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Immobilization of Diphenylamine-Linked Bis(oxazoline) Ligands and Their Application in the Asymmetric Friedel–Crafts Alkylation of Indole Derivatives with Nitroalkenes

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A diphenylamine-linked bis(oxazoline) ligand with *trans*-diphenyl substitution on the oxazoline rings has been immobilized onto one- to three-generation Fréchet-type dendrimers and a C_3-symmetric core structure. The catalytic activities and enantioselectivities of these new ligands were tested in the asymmetric Friedel–Crafts alkylation reactions of indole derivatives with nitroalkenes. The two types of immobilized ligands exhibited similar enantioselectivities and substrate compatibilities to the free ligand *trans*-DPBO we reported previously. No dendrimer effect was observed in the kinetic investigation of the Fréchet-type dendrimer-immobilized ligands. The in situ recycling of the catalysts was also tested to illustrate the effect of reducing catalyst loading and the efficiency of our system.

Introduction

During the past few decades, the progress in homogeneous asymmetric catalysis has changed the state-of-the-art of organic chemistry.[1] More and more chiral products such as drug intermediates and materials can be obtained with high efficiency through the use of chiral coordination catalysts or organocatalysts. However, the wide-spread application of asymmetric catalysis on an industrial scale is still limited due to the relatively high cost of the chiral sources used in ligand preparation, high catalyst loading (1–10 mol-% in most cases) and contamination of the products with heavy metal elements leached from the catalysts. To overcome the drawbacks of homogeneous asymmetric catalytic processes, the development of recovery technology for homogeneous catalysts, which includes the synthesis of recoverable catalysts immobilized on suitable supporting materials and the design of reactors, has attracted the attention of chemists both in academia and in industry laboratories.[2]

On the basis of the number of phases involved in the system, the recovery strategies can be classified into two categories. The first one is the immobilization of catalysts onto insoluble materials to generate a heterogeneous system and the use of simple filtration for catalyst recovery. The insoluble materials used can be polymers functionalized with active groups for the ligation of catalysts[2] or inorganic materials such as zeolites and molecular sieves.[3] The recently developed catalyst immobilization by the self-assembly of ligands, which have been defined as self-supported catalysts, can also be classified into this category.[4,5] Compared with the original homogeneous systems, the heterogeneous systems often show lower reactivity and sometimes lower selectivity as a result of the slow diffusion of substrates to the interface to which the catalysts are linked and unfavourable interactions between the supporting materials and the active catalytic centres.

The second category is the immobilization of catalysts onto soluble macromolecules to maintain the homogeneous system. This strategy has all the advantages of homogeneous systems and the recovery can be facilitated by the addition of another solvent for the catalysts or by using a membrane reactor (also known as nanofiltration technology).[6] The soluble macromolecules used can be poly(ethylene glycols) (PEGs) of different molecular weights and highly branched dendrimer molecules of different sizes. In contrast to PEGs, which are a mixture of polymers of different chain lengths,[7] dendrimers have well-defined structures as well as accurate molecular weights. As one important type of macromolecules, the application of dendrimers in catalyst immobilization has been developed by scientists all over the world.[8] The catalytic centres can be located at the core of the dendrimer (type I) or on the shell (type II), as illustrated in Figure 1. The effects of dendrimer structure (chemical constitution and mode of linking), generation and the position of the active catalytic centres have been investigated and summarized. In some homogeneous catalytic systems, especially the core-modified dendrimers, an

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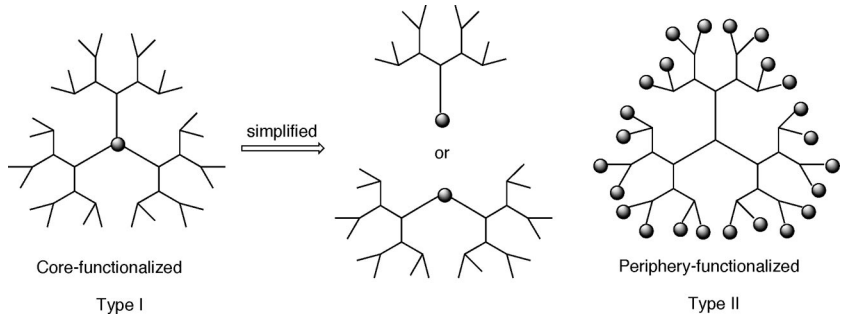


Figure 1. Type I and II dendrimer-immobilized catalysts.

improvement in reactivity can be observed with increasing size and generation of the dendritic catalysts. Such a phenomenon, known as the "positive dendrimer effect", can be attributed to the formation of a microenvironment, which improves the substrate concentration surrounding the catalytic centre (concentrator effect), prevents product inhibition (catalytic pump) and provides better stabilization of the transition state.[9,10]

The diphenylamine-linked bis(oxazoline) ligands reported by Guiry and co-workers[11] and ourselves[12] have been successfully applied in the asymmetric Henry reaction of α-keto esters,[12a,12b] the asymmetric Nozaki–Hiyama–Kishi reaction of aldehydes,[11b,11d] the asymmetric Michael addition of nitroethane to nitroalkenes,[12c] the asymmetric Friedel–Crafts alkylation of different electron-rich heteroaromatics with nitroalkenes[11c,12d–12f] and the asymmetric hydrosilylation of prochiral ketones.[13] Some investigations have focused on the modification of the electronic effect,[12g] the rigidity of the ligand skeleton[12g] and the effect of the ligands without C_2 symmetry.[11c] As a rational extension of our project on the application and modification of diphenylamine-derived chiral ligands, we hoped to facilitate the immobilization of ligands onto dendritic macromolecules in both type I and II fashions and to investigate the effect of the dendrimer structure on the catalytic activity and enantioselectivity, which is important for the further investigation of catalyst recovery in the membrane reactor system. Herein, we would like to document our recent research results.

Results and Discussion

At the beginning of the type I ligand immobilization, we had to choose an appropriate dendrimer system. Because our ligands are usually used in non-polar solvents such as toluene (optimized solvent for asymmetric Friedel–Crafts alkylation), the Fréchet-type dendrimer composed of a phenyl benzyl ether substructure, which was first reported by Fréchet and co-workers in 1990,[14,15] becomes the proper choice because of its good solubility in toluene and inert nature. On the basis of this choice, we designed the ligand structure illustrated in Figure 2. The diphenylamine skeleton was linked to the dendrimer fragment through appropriate linkers, such as an alkyne-based structure, triazole from a click cycloaddition and ether. All the designed linkers were tested in the synthesis of the ligands (Figure 3).

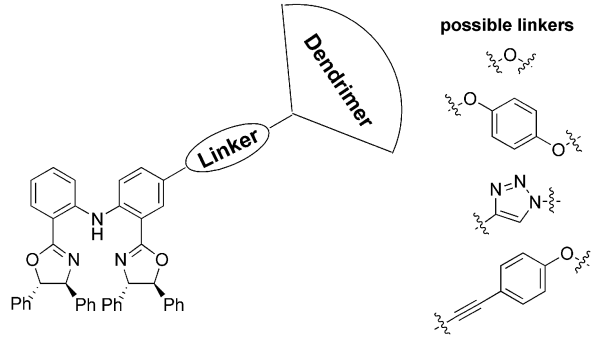


Figure 2. Design of type I immobilized catalysts.

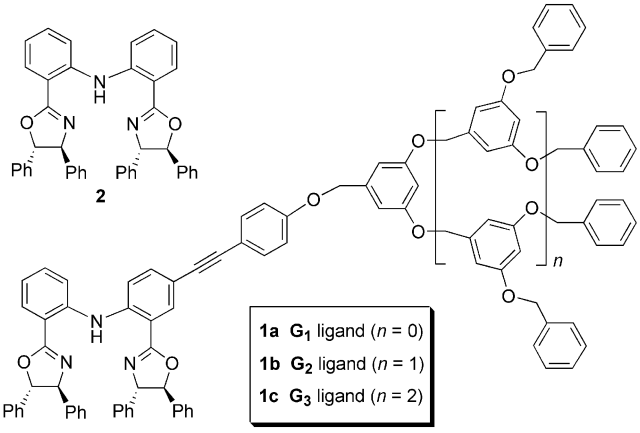
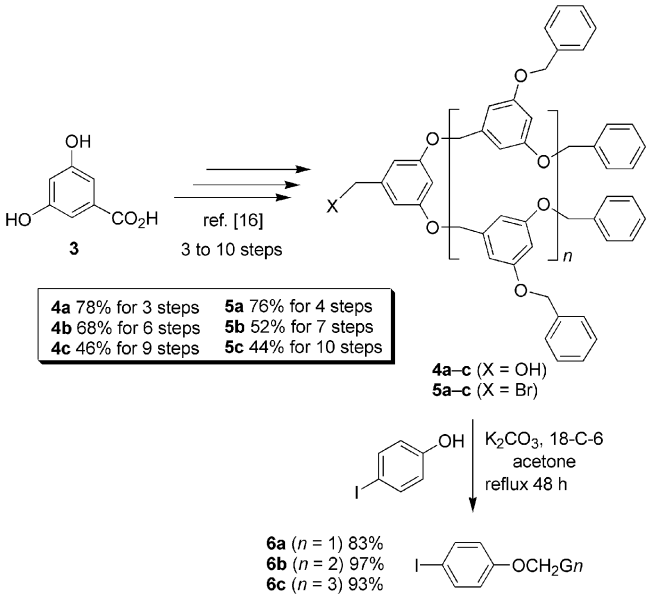


Figure 3. Diphenylamine-linked bis(oxazoline) ligands immobilized on the Fréchet-type dendrimers and the free ligand *trans*-DPBO (**2**).

