Preparation, Structure, and Reactivity of the Nonbonded Organoditantalum(IV) Complexes $(\eta\text{-}C_5Me_4R)_2Ta_2(\mu\text{-}X)_2X_4$ (R = Me, Et; X = Cl, Br), Precursors to the Doubly Bonded Organoditantalum(III) Complexes $(\eta\text{-}C_5Me_4R)_2Ta_2(\mu\text{-}X)_4$

Sir:

Organometallic and inorganic complexes with transition-metal–transition-metal bonds are prepared by a number of strategies,[1] including (1) addition of nucleophilic metal anions to other metal complexes, (2) reductive dimerization of mononuclear, high-valent precursors, or (3) photoinduced or thermally induced elimination of ligands or small covalent molecules (e.g., methane, dihydrogen) from two mononuclear complexes. Method 2 has been used in a number of cases with the early transition metals[2] and constitutes the method of choice for the preparation of dinuclear complexes with metal–metal single and double bonds. In in situ two-electron reduction of high-valent mononuclear complexes to compounds with metal–metal double bonds (eq 1), there

$$MX_nL_m \xrightarrow{e^-} (MX_{n-1}L_m \text{ or } M_2X_{2n-2}L_{2m}) \xrightarrow{e^-} M_2X_{2n-4}L_{2m} \quad (1)$$

is often ambiguity as to the nuclearity of the intervening valency species. For example, the nuclearity of the intermediate Ta(IV) complex is unknown in the preparation[3] of the doubly bonded ditantalum(III) compound $[TaCl_2(PMe_3)_2]_2(\mu\text{-}Cl)_2$ from Ta_2Cl_{10} (presumably $TaCl_5(PMe_3)_n$ in solution), PMe_3, and sodium amalgam, although the singly bonded, possible intermediate ditantalum(IV) complex $[TaCl_2(PMe_3)_2]_2(\mu\text{-}Cl)_4$ has been isolated.[4]

We have recently reported[5] that the mononuclear[6] (peralkylcyclopentadienyl)tantalum(V) complexes $(\eta\text{-}C_5Me_4R)TaX_4$ (**1**, R = Me, Et; X = Cl, Br) can be reductively dimerized with 2 equiv of sodium amalgam to the doubly bonded organoditantalum(III) complexes $(\eta\text{-}C_5Me_4R)_2Ta_2(\mu\text{-}X)_4$ (**3**, Scheme I). These novel complexes are members of a new class of metal–metal double bonds and are highly reactive toward a diverse range of substrates (Scheme I), most significantly in activation of vinylic C–H[7] and borohydride B–H bonds.[8] The several possible Ta(IV) intermediates in the preparation of **3** include mononuclear $(\eta\text{-}C_5Me_4R)TaX_3(solvent)_n$ and dinuclear $(\eta\text{-}C_5Me_4R)_2Ta_2X_6$. There is no literature basis for deciding between mononuclear and dinuclear Ta(IV) intermediates, as mid-valent (peralkylcyclopentadienyl)tantalum chemistry is underdeveloped[2,7,9-11] with most examples containing π-acid ligands such as CO[12] or alkynes.[12a,13]

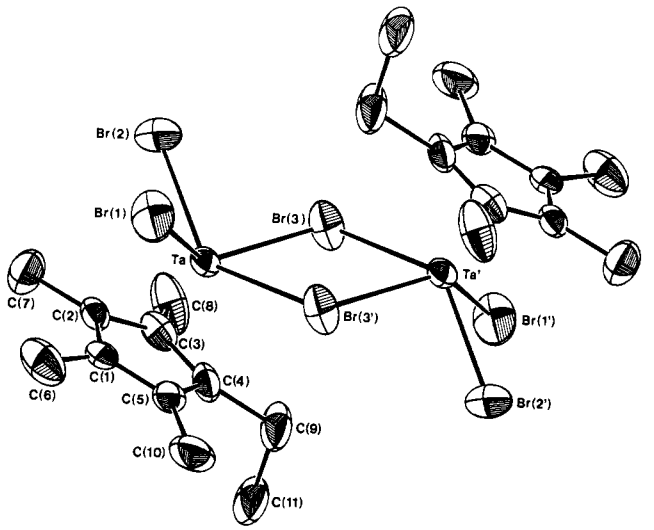


Figure 1. ORTEP drawing of the molecular structure of $(C_5Me_4Et)_2Ta_2(\mu\text{-}Br)_2Br_4$.

