isolated by distillation instead of chromatography. The yield of desulfurization reactions was determined by isolating and weighing the crude products and analyzing the mixture by GC (hydrocarbons C_8–C_{16} were employed as internal standards). Response factors were determined on pure samples of all components encountered in such analyses. Spectral data (^{1}H NMR, IR) and melting and boiling points of the desulfurization products were the same as authentic samples.

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Superoxide Anion Radical ($O_2^{\bullet-}$) Mediated Base-Catalyzed Autoxidation of Enones

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Seventeen variously substituted cyclohex-2-en-1-ones were prepared and reacted with superoxide anion radical ($O_2^{\bullet-}$, generated from KO_2/18-crown-6) in inert nonpolar aprotic media at room temperature. The 4,4,6,6-tetrasubstituted cyclohexenones (**1b**, **1c**, and **1d**) proved to be totally inert, while those cyclohexenones possessing available acidic α'- or γ-hydrogens underwent $O_2^{\bullet-}$-mediated base-catalyzed autoxidation (BCA) generating various products depending on the nature and location of the substituents. Thus, 4,4- and 5,5-disubstituted substrates (**2b**, **2c**, **2e**, **2f** and **3b**, **3d**, **3f**–**3i**, respectively) gave 2-hydroxycyclohexa-2,5-dien-1-ones (**7**) as the major product (>80% yield) upon aqueous acid workup, while the corresponding 2-methoxy analogues **8** are obtained when the reaction is quenched with CH_3I. 2,3-Epoxycyclohexanones **13** and oxidative cleavage products **11** and **12** are formed in the case of the 6,6-disubstituted systems (**4a**–**4c**); these oxidation products are accompanied by dimers **14** when the substituent on **4** is CH_3 or H. Epoxide **23** is the primary isolable product in the 3,4,4-trialkyl system (**5d**). As expected for BCA processes, similar results were observed when these reactions were mediated by KOH (at room temperature) or $KOC(CH_3)_3$ (at −40 °C). In the case of 6,6-diphenylcyclohex-2-en-1-one (**4c**), however, *tert*-butoxide-mediated BCA at −40 °C yielded cyclopentene hydroxy acid **15** in addition to epoxide **13**. The saturated analogue of **4c**, **18**, yielded primarily the corresponding saturated hydroxy acid **19**, as well as several other oxidation products (**20**–**22**) depending on the reaction conditions. The mechanism of these transformations is rationalized in terms of base-induced reactions and rearrangements of the initially formed keto hydroperoxides.

Introduction

Despite the pivotal role of free-radical processes in nature, free-radical damage presents a serious and constant threat to living organisms.[1-3] One of the clearest sources of radicals in the body is superoxide anion radical, $O_2^{\bullet-}$, which is formed in a large number of reactions of biological importance in both enzymic and nonenzymic processes.[4] Fluxes of $O_2^{\bullet-}$, generated enzymatically or photochemically, have been shown to inactivate viruses, induce lipid peroxidation (a suspected source of senescence and carcinogenesis[3,5]), damage membranes, and kill cells.[4]

Given the importance of superoxide in biological processes, it is clearly of value to understand its organic chemistry and thereby its mechanism of action.[6,7] The introduction in 1972 of the KO_2–crown ether reagent[8] as a convenient source of $O_2^{\bullet-}$ in aprotic media allowed the organic chemist to carry out extensive studies on the reactions of $O_2^{\bullet-}$ with various functional groups.[9]

Our own research in this field began in 1975 with an exploration of the enone moiety. We reported that $O_2^{\bullet-}$ reacts with chalcones and tetracyclone via what is presumably an electron transfer to the extended π-system. The resulting substrate anion radical is oxygenated, ultimately producing oxidative cleavage products of these enones.[6,10,11] Dibenzal acetone reacts in a similar fashion.[12]

We next turned our attention to more simple enone systems in which electron transfer is not expected. The complete details[13] of these studies are reported below and,

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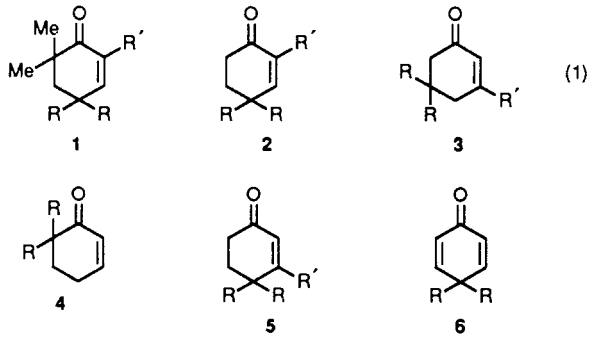
in short, reveal the effectiveness of $O_2^{\bullet-}$ as an initiator of base-catalyzed autoxidation (BCA)[9] and related processes. Extension of this work to steroidal systems has been reported elsewhere.[13e,f]

Synthesis of Starting Materials

For the purpose of this study 17 variously substituted cyclohex-2-en-1-ones and two cyclohexa-1,4-dien-3-ones were prepared: **1b**, **1c**, and **1d**; **2b**, **2c**, **2e**, and **2f**; **3b**, **3d**, **3f**, **3g**, **3h**, and **3i**; **4a**, **4b**, and **4c**; **5d**; **6b** and **6c** (eq 1).



(1)

a: R = R′ = H
b: R = CH_3, R′ = H
c: R = C_6H_5, R′ = H
d: R = R′ = CH_3
e: R = CH_3, R′ = OCH_3
f: R = CH_3, R′ = OC_2H_5
g: R, R = $-(CH_2)_5-$, R′ = OCH_3
h: R = CH_3, R′ = C_6H_5
i: R = CH_3, R′ = t-C_4H_9

Compounds **2b**,[14] **2c**,[15] **2e**,[16] **2f**,[16] and **5d**[14a] were synthesized via Robinson annelation according to literature techniques. Enones **2b** and **2c** were dimethylated with methyl iodide in the presence of sodamide, following the procedure of Russell et al.,[17] yielding **1b** and **1c**, respectively. The Russell procedure was modified by carrying out this base-mediated methylation under an argon atmosphere to prevent BCA.[18] This simple change increased the yield dramatically from 30% to almost 90%. Pentamethylated cyclohexenone **1d** was obtained as a side product in the preparation of **1b** and isolated by GLC. Enones **3b** and **3f** were prepared from dimedone, and **3g** from spiro[5.5]undecane-2,4-dione[19,20] according to the procedure of Gannon and House.[21a] Several other methods were also used to prepare **3f**.[21b-d] Reaction of **3f** with the appropriate Grignard reagents yielded **3h**[21g] and **3i**.[21f] Cyclohexenones **3d** and **4a** were commercially available (Fluka). Compounds **4b**[22,23] and **4c**[24] were prepared from the corresponding cyclohexanones by an α-bromination–dehydrobromination sequence. Finally enones **2b** and **2c** were dehydrogenated with DDQ,[25] yielding the corre-

Table I. Product Yields (percent) from the Oxidation of 4,4- and 5,5-Disubstituted Cyclohex-2-en-1-ones 2 and 3

enone	reaction conditions[a]	enol 7	ether 8	lactol 10	R_2CO 11	acid 12
2b	KO_2; 5 h	89		10		
	KO_2; 5 h; CH_3I		75			
	KOH; 16 h	55				
2c	KO_2; 5 h	80			10	5 (Y = OH)
	KO_2; 5 h; Ar	80			*b*	
	KO_2; 5 h; DMSO	80			*b*	
	KO_2; 5 h; CH_3I		75		15	5 (Y = OCH_3)
	KOH; 16 h	75			*b*	
2e	KO_2; 1 h	84		15		
	KO_2; 16 h			98		
2f	KO_2; 1.3 h	95		3		
	KO_2; 16 h			95		
3b	KO_2; 7 h	80		20		
	KO_2; 7 h; CH_3I		70			
	KOH; 16 h	40				
	$KOC(CH_3)_3$; 1.5 h[c]	75				
	$KOC(CH_3)_3$; 1.5 h; CH_3I[c]		68			
3d	KO_2; 2 h	98				
	KO_2; 2 h; CH_3I		95			
3f	KO_2; 16 h	30		70		
	KOH; 8 h	80		15		
3g	KO_2; 16 h	*d*		95		
	KOH; 7 h	85		15		
3h	KO_2; 3 h	80		15		
	KO_2; 3 h; CH_3I		75			
3i	KO_2; 3 h	80		15		
	KO_2; 2 h; CH_3I		90			

[a] Reactions were carried out at room temperature in benzene or toluene under dry air and quenched with aqueous acid unless otherwise indicated. The ratio of substrate:crown ether:KX ("reactants ratio") was 1:2:4 for enones **2** and **3h**, 1:1:2 for **3b**, 1:1.5:4 for **3d**, 1:2:8 for **3f** and **3g**, and 1:4:8 for 3i. [b] The presence of this compound was determined by TLC. [c] These reactions were carried out at −25 °C in dry toluene to slow down the reaction rate and prevent secondary oxidation of enol **7** to lactol **10**.[28] [d] The enol was observed by TLC but was rapidly converted to the corresponding lactols **10**.[28]

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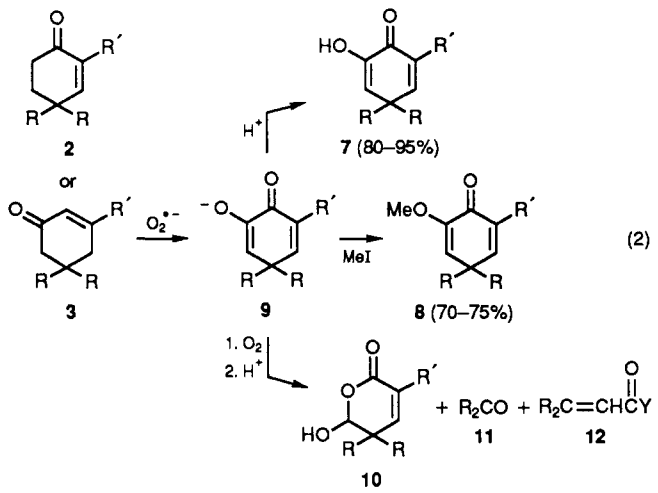
sponding dienones **6b** and **6c**.

Results

Cyclohexenones **1–6** were each reacted with superoxide, generated in sodium-dried benzene or toluene by solubilizing KO_2 with 18-crown-6 polyether. The reactions were generally followed by TLC and, upon disappearance of the substrate, were quenched with either aqueous acid or methyl iodide. A desirable side effect of the latter method is that many of the oxy anions present are methylated, converting, for example, enolates to enol methyl ethers and carboxylates to methyl esters.[26]

Cyclohexenones **1b–1d** and cyclohexadienones **6b** and **6c**, all of which lack acidic (α' or γ) hydrogens,[27] proved totally inert to $O_2^{\bullet-}$ even after contact times of 3 days or more. The 4,4-disubstituted cyclohexenones **2b**, **2c**, **2e**, and **2f**, on the other hand, underwent $O_2^{\bullet-}$ mediated oxidation at the α' position, yielding, upon aqueous acid workup, the corresponding enol **7** in isolated yields of 80–95% (Table I and eq 2). Table I indicates that several



(2)

minor products have been isolated, including lactols **10** (for **2b**, **2e**, and **2f**), and ketones **11** and acrylic acids **12** (for **2c**). These undoubtedly result from secondary oxidation[13d] of enolate **9**, as described further in the accompanying paper.[28] Quenching the reaction with methyl iodide generates the corresponding enol ethers **8** (eq 2).

Interestingly, **7** or **8** are also formed in the reactions of 5,5-disubstituted cyclohexenones **3b** and **3d** with $O_2^{\bullet-}$. In case of **3f** and **3g**, however, the yield of enol, though high in the KOH reactions (vide infra), is very low when the reactions are mediated by the stronger base KO_2. This is because these enol ethers are rapidly oxidized[13d] further under the reaction conditions and converted to the corresponding lactols **10**, a topic discussed in great detail in the accompanying paper.[28] Products **7** and **8** were identified by their spectral data. Enones **7b**,[25b,29a,b] **7c**,[29c] **7d**,[29d] and **8b**[25b,29a,b] are all known compounds. In addition, extensive spectral data on a variety of structurally related steroidal systems has recently been reported.[13e] For reasons that will become clear shortly, we searched but found

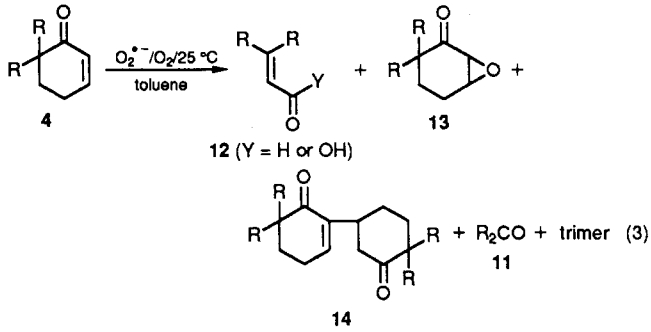
Table II. Product Yields (percent) from the Oxidation of 6,6-Disubstituted Cyclohex-2-en-1-ones 4

enone	reaction conditions[a]	11	12	13	14	misc
4a	KO_2; 4 h				20	trimer (40)
	KO_2; 0.5 h; bubbling O_2			10	3	*b*
4b	KO_2; 16 h			20	40	*b*
	KOH; 16 h				25	*b*
4c	KO_2; 16 h	18	25 (Y = OH)[c] 3 (Y = H)	48		
	KO_2; 16 h; CH_3I	15	35 (Y = OCH_3) 4 (Y = H)	46		
	KOH; 16 h	*d*		36		
	$KOC(CH_3)_3$; 2 h[e]	5		40		**15** (42)[c]
	$KOC(CH_3)_3$; 2 h;[e] CH_3I	5		40		**16** (36) **17** (5)

[a] See note *a* to Table I. The "reactants ratio" was 1:1:1. [b] The acidic fraction consisted of a complex mixture, and its components were not successfully characterized. [c] Identified upon diazotization as its methyl ester; see Experimental Section. [d] The presence of benzophenone was confirmed by TLC. [e] The *tert*-butoxide reactions were carried out at −40 °C in dry toluene.

no evidence for the formation of epoxy ketones[30a] in either the 4,4 or 5,5 systems.

As outlined in eq 3, the 6,6-disubstituted cyclohexenones **4a–4c** yielded a variety of products resulting from both oxidation (e.g., ketone **11** [R_2CO], acid **12** (Y = OH), aldehyde **12** (Y = H), and epoxide **13**) as well as condensation (dimer **14**[30h] and trimer). Table II reveals that the



(3)

product distribution depends primarily on the steric bulk of the substituent R. Thus, diphenylated **4c** yields no condensation product, while the dimethyl analogue **4b** gives both oxidation and condensation products. Dimer **14** and trimer formation is the preferred mode in the unsubstituted cyclohex-2-en-1-one **4a**. Oxidation products **11** and **12** do not result from $O_2^{\bullet-}$-mediated oxidation of the corresponding epoxy ketones **13** since the latter are inert to $O_2^{\bullet-}$.

As seen from Tables I and II, the course of these reactions remains essentially unchanged when DMSO is used as solvent or when the reaction is carried out in an argon atmosphere (after carefully degassing the benzene solvent via five freeze–thaw cycles). What is more, replacing potassium superoxide with the corresponding *tert*-butoxide or hydroxide salts generally yields essentially the same products, with the order of decreasing rates of reaction

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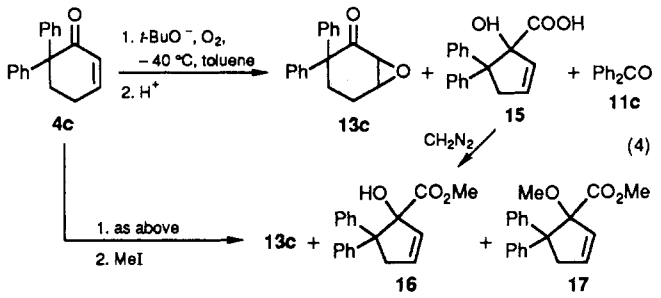
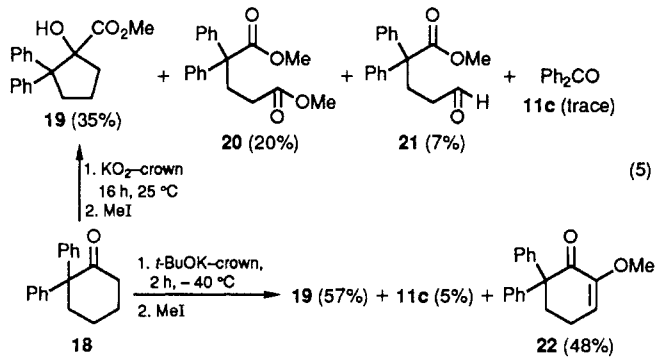
tert-butoxide > superoxide > hydroxide.