The desired $\mathbf{G_{1-3}}$ alcohols **4a**–**c** and benzyl bromides **5a**–**c** were synthesized easily from 3,5-dihydroxybenzoic acid (**3**) in three to ten steps in high yields following literature procedures (Scheme 1).[16] To facilitate the ligation between the ligand part and the dendrimer, a ligation site has to be introduced onto the diphenylamine skeleton. Because of the potential versatile transformations of aryl bromides and iodides, we tested the monohalogenation reaction. To avoid the possible oxidation of the oxazoline segment and the

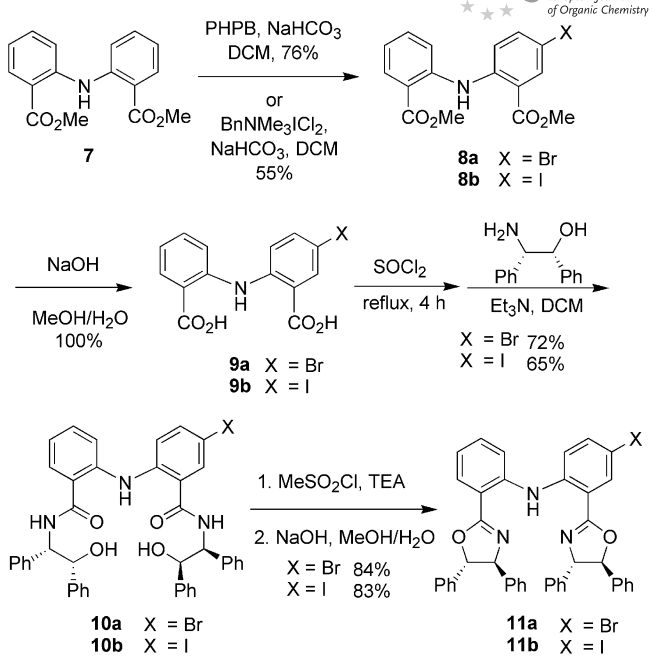
halogenation of the phenyl groups on the oxazoline ring, the halogenation was conducted before the oxazoline formation. After several attempts, the monobromination and -iodination products of dimethyl diphenylamine-2,2′-dicarboxylate (**7**) were obtained in acceptable yields. The selection of the proper halogenation reagent was critical for the successful transformation.[17] Other reagents such as bromine, iodine, NBS, $KBr/(NH)_2MoO_4{\cdot}H_2O$ did not give any desired product. From the monosubstituted esters, the ligands **11a/b** with *trans*-diphenyl substitution on the oxazoline rings (the optimized ligand structure in asymmetric Friedel–Crafts reaction[12e,12f]) were synthesized by saponification of the ester, acyl chloride formation, β-hydroxyamide formation and $MeSO_2Cl$-mediated oxazoline ring-closure (Scheme 2).



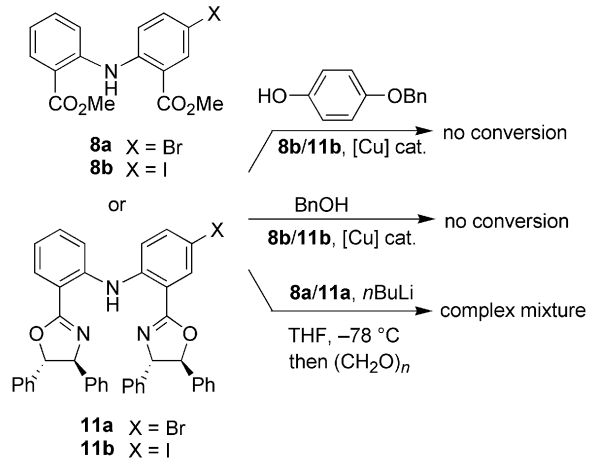
Scheme 1. Synthesis of the dendrimer segments.

Next we tried to introduce a hydroxy group (alcohol or phenol) onto the ligand by the appropriate transformation of the bromine or iodine atom (Scheme 3). To our disappointment, the *n*-BuLi/paraformaldehyde process did not give the hydroxymethyl-derived ligand and neither did the Ullmann-type coupling of either of the Br/I-substituted esters and ligands with benzyl alcohol or 4-benzyloxyphenol show significant conversion at high temperature even after a long reaction time. Such low reactivity may be attributed to the coordination of the ester group or oxazoline to the Cu centre, which deactivates the catalyst.

A similar phenomenon was also observed in our second attempt to introduce the alkynyl group by Sonogashira coupling of the Br/I-substituted ligands. When the reaction was conducted under common conditions using $[Pd(PPh_3)_2Cl_2]$/CuI as catalyst, no conversion was observed because of the deactivation of CuI by the oxazoline fragment. The desired product **13** was obtained in high yield only when the copper-free Sonogashira coupling condition reported by Yi and Hua[18] was used. The application of piperidine as base was critical for the successful coupling reaction as it coordinates

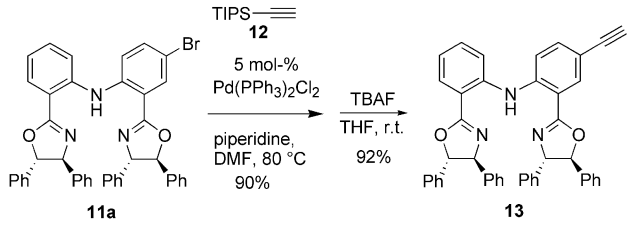


Scheme 2. Synthesis of the Br/I-substituted bis(oxazoline) ligands.



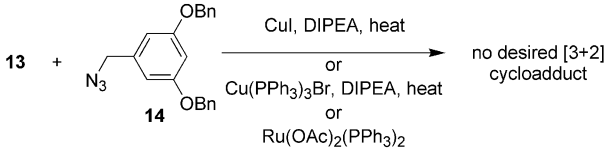
Scheme 3. Attempts to introduce the hydroxy group onto diphenylamine skeleton.

to the Pd centre as a ligand.[19] Because of the easy preparation and good reactivity of the Br-substituted ligand **11a** in the coupling reaction, the reaction of the I-substituted ligand **11b** was not examined (Scheme 4).



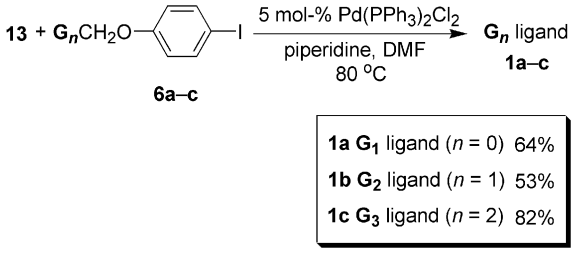
Scheme 4. Copper-free Sonogashira coupling of the Br-substituted ligand **11a** with alkyne **12**.

With the alkynyl-substituted ligand **13** in hand, we tested the click [3+2] cycloaddition with the known azide **14**[20] derived from the G_1 bromide (Scheme 5). Both the Cu^I and Ru^{II} catalysts[21] gave very low conversions of the alkyne at both high and low temperatures, whereas heating the alkyne and azide in toluene without a catalyst led to an inseparable mixture.



Scheme 5. Attempts at the click [3+2] cycloaddition of ligand **13** and azide **14**.

