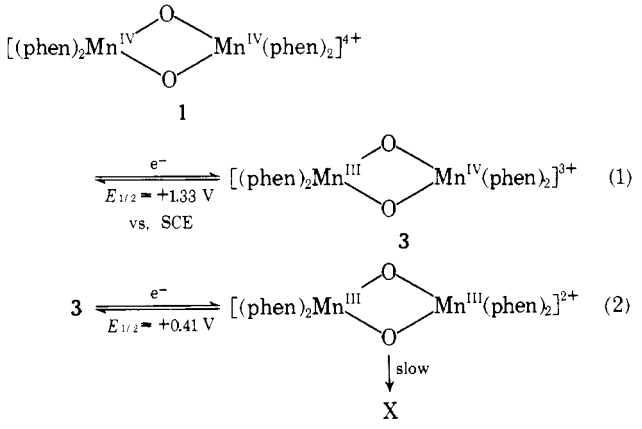
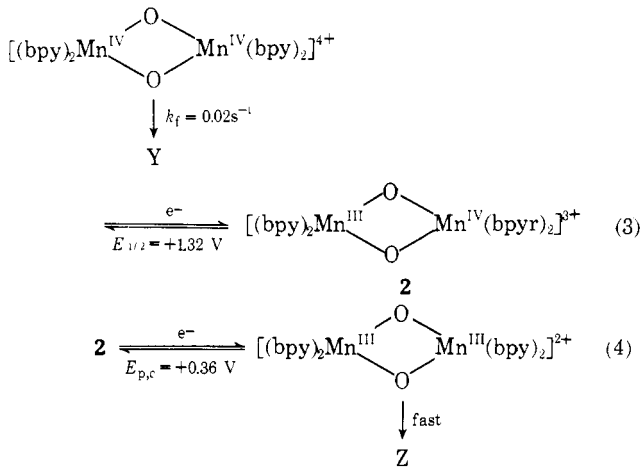
Scheme I. Redox Reactions for Di-μ-oxo Bridged Binuclear Manganese Complexes in Acetonitrile (0.1 M Tetrapropylammonium Perchlorate) (TPAP) at a Platinum Electrode (Scan Rate, 0.1 V/s)

A. 1,10-Phenanthroline Complexes



B. 2,2'-Bipyridyl Complexes

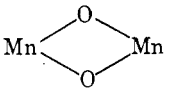


pared to 2.53 μ_B (uncorrected) for the solid by the Guoy method at room temperature[12] and for **3**, μ_{eff} = 2.26 ± 0.08 μ_B.[19,20] The reduced magnetic moments that are observed relative to those for the spin-only condition support the conclusion that the di-μ-oxo bridged species are stable in solution.

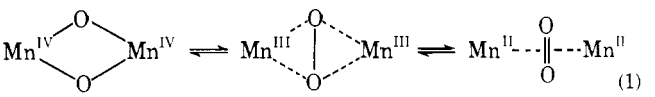
Of the two complexes, the mixed-oxidation state bipyridyl complex (**2**) is slightly easier to oxidize and more difficult to reduce than the corresponding 1,10-phenanthroline derivative. Also, the coupled chemical reactions occur at a faster rate for the bipyridyl complexes. This change in chemical and electrochemical reactivity can be accounted for on the basis of the "floppy" bipyridyl ligand compared to the rigid structure of 1,10-phenanthroline.

A noteworthy feature of the redox chemistry for the di-μ-oxo bridged complexes is the extremely positive potentials for the reversible one-electron (IV-IV)/(IV-III) couples. The 1,10-phenanthroline complex, **1**, appears especially attractive for use as a reagent for one-electron oxidations in nonaqueous media.

The electrochemical data for the



linkage in these complexes confirm that discrete one-electron steps are stabilized. Unfortunately, the stability of this linkage (in association with the bipyridyl and 1,10-phenanthroline ligands) implies that the tautomeric equilibria in this medium must lie far to the left;



the Mn_2(III, III)-peroxo and Mn_2(II, II)-oxygen species have not been detected. Furthermore, preliminary infrared data indicate, as expected from electrostatics, that the Mn-O bond is stronger for the Mn_2(IV, IV) species than for the Mn_2(III, IV) species. From the data presented, evolution of oxygen from di-μ-oxo bridged binuclear manganese(IV) complexes by reaction 1 must involve a displacement of oxide by some other ligand. This possibility is currently under investigation, as is the use of other ligands to promote a shift of the equilibria to the right in eq 1.

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(19) μ_{eff} for **2** is 2.82 ± 0.11 μ_B (corrected) and for **3** is 2.51 ± 0.08 (corrected). Corrections for diamagnetism made according to B. N. Figgis and J. Lewis, *Mod. Coord. Chem.* (1960).
(20) The magnetic moments are for the dimeric groups. On a per metal basis: for **2**, μ_{eff} = 1.81 ± 0.07 μ_B per Mn, and for **3**, μ_{eff} = 1.56 ± 0.05 μ_B per Mn.

