considerable exposure of the porphyrin periphery. In light of this structure and the results of the present work the iron–imidazole–iron "inner-sphere" electron-transfer model for the cytochromes[9] would seem to require an inordinate amount of conformational change. That is to say, the minimum series of movements for electron transfer would require the iron porphyrins of two cytochromes to face out, transfer a ligand, and tuck back into the protein. In contrast, a peripheral interaction of the porphyrin rings of two cytochromes need not involve a conformation change for electron transfer to occur. The latter interaction is consonant with the fast electron-transfer properties of these units. The recently noted reduction of imidazole-bound cytochrome *c* by ascorbic acid[10] is consistent with these views.

The simplest mechanism for exchange upon reduction in our system might be formulated as a hydrogen-atom transfer, eq 2. A complementary formulation could be written for exchange upon oxidation. This sequence is in harmony with the converse generation of magnesium porphyrin radical cations upon one-electron oxidation.[11,12] The implications of peripheral attack in the redox chemistry of metalloporphyrins and hemoproteins is being investigated at all levels.

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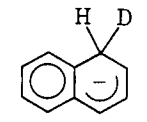
Reactions of Aromatic Radical Anions. IV. Evidence for an Addition Mechanism in the Reaction of Sodium Naphthalene and Hydrogen

Sir:

Recent work has shown that tetrahydrofuran solutions of sodium naphthalene absorb molecular hydrogen and that sodium hydride and naphthalene are stoichiometric reaction products.[1,2] No definitive experiments with regard to the mechanism of this interesting reaction have been reported.

We now wish to report evidence that sodium naphthalene is involved as more than just an electron-transfer agent, and to propose a mechanism for this reaction. Further evidence is proposed by Tamaru and coworkers for an anion intermediate.[3]

Two reasonable mechanisms[4] for the reaction are shown (eq 1–5). While both schemes involve initial electron transfer to molecular hydrogen to give hydride and a hydrogen (H) atom; they differ in the subsequent steps. Mechanism I involves reduction of the H radical to hydride which is expected to be facile based on several analogous reactions,[5–7] whereas mechanism II involves addition of the H radical to the radical anion which also finds analogy,[8,9] followed by loss of hydride to give the observed products. In order to differentiate between these schemes, we have studied the reaction using deuterium (D_2) gas. If mechanism I prevails, the products of reaction with D_2 are NaD and unlabeled naphthalene. If mechanism II prevails, however, the species formed in the addition step has a deuterium atom incorporated in the aromatic nucleus, *viz.*



Unless an unusually large inverse isotope effect operates for step 5, loss of hydride yields naphthalene containing deuterium.

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$$\text{H–H} + \text{Naph}\cdot^- \longrightarrow \text{H}^- + \text{H–Naph}\cdot \xrightarrow{\text{Naph}\cdot^-} \text{H–Naph}^- \longrightarrow \text{H}^- + \text{Naph}$$

The consequences of this mechanism, insofar as the present experiments are concerned, are identical with those of mechanism II. However, we consider this less likely since it involves nucleophilic attack of an extremely soft base on a very hard acid.
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The reaction of sodium naphthalene (50 mmol) in tetrahydrofuran with deuterium gas (Union Carbide Corp.) at 40° was conducted in a three-necked round-bottomed flask. Reaction was followed by assaying the radical anion concentration.[1] After 36 hr the solid product was separated by centrifugation. The liquid layer was treated with water and extracted with ether. After drying and solvent removal, 6.2 g (95% recovery) of naphthalene was obtained.

