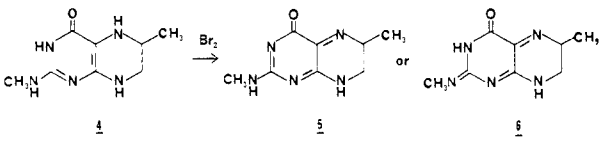
MPH_2, which has been characterized by (1) the resonance of its 4a-carbon in the ^{13}C NMR spectrum (148.0 ppm),[15] (2) its UV spectrum at pH 8.2 (λ_{max} 242 nm (ϵ 6500) 303 (ϵ 8300) 365, sh (ϵ 2800); see also ref 5), and (3) its ability to serve as a cofactor for dihydropteridine reductase (K_m = 35 μM).[6] Chemical oxidation (vide supra) of 6-MPH_4 gives quinonoid-6-MPH_2 with identical properties, indicating that the same species is formed in all cases.

The tautomeric structure of quinonoid-6-MPH_2 was determined by analysis of its 360-MHz NMR spectrum. Figure 1 contrasts the ^1H spectra for the pyrazine ring protons in 6-MPH_4 and quinonoid-6-MPH_2 (generated by Br_2 oxidation) at pD 8.4[16] and 5 °C.[17] The 6-CH_3 resonance has been decoupled from H6 in each case, to facilitate extraction of the apparent first-order coupling constants.

The most striking observation is the downfield shift of 1.08 ppm shown by H6 upon oxidation, while the H7 axial and H7 equatorial protons are shifted downfield by only 0.27 and 0.18 ppm, respectively. Our interpretation of this result is that H6 in quinonoid 6-MPH_2 is adjacent to an imine nitrogen,[25] whereas the protons at C7 are not; that is the para quinonoid (**1** or **3**) is implied, and the ortho tautomer (**2**) is excluded. These chemical shifts do not vary upon changing pD to 7.5 or 6.8, obviating protonation at N5 of quinonoid-6-MPH_2 as the source of this shift.[26] Bromine oxidation of *cis*-6,7-dimethyltetrahydropterin (6,7-$DMPH_4$) and 6-methyltetrahydrolumazine (6-MLH_4)[27] to their quinonoid forms induces very similar shifts at H6 ($\Delta\delta$ = +1.11 and +1.06), $H7_{eq}$ ($\Delta\delta$ = +0.25 and +0.15), and $H7_{ax}$ ($\Delta\delta$ = +0.27).

Bromine oxidation of 2-methylamino-6-MPH_4 (**4**) also produces a quinonoid intermediate (**5**) having similar chemical shifts for the pyrazine ring protons (δ 3.26, $H7_{ax}$, 3.60, $H7_{eq}$; 4.18, H6) but



which shows a pronounced difference in its UV absorption spectrum (λ_{max} 245 nm (ϵ 7100), 323 (ϵ 10800)) from that of quinonoid-6-MPH_2, -6,7-$DMPH_2$, or -3,6-$DMPH_2$,[28] all of which have a λ_{max} of 303 nm. This bathochromic shift of 20 nm was first explained by the fact that the amino group is part of an extended conjugation system,[3] i.e., the exocyclic para tautomer (**6**). However, the failure to observe a large chemical shift change for the 2-methylamino protons (δ 2.82 to 2.96) upon oxidation to quinonoid as expected for the exocyclic form (**6**) implies that the endocyclic tautomer (**5**) is formed in this case. However, it is questionable whether extrapolation of the UV data from **5** to the parent pterin is permissible owing to the perturbation of the tautomeric equilibrium by methyl substitution.[29]

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Registry No. 1, 83650-46-8; **3**, 83650-48-0; **4**, 67129-03-7; **5**, 83650-47-9; 6-MPH_4, 942-41-6; *cis*-6,7-$DMPH_4$, 60378-42-9; 6-MLH_4, 83650-49-1; *cis*-6,7-$DMPH_2$, 83650-50-4; 4a-hydroxy-6-methyltetrahydropterin, 83387-39-7.

(16) pD = pH meter reading + 0.40: Glasoe, P. K.; Long, F. A. *J. Phys. Chem.* **1960**, *64*, 188-190.

