JOC Article

Synthesis and Structural Characterization of Trivalent Amino Acid Derived Chiral Phosphorus Compounds

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Reaction of the *N*-toluenesulfonyl derivatives of (*S*)-alanine, phenylalanine, and valine (**4**−**6**) with $PhPCl_2$ gave in high yield the 4-methyl, benzyl, and isopropyl derivatives (**7**−**9**) of 2-phenyl-1-*p*-toluenesulfonyl-1,3,2-oxazaphospholidin-5-one. The ratios of the (2*S*,4*S*)/(2*R*,4*S*) diastereomers (cis/trans isomers) were 1:1, 2:1, and 10:1 for the methyl, benzyl, and isopropyl derivatives **7a**,**b**, **8a**,**b**, and **9a**,**b**, respectively. For **7a**,**b**, both isomers could be crystallized, but for the others only the major isomers were isolable. The X-ray crystal structure of **9a** shows that the isopropyl and phenyl groups are mutually cis and that the tolyl moiety is oriented s-trans to both the isopropyl and phenyl groups. Reaction of **6** with $Cl_2PCH_2CH_2PCl_2$ (**10**) gave a 56:38:7 mixture of the cis/cis, cis/trans, and trans/trans diphosphorus heterocycles **11a**−**c**. The major isomer could be crystallized and isolated free of the other diastereomers. Reaction of **6** with $EtPCl_2$ gave a 6:1 mixture of cis/trans isomers of the ethyl-substituted heterocycles **12a**,**b** as an inseparable oil but allowed confirmation of the structure of **11a**. Slow epimerization at phosphorus may occur by inversion but more likely by ring opening/closure, since **7b**, **9a**, and **11a** give rise upon standing in solution to mixtures containing starting material and **7a**, **9b**, and **11b**, respectively, along with the free amino acid derivatives **4** and **6**. The NMR spectra, and in particular the coupling constants between the α-hydrogen atom of the amino acid moiety and phosphorus, were used to establish the identities of the cis and trans isomers. Reaction of **9a** with $(THF)W(CO)_5$ gave the phosphorus-ligated adduct (**9a**)$W(CO)_5$ (**13**), and the IR spectrum of this complex shows that **9a** is a strongly electron-withdrawing ligand. The geometry of the sulfonamide moiety is discussed in detail, as are the ^1H NMR coupling constants. The data are consistent with the presence of little steric interaction between the cis isopropyl and phosphorus substituent in **9a**, **11a**, and **12a** and orientation of the tolyl moiety s-cis to the isopropyl group in **9b**, **12b**, and **13**.

Introduction

Organometallic Lewis acids show promise as catalysts for reactions such as the Diels−Alder and aldol reactions,[1−9] but the critical combination of high Lewis acidity and construction of a *chiral* reaction site is difficult to achieve. Phosphines are the auxiliary ligands of choice for low oxidation state carbonyl complexes, but while chiral ligands[10] such as DiPAMP, BINAP, and DuPHOS have great utility,[11−14] they are electron-donating and so are poor choices in the design of chiral Lewis acids. Kündig reported one solution to this problem, describing the use of a relatively electron-deficient fluorinated diaryl phosphinite ligand in asymmetric Diels−Alder catalysis

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§ We dedicate this paper to the memory of Mohammad Salman Hamdani. Sal worked in our labs at Queens College as an undergraduate student from 1998 to 2001 and died as part of the rescue effort at the World Trade Center in New York City, September 11, 2001.

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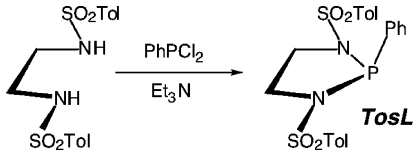
by chiral iron and ruthenium Lewis acids.[15−17] Corey reported a solution for a non-transition-metal Lewis acid, in which higher reactivity was imparted by the presence of a cationic nitrogen center adjacent to the boron Lewis acid site.[18,19] We recently discovered a class of trivalent phosphorus compounds in which one or two electron-withdrawing *N*-sulfonyl moieties are attached to phosphorus.[20] As shown in eq 1, for instance, the compound that we have named TosL is readily prepared from the corresponding sulfonamide and phosphorus dichloride, despite the presumed low nucleophilicity of the nitrogen lone-pairs. Compounds such as TosL can serve as ligands that are exceptionally electron-withdrawing,[20] and consistent with this electronic property, these phosphorus compounds function as effective promoters of rhodium-catalyzed hydroformylation.[21,22]

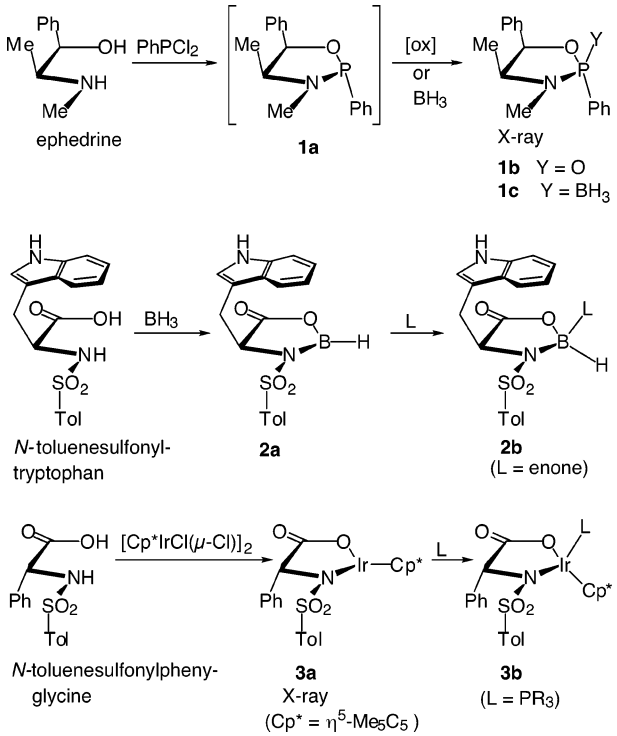


(1)

Related compounds that have been reported in the literature suggested an obvious route to the preparation of a chiral analogue of TosL (Scheme 1). Thus, Jugé and Genet and separately Brown have described the use of ephedrine to prepare the 1,3,2-oxazaphospholidine **1a**.[23−25] In this system, chirality is efficiently and elegantly transmitted from ephedrine 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. The stereochemistry has been assigned on the basis of the X-ray structures of the oxide[26] and borane[27] derivatives **1b**,**c**. We are not aware of this ligand having been tested for its electronic properties in transition-metal adducts, but a prediction of its electronic character would be difficult since the dialkylamino group is electron-donating while the oxygen is electron-withdrawing.[20]

Amino acids possess the same β-amino hydroxy functionality as ephedrine, but the carboxy group should render the oxygen much more electron withdrawing than that in ephedrine, and more importantly, the primary amine is readily sulfonylated to give the electron-withdrawing sulfonamide moiety. A number of amino acid-derived heterocycles that contain boron have been described,[28] of which the 1,3,2-oxazaborolidinone **2a** is a well-known Diels−Alder catalyst.[29] Unlike the phosphorus center in TosL and **1a**, the trivalent boron is an electron acceptor rather than donor, and its geometry is planar. Enone complexation to give **2b** is proposed to occur anti to the toluenesulfonyl moiety and includes a π-acceptor interaction with the electron-rich indole ring. The iridium-containing 1,3,2-oxazirolidinone **3a**[30] is a rare transition-metal heterocycle, and like the boron center in borolidinone **2a** the iridium center is an electron pair acceptor and is coplanar with the attached nitrogen, oxygen, and the centroid of the Cp* ligand. However, attack by phosphine ligands to give **3b** occurs so that the large PR_3 and phenyl groups are mutually trans on the heterocycle as seen for the two phenyl groups in the ephedrine case (**1a**), as well as trans to the toluenesulfonyl group as seen in the boron case (**2a**).

