SHORT PAPER

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Photochromic behaviour of *N*-arylsulfonyl peptides†

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Deep, persistent, but structurally sensitive photoyellowing observed in photochemical studies of a wide range of arylsulfonyl derivatives of amines, amino acids and peptides can be attributed to a novel kind of photochromism in which intramolecular photoinduced electron transfer promotes the formation of a metastable cyanine-type chromophore involving sulfur *d*-orbitals.

Keywords: photochromism, amino acids, intramolecular photoinduced electron transfer

Photochromism is a well-known property of a range of compounds with structural attributes that allow a photochemical transformation to be reversible, either thermally or photochemically. Its actual and potential technological applications as well as its biological relevance ensure it remains an increasingly active field of research.[1] Some of the more useful systems rely on the interconversion of cyclic compounds with isomers containing cyanine-type chromophores absorbing strongly in the visible region of the spectrum (*e.g.* the benzothiazoline photomerocyanin system shown in Scheme 1[2]). The technological potential of photochromism prompts considerable interest in the discovery or development of any new compounds showing this behaviour. We report here a novel but chemically fragile case that may be worthy of further development.

In the course of exploring the scope of photoinduced electron transfer processes found with *N*-tosylglycine[3] in a wide range of arylsulfonyl amines, amino acids and peptides, we observed a striking yellow-orange colouration with particular substrates which we now attribute to the formation of a metastable photoisomer that reverts thermally to the starting material. The structural requirements and conditions of generation and decay suggested the yellow chromophore was of the cyanine type and, while photochromic systems involving such groups are well known,[1] both the mechanism and the participation of sulfur *d*-orbitals implicated in this case appear to be without precedent.

Fig. 1 shows three representative spectra of yellow photoproducts, and the structural requirements for this behaviour among derivatives of arylsulfonyl amino acids are indicated in Table 1. In addition, the β-alanine derivative, $TsNH(CH_2)_2CONHMe$ showed no significant colouration on irradiation.

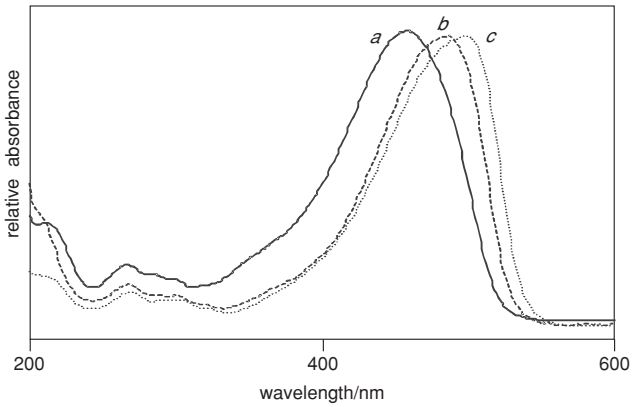
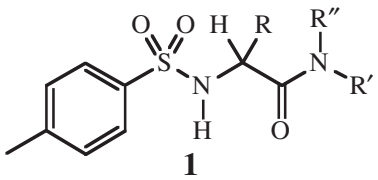


Fig. 1 Spectra of representative yellow photoproducts of $TsNHCH(R^1)CONR^2R^3$ in aqueous acetonitrile: *a,* R^1= R^2 = H, R^3 = Me; *b,* R^1 = $CH_2C_6H_5$, R^2 = H, R^3 = Me; *c,* R^1 = H, R^2R^3 = $(CH_2)_3CH(CO_2H)$.



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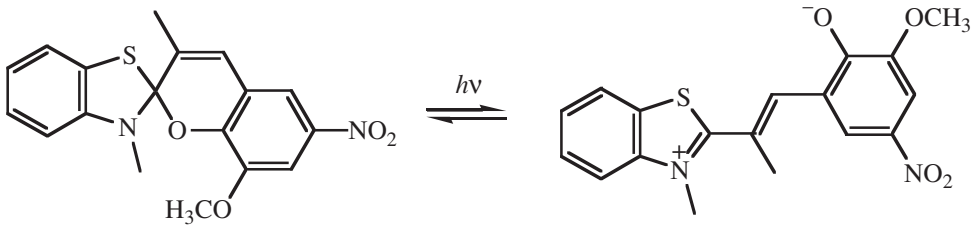
A minimal structure necessary for photoyellowing, **1**, can be derived from the data in Table 1. Firstly, only tosylamino carboxamides exhibit photoyellowing. It is not seen in the tosyl amino acids and their ester derivatives, suggesting that nitrogen is required in the carboxy function. However, the methylamide of tosylproline, a tertiary sulfonamide, did not become yellow, indicating a requirement for hydrogen on the sulfonamide



Scheme 1

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† This is a Short Paper, there is therefore no corresponding material in *J Chem. Research (M).*

