JOC The Journal of Organic Chemistry

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Electrostatically Enhanced Phosphoric Acids and Their Applications in Asymmetric Friedel-Crafts Alkylations

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J. Org. Chem., Just Accepted Manuscript • DOI: 10.1021/acs.joc.9b01741 • Publication Date (Web): 06 Aug 2019

Downloaded from pubs.acs.org on August 8, 2019

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ABSTRACT

A series of electrostatically enhanced phosphoric acid catalysts were synthesized and studied. These compounds possess two positively charged *N*-octylpyridinium or triarylphosphonium ion centers at the 3,3'-positions of the (*R*)-BINOL backbone to enhance reactivity and provide needed steric bulk for enantioselective transformations. Catalytic activities for Friedel-Crafts alkylations of indoles with *trans-* β -nitrostyrenes were studied. Both types of catalysts accelerate reaction conversions relative to noncharged analogues, and good enantioselectivities up to 90% ee are observed with the phosphonium ion tagged phosphoric acids. This transformation also can be scaled up to synthetically useful amounts affording >250 mg of product without losing reactivity or selectivity.

INTRODUCTION

Over the past decade or so a large body of novel Brønsted acids have emerged as effective organocatalysts for a variety of organic transformations.¹ These species are excellent alternatives to metal-containing catalysts as they typically are moisture and air tolerant, and are considered to be environmentally friendlier in nature.² Among these Brønsted acid catalysts, phosphoric acids bearing a 1,1'-bi-2-naphthol (BINOL) backbone have been extensively investigated. Hundreds of derivatives have been prepared as they provide a means for carrying out enantioselective acid-catalyzed processes.³ This includes asymmetric carbon-carbon bond forming transformations⁴ which are extremely valuable, but can be synthetically challenging to carry out.⁵

BINOL-derived phosphoric acids are generally more active catalysts than other chiral Brønsted acids such as BINOL derivatives,⁶ thioureas,⁷ and α, α, α -tetraaryl-1,3-dioxolane-4,5-dimethanols (TADDOLs)⁸ due to their greater acidities.⁹ To broaden their scope and develop more reactive derivatives, several strategies have been employed. These include introducing electron withdrawing groups into the catalyst backbone,¹⁰ modifying the phosphate functional group (e.g., to phosphoramides),¹¹ and employing acidic achiral additives.¹²

More recently, incorporation of positively charged pyridinium ion centers without the introduction of new hydrogen bond donating sites was found to improve the catalytic abilities of achiral phenols,¹³ thioureas,¹⁴ and phosphoric acids¹⁵ by orders of magnitude. In addition, several chiral charge-activated thioureas were reported and found to display excellent reactivities and good enantioselectivities in Friedel-Crafts alkylations of indoles with *trans-β*-nitrostyrenes.¹⁶ Chiral phosphonium ion-containing (*R*)-BINOL-derived phosphoric acids were also recently communicated and found to give good to excellent enantioselectivities in the reactions of indoles with 2,2,2-trifluoroacetophenones.¹⁷ To build upon these efforts a number of new derivatives are

reported, and both charged and noncharged catalysts were investigated using the reaction illustrated in eq. 1 as a well-studied test platform (Figure 1). In this regard it is worth noting that **3b** previously was used for the reaction of indole with *trans-\beta*-nitrostyrene,¹⁸ and the PF₆⁻ salt of **2a** was found to be catalytically inactive for this process.¹⁹



Figure 1. Catalysts used in this work; different counteranions for 2a were also studied.

RESULTS AND DISCUSSION

Our study was initiated by synthesizing 1a and 1b, two (*R*)-BINOL-derived phosphoric acids with *N*-octylpyridinium groups at the 3,3'-backbone positions. A noncoordinating tetrakis[3,5-

bis(trifluoromethyl)phenyl]borate anion (BAr^F₄⁻) was incorporated as the counterion because it enhances reactivity and solubility in nonpolar media.^{15,20} Catalytic activities for the Friedel-Crafts alkylation of indole with *trans-* β -nitrostyrene were examined at different temperatures in CH₂Cl₂ with a 10 mol % catalyst loading and 3 Å molecular sieves (MS) to remove adventitious moisture (Table 1). Disappointingly, the enantioselectivities were poor with the best results of only 21% and 16% ee at -30 °C for **1a** and **1b**, respectively (entries 1-6). These findings led us to examine bulky triaryl phosphonium ion derivatives **2a-2e** as conveniently prepared alternatives.^{17,19,21}

 Table 1. Optimizations of catalysts and reaction conditions^a

entry	cat.	T (°C)	time (h)	yield $(\%)^b$	ee (%) ^c
1	1a	20	24	70	-14
2	1a	0	48	58	-16
3	1a	-30	73	26	-21
4	1b	20	24	70	-12
5	1b	0	48	64	-13
6	1b	-30	73	30	-16
7	2a	20	8	59	35
8	2a	0	24	50	36
9	2a	-30	46	38	40
10	2b	20	5	68	50
11	2b	0	24	75	59
12	2b	-30	46	81	70
13	2c	20	5	67	36
14	2c	0	24	71	46
15	2c	-30	46	83	61
16	2d	20	5	69	34
17	2d	0	24	73	46
18	2d	-30	46	85	61
19	2e	20	5	73	47
20	2e	0	24	63	51
21	2e	-30	46	60	57

^{*a*}Reactions were performed with 0.1 mmol indole, 0.2 mmol *trans-β*-nitrostyrene, 0.01 mmol catalyst and 10 mg of 3 Å MS in 0.5 mL of CH₂Cl₂. ^{*b*}Isolated yield. ^{*c*}Determined by chiral HPLC. Positive ee values correspond to the *S*-enantiomer being the major product.

To our delight, the preliminary screening results for the phosphonium ion-tagged phosphoric acids (entries 7-21) revealed that they are both more reactive and enantioselective than their pyridinium ion-containing analogues. Intriguingly they also led to a reversal in the preferred enantiomer (i.e., the *S*-enantiomer is favored with catalysts $2a-e)^{22,23}$ although this type of finding has been previously noted and rationalized by steric differences in the chiral pocket.³ The parent derivative 2a only gave an ee of 35-40% at temperatures ranging from 20 to -30 °C (entries 7-9), but incorporation of *p*-methyl substituents on each phenyl group led to significant improvements in the reaction conversions and stereoselectivities (entries 10-12). That is, over the same time period at -30 °C, the isolated yield increased from 38% to 81% and the ee improved from 40% to 70%. A further decrease in temperature to -50 °C was not practical in that less than a 10% conversion was observed after 48 hours. Replacement of the *p*-methyl groups by larger ethyl or *n*-propyl substituents had little impact on the product yield, but led to ~10-15% lower ee values over the studied temperature range (entries 13-18).

To address whether the improvement in the stereoselectivity brought about by the *p*-methyl groups is due to steric or electronic effects, the diphenyl(*p*-tolyl)phosphonium ion-tagged BINOL phosphoric acid 2e was prepared and investigated. Its steric requirements should be very similar to those of the unsubstituted phosphoric acid 2a because the Ar₃P group can rotate readily enabling any unfavorable interactions brought about by the methyl group to be minimized. Electronically, 2e should be intermediate in behavior to 2a and 2b since these compounds have 2, 0 and 6 methyl groups, respectively. The observed enantioselectivities with 2e at 20, 0 and -30 °C (entries 19-21) are between the results for 2a and 2b. This indicates that the larger ee values for 2b compared to 2a are primarily due to the electron donating effects of the six methyl groups in the former compound.²⁴ Computations are in accord with this suggestion and indicate that the *S*- enantiomer

of the Friedel-Crafts alkylation product is favored as was observed. More specifically, B3LYP/6-31G(d,p) transition state structures leading to both enantiomers were located for the (*R*)-BINOLderived phosphoric acid catalysts with H, PPh₃, P(*p*-CH₃C₆H₄)₃ and SiPh₃ at the 3 and 3'-positions. Previously reported geometries with simplified biphenyl-substituted phosphoric acid catalysts by Hirata and Yamanaka²⁵ and Li and You et al.²⁶ were used as our starting points and subsequent M06-2X/cc-pVTZ//B3LYP/6-31G(d,p) free energy barriers were obtained. In accord with experiment, **2b** is predicted to be more selective than **2a** or **3b** (i.e., $\Delta G^{\ddagger}(R - S) = 0.60$ (**2b**), 0.35 (**2a**) and 0.32 kcal mol⁻¹ (**3b**) as compared to experimental values of 0.88, 0.41²⁷ and 0.51 kcal mol⁻¹, respectively). The geometries of the transition structures catalyzed by **2a** and **2b** are very similar but the ones that lead to the *S*-enantiomer have C–H •• O interactions that are not present in the geometry leading to the *R*-enantiomer (Figure 2).



