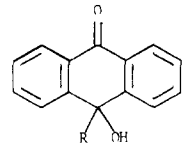


12a: R = Me

b: R = Ph

of anthraquinones in the reaction of **7** with alkoxy and methyl benzaldehydes (entries 2–4, 8) points to complications due to competitive metalation directed by $CONEt_2$ and CH_2O^- groups and steric effects in the cyclization, **3** → **4**. The aerial oxidation step, **4** → **5**, is well precedented.[26,27]

Outside of the specific application presented here, the concept of tandem directed metalation may have broader significance in organic synthesis.[28]

References and Notes

(1) Reviews: H. W. Gschwend and H. R. Rodriguez, *Org. React.*, **26**, 1 (1979); D. W. Slocum and C. A. Jennings, *J. Org. Chem.*, **41**, 3653 (1977); H.-P. Abicht and K. Issleib, *Z. Chem.*, **17**, 1 (1977).

(2) (a) F. E. Ziegler and K. W. Fowler, *J. Org. Chem.*, **41**, 1564 (1976); (b) S. O. de Silva, J. N. Reed, and V. Snieckus, *Tetrahedron Lett.*, 5099 (1978); (c) T. D. Harris, B. Neuschwander, and V. Boekelheide, *J. Org. Chem.*, **43**, 727 (1978).

(3) (a) A. I. Meyers and R. A. Gabel, *Tetrahedron Lett.*, 227 (1978); (b) P. Beak and R. A. Brown, *J. Org. Chem.*, **42**, 1823 (1977); (c) J. J. Fitt and H. G. Gschwend, *ibid.*, **41**, 4029 (1976); (d) R. C. Ronald, *Tetrahedron Lett.*, 3973 (1975); (e) N. Meyer and D. Seebach, *Angew. Chem., Int. Ed. Engl.*, **17**, 521 (1978); (f) M. Uemura, S. Tokuyama, and T. Sakan, *Chem. Lett.*, 1195 (1975); (g) E. F. Perozzi and J. C. Martin, *J. Am. Chem. Soc.*, **101**, 1591 (1979); (h) W. Fuhrer and H. W. Gschwend, *J. Org. Chem.*, **44**, 1133 (1979); (i) H. M. Walborsky and P. Ronman, *ibid.*, **43**, 731 (1978) (this involves α addition to aryl isocyanides followed by ortho metalation); (j) M. F. Semmelhack, J. Bisaha, and M. Czarny, *J. Am. Chem. Soc.*, **101**, 768 (1979); (k) G. A. Kraus and J. O. Pezzanite, *J. Org. Chem.*, **44**, 2480 (1979); (l) N. S. Narasimhan and R. S. Mali, *Synthesis*, 797 (1975).

(4) (a) B. C. Nalliah, D. B. MacLean, R. G. Rodrigo, and R. H. F. Manske, *Can. J. Chem.*, **55**, 922 (1977); (b) B. H. Bhide and V. P. Gupta, *Indian J. Chem., Sect. B*, **15**, 512 (1977); (c) S. O. de Silva and V. Snieckus, *Tetrahedron Lett.*, 5103 (1978); (d) S. O. de Silva, I. Ahmad, and V. Snieckus, *ibid.*, 5107 (1978), and *Can. J. Chem.*, **57**, 1598 (1979); (e) R. C. Ronald and J. M. Lansinger, *J. Chem. Soc., Chem. Commun.*, 124 (1979); (f) J. E. Baldwin and K. W. Blair, *Tetrahedron Lett.*, 2559 (1978); (g) I. Forbes, R. A. Pratt, and R. A. Raphael, *ibid.*, 3965 (1978); (h) R. C. Ronald, *Tetrahedron Lett.*, 4413 (1976); (i) H. P. Plaumann, B. A. Keay, and R. Rodrigo, *Tetrahedron Lett.*, 4921 (1979).

(5) H. W. Gschwend and A. Hamdan, *J. Org. Chem.*, **40**, 2008 (1975); A. I. Meyers and E. D. Mihelich, *ibid.*, **40**, 3158 (1975).

(6) T. D. Harris and G. P. Roth, *J. Org. Chem.*, **44**, 2004 (1979).

(7) J. C. Saddler, P. C. Conrad, and P. L. Fuchs, *Tetrahedron Lett.*, 5079 (1978).

