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Optically Active 1,1′-Spirobiindane-7,7′-diol (SPINOL)-Based Phosphoric Acids as Highly Enantioselective Catalysts for Asymmetric Organocatalysis

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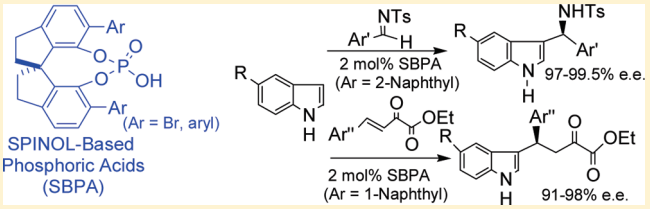
Supporting Information

ABSTRACT: The synthesis and application of a series of optically active 1,1′-spirobiindane-7,7′-diol (SPINOL)-based phosphoric acids are described. These SPINOL-based phosphoric acids were prepared from (*R*)-SPINOL in three steps and exhibited excellent enantioselectivities for the reactions of indoles with aldimines and *β*,*γ*-unsaturated-α-ketoesters. Our study provides a family of promising chiral phosphoric acids to the asymmetric organocatalysis toolbox.



Asymmetric organocatalysis, the use of optically active organic compounds as chiral catalysts, has recently attracted much attention.[1−7] Chiral cyclic phosphoric acids, which contain both a Brønsted acidic site and Lewis basic site, constitute a unique type of organocatalysts.[8−12] The use of chiral cyclic phosphoric acids as catalysts for asymmetric organocatalysis was first reported by Terada and Akiyama in 2004.[13,14] Since then, the tremendous potential of chiral cyclic phosphoric acids was recognized and a number of chiral diol-based phosphoric acids have been developed (Chart 1).[8−28] Axially chiral diol-based, including 1,1′-binaphthyl(BINOL)-based, phosphoric acids **A**−**C** were found to be the most promising chiral phosphoric acids.

While impressive results have been obtained with reported cyclic phosphoric acids as asymmetric organocatalysts, there exists ample room for further development of chiral cyclic phosphoric acids as organocatalysts. For example, the enantioselectivities of reported chiral phosphoric acids and analogues for a number of reactions are not high (ranging from 60% ee to low 90% ee). On the basis of the consideration that the unsatisfactory enantioselectivity for reported chiral phosphoric acids and analogues might in part be due to the conformational flexibility of their axially chiral diol units, such as the BINOL unit, we reasoned that chiral phosphoric acids based on more rigid chiral backbones might be more enantioselective than reported phosphoric acids and analogues. C_2-Symmetrical 1,1′-spirobiindane-7,7′-diol (SPINOL) (**1**)[29−31] and its derivatives (Chart 2),[32,33] which possess very rigid chiral framework, have been demonstrated to exhibit high enantioselectivities for transition metal-catalyzed asymmetric reactions.[32,33] Significantly, SPINOL-based ligands exhibited higher enantioselectivities than the corresponding ligands with axially chiral backbones in most of these reactions, suggesting the unique chiral inducing ability of spirocyclic structures. We thus envision that C_2-symmetrical SPINOLs might be excellent chiral diol units for chiral cyclic phosphoric acids and the rigidity of the spirocyclic framework may render optically active SPINOL-based phosphoric acids and analogues, as represented by (*R*)-**2** (Chart 2), more enantioselective than reported axially chiral diol-based phosphoric acids and analogues. Prompted by recent reports from List and Wang,[34] in this communication, we disclose our results on the preparation of SPINOL-based phosphoric acids and their application as highly active and enantioselective catalysts for the reaction of indoles with aldimines and *β*,*γ*-unsaturated-α-ketoesters.

Our preparation of optically active SPINOL-based phosphoric acids **2** started with (*R*)-SPINOL (**1**)[29−31] (Scheme 1). As shown in Scheme 1, reaction of (*R*)-SPINOL (**1**) with 2.05 equiv of *N*-bromosuccinimide (NBS) at −20 °C selectively yielded (*R*)-6,6′-dibromoSPINOL **3** in 70% yield. Pd-catalyzed cross-coupling reactions of (*R*)-6,6′-dibromoSPINOL **3** with arylboronic acids[35] occurred smoothly to yield 6,6′-diaryl-substituted SPINOLs (*R*)-**4a**−**f** in high yields. Reaction of (*R*)-**4a**−**f** and (*R*)-**3** with $POCl_3$ followed by hydrolysis yielded 6,6′-diaryl-substituted SPINOL-based phosphoric acids (*R*)-**2a**−**g** in moderate to good yields. Phosphoric acids (*R*)-**2a**−**g** are soluble in common organic solvents and are air/moisture-stable.

Optically active SPINOL-based phosphoric acids (*R*)-**2a**−**g** were then tested as organocatalysts for the Friedel−Crafts reaction of indoles with aldimines.[36−38] Such a BINOL-based phosphoric acid-catalyzed reaction was reported by You.[36] Good to excellent enantioselectivity was obtained with 10 mol % of catalyst loading at −60 °C. We found that while (*R*)-**2g** showed a moderate enantioselectivity (Table 1, entry 7), (*R*)-**2a**−**f** exhibited good to excellent enantioselectivities for the reaction

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(Table 1, entries 1−6), with **2c** displaying the highest one (Table 1, entry 3). Further testing showed that $ClCH_2CH_2Cl$ was the best solvent (Table 1, entries 3, 8, and 9). We found that even with 1 mol % of catalyst loading the reaction still occurred with high enantioselectivity (Table 1, entry 10). By carrying out the reaction at 0 °C, 98% ee was observed (Table 1, entry 11). In the reported BINOL-based phosphoric catalyst system, this same enantioselectivity was achieved by employing 10 mol % of BINOL-based phosphoric acid catalyst at −60 °C.[36] It should be noted that in BINOL-based phosphoric acid catalyst system, only 75% ee was observed with 2 mol % of catalyst loading.[14] Under otherwise identical reaction condition, a much higher enantioselectivity (94% ee) was observed with SPINOL-based phosphoric acid **2c** as the catalyst (Table 1, entry 12). We also examined several other aldimines and our results are listed in Table 2. As shown in Table 2, high enantioselectivity (≥97% ee) was universally observed with a 2 mol % of catalyst loading. Significantly, excellent enantioselectivity was also obtained for substrates where lower enantioselectivities were observed with BINOL-based phosphoric acids as catalysts (Table 2, entries 3, 5, and 6). In addition, it was found that excellent enantioselectivity was observed even with the use of 1.05 equiv of indole (Table 2, entries 13 and 14). These results showed that SPINOL-based phosphoric acids are highly efficient organocatalysts, with enantioselectivity comparable to or higher than reported chiral phosphoric acids.

