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Vinylic Radicals Are Intermediates in the Oxidation of Vinylic Lithium Reagents to Lithium Enolates by Dioxygen, But Not by Lithium *tert*-Butyl Peroxide[1]

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Abstract: (*E*)- and (*Z*)-1-lithio-1-propene (**1**) and (*E*)- and (*Z*)-1-lithio-1-phenyl-1-butene (**2**) react with dioxygen at −78 °C and yield the corresponding lithium enolates with partial loss of stereochemistry around the double bond. Reactions of **1** and **2** with lithium *tert*-butyl peroxide yield enolates with retention of configuration. These stereochemical observations implicate free vinylic radicals in reactions of vinylic lithium reagents with dioxygen, and exclude them in reactions with lithium *tert*-butyl peroxide.

Transformation of an organolithium or -magnesium reagent to the corresponding alcoholate by reaction with dioxygen ordinarily occurs in two distinct steps:[3]

$$RM + O_2 \rightarrow ROOM \quad (1)$$

$$ROOM + RM \rightarrow 2ROM \quad (2)$$

Formation of an intermediate organic peroxide by reaction between the organometallic reagent and dioxygen has been proposed to require initial single-electron transfer to dioxygen;[4] this electron transfer may or may not generate a free radical, R·, depending on the solvation or extent of aggregation of the organometallic species.[5] The mechanism(s) of conversion of organic peroxides to alcoholates has not been carefully examined, but a related reaction—that of di-*tert*-butyl peroxide with ethyllithium, yielding, inter alia, lithium *tert*-butoxide and ethyl *tert*-butyl ether—has free alkyl and alkoxyl radical intermediates.[6]

Here we describe stereochemical evidence that indicates that vinylic radicals are intermediates in the oxidation of vinylic lithium reagents to lithium enolates by dioxygen, but not by lithium *tert*-butyl peroxide. *E* and *Z* diastereomers of appropriately substituted vinylic lithium reagents, and of the derived lithium enolates, can be prepared with high stereoselectivity and proved to be stereochemically stable under the conditions required for these oxidations. Vinylic radicals undergo rapid *Z*–*E* isomerization ($k_i = 10^8$–10^{10} s^{-1} for vinyl radical itself).[7-9] Thus, if free vinylic radicals are intermediates in oxidation of diastereomerically pure *Z* or *E* vinylic lithium reagents, the product lithium enolates will be formed as a mixture of diastereomers.[10] Conversely, if the products of reaction are generated with retention (or inversion) of stereochemistry, vinylic radicals are not intermediates.

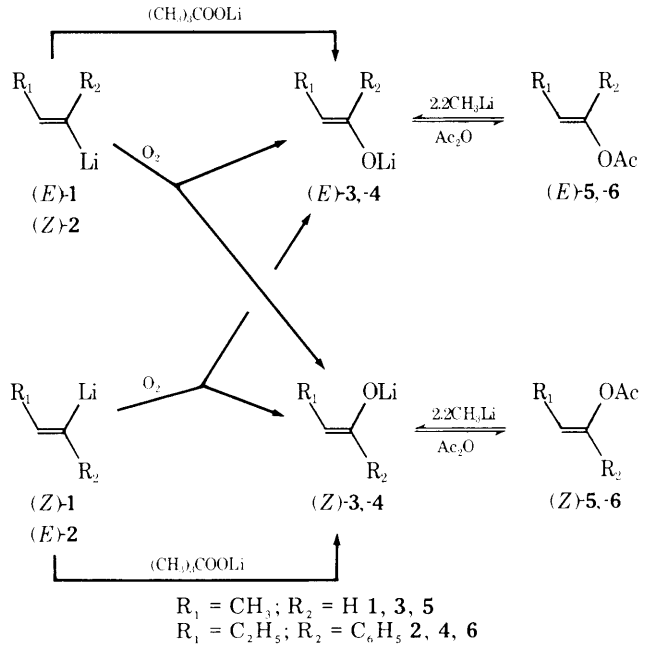
These studies contribute to the body of mechanistic information which will eventually rationalize the nucleophilic and electron-transfer pathways followed in reactions of organometallic compounds. They also provide a new method for the stereoselective generation of enolates, and may have applications in synthesis.[11]

