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Stereodifferentiation in the Decay of Triplets and Biradicals Involved in Intramolecular Hydrogen Transfer from Phenols or Indoles to π,π* Aromatic Ketones

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Laser flash photolysis studies on (*R*,*S*) and (*S*,*S*) diastereoisomers of the bichromophoric compounds **1**−**6** have been used to investigate the possible chiral discrimination in the quenching of triplet excited ketones, resulting in formal hydrogen abstraction. Deuterium isotopic effects show that triplet deactivation in these bichromophores is dominated by hydrogen atom transfer. A remarkable stereodifferentiation is found in the intramolecular quenching of the ketone triplets of **1**−**3** and **5** by the phenolic or indolic moieties, either in methanol or acetonitrile as solvents. This indicates the existence of specific structural requirements for hydrogen transfer. On the other hand, the lifetimes of the generated biradicals show large solvent dependence; solvation appears to slow their reversion to the starting ketone. The considerable stereodifferentiation observed for the biradical lifetimes suggests that the kinetics of biradical decay is faster when the approach of the two radical termini becomes easier.

Introduction

Asymmetric photosensitization with optically active compounds is one of the most promising and less explored fields in mechanistic and synthetic organic photochemistry.[1] As in the case of absolute asymmetric photochemistry with polarized light, chirality transfer takes place during generation of the substrate-derived excited states and may be enhanced via exciplex formation. Excited-state interaction between sensitizer and substrate was believed to be weak and difficult to control; however, some studies have revealed that it is possible to achieve regio- and/or stereochemical control in photosensitized reactions.[2] Enantiodifferentiation can occur either in the quenching of excited chiral sensitizers or in the subsequent decay of the resulting species. In some sensitized photoreactions the asymmetry of exciplex formation seems to be compensated by an opposite asymmetry in the evolution of the exciplexes that leads back to the starting material and to photoproducts. Thus, Rau et al.[1b] have demonstrated that although chiral recognition of triplet ruthenium electron donors by optically active methyl viologens is high, the enantiodifferentiation observed in product formation can be diminished due to competing back electron transfer.

For photoinduced hydrogen abstractions the possibility of conformational control in Norrish-type II reactions or photoenol formation has been reported.[3−6] Geometrical factors, such as the mutual orientation and distance of reactant groups in the initial stages of the reaction, may have an important influence on the kinetics and mechanism of hydrogen or electron-transfer processes.[3−10] This may be due to the different overlap between the electron clouds of donor and acceptor by a through space interaction. In such cases, the trajectory of approach could be a key factor. Thus, in bichromophoric derivatives, Leigh and co-workers have found that the rate of intramolecular H-abstraction of phenolic O−H by ketones depends on the position of attachment of the involved chro-

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mophores to an inert linker.[11] Moreover, in compounds of the type BP$-$O(CH$_2$)$_n$O$-$DPA, containing benzophenone (BP) and diphenylamine (DPA) moieties, generation of an ion pair may or may not be followed by proton transfer, depending on the length of the linker; this competes with direct hydrogen abstraction, to give biradicals as common reaction intermediates.[12] When $n = 2$ almost all the formal hydrogen abstraction is ascribed to proton transfer within the ion pair; however, when $n = 3$ the contribution of this pathway is reduced to around 50%.

In this context, the use of chiral bichromophores containing enantiomerically pure sensitizer and quencher could enable us to investigate the possible chiral discrimination through the quenching rates of the excited sensitizer and/or the lifetimes of the generated intermediates by means of laser flash photolysis.

In the course of our studies on the photobinding of nonsteroidal antiinflammatories tiaprofenic acid (TPA) and suprofen (SUP) to proteins,[13] we became interested in covalently linked bichromophoric compounds as suitable models to study the excited-state interaction between drugs and biomolecules in preassociated complexes. Such models contain a 2-benzoylthiophene (BT) unit (the common chromophore of TPA and SUP) and tyrosine or tryptophan (the main protein reactive sites).

The lowest lying triplet of BT has a π,π^* configuration, involving mainly the thenoyl group, and is generated with a quantum yield close to unity.[14] BT undergoes [2 + 2] photocycloaddition to olefins[14b,15] through either the C=O or the thiophene C=C bonds. On the other hand, excited triplet BT is able to abstract hydrogen from suitable donors, though with low efficiency. Traynard and Blanchi have reported quantum yields of 0.17 for the disappearance of BT upon irradiation in 2-propanol, much lower than the value of 1.23 for benzophenone.[16] Recently,[17] we have performed a detailed study on the intermolecular photoreaction between BT and phenol and indole. Formal hydrogen abstraction by the BT triplet excited state can occur by sequential proton$-$electron transfer processes. Using the laser flash photolysis technique we have been able to observe clearly that the BT triplet, with absorption maxima at 350 ($\epsilon_{\max} = 4800$ M^{-1} cm^{-1}) and 600 nm ($\epsilon_{\max} = 2900$ M^{-1} cm^{-1}),[17] changes upon its conversion into the BT ketyl radical (BTH), with absorption maxima at 350 ($\epsilon_{\max} = 9100$) and 580 nm ($\epsilon_{\max} = 2100$ M^{-1} cm^{-1}). Besides, phenoxy (PhO) and indolyl (In) radicals are formed. Though formation of BTH/PhO and BTH/In radical pairs occurs with quantum yields close to 1, low conversions of the starting reagents to give the final radical coupling products are observed even upon prolonged irradiation. This indicates that regeneration of the starting materials is the major process undergone by the radical pairs. The solvent dependence of the quenching rate constants, together with DFT theoretical studies, indicates fundamental differences between the mechanisms of the reaction of BT triplet with phenol and indole. Thus, data for phenol agree with the involvement of a hydrogen-bonded exciplex BT···HOPh, where concerted electron and proton transfer leads to the BTH···OPh radical pair; however, in the case of indole, electron transfer at the BT···HIn stage precedes proton transfer.

