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# Book of Abstracts

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E-20

# SYNTHESIS AND EVALUATION OF THE ANTIRADICALAR ACTIVITY OF POLYHYDROXY-2-STYRYLCHROMONES

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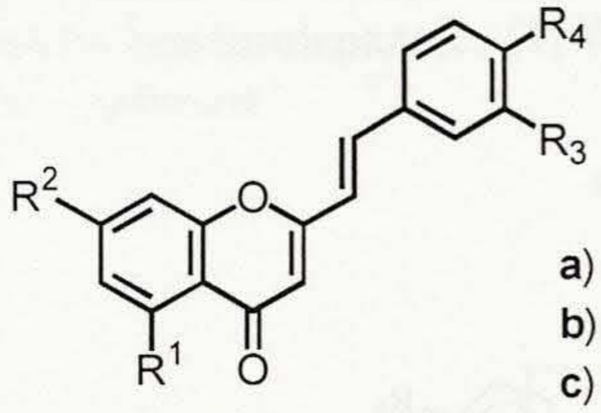
Recent studies have ascribed the cause of several acute and degenerative diseases, including cell aging and carcinogenesis, to the production of free radicals.[1] As a consequence of this, a large number of investigations have been carried out in order to find new, safe and potent antioxidants and to elucidate the corresponding mechanism of action. The evaluation of antioxidant *vs.* antiradicalar activity of phenolic compounds, either of natural or synthetic origin, is nowadays an important area of research in the field of food and medicinal sciences.[1]

We report here the synthesis of several new polyhydroxy-2-styrylchromones **1** starting from 2'-hydroxyacetophenones and cinnamic acid derivatives. The diversity of the substitution pattern, which includes the presence of hydroxyl substituents in 5,7,3' and 4' positions of their skeleton and also a 2,3-double bond was taken into consideration. The evaluation of the antiradicalar efficacy of all synthesised 2-styrylchromones **1** was also carried out by a non-enzymatic method and was performed by the DPPH radical method.[1]

The experimental procedures for the synthesis, for the evaluation of the antiradicalar activity and for the structural characterisation of all synthesised compounds will be presented and discussed.




**1**

**a**) $R^1$ = OH; $R^2$, $R^3$, $R^4$ = H
**b**) $R^1$ , $R^4$ = OH; $R^2$, $R^3$ = H
**c**) $R^1$ , $R^3$ , $R^4$ = OH; $R^2$ = H
**d**) $R^2$ = OH; $R^1$, $R^3$, $R^4$ = H
**e**) $R^2$ , $R^4$ = OH; $R^1$, $R^3$ = H
**f**) $R^2$ , $R^3$ , $R^4$ = OH; $R^1$ = H
**g**) $R^1$ = $R^2$ = OH; $R^3$, $R^4$ = H
**h**) $R^1$ , $R^2$, $R^4$ = OH; $R^3$ = H
**i**) $R^1$ , $R^2$, $R^3$ , $R^4$ = OH

**Acknowledgements**

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1. a) *Handbook of Antioxidants*, Ed. E. Cadenas and L. Packer, Marcel Dekker, New York, **1996**. b) C. A. Rice-Evans, N. J. Miller, G. Paganga, *Free Radic. Biol. Med.*, **1996**, *20*, 933. c) C. A. Rice-Evans and L. Packer, *in* Flavonoids in Health and Disease, Marcel Dekker, New York, **1997**.

