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General Route to Racemic and Enantiomeric Carbo- and Heterocyclic Vinyl Sulfoxides via Tandem Michael Addition/Horner Olefination of α-Phosphorylvinyl Sulfoxides†

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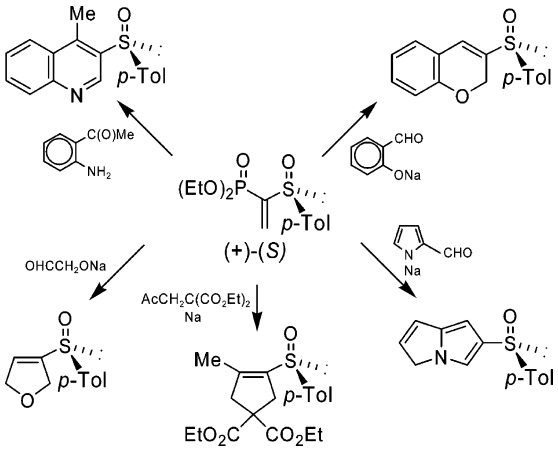

A new one-pot synthesis of heterocyclic and carbocyclic vinyl sulfoxides has been developed which involves reaction of α-phosphorylvinyl sulfoxides with carbonyl compounds bearing oxygen, nitrogen, and carbon nucleophilic centers. Use of optically active α-phosphorylvinyl *p*-tolyl sulfoxides in this tandem Michael addition/Horner olefination reaction leads to the corresponding optically active cyclic sulfoxides. In this way, a variety of optically active chromene, pyrrolizine, chinoline, and cyclopentene sulfoxides have been efficiently prepared.

Introduction

α,*β*-Unsaturated sulfoxides are versatile reagents and useful building blocks in the synthesis of biologically active and natural products.[1] They display three main types of reactivity: (a) electrophilic addition to the carbon−carbon double bond, (b) Michael addition of carbon and various heteroatom nucleophiles, and (c) cycloaddition reactions.[1d] From the viewpoint of synthetic applications, it is important to note that vinyl sulfoxides may be further functionalized via their α-lithiated derivatives.[2,3] In the last two decades interest in this class of compounds was mainly connected with the use of optically active vinyl

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† This paper is dedicated to the late Professor Leopold Horner, the pioneer of the organic chemistry and stereochemistry of phosphorus.

‡ Polish Academy of Sciences.

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(1) (a) Drabowicz, J.; Kiełbasinski, P.; Mikołajczyk, M. In *The Synthesis of Sulfones and Sulfoxides and Cyclic Sulfides*; Patai, S., Rappoport, Z., Stirling, C. J. M., Eds.; John Wiley and Sons: New York, 1994; pp 109−388. (b) Posner, G. H. *The Chemistry of Sulphones and Sulphoxides*; Patai, S., Rappoport, Z., Stirling, C. J. M., Eds.; John Wiley and Sons: New York, 1988; pp 823−849. (c) Oae, S.; Uchida, Y. *The Chemistry of Sulphones and Sulphoxides*; Patai, S., Rappoport, Z., Stirling, C. J. M., Eds.; John Wiley and Sons: New York, 1988; pp 583−664. (d) Drabowicz, J.; Kiełbasinski, P.; Mikołajczyk, M. In *The Chemistry of Sulphones and Sulphoxides*; Patai, S., Rappoport, Z., Stirling, C. J. M., Eds.; John Wiley and Sons: New York, 1988; pp 349−360.

(2) Posner, G. M.; Tang, P.-W.; Mallamo, J. P. *Tetrahedron Lett.* **1978**, *42*, 3995−3998.

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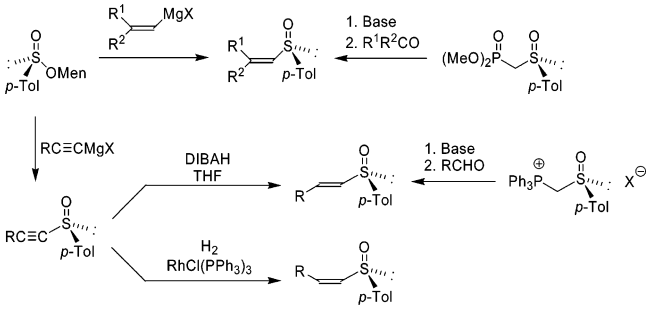
SCHEME 1. General Approaches to Optically Active Acyclic Vinyl Sulfoxides



sulfoxides in asymmetric synthesis.[4−7] This is due to the presence of the sulfinyl group which has been shown to be one of the most efficient chiral auxiliaries.

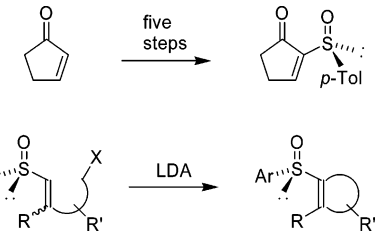
Acyclic, optically active vinyl sulfoxides may be easily prepared by two general methods. The first is based on the Andersen reaction of (−)-(*S*)-menthyl *p*-toluenesulfinate with vinyl Grignard reagents[8] or alkynylmagnesium bromides followed by stereoselective reduction of the resulting 1-alkynyl sulfoxides to the corresponding vinyl sulfoxides of a required E- and Z-geometry[9] (Scheme 1).

