Journal of Applied Pharmaceutical Science 01 (07); 2011: 124-126

Journal of Applied Pharmaceutical Science

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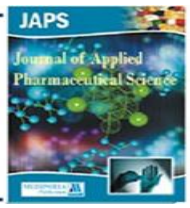

ISSN: 2231-3354
Received on: 26-08-2011
Revised on: 02-09-2011
Accepted on: 10-09-2011

The Study of Base Catalysed Synthesis of 2-Chloro–4–Amino–5-Flouropyrimidine from a biologically active Compound 5-Flouro Pyrimidine

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ABSTRACT

The base catalyzed study of synthesis of 2-chloro-4-Amino-5-flouroPyrimidine to improve the yields and economically viable industrialization process from its biological active pyrimidine derivative of 5-flourouracil.

Key words: Chlorination, Amination of 5-flouro uracil, Base catalyzed synthesis.

INTRODUCTION

Various pyrimidines were synthesized and characterized in various methods among all the Pyrimidines the 2-chloro-4-Amino-5-flouropyrimidine has several Industrial Applications And a very few Methods available for making this product such as Amination of 2, 4,-dichloro-5-flouropyrimidine and one more publication explains its heterocyclic synthesis by using Several routes of synthesis steps these literatures were clearly explained in reference, But no one can study the base catalyzed Chlorination of Hydroxy pyrimidines, which reflects in our Current proposed work and it this study of various Parameters with the help of a base Catalyzed Chlorination process, many of the industrial base Catalyzed methods can get optimized and Economically available industrialized Process could be developed for commercially demanded Products.

MATERIALS AND METHODS

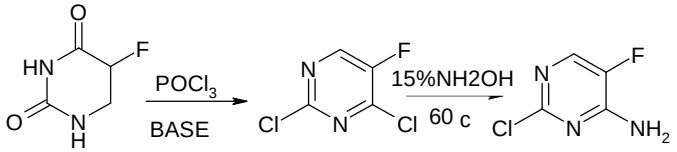
Melting points were determined routinely in open capillary tube. The completion of reaction was routinely checked by TLC on silica gel-G plates of 0.5mm thickness and spots were located by iodine. Elemental analyses of the newly synthesized compounds was carried out on Carlo Reba 1108 analyzer and are found within the range of theoretical value. IR spectra were recorded on Shimadzu-8400 FT-IR spectrometer in Ker (in cm-1). 1H NMR spectra were recorded in CDCl3 on a Bruckner DRX-300 at 300 MHz, all the raw materials were procured from Aldrich chemical catalog company and were tested before going to the synthesis process. Our current work is based on Base catalyzed study of different p Ka strengths of bases and the p Ka strengths of several Acid sand bases were given in the table, to know about p Ka and its strengths.

RESULTS AND DISCUSSIONS

We have synthesized 2-Chloro-5-fluoro-6-Aminopyrimidine by using standard procedures with slight modification in the base catalysts usage, based on their different p Ka values. In the current course of study we have observed several variations like yield, melting point, temperature, and Reaction time cycles. Apart of those parameters reaction flexibility or *Hazop* conditions were excellent for more p Ka containing base catalyst and also they give us more yields with in a short period. The 1HNMR, 13CNMR Analysis was done in a Bruckner DRX-300 at 300 MHz instrument; their spectral results were characterized from their chromatograms as shown as in the figure 1&2.

Experimental

Route of synthesis



Where

BASE: Diethyl amine, Dim ethylformamide, N, N-Dim ethyl aniline and triethyl amine, DMAP.

The Obtained, Observed experimental results are mentioned as shown as in the table-1 and its Chromatographic 1HNMR and 13CNMR are shown as in figure-1& figure-2.

GENERAL PROCEDURES

Stage: 1 (Process for the preparation of 2, 4-Dichloro-5-flouro Pyrimidine

To a clean and dry round bottom flask added 116.51gms of Phosphorous oxy chloride (POCl3, 4 eq) and base (0.5ml) at room temperature under stirring, after 10min 25gm of 5-flouro uracil was added portion wise to the above mixture at room temperature (control the exothermic reaction by adding little ice out side the flask which contain water at room temperature) . Stirr this mixture at room temperature for 20minutes and then slowly rose the temperature 106 -110 deg C for 14 hrs. If TLC complies then cool the reaction mass to room temperature and Pour it into a ice cold water (100ml) under vigorous stirring. The solution pH was adjusted to pH-8, the resulting mixture was stirred for 15 minutes, and the obtained light brown colored solid was filtered, Washed with (2x10ml) water and dried well to report the yield. 1HNMR (CDCl3): 300MHZ, Delta 8.85 (1H, S).

