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Heterocyclizations of Hydroxyketones with Two-Coordinated (Trimethylsilylamino)-phosphines, $(Me_3Si)_2N–P=E–SiMe_3$

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ABSTRACT: *The reaction of two-coordinated (trimethylsilylamino)phosphines* $(Me_3Si)_2N–P=E–SiMe_3$ **1** *(E = N) and* **2** *(E = CH) with hydroxycarbonyl compounds proceeded with four- or five-member heterocyclization to yield derivatives of oxaphosphetane, oxaphospholanes, and oxaphospholes. The reaction rate depends on the structure of hydroxyketones as well as on the type of the two-coordinated phosphorus compound in accordance with the polarity of the P=N and P=C bonds. Thus, reaction was completed in 30 min in the case of the ortho carbonyl phenoxy derivatives with the phosphine* **1***, but required 2 h in the case of the alkyl hydroxy carbonyls. All reactions with the phosphine* **2** *took about 24 h.* © 2004 Wiley Periodicals, Inc. Heteroatom Chem 15:413–417, 2004; Published online in Wiley InterScience (www.interscience.wiley.com). DOI 10.1002/hc.20033

INTRODUCTION

It is well known that the phosphorus center in three-coordinated, three-valent $\sigma^3\lambda^3$ (silylamino) phosphines has nucleophilic character [1–4]. The two-coordinated $\sigma^2\lambda^3$ phosphines, such as $(Me_3Si)_2N–P=N–SiMe_3$ (**1**) and $(Me_3Si)_2N–P=CH–SiMe_3$ (**2**), however, act as electrophilic reactants typically showing addition and cycloaddition [4–8] reactions with various nucleophilic reagents including π-donating systems [8]. Most often the products are three-coordinated $\sigma^3\lambda^5$ and $\sigma^3\lambda^3$ phosphorus compounds. In the latter case, if the reagent contains a second functional group that is suceptible to nucleophilic attack, the reaction continues to form stable, five-valent, four-coordinated phosphorus compounds. Good examples of this behavior are shown by the reaction of **1** with propargyl alcohols to form allenic phosphoranimines (Scheme 1) and the heterocyclization of acetyl acetone **3** in its reactions with both **1** and **2** [6] (Scheme 2).

Knowing that compounds of type **1** and **2** react with alcohols through either 1,1 or 1,2 addition processes to form tricoordinated phosphorus derivatives [5,7], the pathway proposed suggests that the propargyl hydroxyl group reacts initially with **1** to form the three-coordinated phosphine intermediate, and the thus formed nucleophilic phosphine rearranges to the allenic pentavalent phosphorus [P(V)] compound. This mechanism is strongly supported by previous thorough studies on the allenic rearrangement [10].

A similar-two stage mechanism is proposed for the heterocyclization of acetyl acetone. The initial reaction of the hydroxyl group in the enol form of the diketone with the phosphorus center is followed

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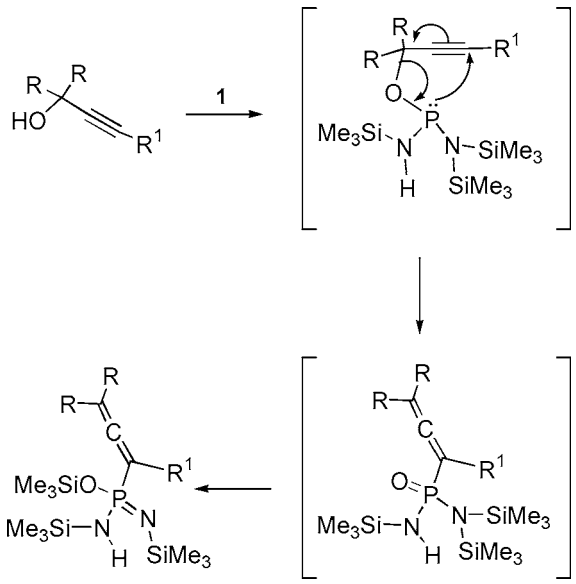
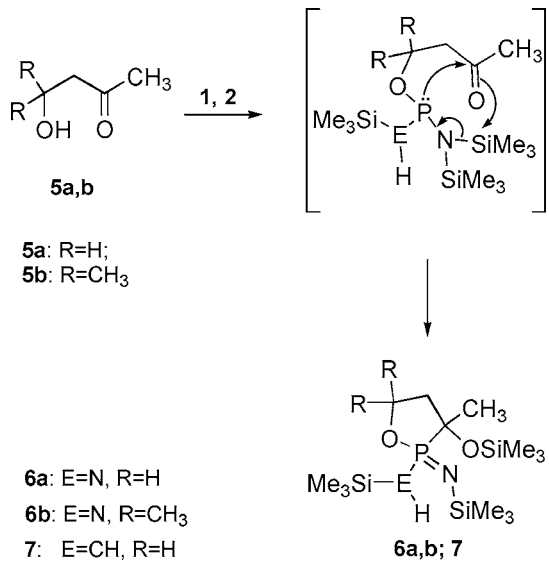


