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Photochemical Reactions of Mercapto/Amino Substituted Alkyl Phenylglyoxylates Induced by Intramolecular Electron Transfer

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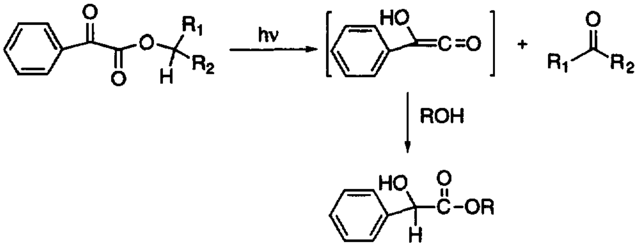
Abstract: *2'-Alkylthio ethyl phenylglyoxylates (1) and 2'-dimethylamino ethyl phenylglyoxylate (10) were synthesized and their photochemistry studied. In contrast to their oxygen analogs 3, which give normal Norrish type II cleavage products, the title compounds undergo intermolecular electron transfer from the heteroatom (sulfur/nitrogen) to the excited carbonyl group, followed by proton transfer and subsequent closing of the resulting biradicals to produce seven-membered (2)/five-membered (11) lactones in high yield. Thiadialkyl phenylglyoxylates (9) react inefficiently due to intramolecular self-quenching of phenylglyoxylate chromophores. The photoreactivity of α-oxothioester (14) was compared with that of its nitrogen (α-oxoamide) and oxygen (phenylglyoxylate) counterparts.* © 1997 Elsevier Science Ltd. All rights reserved.

INTRODUCTION

Alkyl phenylglyoxylates have been the subject of intense mechanistic study[2] and their photoreactions used synthetically.[3] In attempting Norrish type II reactions of α-keto esters (Scheme 1)[4] in laser directed surface reactions on polymer substrates,[5] we found accompanying intermolecular hydrogen abstraction[5] when the concentration of the α-keto ester is high and Paternó-Büchi reaction in the presence of an electron rich alkene.[6] These competitive processes occur partially because the Norrish type II reaction of phenylglyoxylates are slow ($k=6.35\text{x}10^{5}\ s^{-1}$) due to an unfavorable ground state conformation adopted by these ketoesters.[6]

Scheme 1

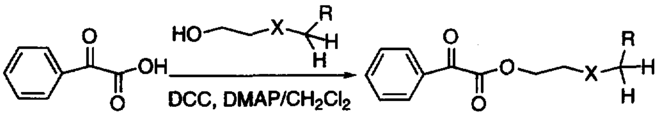


We now report novel ring closures from mercapto/amino substituted alkyl phenylglyoxylates triggered by photoinduced intramolecular electron transfer from the heteroatom to the excited carbonyl group. The closing of biradicals following protonation gives high yields of five-(**11**) or seven-(**2**) membered lactones. The corresponding alkoxyl substituted compounds undergo the Norrish type II process. Thiadialkyl phenylglyoxylates undergo intramolecular self-quenching and no appreciable photochemical products were observed. α-Oxothioesters have also been studied, and their reactions compared with α-oxoamides and phenylglyoxylates.

RESULTS

Mercapto Substituted Alkyl Phenylglyoxylates. 2'-Alkylthio ethyl phenylglyoxylates (**1**) were synthesized in good yields by DCC esterification of benzoylformic acid (Scheme 2). Benzene solutions of **1** (concentrations from 0.01M to 0.1M) gave quantitative yields of seven-membered ring lactones (**2**) (Scheme 3) upon irradiation. Lactone **2b** was produced as a mixture of two separable diastereoisomers with the *cis* to *trans* ratio found to be 1:1.2. No Norrish type II γ-hydrogen abstraction was observed.

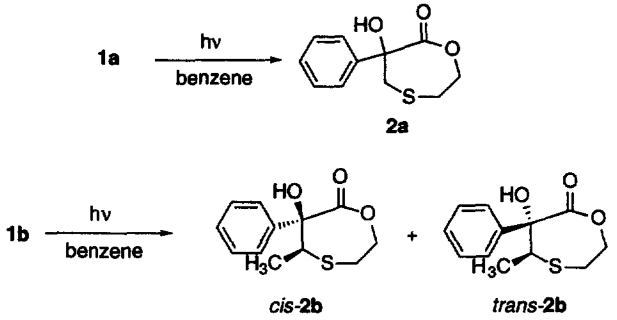
Scheme 2



Compd

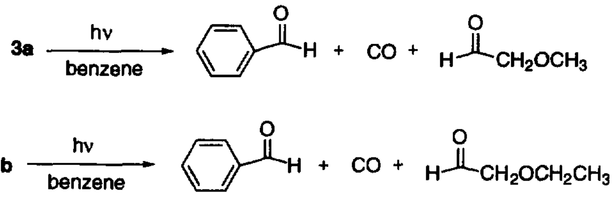
Compd	X	R
1a	S	H
1b	S	CH_3
3a	O	H
3b	O	CH_3

