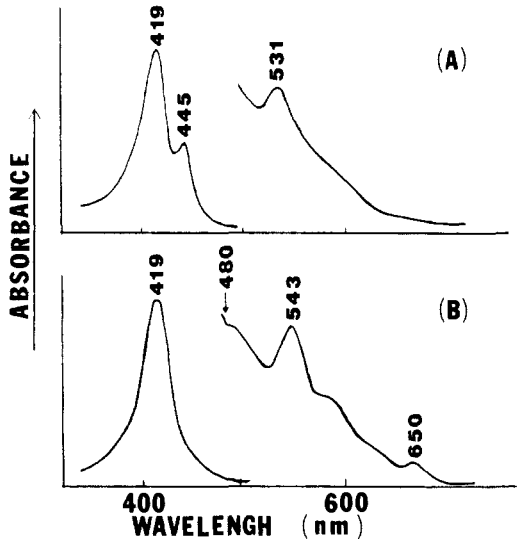

Figure 2. Electronic spectra of (A) Fe(TMP) in toluene at ~ -78 °C and (B) Fe(TMP) + O_2 in toluene at ~ -78 °C.

into (TMP)FeO and (TMP)FeOH, the latter being the final product at room temperature. (This process which is different from the general scheme shown earlier occurs only for Fe(TMP).)[8] In fact, we observed that the ν(FeO) of (TMP)FeO appears at 845 cm^{-1} in toluene when the solution was warmed from ~ -78 to ~ -46 °C.

(3) These bands cannot be assigned to the ν_s(Fe-O) of the μ-oxo dimer (E) since such a vibration should appear near 360 cm^{-1}.[16]

(4) Figure 2 (parts A and B) show the electronic spectra of Fe(TMP) and Fe(TMP) + O_2, respectively, in toluene at ~ -78 °C. These spectra are very similar to those of Fe(TmTP) and Fe(TmTP) + O_2, respectively, obtained under similar experimental conditions (TmTP: tetra-*m*-tolylporphyrinato anion).[2,6] The three λ_{max} values shown in Figure 2B (650, 543, and 480 nm) are close to those of the Fe(TmTP) + O_2 system (630, 540, and 480 nm) which were previously attributed to the Fe-O-O-Fe bridged species.[2] These electronic spectra provide further support to our band assignments.

In the centrosymmetric (TMP)Fe-O-O-Fe(TMP), the antisymmetric Fe-O stretch, ν_{as}(Fe-O), is only IR-active, and its frequency is expected to be much lower than ν_s(Fe-O). For example, the ν_{as}(Co-O) (547 cm^{-1}) of the peroxo-bridged amine complex mentioned above is 95 cm^{-1} lower than the ν_s(Co-O) (642 cm^{-1}).[15] Although its $\nu(O_2^{2-})$ is Raman-active and should appear in the peroxo[2,6-8] region (900-700 cm^{-1}), it was not possible to resonance-enhance this mode with our laser lines (406-676 nm), as are the cases of many other oxyiron porphyrins.[17] It should also be noted that the ν_s(Fe-O) of the bridged species mentioned above can be observed only by excitation in the 406-415-nm region.[12] Thus, this mode must be in resonance with the Soret π-π^*, Fe-O-O-Fe CT transition or a combination of both near 410 nm.

Finally, our RR studies show that (1) (TMP)Fe-O-O-Fe-(TMP) is stable indefinitely in toluene at ~ -78 °C, (2) the step A → C is not reversible, and (3) the ν_s(Fe-O) of the bridged species is observed at ~576 cm^{-1} for analogous TPP and OEP complexes (OEP: octaethylporphyrinato anion).[12]

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Characterization of a Crystalline Synthetic Analogue of Copper(II)-Bleomycin

