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Asymmetric Copper(II)-Catalysed Nitroaldol (Henry) Reactions Utilizing a Chiral C_1-Symmetric Dinitrogen Ligand

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A series of stable chiral C_1-symmetric dinitrogen ligands were conveniently synthesized in high yields by condensation of chiral amines [(–)-*exo*-bornylamine or (+)-(1*S*,2*S*,5*R*)-menthylamine] with various substituted imidazolecarbaldehydes. With the assistance of base, the ligand **L1** in combination with $CuCl_2{\cdot}2H_2O$ (2.5 mol-% or 5.0 mol-%) can efficiently promote nitroaldol (Henry) reactions between a variety of aldehydes and nitromethane. Both aromatic and aliphatic aldehydes were tolerated in our catalytic system, affording the expected nitroalcohol products in high yields (up to 97 %) and with good enantioselectivities (up to 96 %) under mild reaction conditions.

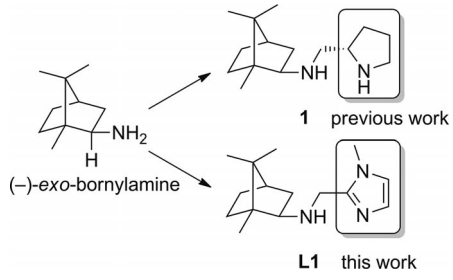
Introduction

The design and synthesis of new chiral ligands play an enduring significant role in asymmetric catalysis.[1] Commercially available chiral amino alcohols derived from amino acids and diamines such as 1,2-cyclohexanediamine and 1,2-diphenylethylenediamine are the most widely used chiral materials for the synthesis of the well-known bis(oxazoline)-type (BOX-type)[2] and salen-type[3] ligands, which are two privileged kinds of C_2-symmetric ligands. Both enjoy extensive utilization in various metal-catalysed enantioselective reactions because of their excellent asymmetric induction abilities.[2,3]

At the same time, C_1-symmetric ligands represent another attractive option, because their structures and electronic properties are more readily adjustable.[4] However, they have been much less focused on until very recently. In general, there are three strategies for the construction of C_1-symmetric ligands: desymmetrization of C_2-symmetric ligands,[5] derivation from natural products[6] and combination of two or more different chiral or achiral parts.[7]

The asymmetric nitroaldol (Henry) reaction, an important methodology for atom-economical construction of carbon–carbon bonds, can generate functionalized β-nitro alcohol adducts that can be transformed into valuable optically active building blocks.[8] Many attempts to develop catalytic asymmetric nitroaldol reaction variants have therefore been made.[9] Out of the great number of metal-based catalysts, copper salts have become the most widely used examples, because copper is a relatively cheap and low-toxicity metal with excellent chelating properties.[10] Although steady progress has been achieved, there is still room for development of new efficient, cheap and easily obtained ligands in this catalytic enantioselective reaction.

Very recently we synthesized (–)-*exo*-bornylamine from D-camphor and applied it in the construction of the new chiral secondary diamine **1** (Scheme 1) as a potential catalyst for enantioselective Henry reactions.[11] As part of our ongoing work on the synthesis and application of C_1-symmetric ligands in asymmetric catalysis, and also in view of the strong coordinating ability of the imidazole group and its successful application in ligand design,[12] we tried to introduce the achiral imidazole group into the ligand scaffold to replace the chiral pyrrolidine ring. In this work we describe another new kind of C_1-symmetric chiral dinitrogen ligand and its successful application in copper-catalysed asymmetric nitroaldol (Henry) reactions.



Scheme 1. Two chiral C_1-symmetric dinitrogen ligands.

Results and Discussion

A series of chiral C_1-symmetric dinitrogen ligands were synthesized from various substituted imidazolecarbaldehydes by the pathways outlined in Scheme 2. Initially, a Schiff base **2** was obtained by condensation of a chiral

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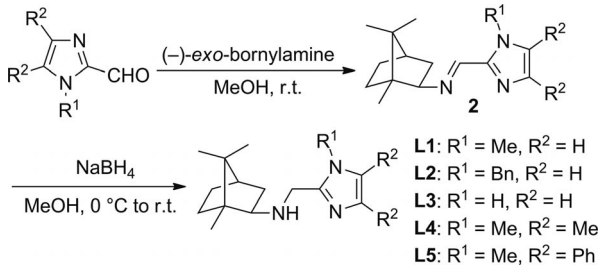
amine [(–)-*exo*-bornylamine or (+)-(1*S*,2*S*,5*R*)-menthylamine] with an imidazolecarbaldehyde (1 equiv.) in methanol at ambient temperature over several hours. Subsequently, the Schiff base **2** could be either separated or reduced in situ with sodium borohydride ($NaBH_4$). A small library of C_1-symmetric chiral dinitrogen ligands (**L1**–**L9**) was thus constructed in a convenient manner through two simple steps under mild reaction conditions in high yields (the total yield for **L1** was 86%). Moreover, most of the chiral ligands are solid and can be stored at room temperature for several months without any special precautions against moisture or air and do not lose any catalytic performance. In the light of our previous work,[11] the set of ligands was evaluated in copper-catalysed enantioselective nitroaldol reactions between aldehydes and nitromethane (Figure 1).



Scheme 2. Synthesis of chiral C_1-symmetric dinitrogen ligands.

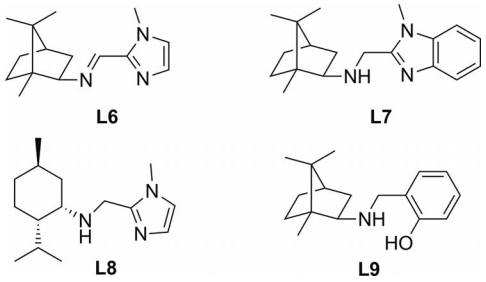
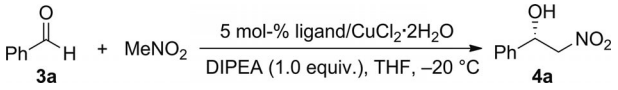


Figure 1. Other chiral C_1-symmetric ligands.

As a result of previously optimized reaction parameters,[11] copper chloride dihydrate ($CuCl_2{\cdot}2H_2O$) was chosen for screening of the new chiral ligands with diisopropylethylamine (DIPEA) as the additive base in THF at –20 °C to catalyse the model reaction between benzaldehyde (**3a**) and nitromethane. The results are listed in Table 1. Of the ligands **L1**–**L9**, **L1** was found to be the best for this reaction, affording the expected nitroaldol product in 95% yield with 92% *ee* after 15 h (Table 1, Entry 1). The ligand **L2**, with a bulkier benzyl group at the N-1 position in the imidazole ring (R^1 substituent), produced a similar enantioselectivity, but with a lower yield (Table 1, Entry 2). On the other hand, when the substituent on the N-1 position was changed from a methyl group to a smaller hydrogen atom (ligand **L3**), an inferior result was also observed (Table 1, Entry 3). After investigation of the effect of the substituent R^1 group, we continued to study the effect of the R^2 substituent. The ligand **L4**, bearing methyl groups at its C-4 and C-5 positions (R^2 substituent), gave both good yield and *ee* value, whereas **L5** could only afford a moderate yield with much lower enantiomeric excess, probably due to its poor solubility in the THF solvent (Table 1, Entries 4 and 5). All these results clearly indicate that the nature of the substituent on the imidazole ring is one of the pivotal factors governing the efficiency of the ligand. A surprising result is that the imine ligand **L6** was not able to promote the reaction at all (Table 1, Entry 6). If the *N*-methylimidazole was re-

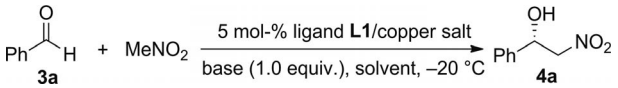
Table 1. Ligand screening.



