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Research Article

ACTION OF ORGANIC AND INORGANIC HALOCOMPOUNDS ON FURFURALDEHYDE DI-N-PROPYLACETAL AT LOW TEMPERATURE

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ABSTRACT

The furfuraldehyde di-n-propylacetal was synthesized and its reactions with halocompounds viz., benzoyl bromide, *p*-chlorobenzyl chloride, N-chlorosuccinimide, phosphorous trichloride, aluminium chloride, phosphorous oxychloride and titanium oxychloride were studied at -20°C. The acetal generated esters with benzoyl bromide and aluminium chloride while ring chloro substituted ester with N-chlorosuccinimide. The acetal produced ether with *p*-chlorobenzyl chloride, but only aldehyde with phosphorous trichloride, and phosphorous oxychloride. Interestingly, the acetal yielded substituted aldehyde alone with titanium oxychloride. Organic and inorganic halocompounds are synthetically very useful reagents and vary widely in their acceptor synthon character and reactivity; hence their application in the present work on the action of halocompounds on furfuraldehyde di-n-propylacetal is a new venture.

Keywords: Furfuraldehyde di-n-propylacetal, Benzoyl bromide, Aluminium chloride, N-chlorosuccinimide, p-chlorobenzyl chloride, Phosphorous trichloride, Phosphorous oxychloride, Titanium oxychloride, Ethanol and acetonitrile.

INTRODUCTION

Acetals play a vital role in bioorganic research[1-5] in exploring, antimalarial[1], antiviral[2], antibacterial[3], anti-inflammatory[4], antitumor[5] and anticancer[5] activities. The action of halo compounds [6,7] and Lewis acids[8]on aromatic and hetero aromatic acetals and the rearrangements of aromatic acetals over solid acids[9] are reported in literature.

Acetal derivatives of aldehyde are valuable in synthesis either as intermediates or as protecting groups. It is known that acetals are susceptible to addition[10], oxidation[11], reduction[12], rearrangement condensation[13]and hydrolysis[14] in presence of catalysts.

The use of titanium chloride[15] and stannic chloride in organic reactions is of relatively recent origin. Titanium tetrachloride and its alkoxy derivatives have been used in many reactions[16].

Studies of substituent effects on aromatic acetals by Lewis acids[15] were investigated by Dr. T.V. Antony on the mechanism of rearrangement of aromatic acetals by the action of $SnCl_4$. The reaction conducted in 1,2-dichloroethane was postulated to pass through carbocation intermediate which on subsequent alkoxide coordination yields ester.

Apart from the metal halides and alkoxides, non-metallic compounds such as boron trifluoride, iodine and its interhalogen compounds have also been used extensively by various researchers[17,18].

Studies on the rearrangement of aromatic acetals with different Lewis Acids[19] were investigated on various aromatic acetals and the mechanisms were proposed based on carbocation intermediate.

The reactions of aliphatic acetals catalyzed by solid acids[9] have been extensively studied by various researchers and in most cases synthetically important α, β-unsaturated ethers have been obtained as the major products. The unsaturated ether was shown to be formed by the elimination of alkoxy group followed by the removal of a proton from the β-carbon of acetal.

The elimination may occur either in a concerted or stepwise manner depending on the nature of the catalyst. The results of the action of halocompounds on furfuraldehyde di-n-propylacetal in acetonitrile and ethanol medium are reported in the present investigation.

MATERIALS

Substrate

The Furfuraldehyde di-n-propylacetal was prepared and its purity was checked spectroscopically.

Solvent

The acetonitrile and ethanol were purified by standard method and used as the solvents.

Reagents

BDH samples of benzoyl bromide, aluminium chloride, N-chlorosuccinimide, *p*-chlorobenzyl chloride, phosphorous trichloride, phosphorous oxychloride and titanium oxychloride were bought and used for the reactions.

MATERIALS AND METHODS

Acetal preparation

Furfuraldehyde di-n-propylacetal

48gm (0.5mol) of freshly vacuum distilled furfuraldehyde and 89gm (1.2mol) of distilled n-propyl alcohol were taken in a 500ml round-bottomed flask fitted with a Dean-Stark apparatus carrying a reflux condenser attached to a calcium chloride guard tube. 0.05g of *p*-toluenesulphonic acid and 80ml of pure dry benzene were added to the solution and the mixture was refluxed for 6 hours.

