

Phosphinite-Thioethers derived from Chiral Epoxides. Modular *P,S*-Ligands for Pd-Catalyzed Asymmetric Allylic Substitutions

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Supporting Information-Table of Contents

1. Experimental details. General Remarks	S2
2. DFT calculations	S3
3. ORTEP view of complexes (10a-syn)•PdCl ₂ and 4m •PdCl ₂	S8
4. References	S10
5. ¹ H and ¹³ C NMR Spectra	S11

1. Experimental details.

General Remarks. All phosphinite thioethers ligands were prepared under argon atmosphere using standard vacuum-line and Schlenk techniques. Tetrahydrofuran, dichloromethane, toluene, dimethylformamide and hexane were dried and deoxygenated by using a Solvent Purification System (SPS).

All flash chromatography was carried out using 60 mesh silica gel and dry-packed columns. Phosphinite thioethers were filtered through a short SiO₂ pad, which was previously dried and deoxygenated with Argon.

The experiment under microwave irradiation was carried out in a CEM discover microwave reactor (the temperature is automatically controlled by a non-contact infrared sensor that monitors and controls the temperature conditions of the reaction vessel).

NMR spectra were recorded in CDCl₃ at room temperature unless otherwise cited operating at 400.13 MHz (¹H), 100.63 MHz (¹³C{¹H}), 100.63 MHz (¹³C{³¹P}), 161.98 MHz (³¹P{¹H}). ¹H NMR chemical shifts are quoted in ppm relative to internal TMS and ¹³C NMR spectra to CDCl₃ whereas ³¹P NMR chemical shifts are quoted in ppm relative to 85% phosphoric acid in water.

[Pd(η³-C₃H₅)Cl]₂ was purchased from Alpha Aesar.

Allylic acetates **S1**, **S2**, and **S3** were prepared following known procedure.¹ Chiral epoxides **1a**², **1b**³, **2a-d**⁴, **11**⁵, compounds **14** and **15**⁶ were prepared as described in the literature.

2. DFT calculations

The Model System

It is known that esters bearing heteroatom-connected substituents at the α or β positions with respect to the ester carbonyl are efficiently hydrolyzed by lithium hydroxide. The rate-increase in the lithium-mediated hydrolysis is assumed to be due to the coordination of lithium to the ester carbonyl group and to the heteroatom at the α or β position, resulting in a five- or six-membered chelate, respectively. Such coordination would make the ester carbonyl more reactive towards the attack of the hydroxide ion. Taking into account that ester solvolysis likely precedes ring-opening, the studied reaction system consisted in one molecule of lithium carboxylate plus one molecule of lithium thiolate. Transition states (TS) for the epoxide openings at C2 (**TS-C2**) and C3 (**TS-C3**) were located and characterized using DFT calculations (B3LYP/6-31G (d)). Both transition states were characterized by analysis of the normal vibration modes corresponding to their imaginary frequencies.

According to the calculations, the transition state for ring-opening at C2 is 14.4 kcal mol⁻¹ above the starting materials, while for attack at C3 is above reactants by 8.9 kcal mol⁻¹.

TS C3

E(RB+HF-LYP) = -1144.06479933 A.U.

Imaginary frequency: - 297.2443 cm⁻¹

Cartesian coordinates

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms)		
			X	Y	Z
1	6	0	-0.118742	0.038430	0.092391
2	6	0	0.072427	0.130614	1.546785
3	8	0	1.408393	0.042903	1.091003
4	1	0	-0.112277	-0.969815	-0.294171
5	1	0	-0.272533	-0.756350	2.092352
6	6	0	-0.291719	1.404460	2.341169
7	8	0	-1.504237	1.565228	2.645611
8	8	0	0.659449	2.187759	2.622252
9	3	0	2.116926	1.618299	1.694004
10	6	0	-0.081496	1.112920	-0.907884
11	6	0	0.187704	0.743159	-2.239118
12	6	0	-0.290442	2.475818	-0.620392
13	6	0	0.263641	1.698034	-3.247919
14	1	0	0.331084	-0.307433	-2.475731
15	6	0	-0.213248	3.430217	-1.633979
16	1	0	-0.527148	2.801566	0.385601
17	6	0	0.066458	3.048024	-2.947725
18	1	0	0.471216	1.389378	-4.268581
19	1	0	-0.384409	4.476281	-1.395252
20	1	0	0.120327	3.796093	-3.733841
21	16	0	-2.953081	-0.328768	-0.250758
22	6	0	-3.593325	-1.975089	0.382931
23	6	0	-4.884462	-2.309935	-0.382135