(8) A. Marxer, H. R. Rodriguez, J. M. McKenna, and H. M. Tsai, *J. Org. Chem.*, **40**, 1427 (1975).

(9) R. M. Sandifer, C. F. Beam, M. Perkins, and C. R. Hauser, *Chem. Ind. (London)*, 231 (1977).

(10) B. M. Trost, M. Reiffen, and M. Crimmin, *J. Am. Chem. Soc.*, **101**, 257 (1979).

(11) A. Dipple, *ACS Monogr.*, **No. 173**, 245 (1973).

(12) Review: M. Sainsbury, *Synthesis*, 437 (1977). Recent work: D. A. Taylor and J. A. Joule, *J. Chem. Soc., Chem. Commun.*, 642 (1979), and references therein.

(13) H. V. Gelboin and P. O. P. Ts'o, Eds., "Polycyclic Aromatic Hydrocarbons and Cancer", Vol. 1, Academic Press, New York, 1978.

(14) M. Hayat, G. Mathé, E. Chenu, M. M. Janot, P. Potier, N. Dat-Xuong, A. Cave, T. Sévenet, C. Kan-Fan, J. Poisson, J. Miet, J. Le Men, F. Le Goffic, A. Gouyette, A. Ahnod, L. K. Dalton, and T. A. Connors, *Biomedicine*, **21**, 101 (1974).

(15) F. U. Ahmed, T. Rangarajan, E. J. Eisenbraun, G. W. Keen, and M. C. Hamming, *Org. Prep. Proc. Int.*, **7**, 267 (1975).

(16) Entry 5 → benz[*a*]anthracene (58%, mp 156–158 °C, lit. mp 158–159 °C); entry 7 → dibenz[*a,c*]anthracene (45%, mp 207 °C, lit. mp 205 °C); entry 11 → dibenz[*a,h*]anthracene (85%, mp 267–268 °C, lit. mp 262–263 °C); entry 12 → benzo[*a*]naphthacene (45%, mp 266–267 °C, lit. mp 263–264 °C). All literature melting points refer to those given in E. Clar, "Polycyclic Hydrocarbons", Vol. 2, Academic Press, New York, 1964.

(17) B. J. Wakefield, "The Chemistry of Organolithium Compounds", Pergamon Press, Oxford, 1974, p 44.

(18) R. J. Sundberg, and H. F. Russell, *J. Org. Chem.*, **38**, 3324 (1973); A. B. Levy, *ibid.*, **43**, 4684 (1978).

(19) 3-Lithiated *N,N*-diethyl, *N,N*-diisopropyl, and *N*-phenyl isonicotinamides are generated using the standard conditions[3b,4c] as evidenced by D_2O quenching experiments (55–100% incorporation): S. O. de Silva and V. Snieckus, unpublished results. For work on the corresponding 2-oxazolinopyridine, see A. I. Meyers and R. Gabel, *Tetrahedron Lett.*, 227 (1978).

(20) We thank Professor Joule, Manchester University, for informing us of a new, substantially different route to compounds of the type **11** completed in his laboratory: D. A. Taylor, M. M. Baradarani, S. J. Martinez, and J. A. Joule, *J. Chem. Res.*, in press; see also *Int. Congr. Heterocycl. Chem., 7th, 1979*, Abstr. T1445P4 (1979).

(21) W. B. Manning, G. M. Muschik, and J. E. Tomaszewski, *J. Org. Chem.*, **44**, 699 (1979).

(22) Identity was established by melting point, mixture melting point, and spectral comparison with an authentic sample kindly provided by Drs. J. Bergman and R. Carlsson, Royal Institute of Technology, Stockholm, Sweden.

(23) **6b:** mp 210 °C lit. mp 209–211 °C [L. K. Dalton, S. Demerac, B. C. Elmes, J. W. Loder, J. M. Swan, and T. Teitei, *Aust. J. Chem.*, **20**, 2715 (1967)]. **6c:** mp 239–240 °C. **6c** was accompanied by a minor amount (5%) of ellipticine.

