Optically Active 6-Membered P-Heterocycles: 1-Phenyl-1,2-Dihydrophosphinine Oxide and 1-Phenyl-3-Diphenylphosphinoyl-1,2,3,6-Tetrahydrophosphinine Oxide

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Abstract: The antipodes of racemic 1-phenyl-1,2-dihydrophosphinine oxides **1A** and **1B** were separated by resolution *via* formation of a diastereomeric complex using (–)-(2*R*,3*R*)-α,α,α',α'-tetraphenyl-1,4-dioxaspiro[4.5]decan-2,3-dimethanol (spiro-TADDOL) **2**. The (+)-antipode of 1-phenyl-3-diphenylphosphinoyl-1,2,3,6-tetrahydrophosphinine oxide **3** was synthesized by the diastereoselective addition of diphenylphosphine oxide to the α,β-double-bond of (–)-1,2-dihydrophosphinine oxide **1A**. The new chiral tetrahydrophosphinine oxide (+)-**3** served, after double deoxygenation, as a novel P-chiral bidentate ligand in the corresponding platinum complex.

Keywords: Resolution, dihydrophosphinine oxide, tetrahydrophosphinine oxide, Michael addition, platinum complex.

1. INTRODUCTION

Among the six-membered P-heterocycles, dihydro- and tetrahydrophosphinine oxides form a representative group [1,2]. Perhaps the most convenient method for the preparation of dihydrophosphinine oxides involves ring enlargement of easily available 2,5-dihydro-1H-phosphole oxides by the dichlorocarbene addition method [3,4]. Thermolysis of the 3-phosphabicyclo[3.1.0]hexane 3-oxides obtained by dichlorocyclopropanation furnished dihydrophosphinine oxides [5,6]. 1,2,3,6-Tetrahydrophosphinine-oxides with a P-function in position 3 have been introduced recently [7,8]. The related diphosphine behaved as a suitable P-ligand to form the corresponding *cis* chelate platinum complex [9].

We aimed at the synthesis of optically active 1-phenyl-3-diphenylphosphinoyl-1,2,3,6-tetrahydrophosphinine oxide from one of the enantiomers of the 1-phenyl-1,2-dihydrophosphinine oxide to make eventually available the corresponding bidentate P-ligand in an optically active form. Optically active P-ligands may be components of transition metal complexes used as enantioselective catalysts in homogeneous catalytic reactions [10]. Especially the homo- and heterobidentate chiral P-ligands, such as BINAP, DIOP, DIPAMP, BINAPHOS are of practical importance [11].

2. RESULTS AND DISCUSSION

Recently, we have elaborated a simple method [12-15] for the resolution of a variety of 3-methyl-3-phospholene 1-oxides *via* molecular complex formation with the chiral host, (–)-(4*R*,5*R*)-4,5-bis(diphenylhydroxymethyl)-2,2-dimethyl-dioxolane (TADDOL) or (–)-(2*R*,3*R*)-α,α,α',α'-tetraphenyl-1,4-dioxaspiro[4.5]decan-2,3-dimethanol (spiro-TADDOL) **2** [16,17].

We could extend the method developed by us to the resolution of methyl-4-chloro-1-phenyl-1,2-dihydrophosphinine 1-oxide **1**. The resolution can be done *via* molecular complex formation using spiro-TADDOL (–)-**2**. In the course of the preparation of 1,2-dihydrophosphinine oxide **1**, a 3:1 mixture of two double-bond isomers (**A** and **B**) were obtained [5] that could not be separated by column chromatography. Therefore, the mixture of dihydrophosphinine oxides **1A** and **1B** was resolved using spiro-TADDOL (–)-**2** in a mixture of acetone and hexane.

Racemic 1-phenyl-1,2-dihydrophosphinine oxide **1** was resolved by adding first half equivalent of spiro-TADDOL (–)-**2** to the hot acetone solution of **1**. The 1:1 crystalline complex (–)-**1**•(–)-**2** was precipitated on the addition of hexane. The ratio of (–)-**1** and resolving agent (–)-**2** was determined by ^{1}H NMR spectoscopy. Complex (–)-**1**•(–)-**2** was analyzed on a chiral HPLC column showing that the enantiomeric excess (*ee*) of major isomer (–)-**1A** was 40%. After two recrystallizations of the (–)-**1**•(–)-**2** complex from a 1:2 mixture of acetone and hexane, complex (–)-**1A**•(–)-**2** was obtained with a 89% *ee* in 33 % yield. The complex could be further purified by a third recrystallization giving the complex with 96.5% *ee*, but the yield became rather low. After flash column chromatography on a silica gel, (–)-**1A** was recovered with an *ee* of 96.5%. Double-bond isomer **1B** did not separate from major isomer **1A** during the process. The enantiomeric excess of minor isomer **1B** was >99.9% after the three recrystallizations and the ratio of the double-bond isomers in the crystalline phase did not change

