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Synthesis and Characterization of Highly Conjugated, Chiral Bridging Ligands

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Received August 24, 2004

This paper describes the synthesis of four chiral derivatives of the electronically highly conjugated tetra-2-pyridylpyrazine (TPPZ) bridging ligand, which are denoted (R)- and (S)-4,5- and 5,6-pinenotetra-2-pyridylpyrazine (PTPPZ). Preparation of these ligands was undertaken through the use of commercially available, enantiomerically pure (1*R*)- and (1*S*)-α-pinene, which was functionalized and subsequently employed in a Kröhnke pyridine synthesis involving a furan-substituted pyridinium salt to yield a chiral, furan-substituted pyridyl intermediate. Oxidative degradation and subsequent reduction of this furan led to a chiral, substituted 2-pyridylaldehyde, which underwent a pyridoin condensation followed by cyclization to produce the final PTPPZ ligands.

Introduction

Bridging ligands and their use in coordination polymers and photoinduced electron-transfer processes have received increased interest over the past several decades. Initial attention to bridging ligands stemmed from the classic studies of thermal electron-transfer rates pioneered by Creutz and Taube.[1] Subsequent studies were stimulated by a strong interest in long-range photoinduced charge separation, a prerequisite for photovoltaic applications. "Photonic" molecular wires can be constructed using bridging ligands; their study often utilizes long-lived excited states in transition-metal complexes (Ru(II), Ir(III), Re(I), etc.) as electron donors which are in turn connected to metal complexes possessing electron acceptor properties, or the inverse of such an arrangement.

A variety of bridging ligands have been explored, and electron-transfer rates for a plethora of such molecular devices have been compared and quantified by Balzani and others.[2] In addition to variables such as reaction medium and temperature and the energetic profile for electron transfer (accounting for the donor and acceptor components), photoinduced electron and energy transfer processes have been studied as a function of the distance between the chromophoric components, the structure and rigidity of the bridging ligands, and the extent of conjugation of the ligand bridges.[3] As a result, considerable attention has been focused on ligand design, specifically in an attempt to tune the ligand so as to achieve the desired optical and electrochemical properties. Whereas early studies were aimed at merely observing photoinduced electron-transfer processes, later work was directed toward enhancing the longevity of the charge-separated state (in order to fully exploit the energy stored there), again through judicious ligand design.[2]

Extending the work on dinuclear complexes are studies involving coordination polymers composed of bridging ligands and metal centers. A variety of synthetic studies employing Ru(II), Cu(I), Ag(I), and Fe(II) metal ions have been explored, and their use in photovoltaic and electrochromic applications has been evaluated.[4] The physical properties of such extended systems depend strongly on the building blocks employed, and it is evident that the electronic structure of the bridging ligand is one of the principal governing factors. A variety of studies targeted the relationship between the degree of electronic conjugation of the ligand backbone and the resulting optical and electrochemical properties.[5] Recent work using a combination of spectroscopic and theoretical methods, ranging from the application of a simple particle-in-a-box model to time-dependent density functional theory calculations (TD-DFT), has further extended our understanding of this interplay.[6]

A relatively new and prominent area of interest is the preparation and application of chiral, bridging ligands.[7] It is the intent of such studies to rely on the chirality of the ligands for endowing large oligomeric and polymeric ensembles with chiral properties. Aesthetically attractive

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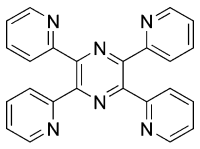
10.1021/jo048515m CCC: $27.50
Published on Web 11/16/2004

helical and double helical polymeric complexes have been prepared and imaged using X-ray crystallography and scanning probe microscopy.[8,9,11] Likewise, the chiroptical properties of helical coordination polymers formed from chiral bridging ligands have been studied in solution with circular dichroism, and films of these materials were used to fabricate electrochromic devices which exhibited absorption dissymmetry.[10,11]

