Supplementary Information for:

Chiral Cyclopropylamines in the Synthesis of New Ligands; First Asymmetric Alkyl-BIAN Compounds

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General procedure for the cyclopropanation of pinene

In a 100 ml two ports Schlenk flask, equipped with a N₂ inlet, a reflux condenser and a magnetic stirring bar, a solution of α or β-pinene (14 mL), CuI (10 mg, 0.05 mmol), Pd(OAc)₂ (10 mg, 0.04 mmol) and 1,2-dichloroethane (10 mL) was heated. An equilibrated dropping funnel was placed on top of the reflux condenser. When reflux temperature was reached, a mixture of ethyl diazoacetate (5 mL) and pinene (14 mL) was added through the dropping funnel during 30 minutes. After the end of the addition, the reaction mixture was refluxed for 10 more min and then cooled. The reaction mixture was filtered through a very short column (3 cm) of basic alumina and eluted with dichloromethane to remove metal compounds. Volatiles were evaporated under vacuum to give yellow solution containing the product and excess pinene. Two of these esters have been isolated by flash chromatography on silica using ethylacetate:hexane = 0:10 to 2:8 as eluent. The reported yields refer to the amounts of the product isolated in pure form and do not correspond to the relative amounts of the isomers as obtained. GC analysis shows that 1S,2S,2'R-I and 1S,2S,2'S-I are initially formed in comparable amounts.

1R,2R,2'R-I

1800 mg, 19% yield, ¹H NMR (300 MHz, CDCl₃, 25 °C) δ = 4.11 (q, J = 7.2 Hz, 2H, O-CH₂), 2.24-2.13 (m, 2H, H7, H4), 1.98-1.77 (m, 4H, H1, 2H3, H5), 1.44 (d, J = 10.2 Hz, 1H, H7), 1.38 (dd, J₁ = 6.0, J₂ = 7.6 Hz, 1H, H2'), 1.32 (dd, J₁ = 1.8, J₂ = 9.3 Hz, 1H, H4), 1.24 (t, J =6.9, Hz, 3H, CH₂CH₃), 1.22 (s, 3H, (CH₃)9), 1.16 (dd, J₁ = 5.4, J₂ = 9.9 Hz, 1H, H3'), 1.04 (dd, J₁ = 4.5, J₂ = 8.1 Hz, 1H, H3'), 0.93 (s, 3H, (CH₃)8).
$\text{C NMR (300 MHz, CDCl}_3, 25 \degree\text{C}) \delta = 172.67\text{ (C=O), 60.43 (O-CH}_2, 43.56 \text{ (C1 or C5), 41.06 (C5 or C1), 40.68 (C6), 32.10 (C2), 28.77 (C4), 27.09 (C7), 26.96 (C9), 25.99 (C2'), 24.72 (C3), 24.59 (C3'), 21.33 (C8), 14.74 (CH}_3CH_2 \text{ ppm. M}^+, 222. C_{14}H_{22}O_2 \text{ requires M}^+, 222.}$

$\text{1R,2R,2'S-1}$

205 mg, 2% yield, $\text{H NMR (300 MHz, CDCl}_3, 25 \degree\text{C}) \delta = 4.13 \text{ (dq, } J^1 = 7.1, J^2 = 14.3 \text{ Hz, 2H, O-CH}_2, 2.22 \text{ (m, 1H, H7), 1.97-1.85 (m, 4H, H5, H3, 2H4), 1.63-1.57 (m, 1H, H3), 1.53 (d, } J = 9.9 \text{ Hz, 1H, H7), 1.37 (dd, } J^1 = 5.4, J^2 = 8.1 \text{ Hz, 1H, H2'), 1.30-1.24 (m, 4H, H3', CH}_2CH_3, 1.23-1.16 \text{ (m, 4H, H1, (CH}_3)_9, 0.97 (s, 3H, (CH}_3)_8) 0.91 \text{ (dd, } J^1 = 4.5, J^2 = 8.1 \text{ Hz, 1H, H3') ppm.}$

$\text{13C NMR (300 MHz, CDCl}_3, 25 \degree\text{C}) \delta = 172.97\text{ (C=O), 60.42 (O-CH}_2, 52.73 \text{ (C1), 41.21 (C6), 40.88 (C5), 31.41 (C2), 27.07 (C7), 26.84 (C9), 26.41 (C2'), 24.07 (C4), 23.73 (C3'), 22.05 (C8), 14.74 (CH}_3CH_2 \text{ ppm. M}^+, 222. C_{14}H_{22}O_2 \text{ requires M}^+, 222.}$