The flask was cooled to room temperature and the contents were washed with 1M sodium bicarbonate solution and then with water. The solution was dried over potassium carbonate. After evaporation of the solvent, the liquid was distilled under reduced pressure. Pure acetal was collected at 142°C (15mm of Hg) and the yield was 75%.

n_D = 1.461 at 31° C

IR: v1040-1150 cm^{-1} (C-O-C)

PMR: δ 0.9 (6H, t, 2XCH_3), 1.45(4H, m, 2XCH_2-CH_3),

3.4(4H, t, 2X O-CH_2), 5.45(1H, S, furyl-CH),6.3-7.3(3H, m, furan-H)

Action of halocompounds on furfuraldehyde di-n-propylacetal

a) Reaction of benzoyl bromide with furfuraldehyde di-n-propylacetal

5 ml of acetal in 10 ml of acetonitrile was taken in a 250 ml conical flask. 3.5 g of benzoyl bromide was dissolved in 10 ml of acetonitrile and was added drop wise to the same flask fitted with a magnetic stirrer. The temperature was maintained at -20 °C throughout the reaction with the help of cooling unit (cold chamber). The reaction mixture was continuously stirred for 1 hour and was washed with water and the products were extracted with diethyl ether. Then, the

resulting reaction mixture was spotted at the TLC (10% diethyl ether and 90% n-hexane) with authenticated sample (ester). Finally, the products were separated by column chromatography and were identified by IR and PMR spectra to be the ester.

b) Reaction of aluminium chloride with furfuraldehyde di-n-propylacetal

5 ml of acetal in 10 ml of acetonitrile was taken in a 250 ml conical flask. 2.7 g of aluminium chloride was dissolved in 10 mL of acetonitrile and was added drop wise to the same flask fitted with a magnetic stirrer. The temperature was maintained at -20°C throughout the reaction with the help of cooling unit (cold chamber). The reaction mixture was continuously stirred for 1 hour and was washed with water and the products were extracted with diethyl ether. Then, the resulting reaction mixture was spotted at the TLC (10% diethyl ether and 90% n-hexane) with authenticated sample (ester). Finally, the products were separated by column chromatography and were identified by IR and PMR spectra to be the ester.

c) Reaction of N-chlorosuccinimide with furfuraldehyde di-n-propylacetal

5 ml of acetal in 10 ml of acetonitrile was taken in a 250 ml conical flask. 3.5 g of N-chlorosuccinimide was dissolved in 10 ml of acetonitrile and was added drop wise to the same flask fitted with a magnetic stirrer. The temperature was maintained at -20°C throughout the reaction with the help of cooling unit (cold chamber). The reaction mixture was continuously stirred for 1 hour and was washed with water and the products were extracted with diethyl ether. Then, the resulting reaction mixture was spotted at the TLC (10% diethyl ether and 90% n-hexane). Finally, the products were separated by column chromatography and were identified by IR and PMR spectra to be the ring chlorinated ester.

d) Reaction of p-chlorobenzyl chloride with furfuraldehyde di-n-propylacetal

5 ml of acetal in 10 ml of acetonitrile was taken in a 250 ml conical flask. 2.7 g of p-chlorobenzyl chloride was dissolved in 10 ml of acetonitrile and was added drop wise to the same flask fitted with a magnetic stirrer. The temperature was maintained at -20°C throughout the reaction with the help of cooling unit (cold chamber). The reaction mixture was continuously stirred for 1 hour and was washed with water and the products were extracted with diethyl ether. Then, the resulting reaction mixture was spotted at the TLC (10% diethyl ether and 90% n-hexane). Finally, the products were separated by column chromatography and were identified by IR and PMR spectra to be the ether.

