Stereo-differentiation in the excited state behaviour of naphthalene-thymine dyads

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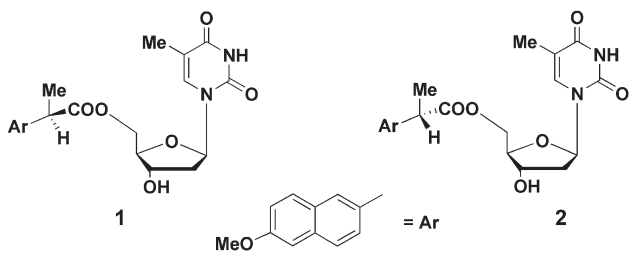
Using two diastereomeric dyads containing naphthalene and thymine units, significant chiral discrimination has been found in the photophysical processes involving the naphthalene excited states: singlet deactivation by hydrogen bonding molecules, singlet–singlet energy transfer from thymine and triplet decay.

In the last two decades, a considerable amount of research effort has been devoted to asymmetric photochemistry;[1,2] however direct photophysical evidence for chiral discrimination in the excited states has only been found in few cases.[3] Moreover, relatively little is still known about diastereomeric differentiation in the intramolecular quenching of excited states.[4]

Previously, it has been shown that bichromophoric compounds containing covalently linked sensitiser and substrate-derived substructures can be useful for modelling photochemical stereoselective events. Thus, in the interaction between excited 2-arylpropionic acid derivatives and biological substrates a high degree of chiral discrimination has been achieved; this has been related to the possible enantioselectivity of the photobiological properties of drugs.[5–7]

Naproxen (NAP, 6-methoxy-α-methyl-2-naphthaleneacetic acid), a non-steroidal anti-inflammatory drug, behaves as a photosensitiser producing DNA damage,[8] among other photobiological effects. In connection with the potential enantioselectivity of drug-photosensitised DNA damage, we have prepared two diastereomeric bichromophores by attaching a chiral NAP to the position 5′ of the thymidine nucleoside (Scheme 1). The synthesis of **2** has been described elsewhere.[9] The new dyad (*R*)-NAP-dThd (**1**) was fully characterized.†

A thorough photophysical study of dyad **2**,[9] showed that a physical deactivation process is the pathway responsible for an efficient excited singlet state quenching in the presence of hydrogen bonding donating solvents. This process (as established by means of femtosecond laser experiments and deuterium effects) involves the formation of a locked complex of the excited dyad with the ROH molecules, as shown in Scheme 2.[9]

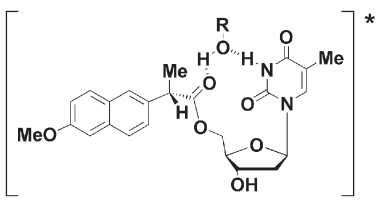


Scheme 1

The present study was undertaken in order to detect a possible chiral discrimination in the photophysical behaviour of the *cisoid* dyads **1** and **2** in the presence of hydrogen bonding donating solvents.

Fluorescence studies on **1** were performed both in acetonitrile and methanol (10^{-4} M); the results were compared with those previously obtained with the stereo-isomeric dyad **2**. The emission spectra featured one band with maximum at about 350 nm in all cases. This band was assigned to the naphthalene chromophore.[9,10] In methanol, the emission of **1** was strongly quenched (Fig. 1), as already found for **2**.

When the fluorescence was analysed in the presence of several hydrogen bonding ROH molecules a significant stereodifferentiation was observed. The emission was measured in aerated acetonitrile, upon addition of increasing amounts of



Scheme 2 Locked conformation of **2** in the presence of hydrogen bonding ROH molecules in the excited state.

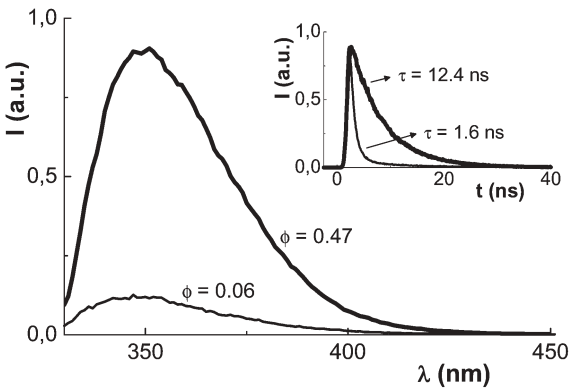


Fig. 1 Fluorescence spectra upon 320 nm excitation of dyad **1** (*ca.* 1×10^{-4} M) in degassed acetonitrile (—) and methanol (—). The solutions were iso-absorptive ($A < 0.2$) at the excitation wavelength. Inset: Decay traces for **1** at 350 nm in degassed acetonitrile (—) and methanol (—).

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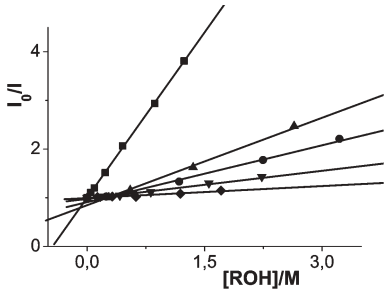

Fig. 2 Stern–Volmer plots for the fluorescence quenching of dyad **1** in ACN, in the presence of increasing concentrations of hydroxylic quenchers, ROH = HFIP (■), H_2O (▲), MeOH (●), EtOH (▼) and iPrOH (◆).

