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Synthesis and Reactions of 5-Hydroxy-pyrido[3,2,1-jk]carbazol-4,6-diones

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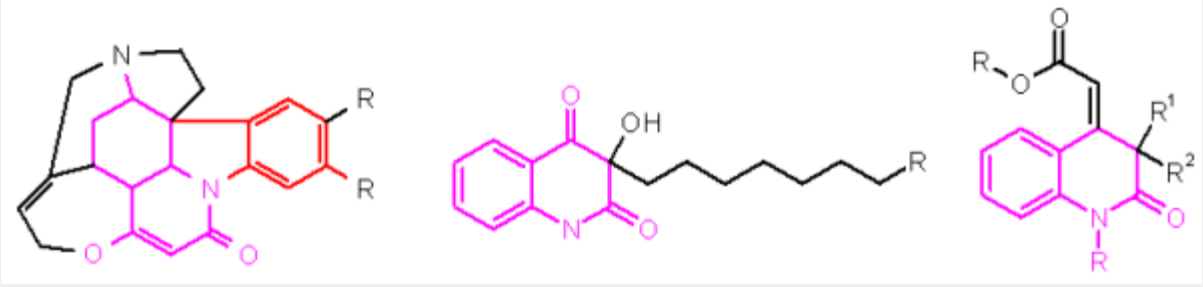
Contents:

Abstract

Oxidative hydroxylation of pyrido[3,2,1-jk]carbazol-6-ones by hydrogen peroxide, peroxy carboxylic acids or nitric acid leads to 5-hydroxypyrido[3,2,1-jk]carbazole-4,6-diones, which give in alkaline solution ring contraction to oxindoles, dioxindoles and ring opening reactions to carbazolyl-hydroxyphenylpropanones depending on the reaction conditions and substituents at position 5.
Wittig olefination of 5-hydroxypyrido[3,2,1-jk]carbazole-4,6-diones gives [2-(3-alkyl-3-hydroxy-2-oxo-1,2,3,4-tetrahydro-quinolinylidene)]-acetates.

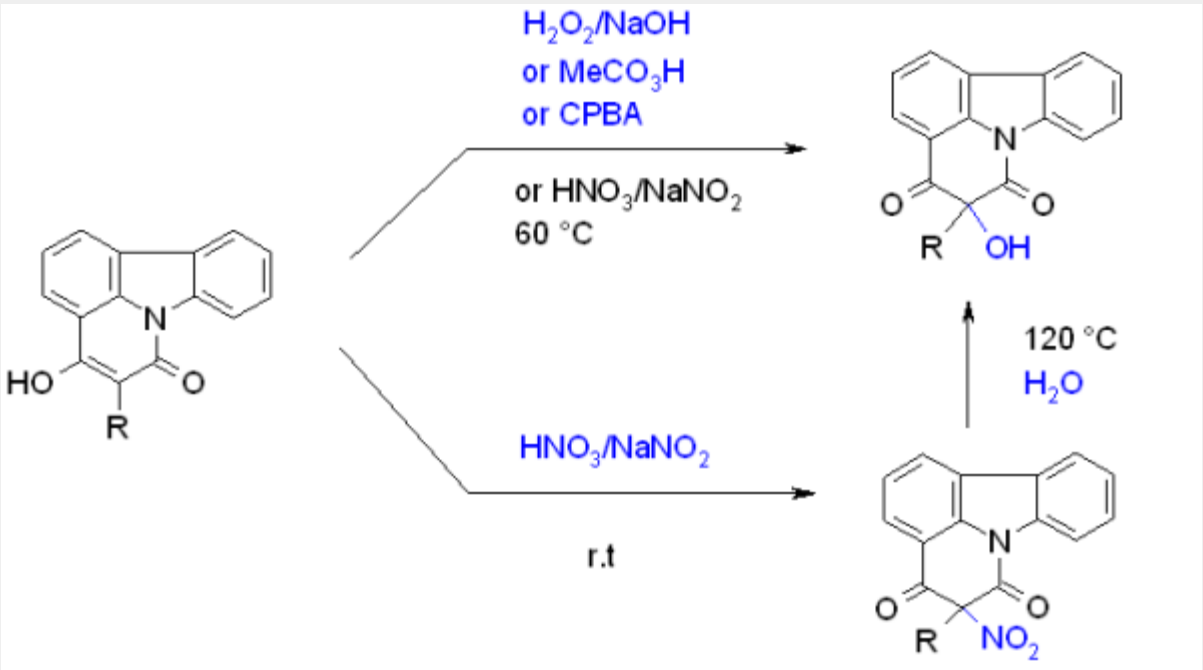
Introduction

Pyrido[3,2,1-jk]carbazol-6-one is part of the heterocyclic skeleton of many natural products (e. g. strychnos alkaloids such as



