

Geometrical Effects on the Intramolecular Quenching of π, π^* Aromatic Ketones by Phenols and Indoles

Julia Pérez-Prieto,^{*,†} Salah-Eddine Stiriba,[†] Francisco Boscá,[‡] Agustín Lahoz,[†]
Luis R. Domingo,[†] Fouad Mourabit,[†] Sandra Monti,[§] and Miguel A. Miranda^{*,‡}

Departamento de Química Orgánica/ICMOL, Universidad de Valencia, Av. Vicent Andrés Estellés s/n, 46100 Burjassot, Valencia, Departamento de Química/Instituto de Tecnología Química UPV-CSIC, Universidad Politécnica de Valencia, Camino de Vera s/n, 46071 Valencia, and Istituto per la Sintesi Organica e la Fotoreattività, CNR, Via Piero Gobetti 101, 40129 Bologna

julia.perez@uv.es

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Laser flash photolysis of a series of bichromophoric compounds **1–12** containing the 2-benzoylthiophene (BT) and phenol (PhOH) or indole (InH) moieties has been used to determine the possible geometrical effects in the intramolecular quenching of triplet excited ketones, resulting in formal hydrogen abstraction. The results are compared with those obtained in the intermolecular process. In both cases, substitution either at the thienyl or the phenyl moiety has a marked influence on the photoreactivity. Time-resolved experiments showed that the rate constants for bimolecular quenching by phenol and indole of 2-benzoylthiophene substituted at the thienyl 5-position were lower than those for BT substituted at the phenyl *p*-position, which agrees with the higher energy found for the excited triplet state of the latter compounds. However, the rate constant for hydrogen abstraction in the bichromophoric compounds by the π, π^* triplet state of the derivatives with the spacer linked to the thienyl 5-position are higher than those of their regioisomers. These results indicate a possible geometry-dependence in the intramolecular quenching process. Theoretical DFT studies have been carried out in order to estimate the optimum conformation for hydrogen abstraction in two pairs of phenolic and indolic bichromophoric regioisomers. The energy profile for photoactivation/deactivation of the aromatic ketone and the structures of the triplet states and biradicals involved in the process have been determined. The observed regiodifferentiation in the experimental studies is consistent with a dependence of the rate constant on orbital overlap between the carbonyl oxygen and the X–H bonds.

Introduction

Although in general, ketones with lowest π, π^* triplet states tend to exhibit lower reactivity than those with lowest n, π^* triplets toward hydrogen abstraction, this is not the case with hydrogen donors containing heteroatoms.¹ It has been suggested that hydrogen abstraction from phenols in aqueous media occurs by a mechanism involving sequential electron transfer and proton transfer.² However, in nonaqueous solvents, the reduction potentials of ketones are higher, making the electron transfer less exergonic. Hence, a mechanism involving initial formation of a hydrogen-bonded triplet exciplex followed by coupled electron/proton transfer has been proposed in the latter case.^{1,3}

In this context, we have recently studied the intermolecular quenching of 2-benzoylthiophene (BT, π, π^* triplet) by phenol (PhOH) or indole (InH) in organic solvents.⁴ The laser flash photolysis technique has enabled us to observe how the BT triplet,⁵ with absorption maxima at 350 ($\epsilon_{\max} = 4800 \text{ M}^{-1} \text{ cm}^{-1}$) and 600 nm ($\epsilon_{\max} = 2900 \text{ M}^{-1} \text{ cm}^{-1}$), is converted with quantum yield close to 1 into the BT ketyl radical (BTH), with absorption maxima at 350 ($\epsilon_{\max} = 9100 \text{ M}^{-1} \text{ cm}^{-1}$) and 580 nm ($\epsilon_{\max} = 2100 \text{ M}^{-1} \text{ cm}^{-1}$), plus phenoxy (PhO) or indolyl (In) radicals. Solvent-dependence of the quenching rate constants, together with density functional theoretical (DFT) calculations for phenol, agree with the involvement of a hydrogen-bonded exciplex BT \cdots HOPh where concerted electron and proton transfer leads to the BTH \cdots OPh radical pair. However, in the case of indole, electron transfer at the BT \cdots HIIn stage precedes proton transfer.

* To whom correspondence should be addressed. Phone: (34)-96-3543050.

[†] Universidad de Valencia.

[‡] Universidad Politécnica de Valencia.

[§] Istituto per la Sintesi Organica e la Fotoreattività.

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The absorption spectra of BT have been assigned by comparison with model compounds containing the same substructures⁶ and by direct studies of the electron density difference maps.⁷ In hexane, the spectrum has maxima at 245 nm (which includes transitions of the benzoyl and thienyl chromophores), 275 nm (due to the π, π^* transition of the 2-thienyl chromophore), and 380 nm (weak and structured 0–0 band due to n, π^* transition).⁶ Alkyl substitution at the thienyl 5-position causes a pronounced bathochromic shift (around 20 nm) of the band assigned to thenoyl chromophore and decreases the energy of the π, π^* excited triplet states. Thus, the 5-methyl-substituted derivative has a triplet energy of 60 kcal mol⁻¹, lower than that of BT (63 kcal mol⁻¹).^{6,8} However, no significant effect has been observed upon substitution at the para position of the benzoyl moiety. Therefore, if the ketone redox potentials in 5-alkyl-2-benzoylthiophenes and their corresponding regioisomers 2-(*p*-alkylbenzoyl)thiophenes are similar, coupled electron/proton-transfer processes should be less exergonic for the former compounds according to the Rehm–Weller equation.

