mL) and extracted with EtOAc (3 × 50 mL). The extracts were dried ($MgSO_4$) and concentrated to give a pale yellow oil, which was purified by flash column chromatography on silica gel (hexane–EtOAc, 1:1) to give (+)-**33** (594 mg, 90%) as a colorless oil: $[\alpha]^{23}_D$ +60.4° (*c* 5.90, $CHCl_3$).

**(2*S*,5*S*)-*N*-[(Benzyloxy)carbonyl]-5-butyl-2-(4-oxobutyl)pyrrolidine [(+)-34].** To a stirred solution of oxalyl chloride (227 mg, 1.79 mmol) in $CH_2Cl_2$ (3 mL) at −78 °C was added dropwise a solution of DMSO (211 mg, 2.70 mmol) in $CH_2Cl_2$ (3 mL), and the mixture was stirred for 30 min at −78 °C. To this mixture was added dropwise a solution of (+)-**33** (149 mg, 0.447 mmol) in $CH_2Cl_2$ (3 mL), and stirring was continued. After 1 h, a solution of $Et_3N$ (364 mg, 3.60 mmol) in $CH_2Cl_2$ (3 mL) was added to the mixture, and the mixture was warmed to ambient temperature and stirred for 15 min. After addition of water (5 mL), the mixture was diluted with $Et_2O$ (150 mL). The organic phase was separated, washed with water (50 mL) and then brine (50 mL), and dried ($MgSO_4$). Evaporation of the solvent and purification of flash column chromatography on silica gel (hexane–EtOAc, 4:1) gave (+)-**34** (140 mg, 94%) as a colorless oil: $[\alpha]^{23}_D$ +65.5° (*c* 1.52, $CHCl_3$).

**(3*S*,5*S*,8a*S*)-3-Butyl-5-methyloctahydroindolidine [(+)-Indolizidine 195B, (+)-1].** Compound (+)-**34** was transformed into (+)-**1** in the same manner as described for the preparation of (−)-**1**: $[\alpha]^{24}_D$ +97.7° (*c* 0.18, MeOH) [lit[4a] $[\alpha]^{16}_D$ +65° (*c* 0.41, MeOH), lit.[4b] $[\alpha]^{24}_D$ +98.0° (*c* 0.30, MeOH)].

**(3*S*,5*S*,8a*S*)-3-Butyl-5-propyloctahydroindolidine [(+)-Indolizidine 223AB, (+)-2].** Compound (+)-**34** was transformed into (+)-**2** in the same manner as described for the preparation of (−)-**2**: $[\alpha]^{24}_D$ +101.1° (*c* 0.36, hexane).

**(3*S*,5*R*,8a*S*)-5-(3-Hydroxypropyl)-3-butyloctahydroindolidine [(+)-Indolizidine 239AB, (+)-3].** Compound (+)-**34** was transformed into (+)-**3** in the same manner as described for the preparation of (−)-**3**: $[\alpha]^{27}_D$ +82.7° (*c* 0.48, MeOH).

**Acknowledgment.** We are indebted to Dr. J. W. Daly, National Institutes of Health, for IR and MS spectra of natural indolizidine **239CD**.

# Preparation of (2*S**,5*S**)-2,5-Dibenzylphospholanic Acid†

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The cheletropic cycloaddition of $[ClP(N\text{-}i\text{-}Pr_2)]^+AlCl_4^-$ with 1-substituted dienes at 0 °C afforded 1-(*N*,*N*-diisopropylamino)-1-chloro-2-alkyl-$\Delta^3$-phospholenium tetrachloroaluminates. The stereoselectivity of these reactions ranged from 5:1 to 100:0. Hydrolysis of the cycloadducts afforded a diastereomeric mixture of 1-(*N*,*N*-diisopropylamino)-1-oxo-2-alkyl-$\Delta^3$-phospholenes. The ratio of the $\Delta^3$-phospholene amides differed significantly from the ratio of the intermediate $\Delta^3$-phospholenium ions, implying that the hydrolysis reactions occurred via five-coordinate phosphoranes which underwent pseudorotation prior to elimination of HCl. Hydrogenation of the $\Delta^3$-phospholene amides afforded saturated phospholane amides which underwent regioselective deprotonation and subsequent stereospecific alkylation reactions with alkyl halides. 1-(*N*,*N*-Diisopropylamino)-1-oxo-2,5-dimethyl- and -2,5-dibenzylphospholanes (**10a** and **10b**) were converted by acid-promoted hydrolysis to (2*R**,5*R**)-2,5-dimethyl- and (2*S**,5*S**)-2,5-dibenzylphospholanic acid (**12a** and **12b**), respectively.

Recently, the potential utility of trans-2,5-disubstituted derivatives of phospholane as chiral reagents in organic[1,2] and organometallic[3,4] chemical transformations has been recognized by ourselves[1] and three other groups.[2-4] We report herein an improved method for the preparation of (2*R**,5*R**)-2,5-dimethyl- and (2*S**,5*S**)-2,5-dibenzylphospholanic acids (**12a** and **12b**).

(*N*,*N*-Diisopropylamino)dichlorophosphine has been shown to undergo chloride ion abstraction by aluminum trichloride to form phosphenium ion[5] **1**. Cowley[6] and Baxter[7] have independently demonstrated that phosphenium ions undergo cycloaddition reactions with 1,3-dienes. We have found that cheletropic cycloaddition of the (*N*,*N*-diisopropylamino)chlorophosphenium ion **1** with *trans*-piperylene at 0 °C afforded a 5:1 mixture of diastereomeric *P*-chloro-*P*-(*N*,*N*-diisopropylamino)-$\Delta^3$-phospholenium tetrachloroaluminates. Aqueous hydrolysis of the phospholenium ions at 0 °C afforded a 2:1 mixture of 1-(*N*,*N*-diisopropylamino)-1-oxo-$\Delta^3$-phospholenes **5a** and **5b**. These compounds possess a phosphinic amide moiety, and such entities will hereafter be referred to as $\Delta^3$-phospholene amides. In a similar fashion *trans*-1-benzyl-1,3-butadiene[8] reacted with phosphenium ion **1** at 0 °C to afford a 10:1 mixture of *P*-chloro-*P*-(*N*,*N*-diisopropylamino)-$\Delta^3$-phospholenium ions which upon aqueous hydrolysis afforded a 3:1 mixture of $\Delta^3$-phospholene amides **6a** and **6b**. (*E*)-1-*tert*-Butyl-1,3-butadiene[9] underwent cycloaddition with **1** to afford a single $\Delta^3$-phospholenium ion. The $\Delta^3$-phospholenium ion then underwent a stereospecific hydrolysis to afford 2-*tert*-butyl-$\Delta^3$-phospholene amide **7a**.

The ratio of diastereomeric *P*-chloro-$\Delta^3$-phospholenium tetrachloroaluminates **3** and **4** obtained in the cheletropic

† Dedicated to Professor David A. Evans.

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**Table I. $^{31}P$ NMR Shifts of Δ3-Phospholenium Ions[a]**

| compd | major isomer | minor isomer | rel ratio |
|---|---|---|---|
| R = Me | 104.0 | 100.2 | 4.7:1 |
| R = $CH_2Ph$ | 103.1 | 98.8 | 10:1 |
| R = *t*-Bu | 93.9 | | 100:0 |

[a] Spectra taken in $CH_2Cl_2$, peaks reported in ppm downfield of external 85% $H_3PO_4$.

reactions was determined by direct $^{31}P$ NMR analysis of aliquots of each reaction mixture. The chemical shifts of the intermediate phospholenium ions appear in Table I. It has not yet been possible to unambiguously assign the relative stereochemical relationship of the vicinal stereogenic centers in the $\Delta^3$-phospholenium ions **3** and **4**. Hence, we do not know for certain which is the major and which is the minor isomer.

