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Photochemical Cleavage and Release of Para-Substituted Phenols from α-Keto Amides

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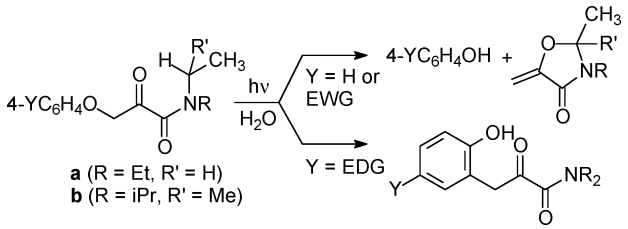

In aqueous media α-keto amides 4-$YC_6H_4OCH_2COCON(R)CH(R')CH_3$ (**5a**, R = Et, R′ = H; **5b**, R = ^{i}Pr, R′ = Me) with para-substituted phenolic substituents (Y = CN, CF_3, H) undergo photocleavage and release of 4-YC_6H_4OH with formation of 5-methyleneoxazolidin-4-ones **7a**,**b**. For both **5a**,**b** quantum yields range from 0.2 to 0.3. The proposed mechanism involves transfer of hydrogen from an *N*-alkyl group to the keto oxygen to produce zwitterionic intermediates **8a**−**c** that eliminate the para-substituted phenolate leaving groups. The resultant imminium ions $H_2C{=}C(OH)CON^+(R){=}C(R')CH_3$ **9a**,**b** cyclize intramolecularly to give **7a**,**b**. The quantum yields for photoelimination decrease in CH_3CN, CH_2Cl_2, or C_6H_6 due to competing cyclization of **8a**,**b** to give oxazolidin-4-one products which retain the leaving group 4-$YC_6H_4O^-$ (Y = H, CN). A greater tendency to undergo cyclization in nonaqueous media is observed for the *N*,*N*-diethyl amides **5a** than the *N*,*N*-diisopropyl amides **5b**. With para electron releasing groups Y = CH_3 and OCH_3 quantum yields for photoelimination significantly decrease and 1,3-photorearrangment of the phenolic group is observed. The 1,3-rearrangement involves excited state ArO−C bond homolysis to give para-substituted phenoxyl radicals, which can be observed directly in laser flash photolysis experiments.

Introduction

Photochemical cleavage reactions have found widespread use in biological applications that require intracellular photochemical release of biologically active substrates[1] or as photoremovable protecting groups and photolinkers for the synthesis of biooligomers.[2] A number of photocleavage reactions have been developed in recent years which release carboxylate and phosphate leaving groups for use in such applications.[3−6] Nevertheless, photochemical elimination reactions that expel leaving group anions remain quite uncommon. Zwitterionic intermediates possess a basic site that, in principle, can be utilized to effect the elimination of leaving groups. Furthermore, intermediates with significant zwitterionic character are thought to be involved in a number of photochemical reactions. One such photoreaction has been the photocyclization of α-keto amides **1** to give oxazolidinones **2** and β-lactams **3** as products (Scheme 1), which can be considered to involve zwitterionic intermediates

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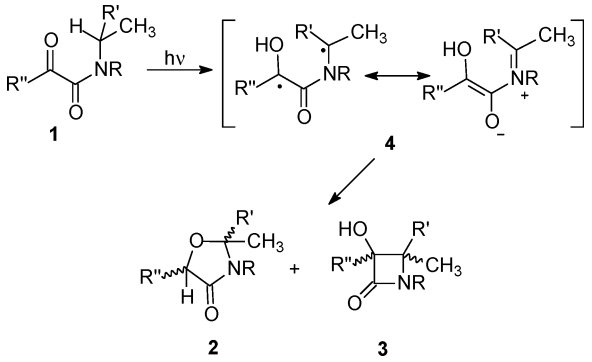
SCHEME 1



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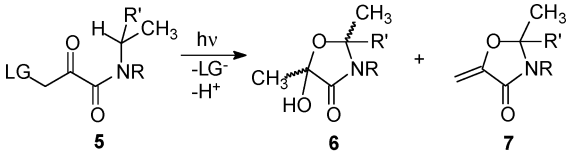
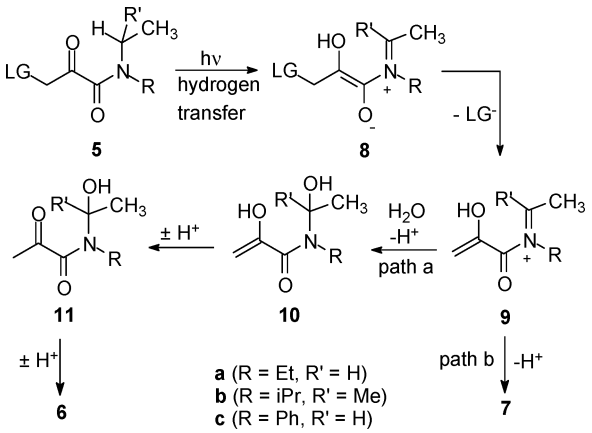


a (R = Et, R' = H)	94	:	6
b (R = iPr, R' = Me)	0	:	100
c (R = Ph, R' = H)	100	:	0

LG = $CH_3CO_2^-$, $PhCH_2CO_2^-$, $C_6H_5CO_2^-$, $4\text{-}NCC_6H_4CO_2^-$, $CH_3CONHCH_2CO_2^-$, BocAla, GABA, Glu

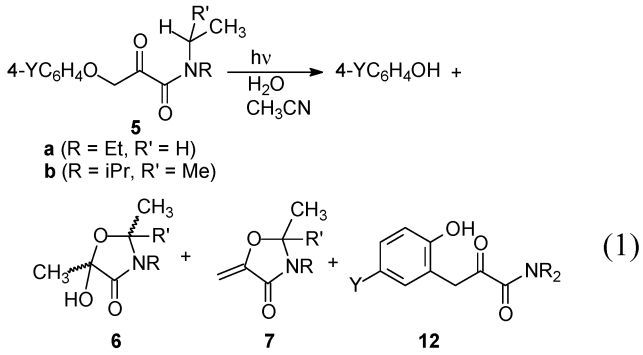
SCHEME 3



a (R = Et, R' = H)
b (R = iPr, R' = Me)
c (R = Ph, R' = H)

4.[7−9] We recently reported evidence that analogous zwitterionic intermediates **8**, photogenerated from α-keto amides **5** (Schemes2 and 3), undergo elimination of carboxylate anions on the microsecond time scale in aqueous solution.[10a,b] The chemical yields of the carboxylic acids and for the formation of the corresponding cleavage coproducts **6** or **7** were essentially quantitative, and quantum yields for the photoeliminations were generally 0.2−0.4 for *N*,*N*-diethyl- or *N*,*N*-diisopropyl amides **5a**,**b** for a wide variety of carboxylate leaving groups (Scheme 2).[10] In these studies the formation of cyclization products analogous to **2** or **3**, which would have retained the carboxylate leaving groups, were never observed.

In a preliminary communication we reported results which extended the photochemical elimination reaction of α-keto amides to effect the release of a variety of para-substituted phenolate leaving groups (eq 1).[11] The results of our studies on

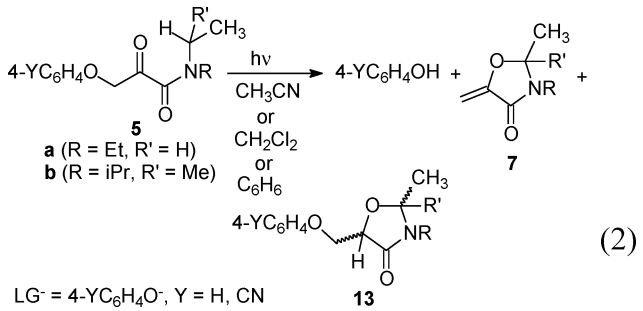


a (R = Et, R' = H)
b (R = iPr, R' = Me)

(1)

$LG^- = 4\text{-}YC_6H_4O^-$, Y = CH_3O, CH_3, H, CF_3, CN

$4\text{-}YC_6H_4O^-$ eliminations can be discussed within the context of our previously proposed[10a,b] mechanism for carboxylate group eliminations (Scheme 3). The obvious difference is that a substantially more basic leaving group is being expelled in the elimination of phenolates $4\text{-}YC_6H_4O^-$ from **8a**,**b**. However, the expected slower rates of elimination are not manifested by significantly reduced quantum yields for $4\text{-}YC_6H_4OH$ formation for Y = H, CF_3, or CN under aqueous conditions. On the other hand, changing to nonaqueous solvents (CH_3CN, CH_2Cl_2, or C_6H_6) sufficiently slows elimination so that a significant fraction of **8a**,**b** undergoes cyclization to give oxazolidinones **13a**,**b** (eq 2).



a (R = Et, R' = H)
b (R = iPr, R' = Me)

(2)

$LG^- = 4\text{-}YC_6H_4O^-$, Y = H, CN

Another difference between the phenolate versus carboxylate anion eliminations in photolyses of **5a**,**b** concerns the partitioning of imminium ion **9** between intermolecular versus intramolecular pathways a and b that form products **6** and **7** under aqueous conditions (Scheme 3). In the case of carboxylate eliminations, path a and product **6a** are favored by *N*,*N*-diethylamides **5a**, whereas product **7b** is exclusively formed via path b in the case of *N*,*N*-diisopropylamides **5b**. In contrast, with phenolate leaving groups product **7a**,**b** is strongly preferred, regardless of whether **5a** or **5b** is the reactant. The preference for intramolecular cyclization of **9a** to give **7a** in the phenolate elimination reactions is explicable in terms of deprotonation of **9a** by the basic phenolate anion in the ion pair initially produced

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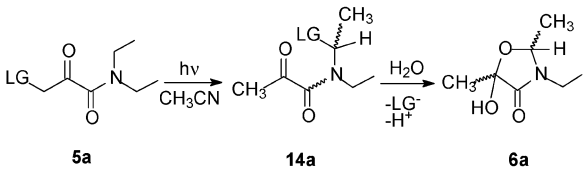
upon elimination in **8a**. A similar phenolate assisted intramolecular cyclization of **9a** to give **7a** persists in the hydrogen-bonded ion pair formed in phenolate eliminations conducted under nonaqueous conditions in CH_3CN, CH_2Cl_2, or C_6H_6, whereas carboxylate anions produced upon photoelimination from **5a** in CH_3CN instead add to the imminium ion carbon of **9a** to give aminal adduct **14a** (eq 3).



