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Registry No. **2a**, 62075-35-8; **3**, 110144-06-4; (*E*)-**4a**, 110144-07-5; (*Z*)-**4a**, 110144-16-6; (*E*)-**4b**, 110144-08-6; (*Z*)-**4b**, 110144-17-7; **5**, 110144-09-7; **6a** (isomer 1), 110144-10-0; **6a** (isomer 2), 110144-18-8; **6b** (isomer 1), 110173-81-4; **6b** (isomer 2), 110144-19-9; **7** (isomer 1), 110144-11-1; **7** (isomer 2), 110144-20-2; **8a**, 110144-12-2; **8b**, 110144-13-3; **8c**, 110144-14-4; **8d**, 110144-15-5; diethyl acetone-1,3-dicarboxylate, 105-50-0; methyl 2-(triphenylphosphoranylidene)propionate, 2605-68-7; methyltriphenylphosphonium iodide, 2065-66-9; γ-elemene, 29873-99-2.

Supplementary Material Available: Experimental procedure for reactions described in Scheme I (7 pages). Ordering information is given on any current masthead page.

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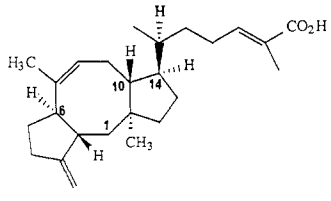
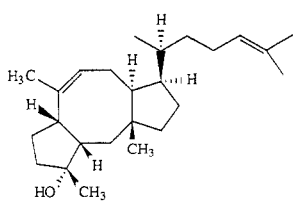
A Synthetic Entry into the Ophiobolane Ring System

Summary: A stereocontrolled construction of the angularly fused 5-8-5 ring system characteristic of the ophiobolin and ceroplastol sesterterpenes is reported. The synthesis is based on the elaboration of a *cis*-hydroazulene intermediate into the dicyclopenta[*a*,*d*]cyclooctane system with control of relative stereochemistry at several critical centers.

Sir: The dicyclopenta[*a*,*d*]cyclooctane ring system is the characteristic structural feature of the ophiobolane class of sesterterpenes. These natural products possess intriguing structural arrays and typically exhibit a wide range of biological activity. Representative examples of these substances are ceroplasteric acid (**1**)[1] and ophiobolin F (**2**).[2]



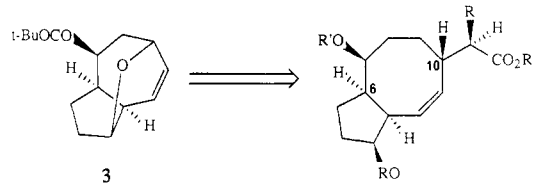
1



2

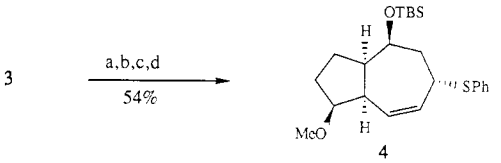
A growing number of additional members of this class of compounds have been isolated as well.[3] Several interesting approaches to the preparation of the ophiobolane system have been reported in the last few years,[4] but no total synthesis has, as yet, been forthcoming.

Our strategic plan centered on the efficient assembly of the 5-8-5 carbon skeleton with concommitant control of the relative stereochemistries at the three critical positions C_6, C_{10}, and C_{14} as found in ceroplasteric acid (**1**). It was envisaged that the highly functionalized and readily available *cis*-hydroazulene **3**[5] would serve admirably as a building block from which to elaborate the elements of the C-ring via a silyl enolate Claisen protocol.[6] Subsequent one-carbon ring expansion to the eight-membered ring would provide a precursor to the requisite 5-8-5 carbon backbone.



3

Treatment of **3** with thiophenol/BF_3·Et_2O at room temperature,[5c,7] followed by protecting group manipulation gave allylic sulfide **4** in 54% overall yield. Formation of



4

(a) BF_3·Et_2O/PhSH, room temprature; (b) NaH, MeI; (c) $LiAlH_4$, Et_2O; (d) TBDMSCl, imidazole

the corresponding sulfoxide with *m*-CPBA at −78 °C followed by a thermally induced [2,3]-sigmatropic rearrangement[8] in the presence of trimethyl phosphite provided the allylically transposed alcohol **5** in 71% yield.