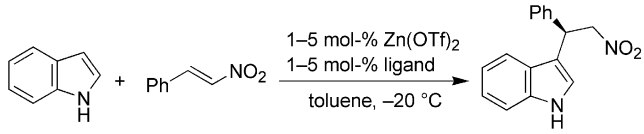
As a result of the success we achieved in the copper-free Sonogashira coupling reaction in the presence of the bis(oxazoline) segment, we turned to the last alkyne-based linker structure (Scheme 6). The G_{1-3} bromides **5a**–**c** were derivatized to the corresponding aryl iodides **6a**–**c** by S_N2 reaction with 4-iodophenol in the presence of K_2CO_3 and crown ether (Scheme 1). Fortunately, the dendrimer-derived aryl iodides coupled with alkyne **13** smoothly under the same reaction conditions used for the synthesis of **13** (Scheme 4). The desired ligands **1a**–**c** (Figure 3) were obtained in moderate-to-good yields after purification by silica gel column chromatography.



Scheme 6. Synthesis of immobilized ligands by copper-free Sonogashira coupling.

With the desired ligands in hand, their catalytic activities were investigated by using the asymmetric Friedel–Crafts alkylation of indole **15a** with β-nitrostyrene (**16a**) as a model system.[22] The G_{1-3} catalysts were generated in situ from **1a**–**c** and $Zn(OTf)_2$ in toluene, as we reported before.[12d–12f] The catalytic reaction was conducted at –20 °C for 24–72 h, corresponding to different catalyst loading. As shown in Table 1, the dendrimer immobilized ligands **1a**–**c** gave excellent yields and enantioselectivities when 5 mol-% catalysts were used (entries 1–3). When the loading of G_3 ligand **3c** was reduced to 2.5 or 1 mol-% (entries 4 and 5), the enantioselectivity was not affected but the reaction rate decreased significantly. For comparison, the free optimized ligand *trans*-DPBO (**2**) was also tested at 1–5 mol-% loading (entries 6–8). No significant variation in enantioselectivity was observed with increasing dendrimer generation and lower reaction rates were observed in the immobilized catalyst system.

Table 1. Catalytic activities of immobilized ligands in asymmetric Friedel–Crafts alkylation of indole with nitrostyrene.[a]



Entry	Catalyst	Loading [mol-%]	Time [h]	Yield[b] [%]	*ee*[c] [%]
1	**1a**	5	24	99	94
2	**1b**	5	24	95	93
3	**1c**	5	24	93	93
4	**1c**	2.5	48	98	93
5	**1c**	1	48	71	93
6	**2**	5	24	96	95
7	**2**	2.5	48	99	95
8	**2**	1	48	96	95

[a] The reactions were conducted on a 0.5 mmol scale when 5 or 2.5 mol-% catalyst loading was used and on a 1.25 mmol scale when 1 mol-% catalyst loading was used. [b] Isolated yield. [c] Determined by HPLC on a Chiralcel OD-H column using *n*-hexane/2-propanol (70:30) as eluent.

To gain further information on the catalytic activity, the rates of reaction under catalysis with 5 mol-% ligands **1a**–**c** and **2** were measured. The conversion of indole was monitored by HPLC on a C18 column using MeOH/H_2O (60:40) as eluent. The results are summarized in Figure 4. In all cases, the reaction proceeded rapidly and >98% conversion was achieved within 4 h at ambient temperature. The differences in the reaction rates are negligible. When the loading of the G_3 ligand **1c** was decreased to 2.5 and 1 mol-%, the reaction rates dropped significantly compared with the case of 5 mol-% loading, as illustrated in Figure 5. Only 96.6 and 92.4% conversions were achieved after 6 h, respectively. No positive dendrimer effect (enhancement of reaction rate or enantioselectivity) was observed in our system.

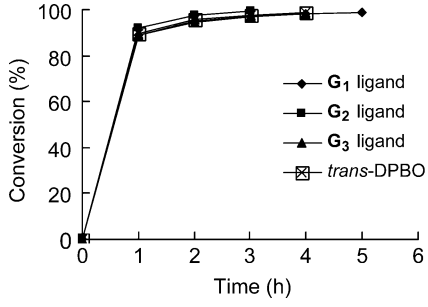


Figure 4. Reaction rates of the Friedel–Crafts reaction of indole and nitrostyrene using G_{1-3} and free ligands.

The G_3 ligand **1c** (2.5 mol-%) was also tested in the Friedel–Crafts alkylation of some representative substrates, as shown in Table 2. Excellent yields and enantioselectivities were achieved in the reactions of aromatic nitroalkenes with both electron-donating and -withdrawing groups at the 4-position (entries 1–3). In the case of the cyclohexyl-containing nitroalkene, only a 36% yield was obtained, much lower than the yield obtained with the *trans*-DPBO (**2**) system reported previously.[12f] Such a phenomenon indicates that

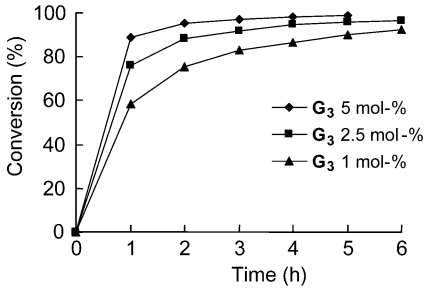
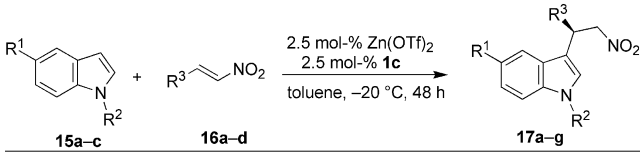


Figure 5. Reaction rates of the Friedel–Crafts reaction of indole and nitrostyrene using the **G$_3$** ligand with different catalyst loading.

the dendrimer-immobilized ligand is more sensitive towards the steric effects of the nitroalkene than the free ligand. When the substituents at the 1- and 5-positions of indole were Me or MeO, good results were also achieved. The moderate yield of **17g** indicates the lower reactivity of the *N*-substituted indole in the nucleophilic reaction. In most cases, the enantioselectivities decreased by only 3–5% compared with the free ligand system.[12f]

Table 2. Application of the **G$_3$** ligand in the asymmetric Friedel–Crafts reaction of indole derivatives with nitroalkenes.[a]



15a–c 16a–d 17a–g

Entry	R^1	R^2	R^3	Product	Yield [%][b]	*ee* [%][c,d]
1	H	H	Ph	**17a**	98	93 (*R*)
2	H	H	4-MeC_6H_4	**17b**	99	92 (*R*)
3	H	H	4-ClC_6H_4	**17c**	99	93 (*R*)
4	H	H	Cyclohexyl	**17d**	36	87 (*R*)
5	H	H	$PhCH_2CH_2$	**17e**	93	86 (*R*)
6	MeO	H	Ph	**17f**	93	94 (*R*)
7	H	Me	Ph	**17g**	78	92 (*R*)

[a] All the reactions were conducted on a 0.5 mmol scale in 3 mL of toluene. [b] Isolated yield. [c] Determined by HPLC on Chiracel OD-H and IA columns using a mixture of hexane and 2-propanol as eluent (for details see the Supporting Information). [d] The absolute configurations were determined by comparison of the optical rotations and the retention times on the chiral HPLC columns with reported results.

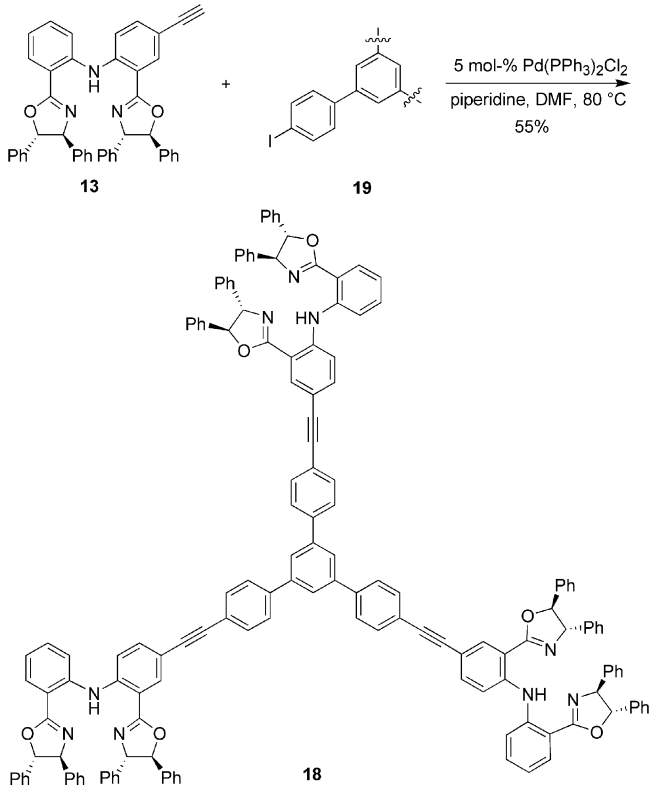
To enhance the efficiency with further reduced catalyst loading, the **G$_3$** ligand **1c** was tested in the in situ recycling process.[23] As shown in Table 3, the asymmetric Friedel–Crafts alkylation of indole **15a** with β-nitrostyrene (**16a**) was performed with 5 mol-% catalyst. After being stirred for 24 h at –20 °C, another portion of each of the two substrates was added without isolation of the product. An excellent accumulative yield and unaffected enantioselectivity were achieved after five cycles. Although the catalytic activity of the catalyst was not inhibited by the product, further recycles were not tested owing to the precipitation of the product from the solution at low temperature.

