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Optically Active 10,10'-spirobi[10*H*-phenoxasilin]-1,1'-diol: Synthesis, Structure, and Application of its Phosphoramidite Derivative to Palladium-catalyzed Asymmetric Allylic Amination

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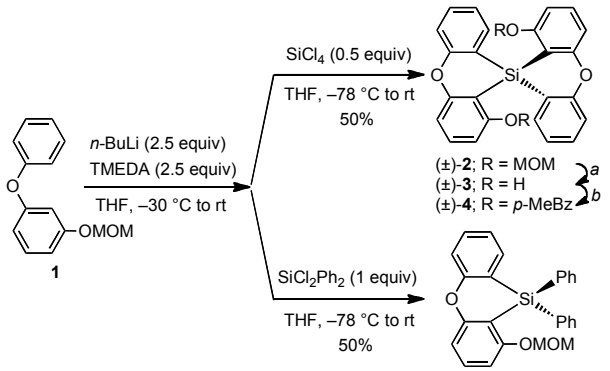
Optically active (*S*)-(+)- and (*R*)-(–)-10,10'-spirobi[10*H*-phenoxasilin]-1,1'-diols were synthesized by the transesterification of their optically active di-*p*-toluoyl derivatives resolved by chiral HPLC. The absolute configurations of the optically active spirosilanes were elucidated by single-crystal X-ray structural analysis. Phosphoramidite derivatives of the optically active diols were applied to Pd-catalyzed asymmetric allylic amination using 1,3-diphenylallyl acetate and benzylamine with moderate enantioselectivity.

Keywords: Optically active spirocyclic diol | Spirosilane | Phosphoramidite

Optically active C_2 symmetric spiro compounds with carbon spiro center which possess axial chirality have attracted much attention because they are potentially useful as chiral ligand scaffolds for transition metal catalyzed asymmetric reactions.[1] Meanwhile, optically active spirosilanes with C_2 symmetry are still rare, which have been mainly obtained by rhodium-catalyzed intramolecular enantioselective hydrosilylation[2] and dehydrogenative silylation[3] of dihydrosilane precursors. However, although a number of spirosilanes with C_2 symmetry have been synthesized,[4] to the best of our knowledge, there is only one report on the optical resolution of the racemate of spirosilane by chiral HPLC.[5]

Optically active spiro diols with C_2 symmetry, such as 1,1'-spirobiindane-7,7'-diol (SPINOL)[6] and 9,9'-spirobixanthene-1,1'-diol (SBIXOL),[7] are of interest as precursors for monodentate spiro phosphorus ligands in metal catalyzed asymmetric reactions with high enantioselectivity.[1,7a,8] However, in the syntheses of the diols, several synthetic steps and chiral resolving agents are necessary for the construction of the spiro framework and the optical resolution of the racemic diols, respectively.[6,7] In contrast, the construction of spirosilane is more readily than that of spiro compounds with carbon spiro center. For instance, 10,10'-spirobi[10*H*-phenoxasilin] has been synthesized by the reaction of $SiCl_4$ with 2,2'-dilithiodiphenyl ether generated from diphenyl ether and *n*-BuLi.[9] Thus, we envisioned that the spiro framework of silicon analogue of SBIXOL could also be readily constructed. Herein, we report on the synthesis and structural characterization of optically active dihydroxy spirosilanes, (*S*)-(+)- and (*R*)-(–)-10,10'-spirobi[10*H*-phenoxasilin]-1,1'-diol [(*S*)-(+)-**3** and (*R*)-(–)-**3**], and their di-*p*-toluoyl derivatives (*S*)-(+)-**4** and (*R*)-(–)-**4**. Also presented are the application of their phosphoramidite derivatives (*S*)-(–)-**6** and (*R*)-(+)-**6** to palladium-catalyzed asymmetric allylic amination of 1,3-diphenylallyl acetate with benzylamine.



Scheme 1. Syntheses of spirosilanes (±)-**2**–**4** and monocyclic silane **5**. *a* *p*-TsOH·H_2O (2.1 equiv), acetone/EtOH (1:1), reflux 27%. *b* NaH (2 equiv), THF, then *p*-toluoyl chloride (2 equiv) 84%.

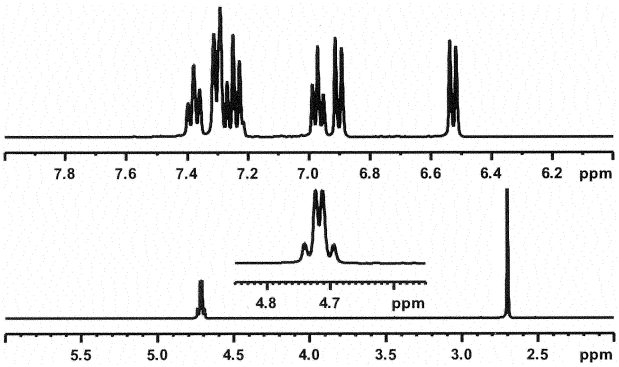


Figure 1. ^{1}H NMR (400 MHz) spectrum of **2** in $CDCl_3$.

