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SYNTHESIS OF 2, 4, 6 – TRIARYL PYRIDINES BY THE REACTION OF 4 – FLUOROPHENACYLIDENE PYRIDINIUM YLIDES WITH α,β – UNSATURATED KETONES

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Abstract

4- Fluoro phenacyl pyridinium bromide was prepared by the interaction of 4 – fluorophenacyl bromide and pyridine, in benzene under reflux temperature. The pyridinium salt on treatment with K2CO3 in aqueous solution, gave 4 – flurophenacylpyridinium ylide. The ylide, on reaction with substituted benzlideneacetophenones in presence of ammonium acetate in acetic acid or methanol, gave symmetrical pyridines having different substituents at 2, 4, 6 – positions. Similarly, when the ylide was coupled with substituted benzylidene – 4 – acetophenones, 2, 6 (4 – fluorophenyl) - 4 – substituted phenyl pyridine, symmetrical pyridines were formed in good yields. Synthesis of symmetrical pyridines having substituents, involving the condensation of 4-fluorobenzylidene pyridinium ylide with 4 – fluorobenzylidene – 4 – fluoroacetophenone in ammonium accetate. All the new pyridines were confirmed by NMR Specteral data.

Keywords: 2, 4, 6 – TRIARYL PYRIDINES, UNSATURATED, KETONES, 4 – FLUOROPHENACYLIDENE PYRIDINIUM YLIDES

Introduction

One of the earlier methods involving azo ring closure leading to the synthesis of substituted pyridines was reported by Tschitschibabin1. The method involves the condensation of aldehydes and methyl ketones in presence of liquid ammonia (Scheme 1).

But this route was not versatile beach. It requires harsh reaction condition and gives poor yields of the pyridines. Subsequent to this report, Frank et al made an improvement by using ammonia and catalytic amount of acetate. Later Krohnke developed a superior method for synthesis of pyridines. This method involves the interaction of pyridinium salts of or ylides with α,β – unsaturated ketones (Scheme 2).

The course of the reaction involves same pentane 1, 5- dionyl intermediate, analogous to the diketo intermediate formed in earlier methods. The intermediate undergoes azo ring closure with ammonium acetate in glacial acetic acid to give 2, 4, and 6- triaryl pyridines. Moreover earlier methods1, 3 were restricted the preparation of symmetrical pyridines having identical substituent's at 2 and 6 –

position of pyridine ring. The krohnke' method allows the synthesis of both symmetrical and asymmetrical pyridines having different substituent's at 6 positions of pyridine nucleus.

Scheme 1

We have reported the synthesis of some symmetrical and asymmetrical fluoro pyridines having various different groups by the condensation of substituted phenacyl pyridinium ylides with α,β – unsaturated ketones.

Preparation of p– Substituted Phenacylpyridinium Bromides

All the reagents were obtained from commercial sources (E. Merck, BDH, and SISCO). Starting materials were prepared according to the procedures reported in literatures.

A solution of 100 mmol of p-substituted phenacyl bromide and 100 mmol of pyridine in 100 ml anhydrous benzene or tetrahydrofuran was boiled for 6-8 hrs. The success of the solvent was evaporated and petroleum ether was added to precipitate the salts which were, then, recrystalise from chloroform, petroleum ether in the ratio 1:2. This procedure was followed to prepare the following salts 8.

1. 4- flurophenacylpyridinium bromide , white crystals, m.p. 205-7oC (m.p. 203-4oC): IR (KBr) : 1685 cm-1 .
2. Phenacyl pyridinium bromide , pale yellow crystals, mp. 192-3°c (m.p. 194- 5-7oC): IR (KBr) 1690 cm-1.
3. 4-chlorophenacylpyridinium bromide , white crystals, m.p. 208 – 10oc (Lit.6 m.p. 207oc): IR (KBr): 1680 cm^{-1} (mu c=o).
4. 4-Bromophenacylpyridinium bromide (1a), white crystals, m.p. 240-42Oc m.p. 242-43oC): IR (KBr) 1695 Cm-1.
5. 4- methylphenacylpyridinium bromide , light reddish crystals, m.p. 201-203oc (m.p. 205oC) : IR (KBr):1680 Cm-1 .
6. 4-Methoxyphenacylpyridinium bromide, white crystals m.p. 206-8oc (Lit.7 m.p. 209 – 10oC): IR (KBr): 1678 Cm-1.