# Synthesis and evaluation of the antiradicalar activity of polyhydroxy-2-styrylchromones

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## INTRODUCTION

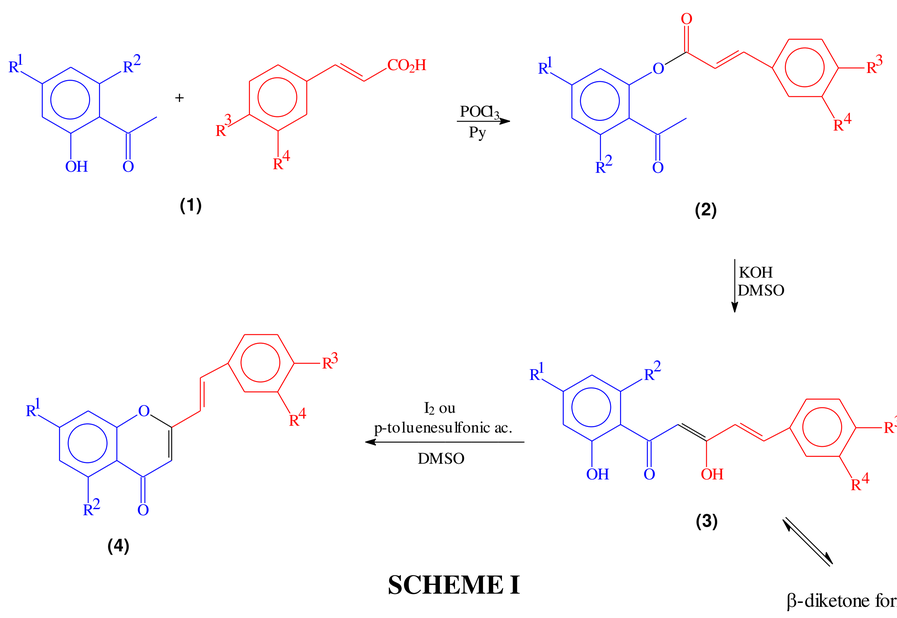
Recent studies have ascribed the cause of several acute and degenerative diseases to the prodution of free radicals.[1] As a consequence of this, a large number of investigations have been carried out in order to find new, safe and potent antioxidants.

The evaluation of antioxidant vs. antiradicalar activity of phenolic compounds, either of natural or synthetic origin, is nowadays an important area of research in the field of food and medicinal sciences.[1]

We report here the synthesis of several new polyhydroxy-2-styrylchromones **(5a-i)** starting from 2'-hydroxyacetophenones and cinnamic acid derivatives.

The evaluation of the antiradicalar efficacy of all synthesised 2-styrylchromones **(5a-i)** was carried out by a non enzimatic method and was performed by the DPPH radical method.[2]

## *Synthesis of benzyloxy-2-styrylchromones*




**(1) - (4)**

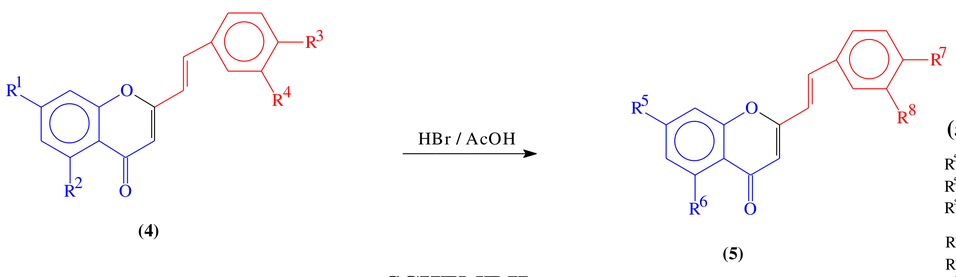
$R^1$ = OBn; $R^2$ = $R^3$ = $R^4$ = H (a)
$R^1$ = OBn; $R^2$ = H; $R^3$ = OBn; $R^4$ = H (b)
$R^1$ = OBn; $R^2$ = H; $R^3$ = $R^4$ = OBn (c)

$R^1$ = H; $R^2$ = OBn; $R^3$ = $R^4$ = H (d)
$R^1$ = H; $R^2$ = $R^3$ = OBn; $R^4$ = H (e)
$R^1$ = H; $R^2$ = $R^3$ = $R^4$ = OBn (f)

$R^1$ = $R^2$ = OBn; $R^3$ = $R^4$ = H (g)
$R^1$ = $R^2$ = $R^3$ = OBn; $R^4$ = H (h)
$R^1$ = $R^2$ = $R^3$ = $R^4$ = OBn (i)

