the temperature results in "fraying", i.e., disappearing of base pairs signals for C·G(10–11) and T·A(9–12), followed by C·G(2–19) and T·A(3–18). Between 42 and 54 °C the signals of the central core (base pairs C·G(4–17) to C·G(8–13)) broaden and disappear. It can be seen (Figure 2a, right) that a lowering of T_m of III-Pt in comparison with III is apparent; the signals of the central core disappear at approximately 42 °C.[12] Surprisingly, however, at low temperature, base pairing is observed *even for the central two G·C base pairs*. The different positions for the imino protons of base pairs C·G(4–17), G·C(5–16), G·C(6–15), and T·A(7–14) in III-Pt compared to III (see Figure 2b) indicate that platinum binding has caused a change in their chemical environment.

Molecular models of a double helix, containing a d(G-G)·cis-Pt part in which the structure of the chelating part was based upon a detailed conformational analysis,[10] clearly indicates that the central two G·C base pairs can be maintained in the duplex after platinum binding but that the vertical stacking interactions between successive base pairs C·G(4–17), G·C(5–16), G·C(6–15), and T·A(7–14) are distorted. Due to platinum binding the guanine bases of G(5) and G(6) cannot maintain a parallel orientation;[10] this implicates a loss of stacking interaction between successive base pairs, which is reflected in the large downfield shifts of the imino protons of G(5) and G(6) in III-Pt compared to III. In addition, base pair T·A(7–14) is deshielded in comparison with III. This deshielding is ascribed to the loss of next-neighboring shielding of G(5). In contrast, C·G(4–17) is shielded in III-Pt with respect to III (Figure 2), indicating a specific interaction between C(4) and G(5).

It is highly surprising that, at low temperatures, a double helix can still occur after platination. Up to now, significant distortions, at 37 °C, have been deduced from other observations[4] on DNA.

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(12) UV melting profiles of III, recorded at 5×10^{-6} M/L (0.8 OD), indicate that at this concentration the melting temperature is 29 °C, concomitant with a ΔH for duplex formation of about 67 kcal/mol. UV melting profiles of III-Pt, recorded under comparable conditions, show a lowering of T_m to 14 °C. A melting profile taken at higher concentration (8.10^{-4} M/L) leads to an estimate of ΔH of 44 kcal/mol.

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Redox Reactions of a Tetrahydro-/Hexahydropyrido[2,3-*d*:6,5-*d*']dipyrimidine Tetrone Couple. A High vs. Low Potential 5-Carba-5-deazaflavin Mimic

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We have recently[1] reported details of the chemistry of 3,7,10-trimethyl-(3*H*,7*H*,9*H*,10*H*)-pyrimido[5,4-*g*]pteridine-2,4,6,8-tetrone (PPT_{ox}) and its 1,5-dihydro reduction product

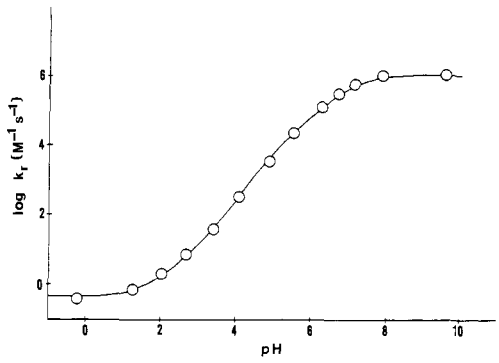
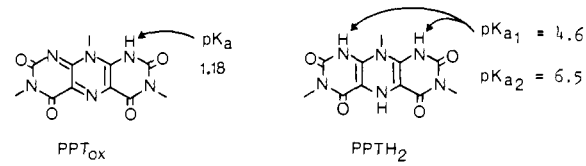
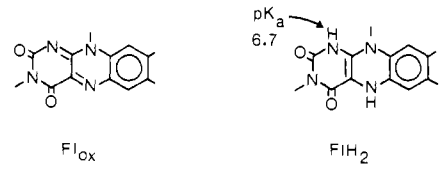


Figure 1. Plot of the log of the second-order rate constants (k_r) for the reduction of *N*-methylacridinium ion by $PPTH_{2T}$ (=$PPTH_2$ + $PPTH^-$ + PPT^{2-}) vs. pH. Points are experimental and the line is generated from eq 2 by use of the constants provided in the text (solvent H_2O, μ = 1, 30 °C).



