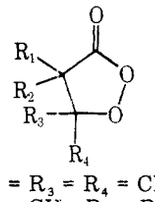
Communications

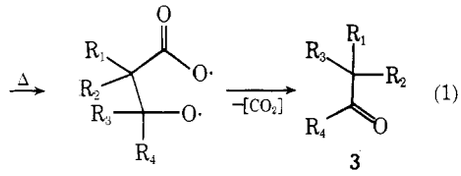
Solvent Effects and Secondary Isotope Effects for Probing Diradical Character in the Thermal Decarboxylation of β-Peroxy Lactones[1]

Summary: The lack of solvent effects on the activation parameters and product distribution and the lack of secondary deuterium isotope effects at the α carbon and β-alkyl migrant substantiate that the thermal decarboxylation of β-peroxy lactones proceeds via a 1,5-diradical.

Sir: On the basis of product distribution and kinetics[2] and stereochemical data[3] we concluded that the mechanism of thermal decarboxylation of β-peroxy lactones **1** involved simple peroxide bond cleavage leading to the 1,5-diradical **2**, which subsequently decarboxylated with concurrent β-alkyl 1,2-migration to afford rearrangement ketone **3** as the major product (eq 1). Since evidence for 1,5-diradicals is scarce[4] and



1a, $R_1 = R_2 = R_3 = R_4 = CH_3$
b, $R_1 = R_2 = CH_3$; $R_3 = R_4 = CD_3$
c, $R_1 = R_2 = H$; $R_3 = CH_3$; $R_4 = Ph$
d, $R_1 = R_2 = H$; $R_3 = CD_3$; $R_4 = Ph$
e, $R_1 = R_2 = D$; $R_3 = CH_3$; $R_4 = Ph$



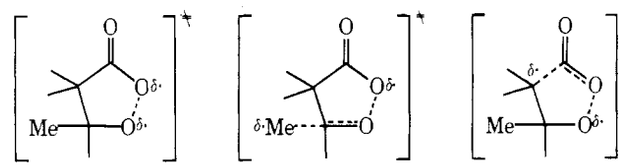
(1)

2 **3**

since the preferred alkyl vs. phenyl 1,2-shift is unusual,[2] it was of interest to confirm the diradical nature of this decarboxylation by exploring the effect of solvent polarity on the kinetics and product distribution in the β-peroxy lactone **1a** and the secondary deuterium isotope effect at the migration origin in β-peroxy lactones **1a** vs. **1b** and **1c** vs. **1d** and at the migration terminus in **1e** vs. **1c**.

The activation parameters $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ of β-peroxy lactone **1a** for the solvents carbon tetrachloride, cyclohexane, benzene, and acetonitrile are summarized in Table I. Only a threefold rate enhancement has been observed between the least and most polar solvents, i.e., c-C_6H_{12} and CH_3CN. If the diradical-like activated complex A were sensitive to solvent polarity by possessing appreciable dipolar character, we would have to expect rate effects by several magnitudes.[5] Also the activation parameters are essentially constant within the experimental error, although a $\Delta H^{\ddagger}$ vs. $\Delta S^{\ddagger}$ plot is linear with an isokinetic temperature $T_{iso} = 583$ K. Whether the latter is mechanistically significant is debatable, but these solvent effect data reflect diradical character with only small dipolar contributions in polar solvents such as acetonitrile.

The isotope effect data is collected in Table I. In β-peroxy lactones **1a** vs. **1b** and **1c** vs. **1d** we were interested in probing whether the β-methyl group (the migrant) was cleaving from the β carbon concurrently with peroxide bond fission via the two-bond breaking activated complex B. Clearly, the negligible isotope effect reveals that neither in **1b** nor in **1d** has any significant methyl group scission taken place in the slow step, i.e., during peroxide bond cleavage.