Figure 2. Computed B3LYP/6-31G(d,p) transition structures with **2b** for the *S* (left) and *R* (right) enantiomers. Most carbon-attached hydrogen atoms were removed for clarity.

The effect of the counterion was examined next by taking the chloride anion precursor to **1a** and converting it to the BF_4^- , PF_6^- and $B(C_6F_5)_4^-$ salts **2f-2h** (eq. 2). These species were com-



pared to the BAr^F₄⁻ salt **2a** at -30 °C and their reactivity order is as follows: BF₄⁻ < PF₆⁻ < B(C₆F₅)₄⁻ < BAr^F₄⁻ (Table 2). The resulting enantioselectivities also seem to track with this order, and is as follows: BF₄⁻ \approx PF₆⁻ < B(C₆F₅)₄⁻ < BAr^F₄⁻. This trend follows their hydrogen bond accepting abilities²⁸ and so additional experiments were carried out with BAr^F₄⁻ salts. It is worth adding that **2g** was previously reported but was found to be catalytically inactive for a series of transformations including the reaction of indole with *trans-β*-nitrostyrene.¹⁹ This differs from our finding and may

 Table 2. Counteranion screening results.^a

entry	cat.	time (h)	yield $(\%)^b$	ee (%) ^c
1	2f	48	18	<1
2	2g	48	23	<1
3	2h	48	33	33
4	2a	46	38	40

^{*a*}Reactions were performed at -30 °C with 0.1 mmol indole, 0.2 mmol *trans-β*-nitrostyrene, 0.01 mmol of the indicated catalyst and 10 mg of 3 Å MS in 0.5 mL of CH₂Cl₂. ^{*b*}Isolated yield. ^{*c*}Determined by chiral HPLC.

be due to the use of a different solvent (i.e., toluene vs dichloromethane) or partially deprotonated catalyst in the previous work since the counterion exchange was done after the acidification of the phosphoric acid.

Reaction additives and media were explored next at -30 °C with **2b** as the catalyst (Table 3). Lower yields and enantioselectivities were found for the reactions carried out without MS or with additives other than 3 Å MS (entries 2-5). Of the single component solvents that were examined with 3 Å MS (entries 1 and 6-11), CH₂Cl₂ gave both the highest yield and ee; 81% and 70%, respectively. 1,2-Dichloroethane (DCE) and chlorobenzene are somewhat worse media for

Table 3.	Reaction	medium	screening. ^a
	1000001011	mount	Servering.

entry	solvent	time (h)	yield $(\%)^b$	ee (%) ^c
1	CH ₂ Cl ₂	46	81	70
2^d	CH_2Cl_2	47	54	67
3 ^e	CH_2Cl_2	48	73	57
4f	CH_2Cl_2	48	62	57
5 ^g	CH ₂ Cl ₂	48	61	62
6	DCE^{h}	46	73	63
7	C ₆ H ₅ Cl	45	77	64
8	CHCl ₃	45	54	41
9	EtOAc	164	trace	-
10	THF	164	trace	-
11	C ₆ H ₅ CN	140	43	63
12	CH ₂ Cl ₂ /C ₆ H ₆ 1:1	46	76	71
13	CH ₂ Cl ₂ /C ₆ H ₅ CH ₃ 1:1	47	83	66
14	CH ₂ Cl ₂ / <i>m</i> -xylene 1:1	47	76	63
15	CH ₂ Cl ₂ /CCl ₄ 1:1	48	86	70
16	CH ₂ Cl ₂ /C ₆ H ₆ 1:2	50	88	72
17	1,2-DCE/C ₆ H ₆ 1:1	45	77	65

^{*a*}Reactions were performed at -30 °C with 0.1 mmol indole, 0.2 mmol *trans-β*-nitrostyrene, 0.01 mmol of **2b** and 10 mg of 3 Å MS (unless otherwise noted) in 0.5 mL of the specified solvent; mixtures are on a volume to volume basis. ^{*b*}Isolated yield. ^{*c*}Determined by chiral HPLC. ^{*d*}No MS were used. ^{*e*}10 mg of 4 Å MS were used. ^{*f*}10 mg of 5 Å MS were used. ^{*g*}10 mg of 13X MS were used. ^{*h*}DCE = 1,2-dichloroethane.

this transformation in terms of both the yield and enantioselectivity, but the results in CHCl₃, surprisingly are much poorer (i.e., a 54% yield and an ee of 41% were obtained; entries 1 and 6-8). Hydrogen bond accepting solvents such as EtOAc and THF completely deactivate the catalyst shutting down product formation (entries 9-10). Benzonitrile, a weaker hydrogen bond acceptor than the two oxygen-containing solvents, does not retard the catalyst as strongly (entry 11) but still is a very ineffective medium, and affords the product with a 7% lower ee than in CH₂Cl₂.

In an attempt to improve these results, a number of binary solvent mixtures with a less polar component (i.e., benzene, toluene, *m*-xylene and carbon tetrachloride) were tested (entries 12-17). A 1:1 (v/v) combination of CH₂Cl₂ and C₆H₆ led to a 5% reduction in yield but a 1% increase in ee relative to the former solvent (entry 12). The opposite trend was observed with a 1:1 CH₂Cl₂/toluene mixture in that the yield was 2% higher but the ee dropped 4% (entry 13). Unfortunately, *m*-xylene was ineffective as a cosolvent in both regards and led to a $\sim 6\%$ decrease in the yield and ee (entry 14). Carbon tetrachloride and dichloromethane in a 1:1 ratio gave an improved vield (86%) without affecting the ee (entry 15). Higher proportions of benzene were also investigated since it is the only cosolvent that led to a higher observed ee. A 1:2 CH_2Cl_2/C_6H_6 mixture afforded our best result, an 88% isolated yield and a 72% ee (entry 16). A further increase in benzene to a 1:3 solvent combination is not feasible because the catalyst does not dissolve in this medium. Finally, a previously reported 1:1 DCE/C₆H₆ solvent combination was examined.²⁴ but it led to a reduction in both the yield and enantioselectivity (entry 17). Clearly, different solvent combinations lead to significant differences presumably due to ion pairing and poorly understood solvation effects.

Under our optimal conditions, the reactivity of charged catalyst **2b** was compared to two similar and well-established noncharged analogues, (R)-3,3'-bis(2,4,6-triisopropylphenyl)-BINOL

phosphoric acid (TRIP, **3a**) and (*R*)-3,3'-bis(triphenylsilyl)-BINOL phosphoric acid (**3b**, Figure 1).^{29,30} The reactions of indole with *trans-β*-nitrostyrene were followed at the same three time points by NMR spectrsocopy, and enantioselectivies were measured by chiral HPLC. Reaction half-lifes, relative rates and the resulting ee values are given in Table 4. Both TRIP and its 3,3'-bis(triphenylsilyl) analogue are similarly effective in this transformation with $t_{1/2} = 74$ (**3a**) and 96 h (**3b**), and ee values of 49% and 48%, respectively (entries 1 and 2). The charged triarylphosphonium ion-containing catalyst **2b** was found to be 6–8 times more reactive and significantly more selective with an ee of 72% (entry 3).

Table 4. Comparison of charged and noncharged catalysts.^a

entry	cat.	$t_{1/2}$ (h) ^b	k _{rel}	ee (%) ^c
1	3a	74	1.3	49
2	3 b	96	1.0	48
3	2b	12	7.9	72

^{*a*}Reactions were carried out at -30 °C with 0.1 mmol indole, 0.2 mmol *trans-β*-nitrostyrene, 0.01 mmol of **2b** and 10 mg of 3 Å MS in 0.5 mL of a 1:2 CH₂Cl₂/C₆H₆ mixture. ^{*b*}Reaction conversions were determined by NMR spectroscopy. ^{*c*}Measured by chiral HPLC.