The $\Delta^3$-phospholene amide diastereomers **5a–b** and **6a–b** were readily separated by flash chromatography on silica gel. The combined yield of diastereomers produced in each reaction was good, being on the order of 65%. The isolated yield of **6a** was 51%, and that of **5a** was 43%. The relative configuration of the phosphorus and carbon stereogenic centers in **5a–b** and **6a–b** was determined by a combination of chemical and spectral means. The carbon–carbon double bond of each pure diastereomer in each series was catalytically reduced over 5% rhodium on carbon. The average yield for this transformation was 95%.

Deprotonation of 1-(*N*,*N*-diisopropylamino)-1-oxo-2-alkylphospholane **9a** or **9b** under kinetic conditions with lithium diisopropylamide followed by alkylation with methyl iodide or benzyl bromide, respectively, afforded phosphinamides **11a** and **11b**. The $^{13}C$ spectra (Table II) of these materials was instructive. The presence of only five resonances in the case of **11a** and nine resonances for **11b** was highly suggestive that these compounds possessed a plane of symmetry, and hence were meso diastereomers. A similar deprotonation/alkylation sequence carried out on phosphinamide **8a** resulted in the formation of 2,5-dimethylphosphinamide **10a** and regioisomer **13** in a ratio of 2.8:1. The isolated yield of the desired isomer **10a** was 55%. The identity of isomer **10a** relative to **13** was established by consideration of $^{13}C$ chemical shifts (Table II), phosphorus–carbon coupling constants ($J_{PC}$, Table III) and phosphorus–hydrogen coupling constants of the two compounds. The most diagnostic piece of spectral evidence for structure **13** was the multiplicity of the hydrogen atoms of the geminal methyl groups attached to C2. The hydrogens of the methyl groups were diastereotopic, resonating at 1.19 and 1.06 ppm, respectively. The hydrogens of each methyl group were coupled only to phosphorus ($J_{PH}$ = 13.2 and 14.8 Hz, respectively), behavior consistent with the geminal disubstitution pattern of **13**. The appearance of 9 resonances in the $^{13}C$ spectrum of **10a** was fully consistent with a trans-2,5-disubstitution pattern. Further evidence for the proposed structure of **10a** was provided by its hydrolysis to the C2 symmetric phosphinic acid **12a**. Since inter- or intramolecular exchange of the phosphinic acid O*H* proton in **12a** is fast on the NMR time scale,[1] the $^{13}C$ spectrum (Table II) of **12a** displayed only three resonances.

The deprotonation/alkylation behavior of phosphinamide **8b** resembled that of **8a**. Deprotonation of **8b** with lithium tetramethylpiperidide (LTMP) in THF at −78 °C under standard kinetic conditions, followed by addition

**Table II. $^{13}C$ Resonances of Phosphinamides[a]**

| compd | C2 | C3 | C4 | C5 | Me[d] | $CH_2$(Ph)[d] | Ph | NCH | $CH(CH_3)CH_3$ |
|---|---|---|---|---|---|---|---|---|---|
| **11a** | 30.3 | 29.6 | 29.6 | 30.3 | 12.9, 12.9 | | | 45.1 | (23.3) 23.3 |
| **11b** | 38.4 | 26.8 | 26.8 | 38.4 | | 34.0, 34.0 | 141.2, 128.9 128.3, 125.9 | 45.2 | (23.3) 23.3 |
| **10a** | 36.7[b] | 32.7[c] | 30.1[c] | 31.3[b] | 14.1, 11.8 | | | 45.2 | (23.42) 23.37 |
| **10b** | 44.6[b] | 30.3[c] | 27.6[c] | 39.4[b] | | 35.8, 33.9 | 141.6[e], 140.6[e] 128.7, 128.5 128.4[f], 126.2 126.0 | 45.7 | (23.9) 23.6 |
| **12a** | 31.7 | 30.5 | 30.5 | 31.7 | 12.9, 12.9 | | | | |
| **12b** | 39.3 | 27.9 | 27.9 | 39.3 | | 34.3, 34.3 | 139.8[e], 128.6 128.3, 126.1 | | |
| **13** | 36.3 | 23.7 | 40.1 | 26.1 | 23.0, 18.8 | | | 46.4 | (23.9) 23.9 |
| **14** | 45.3 | 18.4 | 33.5 | 25.7 | | 40.0, 38.5 | 138.6[e], 138.1[e] 131.1, 130.5 128.1, 127.5 128.1, 127.5 126.4, 125.9 | 46.7 | (28.8) 23.2 |

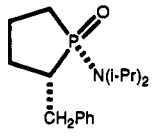
[a] Spectra were recorded in $CDCl_3$; chemical shifts are reported downfield of internal tetramethylsilane. [b] Within a given row, these values may be interchanged. [c] Within a given row, these values may be interchanged. [d] Listed in the order of groups attached to C2 and then C5. It is assumed that the group oriented syn to the diisopropylamino moiety experiences an upfield steric compression shift. [e] Ipso carbon of phenyl ring. [f] This resonance has highest intensity, probably due to an identical chemical shift of a carbon type on each aromatic ring.

**Table III. $J_{PC}$ Coupling Constants of Phosphinamides[a-c]**

| compd | C2 | C3 | C4 | C5 | Me[d] | $CH_2$Ph | Ph(ipso)[d] | PNC |
|---|---|---|---|---|---|---|---|---|
| **11a** | 81.5 | 13.3 | 13.3 | 81.5 | 3.4, 3.4 | | | 4.3 |
| **11b** | 78.6 | 13.2 | 13.2 | 78.6 | | 0 | 12.3 | 4.4 |
| **10a** | 82.4 | 11.1 | 11.5 | 78.1 | 2.3, 2.6 | | | 4.4 |
| **10b** | 79.4 | 11.1 | 11.5 | 76.4 | | 0, 0 | 13.7, 14.5 | 4.5 |
| **12a** | 91.6 | 13.5 | 13.5 | 91.6 | 3.1, 3.1 | | | |
| **12b** | 89.7 | 13.2 | 13.2 | 89.7 | | 1.4 | 13.1 | |
| **13** | 86.5 | 6.6 | 19.7 | 76.4 | 0, 7.8 | | | 3.4 |
| **14** | 82.3 | 8.2 | 19.0 | 75.7 | | 0, 0 | 4.0, 12.6 | 3.2 |

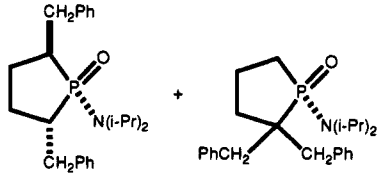
[a] Same meaning as in Table II. [b] Coupling constants are reported in Hz. [c] The coupling constants reported for C2, C3, C4, C5 refer to the chemical shifts cited for these resonances in Table II. [d] Same meaning as in Table II.

of benzyl bromide in the usual manner, produced dibenzyl phosphinamide **14** exclusively. When deprotonation was effected with the less hindered base LDA, both the desired phosphinamide **10b** and regioisomer **14** were produced in a ratio of 1:4.5. When *n*-BuLi was used as the base, the ratio of **10b** to **14** inverted, **10b** now being favored over **14** by a 4:1 margin. The isolated yield of *trans*-2,5-dibenzyl-*N*,*N*-diisopropylphospholanic amide (**10b**) was 70%.