(17) Chemical shifts and coupling constants (CH_3 decoupled) for Figure 1. 6-MPH_4: δ 1.19 (d, J = 6.4 Hz, CH_3), 3.01 (d of d, $H7_{ax}$, 3.12, (d of d, H6), 3.43 (d of d, $H7_{eq}$, $J_{6,7_{ax}}$ = 8.6 Hz, $J_{6,7_{eq}}$ = 2.8 Hz, $J_{7_{eq},7_{ax}}$ = 12.2 Hz). Quinonoid-6-MPH_2: δ 1.40 (d, J = 6.4 Hz, CH_3), 3.28 (d of d, $H_{7_{ax}}$, 3.61 (d of d, $H7_{eq}$), 4.20 (d of d, H6) $J_{6,7_{ax}}$ = 10.6 Hz, $J_{6,7_{eq}}$ = 6.0 Hz, $J_{7_{eq},7_{ax}}$ = 13.8 Hz). The resonance assigned to H6 in both cases is coupled to C4a in the 4a-^{13}C enriched compound.[15] It is also split by the methyl group at C6 if a coupled spectrum is run. In addition this resonance disappears when the proton at C6 is replaced by deuterium.

(18) Conformational studies on various tetrahydropterins[19-21] and tetrahydrofolates[22,23] have demonstrated that the tetrahydropyrazine ring is in a half-chair conformation. The values of the vicinal coupling constants between the pyrazine protons in quinonoid-6-MPH_2 suggest that the conformation in this ring deviates slightly from the pseudochair structure observed for the tetrahydropterins,[19-21] giving a structure which is flattened at N5[24] and shows an increased preference for the pseudochair in which the 6-CH_3 is equatorial. The same trends in $^3J_{6,7_{ax,eq}}$ are evident in the quinonoids of 6,7-$DMPH_2$ and 6-MLH_2.

(19) Ganguly, A. N.; Bieri, J. H.; Viscontini, M. *Helv. Chim. Acta* **1981**, *64*, 367-372.

(20) Webber, R.; Viscontini, M. *Helv. Chim. Acta* **1975**, *58*, 1772-1780.

(21) Armarego, W. L. F.; Schou, H. *J. Chem. Soc., Perkin, Trans. 1* **1977**, 2529-2536.

(22) Poe, M.; Jackman, L. M.; Benkovic, S. J. *Biochemistry* **1979**, *18*, 5527-5530.

(23) Poe, M.; Benkovic, S. J. *Biochemistry* **1980**, *19*, 4576-4582.

(24) Lambert, J. B. *J. Am. Chem. Soc.* **1967**, *89*, 1836-1840.

(25) For example, the chemical shifts for the methyl protons of *N*-benzylmethylamine and *N*-benzylidinemethylamine are 2.36 and 3.41, respectively. Similarly, the chemical shifts for the methylene protons of *N*-benzyl-*N'*,*N'*-dimethylethylenediamine and *N*,*N'*-dibenzylidineethylenediamine are 2.54 and 3.96, respectively: Sadtler Standard Spectra, Sadtler Research Laboratories, Inc., 1978.

(26) This has been confirmed for quinonoid-6,6,7,7-tetramethylpterin, whose N5 $pK_a \simeq 5.2$ (T. C. Bruice, personal communication).

(27) The chemical shifts and coupling constants at pD 8.4. 6,7-$DMPH_4$: δ 1.08 (d, $CH_3(6)$), 1.09 (d, $CH_3(7)$), 3.19 (d of q, H6), 3.58 (d of q, H7, $J_{6,7}$ = 3.3 Hz, $J_{7,CH_3(7)}$ = 6.7 Hz, $J_{6,CH_3(6)}$ = 6.7 Hz). Quinonoid-6,7-$DMPH_2$: δ 1.21 (d, $CH_3(6)$), 1.24 (d, $CH_3(7)$), 3.87 (d of q, H7), 4.30 (d of q, H6, $J_{7,CH_3(7)}$ = 6.7 Hz, $J_{6,CH3(6)}$ = 6.7 Hz, $J_{6,7}$ = 5.5 Hz). The assignment of the resonances was confirmed by replacing the proton at C6 with a deuterium. 6-MLH_4: δ 1.19 (d, J = 6.4 Hz, CH_3), 2.99 (d of d, $H7_{ax}$), 3.09 (d of d (CH_3 decoupled), H6), 3.46, (d of d, H7, $J_{6,7_{eq}}$ = 2.7 Hz, $J_{6,7_{ax}}$ = 8.6 Hz, $J_{7_{eq},7_{ax}}$ = 12.2 Hz). Quinonoid 6-MLH_2: δ 1.39 (d, J = 6.4 Hz, CH_3), 3.26 (d of d, $H7_{ax}$), 3.61 (d of d, $H7_{eq}$), 4.15 (d of d (CH_3 decoupled), H6, $J_{6,7_{ax}}$ = 10.7 Hz, $J_{6,7_{eq}}$ = 6.3 Hz, $J_{7_{ax},7_{eq}}$ = 14.3 Hz).

