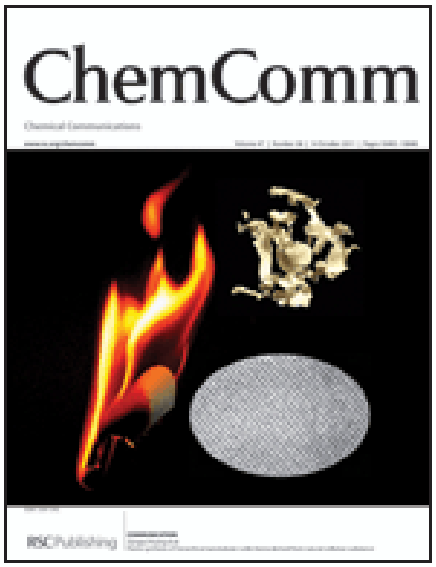

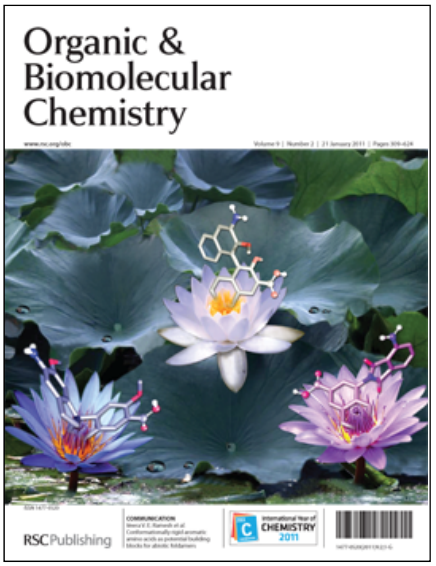

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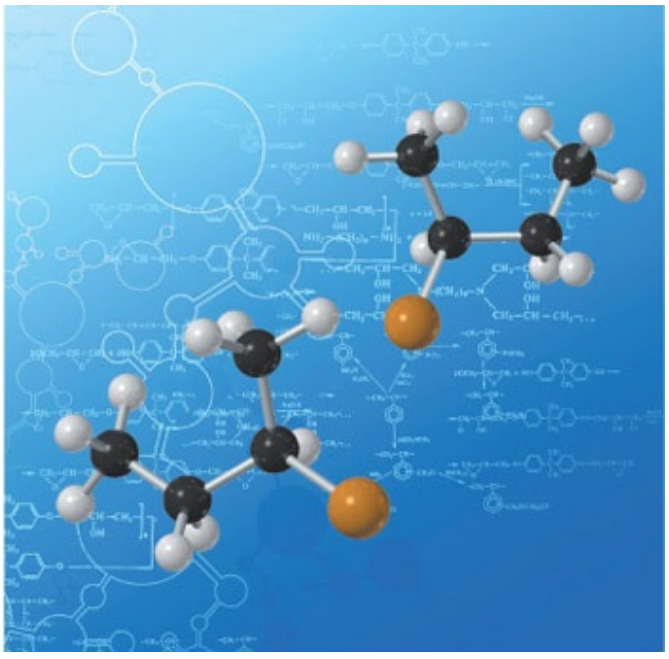

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PAPER

Enantioselective synthesis of fluorene derivatives by chiral *N*-triflyl phosphoramide catalyzed double Friedel–Crafts alkylation reaction†‡

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A highly efficient tandem double Friedel–Crafts reaction between indoles and 2-formylbiphenyl derivatives by chiral *N*-triflyl phosphoramide was realized. Under mild conditions, various 9-(3-indolyl) fluorene derivatives have been obtained in good yield and up to 94% ee. Comparing to their corresponding chiral phosphoric acids, chiral *N*-triflyl phosphoramides catalyzed reactions led to products with opposite absolute configuration.

Introduction

Fluorene is widely existed as the core structure of naturally occurring or synthetic molecules.[1] Some fluorene derivatives such as BMS-201038, amyxin and compound **A** (Fig. 1) have interesting biological activities and can be used as MTP inhibitor, interferon inducers and antitumor compounds respectively. Fluorenes in polymer form have also attracted much attention in recent years due to their wide applications as advanced materials with unique electronic and photonic properties including organic light-emitting diodes, thin film transistors, photovoltaic cells, *etc.* Despite their significant applications and extensive synthetic studies,[2] the asymmetric synthesis of fluorene derivatives has been rarely explored but is certainly highly desirable.

The Friedel–Crafts alkylation reaction is one of the most powerful methods to derivatize aromatic compounds by forming carbon–carbon bond.[3] Chiral phosphoric acids[4] recently proved to be efficient catalysts for the asymmetric Friedel–Crafts alkylation of arenes with various electrophilic partners, such as imines,[5] enamides,[6] α,β-unsaturated carbonyls,[7] and nitroolefins.[8] However, the readily available alcohols have been seldom used in asymmetric Friedel–Crafts alkylation reactions. In 2008, Rueping and co-workers reported the first chiral *N*-triflyl phosphoramide catalyzed enantioselective Friedel–Crafts reaction of indole with alcohol, but with moderate enantioselectivity.[9] Notably, Gong and Rueping independently utilized alcohols in chiral Brønsted acid-catalyzed asymmetric alkylation of enamide and allylic substitution reaction, respectively.[10]

With chiral phosphoric acids as the catalysts, we recently realized a tandem double Friedel–Crafts alkylation reaction[11] of indoles with 2-formylbiphenyl derivatives, leading to 9-(3-indolyl)-fluorene derivatives in high ees (Scheme 1).[12] Interestingly, the reaction features the activation of both aldehyde and alcohol by chiral phosphoric acid and the accomplishment of two Friedel–Crafts alkylation reactions in a tandem fashion. As part of our ongoing efforts to develop chiral Brønsted acid-catalyzed asymmetric reactions,[13] we envisaged the chiral *N*-triflyl phosphoramide,[14] a stronger Brønsted acid than its corresponding phosphoric acid, might be a more efficient catalyst in the above asymmetric tandem double Friedel–Crafts reaction. Notably, since the first introduction of chiral *N*-triflyl phosphoramides as efficient organocatalysts by Yamamoto and co-workers,[15] this unique class of catalysts has been applied successfully in many asymmetric catalytic reactions.[16] Indeed, chiral *N*-triflyl phosphoramide was found to be an efficient catalyst for the synthesis of fluorene derivatives in high ees *via* the above double Friedel–Crafts alkylation reactions. Interestingly, the products were obtained with the opposite absolute configurations compared to those obtained with a chiral phosphoric acid catalyst. In addition, the reaction catalyzed by chiral *N*-triflyl phosphoramide displayed broader substrate scope. In this article, we report the full account of this study.

Results and discussion

We began our study by testing various chiral phosphoramides in the tandem double Friedel–Crafts reaction of **2a** with **3a** in toluene at −15 °C. As summarized in Table 1, all the phosphoramides, particularly *N*-triflyl phosphoramides, proved to be efficient catalysts for this reaction. In most of cases, product **4aa** was obtained in excellent conversions within 2 days. Among these tested chiral *N*-triflyl phosphoramides, (*S*)-**1f** was found to be the optimal one in terms of a combination of yield and ee (>95% conversion, 89% ee, Table 1, entry 6). It is interesting to