Table 1 Structural requirements for photoyellowing of solutions of $TsNR^1C(R^2R^3)COX$ in aqueous acetonitrile

R^1	R^2	R^3	X	λ_{max}/nm[a]	Ref.
H	H	H	OH	–	4
H	H	H	OMe	–	9
H	H	H	NHMe	455[b]	10
H	H	$CH(CH_3)_2$	OH	–	11
H	H	$CH(CH_3)_2$	NHMe	464	4
H	H	$(CH_2)_2SCH_3$	OH	–	12
H	H	$(CH_2)_2SCH_3$	NHMe	466	4
H	H	$CH_2C_6H_5$	OH	–	13
H	H	$CH_2C_6H_5$	OMe	–	14
H	H	$CH_2C_6H_5$	NHMe	486[b]	4
H	H	$CH_2C_6H_4OMe$	NHMe	–	4
$-(CH_2)_3-$		H	NHMe	–	4
H	CH_3	CH_3	NHMe	–	4
H	H	H	$NHCH_2CO_2H$	486	8
H	H	H	$NHCH(CH_3)CO_2H$	457	15
H	H	H	$NHCH[CH(CH_3)_2]CO_2H$	473	16
H	H	H	$-N(CH_2)_3CH(CO_2H)-$	496[b]	17

[a]Blank entries indicate no significant colouration on irradiation. [b]Illustrated in Fig. 1.

nitrogen. Furthermore, only a very slight colouration was seen with the derivative of α-aminobutyric acid, identifying C_α-H as a necessary feature; tosylglycinemethylamide, which has no side-chain, readily becomes yellow. Neither of R′ and R″, however, needs to be hydrogen as the derivative of glycylproline actually gave a more intense colouration than any of the other compounds, perhaps showing that the more polarisable tertiary nitrogen is beneficial. Finally, the absence of photoyellowing with the β-alanine derivative suggests that only those of α-amino acids can show this behaviour.

The yellow colour was stable for a number of weeks if the photolysate was kept in a sealed tube in the dark at < 4 °C. It disappeared within a day when the solutions were exposed to air and light or when diluted. Although attempts to isolate the yellow photoproduct responsible were unsuccessful, analysis of the photolysate of tosylphenylalaninemethylamide by LC-MS with detection at 400 nm gave two peaks that both had MH^+ 333.1 indicating that two compounds isomeric with the substrate are involved.

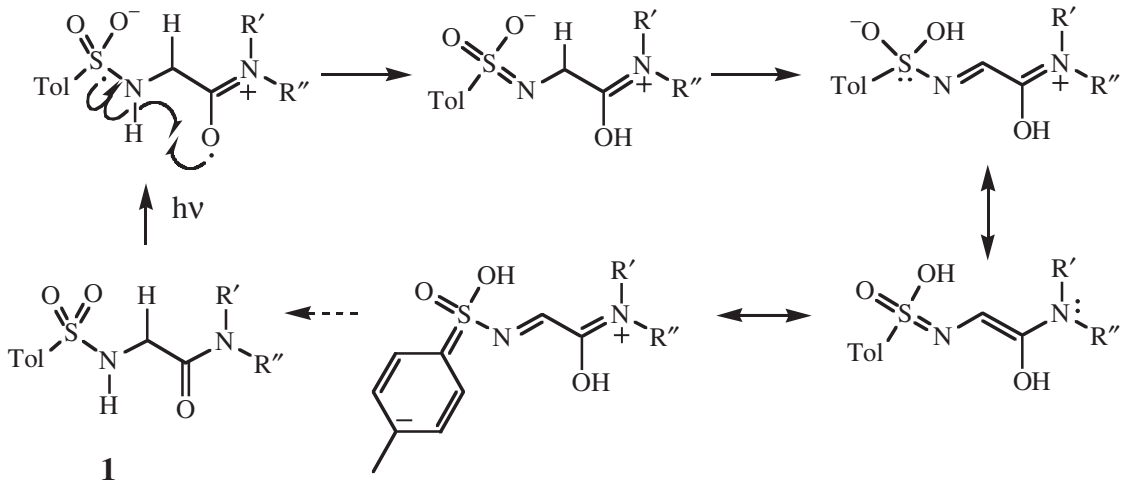
Our earlier detailed product analysis of the aqueous photolysate of tosylglycine supported a mechanism initiated by photoinduced electron transfer.[3] This has been corroborated with similar studies of related compounds, including those in Table 1[4] and offers one explanation for the above structural correlation in which the yellowing may be attributed to the generation of a cyanine-type chromophore (Scheme 2).