We have previously reported⁹ on the results of photo-physical studies performed on diastereoisomeric bichromophoric compounds containing BT and phenol or indole moieties, where triplet lifetime data revealed stereodifferentiation in the intramolecular photoreaction between BT and phenols and indoles. Although a certain degree of regiodifferentiation was also observed in some of the regioisomeric pairs, clear conclusions were masked by the quantitatively more important stereodifferentiation phenomena.

Geometrical factors, such as the mutual orientation and distance between the reactant groups in the initial stages of the reaction, may have an important influence on the kinetics and mechanism of hydrogen abstraction.¹⁰ In particular, in the case of coupled electron/proton transfer in bichromophoric compounds having a *p*- or *m*-phenolic moiety attached via an *m*- or *p*-oxyethyl linkage to acetophenones, it has been found¹¹ that the intramolecular reaction rate depends on the position of attachment of the involved chromophores to the inert linker. To give an explanation for the observed regiodifferentiation, a model based on the spatial overlap between the aryl rings of the carbonyl and phenolic moieties within a hydrogen-bonded triplet exciplex has been suggested. Calculations at the simple Hückel level have

been performed to determine the nodal properties of the orbitals involved in the analogous intermolecular process. The overlap between the two aromatic rings in each of the ketone-phenol regioisomeric pairs was considered to provide some insight into the degree of favorable interaction in the sandwich-like conformation suggested for the process.

However, DFT calculations for the intermolecular quenching of triplet BT by phenol and indole have shown that the optimized geometries relevant for formal hydrogen abstraction are those where the aromatic rings of the donor and the acceptor skew away from each other.⁴ Therefore, we have now investigated in detail the coupled electron/proton-transfer process in a series of model racemic or nonchiral bichromophoric compounds **1–12**, where the linker between the electron donor group (PhOH or InH) and the BT chromophore is attached to either the thienyl 5-position or the benzoyl *p*-position. This structural difference caused a marked influence on the photoreactivity of the 2-benzoylthiophene chromophore. The calculated reduction potentials, together with the triplet energies of the ketones, agree well with the higher bimolecular rate constant for the analogous intermolecular process in the case of 2-(*p*-alkylbenzoyl)thiophenes as compared to the regioisomeric 5-alkyl-2-benzoylthiophenes. Interestingly, the trend observed for the intramolecular quenching process is opposite; high level theoretical calculations have been used here to find a plausible explanation. Thus, DFT studies were performed using four model bichromophoric compounds in order to estimate the energy profile for the photoactivation/deactivation of the aromatic ketone and the structures of the triplet states involved in the process. Calculations suggest that for all four models the approaching rings are slightly skewed away from each other, with the most important intramolecular interaction in the exciplex occurring between the phenolic (or indolic) hydrogen and the carbonyl oxygen. Of interest, the nodal properties of the involved frontier molecular orbitals (MOs) showed a favorable interaction between the atomic orbitals of the phenol oxygen atom (or indole nitrogen atom) and the carbonyl oxygen atom for the 5-alkyl-2-benzoylthiophenes. By contrast, both orbitals in 2-(*p*-alkylbenzoyl)thiophenes have an antisymmetric approach giving an anti bonding overlap.

Results and Discussion

Bichromophores. Compounds **1**, **4**, **7**, and **10** were obtained by condensation of racemic tiaprofenic acid (TPA) or suprofen (SUP) with tyramine or tryptamine. Methylation of TPA or SUP methyl ester in the α position followed by hydrolysis and coupling to tyramine, tyrosine methyl ester, tryptamine or tryptophan methyl ester led to compounds **2**, **3**, **5**, **6**, **8**, **9**, **11**, and **12** (Chart 1). Structures were unambiguously determined by ¹H and ¹³C NMR, GC/MS, and HRMS or elemental analysis (see the Experimental Section).

Compounds **1–3** and **7–9** differ from **4–6** and **10–12**, respectively, in the relative aromatic ketone versus amine or amino acid orientation. Deoxygenated methanolic solutions of **1–12** were irradiated for several hours using Pyrex-filtered light from a mercury lamp. Analysis of the reaction mixtures by ¹H NMR showed that these ketones were photoinert under the irradiation conditions.

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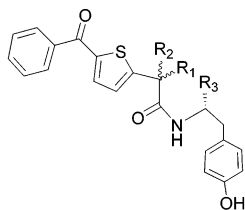
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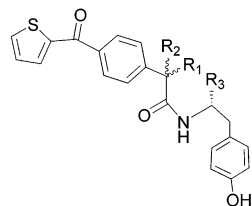
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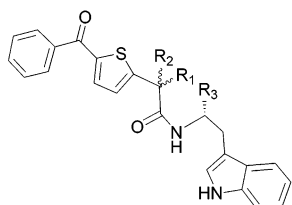
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CHART 1. Bichromophoric Compounds Derived from 5-Alkyl-2-benzoylthiophene (Left) and 2-(*p*-Alkylbenzoyl)benzoylthiophene (Right)


