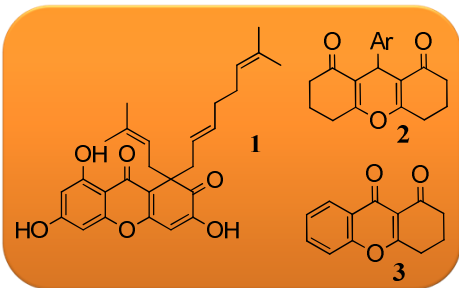


Introduction:



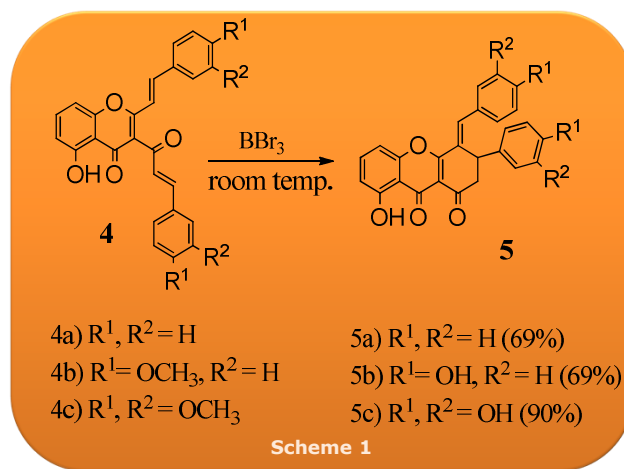
Xanthenediones are scarce in Nature, so far four xanthene-2,9-dione derivatives were found (**1**, as an example),^[1] and one of them showed moderate activity against two strains of *Plasmodium falciparum*.^[2] Synthetic xanthenediones are more frequent, however, the common type of substitution pattern is the 9-aryl-3,4,5,6,7,9-hexahydro-1H-xanthene-1,8(2H)-dione (**2**).^[3] Xanthene-1,9(2H)-diones were not found in Nature and synthetic derivatives seems to be also scarce, only 3,4-dihydro-1H-xanthene-1,9(2H)-dione (**3**) was described.^[4] The well-known biological properties of xanthenes, such as antitumor, anti-inflammatory, antioxidant and anticoagulant/antiplatelet activities,^[5] point out for the possibility of xanthenodione derivatives also present important biological activities.

Synthesis:

- Due to the continuing interest of our group in the synthesis of novel oxygen heterocycles we have recently developed a unique synthetic route towards new xanthenodiones **5** (scheme 1).^[6] The application of this methodology in the cyclization of chromone derivatives **4b,c** bearing methoxyl groups not only promote the cyclization to xanthenedione derivatives but also promote the demethylation leading to the 4-(benzylidene)-8-hydroxy-3-phenyl-3,4-dihydro-1H-xanthene-1,9(2H)-diones **5b,c**.
- This interesting result prompted us to investigate the antioxidant potential of 4-(benzylidene)-8-hydroxy-3-phenyl-3,4-dihydro-1H-xanthene-1,9(2H)-diones **5a-c**.

Antioxidant Activity:

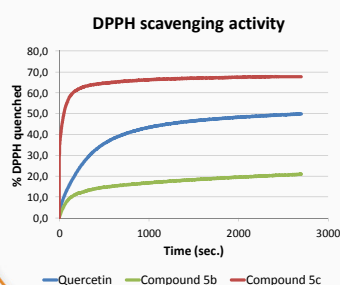
- There are several diseases and symptoms directly related to oxidative stress, such as: atherosclerosis, Alzheimer, cancer, aging process and central nervous system degeneration.^[7] Antioxidant compounds can become important in preventing and/or treat these diseases. In order to evaluate antioxidant activity of xanthenodiones **5a-c**, their ability to scavenge the DPPH radical and to reduce iron (III) was evaluated.



Scheme 1

DPPH radical scavenging activity

- The DPPH method is an assay widely used;^[8]
- Quercetin was used as positive control;
- Our results showed that xanthenodione **5c** can be considered a powerful antioxidant. Probably its high radical scavenge capacity is due to two the catechol moieties present.

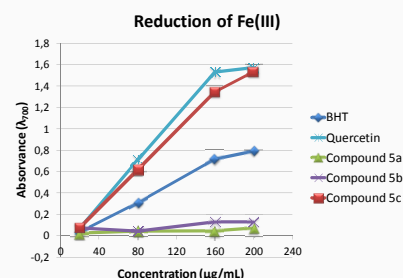


Compound	EC_{50} (mol.dm ⁻³)
Quercetin	$5.97E-6 \pm 1.1E-7$
5b	$> 552E-4^*$
5c	$3.79E-6 \pm 6E-8$

*The EC_{50} of compound **5b** was not obtained due to low solubility in ethanol and at its maximum concentration the remain DPPH was 64%.

Reduction of iron III

- Reducing power is the manifestation of electron donating capacity which is associated with antioxidant activity;^[8]
- Xanthenodiones **5a-c** were tested using potassium ferricyanide reduction method;
- BHT and quercetin were used as reference due to their well-known antioxidant properties;
- All compounds were tested at four concentrations, and the reducing ability increase with concentration;
- Once again xanthenodione **5c** showed high activity, its reduction capacity is higher than BHT and similar to quercetin;
- Another evidence for the importance of the catechol moiety.



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Acknowledgments

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