e) Reaction of phosphorous trichloride with furfuraldehyde di-n-propylacetal

5 ml of acetal in 10 ml of acetonitrile was taken in a 250 ml conical flask. 2.5 g of phosphorous trichloride was dissolved in 10 ml of acetonitrile and was added drop wise to the same flask fitted with a magnetic stirrer. The temperature was maintained at -20°C throughout the reaction with the help of cooling unit (cold chamber). The reaction mixture was continuously stirred for 1 hour and was washed with water and the products were extracted with diethyl ether. Then, the resulting reaction mixture was spotted at the TLC (10% diethyl ether and 90% n-hexane). Finally, the products were separated by column chromatography and were identified by IR and PMR spectra to be the aldehyde.

f) Reaction of phosphorous oxychloride with furfuraldehyde di-n-propylacetal

5 ml of acetal in 10 ml of acetonitrile was taken in a 250 ml conical flask. 2.9 g of phosphorous oxychloride was dissolved in 10 ml of acetonitrile and was added drop wise to the same flask fitted with a magnetic stirrer. The temperature was maintained at -20°C throughout the reaction with the help of cooling unit (cold chamber). The reaction mixture was continuously stirred for 1 hour and was washed with water and the products were extracted with diethyl ether. Then, the resulting reaction mixture was spotted at the TLC (10% diethyl ether and 90% n-hexane). Finally, the products were separated by column chromatography and were identified by IR and PMR spectra to be the aldehyde.

g) Reaction of titanium oxychloride with furfuraldehyde di-n-propylacetal

5 ml of acetal in 10 ml of ethanol was taken in a 250 ml conical flask. 2.3 g of titanium oxychloride was dissolved in 10 ml of ethanol and was added drop wise to the same flask fitted with a magnetic stirrer. The temperature was maintained at -20°C throughout the reaction with the help of cooling unit (cold chamber). The reaction mixture was continuously stirred for 1 hour and was washed with water and the products were extracted with diethyl ether. Then, the resulting reaction mixture was spotted at the TLC (10% diethyl ether and 90% n-hexane). Finally, the products were separated by column chromatography and were identified by IR and PMR spectra to be the substituted aldehyde.

