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

Aryeh A. Frimer,* Pessia Gilinsky-Sharon, Gladis Aljadeff, Vered Marks, and Zilpa Rosental

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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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.

0022-3263/89/1954-4866$01.50/0

Table I. Product Yields in the Superoxide-Mediated Conversion of α-Keto Enols 3 to Lactols 4

enol 3	reaction conditions[a]	yield of lactol 4,[b] %	enol 3	reaction conditions[a]	yield of lactol 4,[b] %
3a	2.5:1:1	50	**3e**	6:3:1	21
3b	2:1:1	50	**3f**	4:2:1	45
3c	4:2:1	80	**3g**	4:2:1	90
3d	4:2:1	80	**3h**	10:5:1	0

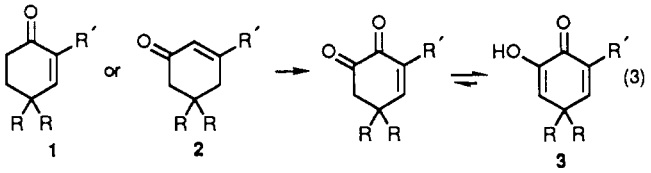
[a] The ratio of substrate:crown ether:KO_2 ("reactants ratio"). Reactions were run overnight (ca. 16 h) at room temperature in benzene or toluene (35 mL/mmol substrate) under dry air and quenched with aqueous acid. [b] Yields are based on converted starting material and were determined by ^1H NMR analysis of the crude mixtures. The remaining product is for the most part a mixture of unidentified acids.

those as weakly acidic as 1-butanol[4] (pK_a = 33 in DMF),[5] apparently cause the instantaneous disproportionation of $O_2^{\bullet-}$. Isopropyl alcohol, on the other hand, requires several minutes for complete reaction, while *tert*-butyl alcohol reacts at appreciable rates only at relatively high concentrations.

Enols, too, undergo facile proton removal by $O_2^{\bullet-}$.[2] Thus, when 3- and 4-hydroxycoumarin are reacted with superoxide, deprotonation of the enolic hydrogen with concomitant dioxygen evolution is the first step.[6] Unlike alkoxy or peroxy anions, however, further C oxidation is generally observed in enolate systems. Thus, our study of the $O_2^{\bullet-}$-mediated autoxidation of 4,4- and 5,5-disubstituted cyclohex-2-en-1-ones (see the accompanying paper)[7] was somewhat complicated by the secondary oxidation of the resulting enols to more polar products. We would now like to report the complete details of our study on this latter transformation.[6a]

Results and Discussion

For the purpose of this study, α-keto enols **3a–h** were prepared by the superoxide or hydroxide mediated base catalyzed autoxidation (BCA) of enones **1b**, **1c**, **1d**, **1h**, **2a**, **2b**, **2c**, **2e**, **2f**, and **2g** (eq 3).[7] Enols **3a–g** (with the notable

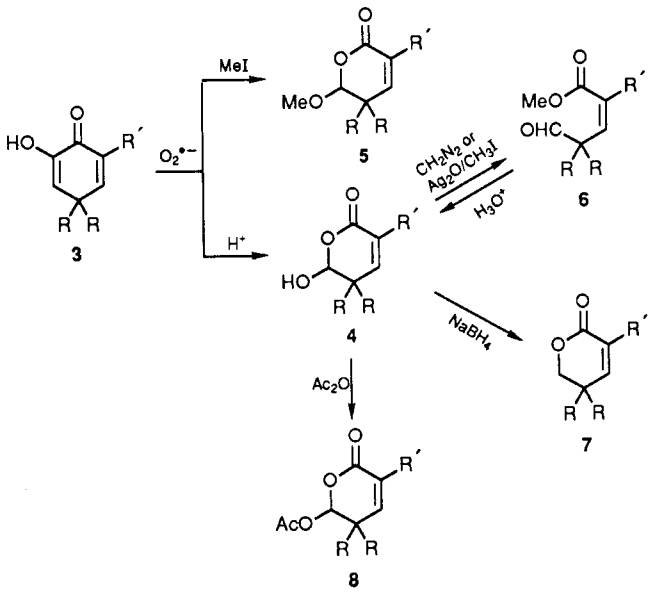


1 2 3

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

exception of **3h**, vide infra) also react with $O_2^{\bullet-}$, generating upon acid workup the corresponding lactols **4a–g** as the major product (Scheme I and Table I). When, however,

Scheme I. Synthetic Outline for the Formation of Products 4–8 from Enols 3



the reaction is quenched with CH_3I prior to workup, methoxy lactone **5** is isolated.[8]

Stable monocyclic lactols such as **4** are generally unknown and appear almost exclusively in the scientific literature as the A-ring of heterosteroids.[9] The structure of the lactols was consistent with the spectral data. Thus, the hemiacetal hydrogen H_5 appears in the ^1H NMR spectrum at ≈5.35, the IR spectrum shows absorptions at around 3400 (br, OH), 1720 (C=O), and 1640 (C=C) cm^{-1}, and the mass spectrum shows loss of CO_2 typical of lactones.[10] As outlined in Scheme I, the identity of the lactols was further confirmed by their conversion to the corresponding aldehydo esters **6** (via diazomethane[11] or silver oxide/methyl iodide[9h]), to lactone **7** (via sodium borohydride reduction[9h,n]), and/or to acetate **8**.[9h] Acid hydrolysis of the aldehydo esters **6** regenerates lactols **4**.

Several pieces of evidence confirm that the superoxide-mediated conversion of enols **3** to lactols **4** involves a base-catalyzed autoxidative (BCA) process.[12] First, the

(4) Sawyer, D. T.; Nanni, Jr., E. J. In *Oxygen and Oxy-Radicals in Chemistry and Biology*; Rodgers, M. A. J., Powers, E. L., Eds.; Academic Press: New York, 1981; pp 15–44.

(5) Nanni, E. J.; Stallings, M. D.; Sawyer, D. T. *J. Am. Chem. Soc.* **1980**, *102*, 4481.

(6) (a) Preliminary report: Frimer, A. A.; Gilinsky-Sharon, P. *Tetrahedron Lett.* **1982**, *23*, 1301. (b) Frimer, A. A.; Aljadeff, G.; Gilinsky-Sharon, P. *Isr. J. Chem.* **1986**, *27*, 39. (c) An extensive review of the oxygenation (including free-radical autoxidation, BCA, singlet oxygenation and $O_2^{\bullet-}$-mediated oxidations) of enones and related enols and enolates has recently been published: Frimer, A. A. In *The Chemistry of Enones*; Patai, S., Rappoport, Z., Eds.; Wiley: New York, 1989; Part 2, Chapter 17, pp 781–921.

(7) (a) Frimer, A. A.; Gilinsky-Sharon, P.; Aljadeff, G.; Gottlieb, H. E.; Hameiri-Buch, J.; Marks, V.; Philosof, R.; Rosental, Z. *J. Org. Chem.*, preceding paper in this issue. (b) Frimer, A. A.; Gilinsky, P. *Tetrahedron Lett.* **1979**, 4331.

