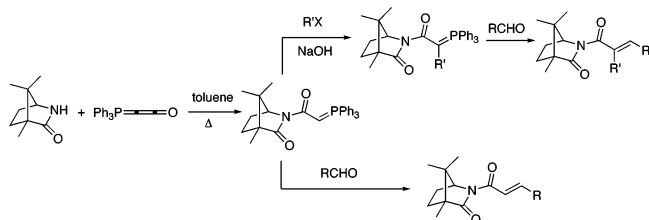


Facile Preparation and Functionalization of Chiral Stabilized Ylides from Common Chiral Auxiliaries Using Triphenylphosphoranylidene ketene (the Bestmann Ylide) and Their Use in Wittig Reactions

Robert K. Boeckman, Jr.,* Xinyi Song, and Joseph E. Pero
 Department of Chemistry, University of Rochester, Rochester,
 New York 14627-0216

rkb@rkbmac.chem.rochester.edu

Received August 21, 2006



Camphor-derived lactams and other related chiral controllers have been found to react with the Bestmann ylide (triphenylphosphoranylidene ketene) upon heating in toluene. The resulting parent ylides provide convenient access to a structurally diverse set of chiral stabilized ylides via functionalization. The utility of these chiral ylides for Wittig reactions has been briefly investigated and the effects of α -substitution noted.

Phosphorus ylides stabilized by a variety of electron-withdrawing groups (EWG) have found wide use in the Wittig reaction.^{1,2} Isolated examples of the preparation of such ylides bearing a removable oxazolidinone or camphor sultam auxiliaries have appeared.^{3,4} Their utility for complex molecule synthesis is increasingly well established as additional examples of their use and the use of the related chiral Horner–Wadsworth–Emmons (HWE) phosphonates are reported.^{5,6} We required a convenient route to sizable quantities of chiral stabilized ylides such as **1–4** (Chart 1). Convenient access to the parent ylides should afford

CHART 1

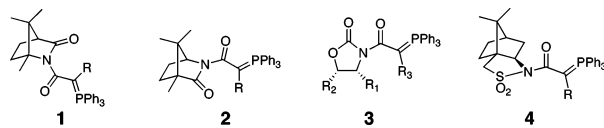
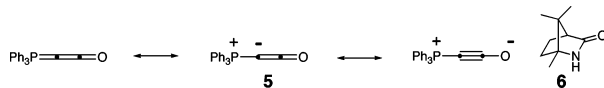


CHART 2



access to their more functionalized counterparts via well-established alkylation and acylation chemistry.⁷

We identified triphenylphosphoranylidene ketene (**5**), the Bestmann ylide, as a likely starting point as it is readily available in multigram quantities in one step from commercial starting materials (Chart 2).^{8,9} Our first attempts involving conversion of camphor lactam **6** to the Li or K salts with *n*BuLi or KH followed by addition of **5** were not promising. Complex mixtures containing high molecular weight materials were observed. This seemed surprising because **5** was well known to react with a variety of electrophiles and nucleophiles, including amines, alcohols, and thiols, and chiral alcohols that afford chiral ester stabilized ylides.^{10,11} Consideration of the electronic structure of **5** suggested that the use of the amide anion was counterproductive. In actuality, ylide **5** reacts smoothly with relatively acidic neutral nucleophiles because proton transfer and not nucleophilic addition is likely the rate-determining step. Although α amino esters,¹² acidic NH heterocycles,^{10a,13} vinylogous amides and thioamides,¹³ and sulfonamides^{10a} have been observed to react, generally nucleophiles with a $pK_a > \sim 18$ (apparent upper limit of the basicity of **5**) such as NH-carboxamides and lactams have not been employed previously in reactions with **5**.