A B C

In the case of β-peroxy lactones **1c** vs. **1e** we were interested in assessing the degree of α-carbon cleavage via the two-bond breaking activated complex C. Again, the negligible isotope effect signifies that peroxide bond rupture is not assisted by substantial α-carbon cleavage in the β-peroxy lactones not bearing α substituents. For example, an appreciable secondary isotope effect ($k_H/k_D = 1.17$) has been observed in *tert*-butyl phenylperacetate on deuteration of the benzylic position.[6] However, in this acyclic case a two-bond cleavage is encouraged, since the incipient benzyl radical is resonance stabilized.[7] In fact, in our cyclic case α substitution does lower the activation free energy by 3 kcal/mol, i.e., **1a** ($\Delta G^{\ddagger} = 28$ kcal/

Table I. Activation Parameters and Secondary Isotope Effects[a] in the Thermal Decarboxylation of β-Peroxy Lactones

β-Peroxy lactone	Solvent	T, K	$k_{avg} \times 10^3$, s^{-1} [b]	$\Delta H^{\ddagger}$,[c] kcal/mol	$\Delta S^{\ddagger}$,[c] gibbs/mol	$\Delta G^{\ddagger}_{383\ K}$,[d] kcal/mol	k_H/k_D
1a	CCl_4	383	0.627 ± 0.012	28.7 ± 0.3	1.7 ± 0.4	28.0 ± 0.4	
1a	c-C_6H_{12}	383	0.518 ± 0.010	28.6 ± 0.2	1.4 ± 0.3	28.1 ± 0.5	
1a	C_6H_6	383	0.916 ± 0.020	28.3 ± 0.4	1.0 ± 1.2	27.9 ± 0.5	
1a	CH_3CN	383	1.47 ± 0.05	26.7 ± 0.2	1.8 ± 0.6	27.4 ± 0.6	
1a	CCl_4	392	1.26 ± 0.04				0.99 ± 0.03
1b	CCl_4	392	1.26 ± 0.03				
1c	CCl_4	403	5.77 ± 0.03				1.01 ± 0.03
1d	CCl_4	403	5.70 ± 0.02				
1c	CCl_4	403	5.77 ± 0.03				0.99 ± 0.03
1e	CCl_4	403	5.85 ± 0.04				
1c	C_6H_6	398	5.92 ± 0.10[e]				1.02 ± 0.02
1d	C_6H_6	398	5.85 ± 0.15[e]				

[a] All deuterated substrates are at least 95% labeled, as confirmed by NMR and/or MS analysis. [b] Measured by disappearance of the 1790-cm^{-1} carbonyl band of 1 in the infrared except for the last two entries. The initial [1] was ~0.01 M. [c] From triplicate runs at 370, 383, and 391 K. [d] Calculated from $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$. [e] These are methyl vs. phenyl migration ratios determined by quantitative GLC of the respective rearrangement ketone **3**. These ratios bear no units.

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mol) vs. **1c** ($\Delta G^{\ddagger}$ = 31 kcal/mol[2]), since a tertiary radical site is generated at the α carbon in the activated complex C.[8]

The β-peroxy lactones **1c** and **1d** were also employed to determine the secondary isotope effect during the 1,2-shift of the β-methyl migrant, i.e., in the destruction of the 1,5-diradical **2** into products. For this purpose, by means of quantitative GLC the migratory aptitudes of methyl (k_{Me}) vs. phenyl (k_{Ph}) as a function of methyl deuteration were measured by determining the amount of β-methyl vs. β-phenyl migration product. From β-peroxy lactones **1c** and **1d** the migratory ratios k_{CH_3}/k_{Ph} and k_{CD_3}/k_{Ph}, respectively, were obtained from which k_H/k_D was calculated. A negligible secondary isotope effect was found. This implies, as expected, that the slow step of the decomposition of β-peroxy lactones is the peroxide bond cleavage into diradical **2**. Subsequently, this diradical **2** decarboxylates with β-alkyl migration via a fast step with a low activation barrier. In such cases the secondary isotope effect is expected to be very small.[9] The error in our product data is too large to pick up such small effects.

The product distribution derived from **1a** was found to be insensitive to solvent polarity. Thus, pinacolone was formed essentially quantitatively (>99% yield) and only small amounts (<0.5%) of acetone and tetramethyloxirane (stable to the thermolysis conditions) could be detected in the various solvents. Consequently, also the destruction of the diradical **2** into pinacolone exhibits negligible dipolar character.