**8b**

1. Base, -78°C
2. $PhCH_2Br$, -78°C




**10b** **14**

| | | |
|---|---|---|
| LTMP | 0 | 100 |
| LDA | 18 | 82 |
| *n*-BuLi | 80 (70% isolated) | 20 |

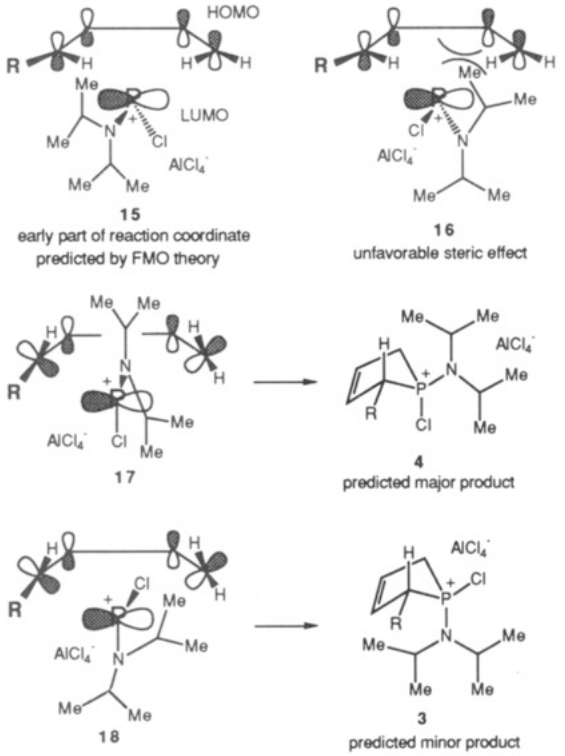
One-bond phosphorus–carbon coupling constants are very large, and in the 1-oxophospholane series[1] are typically 75–80 Hz. Compound **10b** displayed resonances at 44.6 and 39.4 ppm with coupling constants of 82.4 and 78.1 Hz, respectively. These chemical shifts are typical for methine-type carbons adjacent to the phosphinyl moiety in phospholanes.[1] Isomer **14** displayed resonances at 45.3 and 25.7 ppm with large $^1J_{PC}$ values, 82.3 and 75.7 Hz, respectively. Each resonance possessed a positive intensity in the APT spectrum of **14**, implying they were either quaternary- or methylene-type carbons. The chemical shifts observed for C2 and C5 in isomer **14** suggest that C2 is quaternary and C5 is a methylene carbon. Further evidence consistent with this analysis was provided by the hydrolysis of phospholane amide **10b** to the known[1] (2S*,5S*)-2,5-dibenzylphospholanic acid (**12b**).

## Discussion

A regular increase in stereoselection was observed in the cycloaddition of phosphenium ion **1** with dienes **2a–c** as the steric bulk of the substituent attached to the diene increased. Thus, the reaction was moderately stereoselective with piperylene, became highly selective with (*E*)-1-benzylbutadiene and stereospecific with (*E*)-1-*tert*-butylbutadiene. The cycloadditions appear to proceed to completion within 1-h at 0 °C. The cheletropic cycloaddition of a 1,3-diene with a phosphenium ion is believed to proceed via a pericyclic transition state in what is assumed to be a concerted process.[6,7] The cycloaddition process thus appears to involve a disrotatory motion of the termini of the $\pi$ system.[10] In thinking about allowed

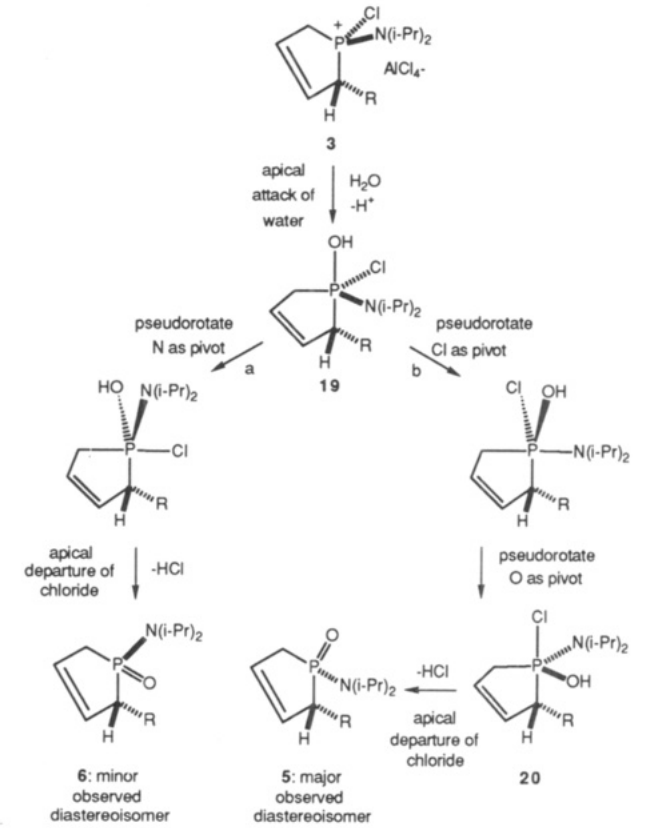
(10) The calculated frontier molecular orbitals for phosphenium cations appear in: Cowley, A. H.; Cushner, M. C.; Lattman, M.; McKee, M. L.; Szobota, J. S.; Wilburn, J. C. *Pur. Appl. Chem.* **1980**, *52*, 789. A detailed analysis for the isolobal $SO_2$–butadiene cycloaddition appears in: Fleming I. *Frontier Orbitals and Organic Chemical Reactions*; Wiley: New York, 1976; pp 95–97.

transition-state geometries for the cyclization reaction, it seems reasonable that the sterically preferred path should resemble **15** wherein the smaller substituent attached to




phosphorus, the chlorine atom, is pointed toward the diene and the bulky diisopropylamine moiety is pointed away from the diene. The major isomer formed in the cycloaddition reaction should be **4**. The $\Delta^3$-phospholenium ions appear to be formed under kinetic control. This premise is supported by the observation that the initial ratio of phospholenium ions **3b** and **4b** was found to be retained when a sample was maintained at 25 °C for 48 h.

Nucleophilic substitution reactions at phosphorus can occur by three mechanistic types: $S_N1(P)$, $S_N2(P)$, and addition–elimination.[11] Since the substrates of the hydrolysis reactions are phosphonium salts **3** and **4** bearing a formal positive charge at phosphorus, an $S_N1(P)$ process involving intermediates bearing a formal $2^+$ charge on phosphorus seems unlikely. In the cases of dienes **2a** and **2b**, the ratio of hydrolysis products **5a–b** and **6a–b** were significantly different from the ratio of intermediate $\Delta^3$-phospholenium tetrachloroaluminates. Therefore, a strict $S_N2(P)$ process did not occur. This suggests that the hydrolysis reaction proceeds by an addition–elimination mechanism.[12] Consider hydrolysis of the presumed major diastereomer **3**. Apical approach of water should produce a phosphorane of trigonal bipyramidal geometry, which by ring strain considerations[13] will force the $\Delta^3$-phospholene moiety to span apical–equatorial positions. Water should approach the phosphonium salt **3** under "steric approach control". The least sterically hindered path of approach produces intermediate **19**. Phosphorane **19** may then partition itself among two competing pathways. Pathway a involves a single Berry pseudorotation[14]




using N as the pivot. Chlorine is expelled from an apical position producing diastereomer **6** with net retention of configuration at phosphorus. Alternatively, phosphorane **19** may undergo two sequential pseudorotations to afford **20**. Apical departure of chloride from **20** affords diastereomer **6** with net inversion at the phosphorus stereogenic center. It is important to note that since phosphorus is incorporated into a five-membered ring these three pseudorotations are geometrically allowed via square pyramidal transition states and represent the most direct paths from phosphonium salt to phosphinamides. A similar dual reaction pathway exists for the diastereomeric phosphonium salt **4**.