Interestingly, we found in the case of **4c** that when the BCA is mediated by *tert*-butoxide in toluene at −40 °C, the two major products are epoxide **13c** and hydroxy acid **15** (eq 4). A methyl iodide workup of this reaction mixture yielded **13c** as before, but in addition methyl esters **16** and **17** were isolated.



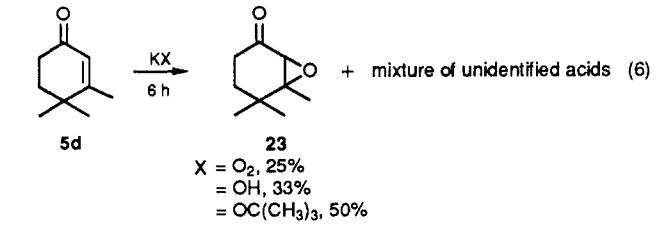
The identity of these products was determined by their spectral data, and in the case of epoxy ketones **13**[30g] and dimers **14**[30h] also by independent synthesis. Methyl 3-phenylcinnamate (**12c** (Y = OCH_3)),[31a] phenylcinnamic acid (**12c** (Y = OH)),[31b] and 3-phenylcinnamaldehyde (**12c** (Y = H))[31c,d] are also known compounds.

For the purpose of comparison, we reacted the saturated analogue of **4c**, 2,2-diphenylcyclohexanone (**18**),[24] with both KO_2 and $KOC(CH_3)_3$ under the same reaction conditions (eq 5). In the case of the room-temperature KO_2 run, the



major isolated product following CH_3I workup was hydroxy ester **19**, along with two oxidative cleavage products, pentanoate esters **20** and **21**. When, however, **18** was reacted at low temperature (−40 °C) with $KOC(CH_3)_3$, hydroxy ester **19** was again the major product, accompanied this time by enol ether **22**.

The final system, **5d**, was studied only briefly and generated epoxy ketone **23** and a mixture of unidentified acids.



As seen from eq 6, the yield of epoxide was lowest with superoxide and greatest with *tert*-butoxide. Unlike epoxy ketones **13b** and **13c**, **23** was further oxidized by $O_2^{\bullet-}$, which may well explain the low yield of **23** and the complexity of the product mixtures.

Discussion

Early researchers in the superoxide field assumed that this radical anion mediated hydrocarbon oxidation via hydrogen atom abstraction, as expected for a typical radical. Recently, however, serious doubts have been raised as to any possible role for $O_2^{\bullet-}$ as a general initiator of oxidative processes by hydrogen abstraction. Liebman and Valentine[32] note that hydrogen atom abstractions occur at appreciable rates only when the bond energy of the bond being formed exceeds that of the bond being broken. These researchers estimate a bond dissociation energy (BDE) for HO_2^- of approximately 66 kcal mol^{-1}. A quick scan of any table of BDEs[33] reveals that only a handful of substrates bear R–H bonds remotely that weak. Nevertheless, many hydrocarbons with high BDEs undergo facile oxidation when reacted with $O_2^{\bullet-}$. For example, the bond energy of the secondary hydrogens in 2-butanone[34] is 92 kcal mol^{-1}; yet, 2-butanone is easily oxidized to the corresponding α-diketone.[9] On the other hand, 1-butene, whose allylic hydrogens have a BDE 9 kcal mol^{-1} lower,[34] is unaffected by $O_2^{\bullet-}$.[9c,d] By contrast, the pK_a of 2-butanone is approximately 20,[35a] whereas that of 1-butene is around 43.[35a] It would seem, therefore, that a substrate's acidity—not its BDE—determines its susceptibility to superoxide mediated oxidation.

Interestingly, the pK_a value (obtained from aqueous pulse radiolysis studies)[35b] of $HOO^{\bullet}$, the conjugate base of superoxide, is 4.69, suggesting that superoxide should be about as basic as acetate. Yet, superoxide is reported to efficiently mediate the oxidations of both oxygen and carbon acids having pK_a's in DMSO as high as 35.[36] Overcoming such pK_a gaps is precedented. Thus, acetate itself is reported to effect the ionization of ketones[35c,d] despite a difference of ≈20 pK_a units. Furthermore, the basicity of $O_2^{\bullet-}$ should be all the more pronounced in aprotic media in which this hard anion is essentially "naked", unencumbered by a stiflingly tight hydration sphere. Indeed, Sawyer[36d] (based on electrochemical studies) has determined a higher pK_a of ≈12 for $HOO^{\bullet}$ in DMF, and this value should be even higher in nonpolar solvents like benzene or toluene.

The data suggest, therefore, that for kinetic reasons $O_2^{\bullet-}$-mediated oxidations are base-catalyzed autoxidative (BCA) processes[13d,18] involving deprotonation (eq 7)—not

(31) (a) Cortese, N. A.; Ziegler, Jr., C. B.; Hrnez, B. J.; Heck, R. F. *J. Org. Chem.* **1978**, *43*, 2952. (b) Sakakibara, T.; Nishimura, S.; Kimura, K.; Minato, I.; Odaira, Y. *J. Org. Chem.* **1970**, *35*, 3884, Table III. (c) Pouchert, C. J.; Campbell, J. R. *The Aldrich Library of NMR Spectra*; Aldrich Chemical Co.: Milwaukee, 1974; Volume VI, spectrum 78B. (d) Kurosawa, K.; Tsujita, T. *Bull. Chem. Soc. Jpn.* **1981**, *54*, 2391.

(32) Liebman, J. F.; Valentine, J. S. *Isr. J. Chem.* **1983**, *23*, 439.

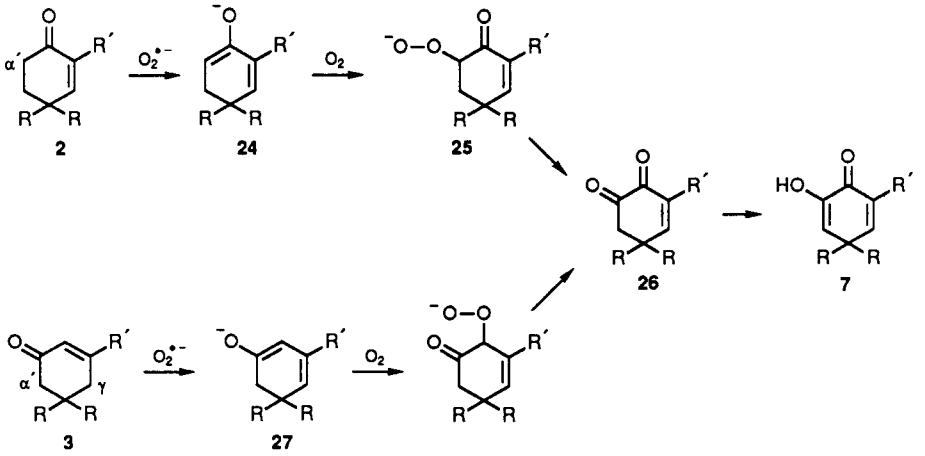
(33) See, for example: *Handbook of Chemistry and Physics*, 61st ed.; Weast, R. C., Ed.; Chemical Rubber Co.: Boca Raton, FL, 1980; p F-233.

(34) Korcek, S.; Chernier, J. H. B.; Howard, J. A.; Ingold, K. U. *Can. J. Chem.* **1972**, *50*, 2285.

(35) (a) March, J. *Advanced Organic Chemistry—Reactions, Mechanisms and Structure*, 3rd ed.; McGraw-Hill: New York, 1985; Table 1, pp 220ff, and references therein. (b) Bielsky, B. H. J. *Photochem. Photobiol.* **1978**, *28*, 645. (c) Bell, R. P.; Lidwell, O. M. *Proc. R. Soc., Ser. A* **1940**, *176*, 88. (d) Jones, J. R. *The Ionization of Carbon Acids*; Academic Press: New York, 1973; p 134.

(36) (a) Frimer, A. A.; Farkash-Solomon, T.; Aljadeff, G. *J. Org. Chem.* **1986**, *51*, 2093. (b) The pK_a at which a substrate is essentially inert to $O_2^{\bullet-}$ has yet to be determined, though recent work from our own laboratory sheds some light on the subject. Frimer et al.[36a] have demonstrated that $O_2^{\bullet-}$ functions as a base when it mediates the oxidation of various ring-substituted diphenylmethanes to the corresponding benzophenones. While (4-methoxyphenyl)phenylmethane reacts very slowly, the 4,4′-dimethoxy analogue proves to be unreactive. Recently, Streitweiser's group[36c] has reported a pK_a of 37.6 for the latter, which would set the pK_a of inertness just below that. (c) Streitweiser, Jr., A.; Vorpagel, E. R.; Chen, C.-C. *J. Am. Chem. Soc.* **1985**, *107*, 6970. (d) Chin, D.-H.; Chiercato, Jr., G.; Nanni, Jr., E. J.; Sawyer, D. T. *J. Am. Chem. Soc.* **1982**, *104*, 1296. (e) Sawyer and co-workers[9] calculate that $O_2^{\bullet-}$ can promote proton transfer from substrates to an extent equivalent to that of a conjugate base of an acid with a pK_a (in H_2O) of approximately 25.

Scheme I. Mechanism for the Formation of Enols 7 from Enones 2 and 3



hydrogen atom abstraction—as the initial step. According to the Russell mechanism[18] for such processes (eq 7–11), the initially formed carbanion (eq 7) is first converted to the corresponding carbon-based radical (eq 8) and is only then oxygenated (eq 9).[37]

$$RH + O_2^{\bullet-} \rightarrow R^- + HO_2^{\bullet} \quad (7)$$

$$R^- + O_2 \rightarrow R^{\bullet} + O_2^{\bullet-} \quad (8)$$

$$R^{\bullet} + O_2 \rightarrow ROO^{\bullet} \quad (9)$$

$$ROO^{\bullet} + O_2^{\bullet-} \rightarrow ROO^- + O_2 \quad (10)$$

$$ROO^- \rightarrow \text{oxidation products} \quad (11)$$

$$HO_2^{\bullet} + O_2^{\bullet-} \rightarrow HO_2^- + O_2 \quad (12)$$

It should be noted that in the presence of excess $O_2^{\bullet-}$ a facile electron transfer (eq 12, $k = 10^8$ M^{-1} s^{-1})[36d] occurs between superoxide and its conjugate acid, $HOO^{\bullet}$, formed in eq 7. This favorable electron-transfer step is vital to the whole process since, by contrast, eq 7 is highly endothermic and its equilibrium lies well to the left. It is mainly the efficiency of eq 12 in inhibiting the reversal of R^- to starting material (for R = H, $K_{7+12} = 2.5 \times 10^8$)[36d] which ultimately enables the conversion of reactants into products.

It would seem certain, then, that C–H linkages with low pK_a values react with $O_2^{\bullet-}$ via initial proton transfer. Indeed, cyclopentadiene[38a] (pK_a 16),[35a] diethyl malonate[38] (pK_a 13),[35a] dibenzoylmethane,[13,27] and 1,3-cyclohexanedione[13,27] are rapidly deprotonated by $O_2^{\bullet-}$, though the resulting anions in the case of the last three are stable to O_2 and superoxide.[13,36a,38b] Similarly, the oxidations of benzoylacetonitrile,[39] malonitrile[40] (pK_a 11),[35a] benzyl cyanide,[40] diphenylacetonitrile,[11] alkyl and aryl malonate esters,[11,38b] and nitroalkanes[41] ($pK_a \approx 10$)[35a] at the α position should be considered BCA processes.

α-Oxidation has been cited in numerous reports[9,27,42,43] on the reaction of $O_2^{\bullet-}$ with saturated ketones (pK_a 20–21).[35a] These reactions are also assumed[27b] to be BCAs, and indeed similar reactions are observed with bona fide bases such as hydroxide and *tert*-butoxide.[18a,e,43b,44] In these cases, the α-diketones or diacids formed presumably result from the decomposition of the corresponding α-hydroperoxy ketones.

Prior to the present study, little was known about the reaction of $O_2^{\bullet-}$ with simple enones,[13d] except for a report by Dietz et al.[45] of a 30% yield of epoxy ketone when cyclohex-2-en-1-one was reacted with electrogenerated $O_2^{\bullet-}$. Our attempts to repeat this observation with KO_2–crown ether were unsuccessful and prompted us to undertake a more detailed study of this system.

The inertness of enones **1b–d** and dienones **6** suggested to us that, unlike extended π systems such as chalcone, tetracyclone, and dibenzal acetone,[6,10,12] the simple enone moiety per se is unreactive to $O_2^{\bullet-}$, be it via electron transfer[46] or Michael addition. By contrast, the reactivity of ketones **2–5** would seem to result, then, from the availability of labile hydrogens.

One indication of the fact that $O_2^{\bullet-}$ is indeed acting as a base in these systems is that the same products are obtained with "naked" hydroxide and *tert*-butoxide. As in all our previous studies[9d,13d,42g] in aprotic nonpolar media in which $O_2^{\bullet-}$ functions as a base, the rate of reaction is $KOC(CH_3)_3 > KO_2 > KOH$. The observation that these

(37) This sequence is required because the concerted oxygenation of carbanions is forbidden by spin conservation principles. It should be noted that unlike Russell and co-workers[18] we have not included in this sequence of reactions a radical coupling between R• and superoxide anion radical (equation 10′), a process with the same outcome as eq 9 and 10 combined:

$$R^{\bullet} + O_2^{\bullet-} \rightarrow ROO^- \quad (10')$$

This is simply because electron transfer rather than radical coupling is generally observed with superoxide.[9c,d]

(38) (a) Stanley, J. P. *J. Org. Chem.* **1980**, *45*, 1413, footnote 20. (b) Allen, P. M.; Hess, U.; Foote, C. S.; Baizer, M. M. *Synth. Commun.* **1982**, *12*, 123.

(39) Gibian, M. J.; Sawyer, D. T.; Ungermann, T.; Tangpoonpholvivat, R.; Morrison, M. M. *J. Am. Chem. Soc.* **1979**, *101*, 640.

(40) (a) Tezuka, M.; Hamada, H.; Ohkatsu, Y.; Osa, T. *Denki Kagaku* **1976**, *44*, 17; *Chem. Abstr.* **1976**, *85*, 26672a. (b) Dibiase, S. A.; Wolak, Jr., R. P.; Dishong, D. M.; Gokel, G. W. *J. Org. Chem.* **1980**, *45*, 3630.

(41) Monte, W. T.; Baizer, M. M.; Little, R. D. *J. Org. Chem.* **1983**, *48*, 803.

(42) (a) Corey, E. J.; Nicolaou, K. C.; Shibasaki, M.; Machida, Y.; Shiner, C. S. *Tetrahedron Lett.* **1975**, *3183*. (b) Frimer, A. A.; Rosenthal, I.; Hoz, S. *Tetrahedron Lett.* **1977**, 4631. (c) Jefford, C. W.; Cadby, P. A. *Helv. Chim. Acta* **1979**, *62*, 1866. (d) Utaka, M.; Matsushita, S.; Yamasaki, H.; Takula, A. *Tetrahedron Lett.* **1980**, *21*, 1063. (e) Galliani, G.; Rindone, B. *Tetrahedron* **1981**, *37*, 2313. (f) Alvarez, E.; Betancor, C.; Freire, R.; Martin, A.; Suarez, E. *Tetrahedron Lett.* **1981**, *22*, 4335. (g) Frimer, A. A.; Aljadeff, G.; Ziv, J. *J. Org. Chem.* **1983**, *48*, 1700. (h) Hocquax, M.; Jaquet, B.; Vidril-Robert, D.; Maurette, M.-T.; Oliveros, E. *Tetrahedron Lett.* **1984**, *25*, 533.

