with MeCu-catalyzed hydroalumination with DIBAL in HMPA/THF followed by trapping the aluminate with chlorotrimethylsilane.[11] Without purification, this labile substance was ozonized[12] and the crude product was treated with sodium borohydride followed by diazomethane to give hydroxy ester **9**, $[\alpha]^{25}_D$ -7.69° (*c* 0.52, $CHCl_3$), in 87% yield. Tosylation of the hydroxy ester **9** followed by exposure to lithium diphenylcuprate[13] gave the corresponding 7-phenylheptanoate. Acidic (HF, CH_3CN) removal of the silyl ether protecting groups resulted in concomitant lactonization to compound (-)-**10**, $[\alpha]^{25}_D$ -45.20° (*c* 0.44, $CHCl_3$) (lit.[10b] $[\alpha]^{20}_D$ +45.6°).

The preparation of lactone (+)-**10** (natural compactin analogue) was performed along similar lines (Scheme II). Compound **6** was transformed into enone **11**, $[\alpha]^{24}_D$ -19.63° (*c* 1.24, $CHCl_3$), in 86% yield via chemoselective oxidation with MnO_2 followed by hydroxy protection as the silyl ether. Treatment of **11** with catalytic MeCu and 2.5 equiv of DIBAL in HMPA/THF followed by MeLi afforded a bisaluminate species, which was treated with *tert*-butyldimethylsilyl trifluoromethanesulfonate (TBSOTf) to give **12** in 90% yield.[14] Silyl enol **12** was converted to natural compactin analogue (+)-**10** in a series of routine manipulations as described in Scheme II. The optical rotation of (+)-**10** was found to be $[\alpha]^{25}_D$ +46.11° (*c* 0.36, $CHCl_3$) (lit.[10a] $[\alpha]^{25}_D$ +48.80° (*c* 0.20, $CHCl_3$)).

We anticipate that the optically active synthon **6** will be applicable to the synthesis of a number of biologically interesting substrates; studies along these lines are continuing in our laboratory.

Acknowledgment. We gratefully acknowledge support by the National Science Foundation.

Supplementary Material Available: Spectral data for compounds **3-12** (8 pages). Ordering information is given on any current masthead page.

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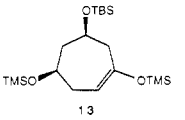
(11) Tsuda, T.; Satomi, H.; Hayashi, T.; Saegusa, T. *J. Org. Chem.* **1987**, *52*, 439.
(12) Stork, G.; Nair, V. *J. Am. Chem. Soc.* **1979**, *101*, 1315. White, J. D.; Fukuyama, Z. Y. *J. Am. Chem. Soc.* **1979**, *101*, 226.
(13) Johnson, C. R.; Dutra, G. A. *J. Am. Chem. Soc.* **1973**, *95*, 7783.
(14) Attempts to prepare compound **13** were successful but ozonation resulted in low yields of the desired product.

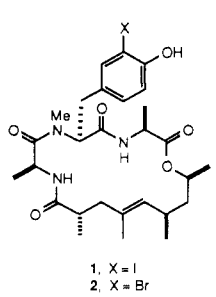


13

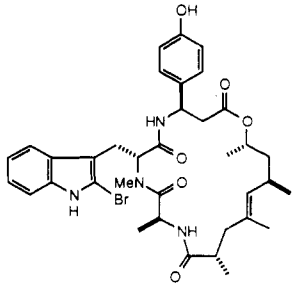
Total Synthesis of Geodiamolide A, a Novel Cyclodepsipeptide of Marine Origin

Summary: Geodiamolide A (**1**), a cyclodepsipeptide isolated from the sponge *Geodia* containing the new amino acid (*R*)-3-iodo-*N*-methyltyrosine, was synthesized from its constituent tripeptide and 8-hydroxynonenoic acid subunits. Final closure of the 18-membered ring was effected via macrolactonization employing dicyclohexylcarbodiimide.

