Table I. NMR Binding Data for Ligand **1a** in Deuteriochloroform

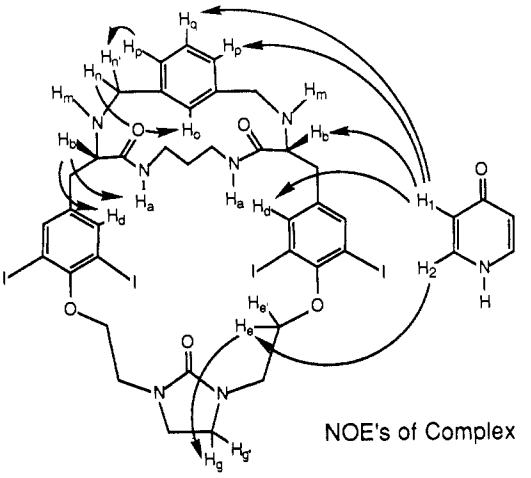
substrate	saturation achieved (%)	association energy[a] saturation[b]	Scatchard[c]	stoichiometry[d]
imidazole	89	-4.3 (0.4)	-4.7 (0.4)	0.90
1-Me imidazole		0.0[e]	0.0[e]	
2-Me imidazole	67	-3.4 (0.3)	-3.5 (0.2)	0.95
4-Me imidazole	85	-4.1 (0.4)	-4.4 (0.4)	0.89
N-Ac Me L-histidine	37	-1.9 (0.4)	-1.7 (0.4)	1.19
N-Ac Me L-phenylalanine		0.0[e]	0.0[e]	
benzimidazole	88	-4.3 (0.5)	-4.9 (0.4)	0.86
2-Me benzimidazole	30	-2.7 (0.2)	-2.6 (0.2)	1.20
benztriazole	58	-3.9 (0.1)	-4.5 (0.2)	0.67
pyrazole		0.0[e]	0.0[e]	
pyrrole		0.0[e]	0.0[e]	
pyridine		0.0[e]	0.0[e]	
2-pyridone	70	-3.7 (0.3)	-3.7 (0.3)	0.99
4-pyridone	95	-5.0 (1.0)	-4.7 (0.7)	1.10
3-hydroxypyridine	74	-3.9 (0.6)	-3.9 (0.6)	0.95
4-aminopyridine	55	-3.0 (0.3)	-3.0 (0.2)	0.99
4-Me_2N pyridine		0.0[e]	0.0[e]	
aniline		0.0[e]	0.0[e]	

[a] Association energies in kcal/mol (error limit). [b] By least-squares nonlinear fit assuming an equilibrium of the type A + B ⇌ AB. [c] By Scatchard which assumes the saturation value determined by the nonlinear fit. [d] Stoichiometry of complex obtained from Scatchard data treatment. [e] No binding of **1a** (5 mM) could be detected.

molecule possesses a deep cleft between the tyrosine phenyls which is occupied in the crystal by solvent.[3] Hydrogen positions were not determined, but the amide and amine hydrogens could be defined by molecular mechanics[4] to create strong hydrogen bonds from the amide hydrogens to the nearby amines. The X-ray of the benzylated **1b** shows this interaction explicitly and further demonstrates that **1** is capable of existing in several distinct conformations having large, well-defined cavities.

The X-ray structures above suggest that certain small heterocycles could indeed fill the cavity of **1** and donate a hydrogen bond to the urea at one end of the binding site and accept a hydrogen bond from an amide at the other. As shown in Table I, **1a** does in fact bind imidazole and a variety of related molecules in $CDCl_3$ with 1:1 stoichiometry according to NMR titrations. Association energies as high as 5 kcal/mol were found and represent minimum values since most of the substrates associate in chloroform.[5] The main feature, which distinguishes substrates which form complexes from those which do not, is their ability to both accept and donate hydrogen bonds to the ligand. Thus binding was found with all imidazoles tested except those having substitution on nitrogen. No binding was observed in DMSO or acetonitrile. The binding site accommodates considerable changes in the distance between the substrate's hydrogen bond donors and acceptors since the H/N distance in imidazole and the H/O distance in 4-pyridone is 3.2 and 5.0 Å, respectively.