S3
1R,2R,2'R-8

1960 mg, 21% yield, $^1$H NMR (300 MHz, CDCl$_3$, 25 °C), $\delta = 4.09$ (q, $J = 7.2$ Hz, 2H, O-CH$_2$), 2.10-1.90 (m, 2H, H7, H4), 1.97 (d, $J = 4.5$ Hz, 1H, H2'), 1.93 (t, $J = 5.4$ Hz, 1H, H1), 1.72-1.63 (m, 2H, H5, H7), 1.52 (dd, $J_1 = 4.5$, $J_2 = 7.2$ Hz, 1H, H3), 1.25 (m, 6H, (CH$_3$)$_9$, CH$_2$CH$_3$), 1.15 (s, 3H, (CH$_3$)$_{10}$) 1.02-0.99 (m, 4H, H4, (CH$_3$)$_8$) ppm.

$^{13}$C NMR (300 MHz, CDCl$_3$, 25 °C) $\delta = 173.74$ (C=O), 60.40 (O-CH$_2$), 47.35 (C1), 41.25 (C5), 41.07 (C6), 31.68 (C2), 30.70 (C2'), 27.06 (C9), 27.06 (C4), 26.60 (C7), 24.18 (C3), 21.21 (C8), 21.21 (C10), 14.77 (CH$_3$CH$_2$) ppm. M$^+$, 222. C$_{14}$H$_{22}$O$_2$ requires M$^+$, 222.

**General procedure for the hydrolysis of the esters**

In a 100 ml round bottom flask with a magnetic stirring bar a mixture of the isolated crude esters (1 or 8) dissolved in methanol (20 mL) and a solution of KOH (3.5 g, 61.4 mmol) in water (10 mL) was refluxed for 24 hr. Excess pinene was extracted with toluene (2×20 mL). Then the aqueous layer was acidified with concentrated HCl then the liberated acid was extracted using dichloromethane (3×20 mL). The organic layer was dried over sodium sulfate, filtered and evaporated to give yellowish white solid.

The reaction has been performed either on one of the isolated ester isomers (1S,2S,2'R-1, 1S,2S,2'S-1 or 1S,2S,2'R-8) or, most commonly, on the crude mixture containing the excess pinene. The characterization given in the following refers to the products obtained starting from the single diastereoisomers.
Overall yield from β-pinene to the mixture of acid isomers (2) (initial reagents amounts as given previously): 5790 mg, 65% yield.
Overall yield from α-pinene to the mixture of acid isomers (7) (initial reagents amounts as given previously): 5295 mg, 59% yield.

1R,2R,2'R-2

From isolated 1R,2R,2'R-1 (1500 mg, 9.1 mmol), yield: 1320 mg, 93% yield, \(^1\)H NMR (300 MHz, CDCl\(_3\), 25 °C), 2.29-2.17 (m, 2H, H7, H4), 2.00-1.79 (m, 4H, H1, 2H3, H5), 1.50 (d, \(J = 10.2\) Hz, 1H, H7), 1.43 (dd, \(J^1 = 6.0, J^2 = 7.8\) Hz, 1H, H2'), 1.35-1.14 (m, 6H, H4, 2H3', (CH\(_3\))9), 0.97 (s, 3H, (CH\(_3\))8) ppm.

\(^{13}\)C NMR (300 MHz, CDCl\(_3\), 25 °C) \(\delta = 43.49\) (C1), 41.02 (C5), 40.76 (C6), 33.69 (C2), 28.80 (C4), 27.04 (C7), 26.98 (C9), 25.73 (C3'), 25.36 (C2'), 24.54 (C3), 21.25 (C8) ppm. Found: C, 74.01; H, 9.50%. C\(_{12}\)H\(_{18}\)O\(_2\) requires C, 74.19; H, 9.34%.
Starting from **1R,2R,2'R-8** (2000 mg, 12.1 mmol), yield: 1780 mg, 95% yield, $^1$H NMR (300 MHz, CDCl$_3$, 25 °C), 2.16-2.10 (m, 2H, H7, H4), 2.06 (d, $J = 4.5$ Hz, 1H, H2'), 2.01 (t, $J = 5.7$ Hz, 1H, H1), 1.76 (m, 1H, H7), 1.74-1.69 (m, 1H, H5), 1.63 (dd, $J_1 = 4.5$, $J_2 = 7.8$ Hz, 1H, H3), 1.31 (s, 3H, (CH$_3$)9), 1.26 (s, 3H, (CH$_3$)10), 1.07-1.04 (m, 4H, H4, (CH$_3$)8) ppm.