Preliminary photophysical studies performed on bichromophoric compounds have shown stereodifferentiation in the intramolecular photoreaction between BT and phenols and indoles.[18,19] In this paper, we wish to report in full our studies on the photophysical and photochemical behavior of BT-derived bichromophoric compounds. Remarkably, we have found chiral recognition not only in the very fast quenching of the triplet state, but also in the subsequent decay of the generated biradicals.

Results and Discussion

Bichromophores. Compounds **1**, **2**, **3**, and **5** were obtained by condensation of racemic TPA and SUP with the methyl esters of the naturally occurring amino acids (*S*)-tryptophan or (*S*)-tyrosine (Chart 1). The resulting amides were purified and resolved into the pure diastereoisomers (*S*,*S*) and (*R*,*S*) by column chromatography and subsequent HPLC. Compounds **4** and **6** were obtained from the corresponding stereoisomers of **3** and **5** by *O*-methylation with diazomethane. Structures were unambiguously determined by X-ray for (*S*,*S*)-**3**, (*S*,*S*)-**5**, and (*R*,*S*)-**5**, thus allowing us to confidently assign the stereochemistries for compounds **3**$-$**6**. Although X-ray analysis only led to determining the relative configurations, the fact that the stereochemistries of the amino acids were known allowed the absolute configuration assignment. Likewise, good crystals were obtained from one of the indolic bichromophores; its structure was determined as (*R*,*S*)-**2** by X-ray analysis. The important angles and distances for all these compounds are reported in Table 1.

For the crystals of the tyrosine-derived bichromophores a short distance (around 1.9 Å) was found between the phenolic OH and the C=O of the diaryl ketone. This is indicative of an intramolecular hydrogen bond. In the case of the tryptophan-derived bichromophores, the only

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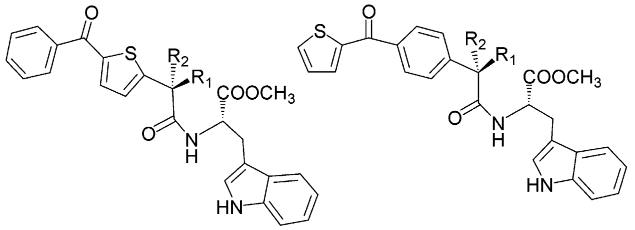
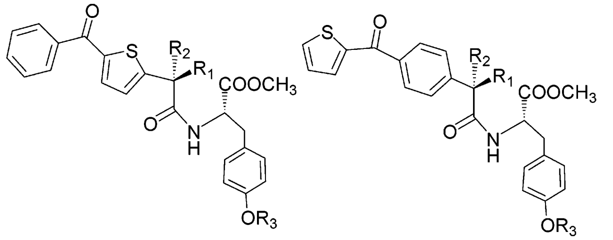
CHART 1. Bichromophoric Compounds



(*R*,*S*)-1 $R_1 = H, R_2 = CH_3$ **(*R*,*S*)-2** $R_1 = H, R_2 = CH_3$

(*S*,*S*)-1 $R_1 = CH_3, R_2 = H$ **(*S*,*S*)-2** $R_1 = CH_3, R_2 = H$



(*R*,*S*)-3 $R_1 = CH_3, R_2 = H, R_3 = H$ **(*R*,*S*)-5** $R_1 = H, R_2 = CH_3, R_3 = H$

(*S*,*S*)-3 $R_1 = H, R_2 = CH_3, R_3 = H$ **(*S*,*S*)-5** $R_1 = CH_3, R_2 = H, R_3 = H$

(*R*,*S*)-4 $R_1 = CH_3, R_2 = H, R_3 = CH_3$ **(*R*,*S*)-6** $R_1 = H, R_2 = CH_3, R_3 = CH_3$

(*S*,*S*)-4 $R_1 = H, R_2 = CH_3\ R_3 = CH_3$ **(*S*,*S*)-6** $R_1 = CH_3, R_2 = H, R_3 = CH_3$

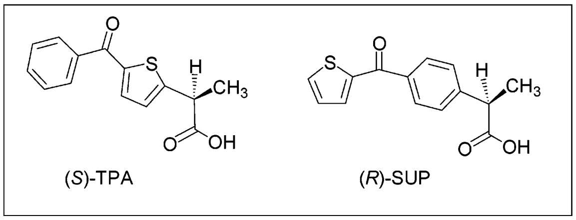


TABLE 1. Important Angles and Distances in Compounds 2, 3, and 5

	angles (deg)[a]		distances (Å)		
compd	Ph−C=O	Ar(S)−C=O	Ph (or Th)/ Tyr (or Trp)[b]	C=O···HO	C=O···X[c]
(*R*,*S*)-**2**	46.7	11.5	3.490		5.547
(*S*,*S*)-**3**	28.9	14.3	3.474	1.950	4.129
(*S*,*S*)-**5**	29.0	10.9	3.285	1.903	3.856
(*R*,*S*)-**5**	30.0	12.8	3.567	1.937	3.905

[a] Dihedral angles between the planes of the phenyl or thienyl ring and the carbonyl group. [b] Ring-to-ring distance between phenyl (or thienyl) and phenol (or indole). [c] Distance between the carbonyl oxygen atom and the X group (X: oxygen atom of the phenolic moiety or nitrogen atom of the indolic moiety).

available X-ray structure is that of (*R*,*S*)-**2**; it also shows a short distance between the aromatic rings connected through the aliphatic chain (see Table 1). However, the N−H bond does not appear to be involved in hydrogen bonding with the carbonyl n-orbital, at least in the solid state.

