amide **25** was desilylated to **26** and then saponified to furnish **27**. Closure of **27** to the 18-membered ring of **1** proved to be surprisingly difficult (cf. ref 3), the only reagent to effect this macrolactonization being one based on dicyclohexylcarbodiimide.[17] Application of this protocol to **27** gave geodiamolide A (**1**) in low yield, identical by comparison of melting point, optical rotation, and IR, ^{1}H NMR, and mass (FAB) spectra with a sample of natural material.

Acknowledgment. We are grateful to Dr. Percy S. Manchand, Hoffmann-LaRoche, Inc., for a sample of natural geodiamolide A and to Professor R. B. Bates, University of Arizona, for helpful advice. Financial support was provided by the National Institutes of Health (AI 10965).

(17) Boden, E. P.; Keck, G. E. *J. Org. Chem.* **1985**, *50*, 2394.

Supplementary Material Available: $[\alpha]_D$, IR, ^{1}H NMR, ^{13}C NMR, and mass spectral data are provided for **5–9**, **12–14**, and **16–27** (7 pages). Ordering information is given on any current masthead page.

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Articles

Syntheses of Vinyl Silane Phosphates: Novel Synthetic Intermediates

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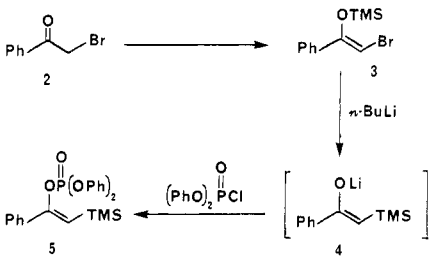
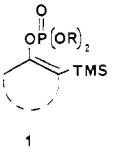
A number of procedures have been developed for the synthesis of vinyl silane phosphates (VSP's), a new type of functional group bearing trialkylsilyl and diaryl (or dialkyl) phosphate groups on adjacent sp^2 carbons. α-Silyl ketone enolates, accessible in a variety of ways, react with phosphorochloridates to give VSP's. Alternatively, in select cases it is possible to trap a β-lithiated vinyl phosphate with a trialkylsilyl chloride to obtain the VSP. Because vinyl silanes are susceptible to electrophilic substitution while at least some vinyl phosphates are subject to nucleophilic substitution, a variety of applications can be envisioned for this new functional group.

We have recently developed an interest in the chemistry of vinyl phosphates, reporting both a rearrangement of cyclic vinyl phosphates, which makes cyclic β-keto phosphonates readily available,[2] and a study of phosphate diene cycloadditions as a route to cyclic vinyl phosphates.[3] These studies of phosphate chemistry have fostered the evolution of a new strategy for olefin synthesis.[4] Specifically, we hypothesized that a new juxtaposition of functionality, with trialkylsilyl and diaryl phosphate groups positioned on adjacent sp^2 carbons, would prove to be readily accessible and amenable to both nucleophilic[5] and electrophilic[6] substitution reactions. In this manuscript we describe several routes that have been developed for preparation of vinyl silane phosphates (VSP's,[7] **1**), as well as the synthesis of a number of individual compounds. In the accompanying paper,[8] we describe representative substitution reactions, whereby VSP's are converted to vinyl silanes with carbon–carbon bond formation.

Scheme I





1

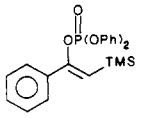
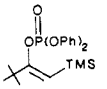
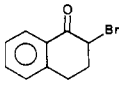
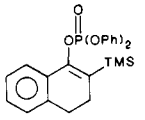
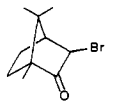
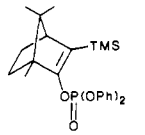
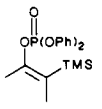
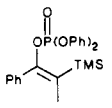
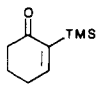
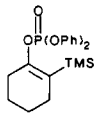
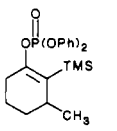
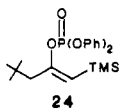
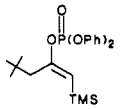
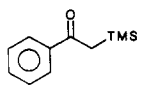
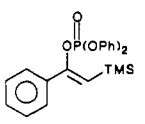
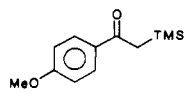
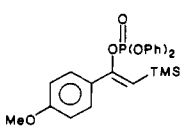
Results and Discussion

The high density of functionality in the VSP system allows a variety of synthetic approaches. By focusing upon ketones as the preferred starting material, assuring the availability of a wide variety of potential substrates, the

(1) Fellow of the Alfred P. Sloan Foundation, 1985–1989.
(2) Hammond, G. B.; Calogeropoulou, T.; Wiemer, D. F. *Tetrahedron Lett.* **1986**, *27*, 4265. Calogeropoulou, T.; Hammond, G. B.; Wiemer, D. F. *J. Org. Chem.* **1987**, *52*, 4185.
(3) Calogeropoulou, T.; Wiemer, D. F. *J. Org. Chem.* **1988**, *53*, 2295. For a closely related study, cf. Liu, H.-J.; Feng, W. M. *Synth. Commun.* **1987**, *17*, 1777.
(4) Portions of this work were reported at the 193rd American Chemical Society National Meeting, Denver, April, 1987.
(5) (a) Blaszczak, L.; Winkler, J.; O'Kuhn, S. O. *Tetrahedron Lett.* **1976**, *49*, 4405. (b) Sum, F.-W.; Weiler, L. *Can. J. Chem.* **1979**, *57*, 1431.
(6) Fleming, I.; Chan, T. H. *Synthesis* **1979**, 761. Colvin, E. W. *Silicon in Organic Synthesis*; Butterworths: London, 1981. Weber, W. P. *Silicon Reagents for Organic Synthesis*; Springer-Verlag: Berlin, 1983.
(7) The systematic names for these compounds are given in the Experimental Section. We have chosen the trivial name of vinyl silane phosphates to emphasize their potential reactivity as both vinyl silanes and vinyl phosphates and to provide a convenient acronym.
(8) Koerwitz, F. L.; Hammond, G. B.; Wiemer, D. F. *J. Org. Chem.*, following paper in this issue.

