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Optimizing the Manufacturing process of N, N DI-METHYLE FORMAMIDE – N, N DI MITHYLE ACETOL

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ABSTRACT

In this work, studies has been done on N,N Di-Methyle Formamide – N,N Di Mithyle acetol Manufacturing Process using semi Batch reactor for improving the purity and yield. The process is carried out with two stages,(i)In the first stage mixing of reactants N,N Di- methyle formamide,N,N Di- methyle sulfate with sodium methoxide in 1:1 mole ratio to form the product (N,N Di- methyle formamide N,N Di- methyle acetol).(ii)Finally in the second stage separation of product will be done by using simple distillation.

The reaction for the process is purly exothermic and the reactants are N,N Di- methyle formamide, N,N Di- methyle sulfate and Sodium methoxide by optimising the time,temperature,concentration and RPM.The reaction is processed at 15-40 ℃ temperature with the changes of reaction time intervals from 30 to 180 minutes under 100-900 stirrer RPM . By using this process by-products has been decreased with improved product (N,N Di-Methyle Formamide – N,N Di Mithyle acetol) purity 91.13% and yield 86% using GC Analytical technique.

KEYWORDS: N,N Di- methyle formamide N,N Di- methyle acetol ,optimization, Batch reactor,conversion.

1. INTRODUCTION

N,N-DimethylformamideDimethylacetol- C5H13NO2 is an intermediate compound for many applications in pharma industry. It's an anti-tumor agent and also used as intermediate for the HIV medicine.

Dimethylformamide Dimethylacetal (DMF-DMA) is an excellent methylating agent for acids, amines, thiols and amino acids, and widely used for **pharma, agro, and cosmetics applications**.

Shah, Bipinchandra Punjalal et al. [1] have examined the salient features of the Process for preparation of Di methyle formamide - Di methyle Acetate.Chemicals for the process is Di methyle formamide,Di methyle sulfate,sodium methoxide,methanol reaction temperature for DMFDMS complex is 85 ℃,3hrs time. Reaction temperature at batch reactor is 20-25℃.Yield is 60-70% and purity is 85%.

Liu,yuxia [2] have studied the Synthesis of N,N-dimethylformamide dimethyl acetal from China and the chemicals are Di methyle formamide,Di methyle sulfate,sodium methoxide,methanol.Reaction temperature at Batch reactor is 3-5 ℃.

LI,Ke[3] have studied the preparation of floxuridine like compounds as antitumor agents.chemicals are

sodium methoxide and r eaction temperature at Batch Reactor is 1-5 ℃ with yield 55% and purity 80%.

jingxi huagng zhongjianti [4]have studied the Optimization on synthesis technology of N,N-d sodium methoxide,the molar ratio of n-sodium methylate and dimethyl sulfate was 1.2:1 Reaction temperature at BatchReactor -5~5℃ yield is 40-60% and purity is 85%.

yu,jianxin [5] preparation of 5'-deoxy-5-fluorocytidine derivatives as antitumor agent.sodium methoxide used for the preparation of Reaction temperature at Batch Reactor is 0-5 ℃. yield is 65% and purity is 88%.

yu, Haibo [6] have studied on synthesis and bio activity of I- Substituted anilino -4 , 4- dimethyl -2 (1H-1,2, 4 - triazol -1 - yl) -1- pentene -3- one. Sodium methoxide is the Reagent yield is 65% and purity is 70%.

Kurbanov D[7] have studied on synthesis and NMR spectra of formamide acetalS. Reagent Is Di methyle formamide and sodium methoxide. condition is two stages. yield is 55% and purity is 65%.

Ahn, Gyeong UK[8] studied on method for the preparation. of 4,4- alifluoro -2-((dialky Iamino) methylene) -3- oxobutanoic acid alkyl ester. methanol is the solvent and condition of the reaction is multisteps.

Lapuka , L.F[9] have studied on molecular complexes of chloroform with ortho esters. sodium Methoxide is the reagent and methanol is the solvent. yield is 55% and purity is 60%.

Mesnard, D[10] studied on Regiospecific synthesis of tertiary amines with a double unsaturated second group. Reagents are Dimethyl sulfate, sodiumretioxide and methanol is the Solvent. condition of the reaction is following multi steps. purity is 55% and yield is 40%.

It is very essential need in pharma industry to produce DMF-DMA above than the purity available in the market. The reason for improving purity and yield is to decrease the available impurities in the product and controlling the losses due to an incomplete reaction and undesirable side reactions.

To the best of our knowledge, from the literature it was observed that most of the studies are done on purity and yield of N,N DI-METHYLE FORMAMIDE – N,N DI MITHYLE ACETOL below 90% . Experimental data is required to vary the pecentage of purity and yield of DMFDMA product .Therefore, the objective of the present study is to develop the product above 90 percent.