($PPTH_2$). In the structures PPT_{ox} and $PPTH_2$, the dimethylbenzo moiety of flavins (Fl_{ox}) and 1,5-dihydroflavins (FlH_2) has been



replaced by uracil. Because of the low pK_a of PPT_{ox} (due to the extensive delocalization of the negative charge of PPT_{ox}^-) and the two enamine functions of $PPTH_2$, the redox potential (E_o' −346 mV) for the $PPTH_2/PPT_{ox}$ couple is 150 mV more negative than that for the related 3-methyllumiflavin/1,5-dihydro-3-methyllumiflavin couple. In many reactions PPT^{2-} behaves as a low potential FlH^- mimic readily reducing such substances as organic disulfides, nicotinamides, and conjugated C–C double bonds. Various aspects of the mechanism for these reactions are intriguing and remain topics of continuing investigation in this laboratory. (As an example, *m*-hydroxybenzaldehyde is reduced by PPT^{2-} to *m*-cresol without the intervention of *m*-hydroxybenzyl alcohol as an intermediate.)[1c]

5-Carba-5-deazaflavins (dFl_{ox} and $dFlH_2$) have served well as isosteric replacements for FMN and FAD in the investigation of various aspects of flavoenzyme chemistry.[2] We report herein our preliminary investigations of $dPPT_{ox}$ and $dPPTH_2$. By analogy to $PPTH_2$ one might anticipate that $dPPTH_2$ would behave as a low-potential $dFlH_2$ mimic. Further, since $E^{\circ\prime}$ for the $dFl_{ox}/dFlH_2$ couple is more negative than that for the Fl_{ox}/FlH_2 couple by 120 mV,[3] $dPPTH_2$ would appear to be a good candidate for

(1) (a) Skibo, E. B.; Bruice, T. C. *J. Am. Chem. Soc.* **1982**, *104*, 4982–4984; (b) *Ibid.* **1983**, *105*, 3304–3315; (c) *Ibid.* **1983**, *105*, 3316–3328.

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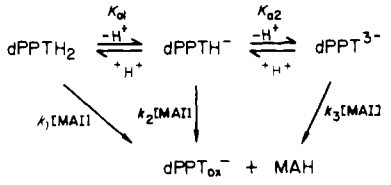
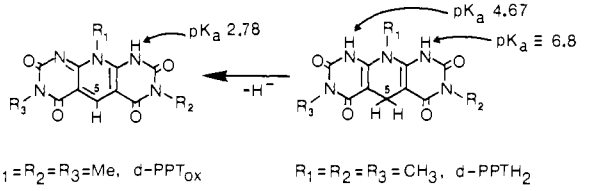
Scheme I

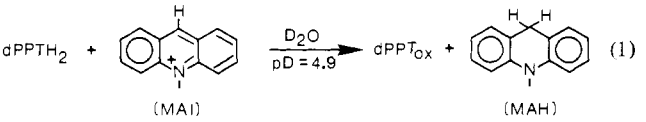


a very effective hydride equivalent reducing agent. Yoneda, Yamamoto, and Ono, however, have made the interesting ob-



servation that $dPPT_{ox}$ and its analogues (R_1, R_2, and R_3 phenyl substitutents) are very effective aerobic autorecycling catalysts for the oxidation of alcohols.[4] The expectation that $dPPT^{2-}$ should be a most effective organic reductant and the finding by Yoneda that $dPPT_{ox}$ and its analogues are good oxidants (at least in the autorecycling process) are explained by the results presented herein.

