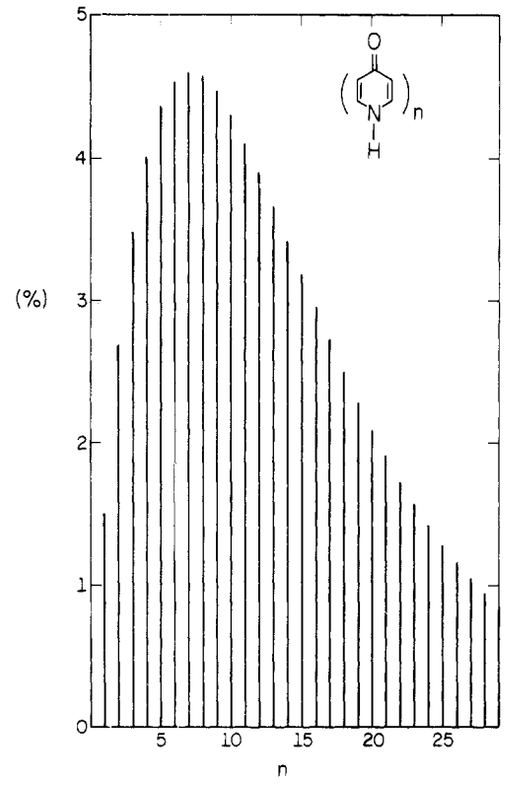
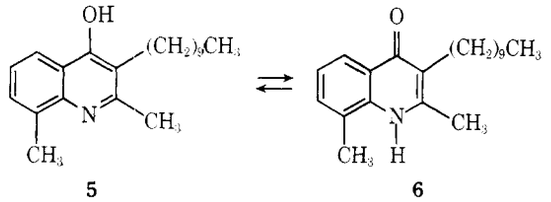


Figure 1. Composition of oligomers to $n = 29$ for 0.025 M 4-pyridone in chloroform.

in terms of the relative energies of the monomers would be erroneous and the significance of the suggested correlation of the overall equilibrium constants of 2-pyridone and 4-pyridone with solvent Z values is open to question.[4,10] It is essential that the nature of the species being compared be known if fundamental understanding of medium effects on protomeric equilibria is to be achieved.

While the complication of association may be removed, in principle, by operating at very low concentrations, for some solvents the necessary dilutions may provide solutions in which the chromophore of interest is beyond the present limits of detection. Another approach is suggested by the studies of 2,6-di-*tert*-butyl-4-hydroxypyridine (**3**)–2,6-di-*tert*-butyl-4-pyridone (**4**) and 3-decyl-2,8-dimethyl-4-hydroxyquinoline (**5**)–3-decyl-2,8-dimethyl-4-quinolone (**6**), compounds which



5 **6**

were chosen by Frank and Katritzky for their favorable solubility.[4] The structures of **3–4** and **5–6** might be expected to offer substantial hindrance to association by hydrogen bonding.[11] In fact, both **3–4** and **5–6** are shown by vapor-pressure osmometry to be essentially monomeric in chloroform at the concentrations used to measure their ultraviolet spectra. The possible association of these compounds in less polar solvents, their position of equilibrium in the vapor, and the effect of substitution on the position of equilibria need to be determined. Compounds which are designed and shown to be monomeric under the conditions of measurement should be useful in providing information about the effect of molecular environment on tautomeric equilibria.

Acknowledgment. We are grateful to the National Science Foundation for support of this work

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(8) The association of 4-pyridone is quite strong and persists in ethanol. Comparison of the association with that of 2-pyridone using the statistical distribution model of Figure 1 shows the free energies of hydrogen bonding in ethanol are: 4-pyridone, −2.6 kcal/mol; 2-pyridone, −1.95 kcal/mol.
(9) It is possible that the equilibrium constant for association of monomers is different from that for addition to the polymer chain. If previous work on amide association is a useful guide the dimer association constant would be less than the subsequent oligomer association constant and the amount of monomer present would be then less than the above estimate: L. L. Graham and C. Y. Chang, *J. Phys. Chem.*, **25**, 776, 784 (1977); M. Davies and D. K. Thomas, *ibid.*, **60**, 763, 767 (1956).
(10) We find that 4-pyridone is monomeric in acetonitrile, the other solvent in which the equilibrium constant for **1–2** was determined for the proposed correlation.[4]
(11) In private discussions with Professor A. R. Katritzky regarding possible problems of association of 2- and 4-pyridones which began in April, 1976, he also noted the possibility that **3–4** and **5–6** would be less associated than the parent materials. The correlations of the equilibrium constants of these substituted systems with Z values may be accorded more significance than those of the parent system.

