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Hetero-cycloreversions Mediated by Photoinduced Electron Transfer

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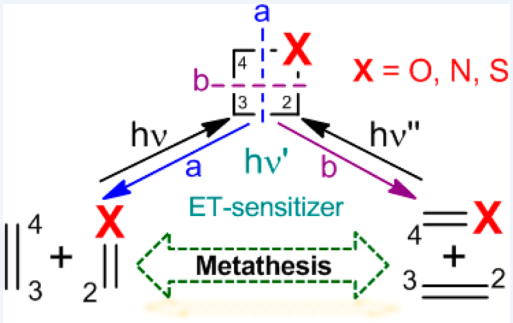
CONSPECTUS: Discovered more than eight decades ago, the Diels−Alder (DA) cycloaddition (CA) remains one of the most versatile tools in synthetic organic chemistry. Hetero-DA processes are powerful methods for the synthesis of densely functionalized six-membered heterocycles, ubiquitous substructures found in natural products and bioactive compounds. These reactions frequently employ azadienes and oxadienes, but only a few groups have reported DA processes with thiadienes. The electron transfer (ET) version of the DA reaction, though less investigated, has emerged as a subject of increasing interest.



In the last two decades, researchers have paid closer attention to radical ionic hetero-cycloreversions, mainly in connection with their possible involvement in the repair of pyrimidine(6−4)pyrimidone photolesions in DNA by photolyases. In biological systems, these reactions likely occur through a reductive photosensitization mechanism. In addition, photooxidation can lead to cycloreversion (CR) reactions, and researchers can exploit this strategy for DNA repair therapies.

In this Account, we discuss electron-transfer (ET) mediated hetero-CR reactions. We focus on the oxidative and reductive ET splitting of oxetanes, azetidines, and thietanes. Photoinduced electron transfer facilitates the splitting of a variety of four-membered heterocycles. In this context, researchers have commonly examined oxetanes, both experimentally and theoretically. Although a few studies have reported the cycloreversion of azetidines and thietanes carried out under electron transfer conditions, the number of examples remains limited.

In general, the cleavage of the ionized four-membered rings appears to occur via a nonconcerted two-step mechanism. The trapping of the intermediate 1,4-radical ions and transient absorption spectroscopy data support this hypothesis, and it explains the observed loss of stereochemistry in the products. In the initial step, either C−C or C−X bond breaking may occur, and the preferred route depends on the substitution pattern of the ring, the type of heteroatom, and various experimental conditions. To better accommodate spin and charge, C−X cleavage happens more frequently, especially in the radical anionic version of the reaction.

The addition or withdrawal of a single electron provides a new complementary synthetic strategy to activate hetero-cycloreversions. Despite its potential, this strategy remains largely unexplored. However, it offers a useful method to achieve C═X/olefin metathesis or, upon ring expansion, to construct six-membered heterocyclic rings.

1. INTRODUCTION

The Diels−Alder (DA) cycloaddition (CA) was discovered more than eight decades ago and remains one of the most versatile tools in synthetic organic chemistry. Hetero-DA processes are powerful methods for the synthesis of densely functionalized six-membered heterocycles, which are ubiquitous substructures found in natural products and bioactive compounds.[1] Azadienes and oxadienes are the most frequently employed synthons for this purpose, whereas only a limited number of DA processes with thiadienes have been reported.[2−4] The electron transfer (ET) version of the DA reaction has been much less investigated, although it is emerging as a subject of increasing interest.[5−16]

Cycloreversion (CR) of four-membered heterocycles via radical ions has attracted considerable interest in connection with its possible role in the photoenzymatic repair of DNA by photolyases.[17] Both the anionic and the cationic pathways have been investigated, in order to gain mechanistic insight. Ring splitting can occur through cleavage of the X−C2/C3−C4 or C2−C3/C4−X bonds, leading to the starting materials of the formal photocycloaddition or, more interestingly, to the metathesis products.

Photorepair of (6−4) DNA lesions by photolyases is thought to involve photoinduced electron transfer (PET) from a catalytic flavin−adenosine cofactor to the dimeric lesion; however, a critical and controversial issue is whether (photo)chemical conversion of the (6−4) photoproducts to oxetanes is actually a necessary step.[18−23]

The idea that (6−4) photoproducts are converted to oxetanes (or azetidines) upon binding to the enzyme in the dark has been questioned based on the crystal structure of a model (6−4) photoproduct in the binding pocket.[24,25] In general, experimental and theoretical studies assume that (6−4) photoproducts are repaired upon absorption of a single photon by the

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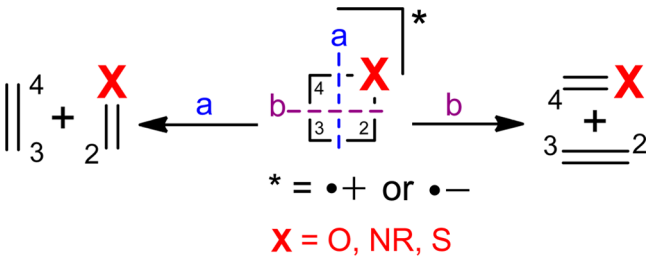
enzyme. However, the possibility of a two-photon process has been recently proposed, whereby a first PET converts the (6−4) lesion into the oxetane and a second one splits the oxetane ring leading to the repaired thymines.[23,26,27]

In addition to photorepair studies, the PET CR of four-membered ring heterocycles has attracted considerable interest from the mechanistic point of view and also as a tool to reveal the transfer of excess electrons in biomolecules by charge trapping.[28]

With this background, this Account deals with ET-mediated hetero-CR reactions (see Chart 1 for a general illustration of the topic). The attention has been focused on the oxidative and reductive ET splitting of oxetanes, azetidines, and thietanes.

