Highly fluorescent biologically active iminocoumarines with interesting spectroscopic properties

FKITMCMXIX

M. Cindrić[1)], N. Perin[1)], K. Starčević[2)], M. Maurić[2)], S. Liekens[3)] and M. Hranjec[1)]

[1)] Department of Organic Chemistry, Faculty of Chemical Engineering and Technology, Marulićev trg 20, HR-10000 Zagreb, Croatia; [2)] Department of Animal Husbandry, Faculty of Veterinary Medicine, University of Zagreb, Heinzelova 55, HR-10000 Zagreb, Croatia; [3)] Rega Institute, Department of Microbiology and Immunology, Herestraat 49, B-3000 Leuven, Belgium;

maleksic@fkit.hr

The coumarin derivatives have been one of the most widely studied classes of fluorescent dyes and probably one of the most frequently used fluorescent compounds. Fluorescent coumarin derivatives have been widely used in many applications from cell biology, medical analysis, lasers, sensors, to the advanced photophysical systems [1]. This work presents highly fluorescent iminocoumarine derivatives as a potential biologically active agents. Their molecular structure incorporate a push-pull functionality, the *N*,*N*-dialkylamino group at the 7-position is an electron donor, while an electron withdrawing group, such as benzimidazole, benzothiazole and imidazopyridine fragment at the 3-position, enhances the fluorescence efficiency. The spectroscopic properties of these compounds were evaluated in several polar and non-polar organic solvents. pH titrations were carried out to explore their potential as chemosensors and pH probes [2,3].

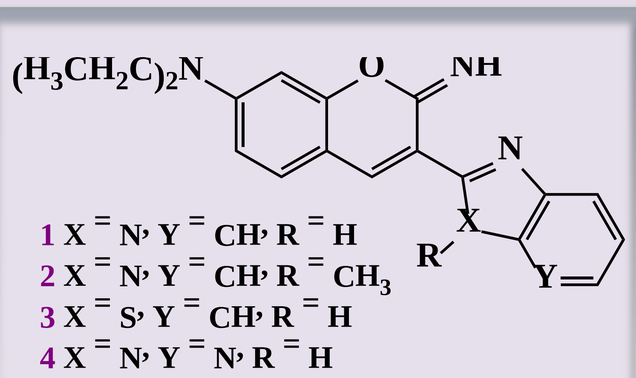

Figure 1. Highly fluorescent iminocoumarine derivatives.

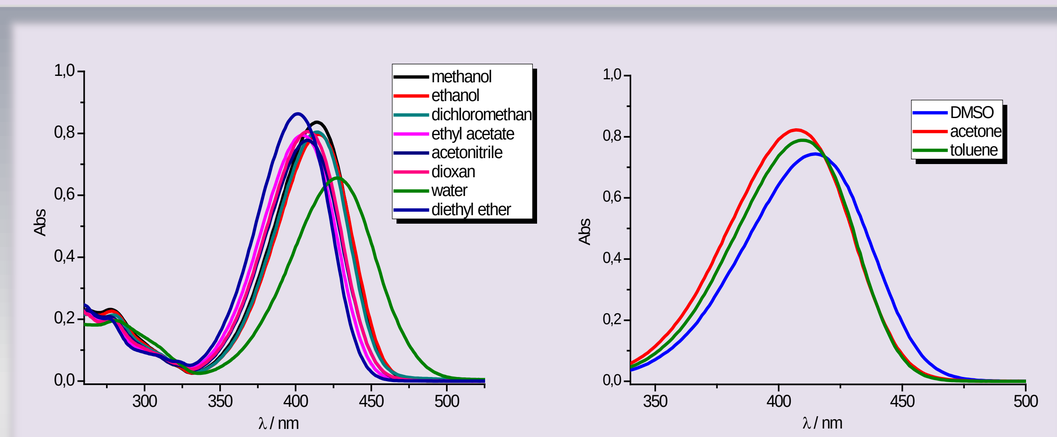

Figure 2. a, b) UV-Vis spectra of 2 (2×10^{-5} moldm^{-3}) in polar and non-polar organic solvents.

