Reaction of Superoxide with Aci-Reductones

Aryeh A. Frimer,* Vered Marks, Pessia Gilinsky-Sharon, Gladis Aljadeff, and Hugo E. Gottlieb

The Ethel and David Resnick Chair in Active Oxygen Chemistry, The Department of Chemistry, Bar-Ilan University, Ramat Gan 52900, Israel

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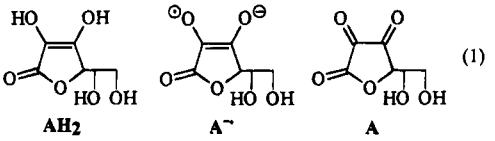
Three reductones, 2,3-dihydroxy-4,4-diphenyl-2,5-cyclohexadien-1-one (**11**), 3,4-dihydroxycoumarin (**35**), and 3,4-dihydroxyspiro[5.5]undecan-3-en-4-one (**64**), were prepared and subsequently reacted with superoxide anion radical ($O_2^{\bullet-}$), generated from KO_2 and 18-crown-6 polyether. The reactions were carried out in aprotic media and quenched with methyl iodide which facilitates the trapping of the various oxyanions formed. While a plethora of products were formed in each case [2-hydroxy-2-methyl-4,4-diphenyl-5-cyclohexene-1,3-dione (**17**), dimethyl 4,4-diphenylglutaconate (**18**), methyl 4,4-diphenyl-3-butenoate (**19**), phenylcinnamaldehyde (**20**), methyl 3-phenylcinnamate (**21**), and benzophenone (**22**) from **11**; 3-hydroxy-2-methoxycoumarin (**39**), 2-carbomethoxy-2-hydroxy-3-coumaranone (**40**), 2-hydroxy-2-methyl-3-coumaranone (**41**), methyl *o*-hydroxyphenylglyoxylate (**42**), methyl salicylate (**43**), and catechol (**44**) from **35**; and 2,4-dihydroxyspiro[5.5]undeca-1,4-dien-3-one (**66**), 2-hydroxyspiro[4.5]dec-1-en-3-one (**70**), dimethyl 1,1-cyclohexanediacetate (**73**), and dimethyl α-keto-1-[(methoxycarbonyl)methyl]cyclohexane-1-propionate) (**75**) from **64**], an overall analysis of the product distribution indicates that the basic elements of the reaction sequence are the same. The first step involves facile deprotonation and the concomitant generation of the reductone monoanion, a process which lends support to the suggestion of Afanas'ev and co-workers (Afanas'ev, I. B.; Grabovetskii, V. V.; Kuprianova, N. S. *J. Chem. Soc. Perkin Trans. 2* **1987,** 281–285). Oxidation of this monoanion yields the corresponding triketone. Of the various options available to this polyketone, superoxide attack at the most electrophilic central carbonyl followed by oxidative cleavage and/or benzylic acid rearrangement are clearly the most prominent. These are followed by a variety of base catalyzed autoxidative processes which are highly dependent on the nature of the substrate.

Introduction

Both the biology[1–3] and chemistry[4] of superoxide anion radical, $O_2^{\bullet-}$, has been extensively examined and discussed over the past two decades. Our interest in the interaction of $O_2^{\bullet-}$ with compounds of biochemical importance lead us to take a second look at vitamin C (ascorbic acid, $\mathbf{AH_2}$ in eq 1), one of the many natural antioxidants which protect the cell against oxidative and/or free radical damage. From a functional group perspective, ascorbic acid can be viewed as a lactone, an enone, an α-keto enol, and a β-keto enol—and over the past twenty years we have had an opportunity to systematically explore the reaction of superoxide with each of these moieties.[5–7]



(1)

However, perhaps the most significant fact about ascorbic acid is that it is an aci-reductone (1-oxo 2-ene-2,3-diol, **1**, eq 2),[8] containing all these moieties simultaneously. Aci-reductones exist in several tautomeric forms (**1**–**5**) and generally undergo oxidation to the corresponding triketones **6** or the related hydration product **7**. The facility of these oxidations depends to a large extent on the nature of the 1-oxo group: alkyl- and arylcarbonyl enediols [**1** (R^1 and R^2 = alkyl or aryl); eq 2] generally autoxidize rapidly under ambient conditions and must be stored at low temperature under inert gas; oxycarbonyl enediols [**1** (R^1 or R^2 = OR′ or OAr); e.g., ascorbic acid], on the other hand, have a relatively long shelf-life under ambient conditions.[4d]

[⊗] Abstract published in *Advance ACS Abstracts,* June 15, 1995.

(1) (a) Halliwell, B. In *Age Pigments,* Sohal, R. S., Ed.; Elsevier/North-Holland Biomedical Press: Amsterdam 1981; pp 1–62. (b) Kehrer, J. P. *Crit. Rev. Toxicol.* **1993**, *23*, 21–48.

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

(3) (a) See the articles of I. Fridovich and J. Fee and the subsequent extensive discussion in *Oxygen and Oxy-Radicals in Chemistry and Biology*; Rodgers, M. A. J., Powers, E. L. Eds.; Academic Press: New York, 1981; pp. 197–239. (b) See the exchange of correspondence between Fridovich and Sawyer and Valentine: Fridovich, I.; Sawyer, D. T.; Valentine, J. S. *Acc. Chem. Res*, **1982**, *15*, 200. (c) Baum, R. M. *Chem. Eng. News*, April 9, 1984, 20–26 and subsequent letters to the editor in the June 4th and July 2nd issues.

(4) For extensive reviews of the organic chemistry of $O_2^{\bullet-}$ see: (a) Frimer, A. A. In *Superoxide Dismutase*; Oberley, L. W., Ed.; Chemical Rubber Co.: Boca Raton, FL, 1982; Vol. II, p 83–125. (b) Frimer, A. A. In *The Chemistry of Peroxides*; Patai, S., Ed.; Wiley: Chichester, 1983; pp 429–461. (c) Roberts, J. L., Jr.; Sawyer, D. T. *Isr. J. Chem.*, **1983**, *23*, 430–438. (d) Frimer, A. A. In *The Chemistry of Enones*- Part 2; Patai, S., Rappoport, Z., Eds.; Wiley: Chichester, 1989; pp 781–921. Please note that the structure assignments of compounds **607** and **608** of Scheme 26 of this review as well as the absence of catechol have been corrected in Scheme 2 of the present paper. (e) Reference 10c.

(5) (a) Rosenthal, I.; Frimer, A. A. *Tetrahedron Lett.* **1975**, 3731–3732. (b) Rosenthal, I.; Frimer, A. A. *Tetrahedron Lett.* **1976**, 2805–2808. (c) Frimer, A. A.; Rosenthal, I. *Radicaux Libres Org., Colloq. (Colloq. Int.* C.N.R.S.) **1978**, *278*, 309–312. (d) Frimer, A. A.; Gilinsky, P. *Tetrahedron Lett.* **1979**, 4331–4334. (e) Frimer, A. A.; Gilinsky-Sharon, P.; Hameiri, J.; Aljadeff, G. *J. Org. Chem.* **1982**, *47*, 2812–2819. (f) Frimer, A. A.; Hameiri-Buch, J.; Ripshtos S.; Gilinsky-Sharon, P. *Tetrahedron* **1986**, *42*, 5693–5706. (g) Frimer, A. A.; Gilinsky-Sharon P.; Aljadeff, G.; Gottlieb, H. E.; Hameiri-Buch, J.; Marks, V.; Philosof, R.; Rosental, Z. *J. Org. Chem.* **1989**, *54*, 4853–4866.

(6) (a)Frimer, A. A.; Gilinsky-Sharon, P. *Tetrahedron Lett* **1982**, *23*, 1301–1304. (b) Frimer, A. A.; Aljadeff, G.; Gilinsky-Sharon, P. *Isr. J. Chem.*, **1986**, *27*, 39–44. (c) Frimer, A. A.; Gilinsky-Sharon P.; Aljadeff, G.; Marks, V.; Rosental, Z. *J. Org. Chem.* **1989**, *54*, 4866–4872.

(7) Frimer, A. A.; Marks, V.; Gilinsky-Sharon P. *Free Rad. Res. Commun.* **1991**, *12*–13, 93–98.

(8) (a) Schank, K. *Synthesis* **1972**, 176–190. (b) Hesse, G. In *Houben-Weyl: Methoden der Organischen Chemie*; Kropf, H., Hesse, G., Eds; Verlag: Stuttgart, 1978; Vol. VI/1d, pp 217–298.

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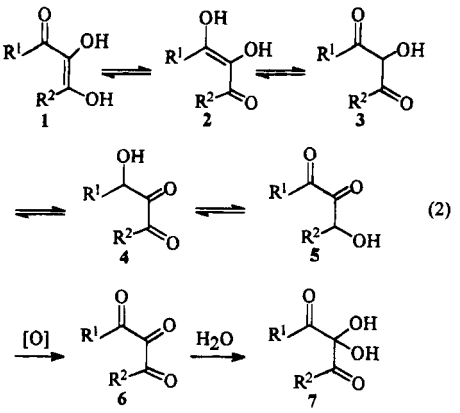


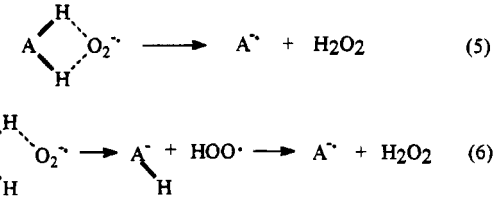
(2)

Two groups have explored the oxidation of ascorbic acid (AH_2) to dehydroascorbic acid (A) in aprotic media mediated by electrogenerated superoxide. Sawyer and co-workers[9] find that $O_2^{\bullet -}$ mediates this process in DMF with the formation of the ascorbate anion radical ($A^{\bullet -}$) and without the generation of molecular oxygen. This latter observation seems to rule out a simple proton abstraction (eq 3). For were such a mode of action by superoxide involved, it would have resulted in the generation of the hydroperoxy radical and the concomitant formation of molecular oxygen (eq 4).

$$O_2^{-\bullet} + AH_2 \rightarrow HO_2^{\bullet} + AH^- \quad (3)$$

$$HO_2^{\bullet} + O_2^{-\bullet} \rightarrow HO_2^- + O_2 \quad (4)$$

As a result of these and related observations, Sawyer has suggested that the initial rate determining step is a concerted (eq 5) or rapid sequential (eq 6) transfer of a



proton and a hydrogen atom to superoxide generating ascorbate anion radical ($A^{\bullet -}$) and H_2O_2. Subsequent reactions involve the proton-induced disproportionation of $A^{\bullet -}$ (eq 7) and oxidation of the resulting ascorbate anion (HA^-) by H_2O_2 to A (eq 8).