Conformational studies on 2-benzoylthiophene have shown that sulfur is on the same side of the carbonyl group and that the thienyl ring is almost coplanar with respect to the plane of the C=O bond.[20] However, the phenyl ring is significantly twisted, with a dihedral angle estimated to be ca. 71°. Thus, the extent of π-conjugation with the carbonyl is higher for the heteroaromatic ring.[20] This is in agreement with all the X-ray structures obtained for the bichromophoric compounds, where the sulfur atom and the carbonyl oxygen are oriented toward the same side, and the phenyl ring is far more deviated from coplanarity than the thienyl group (Table 1).

The stereochemical assignment for compounds **1** was achieved by alternative synthesis, starting from small amounts of the enantiomerically pure TPA (prepared according to literature procedures)[21] and (*S*)-tryptophan methyl ester; short reaction times were used to avoid racemization. Compounds **1**, **3**, and **4** differ from **2**, **5**, and **6**, respectively, in the relative aromatic ketone versus amino acid orientation. It has to be noted that the same spatial orientation of the substituents around the stereocenter in TPA-Tyr(Trp) and SUP-Tyr(Trp) compounds has the opposite *R*/*S* nomenclature due to different priority of the phenyl/thienyl groups (Chart 1).[22]

Deoxygenated methanolic solutions of **1**−**6** were irradiated for several hours with light from a mercury lamp filtered through Pyrex glass. Analysis of the reaction mixtures by ^{1}H NMR showed that these ketones were almost photoinert under the irradiation conditions.

Transient Intermediates: Triplets and Biradicals. The (*R*,*S*) and (*S*,*S*) diastereoisomers of the bichromophoric compounds **1**−**6** could be suitable substrates to study regio- and stereochemical aspects of the intramolecular electron-transfer process between excited benzoylthiophene and phenolic or indolic moieties.

Dynamic studies were performed by using deaerated methanolic solutions ($(7.0-8.0) \times 10^{-4}$ M) at 355 nm (Nd:YAG). Laser flash photolysis of the *O*-methylated phenolic derivatives **4** and **6** could provide an indication of the intrinsic triplet state properties of the chromophore present in all these compounds, taking into account the low reactivity found for anisole toward the 2-benzoylthiophene triplet ($k_q < 10^7$ M^{-1} s^{-1}). Actually, time-resolved absorption spectra obtained after laser irradiation of compounds **4** and **6** [see spectra for (*S*,*S*)-**4** and (*R*,*S*)-**6** in Figure 1A,B] showed the generation of a transient absorbing in the 300−700 nm range with maxima at 350 and 600 nm (lifetime around 2 μs). This absorption could be safely ascribed to the triplet state and is similar to that of 2-benzoylthiophene triplet.[14a,17] The lifetimes (see Table 2) were also similar to that of triplet BT.

In the phenolic bichromophores **3** and **5** there was a diminished transient absorption beyond 625 nm. Also the ratio $\Delta A_{350}/\Delta A_{600}$ was higher and the maximum in the visible region was shifted to 590 nm (Figure 1C,D). Similar spectra were observed for the indolic-derived bichromophores **1** and **2**, but with an enhanced broad

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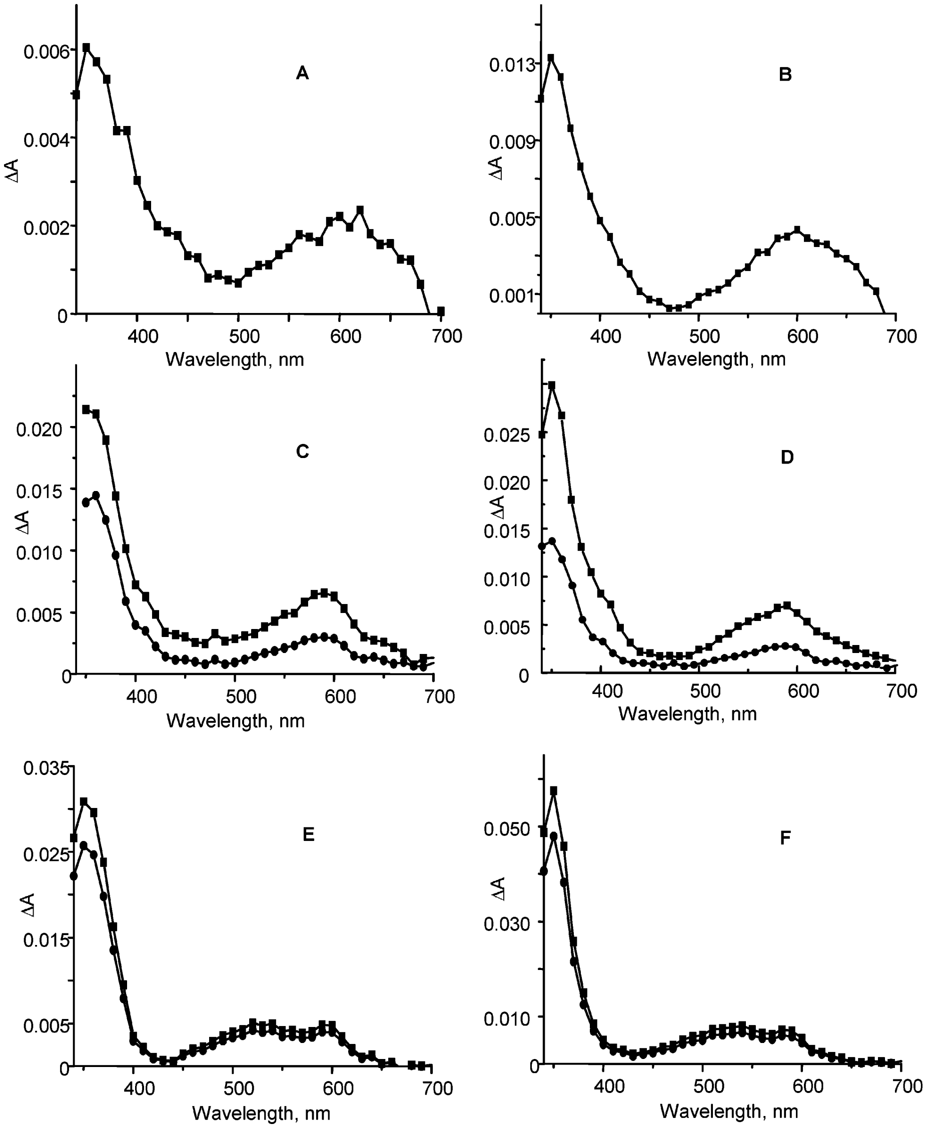