(24) Compounds **12a** (mp 153 °C) and **12b** (mp 216–217 °C) were characterized by melting point, mixture melting point, and IR, NMR, and mass spectral comparison with authentic samples: J. A. Campbell, R. W. Koch, J. V. Hay, and M. A. Ogliaruso, *J. Org. Chem.*, **39**, 146 (1974); J. Rigaudy, M.-C. Perlat, D. Simon, and N. K. Cuong, *Bull. Soc. Chim. Fr.*, 493 (1976). We thank Dr. S. O. de Silva for these results.

(25) Related ortho-lithiated arylcarbinol amine anions have been generated from reaction of *N,N*-dimethylbenzamides with 2 equiv of alkyllithium reagents: L. Barsky, H. W. Gschwend, J. McKenna, and H. R. Rodriguez, *J. Org. Chem.*, **41**, 3651 (1976). See also D. W. Slocum and W. Achermann, *J. Chem. Soc., Chem. Commun.*, 968 (1974).

(26) P. G. Sammes and D. J. Dodsworth, *J. Chem. Soc., Chem. Commun.*, 33 (1979).

(27) We have also found that anthraquinone is produced in 74% yield when a solution of ortho-lithiated *N,N*-diethylbenzamide is warmed to room temperature overnight: S. O. de Silva and V. Snieckus, unpublished results; see also D. W. Slocum and P. L. Gierer, *J. Org. Chem.*, **41**, 3668 (1976). For an analogous dimerization of ortho-lithiated benzoate anion, see W. E. Parham and Y. A. Sayed, *ibid.*, **39**, 2051 (1974).

(28) We gratefully acknowledge the financial support of the Natural Sciences and Engineering Research Council of Canada.

M. Watanabe, V. Snieckus*

Guelph-Waterloo Centre for Graduate Work in Chemistry
University of Waterloo, Waterloo, Ontario N2L 3G1, Canada

Received October 1, 1979

Determination of Rotational Correlation Time from Perturbed Angular Correlations of γ Rays: Apomyoglobin Reconstituted with ^{111}Indium(III) Mesoprotoporphyrin IX[1]

Sir:

Currently popular methods for determining macromolecular rotational correlation time, τ_{rot}, each possess major drawbacks. Fluorescence depolarization (FD)[2] and depolarized light scattering[3] require transparent media. Electron paramagnetic resonance (EPR) "spin labeling"[4] and FD require introduction of an artificial reporter group, linked by one or more flexible bonds to the macromolecule. EPR line-shape analysis is complicated by inhomogeneous (nitrogen hyperfine coupling) broadening, nitrogen nuclear relaxation, and **g**-tensor nonaxial symmetry.[5] NMR relaxation time analysis is complicated by competing relaxation pathways,[6,7] internuclear distance uncertainty,[8] pulse imperfections, and multiexponential relaxation.[9,10]

In contrast, time-resolved emission anisotropy from a perturbed γ-γ angular correlation (PAC) experiment can provide direct determination of τ_{rot},[11-16] in opaque media (even in vivo[17]), at 10^{-12} M, without flexible and/or bulky reporter groups. Unfortunately, previous PAC determinations of τ_{rot} have been complicated by multiple τ_{rot} processes.[14-16] In this communication, we report the PAC results from the successful reconstitution of indium-111 mesoprotoporphyrin IX, In-MPP (see ref 18 for synthesis), into apomyoglobin by the procedure of Srivastava[19] to give a singly labeled protein with unique conformation and chemical form.[20]

The crystal and molecular structure of the closely related tetraphenylporphinatoindium(III) chloride[21] strongly suggests that In-MPP-myoglobin should be isostructural with the Fe(II) heme in deoxymyoglobin or deoxyhemoglobin, because the indium atom is displaced above the mean porphyrin plane by the same distance (0.6 Å) as is Fe(II) in the native proteins.