Results

(*E*)- and (*Z*)-1-lithiopropene ((*E*)- and (*Z*)-**1**) were prepared by reaction of lithium metal with (*E*)-1-chloropropene and (*Z*)-1-bromopropene, respectively, in diethyl ether solution.[10,12] (*Z*)-1-Lithio-1-phenyl-1-butene ((*Z*)-**2**) was obtained by a lithium–halogen exchange reaction between *n*-butyllithium and (*E*)-1-bromo-1-phenyl-1-butene in hexane solution at 22 °C or THF solution at −78 °C,[13] and (*E*)-1-lithio-1-phenyl-1-butene ((*E*)-**2**) by reaction of *n*-butyllithium with (*Z*)-1-bromo-1-phenyl-1-butene in THF solution at −78 °C.[13] The diastereomers of **1** and **2** are configurationally stable at the temperatures used for the oxidation studies (−78 °C).[10,12,13] The lithium enolates **3** and **4**, generated by oxidation of the lithium reagents **1** and **2**, can be assayed for diastereomeric composition by acylation with acetic anhydride, and analysis by GLC of the resulting enol acetates **5** and **6**. The yields and isomeric composition of the enolate anions formed by oxidations of these reagents were determined by quenching the reaction mixtures with excess acetic anhydride, and analyzing the resulting enol acetates by GLC (Scheme I). Before the compositions of these mixtures of enol acetates could be used as the basis for conclusions concerning the stereochemistry of conversion of vinylic lithium reagents to lithium enolates, however, it was necessary to establish that (a) conversion of lithium enolate to enol acetate proceeded in high yield without isomerization, (b) the lithium enolates were stereochemically stable under the oxidative conditions used to generate them from the vinylic lithium reagents, and (c) neither diastereomer of the pairs of enolates was destroyed oxidatively at a much faster rate than the other.

Authentic lithium enolates were prepared by treating enol acetates with an excess of methyllithium. If stereochemically pure (>99%) (*Z*)- or (*E*)-**5** or -**6** was converted to lithium enolate by this procedure, and then quenched with acetic anhydride, the original enol acetate was obtained in >90% yield, with no detectable loss of stereochemistry. The yields and stereochemistry of the enol acetates obtained by acylation with acetic anhydride thus accurately reflect the composition of the lithium enolates from which they were derived.

Scheme I. Interconversions Used in Testing the Stereochemical Course of Oxidation of Vinylic Lithium Reagents to Lithium Enolates



$R_1 = CH_3$; $R_2 = H$ **1, 3, 5**
$R_1 = C_2H_5$; $R_2 = C_6H_5$ **2, 4, 6**

To test the isomeric stability of the lithium enolates to oxidation, isomerically pure samples of (*E*)-**3** and (*Z*)-**3** in ether solution were exposed to dioxygen at 22 and at −78 °C. At both temperatures, enolates were destroyed by autoxidation. At the higher temperature, loss of stereochemistry in the enolate occurred competitively with this autoxidation. Figure 1 shows the absolute yields of (*E*)-**3** and (*Z*)-**3** (estimated as enol acetates **5**) following treatment with acetic anhydride of aliquots from a sample to which increasing volumes of dioxygen were added. The production of *Z* isomer from *E* is evident in this plot. Similar conversions from (*Z*)- to (*E*)-**3** were observed in samples originally highly enriched in the former. At −78 °C, however, no evidence for isomerization of *Z* to *E* (or vice versa) during autoxidation was observed. Whatever the reaction responsible for the isomerization during oxidation, it is unimportant at −78 °C. Oxidations of **1** could, accordingly, be conducted at this temperature with the assurance that the initially formed lithium enolates would not isomerize under the reaction conditions.

The relative rates of autoxidation of the enolates derived from **1**, (*E*)-**3**, and (*Z*)-**3** were established by exposing mixtures of the two to dioxygen at −78 °C, periodically withdrawing aliquots, and converting the remaining enolates to enol acetates and analyzing. The mechanism and the kinetic rate expression for the disappearance of enolate are not known. The simplest realistic assumption about this reaction is that autoxidation of both *Z* and *E* enolates is described by rate expressions that are of the same form (e.g., for (*E*)-**3**, eq 3).

$$d[(E)\text{-}3] = -k_E[(E)\text{-}3]^{\alpha}C\,dt \qquad (3)$$

Here α and C are unknown constants which are the same for (*E*)-**3** and (*Z*)-**3**. If $\alpha = 1$, a plot of $-\ln(E/E_0)$ vs. $-\ln(Z/Z_0)$ should be linear, with slope k_E/k_Z. Figure 2 indicates that the relation is followed experimentally, and that $k_E/k_Z \simeq 1.5$. The significance of this number lies in the fact that it establishes that (*E*)-**3** and (*Z*)-**3** present in the same solution are destroyed by autoxidation at similar rates. It is therefore unnecessary to try to correct the relative amounts of (*E*)- and (*Z*)-**5**, the enol acetates obtained from (*Z*)- and (*E*)-**3**, for differential rates of autoxidation of these enolates before treatment with acetic anhydride, in order to estimate accurately the relative amounts

