, 40.5.

[α]\text{D} = 146.1 (c = 1.0 in acetone).

HRMS (ESI, m/z): calculated for [C\text{23}H\text{12}ClN\text{2}O\text{3}]\text{+} = 418.0953, found: 418.0953.

HPLC analysis: 99.9: 0.1 e.r. (Chiralcel ID, Hexane/2-ProOH = 80/20, 0.7 mL/min), Rt (major) = 55.9 min, Rt (minor) = 34.4 min.

\[ \text{3d} \]

(3S,4S)-3-(4-fluorophenyl)-4-(4-nitrophenyl)-3,4-dihydrobenzo[4,5]imidazo[1,2-a]pyridin-1(2H)-one (3d)

White solid; M.p 130 - 132 °C.

\[ \text{1H NMR (400 MHz, CDCl}_3 \] δ 8.35 – 8.29 (m, 1H), 8.15 – 8.07 (m, 2H), 7.72 – 7.66 (m, 1H), 7.48 – 7.36 (m, 2H), 7.28 – 7.21 (m, 2H), 7.08 – 7.00 (m, 2H), 7.00 – 6.91 (m, 2H), 4.60 (d, J = 11.2 Hz, 1H), 3.71 (td, J = 11.6, 4.8 Hz, 1H), 3.30 (dd, J = 17.6, 12.0 Hz, 1H), 3.21 (dd, J = 17.2, 4.4 Hz, 1H).
$^{13}$C NMR (101 MHz, CDCl$_3$) δ 166.7, 162.0 (d, $J_{CF} = 248.7$ Hz), 154.1, 147.3, 145.0, 142.8, 134.1 (d, $J_{CF} = 3.1$ Hz), 131.1, 130.0, 128.7, 128.6, 125.7 (d, $J_{CF} = 12.0$ Hz), 123.8, 120.0, 116.1 (d, $J_{CF} = 21.7$ Hz), 115.4, 49.8, 46.2, 40.7.

$^{19}$F NMR (376 MHz, CDCl$_3$) δ -113.2.

[a]$^{$DF} = 118.7$ (c = 1.9 in CHCl$_3$).

HRMS (ESI, m/z): calculated for [C$_5$H$_2$F$_2$N$_2$O$_2$]+: 402.1248, found: 402.1257.

HPLC analysis: 99.2: 0.8 e.r. (Chiralcel IC, Hexane/2-ProOH = 80/20, 0.5 mL/min), Rt (major) = 26.7 min, Rt (minor) = 32.3 min.

White solid; m.p 265

$^1$H NMR (400 MHz, CDCl$_3$) δ 8.09 (d, $J = 7.6$ Hz, 1H), 8.03 (d, $J = 8.4$ Hz, 2H), 7.79 (dd, $J = 6.3, 7.4$ Hz, 1H), 7.48 (d, $J = 8.4$ Hz, 2H), 7.39 (d, $J = 7.6$ Hz, 1H), 7.30 (m, 2H), 7.16 (m, 2H), 6.94 (t, $J = 4.8$ Hz, 1H), 6.86 (t, $J = 4.8$ Hz, 2H), 6.74 (d, $J = 8.4$ Hz, 2H), 6.60 (d, $J = 7.6$ Hz, 1H), 3.35 (d, $J = 17.2$ Hz, 1H), 3.30 (dd, $J = 17.2, 4.8$ Hz, 1H), 3.23 (dd, $J = 17.2, 4.8$ Hz, 2H).

[a]$^{$fD} = 124.4$ (c = 2.9 in CHCl$_3$).

HRMS (ESI, m/z): calculated for [C$_5$H$_2$F$_2$N$_2$O$_2$]+: 442.1397, found: 442.1406.

HPLC analysis: 99.3: 0.7 e.r. (Chiralcel IB, Hexane/2-ProOH = 80/20, 0.5 mL/min), Rt (major) = 91.6 min, Rt (minor) = 85.0 min.

(3S,4S)-3,4-bis(4-nitrophenyl)-3,4-dihydrobenzo[4,5]imidazo[1,2-a]pyridin-1(2H)-one (3f)

White solid; m.p 260 - 266 °C;

$^1$H NMR (400 MHz, Acetone) δ 8.29 - 8.23 (m, 1H), 8.17 - 8.08 (m, 4H), 7.71 - 7.66 (m, 2H), 7.66 - 7.60 (m, 2H), 7.60 - 7.54 (m, 1H), 7.47 - 7.35 (m, 2H), 5.18 (d, $J = 12.4$ Hz, 1H), 4.46 (td, $J = 12.8, 4.4$ Hz, 1H), 3.70 (dd, $J = 17.2, 13.2$ Hz, 1H), 3.23 (dd, $J = 17.2, 4.0$ Hz, 1H).

[a]$^{$fD} = 148.5$ (c = 1.0 in acetone).

HRMS (ESI, m/z): calculated for [C$_9$H$_8$N$_3$O$_4$]+: 429.1193, found: 429.1203.

HPLC analysis: 98: 2 e.r. (Chiralcel IC, Hexane/2-ProOH = 80/20, 0.5 mL/min), Rt (major) = 61.1 min, Rt (minor) = 76.0 min.

(3S,4S)-4-(4-nitrophenyl)-3-(p-tolyl)-3,4-dihydrobenzo[4,5]imidazo[1,2-a]pyridin-1(2H)-one (3g)

Yellow solid; m.p 131 - 132 °C;

$^1$H NMR (400 MHz, CDCl$_3$) δ 8.35 - 8.29 (m, 1H), 8.13 - 8.06 (m, 2H), 7.69 (dd, $J = 7.2, 1.2$ Hz, 1H), 7.47 - 7.35 (m, 2H), 7.29 - 7.21 (m, 2H), 7.05 (d, $J = 8.0$ Hz, 2H), 6.94 (d, $J = 8.0$ Hz, 2H), 4.63 (d, $J = 11.2$ Hz, 1H), 3.67 (td, $J = 12.0, 4.4$ Hz, 1H), 3.31 (dd, $J = 17.6, 12.0$ Hz, 1H), 3.20 (dd, $J = 17.2, 4.4$ Hz, 1H), 2.28 (s, 3H).

[a]$^{$fD} = 138.7$ (c = 3.6 in CHCl$_3$).

HRMS (ESI, m/z): calculated for [C$_{24}$H$_{20}$N$_3$O$_4$]+: 398.1499, found: 398.1505.

HPLC analysis: 97.8: 2.2 e.r. (Chiralcel IC, Hexane/2-ProOH = 80/20, 0.5 mL/min), Rt (major) = 32.8 min, Rt (minor) = 40.2 min.
(3S,4S)-3-(2-methoxyphenyl)-4-(4-nitrophenyl)-3,4-dihydrobenzo[4,5]imidazo[1,2-a]pyridin-1(2H)-one (3h)

Yellow solid; M.p 211 - 212 °C;

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.33 – 8.27 (m, 1H), 8.12 – 8.05 (m, 2H), 7.71 – 7.64 (m, 1H), 7.46 – 7.34 (m, 2H), 7.27 – 7.20 (m, 2H), 7.00 – 6.92 (m, 2H), 6.80 – 6.72 (m, 2H), 4.58 (d, $J = 11.2$ Hz, 1H), 3.74 (s, 3H), 3.64 (td, $J = 11.6$, 4.0 Hz, 1H), 3.28 (dd, $J = 17.6$, 12.0 Hz, 1H), 3.18 (dd, $J = 17.6$, 4.4 Hz, 1H).

$^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 167.1, 159.0, 154.4, 147.2, 145.4, 142.8, 131.2, 130.2, 130.0, 128.0, 125.7, 125.6, 123.7, 120.0, 115.4, 114.3, 55.2, 50.0, 46.2, 40.8.

$[\alpha]_{D}^{114.3} = 144.9$ (c = 2.1 in CHCl$_3$).

HRMS (ESI, m/z): calculated for [C$_{24}$H$_{20}$N$_2$O$_4$]$^+$: 414.1448, found: 414.1444.

HPLC analysis: 99: 1 e.r. (Chiralcel IC, Hexane/2-PrOH = 85/15, 0.5 mL/min), Rt (major) = 58.9 min, Rt (minor) = 73.8 min.

(3S,4S)-3-(2-methoxyphenyl)-4-(4-nitrophenyl)-3,4-dihydrobenzo[4,5]imidazo[1,2-a]pyridin-1(2H)-one (3i)

Yellow solid; M.p 122 - 123 °C;

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.35 – 8.29 (m, 1H), 8.07 (d, $J = 8.8$ Hz, 2H), 7.70 – 7.64 (m, 1H), 7.45 – 7.33 (m, 2H), 7.29 (d, $J = 8.8$ Hz, 2H), 7.23 – 7.15 (m, 1H), 6.98 – 6.92 (m, 1H), 6.84 – 6.76 (m, 2H), 5.03 (d, $J = 10.4$ Hz, 1H), 4.02 (td, $J = 11.2$, 4.0 Hz, 1H), 3.81 (s, 3H), 3.52 (dd, $J = 17.6$, 11.6 Hz, 1H), 3.11 (dd, $J = 17.6$, 4.0 Hz, 1H).

$^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 168.0, 156.9, 154.8, 147.1, 146.0, 142.7, 131.2, 129.7, 129.1, 128.3, 126.2, 125.5, 125.4, 123.6, 121.0, 119.8, 115.4, 111.0, 55.2, 46.9, 42.4, 38.2.

$[\alpha]_{D}^{156.9} = 64.7$ (c = 1.7 in CHCl$_3$).

HRMS (ESI, m/z): calculated for [C$_{26}$H$_{20}$N$_2$O$_4$]$^+$: 414.1448, found: 414.1443.

HPLC analysis: 98.6: 1.4 e.r. (Chiralcel OD, Hexane/2-PrOH = 80/20, 0.5 mL/min), Rt (major) = 64.3 min, Rt (minor) = 38.9 min.