The second convenient synthesis elaborated in our laboratory involves the Horner olefination reaction of (+)-(*S*)-dimethoxyphosphorylmethyl *p*-tolyl sulfoxide[10] or the Wittig reaction of (*S*)-(*p*-toluenesulfinyl)methyltriphenylphosphonium ylide with carbonyl compounds[11] (Scheme 1). However, the synthetic approaches to optically active, cyclic vinyl sulfoxides are few in number and devised for the synthesis of specific structures. Thus, for example, the widely used (+)-(*S*)-2-(*p*-toluenesulfinyl)-2-cyclopentenone has been prepared by Posner from cyclopentenone in five steps involving bromination, ketalization, lithiation, Andersen reaction, and carbonyl deprotection, Scheme 2.[12]

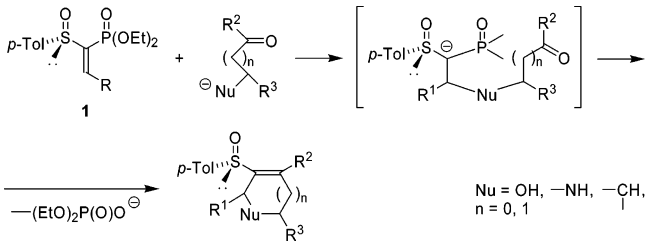
Recently, a novel method for the synthesis of optically active 1-cycloalkenyl sulfoxides has been developed by Tanaka et al.,[13] wherein the key step involves intramolecular alkylation of β-(ω-haloalkyl)vinyl sulfoxides. However, this approach is somewhat lengthy because it requires first the synthesis of acyclic vinyl sulfoxides followed by their multistep elaboration to β-(ω-haloalkyl) analogues.

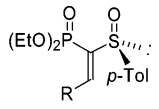
In this paper we wish to disclose a new general approach to the synthesis of optically active mono- and condensed heterocyclic and carbocyclic vinyl sulfoxides that is based on the use of chiral (*S*)-α-(diethoxyphosphoryl)vinyl *p*-tolyl sulfoxides **1**[14,15] as starting reagents.

SCHEME 2. Selected Syntheses of Optically Active Cycloalkenyl Sulfoxides



SCHEME 3. Synthesis of Cyclic Vinyl Sulfoxides by Tandem Michael Addition/Horner Olefination Reaction of Sulfoxides 1





1

1a, R=H, $[\alpha]_D^{20}$ +157 (*c* 2.1, acetone)[14]

1b, R=Ph, $[\alpha]_D^{20}$ +77 (*c* 0.21, acetone)[15]

Results and Discussion

α-Phosphorylvinyl sulfoxides **1** have been shown to be potent Michael acceptors due to the presence of two electron-withdrawing phosphoryl and sulfinyl groups bonded to the olefinic α-carbon atom.[14] As the nucleophilic addition to **1** generates the corresponding α-phosphonate carbanion, which can react with carbonyl compounds, reactions of α-phosphorylvinyl sulfoxides **1** with carbonyl reagents bearing a nucleophilic center in a β- or γ-position to the carbonyl group can provide a useful means for the synthesis of heterocyclic and carbocyclic vinylic sulfoxides as depicted in Scheme 3.

In accord with our expectations, this new tandem Michael addition/Horner olefination reaction was found to afford a variety of cyclic vinylic sulfoxides. The examples discussed below demonstrate the scope and usefulness of this methodology.

Initially, the method was tested with racemic α-(diethoxyphosphoryl)vinyl methyl sulfoxide **2** and 2-hydroxybenzaldehyde (eq 1). The latter was first converted into the sodium salt by sodium hydride in a THF solution and then treated with the sulfoxide (±)-**2**. After refluxing the reaction mixture 1 h and

(3) Okamura, H.; Mitsuhira, Y.; Miura, M.; Takei, H. *Chem. Lett.* **1978**, 517−520.
(4) Carreño, M. C. *Chem. Rev.* **1995**, *95*, 7−1760.
(5) Aversa, M. C.; Barattucci, A.; Bonaccorsi, P.; Giannetto, P. *Tetrahedron: Asymmetry* **1997**, *8*, 1339−1367.
(6) Mikołajczyk, M.; Drabowicz, J.; Kiełbasinski, P. *Chiral Sulfur Reagents: Applications in Asymmetric and Stereoselective Synthesis*; CRC Press: Boca Raton, 1997; pp 144−194.
(7) Pellissier, H. *Tetrahedron* **2006**, *62*, 5559−5601.
(8) (a) Abbot, D. J.; Colonna, S.; Stirling, C. J. M. *J. Chem. Soc., D* **1971**, 472−473; *Perkin Trans. 1* **1976**, 492−498. (b) Posner, G. H.; Tang, P. W. *J. Org. Chem.* **1978**, *43*, 4131−4136.
(9) Kosugi, H.; Kitaoka, M.; Tagami, K.; Takahashi, A.; Uda, H. J. *J. Org. Chem.* **1987**, *52*, 1078−1082.
(10) Mikołajczyk, M.; Midura, W. H.; Grzejszczak, S.; Zatorski, A.; Chefczynska, A. *J. Org. Chem.* **1978**, *43*, 473−478.
(11) Mikołajczyk, M.; Perlikowska, W.; Omelanczuk, J.; Cristau, H.-J.; Perraud-Darcy, A. *J. Org. Chem.* **1998**, *63*, 9716−9722.
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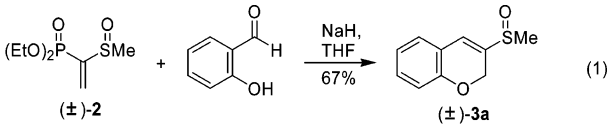
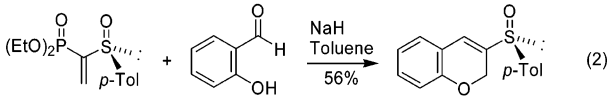
(13) Maezaki, N.; Izumi, M.; Yuyama, S.; Sawamoto, H.; Iwata, Ch.; Tanaka, T. *Tetrahedron* **2000**, *56*, 7927−7945.
(14) (a) Mikołajczyk, M.; Midura, W. H. *Tetrahedron: Asymmetry* **1992**, *3*, 1515−1518. (b) Midura, W. H.; Krysiak, J. A. *Tetrahedron* **2004**, *60*, 12217−12229.
(15) Sulfoxide (+)-(*S*)-**1b** has been prepared according to the procedure elaborated for the dimethoxyphosphoryl analog;[16] for details of the preparation of (+)-**1b**, see Experimental Section of this paper.

