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SYNTHESIS OF CINNOLINE RING FORMATION FROM SOME ARYLHYDRAZONES

PRAKASH KUMAR

Department of Chemistry, Muzaffarpur Institute of Technology,
MUZAFFARPUR – 842003 (Bihar) INDIA

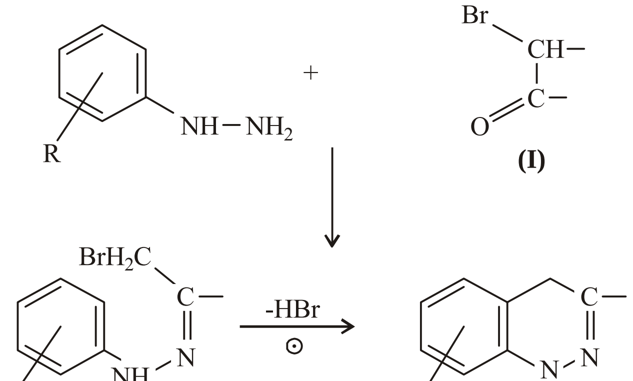
ABSTRACT

Reaction of hydrazones and the conditions, under which Fischer indole synthesis occurs, gave cinnoline ring formation from arylhydrazones.

Key words: Arylhydrazones, Fischer-indole synthesis, Cinnolines, Indolization.

INTRODUCTION

Preparation of arylhydrazones **(II)** of suitable α-halocarbonyl compound **(I)** followed by intramolecular Friedel-Crafts alkylation may give the desired cinnoline **(III)**.



A number of α-halocarbonyl compounds are known to form stable arylhydrazones.

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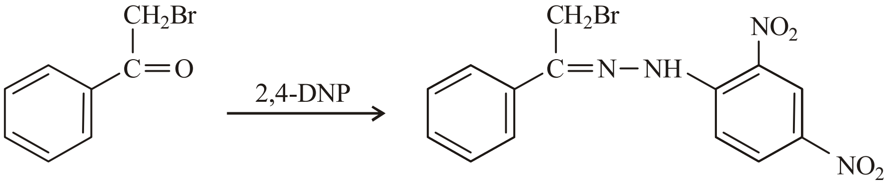
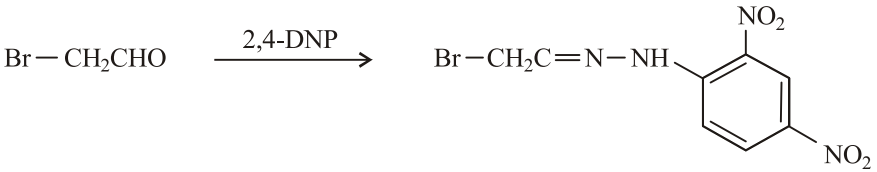
[*] Author for correspondence; E-mail: pk_mit@yahoo.co.in

For example, phenacyl bromide **(IV)** and bromoacetaldehyde **(V)** form their respective 2, 4-dinitrophenylhydrazones **(VI & VII)**.



(IV) **(VI)**



(V) **(VII)**

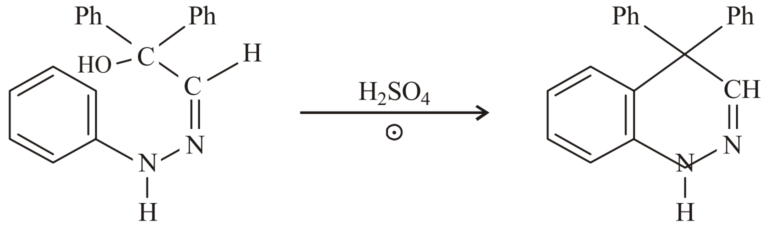
EXPERIMENTAL

Phenacylbromide **(IV)** was chosen as an α-halocarbonyl compound. As its 2,4 – dinitrophenylhydrazone **(VI)** contains two deactivating nitro groups in the benzene ring, Friedel-Crafts reaction was not successful with this compound. Phenacyl bromide **(IV)** was, therefore, converted into phenylhydrazone **(X)** by standard procedure. Friedel-Crafts alkylation was then carried out in CS_2 solution at ordinary temperature. A steady evolution of HBr in the reaction showed that it was occuring in the expected manner. T.L.C. examination was carried out from time to time to monitor the progress of reaction. The product from this reaction furnished a pure crystalline product, which was free from halogen. Indolization of the phenylhydrazone **(X)** would give the indole derivative **(XI)** containing bromine. The compound was analyzed and assigned dihydrocinnoline structure **(XII)**.