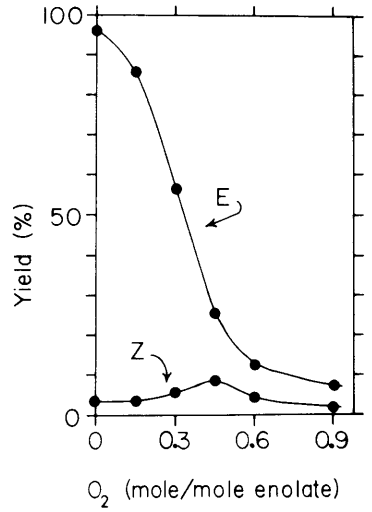


Figure 1. Addition of dioxygen to a solution containing predominantly (*E*)-**3** (0.1 N, Et$_2$O, 22 °C) results in concomitant isomerization of *E* to *Z* enolate and destruction of the enolates. Enolates were analyzed by GLC following conversion to enol acetates with acetic anhydride.

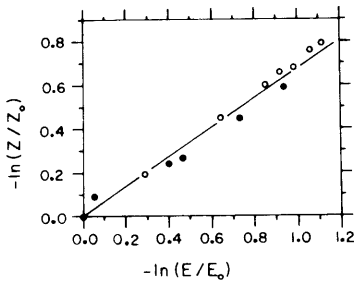


Figure 2. Analysis of competitive autoxidations of mixtures of (*E*)-**1** and (*Z*)-**1** according to eq 3 indicates that $k_E/k_Z \simeq 1.5$. Open and filled circles are data from two independent experiments.

of the diastereomeric enolates generated by oxidations of propenyllithium (**1**).

These studies establish that the diastereomeric composition of the enolates produced by oxidation of **1** can be determined by conversion to enol acetates with acetic anhydride and analysis by GLC, provided that the enolates are not exposed to oxygen at temperatures above −78 °C. Although we have not carried through analogous studies for the enolates **4** explicitly, we assume that the same conclusion applies to their determination; this assumption is justified qualitatively by the results that follow.

Oxidation of Vinylic Lithium Reagents with Lithium and Sodium *tert*-Butyl Peroxides Occurs with Retention of Configuration. The lithium salt of *tert*-butyl hydroperoxide was prepared by slowly adding a solution of methyllithium in ether to a well-stirred solution of *tert*-butyl hydroperoxide in ether (or THF) cooled to −78 °C. The sodium salt was prepared by allowing *tert*-butyl hydroperoxide to react with a suspension of sodium hydride in THF solution at 0 °C.[14] Analysis of the distribution of products obtained by permitting (E)- and (*Z*)-**1** to react with lithium *tert*-butyl hydroperoxide in ether at −78 °C, and (*E*)- and (*Z*)-**2** to react with lithium and sodium *tert*-butyl hydroperoxide in THF at −78 °C, establishes that conversion of the vinylic lithium reagent to lithium enolate occurs cleanly with retention of configuration around the double bond (Table I). Unreacted organolithium reagents present on quenching the reaction mixture with acetic anhydride appear as substituted methyl vinyl ketones. The major side products in the oxidation reactions are olefins. It is not known whether these materials are generated from proton

Table I. Diastereomeric Compositions and Product Yields from Oxidations of Vinylic Lithium Reagents RCHCR'Li with O_2 and Metal *tert*-Butyl Hydroperoxides (ROOM)

				Products, yield, %							
		% E^b		RCH=CR'-OAc		RCH=CR'-$COCH_3$		RCH=CHR'			
RLi[a]	Oxidant	RLi	RCH=CR'OAc	E	Z	E	Z	E	Z	RCH_2COR'	Total[d]
1	ROOLi	95	96	96	4.4						100
		4.1	3.7	2.4	63	33					98
2		80	21 [79]	8.3	32			40	8.8	*e*	89
		13	83 [17]	43	8.8			5.0	39	2.0	98
	ROONa	25	74 [26]	16	5.7			16	45	*e*	83
1[f]	O_2[g]	100	83	15	3.0	37					55
f		100	81	21	5.0	*e*					26
h		97	78	17	5.0	60					82
h		97	80	21	5.3	48					74
i		97	78	12	3.3	74					89
i		97	76	22	7.0	13					42
i		5.3	15	3.0	17	(68)[j,k]					88
i, l		4.5	14	1.5	9.1	(74)[j,m]					84
i, l		4.5	11	4.5	34	(*e*)[j]					38
2[n]		80	51 [49]	29	28	*e*	15	19	1.6	5.9	99
n		80	55 [45]	29	24	*e*	12	29	8.3	5.1	97
n		18	83 [17]	66	14	4.6	*e*	2.6	7.3	8.3	103
n		18	83 [17]	61	13	*e*	*e*	3.7	8.0	9.0	95
o		20	73 [27]	40	15	*e*	*e*	5.7	12	4.0	77
o		10	85 [15]	56	10	*e*	*e*	2.4	4.4	16	89

