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Stereocontrolled Synthesis of Triazacyclopenta[*cd*]pentalenes by Intramolecular 1,3-Dipolar Cycloaddition Reactions of Azomethine Imines

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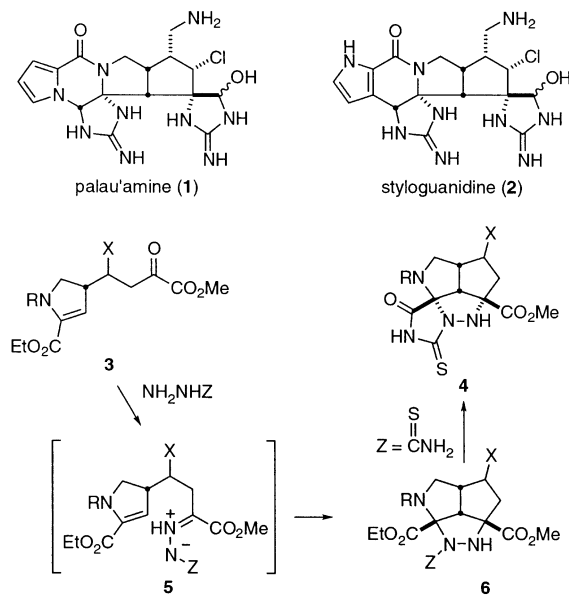
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Received August 2, 2002

Abstract: The construction of triazacyclopenta[*cd*]pentalene diesters **6** by the reaction of dihydropyrrole α -ketoesters **3** with acylated hydrazines was evaluated further as a potential central strategic step in the total syntheses of complex guanidine alkaloids such as palau'amine and styloguanidine. Successful cyclocondensations were realized with acid-stable 2,2,2-trichloroethyl carbazate and thiosemicarbazide, but not *tert*-butyl carbazate. The substituent on the pyrrolidine nitrogen can be alkoxycarbonyl, sulfonyl, or an *N*-alkyl-2-acylpyrrole group. Siloxy substitution at C1 of the α -ketoester side chain is also tolerated.

Cycloaddition of azomethine imines with suitable dipolarophiles is a powerful method for constructing tetrahydropyrazole rings.² Beginning with pioneering investigations by Oppolzer and co-workers in the 1970s,³ intramolecular variants of this class of 1,3-dipolar cycloadditions have found wide utility for synthesis of complex nitrogen heterocycles.² Exemplified in Oppolzer's early studies³ and Jacobi's incisive synthesis of saxitoxin,⁴ the 1,3-dipole is often formed by condensation of a 1-acyl-2-alkylhydrazine with an aldehyde. A second commonly used procedure to generate azomethine imine dipoles is tautomerization of acyl hydrazones.⁵ This latter approach was employed in our recent construction of tetracyclic nitrogen heterocycle **4** (R = Cbz, X = H) during our early studies to uncover routes to complex guanidine alkaloids such as palau'amine (**1**) and styloguanidine (**2**) (Scheme 1).⁶ To the best of our knowledge, hydrazones derived from α -ketoesters or α,β -unsaturated α -amino esters had not been described previously as components of intramo-

SCHEME 1



lecular azomethine imine cycloaddition reactions. In this paper, we report our studies to further explore the scope of this new construction of triazacyclopenta[*cd*]pentalenes in the context of its potential use for the total synthesis of complex guanidine alkaloids of the palau'amine and styloguanidine families.

Synthesis of the Dihydropyrrole α -Ketoester Cycloaddition Components. To explore how the nitrogen substituent of the dipolarophile would influence the cycloaddition, three dihydropyrrole α -ketoesters **12a–c** were prepared (Scheme 2). In two cases, the nitrogen carried an acid-stable protecting group, Cbz or SES (SO₂-CH₂CH₂TMS).⁷ In the third, the nitrogen carried a 2-acylpyrrole group to investigate whether this fragment of palau'amine and styloguanidine could be incorporated early in a synthetic sequence. These syntheses began with readily available amino diester **7**,⁸ which was acylated or sulfonylated in standard fashion to deliver **8a–c** in high yield. Dieckmann cyclization⁹ of **8** using potassium *tert*-butoxide followed by sodium borohydride reduction¹⁰ of the resulting β -ketoesters generated β -hydroxyesters **9a–c** as mixtures of stereoisomers.

