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

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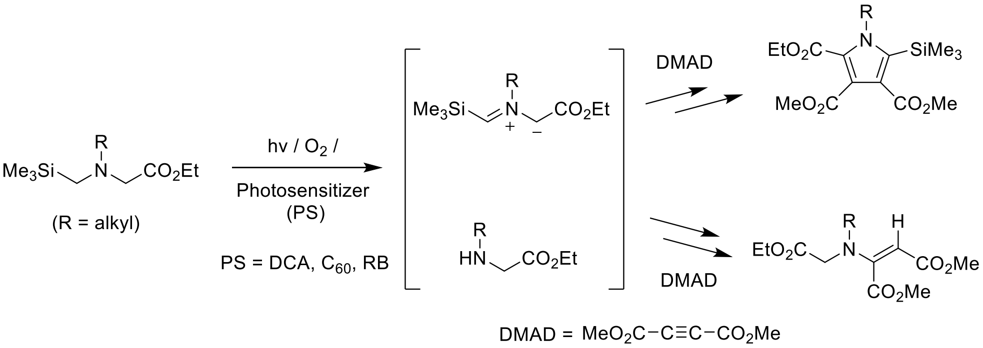
Keyword: Photosensitizer; Photoaddition reaction; *N*-Alkyl glycinates; Azomethine ylide; Pyrrole; Enamino-ester