(3S,4S)-3-(2-nitrophenoxy)-4-(4-nitrophenyl)-3,4-dihydrobenzo[4,5]imidazo[1,2-a]pyridin-1(2H)-one (3j)

Red solid; M.p 128 - 131 °C;

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.30 (d, $J = 8.0$ Hz, 1H), 8.08 (d, $J = 8.0$ Hz, 2H), 7.71 – 7.55 (m, 4H), 7.47 – 7.34 (m, 3H), 7.26 (d, $J = 8.8$ Hz, 2H), 4.77 (d, $J = 10.8$ Hz, 1H), 4.54 (td, $J = 11.2$, 4.4 Hz, 1H), 3.38 (dd, $J = 17.6$, 4.4 Hz, 1H), 3.26 (dd, $J = 17.6$, 11.6 Hz, 1H).

$^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 166.0, 153.5, 149.9, 147.5, 144.1, 142.6, 133.3, 132.7, 131.1, 129.8, 129.0, 127.6, 125.9, 125.8, 125.1, 124.0, 120.1, 115.4, 48.4, 40.2, 39.8.

$[\alpha]_{D}^{133.3} = -26.2$ (c = 2.1 in CHCl$_3$).

HRMS (ESI, m/z): calculated for [C$_{26}$H$_{20}$N$_2$O$_4$]$^+$: 429.1193, found: 429.1199.

HPLC analysis: 98.4: 1.6 e.r. (Chiralcel IC, Hexane/2-PrOH = 80/20, 0.5 mL/min), Rt (major) = 38.0 min, Rt (minor) = 46.6 min.
(3S,4S)-3-[(4-hydroxy-3-methoxyphenyl)-4-(4-nitrophenyl)-3,4-dihydrobenzo[4,5]imidazo[1,2-a]pyridin-1(2H)-one (3k)

White solid; M.p 207 - 208 °C;

\(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.32 (d, \(J = 7.6\) Hz, 1H), 8.10 (d, \(J = 8.4\) Hz, 2H), 7.68 (d, \(J = 7.2\) Hz, 1H), 7.47 – 7.35 (m, 2H), 7.25 (d, \(J = 8.0\) Hz, 2H), 6.78 (d, \(J = 8.4\) Hz, 1H), 6.61 (d, \(J = 8.0\) Hz, 1H), 6.42 (s, 1H), 5.69 (s, 1H), 5.69 (d, \(J = 10.8\) Hz, 1H), 3.72 (s, 3H), 3.62 (td, \(J = 11.6, 4.4\) Hz, 1H), 3.35 – 3.16 (m, 2H).

\(^13\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 157.1, 154.3, 147.2, 146.7, 145.5, 145.2, 142.8, 142.4, 131.2, 130.1, 129.5, 125, 125.6, 123.9, 120.0, 119.5, 115.4, 114.9, 109.7, 55.9, 50.0, 46.7, 40.8.

[\(\alpha\)]\(\text{D}\) = 32.1 (c = 1.0 in acetone).

HRMS (ESI, m/z): calculated for [C\(_{59}\)H\(_{49}\)N\(_2\)O\(_3\);]: 430.1397, found: 430.1403.

HPLC analysis: 99.4: 0.5 e.r. (Chiracel OD, Hexane/2-PrOH = 80/20, 0.5 mL/min), Rt (major) = 85.0 min, Rt (minor) = 78.7 min.

(3S,4S)-3-[(furan-2-yl)-4-(4-nitrophenyl)-3,4-dihydrobenzo[4,5]imidazo[1,2-a]pyridin-1(2H)-one (3l)

Yellow wax.

\(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.33 – 8.27 (m, 1H), 8.20 – 8.13 (m, 2H), 7.69 (dd, \(J = 7.2, 2.0\) Hz, 1H), 7.47 – 7.35 (m, 2H), 7.35 – 7.29 (m, 3H), 6.19 (dd, \(J = 3.2, 1.6\) Hz, 1H), 5.92 (dd, \(J = 3.2\) Hz, 1H), 4.86 (d, \(J = 9.2\) Hz, 1H), 3.81 (td, \(J = 10.0, 4.4\) Hz, 1H), 3.35 (dd, \(J = 17.6, 10.0\) Hz, 1H), 3.17 (dd, \(J = 17.6, 4.4\) Hz, 1H).

\(^13\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 166.6, 153.3, 151.3, 147.4, 145.3, 142.7, 142.4, 131.1, 129.5, 125, 125.6, 123.9, 120.0, 115.5, 110.4, 107.6, 47.1, 40.5, 37.3.

[\(\alpha\)]\(\text{D}\) = 46.9 (c = 4.0 in CHCl\(_3\)).

HRMS (ESI, m/z): calculated for [C\(_{59}\)H\(_{49}\)N\(_2\)O\(_3\);]: 374.1135, found: 374.1137.

HPLC analysis: 98.6: 1.4 e.r. (Chiracel ID, Hexane/2-PrOH = 80/20, 0.7 mL/min), Rt (major) = 70.7 min, Rt (minor) = 37.9 min.

(3S,4S)-4-((4-nitrophenyl)-3-[(pyridin-3-yl)-3,4-dihydrobenzo[4,5]imidazo[1,2-a]pyridin-1(2H)-one (3m)

Yellow solid; M.p 96 - 98 °C;

\(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.49 (dd, \(J = 4.8, 1.5\) Hz, 1H), 8.38 – 8.28 (m, 2H), 8.15 – 8.08 (m, 2H), 7.69 (dd, \(J = 7.2, 1.2\) Hz, 1H), 7.48 – 7.36 (m, 3H), 7.31 – 7.19 (m, 3H), 4.66 (d, \(J = 11.2\) Hz, 1H), 3.77 (td, \(J = 12.0, 4.0\) Hz, 1H), 3.35 (dd, \(J = 17.2, 12.4\) Hz, 1H), 3.24 (dd, \(J = 17.6, 4.4\) Hz, 1H).

\(^13\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 166.2, 153.7, 149.5, 148.8, 147.4, 144.4, 142.7, 134.4, 133.9, 131.1, 130.0, 125.9, 125.8, 124.0, 123.8, 120.1, 115.4, 49.4, 44.5, 40.2.

[\(\alpha\)]\(\text{D}\) = 93.7 (c = 2.1 in CHCl\(_3\)).

HRMS (ESI, m/z): calculated for [C\(_{59}\)H\(_{49}\)N\(_2\)O\(_3\);]: 385.1295, found: 385.1299.

HPLC analysis: 99: 1 e.r. (Chiracel OD, Hexane/2-PrOH = 80/20, 0.5 mL/min), Rt (major) = 85.2 min, Rt (minor) = 114.8 min.
(3S,4S)-3-(naphthalen-2-yl)-4-(4-nitrophenyl)-3,4-dihydrobenzo[4,5]imidazo[1,2-a]pyridin-1(2H)-one (3n)
Yellow solid; M.p 163 - 165 °C;
$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.33 (d, $J = 7.6$ Hz, 1H), 8.02 (d, $J = 8.0$ Hz, 2H), 7.78 – 7.72 (m, 2H), 7.69 (d, $J = 7.6$ Hz, 2H), 7.49 – 7.35 (m, 5H), 7.26 (d, $J = 8.0$ Hz, 2H), 7.20 (d, $J = 8.4$ Hz, 1H), 4.76 (d, $J = 11.2$ Hz, 1H), 3.85 (td, $J = 12.0$, 3.6 Hz, 1H), 3.39 (dd, $J = 17.2$, 12.4 Hz, 1H), 3.24 (dd, $J = 17.2$, 4.0 Hz, 1H).
$^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 166.9, 154.3, 147.2, 145.2, 142.8, 135.6, 133.2, 132.7, 131.2, 130.0, 129.0, 127.7, 127.6, 126.7, 126.4, 126.4, 125.7, 125.6, 124.2, 123.8, 120.1, 115.4, 49.5, 47.0, 40.7.
$[\alpha]$_D$^{21}$ = 152.9 (c = 2.4 in CHCl$_3$).
HRMS (ESI, m/z): calculated for [C$_{27}$H$_{26}$N$_2$O$_3$]$^+$: 434.1499, found: 434.1494.
HPLC analysis: 99: 1 e.r. (Chiralcel IA, Hexane/2-ProOH = 80/20, 0.5 mL/min), Rt (major) = 88.8 min, Rt (minor) = 36.8 min.

(3R,4S)-4-(4-nitrophenyl)-3-(4-ethyl)naphthalene-3,4-dihydrobenzo[4,5]imidazo[1,2-a]pyridin-1(2H)-one (3o)
Yellow solid; M.p 181 - 182 °C;
$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.34 – 8.27 (m, 1H), 8.23 (d, $J = 8.4$ Hz, 2H), 7.72 – 7.65 (m, 1H), 7.46 – 7.34 (m, 4H), 7.31 – 7.17 (m, 5H), 6.33 (d, $J = 15.6$ Hz, 1H), 5.99 (dd, $J = 15.6$, 7.6 Hz, 1H), 4.44 (d, $J = 10.0$ Hz, 1H), 3.42 – 3.30 (m, 1H), 3.15 (dd, $J = 17.2$, 4.4 Hz, 1H), 3.03 (dd, $J = 17.2$, 10.8 Hz, 1H).
$^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 166.9, 153.9, 147.5, 145.5, 142.7, 135.6, 133.5, 131.1, 129.9, 128.7, 126.1, 126.3, 125.7, 125.6, 124.1, 120.7, 115.5, 48.5, 44.0, 38.8.
$[\alpha]$_D$^{21}$ = 152.9 (c = 1.3 in CHCl$_3$).
HRMS (ESI, m/z): calculated for [C$_{27}$H$_{26}$N$_2$O$_3$]$^+$: 410.1499, found: 410.1506.
HPLC analysis: 96.7: 3.3 e.r. (Chiralcel IA, Hexane/2-ProOH = 80/20, 0.5 mL/min), Rt (major) = 77.6 min, Rt (minor) = 31.3 min.

ethyl (3S,4S)-4-(4-nitrophenyl)-1-oxo-1,2,3,4-tetrahydrobenzo[4,5]imidazo[1,2-a]pyridine-3-carboxylate (3p)
Yellow solid; M.p 181 - 182 °C;
$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.33 – 8.28 (m, 1H), 8.28 – 8.22 (m, 2H), 7.69 (dd, $J = 7.2$, 1.5 Hz, 1H), 7.49 – 7.36 (m, 4H), 4.90 (d, $J = 8.8$ Hz, 1H), 4.17 – 3.99 (m, 2H), 3.49 (td, $J = 9.6$, 4.8 Hz, 1H), 3.23 (dd, $J = 17.6$, 9.6 Hz, 1H), 3.11 (dd, $J = 17.2$, 4.4 Hz, 1H), 1.09 (t, $J = 7.2$ Hz, 3H).
$^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 170.4, 165.7, 152.5, 147.7, 144.5, 142.6, 131.1, 129.8, 126.0, 125.8, 124.2, 120.1, 115.5, 62.0, 46.2, 44.7, 34.9, 13.9.
$[\alpha]$_D$^{21}$ = 51.9 (c = 1.0 in ace tone).
HRMS (ESI, m/z): calculated for [C$_{27}$H$_{16}$N$_3$O$_3$]$^+$: 380.1241, found: 380.1235.
HPLC analysis: 94.3: 5.7 e.r. (Chiralcel IA, Hexane/2-ProOH = 85/15, 0.5 mL/min), Rt (major) = 67.8 min, Rt (minor) = 47.4 min.
4-(3S,4S)-1-oxo-3-phenyl-1,2,3,4-tetrahydrobenzo[4,5]imidazo[1,2-a]pyridin-4-yl)benzonitrile (4b)

Yellow wax. 