SCHEME 1

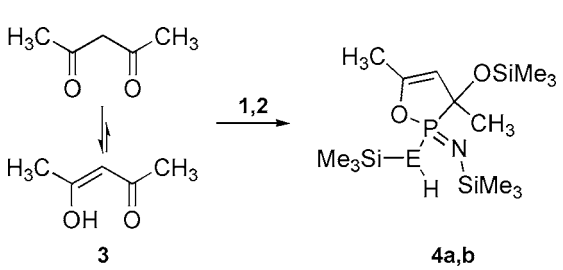


SCHEME 3

by subsequent cycle closure via the well-established Abramov reaction; a two step process in which the P(III) center adds to the carbonyl group [1,2] and involves an intermediate similar to the one depicted in Scheme 3.

However, as there was no direct evidence that the reaction of **3** followed this mechanism, further studies were needed to support the reaction pathway proposed earlier. There is only one reported example of a reaction of a hydroxycarbonyl with the (silylamino)-phosphine **1**. [11]

To develop the chemistry of hydroxycarbonyl compounds with two-coordinated (silylamino)phosphines, we describe herein reactions of 4-hydroxy-2-butanone **5a**, 4-hydroxy-4-methyl-2-pentanone **5b**, 1-(2-hydroxyphenyl)propanone **8b**, and 1-(2-hydroxy-5-methylphenyl)ethanone **8a** with **1** and **2**. In an extension, we also probed the possibilities of this heterocyclization reaction toward the α-hydroxy ketone **11**.



SCHEME 2

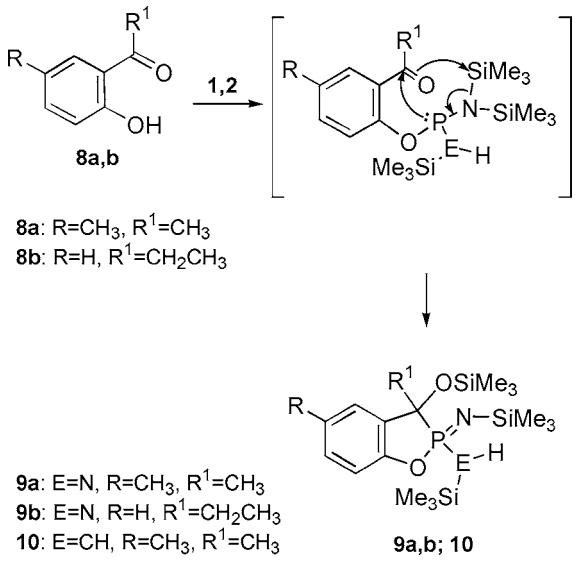
RESULTS AND DISCUSSION

Trimethylsilylaminophosphines **1** and **2** reacted readily with β-hydroxyketones **5a,b** in CH_2Cl_2. The reaction with **1** was essentially complete in 2 h at room temperature, while the reaction with **2** required reaction time of over 24 h at room temperature to achieve completion (Scheme 3).

All products were isolated as colorless liquids by vacuum distillation. The cyclic structure of oxaphospholanes **6a,b** and **7** was confirmed by NMR studies. Thus, in the ^{1}H NMR of **6a** we observed peaks for three trimethylsilyl groups at high field; the NH proton appears at $\delta = 2.43$ ppm as broad singlet, the methyl protons at C-5 as a doublet with a three-bond coupling from phosphorus of 15.2 Hz. The strongest evidence for the cyclization of **6a** was found in the ^{13}C NMR spectrum in which the coupling constant between phosphorus and C-5 is 139.5 Hz, typical for a one-bond coupling. The two other heterocycles have similar NMR spectra. The element analysis corresponds to the proposed structures for **6a,b** and **7**.