To generate the dihydropyrrole α -ketoester cycloaddition components **12** from **9**, the hydroxypyrrolidine ester must be dehydrated and the allyl substituent converted to a 4-carbon α -ketoester side chain. In the Cbz and SES series, the hydroxyl groups of **9a** and **9b** were first mesylated, followed by ozonolysis of the allyl side chain and Horner–Emmons elaboration of the resulting side chain aldehydes (Scheme 3).^{11,12} The use of excess DBU in the condensation step promoted in situ elimination of the mesylate to form the dihydropyrrole. After cleavage

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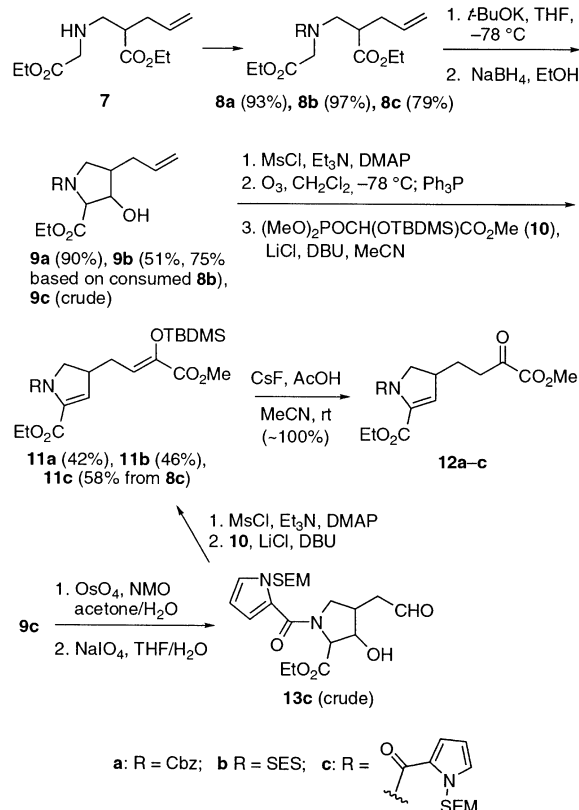
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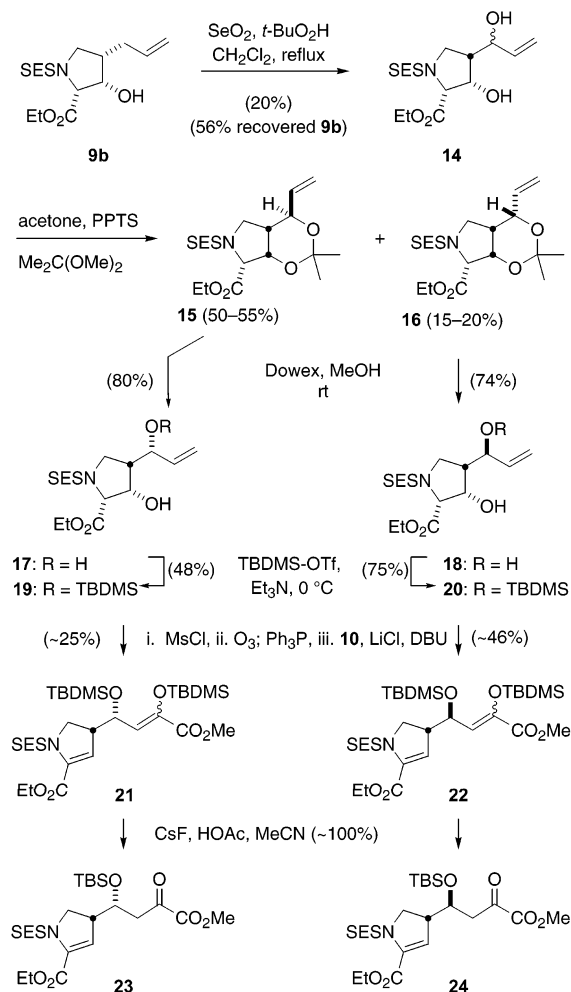
SCHEME 2



