

# SYNTHESIS OF N, N'-DIACETYLOXAMIDE USING SPECIFIC METHODS IN AN ATTEMPT TO ACHIEVE EXCELLENT YIELD OF THE PRODUCT

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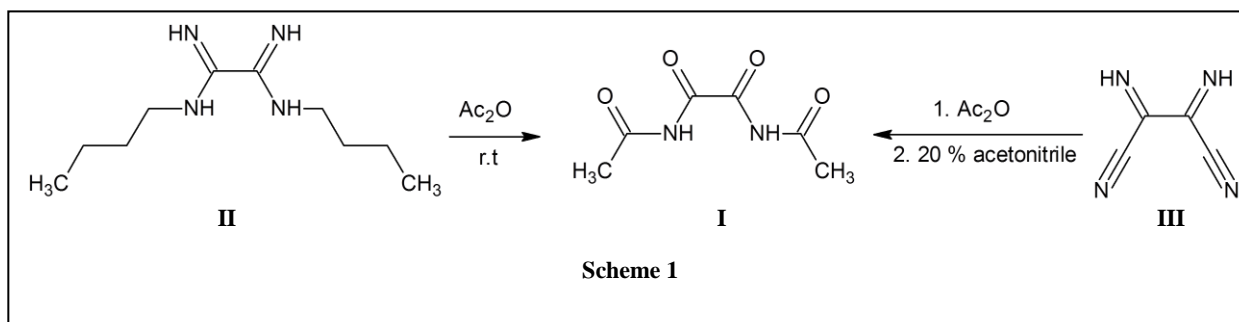
**ABSTRACT:** *N, N'*-diacetyloxamide (**I**) is an important acylated oxamide which is used in the field of detergents, pharmaceuticals, as an activator for inorganic per-compounds and in biologically active compounds. In the present study *N, N'*-diacetyloxamide (**I**) was synthesized from specific ways and characterized on the basis of melting point and FTIR spectral data. Results of the study suggested that the reaction was not successful using base catalysts but strong acid catalysts catalyzed the reaction efficiently in the presence of acetic anhydride as an acylating agent (**Scheme 3**). Among mineral acids perchloric acid ( $\text{HClO}_4$ ) gave the best yield i.e. 82%. Sulfuric acid ( $\text{H}_2\text{SO}_4$ ) and poly phosphoric acid (PPA) also catalyzed the reaction proficiently. Lewis acids i.e. ferric chloride ( $\text{FeCl}_3$ ), zinc chloride ( $\text{ZnCl}_2$ ), phosphoryl chloride ( $\text{POCl}_3$ ) and tin chloride ( $\text{SnCl}_2$ ) offered 40-61% yields. Other catalysts like para toluene sulfonic acid (PTSA), copper (II) chloride ( $\text{CuCl}_2$ ), nickel chloride ( $\text{NiCl}_2$ ), silver chloride ( $\text{AgCl}_2$ ), mercury (II) chloride ( $\text{HgCl}_2$ ), aluminium chloride ( $\text{AlCl}_3$ ), ortho phosphoric acid ( $\text{H}_3\text{PO}_4$ ), trichloroacetic acid ( $\text{CCl}_3\text{COOH}$ ) and trifluoroacetic acid ( $\text{CF}_3\text{COOH}$ ) was also tried but they were unable to catalyze the reaction.

**Key words:** Oxamide; N,N'-diacetyloxamide; Mineral Acid; Lewis Acid; Acetic Anhydride; Acylation; Yield.

## INTRODUCTION

*N,N'*-diacetyloxamide, M.F: ( $\text{C}_6\text{H}_8\text{N}_2\text{O}_4$ ), has also been named as *N, N'*-diacetyloethanediamide, is a secondary amide having M.P. (236-238 °C) [1]. Diacetyloxamide is used in the sector of detergents [2]. The acylated oxamides e.g. diacetyloxamide has been used as activators for inorganic per-compounds and are distinguished by a very good activating action. The oxidation, bleaching and washing agents prepared with the acylated oxamides as activators have been found to have a surprisingly good stability to storage as

compared to known activators [3].  $\alpha$ -Dicarbonyl compounds are valuable synthons in the organic chemistry, and the  $\alpha$ -dioxo bridge is a key moiety of many enlightened compounds. Esters and amides having general formula  $\text{ZCOCOZ}'$  (**V**) ( $\text{Z}, \text{Z}' = \text{OR}, \text{NR}_2$ ) have many industrial uses such as important intermediates in synthesis [4, 5], as a co-component in polymerization [6, 7], biologically active compounds such as pesticides [8, 9], pharmaceuticals etc [10, 11].

