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# Bypassing the Energy Barrier of Homolytic Photodehalogenation in Chloroaromatics through Self-Quenching

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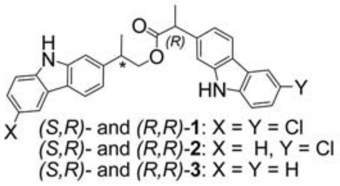
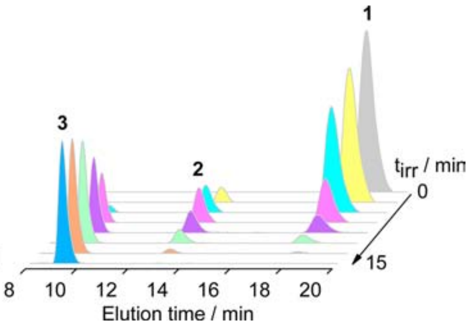
## ABSTRACT



(*S*,*R*)- and (*R*,*R*)-**1**: X = Y = Cl
(*S*,*R*)- and (*R*,*R*)-**2**: X = H, Y = Cl
(*S*,*R*)- and (*R*,*R*)-**3**: X = Y = H



**Reductive photodehalogenation of chloroaromatics is assumed to proceed from the triplet excited state, although its energy is often insufficient to promote a clean homolytic C−Cl cleavage. A clear-cut experimental proof is provided that correlates self-quenching of the directly observed triplet excited states of chlorocarbazole-based dyads 1 and 2 with photoreactivity via intramolecular charge transfer.**

Aryl halides are in general fairly unreactive. As they usually do not participate in conventional nucleophilic aromatic substitution, halogens are only displaced by strong nucleophiles via radical anions; however, the use of light as activating agent has proven to be an efficient way for increasing the reactivity of these substrates in dehalogenation processes.[1]

The photochemistry of aryl halides has attracted considerable interest over the last decades, not only for the mechanistic understanding of carbon−halogen photodissociation dynamics but also for the development of synthetic applications.[2] Moreover, photolysis of persistent polychlorinated biphenyls and other haloaromatic pollutants has

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gained momentum as a tool for environmental remediation.[3]

A variety of mechanisms have been invoked for the photodehalogenation of aryl halides,[1a,b,4] and special attention has been focused on the intriguing pathways of reductive dechlorination.[5] In the case of chloroaromatics, the reaction is assumed to proceed from the triplet excited state, although its energy is often insufficient to promote a clean homolytic C−Cl cleavage leading to aryl radicals and chlorine atoms.[1a,b,6]

As a way to circumvent the unfavorable thermodynamics of this step, it has been proposed that the actual operating mechanism involves formation of triplet excimers.[1a,b,5e,7] However, a clear-cut experimental proof supporting this hypothesis, linking self-quenching of the directly observed triplet excited states with reactivity, is still missing. A possible strategy to obtain such a piece of evidence could be based on the use of dyads containing two identical chloroaromatic subunits covalently attached by means of a spacer. With this purpose, we have designed two diastereomeric dyads, namely (*S*,*R*)-**1** and (*R*,*R*)-**1**, based on carprofen (**CPF**); their chemical structures are shown in Figure 1. This choice is based on the well-known photochemistry of **CPF**, a nonsteroidal anti-inflammatory drug containing a chlorocarbazole chromophore, whose reductive dehalogenation occurs from a detectable triplet excited state.[8] Steady-state irradiation, fluorescence and laser flash photolysis studies have been performed on the dyads, and the results have been compared with those obtained using the methyl ester of **CPF** (**CPFMe**) as reference compound.