SCHEME 1



In this paper, we describe (1) the synthesis of phosphorus analogues of **2a** and **3a**, (2) an example of the high diastereoselectivity at phosphorus like that seen for **1a**, (3) extension to the synthesis of a chiral diphosphorus analogue, (4) a rare example of an X-ray structure of a chiral trivalent phosphorus compound, and (5) the high electron-withdrawing ability of this new moiety as judged by the IR spectrum of the $W(CO)_5$ adduct, like that seen for TosL. Part of this work has been communicated previously.[31]

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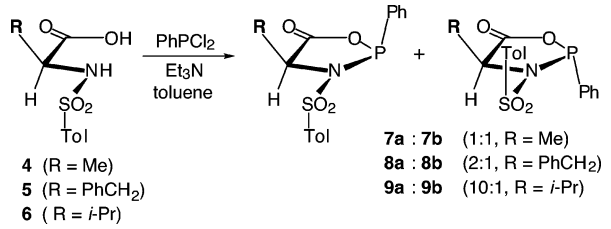
SCHEME 2



Results

Synthesis. Following a procedure similar to that used for the synthesis of TosL,[20] triethylamine was first added to a solution of the *N*-toluenesulfonyl derivatives of *S*-alanine (**4**), phenylalanine (**5**), and valine (**6**) in toluene, each giving a white suspension of what is presumably the Et_3NH^+ salt of the corresponding sulfonamido carboxylate. A solution of $PhPCl_2$ was then added to the stirred suspensions, resulting in a visible change to a merely cloudy white suspension, presumably due to the less voluminous two equivalents of $Et_3NH^+Cl^-$. Stirring was continued for up to 3 h while the reactions were monitored by ^{31}P NMR spectroscopy, after which filtration of the ammonium salt followed by solvent removal gave the products as pale yellow solids in greater than 90% yield (Scheme 2). Analysis of the reaction mixtures by ^{31}P NMR spectroscopy indicated the presence of two new phosphorus-containing compounds with peaks near 130 ppm, subsequently identified as the desired diastereomeric *cis* and *trans*-1,3,2-oxazaphospholidinones **7**−**9**, along with any excess $PhPCl_2$ at 161.5 ppm. The ratio of the new compounds was similar in the reaction solutions to that observed after workup, indicating that no significant isomerization occurred over a short time.

The highest diastereomer ratio was observed for valine derivative **9**, but was somewhat variable in the solvent initially used, ether, 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. The product ratios determined by ^{31}P NMR spectroscopy were confirmed by analysis of the more complex ^1H NMR spectra. Approximately 20 experiments were conducted in which the reaction solvent, time (up to 3 days), temperature, and reactant concentrations were varied, but no correlations with diastereoselectivity emerged. For instance, while a 2.7:1 ratio was observed in refluxing ether, lowering the reaction temperature to −35 °C gave a 6.3:1 ratio, lower than most room temperature runs. Use of methylene chloride, a solvent in which the initially formed Et_3NH^+ salt of the sulfonamido carboxylate was completely soluble and the final product $Et_3NH^+Cl^-$ was partially soluble, gave results that were even less reproducible. Room-temperature reactions gave ratios from 3.3 to 10.6:1, a −78 °C reaction gave a 6.1:1 ratio, and a reaction conducted at reflux gave a 4.3:1 ratio. Most of the room-temperature reactions in CH_2Cl_2 gave ratios greater than 6:1, but the greater reproducibility of the ether and toluene reactions made these the solvents of choice, with toluene giving the most reproducible ratios but ether giving the easiest synthesis in reliable yield. The lack of reproducibility in CH_2Cl_2 is puzzling since all reactions were carried out with strict exclusion of air and water but we presume the cause is the presence of what might be variable concentrations of the weak acid $Et_3NH^+Cl^-$, which is more soluble in CH_2Cl_2 than in ether and toluene. In ether and toluene, by contrast, both the starting amino acid carboxylate and the $Et_3NH^+Cl^-$ are fairly insoluble. One run was carried out in THF at room temperature, and it exhibited solubility characteristics similar to CH_2Cl_2 and gave a relatively low 6.2:1 diastereomer ratio.

Comparison of diastereomer ratios for the three reactions was most reproducibly made in toluene at room temperature, with the alanine derivative giving a 1:1 ratio, phenylalanine a 2:1 ratio, and valine a 10:1 ratio. A single crystallization of the mixture of diastereomers of **9** from ether at −35 °C reproducibly gave a 50% yield of the major isomer **9a** free of any detectable minor isomer **9b**. Subsequent recrystallizations gave the major isomer contaminated by small amounts of the minor isomer, but absent the need for large amounts of the pure diastereomer, no attempt to optimize the yield has been made. To identify the minor product **9b**, fractional crystallization was attempted, since the compounds are too polar to move on TLC. No crystallization solvent could be found that would selectively precipitate **9b** and so numerous crystallizations from ether were carried out to remove **9a**. Since this crystallization also resulted in increasing amounts of precipitation of **9b** as its concentration in the residue increased, the best purification we could achieve was a 1:1 ratio of **9a**/**9b**. This was sufficient to identify all peaks due to **9b** in the ^1H and ^{13}C NMR spectra, and all are simply slightly shifted from those due to **9a**. Elemental analysis of the mixture was consistent with **9b** being an isomer of **9a**, and the optical rotation of the mixture showed that **9b** as expected has a nonzero rotation. There is no reason to suppose that this compound is anything other than the stereoisomer of **9a**, in which the isopropyl and phenyl groups are trans rather than cis to each other (vide infra).

For the other mixtures, the relatively low diastereomer ratios resulted in more difficulty in selective crystallization, but in the case of the alanine derivatives **7a** and **7b** each isomer could be crystallized free of the other, although not in high yield. No prolonged attempt was made to isolate the minor isomer of **8**.

X-ray Structure. Crystals of **9a** suitable for X-ray diffraction were obtained on the first recrystallization from ether. The absolute configuration was assumed to be (*S*) from the naturally occurring amino acid carbon atom, and the refinement was consistent with this.[31] The structure is shown in Figure 1, and selected bond lengths, angles, and torsional angles are given in the Supporting Information for comparison to related compounds. 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.