of the TBDMS group, this sequence provided **12a** and **12b** in ~45% overall yield. In the 2-acylpyrrole series, the aldehyde intermediate was generated in the first step by dihydroxylation of the allyl side chain of **9c**, followed by cleavage of the resulting vicinal diol with NaIO_4 .¹³ Mesylation of the hydroxy aldehyde, condensation of the resulting product with **10**, and desilylation delivered **12c** in 58% overall yield from acyclic amino diester **8c**.

Epimeric cyclization precursors **23** and **24** bearing a protected alcohol at C-1 of the α -ketoester side chain were prepared to study the impact of substitution on the tether joining the cycloaddends (Scheme 3). Oxidation of allylpyrrolidine **9b**¹⁴ with catalytic selenium dioxide using $t\text{-BuO}_2\text{H}$ as the reoxidant provided an inseparable 3:1 mixture of two epimeric diols **14** in low yield, as well as 50–60% of recovered **9b**.^{15,16} The mixture of diols **14** was converted into the corresponding acetonides, which were readily separable by column chromatography. The relative configuration of these epimers was determined by the method of Rychnovsky and co-workers from the diagnostic chemical shifts of the acetonide methyl carbons in the ^{13}C NMR spectra: **15** (25.5 and 24.4 ppm) and **16** (29.9 and 19.6 ppm).¹⁷ The epimeric acetonides were independently cleaved with Dowex 50WX8 acidic resin

SCHEME 3



in methanol to provide the corresponding diols in good yields.¹⁸ Selective silylation of the side chain allylic alcohol of **17** and **18** delivered silyl ethers **19** and **20**.¹⁹ These intermediates were processed identically to the simpler SES analogue **9b** to provide dihydropyrrole α -ketoester epimers **23** and **24**.

Intramolecular Cycloaddition Reactions. Results obtained from our initial survey of the reaction of dihydropyrrole α -ketoester **12a** with various acylhydrazines are summarized in Scheme 4. With 2,2,2-trichloroethyl carbazate (**25**, Z = Troc), cycloaddition took place smoothly in refluxing xylenes to provide cycloadduct **26** in 86% yield. Only a trace of the analogous product was formed from identical reaction with *tert*-butyl carbazate (**25**, Z = Boc), an outcome we ascribe to the instability of the *tert*-butoxycarbonyl group under these conditions.²⁰ Reaction of **12a** with thiosemicarbazide in refluxing

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(13) This procedure was employed as the acylpyrrole reacted slowly with ozone.

(14) This sample was largely (~90%) one stereoisomer. Although not rigorously established, it is likely that this was the all-*cis* stereoisomer that is depicted in Scheme 3.

(15) Umbreit, M. A.; Sharpless, K. B. *J. Am. Chem. Soc.* **1977**, 99, 5526–5528.

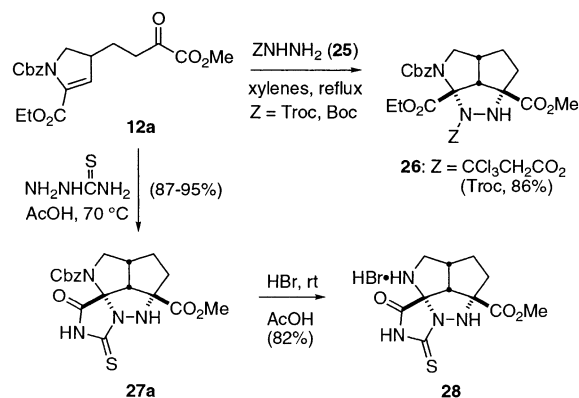
(16) Due to decomposition of **14** under the reaction conditions, the yield of these allylic alcohol products was no higher if the allylic oxidation was carried out for a longer time to ensure complete consumption of **9b**.

(17) Rychnovsky, S. D.; Rogers, B. N.; Yang, G. *J. Org. Chem.* **1993**, 58, 3511–3515.