[a] [RLi] = 0.10 ± 0.01 M, unless noted otherwise. [b] The diastereomeric composition of the vinylic bromides was determined by GLC analysis of the vinylic bromides produced by reaction with 1,2-dibromoethane. The *Z, E* system of nomenclature is such that oxidation of (*Z*)-**2** with retention of configuration generates (*E*)-**6.** The numbers in brackets in the column for enol acetates are simply 100 − % *E*, and are included to facilitate direct comparison with % *E* for RLi. [c] (*E*)- and (*Z*)-pent-3-en-2-one were not distinguished under the GLC conditions used. Both methyl vinyl ketones and 1-bromopropene are derived from unreacted vinylic lithium reagents present in solution. [d] Product balance, based on starting RLi. [e] Not detected (<0.5%). [f] [RLi] = 0.01 N. [g] Oxygen was injected by syringe into the atmosphere over the solution, unless noted otherwise. [h] The solution was equimolar in the lithium enolates of butanal (94% *Z*). Ten percent of the mixture of butanal enolates was oxidized (96% *Z* after oxidation). [i] Oxygen was added at 11 mL/h to the atmosphere above 10 mL of solution in the beveled-bottomed oxidation apparatus described previously: E. J. Panek and G. M. Whitesides, *J. Am. Chem. Soc.*, **94,** 8768 (1972). [j] Values in parentheses are yields of 1-bromopropenes determined after treating with reaction mixture with 1,2-dibromoethane. [k] 5.6% *E*. [l] The solution was 0.1 M in LiBr. [m] 5.9% *E*. [n] THF solution. [o] [RLi] = 0.2 N in hexane solution.

sources included with the *tert*-butyl peroxide salts, from water introduced accidentally, or from other reactions.

The retention of configuration observed in these reactions established that free vinyl radicals are not intermediates in the oxidation of **1** and **2** by *tert*-butyl peroxide salts, and presumably, by analogy, by salts of other hydroperoxides.[15]

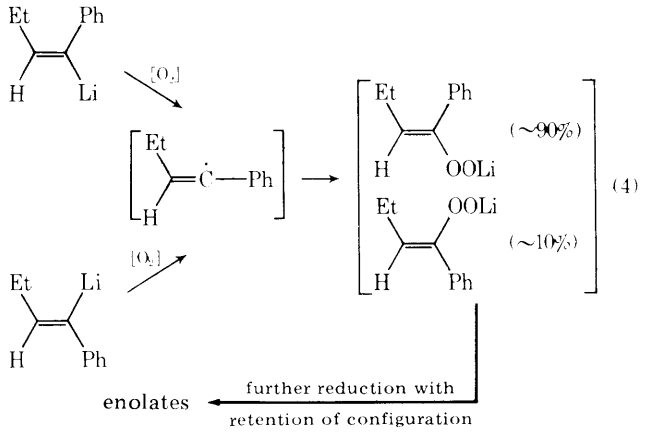
Oxidation of Vinylic Lithium Reagents with Dioxygen Generates Enolates with Significant Loss in Stereochemistry. Reaction of **1** and **2** with dioxygen, followed by acylation of the resulting enolates with acetic anhydride and analysis by GLC, gave mixtures of enol acetates in which some loss in stereochemistry had occurred around the double bond. The extent of loss depended on the structure: (*E*)-**1** showed greater loss than (*Z*)-**1** and (*E*)-**2** greater loss than (*Z*)-**2.** Since (*E*)-**3** is more rapidly oxidized than (*Z*)-**3,** part of this apparent difference in the degree to which stereochemistry is lost may be artifactual. The yields of enol acetates were higher from **2** than from **1.** In control experiments, partially oxidized solutions of organolithium reagents were allowed to react with 1,2-dibromoethane or acetic anhydride, and the stereochemistry of the vinylic moiety of the resulting vinylic bromides or methyl vinyl ketones compared with that of the same materials derived from the original, unoxidized solutions. These comparisons established that the vinylic lithium reagents were not isomerized under the reaction conditions. Several variations in the experimental conditions had no significant qualitative influence on the distribution of products: changes in the rate at which dioxygen was added to the reaction mixtures, alteration of the concentration of vinylic lithium reagent, addition of lithium bromide or of the lithium enolate of butanal to the solutions, and variations in the nature of the solvent, all resulted in reaction mixtures showing the same types of products and some degree of loss in stereochemistry in the enol acetates, although the distribution of products between enol acetates, methyl vinyl ketones, and other products varied with these (and other, unidentified) changes in experimental conditions in ways that have not been rationalized.

