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(6) The more polar ester **7**, $[\alpha]^{25}_D$ +68.5°, was saponified to form dextrorotatory diol **6**, $[\alpha]^{25}_D$ +37.1° (*c* 0.7, in ethanol), which was converted into (*R*)-(+)-2-methyl-2,3-pentanediol by the following sequence: (1) benzoylation of **6** using benzoyl chloride–pyridine to the secondary mono benzoyl derivative, (2) oxidative cleavage by reaction with potassium permanganate–sodium periodate in aqueous *tert*-butyl alcohol to form 3-benzoyloxy-2-pentanone, (3) reaction with excess methylmagnesium bromide in ether to form the 3-benzoate of 2-methyl-2,3-pentanediol, and (4) saponification using potassium hydroxide in aqueous methanol to form dextrorotatory 2-methyl-2,3-pentanediol which is known to have the *R* configuration. See Manwaring, D. G.; Richards, R. W.; Smith, R. M. *Tetrahedron Lett.* **1970**, 1029.
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(14) The levo acid **11** was obtained using (+)-1-α-napthylethylamine for resolution. There is a typographical error in ref 1 which reports "(±)-1-α-naphthylethylamine" as the resolving agent.
(15) This route from the epoxy lactone **12** to the dibenzoate **16** differs from that previously used[1] with racemic intermediates. The present modification was found to be necessary for the preparation of optically active intermediates because of a pronounced tendency of optically active hydroxy lactone **13** to racemize readily under various conditions, including during its formation from epoxy lactone **12** when aluminum amalgam is used as the reductant (see ref 1). The facile racemization of the hydroxy lactone under mild conditions will be discussed in a separate paper. The palladium catalyst used for the presently described conversion of **12** into **13** was prepared according to Pearlman, W. M. *Tetrahedron Lett.* **1967**, 1663.
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(18) The 2-pyridinethiol ester was prepared by reaction of **4** with 1 equiv of triethylamine and 1 equiv of 2-pyridinethiol chloroformate in methylene chloride at 0 °C for 15 min, washing with water, drying, removal of methylene chloride, and azeotropically drying with toluene under reduced pressure three times. For method see Corey, E. J.; Clark, D. *Tetrahedron Lett.*, **1979**, 2875.
(19) The modified Mukaiyama coupling of **3** and **4** following an approach which had been very effective in the synthesis of erythronolide B failed completely with **3** as a component, probably as a result of the instability of the MTM group to some magnesium(II) species present after addition of magnesium bromide to lithiated **3**. To obtain successful coupling of **3** and **4** by the process described herein, *minimum* amounts of THF were used throughout the procedure and the final solvent was alkane–THF (ratio, 1.2:1; total volume, 25 mL/mmol of pyridinethiol ester). The hexane and pentane originated in the organolithium reagents used. The coupling process is very sensitive to changes from these reaction conditions or to the presence of impurities.
(20) For analogous stereochemistry and translactonization in the reduction of the corresponding enone in previous work see ref 2 and also Corey, E. J.; Brunelle, D. J.; Nicolaou, K. C. *J. Am. Chem. Soc.* **1977**, *99*, 7359.
(21) Unless the sulfide component was included in the reaction mixture a very complex assortment of products resulted after this step and ^{1}H NMR analysis indicated loss of the MTM group.
(22) For reasons which are unclear the tris MTM ether **23** could not be prepared directly from **20** in a single step, despite numerous attempts under a variety of conditions.
(23) The conversion of erythronolide A into **24** roughly parallels an analogous previously described sequence for the erythronolide B series. See Corey, E. J.; Nicolaou, K. C.; Melvin, L. S. *J. Am. Chem. Soc.* **1975**, *97*, 654. The details of the preparation of **24** from erythronolide A will be detailed in a separate publication.
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(30) This research was assisted financially by a grant from the National Institutes of Health. We are indebted to the Chas. Pfizer Co. for a generous gift of erythromycin A and to Dr. R. A. LeMahieu for a reference sample of erythronolide A. P.B.H. has been the holder of an NSF graduate fellowship.