Chart 1. Reported Chiral Diol-Based Phosphoric Acids

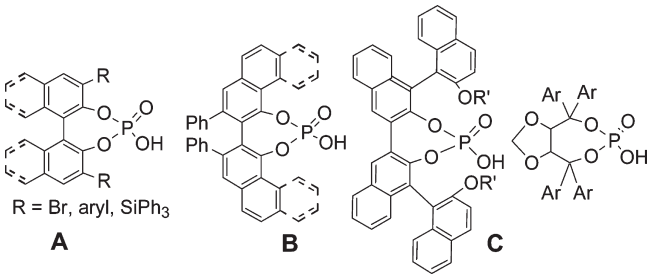
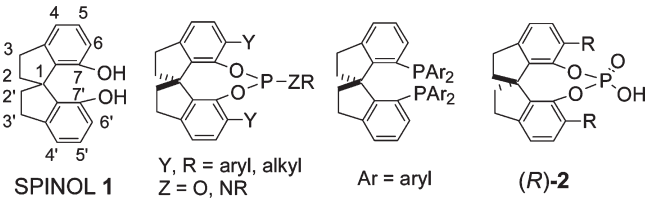


Chart 2. 1,1′-Spirobiindane-7,7′-diol (SPINOL) (1), Its Derivatives, and SPINOL-Based Phosphoric Acids (2)



Scheme 1. Preparation of (*R*)-SPINOL-Based Phosphoric Acids

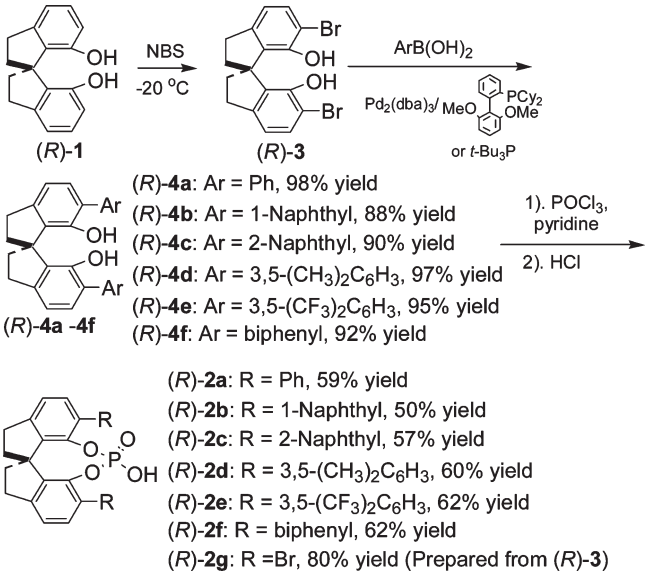
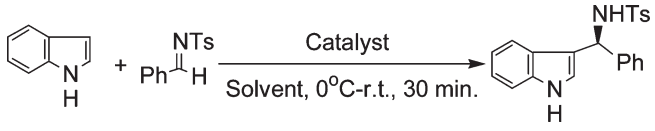


Table 1. SPINOL-Based Phosphoric Acid-Catalyzed Reaction of Indole with Benzaldimine[a]



entry	catalyst	catalyst loading (mol %)	solvent	temp	conv[b] (%)	ee (%)[c]
1	(*R*)-**2a**	10	CH_2Cl_2	rt	84	91.5
2	(*R*)-**2b**	2	CH_2Cl_2	rt	69	89.5
3	(*R*)-**2c**	2	CH_2Cl_2	rt	96	93
4	(*R*)-**2d**	2	CH_2Cl_2	rt	80	86
5	(*R*)-**2e**	2	CH_2Cl_2	rt	84	79
6	(*R*)-**2f**	2	CH_2Cl_2	rt	86	75
7	(*R*)-**2g**	10	CH_2Cl_2	rt	97.5	50
8	(*R*)-**2c**	2	$ClCH_2CH_2Cl$	rt	99	97.5
9	(*R*)-**2c**	2	toluene	rt	99	92
10	(*R*)-**2c**	1	$ClCH_2CH_2Cl$	rt	96	97
11	(*R*)-**2c**	2	$ClCH_2CH_2Cl$	0 °C	99	98[d]
12	(*R*)-**2c**	2	toluene	−60 °C	99	94 (75)[e,f]

[a] Reaction conditions: indole (3.0 equiv), imine (1.0 equiv). [b] Based on ^{1}H NMR analysis. [c] Based on HPLC (Chiracel OD column) analysis. [d] Reaction time: 2 h. [e] Reaction time: 42 h. [f] In parentheses: reported ee value with 2 mol % of BINOL-based phosphoric acids in toluene at −60 °C, see ref 36.

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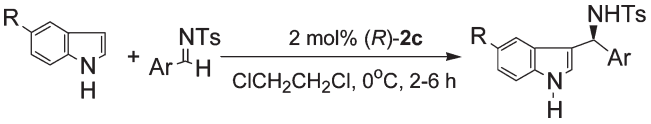
Table 2. SPINOL-Based Phosphoric Acid (*R*)-2c-Catalyzed Friedel–Crafts Reaction of Indoles with Aldimines[a]



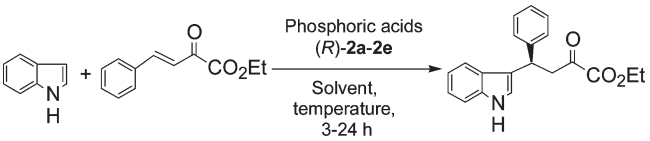
entry	R	Ar	yield (%)[b]	ee (%)[c]
1	H	Ph	98	98 (98)[d]
2	H	4-$CH_3C_6H_4$	95	97 (99)[d]
3	H	4-BrC_6H_4	99	99 (82)[d]
4	H	3-BrC_6H_4	94.5	99
5	H	4-ClC_6H_4	98	99 (94)[d]
6	H	3-$NO_2C_6H_4$	97	99.5 (89)[d]
7	Br	Ph	97	99 (98)[d]
8	Br	4-$CH_3C_6H_4$	92	97
9	Br	4-BrC_6H_4	97	99
10	Br	3-BrC_6H_4	94	99
11	Br	4-ClC_6H_4	95	98
12	Br	3-$NO_2C_6H_4$	93	99.5
13	H	4-BrC_6H_4	94.5	99[e]
14	H	4-BrC_6H_4	90	99[f]

[a] Reaction conditions: indole (3.0 equiv), imine (1.0 equiv), 2 mol % phosphoric acid **2c**, $ClCH_2CHC_2Cl$, 0 °C, 2 h. [b] Isolated yields. [c] Based on HPLC (Chiracel OD or AD-H column) analysis. [d] In parentheses: reported ee value with 10 mol % of BINOL-based phosphoric acids at −60 °C, see ref 36. [e] 1.2 equiv of indole was used. [f] 1.05 equiv of indole was used.

We have also tested the reaction of indoles with β,γ-unsaturated-α-ketoesters.[39−43] This reaction was chosen because it involves the activation of the carbonyl group, and it was reported that BINOL-based phosphoric acids cannot catalyze it. More acidic *N*-triflylphosphoramides[39] or a binary BINOL-based phosphoric acid−MgF_2 catalyst system were needed to realized this reaction.[40] We found not only SPINOL-based phosphoric acids (*R*)-**2a**−**e** can catalyze the reaction (Table 3, entries 1−5), but also a 90% ee was observed with (*R*)-**2b** as the catalyst (Table 3, entry 2). Further testing showed that with 2 mol % of phosphoric acid (*R*)-**2b**, $ClCH_2CH_2Cl$ as the solvent at −20 °C, a 94.5% ee could be obtained. The highest percent ee reported for this substrate with chiral phosphoric acids/phosphoramides as catalysts was 90% ee and was achieved by using 2 mol % BINOL-based phosphoric acids and 0.5 mol % MgF_2 at −70 °C.[40] We also examined other β,γ-unsaturated-α-ketoesters and our results are listed in Table 4. We found that excellent enantioselectivity, higher than reported results with BINOL-based phosphoramides or phosphoric acid−MgF_2 as catalysts, was observed (Table 4). For a comparison purpose, an addition reaction with **2b** as the catalyst was also examined under the reaction condition reported by Chen (toluene, −70 °C).[40] We found higher enantioselectivity was observed for **2b** (93% ee) than BINOL-based phosphoric acid−MgF_2 catalyst (83% ee)[40] (Table 4, entry 7). These results also showed that SPINOL-based phosphoric acids are a family of promising chiral phosphoric acids, with their enantioselectivity higher than those of BINOL-based phosphoric acids.