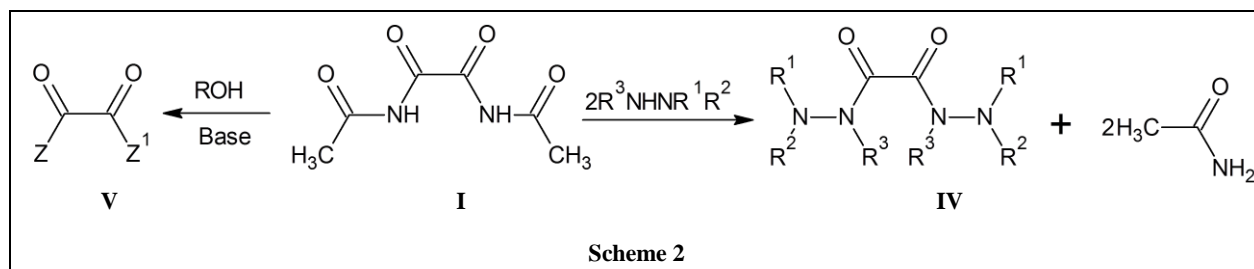


Synthesis of *N,N'*-diacetyloxamide (**I**) with 6% yield from the reaction of di-*n*-butylloxamidine (**II**) with acetic anhydride at room temperature has been reported in the literature [1]. Similarly reaction of diiminisuccinonitrile (DISN) (**III**) with acetic acid yielded (11%) *N, N'*-diacetyldiiminisuccinonitrile which on hydrolysis with 20% aqueous acetonitrile gave *N, N'*-diacetyloxamide (**I**) (**Scheme 1**) [12].

$\alpha$ -Ketoamides have been synthesized via double carbonylation of organic halides with amines using palladium complexes [13, 14, 15, 16]. Oxamates, Oxamides, and oxalates have been prepared by the carbonylation of alcohols or amino alcohols and amines in the presence of palladium (II) catalysts [17, 18, 19, 20]. Carbon monoxide is used in these catalyzed carbonylation reactions since

monocarbonylation take place, majority of these reactions are not selective.  $\alpha$ -diketo derivatives are synthesized by reactive, oxalates, oxamates or oxamides [21, 22] like oxalyldiimidazole [4, 5] or diacetyloxamide [23].

For the preparation of oxalyl- and oxamyl-hydrazides (**IV**) a new method was developed which consists of reacting oxamide or diacetyloxamide with the related hydrazine derivative having formula  $\text{R}^1\text{R}^2\text{N-NHR}^3$  where  $\text{R}^1$  denotes a hydrogen atom or a substituted alkyl, aryl, cycloalkyl or aryl-alkyl group,  $\text{R}^2$  represents a hydrogen atom or substituted alkyl group, or taken together  $\text{R}^1$  and  $\text{R}^2$  with the neighboring nitrogen atom denote a saturated heterocyclic ring, and  $\text{R}^3$  is also a hydrogen atom or substituted alkyl group. Very good yields of these products has been claimed [24].



