C_2-Symmetric Fluorous Diamines and Diimines as Ligands for Metal-Catalysed Asymmetric Cyclopropanation of Styrene

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Perfluoroalkyl-substituted, enantiopure C_2-symmetric N and N,O ligands showing affinity either for standard organic solvents or perfluorocarbons have been conveniently prepared from readily available precursors. Preformed cobalt(II) and in-situ-generated copper(I) complexes of these ligands were tested as catalysts in the metal-catalysed cyclopropanation of styrene with diazoacetates. Under optimised reaction conditions, which include the use of a fluorous biphasic system and short reaction times, the copper complex of a C_2-symmetric diamine afforded promising results (yield = 77%, *trans*/*cis* = 67:33, *ee* of the *trans* isomer = 62%) and could be easily separated from the products by simply decanting the fluorous phase.

Introduction

Asymmetric cyclopropanation was the first example of the use of a chiral metal complex to catalyse the conversion of a prochiral substrate into a chiral product with an excess of one enantiomer.[1] Since then much research has been carried out in order to gain a better understanding of the mechanism of cyclopropanation in which a diazoacetate decomposes to generate a metal carbenoid, which in turn is inserted into the double bond of an olefin.[2] At the same time various metals and ligands have been tested in an effort to improve the *trans*/*cis* selectivity and the enantioselectivity of the reaction.[3] At present, some of the best systems for asymmetric cyclopropanation use C_2-symmetric bis(oxazoline) ligands with Cu^I metal complexes.[4−6] These ligands give high enantioselectivities, up to 99% *ee* for the *trans* isomer and 97% *ee* for the *cis* isomer using ethyl diazoacetate. The *trans*/*cis* selectivity depends heavily on the diazoacetate used but varies between 66:34 and 94:6. However bis(oxazolines) are not the only C_2-symmetric chiral ligand that can be used for cyclopropanation: other ligands such as chiral binaphthyldiimines[7] and bis(ferrocenyl)diamines[8] have been tested. Both the diimines and especially the diamines give good enantioselectivities (up to 96% *ee*) and *trans*/*cis* selectivities (up to 90:10) using ethyl diazoacetate.

Whichever chiral complex is used, they are difficult and expensive to make, so it is desirable to be able to separate the catalyst after the cyclopropanation reaction and to reuse it. To this end bis(oxazolines) (and other ligands) have been attached to heterogeneous inorganic and organic supports to allow filtration and the facile recovery of the catalyst after the reaction.[9] However, while the selectivities of such supported catalysts are equal to those of their homogeneous equivalents, their activities are generally lower. Moreover, although this approach ensures the successful separation of the catalyst from reaction products, recycling of the recovered catalysts is much less effective.[10] A soluble support such as PEG can be used so that the reaction can be run under homogeneous conditions and therefore give similar activities to those of unsupported catalysts. Once the reaction is complete the PEG-supported catalyst can be precipitated out, filtered and reused. Depending on the linker between the bis((oxazoline) and the PEG the catalyst can be recycled up to 13 times.[11] Compared with these now well-established methods, the application of fluorous immobilisation and separation techniques[12−14] to metal-catalysed asymmetric cyclopropanation is much less developed. The only reported example concerns the Cu^I-promoted cyclopropanation of styrene in the presence of chiral fluorous bis(oxazoline) (F-box) ligands.[15] Good selectivities and activities were observed, but attempts to recycle the active metal complex were foiled by decomposition products of the diazoacetates inhibiting the catalyst. Therefore, our interest moved towards the use of alternative C_2-symmetric fluorous N and N,O ligands.

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Results and Discussion

Synthesis of Fluorous Chiral Nitrogen Ligands: In the last few years, we have developed several heavy-fluorous (F con-

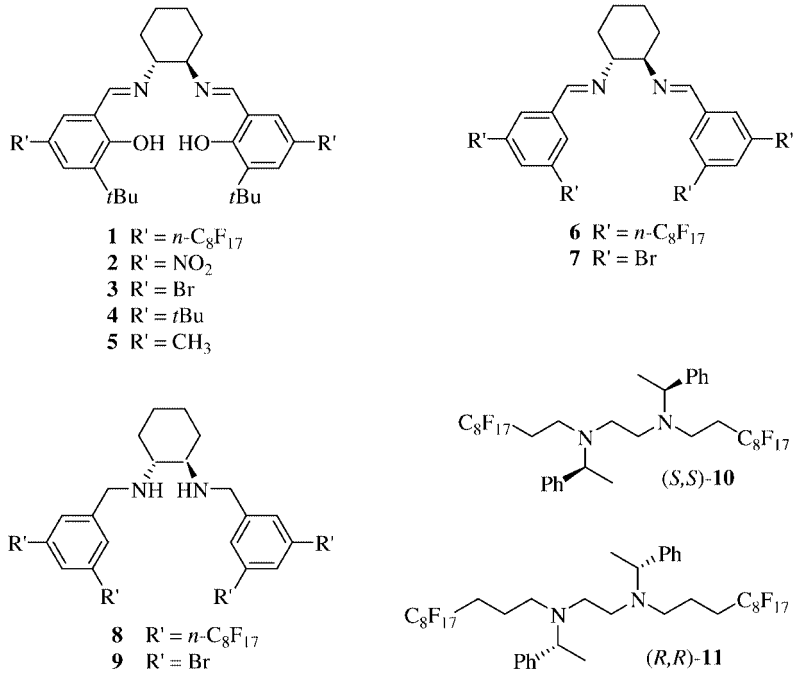
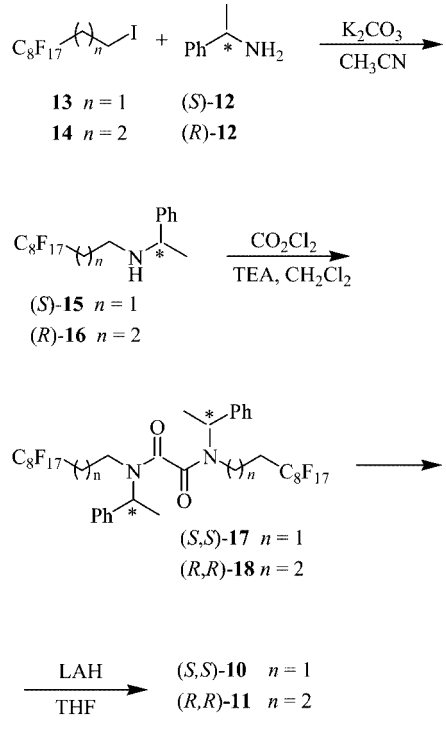