In summary, based on the consideration that the rigidity of the spirocyclic framework may render SPINOL-based phosphoric acids more enantioselective than reported axially chiral diol-based phosphoric acids, a series of optically active (*R*)-SPINOL-based phosphoric acids were prepared from readily available (*R*)-SPINOL in three steps. These SPINOL-based phosphoric acids

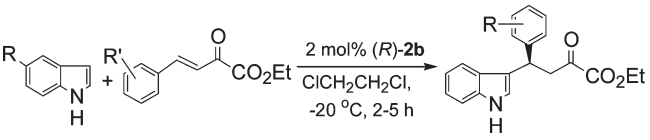
Table 3. SPINOL-Based Phosphoric Acid-Catalyzed Reactions of Indole with a β,γ-Unsaturated-α-ketoester[a]



entry	cat.	cat. loading (mol %)	solvent	temp	ee (%)[b]
1	(*R*)-**2a**	5	CH_2Cl_2	rt	81
2	(*R*)-**2b**	5	CH_2Cl_2	rt	90
3	(*R*)-**2c**	5	CH_2Cl_2	rt	58
4	(*R*)-**2d**	5	CH_2Cl_2	rt	61
5	(*R*)-**2e**	5	CH_2Cl_2	rt	37
6	(*R*)-**2f**	5	CH_2Cl_2	rt	76
7	(*R*)-**2b**	5	$CHCl_3$	rt	89
8	(*R*)-**2b**	5	toluene	rt	85
9	(*R*)-**2b**	5	$(CH_2Cl)_2$	rt	91.5
10	(*R*)-**2b**	2	$(CH_2Cl)_2$	rt	92
11	(*R*)-**2b**	2	$(CH_2Cl)_2$	0 °C	93[c]
12	(*R*)-**2b**	2	$(CH_2Cl)_2$	−10 °C	94[c]
13	(*R*)-**2b**	2	$(CH_2Cl)_2$	−20 °C	94.5[c]

[a] Reaction conditions: indole (1.5 equiv), β,γ-unsaturated-α-ketoester (1.0 equiv), 99% conversion was observed for all entries. [b] Based on HPLC (Chiracel OD or AD-H column) analysis. [c] 3.0 equiv of indole was used.

Table 4. SPINOL-Based Phosphoric Acid-Catalyzed Reactions of Indoles with β,γ-Unsaturated-α-ketoesters[a]



entry	R	R′	yield (%)[b]	ee (%)[c]
1	H	H	84	94.5 (90)[d]
2	H	2-F	96	98 (94)[d]
3	H	4-Me	89.5	94 (87)[d]
4	Br	H	82	91
5	Br	2-F	92	97
6	H	4-Cl	94	94 (83)[d]
7	H	4-Cl	84[e]	93 (83)[d]

[a] Reaction conditions: indole (3.0 equiv), β,γ-unsaturated-α-ketoester (1.0 equiv). [b] Isolated yields. [c] Based on HPLC (Chiracel OD or AD-H column) analysis. [d] In parentheses: reported ee for β,γ-unsaturated-α-ketoesters (methyl esters) with 2 mol % of BINOL-based phosphoric acid−0.5 mol % of MgF_2 catalyst at −70 °C, see ref 40. [e] The reaction was carried out in toluene at −70 °C for 48 h.

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were employed as organocatalysts for the reactions of indoles with aldimines and β,γ-unsaturated-α-ketoesters. They exhibited excellent enantioselectivity in these reactions, comparable to or higher than those reported for phosphoric acids. Our study adds a new family of promising chiral phosphoric acids to the asymmetric organocatalysis toolbox and paves the road for the development of other SPINOL-based phosphoric acids and related Brønsted acidic analogues such as SPINOL-based *N*-triflylphosphoramides.[44−47] Work toward this direction is actively underway.

EXPERIMENTAL SECTION

General. NMR spectra were recorded on 300 or 600 MHz spectrometers (300 or 600 MHz for ^{1}H NMR, 150 M Hz for ^{13}C NMR, and 121 MHz for ^{31}P NMR) with $CDCl_3$ as the solvent. The enantioselectivities were determined by using a HPLC instrument (analysis condition: hexanes/IPA = 70/30 to 90/10, flow rate at 1.0 mL/min, and UV detector λ = 254 nm).

(*R*)-6,6′-Dibromo-1,1′-spirobiindane-7,7′-diol, (*R*)-3. In a round flask, (*R*)-SPINOL (*R*)-**1** (1 g, 4 mmol) and $KHCO_3$ (0.8 g, 8 mmol) were mixed with dichloromethane (40 mL), and the mixture was stirred and cooled to −20 °C. Then, NBS (1.46 g, 8.2 mmol) was added. After being stirred at −20 °C for 2 h, the reaction mixture was poured into HCl (2 N). The reaction mixture was then extracted with dichloromethane. After removal of solvent by rota-evaporation, the residue was subjected to column chromatography (silica gel, hexanes/ethyl acetate (v/v = 20/1−15/1) as eluent), affording the expected compound (*R*)-**3** as a white solid (70% yield). Mp 159−160 °C; ^{1}H NMR δ 7.31 (d, J = 7.8 Hz, 2H), 6.75 (d, J = 8.4 Hz, 2H), 5.26 (s, 2H), 2.95−3.06 (m, 4H), 2.36−2.41 (m, 2H), 2.21−2.25 (m, 2H); ^{13}C NMR δ 148.6, 145.5, 134.3, 131.0, 118.0, 108.0, 59.8, 38.2, 31.2; HRMS (ESI+) m/z calcd for $C_{17}H_{18}Br_2NO_2$ ($[M + NH_4]^+$) 427.9679, found 427.9684.

General Procedure for the Preparation of (*R*)-6,6′-Diaryl-1,1′-spirobiindane-7,7′-diol, (*R*)-4a−f. Under N_2, to a round flask containing (*R*)-**3** (205 mg, 0.5 mmol), arylboronic acid (2−3 mmol), $Pd_2(dba)_3$ (9.2 mg, 2 mol %), S-Phos (16.5 mg, 8 mol %) or *t*-Bu_3P (12 mg, 12 mol %), and K_3PO_4 (3−4 mmol) was added toluene (5 mL) or dioxane (5 mL). The reaction mixture was stirred and heated to 105−110 °C for 8−12 h. After being cooled to room temperature, HCl (2 N) was added to the reaction mixture. The mixture was then extracted with dichloromethane. After removal of solvent by rota-evaporation, the residue was subjected to column chromatography [silica gel, hexanes/ethyl acetate (v/v = 20/1−15/1) or hexanes/dichloromethane (v/v = 1/1) as eluent], affording the expected product as a white solid.

(*R*)-**4a**:[48] 98% yield; mp 200−201 °C; ^{1}H NMR δ 7.47 (d, J = 7.8 Hz, 4H), 7.39 (t, J = 7.2 Hz, 4H), 7.30 (t, J = 7.8 Hz, 2H), 7.19 (d, J = 7.8 Hz, 2H), 6.93 (d, J = 7.8 Hz, 2H), 5.06 (s, 2H), 3.04−3.13 (m, 4H), 2.35−2.45 (m, 4H); ^{13}C NMR δ 149.5, 145.2, 137.5, 132.1, 130.5, 129.3, 128.6, 127.2, 126.9, 117.4, 58.4, 37.8, 31.2; HRMS (ESI+) m/z calcd for $C_{29}H_{28}NO_2$ ($[M + NH_4]^+$) 422.2115, found 422.2119.

