New Methods for the Synthesis of P-Chirogenic Diphosphines: An Application to the Development of an Improved Asymmetric Variation of the Rh(I)-Catalyzed [4+2] Cycloaddition

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Abstract: A series of new P-chirogenic diphosphines has been prepared by efficient and complementary synthetic procedures. The utilization of a series of these bidentate ligands possessing steric linker variations and a conserved P-chirogenic domain in an asymmetric variation of the Rh(I)-catalyzed [4 + 2] enediene cycladdition is described.

Key words: P-chirogenic ligands, dynamic resolution, catalysis, cycloadditions

Introduction

Chiral phosphines have proven invaluable as controller ligands for an exceptional range of asymmetric processes that have found utility in synthesis.1 The vast majority of diphosphines in this category derive their intrinsic conformational bias from chirality established within a carbon based linking element. In contrast, comparatively few P-chirogenic ligands have received scrutiny as asymmetry inducers due to their relative inaccessability.2 Our interest in the development of asymmetric transition-metal-catalyzed carbon–carbon bond forming reactions stimulated us to investigate prospective new procedures for the preparation of this class of ligands. In this communication we describe aspects of our progress in this area and report the first examples of the utilization of P-chirogenic diphosphines in an asymmetric variation of the Rh(I)-catalyzed [4+2] cycladdition.

The Dynamic Thermodynamic Resolution of Lithiated Racemic 2° Phosphine–Boranes with (−)-Sparteine3

The known proclivity of P-lithio 2° phosphine–boranes to undergo stereochemical inversion at phosphorus4 suggested the possibility that optically enriched derivatives might be obtained by a sequence involving dynamic thermodynamic resolution of these species followed by P-alkylation. In a recent study to demonstrate the feasibility of this concept, we found that the lithio derivative of racemic tert-butylphenylphosphine–borane (1) undergoes spontaneous dynamic resolution in the presence of (−)-sparteine in diethyl ether at room temperature.5 Accordingly, treatment of 1 with BuLi (1.0 equiv) in Et2O at −78 °C in the presence of (−)-sparteine (1.3 equiv) furnished a nearly homogeneous solution, which, upon warming, deposited a voluminous precipitate. Subsequent stirring of the resulting suspension for 30 min at ca. 25 °C followed by cooling to −78 °C and alkylative trapping with 2-(chloromethyl)anisole 6 provided the optically enriched phosphine-borane 2 in 95% ee7 and 80% isolated yield. The absolute sense of optical induction was determined to be R by methylation of the (−)-sparteine complex of lithiated 1 to afford the known derivative 38 in 93% ee (Scheme 1). Alkylation of dynamically resolved P-lithio-tert-butylphenylphosphine–borane(−)-sparteine complex prepared in the above manner with representative halides

Scheme 1

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Table 1 Ligand Precursors 4 and 6 Prepared

<table>
<thead>
<tr>
<th>Electrophile</th>
<th>Product</th>
<th>Yield (%)</th>
<th>Ratio of $5:6^a$</th>
<th>ee (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Ph$_2$P(BH)$_3$</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$\text{Cl}$</td>
<td>$\text{Ph}_2$P(BH)$_3$</td>
<td>85</td>
<td>–</td>
<td>95</td>
</tr>
<tr>
<td>$\text{Br}$</td>
<td>$\text{Ph}_2$P(BH)$_3$</td>
<td>90</td>
<td>–</td>
<td>92</td>
</tr>
<tr>
<td>$\text{Br}$</td>
<td>$\text{Ph}_2$P(BH)$_3$</td>
<td>68$^b$</td>
<td>21.7:1</td>
<td>&gt;99$^c$</td>
</tr>
<tr>
<td>$\text{Br}$</td>
<td>$\text{Ph}_2$P(BH)$_3$</td>
<td>71$^b$</td>
<td>11.3:1</td>
<td>&gt;99$^c$</td>
</tr>
<tr>
<td>$\text{Br}$</td>
<td>$\text{Ph}_2$P(BH)$_3$</td>
<td>76$^b$</td>
<td>18.4:1</td>
<td>&gt;99$^c$</td>
</tr>
<tr>
<td>$\text{Br}$</td>
<td>$\text{Ph}_2$P(BH)$_3$</td>
<td>75$^b$</td>
<td>11.8:1</td>
<td>&gt;99$^c$</td>
</tr>
</tbody>
</table>

$^a$ Diastereomeric ratios were determined by NMR.