While none of the complexes could be crystallized and facile protoisomerism made study of the imidazole complexes problematic, the structure of the 4-pyridone/**1a** complex could be elucidated by COSY-aided assignments and NOESY experiments. Important NOE's are shown in the figure below and interestingly are not consistent with a complex of 4-pyridone and the X-ray conformation of **1a**. They are however compatible with a complex having **1a** in a conformation similar to that of the X-ray of **1b**. Molecular mechanics suggests that the two conformations are similar in energy and shows internuclear distances of <4.0 Å in the energy minimized complex for all NOE-related hydrogens.



These results demonstrate the use of specific hydrogen bonding within an enforced cavity to provide well-defined complexes of donor/acceptor substrates and underscore the importance of considering conformational alternatives to X-ray structures when three-dimensional geometry is important.[6]

(6) This work was supported by National Science Foundation Grant CHE-8605891.

(3) Chang, M., to be published elsewhere.

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(5) Imidazole for example: Wang, S.-M.; Lee, L.-Y.; Chen, J.-T. *Spectrochim. Acta* **1979**, *35A*, 765.

Isolation and Structure Determination of the Didemnenones, Novel Cytotoxic Metabolites from Tunicates

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The didemnid tunicates have been a rich source of cytotoxic amino acid derived metabolites.[1-3] We recently investigated the didemnid tunicates *Didemnum voeltzkowi* and *Tridemnum* cf. *cyanophorum* and wish to report the isolation and structure determination of a series of biologically active C_{11} cyclopentenone metabolites **1-4**. These are the first nonnitrogenous metabolites reported from a didemnid tunicate.

The tunicates were collected in widely separated parts of the world. *Didemnum voeltzkowi* is an encrusting tunicate on coral and coralline algae found in the high tidal zone of the fringing reef at Suva Harbor, Fiji. *Tridemnum* cf. *cyanophorum* was collected on the seagrass beds off Shroud Cay, Bahama Islands. Didemnenones A (**1**) and B (**2**) were isolated (0.7% combined dry weight) from the ethyl acetate extracts of *T. cyanophorum*. The extracts were subjected to flash chromatography with iso-

(1) Ireland, C.; Scheuer, P. J. *J. Am. Chem. Soc.* **1980**, *102*, 5688-91.
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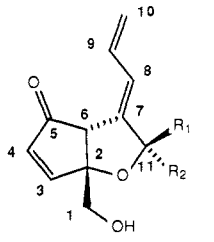
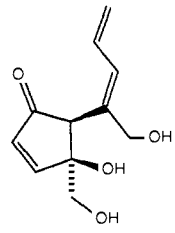
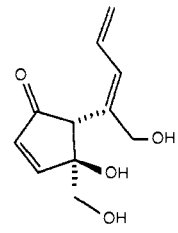


1 R_1 = H, R_2 = OH
2 R_1 = OH, R_2 = H
5 R_1 = H, R_2 = OCH_3
6 R_1 = OCH_3, R_2 = H
7 R_1, R_2 = O



3



4

octane/ethyl acetate mixtures. Compound **5**, produced along with **6** as an artifact of the chromatography,[4] was crystalline, and its relative stereostructure was established by single-crystal X-ray diffraction analysis.[5]

Compound **5** was central to the structure elucidation of compounds **1** through **4**.[6] An important observation on **5** was that irradiation of the proton at C9 (δ 6.85) gave a 13.4% NOE enhancement for the methine proton at C6 (δ 3.61). Similarly, irradiation of the olefinic proton at C8 (δ 6.30) gave a 9% NOE enhancement to the acetal proton at C11. Acetals **5** and **6** could be interconverted with hemiacetals **1** and **2** upon treatment with acid in aqueous THF. The ^{1}H NMR and ^{13}C NMR spectra[7] of didemnenones A (**1**) and B (**2**) were very similar to those for **5**. In addition to the similarity of chemical shifts and coupling constants, the same NOE enhancements could be observed. This establishes that **1** and **2** are related as epimers at C11 and not double bond isomers at C7.