(*R*)-**4b**: 88% yield; mp > 300 °C; ^{1}H NMR δ 7.68−7.92 (m, 5H), 7.31−7.60 (m, 8H), 6.61−7.22 (m, 5H), 4.71−4.90 (m, 2H), 3.05−3.20 (m, 4H), 2.41−2.55 (m, 4H); ^{13}C NMR δ 150.02, 149.98, 149.96, 149.91, 145.54, 145.47, 145.4, 135.2, 135.1, 134.8, 133.9, 133.70, 133.66, 133.60, 132.8, 132.7, 132.4, 132.2, 132.0, 131.9, 131.8, 131.2, 131.0, 130.9, 130.7, 128.4, 128.33, 128.29, 128.25, 128.18, 128.14, 128.11, 128.09, 128.0, 127.95, 126.7, 126.3, 126.22, 126.16, 126.10, 126.05, 126.0, 125.91, 125.88, 125.73, 126.64, 125.59, 125.50, 125.45, 125.21, 125.15, 125.07, 124.96, 116.99, 116.94, 116.84, 116.78, 58.6, 58.5, 38.3, 38.1, 37.8, 37.6, 31.41, 31.36; HRMS (ESI−) m/z calcd for $C_{37}H_{27}O_2$ ($[M - H]^-$) 503.2017, found 503.2020.

(*R*)-**4c**: 90% yield; mp 227−228 °C; ^{1}H NMR δ 7.93 (s, 2H), 7.86 (d, J = 8.4 Hz, 2H), 7.80−7.83 (m, 4H), 7.61 (dd, J = 7.2, 8.4 Hz, 2H), 7.44−7.48 (m, 4H), 7.30 (d, J = 7.8 Hz, 2H), 6.99 (d, J = 7.8 Hz, 4H), 5.20 (s, 2H), 3.08−3.16 (m, 4H), 2.39−2.50 (m, 4H); ^{13}C NMR δ 149.7, 145.4, 135.0, 133.5, 132.4, 132.1, 130.8, 128.1, 128.0, 127.8, 127.62, 127.60, 126.8, 126.2, 126.0, 117.6, 58.5, 37.8, 31.2; HRMS (ESI+) m/z calcd for $C_{37}H_{32}NO_2$ ($[M + NH_4]^+$) 522.2428, found 522.2434.

(*R*)-**4d**:[48] 97% yield; mp 93−94 °C; ^{1}H NMR δ 7.15 (d, J = 7.8 Hz, 2H), 7.07 (s, 4H), 6.94 (s, 2H), 6.90 (d, J = 7.2 Hz, 2H), 5.13 (s, 2H), 3.03−3.10 (m, 4H), 2.40−2.45 (m, 2H), 2.32−2.36 (m, 14H); ^{13}C NMR δ 149.4, 145.0, 138.2, 137.3, 132.3, 130.2, 128.9, 126.96, 126.93, 117.1, 58.5, 37.8, 31.2, 21.3; HRMS (ESI+) m/z calcd for $C_{33}H_{36}NO_2$ ($[M + NH_4]^+$) 478.2741, found 478.2737.

(*R*)-**4e**: 95% yield; mp 222−223 °C; ^{1}H NMR δ 7.97 (s, 4H), 7.79 (s, 2H), 7.29 (d, J = 7.8 Hz, 2H), 7.04 (d, J = 7.8 Hz, 2H), 4.92 (s, 2H), 3.10−3.17 (m, 4H), 2.44−2.47 (m, 2H), 2.33−2.38 (m, 2H); ^{13}C NMR δ 149.8, 147.0, 139.6, 131.6, 131.5 (q, J = 33.3 Hz), 130.6, 129.50, 129.48, 124.6, 123.4 (q, J = 273 Hz), 120.7(m), 118.6, 57.9, 37.6, 31.20, 31.15; HRMS (ESI−) m/z calcd for $C_{33}H_{19}F_{12}O_2$ ($[M - H]^-$) 675.1199, found 675.1209.

(*R*)-**4f**: 92% yield; mp 193−194 °C; ^{1}H NMR δ 7.56−7.63 (m, 10H), 7.43(t, J = 7.2 Hz, 4H), 7.34 (t, J = 7.8 Hz, 2H), 7.25−7.26 (m, 4H), 6.97 (d, J = 7.2 Hz, 2H), 5.11 (s, 2H), 3.06−3.16 (m, 4H), 2.38- 2.47 (m, 4H); ^{13}C NMR δ 149.6, 145.3, 140.8, 140.0, 136.4, 131.9, 130.6, 129.7, 128.8, 127.3, 127.1, 126.6, 117.6, 58.4, 37.8, 31.2; HRMS (ESI+) m/z calcd for $C_{41}H_{36}NO_2$ ($[M + NH_4]^+$) 574.2741, found 574.2747.

General Procedure for the Preparation of SPINOL-Based Phosphoric Acids. In a vial, (*R*)-**3** or (*R*)-**4** (0.25 mmol) was dissolved in anhydrous pyridine (0.5−1.0 mL) and the mixture was stirred under N_2. $POCl_3$ (77 mg, 0.5 mmol) was added dropwise. The reaction mixture was stirred at room temperature or 80 °C for 6−24 h. After being cooled to room temperature, the reaction mixture was transferred to HCl (6 N) carefully and extracted with dichloromethane three times. After removal of the solvent, a white solid was obtained. The white solid was then mixed with acetic acid, 1,2-dichloromethane, and HCl (6 N), and heated to reflux for 5 h to 7 days (monitored by ^{31}P NMR). After the reaction mixture was cooled to room temperature, a white solid was formed. The mixture was poured into HCl (4 N) and extracted with dichloromethane (three times). The organic solution was combined and washed with HCl (2 N) once, followed by filtration through a short silica gel column with dichloromethane/methanol (v/v 20/1) as eluent. The obtained solution was concentrated by rota-evaporation. A few milliliters of methanol was added to dissolve the residue. Then, HCl (2 N) was added slowly with swirling and the precipitate was formed. After standing in a refrigerator for a few hours, the final product was harvested as a white or pale pink solid by filtration, which was washed with water and then dried under vacuum for 2−6 h.

(*R*)-**2a**:[34b] 59% yield; mp >300 °C; ^{1}H NMR δ 7.36−7.39 (m, 4H), 7.26 (d, J = 7.8 Hz, 2H), 7.17 (d, J = 7.8 Hz, 2H), 7.02−7.07 (m, 6H), 3.60 (br, OH), 3.08−3.19 (m, 2H), 2.92 (dd, J = 7.8, 16.2 Hz, 2H), 2.35 (dd, J = 6.3, 11.7 Hz, 2H), 1.97 (dd, J = 10.8, 18.9 Hz, 2H); ^{13}C NMR δ 145.3, 142.31, 142.26, 140.53, 140.51, 137.8, 134.25, 134.23, 130.3, 129.5, 128.3, 126.9, 122.6, 60.03, 60.04, 38.6, 30.2; ^{31}P NMR δ −10.4; HRMS (ESI+) m/z calcd for $C_{29}H_{24}O_4P$ ($[M + H]^+$) 467.1407, found 467.1414.