$^b$ Yield obtained after recrystallization.

$^c$ Enantiomeric excesses were determined after recrystallization.

The Preparation of $(S_S)$-Methylphosphine–Borane Derivatives in a High State of Optical Purity by an Asymmetric Lithiation/Trapping-Reductive Elimination Strategy

Enantioenriched P-chiral 2° phosphine–boranes are extremely useful precursors for the synthesis of P-chirogenic ligands for asymmetric catalysis. The most common route used for the preparation of these compounds involves the synthesis and resolution of diastereomeric derivatives followed by reductive cleavage and protonation.$^{11}$ During the course of our studies on new methods for the synthesis of enantiopure P-chiral phosphines,$^{12}$ we developed an alternative and highly efficient route to P-chiral 2° phosphine–boranes in enantiopure form by an asymmetric lithiation/trapping-ductive elimination procedure that represents an overall “asymmetric demethylation” (Scheme 2).

The requisite achiral dimethylphosphine–borane precursors 7a–d were typically prepared by the method of Muci and Evans$^{38}$ from chlorodimethylphosphine–borane and the corresponding aryl Grignard reagent. Asymmetric lithiation of dimethylphosphine–boranes in the presence of s-BuLi/(−)-sparteine complex (Et$_2$O, –78 °C)$^{2b}$ followed by sequential trapping of the resultant organolithium derivatives with benzophenone and final alkoxide acylation with pivaloyl chloride furnished the enantio-enriched adducts 8a–d in very good yields on a preparative scale. Significantly, these highly crystalline compounds could usually be brought to >99% optical purity by recrystallization from the appropriate solvent system.$^{13}$ In addition, simple reduction of these adducts in the presence of lithium naphthalenide in THF or Li/NH$_3$–THF at –78 °C followed by protonation (MeOH) gave the corresponding 2° phosphine–boranes 9a–d with enantipurities exceeding 99%. The optical purities of 9a–d were determined by prior conversion to appropriate 3° phosphine–boranes by alkylation of the corresponding lithium possessing a secondary ligating moiety or, alternatively, dihalides readily furnished the corresponding ligand precursors 4 or 6 with high efficiency (Table 1). In the case of dihalides, optical amplification$^{36}$ is operative leading to the formation of the desired C$_2$-symmetric diphosphine derivatives 6 admixed with minor amounts of the corresponding meso-diastereomers 5 that could be readily separated by chromatography or recrystallization. Removal of the borane protecting group from the intermediates 4 or 6 to liberate the free phosphines could most readily be achieved by exposure to pyrrolidine (neat, r.t. to 45 °C, 24 h) followed by sublimation of the residual pyrrolidine–borane in vacuo.$^9$
derivatives with 2-(chloromethyl)benzothiophene to give the chiral P/S ligand precursors 10a–d or benzyl bromide (for 9b)\(^{14}\) (Scheme 3). In all cases, stereochemical comparisons were made to authentic racemates by chiral HPLC using a CHIRALPAK AD column. As before, representative alkylations using dihalides provided the corresponding diphosphines 11a,b in high yield. A collection of results obtained via this sequence appear in Table 2.