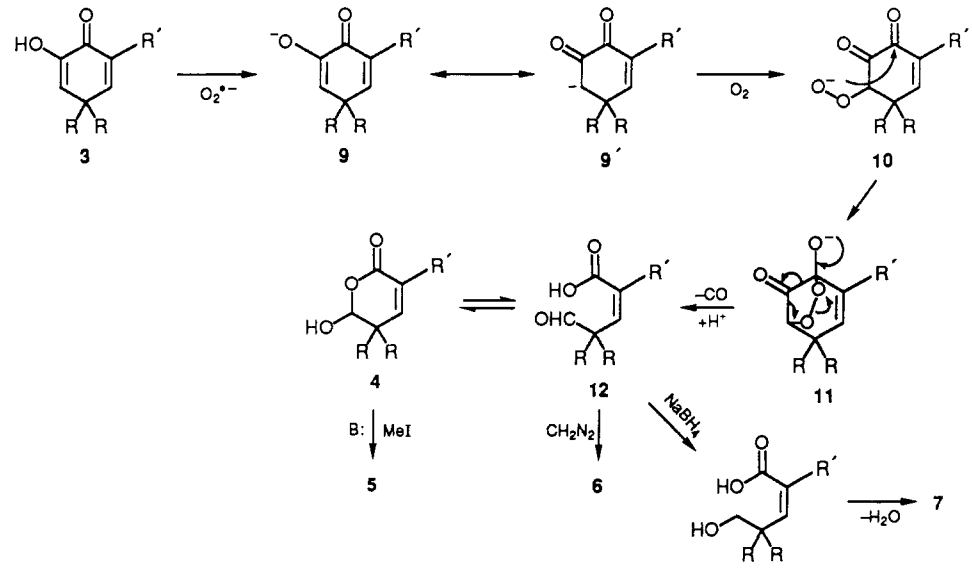
(8) (a) The CH_3I reacts with the excess superoxide generating methoxide and presumably dimethyl ether. A desirable side effect of this quenching method is that many of the oxy anions present are methylated, converting, for example, enolates to enol methyl ethers and carboxylates to methyl esters.[6] (b) The isolation of **5** is in contradistinction to the related steroidal analogues[9m] in which a methyl iodide workup yields aldehydo esters analogous to **6**.

(9) See, for example: (a) Hanna, R.; Ourisson, G. *Bull. Soc. Chim. Fr.* **1961**, 1945. (b) Caspi, E.; Schmid, W.; Kahn, B. T. *Tetrahedron* **1962**, *18*, 767. (c) Caspi, E.; Kahn, B. T.; Balasubrahmanyam, S. N. *Tetrahedron* **1962**, *18*, 1013. (d) Hirschmann, R.; Steinberg, N. G.; Walker, R. *J. Am. Chem. Soc.* **1962**, *84*, 1270. (e) Pappo, R.; Jung, C. J. *Tetrahedron Lett.* **1962**, 365. (f) Pappo, R. U.S. Patent 3101350, Aug 20, 1963. (g) Pappo, R. U.S. Patent 3128283, Apr 7, 1964. (h) Kocar, M.; Kurek, A.; Dabrowski, I. *Tetrahedron* **1969**, *25*, 4257. (i) Chorvat, R. J.; Pappo, R.; Scaros, M. G. U.S. Patent 3644342, Feb 22, 1972. (j) Pappo, R.; Chorvat, R. J. *Tetrahedron Lett.* **1972**, 3237. (k) Frimer, A. A.; Gilinsky-Sharon, P. In *Oxygen and Oxy-Radicals in Chemistry and Biology*; Rodgers, M. A. J., Powers, E. L., Eds.; Academic Press: New York, 1981; p 639. (l) Alvarez, E.; Betancor, C.; Freire, R.; Martin, A.; Suarez, E. *Tetrahedron Lett.* **1981**, *22*, 4335. (m) Frimer, A. A.; Gilinsky-Sharon, P.; Hameiri, J.; Aljadeff, G. *J. Org. Chem.* **1982**, *47*, 2818. (n) Frimer, A. A.; Hameiri-Buch, J.; Ripshtos, S.; Gilinsky-Sharon, P. *Tetrahedron* **1986**, *42*, 5693. (o) Alvarez, E.; Francisco, C. G.; Freire, R.; Hernandez, R.; Salazar, J. A.; Suarez, E.; Betancor, C. *J. Chem. Soc., Perkin Trans. 1* **1986**, 1523. (p) Chorvat, R. J.; Pappo, R. *J. Org. Chem.* **1976**, *41*, 2864.

(10) Reed, R. I. In *Advances in Organic Chemistry*; Raphael, R. A., Taylor, E. S., Wynberg, H., Eds.; Wiley-Interscience: New York, 1963; Vol. 3, p 30.

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

Scheme II. Mechanism for the Formation of Products 4-7 in the Base-Catalyzed Autoxidation of Enols 3



same products are obtained with potassium hydroxide and *tert*-butoxide, with the order of decreasing rates (*tert*-butoxide > superoxide > hydroxide) consistent with previous studies.[13] Furthermore, the rate of $O_2^{\bullet-}$ reaction is essentially the same whether carried out in air or under argon (after carefully degassing the solvent via five freeze–thaw cycles). This observation is most conveniently accommodated[13a] by assuming that $O_2^{\bullet-}$ acts as a base, with the abstracted proton inducing disproportionation of superoxide to molecular oxygen (eq 1 and 2). The resulting substrate anion is then oxygenated (eq 4) via the series of processes typical of BCA.[7a,12]

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

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

$$RO^- + O_2 \rightarrow\rightarrow \text{oxygenation products} \quad (4)$$

A likely and well-precedented mechanism[14] for the oxidation of enols **3** to lactols **4** is outlined in Scheme II and involves the expected C-oxidation of the 3-oxo-1,4-dien-2-olate **9** at C_1. Cyclization of the resulting peroxy anion **10** generates endoperoxide **11**. Elimination of carbon monoxide ultimately yields lactol **4** via aldehydo acid **12**.

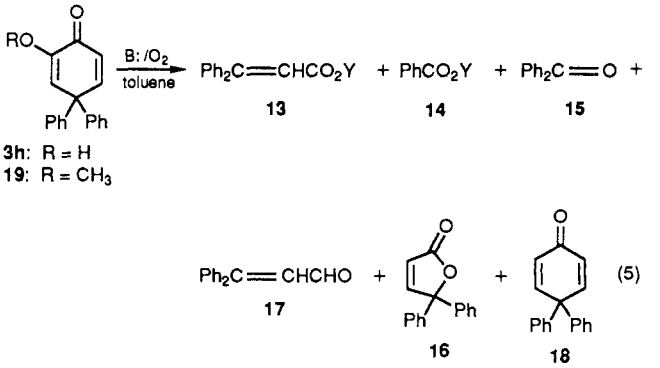
We close this section on the BCA of enols **3a–g** by bringing to the readers attention footnote *b* at the bottom of Table I. The oxidative cleavage of α-diketones to diacids by $O_2^{\bullet-}$ is well-known;[2] hence, the formation of acidic side products in the case of α-keto enols **3a–g** is undoubtedly expected.[6c,14d] What is interesting, however, is that the lactol yield is in excess of 80% in all cases where the double bond in the molecule is an enol ether moiety (**3c**, **3d**, and **3g**). The factors that control the product distribution require further elucidation.

