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ACTION OF ACID CHLORIDES ON BENZALDEHYDE DI-N-BUTYLACETAL AT LOW TEMPERATURE

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ABSTRACT: The benzaldehyde di-n-butylacetal has been synthesized and its reactions with acid chlorides, viz., acetylchloride, benzoylchloride, benzylchloride, perchloricacid, sodiumperchlorate, zirconiumoxychloride and calciumoxychloride have been studied at -20°C. The acetal generates esters with acetylchloride, benzoylchloride and perchloricacid while produced ether with benzylchloride, but only aldehyde with sodiumperchlorate. Interestingly, acetal yields substituted aldehyde alone with zirconiumoxychloride and calciumoxychloride. Acid chlorides 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 acid chlorides on benzaldehyde di-n-butylacetal is a new venture.

Keywords: Benzaldehyde di–n–butylacetal, Acetylchloride, Benzoylchloride, Benzylchloride, Perchloricacid,Sodiumperchlorate, Zirconiumoxychloride, Calciumoxychloride and Acetonitrile.

INTRODUCTION

Acetals play a vital role in bioorganic research in exploring, antimalarial, antiviral, antibacterial, anti-inflammatory, antitumor and anticancer activities. The action of aromatic and heteroaromatic acetals by halo compounds [1, 11], Lewis acids[3] and the rearrangements of aromatic acetals over solid acids[7] 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[8], oxidation[6], reduction[2], rearrangement condensation[4] and hydrolysis[9] in presence of catalysts.

The use of titanium chloride[10] and stannic chloride in organic reactions is of relatively recent origin. Titanium tetrachloride and its alkoxy derivatives have been used in many reactions[12].

Studies of substituent effects on Aromatic Acetals by Lewis cids[10], has investigated the effect of ring substituent on the mechanism of rearrangement of aromatic acetals by the action of $SnCl_4$. The reaction conducted in 1,2-dichloroethane has been postulated to pass through carbocation intermediate which on subsequent alkoxide coordination yields esters.

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[16,17].

Studies on the Rearrangement of aromatic acetals with different Lewis Acids[15] has investigated on various aromatic acetals and proposed mechanism based on carbocation intermediate.

The reactions of aliphatic acetals catalyzed by solid acids[7] 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 acid chlorides on benzaldehyde di–n-butylacetal in acetonitrile medium are reported in the present investigation.

MATERIALS

Benzaldehyde di-n-butylacetal was prepared and its purity was checked spectroscopically. The acetonitrile was purified by standard method and used as a solvent.

EXPERIMENTAL SECTION

a) Reaction of acetylchloride with benzaldehyde di- n-butylacetal

5 mL of acetal in 10 mL of acetonitrile was taken in a 250 mL conical flask, 3.5 g of acetyl 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 ºC 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 benzoylchloride with benzaldehyde di-n-butylacetal

5 mL of acetal in 10 mL of acetonitrile was taken in a 250 mL conical flask, 2.7 g of benzoylchloride was dissolved in 10 mL of acetonitrile and was added drop wise to the same flask, fitted with a magnetic stirrer. The temperature was kept at -20 ºC.The reaction mixture was continuously stirred for 1 hour at -20 ºC. The reaction mixture was washed with water and the products were extracted with 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 perchloricacid with benzaldehyde di-n-butylacetal

5 mL of acetal in 10 mL of acetonitrile was taken in a 250 mL conical flask, 2.1 g of perchloric acid was dissolved in 10 mL of acetonitrile and was added drop wise to the same flask, fitted with a magnetic stirrer. The temperature was kept at -20 ºC.The reaction mixture was stirred and the stirring was continued for 1 hour. The reaction mixture was washed with water and the products were extracted with ether. The resulting reaction mixture was spotted at the TLC (10% diethyl ether and 90% n-hexane). The products were separated by column chromatography and were identified by IR and PMR spectra to be the ester.