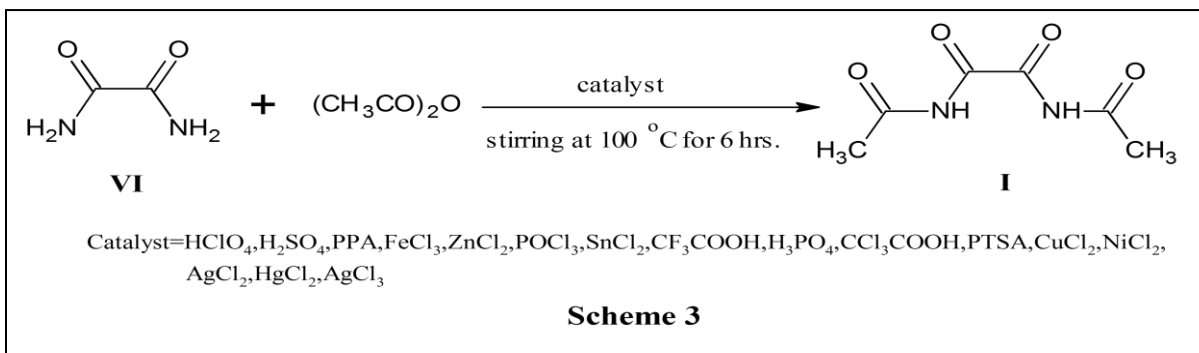
For the preparation of oxalic acid esters and amides of general formula (V) wherein Z designates an —OR or —NR<sup>1</sup>R<sup>2</sup> group, wherein R represents substituted or unsubstituted alkyl, alkenyl, cycloalkyl, aryl, or aryl-alkyl, R<sup>1</sup> is hydrogen or substituted or unsubstituted alkyl, alkenyl, cycloalkyl, aryl, or aryl-alkyl, R<sup>2</sup> represents substituted or unsubstituted alkyl, alkenyl, cycloalkyl, aryl, or aryl-alkyl, or R<sup>1</sup> and R<sup>2</sup> taken together with the adjacent nitrogen atom represent a saturated five, six, seven, eight membered heterocyclic ring, which may contain an additional heteroatom selected from —O—, —S—, and —N(H, Alkyl)—, and optionally endure one or more alkyl or alkenyl substituents, and Z<sup>1</sup> designates an —OR or —NR<sup>1</sup>R<sup>2</sup> group, wherein R, R<sup>1</sup>, and R<sup>2</sup> are as defined before, or a group —NHCOCH<sub>3</sub>, which includes the base-catalyzed reaction of diacetyloxamide (I) with an alcohol ROH or/and an amine

**Acid Catalyzed Synthesis:**

HNR<sup>1</sup>R<sup>2</sup>. The compounds of formula (V) have many industrial utilities, mainly as intermediates and stabilizers in the polymer field (Scheme 2) [25].

### MATERIAL AND METHODS

All chemicals used were bought from “Sigma –Aldrich” and solvents were used after distillation. All reactions were monitored by using silica gel G TLC plates and the spots were detected under UV lamp and with the help of iodine vapors. TLC was also used to find the purity of the compound. IR spectra were recorded on Agilent microlab Cary 630 FTIR (ATR) spectrophotometer. Mass Spectrum of synthesized compound was noted on MAT-312. Melting points were taken by using Gallenkamp melting point apparatus through open capillary method.