Synthesis of a Chiral Diphosphine. Reaction of **6** with tetrachlorodiphosphine **10** in THF gave a mixture that after 5 min of reaction exhibited four peaks in the ^{31}P NMR spectrum: a singlet at 156.7 ppm, a 1:1 pair of doublets at 159.2 and 154.5 ppm with $^3J_{PP} = 6.8$ Hz, and a singlet at 159.3 ppm, in a 56:38:7 molar ratio of

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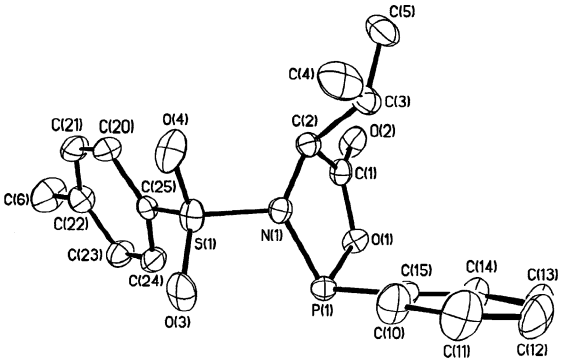
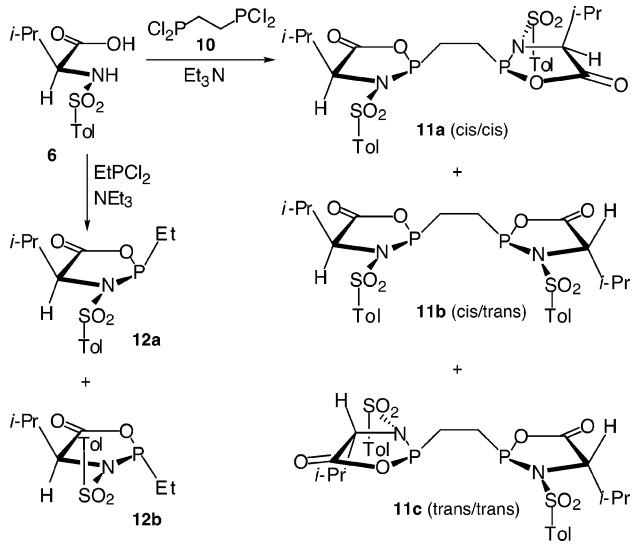


FIGURE 1. ORTEP drawing of **9a**.

SCHEME 3



diphosphines. When the reaction was carried out in toluene, the three compounds were observed to form in a 49:42:9 molar ratio (Scheme 3). The major product is proposed to be cis/cis diastereomer **11a** while the minor product is proposed to be trans/trans diastereomer **11c**, each of which would give a singlet in the ^{31}P NMR spectrum. The last product, cis/trans diastereomer **11b**, would be expected to exhibit a pair of doublets due to 3-bond phosphorus−phosphorus coupling as seen. Since the 2-carbon bridge linking the two phosphorus atoms is different from the phenyl group on phosphorus of **7**−**9**, **6** was combined with $EtPCl_2$ as well (Scheme 3), to better model the alkane linker, to give the cis and trans isomers **12a**,**b**. The initial reaction mixture exhibited two peaks in the ^{31}P NMR spectrum at 163.7 and 169.9 ppm in a 6:1 ratio due to the cis and trans isomers. In contrast to the other reactions, neither isomer could be crystallized and the mixture that was spectroscopically characterized was a clear oil.

Stability. The air, water, and thermal stability of **9a** is surprisingly high. Crystalline **9a** exhibited no decomposition upon exposure to air overnight, as judged by ^{1}H and ^{31}P NMR spectroscopy, but roughly half decomposed in $CDCl_3$ solution upon overnight exposure to air; no product analysis has been carried out. Addition of water (1−15 equiv) to a $CDCl_3$ solution in the air gave only traces of decomposition within 1 h. A sample of **9a** was stored at 18 °C in toluene in a glovebox for 1 week. While there was no immediate change (a sample withdrawn after 0.5 h contained ≤0.2% of the trans isomer **9b**), by the end of 1 week, the diastereomer ratio of **9a**:**9b** was 89:11, and it remained constant as continued decomposition to give increasing amounts of **6** occurred. Since samples enriched in **9b** might isomerize back to this 89:11 mixture, we attempted to optimize the yield of **9a** by allowing the mixtures to stand at room temperature in solution after crystallizing out the **9a**. In fact, a 65:35 mixture of **9a**/**9b** did isomerize to an 86:14 mixture after one week in toluene, but decomposition to **6** was competitive with the isomerization reaction, so no additional **9a** could be crystallized out. Finally, the *solid* 89:11 mixture was allowed to stand at ambient temperature over a 3-week period in order to see if it might be converted to a single isomer as has been seen during the elegant self-resolution process described by Vedejs,[32,33] but in our case no isomerization occurred.

A pure sample of **7b** exhibited similar behavior. After 1 day at 20 °C in toluene, the ratio of **7a**/**7b** was 4:96, and after 1 week, 23:77, but like **9** accompanied by analogous decomposition to **4**. The diphosphorus compound **11a** seemed to isomerize faster than this albeit in $CDCl_3$: after 1 day at room temperature, a 90.2:9.3:0.5 mixture of **11a**/**11b**/**11c** was observed, and after 3 days an 88:12 mixture of **11a**/**11b** with about an equal amount of **6** was observed, but with no detectable **11c**.

NMR Spectra. Peak assignments for **7**−**9**, **11**, and **12** were made by a combination of 2D COSY and HETCOR experiments and for the α-ring hydrogen by selective homonuclear decoupling experiments. In addition, selective heteronuclear decoupling of the ortho phenyl hydrogens resulted in collapse of the broad phosphorus signal (in the undecoupled spectrum) to a doublet, allowing confirmation of coupling of the phosphorus and ring hydrogen. While the determination of the cis/trans stereochemistry was made on the basis of the X-ray structure of **9a**, the NMR coupling constant data allowed all of the other stereochemistries to be determined with reference to this one compound. The key observation is that all of the cis isomers exhibit $^3J_{PH}$ = 3.4−3.7 Hz while all of the trans isomers exhibit $^3J_{PH}$ = 1.4−1.8 Hz for the ring hydrogen. In addition, the trans isomers for valine derivatives **9b**, **11b**,**c**, and **12b** each exhibit, compared to the cis isomers, both an upfield shift of one of the isopropyl methyl groups that suggests anisotropic shielding by the toluenesulfonyl moiety, and a concomitant reduction in $^3J_{HH}$ from ∼7 Hz to 3 Hz, suggesting a conformational rotation of the isopropyl group. The $W(CO)_5$ adduct of **9a**, that is, **13**, exhibited similar changes in the isopropyl group compared to **9a**. These and other data characteristic of the cis/trans isomers are collected in tabular form in the Supporting Information.

Both the decoupled and undecoupled NMR spectra of the diphosphine **11a** were complicated by the presence of virtual coupling, and the critical coupling constant $^3J_{PH}$ could not be measured directly. The undecoupled ^{1}H signal was an apparent doublet of triplets, and simulation of this multiplet as an ABXX′ system (where the phosphorus atoms are the XX′ pair) gave an excellent fit using the observed values $^3J_{HH}$ = 5.8 Hz and $^3J_{PH}$ = 3.6 Hz

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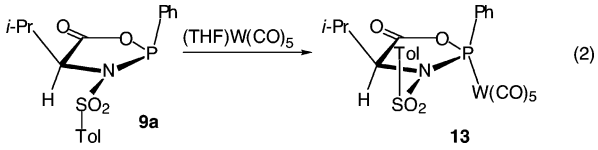
(assumed to be double the observed "triplet" coupling), for values of $^3J_{PP'} \geq 15$ Hz. In fact the value $^3J_{PP'} = 20.4$ Hz was indirectly determined by simulation of the ^{13}C ABX signal for the bridging methylene carbon, where the single ^{13}C renders the phosphorus atoms chemically *in*equivalent (the AB pair) and gives a 6-line pattern.[34] Further confirmation of the stereochemical assignment came from the isopropyl methyl chemical shifts: both are "normal" in **11a** (1.22, 1.15 ppm), but the mixture of all three stereoisomers exhibited doublets at 0.39 and 0.375 ppm for **11c** and **11b**, respectively, characteristic of the high-field signals of the trans isomers **9b** and **12b**.

