J. Org. Chem. 1985, 50, 3573–3580

furan with the same procedure and quenched with heavy water. The ^{2}H NMR spectrum was recorded, Figure 1 part B.

The coal was also reduced in unlabeled tetrahydrofuran and quenched with unlabeled water. No resonances were observed upfield of 7.2 ppm. Hence, the resonances observed in the spectra shown in Figure 1 originated from labeled materials.

Basic Hydrolysis of Reductively Alkylated Coal. An intermediate molecular weight fraction of the tetrahydrofuran-soluble products obtained in the reductive alkylation of Illinois No. 6 coal with 90% methyl-^{13}C iodide was hydrolyzed. The reaction product (35 mg) was treated with tetrahydrofuran (2 mL) and tetrabutylammonium hydroxide (1 mL, 40% by weight in water). This mixture was stirred at room temperature for 25 h before it was acidified with 2 N hydrochloric acid. The acidified coal product was collected and washed with water and dried under a stream of nitrogen overnight. The entire sample was dissolved in chloroform-*d* (5 mL) and the ^{13}C NMR spectrum was recorded. The resonance in region 3 at 51 ppm was reduced virtually to the base line.

Acid Hydrolysis of Reductively Alkylated Coal. A representative GPC fraction of tetrahydrofuran-soluble, hexane- and water-soluble ^{13}C-enriched reductively methylated coal (18.8 mg) was treated with hydrochloric acid (0.5 mL, 0.2 N) in tetrahydrofuran (2 mL). The mixture was stirred for five days before the coal product was isolated and dried. The entire product was dissolved in chloroform-*d* (5 mL) and the ^{13}C NMR spectrum was recorded. Replicate analyses indicated that the area of the region 1 resonance relative to the region 2 resonance was 1.61 in the product compared to 1.5 in the starting material.

Demethylation of Aryl Methyl Ethers. The methyl ether was reacted with a 5–10 molar excess of lithium iodide and an equimolar amont of naphthalene, which was used as an internal standard, in 2,4,6-collidine (5–7 mL). The solution was stirred for 48 h at 170 °C under nitrogen. The organic products were isolated in the usual way and analyzed by gas chromatography by using an OV101 column (4% on Chromosorb W, $^{1}/_{8}$ in. × 20 ft). The results for several representative compounds are summarized in Table II.

Demethylation of Reductively Methylated Coal. A portion of the tetrahydrofuran-soluble, ^{13}C-enriched reductively methylated coal (GPC fractions 18–27, 121 mg), lithium iodide (512 mg, 3.8 mmol) and 2,4,6-collidine (7 mL) were heated at 170 °C under nitrogen; the reaction proceeded for 48 h. The collidine was removed in vacuo and the coal product was collected and washed with 2 N hydrochloric acid and water to remove inorganic salts. The sample was dried in vacuo to give the product (118 mg) which was extracted with pyridine. The dried pyridine-insoluble fraction weighed 28 mg (23%). A portion of the pyridine-soluble fraction (25 mg) was dissolved in pyridine-d_5 (5 mL) and the ^{13}C NMR spectrum was recorded, Figure 3 part A.

The reaction was also carried out for 24 h. The pyridine-soluble fraction (37.4 mg) represented 92% of the recovered product (40.1 mg). A portion of the soluble product (25 mg) was dissolved in pyridine-d_5 (5 mL) and the ^{13}C NMR spectrum was recorded. The *O*-methyl signal strength decreased by 63 ± 2%.

Demethylation of Reductively Methylated Coal under Acidic Conditions. Tetrahydrofuran-soluble, hexane-insoluble, ^{13}C-enriched reductively methylated Illinois No. 6 coal (30 mg) was treated with boron trifluoride–etherate (0.1 mL) and 1,2-ethanedithiol (1.0 mL) under argon in a vial at room temperature for three days. Excess boron trifluoride and 1,2-ethanediol were removed in nitrogen. The coal product was washed with 10% aqueous sodium bicarbonate (100 mL), water (100 mL), and 95% ethanol (50 mL) to remove the residual acid and dithiol. After drying in a stream of nitrogen, the product was suspended in tetrahydrofuran and centrifuged, and the supernatant was collected. The process was repeated until the supernatant was slightly yellow. The insoluble residue was dried under nitrogen and weighed. About 95% of the demethylated coal product was soluble in tetrahydrofuran. The sample was dissolved in chloroform-*d* and the ^{13}C spectrum was recorded, Figure 3 part B.

Acknowledgment. It is a pleasure to acknowledge the support of this work by the United States Department of Energy and by the Illinois State Coal Board. The NMR equipment used in this research was purchased with funds from the National Science Foundation and the National Institutes of Health.

Registry No. Potassium naphthalene (−1), 4216-48-2; methyl iodide, 74-88-4; ethyl iodide, 75-03-6; 1-butyl iodide, 542-69-8.

Reaction of Singlet Oxygen with Enamino Carbonyl Systems. A General Method for the Synthesis of α-Keto Derivatives of Lactones, Esters, Amides, Lactams, and Ketones

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Received September 21, 1984

A general method for the introduction of a ketone α to the carbonyl group of a ketone, lactone, ester, substituted amide, or lactam has been developed involving the formation and dye-sensitized photooxygenation of enamino carbonyl intermediates.

The direct introduction of a ketone α to a carbonyl group is an important functional group transformation which has many applications in natural product synthesis.[1] The conversion of a ketone to an α-diketone, for example, has been employed in the synthesis of colchicine,[1a] strychnine,[1b] and other natural products. There have been important applications of α-keto lactam formation in synthesis, ranging from the preparation of senecio[2] and vasicine alkaloids[3] to the synthesis of β-lactams[4] and derivatives of penams and cephams.[5] In addition, there is intrinsic interest in α-ketopyrrolidones as synthetic targets, due to their reported antibiotic activity, e.g., against *Trichomonas*

[†] Present address: Pfizer, Inc., Groton, CT 06340.

(1) (a) Woodward, R. B. *Harvey Lect.* **1964**, *31*. (b) Woodward, R. B.; Cava, M. P.; Ollis, S. D.; Hunger, A.; Doeniker, H. U.; Schenker, K. *Tetrahedron* **1963**, *19*, 247. (c) Buchi, G.; MacLeod, W. D.; Padilla, J. *J. Am. Chem. Soc.* **1964**, *86*, 4438. (d) Kagawa, S.; Matsumoto, S.; Nishida, S.; Yu, S.; Morita, J.; Ichihara, A.; Shirahama, H.; Matsumoto, T. *Tetrahedron Lett.* **1969**, 3913.

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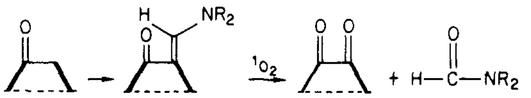
(3) (a) Southwick, P. L.; Casanova, J. *J. Am. Chem. Soc.* **1958**, *80*, 1168. (b) Southwick, P. L.; Cremer, S. E. *J. Org. Chem.* **1959**, *24*, 753. (c) Kuffner, F.; Lenneis, G.; Bauer, H. *Monatsch. Chem.* **1960**, *91*, 1152.

0022-3263/85/1950-3573$01.50/0

Scheme I



foetus and *Streptococcus aureus*.[6]

Many of the existing methods for the preparation of α-keto carbonyl systems are of limited use due to the harsh reaction conditions employed. For example, conventional reagents for oxidizing a ketone to an α-diketone, such as selenium dioxide[7] or alkyl nitrites in acid or base,[8] often lead to further oxidation or side reactions because of the inherently strong reaction conditions. More indirect methods of α-diketone synthesis, such as α-halogenation or α-oxygenation of the starting ketone followed by further oxidation, may also be limited to the most simple ketonic systems.[9]

In reviewing methods for the formation of α-keto lactones and α-keto γ-lactams, one finds an absence of general procedures for the direct introduction of the ketone group on the *intact* parent lactone or lactam. Instead, the α-ketone group is usually introduced prior to ring formation. Thus, the reported syntheses of α-keto lactones are usually limited to the condensation of α-keto esters (acids) with aldehydes followed by lactonization.[10] Many of these procedures are complicated by side reactions such as dehydration of the intermediate γ-hydroxy-α-keto acids, the self-condensation of the aldehyde component, or the dimerization of the α-keto lactone itself.[10e] The reported methods of synthesis for α-keto γ-lactams have included the condensation of ammonia (or a primary amine) with an aldehyde and an α-keto ester[11] or the condensation of β-aminopropionates with diethyl oxalate.[12] More limited alternative methods include the condensation of oxalyl acetate with cyclic imines[13] and the multistep preparation of α-keto piperidones from nicotinic acid.[4a]