0022-3263/89/1954-0738$01.50/0

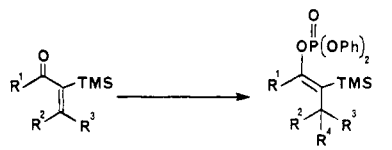
Table I. Synthesis of Vinyl Silane Phosphates

ketone	vinyl silane phosphate	yield, %
2	 5	87
 6	 7	72
 8	 9	64
 10	 11	81
12	 15	8
16	 17	67
 18	 19	82
18	 20	56
21	 24  25	65
 26	 5	70
 27	 28	53[a]

[a] Crude yield.

retrosynthetic analysis can be simplified essentially to those sequences that form the phosphorus–oxygen bond last and sequences that form the carbon–silicon bond last. Although we have prepared one VSP by a route that falls into the latter category, most of our VSP syntheses fall into the former category. They vary in the methods used to form the enolate prior to phosphorylation and in the origin of the trialkylsilyl group.

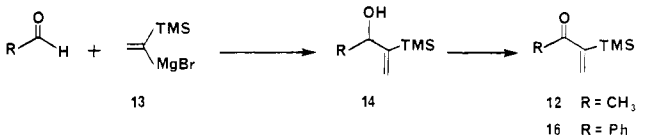
Scheme II



As illustrated in Scheme I with α-bromo acetophenone (**2**), the first VSP synthesis utilizes a 1,3-silicon shift to obtain the C–Si bond and form the α-silyl ketone enolate.[9] The siloxyvinyl bromide **3** can be obtained from the α-bromo ketone upon treatment with lithium hexamethyldisilazide and trimethylsilyl chloride. A subsequent reaction with *n*-BuLi promotes halogen–metal exchange, which is followed by a rapid rearrangement to the α-silyl ketone enolate **4**. If this enolate is trapped by reaction with diphenyl phosphorochloridate, the VSP **5** is obtained. As shown in Table I, this strategy has been applied to several α-bromo ketones, with generally positive results.

With the cyclic VSP's **9** and **11** only a single stereoisomer is possible, but, in theory, this approach to VSP's could give two stereoisomers with acyclic ketones such as **2** and **6**. Only one isomer was detected in each of these acyclic cases however. With the VSP derived from pinacolone (i.e. compound **7**), observation of a large NOE enhancement of the vinylic H upon irradiation of the *tert*-butyl resonance led to an assignment as the *Z* isomer. With the diphenyl VSP derived from acetophenone, the overlap of the 15 aromatic hydrogens complicates an analogous experiment. However, VSP **5** was assigned the *Z* stereochemistry, initially on the basis of the lack of significant spin–spin coupling between phosphorus and the vinylic hydrogen.[10] This assignment was substantiated by later studies with a closely related compound (vide infra).

The first route to VSP's requires an α-halo ketone as the starting material, which may be inconvenient in some cases, and appears to be restricted to systems that lack acidic α′ hydrogen. An alternative approach, which circumvents both these problems, involves utilizing a phosphorochloridate for trapping the enolate generated by conjugate addition to an α-silyl-α,β-unsaturated ketone (Scheme II). Acyclic silyl enones (e.g. **12**) have been known for some time, first having been prepared by Stork and Ganem through addition of the vinyl Grignard reagent **13** to an aldehyde and oxidation of the resulting allylic alcohol (**14**).[11] Both silyl enone **12** and the analogous phenyl compound **16** were prepared by slight variations on this sequence.

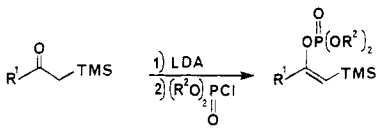


13 **14** **12** R = CH_3; **16** R = Ph

Although acyclic enones usually react with lithium tri-*sec*-butylborohydride (L-Selectride) in a 1,2-manner,[12] treatment of the silyl enone **12** with this reagent and

(9) Sampson, P.; Hammond, G. B.; Wiemer, D. F. *J. Org. Chem.* **1986**, *51*, 4342.
(10) Gaydou, E. M. *Can. J. Chem.* **1973**, *51*, 3412.
(11) Stork, G.; Ganem, B. *J. Am. Chem. Soc.* **1973**, *95*, 6152.
(12) Corey, E. J.; Becker, K. B.; Varma, R. K. *J. Am. Chem. Soc.* **1972**, *94*, 8616. Fortunato, J. M.; Ganem, B. *J. Org. Chem.* **1976**, *41*, 2194. Kowalski, C. J.; Weber, A. E.; Fields, K. W. *J. Org. Chem.* **1982**, *47*, 5088. Crisp, G. T.; Scott, W. J. *Synthesis* **1985**, 335.

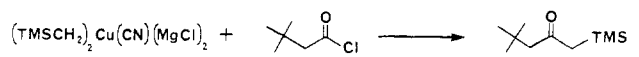
Scheme III



trapping of the resulting enolate with diphenyl phosphorochloridate produced the VSP **15** in low yield. In contrast, when the silyl enone **16** was employed in an analogous reaction sequence, the VSP **17** was obtained in good yield (67% after column chromatography). In both cases, a single stereoisomer of the VSP was obtained. With the VSP **15**, this product was assigned as the *Z* isomer when a small NOE effect was observed between the two methyl resonances. While the stereochemistry of the VSP **17** has not yet been established with certainty, a tentative assignment as the *Z* isomer may be reasonable because the ^1H and ^{13}C shifts of the β-methyl substituent closely parallel those of compound **15**.

Cyclic α-silyl enones such as **18** have been prepared from the analogous enones via their bromo ketals.[13] Conjugate addition of hydride to the silyl enone via reaction with L-Selectride,[12] and trapping of the resulting enolate with diphenyl phosphorochloridate gave the expected VSP (**19**). A variety of VSP's should be accessible through other conjugate additions to the silyl enone system. For example, treatment of the silyl enone **18** with methyl cuprate, and quenching of the resulting enolate by reaction with diphenyl phosphorochloridate, gives the VSP **20** in good yield.

