Synthesis of Fused 1,2-Diazetidinones via an Intramolecular Horner–Emmons Reaction

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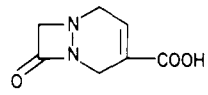
8-Oxo-1,6-diazabicyclo[4.2.0]oct-3-ene-3-carboxylates (6-aza-1-carba-2-cephem-3-carboxylates) have been prepared for the first time by application of the Horner–Emmons reaction to appropriate 1,2-diazetidinone precursors.

A massive effort has been devoted during the past decade to the synthesis of nuclear analogues of the β-lactam antibiotics.[1] We have recently initiated a program aimed at the development of novel, highly strained bridgehead aza analogues of the carbapenems and carbacephems and describe in this paper the synthesis of the first representatives of the 6-aza-1-carba-2-cephem-3-carboxylate system **1**.



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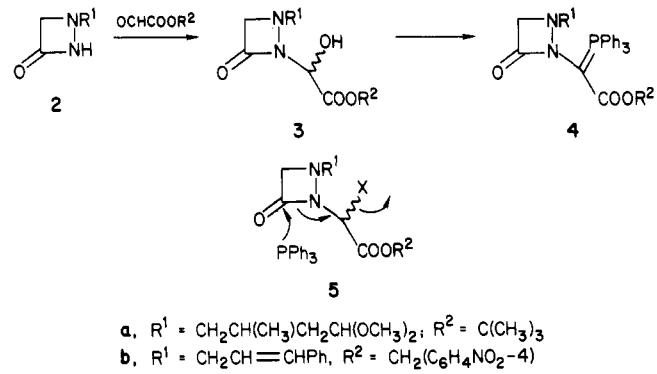
A widely used procedure for the synthesis of fused β-lactams, developed by Woodward,[2] utilizes an intramolecular Wittig reaction for the crucial cyclization step. We have already described the synthesis of 1,2-diazetidinones suitably substituted at N-1 for application of this cyclization strategy.[3] Condensation of **2a** with *tert*-butyl glyoxylate proceeded smoothly to give the hemiaminal **3a** (Scheme I). Purification of **3a** proved difficult because of its propensity to revert to starting materials during chromatography. Unfortunately, all efforts to convert **3a** to the phosphorane **4a** under conditions that are standard in β-lactam chemistry (e.g., CH_3SO_2Cl/Et_3N followed by PPh_3/2,6-lutidine) were unsuccessful. Analysis of the crude reaction mixture by IR clearly revealed that the aza-β-lactam ring had been destroyed. An attempt to convert **3b** to **4b** was also unsuccessful. We have not investigated reasons for the failure of these reactions, but we assume that contributing factors include interference by N-1 in the hydroxyl activation step and probable nucleophilic ring opening of **5** (X = Cl, OSO_2CH_3), by triphenylphosphine.

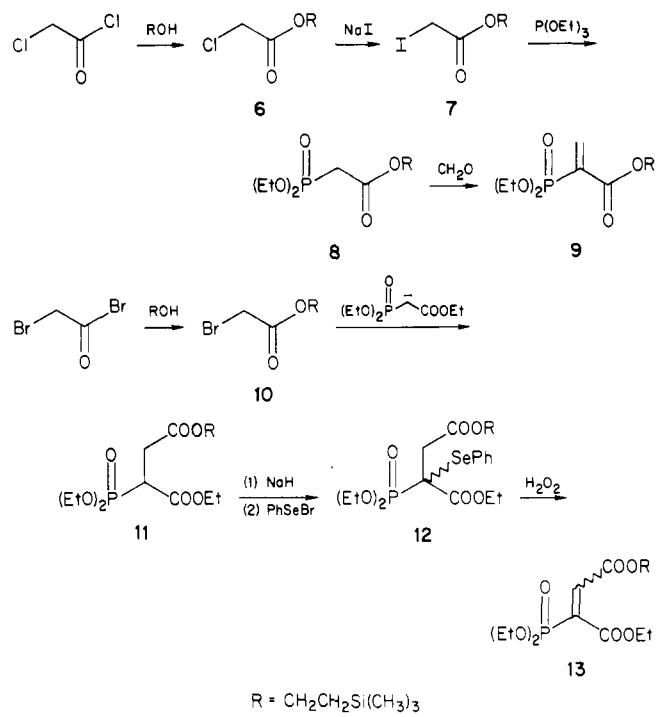
The unexpected failure of these attempts to prepare the phosphoranes **4** led us to investigate the intramolecular Horner–Emmons reaction[4] as an alternative to the intramolecular Wittig reaction. The vinyl phosphonates **9** and **13** were prepared by standard procedures as outlined in Scheme II. Condensation of **14a**[3] with **9** took place in 93% yield simply by stirring the two reactants overnight at room temperature *in the absence of base*. It is noteworthy that the analogous reaction with β-lactam substrates requires the use of *n*-butyllithium as base;[4] our result is a reflection of the much greater nucleophilicity of N-2 in diazetidinones compared with the β-lactam amide nitrogen. Ozonolysis