Stage: 2 (Process for the preparation of 2-chloro-4-Amino-5-flouro Pyrimidine):

The Pure stage-1 material was taken in to a 47.5 ml 15% Aqueous Ammonia solution at Room Temperature slowly rose the temperature to 60^0C and was maintain for 1 hrs. If TLC complies Cool to room temperature. Filter the obtained off white Solid material, Washed with water (2x20ml) and dried at 70-80^0C for half and hour, report the (4 gm) Yield and MR1HNMR (CDCl3+DMSO) : 300MHZ, delta 7.72 (1H,d) , 6.59 (2H, BS) (-NH_2)C13NMR (CDCl3+DMSO): 300MHZ, delta 155 (1C, d), 153(1C, S), 146(1C, S), 140(1C, d)

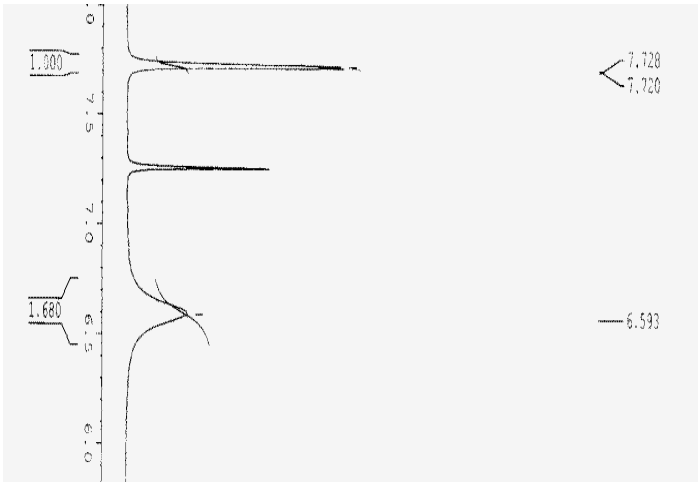


Fig 1: 1H NMR Chromatogram for 2DC5FP.

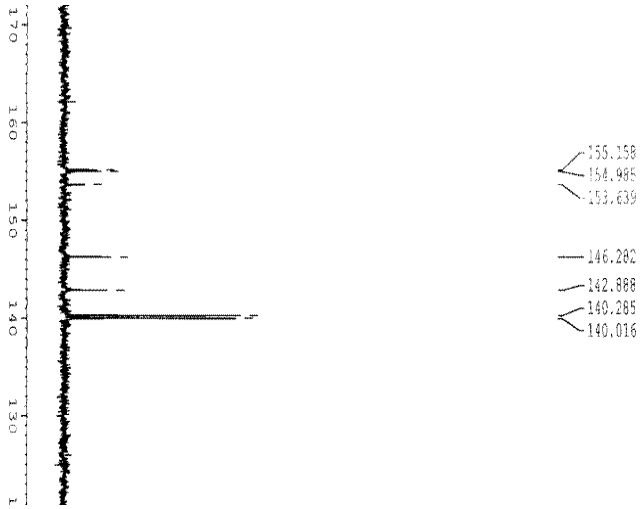


Fig 2: 13C NMR Chromatogram for 2DC5FP.

Table 1: Experimental results with various parameters.

S.No	Base	Temp In ° C	Moles	O.A.yield In %	pKa	Rxn.time In Hours	Melting point In ° C
1.	TEA	106	0.1	80.1	10.75	12	196-199
		106	0.3	65.1		14	195-200
		80	0.1	26.0		16	NI
2.	Dimethyl aniline	106	0.1	55.5	5.15	12	196-200
		106	0.3	55.5		12	196-199
		80	0.1	10.0		10	NI
3.	DMF	106	0.1	66.3	9.5	16	196-200
		106	0.3	50.0		20	196-201
		80	0.1	20.0		24	NI
4.	DMAP	106	0.1	69.8	9.2	14	195-199
		106	0.3	48.2		12	194-198
		80	0.1	35.0		16	195-200
5.	Diethyl Aniline	106	0.1	59.0%	6.61	12	196-200
		106	0.3			16	195-201
		80	0.1			14	196-200

Being study of yields and process safety, we have changed the base and its parameters then We have obtained the following results as shown in table -1.

CONCLUSION

The entire study of catalyst concludes that the highest yields were observed in case of base with highest pKa value. So that the chlorination of Pyrimidine, pyridine or like any nitrogen containing heterocyclic nucleus base compounds, Better to use a highest pKa value containing base catalyst to get better yields and for better commercialized process.

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