Chart 1



2. OXETANES

The PET CR of oxetanes arising from the Paternò−Büchi reaction between thymine, cytosine, or uracil and different carbonyl compounds has been achieved with either electron-donating or electron-accepting photosensitizers (Figure 1).[29−32]

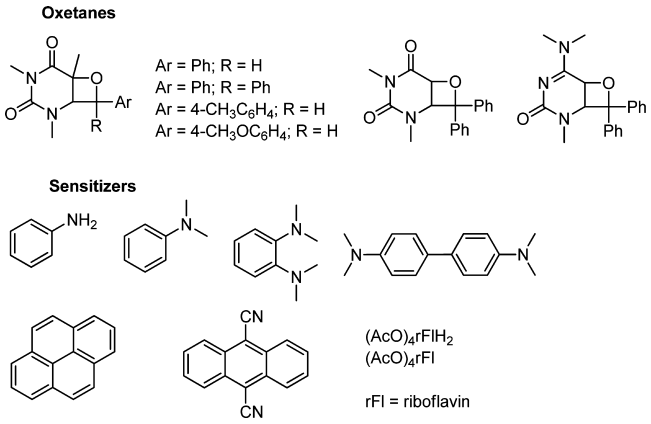


Figure 1. Chemical structures of oxetanes and sensitizers used for the study of PET CR.

In the reductive version, formation of the radical anion of the carbonyl fragment can be monitored by laser flash photolysis (LFP). A lower limit for the rate constant of the splitting reaction has been estimated at 5×10^7 s^{-1}.

Intramolecular PET CR has been investigated in a system containing the oxetane obtained from thymine and benzophenone, covalently linked to a flavin subunit (Figure 2A).[20] Ring splitting occurs through the radical anionic pathway and requires that flavin acts in the reduced and deprotonated state. Related DNA hairpin model compounds (Figure 2B) have been used to prove that excess electrons move through the duplex even over distances as long as 17 Å.[33]

Steady state photolysis, LFP, and fluorescence experiments have provided support for cleavage of oxetane radical anions formally resulting from photocycloaddition between benzophenone and 1,3-dimethylthymine or 2′-deoxyuridine, upon photosensitization by methyl 2-(carbazol-2-yl)propanoate (Figure 3).[34] An interesting feature of this photosensitizer is that it plays the role of a double-edged sword: while it may induce formation of cyclobutane pyrimidine dimers, it can also achieve CR of oxetanes.

The intramolecular version of this process has been investigated with the carbazole chromophore covalently linked to an oxetane unit (Scheme 1).[35] As expected for an ET reaction, a strong medium dependence is observed. In nonpolar solvents, no splitting occurs, charge separation is disfavored, and fluorescence quenching of the carbazole moiety is not observed.

A related oxetane has been covalently linked to β-cyclodextrin, and electron-rich fluorophores such as *N*,*N*-dimethylaniline or indole have been encapsulated within the cavity (Figure 4).[36] Upon irradiation, CR to thymine and benzophenone is confirmed by NMR measurements. In addition, fluorescence quenching occurs in all the investigated systems. The ET mechanism of the splitting reaction is supported by the negative ΔG_{ET} values, estimated in terms of the Rehm−Weller equation.[37] The quantum yields are concentration- and solvent-dependent; they are much higher for the oxetane−indole supramolecular systems than for the equivalent covalently linked models (Figure 4).[38]

The CR of 2-(*p*-cyanophenyl)-4-methyl-3-phenyloxetane has been achieved using 1-methoxynaphthalene as ET photosensitizer.[39] Splitting of the radical anion through cleavage of the O−C2 and C3−C4 bonds leads to acetaldehyde and *p*-cyanostilbene (Scheme 2), whereas construction of the oxetane ring from its precursors by the Paternò−Büchi reaction involves formation of the C2−C3 and O−C4 bonds.

Fluorescence of the sensitizer is quenched by the oxetane ($k_q = 7.4 \times 10^9$ M^{-1} s^{-1}), in agreement with ET from the singlet excited state of the former (Figure 5A). In addition, the radical anion of *trans*-*p*-cyanostilbene, peaking at ca. 500 nm, is detected upon LFP of the mixed reaction partners (Figure 5B).

The intramolecular version of this PET CR process has been investigated using covalently linked dyads (Figure 6), both in acetonitrile and in chloroform.[40] The photoreactivity is higher in the former solvent, where stereodifferentiation is less marked. The (*S*,*R*,*R*) isomer reacts faster, due to the predominancy of its folded conformation, with the naphthalene ring directed toward the oxetane region.

Accordingly, intramolecular fluorescence quenching is more efficient in acetonitrile, but it reveals higher stereodifferentiation in chloroform (Figure 7).

From the synthetic point of view, the metathesis of oxetanes constitutes an attractive tool to obtain carbonyl−olefin pairs. In this context, the behavior of bicyclic oxetanes resulting from photocycloaddition of aromatic aldehydes to 2,3-dihydrofuran has been investigated using 1-methoxy- and 2,7-dimethoxynaphthalene as PET donors.[41] Under these conditions, ring splitting ensues with photometathesis (Scheme 3). The rate constants for quenching of the photosensitizer fluorescence depend on aromatic substitution and range between 5.6×10^9 and 8.9×10^9 M^{-1} s^{-1}. The same trend is observed for triplet quenching, although the values are 1 order of magnitude lower. According to Rehm−Weller, the ET process is only exergonic from the singlet excited state.