$^{13}$C NMR (300 MHz, CDCl$_3$, 25 °C) $\delta = 179.74$ (C=O), 47.52 (C1), 41.23 (C5), 41.18 (C6), 33.32 (C2), 30.49 (C2'), 27.14 (C4), 27.10 (C9), 26.64 (C7), 25.41 (C3), 21.25 (C8), 19.21 (C10), 22.05 ppm. Found: C, 74.01; H, 9.50%. C$_{12}$H$_{18}$O$_2$ requires C, 74.19; H, 9.34%.

**Preparation of the amines:**

In a 100 ml round bottom flask with a magnetic stirring bar, methyl chloroformate (4 mL) was added to a solution of the acids (2) (5.1 g, 26.3 mmol) in THF (40 mL) and triethylamine (10 mL) at -20 °C and this solution was stirred at this temperature for 1 hour. Then a solution of sodium azide (2.5 g, 38.4 mmol) in water (20 mL) was added portion wise at 10 °C over 10 min. Then the reaction mixture was stirred for 2 h at room temperature, the organic content was extracted using dichloromethane, then washed with NaHCO$_3$ (1×20 mL) and with water (2×20 mL), then dried with anhydrous sodium sulfate and the solvent evaporated in vacuo (CAUTION: do not heat the flask while evaporating the solvent). The organic mixture was diluted with benzene (20 mL) and refluxed for 2 h. 6 M HCl (20 mL) was added and the mixture was...
refluxed for 8 h. The reaction mixture was diluted with water then neutralized with saturated solution of NaHCO$_3$. The organic content was extracted using dichloromethane (3×30 mL), dried over sodium sulfate, filtered and evaporated.

Overall yield of (3) from the acid (2): 3043 mg, 70% yield, the isomers have been separated over silica by flash chromatography using ethyl acetate:hexane (2:8 to 5:5) containing 2% triethylamine.

The same procedure was applied to 7, but in this case the reaction was only performed on the isolated 1S,2S,2'R-7 isomer.

**1R,2S,2'R-3**

![1R,2S,2'R-3](image)

$^1$H NMR (300 MHz, CDCl$_3$, 25 °C) $\delta$ = 2.22-1.90 (m, 1H, H7), 2.02-1.70 (m, 5H, H2', H5, H3, 2H4), 1.61-1.45 (m, 3H, NH$_2$, H7), 1.27-1.17 (m, 4H, H3, (CH$_3$)9), 1.12-1.18 (m, 4H, H1, (CH$_3$)8), 0.49 (dd, $J^1$ = 4.5, $J^2$ = 7.5 Hz, 1H, H3'), 0.08 (dd, $J^1$ = 4.5, $J^2$ = 4.5 Hz, 1H, H3') ppm.

M$^+$, 165. C$_{11}$H$_{19}$N requires M$^+$, 165.

**1R,2R,2'R-3**

![1R,2R,2'R-3](image)

950 mg, 22% yield, $^1$H NMR (300 MHz, CDCl$_3$, 25 °C) $\delta$ = 2.31-2.19 (m, 1H, H7), 2.04-1.90 (m, 4H, H2', H1, H3, H4), 1.86-1.74 (m, 2H, H4, H5), 1.51 (s, 2H, NH$_2$), 1.46 (d, $J$ = 9.6 Hz, 1H, H7), 1.22 (m, 4H, H3, (CH$_3$)9), 1.00 (s, 3H, (CH$_3$)8), 0.68 (dd, $J^1$ = 5.1, $J^2$ = 7.2 Hz, 1H, H3'), 0.27 (dd, $J^1$ = 4.6, $J^2$ = 4.6 Hz, 1H, H3') ppm.
\[ \delta = 44.03 \text{ (C1)}, 41.38 \text{ (C5)}, 40.64 \text{ (C6)}, 35.56 \text{ (C2')}, 31.07 \text{ (C2)}, 28.04 \text{ (C7)}, 27.81 \text{ (C3)}, 27.09 \text{ (C9)}, 25.81 \text{ (C3')}, 24.85 \text{ (C4)}, 22.30 \text{ (C8) ppm.} \]
M\(^+\), 165.  
C\(_{11}\)H\(_{19}\)N requires M\(^+\), 165.