Table I. Comparative Structure Data for $(C_5Me_4Et)_2Ta_2(\mu\text{-}Br)_2Br_4$ and $(C_5Me_5)_2Ta_2(\mu\text{-}Br)_4$[5]

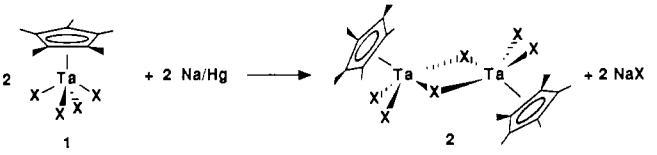
	$(C_5Me_4Et)_2Ta_2(\mu\text{-}Br)_2Br_4$	$(C_5Me_5)_2Ta_2(\mu\text{-}Br)_4$
Ta···Ta, Å	4.1230 (9)	2.748 (2)
Ta–Ta bond order	0	2
Ta–(μ-Br)–Ta, deg	102.68 (5)	63.7 (1), 63.1 (1)
(μ-Br)–Ta–(μ-Br), deg	77.32 (6)	116.2 (2)
Ta–(μ-Br), Å	2.648 (1), 2.632 (1)	2.589 (5)–2.631 (6)
$Ta\text{–}Br_{terminal}$, Å	2.517 (1), 2.534 (2)	
magnetism (soln)	paramagnetic	diamagnetic

Table II. Crystallographic Data for $(C_5Me_4Et)_2Ta_2(\mu\text{-}Br)_2Br_4$

$Ta_2C_{22}H_{34}Br_6$	space group $P2_1/n$ (No. 1014)
fw 1139.81	T = 22 °C
a = 8.566 (2) Å	λ = 0.710 73 Å
b = 13.167 (6) Å	ρ_{calcd} = 2.245 g cm^{-3}
c = 12.854 (6) Å	μ = 258.5 cm^{-1}
β = 94.04 (3)°	transmission coeff 0.85–1.00
V = 1449.71 Å^3	$R(F_o)$ = 0.041
Z = 2	$R_w(F_o)$ = 0.060

We wish to report that a dinuclear organoditantalum(IV) complex is an isolable intermediate in the reductive dimerization of **1** to **3**, that the compound in solution is paramagnetic, and that this complex has a solid-state structure with two bridging halogen atoms and *no* tantalum–tantalum bonding interaction.

Reduction of $(\eta\text{-}C_5Me_4R)TaX_4$ with 1 equiv of sodium amalgam in toluene proceeds straightforwardly to $(\eta\text{-}C_5Me_4R)_2Ta_2X_6$ (**2**) in 70% yield[14] (eq 2). The moderately



(2)

soluble green products are paramagnetic by ^{1}H NMR spectroscopy, with single, broad ($\Delta\nu_{1/2} \approx 250$ Hz) resonances for the

(1) (a) Cotton, F. A.; Wilkinson, G. *Advanced Inorganic Chemistry*, 5th ed.; Wiley-Interscience: New York, 1988. (b) Collman, J. P.; Hegedus, L. S.; Norton, J. R.; Finke, R. G. *Principles and Applications of Organotransition Metal Chemistry*; University Science Books: Mill Valley, CA, 1987. (c) Lukehart, C. M. *Fundamental Transition Metal Organometallic Chemistry*; Brooks/Cole (Wadsworth): Monterrey/Belmont, CA, 1985. (d) Crabtree, R. H. *The Organometallic Chemistry of the Transition Metals*; Wiley-Interscience: New York, 1988.

(2) Messerle, L. *Chem. Rev.* **1988**, *88*, 1229–1254.