The racemate of 1,1'-bis(methoxymethoxy)-10,10'-spirobi[10*H*-phenoxasilin] (±)-**2** could be synthesized in moderate yield (50%) by the reaction of $SiCl_4$ with the dianion generated from 3-(methoxymethoxy)phenyl phenyl ether **1** and *n*-BuLi (Scheme 1). In this synthesis, TMEDA was used as an additive to activate all organolithium species on the reaction pathway because it has been reported that the reaction of $SiCl_4$ with 2,2'-dilithiodiaryl ethers bearing an electron-donating group did not afford the corresponding spirosilanes.[10] The ^{1}H NMR spectrum showed a single resonance for the methyl groups and seven signals in the aromatic region indicative of C_2 symmetry (Figure 1). Endo configuration was demonstrated by spectroscopically non-equivalent methylene protons due to the restriction of

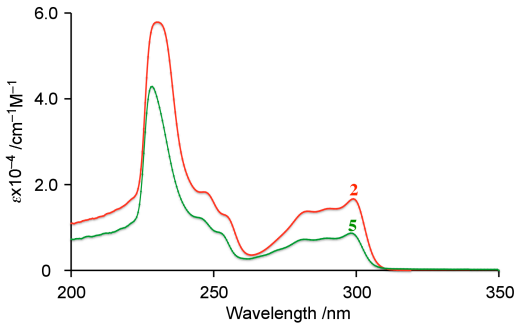


Figure 2. UV-vis spectra (in CH_2Cl_2) of **2** and **5**.

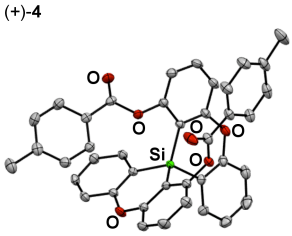
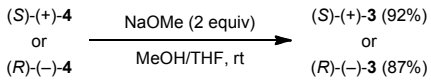


Figure 3. The ORTEP drawing of (+)-**4** showing the thermal ellipsoids at the 50% probability level. All hydrogens are omitted for clarity.

rotation about C–OMOM bond and the absence of an aromatic proton signal without vicinal coupling constants.

The spiro structure of (±)-**2** could also be supported by UV-vis spectroscopic analysis (Figure 2). In the UV-vis spectrum of the spirosilane (±)-**2**, although the spectral shape and λ_{max} were similar to those of monocyclic diphenylsilane **5** synthesized as a reference compound (Scheme 1), the molar extinction coefficient of λ_{max} was approximately 1.5 to 2 times as large as that of **5**. However, because the weak absorption maximum at longer-wavelength (> 300 nm) resulted from HOMO–LUMO transition was not observed, the influence of spiro-conjugation[11] and interaction between σ^* orbital of the Si–C bond on silicon and π^* orbital of two biaryl ether units[12] leading to the narrowing of HOMO–LUMO energy gap could not be evaluated.

Removal of methoxymethyl (MOM) groups from (±)-**2** by TsOH·H_2O under reflux conditions in a mixture of acetone/EtOH 1/1 (v/v) could afford dihydroxy spirosilane (±)-**3** even in low yields (Scheme 1), although unidentifiable decomposition products were mainly obtained. Chiral high-performance liquid chromatography (HPLC) separation of (±)-**3** was not practical because of its low solubility in organic solvents. Thus, the diol (±)-**3** was converted to di-*p*-toluoyl ester (±)-**4** (Scheme 1) followed by the chiral HPLC separation of (±)-**4** performed on recycling preparative HPLC equipped with a CHIRALPAK IA column using a mixture of *n*-hexane/$CHCl_3$ 2/1 (v/v) as the eluent. The crystal structures of (+)-**4** (Figure 3) and (–)-**4** have been determined by the single-crystal X-ray diffraction analyses,[13] and the absolute configurations were assigned to



Scheme 2. Transesterification reactions of (*S*)-(+)-**4** and (*R*)-(–)-**4**.

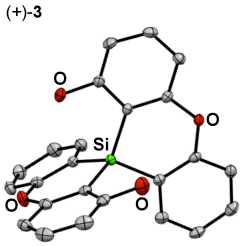


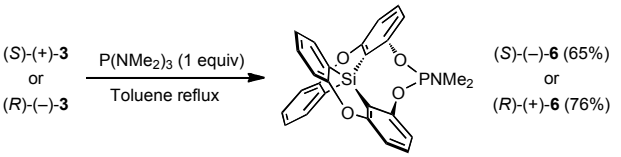
Figure 4. The ORTEP drawing of (+)-**3** showing the thermal ellipsoids at the 50% probability level. All hydrogens are omitted for clarity.

be *S* and *R*,[14] respectively, by means of refinement of the Flack parameter.[15]

