The Rates of Termination of Radicals in Solution. V.[1,2] Ketyl Radicals Derived from α-Keto Acids and Esters

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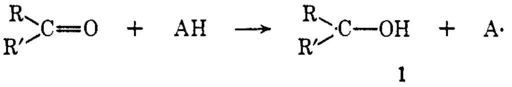
Abstract: The ketyl radicals derived from six α-keto acids and α-keto esters have been observed by irradiation of isopropyl alcohol solutions of these compounds in the cavity of an electron paramagnetic resonance spectrometer. For four of these radicals the bimolecular decay rates have been measured by a light intermittency esr technique. These rates, 2-5 × 10^8 M^{-1} sec^{-1}, are of the same order of magnitude as those of other radical coupling reactions.

The electron paramagnetic resonance spectra of a number of liquids under irradiation have been investigated recently.[1-12] Of particular interest have been those aldehydes and ketones which can form ketyl radicals (**1**) by abstraction of a hydrogen atom from a hydrogen atom donor, generally the solvent. The esr spectra of a number of these radicals have been reported.



$$\mathrm{\overset{R}{\underset{R'}{>}}C{=}O + AH \longrightarrow \underset{\mathbf{1}}{\overset{R}{\underset{R'}{>}}\dot{C}{-}OH} + A\cdot}$$

Our interest in these radicals stems from our attempts to establish structure–reactivity relationships for the rates of radical termination. Previous studies have involved the measurement of the second-order decay rates of carbon radicals[4] and those of the ketyl radicals derived from substituted benzophenones,[3] α-diketones,[1] and quinones.[2] We have extended these studies to include the ketyl radicals derived from α-keto acids and α-keto esters.

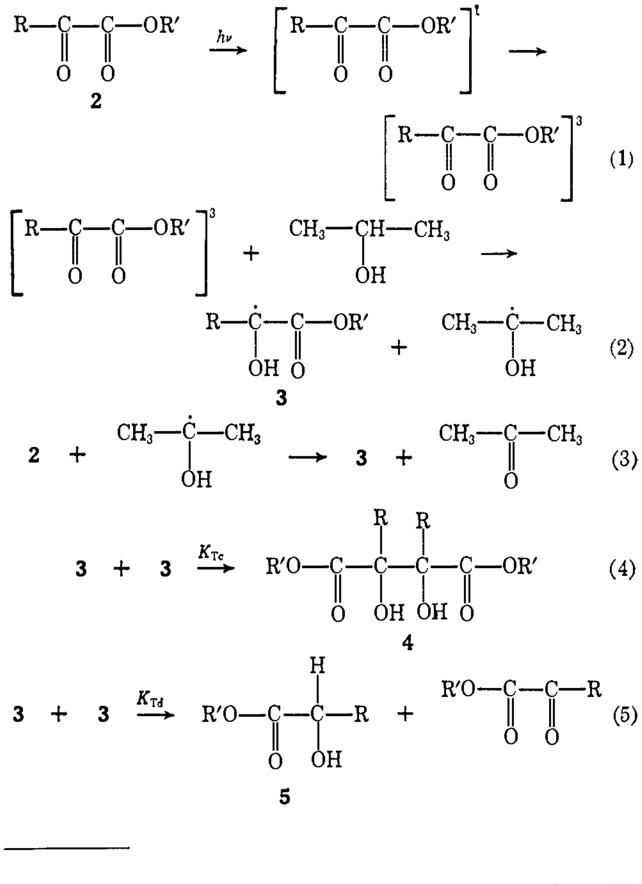
Experimental Section

Materials. Pyruvic acid (Eastman), ethyl pyruvate (Aldrich), and phenylglyoxylic acid (Aldrich) were all commercial materials. *p*-Methoxyphenylglyoxylic acid[13] and *p*-bromophenylglyoxylic acid[14] were prepared by oxidation of the corresponding acetophenones. Ethyl phenylglyoxalate was prepared by esterification of phenylglyoxylic acid. Spectrograde isopropyl alcohol (MCB) was used as solvent in the measurement of radical termination rates.

