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Enantiopure Phosphacymantrene-2-carboxaldehyde and Some of Its Derivatives

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ABSTRACT: *The resolution of η^5(2-formyl-3,4-dimethylphospholyl)(triphenylphosphine)-manganesedicarbonyl* **1** *has been carried out by chromatography of the acetals derived from (S,S)-1,2-diphenylethane-1,2-diol. The enantiopure 2-diphenylphosphinomethyl* **4** *and diphenylmethylimino* **5** *derivatives have been prepared from* **1**. © 2005 Wiley Periodicals, Inc. Heteroatom Chem 16:458–460, 2005; Published online in Wiley InterScience (www.interscience.wiley.com). DOI 10.1002/hc.20130

INTRODUCTION

Recently, more and more interest has been expressed in the synthesis of transition-metal containing non-metallocene ligands for enantioselective catalysis [1]. Among these, cymantrenes have been the subject of two reports [2,3]. In the second one, the replacement of one carbonyl of the $[Mn(CO)_3]$-complexing group by triphenylphosphine has been shown to have a positive effect on the enantioselectivity of the palladium-catalyzed allylic alkylation reaction under study [3]. From another standpoint, the use of phosphaferrocene ligands in asymmetric catalysis is developing rapidly and several very promising results have been reported during the last few years [4–6]. These series of observations led us to envisage the use of phosphacymantrenes for the same purpose. The recent discovery of a simple access to a triphenylphosphine-substituted 2-phosphacymantrenylcarboxaldehyde [7] gave us the necessary starting point for such an investigation. Our preliminary results are described in this note.

RESULTS AND DISCUSSION

The resolution of aldehyde **1** was performed through acetalization with (*S*,*S*)-1,2-diphenylethane-1,2-diol [8]. The resulting diastereomeric acetals $\mathbf{2_{a,b}}$ were separated by flash chromatography on silica gel. The deprotection was achieved by acidic workup on silica gel in the presence of acetone as the solvent (Scheme 1).

The absolute configurations of $\mathbf{1_a}$ and $\mathbf{1_b}$ have not been established. Reduction of $\mathbf{1_a}$ and $\mathbf{1_b}$ by $LiAlH_4$ under mild conditions as previously described [7] afforded the corresponding primary alcohols $\mathbf{3_a}$ and $\mathbf{3_b}$. These alcohols were converted into the diphenylphosphino derivatives $\mathbf{4_a}$ and $\mathbf{4_b}$ in acidic medium, using a technique already employed by Ganter et al. [9] (Scheme 2).

In addition, we prepared the benzhydrylimine $\mathbf{5_b}$ from aminodiphenylmethane. Preliminary catalytic tests were performed on the condensation of sodium

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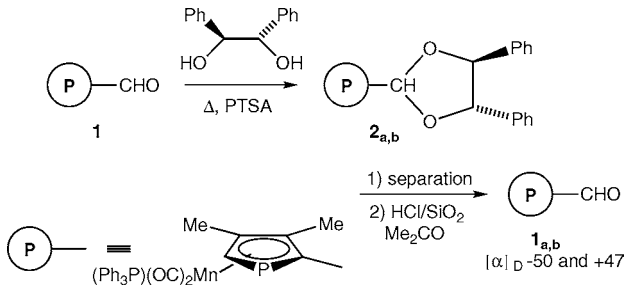
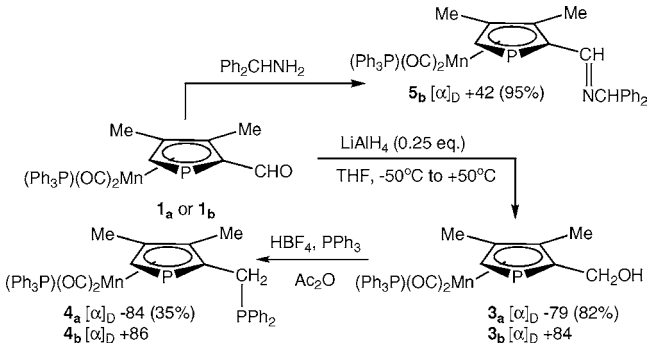
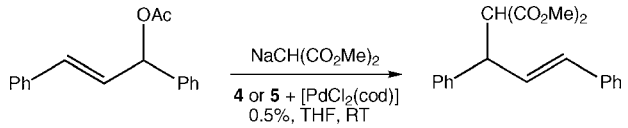


SCHEME 1



SCHEME 2



SCHEME 3

malonate with 1,3-diphenylallyl acetate in the presence of a palladium catalyst (Scheme 3).