Sir: Geodiamolide A (**1**) and B (**2**),[1] along with jasplakinolide (**3**),[2] are novel cyclodepsipeptides isolated by acetone extraction of the sponges *Geodia* and *Jaspis* sp., respectively. Each of these 18-membered cyclodepsipeptides consists of an 11-carbon, propionate-derived hydroxy acid [(2*S*,6*R*,8*S*)-8-hydroxy-2,4,6-trimethyl-4(*E*)-nonenoic acid] linked to a tripeptide containing a unique amino acid. The pharmacological properties of these substances, especially the potent insecticidal and anthelmintic activity of **3**,[2] have attracted attention, and, recently, the syntheses of both **2** and **3** have been reported by Grieco et al.[3,4] Herein we describe the total synthesis of **1** containing the previously unknown amino acid 3-iodo-*N*-methyl-D-tyrosine. The steric demand imposed by the iodo substituent in this subunit compelled us to adopt a sequence significantly different from that employed for the corresponding tripeptide segment of **2**.[4] Also, in contrast to the previous syntheses of **2** and **3**, our route to the nonenoic acid component of **1** takes advantage of the Claisen rearrangement of an orthopropionate, and thereby establishes the desired substitution at C-2 without the need for a separate methylation.[2,5]

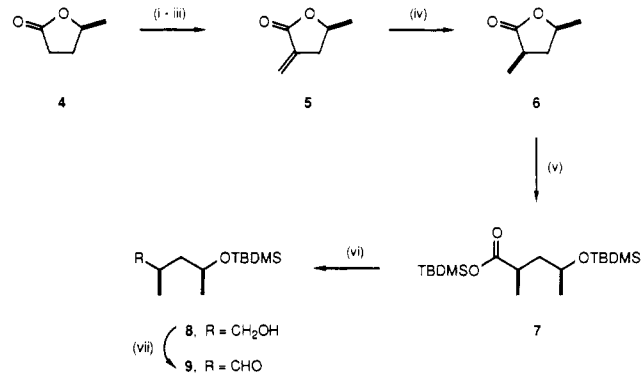


1, X = I
2, X = Br



3

Scheme I[a]



[a] Reagents: (i) HCO_2Me, NaH, Et_2O, 25 °C (93%); (ii) Me_2NH, $NaBH_3CN$, MeOH-HCl, 25 °C (66%); (iii) MeI, MeOH, then 5% $NaHCO_3$, 25 °C (80%); (iv) H_2, 10% Pd/C, EtOH, 25 °C (72%); (v) 2.5 M KOH, THF, 25 °C, then $tBuMe_2SiCl$, imidazole, DMF, 25 °C (70%); (vi) $(iBu)_2AlH$, Et_2O, 25 °C (78%); (vii) $(COCl)_2$, DMSO, Et_3N, CH_2Cl_2, -60 °C → 25 °C (75%).

(1) Chan, W. R.; Tinto, W. F.; Manchand, P. S.; Todaro, L. J. *J. Org. Chem.* **1987**, *52*, 3091.
(2) (a) Crews, P.; Manes, L. V.; Boehler, M. *Tetrahedron Lett.* **1986**, *27*, 2797. (b) Zabriskie, T. M.; Klocke, J. A.; Ireland, C. M.; Marcus, A. H.; Molinski, T. F.; Faulkner, D. J.; Xu, C.; Clardy, J. D. *J. Am. Chem. Soc.* **1986**, *108*, 3123.
(3) Grieco, P. A.; Hons, Y. S.; Perez-Medrano, A. *J. Am. Chem. Soc.* **1988**, *110*, 1630.
(4) Grieco, P. A.; Perez-Medrano, A. *Tetrahedron Lett.* **1988**, *29*, 4225.

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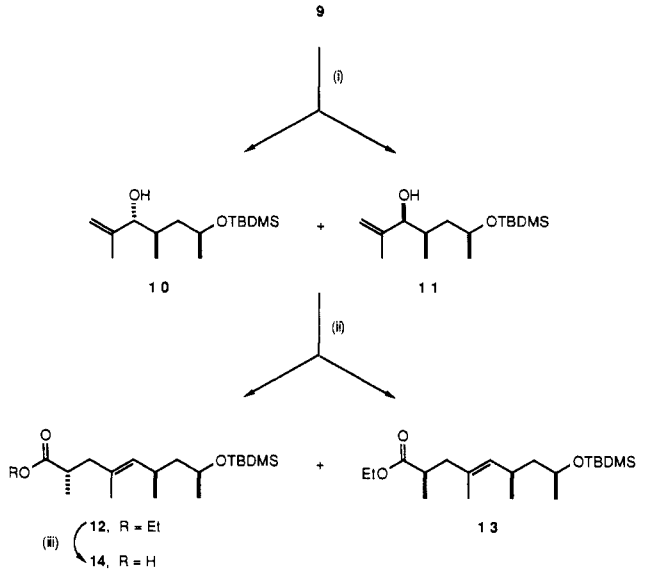
Scheme II[a]