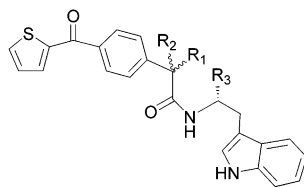
- BTT-OH** $R_1 = R_2 = R_3 = H$
1 $R_1 = H, R_2 = CH_3, R_3 = H$
2 $R_1 = CH_3, R_2 = CH_3, R_3 = H$
3 $R_1 = CH_3, R_2 = CH_3, R_3 = CO_2CH_3$



- BTP-OH** $R_1 = R_2 = R_3 = H$
4 $R_1 = H, R_2 = CH_3, R_3 = H$
5 $R_1 = CH_3, R_2 = CH_3, R_3 = H$
6 $R_1 = CH_3, R_2 = CH_3, R_3 = CO_2CH_3$



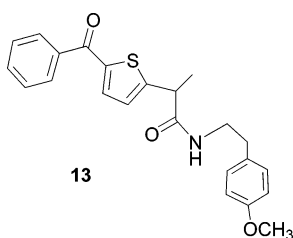
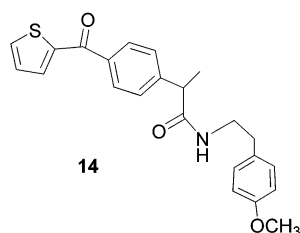
- BTT-NH** $R_1 = R_2 = R_3 = H$
7 $R_1 = H, R_2 = CH_3, R_3 = H$
8 $R_1 = CH_3, R_2 = CH_3, R_3 = H$
9 $R_1 = CH_3, R_2 = CH_3, R_3 = CO_2CH_3$



- BTP-NH** $R_1 = R_2 = R_3 = H$
10 $R_1 = H, R_2 = CH_3, R_3 = H$
11 $R_1 = CH_3, R_2 = CH_3, R_3 = H$
12 $R_1 = CH_3, R_2 = CH_3, R_3 = CO_2CH_3$

Transient intermediates. Bichromophoric compounds **1–12** are suitable substrates to investigate regiochemical aspects of the intramolecular electron-transfer process between excited benzoylthiophene and phenolic or indolic moieties.

Dynamic studies were performed using deaerated methanolic solutions ($7.0\text{--}8.0 \times 10^{-4}$ M) at 355 nm (Nd:YAG). Laser flash photolysis of the *O*-methylated phenolic derivatives **13** and **14** provided information on the intrinsic triplet state properties of the chromophore present in all these compounds, taking into account the low reactivity found for anisole (quenching rate constant of the 2-benzoylthiophene triplet by anisole $k_q < 10^7$ M $^{-1}$ s $^{-1}$).⁹ Thus, time-resolved absorption spectra obtained after laser irradiation of **14** (see spectrum in Figure 1A) showed the triplet transient in the 300–700 nm range, with maxima at 350 and 600 nm (lifetime around 5 μ s), absorption features similar to those of the 2-benzoylthiophene triplet.^{4,5}

**13****14**

The phenolic bichromophores **1–6** displayed a differently shaped transient absorption, characterized by relatively lower intensity beyond 625 nm. In addition, the ratio $\Delta A_{350} / \Delta A_{600}$ was higher and the maximum in the visible region was shifted to 590 nm (see Figure 1B for **5**). Similar spectra were observed for the indole-derived bichromophores **7–12**, but with an enhanced

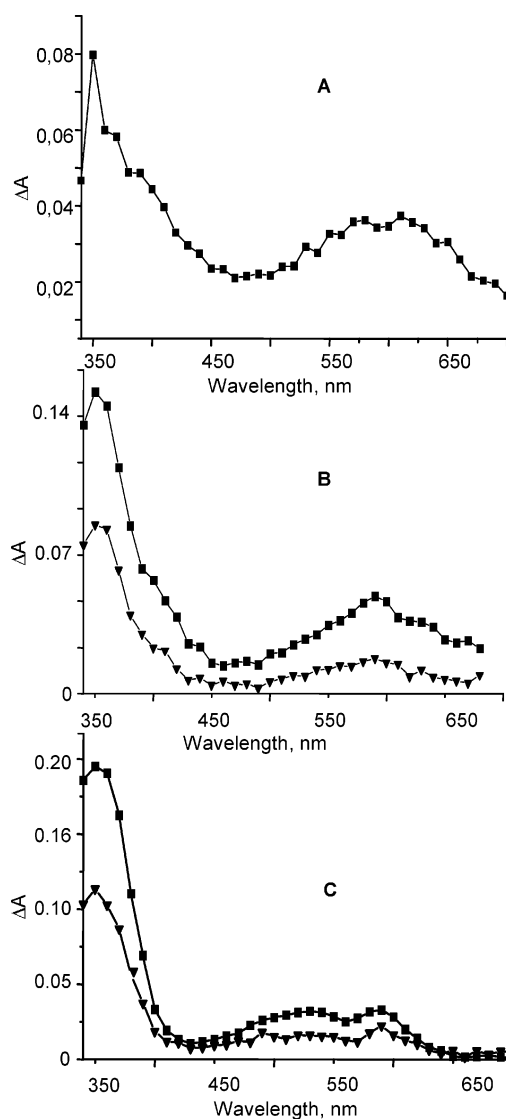


FIGURE 1. Transient absorption spectra recorded following laser excitation (355 nm) in deaerated methanol ($7.0\text{--}8.0 \times 10^{-4}$ M): (A) **14**, 50 ns after the laser pulse; (B) **5**, 20 ns (■) and 200 ns (▼) after the laser pulse; (C) **11**, 5 ns (■) and 200 ns (▼) after the laser pulse.

broad band in the 450–550 nm region (see Figure 1C for **11**). These spectra correspond to the overlap of both triplets and biradicals;⁹ their relative contributions depend on the time elapsed after the laser pulse and the nature of the electron donor moiety. Previous studies⁹ performed on related bichromophores have allowed us to better understand the spectra of the transients formed in these processes and to make a safe assignment. Thus, disappearance of the BT triplet was followed by formation of the ketyl radical (with no absorption beyond 625 nm), accompanied by phenoxy (maxima at 385–405 nm) or indolyl radical (maxima at 320 and 520 nm).