d) Reaction of benzylchloride with benzaldehyde di-n-butylacetal

5 mL of acetal in 10 mL of acetonitrile was taken in a 250 mL conical flask, 2.7 g of benzyl 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 kept at -20 ºC.The reaction mixture was stirred and the stirring was continued for 1 hour. The reaction mixture was washed with water and the products were extracted with ether. The resulting reaction mixture was spotted at the TLC (10% diethyl ether and 90% n-hexane). The products were separated by column chromatography and were identified by IR and PMR spectra to be the ether.

e) Reaction of sodiumperchlorate with benzaldehyde di-n-butylacetal

5 mL of acetal in 10 mL of ethanol was taken in a 250 mL conical flask, 2.5 g of sodiumperchlorate was dissolved in 10 mL of ethanol and was added drop wise to the same flask, fitted with a magnetic stirrer. The temperature was kept at -20 ºC.The reaction mixture was stirred and the stirring was continued for 1 hour. The reaction mixture was washed with water and the products were extracted with ether. The resulting reaction mixture was spotted at the TLC (10% diethyl ether and 90% n-hexane). The products were separated by column chromatography and were identified by IR and PMR spectra to be the aldehyde.

f) Reaction of zirconiumoxychloride with benzaldehyde di-n-butylacetal

5 mL of acetal in 10 mL of ethanol was taken in a 250 mL conical flask, 2.9 g of zirconium 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 kept at -20 ºC.The reaction mixture was stirred and the stirring was continued for 1 hour. The reaction mixture was washed with water and the products were extracted with ether. The resulting reaction mixture was spotted at the TLC (10% diethyl ether and 90% n-hexane).The products were separated by column chromatography and were identified by IR and PMR spectra to be the substituted aldehyde.

g) Reaction of calciumoxychloride with benzaldehyde di-n-butylacetal

5 mL of acetal in 10 mL of ethanol was taken in a 250 mL conical flask, 2.3 g of calcium 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 kept at -20 ºC.The reaction mixture was stirred and the stirring was continued for 1 hour. The reaction mixture was washed with water and the products were extracted with ether. The resulting reaction mixture was spotted at the TLC (10% diethyl ether and 90% n-hexane).The products were separated by column chromatography and were identified by IR and PMR spectra to be the substituted aldehyde.

RESULTS AND DISCUSSION

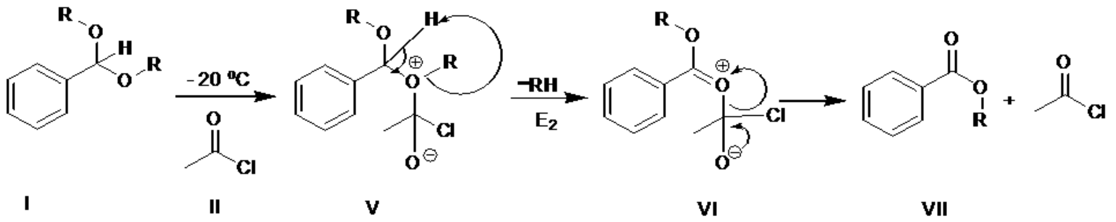
The action of acid chloride compounds on acetal

The acetal (I) contains the benzal carbon[3, 16] atoms which is surrounded by one H atom and the other three bulky groups namely phenyl ring and the two butoxy groups. 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 which may result in the cleavage of one of the groups attached to the methine carbon[15] atom. The requirement of 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 carbonyl carbon atom of the acid chlorides.