Scheme 3

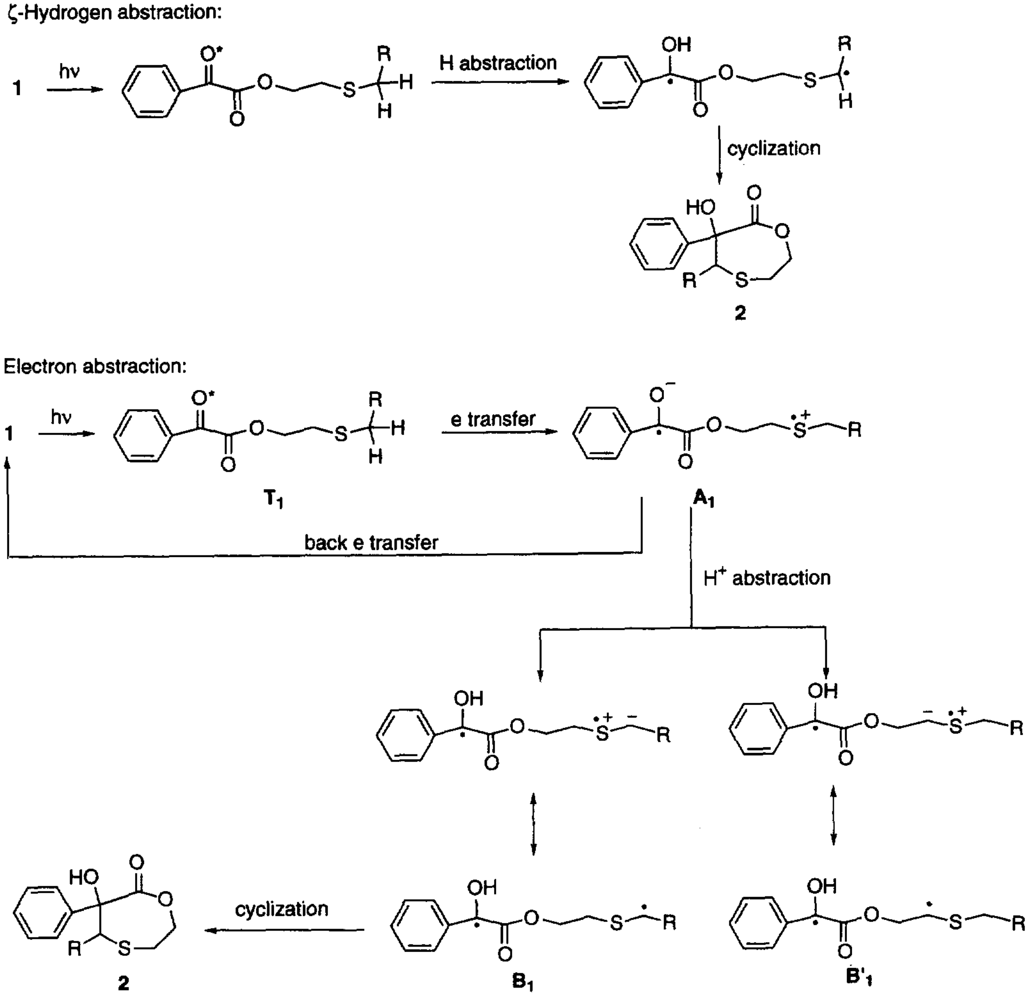


Formation of **2** can be rationalized by at least two different mechanisms (Scheme 4): a) intramolecular hydrogen abstraction, i. e., the triplet carbonyl abstracts a hydrogen α to sulfur (refer to as ζ hydrogen hereafter) followed by subsequent closure of the resulted biradical; or b) intramolecular electron abstraction, i. e., triplet carbonyl is reduced by sulfur and this is followed by proton transfer and ring closure. Considering the intrinsically slow γ-hydrogen abstraction of phenylglyoxylate triplet[5] and that the radical α to sulfur is stabilized by the lone-pair electrons on sulfur,[7] the selectivity of ζ-hydrogen abstraction over γ-hydrogen abstraction [mechanism a)] is not unreasonable. Irradiation of the corresponding oxygen compounds **3** in benzene resulted in exclusive Norrish type II γ-hydrogen abstraction followed by α,β-cleavage.[8] No seven-membered ring lactone was observed. The absence of ζ-hydrogen abstraction in **3** makes ζ-hydrogen abstraction in **1** unlikely.[9] On the other hand, sulfides are known to quench triplet ketones bimolecularly by charge transfer[10] and the rate constants correlate with those of other electron donors.[11] Together these observations favor a rate limiting electron transfer for the formation of lactones **2**.

Scheme 5



Scheme 4



Nanosecond laser flash photolysis of **1a** produced a transient absorption maximum at 420nm which decays biexponentially, Figure 1. The first decay (τ=0.6 μs) is attributed to the triplet state of **1a** and the second decay (τ=8.5 μs) to the radical anion (A_{1a}). The triplet lifetime of **1a** is significantly shorter than that of a typical alkyl phenylglyoxylate (e. g.: the triplet lifetime of methyl phenylglyoxylate is 1.38 μs[5]) in agreement with an electron transfer mechanism in which a rapid electron transfer to give A_{1a} and deactivates the triplet (T_{1a}).

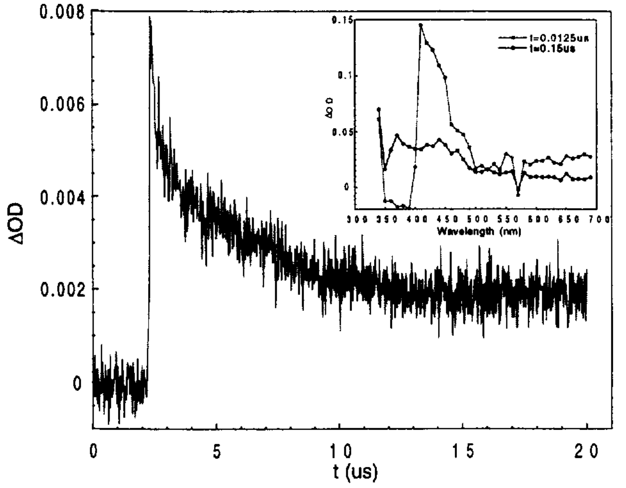


Figure 1. Transient decay trace of **1a** in benzene (0.0036M) monitored at 420 nm. Inserts are the transient absorption spectra.