This paper describes the synthesis of chiral derivatives of the electronically highly conjugated tetra-2-pyridylpyrazine (TPPZ) bridging ligand (**1**). As a bridging ligand, TPPZ is known to exhibit "remarkable coordination versatility,"[12] even effectively bridging bimetallic and trimetallic complexes.[13] Moreover, TPPZ has been shown to be an ideal candidate for a variety of applications. For the study of electron- and energy-transfer processes, TPPZ not only proved to be an optimal ligand for the formation of stable, mixed-valence, dinuclear complexes, but also was observed in each case to be a proficient intermediary for electronic coupling of the metal centers.[14] Langmuir−Blodgett (LB) techniques have been successfully employed to yield stable redox-active surface assemblies of dinuclear Ru(II) complexes with TPPZ.[15] TPPZ, along with other related 2,2′:6′,2″-terpyridine derivatives, has been effectively employed as a bridging ligand for incorporation into metallosupramolecules, facilitating the formation of multinuclear systems designed to study directionally and spatially controlled electron- and/or energy-transfer processes.[16] Finally, metal complexes involving TPPZ as a bridging ligand are found to adsorb well onto gold electrode surfaces, thereby lending themselves as ideal candidates for the formation of modified electrodes.[11a]



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The focus of this paper is the synthesis of both enantiomers of two chiral derivatives of TPPZ [4,5- and 5,6-pinenotetra-2-pyridylpyrazine (PTPPZ) (Figure 1)]. The chiral pinene side groups are utilized to endow the ligand's backbone and π-system with helicity to bestow chiroptical properties on the ligand[17] and, therefore, on the coordination complexes and polymers prepared from it. Moreover, the aliphatic character of the fused pinene groups will also enhance the solubility of the polymeric materials formed from the ligand, a property necessary for producing high degrees of polymerization. We have successfully synthesized these four novel, chiral PTPPZ ligands and have undertaken a preliminary characterization of their optical and chiroptical properties.

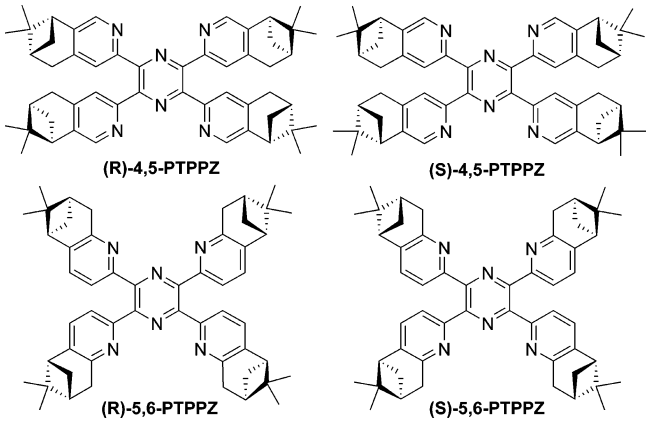
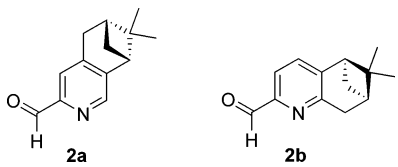


FIGURE 1. Both enantiomers of the 4,5- and 5,6-pinenotetra-2-pyridylpyrazine (PTPPZ) ligands.

Results and Discussion

Traditional preparation of TPPZ involves the self-reaction of a 2-pyridyl aldehyde using a pyridoin condensation[18] and subsequent cyclization.[19] Therefore, the key intermediate for the synthesis of a TPPZ-derived ligand is the substituted 2-pyridinecarboxaldehyde; specifically, for the PTPPZ ligands, it is the chiral aldehydes (**2a**,**b**) shown below. Whereas the unsubstituted aldehyde is commercially available, currently there are few known feasible synthetic pathways to the alkylated species.



2a **2b**

Presently, the most prevalent synthetic approach for the preparation of a pyridyl aldehyde involves allylic oxidation of a methyl-substituted pyridine using selenium dioxide.[20] However, this allylic oxidation is not selective between two or more alkyl substituents, so for the synthesis of the target aldehyde (**2a**,**b**), this strategy proves impractical.