Scheme I



a, $R^1 = CH_2CH(CH_3)CH_2CH(OCH_3)_2$; $R^2 = C(CH_3)_3$
b, $R^1 = CH_2CH{=}CHPh$, $R^2 = CH_2(C_6H_4NO_2\text{-}4)$

Scheme II



R = $CH_2CH_2Si(CH_3)_3$

of the adduct **15a** at −78 °C followed by treatment with dimethyl sulfide gave the unstable aldehyde **16a**. For subsequent conversion, it proved unnecessary to isolate **16a**; addition of 1 equiv of DBU to the crude reaction mixture, followed by warming to room temperature, resulted in formation of the fused aza-β-lactam **17a** in 54% yield (Scheme III). Although N-2 alkylation of 1,2-diazetidinones with alkyl halides occurs only when N-1 is severely sterically hindered,[5] both **14b** and **14c** reacted smoothly with **9** to give the adducts **15b** and **15c** in 83% and 82% yields, respectively. The success of these latter reactions is undoubtedly a consequence of the reversibility

(1) (a) "Chemistry and Biology of β-Lactam Antibiotics"; Morin, R. B., Gorman, M., Eds.; Academic Press: New York, 1982; Vol. 2. (b) Dürckheimer, W.; Blumbach, J.; Lattrell, R.; Scheunemann, K. H. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 180.

(2) (a) Scartazzini, R. von; Peter, H.; Bickel, H.; Heusler, K.; Woodward, R. B. *Helv. Chim. Acta* **1972**, *55*, 408. (b) Scartazzini, R. von; Gosteli, J.; Bickel, H.; Woodward, R. B. *Helv. Chim. Acta* **1972**, *55*, 2567. (c) Ernest, I.; Gosteli, J.; Greengrass, C. W.; Holick, W.; Jackman, D. E.; Pfaendler, H. R.; Woodward, R. B. *J. Am. Chem. Soc.* **1978**, *100*, 8214.

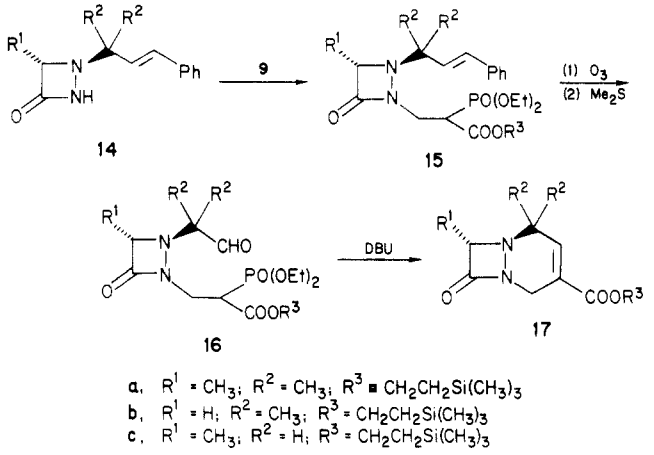
(3) Taylor, E. C.; Davies, H. M. L. *J. Org. Chem.* **1984**, *49*, 4415.

(4) Venugopalan, B.; Hamlet, A. B.; Durst, T. *Tetrahedron Lett.* **1981**, *22*, 191.

(5) Taylor, E. C.; Davies, H. M. L.; Hinkle, J. S., see accompanying article in this issue.