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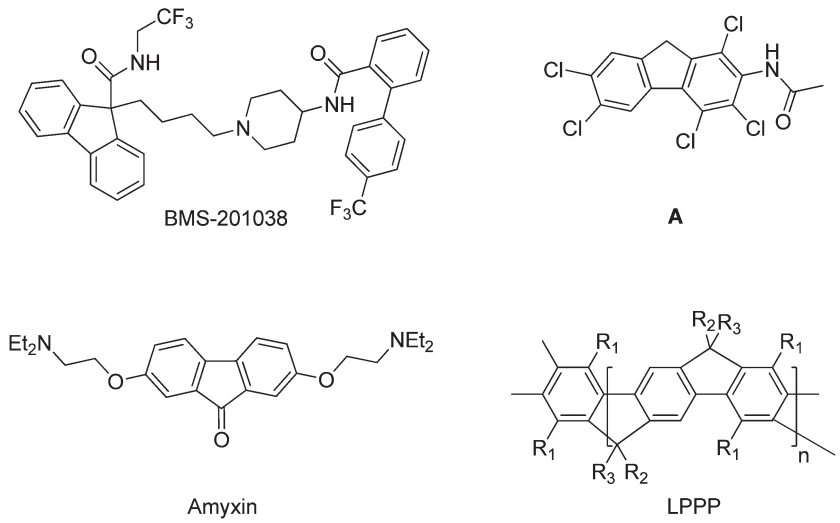
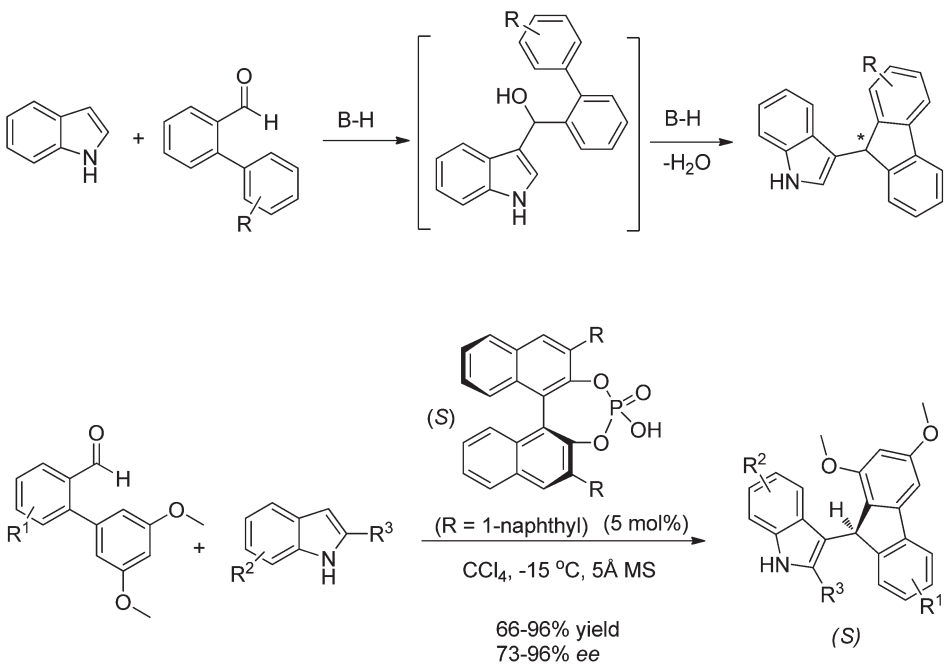


Fig. 1 Selected fluorene derivatives. LPPP: ladder type poly(*para*-phenylene).



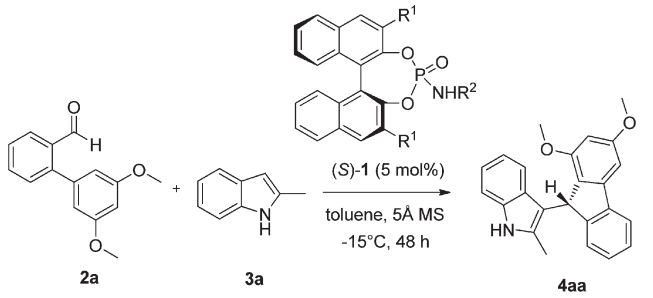
Scheme 1 Chiral phosphoric acid catalyzed tandem double Friedel–Crafts reaction.

note that the absolute configuration of product **4aa** obtained by utilizing (*S*)-*N*-triflyl phosphoramide is *R*, which is opposite of that obtained with (*S*)-phosphoric acid.

With the optimal catalyst (*S*)-**1f** in hand, different reaction parameters including the reaction temperature and solvent were further optimized. As summarized in Table 2, the reaction proceeded smoothly in various solvents and *o*-xylene was found to be the optimal one (92% yield, 90% ee, Table 2, entry 4). Reactions at lower temperature could also proceed smoothly to completion, although the enantioselectivity slightly decreased (Table 2, entry 7).

Under the optimized reaction conditions (Table 2, entry 4), various substituted indoles were investigated to test the generality of the reaction. The results are summarized in Table 3. In general, all the tested 2-methyl indoles with either electron-withdrawing or electron-donating substituents reacted smoothly to give their corresponding cyclization products **4** with satisfactory enantioselectivities. However, when indole was applied, both yield and ee of the product were significantly decreased (Table 3, entry 8). The reaction with 2-phenyl indole proceeded smoothly in 8% yield and 28% ee (Table 3, entry 9). Meanwhile, the scope of 2-formylbiphenyl derivatives was also explored by subjecting them to the optimized reaction conditions with **3a**. As shown in Scheme 2, all the desired fluorene derivatives were obtained with good to excellent yields and enantioselectivities. Notably, products **4fa** and **4ha** were synthesized for the first

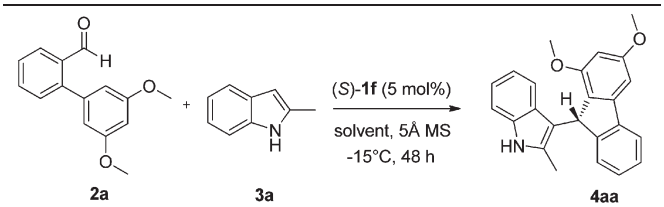
Table 1 Screening the 3,3′-substituents of chiral phosphoramide catalysts[a]



Entry	**1** R^1, R^2	Conv.[b] (%)	ee[c] (%)
1	**1a** 3,5-$(CF_3)_2$-phenyl, Tf	>95	86
2	**1b** biphenyl, Tf	>95	39
3	**1c** $SiPh_3$, Tf	>95	53
4	**1d** pyrenyl, Tf	>95	58
5	**1e** 3,5-$(CH_3)_2$-phenyl, Tf	97	33
6	**1f** 9-anthryl, Tf	>95	89
7	**1g** 9-phenanthryl, Tf	>95	66
8	**1h** 4-NO_2-phenyl, Tf	>95	43
9	**1i** 2,4,6-(^{i}Pr)$_3$-C_6H_2, Tf	>95	51
10	**1j** 3,5-$(CF_3)_2$-biphenyl, Tf	97	53
11	**1k** 3,5-$(CF_3)_2$-phenyl, $SO_2C_8F_{17}$	>95	55

[a] All the reactions were performed using 0.10 mmol **2a**, 0.15 mmol **3a** and 100 mg 5 Å MS in 1.5 mL toluene with 5 mol% of catalyst (*S*)-**1** at −15 °C. [b] Isolated yield for entries 5 and 10. [c] Determined by HPLC analysis (Chiralpak AD-H).

Table 2 Screening reaction temperatures and solvents[a]



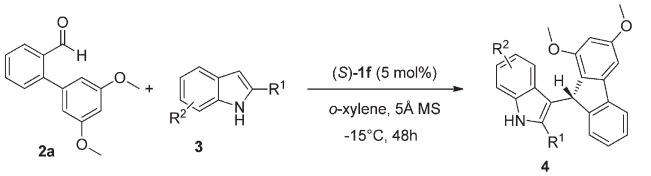
Entry	Solvent	Conv.[b] (%)	ee[c] (%)
1	Et_2O	>95	70
2	DCM	>95	33
3	CCl_4	92	84
4	*o*-Xylene	>95 (92)	90
5	Ph-Cl	96	78
6	Toluene	>95	89
7[d]	Toluene	96	85

[a] All the reactions were performed using 0.10 mmol **2a**, 0.15 mmol **3a** and 100 mg 5 Å MS in 1.5 mL solvent with 5 mol% of catalyst (*S*)-**1f** at −15 °C unless otherwise noted. [b] Isolated yield was listed for entries 3, 4, 5, and 7. [c] Determined by HPLC analysis (Chiralpak AD-H). [d] At −40 °C.

time. When *N*-protected 2-methyl indole was used, complete conversion was achieved yielding product **4aj** with 34% ee (Scheme 2).

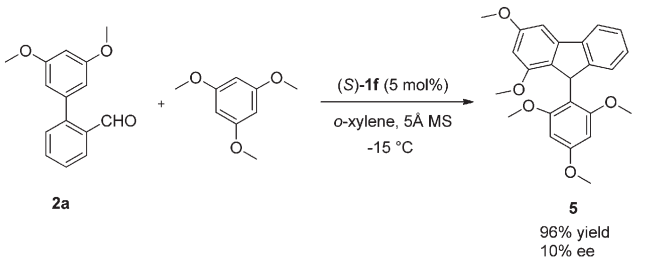
To further explore the substrate scope, 1,3,5-trimethoxybenzene was also tested under the standard reaction conditions with **2a**. The reaction proceeded smoothly to afford the desired product **5** in almost quantitative yield but with only 10% ee (eqn (1)).