We were gratified that simply heating a mixture of **5** and lactam **6** in toluene at reflux smoothly afforded the desired stabilized imide ylide **7** in 90% yield (Table 1). The estimated pK_a of lactam **6** is 20–25. Thus, the apparent upper limit of the basicity of **5** can now be regarded as in that range. We found that the reaction was general for other camphor-derived lactams such as **8** and **9**, as well as other prototypical chiral auxiliaries such as Evan's oxazolidinones **10**¹⁴ and the Oppolzer sultam **11**,¹⁵

(1) Cadogan, J. I. G., Ed.; *Organophosphorus Reagents in Organic Synthesis*; 1979.

(2) (a) Abell, A. D.; Edmonds, M. K. *Organophosphorus Reagents* **2004**, 99–127. (b) Edmonds, M.; Abell, A. *Mod. Carbonyl Olefination* **2004**, 1–17. (c) Nicolaou, K. C.; Harter, M. W.; Gunzner, J. L.; Nadin, A. *Liebigs Ann./Recueil* **1997**, 1283–1301. (d) Maercker, A. *Org. React.* **1965**, *14*, 270–490.

(3) (a) Williams, D. R.; Nold, A. L.; Mullins, R. J. *J. Org. Chem.* **2004**, *69*, 5374–5382. (b) Mamaghani, M.; Tabatabaiean, K.; Badrian, A. *Phosphorus, Sulfur Silicon Relat. Elem.* **2004**, *179*, 1347–1353. (c) Noguchi, H.; Aoyama, T.; Shioiri, T. *Heterocycles* **2002**, *58*, 471–504. (d) Suzuki, M.; Yamazaki, T.; Ohta, H.; Shima, K.; Ohi, K.; Nishiyama, S.; Sugai, T. *Synlett* **2000**, 189–192. (e) Badone, D.; Bernassau, J.-M.; Cardamone, R.; Guzzi, U. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 535–538. (f) Evans, D. A.; Black, W. C. *J. Am. Chem. Soc.* **1993**, *115*, 4497–4513.

(4) Cheng, P. T. W.; Chen, S.; Devasthale, P.; Ding, C. Z.; Herpin, T. F.; Wu, S.; Zhang, H.; Wang, W.; Ye, X.-Y. Bristol-Myers Squibb Co., USA, Patent No. 2004004665, 2004; 543 pp.

(5) Selected recent examples: (a) Kouko, T.; Matsumura, K.; Kawasaki, T. *Tetrahedron* **2005**, *61*, 2309–2318. (b) Ni, Y.; Amarasinghe, K. K. D.; Ksebbati, B.; Montgomery, J. *Org. Lett.* **2003**, *5*, 3771–3773. (c) Lee, K.; Cha, J. K. *J. Am. Chem. Soc.* **2001**, *123*, 5590–5591.

(6) Leading references: (a) Wipf, P.; Hopkins, T. D. *Chem. Commun.* **2005**, 3421–3423. (b) Nicolaou, K. C.; Piscopio, A. D.; Bertinato, P.; Chakraborty, T. K.; Minowa, N.; Koide, K. *Chem.-Eur. J.* **1995**, *1*, 318–333. (c) Broka, C. A.; Ehrler, J. *Tetrahedron Lett.* **1991**, *32*, 5907–5910.

(7) Bestmann, H. J.; Zimmerman, R. *Carbon–Carbon Bond Form.* **1979**, *1*, 353–426.

(8) (a) Schobert, R. *Org. Synth.* **2005**, *82*, 140–145. (b) Bestmann, H. J.; Sandmeier, D. *Chem. Ber.* **1980**, *113*, 274–277.

(9) Schobert, R.; Löffler, J.; Siegfried, S. *Targets Heterocycl. Syst.* **1999**, *3*, 245–264.

(10) (a) Bestmann, H. J.; Schmid, G.; Sandmeier, D. *Chem. Ber.* **1980**, *113*, 912–918. (b) Bestmann, H. J.; Schobert, R. *Angew. Chem.* **1985**, *97*, 783–784. (c) Schobert, R.; Siegfried, S.; Gordon, G. J. *J. Chem. Soc., Perkin Trans. 1* **2001**, 2393–2397.

