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Photochemical Oxidation of *trans*-α,α'-Dimethylstilbene in the presence of α-Terthienyl

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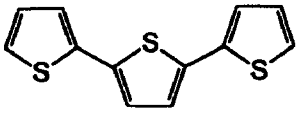
Abstract - *trans*-α,α'-dimethylstilbene gave a new photoproduct when irradiated in the presence of both oxygen and α-terthienyl. This new product is due to an electron transfer process.

α-Terthienyl (α-T, **1**), is a naturally occurring polythiophene isolated in numerous members of *Compositae*. α-T has been extensively studied for its biological properties. In fact, it showed a nematocidal activity that was enhanced in the presence of sunlight (UV-A); similarly, in the presence of UV-A, it showed antibiotic, ovicidal, algicidal, larvicidal, and antifeedant properties. Furthermore, it inhibited germination of some plants and was phototoxic to some aquatic organisms. It could produce hemolysis and phototoxic dermatitis; however, it was not able to induce chromosome damage.[1] More recently photochemical interaction of α-T with supercoiled c-DNA[2] and photobiological activity of α-T against viruses[3] and HIV[4] were reported. The presence of UV-A to have biological activity can be explained considering that α-T is a photosensitizer of singlet oxygen and that singlet oxygen quenchers inhibit the enzymatic inactivation by α-T.



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In aqueous media formation of $\alpha\text{-T}^{+\cdot}$ and $O_2^{-\cdot}$ through an electron transfer mechanism has been suggested.[5] In this case the reduction of ferrycytochrome c in the presence of superoxide dismutase was tested. Nevertheless, numerous reported data are not in agreement with the formation of $\alpha\text{-T}^{+\cdot}$. Photoionization products were not observed both in alcoholic and in aqueous media.[6] Furthermore, in acetonitrile, the efficiency of the electron transfer from α-T to oxygen was estimated to be lower than 1%.[7]

Finally, the $O_2^{-\cdot}$ formation has not been confirmed *in vivo* by using *Escherichia coli*.[8] In conclusion, on the basis of these results, electron transfer could be involved in aqueous medium while this process is not involved in reactions carried out in non-aqueous media.

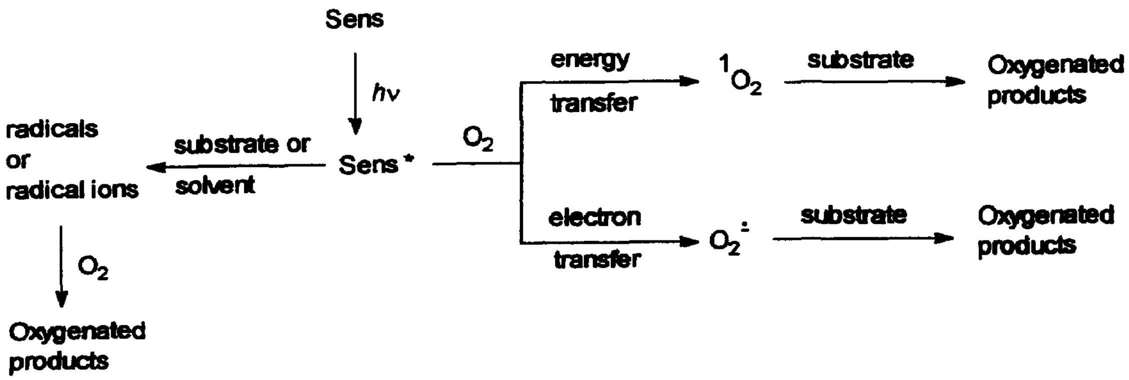
In this paper we want to report our results on electron transfer reactions catalyzed by α-T in acetonitrile.