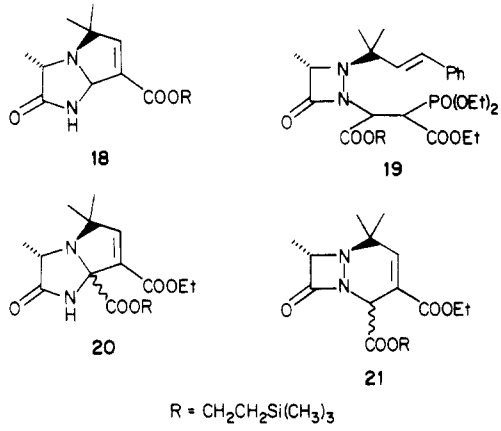
0022-3263/86/1951-1537$01.50/0

Scheme III



of the Michael reaction at N-1. Subsequent ozonolysis of **15b** and **15c**, followed by treatment with dimethyl sulfide and DBU, gave the bicyclic aza-β-lactams **17b** and **17c** in 56% and 24% yield, respectively. A characteristic feature of the NMR spectra of **17a,b** is a well-defined triplet, J = 2 Hz, for the vinyl proton at C-2.

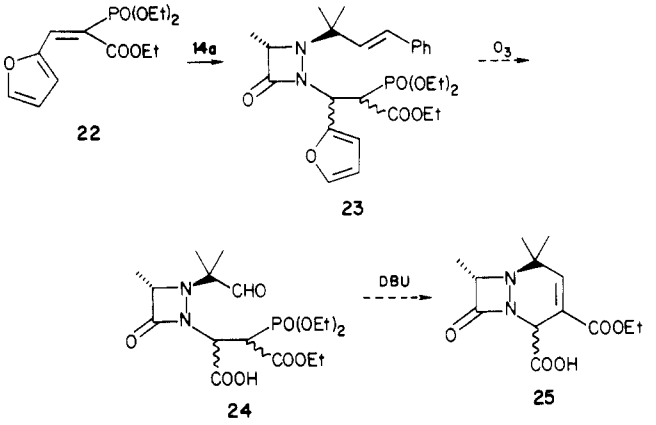
We have previously demonstrated that removal of a proton α to N-2 in a variety of 1,2-disubstituted diazetidinones results in an instantaneous ring-expansion reaction, analogous to the Stevens rearrangement, to give imidazolidinones.[6] Treatment of **17a** with LDA results in a similar ring expansion to give the fused imidazolidinone **18**. Unfortunately, introduction of a carboxylate grouping



at C-4 would be expected to facilitate this ring-expansion reaction, and this indeed proved to be the case. Thus, condensation of **14a** with the vinyl phosphonate **13** gave the adduct **19** which, since it rapidly underwent a retro-Michael reaction upon chromatography, was used without purification. Ozonolysis of **19** followed by treatment with dimethyl sulfide and DBU led only to the rearranged bicyclic imidazolidinone **20**, which was obtained as a mixture of diastereomers. When triethylamine rather than DBU was employed as a base, a mixture of **20** and the unrearranged bicyclic diazetidinone **21** was obtained. Although the latter could not be isolated from the reaction mixture, its formation was confirmed by the presence of two doublets (J = 2 Hz) for the vinyl hydrogens at C-2 of **21** (mixture of diastereomers).

The possibility that this base-promoted ring expansion might be mitigated by use of the free carboxylic acid **24** as a substrate for the Horner–Emmons reaction was briefly examined. The vinyl phosphonate **22**[7] was readily prepared by condensation of furfural with triethyl phosphonoacetate. Reaction of **22** with **14a** led to the adduct **23** in 74% yield (Scheme IV), but ozonolysis of **23**, followed by treatment with dimethyl sulfide and DBU as described above, led only to a dark colored reaction mixture from which none of the desired **25** could be isolated.

Scheme IV



The sodium salts of the acids derived from **17a,b**, **18**, and **20** were prepared by treatment of the above 2-(trimethylsilyl)ethyl esters[8] with tetrabutylammonium fluoride in THF at 20 °C for 18 h, followed by ion exchange using Amberlite CG-120 ($RSO_3^-Na^+$) cation-exchange resin.

Experimental Section

Melting points were determined on a Thomas-Hoover capillary melting point apparatus and are uncorrected. Infrared spectra were determined on a Perkin-Elmer Model 467 spectrophotometer, and NMR spectra were recorded on a Perkin-Elmer R-32 (90 MHz) or JEOL Model FX 90Q spectrometer. Mass spectra were determined on an AEI MS-9 instrument.