On the Rhodium(I)-Catalyzed \([4+2]\) Cycloaddition. The Role of P-Chirogenic Diphosphine Linker Backbone Variations on the Magnitude of Absolute Stereoinduction

The catalysis of formal \([4+2]\) cycloadditions of nonactivated enedienes and dienynes by appropriate Rh(I) complexes has proven to be an extremely useful method for the synthesis of carbocyclic and heterocyclic intermediates.\(^{15}\) In contrast to the corresponding thermal Diels–Alder cycloadditions that require high temperatures and proceed with limited stereoselectivity, the nonconcerted Rh(I)-catalyzed reactions occur at moderate temperatures (ca. 25–70 °C) and give rise to excellent levels of substrate directed stereocontrol. As an additional feature, we have shown that modification of the active Rh(I) center with simple DIOP-like diphosphines provides good levels of absolute stereoinduction for the cyclization of achiral substrates.\(^{15b, 16}\) During the course of the latter investigation, the sterically demanding 2-(trifluoromethyl)phenyl moiety was found to be a particularly effective substituent for phosphorus. As part of the present study, a series of P-chirogenic diphosphines bearing this substituent were evaluated as chirality controllers with the intent of elucidating the stereochemical influence of linker backbone variations on asymmetric induction. Significantly, very little is currently known regarding structural perturbations of this type.\(^{17}\) Consequently, a set of diphosphines possessing a \(S\)-disposed methyl-2-(trifluoromethyl)phenyl P-bonding motif conserved throughout was prepared and evaluated. The diphosphines used in this investigation were synthesized from dimethyl-2-(trifluoromethyl)phenylphosphine–borane (9a) has been shown to be a useful precursor for a variety of P-chiral 3° phosphine–boranes via Cu(I)–Pd(0) cocatalyzed cross coupling with representative aryl iodides (or nonaflates) to provide the corresponding 3° phosphine–boranes 12 with high efficiency (Scheme 4).\(^{12a}\)

**Table 2** Preparation of Enantioenriched 2° Phosphine–Boranes

<table>
<thead>
<tr>
<th>Ar</th>
<th>ee (%) Before Recrystallization</th>
<th>Yield (%)(&gt;99% ee)</th>
<th>Yield (%)(&gt;99% ee)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ph</td>
<td>75</td>
<td>69(^{b})</td>
<td>93</td>
</tr>
<tr>
<td>2-(i)-PrC(_6)H(_4)</td>
<td>&gt;99</td>
<td>70(^{c})</td>
<td>94</td>
</tr>
<tr>
<td>2-MeC(_6)H(_4)</td>
<td>87</td>
<td>76(^{b})</td>
<td>93</td>
</tr>
<tr>
<td>2-MeOC(_6)H(_4)</td>
<td>83</td>
<td>46(^{b})</td>
<td>99</td>
</tr>
</tbody>
</table>

\(^{a}\) Absolute stereochemistry of 9a–d was assigned \((S)\) by analogy.

\(^{b}\) Ee (%) determined by chiral HPLC using a CHIRALPAK AD column.

\(^{c}\) Ee (%) determined by analogy to the corresponding alcohol.

**Scheme 3**

In addition to the results presented above, \((S\_P)\)-methylphenylphosphine–borane (9a) has been shown to be a useful precursor for a variety of P-chiral 3° phosphine–boranes via Cu(I)–Pd(0) cocatalyzed cross coupling with representative aryl iodides (or nonaflates) to provide the corresponding 3° phosphine–boranes 12 with high efficiency (Scheme 4).\(^{12a}\)
nylphosphine–borane (7e) by a direct application of the Evans–Muci procedure. Accordingly, asymmetric lithiation of 7e in the presence of s-BuLi(-)-sparteine complex (Et₂O, -78 °C) followed by oxidation (anhyd CuCl₂) or interception of the resultant organolithium derivative in situ with the appropriate dichlorosilane and final deboration (pyrrolidine) furnished the diphosphines 14a–d (Scheme 5). The immediate precatalysts 15a–d were prepared by the treatment of (NBD)₂Rh⁺⁺⁻⁻SbF₆⁻⁻ (1.0 equiv) with the diphosphine of interest (1.1 equiv) in CH₂Cl₂ at ambient temperature. Catalyst generation was readily achieved by hydrogenative removal of the norbornadiene ligand (H₂) present in 15a–d in rigorously degassed 1,2-dichloroethane (DCE) or trifluoroethanol (TFE). Asymmetric cycloisomerizations of enediene 16 to the hexahydroisoindole 17 in the presence of 2.5 mol% of the active catalysts were then performed at 70 °C over 20 h. In all cases these cyclizations proceeded with excellent (>50:1) diastereoselectivities and respectable to very good enantiomeric excesses. The results of representative asymmetric cyclizations are assembled in Table 3.