0002-7863/80/1502-1460$01.00/0

Table I. Measured and Calculated Properties of Native and Reconstituted Myoglobin

mol wt	T, °C	viscosity, cP	$D_{tr(20°,w)}$	r, Å, from eq 3	τ_{rot}, ns eq 1	eq 2[a]	fluorescence	PAC[b]	$(\omega_0/2\pi)$, MHz	δ[b]	quadrupolar asymmetry parameter[b]
17 000	25	0.0089[c]			4.5	6.2	8.3[e]				
17 000	20	0.0100[c]	11.3×10^{-7} [d]	19.0	5.1	7.1					
17 000	12	0.0128[f]			6.5	9.4	11.9[g]	16^{+3}_{-2}	25 ± 3[h]	0.42 ± 0.04[i]	0.00 ± 0.01[j]

[a] Molecular radius is assumed constant with temperature. [b] This work. [c] Water. [d] "Handbook of Biochemistry—Selected Data for Molecular Biology", H. A. Sober, Ed., Chemical Rubber Co., Cleveland, Ohio, 1970, p C10. [e] J. Yguerabide.[2] [f] Measured for In-MPP-Mb solution. [g] Calculated from value at 25 °C, assuming constant molecular radius. [h] 36 ± 4 MHz for solid sample. [i] 0.37 ± 0.03 for solid sample. [j] 0.01 ± 0.01 for solid sample.

In any case, the PAC τ_{rot} should reflect rotational motion *at the central metal atom*, the first such probe for a heme protein.

PAC apparatus, measurements, and data reduction are as reported in ref 14. The time dependence of the perturbation factor, $G_2(t)$, is fitted to an adiabatic motional model,[12] assuming nonaxial electric field gradient (represented by a quadrupolar asymmetry parameter), a finite spread in quadrupole frequency (characterized by Gaussian distribution parameter, δ), with correction for solid angle effects and finite instrumental time resolution. The results are shown in Figure 1 and summarized in Table I.

Two features demonstrate self-consistency in the PAC analysis. First, the quadrupolar asymmetry parameter is found to be 0, as expected for the square pyramidal metalloporphyrin geometry.[21] Second, the nonmotional parameters (last three columns of Table I) are similar for solution and solid samples.

The two basic ways for computing τ_{rot} (for comparison to the 16-ns experimental PAC value) derive from the Stokes-Einstein relation[22]

$$\tau_{rot} = V\eta/kT \quad (1)$$

in which V is molecular volume, η is viscosity, k is Boltzmann's constant, and T is absolute temperature. In the first method, molecular volume is computed directly from the molecular weight M and the partial specific volume $\bar{v}$

$$\tau_{rot} = (\bar{v}M/N_0)(\eta/kT) \quad (2)$$

where N_0 is Avogadro's number (see Table I, column 6). In the second method, molecular radius, r, is computed from the *translational* diffusion coefficient, D_{tr}

$$r = kT/6\pi\eta D_{tr} \quad (3)$$

and the molecular volume $(4\pi r^3/3)$ substituted into eq 1 (see Table I, column 7). The second method is probably more accurate, since it incorporates (via D_{tr}) any additional water of hydration bound to the macromolecular surface.

The 16-ns τ_{rot} value determined from PAC is larger than that calculated from eq 3, possibly because (a) myoglobin may be nonspherical in solution[13,23] and (b) the calculated value was obtained by extrapolation from 20 to 12 °C assuming constant r, whereas r may well increase at lower temperature from increased hydration (a 21% increase would account for the discrepancy). In corroboration of these notions, the FD value is also larger than that calculated from eq 3, and the difference between the PAC and FD τ_{rot} values may reflect a different rate of rotational diffusion of the principal axis for each interaction. (The fluorescent axis likely lies in the macrocyclic plane of the fluorescent label, while the PAC axis should be perpendicular to the porphyrin plane.)

Future experiments with the 397-keV ^{111m}Cd nucleus will establish the importance of aftereffects of electron capture from the ^{111}In to ^{111}Cd transition.[24] The present preliminary results should, however, suffice to demonstrate the potential value of PAC measurements for determination of macromolecular rotational correlation times.