The photochemical processes of **1a** are outlined in Scheme 6. The triplet decay rate constant of **1a**, k_d, can be derived[12] from the triplet lifetime (12.7 μs) of *tert*-butyl phenylglyoxylate (7.88×10^4 s^{-1}),[5] the latter being photoinert owing to the absence of γ-hydrogens. Based on the triplet lifetime of **1a** (0.6 μs), $k_d + k_i = 1/\tau = 1.6\times10^6$ s^{-1}. Thus $k_i = 1.5\times10^6$ s^{-1}. This is more than twice the normal Norrish type II γ-hydrogen abstraction rate constant found for alkyl phenylglyoxylates. Comparing k_i with a typical value of intermolecular hydrogen abstraction rate constant, $k_I = 2.0\times10^6$ $M^{-1}s^{-1}$,[5] convinces that the intermolecular hydrogen abstraction does not compete with intramolecular electron transfer when the concentration of **1a** is 0.01-0.1M.

Since the bimolecular quenching rate constants of triplet ketones by sulfides are well below the limits of diffusion control,[9] rate constants for the analogous intramolecular quenching process should depend on the equilibrium constants for the formation of the requisite cyclic orientations[13] between the donor orbital, the lone pair on sulfur and the acceptor orbital, the half-empty oxygen n-orbital.[14] It has been demonstrated that charge transfer rate constants between sulfide and triplet carbonyl groups in ketosulfides (**4**) are conformationally controlled and the variation of rate constants reflect the equilibrium stability of the required cyclic conformations (Scheme 7).[7] To achieve overlap of a sulfur lone pair orbital with the carbonyl oxygen n-orbital, it is necessary to form a cyclic ring with n+3 members. Because of the stability associated with five- and six-membered ring transition states, it is not surprising to find quenching rates are high when n=2 and 3. It is also reasonable that quenching rate constant for compound **1a**, which corresponds to n=5, is relatively low. [Our attempts to synthesize 1'-ethylthio methyl phenylglyoxylate (n=4) were, unfortunately not successful. However, it would be expected to give a higher electron transfer rate than **1a**.] The results obtained for α-oxothioester (**14**), *vide infra*, confirm this prediction.

Scheme 6

$$\mathbf{1a} \xrightarrow{h\nu} {}^{1}S_{1a} \qquad (1)$$

$${}^{1}S_{1a} \longrightarrow \mathbf{1a} \qquad (2)$$

$${}^{1}S_{1a} \xrightarrow{ISC} {}^{3}T_{1a} \qquad (3)$$

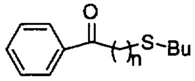
$${}^{3}T_{1a} \xrightarrow{k_d} \mathbf{1a} \qquad (4)$$

$${}^{3}T_{1a} \xrightarrow{k_1} A_{1a} \qquad (5)$$

$$A_{1a} \xrightarrow{k_2} \mathbf{1a} \qquad (6)$$

$$A_{1a} \xrightarrow{H^+ \text{ abstraction}} \text{product} \qquad (7)$$

Scheme 7

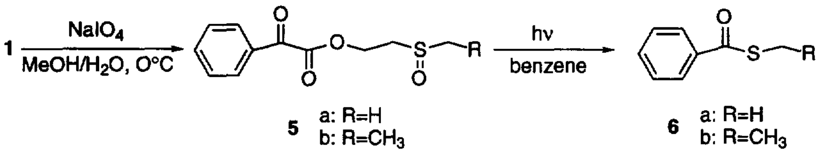


4

n	Rate constants for charge transfer self-quenching (s^{-1})
1	2×10^8
2	55×10^8
3	29×10^8
4	1.7×10^8
5	$< 0.2\times10^8$

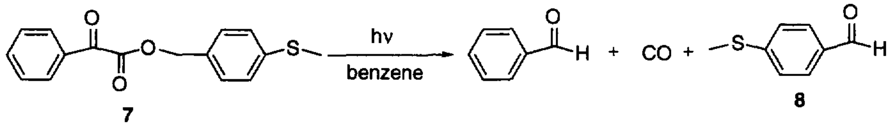
The electron transfer postulate is further confirmed when **1** is oxidized to 2'-alkylsulfinyl ethyl phenylglyoxylate **5** (Scheme 8). Irradiating **5** in benzene produces **6**, the structure of which is confirmed by independent synthesis from benzoyl chloride and the corresponding thiol. Compound **6** is thought to come from intermolecular γ-hydrogen abstraction of **5**.[5] The absence of an electron transfer process in photochemical reactions of **5** is likely due to the increased oxidation potential of a sulfoxide relative to a sulfide. A benzoyl radical and the corresponding aldehyde (2-alkylsulfinyl acetaldehyde) are also produced in this process. One molecule of 2-alkylsulfinyl acetaldehyde will oxidize the other molecule of the same aldehyde to corresponding acid while itself being reduced produce the alkyl sulfide radical. Subsequent coupling of alkyl sulfide radical and benzoyl radical furnishes product **6**.

Scheme 8



We reasoned by increasing the stability of the radical on the γ-carbon and by increasing the distance between the excited carbonyl group and the electron donating sulfur atom, we should be able to observe a Norrish type II reaction that is competitive with electron transfer in mercapto substituted phenylglyoxylates. This thesis is confirmed, Norrish type II products are the only products observed from the irradiation of compound **7** (Scheme 9). 4-Methylthiobenzaldehyde (**8**) is isolated and proven to be identical (^{1}HNMR, ^{13}CNMR, MS, and retention times on two GC columns) to a commercial sample.