**Conclusion**

As is evident from the data presented in Table 3, structural modification of the phosphine linking element can engender synthetically significant increases in enantiomeric excesses associated with metal templated cycloaddition. Although the origin of this effect is not currently known with precision, a probable contributing cause is the restriction of conformer mobility about the phosphorus–aryl bonds resulting from nonbonded interactions with the bulky backbone substituents present in 14c and 14d. Additional examples concerning the correlation of asymmetric cyclizations are assembled in Table 3.

### Table 3  Asymmetric Cyclization 16 to 17

<table>
<thead>
<tr>
<th>Entry</th>
<th>Diphosphine</th>
<th>Reaction Conditions</th>
<th>Isolated Yield (%)</th>
<th>ee (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>14a</td>
<td>DCE, 70 °C, 20 h</td>
<td>62</td>
<td>76</td>
</tr>
<tr>
<td>2</td>
<td>14b</td>
<td>DCE, 70 °C, 20 h</td>
<td>89</td>
<td>62</td>
</tr>
<tr>
<td>3</td>
<td>14c</td>
<td>TFE, 70 °C, 20 h</td>
<td>85</td>
<td>91</td>
</tr>
<tr>
<td>4</td>
<td>14d</td>
<td>DCE, 70 °C, 20 h</td>
<td>71</td>
<td>87</td>
</tr>
</tbody>
</table>

*See text and Scheme 5 for exact reaction conditions starting from diphosphine 14.

*The selectivities were determined by analytical HPLC on an IBM LC/9533 ternary gradient liquid chromatograph with a variable wavelength detector, using a Diacel CHIRALPAK AD column (250 x 4.6 mm), or a Diacel CHIRALCEL OD-H (250 x 4.6 mm) column. In all cases, the ee values were determined by comparison with racemic compounds.
metric induction to P-chirogenic phosphate structure variation will be reported in future accounts from these laboratories.

Melting points were obtained using a Mel-Temp II apparatus equipped with a digital thermometer and are uncorrected. Optical rotations were measured on a Perkin Elmer 241 MC polarimeter with a sodium lamp and reported as follows: [\alpha]_D^20 (c = g/100 mL of solvent). IR spectra were recorded on a Perkin Elmer 1600 FT-IR. Standard KBr pellet procedures were used to obtain IR spectra of solids. \(^1^C\) NMR was recorded on Bruker DPX-300 (300 MHz) spectrometer. Chemical shifts are reported in ppm from tetramethylsilane with residual hydrogen bearing solvent resonance as the internal standard (CDCl\(_3\); \(\delta = 7.26\)). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, pent = pentet, m = multiplet, etc.), integration, coupling constant (Hz), and assignment. \(^1^H\) NMR spectra were recorded on Bruker DPX-300 (75 MHz) spectrometer with complete proton decoupling.

Chemical shifts are reported in ppm from tetramethylsilane with solvent as the internal standard (CDCl\(_3\); \(\delta = 77.0\)). Data reported as follows: chemical shift, multiplicity, coupling constant, and assignment. \(^3^P\) NMR spectra were recorded on a Bruker DPX-300 (121 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in ppm from H\(_3\)PO\(_4\) with H\(_3\)PO\(_4\) as an external standard (\(\delta = 0.0\)). Mass spectra were obtained on a BQ 70 series mass spectrometer, under electron impact conditions at 70 eV.