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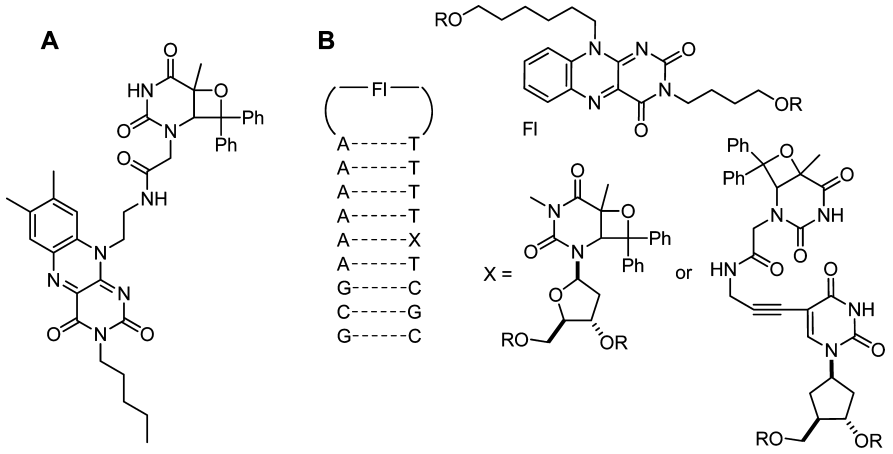


Figure 2. (A) Chemical structure of a covalently linked flavin−oxetane system for model studies on DNA repair. (B) Chemical structures of hairpins for the investigation of excess electron transport in DNA.

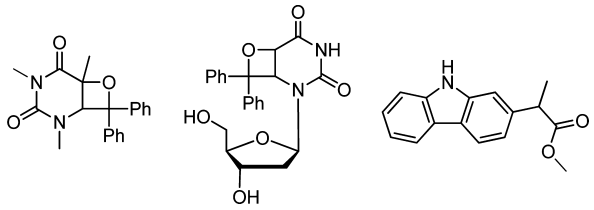
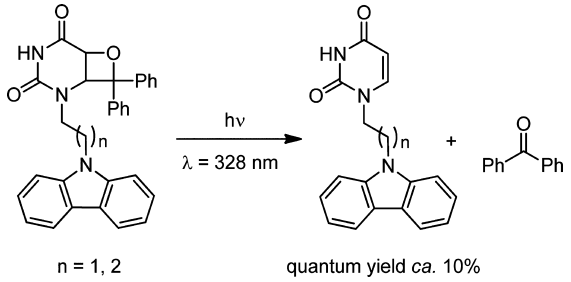


Figure 3. Chemical structures of thymine- and uridine-derived oxetanes and a carbazole photosensitizer.

Scheme 1. Intramolecular PET CR in a Carbazole−Oxetane Linked System



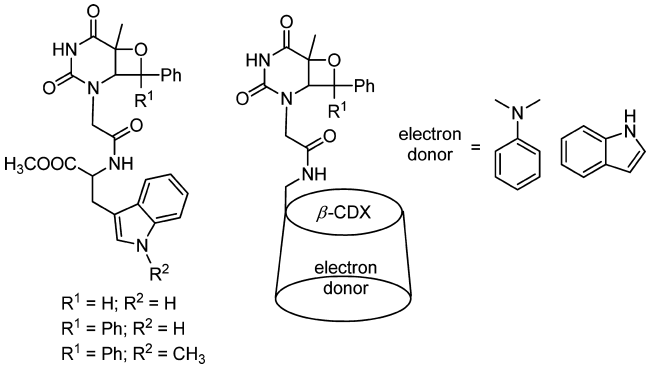
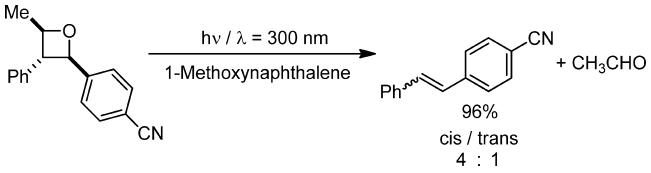


Figure 4. Chemical structures of a thymine-derived oxetane covalently linked to tryptophan and to a cyclodextrin. Structures of encapsulated electron donors.

Although photooxidative cleavage of oxetanes can in principle be used for DNA repair,[42] the reported studies are mainly focused on the interesting mechanistic aspects of this process. In this context, early studies on PET sensitization with cyanonaphthalenes point to involvement of the singlet excited state, in a stepwise CR mechanism involving initial C−C bond breaking.[29,43]

Scheme 2. Reductive PET CR of a Cyanophenyl-Substituted Oxetane



In the case of *trans,trans*-2,3-diphenyl-4-methyloxetane (obtained from *β*-methylstyrene and benzaldehyde), photosensitization by a 2,4,6-triphenylthiapyrylium (TTP^+) salt leads to *trans*-stilbene and acetaldehyde (Scheme 4, path a). The regioselectivity of the ET-mediated CR process can be modified by changing the substituents attached to the aryl groups. Thus, replacement of phenyl with *p*-methoxyphenyl results in *trans*-anethole and benzaldehyde (Scheme 4, path b).[44−48]

In principle, both the singlet and triplet excited states of TTP^+ can be involved, and indeed they are effectively quenched by the oxetane. In addition, LFP of TTP^+ in the presence of the oxetane leads to *trans*-stilbene radical cation, detected at λ_{max} = 470 nm (Figure 8A). Likewise, in the case of the methoxyphenyl substituted oxetane, *trans*-anethole radical cation is detected upon LFP (Figure 8B). Here, initial ionization occurs at the methoxy-substituted aromatic ring. Subsequent C2−C3 bond cleavage generates a 1,4-radical cation, and the observed intermediate is formed after subsequent O−C4 bond splitting (Scheme 5).

The facts that TTP^+ (with a very high intersystem crossing quantum yield) is an efficient sensitizer and that the reaction does not occur in the presence of oxygen point clearly to triplet involvement. The molecular mechanism for oxetane CR has been studied at the UB3LYP/6-31G* level.[46] Calculations are in agreement with an asynchronous process, which allows a favorable rearrangement of the spin electron density from the oxygen atom of the oxetane radical cation to the π system of the alkene radical cation.

