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An Accelerating−Reporting Group for Studies of Radical Heterolysis Reactions and Its Application in an Acid-Catalyzed Fragmentation Reaction of an α,β-Dimethoxy Radical

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The 2,2-diphenylcyclopropyl group was employed to accelerate reactions of α-methoxy radicals containing β-leaving groups, to trap the products of either migration or heterolysis of the leaving group, and to provide a useful chromophore for laser flash photolysis kinetic studies. The reporting group biases reactions in favor of heterolytic fragmentation and most likely intercepts radical cations in ion pairs. The 1-methoxy-1-methyl-2-(diethylphosphatoxy)-2-(2,2-diphenylcyclopropyl)ethyl radical (**3a**) reacted faster than the kinetic resolution of the instrument ($k > 2 \times 10^8$ s^{-1}) in all solvents studied, and the 2-acetoxy analogue (**3b**) reacted much faster than related radicals that do not contain the cyclopropyl group (e.g., $k = 1.1 \times 10^6$ s^{-1} in CH_3CN at ambient temperature). The rate constants and Arrhenius parameters for reactions of **3b** indicated that the rate-limiting step in the reaction was heterolytic cleavage. The 1,2-dimethoxy-1-methyl-2-(2,2-diphenylcyclopropyl)ethyl radical (**26**) reacted in a general acid-catalyzed heterolysis reaction, and rate constants for protonation of the β-methoxy group by a series of carboxylic acids were determined. The results suggest that acid-catalyzed reactions of β-alkoxy radicals might be employed in synthetic conversions.

Radicals with β-leaving groups are attracting increasing interest for synthetic chemistry. In high-polarity media they react by heterolytic cleavage of the leaving group to give radical cations under non-oxidative conditions,[1−5] and in low- and medium-polarity media they react in facile rearrangement and nucleophilic substitution reactions.[6,7] The reaction pathways in high- and low-polarity solvents could be quite similar with initial heterolytic fragmentation to give a contact ion pair (CIP) that recombines to an isomer or reacts with a nucleophile in low-polarity media or diffuses apart via a solvent-separated ion pair (SSIP) to give a free radical cation in high-polarity media (Scheme 1). Alternatively, computational results suggest that radicals with β-leaving groups can react without heterolysis in concerted rearrangements and eliminations and associative nucleophilic substitution reactions.[8]

The time domains of ion pair reactions place a difficult constraint on mechanistic studies of radicals with β-leaving groups. Contact ion pairs react by solvation to SSIPs or collapse on the picosecond time scale, and solvent-

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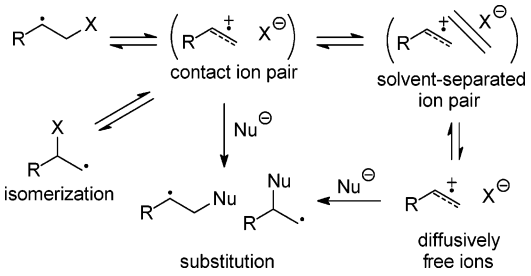
SCHEME 1



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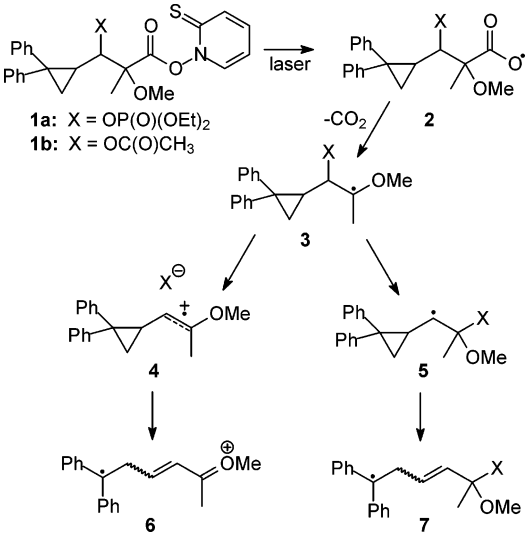
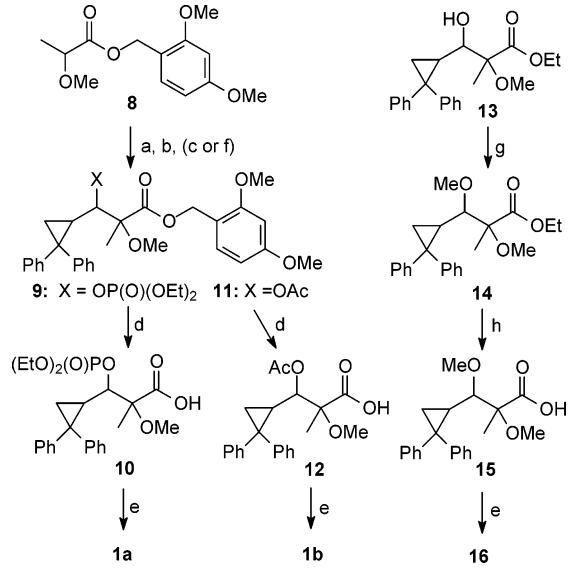