Table II. Product Yields from the Base-Catalyzed Autoxidation of Dienones 3h and 19

substrate	reaction conditions[a]	product yield,[b] % 13	14	15	16	17	18
3h	$O_2^{\bullet-}$, 1 day, H^+, 20%	25[c]	4[c]	50			
	t-BuO^-, 5 days, H^+, 55%	47[c]	17[c]	29	3	1	3
	t-BuO^-, 5 days, CH_3I, 55%	56[d]		35	3	6	
19	*t*-BuO^-, 3 days, CH_3I, 47%	68[d]	8[d]	24			

[a] Base (KO_2 or *t*-C_4H_9OK), reaction time in days, workup (aqueous acid or 10-fold CH_3I), percent conversion of starting material to products. Ratio of base:18-crown-6:substrate was 4:2:1. Reactions were carried out in dry toluene (35 mL/mmol substrate) at ambient temperature under dry air. Percent conversion was determined by the amount of starting material recovered. In the case of CH_3I workup, starting material was isolated as **19**. [b] Yields are based on converted starting material and were determined by ^1H NMR analysis of the crude reaction mixtures. In the case of aqueous acid workup, acids **13** and **14** (Y = H) were isolated and identified as their methyl esters (**13** and **14**, Y = CH_3) after treatment with diazomethane. [c] Y = H. [d] Y = CH_3.

In contradistinction to enols **3a–g**, the 4,4-diphenyl analogue **3h** reacted extremely sluggishly with superoxide anion radical. As seen from eq 5 and Table II, after 24 h of reaction only 20% of the enol reacted, yielding 3-

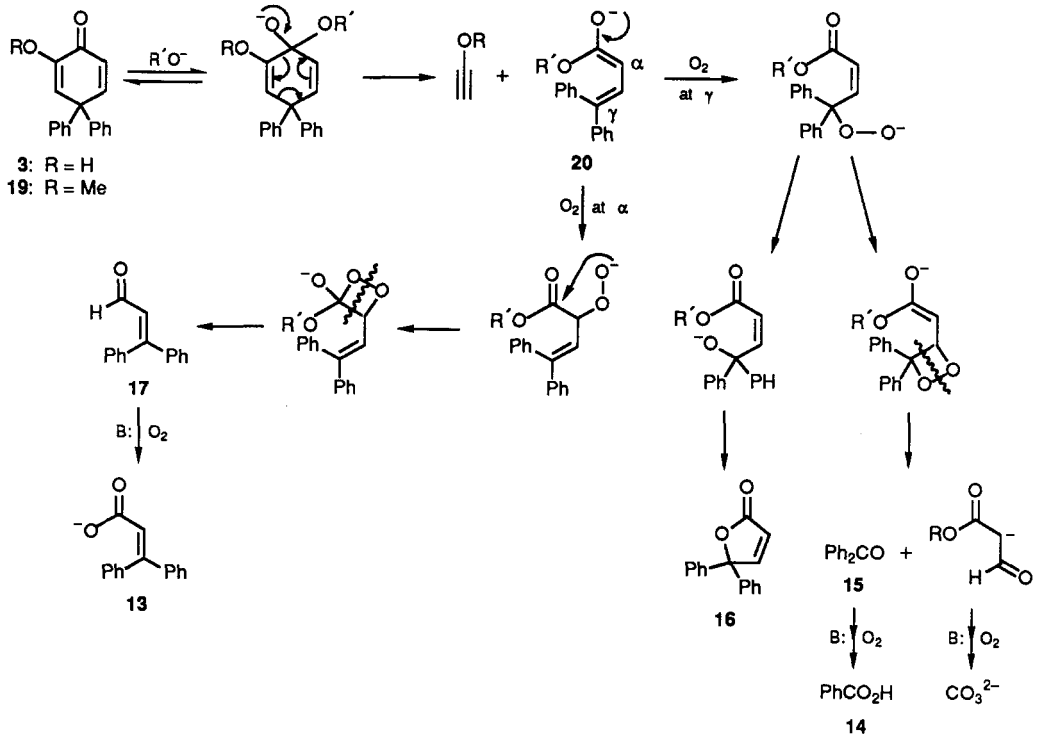


(12) (a) Sosnovsky, G.; Zaret, E. H. In *Organic Peroxides*; Swern, D., Ed.; Wiley: New York, 1970; Vol. I, p 517. (b) Russell, G. A.; Janzen, E. G.; Bemis, A. G.; Geels, E. J.; Moye, A. J.; Mak, S.; Strom, E. T. *Adv. Chem. Ser.* **1965**, *51*, 112. (c) Russell, G. A. *Pure Appl. Chem.* **1967**, *15*, 185. (d) Russell, G. A.; Bemis, A. G.; Geels, E. J.; Janzen, E. G.; Moye, A. J. *Adv. Chem. Ser.* **1968**, *75*, 175. (e) Karnojitzky, V. *Russ. Chem. Rev.* **1981**, *50*, 888.

(13) For further discussion of this point see: Frimer, A. A.; Aljadeff, G.; Ziv, J. *J. Org. Chem.* **1983**, *48*, 1700. (b) Recent data indicate that this order of rates corresponds to the order of solubilities of the respective potassium salts.

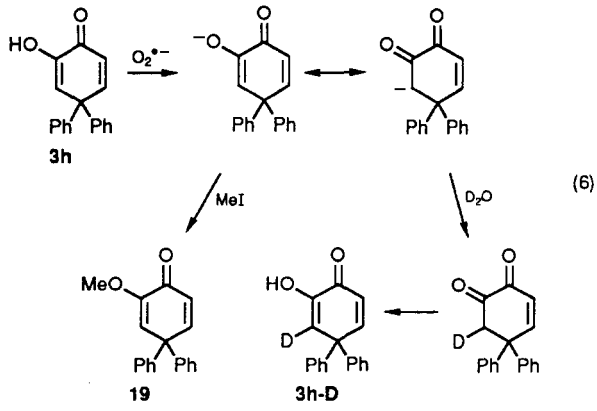
(14) (a) Matsuura, T.; Matsushima, H.; Sakamoto, H. *J. Am. Chem. Soc.* **1967**, *89*, 6370. (b) Nishinaga, A.; Matsuura, T. *J. Chem. Soc., Chem. Commun.* **1973**, 9. (c) Nishinaga, A.; Tojo, T.; Tomita, H.; Matsuura, T. *J. Chem. Soc., Perkin Trans. 1* **1979**, 2511. (d) Utaka, M.; Matsushita, S.; Yamasaki, H.; Takeda, A. *Tetrahedron Lett.* **1980**, *21*, 1063. (e) Rajanada, V.; Brown, S. B. *Tetrahedron Lett.* **1981**, *22*, 4331. (f) Wasserman, H. H.; Pickett, J. E. *J. Am. Chem. Soc.* **1982**, *104*, 4695. (g) Utaka, M.; Nakatani, M.; Takeda, A. *Tetrahedron Lett.* **1983**, *24*, 803. (h) Utaka, M.; Hojo, M.; Fujii, Y.; Takeda, A. *Chem. Lett.* **1984**, 635. (i) Wasserman, H. H.; Pickett, J. E. *Tetrahedron* **1985**, *41*, 2155. (j) Utaka, M.; Nakatani, M.; Takeda, A. *Tetrahedron* **1985**, *41*, 2163. (k) Hayakawa, K.; Ueyama, K.; Kanematsu, K. *J. Org. Chem.* **1985**, *50*, 1963. (l) Utaka, M.; Kuriki, H.; Sakai, T.; Takeda, A. *J. Org. Chem.* **1986**, *51*, 935. (m) Utaka, M.; Nakatani, M.; Takeda, A. *J. Org. Chem.* **1986**, *51*, 1140. (n) See in addition ref 6a, 6c, 9a, 9k, 9l, 9o.