24	1	0	-4.694876	-2.368129	-1.458449
25	1	0	-5.290590	-3.276817	-0.049818
26	1	0	-5.647963	-1.542194	-0.217933
27	6	0	-2.541441	-3.066003	0.123742
28	1	0	-1.615539	-2.866202	0.675930
29	1	0	-2.914996	-4.049640	0.443370
30	1	0	-2.296133	-3.125392	-0.941628
31	6	0	-3.896535	-1.902027	1.889705
32	1	0	-4.281918	-2.861231	2.264657
33	1	0	-2.992735	-1.668731	2.469069
34	1	0	-4.660031	-1.141077	2.101106
35	3	0	-2.857309	0.868708	1.676005

TS C2

E(RB+HF-LYP) = -1144.05750203 A.U.

Imaginary frequency: - 314.9729 cm⁻¹

Cartesian coordinates

Center	Atomic	Atomic	Coordinates (Angstroms)		
Number	Number	Type	X	Y	Z

1	6	0	1.114772	-0.298411	-0.904928
2	6	0	1.024001	-0.213199	0.568923
3	8	0	2.493010	-0.283367	-0.620882
4	1	0	0.759514	-1.265142	-1.287706
5	1	0	1.191485	-1.145713	1.086517
6	6	0	1.263547	1.069671	1.385528
7	8	0	0.886890	1.047548	2.592168
8	8	0	1.837850	2.039200	0.826118
9	16	0	-1.552414	-0.694061	1.118531
10	6	0	-1.666508	-2.496834	1.635332
11	6	0	0.649301	0.835297	-1.806497
12	6	0	-0.617807	1.423373	-1.707105
13	6	0	1.532119	1.290001	-2.799994
14	6	0	-0.975931	2.465854	-2.562207
15	1	0	-1.318961	1.059757	-0.962516
16	6	0	1.171074	2.336396	-3.655406
17	1	0	2.491247	0.788301	-2.928138
18	6	0	-0.083612	2.932232	-3.531651
19	1	0	-1.958430	2.920666	-2.467348
20	1	0	1.864121	2.671791	-4.422770
21	1	0	-0.369202	3.747813	-4.190289
22	3	0	2.812575	1.544017	-0.609255
23	6	0	-0.951432	-2.724636	2.977707
24	1	0	-1.010766	-3.779780	3.279389

25	1	0	0.111685	-2.459689	2.922332
26	1	0	-1.420075	-2.135934	3.779238
27	6	0	-1.034941	-3.383556	0.550119
28	1	0	-1.144513	-4.445291	0.812345
29	1	0	-1.519762	-3.220113	-0.417444
30	1	0	0.035254	-3.180015	0.432816
31	6	0	-3.157826	-2.842017	1.780942
32	1	0	-3.277812	-3.894571	2.075635
33	1	0	-3.636436	-2.217196	2.542676
34	1	0	-3.689207	-2.687721	0.836863
35	3	0	-0.683261	0.307901	2.958616