(*R*)-**2b**:[34b] 50% yield; mp 169−172 °C; ^{1}H NMR δ 7.65−7.77 (m, 2H), 6.76−7.48 (m, 16H), 4.2 (br, OH), 2.92−3.34 (m, 4H), 2.26−2.53 (m, 4H); ^{13}C NMR δ 145.4, 145.1, 145.0, 143.25, 143.19, 142.9, 142.7, 140.8, 140.6, 140.08, 140.06, 139.8, 135.1, 134.9, 134.3, 134.1, 133.8, 133.5, 133.0, 132.8, 132.7, 132.5, 132.3, 132.1, 132.0, 131.9, 131.8, 131.7, 131.5, 131.3, 128.9, 128.8, 128.6, 128.5, 128.0, 127.9, 127.6, 127.35, 127.28, 126.7, 126.4, 125.72, 125.66, 125.58, 125.4, 125.11, 125.07, 125.03, 124.97, 124.94, 124.8, 124.7, 122.4, 121.4, 60.2, 60.0, 59.8, 39.15, 39.06, 38.74, 38.69, 30.53, 30.44, 30.40, 30.32; ^{31}P NMR δ −10.1; HRMS (ESI−) m/z calcd for $C_{37}H_{26}O_4P$ ($[M - H]^-$) 565.1574, found 565.1576.

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(*R*)-**2c**: 57% yield; mp >300 °C; ^{1}H NMR δ 7.67 (s, 2H), 7.53 (d, J = 7.8 Hz, 2H), 7.50 (d, J = 7.8 Hz, 2H), 7.33 (d, J = 7.2 Hz, 2H), 7.21−7.25 (m, 10H), 4.77 (br, OH), 3.14−3.20 (m, 2H), 2.98 (dd, J = 7.8, 16.2 Hz, 2H), 2.37 (dd, J = 6.6, 12.0 Hz, 2H), 2.23 (dd, J = 10.8, 19.8 Hz, 2H); ^{13}C NMR δ 145.29, 145.28, 142.43, 142.38, 140.58, 140.56, 135.2, 134.46, 134.44, 133.1, 132.2, 130.3, 128.0, 127.8, 127.5, 127.4, 127.2, 125.44, 125.37, 122.5, 59.91, 59.90, 38.7, 30.4; ^{31}P NMR δ −11.1; HRMS (ESI+) m/z calcd for $C_{37}H_{31}NO_4P$ ($[M + NH_4]^+$) 584.1985, found 584.1989.

(*R*)-**2d**: 60% yield; mp 235−240 °C; ^{1}H NMR δ 7.23 (d, J = 7.8 Hz, 2H), 7.13 (t, J = 7.8 Hz, 2H), 7.00 (s, 4H), 6.78 (s, 2H), 3.24 (br, OH), 3.08−3.14 (m, 2H), 2.88 (dd, J = 7.8, 16.2 Hz, 2H), 2.32 (dd, J = 6.0, 12.0 Hz, 2H), 2.18 (dd, J = 10.8, 19.2 Hz, 2H), 2.12 (s, 12H); ^{13}C NMR δ 145.04, 145.03, 142.9, 140.8, 138.4, 137.5, 134.9, 130.0, 127.9, 127.6, 122.0, 59.87, 59.86, 38.7, 30.3, 21.0; ^{31}P NMR δ −11.2; HRMS (ESI+) m/z calcd for $C_{33}H_{32}O_4P$ ($[M + H]^+$) 523.2033, found 523.2030.

(*R*)-**2e**:[34b] 62% yield; mp >300 °C; ^{1}H NMR δ 7.66 (s, 4H), 7.44 (s, 2H), 7.26 (s, 2H), 7.16 (d, J = 7.8 Hz, 2H), 3.14−3.20 (m, 2H), 2.99 (dd, J = 7.2, 16.2 Hz, 2H), 2.37 (dd, J = 7.2, 12.0 Hz, 2H), 2.22 (dd, J = 10.2, 19.2 Hz, 2H); ^{13}C NMR δ: 147.15, 147.13, 141.53, 141.48, 140.58, 140.56, 139.4, 132.19, 132.16, 131.4, 131.2, 131.0, 130.8, 130.7, 129.4, 126.0, 124.2, 123.2, 122.4, 120.6, 59.9, 38.5, 30.4; ^{31}P NMR δ −6.8; HRMS (ESI+) m/z calcd for $C_{33}H_{23}F_{12}NO_4P$ ($[M + NH_4]^+$) 756.1168, found 756.1167.

(*R*)-**2f**:[34b] 62% yield; mp 282−290 °C; ^{1}H NMR δ 7.35 (d, J = 7.8 Hz, 4H), 7.27 (d, J = 7.8 Hz, 2H), 7.16−7.24 (m, 16H), 3.67 (br, OH), 3.10−3.16 (m, 2H), 2.92 (dd, J = 7.8, 15.6 Hz, 2H), 2.32 (dd, J = 6.6, 12.0 Hz, 2H), 2.14 (dd, J = 11.4, 19.2 Hz, 2H); ^{13}C NMR δ 145.2, 142.3, 141.1, 140.52, 140.50, 139.8, 136.6, 134.2, 130.1, 129.7, 128.3, 127.2, 127.0, 126.7, 122.6, 60.0, 38.5, 30.3; ^{31}P NMR δ −9.2; HRMS (ESI+) m/z calcd for $C_{41}H_{32}O_4P$ ($[M + H]^+$) 619.2033, found 619.2037.

(*R*)-**2g**: 80% yield; mp >300 °C; ^{1}H NMR δ 7.45 (d, J = 7.8 Hz, 2H), 6.99 (d, J = 7.8 Hz, 2H), 5.14 (br s, OH), 2.98−3.04 (m, 2H), 2.78−2.82 (m, 2H), 2.19−2.22 (m, 2H), 2.03−2.08 (m, 2H); ^{13}C NMR δ 145.3, 142.2, 140.7, 133.0, 123.8, 114.7, 60.7, 38.4, 30.1; ^{31}P NMR δ −9.0; HRMS (ESI+) m/z calcd for $C_{17}H_{17}Br_2NO_4P$ ($[M + NH_4]^+$) 489.9237, found 489.9239.

General Procedure for SPINOL-Based Phosphoric Acids-Catalyzed Reaction of Indoles with Aldimines. In a vial, aldimine (0.2 mmol, 1.0 equiv) and SPINOL-based phosphoric acid (*R*)-**2c** (2.0 mol %) were dissolved in 1,2-dichloroethane (1.6 mL). The mixture was stirred and cooled to 0 °C with an ice-bath. Then, indole (0.6 mmol, 3.0 equiv) was added in one portion. The reaction mixture was stirred at this temperature for 2−6 h until all aldimine was converted (monitored by ^{1}H NMR). Column chromatography on silica gel with dichloromethane as eluent removed excessive indole, with dichloromethane/ethyl acetate (v/v = 20/1) eluent afforded the product, and with dichloromethane/methanol (v/v = 15/1) as eluent recovered the catalyst (*R*)-**2c**.

***N*-((1*H*-Indol-3-yl)(phenyl)methyl)-4-methylbenzenesulfonamide:**[36]**.** white solid, 98% yield, 98% ee (Chiralcel OD, t(minor) = 10.9 min, t(major) = 17.2 min); mp 141−142 °C; ^{1}H NMR δ 7.97 (br, 1H), 7.57 (d, J = 8.4 Hz, 2H), 7.31 (d, J = 7.8 Hz, 1H), 7.20−7.25 (m, 5H), 7.17 (t, J = 7.8 Hz, 1H), 7.12 (d, J = 7.8 Hz, 2H), 7.00 (t, J = 7.8 Hz, 2H), 6.69 (d, J = 1.8 Hz, 1H), 5.86 (d, J = 6.6 Hz, 1H), 4.99 (d, J = 6.6 Hz, 1H), 2.37 (s, 3H); ^{13}C NMR δ 143.0, 140.2, 137.4, 136.5, 129.2, 128.3, 127.4, 127.2, 125.3, 123.7, 122.6, 120.0, 119.3, 116.5, 111.2, 55.0, 21.5.

