cation–arene anion ion pair species than in traditional ether solvents.

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o-Hydroperoxynaphthoquinols. Chemical Transducers for Coupling Oxidation with Acylation: A Vitamin K Model

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Vitamin K is an essential cofactor for a number of important biological processes[1,2] and yet only on the coagulation of blood[3] has a well-defined chemical role for vitamin K been proposed. Suttie has suggested that hydroperoxides of vitamin K[4] are involved in the carboxylation of glutamic acid residues of blood proteins.[5] While the mechanism of this carboxylation is still uncertain, the working hypothesis outlined in Scheme I is consistent with the available data.[4,5a] Our interest in the chemistry of vitamin K peroxides[6] has prompted us to synthesize peroxides related to **1** and to study their chemistry in an effort to evaluate Suttie's proposal.

A number of synthetic approaches to hydroperoxides related to **1** have been examined (Scheme II). These approaches all begin with the hydronaphthoquinone monoacetate **2** which is readily available through partial hydrolysis of the corresponding diacetate.[7] In the initial approach, photochemically generated singlet oxygen was employed as the oxidizing agent. While the hydroperoxide **3** was formed under these conditions, the yields were very poor (∼10%). Subsequently it was found that **3** could be obtained in quantities useful for further study (34%) using cobalt salpr and molecular oxygen.[8] The success of this method is most intriguing since oxygen-binding cobalt complexes of this type are considered to be good models for the iron-containing cytochrome oxidizing agents of biological systems.[9]

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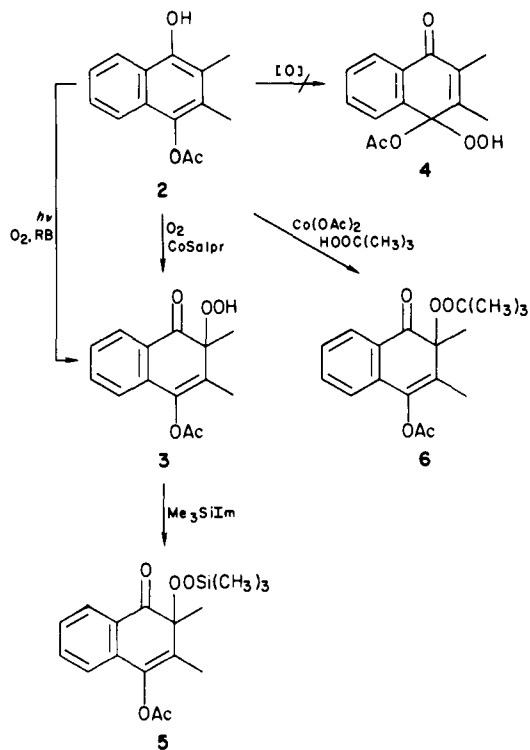
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Scheme I
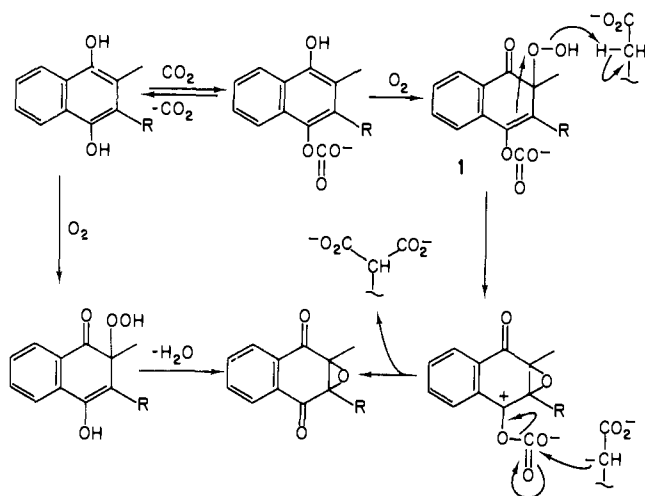
Scheme II

That this hydroperoxide[10] (mp 154.1–156.0 °C) was indeed the ortho hydroperoxide isomer **3** and not the para hydroperoxide isomer **4** is most apparent from the IR spectrum which has ν_{max} at 1760 and 1670 cm^{-1} for the enol acetate and 1695 cm^{-1} for the aryl ketone. In addition, the UV spectrum, λ_{max}(CH$_3$CN) 235 nm (ϵ 24600), 270 (1640), 277 (1730), 287 (1130), and 337 (870), was consistent with **3** but quite different from that of a model containing the cross-conjugated carbonyl chromophore in **4**.[11]

Peroxide derivatives of **3** are also readily available (Scheme II). (Trimethylsilyl)imidazole smoothly converts **3** to **5** (65%, mp 95.8–97.4 °C). The *tert*-butyl peroxide **6** is particularly easy to

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(10) The peroxides reported here have spectroscopic properties and elemental compositions in accord with the proposed structures. They are very labile in crude reaction mixtures and on silica gel at ambient temperature, but may be purified by silica gel chromatography at –15 to –30 °C.