Scheme 9



We further observed that thiadialkyl phenylglyoxylates **9** (Figure 2) react inefficiently under the same irradiation conditions. This is the result of internal quenching of the two phenylglyoxylate chromophores by energy transfer analogous to the well-studied internal quenching of non-conjugate diketones.[15]

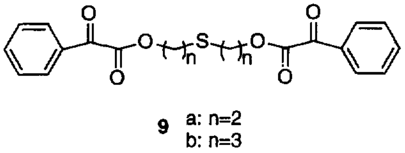
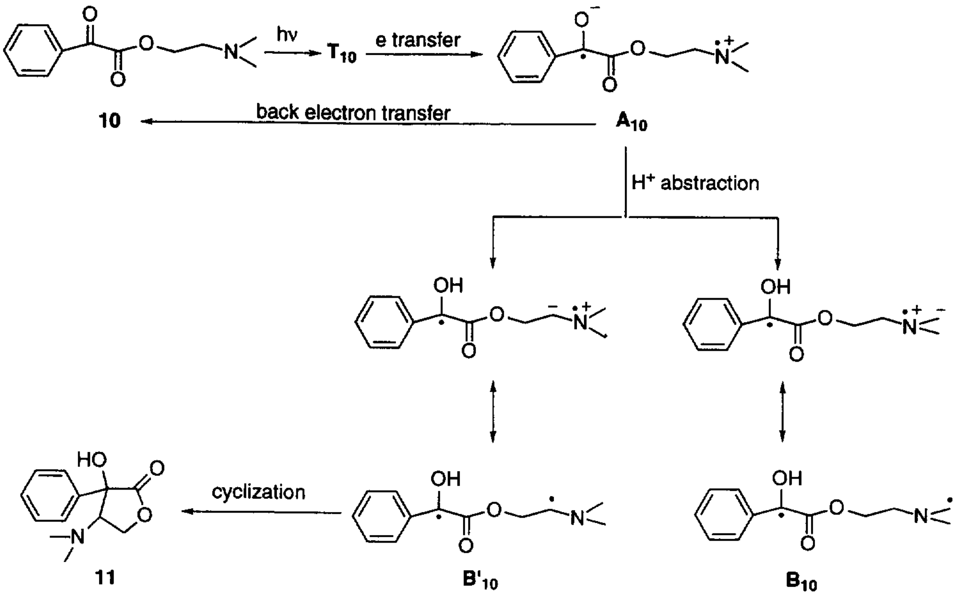


Figure 2

Dimethylamino Substituted Alkyl Phenylglyoxylates. 2'-Dimethylamino ethyl phenylglyoxylate (**10**) was similarly synthesized by DCC esterification and irradiated in benzene producing the five-membered ring lactone **11** in 77% yield. Lactone **11** was isolated as a single stereoisomer. The trans relationship of the phenyl and dimethylamino is tentatively assigned.

Scheme 10



We propose the electron transfer mechanism as outlined in Scheme 10 for this reaction based on similar analysis as for mercapto substituted alkyl phenylglyoxylates (**1**). Nanosecond laser flash photolysis detected no transient absorption for **10**, indicating its triplet state (T_{10}) lifetime is short because of the fast electron transfer leading to radical anion (A_{10}).

In the electron transfer mechanism we proposed for the photochemical reaction of **1** (Scheme 4) and **10** (Scheme 10), electron transfer from the heteroatom to the excited carbonyl group is the rate-determining step. Subsequent proton transfer from the carbon α to the heteroatom by the radical anion (A_1 or A_{10}) is a rapid process. Theoretically, both 1,6-proton transfer and 1,8-proton transfer are possible since all radical centers α to the heteroatom are stabilized to the same degree. The reason why 1,8-proton transfer is favored in A_1 while 1,6-proton transfer is preferred in A_{10} has to be attributed to the geometry imposed by the different heteroatoms to the conformations of the intermediates leading to proton abstractions. Formations of 1,7-biradical (B_1) and 1,5-biradical (B'_{10}) are the dominating processes and subsequently cyclizations result in seven-membered (**2**) and five-membered (**11**) lactones respectively.

Quantum Efficiency. Quantum yields for the disappearance of **1a** and **10** were measured (Table 1). Since **1a** and **2a** could not be separated cleanly on two different GC columns, NMR was chosen to monitor the disappearance of **1a**. The disappearance of **10** was monitored by GC.

Table 1: Quantum yields of starting material disappearance.

Compound	Solvents	
	benzene	Acetonitrile
1a	0.41	0.52
10	0.24	/

Quantum yields for the disappearance of **1a** and **10** in benzene are less than half of those measured for non-mercapto/amino substituted alkyl phenylglyoxylates which react only by hydrogen abstraction.[2, 5] This is attributed to competition between the back electron transfer process in anion (**A**), with the proton transfer. The former leads to ground state of the starting materials. The latter generates biradical (**B**) and subsequently cyclizes to product.[16]

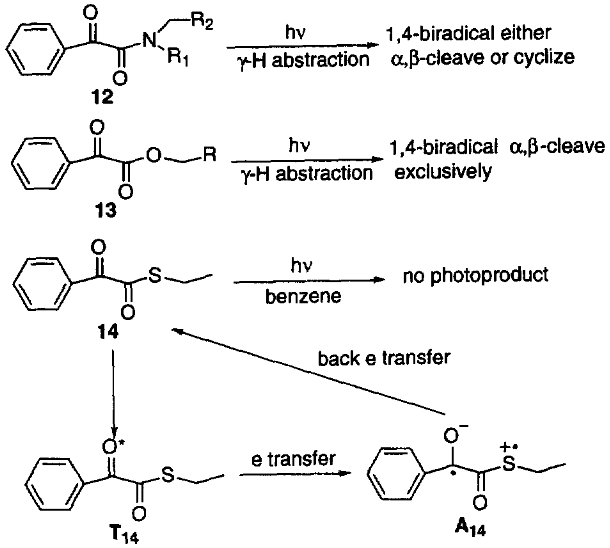
The photochemistry of **10** is even less efficient than that of **1a**. Oxidation of the amino group by the excited carbonyl group is faster than that of a sulfide.[17,18] Thus triplet **10** is quenched more efficiently than triplet **1**, leaving the quantum yield of its photoreaction lower. The more rapid quenching of the triplet carbonyl group by amino rather than sulfide also explains why we can detect triplet of **1a** but not **10** on a nanosecond time scale.