2. MATERIALS AND METHODS

2.1 Materials

Raw materials such as N,N Di- methyl formamide (98%), N,N Di- methyl sulfate (98%) and Sodium methoxide were procured from Avra synthesis Pvt. Ltd. (India).

2.2 Experimental Procedure

The N,N DI-METHYLE FORMAMIDE – N,N DI MITHYLE ACETOL production was carried out in a semi batch reactor.The experimental setup for the process is shown in Figure1. A weighed amount of formed DMF and DMS 1:1 mole ratio is added drop wise by using addition tank to the weighed amount of one mole ratio sodium methoxide in the batch reactor. while adding the DMFDMS to the sodium methoxide the reaction temperature becoming exothermic and the temperature raises above 80℃ but by applying cooling around the reactor the temperature should control below 40℃ for three hours of reaction time.when the reaction is over the solid mass is formed in side the reactor with N,N DI-METHYLE FORMAMIDE – N,N DI MITHYLE ACETOL.Finally using distillation technique separation of product was done.

Like wise,the reaction temperature was controlled from 15℃ to 40℃ for three hours of reaction time.

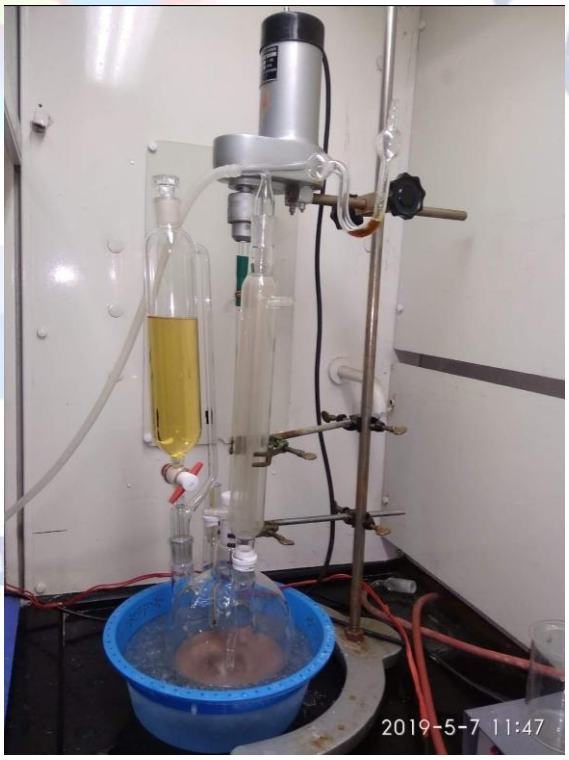

Figure 1. Semi batch reactor

2.3 Reaction mechanism of N,N DI-METHYLE FORMAMIDE – N,N DI MITHYLE ACETOL

The production of DMFDMA is a single step reaction. The amount of dmf and dms is added to the sodium methoxide in 1:1 mole ratio ratio.The reaction is carried out in liquid slurry phase, the rate of reaction between dmfdms and sodium methoxide must be sufficiently fast at practical temperatures. The product selectivity mainly depends upon the reaction conditions.

Reaction mechanism:

$$CH_3NaO + C_5H_{13}NO_5S \rightarrow CH_3NaO_4S + C_5H_{13}NO_2$$

(sodium methoxide) (DMFDMS) (Sodium methyle sulfate) (DMFDMA)

2.4 Analytical techniques

N,N DI-METHYLE FORMAMIDE – N,N DI MITHYLE ACETOL product sample analysis is done by using Gas chromatography with Flame Ionization Detector . The number of compounds present in the sample will decide by the available peaks from the GCgraph . In fig 2. third peak from left to right is the DMFDMA product and the area under the peak is covered,and remaining peaks are traces of di-methyl formamide and methanol.

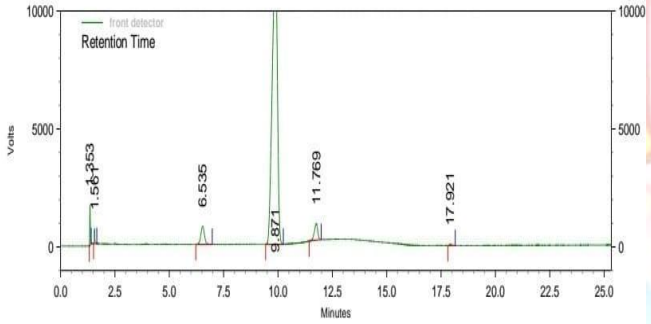

Figure 2. Graph from Gas Chrometography

3. RESULTS AND DISCUSSIONS

In the present study, the production of liquid phase N,N DI-METHYLE FORMAMIDE – N,N DI MITHYLE ACETOL was carried out in a semi batch reactor. The effect of reaction parameters, such as reaction temperature,time and RPM on yield and purity of DMFDMA has been studied.