separated ion pairs desolvate to CIPs or dissociate to free ions in subnanosecond time frames. Thus, unless an exceptionally fast radical reaction is studied, transients can only accumulate to detectable levels when diffusive escape occurs to give free ions. A radical heterolysis reaction in low-polarity solvent followed by ion pair collapse or nucleophilic capture of the radical cation will be indistinguishable from a concerted or associative reaction of the radical, and mechanistic conclusions concerning these reactions typically have been inferred from products or kinetic correlations.[6] To overcome the inherent time constraints in studies of radicals with β-leaving groups, we have explored the use of intramolecular reactions to intercept a radical cation.[5] We report here studies using a cyclopropyl moiety that promotes radical heterolysis reactions and "captures" the radical cation product in an ion pair via an ultrafast ring-opening reaction.

Results and Discussion

The experimental design is shown in Scheme 2. PTOC[9] esters **1** were used as radical precursors. In laser flash photolysis (LFP) reactions, the PTOC esters were cleaved at the weak N−O bond by photolysis with 355-nm light to give acyloxyl radicals **2** that decarboxylated to provide the α-methoxy radicals **3**. Heterolysis of the leaving group X in radicals **3** would give radical cation **4**, and migration

SCHEME 3 [a]



[a] Reagents and conditions: (a) LDA, −80 °C; (b) 2,2-diphenylcyclopropanecarboxaldehyde; (c) $(EtO)_2(O)PCl$; (d) CAN; (e) 2,2′-dithiopyridine-1,1′-dioxide, Bu_3P; (f) Ac_2O, pyridine; (g) BDMAN, $(Me_3O)(BF_4)$; (h) KOH, EtOH.

of the leaving group would give rearranged radicals **5**. The diphenylcyclopropyl group was expected to trap either **4** or **5**, ring opening to give products **6** and **7**, respectively, and the diphenylalkyl radical moieties in **6** and **7** permit UV detection of these products. The 2,2-diphenylcyclopropylcarbinyl radical ring opens with a rate constant of 5×10^{11} s^{-1} at ambient temperature,[10] and ring opening of radical cation **4** was expected to be even faster given that the 2-phenylcyclopropylcarbinyl cation ring opens with no activation energy.[11]

The synthetic routes to the radical precursors are shown in Scheme 3. Deprotonation of ester **8** with LDA followed by addition of 2,2-diphenylcyclopropanecarboxaldehyde and quenching with diethyl chlorophosphate gave compound **9**, which was isolated as a single diastereomer. The dimethoxybenzyl group was removed by ceric ammonium nitrate (CAN) oxidation to give acid **10** that was converted to PTOC ester **1a** by the method of Barton and Samadi.[12] For the preparation of **1b**, a mixture of diastereomers of the β-hydroxy ester was obtained from reaction of the enolate of **8** with the aldehyde. This mixture was converted to the acetate derivatives **11**, and one diastereomer of **11** was isolated by chromatography and converted to acid **12** and then to PTOC ester **1b**. An analogous hydroxyalkylation gave a mixture of diastereomers of β-hydroxy ethyl ester **13**. The mixture was methylated with Meerwein's reagent in the presence of 1,8-bis(dimethylamino)naphthalene (BDMAN) to give α,β-dimethoxy ester **14** that was isolated as one diastereomer. Saponification of **14** gave acid **15** that was converted to PTOC ester **16** (discussed below). Although PTOC esters are unstable at temperatures above ca. 50 °C and react when exposed to visible

(9) The acronym PTOC is for pyridine-2-thioneoxycarbonyl. PTOC esters were originally developed by Barton's group and are also known as Barton esters; see: Barton, D. H. R.; Crich, D.; Motherwell, W. B. *Tetrahedron* **1985**, *41*, 3901−3924.