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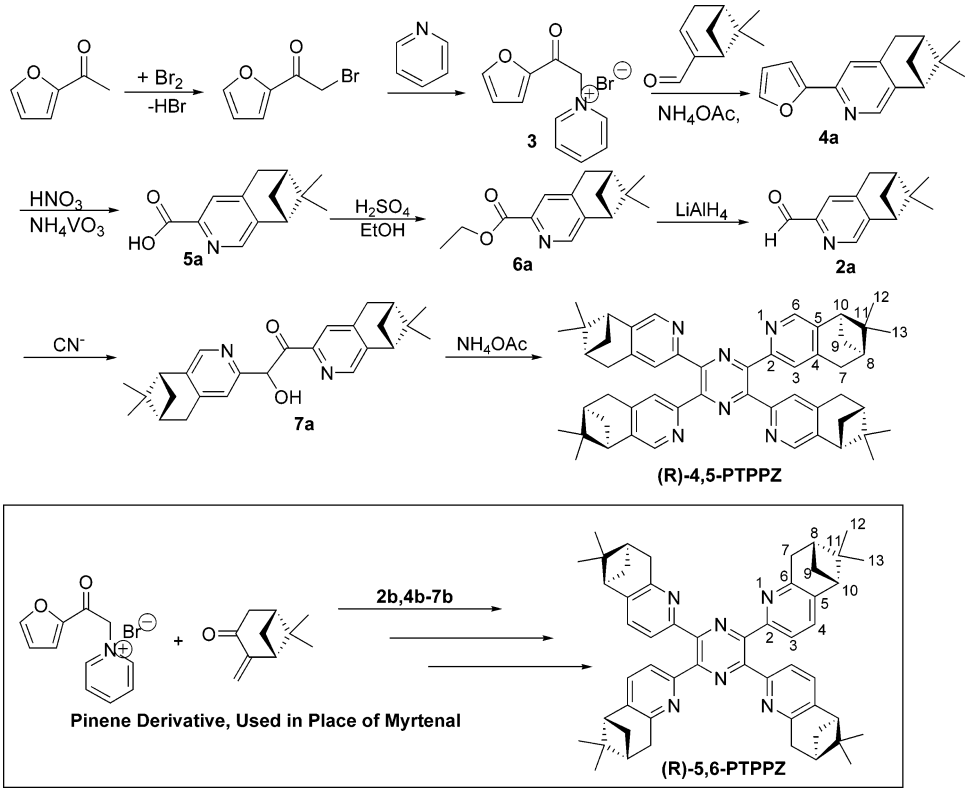
SCHEME 1



Initial attempts were directed toward preparing the aldehyde directly from (1*R*)-(−)-myrtenal and 1-(3-hydroxyimino-2-oxopropyl)pyridinium bromide. The latter was prepared from 3-bromo-2-oxopropionaldehyde oxime,[21] but being extremely hygroscopic, was particularly difficult to handle, especially on the large scale necessary for this reaction. It subsequently became evident that this instability under the conditions needed for cyclization resulted in a failure to form the pyridine ring.

A more indirect pathway through the 2-pyridinecarboxylic acid derivative was then attempted, starting from 1-(3-ethoxy-2,3-dioxopropyl)pyridinium bromide and (1*R*)-(−)-myrtenal. The cyclization was successful, but the transesterification endeavoring to form 2-pyridincarboxamide from reaction with ammonium acetate led to three major products. The mixture was separable on a small scale using column chromatography, but this approach was impractical for synthesis on a larger scale.

Therefore, a path through the 2-furan-2-yl-pyridine intermediate (Scheme 1) became necessary to obtain the aldehyde in adequate quantities. The precursor for this reaction was the air-stable 1-(2-furan-2-yl-2-oxoethyl)-pyridinium bromide. The synthetic pathway followed for this intermediate was similar to previous methods but involved a more direct route with a higher overall reaction yield.[22] Through subsequent reaction of this reagent with (1*R*)-(−)-myrtenal (acting as the α,β-unsaturated reactant), a Kröhnke pyridine synthesis[23] was undertaken to transform the pyridinium bromide into a 2-furan-2-ylpyridine derivative containing a fused pinene moiety in the 4- and 5- positions. The analogous 5,6-pinene-substituted 2-furan-2-ylpyridine was prepared from the same pyridinium precursor reacted with pinocarvone (in place of (1*R*)-(−)-myrtenal), followed by identical conditions for the two isomers throughout the remaining synthesis.

Two pathways were explored for the subsequent oxidative degradation of the furan intermediate. Initial efforts were focused on ozonolysis, which was performed successfully, but proved unfeasible for larger scale reactions. However, oxidation of the furan moiety using nitric acid and ammonium metavanadate[24] led to the desired pinene-substituted 2-pyridinecarboxylic acid. Isolation of this amphoteric and amphiphilic compound proved to be difficult, and the subsequent esterification[25] was performed without prior purification of the acid. Formation of a hemiacetal complex enabled the direct reduction of this ester to the aldehyde in excellent yields using lithium aluminum hydride.[26] It is evident that the aldehyde (**2a**,**b**) and the ester (**6a**,**b**) are useful precursors for the preparation of ligands designed for enantioselective metal-catalyzed reactions, and tests for such activity are currently in progress.