typical workup, (±)-3-methylsulfinyl-2*H*-chromene **3a** was isolated in 67% yield.



(±)-**2** (±)-**3a** (1)

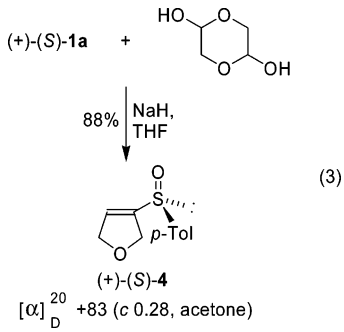


(+)-(*S*)-**1a** (+)-(*S*)-**3b** (2)

$[\alpha]_D^{20}$ +157 (*c* 2.1, acetone) $[\alpha]_D^{20}$ +84 (*c* 0.21, acetone)

When sulfoxide (+)-(*S*)-**1a** was condensed with salicylic aldehyde under the same reaction conditions, the expected chromene **3b** was obtained in low yield. However, using toluene as solvent and refluxing the reaction mixture for 3 h led to (+)-(*S*)-3-*p*-toluenesulfinyl-2*H*-chromene **3b** in 56% yield (eq 2).

Reaction of the sulfoxide (+)-(*S*)-**1a** with aliphatic hydroxyaldehydes was found to occur under milder conditions and more efficiently. For example, its reaction with the sodium salt of α-hydroxyacetaldehyde, generated in situ from the dimer upon treatment with sodium hydride in THF, gave, after stirring for 6 h at room temperature, (+)-(*S*)-3-*p*-toluenesulfinyl-2,5-dihydrofuran **4** in 88% yield (eq 3).

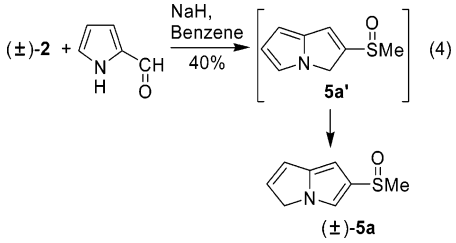


(3)

(+)-(*S*)-**4**

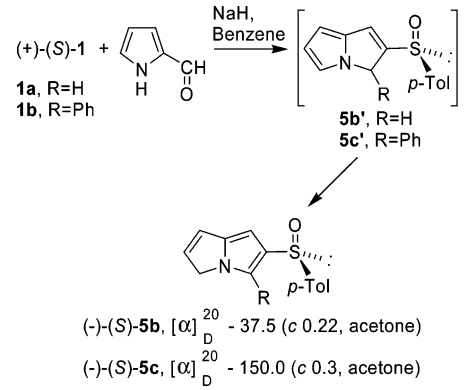
$[\alpha]_D^{20}$ +83 (*c* 0.28, acetone)

In the next step aminoaldehydes and aminoketones were used as reaction partners in the tandem reaction of α-phosphorylvinyl sulfoxides **1**. As in the case of hydroxyaldehydes, the reaction conditions were determined using racemic sulfoxide **2**. It was found that treatment of pyrrole-2-carbaldehyde with an excess of sodium hydride and then with (±)-**2** in benzene gave, after 3 h reflux, the expected cyclic product in 40% isolated yield. Its spectral properties (^{1}H and ^{13}C NMR) indicated, however, that we obtained (±)-6-methylsulfinyl-3*H*-pyrrolizine **5a** and not the tautomeric form **5a′**, which is a primary cyclic product formed as a result of the Horner olefination reaction (eq 4). Most probably, isomerization of **5a′** to the thermodynamically more stable **5a** occurred under basic conditions and at elevated temperatures.



(4)

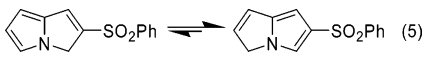
SCHEME 4. Synthesis of Enantiopure Pyrrolizine Sulfoxides 5



(-)-(*S*)-**5b**, $[\alpha]_D^{20}$ - 37.5 (*c* 0.22, acetone)

(-)-(*S*)-**5c**, $[\alpha]_D^{20}$ - 150.0 (*c* 0.3, acetone)

In this context, it is interesting to point out that a very similar isomerization of 2-(phenylsulfonyl)-3*H*-pyrrolizine to 6-(phenylsulfonyl)-3*H*-pyrrolizine has been described by Flitsch and Lubisch, who were able to obtain and characterize both tautomers.[17]



(5)

When (+)-(*S*)-**1a** and pyrrole-2-carbaldehyde were reacted under the conditions elaborated above, the corresponding annulation product (−)-**5b** was obtained in 74% yield. In a similar way, starting from (+)-(*S*)-**1b** led to the pyrrolizine sulfoxide (−)-**5c** in 77% yield (Scheme 4).