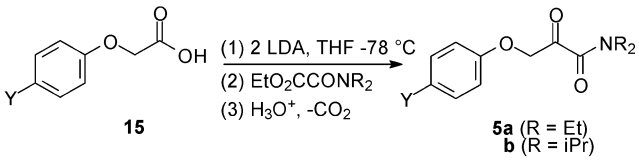
(3)

LG = $CH_3CO_2^-$, $PhCH_2CO_2^-$

With para electron releasing groups Y = CH_3 and OCH_3, the α-keto amides **5a**,**b** (LG^- = 4-$YC_6H_4O^-$) show marked reductions in the efficiencies for release of 4-YC_6H_4OH under aqueous conditions, and 1,3-photorearrangement of the phenolic group to give **12a**,**b** (eq 1) becomes increasingly important or even predominant as a photoprocess. This 1,3-photorearrangement of the phenolic group in **5a**,**b** likely involves C−O bond homolysis and recombination of the radical pair. The corresponding long-lived para-substituted phenoxyl radicals (Y = CH_3, OCH_3) of cage escape were readily observed by laser flash photolysis. Since these radicals were produced rapidly within the duration of the laser pulse, the C−O bond homolysis was thought to occur directly in the excited state as a process that competes with the excited-state transfer of hydrogen from the carboxamide alkyl group to the keto group.

Results

Photochemical Reactants. The series of *N*,*N*-dialkyl α-keto amides **5a**,**b** were prepared by reaction of dilithio dianions of para-substituted phenoxyacetic acids **15** with ethyl *N*,*N*-diethyloxamate or ethyl *N*,*N*-diisopropyloxamate in THF according to the literature method[12] (eq 4).



(4)

The absorption spectra of **5a** showed a maximum below 300 nm that progressively shifted to longer wavelengths by substitution of *p*-Y substituents with increasing electron donating abilities, e.g., Y = CN, λ = 246 nm (ϵ 2050), Y = H, λ = 269 nm (ϵ 2270), and Y = OCH_3, λ = 288 nm (ϵ 3510). Very similar absorption maxima were observed for the *N*,*N*-diisopropyl α-keto amides **5b** bearing para-substituted phenolic groups. The absorption spectra of **5a**,**b** tailed out to longer wavelengths such that photolyses could readily be conducted above 300 nm and laser flash photolysis studies could be performed at 355 nm.

Photolyses in Aqueous Acetonitrile. Photolyses of α-keto amides **5a**,**b** (Y = H, CF_3, CN) in 33% aqueous CH_3CN with Pyrex-filtered light at 25 °C produced 4-YC_6H_4OH and the cleavage coproducts, oxazolidinones **7a**,**b** (eq 1), whereas the diastereomeric hemiacetal **6a** was only observed as a minor product. Cleavage coproducts **6a** and **7a**,**b** were identified by comparison to ^1H, ^{13}C NMR spectra of the authentic samples, which had been isolated and characterized previously.[10] The yields of these cleavage coproducts were similar to the yields of 4-YC_6H_4OH produced in the photolyses (Tables1 and 2).

TABLE 1. Chemical Yields for Photolyses of *N*,*N*-Diethyl α-Keto Amides 5a (LG^- = 4-$YC_6H_4O^-$) in 33% D_2O in CD_3CN[a]

5a, Y =	ArOH, pK_a	ArOH, %	**7a**, %	**6a**, %	**12a**, %	unreacted **5a**, %
4-CN	7.95	98	47	31	0	0
4-CF_3	8.51	30	24	8	0	69
H	9.95	52	43	<5	<5	41
4-CH_3	10.26	16[b]	14	0	19	50
4-CH_3O	10.20	<5	<5	0	64	22

[a] Yields determined by ^1H NMR spectroscopy with DMSO as standard. [b] Yield determined by HPLC analyses, using an internal standard and 254 nm UV detection.

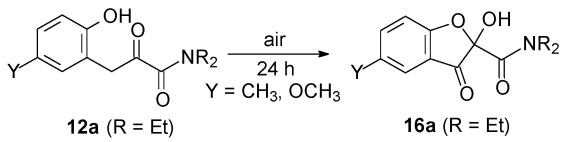
TABLE 2. Chemical Yields for Photolyses of *N*,*N*-Diisopropyl α-Keto Amides 5b (LG^- = 4-$YC_6H_4O^-$) in 33% D_2O in CD_3CN[a]

5b, Y =	ArOH, %	**7b**, %	**12**, %	unreacted **1**, %
4-CN	76	79	0	17
H	59	60	<5	40
4-CH_3	48[b]	49	8	46
4-CH_3O	<5	0	74	22

[a] Yields determined by ^1H NMR spectroscopy with DMSO as standard. [b] Yields determined by HPLC analysis, using an internal standard and 254 nm UV detection.

Substitution of **5a**,**b** by para electron donating groups, Y = CH_3 or OCH_3, led to progressively lower yields of 4-YC_6H_4OH, **6a**, and **7a**,**b**, and the formation of 1,3-photorearrangement products **12a**,**b** was observed by ^1H NMR spectroscopy. Photoproducts **12a** (Y = CH_3, OCH_3) and **12b** (Y = OCH_3) were isolated chromatographically from larger scale photolyses and identified by ^1H, ^{13}C NMR spectroscopy, whereas the yields of **12b** (Y = CH_3) were insufficient for complete characterization. The salient feature of **12a**,**b** was an α-CH_2 group ca. δ 3.9 in the ^1H NMR spectra ($CDCl_3$). The isolated compounds also showed only three aromatic protons and an exchangeable hydroxyl group. In ^{13}C NMR spectra ($CDCl_3$) the α-CH_2 group appeared at ca. δ 42, and there were six peaks corresponding to the nonequivalent carbons of the trisubstituted aryl groups.

In solution the photorearranged *N*,*N*-diethylamide **12a** (Y = CH_3, OCH_3) slowly air-oxidized to form the keto cyclic hemiacetals **16a** (Y = CH_3, OCH_3) (eq 5). The *N*,*N*-diisopropyl



(5)

amide **12b** (Y = OCH_3) showed no evidence of undergoing this reaction. The oxidation of **12a** (Y = CH_3, OCH_3) to **16a** (CH_3, OCH_3) was readily observed by ^1H NMR spectroscopy ($CDCl_3$) by the disappearance of the δ 3.9 peak of **12a** (Y = CH_3, OCH_3) and by an accompanying downfield shift of two out of three aromatic protons (from δ <7.0 to 7.3−7.4). Conversion was essentially complete after 24 h at 25 °C. In the

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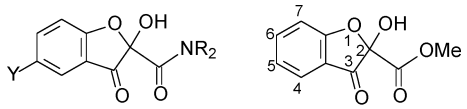
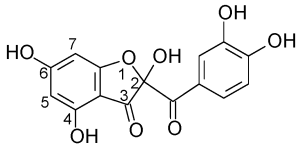
^{13}C NMR spectra ($CDCl_3$) the characteristic feature of products **16a** was a quaternary carbon at δ 98, which was very similar to quaternary carbon chemical shifts reported for model compounds **17**[13] and **18**[14] (vide infra). The structures proposed for **16a** (Y = CH_3, OCH_3) were also consistent with elemental analyses.



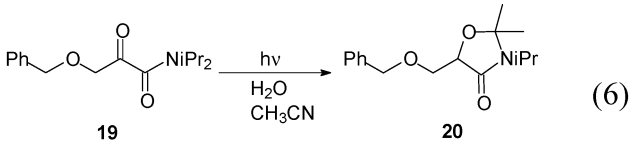
16a (R = Et)
Y = CH_3, OCH_3

17



18

The photochemistry of *N*,*N*-diethyl α-keto amide **19** was studied for comparison to the phenoxy-substituted α-keto amides **5a**,**b** (eq 6). The photolyses of 0.05 M **19** in 30% aqueous



19 16% unreacted → **20** 84% yield (6)

CH_3CN with Pyrex-filtered light gave oxazolidinone **20** as the sole photoproduct in 84% yield at high conversions, according to ^{1}H NMR spectroscopic analyses of the photolyzates. There was no sign of other products, including those analogous to **7b**, which might arise from elimination of the leaving group. Oxazolidinone **20** was isolated chromatographically. Its ^{1}H NMR spectrum ($CDCl_3$) showed the presence of the benzyloxy group and a pair of doublet of doublets at δ 3.69 and 3.77 due to diastereotopic CH_2 protons. In addition, there was a corresponding doublet of doublets at δ 4.39 that was assigned to the lone methine proton in **20**. In the ^{13}C NMR spectrum ($CDCl_3$) the methine carbon appeared at δ 95.2, and the only carbonyl group present was that ascribable to an amide.

