(and at a lesser extent also the HCS splitting of thioketyls) is extremely dependent upon the solvation.[1] In particular, the greater the hydrogen bonding with the solvent, the larger the value of the splitting (e.g., in the aprotic solvent *N,N*-dimethylformamide, the splitting of 1 is reduced to 8.5 G[16] from the 13.0 G observed in methanol[1]). Accordingly, it is conceivable that in the bulkier radical **3** the hydrogen bonding between the HCS moiety and the solvent (ethanol) is lower than in **2**. This would thus contribute to reduce the splitting of **3** with respect to **2**. The balance of the two opposite effects (i.e., the torsion that would increase the splitting and the lesser solvation that would reduce it) thus accounts for the rather moderate increment of the HCS splitting observed in **3** with respect to **2**. On the other hand, the torsion exerted by the *tert*-butyl groups upon the HCO in **4** is smaller than on the HCS moiety in **3**, owing to the shorter C=O bond distance. As a consequence, the contribution of the torsion in modifying the HC=X splitting is less important in **4** with respect to **1** (X = oxygen) than it is in **3** with respect to **2** (X = sulfur). Conversely, the greater polarity of HCO with respect to HCS would make the hydrogen bonding more efficent in **4** than in the corresponding thio radical **3**. In the ketyl radical **4**, the balance of the two opposite effects thus favors the contribution of solvation. This circumstance explains why the HCO splitting is smaller in **4** than in **1**, with a trend opposite to that expected solely on the basis of the conformational properties.

Experimental Section

The ESR spectra were recorded with a Varian E3 ESR spectrometer. Photolysis was carried out with a 500-W high-pressure mercury lamp focused into the ESR cavity. The samples were degassed in a vacuum line by the usual thaw-freezing technique and sealed under vacuum. The *g* factor was measured by comparison with DPPH (2.0037) introduced in a capillary tube inside the sample under investigation.

The derivatives 2,4,6-tri-*tert*-butylbenzaldehyde and 2,4,6-tri-*tert*-buthylthiobenzaldehyde were prepared according to ref 14 and 12: MS, molecular ion at *m/e* 274.2289 (calcd 274.2297) and 290.2071 (calcd 290.2068), respectively.

Acknowledgment. This work was carried out with the financial support of the CNR (Strategic Project: Electron Transfer) and of the Ministry of Public Education, Rome, Italy.

Registry No. **2**, 58712-13-3; benzenethiol, 100-53-8; 2,4,6-tri-*tert*-butylthiobenzaldehyde, 84543-57-7.

---

[16] Steinberger, N.; Fraenkel, G. K. *J. Chem. Phys.* **1964**, *40*, 732.

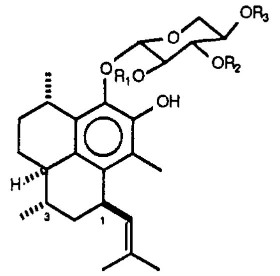
Communications

Total Synthesis of (-)-Pseudopterosin A

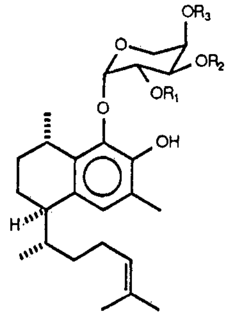
Summary: Pseudopterosin A has been synthesized, in optically active form, from (*S*)-(-)-limonene.

Sir: Pseudopterosins A–D (**1a–d**),[1,2] diterpene pentosides elaborated by the sea whip *Pseudopterogorgia elisabethae*, comprise a newly discovered family of biologically active marine natural products. Pharmacological studies[1] have shown them to possess antiinflammatory and analgesic activity with potencies comparable to that of indomethacin. Moreover, it appears that their mechanism of action is distinct from that of the cyclooxygenase-inhibiting antiinflammatory agents, making them particularly fascinating compounds from a biological standpoint. We record herein the first total synthesis of **1a**, in optically active form, by a route which should also lend itself to preparation of the related secopseudopterosins A–D (**2a–d**).[3]