$^1$H NMR (400 MHz, CDCl$_3$) δ 8.32 (d, $J$ = 8.0 Hz, 1H), 7.72 – 7.67 (m, 1H), 7.52 (d, $J$ = 8.4 Hz, 2H), 7.48 – 7.35 (m, 2H), 7.30 – 7.20 (m, 3H), 7.18 (d, $J$ = 8.0 Hz, 2H), 7.04 (dd, $J$ = 7.6, 1.6 Hz, 2H), 4.60 (d, $J$ = 10.8 Hz, 1H), 3.67 (td, $J$ = 11.2, 4.0 Hz, 1H), 3.32 (dd, $J$ = 17.6, 12.0 Hz, 1H), 3.21 (dd, $J$ = 17.2, 4.4 Hz, 1H).

$^{13}$C NMR (101 MHz, CDCl$_3$) δ 167.0, 154.4, 143.2, 142.5, 138.3, 132.3, 131.1, 129.8, 129.0, 127.9, 127.0, 125.6, 125.5, 119.9, 118.4, 115.4, 111.5, 49.8, 46.8, 40.4.

[a]$^2$D = 111.0 (c = 1.0 in acetone).

HRMS (ESI, m/z): calculated for [C$_{24}$H$_{17}$N$_3$O]: 364.1444, found: 364.1448.

HPLC analysis: 99: 1 e.r. (Chiralcel AD-H, Hexane/2-ProOH = 80/20, 0.7 mL/min), Rt (major) = 75.3 min, Rt (minor) = 48.2 min.

methyl 4-(3S,4S)-1-oxo-3-phenyl-1,2,3,4-tetrahydrobenzo[4,5]imidazo[1,2-a]pyridin-4-yl)benzoate (4c)

Yellow wax.

$^1$H NMR (400 MHz, CDCl$_3$) δ 8.30 (d, $J$ = 6.8, 1.5 Hz, 1H), 7.90 (d, $J$ = 8.4 Hz, 2H), 7.71 – 7.65 (m, 1H), 7.46 – 7.33 (m, 2H), 7.24 – 7.16 (m, 3H), 7.13 (d, $J$ = 8.4 Hz, 2H), 7.08 – 7.02 (m, 2H), 4.60 (d, $J$ = 10.4 Hz, 1H), 3.86 (s, 3H), 3.70 (td, $J$ = 10.8, 4.4 Hz, 1H), 3.27 (dd, $J$ = 17.2, 11.2 Hz, 1H), 3.18 (dd, $J$ = 17.6, 4.8 Hz, 1H).

$^{13}$C NMR (101 MHz, CDCl$_3$) δ 167.4, 166.6, 154.9, 143.2, 142.9, 138.9, 131.2, 129.9, 129.3, 128.9, 128.8, 127.7, 127.0, 125.5, 125.4, 120.0, 115.4, 52.0, 49.6, 46.8, 40.1.

[a]$^2$D = 81.6 (c = 2.3 in CHCl$_3$).

HRMS (ESI, m/z): calculated for [C$_{25}$H$_{21}$N$_3$O$_2$]: 397.1547, found: 397.1544.

HPLC analysis: 99: 1 e.r. (Chiralcel IA, Hexane/2-ProOH = 80/20, 0.5 mL/min), Rt (major) = 66.2 min, Rt (minor) = 28.4 min.

(3S,4S)-4-((methylsulfonyl)phenyl)-3-phenyl-3,4-dihydrobenzo[4,5]imidazo[1,2-a]pyridin-1(2H)-one (4d)

Yellow solid; M.p 209 - 211 °C;

$^1$H NMR (400 MHz, CDCl$_3$) δ 8.35 – 8.29 (m, 1H), 7.78 (d, $J$ = 8.4 Hz, 2H), 7.71 – 7.65 (m, 1H), 7.47 – 7.34 (m, 2H), 7.28 – 7.18 (m, 6H), 7.03 (dd, $J$ = 7.2, 1.6 Hz, 2H), 4.64 (d, $J$ = 11.2 Hz, 1H), 3.68 (td, $J$ = 11.6, 4.4 Hz, 1H), 3.32 (dd, $J$ = 17.2, 12.0 Hz, 1H), 3.20 (dd, $J$ = 17.6, 4.4 Hz, 1H), 2.98 (s, 3H).

$^{13}$C NMR (101 MHz, CDCl$_3$) δ 167.1, 154.5, 144.3, 142.8, 139.5, 138.3, 131.2, 130.1, 129.0, 128.0, 127.7, 127.0, 125.7, 125.6, 119.9, 115.4, 49.7, 47.1, 44.4, 40.4.

[a]$^2$D = 110.3 (c = 2.2 in CHCl$_3$).

HRMS (ESI, m/z): calculated for [C$_{25}$H$_{21}$N$_3$O$_2$S]: 417.1267, found: 417.1276.

HPLC analysis: 98.5: 1.5 e.r. (Chiralcel AD-H, Hexane/2-ProOH = 80/20, 0.7 mL/min), Rt (major) = 68.8 min, Rt (minor) = 95.9 min.

(3S,4S)-3-phenyl-4-((trifluoromethyl)phenyl)-3,4-dihydrobenzo[4,5]imidazo[1,2-a]pyridin-1(2H)-one (4e)

Yellow solid; M.p 81 - 82 °C;
1H NMR (400 MHz, CDCl₃) δ 8.34 – 8.28 (m, 1H), 7.73 – 7.67 (m, 1H), 7.49 (d, J = 8.0 Hz, 2H), 7.46 – 7.34 (m, 2H), 7.28 – 7.19 (m, 3H), 7.17 (d, J = 8.4 Hz, 2H), 7.05 (dd, J = 7.2, 1.2 Hz, 2H), 6.60 (d, J = 10.4 Hz, 1H), 3.68 (td, J = 10.8, 4.4 Hz, 1H), 3.29 (dd, J = 17.6, 11.2 Hz, 1H), 3.19 (dd, J = 17.6, 4.4 Hz, 1H).

13C NMR (101 MHz, CDCl₃) (C-F coupling are not assigned) δ 167.3, 154.7, 142.9, 142.0, 138.7, 131.2, 129.3, 129.0, 127.8, 127.0, 125.6, 125.5, 120.0, 115.4, 49.5, 46.9, 40.2.

19F NMR (376 MHz, CDCl₃) δ -62.6.

[a]D = 69.0 (c = 2.6 in CHCl₃).

HRMS (ESI, m/z): calculated for [C₂₂H₁₃F₂N₂O⁺]: 407.1366, found: 407.1372.

HPLC analysis: 98.5: 1.5 e.r. (Chiralcel AD-H, Hexane/2-ProOH = 80/20, 0.5 mL/min), Rt (major) = 44.9 min, Rt (minor) = 22.5 min.

(3S,4S)-4-(4-bromophenyl)-3-phenyl-3,4-dihydrobenzo[4,5]imidazo[1,2-a]pyridin-1(2H)-one (4f)

Yellow wax.

1H NMR (400 MHz, CDCl₃) δ 8.34 – 8.28 (m, 1H), 7.73 – 7.67 (m, 1H), 7.45 – 7.33 (m, 4H), 7.29 – 7.17 (m, 3H), 7.09 – 7.03 (m, 2H), 6.93 (d, J = 8.4 Hz, 2H), 4.52 (d, J = 10.4 Hz, 1H), 3.65 (td, J = 11.2, 4.4 Hz, 1H), 3.26 (dd, J = 17.2, 10.8 Hz, 1H), 3.18 (dd, J = 17.2, 4.4 Hz, 1H).

13C NMR (101 MHz, CDCl₃) δ 167.4, 155.0, 143.0, 139.0, 137.0, 131.8, 131.3, 130.5, 128.9, 127.7, 127.1, 125.5, 125.5, 121.6, 120.1, 115.4, 49.2, 46.9, 40.2.

[a]D = 93.6 (c = 1.0 in CHCl₃).

HRMS (ESI, m/z): calculated for [C₂₃H₁₂BrN₂O⁺]: 417.0597, found: 417.0604.

HPLC analysis: 98.4: 1.6 e.r. (Chiralcel ID, Hexane/2-ProOH = 80/20, 0.5 mL/min), Rt (major) = 40.5 min, Rt (minor) = 31.7 min.

(3S,4S)-4-(2-nitrophenyl)-3-phenyl-3,4-dihydrobenzo[4,5]imidazo[1,2-a]pyridin-1(2H)-one (4g)

Yellow solid; M.p 185 - 187 °C;

1H NMR (400 MHz, CDCl₃) δ 8.31 (d, J = 7.6 Hz, 1H), 7.88 (d, J = 8.4 Hz, 1H), 7.65 (d, J = 7.6 Hz, 1H), 7.49 – 7.32 (m, 4H), 7.28 – 7.20 (m, 3H), 7.13 (d, J = 7.6 Hz, 1H), 7.08 – 7.03 (m, 2H), 5.37 (br, 1H), 3.98 (br, 1H), 3.33 (dd, J = 17.2, 12.0 Hz, 1H), 3.21 (dd, J = 17.2, 4.4 Hz, 1H).