$$2A^{-\bullet} + H_2A \rightarrow A + 2HA^- \quad (7)$$

$$HA^- + H_2O_2 \rightarrow A + H_2O_2 + HO^- \quad (8)$$

Afanas'ev and colleagues[10] have taken issue with Sawyer's mechanism. They observe the formation of only a 50–70% yield of HA^- when the same reaction is carried out in acetonitrile. The Russian group posits that such a high yield of ascorbate anion can only be explained by a simple deprotonation of H_2A by $O_2^{\bullet -}$ and believe, therefore, that proton abstraction (eq 3) is the main if not sole pathway of interaction between ascorbic acid and superoxide. The Russian team suggests that any oxygen formed via disproportionation (eq 4) is rapidly converted back to $O_2^{\bullet -}$ upon interaction with ascorbate (eq 9). However, disproportionation is prevented by a series of rapid competing processes (eqs 10–13).

$$AH^- + O_2 \rightarrow AH^{\bullet} + O_2^{-\bullet} \quad (9)$$

$$HO_2^{\bullet} + AH_2 \rightarrow H_2O_2 + AH^{\bullet} \quad (10)$$

$$HO_2^{\bullet} + AH^- \rightarrow H_2O_2 + A^{-\bullet} \quad (11)$$

$$HO_2^{\bullet} + AH^{\bullet} \rightarrow H_2O_2 + A \quad (12)$$

$$HO_2^{\bullet} + A^{-\bullet} \rightarrow HO_2^- + A \quad (13)$$

Three separate solvent-dependent considerations have been suggested in an attempt to resolve the conflicting data:[7] (1) Firstly, the discrepancy may result from the substantial viscosity difference between the solvents used by the U. S. and Russian research teams, DMF (0.802 cp at 25 °C)[11a] and acetonitrile (0.345 cp),[11b,c] respectively. As the viscosity increases, so does the likelihood of solvent cage reactions, such as eq 6. With less viscous solvents, such as acetonitrile, HA^- may well escape the cage before being oxidized by HOO·. (2) Alternatively, the pK_a of the substrate is expected to differ in these two solvents, and this may well have an affect on the mode of action of $O_2^{\bullet -}$. (3) Finally, Sawyer and co-workers[9d,e] have found that, because CH_3CN is difficult to dry, all their attempts to electrochemically prepare superoxide in this solvent generally result in the generation of high yields of hydroxide in addition to the desired superoxide; hence, HO^-, not $O_2^{\bullet -}$, may be the active species in Afanas'ev's system.

With the exception of ascorbic acid itself, there have been to our knowledge no other aci-reductones whose interaction with $O_2^{\bullet -}$ has been studied. We report herein on the results of our exploration into the superoxide chemistry of aci-reductones in general, and those of reductones **11**, **35**, and **64** in particular.

Results and Discussion

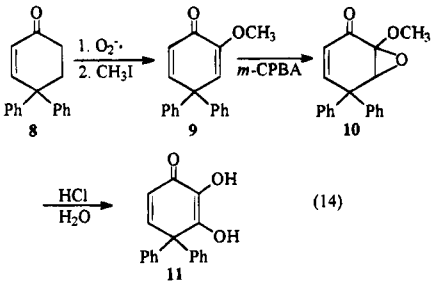
A. Synthesis and Reaction of 2,3-Dihydroxy-4,4-diphenyl-2,5-cyclohexadien-1-one (11) with Superoxide. 1. Synthesis of Reductone 11: The new reductone **11** was prepared as outlined in eq 14. Superoxide-mediated base-catalyzed autoxidation of 4,4-diphenyl-2-cyclohexen-1-one[12] followed by methyl iodide workup yielded methoxy dienone **9**.[5g] Reaction of the latter with buffered *m*-CPBA[13] for 7 days generated epoxy

(9) (a) Sawyer, D. T.; Calderwood, T. S.; Johlman, C. L.; Wilkins, C. L. *J. Org. Chem.* **1985**, *50*, 1409–1412. (b) Sawyer, D. T.; Chiericato, G. Jr.; Tsuchiya, T. *J. Am. Chem. Soc.* **1982**, *104*, 6273–6278. (c) Nanni, E. J., Jr.; Stallings, M. D.; Sawyer, D. T. *J. Am. Chem. Soc.* **1980**, *102*, 4481–4485. (d) Yamagichi, K.; Calderwood, T. S.; Sawyer, D. T. *Inorg. Chem.* **1986**, *25*, 1289–1290. (e) Professor Sawyer has communicated to us (1989) that the yields of HO^- in the attempted electrogeneration of $O_2^{\bullet -}$ can reach as high as 50%.

(10) (a) Afanas'ev, I. B.; Grabovetskii, V. V.; Kuprianova, N. S. *J. Chem. Soc. Perkin Trans. 2* **1987**, 281–285 and references cited therein. (b) Afanas'ev, I. B.; Grabovetskii, V. V.; Kuprianova, N. S.; Gunar, V. I. In *Superoxide and Superoxide Dismutase in Chemistry, Biology and Medicine*; Rotilio, G., Ed.; Elsevier: Amsterdam, 1986; pp 50–52. (c) Afanas'ev, I. B. *Superoxide Ion: Chemistry and Biological Implications, Volume II*; Chemical Rubber Co.: Boca Raton, FL, 1989; p 225ff.

(11) (a) *Du Pont Dimethylformamide*, E. I. du Pont de Nemours, Wilmington, p 3. (b) *Handbook of Chemistry and Physics*; Weast, R. C., Ed.; Chemical Rubber Co.: Boca Raton, FL, 1971; p F-37. (c) Matsuda, Y. In *Practical Lithium Batteries*; Matsuda, Y., Schlaikjer, C. R., Ed.; JEC Press: Cleveland, 1988; pp 13–23.

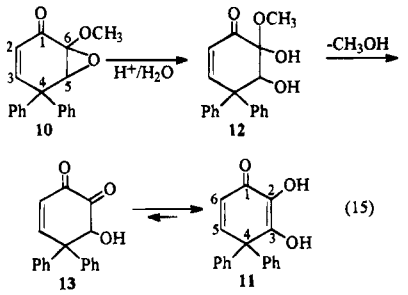
ketone **10**, which rearranged upon acid hydrolysis[14] to the desired reductone **11**.



(14)

Several comments should be made regarding the formation of epoxy ether **10**. Firstly, enol ether epoxides are generally hard to generate with *m*-CPBA since they undergo facile nucleophilic attack at the ether carbon by the acid byproduct.[15] In the present case, however, the ether carbon is α to a carbonyl and, hence, carbonium ion formation is somewhat inhibited. We also note that the *m*-CPBA epoxidation of **9** is presumably electrophilic since oxirane formation is observed only at the enol ether linkage. For related reasons, the epoxidation of enones with *m*-CPBA is rare, though several other cases are known in the literature[16] which also involve enones substituted with electron-donating groups.

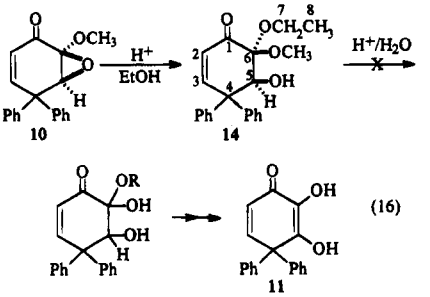
As outlined in eq 15, the hydrolysis of **10** presumably involves the intermediacy of α-keto hemiacetal **12** and hydroxy dione **13**, the tautomer of reductone **11** (cf. eq 2, structure **5**).



(15)

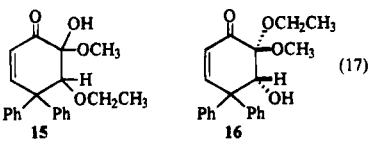
In this regard, we note that while epoxy ketone **10** can be recrystallized from absolute ethanol, heating it briefly (<1 min) in acidic ethanol results in the immediate formation of α-keto ketal **14** (eq 16). Ketal **14** is surprisingly stable to aqueous acid hydrolysis[14] and does not generate reductone **11**.

The assignment of the hydroxyl group in keto ketal **14** to C-5 (rather than to C-6 as in the isomeric hemiacetal **15**) is firmly based on the observed 4.5 Hz coupling



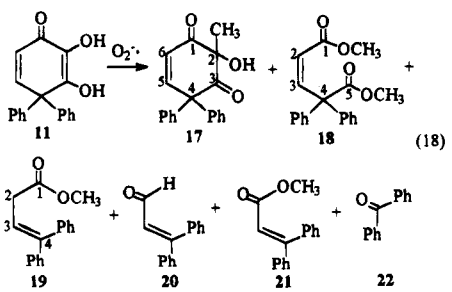
(16)

between hydroxy proton and the geminal H-5. This regiospecificity combined with the formation of only a *single* epimer suggests an attack of ethanol exclusively at C-6 of protonated epoxide **10**, presumably from the side opposite the epoxide linkage, leading to **14** (rather than epimer **16**). In such a reaction, the carbonium ion developing at C-6 (α to the C-1 carbonyl) is stabilized both by the methoxy group, as well as by partial bridging of the epoxide oxygen. The C-4 *gem*-diphenyl group is undoubtedly playing a directing role in this process; indeed, this bulky functional group has been shown[5g] to completely prevent the approach of nucleophiles or electrophiles to the vicinal C-5 carbon. NOE experiments on **14** were inconclusive.



(17)

2. Superoxide Reaction of Reductone 11. The reaction of **11** with superoxide (1:1:1 ratio of subtrate: 18-crown-6:KO_2) in toluene (0.56 cp),[11b] was complete within 1 h and quenched with CH_3I.[12b] Six major products **17**–**22** (eq 18) were generated, along with several unidentified minor products. Of the six, 3-phenylcinnamaldehyde (**20**),[17] methyl 3-phenylcinnamate (**21**),[18] and benzophenone (**22**, Aldrich) are all known. The remaining products were identified by their spectral data. We note that **18** could not be isolated pure (see Experimental Section); hence, its identification should be considered tentative.



(18)

As noted above, alkyl- and arylcarbonyl enediols [**1** (R^1 and R^2 = alkyl or aryl); eq 2] generally autoxidize rapidly under ambient conditions and must be stored under argon at low temperatures. Indeed, we have found that there is substantial autoxidation of **11** after standing in

(12) (a) Newman, M. S. *An Advanced Organic Laboratory Course*; Macmillan: New York, 1972; p 181. (b) Superoxide reactions can be 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. Alcoholates are generally unaffected and phenolates give varying results. See refs 4d (section V. B.5, p.895 therein) and 6b.

(13) Matoba, K.; Karibe, N.; Yamazaki, T. *Chem. Pharm. Bull.* **1984**, *32*, 2639–2645.

(14) (a) Schank, K.; Felzmann, J. H.; Kratzsch, M. *Chem. Ber.* **1969**, *102*, 388–394. (b) Cf. Langin-Lanteri, M. T.; Huet, J. *Synthesis* **1976**, 541–543.