**SCHEME I**

## *Debenzylation of benzyloxy-2-styrylchromones*




**(5)**

$R^5$ = OH; $R^6$ = $R^7$ = $R^8$ = H (a)
$R^5$ = OH; $R^6$ = H; $R^7$ = OH; $R^8$ = H (b)
$R^5$ = OH; $R^6$ = H; $R^7$ = $R^8$ = OH (c)

$R^5$ = H; $R^6$ = OH; $R^7$ = $R^8$ = H (d)
$R^5$ = H; $R^6$ = $R^7$ = OH; $R^8$ = H (e)
$R^5$ = H; $R^6$ = $R^7$ = $R^8$ = OH (f)

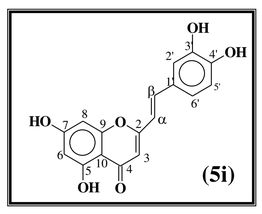
$R^5$ = $R^6$ = OH; $R^7$ = $R^8$ = H (g)
$R^5$ = $R^6$ = $R^7$ = OH; $R^8$ = H (h)
$R^5$ = $R^6$ = $R^7$ = $R^8$ = OH (i)

**SCHEME II**

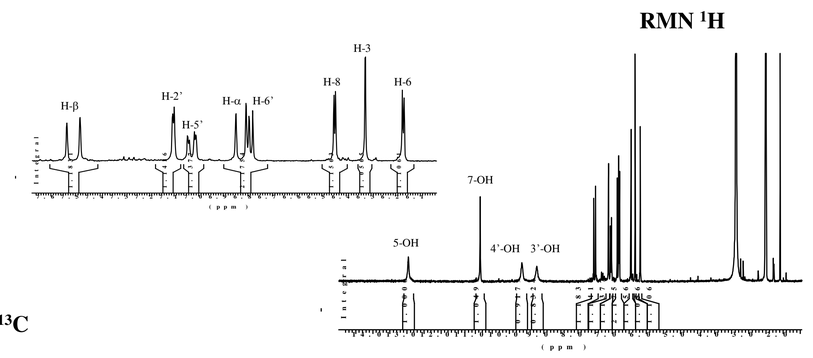
| Compounds | Yield (%) |
|---|---|
| **4(a)** | 93 |
| **4(b)** | 50 |
| **4(c)** | 37 |
| **4(d)** | 95 |
| **4(e)** | 96 |
| **4(f)** | 56 |
| **4(g)** | 84 |
| **4(h)** | 98 |
| **4(i)** | 50 |

| Compounds | Yield (%) |
|---|---|
| **5(a)** | 58 |
| **5(b)** | 51 |
| **5(c)** | 48 |
| **5(d)** | 86 |
| **5(e)** | 63 |
| **5(f)** | 50 |
| **5(g)** | 80 |
| **5(h)** | 55 |
| **5(i)** | 27 |

