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Coumarin Derivatives as Potential Antiradical Agents

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I. INTRODUCTION

Coumarin derivatives are well known anticoagulants, often demonstrate antiproliferative and anti-HIV effects, but 4-hydroxycoumarins [1, 2] and derivatives of coumarin-3-carboxylic acid [3] are known as antioxidants.

II. RESULTS AND DISCUSSION

In order to evaluate structure-antiradical activity relationships we synthesized a range of coumarin-3-carboxylic acids **1** and their *N*-arylamides, 4-hydroxycoumarins **2** (Y=O) and 4-hydroxy-2(1*H*)-quinolinones **2** (Y=NH).

Compounds **1** were obtained by Knoevenagel condensation of Meldrum's acid (**3**) with corresponding *o*-hydroxybenzaldehydes **4**. Derivatives of coumarin-3-carboxylic acid **1** were converted to acylchlorides and treated with anilines **5** – this provided amides **6**. Due to the fact that hydroxycinnamoylanilines are well known antioxidants, we were interested in synthesis of 2-hydroxycinnamanilides **7**, which could be obtained by hydrolysis of lactone ring of *N*-(3-coumarinoyl)-anilines **6**. While hydrolysis of carboxylic acid **1** (R=H) in the presence of piperidine proceeded with decarboxylation providing coumarin and ring opening product – *o*-coumaric acid, anilide **6** (R=H) at such conditions gave amide hydrolysis product - compound **7**.

Synthesis of 4-hydroxycoumarins **2** (Y=O) and 4-hydroxy-2(1*H*)-quinolinones **2** (Y=NH) we realized by intramolecular acylation of malonic acid monoarylesters **8** (Y=O) and *N*-arylmalonic acids **8** (Y=NH) in the presence of Eaton's

reagent; the derivatives of malonic acid **8** were obtained from Meldrum's acid (**3**) in reactions with corresponding phenols **9** (Y=O) or anilines **9** (Y=NH).

4-Hydroxy-*bis*-coumarins are strong radical scavengers and chain-breaking antioxidants [2] – this stimulated us to synthesize a few new *bis*-coumarins **10** by reaction of 4-hydroxycoumarins **2** (Y=O) with aromatic aldehydes **11**.

III. CONCLUSIONS

All synthesized compounds were tested for their antiradical activity against DPPH (diphenyl picryl hidrazyl). A few compounds demonstrated good antiradical activity, even 5 times higher than widely used antioxidant butylated hydroxytoluene.

IV. REFERENCES

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