This isomer has been also prepared from the \(1R,2R,2'R-2\) (1200 mg, 7.3 mmol) by the same method, but again it needs chromatographic purification to separate the traces of the isomerized compounds. 752 mg, 73% yield

**1R,2R,2'S-3**

890 mg, 21% yield, \(^1\)H NMR (300 MHz, CDCl\(_3\), 25 °C) \(\delta = 2.22-1.88 \text{ (m, 6H, H7, H3, H1, 2H4, H2')}, 1.53-1.49 \text{ (m, 3H, H7, NH\(_2\))}, 1.22 \text{ (m, 1H, H3)}\), 1.17 \(\text{s, 3H, (CH\(_3\))9)}\), 1.03-1.00 \(\text{ (m, 4H, H5, (CH\(_3\))8)}\), 0.60 \(\text{ (dd, } J^1 = 5.1, J^2 = 7.5 \text{ Hz, 1H, H3')}\), 0.21 \(\text{ (dd, } J^1 = 4.7, J^2 = 4.7 \text{ Hz, 1H, H3'})\) ppm.
$^{13}$C NMR (300 MHz, CDCl$_3$, 25 ºC) $\delta = 51.33$ (C1), 41.29 (C5), 40.96 (C6), 33.76 (C2'), 27.80 (C7), 26.86 (C9), 25.28 (C2), 24.30 (C4), 23.71 (C3'), 20.82 (C8), 19.82 (C3) ppm. M$^+$, 165. C$_{11}$H$_{19}$N requires M$^+$, 165.

1R,2R,2'R-6

Overall yield starting from 1R,2R,2'R-7 (1850 g, 9.54 mmol): 850 mg, 55% yield. $^1$H NMR (300 MHz, CDCl$_3$, 25 ºC), $\delta = 2.53$ (d, $J = 3.0$ Hz, 1H, H2'), 2.11-1.96 (m, 3H, H7, NH$_2$), 1.84 (dd, $J^1 = 5.7$, $J^2 = 6.3$ Hz, 1H, H1), 1.64 (dd, $J^1 = 2.4$, $J^2 = 18.9$ Hz, 1H, H7), 1.28-0.99 (m, 11H, 2H4, (CH$_3$)8, (CH$_3$)9, (CH$_3$)10), 0.46 (dd, $J^1 = 2.7$, $J^2 = 7.8$ Hz, 1H, H3) ppm.

$^{13}$C NMR (300 MHz, CDCl$_3$, 25 ºC) $\delta = 46.71$ (C1), 41.14 (C5), 38.93 (C2'), 34.58 (C6), 31.46 (C2), 26.86 (C9), 27.00 (C7), 26.10 (C4), 24.95 (C3), 21.17 (C8), 18.84 (C10) ppm. M$^+$, 165. C$_{11}$H$_{19}$N requires M$^+$, 165.
Preparation of picrates

In a side port flask, a saturated solution of picric acid in a mixture of equal amounts of water and methanol (5 mL) was added to chiral amines 1R,2R,2'R-3 or 1R,2R,2'S-3 (180 mg, 1.1 mmol) dissolved in methanol (2 mL). The mixture was warmed on a water bath for 15 min. The products separated on cooling were crystallized from water/methanol.

Chiral BIAN synthesis:

A-By transimination:

In a Schlenk flask, 3,5-(CF₃)₂C₆H₃-BIANZnCl₂ (150 mg, 0.20 mmol) and 1R,2R,2'S-3 (82.5 mg, 0.5 mmol) were suspended in methanol (20 mL). The mixture was stirred under nitrogen at room temperature for 16 h, during which time a yellow solid was formed. The reaction mixture was filtered and washed with methanol. The single crystal was grown by diffusion of hexane into a chloroform solution of the complex.

