Table I. Physical Properties of Some New Five-Coordinate Iron(II) Complexes

	Λ_M	μ_{eff}, BM[c]	d–d electronic spectra[d]	Mossbauer parameters δ, mm/sec[e]	ΔE_Q, mm/sec
[Fe(1,7 CT)Cl]ClO_4	95[a]	5.05	4.7 (7); 12.2 (5)	1.15	3.78
[Fe(1,7 CT)Br]ClO_4	106[a]	5.11	~5 (~5); 12.2 (4.9)	1.14	3.81
[Fe(1,7 CT)I]ClO_4	93[a]	5.15	<5 (~4); 12.2 (4)	1.12	3.34
[Fe(1,3,7,10 CT)Cl]ClO_4	97[a]	5.00	4.65 (3); 11.62 (3)	1.13	3.60
[Fe(1,3,7,10 CT)Br]ClO_4	99[a]	5.14	4.76 (3); 11.66 (3)	1.14	3.78
[Fe(1,3,7,10 CT)I]ClO_4	102[a]	5.10	~5; 11.65	1.10	3.79
[Fe(CRH)Cl]Cl	110[b]	5.20		1.11	3.72
[Fe(CRH)Br]Br	92[b]	5.11		1.12	3.84
[Fe(CRH)I]I	102[b]	5.05		1.08	3.84

[a] Molar conductance obtained in purified nitromethane under N_2 atmosphere; concentrations were in the range 1.5×10^{-3}–0.97×10^{-3} *M*. [b] Obtained in absolute methanol under N_2 atmosphere; concentrations $\sim 10^{-3}$ *M*. [c] Obtained at room temperature using the Faraday technique. [d] Obtained in nitromethane under N_2 atmosphere, absorption maxima in kilokaisers, molar extinction coefficients are given in parentheses. [e] Values are with respect to sodium nitroprusside standard.

The Mössbauer parameters of these five-coordinate complexes were obtained during the course of an extensive investigation of several series of iron complexes of varying coordination number, geometry, spin state, and oxidation state.[5] The strong axial perturbation in these five-coordinate complexes yields a unique range of Mössbauer parameters which appear to be characteristic of iron(II) in this environment. For the five-coordinate [Fe(1,7 CT)X]ClO_4 and [Fe(1,3,7,10 CT)X]ClO_4 series, the isomer shifts (δ) are in the characteristic range for high-spin Fe(II), in agreement with the magnetic data. Quadrupole splitting values (ΔE_Q) are consistently large (3.3–3,8 mm/sec), and together with the δ values form a set of parameters unique among iron coordination compounds. The range of ΔE_Q values for these compounds is the highest yet recorded for iron. The more familar high-spin Fe(II) complexes have quadrupole splittings in the range 2.0–3.0 mm/sec;[6] the ΔE_Q values of so-called ionic salts are normally between 2.5 and 3.5 mm/sec.[7] The relative contributions of the electric field gradient due to the dissymmetry of the electron population and to the ligand environment will be discussed in another paper.

Very few previously reported iron complexes have ΔE_Q values greater than 3.5 mm/sec. One of these is a pyrazolylborate which is a high-spin Fe(II) compound;[8] another is a five-coordinate low-spin iron(III) phthalocyanine complex.[9]

The characteristic range of Mössbauer parameters for five-coordinate high-spin Fe(II) can be helpful in identifying this configuration in other iron compounds. For example, in the series Fe(CRH)X_2 (X = Cl, Br, I) experimental difficulties limit the value of other physical data in attempts to assign the coordination number. For each of these compounds, δ is in the characteristic range for high-spin Fe(II) and ΔE_Q is in the range 3.3–3.8 mm/sec. In the absence of a complete X-ray structural determination, Mössbauer spectra appear to be the most convenient means of establishing the presence of five-coordinate high-spin Fe(II) in the solid state.[10]

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(5) To be reported. Room-temperature Mössbauer spectra were taken with a conventional constant-acceleration time-mode spectrometer, calibrated with sodium nitroprusside, iron metal, and α-Fe_2O_3.