The aldehydes (**2a**,**b**) were subjected to a pyridoin condensation followed by a subsequent ring condensation with ammonium acetate for the preparation of the final chiral PTPPZ ligands (Figure 1). Two enantiomers of both the 4,5- and 5,6-pinene-substituted bridging ligands were prepared and fully characterized using ^{1}H and ^{13}C NMR,

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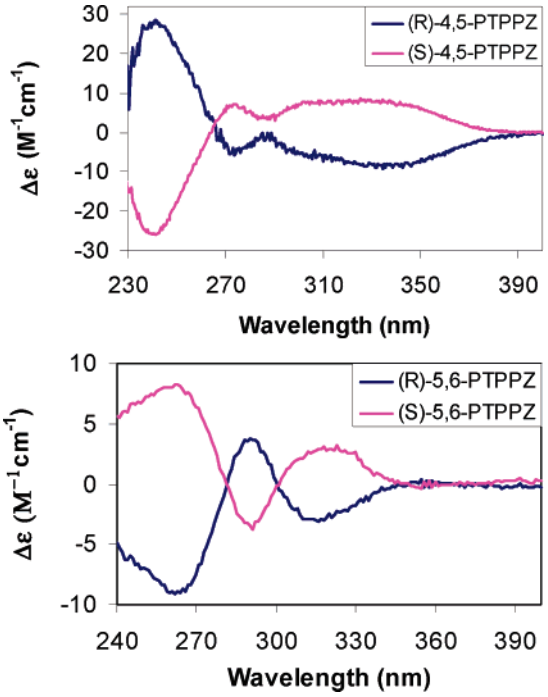

FIGURE 2. CD spectra for both (*R*)- and (*S*)-4,5- and -5,6-PTPPZ ligands. Circular dichroism spectra of the four ligands synthesized were measured at room temperature in a 1.0 cm path length quartz cell. CD data were collected at 1 nm intervals using averaging times of 3 s/nm. The spectral bandwidth was 1.5 nm. Sample concentrations were 25 μM.

HR-MS, and X-ray crystallography. The chiroptical behavior of the ligands was studied using CD spectroscopy. It is notable that the scale-up of this synthesis is straightforward, given that none of the purification steps involved column chromatography.

X-ray Crystallography. The X-ray crystal structures of (*R*)-4,5- and (*S*)-5,6-PTPPZ (see the Supporting Information) provided further evidence that the synthesis of the enantiomerically pure form of these two ligands was successful. The ligands adopt a slightly nonplanar geometry so as to reduce intramolecular steric interactions, as was evidenced by the X-ray structures showing a canted relationship of the pinenopyridyl moieties. Bond angles and distances are provided in the Supporting Information, but a specific distance of interest is the N$\cdots$N distance across the central pyrazine ring. The observed values of this distance for the (*R*)-4,5- and (*S*)-5,6-PTPPZ structures are 2.774(4) and 2.776(3) Å, respectively. Not only are the distances the same for the two structures, as is to be expected, but coordination of both nitrogens to a metal will provide one of the shortest metal-to-metal distances across an aromatic bridging ligand in coordination polymers (an estimated 7 Å, versus 12−42 Å for similar systems,[27] assuming 2 Å for a Ru−N coordination bond) and, accordingly, one of the most electronically coupled coordination systems to date.

Circular Dichroism. The CD spectra of solutions of the enantiomerically pure ligands are presented in Figure 2. Enantiomeric pairs yielded spectra with a mirror image relationship of equal values but opposite sign, as expected. The most prominent transition for the 4,5- and 5,6-PTPPZ ligands is the $\pi-\pi^*$ transition, centered at 241 and 265 nm, respectively. We note the resemblance of our results with reports in the literature for related systems.[28] For molecules of high helicity, $\pi-\pi^*$ transitions can give rise to high magnetic dipole moments and thus values for the dissymmetry factor (g) as large as 6.5×10^{-3} (versus the typical value on the order of $g \leq 5 \times 10^{-3}$).[29] The dissymmetry factor is defined as ($\Delta\epsilon/\epsilon$) and was calculated for the (*R*)- and (*S*)-4,5-PTPPZ ligands to be -2.88×10^{-5} and 3.18×10^{-5}, respectively. Therefore, despite the canted geometry displayed in the X-ray crystal structures, these ligands appear to be fairly coplanar in solution as free ligands. Of course, once coordinated to a metal, their predilection for certain geometries will change dramatically.