Measurement of Decay Constants. All solutions were about 1 *M* in α-keto acid or α-keto ester. The apparatus and procedure used for determination of the decay constants have been described.[4,15] As previously discussed, an error of ±20% is associated with a given termination constant.

Discussion

The photoreduction of α-keto acids and α-keto esters in isopropyl alcohol at room temperature has been studied by several groups of workers.[16-20] The following mechanism is consistent with the experimental evidence.



$$\underset{\mathbf{2}}{\mathrm{R{-}\overset{\displaystyle O}{\overset{\|}{C}}{-}\overset{\displaystyle O}{\overset{\|}{C}}{-}OR'}} \xrightarrow{h\nu} \left[\mathrm{R{-}\overset{O}{\overset{\|}{C}}{-}\overset{O}{\overset{\|}{C}}{-}OR'}\right]^1 \longrightarrow \left[\mathrm{R{-}\overset{O}{\overset{\|}{C}}{-}\overset{O}{\overset{\|}{C}}{-}OR'}\right]^3 \qquad (1)$$

$$\left[\mathrm{R{-}\overset{O}{\overset{\|}{C}}{-}\overset{O}{\overset{\|}{C}}{-}OR'}\right]^3 + \mathrm{CH_3{-}\underset{OH}{\underset{|}{C}}H{-}CH_3} \longrightarrow \underset{\mathbf{3}}{\mathrm{R{-}\underset{OH}{\underset{|}{\dot{C}}}{-}\overset{O}{\overset{\|}{C}}{-}OR'}} + \mathrm{CH_3{-}\underset{OH}{\underset{|}{\dot{C}}}{-}CH_3} \qquad (2)$$

$$\mathbf{2} + \mathrm{CH_3{-}\underset{OH}{\underset{|}{\dot{C}}}{-}CH_3} \longrightarrow \mathbf{3} + \mathrm{CH_3{-}\underset{O}{\underset{\|}{C}}{-}CH_3} \qquad (3)$$

$$\mathbf{3} + \mathbf{3} \xrightarrow{K_{\mathrm{Tc}}} \underset{\mathbf{4}}{\mathrm{R'O{-}\underset{O}{\underset{\|}{C}}{-}\overset{R}{\overset{|}{\underset{OH}{\underset{|}{C}}}}{-}\overset{R}{\overset{|}{\underset{OH}{\underset{|}{C}}}}{-}\underset{O}{\underset{\|}{C}}{-}OR'}} \qquad (4)$$

$$\mathbf{3} + \mathbf{3} \xrightarrow{K_{\mathrm{Td}}} \underset{\mathbf{5}}{\mathrm{R'O{-}\underset{O}{\underset{\|}{C}}{-}\overset{H}{\overset{|}{\underset{OH}{\underset{|}{C}}}}{-}R}} + \mathrm{R'O{-}\underset{O}{\underset{\|}{C}}{-}\underset{O}{\underset{\|}{C}}{-}R} \qquad (5)$$

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[1] Part III: S. A. Weiner, E. J. Hamilton, Jr., and B. M. Monroe, submitted for publication.

[2] Part IV: S. A. Weiner and G. S. Hammond, to be submitted for publication.

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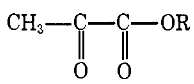
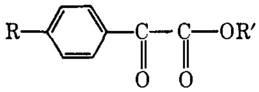
All the nonradical-producing reactions of the photoexcited states (*i.e.*, fluorescence, phosphorescence, etc.) have been omitted. The hydrogen transfer step (3) is completely analogous to the hydrogen transfers found in the photoreduction of other ketones.[21,22] In all the cases reported to date products derived from termination *via* radical coupling (step 4) are the principal or sole observed products. In the photoreduction of ethyl pyruvate a small amount of ethyl lactate was obtained in addition to large amounts of the diethyl ester of dimethyltartaric acid.[18] Since ethyl lactate presumably arises from radical disproportionation (step 5), this may be a minor route of radical termination. However, coupling is the major path of termination for this radical.