Figure 1. Ligands tested in the asymmetric cyclopropanation of styrene

tent > 60%) C_2-symmetric bi- and tetradentate N and N,O ligands which have been successfully used in catalytic asymmetric reactions such as the epoxidation of alkenes and the enantioselective hydrogen transfer reduction of ketones.[16] Most of these ligands are derivatives of commercially available, enantiomerically pure *trans*-1,2-diaminocyclohexane and can be prepared on a multigram scale by straightforward condensation of the chiral diamine with fluorous benzaldehydes, followed by reduction of the imino functionalities when required. Salen ligand **1**,[17] diimine **6** and diamine **8** (Figure 1)[18] were selected from this set of compounds for this study. Two new light-fluorous (F content < 60%) C_2-symmetric diamines, (*S*,*S*)-**10** and (*R*,*R*)-**11** (Figure 1), were also studied as they can be readily prepared from the enantiomers of the inexpensive chiral building block 1-phenylethylamine **12** (Scheme 1).

Perfluoroalkyl iodides **13** and **14** were reacted with (*S*)-**12** and (*R*)-**12**, respectively, in the presence of K_2CO_3 as a base. Under these conditions, the enantiomerically pure primary amine was selectively *N*-alkylated to afford the chiral secondary amines (*S*)-**15** (yield = 55%) and (*R*)-**16** (yield = 70%), respectively, as the only products. A partial loss of the perfluoroalkyl iodide **13** occurred due to HI elimination, which accounts for the lower yield of (*S*)-**15**. This side reaction did not occur with iodide **14**, which has an extra methylene spacer inserted between the perfluoroalkyl chain and the iodine atom. Indeed, unchanged **14** could be recovered from the product mixture at the end of the reaction. Ethanediamides (*S*,*S*)-**17** (yield = 53%) and (*R*,*R*)-**18** (yield = 67%) were obtained by the reaction of two molar equivalents of (*S*)-**15** and (*R*)-**16**, respectively, with oxalyl chloride. These intermediates were reduced to the corresponding diamines (*S*,*S*)-**10** and (*R*,*R*)-**11** using

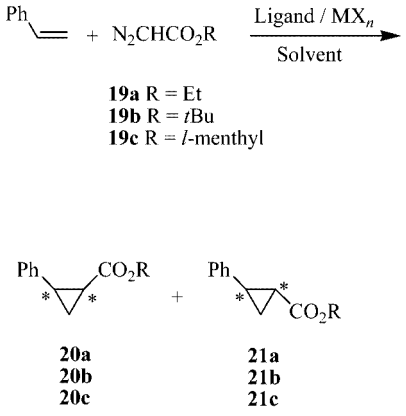


Scheme 1. Synthesis of diamines (*S*,*S*)-**10** and (*R*,*R*)-**11**

LAH in THF at 0 °C. In the event (*S*,*S*)-**10** was recovered in a moderate yield (56%), however the reduction of (*R*,*R*)-**18** was accompanied by product degradation and diamine (*R*,*R*)-**11** was obtained in only 15% yield. Attempts at using milder reducing agents such as $NaBH_4$ and BH_3·THF failed to improve this.

As expected on the basis of the relatively low fluorine content, both (*S*,*S*)-**10** and (*R*,*R*)-**11** are readily soluble in non-fluorinated solvents and show similarly low partition coefficients *P* between perfluorocarbons and organic solvents [e.g. $P = 1$ in C_8F_{18}/dichloromethane (50:50, v/v)].

Catalytic Activity of Co^{II} Complexes: Enantiomerically pure metallosalen complexes are among the most widely investigated chiral catalysts in asymmetric synthesis. Katsuki and co-workers have recently demonstrated that cyclopropanation of styrene with α-diazoacetates (Scheme 2) proceeds with moderate-to-high diastereo- and enantioselectivity in the presence of Co^{II}−salen complexes.[19] Such a reaction was attempted using the Co^{II} complex of salen **1** (Co−**1**), an effective fluorous catalyst for the asymmetric hydrolytic kinetic resolution (HKR) of terminal epoxides.[20] The reaction of styrene with ethyl α-diazoacetate **19a** proceeded slowly in the presence of Co−**1** and *N*-methylimidazole in THF, affording a 1:1 mixture of *cis*- and *trans*-cyclopropanes **20a**/**21a** with moderate enantioselectivity (Table 1, Entry 1). These results are comparable to those obtained with most Co^{II}−salen complexes tested in the literature under the same conditions.[19]



Scheme 2. Cyclopropanation of styrene with α-diazoacetates

Table 1. Asymmetric cyclopropanation of styrene using Co^{II}−salen complexes as catalysts

Entry	Catalyst[a]	Yield (%)[b]	**21a**/**20a**[c]	*ee* **21a** (%)[d][e]
1	Co−**1**	12	50:50	65
2	Co−**2**	10	50:50	60
3	Co−**3**	6	52:48	67
4	Co−**4**	24	54:46	59
5	Co−**5**	15	57:43	66

[a] Catalyst: 5 mol%; $T = 20$ °C; $t = 24$ h; solvent = THF; additive = *N*-methylimidazole (10 mol%). See ref.[19] for experimental details. [b] Overall isolated yield (**20a** + **21a**). [c] Determined by ^1H NMR analysis of the crude reaction products. [d] Determined by HPLC analysis of isolated **21a** (Daicel Chiralcel OD chiral column). [e] Configuration (1*R*,2*R*) as determined by comparison with an authentic sample.