(11) Bestmann, H. J.; Kellermann, W. *Synthesis* **1994**, 1257–1261.

(12) Schobert, R.; Jagusch, C. *Tetrahedron* **2005**, *61*, 2301–2307.

(13) (a) Bestmann, H. J.; Schmid, G.; Sandmeier, D. *Angew. Chem.* **1976**, *88*, 92–93. (b) Nickisch, K.; Klose, W.; Nordhoff, E.; Bohlmann, F. *Chem. Ber.* **1980**, *113*, 3086–3088. (c) Boulos, L. S.; Hafez, T. S.; Fahmy, A. A.; Abdel-Hamid, M. M. *Egypt. J. Pharm. Sci.* **1988**, *29*, 515–520.

(14) Gage, J. R.; Evans, D. A. *Org. Synth.* **1990**, *68*, 77–82.

TABLE 1. Preparation of Parent Stabilized Ylides

Chiral Auxiliary	Chiral Stabilized Ylide	Time (h)	Yield (%)
		~24	90%
		26	88%
		~24	82%
		~24	85%
		6	75%

TABLE 2. Alkylation and Acylation of Ylides 7 and 12

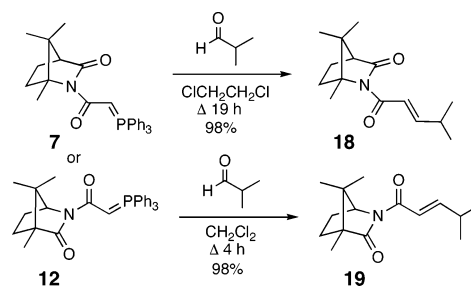
Ylide	Halide	Time (h)	Product	Yield
7	CH ₃ -I	2	16a R = CH ₃	98%
12	CH ₃ -I	2	17a R = CH ₃	98%
7	CH ₃ (CH ₂) ₅ -I	24	16b R = nHexyl	98%
12	CH ₂ =CHCH ₂ Br	1	17b R = allyl	93%
7		1	16c R = (E)-crotyl	85%
7		2	16d R =	88%
12		2	17c R =	85%
12		2	17d R =	95%
12		19	17e R =	91%
7	<i>i</i> PrCOCl	0.5	16e R = C(O) <i>i</i> Pr	98%

affording the imide or sulfonyl amide stabilized ylides **12**, **13** and **14**,^{3c}**15**⁴ in excellent yields (Table 1).

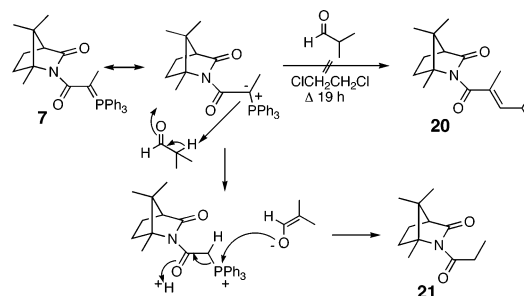
Further functionalization of these ylides occurred smoothly as expected. Alkylation or acylation of the parent ylides **7** or **12** with a variety of alkyl and acyl halides followed by treatment with NaOH afforded the expected substituted ylides **16a–e** and **17a–e** in excellent yields (Table 2).^{16,17}

(15) (a) Towson, J. C.; Weismiller, M. C.; Lal, G. S.; Sheppard, A. C.; Davis, F. A. *Org. Synth.* **1990**, *69*, 158–168. (b) Weismiller, M. C.; Towson, J. C.; Davis, F. A. *Org. Synth.* **1990**, *69*, 154–157. (c) Oppolzer, W. *Tetrahedron* **1987**, *43*, 1969–2004.