Scheme III. Proposed Mechanism for the Formation of Products 13–17



phenylcinnamic acid (**13**)[7a] and benzophenone (**15**) as the major products. A small amount of benzoic acid (**14**) was also observed, but no lactol **4h** could be detected. Since the conversion of enols to lactols is a BCA process, we attempted to force the reaction to go by replacing $O_2^{\bullet-}$ with the stronger base *tert*-butoxide. Thus, both **3h** and, for comparison purposes, its enol ether analogue **19**[7] (which lacks an enolic proton) were contacted with *tert*-butoxide at room temperature for 5 days. Again, **13** and **15** were observed as the major products along with various amounts of **14**, 5,5-diphenyl-2(5*H*)-furanone (**16**),[15] 3-phenylcinnamaldehyde (**17**),[7a,15d] and 4,4-diphenylcyclohexa-2,5-dien-1-one (**18**).[7a]

A priori, the absence of lactol might be attributed to the inhibition of enolate **9** formation as a result of steric blocking by the diphenyl substituents at C_4. This was ruled out, however, by two simple experiments (eq 6). First, the reaction mixtures were quenched with CH_3I, yielding the corresponding enol ether **19**. In the second experiment, the reaction was worked up with D_2O, generating the 3-deuterio analogue of **3h** (**3h-D**).

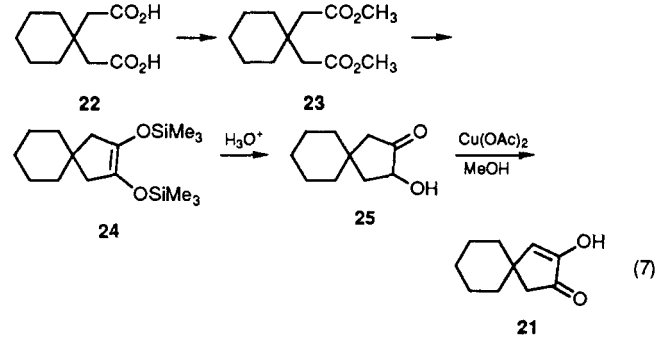


(6)

An alternative explanation is that oxygenation at C_3 is sterically inhibited by the gem-diphenyl group at C_4. Indeed, construction of a space-filling model[16] of **3h** reveals severe steric crowding around C_3, which hinders the approach of electrophiles to the reaction site. This effect is much more pronounced with larger electrophiles such as molecular oxygen, whereas the steric demands of a deuteron are much less severe.

The results of Table II can be rationalized by assuming nucleophilic attack of the base ($O_2^{\bullet-}$ or t-$C_4H_9O^-$) upon the C_1 carbonyl, as shown in Scheme III. We speculate that this induces a retro-Diels–Alder process generating extended enolate **20**, which can undergo oxygenation at either the α- or γ-carbons. The former leads to **13** and **17**, while the latter produces **15** and **16**. Benzoic acid (**14**) is a product of the BCA of benzophenone.[17] The origin of **18** is unclear.

One additional α-keto–enol system was briefly explored in this project. 2-Hydroxyspiro[4.5]dec-1-en-3-one (**21**) was prepared (as outlined in eq 7) via the chlorotrimethylsilane modification of the acyloin condensation[18] using the general procedure of Naoshima and co-workers.[19] Copper acetate oxidation of the resulting acyloin **25** yields the desired enol.

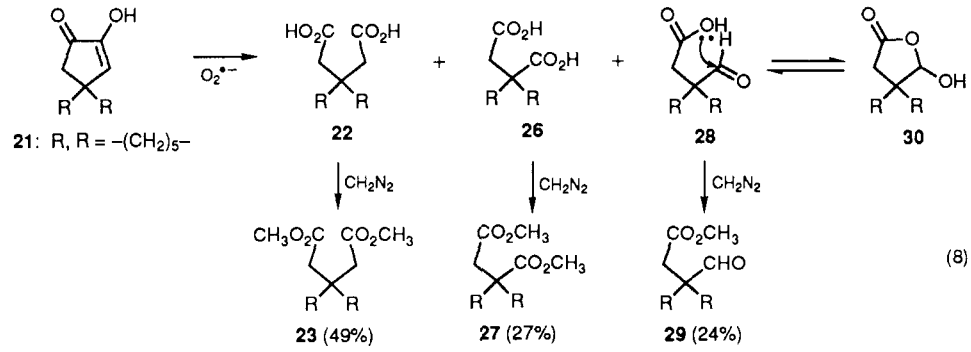


(7)

(15) (a) Brown, R. F. C.; Eastwood, F. W.; Chaichit, N.; Gatehouse, B. M.; Pfeiffer, J. M.; Woodroffe, D. *Aust. J. Chem.* **1981**, *34*, 1467, 1474. (b) Machado-Araujo, F. W. L.; Gore, J. *Tetrahedron* **1982**, *38*, 2897. (c) Grandguillot, J.-C.; Rouessac, F. *Synthesis* **1979**, 607. (d) Kurosawa, K.; Tsujita, T. *Bull. Chem. Soc. Jpn.* **1981**, *54*, 2391. (e) Cannone, P.; Akssira, M.; Fytas, J. *Tetrahedron* **1984**, *40*, 1809.

(16) Courtauld Atomic Models; Griffin and George Ltd.: Alperton, Middlesex, England.

Scheme IV



Reaction of enol **21** with KO_2/18-crown-6 gave a quantitative yield of acidic products, which were diazotized and separated by GLC. Three products were isolated in a ratio of 2:1:1 and identified as diesters **23** and **27** and aldehydo ester **29**, respectively. These three are presumably derived from the corresponding acids **22**, **26**, and **28** (Scheme IV). However, the absence of an aldehyde absorption in the ^1H NMR spectrum of the acid mixture and the presence of a singlet at 5.4 ppm (corresponding to the hemiacetal hydrogen OC*H*OH) indicate that aldehydo acid **28** exists as expected in the closed lactol form **30**.

Regarding the question of mechanism, it is likely that diacid **22** results from $O_2^{\bullet-}$-mediated cleavage of the α-diketone tautomeric form, as suggested above for enols **3a–g**. Similarly, aldehydo acid **28** (or lactol **30**) is formed by the same oxidation–cyclization–decarbonylation sequence invoked above for the formation of lactols **4a–g**. The source of diacid **26** is not clear; it may result either from a secondary BCA of **22** at the α-carbon or via the $O_2^{\bullet-}$-catalyzed autoxidation of the aldehydic functionality[2] in aldehydo acid **28**. Both of these possibilities are well precedented.[2] Indeed, both may well be operational.