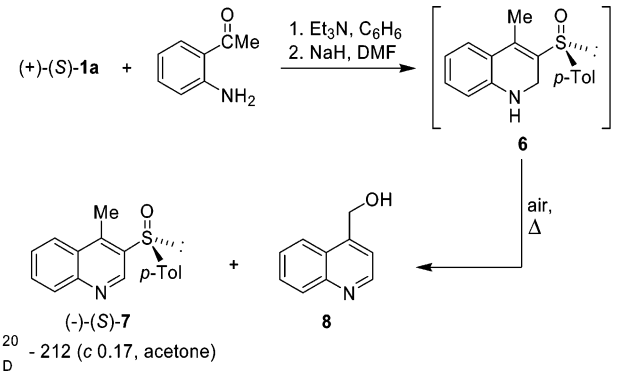
Also in this case, ^{1}H NMR spectra indicated that the products obtained have the structure of **5b** and **5c** and not **5b′** and **5c′**, which were preliminarily formed as shown in Scheme 4. To unequivocally confirm the product structure we took advantage of the fact that the pyrrolizine sulfoxide (−)-**5b** is crystalline and determined its crystal and molecular structure by X-ray diffraction. Inspection of bond lengths in both five-membered heterocyclic rings revealed that the chiral sulfinyl group is attached to the ring with two carbon−carbon double bonds. With regard to stereostructure of the sulfoxide (−)-**5b**, the X-ray data corroborated its absolute configuration *S* at sulfur with full enantiomeric purity because Flack's parameter was found to be zero. Most probably, other optically active cyclic vinyl sulfoxides obtained in this work are also enantiopure because the reaction conditions used for their preparation could not cause racemization of the chiral sulfoxide moiety.

Reaction of (+)-(*S*)-**1a** with *o*-aminoacetophenone requires special comment for two reasons. First, it was performed using a different experimental procedure. Second, it afforded two rather unexpected products. Since both reagents did not react under conditions elaborated for the synthesis of pyrrolizine sulfoxides **5**, we found that it was advantageous to add, in the first place, aminoketone to the sulfoxide (+)-(*S*)-**1a** in the presence of triethylamine in a benzene solution. Then, the diastereomeric adducts (δ_P=21.8 and 20.3 ppm; 9:1) isolated in the crude state were dissolved in DMF, treated with sodium hydride, and refluxed for 2 h. This procedure resulted in formation of two products which were identified as (−)-(*S*)-4-methyl-3-*p*-toluenesulfinyl-chinoline **7** and 4-hydroxymethyl-

(16) Midura, W. H.; Mikołajczyk, M. *Tetrahedron Lett.* **2002**, *43*, 3061−3065.

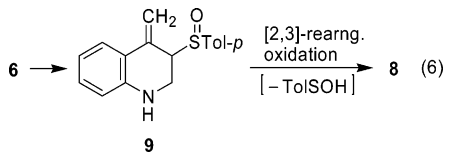
(17) Flitsch, W.; Lubish, W. *Chem. Ber.* **1984**, *117*, 1424−1435.

SCHEME 5. Synthesis of Optically Active Chinoline Sulfoxide 7



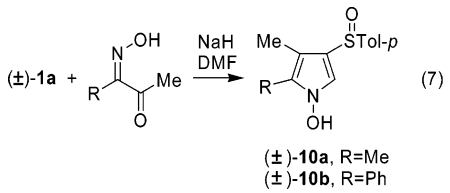
chinoline **8** and isolated in 32% and 45% yield, respectively (see Scheme 5).

Their formation can reasonably be explained by assuming that the expected annulation product **6** is air oxidized to the chinoline sulfoxide (−)-(*S*)-**7**.[18] On the other hand, under forced and basic conditions **6** most probably undergoes isomerization to the corresponding allylic sulfoxide **9** which in turn undergoes [2,3]-sigmatropic rearrangement followed by air oxidation to alcohol **8** (eq 6).[19]



(6)

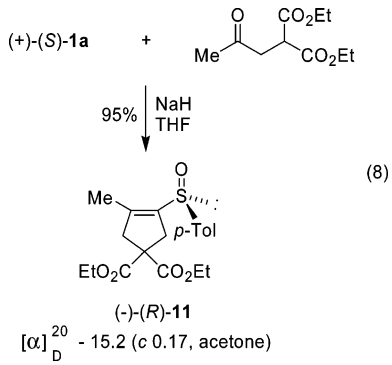
Continuing our work on the synthesis of cyclic vinyl sulfoxides, we also selected ketone monooximes as components of the tandem reaction. Due to the ambident character of the monooxime anion, its addition to **1** could be expected to occur through attack of nitrogen or oxygen on the olefinic *β*-carbon atom to give, after intramolecular Horner reaction, the corresponding pyrrole or 6*H*-oxazine derivatives. We found that treatment of the racemic sulfoxide **1a** with the sodium salt of monooximes of butan-2,3-dione and 2-phenylpropan-1,2-dione in a DMF solution at room temperature gave *N*-hydroxy-2,3-dimethyl-4-(*p*-toluenesulfinyl)pyrrole **10a** (81% yield) and *N*-hydroxy-3-methyl-2-phenyl-4-(*p*-toluenesulfinyl)pyrrole **10b** (78% yield) (eq 7).