(6) L. May, "The Mössbauer Effect and Its Application in Chemistry," R. H. Herber, Ed., American Chemical Society Publications, Washington, D. C., 1967, p 54.

(7) J. Danon, "Chemical Applications of Mössbauer Spectroscopy," V. I. Goldanskii and R. H. Herber, Ed., Academic Press, New York, N. Y., 1968, pp 233–241.

(8) J. P. Jesson, J. F. Weiher, and S. Trofimenko, *J. Chem. Phys.*, **48**, 2058 (1968).

(9) R. Taube, H. Drevs, E. Fluck, and P. Kuhn, *Z. Anorg. Allg. Chem.*, **364**, 297 (1969).

(10) The experimental correlations provide the best justification for the kind of generalization we suggest here. ΔE_Q will depend on the nature of the ground state in C_{4v} symmetry; under a tetragonal distortion the $^5T_2$ state (O_h) is split into $^5B_2$ and ^5E states. The ordering of these states will depend upon the sign of the tetragonal splitting. Actually, the magnitudes of the contributions to the quadrupole splitting from a 3d electron in the $^5B_2$ or in the ^5E state are equal, but the electric field gradients associated with the two states have opposite signs. When the contribution to ΔE_Q from the ligand-field dissymmetry is included, somewhat different splittings may occur for the two states. In all the cases reported here, the monodentate ligand on the pseudofourfold axis is of much weaker ligand-field strength than is the in-plane macrocycle. Consequently the ^5E state is expected to lie lowest.

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Geldanamycin. I. Structure Assignment

Sir:

The ansamycin antibiotics have aroused considerable interest, both on account of their unusual *ansa* structures and because some of these compounds show marked antiviral activity as well as potent inhibition of DNA-dependent RNA polymerase.[1] The members of this class of antibiotics reported until now (rifamycins,[2] streptovaricins,[3] tolypomycins[4]) have all contained naphthoquinone nuclei. In the present report we

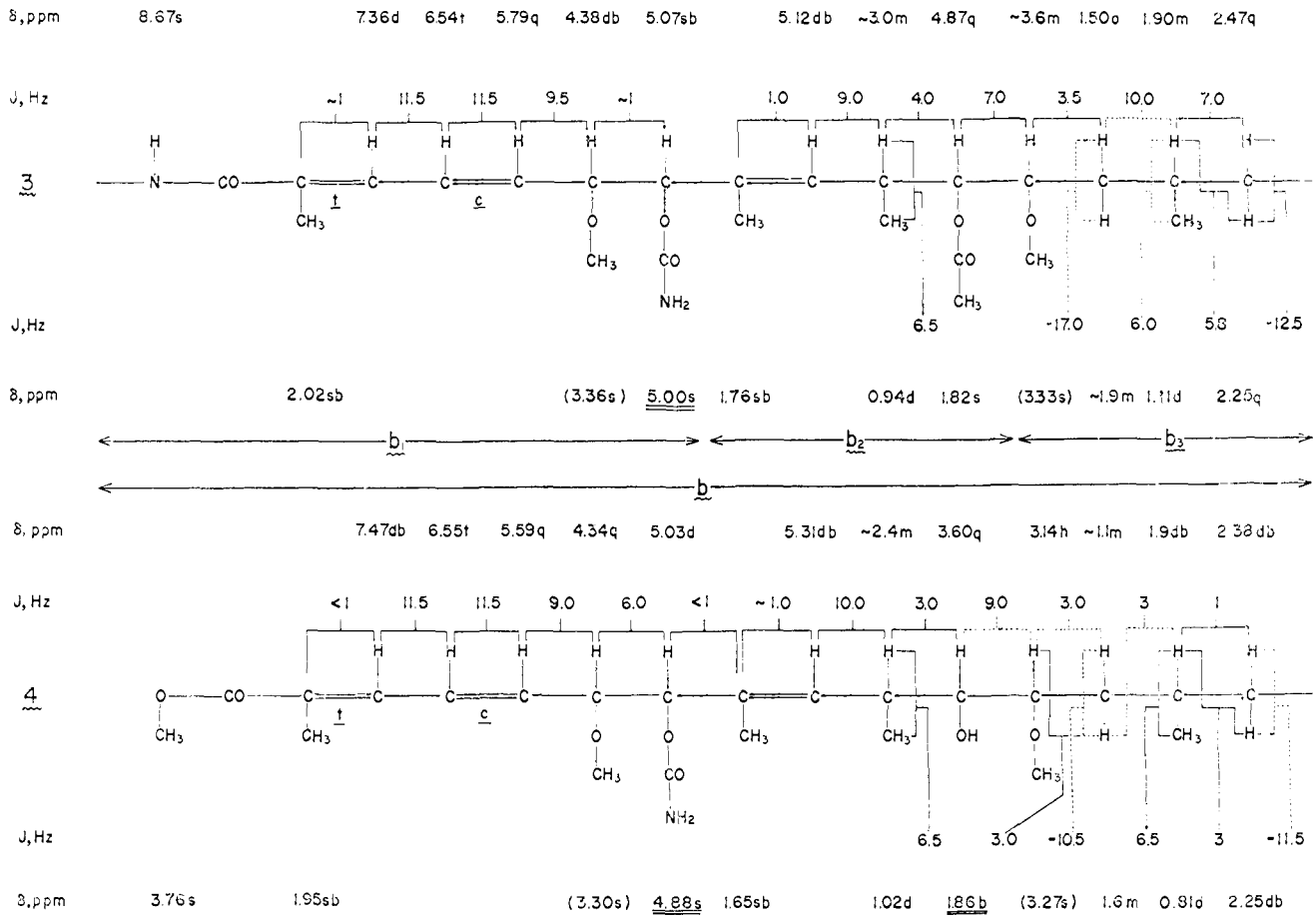
(1) A review of ansamycins: K. L. Rinehart, Jr., submitted for publication.