Entry[a]	Ligand	Time [h]	Yield [%][b]	*ee* [%][c]
1	**L1**	15	95	92
2	**L2**	15	80	90
3	**L3**	40	70	83
4	**L4**	15	85	86
5	**L5**	40	52	25
6	**L6**	40	trace	n.d.[d]
7	**L7**	15	94	88
8	**L8**	15	78	–48
9	**L9**	40	trace	n.d.[d]

[a] Reactions were carried out on a 0.5 mmol scale (benzaldehyde) with nitromethane (10 equiv.) in THF (2.0 mL) in the presence of ligand (5 mol-%), $CuCl_2{\cdot}H_2O$ (5 mol-%), and DIPEA (1.0 equiv.) at –20 °C for the specified times. [b] Isolated yield. [c] Enantiomeric excesses were determined by HPLC analysis on a Chiracel OD-H column; the absolute configuration was established as (*S*) by comparison with literature data. [d] Not determined.

Table 2. Optimization of reaction conditions.



Entry[a]	Copper salt	Solvent	Base	Yield [%][b]	*ee* [%][c]
1	$CuCl_2{\cdot}2H_2O$	THF	DIPEA	95	92
2[d]	$Cu(OAc)_2{\cdot}H_2O$	THF	DIPEA	65	94
3	$CuBr_2$	THF	DIPEA	83	89
4	CuBr	THF	DIPEA	85	87
5	CuCl	THF	DIPEA	78	90
6	$CuCl_2{\cdot}2H_2O$	Et_2O	DIPEA	90	91
7	$CuCl_2{\cdot}2H_2O$	iPr_2O	DIPEA	93	90
8	$CuCl_2{\cdot}2H_2O$	DMF	DIPEA	92	91
9	$CuCl_2{\cdot}2H_2O$	THF	TEA	92	92
10	$CuCl_2{\cdot}2H_2O$	THF	TBA	90	92
11[e]	$CuCl_2{\cdot}2H_2O$	THF	DIPEA	96	92
12[f]	$CuCl_2{\cdot}2H_2O$	THF	DIPEA	78	95
13[g]	$CuCl_2{\cdot}2H_2O$	THF	DIPEA	94	95

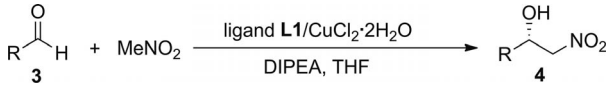
[a] Reactions were carried out with benzaldehyde (0.5 mmol scale) and nitromethane (10 equiv.) in a mixture of solvent (2.0 mL), ligand **L1** (5 mol-%) and copper salt (5 mol-%) in the presence of base additive (1.0 equiv.) at –20 °C for 15 h. [b] Isolated yields. [c] Enantiomeric excesses were determined by HPLC analysis. [d] The reaction time was prolonged to 40 h. [e] 2.5 mol-% of catalyst and 0.1 equiv. of DIPEA were used, and the reaction time was prolonged to 20 h. [f] 2.5 mol-% of catalyst and 1.0 equiv. of DIPEA were used, and the reaction was carried out at –40 °C over 40 h. [g] 5.0 mol-% of catalyst and 1.0 equiv. of DIPEA were used, and the reaction was carried out at –40 °C over 40 h.

placed by *N*-methylbenzimidazole (ligand **L7**) the reaction rate was not affected, but a slight decrease in the *ee* value was observed (Table 1, Entry 7).

(+)-(1*S*,2*S*,5*R*)-Menthylamine was then used in place of (–)-*exo*-bornylamine (ligand **L8**), and the product with the opposite (*R*) configuration was obtained with lower enantioselectivity (Table 1, Entry 8). In addition, the salicylaldehyde-derived ligand **L9** was also tested, but was unable to catalyse the reaction, probably due to the poor coordinating ability of the oxygen atom to the copper centre (Table 1, Entry 9).

Having achieved the preliminary results, we continued to carry out the optimization of the reaction conditions systematically. The results are given in Table 2. Firstly, a series of copper salts were evaluated in combination with the chiral ligand **L1** and DIPEA in THF at –20 °C over 15 h (Table 2, Entries 1–5).[13] Notably, $Cu(OAc)_2{\cdot}H_2O$ gave the highest *ee*, of 94%, but the reaction would not go to completion even when the reaction time was prolonged to 40 h (Table 2, Entry 2). As well as divalent copper salts, monovalent copper salts such as CuCl and CuBr could also promote the reaction with satisfactory enantioselectivities and yields (Table 2, Entries 4 and 5). In terms of yield and enantioselectivity, though, $CuCl_2{\cdot}2H_2O$ still proved to be the preferred catalyst (Table 2, Entry 1). Next, a group of solvents were investigated (Table 2, Entries 6–8), with THF giving the highest *ee* value of 92%. Several ether solvents, as well as DMF, afforded similar results.[14] Some organic bases were then tested as additives, and DIPEA turned out to be the best choice, although TEA and TBA induced almost the same result (Table 2, Entries 9 and 10).[15] Lastly, the influence of the amounts of catalyst and base additive, as well as of reaction temperature, on the course of asymmetric catalysis process were also assessed. It was found that 2.5 mol-% of the catalyst in combination with DIPEA (0.1 equiv.) were sufficient for the reaction to go smoothly

Table 3. Enantioselective nitroaldol reactions between aldehydes and nitromethane.