The scope of this reaction was also addressed (eq 3), and the results are summarized in Table 5. A wide range of indoles (**4a-4k**) and *trans-\beta*-nitrostyrenes (**5a-5f**) bearing electron-donating and electron-withdrawing groups are tolerated and afford high conversions (75 - >99%) with enantiomeric excesses ranging from 60-90%. Indoles **4b-4d** and **4f** with an electron-withdrawing halogen atom at the 5- or 6-position react more slowly than the parent compound (i.e., **4a**) and afforded ~10% lower conversions after an ~33% longer time period, but had little impact upon the ee (i.e., the values ranged from 69-73%, entries 1-4 and 6). A chlorine atom at the 7-position



 Table 5. Substrate scope.^a

entry	reactants	pdt	time (h)	$\begin{array}{c} \text{conv.} \\ (\%)^b \end{array}$	ee (%) ^c
1	4a + 5a	6a	50	88	72
2	4b + 5a	6b	68	81	72
3	4c + 5a	6c	66	75	73
4	4d + 5a	6d	66	79	70
5	4e + 5a	6e	114	88	83
6	4f + 5a	6f	68	78	69
7	4g + 5a	6g	40	97	68
8	4h + 5a	6h	39	96	76
9	4i + 5a	6i	47	92	60
10	4j + 5a	6j	58	99	90
11	4k + 5a	6k	58	98	85
$12^{d,f}$	4a + 5b	61	64	>99	74
13	4a + 5c	6m	39	>99	65
14	4a + 5d	6n	39	>99	74
15 ^{e,g}	4a + 5e	60	64	>99	70
16 ^d	4a + 5f	6p	68	91	79
17^{h}	4j + 5a	6j	64	>99	90

^{*a*}Reactions were carried out at -30 °C with 0.1 mmol of the indole, 0.2 mmol of the *trans-\beta*-nitrostyrene, 0.01 mmol of **2b** and 10 mg of 3 Å MS in 0.5 mL of a 1:2 CH₂Cl₂/C₆H₆ mixture. ^{*b*}Determined by NMR spectroscopy. ^{*c*}Measured by chiral HPLC. ^{*d*}A 1:1 CH₂Cl₂/C₆H₆ mixture was used as the solvent. ^{*e*}A 2:1 CH₂Cl₂/C₆H₆ mixture was used as the solvent. ^{*f*}This reaction was run at half of the typical concentrations. ^{*g*}This reaction was run at 2/3 of the usual concentrations in 1 mL of solvent and with 20 mg of 3 Å MS. ^{*h*}This reaction was scaled up by a factor of 10. Page 13 of 38

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(4e) behaved differently in that it had a bigger influence on the rate of the reaction and the enantioselectivity. That is, significantly more time was needed to produce the product but it also was formed with an increased ee of 83%. An electron donating methoxy substituent at the 5- or 6position (4g and 4h) accelerated the transformation as expected, led to high conversions of 97 and 96%, respectively in shorter time periods, and had little effect ($\pm 4\%$) on the observed ee (entries 7 and 8). Alkyl groups at the 6- and 7-positions (4i-4k) also led to very efficient transformations but had little impact on the speed of the transformation (entries 9-11). A methyl group, however, was found to have the largest influence on the enantioselectivity of all the substituents that were studied. 6-Methylindole (4i) gave the smallest ee (60%) in the reaction with *trans-\beta*-nitrostyrene whereas its 7-methyl isomer (4j) afforded the highest value (90% ee). 7-Ethylindole (4k) also displayed good enantioselectivity (85% ee). These results indicate that subtle changes in the location and size of an indole substituent can influence the enantioselectivity of product formation, and that incorporation of a chlorine, methyl or ethyl group at the 7-position is particularly favorable from a stereochemical point of view. Incorporation of electron-withdrawing halogen atoms or an electron-donating methoxy group into the aromatic ring of *trans-\beta*-nitrostyrene led to a few solubility issues, but in all cases excellent conversions were obtained (entries 12-16). The products were formed with moderate ee ranging from 70-79% except for 5c, which led to a lower value of 65%, presumably because of the *ortho*-chlorine atom. The reaction of **4** with **5a** was also scaled up by a factor of 10 (entry 17) to afford >250 mg of product without any loss in the yield or ee.

1-Methylindole (41) was explored to investigate the role of the N–H •• O=P hydrogen bond in the reaction of indole with *trans-* β -nitrostyrene since this interaction is blocked in this case. This change resulted in a reduction in the isolated yield from 81% to 5% and in the ee from 70% to 30% under the same reaction conditions.³¹ These results indicate that the hydrogen bond between indole and the phosphoryl oxygen of the phosphoric acid is important both in terms of the reaction efficiency and stereoselectivity as previously concluded with noncharged BINOL-derived phosphoric acids.^{18,29a} A kinetic study with catalytic loadings of **2b** ranging from 5-20 mol % was also carried out. A plot of the relative rates vs. the mol % of the catalyst is linear indicating a first-order dependence on the catalyst concentration (Figure 3). Alternatively, the same conclusion is reached by carrying out a normalized time scale analysis.³² Interestingly, even though the background process is not competitive, the ee was found to correlate with the catalyst loading. That is, when 5, 10 and 20 mol % of **2b**, were used, ee values of 60%, 70% and 73% were observed. This may be due to the changes in the medium arising from differences in the catalyst concentration since it is a soluble salt. These results, nevertheless, suggest that the operating mechanism is analogous to noncharged phosphoric acid derivatives,¹⁸ and that a pair of hydrogen bond interactions play a key role in the efficiency and stereoselectivity of this



Figure 3. Linear least squares fit of relative rates vs the catalyst (**2b**) mol %; rel. rate = $0.32 \times 2b$ mol % – 0.840, r² = 0.986. Relative rates and half-lifes follow: 1.0 and 24 h (5 mol %), 2.1 and 12 h (10 mol %) and 5.7 and 4.2 h (20 mol %). Inset is for the normalized time scale analysis.

transformation (Figure 4), which is consistent with previous reports of other phosphoric acid catalysts.³³ Our computations also suggest that a pair of aromatic C–H •• ONO interactions are important in determining the observed enantioselectivity.



Figure 4. Proposed Friedel-Crafts alkylation transition state.

CONCLUSION

In summary, we demonstrated the successful synthesis of a series of electrostatically enhanced pyridinium-containing and phosphonium ion-tagged phosphoric acids, and studied their catalytic performance in the Friedel-Crafts alkylation of indoles with *trans-\beta*-nitrostyrenes. Unfortunately, the pyridinium-containing phosphoric acids failed to afford high stereoselectivity. On the other hand, the phosphonium ion-containing phosphoric acids are good catalysts for a wide range of substrates, promoting higher reactivities and enantioselectivities than their noncharged analogues. Charge activated organocatalysts consequently continue to show promise in the development of new hydrogen bond and Brønsted acid catalysts.

Experimental

Materials and general methods. All the reagents used in this work were obtained from commercial sources and used without further purification. Reaction solvents were dried with oven-activated 3 Å molecular sieves. Proton and carbon chemical shifts are reported in ppm (δ) based upon internal reference signals from the solvent: CDCl₃ (7.26 and 77.0 δ) and CD₂Cl₂ (5.32 and 54.0 δ). For ¹⁹F and ³¹P, external calibrants were used as follows: CF₃COOH (-76.55 δ) and 85% aqueous H₃PO₄ (0.00 δ). High-resolution electrospray ionization mass spectra (HRMS-ESI) were obtained with a TOF instrument using methanol solutions and polyethylene glycol (PEG) or polypropylene glycol (PPG) as an internal standard. HPLC analyses were carried out on chiral 25 cm x 4.6 mm RegisCell and RegisPack columns.

(*R*)-2,2'-Bis(ethoxymethoxy)-1,1'-binaphthyl (7).³⁴ (*R*)-1,1'-Bi-2-naphthol (0.50 g, 1.75 mmol) was transferred into a 250 mL round-bottomed flask under a dry nitrogen atmosphere, and 20 mL of anhydrous THF was added via syringe. The resulting solution was stirred and cooled to -20 °C before adding 0.43 g (3.83 mmol) of potassium *tert*-butoxide in one portion. This mixture was stirred for 15 min before 0.35 mL (0.356 g, 3.83 mmol) chloromethyl ethyl ether was syringed in over 5 min. The resulting solution was allowed to warm to room temperature and stirred for 1 hour, after which brine (30 mL) was added to quench the reaction and the solvent was removed under vacuum. Ethyl acetate (30 mL x 3) was used to extract the crude product and the combined organic material was washed with water (30 mL x 2) and brine (30 mL), dried over MgSO₄, and concentrated to give a yellow oil. Purification by MPLC was carried out using the following protocol: a hexanes wash with a flow rate of 40 mL min⁻¹ was carried out for 5 min, then the eluent was switched via a linear gradient over the course of 5 min to 1:1 hexanes/CH₂Cl₂ and maintained for 20 min. The last fraction was concentrated to afford 0.47 g (67%) of the product as a colorless

viscous oil. ¹H NMR (500 MHz, CD₂Cl₂) δ 8.01 (d, *J* = 9.0 Hz, 2H), 7.94 (d, *J* = 8.2 Hz, 2H), 7.68 (d, *J* = 9.1 Hz, 2H), 7.40 (t, *J* = 7.8 Hz, 2H), 7.28 (t, *J* = 7.6 Hz, 2H), 7.23 (d, *J* = 8.5 Hz, 2H), 5.21 (d, *J* = 7.0 Hz, 2H), 5.09 (d, *J* = 7.0 Hz, 2H), 3.51-3.36 (m, 4H), 1.07 (t, *J* = 7.1 Hz, 2H). ¹³C{¹H} NMR (100 MHz, CDCl₃) δ 152.8, 134.0, 129.8, 129.3, 127.8, 126.2, 125.5, 123.9, 121.2, 117.4, 93.8, 63.9, 14.8. HRMS-ESI: calc for C₂₆H₂₆O₄Na⁺ (M + Na⁺)⁺ 425.1729, found 425.1748.