The alkylation reactions of 1-oxo-2-alkyl phospholane amides **9a** and **9b** were stereospecific. This is in direct contrast to the observed alkylation behavior of the analogous phosphinic esters.[1] Regiospecific deprotonation was effected with a hindered lithium amide base under kinetic conditions. Deprotonation occurred selectively at the methylene rather than the methine position adjacent to the phosphinyl moiety, as expected on steric grounds.[15] The deprotonation behavior of phosphinamides **8a** and **8b** was unexpected and is difficult to rationalize. The key structural element necessary for a highly stereoselective alkylation adjacent to phosphorus appears to be a large difference in steric bulk of groups directly attached to phosphorus. Thus, regardless of the configuration of the stereogenic center at C5 in carbanion **21** ($R_1 = CH_2Ph$ or Me, $R_2 = H$; $R_1 = H$, $R_2 = Me$ or $CH_2Ph$) the anion always alkylated anti to the bulky diisopropylamine moiety attached to phosphorus. Apparently, in the phosphinic

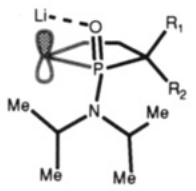
(11) Emsley, J.; Hall, D. *The Chemistry of Phosphorus*; Harper and Row: New York, 1976; Chapter 8.

(12) Marsi, K. L. *J. Am. Chem. Soc.* **1969**, *91*, 4724. Marsi, K. L.; Burns, F. B.; Clark, R. T. *J. Org. Chem.*, **1972**, *37*, 238. Marsi, K. L. *J. Org. Chem.* **1975**, *40*, 1779. Gorenstein, D. G. *J. Am. Chem. Soc.* **1973**, *95*, 8060.

(13) Trippett, S. *Phosphorus Sulfur* **1976**, *1*, 89.

(14) Berry, R. S. *J. Chem. Phys.* **1960**, *32*, 933. Westheimer, F. H. *Acc. Chem. Res.*, **1968**, *1*, 70. Mislow, K. *Acc. Chem. Res.* **1970**, *3*, 321. DeBruin, K. E.; Peterson, J. R. *J. Org. Chem.* **1972**, *37*, 2272. Hudson, R. F.; Brown, C. *Acc. Chem. Res.* **1972**, *5*, 204. Trippett, S. *Pure Appl. Chem.* **1974**, *74*, 545.

(15) Compare to selection rules for kinetic deprotonation of ketones, summarized in: Evans, D. A. In Morrison, J. D., Ed. *Asymmetric Synthesis*; Academic; New York, 1984; Vol. 3, Chapter 1.



21

esters (**21**, replace N(*i*-Pr)$_2$ with O-*i*-Pr), the alkoxy moiety is not large enough to create an appreciable steric effect in the transition state of the alkylation reaction, since in those cases stereoselectivity was a modest 1.5–3:1.[1]

We had anticipated that phosphinamides **10a** and **10b** would serve as ideal precursors of the corresponding phospholanic acids since phosphinic amides are, in general, readily hydrolyzed.[16] In the event, the hydrolysis required heating the phosphinic amides in concentrated HCl for several hours. The phosphinic acids themselves are very robust and were isolated in good yield. It is conceivable that the reluctance of amides **10a** and **10b** toward hydrolysis was due to steric congestion in the vicinity of the phosphinyl moiety which must necessarily undergo nucleophilic attack by water. Presumably, a significant amount of the steric hindrance originates from the diisopropylamino moiety directly attached to phosphorus.

We have thus established a general method for the preparation of *trans*-2,5-dialkyl derivatives of phospholanic acid. Studies directed toward further elucidating the mechanistic details and improving the preparative aspects of the reactions are underway and will be reported in due course.

## Experimental Section

**General.** Melting points are uncorrected. Abbreviations for NMR data are s = singlet, d = doublet, m = multiplet, dd = doublet of doublets. Coupling constants are reported in Hz. $^1$H and $^{13}$C chemical shifts are reported relative to internal tetramethylsilane, and $^{31}$P chemical shifts are reported relative to external 85% $H_3PO_4$. In cases where more than one isomeric product was generated in a reaction, an analytical ratio of unpurified material was determined by capillary GC on a 30-m × 0.32-mm fused silica column coated with DB-5. Dichloromethane, diisopropylamine, 2,2,6,6-tetramethylpiperidine, and all dienes were distilled from calcium hydride. Aluminum trichloride (Aldrich) was sublimed before use. Flash chromatography was carried out on Kieselgel 60 (230–400 mesh), and all reactions except hydrolyses of **10a–b** were run under a nitrogen atmosphere. Microanalyses were performed by MHW laboratories, Phoenix, Az.

**Cheletropic Cycloaddition/Hydrolysis.** A solution of $Cl_2PN(i\text{-}Pr_2)_2$ (1.8 mmol) in $CH_2Cl_2$ (3 mL) was added dropwise to a suspension of $AlCl_3$ (256.9 mg, 1.1 equiv) in $CH_2Cl_2$ (6 mL). The mixture was stirred at rt for 30 min, during which time the $AlCl_3$ dissolved. The resultant solution was cooled to 0 °C, and an icecold solution of the freshly distilled diene (1.75 mmol) in $CH_2Cl_2$ (3 mL) was added dropwise. After 4 h, the reaction solution was slowly cannulated onto a rapidly stirring ice-cold mixture of aqueous saturated $NaHCO_3$ and 0.2 N EDTA (1:1 by volume, 10 mL total). The mixture was stirred for 6 h at 0 °C, stored in the refrigerator overnight, and then extracted several times with $CH_2Cl_2$. The organic extracts were dried ($Na_2SO_4$), filtered, and concentrated, and the residual oil was purified by flash chromatography on silica gel, typically using a gradient of EtOAc → 2.5:97.5 → 5:95 → 7.5:92.5 → 10:90 MeOH–EtOAc. In certain cases, the $\Delta^3$-phospholene amides were purified further by bulb-to-bulb distillation.

**(1*R**,2*R**)-1-(*N*,*N*-Diisopropylamino)-1-oxo-2-methyl-$\Delta^3$-phospholene (5a)**: 42.9%; IR (NaCl, neat) 1180 (s), 680 cm$^{-1}$ (s); $^1$H NMR (300 MHz, $CDCl_3$) δ 5.93 (s, 1 H, =CH), 5.84 (s, 1 H, =CH), 3.31 (m, 2 H, 2NCH, $J_{HH}$ = 6.8, $J_{PH}$ = 15.7), 2.73 (m, 1 H, PC*H*($CH_3$), $J_{HH}$ = 7.6, $J_{PH}$ = 12.6), 2.51 (d, 2 H, $PCH_2$, $J$ = 11.0), 1.31 (d, 6 H, 2NCH(C*H*$_3$)$CH_3$, $J_{HH}$ = 6.8), 1.28 (d, 6 H, 2NCH($CH_3$)C*H*$_3$, $J_{HH}$ = 6.8), 1.21 (dd, 3 H, PCH(C*H*$_3$), $J_{HH}$ = 7.6, $J_{PH}$ = 16); $^{31}$P NMR (121.4 MHz, $CDCl_3$) δ 70.3; $^{13}$C NMR (75 MHz, $CDCl_3$) δ 135.4 (d, =*C*H, $J_{PC}$ = 17.7), 125.2 (d, =CH, $J_{PC}$ = 12.2), 46.0 (d, PNC, $J_{PC}$ = 3.6), 38.4 (d, P*C*H($CH_3$), $J_{PC}$ = 85.4), 32.1 (d, $PCH_2$, $J_{PC}$ = 75.8), 23.2 (NCH(*C*H$_3$)$CH_3$), 22.8 (NCH($CH_3$)*C*H$_3$), 13.3 (d, PCH(*C*H$_3$), $J_{PC}$ = 3.6); MS (CI, $NH_3/CH_4$) *m/e* 216 ($MH^+$, base peak). Anal. Calcd for $C_{11}H_{22}NOP\cdot H_2O$: C, 56.63; H, 10.37. Found: C, 56.85; H, 10.34.