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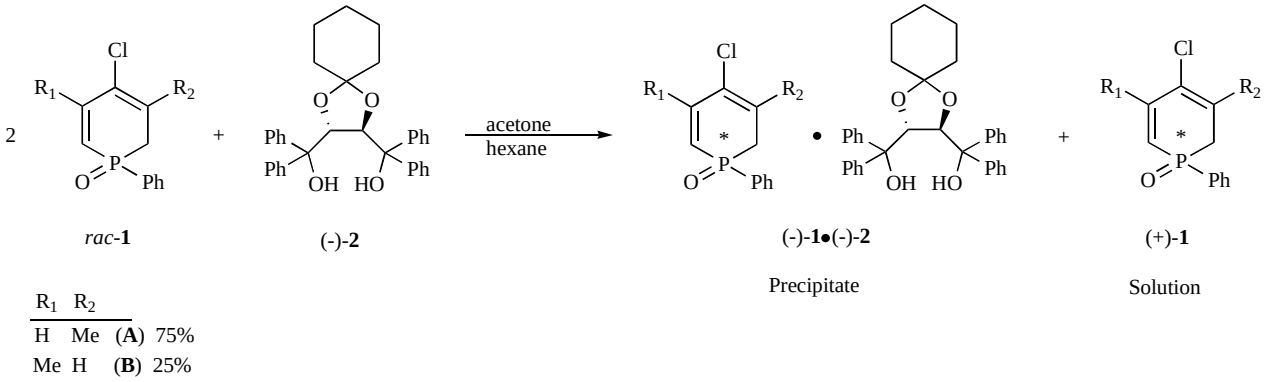


Scheme 1.

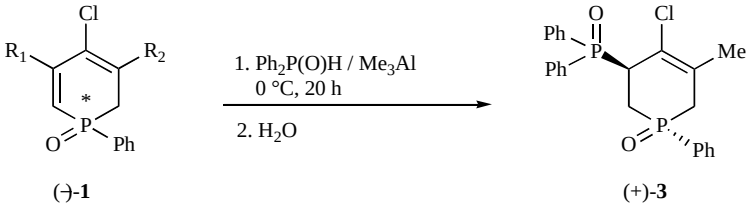
significantly (Scheme **1**). Dihydrophosphinine oxide (+)-(**1A** and **1B**) remained in solution. This is the first case that a 1,2-dihydrophosphinine oxide was obtained in an optically active form.

The resolution of 1-phenyl-1,2-dihydrophosphinine oxide **1** with half equivalent of (–)-**2** was also accomplished from a 2:5 mixture of ethyl acetate and hexane, but in this case, the resolution sequence was less efficient than using a mixture of acetone and hexane. Crystallization of the corresponding supramolecular formation involving 1,2-dihydrophosphinine oxide **1** and TADDOL could not be accomplished.

