that the catalytic activity of the subtilisins in transesterification 1 (and probably other reactions in organic solvents) strongly depended on the water content of the lyophilized enzymes. Hence, in order to keep the water content of different subtilisin preparations constant, the lyophilized samples of the subtilisins were placed in a desiccator containing a vessel with the saturated aqueous solution of LiCl. The desiccator was evacuated and stored at 7 °C for at least 48 h before the enzymes were used. Under these conditions the enzymes, exposed to a constant humidity of 11%,[29] exhibit reproducible activities in organic solvents over the period of at least 7 days. Porcine pancreatic lipase (specific activity of 11 triacetin units/mg of solid) was used as a catalyst in organic solvents directly without any pretreatment.[30]

Chemicals and Solvents. All the alcohols used in this study, including the individual enantiomers of chiral alcohols, were obtained from commercial suppliers [except for the *R* and *S* enantiomers of *sec*-(2-naphthyl)ethyl alcohol, which were obtained by the enzymatic resolution of the racemate[8]] and were of analytical grade or purer. Vinyl butyrate (99%+ pure by gas chromatography) was purchased from American Tokyo Kasei Co. Butyryl esters of chiral alcohols, used as standards in gas chromatographic analyses, were synthesized according to the classical methodology.[31] Organic solvents employed in this work were either purchased in the anhydrous form (in Aldrich Sure/Seal bottles, water content below 0.005%) or dehydrated by shaking with 3-Å molecular sieves (Linde)[10] to bring the water content[32] below 0.01%. Triethylamine was purified by using the literature procedure.[33]

Kinetic Measurements. In a typical experiment, a powdered enzyme sample (prepared as described above) was placed in a 7-mL screw-cap scintillation vial, followed by an addition of 1 mL of a solvent containing vinyl butyrate and an alcohol. Then the vial was closed, subjected to a 5-s sonication (to homogenize the suspension), placed in a controlled-temperature shaker, and shaken at 45 °C and 300 rpm. Periodically, 0.5-μL aliquots were withdrawn and assayed by gas chromatography (10-m HP-5 capillary column coated with 5% phenyl-/95% methylsilicone gum). The reaction rates were determined on the basis of the increase in the concentration of the product butyryl esters (e.g., reaction 1) as a function of time (five to seven data points were usually collected).

Kinetic Calculations. The values of V/K_M (where K_M stands for the Michaelis constant for the alcohol in the enzymatic transesterification) were determined on the basis of the dependencies of the initial rates of the enzymatic reactions on the alcohol concentrations (typically, seven data points were obtained). Nonlinear regression analysis using the software program, Enzfitter, written by R. J. Leatherbarrow and distributed by Elsevier-Biosoft, was employed in all calculations. The enzyme molarity (needed to convert V/K_M into k_{cat}/K_M) was determined from the molecular weight and weight concentrations (mg/mL) of subtilisin Carlsberg used in transesterifications and the following correction factors:[10] the aforementioned 54% purity of the enzyme, the fact that only 68% of all subtilisin molecules are catalytically competent in organic solvents, and the presence of 40% (w/w) of potassium phosphate salts in the lyophilized enzyme samples. Note that any inaccuracies arising from these calculations would affect $(k_{cat}/K_M)_S$ and $(k_{cat}/K_M)_R$ to the same extent and thus would be inconsequential for our conclusions.

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Communications to the Editor

Electronic Structure of *trans*-Dioxorhenium(VI)

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Complexes containing d^2 *trans*-dioxometal units exhibit rich electrochemistry[1-3] and photochemistry.[2,4-6] By employing strongly basic ancillary ligands, we have succeeded in isolating the first d^1 *trans*-dioxo complex, *trans*-$[ReO_2(dmap)_4](PF_6)_2$ [dmap = 4-(dimethylamino)pyridine].[6] Analysis of the structure of the complex cation shows that there is considerable shortening (0.04 Å) in the Re–N bond lengths relative to Re(V) analogues,[6,7] but the Re–oxo bond lengths are virtually the same in both oxidation states (Figure 1A).[8] The structural data confirm that an electron is removed from the d_{xy} orbital upon oxidation of Re(V), as predicted by the standard ligand field (LF) model for axially compressed metal–oxo systems (Figure 1B).[9-11] In order to examine the electronic structure of the *trans*-dioxo framework more closely, we have measured and analyzed the EPR spectrum of *trans*-$[ReO_2(dmap)_4](PF_6)_2$.