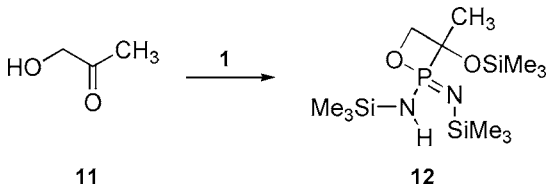
We further investigated the reaction of **1** and **2** with the hydroxyphenyl ketones **8a,b** (Scheme 4). In this case the reactions are exothermic because of the higher acidic character of the hydroxyphenyl group. All experiments were conducted in CH_2Cl_2 at 0°C and were completed in 30 min (monitored by ^{31}P NMR).

These reactions gave the bicyclic compounds **9a,b** and **10** as colorless liquids. The structures were again confirmed by ^{1}H, ^{13}C, and ^{31}P NMR studies.



SCHEME 4

These results suggested that we should examine the reactions of α-hydroxy carbonyls with **1**, with a view of possibly preparing the uncommon oxaphosphetanes containing the tetracoordinated phosphoranimine moiety. Thus, hydroxypropanone **11**, when mixed with **1** in CH_2Cl_2 at 0°C, warmed and allowed to react for 2 h at room temperature, gave the oxaphosphetane **12** in moderate yield (Scheme 5).



SCHEME 5

The structure of **12** was deduced from NMR spectra. In the ^{13}C NMR spectrum we observed a doublet for C-5 at 76.4 ppm with a ^{31}P coupling of 137.3 Hz indicating a direct P—C link. Signals for C-4 and C-6 appeared as doublets with smaller values of the ^{31}P coupling constants consistent with their increased separation from phosphorus. The ^{31}P chemical shift of **12** is 29.9 ppm, which also is in agreement with the typical shifts values displayed by compounds with similar structures [12].

EXPERIMENTAL

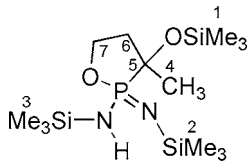
Materials and General Procedures

All operations were carried under Argon. The hydroxy and phenoxy carbonyl compounds, **5a–c, 11, 8a–c**, were obtained from commercial sources and were distilled before use. The (silylamino)phosphines **1** and **2** were prepared according to published procedures [13,14]. Dichloromethane was distilled from CaH_2 and stored over molecular sieves prior to use. ^1H, ^{13}C, and ^{31}P (85% H_3PO_4 as external standard) NMR spectra were recorded on a Varian 300 instrument (operating at 300.13, 75.46, and 121.49 MHz, respectively) in $CDCl_3$.

Reaction of 1 with Hydroxycarbonyl Compounds **5a,b, 11**, *and* **8a,b**. The (silylamino)phosphine **1** (0.84 g, 3 mmol) was added, via syringe, to a stirred solution of the respective ketone (3 mmol) in CH_2Cl_2 (2–3 ml) at 0°C. Reactions with **8a** and **8b** are exothermic and were completed within 30 min. The reactions of **5a**, **5b**, and **11** were conducted in a similar manner. The reaction mixture was stirred at room temperature 2 h. After the solvent was removed, the residues were distilled under vacuum giving the products as colorless liquids.

Reaction of 2 with Hydroxycarbonyl Compounds **5a** *and* **8a**. The (silylamino)phosphine **2** (0.83 g, 3 mmol) was added via syringe to a stirred solution of hydroxyketone (3 mmol) in CH_2Cl_2 (2–3 ml) at 0°C. The reaction mixture was stirred at room temperature overnight. On the next day the solvent was removed and the residues were distilled under vacuum to provide **7** and **10** as colorless liquids.