SCHEME 1. Wittig Reactions of Ylides 7 and 12



SCHEME 2. Attempted Wittig Reaction: Reduction of Ylide 7



The parent ylides **7** and **12** react smoothly with simple aldehydes, affording the expected (*E*)- α,β -unsaturated imides. Exposure of either ylide **7** or **12** to isobutyraldehyde in hot dichloromethane or dichloroethane afforded exclusively the expected (*E*)- α,β -unsaturated imides **18** and **19** in excellent yields (both 98%) as for the parent ylides **14** and **15** (Scheme 1).^{3,4}

Somewhat surprisingly, more functionalized analogues of **7** and **12**—**15** have not been previously reported, and nothing was known of their behavior (e.g., **16** and **17**) upon exposure to aldehydes. Ylides **16** and **17** should behave analogously to the parent ylides **7** and **12**. Surprisingly, the reactivity of these materials differs markedly from the parent ylides.

Thus, upon exposure of **16a** to isobutyraldehyde in refluxing dichloroethane, none of the expected (*E*)-trisubstituted α,β -unsaturated imide **20** was observed. Instead, a complex mixture was obtained containing unreacted aldehyde, aldol condensation products of isobutyraldehyde, and the propionimide **21**,¹⁸ resulting from effective reduction of the ylide.

The precise origin of imide **21** is still uncertain. A plausible mechanism would involve enolization of the aldehyde by the ylide **16a** followed by collapse of the enolate-phosphonium salt ion pair by attack at phosphorus affording the enolate, and, subsequently upon protonation, the propionimide **21** (Scheme 2). Similar results were obtained using the ylide **17a** with isobutyraldehyde. No olefination occurred, and the analogous propionimide **22**¹⁸ was observed (Chart 3).

To examine the role of steric hindrance in the aldehyde, we reacted **16a** with the unbranched butyraldehyde in dichloroethane (80 °C, 18 h), resulting in slow conversion to the expected trisubstituted α,β -unsaturated imide **23** in 31% yield (Chart 3). Because competing formation of imide **21** was noted, the scope

(16) Bestmann, H. J.; Schulz, H. *Tetrahedron Lett.* **1960**, 5–6.

(17) Werkhoven, T. M.; Van Nispen, R.; Lugtenburg, J. *Eur. J. Org. Chem.* **1999**, 2909–2914.

(18) Boeckman, R. K., Jr.; Boehmler, D. J.; Musselman, R. A. *Org. Lett.* **2001**, *3*, 3777–3780.

CHART 3

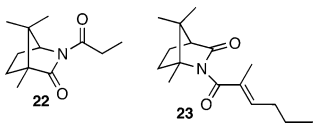
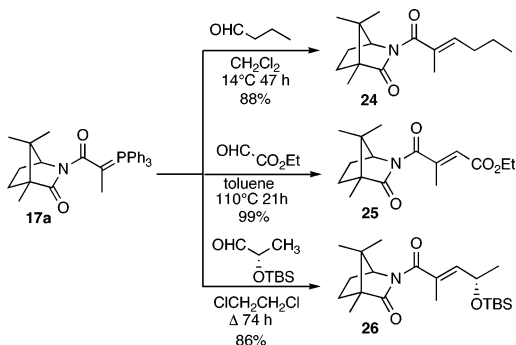
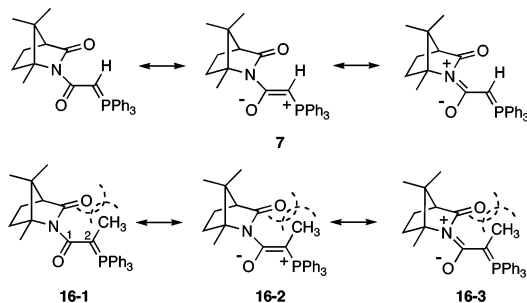
SCHEME 3. Olefination of Ylide **17a**

CHART 4



of reactivity of ylide class **16** seems limited. Thus, we examined reaction of the less congested ylide **17a** with several reactive, unbranched and α -heteroatom branched aldehydes. Reactions with **17a** proceed smoothly in excellent yield (conditions unoptimized) to afford exclusively the expected (*E*)- α,β -unsaturated imides **24**–**26**. However, the reactivity of ylide **17a** is also much lower than the parent ylide **12** (Scheme 3). Use of lower temperatures and longer reaction times was necessary to achieve complete conversion of **17a** and avoid formation of the byproduct imide **22**. The chiral lactaldehyde affords imide **26** as a single diastereomer with no observable epimerization of the chiral center.