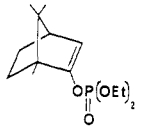
The third route to VSP's (Scheme III) starts with an α-silyl ketone, readily available through a variety of routes.[14] Once the silyl ketone is in hand, generation of the appropriate enolate[15] and reaction with a phosphorochloridate would afford a VSP. To test this hypothesis, we prepared the α-silyl ketone **21** by addition of the cuprate **22** to the acid chloride **23**. The α-silyl ketone thus



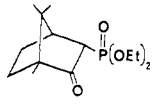
obtained (**21**), after treatment with LDA and reaction with diphenyl phosphorochloridate at −20 °C, gave two stereoisomeric VSP's in a 60:40 ratio. The major isomer was assigned the *Z* stereochemistry, consistent with the observation of a 15% NOE enhancement of the vinylic H upon irradiation of the methylene resonance, the relatively deshielded value of the CH_2 resonance in its ^{13}C NMR spectrum (49.8), and the lack of observable P–H coupling.[10] The minor isomer was assigned structure **25**, i.e. *E* stereochemistry, on the basis of the observation of a relatively shielded CH_2 resonance (46.8), and a P–H coupling (1.7 Hz).[10] When the enolate of silyl ketone **21** was treated with diphenyl phosphorochloridate at −78 °C, only the *Z* stereoisomer **24** was obtained.

Two other VSP's were prepared from their respective α-silyl ketone enolates. Addition of the cuprate **22** to benzoyl chloride gave the α-silyl ketone **26**, and reaction of compound **22** with *p*-methoxybenzoyl chloride gave compound **27**. Upon treatment with base and diphenyl phosphorochloridate, these α-silyl ketones were converted to the VSP's **5** and **28**. In the ^1H NMR spectrum of compound **28**, the four H's of the methoxyphenyl ring are resolved into separate signals (at δ 7.4 and 6.8), which do not overlap with the resonances of the other 10 phenyl protons. Accordingly, it was possible to conduct an NOE experiment, to establish the stereochemistry of this VSP. A significant NOE enhancement of the resonance at δ 7.4 was observed upon irradiation of the vinylic resonance. Upon irradiation of the resonance at δ 7.4, a corresponding increase in the intensity of the vinylic hydrogen was observed, supporting assignment of VSP **28** as the *Z* stereoisomer. Because treatment of the α-silyl ketone **26** under the same reaction conditions gives compound **5**, the earlier stereochemical assignment of compound **5** as the *Z* isomer is further justified.

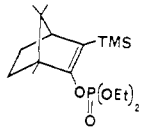
Finally, we have explored one route to VSP's that forms the C–Si bond last. Our studies of the rearrangement of vinyl phosphates to β-keto phosphonates[2] have identified two general classes of reactions: those that proceed via formation of an intermediate allyl anion and those that presumably involve an intermediate vinyl anion. Included in the latter category are those vinyl phosphates that lack allylic hydrogen and those where formation of an allyl anion is precluded by factors such as ring strain. For example, when the diethyl vinyl phosphate of camphor (**29**) is treated with LDA, rearrangement to the keto phosphonate **30** proceeds in good yield.[2] Efforts to trap a vinyl anion in this system by addition of TMSCl were frustrated by the speed of the intramolecular rearrangement of vinyl phosphate anion to keto phosphonate anion. However, upon treatment with LDA in the presence of excess TMSCl, phosphate **29** did give the desired VSP (**31**) in good yield. This approach clearly is restricted to those



29



30



31

cases where formation of an allyl anion is not possible. It also is restricted with respect to the choice of phosphate esters. Treatment of diphenyl vinyl phosphates with LDA can result in a 1,3-phosphorus migration to an ortho position of an aromatic ring,[2,16] precluding the preparation of diphenyl VSP's by this approach.[17] Nevertheless, these experiments indicate that it is possible to form dialkyl VSP's by final formation of the C–Si bond.

In conclusion, this paper describes a number of methods that can be used to prepare vinyl silane phosphates. By these various routes, we have prepared cyclic and acyclic

(13) Guaciaro, M. A.; Wovkulich, P. M.; Smith, A. B., III *Tetrahedron Lett.* **1978**, 4661. Swenton, J. S.; Fritzen, E. L., Jr. *Tetrahedron Lett.* **1979**, 1951.

(14) Among the syntheses of α-silyl ketones are the following: Obayashi, M.; Utimoto, K.; Nozaki, H. *Bull. Chem. Soc. Jpn.* **1979**, *52*, 2646, and references cited therein. Fleming, I.; Pearce, A. *J. Chem. Soc., Perkin Trans. 1* **1981**, 251. Seitz, D. E.; Zapata, A. *Synthesis* **1981**, 557. Kuwajima, I.; Inoue T.; Sato, T. *Tetrahedron Lett.* **1978**, 4887. Hauser, C. R.; Hance, C. R. *J. Am. Chem. Soc.* **1952**, *74*, 5091. Kuwajima, I.; Takeda, R. *Tetrahedron Lett.* **1981**, *22*, 2381. Corey, E. J.; Rucker, Ch. *Tetrahedron Lett.* **1984**, *25*, 4345. Larson, G. L.; Hernandez, D.; Montes de Lopez-Cepero, I.; Torres, L. E. *J. Org. Chem.* **1985**, *50*, 5260.

(15) Inoue, T.; Sato, T.; Kuwajima, I. *J. Org. Chem.* **1984**, *49*, 4671.

(16) Dhawan, B.; Redmore, D. *J. Org. Chem.* **1984**, *49*, 4018. Dhawan, B.; Redmore, D. *J. Org. Chem.* **1986**, *51*, 179.

(17) Because previous studies on vinyl phosphates suggested that displacements of diphenyl phosphates are more facile than those of dialkyl phosphates, we have favored preparation of VSP's containing diphenyl phosphate groups. (cf. ref 5a and Ishihara, T.; Yamana, M.; Ando, T. *Tetrahedron Lett.* **1983**, *24*, 5657. Takai, K.; Sato, M.; Oshima, K.; Nozaki, H. *Bull. Chem. Soc. Jpn.* **1984**, *57*, 108.)