$\mathrm{CH_3{-}\underset{O}{\underset{\|}{C}}{-}\underset{O}{\underset{\|}{C}}{-}OR}$

6, R = H
7, R = C_2H_5



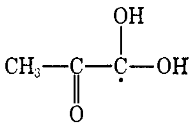
8, R = H; R′ = H
9, R = OCH_3; R′ = H
10, R = Br; R′ = H
11, R = H; R′ = C_2H_5

Observations of the Ketyl Radicals. The ketyl radicals derived from pyruvic acid (**6**), ethyl pyruvate (**7**), phenylglyoxylic acid (**8**), *p*-methoxyphenylglyoxylic acid (**9**), *p*-bromophenylglyoxylic acid (**10**), and ethyl phenylglyoxalate (**11**) were observed by irradiation of degassed isopropyl alcohol solutions of these compounds in the cavity of an esr spectrometer. The observed couplings and their assignments are given in Table I.

Table I. Hyperfine Coupling Constants for Ketyl Radicals

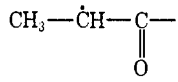
Compound	Protons	Coupling constant, G
Pyruvic acid (**6**)	Methyl	17.08
	α-OH	2.17
Ethyl pyruvate (**7**)	α-Methyl	16.84
	$-CH_2-$	0.82
	α-OH	2.14
Phenylglyoxylic acid (**8**)	*o*- and *p*-H	3.6
	α-OH	1.4
p-Methoxyphenylglyoxylic acid (**9**)	*o*-H	3.2
p-Bromophenylglyoxylic acid (**10**)	*o*-H	3.3
Ethyl phenylglyoxalate (**11**)	*o*- and *p*-H	3.6
	α-OH	1.0

The ketyl radical derived from pyruvic acid has previously been observed in aqueous acid solution from the oxidation of lactic acid by hydroxyl radical generated from titanous ion and H_2O_2 in a flow system.[23] Our measured hyperfine interactions are in reasonable agreement with the previously reported values: $a(CH_3)$ = 17.1 G and $a(OH)$ = 2.0 G. The coupling with the α-hydroxyl is not expected to agree too closely since these couplings have been shown to be solvent dependent.[8,11] No signal which could be ascribed to **11**, a radical which might have been expected based on electronic considerations, was detected.



$\mathrm{CH_3{-}\underset{O}{\underset{\|}{C}}{-}\overset{OH}{\overset{|}{\dot{C}}}{-}OH}$

11



$\mathrm{CH_3{-}\dot{C}H{-}\underset{O}{\underset{\|}{C}}{-}O{-}CH_3}$

12

Similar interactions were observed for the ketyl radical derived from ethyl pyruvate. An additional coupling to the methylene protons of the ethyl group was also observed. Similar long range couplings have been observed in the radicals derived from aliphatic carboxyl esters.[24] A long range coupling of $a(\gamma\text{-}CH_3)$ = 1.3 G was observed for **12**.

Because of the rapid decay of the ketyl radicals derived from the phenylglyoxylic acids only low concentrations of these radicals could be obtained with our light intensities. Consequently, the signals from these radicals were not as well resolved as those from pyruvic acid and ethyl pyruvate so that some of the smaller couplings may not have been observed.

The signal from phenylglyoxylic acid (**8**) was observed as a quartet with 1:3:3:1 relative intensity and a line spacing of 3.6 G. Each of these lines was split to a doublet with a coupling of 1.4 G. An assignment of $a_{o\text{-H}} = a_{p\text{-H}}$ = 3.6 G and a_{OH} = 1.4 G is consistent with the observed spectrum. The coupling to the *m* protons is too small to be observed at our instrument settings. The couplings for the analogous radical derived from benzophenone[9] are: $a_{o\text{-H}}$ = 3.23 G, $a_{m\text{-H}}$ = 1.24 G, $a_{p\text{-H}}$ = 3.69 G, and a_{OH} = 3.4 G. The signal from the ketyl radical of ethyl phenylglyoxalate was similar to that of phenylglyoxylic acid. No coupling to the methylene protons was observed.