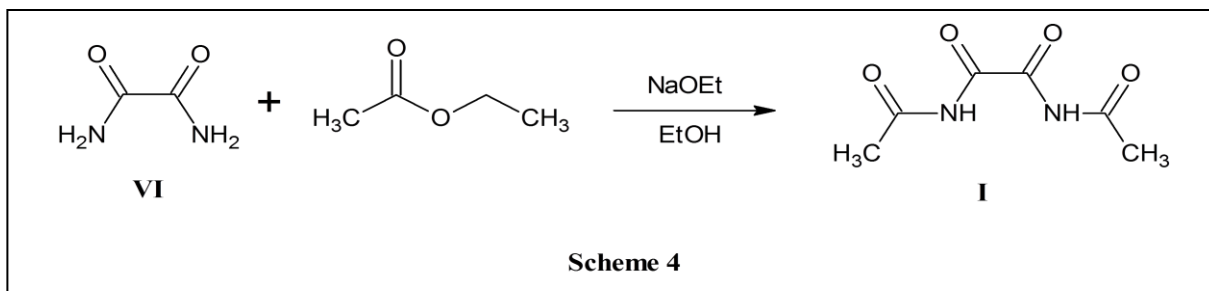


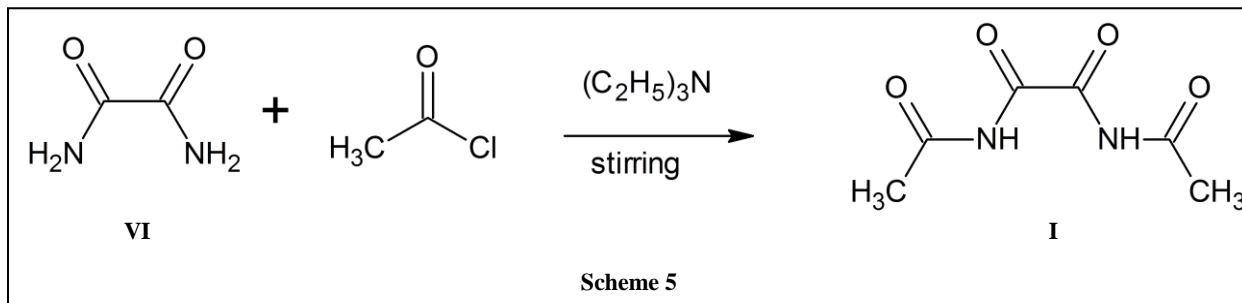
Glacial acetic acid (4 mL, 4.2 g, 0.07 mol) and acetyl chloride (4.98 mL, 5.5 g, 0.07 mol) was stirred with continuous heating until there was no HCl fumes evolution. Then oxamide (VI) (0.44 g, 0.005 mol) and one drop or 0.01 equivalents of catalyst was added in the above mixture. The reaction mixture was stirred for six hours at 100°C. Reaction was conducted under moisture free conditions. The reaction contents were poured into an ice cold distilled water (20 mL) with continuous stirring. The precipitates were filtered, dried and recrystallized from ethyl acetate or ethanol (Scheme 3).

Table 1 indicates percentage yields, melting points and IR spectral data of the products obtained under these conditions; m/z 172.1 (M<sup>+</sup>).

### Sodium Ethoxide (NaOEt) Catalyzed Synthesis:

Chunks of sodium metal (0.02 mol, 0.46 g) were added in excess of ethanol this led to the formation of sodium ethoxide. Ethyl acetate (1.96 mL, 1.76 g, 0.02 mol) was added in the reaction mixture. Then oxamide (VI) (0.88 g, 0.01 mol) was added and the mixture was refluxed with constant stirring. Whole experiment was performed under





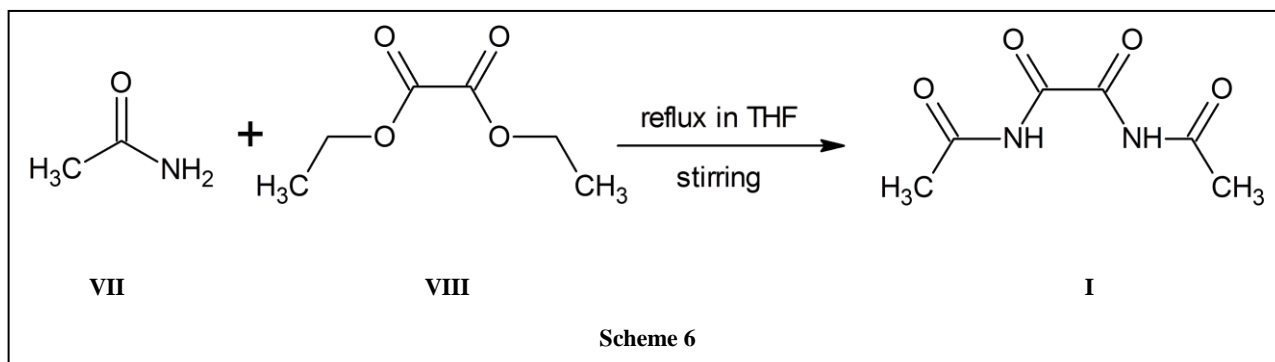
moisture free conditions. The reaction mixture was poured in an ice cold distilled water (20 mL) and it was stirred well. Precipitates formed were filtered, dried and recrystallized from ethyl acetate having M.P. 233°C and Yield: 2%. IR ( $\text{cm}^{-1}$ ) 3382, 3188 (NH- str), 2905 ( $\text{CH}_3$ - str), 1662 (C=O str) (**Scheme 4**).

#### Triethylamine Catalyzed Reaction:

Mixture of Acetyl chloride (5mL as solvent), oxamide (**VI**) (0.44 g, 0.005 mol) and triethylamine (0.505g, 0.7mL, 0.005 mol) was stirred at room temperature under moisture free conditions. The reaction mixture was poured into an ice cold distilled water (20 mL). Precipitates were filtered out, dried and recrystallized from ethyl acetate. Melting point of the precipitates was 274 °C. IR ( $\text{cm}^{-1}$ ): 3382, 3181 (NH<sub>2</sub>- str), 1655 (C=O str) (**Scheme 5**).