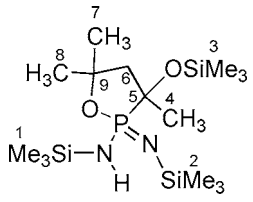
3-Methyl-3-trimethylsilyloxy-2-trimethylsilylamino-2-trimethylsilylimino-[1,2]-oxaphospholane, **6a**



^1H NMR: δ 3.93 (m, 2H, CH_2O); 2.1 (m, 2H, CH_2-C); 2.43 (s, 1H, NH); 1.45 (d, 3H, $^3J_{PH} = 15.2$ Hz, CH_3); 0.13 (s, 9H, $OSi(CH_3)_3$); 0.1 (d, 9H, $^4J_{PH} = 0.9$ Hz, $=NSi(CH_3)_3$); 0.06 (s, 9H, $NHSi(CH_3)_3$). $^{13}C[H]$ NMR: δ 66.9 (d, 1C, $^2J_{PC} = 6.6$ Hz, C-7); 43.1 (d, 1C, $^2J_{PC} = 19.0$ Hz, C-6); 70.0 (d, 1C, $^1J_{PC} = 139.5$ Hz, C-5); 25.9 (d, 1C, $^3J_{PC} = 6.6$ Hz, C-4); 2.6 (s, 3C, C-3); 3.7 (d, 3C, $^3J_{PC} = 2.2$ Hz, C-2); 1.4 (d, 3C, $^3J_{PC} = 2.1$ Hz, C-1). ^{31}P NMR: δ 30.2 ppm. b.p. 77–78°C/0.05 mm, yield 55%,

$C_{13}H_{35}N_2O_2PSi_3$. Calcd (%): C, 42.58; H, 9.62; N 7.64. Found (%): C, 42.48; H, 9.71; N 7.35.

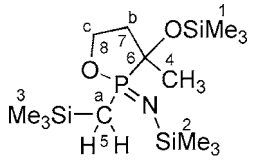
3,5,5-Trimethyl-3-trimethylsilyloxy-2-trimethylsilylamino-2-trimethylsilylimino-[1,2]-oxaphospholane, **6b**



6b

^{1}H NMR: δ 2.02 (d, 1H, $^2J_{PH} = 6.0$ Hz, NH); 1.97 (d, 2H, $^3J_{PH} = 8.6$ Hz); 1.35 (s, 6H, $C(CH_3)_2$) 1.45, 1.50 (s, 3H, CH_3 diastereotopic) 0.18 (s, 9H) $Si(CH_3)_3$); 0.14 (s, 9H, =N $Si(CH_3)_3$); 0.04 (d, 9H, $^4J_{PH} =$ 3.4 Hz, $NHSi(CH_3)_3$). ^{13}C[H] NMR: δ 78.3 (d, 1C, $^2J_{PC} = 5.5$ Hz, C-9); 31.7 (s, 1C, C-8); 29.8 (d, 1C, $^3J_{PC} = 2.2$ Hz, C-7); 50.7 (d, 1C, $^2J_{PC} = 16.5$ Hz, C-6); 76.1 (d, 1C, $^1J_{PC} = 133.0$ Hz, C-5); 22.8 (d, 1C, $^2J_{PC} = 6.6$ Hz, C-4); 2.4 (s, 3C, C-3); 3.64 (d, 3C, $^3J_{PC} = 2.2$ Hz, C-2); 1.27 (d, 3C, $^3J_{PC} = 2.2$ Hz, C-1). ^{31}P NMR: δ 26.55 ppm. b.p. 88–89°C/0.05 mm, yield 22%, $C_{15}H_{39}N_2O_2PSi_3$. Calcd (%): C, 45.64; H, 9.96; N, 7.10. Found (%): C, 45.39; H, 10.01; N, 7.25.

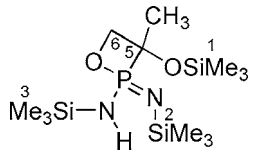
3-Methyl-3-trimethylsilyloxy-2-trimethylsilylmethyl-2-trimethylsilylimino-[1,2]-oxaphospholane, **7**