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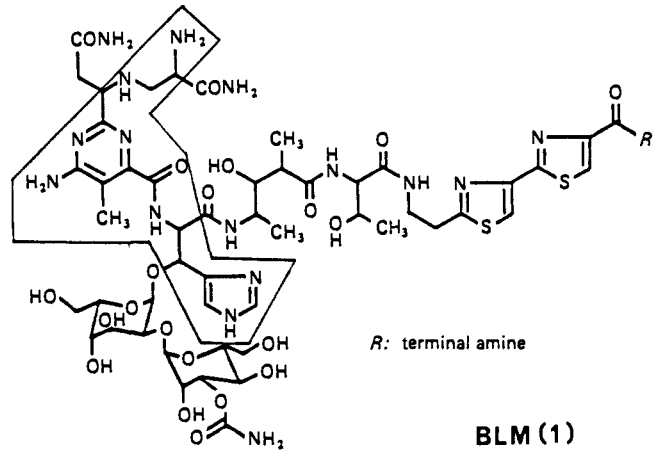
Bleomycins (BLM 1), a family of glycopeptide antitumor drug cause DNA strand cleavage in the presence of metal ions like Fe^{2+} and molecular oxygen. The requirement of a metal ion for the drug action has prompted research in coordination chemistry of BLM and the interaction of metallobleomycins (M-BLMs) with DNA.[1] The coordination structures of various M-BLMs have



BLM (1)

been predicted primarily on the basis of spectroscopic data. The only exception is Cu(II)-BLM in which the assignment of the donor centers around Cu(II) relies on the preliminary crystal structure of a Cu(II) complex of P-3A, a biosynthetic intermediate of BLM.[2,3] Studies on the synthetic analogues of M-BLMs[4,5] reported so far are all restricted to measurements in solutions. In absence of crystallographic studies, precise structure-reactivity correlations with M-BLMs are therefore not available. As part of a systematic synthetic analogue approach to metallobleomycins,[6-9] we report here the synthesis, structure, and selected

† Inquiries related to crystallographic data should be addressed to this author.

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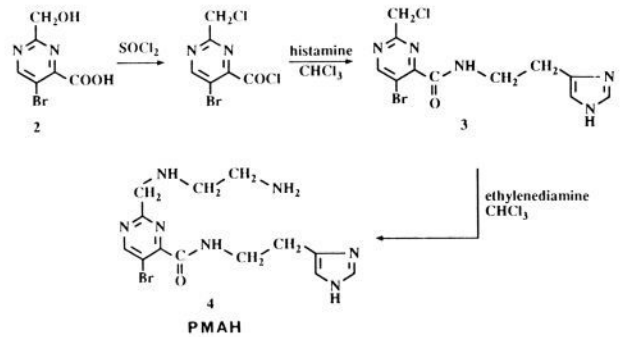
Scheme I



spectral properties of an analogue of Cu(II)–BLM in which all the five proposed coordination centers of BLM around copper have been successfully reproduced for the first time.

The *tailored* ligand PMAH (**4**)[10] used in the present work contains five nitrogen donor centers located in the primary and secondary amines, pyrimidine and imidazole rings, and the amide moiety and thus mimicks a major part of the metal-chelating portion of BLM (boxed area in **1**). The starting material for the synthesis of PMAH (Scheme I) was the substituted pyrimidine ring **2**.[11] Reaction of **2** with excess $SOCl_2$ resulted in the double chloride which afforded the peptide fragment **3**[12] when reacted with 2 equiv of histamine in chloroform (25 °C, 1 h). Further reaction of **3** with 6 equiv of ethylenediamine in chloroform (40 °C, 24 h) followed by removal of ethylenediamine hydrochloride produced the desired ligand **4** in solution. PMAH was isolated as a cream-colored solid[13] in ~80% yield (based on **2**) upon removal of the solvent as well as the excess amine.