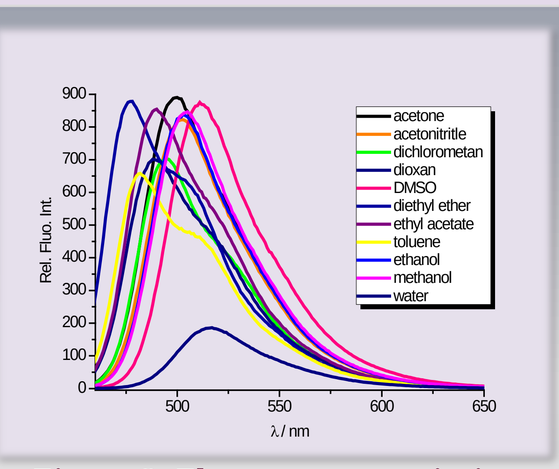

Figure 3. Fluorescence emission spectra of 3 (1×10^{-7} moldm^{-3}) in polar and non-polar organic solvents.

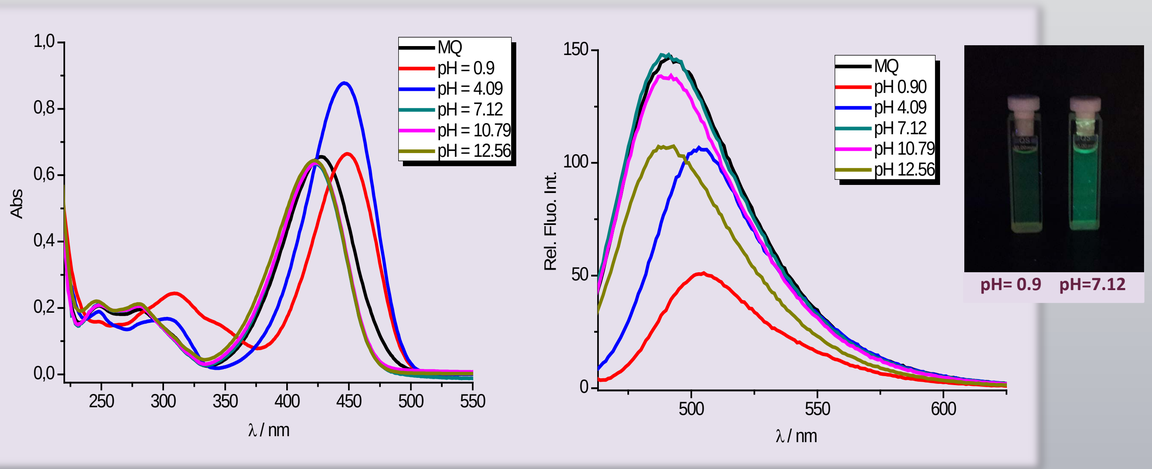

Figure 4. a) UV-Vis spectra of 2 (2×10^{-5} moldm^{-3}) at different pH values; b) Fluorescence emission spectra of 2 (1×10^{-7} moldm^{-3}) at different pH values

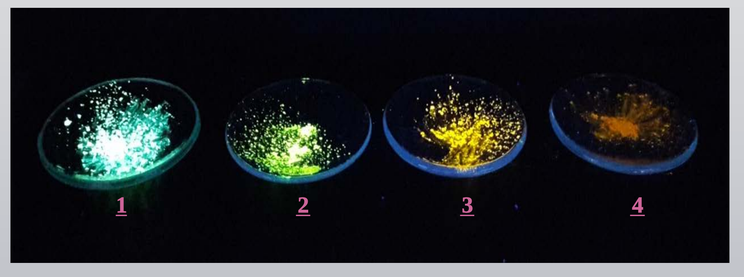

Table 1. Antiproliferative activity *in vitro*

Cpd	IC_{50}* (μM)		
	CEM	HeLa	HMEC-1
1	>100	>100	>100
2	0.059±0.018	0.19±0.00	0.25±0.00
3	>100	>100	>100
4	0.17±0.09	0.68±0.31	1.0±0.4

*50% inhibitory concentration.