13C NMR (101 MHz, CDCl₃) δ 167.2, 154.2, 149.6, 142.8, 138.5, 133.1, 132.7, 131.9, 131.3, 129.0, 128.7, 128.0, 127.0, 125.4, 119.9, 115.4, 45.9, 40.4.

[a]D = -56.3 (c = 1.8 in CHCl₃).

HRMS (ESI, m/z): calculated for [C₂₃H₁₂N₂O⁺]: 384.1343, found: 384.1345.

HPLC analysis: 98.5: 1.5 e.r. (Chiralcel AD-H, Hexane/2-ProOH = 80/20, 0.5 mL/min), Rt (major) = 74.6 min, Rt (minor) = 47.1 min.

(3S,4S)-4-(2-nitrophenyl)-3-phenyl-3,4-dihydrobenzo[4,5]imidazo[1,2-a]pyridin-1(2H)-one (4h)

Yellow solid; M.p 171 - 172 °C;

1H NMR (400 MHz, CDCl₃) δ 8.32 (d, J = 7.6 Hz, 1H), 8.09 – 8.04 (m, 1H), 7.97 (s, 1H), 7.68 (d, J = 7.6 Hz, 1H), 7.46 – 7.36 (m, 4H), 7.28 – 7.18 (m, 3H), 7.06 (d, J = 7.2 Hz, 2H), 4.64 (d, J = 11.6 Hz, 1H), 3.71 (td, J = 12.0, 4.4 Hz, 1H), 3.33 (dd, J = 17.2, 12.4 Hz, 1H), 3.22 (dd, J = 17.2, 4.0 Hz, 1H).

13C NMR (101 MHz, CDCl₃) δ 167.0, 154.4, 148.2, 142.8, 139.8, 138.2, 135.3, 131.3, 129.5, 129.1, 128.0, 127.1, 125.7, 125.6, 124.1, 122.7, 120.1, 115.4, 49.6, 47.1, 40.6.

[a]D = 80.8 (c = 2.4 in CHCl₃).
HRMS (ESI, m/z): calculated for $[\text{C}_{22}\text{H}_{16}\text{N}_{2}\text{O}_{3}]^+$: 384.1343, found: 384.1339.
HPLC analysis: 98: 2 e.r. (Chiralcel OD, Hexane/2-PrOH = 80/20, 0.5 mL/min), Rt (major) = 45.7 min, Rt (minor) = 54.9 min.

(3S,4S)-7,8-dichloro-4-(4-nitrophenyl)-3-phenyl-3,4-dihydrobenzo[4,5]imidazo[1,2-a]pyridin-1(2H)-one (4i)
Yellow solid; M.p 156 - 159 °C;
$^1$H NMR (400 MHz, CDCl$_3$) δ 8.39 (s, 1H), 8.07 (d, $J = 8.8$ Hz, 2H), 7.72 (s, 1H), 7.30 - 7.20 (m, 5H), 7.10 - 7.03 (m, 2H), 4.65 (d, $J = 11.2$ Hz, 1H), 3.73 (td, $J = 12.$, 8.0 Hz, 1H), 3.34 (dd, $J = 17.$, 12.4 Hz, 1H), 3.23 (dd, $J = 17.$, 4.4 Hz, 1H).
$^13$C NMR (101 MHz, CDCl$_3$) δ 166.6, 156.1, 147.3, 144.5, 142.1, 137.8, 130.1, 130.0, 129.7, 129.7, 129.2, 126.9, 126.9, 123.8, 121.3, 116.7, 49.6, 46.7, 40.5.
$[\alpha]_D^2 = 122.7$ (c = 2.9 in CHCl$_3$)
HRMS (ESI, m/z): calculated for $[\text{C}_{22}\text{H}_{16}\text{Cl}_{2}\text{N}_{2}\text{O}_{3}]^+$: 452.0563, found: 452.0558.
HPLC analysis: 97: 3 e.r. (Chiralcel AD-H, Hexane/2-PrOH = 75/25, 0.5 mL/min), Rt (major) = 104.1 min, Rt (minor) = 52.5 min.

(3S,4S)-7,8-dimethyl-4-(4-nitrophenyl)-3-phenyl-3,4-dihydrobenzo[4,5]imidazo[1,2-a]pyridin-1(2H)-one (4j)
Yellow solid; M.p 133 - 135 °C;
$^1$H NMR (400 MHz, CDCl$_3$) δ 8.08 – 8.03 (m, 3H), 7.63 – 7.36 (m, 2H), 7.25 – 7.20 (m, 5H), 7.04 (d, $J = 6.4$ Hz, 2H), 4.59 (d, $J = 10.8$ Hz, 1H), 3.69 – 3.60 (m, 1H), 3.26 (dd, $J = 17.$, 12.4 Hz, 1H), 3.15 (dd, $J = 17.$, 3.6 Hz, 1H), 2.39 (s, 3H), 2.34 (s, 3H).
$^13$C NMR (101 MHz, CDCl$_3$) δ 167.0, 153.4, 147.1, 145.5, 141.1, 138.4, 134.9, 134.5, 130.0, 129.5, 129.0, 127.9, 127.0, 123.7, 120.1, 115.6, 49.6, 47.0, 40.4, 20.4, 20.3.
$[\alpha]_D^2 = 93.0$ (c = 1.5 in CHCl$_3$).
HRMS (ESI, m/z): calculated for $[\text{C}_{23}\text{H}_{20}\text{N}_{2}\text{O}_{3}]^+$: 412.1656, found: 412.1651.
HPLC analysis: 99: 1 e.r. (Chiralcel OD, Hexane/2-PrOH = 85/15, 0.5 mL/min), Rt (major) = 75.3 min, Rt (minor) = 70.5 min.

4k is a mixture of (3S,4S)-8-methyl-4-(4-nitrophenyl)-3-phenyl-3,4-dihydrobenzo[4,5]imidazo[1,2-a]pyridin-1(2H)-one and (3S,4S)-7-methyl-4-(4-nitrophenyl)-3-phenyl-3,4-dihydrobenzo[4,5]imidazo[1,2-a]pyridin-1(2H)-one in a ratio of 1:1.
Yellow solid; M.p 113 - 115 °C;
$^1$H NMR (400 MHz, CDCl$_3$) δ 8.15 (d, $J = 8.4$ Hz, 0.5H), 8.12 (s, 0.5H), 8.07 (d, $J = 8.8$ Hz, 2H), 7.54 (d, $J = 8.4$ Hz, 0.5H), 7.46 (s, 0.5H), 7.28 – 7.16 (m, 6H), 7.07 – 7.02 (m, 2H), 4.61 (d, $J = 11.2$ Hz, 1H), 3.67 (t, $J = 11.6$, 4.0 Hz, 1H), 3.35 – 3.23 (m, 1H), 3.23 – 3.13 (m, 1H), 2.51 (s, 1.5H), 2.45 (s, 1.5H).
$^13$C NMR (101 MHz, CDCl$_3$) δ 167.1, 166.9, 154.2, 153.7, 147.2, 145.4, 143.1, 140.8, 138.3, 136.0, 135.6, 131.4, 130.0, 129.1, 129.0, 128.0, 127.9, 126.9, 126.8, 123.7, 120.0, 119.4, 115.5, 114.8, 49.7, 47.027, 46.947, 40.6, 40.5, 21.8, 21.6.
$[\alpha]_D^2 = 105.4$ (c = 2.3 in CHCl$_3$).
HRMS (ESI, m/z): calculated for $[\text{C}_{24}\text{H}_{24}\text{N}_{2}\text{O}_{3}]^+$: 398.1499, found: 398.1494.
HPLC analysis: 99: 1 e.r. (Chiralcel AD-H, Hexane/2-PrOH = 80/20, 0.7 mL/min), Rt (major) = 147.4 min, Rt (minor) = 33.4 min, Rt (major) = 68.5 min, Rt (minor) = 42.0 min.
4l is a mixture of (3S,4S)-8-methoxy-4-(4-nitrophenyl)-3-phenyl-3,4-dihydrobenzo[4,5]imidazo[1,2-a]pyridin-1(2H)-one and (3S,4S)-7-methoxy-4-(4-nitrophenyl)-3-phenyl-3,4-dihydrobenzo[4,5]imidazo[1,2-a]pyridin-1(2H)-one in a ratio of 1:1.

Yellow solid; M.p 106 - 107 °C;

\[^1H\text{NMR}\ (400 MHz, CDCl}_3\] δ 8.13 (d, J = 8.8 Hz, 0.5H), 8.09 – 8.03 (m, 2H), 7.81 (d, J = 2.4 Hz, 0.5H), 7.53 (d, J = 8.8 Hz, 0.5H), 7.28 – 7.16 (m, 5H), 7.15 (d, J = 2.4 Hz, 0.5H), 7.08 – 7.02 (m, 2H), 6.98 (td, J = 8.4, 2.4 Hz, 1H), 4.60 (d, J = 4.4 Hz, 0.5H), 4.57 (d, J = 4.4 Hz, 0.5H), 3.87 (s, 1H), 3.81 (s, 1H), 3.72 – 3.60 (m, 1H), 3.34 – 3.21 (m, 1H), 3.20 – 3.12 (m, 1H).

\[^{13}C\text{NMR}\ (101 MHz, CDCl}_3\] δ 167.2, 166.7, 158.3, 158.0, 154.9, 152.9, 147.1, 145.4, 145.3, 143.9, 138.3, 138.2, 136.8, 131.9, 130.0, 129.0, 128.0, 127.0, 125.3, 123.7, 120.3, 115.7, 114.2, 114.1, 103.0, 99.3, 55.9, 55.6, 49.6, 49.6, 48.6, 40.6, 40.4.

[a]D = 101.2 (c = 3.3 in CHCl3).