(3) Sattelberger, A. P.; Wilson, R. B.; Huffman, J. C. *Inorg. Chem.* **1982**, *21*, 2392–2396.

(4) (a) Boyd, P. D. W.; Jones, T. C.; Nielson, A. J.; Rickard, C. E. F. *J. Chem. Soc., Chem. Commun.* **1984**, 1086–1088. (b) Boyd, P. D. W.; Nielson, A. J.; Rickard, C. E. F. *J. Chem. Soc., Dalton Trans.* **1987**, 307–314. (c) Cotton, F. A.; Diebold, M. P.; Roth, W. J. *Polyhedron* **1985**, *4*, 1103–1108.

(5) Ting, C.; Baenziger, N. C.; Messerle, L. *J. Chem. Soc., Chem. Commun.* **1988**, 1133–1135.

(6) (a) The complex $(C_5Me_5)TaBr_4$ has the anticipated four-legged piano-stool structure in the solid state. (b) Messerle, L. Unpublished results.

(7) Ting, C.; Messerle, L. *J. Am. Chem. Soc.* **1987**, *109*, 6506–6508.

(8) Ting, C.; Messerle, L. Submitted for publication in *J. Am. Chem. Soc.*

(9) (a) $Cp^*TaCl_3PMe_3$ has been reported[9b,c] by several groups; it is also one of several products from PMe_3 addition[5] to $Cp^*_2Ta_2(\mu\text{-}X)_4$ and has a four-legged piano-stool structure.[9d] (b) McLain, S. J.; Wood, C. D.; Schrock, R. R. *J. Am. Chem. Soc.* **1979**, *101*, 4558–4570. (c) Gibson, V. C.; Bercaw, J. E.; Bruton, W. J.; Sanner, R. D. *Organometallics* **1986**, *5*, 976–979. (d) Ting, C.; Messerle, L. Unpublished results.

(10) (a) Hubert-Pfalzgraf, L.; Riess, J. G. *Inorg. Chim. Acta* **1981**, *52*, 231–236. (b) Foxman, B. M.; McNeese, T. J.; Wreford, S. S. *Inorg. Chem.* **1978**, *17*, 2311–2314.

(11) Belmonte, P. A.; Schrock, R. R.; Day, C. S. *J. Am. Chem. Soc.* **1982**, *104*, 3082–3089.

(12) (a) Curtis, M. D.; Real, J. *Organometallics* **1985**, *4*, 940–942. (b) Burt, R. J.; Leigh, G. J.; Hughes, D. L. *J. Chem. Soc., Dalton Trans.* **1981**, 793–799. (c) Mayer, J. M.; Bercaw, J. E. *J. Am. Chem. Soc.* **1982**, *104*, 2157–2165.

(13) Smith, G.; Schrock, R. R.; Churchill, M. R.; Youngs, W. J. *Inorg. Chem.* **1981**, *20*, 387–393.

(14) Characterization data for $(C_5Me_4Et)_2Ta_2Cl_6$ is a follows. Anal. Calcd for $C_{11}H_{17}Cl_3Ta$: C, 30.24; H, 3.89; Cl, 24.40. Found (combustion with WO_3/V_2O_5): C, 30.48; H, 3.93; Cl, 22.69. ^{1}H NMR (δ, C_6D_6, 25 °C): 50.1 and 48.2 (partially overlapped ring Me and CH_2), 43.5 (ring Me), and 20.3 (ethyl Me). ^{1}H NMR for $(C_5Me_4Et)_2Ta_2Br_4(\mu\text{-}Br)_2$ (δ, C_6D_6, 25 °C): 47.7 and 45.0 (partially overlapped ring Me and CH_2), 42.0 (ring Me), and 18.9 (ethyl Me).

