Fluorescence studies on new potential antitumoral benzothienopyran-1-ones in solution and in lipid membranes

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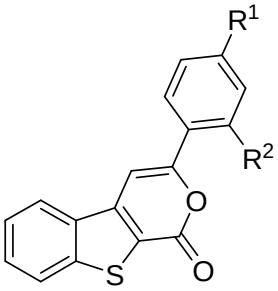
The compounds **1a-d** are novel potential antitumoral 3-(aryl)benzothieno[2,3-*c*]pyran-1-ones [1]. The fluorescence properties of these four compounds were studied in solution and in lipid aggregates of egg yolk phosphatidylcholine (Egg-PC), dioctadecyldimethylammonium bromide (DODAB) and dipalmitoyl phosphatidylcholine (DPPC). Compound **1c** exhibits the largest red shifts in emission with increasing solvent polarity (26 nm between cyclohexane and DMSO), together with significantly higher fluorescence quantum yields relative to the other compounds. The type and position of the substituents strongly influence the photophysical behavior of these molecules in solution.



1a R^1= F, R^2 = H
1b R^1= H, R^2 = F
1c R^1= OMe, R^2 = H
1d R^1= H, R^2 = OMe

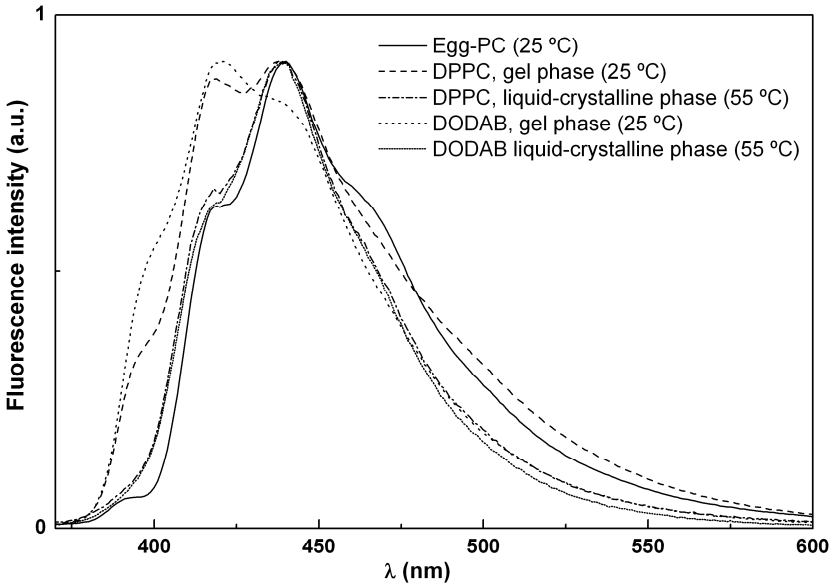


Figure 1 - Normalised fluorescence spectra of compound **1a** in lipid membranes of DPPC, Egg-PC and DODAB.

The antitumoral activity of compounds **1a-c** was evaluated in three representative human tumor cell lines, MCF-7 (breast adenocarcinoma), SF-268 (CNS cancer) and NCI-H460 (non-small cell lung cancer). Compound **1b** was shown to be the most potent against all the cell lines tested, presenting low GI_{50} (the lowest concentration causing 50% of the cell growth inhibition after a continuous exposure of 48 h) values (12-19 μM) [1].
Fluorescence anisotropy measurements of the compounds incorporated in vesicles of DPPC, Egg-PC and DODAB indicate that the four compounds have distinct behaviors in lipid membranes. While compound **1b** is deeply located inside the lipid bilayer, the behaviour of compounds **1a**, **1c** and **1d** point to the presence of two different locations in lipid aggregates (fig. 1), one corresponding to molecules located near the hydrocarbon tails and the other in a more hydrated and less viscous environment. The deeper penetration of compound **1b** in lipid membranes can play an important role on the promising antitumoral activity of this compound.

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References: [1] M.-J.R.P. Queiroz et al., *Eur. J. Med. Chem.* 44 (2009) 1893.