Table 3 Substrate scope[a]



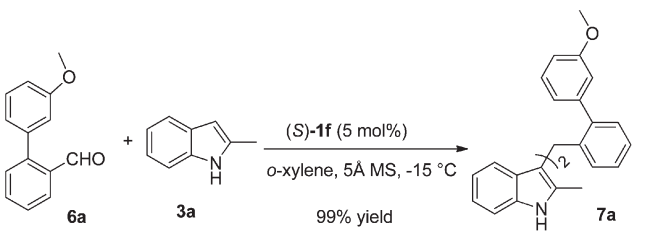
Entry	R^1, R^2	**4**, yield[b] (%)	ee[c] (%)
1	Me, H	**4aa**, 92	90
2	Me, 5-Me	**4ab**, 89	90
3	Me, 5-Br	**4ac**, 97	84
4	Me, 5-Cl	**4ad**, 97	85
5	Me, 5-F	**4ae**, 38	89
6	Me, 5- OCH_3	**4af**, 97	91
7	Me, 7-Br	**4ag**, 67	94
8	H, H	**4ah**, 35	2
9	Ph, H	**4ai**, 8	28

[a] All the reactions were performed using 0.10 mmol **2a**, 0.15 mmol **3** and 100 mg 5 Å MS in 1.5 mL *o*-xylene with 5 mol% of catalyst (*S*)-**1f** at −15 °C. [b] Isolated yield. [c] Determined by HPLC analysis (Chiralpak AD-H).

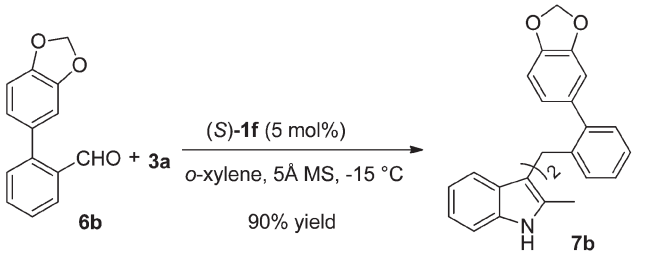


(1)

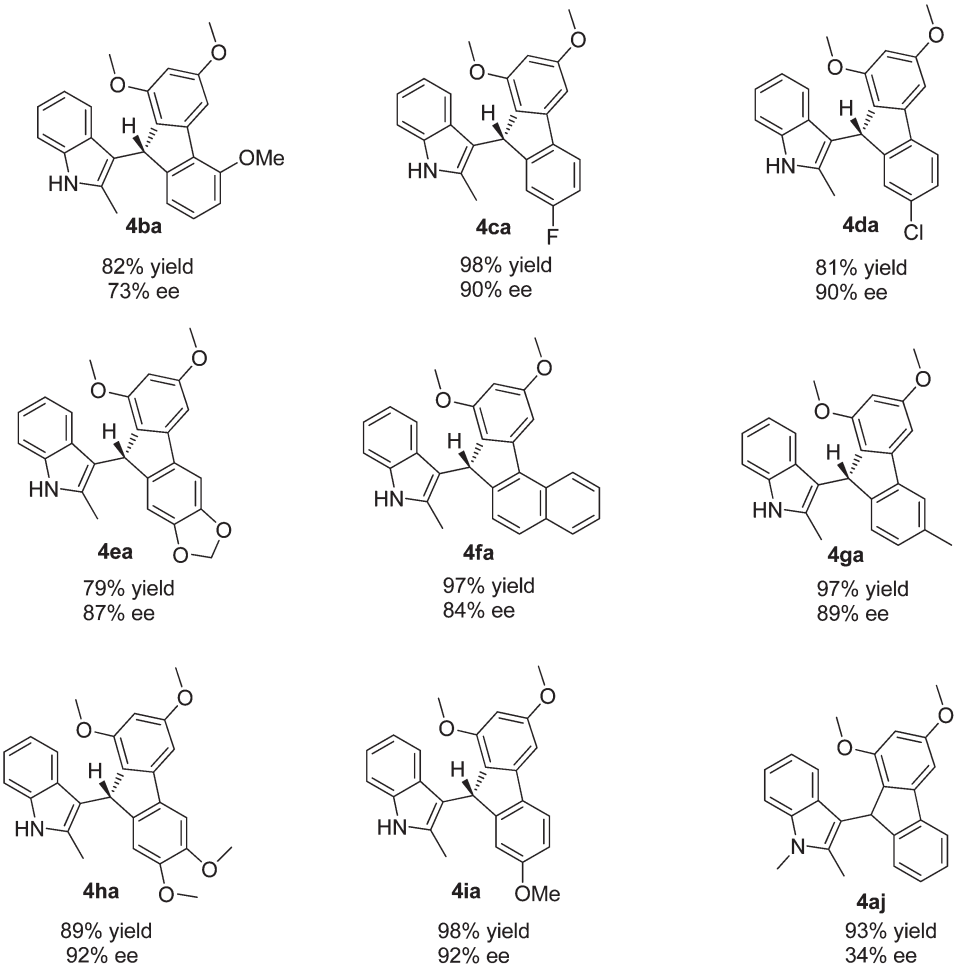
When **6a** and **6b** were used to react with **3a** under the standard conditions, bisindole alkylated products **7a** and **7b** were obtained respectively (eqn (2) and (3)). Interestingly, when the reaction was performed at room temperature, the corresponding fluorene derivatives could be obtained in excellent yields with moderate enantioselectivities (eqn (4) and (5)).



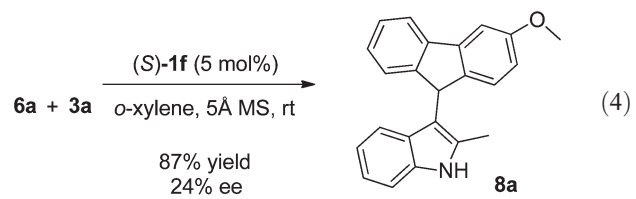
(2)



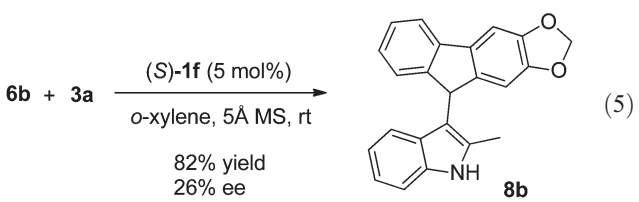
(3)



Scheme 2 Substrate scope of 2-formylbiphenyl derivatives.

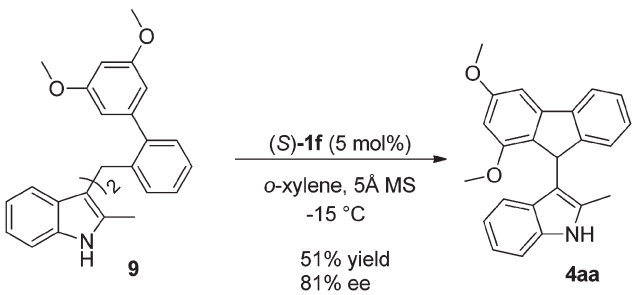


(4)



(5)

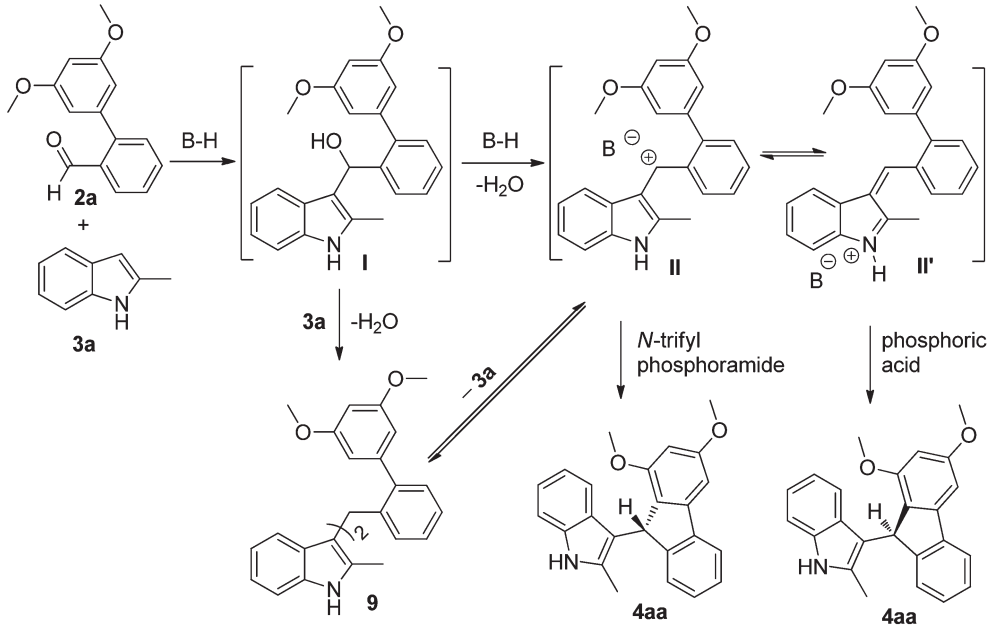
A plausible reaction mechanism was proposed, as depicted in Scheme 3. Chiral Brønsted acid activates the aldehyde through the hydrogen bonding with the carbonyl group, enabling the first Friedel–Crafts reaction between **2a** and **3a**. The secondary alcohol **I** obtained in the presence of chiral Brønsted acid leads to the formation of a close counterion **II** or **II′**, where the anion creates a chiral environment to control the enantioselectivity over the second Friedel–Crafts alkylation reaction. Since bisindole **9** can be observed during the reaction and be converted to corresponding product **4aa** under the optimized reaction conditions (51% yield, 81% ee, eqn (6)), a bypass involving the transformation of **9** to the intermediate **II** (**II′**) is added into the catalytic cycle. The reaction with chiral *N*-triflyl phosphoramide might form different type of counterion comparing to chiral phosphoric acid, which likely contributes the reverse of absolute configuration of the product. The understanding of the actual activation mode by different catalysts (*N*-triflyl phosphoramide or phosphoric acid) still needs further investigation and might provide useful guidance in catalyst design.