Discussion

The oxidation of vinylic lithium reagents **1** and **2** to lithium enolates **3** and **4** by lithium *tert*-butyl peroxide preserves configuration around the double bond.[14] Some loss in stereochemistry occurs during oxidation by dioxygen (Scheme I). To interpret the latter observation, we assume that the sequence of reactions described by eq 1 and 2 describes the conversion of vinylic lithium reagents to lithium enolates, and that the reaction of vinylic lithium compound with lithium vinylic peroxide retains stereochemistry around both vinylic double bonds.

Analysis of the distributions of products from reaction of (*E*)- and (*Z*)-**2** with dioxygen, based on these assumptions, is compatible with the conclusion that both *E* and *Z* diastereomers produce the same mixture of stereoisomers of the (presumed) lithium vinylic peroxide intermediate. In a typical example, reaction of **2** (18% *E* and 82% *Z*) with oxygen yields 83% *E* and 17% *Z* enolate. The yields of enolate derived from reduction of intermediate peroxides are assumed to be half of the total (because no peroxides survive the reaction) and are

calculated to be 41% *E* (0.5 × 82%) and 9% *Z* (0.5 × 18%). Subtraction of these yields from the overall yields gives the yields of the diastereomeric vinylic peroxides derived from initial reaction with dioxygen: 42% *E* (83% − 41%) and 8% *Z* (17% − 9%). A similar calculation on a second reaction of **2** with different diastereomeric composition (80% *E* and 20% *Z*) which yields 55% *E* and 45% *Z* enolate indicates that the yields of the diastereomeric vinylic hydroperoxides derived from this reaction would be 45% *E* and 5% *Z*. These diastereomeric compositions calculated from different reactions are considered to be the same within experimental error. A linear[15] vinylic radical is a plausible intermediate to use in rationalizing this stereochemical equilibration (eq 4).



(4)

Calculation of the diastereomeric composition of intermediate peroxides in the reactions of oxygen with **1** is not as easily justified since oxidation of enolates is a more severe problem, and the enolate yields are lower and less significant than those from **2**. Calculations on reactions with high total product yields indicate that nearly equal amounts of *E* and *Z* peroxides are compatible with the final yields of enolates.

The details of the steps in which free vinylic radical intermediates are generated and consumed in these reactions are not known. The vinyllithium compounds are probably aggregated under the conditions of our experiments.[16] However, the absence of any significant effect of solvent, or lithium halide or enolate concentration, on the reactions of **2** with oxygen suggests that an electron-deficient aggregate, if formed, rapidly releases a free vinyl radical. This result is surprising: neophyllithium shows a marked propensity to react with oxygen by pathways which do not involve release of a free neophyl radical intermediate[5] even though a neophyl radical should be more easily formed than a vinyl radical.[17] Metal–halogen exchange[13,18] and thermal decomposition of organocopper(I) reagents[10,19] provide examples of reactions in which intermediate alkyl radicals are generated, but intermediate vinylic radicals are not. Reaction of dioxygen with organolithium reagents apparently provides an obverse example, but the underlying reasons for the differences between these types of reactions are not obvious.

Qualitative data suggest that the mechanistic scheme outlined by eq 1–3 may also be applicable to the autoxidation of cyclopropyllithium reagents.[20]

Experimental Section

General Methods. All reactions involving organometallic compounds were carried out under atmospheres of prepurified nitrogen using standard techniques.[21] Ether was distilled from lithium aluminum hydride under a nitrogen atmosphere immediately before use. THF was distilled from a dark purple solution of sodium benzophenone dianion under nitrogen. Hexane was purified by scrubbing with concentrated sulfuric acid, drying, and distilling from a suspension of sodium benzophenone ketyl under nitrogen. NMR spectra were run as carbon tetrachloride solutions on Varian A-60 and JEOL MH-100 spectrometers; chemical shifts are reported in parts per million downfield from internal tetramethylsilane and coupling constants in hertz. IR spectra were run as carbon tetrachloride solutions in sodium chloride cells using Perkin-Elmer 237B or Beckman Model 18A grating spectrometers. Boiling points are uncorrected. Microanalyses were performed by Midwest Microlab, Inc., Indianapolis, Ind., and Galbraith Laboratories, Inc., Knoxville, Tenn.

Analytical GLC analyses of reactions of **1** and the enolates of propionaldehyde were performed on F and M Model 810 instruments equipped with flame ionization detectors using a 0.25 in. × 20 ft, 12.5% TCEOP on 80/100 mesh Chromosorb W column operated at 70 °C (for reactions with acetic anhydride) and 35 °C (for reaction with 1,2-dibromoethane). GLC analyses of reactions **2** were performed on a Gow-Mac Model 750 instrument (flame ionization detector) using a 0.125 in. × 10 ft, 7% SE-30 on 80/100 mesh Chromosorb W column operated at 120 °C.