The EPR spectra of d^1 Re(VI) species often are hard to interpret because of the extremely large Re hyperfine and quadrupole coupling constants associated with tetragonal geometries of this ion.[12-15] As a result, the spectra exhibit (1) variations in band

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(8) *trans*-$[ReO_2(dmap)_4](PF_6)_2$ was prepared as previously described.[6] Crystal data: $ReC_{28}H_{40}N_8O_2P_2F_{12}$, M = 996.813, triclinic, space group $P\bar{1}$, a = 8.307 (3) Å, b = 10.911 (5) Å, c = 11.907 (11) Å, α = 96.24 (6)°, β = 108.28 (6)°, γ = 99.42 (6)°, V = 996.1 (11) Å^3, Z = 1, d_{calcd} = 1.662 g/cm^3. Data collection parameters and a summary of the crystal structure analysis are provided in the supplementary material. Refinement of atomic positional and thermal parameters converged at R = 0.0385 over 3482 reflections with $I > 3.0\sigma(I)$.
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Table I. EPR Data for Axially Symmetric Re(VI) Complexes

compound	$g_\perp$	$A_\perp$, cm^{-1}	$g_\parallel$	$A_\parallel$, cm^{-1}	$\|Q\|$, cm^{-1}	ref
$[ReO_2(dmap)_4][PF_6]_2$[a]	1.91	−0.031	1.83	−0.060	0.0075	this work
$[Ph_4As][ReNCl_4]$[b]	1.947	−0.0391	1.918	−0.077	0.0047	12
$ReOCl_4$[c]	1.720	−0.0320	1.968	−0.0630	0.0020	14
$ReOCl_4(NCCH_3)$[d]	1.732	−0.0315	1.970	−0.0621	0.0020	14
$ReOCl_4(OPCl_3)$[e]	1.734	−0.0308	1.97	−0.0616	0.0019	14
$[Ph_4As][ReOCl_5]$[c]	1.740	−0.0305	1.975	−0.0609	0.0020	14
$[H_3O][ReOF_5]$[f]	1.74	−0.0500	1.72	−0.0960	0.0045	13

[a] Frozen 50% aqueous DMSO, 7 K. [b] Single crystal, 110 K. [c] Frozen dioxane, 77 K. [d] Frozen CH_3NO_2, 77 K. [e] Frozen $OPCl_3$, 77 K. [f] Frozen anhydrous HF, 77 K.

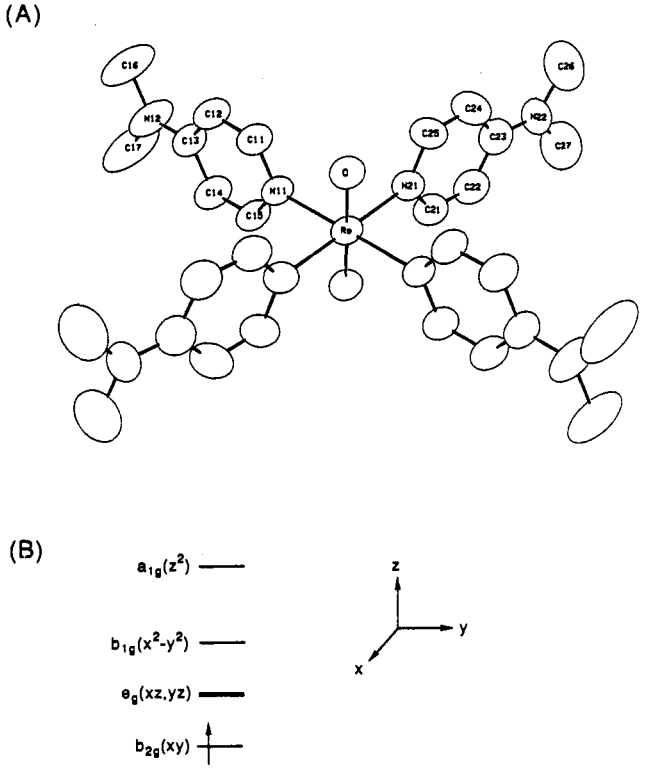

Figure 1. (A) ORTEP diagram of *trans*-$[ReO_2(dmap)_4]^{2+}$ with thermal ellipsoids drawn at the 50% probability level showing the atom numbering scheme. Selected bond distances (Å) and angles (deg): Re–O 1.764 (4), Re–N11 2.108 (4), Re–N21 2.120 (5), O–Re–N11 90.0 (2), O–Re–N21 90.0 (2), N11–Re–N21 91.9 (2). (B) LF diagram for *trans*-$[ReO_2(dmap)_4]^{2+}$.

