

SYNTHESIS OF SOME NEW SPIROPYRANS CONTAINING INDOLINE MOIETY

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Abstract : 3-dicyanomethylidene-2-oxoindolines **1a-c** reacted with different cyclic carbonyl compounds to afford new spiroheterocyclic derivatives **2a-c** to **5a-c** which are analogues of some reported biologically active spiropolycyclic compounds.

Introduction

Nitrils were used as starting materials to prepare a variety of condensed pyrans¹⁻⁵ for their medicinal importance.^{6,7} Pyrano derivatives have well known biological effect such as analgesic and anti-inflammatory activities.⁸ Spiro derivatives have anticonvulsants, antibacterial and anticancer activities.^{9,10} Spiroheterocycles were used as nitric oxide synthesis inhibitors.¹¹ Photochromism of indolinospirochromens containing condensed fragments in the indoline part of the molecule were achieved.¹² As continuation to our interest in this area¹³⁻²¹ encouraged us to suggest the synthesis of some new spiroheterocycles of pyrans containing indoline moiety.

Experimental

The time required for completion of each reaction was monitored by TLC. Melting points are uncorrected and were measured on Gallen Kamp apparatus.

The IR spectra were recorded on a Chimadz 470 IR spectrometer (KBr) ν cm⁻¹. The ¹H-NMR spectra were measured on Varian EM-200, 90 MHz spectrometer with TMS as internal standard. Mass spectra were determined on a Jeol-600 spectrometer. Elemental analyses were performed on an elemental analyses system GmbH varioel V_{2.3}.

Synthesis of 2-amino-3-cyano-5(H)-5-oxo-indano[b]pyran-4-spiro-3'-(N'-substituted-indoline-2'-ones) **2a-c**:

A mixture of indan-1,3-dione (0.01 mol) and/or **1a-c** (0.01 mol) in absolute ethanol (20 ml) in the presence of catalytic amount of triethyl amine (2 ml) was stirred at room temperature for 3hrs., or refluxed for 2hrs. Then the product was precipitated, collected by filtration, dried and recrystallized from glacial acetic acid.

Synthesis of 2-amino-3-cyano-5(H)-5-oxo-6,7,8-trihydrobenzo[*b*]pyran-4-spiro-3'-(N'-substitutedindoline-2'-ones) 3a-c:

A mixture of cyclohexan-1,3-dione (0.01 mol) and/or **1a-c** (0.01 mol) in absolute ethanol (20 ml) and catalytic amount of morpholine (0.5 ml) was stirred at room temperature for 2hrs. The product thus formed was collected by filtration, washed the precipitate several times by methylene chloride, dried and recrystallized from a proper solvent.

Synthesis of 5-amino-3-benzyl-6-cyano-2,2-diphenylpyrano[2,3-*d*]thiazolidine-7-spiro-3'-(N'-substitutedindoline-2'-ones) 4a-c:

A mixture of 3-benzyl-2,2-diphenylthiazolidin-4-one (0.01 mol) and/or **1a-c** (0.01 mol) in absolute ethanol (15 ml) and catalytic amount of triethyl amine (1 ml) was heated under reflux for 6hrs. Then the reaction mixture was cooled to room temperature, then the solvent was removed under reduced pressure, the formed product was collected by filtration, dried and recrystallized from a mixture of ethanol/water (2/1).