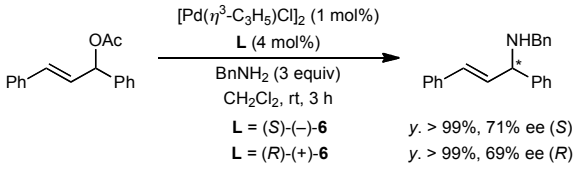
Optically active dihydroxy spirosilanes (+)-**3** and (–)-**3** could be obtained by the transesterification reactions of the di-*p*-toluoyl ester (*S*)-(+)-**4** and (*R*)-(–)-**4**, respectively, with NaOMe in MeOH/THF (Scheme 2). The high enantiomeric purity of the products indicate that there was no racemization of spirosilanes in the reaction through nucleophilic attack of the methoxide anion at silicon spiro center.[3b] The Lewis acidity at silicon in 1,1'-dioxy-10,10'-spirobi[10*H*-phenoxasilin] framework must be decreased owing to π-electron donation from oxygens. The single-crystal X-ray diffraction analyses of (+)-**3** (Figure 4) and (–)-**3**[16] revealed that the absolute configurations were also assigned to be *S* and *R*,[14] respectively, by means of refinement of the Flack parameter.[15] The bond lengths and angles around the silicon atoms of **3** and **4** were comparable with those of the reported six-membered π-conjugated spirosilanes,[9b,11c,17] and the spiro rings of them assumed slightly distorted planar structures. Meanwhile, the tetrahedral geometry around the silicon spiro center was distorted with small endocyclic C–Si–C angles of around 100° in contrast to nearly ideal tetrahedral geometry around the carbon spiro center of SBIXOL[7b] probably due to long Si–C bonds compared with C–C bonds. Additionally, the C–O–C bond angles of around 125° in six-membered spiro rings for the spirosilanes were significantly larger than those of around 119° for SBIXOL,[7b] which would result from the distortion around the silicon spiro center. The low and good yields of the spiro diols (±)-**3** and (±)-SBIXOL[7] in the deprotection reactions with protic acids under reflux conditions should be influenced by the presence and absence of the significant distortion around spiro center, respectively.

To ascertain that the spiro diol **3** can be the chiral ligand scaffold for transition metal catalyzed asymmetric reactions, monodentate phosphoramidite ligand **6** was synthesized for the asymmetric allylic amination. According

to the synthetic procedure for the phosphoramidite ligands from SBIXOL,[7a,8] the optically active ligands (*S*)-(–)-**6** and (*R*)-(+)-**6** were obtained by the reactions of (*S*)-(+)-**3** and (*R*)-(–)-**3**, respectively, with hexamethylphosphorus triamide (HMPT) in refluxing toluene (Scheme 3). It is worth noting that the reaction time (3 h) and yield were shorter and higher, respectively, than those (72 h and 35%)



Scheme 3. Syntheses of optically active phosphoramidite ligands (*S*)-(–)-**6** and (*R*)-(+)-**6**.



Scheme 4. Pd(II)/(*S*)-(–)-**6**- and Pd(II)/(*R*)-(+)-**6**-catalyzed asymmetric allylic amination reaction of *rac*-(2*E*)-1,3-diphenyl-2-propenyl acetate with benzylamine.

for the reaction of SBIXOL.[7a] ^{1}H and ^{13}C NMR spectroscopic analyses of the ligands **6** revealed that the two diaryl ether moieties were spectroscopically unequivalent based on the pyramidal geometry at phosphorus while the NMR spectra of the spirosilanes **2**–**4** were consistent with C_2 symmetric structures. The optically active ligands **6** could be applied to Pd-catalyzed asymmetric allylic amination reaction of *rac*-(2*E*)-1,3-diphenylallyl acetate with benzylamine affording the chiral allylic amine in nearly quantitative yield with moderate enantiomeric excess (Scheme 4). It is noteworthy that the complete conversion of the substrate was achieved in a short reaction time of 3 h compared to the reactions (12–36 h) with other monodentate phosphoramidite ligands under similar reaction conditions.[18]

In summary, first optically active C_2 symmetric spiro diols with silicon spiro center, (*S*)-(+)- and (*R*)-(–)-10,10'-spirobi[10*H*-phenoxasilin]-1,1'-diols [(*S*)-(+)-**3** and (*R*)-(–)-**3**], were synthesized by the transesterification of their optically active di-*p*-toluoyl derivatives **4** resolved by chiral HPLC. The absolute configurations of the optically active spirosilanes **3** and **4** were elucidated by single-crystal X-ray structural analysis. Phosphoramidite derivatives **6** of the optically active diols **3** were synthesized and applied to Pd-catalyzed asymmetric allylic amination reaction of 1,3-diphenylallyl acetate with benzylamine affording the chiral allylic amine in nearly quantitative yield with moderate enantioselectivity. Improved method for the removal of MOM groups from the spirosilane **2** and applications of the optically active ligands **6** to other transition metal-catalyzed asymmetric reactions are under investigations.

Supporting Information is available on http://dx.doi.org/10.1246/cl.******.

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