Table 3. In situ recycling of the catalyst in the asymmetric Friedel–Crafts alkyaltion of indole with β-nitrostyrene.[a]

Entry	β-Nitrostyrene [mmol]	Indole [mmol]	Yield [%][b]	*ee* [%][c]
1	0.25	0.25	93	93
2	0.25	0.25	99[d]	93
3	0.25	0.25	97[e]	92
4	0.25	0.25	98[f]	92
5	0.25	0.25	92[g]	92

[a] The reactions were conducted in 3 mL of toluene at –20 °C under the catalysis of 5 mol-% catalyst. [b] Isolated yield. [c] Determined by chiral HPLC on a Daicel Chiralcel OD-H column using *n*-hexane/2-propanol (70:30) as eluent. [d] Accumulative yield for two cycles. [e] Accumulative yield for three cycles. [f] Accumulative yield for four cycles. [g] Accumulative yield for five cycles.

For type II ligand immobilization, we designed the C_3-symmetric **G$_0$** dendrimer structure **18** (three-centre catalyst), which can be synthesized from alkynyl-substituted ligand **13** and iodide compound **19**[24] by copper-free Sonogashira coupling, as illustrated in Scheme 7. No desired product was obtained when the bromide analogue of **19** was used. The Suzuki–Miyaura coupling of **13** with tris(borate) or tris(boronic acid) analogues of **19** were also tested, but no conversion was observed.

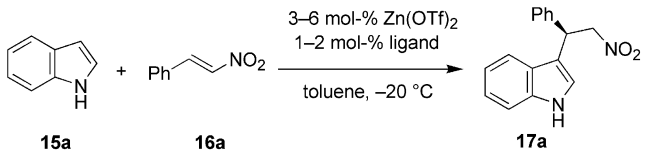


Scheme 7. Synthesis of the designed C_3-symmetric three-centre catalyst by a double copper-free Sonogashira coupling reaction.

With the desired ligand **18** in hand, the catalytic activity of its complex with $Zn(OTf)_2$ was investigated in the asymmetric Friedel–Crafts alkylation of indole **15a** with β-nitrostyrene (**16a**) under the optimized conditions we reported before.[12f] Because there are three bis(oxazoline) moieties

in **18**, 1 and 2 mol-% catalyst loadings were tested, and 3 and 6 mol-% of the free ligand **2** were also tested for comparison. As shown in Table 4, the immobilized ligand gave similar catalytic activity and enantioselectivity to the free ligand.

Table 4. Catalytic activity of the three-centre catalyst and free ligand in the Friedel–Crafts alkylation of indole with nitrostyrene.[a]



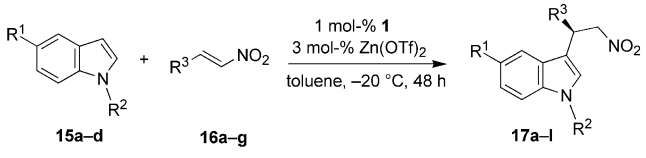
15a **16a** **17a**

Entry	Ligand	Loading [mol-%]	Yield [%][b]	*ee* [%][c]
1	**18**	2	96[d]	92
2	**18**	1	89[e]	93
3	**2**	6	96[d]	95
4	**2**	3	88[e]	95

[a] The reactions were conducted in 3 mL of toluene at –20 °C. [b] Isolated yield. [c] Determined by chiral HPLC on a Daicel Chiralcel OD-H column using *n*-hexane/2-propanol (70:30) as eluent. [d] The reaction time was 24 h. [e] The reaction time was 48 h.

When other indole derivatives and nitroalkenes were used in our system, good yields and enantioselectivities were also achieved in most cases, as shown in Table 5. The yields and enantioselectivities were not sensitive to *para* and *meta* substitutions on the phenyl ring in the aromatic nitroalkenes (entries 1–5). Thiophene-containing and aliphatic nitroalkenes gave lower enantioselectivities than aromatic ones (entries 6 and 7). The 5-chloroindole with an electron-withdrawing group (entry 10) and *N*-methylindole (entry 11) gave low yields because of their low reactivities, whereas the *ee* values were not affected significantly. All the results are similar to those published previously using 5 mol-% of the free ligand **2**. The slightly lower yields can be attributed to the partial precipitation of the complex in toluene at the low temperature. The absolute configurations of the products were determined by comparison of optical rotation values with the literature.[12d,12f]

Table 5. Asymmetric Friedel–Crafts alkyaltion of indole derivatives with nitroalkenes.[a]



15a–d **16a–g** **17a–l**

Entry	R^1	R^2	R^3	Product	Yield [%][b]	*ee* [%][c,d]
1	H	H	C_6H_5	**17a**	89	93 (*R*)
2	H	H	4-$CH_3C_6H_4$	**17b**	95	92 (*R*)
3	H	H	4-ClC_6H_4	**17c**	93	93 (*R*)
4	H	H	4-FC_6H_4	**17h**	85	91 (*R*)
5	H	H	3-BrC_6H_4	**17i**	89	93 (*R*)
6	H	H	2-thienyl	**17j**	79	81 (*R*)
7	H	H	$PhCH_2CH_2$	**17e**	86	85 (*R*)
8	Me	H	C_6H_5	**17k**	89	93 (*R*)
9	MeO	H	C_6H_5	**17f**	97	89 (*R*)
10	Cl	H	C_6H_5	**17l**	41	88 (*R*)
11	H	Me	C_6H_5	**17g**	54	87 (*R*)

[a] The reactions were conducted in 3 mL of toluene at –20 °C for 48 h. [b] Isolated yield. [c] Determined by chiral HPLC (for details, see the Supporting Information). [d] The absolute configurations were determined by comparison of the optical rotations and retention times on a chiral HPLC column with reported results.

To further reduce the catalyst loading, the three-centre bis(oxazoline) ligand **18** was evaluated in the in situ recycling process. As shown in Table 6, the asymmetric Friedel–Crafts alkylation of indole **15a** with β-nitrostyrene (**16a**) was performed with 2 mol-% catalyst. After being stirred for 24 h at –20 °C, another portion of each of the two substrates was added without isolation of the product. An excellent accumulative yield and unaffected enantioselectivity was achieved after four cycles. Although the catalytic activity of the catalyst was not inhibited by the product, further recycles were not tested owing to the precipitation of the product from the solution at low temperature.

Table 6. In situ recycling of catalyst in asymmetric Friedel–Crafts alkylation of indole with β-nitrostyrene.[a]

Run	β-Nitrostyrene [mmol]	Indole [mmol]	Yield [%][b]	*ee* [%][c]
1	0.25	0.25	96	93
2	0.25	0.25	93[d]	93
3	0.25	0.25	92[e]	92
4	0.25	0.25	98[f]	93

[a] The reactions were conducted in 3 mL of toluene at –20 °C with 2 mol-% catalyst. [b] Isolated yield. [c] Determined by chiral HPLC on a Daicel Chiralcel OD-H column using *n*-hexane/2-propanol (70:30) as eluent. [d] Accumulative yield for two cycles. [e] Accumulative yield for three cycles. [f] Accumulative yield for four cycles.

Conclusions

A diphenylamine-linked bis(oxazoline) ligand with *trans*-diphenyl substitution on the oxazoline rings was immobilized onto Fréchet-type dendrimers (generations one to three) and a C_3-symmetric core structure by copper-free Sonogashira coupling. In the asymmetric Friedel–Crafts alkylation of indole derivatives with nitroalkenes, good yields and enantioselectivities were achieved in most cases with values similar to those obtained with the free ligand system reported previously. The in situ recycling of the catalyst was tested in the asymmetric Friedel–Crafts alkylation reaction. Excellent accumulative yields and enantioselectivities were achieved after four or five cycles. No dendrimer effect was observed in the kinetic investigation of the Fréchet-type dendrimer-immobilized ligands. Although the in situ recycling of the catalyst can be recognized as a method for reducing the effective catalyst loading of the reaction, it also provides a potential method for the one-pot large-scale asymmetric catalytic synthesis of chiral compounds. Further application of the catalyst in a membrane reactor system is underway in our laboratory.