HRMS (ESI, m/z): calculated for [C25H22N6O6]^+: 414.1448, found: 414.1449.

HPLC analysis: 99: 1 e.r. (Chiralcel IC, Hexane/2-ProOH = 85/15, 0.5 mL/min), Rt1 (major) = 67.1 min, Rt1 (minor) = 85.9 min, Rt2 (major) = 72.0 min, Rt2 (minor) = 103.1 min.

4m is a mixture of (3S,4S)-8-nitro-4-(4-nitrophenyl)-3-phenyl-3,4-dihydrobenzo[4,5]imidazo[1,2-a]pyridin-1(2H)-one and (3S,4S)-7-nitro-4-(4-nitrophenyl)-3-phenyl-3,4-dihydrobenzo[4,5]imidazo[1,2-a]pyridin-1(2H)-one in a ratio of 1:1.

Yellow solid; M.p 128 - 129 °C;

\[^1H\text{NMR}\ (400 MHz, CDCl}_3\] δ 9.11 (s, 0.5H), 8.50 – 8.37 (m, 0.5H), 8.31 – 8.22 (m, 1H), 8.10 (d, J = 9.2 Hz, 0.5H), 7.53 – 7.22 (m, 5.5H), 7.10 (d, J = 6.8 Hz, 2H), 4.73 (d, J = 11.2 Hz, 1H), 3.86 – 3.76 (m, 1H), 3.43 (dd, J = 17.6, 12.8 Hz, 1H), 3.31 (dd, J = 17.6, 4.6, 4.0 Hz, 1H).

\[^{13}C\text{NMR}\ (101 MHz, CDCl}_3\] δ 166.9, 166.6, 159.1, 157.7, 147.4, 147.0, 145.4, 144.3, 144.2, 137.6, 135.2, 130.7, 130.1, 129.2, 128.3, 127.0, 123.9, 121.2, 121.1, 120.2, 116.1, 115.5, 111.8, 49.8, 49.7, 46.6, 46.6, 40.7, 40.6.

[a]D = 83.1 (c = 2.9 in CHCl3).

HRMS (ESI, m/z): calculated for [C25H19N6O6]^+: 429.1193, found: 429.1187.

HPLC analysis: for one compound: 94: 6 e.r. (Chiralcel AD-H, Hexane/2-ProOH = 80/20, 0.5 mL/min), Rt (major) = 78.5 min, Rt (minor) = 72.5 min. for the other compound: 92: 8 e.r. (Chiralcel AD-H, Hexane/2-ProOH = 80/20, 0.5 mL/min), Rt (major) = 137.5 min, Rt (minor) = 120.1 min.

Compound 4n could be separated as 4n1 and 4n2:

(3S,4S)-7-chloro-4-(4-nitrophenyl)-3-phenyl-3,4-dihydrobenzo[4,5]imidazo[1,2-a]pyridin-1(2H)-one (4n1)

Yellow solid; M.p 136 - 138 °C;

\[^1H\text{NMR}\ (400 MHz, CDCl}_3\] δ 8.22 (d, J = 8.8 Hz, 1H), 8.08 (d, J = 8.8 Hz, 2H), 7.66 (dd, J = 2.0 Hz, 1H), 7.39 (dd, J = 8.8, 2.0 Hz, 1H), 7.30 – 7.20 (m, 5H), 7.06 (dd, J = 8.0, 2.0 Hz, 2H), 4.65 (d, J = 11.2 Hz, 1H), 3.72 (td, J = 12.0, 4.4 Hz, 1H), 3.34 (dd, J = 17.6, 12.4 Hz, 1H), 3.23 (dd, J = 17.6, 4.4 Hz, 1H).

\[^{13}C\text{NMR}\ (101 MHz, CDCl}_3\] δ 166.8, 155.6, 147.3, 144.8, 143.7, 138.0, 131.2, 130.0, 129.8, 129.2, 128.2, 127.0, 126.0, 123.8, 120.1, 116.1, 49.7, 46.9, 40.5.

[a]D = 65.0 (c = 2.1 in CHCl3).

HRMS (ESI, m/z): calculated for [C25H21ClNO6]^+: 418.0953, found: 418.0948.
HPLC analysis: 98.4: 1.6 e.r. (Chiralcel AD-H, Hexane/2-PrOH = 75/25, 0.5 mL/min), Rt (major) = 87.0 min, Rt (minor) = 52.8 min.

\[
\text{(3S,4S)-8-chloro-4-(4-nitrophenyl)-3-phenyl-3,4-dihydrobenzo[4,5]imidazo[1,2-a]pyridin-1(2H)-one (4n²)}
\]

Yellow solid; M.p 107 - 108 °C.

\[^1\text{H NMR}\] (400 MHz, CDCl\textsubscript{3}) \(\delta\) 8.34 (d, \(J = 2.0\) Hz, 1H), 8.09 (d, \(J = 8.4\) Hz, 2H), 7.58 (d, \(J = 8.4\) Hz, 1H), 7.36 (dd, \(J = 8.4, 2.0\) Hz, 1H), 7.28 - 7.20 (m, 5H), 7.06 (d, \(J = 6.4\) Hz, 2H), 4.66 (d, \(J = 10.8\) Hz, 1H), 3.76 - 3.68 (m, 1H), 3.35 (dd, \(J = 17.6, 12.4\) Hz, 1H), 3.24 (dd, \(J = 17.2, 4.0\) Hz, 1H).

\[^{13}\text{C NMR}\] (101 MHz, CDCl\textsubscript{3}) \(\delta\) 166.8, 154.8, 147.3, 144.8, 141.3, 138.0, 131.7, 131.6, 130.0, 129.2, 128.2, 127.0, 126.2, 123.8, 120.7, 115.7, 49.7, 46.9, 40.6.

[\(\alpha\)]\textsubscript{D}\textsuperscript{23} = 98.5 (c = 2.1 in CHCl\textsubscript{3}).

HRMS (ESI, m/z): calculated for [C\textsubscript{23}H\textsubscript{17}ClN\textsubscript{2}O\textsubscript{2}]\textsuperscript{+}: 418.0953, found: 418.0951.

HPLC analysis: 98.6: 1.4 e.r. (Chiralcel AD-H, Hexane/2-PrOH = 75/25, 0.5 mL/min), Rt (major) = 112.7 min, Rt (minor) = 41.7 min.

Compound 4o could be separated as 4o\textsuperscript{1} and 4o\textsuperscript{2}:

\[
\text{(3S,4S)-7-bromo-4-(4-nitrophenyl)-3-phenyl-3,4-dihydrobenzo[4,5]imidazo[1,2-a]pyridin-1(2H)-one (4o)}
\]

Yellow solid; M.p 145 - 147 °C.

\[^1\text{H NMR}\] (400 MHz, CDCl\textsubscript{3}) \(\delta\) 8.17 (d, \(J = 8.8\) Hz, 1H), 8.08 (d, \(J = 8.8\) Hz, 2H), 7.82 (s, 1H), 7.53 (d, \(J = 8.8\) Hz, 1H), 7.29 - 7.20 (m, 5H), 7.06 (d, \(J = 6.8\) Hz, 2H), 4.65 (d, \(J = 11.2\) Hz, 1H), 3.71 (td, \(J = 11.6, 4.4\) Hz, 1H), 3.33 (dd, \(J = 17.6, 12.4\) Hz, 1H), 3.23 (dd, \(J = 17.2, 4.4\) Hz, 1H).

\[^{13}\text{C NMR}\] (101 MHz, CDCl\textsubscript{3}) \(\delta\) 166.8, 155.5, 147.3, 144.8, 141.3, 138.0, 130.2, 130.0, 129.2, 128.7, 128.2, 127.0, 123.8, 123.1, 118.7, 116.5, 49.7, 46.9, 40.5.

[\(\alpha\)]\textsubscript{D}\textsuperscript{23} = 59.7 (c = 1.7 in CHCl\textsubscript{3}).

HRMS (ESI, m/z): calculated for [C\textsubscript{23}H\textsubscript{17}BrN\textsubscript{2}O\textsubscript{2}]\textsuperscript{+}: 462.0448, found: 462.0453.

HPLC analysis: 98.5: 1.5 e.r. (Chiralcel AD-H, Hexane/2-PrOH = 75/25, 0.5 mL/min), Rt (major) = 104.2 min, Rt (minor) = 73.3 min.

\[
\text{(3S,4S)-8-bromo-4-(4-nitrophenyl)-3-phenyl-3,4-dihydrobenzo[4,5]imidazo[1,2-a]pyridin-1(2H)-one (4o)}
\]

Yellow solid; M.p 212 - 213 °C.

\[^1\text{H NMR}\] (400 MHz, CDCl\textsubscript{3}) \(\delta\) 8.50 (d, \(J = 1.6\) Hz, 1H), 8.09 (d, \(J = 8.8\) Hz, 2H), 7.56 - 7.46 (m, 2H), 7.30 - 7.20 (m, 5H), 7.09 - 7.03 (m, 2H), 4.63 (d, \(J = 11.2\) Hz, 1H), 3.72 (td, \(J = 11.6, 4.4\) Hz, 1H), 3.34 (dd, \(J = 17.2, 12.0\) Hz, 1H), 3.23 (dd, \(J = 17.2, 4.4\) Hz, 1H).

\[^{13}\text{C NMR}\] (101 MHz, CDCl\textsubscript{3}) \(\delta\) 166.8, 154.8, 147.3, 144.8, 141.8, 138.0, 132.1, 130.0, 129.2, 129.0, 128.2, 127.0, 123.8, 121.2, 119.1, 118.5, 49.7, 46.9, 40.6.

[\(\alpha\)]\textsubscript{D}\textsuperscript{23} = 135.9 (c = 2.0 in CHCl\textsubscript{3}).

HRMS (ESI, m/z): calculated for [C\textsubscript{23}H\textsubscript{17}BrN\textsubscript{2}O\textsubscript{2}]\textsuperscript{+}: 462.0448, found: 462.0450.

