formation. Moreover, photolyses of substrates lacking alkyl substituents at positions 3 and 5 (entries 7 and 10) were observed to proceed nearly as well as the more highly substituted 4-pyrones. Previous studies had indicated the need for electron-releasing alkyl substituents for both efficient partitioning into the zwitterion manifold and effective nucleophilic capture relative to rearrangement to 2-pyrone.[10] The successful conversion of **8** and **11** into the typical bicyclic photoproducts implies a promising generality of this new reaction. Also of interest is the observation that for at least two substrates, extended photolysis time results in selective destruction of the minor diastereomer (entries 4 and 9).[11] Issues which remain to be addressed in future work include the mechanism and products of this decomposition pathway, the factors which influence diastereoselectivity of the initial closure of excited 4-pyrone to zwitterion, applicability to other tether lengths and other possible pendant nucleophiles.

(10) Electron-releasing substituents at positions 3 and 5 were presumed necessary to confer stability to the electron-deficient allyl cation portion of the zwitterion.[1]

(11) In most cases, the bicyclic cyclopentenone ether products are effectively inert to photolysis during the relatively short (1-3 h) time required for efficient conversion of starting material.

In summary, we have reported a significant new class of synthetic transformations based upon the efficient intramolecular trapping of a photogenerated oxyallyl zwitterion by a nearby hydroxyl moiety. The net conversion of planar heterocyclic 4-pyrone precursors to bicyclic cyclopentenone ethers represents a striking bond reorganization and increase in molecular complexity, providing possible access to a variety of cyclopentanoid targets. Further elaboration of this class of transformations is currently underway in our laboratories.

Acknowledgment. We thank Professor Michael Crimmins for helpful discussions. We also gratefully acknowledge partial support from the University of Utah Research Committee and the American Cancer Society Institutional Research Grant no. IN-178, as well as National Science Foundation Grants CHE-8100424 and CHE-8310031 for funds used for the purchase of departmental mass spectroscopy facilities.

Supplementary Material Available: Representative procedures for the preparation of substrates **7** and **9** and photolysis of **6**, along with physical data for compounds **5**-**18** (7 pages). Ordering information is given on any current masthead page.

Synthesis of the Lichen Metabolite (+)-Bourgeanic Acid and Conformational Analysis of Its Dilactone

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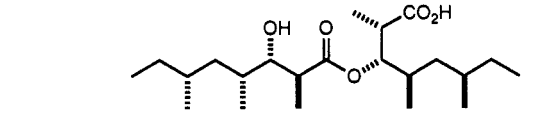
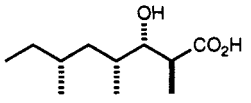
Summary: An enantiospecific synthesis of the depside (+)-bourgeanic acid via (-)-hemibourgeanic acid defines the latter as (2*S*,3*S*,4*R*,6*R*)-3-hydroxy-2,4,6-trimethyloctanoic acid and the former as its self-esterification product. Conformational analysis of the dilactone derived from bourgeanic acid shows that the eight-membered ring adopts a crown conformation with C_2 symmetry and all substituents in equatorial orientation.

The structure of (+)-bourgeanic acid (**1**), an aliphatic depside isolated from species of the lichen *Ramalina*,[1] was deduced by Bodo as the esterification product of two molecules of 3-hydroxy-2,4,6-trimethyloctanoic acid.[1,2] Saponification of **1** gave (-)-hemibourgeanic acid (**2**), the absolute configuration of which was proposed on the basis of an X-ray crystallographic analysis of its *p*-bromophenacyl ester.[3] An interesting property of **1**, noted by Bodo,[2] is the formation of an eight-membered dilactone **3** under mild dehydrating conditions.

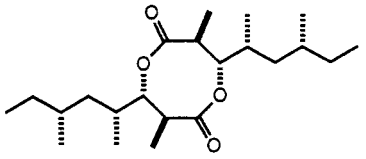
We now describe the first enantioselective synthesis of **1** and offer a rationale for its facile conversion to **3**. A signficant obstacle en route to **1** was self-esterification of the sterically hindered hemibourgeanic acid, for which a solution was devised through the β-lactone derivative of **2**.