**(1*R**,2*R**)-1-(*N*,*N*-Diisopropylamino)-1-oxo-2-methyl-$\Delta^3$-phospholene (5b)**: 21.6%; IR (NaCl, neat) 1180 cm$^{-1}$ (s); $^1$H NMR (300 MHz, $CDCl_3$) δ 5.76–5.84 (m, 1 H, =CH), 5.56–5.74 (m, 1 H, =CH), 3.30 (m, 2 H, 2NCH, $J_{HH}$ = 6.8, $J_{PH}$ = 16.6), 2.81–3.04 (m, 3 H, PCH and $PCH_2$), 1.274 (d, 6 H, 2NCH-(*C*H$_3$)$CH_3$, $J_{HH}$ = 6.8), 1.267 (d, 6 H, 2NCH($CH_3$)C*H*$_3$, $J$ = 6.8); $^{31}$P NMR (121.4 MHz, $CDCl_3$) δ 64.4; $^{13}$C NMR (75 MHz, $CDCl_3$) δ 135.1 (d, =CH, $J_{PC}$ = 17.3), 125.3 (d, =CH, $J_{PC}$ = 12.7), 45.3 (d, NCH, $J_{PC}$ = 3.8), 34.7 (d, P*C*H($CH_3$), $J_{PC}$ = 82.8), 31.7 (d, $PCH_2$, $J_{PC}$ = 80.0), 22.7 (NCH(*C*H$_3$)$CH_3$), 22.6 (NCH($CH_3$)*C*H$_3$), 12.5 (d, PCH(*C*H$_3$); MS (CI, $NH_3/CH_4$) *m/e* 216 ($MH^+$, base peak). Anal. Calcd for $C_{11}H_{22}NOP\cdot H_2O$: C, 56.63; H, 10.37. Found: C, 56.46; H, 10.30.

**(1*S**,2*R**)-1-(*N*,*N*-Diisopropylamino)-1-oxo-2-benzyl-$\Delta^3$-phospholene (6a)**: 51.5%; mp 69–70 °C; IR ($CHCl_3$), 3050 (w); 1150 cm$^{-1}$ (s); $^1$H NMR (300 MHz, $CDCl_3$) δ 7.21–7.35 (m, 5 H, Ph), 5.82–5.90, and 5.94–6.02 (each a m, total of 1 H, =CH), 5.70–5.78 and 5.82–5.90 (each a m, total of 1 H, =CH), 3.38 (m, 2 H, 2NCH, $J_{HH}$ = 6.8, $J_{PH}$ = 16.1), 3.18–3.27 (m, 1 H, C*H*HPh), 2.90–3.03 (m, 1 H, CH*H*Ph), 2.56 (dd, 2 H, $J$ = 11.0, 1.4, $PCH_2$), 2.38–2.48 (m, 1 H, PC*H*($CH_2$Ph), 1.36 (d, 6 H, 2NCH(C*H*$_3$)$CH_3$, $J_{HH}$ = 6.8), 1.33 (d, 6 H, 2NCH($CH_3$)C*H*$_3$, $J_{HH}$ = 6.8); $^{31}$P NMR (121.4 MHz, $CDCl_3$) δ 68.8; $^{13}$C NMR (75 MHz, $CDCl_3$) δ 139.8 (d, $J_{PC}$ = 14.6), 132.9 (d, $J_{PC}$ = 17.5), 128.5, 128.4, 126.2, 126.0 (d, $J_{PC}$ = 12.3), 46.3 (d, PNC, $J_{PC}$ = 4.2), 45.7 (d, P*C*H$CH_2$Ph, $J_{PC}$ = 83.5), 34.8 (*C*$H_2$Ph), 32.5 (d, $PCH_2$, $J_{PC}$ = 76.1), 23.5 (NCH(*C*H$_3$)$CH_3$, 23.1 (NCH($CH_3$)*C*H$_3$); MS (CI, *i*-$C_4H_{10}$) *m/e* 292 ($MH^+$, base peak).

**(1*S**,2*R**)-1-(*N*,*N*-Diisopropylamino)-1-oxo-2-benzyl-$\Delta^3$-phospholene (6b)**: 13.3%; IR ($CHCl_3$), 1180 cm$^{-1}$ (s); $^1$H NMR (300 MHz, $CDCl_3$) δ 7.18–7.35 (m, 5 H, Ph), 5.83–5.89 and 5.92–6.02 (each a m, total of 1 H, =CH), 5.71–5.79 and 5.83–5.89 (each a m, total of 1 H, =CH), 3.27 (m, 2 H, 2NCH, $J_{HH}$ = 6.6, $J_{PH}$ = 17), 3.17–3.26 (m, 1 H, C*H*HPh), 2.35–2.76 (m, 4 H), 1.26 (d, 6 H, 2NCH(C*H*$_3$)$CH_3$, $J_{HH}$ = 6.6), 1.22, (d, 6 H, 2NCH-($CH_3$)C*H*$_3$, $J_{HH}$ = 6.6); $^{31}$P NMR (121.4 MHz, $CDCl_3$) δ 63.1; $^{13}$C NMR (75 MHz, $CDCl_3$) δ 140.8 (d, $J_{PC}$ = 11.5), 133.4 (d, $J_{PC}$ = 17.6), 129.3, 128.7, 126.7 (d, $J_{PC}$ = 12.9), 126.4, 46.0 (d, PNC, $J_{PC}$ = 4.6), 42.9 (d, P*C*H$CH_2$Ph, $J_{PC}$ = 81.0), 34.7 (*C*$H_2$Ph), 32.8 (d, $PCH_2$, $J_{PC}$ = 80), 23.2 (PNCH(*C*H$_3$)$CH_3$); MS (CI, *i*-$C_4H_{10}$) *m/e* 292 ($MH^+$, base peak). Anal. Calcd for $C_{17}H_{26}NOP$: C, 70.08; H, 8.99. Found: C, 68.26; H, 8.73.

**(1*R**,2*S**)-1-(*N*,*N*-Diisopropylamino)-1-oxo-2-*tert*-butyl-$\Delta^3$-phospholene (7a)**: 46%; IR ($CHCl_3$), 1160 cm$^{-1}$ (s); $^1$H NMR (300 MHz, $CDCl_3$) δ 5.96–6.11 (m, 2 H, 2 =CH), 3.42 (m, 2 H, 2NCH, $J_{HH}$ = 6.7, $J_{PH}$ = 15.5), 2.75 (d, 1 H, PCH(*t*-Bu)), 2.40–2.51 (m, 2 H, $PCH_2$), 1.31 (d, 6 H, 2NCH(C*H*$_3$)$CH_3$, $J_{HH}$ = 6.7), 1.28 (d, 6 H, 2NCH($CH_3$)C*H*$_3$, $J_{HH}$ = 6.7), 1.16 (s, 9 H, C(C*H*$_3$)$_3$); $^{31}$P NMR (121.4 MHz, $CDCl_3$) δ 72.4; $^{13}$C NMR (75 MHz, $CDCl_3$) δ 131.8 (d, $J_{PC}$ = 17.6), 125.2 (d, $J_{PC}$ = 10.3), 57.3 (d, $J_{PC}$ = 80.2), 46.8 (PNC), 34.1 (d, $J_{PC}$ = 71.1), 32.1 (d, *C*(CH$_3$)$_3$, $J_{PC}$ = 4.6), 29.2 (d, C(*C*H$_3$)$_3$, $J_{PC}$ = 6.3), 23.3 (NCH($CH_3$)$CH_3$), 22.5 (NCH($CH_3$)*C*H$_3$); MS (CI, *i*-$C_4H_{10}$) *m/e* 258 ($MH^+$, base peak). Anal. Calcd for $C_{14}H_{28}NOP$: C, 65.34; H, 10.97. Found: C, 65.40; H, 10.72.