3.1 Effect of temperature on purity and yield of N,N DI-METHYLE FORMAMIDE – N,N DI MITHYLE ACETOL

To know the effect of reaction temperature on the purity of DMFDMA , the reactions were carried out for different reaction temperatures for a fixed time factor. The obtained results are shown Figure.3.

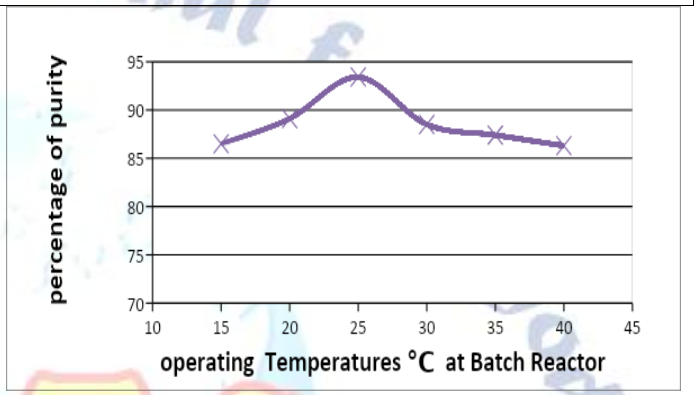

Figure 3. Effect of temperature on yield of DMFDMA reaction

From Figure.3 it can be seen that the purity of DMFDMA is increased with the increment in reaction temperature from 15-30 °C. However, a decreased trend was observed in purity for the temperature of 30-40 °C. The purity of sample is analysed by using gas chromatography,the area and height of the peak in graph decides the purity of product.

To know the effect of reaction temperature on the yield of DMFDMA , the reactions were carried out for different reaction temperatures for a fixed time factor. The obtained results are shown Figure.4.

From Figure.4 it can be seen that the yield of the DMFDMA is increased with the increment in reaction temperature from 15-30 °C. However, a decreased trend was observed in yield for the temperature of 30-40 °C.

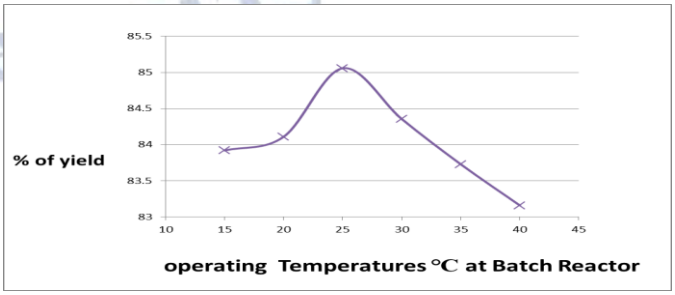

Figure 4. Effect of temperature on yield of DMFDMA reaction

3.2 Effect of time on Purity and yield of N,N DI-METHYLE FORMAMIDE – N,N DI MITHYLE ACETOL

To know the effect of reaction time on the purity of DMFDMA, the reactions were carried out for different reaction times . The obtained results are shown Figure.5.

From Figure .5 it can be seen that the purity of the DMFDMA is increased with the increment in reaction time from 30 to 180 mins.

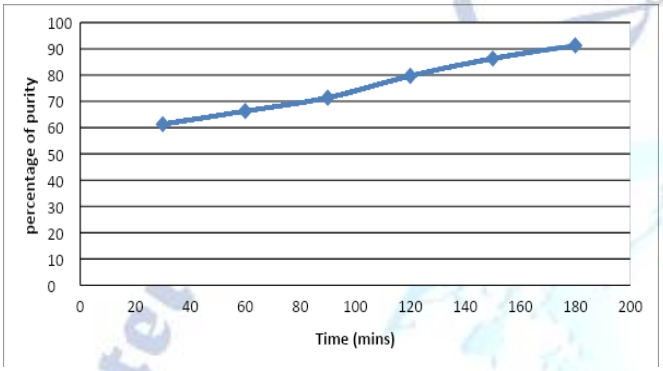

Figure 5. Effect of temperature on purity of DMFDMA reaction

To know the effect of reaction time on the yield of N,N DI-METHYLE FORMAMIDE – N,N DI MITHYLE ACETOL , the reactions were carried out for different reaction times . The obtained results are shown Figure.6.

From Figure.6 it can be seen that the yield of the DMFDMA is increased with the increment in reaction time from 30 to 180 mins.