#### Reaction of Acetamide and Diethyl oxalate:

Acetamide (**VII**) (1.18 g, 0.02 mol) and diethyl oxalate (**VIII**) (1.4 mL, 1.46 g, 0.01 mol) was suspended in



tetrahydrofuran (THF) (20 mL as solvent). The reaction mixture was refluxed for six hours with constant stirring. The reaction contents were cooled in an ice bath. The colorless crystals appeared were filtered, washed thoroughly with n-hexane, dried in air at room temperature. M.P. of the crystals was 78 °C, IR ( $\text{cm}^{-1}$ ): 3305, 3150 (NH<sub>2</sub>- str), 2819 ( $\text{CH}_3$  str), 1735, 1719 (C=O str) (**Scheme 6**).

## RESULTS AND DISCUSSION

In this study N, N'-Diacetyloxamide has synthesized using different methods in an attempt to achieve excellent yield of the product.

#### Acid Catalyzed Synthesis:

In following cases reaction was catalyzed by some acids under above mentioned conditions (**Scheme 3**). Percentage

yields, melting points and IR spectral data of the products from various methods are tabulated in Table 1.

When perchloric acid ( $\text{HClO}_4$ ) was used as catalyst the product obtained has 233°C melting point and FTIR spectra contain peak at  $3251 \text{ cm}^{-1}$  which indicate the presence of (N-H) group, peak at  $2941 \text{ cm}^{-1}$  is due to the presence of ( $-\text{CH}_3$ ) group and peaks at  $1735 \text{ cm}^{-1}$ ,  $1685 \text{ cm}^{-1}$  shows the presence of (C=O) group. Mass spectrum of the prepared compound shows peak at  $m/z$  172.1 ( $\text{M}^+$ ) which is exactly similar to the calculated value (172.1) for  $\text{C}_6\text{H}_8\text{N}_2\text{O}_4$ . All this data indicate the formation of our target molecule *i-e* N, N'-diacetyloxamide having 82% yield

In the presence of sulfuric acid ( $\text{H}_2\text{SO}_4$ ) reaction produced appreciable amount of product having 234 °C melting point and bands in FTIR spectra are at  $3278 \text{ cm}^{-1}$ ,  $3203 \text{ cm}^{-1}$  which may be due to the presence of (N-H) group, at  $2950 \text{ cm}^{-1}$  is due to ( $-\text{CH}_3$ ) group and at  $1750 \text{ cm}^{-1}$ ,  $1700 \text{ cm}^{-1}$  shows the presence of (C=O) group. From this data it is inferred that the reaction was successful with 78% yield.

With poly phosphoric acid (PPA) reaction product has melting point 236 °C and FTIR analysis indicates that product contains (N-H) group showing peaks at  $3278 \text{ cm}^{-1}$ ,  $3203 \text{ cm}^{-1}$  and peak at  $2950 \text{ cm}^{-1}$  is due the ( $-\text{CH}_3$ ) group and bands at  $1752 \text{ cm}^{-1}$ ,  $1700 \text{ cm}^{-1}$  indicate the presence of (C=O) group. From this information it is inferred that PPA give the product with 74% yield.

It is observed that when para toluene sulphonic acid (PTSA) was used to catalyze the reaction melting point of the product was 294°C and in FTIR spectra peaks at  $3374 \text{ cm}^{-1}$ ,  $3173 \text{ cm}^{-1}$  indicate existence of (N-H) group and peak at  $1648 \text{ cm}^{-1}$  shows that (C=O) group is also present but there is no peak around  $2900 \text{ cm}^{-1}$  indicating the absence of methyl ( $-\text{CH}_3$ ) group. This information helps to deduce that PTSA did not

