Evidence for Triplet Sensitization in the Visible-Light-Induced [2+2] Photocycloaddition of Eniminium Ions

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Abstract: Eniminium ions were prepared from the corresponding α,β-unsaturated carbonyl compounds (enones and enals), and were found to be promoted to their respective triplet states by energy transfer. The photoexcited intermediates underwent intra- or intermolecular [2+2] photocycloaddition in good yields (50–78%) upon irradiation at λ = 433 nm or λ = 457 nm. Iridium or ruthenium complexes with a sufficiently high triplet energy were identified as efficient catalysts (2.5 mol% catalyst loading) for the reaction. The intermolecular [2+2] photocycloaddition of an eniminium ion derived from a chiral secondary amine proceeded with high enantioselectivity (88% ee).

While the [2+2] photocycloaddition chemistry of α,β-unsaturated carbonyl compounds (enones and enals) has been extensively explored,[1] the related α,β-unsaturated iminium ions (eniminium ions) have received little attention. Notable studies originate only from the group of Mariano, who investigated the intramolecular [2+2] photocycloaddition of eniminium ions[2] in the context of their pioneering work on the photochemistry of iminium ions.[3] They found that eniminium ions, upon direct excitation at λ > 250 nm, undergo a stereospecific [2+2] photocycloaddition that results from excitation of the respective ππ* transition. Attempts to generate enantioenriched cyclobutanes by using an eniminium ion derived from a chiral secondary amine led to a maximum enantiomeric excess (ee) of 82% at 40% conversion.[3b]

Scheme 1 illustrates the major difference in the photochemical behavior of enones I and eniminium ions II. The lowest-lying singlet state (S1) of enones is of ππ* character and opens, despite its low absorption coefficient, a convenient entry to populate the reactive triplet state T1 by direct excitation at long wavelengths (λ = 300–350 nm) followed by a symmetry-allowed[4] intersystem crossing (ISC). The S1 state of eniminium ions is of ππ* character, and the absorption is shifted hypsochromically relative to the ππ* transition of the enone. As ISC to T1 is notoriously slow[4] for the eniminium ion, subsequent reactions occur exclusively from the S1 state. While it has been known for some time[5] that E/Z isomerization reactions occur from S1 in photoexcited eniminium ions, it has only recently been disclosed by the Melchiorre group that this state can be quenched with appropriate electron donors to achieve enantioselective alkylation reactions.[6]

Considering recent interest in the catalysis of photochemical processes by visible-light-induced triplet sensitization,[7] we have explored the nature of the triplet state T1 of eniminium ions in the present study. We speculated that this state would be accessible by carefully choosing a suitable triplet sensitizer, and we expected it to be an efficient intermediate in [2+2] photocycloaddition reactions. Our preliminary results are described in this Communication.

To investigate our hypothesis, we synthesized 3-(4-pentenyl)cyclohex-2-enone (1)[8] which was readily converted into the eniminium salt 2 by treatment with pyrrolidine and azetropic removal of water[9] (Scheme 2). The respective hexafluorophosphate salt precipitated and was recrystallized from ethanol. Enone 1 absorbs at λ = 233 nm (ε = 15650 M⁻¹ cm⁻¹) and λ = 320 nm (ε = 70 M⁻¹ cm⁻¹). The latter absorption was assigned to the forbidden ππ* transition, and the former absorption to the allowed ππ* transition. The enaminium salt 2 showed an absorption maximum at λ = 270 nm (ε = 21 320 M⁻¹ cm⁻¹). For the reasons mentioned above, the triplet energy of enaminium ion 2 could not be directly measured but its redox potential E1/2(2/2) was determined as −1.39 V vs. SCE.[10] As expected from their absorption spectra, neither enone 1 nor the enaminium ion 2 showed any conversion when excited at an irradiation wavelength of λ = 420 nm.[11] We subsequently attempted to initiate the [2+2] photocycloaddition of enaminium ion 2 by addition of 2.5 mol% of an iridium or ruthenium catalyst (Table 1). The reactions were performed in MeCN solution, 

[References and Supporting Information]
and the intermediate iminium ion rac-3 was hydrolyzed by treatment with aqueous 1 M NaOH solution.

