Table I. ^{1}H NMR Data[a] of Selected Dihydrogen Complexes $[Os^{II}(NH_3)_4(H_2)L]^{2+/1+}$

L	AN	Py	Im	I^-	Cl^-	D_2O	$(CD_3)_2CO$	Br^-
$\delta(H_2)$, ppm	−7.80[c]	−7.44	−7.43	−11.60	−10.78[c]	−11.35	−11.37[b,c]	−11.29
J_{HD}, Hz	20.3	19.6	17.1	12.5	10.2	8.1	4.0	<2.5
T_1, ms (20 °C)	221	148	131	142	1026	346	572	963
T_1, ms (low temperature)	62[d]	38 (min)	63 (min)	129[d]	125[d]	77 (min)	74[d]	107[d]

[a] In $(CD_3)_2CO$ as solvent, at 400 MHz; complexes at ca. 0.010 M level. [b] Identical values of parameters for PF_6^- and $B(C_6H_5)_4^-$ salts. [c] No new peaks at −95 °C or above. [d] No minimum observed at −95 °C or above.

Figure 1. Trans-to-cis isomerization.

used as precipitant. Elemental analysis shows the composition of the solid to correspond to $[Os(en)_2H_2Cl]B(C_6H_5)_4$.[6] The solid was dissolved in acetone and treated with $TlPF_6$ to extract Cl^-. After filtration, ether was added to the solution; the solid was collected, washed with ether, dried, and redissolved in $(CD_3)_2CO$, and the ^{1}H NMR spectrum was recorded. The proton signals for dihydrogen and for en prove to be different from those for the chloro complex.[7] In addition, a peak is observed at $\delta = 2.39$ ppm (3.7 H atoms counted at the first measurement), which disappears ($t_{1/2} \sim 10$ min) without attendant alterations in the other peaks. We ascribe this behavior to the replacement of coordinated $(CH_3)_2CO$ by $(CD_3)_2CO$.

We conclude that in solution each of the 16e$^-$ species $[Os(NH_3)_4H_2]^{2+}$ and $[Os(en)_2H_2]^{2+}$ adopts an additional ligand and that the nitrogen ligands are coplanar in both cases. In contrast to NH_3, the amine moieties in $[Os(en)_2H_2]^{2+}$ are not free to rotate, and thus they respond to the different environments provided by the groups on the opposite faces of the molecular plane. X-ray crystallographic study of three compounds[8] confirmed the trans, octahedral stereochemistry (H_2 being counted as one ligand). All π-acid ligands which we have introduced lead to values of J_{HD} in the high range, suggesting that such ligands cause the hydrogen atoms to draw together. The addition of a very strong π-acid such as $C_6H_5CH_2NC$ leads to the immediate release of H_2. The product is a *trans*-$[Os(en)_2]^{2+}$ complex, which shows ^{1}H NMR signals only for en. Presumably the axial positions are occupied by $(CD_3)_2CO$.

In every one of at least 10 different systems, where the complexes in acetone are kept at room temperature for many hours, the ^{1}H NMR signals change.[9] For ammonia, the 12 protons appear in the ratio 2:1:1, the pattern expected for cis configurations (see Figure 1). For the bis(ethylenediamine) complexes in the cis configuration, a plane of symmetry is lacking even when the addend is a symmetrical ligand such as Cl^-, and for the eight amine as well as the eight methylene protons, four to eight peaks appear, the number depending on the symmetry of the addend. In all cases but one, conversion to the cis forms is more than 98% complete at equilibrium. The sole exception is $[Os(NH_3)_4(H_2)(CH_3CN)]^{2+}$, where the conversion is only 90% complete.

The facile addition of both saturated and unsaturated ligands to the 16e$^-$ moieties dealt with above provides a unique opportunity for a systematic study of the variation of the chemical and physical properties of η^2 complexes with composition and, trans and cis forms being available, also with geometry. Moreover, the use of the moieties as recognition probes, particularly for biological molecules, also suggests itself. Studies along both lines are in progress.