The Co^{II} complexes of ligands **2**−**5**, which bear either electron-withdrawing or -donating substituents at the C5 and C5′ positions, were also examined to better assess the role of the perfluoroalkyl substituents. As shown in Table 1, these catalysts exhibited only minor variations relative to Co−**1**. Complex Co−**2** (Entry 2) with strong electron-withdrawing nitro groups behaved like Co−**1** with no *trans*/*cis* selectivity. Enhancing the electron-donor character of the substituents at C5 and C5′ slightly increased both reaction yields and *trans*−*cis* selectivities (Entries 3−5), which, however, remained low. The stereoelectronic characteristics of the C5 and C5′ substituents have little influence on the enantioselectivity of the reaction: with all the catalysts tested, (1*R*,2*R*)-**21a** was obtained as the major *trans*-enantiomer with *ee*'s in the range of 60−67%.

It was concluded that the low diastereoselectivity and reaction yield observed with Co−**1** cannot be ascribed to the presence of perfluoroalkyl substituents at the C5 and C5′ positions of the ligand. These preliminary experiments convinced us that fluorous Co^{II}−salen complexes are potentially useful catalysts for cyclopropanation reactions, but critical modifications to the ligand design are required to obtain catalytic activities comparable to those of Cu^I complexes of chiral fluorous bis(oxazoline) ligands.

Catalytic Activity of Cu^I Complexes: Catalytic systems based on combinations of bidentate chiral nitrogen ligands and Cu^I salts operate efficiently in the asymmetric cyclopropanation of styrene derivatives. Besides binaphthyldiimines and bis(ferrocenyl)diamine-based systems,[7,8] positive results have been obtained using enantiopure C_2-symmetric diimines and diamines derived from *trans*-1,2-diphenyl-1,2-ethanediamine and related compounds featuring a 1,2-cyclohexanediamine-like skeleton derived from sugars.[21,22]

The cyclopropanation of styrene (5 mol equiv.) with ethyl α-diazoacetate **19a** (1 mol equiv.) was first attempted under fluorous biphasic (FB) conditions identical to those previously reported in the case of F-box-catalysed reactions.[15] Ligand **8** (20 mol %) and Cu(OTf) (10 mol %) were stirred together in degassed perfluorooctane at 50 °C. After 30 minutes the solids had dissolved and the resulting solution was cooled to room temperature. After the addition of styrene, **19a** dissolved in dichloromethane was added dropwise over 10 h using a syringe pump. The biphasic mixture was stirred for a further 14 h. The upper organic layer containing the products and unchanged styrene was separated and the *cis*- and *trans*-cyclopropanes **20a**/**21a** were isolated by flash column chromatography (overall yield based on **19a** = 53%).

As shown in Table 2 (Entry 1), the *ee* of the major *trans*-(1*R*,2*R*)-**21a** isomer was only 11% and the *trans*/*cis* ratio close to 1:1. Such results are in agreement with those obtained in the FB cyclopropanation of styrene catalysed by F-box.

Further experiments showed that the nature of the Cu^I precursor strongly affects the outcome of the FB reaction. The use of $Cu(CH_3CN)_4BF_4$ (Entry 2) and $Cu(CH_3CN)_4PF_6$ (Entry 3) instead of Cu(OTf) led to increases in the reaction yields, the *trans*/*cis* ratios and significantly higher ee's for the major isomer (1*R*,2*R*)-**21a** (approx. 60%).

Table 2. Asymmetric cyclopropanation of styrene: optimisation of reaction conditions

Entry	$Cu^{I}X$[a]	Solvent	Yield (%)[b]	Time (h)	**21a/20a**[c]	*ee* **21a** (%)[d][e]
1	Cu(OTf)	C_8F_{18}/CH_2Cl_2	53	24	53:47	11
2	$Cu(CH_3CN)_4BF_4$	C_8F_{18}/CH_2Cl_2	72	24	67:33	61
3	$Cu(CH_3CN)_4PF_6$	C_8F_{18}/CH_2Cl_2	78	24	66:34	59
4[f]	$Cu(CH_3CN)_4PF_6$	C_8F_{18}/CH_2Cl_2	64	24	66:34	40
5	$Cu(CH_3CN)_4PF_6$	CH_2Cl_2	30	24	64:36	45
6	$Cu(CH_3CN)_4PF_6$	C_8F_{18}/CH_3CN	13	24	63:37	7
7	$Cu(CH_3CN)_4PF_6$	C_8F_{18}/CH_2Cl_2	77	1.5	67:33	62
8[g]	$Cu(CH_3CN)_4PF_6$	C_8F_{18}/CH_2Cl_2	5	1.5	67:33	43
9[h]	$Cu(CH_3CN)_4PF_6$	C_8F_{18}/CH_2Cl_2	97	1.5	82:18[i]	29[j]
10[k]	$Cu(CH_3CN)_4PF_6$	C_8F_{18}/CH_2Cl_2	53	1.5	64:36	13