As additional support for an electron transfer mechanism, the quantum efficiency for the disappearance of **1a** is slightly higher in polar solvents (acetonitrile) than in non-polar solvents (benzene). Polar solvents stabilize the polar charge transfer intermediate leading to increased reaction efficiency.

α-Oxothioester. α-Oxoamides (**12**)[19] undergo Norrish type II γ-hydrogen abstraction and the resulting 1,4-biradical either α,β cleave or cyclize. On the other hand, alkyl phenylglyoxylates (**13**) undergo γ-hydrogen abstraction followed exclusively by α,β cleavage of the resulting 1,4-biradical.[4] α-Oxothioester (**14**) was found to be inert to irradiation in benzene, and nanosecond laser flash photolysis revealed no transient absorption. It is proposed that both electron transfer in the triplet ($\mathbf{T_{14}}$) and back electron transfer in radical anion ($\mathbf{A_{14}}$) (Scheme 11) is sufficiently rapid such that either γ-hydrogen abstraction in $\mathbf{T_{14}}$ or γ-proton transfer in $\mathbf{A_{14}}$ could take place.

It is interesting to note the paradoxical situation presented by comparing the photochemical behaviors of **1** and **10** *vs.* **14** and **12**. The different photochemical properties of **1** and **10** evidence that the dialkyl amino group is a better change transfer quencher than sulfide (*vide supra*). However, that triplet **12** is reactive via the Norrish type II route but triplet **14** is rapidly quenched seems to suggest that thio ester is a better quencher than the amide group. This can be explained by considering the greater size of sulfur 3p orbital as compared to the nitrogen 2p orbital.[7] As mentioned earlier, electron transfer is a conformational controlled process. The larger sulfur 3p orbital thus plays a greater role in helping the molecule to achieve the required electron transfer conformation when the transition state becomes more rigid in **14** (four-membered ring) than it is in **1** (eight-membered ring). As shown in Scheme 12, the 2p orbital of nitrogen is not as large so that the required conformation for electron transfer in α-oxoamide (**12**) is not easily obtained.[20] Triplet **12** is less rapidly quenched and makes Norrish type II γ-hydrogen abstraction possible.

Scheme 11



Scheme 12

DISCUSSION

Electron Abstraction vs. ζ-Hydrogen Abstraction.[21] Since electron abstraction possesses a topologically equivalent correlation diagram to that of hydrogen abstraction, it follows the same behavior qualitatively as hydrogen abstraction.[17] The electron transfer mechanism is established for the photochemical reaction of **1** and **10** based on several observations. Firstly, the rate constants for photochemical reduction by charge transfer pathway are higher than those expected for a hydrogen abstraction.[5] Secondly, because of the existence of back electron transfer, the quantum efficiency of the electron transfer reaction is expected to be lower than that of the hydrogen abstraction reaction. The quantum yields for electron transfer reactions also vary with solvent polarity. We observed that quantum efficiency for **1a** is higher in acetonitrile than in benzene. Thirdly, laser flash photolysis detects a biexponential decay evidencing the radical anion (**A**). Furthermore, no product from Norrish type II γ-hydrogen abstraction is observed in either the case of **1** and as of **10**. This is an indication that the rate of electron transfer is higher than that of γ-hydrogen abstraction. The rate of ζ-hydrogen abstraction could not be larger than that of γ-hydrogen abstraction because of an unfavorable transition state. So ζ-hydrogen abstraction is not expected to be able to compete with electron transfer.

Mercapto/Amino Substituted Alkyl Phenylglyoxylates vs. Keto Sulfides/Dialkylamino Ketones. Intramolecular charge-transfer interactions of triplet keto sulfides[7] and dialkylamino ketones[18a] have been the subject of systemic studies by Wagner et al. Valuable rate constant measures have been deduced from the competition between charge transfer and γ-hydrogen abstraction. Yet, because of the rate of Norrish type II γ-hydrogen abstraction of ketones is higher than that of alkyl phenylglyoxylates, charge transfer rate is comparable with γ-hydrogen abstraction rate for keto sulfides and dialkylamino ketones. This results in a situation in which charge transfer mechanism in keto sulfides and dialkylamino ketones produces no new products in clean yields. It also makes the study of mechanism and obtaining of kinetic data difficult. On the other hand, γ-hydrogen abstraction in alkyl phenylglyoxylates is relatively slow and can not compete with its electron transfer process. Therefore, electron transfer dominants the photochemical reaction of mercapto/amino substituted alkyl phenylglyoxylate like **1** and **10** and produce new products in good yields. The kinetic data obtained from the photochemical reactions of **1** and **10** unequivocally implicate electron transfer processes.

Synthetic Uses. Development of methods for synthesis of carbocyclic molecules containing seven-membered rings is an area of active investigation since such carbon skeletons make up the basic structures of many biologically active natural products.[22] Radical-prompted ring closure has been investigated intensively to construct synthetic intermediates.[23] The photoinduced electron transfer reaction reported for **1** producing seven-membered lactone in quantitative yield is an attractive synthetic methodology to a seven-membered ring skeleton.