strychninolones and brucinolones, picrasidin Q and olivacin alkaloids [1]). It possesses the biological interesting combination of an **indole structure** and of a **2-quinolone**. Introduction of suitable substituents into the quinolone moiety should lead to interesting structures known as antibiotic bacterial contents (e.g. by **hydroxylation** [2]) or by **Wittig or Grignard reaction** to potential antiviral structures [3]).

Synthesis of 5-Hydroxy-pyrido[3,2,1-jk]carbazol-4,6-diones

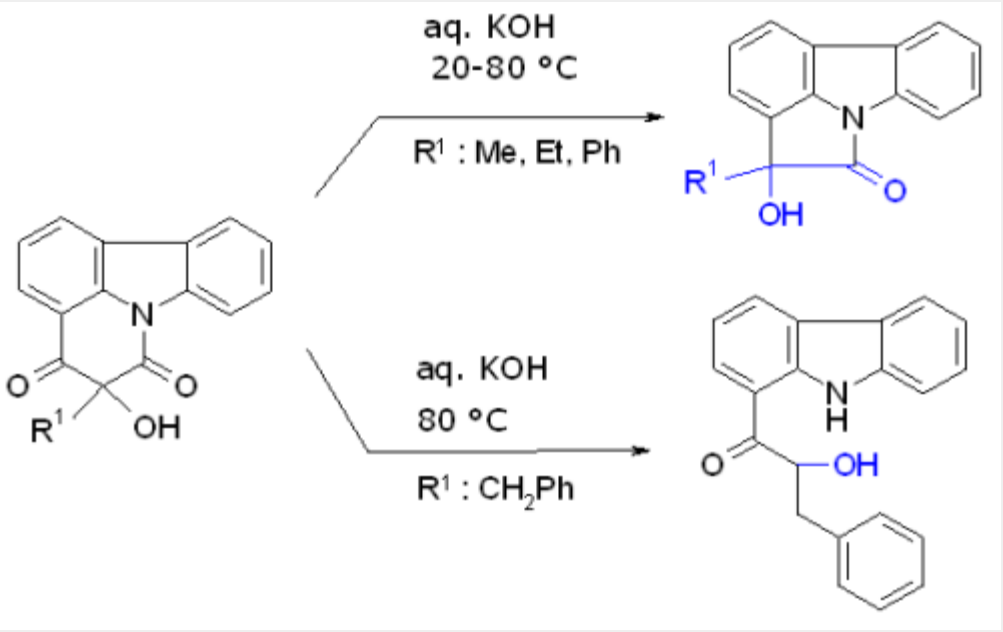


4-Hydroxypyrido[3,2,1-jk]carbazol-6-ones [4] were found to react in a number of oxidation processes to 5-alkyl/aryl-5-hydroxypyrido[3,2,1-jk]carbazol-4,6-diones. Oxidation in alkaline hydrogenperoxide solution is one of the easiest ways, but also reaction with peroxy carboxylic acids such as peroxy acetic acid or m-chloro-peroxybenzoic acid gave good yields.

A suprising pathway was found when we synthesized 5-nitro-pyrido[3,2,1-jk]carbazol-4,6-diones: At low temperatures the desired nitro compound was formed, but at elevated

temperatures the nitro group was exchanged against the hydroxy group. The formed nitro compound was shown also to react slowly on storage to the hydroxy compound.

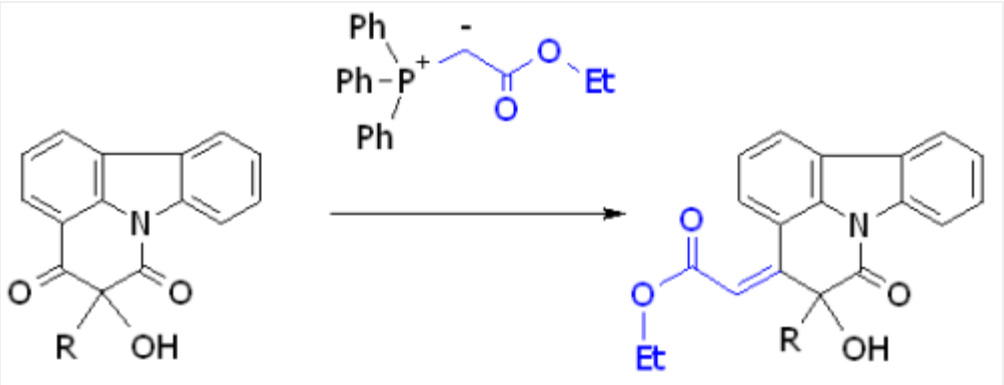
Ringcontraction and Ringopening Reactions of 5-Hydroxy-pyrido[3,2,1-jk]carbazol-4,6-diones