Entry[a]	Aldehyde: R	Cat. [mol-%]/DIPEA [equiv.]	Temp. [°C]	Time [h]	Yield [%][b]	*ee* [%][c]
1	Ph (**3a**)	2.5/0.1	–20	20	96	92
		5.0/1.0	–40	35	94	95
2	2-$O_2NC_6H_4$ (**3b**)	2.5/0.1	–20	20	95	89
		5.0/1.0	–40	30	92	90
3	3-$O_2NC_6H_4$ (**3c**)	2.5/0.1	–20	15	97	92
		5.0/1.0	–40	25	95	94
4	4-$O_2NC_6H_4$ (**3d**)	2.5/0.1	–20	20	94	91
		5.0/1.0	–40	30	93	94
5	4-ClC_6H_4 (**3e**)	2.5/0.1	–20	20	97	92
		5.0/1.0	–40	35	92	95
6	4-FC_6H_4 (**3f**)	2.5/0.1	–20	20	95	93
		5.0/1.0	–40	30	93	96
7	4-MeC_6H_4 (**3g**)	2.5/0.1	–20	20	94	93
		5.0/1.0	–40	35	91	95
8	4-$MeOC_6H_4$ (**3h**)	2.5/0.1	–20	25	95	90
		5.0/1.0	–40	40	92	95
9	2,4-$Cl_2C_6H_3$ (**3i**)	2.5/0.1	–20	20	96	89
		5.0/1.0	–40	40	91	90
10	3,4-$(MeO)_2C_6H_3$ (**3j**)	5.0/1.0	–40	60	89	94
11	1-naphthyl (**3k**)	2.5/0.1	–20	25	93	92
		5.0/1.0	–40	40	90	94
12	2-furyl (**3l**)	2.5/0.1	–20	25	91	92
		5.0/1.0	–40	40	90	96
13	2-thiophenyl (**3m**)	2.5/0.1	–20	25	92	91
		5.0/1.0	–40	40	88	94
14	CH_3CH_2 (**3n**)	2.5/1.0	4	20	93	89
		2.5/1.0	–20	40	88	91
15	$CH_3(CH_2)_2CH_2$ (**3o**)	2.5/1.0	4	20	95	91
		2.5/1.0	–20	40	94	93
16	$(CH_3)_2CHCH_2$ (**3p**)	2.5/1.0	4	20	94	91
		2.5/1.0	–20	40	91	92
17	$(CH_3)_3C$ (**3q**)	2.5/1.0	4	40	85	90
		2.5/1.0	–20	80	82	92
18	$CH_3(CH_2)_4CH_2$ (**3r**)	2.5/1.0	4	20	96	90
		2.5/1.0	–20	40	94	91
19	$Ph(CH_2)_2$ (**3s**)	2.5/1.0	–20	40	92	91

[a] Reactions were carried out with the aldehydes (0.5 mmol scale) and nitromethane (10 equiv.) in mixtures of THF (2.0 mL) and either catalyst (2.5 mol-%) in the presence of DIPEA (0.1 equiv.) at –20 °C or catalyst (5.0 mol-%) in the presence of DIPEA (1.0 equiv.) at –40 °C for the specified times. [b] Isolated yields. [c] Enantiomeric excesses were determined by HPLC analysis.

to completion over 20 h with 96% yield and 92% *ee* (Table 2, Entry 11). When the reaction temperature was lowered to –40 °C, however, 5 mol-% of the catalyst and 1.0 equiv. of DIPEA were necessary for satisfactory yield and enantioselectivity (Table 2, Entries 13 vs. 12).

With the optimized reaction conditions to hand the substrate scope was explored. The results are summarized in Table 3. In general, the steric hindrance and electronic nature of the substituent on the aromatic ring do not exert any obvious influence on the asymmetric catalytic progress. The expected products were obtained above 94% *ee* in most cases when the reactions were performed at –40 °C. Only the 2-substituted aromatic aldehydes produced slight decreases in the enantioselectivity (Table 3, Entries 2 and 9). Heteroaromatic aldehydes were also able to provide the Henry adducts with high enantioselectivitives (Table 3, Entries 12 and 13). The evaluation of our catalyst system was then extended to aliphatic aldehydes (Table 3, Entries 14–19). We were delighted to find that both unbranched (Table 3, Entries 14, 15, 18 and 19) and branched aliphatic aldehydes (Table 3, Entries 16 and 17) were suitable substrates, providing high yields (up to 96%) and good enantioselectivitives (up to 93% *ee*). It is noteworthy that neither the carbon-chain lengths of aliphatic aldehydes nor the steric bulk had any evident effect on the enantioselectivity, whereas the reaction rate of the sterically heavily hindered aldehyde **3q** (Table 3, Entry 17) was relatively much slower.

Conclusions

A series of new stable chiral C_1-symmetric dinitrogen ligands were conveniently synthesized in two simple steps under mild reaction conditions in high yields. Of the ligands, **L1** proved to be an effective catalyst in combination with $CuCl_2{\cdot}2H_2O$ for promoting enantioselective nitroaldol reactions between a wide range of aldehydes and nitromethane with high enantioselectivities and yields under mild reaction conditions. Further investigations into applications of this new chiral dinitrogen ligand are currently underway in our laboratory.

Experimental Section

General: THF was dried with Na and distilled prior to use. Nitromethane was dried with anhydrous $CaCl_2$ and distilled prior to use. Aliphatic aldehydes were obtained from commercial sources and were distilled before use. Aromatic aldehydes were treated by dissolving in CH_2Cl_2 and washing with aqueous NaOH solution (5 M), drying with anhydrous K_2CO_3 and concentration in vacuo. Reactions were monitored by TLC analysis on silica gel (60 Å, F-254) thin layer plates. Flash column chromatography was performed on silica gel (60 Å, 10–40 μm). Optical rotations were measured with a JASCO P1010 polarimeter in the solvent indicated. ^{1}H NMR spectra were recorded with Bruker instruments (400 MHz). Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard ($CDCl_3$, δ = 7.26 ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br. = broad), coupling constants (Hz) and integration. ^{13}C NMR spectra were recorded with Bruker instruments (100 MHz) with complete proton decoupling. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as internal standard ($CDCl_3$, δ = 77.0 ppm). HRMS data were measured with an Apex III (7.0 Tesla) Fourier transform ion cyclotron resonance (FTICR) mass spectrometer (Bruker, Billerica, MA, USA) fitted with an ESI source in the positive-ion mode. Enantiomer ratios were determined by chiral HPLC analysis on Daicel Chiralcel AD-H and OD-H and comparison with authentic racemates. Retention times are given in minutes. The absolute configuration of the nitroaldol adducts was assigned by comparison with literature data.

Synthesis and Characterization of the Ligands

(–)-*exo*-Bornylamine and (+)-(1*S*,2*S*,5*R*)-Menthylamine: These compounds were prepared as described in our previous work.[11]

1-Methylimidazole-2-carbaldehyde: *n*BuLi (40 mmol, 16 mL of a 2.5 mol dm^{-3} solution in hexane) was added dropwise under argon at –78 °C to a stirred solution of 1-methylimidazole (2 mL, 25.8 mmol) in anhydrous THF (30 mL) as described in the literature.[16] After 30 min, dimethylformamide (DMF) (4.6 mL, 59.4 mmol) was added dropwise. The mixture was then allowed to warm to room temperature naturally and stirred for a further 1 h. After the reaction had gone to completion, saturated aqueous ammonium chloride (20 mL) was added, and the organic layer was separated and washed with brine (20 mL), dried with anhydrous Na_2SO_4 and concentrated under vacuum. The crude product was purified by flash chromatography with petroleum ether and ethyl acetate to afford a colourless oil (1.47 g, 52% yield). ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ = 9.82 (s, 1 H, CHO), 7.28 (s, 1 H, ArH), 7.14 (s, 1 H, ArH), 4.03 (s, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ = 182.1, 143.7, 131.5, 127.3, 34.9 ppm.