FIGURE 1. Transient absorption spectra recorded following laser excitation (355 nm) in deaerated methanol (7.0−8.0 × 10^{-4} M): (A) (*S*,*S*)-**4**, 1 μs after the laser pulse; (B) (*R*,*S*)-**6**, 1 μs after the laser pulse; (C) (*S*,*S*)-**3**, 10 (■) and 50 ns (●) after the laser pulse; (D) (*R*,*S*)-**5**, 15 (■) and 50 ns (●) after the laser pulse; (E) (*S*,*S*)-**1**, 15 (■) and 50 ns (●) after the laser pulse; and (F) (*R*,*S*)-**2**, 30 (■) and 50 ns (●) after the laser pulse.

TABLE 2. Lifetimes of Carbonyl Triplets and Biradicals in Methanol at 25 °C[a]

compd	τ_T (ns)	biradical	τ_{br} (ns)[b]
(*R*,*S*)-**1**	17[c]	(*R*,*S*)-**7**	355
(*S*,*S*)-**1**	6[c]	(*S*,*S*)-**7**	170
(*R*,*S*)-**2**	8[c]	(*R*,*S*)-**8**	360
(*S*,*S*)-**2**	12[c]	(*S*,*S*)-**8**	620
(*R*,*S*)-**3**	93[d]−120[c]	(*R*,*S*)-**9**	210
(*S*,*S*)-**3**	27[d]−25[c]	(*S*,*S*)-**9**	56
(*R*,*S*)-**5**	24[d]−26[c]	(*R*,*S*)-**10**	40
(*S*,*S*)-**5**	160[d]−190[c]	(*S*,*S*)-**10**	211
(*R*,*S*)-**6** (**4**)	2300 (2800) [e]		
(*S*,*S*)-**6** (**4**)	2440 (2200) [e]		

[a] Concentrations: 8 × 10^{-4} M for **1**, **3**, **5**, and **6** and 7 × 10^{-4} M for **2**. [b] Biradical lifetime, measured at 360 nm. [c] Measured by the indirect naphthalene method. [d] Directly measured at 630 nm. [e] No significant intramolecular quenching was observed; these τ_T values are similar to that of the 2-benzoylthiophene chromophore under similar conditions (2800 ns).

band in the 450−550 nm region (Figure 1E,F). Although these spectra could be assigned to the ketone triplet states, it is now clear that they can correspond to the overlap of both triplets and biradicals; their relative contributions depend on the time elapsed after the laser pulse and the nature of the electron donor moiety. In this context, a recent detailed study[17] of the intermolecular BT/phenol and BT/indole quenching process has allowed us to better understand the spectra of the transients formed in the intramolecular processes, and to make a safe assignment.

In the intermolecular experiment, disappearance of the BT triplet was followed by formation of the ketyl radical (with no absorption beyond 625 nm) and phenoxy (maxima at 385−405 nm) or indolyl radical (maxima at 320 and 520 nm).[17] Hence, kinetic traces for the triplet of the phenolic bichromophores were recorded in the 630-nm region to avoid contribution of the biradical. For instance, Figure 2 (spectra A and B) shows the decay at 630 nm for compounds (*S*,*S*)-**3** and (*R*,*S*)-**5**, indicating a very fast disappearance of the ketone triplets in the submicrosec-

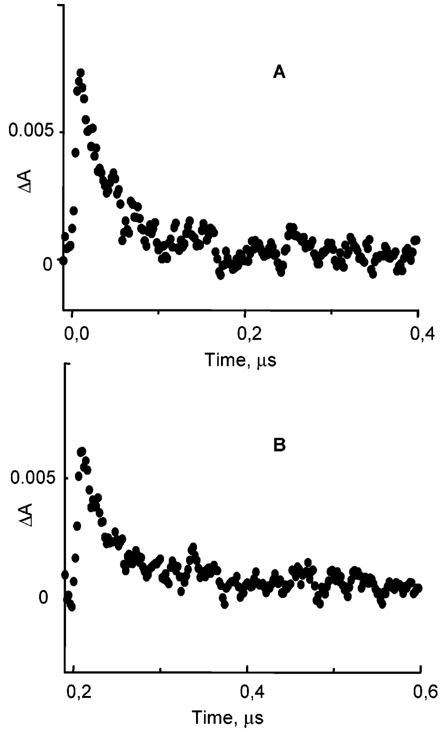


FIGURE 2. Triplet decay monitored at 630 nm, following laser excitation (355 nm) in deaerated methanol (7.0−8.0 × 10^{-4} M): (A) for (*S*,*S*)-**3** and (B) for (*R*,*S*)-**5**.