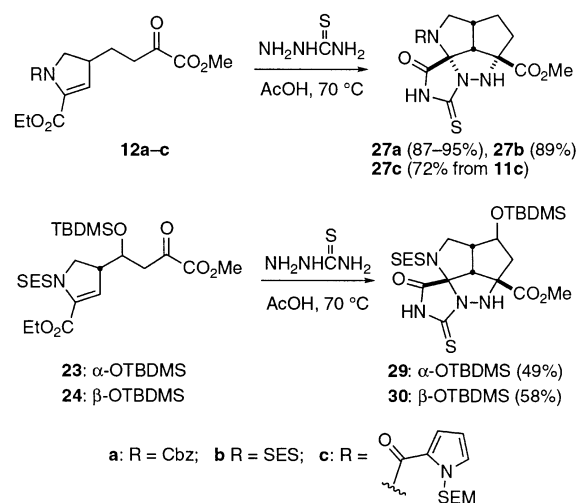
(18) Rychnovsky, S. D.; Khire, U. R.; Yang, G. *J. Am. Chem. Soc.* **1997**, 119, 2058–2059.

(19) Significantly lower yields of **19** were observed due to competitive silylation of the hydroxyl on the pyrrolidine ring of **17**.

SCHEME 4



SCHEME 5



xylenes produced a product mixture containing some of the expected tricyclic cycloadduct as well as tetracycle **27a** resulting from loss of ethanol from this intermediate.²¹ Further investigation showed that the cycloaddition of **12a** with thiosemicarbazide occurred most cleanly in acetic acid at 70 °C over a 24 h period, in which case **27a** was formed in 87–95% yield.²² The structure of this cycloadduct was secured by cleavage of its benzyloxycarbonyl group with HBr in acetic acid to give crystalline **28**, which was amenable to single-crystal X-ray analysis.⁶

The reaction of thiosemicarbazide with dihydropyrrole α -ketoesters **12b,c** was surveyed under identical reaction conditions in acetic acid (Scheme 5). Cycloaddends **12b** and **12c** in which the dihydropyrrole nitrogen is substi-

tuted with SES or *N*-SEM-2-acylpyrrole functionality behaved similarly to the corresponding Cbz-protected substrate and gave tetracyclic adducts **27b** and **27c** in high yield. The SES-protected substrates **23** and **24** having a *tert*-butyldimethylsiloxy group at C1 of the α -ketoester side chain also readily provided the corresponding tetracyclic cycloadducts **29** and **30** when condensed in acetic acid at 70 °C with thiosemicarbazide. We had anticipated that the thiosemicarbazone derived from **23** might be less prone to undergo cycloaddition as the siloxy group would reside on the hindered concave face of the triazacyclopenta[*cd*]pentalene cycloadduct. However, both siloxy epimers provided their respective cycloadducts with nearly equal efficiency.²³

This study shows that dihydropyrrole α -ketoesters of general structure **3** react with acid-stable alkyl carbazates and thiosemicarbazide, but not *tert*-butyl carbazate, to efficiently provide cycloadducts containing the triazacyclopenta[*cd*]pentalene ring system. The substituent on the pyrrolidine nitrogen can be varied widely, as successful cycloadditions were realized when this group was alkoxy carbonyl, sulfonyl, or an *N*-alkyl-2-acylpyrrole group. Moreover, silyloxy substitution at C1 of the α -ketoester side chain is also tolerated. These results encourage us to explore further the utility of the cyclocondensation outlined in Scheme 1 for the total synthesis of complex guanidine alkaloids of the palau'amine (**1**) and styloguanidine (**2**) families.

