Chiral discrimination in the intramolecular abstraction of allylic hydrogens by benzophenone triplets

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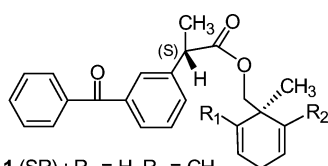
Using two diastereomeric compounds containing benzophenone and olefin units, significant chiral discrimination has been found in all the photophysical and photochemical processes involved in intramolecular hydrogen abstraction: overall quenching of benzophenone triplets, actual hydrogen abstraction step and π-quenching.

Photoreduction of benzophenone is one of the best known photochemical reactions.[1] Chiral benzophenone derivatives tethered to enantiomerically pure 1,4-cyclohexadienes (**1** and **2**, Scheme 1) exhibit significant stereoselectivity in their intramolecular hydrogen abstraction. In this case, the photoreactivity of the *SR* isomer (**1**) was found to be higher than that of the compound with *SS* configuration (**2**).[2] However, direct measurements of the triplet lifetimes, that could reveal a possible excited state stereodifferentiating interaction, were not reported. By contrast, remarkable stereoselectivity has been observed in the electron transfer quenching of π,π^* triplet excited states of 2-benzoylthiophene by tyrosine and tryptophan.[3]

The present study was undertaken in order to detect a possible chiral discrimination in the intramolecular abstraction of allylic hydrogens by benzophenone triplets. For this purpose, esters **1** and **2**, prepared from a chiral benzophenone (*S*-ketoprofen) and *S*- or *R*-1,2-dimethylcyclohexa-2,5-diene-1-methanol were submitted to laser flash photolysis in deaerated acetonitrile (Nd:YAG-Laser at 355 nm). In agreement with previous observations, transient absorption spectra obtained from **1** and **2** 70 ns after the laser pulse were very similar, as expected for the corresponding biradicals. Their assignment was based on the

typical bands with maxima at *ca.* 330 and 545 nm, and their lifetimes were 1.8 and 1.6 μs, respectively.[2] The fact that the two diastereomeric biradicals have nearly the same lifetimes suggests that their decay is mainly controlled by intersystem crossing.[1e] In order to detect transient species with shorter lifetimes, the decay traces were registered in the submicrosecond timescale, close to the resolution limit of the system. When the spectra were monitored just after the laser pulse an earlier intermediate was observed in the two cases (from **1** and **2**), which showed a band with a maximum at *ca.* 525 nm. It was assigned to the triplet–triplet absorption based on the literature data reported for benzophenone and ketoprofen (see Fig. 1).

It was noteworthy that, at first sight, the lifetime of this intermediate appeared to be shorter for **1** than for **2**. Actually, the spectrum obtained 15 ns after the laser pulse in the case of **1** showed a much more significant contribution of the biradical (shoulder at 545 nm). Kinetic analysis of the triplet decay, using a monoexponential function, led to a lifetime of 29 ns for **2**, while it was impossible to make a reliable measurement for **1**.

In view of this difficulty, another set of experiments was performed to obtain more accurate values for the lifetimes of triplet states of **1** and **2**. It has been reported that the short lived

1 (SR) ; R$_1$ = H, R$_2$ = CH$_3$
2 (SS) ; R$_1$ = CH$_3$, R$_2$ = H

Scheme 1
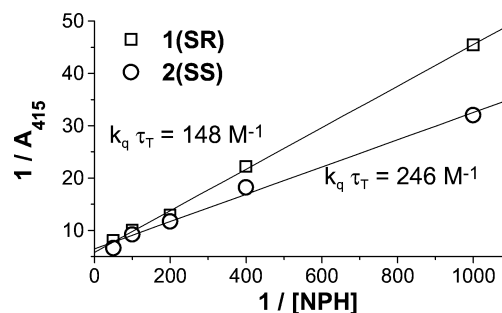
Fig. 2 Double reciprocal plot for quenching of **1** and **2** triplet excited state by NPH in acetonitrile.