At this point, a study was initiated to ascertain the stereochemical course of the enolate–Claisen reaction in our system. The correct configuration at C_{10} (ophiobolane numbering) is assured by virtue of the chirality transfer from the carbon–oxygen bond to the carbon–carbon bond inherent in this process. However, the stereochemistry at C_{14} (ophiobolane numbering) is a consequence of the ester enolate geometry and the transition state of the reaction.[6] Acylation of **5** with propionic anhydride/DMAP/Et_3N and treatment with LDA followed by *tert*-butyldimethylsilyl chloride (TBDMSCl) at −78 °C gave the requisite silyl ketene acetal[9] (Scheme I). Heating this material in re-

(1) Iitake, Y.; Watanabe, I.; Harrison, I. T.; Harrison, S. *J. Am. Chem. Soc.* **1968**, *90*, 1092.

(2) (a) Nozoe, S.; Morisaki, M.; Fukushima, K.; Okuda, S. *Tetrahedron Lett.* **1968**, 4457. (b) Nozoe, S.; Morisaki, M. *J. Chem. Soc. D* **1968**, 1319.

(3) (a) Ishibashi, K.; Nakamura, R. *Agric. Chem. Soc. Jpn.* **1958**, *32*, 739. (b) Rios, T.; Gomez G. F. *Tetrahedron Lett.* **1969**, 2929. (c) Rios, T.; Quijano, L. *Ibid.* **1969**, 1317.

(4) (a) Das, T. K.; Gupta, A. D.; Ghosal, P. K.; Dutta, P. C. *Indian J. Chem., Sect. B* **1976**, *14B*, 238. (b) Das, T. K.; Dutta, P. C. *Synth. Commun.* **1976**, *6*, 253. (c) Das, T. K.; Dutta, P. C.; Kartha, G.; Bermassan, J. M. *J. Chem. Soc., Perkin Trans. 1* **1977**, 1287. (d) Boeckman, R. K., Jr.; Bershas, J. P.; Clardy, J.; Solheim, B. *J. Org. Chem.* **1977**, *42*, 3630. (e) Dauben, W. G.; Hart, D. J. *J. Org. Chem.* **1977**, *42*, 922. (f) Baker, W. R.; Senter, P. D.; Coates, R. M. *J. Chem. Soc., Chem. Commun.* **1980**, 1011. (g) Coates, R. M.; Senter, P. D.; Baker, W. R. *J. Org. Chem.* **1982**, *47*, 3597. (h) Paquette, L. A.; Andrews, D. R.; Springer, J. P. *Ibid.* **1983**, *48*, 1147. (i) Takeshita, H.; Kato, N.; Nakanishi, K. *Chem. Lett.* **1984**, 1495. (j) Coates, R. M.; Muskopf, J. W.; Senter, P. A. *J. Org. Chem.* **1985**, *50*, 3541. (k) Paquette, L. A.; Colapret, J. A.; Andrews, D. R. *Ibid.* **1985**, *50*, 201. (l) Metha, G.; Krishnamurthy, N. *J. Chem. Soc., Chem. Commun.* **1986**, 1319.

(5) (a) Rigby, J. H. *Tetrahedron Lett.* **1982**, *23*, 1863. (b) Rigby, J. H.; Wilson, J. Z. *J. Am. Chem. Soc.* **1984**, *106*, 8217. (c) Rigby, J. H.; Wilson, J. Z. *J. Org. Chem.* **1987**, *52*, 34.

(6) (a) Ireland, R. E.; Mueller, R. H.; Willard, A. K. *J. Am. Chem. Soc.* **1976**, *98*, 2868. (b) Ireland, R. E.; Daub, J. P. *J. Org. Chem.* **1981**, *46*, 479. (c) Ireland, R. E.; Anderson, R. C.; Badoud, R.; Fitzsimmons, B. J.; McGarvey, G. J.; Thaisrivongs, S. *J. Am. Chem. Soc.* **1983**, *105*, 1988.