Experimental Section^{24,25}

Ethyl 2-[[Ethoxycarbonylmethyl-[2'-(trimethylsilyl)ethanesulfonyl]amino]methyl]pent-4-enoate (8b). A stirring solution of **7** (5.50 g, 22.6 mmol),⁸ triethylamine (9.5 mL, 68 mmol), and CH₂Cl₂ (35 mL) was cooled to –78 °C, and a cooled (–78 °C) solution of 2-(trimethylsilyl)ethanesulfonyl chloride (9.00 g, 45.2 mmol) and CH₂Cl₂ (10 mL) was added by cannula. Upon completion of the addition, the reaction flask was placed in a –45 °C bath and left overnight. The resulting solution was allowed to warm to 23 °C, 1 M HCl was added (40 mL), and the aqueous layer was extracted with CH₂Cl₂. The combined organic layers were dried (Na₂SO₄) and concentrated, and the residue was chromatographed (9:1–4:1 pentanes–EtOAc) to yield 8.90 g (97%) of **8b** as a colorless oil: ¹H NMR (500 MHz, CDCl₃) δ 5.73 (1H, ddd, *J* = 17.1, 10.1, 7.0 Hz), 5.10 (2H, m), 4.2–4.0 (6H, m), 3.51 (2H, m), 3.85 (1H, m), 3.01 (2H, m), 2.40–2.21 (2H, m), 1.28 (3H, t, *J* = 7.2 Hz), 1.26 (3H, t, *J* = 7.2 Hz), 1.08 (2H, m), 0.05 (9H, s); ¹³C NMR (125 MHz, CDCl₃) δ 173.9, 136.4, 134.0, 117.6, 61.3, 60.8, 49.6, 49.1, 45.1, 34.4, 14.1, 11.1, 10.0, –2.1; IR (film) 1737 cm^{–1}; MS (CI) *m/z* 408.1877 (408.1876 calcd for C₁₇H₃₄NO₆SSi, MH). Anal. Calcd for C₁₇H₃₄NO₆SSi: C, 50.10; H, 8.16; N, 3.44; S, 7.87. Found: C, 50.19; H, 8.15; N, 3.40; S, 7.97.

(20) (a) Wasserman, H. H.; Berger, G. D.; Cho, K. R. *Tetrahedron Lett.* **1982**, 23, 465–468. (b) Rawal, V. H.; Jones, R. J.; Cava, M. P. *J. Org. Chem.* **1987**, 52, 19–28.

(21) The inefficiency of the cycloaddition in xylenes could be due, in part, to the poor solubility of thiosemicarbazide in this solvent.

(22) Product **27a** forms slowly at room temperature over the course of 10–14 days when the solvent is acetic acid. Although, the cyclocondensation of **12a** with acylhydrazines in refluxing xylenes undoubtedly proceeds as depicted in Scheme 1, an alternative mechanism is possible when the solvent is acetic acid. Dehydroamino esters are well-known to exhibit ambiphilic reactivity. Thus, the finding that the cyclocondensation of **12a** with thiosemicarbazide occurs optimally in acetic acid, and even at room temperature, suggests that this cyclocondensation likely takes place by an asynchronous or stepwise mechanism. In the stepwise limit, the cycloadduct would be the result of an intramolecular Mannich cyclization followed by subsequent cyclization of the acylated hydrazine with an *N*-acyl- or *N*-sulfonyliminium ion intermediate.

(23) Analysis of ¹H NMR coupling constants of **29** and comparison with the X-ray structure of **28** indicates that the siloxy group of **29** assumes a quasi-equatorial orientation.

(24) General experimental details have been described: Ando, S.; Minor, K. P.; Overman, L. E. *J. Org. Chem.* **1997**, 62, 6379–6387. Ether, THF, dichloromethane and toluene were dried by passage through a bed of activated alumina.²⁵ For reactions requiring anhydrous conditions, substrates were dried by azeotropic evaporation with benzene, the reaction flask was flame-dried under vacuum, and the reaction was conducted under an atmosphere of anhydrous nitrogen. High-resolution mass spectra were obtained by CI, ES or FAB methods. IR spectra were recorded by applying substrates as thin films onto a KBr plate. Details of the preparation and characterization of compounds **8a**, **9a**, **11a**, **12a**, **27a**, and **28** have been reported previously in Supporting Information.⁶