The requirement of nitrogen rather than oxygen on the carboxyl function is consistent with N being more polarisable and therefore able to participate more readily in electron-delocalised structures. Also, the proposed rearrangements require hydrogen on the sulfonamide nitrogen and at the α-carbon. The single major absorption band observed in the UV-visible spectra of all the yellow photolysates implies that a single chromophore is involved, which is supported by the cyanine-type structure that does not involve the side-chain. The conjugated system is possible with α-amino acids but not with β-amino acids. The involvement of the peptide bond nitrogen is consistent with the product derived from tosylglycylproline having an absorption maximum at a longer wavelength than the other tosyl dipeptides studied, tertiary amides being more polarisable than secondary amides. Other variations in wavelength shown in Table 1 could arise through conformational factors. Significantly, our product studies with the methylamide of tosyl-*O*-methyltyrosine showed that side-chain cleavage dominates its photochemistry,[4] consistent with the well-known strong electron-donating properties of aryl ethers. This derivative remained colourless on irradiation, as might be expected from Scheme 2, which entails the generation of a chromophore in the main chain. Finally, the apparent formation of two yellow isomers could be accommodated in the scope for *cis* and *trans* configurations within the proposed chromophore.

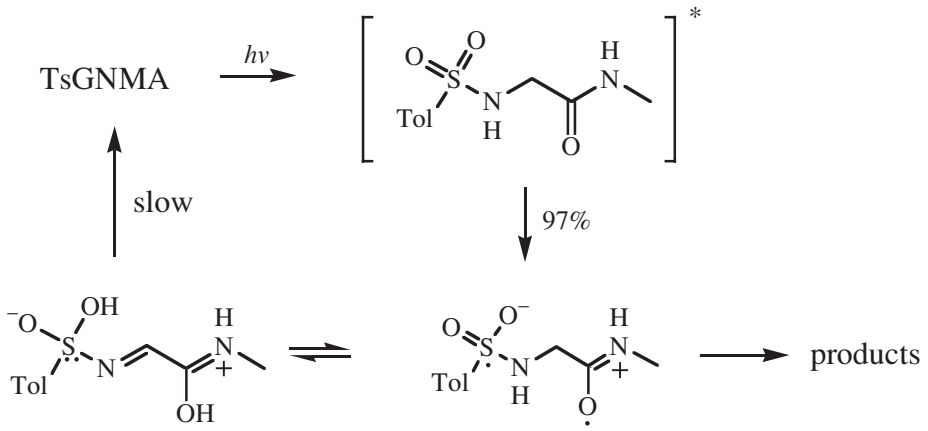
These particular compounds are far too photolabile for photochromic applications (see Scheme 3 for the glycyl derivative[4]) but, as far as we are aware, the behaviour we have observed is unprecedented with both sulfonyl compounds and peptides. Although the participation of sulfur *d*-orbitals in extended conjugated systems is demonstrable,[5] their apparent involvement in photochromism is novel, and may be profitably investigated with more robust systems. For example, the proton shift from the relatively acidic[6] C_α-H in Scheme 2 is also seen in the thermolysis of arylsulfones,[7] and analogous carboxamide and other derivatives may well offer usefully stable photochromic systems.

Experimental

Lancaster Chemicals supplied 2-amino-*iso*-butyric acid, L-proline and triethylamine. β-Alanine, glycyl-DL-alanine, glycylproline, glycyl-DL-valine, hydrochloric acid (ACS), pyruvic acid ethyl ester and tosylglycine were supplied by Sigma Chemical Company. Aldrich Chemical Company supplied all other chemicals. Methylamides of *N*-tosylamino acids and peptides were synthesised by standard methods from the amino acid or dipeptide in the sequence: tosylation,[8] methyl esterification and methyl amidation. Products were fully characterised by comparison with existing data for known compounds[8-17] or with consistent spectral and elemental analytical data.[4]



Scheme 2



Scheme 3

Photolyses: A 10^{-2} M solution of the substrate in water or in 40% aq. acetonitrile was purged with nitrogen for ~1 hr whilst being stirred. Quartz carousel tubes were filled with ~14 cm^3 of the solution, and purged for a further 2 minutes prior to subasealing. The tubes were irradiated in an Applied Photophysics carousel in the inner or outer rings with a 400 W medium pressure Hg lamp for periods of 1–240 min, with an inversion every 30 minutes to ensure homogeneous mixing. The reactions were quenched by cooling in ice for at least 30 min before product analyses[4] the same day or after storage in a refrigerator.

Measurements: UV spectra were recorded in 1 cm quartz cuvettes on a Kontron Model 860 spectrophotometer, or were extracted from HPLC data. Accurate mass and LC-MS data were obtained by Pfizer Global R & D, Sandwich, Kent, the latter using a Waters Alliance System with a Waters 474 scanning fluorescence detector, 712 WISP autosampler and Waters Millenium Software version 3.05 using a Phenomenex Luna phenylhexyl 150 mm × 4.60 mm column at 25 °C with an eluent gradient from 90:10 to 25:75 10 mM ammonium trifluoroacetate (pH 3.0) : acetonitrile and MS in positive ion-mode detection.

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