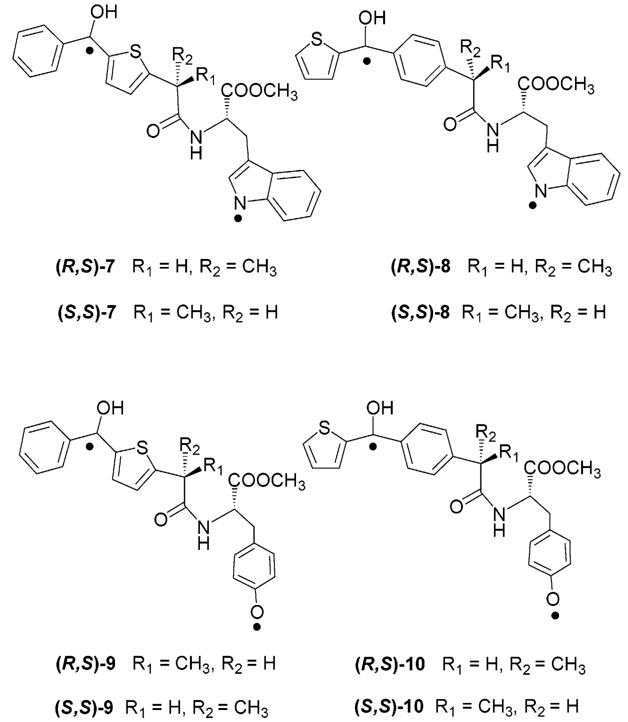
ond time scale. The triplet lifetimes estimated for **3** and **5** (Table 2) were actually much shorter that those found for **4** and **6**.

To rule out the possible contribution of self-quenching, solutions of compounds **3** or **5** with molar concentrations between 1×10^{-4} and 15×10^{-4} M were flash photolyzed, and the decay at 630 nm was examined; no significant effect was observed on the lifetimes of the triplet ketones. On the other hand, variation of the laser power between 4 and 20 mJ/pulse did not have any appreciable influence on the triplet lifetimes, suggesting that triplet−triplet annihilation is not important.

As the kinetic traces at 630 nm found for the indolic compounds were even faster it was not possible to make direct measurement of the triplet lifetimes accurately. However, these data were determined by means of triplet−triplet energy transfer, using the naphthalene (NP) probe method[23] (see below).

Formation of the flexible 1,14- or 1,15-biradicals resulting from formal hydrogen abstraction (**7**−**10**, Chart 2) was observed at very short times after the laser pulse, especially in the case of the indolic derivatives. Thus, the early spectra C and D in Figure 1 result from the overlapping absorptions of the triplet state and the biradical, while those recorded after longer times are mainly due to the biradical. For compounds **1** and **2**, the spectra obtained 15 ns after the laser pulse (Figure 1E,F) were already very similar to those of indolyl plus ketyl radicals, generated by flash photolysis of BT in the presence of indole. The lack of photoproducts in the steady-state studies indicates that all these biradicals decay almost exclusively by back hydrogen transfer, a well-known phenomena in other hydroxy biradicals.[10,11,23a,24] The biradical lifetimes obtained for all the bichromophores are also given in Table 2.

CHART 2. 1,14- and 1,15-Biradicals



(*R*,*S*)-7 R_1 = H, R_2 = CH$_3$
(*S*,*S*)-7 R_1 = CH$_3$, R_2 = H
(*R*,*S*)-8 R_1 = H, R_2 = CH$_3$
(*S*,*S*)-8 R_1 = CH$_3$, R_2 = H
(*R*,*S*)-9 R_1 = CH$_3$, R_2 = H
(*S*,*S*)-9 R_1 = H, R_2 = CH$_3$
(*R*,*S*)-10 R_1 = H, R_2 = CH$_3$
(*S*,*S*)-10 R_1 = CH$_3$, R_2 = H

Indirect Determination of Short Triplet Lifetimes. Addition of NP to methanolic solutions of all the bichromophores led to quenching of the ketone triplets and the "instantaneous" formation of the NP triplet state, easily detectable at 425 nm. The end-of-pulse absorbance at 425 nm was determined as a function of NP concentration. These data were plotted against each other in a double reciprocal form, according to eq 1, where ΔA_{425} is the transient absorption at 425 nm before significant decay takes place, $k_q\tau_T$ is the Stern−Volmer parameter, and α is a constant.

$$1/\Delta A_{425} = \alpha + (\alpha / k_q\tau_T)[\mathrm{NP}] \qquad (1)$$

Figure 3A,B shows the plots obtained for some of the bichromophoric compounds **1**−**3** and **5** (those derived from (*S*)-TPA and (*R*)-SUP), while Table 2 lists the triplet lifetimes (τ_T) obtained for all of them from the intercept-to-slope ratios. The intermolecular k_q values needed for these calculations were experimentally measured and found to be 4.9×10^9 (TPA/NP) and 8.0×10^9 M^{-1} s^{-1} (SUP/NP).