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Preferential 1,4- vs. 1,6-Hydrogen Transfer in a 1,5 Biradical. Photochemistry of β-Ethoxypropiophenone

Sir:

We have obtained evidence that the 1,5 biradical generated photochemically from β-ethoxypropiophenone (**1**) undergoes internal disproportionation by two paths: the minor one is a 1,6-H transfer which regenerates starting ketone; the major one, surprisingly, is a 1,4-H transfer which generates the enol of starting ketone.

Irradiation of **1** produces only two products, the (*Z*)- and (*E*)-oxacyclopentanols **3**, which arise from δ-hydrogen abstraction by triplet ketone[1] (Scheme I). The quantum efficiency for this photocyclization is *lower* in Lewis base solvents than in hydrocarbons, in sharp contrast to the solvent effects observed on quantum efficiencies of product formation resulting from γ-hydrogen abstraction.[2,3] It is widely accepted that hydrogen bonding to solvent by 1-hydroxy-1,4 biradicals suppresses their internal disproportionation back to ground-state ketone. We speculated that in the analogous 1,5 biradicals a 1,4-hydrogen transfer might provide an alternative mode of internal disproportionation, one not affected by hydrogen bonding involving the OH group.

To test this idea we have studied the effect of α deuteration[4] on the photochemistry of **1**. A degassed benzene solution 0.05 M in **1**-α,α-d_2 (**1**-D) was irradiated to ~65% conversion. Unreacted ketone was isolated and analyzed by mass spectrometry. Comparison of isotopic distribution for the M − CH_3, M − CH_2CH_3, M − OCH_2CH_3, and $CH_2OH_2CH_3$ peaks indicated that 20% of the remaining ketone had undergone a deuterium shift specifically from the α to the δ carbon.[5] A similar result was obtained for solutions containing dioxane. This result is readily rationalized only as enolization of the 1,5-biradical intermediate **2**.

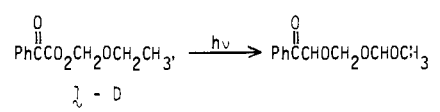

Table I lists *Z*/*E* product ratios and total quantum efficiencies for **1**-D and all protio-**1** (**1**-H) as a function of added *tert*-butyl alcohol or dioxane. As observed previously, added H-bond acceptors lower the overall quantum efficiency and drastically lower the relative yield of (*Z*)-**3**. As expected, if enolization is a major decay mode of the intermediate biradical, a primary isotope effect causes **1**-D to yield products with greater efficiency than does **1**-H.

It is possible to deduce relative values for the rate constants in Scheme I from the measured quantum efficiencies as listed in Table II. These values depend on the following assumptions: (1) that k_{-H} is negligibly small in *tert*-butyl alcohol; (2) that α deuteration affects only k_e; and (3) that biradical solvation

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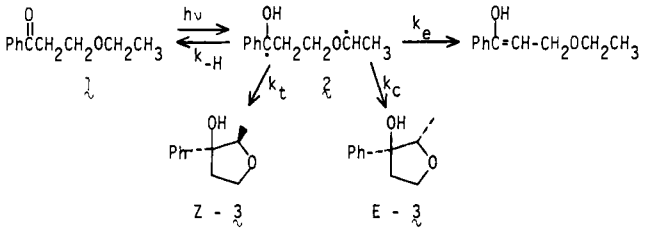
Scheme I



lowers k_t but does not affect k_e or k_c. The first assumption is reasonable because alcohol must decrease the relative value of k_{-H} for 1,4 biradicals by a factor of at least 50 to explain type II quantum efficiencies close to unity.[3,6] The second assumption is reasonable because only secondary isotope effects are involved.