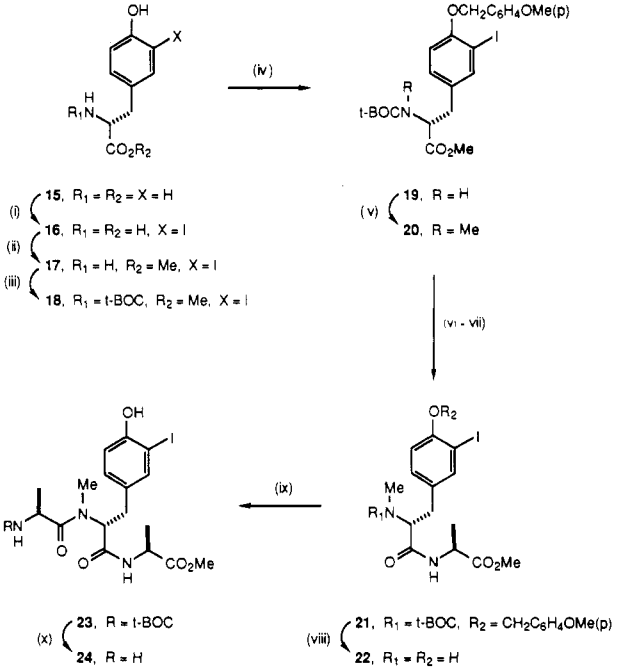


[a] Reagents: (i) $CH_2{=}C(CH_3)MgBr$, THF, reflux (60%); (ii) $CH_3CH_2C(OEt)_3$, $EtCO_2H$, 110 °C (78%, **12**:**13** = 1.5:1); (iii) LiOH, THF–MeOH–H_2O (3:1:1) (86%).

Preparation of the hydroxy acid moiety of **1** began from (4*S*)-4-methylbutyrolactone (**4**),[6] obtained from (*S*)-propylene oxide[7] and the dianion of phenylthioacetic acid.[8] α-Methylenation of **4**[9] afforded **5**, which underwent hydrogenation to give (2*R*,4*S*)-*cis*-2,4-dimethylbutyrolactone (**6**), exclusively[10,11] (Scheme I). Saponification of **6**, followed by silylation, gave **7**, which after reduction yielded alcohol **8**. Swern oxidation of **8** provided the aldehyde **9**. Treatment of **9** with isopropenylmagnesium bromide furnished a mixture of allylic alcohols **10** and **11** (Scheme II), which were separated with difficulty. However, it was found that each alcohol, when reacted with triethyl orthopropionate in the presence of propionic acid at 110 °C, produced the same 1.5:1 mixture of ethyl esters **12** and **13**.[12] Hence, for practical purposes the mixture of **10** and **11** was taken through the ortho ester Claisen rearrangement, and the facile separation of **12** from **13** was effected by HPLC (μ-Porasil, hexane–EtOAc, 99:1). Saponification of **12** gave the carboxylic acid **14** required for coupling with the tripeptide subunit of **1**.[13]

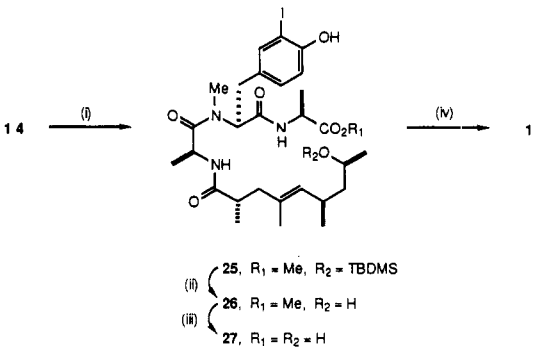
It was apparent, after several futile attempts to prepare a 3-iodo-substituted O-protected D-tyrosinyl derivative, that a carefully designed sequence would be necessary for elaboration of this new amino acid. Direct iodination[14] of

Scheme III[a]



[a] Reagents: (i) I_2, KI, NH_4OH, 25 °C (65%); (ii) $SOCl_2$, MeOH, 0 °C → reflux, then NH_3(g) (79%); (iii) $(tBuOCO)_2O$, THF, 25 °C (89%); (iv) *p*-$MeOC_6H_4CH_2Cl$, (*n*-Bu)$_4$NI, K_2CO_3, Me_2CO, 55 °C (96%); (v) NaH, MeI, DMF, 0 °C → 25 °C (86%); (vi) LiOH, THF–MeOH–H_2O (3:1:1), 25 °C (85%); (vii) L-alanine methyl ester, DCC, HOBT, CH_2Cl_2, 25 °C (73%); (viii) TFA–CH_2Cl_2 (1:1) (85%); (ix) N-t-BOC-L-alanine methyl ester, DCC, HOBT, CH_2Cl_2, 4 °C (76%); (x) TFA–CH_2Cl_2 (1:1), 25 °C (79%).