(7)

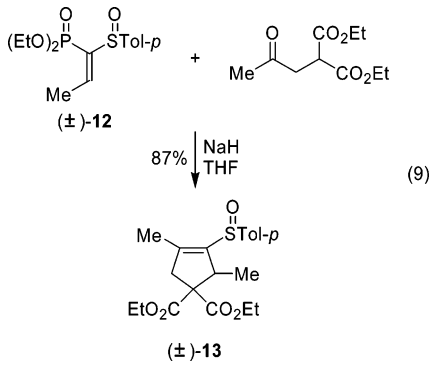
Formation of *N*-hydroxy-pyrroles **10** in this reaction indicates that Michael addition of the monooxime anion takes place by means of nitrogen as the nucleophile. Our findings are in accord with the results of Schweizer and Kopay,[20] who obtained *N*-hydroxy-pyrroles in a closely related tandem reaction of vinyltriphenylphosphonium bromide with monooximes. Interestingly, both tandem reactions represent the only way reported to construct the *N*-hydroxypyrrole ring.

Finally, we focused our interest on the tandem reaction with carbonyl compounds bearing a carbanionic center in hopes of finding a new approach to 1-cycloalkenyl sulfoxides. In fact, when sulfoxide (+)-(*S*)-**1a** was added to the sodium salt of diethyl 2-(2-oxopropyl)malonate in a THF solution with stirring for 3 h at room temperature, the annulation product **11** was isolated in excellent yield (eq 8).



(8)

Similarly, treatment of the sodium salt of the same malonate with racemic 1-(diethoxyphosphoryl)propen-1-yl *p*-tolyl sulfoxide **12** resulted in formation of the corresponding cyclopentenyl sulfoxide (±)-**13** in 87% yield (eq 9). This compound was obtained as a 3:1 mixture of two diastereomers due to generation of a new stereogenic center at C5 in the product.



(9)

Conclusions

In conclusion, a new and efficient method for the synthesis of cyclic (hetero- and carbocyclic) vinyl sulfoxides has been developed which is based on the tandem Michael addition/Horner olefination reaction of α-phosphorylvinyl sulfoxides and carbonyl compounds bearing nucleophilic centers. Using optically active α-phosphorylvinyl sulfoxides this approach delivers a series of enantiomeric cyclic vinyl sulfoxides in which the chiral sulfinyl group is bonded to the chromene, pyrrolizine, chinoline, and cyclopentene rings. All of these sulfoxides are

(18) Aromatization of the dihydrochinoline ring by atmospheric oxygen is a well-known process, see, for example: (a) Barton, J. W.; Pearson, N. D. *J. Chem. Soc., Perkin Trans.1* **1987**, 1541−1545. (b) Gellerman, G.; Babad, M.; Kashman, Y. *Tetrahedron Lett.* **1993**, *34*, 1822−1830. (c) Uno, H.; Okada, S.; Shirashi, Y.; Shimokawa, K.; Suzuki, H. *Chem. Lett.* **1988**, 1165−1168.

(19) For excellent review on [2,3]-sigmatropic rearrangement of allyl sulfoxides, see: Braverman, S. In *The Chemistry of Suphones and Sulphoxides*; Patai, S., Rappoport, Z., Stirling, C. J. M., Eds.; John Wiley and Sons: New York, 1988; pp 717−757.

(20) Schweizer, E. E.; Kopay, Ch. M. *J. Org. Chem.* **1972**, *37*, 1561−1564.

potentially interesting as starting materials for further asymmetric transformations.

Experimental Section

(+)-(*S*)-1-(Diethoxyphosphoryl-2-phenyl)vinyl *p*-Tolyl Sulfoxide (1b). To a solution of benzaldehyde (1.06 g, 10 mmol) in benzene (30 mL) was added piperidine (340 mg, 4 mmol), and the mixture was refluxed for 0.5 h. Then, to a resulting solution cooled to room temperature was added (+)-(*S*)-α-diethoxyphophorylmethyl *p*-tolyl sulfoxide (2.9 g, 10 mmol) and acetic acid (0.25 g, 4.1 mmol). The reaction mixture was refluxed for 2 days. After solvent evaporation, water (20 mL) and CH_2Cl_2 (20 mL) were added to the remaining oil. The organic layer was dried over anhydrous $MgSO_4$ and evaporated in a vacuum. The residue obtained as a yellow oil was purified by column chromatography (hexane/ethyl acetate, 5:1) to give the pure sulfoxide **1b** as a colorless oil (3.6 g, 95%); $[\alpha]^{20}_D$ +77 (c = 0.21, acetone); ^{31}P NMR (81 MHz, $CDCl_3$) δ 12.3; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.12 (t, 3H, J = 7.1 Hz), 1.16 (t, 3H, J = 7.1 Hz), 2.38 (s, 3H), 3.50−4.03 (m, 4H), 7.17 (d, 1H, J = 41.4 Hz), 7.21−7.64 (m, 9H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 19.6, 21.7, 61.4 (d, J = 7.2 Hz), 126.4, 128.5, 129.2, 134.8 (d, J = 181.3 Hz), 140.4, 146.6, 150.4 (d, J = 7.5 Hz). Anal. Calcd for $C_{19}H_{23}O_4PS$ (378.36): C, 60.31; H, 6.13; S, 8.47. Found: C, 60.04; H, 6.23; S, 8.39.