***tert*-Butyl 2-(4,4-Dimethoxy-2-methylbutyl)-α-hydroxy-4-oxo-1,2-diazetidine-1-acetate (3a).** A solution of 1-(4,4-dimethoxy-2-methylbutyl)-1,2-diazetidin-3-one (**2a**) (0.32 g, 1.6 mmol) and *tert*-butyl glyoxylate (0.80 g, 6.2 mmol) in DMF (3 mL) and toluene (10 mL) was stirred in the presence of activated 3-Å molecular sieves (4.0 g) for 3 h. The molecular sieves were then removed by filtration and washed with toluene. The combined washings were evaporated in vacuo, and the residue was chromatographed on silica using ethyl acetate/hexane (1:1) as eluent to give 0.44 g of **3a**, slightly contaminated with excess *tert*-butyl glyoxylate; IR (neat) 3400, 1780, 1740 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.42 (s, 1 H), 4.61 (t, 1 H, J = 5 Hz), 4.10 (s, 2 H), 3.32 and 3.31 (2 s, 6 H), 1.76 and 1.71 (2 d, 2 H, J = 5 Hz), 1.55 (s, 9 H), 1.11 and 1.04 (2 s, 6 H).

***p*-Nitrobenzyl 2-(3-Phenyl-2-propenyl)-α-hydroxy-4-oxo-1,2-diazetidine-1-acetate (3b).** A mixture of 1-(3-phenyl-2-propenyl)-1,2-diazetidin-3-one (**2b**) (0.52 g, 2.8 mmol), *p*-nitrobenzyl glyoxylate (0.75 g, 3.6 mmol), and activated 3-Å molecular sieves (3.0 g) in dichloromethane (40 mL) was stirred for 12 h at 25 °C. The molecular sieves were then filtered and washed with dichloromethane. The combined washings were evaporated in vacuo, and the residue was triturated with pentane to give 1.01 g of **3b** slightly contaminated with excess *p*-nitrobenzyl glyoxylate: mp 106–110 °C; IR (neat) 3480, 1770, 1645, 1605, 1580 cm^{-1}.

2-(Trimethylsilyl)ethyl (Diethoxyphosphinyl)acetate (8). A stirred mixture of triethyl phosphite (8.3 g, 50 mmol) and 7[5] (14.3 g, 50 mmol) was heated for 2 h at 130 °C, and the liberated ethyl iodide was allowed to evaporate. The residue was distilled under reduced pressure to give 11.2 g (76%) of **8** as a colorless liquid: bp 140–145 °C (0.1 mmHg); IR (neat) 1731 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.23–3.90 (m, 6 H), 2.91 (d, 2 H, J = 22 Hz), 1.31 (t,

(6) Taylor, E. C.; Clemens, R. J.; Davies, H. M. L.; Haley, N. F. *J. Am. Chem. Soc.* **1981**, *103*, 7659.

(7) Lennert, W. *Tetrahedron* **1974**, *30*, 301.

(8) Use of the 2-(trimethylsilyl)ethyl ester protecting group in the β-lactam field has been reported recently: Chu, D. T.; Hengeveld, J. E.; Lester, D. *Tetrahedron Lett.* **1983**, *24*, 139.

6 H, J = 7 Hz), 0.98 (m, 2 H), 0.01 (s, 9 H).

Anal. Calcd for $C_{11}H_{25}O_5PSi$: C, 44.58; H, 8.50. Found: C, 44.24; H, 8.53.

2-(Trimethylsilyl)ethyl 2-(Diethoxyphosphinyl)-2-propenoate (9). A stirred mixture of paraformaldehyde (1.52 g, 50.7 mmol), piperidine (0.43 g, 5.1 mmol), and methanol (40 mL) was heated under reflux for 1.5 h. After the mixture cooled to room temperature, **8** (11.0 g, 37.7 mmol) was added, and the mixture was heated under reflux for 12 h. The solution was cooled, and the solvent was evaporated under reduced pressure; benzene was added, and the solvent was again evaporated under reduced pressure. After repeating this procedure, phosphoric acid (85%, 0.4 mL) was added, and the mixture was then distilled under reduced pressure to give 8.92 g (78%) of **9** as a colorless liquid: bp 138–150 °C (0.5 mmHg); IR (neat) 1720 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.00 (dd, 1 H, J = 31, 2 Hz), 6.66 (dd, 1 H, J = 10, 2 Hz), 4.39–3.89 (m, 6 H), 1.32 (t, 6 H, J = 7 Hz), 1.02 (m, 2 H), 0.03 (s, 9 H); LRMS, m/e (relative intensity) 293 (obsd $M^+ - CH_3$, 3), 279 (3), 266 (4), 209 (15), 191 (10), 75 (80), 73 (100); HRMS calcd for $C_{11}H_{22}O_5PSi$ 293.0974, found 292.0965.

