

the leaving phosphoryl group is activated via Mg^{2+} complexation with a resultant pK_a lowering.¹⁵ Detailed kinetic analysis has shown Mg_2PPi to be the true PPase substrate in a stoichiometric, though not necessarily a structural sense.^{3a,18} The two ϕ^R values of 0.9 are well accounted for by a water molecule coordinated to Mg^{2+} , whose protons should each have a ϕ value lying between 0.69, the value for the hydrated proton,¹⁹ and 1.00. In the transition state, a ϕ value of 0.4 for the proton in transit is similar to what has been found in comparable situations,^{11b,20} whereas the proton remaining attached to the oxygen resembles more closely a proton in a neutral water molecule and can be assigned a value of 1.00. Model B depicts a pure $S_N1(P)$ reaction in which extreme leaving group activation is achieved through coordination to arginine and to Mg^{2+} , and to general acid catalysis via a water molecule bound to Mg^{2+} . The proposed transition state could accommodate a second Mg^{2+} if the two Mg^{2+} functions were divided between two different Mg^{2+} ions. The expected ϕ values are again in accord with set I, with two ϕ^R values of 0.9 for water bound to Mg^{2+} , ϕ^T values of 0.4 for the proton in transit, and 1.00 for the proton remaining with the water oxygen. Model C depicts an addition-elimination reaction in which the transition state occurs during a base-catalyzed breakdown of the trigonal bipyramid formed via water addition and rapid internal proton transfer. The trigonal bipyramid is stabilized via bidentate coordination to Mg^{2+} ,^{16,21,22} and coordination to arginine (and possibly a second Mg^{2+}) activates the leaving group. The expected ϕ values may be in accord with set II. All ϕ^R values should be 1.00, and a ϕ^T value of 0.37 for the proton in transit is reasonable. The uncertainty comes in assigning a ϕ^T value of 1.37 to the proton bound to the pentoxyphosphorane, which must be considered speculative since it is not based on any direct precedent. Such a value would not, however, be unreasonable, given the obvious structural analogy between gem diols ($\phi = 1.23-1.28$)²³ and pentoxyphosphoranes and the expected strongly basic nature of the position to which the proton is bound.²⁴

Given the uncertainties inherent in solvent isotope studies on enzymatic mechanisms,^{25,26} it is clear that the experiments presented here do not allow any final conclusions to be reached. Their value lies rather in defining the simplest allowed mechanisms whose validity can then be tested by other approaches. Within this limited context, our results provide evidence for involvement of at least one water molecule in the transition state. They also hint at a direct catalytic role for Mg^{2+} . Thus, both PPase and Mg^{2+} -catalyzed PPi hydrolysis show appreciable solvent isotope effects, whereas simple PPi hydrolysis does not, and at least, for parameter set I, the ϕ values obtained are fully consistent with water bound to Mg^{2+} as an important part of the transition state.

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Nature of the Detectable Intermediate in the Permanganate Oxidation of *trans*-Cinnamic Acid

Sir:

In recent papers,^{1,2} Lee and Brownridge have reported on the stopped-flow detection of an intermediate (at 415 nm) in the oxidation of *trans*-cinnamic acid (TCA) by acidic permanganate. The conclusion has been made that this intermediate is a relatively stable hypomanganate ester. We wish to report the results of experiments performed by the combined stopped-flow-chemical quenching technique, which show that the oxidation state of manganese in the above intermediate cannot be +5. The scheme of the setup is shown in Figure 1. Syringes S_1-S_3 are discharged at constant speed. In the two-jet mixing chamber, M_1 , aqueous TCA is mixed with acidic permanganate. The reacting solution passes down the capillary tube T to a four-jet mixer (M_2), where it is mixed with the quenching solution (aqueous NaI, with starch added in some experiments). Mixer M_2 is part of a stopped-flow instrument with an observation cell at C. Discharge of syringes S_1-S_3 through the two-stage mixing system permits one to (i) monitor the reaction of the short-lived intermediate accumulating in tube T with the quenching reagent and analyze the effluent chemically or (ii) follow the decay of the intermediate without the quenching reagent (aqueous $HClO_4$ in S_3).

Prior to the runs on the two-stage system, stopped-flow experiments were performed to determine the time at which the 415-nm trace reaches its minimum (% T). By varying the flow rate, the length and diameter of capillary T, the residence times in T were set as close as possible to these values. Thus the concentration of the intermediate at M_2 was a maximum in each run. The reaction between starch and NaI/I_2 was found to be complete within the time of mixing; therefore, starch could be used to enhance the sensitivity of detection of iodine at 415 nm.

