Synthesis and characterization of psoralen analogues based on carbazoles

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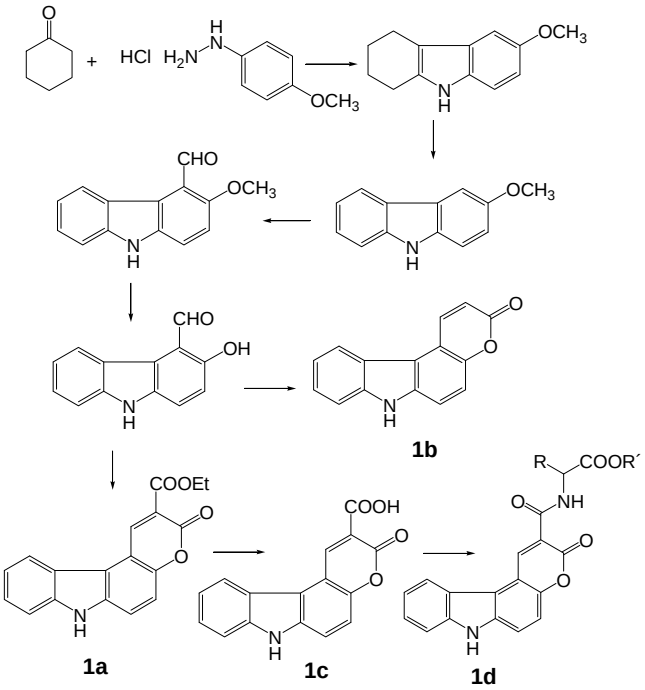
Introduction

Psoralens are plant natural products. They are coumarin derivatives. Their basic characteristic is a furanic ring fused to the coumarin basic structure. They are often photosensitizing drugs, and widely used for the treatment of various skin diseases characterized by hyperproliferative conditions, some infections connected to AIDS and blood decontamination.[1] It was also reported that they can be used in cancer (cutaneous malignant melanoma)[2] and T cell lymphoma[3] treatment as well as in the prevention of rejection in organ transplants,[3] in the treatment of autoimmune diseases[1] and viral diseases such as HIV-1.

Carbazoles constitute an important class of heterocycles that are known for their extensive potential applications in the field of chemistry (photoelectrical materials, dyes, supramolecular recognition etc.) and medicinal chemistry (antitumor, antimicrobial, antihistaminic, anti-oxidative, anti-inflammatory, psychotropic agents etc.).[4] Our group has been involved in the synthesis of psoralen analogues based on dibenzofuran[5], on carbazole and xantone and found that some compounds showed *in vitro* antitumoral activity (MCF-7, NCI-H460, SF-268).[6,7] Here we report the synthesis of new psoralen analogues based on carbazoles.

Results and Discussion

The synthesis of pyrano[2,3-*c*]carbazol-3(7*H*)-one **1** was achieved following scheme 1. For compound **1a**, 3-hydroxycarbazole was obtained by Fischer type synthesis, followed by oxidation. Its formylation (Vilsmeier-Haack) gave an orthoformylhydroxy carbazole which was condensed with diethyl malonate to build the pyranone ring. For the synthesis of compound **1b** (R = H) the method of Harayama and Ishii was used, where the cinnamate was obtained by the Wittig reaction, followed by ring closure. Basic hydrolysis of **1a** gave compound **1c** and coupling to aminoacids gave **1d**. The products were characterized by elemental analysis, melting point, ^{1}H and ^{13}C NMR. The yields and reaction conditions for the seven steps will be presented, as well as details of characterization.



Scheme 1. Synthesis of pyrano[2,3-*c*]carbazol-3(7*H*)-one, **1**

Conclusions

Novel psoralen analogues based on carbazoles were synthesized and characterized.

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