[a] Ligand **8**: 20 mol %; $Cu^{I}X$: 10 mol %; $T = 20$ °C. See Expt. Sect. and text for experimental details. [b] Overall isolated yield for (**20a** + **21a**). [c] Determined by ^1H NMR analysis of the crude reaction products. [d] Determined by HPLC analysis of isolated **21a** (Daicel Chiralcel OD chiral column). [e] Configuration (1*R*,2*R*) as determined by comparison with an authentic sample. [f] Ligand **8**: 10 mol %; $Cu^{I}X$: 10 mol %. [g] $T = 0$ °C. [h] *tert*-Butyl α-diazoacetate (**19b**) was used. [i] **21b/20b**. [j] *ee* **21b**. [k] Ligand **8**: 1 mol %; $Cu^{I}X$: 0.5 mol %.

The ratio of the diamine to the copper is crucial, with a 2:1 ratio giving higher enantioselectivities than a 1:1 ratio (Entry 4). Kanemasa et al. observed the same behaviour in cyclopropanation reactions catalysed by non-fluorous diamines.[21] This was explained by a change in the pre-catalyst structure leading to a change in selectivity, however the change in structure when more diamine is used cannot be explained easily as these complexes are difficult to characterize. Our attempts to isolate and characterize the different fluorous copper species depending on the **8**/Cu^{I} ratio also failed.

The fluorous-tagged diamine **8** is better suited to a FB system as under homogeneous conditions (Entry 5) the copper complex is poorly soluble and therefore is less active. Solvents other than dichloromethane were also tested as the organic phase of the FB mixture, but disappointing results were obtained, as exemplified by the reaction in C_8F_{18}/CH_3CN (Entry 6).

Interestingly, there was no effect on the yield of the FB reaction when addition time was reduced to 60 min and the overall reaction time to 90 min, respectively (Entry 7 vs. Entry 3). Usually in homogeneous catalytic systems faster addition leads to increased diazoacetate self-coupling and a drop in the recovered yield of the cyclopropane.[23] As often observed in FB asymmetric catalysis, lowering the temperature had negative effects on the activity of the system (Entry 8). The complex prepared in situ at 50 °C partly precipitated as a waxy solid when the FB mixture was cooled to 0 °C and, as found in pure organic solvents (Entry 5), the catalytic activity dropped. Attempts to improve the enantioselectivity of the reaction by using more bulky diazoacetates, for example, *tert*-butyl α-diazoacetate **19b** did not work (Entry 9). The presence of the *tert*-butyl group significantly increases the *trans*/*cis* ratio as it makes the *cis* transition state sterically less favourable. However, the major *trans*-cyclopropane isomer (1*R*,2*R*)-**21b** was obtained with an *ee* of only 29%. Finally, lower catalyst to substrate loadings (Entry 10) led to lower enantioselectivities and yields, consistent with those previously observed using F-box catalysts.

Having optimised the catalytic system, the recycling ability of the catalyst under FB conditions was next examined (Table 3, Entries 1−3). The catalyst derived from ligand **8** was easily removed from the reaction mixture by simple phase-separation of the two immiscible organic and fluorous layers. The C_8F_{18} layer was washed twice with CH_2Cl_2 and used as such in a subsequent run. A drop in the enantioselectivity was observed in the second and, even

Table 3. Asymmetric cyclopropanation of styrene using C_2-symmetric bidentate N ligands

Entry	Ligand[a]	Solvent	Yield (%)[b]	**21a/20a**[c]	*ee* **21a** (%)[d]	Conf.
1	**8**	FB conditions[e]	77	67:33	62	(1*R*,2*R*)
2[f]		FB conditions	78	65:35	46	
3[f]		FB conditions	43	61:39	8	
4	**9**	CH_2Cl_2	67	66:34	52	(1*R*,2*R*)
5	**6**	FB conditions	43	60:40	6	(1*S*,2*S*)
6	**7**	CH_2Cl_2	65	66:43	19	(1*S*,2*S*)
7[g]	(*S*,*S*)-**10**	CH_2Cl_2	67	58:42	16	(1*R*,2*R*)
8	(*R*,*R*)-**11**	CH_2Cl_2	57	58:42	11	(1*S*,2*S*)

[a] Ligand: 20 mol %; $Cu(CH_3CN)_4PF_6$: 10 mol %; $T = 20$ °C; $t = 90$ min. See Expt. Sect. and text for experimental details. [b] Overall isolated yield for (**20a** + **21a**). [c] Determined by ^1H NMR analysis of the crude reaction products. [d] Determined by HPLC analysis of isolated **21a** (Daicel Chiralcel OD chiral column). [e] Fluorous biphasic conditions: perfluorooctane/CH_2Cl_2, 1:1 (v/v). [f] Recycling experiment: the fluorous layer recovered from the previous run was used (see Expt. Sect.). [g] $t = 24$ h.

more clearly, in the third run. This was due to the partial decomposition of the chiral ligand, as evidenced by ^1H and ^{19}F NMR analysis of the residue obtained after decomplexation of the ligand with an aqueous solution containing cyanide ions carried out on the recovered fluorous layer.