Conclusion: Cyclization of biradical to lactone following electron transfer from heteroatoms to the excited carbonyl group is the only reaction observed for mercapto/amino substituted alkyl phenylglyoxylates (**1** , **10**) even though both Norrish type II γ-hydrogen abstraction and an ζ-hydrogen abstraction are also possible for these compounds. Very different photochemical properties are observed for alkyl phenylglyoxylate (**13**), α-oxoamide (**12**), and α-oxothioester (**14**).

EXPERIMENTAL SECTION

Materials. Benzene (Aldrich) was dried over sodium under Argon. Other chemicals were obtained from commercial sources and used as received. NMR spectra were taken with either a Varian Gemini 200 NMR spectrometer or a Varian Unity Plus 400 NMR spectrometer using Chloroform-*d* as solvent. Chemical shifts are in ppm with TMS as an internal standard. GC measurements were carried out on a Hewlett-Packard(HP) 5890 Gas Chromatography. GC/MS were taken on Hewlett-Packard 5988 mass spectrometer coupled to a HP 5880A GC, interfaced to a HP 2623A data processor. Thin layer chromatography was performed with Whatman® silica gel coating TLC plates. Silica gel (60Å, 60-200 mesh) used in column chromatography were from J. T. Baker Chemical Company. High Resolution Mass Spectra were obtained from the University of Illinois at Urbana-Champaign.

General procedures for irradiation of samples and isolating products. Samples were dissolved in proper solvent and sealed with a rubber septum bound by sticky parafilm. Degassing was achieved by bubbling dry argon gas through the solution for 10-15 mins. Irradiation was carried out in a Rayonet RPR-100 photoreactor equipped with 16 350nm GE® F8T5·BLB UV lamps. After irradiation, solvent was evaporated on a rotary evaporator and the resulting solution was chromatographied under pressure using hexanes:ethyl acetate as eluting solvent or distilled under vacuum.

Quantum yields. A benzene solution (0.1M) of valerophenone as actinometer ($\Phi_{acetophenone}$ =0.33)[24] was always irradiated parallel to the sample solution on a "merry-go-around." The disappearance of **1a** was monitored by NMR since it can not be separated from its product **2a** on GC. The aromatic protons of the reaction mixture was used as internal standard since **1a** transfer to **2a** quantitatively. Signal from the methyl protons of **1a** was used to indicate the disappearance of **1a**. The disappearance of **10** as well as the appearance of acetophenone in the actinometer were conveniently monitored by GC. GC was calibrated against these compounds using chlorobenzene as an internal standard. Quantum yields reported are averages of three measurements.

Time resolved laser flash photolysis. Nanosecond laser flash photolysis were carried out on a setup described by Ford and Rodgers[25] using the third harmonic of a Q-switched Nd:YAG laser (Continuum, YG660) as excitation source. The sample solution in a quartz curette was purged by Argon for five minutes before and during the experiment. The samples were excited with 355nm pulses (pulse width *ca.* 7ns). Light from a 200W xenon lamp was focused into the sample solution and then into a SPEX1680 0.22mm double spectrometer. A computer controlled kinetic spectrophotometer (Kinetic Instruments) was used in its absorption mode to obtain transient spectra and kinetic data. The spectrometer was interfaced with a digital oscilloscope (Le Croy 9450, 350MHz bandpass).

General procedure for DCC esterification. (Synthesis of compounds **1, 3, 7, 9, 10, 14**) To the appropriate alcohol, benzoylformic acid, and 4-N, N'-dimethylamino pyridine (molar ratio: 1.0:1.1:0.1) in a round bottom flask, dry dichloromethane was added to make an about 0.2M solution. The solution was then placed over ice to cool to 0°C. Equal molar amount of 1,3-dicyclohexylcarbodiimide (DCC) in dry dichloromethane was added dropwise to the stirring solution. Generally, a white precipitation formed instantly. The mixture was then allow to warm up to room temperature and stirred overnight. The precipitation was filtered off and the solvent evaporated in vacuo. The residue was purified by flash column chromatography with indicated eluents.

2'-Methylthio ethyl phenylglyoxylate (1a), (Hexanes: Ethyl acetate=15:1), 92% yield. ^{1}HNMR (200 MHz) δ 2.18 (s, 3H), 2.86 (t, J = 7.0 Hz, 2H), 4.56 (t, J = 7.0 Hz, 2H), 7.48-7.55 (m, 2H), 7.61-7.67 (m, 1H), 8.01-8.07 (m, 2H). ^{13}CNMR (50 MHz) δ 15.66, 32.11, 64.30, 128.75, 129.94, 132.12, 134.87, 163.33, 185.87. MS 51 (12.7), 77 (41.6), 105 (100), 119 (4.5), 224 (0.7). HRMS *m/z* calculated: 224.0507, measured: 224.0505.

2'-Ethylthio ethyl phenylglyoxylate (1b), (Hexanes: Ethyl acetate=15:1), 90% yield. ^{1}HNMR (200 MHz) δ 1.27 (t, J = 7.2 Hz, 3H), 2.61 (q, J = 7.2 Hz, 2H), 2.89 (t, J = 7.0 Hz, 2H), 4.54 (t, J = 7.0 Hz, 2H), 7.47-7.55 (m, 2H), 7.62-7.67 (m, 1H), 8.01-8.07 (m, 2H). ^{13}CNMR (50 MHz) δ 14.60, 26.07, 29.52, 64.77, 128.75, 129.92, 132.12, 134.87, 163.33, 185.87. MS 51 (13.7), 61 (19.8), 77 (44.7), 88 (30.5), 105 (100), 133 (3.8), 238 (0.8). HRMS *m/z* calculated: 238.0664, measured: 238.0665.