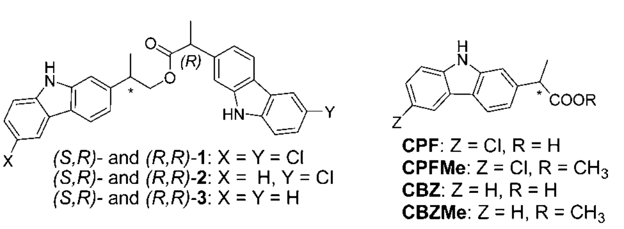

**Figure 1.** Chemical structures of diastereomeric dyads **1**−**3** and model compounds **CPF**, **CPFMe**, **CBZ**, and **CBZMe**.

Bichromophoric dyads (*S*,*R*)- and (*R*,*R*)-**1** were prepared by esterification of (*R*)-**CPF** with the alcohol obtained from reduction of (*S*)- or (*R*)-**CPF** and were fully characterized. Their synthetic details and spectroscopic data are presented in the Supporting Information.

Solutions of (*S*,*R*)- and (*R*,*R*)-**1** in MeCN/N$_2$ ($10^{-4}$ M) were irradiated in a multilamp photoreactor ($\lambda_{max}$ = 300 nm). The course of the reaction was followed by HPLC (reverse phase, MeCN/H$_2$O 80:20 v/v as eluent). The chromatograms of the photomixtures obtained at different times for (*S*,*R*)-**1** are shown in Figure 2A. The starting compound ($t_R$ = 18 min) reacted until complete disappearance after 15 min of irradiation, concomitantly with the appearance of a first photoproduct ($t_R$ = 13.5 min), which emerged at short irradiation times and was completely consumed upon prolonged irradiation. This was accompanied by formation of a second photoproduct ($t_R$ = 9 min), which remained as the only final component of the photolyzate. The two compounds with $t_R$ = 13.5 and 9 min were isolated and fully characterized (Supporting Information). The MH$^+$ value found for the molecular ion of the former in MS was 481 amu, which points to a reductive monodehalogenation of (*S*,*R*)-**1**. In principle, replacement of Cl with H can occur in any of the two carbazole rings, and therefore two different regioisomers with similar spectroscopic patterns can be formed. The chemical structure of this photoproduct was unequivocally assigned as (*S*,*R*)-**2** (Figure 1) by acid-catalyzed methanolysis, followed by GC−MS analysis (experimental details in the Supporting Information). Likewise, the chemical structure of the photoproduct with $t_R$ = 9 min was unambiguously assigned as (*S*,*R*)-**3** on the basis of its MS spectrum (MH$^+$ = 447 amu) and NMR data.

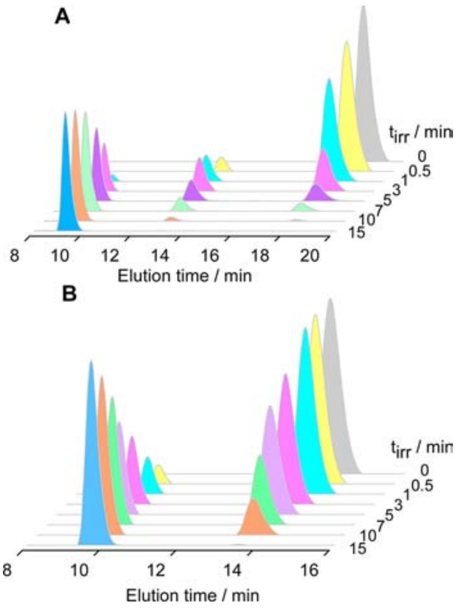

**Figure 2.** HPLC chromatograms obtained for irradiation ($\lambda_{max}$ = 300 nm, MeCN/N$_2$, $10^{-4}$ M concentration) for **A**: (*S*,*R*)-**1** and **B**: (*S*,*R*)-**2**. The detection wavelength was 297 nm.