Analytical TLC was performed on Polygram\® SIL G/UV 254 0.25 mm silica gel plates with fluorescent indicator supplied by Alltech and Scientific Adsorbent. UV-light, \(I_0\), and KMMO\(_4\) accomplished visualization. Flash chromatography was performed on Merck silica gel 60. Solvents for extraction and flash chromatography were reagent grades. Where reported, the enantiomeric excess (ee) was determined by analytical high-performance liquid chromatography (HPLC) on an IBM LC/553 ternary gradient liquid chromatograph with a variable wavelength detector, using a Daicel CHIRALPAK® AD column (250 \(\times\) 4.6 mm), or a Daicel CHIRALCEL® OD-H (250 \(\times\) 4.6 mm) column. In all cases, the ee is determined by comparison with racemic compounds.

All experiments were conducted in oven and/or flame-dried glassware with anhyd solvents under dry argon. (\(\pm\))-Sparteine was distilled from CaH\(_2\) under vacuum and stored at –20 °C. All experiments were conducted in oven and/or flame-dried glassware with anhyd solvents under dry argon.

A 100 mL flame-dried round-bottomed flask was equipped with a Teflon-coated magnetic spinbar and fitted with a rubber septum. The flask was purged with argon, and charged with a solution of (\(\pm\))-sparteine (2.58 g, 11.0 mmol, 1.1 equiv) in Et\(_2\)O (35 mL) at –78 °C. Sec-ButLi (1.3 M in hexane, 8.46 mL, 11.0 mmol, 1.1 equiv) was added dropwise and the mixture was stirred for 10 min after the addition. A solution of 7e (2.20 g, 10.0 mmol, 1.0 equiv) in Et\(_2\)O (5 mL) was added over 5 min via cannula. The mixture was allowed to stir for 3 h at –78 °C, then anhyd CuCl\(_2\) (4.03 g, 30.0 mmol, 3.0 equiv) was added in one batch under a flow of argon whereupon the mixture was warmed to –20 °C and stirred for 18 h. The mixture was quenched with sat. aq NH\(_4\)Cl solution. The aqueous layer was separated and extracted with Et\(_2\)O (3 \(\times\) 10 mL). The organic extracts were combined and washed with 25% aq NH\(_4\)OH (15 mL), H\(_2\)O (15 mL), and brine (15 mL), respectively. The organic layer was dried (MgSO\(_4\)), filtered through a plug of silica gel, and concentrated in vacuo. The residue was purified by flash column chromatography (0–10% EtOAc in hexanes) to provide the title compound (1.71 g, 69%) as a white solid. Recrystallization from 20% EtOAc in hexanes afforded meso-free 13a (1.20 g, 55%) as white crystals; mp 134.1–136.1 °C; [\(\alpha\)]\(_D\)\(^{20}\) = +0.695 (c = 8.07, CH\(_2\)Cl\(_2\)).