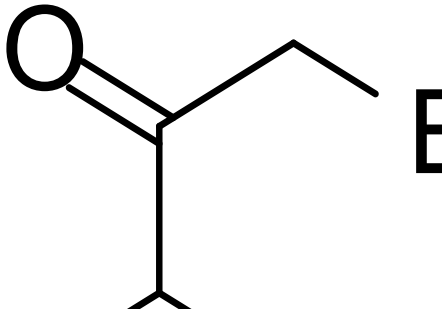
All the substituted benzylideneacetophenononeswere prepared by the reaction of substituted benzaldehydes and substituted acetophenones in presence of alcoholic sodium hydroxide as reported in literature 9-10.

Results and Discussion

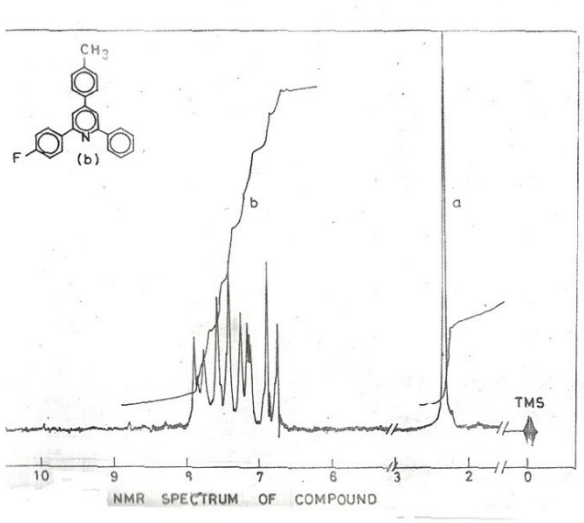
The reaction of pyridine with 4–flourophenacyl

bromine in benzene of THF at reflux temperature gave 4 – flouroacyl pyridinium bromide. The treatment of salt (1) with aqueous K2CO3 gave 4 – flurobenzyl pyridinium ylide which could be isolated but could not be stored due to sensitivity towards atmospheric components. Therefore, the reaction was carried by generating the ylide in situ its corresponding precursor's salt. The structure of salt (1) was evidenced by the comparison of melting point that replied in literature. The IR spectrum of pyridinium salt (1) released led to characteristic absorption band at 1690 cm-1 due to stretching vibration for the carbonyl group. The diagnostic band in the 3300 cm-1 was observed due to C – R stretching vibrations of methylene group attached to the nitrogen atom. The NMR spectrum of the salt displayed a pass at 86.80 (singlet) due to methylene group and other the protons were exhibited in the range 87.20 – 8.45 (Multiple)
The reaction of salt (1) with substituted benzylideneacetophenone in pressure of ammonium acetate and glacial acetic acid, at reflux temperature gave a symmetrical 1 – (4 – fluorophenyl) -4, 6 – di (substituted phenyl) pyridines could in 40 – 70% yield. The same pyridines could also be prepared by the interaction of 4 substituted phenacylpyridinium bromides4-5. With substituted benzyledene 4 fluoroacetophenones using ammonium acetate in glacial acetic acid as cyclysation agent (Scheme 3). Similarly, symmetrical pyridines 2,6 – di (4 – fluoro – phenyl) – 4 – aryl pyridines were synthesized in 50 – 75% yields by the reaction of salt (1) with benzylidene -4-fluoro – acetophenone in mixture of ammonium acetate and acetic acid. Attention was now directed towards the synthesis of pyridine having identical groups at 2, 4, and 6 – positions of the pyridine nucleus. This was achieved by heating salt (1) with 4- fluorobenzyledene 4- fluoroacetophenone in presence of ammonium acetate in acetic acid giving 50% yield. The reaction seems to proceed by the attack of ylide on ? carbon of α,β – unsaturated ketones to form (pentane – 1, 5– dionyl) pyridinium intermediates which, in turn undergo azo ring closure in presence of ammonium acetate to form 2, 4, 6 – triarylpyridines .