Intramolecular nucleophilic trapping of the cationic center has further proven the stepwise mechanism involved in the PET CR of oxetane radical cations. Thus, *trans,trans*-2,3-diphenyl-4-hydroxymethyloxetane has been submitted to steady-state and

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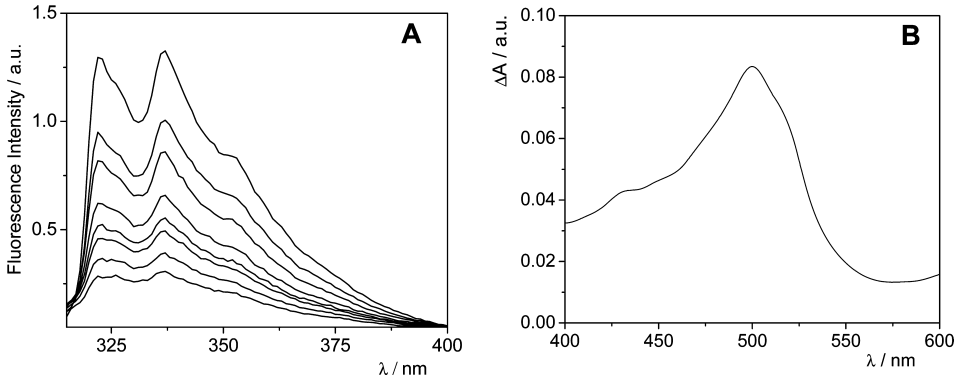


Figure 5. (A) Fluorescence quenching of 1-methoxynaphthalene by increasing amounts of 2-(*p*-cyanophenyl)-4-methyl-3-phenyloxetane (from 0 to 0.023 M). (B) Spectrum obtained 1 μs after LFP (λ_{exc} = 308 nm, MeCN/Ar) of 1-methoxynaphthalene (10^{-4} M) in the presence of 2-(*p*-cyanophenyl)-4-methyl-3-phenyloxetane (1.43×10^{-3} M).

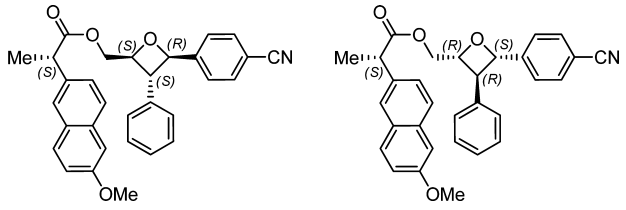
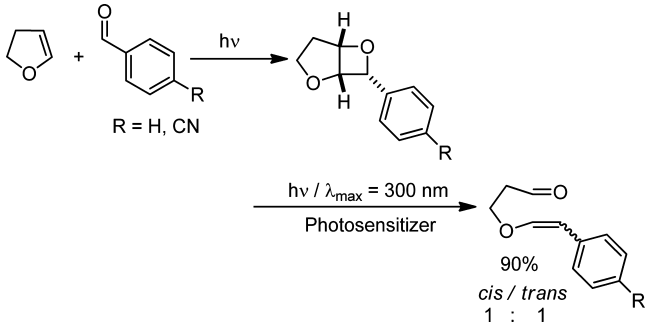


Figure 6. Chemical structures of stereoisomeric dyads constructed by linking methoxynaphthalene and oxetane moieties.

time-resolved photolysis, using (thia)pyrylium salts as ET sensitizers.[49] The isolated photoproducts are stilbene and 2,3-diphenyl-4-hydroxytetrahydrofuran (Scheme 6) in addition to 2,5-dihydroxy-1,4-dioxane (the dimer of hydroxyacetaldehyde). Initial O−C2 cleavage gives rise to a distonic radical cation, where spin and charge are located in the oxygen and the C2 atoms, respectively. This intermediate follows two competing pathways, namely, C−C cleavage and intramolecular nucleophilic attack. After LFP excitation of a sensitizer/oxetane mixture, a transient band is observed centered at ca. 470 nm, corresponding to stilbene radical cation. Its formation is not "instantaneous" and occurs in the submicrosecond time scale. The estimated rate constant of intramolecular nucleophilic attack is 2.7×10^6 s^{-1}.

Intermolecular trapping of a similar 1,4-radical cation intermediate has been achieved in the ET oxidation of *trans,trans*-2-cyclopropyl-4-methyl-3-phenyloxetane.[50] Its TTP^+ sensitized photolysis in acetonitrile leads to *trans*-1-propenylbenzene, cyclopropanecarboxaldehyde, and the solvent adduct *cis,trans*-4-cyclopropyl-2,6-dimethyl-5-phenyl-4*H*-5,6-dihydro-1,3-oxazine. Combined fluorescence and LFP results indicate that the reaction takes place from the singlet excited state of the photosensitizer, which agrees well with the estimation of the free energy changes associated with ET from this excited state. The operating mechanism is summarized in Scheme 7.

Scheme 3. Photometathesis in the PET-CR of a Dihydrofuran-Derived Oxetane



In principle, C2−C3 or O−C2 cleavage can occur. The first pathway leads to a 1,4-radical cation, whose carbocationic site is stabilized by oxygen as an oxonium ion. Subsequent O−C4 bond cleavage affords *trans*-1-propenylbenzene radical cation and cyclopropanecarboxaldehyde. The alternative C2−C3 or O−C2 bond breaking pathway involves formation of a different 1,4-radical cation with spin and charge located at the oxygen and at

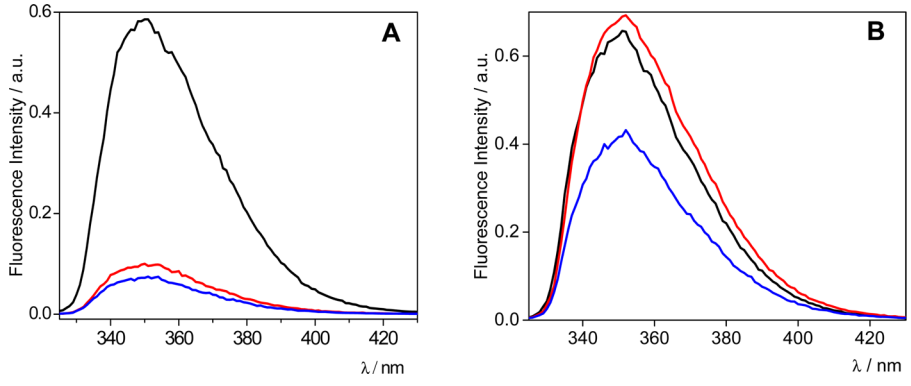


Figure 7. Fluorescence spectra of methoxynaphthalene (black) and methoxynaphthalene−oxetane dyads with (*R,S,S*) (red) or (*S,R,R*) (blue) stereochemistry, recorded after excitation at 320 nm under nitrogen in acetonitrile (A) and in chloroform (B).