Ligand L6: 1-Methylimidazole-2-carboxaldehyde (1.10 g, 10 mmol) and (–)-*exo*-bornylamine (1.53 g, 10 mmol) were added in one portion at room temperature to anhydrous MeOH (50 mL). The reaction solution was stirred at this temperature until no more starting material was detected (4–5 h). The mixture was then directly concentrated under vacuum and purified by flash chromatography with petroleum ether and ethyl acetate to afford a white solid (2.33 g, 95% yield). $[\alpha]_D^{25}$ = –167.5 (*c* = 0.8, EtOH). ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ = 8.13 (s, 1 H, CHN), 7.09 (s, 1 H, ArH), 6.91 (s, 1 H, ArH), 3.95 (s, 3 H, CH_3), 3.13 (dd, *J* = 8.4, 4.4 Hz, 1 H, CHN), 1.84–1.90 (m, 1 H, CH_2), 1.75–1.80 (m, 2 H, CH_2), 1.68–1.73 (m, 1 H, CH_2), 1.55–1.65 (m, 1 H, CH_2), 1.17–1.22 (m, 2 H, CH_2), 1.16 (s, 3 H, CH_3), 0.89 (s, 3 H, CH_3), 0.70 (s, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ = 150.3, 143.5, 128.9, 124.5, 79.7, 50.2, 47.2, 45.5, 39.1, 36.4, 35.6, 27.6, 20.7, 20.4, 12.9 ppm. HRMS (ESI, pos.): calcd. for $C_{15}H_{23}N_3Na$ $[M + Na]^+$ 268.1784; found 268.1781.

Ligand L1: Sodium borohydride (0.91 g, 24 mmol) was added portionwise at 0 °C to a solution of **L6** (1.96 g, 8 mmol) in anhydrous MeOH (30 mL) over a period of 30 min. The mixture was then allowed to warm to room temperature naturally and stirred for several hours until no more starting material was detected. The reaction was then quenched with aqueous HCl, and the MeOH solvent was removed by rotary evaporation. The aqueous phase was extracted with ethyl acetate, and the combined organic layers were dried with anhydrous Na_2SO_4 and concentrated under vacuum. The crude product was purified by flash chromatography with petroleum ether and ethyl acetate to afford a white solid (1.78 g, 90% yield). $[\alpha]_D^{25}$ = –81.5 (*c* = 1.1, EtOH). ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ = 6.90 (s, 1 H, ArH), 6.81 (s, 1 H,

ArH), 3.70–3.78 (m, 2 H, CH_2N), 3.67 (s, 3 H, CH_3), 2.58 (t, J = 6.4 Hz, 1 H, CHN), 1.87 (br. s, 1 H, NH), 1.67 (s, 2 H, CH_2), 1.57–1.60 (m, 2 H, CH_2), 1.16–1.55 (m, 1 H, CH_2), 1.07–1.09 (m, 2 H, CH_2), 1.03 (s, 3 H, CH_3), 0.86 (s, 3 H, CH_3), 0.81 (s, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ = 147.0, 126.8, 121.2, 67.2, 48.5, 46.7, 45.4, 45.3, 38.5, 36.9, 32.8, 27.3, 20.6, 20.4, 12.2 ppm. HRMS (ESI, pos.): calcd. for $C_{15}H_{26}N_3$ $[M + H]^+$ 248.2121; found 248.2115.

1-Benzylimidazole: Imidazole (6.80 g, 100 mmol) and anhydrous potassium carbonate (K_2CO_3, 6.9 g, 50 mmol) were added to anhydrous THF (150 mL) as described in the literature procedure.[17] The mixture was stirred at room temperature for 10 min prior to the addition of benzyl bromide (17.0 g, 100 mmol). The mixture was then stirred under reflux until the reaction was complete. After filtration, the THF was removed under vacuum to give a yellow solid, which was dissolved in dichloromethane (100 mL) and washed with water. The organic layer was then extracted with aqueous HCl, followed by water. The combined acid layers were neutralised with solid $NaHCO_3$ and then extracted with dichloromethane. The combined organic layers were washed with water, dried with anhydrous Na_2SO_4 and concentrated under vacuum. The crude product was purified by flash chromatography with petroleum ether and ethyl acetate to give a yellow oil (10.7 g, 68%). ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ = 7.53 (s, 1 H, ArH), 7.30–7.37 (m, 3 H, ArH), 7.14–7.16 (m, 2 H, ArH), 7.08 (s, 1 H, ArH), 6.89 (s, 1 H, ArH), 5.10 (s, 2 H, CH_2) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ = 137.4, 136.2, 129.8, 129.0, 128.3, 127.3, 119.3, 50.8 ppm.

1-Benzylimidazole-2-carbaldehyde: This compound was obtained according to the same procedure as that used for the synthesis of 1-methylimidazole-2-carbaldehyde by starting from 1-benzylimidazole (3.16 g, 20 mmol) and affording a colourless oil (2.27 g, 61% yield). ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ = 9.84 (s, 1 H, CHO), 7.28–7.36 (m, 4 H, ArH), 7.19–7.21 (m, 2 H, ArH), 7.14 (s, 1 H, ArH), 5.60 (s, 2 H, CH_2) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ = 182.2, 143.3, 135.8, 131.9, 129.0, 128.4, 127.7, 126.3, 50.9 ppm.

***N*-[(1-Benzyl-1*H*-imidazol-2-yl)methylene]-1,7,7-trimethylbicyclo-[2.2.1]heptan-2-amine (L2-1):** This compound was obtained according to the same procedure as that used for the synthesis of **L6** by starting from 1-benzylimidazole-2-carbaldehyde (1.30 g, 7 mmol) and affording a yellow oil (2.09 g, 93% yield). $[\alpha]_D^{25}$ = –110.5 (c = 1.0, EtOH). ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ = 8.20 (s, 1 H, CHN), 7.19–7.35 (m, 3 H, ArH), 7.14 (s, 1 H, ArH), 7.02–7.04 (m, 2 H, ArH), 6.90 (s, 1 H, ArH), 5.78 (d, J = 15.2 Hz, 1 H, CH_2N), 5.72 (d, J = 15.2 Hz, 1 H, CH_2N), 3.11 (dd, J = 8.4, 4.0 Hz, 1 H, CHN), 1.53–1.78 (m, 5 H, CH_2), 1.11–1.18 (m, 2 H, CH_2), 0.93 (s, 3 H, CH_3), 0.81 (s, 3 H, CH_3), 0.58 (s, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ = 150.6, 143.2, 137.3, 129.6, 128.6, 127.5, 126.9, 123.6, 79.8, 50.4, 50.3, 47.1, 45.4, 38.9, 36.5, 27.5, 20.6, 20.3, 12.7 ppm. HRMS (ESI, pos.): calcd. for $C_{21}H_{27}N_3Na$ $[M + Na]^+$ 344.2097; found 344.2092.

