Photosensitizer-Promoted Photoaddition Reactions of \(\alpha\)-Silyl Group Containing \(N\)-Alkyl Glycinates to Dimethyl Acetylenedicarboxylate (DMAD)

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Keyword: Photosensitizer; Photoaddition reaction; \(N\)-Alkyl glycinates; Azomethine ylide; Pyrrole; Enamino-ester
Graphical Abstract

DMAD = MeO₂C−CEC−CO₂Me
Abstract

Photosensitizer-promoted photoaddition reactions of \(N-\alpha\text{-trimethylsilyl-N-alkylglycinates}\) with DMAD were conducted to explore the scope of glycinate substrates and how product distributions can be influenced by structural nature of glycines. The results show that two competitive reaction pathways are involved, in which one route is cycloaddition of in situ formed azomethine ylides to DMAD to generate pyrroles and the other is Michael addition of in situ generated secondary amines to DMAD to produce enamino-esters. Importantly, product distributions patterns are dependent on structural nature of glycines and kinds of photosensitizers. Especially, photoaddition reaction of cyclic glycinate took place chemoselectively to produce pyrrole adduct.
Introduction

Photochemical reactions occurring in organic substances play an important role in the area of organic synthesis, materials and green chemistry. Among the number of diverse photochemical reactions explored so far, single electron transfer (SET)-promoted photoaddition reactions of tertiary amine substrates to electron acceptors possessing high excited state of reduction potentials have been attracting considerable attentions due to the low oxidation potentials. In these reactions, amine radical cations (i.e., aminium radicals) arisen by SET process serve as a synthetically useful intermediate. In particular, aminium radicals are eligible to undergo either α-CH deprotonation to produce α-amino radicals or α-hydrogen atom abstraction to yield iminium ions. Of course, the generated α-amino radicals can be also converted to iminium ions via a secondary SET process. Once these intermediates are formed, a variety of reactions of generated intermediates with either electrophiles or nucleophiles can take place to produce nitrogen containing functional molecules. In earlier studies, we’ve explored SET-promoted photoreactions of α-silyl group containing tertiary amines, in which α-amino radicals generated by sequential SET-desilylation processes play a key intermediates. In recent study, we found that tertiary amines possessing both α-silyl and α-carboxy group at nitrogen atom could serve as efficient azomethine ylide precursors depending on reaction conditions. For instance, in the photochemical reactions of N-α-silyl-N-benzylglycinates with electron deficient fullerene C₆₀, while irradiation of N₂-purged (deoxygenated) solutions containing glycinate and C₆₀ led to production of 1-aminomethyl-1,2-dihydrofullerene via addition of α-amino radicals to C₆₀, irradiation of O₂-purged solutions containing the same reactants gave rise to the formation of fulleropyrrolidines through 1,3-dipolar cycloaddition reactions of in situ formed azomethine ylides to C₆₀. (Scheme 1a) In addition, in the photosensitizer-mediated cycloaddition reactions of glycinate with dimethyl acetylene dicarboxylate (DMAD), the results showed that two competitive pathways were
involved in this reactions, one of which involves azomethine ylide (4a)-forming process (leading to cycloaddition to DMAD to form pyrrole adducts 5a) and the other involves desilylmethylated secondary amine (4b) formation (leading to amination of DMAD to form enaminoesters 5b). Encouraged by these observation, we have expanded our study to explore the scope of glycinate substrates in photosensitizer-mediated photoaddition reactions with DMAD and how the product distributions are changed by the structural nature of glycinates. The results observed in photochemical reactions of various alkyl containing glycinate with DMAD are presented below.

![Scheme 1](image-url)  
Scheme 1. Photoaddition reactions of N-α-silyl-N-benzylglycinate 1.

Results and Discussion
To explore photosensitizer-mediated photoaddition reactions of N-alkylglycinates with DMAD, firstly, both \( \alpha \)-trimethylsilyl and various alkyl group substituted glycinates 8a-8e were prepared by well-known base catalyzed N-alkylation reactions of corresponding primary amines with TMSCH\(_2\)I, followed by similar substitution reactions of resulting amines with ethyl bromoacetate. (Scheme 2) In addition, cyclic glycinate 8f was also successfully prepared by using the same synthetic sequences employed above reactions. (Scheme 3)

**Scheme 2.** Preparation of \( N-\alpha \)-silyl-N-alkyglycinates 8a-8e.

**Scheme 3.** Preparation of cyclic glycinate 8f

With these synthesized glycinates in hand, photochemical reactions were performed. Specifically, oxygenated (O\(_2\)-purged) MeCN or toluene solutions containing glycinates, DMAD and photosensitizer were irradiated with 450W Hanovia medium pressure lamp equipped with flint glass filter (> 310 nm)
for certain period time to bring about complete conversion of glycinates. Then, photolysates were concentrated and the residues were subjected to column chromatography to determine photoproducts and their product yields. The photosensitizers employed in these photoreactions include 1,10-dicyanoanthracene (DCA), rose Bengal (RB), and fullerene C$_{60}$.