Photolyses in Nonaqueous Solvents.. With a sufficiently poor leaving group, such as a strongly basic alkoxide, cyclization to form oxazolidinones such as **20** becomes the predominant photoprocess (eq 6). Although this type of photoreactivity is not observed under aqueous conditions in photolyses of α-keto amides **5a**,**b** with phenolate leaving groups, such photocyclizations could become important if the phenolate photoeliminations are slowed by changing to nonaqueous media. Under these latter conditions, photolyses of **5a**,**b** (Y = H, CN) performed in neat CH_3CN and CH_2Cl_2 show that photocyclization to **13a**,**b** can become an important or even the predominant photoreaction (eq 2, Tables 3 and 4).

In the case of **5a** (Y = H) photolysis in dry CH_3CN produced no phenol or cleavage coproduct **7a**, and the only photoproduct that was observed was that of photocyclization to form oxazolidinone **13a** (Y = H) (Table 3). With the less basic *p*-cyanophenolate leaving group, however, photoelimination almost completely prevailed over photocyclization, and 4-CNC_6H_4OH plus **7a** were the principal photoproducts in CH_3CN. Unlike the *N*,*N*-diethylamide **5a** (Y = H), the *N*,*N*-diisopropylamide **5b** (Y = H) underwent both photoelimination and photocyclization to give phenol, **7a**, and **13b** (Y = H) in both CH_3CN and benzene (Table 4). In the case of **5b** (Y = CN) photoelimination was exclusively observed in CH_3CN, but was retarded by photolyzing in CH_2Cl_2 or benzene, such that the photocyclized product **13b** (Y = CN) was obtained in addition to 4-CNC_6H_4OH and **7b**.

Control experiments were performed to determine whether **13a** (Y = H) and **13b** (Y = H, CN) undergo elimination of 4-YC_6H_4OH to produce **6a** or **7a**,**b** in 33% aqueous CD_3CN. The above solutions were monitored by ^{1}H NMR spectroscopy for periods of 2 weeks. Only unreacted **13a**,**b** were observed and no trace of any other compound was detected in the solutions.

Quantum Yields. The quantum yields for photolyses of 0.01 M **5a**,**b** at 310 nm in 33% aqueous CH_3CN showed that the elimination of the para-substituted phenols 4-YC_6H_4OH is efficient for electron withdrawing groups Y = CN or CF_3 and for Y = H (Table 5). However, the quantum efficiencies strongly decreased for electron donating groups Y = CH_3 and OCH_3, and there was a corresponding increase in the quantum yields for formation of the 1,3-photorearrangement products **12a**,**b**.

TABLE 3. Chemical Yields for Photolyses of *N*,*N*-Diethyl α-Keto Amides 5a (LG^- = 4-$YC_6H_4O^-$) under Nonaqueous Conditions (CD_3CN or C_6D_6)[a]

reactant **5a**, Y =	solvent	ArOH, %	**7a**, %	**13a**, %	unreacted **5a**, %
H	CD_3CN	0	0	44	53
CN	CD_3CN	54	54	trace	38
CN	C_6D_6	40	42	42	12

[a] Yields determined by ^{1}H NMR spectroscopy with DMSO as standard.

TABLE 4. Chemical Yields for Photolyses of *N*,*N*-Diisopropyl α-Keto Amides 5b (LG^- = 4-$YC_6H_4O^-$) under Nonaqueous Conditions (CD_3CN, CD_2Cl_2, or C_6D_6)[a]

reactant **5b**, Y =	solvent	ArOH, %	**7b**, %	**13b**, %	unreacted **5b**, %
H	CD_3CN	30	31	24	43
CN	CD_3CN	44	45	0	52
CN	CD_2Cl_2	45	47	24	27
CN	C_6D_6	39	39	31	26

[a] Yields determined by ^{1}H NMR spectroscopy with DMSO as standard.

TABLE 5. Quantum Yields for Photolyses of 5a,b (LG^- = 4-$YC_6H_4O^-$) in 33% Aqueous CH_3CN for Various Para Substituents, Y[a]

reactant **5a**, Y =	Φ ArOH	Φ **12a**[b]	reactant **5b**, Y	Φ ArOH	Φ **12b**[b]
CN	0.30	0	CN	0.30	0
CF_3	0.30	0			
H	0.26	0	H	0.23	0
CH_3	0.16	0.13	CH_3	0.15	0.10
OCH_3	0.07	0.26	OCH_3	0.07	0.19

[a] HPLC analyses with internal standard used to quantify **5a**,**b** and 4-Y-C_6H_4OH. [b] Taken as $\Phi_{dis} - \Phi_{phenol}$ where Φ_{dis} is the disappearance quantum yield and Φ_{ArOH} is the quantum yield for 4-Y-C_6H_4OH (ArOH).

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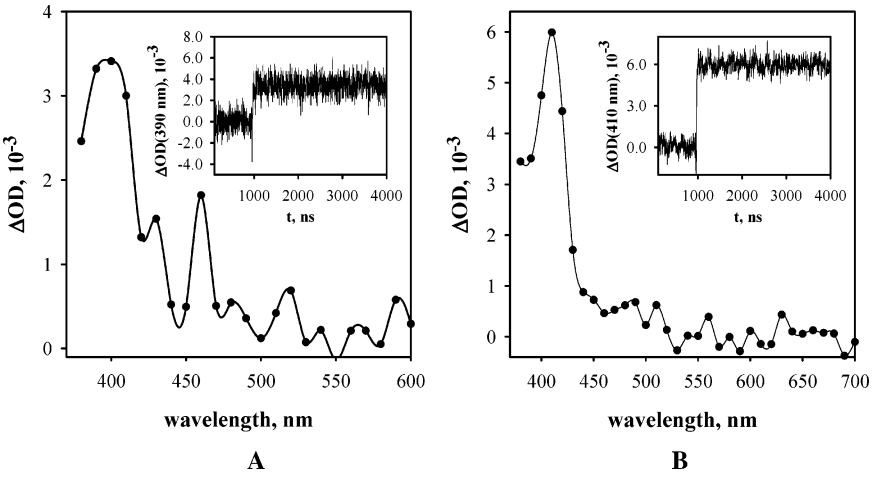


FIGURE 1. (A) Spectrum of *p*-methylphenoxyl radical, λ_{max} = ca. 400 nm, produced from LFP of α-keto amide **5a** (Y = CH_3). (B) Spectrum of *p*-methoxyphenoxyl radical, λ_{max} = ca. 410 nm, produced from LFP of α-keto amide **5b** (Y = OCH_3). Insets are kinetic plots of the intermediates, monitored at 390 and 410 nm, respectively.

For the photoeliminations the quantum yields, Φ_{ArOH}, were determined by measuring the yields of the para-substituted phenol photoproducts by direct phase HPLC, using the internal standard method. We also measured the quantum yields of disappearance, Φ_{dis}, of the reactants **5a**,**b** by the same method. The quantum yields for **12a**,**b** were then obtained by subtracting Φ_{ArOH} from Φ_{dis} (Table 5).

Quantum yield measurements were also made for photolyses of **5a** (Y = H) in CH_3CN and for **5b** (Y = H) in CH_3CN and **5b** (Y = CN) in C_6H_6. In these cases the products were quantified by ^{1}H NMR spectroscopy with use of DMSO as a standard. The quantum yield for formation of the cyclic product **13a** (Y = H) in CH_3CN was $\Phi = 0.20$, which is similar to the value ($\Phi = 0.26$) for photoelimination to produce phenol in 33% aqueous CH_3CN as the solvent. In the case of **5b** (Y = H) in CH_3CN the quantum yield for photoelimination of phenol was lowered due to competition by photocyclization to form **13b**, such that $\Phi = 0.12$ for elimination of C_6H_5OH to form **7b** and $\Phi = 0.11$ for photocyclization to form **13b**. No solvent effect on the total quantum yield ($\Phi = 0.23$) in CH_3CN was observed as compared to 33% aqueous CH_3CN. For photolyses of **5b** (Y = CN) in C_6H_6, the quantum yield for photoelimination of 4-CNC_6H_4OH to form **7b** was $\Phi = 0.081$, whereas $\Phi = 0.073$ for cyclization to form **13b**, and the total quantum yield for formation of products was $\Phi = 0.15$, which is lower than the total quantum in aqueous CH_3CN (Table 5).

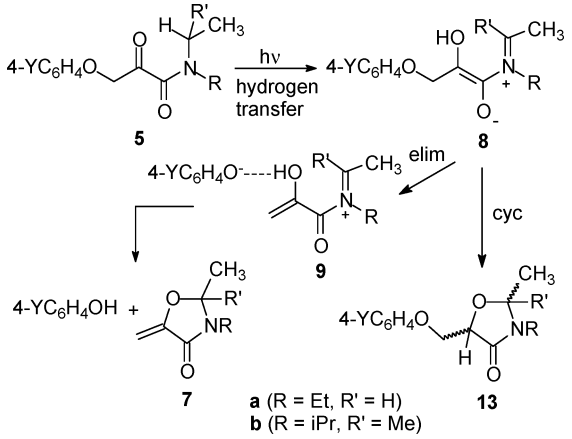
Laser Flash Photolyses. Considering the likelihood that the 1,3-photorearrangement products **12a**,**b** were formed via recombination of radicals produced upon photochemical ArO−C bond homolysis of **5a**,**b** (Y = CH_3, OCH_3), we performed 355 nm nanosecond laser flash photolysis experiments with argon flushed solutions of 0.05 and 0.08 M reactants **5a** (Y = CH_3) and **5b** (Y = OCH_3) in 33% aqeuous CD_3CN in efforts to detect long-lived para-substituted phenoxyl radicals. The flash photolyses produced transient absorptions at 400 (Y = CH_3) and 410 nm (Y = OCH_3) (Figure 1A,B). These absorptions did not decay within the microsecond time scale used for these experiments. The kinetics of formation of the transients were monitored at 390 and 410 nm, respectively, and showed that the transients were produced within the duration of the laser pulse (ca. 10 ns).