Graphical Abstract

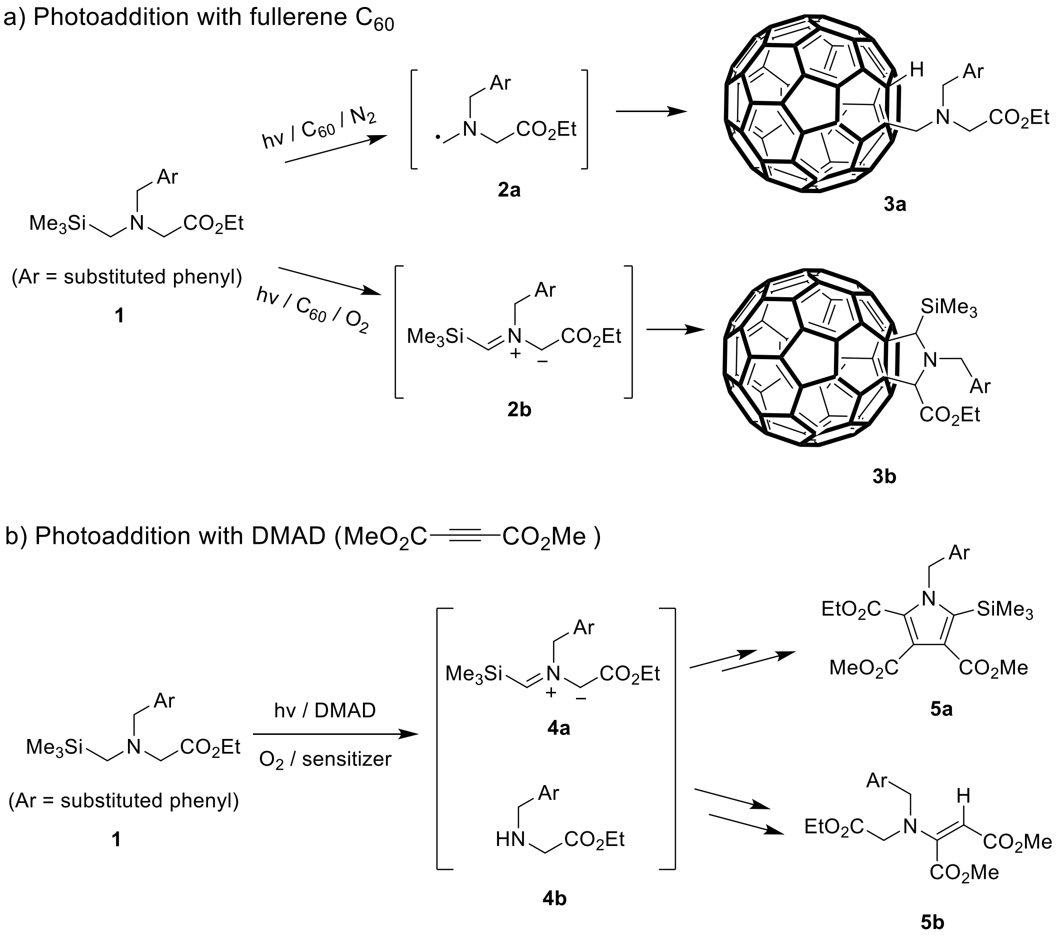


Abstract

Photosensitizer-promoted photoaddition reactions of *N*-α-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 glycinates. 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 glycinates and kinds of photosensitizers. Especially, photoaddition reaction of cyclic glycinate took place chemoselectively to produce pyrrole adduct.

Introduction

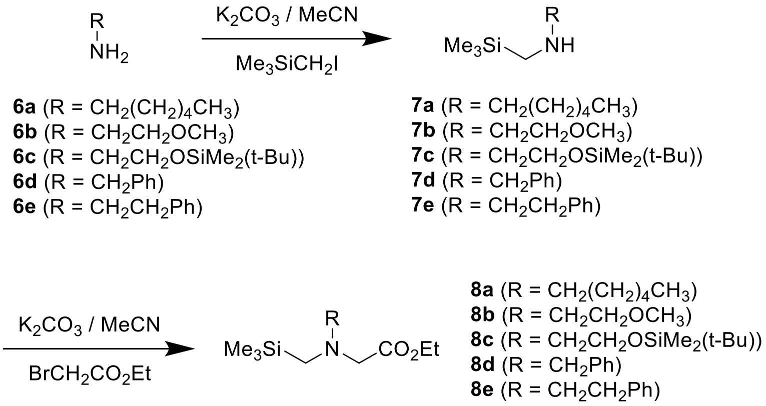
Photochemical reactions occurring in organic substances play an important role in the area of organic synthesis, materials and green chemistry.[1-10] Among the number of diverse photochemical reactions explored so far, single electron transfer (SET)-promoted photoaddition reactions of tertiary amine substrates to electron acceptors possessing high excited state of reduction potentials have been attracting considerable attentions due to the low oxidation potentials.[11,12] 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[13-15] or α-hydrogen atom abstraction to yield iminium ions.[16,17] 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.[10,13,18,19] 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 precusors depending on reaction conditions.[12,20,21] For instance, in the photochemical reactions of *N*-α-silyl-*N*-benzylglycinates **1** with electron deficient fullerene C_{60}, while irradiation of N_2-purged (deoxygenated) solutions containing glycinates **1** and C_{60} led to production of 1-aminomethyl-1,2-dihydrofullerene **3a** *via* addition of α-amino radicals **2a** to C_{60}, irradiation of O_2-purged solutions containing the same reactants gave rise to the formation of fulleropyrrolidines **3b** through 1,3-dipolar cycloaddition reactions of in situ formed azomethine ylides **2b** to C_{60}. (Scheme 1a)[20] In addition, in the photosensitizer-mediated cycloaddition reactions of glycinates **1** with dimethyl acetylene dicarboxylate (DMAD), (Scheme 1b)[21] 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 glycinates with DMAD are presented below.



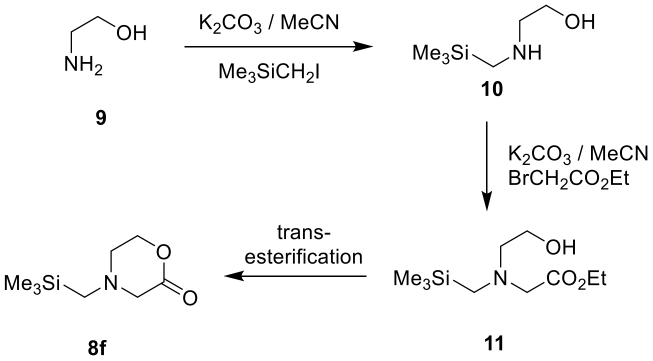
Scheme 1. Photoaddition reactions of *N*-α-silyl-*N*-benzylglycinate **1**.