Experimental Section

Methyl 5-Bromo-2-[(2-methoxycarbonylphenyl)amino]benzoate (8a): $NaHCO_3$ (0.84 g, 10 mmol) was added to a solution of dimethyl 1,1′-diphenylamine-2,2′-dicarboxylate (**7**; 1.425 g, 5 mmol) in dichloromethane (DCM, 10 mL) and MeOH (5 mL). The mixture was cooled to 0 °C and pyridinium hydroperbromide (PHPB, 1.60 g, 5 mmol) was added in portions. After the addition, the mixture was warmed to room temperature and stirred overnight. After being quenched with water, the organic phase was separated and the water phase extracted with DCM (50 mL). The combined organic phases were dried with anhydrous Na_2SO_4. The solvent was removed under vacuum and the crude product was purified by recrystallization in toluene. The product **8a** was obtained as a bright greenish solid (1.420 g, 76% yield); m.p. 139–140 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 11.03 (s, 1 H, NH), 8.10 (s, 1 H, ArH), 7.99 (d, J = 7.8 Hz, 1 H, ArH), 7.35–7.50 (m, 4 H, ArH), 6.94 (t, J = 7.5 Hz, 1 H, ArH), 3.95 (s, 6 H, CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 167.5, 166.5, 143.44, 143.39, 136.0, 134.2, 133.2, 131.8, 120.4, 119.0, 118.2, 117.8, 117.6, 111.1, 52.3, 52.1 ppm. IR (neat): $\tilde{\nu}$ = 3315, 1698, 1581, 1515, 1431, 1316, 1254, 1211, 1082, 967 cm^{-1}. MS (ESI): m/z = 364 [M + H]$^+$. $C_{16}H_{14}BrNO_4$ (364.19): calcd. C 52.77, H 3.87, N 3.85; found C 52.37, H 3.88, N 3.90.

Methyl 5-Iodo-2-[(2-methoxycarbonylphenyl)amino]benzoate (8b): $NaHCO_3$ (3.36 g, 40 mmol) was added to a solution of dimethyl 1,1′-diphenylamine-2,2′-dicarboxylate (**7**; 5.70 g, 20 mmol) in DCM (40 mL) and MeOH (20 mL). The mixture was cooled to 0 °C and $BnN(CH_3)_3ICl_2$ (6.96 g, 20 mmol) was added in portions. The mixture was warmed to room temperature after the completion of the addition and stirred overnight. The reaction was quenched with water and the organic phase was separated. The water phase was extracted with DCM (100 mL) and the combined organic phases were dried with anhydrous Na_2SO_4. The solvent was removed under vacuum to afford the crude product, which was further purified by recrystallization in toluene. The product **8b** was obtained as a yellowish solid (4.483 g, 55% yield); m.p. 153–155 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 11.04 (s, 1 H, NH), 8.27 (d, J = 1.8 Hz, 1 H, ArH), 7.99 (d, J = 7.8 Hz, 1 H, ArH), 7.58 (dd, J_1 = 8.7, J_2 = 2.1 Hz, 1 H, ArH), 7.49 (d, J = 8.1 Hz, 1 H, ArH), 7.29–7.40 (m, 2 H, ArH), 6.94 (t, J = 7.5 Hz, 1 H, ArH), 3.94 (s, 6 H, CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 167.5, 166.4, 144.0, 143.2, 141.6, 140.1, 133.2, 131.8, 120.5, 119.2, 118.6, 118.0, 117.7, 80.3, 52.3, 52.1 ppm. IR (neat): $\tilde{\nu}$ = 3300, 2944, 1697, 1579, 1512, 1451, 1432, 1313, 1252, 1207, 1079, 750 cm^{-1}. MS (ESI): m/z = 412 [M + H]$^+$. $C_{16}H_{14}INO_4$ (411.19): calcd. C 46.74, H 3.43, N 3.41; found C 47.50, H 3.54, N 3.50.

5-Bromo-2-[(2-carboxyphenyl)amino]benzoic Acid (9a): A solution of NaOH (1.0 g, 25 mmol) in water (10 mL) was added to a solution of **8a** (1.407 g, 3.87 mmol) in MeOH (10 mL). The mixture was heated at reflux for 3 h and then cooled to room temperature. After being acidified to pH 1.0 with concentrated HCl (aq.), the product was obtained by filtration as a greenish powder (1.295 g, 100% yield); m.p. >260 °C (dec). ^{1}H NMR (200 MHz, [D$_6$]DMSO): δ = 13.29 (br., 2 H, CO_2H), 11.02 (s, 1 H, NH), 7.98–7.99 (m, 1 H, ArH), 7.96 (d, J = 10.2 Hz, 1 H, ArH), 7.53–7.63 (m, 2 H, ArH), 7.39–7.48 (m, 2 H, ArH), 6.97–7.05 (m, 1 H, ArH) ppm. ^{13}C NMR (50 MHz, [D$_6$]DMSO): δ = 168.1, 167.0, 143.0, 142.6, 135.7, 133.6, 133.2, 131.6, 120.6, 119.2, 118.8, 118.3, 118.0, 110.1 ppm. IR (neat): $\tilde{\nu}$ = 2985, 1676, 1592, 1517, 1456, 1315, 1250, 1218, 1167, 1084, 908 cm^{-1}. MS (ESI): m/z = 334 [M – H]$^+$. $C_{14}H_{10}BrNO_4 \cdot 0.5H_2O$ (345.15): calcd. C 48.72, H 3.21, N 4.06; found C 48.21, H 2.91, N 4.11.

2-[(2-Carboxyphenyl)amino]-5-iodobenzoic Acid (9b): The desired product was prepared from **8b** following the same procedure as used for **9a** on a 4 mmol scale. The product was obtained by filtration as a yellowish powder (1.530 g, 100% yield); m.p. >260 °C (dec). ^{1}H NMR (200 MHz, [D$_6$]DMSO): δ = 13.30 (br., 2 H, CO_2H), 10.92 (s, 1 H, NH), 8.17 (d, J = 2.2 Hz, 1 H, ArH), 7.93 (d, J = 7.6 Hz, 1 H, ArH), 7.71 (dd, J_1 = 9.0, J_2 = 2.2 Hz, 1 H, ArH), 7.48 (d, J = 3.6 Hz, 2 H, ArH), 7.30 (d, J = 8.8 Hz, 1 H, ArH), 6.97–7.05 (m, 1 H, ArH) ppm. ^{13}C NMR (50 MHz, [D$_6$]-DMSO): δ = 168.1, 167.0, 143.5, 142.5, 141.3, 139.5, 133.2, 131.7, 120.6, 119.3, 119.2, 118.3, 118.2, 80.9 ppm. IR (neat): $\tilde{\nu}$ = 2969, 1672, 1586, 1514, 1452, 1316, 1249, 1221, 1168, 912, 835, 743 cm^{-1}. MS (ESI): m/z = 382 [M – H]$^+$. $C_{14}H_{10}INO_4$ (383.14): calcd. C 43.89, H 2.63, N 3.66; found C 43.94, H 2.77, N 3.70.

5-Bromo-2-[(2-{*N*-[(1*S*,2*R*)-2-hydroxy-1,2-diphenylethyl]carbamoyl}phenyl)amino]-*N*-[(1*S*,2*R*)-2-hydroxy-1,2-diphenylethyl]benzamide (10a): Compound **9a** (2.352 g, 7 mmol) and $SOCl_2$ (10 mL) were added to a 50 mL round-bottomed flask. The mixture was heated at reflux for 4 h and excess $SOCl_2$ was removed under vacuum. The crude diacyl chloride was dissolved in CH_2Cl_2 (60 mL) and added dropwise through a dropping funnel to a mixture of (1*R*,2*S*)-2-amino-1,2-diphenylethanol (2.982 g, 14 mmol) and Et_3N (5.0 mL, 35 mmol) in CH_2Cl_2 (30 mL) at 0 °C. The mixture was stirred at room temperature for another 20 h after completion of the addition. After being quenched with saturated NH_4Cl (aq.) and washed with water, the organic phase was dried with anhydrous Na_2SO_4. The bis(β-hydroxyamide) **10a** was isolated by silica gel column chromatography using petroleum ether/ethyl acetate (2:1) as eluent and obtained as a colourless solid (3.663 g, 72% yield); m.p. 127–129 °C. $[\alpha]_D^{20}$ = –54.0 (c = 0.57 g/100 mL, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.40 (s, 1 H, NH), 7.73 (d, J = 8.1 Hz, 1 H, ArH), 7.65 (d, J = 2.1 Hz, 1 H, ArH), 7.56 (d, J = 7.8 Hz, 1 H, ArH), 7.48 (d, J = 7.5 Hz, 1 H, ArH), 7.23–7.36 (m, 3 H, ArH), 6.97–7.10 (m, 12 H, ArH), 6.85–6.94 (m, 10 H, ArH), 5.23–5.32 (m, 2 H, CH), 4.97 (dd, J_1 = 18.0, J_2 = 3.3 Hz, 2 H, CH), 3.32 (br., 2 H, OH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 167.9, 166.2, 142.1, 141.0, 139.8, 139.7, 136.8, 136.7, 134.8, 132.3, 131.8, 128.9, 128.0, 127.8, 127.5, 126.3, 125.8, 123.3, 121.73, 121.68, 121.62, 121.59, 121.5, 119.3, 119.2, 113.9, 75.9, 75.8, 59.4 ppm. IR (neat): $\tilde{\nu}$ = 3310, 3060, 1636, 1579, 1497, 1313, 1265, 1093, 1060, 739, 701 cm^{-1}. MS (ESI): m/z = 726 [M + H]$^+$. $C_{42}H_{36}BrN_3O_4$ (726.66): calcd. C 69.42, H 4.99, N 5.78; found C 69.12, H 5.03, N 5.81.