1



2



3

Using methodology developed independently by Evans[4] and Sonnet,[5] the dilithio enolate of (2*S*)-1-propionyl-2-pyrrolidinemethanol (**4**) was alkylated with (2*R*)-1-iodo-2-methylbutane (**5**)[6] to give amide **6** (Scheme I). Hydrolysis of **6** afforded (2*R*,4*R*)-2,4-dimethylhexanoic acid (**7**), which was reduced to the corresponding hexanol **9** via methyl ester **8**. Oxidation of **9** under Swern conditions[8] led cleanly to aldehyde **10**, which was characterized as its

(1) Bodo, B.; Hebrard, B.; Molho, L.; Molho, D. *Tetrahedron Lett.* **1973**, 1631.

(2) Bodo, B.; *Bull. Mus. Natn. Hist. Nat., Paris*, 3ème sér. **1975**, *349*, 23.

(3) Bodo, B.; Trowitzch-Kienast, W.; Schomburg, D. *Tetrahedron Lett.* **1986**, *27*, 847.

(4) Evans, D. A.; Takacs, J. M. *Tetrahedron Lett.* **1980**, *21*, 4233.

(5) Sonnet, P. E.; Heath, R. R. *J. Org. Chem.* **1980**, *45*, 3137.

(6) The iodide **5** was prepared from methyl (2*S*)-3-(benzyloxy)-2-methylpropionate[7] via (a) reduction ($LiAlH_4$, Et_2O, 98%); (b) bromination of the resulting alcohol (NBS, Ph_3P, CH_2Cl_2, 92%); (c) methylation ($Me_2Cu(CN)Li$, THF-Et_2O, -78 °C → -20 °C, 87%); (d) hydrogenolysis (H_2, 1 atm, 10% Pd-C, THF) followed by tosylation (*p*-TsCl, pyridine, 87%); and (e) displacement by iodide (NaI, acetone, reflux, 81%).

(7) White, J. D.; Reddy, G. N.; Spessard, G. O. *J. Am. Chem. Soc.* **1988**, *110*, 1624.

(8) Mancuso, A. J.; Huang, S.-L.; Swern, D. *J. Org. Chem.* **1978**, *43*, 2480.