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Scheme III*[a]*
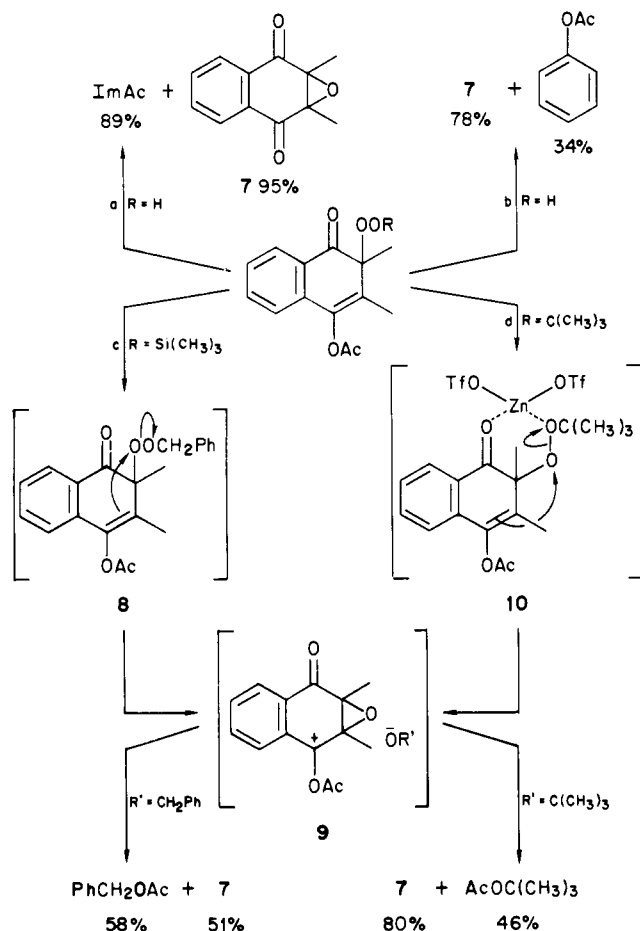
[a] (a) 1.0 equiv of (Im)$_2$CO, CHCl$_3$, room temperature, 2 h; (b) 1.0 equiv of phenol, Zn(OTf)$_2$, CH$_2$Cl$_2$, room temperature, 48 h; (c) *n*-Bu$_4$NF, PhCH$_2$Br, THF, 78 °C, 2 h; (d) Zn(OTf)$_2$, CHCl$_3$, room temperature, 48 h.

prepare from **2** by using *tert*-butyl hydroperoxide and cobalt acetate[12] (44%, mp 107.1–108.1 °C). With these materials in hand, it became possible to test Suttie's acylation proposal.

In these initial studies we have examined only acetylations at nitrogen and oxygen. The hydroperoxide **3** undergoes an extremely smooth reaction with 1 equiv of carbonyl diimidazole (Scheme III) to form the desired quinone epoxide **7** and acetylimidazole in nearly quantitative yield. Zinc triflate is the most effective Lewis acid catalyst found to date for the formation of phenyl acetate from **3** and phenol.[13] With other Lewis acids such as boron trifluoride, the hydroperoxide is converted to quinone epoxide **7**, but no acetylation is observed. Thus, the formation of these acetylation products along with the quinone epoxide is good evidence in support of Suttie's mechanism.

It is thought that the key to success in these reactions lies in finding conditions that will restrict the availability of undesired nucleophiles which might react with the activated acetyl group. To this end we have examined conditions that might be expected to generate the desired nucleophile, alkoxide ions, simultaneously with the activated acetyl species. Desilylation of **5** with fluoride ion in the presence of benzyl bromide should lead to the peroxide **8** (Scheme III) and this species might fragment to form an alkoxide ion and active acylating agent as an ion pair **9**, R′ = CH$_2$Ph. The feasibility of this ion pair hypothesis is indicated by the

formation of quinone epoxide **7** and benzyl acetate in nearly equivalent yields. Unfortunately, the peroxide **8** could not be detected as an intermediate. Thus, **8** would appear to be very labile in contrast to the *tert*-butyl peroxide **6** which is reasonably stable. The same ion pair model for acetylation succeeds with **6** when zinc triflate is used as a catalyst.[13] In this reaction the zinc triflate might complex with the α-peroxy ketone unit as shown in **10** and bias the peroxide linkage in favor of a heterolytic cleavage to form the ion pair **9**, R′ = C(CH$_3$)$_3$.[14]

In summary, this work has demonstrated that peroxy analogues of vitamin K are readily formed from molecular oxygen under conditions closely approximating those found in biological systems. Further, it has been shown that ionic decomposition of these peroxides does lead to active acylating species. Finally, it must be noted that phenolic esters have previously been converted to active acylating species through electrochemical[15] and chemical[16] means. However, this is the first demonstration of a route for coupling oxidation with molecular oxygen to acylation.

(14) The reactions described here afford simple reaction mixtures. Many other conditions examined afford complex mixtures. These intractable mixtures are possibly the result of triggering radical chain modes of peroxide decomposition.

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Lithium-Metalloid Exchange Reactions. Kinetic Evidence for an Intermediate in the Lithium–Iodine Exchange[1]

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The metal–halogen exchanges (Li/Br, Li/I)[2] are the best known of a family of lithium–metalloid exchange reactions, of which the Li/Sn[3] and Li/Se[4] exchanges are also commonly used members. These reactions have achieved special importance for the preparation of functionalized and/or unstable alkyl-, vinyl-, and aryllithium reagents.[2b,3b,c,4b] Kinetic studies of the Li/M exchange

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