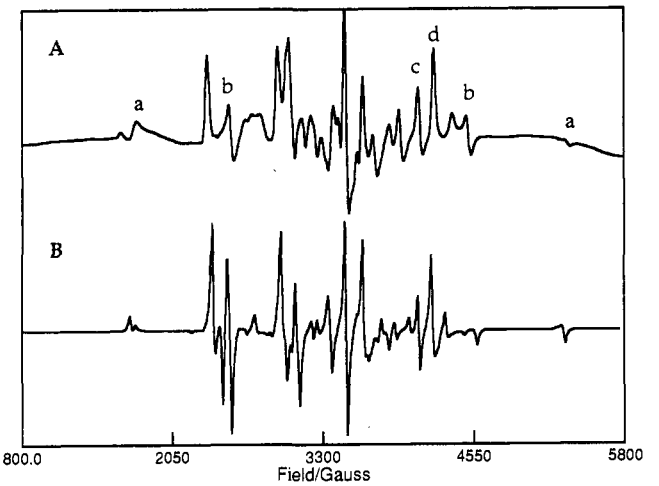

Figure 2. (A) EPR spectrum at 7 K of *trans*-$[ReO_2(dmap)_4](PF_6)_2$ (~10 μM) in 50% DMSO. Microwave frequency: 9.0505 GHz. Modulation frequency: 100 kHz. Modulation amplitude: 10 G. Microwave power: 0.05 mW. (a) Outermost peaks in the parallel manifold. (b) Outermost peaks in the perpendicular manifold. (c) $\Delta M_I = \pm 1$ transition. (d) $\Delta M_I = \sim\pm 2$ transition. (B) Simulated spectrum using $g_\perp = 1.91$, $A_\perp = 0.031$ cm^{-1}, $g_\parallel = 1.83$, $A_\parallel = 0.060$ cm^{-1}, and $Q' = 0.0075$ cm^{-1}.

intensities for $\Delta M_I = 0$ transitions, (2) unequal rhenium hyperfine spacing, (3) the presence of forbidden features due to $\Delta M_I = \pm 1$, ± 2 transitions, and (4) intense features at off-axis turning points.[12] Our analysis of the spectrum of *trans*-$[ReO_2(dmap)_4]^{2+}$ deals with all four of these complexities.

No signal could be detected for *trans*-$[ReO_2(dmap)_4](PF_6)_2$ in CH_3CN, methanol, or acetone solutions.[16] The EPR of a solid (powder) sample gave a single line with $\langle g \rangle \sim 1.91$. In an attempt to obtain a better spectrum, a dilute (~10 μM) 50% aqueous DMSO solution was examined at 7 K (Figure 2A). The large $A_\parallel$ is apparent from the two outermost transitions of the parallel manifold (labeled a). The $A_\perp$ is somewhat smaller; the outermost transitions of the perpendicular manifold are labeled b. The number of lines is greater than the six parallel and six perpendicular features expected for an axially symmetric system with $I = {}^5/_2$. The extra features arise from $\Delta M_I = \pm 1$ (e.g., peak c) and $\Delta M_I = \pm 2$ (e.g., peak d) transitions and their off-axis turning points.[12-15] The strength of these features is indicative of a large quadrupole coupling constant, Q' ($3Q_z/2$ for an axially symmetric system), which increases the probability of forbidden transitions.[15] In some cases, the forbidden transitions are more intense than the allowed transitions.

A simulation that accounts for all of the major transitions and reproduces qualitatively the intensity pattern in the EPR spectrum of *trans*-$[ReO_2(dmap)_4]^{2+}$ is shown in Figure 2B.[17] The spin Hamiltonian parameters are compared with those of related Re(VI) complexes in Table I. The order $g_\parallel < g_\perp < 2.0023$ accords with the LF splitting diagram of Figure 1B.[18,19]

In axially symmetric systems where the unpaired electron is coupled to a nucleus with a high quadrupole moment such as Re

(16) Solvents were reagent grade and Millipore water was used. EPR spectra were recorded on a home-built EPR spectrometer equipped with an Oxford Instruments ESR-900 liquid helium cryostat. This instrument has been described in detail elsewhere: Beck, W. F.; Innes, J. B.; Lynch, J. B.; Brudvig, G. W. *J. Magn. Reson.* **1991**, *91*, 12.