7

^{1}H NMR: δ 1.51–1.55 (m, 2H, CH_2-b); 1.41–1.3 (m, 2h, CH_2-c); 0.67–1.37 (m, 2H, CH_2-a); 1.37 (d,3H, $^3J_{PH} = 15.2$ Hz, CH3); 0.13 (s, 9H, $OSi(CH_3)_3$); 0.12 (d, 9H, $^4J_{PH} = 1.5$ Hz, CH2$Si(CH_3)_3$); 0.09 (d, 9H $^4J_{PH} = 1.9$ Hz, =N $Si(CH_3)_3$). ^{13}C[H] NMR: δ 75.0 (d, 1C, $^1J_{PC} = 96.6$ Hz, C-6); 63.7 (d, 1C, $^2J_{PC} = 6.4$ Hz, C-8); 39.4 (d, 1C, $^2J_{PC} = 17.6$ Hz, C-7); 23.0 (d, 1C, $^2J_{PC} = 9.9$ Hz, C-4); 17.5 (d, 1C, $^1J_{PC} = 86.8$ Hz, C-5); 3.8 (s, 3C, C-1); 2.6 (s, 3C, C-2); 0.32 (d, 3C, $^3J_{PC} = 2.2$ Hz, C-3). ^{31}P NMR: δ 45.5 ppm, (85% H_3PO_4, external standard). b.p. 74–75°C/0.05 mm, yield 58%, $C_{13}H_{36}NO_2PSi_3$. Calcd (%): C, 44.15; H, 10.26; N, 3.96. Found (%): C, 44.59; H, 9.92; N, 3.58.

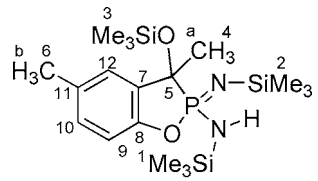
3-Methyl-3-trimethylsilyloxy-2-trimethylsilylamino-2-trimethylsilylimino-[1,2]-oxaphosphetane, **12**



12

^{1}H NMR: δ 3.68 (m, 2H, CH_2O); 2.62 (bs, 1H, NH); 1.35 (d, 3H, $^3J_{PH} = 14.3$ Hz, CH_3); 0.2 (s, 9H, $OSi(CH_3)_3$); 0.17 (s, 9H, =$NSi(CH_3)_3$); 0.11 (s, 9H, $NHSi(CH_3)_3$) ^{13}C[H] NMR: δ 76.4 (d, 1C, $^1J_{PC} = 137.3$ Hz, C-5); 67.4 (d, 1C, $^2J_{PC} = 7.7$ Hz, C-6); 19.8 (d, 1C, $^2J_{PC} = 4.8$ Hz, C-4); 3.4 (s, 3C, C-1); 3.3 (d, 3C, $^4J_{PC} =$ 3.3 Hz, C-2); 0.7 (s, 3C, C-3). ^{31}P NMR: 30.0 ppm. b.p. 85–86°C/0.05 mm, yield 38%, $C_{12}H_{33}N_2O_2PSi_3$. Calcd (%): C, 40.87; H, 9.43; N, 7.95. Found (%): C, 40.80; H, 9.51; N, 7.38.

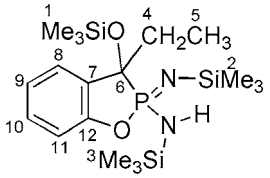
3,5-Dimethyl-3-trimethylsilyloxy-2-trimethylsilylamino-2-trimethylsilylimino-2,3-dihydro-benzo[d]1,2-oxaphosphole, **9a**



9a

^{1}H NMR: δ 7.10–6.83 (3H, aromatic); 2.93 (s, 1H NH); 2.33 (s, 3H, CH_3-b); 1.69 (d, 3H, $^3J_{PH} = 16.5$ Hz); 0.28 (s, 9H, $OSi(CH_3)_3$); 0.02 (s, 9H, =$NSi(CH_3)_3$); −0.11 (s, 9H, $NHSi(CH_3)_3$). ^{13}C[H] NMR: δ 113.6 (d, 1C, $^3J_{PC} = 7.7$ Hz, C-4); 131.3 (s 1C, C-11); 130.6 (s, 1C, C-10); 125.6 (d, 1C, $^3J_{PC} = 12.1$ Hz, C-9); 151.0 (d, 1C, $^2J_{PC} = 8.8$ Hz, C-8); 131.3 (s, 1C, C-7); 20.86 (s, 1C, C-6); 72.7 (d, 1C, $^1J_{PC} = 134.0$ Hz, C-5); 22.1 (d, 1C, $^2J_{PC} = 5.5$ Hz, C-4); 1.85 (s, 3C, C-3); 3.14 (d, 3C, $^3J_{PC} = 3.3$ Hz, C-2); 1.15 (d, 3C, $^2J_{PC} = 2.2$ Hz). ^{31}P NMR: δ 32.06 ppm. b.p. 95–95°C/0.05 mm, yield 79%, $C_{18}H_{37}N_2O_2PSi_3$. Calcd (%): C, 54.35; H, 9.38; N, 7.04. Found (%): C, 54.57; H, 8.96; N 6.89.