Scheme II

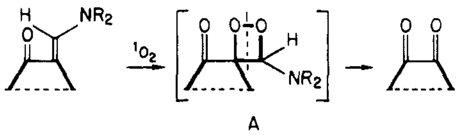
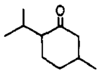
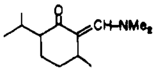
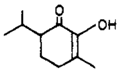
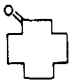
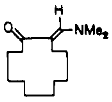
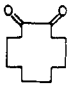
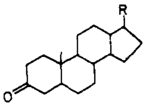
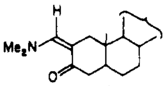
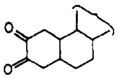
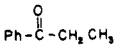
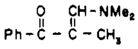
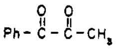
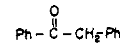
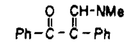
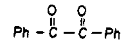
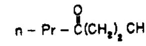
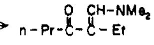
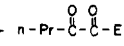


Table I. Conversion of Ketones to α-Diketones[a]

ketone	enamino ketone	α-diketone	overall yield, %
 3	$\xrightarrow[\text{55 °C, 24 h}]{1}$  9	$\xrightarrow{a}$  15	81
 4	$\xrightarrow[\text{60 °C}]{1}$  10	$\xrightarrow{a}$  16	82
 5	$\xrightarrow{1}$  11	$\xrightarrow{a}$  17	87
 $\mathrm{Ph{-}\overset{O}{\overset{\|}{C}}{-}CH_2\,CH_3}$ 6	$\xrightarrow[\text{55 °C, 18 h}]{1}$  $\mathrm{Ph{-}\overset{O}{\overset{\|}{C}}{-}\overset{CH-NMe_2}{\overset{\|}{C}}{-}CH_3}$ 12	$\xrightarrow{a}$  $\mathrm{Ph{-}\overset{O}{\overset{\|}{C}}{-}\overset{O}{\overset{\|}{C}}{-}CH_3}$ 18	68
 $\mathrm{Ph{-}\overset{O}{\overset{\|}{C}}{-}CH_2{-}Ph}$ 7	$\xrightarrow[\text{55 °C, 3 h}]{1}$  $\mathrm{Ph{-}\overset{O}{\overset{\|}{C}}{-}\overset{CH-NMe_2}{\overset{\|}{C}}{-}Ph}$ 13	$\xrightarrow{a}$  $\mathrm{Ph{-}\overset{O}{\overset{\|}{C}}{-}\overset{O}{\overset{\|}{C}}{-}Ph}$ 19	89
 $\mathrm{n{-}Pr{-}\overset{O}{\overset{\|}{C}}(CH_2)_2\,CH_3}$ 8	$\xrightarrow[\text{55 °C}]{1}$  $\mathrm{n{-}Pr{-}\overset{O}{\overset{\|}{C}}{-}\overset{CH-NMe_2}{\overset{\|}{C}}{-}Et}$ 14	$\xrightarrow{a}$  $\mathrm{n{-}Pr{-}\overset{O}{\overset{\|}{C}}{-}\overset{O}{\overset{\|}{C}}{-}Et}$ 20	74

[a] O_2, *hν*, BANT, CH_2Cl_2, −78–25 °C.

We now report the details of a general method for the introduction of a ketonic group α to a carbonyl group which is mild enough to use on complex systems containing sensitive functional groups. The method involves conversion of the starting ketone, lactone, ester, amide, or lactam to the corresponding enamino carbonyl derivative, followed by oxidative cleavage of the enamine double bond by singlet oxygen[14] (Scheme I).

Conversion of Ketones to α-Diketones. Our initial investigation involved the preparation and photooxygenation of enamino ketones derived from β-keto aldehydes. The oxidative cleavage of the carbon–carbon double bond of these vinylogous amides appeared to constitute a potentially useful method for the conversion of ketones to α-diketones. In the early stages of our work, the enamino ketones were prepared by a two-step procedure involving formylation of the starting ketone (HCO_2Et, NaH) followed by condensation with a secondary amine (Et_2NH or morpholine, anhydrous K_2CO_3, ether, 0 °C). Dye-sensitized photooxygenation of the resulting enamino ketone furnished a mixture of the corresponding α-diketone and formamide.

The photooxygenation of this series of enamino ketones yielded products analogous to those obtained in the oxidation of simple aldehyde enamines.[15] The enamino ketones presumably react with singlet oxygen (Scheme II) to form dioxetane intermediates A which decompose exclusively to form the carbon–carbon bond cleavage products—α-diketones and formamides. No additional products corresponding to dioxetane rearrangements (as reported by Rodrigo et al.)[18] or alternative pathways[16] were

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[10] (a) Meyer, K. H. *Liebigs Ann. Chem.* **1913**, *398*, 58. (b) Claisen, L. *Chem. Ber.* **1891**, *24*, 116. (c) Plattner, P. A.; Tamplosky, L. M. *Helv. Chim. Acta* **1943**, *26*, 687. (d) Schintz, H.; Hinder, M. *Ibid.* **1947**, *30*, 1349. (e) Wermuth, C. H. *Bull. Soc. Chim. Fr.* **1966**, 1435 and references cited therein. (f) Ksander, G. M.; McMurray, J. E. *Tetrahedron Lett.* **1976**, 4691.

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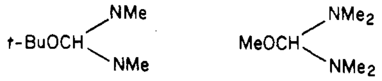
observed. In addition, the α-diketones formed were stable to the oxidation conditions and did not suffer higher oxidation or polymerization.

This two-step formylation and enamine formation sequence proved limited as a general method because of the low overall yields and the need for isolation of the intermediate β-keto aldehydes. We therefore investigated alternative methods for the direct introduction of an enamine group in a single, high yield reaction. Derivatives of dimethylformamide (DMF) are known to react with a variety of active methylene compounds to form the corresponding enamino derivatives directly. The dialkyl acetals of DMF, for example, reportedly react with systems containing strongly acidic methylene groups such as β-diketones, desoxybenzoin, acetophenones, and cyclopentadiene to yield enamino derivatives but fail to react with less activated compounds such as simple ketones.[19] An alternative class of DMF reagents was sought which would be potentially more reactive. Our search revealed that the alkoxybis(dimethylamino)methanes 1 and 2, first reported by Bredereck[20] and Emmons,[21] react with a wide variety of active methylene compounds including the systems in which we were interested. Table I lists a series of enamino ketones prepared by the use of Bredereck's reagent.


$t\text{-BuOCH}(NMe)_2$ $\quad$ $MeOCH(NMe_2)_2$

1 **2**

Our improved sequence for the conversion of ketones to α-diketones involves treatment of the starting ketone with *tert*-butoxybis(dimethylamino)methane (1) to form the intermediate enamino ketone which is then oxidized with singlet oxygen to afford the corresponding α-diketone in high overall yield. (Table I). The reaction of the diamino ethers 1 and 2 with ketones proved to be a mild, high-yield conversion which allowed the direct photooxygenation of the enamino ketone reaction mixture. By this reaction sequence the overall transformation of ketones to α-diketones required no isolation of intermediates. The high yields of α-diketone products (Table I) may be contrasted with their synthesis by using conventional reagents such as selenium dioxide[7] or alkyl nitrites.[8] For example, the oxidation of menthone (3) with selenium dioxide is reported to yield only 15% of buchucamphor (15) along with higher oxidized products.[22] In addition, 3-cholestanone (5) upon treatment with selenium dioxide reportedly gave only 30% of 2,3-cholestanedione (17).[23]

The selectivity and mildness of this transformation has been demonstrated by Ziegler and co-workers[24] in their synthetic approach to eriolangin. The rigid tricyclic intermediate (21), containing cyclopropane, silyl ether, and lactone functionalities, reacted smoothly with methoxybis(dimethylamino)methane (2) to form the desired enamino ketone 22 as a stable intermediate. Photooxygenation of this compound gave the desired α-diketone product 23 as a transient intermediate (85%) which rearranged through the enol 23 to the hydroxy lactone 48.