Acknowledgment. Support of this work by National Institutes of Health Grant GM13638-25 is gratefully acknowledged.

(6) Microanal. Calcd for $[Os(en)_2(H_2)Cl]B(C_6H_5)_4$: C, 50.43; H, 5.69; N, 8.39; Cl, 5.32. Found: C, 50.18; H, 5.46; N, 8.22; Cl, 5.81. (en = $H_2NCH_2CH_2NH_2$). ^{1}H NMR (ppm, in $(CD_3)_2CO$): 5.31 (s, br, 4 H, NH_2), 4.03 (s, br, 4 H, NH_2), 2.67 (m, 4 H, $-CH_2-$), 2.11 (m, 4 H, $-CH_2-$), −12.57 (s, 2 H, OsH_2). $^1J_{HD} = 7.2$ Hz. T_1 (20 °C, 400 MHz) = 254 ms. T_1(min) = 61 ms (400 MHz).

(7) ^{1}H NMR in $(CD_3)_2CO$: 5.75 (s, br, 4 H, NH_2), 4.34 (s, br, 4 H, NH_2), 2.76 (m, 4 H, $-CH_2-$), 2.34 (m, 4 H, $-CH_2-$), 2.39 (s, 3.7 H, $(CH_3)_2CO$), −13.19 (s, 2 H, OsH_2). T_1 (20 °C, 400 MHz) = 145 ms. T_1(min) = 57 ms (400 MHz).

(8) X-ray crystal structure determinations on $[Os(en)_2(\eta^2\text{-}H_2)Cl]Cl$, $[Os(en)_2(\eta^2\text{-}H_2)Br]Br$, and $[Os(en)_2(\eta^2\text{-}H_2)py](PF_6)_2\cdot CH_3OH$ by T. Hasegawa of this laboratory and H. Hope of the University of California, Davis, confirm the trans geometry in these cases. Though data were taken at low temperature, they are not refined enough to place the atoms of dihydrogen. Arrangements have been made with T. F. Koetzle of the Brookhaven National Laboratory for structure determination by neutron diffraction.

(9) For example, on leaving **2** in $(CD_3)_2CO$ for 4 days, the original ^{1}H NMR peaks disappear and are replaced by a set of new peaks, which we assign as *cis*-$[Os(NH_3)_4(H_2)Py][B(C_6H_5)_4]_2$: 8.74 (d, 2 H, Py), 7.70 (t, 1 H, Py), 7.24 (t, 2 H, Py), 7.40–6.70 (m, 40 H, C_6H_5), 4.51 (s, br, 3 H, NH_3), 4.23 (s, br, 6 H, 2 NH_3), 3.58 (s, br, 3 H, NH_3), −7.32 (s, 2 H, OsH_2). $^1J_{HD}$ = 20.2 Hz; T_1 (20 °C, 400 MHz) = 104 ms, T_1(min) = 28 ms (400 MHz).

The Structures of Quartromicins A_1, A_2, and A_3: Novel Macrocyclic Antiviral Antibiotics Possessing Four Tetronic Acid Moieties

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In the course of a search for new antibiotics, novel antiviral antibiotics have been isolated from *Amycolatopsis orientalis* No. Q427-8. Non-ionic resin extraction of the fermentation broth (9.8 L) followed by chromatographic purification resulted in isolation of three active components, quartromicins A_1 (**1**; 57 mg), A_2 (**2**; 87 mg), and A_3 (**3**; 70 mg),[1] which contain a unique macrocarbocyclic ring possessing four tetronic acid moieties.

Quartromicin A_1 (**1**) [$C_{78}H_{88}O_{30}$, negative FABMS m/z 1525 $(M - 2 + Na)^-$, 1541 $(M - 2 + K)^-$] and quartromicin A_3 (**3**) [$C_{78}H_{92}O_{30}$, m/z 1545 $(M - 2 + K)^-$] were isolated as colorless amorphous salts.[2] The ^{13}C NMR spectra of **1** and **3** exhibit 39 well-defined carbon signals, and therefore, both antibiotics must possess symmetrical dimeric structures.