(6)

Conclusions

In conclusion, chiral *N*-triflyl phosphoramide was found an efficient catalyst for the tandem double Friedel–Crafts alkylation



Scheme 3 Proposed reaction mechanism.

reaction of indoles with 2-formylbiphenyl derivatives. With 5 mol% of the optimized catalyst, various fluorene derivatives were obtained in excellent yields and ee. Notably, the fluorene products obtained with the chiral *N*-triflyl phosphoramide have the opposite absolute configuration compared to that obtained with the corresponding chiral phosphoric acid. This allows access to both enantiomers of the products by utilizing different catalysts derived from one enantiomer of binaphthol.

Experimental

General information

Unless stated otherwise, all reactions were carried out in flame-dried glassware under a dry argon atmosphere. All solvents were purified and dried according to standard methods prior to use. ^{1}H and ^{13}C NMR spectra were recorded on a Varian instrument (300 MHz and 75 MHz, 400 MHz and 100 MHz, respectively) and internally referenced to tetramethylsilane signal or residual protio solvent signals. Data for ^{1}H NMR are recorded as follows: chemical shift (δ, ppm), multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet or unresolved, br = broad singlet, coupling constant(s) in Hz, integration). Data for ^{13}C NMR are reported in terms of chemical shift (δ, ppm). The enantioselectivities were determined by HPLC analysis and optical rotation was measured on a polarimeter.

General procedure for the double Friedel–Crafts alkylation reaction of indoles with 2-formyl biphenyl derivatives

In a dry Schlenk tube, *N*-triflyl phosphoramide (*S*)-**1f** (4.4 mg, 0.005 mmol), substituted indole **3** (0.15 mmol) and 5 Å molecular sieves (100 mg) were dissolved in *o*-xylene (1.5 mL) under argon. The solution was stirred for 5 minutes at room temperature and then for another 5 minutes at −15 °C. Subsequently, biphenyl-2-carbaldehyde **2** (0.10 mmol) was added in one portion at −15 °C. After the reaction was complete (monitored by TLC), saturated aqueous $NaHCO_3$ (3 mL) was added to quench the reaction. The mixture was resumed to room temperature and extracted with CH_2Cl_2 (10 mL). The organic layer was separated and dried over anhydrous Na_2SO_4. The solvents were removed under reduced pressure after filtration and the residue was purified by silica gel column chromatography (ethyl acetate/petroleum ether = 1/10–1/5) to afford the product.

3-(1,3-Dimethoxy-9*H*-fluoren-9-yl)-2-methyl-1*H*-indole (4aa).[12] White solid, 92% yield, 90% ee; the enantiomeric ratio was determined by Daicel Chiralpak AD-H (25 cm), hexanes/IPA = 80/20, 1.0 mL min^{-1}, λ = 254 nm, t (minor) = 7.80 min, t (major) = 20.91 min; $[\alpha]_D^{20}$ = +15.6° (*c* = 1.00, acetone); ^{1}H NMR (400 MHz, DMSO-d$_6$) δ 2.69 (s, 3H), 3.60 (s, 3H), 3.87 (s, 3H), 5.24 (s, 1H), 5.84 (d, *J* = 8.0 Hz, 1H), 6.38 (d, *J* = 7.2 Hz, 1H), 6.41–6.42 (m, 1 H), 6.74–6.78 (m, 1H), 7.14 (d, *J* = 8.0 Hz, 1H), 7.18–7.38 (m, 3 H), 7.34–7.37 (m, 1H), 7.94 (d, *J* = 7.6 Hz, 1H), 10.76 (s, 1H).

3-(1,3-Dimethoxy-9*H*-fluoren-9-yl)-2,5-dimethyl-1*H*-indole (4ab).[12] White solid, 89% yield, 90% ee; the enantiomeric ratio was determined by Daicel Chiralpak AD-H (25 cm), hexanes/IPA = 80/20, 1.0 mL min^{-1}, λ = 254 nm, t (minor) = 9.20 min, t (major) = 22.70 min; $[\alpha]_D^{20}$ = +34.2° (*c* = 1.0 acetone); ^{1}H NMR (400 MHz, DMSO-d$_6$) δ 1.92 (s, 3H), 2.68 (s, 3H), 3.62 (s, 3H), 3.88 (s, 3H), 5.24 (s, 1H), 5.64 (s, 1H), 6.44 (s, 1H), 6.60 (d, *J* = 7.6 Hz, 1H), 7.04 (d, *J* = 8.0 Hz, 1H), 7.19–7.23 (m, 3H), 7.37–7.40 (m, 1H), 7.96 (d, *J* = 7.2 Hz, 1H), 10.62 (s, 1H).

5-Bromo-3-(1,3-dimethoxy-9*H*-fluoren-9-yl)-2-methyl-1*H*-indole (4ac).[12] White solid, 97% yield, 84% ee; the enantiomeric ratio was determined by Daicel Chiralpak AD-H (25 cm), hexanes/IPA = 80/20, 1.0 mL min^{-1}, λ = 254 nm, t (minor) = 9.24 min, t (major) = 17.59 min; $[\alpha]_D^{20}$ = +1.8° (*c* = 1.0 acetone); ^{1}H NMR

(400 MHz, DMSO-d_6) δ 2.68 (s, 3H), 3.61 (s, 3H), 3.87 (s, 3H), 5.24 (s, 1H), 5.88 (d, J = 1.6 Hz, 1H), 6.43 (d, J = 2.0 Hz, 1H), 6.86 (dd, J = 2.0, 8.4 Hz, 1H), 7.11 (d, J = 8.4 Hz, 1H), 7.17–7.23 (m, 3H), 7.38–7.40 (m, 1H), 7.97 (d, J = 7.6 Hz, 1H), 11.03 (s, 1H).

5-Chloro-3-(1,3-dimethoxy-9*H*-fluoren-9-yl)-2-methyl-1*H*-indole (4ad).[12] White solid, 97% yield, 85% ee; the enantiomeric ratio was determined by Daicel Chiralpak AD-H (25 cm), hexanes/IPA = 80/20, 1.0 mL min^{-1}, λ = 254 nm, t (minor) = 8.91 min, t (major) = 17.40 min; $[\alpha]_D^{20}$ = +0.52° (c = 1.00, acetone); ^{1}H NMR (400 MHz, DMSO-d_6) δ 2.69 (s, 3H), 3.61 (s, 3H), 3.87 (s, 3H), 5.25 (s, 1H), 5.76 (d, J = 2.0 Hz, 1H), 6.44 (s, 1H), 6.77 (d, J = 8.8 Hz, 1H), 7.15–7.23 (m, 4H), 7.37–7.41 (m, 1H), 7.97 (d, J = 7.2 Hz, 1H), 11.02 (s, 1H).

5-Fluoro-3-(1,3-dimethoxy-9*H*-fluoren-9-yl)-2-methyl-1*H*-indole (4ae).[12] White solid, 38% yield, 89% ee; the enantiomeric ratio was determined by Daicel Chiralpak AD-H (25 cm), hexanes/IPA = 80/20, 1.0 mL min^{-1}, λ = 254 nm, t (minor) = 8.26 min, t (major) = 17.29 min; $[\alpha]_D^{20}$ = −6.0° (c = 1.00, acetone); ^{1}H NMR (400 MHz, DMSO-d_6) δ 2.68 (s, 3H), 3.61 (s, 3H), 3.87 (s, 3H), 5.25 (s, 1H), 5.41–5.44 (m, 1H), 6.43 (d, J = 2.0 Hz, 1H), 6.56–6.21 (m, 1H), 7.12 (dd, J = 4.8, 8.8 Hz, 1H), 7.18–7.22 (m, 3H), 7.36–7.40 (m, 1H), 7.95 (d, J = 7.6 Hz, 1H), 10.89 (s, 1H).