2-[(2-{*N*-[(1*S*,2*R*)-2-Hydroxy-1,2-diphenylethyl]carbamoyl}phenyl)amino]-*N*-[(1*S*,2*R*)-2-hydroxy-1,2-diphenylethyl]-5-iodobenzamide (10b): The iodine-substituted bis(β-hydroxyamide) **10b** was prepared similarly to **10a** on 4 mmol scale. The desired product was obtained as a colourless solid (2.000 g, 65% yield); m.p. 137–139 °C. $[\alpha]_D^{20}$ = –61.2 (c = 0.94 g/100 mL, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.43 (s, 1 H, NH), 7.80 (s, 1 H, ArH), 7.59 (dd, J_1 = 11.4, J_2 = 8.7 Hz, 2 H, ArH), 7.50 (d, J = 7.2 Hz, 2 H, ArH), 7.23–7.31 (m, 2 H, ArH), 7.10 (br., 12 H, ArH), 6.82–6.94 (m, 10 H, ArH), 5.25–5.30 (m, 2 H, CH), 4.97 (dd, J_1 = 9.9, J_2 = 3.0 Hz, 2 H, CH), 3.22 (br., 2 H, OH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 167.7, 166.2, 141.9, 141.7, 140.6, 139.8, 139.7, 137.5, 136.8, 136.7, 132.2, 129.0, 128.0, 127.9, 127.5, 126.3, 125.8, 123.9, 122.0, 121.2, 119.7, 83.3, 75.9, 59.4 ppm. IR (neat): $\tilde{\nu}$ = 3413, 3062, 1636, 1577, 1497, 1314, 1265, 1091, 1060, 1029, 908, 738, 702 cm^{-1}. MS (ESI): m/z = 774 [M + H]$^+$. $C_{42}H_{36}IN_3O_4$ (773.66): calcd. C 65.20, H 4.69, N 5.43; found C 64.80, H 4.72, N 5.47.

4-Bromo-2-[(4*S*,5*S*)-4,5-diphenyloxazolin-2-yl]-*N*-{2-[(4*S*,5*S*)-4,5-diphenyloxazolin-2-yl]phenyl}aniline (11a): $MeSO_2Cl$ (0.61 mL,

7.8 mmol) and Et_3N (2.3 mL, 16 mmol) were added successively to a solution of **10a** (2.562 g, 3.53 mmol) in CH_2Cl_2 (20 mL) at 0 °C. After the addition, the mixture was stirred at room temperature for 10 h. The reaction was quenched with saturated NH_4Cl (aq.), washed with brine and dried with anhydrous Na_2SO_4. After concentration, the residue was dissolved in methanol (10 mL) and mixed with NaOH (1.0 g) in water (10 mL). The mixture was heated at reflux for 2 h and then methanol was removed under vacuum. The residue was extracted with CH_2Cl_2, washed with brine and dried with anhydrous Na_2SO_4. The desired product **11a** was purified by silica gel column chromatography using petroleum ether/ethyl acetate (10:1) as eluent to give a colourless solid (2.041 g, 84% yield); m.p. 108–110 °C. $[\alpha]_D^{20}$ = 78.0 (*c* = 0.60 g/100 mL, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 11.32 (s, 1 H, NH), 8.07 (s, 1 H, ArH), 7.97 (d, *J* = 7.8 Hz, 1 H, ArH), 7.57 (d, *J* = 8.1 Hz, 1 H, ArH), 7.44 (s, 2 H, ArH), 7.38 (d, *J* = 8.1 Hz, 1 H, ArH), 7.29 (br., 6 H, ArH), 7.16 (br., 10 H, ArH), 6.99–7.04 (m, 5 H, ArH), 5.09 (d, *J* = 7.5 Hz, 2 H, CH), 4.90–4.94 (m, 2 H, CH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 163.1, 162.1, 143.0, 142.6, 142.0, 141.7, 140.4, 140.0, 134.4, 132.9, 131.7, 130.8, 128.8, 128.7, 128.5, 128.3, 128.2, 127.4, 126.4, 126.3, 125.8, 125.7, 120.9, 119.3, 116.8, 116.5, 111.0, 87.9, 78.7 ppm. IR (neat): $\tilde{\nu}$ = 3031, 1639, 1577, 1508, 1454, 1310, 1257, 1050, 971, 759, 696 cm^{-1}. MS (ESI): *m*/*z* = 690 [M + H]$^+$. $C_{42}H_{32}BrN_3O_2$ (690.63): calcd. C 73.04, H 4.67, N 6.08; found C 73.67, H 4.84, N 6.09.

2-[(4*S*,5*S*)-4,5-Diphenyloxazolin-2-yl]-*N*-{2-[(4*S*,5*S*)-4,5-diphenyloxazolin-2-yl]phenyl}-4-iodoaniline (11b): $MeSO_2Cl$ (0.37 mL, 4.7 mmol) and Et_3N (1.3 mL, 9.4 mmol) were added successively to a solution of **10b** (1.622 g, 2.1 mmol) in CH_2Cl_2 (20 mL) at 0 °C. After the addition, the mixture was stirred at room temperature for 10 h. The reaction was quenched with saturated NH_4Cl (aq.), washed with brine and dried with anhydrous Na_2SO_4. After concentration, the residue was dissolved in methanol (5 mL) and mixed with NaOH (0.5 g) in water (5 mL). The mixture was heated at reflux for 2 h and methanol was removed under vacuum. The residue was extracted with CH_2Cl_2, washed with brine and dried with anhydrous Na_2SO_4. The desired product **11b** was purified by silica gel column chromatography using petroleum ether/ethyl acetate (10:1) as eluent to give a yellowish solid (1.289 g, 83% yield); m.p. 110–112 °C. $[\alpha]_D^{20}$ = 70.1 (*c* = 1.2 g/100 mL, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 11.33 (s, 1 H, NH), 8.23 (s, 1 H, ArH), 7.97 (d, *J* = 7.5 Hz, 1 H, ArH), 7.56–7.61 (m, 2 H, ArH), 7.34–7.42 (m, 8 H, ArH), 7.16 (br., 9 H, ArH), 7.02 (br., 6 H, ArH), 5.09 (d, *J* = 7.5 Hz, 2 H, CH), 4.91 (t, *J* = 7.2 Hz, 2 H, CH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 163.1, 162.0, 143.7, 142.3, 141.9, 141.7, 140.3, 140.1, 140.0, 138.8, 138.7, 131.6, 130.8, 128.7, 128.54, 128.52, 128.3, 128.2, 127.4, 126.4, 125.8, 125.7, 121.1, 119.6, 119.3, 117.1, 116.7, 87.9, 80.1, 78.6 ppm. IR (neat): $\tilde{\nu}$ = 3031, 1638, 1575, 1507, 1454, 1310, 1264, 1050, 970, 814, 737, 696 cm^{-1}. MS (ESI): *m*/*z* = 738 [M + H]$^+$. $C_{42}H_{32}IN_3O_2$ (737.63): calcd. C 68.39, H 4.37, N 5.70; found C 69.04, H 4.63, N 5.70.