(R)-3,3'-dibromo-2,2'-bis(ethoxymethoxy)-1,1'-binaphthyl (8). (R)-2,2'-Bis(ethoxymethoxy)-1,1'binaphthyl (7, 3.10 g, 7.70 mmol) was dissolved into 50 mL of diethyl ether in a 250 mL roundbottomed flask under a dry nitrogen atmosphere, after which n-butyllithium (9.25 mL, 2.5 M in hexane, 23.1 mmol) was added dropwise at room temperature. The resulting solution was stirred for 2 h before being cooled to -20 °C and slowly adding 1,2-dibromotetrachloroethane (7.52 g, 23.1 mmol) in THF (30 mL). Upon warming to room temperature and stirring overnight, the reaction was guenched with 30 mL of brine. Removal of the solvents with a rotary evaporator afforded a residue which was extracted with EtOAc (30 mL x 3). The combined organic material was washed with 30 mL of water and 30 mL of brine, and then dried over MgSO₄. Evaporation of the solvent under vacuum gave a yellow solid which was purified by MPLC; hexanes were used for 2 min. then a linear gradient to a 9:1 hexanes/EtOAc mixture was applied over a 3 min period, and this binary solution was maintained until the product eluted off the column. It was concentrated under reduced pressure to afford 3.88 g (90%) of a white solid (mp 107 - 113 °C). ¹H NMR (500 MHz, CDCl₃) δ 8.27 (s, 2H), 7.81 (d, J = 8.2 Hz, 2H), 7.43 (t, J = 7.7 Hz, 2H), 7.30 (t, J = 8.2 Hz, 2H), 7.43 (t, J = 7.7 Hz, 2H), 7.30 (t, J = 8.2 Hz, 2H), 7.43 (t, J = 7.7 Hz, 2H), 7.30 (t, J = 8.2 Hz, 2H), 7.43 (t, J = 7.7 Hz, 2H), 7.43 (t, J = 7.7 Hz, 2H), 7.43 (t, J = 8.2 Hz, 2H), 7.43 (t, J = 7.7 Hz, 2H), 7.43 (t, J = 8.2 Hz, 2H), 7.43 (t, J = 7.7 Hz, 2H), 7.43 (t, J = 8.2 Hz, 2H), 7.43 (t, J = 7.7 Hz, 2H), 7.43 (t, J = 8.2 Hz, 2H), 7.43 (t, J = 7.7 Hz, 2H), 7.43 (t, J = 8.2 Hz, 2H), 7.43 (t, J 2H), 7.17 (d, J = 8.5 Hz, 2H), 4.91 (d, J = 5.9 Hz, 2H), 4.84 (d, J = 5.9 Hz, 2H), 3.08-2.98 (m, 2H), 2.72-2.62 (m, 2H), 0.60 (t, J = 7.1 Hz, 6H). ¹³C{¹H} NMR (100 MHz, CDCl₃) δ 150.2, 133.0, 132.9, 131.5, 127.2, 127.0, 126.9, 126.5, 126.0, 117.5, 97.9, 64.8, 14.3. HRMS-ESI: calc for $C_{26}H_{24}O_4Br_2Na^+ (M + Na^+)^+ 582.9919$, found 582.9899.

General procedure for the synthesis of 9a-9b. (R)-3,3'-Dibromo-2,2'-bis(ethoxymethoxy)-1,1'binaphthyl (8) (0.70 g, 1.25 mmol), 3-pyridinylboronic acid (0.54 g, 4.37 mmol) [or 5methylpyridine-3-boronic acid (0.60 g, 4.37 mmol)] and tetrakis(triphenylphosphine)palladium (0.14 g, 0.13 mmol) were mixed together in a 250 mL round-bottomed flask and then dissolved in degassed 1,2-dimethoxylethane (8 mL), after which 3.3 mL of a 2.0 M aqueous Na₂CO₃ solution was added. The resulting mixture was refluxed at 93 °C with stirring for 16 h and upon cooling to room temperature the volatiles were removed with a rotary evaporator. Dichloromethane (30 mL x 3) was used to extract the resulting residue and the combined organic solutions were washed with 30 mL of saturated NH₄Cl and 30 mL of brine before being dried over Na₂SO₄. Concentration of this material under vacuum gave a yellow oil that was purified by MPLC using EtOAc as the eluent. The resulting white solid was dissolved in 5 mL of ethanol and then 1.5 mL of 6.0 M HCl was added dropwise over 5 min with stirring. After 3 h at room temperature a white precipitate had formed and the reaction was guenched with 30 mL of aqueous NaHCO₃. A rotary evaporator was used to remove the ethanol and the remaining material was extracted with EtOAc (50 mL x 2). The combined organic layers were washed with water and brine, and then dried over Na₂SO₄. Concentration of this solution afforded a viscous yellow liquid that was purified by MPLC with EtOAc as the eluent.

(*R*)-3,3'-Di(3-pyridyl)-2,2'-dihydroxyl-1,1'-binaphthyl (**9a**). This compound was obtained as a white solid (0.40 g) in a 73% yield (mp 206 - 212 °C). ¹H NMR (500 MHz, CD₂Cl₂) δ 11.42 (s, 2H), 9.10 (s, 2H), 7.72 (d, *J* = 7.8 Hz, 2H), 7.58 (d, *J* = 7.1 Hz, 2H), 7.35-7.25 (m, 4H), 7.23-7.15 (m, 4H), 6.77 (dd, *J* = 5.0 and 7.6 Hz, 2H), 6.58 (d, *J* = 4.3 Hz, 2H). ¹³C{¹H} NMR (100 MHz, CD₂Cl₂) δ 152.7, 150.2, 144.8, 135.7, 135.6, 134.6, 130.5, 129.6, 129.4, 128.9, 127.2, 125.1, 123.5, 123.3, 116.1. HRMS-ESI: calc for C₃₀H₂₁N₂O₂⁺ (M + H⁺)⁺ 441.1603, found 441.1588.

(*R*)-3,3'-Di[3-(5-methyl)pyridyl]-2,2'-dihydroxyl-1,1'-binaphthyl (9b). This species was obtained as a white solid (0.42 g) in a 72% yield (mp 201 - 208 °C). ¹H NMR (500 MHz, CD₂Cl₂) δ 11.68 (s, 2H), 8.89 (s, 2H), 7.59 (d, *J* = 8.8 Hz, 2H), 7.52 (s, 2H), 7.33-7.26 (m, 4H), 7.19 (d, *J* = 9.3 Hz, 2H), 7.17 (s, 2H), 6.30 (s, 2H), 2.03 (s, 6H). ¹³C{¹H} NMR (100 MHz, CD₂Cl₂) δ 152.9, 147.7, 145.2, 136.0, 135.6, 134.0, 132.7, 130.2, 129.8, 129.7, 128.5, 127.0, 125.1, 123.2, 116.0, 18.7. HRMS-ESI: calc for C₃₂H₂₅N₂O₂⁺ (M + H⁺)⁺ 469.1916, found 469.1933.

General procedure for the synthesis of 10a-10b. Compound 9a or 9b (0.227 mmol) was added into a 100 mL round-bottomed flask under an atmosphere of dry nitrogen and then was dissolved in 15 mL of anhydrous acetonitrile. After stirring for 5 min, 0.164 mL of 1-iodooctane (0.218 g, 0.908 mmol) was syringed into the flask in one portion and the solution was heated to 100 °C and refluxed overnight. Upon cooling to room temperature, the reaction mixture was concentrated under vacuum. The crude product was dissolved in 5 mL of CH_2Cl_2 and triturated by adding it dropwise to 100 mL of hexanes. Filtration of the resulting precipitate and a subsequent wash with hexanes gave the desired product.