(28) Quinonoid-3,6-$DMPH_2$ was too unstable for a ^1H NMR spectrum to be obtained.

(29) Jackman, L. M.; Jen, T. *J. Am. Chem. Soc.* **1975**, *97*, 2811-2818.

H-D Kinetic Isotope Effects of 16 and 22 in the Oxidation of H_2O_2

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In a recent communication we reported a D_2O/H_2O isotope effect of 16.1 for the comproportionation reaction in eq 1.[1] It

$$(bpy)_2(py)Ru^{IV}O^{2+} + (bpy)_2(py)Ru^{II}OH_2^{2+} \rightarrow 2(bpy)_2(py)Ru^{III}OH^{2+} \quad (1)$$

was argued that the origin of the effect was in the proton content of the reagents, which creates a proton demand for the reaction. The direct, outer-sphere electron transfer pathway shown in eq 2 is accessible, but slower (k(25 °C) < 3 × 10^3 M^{-1} s^{-1}) because

$$(bpy)_2(py)Ru^{IV}O^{2+} + (bpy)_2(py)Ru^{II}OH_2^{2+} \rightarrow (bpy)_2(py)Ru^{III}O^{+} + (bpy)_2(py)Ru^{III}OH_2^{3+} \quad (2)$$

of the high-energy nature of the initial products with regard to their proton compositions.[2] Rather, it was argued, a more facile pathway for the system exists in which proton and electron transfer are coupled (eq 3) in a mechanism that could be described as involving "hydrogen atom transfer".

$$(bpy)_2(py)Ru^{IV}{=}O^{2+}, H_2ORu^{II}(py)(bpy)_2^{2+} \rightarrow (bpy)_2(py)Ru^{III}OH^{2+}, HORu^{III}(py)(bpy)_2^{2+} \quad (3)$$

We report here a similar effect in the oxidation of H_2O_2 by both $(bpy)_2(py)Ru^{IV}O^{2+}$ and $(bpy)_2(py)Ru^{III}OH^{2+}$. The reactions occur with the stoichiometries shown in eq 4 and 5. Over the pH range

$$(bpy)_2(py)RuO^{2+} + H_2O_2 \rightarrow (bpy)_2(py)RuOH_2^{2+} + O_2 \quad (4)$$

$$2(bpy)_2(py)RuOH^{2+} + H_2O_2 \rightarrow 2(bpy)_2(py)RuOH^{2+} + O_2 \quad (5)$$

(1) Binstead, R. A.; Moyer, B. A.; Samuels, G. J.; Meyer, T. J. *J. Am. Chem. Soc.* **1981**, *103*, 2897-2899.

(2) Moyer, B. A.; Meyer, T. J. *Inorg. Chem.* **1981**, *20*, 436-444.