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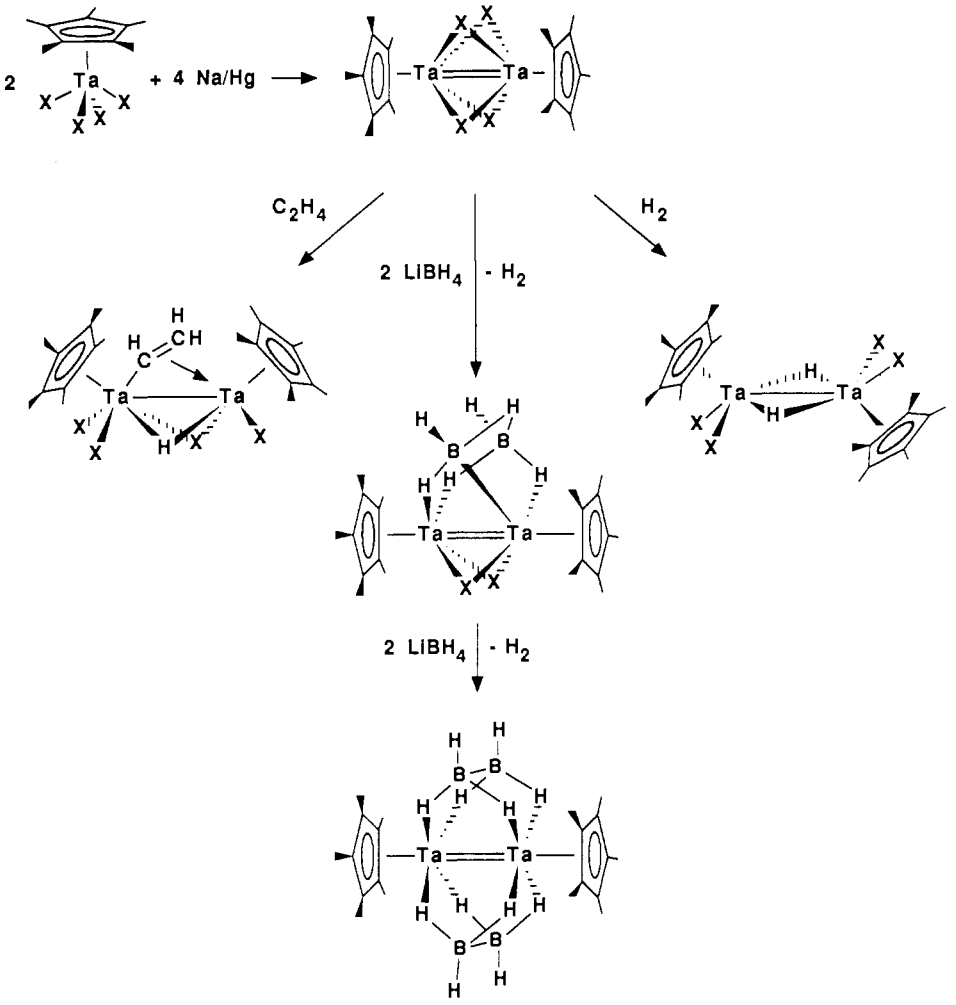
Scheme I



equivalent C_5Me_5 (henceforth abbreviated Cp*) groups at δ 47.9 for X = Cl and at δ 44.4 for X = Br; spectra of the C_5Me_4Et derivatives show that a plane of symmetry passes through the equivalent peralkylcyclopentadienyl groups. An Evans method[15] susceptibility determination shows a μ_{eff} value for $(C_5Me_4Et)_2Ta_2Cl_6$ of 2.92 μ_B consistent with two unpaired electrons per dimer, and the complex exhibits no EPR signal in frozen solution (8 K) as would be expected for a triplet-state complex. The above data suggest that the two Ta(IV) centers are not close enough for a bonding interaction and that two or more bridging halogen atoms must be present.

A single-crystal X-ray diffraction study shows that **2d** (R = Et, X = Br) exists in the solid state as a dinuclear complex (Figure 1) with two bridging bromine atoms and a long, nonbonded tantalum–tantalum separation of 4.1230 (9) Å. The obtuse Ta–(μ-Br)–Ta and acute (μ-Br)–Ta–(μ-Br) angles are also consistent with a lack of bonding between the metal centers, as is emphasized by a comparison of structural parameters for **2d** and the doubly bonded **3c** (R = Me, X = Br) listed in Table I. Table II lists the relevant parameters for the crystallographic determination of **2d**.