VSP's with varying degrees of alkyl and aryl substitution. While many other routes to this functionality can be envisioned, these studies have given facile access to a sufficient variety of structures so that attention can be focused on applications of the VSP system.

Experimental Section

To maintain anhydrous conditions, tetrahydrofuran (THF) was distilled from sodium/benzophenone immediately prior to use, and reactions were conducted under a positive pressure of an inert gas. Flash column chromatography was done on Merck grade 60 silica gel (230–400 mesh), while radial chromatography was performed with a Chromatotron apparatus and Merck PF254 silica gel with $CaSO_4 \cdot 0.5H_2O$. NMR spectra (^1H, ^{13}C, and ^{31}P) were recorded on either a JEOL FX-90Q or a Brucker WM-360 spectrometer, with deuteriochloroform as the solvent. The ^1H and ^{13}C chemical shifts are reported in parts per million relative to $(CH_3)_4Si$, while the ^{31}P chemical shifts are reported in parts per million relative to H_3PO_4 (external standard). Low-resolution electron impact (EI) mass spectra were recorded with a Hewlett-Packard 5985B instrument operating at 70 eV; only selected ions are reported here. High-resolution mass spectra were recorded on a VG Instruments ZAB-HF spectrometer at the University of Iowa Mass Spectrometry Facility. Microanalyses were conducted by Desert Analytics, Tucson, AZ.

(*Z*)-1-Phenyl-2-(trimethylsilyl)vinyl Diphenyl Phosphate (5). General Procedure for VSP Synthesis via Silyl Migrations. To a solution of lithium hexamethyldisilazide in anhydrous THF (5.8 mmol in 8 mL) at −78 °C was added a solution of α-bromoacetophenone (995 mg, 5.0 mmol) in THF (17 mL). After 20 min, chlorotrimethylsilane (TMSCl, 0.75 mL, 6.0 mmol) was added, and the pale yellow solution was allowed to warm to room temperature. One hour after the initial addition, the solution was cooled to −78 °C, and *n*-BuLi (11.6 mmol) was added. The resulting orange solution was stirred for 20 min, and diphenyl phosphorochloridate (1.8 mL, 8.8 mmol) was added slowly. When the addition was complete, the mixture was allowed to warm to room temperature and quenched by addition of a saturated solution of ammonium chloride (25 mL). After extraction with ether (2 × 30 mL), the combined ethereal layers were washed with brine (30 mL) and dried ($MgSO_4$). Concentration in vacuo gave an oil (3.7 g), which was purified by flash chromatography (10% EtOAc, 90% hexane) to afford the vinyl silane phosphate **5** as a colorless oil (1.84 g, 87%): ^1H NMR δ 7.56–7.01 (m, 15 H), 5.6 (s, 1 H), 0.25 (s, 9 H); ^{31}P NMR δ −18.6; ^{13}C NMR δ 156.9 (d, J_{CP} = 8.7 Hz), 150.2 (d, J_{CP} = 7.2 Hz), 135.9, 129.3, 128.8, 127.8, 126.3, 125.0, 119.7 (d, J_{CP} = 5.8 Hz), 115.2 (d, J_{CP} = 8.3 Hz), −0.7; EIMS, *m/z* (relative intensity) 409 (M^+ − 15, 18), 307 (100), 250 (5), 213 (31), 159 (44). Anal. Calcd for $C_{23}H_{25}O_4PSi$: C, 65.07; H, 5.94. Found: C, 65.22; H, 5.94.

(*Z*)-1-*tert*-Butyl-2-(trimethylsilyl)vinyl Diphenyl Phosphate (7). α-Bromopinacolone (0.745 mL, 5.0 mmol) in THF (20 mL) was treated sequentially with LDA (6.0 mmol in 10 mL THF), TMSCl (0.81 mL, 6.4 mmol), *n*-BuLi (12 mmol), and diphenyl phosphorochloridate (1.68 mL, 8.8 mmol) according to the general procedure. Purification by column chromatography (silica, 5% EtOAc, 95% hexane) gave pure VSP **7** (1.34 g, 72%): ^1H NMR δ 7.3–7.14 (m, 10 H), 5.08 (s, 1 H), 1.24 (s, 9 H), 0.20 (s, 9 H); ^{31}P NMR δ −19.6; ^{13}C NMR δ 168.1 (d, J_{CP} = 11.4 Hz), 150.5 (d, J_{CP} = 7.2 Hz), 129.5, 129.4, 119.7 (d, J_{CP} = 4.5 Hz), 109.3 (d, J_{CP} = 5.8 Hz), 38.2, 28.7, −0.4; EIMS, *m/z* (relative intensity) 389 (M^+ − 15, 19), 307 (100), 291 (5), 250 (22), 213 (62), 94 (16), 77 (27), 73 (23); HRMS calcd for $C_{21}H_{29}O_4PSi$ (M^+ − 15) 389.1338, found 389.1339. In a difference NOE experiment, irradiation of the resonance at 1.24 ppm gave a 19% enhancement of the resonance at 5.08 ppm.

Preparation of the Diphenyl VSP Derivative of Tetralone (9). 2-Bromo-3,4-dihydro-1(2*H*)-naphthalenone (1.12 g, 5 mmol) in THF (10 mL) was allowed to react with LDA (6 mmol) in THF (20 mL), and the resulting enolate was treated with TMSCl (0.81 mL, 6.4 mmol), *n*-BuLi (7.5 mL, 12 mmol), and diphenyl phosphorochloridate (1.55 mL, 7.5 mmol) as described above. Purification by column chromatography (silica, 5% EtOAc, 95% hexanes) provided pure compound **9** (1.45 g, 64%): ^1H NMR δ 7.45–7.07 (m, 14 H), 2.67 (t, 2 H, J = 7.5 Hz), 2.31 (m, 2 H), 0.27 (s, 9 H); ^{31}P NMR δ −17.2; ^{13}C NMR δ 150.7 (d, J_{CP} = 7.2 Hz), 150.1 (d, J_{CP} = 9.1 Hz), 137.5, 130.9, 129.6, 128.2, 126.8, 126.2, 125.7 (d, J_{CP} = 7.0 Hz), 125.2, 122.6, 120.1 (d, J_{CP} = 4.4 Hz), 27.9, 26.6, −1.02; EIMS, *m/z* (relative intensity) 450 (M^+, 0.8), 435 (100), 307 (11), 291 (12), 213 (39), 128 (33), 115 (11), 77 (25), 73 (19); HRMS calcd for $C_{25}H_{27}O_4PSi$ (M^+ − 15) 435.1182, found 435.1209.