Thus, (*S*,*R*)-**2** is formed and consumed during the course of the reaction, and (*S*,*R*)-**3** is the result of a double dehalogenation. Expectedly, direct photolysis of (*S*,*R*)-**2** under the same conditions afforded (*S*,*R*)-**3** (Figure 2B),

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**Table 1.** Product Distribution (%) after Monocromatic Irradiation of **1**, **2**, and **CPFMe** at Different Times ($\lambda_{exc}$ = 300 nm, MeCN/$N_2$)

| | (*S*,*R*)-**1**[a] | | | (*R*,*R*)-**1**[a] | | | (*S*,*R*)-**2**[b] | | (*R*,*R*)-**2**[b] | | **CPFMe**[b] | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| time (s) | (*S*,*R*)-**1** | (*S*,*R*)-**2** | (*S*,*R*)-**3** | (*R*,*R*)-**1** | (*R*,*R*)-**2** | (*R*,*R*)-**3** | (*S*,*R*)-**2** | (*S*,*R*)-**3** | (*R*,*R*)-**2** | (*R*,*R*)-**3** | **CPFMe** | **CBZMe** |
| 30 | 96 | 4 | | 95 | 5 | | 98 | 2 | 98 | 2 | >99 | <1 |
| 60 | 95 | 5 | | 93 | 7 | | 93 | 7 | 94 | 6 | >99 | <1 |
| 280 | 83 | 14 | 3 | 85 | 13 | 2 | 80 | 20 | 84 | 16 | 97 | 3 |
| 400 | 76 | 19 | 5 | 78 | 19 | 3 | 77 | 23 | 81 | 19 | 96 | 4 |

[a] $A_{samples}$ = 0.3. [b] $A_{samples}$ = 0.1.

**Table 2.** Photophysical Parameters of Dyads **1**−**3** and Models **CBZMe** and **CPFMe** in MeCN/$N_2$.

| compd | $\lambda_{max}$[a] | $\phi_F$[b] | $\tau_T$ ($\mu$s) | $k_Q \times 10^{-5}$ ($s^{-1}$) | $\phi_T$[c] |
|---|---|---|---|---|---|
| **CBZMe** | 343, 358 | 0.540 | 5.4 | | 0.23 |
| **CPFMe** | 354, 369 | 0.069 | 3.2 | | 0.43 |
| (*S*,*R*)-**1** | 354, 369 | 0.045 | 0.7 | 11.1 | 0.24 |
| (*R*,*R*)-**1** | 354, 369 | 0.046 | 0.9 | 8.0 | 0.25 |
| (*S*,*R*)-**2** | 354, 369 | 0.062 | 1.7 | 2.8 | 0.30 |
| (*R*,*R*)-**2** | 354, 369 | 0.059 | 1.9 | 2.1 | 0.31 |
| (*S*,*R*)-**3** | 345, 360 | 0.509 | 6.0 | | 0.22 |
| (*R*,*R*)-**3** | 345, 360 | 0.515 | 6.1 | | 0.22 |

[a] Maxima of emission, in nm. [b] Determined using **CPF** in MeCN/$N_2$ as standard.[8a] [c] Determined using **CPF** in EtOH/$N_2$ as standard.[8a]

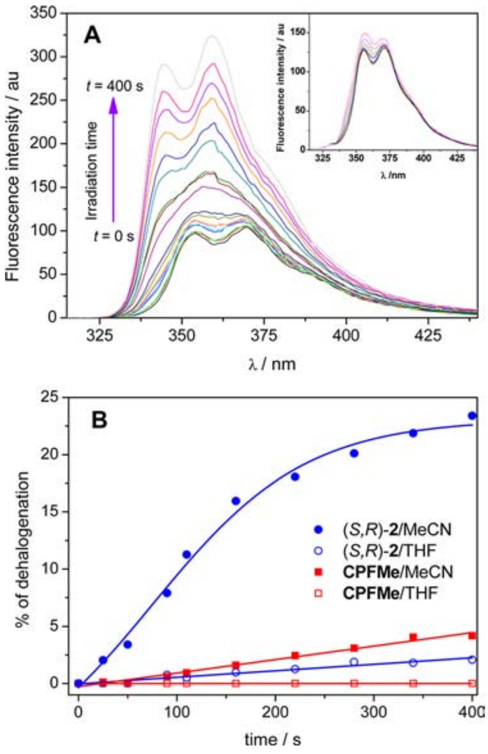

**Figure 3.** (A) Fluorescence spectra obtained after monochromatic irradiation of (*S*,*R*)-**2** at different times ($\lambda_{exc}$ = 300 nm/$N_2$) in MeCN. Inset: in THF. (B) Percentage of dehalogenation for (*S*,*R*)-**2** and **CPFMe** in MeCN and THF (symbols) and their corresponding tendency lines.

