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Production of reactive oxygen species assisted by new [60]fullerene photosensitizers

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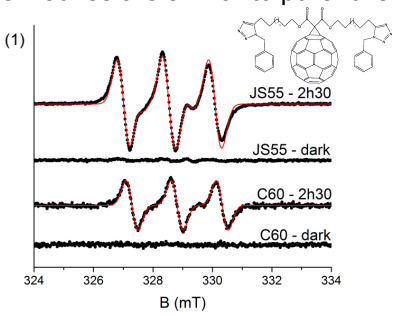
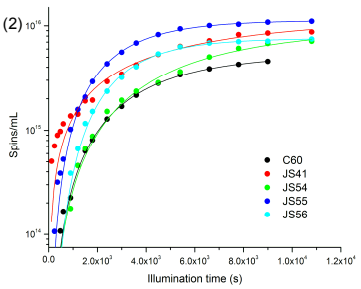
Abstract – The generation of free radicals assisted by fullerenes is of great interest for biological application. As part of this research, seven new C_{60} derivatives modified with tetrazole and oxadiazole units were synthesized and characterized. The photophysical properties of the new compounds were studied by EPR radical spin-trapping technique. The results show that reactive oxygen species (ROS) production can be induced by these C_{60} derivatives under UVA illumination, and suggest they may be used in topic photodynamic therapy (PDT) as photosensitizers.

The fullerene molecules have very interesting photophysical properties, which can be used in biological applications. In the presence of UV light, C_{60} is easily photoexcited, resulting in a short-lived singlet excited-state ($^1C_{60}$), which is readily converted into a long-lived triplet excited-state ($^3C_{60}$) via intersystem crossing [1]. In the presence of molecular oxygen, it may decay from $^3C_{60}$ to its ground state by undergoing one of two possible paths: transferring charge to O_2 molecules and generating superoxide O_2^- (mechanism type I) or transferring energy and producing singlet oxygen $^1O_2$ (mechanism type II). Both superoxide and singlet oxygen are reactive oxygen species (ROS). They are highly cytotoxic species, i.e. they are able to perform DNA cleavage and cellular membrane damage, which makes fullerenes very promising photosensitizers for photodynamic therapy (PDT) [2]. Structural modification of C_{60} may result in compounds with new and attractive properties. Therefore, in this study, we have prepared seven new fullerene derivatives containing either tetrazole or oxadiazole units to investigate and compare their efficiencies in ROS production. These hydrophobic compounds are potential photosensitizers and may be applicable in topic PDT with special pharmaceutical formulations. Furthermore, amphiphilic derivatives can also be obtained, such as tetrazolium salts or complexes with hydrophilic residues, making it possible to study their properties in polar solvents, water, or physiological media. The generation of ROS assisted by C_{60}, and seven new C_{60} derivatives under UVA illumination was studied by electron paramagnetic resonance (EPR) using the spin-trapping technique. The samples were toluene solutions with two compounds: the spin-trap PBN and the photosensitizer (fullerene derivative). In this work we show that new fullerenes modified with tetrazole and oxadiazole units may be prepared and fully characterized. We demonstrate also by EPR spin-trapping method that these derivatives present potentially useful properties, i.e. superoxide radicals are generated from the photoexcited fullerene derivatives under UVA light. For the tetrazole-modified fullerenes the superoxide is produced after conversion of singlet oxygen produced by mechanism type II [3]. The photochemical properties: efficiency, illumination curves and absolute amount of ROS produced per mol of photosensitizer, for all fullerenes derivatives are similar to pure fullerene and point to potentially promising biological applications.

(1)



(2)



(3)

	Number of Spins at saturation (mL^{-1})	Rate constant (s^{-1})
C60	$(5.3 \pm 0.3) \times 10^{15}$	$(3.0 \pm 0.5) \times 10^{-4}$
JS41	$(1.2 \pm 0.2) \times 10^{16}$	$(1.4 \pm 0.5) \times 10^{-4}$
JS54	$(1.0 \pm 0.1) \times 10^{16}$	$(2.0 \pm 0.5) \times 10^{-4}$
JS55	$(1.1 \pm 0.1) \times 10^{16}$	$(4.6 \pm 0.2) \times 10^{-4}$
JS56	$(7.6 \pm 0.2) \times 10^{15}$	$(5.0 \pm 0.4) \times 10^{-4}$

(1) EPR spectra of pure C_{60} and a derivative, before and after 2,5 hours of UVA illumination. (2) Free radical production of C_{60} and derivatives. (3) Table containing number of spin-adducts at saturation and rate constant for each compound.

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References

[1] Y. Yamakoshi, N. Umezawa, A. Ryu, K. Arakane, N. Miyata, Y. Goda, T. Masumizu, and T. Nagano, J. Am. Chem. Soc. 125 (2003) 12803-12809
[2] S. Bosi, T. Da Ros, G. Spalluto and M. Prato, European Journal of Medicinal Chemistry 38 (2003) 913-923
[3] L.J. dos Santos, R.B. Alves, R.P. de Freitas, J.F. Nierengarten, L.E.F. Magalhães, K.Krambrock and M.V.B. Pinheiro, J. Photochem. Photobiol. A: Chem. 200 (2008) 277-281