A Chiral *N*-Sulfonylphosphoramide: Synthesis and X-ray Crystal Structure of a 1,3,2-Oxazaphospholidin-5-one, a Trivalent Electron-Withdrawing Amino Acid-Derived Phosphorus Compound, and Synthesis of Its $W(CO)_5$ Adduct

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Chiral phosphines[1] such as DiPAMP, BINAP, and most recently DuPHOS have great utility in asymmetric synthesis,[2] but they are electron-donating and so are poor choices in the design of the chiral Lewis acids in which we have long been interested.[3] The ephedrine-derived chiral 1,3,2-oxazaphospholidine (**1**; see Chart 1) that Jugé and Brown have each described[4] has an electron-withdrawing oxygen atom attached to phosphorus, but **1** also has a counter-balancing electron-donating nitrogen atom.[5] A number of Lewis acids bearing electron-withdrawing *N*-sulfonyl moieties adjacent to the acidic site such as **2** and **3** have been described.[6] Although ephedrine is *N*-methylated and not subject to ready modification, its use is still attractive due to its ready availability and its efficient (and elegant) transfer of chirality to phosphorus to give a diastereomerically pure material that contains a stereogenic phosphorus atom; presumably, the diastereomer in which the phenyl groups are mutually cis is disfavored due to the higher steric interaction. However, as illustrated by **2** and **3**, amino acids possess both the same β-amino hydroxy functionality as ephedrine as well as a primary amine that is readily sulfonylated to give the electron-withdrawing sulfonamide moiety. In **2** and **3**, coordination at the Lewis acid site occurs anti to the toluenesulfonyl group, but while this is trans to the phenyl (like ephedrine) in **3**, it is cis to the indolyl group in **2**. Guided by these examples, we have begun a program to investigate the properties of *N*-sulfonylphosphoramides. For instance, the achiral compound that we have named TosL (**4**) is readily prepared from the corresponding bis(sulfonamide) and $PPhCl_2$, despite the presumed low nucleophilicity of the nitrogen lone-pairs, and it is exceptionally electron-withdrawing as a ligand.[5] In this paper we describe (1) the synthesis of a phosphorus analogue of **2**, (2) the high diastereoselectivity at phosphorus such as that seen for **1**, (3) a rare example of an X-ray structure of a chiral trivalent phosphorus compound, and (4) the high electron-withdrawing ability of this new chiral ligand as judged by the IR spectrum of the $W(CO)_5$ adduct, like that seen for TosL.

Scheme 1

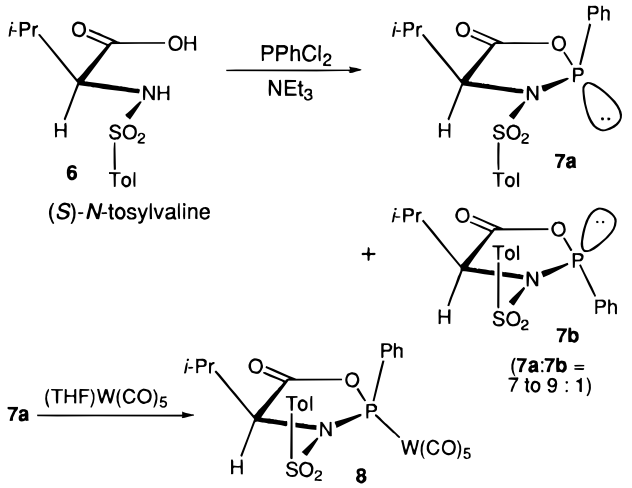
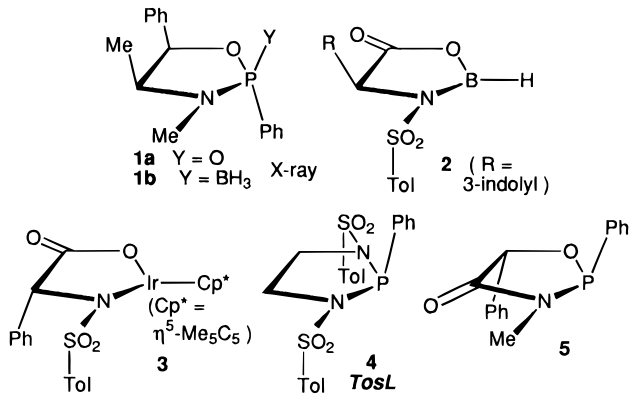


Chart 1



Following a procedure similar to that used for the synthesis of TosL,[5] triethylamine was first added to an ether solution of (*S*)-*N*-tolylsulfonylvaline (**6**), giving a white suspension of what is presumably the Et_3NH^+ salt of the sulfonamido carboxylate. An ether solution of $PPhCl_2$ was then added to the stirred suspension, resulting in a visible change to a merely cloudy white suspension, presumably due to the less voluminous 2 equiv of $Et_3NH^+Cl^-$. Stirring was continued for 1 h, after which filtration of the ammonium salt followed by solvent removal gave the product as a pale yellow solid in greater than 90% yield.[7] Analysis of the reaction mixture by ^{31}P NMR spectroscopy indicated the presence of two new phosphorus-containing compounds at 131.2 and 134.3

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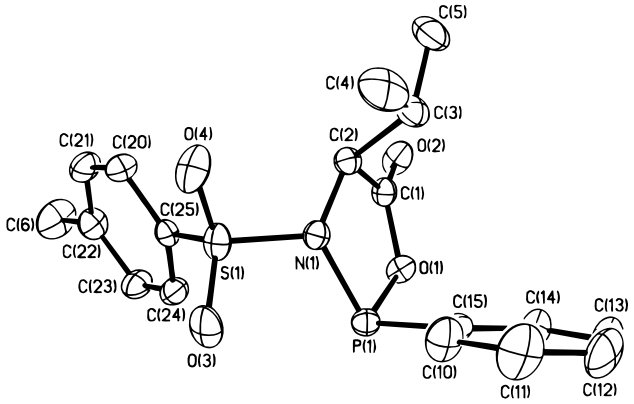