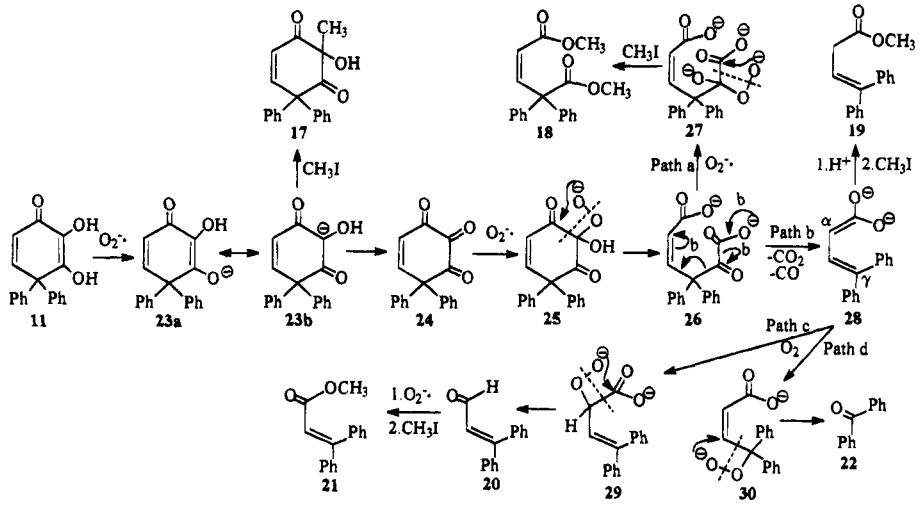
(15) (a) Frimer, A. A. *Synthesis* **1977**, 578–579. (b) Frimer, A. A. *J. Chem. Soc., Chem. Commun.* **1977**, 205–206; corrigendum, *Ibid.*, p 828.

(16) (a) Swern, D. *Organic Reactions*; Wiley: New York, 1953; Vol. 7, p 378. (b) Keane, D. D.; O'Sullivan, W. I.; Philbin, E. M.; Simons, R. N.; Teague, L. C. *Tetrahedron* **1970**, *26*, 2533–2544. (c) Macpeek, D. L.; Starcher, P. S.; Phillips, B. *J. Am. Chem. Soc.* **1959**, *81*, 680.

(17) (a) Pouchert, C. J.; Campbell, J. R. *The Aldrich Library of NMR Spectra;* Aldrich Chemical Co., Milwaukee, 1974; Vol. VI, spectrum 78B. (b) Kurosawa, K.; Tsujita, T. *Bull. Chem. Soc. Jpn.* **1981**, *54*, 2391.

(18) (a) Cortese, N. A.; Ziegler, C. B., Jr.; Hrnez, B. J.; Heck, R. F. *J. Org. Chem.* **1978**, *43*, 2952–2958. (b) For the corresponding acid, see: Sakakibara, T.; Nishimura, S.; Kimura, K.; Minato, I.; Odaira, Y. *J. Org. Chem.* **1970**, *35*, 3884–3887, table 3.

Scheme 1. Product Formation in the Superoxide-Mediated Oxidation of Reductone 17



air for 24 h at room temperature; however, it is negligible for the first hour or so. By contrast, Table 1 reveals that the room temperature superoxide-mediated oxidation of reductone **11** is essentially complete after 15 min, with ester **19** being the major product. The rate of the reaction can be slowed by lowering the reaction temperature to 4 °C, but the product distribution remains essentially the same. Finally, multiple/secondary oxidations can be inhibited by reducing the oxygen concentration, accomplished by carrying out the reaction under argon (after thoroughly degassing the reaction mixture by six freeze-thaw cycles). Under such conditions the only source of oxygen is that generated in the substrate induced disproportionation of superoxide (eq 19–21).[4] As Table 1 reveals, under such conditions hydroxy dione **17** becomes the predominant product.

$$O_2^{-\bullet} + SH \rightarrow HO_2^{\bullet} + S^- \qquad (19)$$

$$HO_2^{\bullet} + O_2^{-\bullet} \rightarrow HO_2^- + O_2 \qquad (20)$$

$$O_2 + S^- \rightarrow SO_2^{-\bullet} \qquad (21)$$

This latter result is significant since it supplies our first clue as to the initial stages of the reaction mechanism. Hydroxy dione **17** is undoubtedly the C-methylation product of monoanion **23**, formed by the deprotonation of reductone **11**. Under conditions in which secondary oxidations are substantially inhibited the initially formed monoanion of reductone **11** accumulates and is trapped by CH_3I. These results correspond well with Afanas'ev's suggestion[10] that $O_2^{\bullet-}$ reacts with reductones primarily, if not solely, as a base.

On the basis of this assumption, we have drawn up a possible mechanism for the production of **17–22**, outlined in Scheme 1. Initial deprotonation of reductone **11** results in the formation of reductone monoanion **23** (trapped by CH_3I as **17**) which undergoes further oxidation by O_2 or $HOO^{\bullet}$ (eq 9 or 11) to triketone **24**. Of the three carbonyls, it is the *central* C-2 carbonyl which is well known to be the most electrophilic.[19] $O_2^{\bullet-}$ attack at this site would generate 1,3-dioxo 2-peroxy anion **25**, which can *a priori* cyclize into either of the flanking carbonyls. Considering, however, that carbonyl adjacent to the *gem*-diphenyl moiety is highly sterically blocked,[5g] cyclization into the C-1 carbonyl would clearly be preferred. The latter process would yield a dioxetane which cleaves to dicarboxylate **26**. Examining the latter, we notice that the carboxylate closer to the *gem*-diphenyl moiety is an α-keto acid, and as such can undergo a well precedented[4] oxidative cleavage to the corresponding acid, trapped as diester **18**. In addition, the α-keto acid is *doubly* activated toward tandem decarbonylation–decarboxylation by the β-double bond and the two aryl groups on the carbon α to the carbonyl moiety.[20] The resulting dienolate **28** (trapped by CH_3I as **19**) can be oxygenated either at the α (path c) or γ (path d) carbons, generating peroxy carbonyls **29** and **30**, respectively. Oxidative cleavage ultimately leads to products **20–22**.[21] Indeed, saponification of ester **19** with superoxide under the reaction conditions, followed by CH_3I workup, generates these very products.

Table 1. Product Distribution in the Reaction of Reductone 11 with KO_2

reaction conditions[a]	conversion (%)	product yield (%)[b]					
		17	**18**	**19**	**20**	**21**	**22**
KO_2, 15 min	100	3.5	1	66	6	5	0.5
KO_2, 1 h, 4 °C	65	3	3	71.5	9	6	0.5
KO_2, 1 h, Ar	100	47	14.5	20	9	4.5	0.5

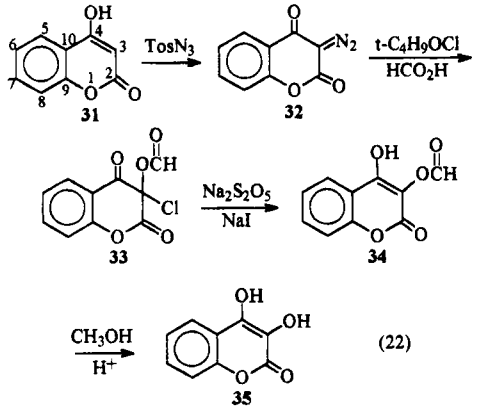
[a] The reactions were carried out at room temperature, under dry air (unless argon is indicated), in dry toluene with a "reactants ratio" (substrate:crown:KX) of 1:1:1 followed by a CH_3I workup. [b] The yields were determined from the ^1H NMR spectrum of the product mixture and are based on the amount of starting material that reacted.

(19) (a) Rubin, M. *Chem. Rev.* **1975**, *75*, 177–202. (b) Schonberg, A.; Singer, E. *Tetrahedron* **1978**, *34*, 1285–1300.

(20) (a) March, J. *Advanced Organic Chemistry-Reactions, Mechanisms and Structure*, 3rd ed.; McGraw-Hill: New York, 1985; Table 1, pp 562–565 and references cited therein. (b) A similar doubly-activated decarboxylation leading to dienolate **28** (and ultimately to **20** and **21**) has been suggested by Frimer and co-workers in the base-catalyzed autoxidation of 6,6-diphenyl-2-cyclohexen-1-one.[5g] In that system, **19** was not observed and the yield of **20** was substantially lower. However, this is presumably due to the much larger reactants ratio of 4:2:1 (*vs* our 1:1:1) which facilitates secondary oxidation.

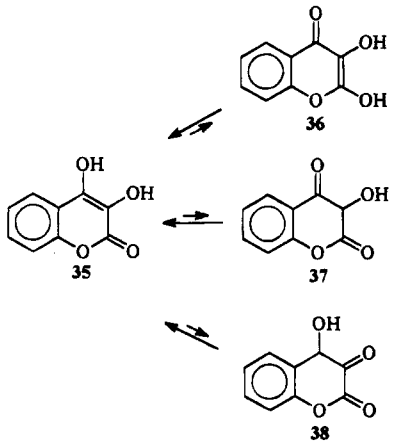
(21) The oxygenation of enolates to α-peroxy carbonyls followed by oxidative cleavage is a well precedented process.[4d] It has also been observed under basic conditions when the carbonyl group is part of an carboxylate moiety.[21a–c] α-Keto acids also undergo oxidative cleavage with alkaline hydrogen peroxide; here too an α-peroxy carboxylate is the putative intermediate.[21d] (a) Jefford, C. W., Cadby, P. A. *Helv. Chim. Acta* **1979**, *62*, 1866–1871. (b) Konen, D. A.; Silbert, L. S.; Pfeffer, P. E. *J. Org. Chem.* **1975**, *40*, 3253–3258. (c) Adam, W.; Cuetto, O. Rebello, H. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 75. (d) Bunton, C. A. In *Peroxide Reaction Mechanisms*; Edwards, J. O., Ed.; Wiley Interscience: New York, 1961; p 16.

B. Synthesis and Reaction of 3,4-Dihydroxycoumarin (35) with Superoxide. The known coumarin reductone **35**[22] was synthesized as outlined in eq 22. Diazocoumarin **32**, prepared[23] from tosyl azide[24] and 4-hydroxycoumarin (**31**, Aldrich), was reacted with *tert*-butyl hypochlorite[25] in formic acid yielding chloroformoylcoumarin **33**. The latter was reduced with sodium iodide/metabisulfite to formyl ester **34**, which yielded the desired reductone **35** upon hydrolysis.[22]



(22)

The ^{13}C NMR spectrum of the reductone shows only a *single* carbonyl absorption at 160.82 ppm. Thus, the carbonyl group must be part of a lactone moiety (ruling out chromone **36** and analogous systems; eq 23), and there can only be one carbonyl in the system (excluding hydroxy dioxo analogs **37** and **38**). The coumarin reductone, thus exists predominantly (if not exclusively) as dihydroxy lactone tautomer **35**.