3-(1,3-Dimethoxy-9*H*-fluoren-9-yl)-5-methoxy-2-methyl-1*H*-indole (4af).[12] White solid, 97% yield, 91% ee; the enantiomeric ratio was determined by Daicel Chiralpak AD-H (25 cm), hexanes/IPA = 80/20, 1.0 mL min^{-1}, λ = 254 nm, t (minor) = 11.75 min, t (major) = 23.50 min; $[\alpha]_D^{20}$ = +18.1° (c = 1.00, acetone); ^{1}H NMR (400 MHz, DMSO-d_6) δ 2.64 (s, 3H), 3.24 (s, 3H), 3.60 (s, 3H), 3.86 (s, 3H), 5.23 (s, 1H), 5.26 (s, 1H), 6.39–6.42 (m, 2H), 6.99 (d, J = 8.4 Hz, 1H), 7.19–7.20 (m, 3H), 7.34–7.37 (m, 1H), 7.93 (d, J = 6.8 Hz, 1H), 10.54 (s, 1H).

7-Bromo-3-(1,3-dimethoxy-9*H*-fluoren-9-yl)-2-methyl-1*H*-indole (4ag).[12] White solid, 67% yield, 94% ee; the enantiomeric ratio was determined by Daicel Chiralpak AD-H (25 cm), hexanes/IPA = 80/20, 1.0 mL min^{-1}, λ = 254 nm, t (minor) = 9.32 min, t (major) = 14.67 min; $[\alpha]_D^{20}$ = −7.8° (c = 1.00, acetone); ^{1}H NMR (400 MHz, DMSO-d_6) δ 2.71 (s, 3H), 3.60 (s, 3H), 3.87 (s, 3H), 5.25 (s, 1H), 5.80 (d, J = 8.0 Hz, 1H), 6.33–6.37 (m, 1H), 6.42 (s, 1H), 6.96 (d, J = 7.6 Hz, 1H), 7.18–7.20 (m, 3H), 7.34–7.36 (m, 1H), 7.93 (d, J = 7.2 Hz, 1H), 10.94 (s, 1H).

3-(1,3-Dimethoxy-9*H*-fluoren-9-yl)-1*H*-indole (4ah).[12] White solid, 35% yield, 2% ee; the enantiomeric ratio was determined by Daicel Chiralpak AD-H (25 cm), hexanes/IPA = 80/20, 1.0 mL min^{-1}, λ = 254 nm, t (minor) = 16.11 min, t (major) = 37.90 min; $[\alpha]_D^{20}$ = −0.4° (c = 1.00, acetone); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.60 (s, 3H), 3.92 (s, 3H), 5.37 (s, 1H), 6.37 (s, 1H), 6.87–6.92 (m, 1H), 7.00–7.07 (m, 4H), 7.15–7.20 (m, 1H), 7.24–7.39 (m, 3H), 7.75 (d, J = 10.0 Hz, 1H), 7.89 (s, 1H).

3-(1,3-Dimethoxy-9*H*-fluoren-9-yl)-2-phenyl-1*H*-indole (4ai).[12] White solid, 8% yield, 28% ee; the enantiomeric ratio was determined by Daicel Chiralcel OD-H (25 cm), hexanes/IPA = 70/30, 1.0 mL min^{-1}, λ = 254 nm, t (major) = 6.46 min, t (minor) = 10.47 min; $[\alpha]_D^{20}$ = −20.0° (c = 1.00, acetone); ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.54 (s, 3H), 3.91 (s, 3H), 5.54 (s, 1H), 6.28 (d, J = 8.4 Hz, 1H), 6.33 (d, J = 1.2 Hz, 1H), 6.58–6.63 (m, 1H), 6.93–6.96 (m, 1H), 7.03 (d, J = 2.1 Hz, 1H), 7.11–7.16 (m, 2H), 7.21–7.23 (m, 1H), 7.29–7.33 (m, 1H), 7.39–7.44 (m, 1H), 7.51–7.55 (m, 2H), 7.77 (d, J = 7.5 Hz, 1H), 7.94–7.97 (m, 3H).

2-Methyl-3-(1,3,5-trimethoxy-9*H*-fluoren-9-yl)-1*H*-indole (4ba).[12] White solid, 82% yield, 73% ee; the enantiomeric ratio was determined by Daicel Chiralpak AD-H (25 cm), hexanes/IPA = 80/20, 1.0 mL min^{-1}, λ = 254 nm, t (minor) = 22.69 min, t (major) = 41.24 min; $[\alpha]_D^{20}$ = +34.8° (c = 1.00, acetone); ^{1}H NMR (400 MHz, DMSO-d_6) δ 2.36 (s, 3H), 2.63 (s, 3H), 3.57 (s, 3H), 3.85 (s, 3H), 5.18 (s, 1H), 5.84 (d, J = 7.6 Hz, 1H), 6.36–6.40 (m, 2H), 6.74–6.76 (m, 1H), 6.98 (d, J = 7.6 Hz, 1H), 7.04 (d, J = 7.2 Hz, 1H), 7.12 (d, J = 8.0 Hz, 1H), 7.16 (d, J = 2.0 Hz, 1H), 7.74 (s, 1H), 10.71 (s, 1H).

3-(7-Fluoro-1,3-dimethoxy-9*H*-fluoren-9-yl)-2-methyl-1*H*-indole (4ca).[12] White solid, 98% yield, 90% ee; the enantiomeric ratio was determined by Daicel Chiralpak AD-H (25 cm), hexanes/IPA = 80/20, 1.0 mL min^{-1}, λ = 254 nm, t (minor) = 8.78 min, t (major) = 17.24 min; $[\alpha]_D^{20}$ = +17.5° (c = 1.00, acetone); ^{1}H NMR (400 MHz, DMSO-d_6) δ 3.20 (s, 3H), 4.07 (s, 3H), 4.33 (s, 3H), 5.75 (s, 1H), 6.47 (d, J = 8.0 Hz, 1H), 6.84 (d, J = 2.0 Hz, 1H), 6.68–6.92 (m, 1H), 7.22–7.26 (m, 1H), 7.39–7.41 (m, 1H), 7.55–7.63 (m, 3H), 8.37 (dd, J = 4.8, 8.0 Hz, 1H), 10.36 (s, 1H).

3-(7-Chloro-1,3-dimethoxy-9*H*-fluoren-9-yl)-2-methyl-1*H*-indole (4da).[12] White solid, 81% yield, 90% ee; the enantiomeric ratio was determined by Daicel Chiralpak AD-H (25 cm), hexanes/IPA = 70/30, 0.6 mL min^{-1}, λ = 254 nm, t (minor) = 10.62 min, t (major) = 19.11 min; $[\alpha]_D^{20}$ = −32.5° (c = 1.00, acetone); ^{1}H NMR (400 MHz, DMSO-d_6) δ 2.66 (s, 3H), 3.59 (s, 3H), 3.86 (s, 3H), 5.26 (s, 1H), 5.84 (d, J = 8.0 Hz, 1H), 6.40–6.42 (m, 2H), 6.75–6.78 (m, 1H), 7.13–7.16 (m, 2H), 7.20–7.22 (m, 1H), 7.41 (d, J = 8.4 Hz, 1H), 7.95 (d, J = 8.0 Hz, 1H), 10.80 (s, 1H).

3-(6,8-Dimethoxy-9*H*-fluoreno[3,2-*d*][1,3]dioxol-9-yl)-2-methyl-1*H*-indole (4ea).[12] White solid, 79% yield, 87% ee; the enantiomeric ratio was determined by Daicel Chiralpak AD-H (25 cm), hexanes/IPA = 80/20, 1.0 mL min^{-1}, λ = 254 nm, t (minor) = 16.79 min, t (major) = 56.69 min; $[\alpha]_D^{20}$ = −21.1° (c = 1.00, acetone); ^{1}H NMR (400 MHz, DMSO-d_6) δ 2.64 (s, 3H), 3.57 (s, 3H), 3.85 (s, 3H), 5.10 (s, 1H), 5.91 (d, J = 8.0 Hz, 1H), 5.99–6.00 (m, 1H), 6.32 (d, J = 2.0 Hz, 1H), 6.41–6.45 (m, 1H), 6.65 (s, 1H), 6.74–6.78 (m, 1H), 7.11–7.14 (m, 2H), 7.54 (s, 1H), 10.72 (s, 1H).