We close this paper with a discussion of the synthetic ramifications of our results. As noted in the opening lines of the Results and Discussion, enols **3a–h** were prepared by the $O_2^{\bullet-}$-induced BCA of 4,4- and 5,5-disubstituted cyclohex-2-en-1-ones **1** and **2** (eq 3).[7] As shown in Table III, the conversion of these enones to the corresponding lactols **4** can in fact be carried out in one pot if the enol, instead of being isolated, is allowed to react further. Indeed, α-keto enols **3c** and **3g** are much more reactive than the corresponding enones **2c** and **2g**, such that the reaction of the latter pair cannot be stopped at the enol stage and proceeds directly to lactol.[7] The facile one-pot oxidation of cyclohexenones **1** to lactols **4** and the subsequent reduction of the latter to lactones **7** represents a convenient two-step method for the conversion of 4,4-disubstituted cyclohex-2-en-1-ones to their 6-oxa analogues, 2,3-unsaturated δ-valerolactones. A practical application of such an approach has been utilized in the synthesis of the pharmacologically active 2-oxa-3-oxo-Δ^4-steroids.[9n]

We are presently exploring other methods for converting α-keto enols to the corresponding lactols. We have found singlet oxygenation[14i,j] to offer the greatest promise. For example, enol **3c** undergoes facile conversion to lactol **4c** upon photosensitized (polymer–Rose Bengal) oxidation in the presence of tetrabutylammonium fluoride.[14i] A complete report on our efforts in this area as well as its application to oxasteroid synthesis[9n] is in preparation.[20]

Table III. Product Yields in the Superoxide-Mediated One-Pot Conversion of Enones 1 and 2 to Lactols 4[a]

enone	yield of lactol 4, %	enone	yield of lactol 4, %
2a	40[b]	**1d**	98
1b	20[b]	**2e**	0[c]
2b	38[b]	**2f**	15[c]
1c	95	**2g**	95
2c	70[c]		

[a] The ratio of KO_2:18-crown-6:substrate was 4:2:1. Reactions were carried out in benzene or toluene at ambient temperature under dry air for 16 h. [b] The remaining product is a mixture of unidentified acids. [c] The remaining product is the corresponding enol **3**.

Experimental Section

The instrumentation utilized and the general experimental techniques, as well as the synthesis of enones **1** and **2**, enols **3**, and enol ether **19**, have been described in the accompanying paper.[7a] GLC was carried out on a 5 ft × $^1/_4$ in. copper column packed with 10% SE-30 on Chromosorb WAWDMCS, unless otherwise indicated.

General Procedure for the Preparation of Lactols 4 and Their Methoxy Analogues 5. Enols **3**[7a] and enones **1** and **2**[7a] were reacted with KO_2/18-crown-6 in benzene or toluene according to the general oxidation procedure[7a] under the conditions indicated in Tables I and III, respectively. Aqueous acid workup acidification of the $NaHCO_3$ extracts, and extraction with ether yielded lactol **4**. Lactols **4e** and **4f** were in the original organic phase. On the other hand, when the reaction was quenched with 10-fold CH_3I prior to workup, methoxy lactol **5** could be isolated from the nonacidic fraction in yields corresponding to that of **4**. The products were generally purified by preparative TLC eluting with 25% acetone in hexane unless otherwise indicated. Retention times (R_f) cited below are for analytical TLC samples run in this solvent system. Acetone-d_6 proved to be the solvent of choice for the ^1H NMR spectra of lactols **4c** and **4d** because in $CDCl_3$ H_3 and H_5 are difficult to distinguish.

4a: ^1H NMR‡ ($CDCl_3$) δ 6.29 (m, 1 H, H_3), 5.35 (br s, 1 H, H_5), 4.83 (br s, 1 H, OH), 1.87 (d, J = 1.5 Hz, 3 H, C_2 methyl), 1.15 (s, 3 H), 1.12 (s, 3 H); IR ($CDCl_3$) 3420 (br, m, OH), 1700 (s, C=O), 1640 (w, C=C) cm^{-1}; MS (CI, 57 eV), m/e 157 (MH^+), 139 ($MH^+ - H_2O$).

5a: ^1H NMR‡ ($CDCl_3$) δ 6.27 (qd, $J_{allylic}$ = 1.5 Hz, $J_{3,5}$ = 1.0 Hz, 1 H, H_3), 4.84 (d, $J_{3,5}$ = 1 Hz, H_5), 3.56 (s, 3 H, OCH_3), 1.88

(17) (a) Galliani, G.; Rindone, B. *Tetrahedron* **1981**, *37*, 2313. (b) Artamkina, G. A.; Grinfel'd, A. A.; Beletskaya, I. P. *Bull. Acad. Sci. USSR, Div. Chem. Sci.* **1983**, 345; *Izv. Akad. Nauk. SSSR, Ser. Khim.* **1983**, 383. (c) Artamkina, G. A.; Grinfel'd, A. A.; Beletskaya, I. P. *Tetrahedron Lett.* **1984**, *25*, 4989.

(18) For a review of this modification see: Reiffers, S.; Wynberg, H. *Synthesis* **1971**, 209.

(19) Naoshima, Y.; Yamagushi, M.; Kawai, M.; Ichimoto, I. *J. Agric. Biol. Chem.* **1974**, *38*, 2273.

(20) (a) Frimer, A. A.; Ripshtos, S., unpublished results, 1987. (b) Ripshtos, S. M.S. Dissertation, Bar-Ilan University, Ramat Gan, Israel, Jan 1988.

(d, $J_{allylic}$ = 1.5 Hz, 3 H, C_2 methyl), 1.15 (s, 3 H), 1.08 (s, 3 H)—assignments were elucidated via double-resonance irradiation at 6.65 and 1.90 ppm; ^{13}C NMR‡ ($CDCl_3$) δ 164.37 (C_1), 148.37 (C_3), 125.64 (C_2), 108.29 (C_5), 57.18 (CH_3O), 36.73 (C_4), 24.89 and 20.80 (gem-dimethyls), 16.66 (C_2-methyl); IR (CCl_4) 1730 (s, C=O) cm^{-1}; MS (CI, 57 eV), *m/e* 171 (MH^+, 100%), 139 (M - OCH_3, 15.48%); MS (EI, 55 eV), *m/e* 171 (MH^+, 4.16%), 141 (M - HCO, 25.39%), 139 (M - OCH_3, 13.20%), 110 (M - CH_3OCHO, 94.02%), 95 (M - OCH_3 - CO_2, 55.08%), 67 (M - OCC_2CH_3, 100%).

4b: ^1H NMR ($CDCl_3$) δ 6.56 (d, $J_{2,3}$ = 9 Hz, 1 H, H_3), 5.90 (d, $J_{2,3}$ = 9 Hz, 1 H, H_2), 5.36 (s, 1 H, H_5), 1.18 (s, 6 H); IR ($CDCl_3$) 3350 (br, m, OH), 1720 (s, C=O), 1640 (w, C=C) cm^{-1}; MS (CI, 70 eV), *m/e* 143 (MH^+).

