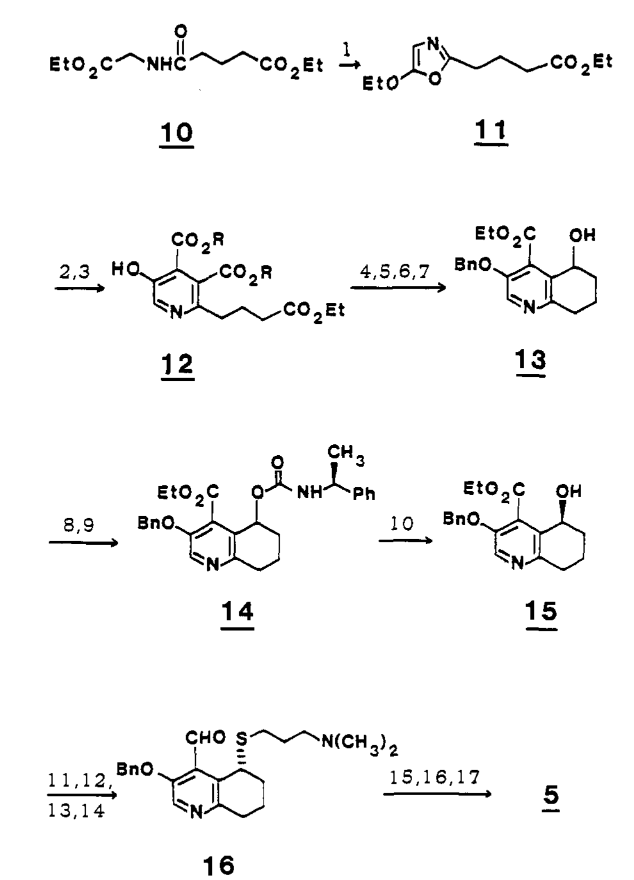
Scheme I[a]



[a] (1) P_2O_5, $CHCl_3$, reflux/54%; (2) maleic anhydride neat; (3) EtOH-saturated HCl_g, reflux/55%; (4) 1,3-diisopropyl-2-benzylisourea, neat, 110 °C/57%; (5) NaOEt-EtOH, PhH, reflux/99%; (6) 2.4 N HCl, EtOH, reflux/41%; (7) $NaBH_4$, EtOH, 5% $NaOH_{aq}$/99%; (8) carbonyldiimidazole, CH_2Cl_2, room temperature; (9) α-1-(−)-phenethylamine, PhH, $BF_3{\cdot}O_2Et$, reflux/58%; (10) MPLC; $HSiCl_3$, Et_3N, PhH, reflux/85%. (11) MsCl, Et_3N, CH_2Cl_2, 0 °C/99%; (12) $HS(CH_2)_3N(CH_3)_2$, NaH, THF, 0 °C-room temperature/82%; (13) LAH, THF, room temperature/58%; (14) $CrO_3{\cdot}Pyr_2$, CH_2Cl_2, room temperature; (15) $HONH_2$, NaOAc, H_2O, EtOH; (16) Zn, HOAc; H_2S, CH_3OH; CM25 sephadex/26% (steps 14–16); (17) 6 N HCl, reflux, 30 min; CM25 sephadex/82%.

Table I. Rates of Conversion of Ketimine to Aldimine in Methanol at "pH 4.00" (30.0 °C) and Optical Inductions in Product Amino Acids[a]

compd	amino acid[b]	k_{obsd}, s^{-1} [c]	rel rate[d]	% conversion[e]	ratio[f] D:L
3	alanine	3.3×10^{-4}	38		
4	alanine	8.7×10^{-6}	1		
5	alanine	1.5×10^{-3}	172	83	93:7
5	alanine			68	91:9
5	norvaline	9.5×10^{-4}	109	68	96:4
5	norvaline			35	95:5
5	tryptophan	1.0×10^{-4}	115	89	94:6
6	norvaline	4.4×10^{-5}	5	75	42:58