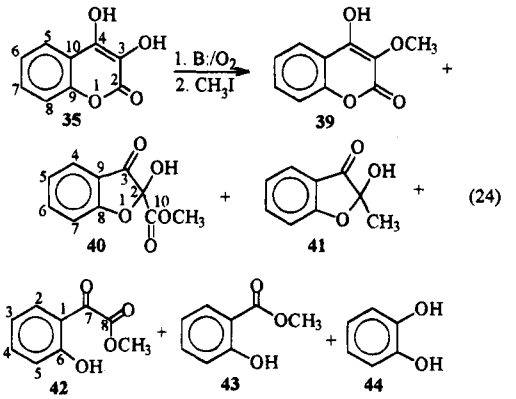
(23)

Reductone **35** reacts rapidly (<10 min) with $O_2^{\bullet-}$ (1:1:1 ratio of subtrate:18-crown-6:KO_2) in THF (0.46 cp).[11c] Upon CH_3I workup,[12b] the reaction mixture gave six products which were identified by their spectral data as **39-44** (eq 24).

Table 2: Product Distribution in the Reaction of 3,4-Dihydroxycoumarin 35 with KO_2, KOH, and *t*-BuOK

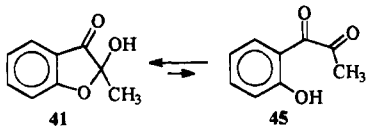
reaction conditions[a]	conversion (%)	product yield (%)[b]					
		39	**40**	**41**	**42**	**43**	**44**
KO_2, 10 min.	100	3.5	3.5	3	36	13.5	0.5
KO_2, 1 h	100	2.5	7.5	4	44	18	5
KO_2, 1 h, Ar	49	21	21	12	6	27.5	1
KOH, 1 h	90	15.5	7	10	38	13	–
KOH, 4 h	100	*c*	–	–	56	38	–
t-BuOK, 0.5–2 h	67	12.5	4	10	60	2	1.5

[a] The reactions were carried out at room temperature, under dry air (unless argon is indicated), in dry THF with a "reactants ratio" (substrate:crown:KX) of 1:1:1 followed by a CH_3I workup. [b] The yields were determined from the ^1H NMR spectrum of the product mixture and are based on the amount of starting material that reacted. [c] A blank space indicates that the product's presence was not detected.



(24)

Of the six products, 3-hydroxy-2-methoxycoumarin (**39**),[26,27] 2-hydroxy-2-methyl-3-coumaranone (**41**),[28] and methyl (*o*-hydroxyphenyl)glyoxylate (**42**)[29] have been previously reported, while methyl salicylate (**43**) and catechol (**44**) are commercially available (Aldrich). 2-Carbomethoxy-2-hydroxy-3-coumaranone (**40**) was identified by its spectral data, which closely resembles that of methyl analog **41**. Regarding lactol **41**, Drewer and coworkers[28] report that in $CDCl_3$, the ^1H NMR reveals the presence of ca. 10% of the open diketo form **45** (eq 25). In our hands, however, both the ^1H and ^{13}C NMR spectra taken in acetone-d_6 show only the presence of lactol.



(25)

As seen from Table 2, essentially the same product distribution is obtained when the oxidation is mediated by other bases (hydroxide and *tert*-butoxide) and suggests that in the case of superoxide too we are observing a base catalyzed autoxidative (BCA) process.[4d,30] This sugges-

(22) (a) Schank, K.; Blattner, R. *Chem. Ber.* **1981**, *114*, 1958–1962. (b) Blattner, R.; Ph.D. Thesis, University of Saarlande, 1980. (c) Schank, K. Personal communication (Aug. 29, 1984). We thank Prof. Schank for sending us photocopies of the NMR and IR spectra of compound **33** and **35** prepared by Dr. Blattner.

(23) (a) Regitz, M.; Stadler, D. *Justus Liebigs Ann. Chem.* **1965**, *687*, 214–225, according to the procedure described for the dimedone analog. (b) For an improved synthesis of 2-diazo-1,3-diketones, see: Popic, V. V.; Korneev, S. V.; Nikolaev, V. A.; Korobitsyna, I. K. *Synthesis* **1991**, 195–198.

(24) Regitz, M.; Hocker, J.; Liedhegener, A. *Organic Syntheses*; **1973**; Coll. Vol. V, pp 179–183.

(25) Mintz, M. J.; Walling, C. *Organic Syntheses*; 1973; Coll. Vol. V, pp 183–187.

(26) Arndt, F.; Loewe, L.; Ün, R.; Ayca, E. *Chem. Ber.* **1951**, *84*, 319–329.

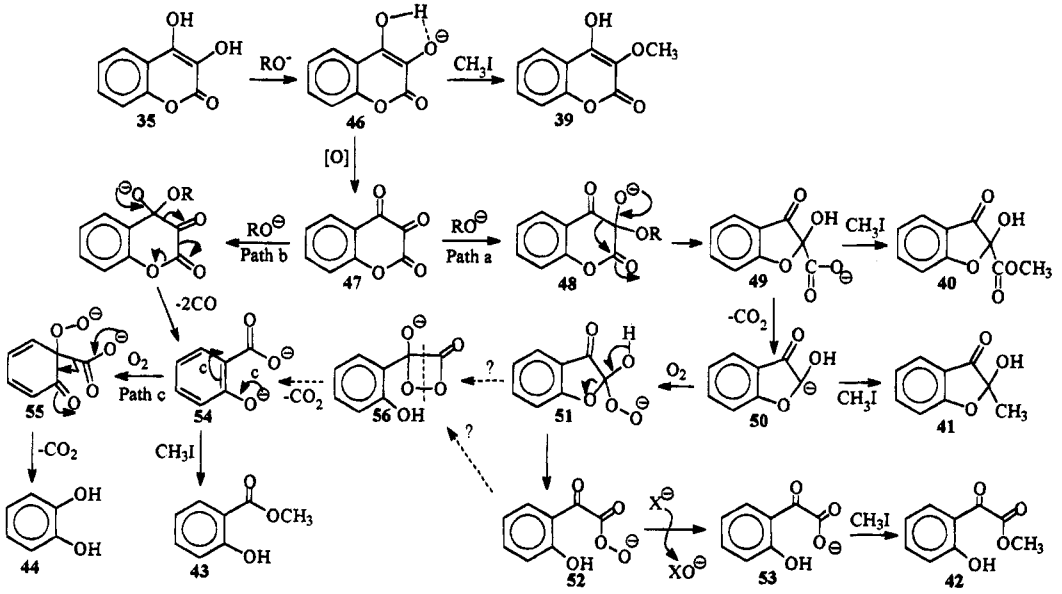
(27) Iguchi, M.; Nishiyama, A.; Eto, H.; Yamamura, S. *Chem. Lett.* **1980**, *11*, 1323–1326.

(28) Drewer, S. D.; Davidson, W. J.; Alix, J. A.; Leppik, R. A. *Aust. J. Chem.* **1971**, *24*, 1883–1898.

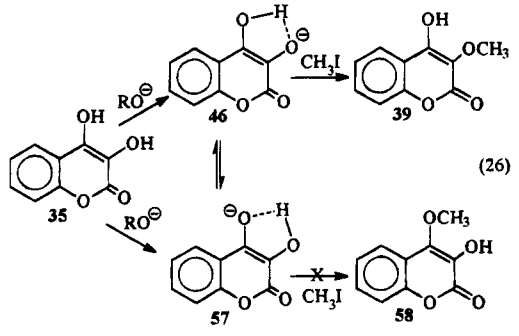
(29) Horspool, W. M.; Khandelwal, G. D. *J. Chem. Soc. (C)* **1971**, 3328–3331.

(30) (a) Sosnovsky, G.; Zaret, E. H. In Organic Peroxides; Swern, D., Ed.; Wiley; New York, 1970; Vol. I, pp 517–557. (b) Russell, G. A.; Janzen, E. G.; Bemis, A. G.; Geels, E. J.; Moye, A. J. Mak, S.; Strom, E. T. *Adv. Chem. Ser.* **1965**, *51*, 112–171. (c) Russell, G. A. *Pure Appl. Chem.* **1967**, *15*, 185–206. (d) Russell, G. A.; Bemis, A. G.; Geels, E. J.; Janzen, E. G.; Moye, A. J. *Adv. Chem. Ser.* **1968**, *75*, 174–215. (e) Karnojitzky, V. *Russian Chem. Rev.* **1981**, *50*, 888–899.

Scheme 2. Mechanism of Product Formation in the BCA of Coumarin Reductone 35



tion is confirmed by the observation that, when the superoxide reaction is carried out under argon (after thoroughly degassing the reaction mixture by six freeze-thaw cycles), there is an accumulation of substantial amounts (>20%) of enol ether **39**, even after reaction times of 1 h. Enol ether **39** is undoubtedly the CH_3I trapping product of the reductone monoanion (see Scheme 2 and eq 26). Considering that both the C-3 and C-4 hydroxyl groups are enolic, deprotonation of either is possible. However, as the enol of a 1,3-dione, the C-4 hydroxyl group is expected to be more acidic. It is somewhat surprising, therefore, that alkylation occurs exclusively at O-3 to give **39**, rather than at O-4 to yield **58**. Nevertheless, O-3 alkylation and acylation are well precedented for aci-reductones in general,[31] and have already been reported for coumarin reductone **35**.[26] In any case, the formation of appreciable amounts of the reductone monoanion is quite significant. Assuming that the active species in this KO_2/crown/THF system is indeed $O_2^{\bullet-}$, these results correspond to Afanas'ev's suggestion[10] that $O_2^{\bullet-}$ reacts with reductones primarily, if not solely, as a base.



(26)

The above argon experiment also indicates that the formation of phenylglyoxylate **42** is highly dependent on the availability of oxygen, but this is not the case for salicylate **43**. Hence, it is unlikely that the key precursor of **42** is along the route to **43**. That two essentially separate product pathways are involved is also confirmed by the KOH mediated results. At longer reaction times and higher conversion, products **42** and **43** increase primarily at the expense of unreacted starting material and products **39**–**41**, rather than each other.