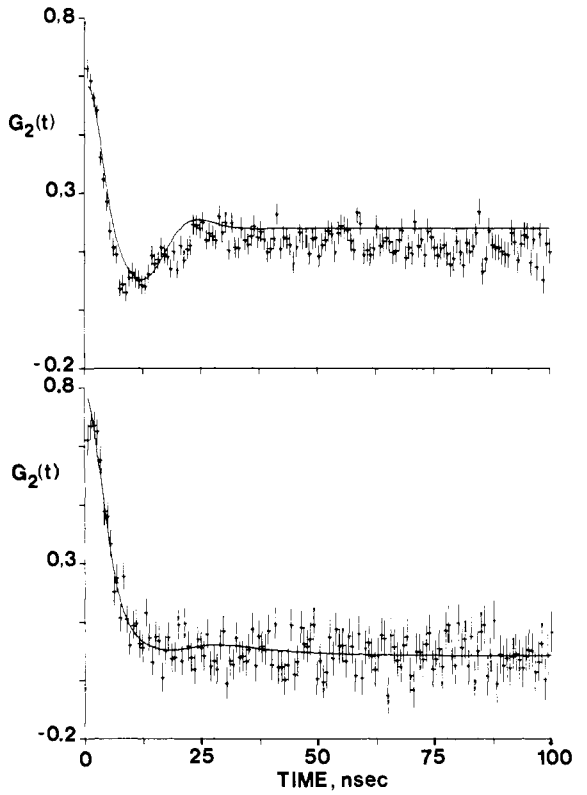


Figure 1. Perturbation factors and associated best theoretical fits for In-MPP-myoglobin: top, solid; bottom, solution (0.05 M phosphate, pH 7.0). T = 12 °C. Time scale is 0.69 ns/channel.

Acknowledgment. The authors thank Professor D. E. Brooks for providing viscosity measurements at 12 °C.

References and Notes

(1) Work was supported by grants from the Natural Sciences and Engineering Research Council of Canada (A.G.M., P.W.M.), University of British Columbia (A.G.M., P.W.M.), and the Alfred P. Sloan Foundation (A.G.M.).
(2) J. Yguerabide, *Methods Enzymol.*, **26** (C), 528 (1972).
(3) D. R. Bauer, S. J. Opella, D. J. Nelson, and R. Pecora, *J. Am. Chem. Soc.*, **97**, 2580 (1975)
(4) L. J. Berliner, Ed., "Spin Labeling: Theory and Applications", Vol. 1 and 2, Academic Press, New York, 1976 and 1979.
(5) D. D. Thomas, L. R. Dalton, and J. S. Hyde, *J. Chem. Phys.*, **65**, 3006 (1976).
(6) W. E. Hull and B. D. Sykes, *J. Mol. Biol.*, **98**, 121 (1975).
(7) J. S. Noggle and R. E. Schirmer, "The Nuclear Overhauser Effect", Academic Press, New York, 1971.
(8) K. Dill and A. Allerhand, *J. Am. Chem. Soc.*, **101**, 4376 (1979).
(9) L. G. Werbelow and A. G. Marshall, *Mol. Phys.*, **28**, 113 (1974).
(10) L. G. Werbelow, *J. Chem. Phys.*, **70**, 5381 (1979).
(11) A. G. Marshall, "Biophysical Chemistry", Wiley, New York, 1978, pp 535–539.
(12) A. G. Marshall and C. F. Meares, *J. Chem. Phys.*, **56**, 1226 (1972).
(13) A. G. Marshall, L. G. Werbelow, and C. F. Meares, *J. Chem. Phys.*, **57**, 364, 4508 (1972).

(14) P. W. Martin, C. A. Kalfas, and K. Skov, *J. Chem. Phys.*, **69**, 1958 (1978).
(15) R. Bauer, P. Limkilde, and J. T. Johansen, *Biochemistry*, **15**, 334 (1976).
(16) J. W. Ball and M. Kaplan, *J. Chem. Phys.*, **70**, 1337 (1979).
(17) D. A. Goodwin, C. F. Meares, and C. H. Song, *Radiology*, **105**, 699 (1972).
(18) K. M. Lee and A. G. Marshall, *J. Labelled Compd. Radiopharm.*, in press.
(19) T. S. Srivastava, *Biochim. Biophys. Acta*, **491**, 599 (1977).
(20) K. M. Lee, M.S. Thesis, University of British Columbia, 1979.
(21) R. G. Ball, K. M. Lee, A. G. Marshall, and J. Trotter, *Inorg. Chem.*, in press.
(22) Reference 11, pp 197–201, 714–721.
(23) S. E. V. Phillips, *Nature (London)*, **273**, 247 (1978).
(24) C. F. Meares, R. G. Bryant, J. D. Baldeschwieler, and D. A. Shirley, *Proc. Natl. Acad. Sci. U.S.A.*, **64**, 1155 (1969).
(25) Alfred P. Sloan Research Fellow, 1976–1980.