[a] Methanol solutions 0.16 mM in pyridoxamine derivative and in zinc acetate and 1.6 mM in ketoacid. Reactions were performed as in ref 4, with the "pH" as read on a glass electrode calibrated against aqueous buffer. [b] Obtained from the corresponding α-keto acid and analyzed as the dansyl derivative. [c] Standard deviations for all runs were <1% with duplicate runs within 10%. [d] Relative to 4 with pyruvic acid. [e] At the time of product isolation, relative to final equilibrium absorbance (UV). [f] Determined by chiral HPLC, as described in ref 4.

a maleic anhydride/oxazole Diels–Alder reaction[8] and a Dieckmann cyclization. The racemic intermediate **13** was resolved[9] by MPLC of its carbamate **14**, and the isomer whose carbamate eluted first was used for the synthesis of **5**[10] and of the related **6**.[10] The steps are detailed in Scheme I. To establish catalysis the compounds were then evaluated (as in our previous work[4]) for the rate at which the ketimines, formed with various α-keto acids in methanol, underwent isomerization to the corresponding aldimines. The data are listed in Table I. Furthermore, the product amino acids, from hydrolysis of the aldimines, were examined for chirality by chiral HPLC[11] of their dansyl derivatives (as in our previous work[4]). These data are also in Table I.

Catalysis by the basic side arm of **5** is clearly established by the significant rate accelerations in Table I relative to the rate for **6**, whose side arm is not basic. The chiral inductions by **5** are striking. Indeed the D/L enantiomeric ratio of 95:5 for norvaline, for instance, is a minimum value. We cannot yet exclude a few percent contamination of **5** by its enantiomer from incomplete resolution or partial racemization. The data in Table I do show that catalyzed racemization of the product amino acids, at the aldimine stage, is not a problem since enantioselectivity did not fall when reactions were allowed to run to higher conversions over longer times.

The mechanism involved in the chiral selectivity and the absolute configuration of **5** are established by the results with compound **6**. Its noncatalytic side chain helps shield the *re* face of the intermediate, leading to some preference for L-norvaline. Since **5** has the same absolute configuration as **6** but shows a strong D preference, **5** must be catalyzing proton transfer along the *re* face.

Even if the few percent nonspecific product from **5** proves to be genuine, rather than the result of optical contamination of **5** itself, the stereospecificity of these biomimetic transaminations is striking. It remains to be seen whether these or related systems will prove to be practical catalysts for chiral amino acid synthesis.

Acknowledgment. This work was supported by a grant from NIH.

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(9) Cf.: Pirkle, W. H.; Hauske, J. R. *J. Org. Chem.* **1977**, *42*, 1839–1844; **1977**, *42*, 2781–2782.
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(11) Lam, S.; Chow, F.; Karmen, A. *J. Chromatogr.* **1980**, *199*, 295–305.

Nucleophilic Attack of a Phosphorus–Phosphorus Double Bond

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Recently, several compounds have been isolated that exhibit double bonding between the heavier main-group elements.[1] Current attention has turned to examining the reactivities of these novel species. In the context of group 5A, it has been found that diphosphenes (RP=PR), phosphaarsenes (RP=AsR), and diarsenes (RAs=AsR) react with electrophiles such as HX,[2] peracids,[3] elemental sulfur,[4] halogens,[5] *t*-BuX radicals,[6] and metal

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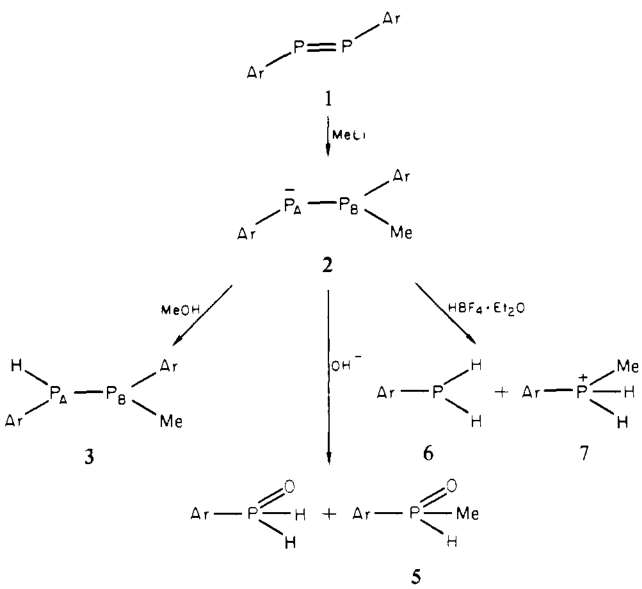
Scheme I[a]



[a] Ar = 2,4,6-(t-Bu)$_3$C$_6$H$_2$.

carbonyl fragments.[7] We present the first evidence that diphosphenes are reactive toward nucleophiles, thus greatly extending the synthetic utility of these compounds.