Results and Discussion

To explore photosensitizer-mediated photoaddition reactions of *N*-alkylglycinates with DMAD, firstly, both α-trimethylsilyl and various alkyl group substituted glycinates **8a-8e** were prepared by well-known base catalyzed *N*-alkylation reactions of corresponding primary amines with $TMSCH_2I$, 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)



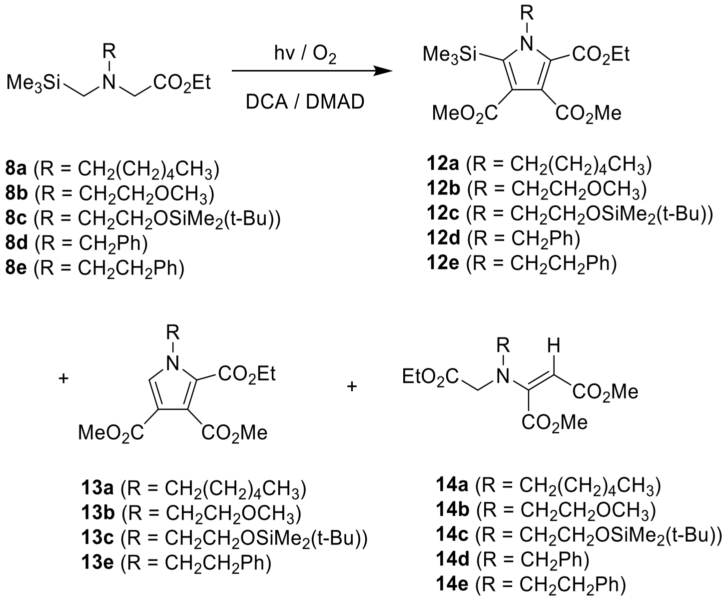
Scheme 2. Preparation of *N*-α-silyl-*N*-alkylglycinates **8a-8e**.



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-sensitizered photoreactions of MeCN solutions containing *N*-α-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)



8a (R = $CH_2(CH_2)_4CH_3$)
8b (R = $CH_2CH_2OCH_3$)
8c (R = $CH_2CH_2OSiMe_2$(t-Bu))
8d (R = CH_2Ph)
8e (R = CH_2CH_2Ph)

12a (R = $CH_2(CH_2)_4CH_3$)
12b (R = $CH_2CH_2OCH_3$)
12c (R = $CH_2CH_2OSiMe_2$(t-Bu))
12d (R = CH_2Ph)
12e (R = CH_2CH_2Ph)

13a (R = $CH_2(CH_2)_4CH_3$)
13b (R = $CH_2CH_2OCH_3$)
13c (R = $CH_2CH_2OSiMe_2$(t-Bu))
13e (R = CH_2CH_2Ph)

14a (R = $CH_2(CH_2)_4CH_3$)
14b (R = $CH_2CH_2OCH_3$)
14c (R = $CH_2CH_2OSiMe_2$(t-Bu))
14d (R = CH_2Ph)
14e (R = CH_2CH_2Ph)

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]

entry	amine	Yield (%)[b]

1	**8a**	**12a** (10), **13a** (9), **14a** (31)
2	**8b**	**12b** (5), **13b** (4), **14b** (40)
3	**8c**	**12c** (7), **13c** (5), **14c** (33)
4	**8d**	**12d** (6), **14d** (50)
5	**8e**	**12e** (9), **13e** (6), **14e** (35)
6[c]	**8a**	none
7[d]	**8a**	none

[a]220 mL of O_2-purged MeCN solutions containing glycinates (3.2 mM), DMAD (3.2 mM) and DCA (0.27 mM) were irradiated for 5 min. [b]Isolation yields. [c]Reaction in N_2-purged solution. [d]No light condition.