The traces in Figure 1 illustrate the efficiency of quenching. The system is originally filled with water, which is discharged up to point 1. In section 1-2, the reacting solution arrives, while in section 2-3 it flows through the observation cell. At point 3 the flow stops. Trace I shows the decay of

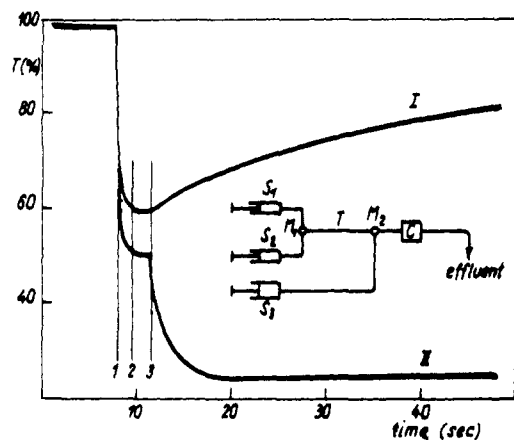


Figure 1. Variation of transmission with time in cell C during discharge of syringes S_1 - S_3 through the two-stage mixer: $[TCA] = 2 \times 10^{-3}$ M; $[MnO_4^-] = 1 \times 10^{-3}$ M; $[HClO_4] = 1$ M; (trace I) decay of the intermediate (1 M $HClO_4$ in S_3); (trace II) quenching of the intermediate with NaI /starch (from S_3).

Table I. Average Oxidation State (OS) of Manganese at the Time Corresponding to Maximum Concentration of the Intermediate (t_{max})^a

$[TCA]_0 \times 10^4$, M	$[MnO_4^-]_0 \times 10^4$, M	$t_{max},^b$ s	OS ^c	OS ^d
5.0	2.0	5.0	3.08	2.98
5.0	2.5	4.2	3.03	3.05
10.0	5.0	2.4	2.85	2.85
15.0	7.5	1.8	2.81	2.82
20.0	10.0	1.3	2.64	2.65

^a $[HClO_4] = 1$ M; temp = 25 °C. ^b Measured at 415 nm; average of two experiments. ^c No pyrophosphate added. ^d $[Pyrophosphate] = 10[MnO_4^-]_0$.

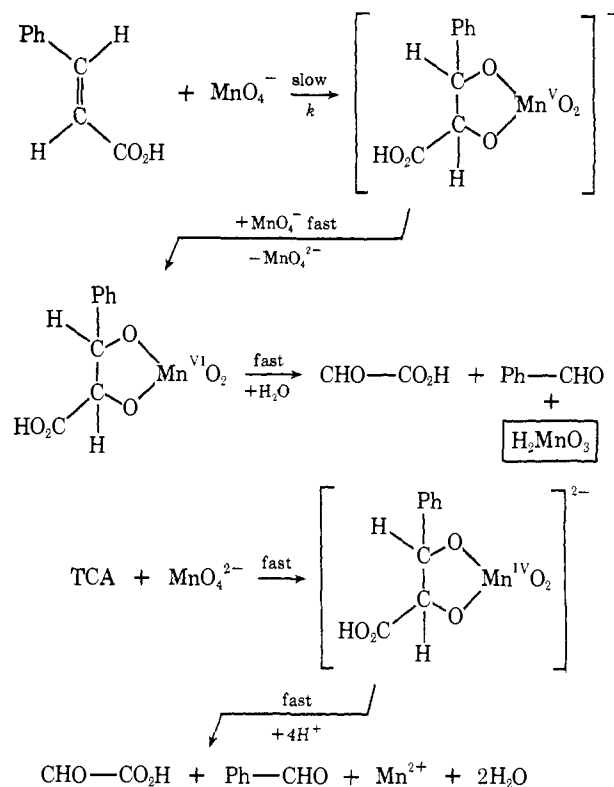
the intermediate without quenching, which is complete only after about 100 s. Trace II was obtained with NaI /starch in S_3 . Clearly, it reaches a steady value within about 5 s; consequently, quenching is much faster than the decay of the intermediate.