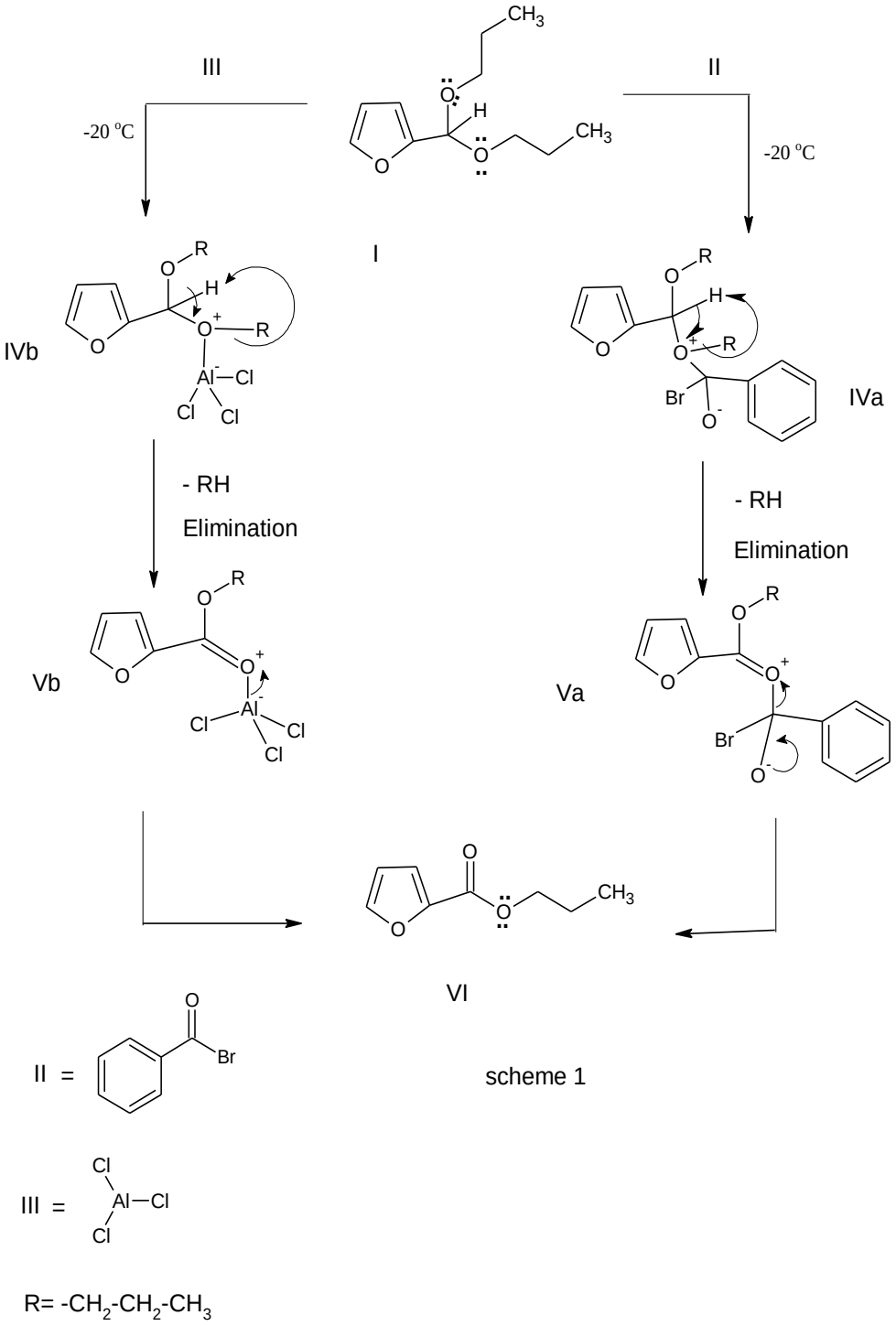
RESULTS AND DISCUSSION

The action of halocompounds on furfuraldehyde di-n-propylacetal

The acetal (I) contains the benzal carbon[17]atom which is surrounded by one H atom and three bulky groups namely phenyl ring and the two butoxy groups. The bulky groups are crowded around the benzal carbon atom. Thus the acetal requires steric relief. So the butoxy oxygen atom with two lone pairs is longing to extend one lone pair to any acceptor synthon giving oxonium ion which may result in the cleavage of one of the groups attached to the methine carbon[19] atom. The requirement of such steric relief from crowding of the groups around the methine (benzal) carbon atom in the acetal is expected to be the driving force for the ethereal oxygen atom of the acetal to coordinate with an acceptor synthon, which may result in the cleavage of the alkoxy group leaving the sp^3 carbon atom to become a roomier sp^2 carbon atom. Such a thirst of the ethereal oxygen atom has been quenched by the partial positive end of the reagent chosen.

In the present investigation the reagents selected are halocompounds which by their partial positive ends can quench the thirst of the ethereal oxygen atom by accepting its lone pair by the partial positive end. Thus the present study on the action of halocompounds on furfuraldehyde di-n-propylacetal is a new venture. The reagents benzoyl bromide and aluminium chloride react on the furfuraldehyde di-n-propylacetal to give ester, while N-chlorosuccinimide gives ring chlorinated ester. The reagent *p*-chlorobenzyl chloride reacts with furfuraldehyde di-n-propylacetal to produce ether. Phosphorous trichloride and phosphorous oxychloride react with furfuraldehyde di-n-propylacetal to yield furfuraldehyde while titanium oxychloride results in substituted benzaldehyde. The formation of ester indicates that this reaction follows the mechanism shown in scheme-1, while for the formation of ring chlorinated ester the reaction follows the mechanism shown in scheme-2. The product ether is formed according to the mechanism shown in scheme-3. The formation of aldehyde indicates that these reactions may pass through the mechanism in scheme–4, while the scheme-5 speaks of the mechanism of formation of substituted aldehyde.