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2-10, the rate laws for both reactions (eq 6 and 7) include both pH-dependent and pH-independent terms. Rate constants for the separate pathways have been obtained from kinetics data obtained by using stopped-flow or simple mixing techniques over the pH range 2-10.

$$-d[(bpy)_2(py)RuO^{2+}]/dt = [H_2O_2][(bpy)_2(py)RuO^{2+}](k_1^{IV} + k_2^{IV}[H^+]^{-1}) \quad (6)$$

$$k_1^{IV}(I = 0.1, 25\ °C) = 2.10 \pm 0.07\ M^{-1}\ s^{-1}$$

$$k_2^{IV}(I = 0.1, 25\ °C) = (6.03 \pm 0.35) \times 10^{-8}\ s^{-1}$$

$$-d[(bpy)_2(py)RuOH^{2+}]/dt = [H_2O_2][(bpy)_2(py)RuOH^{2+}](k_1^{III} + k_2^{III}[H^+]^{-1}) \quad (7)$$

$$k_1^{III}(I = 0.1, 25\ °C) = (5.44 \pm 0.06) \times 10^{-2}\ M^{-1}\ s^{-1}$$

$$k_2^{III}(I = 0.1, 25\ °C) = (6.55 \pm 0.15) \times 10^{-9}\ s^{-1}$$

The oxidations involving Ru(III) must proceed via an initial one-electron step, whereas the Ru(IV) oxidations could proceed, at least in principle, via one- or two-electron steps.[1,3] We have been able to demonstrate that the Ru(IV) reactions also involve initial one-electron steps by stopped-flow spectrophotometry. A two-electron mechanism would necessarily involve the formation of $(bpy)_2(py)RuOH_2^{2+}$ as the initial product. However, because of the comproportionation in eq 1, the Ru(II) complex can only be observed as product at high concentrations of H_2O_2 where the rate of oxidation of H_2O_2 exceeds the rate of comproportionation. We find that under the appropriate conditions ($[H_2O_2] = 0.4$ M, $[Ru^{IV}] = 2.5 \times 10^{-5}$ M) the initial product of the reaction is $(bpy)_2(py)Ru^{III}OH^{2+}$.

The most striking observation in our work is that the acid-independent pathways in D_2O as solvent show the existence of H-D isotope effects of a considerable magnitude: for $(bpy)_2(py)RuO^{2+}$ at 25 °C, $k_{H_2O}/k_{D_2O} = 22.1 \pm 0.6$; for $(bpy)_2(py)RuOH^{2+}$, $k_{H_2O}/k_{D_2O} = 16.7 \pm 0.5$. The existence of such dramatic effects is reminiscent of the comproportionation reaction in eq 1. The origin of the effect is probably closely related and is no doubt reflective of a similarity in mechanisms. As shown in eq 8 and 9, simple outer-sphere electron transfer would result in initial

$$(bpy)_2(py)RuO^{2+} + H_2O_2 \rightarrow (bpy)_2(py)RuO^{+} + H_2O_2^{+} \quad (8)$$

$$(bpy)_2(py)RuOH^{2+} + H_2O_2 \rightarrow (bpy)_2(py)RuOH^{+} + H_2O_2^{+} \quad (9)$$

products having nonequilibrium high-energy structures with regard to proton content. On the other hand, as shown in eq 10 and 11,

$$(bpy)_2(py)Ru^{IV}{=}O^{2+} + H_2O_2 \rightleftharpoons (bpy)_2(py)Ru^{IV}{=}O^{2+}, HOOH$$

$$(bpy)_2(py)Ru^{IV}{=}O^{2+}, HOOH \rightarrow (bpy)_2(py)Ru^{III}OH^{2+}, OOH \quad (10)$$

$$(bpy)_2(py)RuOH^{2+} + H_2O_2 \rightleftharpoons (bpy)_2(py)RuOH^{2+}, HOOH$$

$$(bpy)_2(py)RuOH^{2+}, HOOH \rightarrow (bpy)_2(py)RuOH_2^{2+}, OOH \quad (11)$$

proton-coupled electron transfer would result in the appropriate proton composition in the products, but at the cost of a more complex mechanism. In the coupled mechanism, strong electronic interactions may exist between the $Ru^{IV}{=}O$ group and the OH group of H_2O_2, or if electronic coupling is weak, a long-range proton tunneling must occur between redox sites. As yet, the detailed nature of the proton–electron transfer is unclear and may involve, in part, solvent O-H (or O-D) bonds.