3-Hydroxyl-3-phenyl-5-thia-cycloheptanelactone (2a), obtained from irradiation of **1a** in benzene without further purification. ^{1}HNMR (400 MHz) δ 2.64-2.69 (m, 1H), 2.94-2.97 (m, 1H), 3.05-3.12 (m, 2H), 4.46-4.51 (m, 1H), 4.61-4.66 (m, 1H), 7.30-7.37 (m, 3H), 7.53-7.55 (m, 2H). ^{13}CNMR (50 MHz) δ 34.58, 42.21, 73.32, 83.15, 125.51, 128.24, 128.66, 139.27, 178.09. MS 46 (7.8), 74 (33), 77 (28.3), 91 (5.6), 105 (100), 119 (9.4), 151 (3.7), 178 (0.3), 224 (1.3). HRMS *m/z* calculated: 224.0507, measured: 224.0505.

trans-3-Hydroxyl-4-methyl-3-phenyl-5-thia-cycloheptanelactone (trans-2a), separated from ***cis*-2b** from the mixture obtained by irradiating **1b** in benzene. Stereochemical assignment is based on NOE experiment. Irradiation of the methyl proton enhanced the aromatic proton signals. (Hexanes: Ethyl acetate=5:1 to 3:1) ^{1}HNMR (400 MHz) δ 1.17 (d, J=7.2 Hz, 3H), 2.71-2.75 (m, 1H), 3.25-3.33 (m, 1H), 3.49 (q, J=7.2 Hz, 1H), 3.82 (s, 1H), 4.73-4.80 (m, 2H), 7.26-7.40 (m, 3H), 7.71-7.73 (m, 2H). ^{13}CNMR (50 MHz) δ 14.78, 36.57, 50.85, 76.33, 83.31, 125.73, 128.23, 128.37, 137.96, 179.05. MS 60 (40.7), 77 (38.3), 88 (42.8), 105 (100), 133 (18.7), 194 (1.5), 238 (2.8). HRMS *m/z* calculated: 238.0664, measured: 238.0663.

cis-3-Hydroxyl-4-methyl-3-phenyl-5-thia-cycloheptanelactone *(cis-2a)*, separated from ***trans*-2b** from the mixture obtained by irradiating **1b** in benzene. (Hexanes: Ethyl acetate=5:1 to 3:1) ^{1}HNMR (400 MHz) δ 1.20 (d, J=7.2 Hz, 3H), 2.60-2.66 (m, 1H), 3.09 (q, J=7.2 Hz, 1H), 3.20-3.22 (m, 1H), 3.94 (s, 1H), 4.55-3.58 (m, 1H), 4.74-4.80 (m, 1H), 7.26-7.38 (m, 3H), 7.62-7.64 (m, 2H). ^{13}CNMR (50 MHz) δ 17.44, 28.92, 47.96, 73.23, 85.39, 126.33, 128.24, 138.20, 178.16. MS 60 (40.7), 77 (38.3), 88 (42.8), 105 (100), 133 (18.7), 194 (1.5), 238 (2.8). HRMS *m/z* calculated: 238.0664, measured: 238.0663.

2'-Methoxyl ethyl phenylglyoxylate (3a), (Hexanes: Ethyl acetate=20:1 to 8:1), 93% yield. ^{1}HNMR (400 MHz) δ 3.42 (s, 3H), 3.71-3.73 (m, 2H), 4.53-4.56 (m, 2H), 7.51-7.53 (m, 2H), 7.64-7.68 (m, 1H), 8.01-8.03 (m, 2H). ^{13}CNMR (50 MHz) δ 59.20, 64.83, 70.02, 128.34, 130.06, 132.14, 135.37, 163.88, 186.14. MS 51 (6.9), 77 (27.4), 105 (100), 134 (0.7), 208 (0.2). HRMS *m/z* calculated: 208.0736, measured: 208.0735.

2'-Ethoxyl ethyl phenylglyoxylate (3b), (Hexanes: Ethyl acetate=20:1 to 8:1), 90% yield. ^{1}HNMR (400 MHz) δ 1.23 (t, J = 6.8 Hz, 3H), 3.56 (q, J = 6.8 Hz, 2H), 3.74-3.77 (m, 2H), 4.54-4.56 (m, 2H), 7.49-7.53 (m, 2H), 7.63-7.67 (m, 1H), 8.02-8.05 (m, 2H). ^{13}CNMR (50 MHz) δ 14.98, 64.42, 66.23, 67.89, 128.14, 129.94, 132.01, 134.12, 163.11, 185.79. MS 51 (5.2), 77 (22.8), 105 (100), 117 (3.5), 178 (3.6), 194 (0.05). HRMS *m/z* calculated: 222.0892, measured: 222.0893.

2'-Methylsulfinyl ethyl phenylglyoxylate (5a). 0.5g (2.4 mmol) of **1a** was added portion wise to a stirring solution of 0.59g (2.5 mmol) of sodium metaperiodate in 1:1 mixture of water and methanol held at 0°C. The mixture was stirred at 0°C for 10 hours and then extracted three times with dichloromethane. The combined organic solution was dried over $MgSO_4$. Evaporating solvent in vacuo leaves 0.55g **5a**, yields: 95%. ^{1}HNMR

(400 MHz) δ 2.70 (s, 3H), 3.06-3.09 (m, 1H), 3.18-3.20 (m, 1H), 4.84 (t, J= 4.8 Hz, 2H), 7.52-7.56 (m, 2H), 7.67-7.69 (m, 1H), 8.02-8.04 (m, 2H). ^{13}CNMR (50 MHz) δ 39.20, 52.65, 58.60, 128.99, 130.12, 132.08, 135.23, 162.93, 185.31. MS 51 (6.9), 77 (24.6), 105 (100), 119 (11.1), 177 (1.3), 240 (0.03). HRMS *m/z* calculated: 240.0456, measured: 240.0456.