***N*-((1*H*-Indol-3-yl)(*p*-tolyl)methyl)-4-methylbenzenesulfonamide:**[36]**.** white solid, 95% yield, 97% ee (Chiralcel OD, t(minor) = 9.97 min, t(major) = 17.18 min); mp 143−145 °C; ^{1}H NMR δ 7.97 (br, 1H), 7.57 (d, J = 8.4 Hz, 2H), 7.29 (d, J = 7.8 Hz, 1H), 7.21 (d, J = 7.8 Hz, 1H), 7.15 (t, J = 7.8 Hz, 1H), 7.10−7.12 (m, 4H), 7.97−7.01 (m, 3H), 6.72 (s, 1H), 5.80 (d, J = 6.6 Hz, 1H), 4.99 (d, J = 6.6 Hz, 1H), 2.38 (s, 3H), 2.29 (s, 3H); ^{13}C NMR δ 143.0, 137.5, 137.3, 137.1, 136.6, 129.2, 129.0, 127.2, 127.1, 125.4, 123.7, 122.5, 119.9, 119.3, 116.6, 111.2, 54.9, 21.5, 21.1.

***N*-((4-Bromophenyl)(1*H*-indol-3-yl)methyl)-4-methylbenzenesulfonamide:**[36]**.** white solid, 99% yield, 99% ee (Chiralcel OD, t(minor) = 12.95 min, t(major) = 20.04 min); mp 201−202 °C; ^{1}H NMR δ 8.00 (br, 1H), 7.56 (d, J = 7.8 Hz, 2H), 7.32 (t, J = 9.0 Hz, 3H), 7.17−7.21 (m, 2H), 7.13 (t, J = 7.8 Hz, 4H), 7.01 (t, J = 7.8 Hz, 1H), 6.63 (d, J = 1.8 Hz, 1H), 5.80 (d, J = 6.6 Hz, 1H), 5.05 (d, J = 6.6 Hz, 1H), 2.40 (s, 3H); ^{13}C NMR δ 143.3, 139.3, 137.3, 136.5, 131.4, 129.4, 129.0, 127.2, 125.1, 123.7, 122.8, 121.3, 120.2, 119.1, 115.9, 111.3, 54.5, 21.5.

***N*-((3-Bromophenyl)(1*H*-indol-3-yl)methyl)-4-methylbenzenesulfonamide:**[41]**.** white solid, 94.5% yield, 99% ee (Chiralpak AD-H, t(minor) = 19.89 min, t(major) = 22.77 min); mp 142−143 °C; ^{1}H NMR δ 8.00 (br, 1H), 7.56 (d, J = 8.4 Hz, 2H), 7.31 (d, J = 8.4 Hz, 2H), 7.26−7.28 (m, 2H), 7.18−7.21 (m, 2H), 7.15 (d, J = 7.8 Hz, 2H), 7.08 (t, J = 7.8 Hz, 1H), 7.03 (t, J = 7.8 Hz, 1H), 6.64 (s, 1H), 5.82 (d, J = 6.0 Hz, 1H), 5.01 (d, J = 6.0 Hz, 1H), 2.39 (s, 3H); ^{13}C NMR δ 143.4, 142.4, 137.2, 136.5, 130.5, 130.2, 129.9, 129.4, 127.2, 126.0, 125.1, 123.7, 122.8, 122.4, 120.2, 119.1, 115.8, 111.3, 54.5, 21.5.

***N*-((4-Chlorophenyl)(1*H*-indol-3-yl)methyl)-4-methylbenzenesulfonamide:**[36]**.** white solid, 98% yield, 99% ee (Chiralcel OD, t(minor) = 12.34 min, t(major) = 18.93 min); mp 189−190 °C; ^{1}H NMR δ 7.99 (br, 1H), 7.57 (d, J = 8.4 Hz, 2H), 7.31 (d, J = 7.8 Hz, 1H), 7.17−7.21 (m, 6H), 7.15 (d, J = 7.8 Hz, 2H), 7.01 (t, J = 7.8 Hz, 1H), 6.64 (d, J = 2.4 Hz, 1H), 5.82 (d, J = 6.6 Hz, 1H), 5.02 (d, J = 7.2 Hz, 1H), 2.40 (s, 3H); ^{13}C NMR δ 143.3, 138.8, 137.3, 136.5, 133.2, 129.3, 128.6, 128.4, 127.2, 125.1, 123.7, 122.8, 120.2, 119.1, 116.0, 111.3, 54.4, 21.5.

***N*-((1*H*-Indol-3-yl)(3-nitrophenyl)methyl)-4-methylbenzenesulfonamide:**[36]**.** white solid, 97% yield, 99.5% ee (Chiralcel OD, t(minor) = 9.97 min, t(major) = 19.55 min); mp 203−204 °C; ^{1}H NMR (DMSO-d_6) δ 10.96 (br, 1H), 8.64 (d, J = 7.8 Hz, 1H), 8.06 (s, 1H), 7.97 (d, J = 8.4 Hz, 1H), 7.71 (d, J = 7.8 Hz, 1H), 7.43−7.46 (m, 3H), 7.38 (d, J = 7.8 Hz, 1H), 7.31 (d, J = 7.8 Hz, 1H), 7.05−7.08 (m, 3H), 6.92 (t, J = 7.2 Hz, 1H), 6.76 (d, J = 2.4 Hz, 1H), 5.90 (d, J = 7.2 Hz, 1H), 2.22 (s, 3H); ^{13}C NMR (DMSO-d_6) δ 147.7, 143.7, 142.3, 138.6, 136.6, 134.2, 129.6, 129.2, 126.6, 125.5, 124.2, 121.9, 121.8, 121.7, 119.01, 118.97, 114.9, 111.8, 54.0, 21.0.

***N*-((5-Bromo-1*H*-indol-3-yl)(phenyl)methyl)-4-methylbenzenesulfonamide:**[36]**.** white solid, 97% yield, 99% ee (Chiralcel OD, t(minor) = 7.30 min, t(major) = 15.14 min); mp 202−203 °C; ^{1}H NMR δ 8.04 (br, 1H), 7.61 (d, J = 8.4 Hz, 2H), 7.22−7.26 (m, 6H), 7.15−7.19 (m, 3H), 7.11 (s, 1H), 6.74 (d, J = 2.4 Hz, 1H), 5.74 (d, J = 6.0 Hz, 1H), 4.95 (d, J = 6.6 Hz, 1H), 2.40 (s, 3H); ^{13}C NMR δ 143.4, 140.1, 137.0, 135.1, 129.5, 128.5, 127.7, 127.15, 127.08, 127.06, 125.5, 125.1, 121.6, 116.2, 113.3, 112.7, 54.6, 21.6.