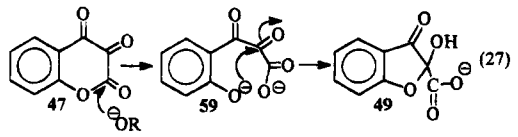
A possible mechanism for the production of **39**–**44** is outlined in Scheme 2 and as noted above assumes that overall we are observing a BCA process[4d,30] mediated by superoxide, hydroxide, or *tert*-butoxide. For reasons cited above, this mechanism invokes the initial formation of reductone monoanion **46** (trapped by CH_3I as enol ether **39**) which undergoes further oxidation by O_2 or $HOO^{\bullet}$ (eq 9 or 11) to coumarin triketone **47**. As noted above in the case of polycarbonyl **24**, triketones in general are well known[19] to undergo base attack at the electrophilic central carbon of the latter (path a). In the present system this is followed by a benzylic acid rearrangement, which generates carboxylate **49** (capped by CH_3I as ester **40**). As an α-keto acid, **49** is expected to undergo facile decarboxylation to enolate **50** (isolated after CH_3I treatment as lactol **41**), which upon oxygenation generates peroxy lactol **51**. The corresponding open form of this peroxy lactol is α-keto percarboxylate **52**, which yields the related ester **42** upon methyl iodide treatment.[32] Returning again to coumarin triketone **47**, base attack at the benzylic carbonyl (path b) followed by unzipping and loss of 2 moles of carbon monoxide yields salicylate **54**, which upon methylation generates ester **43**. Oxygenation of **31** ultimately generates catechol **44**.

Three brief comments are called for at this juncture. We turn first to the facile benzylic acid rearrangement of tricarbonyl **47** (outlined in Scheme 2), a transformation which is totally absent in the corresponding superoxide reaction of dehydroascorbic acid derivatives (of the type **A**, eq 1).[33] The reason seems clear. In the case of **47**, such a contraction–rearrangement leads to the formation

(31) (a) Cabral, J.; Haake, P. *J. Org. Chem.* **1988**, *53*, 5742–5750 and references cited therein. (b) Eistert, B. In *Methoden der Organischen Chemie (Houben-Weyl)-Analytische Methoden*; Muller, E., Ed.; Georg Thieme: Stuttgart, 1953; Vol. II, pp 394–401, p 397. (c) Tolbert, B. M.; Downing, M., Carlson, R. W., Knight, M. K.; Baker, E. M. *Ann. N. Y. Acad. Sci.* **1975**, *258*, 48–69. (d) Nomura, H.; Sugimoto, K. *Chem. Pharm. Bull.* **1966**, *14*, 1039–1044. (e) See also ref 13c *supra*. These authors suggest the involvement of the dianion of ascorbic acid.

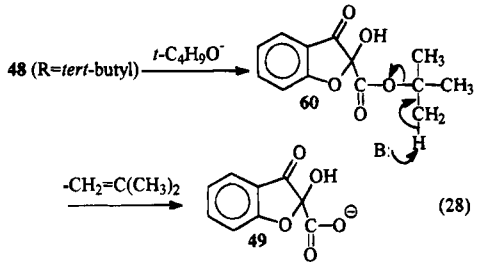
(32) The peroxy anion is presumably reduced to the corresponding alkoxide by iodide formed upon reaction of superoxide with CH_3I. See: (a) Kornblum, N. *Angew. Chem. Int. Ed. Engl.* **1975**, *14*, 734–745. (b) Levonowich, P. F.; Tannenbaum, H. P.; Dougherty, H. C. *J. Chem. Soc., Chem. Commun.* **1975**, 597–598.

of a five-membered ring; by contrast, a more highly strained four-membered analog would be required in the corresponding case of the five-membered dehydroascorbic acid and its derivatives, thus inhibiting this mechanistic route. Our preference for a benzylic acid rearrangement of triketone **47** rather than a saponification–recyclization sequence (eq 27),[6b] is based on our inability to trap the intermediate α,β-diketo acid **59**, in sharp contrast to the case of the corresponding α-keto acid **53** (see Scheme 2).



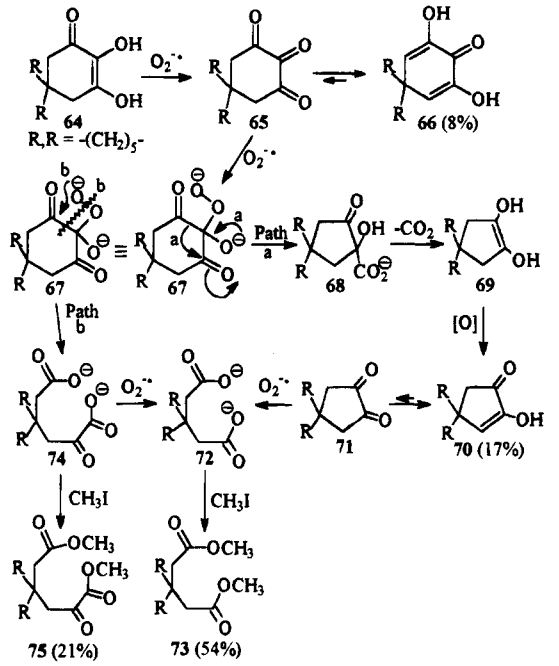
Our second remark relates to the formation of salicylate **54**. This *o*-hydroxy carboxylate could well result, at least in part, from the oxidative cleavage of α-peroxy carbonyl compounds **51** or **52** via dioxetanone **55**.[34] Nevertheless, we have not suggested this as the primary mechanistic route to **43** since, as already mentioned above, the available evidence suggests that the pathways leading to **42** and **43** are essentially independent.

Finally, when the BCA of coumarin reductone **35** is mediated by *tert*-butoxide, one might well ask why no *tert*-butyl esters of **49** or **54** are observed. The answer seems to be that under these strongly basic conditions, such t-BOC esters presumably undergo E_2-elimination generating the corresponding carboxylates and isobutene (eq 28). Such processes have been previously reported.[6b,35,36]

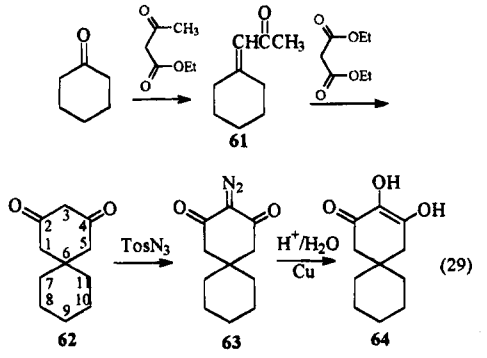


C. Synthesis and Reaction of 3,4-Dihydroxyspiro-[5.5]undec-3-en-2-one (64) with Superoxide. The known spiroreductone **64**[22,37] was synthesized as outlined in eq 29. Cyclohexenylacetone **61**[38] was converted to spiro-β-diketone **62**,[39] which upon reaction with from tosyl azide[24] generates diazo 1,3-dione **63**.[23,37] Copper

Scheme 3. Product Formation in the Superoxide-Mediated Oxidation of Spiroreductone 64



mediated reductive hydrolysis[37] of the latter yields the desired reductone.

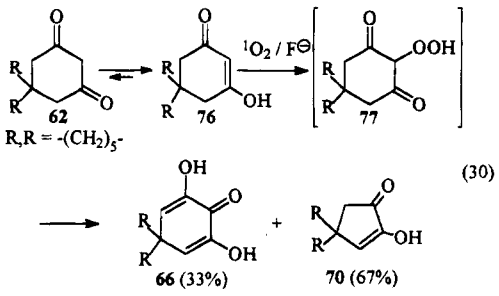


In contradistinction to α-*lactone* enediol **35**, which is relatively stable under neutral ambient conditions, the α-*ketone* enediol **64**, like α-*enone* enediol **11**, is quite susceptible to autoxidation. In order to minimize this process, the shiny white crystals of **64** were stored at reduced temperature (−5 °C) under inert atmosphere until use. In addition, the reaction of spiroreductone **64** with an equimolar amount of $O_2^{\bullet-}$ (1:0.5:1 ratio of subtrate:18-crown-6:KO_2) was carried out in toluene (0.56 cp)[11b] under argon. In this case, there are two sources of molecular oxygen (1) that resulting from the substrate catalyzed disproportionation of the superoxide (analogous to eqs 3 and 4; where AH_2 is now reductone **64**); and (2) adventitious oxygen present in the reaction solvent. CH_3I workup gave a quantitative yield of four products (see Scheme 3), identified by their spectral data as diosphenols **66** (the dienol form of triketone **65**; 8% yield) and **70** (the enol form of dione **71**; 17%), and diesters **73** (54%) and **75** (21%). The preparation and spectral data of diosphenol **66**,[37,40] enol ketone **70**,[6c] and diester **73**[6c] have been reported previously. Diosphenols **66** and **70**

(33) See Frimer, A. A.; Gilinsky-Sharon, P. *J. Org. Chem.*, in press.
(34) Reference 4d, p 791ff.
(35) Pedersen, C. J. *J. Am. Chem. Soc.* **1967**, *89*, 7017–7036; appendix on p 7035.
(36) Analogous thermal and acid catalyzed processes have also been observed: (a) Houlihan, F. M.; Bachman, B. J.; Wilkins, C. W., Jr.; Pryde, C. A. *Macromolecules* **1989**, *22*, 4477–4483 and references cited therein. (b) Ito, H.; Willson, C. G.; Frechet, J.M. J.; Farrall, M. J.; Eichler, E. *Macromolecules* **1983**, *16*, 510–517 and references cited therein. (c) Klemm, L. H.; Antoniades, E. P.; Lind, C. D. *J. Org. Chem.* **1962**, *27*, 519–526.
(37) Eistert, B.; Bock, G.; Kosch, E.; Spalink, F. *Chem. Ber.* **1960**, *93*, 1451–1466, at 1461.
(38) (a) Datta, D. K.; Bagchi, P. *J. Org. Chem.* **1960**, *25*, 932–935. (b) Cf. Norris, G. P.; Thorpe, J. F. *J. Chem. Soc.* **1921**, 1199.
(39) (a) Eistert, B.; Reiss, W. *Chem. Ber.* **1954**, *87*, 92–109. (b) Eistert, B.; Geiss, F. *Tetrahedron* **1959**, *7*, 1–9. Interestingly, since its synthesis more than 40 years ago, NMR spectral data for this compound has been lacking. In the experimental section of this paper we report this data, noting that β-ketone **62** is in a solvent dependent dynamic equilibrium with keto enol **76**. The **62**:**76** ratio in $CDCl_3$, acetone-d_6, and CD3OD is 9:1, 1:3, and 1:60, respectively.

(40) (a) Schank, K.; Blattner, R.; Bouillon, G. *Chem. Ber.* **1981**, *114*, 1951–1957. (b) Schank, K.; Lick, C. *Synthesis* **1983**, 392–395.

were also independently synthesized by fluoride catalyzed singlet oxygenation[41] of spirodione **62** (eq 30).



(30)

A possible mechanism for the superoxide mediated oxidation of reductone **64**, analogous to that suggested for the other reductone systems discussed above, is outlined in Scheme 3. In determining the mechanism of this process, many of the puzzle pieces were known, while a few additional experiments were required to elucidate others:

(1) The isolation of **66**, corresponds well with the aforementioned oxidation of aci-reductones to triones (eq 2).