(*R*)-3,3'-*Di*(3-*N*-octylpyridinium)-2,2'-dihydroxyl-1,1'-binaphthyl iodide (**10a**). A yellow solid (0.16 g) was obtained in a 77% yield (mp 278 - 282 °C). ¹H NMR (500 MHz, CD₂Cl₂) δ 9.98 (s, 2H), 8.86-8.77 (m, 4H), 8.34 (s, 2H), 8.10-8.01 (m, 4H), 7.43 (t, *J* = 7.2 Hz, 2H), 7.33 (t, *J* = 7.4 Hz, 2H), 7.14 (d, *J* = 8.5 Hz, 2H), 4.80-4.65 (m, 4H), 2.09-1.98 (m, 4H), 1.40-1.18 (m, 22H), 0.82 (t, *J* = 6.6 Hz, 6H). ¹³C{¹H} NMR (100 MHz, CD₂Cl₂) δ 149.7, 146.4, 145.6, 145.5, 142.0, 139.6, 135.0, 132.6, 130.1, 129.5, 128.9, 128.5, 125.6, 125.1, 118.6, 62.7, 32.3, 32.2, 29.50, 29.48, 26.5, 23.1, 14.4. HRMS-ESI: calc for C₄₆H₅₃N₂O₂⁺ (M - H⁺ - 2I⁻)⁺ 665.4107, found 665.4139.

(*R*)-3,3'-Di(3-(*N*-octyl-5-methyl)pyridinium)-2,2'-dihy-droxyl-1,1'-binaphthyl iodide (**10b**). A yellow solid (0.19 g) was obtained in an 88% yield (mp 265 - 270 °C). ¹H NMR (500 MHz, CD₂Cl₂)

δ 9.86 (s, 2H), 8.71 (s, 2H), 8.65 (s, 2H), 8.30 (s, 2H), 8.04 (d, J = 7.9 Hz, 2H), 7.45 (t, J = 7.8 Hz, 2H), 7.35 (t, J = 8.3 Hz, 2H), 7.14 (d, J = 8.3 Hz, 2H), 6.53 (s, 2H), 4.79-4.62 (m, 4H), 2.67 (s, 6H), 2.12-2.00 (m, 4H), 1.42-1.18 (m, 20H), 0.83 (d, J = 6.8 Hz, 6H). ¹³C {¹H} NMR (100 MHz, CD₂Cl₂) δ 149.5, 146.2, 144.2, 141.3, 139.8, 139.0, 135.0, 132.5, 130.2, 129.5, 128.9, 125.7, 125.3, 125.1, 118.5, 62.5, 32.3, 32.2, 29.53, 29.51, 26.5, 23.1, 19.2, 14.4. HRMS-ESI: calc for C₄₈H₅₇N₂O₂⁺ (M - H⁺ - 2I⁻)⁺ 693.4420, found 693.4401.

General procedure for the synthesis of 11a-11b. Iodide salt 10a or 10b (0.218 mmol) was dissolved into 20 mL of anhydrous acetonitrile under a N₂ atmosphere and 64 μ L (0.10 g, 0.654 mmol) of POCl₃ was added with stirring in one portion followed by 44 μ L (0.044 g, 0.544 mmol) of anhydrous pyridine. The resulting solution was heated to 90 °C and refluxed for 16 h before cooling to room temperature and adding 0.5 mL of water. This material was heated back to 90 °C for 1 h and then allowed to return to room temperature. Removal of the solvent under vacuum afforded a residue which was dissolved in 40 mL of CH₂Cl₂ and washed with 2.0 M HCl (15 mL), 15 mL of brine and then dried over Na₂SO₄. Rotary evaporation of this material gave a brown oil that was purified by MPLC. A linear gradient from EtOAc to a 1:1 EtOAc/MeOH mixture over 10 min followed by a 10 min wash with this solution eluted the product. This material was concentrated under reduced pressure to give the desired compound as a yellow solid.

(R)-3,3'-(4-Hydroxy-4-oxidodinaphtho[2,1-d:1',2'-f][1,3,2]dioxaphosphepine-2,6-diyl)bis(1-

octylpyridin-1-ium) chloride (11a). This compound (0.12 g) was generated in a 69% yield (mp 195 - 202 °C). ¹H NMR (500 MHz, CD₂Cl₂) δ 10.38 (s, 2H), 9.11 (d, *J* = 5.6 Hz, 2H), 8.82 (d, *J* = 7.7 Hz, 2H), 8.20 (s, 2H), 8.08-7.95 (m, 4H), 7.48 (t, *J* = 7.3 Hz, 2H), 7.30 (t, *J* = 7.9 Hz, 2H), 7.19 (d, *J* = 8.7 Hz, 2H), 4.86-4.60 (m, 4H), 2.19 (bs, OH, 1H) 2.10-1.93 (m, 4H), 1.37-1.15 (m, 20H), 0.82 (t, *J* = 6.7 Hz, 6H). ¹³C{¹H} NMR (100 MHz, CD₂Cl₂) δ 155.31, 155.26, 153.64, 153.58,

137.64, 137.58, 137.0, 136.7, 136.6, 129.7, 128.7, 123.9, 123.8, 121.0, 120.9, 63.0, 32.2, 32.1, 29.5, 29.4, 26.6, 23.1, 14.4. ³¹P NMR (162 MHz, CD₂Cl₂) δ 5.64. HRMS-ESI: calc for C₄₆H₅₂N₂O₄P⁺ (M - H⁺ - 2Cl⁻)⁺ 727.3665, found 727.3677.

(*R*)-5,5'-(4-Hydroxy-4-oxidodinaphtho[2,1-d:1',2'-f][1,3,2]dioxaphosphepine-2,6-diyl)bis(3methyl-1-octylpyridin-1-ium) chloride (11b). This compound (0.15 g) was produced in an 83% yield (mp 194 - 200 °C). ¹H NMR (500 MHz, CD₂Cl₂) δ 10.25 (s, 2H), 9.19 (s, 2H), 8.62 (s, 2H), 8.20 (s, 2H), 8.02 (d, *J* = 8.2 Hz, 2H), 7.47 (t, *J* = 7.1 Hz, 2H), 7.30 (t, *J* = 8.5 Hz, 2H), 7.21 (d, *J* = 8.6 Hz, 2H), 4.72 (t, *J* = 7.3 Hz, 4H), 2.63 (s, 6H), 2.54 (bs, OH, 1H), 2.15-1.95 (m, 4H), 1.45-1.14 (m, 20H), 0.82 (t, *J* = 6.8 Hz, 6H). ¹³C {¹H} NMR (100 MHz, CD₂Cl₂) δ 147.2, 146.5, 144.7, 142.6, 139.7, 138.8, 133.9, 132.5, 131.0, 129.4, 128.1, 127.6, 127.3, 126.4, 124.0, 62.6, 32.3, 32.1, 29.6, 29.5, 26.7, 23.1, 19.0, 14.4. ³¹P NMR (162 MHz, CD₂Cl₂) δ 6.19. HRMS-ESI: calc for C₄₈H₅₆N₂O₄P⁺ (M - H⁺ - 2Cl⁻)⁺ 755.3978, found 755.4002.

General procedure for the synthesis of 1a-1b. Chloride salt 11a or 11b (0.0755 mmol), sodium tetrakis[3,5-bis(trifluoromethyl)phenyl]borate (0.141 g, 0.159 mmol) and 3 Å molecular sieves (0.10 g) were mixed in a 23 x 85 mm vial, and then 7 mL of CH_2Cl_2 was added. The resulting solution was stirred at room temperature for 3 h before being filtered through a 0.45 µm polytetrafluoroethylene (PTFE) membrane. The filtered solution was washed with 2.0 M H_2SO_4 (7 mL x 2) and water (7 mL x 3), and then was dried over Na₂SO₄ before being concentrated to afford the product.