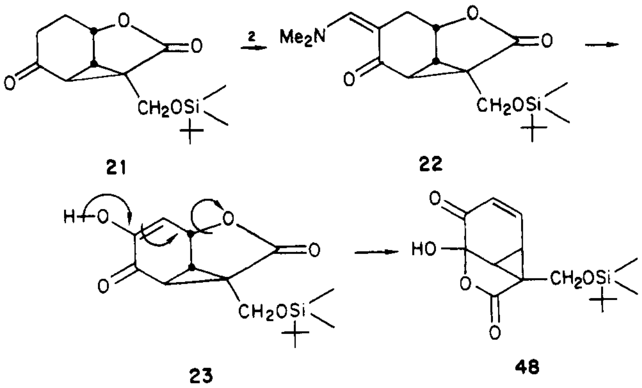
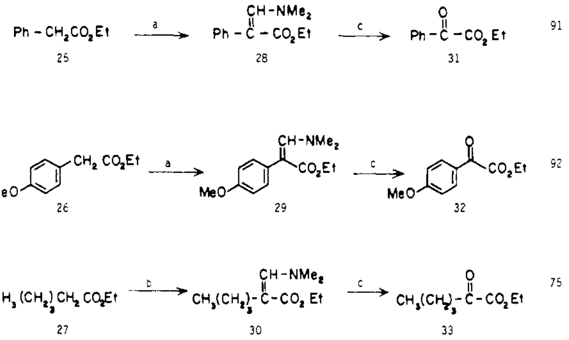


Table II. Conversion of Esters to α-Keto Esters[a]

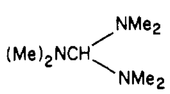


ester	enamino ester	α-keto ester	overall yield, %
$Ph-CH_2CO_2Et$ **25**	$Ph-\overset{CH-NMe_2}{\overset{\|}{C}}-CO_2Et$ **28**	$Ph-\overset{O}{\overset{\|}{C}}-CO_2Et$ **31**	91
$p\text{-}MeOC_6H_4CH_2CO_2Et$ **26**	$p\text{-}MeOC_6H_4C(=CH-NMe_2)CO_2Et$ **29**	$p\text{-}MeOC_6H_4COCO_2Et$ **32**	92
$CH_3(CH_2)_3CH_2CO_2Et$ **27**	$CH_3(CH_2)_3-\overset{CH-NMe_2}{\overset{\|}{C}}-CO_2Et$ **30**	$CH_3(CH_2)_3-\overset{O}{\overset{\|}{C}}-CO_2Et$ **33**	75

[a] a, Methoxybis(dimethylamino)methane (2), 60 °C; b, LDA, −78 °C; DMF–dimethyl sulfate adduct, 50 °C; c, O_2, *hν*, BANT, −78 °C; $CHCl_2$.

Conversion of Lactones or Esters to α-Keto Lactones or α-Keto Esters. The successful development of a method for the conversion of ketones to α-diketones led us to explore further applications of this method to lactones and esters. Initial attempts to prepare enamino lactones and esters by using similar conditions employed for the ketones failed for all but the most activated esters (phenylacetates). Prolonged heating of lactones and aliphatic esters with the bis(dimethylamino) DMF derivatives 1 and 2 at elevated temperatures gave only partial conversion to enamine derivatives.

To circumvent this problem, we employed the more reactive DMF reagent reported by Martin and Moore,[25] tris(dimethylamino)methane[26] (24) for the conversion of


$(Me)_2NCH(NMe_2)_2$

24

lactones and esters to the corresponding enamine systems. The reaction of lactones with the tris derivative 24 furnished the corresponding α-enamino derivatives which could then be oxidized smoothly by $^1O_2$ to give α-keto

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[17] (a) Ando, W.; Saiki, T.; Migita, T. *J. Am. Chem. Soc.* **1975**, *97*, 5028. (b) Wasserman, H. H.; Ives, J. L., unpublished results.

[18] Orito, K.; Manske R. H.; Rodrigo, R. *J. Am. Chem. Soc.* **1974**, *96*, 1944.

[19] (a) Arnold, Z.; Kormilov, M. *Collect. Czech. Chem. Commun.* **1964**, *29*, 645. (b) Fohlisch, B. *Chem. Ber.* **1971**, *104*, 348. (c) Meerwein, H.; Forian, W.; Schon, N.; Stopp, G. *Liebigs Ann. Chem.* **1961**, *641*, 1. (d) Buchi, G.; Carlson, J. A. *J. Am. Chem. Soc.* **1968**, *90*, 5336.

[20] Bredereck, H.; Effenberger, F.; Simchen, G. *Angew. Chem., Int. Ed. Engl.* **1962**, *1*, 331. (b) Bredereck, H.; Effenberger, F.; Simchen, G. *Chem. Ber.* **1963**, *96*, 1350. (c) Bredereck, H.; Effenberger, F.; Simchen, G. *Ibid.* **1965**, *98*, 1078. (d) Bredereck, H.; Simchen, G.; Rebsdat, S.; Katlehner, W.; Horn, P.; Wahl, R.; Hoffman, H.; Grieschaber, P. *Ibid.* **1968**, *101*, 41.

[21] Clemens, D. H.; Emmons, W. D. *J. Am. Chem. Soc.* **1961**, *83*, 2588.

[22] (a) Riley, H. L.; Morely, J. F.; Friend, N. A. C. *J. Chem. Soc.* **1932**, 1875. (b) Hirayama, S. *J. Chem. Soc. Jpn.* **1937**, *58*, 1383.

[23] Stiller, E. T.; Rosenheim, O. *J. Chem. Soc.* **1938**, 353.

[24] Ziegler, F. E.; Cady, M. A.; Nelson, R. V.; Photis, J. M. *Tetrahedron Lett.* **1979**, 2741.

[25] Martin, S. F.; Moore, D. R. *Tetrahedron Lett.* **1976**, 4459.

[26] (a) Bredereck, H.; Effenberger, F.; Brendle, T. *Angew. Chem., Int. Ed. Engl.* **1966**, *5*, 132. (b) Bredereck, H.; Effenberger, F.; Brendle, T.; Muffler, H. *Chem. Ber.* **1968**, *101*, 1885. (c) Weingarten, H.; White, W. A. *J. Am. Chem. Soc.* **1966**, *88*, 850. (d) Weingarten, H.; Edelmann, N. K. *J. Org. Chem.* **1967**, *32*, 3293.

lactones.[27] Unlike the previously described α-diketone procedure, the photooxygenation of *crude* enamino lactones gave reduced yields of α-keto lactones and necessitated isolation of the intermediate enamino lactones.

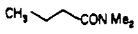
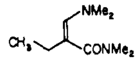
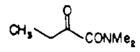
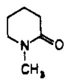
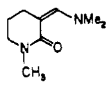
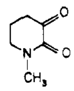
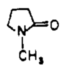
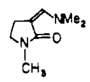
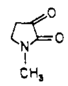
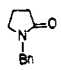
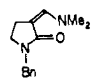
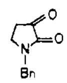
The advantage of this method over previously reported syntheses[10] of α-keto lactones is that the sequence is generally applicable to five-, six-, and larger-member lactones. This mode of introduction of the ketone on the *intact* parent lactone is mild and selective and should have general application in more complex systems.

Several esters were successfully converted to the corresponding α-keto esters by using similar chemistry (Table II). The phenylacetates (**25 and 26**) reacted readily with the DMF derivative (**2**) in high yield to give the corresponding enamino esters (**28 and 29**). Subsequent photooxygenation gave α-keto esters (**31 and 32**) in excellent yield. The less reactive ester (**27**) failed to react completely with **1** or **2** or the tris derivative (**24**) even at elevated temperatures and prolonged reaction times. We therefore employed a method reported by Hafner et al.[28] for introducing the enamine group in systems containing less reactive carbonyl groups such as the ester (**27**). Condensation of the enolate of ester **27** (LDA–78 °C) with the 1:1 adduct of DMF and dimethyl sulfate (an intermediate in the preparation of **1** and **2**) gave a good yield of enamino ester (**30**). Subsequent photooxygenation proceeded smoothly to give the desired α-keto ester (**33**).

Preparation and Photooxygenation of Enamino Lactams and Amides. The extension of our method to the synthesis of α-keto lactams and amides initially encountered unexpected difficulties both in the preparation and photooxygenation of enamino lactams and amides. Our first studies on the preparation of the enamino derivatives of **34** and **35** (Table III) centered on the previously successful use of DMF derivatives **1**, **2**, and **24** with ketones and lactones. However, reaction of amides and lactams (e.g., **34** and **35**) with these reagents under a variety of reactions conditions (prolonged heating, co-solvents, catalytic base) failed to produce the desired enamine derivatives.