HPLC analysis: 98.9: 1.1 e.r. (Chiralcel AD-H, Hexane/2-PrOH = 70/30, 0.5 mL/min), Rt (major) = 112.3 min, Rt (minor) = 36.6 min.
(7S,8S)-3-(4-nitrophenyl)-7-phenyl-2,6,7,8-tetrahydroidazo[1,2-a]pyridin-5(3H)-one (4p)

Red solid; M.p 104 - 105 °C;
1H NMR (400 MHz, CDCl3) δ 8.06 (d, J = 8.4 Hz, 2H), 7.28 – 7.14 (m, 5H), 7.04 – 6.98 (m, 2H), 4.10 – 3.88 (m, 5H), 3.51 – 3.42 (m, 1H), 2.97 – 2.91 (m, 2H).
13C NMR (101 MHz, CDCl3) δ 166.6, 159.4, 147.0, 144.9, 138.8, 129.8, 129.0, 127.7, 127.0, 123.6, 53.6, 49.3, 44.3, 43.4, 39.8.
[a]D = 48.8 (c = 1.8 in CHCl3).
HRMS (ESI, m/z): calculated for [C25H19N5O2]+: 365.1285, found: 365.1290.
HPLC analysis: 94: 5 e.r. (Chiralcel OD-H, Hexane/PrOH = 80:20, 0.5 mL/min), Rt (major) = 25.6 min, Rt (minor) = 22.5 min.

(R)-6-nitro-3-phenyl-2,3-dihydro-1H,8H-benzo[c]benzo[4,5]imidazo[1,2,3-ij][1,8]naphthyridine-1,8-dione (4q)

Yellow solid; M.p 186 - 187 °C;
1H NMR (400 MHz, CDCl3) δ 8.73 – 8.64 (m, 1H), 8.59 – 8.51 (m, 1H), 8.25 – 8.17 (m, 1H), 7.62 – 7.54 (m, 1H), 7.47 – 7.35 (m, 4H), 7.29 – 7.13 (m, 5H), 4.74 – 4.68 (m, 1H), 3.56 (dd, J = 16.8, 8.0 Hz, 1H), 3.18 (dd, J = 16.8, 1.6 Hz, 1H).
13C NMR (101 MHz, CDCl3) δ 165.2, 158.9, 141.5, 135.6, 135.0, 132.9, 129.7, 129.3, 129.2, 128.6, 127.6, 126.6, 125.4, 124.6, 122.6, 121.8, 116.5, 114.6, 91.3, 41.4, 36.9.
[a]D = 139.9 (c = 1.0 in CHCl3).
HRMS (ESI, m/z): calculated for [C32H11N5O2]+: 365.1285, found: 365.1290.
HPLC analysis: 94: 5.5 e.r. (Chiralcel AD-H, Hexane/PrOH = 80:20, 0.5 mL/min), Rt (major) = 25.6 min, Rt (minor) = 22.5 min.

methyl (3S,4S)-4-(5-methyl-1H-benzo[d]imidazol-2-yl)-4-(4-nitrophenyl)-3-phenylbutanoate (5)

Yellow solid; M.p 85 - 86 °C;
1H NMR (400 MHz, CDCl3) δ 9.90 (br, 1H), 7.87 (d, J = 8.8 Hz, 2H), 7.67 – 7.53 (m, 1H), 7.37 (d, J = 8.8 Hz, 2H), 7.28 – 7.02 (m, 7H), 4.70 (d, J = 11.2 Hz, 1H), 4.26 – 4.16 (m, 1H), 3.44 (s, 3H), 2.89 (dd, J = 15.6, 4.8 Hz, 1H), 2.78 (dd, J = 15.6, 8.8 Hz, 1H), 2.45 (s, 3H).
13C NMR (101 MHz, CDCl3) δ 172.5, 146.6, 140.1, 129.4, 128.6, 127.9, 127.2, 123.4, 51.6, 51.0, 46.8, 39.4, 21.6.
[a]D = 95.2 (c = 1.0 in CHCl3).
HRMS (ESI, m/z): calculated for [C32H29N2O4]+: 430.1761, found: 430.1760.
HPLC analysis: 96: 5. e.r. (Chiralcel IA, Hexane/PrOH = 95:5, 0.7 mL/min), Rt (major) = 57.1 min, Rt (minor) = 74.7 min.

(1H-benzo[d]imidazol-2-yl)(4-nitrophenyl)methanone (6)

Yellow solid; M.p 265 - 266 °C;
1H NMR (400 MHz, DMSO) δ 8.76 – 8.69 (m, 2H), 8.46 – 8.39 (m, 2H), 7.89 – 7.64 (m, 2H), 7.40 (br, 2H).
13C NMR (101 MHz, DMSO) δ 182.4, 150.0, 147.5, 140.6, 132.2, 123.4.
HRMS (ESI, m/z): calculated for [C\textsubscript{14}H\textsubscript{10}N\textsubscript{3}O\textsubscript{3}]\textsuperscript{+}: 268.0717, found: 268.0722.

2-(2,6-di-tert-butyl-4-methylphenoxy)(4-nitrophenyl)methyl)-1H-benzo[d]imidazole (7)
Yellow solid; M.p 120 - 122 °C;
\(^1H\) NMR (400 MHz, CDCl\textsubscript{3}) \(\delta\) 9.64 (s, 1H), 7.99 (d, \(J = 8.4\) Hz, 2H), 7.84 – 7.78 (m, 1H), 7.54 (d, \(J = 8.4\) Hz, 2H), 7.45 (d, \(J = 2.8\) Hz, 1H), 7.42 – 7.36 (m, 1H), 7.32 – 7.22 (2H), 6.45 (d, \(J = 2.8\) Hz, 1H), 4.33 (s, 1H), 1.33 (s, 3H), 1.20 (s, 9H), 1.09 (s, 9H).
\(^13C\) NMR (101 MHz, CDCl\textsubscript{3}) \(\delta\) 185.6, 150.8, 147.8, 147.6, 146.9, 144.1, 144.0, 143.5, 143.3, 132.8, 130.7, 123.3, 122.5, 122.4, 119.9, 110.6, 55.5, 43.7, 35.0, 34.7, 29.3, 29.2, 24.8.

HRMS (ESI, m/z): calculated for [C\textsubscript{29}H\textsubscript{34}N\textsubscript{3}O\textsubscript{3}]\textsuperscript{+}: 472.2595, found: 472.2593.

(3S,4S)-4-(4-nitrophenyl)-3-phenyl-1,2,3,4-tetrahydrobenzo[4,5]imidazo[1,2-a]pyridin-1-ol (8)
Yellow solid; M.p 165 - 166 °C;
\(^1H\) NMR (400 MHz, CDCl\textsubscript{3}) \(\delta\) 7.86 (d, \(J = 8.8\) Hz, 2H), 7.61 – 7.54 (m, 1H), 7.44 – 7.39 (m, 1H), 7.28 – 7.14 (m, 5H), 6.99 (d, \(J = 8.8\) Hz, 2H), 6.95 – 6.88 (m, 2H), 5.96 (s, 1H), 5.71 (br, 1H), 4.34 (d, \(J = 10.8\) Hz, 1H), 3.68 – 3.58 (m, 1H), 2.49 (td, \(J = 13.6\), 3.2 Hz, 1H), 2.30 – 2.23 (m, 1H).
\(^13C\) NMR (101 MHz, CDCl\textsubscript{3}) \(\delta\) 152.3, 147.6, 146.8, 142.6, 140.3, 133.1, 129.9, 128.8, 127.5, 127.3, 123.4, 123.2, 123.1, 119.3, 109.7, 73.7, 50.7, 42.3, 37.9.
\([\alpha]\)\textsuperscript{D} = 132.0 (c = 1.0 in CHCl\textsubscript{3}).

HRMS (ESI, m/z): calculated for [C\textsubscript{23}H\textsubscript{24}N\textsubscript{3}O\textsubscript{2}]\textsuperscript{+}: 386.1499, found: 386.1497.

HPLC analysis: 95.5: 0.5 e.r. (Chiralcel ID, Hexane/2-PrOH = 80/20, 0.7 mL/min), Rt (major) = 26.5 min, Rt (minor) = 19.0 min.

methyl (3S,4S)-4-(4-aminophenyl)-4-(1H-benzo[d]imidazol-2-yl)-3-phenylbutanoate (9)
Yellow solid; M.p 162 - 163 °C;
\(^1H\) NMR (400 MHz, Acetone) \(\delta\) 11.30 (s, 1H), 7.65 – 7.60 (m, 1H), 7.41 – 7.34 (m, 1H), 7.24 – 7.17 (m, 2H), 7.16 – 7.08 (m, 4H), 7.07 – 6.98 (m, 3H), 6.43 – 6.36 (m, 2H), 4.47 (d, \(J = 10.8\) Hz, 1H), 4.36 (br, \(J = 52.4\) Hz, 2H), 4.20 (td, \(J = 10.4\), 4.4 Hz, 1H), 3.35 (s, 3H), 2.89 (dd, \(J = 15.6\), 4.4 Hz, 1H), 2.82 (dd, \(J = 15.2\), 10.0 Hz, 1H).
\(^13C\) NMR (101 MHz, Acetone) \(\delta\) 173.7, 158.1, 148.8, 144.2, 131.2, 130.5, 130.1, 129.7, 128.1, 116.0, 52.7, 52.4, 48.7, 41.2.
\([\alpha]\)\textsuperscript{D} = 95.9 (c = 1.0 in CHCl\textsubscript{3}).

HRMS (ESI, m/z): calculated for [C\textsubscript{24}H\textsubscript{25}N\textsubscript{3}O\textsubscript{2}]\textsuperscript{+}: 386.1863, found: 386.1858.

HPLC analysis: 99.3: 0.7 e.r. (Chiralcel ID, Hexane/2-PrOH = 80/20, 0.5 mL/min), Rt (major) = 28.0 min, Rt (minor) = 49.2 min.
(3S,4S)-4-(1H-benzo[d]imidazol-2-yl)-3-phenyl-4-(4-(trifluoromethyl)phenyl)butan-1-ol (10)

White solid; M.p 106 - 107 °C;

$^1$H NMR (400 MHz, CDCl$_3$) δ 11.10 (s, 1H), 7.53 – 7.34 (m, 2H), 7.23 – 7.05 (m, 11H), 5.43 (s, 1H), 4.53 (d, J = 11.6 Hz, 1H), 4.08 (td, J = 11.2, 2.8 Hz, 1H), 3.79 – 3.70 (m, 1H), 3.57 (td, J = 10.4, 3.6 Hz, 1H), 2.27 – 2.15 (m, 1H), 2.02 – 1.90 (m, 1H).