A sample of the naphthalene was purified by preparative-scale glpc and analyzed by mass spectrometry. From the ratio of the intensities of the *m/e* peaks at 128 and 129 the amount of deuterated naphthalene was established as 6.0 ± 0.5%.[10]

Since the sodium deuteride is produced in an exceedingly active form,[1] a control experiment, to demonstrate the absence of exchange by the path illustrated in eq 6, was required. Such exchange would obscure

$$C_{10}H_8 + NaD \longrightarrow C_{10}H_7D + NaH \qquad (6)$$

the significance of the above results. Accordingly, naphthalene was brought into contact with the sodium deuteride prepared above in THF at 40° for 51 hr under a nitrogen atmosphere. The recovered naphthalene was analyzed by mass spectrometry and showed no deuterium incorporation. Therefore, the results in the presence of deuterium gas are not complicated by this conceivable artifact.

The results indicate that, even though naphthalene is recovered quantitatively, the mechanism involves addition to sodium naphthalene radical anion and not solely electron transfer. If mechanism II were uniquely operative and if there were no kinetic isotope effect for step 5, then a maximum value of 25% of the recovered naphthalene would be deuterated.[11] Our value is substantially less than this maximum and probably indicates that both mechanisms are operative. Such a conclusion is in accord with the conclusions regarding the reaction of alkyl radicals and sodium naphthalene.[8,9]

These mechanistic conclusions are supported by the results of Tamaru and coworkers,[3] who find a peak appearing at 435 mμ when hydrogen gas is introduced into an EDA complex solution of sodium naphthalene in THF which might be attributed to the monohydro anion. We have prepared this anion by an independent route and find the maximum to occur at 437 mμ.

When considered together, the results of Tamaru and coworkers[3] and those reported in this communication present strong support for the intermediacy of the monohydro anion.

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(10) There was no evidence for naphthalene-d_2 within the limits of experimental accuracy (±0.5%).

(11) This value is obtained by assuming that 50% of the hydride is formed in an initial step that does not give exchange. With no isotope effect for the potential exchange step (eq 5), then 25% of the recovered naphthalene would be deuterated.

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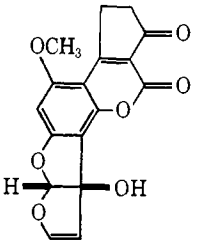
The Total Synthesis of Racemic Aflatoxin-M_1 (Milk Toxin)

Sir:

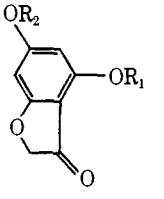
Aflatoxin-M_1 was first detected in the milk of aflatoxin-B_1-fed cows.[1,2] Metabolites with similar properties were subsequently isolated from the urine of sheep[3,4] and the livers of rats[5] dosed with aflatoxin-B_1. Subsequent work established the identity of the milk factor and the urinary metabolite.[4,6] Structural investigations led to the conclusion that aflatoxin-M_1 is a hydroxyaflatoxin-B_1 as represented by structure **1**.[4]



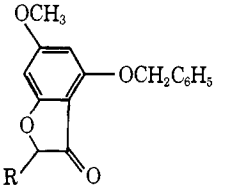
1

Although the acute toxicity[7] of M_1 seems established, the more important question concerning its carcinogenicity remains unanswered because hitherto only minute quantities of the metabolite have been available for biological studies. We wish to describe a total synthesis which makes racemic aflatoxin-M_1 (**1**) a relatively accessible substance.

Methylation of 4,6-dihydroxycoumaran-3-one (**2**)[8] in refluxing glyme with dimethyl sulfate in the presence of potassium carbonate gave the dimethyl ether **3**, mp 138–140° (78% yield).[9] Partial ether cleavage with 2 equiv of aluminum chloride in hot methylene chloride afforded the monomethyl ether **4**, mp 140–142°,[10] which in its crude form was transformed into the benzyl ether **5**, mp 172–173° (45% from **3**), by alkylation with benzyl bromide in refluxing glyme–dimethylformamide containing suspended potassium carbonate.



2, $R_1 = R_2 = H$
3, $R_1 = R_2 = CH_3$
4, $R_1 = H$; $R_2 = CH_3$
5, $R_1 = CH_2C_6H_5$; $R_2 = CH_3$



6, R = Br
7, R = $OCH_2C_6H_5$

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