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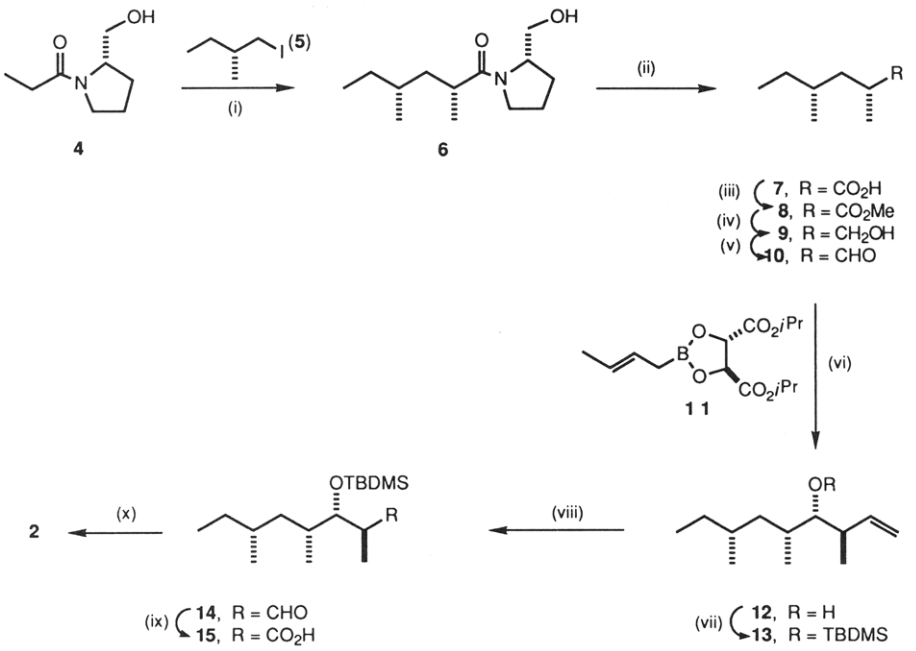
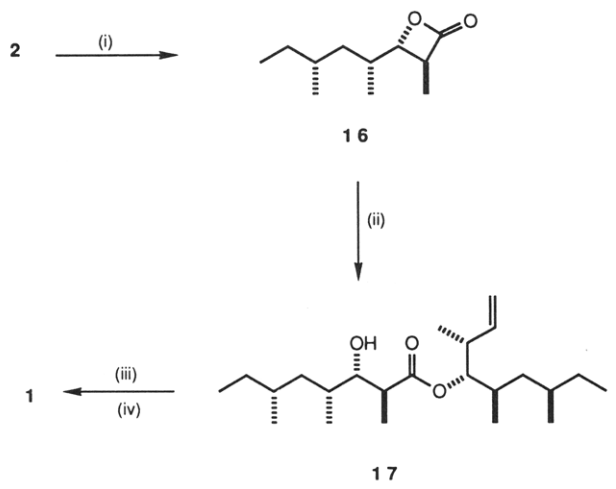
Scheme I[a]



[a] (i) LDA (2 equiv), THF, 25 °C, 1 h, HMPA **5**, then, −78 °C, 72 h (55%); (ii) 1 M HCl, reflux (95%); (iii) CH_2N_2, Et_2O; (iv) $LiAlH_4$, Et_2O, 0 °C (79% from **7**); (v) $(COCl)_2$, DMSO, Et_3N, CH_2Cl_2, −78 °C→0 °C (98%); (vi) **11**, toluene, 4Å sieves, −78 °C (76%); (vii) *tert*-$BuMe_2SiOTf$, 2,6-lutidine, CH_2Cl_2 (97%); (viii) O_3, CH_2Cl_2, −78 °C, then Me_2S, reflux (75%); (ix) $NaClO_2$, 2-methyl-2-butene, *t*-BuOH, pH 4 (97%); HF, THF–MeCN, 25 °C (89%).

Scheme II[a]



[a] (i) $PhSO_2Cl$, pyridine, 0 °C (86%), (ii) **12**, *n*-BuLi, THF, 0 °C (61%); (iii) O_3, EtOAc, −78 °C; (iv) H_2O_2, HOAc, 25 °C (47% from **17**).

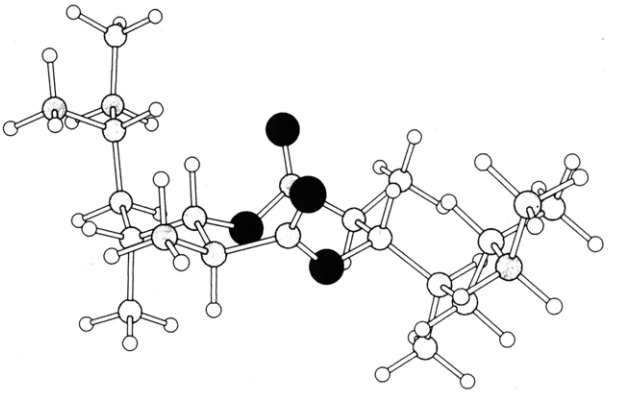


Figure 1. Calculated (MMX) minimum energy conformation of bourgeanic acid dilactone (**3**).