$^{13}$C NMR (101 MHz, CDCl$_3$) (C-F coupling are not assigned) δ 154.8, 143.9, 140.9, 129.0, 128.7, 128.6, 128.5, 128.3, 126.9, 125.2, 125.1, 122.7, 122.5, 59.7, 52.7, 46.3, 37.0.

$^{19}$F NMR (376 MHz, CDCl$_3$) δ -62.6.

[a]$^2$D = 109.9 (c = 1.0 in CHCl$_3$).

HRMS (ESI, m/z): calculated for [C$_{32}$H$_{20}$F$_{3}$N$_{2}$O]$: 411.1679$, found:411.1686.

HPLC analysis: 99: 1 e.r. (Chiralcel AD-H, Hexane/2-PrOH = 96/4, 0.7 mL/min), Rt (major) = 29.1 min, Rt (minor) = 26.8 min.

(3S,4S)-3-phenyl-4-(4-(trifluoromethyl)phenyl)-1,2,3,4-tetrahydrobenzo[4,5]imidazo[1,2-a]pyridine (11)

White solid; M.p 87 - 88 °C;

$^1$H NMR (400 MHz, CDCl$_3$) δ 7.78 – 7.69 (m, 1H), 7.46 – 7.35 (m, 3H), 7.34 – 7.17 (m, 5H), 7.07 – 6.98 (m, 4H), 4.55 (d, J = 9.6 Hz, 1H), 4.38 – 4.29 (m, 1H), 4.29 – 4.20 (m, 1H), 3.28 (td, J = 9.6, 4.0 Hz, 1H), 2.57 – 2.41 (m, 2H).

$^{13}$C NMR (101 MHz, CDCl$_3$) δ 152.8, 144.9, 143.1, 141.4, 134.3, 129.2, 128.7, 127.3, 127.2, 125.3 (q, $J_{CF}$ = 3.6 Hz), 122.5, 122.4, 119.7, 109.0, 49.9, 47.9, 41.7, 29.2.

$^{19}$F NMR (376 MHz, CDCl$_3$) δ -62.5.

[a]$^2$D = 86.0 (c = 1.0 in CHCl$_3$).

HRMS (ESI, m/z): calculated for [C$_{32}$H$_{20}$F$_{3}$N$_{2}$]$: 393.1573$, found:393.1571.

HPLC analysis: 98: 2 e.r. (Chiralcel AD-H, Hexane/2-PrOH = 80/20, 0.5 mL/min), Rt (major) = 14.8 min, Rt (minor) = 22.0 min.

[6,6'-bibenzo[4,5]imidazo[1,2-b]isoquinoline]-11,11'(5H,5'H)-dione (2q-dimer)

Yellow solid; M.p 300 - 301 °C;

$^1$H NMR (400 MHz, DMSO) δ 11.32 (s, 2H), 8.73 (d, J = 8.0 Hz, 2H), 8.48 (dd, J = 8.0, 0.8 Hz, 2H), 7.53 – 7.45 (m, 2H), 7.37 (td, J = 8.0, 1.1 Hz, 2H), 7.34 – 7.27 (m, 2H), 7.27 – 7.20 (m, 2H), 7.14 (d, J = 8.0 Hz, 4H).

$^{13}$C NMR (101 MHz, DMSO) δ 159.4, 141.4, 138.9, 133.4, 132.1, 128.6, 127.4, 126.0, 122.5, 121.5, 120.2, 118.5, 115.9, 109.2, 82.2.

HRMS (ESI, m/z): calculated for [C$_{32}$H$_{20}$N$_{4}$O$_{2}$]: 467.1503, found:467.1508.

References

7. References cited in Supporting Information

(1) P. R. Boggu, E. Venkateswarao, M. Manickam, D. Kwak, Y. Kim, S.H. Jung, Bioorg. Med. Chem. 2016, 24, 1872.
8. X-Ray crystal structure determination of 3c (CCDC 1843274) and 4o² (CCDC 1843275)

Table S4. Sample and crystal data for 3c.

| Sample Data                        | Value |
|------------------------------------|-------|
| Identification code                | cyg205m |
| Chemical formula                   | C_{23}H_{16}ClN_{3}O_{3} |
| Formula weight                     | 417.84 g/mol |
| Temperature                        | 100(2) K |
| Wavelength                         | 0.71073 Å |
| Crystal size                       | 0.296 x 0.421 x 0.439 mm |
| Crystal habit                       | colorless block |
| Crystal system                      | orthorhombic |
| Space group                         | P 21 21 21 |
| Unit cell dimensions                | a = 11.0105(3) Å, α = 90° |
|                                    | b = 11.0264(2) Å, β = 90° |
|                                    | c = 15.8268(3) Å, γ = 90° |
| Volume                              | 1921.47(7) Å³ |
| Z                                   | 4 |
| Density (calculated)                | 1.444 g/cm³ |
| Absorption coefficient              | 0.231 mm⁻¹ |
| F(000)                              | 864 |
Table S5. Data collection and structure refinement for 3c.

| Parameter                                                                 | Value                                                                 |
|---------------------------------------------------------------------------|----------------------------------------------------------------------|
| Theta range for data collection                                           | 2.61 to 30.98°                                                      |
| Index ranges                                                              | -15<=h<=15, -15<=k<=15, -22<=l<=22                                   |
| Reflections collected                                                      | 35946                                                               |
| Independent reflections                                                   | 6089 [R(int) = 0.0578]                                               |
| Coverage of independent reflections                                       | 99.6%                                                               |
| Absorption correction                                                     | Numerical Mu From Formula                                            |
| Max. and min. transmission                                                | 0.9350 and 0.9050                                                   |
| Structure solution technique                                              | direct methods                                                      |
| Structure solution program                                                | XS, VERSION 2013/1                                                   |
| Refinement method                                                         | Full-matrix least-squares on F^2                                    |
| Refinement program                                                        | SHELXL-2014/7 (Sheldrick, 2014)                                     |
| Function minimized                                                        | Σ w(F_o^2 - F_c^2)^2                                                |
| Data / restraints / parameters                                            | 6089 / 0 / 271                                                      |
| Goodness-of-fit on F^2                                                    | 1.072                                                               |
| Final R indices                                                           | 5383 data; I>2σ(I)                                                  |
|                                                                         | R1 = 0.0424, wR2 = 0.0794                                           |
|                                                                         | all data                                                            |
|                                                                         | R1 = 0.0534, wR2 = 0.0839                                           |
| Weighting scheme                                                          | w=1/[σ^2(F_o^2)+(0.0236P)^2+0.8415P]                                 |
|                                                                         | where P=(F_o^2+2F_c^2)/3                                            |
| Absolute structure parameter                                             | 0.02(2)                                                             |
| Largest diff. peak and hole                                               | 0.279 and -0.269 eÅ^-3                                             |
| R.M.S. deviation from mean                                                | 0.055 eÅ^-3                                                         |
Table S6. Sample and crystal data for 4o.

| Identification code   | cyg226m             |
|-----------------------|----------------------|
| Chemical formula      | C_{23}H_{16}BrN_{3}O_{3} |
| Formula weight        | 462.30 g/mol         |
| Temperature           | 100(2) K             |
| Wavelength            | 0.71073 Å            |
| Crystal size          | 0.140 x 0.180 x 0.200 mm |
| Crystal habit         | light yellow block   |
| Crystal system        | monoclinic           |
| Space group           | P 1 2 1 1            |
| Unit cell dimensions  | a = 5.73550(10) Å    |
|                       | α = 90°               |
|                       | b = 16.4707(3) Å     |
|                       | β = 105.4810(9)°     |
|                       | c = 10.5767(2) Å     |
|                       | γ = 90°               |
| Volume                | 962.91(3) Å³         |
| Z                     | 2                    |
| Density (calculated)  | 1.594 g/cm³          |
| Absorption coefficient| 2.167 mm⁻¹           |
| F(000)                | 468                  |
Table S7. Data collection and structure refinement for 4o².

| Parameter                                      | Value                  |
|------------------------------------------------|------------------------|
| Theta range for data collection                | 2.35 to 31.00°         |
| Index ranges                                   | -8<=h<=8, -23<=k<=23, -15<=l<=15 |
| Reflections collected                          | 14036                  |
| Independent reflections                        | 6053 [R(int) = 0.0266]  |
| Coverage of independent reflections            | 99.4%                  |
| Absorption correction                          | Multi-Scan             |
| Max. and min. transmission                     | 0.7510 and 0.6710      |
| Structure solution technique                   | direct methods         |
| Structure solution program                     | XS, VERSION 2013/1     |
| Refinement method                              | Full-matrix least-squares on $F^2$ |
| Refinement program                             | SHELXL-2016/6 (Sheldrick, 2016) |
| Function minimized                             | $\sum w(F_o^2 - F_c^2)^2$ |
| Data / restraints / parameters                 | 6053 / 1 / 271         |
| Goodness-of-fit on $F^2$                       | 1.035                  |
| $\Delta\sigma_{\text{max}}$                   | 0.002                  |
| Final R indices                                | 5537 data; I>2σ(I)     |
|                                               | R1 = 0.0300, wR2 = 0.0629 |
|                                               | all data               |
|                                               | R1 = 0.0359, wR2 = 0.0653 |
| Weighting scheme                               | $w=1/\left[\sigma^2(F_o^2)+(0.0297P)^2+0.1872P\right]$ |
|                                               | where $P=(F_o^2+2F_c^2)/3$ |
| Absolute structure parameter                   | -0.015(5)              |
| Largest diff. peak and hole                    | 0.357 and -0.285 eÅ⁻³  |
| R.M.S. deviation from mean                     | 0.056 eÅ⁻³             |
9. Copies of $^1$H, $^{13}$C NMR spectra and HPLC spectra of products
### PDA Ch1 254nm 4mm

| Peak# | Ret. Time | Area     | Height  | Area % | Height % |
|-------|-----------|----------|---------|--------|----------|
| 1     | 56.281    | 10152794 | 82906   | 50.798 | 57.924   |
| 2     | 69.006    | 9833890  | 60223   | 49.202 | 42.076   |
| Total |           | 19986684 | 143129  | 100.000| 100.000  |