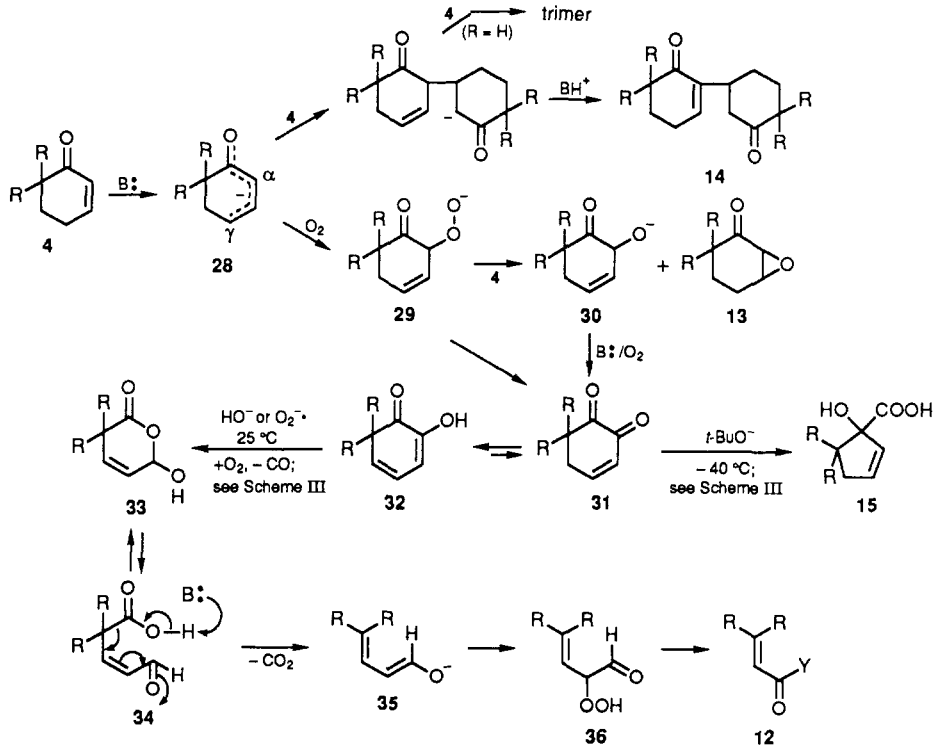
(43) (a) San Fillipo, Jr., J.; Chern, C. I.; Valentine, J. S. *J. Org. Chem.* **1976**, *41*, 1077. (b) Caton, M. P. L.; Darnbrough, G.; Parker, T. *Tetrahedron Lett.* **1980**, *21*, 1685.

(44) (a) House, H. O. *Modern Synthetic Reactions*, 2nd ed.; W. H. Benjamin: Menlo Park, CA, 1972; pp 349ff, and references therein. (b) Rao, D. V.; Stuber, F. A.; Ulrich, H. *J. Org. Chem.* **1979**, *44*, 456.

(45) Dietz, R.; Forno, A. E. J.; Larcombe, B. E.; Peover, M. E. *J. Chem. Soc. B* **1970**, 816.

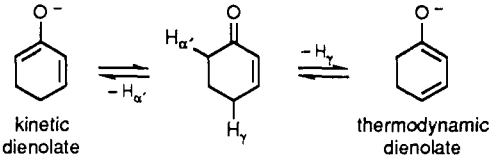
(46) Some reversible electron transfer does seem to occur, however; see: Gibian, M. J.; Russo, S. *J. Org. Chem.* **1984**, *49*, 4304.

Scheme II. Base-Catalyzed Autoxidation of Cyclohexenones 4 with $O_2^{\bullet-}$ or HO^- (at 25 °C) and t-$C_4H_9O^-$ (at −40 °C)



$O_2^{\bullet-}$-mediated reactions proceed essentially unchanged when carried out under argon is also indicative[42] of the role of base played by superoxide in these oxidations, since deprotonation by $O_2^{\bullet-}$ results in O_2 generation (eq 7 and 12).

Overall, then, the data point toward a BCA in which the diversity of products formed results from the fact that in α,β-unsaturated carbonyl systems *two* acidic protons are generally present, positioned at the α' and γ carbons. Of the two, $H_{\alpha'}$ is more acidic for inductive reasons; nevertheless, abstraction of H_γ is thermodynamically preferred since the completely conjugated dienolate ion formed is more stable than its cross-conjugated isomer (eq 13).[47]



(13)

It is not surprising, then, that both 4,4- and 5,5-disubstituted cyclohex-2-en-1-ones (**2** and **3**, respectively) yield the corresponding 2-hydroxycyclohexa-2,5-dien-1-ones **7** (eq 2 and Scheme I). In the case of **2**, it is the $H_{\alpha'}$ that is removed (since the γ position is blocked), and oxygenation of the cross-conjugated dienolate **24** yields the diketone **26**, which in turn enolizes to **7**. For **3**, H_γ abstraction is the preferred mode. We note, of course, that in **3d** (R = R′ = CH_3) both ring and methyl γ hydrogens are available. Nevertheless, removal of a ring H_γ yields the more highly substituted and, hence, the more stable dienolate **27**. Oxygenation of anion **27** proceeds as expected[47e] preferentially α to the carbonyl, leading to diketone **26** and enol **7** (Scheme I). We also note in passing that although **2f** and **3f** yield the same enol **7f**, Table I reveals a discrepancy in the yields of lactol **10f** after 16 h of reaction. We attribute this to the slower rate of H_γ abstraction and enol formation in the case of **3f** due to combined steric blocking by the gem-dimethyl group at C_5 and the ethoxy group at C_3.

6,6-Disubstituted cyclohex-2-en-1-ones **4** yield a variety of products depending on the nature of the substituent. Since similar results were obtained with the bases KOH and $KOC(CH_3)_3$, the mechanism (Scheme II) most likely involves initial H_γ deprotonation generating dienolate **28**. As in the case of dienolate **27**, the point of reaction in such systems is specifically α to the carbonyl.[47e] Dimers **14a** and **14b** as well as the trimer of **4a** (MW = 288) undoubtedly result from intermolecular Michael-type additions.[48] We have already noted in the Results that the data of Table II indicate that the rate of dimerization is quite sensitive to the steric size of the substituents at carbon-6, which is consistent with the observation of others.[48a] Thus, while **4a** (R = H) dimerizes readily (12 h) with aqueous base at room temperature,[30] **4b** (R = CH_3) does so only at 75 °C (16 h), and **4c** (R = Ph) not at all. This steric sensitivity is presumably why no dimerization is observed with the 4,4- and 5,5-disubstituted cyclohexenone systems **2** and **3**. It has been reported[49] that the dimerization of **3b** takes 3 days when mediated by methoxide in methanol.

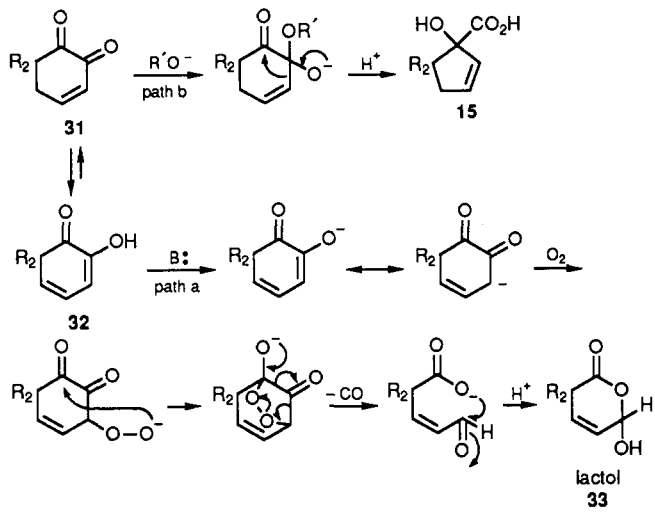
With the dimerization slowed substantially for enones **4b** and **4c**, autoxidative (BCA) processes resulting from the oxygenation of dienolate **28** and the generation of α-keto hydroperoxide **29** can now compete. We believe that **29** is the precursor the oxidation products **12**, **13**, and **15**. Regarding epoxide **13**, it should be noted that the BCA epoxidation of α,β-unsaturated ketones has been known

(47) (a) Malhotra, S. K.; Ringold, H. J. *J. Am. Chem. Soc.* **1964**, *86*, 1997. (b) Volger, H. C.; Brackman, W. *Recl. Trav. Chim. Pays-Bas* **1965**, *84*, 1017 (see especially pp 1030–1032). (c) Reference 44a, pp 502ff. (d) Lee, R. A.; McAndrews, C.; Patel, K. M.; Reusch, W. *Tetrahedron Lett.* **1973**, 965. (e) Tran Huu Dau, M.-T.; Fetizon, M.; Trong Anh, N. *Tetrahedron Lett.* **1973**, 851. (f) Nedelec, L.; Gasc, J. C.; Bucourt, R. *Tetrahedron* **1974**, *30*, 3263. (g) d'Angelo, J. *Tetrahedron* **1976**, *32*, 2979.

(48) (a) Baizer, M. M.; Churna, N.; White, D. A. *Tetrahedron Lett.* **1973**, 5209. (b) Cf.: Chen, H. L. J.; Bersohn, M. *Mol. Phys.* **1967**, *13*, 573.

(49) (a) Engelhardt, J. E.; McDivitt, J. R. *J. Org. Chem.* **1971**, *36*, 367. (b) Cf.: House, H. O.; Fischer, Jr., W. F. *J. Org. Chem.* **1969**, *34*, 3615.

Scheme III. Mechanism of the Base-Mediated β-Oxygenation (Path a) and Benzilic Acid Rearrangement (Path b) of α-Diketone 31



since the early thirties,[13d,18a,e] but no mechanistic studies have been carried out. Karnojitzky[18e] suggests that hydrogen peroxide (formed by the hydrolysis of the initially formed allylic hydroperoxides) can serve as the epoxidizing agent.[30e,50] While plausible in wet solvents, it would seem unlikely in our dry aprotic media. On the other hand, hydroperoxy anion might well be formed in our system by the disproportionation of superoxide anion radical which is initiated by proton transfer from the substrate (eq 7 and 12). However, this would not explain why similar results are obtained with hydroxide and *tert*-butoxide. We have, therefore, suggested in Scheme II that **29**, the hydroperoxy anion of the substrate itself, is the epoxidizing agent. (A similar process would rationalize the formation of epoxy ketones from **5d**.) Such a mechanism finds precedent in the work of Muckensturm[51] on the BCA epoxidation of 9-benzylidenefluorene and in the alkaline *tert*-butyl hydroperoxide epoxidation of enones.[52] We should note, however, that our attempts to reduce **29** in situ with DMSO[53] and thereby inhibit epoxidation proved unsuccessful.[54,55]

The epoxidation mechanism outlined in Scheme II requires the concomitant formation of alkoxide **30**. Considering that epoxide **13** represents 40–50% of the product yield and furthermore that the corresponding alcohol was not isolated from the product mixture, we are led to conclude that **30** is rapidly oxidized to some or all the remaining products. This is, in fact, exactly as expected since α-hydroxy-β,γ-enone **30** is *doubly* activated toward H_α deprotonation and oxygenation at C-2 by the β,γ double bond[56,57] and the C-2 hydroxyl group.[58,59]

α-Oxidation of **30** as outlined above should produce α-diketone **31** and/or its tautomer α-keto enol (diosphenol) **32**. Such systems are well-known[13d,60] to react further under basic conditions to yield the corresponding lactols (via the β-oxygenation sequence outlined in Scheme III, path a) and/or hydroxy acids (via benzilic acid rearrangement; see Scheme III, path b), depending on the reaction conditions. Indeed, we succeeded in isolating both epoxy ketone **13c** and hydroxy acid **15** when the BCA of **4c** was mediated by *tert*-butoxide at low temperatures.

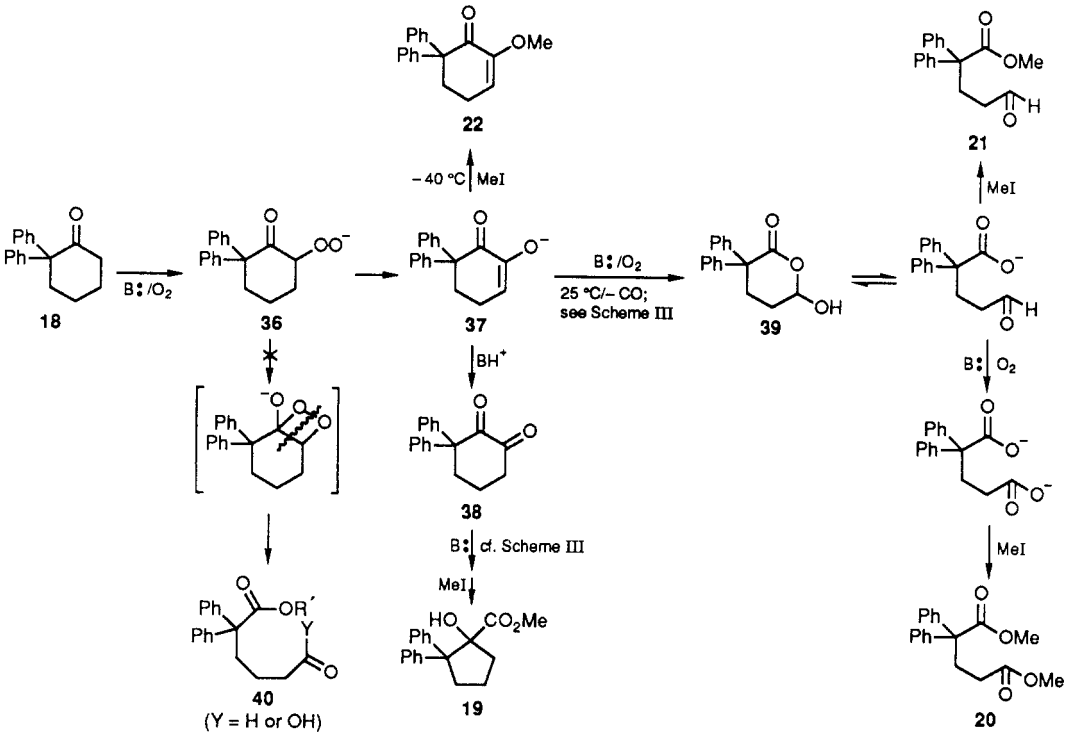
Nevertheless, when the room temperature BCA of **4c** is mediated by KO_2/crown, neither **15** nor the alternately possible lactol **33c** were observed; instead, only cinnamaldehydes and cinnamic acids (**12c**, Y = H or OH) were obtained. This, too, can be readily explained, as shown in Scheme II. The tautomeric open form of lactol **33**, namely, glutaconic aldehydo acid **34**, is *doubly* activated toward decarboxylation by the β,γ double bond and the two aryl groups on the carbon α to carboxyl moiety.[61] Extremely facile loss of CO_2 from **34c** under the strongly basic reaction conditions, oxygenation of the resulting enolate **35c** α to the carbonyl,[47e] and subsequent oxidative cleavage[13d,18e,27,44,55b] of the α-hydroperoxy aldehyde generated all lead quite smoothly and via well-precedented steps to the observed 3-phenylcinnamic aldehyde and acid **12c** (Y = H and OH).

Having explained the results of Table II with the aid of Scheme II, there remain several tissues upon which we would like to comment further. Let us first turn to the formation of hydroxy acid **15** (from aqueous acid workup) or the corresponding methyl esters **16** and **17** (from CH_3I workup). As noted above, the literature[13d] is replete with examples of the base-mediated conversion of dienones to either hydroxy acids or lactols. Nearly all these studies were carried out in protic media where, as a general rule, nucleophilic bases (e.g., HO^-, CH_3O^-, $C_2H_5O^-$) favor benzilic acid rearrangement to a hydroxy acid, while the stronger nonnucleophilic base *tert*-butoxide favors lactol formation. This is consistent with the mechanistic details of these two reactions (Scheme III): the benzilic acid rearrangement involves initial nucleophilic attack of the base upon the carbonyl; on the other hand, α-deprotonation and BCA of the resulting enolate generate lactol.