4c: R_f (25% acetone in hexane) 0.15; ^1H NMR ($CDCl_3$) δ 5.33 (br s, 2 H, H_3 and H_5), 4.93 (br s, 1 H, OH), 3.78 (q, *J* = 6 Hz, 2 H, ethoxy methylene), 1.33 (t, *J* = 6 Hz, 3 H, ethoxy methyl), 1.17 (s, 6 H, C_4 gem-dimethyl); ^1H NMR‡ (acetone-d_6) δ 6.57 (br s, 1 H, OH), 5.53 (s, 1 H, H_3), 5.32 (s, 1 H, H_5), 3.77 (q, *J* = 7 Hz, 2 H, ethoxy methylene), 1.26 (t, *J* = 7 Hz, 3 H, ethoxy methyl), 1.13 (s, 6 H, C_4 gem-dimethyl); ^{13}C NMR‡ ($CDCl_3$) δ 160.65 (C_1), 141.66 (C_2), 118.59 (C_3), 100.83 (C_5), 63.05 (ethoxy methylene), 35.71 (C_4), 24.90 and 20.51 (gem-dimethyl at C_4), 13.18 (ethoxy methyl); IR ($CDCl_3$) 3360 (br, m, OH), 1720 (s, C=O), 1630 (s, C=C) cm^{-1}; UV (absolute ethanol) λ_{max} (ϵ_{max}) = 248 (3868) nm; MS (40 eV), *m/e* 186 (M^+), 169 (M - OH), 140 (M - HOCHO), 113 (M - CH_3CH_2OCO).

5c: R_f (25% acetone in hexane) 0.53; ^1H NMR ($CDCl_3$) δ 5.33 (s, 1 H, H_3), 4.83 (s, 1 H, H_5), 3.80 (q, *J* = 8 Hz, 2 H, ethoxy methylene), 3.57 (s, 3 H, OCH_3), 1.40 (t, *J* = 8 Hz, 3 H, ethoxy methyl), 1.17 and 1.13 (s, 3 H each, gem-dimethyl); IR (neat) 1730 (s, C=O), 1630 (s, C=C) cm^{-1}; MS (70 eV), *m/e* 200 (M^+), 185 (M - CH_3), 171 (M - C_2H_5), 140 (M - OC_2H_5 - CH_3).

4d: R_f (25% acetone in hexane) 0.09; ^1H NMR (acetone-d_6) δ 6.63 (br s, 1 H, OH), 5.50 (s, 1 H, H_3), 5.33 (s, 1 H, H_5), 3.56 (s, 3 H, OCH_3), 1.16 (s, 6 H, gem dimethyl); IR (neat) 3460 (br, s, OH), 1700 (s, C=O), 1620 (m, C=C) cm^{-1}; MS (70 eV), *m/e* 172 (M^+), 155 (M - OH), 141 (M - CH_3OH), 126 (M - HOCHO).

4e: R_f (25% acetone in hexane) 0.22; ^1H NMR‡ ($CDCl_3$) δ 7.49–7.31 (m, 6 H, aryl and OH), 6.65 (s, 1 H, H_3), 5.45 (s, 1 H, H_5), 1.25 (s, 6 H, gem-dimethyl); ^{13}C NMR‡ ($CDCl_3$) δ 163.78 (C_1), 150.77 (C_3), 134.86 (ipso), 130.50 (C_2), 128.43 and 128.22 (ortho and meta), 128.33 (para), 101.21 (C_5), 37.42 (C_4), 24.75 and 20.36 (gem-dimethyl at C_4); FTIR (KBr) 3413.3 (br, m, OH), 1717 (s, CO), 1696 (br, s, C=C) cm^{-1}; UV (absolute ethanol) λ_{max} (ϵ_{max}) = 237.0 (9090) nm; MS (30 eV, EI), *m/e* 172 (M - H_2CO_2, 1.34%), 129 (M - HOCHOCO, 100%); MS (55 eV, CI), *m/e* 219 (MH^+, 50.23%), 202 (M - OH, 100%), 173 (M - HOCHO, 14.41%).

4f: mp (following workup, without further purification) 89–90 °C; R_f (25% acetone in hexane) 0.30; ^1H NMR‡ ($CDCl_3$) δ 6.56 (br s, 1 H, OH), 6.28 (s, 1 H, H_3), 5.23 (s, 1 H, H_5), 1.25 (s, 6 H, gem dimethyl); ^{13}C NMR‡ ($CDCl_3$) δ 163.86 (C_1), 146.75 (C_3), 137.78 (C_2), 100.47 (C_5), 36.67 (C_4), 34.16 (4° of *tert*-butyl), 29.18 (*tert*-butyl methyls), 24.84 and 20.27 (gem-dimethyl at C_4); FTIR ($CDCl_3$) 3365.3 (br, m, OH), 1717.5 (s, CO), 1683.5 (br, s, C=C) cm^{-1}; UV ($CHCl_3$) λ_{max} (ϵ_{max}) = 237.2 (3120) nm; MS (55 eV), *m/e* 199 (MH^+, autoprotonation, 43.50%), 181 (MH^+ - H_2O, 59.02%), 165 (M - OH - CH_3, 10.71%), 152 (M - OCHOH, 100%), 137 (M - OCHOH - CH_3, 56.01%), 109 (M - OCHOH - C_3H_7, 66.63%).

4g: R_f (25% acetone in hexane) 0.12; mp ($CHCl_3$–hexane) 86–88 °C; ^1H NMR[21a] ($CDCl_3$) δ 5.60 (s, 1 H, H_3), 5.40 (s, 1 H, H_5), 4.98 (br s, 1 H, OH), 3.68 (s, 3 H, OCH_3), 2.10–1.20 (br s, 10 H, ring); IR[21b] (neat) 3140 (br, m, OH), 1720 (s, C=O), 1640 (m, C=C) cm^{-1}; UV (absolute ethanol) λ_{max} (ϵ_{max}) = 251 (5724) nm; MS (40 eV), *m/e* 212 (M^+), 166 (M - HOCHO), 123 (M - HOCHOCO - CH_3). Anal. Calcd for $C_{11}H_{16}O_4$: C, 62.26; H, 7.54. Found: C, 62.42; H, 7.52.

Methyl 2,4,4-Trimethyl-5-oxo-2-pentenoate (6a). Lactol **4a** was reacted with diazomethane,[11] and the products were separated by preparative TLC. The aldehydo ester **6a** was isolated in a 60% yield.

6a: ^1H NMR ($CDCl_3$) δ 9.43 (s, 1 H, aldehydic), 5.87 (s, 1 H, H_3), 3.66 (s, 3 H, OCH_3), 1.96 (s, 3 H, C_2 methyl), 1.23 (s, 6 H, C_4 gem-dimethyl); IR (neat) 2700 (w, aldehydic C–H), 1720 (s, C=O), 1630 (w, C=C) cm^{-1}; MS (CI, 70 eV), *m/e* 171 (MH^+).