2-(Trimethylsilyl)ethyl Bromoacetate (10). This compound was prepared from 2-(trimethylsilyl)ethanol and bromoacetyl bromide by an analogous procedure to that used for the preparation of **6**;[5] 91% yield; bp 69–76 °C (0.2 mmHg); IR (neat) 1735 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.25 (m, 2 H), 3.79 (s, 2 H), 1.01 (m, 2 H), 0.04 (s, 9 H).

Anal. Calcd for $C_7H_{15}ClO_2Si$: C, 35.15; H, 6.32; Br, 33.41. Found: C, 34.96; H, 6.32; Br, 33.62.

1-Ethyl 4-[2-(Trimethylsilyl)ethyl] 2-(Diethoxyphosphinyl)butanedioate (11). Sodium hydride (2.20 g, 60% dispersion in oil, 55 mmol, washed three times with pentane) was suspended in freshly distilled THF (50 mL). After the mixture was cooled to 0 °C, triethyl phosphonoacetate (11.21 g, 50 mmol) was added dropwise over 10 min. After 1 h, 2-(trimethylsilyl)ethyl bromoacetate (11.95 g, 50 mmol) was added, and the mixture was stirred for 12 h at 20 °C. The mixture was washed with dilute hydrochloric acid and saturated sodium chloride solution and dried ($MgSO_4$), and the solvent was evaporated in vacuo. The residue was distilled under reduced pressure to give 12.25 g (64%) of **11** as a colorless liquid: bp 168–173 °C (0.25 mmHg); IR (neat) 1733 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.33–4.03 (m, 8 H), 3.60–2.79 (m, 3 H), 1.39–1.19 (m, 9 H), 0.95 (m, 2 H), 0.01 (s, 9 H).

Anal. Calcd for $C_{15}H_{31}O_7PSi$: C, 47.11; H, 8.17; P, 8.10. Found: C, 46.94; H, 7.89; P, 8.07.

1-Ethyl 4-[2-(Trimethylsilyl)ethyl] 2-(Diethoxyphosphinyl)-2-(phenylseleno)butanedioate (12). Sodium hydride (0.96 g, 60% dispersion in oil, 24 mmol) was washed three times with pentane under nitrogen and suspended in freshly distilled THF (30 mL). After the mixture was cooled to 0 °C, the phosphonate[11] (7.64 g, 20 mmol) in THF (5 mL) was added dropwise and the mixture was stirred for 2 h at 20 °C. Phenylselenyl bromide [24 mmol, prepared by adding bromide (0.65 mL) to a stirred solution of diphenyl diselenide (3.85 g) in THF at 20 °C followed by further stirring for 10 min] was then added, the mixture was stirred for 12 h at 20 °C and partitioned between dilute HCl and dichloromethane, and the organic layer was separated, washed with saturated sodium bicarbonate solution, and dried over $MgSO_4$. The solvent was then evaporated under reduced pressure, and the residue was chromatographed on silica gel with ether/petroleum ether (10:90 to 70:30) as solvent gradient to give 6.95 g (65%) of **12** as a pale yellow gum: IR (neat) 1730 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.76 (m, 2 H), 7.32 (m, 3 H), 4.40–3.95 (m, 8 H), 3.60–2.40 (m, 3 H), 0.90 (m, 2 H), 0.01 (s, 9 H).

Anal. Calcd for $C_{21}H_{36}O_7PSeSi$: C, 46.42; H, 6.56; P, 5.76. Found: C, 46.60; H, 6.79; P, 5.60.

1-Ethyl 4-[2-(Trimethylsilyl)ethyl] (*Z*)-2-(Diethoxyphosphinyl)-2-butanedioate (13). Hydrogen peroxide (30%, 2.5 g) and water (0.5 mL) were added to a stirred solution of **12** (1.73 g) in dichloromethane (15 mL) at such a rate that the temperature remained above 30 °C. After being stirred for 1 h at 20 °C, the mixture was washed with saturated sodium bicarbonate solution and dried over $MgSO_4$, and the solvent was evaporated under reduced pressure. The residue was distilled under reduced pressure to give 1.02 g (83%) of **13** as a colorless liquid: bp 175 °C (0.2 mmHg); IR (neat) 1728 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.76 (d, 1 H, J = 22 Hz), 4.35–3.98 (m, 8 H), 1.33 (t, 6 H, J = 7 Hz), 1.31 (t, 3 H, J = 7 Hz), 1.00 (m, 2 H), 0.02 (s, 9 H).