which was found to be photostable (Supporting Information). A parallel behavior was observed for the (*R*,*R*)-dyads (Supporting Information). Irradiation of the reference compound **CPFMe**, under the same conditions, led to **CBZMe** (Figure 1) as the only photoproduct.

After completing the product studies, the photodehalogenation kinetics of (*S*,*R*)- and (*R*,*R*)-**1** were investigated at lower concentration, using monochromatic light ($\lambda_{exc}$ = 300 nm, absorbance of the samples ca. 0.3), until conversions lower than 25% were reached. The product distributions are shown in Table 1. In the case of (*S*,*R*)- and (*R*,*R*)-**2**, the huge fluorescence changes associated with the reaction allowed us to follow its progress by direct steady-state emission measurements on the photomixtures. The values obtained for the emission maxima ($\lambda_{max}$) and fluorescence quantum yields ($\phi_F$) of the dyads and their photoproducts are summarized in Table 2. The coincidence between the photophysical properties of **1** and **2** revealed a thermodynamically favored singlet singlet energy transfer in **2** from the carbazole to the chlorocarbazole unit, which is the dominating chromophore. By contrast, the absence of Cl in dyads **3** and also in **CBZMe** resulted in a dramatic enhancement of the $\phi_F$ value (Table 2) (Supporting Information).

The fluorescence changes observed during the course of the photoreaction are shown in Figure 3A for (*S*,*R*)-**2**. For comparison, the photodehalogenation of **CPFMe** was followed in a similar way (Figure 3B and Table 1).

In agreement with the proposed dehalogenation mechanism, the results clearly show that dyads **1** and **2** are much more reactive than model **CPFMe**. Thus, after 400 s only a 4% of **CPFMe** was reacted, a value that was ca. 6 times higher for **1** and **2**. No significant stereodifferentiation was observed for the dyads.

Laser flash photolysis experiments ($\lambda_{exc}$ = 308 nm, MeCN/$N_2$) were performed on the substrates, to prove the involvement of triplet excited state and self-quenching in the mechanism of the photochemical reaction. For **1**, **2**, and **CPFMe**, the transient absorption spectra displayed the characteristic T-T band with maximum at 430 nm (Supporting Information); however, the quantum yields and the kinetic decays of these species were markedly different (see Table 2 and Figure 4A), with triplet lifetime values

($\tau_T$) much higher for **CPFMe** (3.2 $\mu$s) than for the mono- (1.7−1.9 $\mu$s) and dihalogenated dyads (0.7−0.9 $\mu$s). The triplet quenching rate constants were estimated using the relationship $k_Q = 1/\tau_{T(\mathrm{dyad})} - 1/\tau_{T(\mathbf{CPFMe})}$ and are in the range of $10^5$−$10^6$ $s^{-1}$ (Table 2).