(*R*)-3,3'-(4-Hydroxy-4-oxidodinaphtho[2,1-d:1',2'-f][1,3,-2]dioxaphosphepine-2,6-diyl)bis(1octylpyridin-1-ium) tetrakis[3,5-bis(trifluoromethyl)phenyl]borate (1a). A yellow solid (0.17 g) was formed in a 92% yield (mp 77 - 81 °C). ¹H NMR (500 MHz, CD₂Cl₂) δ 9.54 (s, 2H), 8.90 (d, J = 7.8 Hz, 2H), 8.29 (d, J = 5.9 Hz, 2H), 8.12 (s, 2H), 8.06 (d, J = 8.3 Hz, 2H), 8.00 (dd, J = 5.9 and 7.9 Hz, 2H), 7.77 (s, 16H), 7.65-7.57 (m, 10H), 7.47 (t, J = 8.3 Hz, 2H), 7.35 (d, J = 8.8 Hz, 2H), 4.62-4.44 (m, 4H), 2.60 (bs, OH, 1H) 2.07-1.93 (m, 4H), 1.36-1.21 (m, 20H), 0.84 (t, J = 6.9 Hz, 6H). ¹³C{¹H} NMR (100 MHz, CD₂Cl₂) δ 162.4 (q, J = 48.9 Hz), 147.1, 145.7, 145.4, 141.4, 140.7, 140.5, 135.5, 134.0, 133.1, 131.3, 129.5 (qq, J = 2.92 and 31.4 Hz), 128.6, 127.9, 127.7, 127.2, 125.9, 125.2 (q, J = 270 Hz), 124.1, 118.2 (septet, J = 3.64 Hz), 63.9, 32.1, 32.0, 29.4, 29.3, 26.6, 23.0, 14.2. ¹⁹F NMR (376 MHz, CD₂Cl₂) δ -62.68. ³¹P NMR (162 MHz, CD₂Cl₂) δ 6.76. HRMS-ESI: calc for C₄₆H₅₂N₂O₄P⁺ (M - H⁺ - 2BAr^F₄⁻)⁺ 727.3665, found 727.3679.

(*R*)-5,5'-(4-Hydroxy-4-oxidodinaphtho[2,1-d:1',2'-f][1,3,-2]dioxaphosphepine-2,6-diyl)bis(3methyl-1-octylpyridin-1-ium) tetrakis[3,5-bis(trifluoromethyl)phenyl]borate (1b). A yellow solid (0.17 g) was generated in a 91% yield (mp 54 - 58 °C). ¹H NMR (500 MHz, CD₂Cl₂) δ 9.06 (s, 2H), 8.55 (s, 2H), 8.21 (s, 2H), 8.13 (s, 2H), 8.06 (d, *J* = 7.8 Hz, 2H), 7.74 (s, 16H), 7.63 (t, *J* = 7.1 Hz, 2H), 7.56 (s, 8H), 7.48 (t, *J* = 8.5 Hz, 2H), 7.34 (d, *J* = 8.3 Hz, 2H), 4.83 (bs, OH, 1H), 4.45 (t, *J* = 7.3 Hz, 4H), 2.55 (s, 6H), 2.07-1.90 (m, 4H), 1.36-1.17 (m, 20H), 0.82 (t, *J* = 6.8 Hz, 6H). ¹³C {¹H} NMR (100 MHz, CD₂Cl₂) δ 162.3 (q, *J* = 49.6 Hz), 147.6, 143.9, 142.5, 141.6, 141.3, 139.0, 135.4, 133.65, 133.63, 131.7, 129.5 (qq, *J* = 2.92 and 31.4 Hz), 128.4, 127.3, 125.47, 125.45, 125.2 (q, *J* = 270 Hz), 123.58, 123.56, 118.1 (septet, *J* = 3.64 Hz), 63.7, 32.1, 32.0, 29.4, 29.3, 26.6, 23.0, 19.1, 14.2. ¹⁹F NMR (376 MHz, CD₂Cl₂) δ -62.76. ³¹P NMR (162 MHz, CD₂Cl₂) δ 5.68. HRMS-ESI: calc for C₄₈H₅₆N₂O₄P⁺ (M - H⁺ - 2BAr^F₄-)⁺ 755.3978, found 755.3998

General procedure for the synthesis of 2f-2g. In a 23 x 85 mm vial, (*R*)-(4-hydroxy-4oxidodinaphtho[2,1-d:1',2'-f][1,3,2]dioxaphosphepine-2,6-diyl)bis(triphenylphosphonium) chloride (0.188 g, 0.200 mmol), sodium tetrafluoroborate (0.046 g, 0.420 mmol) or potassium hexafluorophosphate (0.077 g, 0.420 mmol) and 3 Å molecular sieves (0.50 g) were mixed together and then 3 mL of methanol was added. After stirring at room temperature for 2 h, 10 mL

of CH_2Cl_2 was added and the reaction was stirred for an additional 1 h before filtering the solution through a 0.45 µm PTFE membrane. The solvent was removed under vacuum and the residue was redissolved in 8 mL of CH_2Cl_2 . It was then washed twice with 8 mL of 2.0 M H₂SO₄ and three times with 8 mL of water before being dried over Na₂SO₄. Concentration of the solution under reduced pressure afforded the desired product.

(*R*)-(4-Hydroxy-4-oxidodinaphtho[2,1-d:1',2'-f][1,3,2]dioxaphosphepine-2,6-diyl)bis(triphenylphosphonium) tetrafluoroborate (2f). A yellow solid (0.141 g) was afforded in a 67% yield (mp 233 – 236 °C). ¹H NMR (500 MHz, CDCl₃) δ 8.00 (d, *J* = 16.3 Hz, 2H), 7.87 (d, *J* = 7.7 Hz, 2H), 7.83-7.72 (m, 18H), 7.68-7.62 (m, 12H), 7.57-7.48 (m, 4H), 7.28 (d, *J* = 8.3 Hz, 2H), 1.25 (bs, OH, 1H). ¹³C {¹H} NMR (100 MHz, CDCl₃) δ 150.7 (d, *J* = 9.9 Hz), 141.0 (d, *J* = 8.4 Hz), 136.2 (d, *J* = 2.4 Hz), 135.03, 134.95 (d, *J* = 10.5 Hz), 131.0, 130.0 (d, *J* = 13.1 Hz), 129.8, 129.2 (d, *J* = 14.3 Hz), 127.0, 126.5, 124.5 (d, *J* = 10.1 Hz), 118.9 (d, *J* = 90.4 Hz), 110.8 (d, *J* = 91.0 Hz). ¹⁹F NMR (376 MHz, CD₂Cl₂) δ -154.11. ³¹P NMR (162 MHz, CD₂Cl₂) δ 22.93, 0.87. HRMS- ESI: calc for C₅₆H₄₀O₄P₃⁺ (M - H⁺ - 2BF₄⁻)⁺ 869.2134, found 869.2103.

(*R*)-(*4*-Hydroxy-4-oxidodinaphtho[2,1-d:1',2'-f][1,3,2]dioxaphosphepine-2,6-diyl)bis(triphenylphosphonium) hexafluorophosphate (2g). A yellow solid (0.177 g) was produced in a 76% yield (mp 225 – 230 °C). ¹H NMR (500 MHz, CDCl₃) δ 8.00 (d, *J* = 16.3 Hz, 2H), 7.88 (d, *J* = 7.7 Hz, 2H), 7.81-7.72 (m, 18H), 7.68-7.62 (m, 12H), 7.58-7.50 (m, 4H), 7.28 (d, *J* = 8.3 Hz, 2H), 2.11 (bs, OH, 1H). ¹³C {¹H} NMR (100 MHz, CDCl₃) δ 144.7 (d, *J* = 8.6 Hz), 141.0 (d, *J* = 8.4 Hz), 136.2 (d, *J* = 2.9 Hz), 135.1, 135.0 (d, *J* = 10.6 Hz), 131.0, 130.1 (d, *J* = 13.2 Hz), 129.8, 129.2 (d, *J* = 14.4 Hz), 127.0, 126.5, 124.5 (d, *J* = 7.0 Hz), 118.9 (d, *J* = 90.5 Hz), 110.7 (d, *J* = 91.1 Hz). ¹⁹F NMR (376 MHz, CDCl₃) δ -73.62 (d, *J* = 712 Hz). ³¹P NMR (162 MHz, CDCl₃) δ 22.94, 0.77, -144.43 (septet, *J* = 712 Hz). HRMS- ESI: calc for C₅₆H₄₀O4P₃⁺ (M - H⁺ - 2PF₆⁻)⁺ 869.2134, found

869.2155.