At first, the low reactivity and apparently higher basicity of these chiral ylides seemed anomalous. However, it can be seen that these properties have their origin in the structure and conformational requirements of the substituted ylides **16** and **17**. Strain imparted by delocalization of the nitrogen lone pair onto the endocyclic carbonyl group of imides derived from bicyclic lactams such as **6**–**8** raises the energy of this resonance contributor as shown by the participation of the exocyclic carbonyl group in anchimeric assistance.¹⁹

The major contributors to that stabilization are those depicted for **7** (Chart 4). Strong dipole forces orient the carbonyl groups anti in the absence of a chelating metal ion. That places the hydrogen or alkyl substituent in **7** and the related ylides in a very congested environment because the delocalization requires coplanarity of the *N*-acyl substituent and the endocyclic carbonyl group. It has previously been seen that reactivity and enanti-

(19) Boeckman, R. K., Jr.; Wroblewski, S. T. *J. Org. Chem.* **1996**, *61*, 7238–7239.

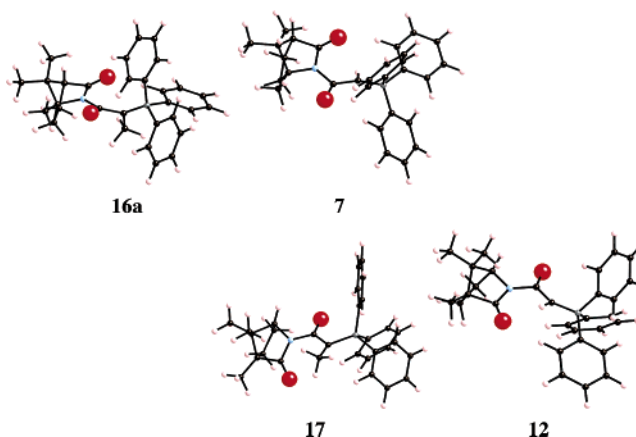


FIGURE 1. Model (HF 3-21G* Spartan 2004) of ylides **16a**, **7**, **17a**, and **12**.

oselectivity of reactions of α -substituted enones bearing typical chiral controller units were significantly diminished because of unfavorable allylic strain derived from interactions between the chiral controller moiety and the α substituent.^{20,21}

We wished to probe the origin of the apparently higher basicity and relatively low reactivity of the α -substituted ylides **16a** and **17a**, which could arise from steric inhibition of delocalization of the negative charge of the ylide moiety by the α substituent. Thus, resonance form **16-1** (Chart 4) is rendered the major contributor due to twisting about the N–C₁ and/or the C₁–C₂ side chain bonds, reducing the stabilization and increasing the basicity of **16a** and **17a**.

Examination of a computational model (HF 3-21G* Spartan 2004) of ylide **16a** (Figure 1) lends some support to this argument. A relatively small (absolute value of the OC₁C₂P dihedral angle: 23°) twist occurs about the C₁–C₂ bond. The parent ylide **7** is only slightly twisted (absolute value of the OC₁C₂P dihedral angle: 2°), so substantial delocalization should be possible for both. However, the ylide carbon in **16a** is effectively buried within the molecular framework, shielded on both faces by a combination of the bridgehead methyl, endocyclic carbonyl, and two P-phenyl groups. It is actually quite remarkable that any reactivity is seen at all. Torsional strain about the C₁–C₂ bond is reduced in ylides **17a** and **12** as is evident from the observed OC₁C₂P dihedral angles 4° and 1° as shown in Figure 1. Thus, some combination of resonance stabilization and reduction steric shielding appears to be responsible for the more normal reactivity and basicity observed for ylide **17a**. As can be seen, the lower face of ylide **17a** appears more accessible (from the bottom as depicted in Figure 1), that is partially shielded by two P-phenyl moieties.