In the case of the fluorous diamines derived from *trans*-1,2-cyclohexanediamine, the presence of perfluoroalkyl chains does not interfere to any significant extent with the formation of the chiral catalytic species. Indeed, homogeneous reactions run in the presence of diamine **9**, which features bromine atoms at the C3, C3′, C5 and C5′ positions, gave slightly lower activity and selectivity than those obtained using the fluorous diamine **8** in a FB system (Entry 4). There was a major difference between the fluorous diamine **8** and the corresponding diimine ligand **6**, the latter showing lower enantioselectivity and the opposite enantiomer was favoured (Entry 5). The same behaviour was observed when the reaction was run in the presence of the non-fluorous diimine **7** (Entry 6). This is due to the diamines and diamines having different modes of coordination. Indeed, some C_2-symmetric diamines are able to create a narrow five-membered *transoid* chiral pocket around the copper, enabling efficient enantioface discrimination by the approaching olefin.[24] As experimentally confirmed in the case of diamino ligands derived from α-D-glucose, enantiomerically pure *trans*-cyclohexanediamine-like structures are able to retain their C_2-symmetry upon coordination to the copper ion, giving rise to such a chiral pocket.[22] Diamine **8** seems to work similarly, whereas the light-fluorous diamines (*S*,*S*)-**10** (Entry 7) and (*R*,*R*)-**11** (Entry 8) are possibly too flexible to generate a stereodifferentiating environment around the reactive metal center.

Conclusions

Enantiopure α-diamines and diimines possessing C_2 symmetry are particularly attractive in asymmetric synthesis and organometallic asymmetric catalysis. In this work, enantiopure fluorous derivatives of *trans*-1,2-diaminocyclohexane and two new light-fluorous C_2-symmetric diamines derived from 1-phenylethylamine **12** have been used as ligands in the asymmetric cyclopropanation of styrene promoted by Co^{II} or Cu^{I}. We have shown that neither the introduction of perfluoroalkyl substituents in the ligand structure nor the use of FB conditions has a detrimental effect on the chemical yields and selectivities. This is in contrast with that observed for cyclopropanations carried out in the presence of fluorous bis(oxazolines).[15] FB conditions proved to be superior to homogeneous conditions when relatively rigid diamines derived from *trans*-1,2-diaminocyclohexane were tested in Cu^{I}-catalysed reactions. Under optimised FB reaction conditions the copper complex of diamine **8** afforded promising results (yield = 77%, *trans*/*cis* = 67:33, *ee trans* isomer = 62%) and could be quickly separated from the products by simply decanting the fluorous phase. However, the issue of catalyst recycling remains open, since partial decomposition of the ligand occurs.

The application of enantiopure fluorous diamines in other catalytic reactions is currently in progress in our laboratories.

Experimental Section

General Remarks: Solvents were purified by standard methods and dried if necessary, except for perfluorocarbons that were used as received. All commercially available reagents were used as received. Co^{II}−salen complexes **1**−**5**,[19,20,25,26] diimines **6**[18] and **7**,[27] and diamine **8**[18] were prepared as described in the literature. Melting points (uncorrected) were determined using a capillary melting point apparatus Büchi SMP-20. Optical rotations were measured with a Perkin−Elmer 241 polarimeter in a 1-dm cell at 20 °C. ^1H (300 MHz), ^{13}C (75.4 MHz) and ^{19}F NMR (282 MHz) spectra were recorded in $CDCl_3$ with a Bruker AC 300 spectrometer with tetramethylsilane (δ = 0 ppm), $CDCl_3$ (δ = 77 ppm) and $CFCl_3$ (δ = 0 ppm) as internal standards, respectively. Mass spectrometry was performed with the following instruments: Electrospray ionization (ESI) mass spectrometry: Bruker APEX II ICR-FTMS mass spectrometer (source: nano ESI at 45°); matrix-assisted laser desorption ionisation-time of flight (MALDI-TOF) mass spectrometry: TOF-Spec-2E high performance mass spectrometer. Cyclopropanation reactions catalysed by Co^{II}−salen complexes were carried out as described in ref.[19]. The *ee* of compound **21a** was determined by HPLC on a chiral stationary phase (column: Chiracel OD; eluent: hexane/*i*PrOH, 99:1; flow rate: 1 mL·min^{-1}; λ = 210 nm; t_R of (1*R*,2*R*)-**21*a*** = 6.65 min; t_R of (1*S*,2*S*)-**21*a*** = 10.31 min). The absolute configurations of the enantiomers were determined by comparison of the retention times with those of authentic samples. Abbreviations used in this article: R^f for perfluoroalkyl.

(1*R*,2*R*)-*N*,*N*′-Bis(3,5-dibromobenzyl)cyclohexane-1,2-diamine (9): In a flame-dried Schlenk tube the diimine **7** (1.50 g, 2.46 mmol) was dissolved in dry CH_2Cl_2 (25 mL). $NaBH(OAc)_3$ (1.56 g, 7.38 mmol) was added followed by CH_3COOH (0.5 mL). The mixture was stirred at room temp. for 24 h. Aqueous 10% NaOH (5 mL) was added and the reaction stirred for a further 30 min. The reaction was extracted three times with CH_2Cl_2 and the combined organic layers were washed with H_2O, brine and dried with Na_2SO_4. The solvent was evaporated to leave a brown sticky residue, which was purified by column chromatography (silica gel, hexane/EtOAc, 1:1) to yield **9** (1.37 g, 91%) as a white solid. $[\alpha]_D^{20}$ = +52 (*c* = 0.1, CH_2Cl_2). ^1H NMR (300 MHz, $CDCl_3$): δ = 0.90−1.40 (m, 4 H), 1.60−1.80 (m, 2 H), 2.00−2.30 (m, 4 H), 3.63 (d, *J* = 21 Hz, 2 H), 3.87 (d, *J* = 21 Hz, 2 H), 7.42 (d, *J* = 2.6 Hz, 2 H), 7.54 (t, *J* = 2.6 Hz, 4 H) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 24.9 (CH_2CH_2CHN), 31.5 (CH_2CH_2CHN), 49.9 (CH_2CH_2CHN), 70.0 ($ArCH_2N$), 122.9 (arom. quat. C), 129.8 (arom.), 132.5 (arom. C), 145.1 (arom. quat. C) ppm. HRMS (ESI): *m*/*z* = 610.8503 $[M + H]^+$; calcd. for $[C_{20}H_{23}Br_4N_2]^+$ 610.8554.