Conclusions

We have successfully synthesized four novel, chiral PTPPZ ligands (Figure 1) and have undertaken a preliminary characterization of their optical and chiroptical properties. An enantiomerically pure derivative of pinene (either myrtenal or pinocarvone for 4,5- and 5,6-PTPPZ, respectively) underwent a Kröhnke pyridine synthesis,[23] followed by oxidation of the resulting substituted pyridyl furan. Subsequent esterification and reduction yielded the chiral, substituted pyridylaldehyde (**2a**,**b**), and final pyridoin condensation followed by cyclization produced the four chiral PTPPZ ligands in at least 35% yield (from the pyridoin intermediate).

Experimental Section

Pyridinium Salt (3). A solution of 2-acetylfuran (25 g, 0.227 mol) and a pinch of steel wool in chloroform (192 mL) was heated to 60 °C. Then a solution of bromine (36 g, 0.227 mol) in chloroform (113 mL) was added slowly, and the reaction mixture was stirred for 3 h at 60 °C, with nitrogen bubbling through the solution. The reaction mixture was then filtered through a plug of silica gel, concentrated to approximately 200 mL on a rotary evaporator, and cooled to 0 °C. Pyridine (39 mL) was added slowly, and the reaction mixture was stirred at room temperature overnight. The formed precipitate was filtered and washed with cold ether: yield 42 g (69% from 2-acetylfuran); brown powder; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.30 (s, 2H), 6.86 (dd, $J_1 = 1.7$ Hz, $J_2 = 3.7$ Hz, 1H), 7.70 (d, $J = 3.4$ Hz, 1H), 8.19 (d, $J = 1.7$ Hz, 1H), 8.25 (t, $J = 6.8$ Hz, 1H), 8.70 (t, $J = 6.5$ Hz, 1H), 9.02 (t, $J = 1.3$ Hz, 2H); δ MS (EI) *m/z* 188 [$M^+ - Br^-$] (100).

(*R*)-4,5-Furan (4a). (1*R*)-(−)-Myrtenal (24 g, 0.156 mol) was added to a solution containing pyridinium salt **3** (42 g, 0.156 mol) and ammonium acetate (98 g, 1.27 mol) in 252 mL of acetic acid, and the reaction mixture was stirred at 120 °C overnight. The reaction mixture was then poured into water (100 mL) and extracted with hexanes (3 × 150 mL). The combined organic layers were washed with water (2 × 150 mL), dried over sodium sulfate, and concentrated on a rotary evaporator: yield 23 g (62%); dark brown oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.64 (s, 3H), 1.22 (d, $J = 9.6$ Hz, 1H), 1.40 (s, 3H), 2.27−2.32 (m, 1H), 2.66−2.73 (m, 1H), 2.82 (t, $J = 5.4$ Hz, 1H), 3.00 (d, $J = 2.0$ Hz, 2H), 6.51 (t, $J = 1.5$ Hz, 1H), 6.98 (d, $J = 3.3$ Hz, 1H), 7.50 (s, 2H), 8.14 (s, 1H); ^{13}C (125 MHz, $CDCl_3$) δ 21.6, 26.2, 32.1, 33.1, 39.6, 40.3, 44.7, 107.8,

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112.2, 118.5, 141.5, 143.0, 145.7, 145.8, 147.8, 154.1; MS (EI) *m/z* 239 [M^+] (27), 196 [$M^+ - C_3H_8$] (100), 167 (20), 141 (5), 95 (3). **(*R*)-5,6-Furan (4b).** Same experimental procedure as **4a**, except that (1*R*)-pinocarvone (made from (*S*)-(−)-α-pinene)[31] was used in place of the (1*R*)-(−)-myrtenal listed above: yield 29 g (52%); dark brown oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.64 (s, 3H), 1.26 (d, J = 9.5 Hz, 1H), 1.38 (s, 3H), 2.34−2.36 (m, 1H), 2.62−2.68 (m, 1H), 2.73 (t, J = 5.6 Hz, 1H), 3.13 (d, J = 2 Hz, 2H), 6.47 (dd, J_1 = 1.8 Hz, J_2 = 3.4 Hz, J_3 = 5.1 Hz, 1H), 6.93 (d, J = 2.9 Hz, 1H), 7.19 (d, J = 7.8 Hz, 1H), 7.35 (d, J = 7.8 Hz, 1H), 7.47 (d, J = 1.2 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.6, 26.3, 32.2, 36.9, 39.8, 40.4, 46.7, 107.5, 112.0, 115.8, 133.8, 140.8, 142.9, 147.0, 154.2, 157.2; MS (EI) *m/z* 239 [M^+] (60), 224 (50), 210 (20), 196 (100), 167 (18) 128 (8), 105 (7), 77 (7).