(2) The formation of **70** is consistent with the well precedented base catalyzed conversion of triones to diones,[19,42] which presumably involves a base induced benzylic acid rearrangement (path a) of **67** to **68**, decarboxylation of the generated β-keto acid **68**, and facile oxidation of the resulting enediol. Indeed, when **66** is reacted with $O_2^{\bullet-}$ at 0–5 °C (rather than at room temperature to slow down the reaction) three products are observed: **70** (5% yield), **73** (30%), and **75** (60%).

(3) Diester **73** has already been reported[6c] to be the primary product from $O_2^{\bullet-}$ mediated oxidative cleavage of **70** (or its tautomer diketone **71**). By the same token, the above mentioned reaction of **66** with $O_2^{\bullet-}$ makes it clear that **75** is the direct (i.e., not involving path a; see section 2) oxidative cleavage product of **66** (or its tautomer triketone **65**). Presumably, this involves 2-peroxy-1,3-dicarbonyl intermediate **67**, as outlined in path b.

(4) In light of the above, the formation of diesters **73** and **75** as the major products, led us to suspect that the primary products are actually **66** and **70**, which in the presence of even small amounts of oxygen undergo successive oxidation. Hence, we repeated the reaction of spiroreductone **64** with an equimolar amount of $O_2^{\bullet-}$, but this time oxygen was scrupulously removed from the reactants and solvent prior to reaction (by six freeze-thaw cycles). In the latter instance, diosphenols **66** and **70** were formed in a 90% yield and in a 2:1 ratio. These results suggest that in the presence of even small amounts of oxygen, various autoxidative processes can come into effect, in which molecular oxygen and/or bases other than $O_2^{\bullet-}$ may be playing assorted roles.

Conclusion

In this paper, we have explored three distinct aci-reductone systems: α-*enone* enediol **11**, α-*lactone* enediol **35**, and α-*ketone* enediol **64**. While the exact course of reaction and product distribution is highly dependent on the structure of the starting dihydroxy enone, all three reaction mechanisms share several important features in common. Firstly, the evidence in all three systems strongly supports the suggestion of Afanas'ev[10] that, at least in solvents less viscous than toluene (0.56 cp),[11b] the first step in the reaction of superoxide with reductones is a facile deprotonation; in other words, $O_2^{\bullet-}$ reacts with reductones primarily, if not solely, as a base. The next major product along the reaction pathway following the formation of reductone monoanion is the corresponding triketone. Of the various options available to this polyketone, superoxide attack at the central carbonyl followed by oxidative cleavage and/or benzylic acid rearrangement are clearly the most prominent. These are followed by a variety of base catalyzed autoxidative processes which are highly dependent on the nature of the substrate.

Experimental Section

^{1}H NMR and ^{13}C NMR (75 MHz) spectra were generally obtained on 200 or 300 MHz Fourier transform spectrometers. Assignments (see supporting information) 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. The spectral data of known compounds are not given unless they are missing from the literature (most common for ^{13}C NMR data), in error, or otherwise substantially lacking. High resolution mass spectra (HRMS) were performed on a VG-Fison AutoSpecE high resolution spectrometer. Preparative thin layer chromatography (TLC) was carried out on Merck silica gel F_{254} precoated plates, while analytical runs were performed using Riedel-De Haen microcards. The retention times given are based on the analytical runs. Gas chromatograms[43] were obtained using a Varian Aerograph Model 920 preparative GLC with peak areas determined by triangulation. Potassium superoxide (Alfa Inorganics, as small chunks; or Callery, as a fine powder), *tert*-butoxide (Fluka), and hydroxide (Frutarom) salts were ground into fine powders in a glove bag 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)[44] and stored along with the above potassium salts in a desiccator. Methyl iodide was distilled and stored at −10 °C under argon.

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 toluene (or P_2O_5-dried THF when specified). The "reactants ratio" (i.e., the molar ratio of substrate: crown: KX) and reaction times were optimized for each substrate. Approximately 35 mL of solvent were used per mmol 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 one of two methods. (a) **Aqueous quenching**: The reaction was acidified with 10% HCl, which is quite commonly accompanied by a sudden change of color in the reaction mixture as neutrality is approached. (In reactions run in THF, 1 vol equiv of benzene

(41) (a) Wasserman, H. H.; Pickett, J. E. *J. Am. Chem. Soc.* **1982**, *104*, 4695–4696. (b) Wasserman, H. H.; Pickett, J. E. *Tetrahedron* **1985**, *41*, 2155–2162 following the procedure for dimedone. (c) Frimer, A. A.; Ripstos, S.; Marks, V.; Aljadeff, G.; Hameiri-Buch, J.; Gilinsky-Sharon, P. *Tetrahedron* **1991**, *47*, 8361–8372. (d) The mechanism for the formation of diosphenol **66** where R = CH_3 from dimedone has been described[41a,b] and involves the intermediacy of hydroperoxide **77**. The simultaneous formation of keto enol **70** (R,R = $-(CH_2)_5$-) in our system is unprecedented and is deserving of further study.

(42) Russell, G. A.; Blankespoor, R. L.; Trahanovsky, K. D.; Chung, C. S. C.; Whittle, P. R.; Mattox, J.; Myers, C. L., Penny, R.; Ku, T.; Kasugi, Y.; Givens, R. S. *J. Am. Chem. Soc.* **1975**, *97*, 1907–1914.

(43) (a) 1.5 ft × 0.25 in copper column packed with 10% SE-30 on Chromosorb W. (b) 8 ft × 0.25 in copper column packed with 20% SE-30 on Chromosorb WAW.

(44) Gokel, G. W.; Cram, D. J.; Liotta, C. L.; Harris, H. P.; Cook, F. L. *J. Org. Chem.* **1974**, *39*, 2445–2446.

was added at this juncture prior to the aqueous washings.) 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. (b) **Methyl iodide quenching**: Alternatively, excess (generally 10 mol equiv based on substrate) of CH_3I was added, 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). (In reactions run in THF, a volume equivalent of benzene was added at this juncture prior to the aqueous washings.) The reaction mixture was 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.

General Procedure for the Rigorous Exclusion of Atmospheric Oxygen: Reactions carried out with the rigorous exclusion of atmospheric oxygen were performed using a bulb-to-bulb distillation apparatus [an inverted flattened U-tube, fitted at its ends with two male joints and at its center with a gas inlet] as the reactor. The gas inlet was connected to a three-way stopcock, permitting alternating connection of the apparatus to a vacuum pump or argon cylinder. One round bottom flask, fitted with a septum-capped opening for syringe sampling, was charged with crown ether, solvent, and a magnetic stirrer, and the other with reductone dissolved in the reaction solvent. The contents of both reactants flasks were frozen in liquid N_2, the system was evacuated, and the reaction flasks were allowed to warm to room temperature. This freeze-thaw cycle was repeated a total of six times, at which time the reductone solution was added to the KO_2/crown ether solution. The system was filled with argon and maintained under a positive argon pressure while the reaction was allowed to proceed for a designated period, during which time the reaction was followed by TLC. The reaction was then quenched and worked-up as usual.

5,6-Epoxy-4,4-diphenyl-6-methoxy-2-cyclohexen-1-one (10). The title compound was prepared by reacting methoxy dienone **9**[5g] with a 4-fold excess of *m*-CPBA at room temperature for 1 week according to the procedure of Matoba.[13] Following workup,[45] the product was isolated in 40% yield by preparative TLC eluting with 15% acetone in hexane. Recrystallization from absolute ethanol yielded white crystals of the epoxide. If the ethanol is slightly acidic, the epoxide hydrolyzes within minutes to α-keto ketal **14**. The numbering of **10** and **14** is shown in eqs 15 and 16, respectively.

10: mp 105–107 °C; R_f (25% acetone in hexane) 0.34; ^{1}H NMR ($CDCl_3$) δ 7.42–7.14 (overlapping m, 10H), 6.82 (dd, J = 10 Hz, J = 2 Hz, 1H), 6.09 (d, J = 10 Hz, 1H), 4.24 (d, $J_{3,5}$ = 2 Hz, 1H), 3.62 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 190.50 (C-1), 149.79, 141.61, 141.10, 129.15, 128.80, 128.23, 127.74, 127.89, 127.74, 124.77, 82.57, 66.12, 54.46, 52.98; FTIR (KBr) 1688.66 (s, C=O) cm^{-1}; UV λ_{max} ($CHCl_3$, ϵ_{max}) 227 (10,520 shoulder), 244.7 (12,000) nm; HRMS calcd ($C_{19}H_{16}O_3$, M^+) 292.1099, obsd 292.1097; MS (EI, 70 eV) *m/e* 292 (M^+, 4.09%), 263 (M – HCO, 3.03%), 233 (M – OCH_3 – CO, 100%), 205 (M – C(O)(CO)-OCH_3, 28.09%), 191 (CH(O)C(CO)OCH_3, 16.74%).

14: mp 145–146 °C; R_f (25% acetone in hexane) 0.31; ^{1}H NMR (acetone-d_6) δ 7.51 (dd, J = 11 Hz, J = 1.5 Hz, 1H) 7.46–7.38 (m, 4H), 7.31–7.21 (m, 4H), 7.19–7.12 (m, 2H), 6.19 (d, J = 11 Hz, 1H), 5.19 (dd, J = 4.5 Hz, J = 1.5 Hz, 1H), 4.15 (d, $J_{5,OH}$ = 4.5 Hz, 1H), 3.35 and 3.24 (ABq of q [ABX_3], J = 10 Hz, J = 7 Hz, 2H), 3.19 (s, 3H), 0.74 (t, J = 7 Hz, 3H); ^{1}H NMR ($CDCl_3$) δ 7.4–7.2 (11H), 6.30, 5.05, 3.52, 3.36, 3.20, 2.35 (OH), 0.9; ^{13}C NMR ($CDCl_3$) δ 192.73, 152.49, 144.67, 142.71, 129.41, 128.08, 127.99, 127.80, 126.86, 126.46, 126.70, 97.72, 73.04, 59.31, 55.27, 49.20, 14.78; FTIR (KBr) 3473.45 (bs, OH), 1697.06 (s, C=O), 1623.69 (s, C=O) cm^{-1}; UV λ_{max} ($CHCl_3$, ϵ_{max}) 242 (13,010), 193.2 (11,420) nm; HRMS calcd ($C_{21}H_{22}O_4$, M^+) 338.1518, obsd 338.1497; MS (EI, 70 ev) 338 (M^+, 10.29%), 220 (M – 118, 66.47%), 118 (CH(OH)C(OCH_3)OCH_2CH_3, 100%).