1R,2R,2'S-4-ZnCl₂

Yield: 25 mg, 20% yield, ¹H NMR (300 MHz, CDCl₃, 25 °C) δ = 8.24 (d, J = 8.4 Hz, 2H, Hp), 8.14 (d, J = 7.2 Hz, 2H, Ho), 8.24 (t, J = 7.5 Hz, 2H, Hm), 3.34 (dd, J₁ = 4.2, J₂ = 6.6 Hz, 2H, H2'), 2.43-2.36 (m, 2H, H7), 2.02-1.90 (m, 8H, H5, H3', 2H4), 1.75-1.56 (m, 8H, H1, H3', 2H3), 1.42 (d, J = 9.9 Hz, 2H, H7), 1.21 (s, 6H, (CH₃)9), 1.10 (s, 6H, (CH₃)8) ppm.
B-By direct amination reaction:

In a side port flask, acenaphthenequinone (60 mg, 0.33 mmol), 1R,2R,2'R-3, 1R,2R,2'S-3 (150 mg, 0.91 mmol) and titanium isopropoxide (0.3 mL, 1.0 mmol) were suspended in dry THF (20 mL). The reaction mixture was stirred at room temperature for 24 hr then evaporated in vacuo. The residue was suspended in CH\textsubscript{2}Cl\textsubscript{2} (4mL) and vigorously stirred with a solution of K\textsubscript{2}C\textsubscript{2}O\textsubscript{4} (0.99 mmol) in water (5mL). This removed most of the bound titanium, but some was apparently still present. The ligand was further purified by passing it over a pad of silica gel using ethylacetate:hexane = 2:8 and 2% triethylamine as eluent.

Yield: 126 mg, 80% yield, \textsuperscript{1}H NMR (300 MHz, C\textsubscript{6}D\textsubscript{6}, 25 \textdegree C) \(\delta = 8.06 \) (d, \(J = 6.9\) Hz, 1H, Ho'), 7.99 (d, \(J = 7.2\) Hz, 1H, Ho), 7.63 (d, \(J = 8.1\) Hz, 1H, Hp), 7.58 (d, \(J = 8.1\) Hz, 1H, Hp'), 7.39 (t,
$J = 8.1$ Hz, 1H, Hm'), 7.34 (t, $J = 8.1$ Hz, 1H, Hm), 5.64 (dd, $J' = 3.9$, $J^2 = 7.2$ Hz, 1H, H2' syn), 3.68 (dd, $J' = 3.9$, $J^2 = 7.5$ Hz, 1H, H2' anti), 2.84 (t, $J = 5.4$ Hz, 1H), 2.64-2.39 (m, 4H), 2.23-1.89 (m, 6H), 1.75 (d, $J = 9.9$ Hz, 1H), 1.68-1.18 (m, 20H) ppm.

$^1$H NMR (300 MHz, C$_6$D$_6$, 25 °C) δ = 8.15 (d, $J = 6.9$ Hz, 1H, Ho'), 7.95 (d, $J = 7.2$ Hz, 1H, Ho), 7.56 (d, $J = 8.4$ Hz, 1H, Hp), 7.53 (d, $J = 8.1$ Hz, 1H, Hp'), 7.47 (t, $J = 8.1$ Hz, 1H, Hm'), 7.37 (t, $J = 8.1$ Hz, 1H, Hm), 5.63 (dd, $J' = 3.9$, $J^2 = 6.6$ Hz, 1H, H2' syn), 3.85 (dd, $J' = 3.6$, $J^2 = 7.2$ Hz, 1H, H2' anti), 2.78-2.67 (m, 1H), 2.53-1.99 (m, 11H), 1.76 (d, $J = 9.9$ Hz, 1H), 1.68-1.47 (m, 5H), 1.40-1.17 (m, 14H) ppm.

Yield: 113 mg, 72% yield, $^1$H NMR (300 MHz, C$_6$D$_6$, 25 °C) δ = 8.15 (d, $J = 6.9$ Hz, 1H, Ho'), 7.95 (d, $J = 7.2$ Hz, 1H, Ho), 7.56 (d, $J = 8.4$ Hz, 1H, Hp), 7.53 (d, $J = 8.1$ Hz, 1H, Hp'), 7.47 (t, $J = 8.1$ Hz, 1H, Hm'), 7.37 (t, $J = 8.1$ Hz, 1H, Hm), 5.63 (dd, $J' = 3.9$, $J^2 = 6.6$ Hz, 1H, H2' syn), 3.85 (dd, $J' = 3.6$, $J^2 = 7.2$ Hz, 1H, H2' anti), 2.78-2.67 (m, 1H), 2.53-1.99 (m, 11H), 1.76 (d, $J = 9.9$ Hz, 1H), 1.68-1.47 (m, 5H), 1.40-1.17 (m, 14H) ppm.