Materials. *n*-Butyllithium was purchased from lithium Corp. of America as a hexane solution. Methyllithium (from methyl chloride) was purchased from Foote as an ether solution. (*E*)- and (*Z*)-**1**[10,12] and -**2**[13] were prepared as described previously. Concentrations and diastereomeric compositions of organolithium reagent solutions were determined by the Gilman double-titration method with 1,2-dibromoethane and GLC analysis.[10,12,13] The *E* and *Z* enol acetates of butyrophenone are described elsewhere.[22] *tert*-Butyl hydroperoxide was purchased from MCB and purified by reduced pressure distillation before use.

(*E*)- and (*Z*)-1-Propenyl Acetate. A mixture of 250 g (2.5 mol) of acetic anhydride, 20 g of potassium acetate, and 100 g (1.67 mol) of propionaldehyde was refluxed for 19 h.[23] Products which distilled below 118 °C were collected and neutralized with saturated aqueous Na_2CO_3, washed with brine, and dried ($MgSO_4$). Twelve grams of material (10% yield) was obtained. Distillation on a Teflon annular spinning band column yielded a fraction with bp 101 °C (5.7 g, 99.4% *Z* by GLC) and another fraction with bp 105 °C (3.0 g, 99.7% *E* by GLC).

NMR spectra were used to assign the geometrical configurations of these products. (*E*)-1-Propenyl acetate: IR 1761, 1670, 927 cm^{-1}; NMR δ 6.90 (1 H, d, J = 11.0 Hz, of q, J = 1.5 Hz), 5.20 (1 H, d, J = 11.0 Hz, of q, J = 6.2 Hz) 2.01 (3 H, s), 1.58 (3 H, d, J = 6.2 Hz, of d, J = 1.5 Hz). (*Z*)-1-Propenyl acetate: IR 1760, 1675 cm^{-1}; NMR δ 6.87 (1 H, d, J = 5.7 Hz, of q, J = 6.5 Hz), 2.05 (3 H, s), 1.62 (3 H, d, J = 6.5 Hz, of d, J = 1.6 Hz).

Anal. Calcd for $C_5H_8O_2$: C, 59.98; H, 8.05. Found (*E*): C, 59.96; H, 8.06. (*Z*): C, 59.82; H, 7.94.

(*E*)- and (*Z*)-1-Butenyl Acetate. The method of preparation is the same as that described above except that the material distilling between 70 and 141 °C was collected and neutralized. Upon distillation through a Teflon annular spinning band column fractions with boiling points 121 °C (99% *Z* by GLC) and 130 °C (100% *E* by GLC) were obtained. The spectra are similar to those reported above. (*E*)-1-Butenyl acetate: IR 1762, 1670, 935 cm^{-1}; NMR δ 6.92 (1 H, d, J = 11.1 Hz, of t, J = 1.3 Hz), 5.25 (1 H, d, J = 11.1 Hz, of t, J = 6.2 Hz). (*Z*)-1-Butenyl acetate: IR 1760, 1670 cm^{-1}; NMR δ 6.82 (1 H, d, J = 5.7 Hz, of t, J = 1.4 Hz), 4.70 (1 H, d, J = 5.7 Hz, of t, J = 6.5 Hz).

Anal. Calcd for $C_6H_{10}O_2$: C, 63.14; H, 8.83. Found (*E*): C, 63.24; H, 8.90. (*Z*): C, 62.75; H, 8.79.

(*E*)-Pent-3-en-2-one. A mixture of 6.2 g (15 mmol) of acetylmethylenetriphenylphosphorane[24] and 1.7 g (39 mmol) of acetaldehyde in 20 mL of methylene chloride was stirred at room temperature for 2 days, 25 mL of pentane was added, and the precipitated triphenylphosphine oxide was removed by filtration. The solvent was removed by distillation through an 80-cm Vigreux column and the resultant red solution was distilled through a short-path column to yield 1.14 g (14 mmol, 93% yield) of a colorless liquid with bp 115–121 °C (lit.[25] 113–119 °C), having IR spectrum ($CHCl_3$) indistinguishable from that reported.[26]

1-Phenylbuten-1-yl Acetate (4). The *Z* enol acetate of butyrophenone was the predominant (>95%) product formed in both acid- and base-catalyzed reactions of butyrophenone with acetic anhydride.[22] The pure *E* and *Z* isomers were obtained by preparative GLC separation.[22] Their configurations were assigned by comparison of the vinyl proton chemical shifts with those reported for the enol acetates of propiophenone[27] and with those calculated by Fobey's method.[28]