Preparation of the Diphenyl VSP Derivative of Camphor (11). A solution of α-bromocamphor (1.13 g, 4.9 mmol) in THF (17 mL) was added to $LiN(TMS)_2$ in THF (5.8 mmol in 8 mL) at −78 °C. The resulting enolate was treated with TMSCl (0.80 mL, 6.3 mmol), *n*-BuLi (11.6 mmol), and diphenyl phosphorochloridate (1.8 mL, 8.8 mmol) in the usual manner. Standard workup and purification by flash chromatography (silica, 20% EtOAc, 80% hexane) yielded pure VSP **11** (1.8 g, 81%): ^1H NMR δ 7.33–7.14 (m, 10 H), 2.39 (d, 1 H, J = 3.6 Hz), 1.87 (m, 1 H), 1.58 (m, 3 H), 1.06 (s, 3 H), 0.91 (s, 3 H), 0.75 (s, 3 H), 0.13 (s, 9 H); ^{31}P NMR δ −18.6; ^{13}C NMR δ 162.8, 150.7 (d, J_{CP} = 7.3 Hz), 150.6 (d, J_{CP} = 7.3 Hz), 129.7, 126.3 (d, J_{CP} = 7.7 Hz), 125.2 (d, J_{CP} = 3.3 Hz), 120.1 (d, J_{CP} = 5.3 Hz), 120.0 (d, J_{CP} = 6.3 Hz), 57.1, 55.4, 53.4, 31.1, 25.8, 20.1, 19.5, 10.3, −1.3; EIMS, *m/z* (relative intensity) 456 (M^+, 2), 441 (59), 413 (25), 307 (43), 213 (100), 133 (28), 91 (29), 77 (62), 73 (96). Anal. Calcd for $C_{25}H_{33}O_4PSi$: C, 65.76; H, 7.29. Found: C, 66.04; H, 7.51.

(*Z*)-1,2-Dimethyl-2-(trimethylsilyl)vinyl Diphenyl Phosphate (15). To a solution of L-Selectride (5.28 mmol) in THF (30 mL) at −78 °C was added a solution of the α-silyl enone **12** (500 mg, 3.5 mmol) in THF (4 mL). After 20 min, diphenyl phosphorochloridate (1.45 mL, 7.0 mmol) was added. The resulting mixture was allowed to warm up to room temperature and then quenched by addition of saturated ammonium chloride (40 mL) and ether (40 mL). The layers were separated, and the ethereal layer was washed with water (2 × 35 mL), and brine (1 × 35 mL). The combined aqueous layers were extracted with ether (2 × 25 mL), and then the combined ethereal extracts were dried ($MgSO_4$). Concentration in vacuo, and purification by radial chromatography (silica, 10% EtOAc, 90% hexane), provided the VSP **15** as a colorless oil (0.11 g, 8.4%): ^1H NMR δ 7.26–7.08 (m, 10 H), 2.09 (dd, 3 H, J_{HP} = 1.6 Hz, J = 1.0 Hz), 1.57 (dd, 3 H, J_{HP} = 2.2 Hz, J = 1.0 Hz), 0.05 (s, 9 H); ^{31}P NMR δ −17.9; ^{13}C NMR δ 150.5 (d, J_{CP} = 6.9 Hz), 150.3 (d, J_{CP} = 7.3 Hz), 129.7, 125.2, 120.0 (d, J_{CP} = 5.4 Hz), 117.9 (d, J_{CP} = 11.7 Hz), 17.1, 15.8 −0.8; EIMS, *m/z* (relative intensity) 376 (M^+, 0.2), 361 (1), 323 (27), 307 (20), 213 (22), 88 (18), 77 (23), 73 (100); HRMS calcd for $C_{19}H_{25}O_4PSi$ 376.1259, found 376.1232. In a difference NOE experiment, irradiation of the resonance at 1.57 ppm gave a 4.4% enhancement of the resonance at 2.10 ppm.

(*Z*)-2-Methyl-1-phenyl-2-(trimethylsilyl)vinyl Diphenyl Phosphate (17). To a solution of L-Selectride in THF (3.77 mmol in 24 mL) at −78 °C was added a solution of the α-silyl ketone **16**[18] (700 mg, 3.43 mmol) in THF (2 mL). After 25 min, one equiv of HMPA (0.66 mL, 3.77 mmol) and 1.8 equiv of diphenyl phosphorochloridate (1.28 mL, 6.17 mmol) were added successively. The resulting mixture was allowed to warm to room temperature and quenched by addition of saturated ammonium chloride (40 mL) and ether (40 mL). After the layers were separated, the ethereal layer was washed with water (2 × 35 mL) and brine (35 mL), and then the combined aqueous layers were extracted with ether (2 × 25 mL). The combined ethereal layers were dried ($MgSO_4$) and concentrated in vacuo. Purification of the residue by flash chromatography (silica, 10% EtOAc, 90% hexane) provided VSP **17** (1.01 g, 67%) as a white solid, which could be crystallized from petroleum ether as very fine needles: mp 77.5–78.5 °C; ^1H NMR δ 7.37–6.89 (m, 15 H), 1.62 (d, 3 H, J_{HP} = 2.7 Hz[10]), 0.26 (s, 9 H); ^{31}P NMR δ −18.3; ^{13}C NMR δ 151.3 (d, J_{CP} = 8.7 Hz), 150.3 (d, J_{CP} = 7.2 Hz), 134.4, 129.8, 129.4, 128.5, 127.9, 124.9, 121.3 (d, J_{CP} = 7 Hz), 119.8 (d, J_{CP} = 5.7 Hz), 16.7, −0.80; EIMS, *m/z* (relative intensity) 438 (M^+, 0.1), 423 (0.3), 395 (2), 323 (100), 307 (89), 251 (6), 231 (10), 213 (50), 188 (40), 151 (17). Anal. Calcd for $C_{24}H_{27}O_4PSi$: C, 65.73; H, 6.21. Found: C, 65.98; H, 6.33.