Figure 1. ORTEP drawing of **7a**. Selected bond lengths (Å) and angles (deg): P−O(1), 1.678 (3); P−N, 1.744 (4); P−C(15), 1.824 (5); O(1)−P−N, 90.9 (2); O(1)−P−C(15), 101.1 (2); N−P−C(15), 99.9 (2).

ppm, subsequently identified as the desired diastereomeric 1,3,2-oxazaphospholidinones **7a** and **7b** (Scheme 1). The ratio of **7a**:**7b** was somewhat variable, ranging from a low of 6.2:1 to a high of 9.8:1 for room-temperature reactions, although typically the ratio was 7 to 9:1.

A single crystallization of the mixture of diastereomers from ether at −35 °C reproducibly gave a 50% yield of the major isomer **7a** free of any detectable minor isomer **7b**. Subsequent recrystallizations gave the major isomer contaminated by small amounts of the minor isomer, but because there was no need for large amounts of the pure diastereomer, no attempt to optimize the yield was made. We are aware of five previous syntheses of 1,3,2-oxazaphospholidinones formally derived from α-amino acids,[8] but none of these reports was concerned with chirality. A diastereoselective synthesis of the related *amido* alcohol-derived compound 2,5-diphenyl-3-methyl-1,3,2-oxazaphospholidin-4-one (**5**)[9] gave the trans isomer (85:15 trans:cis) under thermodynamic control, just as with ephedrine (**1**);[4c] evidently the carbonyl does not affect the stereochemical preference.

Crystals of **7a** suitable for X-ray diffraction were obtained on the first recrystallization from ether. The absolute configuration was assumed to be that (*S*) from the naturally occurring amino acid carbon atom, and the refinement was consistent with this. The structure[10] (Figure 1) is unique; to the best of our knowledge it is the only 1,3,2-oxazaphospholidinone, the only acetoxyphosphine, and just the second *trivalent* 1,3,2-oxazaphospholidine structure;[11] a trivalent 1,3,2-oxazaphosphorinane (six-membered ring) has been characterized by X-ray[12] as have a number of ephedrine-derived *tetravalent* phosphine oxides, sulfides, and boranes analogous to **1a**,**b**.[13] Nevertheless, the key results are stereochemical: the isopropyl and phenyl groups are cis to each other, and the tolyl moiety is in the s-trans conformation relative to these 1,3-substituents on the heterocycle. It is reasonable to propose that the isopropyl forces the tolyl ring to be in the anti conformation, which then forces the phenyl to be anti to it. However, examination of **7a** using molecular modeling software does not reveal any compelling steric reasons for the preference of **7a** over **7b**, in part due to the intervening SO_2 which extends the distance from the tolyl moiety to the other ring substituents. Sulfonamide geometry is an active area of research[14] and will be discussed in detail in the full account of this work; for now we note that the nitrogen is slightly pyramidalized and the sulfonamide lies in a staggered conformation with the tolyl roughly anti to the nitrogen lone pair. In **7b** on the other hand, the tolyl group is proposed to be s-cis to the isopropyl group rather than the phenyl as shown in Scheme 1 on the basis of $^3J_{HH}$ for the isopropyl and ring methines; in **7a** it is 7.1 Hz, consistent with a 180° dihedral angle (X-ray: 168°) while in **7b** it is 3.0 Hz, consistent with a 60° dihedral angle, as the isopropyl rotates to avoid contact with the tolyl group.

To assess the electronic properties of **7a**, as we have done before,[5] it was combined with (THF)$W(CO)_5$ to give the adduct **8** (Scheme 1) in 63% yield. The infrared spectrum exhibits unusually high-frequency carbonyl stretching frequencies[7] placing **7a** second only to $P(CF_3)_3$ as the most electron-withdrawing ligand in $LW(CO)_5$ complexes.[5] In fact, while the sulfonamide moiety was expected to be electron-withdrawing, one unexpected feature of this work is that **7a** is evidently more electron-withdrawing than TosL, so the carboxylate group appears to be even more electron-withdrawing than the sulfonamide. We also note that $^3J_{HH} = 3.4$ Hz for the isopropyl and ring methines, consistent with the bulky $W(CO)_5$ moiety forcing the tolyl to be anti to it rather than phenyl, as shown in Scheme 1.

In conclusion, reaction of an inexpensive and readily available amino acid derivative with $PhPCl_2$ gives a near-quantitative yield of a new phosphorus heterocycle in high diastereomeric purity. A single crystallization gives one diastereomer in overall 50% yield, and so constitutes one of the simplest syntheses of an enantiomerically pure trivalent phosphorus compound. This work extends the number of sulfonamide-substituted heterocycles that exhibit interesting and high stereoselectivity,[6a,c] so exploration of the steric space of this substituent appears to be in order. Future research will be directed toward understanding the factors that contribute to diastereoselectivity at phosphorus, stereospecific transformations of this new phosphorus heterocycle, and use in catalytic reactions.

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Supporting Information Available: Details of the syntheses and analytical data for **6**−**8** and X-ray data, atomic coordinates, isotropic and anisotropic displacement coefficients, and bond lengths and angles for **7a** (11 pages). Ordering information is given on any current masthead page.

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(7) Complete synthetic details and spectral and analytical data are given in the Supporting Information.

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(10) Crystallographic data have been deposited with the Cambridge Structural Database and may be accessed by the refcode HIGPOC. See the Supporting Information for details of the structure determination.

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