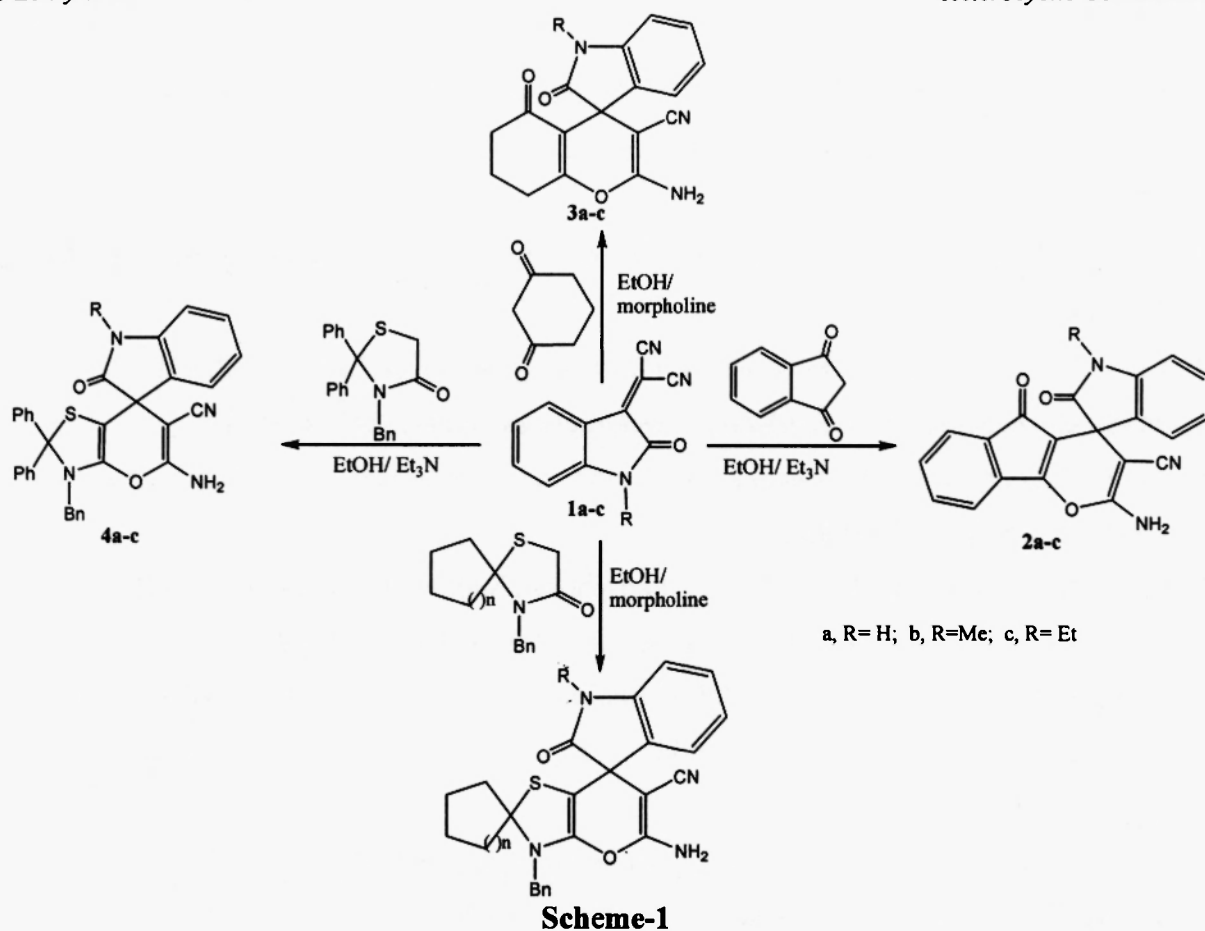
Synthesis of 5-amino-3-benzyl-6-cyanopyrano[2,3-*d*]thiazolidine-2-spiro(cycloalkane)-7-spiro-3'-(N'-substitutedindoline-2'-ones) 5a-c and/or 6a-c:

A mixture of 1-thia-4-benzylazaspiro[4.4]nonan-3-one (0.01 mol) or 1-thia-4-benzylazaspiro[4.5]decan-4-one (0.01 mol) and/or **1a-c** (0.01 mol) in absolute ethanol (20 ml) and catalytic amount of morpholine (1 ml) and DMF (0.5 ml) was stirred at room temperature for 12hrs. The solid product thus formed was collected by filtration, dried and recrystallized from a mixture of ethanol/acetic acid (2/1).

Results and Discussion

3-dicyanomethylidene-2-oxoindolines^{21,22} **1a-c** reacted with indan-1,3-dione, cyclohexan-1,3-dione, 3-benzyl-2,2-diphenylthiazolidin-4-one, 1-thia-4-benzylazaspiro[4.4]nonan-3-one, and/or 1-thia-4-benzylazaspiro[4.5]decan-4-one to afford 2-amino-3-cyano-5(H)-5-oxo-indano[*b*]pyran-4-spiro-3'-(N'-substituted-indoline-2'-ones) **2a-c**, 2-amino-3-cyano-5(H)-5-oxo-6,7,8-trihydrobenzo[*b*]pyran-4-spiro-3'-(N'-substitutedindoline-2'-ones) **3a-c**, 5-amino-3-benzyl-6-cyano-2,2-diphenylpyrano[2,3-*d*]thiazolidine-7-spiro-3'-(N'-substitutedindoline-2'-ones) **4a-c**, 5-amino-3-benzyl-6-cyanopyrano[2,3-*d*]thiazolidine-2-spiro(cycloalkane)-7-spiro-3'-(N'-substitutedindoline-2'-ones) **5a-c** and/or **6a-c** respectively (Scheme-1).

The structures of compounds **2a-c** to **6a-c** were established from their elemental analyses and spectral data.



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Received on September 13, 2007.