(2) W. Oppolzer, V. Prelog, and P. Sensi, *Experientia*, 20, 336 (1964).

(3) K. L. Rinehart, Jr., H. H. Mathur, K. Sasaki, P. K. Martin, and C. E. Coverdale, *J. Amer. Chem. Soc.*, 90, 6241 (1968).

(4) T. Kishi, S. Horada, M. Asai, M. Muroi, and K. Mizuno, *Tetrahedron Lett.*, 97 (1969).

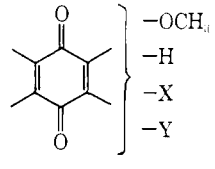
Chart I



assign structure **1** to geldanamycin, the first ansamycin shown to contain a benzoquinone nucleus. Geldanamycin, a yellow antibiotic produced by *Streptomyces hygroscopicus* var. *geldanus* var. *nova* (UC-5208), was recently reported to be especially active against *Tetrahymena pyroformis* and *Crithidia fasciculata*.[5] With primarily antiparasitic activity, geldanamycin thus differs from the other ansamycins in its antimicrobial spectrum, since the others are primarily active against Gram-positive bacteria.[1]

In the earlier report[5] geldanamycin was assigned the molecular formula $C_{29}H_{40}N_2O_9$ and this is substantiated by high-resolution mass spectrometry (Calcd for $C_{29}H_{40}N_2O_9$: 560.273. Found: 560.273).[6] The high degree of unsaturation and the color of the antibiotic suggest its aromatic character. This is defined as a benzoquinone nucleus by reduction of **1** by zinc dust and acetic acid to a colorless reduction product (λ_{max} 244 nm) which is rapidly reoxidized in air to **1**, as well as by the reductive acetylation (zinc dust–acetic anhydride) of **1** to diacetyldihydrogeldanamycin (**2**) ($C_{33}H_{46}N_2O_{11}$);[8,9] λ_{max} 268 nm (ϵ_{max} 26,400). These ultraviolet data are appropriate for a substituted benzene but not for a substituted naphthalene.[10]

The nmr spectrum ($CDCl_3$) of geldanamycin indicates that there are attached to the benzoquinone nucleus a methoxyl group (at δ 4.13, too low for all but aromatic methoxyls)[11] and a single hydrogen (δ 7.35, singlet). Thus, the unit **a** is established.