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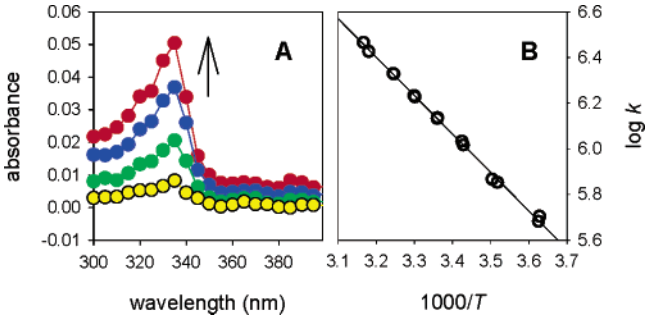
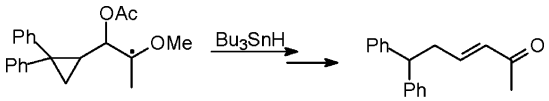


FIGURE 1. (A) Time-resolved spectrum for reaction of radical **3b** in CH_3CN. The time slices are at 0.6, 0.8, 1.2, and 1.8 μs with the spectrum at 0.5 μs subtracted to give a baseline. (B) Arrhenius function for reaction of radical **3b** in CH_3CN.

SCHEME 4



3b **17**

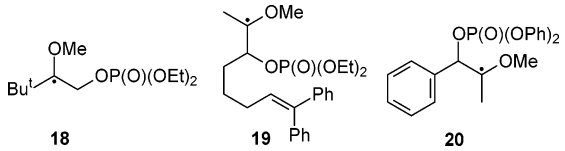
light, compounds **1a**, **1b**, and **16** were adequately robust for electrospray ionization conditions and were characterized by NMR spectroscopy and HRMS analyses.

The β-phosphate radical **3a** was studied to characterize the reactivity of the probe system. Laser flash photolysis (LFP) studies of dilute solutions of **1a** were conducted in a kinetic spectrometer unit with nanosecond resolution. Unexpectedly, radical **3a** reacted faster than the resolution of the unit in several solvents, including nonpolar cyclohexane. Thus, the UV spectrum of a diphenylalkyl radical product was obtained "instantly" following the laser pulse ($k > 2 \times 10^8$ s^1).

The β-acetoxy radical **3b** also reacted rapidly, but rate constants for the reactions of this radical could be measured. Figure 1A shows a portion of the time-resolved spectrum for reaction of **3b** in acetonitrile. The growing signal with $\lambda_{max} \approx 335$ nm is typical for a diphenylalkyl radical,[13] indicating the formation of either **6** or **7**. In a preparative reaction, PTOC ester **1b** was allowed to react in THF in the presence of 0.1 M Bu_3SnH at room temperature, and ketone **17** (Scheme 4) was obtained, indicating that radical **3b** reacted in a heterolysis reaction that gave radical cation **6**.

In THF at room temperature, radical **3b** reacted with a rate constant of $k = 2 \times 10^5$ s^{-1}, and in acetonitrile at ambient temperature the rate constant for reaction was $k = 1.1 \times 10^6$ s^{-1}. Rate constants were obtained at various temperatures in CH_3CN to give the results shown graphically in Figure 1B. The Arrhenius function obtained from these data is $\log k = (11.8 \pm 0.1_4) - (7.7 \pm 0.2)/2.3RT$ (in kcal/mol), where the errors are 2σ.

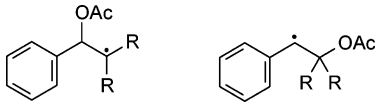
The reactions of radicals **3a** and **3b** are much faster than reactions of analogous α-methoxy radicals lacking the cyclopropyl group. Radical heterolysis reactions are sensitive to solvent polarity, which makes the fast reaction of **3a** in the low-polarity solvent cyclohexane ($k > 2 \times 10^8$ s^{-1}) quite unusual. For comparison, the α-methoxy-β-phosphate radical **18** heterolyzed to give a diffusively free enol ether radical cation with a rate constant of $k = 3 \times 10^6$ s^{-1} in the highly polar medium 5% 2,2,2-trifluoroethanol (TFE) in CH_3CN,[4] and β-phosphate radical **19** heterolyzed with a rate constant of $k = 4 \times 10^7$ s^{-1} in the medium-polarity solvent CH_3CN.[5] Radical **20** provides a more dramatic comparison. In **20**



18 **19** **20**

the diphenyl phosphate leaving group is inherently more reactive than the diethyl phosphate leaving group in radical **3a**, and the radical cation formed by heterolysis of **20** is stabilized by both the phenyl group and the methoxy group. Nonetheless, radical **20** reacted slower in medium-polarity THF ($k = 3.4 \times 10^6$ s^{-1})[3] than did **3a** in low-polarity cyclohexane.