(*S*)-(-)-Limonene was chosen as the starting material for this synthesis and converted into diols **3** by treatment with thexylborane according to the procedure of Brown.[4] The epimeric mixture was converted by routine operations into the hydroxy acid **4** and then lactonized to afford **5**, still as a mixture of epimers. Selenation–oxidation then gave α-methylene lactone **6** (Scheme I).[5]



1a: R$_1$ = R$_2$ = R$_3$ = H
1b: R$_1$ = Ac, R$_2$ = R$_3$ = H
1c: R$_2$ = Ac, R$_1$ = R$_3$ = H
1d: R$_3$ = Ac, R$_1$ = R$_2$ = H



2a: R$_1$ = R$_2$ = R$_3$ = H
2b: R$_1$ = Ac, R$_2$ = R$_3$ = H
2c: R$_2$ = Ac, R$_1$ = R$_3$ = H
2d: R$_3$ = Ac, R$_1$ = R$_2$ = H

Having constructed the rigid bicyclic system **6** we were now in a position to establish the correct stereochemistry at that center destined to become C-3 of our target. Dropwise addition of **6** (in THF) to a mixture of vinylmagnesium bromide (2.25 equiv), copper(I) iodide (0.15 equiv), dimethyl sulfide (2 equiv), and trimethylsilyl chloride (5 equiv) in THF at -40 °C provided **7** in excellent yield as a single stereoisomer after aqueous workup. The presence of trimethylsilyl chloride[6] is essential to the success of this reaction as is the order of addition (lactone to vinylcopper reagent). Upon workup, hydrolysis of the initially formed silyl ketene acetal occurs with proton

---

[1] Look, S. A.; Fenical, W.; Jacobs, R. S.; Clardy, J. *Proc. Natl. Acad. Sci. U.S.A.* **1986**, *83*, 6238.

[2] Look, S. A.; Fenical, W.; Matsumoto, G. K.; Clardy, J. *J. Org. Chem.* **1986**, *51*, 5140.

[3] Look, S. A.; Fenical, W. *Tetrahedron* **1987**, *43*, 3363. The absolute configuration of the arabinose moiety in the secopseudopterosins is not known with certainty at this time.

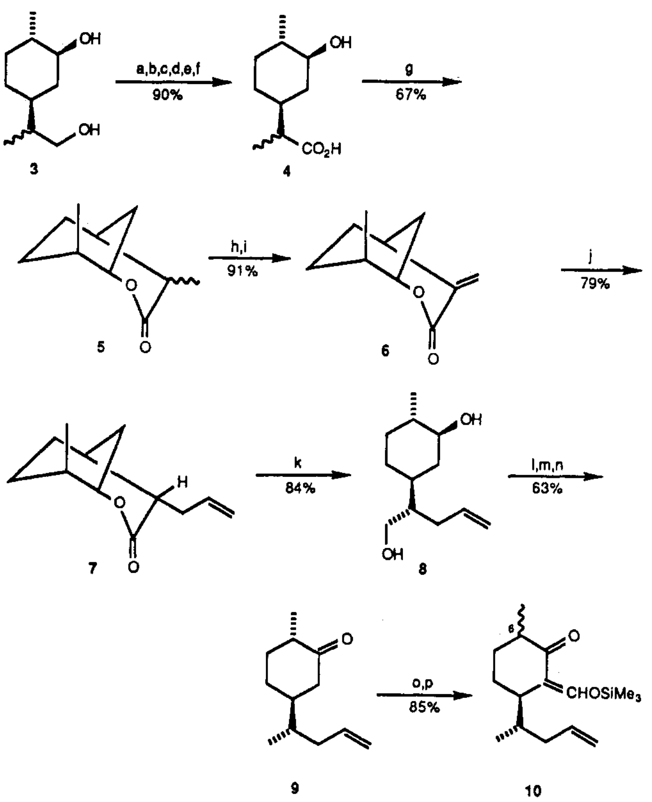
[4] Brown, H. C.; Pfaffenberger, C. D. *J. Am. Chem. Soc.* **1967**, *89*, 5475.

[5] Grieco, P. A.; Miyashita, M. *J. Org. Chem.* **1974**, *39*, 120.

[6] (a) Corey, E. J.; Boaz, N. W. *Tetrahedron Lett.* **1985**, 6015, 6019. (b) Alexakis, A.; Berlan, J.; Besace, Y. *Tetrahedron Lett.* **1986**, 1047.