(±)-3-Methanesulfinyl-2*H*-chromene (3a). To a solution of salicylaldehyde (61 mg, 0.5 mmol) in THF (20 mL) 50% NaH (24 mg, 1 mmol, suspension in mineral oil) in THF (5 mL) was added. After stirring for 5 min, vinyl sulfoxide (±)-**2** (113 mg, 0.5 mmol) in THF (5 mL) was added dropwise. The reaction mixture was then refluxed for 1 h. After cooling the reaction mixture to room temperature an aqueous solution of NH_4Cl (15 mL) was added, and the product was extracted with $CHCl_3$ (3 × 10 mL). The combined extracts were dried over anhydrous $MgSO_4$ and evaporated to give the crude product **3a**, which was purified by column chromatography on silica gel (benzene/acetone, 1:20); yellow oil, 65 mg (67%); ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.69 (s, 3H), 4.92 (AB system, 2H, J = 12 Hz)), 6.82−7.35 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 38.9, 61.6, 103.9, 116.0, 122.0, 126.1, 127.9, 131.2. Anal. Calcd for $C_{10}H_{10}O_2S$ (194.24): C, 61.83; H, 5.19; S, 16.50. Found: C, 61.68; H, 5.27; S, 16.45.

(*S*)-3-*p*-Toluenesulfinyl-2*H*-chromene (3b). According to the procedure described above, the sulfoxide (+)-**1a** (151 mg, 0.5 mmol) and salicylaldehyde (61 mg, 0.5 mmol) in toluene (3 h reflux) gave the chromene sulfoxide **3b**; light-yellow crystals, mp 94−95 °C, 76 mg (56%); $[\alpha]^{20}_D$ +84 (c = 0.21, acetone); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.41 (s, 3H), 4.53 and 6.66 (AB system, 2H, J = 14.2 Hz), 6.78−7.26 (m, 5H), 7.32 and 7.55 (AA′BB′ system, 4H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 21.4, 61.8, 116.2, 120.8, 122.0, 125.1, 127.4, 128.2, 130.2, 131.5, 135.6, 138.0 142.1, 154.0. Anal. Calcd for $C_{16}H_{14}O_2S$ (270.32): C, 71.09; H, 5.22; S, 11.86. Found: C, 70.97; H, 5.11; S, 11.95.

(*S*)-3-*p*-Toluenesulfinyl-2,5-dihydrofuran (4). To 50% NaH (48 mg, 2 mmol; suspension in mineral oil) in THF (10 mL) was added glycolaldehyde (60 mg, 1 mmol) dropwise. After vigorous stirring for 30 min at room temperature a solution of sulfoxide (+)-**1a** (302 mg, 1 mmol) in THF (10 mL) was added, and the reaction mixture was stirred for 6 h. Then, saturated ammonium chloride solution (5 mL) was added, and the reaction solution was extracted with $CHCl_3$ (3 × 10 mL). The combined organic phases were dried over $MgSO_4$. After solvent evaporation, the crude product was purified by chromatography on silica gel (hexane/acetone, 24:1) to afford the product **4** as a yellow oil (183 mg, 88%); $[\alpha]^{20}_D$ +83 (c = 0.28, acetone); ^{1}H NMR (200 MHz, C_6D_6) δ 2.38 (s, 3H), 4.39−4.60 (m, 2H), 4.73−4.80 (m, 2H), 6.57 (m, 1H), 7.32 and 7.50 (AA′BB′ system, 4H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 21.1, 71.9, 76.1, 124.5, 130.5, 131.9, 133.1, 140.2, 142.1. Anal. Calcd for $C_{11}H_{12}O_2S$ (208.27): C, 63.44; H, 5.81; S, 15.39. Found: C, 63.67; H, 5.70; S, 15.45.

General Procedure for the Preparation of Pyrrazoline Sulfoxides 5. To a solution of pyrrole-2-carbaldehyde (94 mg, 1 mmol) in benzene (10 mL) was added 50% NaH (48 mg, 2 mmol, suspension in mineral oil). The mixture was stirred for 0.5 h, and a solution of vinyl sulfoxide [(±)-**2**, (+)-**1a**, (+)-**1b**] (1 mmol) in benzene (5 mL) was added. After 3 h reflux, the reaction was quenched by addition of aqueous ammonium chloride solution (15 mL). The water phase was extracted with $CHCl_3$ (3 × 10 mL), and combined organic phases were dried over anhydrous $MgSO_4$. Evaporation of solvents gave the crude product **5**, which was purified by chromatography (acetone/benzene, 1:25).

(±)-6-Methanesulfinyl-3*H*-pyrrolizine (5a). Yellow oil (80 mg, 48%); ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.82 (s, 3H), 4.46−4.49 (m, 2H), 6.11 (s, 1H), 6.30 (m, 1H), 6.96 (m, 1H), 7.29 (dd, 1H, J = 1.4 and 2.8 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 38.1, 49.2, 106.1, 108.1, 119.0, 122.9, 142.3, 148.9. Anal. Calcd for C_8H_9NOS (167.22): C, 57.46; H, 5.42; N, 8.38; S, 19.17. Found: C, 57.34; H, 5.22; N, 8.63; S, 18.99.