(*R*)-4,5-Ester (6a). To a suspension of **4a** (10 g, 0.418 mol) and ammonium metavanadate (0.70 g, 5.98 × 10^{-3} mol) in water (200 mL) was added concentrated nitric acid (132 mL), and the mixture was stirred at reflux for 3−4 h. The water and nitric acid were removed by distillation at 180 °C, with vacuum applied at the very end of the distillation to ensure dryness of the reaction mixture. Ethanol (80 mL) and sulfuric acid (20 mL) were added to the reaction flask, and the mixture was stirred at reflux overnight. The reaction mixture was then poured into hexanes (150 mL) and neutralized with an aqueous solution of saturated sodium bicarbonate. The water layer was extracted with hexanes (3 × 100 mL), and the combined organic layers were then washed with water (3 × 100 mL), dried over sodium sulfate and concentrated on a rotary evaporator: yield 5.7 g (56%); brown oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.60 (s, 3H), 1.19 (d, J = 9.7 Hz, 1H), 1.40−1.45 (m, 6H), 2.32 (quint, J_1 = 2.9 Hz, J_2 = 5.6 Hz, J_3 = 8.6 Hz, J_4 = 11.5 Hz, 1H), 2.66−2.74 (m, 1H), 2.88 (t, J = 5.4 Hz, 1H), 3.01 (d, J = 2.8 Hz, 2H), 4.45 (q, J_1 = 6.5 Hz, J_2 = 7.1 Hz, J_3 = 7.7 Hz, 2H), 7.91 (s, 1H), 8.26 (s, 1H); ^{13}C (125 MHz, $CDCl_3$) δ 14.6, 21.5, 26.1, 31.7, 33.0, 39.2, 40.1, 44.9, 61.9, 124.8, 145.8, 146.6, 146.7, 146.8, 166.0. MS (EI) *m/z* 244 [M^+ − H] (23), 202 (90), 223 (45), 173 (95), 156 (100), 129 (87), 91 (45), 77 (73). **(*R*)-5,6-Ester (6b):** yield 4.8 g (47%); brown oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.60 (s, 3H), 1.23 (d, J = 9.7 Hz, 1H), 1.36 (t, J = 6.4 Hz, 3H), 1.38 (s, 3H), 2.33−2.39 (m, 1H), 2.63−2.71 (m, 1H), 2.80 (t, J = 5.7 Hz, 1H), 3.19 (d, J = 2.9 Hz, 2H), 4.38−4.48 (m, 2H), 7.29 (d, J = 7.7 Hz, 1H), 7.82 (d, J = 7.46 Hz, 1H); ^{13}C (125 MHz, $CDCl_3$) δ 14.6, 21.5, 26.2, 31.8, 36.9, 39.6, 40.2, 47.0, 61.9, 122.8, 133.6, 145.8, 146.5, 157.9, 165.9; MS (EI) *m/z* 245 [M^+ − H] (5), 230 (4), 216 (7), 200 (30), 186 (37), 170 (39), 158 (100), 141 (27), 128 (79), 117 (23), 103 (24), 84 (22), 77 (68), 69 (40).