***N*-((5-Bromo-1*H*-indol-3-yl)(*p*-tolyl)methyl)-4-methylbenzenesulfonamide:** white solid, 92% yield, 97% ee (Chiralcel OD, t(minor) = 8.39 min, t(major) = 19.83 min); mp 183−185 °C; H NMR δ 8.04 (br, 1H), 7.61 (d, J = 8.4 Hz, 2H), 7.21 (dd, J = 1.8, 8.4 Hz, 1H), 7.14−7.19 (m, 3H), 7.10−7.13 (m, 3H), 7.05 (d, J = 7.8 Hz, 2H), 6.78 (d, J = 2.4 Hz, 1H), 5.68 (d, J = 6.0 Hz, 1H), 4.92 (d, J = 5.4 Hz, 1H), 2.40 (s, 3H), 2.31 (s, 3H); ^{13}C NMR δ 143.3, 137.4, 137.2, 137.0, 135.1, 129.5, 129.2, 127.14, 127.07, 126.98, 125.4, 125.1, 121.6, 116.2, 113.2, 112.7, 54.5, 21.6, 21.1; HRMS (ESI−) m/z calcd for $C_{23}H_{20}BrN_2O_2S$ ($[M - H]^-$) 467.0434, found 467.0439.

***N*-((5-Bromo-1*H*-indol-3-yl)(4-bromophenyl)methyl)-4-methylbenzenesulfonamide:** white solid, 97% yield, 99% ee (Chiralcel OD, t(minor) = 7.16 min, t(major) = 17.84 min); mp 220−221 °C; ^{1}H NMR (DMSO-d_6) δ 11.12 (br, 1H), 8.48 (d, J = 8.4 Hz, 1H), 7.48 (d, J = 8.4 Hz, 2H), 7.35 7.37 (m, 3H), 7.26 (d, J = 8.4 Hz, 1H), 7.21 (d, J = 8.4 Hz, 2H), 7.14 (d, J = 9.0 Hz, 3H), 6.78 (d, J = 2.4 Hz, 1H), 5.67 (d, J = 8.4 Hz, 1H), 2.30 (s, 3H); ^{13}C NMR (DMSO-d_6) δ 142.2, 140.9, 138.3, 135.1, 130.8, 129.34, 129.29, 129.14, 129.08, 127.1, 126.4, 125.8, 125.7, 123.9, 123.8, 119.9, 114.8, 113.5, 111.4, 53.42, 53.39,

21.05, 21.02; HRMS (ESI−) m/z calcd for $C_{22}H_{17}Br_2N_2O_2S$ ([M + HCOO]$^-$) 530.9383, found 530.9381.

***N*-((5-Bromo-1*H*-indol-3-yl)(3-bromophenyl)methyl)-4-methylbenzenesulfonamide:** white solid, 94% yield, 99% ee (Chiralcel OD, t(minor) = 7.12 min, t(major) = 12.04 min); mp 187−188 °C; ^{1}H NMR δ 8.06 (br, 1H), 7.63 (d, J = 8.4 Hz, 2H), 7.37 (d, J = 7.8 Hz, 1H), 7.33 (s, 1H), 7.23−7.25 (m, 4H), 7.19 (d, J = 8.4 Hz, 1H), 7.15 (t, J = 7.8 Hz, 1H), 7.11 (s, 1H), 6.69 (d, J = 2.4 Hz, 1H), 5.71 (d, J = 5.4 Hz, 1H), 4.88 (d, J = 6.0 Hz, 1H), 2.43 (s, 3H); ^{13}C NMR δ 143.8, 142.4, 136.8, 135.0, 130.7, 130.2, 130.0, 129.7, 127.1, 126.9, 125.83, 125.81, 125.2, 122.6, 121.3, 115.6, 113.6, 112.8, 54.0, 21.7; HRMS (ESI−) m/z calcd for $C_{22}H_{17}Br_2N_2O_2S$ ([M − H]$^-$) 530.9383, found 530.9388.

***N*-((5-Bromo-1*H*-indol-3-yl)(4-chlorophenyl)methyl)-4-methylbenzenesulfonamide:** white solid, 95% yield, 98% ee (Chiralcel OD, t(minor) = 6.85 min, t(major) = 16.10 min); mp 196−197 °C; ^{1}H NMR δ 8.09 (br, 1H), 7.61 (d, J = 7.8 Hz, 2H), 7.20−7.25 (m, 7H), 7.16 (d, J = 8.4 Hz, 1H), 7.07 (s, 1H), 6.66 (d, J = 1.8 Hz, 1H), 5.69 (d, J = 6.6 Hz, 1H), 5.00 (d, J = 6.6 Hz, 1H), 2.43 (s, 3H); ^{13}C NMR δ 143.7, 138.7, 136.8, 135.0, 133.4, 129.7, 128.6, 128.5, 127.1, 126.9, 125.7, 125.1, 121.3, 115.7, 113.5, 112.8, 54.0, 21.6; HRMS (ESI−) m/z calcd for $C_{22}H_{17}BrClN_2O_2S$ ([M − H]$^-$) 486.9888, found 486.9894.

***N*-((5-Bromo-1*H*-indol-3-yl)(3-nitrophenyl)methyl)-4-methylbenzenesulfonamide:** white solid, 93% yield, 99.5% ee (Chiralcel OD, t(minor) = 9.22 min, t(major) = 16.66 min); mp 221−223 °C; ^{1}H NMR (DMSO-d_6) δ 11.17 (br, 1H), 8.65 (d, J = 8.4 Hz, 1H), 8.11 (s, 1H), 8.00 (dd, J = 2.4, 8.4 Hz, 1H), 7.74 (d, J = 7.2 Hz, 1H), 7.47−7.50 (m, 3H), 7.43 (d, J = 1.2 Hz, 1H), 7.28 (d, J = 9.0 Hz, 1H), 7.16 (dd, J = 1.2, 8.4 Hz, 1H), 7.11 (d, J = 7.8 Hz, 2H), 6.77 (d, J = 2.4 Hz, 1H), 5.89 (d, J = 7.8 Hz, 1H), 2.25 (s, 3H); ^{13}C NMR (DMSO-d_6) δ 147.6, 143.5, 142.3, 138.1, 135.1, 134.0, 133.9, 129.5, 129.2, 129.1, 127.1, 126.5, 126.1, 125.9, 124.1, 124.0, 121.8, 121.7, 121.1, 114.5, 113.64, 113.61, 111.6, 53.19, 53.17, 20.94, 20.90; HRMS (ESI−) m/z calcd for $C_{22}H_{17}BrN_3O_4S$ ([M − H]$^-$) 498.0129, found 498.0135.

General Procedure for SPINOL-Based Phosphoric Acids-Catalyzed Reaction of Indoles with β,γ-Unsaturated-α-ketoesters. In a vial, β,γ-unsaturated-α-ketoester (0.2 mmol, 1.0 equiv) and SPINOL-based phosphoric acid (*R*)-**2b** (2.0 mol %) were dissolved in 1,2- dichloroethane (1 mL). The mixture was stirred and cooled to −20 °C. Then, indole (0.6 mmol, 3.0 equiv) was added in one portion. The reaction mixture was stirred at this temperature for 2−5 h until β,γ-unsaturated-α-ketoester was fully reacted (monitored by ^{1}H NMR). Column chromatography on silica gel with hexanes/ethyl acetate (v/v = 3/1) afforded the product and with dichloromethane/methanol (v/v = 15/1) as eluent recovered the catalyst (*R*)-**2b**.