The results summarized in Table II as rationalized by Scheme II were, therefore, somewhat surprising since it was *tert*-butoxide, not the "supernucleophilic"[9] $O_2^{\bullet-}$, that

(50) House, H. L.; Wasson, R. L. *J. Am. Chem. Soc.* **1957**, *79*, 1488.
(51) (a) Lombard, R.; Muckensturm, B. *C. R. Acad. Sci., Ser. C* **1967**, *265*, 193. (b) Muckensturm, B. *Tetrahedron Lett.* **1968**, 6139.
(52) (a) Yang, C.; Finnegan, R. A. *J. Am. Chem. Soc.* **1958**, *80*, 5845. (b) Payne, G. B. *J. Org. Chem.* **1960**, *25*, 275.
(53) (a) Howard, J. A. In *Free Radicals*; Kochi, J. K., Ed.; Wiley: New York, 1973; p 38. (b) Gibian, M. J.; Ungermann, T. *J. Org. Chem.* **1976**, *41*, 2500. (c) Chern, C.-I.; DiCosimo, R.; De Jesus, R.; San Fillipo, Jr., J. *J. Am. Chem. Soc.* **1978**, *100*, 7317.
(54) Jefford and Rimbault[55] have reported the chemically induced transformation of an allylic hydroperoxide to the corresponding epoxide initiated by homolytic cleavage of the oxygen–oxygen bond. Such a process might be metal catalyzed as well. Its involvement in our systems could not be excluded.
(55) (a) Jefford, C. W.; Rimbault, C. G. *J. Org. Chem.* **1978**, *43*, 1908. (b) See also: Frimer, A. A. *Chem. Rev.* **1979**, *79*, 359.
(56) That β,γ-enones are substantially more susceptible to BCA than the corresponding α,β-analogues is well documented in the literature.[13d,57]
(57) (a) Stern, B. M.S. Thesis, Bar-Ilan University, Ramat Gan, Israel, 1987. (b) Frimer, A. A.; Stern, B., unpublished results, 1987. (c) Sherico Ltd., Netherland Patent Appl. 6400153 (1964); *Chem. Abstr.* **1965**, *62*, 9201. (d) Joly, R.; Warnant, J.; Joly, J.; Malthieu, J. *C. R. Acad. Sci.* **1964**, *258*, 5669. (e) Brown, J. J.; Bernstien, S. *Steroids* **1966**, *8*, 87.
(58) For example, BCA of α,β-unsaturated carbonyl systems generally occurs at the α′ or γ carbons. However, nearly exclusive α′-oxidation is observed when the α′-carbon is already partially oxidized.[13d,59]
(59) (a) Clarke, R. L. *J. Am. Chem. Soc.* **1960**, *82*, 4629. (b) Rao, P. N.; Axelrod, L. R. *J. Am. Chem. Soc.* **1960**, *82*, 2830. (c) Lack, R. E.; Ridley, A. B. *J. Chem. Soc. C* **1968**, 3017.
(60) The conversion of enols to lactols will be discussed in detail in the accompanying paper.[28] Examples in which benzilic acid rearrangement (yielding hydroxy acids) competes with lactol formation are cited below: (a) Curtis, R. G.; Schoenfeld, R. *Aust. J. Chem.* **1955**, *8*, 258. (b) Lavie, D.; Szinai, S. *J. Am. Chem. Soc.* **1958**, *80*, 707, 710. (c) Hirschman, R.; Bailey, G. A.; Walker, R.; Chemedra, J. M. *J. Am. Chem. Soc.* **1959**, *81*, 2822. (d) Rajic, M.; Rull, T.; Ourisson, G. *Bull. Soc. Chim. Fr.* **1961**, 1213. (e) Hanna, R.; Ourisson, G. *Bull Soc. Chim. Fr.* **1961**, 1948. (f) Chandry, G. R.; Halsall, T. G.; Jones, E. R. H. *J. Chem. Soc.* **1961**, 2725. (g) Mori, H.; Gandhi, V. S.; Schwenck, E. *Chem. Pharm. Bull.* **1961**, *10*, 842. (h) Nace, H. R.; Inaba, M. *J. Org. Chem.* **1962**, *27*, 4024. (i) Biellmann, J. F.; Rajic, M. *Bull. Soc. Chim. Fr.* **1962**, 441. (j) Bailey, E. J.; Barton, D. H. R.; Elks, J.; Templeton, J. F. *J. Chem. Soc.* **1962**, 1578. (k) Hanna, R.; Ourisson, G. *Bull. Soc. Chim. Fr.* **1967**, 3742. (l) Utaka, M.; Matsushita, S.; Yamasaki, H.; Takeda, A. *Tetrahedron Lett.* **1980**, *21*, 1063. (m) Nishihama, T.; Takahashi, T. *Bull. Chem. Soc. Jpn.* **1987**, *60*, 2117.
(61) Reference 35a, pp 562–565, and references therein.

Scheme IV. Mechanism for the Oxidation of 2,2-Diphenylcyclohexanone 18



gave us the hydroxy acid product. We were also a bit surprised that the suggested peroxy ketone or diketone intermediates, **29** and **31**, respectively, did not undergo oxidative cleavage by $O_2^{\bullet-}$ to the corresponding diacids.[9,27,42,43] To get better insight into these reactions, we reacted the dihydro analogue of **4c**, 2,2-diphenylcyclohexanone, **18**,[24] with superoxide and *tert*-butoxide under the same reaction conditions as described for **4c**. The product distribution for these reactions is shown above in eq 5, while Scheme IV outlines a proposed mechanism for their formation.

The products obtained with KO_2/crown at room temperature were hydroxy ester **19** as well as pentane-1,5-dioate diester **20** and 5-oxopentanoate ester **21**. As before (Scheme III), the former is the benzilic acid rearrangement product of dione **38** (Scheme IV). The esters, it should be noted, are not the simple oxidative cleavage products of α-hydroperoxy ketone **36**; in such a case, the C_6 homologues (**40**) should have been obtained. As shown in Scheme IV, aldehydo ester **21** is merely a methylated open form of lactol **39**, about which we will have more to say in the accompanying paper,[28] while **20** is its oxidized form. At −40 °C, further oxidation of enolate **37** is inhibited, and only enol ether **22** and hydroxy ester **19** are isolated.

Thus, in glaring contradistinction to the superoxide-mediated oxidation of other cycloalkanones where oxidative cleavage occurs almost exclusively,[27] the results, shown in eq 5, indicate that the 2,2-diphenyl system greatly prefers dehydration of the intermediate α-hydroperoxy ketone (**36**) to α-dione (**38**) and subsequent benzilic acid rearrangement or alternatively further oxidation to lactol (**39**). Lowering the reaction temperature inhibits the latter process. This is exactly what was observed in the case of the unsaturated analogue **4c** and strengthens the mechanism proposed in Scheme II.

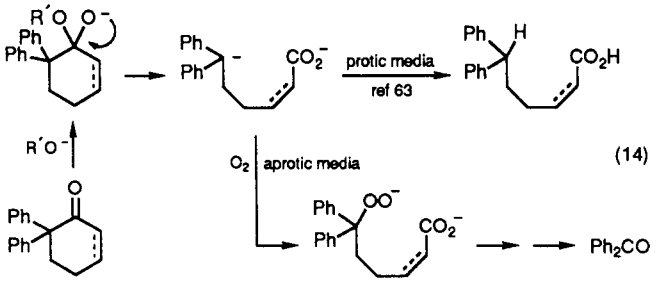
We turn now to the formation of epoxides **13**. We have already noted above that the absence of epoxide in the reaction of **4a** with KO_2/crown would seem to contradict the results of Dietz and co-workers,[45] who report a 30% yield of epoxy ketone using electrogenerated superoxide. Dietz's results have been reconfirmed by Sugawara and Baizer,[11] who suggest that in the standard KO_2/crown procedure excess molecular oxygen is absent. As a result the anion of **4a** has too little opportunity to form a hydroperoxide essential for the epoxidation reaction and reacts by the readily available alternate Michael addition pathway to generate dimer and trimer.

To test this hypothesis, the reaction of **4a** with KO_2/crown was repeated, but this time the reaction mixture was continually bubbled with O_2. An ^1H NMR analysis of the product mixture following aqueous acid workup indicated the formation of epoxide in a yield of approximately 10%. A small amount of dimer (3%) was formed, but no trimer could be detected. The remaining products seem to be the result of multiple oxidation and could not be characterized.

Superoxide-mediated epoxidation has also been observed by Saito and co-workers,[62] who explored the reaction of KO_2/crown with 2,3-dimethyl-1,4-naphthoquinone and other vitamin K related compounds. These authors raise the possibility of either an electron-transfer mechanism or a direct nucleophilic attack by $O_2^{\bullet-}$ on the enone system as the initial step. However, on the basis of the results described above for enones **4** and **5** and the mechanism of Scheme II, a BCA process may be invoked entailing initial γ-proton abstraction from the methyl groups straddling the quinone double bond.[9c,d,13d]

Some comments as to origin of the benzophenone (**11c**) formed in the oxidation of **2c** and **4c** are also in order. In the case of the former, it presumably results as a secondary oxidation product of enol **7c**,[28] and related processes may be involved in the case of **4c** as well. However, in the 6,6-diphenyl system an additional mechanism is possible (eq 14). Calas et al.[63] report that **18c** is cleaved in refluxing isopropanolic solutions of KOH to 6,6-diphenylhexanoic acid. Were a similar mechanism operative in our aprotic media systems, then the intermediate diphenyl carbanion would most likely undergo oxygenation (instead

(62) Saito, I.; Otsuki, T.; Matsuura, T. *Tetrahedron Lett.* **1979**, 1693.
(63) Calas, M.; Calas, B.; Giral, L. *Bull. Soc. Chim. Fr.* **1973**, 2078.



(14)

of protonation). Cleavage of the resulting peroxyanion would yield the observed benzophenone.

We note in closing that enols 7 and enol ethers 8 undergo the acid-catalyzed dienone–phenol rearrangement. The latter process proceeds under *electronic*—not *steric*—control, as is commonly assumed. These results will be discussed in greater detail in a forthcoming publication.

In summary, this paper has further demonstrated the effectiveness and convenience of the superoxide anion radical/18-crown-6 complex in mediating base-catalyzed autoxidative processes in nonpolar aprotic media. We have also gained further insight into the factors that control the secondary rearrangements of the quite labile keto hydroperoxide system.

Experimental Section

^{1}H NMR spectra were obtained on Varian HA-60, Varian HA-100 (asterisked values), and Bruker AM 300 Fourier transform (double-daggered values) spectrometers, while ^{13}C NMR spectra were taken with a Varian CFT-20 or the above 300 (double-daggered values) instrument. Assignments were facilitated by correlating proton and carbon chemical shifts through analysis of residual couplings in off-resonance decoupled spectra. In all cases, TMS served as the internal standard. IR spectrometers used were generally Perkin Elmer Models 457 and 621, though spectra designated FTIR were taken with the Nicolet 60 SXB FTIR spectrometer. Mass spectra were run on a Finnigan-4000 GC/MS machine. UV–visible spectra were taken with a Varian DMS-100 spectrometer. Preparative thin-layer chromatography (TLC) was carried out on Merck silica gel F_{254} precoated plates, while analytical runs were performed by using Riedel-De Haen microcards. The retention times given are for the analytical runs. Gas chromatograms were obtained by using a Varian Aerograph Model 920 preparative GLC with peak areas determined by triangulation. Copper columns ($^1/_4$ in.) were packed with 20% Carbowax 20M on Chromosorb W AW DMCS. Injector and detector temperatures were at least 25 °C above the column temperature given and were generally set at 200 ± 25 °C.[64] Potassium superoxide (Alfa inorganics, 96.5%), *tert*-butoxide (Fluka), and hydroxide (Frutarom) salts were ground into fine powders in a glovebag under dry argon prior to use. 18-Crown-6 polyether (Fluka) was used as supplied (if dry and crystalline; otherwise, it was recrystallized from acetonitrile)[65] and stored along with the above potassium salts in a desiccator. Methyl iodide was distilled and stored at −10 °C under argon.

4,4,6,6-Tetramethyl- and 2,4,4,6,6-Pentamethylcyclohex-2-en-1-one (1b and 1d, Respectively). The title compounds were prepared by methylating enone **2b** according to the procedure of Russell and Stevenson.[17] Yields were improved substantially (from 30 to almost 90%) by carrying out the reaction in inert atmosphere (Ar or N_2), thus preventing competitive base-catalyzed autoxidation (BCA).[18] The product mixture was fractionally distilled at 75–80 °C/17 Torr. TLC analysis (10% acetone in hexane) of the distillate showed only a single spot (R_f = 0.49); however, NMR revealed it to be a mixture of **1b** and **1d** in a ratio of 4:1. The enones were separated by GLC[64d] at 95 °C with **2b** eluting first (retention time 18 min; flow rate 80 cm^3/min).

1b: ^{1}H NMR* ($CDCl_3$) δ 6.52 (d, $J_{2,3}$ = 10 Hz, 1 H, H_3), 5.77 (d, $J_{2,3}$ = 10 Hz, 1 H, H_2), 1.78 (s, 2 H, H_5), 1.17 (s, 6 H, gem-dimethyl at C_4), 1.15 (s, 6 H, gem-dimethyl at C_6); ^{1}H NMR (C_6D_6) δ 6.05 and 5.78 (AB quartet, J = 10 Hz, 2 H), 1.47 (s, 2 H), 1.17 (s, 6 H), 0.9 (s, 6 H); MS (70 eV), m/e 152 (M^+).

1d: ^{1}H NMR (C_6D_6) δ 5.97 (br s, 1 H, H_3), 1.90 (d, J = 2 Hz, 3 H, C_2 methyl), 1.53 (s, 2 H, H_5), 1.20 (s, 6 H, gem-dimethyl at C_4), 0.95 (s, 6 H, gem-dimethyl at C_6); MS (70 eV), m/e 166 (M^+).

6,6-Dimethyl-4,4-diphenylcyclohex-2-en-1-one (1c). This enone was prepared in a 65% yield according to the procedure of Russell and Stevenson,[17] but under Ar as noted in the preparation of **1b**. The product was recrystallized from 95% ethanol as a yellow powder; mp 95 °C.

1c: ^{1}H NMR ($CDCl_3$) δ 7.22 (m, 11 H, Ar + H_3), 6.12 (d, $J_{2,3}$ = 12 Hz, 1 H, H_2) 2.70 (s, 2 H, H_5), 0.95 (s, 6 H, gem-dimethyl); MS (70 eV), m/e 276 (M^+), 261 ($M - CH_3$), 248 (M − CO). Anal. Calcd for $C_{10}H_{20}O$: C, 86.95; H, 7.25. Found: C, 86.83; H, 7.33.

4,4-Dimethylcyclohex-2-en-1-one (2b). Enone **2b** was prepared according to the procedure of Dauben et al.[14a] The product was distilled through a 40-cm Vigreux column, and the fraction distilling at 48–56 °C/4 Torr contained the desired enone in a 40% yield. The product was purified from isobutyraldehyde by GLC[64c] at 100 °C and had a retention time of 13.5 min when the flow rate was 90 cm^3/min; R_f (25% acetone in hexane) 0.52. The spectral properties of **2b** were consistent with those previously reported.[14]

4,4-Diphenylcyclohex-2-en-1-one (2c). This compound was synthesized by condensing diphenylacetaldehyde (Aldrich) with methyl vinyl ketone (Aldrich) by using the Newman[15a] modification of the Zimmerman procedure.[15b]

2c: R_f (1:1 $CHCl_3$–benzene) 0.46; ^{1}H NMR‡ ($CDCl_3$) δ 7.32 (m, 2 H, para), 7.31 (dt, $J_{2,3}$ = 10.2 Hz, $J_{3,5}$ = 1.0 Hz, 1 H, H_3), 7.30 (m, 4 H, meta), 7.23 (m, 4 H, ortho), 6.21 (d, $J_{2,3}$ = 10.2 Hz, H_2), 2.70 (dt, $J_{5,6}$ = 7 Hz, $J_{3,5}$ = 1 Hz; additional AA′XX′ splittings, 2 H, H_5) 2.42 (t, $J_{5,6}$ = 7 Hz, additional AA′XX′ splittings, 2 H, H_6)—assignments were elucidated via double-resonance irradiation at 6.21 and 2.70 in conjunction with 5 Hz/cm resolution; ^{13}C NMR‡ ($CDCl_3$) δ 198.75 (C_1), 156.11 (C_3), 145.35 (ipso), 128.92 (C_2), 128.53 (meta), 127.60 (ortho), 126.81 (para), 49.29 (C_4), 35.90 (C_5), 34.92 (C_6); IR (Nujol) 1660 (s, C=O), 1570 (w, C=C) cm^{-1}; MS (55 eV), m/e 248 (M^+, 10.67%), 220 (M − CO and/or M − C_2H_4, 15.91%), 219 (M − HCO, 20.16%), 204 (M − CH_2CO), 205 (25.21%), 191 (M − C_2H_4 − HCO, 40.06%), 180 (M − CH_2CO − C_2H_2, 9.31%), 165 ($C_6H_5CC_6H_4$, 25.59%).

2-Methoxy- and 2-Ethoxy-4,4-dimethylcyclohex-2-en-1-one (2e and 2f). These enol ethers were prepared according to Wenkert et al.[16a] from the corresponding 1,4-dialkoxy-2-butanones[16b] in a 60% yield. The products were distilled at 0.1 Torr (bp 65 °C for **2e** and 87 °C for **2f**) and further purified by GLC[64b] at 200 °C. With a flow rate of 100 cm^3/min, the retention times of **2e** and **2f** were 7 and 3 min, respectively. In the case of **2e**, the spectral data were consistent with the literature values.[16] The R_f of **2e** eluting with 5% acetone in pentane was 0.125. The spectral data for **2f** is given below.

2f: R_f (25% acetone in hexane) 0.42; ^{1}H NMR ($CDCl_3$) δ 5.50 (s, 1 H, H_3), 3.70 (q, J = 6 Hz, 2 H, OCH_2), 2.50 (t, $J_{5,6}$ = 6 Hz, 2 H, H_6), 1.76 (t, $J_{5,6}$ = 6 Hz, 2 H, H_5), 1.33 (t, J = 6 Hz, 3 H, ethoxy methyl), 1.16 (s, 6 H, gem-dimethyl); IR (neat) 1675 (s), 1610 (s) cm^{-1}; MS (55 eV), m/e 168 (M^+), 153 ($M - CH_3$), 139 ($M - CH_2CH_3$), 124 ($M - CH_3 - CH_2CH_3$).