In order to prepare the enamino derivatives of lactams and amides, we again resorted to the method of Hafner.[28] Reaction of amide **34** and lactams **35–37** with lithium diisopropylamide (LDA) gave the corresponding lithium enolates which were subsequently treated with the DMF–dimethyl sulfate adduct to afford the desired enamino derivatives **38–41**. (Table III). The impure state of the crude reaction mixtures obtained by this method necessitated the isolation and purification of the enamino intermediates before attempting the second-stage photooxygenations. An alternative route to enamino lactams has recently been reported by L'Eplattenier.[29] By this method, the reaction of five- and six-membered lactams with orthoformates and aniline in ethylene glycol reportedly forms the corresponding anil lactams in good yield. Unfortunately, the subsequent oxidation of these systems would yield the nonvolatile phenylformamide as a byproduct, complicating the isolation of desired products.

Table III. Conversion of Lactams (Amides) to α-Keto Lactams (Amides)[a]

lactam (amide)		enamino lactam (amide) (yield)		α-keto lactam (amide) (yield)
 34	$\xrightarrow{a}$	 38 (58%)	$\xrightarrow{b}$	 42 (81%)
 35	$\xrightarrow{a}$	 39 (67%)	$\xrightarrow{c}$	 43 (78%)
 36	$\xrightarrow{a}$	 40 (62%)	$\xrightarrow{c}$	 44 (74%)
 37	$\xrightarrow{a}$	 41 (68%)	$\xrightarrow{c}$	 45 (58%)

[a] a, LDA, −78 °C; DMF–dimethyl sulfate adduct, 50 °C; b, O_2, *hν*, BANT, CH_2Cl_2/ether, −78–25 °C; c, O_2, *hν*, Rose Bengal, dichromate filter, CH_2Cl_2, −78–25 °C.

The photooxygenation of enamino amide **38** in the usual manner proceeded smoothly to afford the desired α-keto amide (**42**) in 81% yield. However, difficulties were encountered in the oxidation of enamino lactams **39–41**, under conditions identical with those employed in the oxidation of enamino ketones, lactones, and esters. While the enamino lactams **39–41** reacted rapidly with 1 equiv of singlet oxygen at low temperature to form a peroxide-free solution, the reaction mixture rapidly decomposed to a viscous tar on warming and concentrating. For example, the photooxygenation of **39–41** in methylene chloride, ether–methylene chloride, methanol, or benzene gave no α-keto lactams (**43–45**). Change of solvent, dilution, or lowering of the temperature had little favorable effect in promoting the desired reaction.

Initially, we believed that the photooxygenation most probably yielded the desired α-keto lactams which then decomposed rapidly upon warming. The facile self-condensation of α-keto lactams has been reported to occur on standing or in the presence of acid or base.[3,4] This condensation is so rapid that chromatography on silica gel or storage at 0 °C for several days must be avoided. In order to understand the chemistry and stability of these systems, the known α-keto lactams (**44 and 45**) were synthesized by the method of Southwick.[3a,b] The conjugate addition of a primary amine (R = methyl or benzyl) with ethyl acrylate gave the corresponding β-aminopropionates which were further condensed with diethyl oxalate. The resulting β-keto esters were hydrolyzed and decarboxylated to produce the desired α-keto lactams (**44 and 45**). The α-keto lactam **44** (R = methyl) proved to be stable upon standing at room temperature for several days. The α-keto lactam **45** (R = benzyl), however, proved remarkably unstable, undergoing self-condensation simply upon recrystallization.

To simulate the photooxygenation workup procedure, 1 equiv of a α-keto lactam and 1 equiv of DMF were dissolved in methylene chloride containing the sensitizer, bisacenaphthalenethiophene (BANT), and allowed to stand at room temperature. After several hours, the mixtures were concentrated to give only unreacted α-keto lactam **44** (R = methyl) or condensed α-keto lactam **45** (R = benzyl).

The apparent stability of the α-keto lactam **44** and the ready self-condensation of α-keto lactam **45** did not offer a rationale for the observed decomposition of the photo-

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[27] Wasserman, H. H.; Ives, J. L. *J. Org. Chem.* **1978**, 3238.

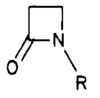
[28] Hafner, K.; Vopel, K. H.; Ploss, G.; Konig, C. *Org. Synth.* **1967**, *47*, 52.

[29] L'Eplattenier, F. A.; Vuitel, L.; Junek, H.; Wolfbeis, O. S. *Synthesis* **1976**, 543.

oxygenation reactions. The use of BANT as the sensitizer (λ_{max} 445, 378, 356) requires the irradiation of the reaction mixture with high-intensity visible light filtered only through Pyrex (UV cutoff 310–330 nm). Under these conditions, the α-keto lactams **44** and **45** (λ_{max} 356 nm) could undergo a photochemical reaction leading to decomposition. To test this possible complication, the enamino lactams **39–41** were photooxygenated at low temperature with Rose Bengal (λ_{max} 550 nm) as the sensitizer and a potassium dichromate filter to remove undesired ultraviolet light (UV cutoff 540 nm). We were pleased to find that the oxidations proceeded rapidly and ceased after 1 equiv of oxygen was consumed. When the reaction mixtures were then warmed and concentrated, decomposition was not observed, but rather, the desired α-keto lactams and DMF were isolated as the only products. Removal of the DMF under high vacuum gave crude α-keto lactams (**43–45**) which were purified by recrystallization or sublimation (Table III).

The conversion of lactams (amides) to α-keto lactams (amides) by this modified sequence offers an alternative method for the synthesis of these versatile synthetic intermediates. Unlike previously reported methods[11-13] for preparing α-keto lactams, this procedure is generally applicable to lactams of varying ring size. For example, the simplicity of the method for preparing α-ketopiperidone (**43**) contrasts sharply with the multistep preparation from nicotinic acid.[4a,b] In addition, the sequence begins with the *intact* parent lactam and does not involve the introduction of the ketone in a ring-forming reaction. Finally, the formation of α-keto lactams under neutral conditions at low temperatures should minimize their self-condensation and permit the isolation of α-keto lactam systems previously unobtainable.

The successful conversion of five- and six-membered lactams to α-keto lactams prompted us to test this method with the β-lactam system. Simple β-lactams (**43** and **47**) were prepared by literature procedures[30] and treated under a variety of reaction conditions with DMF derivatives (**1**, **2**, or **24**). No enamino derivatives could be isolated from the reaction mixture which contained ring-fragmentation products and polymers. Likewise, treatment of lactams **46** and **47** with LDA at low temperatures (−78 °C) followed by the DMF–dimethyl sulfate adduct failed to yield enamino derivatives and gave only starting β-lactam.



46, R = *t*-Bu
47, R = cyclohexyl

Experimental Section

Melting points were obtained with a Melt-Temp apparatus and are uncorrected. Infrared spectra were recorded in chloroform or neat using a Perkin-Elmer 700A spectrometer. Proton NMR spectra were obtained with either a Perkin-Elmer R-32 90-MHz instrument or a Bruker 270-MHz instrument using tetramethylsilane as an internal standard. Mass spectra were recorded on a Hitachi RMU-6 spectrometer operated at 70 eV. Elemental analyses were performed by Dr. Robert Rittner, Olin Laboratories, New Haven, CT.

All singlet oxygen reaction solutions were tested for peroxides prior to concentration by using potassium iodide–starch test paper and 10% aqueous acetic acid.

Methoxybis(dimethylamino)methane (2). When the procedure of Bredereck et al.[20] was followed, a mixture of 146.0 g (2.0 mol) of dry dimethylformamide and 252.0 g (2.0 mol) of dimethyl sulfate was stirred under nitrogen at room temperature. After the initial exothermic reaction subsided, the mixture was heated for 3 h at 60 °C and then cooled to give 398.0 g of dimethylformamide–dimethyl sulfate adduct.

To a stirred solution of 22.5 g (0.50 mol) of dimethylamine in 300 mL of dry benzene at 10 °C was added dropwise over 1 h 50.0 g (0.25 mol) of dimethylformamide–dimethyl sulfate adduct. The mixture was refluxed 1 h, cooled, and separated. The lower golden layer was washed twice with anhydrous ether and dried under vacuum to give the *N,N,N′,N′*-tetramethylformamidinium methyl sulfate as a low melting solid.