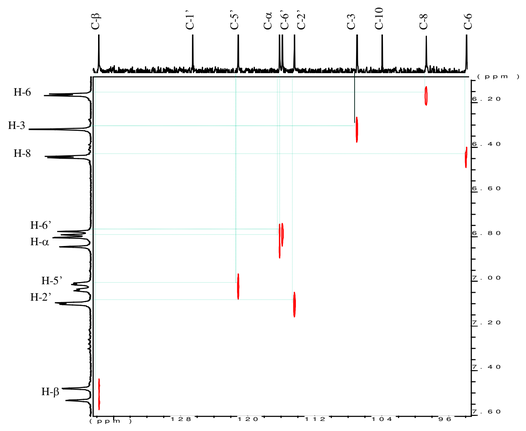
## *Spectroscopic NMR characterisation*



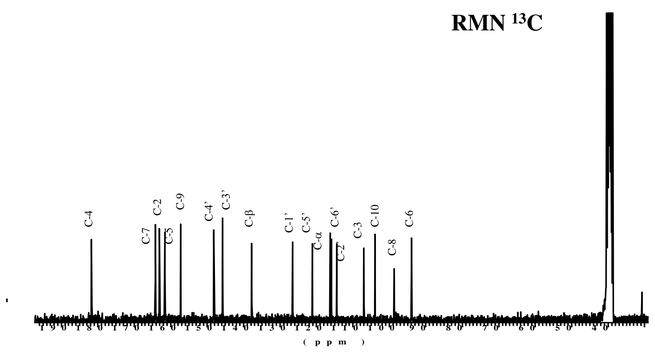

**RMN $^1$H**




**HETCOR $^1$H / $^{13}$C**



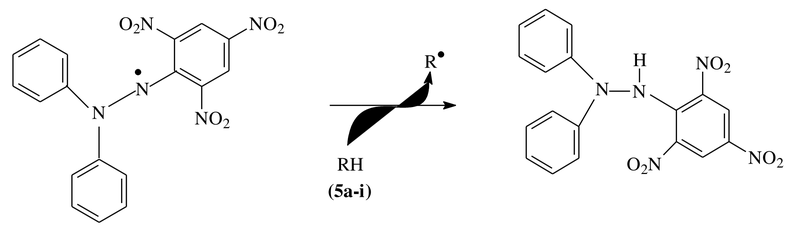

**RMN $^{13}$C**




## EVALUATION OF THE ANTIRADICALAR ACTIVITY

### *General procedure*

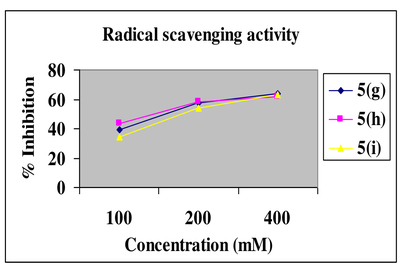
The free radical scavenging activity of the tested compounds were measured using DPPH radical method. The experimental procedure was adapted from Ohnishi et al..[2] The reaction mixture containing a total volume of 2,5 ml: 2 ml of 0,1 mM DPPH$^\bullet$ (in 10% DMSO and 90% EtOH) and 0,5 ml of the test compound (in 10% DMSO and 90% EtOH). The reduction of DPPH$^\bullet$ was followed by monotoring the decrease of absorbance at 517 nm for 20 minutes. The scavenging activity was measured as the decrease of the absorvance of the DPPH$^\bullet$ expressed as a % of the absorbance of a control solution without test substances. The mean value was obtained from triplicate experiments.




DPPH$^\bullet$ DPPH-H

### *Results and discussion*

| Compounds | %Inhibition mol DPPH$^\bullet$/mol antioxidant = 0,5 |
|---|---|
| **5(a)** | 1,4 |
| **5(b)** | 0,6 |
| **5(c)** | 4,2 |
| **5(d)** | 6,6 |
| **5(e)** | 5,2 |
| **5(f)** | 5,3 |
| **5(g)** | 57,5 |
| **5(h)** | 57,9 |
| **5(i)** | 54,2 |




➢ The more rapidly the absorbance decreases, the more potent the antioxidant activity of the compound in terms of hidrogen donating ability.

➢ Almost no decrease in absorbance occurred with the addition of **5(a)** or **5(b)** while the compounds **5(c)-(f)** showed only a slight decrease. However, the presence of the 3',4'-dihydroxy substituents on the B ring of 2-styrylchromones **[5(g)-(i)]** demonstrated the highest inhibition efficiency.

➢ DPPH radical scavenging activities of these compounds increased dose-dependently of the concentration. The more active compounds **[5(g)-(i)]** were tested at concentrations 100, 200 and 400 mM and showed an increase in scavenging activity.

## References

1. **a)** Handbook of Antioxidants, Ed. E. Cadenas and L. Packer, Marcel Dekker, New York, **1996**.
   **b)** C. A.Rice-Evans, N. J. Miller, G. Paganga, Free Radic.Biol. Med., **1996**, 20, 933.
   **c)** C. A. Rice-Evans and L. Packer, in Flavonoids in Health and Disease, Marcel Dekker, New York, **1997**.
2. M. Ohnishi, H. Morishita, H. Iwahshi, S. Toda, Y. Shirataki, M. Kimura and R. Kido, Phytochemistry, **1994**, 36, 579.

## Acknowledgements

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