2,3-Dihydroxy-4,4-diphenyl-2,5-cyclohexadien-1-one (11): Reductone **11** was prepared according to the procedure of Schank.[22] Epoxide **10** was dissolved in dioxane and an equal volume portion of 1 N HCl was added. The reaction solution immediately turned yellow (reductone) and after 1 h, TLC revealed that all of the substrate had reacted. Water and diethyl ether were then added to the reaction flask, the phases were separated, and the aqueous phase was extracted thrice with ether. The ether extracts were combined with the organic phase, washed once with water, and dried over $MgSO_4$. Filtration and evaporation of the solvent gave the desired reductone in 95% yield. Two experimental comments should be noted: (1) The $MgSO_4$ was allowed to remain in the ether phase for only a short time since it seems to complex with the reductone; if contact time is too long, the yield will be substantially diminished. (2) Dioxane also tends to complex well with the product. In order to remove all traces of this solvent, the product was dissolved in a small amount of ether and evaporated under vacuum (0.1 torr) to dryness. This procedure was repeated 2–3 times more. Attempts to recrystallize the reductone were unsuccessful.

11: R_f (25% acetone in hexane) 0.12; ^{1}H NMR ($CDCl_3$) δ 7.38–7.23 (overlapping m, 10 H), 6.90 (d, J = 10 Hz, 1H), 6.32 (d, J = 10 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 148.83, 140.30, 131.59, 128.79, 128.48, 127.67, 122.53, 57.94 (2C were not detected in this solvent; ^{13}C NMR (acetone-d_6, −40 °C) δ 181.52, 152.58, 149.83, 141.89, 132.83, 129.47, 128.90, 127.98, 124.24, 57.38; HRMS calcd ($C_{18}H_{14}O_3$, M^+) 278.0943, obsd 278.0946; MS (EI, 70 eV) 278 (M^+, 78.30%), 260 (M – H_2O, 11.50%), 220 (M – HOCCOH, 65.02%), 191 (M – HOCCOH – CO – H, 33.65%), 105 (PhCO [from rearrangement], 100%).

Reaction of Cyclohexenone Reductone (11) with KO_2. Reductone **11** was reacted with $O_2^{\bullet-}$ in toluene according to the "General Oxidation Procedure" in a "reactants ratio" of 1:1:1, quenched with excess of CH_3I, and worked up as usual. The reaction was followed by TLC (15% acetone in hexane) and was essentially complete after about 0.25 h, but was generally quenched only after 1 h. The product mixture contained six major components, products **17**–**22**, along with several unidentified minor products, which were separated by silica column chromatography and identified by their spectral data. The product yields are found in Table 2. If the separation of the fractions was not complete, products were further purified by preparative TLC eluting with 10% acetone in hexane. Of the six products, 3-phenylcinnamaldehyde (**20**),[18] methyl 3-phenylcinnamate (**21**),[19] and benzophenone (**22**, Aldrich) are all known. The remaining products 2-hydroxy-2-methyl-4,4-diphenyl-5-cyclohexene-1,3-dione (**17**), dimethyl 4,4-diphenylglutaconate (**18**), and methyl 4,4-diphenyl-3-butenoate (**19**)[41c] were identified by their spectral data. We note that **18** could not be isolated pure; hence, its identification should be considered tentative.

The above reaction was repeated at 4 °C and one further time at room temperature with the rigorous exclusion of atmospheric oxygen (as described in the general procedure above). In the latter case, after mixing the reactants, the system was connected to argon and allowed to proceed for one more hour, during which time the reaction was followed by TLC. The reaction mixture was then quenched with CH_3I, which was syringed in through the septum cap. Workup in both cases gave the same six reaction products (see Table 1 for product distribution data).

17: R_f (15% acetone in hexane) 0.25; ^{1}H NMR ($CDCl_3$) δ 7.45 (m, 5H), 7.30 (d, J = 10 Hz, 1H), 7.28 (m, 3H), 6.81 (m, 1H), 6.47 (d, J = 10 Hz, 1H), 1.21 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 206.00, 197.27, 150.53, 140.81, 136.94, 129.39, 127.85, 128.83 128.56, 127.85, 127.75, 124.67, 85.86, 63.73, 28.80; HRMS calcd ($C_{19}H_{16}O_3$, M^+) 292.1099, obsd 292.1097. MS (EI, 70 eV) 292 (M^+, 13.24%), 264 (M – CO, 83.04%), 250 (M – CH_2CO, 42.25%), 221 (M – CH_3COCO, 85.51%), 193 (M – CH_3COCO – CO, 85.58%), 115 (C_7H_6CCH, 100%), 105 (C_6H_5CO, 42.35%).

18: ^{1}H NMR ($CDCl_3$) δ 7.41–7.21 (m, 10H, aromatic), 7.07

(45) Fieser, L. F.; Fieser, M. *Reagents for Organic Synthesis*; Wiley: New York, 1967; Vol. 1, p 135.

(d, J = 12 Hz, 1H), 6.60 (J = 12 Hz, 1H), 3.80 (s, 3H), 3.74 (s, 3H); MS (CI, 70 eV) 311 (MH^+, 100%), 293 (MH − H_2O, %), 279 (MH − CH_3OH, %), 249 (MH − $2CH_3O$, %).

19: ^1H NMR ($CDCl_3$) δ 7.42−7.16 (m, 10H), 6.25 (t, J = 7.5 Hz, 1H), 3.69 (s, 3H), 3.16 (d, J = 7.5 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 172.22, 144.85, 141.95, 139.30, 129.73, 128.35, 128.11, 127.39, 120.28, 51.84, 35.29; HRMS calcd ($C_{17}H_{16}O_2$, M^+) 252.1150, obsd 252.1158.

3,4-Dihydroxycoumarin (35): The known[22] 3-diazo-2,4-dioxocoumarin (**32**) was prepared[23] from tosyl azide[24] and 4-hydroxycoumarin (**31**, Aldrich). Noteworthy is the chemical shift of the C-3 carbon attached to the diazo group which appears at 76.3 ppm. For the purpose of comparison the central carbon of diphenyldiazomethane resonates at 62.5 ppm.[46] Diazocoumarin **32** was reacted with *tert*-butyl hypochlorite[25] in formic acid yielding chloroformoylcoumarin **33**. The latter was reduced with sodium iodide/metabisulfite to 2-hydroxy-3-formoylcoumarin (**34**).[22] The NMR data makes it clear that the latter actually exists in its enol form and not as the 3-formoyl-2,4-diketo tautomer. Hydrolysis of the latter yielded the desired reductone **35**.[22] Only limited physical (mp) and spectral data (IR, UV) are available in the literature[22] for each of these compounds; the NMR absorptions are therefore given below.

32: R_f = 0.35 (35% acetone in hexane); ^1H NMR ($CDCl_3$) δ 8.04 (ddd, J = 8 Hz, J = 2 Hz, J = 0.5 Hz, 1H), 7.67 (ddd, J = 8.5 Hz, J = 7.5 Hz, J = 2 Hz, 1H), 7.35 (ddd, J = 8 Hz, J = 7.5 Hz, J = 1 Hz, 1H), 7.28 (ddd, J = 8.5 Hz, J = 1 Hz, J = 0.5 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 173.89, 157.86, 153.84, 136.03, 125.83, 125.18, 119.04, 117.89, 76.3; MS (EI, 70 eV) m/e 188 (M^+, 65%), 160 (M − N_2, 2%), 120 (M − CN_2 − CO, 16%), 104 (M − CN_2 − CO_2, 67%), 92 (M − CN_2 − CO − H_2O, 12%), 76 (M − CN_2 − CO_2 − H_2O, 100%).

34: R_f = 0.52 (35% acetone in hexane); ^1H NMR (acetone-d_6) δ 8.34 (s, 1H), 7.95 (ddd, J = 8 Hz, J = 2 Hz, J = 0.5 Hz, 1H), 7.69 (ddd, J = 8.5 Hz, J = 7.5 Hz, J = 2 Hz, 1H), 7.44 (ddd, J = 8 Hz, J = 7.5 Hz, J = 1 Hz, 1H), 7.41 (ddd, J = 8.5 Hz, J = 1 Hz, J = 0.5 Hz, 1H); ^{13}C NMR (CD_3OD) δ 174.70, 163.15, 162.87, 150.38, 130.31, 125.28, 124.09, 123.45, 118.82, 116.91; MS (CI, 70 eV) m/e 207 (MH^+, 4%), 179 (MH^+ − CO, 100%).

35: R_f = 0.42 (35% acetone in hexane); ^1H NMR (acetone-d_6) δ 7.82 (ddd, J = 8 Hz, J = 2 Hz, J = 0.5 Hz, 1H), 7.50 (ddd, J = 8.5 Hz, J = 7.5 Hz, J = 2 Hz, 1H), 7.36 (ddd, J = 8 Hz, J = 7.5 Hz, J = 1 Hz, 1H), 7.31 (ddd, J = 8.5 Hz, J = 1 Hz, J = 0.5 Hz, 1H); ^{13}C NMR (acetone d_6) δ 160.82, 149.88, 145.10, 130.03, 125.00, 123.88, 123.00, 118.18, 116.74; MS (CI, 70 eV) m/e 179 (MH^+, 100%), 121 (MH^+ − $C_2H_2O_2$, 100%).

Reaction of Coumarin Reductone (35) with KO_2, KOH, and KOBu-*t*. - Reductone **35** was reacted for varying times (ranging from 5 min up to 1 h) with $O_2^{\bullet-}$ in THF according to the "General Oxidation Procedure" in a "reactants ratio" of 1:1:1, quenched with excess of CH_3I, and worked up as usual. The reaction was followed by TLC (petroleum ether:acetone:HOAc 85:15:1) and the product mixture in each case contained six components, products **39**−**44** (R_f = 0.36, 0.23; 0.27, 0.49, 0.71, 0.95, respectively), which were separated by silica column chromatography and identified by their spectral data. The product yields for reaction times of 10 min and 1 h are found in Table 2. Products **39**−**41** were eluted using a solvent mixture of petroleum ether, acetone, and acetic acid in a 90:10:1 ratio. The solvent ratio was changed to 85:15:2 to elute **42** and **43** and once again to 80:20:3 to elute catechol **44**. Of the six products, salicylate **43** and catechol **44** are commercially available (Aldrich), while 3-methoxycoumarin **39**,[26,27] 3-coumaranone **41**,[28] and phenylglyoxylate **42**[29] have been previously reported. In the case of the latter three, some NMR data is lacking in the literature references and is supplied below, with the carbon numbering as given in eq 24. Coumaranone **40** was identified by its spectral data, which closely resembles that of methyl analog **41**. Both **40** and **41** exist in acetone-d_6 exclusively as lactols.