2-(Trimethylsilyl)cyclohexenyl Diphenyl Phosphate (19). To a solution of L-Selectride in THF (1.19 mmol in 11 mL) at −78 °C, was added a solution of the α-silyl ketone **18** in THF (200

(18) Matsuda, I. P.; Sato, S.; Izumi, Y. *Tetrahedron Lett.* **1983**, *24*, 2787.

mg, 1.19 mmol in 2 mL). After 30 min, diphenyl phosphorochloridate (0.37 mL, 1.78 mmol) was added, and the resulting mixture was allowed to warm to room temperature overnight. After addition of saturated ammonium chloride (25 mL) and ether (25 mL), the layers were separated, and the ethereal layer was washed with brine (20 mL) and dried ($MgSO_4$). Concentration in vacuo and purification of the residue by radial chromatography (silica, 5% EtOAc, 95% hexane) provided compound **19** as a colorless oil (395 mg, 82%): ^1H NMR δ 7.34–7.12 (m, 10 H, 2.52–2.48 (m, 2 H), 2.13–2.09 (m, 2 H), 1.73–1.67 (m, 2 H), 1.57–1.52 (m, 2 H), 0.11 (s, 9 H); ^{31}P NMR δ −18.5; ^{13}C NMR δ 153.2 (d, J_{CP} = 7.7 Hz), 150.5 (d, J_{CP} = 7 Hz), 129.6, 125.2, 120.3 (d, J_{CP} = 4.8 Hz), 120.0, 28.8, 27.1, 23.0, 22.1, −1.1; EIMS, m/z (relative intensity) 403 (M^+ + 1, 15), 388 (60), 307 (25), 213 (100), 156 (31), 228 (20), 77 (32), 73 (23); HRMS calcd for $C_{21}H_{27}O_4PSi$ 402.1416, found 402.1444.

3-Methyl-2-(trimethylsilyl)cyclohexenyl Diphenyl Phosphate (20). To a solution of CuCN in THF (358 mg, 4 mmol, in 20 mL) was added methyllithium (1.4 M in ether, 8.0 mmol) at −78 °C. The resulting solution was stirred for 45 min before addition of the α-silyl enone **18** (500 mg, 3 mmol) as a solution in THF (5 mL). The mixture was allowed to warm to −20 °C and then was treated with diphenyl phosphorochloridate (1.87 mL, 9.0 mmol). After 90 min, the reaction mixture was quenched by addition of saturated ammonium chloride (40 mL) and ether (40 mL). The layers were separated, and the ethereal layer was washed with saturated ammonium chloride (20 mL) and brine (20 mL). Filtration through a Florisil pad, concentration in vacuo, and purification by radial chromatography (silica, 5% EtOAc, 95% hexane) provided the VSP **20** (690 mg, 56%): ^1H NMR δ 7.36–7.14 (m, 10 H), 2.54–2.45 (m, 3 H), 1.81–1.41 (m, 4 H), 1.25 (d, 3 H, J = 6.9 Hz), 0.14 (s, 9 H); ^{31}P NMR δ −18.1; ^{13}C NMR δ 153.9 (d, J_{CP} = 7 Hz), 150.5 (d, J_{CP} = 7 Hz), 130.0, 125.1, 124.5 (d, J_{CP} = 7 Hz), 119.9 (d, J_{CP} = 4.8 Hz), 30.8, 29.1, 28.5, 21.4, 18.3, −0.4; EIMS, m/z (relative intensity) 416 (M^+, 2), 307 (19), 251 (15), 213 (72), 155 (43), 91 (24), 77 (74), 73 (100). Anal. Calcd for $C_{22}H_{29}O_4PSi$: C, 63.44; H, 7.02. Found: C, 63.39; H, 7.10.

4,4-Dimethyl-1-(trimethylsilyl)pentan-2-one (21). General Procedure for Preparation of α-Silyl Ketones from Acid Chlorides. The α-silyl ketone was prepared in a manner similar to that of Akiba and co-workers,[19] although CuCN was used in place of CuI. To a solution of CuCN (1.34 g, 15 mmol) in THF (40 mL) at −78 °C was added $TMSCH_2MgCl$ (1.0 M in ether, 30 mmol). The reaction mixture was allowed to warm slowly until the solution became clear, to ensure formation of the corresponding cuprate, and then cooled to −78 °C before addition of *tert*-butylacetyl chloride (2.06 mL, 14.9 mmol) via syringe. Over the course of 4 h, this mixture was allowed to warm to room temperature. It was then partitioned between ether (75 mL) and a mixture of ammonium chloride–ammonium hydroxide (4:1, 25 mL), and the ether layer was washed with a solution of ammonia in brine (5%, 50 mL) and brine (25 mL) and dried ($MgSO_4$). Concentration in vacuo gave silyl ketone **21**, which was purified by bulb-to-bulb distillation (2.34 g, 85%): ^1H NMR δ 2.18 (s, 2 H), 2.16 (s, 2 H), 0.97 (s, 9 H), 0.07 (s, 9 H); ^{13}C NMR δ 209.3, 56.6, 40.4, 31.0, 29.7, −1.1; EIMS, m/z (relative intensity) 186 (M^+, 3), 171 (5), 130 (15), 115 (100), 91 (8), 75 (30), 73 (75), 57 (17). HRMS calcd for $C_{10}H_{22}OSi$ 186.1440, found 186.1415.