Scheme IV[a]



[a] Reagents: (i) $(PhO)_2PON_3$, Et_3N, **24**, DMF, 0 °C → 25 °C (57%); (ii) 5% HF–MeCN, 25 °C (83%); (iii) LiOH, THF–MeOH–H_2O (3:1:1), 25 °C (95%); (iv) DCC, DMAP, DMAP–TFA, 4-Å molecular sieves, $CHCl_3$, reflux (20%).

D-tyrosine (**15**) furnished **16** in acceptable yield, and the latter was converted to its methyl ester **17** and then to the *N*-t-BOC derivative **18** (Scheme III). Etherification of **18** with *p*-methoxybenzyl iodide at elevated temperature led to **19**, N-methylation of which produced **20**. This ester was saponified, and the amino acid was coupled[15] to L-alanine methyl ester to give the dipeptide **21**. The latter was deblocked with acid at both the amine and phenol to yield **22**, which was coupled[15] with *N*-t-BOC-L-alanine to provide tripeptide **24** after removal of N-protection from **23**.

The seco acid of **1** was assembled by linking **24** to the acyl azide[16] derived from **14** (Scheme IV). The resulting

(5) A preparation of the nonenoic acid subunit of **1**, **2**, and **3** employing this methodology has been reported independently: Schmidt, U.; Siegel, W.; Mundinger, K. *Tetrahedron Lett.* **1988**, *29*, 1269.

(6) White, J. D.; Somers, T. C.; Reddy, G. N. *J. Am. Chem. Soc.* **1986**, *108*, 5352.

(7) Ghirardelli, R. G. *J. Am. Chem. Soc.* **1973**, *95*, 4987.

(8) Iwai, K.; Kosugi, H.; Uda, H.; Kawai, M. *Bull. Chem. Soc. Jpn.* **1977**, *50*, 242.

(9) Barbier, P.; Benezra, C. *J. Med. Chem.* **1982**, *25*, 943.

(10) Barrett, A. G. M.; Carr, R. E.; Attwood, S. V.; Richardson, G.; Walshe, N. D. A. *J. Org. Chem.* **1986**, *51*, 4840.

(11) Satisfactory analytical and spectral data were obtained for all new compounds. Elemental compositions were determined by combustion analysis and/or high-resolution mass spectrometry.

(12) For a discussion of stereochemical aspects of the ortho ester Claisen rearrangement, see: Daub, G. W.; Shanklin, P. L.; Tata, C. *J. Org. Chem.* **1986**, *51*, 3402.

(13) Confirmatory evidence for the C-2 configuration of **14** was obtained by ozonolysis of its methyl ester to methyl (2*S*)-2-methyl-4-oxopentanoate; the latter was correlated with methyl (2*S*)-3-hydroxy-2-methylpropionate via Baeyer–Villiger oxidation.

(14) Harrington, C. R. *Biochem. J.* **1928**, *22*, 1434.

(15) Windridge, G. C.; Jorgensen, E. C. *J. Am. Chem. Soc.* **1971**, *93*, 6318.

(16) Shioiri, T.; Ninomiya, K.; Yamada, S. *J. Am. Chem. Soc.* **1972**, *94*, 6203.

amide **25** was desilylated to **26** and then saponified to furnish **27**. Closure of **27** to the 18-membered ring of **1** proved to be surprisingly difficult (cf. ref 3), the only reagent to effect this macrolactonization being one based on dicyclohexylcarbodiimide.[17] Application of this protocol to **27** gave geodiamolide A (**1**) in low yield, identical by comparison of melting point, optical rotation, and IR, ^{1}H NMR, and mass (FAB) spectra with a sample of natural material.

Acknowledgment. We are grateful to Dr. Percy S. Manchand, Hoffmann-LaRoche, Inc., for a sample of natural geodiamolide A and to Professor R. B. Bates, University of Arizona, for helpful advice. Financial support was provided by the National Institutes of Health (AI 10965).

