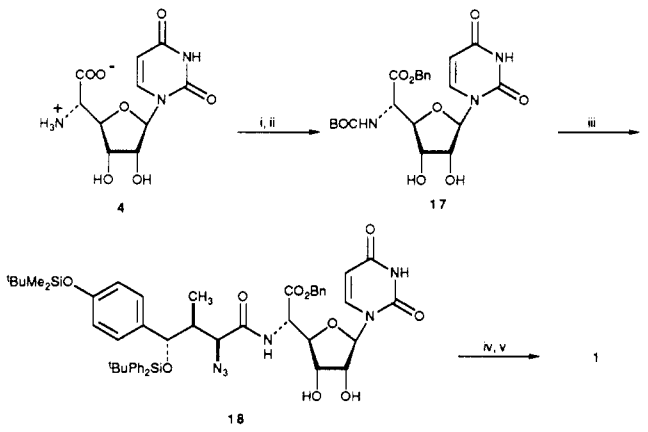
Scheme III[a]



[a] Reagents: (i) 1:1 dioxane-H_2O, K_2CO_3, BOC anhydride, 25 °C, 3.5 h; (ii) MeOH, $PhCHN_2$, 25 °C, 72%; (iii) TFA, EtOAc, 0 °C to 25 °C, 30 min, evaporate; 2 equiv of *N*-methylmorpholine, DMF, **16**, 25 °C, 72 h, 53%; (iv) TBAF, THF, 25 °C, 30 min; (v) 10% $Pd/BaSO_4$ (prehydrogenated overnight), $MeOH/H_2O$, H_2, 25 °C, 30 min, 39%.

Although saponification of the ester **13** led to undesired desilylation and lactonization, ester **13** could be hydrolyzed under nonaqueous conditions developed in this laboratory.[22] Transesterification of **13** in the presence of 3-buten-1-ol and $Ti(Oi\text{-}Pr)_4$[23] gave the ester **14** (91%), which was protected as the *tert*-butyldimethylsilyl ether **15** (95%).[24] Ozonolysis of the butene residue afforded the aldehyde which, after treatment with DBU[22] in situ, gave the α-azido acid. Without isolation, treatment of the acid with *p*-nitrophenol and DCC in THF[25] afforded the activated ester **16** (61%) as a single diastereoisomer.

p-Nitrophenyl esters are widely used to facilitate peptide bond formation.[25,26] In fact, a variety of *p*-nitrophenyl esters of N-protected α-amino acids have been utilized in the peptide-coupling reaction with α-amino nucleosides including the C-terminal amino acid, uracil polyoxin C (**4**).[27] Unfortunately, reaction of the C-terminal amino acid **4** with the activated ester **16** in DMF[27b] failed to afford any coupled product. However, after protecting nucleoside **4**, formation of the amide bond was achieved. The α-amino acid was first protected as the BOC derivative[28] followed by formation of the benzyl ester **17** using $PhCHN_2$,[29] (72% over 2 steps) (Scheme III). Liberation of the amine moiety by treatment with trifluoroacetic acid[26] gave the corresponding ammonium trifluoroacetate which was used directly in the peptide coupling reaction in DMF using N-methylmorpholine,[27] affording amide **18** (53%). Desilylation[17] of **18** and subsequent chemoselective hydrogenation over 10% $Pd/BaSO_4$ in aqueous methanol[11c] afforded the nucleoside dipeptide amino acid nikkomycin B (**1**) (39%).[30]

In conclusion, a potentially general route to the (2*S*,3*S*,4*S*)-γ-hydroxy-β-methyl-α-aminobutanoic acid moiety, a common feature of the nikkomycin N-terminal amino acid residues, has been described. The protected α-amino nucleoside fragment **17** has been successfully coupled with the activated *p*-nitrophenyl ester **16**, completing the total synthesis of nikkomycin B (**1**).

Acknowledgment. We thank the National Institutes of Health (AI-22252) for the support of this program and for the purchase of a 400-MHz NMR spectrometer (RR-01672) and a high-resolution mass spectrometer (RR-03245) used in these studies. We additionally thank Dr. Colin Smith of Glaxo Research Group, Greenford, Middlesex, U.K., for most generously providing authentic uracil polyoxin C (**4**) for studies on the peptide coupling reaction, G. D. Searle and Co., Skokie, IL, for microanalytical services, and Dr. Xiao-an Zhang for preliminary studies.