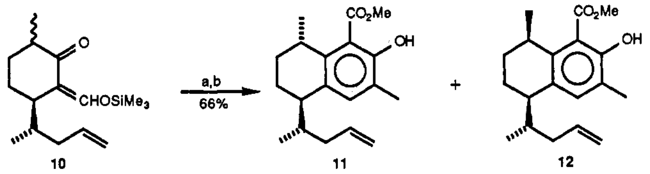
0022-3263/88/1953-1584$01.50/0

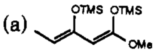
Scheme I[a]



[a] (a) Piv-Cl (1.1 equiv); pyr; (b) DHP, PPTS (cat.), CH_2Cl_2; (c) aqueous KOH; (d) PCC, NaOAc, CH_2Cl_2; (e) $NaClO_2$, aqueous *t*-BuOH, 2-methyl-2-butene; (f) $AcOH-H_2O/80$ °C; (g) *p*-TsOH, toluene reflux; (h) LDA, PhSeCl, HMPA; (i) H_2O_2; (j) vinylmagnesium bromide, CuI-DMS, TMSCl, THF (−40 °C); (k) LAH, THF; (l) $PhSO_2Cl$ (1.1 equiv); NEt_3, DMAP, CH_2Cl_2; (m) $LiBHEt_3$, THF; (n) PCC, CH_2Cl_2; (o) HCO_2Et, NaH, dioxane; (p) TMSCl, NEt_3, hexane.

Scheme II[a]

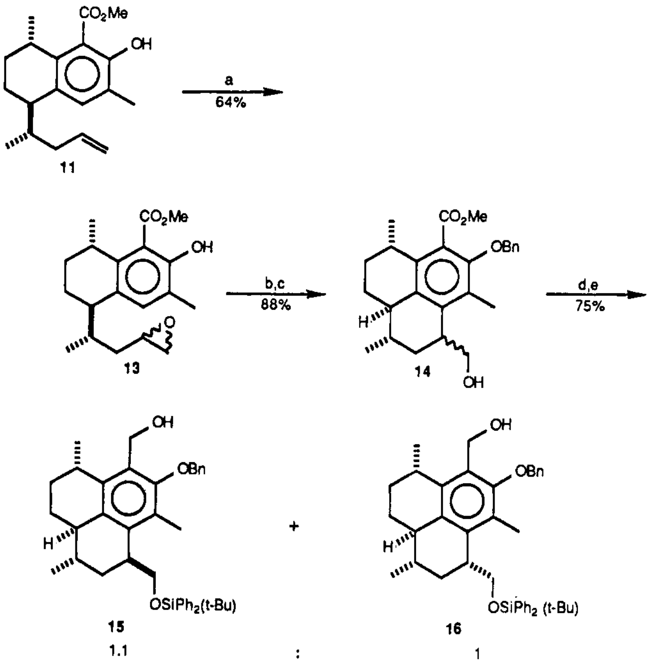


[a] (a)  , $TiCl_4$, CH_2Cl_2 (−78 °C, 4 h); (b) NaOMe, MeOH (24 h).

delivery from the more accessible exo face, accounting for the stereoselectivity of this reaction. Reduction of 7 to 8 (LAH, THF, 25 °C, 1 h) followed by selective sulfonylation of the primary hydroxy function, treatment with lithium triethylborohydride[7] and PCC oxidation furnished ketone **9** as a single stereoisomer. Conversion of **9** to its hydroxymethylene derivative[8] proceeded in good yield but resulted in loss of stereochemistry at C-6. Silylation of this product delivered **10**, again as an epimeric mixture (ratio ~1:1).