(*R*)-4,5-Aldehyde (2a) A solution of **5a** (5.2 g, 2.13 × 10^{-2} mol) in tetrahydrofuran (100 mL) was cooled to −78 °C, under nitrogen. A lithium aluminum hydride solution (26 mL, 1 M in diethyl ether, 2.56 × 10^{-2} mol) was then added slowly, and the resulting solution was stirred at −78 °C for 1 h. Acetic acid (11 mL) was added to the reaction mixture at −78 °C, and the resulting solution was added to hexanes (300 mL). The mixture was then poured into water (300 mL) and extracted with hexanes (3 × 300 mL). The combined organic layers were washed with water (2 × 100 mL), dried over sodium sulfate, and concentrated on a rotary evaporator: yield 2.7 g (64%); reddish-orange oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.59 (s, 3H), 1.18 (d, J = 9.8 Hz, 1H), 1.40 (s, 3H), 2.28−2.34 (m, 1H), 2.66−2.74 (m, 1H), 2.89 (t, J = 5.4 Hz, 1H), 3.00 (d, J = 2.8 Hz, 2H), 7.73 (s, 1H), 8.28 (s, 1H), 9.98 (s, 1H); ^{13}C (125 MHz, $CDCl_3$) δ 21.6, 26.1, 31.6, 33.1, 39.3, 40.0, 45.2, 121.4, 146.0, 147.0, 148.4, 152.0, 193.8; MS (EI) *m/z* 201 [M^+] (26), 170 (52), 158 (100), 141 (53), 130 (82), 117 (21), 103 (32), 89 (16), 83 (5), 77 (83), 69 (12). **(*R*)-5,6-Aldehyde (2b):** yield 3.6 g (85%); reddish-orange oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.62 (s, 3H), 1.32 (d, J = 9.8 Hz, 1H), 1.43 (s, 3H), 2.40−2.45 (m, 1H), 2.71−2.80 (m, 1H), 2.86 (t, J = 5.7 Hz, 1H), 3.20 (d, J = 2.9 Hz, 2H), 7.36 (d, J = 7.6 Hz, 1H), 7.69 (d, J = 7.6 Hz, 1H), 10.0 (s, 1H); ^{13}C (125 MHz, $CDCl_3$) δ 21.5, 26.2, 31.8, 36.6, 39.7, 40.2, 47.2, 120.0, 133.8, 147.9, 150.9, 158.2, 193.5; MS (EI) *m/z* 200 [M^+ − H] (25), 186 (26), 158 (100), 130 (34), 77 (10).

(*R*)-4,5-Pyridoin (7a). A solution of **2a** (3.1 g, 1.55 × 10^{-2} mol) in pyridine (19 mL) was heated to 100 °C. Sodium cyanide was added (0.21 g, 4.25 × 10^{-3} mol), and the resulting mixture was stirred at 100 °C for 0.5 h. To this solution was added water (6 mL), and the mixture was stirred at 100 °C for 0.5 h. The mixture was then cooled to 0 °C and stirred for 1−1.5 h. The formed precipitate was filtered and washed with cold methanol (5 mL): yield 1.7 g (56%); orange crystalline solid; ^{1}H NMR (400 MHz, acetone-d_6) δ 0.68 (s, 6H), 1.24 (d, J = 9.62 Hz, 2H), 1.44 (s, 6H), 2.32−2.38 (m, 2H), 2.74−2.80 (m, 3H), 2.92 (t, J = 5.46 Hz, 2H), 3.12 (d, J = 2.37 Hz, 4H), 7.66 (s, 2H), 8.12 (s, 2H), 13.1 (wide s, exchangeable H); ^{13}C (125 MHz, $CDCl_3$) δ 20.9, 21.0, 25.4, 25.6, 31.2, 31.8, 32.8, 33.0, 38.9, 39.3, 40.0, 40.2, 44.6, 44.9, 118.5, 121.2, 140.8, 142.0, 146.2, 146.8, 148.3, 155.4, 197.7; MS (EI) *m/z* 402 [M^+] (56), 343 (21), 202 (34), 158 (100), 130 (69), 103 (21), 77 (76). **(*R*)-5,6-Pyridoin (7b):** yield 3.3 g (53%); yellow crystalline solid; ^{1}H NMR (400 MHz, acetone-d_6) δ 0.66 (s, 6H), 1.30 (d, J = 9.6, 2H), 1.42 (s, 6H), 2.30−2.40 (m, 2H), 2.73−2.82 (m, 3H), 2.86 (t, J = 5.6 Hz, 2H), 3.11 (d, J = 2.4 Hz, 4H), 7.50 (d, J = 8.0 Hz, 2H), 7.54 (d, J = 7.8 Hz, 2H), 12.9 (s, 1H); ^{13}C (125 MHz, $CDCl_3$) δ 20.8, 25.6, 32.0, 35.8, 39.8, 40.3, 46.4, 95.0, 134.9; MS (EI) *m/z* 402 [M^+] (55), 372 (40), 329 (50), 301 (20), 276 (10), 224 (5), 202 (37), 172 (100), 158 (90), 145 (29), 130 (91), 103 (42), 91 (26), 77 (58), 69 (38).