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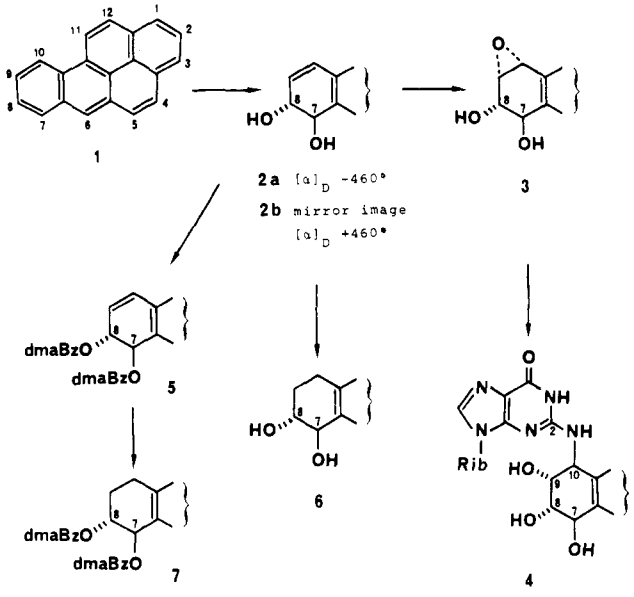
Absolute Configuration of a Ribonucleic Acid Adduct Formed in Vivo by Metabolism of Benzo[*a*]pyrene

Sir:

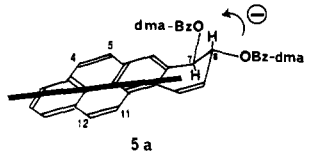
Incubation of the potent carcinogen benzo[*a*]pyrene (**1**) with bovine bronchial explants followed by extraction and digestion of the cellular RNA led to the isolation of an adduct **4**[1,2] which, by high pressure liquid chromatographic (HPLC) analysis, was shown to correspond to one of the diastereoisomeric in vitro products resulting from reaction of (±)-**3** with poly(G).[3,4] Spectral and chemical data established that the in vivo adduct is represented either by structure **4** or its mirror image at chiral centers C-7 through C-10. The following data now show that the absolute configuration is as shown in **4**. This work, together with our previous studies on the adduct formed between 7,12-dimethylbenz[*a*]anthracene 5,6-oxide and poly(G),[5] constitutes the first full structure determinations of both in vivo and in vitro[5] products derived from the carcinogenic polycyclic aromatic hydrocarbons.

In the present study, the absolute configuration of **2a** is derived from the exciton split CD spectrum[6] of its 7,8-bis-*p*-dimethylaminobenzoate, **5**, which is corroborated by the split CD of its hydrogenation product **7**.[7,8]



Racemic **2**[9] was resolved by HPLC[10] of the diastereoisomeric menthoxyacetates, prepared by reaction with (−)-menthoxyacetyl chloride,[11] and subsequent release of the two enantiomeric free dihydrodiols[12] by bubbling ammonia at 0 °C for 1 h through a methanol solution of the esters.

All the following UV, CD, and ^{1}H NMR spectral measurements were obtained in chloroform. The UV spectrum of the dma-dibenzoate, **5** (Figure 1), prepared from ca. 3 mg of (−)-**2**, shows that the conspicuous dma-dibenzoate longitudinal polarization band at 316 nm is located between the pyrenoid bands at 284–295 nm (longitudinal, see **5a**,[13,14]) and at 334–370 nm (transverse, running through C-4/C-5 and C-11/C-12 in **5a**); the *p*-dimethylamino substituent was chosen[15] so as to minimize the interaction between the dibenzoate and pyrenoid transitions.



5a

The CD curve of **2a** is weak in comparison with its dma-dibenzoate, **5** (Figure 1), which shows strong peaks at 322 ($\Delta\epsilon$ − 77.9) and 292 ($\Delta\epsilon$ + 73.7). Although the difference in the CD spectra above 340 nm indeed shows that the pyrenoid chromophore is interacting with the benzoate groups, it can be safely assumed that the strong intensities and locations of the extrema at 322 and 292 nm[16] arise mainly from coupling between the two dma-benzoate groups. The ^{1}H NMR spectrum of **5** shows that its flexible terminal ring adopts conformation **5a** where the two dibenzoates are *e'*: 7-H, 7.02 ppm, d, J = 8 Hz; and 8-H, 6.16 ppm, two multiplets split by 8 Hz. Molecular models show that in conformation **5a** there is little or no interaction between the pyrenoid transitions (longitudinal and transverse) and the dibenzoate transitions because they either lie in close-to-parallel planes, e.g., longitudinal pyrenoid and 8-dma-benzoate transitions, or because the two transitions intersect (lie in the same plane), e.g., longitudinal pyrenoid and 7-dma-benzoate transition.