(7) An easily separated mixture of sulfide **4** and its allylically transposed isomer were isolated from this reaction in a 9:1 ratio, respectively.

(8) Andrews, G. C.; Evans, D. A. *Acc. Chem. Res.* **1974**, *7*, 147.

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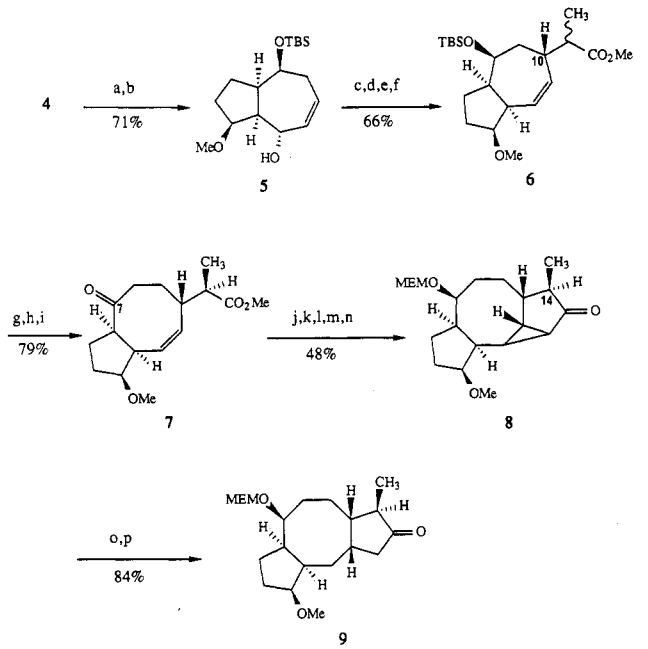
Scheme I[a]



[a] (a) *m*-CPBA, −78 °C; (b) $(MeO)_3P$, 65 °C; (c) $(C_2H_5CO)_2O$, Et_3N, DMAP; (d) LDA, TBDMSCl, −78 °C; (e) 110 °C, MePh; (f) CH_2N_2, Et_2O; (g) Bu_4NF, room temperature; (h) $(COCl)_2$, DMSO, Et_3N, −78 °C; (i) $TMSCHN_2$, $BF_3{\cdot}Et_2O$, −40 °C; (j) $NaBH_4$, 0 °C; (k) MEMCl, Et_2-*i*-PrN; (l) LiSPr, HMPA, room temperature; (m) $(COCl)_2$/collidine; (n) CH_2N_2, $Cu/CuSO_4/C_6H_{12}$/reflux; (o) Li/NH_3; (p) PDC.

fluxing toluene for several hours provided the rearranged product **6** as an easily separable 85:15 mixture of epimers at the side-chain methyl substituent in 66% overall yield. This mixture was isolated as the methyl esters (CH_2N_2, Et_2O). The major isomer was separated and carried through the remainder of the synthesis. Removal of the TBDMS group from the C_{10} alcohol and Swern oxidation[10] gave the corresponding cycloheptanone in 90% yield. Exposure of this ketone to (trimethylsilyl)diazomethane in the presence of $BF_3{\cdot}Et_2O$ at −40 °C[11] resulted in a smooth, regiospecific one-carbon ring expansion to the cyclooctanone **7** (mp 57–58 °C; C=O ν_{max} 1710 cm^{-1}) in 88% yield. Interestingly, none of the regioisomeric ketone was detected in this reaction. This observation is consistent with previous results in which the sterically less congested carbon migrates preferentially.

At this crucial juncture in the synthetic scheme, a single-crystal X-ray structure was obtained on compound **7**, which verified the direction of the ring expansion and, more importantly, established the relative stereochemistry of the vicinal protons at the side chain as being correct for ceroplasteric acid (**1**).