Kinetic traces for the triplet decay in the case of the phenolic bichromophores were recorded in the 630 nm region to avoid contribution of the biradical. For instance, Figure 2 shows the decay at 630 nm for regioisomeric compounds **3** and **6**, indicating a very fast disappearance of the ketone triplets in the sub-microsecond time scale, much shorter than that found for **14**.

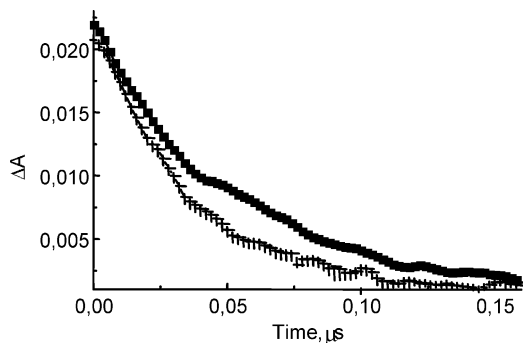


FIGURE 2. Triplet decay monitored at 630 nm, following laser excitation (355 nm) in deaerated methanol ($7.0\text{--}8.0 \times 10^{-4}$ M) for **3** (+) and **6** (■).

TABLE 1. Lifetimes of Carbonyl Triplets in Methanol at 25°C^a

compd	τ_T (ns)	$k_q \times 10^8$ ^b	compd	τ_T (ns)	$k_q \times 10^8$ ^b
1	$35^c\text{--}30^d$	0.30	4	$50^c\text{--}66^d$	0.15
2	$50^c\text{--}65^d$	0.15	5	$60^c\text{--}56^d$	0.18
3	$22^c\text{--}35^d$	0.29	6	$35^c\text{--}45^d$	0.22
7	11^d	0.91	10	18^d	0.56
8	11^d	0.91	11	9^d	1.11
9	4^d	2.50	12	6^d	1.67

^a Concentrations: 7×10^{-4} M for **1–3** and **7–9** and 8×10^{-4} M for **4–6** and **10–12**. ^b Quenching rate constant in the intramolecular quenching of the bichromophores are obtained by using the equation $k_q = 1/\tau - 1/\tau_0$, where τ_0 is $4.4 \mu\text{s}$. ^c Directly measured at 630 nm. ^d Measured by the indirect naphthalene method.

As the decay at 630 nm was very fast, especially for the indolic compounds, triplet lifetimes were accurately determined by means of triplet–triplet energy transfer, using the naphthalene (NP) probe method.¹² Thus, addition of NP to methanolic solutions of all the bichromophores led to quenching of the ketone triplets and “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.

$$1/\Delta A_{425} = \alpha + (\alpha/k_q \tau_T)[\text{NP}]^{-1} \quad (1)$$

Table 1 lists the triplet lifetimes (τ_T) obtained for bichromophoric compounds **1–12** from the intercept-to-slope ratios. The intermolecular k_q values needed for these calculations were experimentally measured and found to be $4.9 \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$ (TPA/NP) and $8.0 \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$ (SUP/NP).

In a number of cases (**1** vs **4**, **3** vs **6**, and **7** vs **10**), remarkable regiodifferentiation was found for the triplet lifetimes of the bichromophores. In general, quenching rate constants were higher for 5-alkyl-2-benzoylthiophenes than for their corresponding regioisomers 2-(*p*-alkylbenzoyl)thiophenes. Even when the photoreactivities

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CHART 2. Biradicals

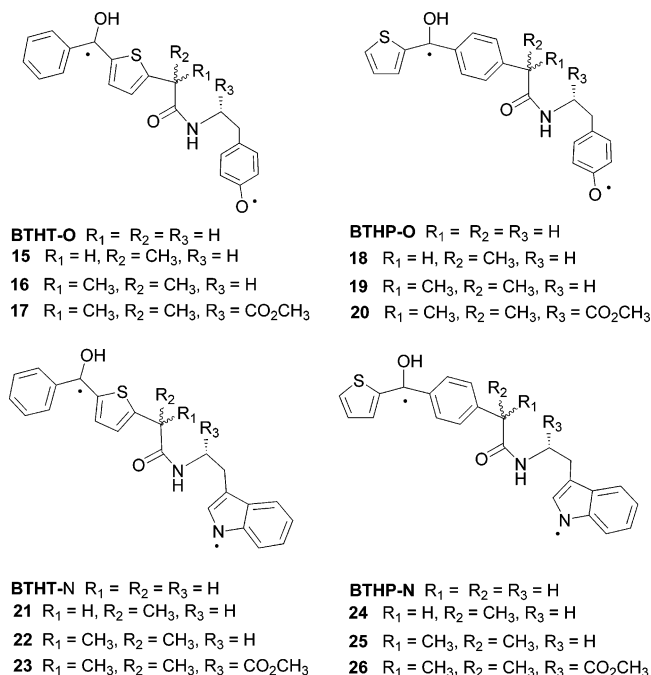


TABLE 2. Lifetimes of Biradicals in Methanol at 25°C^a

species	τ_T (ns)	species	τ_T (ns)
15	130	21	116
16	160	22	195
17	65	23	85
18	245	24	530
19	235	25	405
20	145	26	230