(R)-(4-Hydroxy-4-oxidodinaphtho[2,1-d:1',2'-f][1,3,2]dioxaphosphepine-2,6-divl)bis(triphenylphosphonium) tetrakis(pentafluorophenyl)borate (2h). In a 23 x 85 mm vial, (R)-(4-hydroxy-4oxidodinaphtho[2,1-d:1',2'-f][1,3,2]dioxaphosphepine-2,6-diyl)bis(triphenylphosphonium) chloride (0.188 g, 0.200 mmol), potassium tetrakis(pentafluorophenyl)borate (0.302 g, 0.420 mmol) and 3 Å molecular sieves (0.50 g) were mixed together and then 8 mL of CH₂Cl₂ was added. The solution was stirred at room temperature for 3 h and then filtered through a 0.45 µm PTFE membrane. It was subsequently washed twice with 2.0 M H₂SO₄ and three times with water before being dried over Na₂SO₄. Removal of the CH₂Cl₂ gave **2h** as a yellow solid (0.337 g) in a 76% yield (mp 178 – 182 °C). ¹H NMR (500 MHz, CD₂Cl₂) δ 8.10 (d, J = 16.5 Hz, 2H), 7.91 (d, J = 8.1 Hz, 2H), 7.84-7.77 (m, 6H), 7.77-7.69 (m, 12H), 7.69-7.59 (m, 14H), 7.54 (d, J = 8.1 Hz, 2H), 7.29 (d, J = 8.5 Hz, 2H), 2.20 (bs, OH, 1H). ¹³C{¹H} NMR (100 MHz, CD₂Cl₂) δ 149.7 (d, J = 9.4Hz), 148.7 (d, J = 236.4 Hz), 142.5 (d, J = 8.5 Hz), 138.8 (d, J = 242.9 Hz), 136.9 (d, J = 231.2Hz), 135.7 (d, J = 3.0 Hz), 136.7, 135.5 (d, J = 10.5 Hz), 132.0, 130.6 (d, J = 13.1 Hz), 130.5, 130.2 (d, J = 14.3 Hz), 128.1, 127.0, 124.7 (d, J = 6.9 Hz), 124.2 (m), 119.1 (d, J = 90.6 Hz), 110.6 (d, J = 91.2 Hz). ¹⁹F NMR (376 MHz, CD₂Cl₂) δ -133.12, -163.39 (t, J = 20.4 Hz), -167.38 (t, J =17.1 Hz). ³¹P NMR (162 MHz, CD₂Cl₂) δ 22.81, 0.89. HRMS- ESI: calc for C₅₆H₄₀O₄P₃⁺ (M - H⁺ $-2B(C_6F_5)_4^{-})^+$ 869.2134, found 869.2116.

General procedure for the Friedel-Crafts alkylations. A 23 x 85 mm vial was charged with a catalyst (10 mol %) and 3 Å molecular sieves (10 mg), and then was sealed followed by a 1 min purge with dry nitrogen. After adding 250 μ L of CH₂Cl₂ via syringe, the resulting solution was cooled if the reaction was being carried out at subambient temperature. Indole (0.100 mmol) and *trans-β*-nitrostyrene (0.200 mmol) were dissolved in 250 μ L of CH₂Cl₂ and this solution was then

added dropwise over 10-15 s. The reaction mixture was shaken and the transformation was allowed to proceed over the course of 5-164 h. Reaction conversions were determined by removing 1-2 drops of the reaction mixture and dissolving it in 0.5 mL of CDCl₃ after flowing dry nitrogen over the sample for ≤ 15 s to evaporate the CH₂Cl₂. Upon completion of reaction, the solution was injected on to a 4 g silica gel column followed by 0.2-0.3 mL of CH₂Cl₂ that had been used to rinse the molecular sieves. MPLC purification was carried out first with hexanes (1 min) followed by a linear gradient to 100% CH₂Cl₂ over the course of 7 min, and then this solvent was maintained until all of the components eluted off the column. Racemic reference materials were obtained in the same way using diphenylphosphate as the reaction catalyst.

Analytical data for the Friedel-Crafts products. *3-(2-Nitro-1-phenylethyl)-1H-indole (6a)*.^{18 1}H NMR (500 MHz, CDCl₃) δ 8.10 (bs, NH, 1H), 7.46 (d, *J* = 8.0 Hz, 1H), 7.39-7.30 (m, 5H), 7.29-7.24 (m, 1H), 7.23-7.18 (m, 1H), 7.12-7.06 (m, 1H), 7.03 (d, *J* = 2.5 Hz, 1H), 5.20 (t, *J* = 8.2 Hz, 1H), 5.07 (dd, *J* = 7.7 and 12.6 Hz, 1H), 4.95 (dd, *J* = 8.4 and 12.5 Hz, 1H). ¹³C{¹H} NMR (100 MHz, CDCl₃) δ 139.2, 136.5, 128.9, 127.7, 127.5, 126.1, 122.7, 121.6, 119.9, 118.9, 114.4, 111.4, 79.5, 41.5. HRMS-ESI: calc for C₁₆H₁₃N₂O₂⁻ (M - H⁺)⁻ 265.0977, found 265.0971. Enantiomeric excess was determined with a Regiscell column (75:25 hexanes/iPrOH, 1.0 mL min⁻¹, 20 °C, 250 nm, $\tau_{maior} = 17.0$ min, $\tau_{minor} = 20.1$ min).

5-*Fluoro-3-(2-nitro-1-phenylethyl)-1H-indole (6b)*.³⁵ Reaction conversion was determined by relative integration of the ¹H NMR signals at δ 6.42 (4b) and 4.78 (6b). Enantiomeric excess was measured with a Regiscell column (92:8 hexanes/iPrOH, 1.0 mL min⁻¹, 20 °C, 254 nm, $\tau_{major} = 56.1 \text{ min}, \tau_{minor} = 48.2 \text{ min}$).

5-Chloro-3-(2-nitro-1-phenylethyl)-1H-indole (6c).^{18,36} Reaction conversion was determined by relative integration of the ¹H NMR signals at δ 6.41 (4c) and 4.82 (6c). Enantiomeric excess was

measured with a Regiscell column (80:20 hexanes/iPrOH, 1.0 mL min⁻¹, 20 °C, 250 nm, $\tau_{\text{major}} = 16.8 \text{ min}, \tau_{\text{minor}} = 13.8 \text{ min}$).

6-Chloro-3-(2-nitro-1-phenylethyl)-1H-indole (6d).³⁷ Reaction conversion was determined by relative integration of the ¹H NMR signals at δ 6.43 (4d) and 4.82 (6d). Enantiomeric excess was measured with a Regiscell column (85:15 hexanes/iPrOH, 1.0 mL min⁻¹, 20 °C, 250 nm, $\tau_{major} = 21.2 \text{ min}, \tau_{minor} = 19.8 \text{ min}$).

7-*Chloro-3-(2-nitro-1-phenylethyl)-1H-indole (6e)*. A yellow solid was isolated with a mp of 58 - 62 °C. ¹H NMR (500 MHz, CDCl₃) δ 8.32 (bs, NH, 1H), 7.37-7.29 (m, 5H), 7.29-7.26 (m, 1H), 7.20 (d, J = 7.6 Hz, 1H), 7.13 (d, J = 2.4 Hz, 1H), 7.00 (t, J = 7.8 Hz, 1H), 5.17 (t, J = 8.0 Hz, 1H), 5.06 (dd, J = 8.0 and 12.5 Hz, 1H), 4.95 (dd, J = 8.0 and 12.5 Hz, 1H). ¹³C {¹H} NMR (100 MHz, CDCl₃) δ 138.8, 133.8, 129.0, 127.71, 127.691, 127.688, 127.5, 122.1, 120.8, 117.6, 116.9, 115.6, 79.4, 41.5. HRMS-ESI: calc for C₁₆H₁₂N₂O₂Cl⁻ (M - H⁺)⁻ 299.0587 and 301.0558, found 299.0577 and 301.0553. Reaction conversion was determined by relative integration of the ¹H NMR signals at δ 6.60 (**4e**) and 4.95 (**6e**). Enantiomeric excess was measured with a Regiscell column (75:25 hexanes/iPrOH, 1.0 mL min⁻¹, 20 °C, 250 nm, $\tau_{major} = 34.7$ min, $\tau_{minor} = 39.6$ min).

5-Bromo-3-(2-nitro-1-phenylethyl)-1H-indole (6f).¹⁸ Reaction conversion was determined by relative integration of the ¹H NMR signals at δ 6.40 (4f) and 4.82 (6f). Enantiomeric excess was measured with a Regiscell column (75:25 hexanes/iPrOH, 1.0 mL min⁻¹, 20 °C, 250 nm, $\tau_{major} = 12.1 \text{ min}, \tau_{minor} = 10.8 \text{ min}$).

5-Methoxy-3-(2-nitro-1-phenylethyl)-1H-indole (**6g**).³⁶ Reaction conversion was determined by relative integration of the ¹H NMR signals at δ 6.39 (**4g**) and 4.84 (**6g**). Enantiomeric excess was measured with a Regiscell column (75:25 hexanes/iPrOH, 1.0 mL min⁻¹, 20 °C, 250 nm, $\tau_{major} = 12.9 \text{ min}, \tau_{minor} = 11.4 \text{ min}$).