Preparation of (*Z*)- and (*E*)-1-(2,2-Dimethylpropyl)-2-(trimethylsilyl)vinyl Diphenyl Phosphate (24 and 25). General Procedure for Preparation of VSP's from α-Silyl Ketones. A solution of α-silyl ketone **21** (2.28 g, 9 mmol) in THF (5 mL) was added to LDA (1.1 equiv in 35 mL of THF) at −78 °C. The resulting solution was allowed to warm to −10 °C over 2.5 h, and diphenyl phosphorochloridate (2.8 mL, 13.5 mmol) was added via syringe. The reaction mixture was allowed to warm to room temperature over 4 h and then quenched by addition of saturated ammonium chloride (30 mL). After extraction with ether (2 × 50 mL), the combined organic layers were washed with water (50 mL) and brine (50 mL), dried ($MgSO_4$), and concentrated in vacuo. Purification by column chromatography (silica, 25% EtOAc, 75% hexane) provided a 60:40 mixture[20] of the *Z* (**24**) and *E* (**25**) stereoisomers (total of 2.43 g, 65%): EIMS, m/z (relative intensity) 403 (M^+ − 15, 12), 323 (14), 307 (100), 251 (91), 213 (86), 94 (20), 77 (37), 73 (66), 57 (39). Anal. Calcd for $C_{22}H_{31}O_4PSi$: C, 63.13; H, 7.47. Found: C, 63.37; H, 7.75.

The individual isomers could be separated by radial chromatography, with an acetonitrile/hexane partition: ***Z* isomer (24)**: ^1H NMR δ 7.31–7.16 (m, 10 H), 4.86 (s, 1 H), 2.39 (d, 2 H, J_{HP} = 0.98 Hz), 0.94 (s, 9 H), 0.14 (s, 9 H); ^{31}P NMR δ −18.7; ^{13}C NMR δ 158.7 (d, J_{CP} = 7.6 Hz), 150.5 (d, J_{CP} = 7.2 Hz), 129.6, 125.2, 120.0 (d, J_{CP} = 4.2 Hz), 115.8 (d, J_{CP} = 8.8 Hz), 49.8, 31.2, 29.3, −0.5. In a difference NOE experiment, irradiation of the resonance at 2.39 ppm gave a 15% enhancement of the resonance at 4.86 ppm. ***E* isomer (25)**: ^1H NMR δ 7.36–7.16 (m, 10 H), 5.34 (d, 1 H, J_{HP} = 1.7 Hz), 2.16 (d, 2 *H*, J_{HP} = 0.95 Hz), 0.93 (s, 9 H), 0.12 (s, 9 H); ^{31}P NMR δ −18.6; ^{13}C NMR δ 157.3 (d, J_{CP} = 9.3 Hz), 150.6 (d, J_{CP} = 7.2 Hz), 129.6, 125.2, 120.1 (d, J_{CP} = 4.7 Hz), 111.3 (d, J_{CP} = 4.0 Hz), 46.8, 31.0, 30.1, 0.2.

Preparation of VSP 5 from Benzoyl Chloride. Treatment of benzoyl chloride (1.16 mL, 10 mmol) with 1 equiv of $(TMSCH_2)_2Cu(CN)(MgCl)_2$ (prepared in situ from CuCN (0.895 g, 10 mmol) and $TMSCH_2MgCl$ (20 mmol in 40 mL of THF)) at −78 °C gave the α-silyl ketone **26**, identical with material prepared by an alternate route.[9]

To a solution of LDA (11 mol) in THF (25 mL) at −78 °C was added a solution of the α-silyl ketone **26** (ca. 10 mmol) in THF (5 mL). The resulting transparent yellow solution was allowed to warm to −55 °C over a period of 1 h and subsequently was quenched with diphenyl phosphorochloridate (3.1 mL, 15 mmol). Addition of saturated ammonium chloride (20 mL) and ether (30 mL) was followed by separation of the organic and aqueous layers. The ethereal layer was washed with brine (50 mL), dried ($MgSO_4$), and concentrated in vacuo. The resulting oil was purified by column chromatography (silica; 25% EtOAc, 75% hexane) to yield pure VSP **5** (2.95 g, 70% from benzoyl chloride), identical with the material prepared earlier from α-bromoacetophenone.

(*Z*)-1-(4-Methoxyphenyl)-2-(trimethylsilyl)vinyl Diphenyl Phosphate (28). The α-silyl ketone **27** was prepared by treatment of *p*-anisoyl chloride (0.853 g, 5 mmol) with $(TMSCH_2)_2Cu(CN)(MgCl)_2$ according to the general procedure. Standard workup afforded α-silyl ketone **27**, with ^1H NMR and mass spectra in agreement with the reported data.[21]

The α-silyl ketone **27** (4.5 mmol) in THF (3 mL) was treated sequentially with LDA (4.95 mmol in 15 mL of THF) and diphenyl phosphorochloridate (1.4 mL, 6.75 mmol) according to the general procedure. Standard workup and concentration in vacuo gave crude compound **28** (1.11 g, 53%). Impurities, originating in decomposition of the α-silyl ketone, were removed by gel permeation chromatography using Sephadex LH-20 (80% methylene chloride, 20% hexane) to obtain analytically pure VSP **28**: ^1H NMR δ 7.48 (d, 2 H, J = 8.9 Hz), 7.27–7.04 (m, 10 H), 6.81 (d, 2 H, J = 8.8 Hz), 5.46 (s, 1 H), 3.78 (s, 3 H), 0.23 (s, 9 H); ^{31}P NMR δ −18.7; ^{13}C NMR δ 160.2, 157.0 (d, J_{CP} = 8.4 Hz), 150.6, 129.8, 129.6, 128.0, 125.2, 120.1, 113.5, 113.4 (d, J_{CP} = 6 Hz), 55.3, −0.4; EIMS, m/z (relative intensity) 335 (11), 322 (64), 307 (75), 289 (19), 250 (57), 231 (30), 213 (100), 166 (84), 151 (28), 135 (35). Anal. Calcd for $C_{24}H_{27}O_5PSi$: C, 63.42; H, 5.99. Found: C, 63.31; H, 5.96. In a difference NOE experiment, irradiation of the resonance at 7.48 ppm gave an 18% enhancement of the resonance at 5.46 ppm; irradiation at 5.46 ppm gave a 14% enhancement of the resonance at 7.48 ppm.