Ligand L2: This compound was obtained according to the same procedure as that used for the synthesis of **L1** by starting from **L2–1** (0.96 g, 3 mmol) and affording a yellow oil (0.77 g, 80% yield). $[\alpha]_D^{25}$ = –56.8 (c = 0.7, EtOH). ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ = 7.26–7.34 (m, 3 H, ArH), 7.08–7.10 (m, 2 H, ArH), 6.97 (s, 1 H, ArH), 6.83 (s, 1 H, ArH), 5.25 (s, 2 H, CH_2), 3.75 (d, J = 13.2 Hz, 1 H, CH_2N), 3.68 (d, J = 13.2 Hz, 1 H, CH_2N), 2.55 (t, J = 6.4 Hz, 1 H, CHN), 2.25 (br. s, 1 H, NH), 1.66–1.69 (m, 2 H, CH_2), 1.44–1.55 (m, 3 H, CH_2), 1.04–1.09 (m, 2 H, CH_2), 0.98 (s, 3 H, CH_3), 0.82 (s, 3 H, CH_3), 0.79 (s, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ = 137.0, 136.9, 128.8, 127.8, 127.3, 126.9, 120.6, 67.2, 49.5, 48.5, 46.7, 45.5, 45.3, 38.5, 36.9, 27.3, 20.6, 20.5, 12.1 ppm. HRMS (ESI, pos.): calcd. for $C_{21}H_{30}N_3$ $[M + H]^+$ 324.2434; found 324.2434.

1-(Triphenylmethyl)imidazole: NaH (75 mmol, 3.0 g, 60 wt.-% in mineral oil) was added portionwise at 0 °C to a solution of imidazole (3.4 g, 50 mmol) in anhydrous THF (100 mL) over a period of 30 min as described in the literature procedure.[18] Chlorotriphenylmethane (16.7 g, 60 mmol) was then added to the mixture in one portion. The solution was allowed to warm to room temperature naturally and stirred for several hours until no more starting material was detected. The reaction was then quenched with aqueous HCl, and the THF solvent was removed by rotary evaporation. The aqueous phase was extracted with ethyl acetate, and the combined organic layers were dried with anhydrous Na_2SO_4 and concentrated under vacuum. The crude product was recrystallized and used directly for the next step without further purification (5.43 g, 35% yield). ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ = 7.48 (s, 1 H, ArH), 7.30–7.31 (m, 9 H, ArH), 7.13–7.15 (m, 6 H, ArH), 7.06 (s, 1 H, ArH), 6.82 (s, 1 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ = 142.6, 139.0, 129.8, 129.6, 128.3, 128.1, 121.7, 75.3 ppm.

1-(Triphenylmethyl)imidazole-2-carbaldehyde: This compound was obtained according to the same procedure as that used for the synthesis of 1-methylimidazole-2-carbaldehyde by starting from 1-(triphenylmethyl)imidazole (3.16 g, 20 mmol) and affording a yellow oil (2.27 g, 61% yield). ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ = 9.22 (s, 1 H, CHO), 7.31–7.32 (m, 10 H, ArH), 7.10–7.15 (m, 6 H, ArH), 7.02 (s, 1 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ = 178.7, 145.6, 145.2, 142.1, 130.4, 129.7, 129.6, 128.2, 128.1, 127.9, 127.0, 126.9, 77.0 ppm.

Imidazole-2-carbaldehyde: This compound was obtained according to a literature procedure[19] by heating a solution of 1-(triphenylmethyl)imidazole-2-carbaldehyde (1.01 g, 3 mmol) in acetic acid in methanol (5%, 20 mL) at reflux for 2 h. After evaporation of the solvent, the mixture was basified with saturated aqueous $NaHCO_3$ (20 mL) and then extracted with ethyl acetate, and the combined organic layers were dried with anhydrous Na_2SO_4 and concentrated under vacuum. The crude product was purified by flash chromatography with petroleum ether and ethyl acetate to afford a yellow solid (0.20 g, 70% yield). ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ = 9.74 (s, 1 H, CHO), 7.09 (s, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ = 181.1, 151.7, 127.0 ppm.

***N*-[(1*H*-Imidazol-2-yl)methylene]-1,7,7-trimethylbicyclo[2.2.1]heptan-2-amine (L3-1):** This compound was obtained according to the same procedure as that used for the synthesis of **L6** by starting from imidazole-2-carbaldehyde (0.20 g, 2 mmol) and affording a yellow oil (0.40 g, 86% yield). $[\alpha]_D^{25}$ = –146.3 (c = 0.9, EtOH). ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ = 8.03 (s, 1 H, CHN), 7.16–7.29 (m, 2 H, ArH), 7.12 (br. s, 1 H, NH), 3.22 (dd, J = 8.4, 4.4 Hz, 1 H, CHN), 1.84–1.90 (m, 1 H, CH_2), 1.74–1.80 (m, 2 H, CH_2), 1.66–1.72 (m, 1 H, CH_2), 1.57–1.65 (m, 1 H, CH_2), 1.16–1.18 (m, 2 H, CH_2), 1.14 (s, 3 H, CH_3), 0.88 (s, 3 H, CH_3), 0.69 (s, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ = 148.5, 145.5, 130.4, 127.9, 126.9, 78.4, 50.5, 47.2, 45.6, 38.8, 36.6, 27.5, 20.7, 20.6, 12.7 ppm. HRMS (ESI, pos.): calcd. for $C_{14}H_{21}N_3Na$ $[M + Na]^+$ 254.1628; found 254.1625.

Ligand L3: This compound was obtained according to the same procedure as that used for the synthesis of **L1** by starting from **L3–1** (0.35 g, 1.5 mmol) and affording a yellow oil (0.25 g, 72% yield). $[\alpha]_D^{25}$ = –65.0 (c = 1.0, EtOH). ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ = 6.98 (s, 2 H, ArH), 3.86 (d, J = 14.4 Hz, 1 H, CH_2N), 3.81 (d, J = 14.8 Hz, 1 H, CH_2N), 2.56 (dd, J = 8.0, 5.2 Hz, 1 H, CHN), 1.47–1.72 (m, 5 H, CH_2), 1.05–1.09 (m, 2 H, CH_2), 1.02 (s, 3 H,

CH_3), 0.89 (s, 3 H, CH_3), 0.82 (s, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ = 148.2, 121.6, 66.7, 48.5, 46.8, 46.1, 45.2, 38.8, 36.9, 27.2, 20.7, 20.6, 12.2 ppm. HRMS (ESI, pos.): calcd. for $C_{14}H_{24}N_3$ $[M + H]^+$ 234.1965; found 234.1959.