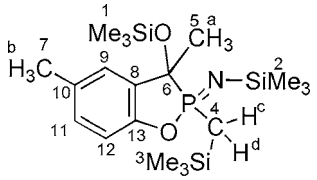
3-Ethyl-3-trimethylsilyloxy-2-trimethylsilylamino-2-trimethylsilylimino-2,3-dihydro-benzo[d]1,2-oxaphosphole, **9b**



9b

^{1}H NMR: δ 7.29–6.91 (m, 4H, aromatic); 3.1 (s, 1H, NH); 2.17–1.96 (m, 2H, CH_2); 1.17 (t, 3H, $^3J_{HH}$ = 7.0 Hz); 0.28 (s, 9H, $OSi(CH_3)_3$); −0.2 (s, 9H, NH $Si(CH_3)_3$); −0.11 (s, 9H, =N $Si(CH_3)_3$). ^{13}C[H] NMR: δ 154.0–114.1 (6C, aromatic); 75.4 (d, 1C, $^1J_{PC}$ = 134.0 Hz, C-6); 27.3 (d, 1C, $^2J_{PC}$ = 5.5 Hz, C-4); 8.5 (d, 1C, $^3J_{PC}$ = 4.4 Hz, C-5); 2.9 (d, 3C, $^3J_{PC}$ = 3.3 Hz, C-2); 1.3 (s, 3C, C-1); 1.1 (s, 3C, C-3). ^{31}P NMR: δ 29.9 ppm. b.p. 94–95°C/0.05 mm, yield 84%, $C_{18}H_{37}N_2O_2PSi_3$. Calcd (%): C, 54.35; H, 9.38; N, 7.04. Found (%): C, 53.88; H, 9.41; N, 6.92.

3,6-Dimethyl-3-trimethylsilyloxy-2-trimethylsilylmethyl-2-trimethylsilylimino-2,3-dihydro-benzo[d] 1,2-oxaphosphole, **10**



10

^{1}H NMR: δ 7.14–6.80 (3h, aromatic); 2.33 (s, 3h, CH_3-b); 1.67 (d, 3H, $^3J_{PH}$ = 15.9 Hz, CH_3-a); 1.11(sdd, 1h, $^2J_{PH}$ = 24.5 Hz, $^2J_{HH}$ = 12.9 Hz, CH-d); 0.189s, 9H, $OSi(CH_3)_3$); 0.06 (s, 9H, =N$Si(CH_3)_3$); −0.03 (s, 9H, $CH_2Si(CH_3)_3$). ^{13}C[H] NMR: δ 151.3–113.8 (6C, aromatic); 21.0 (s, 1C, C-7); 74.52 (d, 1C, $^1J_{PC}$ = 198 Hz, C-6); 22.3 (d, 1C, $^2J_{PC}$ = 8.8 Hz, C-5); 4.6 (d, 1C, $^1J_{PC}$ = 82.3 Hz, C-4); 3.8 (d, 3C, $^3J_{PC}$ = 3.3 Hz, C-1); 2.12 (s, 3, C-2); 0.33 (s, 3C, C-3). ^{31}P NMR: δ 49.1 ppm. b.p. 108–109°C/0.05 mm, $C_{19}H_{38}NO_2PSi_3$. Calcd (%): C, 53.35; H, 8.95; N, 3.27. Found (%): C, 53.58; H, 8.77; N, 3.16.

CONCLUSION

Reactions of the two-coordinated phosphines **1** and **2** with the hydroxy ketones yielded the heterocyclic compounds **6a,b, 7, 9a,b**, and **10** thus in accord with the previously proposed two-step mechanism for cyclization of acetyl acetone and similar β-dicarbonyl compounds. These reactions provide a new, mild, and convenient route to heterocyclic phosphoranimines. This heterocylization approach was extended to the synthesis of four-membered cycles and the new phosphoranimine **12** was thereby prepared in moderate yield.

Further investigations in this field will explore the scope and limitations of the approach and will develop applications for the synthesis of new biologically active organophosphorus compounds.

ACKNOWLEDGMENTS

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