Preparation of the Diethyl VSP Derivative of Camphor (31). To a solution of LDA (2.42 mmol) and TMSCl (0.8 mL, 7 mmol) in THF (6 mL) at −78 °C was added via syringe pump a solution of the diethyl vinyl phosphate of camphor (**29**)[2] (0.278 g, 0.96 mmol) in THF (10 mL) over 1 h. The mixture was allowed to warm to room temperature over a 3-h period and then quenched with a saturated solution of ammonium chloride (20 mL). The layers were separated, and the aqueous layer was extracted with

(19) Yamamoto, Y.; Ohdoi, K.; Nakatani, M.; Akiba, K. *Chem. Lett.* **1984**, 1967.

(20) The pure *Z* isomer could be obtained by adding the phosphorochloridate to a solution of the α-silyl ketone enolate kept at −78 °C. Alternatively, by using a slight excess of the ketone and adding the phosphorochloridate after the reaction mixture had warmed to room temperature, a 20:80 ratio of the *Z*/*E* isomers was obtained.

(21) Fiorenza, M.; Mordini, A.; Ricci, A. *J. Organomet. Chem.* **1985**, *280*, 177.

ether (2 × 30 mL). The combined organic layers were washed with water (25 mL) and brine (25 mL), dried ($MgSO_4$), and concentrated in vacuo to give VSP **31** (0.52 g). Final purification by flash chromatography (silica, 30% EtOAc, 70% hexane) afforded pure compound **31** (0.272 g, 80%): ^1H NMR δ 4.12–4.00 (m, 4 H), 2.28 (d, 1 H, J = 3.6 Hz), 1.81–1.76 (m, 1 H), 1.55–1.38 (m, 3 H), 1.32–1.27 (m, 6 H), 0.99 (s, 3 H), 0.81 (s, 3 H), 0.69 (s, 3 H), 0.08 (s, 9 H); ^{31}P NMR δ −7.19. EIMS, m/z (relative intensity) 360 (M^+, 1), 345 (29), 317 (20), 227 (14), 183 (20), 155 (100), 91 (30), 73 (57); HRMS calcd for $C_{17}H_{33}O_4PSi$ (M^+) 360.1885, found 360.1871.

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Registry No. **2**, 70-11-1; **5**, 118297-82-8; **6**, 5469-26-1; **7**, 118297-83-9; **8**, 13672-07-6; **9**, 118297-84-0; **10**, 76-29-9; **11**, 118297-85-1; **12**, 43209-86-5; **15**, 118297-86-2; **16**, 83845-70-9; **17**, 118297-87-3; **18**, 72162-99-3; **19**, 118297-88-4; **20**, 118297-89-5; **21**, 118297-90-8; **23**, 7065-46-5; **24**, 118297-91-9; **25**, 118297-92-0; **26**, 13735-78-9; **27**, 96574-65-1; **28**, 118297-93-1; **29**, 65898-11-5; **31**, 118297-94-2; $LiN(TMS)_2$, 4039-32-1; TMSCl, 75-77-4; $TMSCH_2MgCl$, 13170-43-9; diphenyl phosphorochloridate, 2524-64-3; benzoyl chloride, 98-88-4; *p*-anisoyl chloride, 100-07-2.

Synthesis of Vinyl Silanes from Vinyl Silane Phosphates

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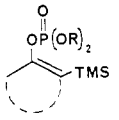
To develop a new synthesis of vinyl silanes, a representative set of vinyl silane phosphates (VSP's) has been treated with several organocuprate reagents. With acyclic VSP's, phosphate substitution proceeds in generally good yields, giving a single stereoisomer of the vinyl silane with retention of the VSP stereochemistry. In the cyclic systems examined, yields are generally somewhat lower under the same reactions conditions. However, this new sequence offers a regiochemistry complementary to other syntheses of cyclic vinyl silanes, and an approach to highly substituted vinyl silanes applicable to both cyclic and acyclic systems.

As vinyl silanes have gained popularity as synthetic intermediates,[2] the need for more general syntheses of this functionality has grown as well.[2,3] Furthermore, while many types of vinyl silanes are readily available, synthesis of certain classes is still problematic. For example, the regiospecific synthesis of cyclic vinyl silanes can be troublesome,[4] and it is difficult to prepare highly substituted vinyl silanes in either cyclic or acyclic systems.[2] In an earlier paper,[5] we described several syntheses of vinyl silane phosphates (VSP's, **1**), a novel juxtaposition of functionality with a variety of potential applications in organic synthesis. In this report, we describe a synthesis of vinyl silanes from representative VSP's.[6]



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The most straightforward conversion of a VSP into a vinyl silane formally requires displacement of a phosphate ester with concomitant carbon–carbon (or carbon–hydrogen) bond formation. While substitutions of vinyl phosphates by alkyl groups upon treatment with various cuprates are known, in simple systems this is a difficult transformation, which often proceeds in low yield.[7] In contrast, vinyl phosphates in conjugation with a group capable of stabilizing a negative charge, e.g. the vinyl phosphate derivatives of β-keto esters or β-diketones, react with alkyl cuprates in an efficient C–C bond forming reaction.[8] Therefore, with respect to the potential for cuprate substitution in VSP's, the central question could be whether or not the trialkylsilyl group provides stabilization in a fashion analogous to the carbonyl group of conjugated vinyl phosphates. While there is evidence to support the view that a trialkylsilyl group can stabilize an α-anion,[9] the significance of this fact to cuprate substitutions in VSP's is less apparent.

Preparations of organocuprates are legion,[10] and their reactivity in additions to enones is known to vary with the nature of the copper salt and solvent, as well as the cuprate order.[11] Initially, two representative systems, the VSP derivatives of pinacolone (**2**) and acetophenone (**4**), were treated with several copper-based reagents. With a standard preparation of lower order methyl cuprate[10a] (from CuI and MeLi), the desired vinyl silanes **3a** and **5a**

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(11) (a) Bertz, S. H.; Gibson, C. P.; Dabbagh, G. *Tetrahedron Lett.* **1987**, *28*, 4251. (b) Lipshutz, B. H. *Synthesis* **1987**, 325. (c) Lipshutz, B. H.; Wilhelm, R. S.; Kozlowski, J. A. *Tetrahedron* **1984**, *40*, 5005.

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