Anal. Calcd for $C_{15}H_{29}O_7PSi$: C, 47.36; H, 7.68; P, 8.14. Found: C, 47.37; H, 7.76; P, 8.36.

Preparation of the Michael Adducts 15: General Procedure. A solution of the diazetidinone (1 equiv) and the vinyl phosphonate (1.05 equiv) in ether or dichloromethane was stirred at 25 °C for 18 h. The solvent was then evaporated under reduced pressure, and the residue was chromatographed on silica with ether/petroleum ether (30:70) to ether as solvent gradient to give the product.

15a: 93% yield, gum; IR (neat) 1770, 1728, 1250 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.33–7.18 (m, 5 H), 6.40 (m, 2 H), 4.30–3.10 (m, 10 H), 1.27 (m, 15 H), 1.04 (m, 2 H), 0.01 (s, 9 H).

Anal. Calcd for $C_{26}H_{43}N_2O_6PSi$: C, 57.97; H, 8.05; N, 5.20; P, 5.75. Found: C, 57.73; H, 8.13; N, 5.34; P, 5.52.

15b: 83% yield, gum; IR (neat) 1775, 1730, 1250 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.25 (m, 5 H), 6.40 (m, 2 H), 4.30–3.10 (m, 11 H), 1.25 (m, 12 H), 1.02 (m, 2 H), 0.01 (s, 9 H).

Anal. Calcd for $C_{25}H_{41}N_2O_6PSi$: C, 57.23; H, 7.88; N, 5.34; P, 5.90. Found: C, 57.43; H, 7.72; N, 5.49; P, 6.18.

15c: 82% yield, gum; IR (neat) 1780, 1730, 1250 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.30 (br s, 5 H), 6.58 (d, 1 H, J = 16 Hz), 6.19 (dt, 1 H, J = 16, 7 Hz), 4.33–3.28 (m, 13 H), 1.28 (m, 9 H), 1.00 (m, 2 H), 0.01 (s, 9 H).

Anal. Calcd for $C_{24}H_{39}N_2O_6PSi$: C, 56.45; H, 7.70; N, 5.48; P, 6.07. Found: C, 56.21; H, 7.60; N, 5.56; P, 6.06.

Preparation of 17: General Procedure. Ozone was bubbled through a solution of **15** (5 mmol) in dichloromethane (75 mL) at −78 °C until the color turned blue. Dimethyl sulfide (1 mL) was then added and after a further 10 min, DBU (5 mmol) was added. After the mixture was slowly warmed to 20 °C over 2 h, the solvent was evaporated in vacuo, and the residue was chromatographed on alumina with ether/petroleum ether (1:1) as eluent to give **17**.

2-(Trimethylsilyl)ethyl 5,5,7-Trimethyl-8-oxo-1,6-diazabicyclo[4.2.0]oct-3-ene-3-carboxylate (17a): 54% yield, gum; IR (neat) 1765, 1712, 1645 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.76 (t, 1 H, J = 2 Hz), 4.32–4.05 (m, 5 H), 1.43 (d, 3 H, J = 7 Hz), 1.23 and 1.16 (2 s, 6 H), 0.98 (m, 2 H), 0.02 (s, 9 H); ^{13}C NMR ($CDCl_3$) δ 164.5 (s), 164.3 (s), 144.8 (d), 122.9 (s), 67.6 (d), 63.1 (t), 55.7 (s), 40.2 (t), 25.3 (q), 18.3 (q), 17.1 (t), 14.8 (q), −1.7 (q); LRMS, m/e (relative intensity) 310 (obsd M^+, 8), 296 (3), 282 (4), 267 (6), 183 (10), 73 (100).

Anal. Calcd for $C_{15}H_{26}N_2O_3Si$: C, 58.03; H, 8.44; N, 9.02. Found: C, 57.84; H, 8.44; N, 9.07.

2-(Trimethylsilyl)ethyl 5,5-Dimethyl-8-oxo-1,6-diazabicyclo[4.2.0]oct-3-ene-3-carboxylate (17b): 56% yield, gum; IR (neat) 1758, 1715, 1640 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.77 (t, 1 H, J = 2 Hz), 4.33–4.09 (m, 6 H), 1.19 and 1.15 (2 s, 6 H), 0.98 (m, 2 H), 0.01 (s, 9 H); ^{13}C NMR ($CDCl_3$) δ 164.3 (s), 160.9 (s), 144.4 (d), 122.8 (s), 63.1 (t), 59.8 (t), 55.7 (s), 40.1 (t), 24.7 (q), 17.5 (q), 17.0 (t), −1.8 (q); LRMS, m/e (relative intensity) 296 (obsd M^+, 5), 282 (2), 267 (2), 253 (5), 183 (8), 108 (15), 73 (100); HRMS calcd for $C_{14}H_{24}N_2O_3Si$ 296.1556, found 296.1543 ± 0.003.