The assignment of the transients 4-YC_6H_4O radicals was made on the basis of independent generation of the radical intermediates through laser flash photolysis of 0.01 M benzophenone in the presence of ca. 0.007 M of the corresponding para-substituted phenols under identical conditions to the above experiments with **5a** (Y = CH_3) and **5b** (Y = OCH_3). In addition to the para-substituted phenoxyl radicals, accompanying absorption was observed due to benzophenone ketyl radicals in the 550 nm region. Absorption due to the triplet excited state of the benzophenone, which is usually observed in this region, was largely quenched under the above conditions. Quenching of the triplet excited state of benzophenone by phenol also was used to generate unsubstituted phenoxyl radicals, which were readily observed at 400 nm. However, transient absorption attributable to such phenoxyl radicals was not observed upon laser flash photolysis of **5a** (Y = H).

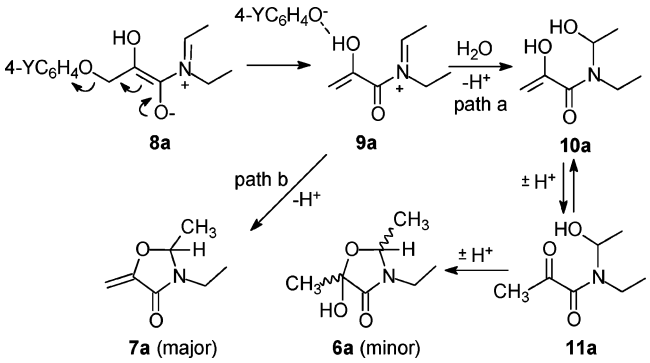
Discussion

Both the *N*,*N*-diethyl and *N*,*N*-diisopropyl amides **5a** and **5b** with para electron accepting substituents Y = H, CF_3, or CN on the phenolic ring exclusively undergo excited state hydrogen transfer and subsequent expulsion of the corresponding phenolate leaving groups to form primarily **7a**,**b** as the cleavage coproducts in aqueous CH_3CN. The phenolate eliminations do not appear to be occurring directly in the excited state, but in a ground-state intermediate thought to be the zwitterionic species **8a**,**b** (Scheme 4). Quantum yields are essentially the same for photoelimination of carboxylate and 4-$YC_6H_4O^-$ (Y = H, CF_3, CN) groups in aqueous CH_3CN. In dry CH_3CN the expulsions of 4-$YC_6H_4O^-$ (Y = H, CF_3, CN) are sufficiently slow such that intermediates **8a**,**b** undergo competitive cyclization to give **13a**,**b**. The cyclization of **8a**,**b** to give **13a**,**b** increases in proportion to elimination when the solvent is changed from CH_3CN to CH_2Cl_2 or benzene. Such cyclizations in CH_3CN are not observed when the leaving group is a carboxylate group.[10] In dry CH_3CN elimination of acetate anion occurs in the case of **5a** ($LG^- = CH_3CO_2^-$) to give the aminal recombination product **14a** in the ion pair (eq 3), whereas **5b** ($LG^- = CH_3CO_2^-$) gives only **7b** and acetic acid.[10a] Aside from the ability of the phenolate substituted intermediates **8a**,**b** to undergo competitive cyclization under nonaqueous conditions, the mechanism for elimination of 4-$YC_6H_4O^-$ (Y = H, CF_3, CN) groups is considered to be similar to that proposed previously[10a,b] for expulsion of carboxylate groups from **5a**,**b** (Scheme 3). Impor-

SCHEME 4



SCHEME 5

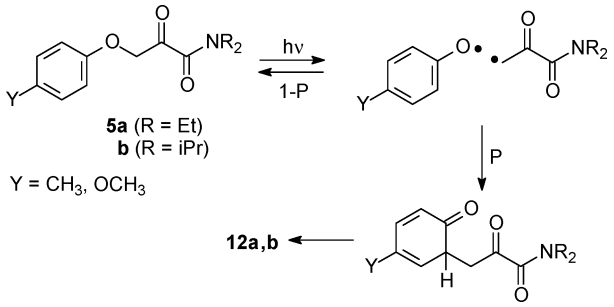


tantly, control experiments show that the phenolate eliminations do not occur in a dark reaction of the cyclized products **13a**,**b**. These products are stable for weeks in 33% aqueous CH_3CN.

Although the photoeliminations to give 4-YC_6H_4OH and **7a**,**b** become less efficient due to competing cyclization of **8a**,**b** in CD_3CN, CD_2Cl_2, or C_6D_6, appreciable yields of these products are observed under such nonaqueous conditions (Tables 3 and 4). These photoeliminations are thought to proceed via initial formation of a hydrogen bonded ion pair involving the phenolate anion and the enolic imminium ion **9a**,**b**. A related issue is the formation of **7a** as the major cleavage coproduct from *N*,*N*-diethyl amides **5a** in aqueous CH_3CN. Under aqueous conditions we invariably observe hemiacetal **6a** rather than methyleneoxazolidinone **7a** as the major product when the leaving group is carboxylate rather than phenolate.[10a] The basic phenolate anion evidently promotes formation of **7a** by enhancing the nucleophilicity of the enolic oxygen in **9a** (Scheme 5). Proton transfer from **9a** to phenolate is envisioned to favor the intramolecular cyclization (path b) leading to **7a** over the intermolecular addition of water (path a), which would give the hemiacetal **6a**. On the other hand, for the *N*,*N*-diisopropyl amides **5b** the only cleavage coproduct observed under aqueous or nonaqueous conditions is **7b**, regardless of whether the leaving group is a phenolate or carboxylate group.

In the foregoing discussion, paths a and b in Schemes 3 and 5 are mechanistically distinct pathways, each leading to its respective product **6a** or **7a**,**b**. From previously reported control experiments it is known that compounds **6a** and **7a** do not interconvert under aqueous conditions at pH as low as 2.[10a] In addition, deuterium labeling studies with D_2O in CD_3CN show that no deuterium is incorporated into the terminal position of the double bond of **7a**,**b**.[10] For **6a** the corresponding CH_3 group always becomes monodeuterated, consistent with the tautomerization step in its mechanism for formation (Scheme 5). Such a tautomerization step does not occur prior to the formation of **7a**,**b**, and these products do not come from **6a** or unobserved **6b**.

SCHEME 6



The photoelimination quantum yields rather abruptly decrease, and 1,3-photorearrangement of the phenolic group to give **12a**,**b** becomes an important, even dominant photoprocess (Table 5) when the remote para substituent Y on the phenolic ring of **5a**,**b** is varied from Y = H to Y = CH_3 to OCH_3. The mechanism for 1,3-photorearrangement likely involves scission of the ArO−C bond of **5a**,**b** to give a para-substituted phenoxyl radical and an α-keto amide radical as a caged radical pair. Recombination at the ortho position of the phenoxyl radicals followed by tautomerization would give **12a**,**b** (Scheme 6).

The formation of para-substituted phenoxyl radicals has previously been observed upon photolysis of α-(*p*-methoxyphenoxy)acetophenone[15] and α-(*p*-methoxyphenoxy)acetone.[16] These radical cleavages are known to occur in the excited states of these α-substituted ketones with rate constants of 10^7-10^9 s^{-1}. In the cases of **5a**,**b** the para-substituted phenoxyl radicals (4-YC_6H_4O, Y = CH_3, OCH_3) are detected in laser flash photolysis experiments and exhibit long-lived transient absorption in the 390−410 nm region. These absorption maxima are identical with those observed upon independent generation of these radicals by photolysis of benzophenone in the presence of various concentrations of 4-YC_6H_4OH. We also find from analysis of the rise times of the transient absorptions of the substituted phenoxyl radicals that they are produced within the duration of the laser pulse, suggesting that the radical cleavages occur directly in the excited state of **5a**,**b** (Y = CH_3, OCH_3).

The rate constants for ArO−C cleavage of α-(4-YC_6H_4O)-substituted acetophenones have been found to correlate to σ^+ constants of the Y para substituents.[15a] The photochemical homolyses observed for 5**a**,**b** (Y = CH_3, OCH_3) are consistent with the known ArO−C bond[17] weakening by para electron donors. Phenoxyl radicals are not detected in flash photolyses of **5a** (Y = H), and no 1,3-photorearrangement products are observed for **5a**,**b** (Y = H, CF_3, CN), which would be consistent with the known substantial ArO−C bond strengthening effect of para electron withdrawing groups (EWG). In these latter cases the predominant excited state reaction is hydrogen transfer to give elimination products of **8a**,**b** in aqueous CH_3CN.

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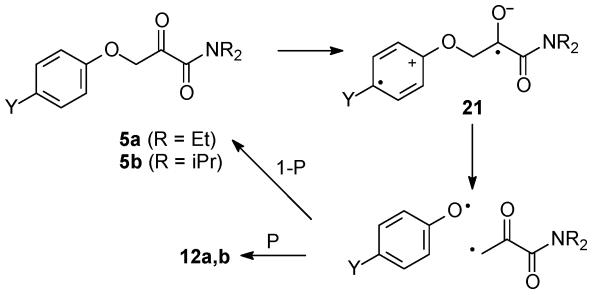
(16) Grimme, S.; Dreeskamp, H. *J. Photochem. Photobiol., A* **1992**, *65*, 371−382.

(17) (a) Pratt, D. A.; de Heer, M. I.; Mulder, P.; Ingold, K. U. *J. Am. Chem. Soc.* **2001**, *123*, 5518−5526. (b) Suryan, M. M.; Kafafi, S. A.; Stein, S. E. *J. Am. Chem. Soc.* **1989**, *111*, 4594−4600.