^a Directly measured at 360 nm.

were similar (**2** vs **5**, **8** vs **11**, and **9** vs **12**), the common trend was to deviate from the intermolecular process, where quenching of 2-(*p*-alkylbenzoyl)thiophenes was faster (see below).

By checking the influence of the molar concentration and variation of laser power on the triplet lifetimes it was clear that there was neither important self-quenching nor triplet–triplet annihilation in solutions of these compounds under the experimental conditions used in the studies.

Formation of flexible biradicals resulting from formal hydrogen abstraction (**15–26**, Chart 2) was observed at very short times after the laser pulse, especially in the case of the indolic derivatives. The lack of photoproducts in the steady-state studies indicates that all these biradicals decay almost exclusively by back-hydrogen-transfer, a well-known phenomenon in other hydroxy biradicals.^{12–15} The biradical lifetimes obtained for all the bichromophores are given in Table 2. Here too, a marked regiodifferentiation was observed in kinetics of the back-

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hydrogen-transfer process, which controls the decay of these intermediate species. This is in agreement with previous observations on related systems.⁹

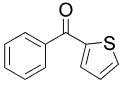
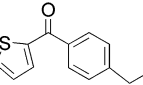
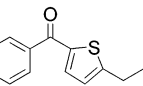
Intermolecular Processes. Rate constants for quenching of 5-ethyl-2-benzoylthiophene and 2-(*p*-ethylbenzoyl)thiophene by indole and phenol were determined in deoxygenated methanol and acetonitrile solutions by monitoring the decay of the triplet–triplet absorption spectra of the ketones at 630 nm. Bimolecular rate constants were determined from plots of the ketone triplet decay versus donor concentration [Q] according to the following equation


$$k_{\text{decay}} = k_0 + k_q[\text{Q}]$$


where k_0 is the pseudo-first-order rate constant for triplet decay in the absence of quencher. Data were compared to those found for 2-benzoylthiophene, showing that the reactivity of the ketone increases with the triplet energy. The differences of the free energy changes ($\Delta\Delta G_{\text{et}}$) associated with the electron-transfer step for two regioisomers containing the same donor depends not only on the triplet energy of the excited ketone but also on its reduction potential (see Chart 3). Cyclic voltammetry for 5-ethyl-2-benzoylthiophene and 2-(*p*-ethylbenzoyl)thiophene measured in acetonitrile (0.2 M Bu₄NPF₄) gave an $E_{1/2} = -1.62$ and -1.58 V vs Ag/AgCl, respectively. Under the same conditions, a value of -1.67 V was obtained for 2-benzoylthiophene. In all the bichromophoric compounds, the $E_{1/2}$ values were between -1.51 and -1.56 V vs Ag/AgCl (see the Supporting Information for representative cyclic voltammograms). From the above data it should be expected a less exergonic process for the 5-alkyl-2-benzoylthiophenes than for their corresponding regioisomers 2-(*p*-alkylbenzoyl)thiophenes; this originates mainly from the different values of their triplet energies.

Theoretical Calculations. The intramolecular excited-state hydrogen transfer process for the simple analogues **BTT-OH**, **BTP-OH**, **BTT-NH**, and **BTP-NH** (Chart 1) has been studied using DFT methods. The lowest lying triplet state of these compounds is involved in an intramolecular proton/electron transfer from the phenol or indole moiety to the 2-benzoylthiophene substructure.

CHART 3

	E_{T} (kcal mol ⁻¹)	$-E_{1/2}$ (V)	k_q (M ⁻¹ s ⁻¹)			
			CH ₃ CN	CH ₃ OH	CH ₃ CN	CH ₃ OH
	63	1.67	5×10^8	50×10^8	1×10^8	0.7×10^8
	63	1.58	4×10^8	50×10^8	1×10^8	0.6×10^8
	58	1.62	0.5×10^8	20×10^8	0.5×10^8	0.2×10^8