Didemnenones C (**3**, 0.007% dry weight) and D (**4**, 0.006% dry weight) were isolated from the methanol extract of *D. voeltzkowi* following solvent partitioning and Sephadex LH-20 (MeOH/$CHCl_3$, 1/1) chromatography. Their ^{1}H NMR spectra were essentially identical and showed many similarities with the spectra of didemnenones A (**1**) and B (**2**).[8,9] A decisive experiment was the MnO_2 oxidation of didemnenone C (**3**) to give γ-lactone **7** (1751 cm^{-1}). Lactone **7** was also formed on MnO_2 oxidation of **1** and **2**. This oxidation established the relative stereostructure of didemnenone C (**3**). Similar oxidation of didemnenone D (**4**) gave the C11 aldehyde which did not form a γ-lactol, indicating that the C2 hydroxyl and the C6 side chain were trans. The aldehyde from **4** ultimately formed a δ-lactol in protic solvents. Most plausibly, didemnenones C (**3**) and D (**4**) were epimeric at C6 with the relative stereochemistries shown.

Surprisingly, the optical rotation of lactone **7** depended on the source organism. Lactone **7** prepared by the oxidation of didemnenone C (**3**) from *D. voeltzkowi* had a negative rotation at 589, 578, 546, 436, 365, and 302 nm. In contrast, lactone **7** from the oxidation of didemnenones A and B (**1** and **2**) from *T. cyanophorum* had a positive rotation at the same wavelengths. Thus the two different organisms produce related metabolites in enantiomeric series.

Didemnenones C and D exhibit cytotoxicity in an in vitro L1210 murine leukemia cell line with IC_{50}'s of 5.6 μg/mL. Didemnenones A and B showed antibacterial activity against a variety of microorganisms and antifungal activity against the pathogenic marine fungus *Lagenidium callinectes*.

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Registry No. **1**, 110935-52-9; **2**, 111056-70-3; **3**, 110935-53-0; **4**, 111056-71-4; **5**, 110935-54-1; **6**, 111056-72-5; **7**, 110935-55-2.

Supplementary Material Available: Tables of fractional coordinates, thermal parameters, interatomic distances, interatomic angles, perspective drawing for **5**, and chiroptical data for **7** (5 pages). Ordering information is given on any current masthead page.

(4) The crude extract was dissolved in MeOH, mixed with silica gel, and evaporated to dryness prior to chromatography.

(5) Compound **5** crystallized in the monoclinic space group $P2_1$ with a = 7.662 (1) Å, b = 7.709 (1) Å, c = 9.808 (1) Å, and β = 104.308 (13)°, and one molecule of composition $C_{12}H_{14}O_4$ forming the asymmetric unit. The structure was solved with direct methods and refined to a conventional crystallographic residual of 0.042. Additional details can be found in the paragraph entitled Supplementary Material at the end of this paper.

(6) Spectral data for **5**: HREIMS, m/z 222.0877 ($C_{12}H_{14}O_4$ requires 222.0892); UV (MeOH) λ_{max} 236 (ϵ = 21 000); IR ($CHCl_3$) 3690, 3550, 1720, 1215, 1075, 1020 cm^{-1}; $[\alpha]_D$ = +371.8° (c 0.86 g/100 mL, $CHCl_3$); ^{13}C NMR (acetone-d_6) δ 65.3 (t, C1), 94.7 (s, C2), 163.7 (d, C3), 128.4 (d, C4), 203.5 (s, C5), 52.9 (d, C6), 138.8 (s, C7), 135.2 (d, C8), 134.4 (d, C9), 120.2 (t, C10), 108.6 (d, C11), 54.2 (q, C12); ^{1}H NMR ($CDCl_3$) δ 3.90 (dd, 11.0, 3.0, C1), 3.71 (dd, 11.0, 7.0, C1), 7.57 (d, 5.5, C3), 6.17 (d, 5.5, C4), 3.61 (d, 2.0, C6), 6.30 (dd, 10.5, 2.0, C8), 6.85 (ddd, 17.0, 10.5, 10.5, C9), 5.39 (d, 17.0, C10), 5.36 (d, 10.5, C10), 5.33 (s, C11), 3.34 (s, C12, 3H), 2.03 (dd, 7.0, 3.0, exch.).