With $\mathbf{4}_{a,b}$ as the ligands, the rate of the reaction appeared to be rather high (100% conversion in 2 h at RT), but the enantiomeric excesses were disappointing (10%). Similar results (20% ee) were obtained with $\mathbf{5}_b$. We plan to replace the two phenyl groups of the diphenylphosphino substituent by bulky groups such as *tert*-butyls. In so doing, three quadrants in the coordination sphere will be blocked and the only one left free will be situated above the phospholyl plane at the opposite of the $[Mn(CO)_2(PPh_3)]$ complexing group. Such geometries are known to favor enantioselection [10].

EXPERIMENTAL

NMR spectra were recorded on a multinuclear Bruker AVANCE 300 MHz spectrometer operating at 300.13 for ^1H, 75.47 for ^{13}C and 121.50 MHz for ^{31}P. Chemical shifts are expressed in parts per million (ppm) downfield from internal tetramethylsilane (^1H and ^{13}C) and external 85% aqueous H_3PO_4 (^{31}P). Rotations have been measured in dichloromethane [c 0.01].

Diastereomeric Acetals $\mathbf{2}_{a,b}$

Aldehyde **1** (0.2 g, 0.39 × 10^{-3} mol) and (*S,S*)-1,2-diphenylethane-1,2-diol (0.092 g, 0.43 × 10^{-3} mol) were stirred in toluene (10 mL) for 3 h at 50°C in the presence of a small amount of *para*-toluenesulfonic acid. One normal and one flash (under pressure) chromatographies on silica gel with hexane/dichloromethane (50/50) as the eluent allow to isolate $\mathbf{2}_a$ and $\mathbf{2}_b$ (total: 0.24 g, 87% pure $\mathbf{2}_a$ 0.053 g, 19%, pure $\mathbf{2}_b$ 0.068 g, 25%).

$\mathbf{2}_a$: ^1H NMR ($CDCl_3$): δ 1.92 (s, 3H, Me), 2.19 (s, 3H, Me), 3.02 (dd, 1H, $^2J_{H\text{-}P} = 40.0$ Hz, $^3J_{H\text{-}P} = 4.7$ Hz, CH-P), 4.94 (AB system, 2H, $^3J_{H\text{-}H} = 7.6$ Hz, PhCH), 6.09 (d, 1H, $^3J_{H\text{-}P} = 6.0$ Hz, CH-O); ^{13}C NMR ($CDCl_3$) : δ 13.36 (s, Me), 15.69 (s, Me), 85.82 (s, O-CHPh), 88.35 (s, O-CHPh), 96.35 (d, $^1J_{C\text{-}P} = 62.8$ Hz, CH-P), 102.49 (broad s, CH-O), 103.68 (broad s, Me-C), 114.44 (broad s, Me-C), 231.80 (m, CO); ^{31}P NMR ($CDCl_3$): δ −51.2 (cyclic P), 90.0 (PPh_3).

$\mathbf{2}_b$: ^1H NMR ($CDCl_3$) δ 1.96 (s, 3H, Me), 2.22 (s, 3H, Me), 2.91 (dd, 1H, $^2J_{H\text{-}P} = 35.5$ Hz, $^3J_{H\text{-}P} = 4.5$ Hz, CH-P), 4.85 (s, 2H, PhCH), 6.15 (d, 1H, $^3J_{H\text{-}P} = 6.6$ Hz, CH-O); ^{13}C NMR ($CDCl_3$) : δ 13.99 (s, Me), 16.38 (s, Me), 85.77 (s, O-CHPh), 88.15 (s, O-CHPh), 97.39 (d, $^1J_{C\text{-}P} = 60.4$ Hz, CH-P), 102.33 (broad s, CH-O), 104.20 (broad s, Me-C), 115.66 (broad s, Me-C), 231.30 (m, CO); ^{31}P NMR ($CDCl_3$): δ −50.2 (cyclic P), 90.0 (PPh_3).

Enantiopure Aldehydes **1a** *and* **1b**

A mixture of 11 N HCl (0.5 mL), acetone (0.5 mL) with a small amount of silica gel was added to a solution of $\mathbf{2}_a$ or $\mathbf{2}_b$ (0.1 g, 0.2 × 10^{-3} mol) in dichloromethane (5 mL). The mixture was stirred for 1.5 h at RT and chromatographed on silica gel with dichloromethane as the eluent. Yield of $\mathbf{1}_a$ or $\mathbf{1}_b$: 0.06 g (80%). $[\alpha]_D^{25}$ −50 (a) or +47 (b) in CH_2Cl_2.