The ^{1}H and ^{13}C NMR spectra[3] of **1**, **2**, and **3** suggest the presence of a sugar, which was identified as D-galactose after isolation from the acid hydrolysis (MeOH/HCl) products. Although the aglycons, degalactosylquartromicins A_1–A_3,[4] were isolated, the yield was rather poor (ca. 50%) and the aglycons were poorly soluble in NMR solvents. Because **3** could be purified most easily, structure determination was performed largely on the salt of **3**. (Structure elucidation will be interpreted on the monomeric fragments hereafter.)

Routine 2D NMR[3] analyses led to partial structures **4** and **5**, which accounted for 33 of 39 carbons in the monomeric fragment of **3**, but the following spectral properties, which were assigned

(1) Tsunakawa, M.; Tenmyo, O.; Tomita, K.; Naruse, N.; Kotake, C.; Miyaki, T.; Konishi, M.; Oki, T. *J. Antibiot.*, submitted for publication.

(2) The metal composition of the salt (mol %) of **3** was analyzed as follows: Na, 70%: K, 19%: Ca, 10%: Mg, 1%.

(3) The 1D and 2D NMR spectra are available as supplementary material.

(4) Degalactosyl-**1**: $C_{66}H_{68}O_{20}$, negative FABMS m/z 1201 $(M - 2 + Na)^-$, 1217 $(M - 2 + K)^-$.

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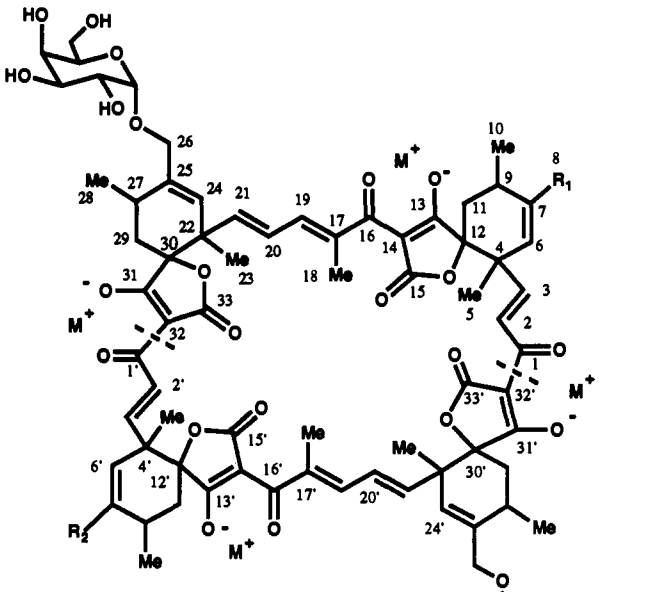


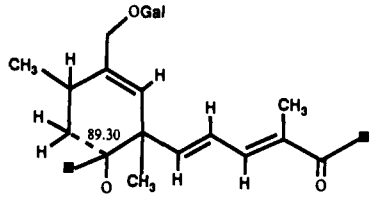
1; R_1 = R_2 = CHO

2; R_1 = CH_2OH, R_2 = CHO

3; R_1 = R_2 = CH_2OH

M = Na^+, K^+, Ca^{++}

to the remaining six carbons, were quite puzzling: (1) The IR spectrum of **3** exhibits intense and broad bands at 1620 and 1450 cm^{-1}, which are reminiscent of a carboxylate group. The bands, however, show no change on acidification (1 N HCl). (2) The ^{13}C NMR signals of the six unassigned carbons appeared to be composed of two sets of carbonyl and olefin groups (δ 201.29/201.17; 179.68/178.51; 101.73/99.95), which indicates the existence of two similar functional groups. Most of these carbons, however, exhibit no correlation peaks to any protons in the COLOC[5] or LSPD[6] spectra. (3) The UV maximum at 300 nm (ϵ 50 000) [another at 236 nm (ϵ 57 000); neither of which changes on addition of 1 N NaOH solution] cannot be interpreted as being due to the chromophores which are present in the partial structures **4** and **5**.