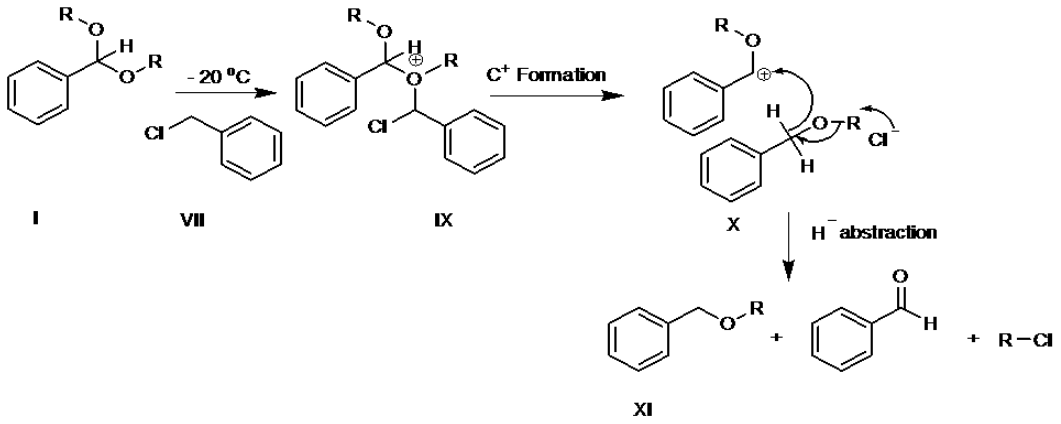
In the place of Lewis acids the reagents selected in the present investigation is acid chloride which can quench the thirst of the ethereal oxygen atom by accepting its lone pair by the partial positive carbonyl carbon atom. Thus the present study on the action of acid chlorides on benzaldehyde di-n-butylacetal is a new venture. The action of acetylchloride, benzoylchloride, perchloricacid, benzylchloride, sodium perchlorate, zirconiumoxychloride and calciumoxychloride on *benzaldehyde di-n-butylacetal* gave the corresponding ester, ether, aldehyde and substituted aldehyde. The formation of ester indicates that these reactions may pass through the E_2 mechanism as shown in scheme–1, while the formation of ether indicates that these reactions may pass through the mechanism involving carbocation intermediate as shown in scheme–2. And the formation of substituted aldehyde indicates that these reactions may pass through the electrophilic substitution on benzene nucleus shown in scheme–4.

A direct observation of the formation of a carbocation was made by Robinovitz et al.[13] 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[14, 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[16] 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.

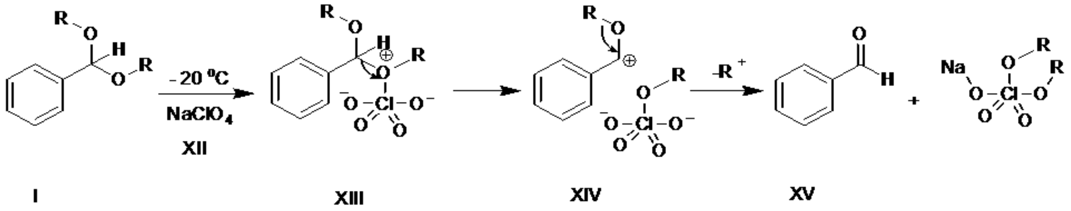
Masaki[17] investigated the backbone rearrangement of 5α, 10α-epoxy alnusan-3β-yl acetate to multiflora 5, 8-dien-3β-yl acetate effected by boron trifluoride and the epoxide ring was found to be cleaved to yield a carbocation which initiated the migration of a hydride.Henbest[16] has also observed such 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[14] involved carbocation intermediate that abstracts the hydride.