To a mechanically stirred suspension of 33.0 g (0.60 mol) of sodium methoxide in 200 mL of anhydrous ether was added dropwise over 15 min 106 g (0.50 mol) of the formamidinium methyl sulfate adduct. The resulting suspension was refluxed for 1 h, cooled, filtered, and fractionally distilled to give 43 g (65%) of methoxybis(dimethylamino)methane (**2**): bp 126–128 °C (lit.[20] bp 128 °C); IR (neat) 2900, 1460, 1070 cm^{-1}; NMR (C_6D_6) δ 3.52 (s, 1 H), 3.21 (s, 3 H), 2.30 (s, 12 H); MS, *m/e* 101, 89, 86, 75, 73.

***tert*-Butoxybis(dimethylamino)methane (1).** When the procedure of Bredereck et al.[20] was followed, a mechanically stirred suspension of 9.02 g (80.0 mmol) of potassium *tert*-butoxide in 150 mL of anhydrous ether was treated over 1 h with 15.50 g (73.0 mmol) of *N,N,N′,N′*-tetramethylformamidinium methyl sulfate. The mixture was stirred for 1 h, filtered, and concentrated by fractional distillation of the solvent. Vacuum distillation of the residue gave 7.52 g (67%) of *tert*-butoxybis(dimethylamino)methane (**1**): bp 48–52 °C (10 mm) (lit.[20] bp 48–52 °C (10–12 mm)); IR (neat) 2950–2750, 1460, 1050, 1020 cm^{-1}; NMR (C_6D_6) δ 4.05 (s, 1 H), 2.30 (s, 12 H), 1.18 (s, 9 H).

Tris(dimethylamino)methane (24). When essentially the procedure of Bredereck et al.[26a] was followed, a mixture of 94.00 g (1.30 mol) of dry dimethylformamide and 57.00 g (0.53 mol) of dimethylcarbamyl chloride was heated at 120 °C under nitrogen for 24 h. The reaction mixture was cooled to room temperature and the resulting white crystals were filtered, washed several times with dimethylformamide, and dried under vacuum to give 44.89 g (62%) of the *N,N,N′,N′*-tetramethylformamidinium chloride.

A solution of 0.12 mol of lithium dimethylamide was prepared by adding dropwise 54 mL (0.12 mol) of a 2.2 M solution of *n*-butyllithium in hexane to a stirred solution of excess dimethylamine in 500 mL of dry THF at −78 °C. The resulting solution was warmed to 0 °C for 30 min, cooled to −78 °C, and treated in several portions with 13.50 g (0.10 mol) of *N,N,N′,N′*-tetramethylformamidinium chloride. The resulting slurry was warmed to room temperature and stirred for 18 h. Removal of the solvent by fractional distillation followed by vacuum distillation of the residue gave 7.40 g (51%) of tris(dimethylamino)methane (**24**): bp 48 °C (12 mm) (lit.[26a] bp 40–43 °C (12 mm)); IR (neat) 3000–2700, 1475, 1450, 1345 cm^{-1}; NMR ($CDCl_3$) δ 3.05 (s, 1 H), 2.31 (s, 18 H); MS, *m/e* 102, 44, 43.

2-[(Dimethylamino)methylene]-3-methyl-6-isopropylcyclohexanone (9). A mixture of 1.05 g (7.16 mmol) of menthone (**3**) and 1.50 g (8.60 mmol) of *tert*-butoxybis(dimethylamino)methane (**1**) was heated at 55 °C under nitrogen with stirring for 36 h. Vacuum distillation of the reaction mixture gave 1.30 g (87%) of enamino ketone (**9**) as a pale yellow liquid: bp 108 °C (0.01 mm); IR (neat) 1640, 1550 cm^{-1}; NMR ($CDCl_3$) δ 7.30 (d, 1 H), 3.05 (s, 3 H), 3.00 (s, 3 H), 2.0 (m, 2 H), 1.20–0.80 (m, 14 H).

Anal. Calcd for $C_{13}H_{23}NO$: C, 74.59; H, 11.07; N, 6.69. Found: C, 74.30; H, 11.06; N, 6.74.

1-(*N,N*-Dimethylamino)-2-ethyl-1-hexen-3-one (14). A mixture of 0.74 g (6.56 mmol) of 4-heptanone (**8**) and 1.37 g (7.90 mmol) of *tert*-butoxybis(dimethylamino)methane (**1**) was stirred under nitrogen at 55 °C for 18 h. The reaction mixture was vacuum distilled to give 0.92 g (83%) of enamino ketone (**14**) as a pale yellow liquid: bp 72 °C (0.06 mm); IR (neat) 1640, 1600–1575 cm^{-1}; NMR ($CDCl_3$) δ 7.12 (s, 1 H), 3.06 (s, 6 H), 2.44 (t, 4 H), 1.56 (m, 2 H), 0.98 (t, 3 H), 0.90 (t, 3 H).

Anal. Calcd for $C_{10}H_{19}NO$: C, 70.96; H, 11.31; N, 8.27. Found: C, 70.88; H, 11.23; H, 8.15.

3-(*N,N*-Dimethylamino)-2-methyl-1-phenylpropenone (12). A mixture of 0.90 g (6.70 mmol) of propiophenone (**6**) and 1.24 g (7.20 mmol) of *tert*-butoxybis(dimethylamino)methane (**1**) was

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[30] (a) Birkofer, L.; Schramm, *J. Liebigs Ann. Chem.* **1975**, 2195. (b) Marvell, C. S.; Moyer, W. W. *J. Org. Chem.* **1957**, *22*, 1065.

heated at 55 °C under nitrogen for 18 h. Vacuum distillation of the reaction mixture gave 1.03 g (81%) of enamino ketone (**12**): bp 126 °C (0.10 mm) (lit.[31] bp 169–172 °C (5 mm)); IR (neat) 1630, 1550 cm^{-1}; NMR (CDCl$_3$) δ 7.33 (bs, 5 H), 6.85 (s, 1 H), 2.95 (s, 6 H), 2.10 (s, 3 H).

1,2-Diphenyl-3-(*N*,*N*-dimethylamino)propenone (13). A mixture of 1.10 g (5.60 mmol) of desoxybenzoin (**7**) and 1.36 g (7.84 mmol) of *tert*-butoxybis(dimethylamino)methane (**1**) was heated at 55 °C under nitrogen for 36 h. The crude product was dried under vacuum and recrystallized from ether–hexane (1:4) to give 1.20 g (85%) of enamino ketone (**13**): mp 128–129 °C (lit.[32] mp 129–130.5 °C); IR (CHCl$_3$) 1630, 1600, 1550 cm^{-1}; NMR (CDCl$_3$) δ 7.44–7.08 (m, 11 H), 2.68 (s, 6 H).

2-[(*N*,*N*-Dimethylamino)methylene]cyclododecanone (10). A mixture of 1.68 g (9.20 mmol) of cyclododecanone (**4**) and 1.70 g (9.7 mmol) of *tert*-butoxybis(dimethylamino)methane (**1**) was heated at 55 °C under nitrogen atmosphere for 24 h. Vacuum distillation of the reaction mixture gave 2.06 g (94%) of enamino ketone (**10**) as a clear liquid which solidified on standing: bp 130 °C (0.03 mm); IR (neat) 1640, 1590 cm^{-1}; NMR (CDCl$_3$) δ 7.15 (s, 1 H), 3.05 (s, 6 H), 2.55 (t, 4 H), 1.65 (m, 4 H), 1.55 (bs, 12 H).

Anal. Calcd for $C_{15}H_{27}NO$: C, 75.90; H, 11.56; N, 5.90. Found: C, 75.66; H, 11.32; N, 6.14.

2-[(*N*,*N*-Dimethylamino)methylene]-3-cholestanone (11). (11). A stirred mixture of 1.00 g (2.60 mmol) of 3-cholestanone (**5**) and 0.50 g (2.90 mmol) of *tert*-butoxybis(dimethylamino)methane (**1**) was heated at 55 °C under nitrogen atmosphere for 18 h. The reaction mixture was dried under vacuum and recrystallized from hexane to give 0.98 g (89%) of enamino ketone (**11**) as a white powder: mp 171–173 °C; IR (CHCl$_3$) 1635, 1530 cm^{-1}; NMR (CDCl$_3$) δ 7.45 (s, 1 H), 3.10 (s, 6 H), 2.25–0.75 (m, 44 H).