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Received September 20, 1977

New Synthetic Methods for the Regioselective Annelation of Aromatic Rings: 1-Hydroxy-2,3-disubstituted Naphthalenes and 1,4-Dihydroxy-2,3-disubstituted Naphthalenes

Summary: Respective condensation of the anion of ethyl 2-carboxybenzyl phenyl sulfoxide and 1*H*-2-benzofuran-1-one 3-(phenyl sulfone) with α,β-unsaturated esters and ketones results in regioselective formation of 1-hydroxy-2,3-disubstituted naphthalenes in moderate yield and 1,4-dihydroxy-2,3-disubstituted naphthalenes in good yield.

Sir: Extension of our recently reported strategy for the construction of linear polynuclear aromatic systems[1,2] has resulted in the development of two new methods for the regioselective annelation of aromatic rings. Each route can be incorporated into the original strategy with the notable advantage that abbreviated syntheses of naphthalenes with a

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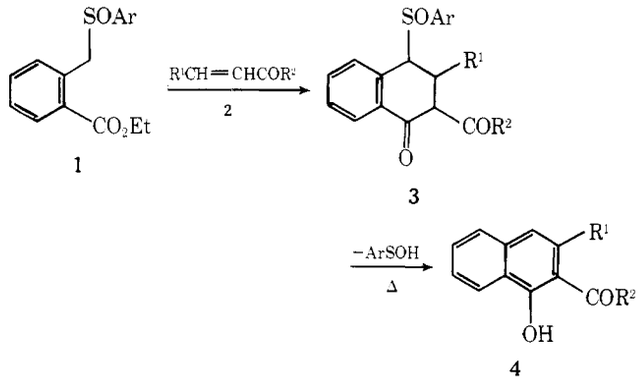
Table I. Regiospecifically Prepared 1-Hydroxy-2,3-disubstituted Naphthalenes (4) Prepared from Sulfoxide 1 and Various Michael Acceptors 2

R_1	R_2	% yield	Mp, °C
H	OEt	28	48–49 (lit.[8] 49)
H	CH_3	37	100–101 (lit.[9] 101)
CH_3	OEt	44	58–59 (lit.[10] 56–59)
CH_3	CH_3	70	93–93.5
CH_2SCH_3	OEt	64	59–60
$-(CH_2)_3-$		0	

Scheme I



broader diversity of functionalities[3] is facilitated. In both cases regiochemical control over the product is vested in the precursors.

Scheme I shows the route devised for the preparation of 1-hydroxy-2,3-disubstituted naphthalenes (**4**). Ethyl 2-carboxybenzyl phenyl sulfoxide (**1**)[4,6] was converted to an anion using lithium diisopropylamide (LDA) in tetrahydrofuran at −78 °C, then allowed to react with various Michael acceptors **2**. The initially formed conjugate addition product underwent intramolecular condensation to yield tetralone **3**.[7] Aromatization of tetralone **3** to 1-hydroxy-2,3-disubstituted naphthalene **4** by thermal elimination of phenylsulfenic acid was accomplished by heating the reaction mixture under reflux for 2 h. In this scheme, the sulfoxide group serves two purposes: initially, it provides essential stabilization for the carbanion generated on the benzyl carbon,[11] and later, it becomes a leaving group allowing aromatization of the newly formed ring. Table I lists 1-hydroxynaphthalenes **4** prepared by this procedure.

Modification of the previous approach accomplished the regioselective preparation of 1,4-dihydroxy-2,3-disubstituted naphthalenes (**7**) (Scheme II). The 1*H*-2-benzofuran-1-one 3-(phenyl sulfone) (**5**, R = H, mp 209–211 °C) was prepared in 87% overall yield by condensing phthaldehydic acid[12] with benzenethiol in benzene[13] followed by oxidation of the sulfide product with 2 equiv of *m*-chloroperbenzoic acid[14,15] in methylene chloride. Addition of **5** to a solution of LDA in tetrahydrofuran at −78 °C generated the corresponding yellow anion, which was allowed to react with Michael acceptors **2**.[16,17] The reaction proceeded through intermediate **6** to afford directly 1,4-dihydroxynaphthalenes **7** in good yield. Since the 1,4-dihydroxynaphthalene products **7** readily underwent air oxidation to naphthoquinones, they were converted to the dimethyl ethers **8** prior to final purification (Table II). This procedure provides a fundamentally new synthetic route to naphthoquinones.