The radicals derived from the substituted phenylglyoxylic acids were observed as ill-resolved triplets. The radical from *p*-methoxyphenylglyoxylic acid (**9**) showed a coupling of 3.2 G and that from *p*-bromophenylglyoxylic acid (**10**) a coupling of 3.3 G. These couplings are assigned to the protons of the phenyl group. No couplings were observed for the *m* protons or for the hydroxyl hydrogen. However, couplings as large as 1.5 G would not have been detected at our instrument settings.

Radical Termination Rates. Second-order radical decay rates were determined for the ketyl radicals derived from pyruvic acid (**6**), ethyl pyruvate (**7**), *p*-methoxyphenylglyoxylic acid (**9**), and ethyl phenylglyoxalate (**11**). Because of the rapid depletion of the samples under intense irradiation it was not possible

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to measure the decay rates for **8** and **10**. The values for the steady-state radical concentration and second-order decay constants are given in Table II.

Table II. Decay of Ketyl Radicals in Isopropyl Alcohol Solution

Compound	$[R_0] \times 10^6\ M$	$K_t[R_0] \times 10^{-2}$ sec^{-1}	$K_t \times 10^{-8}\ M^{-1}$ sec^{-1}
Pyruvic acid (**6**)	6.0	11.4	1.9
Ethyl pyruvate (**7**)	4.7	14.0	3.0
p-Methoxyphenylglyoxylic acid (**9**)	3.1	9.9	3.2
	1.9	8.0	4.2
Ethyl phenylglyoxalate (**11**)	3.2	1.5	4.7
	3.1	1.1	3.5

Product studies have shown that the radicals derived from pyruvic acid, ethyl pyruvate, and ethyl phenylglyoxalate terminate almost entirely by coupling (step 4).[17–20] Although the photochemistry of **9** has not been studied, it should be similar to that of **8** which yields a radical coupling product.[16]

The observed second-order decay rates are of the same order of magnitude as those previously observed for coupling of other ketyl radicals. Representative values are given in Table III.

It can be seen that the rates of coupling for ketyl radicals which have been studied fall in the range 5×10^7 M^{-1} sec^{-1} to 5×10^8 M^{-1} sec^{-1} although the radicals are derived from monoketones, α-diketones, α-keto acids, or α-keto esters.

Table III. Representative Rates of Radical Coupling in Isopropyl Alcohol

Compound	Rate $\times 10^{-8}$ M^{-1} sec^{-1}	Ref
3,4-Dimethylbenzophenone	4.8	3
Benzophenone	1.1	3
p-Bromobenzophenone	0.50	3
Biacetyl	3.9	1
Benzil	3.3	1
Anisil	4.2	1

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Solvolysis of Bicyclo[4.2.0]octyl and Bicyclo[3.2.0]heptyl 1-(3,5-Dinitrobenzoates)[1]

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Abstract: The synthesis of *trans*-fused bridgehead substituted derivatives is described, along with data regarding the carbon–carbon bond cleavage in the lithium aluminum hydride reduction of cyclobutene oxides. The rates and products of solvolysis are determined for both *cis*- and *trans*-fused derivatives. The two isomers and the corresponding spiro cyclopropylcarbinyl derivatives give the same product mixtures which contain both cyclobutanols and cyclopropylcarbinols. The details of the reactions and the possibility of hydrogen migration with the *trans*-fused compounds are discussed.

It now seems fairly clear from our work[3] and that of others[4] that the conformation of the cyclobutane ring and of its substituents is of major importance in determining the reactivity of cyclobutyl derivatives. In most cases, one has little control over the conformation of the ring. However, a 1,2 bridge has the potential for considerable conformational control.

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(1) This investigation was supported by Public Health Service Grant GM12800 from the National Institute of General Medical Science.

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