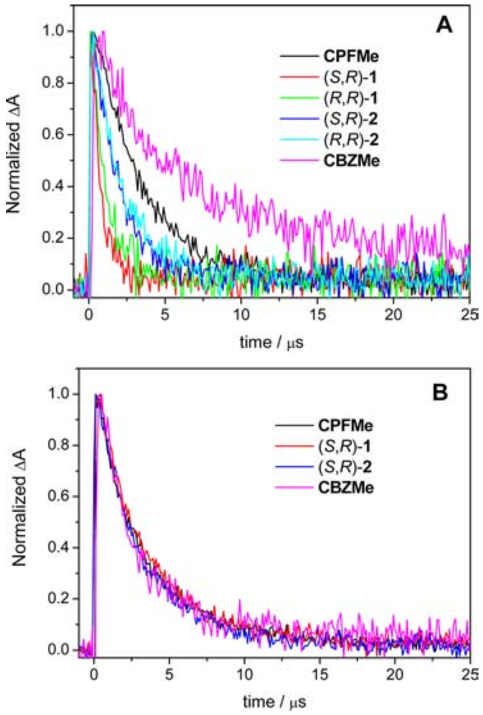

**Figure 4.** Decays monitored at 430 nm after laser flash photolysis ($\lambda_{exc}$ = 308 nm/$N_2$) for dyads and reference compounds (A) in MeCN and (B) in THF.

The observed self-quenching deactivation pathway can give rise to charge-separated species (excimers/exciplexes or radical ion pairs). To discriminate between both possibilities, Rehm−Weller equations[9] were applied. Taking into account the oxidation potential of chlorocarbazole (1.2 V),[10] the reduction potential of **CPFMe** (determined as −1.8 V by cyclic voltammetry, Supporting Information), the dielectric constant of MeCN (37.5)[11] and the triplet excited state energy of **CPF** (69 kcal mol$^{-1}$),[8a] electron transfer was found to be feasible ($\Delta G_{ET}$ = −1.2 kcal mol$^{-1}$), while excimer formation was disfavored ($\Delta G_{ex}$ = +3.9 kcal mol$^{-1}$).

The required geometrical arrangement for self-quenching can only be achieved in folded conformations, where interchromophoric interactions would be maximized. Interestingly, the X-ray structure of (*S*,*R*)-**1** (the only dyad that was obtained in crystalline form) exhibited such a folded conformation (Figure 5).

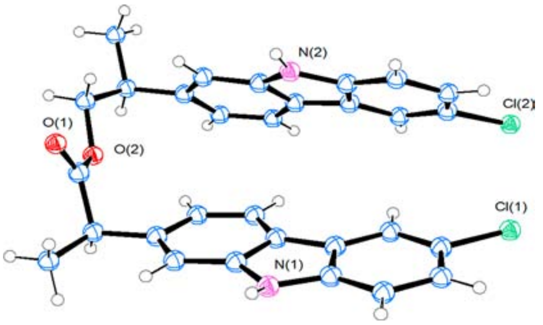

**Figure 5.** X-ray structure of compound (*S*,*R*)-**1**.

To obtain further support for the involvement of charge separated species in the reaction, irradiation was also performed in THF, a solvent of much lower dielectric constant ($\varepsilon$ = 7.6). Here, the Rehm−Weller equations predict endergonic values for both electron transfer and excimer formation (by +5.1 and +5.2 kcal mol$^{-1}$, respectively).[11] Accordingly, photodehalogenation was dramatically reduced in this solvent, as revealed by the comparison between (*S*,*R*)-**2** and **CPFMe** in THF and MeCN (Figure 3B). Noteworthy, the kinetic traces of the triplet excited state were practically coincident for **1**, **2**, and **CPFMe** (Figure 4B), underlining the absence of quenching, as expected from the low reactivity of the triplet excited state.

In summary, self-quenching of the directly observed triplet excited states of **CPF**-based dyads **1** and **2** has been demonstrated. This process can be clearly correlated with reductive photodehalogenation, which occurs from the resulting charge separated species. The trends observed in the triplet lifetimes, as well as the solvent effects on photoreactivity, are in full agreement with this mechanistic picture.

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**Supporting Information Available.** Additional experimental details and experiments, spectroscopic data of the new compounds, NMR spectra of dyads **1**−**3**, and X-ray structure of (*S*,*R*)-**1**. This material is available free of charge via the Internet at http://pubs.acs.org

The authors declare no competing financial interest.

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