Alan G. Marshall,*[25] K. M. Lee
Department of Chemistry, University of British Columbia Vancouver, British Columbia V6T 1W5, Canada

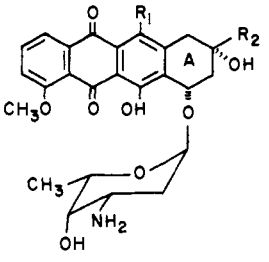
Peter W. Martin*
Department of Physics, University of British Columbia Vancouver, British Columbia V6T 1W5, Canada

Received September 4, 1979

Structures of Novel Anthracycline Antitumor Antibiotics from *Micromonospora peucetica*

Sir:

In our continuing search for new natural[1,2] and semisynthetic[3] analogues of the useful anticancer drugs daunorubicin (**1a**)[4] and doxorubicin (**1b**),[5] we have examined the fermentation broths of *Micromonospora peucetica* n. sp. This has given an anthracycline complex whose glycosidic constituents represent a novel structural class within the family of doxorubicin related anthracyclines. In this communication we report the isolation and structure determination of the new, biologically active anthracyclines 11-deoxydaunorubicin (**2**), 11-deoxydoxorubicin (**3**), 11-deoxy-13-dihydrodaunorubicin (**4**), and 11-deoxy-13-deoxodaunorubicin (**5**).

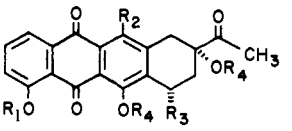


1a: R_1 = OH; R_2 = $COCH_3$
1b: R_1 = OH; R_2 = $COCH_2OH$
2: R_1 = H; R_2 = $COCH_3$
3: R_1 = H; R_2 = $COCH_2OH$
4: R_1 = H; R_2 = $CHOHCH_3$
5: R_1 = H; R_2 = CH_2CH_3

Purification of the anthracycline complex (6 g), isolated in the usual way,[2] on a silica gel column[6] gave **2** (0.4 g) ($C_{27}H_{29}NO_9 \cdot HCl$[7], mp 175–176 °C dec, $[\alpha]^{23}_D$ +139°), **3** (0.6 g) ($C_{27}H_{29}NO_{10} \cdot HCl$, mp 171–173 °C dec, $[\alpha]^{23}_D$ +111°), **4** (0.2 g) ($C_{27}H_{31}NO_9 \cdot HCl$, mp 163–164 °C dec, $[\alpha]^{23}_D$ +107°), and **5** (0.2 g) ($C_{27}H_{31}NO_8 \cdot HCl$, mp 142–146 °C dec).

The UV and visible spectra [λ_{max} (MeOH) 228, 260, 418 nm] suggested the presence of the same hydroxyanthraquinone chromophore in all four compounds,[8] while the IR (KBr) indicated the presence[9] of both nonhydrogen bonded (1670 cm^{-1}) and hydrogen bonded (1625 cm^{-1}) quinone carbonyl groups and an additional carbonyl function in **2** (1710 cm^{-1}) and **3** (1725 cm^{-1}).

Mild acid hydrolysis (0.2 N HCl, 100 °C, 1 h) of the four glycosides afforded the same amino sugar, identified as daunosamine[10] by direct comparison with an authentic sample, and four aglycones differing only in the side chain. Acid hydrolysis of **2** yielded the aglycone **6**: $C_{21}H_{18}O_7$; mp 213–215 °C; IR (KBr) 1710 (CO), 1670 and 1620 cm^{-1} (quinone bands); ^1H NMR ($CDCl_3$) δ 2.42 (s, 3 H, $COCH_3$), 4.02 (s, 3 H, $ArOCH_3$), 5.33 (br, 1 H, C-7), 7.25–7.73 (m, 4 H, ArH), 13.60 (s, 1 H, ArOH). Upon acetylation (Ac_2O, pyr), **6** gave the corresponding tri-*O*-acetyl derivative **7**: $C_{27}H_{24}O_{10}$; mp 120–124 °C dec; IR (KBr) 1775 (phenolic Ac), 1735–1725 cm^{-1} (aliphatic Ac and CO); ^1H NMR ($CDCl_3$) δ 2.05 and 2.25 (two s, 9 H, C-7 OAc, C-9 OAc, and $COCH_3$), 2.48 (s, 3 H, ArOAc), 6.45 (dd, 1 H, C-7), 7.30–8.00 (m, 4 H, ArH). This confirmed the presence of one phenolic OH and two OH's on the alicyclic ring.



