Letters to the Editor

First phosphite ligand based on ((4*R*,5*S*)-5-(hydroxymethyl)-2,2-dimethyl-1,3-dioxolan-4-yl)-diphenylmethanol

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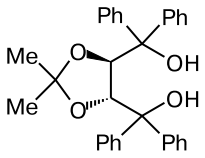
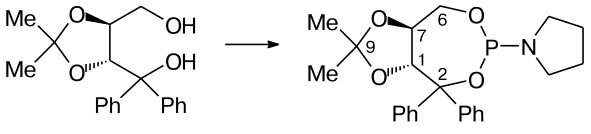
((4*R*,5*R*)-2,2-Dimethyl-1,3-dioxolan-4,5-diyl)bis-(diphenylmethanol) (TADDOL) is one of the most accessible enantiopure C_2 symmetric diols extensively used as versatile chiral ligand/auxiliary.[1—3] TADDOL-derived phosphites revealed themselves to be efficient chiral ligands for a wide range of metal-catalyzed asymmetric reactions.[3—8] To date, no phosphite derivatives of ((4*R*,5*S*)-5-(hydroxymethyl)-2,2-dimethyl-1,3-dioxolan-4-yl)diphenylmethanol (**1**) were described. 1,4-Diol **1**, analog of TADDOL with the pronounced C_1 symmetry, is readily accessible from available monomethyl (*R*,*R*)-tartrate.[9]



TADDOL

Amidophosphite **2** with P*-stereocenter was synthesized by treatment of diol **1** with PCl_3 followed by the reaction with pyrrolidine (Scheme 1). In this reaction, pyrrolidine plays a role of both the reagent and the HCl scavenger. Note that the synthesis of compound **2** is fast due also to the intermediate formation of the corresponding chlorophosphite in the PCl_3 medium in the presence of catalytic amount of *N*-methylpyrrolidone. Amidophosphite **2** was purified by flash column chromatography; this compound is relatively stable in air and at long-term storage in a dry atmosphere.

Scheme 1



1 **2**

Reagents and conditions 1) PCl_3, *N*-methylpyrrolidone, reflux, 5 min, 2) $(CH_2)_4NH$, toluene.

Synthesis of ligand **2** is diastereoselective, the ratio of the epimers at the P*-stereocenter is 19 : 1. This ratio was

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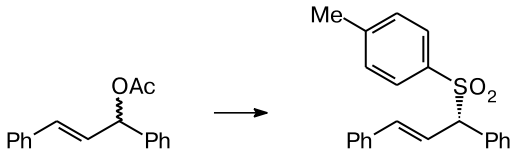
determined from ^{31}P NMR ($CDCl_3$) spectra of compound **2** exhibiting two narrow singlets at δ_P 144.9 (95%) and 137.3 (5%). It should be emphasized that the presence of the P*-stereogenic donor atom in the ligand **2** facilitates the chirality transfer on the key step of the catalytic cycle.[10,11]

Stereodifferentiating ability of amidophosphite **2** was estimated using enantioselective Pd-catalyzed allylic sulfonylation of (*E*)-1,3-diphenylallyl acetate (**3**) (Scheme 2, Table 1) as a model reaction. It is of note that chiral allyl sulfones are of considerable interest for the stereoselective organic synthesis.[11]

Scheme 2



3 **4**

Reagents and conditions: 1) $[Pd(allyl)Cl]_2$, ligand **2**, THF, 20 °C, 15 min, 2) *p*-$TolSO_2Na$, 20 °C, 48 h.

As a pre-catalyst, $[Pd(allyl)Cl]_2$ was used. Allylic sulfone (*S*)-**4** was obtained in high yield and high enantioselectivity up to 90% *ee* (see Table 1). In this reaction, the known TADDOL-derived bis-phosphine ligand gives no more than 68% *ee*.[9] Thus, amidophosphite **2** is a promising chiral ligand and its application in asymmetric catalysis is now extensively studied in our research group.