SCHEME 7



When ArO−C homolysis competes with hydrogen transfer in the excited state, the disappearance quantum yields, Φ_{dis}, of **5a**,**b** will not necessarily increase in going from Y = EWG to Y = EDG. The Φ_{dis} remain nearly constant as the Y substituent is varied (Table 5), likely because homolysis to generate the radical pair results in recombination to give ground-state reactant in addition to giving 1,3-rearrangement product **12a**,**b**. If the probability that recombination gives 1,3-rearrangement product is some fraction *P*, then $\Phi_{dis} = \Phi_{HO}P + \Phi_H$, where Φ_{HO} and Φ_H are the quantum yields for homolysis and hydrogen transfer. This is also expressed by eq 7 , where k_{ho} and k_H are the

$$\Phi_{dis} = \frac{k_{ho}P}{k_{ho} + k_H + k_d} + \frac{k_H}{k_{ho} + k_H + k_d} \qquad (7)$$

respective rate constants and k_d is the rate constant for radiationless decay of the reactive excited state. If $P \approx \Phi_H$, then Φ_{dis} will remain essentially constant even when homolysis occurs at a very much faster rate than hydrogen transfer. From Table 5 the Φ_H values for 5a,b are ca. 0.3. For P = 0.3, Φ_{dis} will be essentially constant at 0.3, whereas for P much larger than 0.3, Φ_{dis} will increase as k_{ho} increases relative to k_H and k_d, and for P much less that 0.3, Φ_{dis} will decrease as k_{ho} increases.

It is possible that ArO−C homolysis involves an intramolecular electron transfer from the easily oxidized para-substituted phenoxy groups (Y = CH_3 and OCH_3), which would produce an anion radical/cation radical intermediate (Scheme 7). The electron transfer from the phenolic group would be energetically feasible. This step could be exergonic by 10−14 kcal mol^{-1} for **5a**,**b** (Y = CH_3, OCH_3) in CH_3CN, based on our measured reduction potential of *N*,*N*-diethyl-2-oxopropanamide of −1.85 V in CH_3CN (SCE) and the oxidation potentials of 1,4-$CH_3C_6H_4OCH_3$ (1.52 V, SCE[18a]) and 1,4-$CH_3OC_6H_4OCH_3$ (1.34 V vs SCE[18b]) as model compounds. The estimate uses an excited state energy of 79 kcal mol^{-1}, which would be the $^1n,\pi^*$ excited state of pyruvamide.[19] The multiplicity of the reactive excited state in α-keto amide photochemistry is not known for certain.[9] If the lowest $^3n,\pi^*$ (pyruvamide, E_T = ca. 67−69 kcal mol^{-1} [19]) is instead involved, then $\Delta G° = -2$ to 0 or −2 to −4 kcal mol^{-1} for Y = CH_3 and OCH_3, respectively.

Conclusion

Photolyses of **5a**,**b** with a variety of phenolic leaving groups, 4-$YC_6H_4O^-$, in aqueous CH_3CN results in photoelimination of the phenolate leaving group for para EWG or H. 1,3-Photorearrangement of the phenolic group occurs for para EDG. In both cases, the photoreactions are efficient under aqueous conditions, with total quantum yields of 0.2−0.3. The zwitterionic intermediates **8a**,**b** are postulated as the key intermediates in the photoelimination of the phenolate anions. Direct cyclization of these intermediates to give oxazolidinones which retain the leaving group is observed in nonaqueous media such as CH_3CN, CH_2Cl_2, or benzene. For those para-substituted phenolate groups with electron releasing substituents (Y = CH_3, OCH_3), 1,3-photorearrangement at the phenolic substituent becomes an important even predominant photoprocess. Laser flash photolyses show that the mechanism likely involves excited state homolysis to radicals which recombine. The homolytic cleavage could occur directly in the excited state or via a photoinduced electron-transfer mechanism with those para-substituted phenols that are good electron donors.

Experimental Section

Preparation of *N*,*N*-Diethyl-3-(4-methylphenoxy)-2-oxopropanamide 5a (LG$^-$ = 4-$CH_3C_6H_4O^-$). To 80 mL of freshly distilled THF in a 250 mL three-neck round-bottom flask cooled in dry ice−acetone bath under nitrogen was added 60.0 mL (120 mmol) of 2 M LDA in THF via a long-needle syringe. To the stirred LDA at −72 °C was added 10.0 g (60.0 mmol) of 4-methylphenoxyacetic acid in 60 mL of THF during 15 min. After 40 min of reaction, 10.0 g (58.0 mmol) of ethyl *N*,*N*-diethyloxamate, dissolved in the 40 mL of THF, was added dropwise to the mixture over 2 min. After 30 min, the ice bath was removed. The reaction was allowed to warm to room temperature, 50 mL of 2 N HCl was added to the solution to adjust the pH to 1, and then 50 mL of concentrated HCl was added. After the reaction was stirred for 30 min, 80 mL of ether was added, and the aqueous phase, which was separated, was extracted by 80 mL of ether. The combined ether extracts were washed twice by 40 mL of water, twice by 40 mL of 2 N NaOH, and once by saturated NaCl, then dried over Na_2SO_4. After concentration in vacuo, the residue was purified by medium-pressure liquid chromatography on 230−400 mesh silica gel (MPLC), eluting with 10% EtOAc in hexane to give 9.3 g (62% yield) of product as colorless oil. The spectral data were as follows: ^{1}H NMR ($CDCl_3$) δ 1.21(t, J = 7.2 Hz, 3H), 1.22 (t, J = 7.2 Hz, 3H), 2.30 (s, 3H), 3.35 (q, J = 7.2 Hz, 2H), 3.44 (q, J = 7.2 Hz, 2H), 5.03 (s, 2H), 6.81(d, J = 9.0 Hz, 2H), 7.07(d, J = 9.0 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 13.3, 15.2, 21.2, 40.3, 42.6, 71.2, 114.2, 129.7, 130.8, 154.9, 163.9, 195.0. Anal. Calcd for $C_{14}H_{19}NO_3$: C, 67.45; H, 7.68; N, 5.62. Found: C, 67.18; H, 7.96; N, 5.34.

Preparation of *N*,*N*-Diethyl-2-oxo-3-phenoxypropanamide 5a (LG$^-$ = $C_6H_5O^-$). The same method as that used for the synthesis of *N*,*N*-diethyl-3-(4-methylphenoxy)-2-oxopropanamide **5a** (LG$^-$ = 4-$CH_3C_6H_4O^-$) was used to prepare 3.0 g (47% yield) of *N*,*N*-diethyl-2-oxo-3-phenoxypropanamide **5a** (LG$^-$ = $C_6H_5O^-$) from 4.7 g (27.1 mmol) of ethyl *N*,*N*-diethyloxamate and 5.0 g (32.0 mmol) of phenoxyacetic acid. The spectral data were as follows: ^{1}H NMR ($CDCl_3$) δ 1.17 (t, J = 7.2 Hz, 3 H), 1.21 (t, J = 7.2 Hz, 3 H), 3.33 (q, J = 7.2 Hz, 2H), 3.43 (q, J = 7.2 Hz, 2H), 5.05 (s, 2H), 6.91 (d, J = 8.2 Hz, 1 H), 6.99 (t, J = 8.0, 2.7 Hz, 1H), 7.28 (t, J = 8.2 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 12.9, 14.8, 40.3, 42.5, 67.5, 128.7, 130.1, 133.7, 164.1, 166.2, 193.2. Anal. Calcd for $C_{13}H_{17}NO_3$: C, 66.36; H, 7.28; N, 5.95. Found: C, 66.09; H, 7.07; N, 6.02.

Preparation of *N*,*N*-Diethyl-3-(4-methoxyphenoxy)-2-oxopropanamide 5a (LG$^-$ = 4-$CH_3OC_6H_4O^-$). The same method as that used for the synthesis of *N*,*N*-diethyl-3-(4-methylphenoxy)-2-oxopropanamide **5a** (LG$^-$ = 4-$CH_3C_6H_4O^-$) was used to prepare 5.0 g (56% yield) of α-keto amide **5a** (LG$^-$ = 4-$CH_3OC_6H_4O^-$)

(18) (a) Dileesh, S.; Gopidas, K. R. *J. Photochem. Photobiol., A* **2004**, *162*, 115−120. (b) Rathore, R.; Kochi, J. K. *Adv. Phys. Org. Chem.* **2000**, *35*, 193−317.

(19) Larson, Donald B.; Arnett, J. F.; Seliskar, C. J.; McGlynn, S. P. *J. Am. Chem. Soc.* **1974**, *96*, 3370−3380.

from 6.5 g (37.5 mmol) of ethyl *N*,*N*-diethyloxamate and 8.0 g (43.9 mmol) of *p*-methoxyphenoxyacetic acid. The product was a colorless oil. The spectral data were as follows: ^{1}H NMR ($CDCl_3$) δ 1.21 (t, J = 7.2 Hz, 3H), 1.23 (t, J = 7.2 Hz, 3H), 3.34 (q, J = 7.2 Hz, 2H), 3.45 (q, J = 7.2 Hz, 2H), 3.77 (s, 3H), 5.01 (s, 2H), 6.84 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 13.4, 15.2, 40.4, 42.7, 56.1, 72.0, 114.5, 115.6, 151.3, 154.0, 164.0, 195.2. Anal. Calcd for $C_{14}H_{19}NO_4$: C, 63.38; H, 7.22; N, 5.28. Found: C, 63.36; H, 7.53; N, 5.10.