**Reduction Procedure.** A suspension of 5% Rh/C (75 mg) in THF (10 mL) was prereduced under a balloon of hydrogen for 20–24 h. A solution of $\Delta^3$-phospholene amide **6a** (152.9 mg) in THF (4 mL) was added via syringe and then the syringe rinsed with an additional 2 mL of THF and the rinse added to the reaction vessel. After 4–6 h the mixture was filtered through Celite, the Celite pad washed thoroughly with THF, the filtrate concentrated and chromatographed on 1 in. × 5 in. of silica gel eluting with 5:95 → 7.5:92.5 → 10:90 MeOH–EtOAc gradient. This process afforded **9a** as a colorless oil: 146.4 mg, 94.9%.

(16) Haake, P.; Koizumi, T. *J. Am. Chem. Soc.* **1972**, *95*, 8073.

**(1*R**,2*R**)-1-(*N*,*N*-Diisopropylamino)-1-oxo-2-methylphospholane (8a)**: 94%; bp 145 °C (0.15 mmHg); IR ($CHCl_3$), 1190 $cm^{-1}$ (s); $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 3.30 (m, 2 H, 2NCH, $J_{HH}$ = 7.2, $J_{PH}$ = 15.8), 2.08–2.24 (m, 1 H, PC*H*($CH_3$)), 1.74–2.04 (m, 6 H), 1.32 (d, 6 H, 2NCH($CH_3$)$CH_3$), 1.27 (d, 6 H, 2NCH-($CH_3$)$CH_3$), 1.14 (dd, 3 H, PCH($CH_3$), $J_{HH}$ = 7.2, $J_{PH}$ = 14.1); $^{31}P$ NMR (121.4 MHz, $CDCl_3$) $\delta$ 70.9; $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 46.4 (d, PNC, $J_{PC}$ = 3.8), 36.2 (d, P*C*H($CH_3$), $J_{PC}$ = 85.7), 33.9 (d, $J_{PC}$ = 13.8), 27.1 (d, $PCH_2$, $J_{PC}$ = 76.4), 23.6 (NC($CH_3$)$_2$), 21.3 (d, $J_{PC}$ = 8.4), 14.3 (d, PCH($CH_3$), $J_{PC}$ = 2.1); MS (CI, $NH_3/CH_4$) *m/e* 218 ($MH^+$, base peak). Anal. Calcd for $C_{11}H_{24}NOP$: C, 60.80; H, 11.13. Found: C, 60.69; H, 11.33.

**(1*S**,2*R**)-1-(*N*,*N*-Diisopropylamino)-1-oxo-2-methylphospholane (9a)**: 95%; bp 125 °C (0.1 mmHg); IR ($CHCl_3$) 1160 $cm^{-1}$ (s); $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 3.28 (m, 2 H, 2NCH, $J_{HH}$ = 5.6, $J_{PH}$ = 16.1), 1.49–2.10 (m, 7 H), 1.27 (d, 6 H, 2NCH-($CH_3$)$CH_3$, $J_{HH}$ = 5.6), 1.26 (d, 6 H, 2NCH($CH_3$)$CH_3$, $J_{HH}$ = 5.6), 1.18 (dd, 3 H, PCH($CH_3$), $J_{HH}$ = 6.6, $J_{PH}$ = 14.6); $^{31}P$ NMR (121.4 MHz, $CDCl_3$) $\delta$ 67.7; $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 45.2 (d, PNC, $J_{PC}$ = 4.8), 31.8 (d, $J_{PC}$ = 14.6), 31.5 (d, $J_{PC}$ = 83.5), 27.3 (d, $J_{PC}$ = 80.5), 23.0 (NCH($CH_3$)$CH_3$), 22.9 (NCH($CH_3$)$CH_3$), 21.8 (d, $J_{PC}$ = 7.6), 11.8 (d, PCH($CH_3$), $J_{PC}$ = 2.8); MS (CI, $NH_3/CH_4$) 218 ($MH^+$, base peak). Anal. Calcd for $C_{11}H_{24}NOP\cdot H_2O$: C, 56.15; H, 10.67. Found: C, 56.90; H, 10.67.

**(1*R**,2*S**)-1-(*N*,*N*-Diisopropylamino)-1-oxo-2-benzylphospholane (8b)**: 95%; bp 170 °C (1 mmHg; IR ($CHCl_3$) 1180 $cm^{-1}$ (s); $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.15–7.35 (m, 5 H, Ph), 3.35 (m, 2 H, 2NCH, $J_{HH}$ = 6.6, $J_{PH}$ = 16.2), 3.18–3.26 (m, 1 H, C*H*HPh), 2.31–2.43 (m, 1 H, CH*H*Ph), 1.70–2.23 (m, 7 H), 1.38 (d, 6 H, 2NCH($CH_3$)$CH_3$, $J_{HH}$ = 6.6), 1.32 (d, 6 H, 2NCH-($CH_3$)$CH_3$, $J_{HH}$ = 6.6); $^{31}P$ NMR (121.4 MHz, $CDCl_3$) $\delta$ 69.2; $^{13}C$ NMR (75 MHz, $CDCl_3$) 140.5 (d, $J_{PC}$ = 14.7), 128.4, 128.3, 126.0, 46.0 (d, PNC, $J_{PC}$ = 4.3), 43.5 (d, P*C*HCH$_2$Ph, $J_{PC}$ = 82.4), 34.9 ($CH_2$Ph), 30.7 (d, $J_{PC}$ = 13.7), 27.0 (d, $PCH_2$, $J_{PC}$ = 76.4), 23.3 (NCH($CH_3$)$CH_3$), 23.2 (NCH($CH_3CH_3$), 20.7 (d, $J_{PC}$ = 8.2); MS (CI, *i*-$C_4H_{10}$) *m/e* 294 ($MH^+$, base peak). Anal. Calcd for $C_{17}H_{28}NOP$: C, 69.60; H, 9.62. Found: C, 69.79; H, 9.74.

**(1*S**,2*S**)-1-(*N*,*N*-Diisopropylamino)-1-oxo-2-benzylphospholane (9b)**: 95%; IR ($CHCl_3$) 1160 $cm^{-1}$ (s); $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.15–7.32 (m, 5 H, Ph), 3.28 (m, 2 H, 2NCH, $J_{HH}$ = 6.8, $J_{PH}$ = 16.6), 3.08–3.18 (m, 1 H, C*H*HPh), 2.61–2.72 (m, 1 H, CH*H*Ph), 1.73–2.10 (m, 5 H), 1.43–1.63 (m, 2 H), 1.28 (d, 12 H, 2NCH($CH_3$)$CH_3$, $J_{HH}$ = 6.8); $^{31}P$ NMR (121.4 MHz, $CDCl_3$) $\delta$ 66.7; $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 141.2 (d, $J_{PC}$ = 13.0), 128.6, 128.2, 125.8, 45.3 (d, PNC, $J_{PC}$ = 4.6), 39.2 (d, P*C*HCH$_2$Ph, $J_{PC}$ = 81.5), 33.6 ($CH_2$Ph), 29.2 (d, $J_{PC}$ = 15.1), 27.6 (d, $PCH_2$, $J_{PC}$ = 80.1), 23.2 (NCH($CH_3$)$CH_3$), 23.0 (NCH($CH_3$)$CH_3$), 21.8 (d, $J_{PC}$ = 7.9); MS (CI, *i*-$C_4H_{10}$) *m/e* 294 ($MH^+$, base peak). Anal. Calcd for $C_{17}H_{28}NOP$: C, 69.60; H, 9.62. Found: C, 69.44; H, 9.67.