The long, nonbonded tantalum···tantalum distance in **2d** is striking when compared to the averaged Ta–Ta distance of 2.835 Å in the diamagnetic $(C_5Me_4Et)_2Ta_2Cl_3Me(\mu\text{-}H)_2$, which has been assigned as a Ta(IV)–Ta(IV) single bond.[11] However, metal–metal distances are usually if not always substantially shorter in hydrido-bridged dinuclear complexes when compared to those in the corresponding halogen-bridged analogues. Examples of this trend of metal–metal distance shortening upon replacement of three-center, three-electron bonds with three-center, two-electron bonds include $[Cp^*IrCl]_2(\mu\text{-}Cl)_2$ (3.769 (1) Å) versus $[Cp^*IrCl]_2(\mu\text{-}H)(\mu\text{-}Cl)$ (2.903 (1) Å) and analogous dirhodium complexes.[16] Hydride-related metal–metal bond shortening has also been noted in ditantalum complexes, such as $[TaCl_2(PMe_3)_2]_2(\mu\text{-}Cl)_2$ (2.721 (1) Å)[3] compared to $[TaCl_2(PMe_3)_2]_2(\mu\text{-}H)_2$ (2.545 (1) Å)[17] and $[TaCl_2(PMe_3)_2]_2(\mu\text{-}Cl)_4$ (2.830 (1) Å)[4b,c] compared to $[TaCl_2(PMe_3)_2]_2(\mu\text{-}H)_2(\mu\text{-}Cl)_2$ (2.621 (1) Å)[18] and $[TaCl_2(PMe_3)_2]_2(\mu\text{-}H)_4$ (2.511 (2) Å).[17]

There are several reports of (cyclopentadienyl)niobium(IV) and -tantalum(IV) complexes in the literature. The compound $CpNbBr_3$ has been obtained from the reaction of $CpSnMe_3$ with $NbBr_5$,[19] and $CpNbCl_3$ has been prepared[20] and attached to a polymer.[21] A green, sparingly soluble compound to which was ascribed the formulation Cp^*TaCl_3 was reported[9b] as one product from thermolysis of $Cp^*TaCl_2(MeCH{=}CH_2)$ in PhCl.

Complex **2** is the probable intermediate in the reductive dimerization of **1** to **3** since it can be reduced directly to **3** in essentially quantitative yield (eq 3). Complex **2** reacts readily with a variety of small molecules, including CO, H_2, PMe_3, and

(15) (a) Evans, D. F. *Proc. Chem. Soc., London* **1958**, 115. (b) Evans, D. F. *J. Chem. Soc.* **1959**, 2003–2005. (c) Deutsch, J. L.; Poling, S. M. *J. Chem. Educ.* **1969**, *46*, 167–168. (d) Loliger, J.; Scheffold, R. *J. Chem. Educ.* **1972**, *49*, 646–647.

(16) Churchill, M. R.; Julis, S. A. *Inorg. Chem.* **1977**, *16*, 1488–1494 and references therein.

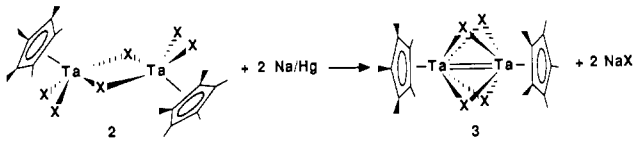
(17) Scioly, A. J.; Luetkens, M. L.; Wilson, R. B.; Huffman, J. C.; Sattelberger, A. P. *Polyhedron* **1987**, *6*, 741–757.

(18) Sattelberger, A. P.; Wilson, R. B.; Huffman, J. C. *Inorg. Chem.* **1982**, *21*, 4179–4184.

(19) Burt, R. J.; Chatt, J.; Leigh, G. J.; Teuben, J. H.; Westerhof, A. *J. Organomet. Chem.* **1977**, *129*, C33–C35.