The above reaction was repeated with the rigorous exclusion of atmospheric oxygen as described in the general procedure above. After mixing the reactants, the system was connected to argon and allowed to proceed for one more hour, during which time the reaction was followed by TLC. The reaction mixture was then quenched with CH_3I, which was syringed in through the septum cap. Workup gave the same six reaction products (see Table 2 for conversion and product distribution data).

The reaction was repeated again with KOH (at room temperature, for up to 4 h) and with KOBu-*t* (at −68 ± 1 °C for up to 2 h) replacing KO_2 (see Table 2 for conversion and product distribution data).

39: ^1H NMR (acetone-d_6) δ 7.76 (ddd, J = 8 Hz, J = 2 Hz, J = 0.5 Hz, 1H), 7.49 (ddd, J = 8 Hz, J = 7 Hz, J = 2 Hz, 1H), 7.34 (ddd, J = 8 Hz, J = 7 Hz, J = 1 Hz, 1H), 7.32 (ddd, J = 8 Hz, J = 1 Hz, J = 0.5 Hz, 1H), 4.3 (s, 3H); ^{13}C NMR (acetone-d_6) δ 162.00, 148.95, 144.68, 129.91, 127.51, 125.24, 123.23, 119.43, 116.65, 60.08; MS (CI, 70 eV) m/e 193 (MH^+, 100%).

40: ^1H NMR (acetone-d_6) δ 7.80 (ddd, $J_{6,7}$ = 8.5 Hz, $J_{5,6}$ = 7.5 Hz, $J_{4,6}$ = 1 Hz, 1H, H-6), 7.69 (ddd, $J_{4,5}$ = 8 Hz, $J_{4,6}$ = 1 Hz, $J_{4,7}$ = 0.5 Hz, 1H, H-4), 7.12 (ddd, $J_{4,5}$ = 8 Hz, $J_{5,6}$ = 7 Hz, $J_{5,7}$ = 1.5 Hz, 1H, H-5), 7.09 (ddd, $J_{6,7}$ = 8.5 Hz, $J_{5,7}$ = 1.5 Hz, $J_{4,7}$ = 0.5 Hz, 1H, H-7), 1.56 (s, 3H, CH_3); ^{13}C NMR (acetone-d_6) δ 194.76 (C-3), 171.96 (C-10), 167.00 (C-8), 139.99 (C-6), 125.60 (C-4), 123.77 (C-5), 119.63 (C-9), 114.18 (C-3), 100.10 (C-2), 53.63 (OCH_3); MS (EI, 70 eV) m/e 208 (M^+, 22.91%), 149 (M − CO_2CH_3, 48.42%), 121 (M − CH_3OCOCO, 100%); HRMS calcd ($C_{10}H_8O_5$, M^+) 208.0372, obsd 208.0263.

41: ^1H NMR (acetone-d_6) δ 7.72 (ddd, J = 8.5 Hz, J = 7 Hz, J = 1.5 Hz, 1H), 7.61 (ddd, J = 8 Hz, J = 1.5 Hz, J = 0.5 Hz, 1H), 7.12 (ddd, J = 8 Hz, J = 7 Hz, J = 1.5 Hz, 1H, 7.09 (ddd, J = 8.5 Hz, J = 1.5 Hz, J = 0.5 Hz, 1H), 1.56 (s, 3H); ^{13}C NMR (acetone-d_6) δ 199.41, 170.78, 139.53, 125.37, 122.59, 119.82, 114.03, 104.73, 22.07; MS (CI, 70 eV) m/e 165 (MH^+, 100%), 148 (MH^+ − H_2O, 32%), 121 (MH^+ − CH_3COH, 14%).

42: ^1H NMR (acetone-d_6) δ 10.85 (s, 1H), 7.78 (ddd, J = 7 Hz, J = 2 Hz, J = 0.5 Hz, 1H), 7.65 (ddd, J = 8 Hz, J = 6.5 Hz, J = 2 Hz, 1H), 7.05 (ddd, J = 8 Hz, J = 1 Hz, J = 0.5 Hz, 1H), 7.03 (ddd, J = 7 Hz, J = 6.5 Hz, J = 1 Hz, 1H), 3.99 (s, 3H); ^{13}C NMR (acetone-d_6) δ 190.47, 164.54, 163.16, 138.89, 132.64, 120.42, 117.94, 113.80, 53.27; MS (CI, 70 eV) m/e 181 (MH^+, 100%), 121 (M − CH_3OCO, 14%).

Spiro[5.5]undecane-2,4-dione (62). Spirodione **62** was prepared as described previously.[39] The product is slightly soluble in $CHCl_3$ and acetone and moderately soluble in methanol. Diketone **62** was recrystallized from $CHCl_3$, rather than from the suggested[39] CH_3OH, because in our hands this yielded the 3-methoxy analog of **76**, 4-methoxyspiro[5.5]-undecan-2,4-dione.[5g] The NMR data reveals the presence of both the 1,3-diketone **62** and the 3-hydroxy 2-en-1-one **76** tautomers. The **62:76** ratio of the tautomers is solvent-dependent: $CHCl_3$, 9:1; acetone, 1:3; and methanol, 1:60. The numbering of the carbons is as shown in eq 29. We note that, as expected, the relatively acidic C-3 methylene undergoes rapid deuterium exchange in methanol-d_4 and is therefore absent in the ^1H NMR spectra below.

62: R_f (acetone) 0.46; ^1H NMR ($CDCl_3$) δ 3.35 (s, 2H), 2.62 (s, 4H), 1.50 (bs, 10H); (acetone-d_6) δ 3.40 (s, 2H), 2.50 (s, 4H), 1.50 (bs, 10H); (CD_3OD) δ 2.62 (s, 4H), 1.50 (bs, 10H); IR (Nujol) 1610, 1580; MS (EI, 70 eV) m/e 180 (M^+), 179 (M − 1), 152 (M − CO), 140 (M − C_2HO), 123 (M − C_3H_3O).

76: ^1H NMR ($CDCl_3$) δ 5.45 (s, 1H), 2.40 (s, 4H), 1.50 (bs, 10H); (acetone-d_6) δ 5.25 (s, 1H), 2.30 (s, 4H), 1.50 (bs, 10H); (CD_3OD) δ 2.36 (s, 4H), 1.50 (bs, 10H); ^{13}C NMR (CD_3OD) δ 103.20, 102.93 (2C), 44.96 (2C), 37.50 (2C), 36.48, 27.73, 22.73 (2C).

2-Diazospiro[5.5]undecan-2,4-dione (63): The known[37] diazodione **63** was prepared by the procedure of Eistert and Reiss.[39] The numbering of the carbons is as shown in eq 29 for the analogous spirodiketone **62**.

63: ^1H NMR ($CDCl_3$) δ 2.50 (s, 4H), 1.46 (bs, 10H); ^{13}C NMR ($CDCl_3$) δ 189.74, 174.77, 48.50, 36.16, 33.97, 25.67, 21.36.

(46) For a general discussion of the ^{13}C NMR of diazoalkanes see: Kalinowski, H.-O.; Berger, S.; Braun, S. *13C NMR Spektroskopie*; Georg Thieme Verlag: Stuttgart, 1984; p 226.

Reaction of 3,4-Dihydroxyspiro[5.5]undecan-3-en-4-one (64) with KO_2. The known reductone (**64**)[22,37] was reacted with $O_2^{\bullet-}$ under an argon atmosphere for 40 min. according to the "General Oxidation Procedure" in a "reactants ratio" of 1:0.5:1, followed by a CH_3I workup. The reaction was followed by TLC (25% acetone in hexane). Alternatively, reaction samples were treated with lead acetate solution; the formation of a gray precipitate indicates that unreacted reductone remains. The products were isolated by GC[43a] (flow rate: 100 cc/min; oven: 120 °C; injector: 200 °C; detector: 220 °C). Four products were obtained with retention times of 9, 18, 27, and 51 min which were identified by their spectral data as 2-hydroxyspiro[4.5]dec-1-en-3-one (**70**),[6c] dimethyl 1,1-cyclohexanediacetate (**73**),[6c] 2,4-dihydroxyspiro[5.5]undeca-1,4-dien-3-one (**66**),[40] and methyl α-keto-1-[(methoxycarbonyl)-methyl]cyclohexane-1-propionate) (**75**), respectively.

The above reaction was repeated with the rigorous exclusion of atmospheric oxygen as described in the general procedure above. After mixing the reactants, the system was connected to argon and allowed to proceed for two more hours, during which time the reaction was followed by TLC. The reaction mixture was then quenched with CH_3I, which was syringed in through the septum cap. Workup gave a nearly quantitative yield of three products **66**, **70**, and **73** in a 60:30:10 ratio, respectively. The products were isolated by GC as described above.

75: ^1H NMR ($CDCl_3$) δ 3.86 (s, 3H), 3.61 (s, 3H), 3.05 (s, 2H), 2.57 (s, 2H), 1.65–1.40 (m, 10H); ^{13}C NMR ($CDCl_3$) δ 21.26, 25.60, 35.67, 36.01, 40.38, 44.46, 50.98, 52.61, 161.57, 172.19, 193.04; IR (neat) 1770 (shoulder, CO) 1720 (s, CO) cm^{-1}; MS (EI, 70 eV) 256 (M^+), 225 (M − CH_3O), 197 (M − CO_2CH_3), 155 (M − $CH_2COCO_2CH_3$), 123 (M − $CH_2COCO_2CH_3$ − OCH_2); HRMS calcd ($C_{13}H_{20}O_5$, M^+) 256.1311, obsd 256.1321.

Reaction of 2,4-Dihydroxyspiro[5.5]undeca-1,4-dien-3-one (66) and 2-hydroxyspiro[4.5]dec-1-en-3-one (70) with KO_2. The dienol (**66**) was reacted with $O_2^{\bullet-}$ under an argon atmosphere for 5 h at 0–5 °C according to the "General Oxidation Procedure" in a "reactants ratio" of 1:1:1. The reaction mixture was then allowed to stand overnight in the refrigerator (5 °C) at which time TLC indicated that the starting material had disappeared. CH_3I workup yielded three products which were separated by preparative GC,[43a] as described above, and identified as **70** (5% yield), **73** (30%), and **75** (60%). Under the same reaction conditions, diosphenol **70** yields diester **73**.

Singlet Oxygenation of β-Diketone 62/Keto enol 76. The title compound was reacted with $^1O_2$ as previously described.[41c] The irradiation was complete within 2 h. Compounds **66** and **70** were obtained in essentially an overall quantitative yield, in a 1:2 ratio, and isolated by GC[43b] (flow rate: 96 cc/min; oven: 175 °C; injector: 180 °C; detector: 200 °C) at 4.5 and 6 min, respectively.

Supporting Information Available: ^1H NMR spectra of **10**, **11**, **14**, **17**, **19**, and **75**, a ^{13}C NMR spectrum of **40**, and the complete ^1H and ^{13}C NMR peak assignments for the compounds described in the Experimental Section (10 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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