^{31}P, ^1H, and ^{13}C NMR spectra were run on Bruker Avance 400 (161.98 (^{31}P), 400.13 (^1H), and 100.61 MHz (^{13}C)) and Bruker Avance III 600 (242.94 (^{31}P), 600.13 (^1H), and 150.9 MHz (^{13}C)) spectrometers relative to 85% H_3PO_4 in D_2O (^{31}P) and Me_4Si (^1H and ^{13}C). The signals in the ^1H and ^{13}C NMR spectra were assigned using COSY, DEPT, and HSQC NMR techniques and taking in account published data.[9] Electron impact mass spectra (EI, 70 eV) were obtained on a Varian MAT-311 instrument. Enantiomeric analyses of the product of allylic sulfonylation were performed on a Stayer HPLC system. For elemental analyses, Carlo Erba EA1108 CHNS-O microanalyzer was used.

Table 1. Pd-catalyzed asymmetric allylic sulfonylation[a] of diphenylallyl acetate **3** with sodium *p*-toluenesulfinate in the presence of ligand **2**

Entry	Ratio ligand **2** : Pd (mol/mol)	Yield of **4** (%)	*ee* (%)[b,c]
1	1	87	90 (*S*)
2	2	92	85 (*S*)

[a] Reaction conditions: $[Pd(allyl)Cl]_2$ (2 mol.%), THF, 20 °C, 48 h.

[b] Enantiomeric excesses of product **4** were determined by HPLC (chiral column Daicel Chiralcel OD-H, elution with C_6H_{14}—Pr^iOH (4 : 1), eluent flow rate 0.5 mL min^{-1}, detection at λ = 254 nm, retention times $t(R)$ = 16.3 min, $t(S)$ = 18.5 min).

[c] Configuration of the product is given in parentheses.

All reactions were carried out in anhydrous solvents under dry argon. ((4*R*,5*S*)-5-(Hydroxymethyl)-2,2-dimethyl-1,3-dioxolan-4-yl)diphenylmethanol (**1**) were synthesized by the known procedure.[9] The starting compounds, (*E*)-1,3-diphenylallyl acetate (**3**) and complex $[Pd(allyl)Cl]_2$, were synthesized as earlier described.[12] Pd-catalyzed asymmetric allylic sulfonylation of compound **3** with sodium *p*-toluenesulfinate and determination of enantiomeric excesses of product **4** were performed following the published procedures.[13]

Pyrrolidine, *N*-methylpyrrolidone, and sodium *p*-toluenesulfinate are commercially available from Fluka and Aldrich.