The stage was now set to complete the construction of the 5-8-5 tricycle with the required relative stereochemistries at C_6, C_{10}, and C_{14}. The C_7 ketone in compound **7** was reduced with $NaBH_4$ at 0 °C to give a 94% yield of a single alcohol, which was presumed to be the β-configuration based on examination of molecular models. The resultant hydroxyl group was then protected as the MEM ether. Next, the methyl ester was cleaved to the corresponding carboxylic acid via a mild S_n2-type dealkylation procedure employing excess lithium thiopropoxide in HMPA at room temperature.[12] This method for obtaining the acid from the ester was deemed prudent at this stage of the synthesis in order to minimize the risk of epimerization at the side-chain methyl substituent. Routine conversion into the diazo ketone via the corresponding acid chloride and copper-mediated insertion[13] into the cyclooctene double bond gave the desired cyclopropyl ketone **8** as a single isomer in 48% yield for the six steps. Reductive cleavage of the cyclopropane bond which was best aligned with the C_{13} carbonyl group under dissolving metal conditions (Li/NH_3)[14] followed to give, after PDC oxidation, the tricyclic ketone **9** (C=O ν_{max} 1744 cm^{-1}) in 84% yield.[15]

Ketone **9** possesses most of the key structural features of the hydrodicyclopenta[*a*,*d*]cyclooctane ring system as well as displaying the correct stereochemical arrangements at several important positions. Work is now under way to utilize this strategy in the total synthesis of ceroplasteric acid and related natural products.

Acknowledgment. This research was funded by the National Institutes of Health through grant GM-30771. We thank Paul Kierkus for obtaining the X-ray structure of compound **7**.

Supplementary Material Available: Spectral and analytical data for compounds **3–9** and fractional coordinates and temperature parameters, bond distances, and angles for **7** (3 pages). Ordering information is given on any current masthead page.

(9) Efforts to establish the geometry of the silyl ketone acetal employed in the rearrangement were unsuccessful.
(10) Swern, D.; Omura, K. *Tetrahedron* **1978**, *34*, 1651.
(11) (a) Mori, S.; Sakai, I.; Aoyama, T.; Shioiri, T. *Chem. Pharm. Bull.* **1982**, *30*, 3380. (b) Hashimoto, N.; Aoyama, T.; Shioiri, T. *Ibid.* **1982**, *30*, 119.
(12) Bartlett, P. A.; Johnson, W. S. *Tetrahedron Lett.* **1970**, 4459.
(13) Mori, K.; Ohki, M.; Kobayashi, A.; Matsui, M. *Tetrahedron* **1970**, *26*, 2815.
(14) Turner, J. V.; Anderson, B. F.; Mander, L. N. *Aust. J. Chem.* **1980**, *33*, 1061.
(15) The identity of all new compounds reported in this paper was established by IR, ^1H NMR, ^{13}C NMR, and MS. The elemental compositions were determined by combustion analysis or HRMS.

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A New Method for the Synthesis of O-Glycosides from S-Glycosides

Summary: Treatment of S-glycosides with $NOBF_4$ produced highly reactive glycosyl donors which in the presence of glycosyl acceptors gave O-glycosides in high yields.

Sir: Stereospecific construction of O-glycosidic linkages is of paramount importance in natural product chemistry.[1] One of the problems involved is the generation, from stable precursors, of a reactive glycosylating species[2] which can form a covalent bond with the glycosyl acceptor in a stereospecific fashion. Disadvantages of glycosyl halides, which are still the most frequently used glycosyl donors, have been well-documented.[2b] 1-O-Acetates of mono- and

(1) For some recent examples, see: (a) Nicolaou, K. C.; Ladduwahetty, T.; Randall, J. L.; Chucholowski, A. *J. Am. Chem. Soc.* **1986**, *108*, 2466 and references cited therein. (b) Katano, K.; Millar, A.; Pozsgay, V.; Primeau, J. L.; Hecht, S. M. *J. Org. Chem.* **1986**, *51*, 2927. (c) Roush, W. R.; Straub, J. A. *Tetrahedron Lett.* **1986**, *27*, 3349.
(2) For recent reviews, see: (a) Paulsen, H. *Angew. Chem.* **1982**, *94*, 184; *Angew, Chem., Int. Ed. Engl.* **1982**, *21*, 155. (b) Schmidt, R. R. *Angew. Chem.* **1986**, *98*, 213; *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 212.

0022-3263/87/1952-4635$01.50/0