6-Methoxy-3-(2-nitro-1-phenylethyl)-1H-indole (6h). A white solid was isolated with a mp of 82 - 85 °C. ¹H NMR (500 MHz, CDCl₃) δ 7.96 (bs, NH, 1H), 7.35-7.29 (m, 4H), 7.29-7.24 (m, 2H), 6.92 (dd, J = 0.8 and 2.3 Hz, 1H), 6.83 (d, J = 2.2 Hz, 1H), 6.74 (dd, J = 2.3 and 8.8 Hz, 1H), 5.14(t, J = 8.1 Hz, 1H), 5.05 (dd, J = 7.7 and 12.4 Hz, 1H), 4.92 (dd, J = 8.3 and 12.5 Hz, 1H), 3.82 (s, J = 8.3 and 12.5 Hz, 100 Hz, 1003H). ${}^{13}C{}^{1H}$ NMR (100 MHz, CDCl₃) δ 156.9, 139.2, 137.3, 128.9, 127.7, 127.5, 120.5, 120.3, 119.6, 114.4, 110.0, 94.7, 79.6, 55.6, 41.6. HRMS-ESI: calc for $C_{17}H_{16}N_2O_3Na^+$ (M + Na⁺)⁺ 319.1059, found 319.1074. Reaction conversion was determined by relative integration of the ¹H NMR signals at δ 6.39 (4h) and 4.92 (6h). Enantiometric excess was measured with a Regiscell column (75:25 hexanes/iPrOH, 1.0 mL min⁻¹, 20 °C, 250 nm, $\tau_{\text{maior}} = 20.7 \text{ min}, \tau_{\text{minor}} = 16.6 \text{ min}$). 6-Methyl-3-(2-nitro-1-phenylethyl)-1H-indole (6i). This compound was isolated as a colorless viscous oil. ¹H NMR (500 MHz, CDCl₃) § 7.94 (bs, NH, 1H), 7.41-7.28 (m, 5H), 7.28-7.23 (m, 1H), 7.15 (s, 1H), 6.94 (d, J = 2.4 Hz, 1H), 6.92 (d, J = 8.1 Hz, 1H), 5.17 (t, J = 8.0 Hz, 1H), 5.06 (dd, J = 7.7 and 12.5 Hz, 1H), 4.94 (dd, J = 8.4 and 12.5 Hz, 1H), 2.44 (s, 3H). ¹³C{¹H} NMR (100 MHz, CDCl₃) & 139.2, 136.9, 132.6, 128.9, 127.7, 127.5, 123.9, 121.7, 120.9, 118.5, 114.3, 111.3, 79.5, 41.6, 21.6. HRMS-ESI: calc for $C_{17}H_{15}N_2O_2^-$ (M - H⁺)⁻ 279.1134, found 279.1149. Reaction conversion was determined by relative integration of the ¹H NMR signals at δ 6.51 (4i) and 4.94 (6i). Enantiomeric excess was measured with a Regiscell column (75:25 hexanes/iPrOH, 1.0 mL min⁻¹, 20 °C, 250 nm, $\tau_{\text{major}} = 13.1$ min, $\tau_{\text{minor}} = 12.0$ min).

7-*Methyl-3-(2-nitro-1-phenylethyl)-1H-indole* (**6j**).¹⁸ Reaction conversion was determined by relative integration of the ¹H NMR signals at δ 6.57 (**4j**) and 4.95 (**6j**). Enantiomeric excess was measured with a Regispack column (97:3 hexanes/iPrOH, 1.0 mL min⁻¹, 20 °C, 250 nm, $\tau_{major} = 40.1 \text{ min}, \tau_{minor} = 35.6 \text{ min}$).

7-*Ethyl-3-(2-nitro-1-phenylethyl)-1H-indole* (**6***k*).³⁸ Reaction conversion was determined by relative integration of the ¹H NMR signals at δ 6.58 (**4***k*) and 4.96 (**6***k*). Enantiomeric excess was measured with a Regispack column (97:3 hexanes/iPrOH, 1.0 mL min⁻¹, 20 °C, 250 nm, $\tau_{major} = 33.3 \text{ min}, \tau_{minor} = 29.7 \text{ min}$).

3-(1-(4-Fluorophenyl)-2-nitroethyl)-1H-indole (61).³⁹ Reaction conversion was determined by relative integration of the ¹H NMR signals at δ 6.47 (4a) and 4.79 (6l). Enantiomeric excess was measured with a Regiscell column (75:25 hexanes/iPrOH, 1.0 mL min⁻¹, 20 °C, 250 nm, $\tau_{major} = 18.1 \text{ min}, \tau_{minor} = 22.8 \text{ min}$).

3-(1-(2-Chlorophenyl)-2-nitroethyl)-1H-indole (6m).⁴⁰ Reaction conversion was determined by relative integration of the ¹H NMR signals at δ 6.47 (4a) and 5.64 (6m). Enantiomeric excess was measured with a Regiscell column (75:25 hexanes/iPrOH, 1.0 mL min⁻¹, 20 °C, 250 nm, $\tau_{major} = 20.5 \text{ min}, \tau_{minor} = 13.3 \text{ min}$).

3-(1-(3-Bromophenyl)-2-nitroethyl)-1H-indole (6n).⁴⁰ Reaction conversion was determined by relative integration of the ¹H NMR signals at δ 6.47 (**4a**) and 4.81 (**6n**). Enantiomeric excess was measured with a Regiscell column (75:25 hexanes/iPrOH, 1.0 mL min⁻¹, 20 °C, 250 nm, $\tau_{major} = 20.2 \text{ min}, \tau_{minor} = 27.7 \text{ min}$).

3-(1-(4-Bromophenyl)-2-nitroethyl)-1H-indole (60).⁴⁰ Reaction conversion was determined by relative integration of the ¹H NMR signals at δ 6.47 (4a) and 4.81 (60). Enantiomeric excess was measured with a Regiscell column (75:25 hexanes/iPrOH, 1.0 mL min⁻¹, 20 °C, 250 nm, $\tau_{major} = 21.7 \text{ min}, \tau_{minor} = 27.0 \text{ min}$).

3-(1-(4-Methoxylphenyl)-2-nitroethyl)-1H-indole (6p).¹⁸ Reaction conversion was determined by relative integration of the ¹H NMR signals at δ 6.47 (4a) and 4.79 (6p). Enantiomeric excess was

measured with a Regiscell column (80:20 hexanes/iPrOH, 1.0 mL min⁻¹, 20 °C, 250 nm, $\tau_{major} = 25.3 \text{ min}, \tau_{minor} = 27.9 \text{ min}$).

3-(2-Nitro-1-phenylethyl)-1-methylindole (6q).⁴¹ ¹H NMR (500 MHz, CDCl₃) δ 7.54 (d, J = 8.0 Hz, 1H), 7.45-7.27 (m, 7H), 7.16 (t, J = 7.0 Hz, 1H), 6.91 (s, 1H), 5.25 (t, J = 8.1 Hz, 1H), 5.09 (dd, J = 7.6 and 12.6 Hz, 1H), 4.98 (dd, J = 8.5 and 12.6 Hz, 1H), 3.75 (s, 3H). ¹³C{¹H} NMR (100 MHz, CDCl₃) δ 139.3, 137.2, 128.8, 127.6, 127.4, 126.4, 126.2, 122.1, 119.3, 118.9, 112.6, 109.4, 79.4, 41.4, 32.6. HRMS-ESI: calc for C₁₇H₁₆N₂O₂Na⁺ (M + Na⁺)⁺ 303.1109, found 303.1118. Enantiomeric excess was measured with a Regiscell column (95:5 hexanes/iPrOH, 1.0 mL min⁻¹, 20 °C, 250 nm, $\tau_{major} = 59.6$ min, $\tau_{minor} = 56.6$ min).

Computations. DFT calcuations were carried out with Gaussian 09⁴² at the Minnesota Supercomputer Institute for Advanced Computational Research. Full B3LYP/6-31G(d,p) geometry optimizations were performed and subsequent vibrational frequencies and M06-2X/cc-pVTZ single point energies were computed.^{43,44} Stationary points that correspond to energy minima have no imaginary frequencies while those that correspond to transition structures have one negative value.

Supporting Information

Illustrated synthetic route for the preparation of pyridinium ion-containing phosphoric acids **1a** and **1b**, kinetic data, NMR spectra, HPLC chromatograms, computed geometries and energies and the complete citation to ref. 42. This material is available free of charge via the internet at http://pubs.acs.org.

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The authors declare no competing financial interests.

ACKNOWLEDGMENT.

Generous support from the National Science Foundation (CHE-1665392) and the Petroleum Research Fund (55631-ND4) as administered by the American Chemical Society are gratefully acknowledged.

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