Facile introduction of a chiral controller unit by olefination enables diastereoselective conjugate addition,²² reduction,²³ and alkylation,²⁴ making these attractive reagents for stereoselective

(20) Evans, D. A.; Chapman, K. T.; Bisaha, J. *J. Am. Chem. Soc.* **1988**, *110*, 1238–1256.

(21) Boeckman, R. K., Jr.; Liu, Y. *J. Org. Chem.* **1996**, *61*, 7984–7985.

(22) (a) Williams, D. R.; Nold, A. L.; Mullins, R. J. *J. Org. Chem.* **2004**, *69*, 5374–5382. (b) Oppolzer, W.; Kingma, A. *J. Helv. Chim. Acta* **1989**, *72*, 1337–1345.

(23) Prasad, M.; Liu, Y.; Kim, H.-Y.; Repic, O.; Blacklock, T. J. *Tetrahedron: Asymmetry* **1999**, *10*, 3479–3482.

(24) (a) Oppolzer, W.; Moretti, R.; Thomi, S. *Tetrahedron Lett.* **1989**, *30*, 5603–5606. (b) Evans, D. A.; Mathre, D. J.; Scott, W. L. *J. Org. Chem.* **1985**, *50*, 1830–1835.

functionalization of acyclic systems. An application of such chiral ylides to complex molecule synthesis has been recently reported.²⁵

Experimental Section²⁶

General Procedure for the Preparation of Chiral Ylides 7, 12–15. A mixture of triphenylphosphoranylideneacetone (the Bestmann ylide) **5**⁸ (1.0–1.5 equiv) and 1.0 equiv of the chiral auxiliary (**6**, **8–11**) in toluene (1–2 M) was heated to reflux (6–26 h) until no starting material was detected (monitored by ¹H NMR). The reaction mixture was concentrated in vacuo, and the residue was isolated and purified by chromatography on SiO₂ and/or recrystallization to provide the stabilized ylides as a solid (**7**, **12–15**).

(1R,4S)-1,7,7-Trimethyl-2-[2-(triphenylphosphanylidene)acetyl]-2-aza-bicyclo[2.2.1]heptan-3-one (7). According to the general procedure above, ketene **5**⁸ (18.8 g, 0.062 mol, 1.5 equiv) and lactam **6** (6.3 g, 0.041 mol) were dissolved in 21 mL of toluene, and the resulting mixture was heated until no more **6** could be detected by ¹H NMR (~24 h). The solvent was removed in vacuo, and the residue was recrystallized from ethyl acetate at –20 °C, affording 17.0 g (90%) of ylide **7** as a tan solid having mp 182–184 °C, [α]_D²⁰ –55.9° (*c* 3.1, CH₂Cl₂), and spectral characteristics: ¹H NMR (400 MHz, CDCl₃) 7.71–7.66 (m, 6H), 7.56–7.53 (m, 3H), 7.47–7.44 (m, 6H), 4.22 (d, *J* = 25 Hz, 1H), 2.31 (d, *J* = 4 Hz, 1H), 2.17–2.13 (m, 1H), 2.00–1.94 (m, 1H), 1.80–1.77 (m, 1H), 1.69–1.66 (m, 1H), 1.46 (s, 3H), 1.06 (s, 3H), 0.86 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) 177.8, 167.4, 133.2, 131.9, 128.8, 127.5 (d, *J*_{C–P} = 91 Hz), 71.9, 56.1, 48.2, 43.6 (d, *J*_{C–P} = 116 Hz), 33.0, 23.8, 18.7, 17.8, 13.4; ³¹P NMR (160 MHz, CDCl₃) 14.5; IR (film) 2966, 1708, 1567, 1431 cm^{–1}. HRMS (EI). Calcd for C₂₉H₃₁NO₂P (M + H)⁺: 456.2092. Found: 456.2091.