2-(Trimethylsilyl)ethyl 7-Methyl-8-oxo-1,6-diazabicyclo[4.2.0]oct-3-ene-3-carboxylate (17c): 21% yield, gum; IR (neat) 1762, 1710, 1648 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.01 (m, 1 H), 4.41 and 4.04 (2 br d, 2 H, J = 18 Hz), 4.26 (m, 2 H), 3.85 (superimposed br d, J = 16 Hz, + q, J = 7 Hz, total 2 H), 3.25 (br d, 1 H, J = 16 Hz), 1.52 (d, 3 H, J = 7 Hz), 1.01 (m, 2 H), 0.03 (s, 9 H); ^{13}C NMR ($CDCl_3$) δ 164.2 (s), 163.4 (s), 134.0 (d), 125.1 (s), 78.0 (d), 63.3 (t), 53.3 (t), 40.5 (t), 17.3 (t), 14.4 (q) −1.5 (q); LMRS, m/e (relative intensity) 282 (obsd M^+, 6), 268 (1), 255 (4), 239 (4), 153 (20), 73 (100).

Anal. Calcd for $C_{13}H_{22}N_2O_3Si$: C, 55.29; H, 7.85; N, 9.92. Found: C, 54.93; H, 7.84; N, 9.64.

Base-Initiated Rearrangement of 17a: Preparation of 18. A solution of **17a** (0.25 g, 0.81 mmol) in THF (5 mL) was added to a stirred solution of LDA (1.2 mmol) in THF at −78 °C under nitrogen. After the mixture was stirred for 10 min, saturated ammonium chloride solution was added. The mixture was extracted with ether, the organic layer was dried over $MgSO_4$, and the solvent was evaporated in vacuo. The residue was chromatographed on alumina with ether/petroleum ether (2:3 to 3.2) as solvent gradient to give recovered **17a** (0.11 g, 44%) and the

rearranged product **18** (0.065 g, 26%): mp 100–102 °C; IR (Nujol) 3200, 1730, 1695, 1662 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.73 (d, 1 H, J = 1 Hz), 6.22 (br s, 1 H), 5.58 (br s, 1 H), 4.25 (m, 2 H), 3.53 (q, 1 H, J = 7 Hz), 1.30 (d, 3 H, J = 7 Hz), 1.28 and 1.26 (2 s, 6 H), 0.04 (s, 9 H); ^{13}C NMR ($CDCl_3$) δ 177.9 (s), 163.3 (s), 151.5 (d), 131.3 (s), 77.9 (d), 68.7 (s), 63.2 (t), 54.7 (d), 30.1 (q), 23.5 (q), 19.3 (q), 17.4 (t), −1.6 (q).

Anal. Calcd for $C_{16}H_{26}N_2O_3Si$: C, 58.03; H, 8.44; N, 9.02. Found: C, 57.96; H, 8.18; N, 8.94.

Preparation of 20 by Base-Initiated Rearrangement: A mixture of **14a** (1 equiv) and **13** (1 equiv) in dichloromethane (50 mL) was stirred for 12 h at 20 °C. The solvent was evaporated under reduced pressure to give the crude Michael adduct **19** which was unstable to chromatography.

Ozone was bubbled through a solution of **19** (1.00 g, 1.6 mmol) in dichloromethane (50 mL) at −78 °C until the color turned blue. Dimethyl sulfide (1 mL) was then added, and after 10 min, DBU (0.27 mL, 1.8 mmol) was added. The mixture was slowly warmed to 20 °C over the course of 2 h, and the solvent was then evaporated under reduced pressure. The residue was chromatographed on alumina with ether/petroleum ether (1:1) as eluent to give crude **20**, which was further purified by trituration with pentane: 0.085 g (14% yield); mp 104–106 °C; IR (Nujol) 3160, 3080, 3020, 1740, 1716, 1657 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.80 and 6.44 (2 s, 1 H), 6.36 (br s, 1 H), 4.30–4.10 (m, 5 H), 1.32–1.17 (m, 12 H), 0.95 (m, 2 H), 0.00 (s, 9 H); LRMS m/e (relative intensity) 237 (obsd $M^+ - COOCH_2CH_2Si(CH_3)_3$, 15), 75 (75), 59 (100); HRMS calcd for $C_{12}H_{17}N_2O_3$ 237.1239, found 237.1232 ± 0.0024.