Coordination to W(CO)$_5$. To assess the electronic properties of **9a**, as we have done before[20] it was combined with (THF)W(CO)$_5$ to give the adduct **13** (eq 2) in 63% yield.



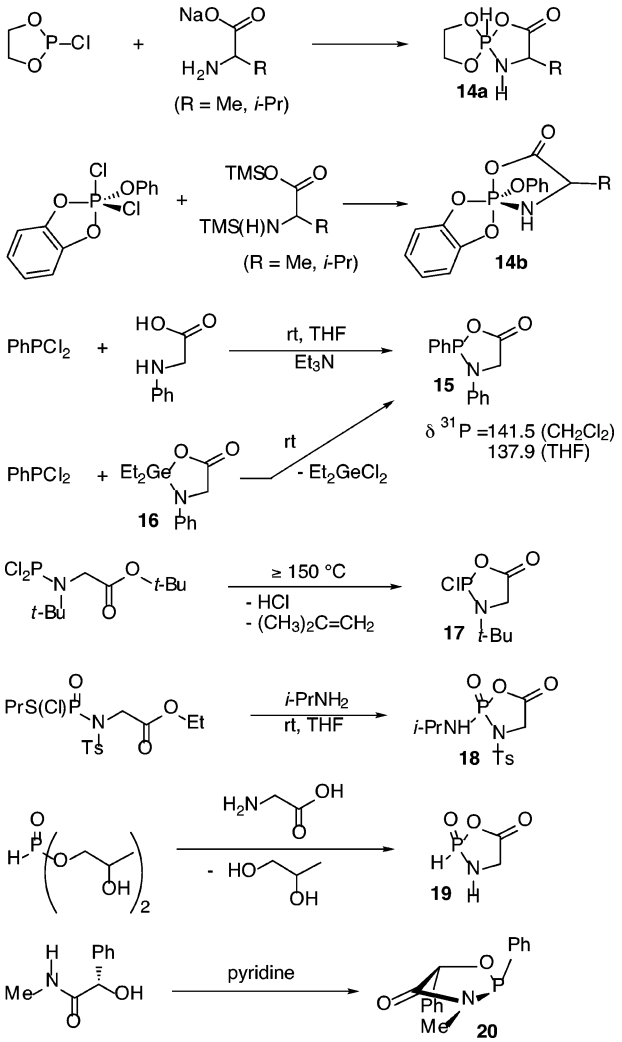
(2)

Coordination of **9a** to tungsten via phosphorus was evident from the change in the ^{31}P NMR chemical shift from 133.0 ppm in **9a** to 146.9 ppm in **13**, as well as from the presence of the characteristic tungsten−phosphorus satellites due to the 14% natural abundance of ^{183}W, giving $^1J_{PW} = 346$ Hz. The ^1H NMR exhibited features of both **9a** and **9b**, with a phosphorus−hydrogen coupling constant for the ring methine characteristic of **9a** ($^3J_{PH} = 3.4$ Hz) but also a hydrogen-isopropyl hydrogen coupling constant for the ring methine characteristic of **9b** ($^3J_{HH} = 3.4$ Hz). Also like **9b**, one of the isopropyl methyl doublets was shifted upfield to 0.32 ppm. In the ^{13}C NMR spectrum, the tungsten carbonyl ligands exhibited the characteristic trans ($^2J_{PC} = 38.4$ Hz) and cis ($^2J_{PC} = 8.5$ Hz) phosphorus−carbon coupling constants of phosphine tungsten pentacarbonyl complexes.[20] The infrared spectrum exhibited unusually high-frequency carbonyl stretching frequencies indicative of an electron-withdrawing ligand, along with the anhydride-like carbonyl stretch for the P−OC=O moiety at 1811 cm^{-1}.

Discussion

Survey of 1,3,2-Oxazaphospholidinone Synthesis, Stereochemistry, and Stability. Only a limited number of syntheses of 1,3,2-oxazaphospholidinones, formally derived from α-amino acids, as well as one diastereoselective synthesis of a related 1,3,2-oxazaphospholidin-4-one, have been reported (Scheme 4). The first to be reported were prepared from amino acids via substitution reactions at phosphorus similar to those in Scheme 2, to give a number of related spirophosphoranes such as **14a**,[35,36] and while these first examples included chiral amino acids, diastereomeric purity of the products was not discussed nor was data reported that could allow the de to be evaluated. More recently, related spirophosphoranes such as **14b** have been prepared by base-free elimination of TMSCl from the phosphorus chloride and *N*,*O*-bis(trimethylsilyl)-α-amino acids,[37−40] and while again diastereomeric purity of the products has not been discussed, one spectrum was published and showed the ratio to be close to unity.[40] Synthesis of trivalent phosphorus heterocycles by substitution of glycine derivatives, again in a manner similar to that seen in Scheme 2, has also been described; the ^{31}P NMR chemical shift of the glycine-derived 2-phenyl substituted 1,3,2-oxazaphospholidinone **15** is very similar to those of **7**−**9**.[41] Heterocycle **15** has also been prepared by a room-temperature exchange reaction of germanium heterocycle **16**.[42] Both a trivalent and pentavalent phosphorus heterocycle have been prepared by elimination reactions from acyclic precursors. While **17** forms at 150 °C and so demon-

SCHEME 4



(34) Hersh, W. H. *J. Chem. Educ.* **1997**, *74*, 1485−1489.
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strates the potentially high stability of the P−O linkage,[43] **18** only forms in low yields.[44] Elimination of 2,3-propanediol to give cyclic glycine derivatives such as **19** occurs under mild conditions.[45] The final reaction in Scheme 4 was reported to give *cis*-**20** as the major product at −5 °C (>2:1 cis/trans), but upon refluxing, *trans*-**20** was obtained as the major product (1:5 cis/trans).[46]

As this survey makes clear, transfer of chirality from the organic fragment to phosphorus is not observed (**14a**,**b**) or has not been sought (**15**−**19**) in most cases. Only for **20** where moderate selectivity was observed and of course for ephedrine (**1a**, Scheme 1) has diastereoselectivity been reported previously. The synthesis of ephedrine-derived **1b**,**c** has been reported to give a 1:1 mixture of cis and trans diastereomers initially, followed by isomerization to give exclusive formation of the trans diastereomer **1a** before oxidation or reaction with BH_3 as shown in Scheme 1. Both in this case and that of **20**, formation of the trans product is evidently favored thermodynamically, in apparent contrast to the cis-selectivity for *N*-toluenesulfonyl heterocycles **8**, **9**, **11**, and **12**. With the exception of this study, no attempts to correlate steric effects with diastereoselectivity at phosphorus have been reported. Clearly, the correlation of cis/trans ratio with steric bulk here suggests a mechanism by which the cis product is favored: the toluenesulfonyl moiety adopts a conformation that is predominantly s-trans to the α-amino acid substituent, so that if P−O bond formation occurs first due to the higher acidity of the carboxylic acid, then subsequent nucleophilic attack of nitrogen on phosphorus occurs so as to minimize the steric interaction of the toluenesulfonyl and the phenylphosphorus groups, leaving the larger α-amino acid substituent and phenyl groups mutually cis. For the isopropyl moiety, not only was a 10:1 cis:trans ratio observed for the phenyl moiety of **9**, but a 6:1 cis:trans ratio was observed for the smaller ethyl moiety of **12**. For **11**, the observed 56:38:7 ratio would be generated by a 3:1 cis/trans ratio for each of the two ring-forming steps pitting the isopropyl group against the two-carbon bridge, a ratio which seems low given the size of this group, but we have no explanation for this result.