**Alkylation Procedure.** A 0.2 M solution of lithium diisopropylamide (1.4–1.8 equiv) in THF was prepared at 0 °C and cooled to −78 °C. A 0.25 M solution of the phosphinamide in THF was added dropwise, and the resultant solution was stirred at −78 °C for 1 h. A 2 M solution of either methyl iodide or benzyl bromide (5 equiv) was then added. The solution was stirred at −78 °C for 1 h, quenched with 1 N HCl (6 mL), and warmed to rt and the THF removed on a rotary evaporator. The residue was extracted 4× with $CH_2Cl_2$, dried ($Na_2SO_4$), filtered, and concentrated and the resultant oil purified by flash chromatography on silica gel.

For alkylation reactions in which *n*-BuLi was employed as base, *n*-BuLi in hexanes (1.7 equiv) was added to THF at −78 °C to generate the cold *n*-BuLi solution. The deprotonation, alkylation, workup, and purification methods were exactly the same as described above.

**(2*R**,5*R**)-1-(*N*,*N*-Diisopropylamino)-2,5-dimethyl-1-oxophospholane (10a)**: 55%; mp 73–75 °C; IR ($CHCl_3$) 1153 $cm^{-1}$ (s); $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 3.12 (m, 2 H, 2NCH, $J_{HH}$ = 6.6, $J_{PH}$ = 16.2), 1.82–2.18 (m, 4 H), 1.61–1.74 (m, 1 H), 1.32–1.43 (m, 1 H), 1.22 (d, 6 H, 2NCH($CH_3$)$CH_3$, $J_{HH}$ = 6.6), 1.17 (d, 6 H, 2NCH($CH_3$)$CH_3$, $J_{HH}$ = 6.6), 1.13 (dd, 3 H, PCH($CH_3$), $J_{HH}$ = 6.4, $J_{PH}$ = 15.0), 1.11 (dd, 3 H, PCH($CH_3$), $J_{HH}$ = 4.9, $J_{PH}$ = 15.5); $^{31}P$ NMR (121.4 MHz, $CDCl_3$) $\delta$ 68.8; $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 45.2 (d, PNC, $J_{PC}$ = 4.4), 36.7 (d, PC, $J_{PC}$ = 82.4), 32.7 (d, $J_{PC}$ = 11.1), 31.3 (d, PC, $J_{PC}$ = 78.1), 30.1 (d, $J_{PC}$ = 11.5), 14.1 (d, PCH($CH_3$), $J_{PC}$ = 2.3), 11.8 (d, PCH($CH_3$), $J_{PC}$ = 2.6); MS (CI, $NH_3/CH_4$) *m/e* 232 ($MH^+$, base peak). Anal. Calcd for $C_{12}H_{26}NOP$: C, 62.31; H, 11.33. Found: C, 62.26; H, 11.34.

**(2*S**,5*S**)-1-(*N*,*N*-Diisopropylamino)-2,5-dibenzyl-1-oxophospholane (10b)**: 70.4%; mp 127–135 °C; IR (NaCl) 1170 $cm^{-1}$ (s); $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.18–7.35 (m, 10 H, 2Ph), 3.31 (m, 2NCH, $J_{PH}$ = 16.5, $J_{HH}$ = 6.6), 3.21–3.30 (m, 1 H, C*H*HPh), 3.10–3.20 (m, 1 H, C*H*HPh), 2.65–2.80 (m, 1 H, CH*H*Ph), 2.35–2.45 (m, 1 H, CH*H*Ph), 2.14–2.32 (m, 1 H), 1.77–2.04 (m, 4 H), 1.39 (d, 6 H, 2NCH($CH_3$)$CH_3$, $J_{HH}$ = 6.6), 1.35 (d, 6 H, 2NCH-($CH_3$)$CH_3$, $J_{HH}$ = 6.6), 1.05–1.12 (m, 1 H); $^{31}P$ NMR (121.4 MHz, $CDCl_3$) $\delta$ 66.2; $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 141.1 (d, $J_{PC}$ = 13.7), 140.6 (d, $J_{PC}$ = 14.5), 128.7, 128.5, 128.4, 126.2, 126.0, 45.7 (d, PNC, $J_{PC}$ = 4.5), 44.6 (d, PC, $J_{PC}$ = 79.4), 39.4 (d, PC, $J_{PC}$ = 76.4), 35.8 ($CH_2$Ph), 33.9 ($CH_2$Ph), 30.3 (d, $J_{PC}$ = 11.1), 27.6 (d, $J_{PC}$ = 11.5), 23.9 (NCH($CH_3$)$CH_3$), 23.6 (NCHCH$_3$)$CH_3$); MS (CI, $NH_3/CH_4$) *m/e* 384 ($MH^+$, base peak). Anal. Calcd for $C_{24}H_{34}NOP$: C, 75.16; H, 8.94. Found: C, 75.02; H, 8.77.

***meso*,*cis*-1-(*N*,*N*-Diisopropylamino)-2,5-dimethyl-1-oxophospholane (11a)**: 94%; bp 140 °C (0.3 mmHg); mp 72.5–75 °C; IR ($CHCl_3$) 1157 $cm^{-1}$ (s); $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 3.23 (m, 2 H, 2NCH, $J_{HH}$ = 6.7, $J_{PH}$ = 16.3), 1.70–1.85 (m, 4 H), 1.50–1.60 (m, 2 H), 1.23 (d, 12 H, 2NCH($CH_3$)$CH_3$, $J_{HH}$ = 6.7), 1.12 (dd, 6 H, 2PCH($CH_3$), $J_{HH}$ = 7.0, $J_{PH}$ = 14.6); $^{31}P$ NMR (121.4 MHz, $CDCl_3$) $\delta$ 67.2; $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 45.1 (d, PNC, $J_{PC}$ = 4.3), 30.3 (d, PC, $J_{PC}$ = 81.2), 29.6 (d, $J_{PC}$ = 13.3), 23.3 (NCH($CH_3$)$_2$), 12.9 (d, 2PCH($CH_3$), $J_{PC}$ = 3.4); MS (CI, $NH_3/CH_4$) *m/e* 232 ($MH^+$, base peak). Anal. Calcd for $C_{12}H_{26}NOP$: C, 62.31; H, 11.33. Found: C, 62.12; H, 11.20.

***meso*,*cis*-1-(*N*,*N*-Diisopropylamino)-2,5-dibenzyl-1-oxophospholane (11b)**: 86.4%, mp 142–144 °C. IR ($CHCl_3$) 1190 $cm^{-1}$ (s); $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.15–7.34 (m, 10 H, 2Ph), 3.26 (m, 2 H, 2NCH, $J_{HH}$ = 6.6, $J_{PH}$ = 16.7), 3.10–3.21 (m, 2 H, 2C*H*HPh), 2.62–2.76 (m, 2 H, 2CH*H*Ph), 1.96 (m, 2PCH), 1.60–1.72 (m, 4 H), 1.25 (d, 12 H, 2 NCH($CH_3$)$CH_3$, $J_{HH}$ = 6.6); $^{31}P$ NMR (121.4 MHz, $CDCl_3$) $\delta$ 65.3; $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 141.2 (d, $J_{PC}$ = 12.3), 128.9, 128.3, 125.9, 45.2 (d, PNC, $J_{PC}$ = 4.4), 38.4 (d, 2PC, $J_{PC}$ = 78.6), 34.0 (2$CH_2$Ph), 26.8 (d, $J_{PC}$ = 13.2), 23.3 (2NCH($CH_3$)$_2$); MS (CI, *i*-$C_4H_{10}$) *m/e* 384 ($MH^+$, base peak). Anal. Calcd for $C_{24}H_{34}NOP$: C, 75.16; H, 8.94. Found: C, 75.19; H, 8.82.