(1S,4R)-4,7,7-Trimethyl-2-[2-(triphenylphosphanylidene)acetyl]-2-aza-bicyclo[2.2.1]heptan-3-one (12). According to the general procedure above, ketene **5** (9.07 g, 0.03 mol, 1.5 equiv) and lactam **8** (3.07 g, 0.041 mol) were dissolved in 10 mL of anhydrous toluene, and the resulting mixture was heated until no more **8** could be detected by ¹H NMR (26 h). The solvent was removed in vacuo, and the residue was purified by chromatography on SiO₂ with elution by 20–50% ethyl acetate in hexane, followed by recrystallization from ethyl acetate at –20 °C, affording 7.98 g of ylide **12** (88%) as a pale yellow solid having mp 222–224 °C, [α]_D²⁰ +45.5° (*c* 2.67, CH₂Cl₂), and spectral characteristics: ¹H NMR (400 MHz, CDCl₃) 7.77–7.65 (m, 6H), 7.55–7.52 (m, 3H), 7.47–7.42 (m, 6H), 4.84 (d, *J* = 25 Hz, 1H), 4.36 (s, 1H), 1.94–1.90 (m, 1H), 1.76–1.56 (m, 3H), 1.06 (s, 3H), 0.97 (s, 3H), 0.88 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) 178.7, 165.7, 133.3, 131.9, 129.1, 127.5 (d, *J*_{C–P} = 91 Hz), 63.1, 56.5, 47.9, 39.8 (d, *J*_{C–P} = 119 Hz), 30.3, 27.3, 18.6, 18.0, 9.77; ³¹P NMR (160 MHz, CDCl₃) 14.4; IR (film) 2955, 1708, 1561, 1478, 1431 cm^{–1}. HRMS (EI). Calcd for C₂₉H₃₁NO₂P (M + H)⁺: 456.2092. Found: 456.2097.

General Procedure: Alkylation of Ylides 7 and 12. A mixture of ylide **7** (1.0 equiv) and alkyl bromide or iodide, or acyl chloride (2.0 equiv), in anhydrous acetonitrile (0.5 M) was heated to reflux. The resulting homogeneous mixture was kept at reflux for the time period as specified (0.5–24 h). The reaction mixture was concentrated in vacuo, and the residue was redissolved in dichloromethane (0.25 M). A 1 M solution of aqueous NaOH (2.0 equiv) was added, and the mixture was stirred vigorously at room temperature for 2 h. The phases were separated, the aqueous phase was extracted with twice the volume of dichloromethane, and the combined organic phases were dried over magnesium sulfate and concentrated

in vacuo to give a solid residue. This solid residue was purified by chromatography on SiO₂ with elution with 50–100% ethyl acetate in hexane to provide the alkylated ylides **16a–d**, **17a–e** mainly as white solids in 85–98% yield.

General Procedure for Condensation of Ylides 7, 12, 16a, and 17a with Aldehydes. A solution of the ylide **7**, **12**, **16a**, or **17a** (1.5 equiv) and the aldehyde (1.0 equiv) in anhydrous CH₂Cl₂, (CH₂Cl)₂, or toluene was heated at 40–100 °C in a sealed tube until no aldehyde could be detected by TLC analysis (4–74 h). The reaction mixture was cooled to room temperature and concentrated in vacuo to provide crude oily products. The oily residue was purified by chromatography on SiO₂ with elution by 5% ethyl acetate in hexane to provide the unsaturated carbonyl compounds as a colorless oil in 31–99% yields.