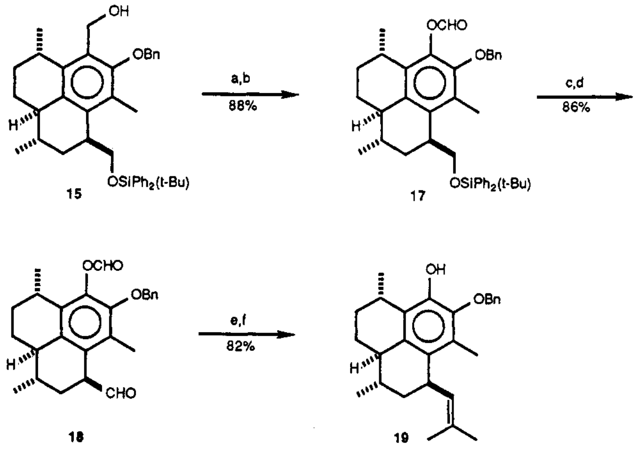
Installation of the requisite aromatic nucleus was accomplished by a slight modification of the procedure of Chan and Brownbridge[9] (Scheme II). In our case the

Scheme III[a]



[a] (a) MCPBA, $NaHCO_3$, $CHCl_3$, 55 °C; (b) $SnCl_4$, CH_2Cl_2 (20 °C); (c) BnBr, DMSO, K_2CO_3; (d) (*t*-Bu)Ph_2SiCl, imidazole, DMF, 45 °C; (e) DIBAL, CH_2Cl_2 (20 °C).

Scheme IV[a]



[a] (a) PCC, CH_2Cl_2; (b) MCPBA, Na_2HPO_4, $CHCl_3$ (20 °C, 3 h); (c) TBAF, AcOH, THF; (d) $(COCl)_2$, $DMSO/CH_2Cl_2$, −60 °C; NEt_3, −40 °C; (e) Me_2CLiCO_2Li, THF (20 °C, 30 min); (f) (dimethylamino)formaldehyde dineopentyl acetal, $CHCl_3$, 4,4′-methylenebis(2,6-di-*tert*-butylphenol) (55 °C, 3 days).

$TiCl_4$-promoted reaction of **10** with the indicated diene failed to give phenolic products directly. Instead, a complex mixture was obtained, the NMR spectrum of which suggested that the intermediate condensation products had not undergone aromatization under the influence of $TiCl_4$. Base treatment of this mixture gave phenols **11** and **12** (ratio 2:3) as the only isolable products in 66% overall yield. Preparative TLC on silica gel (4:1 benzene/hexane, two successive developments) afforded the desired product **11** as the higher running epimer.

Peracid oxidation of **11** led to the epoxides **13** as an inseparable mixture. Closure of the final ring of the amphilectane skeleton was achieved by an intramolecular Friedel–Crafts alkylation using excess $SnCl_4$ as the Lewis

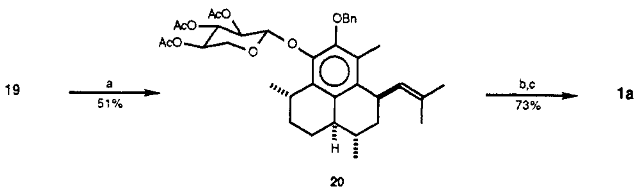
---

(7) Krishnamurthy, S.; Brown, H. C. *J. Org. Chem.* **1976**, *41*, 3064.

(8) Corey, E. J.; Cane, D. E. *J. Org. Chem.* **1971**, *36*, 3070. See also: Corey, E. J.; Nozoe, S. *J. Am. Chem. Soc.* **1963**, *85*, 3527. Sykora, V.; Cerny, J.; Herout, V.; Sorm, F. *Collect. Czech. Chem. Commun.* **1954**, *19*, 566.

(9) Chan, T. H.; Brownbridge, P. *Tetrahedron Suppl.* **1981**, *37*, 387.

Scheme V[a]



[a] (a) 1α-Bromo-2,3,4-triacetyl-D-xylose[15] (8 equiv), AgOTf (8 equiv), tetramethylurea (10 equiv), CH_2Cl_2, 20 °C; (b) KOH, MeOH; (c) Li/NH_3–THF.

acid (Scheme III).[10] Selective benzylation of the phenolic hydroxy group then provided **14**. Silylation and DIBAL reduction of **14** gave rise to a mixture of **15** and **16**, which was separated by preparative TLC on silica gel (6:1 hexane/EtOAc).[11]