Stereo- and Regiodifferentiation. Remarkable stereodifferentiation was found for the triplet lifetimes of the bichromophores (Table 2). Thus, inversion of the configuration in one stereocenter produced a marked variation (up to 7.3-fold in the case of the two diastereomers of **5**)

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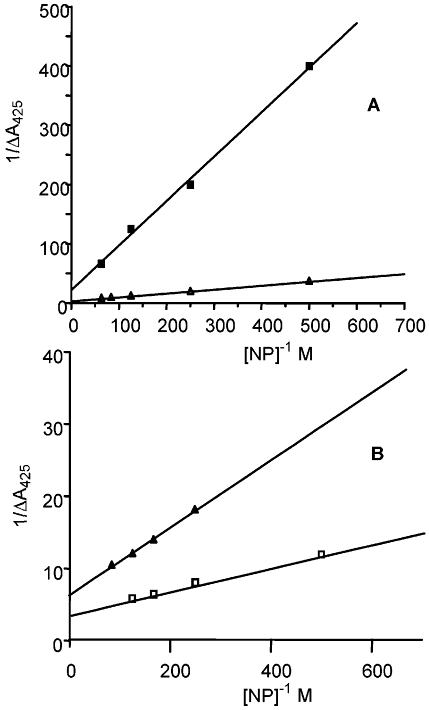

FIGURE 3. (A) Double reciprocal plots for quenching of the ketone triplets generated by laser flash photolysis at 355 nm in deaerated methanolic solutions of (A) (*S*,*S*)-**1** (■) and (*R*,*S*)-2 (△) and (B) (*S*,*S*)-**3** (▲) and (*R*,*S*)-**5** (□).

of this parameter, indicating that there are specific structural requirements for the intramolecular quenching of ketone triplets. The fast triplet decay found for **1**−**3** and **5**, compared to that of the isolated chromophores, suggests that the geometry for intramolecular hydrogen transfer in these compounds maximizes interaction between the π-systems of the donor moieties and the aromatic ketones. Particularly, in the case of the phenolic-derived compounds, triplets could be forced to a sandwich-like geometry due to the O−H ability to achieve the right relative orientation toward the carbonyl group as to make a hydrogen bond. This would clearly be expected to facilitate hydrogen abstraction by an exciplex-mediated mechanism, which has been shown to apply for the intermolecular processes.[17] Such sandwich-like conformations were actually found on the solid state.

Interestingly enough, configurational dependence was also observed for the biradical lifetimes (Table 2 and Figure 4), indicating that there also are specific requirements that must be met for the biradical decay to the starting material.

Finally, it is worth mentioning that some degree of regiodifferentiation was observed in the lifetimes of both triplets and biradicals, mainly for the indolic-derived bichromophores (compare, for instance, the data for (*R*,*S*)-**1** vs (*S*,*S*)-**2** and (*R*,*S*)-**7** vs (*S*,*S*)-**8** in Table 2).

Influence of the Reaction Medium. We have recently[17] studied the solvent influence on quenching of BT triplet by phenol and indole. Results agree with solvent polarity/polarizability being by far the most important factor determining the value of the rate constants for both quenchers. By contrast, the contribution of the hydrogen bonding acceptor ability of the solvent was found to be very small for indole, and became negative in the case of phenol, which was explained as due to a decreased concentration of free phenol due to hydrogen bonding to the solvent.

In the present work, similar studies have been performed with some representative bichromophoric com-