Limited examples of β-acetoxy radical reactions are available for comparison to radical **3b**, but the high reactivity of **3b** is apparent nonetheless. The β-phenyl-β-acetoxy radicals **21** react by acetate migration (assumed to occur by heterolysis followed by ion recombination)[14] to give the benzylic radical products **22**. The rate con-



21a: R = Me
21b: R = H

22a: R = Me
22b: R = H

stants for these rearrangement reactions are $k \approx 5 \times 10^3$ s^{-1} for reaction of **21a** in acetonitrile at ambient temperature and $k = 4 \times 10^4$ s^{-1} for reaction of **21b** in benzene at 70 °C.[14,15] The reaction of β-acetoxy radical **21a** is more than 3 orders of magnitude slower than the reaction of the corresponding β-diphenyl phosphate radical in the same solvent,[14] and thus one would predict that the β-acetoxy radical analogue to radical **20** will react in THF with a rate constant on the order of 10^3 s^{-1}. Radical **3b** does not contain a phenyl group for stabilization of the product radical cation, but it reacted in THF with a rate constant of $k = 2 \times 10^5$ s^{-1}.

Two kinetic effects can contribute to the high reactivity of radicals **3a** and **3b**. A cyclopropyl group results in a 3-kcal/mol stabilization of an adjacent radical center,[16] which is much less than the 12-kcal/mol radical stabilization afforded by a phenyl group.[17] In the case of carbocations, however, adjacent cyclopropyl and phenyl groups result in approximately the same degree of thermodynamic stabilization,[18] and the cyclopropyl group accelerates heterolysis reactions of closed shell molecules

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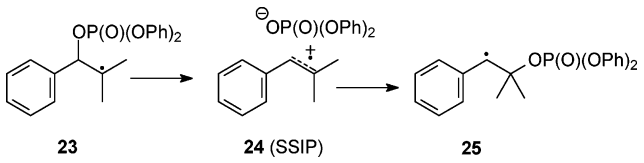
SCHEME 5



to a greater extent than does a phenyl group,[19] in part because the transition state for heterolysis of a cyclopropylcarbinyl system is readily achieved. It is reasonable to expect that the cyclopropyl groups in radicals **3a** and **3b** accelerate the heterolysis reactions appreciably, even though the products are radical cations instead of carbocations, and this effect could be greater than the acceleration by the phenyl group in radical **20**. In any event, the large kinetic acceleration found in reactions of radicals **3** is consistent with a heterolysis pathway. In concerted migration reactions where the incipient products develop radical character, one would expect phenyl-substituted systems to react faster than cyclopropyl-substituted systems.

Cyclopropyl group acceleration of the heterolysis reaction might account entirely for the high reactivity of radicals **3a** and **3b**, but another property of these systems can affect the observed kinetics. The diphenylcyclopropyl reporter group in radical cation **4** will fragment rapidly to give the ring-opened distonic radical cation product **6** that is observed. The rate constant for ring opening of the 2,2-diphenylcyclopropylcarbinyl radical is 5×10^{11} s^{-1} at ambient temperature,[10] and fragmentation of this moiety in radical cation **4** should be even faster. It is likely that the fragmentation reaction competes with ion collapse of a contact ion pair (CIP) and diverts this species to product **6** such that ion recombination does not occur. Thus, the observed rate constants for reactions of radicals **3** are expected to be the rate constants for the initial heterolysis reactions giving the CIP. When diffusively free radical cations are detected, as was the case for radical **18**, the kinetics reflect equilibrations between the CIP and the radical and between the SSIP and the CIP coupled with the rate constant for escape from the SSIP. Radical **19** contains an internal reporter group that was estimated to cyclize with a rate constant of $k \approx 2 \times 10^9$ s^{-1}, but this reaction is not likely to be fast enough to intercept the CIP in competition with ion collapse to the neutral radical; thus, the kinetics for radical **19** might be those for equilibration between the CIP and the neutral radical coupled with solvation of the CIP to the SSIP.