The isotope effect data for the inverse acid path support the importance of proton content in determining the redox mechanism. The most straightforward interpretation of the proton dependence is that the pathways involve the oxidation of HO_2^-, as shown in eq 12 and 13, with $(bpy)_2(py)RuO^{2+}$ as oxidant. With this interpretation, k_2^{III} and k_2^{IV} are the product of the acid dissociation constant for H_2O_2, $K_a(H_2O_2)$,[4] and the rate constant for HO_2^- oxidation (k_2^{III}(redox) and k_2^{IV}(redox)). With the value of $K_a(H_2O_2) = 2.28 \times 10^{-12}$ at 25 °C and $I = 0.1$ M, k_2^{III}(redox) $= (2.64 \pm 0.16) \times 10^4\ M^{-1}\ s^{-1}$ and k_2^{IV}(redox) $= (2.87 \pm 0.65) \times 10^3\ M^{-1}\ s^{-1}$. Although the H-D isotope effect for k_2^{IV}(redox) is large, $k_{H_2O/D_2O} = 9.91$, a considerable fraction of the effect is no doubt from the acid–base preequilibrium for H_2O_2 (note that $K_a(H_2O)/K_a(D_2O) = 7.28$),[5] and the reactions with HO_2^- may be outer-sphere, giving HO_2 directly as shown in eq 13.

$$H_2O_2 \xrightleftharpoons{K_a(H_2O_2)} HO_2^- + H^+ \quad (12)$$

$$(bpy)_2(py)RuO^{2+} + HO_2^- \rightarrow (bpy)_2(py)RuO^{+} + HO_2 \quad (13)$$

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Registry No. D_2, 7782-39-0; H_2O_2, 7722-84-1; $(bpy)_2(py)Ru^{III}OH^{2+}$, 75495-07-7; $(bpy)_2(py)Ru^{IV}O^{2+}$, 67202-43-1.

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Longer-Range Chiroptical Effects in Conjugated Cisoid Dienes: Contributions by Homoallylic and Bis-Homoallylic Alkyl Groups[1]

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Although contributions by allylic substituents to the lowest-energy Cotton effects (CEs) of chiral conjugated cisoid dienes in relation to the helicity of the diene have generated considerable interest and debate,[2] chiroptical effects of more remote groups have received only scant attention. In investigating this question, we have found significant CE influences by homoallylic (β) and bis-homoallylic (γ) methyl groups in a pertinent series of *trans*-$\Delta^{1,3}$-hexalins.

Overall, we find that when the group is axial and close enough to one of the double bonds for a through-space interaction with the π or π^* orbital,[3] it makes an overriding contribution to the CE with the same sign as the helicity of the diene. When it is equatorial and lies in a coplanar "W" path to one end of the diene, it transmits an opposite, weaker effect, apparently by a through-bond mechanism.[4] Formally equivalent results in terms of either a *P* (right handed) or *M* (left handed) diene helicity are obtained from a multisector interpretation (Figure 1) derived by simultaneous application of the Scott-Wrixon olefin octant rule[5] to both double bonds.

Significantly, both approaches anticipate the CE reversal encountered in *trans*-$\Delta^{1,3}$-hexalins when axial allylic alkyl (methyl) groups are replaced by hydrogen.[2] The resulting CE is opposite in sign to the helicity of the diene and is governed by chirality contributions of substituents or bonds lying between the lateral planes of the two double bonds.

(1) Presented in part at the 17th Midwest Regional Meeting of the American Chemical Society, Columbia, MO, Nov 5-6, 1981; paper no. 646; also at the 184th National ACS Meeting, Kansas City, MO, Sept 12-17, 1982; ORGN 160.

(2) For references and recent discussion, see: Lightner, DA.; Bouman, T.; D.; Gawroński, J. K.; Gawrońska, K.; Chappuis, J. L.; Crist, B. V.; Hansen, A. E. *J. Am. Chem. Soc.* **1981**, *103*, 5314-5327.

(3) Cf.: Zushi, S.; Kodama, Y.; Fukuda, Y.; Nishihata, K.; Nishio, M.; Hirota, M.; Uzawa, J. *Bull. Chem. Soc. Jpn.* **1981**, *54*, 2113-2119.

(4) Similar effects are found in the CEs of substituted decalones: Kirk, D. N.; Klyne, W. *J. Chem. Soc., Perkin Trans. 1* **1974**, 1076-1112. Kirk, D. N. *Ibid.* **1980**, 1810-1819.

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