Preparation of *N*,*N*-Diethyl-3-(4-cyanophenoxy)-2-oxopropanamide 5a (LG$^-$ = 4-CNC$_6$H$_4$O$^-$). The same method as that used for the synthesis of *N*,*N*-diethyl-3-(4-methylphenoxy)-2-oxopropanamide **5a** (LG$^-$ = 4-CH$_3$C$_6$H$_4$O$^-$) was used to prepare 6.6 g (56% yield) of α-keto amide **5a** (LG$^-$ = 4-CNC$_6$H$_4$O$^-$) from 7.8 g (45.1 mmol) of ethyl *N*,*N*-diethyloxamate and 9.8 g (55.0 mmol) of *p*-cyanophenoxyacetic acid.[20] The product was obtained as a colorless solid, mp 77−79 °C after MPLC, eluting with 50% EtOAc in hexane. The spectral data were as follows: ^{1}H NMR ($CDCl_3$) δ 1.21 (t, J = 7.2 Hz, 3H), 1.23 (t, J = 7.2 Hz, 3H), 3.39 (q, J = 7.2 Hz, 2H), 3.46 (q, J = 7.2 Hz, 2H), 5.18 (s, 2H), 6.98 (d, J = 8.7 Hz, 2H), 7.61 (d, J = 8.7 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 12.9, 14.9, 40.6, 42.6, 70.9, 105.4, 115.4, 119.0, 134.3, 160.9, 163.7, 193.7. Anal. Calcd for $C_{14}H_{16}N_2O_4$: C, 64.60; H, 6.19; N, 10.76. Found: C, 64.39; H, 6.23; N, 10.59.

Preparation of *N*,*N*-Diethyl-3-(4-trifluoromethylphenoxy)-2-oxapropanamide 5a (LG$^-$ = 4-CF$_3$C$_6$H$_4$O$^-$). The same method as that used for the synthesis of *N*,*N*-diethyl-3-(4-methylphenoxy)-2-oxopropanamide **5a** (LG$^-$ = 4-CH$_3$C$_6$H$_4$O$^-$) was used to prepare 4.5 g (80% yield) of α-keto amide **5a** (LG$^-$ = 4-CF$_3$C$_6$H$_4$O$^-$) from 3.9 g (22.5 mmol) of ethyl *N*,*N*-diethyloxamate and 5.0 g (29.4 mmol) of *p*-trifluoromethylphenoxyacetic acid.[21] The product was a colorless oil, after MPLC, eluting with 50% EtOAc in hexane. The spectral data were as follows: ^{1}H NMR ($CDCl_3$) δ 1.20(t, J = 6.9 Hz, 3H), 1.22 (t, J = 7.2 Hz, 3H), 3.37 (q, J = 6.9 Hz, 2H), 3.45 (q, J = 7.2 Hz, 2H), 5.14 (s, 2H), 6.98 (d, J = 9.0 Hz, 2H), 7.54 (d, J = 9.0 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 12.8, 14.8, 40.4, 42.5, 70.9, 115.0, 124.1 (q, J = 32.7 Hz, 1C), 124.3 (q, J = 269.1 Hz, 1C), 127.2 (q, J = 3.8 Hz, 1C), 160.0, 164.0, 194.4. Anal. Calcd for $C_{14}H_{16}F_3NO_3$: C, 55.45; H, 5.32; N, 4.62. Found: C, 55.40; H, 5.39; N, 4.45.

Preparation of *N*,*N*-Diisopropyl-2-oxo-3-phenoxypropanamide 5b (LG$^-$ = C$_6$H$_5$O$^-$).[12] The same method as that used for the synthesis of *N*,*N*-diethyl-3-(4-methylphenoxy)-2-oxopropanamide **5a** (LG$^-$ = 4-CH$_3$C$_6$H$_4$O$^-$) was used to prepare 1.4 g (yield 30%) of *N*,*N*-diisopropyl-3-phenoxy-2-oxopropanamide **5b** (LG$^-$ = C$_6$H$_5$O$^-$) from 3.6 g (18 mmol) of *N*,*N*-diisopropyloxamate and 3.0 g (20 mmol) of phenoxyacetic acid. The product was obtained as a colorless oil after MPLC, eluting with 10% EtOAc in hexane. The spectral data were as follows: ^{1}H NMR ($CDCl_3$) δ 1.18 (d, J = 7.2 Hz, 6H), 1.50 (d, J = 7.2 Hz, 6H), 3.50 (septet, J = 7.2 Hz, 1H), 3.78 (septet J = 7.2 Hz, 1H), 4.96 (s, 2H), 6.92 (d, J = 8.5 Hz, 1H), 6.98 (t, J = 8.0 Hz, 1H), 7.30 (t, J = 8.2 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 20.4, 20.9, 46.4, 50.3, 70.7, 114.6, 122.0, 129.8, 157.6, 165.7, 196.4. Anal. Calcd for $C_{15}H_{21}NO_3$: C, 68.41; H, 8.04; N, 5.32. Found: C, 68.48; H, 8.15; N, 5.10.

Preparation of *N*,*N*-Diisopropyl-3-(4-methoxyphenoxy)-2-oxopropanamide 5b (LG$^-$ = 4-CH$_3$OC$_6$H$_4$O$^-$). The same method as that used for the synthesis of *N*,*N*-diethyl-3-(4-methylphenoxy)-2-oxopropanamide **5a** (LG$^-$ = 4-CH$_3$C$_6$H$_4$O$^-$) was used to prepare 5.7 g (78% yield) of α-keto amide **5b** (LG$^-$ = 4-CH$_3$OC$_6$H$_4$O$^-$) from 5.0 g (25.0 mmol) of ethyl *N*,*N*-diisopropyloxamate and 5.2 g (28.6 mmol) of *p*-methoxyphenoxyacetic acid. The product was a obtained as a colorless solid, mp 56−57 °C, by MPLC, eluting with 10% EtOAc in hexanes. The spectral data were as follows: ^{1}H NMR ($CDCl_3$) δ 1.19(d, J = 7.2 Hz, 6H), 1.45 (d, J = 7.2 Hz, 6H), 3.53 (septet, J = 7.2 Hz, 1H), 3.76 (s, 3H), 3.79 (septet J = 7.2 Hz, 1H), 4.87 (s, 2H), 6.84 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 20.4, 21.0, 49.4, 50.3, 55.9, 71.6, 114.9, 115.7, 151.9, 154.6, 165.9, 196.8. Anal. Calcd for $C_{16}H_{23}NO_4$: C, 65.51; H, 7.90; N, 4.77. Found: C, 65.76; H, 8.21; N, 4.52.

Preparation of *N*,*N*-Diisopropyl-3-(4-methylphenoxy)-2-oxopropanamide 5b (LG$^-$ = 4-CH$_3$C$_6$H$_4$O$^-$). The same method as that used for the synthesis of *N*,*N*-diethyl-3-(4-methylphenoxy)-2-oxopropanamide **5a** (LG$^-$ = 4-CH$_3$C$_6$H$_4$O$^-$) was used to prepare 6.1 g (73% yield) of α-keto amide **5b** (LG$^-$ = 4-CH$_3$C$_6$H$_4$O$^-$) from 6.0 g (30.0 mmol) of ethyl *N*,*N*-diisopropyloxamate and 5.8 g (35.0 mmol) of *p*-methylphenoxyacetic acid. The product was obtained as a colorless solid, mp 80−82 °C, after MPLC, eluting with 10% EtOAc in hexane. The spectral data were as follows: ^{1}H NMR ($CDCl_3$) δ 1.18 (d, J = 7.2 Hz, 6H), 1.46 (d, J = 7.2 Hz, 6H), 2.28 (s, 3H), 3.52 (septet, J = 7.2 Hz, 1H), 3.79 (septet J = 7.2 Hz, 1H), 4.89 (s, 2H), 6.81 (d, J = 8.4 Hz, 2H), 7.08 (d, J = 8.4 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 20.4, 20.8, 20.9, 46.4, 50.3, 71.0, 114.5, 130.2, 131.3, 155.6, 165.8, 196.7. Anal. Calcd for $C_{16}H_{23}NO_3$: C, 69.29; H, 8.36; N, 5.05. Found: C, 69.55; H, 8.43; N, 4.95.

Preparation of *N*,*N*-Diisopropyl-3-(4-cyanophenoxy)-2-oxopropanamide 5b (LG$^-$ = 4-CNC$_6$H$_4$O$^-$). The same method as that used for the synthesis of *N*,*N*-diethyl-3-(4-methylphenoxy)-2-oxopropanamide **5a** (LG$^-$ = 4-CH$_3$C$_6$H$_4$O$^-$) was used to prepare 4.6 g (76% yield) of α-keto amide **5b** (LG$^-$ = 4-CNC$_6$H$_4$O$^-$) from 4.2 g (21.0 mmol) of ethyl *N*,*N*-diisopropyloxamate and 4.2 g (24.0 mmol) of *p*-cyanophenoxyacetic acid.[20] The product was obtained as a colorless solid, mp 79−82 °C, after MPLC, eluting with 50% EtOAc in hexane. The spectral data were as follows: ^{1}H NMR ($CDCl_3$) δ 1.21 (d, J = 7.2 Hz, 6H), 1.44 (d, J = 7.2 Hz, 6H), 3.55 (septet, J = 7.2 Hz, 1H), 3.83 (septet, J = 7.2 Hz, 1H), 5.03 (s, 2H), 6.98 (d, J = 8.4 Hz, 2H), 7.60 (d, J = 8.4 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 20.4, 21.0, 47.2, 50.3, 70.7, 105.5, 115.4, 119.0, 134.3, 160.8, 165.2, 194.4. Anal. Calcd for $C_{16}H_{22}N_2O_3$: C, 66.18; H, 7.63; N, 9.65. Found: C, 66.40; H, 7.36; N, 9.59.