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Ethyl *N*-[2'-(Trimethylsilyl)ethanesulfonyl]-3-hydroxy-4-allylpyrrolidine-2-carboxylate (9b**).** A stirring solution of **8b** (1.10 g, 2.70 mmol) and THF (35 mL) was cooled to -78°C , and a solution of potassium *tert*-butoxide (340 mg, 3.0 mmol) and THF (30 mL) was added dropwise by cannula. The reaction was maintained at -78°C for 5 min, quenched at this temperature by adding 1 M HCl (20 mL), allowed to warm to 23°C , and extracted with EtOAc. The combined organic extracts were washed with brine, dried (Na_2SO_4), and concentrated to yield 1.0 g of the crude β -ketoester product as a slightly yellow oil, which was used in the next step without further purification. A small sample was chromatographed (4:1–1:1 hexanes–EtOAc) to yield a pure specimen as a colorless oil, diagnostic data: ^1H NMR (500 MHz, CDCl_3 , ~1:1 mixture of diastereomers) δ 5.72 (1H, m), 5.08 (2H, m), 4.29–4.20 (4H, m), 3.48 (1H, m), 3.09 (2H, m), 2.87 (1H, m), 2.50–2.10 (2H, m), 1.30 (3H, m), 1.27 (2H, m), 0.07 (9H, s); IR (film) 1770, 1739, 1642 cm^{-1} .

A suspension of sodium borohydride (200 mg, 5.4 mmol) in MeOH (4 mL) was added dropwise to a solution of this unpurified Dieckman product (1.0 g) and MeOH (50 mL) at -78°C . The cooling bath was removed after 10 min and the solution was maintained at 23°C for 1 h. Acetone (10 mL) was added and the solution was concentrated. Saturated aqueous NaHCO_3 (40 mL) was added to the residue and the resulting mixture was extracted with 1:1 hexanes–EtOAc. The combined organic extracts were dried (Na_2SO_4), concentrated and the residue was chromatographed (2:1–1:1 hexanes–EtOAc) to yield 350 mg of recovered **8b** and 498 mg (51%, 75% overall based on consumed **8b**) of **9b**, a mixture of stereoisomers, as a nearly colorless oil: ^1H NMR (500 MHz, CDCl_3 , major diastereomer only) δ 5.82 (1H, m), 5.09 (2H, ddd, $J = 17.1, 10.2, 1.5$ Hz), 4.73 (1H, d, $J = 4.7$ Hz), 4.61 (1H, m), 4.24 (2H, m), 3.92 (1H, m), 3.20–3.10 (2H, m), 3.00 (1H, m), 2.45 (1H, d, $J = 5.6$ Hz), 2.40–2.20 (2H, m), 1.30 (3H, t, $J = 7.1$ Hz), 1.09 (2H, m), 0.06 (9H, s); ^{13}C NMR (125 MHz, CDCl_3 , of the major diastereomer only) δ 169.8, 135.6, 117.2, 74.2, 67.9, 61.9, 52.0, 51.0, 44.9, 30.7, 14.6, 10.3, -1.4 ; IR (film) 1738, 1642 cm^{-1} ; MS (CI) m/z 364.1612 (364.1614 calcd for $\text{C}_{15}\text{H}_{30}\text{NO}_5\text{SSi}$, MH).

Ethyl *N*-[2'-(trimethylsilyl)ethanesulfonyl]-4-[(3'-*tert*-butyldimethylsiloxy)-3'-methoxycarbonylallyl]-4,5-dihydro-1*H*-pyrrole-2-carboxylate (11b**).** Methanesulfonyl chloride (320 μL , 4.8 mmol) was added to a solution of **9b** (580 mg, 1.6 mmol), triethylamine (1.1 mL, 4.8 mmol), DMAP (48 mg, 0.40 mmol) and benzene (45 mL) at 0°C . The resulting mixture was allowed to warm to 23°C over 1 h and then was cooled to 0°C . Saturated aqueous NaH_2PO_4 (40 mL), Et_2O (60 mL) and water (20 mL) were added and the resulting mixture was stirred as it warmed to 23°C . The organic layer was separated, washed with saturated aqueous NaH_2PO_4 (2×20 mL), dried (Na_2SO_4) and concentrated to yield ~600 mg of a slightly yellow oil. A ozone/oxygen gas mixture was bubbled through a solution of this crude mesylate and CH_2Cl_2 (10 mL) at -78°C until a blue color persisted. The solution was then purged with N_2 until the blue color disappeared. Triphenylphosphine (500 mg, 1.9 mmol) was added and the resulting solution was allowed to warm to 23°C . This solution was concentrated and the residual crude aldehyde was dried azeotropically with benzene (3×25 mL).