The Arrhenius function for reaction of radical **3b** in acetonitrile is consistent with the heterolysis reaction pathway. The entropic term, log $A = 11.8$, is similar to that found in radical reactions that were demonstrated or thought to occur by heterolysis of the leaving group. The most important comparison is with radical **23**, which was found to heterolyze to an observable solvent-separated ion pair (**24**) that collapsed to rearranged product **25** (Scheme 5); the entropic term in the heterolysis reaction of radical **23** was log $A = 11.0$.[20] A related β-phosphate radical that gave a mixture of diffusively free radical cation and rearrangement product in acetonitrile reacted with an entropic term of log $A = 10.6$.[2] The α-methoxy radical **19**, which is closely related to radical **3a** in that it has the same leaving group, reacted by rate-limiting heterolysis, presumed to give the SSIP, with log $A = 10.3$.[5] All of these reactions appear to have similar organizational demands in the transition states for heterolysis.

In a demonstration of the sensitivity of the hypersensitive probe approach, we applied it in a study of an α,β-dimethoxy radical. A considerable amount of computational results has been reported for reactions of the related α,β-dihydroxy radical (the ethylene glycol radical) because this species is an intermediate in the rearrangement catalyzed by diol dehydratase enzymes. The computational works agree that a concerted migration of a hydroxy group in the neutral 1,2-dihydroxyethyl radical to give the 2,2-dihydroxyethyl radical is a high-energy process.[21−25] An acid-catalyzed migration reaction was postulated years ago,[21] but the acid-catalyzed process was later computed to result in a dissociation reaction.[22] Recent works by Golding and Radom have focused on the possibility that concerted migration of the β-hydroxy group can occur with "partial protonation" by an acid (hydrogen bonding to an acid)[23] and a more complex reaction pathway with "partial protonation" of the migrating hydroxy group and "partial deprotonation" of the hydroxy group at the radical center.[25] Experimentally, acid-catalyzed reactions of the ethylene glycol radical, presumed to involve formation of a radical cation by dissociation of water, have been known for many years.[26]

Photolysis of PTOC ester **16** gave the α,β-dimethoxy radical **26** (Scheme 6). In acetonitrile solution, no diphenylalkyl radical product was formed ($k < 1000$ s^{-1}), but in the presence of carboxylic acids, radical **26** reacted to give a diphenylalkyl radical product with a UV spectrum similar to that observed from reaction of radical **3b** (Figure 2A). The observed rate constants for reactions with several carboxylic acids were linearly dependent on acid concentrations (Figure 2B), indicating rate-limiting protonation reactions, that is, general acid catalysis. Although specific acid catalysis of glycol radical reactions is well-known,[26] we are not aware of previous reports of general acid catalysis. Second-order rate constants for protonation (k_{prot}) are listed in Table 1; these values were determined from eq 1 , where k_{obs} is the observed rate

$$k_{obs} = k_0 + k_{prot}[\text{acid}] \qquad (1)$$

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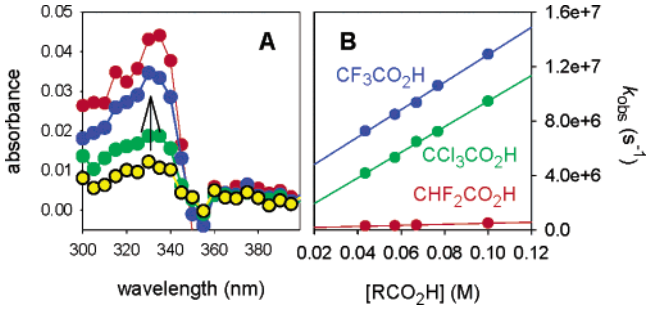

FIGURE 2. (A) Time-resolved spectrum from reaction of radical **26** in CH_3CN containing ca. 0.03 M CF_3CO_2H. The time slices are at 96, 146, 296, and 596 ns with the spectrum at 56 ns subtracted to give a baseline. (B) Observed rate constants for reactions of radical **26** in the presence of representative acids.

SCHEME 6

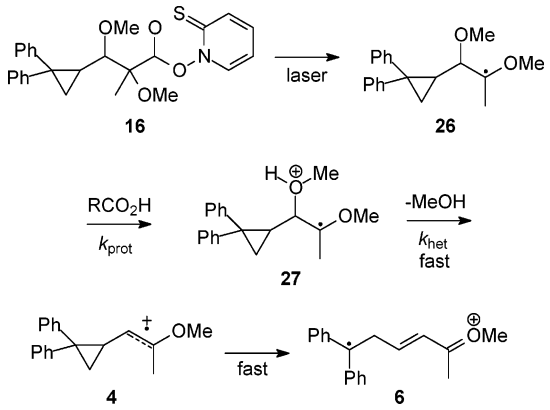

TABLE 1. Second-Order Rate Constants for Acid-Catalyzed Reactions of Radical 26[a]

acid	pK_a[b]	k_{prot} (M^{-1} s^{-1})
CF_3CO_2H	0.23	1.0×10^8
CCl_3CO_2H	0.65	9.4×10^7
CHF_2CO_2H	1.24	3.9×10^6
$CHCl_2CO_2H$	1.29	3.3×10^6
CH_3CO_2H	4.76	1.3×10^6