3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-Heptadecafluoro-*N*-[(1*S*)-1-phenylethyl]-1-decanamine [(*S*)-15]: A mixture of (1*S*)-1-phenylethylamine (*S*)-**12** (1.69 g, 13.9 mmol), K_2CO_3 (2.07 g, 15 mmol) and 3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluorodecyl iodide (**13**, 4.01 g, 7.0 mmol) in dry CH_3CN (30 mL) was refluxed with stirring under nitrogen for 24 h. After filtration of the solid the solvent was evaporated, and the product was purified by column chromatography (silica gel, hexane/EtOAc, 7:3) to yield the title compound (2.1 g, 54%) as a yellow oil. $[\alpha]_D^{20}$ = −16.2 (*c* = 0.5, CH_2Cl_2). ^1H NMR (300 MHz, $CDCl_3$): δ = 1.32 (d, *J* = 6.6 Hz, 3 H, CH_3), 1.40 (br. s, 1 H, N*H*), 2.11−2.41 (m, 2 H, CH_2R^f),

2.69−2.90 (m, 2 H, CH_2NH), 3.78 (q, J = 6.6 Hz, 1 H, CH), 7.21−7.38 (m, 5 H, arom. C) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 24.3 (*C*H$_3$), 31.6 (t, $^2J_{C,F}$ = 21.5 Hz, R^f*C*H$_2$), 39.2 (t, $^3J_{C,F}$ = 3.8 Hz, NH*C*H$_2$), 58.3 (*C*H), 107.5−122.3 (m, C_8F_{17}), 126.4, 127.1, 128.6, 145.0 (arom. C) ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = −126.7 (br. s, 2 F), −124.2 (br. s, 2 F), −123.7 (br. s, 2 F), −122.8 to −121.7 (m, 6 F), −114.2 (br. s, 2 F), −81.6 to −81.2 (m, 3 F, CF_3) ppm. HRMS (CI): m/z = 568.0914 [M + H]$^+$; calcd. for $[C_{18}H_{15}F_{17}N]^+$ 568.0933.

***N*^{1},*N*^{2}-Bis(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluorodecyl)-*N*^{1},*N*^{2}-bis[(1*S*)-1-phenylethyl]ethanediamide [(*S*,*S*)-17]:** Oxalyl chloride (0.12 mL, 1.3 mmol) was added dropwise to a solution of the amine (*S*)-**15** (1.36 g, 2.4 mmol) and Et_3N (0.5 mL, 3.6 mmol) in dry CH_2Cl_2 (20 mL) at 0 °C. The mixture was stirred under nitrogen for 6 h. The organic layer was washed with water (20 mL), a saturated $CuSO_4$ solution (20 mL) and then dried with $MgSO_4$. The solvents were evaporated to give the title compound as a mixture of four rotamers in a ratio of 2:2:1:0.5 (white solid, 0.74 g, 53%), which was used in the next step without further purification.[28] ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.74 (d, J = 7.1 Hz, 6 H, CH_3), 2.35−2.60 (m, 4 H, CH_2R^f), 3.27−3.56 (m, 4 H, CH_2NH), 5.49 (q, J = 6.6 Hz, 2 H, CH), 7.30−7.47 (m, 10 H, arom. C) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 17.5 (*C*H$_3$), 34.4, (t, $^2J_{C,F}$ = 24.9 Hz, R^f*C*H$_2$), 36.7 (N*C*H$_2$), 51.9 (*C*H), 108.0−120.3 (m, C_8F_{17}), 127.2, 128.5, 128.7, 128.9, 129.0, 129.1 (arom. C), 138.2 (arom. quat. C), 164.9 (*C*=O) ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = −127.5 to −126.1 (m, 4 F), −124.9 to −123.1 (m, 4 F), −123.5 to −120.9 (m, 16 F), −115.9 to −114.9 (m, 4 F), −81.8 to −81.1 (m, 6 F, CF_3) ppm. HRMS (MALDI-TOF): m/z = 1211.1008 [M + Na]$^+$; calcd. for $[C_{38}H_{26}F_{34}N_2O_2Na]^+$ 1211.1004.