In conclusion, our present solvent and isotope effect data substantiate the previously proposed diradical mechanism (eq 1).[2,3] The intervention of the 1,5-diradical is established; however, we have no information on its lifetime. Experiments to trap **2** have failed so far, which implies that the 1,5-diradical must be shorter lived than 10^{-7} s. A carbonyl-^{18}O labeling experiment is in progress to estimate the lower lifetime limit of this 1,5-diradical.

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Waldemar Adam,*[10] Omar Cueto, Luis N. Guedes[11] Luis O. Rodriguez[12]

Department of Chemistry, University of Puerto Rico Río Piedras, Puerto Rico 00931

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Superoxide in Organic Synthesis: A New Mild Method for the Oxidation of Amines to Carbonyls via *N*-Chloramines

Summary: Conversion of amines to their chloramines followed by reaction with potassium superoxide is a mild method of oxidizing amines to carbonyl compounds.

Sir: *N*-Chloramines have been used as effective intermediates for converting amines to their carbonyl derivatives in a number of synthetic schemes.[1,2] We wish to report here a new, mild method employing potassium superoxide and the results of our study on seven representative amines, including several unsymmetrical secondary amines.

We have converted a series of amines to their corresponding *N*-chloramines in ether solution utilizing the method of Bachmann[2] and without prior isolation reacted the chloramines with potassium superoxide (see Scheme I). In a typical experiment *N*-methylbutylamine (**1g**) (20 mmol) in ether (50 mL) was converted to its chloramine. Additional ether (50 mL) was then added and the solution washed with water (1 × 50 mL), 1.5 M sulfuric acid (1 × 50 mL), and again with water (2 × 50 mL). It was then dried for at least 1 h over a mixture of magnesium sulfate, potassium carbonate, and molecular sieves.[3] After filtration the ether solution was slurried at room temperature with potassium superoxide (2.2 equiv) in the presence of 18-crown-6 polyether (80 mg). When the yellow superoxide color had completely faded (4–6 h), the mixture was filtered and the filtrate was poured into 2,4-dinitrophenylhydrazine reagent.[4] The ether was evaporated on a rotary evaporator and the crude 2,4-dinitrophenylhydrazone (2,4-DNP) of *n*-butyraldehyde was isolated (82% yield). Analysis of the product by TLC (silica, ether/petroleum ether, 20:80) showed only a minor trace of a material with an R_f similar to that of formaldehyde 2,4-DNP.[5] After recrystallization the melting point and mixed melting point confirmed the product to be *n*-butyraldehyde 2,4-DNP. See Table I for other examples.

The aldimines derived from diisobutylamine, di-*n*-pentylamine, and di-2-methylbutylamine have been isolated and their structures confirmed by IR (C=N stretch, 1670 cm^{-1}) and NMR (δ 7.6, 1 H, aldiminic). In the case of diisobutylamine pure *N*-chloramine was isolated and found to react in anhydrous ether to give imine[6] in 88% yield by analytical VPC, showing the reaction of KO_2 with *N*-chloramines is a clean, high-yield reaction.

An interesting result of our studies is our observation that elimination from unsymmetrical chloramines shows a preference for the more highly alkylated double bond, especially in the case of secondary methylamines. Thus *N*-chloro-*N*-methylbutylamine gives an overwhelming predominance of butylidenemethylamine on reaction with KO_2. Although imines have been shown to form from *N*-choramines, very little work has been done with chloramines of secondary amines and we are unaware of any studies on product yields from unsymmetrical amines. We believe the high regioselectivity we have observed, the mild conditions required, and the easy workup may have valuable synthetic applications in the removal of NCH_3 units from secondary methylamines.

Although the yield of carbonyl product from *n*-hexylamine was only moderate, no attempt was made to maximize the yield. Reaction of *N*-chlorohexylamine with KO_2 was more vigorous than with the secondary *N*-chloramines. Lowering the temperature of the reaction might enhance the yield.

Scheme I

$$R_2CHNHR' \xrightarrow{t\text{-BuOCl}} R_2C(Cl)NHR' \xrightarrow{KO_2} R_2C{=}NR \xrightarrow{H^+} R_2C{=}O$$

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