[a] In acetonitrile solvent at (20 ± 2) °C. [b] Aqueous pK_a value.

constant, k_0 is the background rate constant, k_{prot} is the second-order protonation rate constant, and [acid] is the concentration of acid. The protonation rate constants for reactions in CH_3CN correlate crudely with aqueous pK_a values.

The reaction pathway for radical **26** apparently involves rate-limiting protonation of the β-methoxy group followed by fast heterolysis of the distonic radical cation **27** by loss of methanol to give radical cation **4**, which gives observable product **6** (Scheme 6). The neutral alcohol leaving group in **27** is expected to cleave faster than the diethyl phosphate anionic leaving group in radical **3a**, which reacted too fast for kinetic measurements in all solvents. Therefore, protonation would be the "slow" reaction in the sequence, consistent with the experimental observation of general acid catalysis.

The heterolysis pathway was supported by the results of a preparative reaction of PTOC ester **16** in THF in the presence of 0.05 M CF_3CO_2H and 0.1 M Bu_3SnH. Ketone **17** was isolated from this reaction, and there was no evidence of formation of the dimethylacetal (from methoxy group migration) in the NMR spectrum of the crude reaction mixture. Although computational results predict that protonation of the β-hydroxy group in the ethylene glycol radical will reduce the barrier for a concerted migration,[23] the low-energy pathway for reaction of radical **26** in the presence of acids apparently is heterolytic fragmentation of the methoxy group.

It is important to emphasize that the slow step in the acid-catalyzed heterolysis of radical **26** is the protonation reaction and not the fragmentation reaction. Thus, the accelerating influence of the cyclopropyl group on the heterolysis has no bearing on the potential utility of the reaction sequence in synthesis. In α,β-dialkoxy radicals that lack the cyclopropyl group, heterolysis of the β-alkoxy group following protonation will be faster than heterolysis of an acetate group and is likely to be faster than heterolysis of a dialkyl phosphate group. Thus, in a case where, for example, a β-phosphate ester radical has been employed in a synthetic conversion,[6,7] it should be possible to substitute a β-alkoxy radical and an acid such as CF_3CO_2H.

In summary, the diphenylcyclopropyl moiety promotes rapid heterolysis reactions in radicals containing β-leaving groups and intercepts the radical cations in ion pairs to give UV-detectable distonic radical cations. This "accelerating−reporting" element provides a new approach for studying radicals that contain poor β-leaving groups and would not be expected to give diffusively free radical cations even in polar solvents. The kinetic characterization of the heterolysis of the β-acetoxy radical **3b** demonstrates that the entropic demands in the transition states for a variety of radical heterolysis reactions are similar, and the acid-catalyzed heterolysis reaction of the β-methoxy group in the α,β-dimethoxy radical **26** suggests the possibility that β-alkoxy-substituted radicals might be employed synthetically in acid-catalyzed nucleophilic substitution and isomerization reactions.

Experimental Section

2,4-Dimethoxybenzyl 3-(Diethylphosphatoxy)-3-(2,2-diphenylcyclopropyl)-2-methoxy-2-methylpropionate (9). To a solution of diisopropylamine (0.72 mL, 5.12 mmol) in THF at 0 °C under nitrogen was added 1.6 M BuLi in hexanes (2.95 mL, 4.72 mmol). After being stirred for 15 min at 0 °C, the reaction mixture was cooled to −78 °C, and a solution of 2,4-dimethoxybenzyl 2-methoxypropionate[3] in THF (1.0 g, 3.93 mmol) was added dropwise. The mixture was allowed to stir at −78 °C for 1 h. A solution of 2,2-diphenylcyclopropanecarboxaldehyde[27] (0.874 g, 3.93 mmol) in THF was added dropwise, and the reaction mixture was stirred for another 2 h at −78 °C. The reaction mixture was quenched by addition of diethyl chlorophosphate (0.625 mL, 4.33 mmol), and the mixture was allowed to warm to room temperature. The mixture was diluted with ether, washed with saturated aqueous NH_4Cl solution and brine, and dried over $MgSO_4$. The solvent was removed, and the crude product mixture was subjected to column chromatography on silica gel (EtOAc/hexanes 1:5). One diastereomer of the desired diethylphosphatoxy ester (0.88 g, 37%) was isolated from the mixture for further use. ^1H NMR δ 7.42−7.15 (m, 11H), 6.49−6.46 (m, 2H), 5.26 (d, 1 H, J = 12 Hz), 5.07 (d, 1 H, J = 12 Hz), 4.06 (dd, 1 H, J = 12.6, 10.2 Hz), 3.97−3.86 (m, 4 H), 3.82 (s, 3 H), 3.77