(17) Boden, E. P.; Keck, G. E. *J. Org. Chem.* **1985**, *50*, 2394.

Supplementary Material Available: $[\alpha]_D$, IR, ^{1}H NMR, ^{13}C NMR, and mass spectral data are provided for **5–9**, **12–14**, and **16–27** (7 pages). Ordering information is given on any current masthead page.

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Articles

Syntheses of Vinyl Silane Phosphates: Novel Synthetic Intermediates

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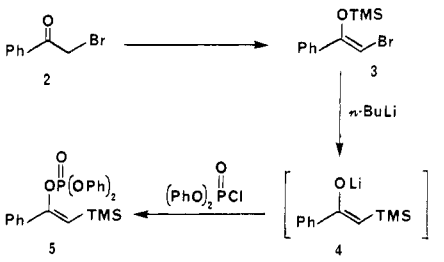
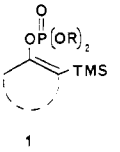
Received July 15, 1988

A number of procedures have been developed for the synthesis of vinyl silane phosphates (VSP's), a new type of functional group bearing trialkylsilyl and diaryl (or dialkyl) phosphate groups on adjacent sp^2 carbons. α-Silyl ketone enolates, accessible in a variety of ways, react with phosphorochloridates to give VSP's. Alternatively, in select cases it is possible to trap a β-lithiated vinyl phosphate with a trialkylsilyl chloride to obtain the VSP. Because vinyl silanes are susceptible to electrophilic substitution while at least some vinyl phosphates are subject to nucleophilic substitution, a variety of applications can be envisioned for this new functional group.

We have recently developed an interest in the chemistry of vinyl phosphates, reporting both a rearrangement of cyclic vinyl phosphates, which makes cyclic β-keto phosphonates readily available,[2] and a study of phosphate diene cycloadditions as a route to cyclic vinyl phosphates.[3] These studies of phosphate chemistry have fostered the evolution of a new strategy for olefin synthesis.[4] Specifically, we hypothesized that a new juxtaposition of functionality, with trialkylsilyl and diaryl phosphate groups positioned on adjacent sp^2 carbons, would prove to be readily accessible and amenable to both nucleophilic[5] and electrophilic[6] substitution reactions. In this manuscript we describe several routes that have been developed for preparation of vinyl silane phosphates (VSP's,[7] **1**), as well as the synthesis of a number of individual compounds. In the accompanying paper,[8] we describe representative substitution reactions, whereby VSP's are converted to vinyl silanes with carbon–carbon bond formation.

Scheme I





1

Results and Discussion

The high density of functionality in the VSP system allows a variety of synthetic approaches. By focusing upon ketones as the preferred starting material, assuring the availability of a wide variety of potential substrates, the

(1) Fellow of the Alfred P. Sloan Foundation, 1985–1989.
(2) Hammond, G. B.; Calogeropoulou, T.; Wiemer, D. F. *Tetrahedron Lett.* **1986**, *27*, 4265. Calogeropoulou, T.; Hammond, G. B.; Wiemer, D. F. *J. Org. Chem.* **1987**, *52*, 4185.
(3) Calogeropoulou, T.; Wiemer, D. F. *J. Org. Chem.* **1988**, *53*, 2295. For a closely related study, cf. Liu, H.-J.; Feng, W. M. *Synth. Commun.* **1987**, *17*, 1777.
(4) Portions of this work were reported at the 193rd American Chemical Society National Meeting, Denver, April, 1987.
(5) (a) Blaszczak, L.; Winkler, J.; O'Kuhn, S. O. *Tetrahedron Lett.* **1976**, *49*, 4405. (b) Sum, F.-W.; Weiler, L. *Can. J. Chem.* **1979**, *57*, 1431.
(6) Fleming, I.; Chan, T. H. *Synthesis* **1979**, 761. Colvin, E. W. *Silicon in Organic Synthesis*; Butterworths: London, 1981. Weber, W. P. *Silicon Reagents for Organic Synthesis*; Springer-Verlag: Berlin, 1983.
(7) The systematic names for these compounds are given in the Experimental Section. We have chosen the trivial name of vinyl silane phosphates to emphasize their potential reactivity as both vinyl silanes and vinyl phosphates and to provide a convenient acronym.
(8) Koerwitz, F. L.; Hammond, G. B.; Wiemer, D. F. *J. Org. Chem.*, following paper in this issue.

0022-3263/89/1954-0738$01.50/0