1,4,5-Trimethylimidazole: Formaldehyde (3.0 g, 100 mmol), methylamine hydrochloride (12.2 g, 180 mmol) and ammonium hydroxide (50 mL) were mixed as described in a literature procedure.[20] After having been stirred vigorously for several minutes, the reaction mixture had become homogeneous, and then butanedione (5.16 g, 60 mmol) was added, and the mixture was maintained at 100 °C and kept at reflux for several hours until the reaction was completed. The cold reaction mixture was extracted with dichloromethane, and the organic phase was dried with anhydrous Na_2SO_4 and concentrated under vacuum. The product was obtained after vacuum distillation (5.0 g, 76% yield). ^1H NMR (400 MHz, $CDCl_3$, TMS): δ = 7.14 (s, 1 H, ArH), 3.35 (s, 3 H, CH_3), 2.02 (s, 3 H, CH_3), 1.98 (s, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ = 135.1, 133.4, 122.5, 31.3, 12.6, 8.1 ppm.

1,4,5-Trimethylimidazole-2-carbaldehyde: This compound was obtained according to the same procedure as that used for the synthesis of 1-methylimidazole-2-carbaldehyde by starting from 1,4,5-trimethylimidazole (3.3 g, 30 mmol) and affording a yellow oil (2.21 g, 53% yield). ^1H NMR (400 MHz, $CDCl_3$, TMS): δ = 9.65 (s, 1 H, CHO), 3.89 (s, 3 H, CH_3), 2.24 (s, 3 H, CH_3), 2.21 (s, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ = 180.9, 142.0, 138.3, 132.0, 31.8, 12.8, 8.6 ppm.

1,7,7-Trimethyl-*N*-[(1,4,5-trimethyl-1*H*-imidazol-2-yl)methylene]bicyclo[2.2.1]heptan-2-amine (L4-1): This compound was obtained according to the same procedure as that used for the synthesis of **L6** by starting from 1,4,5-trimethylimidazole-2-carbaldehyde (0.69 g, 5 mmol) and affording a white solid (1.23 g, 90% yield). $[a]_D^{25}$ = –174.6 (c = 1.0, EtOH). ^1H NMR (400 MHz, $CDCl_3$, TMS): δ = 8.03 (s, 1 H, CHN), 3.84 (s, 3 H, CH_3), 3.08 (dd, J = 8.4, 4.4 Hz, 1 H, CHN), 2.18 (s, 3 H, CH_3), 2.14 (s, 3 H, CH_3), 1.83–1.89 (m, 1 H, CH_2), 1.73–1.79 (m, 2 H, CH_2), 1.66–1.71 (m, 1 H, CH_2), 1.56–1.62 (m, 1 H, CH_2), 1.18–1.23 (m, 2 H, CH_2), 1.16 (s, 3 H, CH_3), 0.88 (s, 3 H, CH_3), 0.69 (s, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ = 150.4, 141.4, 134.2, 127.3, 79.6, 50.1, 47.1, 45.5, 39.2, 36.4, 32.1, 27.6, 20.6, 20.4, 12.8, 12.6, 8.7 ppm. HRMS (ESI, pos.): calcd. for $C_{17}H_{27}N_3Na$ $[M + Na]^+$ 296.2097; found 296.2091.

Ligand L4: This compound was obtained according to the same procedure as that used for the synthesis of **L1** by starting from **L4–1** (0.95 g, 3.5 mmol) and affording a white solid (0.82 g, 85% yield). $[a]_D^{25}$ = –76.5 (c = 1.0, EtOH). ^1H NMR (400 MHz, $CDCl_3$, TMS): δ = 3.71 (d, J = 12.8 Hz, 1 H, CH_2N), 3.61 (d, J = 12.8 Hz, 1 H, CH_2N), 3.49 (s, 3 H, CH_3), 2.58 (t, J = 6.6 Hz, 1 H, CHN), 2.11 (s, 3 H, CH_3), 2.09 (s, 3 H, CH_3), 1.68–1.71 (m, 2 H, CH_2), 1.58–1.61 (m, 2 H, CH_2), 1.46–1.53 (m, 1 H, CH_2), 1.07–1.09 (m, 2 H, CH_2), 1.03 (s, 3 H, CH_3), 0.85 (s, 3 H, CH_3), 0.80 (s, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ = 144.7, 131.0, 123.1, 67.3, 48.5, 46.8, 46.7, 45.4, 38.6, 36.9, 30.2, 27.4, 20.6, 20.5, 12.5, 12.2, 8.8 ppm. HRMS (ESI, pos.): calcd. for $C_{17}H_{30}N_3$ $[M + H]^+$ 276.2434; found 276.2427.

1-Methyl-4,5-diphenylimidazole: 1,2-Diphenylethanedione (10.50 g, 50 mmol), formaldehyde (1.50 g, 50 mmol), methylamine (50 mmol, 8.0 mL of a 25% solution in ethanol), ammonium acetate (3.85 g, 50 mmol) and L-proline (0.86 g, 7.5 mmol) were added to MeOH (60 mL) as described in a literature procedure.[21] The mixture was then kept at reflux for several hours until the reaction had gone to completion. After evaporation of the MeOH solvent, water was added to the mixture, which was then extracted with ethyl acetate, and the combined organic layers were dried with anhydrous Na_2SO_4 and concentrated under vacuum. The pure product was obtained by crystallization from ethanol as light yellow crystals (9.7 g, 83% yield). ^1H NMR (400 MHz, $CDCl_3$, TMS): δ = 7.56 (s, 1 H, ArH), 7.48–7.50 (m, 2 H, ArH), 7.41–7.45 (m, 3 H, ArH), 7.31–7.33 (m, 2 H, ArH), 7.18–7.21 (m, 2 H, ArH), 7.10–7.15 (m, 1 H, ArH), 3.45 (s, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ = 138.2, 137.5, 134.7, 130.7, 130.6, 129.0, 128.9, 128.6, 128.2, 126.6, 126.3, 32.2 ppm.

1-Methyl-4,5-diphenylimidazole-2-carbaldehyde: This compound was obtained according to the same procedure as that used for the synthesis of 1-methylimidazole-2-carbaldehyde by starting from 1-methyl-4,5-diphenylimidazole (4.68 g, 20 mmol) and affording the product as a yellow oil (2.38 g, 45% yield). ^1H NMR (400 MHz, $CDCl_3$, TMS): δ = 9.92 (s, 1 H, CHO), 7.46–7.50 (m, 5 H, ArH), 7.32–7.35 (m, 2 H, ArH), 7.20–7.26 (m, 3 H, ArH), 3.83 (s, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ = 182.3, 143.1, 141.3, 135.7, 133.3, 130.5, 129.7, 129.3, 128.7, 128.4, 127.4, 127.1, 32.9 ppm.