Primary Alcohols **3a** *and* **3b**

Enantiopure $\mathbf{1}_a$ or $\mathbf{1}_b$ was reduced as described in [7]. Yield 82%. $[\alpha]_D^{25}$ −79 (a) or +84 (b) in CH_2Cl_2.

Phosphines **4a** *and* **4b**

A mixture of alcohol $\mathbf{3}_a$ or $\mathbf{3}_b$ (0.09 g, 0.18 × 10^{-3} mol), acetic anhydride (20 μL, 0.21 × 10^{-3} mol) and diphenylphosphine (60 μL, 0.35 × 10^{-3} mol) in

dichloromethane (3 mL) was cooled at −78°C and HBF_4(30 μL, 55% in Et_2O, 0.21 × 10^{-3} mol) was added. The mixture was allowed to warm to RT and neutralized with 10% aqueous NaOH. The organic phase was washed with a saturated aqueous solution of NaCl and dried on magnesium sulfate. After evaporation, the crude residue was chromatographed on silica gel with hexane/dichloromethane 60/40 as the eluent. Yield 0.045 g (35%). $[\alpha]_D^{25}$ −84 (a) or +86 (b) in CH_2Cl_2.

4: ^{1}H NMR (CD_2Cl_2): δ 1.90 (s, 3H, Me), 1.92 (s, 3H, Me), 2.70 (m, 2H, CH_2), 3.44 (dd, 1H, $^2J_{H\text{-}P}$ = 35.5 Hz, $^3J_{H\text{-}P}$ = 4.3 Hz, CH-P); ^{13}C NMR (CD_2Cl_2): δ 13.32 (s, Me), 16.14 (s, Me), 30.43 (s, CH_2), 96.84 (d, $^1J_{C\text{-}P}$ = 59.8 Hz, CH-P),105.30 (s, Me-C), 110.72 (d, $^2J_{C\text{-}P}$ = 6.6 Hz, Me-C), 112.02 (dd, $^1J_{C\text{-}P}$ = 57.2 Hz, $^2J_{C\text{-}P}$ = 19.3 Hz, C-CH_2-P); ^{31}P NMR (CD_2Cl_2): δ −40.7 (d, $^3J_{P\text{-}P}$ = 25.0 Hz, cyclic P), −9.8 (d, $^3J_{P\text{-}P}$ = 25.0 Hz, PPh_2), 89.5 (s, PPh_3).

Imine **5b**

Aldehyde $\mathbf{1_b}$ (0.26 g, 0.51 × 10^{-3} mol) and aminodiphenylmethane (0.1 mL, 0.58 × 10^{-3}mol) were stirred in dichloromethane (10 mL) for 18 h at 50°C in the presence of a small amount of *para*-toluenesulfonic acid and magnesium sulfate. After filtration on celite and evaporation, imine $\mathbf{5_b}$ was obtained as a yellow solid in 95% yield. $[\alpha]_D^{25}$ +42 in CH_2Cl_2.

$\mathbf{5_b}$: ^{1}H NMR (CD_2Cl_2): δ 1.79 (s, 3H, Me), 2.20 (s, 3H, Me), 3.51 (d, 1H, $^2J_{H\text{-}P}$ = 34.7 Hz, CH-P), 5.24 (s, 1H, Ph_2CH), 7.67 (d, 1H, $^3J_{H\text{-}P}$ = 5.6 Hz, CH=N); ^{13}C NMR ($CDCl_3$): δ 12.44 (s, Me), 14.09 (s, Me), 97.62 (d, $^1J_{C\text{-}P}$ = 59.2 Hz, CH-P), 104.15 (d, $^2J_{C\text{-}P}$ = 4.8 Hz, Me-C), 105.36 (d, $^1J_{C\text{-}P}$ = 53.8 Hz, C-P), 110.72 (d, $^2J_{C\text{-}P}$ = 7.5 Hz, Me-C), 158.60 (d, $^2J_{C\text{-}P}$ = 18.7 Hz, CH=N), 229.56 (s, CO), 229.91(s, CO); ^{31}P NMR (CD_2Cl_2): δ −40.7 (cyclic P), 87.3 (PPh_3).

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