Anal. Calcd for $C_{30}H_{51}N$: C, 81.57; H, 11.64; N, 3.17. Found: C, 81.33; H, 11.53; N, 3.12.

Photooxygenation of Enamino Ketones, General Procedure. A solution of 5 mmol of enamino ketone **9–14** and 5 mg of bisacenaphthalenethiophene in 100 mL of dry methylene chloride was photooxygenated at −78 °C with a Sylvania DWY 650-W lamp operated at 70 V as a light source. After the uptake of oxygen ceased (1.1 equiv of oxygen, 40 min), the irradiation was stopped and the reaction mixture was allowed to warm slowly to room temperature. Evaporation of the solvent gave crude oils which were dissolved in ether, washed thoroughly with water, dried over magnesium sulfate, and clarified with activated charcoal. Filtration through Celite and evaporation gave the corresponding α-diketones in the high yields.

Alternatively, the α-diketones **15–20** were prepared directly from the corresponding ketones **3–8** without isolation of the intermediate enamino ketones. Thus, a mixture of 5.0 mmol of a ketone and 1.5 g (8.6 mmol) of *tert*-butoxybis(dimethylamino)methane (**1**) was heated at 55 °C under nitrogen with stirring for 12–24 h. The resulting product was dissolved in 150 mL of dry methylene chloride containing 5 mg of bisacenaphthalenethiophene and photooxygenated at −78 °C in the usual manner. Workup as previously described afforded the corresponding α-diketones **15–20**, identical in all respects (IR, NMR, MS, mp) with compounds prepared from the photooxygenation of the isolated enamino ketones.

2-Hydroxy-3-methyl-6-isopropyl-2-cyclohexen-1-one (15): 81%; mp 82 °C (lit.[33] mp 83–84 °C); IR (CHCl$_3$) 3600–3100, 1680, 1640 cm^{-1}; NMR (CDCl$_3$) δ 6.10 (s, 1 H), 2.32 (m, 3 H), 1.88 (s, H), 1.20–0.80 (m, 9 H); MS, *m/e* 168 (M$^+$), 145, 126, 127.

3,4-Heptanedione (20): 74%; IR (neat) 2850, 1705 cm^{-1}; NMR (CDCl$_3$) δ 2.68 (t, 4 H), 1.60 (m, 2 H), 1.06 (t, 3 H), 1.0 (t, 3 H). DNP derivative mp 256–260 °C (lit.[34] mp 263–264 °C).

1-Phenyl-1,2-propanedione (18): 68%; identical in all respects (IR, NMR, TLC) with an authentic sample (Eastman Chemical Co.); IR (neat) 1700, 1660, 1600 cm^{-1}; NMR (CDCl$_3$) δ 7.64–7.40 (m, 5 H), 2.48 (s, 3 H).

1,2-Diphenylethanedione (19): 89%; identical in all respects (IR, NMR, TLC, mp) with an authentic sample (Aldrich Chemical Co.); mp 94–95 °C; IR (CHCl$_3$) 1670, 1600, 1450 cm^{-1}; NMR (CDCl$_3$) δ 7.88 (m, 4 H), 7.44 (m, 6 H).

1,2-Cyclododecanedione (16): 82%; bp 72 °C (0.2 mm) (lit. bp 98–100 °C (1.5 mm)); IR (CHCl$_3$) 1700, 1450, 1265 cm^{-1}; NMR (CDCl$_3$) δ 2.75 (t, 4 H), 1.70 (m, 4 H), 1.25 (br s, 12 H); MS, *m/e* 196 (M$^+$), 125, 111, 112, 298, 97; UV (CHCl$_3$) λ_{max} 304, 414 nm.

2,3-Cholestanedione (17): 87%; mp 142–144 °C (lit.[23] mp 144–145 °C); IR (CHCl$_3$) 2850, 1720 cm^{-1}; NMR (CDCl$_3$) δ 2.24 (t, 4 H), 1.52–0.80 (m, 4 H).

Ethyl 3-(*N*,*N*-Dimethylamino)-2-phenylpropenoate (28). A mixture of 1.04 g (6.33 mmol) of ethyl phenylacetate (**25**) and 1.29 g (9.75 mmol) of methoxybis(dimethylamino)methane (**2**) was stirred under nitrogen atmosphere at 60 °C for 18 h. The reaction mixture was dried under vacuum and then vacuum distilled (bulb-to-bulb) to afford 1.30 g (93%) of enamino ester (**28**) as a clear liquid: bp 110 °C (0.10 mm); IR (neat) 1680, 1620, 1590, 1440, 1300 cm^{-1}; NMR (CDCl$_3$) δ 7.58 (s, 1 H), 7.22 (br s, 5 H), 4.12 (q, 2 H), 2.64 (s, 6 H), 1.18 (t, 3 H).

Anal. Calcd for $C_{13}H_{17}NO_2$: C, 71.21; H, 7.81; N, 6.39. Found: C, 71.14; H, 7.79; N, 6.28.

Ethyl 3-(*N*,*N*-Dimethylamino)-2-(*p*-methoxyphenyl)propenoate (29). A mixture of 1.35 g (7.00 mmol) of ethyl (*p*-methoxyphenyl)acetate (**26**) and 1.36 g (10.20 mmol) of methoxybis(dimethylamino)methane (**2**) was stirred under nitrogen atmosphere at 60 °C for 48 h. The reaction mixture was vacuum distilled (bulb-to-bulb) to afford 1.69 g (97%) of enamino ester **29** as a pale yellow oil: bp 115 °C (0.50 mm); IR (neat) 1675, 1610, 1600, 1280, 1100 cm^{-1}; NMR (CDCl$_3$) δ 7.55 (s, 1 H), 7.12 (d, 2 H), 6.84 (d, 2 H), 4.15 (q, 2 H), 3.82 (s, 3 H), 2.70 (s, 6 H), 1.24 (t, 3 H).

Anal. Calcd for $C_{14}H_{19}NO_3$: C, 67.45; H, 7.68; N, 5.62. Found: C, 67.41; H, 7.57; N, 5.59.

Ethyl 2-Butyl-3-(*N*,*N*-dimethylamino)propenoate (30). To a stirred solution of 2.02 g (20 mmol) of diisopropylamine in 50 mL of dry THF maintained under a nitrogen atmosphere at −78 °C was added dropwise 4.80 mL (20 mmol) of a 2.1 M solution of *n*-butyllithium in hexane. The resulting solution was stirred for 30 min and then treated dropwise with a solution of 2.59 g (18 mmol) of ethyl caproate in 10 mL of THF. The resulting enolate solution was stirred for 30 min and then treated with 4.0 g (20 mmol) of *N*,*N*-dimethylformamide–dimethyl sulfate adduct. The reaction mixture was warmed to room temperature, heated at 50 °C for 96 h, and poured onto 150 mL of water. The aqueous mixture was extracted with methylene chloride and the combined extracts were dried over magnesium sulfate, evaporated and vacuum distilled (bulb-to-bulb) to give 2.90 g (81%) of enamino ester **30** as a pale yellow liquid: bp 90 °C (0.2 mm); IR (neat) 1680, 1640–1600 cm^{-1}; NMR (CDCl$_3$) δ 7.28 (s, 1 H), 4.15 (q, 2 H), 3.00 (s, 6 H), 2.40 (m, 2 H), 1.40 (m, 4 H), 1.25 (t, 3 H), 0.95 (t, 3 H); MS, *m/e* 199 (M$^+$), 156, 154.

Anal. Calcd for $C_{11}H_{21}NO_2$: C, 66.29; H, 10.62; N, 7.03. Found: C, 66.13; H, 10.34; N, 6.86.

Photooxygenation of Enamino Esters. General Procedure. A solution of 3–5 mmol of enamino ester and 5 mg of bisacenaphthalenethiophene in 150 mL of dry methylene chloride was photooxygenated at −78 °C with a constant circulating oxygen supply and a Sylvania DWY 650-W lamp operated externally through Pyrex at 70 V. The uptake of oxygen was rapid and ceased after 30 min and 1.2 equiv of oxygen. The irradiation was stopped, the reaction mixture was allowed to warm slowly to room temperature and the mixture was concentrated. The α-keto esters were isolated by bulb-to-bulb vacuum distillation. The oxidation of lactones by this procedure has been described in a separate communication.[27]

Ethyl 2-oxophenylacetate (31): 97%, bp 80 °C (0.2 mm) (lit.[36] bp 118 °C (5 mm)); IR (neat) 1740, 1690, 1600, 1455 cm^{-1}; NMR (CDCl$_3$) δ 8.15–7.40 (m, 5 H), 4.45 (q, 2 H), 1.40 (t, 3 H).