1,7,7-Trimethyl-*N*-[(1-methyl-4,5-diphenyl-1*H*-imidazol-2-yl)methylene]bicyclo[2.2.1]heptan-2-amine (L5-1): This compound was obtained according to the same procedure as that used for the synthesis of **L6** by starting from 1-methyl-4,5-diphenylimidazole-2-carbaldehyde (1.31 g, 5 mmol) and affording a white solid (1.68 g, 85% yield). $[a]_D^{25}$ = –133.2 (c = 1.0, EtOH). ^1H NMR (400 MHz, $CDCl_3$, TMS): δ = 8.28 (s, 1 H, CHN), 7.42–7.47 (m, 5 H, ArH), 7.31–7.34 (m, 2 H, ArH), 7.13–7.21 (m, 3 H, ArH), 3.77 (s, 3 H, CH_3), 3.18 (dd, J = 8.4, 4.4 Hz, 1 H, CHN), 1.88–1.94 (m, 1 H, CH_2), 1.70–1.80 (m, 3 H, CH_2), 1.59–1.64 (m, 1 H, CH_2), 1.19–1.24 (m, 2 H, CH_2), 1.16 (s, 3 H, CH_3), 0.89 (s, 3 H, CH_3), 0.74 (s, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ = 150.8, 143.1, 138.5, 134.3, 132.7, 130.9, 130.3, 129.0, 128.9, 128.2, 126.9, 126.6, 79.9, 50.3, 47.2, 45.6, 39.2, 36.5, 33.6, 27.6, 20.7, 20.5, 13.0 ppm. HRMS (ESI, pos.): calcd. for $C_{27}H_{31}N_3Na$ $[M + Na]^+$ 420.2410; found 420.2403.

Ligand L5: This compound was obtained according to the same procedure as that used for the synthesis of **L1** by starting from **L5–1** (1.19 g, 3 mmol) and affording a white solid (1.00 g, 83% yield). $[a]_D^{25}$ = –58.0 (c = 1.1, EtOH). ^1H NMR (400 MHz, $CDCl_3$, TMS): δ = 7.42–7.45 (m, 5 H, ArH), 7.32–7.34 (m, 2 H, ArH), 7.16–7.20 (m, 2 H, ArH), 7.09–7.12 (m, 1 H, ArH), 3.87 (d, J = 13.2 Hz, 1 H, CH_2N), 3.79 (d, J = 13.2 Hz, 1 H, CH_2N), 3.48 (s, 3 H, CH_3), 2.67 (t, J = 6.2 Hz, 1 H, CHN), 1.65–1.71 (m, 5 H, CH_2), 1.49–1.56 (m, 1 H, CH_2), 1.10–1.13 (m, 2 H, CH_2), 1.06 (s, 3 H, CH_3), 0.90 (s, 3 H, CH_3), 0.82 (s, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ = 146.7, 136.2, 134.8, 131.2, 130.9, 129.7, 128.9, 128.4, 128.1, 126.7, 126.1, 67.5, 48.6, 46.8, 46.1, 45.4, 38.6, 36.9, 31.2, 27.4, 20.6, 20.5, 12.3 ppm. HRMS (ESI, pos.): calcd. for $C_{27}H_{34}N_3$ $[M + H]^+$ 400.2747; found 400.2742.

1-Methylbenzimidazole: This compound was obtained according to the same procedure as that used for the synthesis of 1-(triphenylmethyl)imidazole by starting from benzimidazole (2.36 g, 20 mmol) and iodomethane (3.12 g, 22 mmol) and affording the product as light yellow solid (2.16 g, 82% yield). ^1H NMR (400 MHz, $CDCl_3$, TMS): δ = 7.82–7.84 (m, 2 H, ArH), 7.30–7.38 (m, 3 H, ArH), 3.81 (s, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ = 143.8, 143.5, 134.6, 122.9, 122.1, 120.3, 109.3, 30.9 ppm.

1-Methylbenzimidazole-2-carbaldehyde: This compound was obtained according to the same procedure as that used for the synthesis of 1-methylimidazole-2-carbaldehyde by starting from 1-methylbenzimidazole (1.98 g, 15 mmol) and affording the product as a

yellow oil (0.84 g, 35% yield). ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ = 10.13 (s, 1 H, CHO), 7.30 (d, J = 8.4 Hz, 2 H, ArH), 7.48–7.50 (m, 2 H, ArH), 7.39–7.43 (m, 1 H, ArH), 4.17 (s, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ = 185.1, 146.2, 142.8, 137.0, 126.9, 124.1, 122.4, 110.7, 31.4 ppm.

1,7,7-Trimethyl-*N*-[(1-methyl-4,5-diphenyl-1*H*-imidazol-2-yl)methylene]bicyclo[2.2.1]heptan-2-amine (L7-1): This compound was obtained according to the same procedure as that used for the synthesis of **L6** by starting from 1-methylbenzimidazole-2-carbaldehyde (0.64 g, 4 mmol) and affording a white solid (0.92 g, 78% yield). $[\alpha]_D^{25}$ = –192.2 (c = 0.9, EtOH). ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ = 8.35 (s, 1 H, CHN), 7.80 (d, J = 8.0 Hz, 2 H, ArH), 7.26–7.40 (m, 3 H, ArH), 4.13 (s, 3 H, CH_3), 3.24 (dd, J = 8.4, 4.4 Hz, 1 H, CHN), 1.92–1.98 (m, 1 H, CH_2), 1.73–1.84 (m, 3 H, CH_2), 1.62–1.67 (m, 1 H, CH_2), 1.23–1.26 (m, 2 H, CH_2), 1.21 (s, 3 H, CH_3), 0.92 (s, 3 H, CH_3), 0.74 (s, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ = 151.6, 147.9, 142.6, 137.0, 124.2, 122.7, 120.6, 109.8, 80.1, 50.6, 47.3, 45.5, 39.0, 36.4, 32.0, 27.6, 20.7, 20.5, 12.9 ppm. HRMS (ESI, pos.): calcd. for $C_{19}H_{25}N_3Na$ [M + Na]$^+$ 318.1941; found 318.1936.

Ligand L7: This compound was obtained according to the same procedure as that used for the synthesis of **L1** by starting from **L7–1** (0.74 g, 2.5 mmol) and affording a white solid (0.59 g, 80% yield). $[\alpha]_D^{25}$ = –80.9 (c = 0.8, EtOH). ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ = 7.71–7.73 (m, 1 H, ArH), 7.22–7.33 (m, 3 H, ArH), 3.99 (d, J = 13.2 Hz, 1 H, CH_2N), 3.91 (d, J = 13.2 Hz, 1 H, CH_2N), 3.83 (s, 3 H, CH_3), 2.65 (t, J = 6.6 Hz, 1 H, CHN), 1.61–1.70 (m, 5 H, CH_2), 1.49–1.55 (m, 1 H, CH_2), 1.07–1.10 (m, 2 H, CH_2), 1.04 (s, 3 H, CH_3), 0.88 (s, 3 H, CH_3), 0.81 (s, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ = 153.5, 142.3, 136.2, 122.4, 121.8, 119.5, 109.1, 67.5, 48.7, 46.8, 46.1, 45.4, 38.6, 36.9, 30.1, 27.3, 20.6, 20.5, 12.2 ppm. HRMS (ESI, pos.): calcd. for $C_{19}H_{28}N_3$ [M + H]$^+$ 298.2278; found 298.2276.