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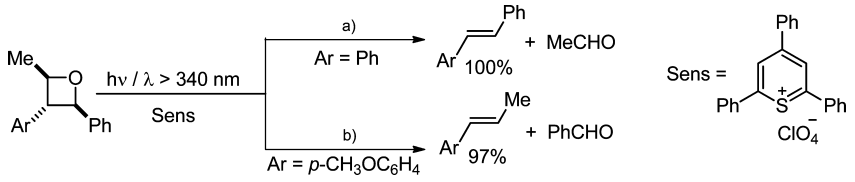
Scheme 4. Thiapyrylium-Sensitized Photoreaction of *trans,trans*-2,3-Diaryl-4-methyloxetanes



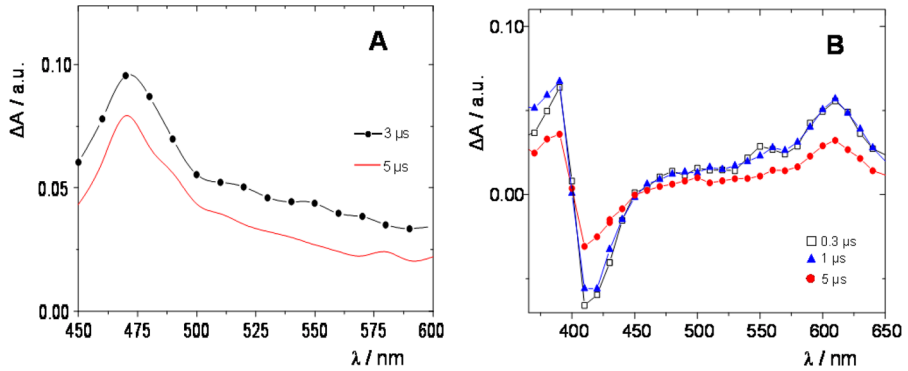
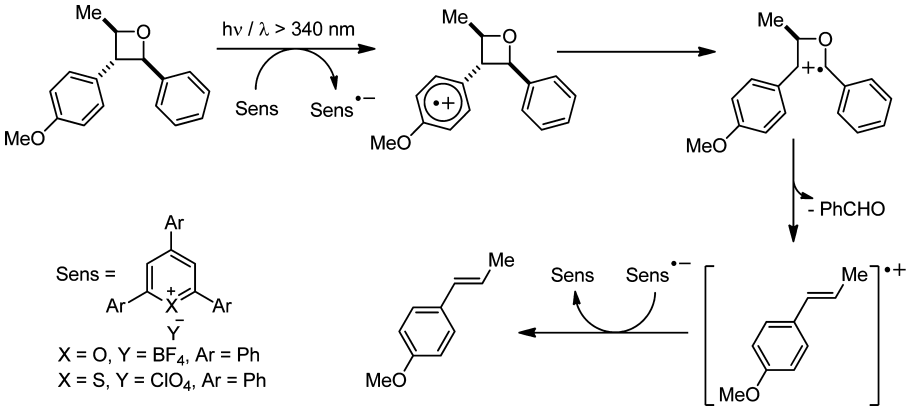
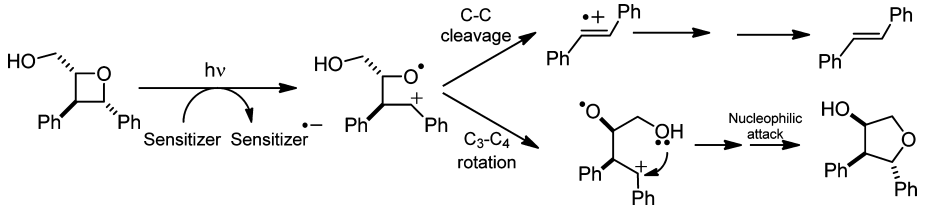


Figure 8. Transient absorption spectra obtained at the indicated delays after LFP (λ_{exc} = 355 nm, MeCN, Ar) of oxetanes in the presence of TTP^{+}: (A) *trans,trans*-2,3-diphenyl-4-methyloxetane; (B) *trans,trans*-3-(4-methoxyphenyl)-2-phenyl-4-methyloxetane.

Scheme 5. Photosensitized ET Ring Splitting of *trans,trans*-3-(4-Methoxyphenyl)-2-phenyl-4-methyloxetane



Scheme 6. Intramolecular Trapping in the PET Reaction of *trans,trans*-2,3-Diphenyl-4-hydroxymethyloxetane



C2, respectively. The higher degree of charge localization favors now nucleophilic attack by acetonitrile at C2, leading to a nitrilium derivative; ring closure and back-electron transfer affords the solvent adduct. This is a new reaction, which formally constitutes the creation of a six-membered heterocyclic ring from C═C, C═O, and C═N units. The absence of acetaldehyde and *trans*-2-cyclopropyl-1-phenylethene in the photomixture indicates that nucleophilic attack by acetonitrile occurs faster than C3−C4 cleavage. Since the initial *trans* arrangement of phenyl and cyclopropyl groups in the oxetane is no longer maintained in the oxazine, bond rotation must occur along the reaction path. Theoretical calculations at the UMP2(FC)/6-31G(d) level support the mechanism assignment (see Figure 9).