Supplementary Material Available: Experimental procedure for the conversion of **18** into nikkomycin B (**1**) and spectroscopic data for **1** (2 pages). Ordering information is given on any current masthead page.

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(29) Adamson, J. R.; Bywood, R.; Eastlick, D. T.; Gallagher, R.; Walker, D.; Wilson, E. M. *J. Chem. Soc., Perkin Trans. 1* **1975**, 2030.
(30) We have been unable to obtain an authentic sample of nikkomycin B (**1**). Our structural assignment is based upon comparison of spectroscopic data for our synthetic material with the data reported by Konig for nikkomycin B_x (**2**). See ref 6 and the supplementary material.

Short Synthesis of (±)-Sterpurene

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Summary: The tricyclic fungal metabolite sterpurene (**1**) has been synthesized by a very short route employing a cyclopentane annulation as the key transformation.

Sterpurene (**1**) was first reported by Ayer in 1981 as a metabolite of *Stereum purpureum*, a fungus that is responsible for silver leaf disease.[1] Syntheses of racemic and nonracemic sterpurene have been reported by Murata, Little, and Okamura.[2] Herein we report our synthesis of (±)-sterpurene.

(1) Ayer, W. A.; Saeedi-Ghomi, M. H. *Can. J. Chem.* **1981**, *59*, 2536.
(2) (a) Murata, Y.; Ohtsuka, T.; Shirahama, H.; Matsumoto, T. *Tetrahedron Lett.* **1981**, *22*, 4313. (b) Moëns, L.; Baizer, M. M.; Little, R. D. *J. Org. Chem.* **1986**, *51*, 4497. (c) Gibbs, R. A.; Okamura, W. H. *J. Am. Chem. Soc.* **1988**, *110*, 4062. (d) Gibbs, R. A.; Bartels, K.; Lee, R. W. K.; Okamura, W. H. *Ibid.* **1989**, *111*, 3717.

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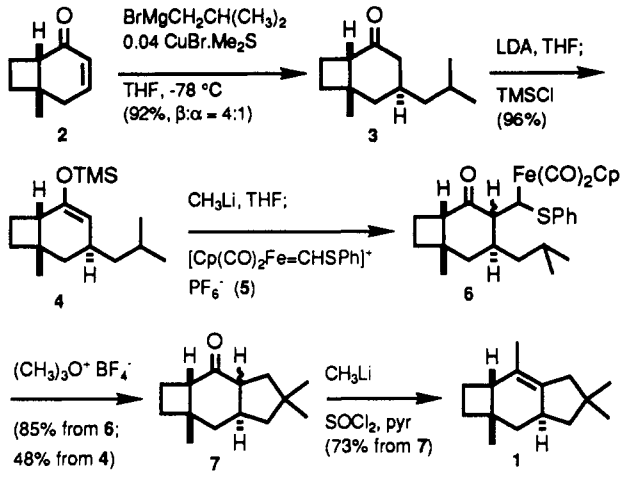
Scheme I



cis-6-Methylbicyclo[4.2.0]oct-3-en-2-one (**2**)[3] undergoes copper-catalyzed conjugate addition[4] of isobutylmagnesium bromide to give the ketone **3** as a 4:1 mixture of the β and α isomers favoring the desired β-substituted isomer. Enolate generation followed by addition of $[Cp(CO)_2Fe{=}CHSPh]^+PF_6^-$ (**5**, Cp = η^5-C_5H_5)[5] gives the intermediate **6** which when treated with trimethyloxonium tetrafluoroborate gives the epimeric tricyclic ketones **7**[6] (Scheme I). This product is obtained in 80–90% yields from **6**, but the overall cyclopentane annulation is made operationally simpler when **6** is not isolated or purified, in which case the overall yield of **7** is 48% from the enol silyl ether **4**. The main limitation in the yield for the overall annulation process appears to be incomplete reaction of the enolate generated from **4** in that 20–30% of the ketone **3** is recovered after the reaction of the enolate with **5**. The synthesis is completed as in Little's route[2b] by addition of methyllithium and dehydration of the resulting tertiary alcohol. The sterpurene thus obtained is identical to the previously obtained material according to direct comparison of ^1H and ^{13}C NMR spectra.[1,2d]

This synthesis provides sterpurene by an attractively simple, short route, and it demonstrates the utility of the new organoiron-based cyclization reaction.[6]

Acknowledgment. We thank Professors Ayer and Okamura for generously providing us with copies of NMR spectra of sterpurene. We also thank Dr. Bruce Plashko (Notre Dame) for mass spectrometric measurements. We are grateful to the National Science Foundation and the donors of the Petroleum Research Fund, administered by the American Chemical Society, for financial support of this work.