Typically, ArP=PAr (**1**)[5] (Ar = 2,4,6-(t-Bu)$_3$C$_6$H$_2$) was treated with an equimolar quantity of MeLi in THF at −78 °C affording a deep red solution. The presence of the novel anion **2** (Scheme I) was established unequivocally by the ^{31}P{^{1}H} NMR[8] spectrum, which comprised an AB pattern with δ_A −94.0, δ_B −43.0, and $^1J_{P_AP_B}$ = 408 Hz. Treatment of a solution of **2** with MeOH resulted in the new diphosphine **3**.[9] ^{31}P{^{1}H} NMR for **3**: AB pattern with δ_A −60.5, δ_B −45.0, $^1J_{P_AP_B}$ = 201 Hz. The corresponding proton-coupled spectrum was of the ABR$_3$X type with $^1J_{P_AH}$ = 207.0, $^2J_{P_BH}$ = 12.0, $^2J_{P_BMe}$ = 5.7, and $^3J_{P_AMe}$ = 1.0 Hz. Quenching of **2** with aqueous LiOH resulted in equimolar quantities of the known phosphine oxide **4**[10] and the new phosphine oxide **5**. ^{31}P NMR for **5**: δ +24.0 (d, $^1J_{PH}$ = 575 Hz). Compounds **4** and **5** presumably arise via Arbuzov rearrangements of initially formed Ar(R)POH (R = H, Me). Treatment of **2** with HBF$_4$·OEt$_2$ also resulted in P–P bond cleavage. With a 100% excess of HBF$_4$·OEt$_2$, the isolated products were ArPH$_2$ (**6**)[11] and the new phosphonium salt [ArP(Me)H$_2$][BF$_4$] (**7**). ^{31}P NMR for **7**: δ −28.5 (t of q, $^1J_{PH}$ = 521, $^2J_{PH}$ = 17 Hz).

Initially, the ^{31}P{^{1}H} spectra of mixtures of **1** and t-BuLi in THF were complex. However, after ~12 h at 25 °C, the spectra anticipated for the anion [ArP–P(Ar)(t-Bu)]$^-$ (**8**) were detected.[12] ^{31}P{^{1}H} NMR for **8**: AB pattern, δ_A −57.0, δ_B +72.5, $^1J_{P_AP_B}$ = 325 Hz. The diphosphine, Ar(H)P–P(Ar)(t-Bu) (**9**), plus traces of **6** and Ar(t-Bu)PH (**10**) were detected upon treatment of the reaction mixture with MeOH. ^{31}P{^{1}H} NMR for **9**: AB pattern with δ_A −78.9, δ_B +42.4, $^1J_{P_A,P_B}$ = 325 Hz. ^{31}P NMR for **10**: δ −72.0 (d, $^1J_{PH}$ = 218 Hz).

The reaction of **1** with K[s-Bu$_3$BH] in THF is slow (~4 days at 25 °C), and the only species detectable by ^{31}P NMR is the diphosphine Ar(H)P–P(H)(Ar) (**11**).[11] In turn, **11** disproportionates to **1** and **6** upon standing ~2 weeks at 25 °C.[13] It was not possible to detect the anion, [ArP–P(H)(Ar)]$^-$ (**12**) in these reaction mixtures; moreover, treatment of **11** with n-BuLi resulted in ArPHLi (**13**)[11] rather than **12**.

Further studies of nucleophilic reactivity are in progress.

Acknowledgment. The authors are grateful to the National Science Foundation (Grant CHE-8205871) and the Robert A. Welch Foundation for generous financial support.

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(8) All ^{31}P NMR spectra measured at a spectrometer frequency of 32.384 MHZ.

(9) Al new compounds except the anions **2** and **8** were characterized by high-resolution mass spectroscopy and/or elemental analysis. These and other details will be furnished in a subsequent full paper.