Oxidative removal of the benzylic methylene unit was accomplished by conversion of **15** to the aldehyde (PCC, CH_2Cl_2) followed by Baeyer–Villiger oxidation (Scheme IV) effected with MCPBA in chloroform (using Na_2HPO_4 as buffer).[12] It was found that desilylation of **17** with excess TBAF in THF could be made to proceed without hydrolysis of the formyl unit if the pH of the reaction mixture was adjusted to about 7 by the addition of acetic acid. Swern oxidation of the resulting alcohol gave **18** in excellent yield and without detectable aldehyde epimerization. Treatment of **18** with the dianion of isobutyric acid produced the expected β-hydroxy acid and also cleaved the formate ester. The product, without purification, was carried on to **19** by reaction with excess (dimethylamino)formaldehyde dineopentyl acetal[13] in warm chloroform containing a small quantity of 4,4′-methylenebis(2,6-di-*tert*-butylphenol).

Of a considerable number of glycosidation protocols which were investigated, that outlined in Scheme V provided the best results. Although it was necessary to employ a considerable excess of the bromo sugar, **20** could be obtained in acceptable yield and with good stereoselectivity. This material was identical with an authentic sample prepared from natural pseudopterosin C.[14] Deacetylation followed by cleavage of the benzyl unit with Li in NH_3 gave (–)-pseudopterosin A (**1a**) identical with material produced by hydrolysis of natural pseudopterosin C (**1c**).[2]

Acknowledgment. We thank the Research Board of the University of Illinois, Research Corporation, and the donors of the Petroleum Research Fund, administered by the American Chemical Society, for their support of this work. We are also grateful to Professor W. Fenical for a generous gift of pseudopterosin C.

Registry No. **1a**, 104855-20-1; **3** (epimer 1), 113161-35-6; **3** (epimer 2), 113161-49-2; **4** (epimer 1), 113161-36-7; **4** (epimer 2), 113161-50-5; **5** (epimer 1), 113161-37-8; **5** (epimer 2), 113216-82-3; **6**, 113161-38-9; **7**, 113161-39-0; **8**, 113161-40-3; **9**, 113161-41-4; **10** (epimer 1), 113161-42-5; **10** (epimer 2), 113216-83-4; **11**, 113161-43-6; **12**, 113216-81-2; **13** (epimer 1), 113161-44-7; **13** (epimer 2), 113216-84-5; **14** (epimer 1), 113161-45-8; **14** (epimer 2), 113216-85-6; **15**, 113180-37-3; **16**, 113299-29-9; **17**, 113180-38-4; **18**, 113161-46-9; **19**, 113161-47-0; **20**, 113161-48-1; $CH_3CH{=}C(OSiMe_3)CH{=}C(OSiMe_3)OMe$, 78133-88-7; Me_2CLiCO_2Li, 16423-62-4; $Me_2NCH(OCH_2CMe_3)_2$, 4909-78-8; (–)-(*S*)-limonene, 5989-54-8; 1α-bromo-2,3,4-triacetyl-D-xylopyranose, 3068-31-3.

Supplementary Material Available: Experimental and spectral data for compounds **4–9** and **11–20** (4 pages). Ordering information is given on any current masthead page.

Chris A. Broka,* Samantha Chan, Barry Peterson
Roger Adams Laboratory
School of Chemical Sciences
University of Illinois at Urbana—Champaign
Urbana, Illinois 61801

Received September 15, 1987

---

[10] (a) Taylor, S. K.; Hockerman, G. H.; Karrick, G. L.; Lyle, S. B.; Schramm, S. B. *J. Org. Chem.* **1983**, *48*, 2449. (b) Taylor, S. K.; Davisson, M. E.; Hissom, B. R., Jr.; Brown, S. L.; Pristach, H. A.; Schramm, S. B.; Harvey, S. M. *J. Org. Chem.* **1987**, *52*, 425.

[11] Since chemoselective oxidation of the benzylic hydroxy group of the diol corresponding to **15** should be possible, the silylation of the other hydroxy group would appear to be unnecessary. However, we elected to postpone attempts to close the last ring of the system stereoselectively in order to first determine whether the isobutenyl moiety could be successfully introduced. We thus required a means of separating the C-1 epimers and this was most easily accomplished through the derivatives **15** and **16**.

[12] (a) Nakatsubo, F.; Cocuzza, A. J.; Keeley, D. E.; Kishi, Y. *J. Am. Chem. Soc.* **1977**, *99*, 4835. (b) Gammill, R. B.; Hyde, B. R. *J. Org. Chem.* **1983**, *48*, 3863.