This explanation for thermodynamic product formation requires that the intermediate chlorophosphine be allowed to epimerize, if (as seems likely) the initial attack of carboxylate on phosphorus is not diastereoselective. We have noticed that reaction of **6** with PCl_3 gives a heterocycle that undergoes rapid epimerization in the presence of $Et_3NH^+Cl^-$ on the NMR time scale, but gives sharp peaks in the NMR when it is crystalline.[47] A recent paper similarly shows that HCl can catalyze chlorophosphine epimerization,[48] and the epimerizations of both **1a** and **20** occur in the presence of trialkylammonium salts.[25,46] The source of the variability in diastereoselectivity for the synthesis of **9** as a function of solvent and temperature is most reasonably attributed to the presence of unpredictable amounts of acid in solution at this epimerization stage. Once the heterocycle forms from the rapidly inverting chlorophosphine, however, we propose that the ring closure is essentially irreversible, and monitoring of reactions at early reaction time has never given any indication of different stereoselectivities.

An alternative explanation for thermodynamic product formation is intramolecular isomerization by inversion at phosphorus; while there is no evidence for it in any of these cases, it is not precluded. For instance, measured barriers to phosphorus inversion are relatively low in a 1,3,2-dioxaphospholane[49] as well as in acylphosphines[50] where the electron-withdrawing acyl group allows analogy to the carboxylate and sulfonamide groups here. Nevertheless, epimerization of **7** and **9** is always accompanied by decomposition with formation of the free *N*-toluenesulfonyl amino acid, so the isomerization here might most reasonably arise via P−O or P−N cleavage followed by ring-closure. Regardless of mechanism, the observed isomerization of **7b** to **7a**, and of the 65:35 mixture of **9a**/**9b** back toward the 89:11 mixture, suggests the cis diastereomer is indeed thermodynamically favored for these *N*-sulfonyl-1,3,2-oxazaphospholidinones.

One might suppose that the P−O−C(=O)R linkage, which is rigorously a mixed anhydride formed from the corresponding phosphorus acid chloride and carboxylic acid would be only somewhat less reactive than a PCl linkage, albeit with the potential for added instability due to Arbuzov-type rearrangement due to the presence of the P−O bond.[51] In fact, acyclic analogues are known[51−56] and, consistent with the range of syntheses and reaction conditions in Scheme 4, show that this can be a surprisingly robust linkage. Interesting examples of both stable and unstable mixed anhydrides are known in biological systems. The former include pyrophosphate analogues[55,56] and aminoacyl-adenylate, the high-energy intermediate used at the outset of protein biosynthesis to charge tRNA.[57] The latter *un*stable mixed anhydrides include, perhaps surprisingly, amino acid-derived heterocycles proposed to be present only as transient intermediates in solvolysis reactions of acyclic phosphonamides (**21**),[58,59] and pentavalent phosphorus intermediates proposed to be present in a laboratory peptide oligomerization sequence (**22**) and perhaps in prebiotic polypeptide synthesis and/or protein biosynthesis (**23**).[60]

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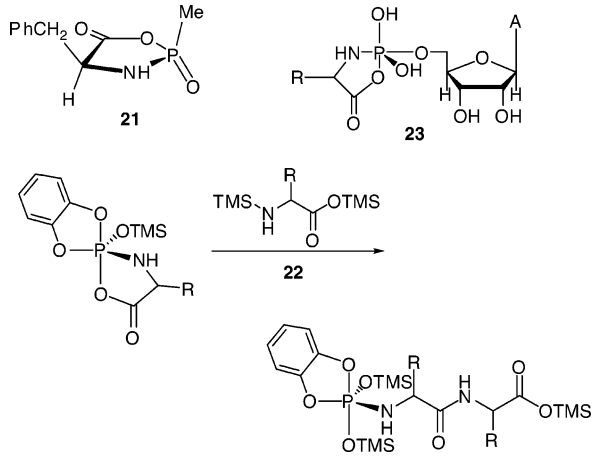
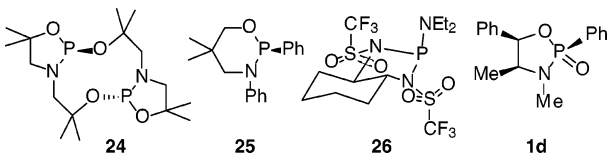
(60) Fu, H.; Li, Z.-L.; Zhao, Y.-F.; Tu, G.-Z. *J. Am. Chem. Soc.* **1999**, *121*, 291−295.



Heterocycle X-ray Structure. The structure determination of **9a** is unique − to the best of our knowledge it is the only 1,3,2-oxazaphospholidin*one* and the only acetoxyphosphine and just the second *trivalent* 1,3,2-oxazaphospholidine structure.[61] Most 1,3,2-oxazaphospholidine structures both are based on the amino alcohol ephedrine and are *tetrahedral* phosphine oxides, sulfides, or boranes.[26,27,62−66] X-ray structures of *tri*valent phosphines such as **9a** include one of a 1,3,2-oxazaphospholidine that is itself part of a larger macrocycle (**24**)[61] and one of a 1,3,2-oxazaphosphorinane (**25**),[67] a six-membered ring heterocycle that like **9a** has a phenyl on phosphorus as well. Comparison of data for these compounds, a recently reported sulfonamide analogue of TosL (**26**),[68] and a representative tetrahedral phosphine oxide (**1d**)[26] chosen since the ring substituents are mutually cis, shows that neither the presence of the carbonyl nor the sulfonyl moiety has much effect on the structure of the heterocycle. The P−O and P−N bonds in **9a** are slightly



longer (∼0.05 Å) than those in **24** and **25**, which might be ascribed both to a weaker anomeric effect in **9a**,[26] and the presence of the less basic carboxylate and sulfonamide moieties. These bonds are also ∼0.1 Å longer than those in **1d**, but this can be a result of the switch from trivalent phosphine to pentavalent phosphine oxide. Other bond lengths are comparable for similarly hybridized atoms. The ring itself is close to planar, with the ring alkane carbon bonded to the nitrogen ring atom being the envelope carbon atom. In most of the known structures, it is this same carbon atom that is the furthest removed from the mean plane.[26,61,63,66,69,70] The nitrogen itself is slightly pyramidalized in **9a**, since the sum of the angles about nitrogen (ΣN) is 350°; planar sp^2-hybridized nitrogen would yield ΣN = 360°, while for sp^3-hybridized nitrogen ΣN ≈ 320°. For instance, pyramidalization in **1d** and **25** is small, while in **26**, the nitrogen with the CF_3 moiety anti to the P−NEt_2 moiety, comparable to the anti orientation of the tolyl and phenyl groups in **9a**, is fairly planar, while the other nitrogen with the syn CF_3 group is almost as pyramidalized as that in **9a**. The effect of the pyramidalization is to increase the distance between the syn groups. Further details of the sulfonamide geometry in **9a** and **26** will be described below (vide infra).