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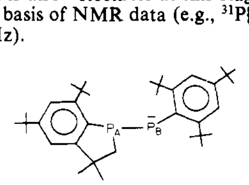
(12) A second anion is also detectable at this stage. We assign the following structure on the basis of NMR data (e.g., ^{31}P{^{1}H} NMR δ_A +7.0, δ_B −116.0, $^1J_{P_AP_B}$ = 458 Hz).



(13) A somewhat similar reaction, viz., 5(PhPH)$_2$ ⇄ 5PhPH$_2$ + (PhP)$_5$, has been observed by Albrand and Gagnaire (Albrand, J. P.; Gagnaire, J. P. *J. Am. Chem. Soc.* **1972**, *94*, 8630).

Novel Cyclophane-Based Hosts with Functionally Neutral Cavities

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Boxlike molecules,[1] those containing cavities capable of accommodating molecular guests, are of current interest as a structural basis for constructing enzymelike catalysts. In this context we wish to report the novel naphthalenophanes **2-C_2** and **2-σ**, molecular boxes having cavities of 5.2 × 5.6 × 3.7 Å. We describe here their synthesis and structure and evidence for their well-defined cavity and interaction with guest molecules via insertion into the hole.

Cyclization precursors **1a–d**[2] were synthesized from 5-methylnaphthalene-1,4-diol as in Scheme I. Cyclization of **1b** (Cu(OAc)$_2$, pyridine, 40 °C, 60–90 min) gave in 25–40% yield a separable mixture of two cyclophanes **2b-σ** and **2b-C_2** (both mp >300 °C) in a ratio of 1.5–9:1. Conversion of the two proton methylene singlets of **1b** to AB quartets in their proton NMR spectra[3] was consistent with formation of a rigid cagelike structure.

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(2) All new compounds are characterized by elemental analysis and appropriate spectra.

(3) **2b-σ**: ^{1}H NMR (CDCl$_3$, 270 MHz) 8.04 (2 H, d, J = 8.6 Hz, H8), 7.89 (2 H, br s, H5), 7.60 (2 H, d of d, J = 8.6, 1.3 Hz, H7), 7.46 (4 H, d, J = 8.3 Hz, tosyl), 7.29 (4 H, d, J = 8.3 Hz, tosyl), 6.94 (4 H, s, phenylene), 6.58 (4 H, s, H2/H3), 5.22 (2 H, d, J = 15.5 Hz, ArCH$_2$N), 4.94 (2 H, d, J = 16.8 Hz, ArOCH$_2$), 4.92 (2H, d, J = 16.4 Hz, ArOCH$_2$'), 4.87 (2 H, d, J = 16.8 Hz, ArOCH$_2$), 4.82 (2 H, d, J = 16.4 Hz, ArOCH$_2$'), 4.63 (2 H, d, J = 15.5 Hz, ArCH$_2$N), 2.49 (6 H, s, tosyl CH$_3$). **2b-C_2**: ^{1}H NMR (CDCl$_3$, 270 MHz) 8.12 (2 H, d, J = 8.8 Hz, H8); 7.81 (2 H, d of d, J = 8.8, 1.1 Hz, H7), 7.73 (2 H, br s, H5), 7.42 (4 H, d, J = 8.3 Hz, tosyl), 7.33 (4 H, d, J = 8.3 Hz, tosyl), 6.93 (4 H, s, phenylene), 6.67 (2 H, d, J = 8.4 Hz, H2), 6.55 (2 H, d, J = 8.4 Hz, H3), 5.43 (2 H, d, J = 15.1 Hz, ArCH$_2$N), 4.98 (2 H, d, J = 17.4 Hz, ArOCH$_2$), 4.90 (2 H, d, J = 17.4 Hz, ArOCH$_2$), 4.88 (2 H, d, J = 17.2 Hz, ArOCH$_2$'), 4.75 (2 H, d, J = 17.2 Hz, ArOCH$_2$'), 4.32 (2 H, d, J = 15.1 Hz, ArCH$_2$N), 2.48 (6 H, s, tosyl CH$_3$). (All compounds **2a–d-σ** and **2a–d-C_2** melt >300 °C.)

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