Preparation of *N*,*N*-Diisopropyl-3-benzyloxy-2-oxopropanamide 19. The same method as that used for the synthesis of **5a** (LG$^-$ = 4-CH$_3$C$_6$H$_4$O$^-$) was used to prepare 4.7 g (74% yield) of α-keto amide **19** from 3.9 g (19.0 mmol) of *N*,*N*-diisopropyloxamate and 3.8 g (23.0 mmol) of benzyloxyacetic acid.[22] The product was a colorless oil. The spectral data were as follows: ^{1}H NMR ($CDCl_3$) δ 1.17 (d, J = 6.6 Hz, 6H), 1.43 (d, J = 6.9 Hz, 6H), 3.49 (septet, J = 7.2 Hz, 1H), 3.72 (septet, J = 7.2 Hz, 1H), 4.39 (s, 2H), 4.64 (s, 2H), 7.33 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 20.3, 20.9, 46.2, 50.1, 73.0, 74.1, 128.0, 128.1, 128.5, 137.0, 166.5, 198.5. Anal. Calcd for $C_{16}H_{23}NO_3$: C, 69.29; H, 8.36; N, 5.05. Found: C, 69.20; H, 8.44; N, 4.83.

Preparative Photolyses of α-Keto Amides 5a (LG$^-$ = C$_6$H$_5$O$^-$, 4-CNC$_6$H$_4$O$^-$, 4-F$_3$CC$_6$H$_4$O$^-$) in Aqueous CH$_3$CN. A solution of 0.86 g (3.6 mmol) of **5a** (LG$^-$ = C$_6$H$_5$O$^-$) in 25 mL of 33% aqueous acetonitrile in a quartz tube was irradiated through a Pyrex filter with a Hanovia 450 W medium-pressure mercury lamp for 2 h at room temperature. NMR analysis of an aliquot showed over 70−90% conversion. The photolyzate was extracted three times with ethyl acetate. After concentration in vacuo the oxazolidinone **7a**, diastereomeric hemiacetals **6a**, and the phenol were isolated by MPLC, eluting with 10% EtOAc in hexane (Table 1). A similar procedure was used for the photolyses of **5a** (LG$^-$ = 4-CNC$_6$H$_4$O$^-$, 4-CF$_3$C$_6$H$_4$O$^-$).

Preparative Photolyses of α-Keto Amides 5a (LG$^-$ = 4-CH$_3$OC$_6$H$_4$O$^-$, 4-CH$_3$C$_6$H$_4$O$^-$) in Aqueous CH$_3$CN. A solution of 4.0 mmol of **5a** (LG$^-$ = 4-CH$_3$OC$_6$H$_4$O$^-$ or 4-CH$_3$C$_6$H$_4$O$^-$) in 25 mL of 33% aqueous acetonitrile in a quartz tube was irradiated through a Pyrex filter with a Hanovia 450 W medium-pressure mercury lamp for 3 h at room temperature. The photolyzate was

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extracted three times with ethyl acetate and concentrated in vacuo. Only a trace amount of oxazolidinone **7a** and the para-substituted phenol were isolated by MPLC, eluting with 10% EtOAc in hexane. The major products isolated were 1,3-rearrangement products **12a** (Y = CH_3O, CH_3), which were colorless oils that readily underwent further oxidation to **16a** (Y = CH_3O, CH_3). The spectral data of **12a** (Y = CH_3O) were as follows: ^{1}H NMR ($CDCl_3$) δ 1.08 (t, J = 7.2 Hz, 3H), 1.11 (t, J = 7.2 Hz, 3H), 3.27 (q, J = 7.2 Hz, 2H), 3.36 (q, J = 7.2 Hz, 2H), 3.74 (s, 3H), 3.95 (s, 2H), 6.68 (d, J = 3.0 Hz, 1H), 6.74 (dd, J = 3.0, 8.7 Hz, 1H), 6.88 (d, J = 8.7 Hz, 1H), 7.46 (br, 1H); ^{13}C NMR ($CDCl_3$) δ 12.7, 14.8, 41.1, 42.7, 42.9, 56.1, 115.1, 116.3, 119.5, 120.5, 148.9, 154.0, 166.3, 196.4.

The spectral data of **12a** (Y = CH_3) were as follows: ^{1}H NMR ($CDCl_3$) δ 1.10 (t, J = 7.2 Hz, 3H), 1.11 (t, J = 7.2 Hz, 3H), 2.25 (s, 3H), 3.27 (q, J = 7.2 Hz, 2H), 3.37 (q, J = 7.2 Hz, 2H), 3.94 (s, 2H), 6.82 (d, J = 8.1 Hz, 1H), 6.95 (s, 1H), 6.98 (d, J = 8.1 Hz, 1H), 7.62 (br, 1H); ^{13}C NMR ($CDCl_3$) δ 12.6, 14.6, 40.8, 42.3, 42.8, 117.9, 119.2, 130.1, 130.4, 132.0, 152.6, 166.4, 196.8.

In solution, compound **12a** (Y = CH_3) was slowly oxidized in air to form **16a** (Y = CH_3), which was obtained as a colorless solid, mp 140−143 °C, after MPLC, eluting with 50% EtOAc in hexanes. The spectral data of **16a** (Y = CH_3) were as follows: ^{1}H NMR ($CDCl_3$) δ 0.99 (t, J = 7.2 Hz, 3H), 1.20 (t, J = 7.2 Hz, 3H), 2.38 (s, 3H), 2.84 (q, J = 7.2 Hz, 1H), 2.91 (q, J = 7.2 Hz, 1H), 3.43 (dq, J = 14.0, 7.2 Hz, 1H), 3.49 (dq, J = 14.0, 7.2 Hz, 2H), 7.03 (s, OH), 7.04 (dd, J = 0.9, 8.1 Hz, 1H), 7.49 (dd, J = 8.1, 0.9 Hz, 1H), 7.51(s, 1H); ^{13}C NMR ($CDCl_3$) δ 12.7, 13.5, 21.0, 42.8, 42.3, 98.2, 113.5, 118.9, 124.9, 133.9, 140.4, 164.7, 168.9, 195.4. MS (*m*/*z*) 263 (0.44), 235 (1.5), 163 (4.5), 135 (16.5), 100 (100), 72 (73.1), 78 (12.1), 44 (21.1). Anal. Calcd for $C_{14}H_{17}NO_4$: C, 63.86, H, 6.51; N, 5.32. Found: C, 63.62; H, 6.59; N, 5.14.

In solution, compound **12a** (Y = CH_3O) was slowly oxidized in air to form **16a** (Y = CH_3O), which was obtained as a colorless solid, mp 120−122 °C, after MPLC, eluting with 50% EtOAc in hexane. The spectral data of **16a** (Y = CH_3O) were as follows: ^{1}H NMR ($CDCl_3$) δ 1.00 (t, J = 7.2 Hz, 3H), 1.20 (t, J = 7.2 Hz, 3H), 2.85 (q, J = 7.2 Hz, 1H), 2.92 (q, J = 7.2 Hz, 1H), 3.43 (dq, J = 14.0, 7.2 Hz, 1H), 3.49 (dq, J = 14.0, 7.2 Hz, 1H), 3.83 (s, 3H), 7.04 (s, OH), 7.06 (d, J = 8.7 Hz, 1H), 7.12 (d, J = 3.0 Hz, 1H), 7.30 (dd, J = 3.0, 8.7 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 12.7, 13.5, 42.3, 42.8, 56.2, 98.7, 105.5, 114.8, 118.9, 128.7, 155.8, 164.4, 165.7, 195.6. MS (*m*/*z*) 279, 251, 179, 151, 108, 100 (100), 79, 72. Anal. Calcd for $C_{14}H_{17}NO_5$: C, 60.21, H, 6.13; N, 5.01. Found: C, 60.35; H, 6.16; N, 5.14.

Preparative Photolysis of α-Keto Amide 5b (LG$^-$ = 4-$CH_3OC_6H_4O^-$, 4-$CH_3C_6H_4O^-$) in Aqueous CH_3CN. A solution of 3.0 mmol of **5b** (LG$^-$ = 4-$CH_3OC_6H_4O^-$, 4-$CH_3C_6H_4O^-$) in 25 mL of 33% aqueous acetonitrile in a quartz tube was irradiated through a Pyrex filter with a Hanovia 450 W medium-pressure mercury lamp for 3 h at room temperature. For **5b** (4-$CH_3C_6H_4O^-$), the photolyzate was extracted three times with ethyl acetate and concentrated in vacuo. The major product, oxazolidinone **7b**, and 4-$CH_3C_6H_4OH$ were isolated by MPLC. A small amount of **12b** (Y = CH_3) was obtained, which could not be further purified by MPLC. For **5b** (LG$^-$ = 4-$CH_3OC_6H_4O^-$) the major product was the 1,3-rearrangement product **12b** (Y = CH_3O), which was obtained as a colorless oil by MPLC, eluting with 10% ethyl acetate in hexane. The spectral data of **12b** (Y = CH_3O) were as follows: ^{1}H NMR ($CDCl_3$) δ 0.99 (d, J = 6.9 Hz, 6H), 1.32 (d, J = 6.9 Hz, 6H), 3.38 (septet, J = 6.9 Hz, 1H), 3.74 (s, 3H), 3.76 (septet J = 6.9 Hz, 1H), 3.91 (s, 2H), 6.66 (d, J = 3.0 Hz, 1H), 6.76 (dd, J = 3.0, 8.7 Hz, 1H), 6.91 (d, J = 8.7 Hz, 1H), 7.02 (br s, 1 H); ^{13}C NMR ($CDCl_3$) δ 20.1, 20.7, 42.5, 46.7, 50.5, 56.0, 115.2, 116.2, 120.0, 120.5, 148.7, 154.2, 168.2, 196.5. Anal. Calcd for $C_{16}H_{23}NO_4$: C, 65.51; H, 7.90; N, 4.77. Found: C, 65.15; H, 7.72; N, 4.78.