3-(8,10-Dimethoxy-7*H*-benzo[*c*]fluoren-7-yl)-2-methyl-1*H*-indole (4fa). White solid, 97% yield, 84% ee; the enantiomeric ratio was determined by Daicel Chiralpak AD-H (25 cm), hexanes/IPA = 80/20, 1.0 mL min, λ = 254 nm, t (major) = 28.05 min, t (minor) = 33.29 min; $[\alpha]_D^{20}$ = +148.1° (c = 0.8, acetone); Mp = 203–205 °C; ^{1}H NMR (300 MHz, $CDCl_3$), δ 2.72 (s, 3H), 3.64 (s, 3H), 3.95 (s, 3H), 5.31 (s, 1H), 5.77 (d, J = 7.8 Hz, 1H), 6.29 (t, J = 7.5 Hz, 1H), 6.52 (s, 1H), 6.71 (t, J = 7.5 Hz, 1H), 7.13 (d, J = 8.1 Hz, 1H), 7.34 (d, J = 8.4 Hz, 1H), 7.57 (t, J = 7.2 Hz, 1H), 7.66 (s, 1H), 7.70–7.78 (m, 2H), 7.99 (d, J = 7.8 Hz, 1H),

8.87 (d, J = 8.4 Hz, 1H), 10.82 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 11.7, 43.0, 55.3, 97.0, 100.5, 106.8, 110.2, 117.3, 117.5, 119.3, 123.3, 123.6, 125.1, 126.2, 126.9, 127.3, 128.0, 128.7, 129.1, 133.1, 133.8, 134.1, 135.1, 143.1, 148.3, 156.6, 160.8; IR (thin film): ν_{max} (cm^{-1}) = 3394, 3055, 2921, 2834, 1759, 1596, 1482, 1461, 1426, 1383, 1364, 329, 1305, 1266, 1245, 1214, 1196, 1153, 1132, 1079, 1055, 1016, 936, 817, 786, 766, 738, 661, 620; MS (EI, *m*/*z*, rel. intensity) 405 (M^+, 100); HRMS (EI): Exact mass calcd for $C_{28}H_{23}NO_2$: 405.1729, Found: 405.1726.

3-(1,3-Dimethoxy-6-methyl-9*H*-fluoren-9-yl)-2-methyl-1*H*-indole (4ga).[12] White solid, 97% yield, 89% ee; the enantiomeric ratio was determined by Daicel Chiralpak AD-H (25 cm), hexanes/IPA = 80/20, 1.0 mL min^{-1}, λ = 254 nm, t (minor) = 7.34 min, t (major) = 17.01 min; $[\alpha]_D^{20}$ = +3.5° (c = 1.00, acetone); ^{1}H NMR (400 MHz, DMSO-d_6) δ 2.38 (s, 3H), 2.65 (s, 3H), 3.54 (s, 3H), 3.85 (s, 3H), 5.18 (s, 1H), 5.85 (d, J = 8.0 Hz, 1H), 6.36–6.40 (m, 2H), 6.71–6.76 (m, 1H), 6.98 (d, J = 7.6 Hz, 1H), 7.04 (d, J = 7.6 Hz, 1H), 7.12 (d, J = 8.0 Hz, 1H), 7.16 (d, J = 2.0 Hz, 1H), 7.74 (s, 1H), 10.71 (s, 1H).

2-Methyl-3-(1,3,6,7-tetramethoxy-9*H*-fluoren-9-yl)-1*H*-indole (4ha). White solid, 89% yield, 92% ee; the enantiomeric ratio was determined by Daicel Chiralpak AD-H (25 cm), hexanes/IPA = 80/20, 0.7 mL min, λ = 254 nm, t (minor) = 19.10 min, t (major) = 26.71 min; $[\alpha]_D^{20}$ = −19.4° (c = 0.5, acetone); Mp = 257–259 °C; ^{1}H NMR (300 MHz, DMSO-d_6), δ 2.66 (s, 3H), 3.58 (s, 3H), 3.61 (s, 3H), 3.86 (s, 3H), 3.90 (s, 3H), 5.14 (s, 1H), 5.88 (d, J = 7.8 Hz, 1H), 6.31 (s, 1H), 6.41 (d, J = 7.5 Hz, 1H), 6.72 (s, 1H), 6.75 (t, J = 7.5 Hz, 1H), 7.12 (t, J = 8.1 Hz, 1H), 7.17 (s, 1H), 7.60 (s, 1H), 10.71 (s, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 11.7, 42.5, 55.1, 55.3, 55.5, 55.7, 96.3, 96.7, 103.7, 107.9, 108.2, 110.1, 117.4, 117.7, 119.2, 126.2, 126.3, 133.0, 133.3, 135.1, 141.1, 143.0, 148.4, 148.8, 156.5, 160.7; IR (thin film): ν_{max} (cm^{-1}) = 3388, 3200, 3054, 3000, 2956, 2925, 2854, 2023, 1899, 1866, 1789, 1711, 1601, 1585, 1502, 1462, 1422, 1406, 1362, 1322, 1302, 1265, 1230, 1201, 1185, 1155, 1138, 1091, 1045, 987, 934, 844, 818, 764, 735, 689, 672, 631, 609; MS (EI, *m*/*z*, rel. intensity) 415 (M^+, 28), 43 (100); HRMS (EI) calcd for $C_{26}H_{25}NO_4$ (M^+): 415.1784, Found: 415.1790.

2-Methyl-3-(1,3,7-trimethoxy-9*H*-fluoren-9-yl)-1*H*-indole (4ia).[12] White solid, 98% yield, 92% ee; the enantiomeric ratio was determined by Daicel Chiralpak AD-H (25 cm), hexanes/IPA = 60/ 40, 0.8 mL min^{-1}, λ = 254 nm, t (minor) = 8.95 min, t (major) = 29.32 min; $[\alpha]_D^{20}$ = −38.5° (c = 1.00, acetone); ^{1}H NMR (400 MHz, DMSO-d_6) δ 2.66 (s, 3H), 3.57 (s, 3H), 3.66 (s, 3H), 3.85 (s, 3H), 5.19 (s, 1H), 5.89 (d, J = 7.6 Hz, 1H), 6.30 (d, J = 2.0 Hz, 1H), 6.38–6.42 (m, 1H), 6.69 (d, J = 1.6 Hz, 1H), 6.73–6.77 (m, 1H), 6.93 (dd, J = 2.4, 8.4 Hz, 1H), 7.09 (d, J = 2.4 Hz, 1H), 7.12 (d, J = 8.0 Hz, 1H), 7.83 (d, J = 8.4 Hz, 1H), 10.72 (s, 1H).

3-(1,3-Dimethoxy-9*H*-fluoren-9-yl)-1,2-dimethyl-1*H*-indole (4aj).[12] White solid; 93% yield, 34% ee; the enantiomeric ratio was determined by Daicel Chiralpak AD-H (25 cm), hexanes/IPA = 80/20, 0.7 mL min^{-1}, λ = 254 nm, t (major) = 8.91 min, t (minor) = 25.49 min; $[\alpha]_D^{20}$ = −3.0° (c = 1.0, acetone); ^{1}H NMR (400 MHz, DMSO-d_6) δ 2.69 (s, 3H), 3.59 (s, 3H), 3.69 (s, 3H), 3.87 (s, 3H), 5.31 (s, 1H), 5.85 (d, J = 8.0 Hz, 1H), 6.40–6.42 (m, 2H), 6.80–6.84 (m, 1H), 7.16–7.37 (m, 4H), 7.34–7.37 (m, 1H), 7.94 (d, J = 7.6 Hz, 1H).

1,3-Dimethoxy-9-(2,4,6-trimethoxyphenyl)-9*H*-fluorene (5). White solid, 96% yield, 10% ee; the enantiomeric ratio was determined by Daicel Chiralpak AD-H (25 cm), hexanes/IPA = 80/20, 0.8 mL min, λ = 254 nm, t (major) = 12.73 min, t (minor) = 30.10 min; $[\alpha]_D^{20}$ = −7.8° (c = 1.0, acetone); ^{1}H NMR (300 MHz, DMSO), δ 2.93 (s, 3H), 3.62 (s, 3H), 3.76 (s, 3H), 3.89 (s, 3H), 3.98 (s, 3H), 5.58 (s, 1H), 5.91 (d, J = 2.1 Hz, 1H), 6.28 (d, J = 2.1 Hz, 1H), 6.35 (d, J = 1.8 Hz, 1H), 6.96 (d, J = 2.1 Hz, 1H), 7.17–7.30 (m, 1H), 7.70 (d, J = 7.2 Hz, 1H); ^{13}C NMR (75 MHz, DMSO) δ 41.3, 55.1, 55.5, 55.7, 56.6, 91.6, 92.7, 96.2, 97.9, 111.2, 119.2, 123.6, 125.9, 126.6, 128.0, 141.2, 143.3, 149.5, 156.6, 159.4, 159.5, 160.2; MS (EI, *m*/*z*, rel. intensity) 415 (M + Na); HRMS (EI) calcd for $C_{24}H_{24}O_5Na$ (M^+): 415.1516, Found: 415.1520.