The reagents benzoyl bromide (II) and aluminium chloride (III) are halocompounds which are ready to draw donor synthons towards the benzoyl carbon atom and the aluminium atom respectively. The acetal (I) makes use of its alkoxy oxygen atom to coordinate the above acceptor synthons and forms the corresponding oxonium ions (IVa & IVb). The oxonium ion intermediates experience a very high steric hindrance and result in the elimination of RH converting the sp^3 methine carbon atom into roomier sp^2 carbon atom of the oxonium ions (Va & Vb). The reagents benzoyl bromide and aluminium chloride have acted as catalysts producing the ester (VI) as the product shown in scheme-1. The formation of ester by the action of Lewis acid $SnCl_4$ has already been confirmed by T.V. Antony[15].



scheme 1

The reagent N-chlorosuccinimide (VII) is susceptible for releasing the acceptor synthon chloronium ion towards the acetal (I) resulting in the oxonium ion (VIII). The intermediate oxonium ion (VIII) undergoes elimination of RH to form the intermediate (IX).

The instability of the chloro oxonium ion and the proximity of the benzene ring to the chlorine atom drive to the formation of the six membered cyclic transition state (X), which is transformed into the σ- complex (XI). The succinimide anion base abstracts the proton which results in the ring chloro substituted ester (XII) as shown in scheme-2.

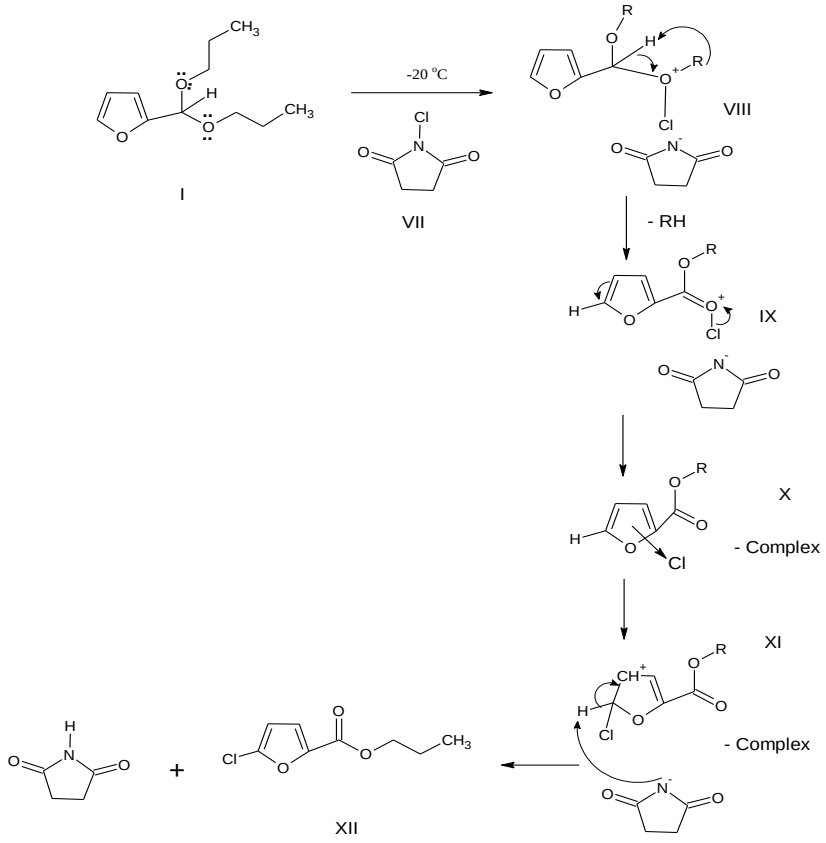
The formation of ring substituted ester is confirmed by the evidence that acetals have undergone oxidative C-O bond cleavage and simultaneous bromination with N,N-dibromobenzene sulphonamide to result in ester and alkyl bromide or brominated ester[21].

Swain and Crist[22] observed ring chlorination of anisole by hypochlorous acid, in which the ethereal oxygen atom is approached by the synthon, chloronium ion Cl^+, resulting in ring substitution.