Similar product distribution were observed in the C_{60}-sensitized photoreactions of **8a**-**8e** with DMAD under the O_2-purged toluene solution. In here, it is noteworthy to mention that, due to the limited solubility of C_{60}, toluene was chosen as reaction solvent. As can be seen from Table 2, 10 min irradiation of toluene solutions containing glycinates **8a**-**8c** and **8e**, DMAD and C_{60} produce corresponding enamino esters as a major adduct and pyrroles as a minor one. However, product distributions resulting from the C_{60}-sensitized reaction of benzyl-substituted glycinate **8d** with DMAD was quite interesting. Specifically, when the toluene solution containing **8d**, DMAD and C_{60} 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 C_{60}-sensitized photoreactions of glycinates **8a**-**8e** with DMAD[a]

entry	amine	Yield (%)[b]
1	**8a**	**12a** (11), **13a** (6), **14a** (35)
2	**8b**	**12b** (5), **14b** (45)

3	**8c**	**12c** (8), **13c** (5), **14c** (34)
4	**8d**	**12d** (38), **14d** (21)
5	**8e**	**12e** (5), **13e** (8), **14e** (40)
6[c]	**8a**	none

[a]220 mL of O_2-purged toluene solutions containing glycinates (3.2 mM), DMAD (3.2 mM) and C_{60} (0.32 mM) were irradiated for 10 min. [b]Isolation yields. [c]Reaction in N_2-purged solution.

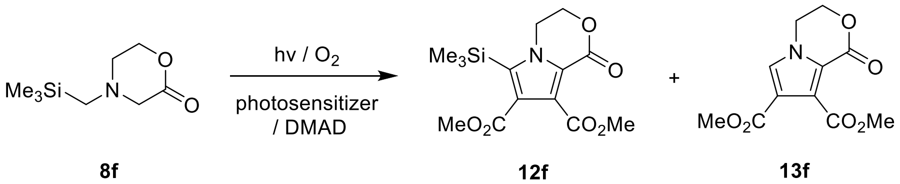
RB-sensitized photoreactions of glycinates with DMAD were also conducted and the product yields were depicted in Table 3. The product distributions observed in these reactions were highly comparable with those made from DCA or C_{60}-promoted photoreactions. Specifically, the RB-sensitized reactions 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[a]

entry	amine	Yield (%)[b]
1	**8a**	**12a** (32), **13a** (8), **14a** (21)
2	**8b**	**12b** (24), **13b** (1), **14b** (45)
3	**8c**	**12c** (27), **14c** (26)
4	**8d**	**12d** (11), **14d** (49)
5	**8e**	**12e** (19), **13e** (6), **14e** (25)

[a]220 mL of O_2-purged toluene solutions containing glycinates (3.2 mM), DMAD (3.2 mM) and RB (0.32 mmol) were irradiated for 10 min. [b]Isolation yields.

In contrast to those of acyclic glycinates **8a-8e**, photoreactions of cyclic glycinate **8f** with DMAD took place with a highly chemoselective manner. As the results depicted in Sheme 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.