2'-Ethylsulfinyl ethyl phenylglyoxylate (5b), Similar procedure as outlined for **5a** begin with **1b** produced this compound in 96% yield. ^{1}HNMR (400 MHz) δ 1.34-1.40 (m, 3H), 2.81-2.86 (m, 2H), 3.02-3.06 (m, 1H), 3.12-3.17 (m, 1H), 4.82.4.85 (m, 2H), 7.51-7.55 (m, 2H), 7.66-7.70 (m, 1H), 8.01-8.04 (m, 2H). ^{13}CNMR (50 MHz) δ 6.63, 46.17, 49.70, 58.69, 128.86, 129.95, 131.94, 135.09, 162.89, 185.31. MS 51 (25.2), 77 (68.8), 105 (100), 133 (3.9), 149 (2.7), 177 (2.7), 254 (0.3). HRMS *m/z* calculated: 254.0614, measured: 254.0613.

4'-Methylthiophenyl methyl phenylglyoxylate (7), (Hexanes: Ethyl acetate=10:1), 91% yield. ^{1}HNMR (200 MHz) δ 2.46 (s, 3H), 5.35 (s, 2H), 7.22-7.26 (m, 2H), 7.34-7.38 (m, 2H), 7.43-7.45 (m, 2H), 7.59-7.64 (m, 1H), 7.93-7.97 (m, 2H). ^{13}CNMR (50 MHz) δ 15.35, 67.32, 126.24, 128.77, 129.17, 129.86, 130.92, 132.21, 134.83, 139.54, 163.47, 185.87. MS 51 (10.7), 77 (28.8), 105 (32), 122 (17.1), 137 (100), 286 (2.5). HRMS *m/z* calculated: 286.0664, measured: 286.0664.

Thiadiethyl phenylglyoxylate (9a), (Hexanes: Ethyl acetate=3:1), 84% yield. ^{1}HNMR (400 MHz) δ 2.99 (t, J=6.8 Hz, 4H), 4.57 (t, J=6.8 Hz, 4H), 7.49-7.53 (m, 4H), 7.64-7.68 (m, 2H), 8.02-8.04 (m, 4H). ^{13}CNMR (50 MHz) δ 30.52, 64.79, 128.87, 130.05, 132.23, 134.99, 163.28, 185.75. MS 51 (16.6), 77 (52.2), 105 (100), 177 (7.3), 236 (8.6), 356 (0.6). HRMS *m/z* calculated: 386.0841, measured: 386.0839.

Thiadipropyl phenylglyoxylate (9b), (Hexanes: Ethyl acetate=3:1), 81% yield. ^{1}HNMR (400 MHz) δ 2.04-2.10 (m, 4H), 2.66 (t, J=7.2 Hz, 4H), 4.49 (t, J=7.2 Hz, 4H), 7.50-7.53 (m, 4H), 7.64-7.68 (m, 2H), 7.99-8.01 (m, 4H). ^{13}CNMR (50 MHz) δ 28.17, 64.48, 128.88, 129.95, 132.30, 134.95, 163.66, 186.10. MS 51 (13), 77 (39), 105 (100), 263 (3.3). HRMS *m/z* calculated: 414.1137, measured: 414.1135.

2'-Dimethylamino ethyl phenylglyoxylate (10), Purified by vacuum distillation in 45% yield. Its boiling point is 120°C/0.005 torr. ^{1}HNMR (400 MHz) δ 2.26 (s, 6H), 2.65 (t, J=5.6 Hz, 2H), 4.43 (t, J=5.6 Hz, 2H), 7.41-7.46 (m, 2H), 7.56-7.60 (m, 1H), 7.96-7.99 (m, 2H). ^{13}CNMR (50 MHz) δ 44.78, 57.20, 63.51, 128.13, 129.94, 132.01, 134.56, 162.87, 185.63. MS 42 (8.8), 58 (100), 77 (19.3), 105 (18.2), 116 (0.4), 177 (0.2), 221 (0.4). HRMS *m/z* calculated: 221.1052, measured: 221.1052.

4-Dimethylamino-3-hydroxyl-3-phenyl-cyclopentanelactone (11), Purified by vacuum distillation from the mixture of irradiating **10** in benzene. Its boiling point is 135°C/0.005 torr. ^{1}HNMR (400 MHz) δ 2.16 (s, 3H), 2.45 (s, 3H), 4.00-4.06 (m, 1H), 4.14-4.31 (m, 2H), 7.39-7.41 (m, 5H). ^{13}CNMR (50 MHz) δ 44.91, 45.98, 68.21, 71.90, 77.84, 126.23, 128.18, 128.74, 137.53, 175.77. MS 43 (24.2), 58 (17.0), 77 (24.4), 88 (100), 105 (27.4), 221 (11.7). HRMS *m/z* calculated: 221.1052, measured: 221.1052.

Ethylthio benzoylformic ester (14), (Hexanes: Ethyl acetate=10:1), 86% yield. ^{1}HNMR (200 MHz) δ 1.37 (t, J=7.4 Hz, 3H), 3.06 (q, J=7.4 Hz, 2H), 7.47-7.54 (m, 2H), 7.62-7.68 (m, 1H), 8.10-8.15 (m, 2H). ^{13}CNMR (50 MHz) δ 14.23, 23.29, 128.76, 130.68, 131.60, 134.76, 186.33, 192.93. MS 51 (13.6), 77 (44.8), 105 (100), 166 (7.5), 194 (0.1). HRMS *m/z* calculated: 194.0402, measured: 194.0399.

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