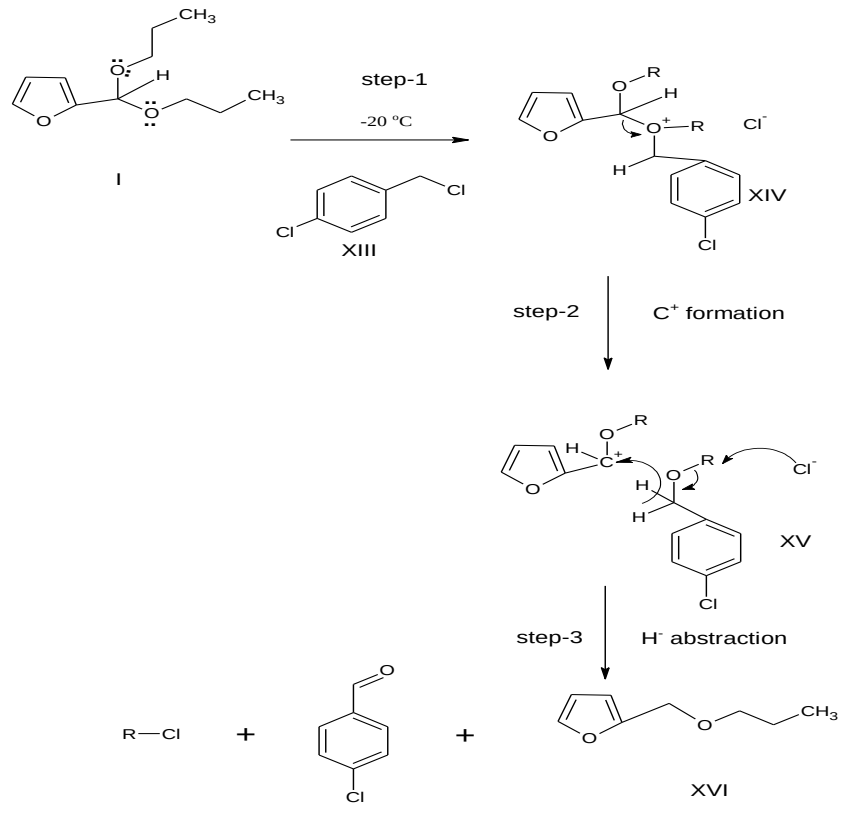
The aromatic electrophilic substitution is further affirmed from the migration of halogen in the Orton[23] rearrangement.

The above evidences strongly support the mechanism in which the substrate acetal had resulted in ring halogenated ester.

The formation of ring ester can be explained by E2 mechanism. The mechanistic steps are similar to those reported in the work of Xavier and Arulraj[9]. In their study the ester formation had occurred in a concerted way with the removal of the benzylic proton with the concomitant cleavage of the σ-bond of the alkyl group.



Scheme-2



Scheme 3

The reagent *p*-chlorobenzyl chloride (XIII) is acting as the substrate for aliphatic nucleophilic substitution reaction, the reaction centre being the benzyl carbon atom, the nucleophile being the butoxy oxygen atom of the acetal and the nucleofuge being the Cl^-ion. The substitution product is the oxonium ion (XIV). The steric strain of the oxonium ion is relieved by its conversion into the carbocation (XV). The carbocation (XV), gets stabilized by abstracting hydride ion as shown in step-3 resulting in the ether (XVI) in scheme-3.

The formation of ether might have passed through the mechanism involving carbocation intermediate that has been supported by several lines of evidences[17,20].

Reactions of some epoxy steroids[17] with boron trifluoride etherate had shown that the lone pair on the epoxy oxygen atom had coordinate with boron trifluoride etherate resulting in bond fission followed by the formation of a stable carbocation. Many similar reactions[20,24] of boron trifluoride etherate had clearly shown that such reactions passed through the carbocation intermediate.