Oxidations of the lithium enolates of propionaldehyde (3) were carried out using one of two procedures. (A) Into a flame-dried 40-mL

centrifuge tube containing a Teflon-coated magnetic stirring bar were weighed 100 mg (1.00 mmol) of 1-propenyl acetate (**5**) and 15 mg of *n*-decane. After the tube had been flushed with nitrogen, 8 mL of ether was added by cannula. The enolate was generated by addition of 1.3 mL of a 1.6 N solution of methyllithium (2.08 mmol). Hydrolysis of a 0.5-mL aliquot of this solution after 10 min showed that no enol acetate remained. (The reaction mixtures that were not oxidized were stirred at room temperature for 45 min.) A 1-mL aliquot of the solution was transferred by cannula under nitrogen into a 12-mL centrifuge tube stoppered with a No-Air stopper containing 1 mL of acetic anhydride (bp 140 °C). Then, while stirring at the desired temperature, 10 mL of oxygen was added all at once by gas-tight syringe to the atmosphere above the remaining solution of the enolate. The reactions were stirred for times varying from 15 to 60 min before a 1-mL aliquot was removed by cannula and quenched with acetic anhydride as above. These samples were analyzed by GLC without further treatment. The samples which were not analyzed immediately were stored under nitrogen at −20 °C.

(B) Oxygen was added by gas-tight syringe to the atmosphere over the stirred enolate solution. After a 10- or 15-min reaction time, a 1-mL aliquot of the solution was transferred by cannula under nitrogen to a 12-mL centrifuge tube containing 1 mL of acetic anhydride. More oxygen was then added to the atmosphere over the solution.

Oxidations of 1-Lithiopropene. These oxidations were carried out at −78 °C by adding oxygen to the atmosphere above stirred or unstirred solutions in 40-mL centrifuge tubes or in the beveled-bottomed flask apparatus; reaction aliquots were quenched with acetic anhydride or 1,2-dibromoethane as above.

The dilute sample (0.01 N) was prepared by transferring ca. 70 mL of a 0.1 N solution of 1-lithiopropene by cannula to one side of a flame-dried double Schlenk tube containing a magnetic stirring bar on each side. The tube was degassed and sealed under vacuum at liquid nitrogen temperature. After the solvent had melted, the solution was sloshed around to destroy traces of oxygen and water on the inside of the tube. Approximately 7 mL of solution was poured into one side, and the rest of the solvent was distilled over into that side. The solvent was frozen with liquid nitrogen and the tube separated by sealing the connecting arm. The tube containing the diluted solution was opened on the vacuum line and surrounded by a bath of the desired temperature. While the solution was stirred, oxygen was injected into the isolated portion of the vacuum line. The solution was allowed to react with the oxygen for ca. 1 h before an aliquot was removed. After the oxidation reaction was complete, a 20 30-mL portion of the solution was titrated to determine the total base concentration.

In the experiment of Table I in which the enolate of butanal was included, 352 mg (3.09 mmol) of 1-butenyl acetate (94.2% *Z*) dissolved in 30 mL of ether was allowed to react with 4.0 mL of a 1.6 N methyllithium solution (6.4 mmol) for 30 min at room temperature. Hydrolysis of an aliquot of this solution showed that no enol acetate remained. (*E*)-1-Lithiopropene (30 mL of a 0.10 N ether solution, 3.0 mmol) was added to the ether solution containing the butanal enolate. Titration of an aliquot of this solution with 0.10 N HCl to a phenolphthalein end point indicated that the total base concentration was 0.26 N. Thus, the concentrations of (*E*)-1-lithiopropene and butanal enolate were ca. 0.09 N. A 20-mL aliquot (1.8 mmol of each component) of this solution was transferred to a flame-dried 40-mL centrifuge tube equipped with a magnetic stirring bar and sealed with a No-Air stopper. The tube was immersed in a dry ice/acetone bath and, while stirring, 10 mL of oxygen was injected into the atmosphere over the solution. The reaction was allowed to proceed for 1 h. Then a 3-mL aliquot of the solution was allowed to react with 2 mL of acetic anhydride as described above.

Oxidations of 1-lithio-1-phenyl-1-butene were also carried out at −78 °C in flame-dried 40-mL centrifuge tubes equipped with magnetic stirring bars and sealed with No-Air stoppers. In a typical experiment 3.5 mL of a 0.2 N solution of **2** was prepared by adding 0.45 mL of *n*-butyllithium as a hexane solution (1.6 N, 0.72 mmol) to a cooled (−78 °C) THF solution (3.0 mL) of (*E*)-1-bromo-1-phenyl-1-butene (149 mg, 0.7 mmol) and *tert*-butylbenzene (26.6 mg). After stirring for a few minutes, 0.2-mL aliquots were removed and quenched with ethanol and 1,2-dibromoethane. Ten milliliters of oxygen was injected into the atmosphere over the remaining solution. The oxidation reaction was quenched by adding to acetic anhydride (4.0 mL) 20 min after the oxygen was added.