Preparation and Hydrolysis of Methyl 2-Ethoxy-4,4-dimethyl-5-oxo-2-pentenoate (6c). Lactol **4c** was methylated with CH_2N_2[11] or with CH_3I/Ag_2O,[9h] yielding ester **6c** as the major product (80% yield). The ester was purified either by preparative TLC or GLC (oven, 100 °C; flow, 70 cm^3/min; retention time, 17 min). The identity of the lactol was further verified by hydrolyzing it back to lactol **4c** as follows: A 10% HCl solution (30 mL) was added to 30 mL of ether containing 0.5 mmol of ester **6c** and stirred for 16 h, at which time TLC revealed that all the ester had been converted to lactol. The ether layer was then separated, dried, and evaporated to yield lactol **4c**.

6c: R_f (25% acetone in hexane) 0.43; ^1H NMR ($CDCl_3$) δ 9.47 (s, 1 H, aldehydic), 5.10 (s, 1 H, H_3), 3.73 (s, 3 H, CH_3O), 3.80 (q, *J* = 7 Hz, 2 H, ethoxy methylene), 1.36 (t, *J* = 7 Hz, 2 H, ethoxy methyl), 1.25 (s, 6 H, C_4 gem-dimethyl); IR (neat) 2700 (w, aldehydic CH), 1730 (s, C=O), 1620 (w, C=C) cm^{-1}; UV (absolute ethenol) λ_{max} (ϵ_{max}) = 248.5 (3218) nm; MS (70 eV), *m/e* 200 (M^+), 172 (M - 28).

5,6-Dihydro-5,5-dimethyl-3-ethoxy-2*H*-pyran-2-one (7c). Lactol **4c** (2.6 mmol) was reduced with $NaBH_4$ as described by Kocar et al.[9h] for related steroidal systems. The reaction was acidified with 10% HCl and extracted with $CHCl_3$. The organic phase was dried ($MgSO_4$) and evaporated to give an 80% yield of lactone **7c**. The latter was purified either by preparative TLC or GLC (oven, 120°; flow, 85 cm^3/min; retention time, 5 min).

7c: R_f (25% acetone in hexane) 0.32; ^1H NMR ($CDCl_3$) δ 5.40 (s, 1 H, H_4), 3.97 (br s, 2 H, H_6), 3.73 (q, *J* = 7 Hz, 2 H, ethoxy methylene), 1.33 (t, *J* = 7 Hz, 2 H, ethoxy methyl), 1.13 (s, 6 H, C_5 gem-dimethyl); IR (neat) 1720 (s, C=O), 1630 (w, C=C) cm^{-1}; MS (70 eV), *m/e* 170 (M^+), 155 (M - CH_3), 126 (M - CO_2).

6-Acetoxy-5,6-dihydro-5,5-dimethyl-3-ethoxy-2*H*-pyran-2-one (8c). The Kocar procedure[9h] was utilized. Lactol **4c** (2.7 mmol) dissolved in acetic anhydride was added to pyridine, and the resulting solution was stirred for 12 h. The reaction mixture was then diluted with acetic acid and ether, and the ether phase was subsequently washed seven times with 10% HCl [to remove pyridine (TLC)] and once with water, dried, and evaporated to give a 70% yield of acetate **8c**. The latter was contaminated with unreacted starting material and required further purification by preparative TLC. Recrystallization from petrolum ether (40–60 °C) gave the desired product as white needles; mp 73–74 °C.

8c: R_f (25% acetone in hexane) 0.63; ^1H NMR[21c] ($CDCl_3$) δ 6.20 (s, 1 H, H_6), 5.37 (s, 1 H, H_4), 3.78 (q, *J* = 6 Hz, 2 H, ethoxy methylene), 2.15 (s, 3 H, acetoxy methyl), 1.40 (t, *J* = 6 Hz, 3 H, ethoxy methyl), 1.26 and 1.18 (s, 3 H each, C_5 gem-dimethyls); IR ($CDCl_3$)[21d] 1765, 1758 and 1745 (s, C=O), 1644 (m, C=C) cm^{-1}; UV (absolute ethanol) λ_{max} (ϵ_{max}) = 248 (7843) nm; MS (70 eV), *m/e* 228 (M^+), 214 (M - CH_2), 169 (M - CH_3CO_2), 156 (M - CH_3CO_2CH). Anal. Calcd for $C_{11}H_{16}O_5$: C, 57.89; H, 7.01. Found: C, 57.90; H, 7.16.

General Procedure for the Oxidation of 3h and 19. Enol **3h**[7] and enol ether **19**[7] were reacted with KO_2 or $KOC(CH_3)_3$ in toluene containing 18-crown-6 according to the general oxidation procedure[7] under the conditions indicated in Table II. Reactions were quenched with either 10% HCl or 10-fold CH_3I, as indicated in Table II. In the former case, the $NaHCO_3$ extracts were acidified and extracted with ether. These ether extracts were dried, concentrated, and treated with diazomethane.[11] The products were isolated by preparative TLC and identified by their spectral data. The product yields were determined from the integration of the distinctive peaks in the ^1H NMR of the crude product mixture prior to separation. All the products observed are known. The literature cites extensive spectral data for furanone **16**,[15] except that the ^1H NMR values reported fluctuate ±0.04; hence, we cite our data below.

16: ^1H NMR‡ ($CDCl_3$) δ 7.93 (d, *J* = 5.5 Hz, H_4), 7.32 (m, 10 H), 6.19 (d, *J* = 5.5 Hz, H_3).

3-Deuterio-2-hydroxy-4,4-diphenylcyclohexa-2,5-dien-1-one (3h-D). Enol **3h** (27 mmol) was reacted for 24 h with KO_2 as outlined in Table II. D_2O (3 mL) was then added to the reaction mixture, which was then allowed to continue stirring overnight. The organic phase was washed with 3 mL of D_2O, dried over $MgSO_4$, and evaporated. The product was identified as **3h-D** contaminated by a small amount of benzophenone.

(21) These spectra are cited in: *The Sadtler Standard Spectra Supplements*; Sadtler Research Laboratories: Philadelphia, 1985. (a) NMR 41446m; (b) IR 68876k; (c) NMR 41447m; (d) IR 68877k.

3h-D: ^{1}H NMR‡ ($CDCl_3$) δ 7.39 (d, $J_{5,6}$ = 10 Hz, 1 H, H_5), 7.32 and 7.29 (overlapping m, 6 H, meta and para), 7.23 (m, 4 H, ortho), 6.45 (d, $J_{5,6}$ = 10 Hz, 1 H, H_6), 6.35 (br s, 1 H, OH)—the assignments of the hydroxyl peak was confirmed by double-resonance irradiation of the water peak at 1.6 ppm. Only trace amounts of a doublet ($J_{3,5}$ = 3 Hz, H_3 of **3h**) could be detected. ^{13}C NMR‡ ($CDCl_3$) δ 181.48 (C_1), 156.52 (C_5), 145.48 (C_2), 142.39 (ipso), 128.86 (meta), 127.78 (ortho), 127.61 (para), 124.45 (C_6), 54.74 (C_4)—absorptions at ca. 123.04 (C_3) were not detected; assignments of the vinyl carbons were confirmed by correlating the residual CH coupling in two off-resonance decoupled spectra to the known proton absorptions; MS (55 eV), *m/e* 263 (M^+, 16.04%), 246 (M - OH, 5.01%), 235 (M - CO, 7.11%), 216 (M - CO - OHD, 6.28%), 158 (5.44%), 129 (11.31%), 105 (PhCO, 100%).