Preparative Photolysis of *N*,*N*-Diisopropyl-3-benzyloxy-2-oxopropanamide 19 (LG$^-$ = $C_6H_5CH_2O^-$) in Aqueous CH_3CN. A solution of 0.5 g (3.6 mmol) of **19** (LG$^-$ = $C_6H_5CH_2O^-$) in 25 mL of 33% aqueous acetonitrile in a quartz tube was irradiated through a Pyrex filter with a Hanovia 450 W medium-pressure mercury lamp for 2 h at room temperature. The photolyzate was extracted three times with EtOAc. After concentration in vacuo, the oxazolidinone **20** was isolated as a colorless oil by MPLC, eluting with 10% EtOAc in hexane. The spectral data were as follows: ^{1}H NMR ($CDCl_3$) δ 1.42 (d, J = 7.2 Hz, 3 H), 1.44 (s, 3 H), 1.45 (d, J = 7.2 Hz, 3 H), 1.49 (s, 3 H), 3.36 (septet, J = 7.2 Hz, 1 H), 3.69 (dd, J = 5.1, 10.5 Hz, 1 H), 3.77 (dd, J = 2.4, 10.5 Hz, 1 H), 4.39 (dd, J = 2.4, 5.1 Hz, 1 H), 4.55 (d, J = 12.3 Hz, 1 H), 4.63 (d, J = 12.3 Hz, 1 H), 7.31 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 20.2, 20.5, 27.1, 27.5, 49.1, 70.3, 70.6, 76.8, 95.2, 127.6, 127.6, 128.3, 138.1, 168.2. Anal. Calcd for $C_{16}H_{23}NO_3$: C, 69.29; H, 8.36; N, 5.05. Found: C, 68.90; H, 8.08; N, 5.05.

Preparative Photolysis of α-Keto Amide 5a (LG$^-$ = $C_6H_5O^-$) in CH_3CN. A solution of 1.0 g (4.25 mmol) of **5a** (LG$^-$ = $C_6H_5O^-$) in 30 mL of CH_3CN in a quartz tube mounted beside a water-jacketed Hanovia 450 W medium-pressure mercury lamp was irradiated through a Pyrex filter for several hours at room temperature until no starting material remained. The photolyzate was concentrated in vacuo. MPLC of the residue, eluting with 10% EtOAc in hexane, gave a major diastereomer of a photoproduct containing a minor diastereomer, which eluted in the leading edge of the peak. The major diastereomer was rechromatographed five times, cutting the leading edge of the peak each time, to obtain 0.26 g (26% yield) of pure major diastereomer of the cyclization product **13a** (LG$^-$ = $C_6H_5O^-$) as colorless crystals, mp 63.0−64.5 °C. The minor diastereomer was rechromatographed six times, cutting the trailing edge of the peak each time, to obtain 60 mg (6.0% yield) of NMR pure minor diastereomer of the cyclization product as an oil.

The spectral data of the major diastereomer of the cyclization product **13a** (LG$^-$ = $C_6H_5O^-$) were as follows: ^{1}H NMR ($CDCl_3$) δ 1.18 (t, J = 7.2 Hz, 3 H), 1.48 (d, J = 5.4 Hz, 3 H), 3.20 (m, 1 H), 3.58 (m, 1 H), 4.24 (m, 1H), 4.58 (m, 1H), 5.31 (m, 1H), 6.91 (d, J = 9.0 Hz, 2H), 6.93 (t, J = 9.0 Hz, 1H), 7.25 (t, J = 9.0 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 13.4, 21.4, 35.0, 67.9, 77.4, 87.0, 114.8, 121.2, 129.5, 158.5, 168.1. Anal. Calcd for $C_{13}H_{17}NO_3$: C, 66.36; H, 7.28; N, 5.95. Found: C, 66.23 H, 7.28; N, 5.98.

The spectral data of the minor diastereomer of the cyclization product **13a** (LG$^-$ = $C_6H_5O^-$) were as follows: ^{1}H NMR ($CDCl_3$) δ 1.19 (t, J = 7.2 Hz, 3 H), 1.44 (d, J = 5.4 Hz, 3 H), 3.11(m, 1 H), 3.67 (m, 1 H), 4.27 (d, J = 3.0 Hz, 2 H), 4.66(q, J = 3.0 Hz, 1H), 5.43 (m, 1H), 6.86 (d, J = 9.0 Hz, 2H), 6.93 (t, J = 9.0 Hz, 1H), 7.25 (t, J = 9.0 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 13.1, 21.2, 35.0, 68.5, 77.0, 87.6, 114.7, 121.3, 129.5, 158.4, 168.7.

Preparative Photolysis of α-Keto Amide 5b (LG$^-$ = $C_6H_5O^-$) in CH_3CN. A solution of 1.2 g (4.56 mmol) of **5b** (LG$^-$ = $C_6H_4O^-$) in 30 mL of CH_3CN in a quartz tube mounted beside a water-jacketed Hanovia 450 W medium-pressure mercury lamp was irradiated through a Pyrex filter for several hours at room temperature. The photolyzate was concentrated in vacuo. MPLC of the residue eluting with 20% EtOAc in hexane gave unreacted **5b** (LG$^-$ = $C_6H_5O^-$) together with methyleneoxazolidinone **7b**, followed by 0.27 g (23% yield) of NMR pure cyclization product **13b** (LG$^-$ = $C_6H_5O^-$) as an oil.

The spectral data of cyclization product **13b** (LG$^-$ = $C_6H_5O^-$) were as follows: ^{1}H NMR ($CDCl_3$) δ 1.62 (s, 3 H), 1.64 (s, 3 H), 1.73 (s, 3 H), 1.84 (s, 3 H), 3.92 (m, 1H), 4.54 (s, 2 H, in CD_3CN, m), 7.16 (d, J = 7.2 Hz, 2H), 7.24 (d, J = 7.2 Hz, 1H), 7.63 (t, J = 7.2 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 21.9, 22.1, 23.3, 44.2, 66.2, 67.8, 85.0, 114.7, 121.5, 129.6, 158.4, 167.6.

Preparative Photolysis of α-Keto Amide 5a (LG$^-$ = 4-$CNC_6H_5O^-$) in C_6H_6. A solution of 0.30 g (1.2 mmol) of **5a** (LG$^-$ = 4-CN $C_6H_5O^-$) in 20 mL of C_6H_6 in a quartz tube mounted beside a water-jacketed Hanovia 450 W medium-pressure mercury lamp was irradiated through a Pyrex filter for several hours at room temperature until no starting material remained. The photolyzate was concentrated in vacuo. MPLC of the residue, eluting with 50%

EtOAc in hexane, gave 0.10 g (33% yield) of pure cyclization product **13a** ($LG^- = 4\text{-}CNC_6H_5O^-$) as colorless liquid.

The spectral data of the cyclization product **13a** ($LG^- = 4\text{-}CNC_6H_5O^-$) were as follows: ^1H NMR ($CDCl_3$) δ 1.19 (t, J = 7.2 Hz, 3 H), 1.46 (d, J = 5.1 Hz, 3 H), 3.21 (m, 1 H), 3.58 (m, 1 H), 4.29 (m, 1H), 4.59(m, 1H), 5.32 (m, 1H), 6.97 (d, J = 9.0 Hz, 2H), 7.57 (d, J = 9.0 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 13.2, 21.3, 35.1, 68.0, 77.1, 87.0, 104.8, 115.6, 119.2, 134.2, 161.9, 167.8.

Preparative Photolysis of α-Keto Amide 5b ($LG^- = 4\text{-}CNC_6H_4O^-$) in CH_2Cl_2. A solution of 0.80 g (2.77 mmol) of **5b** ($LG^- = 4\text{-}CNC_6H_4O^-$) in 20 mL of CH_2Cl_2 in a quartz tube mounted beside a water-jacketed Hanovia 450 W medium-pressure mercury lamp was irradiated through a Pyrex filter for several hours at room temperature. The photolyzate was concentrated in vacuo. MPLC of the residue eluting with 60% EtOAc in hexane gave, in order of elution, unreacted starting material **5b** ($LG^- = 4\text{-}CNC_6H_4O^-$) together with methyleneoxazolidinone **7b**, followed by 0.16 mg (20% yield) of NMR pure cyclization product **13b** ($LG^- = 4\text{-}CNC_6H_4O^-$) as an oil.

The spectral data of the cyclization product **13b** ($LG^- = 4\text{-}CNC_6H_4O^-$) were as follows: ^1H NMR ($CDCl_3$) δ 1.44 (d, J = 6.9 Hz, 3 H), 1.46 (d, J = 6.9 Hz, 3 H), 1.47 (s, 3 H), 1.50 (s, 3 H), 3.43 (m, 2H), 4.54 (m, 1 H), 6.91 (d, J = 9.0 Hz, 2H), 7.50 (d, J = 9.0 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 20.1, 20.5, 27.2, 27.5, 46.4, 68.4, 75.8, 95.8, 104.6, 115.6, 119.3, 134.2, 162.0, 167.3.

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Supporting Information Available: ^1H, ^{13}C NMR spectral data for major and minor diastereomers of **13a** ($LG^- = C_6H_5O^-$), **13b** ($LG^- = C_6H_5O^-$) in CD_3CN and $CDCl_3$, and **13a,b** ($LG^- = 4\text{-}CNC_6H_4O^-$). This material is available free of charge via the Internet at http://pubs.acs.org.

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