3-(9*H*-1,3-Dioxa-cyclopenta[*b*]fluoren-9-yl)-2-methyl-1*H*-indole (8b). Light yellow solid, 87%, 24% ee; The enantiomeric ratio was determined by Daicel Chiralpak AD-H (25 cm), hexanes/IPA = 70/30, 0.5 mL min, λ = 254 nm, t (minor) = 38.21 min, t (major) = 42.54 min; $[\alpha]_D^{20}$ = +4.7° (c = 1.0, acetone); Mp = 187–190 °C; ^{1}H NMR (300 MHz, DMSO), δ 2.73 (s, 3H), 5.24 (s, 1H), 5.88 (d, J = 8.1 Hz, 1H), 6.05 (d, J = 4.2 Hz, 2H), 6.46 (t, J = 7.8 Hz, 1H), 6.75 (s, 1H), 6.82 (t, J = 7.5 Hz, 1H), 7.14–7.22 (m, 3H), 7.36 (t, J = 6.6 Hz, 1H), 7.61 (s, 1H), 7.89 (d, J = 7.8 Hz, 1H); ^{13}C NMR (75 MHz, DMSO) δ 11.5, 44.8, 100.7, 101.1, 105.6, 108.2, 110.3, 117.7, 117.8, 119.1, 119.7, 124.6, 125.8, 125.9, 126.8, 133.8, 134.0, 135.4, 140.5, 142.0, 146.9, 147.1, 148.0; IR (thin film): ν_{max} (cm^{-1}) = 3401, 3059, 2923, 2855, 2770, 2945, 1878, 1708, 1614, 1499, 1473, 1454, 1438, 1339, 1289, 1261, 1230, 1191, 1149, 1100, 1073, 1036, 937, 908, 856, 804, 766, 739, 663, 615; MS (EI, *m*/*z*, rel. intensity) 339 (M^+, 100); HRMS (EI) calcd for $C_{23}H_{17}NO_2$ (M^+): 339.1259, Found: 339.1260.

3-[(3′-Methoxy-biphenyl-2-yl)-(2-methyl-3a,7a-dihydro-1*H*-indol-3-yl)-methyl]-2-methyl-1*H*-indole (7a). White solid, 99% yield; Mp = 196–198 °C; ^{1}H NMR (300 MHz, $CDCl_3$), δ 1.87 (s, 6H), 3.31 (s, 3H), 5.84 (s, 1H), 6.39 (s, 1H), 6.76–6.90 (m, 6H), 7.01 (t, J = 7.8 Hz, 2H), 7.13–7.28 (m, 5H), 7.42 (d, J = 7.8 Hz, 1H), 7.62 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.0, 37.2, 54.6, 109.8, 113.4, 119.0, 120.4, 121.0, 126.0, 127.1, 128.5, 129.2, 129.8, 131.7, 135.0, 141.4, 142.2, 143.3, 158.7; IR (thin film): ν_{max} (cm^{-1}) = 3392, 3055, 2923, 2854, 1929, 1887, 1704, 1594, 1460, 1421, 1340, 1300, 1246, 1217, 1178, 1158, 1095, 1040, 1018, 995, 909, 875, 792, 745, 705; MS (EI, *m*/*z*, rel. intensity) 456 (M^+, 100); HRMS (EI) calcd for $C_{32}H_{28}N_2O$ (M^+): 456.2203, Found: 456.2202.

3-[(2-Benzo[1,3]dioxol-5-yl-phenyl)-(2-methyl-3a,7a-dihydro-1*H*-indol-3-yl)-methyl]-2-methyl-1*H*-indole (7b). White solid, 90% yield; Mp = 252–254 °C; ^{1}H NMR (300 MHz, $CDCl_3$), δ 1.88 (s, 6H), 5.86–5.88 (m, 3H), 6.49–6.53 (m, 2H), 6.64 (d, J = 8.1 Hz, 1H), 6.80–6.91 (m, 4H), 7.00–7.05 (m, 2H), 7.16–7.26 (m, 5H), 7.40–7.43 (m, 1H), 7.64 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.1, 37.1, 100.7, 107.5, 109.5, 109.8, 113.7, 119.0,

119.3, 120.4, 122.1, 126.0, 127.0, 129.1, 129.9, 130.0, 131.7, 134.9, 141.8, 146.0, 146.7; IR (thin film): ν_{max} (cm^{-1}) = 3378, 2918, 1608, 1556, 1500, 1474, 1459, 1426, 1338, 1303, 1244, 1220, 1125, 1098, 1038, 1014, 930, 894, 861, 821, 766, 746, 641; MS (EI, *m*/*z*, rel. intensity) 470 (M^+, 100); HRMS (EI) calcd for $C_{32}H_{26}N_2O_2$ (M^+): 470.1994, Found: 470.1995.

3,3′-((3′,5′-Dimethoxybiphenyl-2-yl)methylene)bis(2-methyl-1*H*-indole) (9).[12] White solid; ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.89 (s, 6H), 3.39 (s, 6H), 5.76 (s, 1H), 6.16 (d, J = 2.0 Hz, 2H), 6.34–6.35 (m, 1H), 6.67–6.68 (m, 2H), 6.73 (d, J = 8.0 Hz, 2H), 6.86–6.90 (m, 2H), 7.18–7.20 (m, 3H), 7.23–7.27 (m, 2H), 7.36–7.38 (m, 1H), 10.69 (s, 1H).

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References

1 (*a*) R. Sulsky, J. A. Robl, S. A. Biller, T. W. Harrity, J. Wetterau, F. Connolly, K. Jolibois and L. Kunselman, *Bioorg. Med. Chem. Lett.*, 2004, **14**, 5067; (*b*) S. A. Lyakhov, E. A. Lyakhova, A. S. Karpenko, G. V. Mal'tsev, I. V. Vel'cheva, L. A. Litvinova, M. N. Lebedyuk, G. A. Khorokhorina and V. P. Fedchuk, *Pharm. Chem. J.*, 2004, **38**, 128; (*c*) L. R. Morgan, K. Thangaraj, B. LeBlanc, A. Rodgers, L. T. Wolford, C. L. Hooper, D. Fan and B. S. Jursic, *J. Med. Chem.*, 2003, **46**, 4552; (*d*) R. Doisy and M.-S. Tang, *Biochemistry*, 1995, **34**, 4358; (*e*) U. Scherf and E. J. W. List, *Adv. Mater.*, 2002, **14**, 477.

2 For reviews: (*a*) W.-Y. Wong, *Coord. Chem. Rev.*, 2005, **249**, 971; (*b*) J. Rault-Berthelot, *Curr. Top. Electrochem.*, 2004, **10**, 971; (*c*) K. Ono and K. Saito, *Heterocycles*, 2008, **75**, 2381. For recent synthesis of fluorenes: (*d*) K. Fuchibe and T. Akiyama, *J. Am. Chem. Soc.*, 2006, **128**, 1434; (*e*) G. Li, E. Wang, H. Chen, H. Li, Y. Liu and P. G. Wang, *Tetrahedron*, 2008, **64**, 9033.

3 For reviews on asymmetric Friedel–Crafts reaction: (*a*) M. Bandini, A. Melloni and A. Umani-Ronchi, *Angew. Chem., Int. Ed.*, 2004, **43**, 550; (*b*) M. Bandini, A. Melloni, S. Tommasi and A. Umani-Ronchi, *Synlett*, 2005, 1199; (*c*) Y.-F. Sheng, A. J. Zhang, X.-J. Zheng and S.-L. You, *Chin. J. Org. Chem.*, 2008, **28**, 605; (*d*) T. B. Poulsen and K. A. Jørgensen, *Chem. Rev.*, 2008, **108**, 2903; (*e*) S.-L. You, Q. Cai and M. Zeng, *Chem. Soc. Rev.*, 2009, **38**, 2190; (*f*) M. Zeng and S.-L. You, *Synlett*, 2010, 1289; (*g*) V. Terrasson, R. M. de Figueiredo and J. M. Campagne, *Eur. J. Org. Chem.*, 2010, 2635.