6: R_1 = CH_3, R_2 = R_4 = H, R_3 = OH
7: R_1 = CH_3, R_2 = H, R_3 = OAc, R_4 = Ac
8: R_1 = CH_3, R_2 = R_3 = OH, R_4 = H
9: R_1 = CH_3, R_2 = R_3 = R_4 = H
10: R_1 = R_2 = R_4 = H, R_3 = OH

Thus the chemical and spectral properties of **6**, which indicated the presence of an anthraquinone chromophore bearing both an OH and an OCH_3, and an alicyclic ring with one acetyl group and two OH's, showed a close relationship to daunomycinone (**8**).[4] Furthermore Zn dust distillation of **6** and **8** gave the same benz[*a*]anthracene, establishing a linear tetracyclic system in **6**.

Catalytic hydrogenolysis (5% $Pd/BaSO_4$, H_2O, 1 h) of **2** afforded daunosamine and a new aglycone **9**: $C_{21}H_{18}O_6$; mp 186–189 °C; IR (KBr) 1710 (CO), 1670 and 1625 cm^{-1} (quinone bands); ^1H NMR ($CDCl_3$) δ 2.25 (s, 3 H, $COCH_3$), 4.02 (s, 3 H, $ArOCH_3$), 7.10–7.90 (m, 4 H, ArH), 13.60 (s, 1 H, ArOH). This showed that the sugar moiety was attached to a benzylic position. Compound **9** can also be obtained by catalytic hydrogenolysis of **6** (5% $Pd/BaSO_4$, dioxane, 1 h).

Demethylation ($AlBr_3$, CH_2Cl_2, 40 °C, 1 h) of **6** yielded **10**: $C_{20}H_{16}O_7$; mp 140–142 °C; ^1H NMR ($CDCl_3$) δ 2.39 (s, 3 H, $COCH_3$), 5.30 (br, 1 H, C-7), 7.25–7.80 (m, 4 H, ArH), 11.87 and 12.57 (two s, 2 H, ArOH). The presence in the IR (KBr) of **10** of nonhydrogen-bonded (1670 cm^{-1}) and hydrogen-bonded (1620 cm^{-1}) quinone carbonyl groups confirmed[10] that the methoxy and hydroxy substituents had to both be peri to the same quinone carbonyl group.

We next addressed the substitution pattern and the stereochemistry of ring A. The ^1H NMR and ^{13}C NMR spectra of **6**, when compared with those of daunomycinone (**8**),[4,11] indicated the presence of a quaternary carbon bearing hydroxyl and acetyl groups. The cis configuration of the two aliphatic OH's was shown by the preparation from **6** [$CH_3C(OCH_3)_2CH_3$, *p*-TsOH, dioxane, 72 h] of the corresponding *O*-isopropylidene derivative **11**: $C_{24}H_{22}O_7$; mp 84–88 °C; ^1H NMR ($CDCl_3$) δ 1.18 and 1.55 (two s, 6 H, $>C(CH_3)_2$), 2.42 (s, 3 H, $COCH_3$), 4.01 (s, 3 H, $ArOCH_3$), 7.25–7.78 (m, 4 H, ArH), 13.10 (s, 1 H, ArOH). Acetylation of **11** yielded a mono-*O*-acetyl derivative (**12**): $C_{26}H_{24}O_8$; mp 157–160 °C; IR (KBr) 1770 (ArOAc), 1710 (CO), 1670 cm^{-1} (quinone band); ^1H NMR ($CDCl_3$) δ 1.09 and 1.42 (two s, 6 H, $>C(CH_3)_2$), 2.38 and 2.50 (two s, 6 H, ArOAc, $COCH_3$), 4.00 (s, 3 H, OCH_3), 5.25 (br, 1 H, C-7), 7.25–7.90 (m, 4 H, ArH). When **12** was subjected to mild acid hydrolysis [$(CH_3)_2CO$, H_2O, H_2SO_4, 0.5 h] it gave **13**: $C_{23}H_{20}O_8$; mp

0002-7863/80/1502-1462$01.00/0