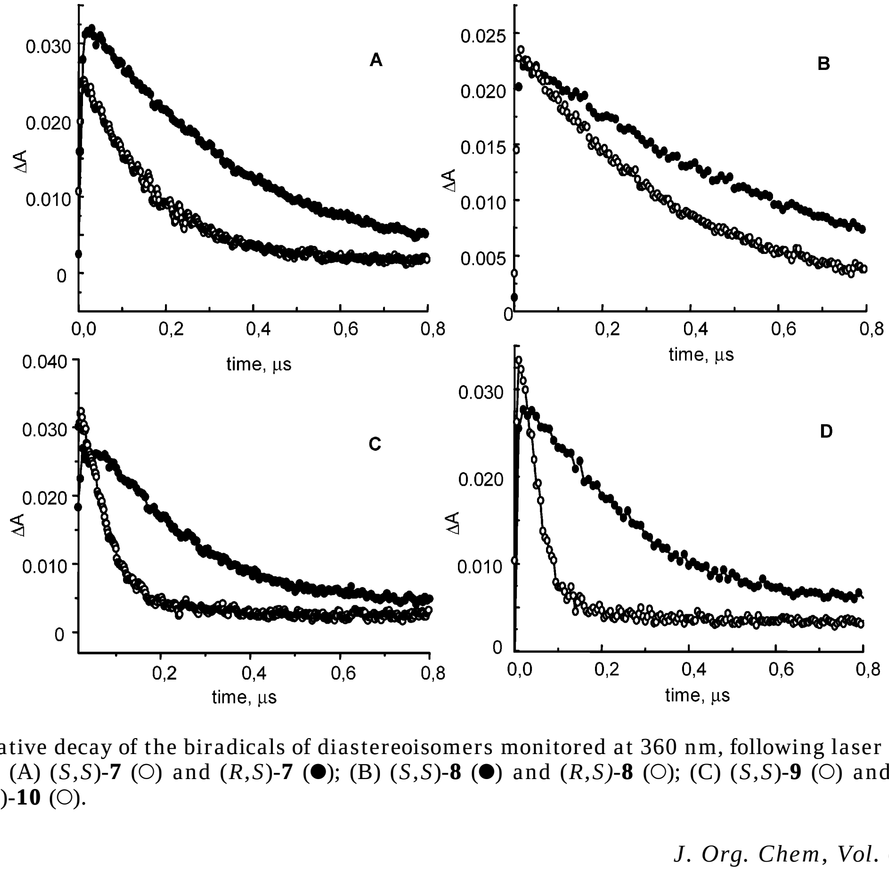

FIGURE 4. Comparative decay of the biradicals of diastereoisomers monitored at 360 nm, following laser excitation (355 nm) in deaerated methanol: (A) (*S*,*S*)-**7** (○) and (*R*,*S*)-**7** (●); (B) (*S*,*S*)-**8** (●) and (*R*,*S*)-**8** (○); (C) (*S*,*S*)-**9** (○) and (*R*,*S*)-**9** (●); and (D): (*S*,*S*)-**10** (●) and (*R*,*S*)-**10** (○).

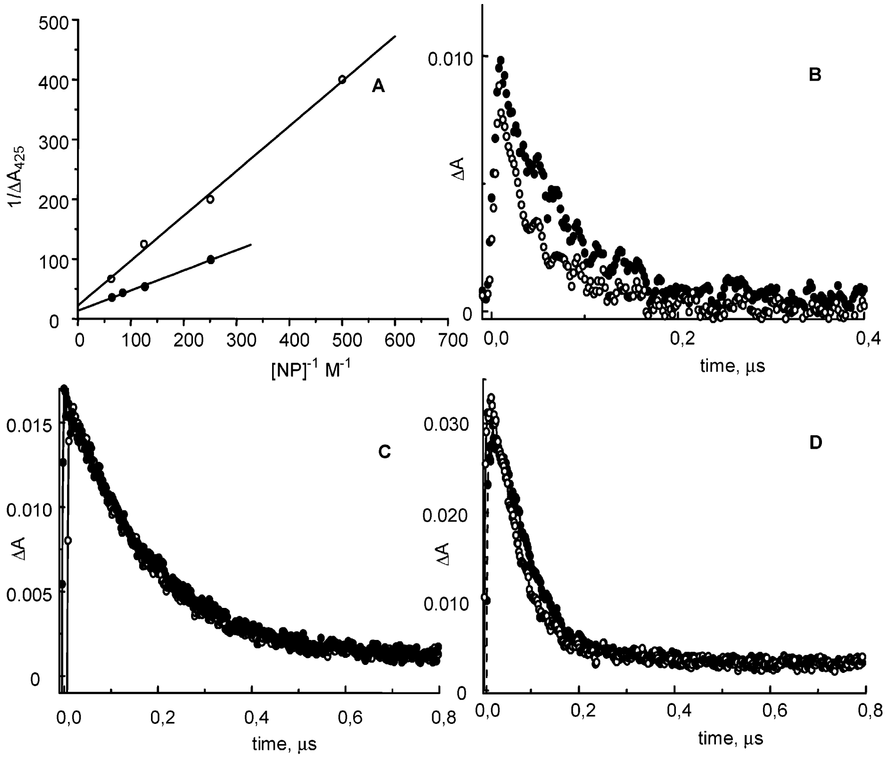

FIGURE 5. Isotopic effects in deaerated CH_3OH (○) or CH_3OD (●) solutions. (A) Double reciprocal plots for quenching of triplet (*S*,*S*)-**1** by naphthalene. Comparative decays of triplet (*S*,*S*)-**3** (B) and biradicals (*S*,*S*)-**7** (C) and (*R*,*S*)-**9** (D).

TABLE 3. Triplet and Biradical Lifetimes in Acetonitrile

triplet	τ_T[a]	τ_T(MeCN)/ τ_T(MeOH)[a]	biradical	τ_{br}[b]	τ_{br}(MeCN)/ τ_{br}(MeOH)
(*R*,*S*)-**1**	25	1.5	(*R*,*S*)-**7**	125	0.4
(*S*,*S*)-**1**	8	1.3	(*S*,*S*)-**7**	52	0.3
(*R*,*S*)-**3**	51	0.4	(*R*,*S*)-**9**	140	0.7
(*S*,*S*)-**3**	12	0.5	(*S*,*S*)-**9**	32	0.6

[a] Measured by the naphthalene method. [b] Measured at 360 nm.

pounds; the results follow the same trend as those obtained in the intermolecular quenching of BT triplet. Thus, triplet lifetimes for the indolic derivatives were higher in acetonitrile than in methanol, while the reverse was true for the phenolic derivatives (Table 3). For the intermolecular process, hydrogen abstraction from phenol by BT triplet proceeds through a hydrogen-bonded exciplex that collapses to radical pairs by coupled electron and proton transfer; however, in the case of indole, charge transfer assists hydrogen abstraction in a π-type exciplex, without prior hydrogen bonding.

To gain further insight into the reaction mechanisms, triplet lifetimes were measured in deuterated methanol for some representative bichromophores and compared to those obtained in methanol. In this solvent, both phenolic OH and indolic NH groups undergo full H/D exchange, as indicated by the disappearance of the ^{1}H NMR signals at ca. 7.4 and 6.0 ppm, respectively. Interestingly, an isotopic effect of 1.5 was obtained through the indirect energy transfer method for the short-lived triplet of (*S*,*S*)-**1** (Figure 5A). In the case of (*S*,*S*)-**3** a similar k_H/k_D value (1.6) was directly measured from the triplet decay traces (Figure 5B). These kinetic effects might indicate that hydrogen transfer is involved in the rate-determining step, while the conformational motions required to achieve the active sandwich-like folded arrangement would occur on a shorter time scale. However, the observed isotope effects may also be secondary due to change in O and N electron density, charge transfer being the rate-determining step. This possibility cannot be ruled out at the basis of the available experimental data.