The literature-reported cyclobutane rac-4\(^{[8]}\) was isolated as a single diastereoisomer from the reactions that were catalyzed by iridium complexes 5 and 6 (entries 1 and 2). The other catalysts, 7, Ir(ppy)_3, (ppy = 2-phenylpyridine), and Ru(bpy)_3(PF_6)_2 (bpy = 2,2’-bipyridine), failed to induce the desired transformation (entries 3–5), and the starting material was recovered unchanged. The direct reaction of enone 1 to product rac-4 was not catalyzed by complex 5 or 6. In combination with the fact that iminium salt rac-3 could be isolated from the reaction mixture in 75% yield (entry 6), it is clear that the reaction proceeds via the eniminium ion and not via the enone. Further optimization experiments revealed that ketone rac-4 was obtained in higher yields upon irradiation at \(\lambda = 433 \text{ nm}\)\(^{[13]}\) and upon work-up with 3 M NaOH solution (entries 7 and 8). Under the conditions of entry 7, other eniminium ions 8 reacted equally well, and products rac-9 were obtained in good yields (Scheme 3).

Most of the redox potentials and triplet energies of the photoexcited catalysts shown in Table 1 have been reported.\(^{[14]}\) The triplet energy of compound 5 was determined from its luminescence emission\(^{[15]}\) in MeCN solution (see the Supporting Information). We found no correlation between the excited-state redox potential of the catalysts and their viability in affording the cyclobutane product rac-4. The strongly reducing iridium complexes 7 and Ir(ppy)_3 failed to catalyze the [2+2] photocycloaddition while the much weaker reducer 6 \([E_{1/2}(\text{Ir}^{	ext{III}}/\text{Ir}^{	ext{II}})) = –0.55 \text{ V}\) was a very efficient catalyst. When comparing the tabulated triplet energies for the individual complexes (Table 1), there is, however, a very clear correlation. The [2+2] photocycloaddition ceases if the triplet energy \(E_T\) of the catalyst is below 250 kJ mol\(^{-1}\). Vice versa, this figure provides an estimate for the triplet energy of the elusive \(T_1\) state of eniminium ion 2. The observation that enone 1 did not undergo an Ir-catalyzed [2+2] photocycloaddition (see above) is readily explained by its higher triplet energy compared to that of the eniminium ion.\(^{[17]}\)

To gain more insight into the interaction between the photoactivated catalyst and eniminium salt 2, quenching studies were performed in MeCN solution at a concentration of \(c = 10 \mu \text{ M}\). Luminescence quenching was observed for catalyst 5 (Figure 1a), and the Stern–Volmer constant \((K_{SV})\) extracted

![Scheme 2. Preparation of eniminium ion 2, its sensitized [2+2] photocycloaddition reaction to products rac-3 and rac-4, and structure of iridium complexes 5–7.](image)

![Table 1: [2+2] Photocycloaddition of eniminium salt 2 in the presence of various catalysts (see Scheme 2).](table)

![Figure 1. Quenching experiments of photoexcited iridium catalysts 5, 6, and Ir(ppy)_3 with eniminium ion 2 in MeCN solution. a) Decrease in the luminescence intensity of compound 5 upon addition of iminium salt 2. Stern–Volmer plots \((K_{SV} = \text{Stern–Volmer constant})\) of the luminescence quenching for b) catalyst 5, c) catalyst 6, and d) Ir(ppy)_3.](figure)
from a plot of $I/I_0$ versus the eninium concentration was 7.49 M$^{-1}$ (Figure 1b). The lifetime $\tau^*$ of the excited state of catalyst 5 was determined to be 970 ns, and it was shown that a dynamic quenching mechanism applies (see the Supporting Information). The quenching rate constant was calculated from $K_{SV}$ and $\tau^*$ as $k_q = 7.7 \times 10^5$ M$^{-1}$ s$^{-1}$. The luminescence intensity of catalyst 6 was similarly quenched by increasing concentrations of eninium ion 2 (Figure 1c). The Stern–Volmer constant was calculated to be 7.69 M$^{-1}$ in the case of catalyst 6. The luminescence of the inactive iridium catalyst Ir(ppy)$_3$ (Table 1, entry 4) was not quenched by addition of eninium ion 2 (Figure 1d). These results suggest that the photochemical reaction of eninium ion 2 is initiated upon energy transfer from compounds 5 and 6 while energy transfer from Ir(ppy)$_3$ is not feasible based on the data from Table 1.