(*S*)-6-(*p*-Toluenesulfinyl)-3*H*-pyrrolizine (5b). After crystallization from a mixture of petroleum ether/methylene chloride (3:1) the product **5b** was obtained in the form of yellow crystals (180 mg, 74%); mp 123−125 °C; $[\alpha]^{20}_D$ −37.5 (c = 0.22, acetone); ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.39 (s, 3H), 4.44 (m, 2H), 5.93 (s, 1H), 6.26 (dt, 1H, J = 2.1 and 6.1 Hz), 6.49 (dt, 1H, J = 2.1 and 6.1 Hz), 7.27 and 7.53 (AA′BB′ system, 4H and 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 21.3, 52.3, 95.8, 119.8, 122.9, 124.5, 128.1, 128.9, 129.3, 130.5, 140.2, 142.8. Anal. Calcd for $C_{14}H_{13}NOS$ (243.31): C, 69.11; H, 5.39; N, 5.76; S, 13.18. Found: C, 69.34; H, 5.22; N, 5.83; S, 12.99.

(*S*)-5-Phenyl-6-(*p*-toluenesulfinyl)-3*H*-pyrrolizine (5c). Brown oil (245 mg, 77%); $[\alpha]^{20}_D$ −150 (c = 0.3, acetone); ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.39 (s, 3H), 4.42−4.67 (m, 2H), 5.92 (s, 1H), 6.27 (dt, 1H, J = 2.1 and 6.1 Hz), 6.53 (dt, 1H, J = 2.1 and 6.1 Hz), 7.26−7.50 (AA′BB′ system, 4H), 7.33−7.75 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 21.3, 52.2, 97.3, 119.2, 123.2, 124.7, 127.6, 128.3, 128.5, 129.4, 140.2, 142.1. Anal. Calcd for $C_{20}H_{17}NOS$ (319.41): C, 75.20; H, 5.36; N, 4.39; S, 10.04. Found: C, 75.45; H, 5.09; N, 4.44; S, 9.96.

Reaction of (+)-1a with *o*-Aminoacetophenone. To vinyl sulfoxide (+)-**1a** (151 mg, 0.5 mmol) dissolved in benzene (5 mL) *o*-aminoacetophenone (67 mg, 0.5 mmol) and 3 drops of triethylamine were added. The mixture was kept at room temperature, and benzene was evaporated. The crude adduct was dissolved in DMF (3 mL), and NaH (24 mg, 1 mmol, 50% dispersion in oil) was added. The mixture was refluxed for 2 h. The reaction was quenched by addition of aqueous ammonium chloride solution (15 mL), and the water phase was extracted with $CHCl_3$ (3 × 10 mL). The combined extracts were dried over anhydrous $MgSO_4$. After evaporation of solvents (DMF was removed by Kugelrohr distillation) the reaction products were separated by column chromatography (hexane/ethyl acetate, 10:1).

(*S*)-4-Methyl-3-(*p*-toluenesulfinyl)quinoline (7). Red oil (45 mg, 32%); $[\alpha]^{20}_D$ −212 (c = 0.17, acetone); ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.35 (s, 3H), 2.88 (s, 3H), 7.26 and 7.56 (AA′BB′ system, 4H), 7.59−7.67 (m, 1H), 7.75−7.82 (m, 1H), 8.03−8.14 (m, 2H), 9.20 (s, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 14.4, 21.3, 111.6, 124.1, 125.0, 127.6, 130.2, 131.0, 130.4, 138.2, 142.7, 145.5, 146.2. MS (EI) m/z 281 $[M]^+$. Anal. Calcd for $C_{17}H_{15}NOS$ (281.36): C, 72.57; H, 5.37; N, 4.98. Found: C, 72.36; H, 5.67; N, 5.01.

4-(Hydroxymethyl)quinoline (8). Red oil (36 mg, 45%), mp 91−92 °C (lit. 97−98 °C[21]); ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.23 (s, 2H), 7.52−7.61 (m, 2H), 7.68−7.76 (m, 1H), 7.93−7.98 (m, 1H), 8.11−8.16 (m, 1H), 8.87 (d, 1H, J = 4.4 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 60.7, 118.1, 123.0, 125.9, 126.8, 129.7, 147.4, 147.6, 150.3; MS (CI) m/z 159 $[M + H]^+$. Anal. Calcd for $C_{10}H_9$-

(21) Wender, P. A.; Beckham, S.; Oleary, J. G. *Synthesis* **1994**, 1278−1283; Philips, A. P. *J. Am. Chem. Soc.* **1946**, *68*, 2568−2569.

NO (159.18): C, 75.45; H, 5.70; N, 8.80. Found: C, 75.16; H, 7.54; N, 9.01.

General Procedure for the Preparation of *N*-Hydroxypyrroles (10). To a solution of dione monooxime (0.25 mmol) in DMF (10 mL) 50% NaH (12 mg, 0.5 mmol, dispersion in oil) and vinyl sulfoxide (±)-**1a** (75 mg, 0.25 mmol) dissolved in DMF (1 mL) were added. The mixture was kept at room temperature for 4 h. After this time aqueous ammonium chloride solution (15 mL) was added, and the reaction solution was extracted with $CHCl_3$ (3 × 10 mL). The extracts were combined, dried over anhydrous $MgSO_4$, and evaporated. The crude product was purified by column chromatography (hexane/ethyl acetate, 12:1 or 20:1).