Firstly, DCA-sensitized photoreactions of MeCN solutions containing $N$-$\alpha$-trimethylsilyl-$N$-alkyl glycinates 8a-8e with DMAD were performed. In the oxygenated condition, as depicted in Scheme 4 and Table 1, 5 min irradiation of MeCN solutions of 8a-8e and DMAD gave rise to predominant formation of enamino esters 14a-14e, along with silyl (12a-12e) and non-silyl (13a-13c and 13e) containing pyrroles as a minor adduct. Interestingly, the reaction of 8d with DMAD did not give rise to formation of non-silyl containing pyrrole. (entry 4 in Table 1) The control experiments showed that no reaction took place without either light or molecular oxygen. (entries 6-7 in Table 1)

Scheme 4. DCA-sensitized photoreactions of glycinates 8a-8e with DMAD.

Table 1. Product and yields of DCA-sensitized photoreactions of glycinates 8a-8e with DMAD$^a$

<table>
<thead>
<tr>
<th>entry</th>
<th>amine</th>
<th>Yield (%)$^b$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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<td></td>
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</tbody>
</table>

$^a$ entries 6-7 in Table 1
Similar product distribution were observed in the C60-sensitized photoreactions of 8a-8e with DMAD under the O2-purged toluene solution. In here, it is noteworthy to mention that, due to the limited solubility of C60, toluene was chosen as reaction solvent. As can be seen from Table 2, 10 min irradiation of toluene solutions containing glycinate 8a-8c, DMAD and C60 produce corresponding enamino esters as a major adduct and pyrroles as a minor one. However, product distributions resulting from the C60-sensitized reaction of benzyl-substituted glycinate 8d with DMAD was quite interesting. Specifically, when the toluene solution containing 8d, DMAD and C60 was irradiated, product yield of silyl tethered pyrrole adduct 12d was significantly increased (from 6% to 38%), which made 12d (38%) to be a major adduct 14d (21%) to be a minor one. (entry 4 in Table 2)

Table 2. Product and yields of C60-sensitized photoreactions of glycinites 8a-8e with DMAD

<table>
<thead>
<tr>
<th>entry</th>
<th>amine</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>8a</td>
<td>12a (11), 13a (6), 14a (35)</td>
</tr>
<tr>
<td>2</td>
<td>8b</td>
<td>12b (5), 14b (45)</td>
</tr>
</tbody>
</table>
RB-sensitized photoreactions of glycinates with DMAD were also conducted and the product yields were depicted in Table 3. The product distributions observed in these reactions were highly comparable with those made from DCA or C₆₀-promoted photoreactions. Specifically, the RB-sensitized reactions of 8a-8c and 8e with DMAD produced pyrroles and enamino esters competitively. Even in the reactions of 8a, pyrrole adducts 12a + 13a were produced more dominantly than enamino ester 14a. However, similarly to those obtained from DCA-sensitized reaction of 8d, the results of RB-catalyzed reaction of 8d with DMAD showed that enamino ester 14a was still predominant photoadduct. In the current stage, it is difficult to explain chemoselectivity depending on photosensitizers employed in the reaction. Further study seems to be required.

Table 3. Product and yields of RB-sensitized photoreactions of glycinates 8a-8e with DMAD

<table>
<thead>
<tr>
<th>entry</th>
<th>amine</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>8a</td>
<td>12a (32), 13a (8), 14a (21)</td>
</tr>
<tr>
<td>2</td>
<td>8b</td>
<td>12b (24), 13b (1), 14b (45)</td>
</tr>
<tr>
<td>3</td>
<td>8c</td>
<td>12c (27), 14c (26)</td>
</tr>
<tr>
<td>4</td>
<td>8d</td>
<td>12d (11), 14d (49)</td>
</tr>
<tr>
<td>5</td>
<td>8e</td>
<td>12e (19), 13e (6), 14e (25)</td>
</tr>
</tbody>
</table>

*220 mL of O₂-purged toluene solutions containing glycinates (3.2 mM), DMAD (3.2 mM) and C₆₀ (0.32 mM) were irradiated for 10 min. †Isolation yields. ‡Reaction in N₂-purged solution.
In contrast to those of acyclic glycines 8a-8e, photoreactions of cyclic glycinate 8f with DMAD took place with a highly chemoselective manner. As the results depicted in Scheme 5 and Table 4 show, photoreactions of 8f with DMAD gave rise to formation of silyl (12f) and non-silyl (13f) containing pyrroles and, noticeably, no enamino-ester was produced regardless of kinds of photosensitizers employed.