5,5-Dimethylcyclohex-2-en-1-one (3b), 3-Methoxy- and 3-Ethoxy-5,5-dimethylcyclohex-2-en-1-one (3d and 3f), and 4-Methoxyspiro[5.5]undec-3-en-2-one (3g). Enone **3d** was commercially available from Fluka. **3b** (60% yield) and **3f** (75% yield) were prepared from dimedone, and **3g** (80% yield) was prepared from spiro[5.5]undeca-2,4-dione[19,20] according to the procedure of Gannon and House.[21a] Several other methods were also used to prepare **3f**.[21b-d] **3b** was distilled (60 °C/8 Torr), and its spectral data were consistent with literature values.[14a] Enone **3f** solidified after distillation (85 °C/5 Torr) and was recrystallized from petroleum ether (40–60 °C), yielding white shiny cubic crystals (mp 56–57 °C). **3g** was obtained as a yellowish solid which was crystallized from methanol (mp 49–50 °C). The spectral data for these latter two enones are given below.

3f: R_f (25% acetone in hexane) 0.43; ^{1}H NMR ($CDCl_3$) δ 5.31 (s, 1 H, H_2), 3.88 (q, J = 8 Hz, 2 H, OCH_2), 2.23 (s, 2 H, H_4), 2.17 (s, 2 H, H_6), 1.30 (t, J = 8 Hz, 3 H, ethoxy methyl), 1.07 (s, 6 H, gem-dimethyl); IR (Nujol) 1650 (s), 1600 (s) cm^{-1}; MS (70 eV),

(64) Column lengths used were (a) 2.5 m, (b) 4 m, (c) 6.5 m, (d) 8 m.
(65) Gokel, G. W.; Cram, D. J.; Liotta, C. L.; Harris, H. P.; Cook, F. L. *J. Org. Chem.* **1974**, *39*, 2445.

m/e 168 (M^+), 153 (M – CH_3), 140 (M – CO), 112 (M – CO – CH_2CH_2).

3g: R_f (25% acetone in hexane) 0.30; ^1H NMR ($CDCl_3$) δ 5.30 (s, 1 H, H_2), 3.66 (s, 3 H, OCH_3), 2.33 (s, 2 H, H_4), 2.27 (s, 2 H, H_6), 1.43 (br s, 10 H, ring); IR (Nujol) 1640 (m), 1610 (s) cm^{-1}; MS (70 eV), m/e 194 (M^+), 179 (M – CH_3), 161 (M – CH_3 – H_2O).

3-Phenyl- and 3-*tert*-Butyl-5,5-dimethylcyclohex-2-en-1-one (3h and 3i, Respectively). These two enones were prepared under nitrogen by adding enol ether **3f** to an etherial solution of either phenylmagnesium bromide or *tert*-butylmagnesium bromide, prepared from the corresponding bromides by standard procedures.[66] The reaction mixtures were refluxed for 5 h and were then stirred overnight at room temperature. Standard acid workup and silica column chromatography (eluting with 15% acetone in hexane) gave the desired products **3h** and **3i** in 60% and 14% yields, respectively. **3h** was recrystallized from petroleum ether; mp 52.5 °C (lit.[21e] 54–54.5 °C). The spectral data for **3i** were consistent with those previously reported.[21f] The 300-MHz NMR data are cited below.

3h: R_f (15% acetone in hexane) 0.48; ^1H NMR‡ ($CDCl_3$) δ 7.56–7.51 (m, 2 H, ortho), 7.44–7.39 (m, 3 H, meta and para), 6.42 (t, $J_{2,4}$ = 1.5 Hz, 1 H, H_2), 2.66 (d, $J_{2,4}$ = 1.5 Hz, 2 H, H_4), 2.35 (s, 2 H, H_6), 1.14 (s, 6 H, gem-dimethyl); ^{13}C NMR‡ ($CDCl_3$) δ 199.99 (C_1), 157.55 (C_3), 139.08 (ipso), 129.89 (para), 128.73 (meta), 126.12 (ortho), 124.43 (C_2), 50.99 (C_6), 42.40 (C_4), 37.76 (C_5), 28.43 (methyls at C_5).

3i: R_f (15% acetone in hexane) 0.32; ^1H NMR‡ ($CDCl_3$) δ 5.95 (t, $J_{2,4}$ = 1 Hz, 1 H, H_2), 2.22 (d, $J_{2,4}$ = 1 Hz, 2 H, H_4), 2.21 (s, 2 H, H_6), 1.12 (s, 9 H, *tert*-butyl), 1.03 (s, 6 H, gem-dimethyl at C_4); ^{13}C‡ NMR ($CDCl_3$) δ 200.88 (C_1), 171.06 (C_3), 121.91 (C_2), 51.01 (C_6), 40.23 (C_4), 36.52 (4° carbon of *tert*-butyl), 33.66 (C_5), 28.07 (methyls at C_5), 28.01 (*tert*-butyl methyls).

6,6-Dimethylcyclohex-2-en-1-one (4b). This compound was prepared from 2,2-dimethylcyclohexanone[22a] via a bromination[22b]–dehydrobromination[23] sequence. The yields from the last step were variable but generally quite poor (<30%). The crude product was vacuum distilled through a Vigreux column, and the fraction boiling in the range 94–100 °C/40–45 Torr was collected. Enone **4b** was further purified via GLC[64d] at 180 °C (retention time of 19 min with flow rate of 80 cm^3/min). The spectral data of 2,2-dimethylcyclohexanone have been reported.[67]

2-Bromo-6,6-dimethylcyclohexanone: ^1H NMR ($CDCl_3$) δ 4.80 (m, 1 H, H_2), 1.77 (m, 6 H, H_3, H_4, and H_5), 1.33 (s, 6 H, gem-dimethyl); MS (70 eV), m/e 206 (M^+ + 2), 204 (M^+), 178 (M + 2 – CO), 176 (M – CO).

4b: R_f (10% acetone in hexane) 0.30; ^1H NMR ($CDCl_3$) δ 6.82 (dt, $J_{2,3}$ = 10 Hz, $J_{3,4}$ = 3 Hz, 1 H, H_3), 5.85 (d, $J_{2,3}$ = 10 Hz, 1 H, H_2), 2.27 (m, 2 H, H_4), 1.77 (t, $J_{4,5}$ = 6 Hz, 2 H, H_5), 1.05 (s, 6 H, gem-dimethyl); MS (70 eV), m/e 124 (M^+), 96 (M – CO).

6,6-Diphenylcyclohex-2-en-1-one (4c) and 2,2-Diphenylcyclohexanone (18). The multistep procedure of Burger and Bennet[24] was followed. The cyanohydrin of cyclopentanone was hydrolyzed and esterified,[66] yielding methyl 1-hydroxycyclopentanecarboxylate (**41**). Addition of phenyl Grignard reagent[66] to the latter produces the corresponding glycol 1-(diphenylhydroxymethyl)-1-hydroxycyclopentane (**42**), which undergoes pinacol–pinacolone rearrangement generating 2,2-diphenylcyclohexanone (**18**). All the above steps proceed quite smoothly as described.[24] However, subsequent bromination of **18** to generate 6-bromo-2,2-diphenylcyclohexanone (**43**) proved a bit troublesome. When carried out in CCl_4 at room temperature,[23b,24] reaction (i.e., decoloration) occurred, in some cases only after a long incubation period of an hour or so (80% yield) and in others not at all. Reaction under reflux[68] did occur, but recrystallization of the crude product mixture from benzene–ligroin gave the desired bromo ketone in varying (25–75%) yields. The final dehydrobromination, using either the collidine procedure of Burger and Bennet[24] or the Warnhoff[69] lithium chloride method, was also problematic; the Zimmerman[23b] conditions, however, proved somewhat more successful. Column chromatography of the crude reaction mixture on deactivated silica gel (30% water w/w, eluting with 5% ether in hexane)[23b] gave the desired enone **4c** (in a 42% yield) along with a variety of side products including 6,6-diphenylcyclohex-3-en-1-one (**44**, 0.5%), 1,2-epoxy-3,3-diphenylcyclohexane (**45**, 0.5%), 6,6-diphenylcyclohexa-2,4-dien-1-one (**46**, 5%), and **18** (5%). The identity of the above compounds was confirmed by their spectral data, which are sparse or nonexistent in the literature and are, therefore, cited below. In the case of **44** and **45**, these data were extracted from spectra of a fraction containing **18**, **44**, and **45** in a 5:1.5:1 ratio. GC MS (Chromosorb Q 100/120, temperature programming 80–250 °C at 8 °C/min) yielded the MS data for **44**. Epoxide **45** was independently synthesized by treating 3,3-diphenylcyclohexene[23c,24c] with MCPBA. Similarly, the data for **46** were obtained from a fraction containing a 2:1 mixture of **4c**:**46**. NMR assignments were facilitated by correlating proton and carbon chemical shifts through analysis of residual couplings in off-resonance decoupled spectra.

4c: R_f (10% acetone in hexane) 0.28; ^1H NMR‡ ($CDCl_3$) δ 7.32–7.15 (m, 6 H, meta and para), 7.12–7.04 (m, 4 H, ortho), 6.80 (dt, $J_{2,3}$ = 10 Hz, $J_{3,4}$ = 4 Hz, 1 H, H_3), 6.20 (dt, $J_{2,3}$ = 10 Hz, $J_{2,4}$ = 2 Hz, 1 H, H_2), 2.80 (t, $J_{4,5}$ = 6 Hz, 2 H, H_5), 2.30 (tdd, $J_{4,5}$ = 6 Hz, $J_{3,4}$ = 4 Hz, $J_{2,4}$ = 2 Hz, 2 H, H_4); ^{13}C NMR‡ ($CDCl_3$) δ 199.90 (C_1), 148.95 (C_3), 141.67 (ipso), 130.07 (C_2), 128.32 (ortho), 127.96 (meta), 126.77 (para), 59.52 (C_6), 35.03 (C_5), 24.45 (C_4); FTIR (KBr) 1672.3 (s, CO) cm^{-1}; MS (55 eV), m/e 248 (M^+, 16.54%), 180 (Ph_2CCH_2, 100%), 179 (40.28%), 165 ($PhCC_6H_4$, 51.45%).

18:[24c] R_f (10% acetone in hexane) 0.36; ^1H NMR‡ ($CDCl_3$) δ 7.36–7.21 (m, 6 H, meta and para), 7.10–7.02 (m, 4 H, ortho), 2.60 (dd with additional splitting, $J_{3,4}$ = 6.5 and 5.5 Hz, 2 H, H_3), 2.51 (dd, $J_{5,6}$ = 7 and 6 Hz, 2 H, H_6), 2.01–1.90 (m, 2 H, H_5), 1.89–1.79 (m, 2 H, H_4); ^{13}C NMR‡ ($CDCl_3$) δ 211.20 (C_1), 142.30 (ipso), 128.52 (ortho), 128.30 (meta), 126.79 (para), 63.91 (C_2), 40.70 (C_3), 39.18 (C_6), 27.78 (C_5), 22.13 (C_4); FTIR (KBr) 1706.3 (s, CO) cm^{-1}; MS (44 eV), m/e 250 (M^+, 28.35%), 222 (M – CO, 17.70%), 206 (M – HO – $CHCH_2$, 91.48%), 193 (M – $HCOCH_2CH_2$, 87.72%), 178 (Ph_2C_2, 52.57%), 165 (Ph_2C – H, 64.66%), 131 (39.22%), 115 (100%); MS (55 eV, CI, butane), m/e 251 (MH^+, 100%), 173 (MH^+ – PhH, 19.21%).

41: bp 85–86 °C/17 Torr (lit.[70] bp 87 °C/23 Torr, 84 °C/16 Torr); ^1H‡ NMR ($CDCl_3$) δ 3.78 (s, 3 H, OCH_3), 3.19 (br s, 1 H, OH), 2.12–1.99 (m, 2 H), 1.96–1.69 (m, 7 H); ^{13}C‡ NMR ($CDCl_3$) δ 177.70 (CO), 81.76 (C_1), 52.54 (CH_3O), 39.57 (C_2 and C_4), 24.76 (C_3 and C_4).

42: R_f (10% acetone in hexane) 0.23; ^1H NMR‡ ($CDCl_3$) δ 7.62–7.55 (m, 4 H, ortho), 7.32–7.19 (m, 6 H, meta and para), 2.73 (br s, 1 H, OH), 2.20–2.07 (m, 2 H), 1.86–1.70 (m, 3 H), 1.70–1.42 (m, 6 H); ^{13}C NMR‡ ($CDCl_3$) δ 145.18 (ipso), 128.03 (ortho), 127.68 (meta), 126.97 (para), 98.08 (C_6), 87.79 (C_1), 37.48 (C_2 and C_5), 24.81 (C_3 and C_4); FTIR (KBr) 3544.9 (m, OH), 3419.0 (m, OH) cm^{-1}; MS (55 eV, CI, ammonia), m/e 268 (M^+, 100%), 251 (MH^+ – H_2O, 68.54%), 183 (Ph_2COH, 3.19%); MS (55 eV), m/e 251 (M – OH, 20.76%), 234 (M – $2H_2O$, 1.29%), 184 (Ph_2COH_2, 100%), 173 (M – Ph – H_2O, 17.04%), 165 ($PhCC_6H_4$, 16.94%), 105 (PhCO, 52.52%).

43: mp (ethanol) 115 °C; R_f (10% acetone in hexane) 0.34; ^1H NMR‡ ($CDCl_3$) δ 7.49–7.17 (m, 8 H, aryl), 6.87–6.83 (m, 2 H, cis-ortho), 4.86 (dd, $J_{5ax,6ax}$ = 13 Hz, $J_{5eq,6ax}$ = 6 Hz, 1 H, H_6), 2.88 (ddd, J = 15, 7 and 3 Hz, 1 H, H_{3ax}), 2.64–2.53 (m, 1 H, H_{3eq}), 2.51–2.25 (m, 2 H, H_5), 2.10–1.86 (m, 2 H, H_4); ^{13}C NMR‡ ($CDCl_3$) δ 201.51 (C_1), 143.76 + 139.02 (ipso), 128.51 + 128.09 (ortho), 129.41 + 127.70 (meta), 127.70 + 126.78 (para), 64.45 (C_2), 55.74 (C_6), 39.77 (C_5 or C_3), 38.63 (C_3 or C_5), 22.92 (C_4); FTIR (KBr) 1729.6 (s, CO) cm^{-1}; MS (55 eV, CI, ammonia), m/e 348 (MNH_4^+ + 2, 79.80%), 346 (MNH_4^+, 100%), 331 (MH^+ + 2, 4.85%), 329 (MH^+, 5.93%), 268 (MNH_4^+ – Br, 28.83%), 251 (MH_2^+ – Br, 10.27%), 249 (M – Br, 5.17%).

44: ^1H NMR‡ ($CDCl_3$) δ 7.33–7.28 (m, 6 H, meta and para), 7.12–7.07 (m, 4 H, ortho), 5.97 (dtt, $J_{3,4}$ = 10 Hz, $J_{4,5}$ = 4 and 2 Hz, 1 H, H_4), 5.60 (dtt, $J_{3,4}$ = 10 Hz, $J_{2,3}$ = 3.5 and 1.5 Hz, 1 H, H_3), 3.12 (qd, J = 5 Hz, $J_{4,5}$ = 4 Hz, 2 H, H_5), 2.93 (dq, $J_{2,3}$ = 3.5, J = 2 Hz, 2 H, H_2); ^{13}C NMR‡ ($CDCl_3$) δ 207.94 (C_1), 141.41 (ipso), 128.74 (ortho), 128.10 (meta), 126.98 (para), 125.92 (C_4), 124.45

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(C_3), 62.42 (C_6), 40.00 (C_5), 38.87 (C_2); MS (55 eV, CI, methane), m/e 249 (MH^+, 49.59%), 231 ($MH^+ - H_2O$, 8.47%), 171.10 (MH^+ - PhH, 18.18%), 143 (MH^+ - PhH - CO, 25.41%), 105 (PhCO).

45: ^1H NMR‡ ($CDCl_3$) δ 7.34–7.26 (m, 6 H, aryl), 7.25–7.16 (m, 4 H, aryl), 3.69 (br d, $J_{1,2}$ = 3.5 Hz, 1 H, H_2), 3.49 (m, 1 H, H_1), 2.40 (ddd, J_{gem} = 13 Hz, $J_{4ax,5ax}$ = 12.5, $J_{4ax,5eq}$ = 3 Hz, 1 H, H_{4ax}), 1.98–1.91 (m, 2 H, H_6), 1.76 (br ddd, J_{gem} = 13 Hz, $J_{4eq,5eq}$ = 6 Hz, $J_{4eq,5ax}$ = 3 Hz, 1 H, H_{4eq}), 1.44–1.32 (m, 1 H, H_{5eq}), 1.21 (dddd, J = 14, 12.5, 8.5, 7.0, 1 H, H_{5ax}); ^{13}C NMR‡ ($CDCl_3$) δ 147.02 and 146.59 (ipso), 128.21 (both orthos), 128.07 and 127.73 (meta), 126.28 and 126.23 (para), 60.07 (C_2), 54.69 (C_1), 47.15 (C_3), 31.19 (C_4), 22.54 (C_6), 16.61 (C_5); MS (55 eV, CI, CH_4), m/e 251 (MH^+, 19.13%), 233 (M - H_2O, 100%), 173 (M - C_6H_5, 41.55%), 167 (Ph_2CH, 61.69%), 145 (M - C_6H_5 - CO, 46.76%).