Ethyl 2-oxo-*p*-methoxyphenylacetate (32): 95%; bp 110 °C (0.55 mm) (lit.[37] bp 178–183 °C (20 mm)); IR (neat) 1735, 1675,

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1600, 1570 cm^{-1}; NMR ($CDCl_3$) δ 8.0 (d, 2 H), 6.98 (d, 2 H), 3.86 (s, 3 H), 1.40 (t, 3 H).

Ethyl 2-oxohexanoate (33): 92%; bp 90 °C (0.2 mm) Kugelrohr) (lit.[38] bp 84 °C (10 mm)); IR (neat) 1735, 1470, 1280 cm^{-1}; NMR ($CDCl_3$) δ 4.32 (q, 2 H), 2.82 (t, 2 H), 1.80–1.20 (m, 4 H), 1.38 (t, 3 H), 0.95 (t, 3 H); MS, *m/e* 158 (M^+), 86, 85.

***N*,*N*-Dimethyl-3-(dimethylamino)-2-ethylpropenamide (38).** To a stirred solution of 2.03 g (20 mmol) of diisopropylamine in 50 mL of dry THF under nitrogen at −78 °C was added dropwise 8.26 mL (20 mmol) of 2.42 M solution of *n*-butyllithium in hexane. The solution was stirred for 30 min and then 2.08 g (18 mmol) of *N*,*N*-dimethylbutyramide (**34**) in 15 mL of THF was added dropwise over 15 min. The enolate was stirred for 1 h at −78 °C and then treated with 4.0 g (20 mmol) of *N*,*N*-dimethylformamide–dimethyl sulfate adduct. The reaction mixture was warmed slowly to room temperature and then heated at 50 °C for 48 h. The solution was poured onto 150 mL of water and extracted with three 100-mL portions of methylene chloride. The combined extracts were dried over magnesium sulfate, evaporated, and vacuum distilled (bulb-to-bulb) to give 1.78 g (58%) of enamino amide (**38**) as a clear liquid: bp 90–100 °C (0.2 mm); IR (neat) 1660–1600, 1490, 1450, 1400 cm^{-1}; NMR ($CDCl_3$) δ 5.72 (s, 1 H), 3.00 (s, 6 H), 2.65 (s, 6 H), 2.18 (q, 2 H), 1.00 (t, 3 H); MS, *m/e* 170 (M^+), 127, 126, 98, 97.

Anal. Calcd for $C_9H_{18}N_2$: C, 63.49; H, 10.66; N, 16.45. Found: C, 63.20; H, 10.82; N, 16.22.

3-[(*N*,*N*-Dimethylamino)methylene]-1-methyl-2-piperidone (39). To a stirred solution of 1.0 g (10.0 mmol) of diisopropylamine in 20 mL of dry THF at −78 °C under nitrogen atmosphere was added dropwise 4.8 mL (10.0 mmol) of a 2.1 M solution of *n*-butyllithium in hexane. The solution was stirred 30 min and then treated dropwise with 1.02 g (9.00 mmol) of 1-methyl-2-piperidone (**35**) in 5 mL of THF. After 1 h, the enolate solution was treated with 3.6 g (18 mmol) of *N*,*N*-dimethylformamide–dimethyl sulfate adduct, warmed to room temperature, and heated at 50 °C for 48 h. The mixture was poured onto 200 mL of water and extracted several times with methylene chloride. The combined extracts were drived over magnesium sulfate and evaporated and the residue vacuum distilled (bulb-to-bulb) to give 1.01 g (67%) of enamino lactam **39**: bp 90 °C (0.2 mm); IR (neat) 1650, 1570, 1335, 1205 cm^{-1}; NMR ($CDCl_3$) δ 7.35 (t, 1 H), 3.29 (t, 2 H), 2.96 (br s, 9 H), 2.68 (t, 2 H), 1.80 (m, 2 H); MS, *m/e* 168 (M^+), 154, 96, 82.

Anal. Calcd for $C_9H_{16}N_2$: C, 64.25; H, 9.59; N, 16.65. Found: C, 64.28; H, 9.60; N, 16.51.

3-[(*N*,*N*-Dimethylamino)methylene]-1-methyl-2-pyrrolidinone (40). To a stirred solution of 2.0 g (20.0 mmol) of diisopropylamine in 30 mL of dry THF at −78 °C under nitrogen atmosphere was added dropwise 9.60 mL (20.0 mmol) of a 2.1 M solution of *n*-butyllithium in hexane. The solution was stirred for 30 min, then treated dropwise with 1.78 g (18.0 mmol) of 1-methyl-2-pyrrolidone (**36**) in 5 mL of THF. After stirring 1 h at −78 °C, the resulting enolate was treated with 4.0 g (20 mmol) of *N*,*N*-dimethylformamide–dimethyl sulfate adduct, warmed to room temperature and heated at 50 °C for 48 h. The reaction mixture was poured onto 150 mL of water and extracted three times with methylene chloride. The combined extracts were dried over sodium sulfate, evaporated, and vacuum distilled (bulb-to-bulb) to give 1.72 g (62%) of enamino lactam **40**: bp 110 °C (0.20 mm); IR ($CHCl_3$) 1670, 1620, 1385, 1300 cm^{-1}; NMR ($CDCl_3$) δ 6.88 (t, 1 H), 3.31 (t, 2 H), 2.98 (t, 2 H), 2.95 (s, 6 H), 2.85 (s, 3 H); MS, *m/e* 154 (M^+), 139, 111, 83.

Anal. Calcd for $C_8H_{14}N_2O$: C, 62.31; H, 9.15; N, 18.17. Found: C, 62.08; H, 9.00; N, 17.95.

1-Benzyl-3-[(*N*,*N*-dimethylamino)methylene]-2-pyrrolidone (41). To a stirred solution of 2.0 g (20.0 mmol) of diisopropylamine in 30 mL of dry THF at −78 °C under nitrogen atmosphere was added dropwise 9.6 mL (20.0 mmol) of a 2.1 M solution of *n*-butyllithium in hexane. The solution was stirred for 30 min then treated dropwise with 3.15 g (18.0 mmol) of 1-benzyl-2-pyrrolidone (**37**) in 5 mL of THF. After 1 h, the enolate solution was treated with 4.0 g (20.0 mmol) of *N*,*N*-dimethylformamide–dimethyl sulfate adduct, allowed to warm to room temperature, and then heated at 50 °C for 48 h. The reaction mixture was poured onto 100 mL of water and extracted several times with methylene chloride. The combined extracts were dried over sodium sulfate, evaporated, and crystallized from ether to afford 2.88 g (68%) of enamino lactam **41** as pale yellow needles: mp 101–102 °C; IR ($CHCl_3$) 1670, 1610, 1390, 1305, 1100 cm^{-1}; NMR ($CDCl_3$) δ 7.22 (s, 5 H), 6.93 (t, 1 H), 4.45 (s, 2 H), 3.30–2.75 (m, 4 H), 2.90 (s, 6 H); MS, *m/e* 230 (M^+), 139, 91, 86; UV ($CHCl_3$) λ_{max} 310 nm.

Anal. Calcd for $C_{14}H_{18}N_2O$: C, 73.01; H, 7.88; N, 12.16. Found: C, 72.78; H, 7.66; N, 12.35.

***N*,*N*-Dimethyl-2-oxobutyramide (42).** A solution of 565 mg (3.32 mmol) of enamino amide **38** and 5 mg of bis-acenaphthalenethiophene in 150 mL of ether and methylene chloride (1:1) was photooxygenated at −78 °C with a Sylvania DWY 650-W lamp operated externally at 70 V as a light source. After 75 min, the uptake of oxygen ceased and the irradiation was stopped. The reaction mixture was warmed to room temperature, concentrated, and vacuum distilled (bulb-to-bulb) to yield 347 mg (81%) of α-keto amide **42** as a clear liquid: bp 80–85 °C (0.6 mm); IR (neat) 1705, 1640, 1410, 1100 cm^{-1}; NMR ($CDCl_3$) δ 3.05 (s, 6 H), 2.82 (q, 2 H), 1.18 (t, 2 H).

Anal. Calcd for $C_6H_{11}NO_2$: C, 55.80; H, 8.58; N, 10.84. Found: C, 55.84; H, 8.44; N, 10.80.