a

The benzoquinone unit accounts for five elements of unsaturation. The remaining six are found in conjugated dienamide, isolated olefin, and carbamate groups. The latter grouping (H_2N–CO–O–) is indicated by a carbonyl band at 1730 cm^{-1} ($CHCl_3$)[12] and by the identity of the NH region of **1** with that of novobiocin,[13] by the very facile mass spectral loss of HNCO from the parent ion of **1** to give an intense peak at *m/e* 517.270 (Calcd for $C_{28}H_{39}NO_8$: 517.268), and by hydrogenolysis (5 mol of uptake over 10% palladium/carbon) to give carbon dioxide (collected in barium hydroxide) and ammonia (collected in Nessler's reagent); on treatment with sodium hydroxide 1 mol of base was evolved. The remaining 4 mol of hydrogen is

(5) C. De Boer, P. A. Meulman, R. J. Wnuk, and D. H. Peterson, *J. Antibiot.*, 23, 442 (1970).

(6) The peak at *m/e* 560 is nearly always accompanied by a peak, of varying intensity, at *m/e* 562 (562.289 by HRMS). We attribute this to reduction of a quinone to a hydroquinone in the ion source, a recognized phenomenon.[7]

(7) *I.e.*, B. C. Das, M. Launasmaa, C. Tendille, and E. Lederer, *Biochem. Biophys. Res. Commun.*, **21**, 318 (1965).

(8) Acceptable microanalyses were obtained.

(9) The molecular weight was substantiated by (a) low-resolution mass spectrometry, (b) high-resolution mass spectrometry.

(10) A. I. Scott, "Interpretation of the Ultraviolet Spectra of Natural Products," Pergamon Press, New York, N. Y., 1964, Chapter 3.

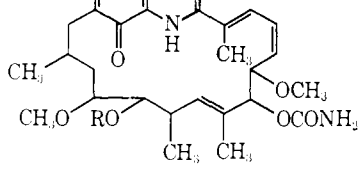
(11) "High Resolution NMR Spectra Catalog," Vol. 2, Varian Associates, Palo Alto, Calif., 1963, p 12.

(12) S. Pinchas and D. Ben-Ishai, *J. Amer. Chem. Soc.*, 79, 4099 (1957).

(13) E. C. Olson, unpublished data.

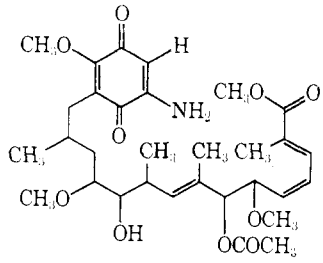
consumed by the dienamide (2 mol), the isolated olefin (1 mol), and the quinone (1 mol) groups. The dienamide group is assigned from the ultraviolet spectrum (λ_{max} 257 nm, ϵ 16,900)[14] and the nmr spectral properties discussed below; the isolated olefin is assigned from the nmr spectra.

The juxtaposition of the three unsaturated groups is established as in **b** by the nmr data shown for geldanamycin acetate (**3**, $C_{31}H_{42}N_2O_{10}$),[8,9] obtained on acetic anhydride–pyridine acetylation of **1** (see Chart I). Solid lines indicate proximate protons located by spin decoupling, dotted lines those assumed to be proximate but not established by decoupling. Chemical shifts in parentheses may be interchanged; those underlined are for exchangeable protons. These nmr data are substantiated by those for the methanolysis product **4** ($C_{30}H_{44}N_2O_{10}$),[8,9] the product obtained by treating geldanamycin with potassium carbonate in refluxing methanol–chloroform (1:1). Alternative structures derived from other junctures of the units $\mathbf{b}_1$, $\mathbf{b}_2$, and $\mathbf{b}_3$ would not fit the chemical shift and coupling data. Detailed arguments will be presented in the full paper.



1, R = H

3, R = $COCH_3$



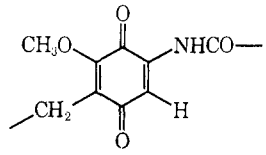
4

The sum of the molecular formulas of units **a** ($C_7H_4O_3$) and **b** ($C_{24}H_{38}N_2O_7$) is $C_{31}H_{42}N_2O_{10}$, the molecular formula of **3**. Thus, the complete structure of **3** (and **1**) is assigned by joining the ends of the unit **b** to two positions of the benzoquinone unit **a**.