1R,2R,2'S-4

$^1$H NMR (300 MHz, C$_6$D$_6$, 25 °C) δ = 8.15 (d, $J = 6.9$ Hz, 1H, Ho'), 7.95 (d, $J = 7.2$ Hz, 1H, Ho), 7.56 (d, $J = 8.4$ Hz, 1H, Hp), 7.53 (d, $J = 8.1$ Hz, 1H, Hp'), 7.47 (t, $J = 8.1$ Hz, 1H, Hm'), 7.37 (t, $J = 8.1$ Hz, 1H, Hm), 5.63 (dd, $J' = 3.9$, $J^2 = 6.6$ Hz, 1H, H2' syn), 3.85 (dd, $J' = 3.6$, $J^2 = 7.2$ Hz, 1H, H2' anti), 2.78-2.67 (m, 1H), 2.53-1.99 (m, 11H), 1.76 (d, $J = 9.9$ Hz, 1H), 1.68-1.47 (m, 5H), 1.40-1.17 (m, 14H) ppm.
\[ ^{13}\text{C} \text{NMR} \ (300 \text{ MHz, C}_6\text{D}_6, \ 25 \ ^\circ\text{C}) \ \delta = 160.36, 158.63, 138.88, 137.87, 132.34, 131.52, 128.78 \ (Cm), 131.38(Cm', Cm'), 126.49 \ (Cm), 122.84 \ (Cp), 117.98 \ (Co), 52.27, 51.38, 46.22, 44.74, 41.69, 41.62, 41.47, 34.10, 32.36, 30.52, 28.79, 28.14, 27.71, 27.08, 26.95, 24.91, 24.59, 23.21, 23.14, 22.29, 22.15 \ \text{ppm}. \text{ Found: C, 85.73; H, 8.45; N, 5.60\%}. \ \text{C}_{34}\text{H}_{40}\text{N}_{2} \text{ requires C, 85.67; H, 8.46; N, 5.88\%.}

\text{Chiral DAB synthesis:}

\text{In a Schlenk flask, glyoxal (97.5 mg, 1.8 mmol) and 1R,2R,2'R-3 or 1R,2R,2'S-3 (550 mg, 3.4 mmol) were dissolved in MeOH (10 mL) at room temperature. The mixture was then stirred for 3 h at 70 \ ^\circ\text{C}, the reaction mixture was evaporated to dryness. The crude material was purified by short flash column chromatography using dichloromethane:hexane = 3:7}

\text{1R,2R,2'R-5}

\text{Yield: 450 mg, 76\% yield, } ^{1}\text{H NMR (400 MHz, CDCl}_3, \ 25 \ ^\circ\text{C}), 8.00 (s, 2H, CH=N), 2.56 (dd, } J_1' = 4.0, J_2' = 7.2 \text{ Hz, 2H, H2'), 2.23-2.19 \text{ (m, 2H, H7), 2.01-1.94 \text{ (m, 8H, H3, H1, H4, H5), 1.87-1.80 \text{ (m, 2H, H4), 1.34-1.24 \text{ (m, 8H, H3, (CH}_3)_9), 1.20 \text{ (dd, 2H, } J_1' = 5.2, J_2' = 7.2 \text{ Hz, H3'), 1.14-1.11 \text{ (m, 2H, H3'), 1.03 (s, 6H, (CH}_3)_8 \text{ ppm.}}

S13
\(^{13}\)C NMR (400 MHz, CDCl\(_3\), 25 °C) \(\delta = 159.24\) (C=N), 53.42 (C2'), 44.98 (C1), 40.56 (C5) 40.41 (C6), 31.43 (C2), 28.11 (C3'), 27.51 (C3), 26.99 (C7), 26.56 (C9), 24.37 (C4), 21.83 (C8) ppm. Found: C, 81.89; H, 10.10; N, 7.80%. C\(_{24}\)H\(_{36}\)N\(_2\) requires C, 81.76; H, 10.29; N, 7.95%.

**1R,2R,2'S-5**

Yield: 467 mg, 79% yield, \(^1\)H NMR (300 MHz, CDCl\(_3\), 25 °C), 8.04 (s, 2H, CH=N), 2.57 (dd, \(J' = 3.9, J = 6.9\) Hz, 2H, H2'), 2.23-2.08 (m, 4H, H7, H4), 2.04-1.78 (m, 8H, H5, H3', 2H3), 1.52 (dd, \(J' = 9.0, J = 14.7\) Hz, 2H, H4), 1.43 (d, \(J = 9.9\) Hz, 2H, H7), 1.26-1.15 (m, 8H, H1, (CH\(_3\))9), 1.13-1.06 (m, 2H, H3'), 1.03 (s, 6H, (CH\(_3\))8) ppm.