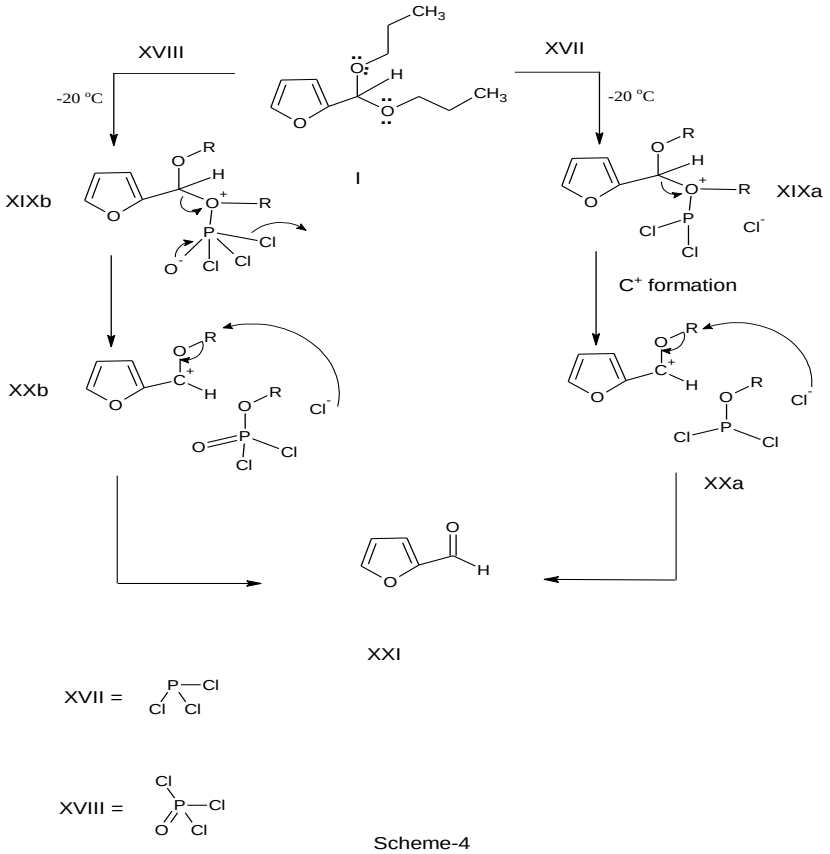
A direct observation of the formation of a carbocation was made by Robinovitz et al[14]. In their PMR study, they observed the formation of stable aryl-alkoxy carbocation when acetals of aromatic aldehydes were treated with boron fluoride in $CDCl_3$.

When Lewis acids act on aromatic acetals, there are evidences[15,16] for the formation of a coordination complex of the acetal with the Lewis acid and the subsequent cleavage of the alkoxy group producing a carbocation.

Reactions of acetals on active catalyst like aluminium phosphate[24] at elevated temperature also proved that the mechanism followed carbocation intermediate. The resultant carbocation intermediate would follow the pathway of abstracting hydride to form ether.

Masaki[17]investigated the backbone rearrangement of 5α,10α-epoxy alnusan-3β-yl acetate to multiflora 5, 8-dien-3β-yl acetate effected by boron trifluoride and the epoxide ring was found to be cleaved to yield a carbocation which initiated the migration of a hydride. Henbest[17] has also observed such hydride abstraction by the carbocation formed during the reactions of some epoxy steroids with boron trifluoride etherate. The action the same boron trifluoride etherate on methyl isopimarate 7, 8-epoxides studied by Tartan[20] involved carbocation intermediate that abstracts the hydride.

Similar abstraction of the hydride ion by the carbocation is postulated in the present mechanism and also the detection of aliphatic aldehyde of the type R'CHO evidently indicates the possible of this mechanism. It has been reported that acetals on alumina surface produce alkoxide which would readily transfer a hydride ion to reduce the carbocation yielding ether.