Ethyl 4-(1*H*-indol-3-yl)-2-oxo-4-phenylbutanoate:[38]**.** 84% yield, 94.5% ee (Chiralcel OD, t(major) = 37.72 min, t(minor) = 44.68 min); ^{1}H NMR δ 8.01 (br, 1H), 7.42 (d, J = 7.8 Hz, 1H), 7.32−7.33 (m, 3H), 7.25−7.27 (m, 2H), 7.14−7.19 (m, 2H), 7.01−7.04 (m, 2H), 4.92 (t, J = 7.8 Hz, 1H), 4.19−4,24 (m, 2H), 3.68 (dd, J = 7.2, 17.4 Hz, 1H), 3.60 (dd, J = 7.8, 16.8 Hz, 1H), 1.27 (t, J = 7.2 Hz, 3H); ^{13}C NMR δ 193.0, 160.9, 143.2, 136.5, 128.5, 127.8, 126.6, 126.4, 122.3, 121.5, 119.5, 119.4, 118.4, 111.1, 62.4, 45.6, 37.8, 13.9.

Ethyl 4-(1*H*-indol-3-yl)-2-oxo-4-*p*-tolylbutanoate: 89.5% yield, 94% ee (Chiralpak AD-H, t(major) = 17.06 min, t(minor) = 20.95 min); ^{1}H NMR δ 7.98 (br, 1H), 7.43 (d, J = 7.8 Hz, 1H), 7.32 (d, J = 8.4 Hz, 1H), 7.21 (d, J = 7.8 Hz, 2H), 7.15 (t, J = 7.2 Hz, 1H), 7.07 (d, J = 7.8 Hz, 2H), 7.02 (t, J = 7.2 Hz, 2H), 4.88 (t, J = 7.8 Hz, 1H), 4.19−4,23 (m, 2H), 3.66 (dd, J = 7.2, 16.8 Hz, 1H), 3.57 (dd, J = 7.8, 16.8 Hz, 1H), 2.28 (s, 3H), 1.27 (t, J = 7.2 Hz, 3H); ^{13}C NMR δ 193.2, 161.0, 140.2, 136.5, 136.0, 129.2, 127.6, 126.4, 122.2, 121.4, 119.5, 119.4, 118.6, 111.1, 62.4, 45.7, 37.4, 21.0, 13.9; HRMS (ESI−) m/z calcd for $C_{21}H_{20}NO_3$ ([M − H]$^-$) 334.1449, found 334.1454.

Ethyl 4-(4-chlorophenyl)-4-(1*H*-indol-3-yl)-2-oxobutanoate: 94% yield, 94% ee (Chiralpak AD-H, t(major) = 17.44 min, t(minor) = 24.99 min); mp 80−82 °C; ^{1}H NMR δ 8.02 (br, 1H), 7.37 (d, J = 7.8 Hz, 1H), 7.33 (d, J = 8.4 Hz, 1H), 7.22−7.27 (m, 4H), 7.17 (t, J = 7.2 Hz, 1H), 7.02−7.04 (m, 2H), 4.89 (t, J = 7.2 Hz, 1H), 4.21−4.25 (m, 2H), 3.65 (dd, J = 7.2, 17.4 Hz, 1H), 3.57 (dd, J = 8.4, 17.4 Hz, 1H), 1.29 (t, J = 7.2 Hz, 3H); ^{13}C NMR δ 192.7, 160.9, 141.8, 136.6, 132.3, 129.2, 128.7, 126.2, 122.5, 121.4, 119.7, 119.3, 117.9, 111.2, 62.6, 45.4, 37.1, 13.9; HRMS (ESI−) m/z calcd for $C_{20}H_{17}ClNO_3$ ([M − H]$^-$) 354.0902, found 354.0909.

Ethyl 4-(2-fluorophenyl)-4-(1*H*-indol-3-yl)-2-oxobutanoate: 96% yield, 98% ee (Chiralpak AD-H, t(major) = 15.55 min, t(minor) = 21.48 min); mp 99−101 °C; ^{1}H NMR δ 8.02 (br, 1H), 7.49 (d, J = 8.4 Hz, 1H), 7.33 (d, J = 7.8 Hz, 1H), 7.23−7.26 (m, 1H), 7.14−7.18 (m, 2H), 7.09 (d, J = 2.4 Hz, 1H), 7.00−7.07 (m, 3H), 5.22 (t, J = 7.8 Hz, 1H), 4.22−4.27 (m, 2H), 3.74 (dd, J = 7.2, 16.8 Hz, 1H), 3.59 (dd, J = 7.8, 17.4 Hz, 1H), 1.29 (t, J = 7.2 Hz, 3H); ^{13}C NMR δ 192.6, 161.3, 160.9, 159.7, 136.4, 130.04, 129.95, 129.33, 129.31, 128.27, 128.22, 126.4, 124.19, 124.17, 122.4, 121.7, 119.6, 119.1, 117.0, 115.7, 115.5, 111.1, 62.5, 44.4, 31.04, 31.02, 13.9; HRMS (ESI−) m/z calcd for $C_{20}H_{17}FNO_3$ ([M − H]$^-$) 338.1198, found 338.1203.

Ethyl 4-(5-bromo-1*H*-indol-3-yl)-2-oxo-4-phenylbutanoate: 82% yield, 91% ee (Chiralpak AD-H, t(major) = 40.45 min, t(minor) = 50.83 min); ^{1}H NMR δ 8.06 (br, 1H), 7.54 (s, 1H), 7.26−7.30 (m, 4H), 7.17−7.23 (m, 3H), 7.04 (m, 1H), 4.85 (t, J = 7.8 Hz, 1H), 4.21−4.25 (m, 2H), 3.64 (dd, J = 7.8, 17.4 Hz, 1H), 3.57 (dd, J = 7.8, 16.8 Hz, 1H), 1.29 (t, J = 7.2 Hz, 3H); ^{13}C NMR δ 192.8, 160.9, 142.7, 135.1, 128.6, 128.2, 127.6, 126.8, 125.2, 122.7, 121.9, 118.0, 112.8, 112.6, 62.5, 45.6, 37.5, 13.9; HRMS (ESI−) m/z calcd for $C_{20}H_{17}BrNO_3$ ([M − H]$^-$) 398.0397, found 398.0404.

Ethyl 4-(5-bromo-1*H*-indol-3-yl)-4-(2-fluorophenyl)-2-oxobutanoate: 92% yield, 97% ee (Chiralcel OD, t(major) = 17.42 min, t(minor) = 22.15 min); mp 139−140 °C; ^{1}H NMR (DMSO-d_6) δ 11.17 (br, 1H), 7.55 (s, 1H), 7.40 (t, J = 7.2 Hz, 1H), 7.30−7.32 (m, 2H), 7.21−7.24 (m, 1H),7.13−7.17 (m, 2H), 7.11 (t, J = 7.8 Hz, 1H), 4.94 (t, J = 7.8 Hz, 1H), 4.20 (q, J = 7.2 Hz, 2H), 3.77 (dd, J = 7.2, 18.6 Hz, 1H), 3.61 (dd, J = 7.8, 18.0 Hz, 1H), 1.24 (t, J = 7.2 Hz, 3H); ^{13}C NMR (DMSO-d_6) δ 192.2, 160.6, 160.3, 158.9, 134.9, 130.6, 130.5, 129.2, 128.2, 127.8, 124.47, 124.43, 124.22, 124.18, 123.7, 123.6, 120.3, 115.8, 115.4, 115.3, 113.58, 113.56, 111.2, 61.8, 43.7, 29.4, 29.3, 13.78, 13.72; HRMS (ESI−) m/z calcd for $C_{20}H_{16}BrFNO_3$ ([M − H]$^-$) 416.0303, found 416.0310.

■ ASSOCIATED CONTENT

Supporting Information. General procedures and characterization of SPINOL-based phosphoric acids and products of their catalyzed reactions. This material is available free of charge via the Internet at http://pubs.acs.org.

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