(1R,4S)-1,7,7-Trimethyl-2-[(2E)-4-methyl-pent-2-enoyl]-2-aza-bicyclo[2.2.1]heptan-3-one (18). A solution of 91.1 mg (0.2 mmol, 1.5 equiv) of ylide **7** and isobutyraldehyde (12.2 μL, 9.62 mg, 0.13 mmol) in anhydrous ClCH₂CH₂Cl was heated at ~83 °C in a sealed tube until no aldehyde could be detected by TLC analysis (19 h). The reaction mixture was cooled to room temperature and concentrated in vacuo to provide crude oily products. The oily residue was purified by chromatography on SiO₂ with elution by 5% ethyl acetate in hexane to provide 44.5 mg (89%) of unsaturated imide **18** as a colorless oil having the spectral characteristics: ¹H NMR (400 MHz, CDCl₃) 6.94 (dd, *J*₁ = 15 Hz, *J*₂ = 6 Hz, 1H), 6.86 (d, *J* = 16 Hz, 1H), 2.50–2.49 (m, 1H), 2.34 (d, *J* = 4 Hz, 1H), 2.04–2.00 (m, 2H), 1.84–1.81 (m, 1H), 1.61–1.60 (m, 1H), 1.48 (s, 3H), 1.07 (d, *J* = 7 Hz, 6H), 1.03 (s, 3H), 0.91 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) 178.5, 167.3, 154.8, 121.9, 72.9, 55.4, 47.5, 32.1, 23.7, 21.4, 21.3, 18.6, 17.5, 13.3; IR (film) 2965, 1746, 1679, 1634, 1456 cm^{–1}. HRMS (EI). Calcd for C₁₅H₂₄NO₂ (M + H)⁺: 250.1807. Found: 250.1804.

(1S,4R)-4,7,7-Trimethyl-2-[(2E,4S)-2-methyl-4-tert-butylidimethylsilyloxy-pent-2-enoyl]-2-aza-bicyclo[2.2.1]heptan-3-one (26). A solution of 704.4 mg (1.5 mmol, 1.5 equiv) of ylide **17a** and 188.3 mg of TBS protected (*S*)-lactaldehyde (1.0 mmol) in anhydrous ClCH₂CH₂Cl was heated at ~83 °C in a sealed tube until no aldehyde could be detected by TLC analysis (74 h). The reaction mixture was cooled to room temperature and concentrated in vacuo to provide crude oily products. The oily residue was purified by chromatography on SiO₂ with elution by 5% ethyl acetate in hexane to provide 0.353 g (86%) of unsaturated imide **26** as a colorless oil having the spectral characteristics: ¹H NMR (400 MHz, CDCl₃) 5.81 (d, *J* = 8 Hz, 1H), 4.62–4.55 (m, 1H), 4.11 (d, *J* = 2 Hz, 1H), 2.01–1.93 (m, 1H), 1.82 (d, *J* = 1 Hz, 3H), 1.81–1.67 (m, 2H), 1.57–1.50 (m, 1H), 1.25 (d, *J* = 6 Hz, 3H), 1.03 (s, 3H), 0.97 (s, 3H), 0.92 (s, 3H), 0.85 (s, 9H), 0.05 (s, 3H), 0.01 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) 177.2, 171.0, 141.5, 129.3, 65.8, 64.8, 56.3, 47.2, 30.8, 26.6, 25.8, 23.2, 18.7, 18.1, 17.7, 13.5, 9.6, –4.6, –4.9; IR (film) 2959, 2939, 2857, 2360, 1752, 1672, 1473 cm^{–1}. HRMS (EI). Calcd for C₂₁H₃₇NNaO₃Si (M + Na)⁺: 402.2440. Found: 402.2463

Acknowledgment. We thank the National Science Foundation (CHE-0305790) for support of these studies.

Supporting Information Available: A description of general experimental methods, additional detailed experimental procedures, analytical data, and the ¹H NMR and selected ¹³C, ³¹P, and IR spectra for **7**, **12–15**, **16a–e**, **17a–e**, **18**, **19**, and **24–26**. This material is available free of charge via the Internet at <http://pubs.acs.org>.

JO061732Y

(25) Boeckman, R. K., Jr.; Pero, J. E.; Boehmler, D. J. *J. Am. Chem. Soc.* **2006**, *128*, 11032–11033.

(26) General experimental methods section and additional experimental procedures and characterization data may be found in the Supporting Information.