Mass spectra of 5-hydroxypyrido[3,2,1-jk]carbazol-4,6-diones gave with the with APCI (chemical ionization) method mass peaks of M - 28, which can be explained by the elimination of CO and ring contraction. The synthetic application of these findings gave surprising results: 5-Hydroxy-pyrido[3,2,1-jk]carbazol-4,6-diones react in alkaline solutions either by ring contraction or ringopening reactions. The methyl derivative (R^1=Me) gave already at room temperature in aqueous sodium hydroxide a ring contraction by cleavage of CO, and the oxindole derivative, 4-hydroxy-4-methylpyrrolo[3,2,1-jk]carbazol-5(4H)-one, was formed. At 80 °C, suprisingly, 4,4-dihydroxypyrrolo[3,2,1-jk]carbazol-5(4H)-one (R^1=OH) was formed by further exchange of the methyl group.
Ethyl and phenyl derivatives did not react at room temperature, but at 80 °C the reaction to 4-substituted 4-hydroxy-pyrrolo[3,2,1-jk]carbazol-5(4H)-one took place in good yields. No dihydroxy derivative was obtained. The benzyl derivative, however, gave at these temperature 1-(9H-carbazol-1-yl)-2-hydroxy-3-phenylpropan-1-one by ring opening.

Wittig Reaction of 5-Hydroxy-pyrido[3,2,1-jk]carbazol-4,6-diones

The conversion of the 4-oxo group of pyridocarbazolediones should lead to structures, which are similar to those in the quinoline series showing interesting antiviral properties [3]. In



the literature only symmetrically C-5-substituted derivatives were synthesized by a Grignard reaction. Our investigation was directed to unsymmetrically C-5-substituted derivatives, which can be derived from 5-hydroxy-pyridocarbazolediones accessible by a Wittg reaction with (ethoxy-carbonylmethylene)-triphenylphosphorane.

Experimental

5-Nitropyrido[3,2,1-jk]carbazol-4,6-diones: To a mixture of 4-hydroxy-pyridocarbazolones and sodium nitrite in glacial acetic acid was dropped concentrated nitric acid and stirred at room temperature. The reaction mixture was poured into crushed ice/water.
5-Hydroxypyrido[3,2,1-jk]carbazol-4,6-diones: A) A solution of 4-hydroxy-pyridocarbazolones was stirred in acetic acid and peroxyacetic acid was added. The reaction temperature was reduced and the mixture stirred. After cooling, the reaction mixture was poured into crushed ice/water.
B) A solution of 4-hydroxy-pyridocarbazolones was stirred in aq. sodium hydroxide until it was dissolved completely. To the solution was dihydrogenphosphate added. The reaction mixture was heated and stirred intensively and then hydrogen peroxide was added, then the reaction mixture was stirred. A precipitate was formed; the reaction mixture was cooled , filtered by suction and washed with water.
4-Hydroxy-pyrrolo[3,2,1-jk]carbazol-5(4H)-ones: A solution of 5-Hydroxypyrido[3,2,1-jk]carbazol-4,6-diones and potassium hydroxide in toluene was stirred at room temperature, the toluene phase was separated and poured into dry potassium carbonate, then filtered and the solvent removed under vacuum. The residue was dissolved in acetone and then water was added. The precipitated solid was filtered by suction and separated by dry flash chromatography.
Ethyl[4-(5-alkyl-5-hydroxy-6-oxo-pyrido[3,2,1-jk]carbazolylidene)]-acetates: A solution of 5-hydroxypyrido[3,2,1-jk]carbazol-4,6-dione and ethyl-(triphenyl-phosphoranyliden)-acetate in xylene (30 ml) was heated under reflux. After evaporating the solvent in vacuo the residue was purified by column chromatography on alumina.

Acknowledgement

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