Addendum

L. V. Reis, J. P. C. Serrano, P. Almeida, P. F. Santos, *Synlett*, **2002**, 1617

New Synthetic Approach to Aminosquarylium Cyanine Dyes

The basic concept of methylation of a squarylium cyanine dye on one of the central bridge oxygens, by the action of a known methylating agent, is *not* novel in the light of the cited prior art: the only novelty that could be attributed to the above paper would lie in the specific methylating agent and conditions described therein.

The facile replacement of the so-formed methoxy function by a primary or secondary alkylamine is also *not* novel in the light of the cited prior art. Furthermore, the use of this basic reaction as a inventive means to introduce new functionality into a squarylium cyanine dye (such as reactive groups for covalent attachment) is clearly described and demonstrated in EP 0898596.

We accept that patent literature may not be as widely read by the scientific community as scientific journals; nevertheless they are still means of disclosing scientific progress. We would also like to stress that no disrespect to Professor Santos is intended via this action.

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We appreciate the understanding that indeed it is an increasingly difficult task to search thoroughly existing published literature. In fact we have used an accurate structure search in STN International when preparing the compounds in the beginning of our research project, which clearly showed that the targeted aminosquarylium cyanine dyes derived from benzothiazole, benzoselenazole and quinoline were not reported. In view of this information, we have written ‘to the best of our knowledge, the few hitherto reported examples of aminosquarylium cyanine dyes were synthesized by condensation of monoalkylaminosquarates and 1-ethyl-2,3,3-trimethylindolenium iodide in very low yield’ in a paper from Prof. Sung Hoon Kim (Dyes & Pigments, 1998). Also, we have noticed in the US 535 4873 from Polaroid (1994), listed in our previous literature searches, a method for assembling non-cyanine aminosquarylium dyes using dimethylsulfate. However, this synthetic approach had not been to our knowledge applied to aminosquarylium dyes of the cyanine type. That was the reason we have given to our paper the title ‘New Synthetic Approach to Aminosquarylium Cyanine Dyes’.

It seems that the main document we would need to access was unfortunately not listed in all our searches: EP 0898596 (1997) and WO 97/40104 (1997) from Amersham Biosciences. We believe the reason was related with the lack of systematic nomenclature for this class of compounds, namely because we followed the most common terms ‘*squarylium*’ and ‘*squaraine*’ as described in a review from Dr. Kock-Yee Law *(Chem. Rev.*).

In view of the cited patents we accept that the information therein raises, in the ambit of intellectual property, the novelty of your synthetic approach. However, we would like to emphasise that the process we have developed for the synthesis of several novel aminosquarylium cyanine dyes uses a methylating agent and conditions different from those previously described. Whether this, in the scope of a scientific journal, when published in a paper comprehending a complete description of the experimental conditions, product yields and physical properties might be considered as a criterion for novelty is certainly not consensual.

In the present time we truly apologize for any inconvenience that the paper might have caused. We hope that there is enough evidence that we were in good faith publishing this step of a broader project concerning the synthesis and evaluation of squarylium cyanine dyes as potential sensitizers for Photodynamic Therapy.

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