46: ^1H NMR‡ ($CDCl_3$) δ 7.32–7.14 (m, 6 H, meta and para), 7.12–7.07 (m, 4 H, ortho), 6.99 (ddd, $J_{2,3}$ = 10 Hz, $J_{3,4}$ = 6 Hz, $J_{3,5}$ = 2 Hz, 1 H, H_3), 6.69 (ddd, $J_{4,5}$ = 9.5 Hz, $J_{3,5}$ = 2 Hz, $J_{2,5}$ = 1 Hz, 1 H, H_5), 6.29 (ddd, $J_{4,5}$ = 9.5 Hz, $J_{3,4}$ = 6 Hz, $J_{2,4}$ = 1 Hz, 1 H, H_4), 6.03 (ddd, $J_{2,3}$ = 10 Hz, $J_{2,4}$ = 1 Hz, $J_{3,4}$ = 1 Hz, 1 H, H_2); ^{13}C NMR‡ ($CDCl_3$) δ 201.56 (C_1), 146.20 (C_5), 141.82 (ipso), 140.94 (C_3), 128.70 (ortho), 128.39 (meta), 127.28 (para), 125.43 (C_4), 119.56 (C_2), 64.75 (C_6); MS (55 eV, CI, methane), m/e 247 (MH^+, 41.29%), 171 (MH^+ - Ph, 25.65%), 105 (PhCO, 100%).

3,4,4-Trimethylcyclohex-2-en-1-one (5d). The synthetic procedure of Dauben et al.[14a] was used, and the product was distilled at 48.5 °C/2 Torr. ^1H NMR revealed the distillate to be a mixture of **5d** and its 3,6,6 isomer, which could be conveniently separated on a silica gel column eluting with 10% acetone in hexane. Their spectral data were consistent with the literature values.[71]

4,4-Dimethyl- and 4,4-Diphenylcyclohexa-2,5-dien-1-one (6b and 6c). Enones **2b** and **2c** were dehydrogenated[25] with DDQ, yielding the title dienones. The ^1H NMR,[72] ^{13}C NMR,[73] and IR[74] data have been reported.

6,6-Dimethyl- and 6,6-Diphenyl-2,3-epoxycyclohexan-1-one (13b and 13c). These epoxy ketones were prepared according to the general procedure of Wasson and House[30e] in a 75% yield. Epoxide **13b** was distilled (38 °C/2 Torr) and purified by GLC[64a] at 100 °C (flow rate 80 cm^3/min; retention time 24 min), while **13c** was recrystallized from pentane as white needles (mp 107–109 °C).

13b: R_f (10% acetone in hexane) 0.24; ^1H NMR* ($CDCl_3$) δ 3.53 (m, 1 H, H_3), 3.20 (d, $J_{2,3}$ = 3 Hz, 1 H, H_2), 2.03 (m, 2 H, H_4), 1.83 (m, 2 H, H_5), 1.13 (s, 3 H, CH_3), 1.03 (s, 3 H, CH_3); ^{13}C NMR ($CDCl_3$) δ 209 (C_1), 53.50, 54.54 (C_2 and C_3), 41.72 (C_6), 29.28 (C_4), 25.48 (CH_3), 25.01 (CH_3), 20.49 (C_5); IR (neat) 1700 (s, CO) cm^{-1}; MS (70 eV), m/e 140 (M^+). Anal. Calcd for $C_8H_{12}O_2$: C, 68.57; H, 8.57. Found: C, 68.73; H, 8.62.

13c: R_f (10% acetone in hexane) 0.17; ^1H NMR‡ ($CDCl_3$) δ 7.41–7.14 (m, 8 H, aryl), 6.96–6.91 (m, 2 H, ortho), 3.47 (br d, $J_{2,3}$ = 3.6 Hz, $J_{3,4eq}$ = 2.5 Hz, $J_{3,4ax}$ = 1.2 Hz, $J_{3,5eq}$ = 0.8 Hz, 1 H, H_3), 3.40 (br d, $J_{2,3}$ = 3.6 Hz, $J_{2,4eq}$ = 0.6 Hz, 1 H, H_2), 2.70 (ddd, $J_{5ax,5eq}$ = 14.4 Hz, $J_{4ax,5ax}$ = 13.0 Hz, $J_{4eq,5ax}$ = 4.4 Hz, 1 H, H_{5ax}), 2.31 (m, $J_{5ax,5eq}$ = 14.4 Hz, $J_{4ax,5eq}$ = 4.6 Hz, $J_{4eq,5eq}$ = 2.8 Hz, $J_{3,5eq}$ = 0.8 Hz, 1 H, H_{5eq}), 2.26 (m, $J_{4ax,4eq}$ = 15.2 Hz, $J_{4eq,5ax}$ = 4.4 Hz, $J_{4eq,5eq}$ = 2.8 Hz, $J_{3,4eq}$ = 2.5 Hz, $J_{2,4eq}$ = 0.6 Hz, 1 H, H_{4eq}), 1.90 (dddd, $J_{4ax,4eq}$ = 15.2 Hz, $J_{4ax,5ax}$ = 13.0 Hz, $J_{4ax,5eq}$ = 4.6 Hz, $J_{3,4ax}$ = 1.2 Hz, 1 H, H_{4ax}); ^{13}C NMR‡ ($CDCl_3$) δ 204.64 (C_1), 145.17 and 139.00 (ipso), 128.84, 128.42, 128.34 and 127.86 (ortho and meta), 126.77 and 127.38 (para), 60.28 (C_6), 54.23 and 54.02 (C_2 and C_3), 27.67 (C_5), 21.25 (C_4); IR ($CDCl_3$) 1700 (s, CO) cm^{-1}; MS (70 eV), m/e 264 (M^+), 236 (M^+ - CO).

4,4-Diphenyl-2,3-epoxycyclohex-2-en-1-one (epoxy-2c): Enone **2c** was epoxidized[75] with 1.1 equiv of MCPBA in CH_2Cl_2. The epoxide was obtained in 50% yield and was recrystallized from ether–petroleum ether (60–80 °C); mp 83–84 °C. The spectral data were consistent with those reported by Matoba and co-workers.[30a,g]

Epoxy-2c: R_f (25% acetone in hexane) 0.41; ^{13}C NMR ($CDCl_3$) δ 204.20 (C_1), 128.90, 128.53, 127.54, 127.23 and 126.88 (aryl), 62.50 and 57.00 (C_2 and C_3), 47.35 (C_4), 33.74 and 27.83 (C_5 and C_6).

2-(3′-Oxo-6′,6′-dimethylcyclohexyl)-6,6-dimethylcyclohex-2-en-1-one (14b): Cyclohexenone **4b** was dimerized in aqueous NaOH according to the procedure of Leonard and Musliner[30h] (described for **4a**) except that the reaction mixture was heated overnight at 70–80 °C. The unreacted starting material was distilled (50 °C/2 Torr) away from the product (25% yield), which was purified by preparative TLC.

14b: R_f (10% acetone in hexane) 0.24; ^1H NMR ($CDCl_3$) δ 6.50 (t, $J_{3,4}$ = 3 Hz, 1 H, H_3), 2.73–2.13 (m, 5 H), 2.13–1.5 (m, 6 H), 1.15 (s, 3 H), 1.03 (s, 9 H); IR ($CDCl_3$) 1700 (s, CO), 1660 (C=C) cm^{-1}; MS (70 eV), m/e 248 (M^+), 233 (M - CH_3), 218 (M - $2CH_3$), 203 (M - $3CH_3$), 192 (M - $(CH_3)_2CCH_2$), 178 (M - $COC(CH_3)_2$), 164 (M - $COC(CH_3)_2CH_2$).

General Oxidation Procedure Using KO_2, KOH, and $KOC(CH_3)_3$. Reactant, 18-crown-6, and powdered KX [X = O_2, OH, or $OC(CH_3)_3$] were added in that order to sodium-dried benzene or toluene. The reactants ratio, i.e., the molar ratio of substrate:crown:KX, is given in Tables I and II. Approximately 35 mL of solvent were used per millimole of substrate. The reaction mixture was stirred magnetically under dry air (unless otherwise indicated) at room temperature until TLC indicated that all the starting material had been consumed. The reaction was then quenched by acidifying with 10% HCl. (Quite commonly, this acidification is accompanied by a sudden change of color in the reaction mixture as neutrality is approached.) The organic layer is then washed thrice with 10% $NaHCO_3$ to remove inorganic salts, crown ether, and acidic products. The organic phase containing the nonacidic products was dried over $MgSO_4$ and concentrated, and the products were then isolated. The combined $NaHCO_3$ extracts were acidified and extracted three times with ether. The combined ether extracts were dried and concentrated, and the products isolated. Alternatively, the reaction can be quenched with CH_3I (10 mol equiv based on substrate), which consumes the unreacted base and methylates various oxyanions in the product. The reaction mixture was generally allowed to react overnight with the CH_3I (though shorter reaction times may well have sufficed) and washed with water to remove inorganic salts, methanol, crown ether, and excess methyl iodide. The organic layer was then dried and concentrated, and the products were isolated.

Reaction of 2b and 3b. The title enones were reacted with KO_2 as described in the general procedure and Table I. Following acid workup, the major product, 2-hydroxy-4,4-dimethylcyclohexa-2,5-dien-1-one (**7b**), was isolated from the nonacidic fraction. This enol was purified by GLC[64a] at 120 °C (retention time 19.5 min with flow rate of 80 cm^3/min) and obtained as long white needles (mp 56 °C), not as a liquid as previously reported.[29a,b] The acidic fraction yielded an additional minor product, lactol **9b**, resulting from the secondary oxidation of **7b** under the reaction conditions.[28] When the reaction is quenched with CH_3I, the methoxy analogue of **7b**, 2-methoxy-4,4-dimethylcyclohexa-2,5-dien-1-one (**8b**), is isolated as the major product. The UV, IR, and ^1H NMR data have already been reported,[25b,29a,b] although, for the latter, we do find several minor discrepancies in the chemical shifts and splitting constants.

7b: R_f (25% acetone in hexane) 0.34; ^1H NMR ($CDCl_3$) δ 6.90 (dd, $J_{5,6}$ = 10 Hz, $J_{3,5}$ = 3 Hz, 1 H, H_5), 6.23 (d, $J_{5,6}$ = 10 Hz, 1 H, H_6), 6.23 (br s, 1 H, OH), 6.07 (d, $J_{3,5}$ = 3 Hz, 1 H, H_3), 1.27 (s, 6 H); ^{13}C NMR ($CDCl_3$) δ 160.18 (C_5), 145.98 (C_2), 125.28 and 124.34 (C_3 and C_6), 38.68 (C_4), 27.37 (CH_3); MS (70 eV), m/e 138 (M^+), 123 (M - CH_3), 110 (M - CO), 95 (M - CH_3 - CO).

8b: ^1H NMR ($CDCl_3$) δ 6.93 (dd, $J_{5,6}$ = 10 Hz, $J_{3,5}$ = 3 Hz, 1 H, H_5), 6.15 (d, $J_{5,6}$ = 10 Hz, 1 H, H_6), 5.76 (d, $J_{3,5}$ = 3 Hz, 1 H, H_3), 3.63 (s, 3 H, OCH_3), 1.33 (s, 6 H, gem-dimethyl); MS (70 eV), m/e 152 (M^+), 137 (M - CH_3), 124 (M - CO), 109 (M - CH_3 - CO).

Reaction of 2c. The reaction of **2c** with KO_2 led to an 80% yield of 2-hydroxy-4,4-diphenylcyclohexa-2,5-dien-1-one (**7c**) upon aqueous acid workup and a 75% yield of the corresponding 2-methoxy-4,4-diphenylcyclohexa-2,5-dien-1-one (**8c**) upon CH_3I

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quenching. When an acid workup was employed, NMR analysis of the reaction mixture revealed that the acid fraction contained a 5% yield of 3-phenylcinnamic acid (**12c**, Y = OH),[31b] while the same yield of the corresponding methyl 3-phenylcinnamate (**12c**, Y = OCH_3)[31a] was detected when CH_3I was used to stop the reaction. In both cases, the above products were accompanied by a 10–15% yield of benzophenone (**11c**); there was no evidence, however, of lactol[28] (**10c**) or epoxy ketone[29] (**epoxy-2c**) formation. The major products were isolated by preparative TLC eluting with 1:1 benzene–chloroform or by crystallization. Enol **7c** was independently prepared via the *tert*-butoxide-mediated autoxidation of **2c** in *tert*-butyl alcohol, according to the general procedure developed by Barton's group.[29c]

7c: R_f (1:1 C_6H_6–$CHCl_3$) 0.42; mp (petroleum ether 60 °C) 145 °C; ^1H NMR‡ ($CDCl_3$) δ 7.39 (dd, $J_{5,6}$ = 10 Hz, $J_{3,5}$ = 3 Hz, 1 H, H_5), 7.32 and 7.29 (overlapping m, 6 H, meta and para), 7.23 (m, 4 H, ortho), 6.50 (d, $J_{3,5}$ = 3 Hz, 1 H, H_3), 6.45 (d, $J_{5,6}$ = 10 Hz, 1 H, H_6), 6.40 (br s, 1 H, OH); ^{13}C NMR‡ ($CDCl_3$) δ 181.45 (C_1), 156.53 (C_5), 145.33 (C_2), 142.37 (ipso), 128.84 (meta), 127.77 (ortho), 127.59 (para), 124.43 (C_6), 123.04 (C_3), 54.80 (C_4)—assignments of the vinyl carbons were confirmed by correlating the residual CH coupling in two off-resonance decoupled spectra to the known proton absorptions; IR (Nujol) 3360 (s, OH), 1640 (s, CO) cm^{-1}; UV (absolute ethanol) λ_{max} (ϵ_{max}) = 241 (19 240), 277 (11 462) nm; MS (55 eV), *m/e* 262 (M^+, 100%), 245 (M – OH, 13.77%), 234 (M – CO, 25.19%), 215 (M – HCO – HO, 24.24%), 128 (13.05%), 105 (PhCO, 81.86%). Anal. Calcd for $C_{18}H_{14}O_2$: C, 82.44; H, 5.34. Found: C, 82.21; H, 5.42.

8c: mp (benzene–petroleum ether) 157 °C; ^1H NMR‡ ($CDCl_3$) δ 7.33 and 7.27 (overlapping m, 10 H, aryl), 7.28 (dd, $J_{5,6}$ = 10 Hz, $J_{3,5}$ = 3 Hz, 1 H, H_5), 6.39 (d, $J_{5,6}$ = 10 Hz, 1 H, H_6), 6.16 (d, $J_{3,5}$ = 3 Hz, 1 H, H_3; $\upsilon_{1/2}$ = 1.2 Hz as compared to $\upsilon_{1/2}$ = 0.5 Hz of TMS with broadening due to $^5J_{HH}$ from OCH_3), 3.72 (s, OCH_3; $\upsilon_{1/2}$ = 1.1 Hz with broadening due to $^5J_{HH}$ from H_3)— assignments confirmed by double-resonance experiments irradiating at 3.72, 6.39, and 7.28 ppm; ^{13}C NMR‡ ($CDCl_3$) δ 180.76 (C_1), 153.56 (C_5), 149.80 (C_2), 142.84 (ipso), 128.83 (meta), 127.68 (ortho), 127.54 (para), 126.72 (C_6), 121.57 (C_3), 54.90 (methoxy), 54.69 (C_4); MS (55 eV), *m/e* 276 (M^+, 100%), 261 (M – CH_3, 11.95%), 248 (M – CO, 12.25%), 245 (M – OCH_3, 11.52%), 244 (M – CH_3OH, 31.66%), 233 (M – CO – CH_3, 50.51%), 218 (M – CH_3OH – C_2H_2, 12.54%), 217 (30.54%), 216 (15.41%), 215 (M – CH_3OH – HCO, 31.44%), 205 (M – $COCH_3$ – CO, 21.91%).