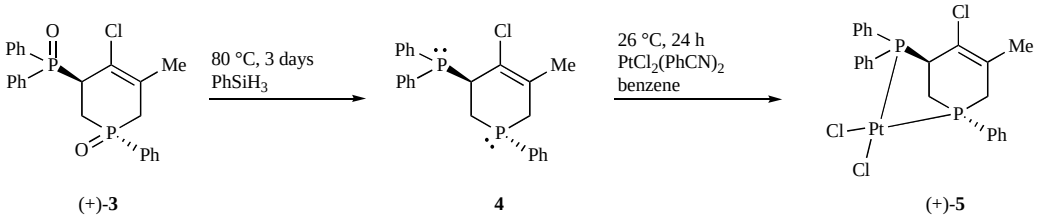
We wished to synthesize optically active 1-phenyl-3-diphenylphosphinoyl-1,2,3,6-tetrahydrophosphinine oxide **3** by the *Michael* addition of diphenylphosphine oxide on the electron-poor α,β-double-bond of the (–)-1-phenyl-1,2-dihydrophosphinine oxide **1A** to obtain the precursor of an optically active bidentate P-ligand. The *ee* value of the starting (–)-1-phenyl-1,2-dihydrophosphinine oxide **1A** was 89%. To activate the diphenylphosphine oxide, it was first reacted with trimethylaluminium at 0°C in chloroform. Then, the corresponding $([Ph_2P(O)])^-$ anion so formed reacted easily with the α,β-double-bond of the (–)-dihydrophosphinine oxide **1A** added to the reaction mixture at 0°C furnishing the (+)-1-phenyl-3-diphenylphosphinoyl-1,2,3,6-tetrahydrophosphinine oxide **3**. The unreactivity of isomer **1B** in the *Michael* addition is a consequence of steric hindrance due to the methyl group in position 5. Due to a selectivity observed earlier [7,8], only one of the two possible diastereomers was obtained. Column chromatography afforded tetrahydrophosphinine oxide (+)-**3** in 50% yield. The *ee* value of product (+)-**3** was determined by chiral HPLC. The structure of (+)-**3** was confirmed by ^{31}P and ^{1}H NMR spectral data (Scheme **2**).

A *twist-boat* conformer was established earlier for 1-phenyl-3-diphenylphosphinoyl-1,2,3,6-tetrahydrophosphinine oxide by DFT calculations [8]. Single crystal X-ray analysis suggested a *twist-boat/cis* conformer containing the $Ph_2P(O)$ moiety and the oxygen atom of the ring P=O moiety in the *cis* disposition [18].

The new chiral tetrahydrophosphinine oxide (+)-**3** may serve, after deoxygenation, as a novel P-chiral bidentate ligand in transition metal complexes. The bis(phosphine oxide) (+)-**3** was deoxygenated applying phenylsilane at 80 ˚C to give diphosphine **4**. The silane reductions are known to proceed with retention of configuration [19]. Diphosphine **4** was then reacted with one equivalent of dichlorodiben-zonitrile platinum(II) in benzene to afford *cis* chelate complex (+)-**5** (Scheme **3**). The structure of (+)-**5** was confirmed by ^{31}P NMR spectral data [9].



Scheme 2.



Scheme 3.

3. CONCLUSION

In summary, the (–)-antipode of 1-phenyl-1,2-dihydrophosphinine oxide **1** was made available by a novel resolution method applying a TADDOL derivative (–)-**2**. Diastereoselective hydrophosphinoxidation led to the corresponding (+)-$Ph_2P(O)$-1,2,3,6-tetrahydrophosphinine oxide **3** that, after double deoxygenation, was a suitable optically active bidentate P-ligand in a *cis* chelate platinum complex (+)-**5**.

4. EXPERIMENTAL

4.1. General

The ^1H and ^{31}P NMR spectra were recorded on a Bruker DRX-500 spectrometer operating at 500 and 202.4 MHz, respectively. Chemical shifts are downfield relative to TMS and 85% H_3PO_4. The coupling constants are given in Hertz. Optical rotations were determined on a Perkin-Elmer 241 polarimeter.

The enantiomeric excesses were determined by chiral HPLC. The *ee* of **1** was determined by chiral HPLC (Daicel Chem. Ind., having a Chiralpack AD-H column 250*4.6 mm ID, using hexane/isopropanol 85/15 as the eluent with a flow rate of 0.8 ml/min, T=20 ˚C, UV detector λ=254 nm). The *ee* of **3** was determined by chiral HPLC (Daicel Chem. Ind., having a Chiralcel OD column 250*4.6 mm ID, using hexane/isopropanol 75/25 as the eluent with a flow rate of 0.8 ml/min, T=20 ˚C, UV detector λ=254 nm).

The starting 1-phenyl-1,2-dihydrophosphinine oxide [5] **1** and (–)-(2*R*,3*R*)-α,α,α',α'-tetraphenyl-1,4-dioxaspiro [4.5] decan-2,3-dimethanol [16] (–)-**2** were synthesized as described earlier. Trimethylaluminium, 2.0 M sol. in heptane and *cis*-$PtCl_2(PhCN)_2$ were purchased from Aldrich Chemical Co.