**Table-1: Summary of Different Acid Catalyzed Reactions used to Synthesize N, N'-Diacetyloxamide (I):**

Sr.No.	Sample Code	Catalyst	M.P (°C)	IR Stretching (cm <sup>-1</sup> )			Yield (%)
				N-H	CH <sub>3</sub>	C=O	
01	Ra-4	HClO <sub>4</sub>	233	3251	2941	1735, 1685	82
02	RA-5 16	H <sub>2</sub> SO <sub>4</sub>	234	3278, 3203	2950	1750, 1700	78
03	RO-7	PPA	236	3278, 3203	2950	1752, 1700	74
04	RA-12	FeCl <sub>3</sub>	234	3276, 3203	2946	1749, 1700	64
05	RA-10	ZnCl <sub>2</sub>	232	3278	2987, 2950	1752, 1700	61
06	RA-18	POCl <sub>3</sub>	234	3275, 3203	2920	1746, 1698	47
07	RA-13	SnCl <sub>2</sub>	236	3278, 3203	2946	1747, 1700	40
08	RA-9	CF <sub>3</sub> COOH	290	3375, 3170	-	1649, 1606	Reactant recovered
09	RO-6	H <sub>3</sub> PO <sub>4</sub>	290	3377, 3173	-	1655	Reactant recovered
10	RA-8	CCl <sub>3</sub> COOH	278-292	3382, 3173	-	1655, 1610	Reactant recovered
11	RA-6	PTSA	294	3382, 3181	-	1662	Reactant recovered
12	RO-11	CuCl <sub>2</sub>	276	3374, 3173	-	1648, 1610	Reactant recovered
13	RA-14	NiCl <sub>2</sub>	286-312	3375, 3172	-	1644, 1609	Reactant recovered
14	RA-15	AgCl <sub>2</sub>	288-320	3373, 3168	-	1642, 1605	Reactant recovered
15	RA-16	HgCl <sub>2</sub>	264	3373, 3168	-	1642, 1605	Reactant recovered
16	RA-17	AlCl <sub>3</sub>	244-290	3375, 3164	-	1654, 1606	Reactant recovered

work in catalysis of this reaction. Similar results were obtained with H<sub>3</sub>PO<sub>4</sub>, CCl<sub>3</sub>COOH and CF<sub>3</sub>COOH.

N, N'-Diacetyloxamide was prepared from same methodology (**scheme 3**) the only difference was the catalyst, here Lewis acids were used to catalyze the reaction.

When reaction was carried out in the presence of zinc chloride (ZnCl<sub>2</sub>), melting point of the product was 232 °C which is near the melting point reported in literature [1] and FTIR analysis shows peaks at 3278 cm<sup>-1</sup> which is due to (N-H) group, at 2987 cm<sup>-1</sup>, 2950 cm<sup>-1</sup> due to (-CH<sub>3</sub>) group and at 1752cm<sup>-1</sup>, 1700 cm<sup>-1</sup> because of (C=O) functional group. This data tells us the presence of acetyl group in the molecule giving an indication of accomplishment of reaction with 61% yield

From ferric chloride (FeCl<sub>3</sub>) catalyzed reaction the product has melting point 234°C and FTIR spectra shows peaks at 3276 cm<sup>-1</sup>, 3203 cm<sup>-1</sup> indicating (N-H) group, at 2946 cm<sup>-1</sup> due to (-CH<sub>3</sub>) group, and at 1749 cm<sup>-1</sup>, 1700 cm<sup>-1</sup> because of (C=O) functionality. This data leads to the inference that acetylation of oxamide has successfully occurred giving product with 64% yield.

The product obtained from tin chloride catalyzed reaction has melting point 236 °C which is in close proximity of reported melting point [1] and FTIR analysis showing peaks at 3278 cm<sup>-1</sup>, 3203 cm<sup>-1</sup> due to (N-H) group, at 2946 cm<sup>-1</sup> because of (-CH<sub>3</sub>) group and bands at 1747 cm<sup>-1</sup>, 1700 cm<sup>-1</sup>, notify the existence of (C=O) moiety, indicate the effectiveness of SnCl<sub>2</sub> in catalysis of this reaction. Percentage yield of the product was 40%.

When phosphoryl chloride (POCl<sub>3</sub>) was used as catalyst the yield was 47% and melting point of the product was 234 °C which is close to the melting point given in literature [1]. In FTIR spectra bands at 3275 cm<sup>-1</sup>, 3203 cm<sup>-1</sup> indicate the presence of (N-H) moiety, at 2920 cm<sup>-1</sup> shows the existence of (-CH<sub>3</sub>) group and at 1746 cm<sup>-1</sup>, 1698 cm<sup>-1</sup> may be due to (C=O) functionality. All of the information given above is evident in favor of formation of N, N'-Diacetyloxamide.