Preparation of Michael Adduct 23. A solution of **14a** (2.10 g, 9.1 mmol) and **22**[7] (2.80 g, 9.2 mmol) in dichloromethane (50 mL) was stirred for 12 h. The solvent was then evaporated in vacuo, and the residue was chromatographed on silica with ether/petroleum ether (1:1) as eluent to give 3.97 g (74%) of **23** as a pale yellow gum: ^1H NMR ($CDCl_3$) δ 7.53 (br s, 1 H), 7.34 (m, 5 H), 6.88 (d, 1 H, J = 4 Hz), 6.49 (m, 3 H), 4.50–4.00 (m, 9 H), 1.50–1.30 (m, 18 H).

Anal. Calcd for $C_{27}H_{36}N_2O_6P$: C, 62.90; H, 7.04; N, 5.43; P, 6.01. Found: C, 62.64; H, 6.95; N, 5.52; P, 5.88.

Preparation of Sodium Salts. General Procedure. Tetrabutylammonium fluoride (1 M in THF, 1 equiv) was added to a stirred solution of the trimethylsilyl ester (1 equiv) in dry THF, and the mixture was stirred for 12 h. The solvent was evaporated in vacuo, and the residual gum was washed with ether/pentane (1:2). The gum was then passed through an Amberlite CG-120 cation-exchange resin ($RSO_3^-Na^+$) to give the product as its sodium salt.

Sodium salt of **17a**: 89% yield; IR (Nujol) 1740, 1648 cm^{-1}; ^1H NMR (D_2O) δ 6.37 (br s, 1 H), 4.31 (q, 1 H, J = 7 Hz), 4.15 and 3.79 (2 d, 2 H, J = 17 Hz), 1.25 (d, 3 H, J = 7 Hz), 1.08 and 1.01 (2 s, 6 H).

Sodium salt of 17b: 87% yield; IR (Nujol) 1730, 1645 cm^{-1}; ^1H NMR (D_2O) δ 6.39 (br s, 1 H), 4.18 and 3.78 (2 d, 2 H, J = 16 Hz), 4.08 (s, 2 H), 1.05 and 1.00 (2 s, 6 H).

Sodium salt of 18: 96% yield; IR (KBr) 1680, 1650 (sh) cm^{-1}; ^1H NMR (D_2O) δ 6.37 (s, 1 H), 5.37 (s, 1 H), 3.52 (q, 1 H, J = 7 Hz), 1.12 (d, 3 H, J = 7 Hz), 1.08 (s, 6 H).

Sodium salt of 20: 95% yield; ^1H NMR (D_2O) δ 6.84 (s, 1 H), 4.08 (q, 2 H, J = 7 Hz), 3.57 (q, 1 H, J = 7 Hz), 1.10 (d, 3 H, J = 7 Hz), 1.15 and 1.06 (2 s, 6 H), 1.06 (t, 3 H, J = 7 Hz).

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Registry No. **2a**, 100604-41-9; **2b**, 79559-06-1; **3a**, 100604-42-0; **3b**, 100604-43-1; **7**, 100297-90-3; **8**, 83863-17-6; **9**, 100604-44-2; **10**, 79414-13-4; **11**, 100604-45-3; **12**, 100604-46-4; **13**, 100604-47-5; **14a**, 92184-64-0; **14b**, 89773-81-9; **14c**, 92184-58-2; **15a**, 100604-48-6; **15b**, 100604-49-7; **15c**, 100604-50-0; **17a**, 100604-51-1; **17a**·Na, 100604-57-7; **17b**, 100604-52-2; **17b**·Na, 100604-58-8; **17c**, 100604-53-3; **18**, 100604-54-4; **18**·Na, 100604-59-9; **19**, 100655-29-6; **20** (isomer 1), 100604-55-5; **20** (isomer 2), 100604-61-3; **20**·Na (isomer 1), 100604-60-2; **20**·Na (isomer 2), 100604-62-4; **22**, 37176-95-7; **23**, 100604-56-6; *tert*-butyl glyoxylate, 7633-32-1; 4-nitrobenzyl glyoxylate, 64370-35-0; 2-(trimethylsilyl)ethanol, 2916-68-9; bromoacetyl bromide, 598-21-0; triethyl phosphonoacetate, 867-13-0.