Table 1 Fluorescence quenching rate constants for **1** and **2** in the presence of hydrogen bond donating ROH molecules[a]

	$k_q \times 10^{-7}$, M^{-1} s^{-1}				
	HFIP	H_2O	MeOH	EtOH	iPrOH
1	31.0	8.2	5.3	2.6	<1.0
2[b]	22.0	7.3	3.4	2.0	<1.0

[a] Room temperature. Aerated solvents. λ_{exc} = 320 nm. Lifetimes in aerated pure acetonitrile are 7.3 ns and 8.0 ns for **1** and **2**, respectively. [b] Taken from Ref. 9.

hexafluoroisopropanol (HFIP), water, methanol, ethanol and isopropanol (in a decreasing order of hydrogen bond donating ability),[11] and the rate constants (k_q) were calculated from the Stern–Volmer plots (see, for instance, Fig. 2) together with the fluorescence lifetime in pure acetonitrile.[9] The obtained values for both dyads are given in Table 1 and clearly show that the quenching process is faster in the case of **1**.

Plots based on emission intensity, quantum yield or lifetime were coincident; thus, the quenching observed for both compounds is dynamic in nature.[12]

As expected from the involved decay mechanism (see above),[9] the obtained values for the rate constants (k_q) correlate well with the hydrogen-bond donor ability of the solvents.

When the excitation spectra (λ_{em} = 350 nm) were compared, significant differences were observed between **1** and **2**. By contrast, the absorption spectra were identical. As shown in Fig. 3 the band at 280 nm increased in the case of both dyads relative to NAP due to the contribution of thymine absorption at this wavelength. Thus, a singlet–singlet energy transfer process takes place from

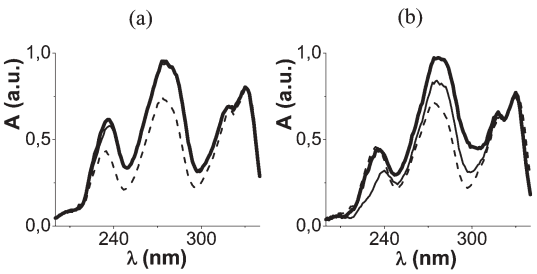

Fig. 3 Excitation spectra obtained under fixed emission at 350 nm of **1** (—), **2** (—) and NAP (---) in (a) acetonitrile and (b) methanol. The solutions were degassed and iso-absorptive ($A < 0.2$ at 280 nm).

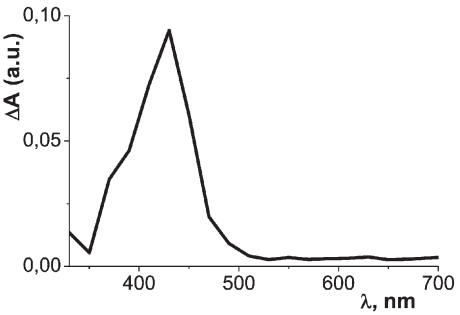

Fig. 4 Transient absorption spectrum of dyad **1** 2.5 μs after the laser pulse (308 nm) in methanol.

thymine to naphthalene in the dyads. It is remarkable that in methanol (Fig. 3b) such energy transfer seems to be stereoselective, as the 280 nm band in the excitation spectra of **1** is somewhat more intense. Again, the involvement of a locked, ROH bridged conformation (see Scheme 2) could account for this observation. Accordingly, no difference was found between **1** and **2** in acetonitrile (Fig. 3a).

Finally, both diastereomers were submitted to laser flash photolysis in deaerated acetonitrile and methanol. No differences were observed in the former solvent, where the decay of the triplet–triplet absorption at 430 nm was similar for **1** and **2** (τ_T *ca.* 7 μs). However, the naphthalene triplet generated in methanol (Fig. 4) exhibited configuration-dependent lifetimes (τ_T(**1**) = 8 μs and τ_T(**2**) = 12 μs).

The origin of this stereo-differentiation in the excited triplet state is currently being investigated.

Summarising, the steady-state and time-resolved studies performed with compounds **1** and **2** show that there is a relevant chiral discrimination involving the naphthalene excited states: (a) physical singlet deactivation mediated by hydrogen-bonding molecules, (b) singlet–singlet energy transfer from thymine to naphthalene and (c) decay of the naphthalene triplet excited state.

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Notes and references

† Characterization of **1**: Colourless crystals; m.p. = 159–160 °C; ^{1}H NMR δ_H (300 MHz; CD_3OD): 7.05–7.70 (m, 7H, ArH + HC=), 6.10 (dd, J = 7.8, 5.7 Hz, 1H, H-1′), 4.60 (m, 1H, H-5′), 4.20–4.42 (m, 2H, H-5′ + H-3′), 3.88 (s, 3H, OCH_3), 3.85–4.10 (m, 2H, H-4′ + C*H*CH_3), 2.05–2.15 (m, 1H, H-2′), 1.72–1.88 (m, 1H, H-2″), 1.67 (s, 3H, =CCH_3), 1.56 (d, J = 7.2 Hz, 3H, CHCH_3). ^{13}C NMR δ_C (75 MHz, CD_3OD): 175.7 (C), 165.9 (C), 158.8 (C), 151.7 (C), 136.8 (CH), 136.1 (C), 134.9 (C), 130.0 (C), 129.9 (CH), 128.1 (CH), 126.8 (CH), 126.6 (CH), 119.9 (CH), 111.0 (C), 106.4 (CH), 86.3 (CH), 85.5 (CH), 72.1 (CH), 65.3 (CH_2), 55.7 (CH_3), 46.3 (CH), 40.5 (CH_2), 18.6 (CH_3), 12.5 (CH_3). MS (EI) *m/z* calcd for $C_{24}H_{26}O_7N_2$, 454.1740; found, 454.1754.

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