On the other hand, it is known that the lifetimes of hydroxy biradicals show large solvent dependence. Thus, a Lewis base can produce a significant increase of biradical lifetimes due to solvation by hydrogen bonding.[24] To investigate the influence of this factor, the lifetimes of some representative biradicals were also studied in acetonitrile. Taking into account that the index for hydrogen bonding acceptor basicity of both solvents is $\beta = 0.40$ and 0.66, respectively,[25] these data indicate that solvation retards the reversion of biradicals to the starting bichromophores. On the basis of the remarkable photostability of these compounds, back hydrogen transfer appears to be the main reaction of biradicals. Moreover, biradical decays were also measured in deuterated methanol and compared to those obtained in the nondeuterated solvent. By contrast with the triplet case, no significant isotopic effect was observed for biradical lifetimes (Figure 5C,D).

Conclusion

From the T−T transient spectra, as well as the solvent effects and the deuterium isotopic effects on the lifetimes, it is clear that triplet deactivation in bichromophores **1**−**3** and **5** is dominated by hydrogen atom transfer. The remarkable stereodifferentiation found in methanol and acetonitrile indicates that there are specific structural requirements for intramolecular quenching of the ketone triplets by both phenol and indole moieties. On the other hand, biradical lifetimes also show large solvent dependence; solvation appears to slow their reversion to the starting ketone. Finally, considerable stereodifferentiation has been found for the biradical lifetimes; this suggests that faster intersystem crossing occurs when the approach of the two radical termini becomes easier.

Experimental Section

Synthesis of Bichromophores 1−3 and 5. The corresponding propanoic acid (300 mg, 1.2 mmol), the (L)-amino acid methyl ester (1.4 mmol), EDC (270 mg, 1.4 mmol), and HBT (200 mg, 1.4 mmol) were combined in dry, degassed DMF (10 mL) at room temperature. The pH was adjusted to 9.0−9.5 with triethylamine and the mixture was stirred overnight. Afterward, the solvent was removed in vacuo, and the residue was treated with 10% HCl (30 mL) and extracted with ethyl acetate (3 × 10 mL). The combined organic layers were washed with 10% HCl (1 × 10 mL), saturated sodium bicarbonate (2 × 10 mL), and brine (1 × 10 mL) and dried over sodium sulfate. Solvent was removed under reduced pressure to give a yellow oil. The residue was chromatographed (hexane/ethyl acetate, 2:1) leading to the corresponding bichromophore as a 1:1 diasteroisomeric mixture. Separation of diasteroisomers was accomplished by HPLC: mobile phase, potassium dihydrogen phosphate (0.06 M):acetonitrile:triethylamine (317:183: 0.1); flow rate, 1.5 mL min^{-1}; UV detection, $\lambda = 310$ nm.

***O*-Methylation of the Tyrosine-Derived Bichromophores.** An ethereal solution containing compounds **3** or **5**, as a diastereoisomeric mixture (300 mg, 0.7 mmol), was treated with 20 mmol of freshly prepared diazomethane[26] at 0 °C. The mixture was allowed to warm to room temperature and stirred overnight. Afterward, the excess of diazomethane was removed under reduced pressure and the resulting yellow oil was chromatographed (hexane/ethyl acetate, 3:1) leading to the corresponding bichromophore as a 1:1 diasteromeric mixture. Separation of the diasteroisomers was accomplished by HPLC: stationary phase, Silica column; mobile phase, hexane:ethyl acetate (4:1 by volume); flow rate, 2 mL min^{-1}; detection by refractive index.

Determination of the Absolute Configuration of the Bichromophoric Compounds. Well-shaped crystals of (*R*,*S*)-**2**, (*S*,*S*)-**3**, (*S*,*S*)-**5**, and (*R*,*S*)-**5** were obtained by slow diffusion of hexane in chloroform solutions of these compounds. Their respective structures and configurations were established unambiguously by X-ray diffraction. The exact configurations of the two diasteroisomers of **1** were confirmed by synthesis starting from the enantiomerically pure TPA and (*S*)-Tryptophan methyl ester. Resolution of the racemic tiaprofenic acid was performed as described elsewhere.[21]

Laser Flash Photolysis. These experiments were carried out with a pulsed Nd-YAG Spectrum laser system instrument. The single pulses were ca. 10 ns duration and the energy was ca. 10 mJ/pulse. A Xenon lamp was employed as the detecting light source. The laser flash photolysis apparatus consisted of the pulsed laser, the Xe lamp, a monochromator, a photomultiplier (PMT) system made up of side-on PMT, PMT housing, and a PMT power supply. The output signal from the oscilloscope was transferred to a personal computer for study. Samples were contained in 7 × 7 mm^2 cells made of Suprasil quartz and were deaerated with dry nitrogen prior to the experiments. Concentrations for bichromophoric compounds **1**−**3** and **5** were adjusted to yield and absorbance of 0.35 at 355 nm.

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Supporting Information Available: Additional transient absorption spectra, triplet decays, and double reciprocal plots in methanol and acetonitrile for triplets and biradicals; also, characterization data for bichromophoric compounds **1**−**6** and crystallographic data for (*R*,*S*)-**2**, (*S*,*S*)-**3**, (*R*,*S*)-**5**, and (*S*,*S*)-**5**. This material is available free of charge via the Internet at http://pubs.acs.org.

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