(1*S*,2*S*,5*R*)-2-Isopropyl-5-methyl-*N*-[(1-methyl-1*H*-imidazol-2-yl)-methylene]cyclohexanamine (L8-1): This compound was obtained according to the same procedure as that used for the synthesis of **L6** by starting from 1-methylimidazole-2-carbaldehyde (0.88 g, 8 mmol) and (+)-(1*S*,2*S*,5*R*)-menthylamine (1.24 g, 8 mmol) and affording a yellow oil (1.70 g, 86% yield). $[\alpha]_D^{25}$ = –5.6 (c = 0.7, EtOH). ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ = 8.35 (s, 1 H, CHN), 7.10 (s, 1 H, ArH), 6.92 (s, 1 H, ArH), 3.99 (s, 3 H, CH_3), 3.60 (d, J = 1.6 Hz, 1 H, CHN), 1.73–1.85 (m, 3 H, 3 CH), 1.55–1.64 (m, 2 H, CH_2), 1.32–1.39 (m, 1 H, CH_2), 1.18–1.27 (m, 1 H, CH_2), 1.06–1.14 (m, 1 H, CH_2), 0.96–1.04 (m, 1 H, CH_2), 0.80–0.93 (m, 9 H, 3 CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ = 150.9, 143.7, 128.8, 124.6, 68.1, 48.3, 44.5, 35.8, 35.7, 29.5, 26.6, 25.6, 22.7, 20.9, 20.4 ppm. HRMS (ESI, pos.): calcd. for $C_{15}H_{25}N_3Na$ [M + Na]$^+$ 270.1941; found 270.1937.

Ligand L8: This compound was obtained according to the same procedure as that used for the synthesis of **L1** by starting from **L8–1** (0.99 g, 4 mmol) and affording a yellow oil (0.82 g, 82% yield). $[\alpha]_D^{25}$ = +59.1 (c = 1.2, in EtOH). ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ = 6.82 (d, J = 1.2 Hz, 1 H, ArH), 6.74 (d, J = 0.8 Hz, 1 H, ArH), 3.85–3.91 (m, 1 H, CH_2), 3.58–3.62 (m, 4 H, CH_3, CH_2), 2.87 (s, 1 H, CHN), 1.92–1.95 (m, 1 H, CH_2), 1.56–1.63 (m, 4 H, CH_2), 1.43–1.49 (m, 1 H, CH_2), 1.00–1.10 (m, 1 H, CH_2), 0.73–0.83 (m, 12 H, 3 CH_3, CH_2) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ = 147.1, 126.8, 121.2, 53.4, 48.4, 44.1, 37.6, 35.3, 32.7, 28.8, 25.7, 24.9, 22.5, 21.4, 20.6 ppm. HRMS (ESI, pos.): calcd. for $C_{15}H_{28}N_3$ [M + H]$^+$ 250.2278; found 250.2275.

***N*-(2-Hydroxybenzylidene)-1,7,7-trimethylbicyclo[2.2.1]heptan-2-amine (L9-1):** This compound was obtained according to the same procedure as that used for the synthesis of **L6** by starting from salicylaldehyde (0.98 g, 8 mmol) and (–)-*exo*-bornylamine (1.22 g, 8 mmol) and affording a yellow solid (1.70 g, 83% yield). $[\alpha]_D^{25}$ = –127.0 (c = 1.0, EtOH). ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ = 13.67 (s, 1 H, OH), 8.18 (s, 1 H, CHN), 7.22–7.30 (m, 2 H, ArH), 6.93–6.97 (m, 1 H, ArH), 6.84–6.88 (m, 1 H, ArH), 3.19 (dd, J = 8.4, 4.4 Hz, 1 H, CHN), 1.92–1.97 (m, 1 H, CH_2), 1.75–1.83 (m, 3 H, CH_2), 1.62–1.69 (m, 1 H, CH_2), 1.17–1.23 (m, 2 H, CH_2), 1.14 (s, 3 H, CH_3), 0.90 (s, 3 H, CH_3), 0.76 (s, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ = 162.4, 161.3, 132.0, 131.2, 118.9, 118.5, 116.9, 77.9, 50.1, 47.3, 45.3, 39.3, 36.5, 27.4, 20.5, 20.4, 12.8 ppm. HRMS (ESI, pos.): calcd. for $C_{17}H_{23}NNaO$ [M + Na]$^+$ 280.1672; found 280.1677.

Ligand L9: This compound was obtained according to the same procedure as that used for the synthesis of **L1** by starting from **L9–1** (1.03 g, 4 mmol) and affording a white solid (0.91 g, 88% yield). $[\alpha]_D^{25}$ = –76.8 (c = 0.9, EtOH). ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ = 7.14–7.18 (m, 1 H, ArH), 6.98 (d, J = 7.2 Hz, 1 H, ArH), 6.82–6.84 (m, 1 H, ArH), 6.75–6.79 (m, 1 H, ArH), 4.00 (d, J = 14.0 Hz, 1 H, CH_2N), 3.77 (d, J = 13.6 Hz, 1 H, CH_2N), 2.60 (dd, J = 8.0, 4.8 Hz, 1 H, CHN), 1.67–1.78 (m, 4 H, CH_2), 1.52–1.60 (m, 1 H, CH_2), 1.06–1.14 (m, 2 H, CH_2), 0.98 (s, 3 H, CH_3), 0.95 (s, 3 H, CH_3), 0.85 (s, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ = 158.3, 128.7, 128.2, 123.0, 118.9, 116.4, 66.3, 51.6, 48.6, 46.9, 45.0, 38.3, 37.0, 27.1, 20.6, 20.5, 12.3 ppm. HRMS (ESI, pos.): calcd. for $C_{17}H_{26}NO$ [M + H]$^+$ 260.2009; found 260.2005.

HRMS Analysis of the L1/$CuCl_2$ Complex: Ligand **L1** (3.1 mg, 0.0125 mmol) and $CuCl_2{\cdot}2H_2O$ (2.1 mg, 0.0125 mmol) were added to a test tube containing EtOH (2 mL), and the mixture was stirred at ambient temperature for 30 min to generate the catalyst. The mixture was diluted and analysed directly by HRMS (ESI, pos.): calcd. for $C_{15}H_{25}ClCuN_3$ [M + CuCl]$^+$ 245.1028; found 245.1030.

General Procedure for the Asymmetric Nitroaldol Reactions: Ligand **L1** (6.2 mg, 0.025 mmol, 5 mol-%) and $CuCl_2{\cdot}2H_2O$ (4.2 mg, 0.025 mmol, 5 mol-%) were added to a test tube containing absolute THF (2.0 mL). The solution was stirred at room temperature for 1 h to give a blue solution. The aldehyde (0.5 mmol), nitromethane (5.0 mmol, 10 equiv.) and DIPEA (87 μL, 0.5 mmol, 1.0 equiv.) were added successively to the resulting solution, and the tube was introduced into a bath at the reaction temperature without special precautions to exclude moisture or air. After the indicated time, aqueous HCl (3 M, 180 μL) was added, and the mixture was concentrated and directly purified by column chromatography on silica gel with petroleum ether and ethyl acetate to afford the expected nitroaldol product.

Supporting Information (see footnote on the first page of this article): Characterization data for all new compounds as well as NMR spectra and HPLC chromatograms of the nitroaldol products.

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