Supplementary Material Available: ^1H and ^{13}C NMR spectra of *trans*-**7** and the synthetic sterpurene (8 pages). Ordering information is given on any current masthead page.

(3) Enone **2** was obtained as previously reported from the photocycloaddition of ethylene to 3-methyl-2-cyclohexenone followed by bromination/dehydrobromination: (a) Zurflüh, R.; Dunham, L. L.; Spain, V. L.; Siddall, J. B. *J. Am. Chem. Soc.* **1970**, *92*, 425. (b) Cargill, R. L.; Dalton, J. R.; Morton, G. H.; Caldwell, W. E. *Org. Synth.* **1984**, *62*, 118. (c) Jacques, J.; Marquet, A. *Organic Syntheses*; Wiley: New York, 1988; Collect. Vol. VI, p 175. (d) House, H. O.; Bashe, R. W. II *J. Org. Chem.* **1965**, *30*, 2942.

(4) (a) Horiguchi, Y.; Matsuzawa, S.; Nakamura, E.; Kuwajima, I. *Tetrahedron Lett.* **1986**, *27*, 4025. (b) Bal, S. A.; Marfat, A.; Helquist, P. *J. Org. Chem.* **1982**, *47*, 5045. Direct trapping of the enolate resulting from the conjugate addition was performed using TMSCl, and direct trapping of the enolate resulting from proton abstraction from ketone **3** was performed using iron reagent **5**, but superior results were obtained with the more stepwise route described in the text.

(5) (a) Knors, C.; Kuo, G.-H.; Lauher, J. W.; Eigenbrot, C.; Helquist, P. *Organometallics* **1987**, *6*, 988. (b) Knors, C.; Helquist, P. *Organomet. Synth.* **1988**, *4*, 205.

(6) Zhao, S.-K.; Knors, C.; Helquist, P. *J. Am. Chem. Soc.* **1989**, *111*, 8527.

Addition of Amino Lactams to Vinyl Vicinal Tricarbonyls. Formation of Tricyclic 2-Azadethiapenams and 3-Azadethiacephams

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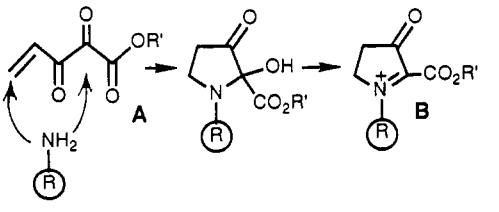
Summary: Amino lactams react as trinucleophiles with vinyl vicinal tricarbonyl esters to form tricyclic derivatives. Products of particular interest resulting from this reaction sequence are 2-azadethiapenams and 3-azadethiacephams.

We have recently shown[1] that the addition of primary amines to vinyl tricarbonyl reagents A generates ketopyrrolinium carboxylates B (Scheme I), which may serve as powerful electrophilic acceptors for nucleophilic residues attached to the primary amine (Figure 1). These nucleophiles have included indole groups, activated aromatic rings, enol ethers, vinylsilanes, propargylsilanes, and pyrroles.[1-3] We now report that the amide NH of a lactam

Scheme I



residue will add to the intermediate iminium group, forming fused-ring 2-(acylamino)-1-oxopyrrolidinecarboxylates.[4] This process constitutes a facile route to

(1) Wasserman, H. H.; Fukuyama, J.; Murugesan, N.; van Duzer, J.; Lombardo, L.; Rotello, V.; McCarthy, K. *J. Am. Chem. Soc.* **1989**, *111*, 371–372.

(2) Wasserman, H. H.; Amici, R. M. *J. Org. Chem.* **1989**, *54*, 5843–5844.

(3) Wasserman, H. H.; Cook, J. D.; Vu, C. B. *J. Org. Chem.* **1990**, *55*, 1701–1702.

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