The most striking feature of these heterocycles is the geometry at phosphorus. The O−P−N angles are extremely acute in **9a** (90.9°) and **24** (91.9°) as is the corresponding N−P−N angle in **26** (85.5°), while in the six-membered ring compound **25** this angle is 101° and in the tetrahedral phosphine oxide **1d**, 95.6°. If this bending were due to the constraints of the ring (it is not simply a geometric consequence of the longer phosphorus bonds), one might expect the third group attached to trivalent phosphorus to be held at a much less acute angle, but with average O−P−R and N−P−R angles (where R is the nonring substituent) of 100.5−101.5° for **9a**, **24**, and **25**, this does not seem to be the case although for **26** with an average N−P−R angle of 104.6° it might be. The normal angle about phosphorus in acyclic trivalent alkyl and aryl phosphines is 102−103°,[71] so in fact the observed angles for the nonring substituent are close to those expected for unstrained bond angles, as is that for the O−P−N ring angle in the six-membered ring compound **25**. Hence neither the deviation from a tetrahedral angle for the nonring substituent nor the acute ring angle, which is normal for phospholidines, is a consequence of the heteroatoms or sulfonamide moiety.

On the basis of the X-ray structure of **9a**, the 1,3-interaction between the isopropyl and phenyl groups is evidently small. The distance between the isopropyl hydrogen atom and the phenyl ring is 2.94 Å, while the sum of the van der Waals radii is ∼2.97 Å.[72] As a first guess 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, as previously discussed from a kinetic point of view. The diastereomer **9b** requires that the sulfonyl tolyl be s-cis to either the isopropyl or phenyl substituents, but the use of molecular modeling software suggests that the steric contacts are minor due to the intervening SO_2, which extends the distance from the tolyl moiety to the other ring substituents. We therefore next consider data directly relevant to the sulfonamide geometry.

NMR Determination of Ring Stereochemistry. The solution NMR data that are relevant to the confor-

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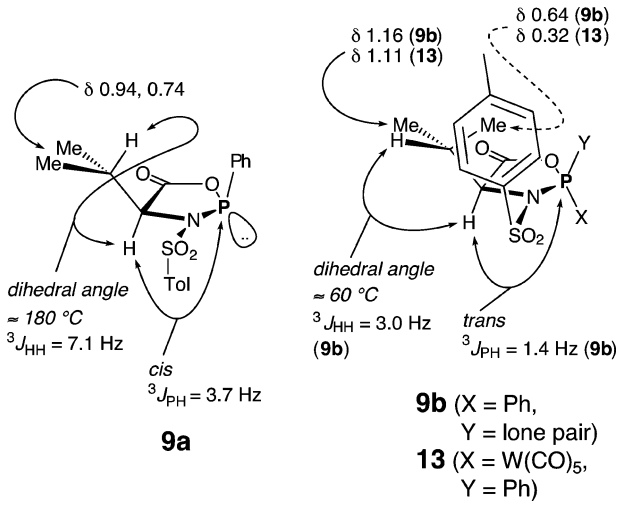
SCHEME 5



mations of **9a** and **9b** are the methine and ring hydrogen coupling constants, as well as the isopropyl methyl chemical shifts. The X-ray structure of **9a** exhibits a H−C−C−H dihedral angle of 168°, and $^3J_{HH} = 7.1$ Hz is consistent with this. In **9b** on the other hand, $^3J_{HH} = 3.0$ Hz, which would be the result of a 52° dihedral angle using the Karplus equation.[73] Such an angle would be consistent with rotation of the isopropyl moiety to another staggered conformation, as might occur to relieve tolyl−methyl interactions if the tolyl were s-cis to the isopropyl group, as drawn in Scheme 5. Consistent with this, the chemical shift of one of the isopropyl methyl signals is unusually far upfield, due to its position above the face of the arene ring. Furthermore, upon coordination of **9a** to tungsten, $^3J_{HH} = 3.4$ Hz in **13**, and one interpretation of this is that the bulky $W(CO)_5$ moiety forces the tolyl to be anti to it rather than to the phenyl, again as drawn in Scheme 5, so that as in **9b** rotation of the isopropyl moiety occurs. Since the same patterns in isopropyl moiety chemical shift and coupling constant occur in **12b** and in **11b**,**c**, the toluenesulfonyl moiety is evidently syn to the isopropyl in these cases as well. Interestingly, the parent toluenesulfonylamino acid **6** also exhibits a coupling constant ($^3J_{HH} = 4.7$ Hz) suggestive of a 60° H−C−C−H dihedral angle; a simple PM3 calculation shows this to be a reasonable outcome of a hydrogen-bonded seven-membered ring structure comparable to those seen for *t*-Boc-α-amino acids;[74] a similar geometry is in fact observed in two X-ray structures incorporating valine-analogues in sulfonamidopeptide mimetics.[75]

The other available coupling constant, $^3J_{PH}$, has been considered by several groups in both five and six-member ring heterocycles, with the conclusion that P−N−C−H coupling constants are too variable for evaluation of the dihedral angle.[26,67,76,77] Generally $^3J_{PH} \approx 0$ Hz for dihedral

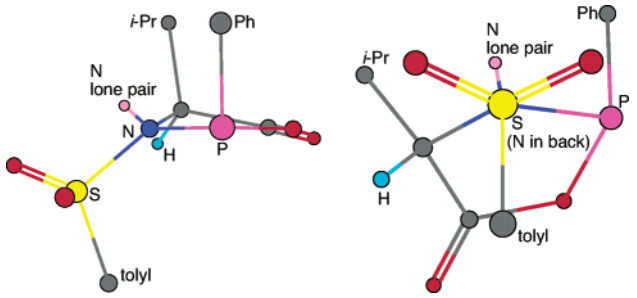


FIGURE 2. View of **9a** (partial structure) along the N−P−O−C plane and Newman projection of of **9a**, viewed down the S−N bond.

angles near 90° and is greater than 10 Hz for dihedral angles near 180° in tetrahedral 2-*oxo*-1,3,2-oxazaphospho*lidines* but ∼3−5 Hz in trivalent 1,3,2-oxazaphospho*rinanes* and 1,3,2-*diaza*phosphor*inanes*. The presence or absence of a phosphorus lone pair may influence the magnitude of this coupling constant, and the value of 3.7 Hz in **9a** for the P−N−C−H dihedral angle of 139° taken from the X-ray structure suggests that the six-membered ring phosphorinanes provide the better comparison since like **9a** and **9b** they are trivalent. The 1.4 Hz value in **9b** suggests that the dihedral angle is closer to 90° and so the ring hydrogen is increasingly axial compared to that in **9a**. This result is sensible in terms of avoiding steric interactions between the isopropyl and tolyl moiety, by making the isopropyl increasingly equatorial. The coupling constant in **13**, by this argument, cannot be directly compared, since now the phosphorus lone pair is tied up by coordination to tungsten. That is, the 3.4 Hz value in **13** might be considered to be low, if the proper comparison is to the 2-*oxo*-1,3,2-oxazaphospholidines which would suggest a dihedral angle closer to 90°, and so the bulky $W(CO)_5$ moiety not only results in the tolyl and isopropyl moieties adopting an s-cis conformation, but in forcing the isopropyl to be more equatorial, just as in **9b**.