3. ORTEP view of complexes **(10a-syn)·PdCl₂** and **4m·PdCl₂**

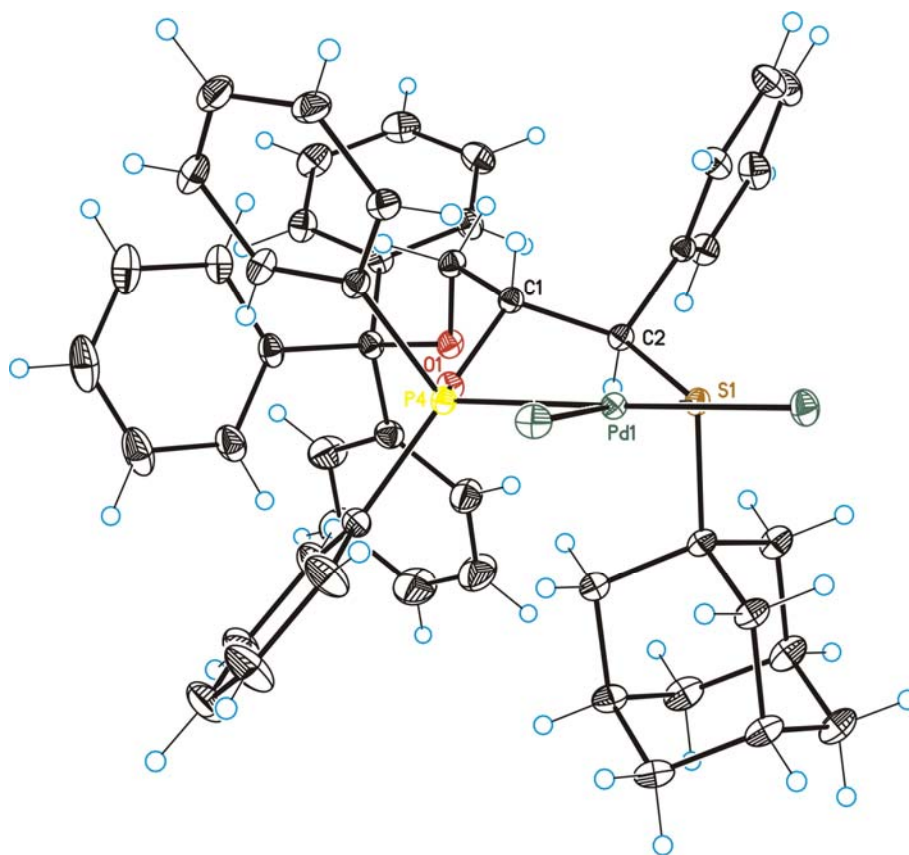


FIGURE 1. Displacement ellipsoid plot (50% probability level) of the crystal structure of **(10a-syn)·PdCl₂**. Selected bond lengths [Å]: Pd1–S1 2.3026(2), Pd1–Cl1 2.3590(2), Pd1–Cl2 2.3124(2), Pd1–P4 2.2107(2).

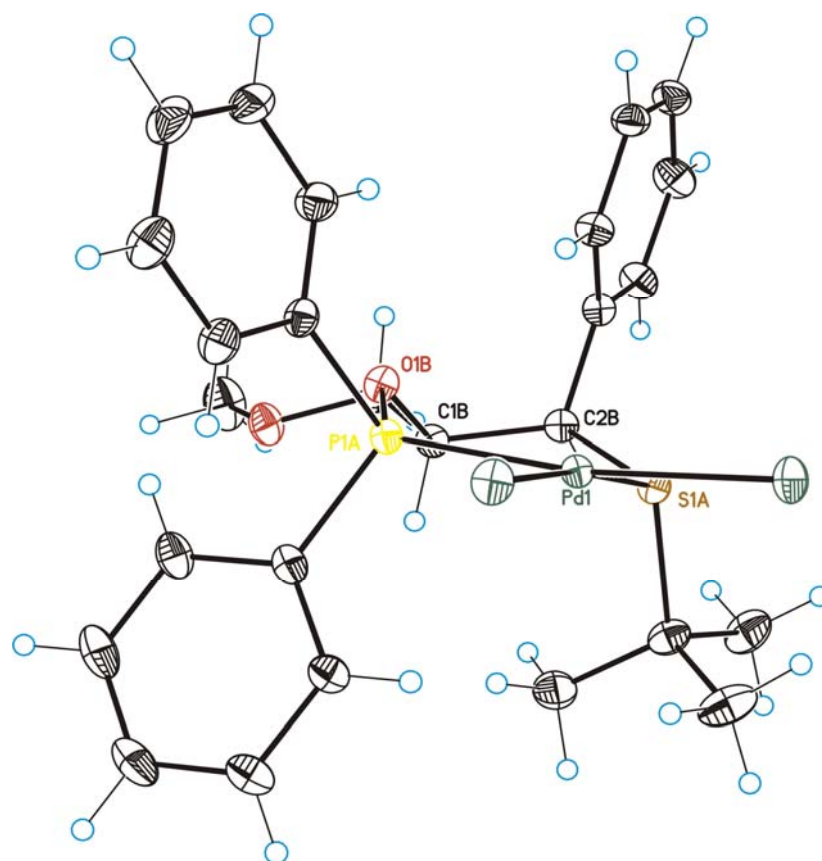


FIGURE 2. Displacement ellipsoid plot (50% probability level) showing the structure of **4m-PdCl₂**. Selected bond lengths [Å]: Pd1–S1A 2.3005(5), Pd1–Cl2 2.3612(4), Pd1–Cl1A 2.3167(5), Pd1–P1A 2.2113(4).

3. References:

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4. ^1H and ^{13}C NMR Spectra