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(18) Expressions for $g_\parallel$ and $g_\perp$ of D_{4h} *trans*-$[ReO_2(L)_4]^{2+}$ are as follows:[4,9] $g_\perp = 2[1 - (c_1^*)^2\xi/\Delta E(^2B_{2g} \rightarrow {}^2E_g)]$ and $g_\parallel = 2[1 - (c_1^*)^2 4\xi/\Delta E(^2B_{2g} \rightarrow {}^2B_{1g})]$; where ξ is the spin–orbit coupling constant of the metal, ΔE is a LF energy, and c_1^* is the coefficient of the LF orbital of the excited state in question. LF energies for *trans*-$[ReO_2(dmap)_4]^{2+}$ are estimated to be 25 000 ($^2B_{2g} \rightarrow {}^2E_g$) and 36 000 cm^{-1} ($^2B_{2g} \rightarrow {}^2B_{1g}$).[6b] The value of ξ(Re) is estimated as follows: By plotting ξ versus the charge (z) of the free rhenium ion, a linear relationship is obtained:[6b] $\xi = [540(z) + 1000]$ cm^{-1}. If we assume that (due to charge neutralization effects) the residual charge on rhenium is 2+, then $\xi = 2080$ cm^{-1}. With these values of the LF and spin–orbit parameters, we find $c_1^*(d_{xz},d_{yz}) = 0.735$ and $c_1^*(d_{x^2-y^2}) = 0.606$, indicating appreciable covalency in both the Re–oxo and Re–N bonds. It also is likely that there is significant mixing of the b_{2g} (d_{xy}) and π (dmap) levels in $[ReO_2(dmap)_4]^{2+}$ (the lowest energy electronic transition is dmap → Re LMCT).[6]

(19) The order of g values predicted by the LF model is not observed for oxorhenium(VI) chlorides (Table I). In these cases, the order $g_\parallel > g_\perp$ is attributable to the effect of spin–orbit coupling of a $(Cl)_4$ d_{xy}-symmetry hole associated with in-plane π-bonding between the Re d_{xy} and equatorial ligand π-orbitals: Marov, I. N.; Dubrov, Y. N.; Belyaeva, V. K.; Ermakov, A. N. *Russ. J. Inorg. Chem.* **1972**, *17*, 1396.

[$Q(^{185}Re) = 2.8 \times 10^{24}/cm^2$, $Q(^{187}Re) = 2.6 \times 10^{24}/cm^2$], the magnitude of Q' reflects the concentration of charge along the z axis, which induces a large electric field gradient in the complex.[15] As evident in Table I, Q' generally increases in the order $ReO^{4+} < ReN^{3+} < ReO_2^{2+}$. In addition, estimated LF energies ($d_{xy} \rightarrow d_{xz}, d_{yz}$) increase with Q',[12-14,18] consistent with an increase in π-bonding on going from monooxo to mononitrido to *trans*-dioxo axial units. Thus the combined spectroscopic evidence emphasizes dramatically the strong axially compressed tetragonal ligand field associated with the *trans*-dioxo moiety.

Acknowledgment. This research was supported by National Science Foundation Grant CHE88-22988 (H.B.G.) and by National Institutes of Health Grants GM32715 and GM36442 (G.W.B.). EPR analysis software was furnished by the Illinois EPR Research Center, NIH Division of Research Resources, Grant No. RR01811. J.C.B. acknowledges B. P. America for a predoctoral fellowship in chemical catalysis.

Registry No. *trans*-$[ReO_2(dmap)_4]PF_6$, 131892-43-8; *trans*-$[ReO_2(dmap)_4]^{2+}$, 131892-42-7.

Supplementary Material Available: Tables of crystallographic data, bond lengths, angles, positional parameters, and thermal parameters for *trans*-$[ReO_2(dmap)_4](PF_6)_2$ and description of EPR simulation procedure (13 pages); table of observed and calculated structure factors for *trans*-$[ReO_2(dmap)_4](PF_6)_2$ (15 pages). Ordering information is given on any current masthead page.

