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Reactions of Chlorine Gas on Benzaldehyde-di-*n*-alkyl Acetals

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Abstract: Reactions of chlorine gas on six aromatic acetals, the benzaldehyde di-*n*-alkyl acetals, $C_6H_4-CH(OR)_2$ where R=ethyl (**1a**), *n*-propyl (**2a**), *n*-butyl (**3a**), isobutyl (**4a**), *n*-amyl (**5a**) and isoamyl (**6a**) were studied. The products were analyzed by IR and 1H NMR spectroscopic techniques and were found to be ring chlorinated alkyl benzoates. A plausible mechanism has been proposed based on the experimental observations and the effect of the alkyl groups on the product yield.

Keywords: Acetals, Chlorine gas, Benzoate esters, Electrophilic aromatic substitution.

Introduction

Acetals play a vital role in bioorganic research in exploring anti-malarial¹, anti-viral², anti-bacterial³, anti-tumor⁴, and anti-cancer activities. The studies of enzymes⁵, thrombin inhibitors⁶, ADP-ribose linkages to proteins⁷, bioprosthetic devices⁸, and knee replacement⁹ have been made through the investigation of acetals. The acetal research has contributed much towards the synthesis of catalytic antibodies, oligonucleotide and hypolipidemic agents. Acetal derivatives of aldehydes are valuable in synthesis either as intermediates or as protecting groups^{10,11}. It is known that acetals are susceptible to addition¹², oxidation¹³, reduction^{14,15}, rearrangement¹⁶, condensation¹⁷ and hydrolysis¹⁸ in presence of catalysts. The literature contains a few references on the preparations^{19, 20}, and reactions^{21,22} of aromatic and heteroaromatic acetals resulting in synthetically important compounds as major products^{23, 24}. But the literature lacks detailed study on the action of halogens on aromatic acetals.

Action of Lewis acids on acetals in homogeneous and heterogeneous media have been investigated by various researchers and in most of the cases synthetically important compounds such as alkoxy alcohols, ethers and esters have been obtained.^{16,25} 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 to coordinate with an acceptor synthon, which may result in the cleavage of the alkoxy group leaving the methine sp^3 carbon atom to become a roomier sp^2 carbon atom. The Lewis acids have quenched such a thirst of the ethereal oxygen. The effect has been studied and the products have been analyzed by researchers.

In the place of Lewis acids the reagent selected in the present investigation is Cl_2 , which can quench the thirst of the ethereal oxygen atom by accepting its lone pair. Thus the present study aims on the action of Cl_2 on some aromatic acetals derived from benzaldehyde and alcohols of different alkyl group size and is a new venture. The following benzaldehyde *di*-alkyl acetals have been synthesized and taken for study in CCl_4 medium.

- 1a. Benzaldehyde diethyl acetal
- 2a. Benzaldehyde di-*n*-propyl acetal
- 3a. Benzaldehyde di-*n*-butyl acetal
- 4a. Benzaldehyde di-isobutyl acetal
- 5a. Benzaldehyde di-*n*-amyl acetal
- 6a. Benzaldehyde di-isoamyl acetal

Experimental

Benzaldehyde and the alcohols were procured from SDS fine chemicals, Mumbai and were distilled before use. IR spectra were recorded in Perkin Elmer 1800 FT IR spectrophotometer and the 1H NMR spectra on a DRX-300 spectrometer (300 MHz) using TMS as internal standard.

Preparation of 1a²⁶

The aldehyde was refluxed with ethylorthoformate and anhydrous ethanol in the presence of ammonium chloride as catalyst for 6 hours. Then the reaction mixture was cooled and ammonium chloride was filtered off. The alcohol was removed by atmospheric distillation and the remaining liquid was distilled under vacuum.

IR (ν_{max} , cm^{-1}) : 1040-1050
 1H NMR (δ , ppm) : 1.2 (6H, t, $2 \times CH_3$), 3.5 (4H, q, $2 \times CH_2$), 5.5 (1H, s, Ph-H), 7.2-7.6 (5H, m, Ph-H)

Preparation of 2a

This acetal was synthesized using *p*-toluene sulphonic acid as the catalyst²⁷. The aldehyde was refluxed for 8 hours with the alcohol in benzene containing a little *p*-toluene sulphonic acid. The equilibrium was driven toward the product by collection of the water formed using a Dean-Stark trap. When no more water was collected, the benzene solution was cooled, 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.

IR (ν_{max} , cm^{-1}) : 1040-1050
 1H NMR (δ , ppm) : 0.9 (6H, t, $2 \times CH_3$), 1.5 (4H, m, $2 \times CH_2-CH_3$), 3.4 (4H, t, $2 \times O-CH_2$), 5.45 (1H, s, Ph-H), 7.15-7.5 (5H, m, Ph-H)

*Preparation of 3a-6a*²⁸

Molecular proportions of the aldehyde and alcohol containing 7% by weight of anhydrous calcium chloride in pure dry benzene were refluxed in an apparatus equipped with a Dean-Stark trap carrying a reflux condenser until no more water was collected. The benzene added was to facilitate water separation. The acetals were preserved over potassium carbonate and distilled prior to use.