Table 1 Photophysical and photochemical parameters of **1** and **2** in acetonitrile

Parameters	**1** (*SR*)	**2** (*SS*)	Stereoselectivity factor (**1**/**2**)
τ_T (ns)	18	31	—
k_{iq} ($\times 10^7$ s^{-1})[a]	5.4	3.2	1.68
k_H ($\times 10^7$ s^{-1})[b]	5.1	2.2	2.30
k_π ($\times 10^7$ s^{-1})[b]	0.3	1.0	0.30
$\Phi_{biradical}$[c]	0.95	0.70	1.35

[a] The intramolecular quenching rate constants were obtained by using the equation $k_{iq} = 1/\tau_i - 1/\tau_0$, where τ_i are the lifetimes of the ketone triplets in compounds **1** and **2** and τ_0 is the *S*-ketoprofen triplet lifetime (1.4 μs). [b] The rate constants for hydrogen abstraction and physical quenching by the π system were obtained using the following equations: $k_H = k_{iq} \times \Phi_{biradical}$ and $k_{iq} = k_H + k_\pi$. [c] The quantum yield of biradicals formation was determined by the comparative method, using benzophenone as standard and assuming the same extinction coefficient for the biradicals and the benzophenone ketyl radical (see literature ref. 5).
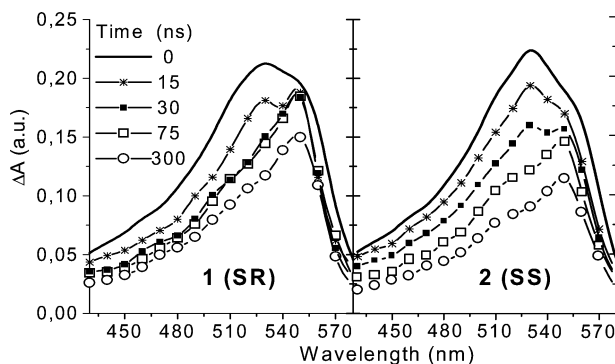
Fig. 1 Transient absorption spectra obtained at different times after laser pulse (355 nm) for **1** and **2** in acetonitrile (5 × 10^{-4} M).

Table 2 Calculated MM2 data for the sandwich conformers of **1** and **2**

Parameters	**1** (*SR*)				**2** (*SS*)			
	A	B	C	D	A′	B′	C′	D′
Energy (kcal mol^{-1})^a	49.5	49.7	49.8	48.5	48.7	49.0	49.1	47.9
Distances (Å)								
d_H (CO–HC)	2.78	2.71	2.91	2.70	2.78	2.77	4.40	2.92
d_π (O–C$_\pi$)^b	3.82	> 4	3.53	> 4	3.96	> 4	3.55	3.50
Dihedral angles (°)								
Δ (C=O–HC)	79	89	70	84	77	86	70	94
ω (CO$_\pi$–HC)^c	79	40	75	60	87	60	70	45
θ (CO–H–C)	143	148	130	155	149	165	95	125

^{a} Calculated MM2 energy for the conformers of **1** and **2**. ^{b} Shortest O–C distance between the carbonyl oxygen and the cyclohexadiene π systems. ^{c} Dihedral angle made by the hydrogen with respect to the nodal plane of the carbonyl π bond.
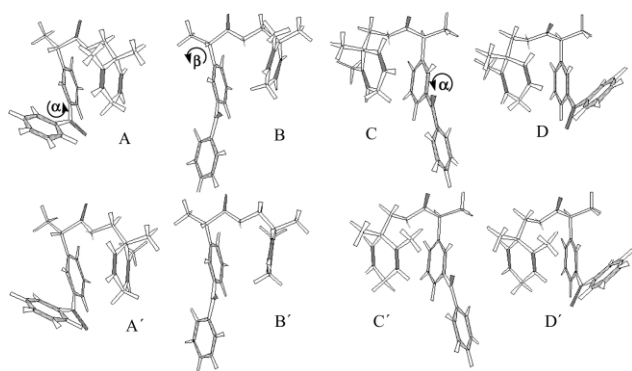
Scheme 2 Most stable sandwich conformers of **1** (*SR*) and **2** (*SS*).

triplets of some ketones can be quenched by naphthalenes.[4] In the case of **1** and **2**, naphthalene (NPH) was used as energy acceptor. Laser flash photolysis of **1** and **2** was performed at the excitation wavelength of 355 nm in the presence of increasing amounts of NPH, and the triplet–triplet absorption of NPH was observed and monitored at 415 nm. When the transient absorbance at 415 nm was plotted against the concentration of NPH two straight lines were obtained (see Fig. 2).