Theoretical and Structural Survey of Sulfonamide Geometry. To understand the steric effect of the toluenesulfonyl moiety, it is necessary to know if the observed geometry is the norm. As shown in Figure 2, the sulfonamide moiety lies in a staggered conformation, with the tolyl roughly anti to the putative nitrogen lone pair (vide infra). There is no indication of any π-overlap between either of the sulfonyl oxygen double bonds and the nitrogen lone pair, and the pyramidalization of the nitrogen provides further evidence of the absence of π-delocalization of the lone pair, and also allows the steric interaction of the cis phenyl and isopropyl groups to be minimized. Stereoelectronic effects have been investigated in the six-membered ring cases of which **25** is representative,[67,78] including the anomeric effect which would be the stabilizing interaction of both the nitrogen and oxygen lone pairs with the P−Ph σ^* orbital when the phenyl is axial,[67,78] and nitrogen−phosphorus lone pair repulsion, which would complement the anomeric effect.[79] On this basis both the anomeric n−σ^* and the nitrogen−phosphorus lone pair-lone pair repulsion interactions would be operative since the electron-with-

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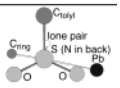
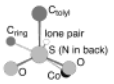
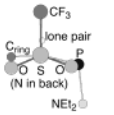
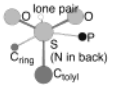
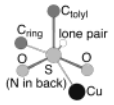
TABLE 1. Nitrogen Pyramidalization and Conformation about the S−N Bond in *N*-Sulfonyl-1,3,2-oxazaheterolidines

Compd	ΣN[a]	l.p. angle[b]	l.p.-N-S-C[c]	Newman Projection
27	360.0	90.7	10.5	
28	359.6	92.2	17.6	
29	359.5	92.3	28.2	
3a	358.5	94.0	21.8	
26	358.0	94.7	5.9	
30	357.4	95.4	169.7	
26	352.4	99.2	4.3	
9a	350.9	100.0	169.8	
31	350.2	100.5	38.0	
32	349.8	100.7	205.2	

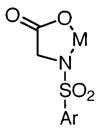
[a] Sum of the three angles at nitrogen. [b] Calculated angle for lone pair to be equiangular to each atom attached to nitrogen. [c] Counterclockwise angle starting from the lone pair on nitrogen.

drawing character of the toluenesulfonyl group is evidently an inductive effect. In the absence of π-effects, it is stereoelectronically comparable to the alkyl or aromatic groups seen in compounds such as **24** and **25**.

Theoretical study of sulfonamide geometry is an active area of research.[80−82] Some relevant conclusions are that (1) conjugation of the type present in planar amides is absent, (2) the nitrogen is pyramidal but the total energy is relatively insensitive to nitrogen hybridization and so X-ray structures may be somewhat misleading, (3) there is a 2-fold torsional barrier with a minimum at the conformation where the nitrogen lone-pair roughly eclipses the carbon attached to sulfur and the nitrogen substituents eclipse the sulfonyl oxygen atoms, and a secondary minimum in which the groups are staggered and the nitrogen lone pair is now anti to the carbon attached to sulfur, (4) these conformations interconvert by nitrogen inversion with a lower energy barrier than they would by rotation, and (5) X-ray structures reveal a range of conformations[83] with a preference for the secondary minimum energy conformation over the global minimum conformation.[82]

The geometry observed in **9a** as shown in Figure 2 is in fact the secondary minimum energy conformation. Inversion at nitrogen would clearly have the effect of pushing the axial phenyl and isopropyl groups closer together, while 180° rotation about the S−N bond would place all three ring substituents on the same side of the ring. Thus, there are good steric reasons for supposing that the observed sulfonamide conformation is preferred. However, inspection of models does not reveal any compelling reasons for preference of this diastereomer over the phosphorus epimer, particularly given the possibility of inversion at nitrogen.

A number of X-ray structures of *N*-sulfonamido-1,3,2-oxazametallacycles formed from α-amino acids have been carried out.[30,84−87] The geometry of the toluenesulfonyl moiety appears not to have been discussed previously. Data from our analysis of a few recent examples (**3a**, **27**−**32**) together with those of **9a** and **26** is collected in Table



3a M = IrCp*
27 M = Pb(H_2O)
28 M = Co(bipy)$_2$
29 M = Hg(bipy)$_2$
30 M = Cu(H_2O)$_3$
31 M = Cu(H_2O)$_2$
32 M = Cu(N-tosylalaninato)$^{2-}$

29: Ar = *o*-nitrophenyl
3a, **27**, **28**, **30** - **32**: Ar = *p*-tolyl

1. The position of the putative nitrogen lone pair was calculated as being equiangular from the three observed nitrogen substituents, and this provides a more intuitive measure of pyramidalization at nitrogen. Half of the amino acid examples are essentially planar at nitrogen, and interestingly, each of these exhibits a nearly eclipsed conformation, with the arene and lone pair syn periplanar,[88] which formally corresponds to the minimum energy eclipsed conformation. The more pyramidalized examples exhibit staggered conformations, and the tolyl and lone pair are anti periplanar in three of the four amino acid examples, which corresponds to the calculated secondary minimum energy conformation. Only the triflate example (**26**) is different, giving as noted above sulfonamide nitrogen atoms that differ in pyramidalization, and that exhibit the minimum energy eclipsed conformation, so it would be interesting to examine amino acid analogues, for which no X-ray structures are available. Given this modest range of amino acid analogues that exhibit similar conformations it is possible that the observed

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geometry is preferred not only for steric reasons but for electronic reasons as well.

We began this account by noting the similarities of ephedrine-derived heterocycles to the boron and iridium heterocycles **2** and **3** (Scheme 1). Addition of a ligand to boron yields **2b** in which the 1,3-substituents are mutually cis as well as mutually anti to the sulfonyl tolyl moiety, exactly as seen in **9a** albeit in contrast to **1a**. The stereochemistry in the boron case was considered to be controlled by a π-stacking interaction between the enone and the indole ring, but our results suggest the steric interaction with the intervening toluenesulfonyl moiety must be important in giving the 1,3-cis substitution. The absence of this bulky group allows the trans stereochemistry to predominate in **1a**. The iridium case is better compared to **13**, where addition of the bulky $W(CO)_5$ moiety to **9a** forces the toluenesulfonyl moiety to rotate placing all three substituents on the same side of the ring, much like **3b**.

Electron-Withdrawing Character of 9a. A byproduct of the design of this new type of ligand is the surprising discovery that it is apparently even more electron-withdrawing than the prototype sulfonylphosphoramide TosL (eq 1), on the basis of the high CO vibrational frequencies of the $W(CO)_5$ adducts. Comparative data for TosL and a variety of phosphorus ligands have been published,[20] and all three CO bands for **13**, the $W(CO)_5$ adduct of **9a**, are higher in frequency than the $W(CO)_5$ adducts of both $P(OMe)_3$ and TosL. As far as we are aware the electronic properties of the acetoxy functional group on phosphorus basicity and acidity have not been assessed, any more than that of the sulfonamido group before our report.[20] Last, when ^{31}P NMR data was examined for the presence of correlation with ligating properties,[20] only the tungsten−phosphorus coupling constant $^1J_{PW}$ had any utility. In this case, it is still highest for $P(OMe)_3$ (386 Hz) but now is second-highest for **9a** (346 Hz) with TosL yet lower (329 Hz), but it is unclear if the value reflects higher electron-withdrawing character for **9a** relative to TosL or is merely due to the oxygen atom bound to phosphorus.