(20) Lau, C. P. Ph.D. Dissertation, Michigan State University, East Lansing, MI, 1977, cited in ref 21.

(21) Kilmer, N. H.; Brubaker, C. H. *Inorg. Chem.* **1979**, *18*, 3283–3284.



2 3 (3)

N_2O, and product characterizations are in progress. The high reactivity of **2**, as also noted for **3**,[5,7,8] suggests that it should prove to be a useful synthon for the preparation of other Ta(IV) and, through oxidative addition, Ta(V) organometallics.

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Supplementary Material Available: Tables of crystallographic data collection parameters, atomic coordinates, bond lengths (non-hydrogen atom), and bond angles (non-hydrogen atom) (4 pages). Ordering information is given on any current masthead page.

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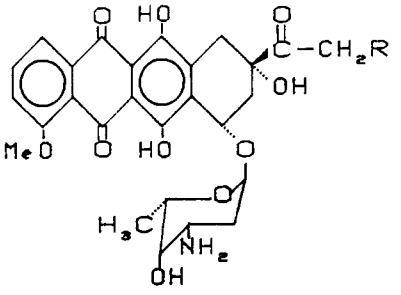
Structural Model for the Binding of Iron by Anthracycline Drugs

Sir:

The anthracycline drugs daunorubicin (R = H) and doxorubicin (R = OH) (structure **1**) have been in clinical use for nearly 2 decades in the treatment of various human cancers.[1-4] Recently,



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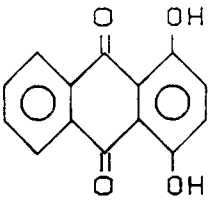
these drugs have also been found to inhibit the infectivity and replication of human immunodeficiency virus (HIV) in vitro and may find applicability as antiviral agents in the treatment of acquired immune deficiency syndrome (AIDS) and AIDS-related complex (ARC).[5-7] The popularity of these drugs in cancer chemotherapy stems in part from their potency against a wide range of maligancies, but is tempered by toxic side effects, which include cardiotoxicity.[4] Despite the widespread use of the drugs and many years of intensive investigation, little information is available concerning their in vivo cytotoxicity. One possibility involves coordination of iron to form a catalyst for the production of reactive oxygen species including hydroxyl radicals,[1,8-13] which could account for all of the known cytotoxic effects of the drugs (including damaging DNA[1,14-18] and cell membranes[1,19-21]) as well as account for their cardiotoxicity.

The drugs are recognized as good iron chelators,[22-24] capable of acquiring iron from ferritin[25] or from transferrin in acidic intracellular compartments.[26] The hydroxyquinone groups found in both drugs have been shown by resonance Raman spectroscopic experiments to play a role in binding metals,[27-29] yet no complex of this type has been structurally characterized. We wish to report the synthesis of complexes of daunorubicin and doxorubicin with Fe(salen),[30] their characterization in solution using spectroscopic techniques, and the structural characterization by single-crystal X-ray diffraction of a model of these complexes employing 1,4-dihydroxy-9,10-anthraquinone, or quinizarin (Qz) (structure **2**),



quinizarin (**2**)

to model the interaction of the drugs with Fe(salen). The complex, $[Fe(salen)]_2Qz$, is the first structurally characterized complex with direct structural relevance to iron binding by anthracycline drugs.

The combination of anaerobic solutions of daunorubicin hydrochloride or doxorubicin hydrochloride in dry acetonitrile containing 1 mM Et_3N with a solution of Fe(salen)OAc in the same solvent mixture, gives rise to spectra like that shown in Figure 1. In addition to the strong absorbance near 480 nm present in the solution of the drug itself, new bands at 593 and 643 nm are observed. These bands are assigned to ligand-to-metal charge-transfer (LMCT) transitions on the basis of resonance Raman data (using a 633-nm excitation) that reveal several peaks in the