**1-(*N*,*N*-Diisopropylamino)-2,2-dimethyl-1-oxophospholane (13)**: 20%; bp 115 °C (5 mmHg): mp 78–82 °C; IR ($CHCl_3$) 1180 $cm^{-1}$ (s); $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 3.32 (m, 2 H, 2NCH, $J_{HH}$ = 6.8, $J_{PH}$ = 15.4), 1.44–2.02 (m, 6 H), 1.26 (d, 6 H, 2NCH-($CH_3$)$CH_3$, $J_{HH}$ = 6.8), 1.24 (d, 6 H, 2NCH($CH_3$)$CH_3$, $J_{HH}$ = 6.8), 1.19 (d, 3 H, PC($CH_3$)$CH_3$, $J_{PH}$ = 13.2), 1.06 (d, 3 H, PC($CH_3$)$CH_3$, $J_{PH}$ = 14.8); $^{31}P$ NMR (121.4 MHz, $CDCl_3$) $\delta$ 70.1; $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 46.4 (d, PNC, $J_{PC}$ = 3.4), 40.1 (d, $J_{PC}$ = 19.7), 36.3 (d, P$C(CH_3)_2$, $J_{PC}$ = 86.5), 26.1 (d, $PCH_2$, $J_{PC}$ = 76.4), 23.9, 23.7, 23.6, 23.0, 18.8 (d, $J_{PC}$ = 7.8); MS (CI, $NH_3/CH_4$) *m/e* 232 ($MH^+$, base peak). Anal. Calcd for $C_{12}H_{26}NOP$: C, 62.31; H, 11.33. Found: C, 62.15; H, 11.12.

**1-(*N*,*N*-Diisopropylamino)-2,2-dibenzyl-1-oxophospholane (14)**: 17.8%; mp 100–103.5 °C; IR ($CHCl_3$) 1180 $cm^{-1}$ (s); $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.10–7.27 (m, 10 H, 2Ph), 3.37 (m, 2 H, 2NCH, $J_{HH}$ = 6.6, $J_{PH}$ = 15.4), 3.23–3.40 (m, 1 H, C*H*HPh), 2.85–2.95 (m, 3 H, 3 benzylic H), 1.86–1.98 (m, 1 H), 1.53–1.77 (m, 4 H), 1.36 (d, 6 H, 2NCH($CH_3$)$CH_3$, $J_{HH}$ = 6.6), 1.31 (d, 6 H, 2NCH-($CH_3$)$CH_3$, $J_{HH}$ = 6.6), 0.90–1.02 (m, 1 H); $^{31}P$ NMR (121.4 MHz, $CDCl_3$) $\delta$ 74.2; $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 138.6 (d, $J_{PC}$ = 4.0), 138.1 (d, $J_{PC}$ = 12.6), 131.1, 130.5, 128.1, 127.5, 126.4, 125.9, 46.7 (d, PNC, $J_{PC}$ = 3.2), 45.3 (d, PC, $J_{PC}$ = 82.3), 40.0 ($CH_2$Ph), 38.5 ($CH_2$Ph), 33.5 (d, $J_{PC}$ = 19.0), 25.7 (d, $PCH_2$, $J_{PC}$ = 75.7), 23.8 (NCH($CH_3$)$CH_3$), 23.2 (NCH($CH_3$)$CH_3$), 18.4 (d, $J_{PC}$ = 8.2); MS (CI, *i*-$C_4H_{10}$) *m/e* 384 ($MH^+$, base peak). Anal. Calcd for $C_{24}H_{34}NOP$: C, 75.16; H, 8.94. Found: C, 74.99; H, 8.97.

**Hydrolysis Procedure.** The phosphinamide (50–75 mg) was dissolved (for **10a**) or suspended (for **10b**) in concd HCl (3 mL). The resulting solution or suspension was heated at 117–120 °C for 30 (for **10a**) or 144 h (for **10b**). The cooled mixture was extracted 4× with $CH_2Cl_2$. The organic extracts were dried ($Na_2SO_4$), filtered, and concentrated and the residue purified by bulb-to-bulb distillation.

**(2*R**,5*R**)-2,5-Dimethylphospholanic acid (12a)**: 68%; bp 230 °C 0.02 mmHg); IR ($CHCl_3$) 1183 $cm^{-1}$ (s); $^1H$ NMR (300

MHz, $CDCl_3$) δ 9.60 (bs, 1 H, OH), 2.06–2.17 (m, 1 H), 1.92–2.05 (m, 1 H), 1.77–1.89 (m, 2 H, 2PCH), 1.20–1.41 (m, 2 H), 1.19 (dd, 6 H, $2PCH(CH_3)$, $J_{HH}$ = 7.0, $J_{PH}$ = 15.6); $^{31}P$ NMR (121.4 MHz, $CDCl_3$) δ 77.7; $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 31.7 (d, 2PC, $J_{PC}$ = 91.6), 30.5 (d, $2CH_2$, $J_{PC}$ = 13.5), 12.9 (d, $2PCH(CH_3)$, $J_{PC}$ = 3.1); MS (CI, $NH_3/CH_4$) *m/e* 149 ($MH^+$, base peak). Anal. Calcd for $C_6H_{13}O_2P$: C, 48.65; H, 8.84. Found: C, 48.42; H, 8.68.

**(2S*,5S*)-2,5-Dibenzylphospholanic acid (12b):**[1] 70%.

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# Pseudorotational, Conformational, and NOE Studies of Pentacovalent Spirophospholenes Derived from Ephedrine and α-Diketones

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Variable-temperature NMR studies showed the chiral pentacovalent dioxaphospholenes **1–3** to be pseudorotationally stable below 60 °C. $\Delta G^{\ddagger}_{PSDRTN}$ for **1** and **2** were determined to be 22.0 ± 2.1 kcal/mol and 33.0 ± 2.6 kcal/mol, respectively. The $\Delta G^{\ddagger}_{PSDRTN}$ for **2** is the largest value reported to date. $^1H$ NMR nuclear Overhauser effect studies on the major isomer of **1** confirmed that it was **1a** and not **1b**. Conformational analysis of the $^1H$ NMR data indicated a twist-envelope conformation for the ephedrine-derived five-membered ring.

## Introduction

Phosphorus-containing compounds (generally phosphates and phosphonates) are of biological interest as enzyme modulators, inhibitors, and active-site probes.[3] Many of these compounds also have medicinal value as antivirals,[4] antibiotics,[5] and antiacidosis agents,[6] and for the treatment of calcification diseases.[7] Proposed modes of action of these compounds generally include attack on the phosphorus by a nucleophile (e.g., an enzyme or water) to form a trigonal bipyramidal pentacovalent phosphorus transition state or intermediate, which can then either trigger the enzyme into action or short-circuit it by failure of the appropriate ligand on phosphorus to cleave (generally a P–C bond).[3]

In order to adequately model these transition states and predict reactivities of the organophosphorus compounds, pseudorotational and conformational studies of trigonal bipyramidal pentacovalent organophosphorus compounds have seen renewed interest.[8] Berry pseudorotation is the accepted mechanism whereby the apical ligands on pentacovalent organophosphorus compounds in a trigonal bipyramidal geometry are exchanged for the equatorial ones.[9] Recent emphasis has been on cAMP models,[8f–h] where it has been proposed that activated cAMP involves a pentacovalent phosphorus species in a trigonal bipyramidal geometry. The studies of these systems have extensively involved X-ray crystallographic, and more recently, solution NMR spectroscopic investigations of these models. The conformations of the six-membered rings in these pentacovalent phosphorus-containing models were also determined.

In connection with our interest in the utilization of pentacovalent (P(V)) organophospholenes as synthetic reagents,[10] we are investigating the production of chiral, and therefore configurationally stable, P(V) phospholenes. In order to produce configurationally defined P(V) compounds, pseudorotation must be prohibited at reaction

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