The quenching experiments were performed by collecting the effluent and titrating the iodine formed with thiosulfate. Runs were also made with a tenfold excess of pyrophosphate over MnO_4^- to ensure that any manganese(III), if formed, should be prevented from disproportionation. If $Mn(III)$ is an intermediate in similar reactions, it is readily trapped by pyrophosphate³ and the pyrophosphatomanganese(III) formed can be recognized by its spectrum. It is important that no $Mn(III)$ can be observed at any time during the oxidation of TCA.

The results of quenching experiments are shown in Table I as the average oxidation state of manganese at the moment of quenching, which, according to the table, at maximum concentration of the intermediate is equal to or less than +3. Since $Mn(III)$ cannot be observed, we suggest that the intermediate detected is a soluble manganese(IV) species, possibly H_2MnO_3 ,⁴ formed not via disproportionation of $Mn(III)$ but directly from higher oxidation states. Its disappearance probably occurs via reaction with the organic intermediates ($CHO-CO_2H$, $Ph-CHO$ ^{1,2}) or possibly with TCA, but with skipping of the $Mn(III)$ state.

The quenching results are at variance with the conclusions of Lee and Brownridge,^{1,2} who regarded the intermediate as a hypomanganate ester, since in this case the average oxidation state should have been around +5. Obviously, the mechanism is more complex than assumed previously.^{1,2} Lee and Brownridge have provided convincing evidence for

Scheme I



a manganese(V) intermediate, based on an inverse secondary isotope effect. However, this is *not* identical with the transient species detected by the stopped-flow technique. Manganese(V) is probably involved in the reaction but escapes detection due to its short lifetime. The formation of longer-lived hypomanganate esters is conceivable with sterically rigid olefins.⁵ The direct determination of the oxidation state may unequivocally define the nature of such intermediates.

The process yielding the intermediate obeys first-order kinetics with respect to both TCA and MnO_4^- , as reported earlier.^{1,2} We have found that TCA and MnO_4^- are consumed in a 1:2 ratio, i.e., the rate-determining step is followed by a fast reaction of a second MnO_4^- . At a 1:1 ratio of the reactants, the 530-nm trace characteristic of the disappearance of MnO_4^- yields excellent linear plots of $\log(1 + A_0/A)$ vs. time, which is based on $\Delta[TCA]/\Delta[MnO_4^-] = 1/2$; at the same time, the plots of $1/A - 1/A_0$ vs. time, based on $\Delta[TCA]/\Delta[MnO_4^-] = 1$, invariably show strong curvatures. The second-order rate constant k (Scheme I) is 1.0×10^3 M⁻¹ s⁻¹ in 1 M $HClO_4$, in agreement with the value reported^{1,2} if the consumption ratio is taken into account.

A mechanism consistent with the available information is outlined in Scheme I, describing the *formation* of the intermediate, H_2MnO_3 , which disappears in a slower reaction with the organic intermediates (trace I in Figure 1).⁶ The mechanism includes some of the steps proposed for olefin oxidation in alkaline media.⁷⁻¹⁰ The formation of manganese esters in acid solutions of TCA was also considered as a possible alternative for the disappearance of hypomanganate.² Manganese (VI) and (V) are regarded as short-lived, undetectable intermediates. Inherent in the proposed mechanism is the assumption that in acid solutions manganese(VI) is a more reactive oxidant, which is not inconsistent with its increased rate of disproportionation. The latter process, however, remains suppressed due to the relatively large excess of TCA under reaction conditions.

The mechanism proposed here accounts for the key facts

that (i) manganese(III) is not an intermediate in the process and (ii) the single detectable intermediate contains 1 oxidn equiv referred to overall manganese: at maximum concentration of the intermediate a 1:1 mixture of Mn(IV) and Mn(II) is present.

The kinetic isotope effect and the substituent effect exhibited by the decomposition of the detectable intermediate^{1,2} do not contradict Scheme I as manganese(IV) should disappear by oxidizing TCA and/or the organic intermediates, and obviously, both reactions may be subject to the above effects. Soluble manganese(IV) may be involved in permanganate oxidations more extensively than recognized thus far.