3. AZETIDINES

The azetidine ring is found in a variety of natural products and biologically active substances. In addition, it is a key substructure of synthetic intermediates and conformationally constrained amino acids used for the design of novel peptides. The PET CR of azetidines has also been the subject of experimental and theoretical work related to UVB-induced DNA repair.[21,22] Moreover, the generation and fate of azetidine radical ions in

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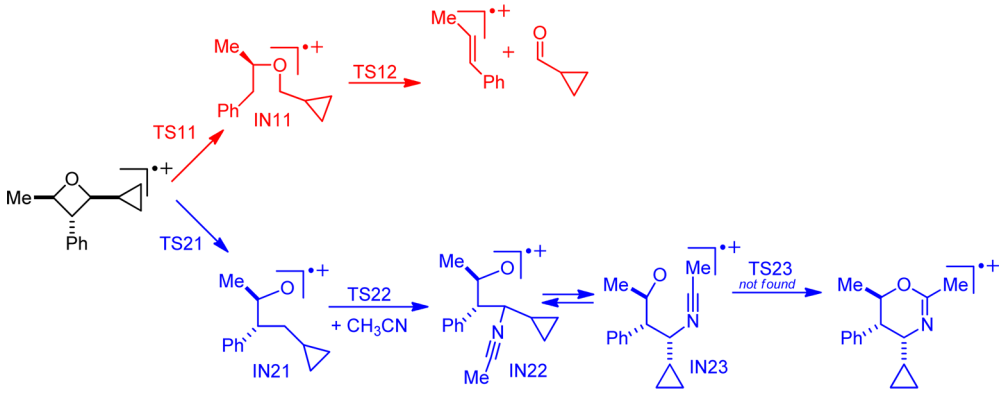
Scheme 7. Reaction Pathways of *trans,trans*-2-Cyclopropyl-4-methyl-3-phenyloxetane in the Absence and in the Presence of Acetonitrile



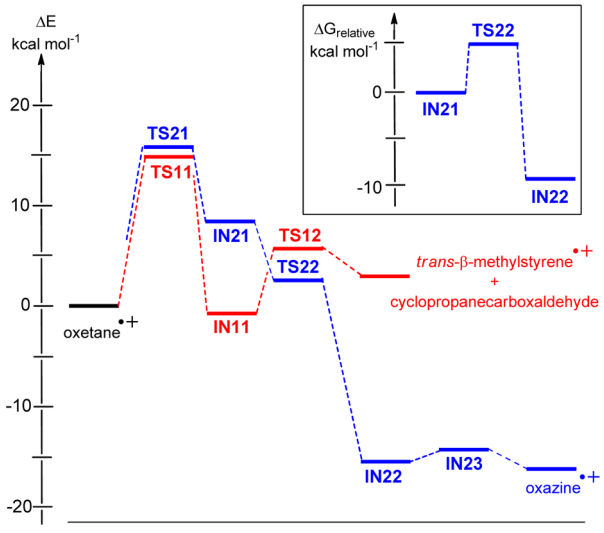


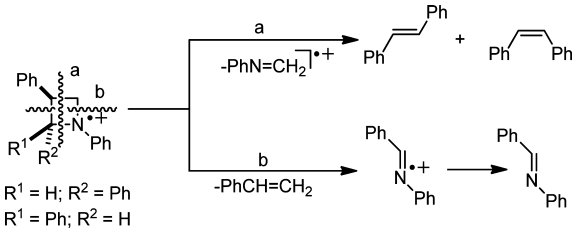
Figure 9. Diagram showing the relative energies of the transition states and intermediates involved in the PET CR of *trans,trans*-2-cyclopropyl-4-methyl-3 phenyloxetane. Inset: relative free energies of transition state TS22 and intermediates IN21 and IN22, taking into account the entropy contribution due to the bimolecular nature of this step.

the gas phase has been reported in the course of mass spectrometric studies.[51]

Reaction of *cis*- and *trans*-1,2,3-triphenylazetidine with tris(4-bromophenyl)aminium hexachloroantimonate (BAHA) as ET-oxidizing agent leads to *cis*- and *trans*-stilbene, together with *N*-benzylideneaniline.[52] In this context, LFP of neutral tris(4-bromophenyl)amine leads to photoionization (Figure 10A), and the resulting aminium radical cation is quenched by both azetidine stereosisomers (Figure 10B), with a rate constant of 2×10^9 M^{-1} s^{-1}. This is assumed to occur by ET, on the basis of the favorable free energy changes associated with the process.

By contrast, no quenching of the aminium radical cation is observed in the presence of *cis*- or *trans*-stilbenes. This supports that twisting around the C2−C3 bond occurs in the 1,4 intermediate, through a stepwise CR of the azetidine radical cation. Furthermore, no new transient absorption spectrum corresponding to *cis*- or *trans*-stilbene radical cations is detected, indicating that CR of the azetidine along pathway a (Scheme 8)

Scheme 8. Fragmentation of *cis*- and *trans*-1,2,3-Triphenylazetidine Radical Cations



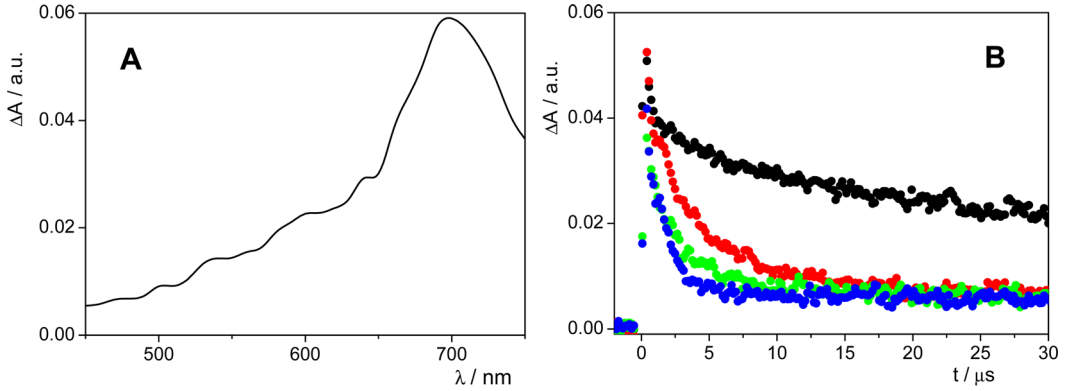


Figure 10. (A) Spectrum obtained upon LFP of tris(4-bromophenyl)amine (λ = 355 nm, $MeCN/N_2$). (B) Quenching of the resulting radical cation at 690 nm by increasing amounts of *trans*-azetidine. Concentration of amine is 2.5×10^{-4} M in all cases. The decay traces correspond to amine/azetidine ratios equal to 1:0 (black), 1:0.5 (red), 1:1 (green), and 1:2 (blue).