It has been observed that with copper (II) chloride(CuCl<sub>2</sub>), product has 276°C melting point and FTIR spectra has peaks

at 3374 cm<sup>-1</sup>, 3173 cm<sup>-1</sup> due to (N-H) group, and at 1648 cm<sup>-1</sup> due to the (C=O) group of the oxamide. There is no peak around 2900 cm<sup>-1</sup> which indicate that compound do not has acetyl group. From melting point and FTIR data it is deduced that CuCl<sub>2</sub> did not catalyze the reaction. Almost similar results have been observed with NiCl<sub>2</sub>, AgCl<sub>2</sub>, HgCl<sub>2</sub>, and AlCl<sub>3</sub>.

#### Base Catalyzed Synthesis:

In sodium ethoxide (NaOEt) catalyzed reaction (**Scheme 4**) FTIR spectra of product shows peaks at 3382 cm<sup>-1</sup>, 3188 cm<sup>-1</sup> which indicate the presence of (N-H) group in the molecule, peak at 2905 cm<sup>-1</sup> indicate that the molecule contain (-CH<sub>3</sub>) group which is the strong indication of the presence of acetyl group in the compound because this peak is absent in the reactant molecule. Band at 1662 cm<sup>-1</sup> shows the presence of (C=O) functional group in the molecule. This information confirmed the synthesis of N, N'-Diacetyloxamide.

From FTIR spectra peaks at 3382 cm<sup>-1</sup>, 3181 cm<sup>-1</sup> shows the presence of (N-H) group in the molecule and bands at 1655 cm<sup>-1</sup> shows the (C=O) group of oxamide. There is no peak in 2900 cm<sup>-1</sup> region which indicate that the reaction did not take place. Melting point i-e. 278 °C also shows that the reactant was recovered.

#### Synthesis of N, N'-Diacetyloxamide from Acetamide and Diethyl oxalate:

Melting point of the product was 78 °C which is very close to the reported melting point and peaks in FTIR spectra are at 3305 cm<sup>-1</sup>, 3150 cm<sup>-1</sup> indicating (N-H) group of amide, 2819 cm<sup>-1</sup> band representing (CH<sub>3</sub>) group and 1676 cm<sup>-1</sup>, 1670 cm<sup>-1</sup> peaks may be due to (C=O) group. From this data it is inferred that reactant was recovered.

#### CONCLUSION

We have synthesized N, N'-diacetyloxamide (**I**) from specific methods using various catalysts and characterized on the basis of physical data i-e. melting point and FTIR spectral data. In FTIR peak at 2950 cm<sup>-1</sup> gives the strong indication of the presence of (-CH<sub>3</sub>) group in the molecule which is not present in the reactant molecule. Further confirmation is

given by melting point data. From our study we deduced that reactions catalyzed by strong acids are successful. Among mineral acids perchloric acid ( $\text{HClO}_4$ ) gives the best yield i.e. 82%. Sulfuric acid ( $\text{H}_2\text{SO}_4$ ) and poly phosphoric acid (PPA) also give appreciable yields (78% and 74% respectively) while para toluene sulfonic acid (PTSA), ortho phosphoric acid ( $\text{H}_3\text{PO}_4$ ), trichloroacetic acid ( $\text{CCl}_3\text{COOH}$ ) and trifluoroacetic acid ( $\text{CF}_3\text{COOH}$ ) are unable to catalyze the reaction. Amongst Lewis acid ferric chloride ( $\text{FeCl}_3$ ), zinc chloride ( $\text{ZnCl}_2$ ), phosphoryl chloride ( $\text{POCl}_3$ ) and tin chloride ( $\text{SnCl}_2$ ) give 61-40% yields. Copper (II) chloride ( $\text{CuCl}_2$ ), nickel chloride ( $\text{NiCl}_2$ ), silver chloride ( $\text{AgCl}_2$ ), mercury (II) chloride ( $\text{HgCl}_2$ ) and aluminium chloride ( $\text{AlCl}_3$ ) catalyzed reactions are not useful to synthesize this compound. In the presence of sodium ethoxide yield (2%) is very poor. In case of triethylamine catalyzed reaction and reaction between acetamide and oxalyl chloride reactant has recovered.

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