A solution of methyl 2-(*tert*-butyldimethylsiloxy)-2-(dimethylphosphono)acetate¹¹ (750 mg, 2.4 mmol), LiCl (120 mg, 2.8 mmol), DBU (1.2 mL, 8.0 mmol) and dry MeCN (25 mL) was prepared and maintained for 1 h at 0°C .¹² A solution of the crude aldehyde and acetonitrile (9.5 mL) was added and the resulting solution was maintained at 0°C for 2 h. Hexanes (25 mL), EtOAc (25 mL) and saturated aqueous NaH_2PO_4 (40 mL) were added and the layers were separated. The organic layer was washed sequentially with water and brine, dried (Na_2SO_4), and concentrated. The residue was chromatographed (4:1 hexanes–EtOAc) to yield 389 mg (46%) of **11b**, a colorless oil that was a 4.5:1 mixture of *E* and *Z* alkene stereoisomers (by NMR analysis): ^1H NMR (500 MHz, CDCl_3) δ 6.13 (1H, d, $J = 6.1$ Hz), 5.42 (1H, t, $J = 8.1$ Hz), 4.24 (2H, dd, $J = 7.2, 7.1$ Hz), 4.10 (1H, dd, $J = 11.3, 9.2$ Hz), 3.75 (3H, s), 3.74 (1H, m), 3.35 (2H, m), 3.09 (1H, m), 2.61 (2H, m), 1.30 (3H, t, $J = 7.1$ Hz), 1.07 (2H, m), 0.94

(9H, s), 0.12 (6H, s), 0.05 (9H, s); ^{13}C NMR (125 MHz, CDCl_3 , of the major diastereomer only) δ 164.8, 161.2, 142.0, 137.1, 128.2, 120.3, 117.8, 61.3, 55.6, 51.3, 42.6, 30.0, 25.5, 14.1, 10.2, -2.0 , -4.9 ; IR (film) 1728 cm^{-1} ; MS (CI) m/z 534.2373 (534.2376 calcd for $\text{C}_{23}\text{H}_{44}\text{NO}_7\text{SSi}_2$ MH).

General Procedure for Generation of Dihydropyrrole α -Ketoesters from Silyl Precursors and Condensation with Thiosemicarbazide. Preparation of **12b and Cycloadduct **27b**.** Acetic acid (160 μL , 2.8 mmol) and CsF (230 mg, 1.5 mmol) were added to a solution of **11b** (250 mg, 0.47 mmol) and dry MeCN (4 mL) at 0°C . The resulting mixture was stirred at 0°C for 30 min and at 23°C for 4 h. The reaction mixture was diluted with hexanes and EtOAc (50 mL each) and washed with saturated aqueous NaHCO_3 . The organic layer was dried (Na_2SO_4) and concentrated to give 200 mg of crude **12b** (judged >95% pure by ^1H NMR analysis) as an unstable colorless oil, which was used immediately: ^1H NMR (500 MHz, CDCl_3) δ 6.15 (1H, d, $J = 3.0$ Hz), 4.25 (2H, dd, $J = 7.2, 7.1$ Hz), 4.07 (1H, dd, $J = 11.4, 9.1$ Hz), 3.87 (3H, s), 3.79 (1H, dd, $J = 11.4, 5.6$ Hz), 3.35 (2H, m), 2.99 (1H, m), 2.92 (2H, m), 1.83 (2H, m), 1.32 (3H, t, $J = 7.1$ Hz), 1.06 (1H, m), 0.06 (9H, s); ^{13}C NMR (125 MHz, CDCl_3) δ 193.1, 161.1, 161.0, 137.4, 127.5, 61.5, 55.8, 53.1, 51.5, 41.0, 36.4, 26.2, 14.1, 10.2, -2.0 ; IR (film) 1732, 1622, cm^{-1} .