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leads to spin and charge located at the more easily oxidizable imine fragment. The same is true for CR through pathway b in Scheme 8, which leads to the radical cation of *N*-benzylideneaniline. Overall, the results correlate well with the fragmentation routes observed in the gas phase upon electron impact ionization.

4. THIETANES

Although bipyrimidine-derived oxetanes and azetidines are thought to be the primary intermediates leading to (6–4) photoproducts, they are not sufficiently stable at room temperature to investigate the mechanism of DNA repair. However, the corresponding thietanes are much longer lived and can therefore be conveniently employed for model studies in the field.[53−55]

In this context, reductive CR of a thietane has been achieved by intramolecular PET from a covalently linked flavin moiety (Figure 11).[56] However, thietanes derived from pyrimidine/thiopyrimidine dinucleotides are not enzymatically repaired,[57] which can be attributed to inefficient binding rather than to lack of ET reactivity.

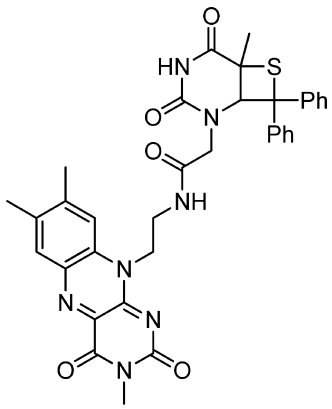


Figure 11. Thietane model containing a covalently linked flavin for intramolecular PET studies.

As regards the oxidative version of thietane CR, photosensitization of 3-cyano- or 3-ethoxy-2,2-diarylthietane by 9,10-dicyanoanthracene affords selectively 1,1-diarylethenes.[58] The reaction is thought to involve PET from the sulfur atom to the singlet excited state of the sensitizer, followed by S−C2 cleavage of the sulfide radical cation. This assumption is based on the observed quenching of dicyanoanthracene fluorescence by the thietanes.

A deeper mechanistic insight into the oxidative CR of thietanes has been gained by a combination of product studies, LFP, and theoretical calculations at the UB3LYP/6-31G* level.[59,60] Photosensitization of 2,2,3-triarylthietanes by TTP^+ leads to thiobenzophenone and the corresponding alkenes, eventually followed by secondary [4 + 2] CA (Scheme 9). Crossover experiments are in agreement with formation of ion−molecule complexes, and final product distribution depends on the escape ability of fragments.

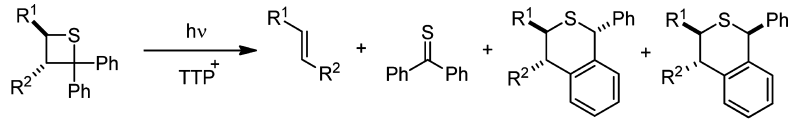
The triplet excited state of TTP^+ is quenched by thietanes at diffusion-controlled rate. In the case of the methyl-substituted derivatives, a new transient peaking at 500 nm appears concomitantly with the diminution of the T−T band (Figure 12A); this species is assigned to the isothiochromane radical cation. For the substrate bearing a methoxyphenyl substituent, the anethole radical cation is also observed at 600 nm. Excitation of TTP^+ at 355 nm in the presence of the tetraphenyl substituted analogue gives rise to stilbene radical cation (centered at 470 nm), whose growth kinetics becomes faster in the presence of increasing thietane concentrations (Figure 12B). All these data unambiguously confirm the involvement of an ET process from the triplet excited state of the photosensitizer.

Overall, the results support formation of thietane radical cations through PET from their neutral precursors to the triplet excited state of TTP^+. Ring-splitting through C2−C3/C4−S bond scission is followed by formation of an ion−molecule complex. Escape of free radical ions from this complex constitutes a critical event. Back electron transfer leads to the alkenes plus thiobenzophenone. An alternative pathway is [4 + 2] CA, followed by rearrangement and back electron transfer, to give eventually the isothiochromanes. Competition between escape and [4 + 2] CA depends on the relative energy barriers: the former is clearly favored in the case of the tetraphenyl derivative, whereas the latter largely predominates with the triphenyl analogue as starting material. The situation for the methoxyphenyl substituted thietane is intermediate.

Actually, the feasibility of ET-mediated [4 + 2] CA between thiobenzophenone and arylalkenes (*trans*-1-propenylbenzene, *trans*-anethole, and *trans*-4-chloro-1-propenylbenzene) has been proven in separate experiments.[61] Based on transient absorption spectroscopic evidence, quenching of the triplet excited state of TTP^+ by both thiobenzophenone and the arylakenes is observed, and the radical cations of the latter are effectively detected. Thus, the spectrum obtained after LFP of TTP^+ exhibits the characteristic band of the triplet excited state, while in the presence of *trans*-anethole the alkene radical cation is clearly observed; its intensity decreases upon addition of thiobenzophenone (Figure 13). The estimated ΔG_{ET} values (between −10.3 and −7.9 kcal mol^{-1}) indicate that ET from the three arylalkenes to $^3TTP^{+}$* is exergonic.