Photodynamic activity is usually divided into two processes named *Type I* and *Type II*.[9] In *Type I* reaction triplet sensitizer reacts with substrate or solvent to give hydrogen abstraction or electron transfer. In *Type II* reaction triplet sensitizer reacts with oxygen to give, *via* energy transfer, singlet oxygen or, *via* electron transfer, superoxide ion (Scheme 1). Recently it was reported that the irradiation of *trans*-α,α'-dimethylstilbene (**2**) in acetonitrile in the presence of both oxygen and a suitable sensitizer gave only compound **3** when the sensitizer can produce singlet oxygen *via* a *Type II* reaction, while, if the sensitizer can give a *Type I* process, a completely different product mixture was obtained (Scheme 2).[10]

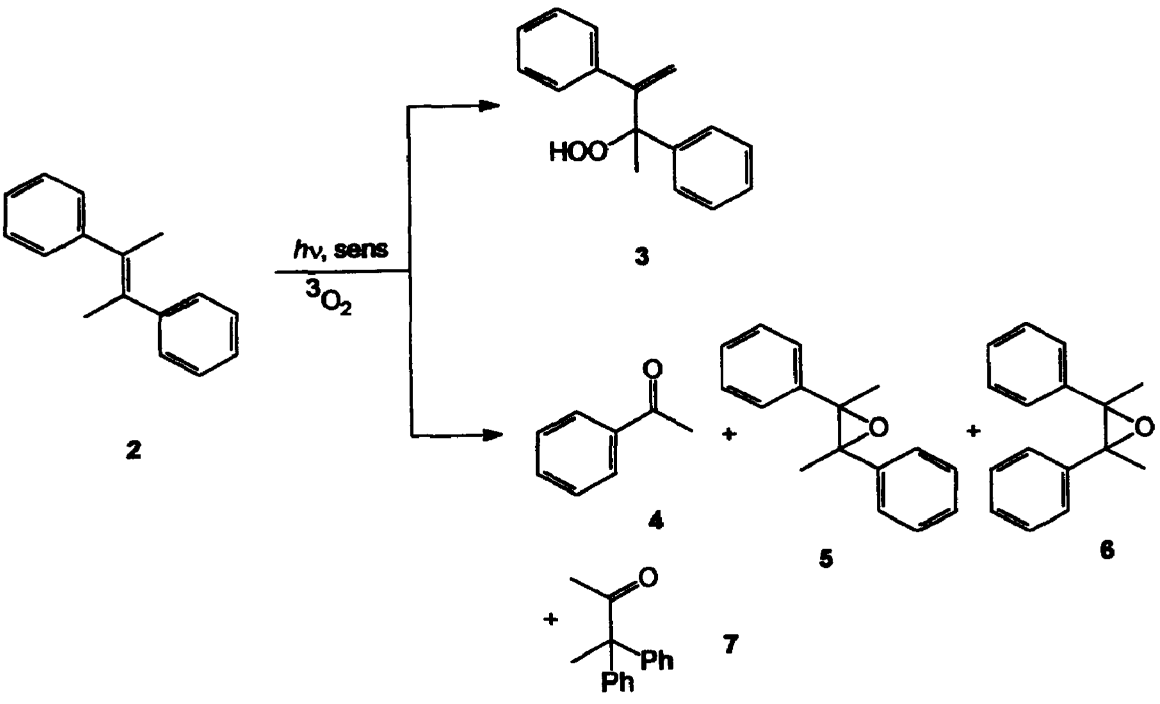
This behaviour showed to be an useful method to distinguish between *Type I* and *Type II* photosensitizers giving good results with both singlet oxygen[11-14] and electron transfer sensitizers.[15,16] Furthermore, *trans*-α,α'-dimethylstilbene (**2**) has been depicted as an efficient $^1O_2$ acceptor in order to explain the absence of electron transfer products in competition reactions.[17] Then **2** is a suitable substrate to study singlet oxygen sensitizers.