2-[(4*S*,5*S*)-4,5-Diphenyloxazolin-2-yl]-*N*-{2-[(4*S*,5*S*)-4,5-diphenyloxazolin-2-yl]phenyl}-4-ethynylaniline (13): Compound **11a** (414 mg, 0.60 mmol), $[Pd(PPh_3)_2Cl_2]$ (21 mg, 0.03 mmol), (triisopropylsilyl) acetylene (**12**; 0.18 mL, 0.8 mmol) and DMF (1 mL) were added to a Schlenk tube under argon. The mixture was heated to 80 °C and the reaction was initiated by the addition of piperidine (90 μL, 0.92 mmol). After being stirred at 80 °C for 12 h, the mixture was cooled and the reaction was quenched by the addition of water. The mixture was extracted with DCM (10 mL). The organic phase was dried with anhydrous Na_2SO_4, concentrated under vacuum and purified by silica gel flash chromatography using petroleum ether/ethyl acetate (15:1) as eluent to afford the TIPS-protected alkyne (427 mg, 90% yield). The TIPS protecting group was removed by addition of a 1 M solution of TBAF in THF (3.0 mL, 3 mmol). After being stirred at room temperature until full conversion of the material, the mixture was concentrated, dissolved in DCM (10 mL), washed with water and dried with anhydrous Na_2SO_4. The crude product was purified by silica gel column chromatograph using petroleum ether/ethyl acetate (10:1) as eluent and **13** was obtained as a colourless solid (316 mg, 92% yield); m.p. 104–106 °C. $[\alpha]_D^{20}$ = 76.9 (*c* = 0.64 g/100 mL, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 11.49 (s, 1 H, NH), 8.14 (s, 1 H, ArH), 7.98 (d, *J* = 7.8 Hz, 1 H, ArH), 7.62 (d, *J* = 8.4 Hz, 1 H, ArH), 7.46 (s, 2 H, ArH), 7.41 (d, *J* = 8.1 Hz, 1 H, ArH), 7.30 (br., 7 H, ArH), 7.17 (br., 9 H, ArH), 7.04 (br., 5 H, ArH), 5.08–5.12 (m, 2 H, CH), 4.91 (dd, J_1 = 13.2, J_2 = 7.5 Hz, 2 H, CH), 3.00 (s, 1 H, C≡CH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 163.1, 162.5, 144.7, 141.9, 141.82, 141.77, 140.3, 140.1, 135.2, 134.6, 131.6, 130.8, 128.73, 128.70, 128.5, 128.3, 128.2, 127.3, 126.4, 126.3, 125.8, 125.7, 121.7, 120.7, 118.1, 116.3, 113.6, 112.0, 88.1, 87.6, 83.5, 78.7, 75.9 ppm. IR (neat): $\tilde{\nu}$ = 3293, 3032, 2102, 1640, 1579, 1508, 1454, 1319, 1268, 1050, 973, 758, 697 cm^{-1}. MS (ESI): *m*/*z* = 636 [M + H]$^+$. $C_{44}H_{33}N_3O_2$ (635.75): calcd. C 83.13, H 5.23, N 6.61; found C 82.68, H 5.27, N 6.56.

G_1-Derived Iodobenzene 6a: K_2CO_3 (1.24 g, 9 mmol) and KI (498 mg, 3 mmol) were added to a solution of 4-iodophenol (660 mg, 3 mmol) in acetone (25 mL). The mixture was then heated at reflux for 0.5 h under argon. Then **G_1**-derived bromide **5a** (1.149 g, 3 mmol) and 18-crown-6 (40 mg, 0.15 mmol) were added and the mixture was heated at reflux for another 8 h. The solvent was removed under vacuum and the residue was dissolved in water and extracted with DCM (50 mL). After being dried with anhydrous Na_2SO_4, the solvent was removed under vacuum and the product **6a** was obtained by crystallization in diethyl ether as a white solid (1.298 g, 83% yield); m.p. 85–87 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.50 (d, *J* = 8.7 Hz, 2 H, ArH), 7.29–7.39 (m, 10 H, ArH), 6.68 (d, *J* = 8.7 Hz, 2 H, ArH), 6.62 (s, 2 H, ArH), 6.56 (s, 1 H, ArH), 4.99 (s, 4 H, OCH_2), 4.91 (s, 2 H, OCH_2) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 160.1, 158.4, 138.9, 138.2, 136.7, 128.5, 128.0, 127.5, 117.2, 106.2, 101.6, 83.1, 70.0, 69.8 ppm. IR (neat): $\tilde{\nu}$ = 3032, 2869, 1595, 1484, 1452, 1376, 1283, 1239, 1156, 1059, 1027, 819, 737, 696 cm^{-1}. MS (ESI): *m*/*z* = 523 [M + H]$^+$. $C_{27}H_{23}IO_3$ (522.37): calcd. C 62.08, H 4.44; found C 62.56, H 4.48.

G_2-Derived Iodobenzene 6b: K_2CO_3 (414 mg, 3 mmol) and KI (166 mg, 3 mmol) were added to a solution of 4-iodophenol (220 mg, 1 mmol) in acetone (15 mL). The mixture was then heated at reflux for 0.5 h under argon. Then **G_2**-derived bromide **5b** (807 mg, 1 mmol) and 18-crown-6 (20 mg, 0.075 mmol) were added and the mixture was heated at reflux for another 12 h. The solvent was removed under vacuum and the residue was dissolved in water and extracted with DCM (20 mL). After being dried with anhydrous Na_2SO_4, the solvent was removed under vacuum and the product **6b** was obtained by crystallization in diethyl ether as a white solid (913 mg, 97% yield); m.p. 105–106 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.49 (d, *J* = 8.4 Hz, 2 H, Ar), 7.29–7.37 (m, 20 H, ArH), 6.52–6.69 (m, 11 H, ArH), 4.99 (s, 8 H, OCH_2), 4.93 (s, 4 H, OCH_2), 4.90 (s, 2 H, OCH_2) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 160.1, 160.0, 158.4, 139.1, 138.9, 138.2, 136.7, 128.5, 127.9, 127.5, 117.3, 117.2, 106.4, 106.3, 101.6, 83.1, 70.0, 69.93, 69.85 ppm. IR (neat): $\tilde{\nu}$ = 3032, 1595, 1484, 1452, 1375, 1294, 1239, 1153, 1055, 829, 735, 698 cm^{-1}. MS (ESI): *m*/*z* = 947 [M + H]$^+$. $C_{55}H_{47}IO_7$ (946.86): calcd. C 69.77, H 5.00; found C 69.52, H 4.96.

G_3-Derived Iodobenzene 6c: K_2CO_3 (414 mg, 3 mmol) and KI (166 mg, 3 mmol) were added to a solution of 4-iodophenol

(220 mg, 1 mmol) in acetone (15 mL). The mixture was then heated at reflux for 0.5 h under argon. Then **G_3**-derived bromide **5c** (1.655 g, 1 mmol) and 18-crown-6 (20 mg, 0.075 mmol) were added and the mixture was heated at reflux for another 24 h. The solvent was removed under vacuum and the residue was dissolved in water and extracted with DCM (30 mL). After being dried with anhydrous Na_2SO_4, the solvent was removed under vacuum and the product **6c** was obtained by crystallization in diethyl ether as a white solid (1.673 g, 93% yield); m.p. 73–75 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.46 (d, J = 8.1 Hz, 2 H, ArH), 7.26–7.35 (m, 40 H, ArH), 6.64 (s, 15 H, ArH), 6.54 (s, 8 H, ArH), 4.96 (s, 16 H, OCH_2), 4.90 (s, 12 H, OCH_2), 4.85 (s, 2 H, OCH_2) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 160.1, 160.0, 158.4, 139.15, 139.12, 139.0, 138.1, 136.7, 128.5, 127.9, 127.5, 117.3, 117.2, 106.4, 106.3, 101.6, 101.5, 83.1, 70.1, 70.0, 69.9, 69.8 ppm. IR (neat): $\tilde{\nu}$ = 3032, 1594, 1452, 1374, 1295, 1153, 1054, 834, 737, 695 cm^{-1}. MS (ESI): m/z = 1796 [M + H]$^+$. $C_{111}H_{95}IO_{15}$ (1795.84): calcd. C 74.24, H 5.33; found C 74.48, H 5.31.