***N*^{1},*N*^{2}-Bis(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluorodecyl)-*N*^{1},*N*^{2}-bis[(1*S*)-1-phenylethyl]-1,2-ethanediamine [(*S*,*S*)-10]:** A solution of (*S*,*S*)-**17** (0.74 g, 0.63 mmol) in dry THF (5 mL) was added by syringe to a suspension of LAH (0.12 g, 3.1 mmol) in THF (5 mL) at 0 °C. The reaction mixture was stirred under nitrogen for 12 h at room temp. The excess of hydride was then destroyed by adding water dropwise until white crystals were formed. The suspension was then filtered and the solid washed with diethyl ether. The combined organic layers were collected and dried with $MgSO_4$. The solvents were evaporated to afford compound (*S*,*S*)-**10** as a white solid that was recrystallised from Et_2O/MeOH (0.41 g, 56%). $[\alpha]_D^{20}$ = +6.47 (c = 0.14, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.22 (d, J = 6.7 Hz, 6 H, CH_3), 1.92−2.13 (m, 4 H, CH_2R^f), 2.26−2.45 (m, 4 H, CH_2CH_2), 2.55−2.83 (m, J = 7.8 Hz, 4 H, R^{f}CH_2NH), 3.64 (q, J = 6.7 Hz, 1 H, CH), 7.11−7.26 (m, 10 H, arom. C) ppm. ^{13}C NMR (75.4, $CDCl_3$): δ = 16.9 (*C*H$_3$), 29.5 (t, $^2J_{C,F}$ = 20.4 Hz, R^f*C*H$_2$), 42.4 (NH*C*H$_2$), 49.6 (NH*C*H$_2$*C*H$_2$NH), 60.1 (*C*H), 105.0−122.3 (m, C_8F_{17}), 127.05, 127.5, 128.2 (arom. C), 143.5 (arom. quat. C) ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = −126.8 to −126.5 (m, 4 F), −124.2 to −123.8 (m, 4 F), −123.3 (br. s, 2 F), −122.7 to −122.1 (m, 12 F), −114.8 to −114.4 (m, 4 F), −81.3 (t, $^3J_{F,F}$ = 10.3 Hz, 6 F, CF_3) ppm. HRMS (MALDI TOF): m/z = 1161.1932 [M + H]$^+$; calcd. for $[C_{38}H_{31}F_{34}N_2]^+$ 1161.1943.

4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,11-Heptadecafluoro-*N*-[(1*R*)-1-phenylethyl]-1-undecanamine [(*R*)-16]: A mixture of (1*R*)-1-phenylethylamine (*R*)-**12** (0.37 g, 3.0 mmol), K_2CO_3 (1.38 g, 10 mmol) and 4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,11-heptadecafluoroundecyl iodide **14** (1.82 g, 3.1 mmol) in dry CH_3CN (20 mL) was refluxed with stirring under nitrogen for 8 h. The suspension was cooled to room temperature and diluted with Et_2O (40 mL). After filtration of the inorganic salts, the liquid layer was washed with H_2O (2 × 15 mL), saturated aqueous NH_4Cl (15 mL) and dried with $MgSO_4$. The solvent was evaporated under vacuum and the residue was purified by flash column chromatography (silica gel, hexane/EtOAc, 4:1) to yield (*R*)-**16** (1.22 g, 70%) as a pale yellow oil. $[\alpha]_D^{20}$ = +13.2 (c = 0.2, Et_2O). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.45 (d, J = 6.6 Hz, 3 H, CH_3), 1.65−1.76 (m, 2 H, R^f−CH_2−CH$_2$), 1.98−2.20 (m, 2 H, R^f−CH$_2$−CH_2), 2.43−2.63 (m, 2 H, CH_2−NH), 3.73 (q, J = 6.6 Hz, 1 H, CH), 7.23−7.35 (m, 5 H, arom. C) ppm. ^{13}C NMR (75.4, $CDCl_3$): δ = 21.1 (*C*H$_3$), 24.4 (CH$_2$−*C*H$_2$−CH$_2$), 28.8 (t, $^2J_{C,F}$ = 21.9 Hz, R^f−*C*H$_2$), 46.4 (NH−*C*H$_2$), 58.4 (*C*H), 107.5−122.3 (m, C_8F_{17}), 126.1, 127.9, 128.6 (arom. C), 145.5 (arom. quat. C) ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = −126.5 (br. s, 2 F), −123.9 to −123.1 (m, 4 F), −123.3 (br. s, 6 F), −114.7 (br. s, 2 F), −81.2 (br. s, 3 F, CF_3) . HRMS (ESI): m/z = 582.1129 [M + H]$^+$; calcd. for $[C_{19}H_{17}F_{17}N]^+$ 582.1089.

***N*^{1},*N*^{2}-Bis(4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,11-heptadecafluoroundecyl)-*N*^{1},*N*^{2}-bis[(1*R*)-1-phenylethyl]ethanediamide [(*R*,*R*)-18]:** Amine (*R*)-**16** (1.15 g, 1.97 mmol) and Et_3N (0.39 mL, 2.81 mmol) were dissolved in dry Et_2O (20 mL) and the solution was cooled to 0 °C. Oxalyl chloride (0.08 mL, 0.94 mmol) dissolved in dry Et_2O was added dropwise to the solution. The solution was stirred at 0 °C for one hour then warmed to room temperature and left stirring overnight. The reaction was filtered and the filtrate washed with water and brine and dried with Na_2SO_4. The diethyl ether was removed under vacuum and the crude product purified by column chromatography (silica gel, hexane/EtOAc, 4:1) to afford the title compound as a mixture of four rotamers in a ratio of 2:1:1:0.2 (colourless oil, 0.76 g, 67%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.56−2.03 (m, 14 H, CH_3 and R^f−CH_2−CH_2), 3.07−3.31 (m, 4 H, NCH_2), [5.04 (q, J = 7.2 Hz), 5.15 (q, J = 7.2 Hz), 5.79 (q, J = 7.2 Hz), 5.92, (q, J = 7.2 Hz)] (ratio = 1:2:0.2:1, 2 H, PhCH), 7.27−7.42 (m, 10 H, arom. C) ppm. ^{13}C NMR (75.4, $CDCl_3$): δ = 16.9, 17.1, 18.2, 18.7 (*C*H$_3$), 19.9, 21.9, 22.2 (R^{f}CH$_2$*C*H$_2$), 28.8, 29.1 (t, $^2J_{C,F}$ = 22.9 Hz, R^f*C*H$_2$), 41.3, 41.6, 44.4, 44.8 (N*C*H$_2$), 52.0, 52.2, 56.4, 56.6 (*C*H), 108.0−120.3 (m, C_8F_{17}), 127.7, 127.8, 127.9, 128.5, 128.7, 128.8, 129.2 (arom. C), 139.0, 139.3, 139.9 (arom. quat. C), 165.4, 165.6 (*C*=O) ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = −126.6 (br. s, 4 F), −124.0 (br. s, 4 F), −123.2 (br. s, 4 F), −122.4 (br. s, 12 F), −114.8 to −114.3 (m, 4 F), −81.3 to −81.1 (m, 6 F, CF_3) ppm. HRMS (ESI): m/z = 1239.1742 [M + Na]$^+$; calcd. for $[C_{40}H_{30}F_{34}N_2O_2Na]^+$ 1239.1661.