A solution of this sample of crude **12b**, glacial acetic acid (50 mL) and thiosemicarbazide (128 mg, 1.4 mmol) was maintained at 70°C for 48 h. After cooling to 23°C , the reaction mixture was concentrated and the residue was azeotropically dried with heptane ($2 \times$) to remove residual acetic acid. The residue was chromatographed (1:19 MeOH– CH_2Cl_2) to give 187 mg of **27b** (89%) as a colorless amorphous solid: ^1H NMR (500 MHz, CDCl_3) δ 8.95 (1H, br s), 5.40 (1H, s), 4.06 (1H, d, $J = 9.5$ Hz), 3.92 (1H, dd, $J = 9.7, 6.4$ Hz), 3.73 (3H, s), 3.62 (1H, d, $J = 9.7$ Hz), 3.09 (2H, m), 2.95 (1H, m), 2.19 (1H, m), 2.07 (1H, m), 2.05 (1H, m), 1.07 (2H, m), 0.04 (9H, s); ^{13}C NMR (125 MHz, CDCl_3) δ 186.2, 171.8, 169.6, 92.4, 81.5, 63.6, 55.5, 53.3, 49.8, 40.5, 34.1, 31.2, 9.6, -2.0 ; IR (KBr) 3225, 1766 cm^{-1} ; MS (EI) m/z 446.1109 (446.1114 calcd for $\text{C}_{16}\text{H}_{26}\text{N}_4\text{O}_5\text{S}_2\text{Si}$, M).

Cycloaddition of **12a with 2,2,2-Trichloroethyl Carbazate To Form Cycloadduct **26**.** A solution of **12a** (110 mg, 0.28 mmol), 2,2,2-trichloroethyl carbazate (280 mg, 1.3 mmol) and xylenes (4 mL) was degassed (by gentle nitrogen bubbling into the solution for 10 min) and heated at reflux for 30 h. After cooling to 23°C , the mixture was concentrated and the residue was chromatographed (2:1 hexanes–EtOAc) to give 140 mg (86%) of **26** as a colorless oil: ^1H NMR (500 MHz, CDCl_3 , mixture of rotamers) δ 7.32 (5H, br s), 6.36 (1H, br s), 5.32–5.27 (2H, br s), 4.75–3.84 (6H, multiplets), 3.77 (3H, br s), 3.48 (1H, br d, $J = 8.5$ Hz), 2.88 (1H, br s), 2.31–1.80 (4H, multiplets), 1.25–1.10 (3H, multiplets); ^{13}C NMR (125 MHz, CDCl_3 , mixture of rotamers) δ 172.4, 166.3, 151.0, 136.1, 128.5, 128.3, 128.0, 95.5, 88.1, 75.4, 74.5, 73.2, 71.4, 67.5, 62.6, 53.4, 52.9, 40.9, 34.8, 31.3, 13.7; IR (film) 3352, 1732, 1408 cm^{-1} ; HRMS (FAB) 577.0782 (577.0785 calcd for $\text{C}_{23}\text{H}_{26}\text{Cl}_3\text{N}_3\text{O}_8$, M).

Acknowledgment. Support from the National Heart, Lung, and Blood Institute (HL-25854), NIH NRSA postdoctoral fellowship support to B.N.R. (CA-73122) and J.E.T. (GM-16617), F.C.A.R.-Québec postdoctoral fellowship to G.B., and graduate fellowship support to W.C.T. from the Department of Education and Abbott Laboratories are gratefully acknowledged. NMR and mass spectra were determined at UC Irvine using instruments acquired with the assistance of NSF and NIH shared instrumentation grants.

Supporting Information Available: Experimental procedures and characterization for the preparation of **8c**, **11c**, **15–20**, **27c**, **29**, and **30**; copies of ^1H NMR spectra for new isolated and fully purified compounds: **8bc**, **9b**, **11bc**, **12bc**, **15–20**, **26**, **27bc**, **29**, and **30**. This material is available free of charge via the Internet at <http://pubs.acs.org>.

JO026282Y