(*R*)-4,5-PTPPZ. A mixture of **7a** (0.39 g, 9.69 × 10^{-4} mol) and ammonium acetate (2.0 g, 2.56 × 10^{-2} mol) was heated without solvent at 180 °C for 1 h. The liquid mixture was then cooled to room temperature, and methanol was added (∼5 mL). Slowly, the formed suspension was warmed in an oil bath until the solution began to reflux and then cooled again to room temperature. The precipitate was filtered and washed with methanol. The product powder was recrystallized from a dichloromethane/methanol (1:2) solution: yield 0.13 g (35%); yellow crystalline solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.67 (s, 12H, H(12)), 1.22(d, J = 9.5 Hz, 4H, H(9a)), 1.40 (s, 12H, H(13)), 2.26−2.30 (m, 4H, H(8)), 2.64−2.71 (m, 4H, H(9b)), 2.79 (t, J = 5.71 Hz, 4H, H(10)), 2.94−2.96 (m, 8H, H(7a,b)), 7.63 (s, 4H, H(6)), 7.96 (s, 4H, H(3)); ^{13}C (125 MHz, $CDCl_3$) δ 21.6, 26.3, 32.0, 33.1, 39.4, 40.3, 44.7, 109.2, 124.4, 142.3, 145.3, 150.2, 155.1; HRMS calcd for $C_{52}H_{56}N_6$ + H 765.4566, found [M + H]$^+$ 765.4664. **(*R*)-5,6-PTPPZ:** yield 2.6 g (69%); yellow crystalline solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.64 (s, 12 H, H(12)), 1.19 (d, J = 9.5 Hz, 4H, H(9a)), 1.38 (s, 12H, H(13)), 2.23−2.38 (m, 4H, H(8)), 2.61−2.69 (m, 4H, H(9b)), 2.76 (t, J = 5.5 Hz, 4H, H(10)), 2.84−2.89 (m, 8H, H(7a,b)) 7.25 (d, J = 7.5 Hz, 4H, H(4)), 7.64 (d, J = 7.8 Hz, 4H, H(3)); ^{13}C (125 MHz, $CDCl_3$) δ 21.7, 26.3, 32.3, 36.6, 39.6, 40.4, 46.7, 121.7, 133.3, 141.4, 149.9, 154.4, 155.8; HRMS calcd for $C_{52}H_{56}N_6$ + H 765.4566, found [M + H]$^+$ 765.4653.

For the (*S*) enantiomers of the compounds listed above, (*R*)-(+)-α-pinene was used to make the (*S*)-enantiomers of myrtenal[30] and pinocarvone,[31] in place of the aforementioned (*R*)-enantiomers of myrtenal and pinocarvone used to make (*R*)-4,5-PTPPZ and (*R*)-5,6-PTTPZ, respectively.

X-ray Crystallographic Procedures. A Nonius KappaCCD diffractometer was employed to collect X-ray data using graphite-monochromated Mo Kα radiation (λ = 0.71073 Å). The data were processed using DENZO-SMN and SCALEPACK,[32] and the structures were solved by direct methods and refined by full-matrix least-squares methods using SHELXTL.[33] The SQUEEZE/BYPASS[34] procedure imple

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mented in PLATON[35] was used (for (*R*)-4,5-PTPPZ) to account for the solvent electron density. The positional and anisotropic displacement coefficients for all of the non-hydrogen atoms were refined, as were the hydrogen isotropic displacement coefficients, and a riding model was used for the hydrogen positional parameters. Specific crystal, reflection and refinement data are contained in Table 1 (Supporting Information), and full details are provided in the Supporting Information.

Acknowledgment. This work was partially supported by the NSF through Grant No. DMR-0213706 to the MRSEC-Princeton Center for Complex Materials. S.B. gratefully acknowledges support from a Camille and Henry Dreyfus Foundation New Faculty Award. We thank J. Carey for the use of the circular dichroism spectropolarimeter and W. B. Peters for his assistance in using it to acquire the data.

Supporting Information Available: Crystal structure reports for (*R*)-4,5- and (*S*)-5,6-PTPPZ (including full experimental details, tables, and figures) and ^{1}H NMR spectra and ^{13}C NMR spectra of compounds **2a**,**b**, **3**, **4a**,**b**−**7a**,**b**, and (*R*)- and (*S*)-4,5- and -5,6-PTPPZ. This material is available free of charge via the Internet at http://pubs.acs.org.

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