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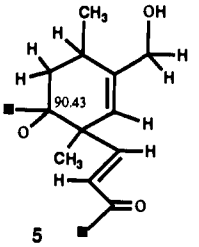

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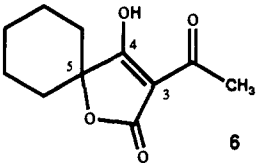
Chemical reactions a–c were carried out to uncover the structure of the hidden atoms. (a) Sodium borohydride reduction of **3** gave the product [C(1)=O and C(16)=O are reduced], which exhibits a UV maximum at 258 nm. (b) Hydrogenated product (Pd/C, 48 h) [C(2)=C, C(17)=C, and C(20)=C are saturated, but C(6)=C and C(24)=C were left intact, possibly owing to steric hindrance] shows absorption maxima at 233 and 267 nm and strong IR bands at 1620 and 1460 cm^{-1}. (c) On further treatment of the hydrogenation product with sodium borohydride, the UV maximum shifted to 258 nm.

The UV properties of the hydride reduction products are reminiscent of tetronate moieties (λ_{max} ca. 260 nm).[7] Therefore, the original chromophore was a 3-acyltetronate group in which only the acyl group is reduced by the hydride reducing agent, and the tetronate subunit is intact. The UV maxima of the hydrogenation product (b) resemble those of a sodium 3-acetyltetronate (λ_{max} 231, 256 nm).[8] The ^{13}C NMR signals of the aforementioned six carbons suggested the presence of two tetronate moieties. The chemical shifts (δ 90.43/89.30) of the two quaternary carbons can be assigned to sp^3 carbons linked by an oxygen atom [C(12), C(30)]. Therefore, structure **3** was deduced for quartromicin A_3. The IR spectrum of the sodium salt of synthetic **6**[9] exhibits intense bands at 1630 and 1450 cm^{-1}. Its ^{13}C NMR signals[10] are in good agreement with the corresponding signals of **3**.



6

The structures of quartromicins A_1 (**1**) and A_2 (**2**) have been determined by analogous spectroscopic analyses and chemical correlation with **3**.[11]

There are very few macrocyclic antibiotics whose carbon frameworks are composed of only C–C linkages.[12] Quartromicins A_1–A_3 are the largest members of this category.

Quartromicins A_1–A_3 exhibit good in vitro antiviral activity against herpes simplex virus type 1 infected on Vero cells with ID_{50} values around 10 μg/mL by the cytopathic effect reduction assay.

Supplementary Material Available: Listings of ^1H and ^{13}C NMR data for the aglycon and galactose parts of **3** (2 pages). Ordering information is given on any current masthead page.

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(10) ^{13}C NMR (CD_3OD): δ 204.29, 199.32, 180.39, 99.24, 88.25, 36.16, 31.22, 28.59, 25.54.
(11) When treated with $NaBH_4$ for a few minutes, **1** was rapidly converted to **3**. Similarly **2** was smoothly reduced to **3**.
(12) For example, see: Mallams, A. K.; Puar, M. S.; Rossman, R. R.; McPhail, A. T.; MacFarlane, R. D.; Stephen, R. L. *J. Chem. Soc., Perkin Trans. 1* **1983**, 1497. Kobinata, K.; Uramoto, M.; Mizuno, T.; Isono, K. *J. Antibiot.* **1980**, *33*, 244.

Binding of Thallium(I) to a [3Fe-4S] Cluster: Evidence for Rapid and Reversible Formation of $[Tl3Fe\text{-}4S]^{2+}$ and $[Tl3Fe\text{-}4S]^{1+}$ Centers in a Ferredoxin

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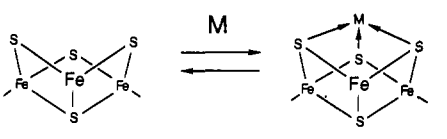
A number of proteins contain [3Fe-4S] centers that bind certain metal ions reversibly to form cubane-like clusters of the type [M3Fe-4S].[1-7]



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