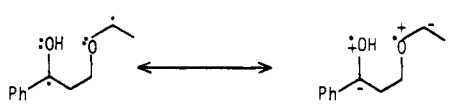
$$1 - \Phi_3 = \frac{k_{-H} + k_e}{k_{-H} + k_e + k_c + k_t} \qquad (1)$$

Introduction of the data for **1**-H and **1**-D in *tert*-butyl alcohol into eq 1 and solution of the resulting simultaneous equations (with $k_{-H} = 0$) leads directly to a k_e^H/k_e^D value of 3.0. This is just the isotope effect expected from Gibian's study of 1-phenylethyl radicals.[7] Application of the same isotope effect to the data in benzene provides a k_e/k_{-H} ratio of 2.25 for **1**-H. The relative rate constant values for **1**-H in benzene are measured quantum yields (sum = 100). The third assumption is not really crucial; its application leads to the relative rate constants in alcohol. Although solvation may well affect all biradical rate constants significantly, it is noteworthy that the ratios of k_e/k_c for both **1**-H and **1**-D are solvent independent. The third assumption thus could be reexpressed as a tentative conclusion: the easiest way for a ratio of rate constants describing two quite different reactions to remain constant is for there to be no change in either.

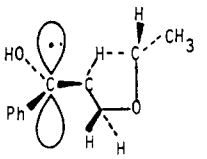
The preference for 1,4- over 1,6-hydrogen transfer in **2**-H is unprecedented. For example, triplet **1** has a similar choice but undergoes no detectable β-hydrogen abstraction.[8] The overall 1,4:1,6 ratio from **2** is compounded of two competitions: (1) C–H vs. O–H reactivity; and (2) ring size of the transition state. It is worth note that the kinetically favored product arises from the less exothermic reaction, another of many examples that biradical reactions are not influenced significantly by product stability.

It is now well established that aliphatic hydroxy radicals disproportionate to yield enolic as well as keto products.[9] No quantitative measurements have been made with hydroxybenzyl radicals, since disproportionation competes so poorly with coupling.[10] The present results may be interpreted as showing a preference for C–H vs. O–H disproportionation, as modified by ring-size effects.

The electron distribution in **2** makes the amount of 1,4-H transfer even more remarkable. Both carbons 1 and 5 are electron rich because of conjugation with the adjoining oxygens' lone pairs; 1,6-H transfer seems far better electrostatically than 1,4 transfer.



The well-known preference for 1,5 intramolecular hydrogen atom transfers[11] is now understood to reflect a strain- and torsion-free transition state.[1,12] The rarity of 1,4 transfers had been thought to corroborate the early suggestion that H-atom transfers prefer a linear transition state.[13] The behavior of **2** indicates that the C···H···C angle can vary significantly from 180°. The γ oxygen in **1** imparts a unique characteristic to **2**; the five-atom cyclic transition state leading to enol is free of any significant eclipsing interactions.



Therefore we cannot assess the general importance of 1,4-H transfer in 1,5 biradicals. However, the oxygen also allows a relatively torsion-free transition state for 1,6-H transfer. We are currently studying competitive disproportionations in other biradicals.[14]

Table I. Product Ratios and Quantum Yields from 313-nm Irradiation of 0.05 M β-Ethoxypropiophenone in Degassed Benzene Solutions

ketone	additive	(*Z*/*E*)-**3**	$\Phi_{3(c+t)}$
1-H	none	4.6	0.49
1-H	1.0 M *t*-BuOH	1.6	0.50
1-H	6.0 M *t*-BuOH	0.76	0.29
1-H	6.0 M dioxane	1.8	0.27
1-D	none	4.3	0.64
1-D	1.0 M *t*-BuOH	1.5	0.60
1-D	6.0 M *t*-BuOH	0.73	0.54

Table II. Effects of Solvent and α-Deuteration on Relative Rate Constants for Reactions of Biradical **2**

ketone	solvent	k_{-H}	k_e	k_t	k_c
1-H	benzene	16	35	40	9
1-H	alcohol	<1	36	6	8
1-D	benzene	16	12	40	9
1-D	alcohol	<1	12	6	8

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(5) In unirradiated **1**-D, *m*/e (60 + 61)/59 = 0.07; (149 + 150)/151 = 0.09; 134/135 = 0.49. After irradiation, the ratios were 0.28, 0.37, and 0.71, respectively.
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(14) We gratefully acknowledge continuing support of this research by the National Science Foundation (Grant No. CHE-76-11892) and partial support by the Petroleum Research Fund, administered by the American Chemical Society.

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