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STEREOSELECTIVE SYNTHESIS OF β-LACTAM DERIVED FROM CHRYSENYL IMINE

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Abstract: Synthesis of *cis*-α-acetoxy-β-lactam has been achieved through sodium borohydride reduction of α-keto-β-lactam followed by acetylation.

Keywords: β-Lactam, Imine, Synthesis

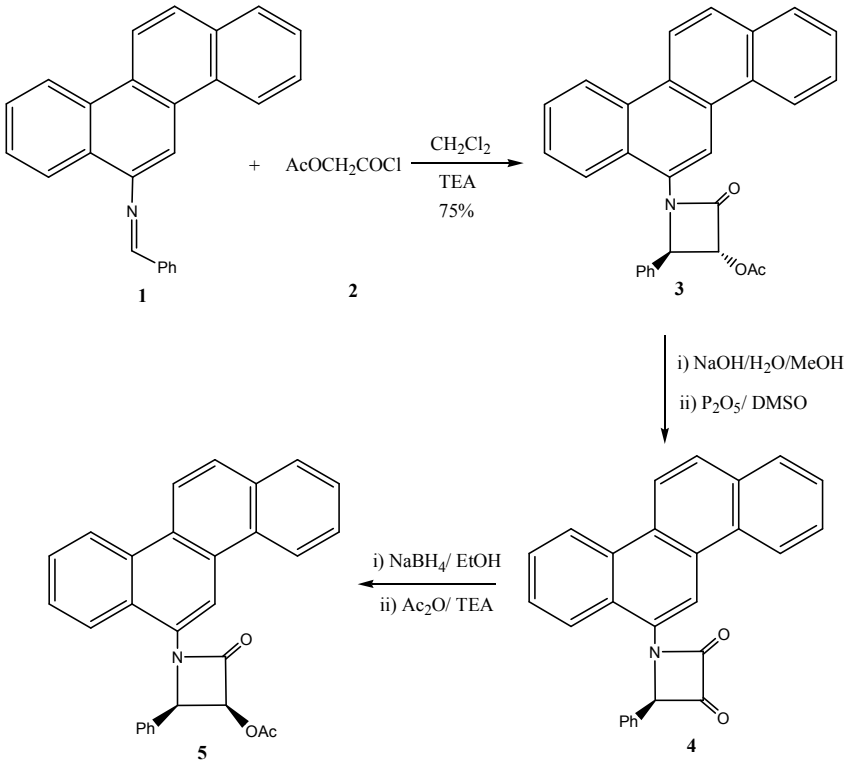
Introduction:
Stereoselective synthesis of new of β-lactams with polyaromatic compounds is not explored except our own studies in this field. Research on these types of molecules can be very intriguing because of their anticancer activities. Despite efforts, synthesis of *cis*-β-lactams that have a chrysene ring at nitrogen could not been achieved. In this paper, an alternative strategy is described for the synthesis of *cis*-1-N-chrysenyl-3-acetoxy-4-phenyl-2-azetidinone by reduction of the corresponding 3-keto-β-lactam with sodium borohydride in ethanol followed by acetylation.

Results and Discussion:
Imines derived from polyaromatic amines resulted in the formation of *trans* β-lactams as the only isolated products.[1]A similar reaction using specific imines derived from polyaromatic aldehydes produced *cis* β-lactams. However, in these examples, the polyaromatic groups were connected to the C_4-position of the β-lactam rings. The stereochemistry of the products was confirmed by NMR data. Interestingly the *trans* β-lactams demonstrated anticancer activities against a number of cancer cell lines *in vitro*.[1] But, the isomeric *cis* β-lactams in which the polyaromatic groups at C_4 had no effects on these cancer cell lines. It is obvious, an isomeric *cis* structure in which polyaromatic group at nitrogen of the β-lactams ring is highly essential to have direct comparative study as their anticancer effects. Earlier, all attempts to prepare *cis* β-lactams using polyaromatic imines derived from polyaromatic amines failed under various reaction conditions. The formation of *trans* β-lactams was explained by advancing a suitable mechanism.[1C] The formation of *cis*-β-lactams was also investigated.[2]

The growing interest in this subject has prompted us to investigate the synthesis of *cis* β-lactam with N-chrysenyl group. The *trans* acetoxy β-lactam **3** was prepared following cycloaddition

chemistry from imine **1** and acetoxyacetyl chloride **2**. The acetate group was hydrolyzed with cold sodium hydroxide solution to hydroxy compound in quantitative yield. The hydroxy group was then oxidized to the keto group **4** using P2O5 and DMSO. Sodium borohydride reduction of the keto group in **4** was then followed to the cis hydroxy compound which was then converted to the acetate **5**. It is fascinating to note that sodium borohydride reduction of the keto group proceeded from one side only despite the presence of a bulky N-polyaromatic system at the nitrogen of the ring. The resulting β-lactam **5** is isomeric to our anticancer β-lactam **3** that we reported earlier (**Scheme 1**).

Scheme 1



Conclusion:
A simple sodium borohydride-induced reduction of a keto group has been accomplished for the preparation of isomeric *cis* β-lactam. Availability of this *cis*-isomer will be extremely helpful to conduct a systematic structure-activity relationships study with respect to the *trans*-isomer.

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