***N*^{1},*N*^{2}-Bis(4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,11-heptadecafluoroundecyl)-*N*^{1},*N*^{2}-bis[(1*R*)-1-phenylethyl]ethanediamine [(*R*,*R*)-11]:** LAH (35 mg, 0.91 mmol) was suspended in dry THF (10 mL) and cooled to 0 °C. Ethanediamide (*R*,*R*)-**18** (0.55 g, 0.45 mmol) was dissolved in dry THF (10 mL) and added dropwise to the suspension. The reaction was stirred for 30 minutes at 0 °C and then hydrolysed by the dropwise addition of water until a white precipitate formed. The reaction was filtered and the filtrate dried with Na_2SO_4. The solvent was evaporated to leave a residue which was purified by column chromatography (silica gel, hexane/EtOAc, 4:1). Finally the crude product was recrystallised from Et_2O/MeOH to give pure (*R*,*R*)-**11** as a white solid (80 mg, 15%). M.p. 64−66 °C. $[\alpha]_D^{20}$ = −1 (c = 0.2, Et_2O). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.27 (d, J = 6.7 Hz, 6 H, CH_3), 1.51−1.63 (m, 4 H), 1.83−2.08 (m, 4 H), 2.27−2.51 (m, 8 H), 3.74 (q, J = 6.7 Hz, 2 H, CH), 7.18−7.30 (m, 10 H, arom. C) ppm. ^{13}C NMR (75.4, $CDCl_3$): δ = 16.3 (*C*H$_3$), 19.2 (R^{f}CH$_2$*C*H$_2$), 29.0 (t, $^2J_{C,F}$ = 21.5 Hz, R^f−*C*H$_2$), 49.9 (R^{f}CH$_2$CH$_2$*C*H$_2$N), 50.2 (N*C*H$_2$*C*H$_2$N), 60.0 [Ph*C*H(CH$_3$)N], 105.0−122.3 (m, R^f), 127.2, 128.0, 128.4 (arom. C), 144.3 (arom. quat. C) ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = −126.6 (br. s, 4

F), −124.0 (br. s, 4 F), −123.2 (br. s, 4 F), −122.4 (br. s, 12 F), −114.5 (br. s, 4 F), −81.2 (t, $^3J_{F,F}$ = 10.5 Hz, 6 F, CF_3) ppm. HRMS (ESI): *m/z* = 1189.2271 [M + H]$^+$; calcd. for $[C_{40}H_{35}F_{34}N_2]^+$ 1189.2256.

Cyclopropanation of Styrene: The following reactions carried out with ligands **8** and **9** are illustrative of FB and homogeneous cyclopropanation, respectively.

Fluorous Biphasic Conditions: Diamine **8** (118 mg, 0.06 mmol) and $Cu(CH_3CN)_4PF_6$ (11 mg, 0.03 mmol) were stirred together in degassed perfluorooctane (2 mL) at 50 °C. After 30 minutes the solid had dissolved and the solution had become dark blue. The reaction mixture was cooled to room temperature and styrene (0.16 mL, 1.5 mmol) was added; the mixture was stirred for a further 5 minutes. Ethyl diazoacetate **19a** (0.034 mL, 0.3 mmol) dissolved in degassed CH_2Cl_2 (2 mL) was added dropwise over one hour using a syringe pump. After its addition the reaction mixture was stirred for a further 30 minutes, after which stirring was stopped to allow the two phases to separate under nitrogen. The dichloromethane layer containing the products was removed and the fluorous phase was stirred with dichloromethane (2 mL) for 5 minutes and then this too was removed. More styrene was added to the fluorous layer and the reaction repeated as before (Table 3). The combined CH_2Cl_2 layers were evaporated to leave a residue, an aliquot of which was analysed by ^{1}H NMR to determine the relative amounts of the two diastereoisomers. The residue was purified by flash column chromatography (silica gel, hexane/EtOAc, 95:5) to give a mixture of **20a** and **21a**. Pure **21a** for HPLC determination of the *ee* was obtained by flash column chromatography of the **20a**/**21a** mixture (silica gel, hexane/EtOAc, 95:5). R_f (**21a**) = 0.22, R_f (**20a**) = 0.16.

Homogeneous Conditions: Diamine **9** (37 mg, 0.06 mmol) and $Cu(CH_3CN)_4PF_6$ (11 mg, 0.03 mmol) were stirred together in degassed CH_2Cl_2 (2 mL) for 10 minutes at room temperature until the reaction became a deep blue colour. Styrene (0.16 mL, 1.5 mmol) was added to the reaction, which was stirred for a further 5 minutes. Ethyl diazoacetate **19a** (0.034 mL, 0.3 mmol) dissolved in CH_2Cl_2 (2 mL) was added dropwise over one hour using a syringe pump. After its addition the reaction was stirred for a further 30 minutes, after which the volatiles were evaporated under vacuum to leave the crude products, which were separated and analysed as described above.

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