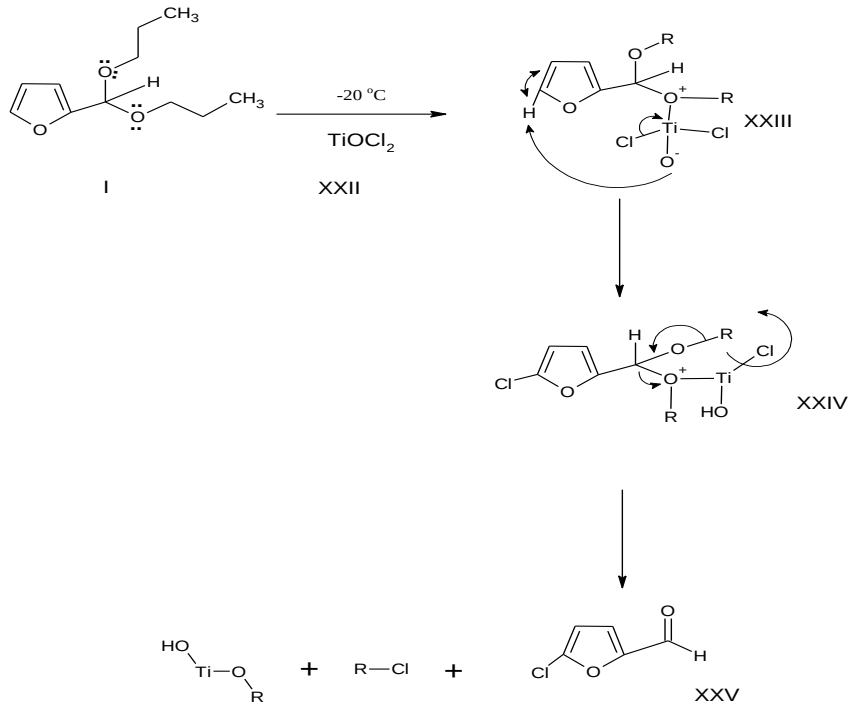


Scheme-4

The reagents phosphorous trichloride (XVII) and phosphorous oxychloride (XVIII) are halocompounds, which are ready to draw donor synthons towards the phosphorous atoms. The acetal (I) makes use of its alkoxy oxygen atom to coordinate with the above acceptor synthons and forms the corresponding oxonium ions (XIXa & XIXb). The steric strain of the oxonium ion is relieved by its conversion into the carbocation (XXa & XXb) in scheme-4. Eventhough the carbocation is formed in scheme-4 as in scheme-3, the carbocation is unable to get stabilized by the H^- abstraction in scheme-4 due to the non-availability of H^-. On the other hand the stability is achieved by expelling the R^+ to Cl^- resulting in the aldehyde (XXI).

The formation of aldehyde of aromatic nature has been confirmed by Xavier and Arulraj[9] when aromatic acetals in vapor phase were poured over γ-alumina.

The reagent titanium oxychloride (XXII) is susceptible for nucleophilic attack at the acetal (I) resulting in the oxonium ion (XXIII). In this case, since the acceptor synthon is only titanium oxychloride, the titanium is reduced and hence the sterically crowded methane carbon atom relieves the alkoxy substituted titanium. The Cl^- from the group departed cleaves R from the intermediate XXIV and produce the product ring chlorinated aldehyde in scheme-5.



Scheme-5

The formation of ring chlorinated aldehyde is further evidence from the work of K.Josephsanthanaraj[7]in the action of $SnCl_4$ on acetal.

CONCLUSION

The reactions of the furfuraldehyde di-n-propylacetal with halocompounds were studied at -20°C. The products formed and the mechanisms followed are given. The reagents benzoyl bromide and aluminium chloride produced ester, while N-Chlorosuccinimide produced ring chlorinated ester. *p*-chlorobenzyl chloride gave ether. The phosphorous trichloride and phosphorous oxychloride resulted in aldehyde. But titanium oxychloride is found to yield the product ring substituted aldehyde.

The formation of ester indicates that this reaction follows the mechanism shown in scheme-1. The ester formation would occur in a concerted way with simultaneous expulsion of both R & H as RH. The mechanism of ring substituted ester formation is explained in scheme-2, while the formation of ether is explained by the mechanism involving carbocation intermediate followed by the hydride abstraction in scheme-3. The formation of aldehyde is explained in scheme-4. The titanium oxychloride produced ring substituted aldehyde according to the scheme-5.

Just as the benzoyl bromide, aluminium chloride, N-chlorosuccinimide, *p*-chlorobenzyl chloride, phosphorous trichloride, phosphorous oxychloride and titanium oxychloride many more acceptor synthons can be used to react with the acetals and such reactions can be run. Many more aromatic nuclei like furan, pyrrole, thiophene, pyridine etc. other than the benzene nucleus can be used in the synthesis of the acetals. The same reagents used in the present study can also be treated with aliphatic acetals. The same reactions can also be conducted in different solvents as well as in different temperatures.

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