The mechanistic aspects of the process have been analyzed using DFT methods at the UB3LYP/6-31G* level.[62] After generation of the radical cations, formation of a molecular complex (MC) initiates a stepwise mechanism, where ring closure is the rate-determining step. The reaction mechanism for this novel ET CA reaction is outlined in Scheme 10.

Scheme 9. Photosensitized Irradiation of 2,2,3-Triarylthietanes in the Presence of TTP^+



$R^1 = CH_3$, R^2 = Ph	-	-	48%	52%
$R^1 = CH_3$, R^2 = 4-$CH_3OC_6H_4$	26%	28%	33%	39%
$R^1 = R^2$ = Ph	100%	85%	-	-

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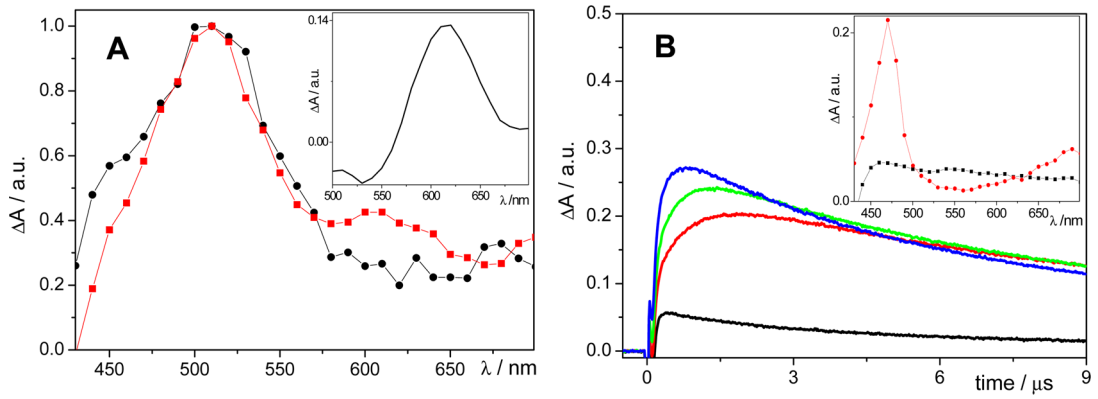

Figure 12. (A) Normalized spectra obtained 0.4 μs after LFP (λ = 355 nm, MeCN, Ar) of TTP^+ (0.06 mM) in the presence of 1 mM 4-methyl-2,2,3-triphenylthietane (black) or 1 mM 2,2-diphenyl-3-(4-methoxyphenyl)-4-methylthietane (red). Inset: Difference spectrum of both traces (smooth fitting). (B) Kinetics monitored at 470 nm after 355 nm LFP of TTP^+ (0.06 mM) in the presence of increasing amounts of 2,2,3,4-tetraphenylthietane: 0 M (black), 0.05 mM (red), 0.1 mM (green), and 0.2 mM (blue). Inset: Transient absorption obtained for TTP^+ (0.06 mM) in the absence (black) and in the presence of 2,2,3,4-tetraphenylthietane (1 mM) (red).

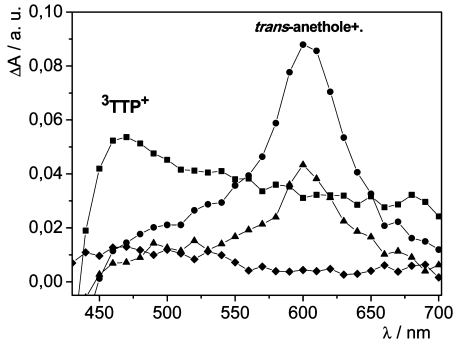

Figure 13. Transient absorption spectra obtained 1 μs after LFP (λ = 355 nm, MeCN, Ar) of TTP^+ (0.06 mM) in the absence of *trans*-anethole (■) and in the presence of 1 mM *trans*-anethole (●), 1 mM *trans*-anethole and 0.05 mM thiobenzophenone (▲), or 0.05 mM thiobenzophenone (♦).

5. CONCLUDING REMARKS

Radical ionic hetero-cycloreversions are emerging as an active research field. Especially, they have attracted considerable interest from a photobiological point of view, in connection with repair of pyrimidine(6−4)pyrimidone photolesions in DNA by photolyases and, to a lesser extent, with excess electron transport in DNA. These reactions have only been explored with four-membered heterocycles, with oxetanes as the most thoroughly investigated systems. In general, ring cleavage occurs through a nonconcerted two-step mechanism. This is consistent with the stereochemistry of the obtained products, with the results of trapping experiments, and with theoretical calculations. Direct mechanistic evidence is provided by fluorescence and laser flash photolysis studies. The initial step can be either C−C or C−X bond breaking; the latter is more frequent, especially in the radical anionic version. Finally, activation of cycloreversion by ionization of the heterocycle provides a new synthetic strategy, which deserves further investigation, in view of its potential to produce new chemistry. As an example, it can in principle be exploited for achieving C═X/olefin metathesis or for ring expansion to create complex six-membered heterocyclic systems.

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Notes

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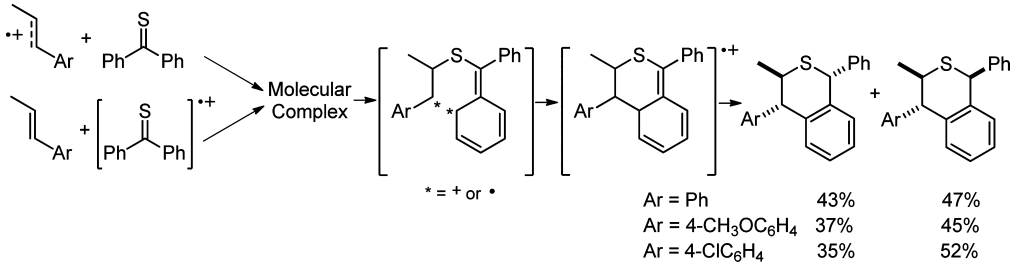
Scheme 10. Radical Cationic Cycloaddition between Thiobenzophenone and Arylalkenes



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