4.2. Resolution of methyl-4-chloro-1-phenyl-1,2-dihydrophosphinine 1-oxide 1 with spiro-TADDOL (–)-2

To 0.43 g (1.80 mmol) of racemic 3- and 5-methyl-4-chloro-1-phenyl-1,2-dihydrophosphinine 1-oxide **1A** (75%) and **1B** (25%) and 0.46 g (0.90 mmol) of spiro-TADDOL (–)-**2** in 2.1 mL of hot acetone was added 4.3 mL of hexane. After the addition, crystals of the complex started to appear immediately. After 1 h, the crystals were separated by filtration to give 0.54 g (80%) of complex consisting of (–)-**1A**•(–)-**2** (75%) with an *ee* of 40% and **1B•2** (25%) with an *ee* of 55%. The complex was further purified by two recrystallizations from acetone–hexane (2.1 mL/4.3 mL) to afford 0.22 g (33%) of complex (–)-**1A**•(–)-**2** with an *ee* of 89% and **1B•2** with an *ee* of 95%, respectively, $[\alpha]_D^{25}$ = –90.2 (*c* 1, $CHCl_3$). Column chromatography (silica gel, 3% methanol in chloroform) of the complex regenerated 0.07 g (0.3 mmol, 31%) of (–)-3- and 5-methyl-4-chloro-1-phenyl-1,2-dihydrophosphinine 1-oxides **1A** and **1B**, **1A** (δ_P 16.1 [δ_P^{lit} 15.3] [5]) with an ee of 89%, **1B** (δ_P 15.0 [δ_P^{lit} 14.2] [5]) with an ee of 95%), $[\alpha]_D^{25}$ = –169.1 (*c* 0.5, $CHCl_3$). Based on ^{31}P NMR, the ratio of **1A** and **1B** remained ca. 3:1. Retention times: 13.5 and 15.9 min for **1A**, 15.0 and 18.1 min for **1B**.

4.3. Preparation of (+)-4-chloro-5-methyl-1-phenyl-3-diphenylphosphinoyl-1,2,3,6-tetrahydrophosphinine 1-oxide 3

Tetrahydrophosphinine 1-oxide (+)-**3** was prepared from (–)-**1** as described earlier for the racemic case [7]. *Ee* of (+)-**3**: 89%; yield: 50%. ^{31}P NMR ($CDCl_3$), δ 33.0 (d, $^3J_{P\text{-}P}$ = 13.8, P1), 34.0 (d, $^3J_{P\text{-}P}$ = 13.8, P2), [δ_P^{lit} 34.0 (d, $^3J_{P\text{-}P}$ = 13.8, P1), 34.8 (d, $^3J_{P\text{-}P}$ = 13.8, P2)] [7], $[\alpha]_D^{25}$ = +257.6 (*c* 0.5, $CHCl_3$). Retention times: 26.2 min for (–)-**3** and 36.5 min for (+)-**3**.

4.4. Deoxygenation of the bis(phosphine oxide) precursor (+)-3 and complexation of the bisphosphine 4 by $PtCl_2(PhCN)_2$

23.0 mg (0.05 mmol, ee 89%) of 1-Phenyl-3-diphenylphosphinoyl-1,2,3,6-tetrahydrophosphinine-1-oxide (+)-**3** and 32 μL (0.26 mmol) of phenylsilane was kept at 80 ˚C under nitrogen for 3 days. Then, the mixture was taken up in 4 mL of degassed benzene, the bisphosphine **4** so obtained was immediately reacted with 25.0 mg (0.05 mmol) of dichlorodibenzonitrile platinum(II) and the mixture was stirred at room temperature for 24 h under nitrogen. After crystallization from the benzene solution, 32.0 mg (+)-**5** (93%) was obtained, ^{31}P NMR ($CDCl_3$), δ_P 14.4 ($J_{Pt\text{-}P}$ = 3496, $J_{P\text{-}P}$ = 7.4, P1), 47.6 ($J_{Pt\text{-}P}$ = 3678, $J_{P\text{-}P}$ = 7.4, C3-P), [δ_P^{lit} 17.7 ($J_{Pt\text{-}P}$ = 3496, $J_{P\text{-}P}$ = 6.7, P1), 50.3 ($J_{Pt\text{-}P}$ = 3681, $J_{P\text{-}P}$ = 6.7, C3-P] [9], $[\alpha]_D^{25}$ = +47.7 (*c* 0.5, $CHCl_3$).

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