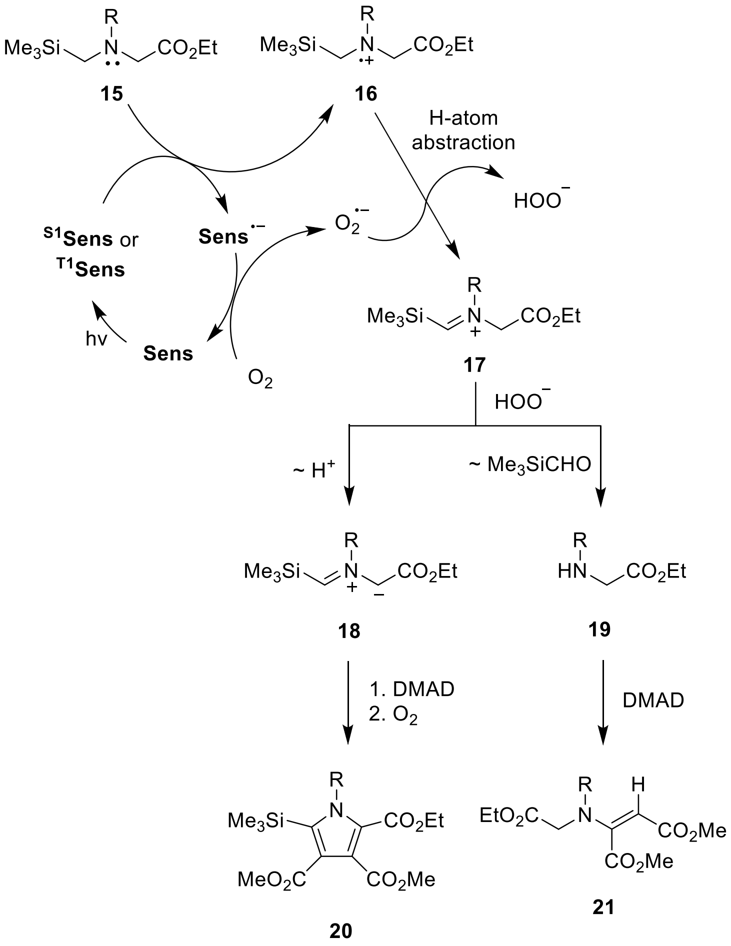
In particular, silyl-containing pyrrole **12f** was exclusively generated. These observation showed that although further information must be accumulated to explain how structural nature of glycinates influence the formation of reaction intermediates as well as photoproducts, however, it is clear that 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 glycinates **8f** with DMAD[a]

reaction condition	irradiation time (min)	Yield (%)[b]
DCA in MeCN,	5	**12f** (51), **13f** (2)
C_{60} in toluene	10	**12f** (44), **13f** (1)
RB in MeCN	5	**12f** (48), **13f** (1)

[a]220 mL of O_2-purged toluene solutions containing glycinates (3.2 mM), DMAD (3.2 mmol) and photosensitizer (0.27 mM of DCA, 0.32 mM of C_{60}, or 0.32 mM of RB) were irradiated for 10 min. [b]Isolation yields.

Based on the analysis of photoadducts generated from above photosensitizer-promoted photoaddition reactions occurring between *N*-α-trimethylsilyl-*N*-alkyl glycinates and DMAD as well as the observation made from earlier studies,[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 (*i.e.*, oxidation potentials of glycinates, E_{ox}) and photosensitizer (*i.e.*, excited state reduction potentials of photosensitizers, $^{*}E_{red}$),[21] the SET process from glycinates to photosensitizers (e.g., DCA, C_{60} and RB) should be thermodynamically favorable.[25] Since this favorable SET event takes place, as a result, aminium radicals of glycinates **16** and radical anions of photosensitizers ($Sens^{\bullet -}$) are formed, in which $Sens^{\bullet -}$ are subsequently interacted with molecular oxygen (O_2), resulting in both ground state sensitizers and radical anions of oxygen ($O_2^{\bullet -}$). Then, aminium radicals **16** undergo $O_2^{\bullet -}$ - assisted H-atom abstraction at α-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 (~ H^+) from α-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**.[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 $O_2^{\bullet -}$ - 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*-α-trimethylsilyl-*N*-alkyl glycinates with DMAD were conducted to explore the scope of glycinate substrates and how product distributions can be influenced by structural nature of glycinates. 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 glyciantes to photosensitizers, followed H-atom abstraction process of generated aminum radicals. Importantly, product distributions patterns are dependent on structural nature of glycinates 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

Acknowledgements

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