1-Methyl-3-oxo-2-piperidone (43). A solution of 320 mg (1.93 mmol) of enamino lactam **39** and 10 mg of Rose Bengal in 150 mL of dry methylene chloride was photooxygenated at −78 °C with a Sylvania DWY 650-W lamp operated externally at 70 V through a 3% aqueous potassium dichromate filter. After the uptake of oxygen ceased (1 h, 1.1 equiv of oxygen), the irradiation was stopped and the reaction mixture was allowed to warm slowly to room temperature. Evaporation of the solvent left a crude powder which was sublimed at 50 °C (0.01 mm) to give 190 mg (78%) of α-keto lactam **43** as white needles: mp 77–78 °C; IR ($CHCl_3$) 1740, 1670 cm^{-1}; NMR ($CDCl_3$) δ 3.60 (t, 2 H), 3.08 (s, 3 H), 2.74 (t, 2 H), 2.22 (m, 2 H); MS, *m/e* 127 (M^+), 99, 98, 88, 86.

Anal. Calcd for $C_6H_9NO_2$: C, 56.68; H, 7.13; N, 11.02. Found: C, 56.89; H, 7.00; N, 11.28.

1-Methyl-3-oxo-2-pyrrolidone (44). A solution of 200 mg (1.30 mmol) of enamino lactam **40** and 10 mg of Rose Bengal in 100 mL of dry methylene chloride was photooxygenated at −78 °C with a Sylvania DWY 650-W lamp operated externally at 70 V through a 3% aqueous potassium dichromate filter. After the uptake of oxygen ceased (1 h, 1.1 equiv. of oxygen), the irradiation was stopped and the reaction mixture was allowed to warm slowly to room temperature. Evaporation of the solvent followed by sublimation at 90 °C (0.01 mm) gave 108 mg (74%) of α-keto lactam **44** as a white powder, identical in all respects (IR, NMR, mp) with an authentic sample prepared by the method of Southwick et al.:[12c] mp 89–90 °C (lit.[4d] mp 89–91 °C); IR ($CHCl_3$) 1767, 1701 cm^{-1}; NMR ($CDCl_3$) δ 3.74 (t, 2 H, J = 5.5 Hz), 3.13 (s, 3 H), 2.75 (t, 2 H, J = 5.5 Hz); UV ($CHCl_3$) λ_{max} 370, 356 nm.

1-Benzyl-3-oxo-2-pyrrolidone (45). A solution of 240 mg (1.04 mmol) of enamino lactam **41** and 10 mg of Rose Bengal in 100 mL of dry methylene chloride was photooxygenated at −78 °C with a Sylvania DWY 650-W lamp operated externally through a 3% aqueous potassium dichromate filter. Afer the uptake of oxygen ceased (1 h), the irradiation was stopped and the solution was allowed to warm to room temperature. Evaporation of the solvent left a solid residue which was dissolved in 150 mL of brine and extracted several times with methylene chloride. The combined extracts were dried and concentrated to give 114 mg (58%) of α-keto lactam **45** which crystallized on standing: mp 99–100 °C (lit.[12c] mp 99–100 °C); IR ($CHCl_3$) 1765, 1700, 1500, 1440 cm^{-1}; NMR ($CDCl_3$) δ 7.30 (m, 5 H), 4.65 (s, 2 H), 3.54 (t, 2 H), 2.64 (t, 2 H).

The α-keto lactam **45** was identical in all respects (mp, IR, NMR) with an authentic sample prepared by the method of Southwick et al.[12c]

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Registry No. **1**, 5815-08-7; **2**, 1186-70-5; **3**, 89-80-5; **4**, 830-13-7; **5**, 15600-08-5; **6**, 93-55-0; **7**, 451-40-1; **8**, 123-19-3; **9**, 61223-73-2;

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Simple Enols. 4. Generation of Some New Simple Enols in Solution and the Kinetics and Mechanism of Their Ketonization

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The simple enols [O-^{2}H]-2-hydroxypropene, [O-^{2}H]-3-chloro-2-hydroxypropene, 2,2-dichlorovinyl alcohol, and hydroxypropadiene have been generated from reactive precursors in solution and characterized by NMR spectroscopy. The kinetics of ketonization of 3-chloro-2-hydroxypropene, hydroxypropadiene, and of the previously described (Z)-prop-1-en-1-ol and 2-methylprop-1-en-1-ol were studied by UV spectrophotometry at 15 °C. It was found that k_0 varied with pH according to the equation $k_0 = k_{H_2O} + (k_{H^+}10^{-pH}) + (k_{HO^-}K_w)/10^{-pH}$ and values of k_{H_2O}, k_{H^+}, and k_{HO^-} were evaluated for these four enols. Solvent isotope effects, k_{H^+}/k_{D^+}, were determined and the acid-catalyzed ketonization of 3-chloro-2-hydroxypropene and 2-methylprop-1-en-1-ol were studied in water–Me_2SO mixtures. The kinetics of the acid-catalyzed hydrolyses of the methyl enol ethers that correspond to these enols were also investigated. It is concluded that the kinetic results were best explained by concerted mechanisms for the hydronium ion catalyzed and spontaneous ketonization and by a stepwise mechanism for the hydroxide ion catalyzed ketonization.

We have recently shown how vinyl alcohol may be generated in solution from reactive precursors and characterized by NMR spectroscopy, and the kinetics of its conversion into acetaldehyde have been studied by UV spectrophotometry.[2,3] An investigation of the NMR spectra of (E)- and (Z)-prop-1-en-1-ol and of 2-methylprop-1-en-1-ol led to the conclusion that vinyl alcohol and (E)-prop-1-en-1-ol exist predominently in the S–cis conformation and that (Z)-prop-1-en-1-ol and 2-methylprop-1-en-1-ol exist predominantly in the S–trans conformation.[4] We now report how a variety of other enols may be generated in similar ways and describe an investigation of the kinetics of ketonization of some of them.

Generation and Characterization of Enols

The NMR spectral data of the enols and their precursors and the conditions under which the enols were generated are given in Table I.

[O-^{2}H]-2-Hydroxypropene (1). This is the enol of acetone. It has previously been generated photochemically and characterized by IR spectroscopy,[5] CIDNP,[6,7] NMR spectroscopy,[8] and UV spectroscopy.[9] It has also been generated thermally by flash thermolysis of its Diels–Alder adduct with anthracene.[10] In the slightly acidic solutions that we used for its generation 2-hydroxypropene undergoes ketonization more rapidly than vinyl alcohol and we were unable to convert the precursor **2** completely into **1** before it was partially converted into [^{2}H]acetone. This appears to be similar to what was found with the other methods of generation. Under our conditions the chemical shifts of the two vinyl protons were identical with δ 3.96. Henne and Fischer who used acetonitrile as solvent reported two signals with δ 3.97 and 3.71. Our value for the chemical shift of the methyl group (δ 1.74) is almost identical with that of the value of Henne and Fischer (δ 1.75).

[O-^{2}H]-3-Chloro-2-hydroxypropene (3). The introduction of a chlorine into 2-hydroxypropene decreases the rate of ketonization in acidic solution and [O-^{2}H]-3-chloro-2-hydroxy-propene (**3**) could be generated from both precursors **4** and **5** without any conversion into [^{2}H]-chloroacetone.

2,2-Dichlorovinyl Alcohol (6). Both the OH and OD forms of this enol which is tautomeric with 2,2-dichloroacetaldehyde were generated. It is much more stable in acidic solutions than vinyl alcohol and was obtained from ketal **7** and orthoformate **8** precursors in slightly aqueous acetone which contained a small amount of acid (Table I). It was not possible to detect the signal of the OH proton of this enol in a similar way to which that of vinyl alcohol was detected.[2] On cooling a solution in 99.5% CD_3COCD_3–0.5% H_2O which contained 5×10^{-4} M HCl to −100 °C, no signal for the OH proton could be detected, but there was some broadening of the signal of the α-CH proton at δ 6.98. This suggests that exchange of the OH proton of this enol is much faster than that of vinyl alcohol, which would be expected on the basis of the electron-withdrawing effects of the chlorines.

Hydroxypropadiene (9). This is the enol of acrylaldehyde. It was first generated from the orthoacetate precursor **10** under the conditions given in Table I. The α-CH was a triplet (δ 6.69) and the γ-CH a doublet (δ 5.19)

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