2-Hydroxyspiro[4.5]dec-1-en-3-one (21). The enol was prepared according to the general procedure of Naoshima et al.[19] 1,1-Cyclohexanediacetic acid (**22**, 10 g, 0.5 mol, Aldrich) was dissolved in 35 mL of methanol containing 3.5 mL of concentrated H_2SO_4 and refluxed for 3 h to give a nearly quantitative yield (11.2 g, 0.5 mol) of diester **23**. The latter was reacted with freshly distilled trimethylsilyl chloride (25.4 mL, 0.2 mol) and sodium as described[19] to yield 2,3-bis(trimethylsiloxy)spiro[4.5]dec-2-ene (**24**). Crude **24** was hydrolyzed[19] to acyloin **25**, a small portion of which was purified by preparative TLC. The bulk of crude **25** was refluxed overnight with copper acetate in methanol until a red copper precipitate was formed. After workup, the product mixture was distilled (80 °C/2 Torr) to yield 1 g (12% overall yield) of the desired α-keto enol **21**. The latter was further purified by GLC (3 ft × $^1/_4$ in. copper column packed with 10% SE-30 on Chromosorb P; oven, 140 °C; flow, 100 cm^3/min; retention time, 8 min).

21: R_f (25% acetone in hexane) 0.30; ^{1}H NMR ($CDCl_3$) δ 6.50 (s, 1 H, vinyl), 5.43 (br s, 1 H, OH), 2.27 (s, 2 H), 1.47 (br s, 10 H); IR (neat) 3340 (br, s, OH), 1690 (s, C=O), 1640 and 1620 (m, C=C) cm^{-1}; MS (70 eV), *m/e* 166 (M^+), 138 (M - CO), 123 (M - CH_2COH), 95 (M - CH_2COCOH).

23: ^{1}H NMR ($CDCl_3$) δ 3.63 (s, 6 H, CH_3O), 2.50 (s, 4 H, CH_2CO), 1.46 (br s, 10 H, ring); IR (neat) 1730 (s, C=O) cm^{-1}; MS (70 eV), *m/e* 228 (M^+), 197 (M - OCH_3), 155 (M - $CH_3O_2CCH_2$), 123 (M - $CH_3O_2CCH_2$ - OCH_3), 95 (M - CH_3O_2-CCH_2 - CH_3OCO).

24: ^{1}H NMR ($CDCl_3$) δ 2.40 (s, 2 H), 2.13 (s, 2 H), 1.47 (br s, 10 H), 0.23 (s, 18 H).

25: R_f (25% acetone in hexane) 0.27; ^{1}H NMR ($CDCl_3$) δ 4.26 (t, J = 10 Hz, 1 H), 2.23-2.13 (m, 4 H), 1.47 (br s, 10 H).

Reaction of 21 with $O_2^{\cdot-}$. Enol **21**, KO_2, and 18-crown-6 in an equimolar ratio were added to toluene and allowed to react for 8 h according to the general oxidation procedure.[7a] Acidic products in a 90% yield were isolated and diazotized.[11] The resulting methyl esters were separated by GLC (7 ft × $^1/_4$ in. copper column packed with 7% SE-52 on Chromosorb P; oven, 115 °C; flow, 100 cm^3/min) to give three peaks in a ratio of 1:1:2 with retention times of 12, 18, and 33 min. On the basis of their spectral data, these products were identified as aldehydo ester **29** and diesters **27** and **23**, respectively.

27: ^{1}H NMR ($CDCl_3$) δ 3.73 (s, 3 H, CH_3O), 3.66 (s, 3 H, CH_3O), 2.63 (s, 2 H, CH_2CO), 1.53 (br s, 10 H, ring); IR (neat) 1735 (s, C=O) cm^{-1}; MS (70 eV), *m/e* 214 (M^+), 183 (M - OCH_3), 155 (M - CO_2CH_3), 95 (M - CO_2CH_3 - HCO_2CH_3).

29: ^{1}H NMR ($CDCl_3$) δ 9.69 (s, 1 H, aldehydic), 3.67 (s, 3 H, CH_3O), 2.56 (s, 2 H, CH_2CO), 1.50 (br s, 10 H, ring); IR (neat) 1735 and 1700 (s, C=O) cm^{-1}; MS (70 eV), *m/e* 183 (M - H), 155 (M - CHO), 123 (M - CO_2CH_3).

Photosensitized Cis/Trans Isomerization of 1-(1-Propenyl)cycloalkenes[1]

Wayne D. Inman, Kenneth A. J. Sanchez, Manuel A. Chaidez, and Donald R. Paulson*

Department of Chemistry and Biochemistry, California State University, Los Angeles, Los Angeles, California 90032

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The photosensitized cis/trans isomerization of a series of 1-(1-propenyl)cycloalkenes is reported. A plot of the photostationary state trans/cis ratio vs the sensitizer triplet energy for 1-(1-propenyl)cyclopentene shows a constant trans/cis ratio of ~1.0 with high-energy sensitizers (E_T > 61 kcal/mol). The plot shows one maxima at E_T ~ 55 kcal/mol with low-energy sensitizers (E_T < 61 kcal/mol). This type of plot is very similar to those obtained with acyclic dienes such as piperylene. The 1-(1-propenyl)cyclohexene system shows a similar plot with high-energy sensitizers, but with low-energy sensitizers this system shows two maxima occurring at 56 and 47 kcal/mol, respectively. This double-maxima plot is rationalized by an unusually low trans/cis decay ratio for the s-cis relaxed triplet state of the 1-(1-propenyl)cyclohexene system. This double maxima is not observed in other diene systems due to a high trans/cis decay ratio for their s-cis relaxed triplet states. The photosensitized cis/trans isomerization of 2-ethylidene-10-methyl-1(9)-octalin was also studied as a model for a conformationally locked s-trans system. The 1-(1-propenyl)cycloheptene system undergoes photosensitized cis/trans isomerization, but photostationary cis/trans isomerization data could not be obtained due to a very efficient photosensitized dimerization of this diene system.

Introduction

The triplet sensitized cis/trans isomerization of conjugated dienes has been extensively studied over the past 25 years, resulting in a fairly clear mechanistic picture.[2] The generally accepted mechanism, shown in Scheme I, involves excitation of the ground-state sensitizer (sens^0) to the first excited singlet state (sens^1) followed by intersystem crossing to the triplet state (sens^3). Collisional deactivation of the sensitizer triplet state by the ground-state diene results in formation of the vertical diene triplets. Havinga first demonstrated the importance of ground-state conformations on the photochemistry of polyenes.[3] The s-trans and s-cis conformational isomers are included for each cis and trans configurational isomer as their importance has been demonstrated by Saltiel.[4]

(1) (a) The initial phase of this work was presented at the 178th National Meeting of the American Chemical Society, Washington, D.C., Sept 1979, Abstract ORGN 171. (b) Taken, in part, from the undergraduate honors thesis of W. D. Inman. (c) Taken, in part, from the M.S. Thesis of M. A. Chaidez.

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