The Cu(II) complex of PMAH, $[Cu(II)–PMA]BF_4$ (**5a**), was synthesized by allowing 1 mmol of Copper(II)–acetate monohydrate to react with 1.2 mmol of PMAH in 40 mL of methanol. After addition of 3 equiv of Et_4NBF_4, the deep blue solution was filtered to remove a trace of suspended particles and was allowed to evaporate at room temperature. The dark bluish green blocks (48%) were collected by filtration after 24 h.[14] $[Cu(II)–PMA]ClO_4$ (**5b**) was synthesized by following a similar procedure and by using $LiClO_4$ instead of Et_4NBF_4 (yield: 65%).[14] The IR, optical, and EPR properties of **5a** and **5b** are identical.[15]

The structure[17] of $[Cu(II)–PMA]^+$ in **5a** is shown in Figure 1. The coordination geometry around copper is distorted square pyramidal. Four nitrogens from the pyrimidine, imidazole, secondary amine, and the deprotonated amide group form the basal

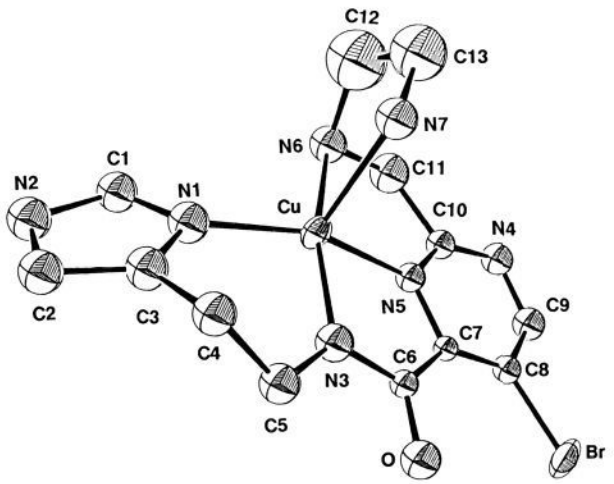


Figure 1. ORTEP drawing of $[Cu(II)–PMA]^+$, 30% thermal elipsoids are shown; hydrogen atoms are omitted for clarity. Selected bond distances are in Å: Cu–N1, 2.10 (3); Cu–N3, 1.86 (2); Cu–N5, 2.17 (2); Cu–N6, 2.18 (2); Cu–N7, 2.19 (2). Selected bond angles are in deg: N1–Cu–N3, 82.7 (9); N1–Cu–N5, 160.4 (8); N1–Cu–N6, 117.5 (8); N1–Cu–N7, 96.3 (7); N3–Cu–N5, 91.6 (9); N3–Cu–N6, 157 (1); N3–Cu–N7, 105.8 (8); N5–Cu–N6, 65.7 (8); N5–Cu–N7, 103.3 (6); N6–Cu–N7, 83.8 (7).

plane of coordination while the primary amine nitrogen occupies the axial position. The copper atom is displaced 0.23 Å from the mean basal plane in the direction of the apical nitrogen. The Cu(II)–N distances range from 1.86 (2) to 2.18 (2) Å and are comparable to those found in related compounds.[2,6,18] Significant deviations from 90° are observed for the N–Cu–N angles due to formation of three five-membered chelate rings. The sixth coordination site on copper is partially blocked due to such distortion, and the metal center remains pentacoordinated both in solid state and in solution.[19]

The deep blue color of $[Cu(II)–PMA]^+$ arises from an absorption with λ_{max} at 612 nm (water, pH 7.2, ϵ = 125 M^{-1} cm^{-1}).[19] Cu(II)–BLM exhibits a similar band at slightly higher energy (595 nm, ϵ = 120).[4] The EPR spectrum of $[Cu(II)–PMA]^+$ at 120 K in glycerol/water glass (3:7)[19] (pH 7.0, $g_\perp$ = 2.052, $g_\parallel$ = 2.210, $A_\parallel$ = 184 G, Supplementary Material) is, however, virtually identical with that of Cu(II)–BLM ($g_\perp$ = 2.055, $g_\parallel$ = 2.211, $A_\parallel$ = 183 G).[4] Clearly, $[Cu(II)–PMA]^+$ resembles Cu(II)–BLM more closely than Cu(II)–P-3A.[21]

In summary, the crystal structure of a synthetic analogue of Cu(II)–BLM has been determined, and its spectroscopic properties have been compared with those of Cu(II)–BLM and related species. Prior to this report, no synthetic analogue of M–BLM has been isolated in crystalline form.