Conclusions

Reaction of the inexpensive and readily available toluenesulfonyl derivative of valine 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; the method has been extended to give a C_2-symmetric chiral diphosphine as well. In contrast to the well-known ephedrine-derived 1,3,2-oxazaphospholidine, the ring substituents are cis to each other. High diastereoselectivity is only achieved with the relatively large isopropyl substituent of valine; hence the cis stereochemistry is apparently mediated by steric interactions with the intervening *N*-sulfonyl moiety, which evidently does not interact with the smaller methyl substituent of alanine. One unexpected feature of this work is the highly electron-withdrawing nature of **9a** as a transition-metal ligand. The sulfonamide moiety was expected to be electron-withdrawing, but the carboxylate seems to be even more so. This work extends the number of sulfonamide-substituted heterocycles that exhibit interesting and high stereoselectivity, so exploration of the steric space of this substituent appears to be in order. Future research will be directed toward extensions of this substituted amino acid methodology for the synthesis of new chiral phosphorus compounds.

Experimental Section

Compounds **7a**,**b**, **8a**, **9a**, **11a**, and **12a**,**b** were made by analogous procedures, although details of the purifications differ. The procedure for **9a** and the partial purification of **9b** is representative.

(2*S*,4*S*)- and (2*R*,4*S*)-4-Isopropyl-5-oxo-2-phenyl-3-*p*-toluenesulfonyl-1,3,2-oxazaphospholidine (9a,b). In an inert atmosphere glovebox under recirculating nitrogen was added a solution of Et_3N (1.31 g, 13.0 mmol) in 3 mL of toluene to a suspension of **6** (1.00 g, 3.69 mmol) in 20 mL of toluene to give at first a nearly clear solution after which a thick suspension precipitated out. Toluene was added (10 mL), and then a solution of $PhPCl_2$ (0.93 g, 5.17 mmol) in 5 mL of toluene was added dropwise. The mixture was allowed to stir for 3 h, and ^{31}P NMR analysis of a few drops of the solution in $CDCl_3$ at both 15 min and 3 h exhibited a 91:9 ratio of **9a**/**9b**. The mixture was then filtered through Celite, the solid was washed successively with ether and benzene, and then the solvent was removed in vacuo. The yellow crude product (1.53 g) was crystallized from 40 mL of ether at −35 °C to give 0.25 g of white crystals. Three more crystallizations from (successively) 20, 10, and 5 mL of ether at −35 °C gave a total of 0.79 g (57% yield) of **9a** contaminated by 0.5% of **9b**.

For more convenient large-scale synthesis, in a similar manner 4.15 mL (29.8 mmol, 3.5 equiv) of triethylamine, 2.31 g (8.51 mmol, 1 equiv) of **6**, and 2.13 g (11.9 mmol, 1.4 equiv) of $PPhCl_2$ were combined in 80 mL of ether, and the mixture was stirred at room temperature for 1 h. The suspended $Et_3NH^+Cl^-$ was removed by filtration and washed with 3 × 5 mL of ether. The solvent was removed from the combined ethereal solution in vacuo giving a pale yellow solid in a clear yellow oil. This residue was heated under vacuum at 50 °C for 1.5 h to remove unreacted $PPhCl_2$, resulting in formation of a pale yellow powder (2.91 g, 91% yield) consisting of a spectroscopically pure mixture of **9a** and **9b** in a 9.2:1 ratio. Fractional crystallization then proceeded as follows. Inside the glovebox, the 2.91 g of the mixture was dissolved in 45 mL of ether and the solution was allowed to stand at −35 °C for several days to give 1.62 g (50% yield) of small pale yellow crystals. The filtrate was stripped to dryness and the residue (1.30 g) was recrystallized from 20 mL of ether at −35 °C to give 0.33 g (10% yield) of a second crop of small white crystals. Recrystallization (0.89 g residue from 10 mL ether) gave a third crop of crystals (0.18 g, 6% yield). The first crop contained no detectable **9b**, the second crop contained 1% **9b**, and the third crop 9% of **9b**. The final residue (0.70 g) consisted of a 1.04:1 mixture of **9a**/**9b**. Major isomer **9a**: mp 129−131 °C; $[\alpha]^{27}_D = +84.83$ ($c = 2.426$, C_6H_6); IR ($CHCl_3$) 3023, 1791, 1360, 1164 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.84 (d, $J = 8.2$ Hz, 2H), 7.60 (m, 2H), 7.46 (m, 3H); 7.38 (d, $J = 8.2$ Hz, 2H), 3.53 (dd, $^3J_{HH} = 7.1$ Hz, $^3J_{PH} = 3.7$ Hz, 1H; assignment of the 7.1 Hz coupling constant to $^3J_{HH}$ was made by homonuclear decoupling of the 3.53 ppm signal by irradiation at δ 1.71), 2.47 (s, 3H); 1.71 (octet, $J = 6.9$ Hz, 1H), 0.94 (d, $J = 6.9$ Hz, 3H), 0.74 (d, $J =$

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6.8 Hz, 3H). ^{31}P NMR ($CDCl_3$) 133.0 ppm; ^{13}C NMR ($CDCl_3$) 171.3 (d, J_{PC}=12.4 Hz), 145.2, 139.6 (d, J_{PC} = 38.6 Hz), 134.7, 131.3, 130.3, 128.9 (d, J_{PC} = 4.4 Hz), 128.3 (d, J_{PC} = 18.8 Hz), 127.7 (d, J_{PC} = 4.8 Hz), 61.6, 31.5, 21.7, 19.7, 18.2 ppm. **Minor isomer 9b**: $[\alpha]^{27}_D$ = +93.8 (calculated from $[\alpha]^{27}_D$ = +88.65 (c = 2.14, C_6H_6) for a sample consisting of a 57.4:42.6 mixture of **9a**/**9b**); ^{1}H NMR ($CDCl_3$) δ 7.60 (m, 3H), 7.46 (m, 4H), 7.21 (d, J = 8.2 Hz, 2H), 4.06 (dd, $^3J_{HH}$=3.0 Hz, $^3J_{PH}$=1.4 Hz, 1H; assignment of the 3.0 Hz coupling constant to $^3J_{HH}$ was made both by simulation of the observed isopropyl CH multiplet and by homonuclear decoupling of the 4.06 ppm signal by irradiation at δ 2.50), 2.50 (d of septets, $J \approx$ 3.1, 6.8 Hz, 1H), 2.41 (s, 3H), 1.16 (d, J = 7.1 Hz, 3H), 0.64 (d, J = 6.7 Hz, 3H); ^{31}P NMR ($CDCl_3$) 136.7 ppm; ^{13}C NMR ($CDCl_3$) 171.0 (d, J_{PC} = 13.0 Hz), 144.5, 139.4 (d, J_{PC} = 50.4 Hz), 136.8, 132.6, 130.5 (d, J_{PC} = 25.8 Hz) 129.7, 128.9 (d, J_{PC} = 5.3 Hz) 127.1, 60.9, 29.2, 21.6, 18.0, 14.9 ppm. Anal. Calcd for $C_{18}H_{20}NO_4SP$: C, 57.29; H, 5.34; N, 3.71. Found: C, 57.15; H, 5.24; N, 3.64 for **9a**; C, 56.47; H, 5.23; N, 3.58 for the noncrystalline 57:43 mixture of **9a**/**9b** used above for the optical rotation.

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Supporting Information Available: Preparation of compounds **6**, **7a**,**b**, **8a**, **11a**, **12a**,**b**, and **13**; IR and ^{1}H, ^{13}C, and ^{31}P NMR spectra for compounds **4**−**9** and **11**−**13**; decoupling results for **9a**; the X-ray structure determination of **9a**; and tables of comparative NMR and X-ray data. This material is available free of charge via the Internet at http://pubs.acs.org.

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