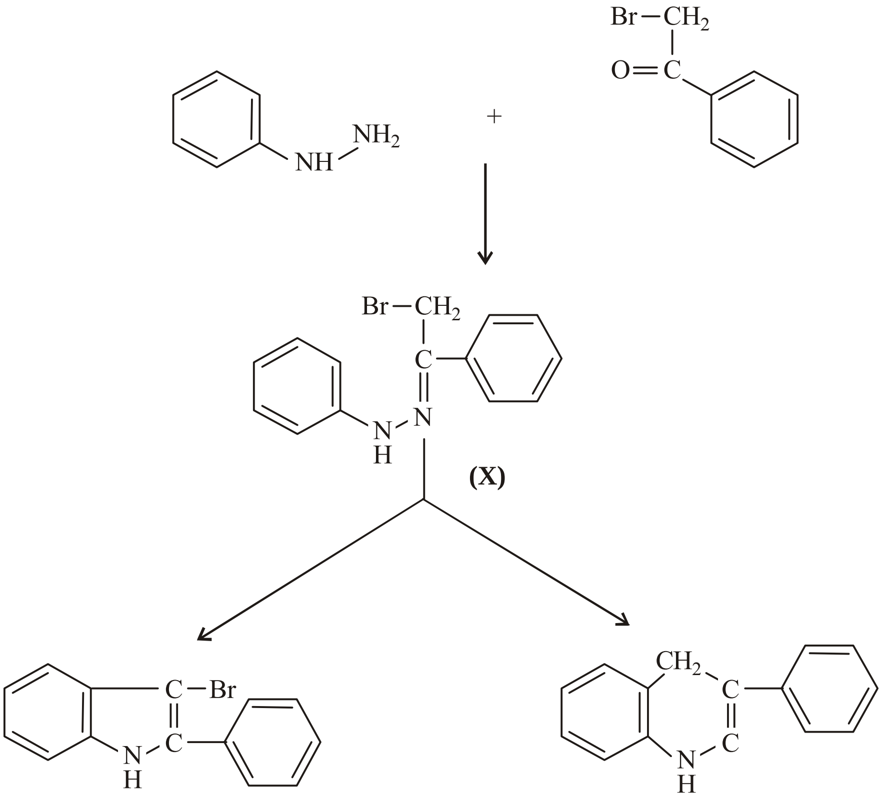
RESULTS AND DISCUSSION

The transformation of the arylhydrazones of the type **(II)** to 1, 4-dihydrocinnolines derivatives **(III)** was proposed to be brought about by Friedel-Crafts alkylation reaction. Since this reaction can be carried out in neutral solvent such as CS_2 under sufficiently mild conditions, there could be no possibility of indolisation taking place by rearrangement of the arylhydrazones. Alkylation could then be expected to occur at the reactive ortho-position.

It has been reported that diphenyl hydroxyl acetaldehyde obtained by reaction between diazo acetic ester and phenyl magnesium bromide with H_2SO_4 (N solution) yields the 1, 4-dihydrocinnoline **(IX)** as a red crystalline solid[1], m.p. 69-70°C.



(VIII) **(IX)**



(X)

(XI) **(XII)**

Further proof of the structure was obtained by spectral evidences. The IR spectrum of the compound had absorption at 1580 cm^{-1} for C = N stretching, 1610 cm^{-1} for substituted benzene ring, 2920 cm^{-1} for C-H stretching (showing the presence of -CH_2 – group) and 3250 cm^{-1} for N-H stretching.

The NMR spectra of the compound had absorption for three sets of protons. The nine aromatic protons had resonance (multiplet) at δ 7.4, a singlet corresponding to two protons at δ 2.7 due to benzylic – CH_2- group and a singlet for one proton at δ 4.3 for the N-H group. Thus, the product obtained in this cyclization reaction was 3-phenyl-1, 4-dihydrocinnoline **(XII)**.

CONCLUSION

Having succeeded in synthesizing 1, 4-dihydrocinnoline from phenylhydrazone of phenacyl bromide, then it was extended to different substituted phenylhydrazones.

p-Methoxyphenylhydrazine, o-bromomethylhydrazine and o-chlorophenylhydrazine were prepared by diazotizing the corresponding substituted anilines and reducing them with sodium sulphite. Phenacyl bromide was condensed with phenylhydrazines to give the corresponding phenylhydrazones, respectively, which were then cyclized as above to give 3-phenyl-6-methoxy-1, 4-cinnoline, 3-phenyl-6-boromo-1, 4-cinnoline and 3-phenyl-8-chloro-1, 4-dihydrocinnoline, respectively. In all these cases, evoluation of hydrogen bromide indicated that cylclization was taking place as expected.

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