(±)-2,3-Dimethyl-*N*-hydroxy-4-(*p*-toluenesulfinyl)pyrrole (10a). Red oil (50 mg, 81%); ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.79 (s, 3H), 2.01 (s, 3H), 2.36 (s, 3H), 6.33 (s, 1H), 7.38 and 7.21 (AA′BB′ system, 4H), 11.26 (s, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 8.9, 9.7, 21.3, 110.6, 115.2, 125.0, 125.7, 129.7, 138.9, 140.8, 152.8; IR (film) 3142, 2924, 1688, 1023 cm^{-1}. Anal. Calcd for $C_{13}H_{15}NO_2S$ (249.32): C, 62.63; H, 6.06; N, 5.62. Found: C, 62.39; H, 5.87; N, 5.81.

(±)-*N*-Hydroxy-3-methyl-2-phenyl-4-(*p*-toluenesulfinyl)pyrrole (10b). Red oil (61 mg, 78%); ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.04 (s, 3H), 2.39 (s, 3H), 6.44 (s, 1H), 7.18−7.46 (m, 9H), 11.3 (s, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 11.0, 21.4, 106.7, 114.7, 125.1, 126.2, 126.7, 129.7, 131.4, 131.5, 134.0, 141.8, 141.9. Anal. Calcd for $C_{18}H_{17}NO_2S$ (311.39): C, 69.43; H, 5.50; N, 4.50. Found: C, 69.63; H, 5.38; N, 4.31.

(*R*)-4,4-Di(ethoxycarbonyl)-2-methyl-1-(*p*-toluenesulfinyl)cyclopent-1-ene (11). To a solution of diethyl 2-(2-oxopropyl)-malonate (1.4 g, 6.5 mmol) in THF (30 mL) 50% NaH (0.299 g, 13 mmol) was added. After stirring for ca. 20 min, vinyl sulfoxide (+)-**1a** (1.969 g, 6.5 mmol) was slowly added and the deeply red reaction solution was stirred at room temperature for additional 3 h. Then, a water solution (10 mL) of ammonium chloride was added. The water phase was extracted with $CHCl_3$ (3 × 20 mL), and the combined organic phase was dried over anhydrous $MgSO_4$ and evaporated to give the crude product **11**, which was subjected to column chromatography (petroleum ether/acetone, 15:1). The product **11** was obtained pure as a brown oil (2.25 g, 95%); $[\alpha]^{20}_D$ −15.2 (c = 0.17, acetone); ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.07 and 1.18 (2xt, 3H, J = 7.1 Hz), 2.10 (m, 3H), 2.37 (s, 3H), 2.61 (m, 1H), 2.97 (m, 1H), 3.20 (m, 1H), 3.29 (m, 1H), 4.08 (2xq, 4H, J = 7.1 Hz), 7.26 and 7.38 (AA′BB′ system, 4H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 14.1, 18.7, 21.6, 34.6, 34.8, 51.2, 61.5, 126.3, 124.8, 129.4, 134.5, 141.8, 144.6, 169.3. HRMS calcd for $C_{19}H_{24}O_5S$ (M + H), 365.1422; found, 365.1427.

(±)-4,4-Di(ethoxycarbonyl)-2.5-dimethyl-1-(*p*-toluenesulfinyl)-cyclopent-1-ene (13). According to the procedure described above, malonate (1.4 g, 6.5 mmol) and vinyl sulfoxide (±)-**12** (2.06 g, 6.5 mmol) produced the cyclopentene sulfoxide (±)-**13** (mixture of diastereomers in a 3:1 ratio) as a yellow oil (2.14 g, 87%); ^{1}H NMR (200 MHz, $CDCl_3$) major diastereomer δ 1.11 (9t, 3H, J = 7.2 Hz), 1.14 (d, 3H, J = 7.1 Hz), 1.19 (d, 3H, J = 7.2 Hz), 2.14 (m, 3H), 2.42 (s, 3H), 2.79 (dq, 1H, J = 18.0 and 0.8 Hz), 3.38 (qdq, 1H, J = 7.1, 1.6 and 1.3 Hz), 3.50 (ddq, 1H, J = 18.0, 1.6 and 1.4 Hz), 3.90−4.25 (m, 4H), 7.33 and 7.44 (AA′BB′ system, 4H); ^{1}H NMR (200 MHz, $CDCl_3$) minor diastereomer δ 0.63 (d, 3H, J = 7.2 Hz), 1.09 (t, 3H, J = 7.2 Hz), 1.17 (t, 3H, J = 7.2 Hz), 2.10 (m, 3H), 2.38 (s, 3H), 2.84 (m, 1H), 2.96−3.35 (m, 2H), 3.90 (m, 4H), 7.33−7.44 (AA′BB′ system, 4H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 13.8, 14.1, 19.7, 21.6, 32.0, 46.8, 58.2, 62.5, 124.5, 126.3, 134.4, 136.5, 141.8, 143.6, 167.5. HRMS calcd for $C_{20}H_{26}O_5S$ (M + H), 379.1579; found, 379.1583.

Supporting Information Available: General experimental methods, ^{31}P NMR spectrum of (+)-**1b**, ^{1}H and/or ^{13}C NMR spectra of compounds **3a**, **4**, **5a**−**c**, **7**, **10a**,**b**, and **13**, X-ray crystallographic data in CIF format, and Figure 1 (ORTEP view of (−)-**5b** with discussion of bond lengths in the pyrrolizine ring). This material is available free of charge via the Internet at http://pubs.acs.org.

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