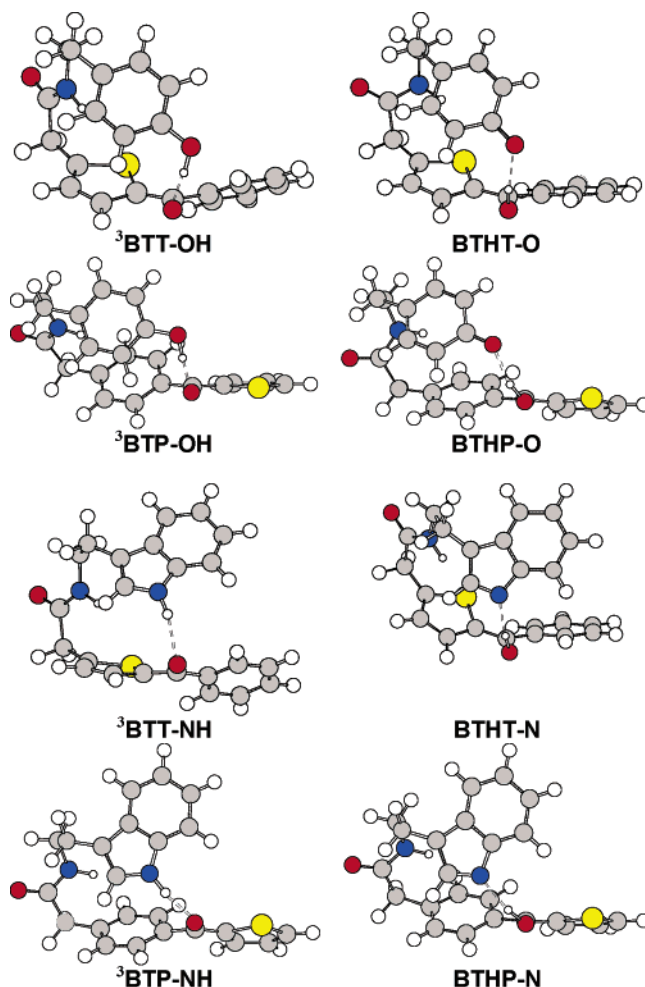


FIGURE 3. (U)B3LYP/6-31G*-optimized geometries of the triplet state and the biradical for **BTT-OH**, **BTP-OH**, **BTT-NH**, and **BTP-NH**.

The geometries corresponding to the triplets and the biradical species are depicted in Figure 3, while those corresponding to the ground states, extended and folded conformations, are given in the Supporting Information (Figure S12). The (U)B3LYP/6-31G* energetic results and

TABLE 3. (U)B3LYP/6-31G* Total (E , in au) and Relative Energies (ΔE , in kcal mol⁻¹, Values in Parentheses Correspond with the Vertical Excitation), Geometrical Parameters (lengths in Å, Dihedral Angles in deg), and Charge Transfer (CT, in e) of the Reactants, the Triplet States, and the Biradicals of BTT-OH, BTP-OH, BTT-NH, and BTP-NH

	E	ΔE	X-H	XH...O	OCCS	OCCC	CT
BTT-OH	-1490.303751		0.977	1.973	150.5	-31.7	
³BTT-OH	-1490.215294	55.5 (65.3)	0.983	1.865	158.5	-27.4	0.00
BHT-O	-1490.234246	43.6	1.883	0.984	158.9	-18.7	0.02
BTP-OH	-1490.306219		0.977	1.983	-10.6	-37.4	
³BTP-OH	-1490.209727	60.5 (69.1)	0.983	1.856	-5.2	-36.5	0.03
BTHP-O	-1490.236979	43.4	1.851	0.985	-13.9	-24.9	0.01
BTT-NH	-1546.655357		1.016	2.132	141.3	-20.9	
³BTT-NH	-1546.565850	56.2 (66.7)	1.017	2.072	153.3	-15.5	0.02
BHT-N	-1546.579400	47.7	1.910	0.993	145.0	-13.2	0.02
BTP-NH	-1546.659265		1.017	2.076	-8.6	-40.9	
³BTP-NH	-1546.564674	59.4 (67.9)	1.035	1.791	-5.4	-36.1	0.24
BTHP-N	-1546.583452	47.6	1.876	0.995	-11.6	-30.0	0.01

the more relevant geometrical parameters are given in Table 3.

At the ground states, the folded hydrogen-bonded conformations are between 3 and 5 kcal mol⁻¹ below the corresponding extended ones. Conformational analysis at these minima shows that for **BTT-OH** and **BTT-NH** the *anti* arrangement of sulfur relative to the carbonyl oxygen is lower in energy than the *syn* one; by contrast, for **BTP-OH** and **BTP-NH** (as for the parent compound BT) the *syn* conformations are favored. Therefore, both conformations have been used along the present study.

Vertical excitation energies to the lowest-lying triplet states of these compounds are in the range of 65.3–69.1 kcal mol⁻¹. Geometry relaxation of the vertical triplets produces a molecular stabilization between 8.5 and 10.5 kcal mol⁻¹, which is larger for the **BTT-OH** and **BTT-NH** regioisomers. The energies for adiabatic triplet excitation (55.5–60.5 kcal mol⁻¹) are close to those obtained for phenol- or indole-BT H-bonded bimolecular species.⁴

The lowest lying triplet states undergo an intramolecular electron/proton-transfer process. The resulting biradical species lie below the triplet states. This hydrogen abstraction process is less favored for **BTT-OH** and **BTT-NH** (–11.9 and –8.8 kcal mol⁻¹) than for the **BTP-OH** and **BTP-NH** regioisomers (–17.1 and –11.8 kcal mol⁻¹).

As regards the geometrical parameters, the most relevant data are the distances between the acidic hydrogen atom of phenol or indole and the corresponding heteroatom X (O or N) or the carbonyl oxygen atom, together with the O–C–C–S (D1) and the O–C–C–C (D2) dihedral angles, which indicate the degree of coplanarity of the thienyl and phenyl rings relative to the carbonyl group in the BT chromophore (see Table 3).