A 100 mL flame-dried round-bottomed flask was equipped with a Teflon-coated magnetic spinbar and fitted with a rubber septum. The flask was purged with argon, and charged with a solution of (\(\pm\))-sparteine (2.58 g, 11.0 mmol, 1.1 equiv) in Et\(_2\)O (35 mL) at –78 °C. Sec-ButLi (1.3 M in hexane, 8.46 mL, 11.0 mmol, 1.1 equiv) was added dropwise and the mixture was stirred for 10 min after the addition. A solution of 7e (2.20 g, 10.0 mmol, 1.0 equiv) in Et\(_2\)O (5 mL) was added over 5 min via cannula. The reaction mixture was allowed to stir for 3 h at –78 °C, then dichlorodimethylsilane (645 mg, 5.0 mmol, 0.5 equiv) was added via syringe and the resulting mixture was warmed to –20 °C and stirred for 18 h. The mixture was quenched with sat. aq NH\(_4\)Cl solution (5 mL). The aqueous layer was separated and extracted with Et\(_2\)O (3 \(\times\) 10 mL). The organic extracts were combined and washed with H\(_2\)O (15 mL) and brine (15 mL), respectively. The organic layer was dried (MgSO\(_4\)), filtered through a plug of silica gel, and concentrated in vacuo. The residue was purified by flash column chromatography (0–10% EtOAc in hexanes) to provide the title compound (1.71 g, 69%) as a white solid. Recrystallization from hot Et\(_2\)O afforded meso-free 13b (1.41 g, 57%) as white crystals; mp 76.8–77.6 °C; [\(\alpha\)]\(_D\)\(^{20}\) = +1.69 (c = 2.60, CH\(_2\)Cl\(_2\)).
A 100 mL flame-dried round-bottomed flask was equipped with a Teflon-coated magnetic spinbar and fitted with a rubber septum and purged with argon. The flask was charged with a solution of (−)-sparteine (2.58 g, 11.0 mmol, 1.1 equiv) in Et₂O (35 mL) at −78 °C, then sec-BuLi (1.3 M in hexane, 8.46 mL, 11.0 mmol, 1.1 equiv) was added dropwise and the mixture was stirred for 10 min. Once the addition was complete a solution of 7e (2.20 g, 10.0 mmol, 1.0 equiv) in Et₂O (5.0 mL) was added over 5 min via cannula. The reaction mixture was allowed to stir for 3 h at −78 °C, then dichlorodicyclohexylsilane (645 mg, 5.0 mmol, 0.5 equiv) was added via syringe whereupon the mixture was warmed to −20 °C and stirred for 42 h. The mixture was quenched with sat. aq NH₄Cl solution (5 mL). The aqueous layer was separated and extracted with Et₂O (3 × 10 mL). The organic extracts were combined and washed with H₂O (15 mL) and brine (15 mL), respectively. The organic layer was dried (MgSO₄), filtered through a plug of silica gel, and concentrated in vacuo. The residue was dissolved in degassed CH₂Cl₂ and passed through a plug of degassed silica gel, and stirred for 3 d. The mixture was sublimed from the product under high vacuum at temperatures not exceeding 70 °C to yield the corresponding deprotected diphosphine 13a–d in quantitative yield.

Deprotection of Diphosphines 13a–d; General Procedure

A flame-dried round-bottomed flask was equipped with a Teflon-coated magnetic spinbar and fitted with a rubber septum. The flask was purged with argon, and charged with a solution of the appropriate phosphine–borane 13a–d in anhydrous pyridine (approximately 2 mL per 1 mmol of phosphine–borane). The reaction mixture was stirred at 45 °C for 24 h. After cooling to r.t., the excess pyridine was removed in vacuo. The residue was dissolved in degassed CH₂Cl₂ and passed through a plug of degassed silica gel, then concentrated in vacuo. The pyridine–borane complex was sublimed from the product under high vacuum at temperatures not exceeding 70 °C to yield the corresponding deprotected diphosphines 14a–d in quantitative yield.
SPECIAL TOPIC

Synthesis of P-Chirogenic Diphosphines

Rhodium(I)-Catalyzed [4+2] Cycloadditions

Representative Precatalyst Synthesis: A flame-dried round-bottomed flask with a magnetic Teflon-coated spinbar was charged with [Rh(NBD)2][SbF6]2 (89 mg, 0.170 mmol, 1.0 equiv) and CH2Cl2 (3 mL) under argon. To this solution was added the diphosphine corresponding to 13c (102 mg, 0.187 mmol, 1.1 equiv) dissolved in CH2Cl2 (3 mL) dropwise at r.t. An immediate color change from light orange to deep orange was observed. After the addition was complete (TLC), the solution was diluted with Et2O and precipitated an orange solid. The solids were collected and washed with Et2O to provide complex 15c (156 mg, 91%) that was subsequently dried under high vacuum prior to use.