Thus the CD splitting is interpreted as being caused mostly by coupling between the two dma-benzoate chromophores,

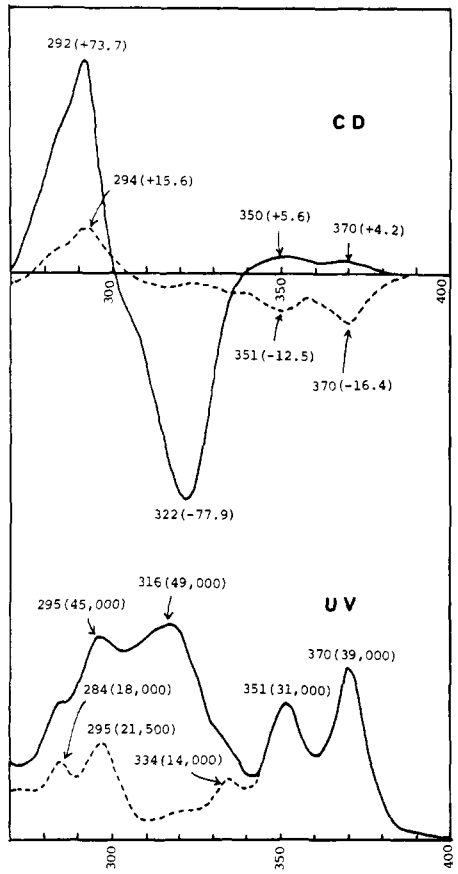
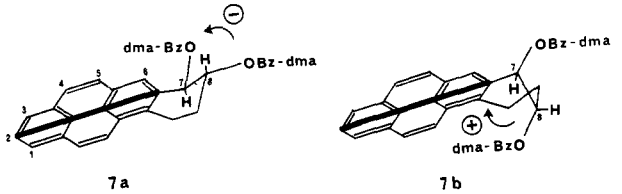


Figure 1. Measurements in $CHCl_3$. UV and CD curves of dihydrodiol **2a** (- - -) and its dma-dibenzoate **5** (—). Only regions above 270 nm are shown due to difficulty in CD measurements. The absorption, centered at 295 and 351 nm, is due to the longitudinal and transverse transitions of the dihydrobenzo[*a*]pyrene moiety, respectively.

which is negative, and this leads to the absolute configuration **5a** or **5**.

The tetrahydrodiol **6** and its dma-dibenzoate **7** were obtained by reduction of **2a** and **5**, respectively. Here the dma-dibenzoate (316 nm) and pyrene (316–347 nm) transitions partly overlap (Figure 2). Again a split CD is seen at 321/295 nm, the interpretation of which is basically similar to that presented for the dihydrodiol case. However, because the pyrene ca. 281 nm longitudinal transition runs through C-2 and C-7 rather than being slanted as in **5a**, there is no coupling between this transition and the C-7 dma-benzoate transition (see **7**). The ^{1}H NMR coupling constant between 7-H (6.85 ppm, d) and 8-H (5.64 ppm, m) is 6 Hz, which shows that conformation **7a** having diequatorial dma-dibenzoates is favored over **7b**.[17] In **7a** the pyrene longitudinal and 8-benzoate transitions lie on roughly parallel planes and therefore the interaction is small. Similar to the previous case, the CD spectrum can be interpreted as mainly arising from two coupled benzoate interactions, and this leads to the absolute configuration **7**.



7a 7b

Racemic **2** was oxidized to (±)-**3**, and the latter reacted with poly(G). Hydrolysis of the modified nucleic acid gave two major products when separated by HPLC, the CD of which

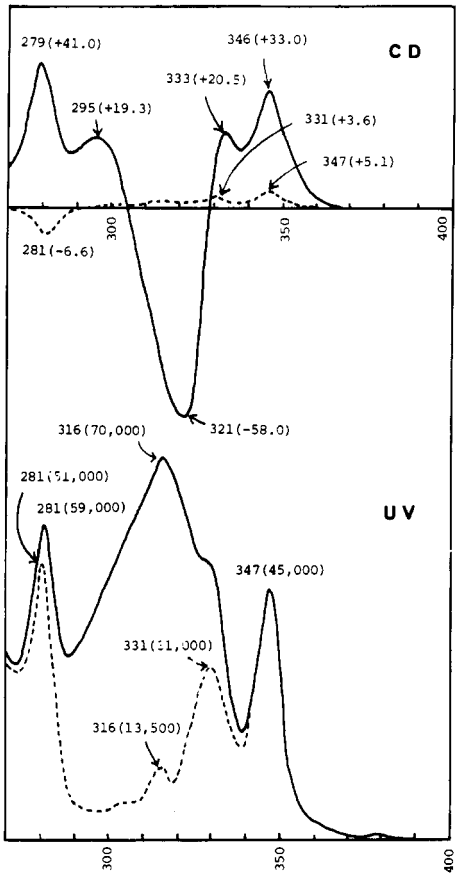


Figure 2. Measurements in $CHCl_3$. UV and CD curves of tetrahydrodiol **6** (- - -) and its dma-dibenzoate **7** (—). Only regions above 270 nm are shown due to difficulty in measurements. The absorption centered at 281 and 331 nm are due to the longitudinal and transverse transitions of the pyrene moiety, respectively.