Spectral characteristics of 3a

IR ($\nu_{\max}$, cm^{-1}) : 1040-1150
 ^1H NMR (δ , ppm) : 0.9 (6H, t, $2\times\text{CH}_3$), 1.45 (8H, m, $2\times\text{CH}_2\text{-CH}_2\text{-CH}_3$),
 3.4 (4H, t, $2\times\text{O-CH}_2$), 5.45 (1H, s, Ph-H), 7.3 (5H, m, Ph-H)

Spectral characteristics of 4a

IR ($\nu_{\max}$, cm^{-1}) : 1040-1150
 ^1H NMR (δ , ppm) : 1.0 (12H, t, $4\times\text{CH}_3$), 1.6-2.1 (2H, m, $2\times\text{CH}(\text{CH}_3)_2$),
 3.2 (4H, d, $2\times\text{O-CH}_2$), 5.5 (1H, s, Ph-H), 7.1-7.5 (5H, m, Ph-H)

Spectral characteristics of 5a

IR ($\nu_{\max}$, cm^{-1}) : 1020-1140
 ^1H NMR (δ , ppm) : 0.9 (6H, t, $2\times\text{CH}_3$), 1.2-1.8 (12H, m, $2\times\text{CH}_2\text{-CH}_2\text{-CH}_2\text{-CH}_3$),
 3.4 (4H, t, $2\times\text{O-CH}_2$), 5.4 (1H, s, Ph-H), 7.1-7.5 (5H, m, Ph-H)

Spectral characteristics of 6a

IR ($\nu_{\max}$, cm^{-1}) : 1020-1140
 ^1H NMR (δ , ppm) : 0.9 (12H, t, $4\times\text{CH}_3$), 1.3-1.9 (6H, m, $2\times\text{CH}_2\text{-CH}(\text{CH}_3)_2$),
 3.4 (4H, t, $2\times\text{O-CH}_2$), 5.4 (1H, s, Ph-H), 7.1-7.5 (5H, m, Ph-H)

Preparation of chlorine gas

Concentrated hydrochloric acid was added in drops on potassium permanganate crystals and the chlorine gas evolved was allowed to pass through concentrated sulphuric acid solution, got dried and used for the reactions.

Results and Discussion*Action of chlorine on acetals*

0.2 mol of acetal in 50mL of purified CCl_4 was taken in a 250mL three-necked round bottomed flask, fitted with a delivery tube to pass the dry chlorine gas, a mercury thermometer sealed stirrer and a calcium chloride guard tube. The flasks were cooled in an ice bath. To the well-stirred acetal solution kept at 0 °C, pure dry chlorine gas was passed for 15 minutes. Stirring was continued for another half an hour. The reactions were stopped and 25mL of 10% sodium hydroxide solution was added to remove the excess chlorine gas as water-soluble sodium chloride and sodium hypochlorite. The aqueous layer was discarded and the organic layer was dried over anhydrous sodium sulphate and the solvent was distilled off. After isolating the individual compounds by column chromatography and thin layer chromatography, each one of the products was tested for the presence of chlorine in the nucleus as well as in the side chain. They were characterized by IR and PMR spectra (Table 1). Further they were quantitatively analyzed by GLC, with authentic samples co injected as references. The products were characterized and identified to be the ring chlorinated esters.

Table 1. Spectra characterizations of ring chlorinated esters

Structure	Acetal	IR		PMR	
		$\nu_{\max}$, cm^{-1}	Functional group	δ , ppm	Nature of protons
1a	1120 1300 1730	O=C-O-C- 	1.35(3H,t), 4.3&(2H,q) 7.1-8.1(4H,m)	Ethyl Ph-H
2a	1100 1280 1730	O=C-O-C- 	1.0 (3H,t), 1.7(2H,m)&4.2 (2H,t) 7.1-7.9(4H, m)	<i>n</i> -propyl Ph-H
3a	1130 1300 1740	O=C-O-C- 	0.9(3H, t), 1.7(2H,m) &4.2(2H, m) 7.1-7.95 (4H, m)	<i>n</i> -butyl Ph-H
4a	1120 1280 1730	O=C-O-C- 	0.95(6H,d),2.0 (1H,m)&4.0(2H,d) 7.1-7.95(4H,m)	Isobutyl Ph-H
5a	1120 1280 1740	O=C-O-C- 	1.0(3H,t), 1.3- 1.8(6H,m) &4.2(2H,t) 7.1-7.95(4H,m)	<i>n</i> -amyl Ph-H
6a	1120 1280 1730	O=C-O-C- 	1.0(6H,d),1.4- 1.8(3H,m)& 4.3(2H,d) 7.1-7.95(4H,m)	isoamyl Ph-H

The formations of esters during the action of chlorine on acetals indicate that the reactions involve E_2 mechanism followed by ring halogenation (Scheme 1)

Scheme 1. Mechanism of ring chlorination of acetals by the action of chlorine

Such a ring substitution has been reported in the nitration reaction²⁹ of methyl phenethyl ether using dinitrogen pentoxide, ring chlorination of anisole by hypochlorous acid³⁰, migration of halogen in the Orton rearrangement.³¹ The formation of ring halogenated ester from acetals by as explained by the E₂ mechanism (Scheme 1) is also very similar to those reported in the work of Xavier and Arulraj.¹⁶ In their study the ester formation had occurred in a concerted way with the removal of the benzal proton with the concomitant cleavage of the σ bond of the alkyl group.

Effect of alkyl group on the product yield

Studies on the effect of alkyl group in the halogenated ester formation is shown in Table 2

Table 2. Percentage distribution of ring chlorinated ester products of acetals by the action of chlorine

Acetal	% Chloroester formed
1a	75
2a	70
3a	62
4a	55
5a	47
6a	28

Table 2 shows low percentage of products as the size of the alkyl group increases. It is self evident that the chlorine-oxygen intermolecular bond would be sensitive to steric effect caused by the alkoxy groups because branching of alkyl group would prevent chlorine from close approach³².

Conclusions

The reactions of six aromatic acetals with chlorine gas were studied at 0°C. An E2 mechanism can successfully explain the formation of ring chlorinated esters formed. Chlorination occurs through electrophilic attack of chloronium ions on the benzene ring. The effect of alkyl groups on the reaction mechanism proposed is also supported by the product yields.

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