The juxtaposition of substituents on the benzoquinone nucleus can be assigned as shown in **1**. Of the six theoretically possible arrangements of **a** and **b**, those in which the benzylic methylene group and aromatic proton are adjacent are eliminated by the lack of coupling between those two groups in the nmr spectrum of **3** (and **4**, *vide infra*). Positive evidence in favor of an arrangement with the amide group and aromatic hydrogen on adjacent positions is provided by the nmr spectrum of **4**. The aromatic proton of **4** is found at δ 5.51, 1.66-ppm upfield from its position in **1**, and is accompanied by an Ar–NH_2 singlet at δ 5.33. The upfield shift would be best explained by an attachment of the amide adjacent to the aromatic proton as in formula **1**.

(14) D. Peters, *J. Chem. Soc.*, 1832 (1960).

The aromatic chromophore of **4** gives maxima at 307 and 485 nm (ϵ 12,700 and 1245, respectively), and the methyl dienoate chromophore occurs at 265 nm (ϵ_{max} 23,000)[15] [*vs.* λ_{max} 257 (ϵ_{max} 16,900),[15] 305 (19,000), 400 nm (991) for **1**]. While the alternative arrangement **c** of substituents on the quinone can only be eliminated



c

by the synthesis of model chromophores,[16] the close similarity between the aromatic chromophore maxima of **4** and those reported for 2-methoxy-5-dimethylaminobenzoquinone [λ_{max} 218 (ϵ_{max} 18,500), 305 (13,900), 490 nm (3900)][17] argues forcefully for structure **1** for geldanamycin.[16]

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(15) Methyl sorbate has λ_{max} 258 nm (ϵ 25,700) *vs.* λ_{max} 254 nm (ϵ 26,900) for sorbamide.[14]

(16) Recently completed syntheses of model chromophores (both for **1** and **c**) strengthen the argument in favor of **1** [C. D. Tipton, M. W. McMillan, and K. L. Rinehart, Jr., to be submitted].

(17) J. S. Webb, D. B. Cosulich, J. H. Mowat, J. B. Patrick, R. W. Broschard, W. E. Meyer, R. P. Williams, C. F. Wolf, W. Fulmor, C. Pidacks, and J. E. Lancaster, *J. Amer. Chem. Soc.*, **84**, 3185 (1962).

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A New Endocyclic Enamine Synthesis

Sir:

In recent years the concept of using cyclic enamines[1] as versatile synthetic intermediates has played a prominent role in the design of numerous alkaloid syntheses.[2] Several recent examples where such methodology has been utilized successfully are illustrated in the synthesis of minovine,[3] mesembrine,[4] and cepharamine.[5] As an outgrowth of our work which has been focused on the synthesis of cepharamine and other related hausbanan alkaloids,[5b] we have had the

(1) K. Blaha and O. Cervinka, *Advan. Heterocycl. Chem.*, **6**, 147 (1966).

(2) E. Wenkert, *Accounts Chem. Res.*, **1**, 78 (1968).

(3) F. E. Ziegler and E. B. Spitzner, *J. Amer. Chem. Soc.*, **92**, 3492 (1970).

(4) (a) S. L. Keely, Jr., and F. C. Tahk, *ibid.*, **90**, 5584 (1968); (b) R. V. Stevens and M. P. Wentland, *ibid.*, **90**, 5580 (1968); (c) T. J. Curphey and H. L. Kim, *Tetrahedron Lett.*, 1441 (1968).

(5) (a) A formal total synthesis of cepharamine has recently been completed: S. L. Keely, Jr., A. J. Martinez, and F. C. Tahk, *Tetrahedron*, in press. (b) The synthesis of the hasubanan alkaloid skeleton has been reported: D. A. Evans, *Tetrahedron Lett.*, 1573 (1969); D. A. Evans, C. A. Bryan, and G. M. Wahl, *J. Org. Chem.*, **35**, 4122 (1970).