indicated a diastereoisomeric relationship.[1,3] The later eluting product (designated peak 3 in ref 1) and the in vivo product were identical. We have now separately converted **2a** and **2b** into the guanosine adducts **4** via oxidation to **3,** reaction with poly(G), and hydrolysis, and found that the product derived from **2a** corresponded to the in vivo peak **3** material. Hence the absolute configuration of the in vivo product is represented by **4.**

A second in vivo product was found which corresponded to the minor component (designated peak 2 in ref 1) resulting from hydrolysis of the racemic **3**-modified poly(G).[1] Recent HPLC studies[18] indicate that this in vivo product is derived from the same enantiomer of **3** and that it is probably the corresponding 9,10-cis addition product.[4,19]

The formation of adducts from only one enantiomer of **3** in vivo[1] is consistent with recent evidence that only **3** derived from **2a** is formed during the in vitro microsomal oxidation of **1.**[20] Nucleic acids themselves are highly asymmetric and hence, the absolute stereochemistry of these in vivo adducts is intimately related to their interaction with and modification of nucleic acid structure.[21]

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(8) The absolute configurations of dihydroanthracene-1,2-diols have been determined by related methods: M. N. Akhtar, D. R. Boyd, N. J. Thompson, M. Koreeda, D. T. Gibson, V. Mahadeven, and D. M. Jerina, *J. Chem. Soc., Perkin Trans. 1,* 2506 (1975).

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(10) LiChrosorb Si-60, 20μ, 50 cm × 0.6 cm column, 300–350 psi, elution with 1:4 hexane–CH_2Cl_2, monitored at 332 nm. The two products were recrystallized from ether–petroleum ether, mp 153–154 °C, $[\alpha]_D$ −300° and mp 180–180.5 °C, $[\alpha]_D$ +160°. The NMR and UV spectra of both isomers were virtually identical and consistent with the proposed structures.

(11) J. Booth, E. Boyland, and E. E. Turner, *J. Chem. Soc.*, 2808 (1950).

(12) The menthoxy derivatives with $[\alpha]_D$ values of −300° and +160° gave, after hydrolysis and recrystallizations from CCl_4, **2a** $[\alpha]_D$ −460° and **2b** $[\alpha]_D$ +460°, respectively.

(13) H. H. Jaffé and M. Orchin, "Theory and Applications of Ultraviolet Spectroscopy", Wiley, 1962, p 334.

(14) In view of the effect of the 9-ene, the pyrenoid longitudinal transition, does not run through C-2 and C-7; it is drawn slanted towards the 9-ene, but the exact location of it is unknown.

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(16) Values for a typical isolated *vic*-dma-dibenozate system are exemplified by 5α-cholestane-2β,3β-diol bis-*p*-dma-dibenzoate (Figure 8 in ref 6c), $\Delta\epsilon_{320}$ + 61.7 and $\Delta\epsilon_{295}$ −33.2 in ethanol, which adopts a dihedral angle of ca. 60°. The imbalance in the intensities of the two extrema is rationalized by the shape of the electronic transitions.[6c] In the case of the present dihydrodiol dma-dibenzoate, **5,** there is clearly interaction between the dma-dibenzoate 316-nm absorption and the pyrenoid 284/295-nm absorption.

(17) The ^{1}H NMR spectrum of **7** at −50 °C remained virtually unchanged from that at ambient temperature, and hence showed that **7b** was either nonexistent or that the **7a** (major) ⇄ **7b** (minor) equilibrium was rapid.

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(21) This work was supported by NIH Grants CA 11572 (K.N.), CA 02332 (I.B.W.), and American Cancer Society Grant BC-132 and NIH Research Contract CP-033385 (R.G.B.).

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The Stereochemistry of Sterols at C-20 and Its Biosynthetic Implications

Sir:

While the three-dimensional character of the dominant sterols[1] in biological systems has been well established in terms of absolute configurations at the various asymmetric centers in the nucleus[2] and more recently at C-24,[3-9] conformational isomerism of the side chain in all sterols[10] and the configuration at C-20 in most of them have remained enigmatic. Rotation about the 17(20)-bond is especially interesting, because in the