(1*R*,7*S*)-9,9-Dimethyl-2,2-diphenyl-4-(pyrrolidin-1-yl)-3,5,8,10-tetraoxa-4-phosphabicyclo[5.3.0]decane (2). To a vigorously stirred suspension of compound **1** (0.63 g, 2 mmol) in PCl_3 (4 mL, 45.5 mmol), *N*-methylpyrrolidone (0.01 g, 0.1 mmol) was added and the mixture was refluxed for 5 min until homogeneity. The PCl_3 excess was removed *in vacuo* (40 Torr), the residue was dried *in vacuo* (30 min, 1 Torr) to remove the PCl_3 traces and dissolved in toluene (12 mL). To the obtained solution, pyrrolidine (0.4 mL, 4.8 mmol) was added at 20 °C under vigorous stirring. The reaction mixture was refluxed for 15 min, cooled to 20 °C, and filtered through an alumina pad. The filtrate was concentrated *in vacuo* (40 Torr). Purification of the residue by flash column chromatography (silica gel, elution with CH_2Cl_2) afforded compound **2** in the yield of 0.59 g (71%), colorless oil. Found (%): C, 67.05; H, 6.76; N, 3.24. $C_{23}H_{28}NO_4P$. Calculated (%): C, 66.82; H, 6.83; N, 3.39. ^{13}C NMR ($CDCl_3$), δ: 25.4 (s, CH_3); 25.9 (d, CH_2, $^3J_{C,P}$ = 5.4 Hz); 27.4 (s, CH_3); 44.5 (d, CH_2N, $^2J_{C,P}$ = 15.0 Hz); 65.6 (d, C(6), $^2J_{C,P}$ = 10.0 Hz); 75.3 (d, C(7), $^3J_{C,P}$ = 3.8 Hz); 80.6 (d, C(2), $^2J_{C,P}$ = 5.7 Hz); 86.2 (d, C(1), $^3J_{C,P}$ = 19.1 Hz); 110.7 (s, C(9)); 126.8 (s, CH_{Ph}); 126.9 (s, CH_{Ph}); 127.0 (s, CH_{Ph}); 127.3 (s, CH_{Ph}); 128.0 (s, CH_{Ph}); 128.4 (s, CH_{Ph}); 141.3 (s, C_{Ph}); 146.7 (s, C_{Ph}). ^1H NMR ($CDCl_3$), δ: 0.66 (s, 3 H, CH_3); 1.46 (s, 3 H, CH_3); 1.84—1.91 (m, 4 H, CH_2); 3.24—3.29 (m, 2 H, CH_2N); 3.39—3.44 (m, 2 H, CH_2N); 3.89 (ddd, 1 H, C(6)H, $^2J_{H,H}$ = 11.2 Hz, $^3J_{H,H}$ = 9.2 Hz, $^3J_{H,P}$ = 2.4 Hz); 4.18 (td, 1 H, C(7)H, $^3J_{H,H}$ = 9.2 Hz, $^3J_{H,H}$ = = 3.6 Hz); 4.33 (ddd, 1 H, C(6)H, $^2J_{H,H}$ = 11.2 Hz, $^3J_{H,H}$ = 3.6 Hz, $^3J_{H,P}$ = 28.2 Hz); 4.96 (dd, 1 H, C(1)H, $^3J_{H,H}$ = 9.1 Hz, $^4J_{H,P}$ = = 3.9 Hz); 7.22 (t, 1 H, CH_{Ph}, ^3J = 7.4 Hz); 7.28 (t, 2 H, CH_{Ph}, ^3J = 7.4 Hz); 7.30—7.34 (m, 2 H, CH_{Ph}); 7.39 (t, 1 H, CH_{Ph}, ^3J = 7.5 Hz); 7.41 (d, 2 H, CH_{Ph}, ^3J = 7.6 Hz); 7.65 (d, 2 H, CH_{Ph}, ^3J = 7.6 Hz). MS, *m*/*z* (I_{rel} (%)): 413 $[M]^+$ (100).

Asymmetric allylic sulfonylation of (*E*)-1,3-diphenylallyl acetate (3) with sodium *p*-toluenesulfinate. A solution of $[Pd(allyl)Cl]_2$ (0.0019 g, 0.005 mmol) and ligand **2** (0.004 g, 0.01 mmol or 0.008 g, 0.02 mmol) in THF (1.5 mL) was stirred for 40 min. Then (*E*)-1,3-diphenylallyl acetate (**3**) (0.05 mL, 0.25 mmol) was added. After 15 min stirring, sodium *p*-toluenesulfinate (0.089 g, 0.5 mmol) was added and stirring was continued for 48 h. To the reaction mixture, brine (3 mL) was added, the mixture was stirred for 1 h and extracted with THF (3×2 mL). The organic layer was washed with brine (2×2 mL), dried with $MgSO_4$, and filtered through Celite. The solvent was removed *in vacuo*

(40 Torr). Crystallization of the residue from 95% EtOH followed by drying *in vacuo* (10 Torr) afforded product **4**, milk-white crystals. IR and NMR ^{1}H spectral data for compound **4** are in good agreement with that published earlier.[9] Enantiomeric excesses of product **4** (see Table 1) were determined by HPLC on a chiral stationary phase.

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