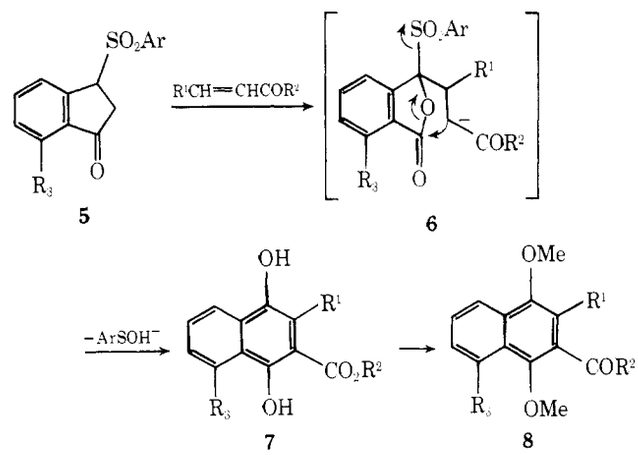
In each route to hydroxynaphthalenes (Schemes I and II) yields were highest when the Michael acceptors had a substituent on the β carbon. The increased yields of products from the phthalide sulfone reaction as compared with those obtained from the sulfoxide reaction are probably due to the enhanced carbanion stabilization afforded by the sulfone.[18] Moreover, this may account for the fact that the phthalide sulfone **5** reacted smoothly with the poor Michael acceptor 2-cyclohexen-1-one,[19] while the corresponding yield of adduct from the sulfoxide was negligible. Since no effort was made to optimize reaction conditions, further studies undoubtedly will result in improved yields. An indication of the scope of the synthetic procedure for preparing 1-4-dihydroxynaphthalenes (Scheme II) is provided by the fact that condensation of methoxyl-substituted phthalide sulfone **5** ($R_3 = OCH_3$) with ethyl crotonate afforded the regiospecifically substituted naphthoate **8** ($R_1 = CH_3$, R_2 = OEt, $R_3 = OCH_3$) in virtually identical yield with that of the unsubstituted compound.

Table II. Regiospecifically Prepared 1,4-Dimethoxynaphthalenes (8) from Phthalide Sulfone 5 and Michael Acceptors 2

R_1	R_2	R_3	% yield	Mp, °C
H	OEt	H	32	*a*
H	CH_3	H	29	59–60
CH_3	OEt	H	70	*a*
CH_3	CH_3	OCH_3	68	*a*
CH_3	CH_3	H	86	70–72
CH_2SCH_3	OEt	H	28	*a*
$-(CH_2)_3-$		H	69	119–120

[a] Oil.

Scheme II



Acknowledgments. The authors wish to thank the National Cancer Institute of DHEW, Grant no. CA 18141, for support of this work.

Supplementary Material Available: Full ^1H NMR data for all the new products listed in Tables I and II as well as the procedures used to prepare and isolate these compounds (3 pages). Ordering information is given on any current masthead page.

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(2) F. M. Hauser and R. P. Rhee, *J. Org. Chem.*, accepted for publication.
(3) The previously reported route[1] accomplished only the incorporation of a carboethoxy functionality.
(4) Ethyl 2-carboxybenzyl phenyl sulfoxide (**1**), an oil, was prepared by initial allylic bromination of ethyl *o*-toluate with *N*-bromosuccinimide followed by bromide displacement with sodium thiophenoxide in ethanol, and finally, oxidation with sodium periodate.[5]
(5) C. R. Johnson and J. E. Keiser, *Org. Synth.*, **46**, 78 (1966).
(6) Satisfactory mass, ^1H HMR, and IR spectra were obtained for all new compounds.
(7) Tetralone **3** was not isolated because it was unstable, slowly decomposing at room temperature to naphthalenes **4**. The available evidence does not completely rule out the possibility that the product observed (TLC analysis) is the initial uncyclized adduct from Michael addition.
(8) R. Schmitt and E. Burkland, *Ber.*, **20**, 2700 (1887).

(9) M. Imoto, *J. Chem. Soc. Jpn.*, **58**, 932 (1937).
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(11) Generation of the anion of ethyl *o*-toluate with LDA at −78 °C followed by attempted trapping with an ethyl crotonate resulted in the formation of the ethyl *o*-toluate dimer, 3-(2-methylphenyl)-1*H*-2-benzopyran-2-one.
(12) 6-Methoxyphthaldehydic acid was prepared from ethyl 2-methyl-6-methoxybenzoate by dibrominating the 2-methyl group followed by hydrolysis in acetic acid–hydrochloric acid medium. This conversion of an aromatic methyl group to an aldehyde follows a procedure described by E. L. Eliel, D. E. Rivard, and A. W. Burgstahler, *J. Org. Chem.*, **18**, 1679 (1953).
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(16) The 3-phenylsulfoxide analogue was successfully used in the annelation reaction; however, the reaction was not as clean as with the sulfone compound (**5**).
(17) Initially, we intended to prepare the 3-cyano analogue of sulfone **5** and employ it in the condensation. The preparation of this compound was not accomplished in satisfactory yield.
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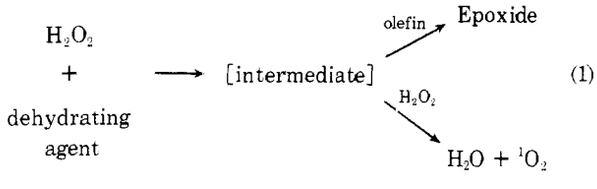
Received July 29, 1977