2,4-dinitrophenylhydrazone. This derivative was previously reported by Bodo[2] from degradation of bourgeanic acid.[9] Condensation of **10** with (*E*)-crotylboronate **11**,[10] prepared from (*S,S*)-tartrate by Roush's modified procedure,[11] yielded **12** in >95% stereochemical purity. After protection of this alcohol as its *tert*-butyldimethylsilyl (TBDMS) ether **13**, ozonolysis followed by reductive workup gave aldehyde **14**. Oxidation and removal of the silyl protecting group from **15** furnished (−)-hemibourgeanic acid (**2**), identical with material obtained by saponification of a sample of natural **1**.

Attempts to esterify the hindered hydroxyl group of **12** with derivatives of **2** by conventional methods were unsuccessful and we therefore resorted to acylation with the β-lactone **16**[2] of hemibourgeanic acid (Scheme II). Lactone **16**, prepared in high yield from **2** via the mixed sulfonic anhydride, was reacted with the lithium alkoxide of **12** to give hydroxy ester **17** in good yield. Ozonolysis, followed by oxidation, afforded **1**, $[\alpha]_D$ +7.3°, identical in all respects with an authentic sample of bourgeanic acid. The natural depside is thus the ester of (2*S*,3*S*,4*R*,6*R*)-hemibourgeanic acid.

The facile conversion of **1** to **3** observed by Bodo[2] was confirmed upon exposure of bourgeanic acid to phenylsulfonyl chloride at 0 °C, which furnished the dilactone in quantitative yield. Examination of the conformation of this lactone suggested two plausible conformers containing syn and anti carbonyl groups, with the former possessing a C_2 axis of symmetry. A MMX calculation unambiguously defined the global minimum as the syn

(9) Physical properties of the 2,4-dinitrophenylhydrazone of synthetic **10** (mp 112–113 °C (EtOH) and $[\alpha]^{23}_D$ −37.6° (*c* 0.25, EtOH)) are significantly different from those reported for the naturally derived material and suggest that the latter is a diastereomeric mixture.

(10) Roush, W. R.; Palkowitz, A. D.; Palmer, M. A. J. *J. Org. Chem.* **1987**, *52*, 316.

(11) Roush, W. R.; Ando, K.; Powers, D. B.; Palkowitz, A. D.; Halterman, R. L. *J. Am. Chem. Soc.* **1990**, *112*, 6339.

structure shown in Figure 1.[12] Theory was confirmed by the ^{13}C NMR spectrum of **3**, which showed only 11 signals, thereby proving that the dilactone possesses C_2 symmetry. The conformation depicted in Figure 1 places all four substituents on the perimeter of **3** in equatorial orientations, a feature that undoubtedly contributes to the ready formation of this eight-membered ring.[13]

(12) Calculations carried out with the MMX 87 force field found a global minimum for the syn conformer (Figure 1) below that of the anti confomer by ~8.5 kcal/mol. The difference ($E_{anti} - E_{syn}$) was found to reside primarily in torsional strain (~5.7 kcal/mol), with an additional ~1.9 kcal/mol resulting from 1,4-interactions.

(13) A MMX calculation on bourgeanic acid (1) found a global minimum in which the two chains are orthogonal, the carbonyl groups are syn, and the hydroxyl and carboxyl groups are oriented toward each other at a distance of 4.6 Å.

Acknowledgment. We are indebted to Dr. Bernard Bodo, Museum national d'Histoire naturelle, Paris, for a sample of natural bourgeanic acid. A.T.J. is grateful to the Division of Organic Chemistry, American Chemical Society, for a graduate fellowship sponsored by the Procter and Gamble Company. Financial support for this work was provided by the National Science Foundation (CHE-8619029).

Supplementary Material Available: Characterization data for **6**, **7**, **9**, **10**, **12**, **13**, **14**, **15**, **2**, **16**, **17**, and **1** (3 pages). Ordering information is given on any current masthead page.