\(^{13}\)C NMR (300 MHz, CDCl\(_3\), 25 °C) \(\delta = 159.98\) (C=N), 52.25 (C2'), 51.44 (C1), 41.24 (C6), 41.16 (C5), 31.38 (C2), 27.45 (C3'), 27.40 (C7), 26.90 (C9), 24.43 (C3), 22.46 (C4), 22.21 (C8) ppm. Found: C, 81.89; H, 10.10; N, 7.80%. C\(_{24}\)H\(_{36}\)N\(_2\) requires C, 81.76; H, 10.29; N, 7.95%.

S14
X-ray crystal structure determination

The structure of the two main isomers 1R,2R,2'R-3 and 1R,2R,2'S-3 was confirmed by X-ray crystallography of their picrate salts. We also measured 1R,2R,2'R-7 and the ZnCl$_2$(1R,2R,2'S-4) complex. All single crystals were mounted in air on glass fibers and measured on a Bruker APEXII CCD diffractometer, using 50 kV and 30 mA generator setting and Mo Kα radiation (0.5 mm collimated).

The raw integrated intensities of all datasets were corrected for crystal anisotropies by SADABS (Sheldrick, G. M. SADABS v2.10, University of Göttingen, Germany, 2003) and a spherical absorption correction was then applied. Structures were solved using direct methods with SIR97 (Altomare, A.; Burla, M.C.; Camalli, M.; Cascarano, G.L.; Giacovazzo, C.; Guagliardi, A.; Moliterni, A.G.G.; Polidori, G.; Spagna R. J. Appl. Cryst. 1999, 32, 115-119.) and refined based on full-matrix least squares on $F^2$ with SHELX97 (Sheldrick, G. M. SHELX97-Program for the refinement of Crystal Structure., University of Göttingen, Germany, 1997), within the WINGX package (Farrugia, L. J. J. Appl. Cryst., 1999, 32, 837-838).

![X-ray structure of the picrate salt of 1R,2R,2'R-3.](image)

**Figure S1** X-ray structure of the picrate salt of 1R,2R,2'R-3. (note only one of the four ionic pairs present in the asymmetric unit is shown). Thermal ellipsoids are drawn at 30% probability level.
Crystal data for (1R,2R,2'R-3)(picrate): C_{17}H_{22}N_{4}O_{7}, M=394.39; a = 14.079(4) Å, b = 12.207(3) Å; c = 22.502(6) Å, α, γ = 90°, β = 102.181(7) °; V = 3780.2(17) Å³; Z = 4; space group P2_1, monoclinic. μ = 0.109 mm⁻¹. T = 293(2) K Measured/independent reflections: 22668/9221 ; R_{int} = 0.0471; R_σ = 0.0828; R_1 (I > 2σ(I)): 0.0685; wR_2(I > 2σ(I)): 0.1712; n° parameters: 986 (6 restraints); θ_{max} = 22. The scarce diffraction at high angle did not allow including higher resolution reflections (not measurable).

Figure S2 X-ray structure of the picrate salt of 1R,2R,2'S-3.

Crystal data for (1R,2R,2'S-3)(picrate): C_{17}H_{22}N_{4}O_{7}, M=394.39; a = 7.033(3) Å, b = 11.108(4) Å; c = 24.782(9) Å, α, β, γ = 90°; V = 1936.0(13) Å³; Z = 4; space group P2_12_1_2_1, orthorhombic. μ = 0.106 mm⁻¹. T = 298(2) K Measured/independent reflections: 15810/2783 ; R_{int} = 0.0465; R_σ = 0.0350; R_1 (I > 2σ(I)): 0.0774; wR_2(I > 2σ(I)): 0.1969; n° parameters: 253; θ_{max} = 23.5.
Figure S3 X-ray structure of the of 1R,2R,2'R-7. All four molecules in the asymmetric unit are shown. For sake of clarity only few atoms are labeled.

Crystal data for 1R,2R,2'R-7 C_{12}H_{18}O_{2}, M= 194.26; a = 7.419(2) Å, b = 20.487(6) Å; c = 28.422(8) Å, α, β, γ = 90°; V = 4320(2) Å³; Z = 4; space group P2_12_12_1, orthorhombic. μ = 0.079 mm⁻¹. T = 298(2) K Measured/independent reflections: 29013/8298 ; R_{int} = 0.0416; R_{σ} = 0.0457; R_1 (I > 2σ(I)): 0.0505; wR_2(I > 2σ(I)): 0.1129; n° parameters: 505; θ_{max} = 26.5.