(7) All attempts to separate didemnenones A (**1**) and B (**2**) were unsuccessful. The spectral data for the approximately 1:1 mixture are the following: HREIMS, m/z 208.0747 ($C_{11}H_{12}O_4$ requires 208.0736), 190.0616, 177.0549; UV (CH_3CN) λ_{max} 238 (ϵ = 13 000), irreversibly base shifted to 243 nm; IR (Nujol) 3100–3500, 1710, 1272, 1255, 1203, 1083, 1045, 1005, 995 cm^{-1}; $[\alpha]_D$ = +576.1° (c 0.49 g/100 mL, DMSO); ^{13}C NMR (MeOH-d_4), δ 203.5 (s), 203.1 (s), 164.5 (d), 163.1 (d), 139.8 (s), 139.0 (s), 134.3 (d), 134.1 (d), 133.8 (d), 132.8 (d), 126.5 (d), 126.1 (d), 119.8 (t), 119.6 (t), 100.7 (d), 98.6 (d), 92.9 (s), 89.3 (s), 63.9 (t, 2C), 52.5 (d), 52.4 (d); ^{1}H NMR (MeOH-d_4) δ 7.62 (d, 5.5, 1 H), 7.55 (d, 5.5, 1 H), 6.90 (ddd, 17.0, 10.8, 9.8, 2 H), 6.28 (br d, 10.8 2 H), 6.21 (d, 5.5, 1H), 6.12 (d, 5.5, 1 H), 5.73 (s, 1 H), 5.51 (br s, 1 H), 5.35 (d, 17.0, 2 H), 5.28 (d, 9.8, 2 H), 3.81–3.62 (m, 6 H).

(8) Spectral data for **3**: HREIMS obsd 210.0893, calcd for $C_{11}H_{14}O_4$ 210.0888; UV (MeOH) λ_{max} 231 nm (ϵ 16 000); $[\alpha]_D$ −25.3° (c 0.08 g/100 mL, MeOH); IR ($CHCl_3$) 3600–3000, 1704 cm^{-1}; ^{1}H NMR (MeOH-d_4) δ 3.59 (d, 10.5, 1 H), 3.69 (d, 10.5, 1 H), 3.88 (s, 1 H), 3.96 (d, 12.6, 1 H), 4.24 (d, 12.6, 1 H), 5.21 (d, 10.6, 1 H), 5.31 (d, 16.5, 1 H), 6.25 (d, 6, 1 H), 6.38 (d, 11.2, 1 H), 6.65 (ddd, 10.6, 11.2, 16.5, 1 H), 7.51 (d, 6, 1 H); ^{13}C NMR (MeOH-d_4) δ 53.0 (d), 65.3 (t), 66.6 (t), 82.2 (s), 119.8 (t), 133.5 (d), 133.7 (d), 135.0 (d), 136.1 (s), 166.4 (d), 210.0 (s).

(9) Spectral data for **4**: HREIMS m/z obsd 210.090, calcd for $C_{11}H_{14}O_4$, 210.0888; UV (MeOH) 231 nm (ϵ 20 000); $[\alpha]_D$ −12.6° (c 0.15 g/100 mL, MeOH); IR ($CHCl_3$) 3600–3200, 1708 cm^{-1}; ^{1}H NMR (MeOH-d_4) δ 7.58 (d, 6, 1 H), 6.41 (m, 10, 11, 16.4, 1 H), 6.26 (d, 11, 1 H), 6.15 (d, 6, 1 H), 5.27 (d, 16.4, 1 H), 5.16 (d, 10, 1 H), 4.20 (d, 13.8, 1 H), 4.05 (d, 13.8, 1 H), 3.31 (s, overlapped signals, 3 H); ^{13}C NMR (MeOH-d_4) δ 208.6, 165.7, 136.7, 134.5, 134.3, 132.6, 119.5, 83.7, 65.8, 65.3, 58.7.

X-ray Absorption Study of Octafluorodirhenate(III): EXAFS Structures and Resonance Raman Spectroscopy of Octahalodirhenates

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The structure, bonding, spectroscopy, and photophysics of transition-metal complexes containing quadruple metal–metal bonds are subjects of intense and general interest.[1,2] For both historic and fundamental reasons, the octahalodirhenate(III) ions have become the paradigms of this field.[1] Extensive spectroscopic and photophysical studies exist for the entire $Re_2X_8^{2-}$ series (X = F, Cl, Br, and I).[1-11] However, while excellent structural data

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