**Scheme 5.** Photosensitizer-mediated photoreactions of glycinate 8f with DMAD.

In particular, silyl-containing pyrrole 12f was exclusively generated. These observation showed that although further information must be accumulated to explain how structural nature of glycines influence the formation of reaction intermediates as well as photoproducts, however, it is clear that cyclic conformation of glycinate seems to prefer azomethine ylide-forming pathway to other intermediate-forming pathways. Further studies are underway to accumulate the information about the origin of chemoselectivity.

**Table 4.** Product and yields of photosensitizer-mediated reactions of glycinate 8f with DMAD

<table>
<thead>
<tr>
<th>reaction condition</th>
<th>irradiation time (min)</th>
<th>Yield (%)&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>DCA in MeCN,</td>
<td>5</td>
<td>12f (51), 13f (2)</td>
</tr>
<tr>
<td>C&lt;sub&gt;60&lt;/sub&gt; in toluene</td>
<td>10</td>
<td>12f (44), 13f (1)</td>
</tr>
<tr>
<td>RB in MeCN</td>
<td>5</td>
<td>12f (48), 13f (1)</td>
</tr>
</tbody>
</table>

<sup>a</sup>220 mL of O<sub>2</sub>-purged toluene solutions containing glycines (3.2 mM), DMAD (3.2 mM) and RB (0.32 mmol) were irradiated for 10 min. <sup>b</sup>Isolation yields.
Based on the analysis of photoadducts generated from above photosensitizer-promoted photoaddition reactions occurring between $N$-$\alpha$-trimethylsilyl-$N$-alkyl glycinates and DMAD as well as the observation made from earlier studies,\textsuperscript{21-23} feasible mechanistic pathways involved in both pyrroles and enamino-esters formation can be suggested, where in situ generated azomethine ylides and secondary amines are key intermediates. Specifically, as described in Scheme 6, a photochemical process is initiated by a SET process from glycinates 15 to excited state of photosensitizer ($^{S1}$Sens and/or $^{T1}$Sens). Taking into redox potentials of glycinates (\textit{i.e.}, oxidation potentials of glycinates, $E_{ox}$) and photosensitizer (\textit{i.e.}, excited state reduction potentials of photosensitizers, $^{*}E_{red}$),\textsuperscript{21} the SET process from glycinates to photosensitizers (e.g., DCA, C$_{60}$ and RB) should be thermodynamically favorable.\textsuperscript{25} Since this favorable SET event takes place, as a result, aminium radicals of glycinates 16 and radical anions of photosensitizers (Sens$^{-}$) are formed, in which Sens$^{-}$ are subsequently interacted with molecular oxygen (O$_{2}$), resulting in both ground state sensitizers and radical anions of oxygen (O$_{2}^{-}$). Then, aminium radicals 16 undergo O$_{2}^{-}$-assisted H-atom abstraction at $\alpha$-carbon position located adjacent to silyl group to yield iminium ions 17 and hydrogen peroxide anion (HOO$^{-}$). The generated iminium ions 17 seems to confront two competitive pathways, in which one of them is HOO$^{-}$-assisted deprotonation ($\sim$ H$^{+}$) from $\alpha$-carbon position adjacent to carboxy group to result in azomethine ylide intermediates 18 and the other is HOO$^{-}$-assisted hydrolysis to lead to the formation of non-silyl containing secondary amines 19.\textsuperscript{16,17,21} Noticeably, the extent of competition taking place between these two processes seems to be dependent on structural nature of glycinates and photosensitizers. Finally, both of generated intermediates 18 and 19 add to DMAD to produce pyrrole 20 (from azomethine ylides 18) and enamino esters 21 (from secondary amines 19). As for production of non-silyl pyrroles, it is assumed that O$_{2}^{-}$-assisted desilylation from 16, leading to non-silyl containing iminium, is probably involved.
Scheme 6. Feasible mechanistic pathways resulting in photoadducts, pyrroles 20 and enamino-esters 21

Conclusion

In summary, photosensitizer-promoted photoaddition reactions of \( N-\alpha \)-trimethylsilyl-\( N \)-alkyl glycines with DMAD were conducted to explore the scope of glycinate substrates and how product distributions can be influenced by structural nature of glycines. The results show that two competitive reaction pathways are involved in this photoaddition reactions, where one of which is cycloaddition of in situ formed azomethine ylides to DMAD to generate pyrroles and the other is Michael addition of in situ generated secondary amines to DMAD to produce enamino esters. The formation of two
intermediates are initiated by single electron transfer (SET) process from glycianates to photosensitizers, followed H-atom abstraction process of generated aminum radicals. Importantly, product distributions patterns are dependent on structural nature of glycines and kinds of photosensitizers. Especially, photoaddition reaction of cyclic glycinate took place chemoselectively to produce pyrrole adduct.

Supporting Information

Synthetic and photochemical procedures and \(^1\)H and \(^{13}\)C NMR spectra of reported compounds

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