Articles

Hydrolysis Rates of Saturated Acyclic and Cyclic Sulfinamides: X-ray Crystal Structures of an Acyclic Sulfinamide and γ-Ammoniopropanesulfinate

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The rates of the neutral hydrolysis of a saturated acyclic sulfinamide, *N,N*-dimethylmethanesulfinamide ($CH_3S(O)N(CH_3)_2$), the monocyclic compounds (isothiazolidine 1-oxide, 2-(1-phenylethyl)isothiazolidine 1-oxide, tetrahydrothiazine 1-oxide) and the bicyclic compounds (9-thia-1-azabicyclo[4.3.0]nonane 9-oxide and 2-thia-1-azabicyclo[4.3.0]nonane 2-oxide) were determined in D_2O using ^1H NMR at 65 °C. The first-order rate constants are similar to those of β-lactams. Activation parameters were determined for the acyclic, one cyclic, and one bicyclic sulfinamide. The striking feature which arises is that the parameters for the hydrolysis of the acyclic sulfinamide ($\Delta H^{\ddagger} = 11 \pm 4$ kcal mol^{-1}; $\Delta S^{\ddagger} = -47 \bullet 11$ cal mol^{-1} K^{-1}) are much different from both the monocyclic sulfinamide and the bicyclic sulfinamide ($\Delta H^{\ddagger} \sim 23 \pm 2$ kcal/mol^{-1}; $\Delta S^{\ddagger} \sim -15 \pm 4$ cal mol^{-1} K^{-1}, respectively). As a consequence, the acyclic sulfinamide hydrolyzes about 25 times faster than the cyclic sulfinamides. Most other heterocyclic compounds hydrolyze more rapidly than their acyclic analogues. Thus, the factors influencing the relative rates of hydrolysis of sulfinamides appear to be acting in a unique manner. The X-ray crystal structure of the first simple sulfinamide, *N*-(1-phenylethyl)methanesulfinamide, and a zwitterionic ammoniosulfinate, 3-((1-phenylethyl)ammonio)propanesulfinate, are also reported.

Introduction

A few years ago, we prepared the first saturated cyclic sulfinamides which represented a missing class of heterocyclic compounds.[1,2] Since these compounds are prepared by the oxidative cyclization of appropriately substituted amine disulfides with iodine in aqueous solution, they must be hydrolytically stable. As a first step to an understanding of the chemistry of saturated mono- and bicyclic sulfinamides, we embarked on a study of their rates of hydrolysis in aqueous solution in order to compare their relative reactivity with related heterocyclic compounds such as sultines and lactams. As a frame of reference for the hydrolysis of sulfinamides in general, we studied the rates of hydrolysis of an acyclic model compound, *N,N*-dimethylmethanesulfinamide ($CH_3S(O)N(CH_3)_2$), and compared these rates to those of the monocyclic compounds, isothiazolidine 1-oxide, 2-(1-phenylethyl)isothiazolidine 1-oxide, tetrahydrothiazine 1-oxide, and of the bicyclic compounds, 9-thia-1-azabicyclo[4.3.0]nonane 9-oxide and 2-thia-1-azabicyclo[4.3.0]nonane 2-oxide. Activation parameters were determined for the acyclic, one cyclic, and one bicyclic sulfinamide.

The X-ray crystal structures of the first simple sulfinamide, *N*-(1-phenylethyl)methanesulfinamide, and a zwitterionic ammoniosulfinate, 3-((1-phenylethyl)ammonio)propanesulfinate, are also reported.

(1) Doi, J. T.; Musker, W. K. *J. Am. Chem. Soc.* **1984**, *106*, 1887.
(2) Doi, J. T.; Musker, W. K. *J. Org. Chem.* **1985**, *50*, 1.

Results

The hydrolysis of the sulfinamides in deuterium oxide were determined by use of ^1H NMR. As the reaction proceeds, the sulfinamide peaks decrease in area and peaks corresponding to the sulfinate and the ammonium ion increase in area. All reactions were followed through at least 80% completion, and at least 10 data points were taken. The neutral hydrolysis of the sulfinamides, *N,N*-dimethylmethanesulfinamide, isothiazolidine 1-oxide, 2-

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