Reaction of 2e, 2f, and 3f. The title enones were reacted according to the general oxidation procedure and as outlined in Table I, yielding 2-methoxy- and 2-ethoxy-6-hydroxy-4,4-dimethylcyclohexa-2,5-dien-1-one (enols **7e** and **7f**, respectively). The remaining product in each case is the secondary oxidation product of these enols,[28] namely, the corresponding lactol **10e** or **10f**,[28] which was isolated from the acidic fraction. The enols were purified by preparative TLC eluting with 25% acetone in hexane. Enol **7f** can also be purified by GLC[64b] at 170 °C (retention time 30 min with flow rate 80 cm^3/min) or recrystallized from ether–petroleum ether (40–62 °C); mp 81–82 °C.

7e: R_f (25% acetone in hexane) 0.18; ^1H NMR ($CDCl_3$) δ 6.30 (br s, 1 H, OH), 6.13 (d, $J_{3,5}$ = 2 Hz, 1 H, H_3), 5.87 (d, $J_{3,5}$ = 2 Hz, 1 H, H_5), 3.66 (s, 3 H, OCH_3), 1.30 (s, 6 H, gem-dimethyl); IR ($CDCl_3$) 3460 (m, OH), 1630 (s, CO), 1605 (s, C=C) cm^{-1}; UV (absolute ethanol) λ_{max} (ϵ_{max}) = 272 (9968) nm; MS (70 eV), *m/e* 168 (M^+), 153 (M – CH_3), 140 (M – CO), 125 (M – CH_3 – CO).

7f: R_f (25% acetone in hexane) 0.30; ^1H NMR ($CDCl_3$) δ 6.23 (s, 1 H, OH), 6.07 (d, $J_{3,5}$ = 2 Hz, 1 H, H_3), 5.83 (d, $J_{3,5}$ = 2 Hz, 1 H, H_5), 3.85 (q, J = 8 Hz, 2 H, OCH_2), 1.33 (t, J = 8 Hz, 3 H, ethoxy CH_3), 1.26 (s, 6 H, gem-dimethyl); ^{13}C NMR ($CDCl_3$) δ 177.60 (C_1), 145.94 and 145.43 (C_2 and C_6), 128.29 and 125.72 (C_3 and C_5), 63.65 (CH_2O), 36.13 (C_4), 28.68 (gem-dimethyls), 14.28 (ethoxy methyl); IR (CCl_4) 3420 (br, m, OH), 1620 (s, CO), 1590 (s, C=C) cm^{-1}; UV (absolute ethanol) λ_{max} (ϵ_{max}) = 275 (9968) nm; MS (70 eV), *m/e* 182 (M^+), 168 (M – CH_2), 155 (M – CO + H), 137 (M – CO – OH). Anal. Calcd for $C_{10}H_{14}O_3$: C, 65.93; H, 7.69. Found: C, 65.90; H, 7.59.

Reaction of Enone 3d. Oxidation of enone **3d**, according to the general procedure and Table I, followed by aqueous acid workup yielded the corresponding enol 2-hydroxy-4,4,6-trimethylcyclohexa-2,5-dien-1-one (**7d**) nearly quantitatively. It should be noted that both the starting enone and the resulting enol have the same TLC R_f values, and hence the reaction was perforce followed by quenching the TLC samples only with CH_3I. The enol was recrystallized from pentane as a white solid melting at 56.5–57.5 °C. The UV of **7d** is nearly identical with that of **7b**.[29a] When CH_3I is used to quench the reaction 2-methoxy-4,4,6-trimethylcyclohexa-2,5-dien-1-one (**8d**) is obtained in a 95% yield.

7d: R_f (25% acetone in hexane) 0.37; ^1H NMR‡ ($CDCl_3$)[29d] δ 6.72 (dq, $J_{3,5}$ = 3.5 Hz, $J_{allylic}$ = 1.5 Hz, 1 H, H_5), 6.35 (br s, 1 H, OH), 6.07 (dq, $J_{3,5}$ = 3.5 Hz, 1 H, H_3), 1.90 (d, $J_{allylic}$ = 1.5 Hz, 3 H, C_6-methyl), 1.26 (s, 6 H, gem-dimethyl); ^{13}C NMR‡ ($CDCl_3$) δ 182.45 (C_1), 155.83 (C_5), 145.39 (C_2), 130.80 (C_6), 125.02 (C_3), 37.30 (C_4), 27.54 (gem-dimethyls), 15.51 (C_6-methyl); IR ($CDCl_3$) 3420 (br, m, OH), 1640 (s, CO), 1620 (s, C=C) cm^{-1}; MS (70 eV), *m/e* 152 (M^+), 137 (M – CH_3), 124 (M – CO), 109 (M – CH_3 – CO).

8d: R_f (25% acetone in hexane) 0.34; ^1H NMR‡ ($CDCl_3$) δ 6.65 (dq, $J_{3,5}$ = 2.5 Hz, $J_{allylic}$ = 1.5 Hz, 1 H, H_5), 5.77 (dq, $J_{3,5}$ = 2.5 Hz, 1 H, H_3), 3.65 (s, 3 H, OCH_3), 1.91 (d, $J_{allylic}$ = 1.5 Hz, 3 H, C_6-methyl), 1.27 (s, 6 H, gem-dimethyl)—assignments were elucidated by double-resonance irradiation at 1.90 and 6.65 ppm; ^{13}C NMR‡ ($CDCl_3$) δ 181.04 (C_1), 152.80 (C_5), 149.78 (C_2), 132.63 (C_3), 123.63 (C_3), 54.82 (methoxy), 37.09 (C_4), 28.21 (gem-dimethyls), 15.90 (C_6 methyl); MS (55 eV), *m/e* 166 (M^+, 43.64%), 151 (M – CH_3, 41.57%), 138 (M – CO, 60.70%), 135 (M – OCH_3, 34.38%), 123 (M – C_3H_7, 100%), 95 (M – CO – C_3H_7, 75.80%), 91 (M – C_3H_7 – CH_3OH, 51.71%); IR (CCl_4) 1643 (s, CO), 1618 (s, C=C) cm^{-1}.

Reaction of Enone 3g. Enone **3g** reacted slowly with KO_2 yielding almost exclusively lactol **10g**.[28] The intermediate enol 1-hydroxy-4-methoxyspiro[5.5]undeca-1,4-dien-3-one (**7g**) could be detected by TLC but not isolated from the reaction mixture. The enol could be isolated in an 85% yield by oxidizing **3g** with the less vigorous base KOH for 7 h.

7g: R_f (25% acetone in hexane) 0.22; ^1H NMR ($CDCl_3$) δ 6.43 (d, $J_{3,5}$ = 2 Hz, 1 H, H_3), 6.23 (br s, 1 H, OH), 6.06 (d, $J_{3,5}$ = 2 Hz, 1 H, H_5), 3.70 (s, 3 H, OCH_3), 1.66 (br s, 10 H, ring); IR ($CDCl_3$) 3640 (m, OH), 1640 (s, CO), 1605 (m, C=C) cm^{-1}; MS (50 eV), *m/e* 208 (M^+), 193 (M – CH_3), 180 (M – CO), 165 (M – CO – CH_3).

Reaction of Enone 3h. Oxidation of enone **3h**, according to the general procedure and Table I, followed by aqueous acid workup yielded the corresponding enol 2-hydroxy-4,4-dimethyl-6-phenylcyclohexa-2,5-dien-1-one (**7h**, 80%) contaminated by the corresponding lactol **10h** (15%). The product mixture was separated by silica gel column chromatography, eluting with 15% acetone in hexane. It should be noted that, as in the case of **3d**, the starting enone and the resulting enol have the same TLC R_f value. The reaction was, therefore, followed by quenching the TLC samples only with CH_3I. When CH_3I is used to quench the entire reaction mixture, 2-methoxy-4,4-dimethyl-6-phenylcyclohexa-2,5-dien-1-one (**8h**) is obtained in a 75% yield.

7h: R_f (25% acetone in hexane) 0.38; ^1H NMR‡ ($CDCl_3$) δ 7.48–7.31 (m, 5 H, aryl), 7.01 (d, $J_{3,5}$ = 2.5 Hz, 1 H, H_5), 6.52 (br s, 1 H, OH), 6.16 (d, $J_{3,5}$ = 2.5 Hz, 1 H, H_3), 1.37 (s, 6 H, gem-dimethyl); ^{13}C NMR‡ ($CDCl_3$) δ 180.63 (C_1), 157.61 (C_5), 145.86 (C_2), 135.08 (ipso), 134.96 (C_6), 128.52 (meta), 128.14 (ortho), 128.06 (para), 124.32 (C_3), 37.52 (C_4), 27.65 (gem-dimethyls at C_4)—the assignment of the ipso and C_6 carbons is based on the expected higher integration of the former because of the presence of more H neighbors; FTIR (KBr) 3482.0 (br, m, OH), 1742.5 (s, CO), 1648.8 (s, C=C) cm^{-1}; MS (55 eV), *m/e* 214 (M^+, 61.12%), 213 (M – 1, 13.88%), 199 (M – CH_3, 15.60%), 197 (M – OH, 14.29%), 186 (M – CO, 58.71%), 184 (M – $2CH_3$, 44.80%), 171 (M – CO – CH_3 and/or $(CH_3)_2CH$, 65.86%), 152 (23.24%), 143 (M – $COC(OH)CH_2$, 24.15%), 128 (M – $COC(OH)CH_2$ – CH_3, 82.44%), 115 (28.80%), 108 (21.81%), 105 (PhCO, 100%); UV ($CHCl_3$) λ_{max} (ϵ_{max}) = 271.8 (7230), 237.2 (9550) nm.

8h: R_f (15% acetone in hexane) 0.31; ^1H NMR‡ ($CDCl_3$) δ 7.45–7.28 (m, 5 H, aryl), 6.89 (d, $J_{3,5}$ = 2.5 Hz, 1 H, H_5), 5.8 (d, $J_{3,5}$ = 2.5 Hz, 1 H, H_3), 3.68 (s, 3 H, OCH_3), 1.36 (s, 6 H, gem-dimethyl); ^{13}C NMR‡ ($CDCl_3$) δ 179.63 (C_1), 154.70 (C_5), 150.27 (C_2), 136.91 (C_6), 135.76 (ipso), 128.77 (meta), 128.00 (ortho), 127.80 (para), 122.73 (C_3), 55.00 (CH_3O), 37.31 (C_4), 28.41 (gem-dimethyls at C_4)—the assignment of the ipso and C_6 carbons is based on the expected higher integration of the former because of the presence of more H neighbors; FTIR (neat) 1727.2 (s, CO), 1655.7

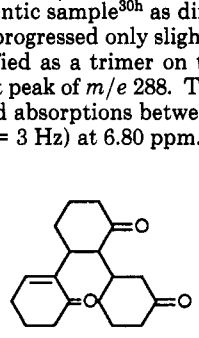
(s, C=C) cm^{-1}; MS (55 eV), m/e 228 (M^+, 100%), 213 (M - CH_3, 14.34%), 200 (M - CO, 22.82%), 196 (M - CH_3OH, 26.06%), 185 (M - CO - CH_3, 36.20%), 157 (M - CH_3OCCO, 15.05%), 141 (17.83%), 127 (10.70), 115 (10.30), 105 (PhCO, 15.81%); UV ($CHCl_3$) λ_{max} (ϵ_{max}) = 269.0 (4081), 237.2 (6516) nm.

Reaction of Enone 3i. Oxidation of enone **3i**, according to the general procedure and Table I, followed by aqueous acid workup yielded the corresponding enol 2-hydroxy-4,4-dimethyl-6-*tert*-butylcyclohexa-2,5-dien-1-one (**7i**, 80%) contaminated by the corresponding lactol **10i** (15%). The product mixture was separated silica gel column chromatography, eluting with 5% acetone in hexane. When CH_3I is used to quench the entire reaction mixture, 2-methoxy-4,4-dimethyl-6-*tert*-butylcyclohexa-2,5-dien-1-one (**8i**) is obtained in a 90% yield.

7i: mp (petroleum ether) 93–95 °C; R_f (25% acetone in hexane) 0.52; ^1H NMR‡ ($CDCl_3$) δ 6.70 (d, $J_{3,5}$ = 3.0 Hz, 1 H, H_5), 6.55 (br s, 1 H, OH), 6.02 (d, $J_{3,5}$ = 3.0 Hz, 1 H, H_3), 1.25 (s, 15 H, *tert*-butyl methyls and gem-dimethyls at C_4); ^{13}C NMR‡ ($CDCl_3$) δ 181.74 (C_1), 153.61 (C_5), 146.01 (C_2), 141.61 (C_6), 122.92 (C_3), 36.81 (C_4), 34.29 (4° of *tert*-butyl), 28.99 (*tert*-butyl methyls), 27.87 (gem-dimethyls at C_4); FTIR (KBr) 3747.4 (m, OH), 1715.1 (s, CO), 1696.0 (s, C=C) 1649.2 (s, C=C) cm^{-1}; MS (55 eV), m/e 194 (M^+, 33.51%), 179 (M - CH_3, 22.84%), 166 (M - CO, 13.70%), 161 (M - CH_3 - H_2O, 17.58%), 151 (M - CH_3 - CO, 100%), 138 (M - $(CH_3)_2CH_2$ and/or M - COCO, 99.71%), 137 (M - $(CH_3)_3C$ and/or M - COCOH, 52%); UV ($CHCl_3$) λ_{max} (ϵ_{max}) = 290.0 (1660), 250.9 (4470) nm.

8i: mp (following workup, without further purification) 104–105 °C; R_f (25% acetone in hexane) 0.40; ^1H NMR‡ ($CDCl_3$) δ 6.60 (d, $J_{3,5}$ = 3.0 Hz, 1 H, H_5), 5.66 (d, $J_{3,5}$ = 3.0 Hz, 1 H, H_3), 3.63 (s, 3 H, OCH_3), 1.26 (s, 6 H, gem-dimethyls at C_4), 1.24 (s, 9 H, *tert*-butyl methyls); ^{13}C NMR‡ ($CDCl_3$) δ 180.74 (C_1), 150.42 (C_5), 150.42 (C_2), 143.38 (C_6), 121.42 (C_3), 54.87 (OCH_3), 36.53 (C_4), 34.42 (4° of *tert*-butyl), 29.15 (*tert*-butyl methyls), 28.63 (gem-dimethyls at C_4); FTIR ($CDCl_3$) 1715.9 (s, CO), 1651.3 (br, s, C=C) cm^{-1}; MS (55 eV), m/e 208 (M^+, 28.02%), 193 (M - CH_3, 67.41%), 180 (M - CO, 15.30%), 165 (M - $(CH_3)_2CH$, 100.00%), 161 (M - CH_3OH - CH_3, 45.46%), 152 (M - $(CH_3)_2CCH_2$, 99%), 137 (M - $(CH_3)_2CCH_2$ - CH_3, 50.68%), 109 (M - $(CH_3)_2CCH_2$ - $(CH_3)_2CH$, 13.74%); UV ($CHCl_3$) λ_{max} (ϵ_{max}) = 240.0 (8330), 193.2 (10 360) nm.

Reaction of Cyclohex-2-en-1-one (4a). Cyclohexenone was reacted with KO_2 under the reaction conditions given in Table II. The reaction mixture turned black almost immediately. Aqueous workup resulted in a 60% yield of neutral product. Preparative TLC, eluting with 25% acetone in hexane, gave two major bands. One had an R_f of 0.37 and was identified by comparison with an authentic sample[30h] as dimer **14a**. The second band was yellow and progressed only slightly above the point of origin. It was identified as a trimer on the basis of the mass spectral (70 eV) parent peak of m/e 288. The ^1H NMR spectrum ($CDCl_3$) showed broad absorptions between 1.33 and 3.35 ppm as well as a triplet (J = 3 Hz) at 6.80 ppm. A possible structure for the trimer is



The reaction was repeated while bubbling continuously with oxygen. After 30 min, a CH_3I workup was employed in the hope of trapping some of the water-soluble acidic products. Nevertheless, only a 25% yield of neutral products could be isolated, which consisted primarily of starting material, epoxy ketone **13a**,[30f] and dimer **14a** (see Table II).

Reaction of Enone 4b. Aqueous acid workup of the superoxide reaction of **4b** gave a neutral fraction in a 60% yield and an acidic fraction in the remaining 40%. Spectral analysis of the latter intractable mixture showed very broad ^1H NMR absorptions and high molecular weights, both suggesting extensive polymerization and/or oxidation. The neutral fraction was separated by preparative TLC eluting with 10% acetone in hexane. NMR analysis of the major fraction revealed it to be a 2:1 mixture of dimer **14b** to epoxy ketone **13b**, both of which have the same R_f. Epoxide **13b** was separated from **14b** by vacuum distillation (50 °C/2 Torr for 4 h). The products were identified by comparison of their spectral data to those of authentic samples independently prepared as described above.