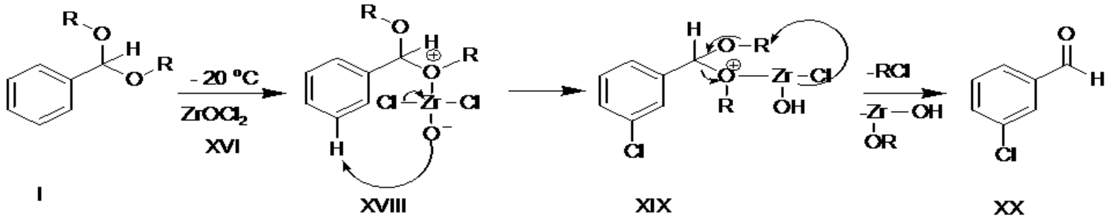
Sheme-1



Sheme-2



Scheme - 3



Scheme - 4

The reagents acetylchloride (II), benzoylchloride (III) and perchloricacid (IV) are acid chlorides which are ready to draw donor synthons towards them, since the chlorine and oxygen atoms are having electron withdrawing inductive effect (-I effect) thus the acetal (I) makes use of its alkoxy oxygen and forms oxonium ion (V).

The oxonium ion intermediate (V) experiences a very high steric hindrance and results in the elimination of RH converting the sp^3 methine carbon atom into roomier sp^2 carbon atom of the oxonium ion. Thus the intermediate (VI) is resulted. The reagents acetylchloride, benzoylchloride and perchloricacid have acted as catalysts producing the ester (VII) as the product shown in scheme-1.

The reagent benzylchloride (VIII) is susceptible for nucleophilic attack like (V) at the acetal (I) resulting in the oxonium ion (IX).The intermediate oxonium ion (IX), forms carbocation (X). The carbocation (X) can undergo hydride abstraction leading to ether with the simultaneous formation of benzaldehyde and aliphatic chloride. The reagent benzylchloride has acted as the catalyst producing the ether (XI) as the product shown in scheme -2.

The reagent sodiumperchlorate (XII) is susceptible for nucleophilic attack like (V) at the acetal (I) resulting in the oxonium ion (XIII).Since the four oxygen atoms are having electron withdrawing inductive effect (-I effect) and cause the steric hindrance to the R group of the alkoxy oxygen atom of the oxonium ion. The steric hindrance experienced by the R group is the driving force for the R to get cleaved as $R\text{-}OClO_4$. Thus the intermediate (XIV) is resulted. The reagent sodiumperchlorate has acted as catalyst and is relieved as sodiumdialkylperchlorate when the aldehyde (XV) is formed as the product as shown in scheme-3.

The reagents zirconiumoxychloride (XVI) and calciumoxychloride (XVII) are susceptible for nucleophilic attack like (V) at the acetal (I) resulting in the oxonium ion (XVIII). In this case, since the acceptor synthons are only zirconiumoxychloride and calciumoxychloride, the zirconium is reduced, hence the R group attached to the oxonium oxygen is not so much sterically hindered as in the case of (XIII). Thus the intermediate (XIX) is resulted. Hence the R group found in the other alkoxy group is cleaved as RCl resulting in substituted aldehyde (XX) is formed as the product shown in scheme-4.

CONCLUSION

The reactions of the benzaldehyde di-n-butylacetal with acid chloride compounds were studied at -20 °C. The products formed and the mechanisms followed are given. The reagents acetylchloride, benzoylchloride and perchloricacid produced ester, while benzylchloride gave ether. Sodiumperchlorate resulted in aldehyde. But zirconiumoxychloride and calcium oxychloride were found to yield the product substituted aldehyde.

The formation of ester is explained by the E_2 mechanism in scheme-1. The ester formation would occur in a concerted way with simultaneous intervention of both functions; the removal of a benzylic proton by R group takes place following the expulsion of the acid chloride, while the formation of ether is explained by the mechanism involving carbocation intermediate followed by the hydride abstraction in scheme-2. But the formation of substituted aldehyde is the Cl atom from the zirconiumoxychloride part in the oxonium ion is relieved as the electrophile and attacks the benzene nucleus resulting in the substituted aldehyde shown in scheme-4.

Just as the acetylchloride, benzoylchloride, perchloricacid, benzylchloride, sodium perchlorate, zirconiumoxychloride and calciumoxychloride 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, heteroaromatic acetals with different hetero atoms such as N, S and O.

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