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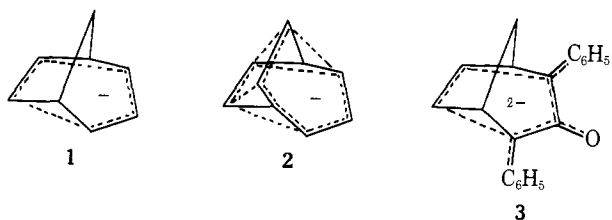
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On the Use of Proton Nuclear Magnetic Resonance As a Tool in Determining Long Range π -Interactions in Carbanions

Sir:

A number of reports have appeared in the recent literature describing long range π -interactions between a carbanionic center and a suitably placed carbon-carbon double bond, to produce such species as **1**,¹ **2**,² **3**,³ and others.⁴

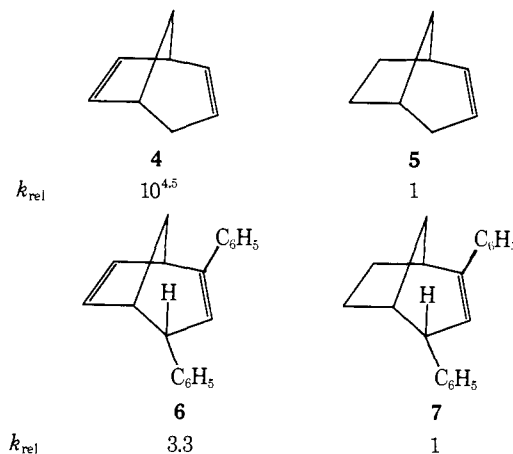


In the majority of cases^{2a,3,4a-c} the experimental evidence in support of π -electron participation in these anions was based exclusively on their ¹H NMR spectra. Most significantly, sizable upfield shifts (ca. 1–2.5 ppm) in the resonance of the protons directly attached to the remote carbon-carbon double bond have been interpreted as evidence indicating considerable charge delocalization in these species.

However, despite the strong reliance on ¹H NMR as a tool for detecting the presence and/or extent of π -participation in carbanions, the effect of the negative charge on the

chemical shift of the vinylic and other neighboring protons *in the absence of π -participation* has received very little,^{2a} if any, consideration.

Recently, we have reported⁵ that replacement of the hydrogens at C(2) and C(4) in the bicyclic systems **4** and **5** by phenyl groups reduces the rate difference of the base-catalyzed hydrogen-deuterium exchange of their allylic hydrogens from 10^{4.5} to 3.3, clearly indicating that the stabilization rendered by the phenyl groups to the incipient carbanion **8** has totally eliminated the charge delocalization from the allylic part of the system to the C(6)–C(7) double bond.^{6,8}

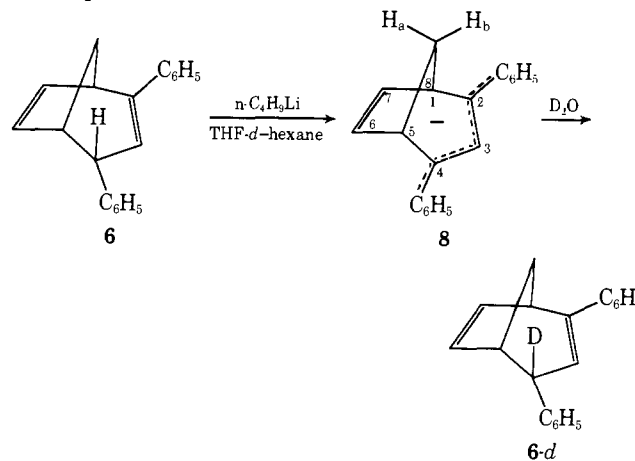


It occurred to us that a study of the ¹H NMR spectrum of carbanion **8**, and especially a comparison of this spectrum with that of anion **1**, previously reported by Winstein and his co-workers,^{1c} would be ideally suited in providing information concerning the effect of the negative charge on the chemical shift of neighboring protons in the absence of long range π -interactions, and more generally in answering questions about the appropriateness of employing proton NMR *alone* as a tool in detecting long range π -interactions and homoaromaticity in carbanions.

The present report describes our findings with regard to the formation, ¹H NMR spectrum, and deuteration of carbanion **8**.

2,4-Diphenylbicyclo[3.2.1]octadienyl anion **8** was obtained from the corresponding hydrocarbon⁵ **6** in practically quantitative yield by treatment of **6** with *n*-butyllithium in THF-*d*₈-hexane (Scheme I). In a typical experiment, 1.9

Scheme I



mmol of hydrocarbon **6** was dissolved in 2.5 ml of THF-*d*₈, the solution was cooled to –5°, and 1.13 ml (2.5 mmol) of a 2.2 M solution of *n*-butyllithium in hexane was added. The reaction mixture was stirred at 0–5° for 30 min and at room