In the hydrogen-bonded ground states, the distances between the phenol hydrogen and the carbonyl oxygen in **BTT-OH** and **BTP-OH** are 1.973 and 1.983 Å, respectively. Similar distances are found between the indole hydrogen and the carbonyl oxygen in **BTT-NH** and **BTP-NH** (2.132 and 2.076 Å, respectively). The values are somewhat smaller (between 0.06 and 0.29 Å) in the corresponding excited triplet states. In the biradical species the distances between the acidic hydrogen and the carbonyl oxygen atom are dramatically shorter (between 0.984 and 0.995 Å), indicating that the hydrogen atom has been transferred. Accordingly, the X–H

distances are much longer (1.883 and 1.910 Å) than in the excited triplet state.

Table 3 also gives the D1 (O–C–C–S) and D2 (O–C–C–C) dihedral angles associated with twisting of the thienyl and phenyl rings relative to the plane of the BT carbonyl group. The observed deviations from the planar arrangement result from (a) the geometrical requirements to attain the folded hydrogen-bonded conformation and (b) the steric hindrance due to the hydrogen atoms *ortho* to the carbonyl group.

To understand the electronic features of the formal hydrogen abstraction process, the degree of charge transfer at the excited triplet state and the subsequent biradical species was analyzed. The natural charges were shared between the donor (phenol or indole) and the acceptor (BT) fragments. The results given in Table 3 indicate that for phenol both fragments remain basically unchanged along the reaction process, suggesting that one electron and one proton are transferred in a concerted fashion. By contrast, for the indole derivative **BTP-NH** there is a substantial charge transfer at the triplet state (0.24 e). This behavior, previously found for the intermolecular process, suggests that electron transfer clearly occurs preceding proton transfer.⁴ The higher degree of charge-transfer character for **³BTP-NH** can be associated with the shorter XH...O bond length.

In these molecules, fast electron/proton transfer in the hydrogen-bonded triplet is expected to require good spatial overlap between the frontier molecular orbitals (FMO) associated with phenol or indole and BT. The FMO approach at the triplet state requires an analysis of the α and β spin MOs to analyze the HOMO–LUMO interactions in the interacting molecules. A schematic representation of the α MOs of phenol (in blue) and BT (in red) associated with the intermolecular process is given in Figure 4a. In the intermolecular mode, electron transfer will take place from the HOMO_{phenol} to the LUMO_{BT}. A more complex analysis is done for the intramolecular process because the MOs belonging to both moieties are mixed in the supermolecule. However, a contour analysis of the MOs for the bichromophore allows us to assign the different MOs to both fragments. A schematic representation of the most relevant α MOs associated with the intramolecular process is given in Figure 4b. In this representation, the MOs associated mainly with the phenol fragment are given in blue, while those associated mainly with the BT one are given in red. Now the HOMO–LUMO interaction

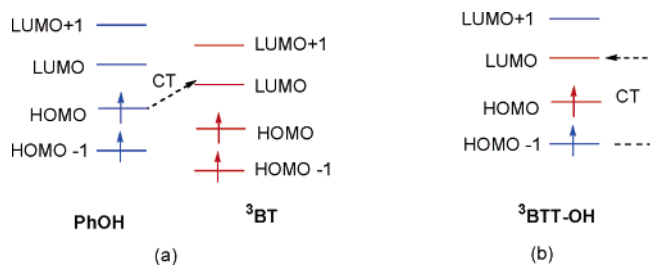


FIGURE 4. Frontier molecular orbital interactions at the triplet state for (a) the intermolecular process between phenol and BT and (b) the intramolecular process in the bichromophore $^3\text{BTT-OH}$.

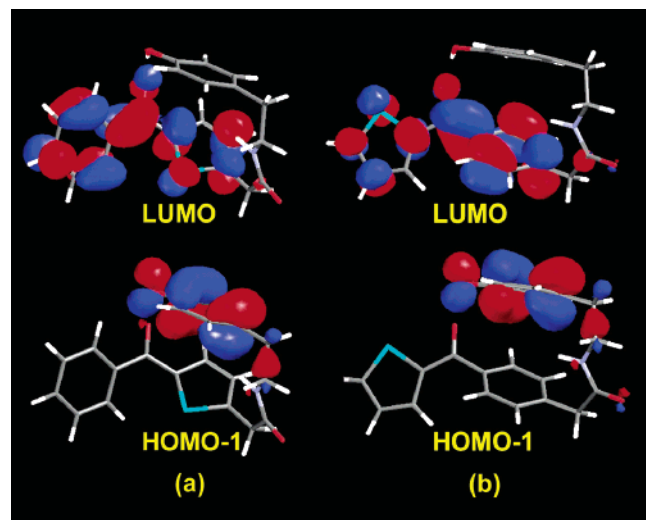


FIGURE 5. α HOMO-1 and α LUMO of (a) $^3\text{BTT-OH}$ and (b) $^3\text{BTP-OH}$.

does not allow an effective electron transfer between both fragments since these α MOs belong to the same BT subunit. However, the HOMO-1–LUMO interaction allows an effective electron transfer because these MOs are associated with the two different subunits, phenol and BT. Hence, these MOs will be further used in the FMO analysis.