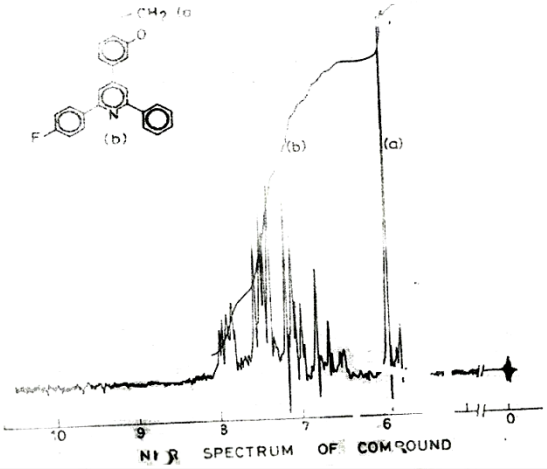
Scheme 3



Various new fluoropyridines synthesized by the above method. All the pyridines gave satisfactory elementary analysis. The spectral data confirmed the proposed structures of pyridines. The IR spectra showed characteristic absorption in the region 3050-3000 cm-1, which were assigned to the C-H stretching mode of pyridine rings. Two bands in the region 1000 cm-1 and 1500 cm-1 were due to the interaction between C – C and C – N vibrations of the pyridine ring 6-7. The NMR spectra of the pyridines showed two pyridyl protons in the range 8.35 – 6.65 and aromatic protons in the region 8.40- 8.900.



NMR SPECTRUM OF COMPOUND



NMR SPECTRUM OF COMPOUND

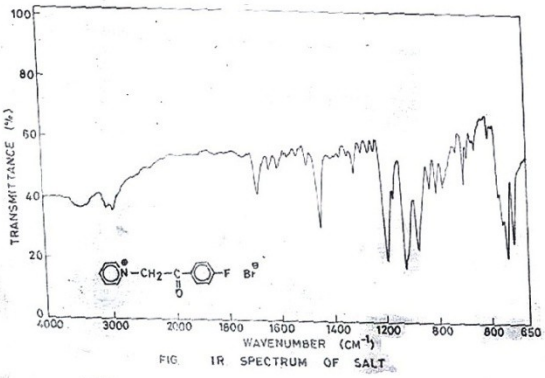
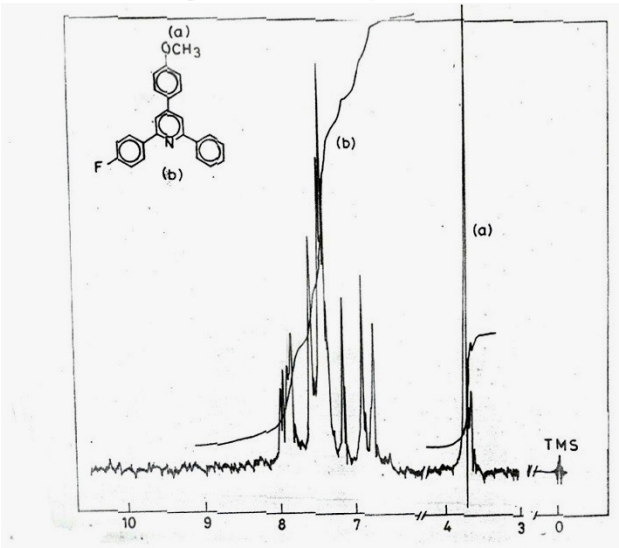
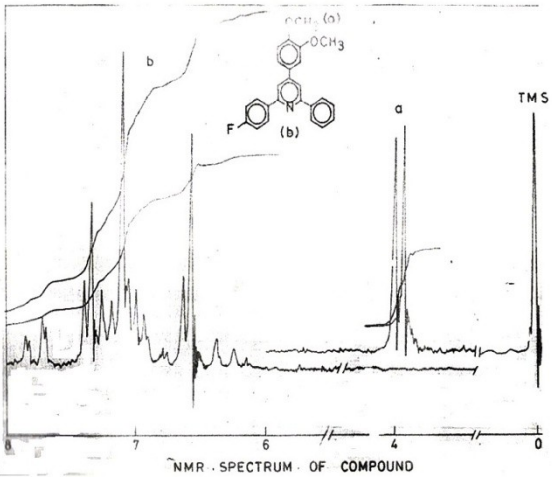


FIG. IR SPECTRUM OF SALT





NMR SPECTRUM OF COMPOUND

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