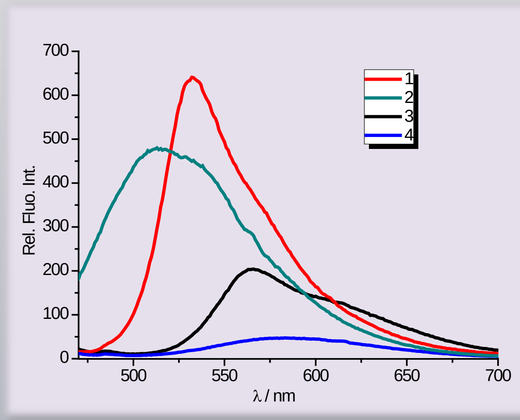

Figure 6. Fluorescence emission in the solid state of 1–4.

Antiproliferative activity *in vitro* of prepared compounds was tested against three human cancer cells, T-lymphocyte cells (CEM), cervix carcinoma cells (HeLa) and dermal microvascular endothelial cells (HMEC). Compounds 2 and 4 showed very strong antiproliferative activity in submicromolar range and they exerted selectivity towards CEM cells.

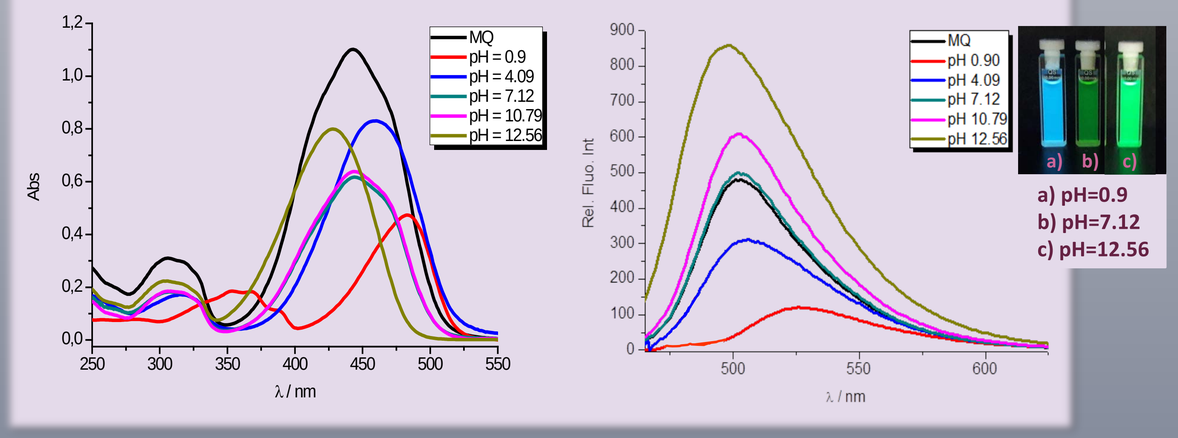

Figure 5. a) UV-Vis spectra of 4 (2×10^{-5} moldm^{-3}) at different pH values; b) Fluorescence emission spectra of 4 (1×10^{-7} moldm^{-3}) at different pH values

Table 2. Antioxidative activity *in vitro*

Cpd	ABTS/% 150 μM	FRAP mmolFe^{2+}/mmolc
1	11.1±0.3	18.9±0.40
2	3.±0.5	14.4±2.03
3	-	154.4±6.40
4	12.6±0.2	14.1±1.05
BHT	28.0±2.3	679.2±37.48

Antioxidative activity of prepared compounds was evaluated by *in vitro* ABTS and FRAP methods. Butylated hydroxytoluene (BHT) was used as a standard antioxidant. Compound 3 showed highest FRAP value, while compounds 1 ,2 and 4 showed lower antioxidative activity then BHT.

[1] S.B. Chemate, N. Sekar, *J. Fluoresc.* **2015**, *25*, 1615–1628.

[2] N. Perin, M. Hranjec, G. Pavlović, G. Karminski-Zamola, *Dyes Pigm.* **2011**, *91*, 79-88.

[3] M. Cindrić, I. Sović, I. Martin-Kleiner, M. Kralj, T. Mašek, M. Hranjec, K. Starčević, *Med. Chem. Res.*, **2017**, *26*, 2024-2037.

HRZZ Croatian Science Foundation

This work was funded by the Croatian Science Foundation (project HRZZ-5596).

CECP

February 4-8. 2018
Bad Hofgastein, Austria