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NOVAL ROUTE THROUGH O–C BOND FORMATION FOR THE SYNTHESIS OF DIASTEREOMERIC 2, 4-DISUBSTITUTED PYRANO [2, 3-B] QUINOLINES FROM 3-FORMYL-2-QUINOLONES VIA INTRAMOLECULAR ELECTROPHILIC CYCLIZATION

Chemistry

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ABSTRACT

One-pot, One-step synthesis of 2, 4-disubstituted pyrano[2,3-b]quinolines from 3-formyl-2-quinolones is described from 3-formyl-2-quinolones via intramolecular electrophilic cyclization.

KEYWORDS

Electrophilic Cyclization, Pyranoquinoline, Cycloaddition Reactions

Many alkaloids such as flindersine, oricine and verprisine [1] which are from Rutaceae family [2], having Pyranoquinoline moiety. They posses broad range of bioactivity such as anti-allergic, psychotropic, anti-inflammatory and estrogenic activities [3]. and have wide applications as drugs, pharmaceuticals and agrochemicals. They have great attention in synthetic as well as medicinal field. Thus, to discover new method for the synthesis of this compound attracts much attention. Although various methods for their synthesis and their annulated analogues described in the literature [4].

The most common method for the synthesis of tri- and tetracyclic pyranoquinolines [5] are cycloaddition reactions.

Bhuyan et al. for the synthesis of tetracyclic pyranoquinolines have reported an intramolecular 1, 3-dipolar cycloaddition reaction 6. Using 1,3 dipoles such as nitrones, nitrile imines, nitrile oxides5, (m.s paper), polyphosphoric acid.2e, DDQ [6], and Prevost reaction [7].

Reaction next to cycloaddition reactions is acid-catalyzed cyclization for the syntheses of pyranoquinoline derivatives.

But all these conditions posses drawbacks such as expensive starting materials and poor yields of both starting materials and final products. Thus, to overcome these difficulties it is essential to develop new and efficient synthetic routes for the preparation of this class of compounds.

Precursor, 2-chloro-3-formylquinolines 1, [8] is synthesis via a Vilsmeier–Haack approach using acetanilide, DMF and $POCl_3$. We have used 3-cyanoquinoline and 3-methoxywuinoline derivative of quinoline for the synthesis of annulated carbocycles [9], sulfur, and nitrogen-containing heterocycles [10]. All these posses broad range of bioactivities.

Further, we have synthesis stereo controlled cis-disubstituted pyrano[2,3-b] in continuation of our research from 3-formyl-2-quinolones 2.

Precursor, 3-formyl-2-quinolones hasbeen synthesis via intramolecular electrophilic cyclization through O–C bond formation from 3-formyl-2-quinolines 1, (Scheme 2, Table 1).

Table 1: Synthesis of diastereomeric cis/trans-4-hydroxy-2-iodomethylpyrano [2,3-b]quinolines from 3-homoallyl-2-quinolones 3

Entry	Substrate	R	Time (h)	Product	Ratio (cis/trans)	Yield (%)
1	3a	H	4	4a/5a	77:23	88
2	3b	6Me	2.5	4b/5b	90:10	81
3	3c	7Me	4	4c/5c	79:21	84
4	3d	6MeO	3	4d/5d	84:16	83
5	3e	7MeO	3.5	4e/5e	100	85
6	3f	8Et	2.5	4f/5f	100	88

Different analogous have been synthesis from 2-chloro-3-formylquinolines.

via different routes[5,11].

3-Formyl-2-quinolones 2 were prepared by refluxing 2-chloro-3-formylquinolines 1 in aqueous acetic acid. Product is obtained in quantitative yield.

Further, allylation of 3-Formyl-2-quinolones using ally indium bromide and DMF, give 3-homoallyl-2-quinolones 3 at room temperature in excellent yields (89–94%). The structure of compound 3a analyze from spectral analysis.

Compound 3a when treated with I_2 and sodium bicarbonate using THF as solvent at room temperature provide a mixture of 4a/5a, 14 in 88% yield (Scheme 1, 2). In mixture of compound cis for is more dominating 4a which is illustrated out through spectral analysis (^1H NMR spectroscopy).

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