4 Reviews on chiral phosphoric acid catalysis: (*a*) M. S. Taylor and E. N. Jacobsen, *Angew. Chem., Int. Ed.*, 2006, **45**, 1520; (*b*) T. Akiyama, J. Itoh and K. Fuchibe, *Adv. Synth. Catal.*, 2006, **348**, 999; (*c*) S. J. Connon, *Angew. Chem., Int. Ed.*, 2006, **45**, 3909; (*d*) T. Akiyama, *Chem. Rev.*, 2007, **107**, 5744; (*e*) X. Yu and W. Wang, *Chem.–Asian J.*, 2008, **3**, 516; (*f*) M. Terada, *Chem. Commun.*, 2008, 4097.

5 (*a*) D. Uraguchi and M. Terada, *J. Am. Chem. Soc.*, 2004, **126**, 5356; (*b*) Q. Kang, Z.-A. Zhao and S.-L. You, *J. Am. Chem. Soc.*, 2007, **129**, 1484; (*c*) M. Terada, S. Yokoyama, K. Sorimachi and D. Uraguchi, *Adv. Synth. Catal.*, 2007, **349**, 1863; (*d*) G. Li, G. B. Rowland, E. B. Rowland and J. C. Antilla, *Org. Lett.*, 2007, **9**, 4065; (*e*) G.-W. Zhang, L. Wang, J. Nie and J.-A. Ma, *Adv. Synth. Catal.*, 2008, **350**, 1457; (*f*) M. J. Wanner, P. Hauwert, H. E. Schoemaker, R. de Gelder, J. H. van Maarseveen and H. Hiemstra, *Eur. J. Org. Chem.*, 2008, 180; (*g*) Q. Kang, X.-J. Zheng and S.-L. You, *Chem.–Eur. J.*, 2008, **14**, 3539; (*h*) Q. Kang, Z.-A. Zhao and S.-L. You, *Tetrahedron*, 2009, **65**, 1603; (*i*) S. Nakamura, Y. Sakurai, H. Nakashima, N. Shibata and T. Toru, *Synlett*, 2009, 1639; (*j*) F. Xu, D. Huang, C. Han, W. Shen, X. Lin and Y. Wang, *J. Org. Chem.*, 2010, **75**, 8677; (*k*) M. Rueping, S. Raja and A. Núñez, *Adv. Synth. Catal.*, 2011, **353**, 563; (*l*) C.-H. Xing, Y.-X. Liao, J. Ng and Q.-S. Hu, *J. Org. Chem.*, 2011, **76**, 4125.

6 (*a*) M. Terada and K. Sorimachi, *J. Am. Chem. Soc.*, 2007, **129**, 292; (*b*) Y.-X. Jia, J. Zhong, S.-F. Zhu, C.-M. Zhang and Q.-L. Zhou, *Angew. Chem., Int. Ed.*, 2007, **46**, 5565; (*c*) G. Li and J. C. Antilla, *Org. Lett.*, 2009, **11**, 1075.

7 (*a*) H.-Y. Tang, A.-D. Lu, Z.-H. Zhou, G.-F. Zhao, L.-N. He and C.-C. Tang, *Eur. J. Org. Chem.*, 2008, 1406; (*b*) Q. Cai, Z.-A. Zhao and S.-L. You, *Angew. Chem., Int. Ed.*, 2009, **48**, 7428.

8 (*a*) J. Itoh, K. Fuchibe and T. Akiyama, *Angew. Chem., Int. Ed.*, 2008, **47**, 4016; (*b*) Y.-F. Sheng, G.-Q. Li, Q. Kang, A.-J. Zhang and S.-L. You, *Chem.–Eur. J.*, 2009, **15**, 3351; (*c*) Y.-F. Sheng, Q. Gu, A.-J. Zhang and S.-L. You, *J. Org. Chem.*, 2009, **74**, 6899.

9 M. Rueping, B. J. Nachtsheim, S. A. Moreth and M. Bolte, *Angew. Chem., Int. Ed.*, 2008, **47**, 593.

10 (*a*) Q.-X. Guo, Y.-G. Peng, J.-W. Zhang, L. Song, Z. Feng and L.-Z. Gong, *Org. Lett.*, 2009, **11**, 4620; (*b*) M. Rueping, U. Uria, M.-Y. Lin and I. Atodiresei, *J. Am. Chem. Soc.*, 2011, **133**, 3732.

11 For a double Friedel–Crafts reaction of indole with divinyl ketones: A. C. Silvanus, S. J. Heffernan, D. J. Liptrot, G. Kociok-Köhn, B. I. Andrews and D. R. Carbery, *Org. Lett.*, 2009, **11**, 1175.

12 F.-L. Sun, M. Zeng, Q. Gu and S.-L. You, *Chem.–Eur. J.*, 2009, **15**, 8709.

13 (*a*) Q. Gu, Z.-Q. Rong, C. Zheng and S.-L. You, *J. Am. Chem. Soc.*, 2010, **132**, 11418; (*b*) Q. Cai, C. Zheng and S.-L. You, *Angew. Chem., Int. Ed.*, 2010, **49**, 8666; (*c*) F.-L. Sun, X.-J. Zheng, Q. Gu, Q.-L. He and S.-L. You, *Eur. J. Org. Chem.*, 2010, 47; (*d*) Q. Yin and S.-L. You, *Chem. Sci.*, 2011, **2**, 1344.

14 For a recent comprehensive review: C. H. Cheon and H. Yamamoto, *Chem. Commun.*, 2011, **47**, 3043.

15 (*a*) D. Nakashima and H. Yamamoto, *J. Am. Chem. Soc.*, 2006, **128**, 9626; (*b*) C. H. Cheon and H. Yamamoto, *J. Am. Chem. Soc.*, 2008, **130**, 9246; (*c*) P. Jiao, D. Nakashima and H. Yamamoto, *Angew. Chem., Int. Ed.*, 2008, **47**, 2411; (*d*) C. H. Cheon and H. Yamamoto, *Org. Lett.*, 2010, **12**, 2476.

16 (*a*) M. Rueping, W. Ieawsuwan, A. P. Antonchick and B. J. Nachtsheim, *Angew. Chem., Int. Ed.*, 2007, **46**, 2097; (*b*) M. Rueping, B. J. Nachtsheim, S. A. Moreth and M. Bolte, *Angew. Chem., Int. Ed.*, 2008, **47**, 593; (*c*) D. Enders, A. A. Narine, F. Toulgoat and T. Bisschops, *Angew. Chem., Int. Ed.*, 2008, **47**, 5661; (*d*) M. Rueping, T. Theissmann, A. Kuenkel and R. M. Koenigs, *Angew. Chem., Int. Ed.*, 2008, **47**, 6798; (*e*) M. Zeng, Q. Kang, Q.-L. He and S.-L. You, *Adv. Synth. Catal.*, 2008, **349**, 2169; (*f*) M. Rueping and W. Ieawsuwan, *Adv. Synth. Catal.*, 2009, **351**, 78; (*g*) S. Lee and S. Kim, *Tetrahedron Lett.*, 2009, **50**, 3345; (*h*) Z. Feng, Q.-L. Xu, L.-X. Dai and S.-L. You, *Heterocycles*, 2010, **80**, 765; (*i*) M. Rueping and B. J. Nachtsheim, *Synlett*, 2010, 119; (*j*) M. Rueping and M.-Y. Lin, *Chem.–Eur. J.*, 2010, **16**, 4169; (*k*) V. N. Wakchaure and B. List, *Angew. Chem., Int. Ed.*, 2010, **49**, 4136; (*l*) D. Enders, M. Seppelt and T. Beck, *Adv. Synth. Catal.*, 2010, **352**, 1413; (*m*) M. Rueping, B. J. Nachtsheim, R. M. Koenigs and W. Ieawsuwan, *Chem.–Eur. J.*, 2010, **16**, 13116; (*n*) M. Rueping, E. Merino and R. M. Koenigs, *Adv. Synth. Catal.*, 2010, **352**, 2629; (*o*) S. Vellalath, I. Čorić and B. List, *Angew. Chem., Int. Ed.*, 2010, **49**, 9749; (*p*) J.-W. Zhang, Q. Cai, X.-X. Shi, W. Zhang and S.-L. You, *Synlett*, 2011, 1239; (*q*) M. Yang, Y.-M. Zhao, S.-Y. Zhang, Y.-Q. Tu and F.-M. Zhang, *Chem.–Asian J.*, 2011, **6**, 1344; (*r*) T. Hashimoto, H. Nakatsu, K. Yamamoto and K. Maruoka, *J. Am. Chem. Soc.*, 2011, **133**, 9730; (*s*) M. Rueping and W. Ieawsuwan, *Chem. Commun.*, 2011, **47**, 11450.