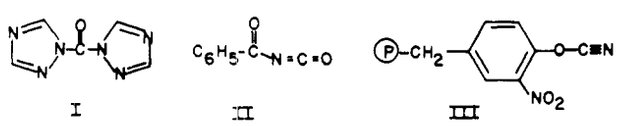
Singlet Oxygen and Epoxidation from the Dehydration of Hydrogen Peroxide

Summary: New epoxidizing reagents and chemical sources of singlet oxygen result from the action of dehydrating agents on hydrogen peroxide.

Sir: We have recently reported that the action of dehydrating agents I or II on H_2O_2 produces intermediates capable of olefin epoxidation.[1] Here we relate that a variety of dehydrating agents behave similarly (eq 1) and that the intermediates involved also lead to the production of singlet molecular oxygen.



(1)



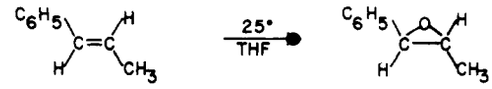
When compounds I or II are added to THF solutions of H_2O_2, CO_2 and oxygen are rapidly evolved. That the oxygen is generated in its singlet ($^1O_2$) state can be demonstrated by its trapping with 9,10-diphenylanthracene (DPA).[2a] Table I shows the yields of $^1O_2$ as indicated by the formation of the endoperoxide of DPA and the β value (rate ratio of $^1O_2$ decay to trapping) determined for DPA in THF.[2b] The polymer-bound cyanate III[3] is also an efficient $^1O_2$ source. The reduced yield of $^1O_2$, probably due to quenching and diffusion effects of the polystyrene matrix, is offset by thee ase of handling and recyclability of this insoluble reagent.[2d] Compounds IV,[4] V,[5] and VI[6] also produce $^1O_2$ slowly under these conditions, but with much reduced efficiency.[2c]

Table I

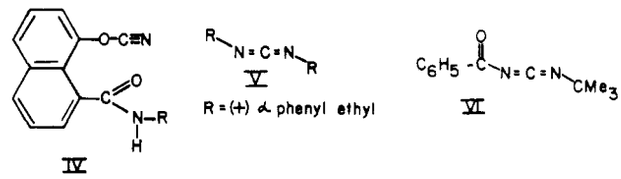
agent + H_2O_2 (4 M) $\xrightarrow[25\ °C]{THF}$ $^1O_2$

	I	II	III
Yield of $^1O_2$, %	94	98	61
Half-life, min	<10	<10	30

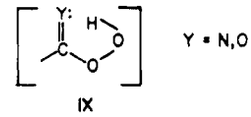
Table II



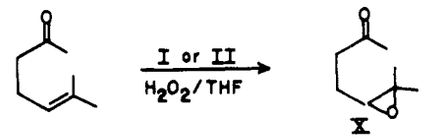
Compound	IV	VII[12]	VIII[13]	V
Asymmetric induction, %	7.5	7.1	5.2	2.0



The intermediates produced in these systems can be intercepted by olefins and epoxidation occurs at the expense of $^1O_2$ generation. Both products are formed in the presence of monoalkylethylenes, but di- and higher alkyl-substituted olefins divert the intermediates to the epoxidation pathway exclusively. Competition studies with a wide variety of olefins revealed that the behavior of these intermediates in epoxidation reactions resembles that of peracids. Epoxidation rates as a function of olefin substituents,[7] selectivities toward cis vs. trans olefins[8] or cyclohexene vs. norbornene,[9] and Baeyer–Villiger oxidations of 2-allylcyclohexanone[10] are, with minor variations, those found for typical peracids. Therefore, while the structures of the actual epoxidizing agents are unknown, intermediates such as IX are not unlikely. Indeed such structures, incorporating the peculiar intramolecular hydrogen bond of peracids, have provided the model for our selection of dehydrating agents.



For preparative epoxidations, reagents I and II were consistently the most effective, e.g., either of these reagents permitted the isolation of the labile epoxide X in >90% yield.



Further, a recent report[11] of the successful isolation of an arene oxide from an H_2O_2–carbodiimide epoxidation should encourage the increased use of such systems, since these reagents lead to products of low acidity. Somewhat less encouraging is the stereospecificity of the optically active reagents tested (Table II) for epoxidations of *trans*-β-methylstyrene. Compared to monoperoxycamphoric acid (4.1%)[15] these reagents offer only modest advantages at best.[14] The design of more effective systems is one of our present goals.

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