A representation of the α HOMO-1 and the α LUMO for the $^3\text{BTT-OH}$ and $^3\text{BTP-OH}$ species is given in Figure 5, while the analogous representation for the $^3\text{BTT-NH}$ and $^3\text{BTP-NH}$ species is given in Supplementary Information (see Figure S13). A detailed analysis of these MOs shows that while the p_z of the phenol oxygen atom participates at the α HOMO-1, the p_z of the carbonyl oxygen atom of BT participates at the α LUMO. However, a different behavior is found for both regioisomers: while for $^3\text{BTT-OH}$ the symmetry of both p_z atomic orbitals allows a favorable overlap between the two fragments, for $^3\text{BTP-OH}$ both p_z atomic orbitals present an antisymmetric approach giving an antibonding overlap. This behavior, also found in the $^3\text{BTT-NH}$ and $^3\text{BTP-NH}$ pair, could explain the faster electron/proton transfer in the $^3\text{BTT-OH}$ and the $^3\text{BTT-NH}$ regioisomers. The MO analysis performed at the *syn* conformer of $^3\text{BTT-OH}$ shows a similar bonding overlap, indicating that the difference found between both regioisomers is not merely a consequence of the *syn/anti* arrangement of the thienyl ring.

Conclusion

From the evolution of the T–T transient spectra it is clear that triplet deactivation in bichromophores **1–12** is dominated by hydrogen atom transfer. Theoretical DFT studies indicate fundamental mechanistic variations in the studied 2-(*p*-alkylbenzoyl)thiophenes: a concerted, not necessarily simultaneous, electron and proton transfer in the hydrogen-bonded exciplex appears to be involved in the phenolic derivatives, by comparison with electron-transfer preceding proton transfer in the indolic analogues. By contrast, in the case of the 5-alkyl-2-benzoylthiophenes the triplet energy is lower, and hydrogen abstraction occurs always through a concerted electron and proton transfer.

Time-resolved experiments have shown that the rate constants for the bimolecular quenching of 2-benzoylthiophene substituted at the thienyl 5-position are lower than those for BT substituted at the phenyl *p*-position, which is in accordance with the higher energy found for the excited triplet state of the latter compounds. However, the regiodifferentiation observed in the intramolecular quenching of the ketone triplet between 2-(*p*-alkylbenzoyl)thiophenes and the regioisomeric 5-alkyl-2-benzoylthiophenes agrees with kinetic control of the process. Theoretical studies provide a plausible explanation: frontier molecular orbitals for the model bichromophoric compounds show a more favorable orbital interaction of the approaching atoms in the exciplex of the 5-alkyl-2-benzoylthiophenes.

Experimental Part

Chemicals. 2-(5-Benzoylthien-2-yl)propanoic acid (tiaprofenic acid, TPA) was extracted from commercial samples using methanol as solvent. 2-[4-(Thien-2-ylcarbonyl)phenyl]propanoic acid (suprofen, SP), L-tyrosine methyl ester, L-tryptophan methyl ester, tyramine, tryptamine, 4-methoxytyramine, [1-ethyl-3-(3-(dimethylamino)propylcarbodiimide) (EDC), and 1-hydroxybenzotriazole (HBT) were commercially available. 2-(5-Benzoylthiophen-2-yl)-2-methylpropionic acid¹⁶ and 2-methyl-2-[4-thiophene-2-carbonyl]phenyl]propionic acid¹⁷ were synthesized from 2-(5-benzoylthiophen-2-yl)propionic acid methyl ester^{16,18} and 2-[4-thiophene-2-carbonyl]phenyl]propionic acid methyl ester,¹⁷ respectively, following a procedure described in the literature.¹⁶

General Procedure. All synthetic procedures were performed under nitrogen atmosphere using purified dried solvents. ^1H and ^{13}C NMR spectra were recorded in a 300 MHz spectrometer, chemical shifts (δ) are reported in ppm relative to TMS. The coupling constants (J) are in hertz (Hz). Column chromatography was performed on silica gel (230–400 mesh). Eluent composition is given as volume/volume mixtures unless specified otherwise. HPLC was carried out using a C-18 column or a silica column.

Synthesis of Bichromophores 1–12. The corresponding propanoic acid (1.2 mmol), the amine or 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

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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.

Laser Flash Photolysis. These experiments were carried out using 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 detecting light source. The laser flash photolysis apparatus consisted of the pulsed laser, the Xe lamp, a monochromator, and 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 cells made of Suprasil quartz and were deaerated with dry nitrogen prior to the experiments. Concentrations for bichromophoric compounds **1–14** were adjusted to yield and absorbance of 0.35 at 355 nm.

Computational Methods. Density functional theory¹⁹ (DFT) calculations have been carried out using the UB3LYP²⁰ exchange-correlation functional, together with the standard 6-31G* basis set.²¹ The optimizations were carried out using the Berny analytical gradient optimization method.²² The electronic structures of stationary points were analyzed by the

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natural bond orbital (NBO) method.²³ All calculations were carried out with the Gaussian 98 suite of programs.²⁴

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Supporting Information Available: Analytical and spectroscopic data for compounds **1–14**, representative cyclic voltammograms, computational data for **BTT-OH**, **³BTT-OH**, **BTHT-O**, **BTP-OH**, **³BTP-OH**, **BTP-O**, **BTT-NH**, **³BTT-NH**, **BTHT-N**, **BTP-NH**, **³BTP-NH**, and **BTP-N**, and additional transient absorption spectra for bichromophoric compounds **1–4**, **6–10**, and **12**. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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