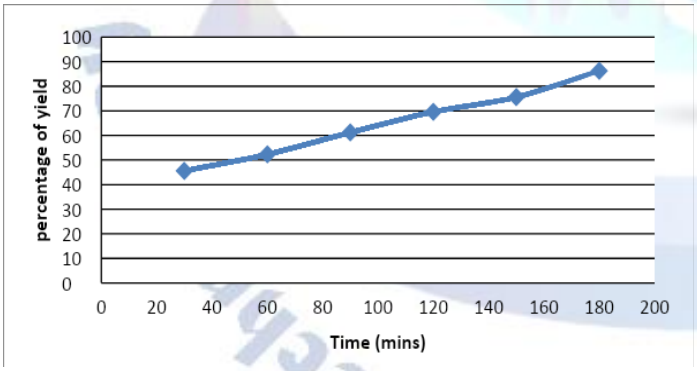

Figure 6. Effect of temperature on yield of DMFDMA reaction

3.3 Effect of RPM on purity and yield of N,N DI-METHYLE FORMAMIDE – N,N DI MITHYLE ACETOL

The observation was done to know the effect of RPM (revolutions per minute) of the stirrer in batch reactor on the purity of N,N DI-METHYLE FORMAMIDE – N,N DI MITHYLE ACETOL , the reactions were carried out for different RPM . The obtained results are shown Figure.7.

From Figure.7 it can be seen that the purity of the DMFDMA is increased with the increment of stirrer speed from 100 to 180 RPM.

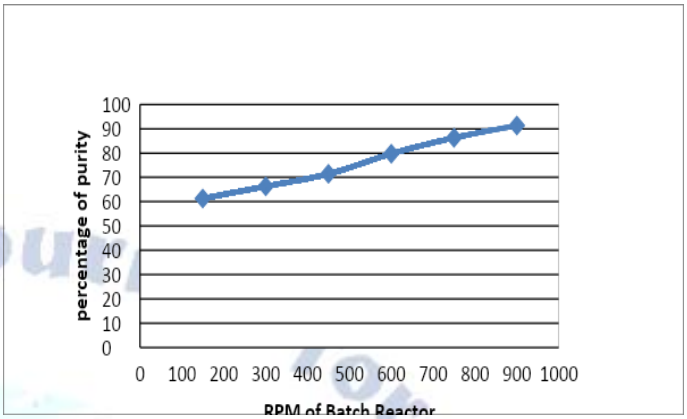

Figure 7. Effect of temperature on yield of N,N DMFDMA reaction

The work was extended to know the effect of RPM (revolutions per minute) of the stirrer in batch reactor on the yield of N,N DI-METHYLE FORMAMIDE – N,N DI MITHYLE ACETOL , the reactions were carried out for different RPM . The obtained results are shown Figure.8.

From Figure.8 it can be seen that the yield of the DMFDMA is increased with the increment of stirrer speed from 100 to 180 RPM.

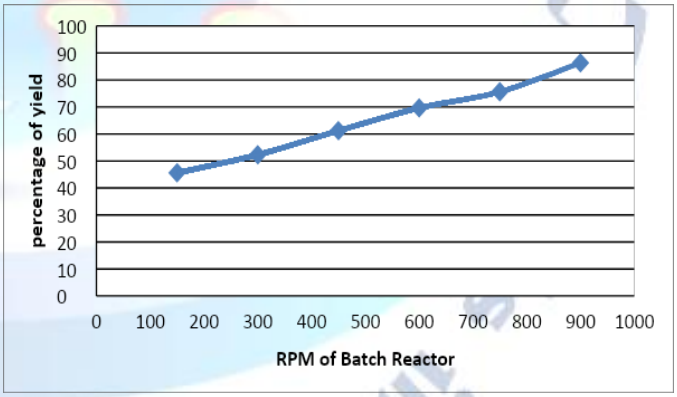

Figure 8. Effect RPM on yield of DMFDMA reaction

4. CONCLUSIONS

- In the work, the process for production of N,N DI-METHYLE FORMAMIDE – N,N DI MITHYLE ACETOL was carried out in semi batch reactor.
- The known weighed quantity of dmf and dms is added to the weighed quantity of sodium methoxide in 1:1 mole ratio.The following reaction is exothermic carried under different operating temperatures from 15℃ to 40℃.Further,it was observed in the study that purity and yield of the product N,N DI-METHYLE

FORMAMIDE – N,N DI MITHYLE ACETOL is increased by increment in reaction temperature from 15-30 ◎C. However, a decreased trend was observed in yield for the temperature of 30-40 ◎C.Finally it is observed that the reaction temperatue at 25℃ got 91.13 % purity.

- The effect of reaction time was studied on the reaction and it was observed that, the purity and yield is increased by increasing the reaction time from 30 mins to 180 mins.Finally the effect of stirrer speed was studied on the reaction and it is noted that, the purity and yield is increased by increasing the RPM of stirrer from 100 to 900.

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Conflict of interest statement

Authors declare that they do not have any conflict of interest.

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