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(s, 3 H), 3.35 (s, 3 H), 2.33 (ddd, 1 H, J = 9.6, 6.3, 3.3 Hz), 1.59−1.54 (m, 4 H), 1.25−1.16 (m, 7 H). ^{13}C NMR δ 171.9, 161.1, 158.7, 145.9, 140.0, 131.2, 129.4 (2 C), 127.9, 127.6, 125.9 (2 C), 115.9, 103.8, 98.2, 82.7, 82.0 (d, J = 7.3 Hz), 63.2 (d, J = 5.2 Hz), 63.0 (d, J = 5.2 Hz), 62.1, 55.2, 55.1, 51.9, 34.8, 27.3, 17.3, 17.0, 15.8, 15.7. HRMS [M + Na]$^+$ calcd for $C_{33}H_{41}O_9NaP$ 635.2386, found 635.2402.

3-(Diethylphosphatoxy)-3-(2,2-diphenylcyclopropyl)-2-methoxy-2-methylpropionic Acid (10). To a solution of **9** (0.391 g, 0.66 mmol) in 10:1 acetonitrile/water (8 mL) was added ceric ammonium nitrate (0.791 g, 1.4 mmol). The reaction was stirred at room temperature for 1 h and quenched by addition of water (10 mL). The resulting solution was extracted in EtOAc (3 × 10 mL). The organic layers were combined, washed with brine, and dried over $MgSO_4$. The solvent was evaporated to give an orange oil. The oil was taken up in EtOAc (20 mL), and the mixture was stirred with 15% $NaHSO_3$ (20 mL) for 2 h. The layers were separated, and the organic layer was washed with saturated $NaHCO_3$ solution (2 × 20 mL). The aqueous layer was separated, acidified with HCl, and extracted into ether (2 × 40 mL). The ether layer was washed with brine and dried over $MgSO_4$. Evaporation of the solvent yielded 0.15 g (50%) of acid **10**. ^{1}H NMR δ 7.32−7.17 (m, 10 H), 4.12−4.02 (m, 2 H), 3.90−3.80 (m, 2 H), 3.69 (dd, 1 H, J = 10.5, 5.7 Hz), 3.32 (s, 3 H), 2.13 (ddd, 1 H, J = 9.9, 6.0, 3.9 Hz), 1.65 (t, 1 H, J = 6.0 Hz), 1.53 (s, 3 H), 1.42 (dd, 1 H, J = 10.2, 4.5 Hz), 1.33 (t, 3 H, J = 6.9 Hz), 1.12 (t, 3 H, J = 6.9 Hz), (COOH not observed). ^{13}C NMR δ 172.3, 145.0, 139.2, 129.6, 128.8, 128.1, 127.9, 126.3, 126.2, 84.3, 83.9 (d, J = 8.3 Hz), 64.0 (d, J = 5.2 Hz), 63.8 (d, J = 5.2 Hz), 51.9, 34.9, 26.4 (d, J = 10.3 Hz), 18.0, 17.3, 15.9 (d, J = 7.2 Hz), 15.6 (d, J = 7.2 Hz). HRMS [M + Na]$^+$ calcd for $C_{24}H_{31}O_7NaP$ 485.1705, found 485.1713.