We tested this reaction with α-T (Scheme 3). A solution (50 ml) containing 2×10^{-4} M **1** and 5×10^{-2} M *trans*-α,α'-dimethylstilbene[18] in acetonitrile was irradiated in the presence of oxygen in a Pyrex tube surrounded by a Pyrex water jacket connected to a Haake F3 thermostat to maintain the temperature at 13.0 ± 0.1°C in a Rayonet chamber with 8 W lamps whose output was centered at 350 nm. After 2 h, the solvent was removed under vacuum and the residual oil was analyzed *via* ^{1}H NMR. Compound **3** showed peaks at δ 1.84 (3 H, s, CH_3), 5.49 (2 H, dd, $J_1 = 7.9$ Hz, $J_2 = 1.0$ Hz, $C{=}CH_2$), and 7.0 - 7.5 ppm (10 H, m, aromatic protons). However, in the reaction mixture we found some other signals that can not be explained with the formation of compound **4** -**7**. We observed in ^{1}H NMR spectra peaks at δ 2.42 (1.5 H, s), 2.58 (1.5 H, s), 5.97 (0.5 H, s), and 6.18 ppm (0.5 H, s), clearly in agreement with a 1:1 mixture of two products. GC-MS of these mixture showed peaks at *m/z* 223 (12%), 222 (70), 221 (4), 120 (22), 106 (7), 105 (91), 104 (21), 103 (100), 102 (15), 91 (7), 78 (29), 77 (68), 76 (7), 63 (6), and 51 (29). These data are in agreement with the formation of compound **8** as a 1:1 mixture of *E,Z* isomers. The observed ratio between **3** and **8** was 1.7:1.

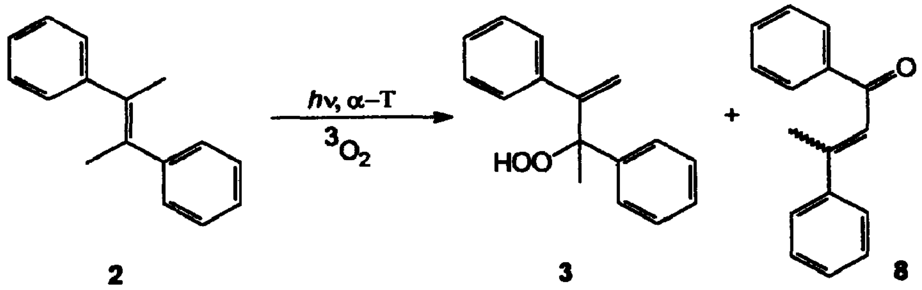
Scheme 1



Scheme 2



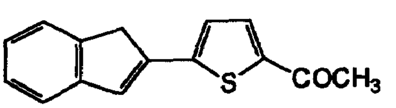
Scheme 3



In order to elucidate the origin of **8** we carried out the above described reaction using Rose bengal as sensitizer and as irradiating source a 400 W sodium lamp (Helios-Italquartz). In fact, the formation of about 20% superoxide ion *via* electron transfer from rose bengal to triplet oxygen was reported.[19] In this case ca. 5% of **8** was recovered in the reaction mixture. Then, compound **8** is formed *via* oxidation of dimethylstilbene with superoxide ion generated from electron transfer between the sensitizer and triplet oxygen. Probably, superoxide ion oxidizes a methyl group and the following phenyl migration gave **8**.

This is the first example of an oxidation reaction sensitized by α-T where there is evidence of a non-singlet oxygen oxidation.

Recently we have reported that indenylthiophene derivatives **9** and **10** are singlet oxygen sensitizers.[12] In singlet oxygen oxidation of 2,5-dimethylfuran we found that the rate of oxidation were in the ratio 1, 0.9, and 1.3 for **1**, **9**, and **10** respectively. On the other hand Φ_T for **9** and **10** was only 0.23 while Φ_T for α-T has been extimated to be 0.95.[20] Furthermore, photobiological experiments on these compounds showed that the expected reactivity order was obtained only with *Daphnia magna* while with erythrocytes, mosquito larvae, and fish (*P. promelas*) α-T is more reactive than **9** and **10**.[21]



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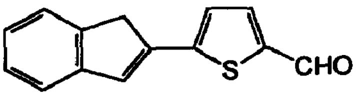

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Observation of superoxide ion formation offers an interesting way of interpreting these controversial data: i.e., if α-T can give both singlet oxygen and superoxide ion, the observed differences between Φ_T and reactivity order between **1** and **9** can be understood. On the other hand, the different photobioactivity could be related to different sensitivity of target organisms to superoxide ion.

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