In a second set of experiments, we studied the intramolecular [2+2] photocycloaddition of eninium ions derived from cinnamaldehyde 10. Eninium ion 11 was readily prepared by treatment of aldehyde 10 with trimethylsilyl (TMS) triflate and N-trimethylsilyl pyrrolidine in diethyl ether (Scheme 4).[18] The absorption spectrum of compound 11 shows a maximum at $\lambda = 330$ nm ($\epsilon = 36.840$ M$^{-1}$ cm$^{-1}$) but its triplet energy could not be determined. The redox potential $E_{1/2}(11^*/11)$ was found to be $-0.83$ V[19] Neither aldehyde 10 nor eninium ion 11 showed any conversion when their solutions in MeCN were irradiated at $\lambda = 457$ nm[20] in the presence of 2,3-dimethylbutadiene. To our delight, we found that the desired [2+2] photocycloaddition of eninium ion 11 could be triggered by the addition of 2.5 mol% of Ru(bpy)$_3$Cl$_2$. The reaction was complete after four hours, and product rac-12 was obtained upon hydrolysis in 69% as a mixture of two diastereomers. The relative configuration at C3 was different in the two diastereomers, and NOESY studies revealed that the major isomer rac-12a places the methyl group in cis orientation relative to the phenyl group. Under the same irradiation conditions, aldehyde 10 underwent hardly any conversion ($\leq 10\%$) to product rac-12.

The following observations (see the Supporting Information) provide evidence for the fact that the ruthenium-catalyzed reaction proceeds via triplet energy transfer and not via electron transfer: a) The ruthenium complex Ru(bpy)$_3$Cl$_2$ (PF$_6$)$_2$ (bpy = 2,2'-bipyrazine), which is known to be a weak reductant in its excited state [$E_{1/2}(Ru(bpy)^{III}/Ru(bpy)^{II}) = -0.26$ V], promoted the [2+2] photocycloaddition as efficiently as Ru(bpy)$_3$Cl$_2$; b) Eosin Y (EY), with a triplet energy of 2.58 $k_B$ mol$^{-1}$ and an excited-state reduction potential of $E_{1/2}(EY^*/EY)^{[20]} = -1.11$ V, did not catalyze the reaction at $\lambda = 512$ nm. c) The reaction was catalyzed by typical triplet sensitzers such as benzil and thioxanthone,[21] albeit upon irradiation at short wavelengths. d) The regioselectivity of the [2+2] photocycloaddition can only be explained by a triplet pathway that proceeds via a 1,4-diradical. Addition of an intermediate radical 11- to 2,3-dimethylbutadiene would lead to the opposite regioisomer.

In a preliminary study of the substrate scope, other olefins were shown to react with eninium ion 11 (Figure 2). Isoprene gave rac-13 in a yield that was comparable to the yield recorded for rac-12. The lower diastereomeric ratio reflects the smaller size of the ethenyl group as compared to the 2-propenyl group. Likewise, 1,3-butadiene gave rac-14 with a low diastereoselectivity at carbon atom C3. Alkynyl-substituted olefins, such as 2-methylhex-1-en-3-yn and (3-methylbut-3-en-1-ynyl)trimethylsilane, reacted smoothly to give products rac-15 and rac-16.

Additionally, we evaluated the potential of the triplet-sensitized [2+2] photocycloaddition of eninium ions for enantioselective synthesis.[22] To meet this end, the known eninium ion 17[23] was prepared and subjected to a ruthenium-catalyzed reaction with 2,3-dimethylbutadiene (Scheme 5). The reaction was performed at $-40^\circ$C with 2.5 mol% of Ru(bpy)$_3$(PF$_6$)$_2$ in MeCN.
conducted only via the respective singlet intermediate by short-wavelength irradiation (λ = 250–300 nm). More importantly, the hypothesis that the triplet state of an eniminium ion is lower in energy than the triplet state of the respective α,β-unsaturated carboxylic compound has been substantiated. Under conditions that allowed for sensitized [24] photo-cycloaddition reactions of the eniminium ions 2 and 11, there was no or little conversion of the corresponding carboxylic compounds 1 and 10. Along with thermal eniminium ion catalysis[8] and photoinduced electron transfer (PET) to eniminium ions,[6,24,25] triplet sensitization seems to offer another promising avenue for the in situ activation of carboxylic groups to explore new reactivity patterns.

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Conflict of interest

The authors declare no conflict of interest.

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