These results are in agreement with expectations, as the relationship between the sets of values must follow eqn. (1):

$$1/A_{415} = \alpha + \alpha/(k_q \times \tau_T \times [\text{NPH}]) \tag{1}$$

where A_{415} is the absorbance of the triplet of NPH at 415 nm, before significant decay takes place, k_q is the bimolecular rate constant for triplet quenching by NPH, τ_T is the triplet lifetime of **1** or **2** in the absence of NPH and α is a constant. The Stern–Volmer parameters ($k_q \times \tau_T$) were obtained from the intercept-to-slope ratios (Fig. 2 and eqn. (1)). They were found to be 148 M^{-1} (**1**) and 246 M^{-1} (**2**). On the other hand, the intermolecular k_q, determined in acetonitrile for *S*-ketoprofen, was 8×10^9 M^{-1} s^{-1}, which was assumed to be the same for **1** and **2**. With these data, the values calculated for the triplet lifetimes of **1** and **2** were 18 and 31 ns, respectively.

This appears to be a satisfactory estimation, in view of the good agreement with the triplet lifetime found for compound **2** by the direct method (29 ns). The τ_T values, together with other important photophysical and photochemical parameters of compounds **1** and **2**, are summarized in Table 1.

It is worth mentioning that the quenching process is stereoselective, as evidenced by the intramolecular quenching rate constant (k_{iq}) calculated from the triplet lifetimes of isomers **1** and **2** and that of the parent chromophore *S*-ketoprofen. However, it is known that the intermolecular interaction of triplet benzophenones with allylic systems leads not only to hydrogen abstraction but also to physical quenching by the π systems, *via* reversible formation of a carbon–oxygen bond.[6] In this context, although the triplet excited states of both isomers are fully quenched by their respective intramolecular hydrogen donors, the quantum yield of biradicals formation ($\Phi_{\text{biradical}}$) is lower for **2** than for **1** (Table 1) as determined by the

comparative method. Based on these data, it is possible to calculate the rate constants for hydrogen abstraction (k_H) and physical quenching (k_π). As shown in Table 1, both processes are even more stereoselective than the overall quenching. Interestingly enough, while k_H (**1**) is higher than k_H (**2**), the reverse is true for the corresponding k_π values.

In an attempt to understand the observed stereoselectivities, the sandwich conformations of **1** and **2** at the energy minima were studied by MM2 computation, using two dihedral drivers for rotation (α and β, Scheme 2). Since the C=O bond is longer in the nπ* triplet than in the ground state, it was locked at 1.5 Å.[7] Results revealed four energy minima for each compound (A–D and A′–D′, Scheme 2). Their energies, together with their geometric factors, are summarized in Table 2.

In connection with hydrogen abstraction, it is remarkable that any $d_H > 3.1$ Å (as in C′) is too long for reaction to occur. Also, when ω approaches 90° (as in A′) the reactivity has been predicted to vanish.[8] All other d, Δ, ω and θ values fall into the previously observed ranges. As regards π quenching, the most striking feature is the long O⋯C distance (> 4 Å) between the interacting systems in B, D and B′. Overall, these results are compatible with the observed stereoselectivities.

Summarizing, the time-resolved studies performed with compounds **1** and **2** show that there is significant chiral discrimination in all the photophysical and photochemical processes involved in intramolecular hydrogen abstraction. This is observed not only in the quenching of benzophenone triplets, but also in the actual hydrogen abstraction step and in the competing π-quenching.

Notes and references

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