Representative Cycloaddition: A flame-dried 10 mL Schlenk tube with a magnetic Teflon-coated spinbar was charged with chiral precatalyst 15c (4.6 mg, 2.5 mol%) and fitted with a rubber septum. The flask was evacuated under high vacuum and back-filled with argon. The precatalyst was dissolved in TFE (2 mL), allowed to stir with stirring for 5 min, then purged with H2 and rapidly stirred for an additional 30 min. The H2 was removed by the freeze-pump-thaw method followed by back-filling with argon. The enedione 16 (57 mg) in TFE (0.1 mL) was then added by gas tight syringe and the reaction mixture was warmed to 70 °C with stirring for 20 h. After the cycloaddition was complete (TLC), the solution was diluted with Et2O and passed through a plug of neutral alumina. Purification by flash column chromatography on silica gel (0 to 15% EtOAc–hexanes for elution) provided hexahydroisoindole 17 (49 mg, 85%) as a colorless solid.

**Figure 5 Chemical structure of 17**

Mp 73.5–75.5 °C.

1H NMR (300 MHz, CDC13): δ = 7.71 (d, JHH = 8.1, 2 H, ArH), 7.32 (d, JHH = 8.1, 2 H, ArH), 5.54(br s, 2 H, CH=CH), 3.54 (dd, JHH = 9.3, 8.5 Hz, 1 H, NCH), 3.45 (dd, JHH = 10.1, 6.5 Hz, 1 H, NCCH), 3.08 (dd, JHH = 10.2, 1.2 Hz, 1 H, NCH=CH), 2.81 (app. t, JHH = 9.9 Hz, 1 H, NCH=CH), 2.53 (m, 1 H, CH2CH=CH), 2.34 (s, 3 H, ArCH3), 2.23 (m, 1 H, CH=CHCH3), 2.11 (m, 1 H, CHCH=CH), 1.47 (app. dt, JHH = 12.9, 4.5 Hz, 1 H, CH2CH=CH), 0.87 (d, JHH = 7.1 Hz, CH3), 0.65 (app. dt, JHH = 13.1, 11.1 Hz, 1 H, CHCH=CHCH3).

13C NMR (75 MHz, CDCl3): δ = 143.7 (C), 136.0 (CH), 134.2 (C), 130.0 (CH), 128.0 (CH), 124.7 (CH), 54.6 (CH2), 52.8 (CH2), 38.2 (CH3), 37.0 (CH), 34.1 (CH), 30.5 (CH), 21.9 (CH2), 21.8 (CH3).

IR (KBr): 3061, 3014, 2951, 2916, 2892, 2868, 2856, 2837, 1646, 1600, 1495, 1485, 1473, 1453, 1396, 1384, 1368, 1338, 1305, 1290, 1274, 1214, 1159, 1130, 1120, 1096, 1087, 1052, 949, 836, 742 cm−1.

HRMS (EI): m/z calcd for C16H21NO2S (M+) requires 291.1293, found 291.1293.

Acknowledgement

Generous financial support for this research by a grant from the National Science Foundation is gratefully acknowledged.

References


(6) The use of this substrate gave exceptionally well resolved HPLC traces so that optimization of the conditions for dynamic resolution could be readily achieved.

(7) In all instances involving monohalide trapping agents, an authentic sample of racemic phosphine–borane was prepared for comparison by chiral HPLC.


(9) Reproduction of the diphosphines derived from 4b, 6c, 6d and 6e with BH3·THF and analysis by HPLC (CHIRALPAK AD) established that no epimerization occurs during the pyridoline mediated deprotection reaction.


(13) In general, recrystallization to near optical purity could most readily be achieved by solvent diffusion in a closed system.

(14) In the case of 9b, separation of the isomers 10b in an authentic racemic mixture by chiral HPLC was not achieved. For this reason, optical purity was established for the corresponding P-benzyl derivative.


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