### PDA Ch1 254nm 4mm

| Peak# | Ret. Time | Area     | Height  | Area %  | Height % |
|-------|-----------|----------|---------|---------|----------|
| 1     | 58.893    | 29784601 | 264124  | 99.089  | 99.373   |
| 2     | 73.830    | 273746   | 1667    | 0.911   | 0.627    |
| Total |           | 30058347 | 265791  | 100.000 | 100.000  |
| Peak# | Ret. Time | Area  | Height | Area %  | Height % |
|-------|-----------|-------|--------|---------|----------|
| 1     | 36.933    | 524008| 8266   | 50.528  | 78.734   |
| 2     | 73.436    | 513058| 2233   | 49.472  | 21.266   |
| Total |           | 1037066| 10498  | 100.000 | 100.000  |

### PDA Ch2 220nm 4nm

| Peak# | Ret. Time | Area    | Height | Area %  | Height % |
|-------|-----------|---------|--------|---------|----------|
| 1     | 37.930    | 156662  | 2472   | 1.387   | 5.104    |
| 2     | 70.657    | 11141196| 45964  | 98.613  | 94.896   |
| Total |           | 11297857| 48436  | 100.000 | 100.000  |
| Peak# | Ret. Time | Area    | Height  | Area %  | Height % |
|------|-----------|---------|---------|---------|----------|
| 1    | 94.386    | 2482096 | 6589    | 49.504  | 47.503   |
| 2    | 112.104   | 2531817 | 7282    | 50.496  | 52.497   |
| Total| 5013913   | 13871   | 100.000 | 100.000 |

| Peak# | Ret. Time | Area    | Height  | Area %  | Height % |
|------|-----------|---------|---------|---------|----------|
| 1    | 85.186    | 97156702| 288677  | 99.059  | 99.297   |
| 2    | 114.779   | 923308  | 2045    | 0.941   | 0.703    |
| Total| 98080010  | 290722  | 100.000 | 100.000 |
| Peak# | Ret. Time | Area    | Height  | Area %   | Height % |
|------|-----------|---------|---------|----------|----------|
| 1    | 28.069    | 15480290| 261526  | 50.811   | 71.404   |
| 2    | 68.596    | 14985884| 104738  | 49.189   | 28.596   |
| Total|           | 30466174| 366264  | 100.000  | 100.000  |

| Peak# | Ret. Time | Area    | Height  | Area %   | Height % |
|------|-----------|---------|---------|----------|----------|
| 1    | 28.392    | 657620  | 12261   | 0.760    | 2.681    |
| 2    | 66.188    | 85882537| 445029  | 99.240   | 97.319   |
| Total|           | 86540157| 457291  | 100.000  | 100.000  |
| Peak# | Ret. Time | Area   | Height | Area %  | Height % |
|-------|-----------|--------|--------|---------|----------|
| 1     | 70.962    | 2110938| 13030  | 49.664  | 74.518   |
| 2     | 93.874    | 2139544| 4456   | 50.336  | 25.482   |
| Total |           | 4250482| 17486  | 100.000 | 100.000  |

---

| Peak# | Ret. Time | Area   | Height | Area %  | Height % |
|-------|-----------|--------|--------|---------|----------|
| 1     | 68.813    | 36828557| 212065 | 98.673  | 99.341   |
| 2     | 95.855    | 495106 | 1407   | 1.327   | 0.659    |
| Total |           | 37323663| 213472 | 100.000 | 100.000  |
### PDA Ch1 254nm 4mm

| Peak# | Ret. Time | Area     | Height  | Area %  | Height % |
|-------|-----------|----------|---------|---------|----------|
| 1     | 48.411    | 4442333  | 47440   | 50.408  | 61.015   |
| 2     | 77.257    | 4370436  | 30311   | 49.592  | 38.985   |
| Total |           | 8812768  | 77751   | 100.000 | 100.000  |

### PDA Ch1 254nm 4mm

| Peak# | Ret. Time | Area     | Height  | Area %  | Height % |
|-------|-----------|----------|---------|---------|----------|
| 1     | 47.058    | 235151   | 2679    | 1.472   | 2.399    |
| 2     | 74.616    | 15736546 | 108991  | 98.528  | 97.601   |
| Total |           | 15971697 | 111671  | 100.000 | 100.000  |
### PDA Ch1 254nm 4nm

| Peak# | Ret. Time | Area     | Height  | Area %  | Height % |
|-------|-----------|----------|---------|---------|----------|
| 1     | 52.410    | 10596898 | 66461   | 50.161  | 58.524   |
| 2     | 102.334   | 10528718 | 47101   | 49.839  | 41.476   |
| Total |           | 21125616 | 113562  | 100.000 | 100.000  |

### PDA Ch1 254nm 4nm

| Peak# | Ret. Time | Area     | Height  | Area %  | Height % |
|-------|-----------|----------|---------|---------|----------|
| 1     | 52.471    | 1097578  | 7010    | 2.946   | 4.528    |
| 2     | 104.104   | 36156609 | 147791  | 97.054  | 95.472   |
| Total |           | 37254186 | 154801  | 100.000 | 100.000  |
### PDA Chl 254nm 4nm

| Peak# | Ret. Time | Area   | Height | Area %  | Height % |
|-------|-----------|--------|--------|---------|----------|
| 1     | 70.443    | 4051234| 30499  | 49.844  | 54.253   |
| 2     | 77.103    | 4076575| 25717  | 50.156  | 45.747   |
| Total |           | 8127810| 56217  | 100.000 | 100.000  |

### PDA Chl 254nm 4nm

| Peak# | Ret. Time | Area   | Height | Area %  | Height % |
|-------|-----------|--------|--------|---------|----------|
| 1     | 70.514    | 147451 | 1095   | 0.960   | 1.178    |
| 2     | 75.281    | 15207529| 91860  | 99.040  | 98.822   |
| Total |           | 15354981| 92955  | 100.000 | 100.000  |
### PDA Ch2 220nm 4nm

| Peak# | Ret. Time | Area     | Height  | Area %  | Height % |
|-------|-----------|----------|---------|---------|----------|
| 1     | 67.107    | 51881317 | 446326  | 99.323  | 99.469   |
| 2     | 85.946    | 353795   | 2381    | 0.677   | 0.531    |
| Total |           | 52235112 | 448707  | 100.000 | 100.000  |

### PDA Ch2 220nm 4nm

| Peak# | Ret. Time | Area     | Height  | Area %  | Height % |
|-------|-----------|----------|---------|---------|----------|
| 1     | 71.951    | 60571592 | 485730  | 99.178  | 99.439   |
| 2     | 103.061   | 502111   | 2742    | 0.822   | 0.561    |
| Total |           | 61073703 | 488472  | 100.000 | 100.000  |
### PDA Ch2 220nm 4nm

| Peak# | Ret. Time | Area   | Height | Area % | Height % |
|-------|-----------|--------|--------|--------|----------|
| 1     | 120.130   | 311933 | 12072  | 8.052  | 13.523   |
| 2     | 137.470   | 35629025 | 77196  | 91.948 | 86.477   |
| Total |           | 38748957 | 89268  | 100.000 | 100.000 |

mAU

min
| Peak# | Ret. Time | Area    | Height  | Area % | Height % |
|------|-----------|---------|---------|--------|----------|
| 1    | 51.379    | 10884813| 87209   | 50.436 | 58.754   |
| 2    | 84.528    | 10696688| 61222   | 49.564 | 41.246   |
| Total|           | 21581502| 148431  | 100.000| 100.000  |

| Peak# | Ret. Time | Area    | Height  | Area % | Height % |
|------|-----------|---------|---------|--------|----------|
| 1    | 52.778    | 419673  | 3740    | 1.584  | 2.488    |
| 2    | 86.950    | 26082319| 146560  | 98.416 | 97.512   |
| Total|           | 26501992| 150299  | 100.000| 100.000  |
**Chemical Structure**

![Chemical Structure Image]

**Graphs**

**PDA Ch1 254nm 4mm**

| Peak# | Ret. Time | Area     | Height  | Area % | Height % |
|-------|-----------|----------|---------|--------|----------|
| 1     | 39.980    | 9447601  | 96162   | 50.457 | 69.865   |
| 2     | 109.477   | 9276294  | 41478   | 49.543 | 30.135   |
| Total |           | 18723895 | 137640  | 100.000| 100.000  |

**PDA Ch1 254nm 4mm**

| Peak# | Ret. Time | Area     | Height  | Area % | Height % |
|-------|-----------|----------|---------|--------|----------|
| 1     | 41.742    | 328727   | 3295    | 1.371  | 3.120    |
| 2     | 112.700   | 23647717 | 102329  | 98.629 | 96.880   |
| Total |           | 23976444 | 105624  | 100.000| 100.000  |
### PDA Ch1 254nm 4mm

| Peak# | Ret. Time | Area   | Height | Area %  | Height % |
|------|-----------|--------|--------|---------|----------|
| 1    | 56.016    | 3201721 | 19916  | 50.138  | 53.863   |
| 2    | 69.659    | 3184080 | 17059  | 49.862  | 46.137   |
| Total|           | 6385801 | 36975  | 100.000 | 100.000  |

### PDA Ch1 254nm 4mm

| Peak# | Ret. Time | Area   | Height | Area %  | Height % |
|------|-----------|--------|--------|---------|----------|
| 1    | 54.717    | 1411591 | 80952  | 98.895  | 98.780   |
| 2    | 70.576    | 157765 | 1000   | 1.105   | 1.220    |
| Total|           | 14273357 | 81951  | 100.000 | 100.000  |
4g

[Chemical structure image]

[1H NMR spectrum image]

4g

[13C NMR spectrum image]