Identification of the Reaction Products. Large-scale oxidation reactions of 1-lithiopropene (6.0 mmol in 60 mL of ether, 99% *E*, 70% *E*, and 98% *Z*) at −78 °C were quenched with excess acetic anhydride. After the lithium acetate had been removed by filtration, the reaction mixtures were distilled on a Teflon annular spinning band column and the fractions with bp 100–125 °C were collected. The (*E*)- and (*Z*)-1-propenyl acetates formed in each reaction were collected from a 10-ft, 10% TCEOP on Chromosorb W column at 85 °C and their IR spectra were compared with those of authentic samples. In addition, a sample of (*E*)-pent-3-en-2-one was collected from the 99% *E* oxidation reaction mixture and its infrared spectrum compared with that of the authentic sample.

A large-scale oxidation of 1-lithio-1-phenyl-1-butene (7.1 mmol in 35 ml of THF, 80% *Z*) was quenched with excess acetic anhydride and worked up in the usual fashion. The (*E*)- and (*Z*)-1-acetoxy-1-phenyl-1-butene formed were collected from a 10-ft, 10% SE-30 on Chromosorb W column at 130 °C and their IR spectra were compared with those of authentic samples.

Reaction of 1-Lithiopropene with Lithium *tert*-Butyl Peroxide. To a stirred 10-mL ether solution of 0.090 g (1.0 mmol) of *tert*-butyl hydroperoxide at −78 °C, 0.70 mL of a 1.5 N methyllithium solution in ether (1.0 mmol) was slowly added by a 1.00-mL syringe. After stirring for a few minutes, 10 mL of a 0.10 N solution of 1-lithiopropene (1.0 mmol) was added by cannula. The reaction mixture was stirred at 0 °C for 2 h before a 2.0-mL aliquot was added by cannula to 2.0 mL of acetic anhydride in a 12-mL centrifuge tube.

Reaction of 2 with Lithium or Sodium *tert*-Butyl Peroxide. One millimole of lithium *tert*-butylperoxide was prepared in 10 mL of THF at −78 °C by reaction of *tert*-butyl hydroperoxide with methyllithium. This solution was transferred by cannula to 5.0 mL of a 0.2 N THF solution of **2** (1.0 mmol) also cooled to −78 °C. The reaction was allowed to proceed for 1 h at −78 °C before adding to excess acetic anhydride.

Sodium *tert*-butyl peroxide was prepared by adding a cooled (0 °C) THF solution (15 mL) of *tert*-butyl hydroperoxide (180 mg, 2.0 mmol) to 2.0 mmol of sodium hydride which had been freed of mineral oil by washing with hexane.[29] Hydrogen evolution was rapid but the reaction mixture was stirred at 0 °C for 1 h. The solution was then cooled to −78 °C and added by cannula to 10 mL of a 0.2 N THF solution of **2** (2.0 mmol). The reaction mixture was stirred for 1 h at −78 °C before adding to excess acetic anhydride.

Reaction of 2 with Lithium or Sodium *m*-Chloroperbenzoate. Sodium *m*-chloroperbenzoate was prepared by adding a THF solution (15 mL) of *m*-chloroperbenzoic acid (344 mg, 2.0 mmol) to 2.0 mmol of sodium hydride which had been freed of mineral oil by washing with hexane.[14] The reaction mixture was refluxed for 8 h, the salt, a white solid, was not isolated. The suspension was cooled to −78 °C and 10 mL of a 0.2 N THF solution of **2** (85% *Z*, 2.0 mmol) at −78 °C was added by cannula. The reaction mixture was stirred at −78 °C for 1 h before adding to acetic anhydride (8 mL) at 22 °C. The enol acetates were formed in 20% yield (86% *E*). Thus the reaction is stereospecific but low yield.

Lithium *m*-chloroperbenzoate was prepared at −78 °C in THF solution by slowly adding methyllithium in ether solution to a solution of *m*-chloroperbenzoic acid. The reactions with **2** were done as described above.

Small samples of **(*E*)- and (*Z*)-3-phenyl-3-hexen-2-one** were prepared by reacting (*Z*)- and (*E*)-**2**, respectively, with acetic anhydride in THF solution at −78 °C. These compounds were not characterized. The reaction mixtures were analyzed by GLC to ensure that products from the reaction of **2** with acetic anhydride were not interfering with the analysis of the enol acetates.

References and Notes

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