(1) Myers, C.; Gianni, L.; Zweier, J.; Muindi, J.; Sinha, B. K.; Eliot, H. *Fed. Proc., Fed. Am. Soc. Exp. Biol.* **1986**, *45*, 2792–2797.
(2) Arcamone, F. *Med. Res. Rev.* **1984**, *4*, 153–188.
(3) Naff, M. B.; Plowman, J.; Narayanan, V. L. In *Anthracycline Antibiotics*; El Khadem, H. S., Ed.; Academic Press: New York, 1982; pp 1–57.
(4) Young, R. C.; Ozols, R. F.; Myers, C. E. *Clin. Rev.* **1981**, *305*, 139–153.
(5) Nakashima, H.; Yamamoto, N. *J. Antibiot.* **1987**, *40*, 396–399.
(6) Wondrak, E. M.; Löwer, J.; Kurth, R. *J. Antimicrob. Chemother.* **1988**, *21*, 151–161.
(7) De Clercq, E. *Arzneim.-Forsch.* **1985**, *35*, 1007–1008.
(8) Lown, J. W. *Adv. Free Radical Biol. Med.* **1985**, *1*, 225–264.
(9) Gianni, L.; Zweier, J. L.; Levy, A.; Myers, C. E. *J. Biol. Chem.* **1985**, *260*, 6820–6826.
(10) Zweier, J. L.; Gianni, L.; Muindi, J.; Myers, C. E. *Biochim. Biophys. Acta* **1986**, *884*, 326–336.
(11) Zweier, J. L. *J. Biol. Chem.* **1984**, *259*, 6056–6058.
(12) Doroshow, J. H. *Cancer Res.* **1983**, *43*, 4543–4551.
(13) Doroshow, J. H. *Biochem. Biophys. Res. Commun.* **1986**, *135*, 330–335.
(14) Sugioka, K.; Nakano, H.; Nakano, M.; Tero-Kubota, S.; Ikegami, Y. *Biochim. Biophys. Acta* **1983**, *753*, 411–421.
(15) Muindi, J. R. F.; Sinha, B. K.; Gianni, L.; Myers, C. E. *FEBS Lett.* **1984**, *172*, 226–230.
(16) Eliot, H.; Gianni, L.; Myers, C. *Biochemistry* **1984**, *23*, 928–936.
(17) Gutteridge, J. M. C.; Toeg, D. *FEBS Lett.* **1982**, *149*, 228–232.
(18) Gutteridge, J. M. C.; Quinlan, G. J. *Biochem. Pharmacol.* **1985**, *34*, 4099–4103.
(19) Muindi, J.; Sinha, B. K.; Gianni, L.; Myers, C. *Mol. Pharmacol.* **1985**, *27*, 356–365.
(20) Goormaghtigh, E.; Ruysschaert, J. M. *Biochim. Biophys. Acta* **1984**, *779*, 271–288.
(21) Praet, M.; Pollakis, G.; Goormaghtigh, E.; Ruysschaert, J. M. *Cancer Lett.* **1984**, *25*, 89–96.
(22) Myers, C. E.; Gianni, L.; Simone, C. B.; Klecker, R.; Greene, R. *Biochemistry* **1982**, *21*, 1707–1713.
(23) Kiraly, R.; Martin, R. B. *Inorg. Chim. Acta* **1982**, *67*, 13–18.
(24) May, P. M.; Williams, G. K.; Williams, D. R. *Inorg. Chim. Acta* **1980**, *46*, 221–228.
(25) Demant, E. J. F. *FEBS Lett.* **1984**, *176*, 97–100.
(26) Demant, E. J. F.; Nørskov-Lauritsen, N. *FEBS Lett.* **1986**, *196*, 321–324.
(27) Dutta, P. K.; Hutt, J. A. *Biochemistry* **1986**, *25*, 691–695.
(28) Beraldo, H.; Garnier-Suillerot, A.; Tosi, L.; Lavelle, F. *Biochemistry* **1985**, *24*, 284–289.
(29) Beraldo, H.; Garnier-Suillerot, A.; Tosi, L. *Inorg. Chem.* **1983**, *22*, 4117–4124.
(30) salen = bis(salicylaldehyde) ethylenediimine.

0020-1669/89/1328-0173$01.50/0