The reduction of *N*-methylacridinium iodide (MAI) by $dPPTH_2$ in D_2O was shown to yield (eq 1) *N*-methylacridan (MAH) devoid

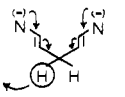


(1)

of deuterium substituent (by proton NMR). The kinetics of the reaction were followed in H_2O at 30 °C between pH 9.58 and −0.20 under pseudo-first-order conditions, with [MAI] in excess over $[dPPTH_2]_T = 7.5 \times 10^{-5}$ M by minimally 10-fold. The appearance of $dPPT_{ox}$ and $dPPT_{ox}^-$ was followed between 370 and 385 nm. Reactions followed the first-order rate law and the pseudo-first-order rate constants (k_{obsd}) were found to be independent of buffer concentration. Plots of k_{obsd} vs. [MAI] were found to be linear at each pH. The slopes of such plots provide the apparent second-order rate constant k_r. In Figure 1 there is plotted the log of k_r as a function of pH. The points of Figure 1 are experimental and the best fit line correlating the points was generated from eq 2 where $k_1 = 4.58 \times 10^{-1}$ M^{-1} s^{-1}, $k_2 = 4.70$

$$k_r = \frac{k_1 a_H^2 + k_2 K_{a1} a_H + k_3 K_{a1} K_{a2}}{K_{a1} K_{a2} + K_{a1} a_H + a_H^2} \qquad (2)$$

$\times 10^2$ M^{-1} s^{-1}, $k_3 = 1.30 \times 10^6$ M^{-1} s^{-1}, $pK_{a1} = 4.57$, and $pK_{a2} = 7.20$. Equation 2 may be derived for Scheme I. The kinetic pK_{app} values (i.e., 4.57 and 7.20) may be compared to the tritrimetric pK_{a1} and pK_{a2} values for stepwise dissociation of $dPPTH_2$ (i.e., 4.67 an 6.5–7.0, this study). From the values of k_1, k_2, and k_3 it may be seen that dissociation of a proton from $dPPTH_2$ to provide $dPPTH^-$ increases the rate of hydride transfer to *N*-methylacridinium cation by 1×10^3 while dissociation of $dPPTH^-$ to give $dPPT^{2-}$ provides an additional rate increase of 2.8×10^3. Thus, the rate for *N*-methylacridinium ion reduction is increased by ca. three-million fold on complete dissociation of $dPPTH_2$ to give $dPPT^{2-}$. Various *N*-alkylpyridine-substituted nicotinamides reduce *N*-methylacridinium ion with second-order rate constants ranging from 4×10^1 to 2×10^3,[5] so that they are kinetically more effective reductants of MAI than is $dPPTH_2$ by minimally $\sim 10^3$ while the most reactive *N*-alkylnicotinamides are kinetically comparable to $dPPT^-$. The species $dPPT^{2-}$ owes its very large hydride transfer potential to the dienamine anion portion of its structure. We find that $dPPT^{2-}$ reduces *m*-hydroxybenzaldehyde



to benzyl alcohol (pH 7.0) via hydride transfer and that undissociated $dPPT_{ox}$ is a mild oxidant capable of the "autorecycling" conversion of cyclohexanol to cyclohexanone. The latter observation was previously described by Yoneda and co-workers for certain phenyl-substituted $dPPT_{ox}$ molecules.[4]

Acknowledgment. This work was supported by a grant from the National Institutes of Health.

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Remarkable Optical Induction in the Reduction of α-Keto Esters with *B*-(3-Pinanyl)-9-borabicyclo[3.3.1]nonane. Synthesis of α-Hydroxy Esters of 100% Optical Purity

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The asymmetric synthesis of chiral α-hydroxy esters is an objective of considerable current importance and activity of organic chemists.[1] Optical purities in the range of 90% ee are no longer exceptional. We now report a simple procedure to achieve the reduction of α-keto esters in optical purities approaching 100%.

Recently we reported an improved procedure for the asymmetric reduction of prochiral ketones with the chiral trialkylborane *B*-(3-pinanyl)-9-borabicyclo[3.3.1]nonane (**1**; Alpine-Borane, Midland's reagent).[2,3] In our procedure we utilized either the neat reagent or highly concentrated (~2 M) solution instead of the relatively dilute solutions employed by the original workers.[4] This led to vastly improved optical induction by greatly increasing the rate of reduction by the desirable bimolecular process in comparison to the rate of dissociation of the reagent into the undersirable 9-borabicyclo[3.3.1]nonane and α-pinene.[5] Another means of increasing the rate of reduction is by substituting the electron-withdrawing groups on the carbonyl compound.[4a] While

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(5) Midland and co-workers have overcome this problem recently by carrying out the reduction under extremely high hydrostatic pressure (5000 atm). They were able to achieve the reduction of acetophenone with 100% ee.

0002-7863/84/1506-1531$01.50/0