G_1-Dendrimer Ligand 1a: Alkyne **13** (127 mg, 0.2 mmol), **G_1**-derived iodobenzene **6a** (104 mg, 0.2 mmol), $[Pd(PPh_3)_2Cl_2]$ (7 mg, 0.01 mmol) and DMF (1 mL) were added to a Schlenk tube under argon. The mixture was heated to 80 °C and the reaction was initiated by the addition of piperidine (30 μL, 0.31 mmol). The mixture was stirred at 80 °C for 24 h and the reaction was quenched by the addition of water at room temperature. The mixture was then extracted with DCM (20 mL). The organic phase was dried with anhydrous Na_2SO_4, concentrated under vacuum and purified by silica gel column chromatography using DCM as eluent. The desired product **1a** was obtained as a light-pink foam (132 mg, 64% yield); m.p. 97–99 °C. $[\alpha]_D^{20}$ = –9.1 (c = 0.47 g/100 mL, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 11.47 (s, 1 H, NH), 8.16 (s, 1 H, ArH), 7.97 (d, J = 6.9 Hz, 1 H, ArH),6.88–7.64 (m, 39 H, ArH), 6.66 (s 2 H, ArH), 6.57 (s, 1 H, ArH), 4.89–5.10 (m, 10 H, CH, OCH_2) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 163.2, 162.7, 160.1, 158.4, 143.8, 142.1, 141.9, 140.3, 140.1, 139.1, 136.7, 134.5, 133.9, 132.8, 131.6, 130.8, 128.7, 128.5, 128.3, 128.2, 128.0, 127.5, 127.3, 126.4, 125.8, 125.7, 121.3, 120.3, 117.6, 116.7, 116.0, 114.9, 114.1, 113.9, 106.3, 101.6, 88.2, 88.0, 87.6, 78.6, 70.1, 69.9 ppm. IR (neat): $\tilde{\nu}$ = 3033, 2921, 1638, 1597, 1513, 1454, 1305, 1256, 1156, 1051, 971, 829, 747, 696 cm^{-1}. HRMS (ESI): calcd. for $C_{71}H_{56}N_3O_5$ [M + H]$^+$ 1030.42200; found 1030.41944.

G_2-Dendrimer Ligand 1b: Alkyne **13** (127 mg, 0.2 mmol), **G_2**-derived iodobenzene **6b** (189 mg, 0.2 mmol), $[Pd(PPh_3)_2Cl_2]$ (7 mg, 0.01 mmol) and DMF (1 mL) were added to a Schlenk tube under argon. The mixture was heated to 80 °C and the reaction was initiated by the addition of piperidine (30 μL, 0.31 mmol). The mixture was stirred at 80 °C for 24 h and the reaction was quenched by the addition of water at room temperature. The mixture was then extracted with DCM (20 mL). The organic phase was dried with anhydrous Na_2SO_4, concentrated under vacuum and purified by silica gel column chromatography using DCM as eluent. The desired product **1b** was obtained as a light-pink foam (155 mg, 53% yield); m.p. 94–96 °C. $[\alpha]_D^{20}$ = 4.0 (c = 0.80 g/100 mL, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 11.51 (s, 1 H, NH), 8.17 (s, 1 H, ArH), 7.98 (d, J = 7.8 Hz, 1 H, ArH), 7.28–7.65 (m, 34 H, ArH), 7.17 (s, 9 H, ArH), 7.05 (s, 4 H, ArH), 6.88 (d, J = 7.8 Hz, 2 H, ArH), 6.65 (s, 6 H, ArH), 6.56 (s, 2 H, ArH), 4.89–5.10 (m, 18 H, CH, OCH_2) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 163.1, 162.6, 160.1, 160.0, 158.4, 143.8, 142.1, 141.9, 141.8, 140.3, 140.1, 139.14, 139.07, 136.7, 134.5, 133.8, 132.8, 131.5, 130.7, 128.68, 128.66, 128.5, 128.22, 128.17, 127.9, 127.5, 127.3, 126.35, 126.32, 125.8, 125.7, 121.3, 120.2, 117.5, 116.7, 116.0, 114.8, 114.0, 113.8, 106.3, 106.2, 101.5, 88.2, 88.0, 87.9, 87.6, 78.7, 70.0, 69.9, 69.8 ppm. IR (neat): $\tilde{\nu}$ = 3030, 2923, 1639, 1595, 1513, 1453, 1374, 1295, 1155, 1050, 973, 830, 738, 696 cm^{-1}. HRMS (ESI): calcd. for $C_{99}H_{80}N_3O_9$ [M + H]$^+$ 1454.58946; found 1454.58207.

G_3-Dendrimer Ligand 1c: Alkyne **13** (127 mg, 0.2 mmol), **G_3**-derived iodobenzene **6c** (359 mg, 0.2 mmol), $[Pd(PPh_3)_2Cl_2]$ (7 mg, 0.01 mmol) and DMF (1 mL) were added to a Schlenk tube under argon. The mixture was heated to 80 °C and the reaction was initiated by the addition of piperidine (30 μL, 0.31 mmol). The mixture was stirred at 80 °C for 24 h and the reaction was quenched by the addition of water at room temperature. The mixture was then extracted with DCM (20 mL). The organic phase was dried with anhydrous Na_2SO_4, concentrated under vacuum and purified by silica gel column chromatography using DCM as eluent. The desired product **1c** was obtained as a light-orange foam (378 mg, 82% yield); m.p. 85–87 °C. $[\alpha]_D^{20}$ = –1.2 (c = 0.90 g/100 mL, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 11.49 (s, 1 H, NH), 8.16 (s, 1 H, ArH), 7.98 (d, J = 7.5 Hz, 1 H, ArH), 7.30–7.64 (m, 54 H, ArH), 7.15–7.19 (m, 9 H, ArH), 7.04 (d, J = 4.2 Hz, 5 H, ArH), 6.87 (d, J = 8.4 Hz, 1 H, ArH), 6.66 (s, 14 H, ArH), 6.55 (s, 7 H, ArH), 4.88–5.11 (m, 34 H, CH, OCH_2) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 163.1, 162.6, 160.1, 160.0, 158.4, 143.8, 142.1, 141.94, 141.86, 140.3, 140.1, 139.2, 136.7, 134.5, 133.8, 132.8, 131.6, 130.8, 128.70, 128.68, 128.5, 128.24, 128.19, 127.9, 127.5, 127.3, 126.4, 126.3, 125.8, 125.7, 121.3, 120.2, 117.5, 116.7, 116.0, 114.8, 114.1, 113.9, 106.3, 101.6, 88.3, 88.01, 87.96, 87.6, 78.7, 70.0, 69.9, 69.8 ppm. IR (neat): $\tilde{\nu}$ = 2922, 1639, 1595, 1513, 1452, 1374, 1296, 1153, 1051, 830, 735, 696 cm^{-1}. HRMS (ESI): calcd. for $C_{155}H_{128}N_3O_{17}$ [M + H]$^+$ 2302.92437; found 2302.92691.

***C_3*-Symmetric Dendrimer-Immobilized Ligand (18):** Alkyne **13** (222 mg, 0.35 mmol), iodide compound **19** (68 mg, 0.1 mmol), $[Pd(PPh_3)_2Cl_2]$ (11 mg, 0.015 mmol, 5 mol-% with respect to iodine atom) and DMF (1 mL) were added to a Schlenk tube under argon. The mixture was heated to 80 °C and the reaction was initiated by the addition of piperidine (55 μL, 0.57 mmol). The mixture was stirred at 80 °C for 48 h and the reaction was quenched by the addition of water at room temperature. The mixture was then extracted with CH_2Cl_2 (20 mL). The organic phase was dried with anhydrous Na_2SO_4, concentrated under vacuum and purified by silica gel column chromatography using CH_2Cl_2 as eluent. The desired product **18** was obtained as a light-pink solid (121 mg, 55% yield); m.p. 165–167 °C. $[\alpha]_D^{20}$ = –86.5 (c = 0.52 g/100 mL, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 11.53 (s, 3 H, NH), 8.21 (s, 3 H, ArH), 7.99 (d, J = 7.5 Hz, 3 H, ArH), 7.79 (s, 3 H, ArH), 7.42–7.66 (m, 25 H, ArH), 7.06–7.30 (m, 62 H, ArH), 5.12 (t, J = 6.9 Hz, 6 H, CH), 4.93 (t, J = 8.7 Hz, 1 H, CH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 78.7, 87.6, 88.0, 88.2, 90.3, 113.3, 113.9, 116.6, 117.9, 120.6, 121.5, 121.6, 123.0, 124.97, 125.01, 125.7, 125.9, 126.4, 127.2, 127.3, 128.26, 128.29, 128.32, 128.5, 128.7, 130.9, 131.6, 131.9, 134.2, 134.7, 140.1, 140.2, 140.3, 141.7, 141.87, 141.93, 144.3, 162.6, 163.1 ppm. IR (neat): $\tilde{\nu}$ = 2923, 1637, 1580, 1515, 1456, 1321, 1258, 1050, 977, 828, 752, 698 cm^{-1}. HRMS (ESI): calcd. for $C_{156}H_{112}N_9O_6$ [M + H]$^+$ 2206.87301; found 2206.87217.

Supporting Information (see also the footnote on the first page of this article): Experimental protocols for the synthesis of all Friedel–Crafts adducts, ^{1}H and ^{13}C NMR spectra of the new compounds and HPLC spectra.

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