Structural and spectroscopic studies on the various metal complexes of PMAH, currently under progress in this laboratory, are expected to establish the coordination structures of metallobleomycins with more certainty.

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Supplementary Material Available: Tables of positional and thermal parameters and EPR spectrum of **5a** in glycerol/water glass (120 K) (3 pages). Ordering information is given on any current masthead page.

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(12) Peptide **3** is unstable in pure state and decomposes to unknown products even when kept at −20 °C: ^1H NMR ($(CD_3)_2SO$, 298 K, ppm from TMS) δ 2.79 (t, 2 H, CH_2), 3.59 (m, 2 H, CH_2), 4.84 (s, 2 H, CH_2), 6.91 (s, 1 H, Im), 7.63 (s, 1 H, Im), 9.16 (s, 1 H, Pm).
(13) PMAH (**4**) is sensitive to both moisture and oxygen. When kept at −20 °C under dry N_2, the compound is stable for at least a week: NMR data ($(CD_3)_2SO$, 298 K, 300 MHz, ppm from TMS) ^1H NMR: δ 2.66 (m, 4 H, CH_2s), 2.81 (t, 2 H, CH_2), 3.54 (t, 2 H, CH_2), 3.92 (s, 2 H, CH_2), 4.96 (br NH and NH_2), 6.91 (s, 1 H, Im), 7.58 (s, 1 H, Im), 9.07 (s, 1 H, Pm); ^{13}C NMR δ 26.72, 39.57, 40.98, 50.80, 54.14, 114.23, 116.52, 134.53, 134.81, 158.42, 160.54, 163.34, 167.28; ν_{CO} 1670 cm^{-1}; MS, 368,370 $(M + H)^+$.
(14) Chemical Anal. Calcd for $[Cu(II)–PMA]BF_4$, $CuC_{13}H_{17}N_7OBrBF_4$: C, 30.15; H, 3.31; N, 18.95. Found: C, 30.62; H, 3.21; N, 18.75. Anal. Calcd for $[Cu(II)–PMA]ClO_4$, $CuC_{13}H_{17}N_7O_5ClBr$: C, 29.43; H, 3.23; N, 18.50; Cl, 6.69. Found: C, 29.23; H, 3.21; N, 18.56; Cl, 6.81.
(15) For both compounds, ν_{CO} appears at 1600 cm^{-1}, suggestive of coordination of the deprotonated amido N to copper.[16]
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(17) X-ray analysis: bluish black blocks from methanol; $CuC_{13}H_{17}N_7OBrBF_4$ (**5a**) orthorhombic space group *Pbca*, a = 15.041 (8) Å, b = 17.733 (7) Å, c = 15.206 (6) Å, V = 4082 (4) Å^3, Z = 8, d_{calcd} = 1.70 g/cm^3, d_{obsd} = 1.71 (1) g/cm^3. The present value of R = 0.088 and R_w = 0.093. The Br and Cu atom positions were determined by direct methods (SHELX-76), and the remaining non-hydrogen atoms were located from difference Fourier map calculations. Full details will be reported elsewhere.
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(19) Electronic spectrum: $[Cu(II)–PMA]^+$, water, λ_{max} nm (ϵ, M^{-1} cm^{-1}) 612 (125), 320 sh (2700), 290 sh (4700). The spectrum remains unchanged in glycerol/water (3:7) mixture. Since the visible band maximum hardly changes with change of solvent (water, DMF, DMSO), axial coordination by solvent molecule appears unlikely.[20]
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(21) Cu(II)–P-3A (water, pH 7.2) exhibits one visible band at 625 nm (ϵ = 120). The EPR spectrum of Cu(II)–P-3A is rhombic ($g_z \approx$ 2.214, g_x = 2.133, g_y = 2.078, $A_\parallel$ = 167 G).[4]