[13] Aristoff, P. A.; Johnson, P. D.; Harrison, A. W. *J. Org. Chem.* **1983**, *48*, 5341.

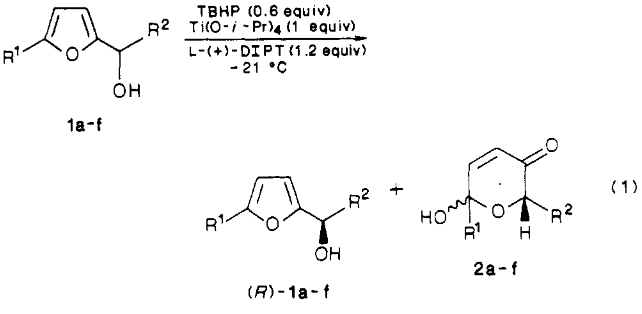
[14] Compound **20** was prepared from **1c** by using methods derived from the work of Fenical [(i) BnBr, K_2CO_3, DMSO; (ii) Ac_2O/pyr].

[15] *Methods in Carbohydrate Chemistry*; Whistler, R. L., Wolfrom, M. L., BeMiller, J. N., Shafizadeh, F., Eds.; Academic: New York/London, 1962; Vol. 1, p 183.

Preparation of Optically Active 2-Furylcarbinols by Kinetic Resolution Using the Sharpless Reagent

Summary: Enantioselective oxidation using TBHP and an asymmetric titanium–tartrate complex provides direct access to a variety of optically active 2-furylcarbinols.

Sir: 2-Furylcarbinols (**1**) have been recognized as versatile compounds in organic synthesis.[1] There is, however, no general method for preparation of optically active **1**.[2] We wish to report here that the Sharpless reagent for asymmetric kinetic resolution of secondary allylic alcohols[3] can be used for the resolution of racemic **1**, thus providing a highly efficient method for preparation of optically active **1** (eq 1).[4] Though the oxidation of **1** using *tert*-butyl hydroperoxide (TBHP) catalyzed by early transition metals to provide racemic **2** has been reported,[5] this example is the first in which the oxidation is carried out in



---

[1] Piancatelli, G.; Scettri, A.; Barbadoro, S. *Tetrahedron Lett.* **1976**, 3555. Piancatelli, G.; Scettri, A. *Tetrahedron Lett.* **1977**, 1131. Laliberté, R.; Médawar, G.; Lefebvre, Y. *J. Med. Chem.* **1973**, *16*, 1084. Georgiadis, M. P. *J. Med. Chem.* **1976**, *19*, 346. DeShong, P.; Ramesh, S.; Elango, V.; Perez, J. J. *J. Am. Chem. Soc.* **1985**, *107*, 5219.

[2] Suzuki, K.; Yuki, Y.; Mukaiyama, T. *Chem. Lett.* **1981**, 1529. Pikul, S.; Raczko, J.; Ankner, K.; Jurczak, J. *J. Am. Chem. Soc.* **1987**, *109*, 3981. Brown, J. M.; Cutting, I. *J. Chem. Soc., Chem. Commun.* **1985**, 578.

[3] Martin, V. S.; Woodard, S. S.; Katsuki, T.; Yamada, Y.; Ikeda, M.; Sharpless, K. B. *J. Am. Chem. Soc.* **1981**, *103*, 6237.

[4] For other examples of kinetic resolution using the Sharpless reagent, see the following. β-Hydroxy sulfides and α-acetylenic alcohols: Sharpless, K. B.; Behrens, C. H.; Katsuki, T.; Lee, A. W. M.; Martin, V. S.; Takatani, M.; Viti, S. M.; Walker, F. J.; Woodard, S. S. *Pure Appl. Chem.* **1983**, *55*, 589. β-Hydroxy amines: Miyano, S.; Lu, L. D.-L.; Viti, S. M.; Sharpless, K. B. *J. Org. Chem.* **1985**, *50*, 4350.

[5] Ho, T.-L.; Sapp, S. G. *Synth. Commun.* **1983**, *13*, 207.

0022-3263/88/1953-1586$01.50/0