(1*H*)-2-Thioxo-1-pyridyl 3-(Diethylphosphatoxy)-3-(2,2-diphenylcyclopropyl)-2-methoxy-2-methylpropionate (1a). The method of Barton and Samadi was used.[12] To a solution of the acid **10** (0.137 g, 0.33 mmol) and 2,2′-dithiopyridine-1,1′-dioxide (0.09 g, 0.36 mmol) in CH_2Cl_2 was added Bu_3P (0.04 mL, 0.16 mmol) at 0 °C under nitrogen. The reaction was allowed to warm to room temperature and was stirred for 1.5 h. The reaction mixture was washed with saturated $NaHCO_3$ solution and brine and dried over $MgSO_4$. Flash chromatography (silica gel, EtOAc:hexanes 1:3, v:v) in the dark afforded (0.1 g, 55%) PTOC ester **1a**. ^{1}H NMR δ 8.26 (d, 1 H, J = 6.9 Hz), 7.67 (dd, 1 H, J = 9.0 Hz, 1.5 Hz), 7.44 (d, 2 H, J = 7.2 Hz), 7.32−7.14 (m, 9 H), 6.67−6.65 (m, 1 H), 4.16 (t, 1 H, J = 9.3 Hz), 4.03−3.75 (m, 4 H), 3.62 (s, 3 H), 2.11 (ddd, 1 H, J = 9.3, 6.3, 2.7 Hz), 1.99 (t, 1 H, J = 6.0 Hz), 1.82 (s, 3 H), 1.37 (dd, 1 H, J = 9.3, 5.4 Hz), 1.25 (t, 3 H, J = 6.9 Hz), 1.16 (t, 3 H, J = 7.2 Hz). ^{13}C NMR δ 161.6, 145.6, 139.2, 138.8, 136.5, 133.2, 129.4, 129.3, 128.0, 127.7, 126.2 (2 C), 112.8, 84.0, 80.2 (d, J = 7.5 Hz), 63.7 (d, J = 5.2 Hz), 63.6 (d, J = 5.2 Hz), 53.3, 34.8, 27.4, 16.6, 15.8 (d, J = 7.2 Hz), 15.7 (d, J = 7.2 Hz), 14.9 (thione C not observed). HRMS [M + Na]$^+$ calcd for $C_{29}H_{34}NO_7NaPS$ 594.1691, found 594.1675.

Laser Flash Photolysis Studies. The LFP experimental method was the same as that previously described.[14] A Continuum Nd:YAG laser producing ca. 50 mJ of 355-nm light in a 7-ns pulse was employed. Reactions of radical **3a** were studied in various solvents (acetonitrile, THF, cyclohexane), and in all cases the UV−vis spectrum of **6** or **7** was completely formed "instantly" ($k > 2 \times 10^8$ s^{-1}). Radical **3b** was studied in THF and in acetonitrile, and a portion of the time-resolved spectrum from reaction of **3b** is shown in Figure 1. Radical **26** showed no apparent reaction in acetonitrile, but reactions were observed when carboxylic acids were present; a portion of the time-resolved spectrum is shown in Figure 2. The results of kinetic measurements of reactions of radical **26** are in Table S1 of the Supporting Information.

Preparative Reaction of 1b. A solution of PTOC ester **1b** (0.112 g) was dissolved in THF (10 mL) containing 0.1 M Bu_3SnH. The solution mixture was irradiated with a 150-W flood lamp and stirred for 2 h. The solvent was evaporated, and the crude mixture was purified by chromatography on silica gel to give 6,6-diphenylhex-3-ene-2-one (**17**) (0.02 g, 35%). ^{1}H NMR δ 7.33−7.17 (m, 10 H), 6.67 (dt, 1 H, J = 15.9, 6.9 Hz), 6.06 (d, 1 H, J = 15.9 Hz), 4.10 (t, 1 H, J = 7.8 Hz), 2.98 (dd, 2 H, J = 8.9, 6.9 Hz), 2.14 (s, 3 H). ^{13}C NMR δ 145.7, 143.3, 132.5, 128.4, 127.5, 126.3, 50.2, 38.3, 26.6 (carbonyl C not observed). HRMS [M$^{\bullet}$]$^+$ calcd for $C_{18}H_{18}O$ 250.1358, found 250.1370.

Preparative Reaction of 16. PTOC ester **16** (0.121 g) was dissolved in THF (10 mL) containing 0.1 M Bu_3SnH and 0.05 M TFA. The mixture was irradiated with a 150-W flood lamp and was stirred for 2 h. The solvent was evaporated, and an NMR spectrum of the crude mixture showed no signals consistent with methoxy peaks in a dimethylacetal. The crude mixture was purified by chromatography on silica gel to yield 6,6-diphenylhex-3-ene-2-one (**17**) (0.015 g, 22%).

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Supporting Information Available: Kinetic results for reactions of radical **26**, synthetic details for preparation of compounds **11**, **12**, **1b**, **14**, **15**, and **16**, and NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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