Superoxide- and *tert*-Butoxide-Mediated Oxidation of Diphenyl Enone 4c. Aqueous workup of the reaction mixture from the room-temperature $O_2^{\bullet-}$-mediated oxidation of the title enone (see Table II for reaction conditions and product distribution) yielded a neutral and an acidic fraction in a 3:1 ratio. The latter was treated with excess diazomethane[76] and allowed to stand overnight. The products were separated by silica gel column chromatography (15% acetone in hexane), and identified by their spectral data as epoxy ketone **13c** (independently synthesized as described above), benzophenone **11c**, and 3-phenylcinnamaldehyde (**12c**, Y = H)[31c,d] in the neutral fraction and methyl 3-phenylcinnamate (**12c**, Y = OCH_3)[31a] from the acid fraction. The product yields were determined via ^1H NMR analysis of the crude reaction mixture, which revealed, in addition to the aforementioned products, the presence of some unreacted substrate (indicating a 75% conversion). Similar results were obtained when the reaction was quenched with CH_3I, except that now all the above products were isolated from the neutral fraction.

When the BCA of **4c** is effected by potassium *tert*-butoxide at −40 °C (see Table II for conditions and yields; 100% conversion), aqueous workup, diazotization, and product separation as before yielded epoxide **13c**, ketone **11c**, and methyl 1-hydroxy-5,5-diphenylcyclopent-2-ene-1-carboxylate (**16**). Methyl iodide quenching generated, in addition to these three products, the 1-methoxy analogue of **16**, ester **17**, which like **16** was thoroughly characterized by its spectral data.

16: R_f (25% acetone in hexane) 0.45; ^1H NMR‡ ($CDCl_3$) δ 7.42–7.14 (m, 10 H, aryl), 6.31 (ddd, $J_{2,3}$ = 5.9 Hz, $J_{3,4'}$ = 3.2 Hz, $J_{3,4}$ = 2.0 Hz, 1 H, H_3), 5.78 (ddd, $J_{2,3}$ = 5.9 Hz, $J_{2,4}$ = 2.8 Hz, $J_{2,4'}$ = 1.0 Hz, 1 H, H_2), 3.78 (br s, 1 H, OH), 3.62 (ddd, $J_{4,4'}$ = 15.7 Hz, $J_{2,4}$ = 2.8 Hz, $J_{3,4}$ = 2.0 Hz, 1 H, H_4), 3.29 (s, 3 H, OCH_3), 3.08 (ddd, $J_{4,4'}$ = 15.7 Hz, $J_{3,4'}$ = 3.2 Hz, $J_{2,4'}$ = 1.0 Hz, 1 H, H4′)—assignments and splitting constants were elucidated with the aid of a double-resonance irradiation at 6.32; ^{13}C NMR‡ ($CDCl_3$) δ 175.92 (ester C=O), 144.62 and 143.64 (ipso), 129.00 and 127.97 (meta), 127.72 and 127.38 (ortho), 126.47 and 126.25 (para), 135.08 (C_3), 134.26 (C_2), 91.07 (C_1), 63.98 (C_5), 52.59 (methoxy), 46.03 (C_4); IR (neat) 3480 (br, s, OH), 1720 (m, CO), 1650 (m, C=C) cm^{-1}; MS (55 eV), m/e 294 (M^+, 53.15%), 279 (M - CH_3, 29.72%), 277 (M - OH, 75.96%), 253 ($Ph_2CCOCO_2CH_3$, 10.34%), 245 (M - OH - CH_3OH, 14.16%), 235 (M - CO_2CH_3, 88.76%), 223 ($Ph_2CC(OH)CO$, 50%), 217 (M - Ph, 37%), 205 (M - CH_3O_2CCHOH, 70.34%), 192 ($Ph_2CC_2H_2$, 100%), 180 (Ph_2CCH_2, 45%), 167 (Ph_2CH, 88.76%), 165 ($PhCC_6H_4$, 65.28%).

17: ^1H NMR‡ ($CDCl_3$) δ 7.42–7.14 (m, 10 H, aryl), 6.59 (ddd, $J_{2,3}$ = 6.0 Hz, $J_{3,4'}$ = 2.9 Hz, $J_{3,4}$ = 2.1 Hz, 1 H, H_3), 5.78 (ddd, $J_{2,3}$ = 6.0 Hz, $J_{2,4}$ = 2.9 Hz, $J_{2,4'}$ = 1.6 Hz, 1 H, H_2), 3.51 (ddd, $J_{4,4'}$ = 16.6 Hz, $J_{3,4'}$ = 2.9 Hz, $J_{2,4'}$ = 1.6 Hz, 1 H, $H_{4'}$), 3.28 (ddd, $J_{4,4'}$ = 16.6 Hz, $J_{2,4}$ = 2.9 Hz, $J_{3,4}$ = 2.1 Hz, 1 H, H_4), 3.18 (s, 3 H, OCH_3 of ester), 3.11 (s, 3 H, OCH_3 at C_1); ^{13}C NMR‡ ($CDCl_3$) δ 172.01 (ester C=O), 144.61 and 143.93 (ipso), 129.77 and 128.41 (meta), 127.50 and 127.41 (ortho), 126.16 and 126.02 (para), 137.37 (C_3 and C_2), 96.46 (C_1), 62.51 (C_5), 52.63 (OCH_3 of ester), 51.60 (OCH_3 at C_1), 47.11 (C_4); FTIR ($CDCl_3$) 1736.2 (s, CO), 1659.8 (m, C=C) cm^{-1}; MS (55 eV), m/e 308 (M^+, 50.35%), 276 (M - OCH_3, 10.43%), 249 (M - CO_2CH_3, 100%), 233 (M - CH_3 - CO_2CH_3 - H, 29.50%), 217 (M - OCH_3 - CO_2CH_3 - H, 35.18%), 205 (M - $CH_3OCHCO_2CH_3$, 28.44%), 191 (Ph_2CC_2H, 20.00%), 165 ($PhCC_6H_4$, 10.92%).

Superoxide- and *tert*-Butoxide-Mediated Oxidation of 6,6-Diphenylcyclohexanone 18. Ketone **18** was subjected to superoxide- and *tert*-butoxide-mediated BCA under the same conditions as its unsaturated analogue **4c** (see eq 5, Table II, and the previous subsection). The reactions were quenched only with CH_3I, and the products were separated by silica gel column chromatography (15% acetone in hexane). These were identified by their spectral data as benzophenone (**11c**), methyl 1-hydroxy-2,2-diphenylcyclopentane-1-carboxylate (**19**), dimethyl 2,2-diphenylglutarate (**20**), and methyl 5-oxo-2,2-diphenyl-

(76) (a) McKay, A. F. *J. Am. Chem. Soc.* **1948**, *70*, 1974. (b) Arndt, F. In *Org. Synth.* **1943**, *Coll. Vol. II*, 165.

pentanoate (21) from the room-temperature $O_2^{\bullet-}$ reaction and as 11c, 19, and 1-methoxy-6,6-diphenylcyclohex-2-en-1-one (22) from the low-temperature (-40 °C) *tert*-butoxide reaction. (The spectral data of diester 20 were determined from a fraction containing a 1:1 mixture of 19 and 20.) The product yields and the percent conversion of starting material to products (approximately 60% in both cases) were determined via ^1H NMR analysis of the crude reaction mixture.

19: ^1H NMR‡ ($CDCl_3$) δ 7.37-7.12 (m, 10 H, aryl), 3.46 (s, 3 H, OCH_3), 2.99 (ddd, $J_{3,3'}$ = 13 Hz, $J_{3,4'}$ = 10 Hz, $J_{3,4}$ = 8 Hz, 1 H, H_3), 2.51 (ddd, $J_{3,3'}$ = 13 Hz, $J_{3',4'}$ = 8.5 Hz, $J_{3',4}$ = 3.5 Hz, 1 H, $H_{3'}$), 2.38-2.27 (m, 1 H, H_5), 2.21-2.11 (m, 1 H, $H_{5'}$), 2.11-1.90 (m, 2 H, H_4 and $H_{4'}$); ^{13}C NMR‡ ($CDCl_3$) δ 176.97 (ester CO), 145.91 and 145.62 (ipso), 129.31 and 127.74 (ortho), 127.56 and 127.50 (meta), 126.23 and 125.92 (para), 61.62 (C_2), 52.51 (OCH_3), 38.10 (C_3), 37.41 (C_5), 20.20 (C_4); FTIR ($CDCl_3$) 3617.7 (br, m, OH), 1717.9 (s, CO) cm^{-1}; MS (55 eV, CI, methane), *m/e* 297 (M^+ + 1, 40.23%); MS (32 eV), *m/e* 296 (M^+, 64.79%); MS (55 eV), *m/e* 296 (M^+, 1.58%), 279 (M - OH, 5.09%), 253 (M - C_3H_7, 22.99%), 247 (M - OH - CH_3OH, 16.18%), 237 (M - CO_2CH_3, 14.79%), 219 (M - Ph and/or M - CH_3CO_2 - H_2O, 100%), 201 (M - Ph - H_2O, 17.75%), 193 (M - CH_3CO_2 - OH - C_3H_3, 6.63%), 159 (M - Ph - H_2O - C_2H_3, 15.27%).

20: ^1H NMR‡ ($CDCl_3$) δ 7.36-7.13 (m, 10 H, aryl), 3.68 (s, 3 H, CH_3O at C_1), 3.59 (s, 3 H, CH_3O at C_5), 2.78-2.69 (m, 2 H, H_4), 2.19-2.09 (m, 2 H, H_3); ^{13}C NMR‡ ($CDCl_3$) δ 174.21 and 173.63 (C_1 and C_5 carbonyls), 142.09 (ipso), 128.74 (ortho), 128.02 (meta), 126.99 (para), 59.63 (C_2), 52.42 and 51.52 (CH_3O at C_1 and C_5), 33.14 (C_3), 30.46 (C_4); MS (55 eV, CI), *m/e* 313 (M^+ + 1, 73.14%), 296 (M + 1 - OH, 13.94%), 253 (M - CO_2CH_3, 68.37%), 219 (M - Ph - OH, 100%).

21: ^1H NMR‡ ($CDCl_3$) δ 9.59 (t, $J_{4,5}$ = 1 Hz, 1 H, aldehydic H_5), 7.35-7.2 (m, 10 H, aryl), 3.70 (s, 3 H, OCH_3), 2.73 (td, $J_{3,4}$ = 8 Hz, $J_{4,5}$ = 1 Hz, 2 H, H_4), 2.32 (t, $J_{3,4}$ = 8 Hz, 2 H, H_3); ^{13}C NMR‡ ($CDCl_3$) δ 201.33 (C=O at C_1), 174.26 (C=O at C_5), 142.16 (ipso), 128.72 (ortho), 128.10 (meta), 127.11 (para), 59.57 (C_2), 52.49 (CH_3O), 40.57 (C_4), 30.50 (C_3); MS (55 eV, CI, methane), *m/e* 281 (M^+ - 1, 2.8%), 265 (M - OH, 10.8%), 253 (M - CHO, 11.2%), 239 (M - CH_2CHO, 12.5%), 223 (M - CO_2CH_3, 86.3%), 209 (M^+ + 1 - CH_2CHO - OCH_3, 20.8%), 205 (M - CO_2CH_3 - H_2O, 100%); MS (55 eV), *m/e* 223 (M - CO_2CH_3, 47.7%), 205 (M - CO_2CH_3 - H_2O, 20.45%), 193 (M - CO_2CH_3 - CHO - H, 26.8%), 180 (Ph_2CCH_2, 26.8%), 178 (Ph_2C_2, 18.6%), 165 ($PhCC_6H_4$, 62.3%), 115 (33.18%), 105 ($PhCH_2CH_2$, 100%).

22: ^1H NMR‡ ($CDCl_3$) δ 7.45-7.18 (m, 6 H, meta and para), 7.05-7.00 (m, 4 H, ortho), 5.61 (t, $J_{3,4}$ = 4.5 Hz, 1 H, H_3), 3.53 (s, 3 H, OCH_3), 2.67 (t, $J_{4,5}$ = 5.8 Hz, 2 H, H_5), 2.30 (td, $J_{4,5}$ = 5.8 Hz, $J_{3,4}$ = 4.5 Hz, 2 H, H_4); ^{13}C NMR‡ ($CDCl_3$) δ 195.16 (C_1), 151.52 (C_2), 141.27 (ipso), 128.55 (para), 128.36 and 128.08 (ortho and meta), 114.60 (C_3), 59.96 (C_6), 35.29 (C_5), 21.73 (C_4); FTIR ($CDCl_3$) 1730.9 (s, CO), 1602.0 (m, C=C) cm^{-1}; MS (55 eV), *m/e* 278 (M^+, 16.11%), 264 (M - CH_2, 1.60%), 250 (M - CO and/or M - C_2H_4, 2.98%), 238 (M - C_3H_4, 11.50%), 223 (M - CH_3OC_2, 8.98%), 206 (M - $COCHOCH_3$, 11.99%), 193 (M - Ph_2CCH_2CH, 20.90%), 183 (48.57%), 165 ($PhCC_6H_4$, 33.16%), 149 (17.05%), 115 (22.44), 111 (14.36), 105 ($PhCH_2CH_2$, 100%).

Superoxide Anion Radical ($O_2^{\bullet-}$) Mediated Base-Catalyzed Autoxidation of α-Keto Enols

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Eight 4,4-disubstituted 2-hydroxycyclohexa-2,5-dien-1-ones were prepared by the base-catalyzed autoxidation (BCA) of the corresponding 4,4- or 5,5-disubstituted cyclohex-2-en-1-ones. Upon reaction with superoxide anion radical ($O_2^{\bullet-}$, generated from KO_2/18-crown-6) in inert nonpolar aprotic media at room temperature, α-keto enols **3a-g** undergo initial deprotonation of the enol hydrogen followed by BCA at C_3 of the resulting enolate. Aqueous acid workup of the reaction mixture yields lactols **4**, while methyl iodide quenching generates methoxy lactones **5**. Lactols **4** can be readily converted to their acetoxy analogues **8**, opened to aldehydo methyl esters **6**, or reduced to the related lactones **7**. The latter suggests a convenient one-pot synthesis of 2,3-unsaturated δ-valerolactones from the corresponding cyclohex-2-en-1-ones. 4,4-Diphenyl enol **3h**, by contrast, resists BCA (whether mediated by $O_2^{\bullet-}$ or t-$C_4H_9O^-$) to the corresponding lactol yielding instead a variety of oxidative cleavage products **13-18**. 2-Hydroxyspiro[4.5]dec-1-en-3-one (**21**) also underwent $O_2^{\bullet-}$-mediated BCA, yielding diacids **22** and **26** as well as lactol **30**. The synthetic applications of these results are also discussed.

Introduction

Over the past decade, the international scientific community has become increasingly aware of the crucial role superoxide anion radical ($O_2^{\bullet-}$) plays in a vast spectrum of metabolic processes.[1] Recent research[2] on the organic chemistry of $O_2^{\bullet-}$ has attempted to uncover the various modes of action available to this radical anion in both the hydrophilic as well as the hydrophobic/lipophilic areas of the cell. In aprotic media, $O_2^{\bullet-}$ reacts with organic substrates via deprotonation, nucleophilic attack, electron transfer, and, in some isolated instances, perhaps by hydrogen atom abstraction.[2]

The first mode of action tends to predominate whenever labile hydrogens are available. Thus, phenols, alcohols, and hydroperoxides induce the disproportionation of $O_2^{\bullet-}$ to dioxygen and hydrogen peroxide (eq 1 and 2), generating

$$ROH + O_2^{\bullet-} \rightarrow RO^- + HO_2^{\bullet} \quad (1)$$

$$HO_2^{\bullet} + O_2^{\bullet-} \rightarrow HOO^- + O_2 \quad (2)$$

the corresponding phenoxides, alkoxides and peroxy anions.[2] Stanley[3] reports that steric considerations seem to control the rate of this reaction. Primary alcohols, even

(1) See the collection of articles in: *Superoxide Dismutase*; Oberley, L. W., Ed.; Chemical Rubber Co.: Boca Raton, FL, 1982, Vol. I and II; 1985, Vol. III.

(2) For recent reviews on the organic chemistry of $O_2^{\bullet-}$ see: (a) Sawyer, D. T.; Gibian, M. J. *Tetrahedron* **1979**, *35*, 1471. (b) Wilshire, J. T.; Sawyer, D. T. *Acc. Chem. Res.* **1979**, *12*, 105. (c) Frimer, A. A. In ref 1, Vol. II, pp 83-125. (d) Frimer, A. A. In *The Chemistry of Peroxides*; Patai, S., Ed.; Wiley: Chichester, 1983; pp 429-461. (e) Roberts, Jr., J. L.; Sawyer, D. T. *Isr. J. Chem.* **1983**, *23*, 430. (f) Frimer, A. A. In *Oxygen Radicals in Biology and Medicine*; Simic, M. G., Taylor, K. A., Ward, J. F., von Sonntag, C., Eds.; Plenum: New York, 1989; pp 29-38. (g) See also ref 6c.

(3) Stanley, J. P. *J. Org. Chem.* **1980**, *45*, 1413.

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