Figure S4 Two views of the X-ray structure of ZnCl₂(1R,2R,2'S-4).
Crystal data for ZnCl$_2$(1R,2R,2'S-4): C$_{34}$H$_{40}$Cl$_2$N$_2$Zn, M=612.97; a, b = 11.573(2) Å; c = 19.653(7) Å, α, β = 90°, γ = 120°; V = 2279.6(1) Å$^3$; Z = 3; space group P3$_2$1, trigonal. μ = 1.010 mm$^{-1}$. T = 298(2) K Measured/independent reflections: 11007/1577 ; $R_{int}$ = 0.1616; $R_σ$ = 0.1527; $R_1$ (I > 2σ(I)): 0.0519; wR$_2$(I > 2σ(I)): 0.0798; n° parameters: 178; θ$\text{max}$ = 20. The scarce diffraction at high angle did not allow to include higher resolution reflections (not measurable).

Calculations of the relative stability of the amines and of the ZnCl$_2$ complex

Figure S5 Relative energy of the different isomers of amine 3
The relative electronic energy of the zinc chloride complexes of the chiral BIAN of the isomers 1R,2R,2’S-4 and 1R,2R,2’R-4 ligands was calculated at B3LYP/LanL2DZ level. The tilting angle between the Zn, Cl, Cl plane and the average Zn, N, C, C, N was calculated to be 84.12° for 1R,2R,2’S-4 (84.32(10) from the experimental X-ray determination) and 76.60° for 1R,2R,2’R-4.

Figure S5a  Calculated structure for ZnCl₂(1R,2R,2’S-4) (relative energy + 0.0 Kcal/mol)

Figure S5b  Calculated structure for ZnCl₂(1R,2R,2’R-4) (relative energy 3.7 Kcal/mol)
$^1$HNMR of 1R,2R,2'R-1
COSY of 1R,2R,2'R-1
HSQC of 1R,2R,2'R-1
APT of 1R,2R,2'R-1
$^1$HNMR of $^{1}$H$_{R2}$R$_2$S-1
COSY of 1R,2R,2'S-1
HSQC of 1R,2R,2'S-1
APT of 1R,2R,2'S-1
$^1$HNMR of 1R,2R,2'R-2
COSY of 1R,2R,2'R-2
HSQC of 1R,2R,2'R-2
APT of 1R,2R,2'R-2
$^1$HNMR of 1R,2R,2'R-3
COSY of 1R,2R,2'R-3
HSQC of 1R,2R,2'R-3
APT of 1R,2R,2'R-3
$^1$HNMR of 1R,2R,2'S-3
COSY of 1R,2R,2'S-3
HSQC of 1R,2R,2'S-3
APT of 1R,2R,2'S-3
$^1$HNMR of 1R,2R,2'R-4
COSY of 1R,2R,2'R-4
HSQC of 1R,2R,2'R-4
APT of 1R,2R,2′R-4
$^1$HNMR of \textbf{1R,2R,2'S-4}
COSY of 1R,2R,2'S-4
HSQC COSY of 1R,2R,2'S-4
APT of 1R,2R,2'S-4
$^1$HNMR of $1\text{R,2R,2'S-4-ZnCl}_2$
COSY of 1R,2R,2'S-4-ZnCl₂
HSQC of 1R,2R,2'S-4-ZnCl₂
APT of 1R,2R,2'S-4-ZnCl₂
$^1$HNMR of 1R,2R,2'R-5
COSY of 1R,2R,2'R-5
HSQC of 1R,2R,2'R-5
APT of 1R,2R,2'R-5
^1H NMR of 1R,2R,2'S-5
COSY of 1R,2R,2'S-5
HSQC of 1R,2R,2'S-5
APT of 1R,2R,2'S-5
\(^1\)HNMR of 1R,2R,2'R-8
COSY of 1R,2R,2'R-8
HSQC of 1R,2R,2'R-8
HSQC of 1R,2R,2'R-8
$^1$HNMR of 1R,2R,2'R-7
COSY of 1R,2R,2'R-7
HSQC of 1R,2R,2'R-7
APT of 1R,2R,2'R-7
$^1$HNMR of 1R,2R,2'R-6
COSY of 1R,2R,2'R-6
HSQC of 1R,2R,2'R-6
APT of 1R,2R,2'R-6