Hennoxazoles: Bioactive Bisoxazoles from a Marine Sponge

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Oxazole-containing marine alkaloids,[1] first described in 1986 from nudibranch egg masses[2,3] and subsequently from sponges,[4-7] possess significant bioactivities including antifungal, cytotoxic, anthelmintic, and tumor-promoting properties. We now report hennoxazoles A-D (**1-4**) from a sponge, *Polyfibrospongia* sp.[8]

Table I. NMR Data for Hennoxazole A (**1**) in Acetone-d_6

C no.	δ_C	δ_H (J, Hz)	HMBC	COSY
1	23.9, q	1.23, 3 H, s		
2	99.9, s		1, 29	
3	45.7, t	1.98, 1 H, ddd (12.6, 4.6, 1.6)	1, OH	3′, 4
3′		1.22, 1 H, t (11.7)		3, 4
4	64.1, d	3.89, 1 H, m	OH	3,3′, 5,5′, OH
5	41.4, t	1.89, 1 H, dtd (12.4, 4.5, 2.3)	7, OH	4, 5′
5′		1.11, 1 H, q (11.6)		4, 5, 6
6	66.3, d	3.51, 1 H, m	7, 8	5′, 7
7	41.2, t	2.06, 2 H, m	8	6, 8
8	73.1, d	4.45, 1 H, dd (7.7, 6.5)	7, 28	7
9	156.1, s		7, 8	
10	137.5, d	7.96, 1 H, s	8	
11	142.1, s		10	
12	131.2, s			
13	139.4, d	8.38, 1 H, s		
14	165.9, s		13, 15, 16	
15	28.4, t	2.88, 2 H, t (7.5)	16, 17	16
16	30.2, t	2.49, 2 H, q (6.9)	15, 17, 18	15, 17
17	129.5, d	5.50, 1 H, dt (15.3, 6.2)	16, 18	16, 18
18	129.9, d	5.44, 1 H, dt (15.3, 6.1)	16, 17	17, 19
19	35.6, t	2.67, 2 H, m	17, 18, 21, 27	18
20	132.5, s		27	
21	130.8, d	4.94, 1 H, d (9.3)	26, 27	22, 27
22	35.7, d	3.01, 1 H, m	24, 26	21, 23
23	136.8, d	5.32, 1 H, m	25, 26	22, 25
24	122.7, d	5.32, 1 H, m	25	25
25	17.9, q	1.58, 3 H, br s	23	23, 24
26	21.6, q	0.94, 3 H, d (6.9)		
27	23.3, q	1.58, 3 H, br s		21
28	56.1, q	3.21, 3 H, s	8	
29	47.7, q	3.01, 3 H, s	2	
OH		3.74, 1 H, d (4.8)		4

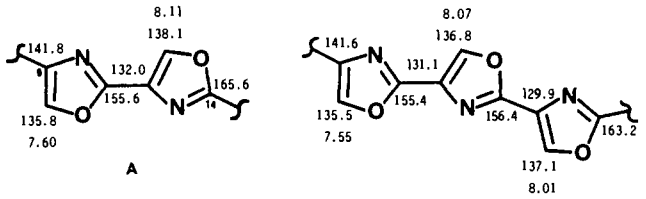
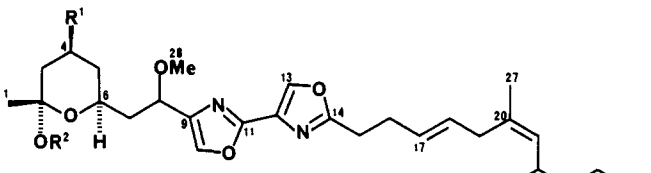


Figure 1. Comparison of NMR data ($CDCl_3$) for partial structure A and the trisoxazole moiety of kabiramide A.

Hennoxazole A (**1**) is active against herpes simplex virus type 1 (IC_{50} 0.6 μg/mL) and displays peripheral analgesic activity comparable with that of indomethacin, when assayed in the phenylquinone-induced writhing assay in mice.[9]



	R^1	R^2
1	OH	$^{29}CH_3$
2	OH	$^{29}CH_2{}^{30}CH_3$
3	OH	$^{29}CH_2CH_2CH_2{}^{32}CH_3$
4	H	$^{29}CH_3$

Polyfibrospongia sp. (4.5 kg) collected by scuba divers was extracted by steeping in acetone. After concentration, the resulting aqueous suspension was extracted with chloroform, yielding an oil (20 g), which was separated by vacuum flash chromatography on silica gel with a stepwise gradient of hexane/ethyl acetate/methanol. A fraction eluting with ethyl acetate was chromato-

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(8) The sponge classified tentatively as a species of the genus *Polyfibrospongia* (family Thorectidae, order Dictyoceratida) is bowl-shaped with a diameter of 10-20 cm and many processes on the surface. It was found sporadically on rock walls at a depth of 20-35 m, where underwater currents are fairly strong. The names of the compounds are derived from the collection site, Agari*hen*nazaki on the island of Miyako, Okinawa, Japan.
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