HETEROCYCLIC TERTIARY AMINES AS INITIATORS FOR HALOALDEHYDE OLIGOMERIZATION

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Abstract - Heterocyclic tertiary amines, such as pyridine, strychnine, sparteine, nicotine, cinchonine, cinchonidine, quinine and quinidine were found to be excellent initiators for the oligomerization of chloral and bromal. Treatment of the chloral oligomer mixture with acetic anhydride gave symmetrical chloral oligomer diacetates. Sparteine initiation of bromal gave bromal oligomer diacetates.

INTRODUCTION

Many nucleophiles are effective initiators for the polymerization but also for the oligomerization of aldehydes, particularly of perhaloacetaldehydes.[1-5] Most notable examples are alkoxides, acylates, chlorides; tertiary amines and phosphines are also excellent initiators.[6,7] The initiation of trichloroacetaldehyde (chloral) with tertiary phosphines, for example triphenylphosphine was studied in greater detail. It was found that this initiation was not a direct addition of the phosphorus atom of triphenyl-

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This paper is dedicated to Professor Edward C. Taylor on the occasion of his 70th birthday with our warmest wishes.

phosphine to the carbonyl carbon atom of chloral, although this reaction probably occurred initially. Further reaction and rearrangement occurred almost immediately resulting in the formation of triphenyl(dichloroethyleneoxy)phosphonium chloride (A) and this compound was found to be the actual initiator and the chloride anion was the initiating species. A was well characterized by single crystal X-ray analysis.[8] Since this type of chloral initiation had been well established, we assumed that the tertiary amine initiation functioned somehow the same way, namely that the tertiary amine is added to chloral initially. We further believed that the intermediate reaction product of chloral with the tertiary amine, a zwitterion alkoxide would undergo further reaction to an ammonium chloride and the chloride anion was again the actual initiator for the polymerization (or oligomerization) of chloral. We have recently reinvestigated the initiation of the trihaloacetaldehyde oligomerization with tertiary amines, especially the oligomerization of chloral. We found that the proposal of chloride initiation as a consequence of the use of tertiary amines as initiators was not justified.[9]

In our recent studies of the oligomerization of chloral (with lithium tertiary butoxide) we have determined the structure and the absolute configuration of individual compounds formed during the oligomerization of chloral.[10-13]

We had found earlier, that polychloral prepared by initiation with a chiral alkoxide was optically active; the activity was caused by macromolecular asymmetry - helicity.[14] We had also shown that some of the chloral oligomers form rigid helices and maintain the helical conformation also in solution. They could be separated on a chiral column into the RRR..R and SSS..S isomers and we demonstrated that these compounds have a helical structure. The RRR..R isomer adopts a right handed helical conformation and the SSS..S isomer a left-handed conformation. Nmr studies confirmed this observation and single crystal determination of the (-)-enantiomer of the pentamer established the absolute configuration.[15]

The stability of the one-handed helices of chloral oligomers was found to depend primarily on the degree of polymerization, but also on the size of the end groups.[16]

Taking this background information into consideration it was believed to be possible to prepare chloral oligomer diacetates with optical activity based on helicity by initiating the oligomerization with chiral tertiary amines, "capping" the oligomeric oxides by acetylation and displacing the initiating ammonium group with the acetate group. We selected a few common alkaloids, heterocyclic tertiary amines, for our oligomerization studies.

RESULTS AND DISCUSSION

Oligomerization of chloral was initiated with eight heterocyclic tertiary amines; they included optically active strychnine, sparteine, nicotine, cinchonine, cinchonidine, quinine, quinidine and also pyridine. Sparteine was used as initiator for the oligomerization of bromal.

The initiated mixtures of the chloral oligomerization were cooled to specified temperatures, which established an equilibrium of oligomeric alkoxides and a solid which consisted of polymeric alkoxides of higher molecular weight. In order to "freeze" this equilibrium, the suspension was treated with acetic anhydride to acetylate the oligomeric and polymeric alkoxides. The composition of the oligomer mixture has an equilibrium concentration of individual oligomers which is dictated by the so-called ceiling temperature of polymerization (Tc).[17] The Tc of chloral (1 molar solution) is near room temperature, at 16°C, but for bromal, it is -75°C. The temperature at which acetylation was carried out (taking into account the exotherm of the acetylation reaction), determined the composition of the oligomer mixture.

The chloral oligomer mixture was subjected to capillary GC; the chromatograms showed several peaks which suggested that the expected oligomer mixture had been obtained (Figure 1).

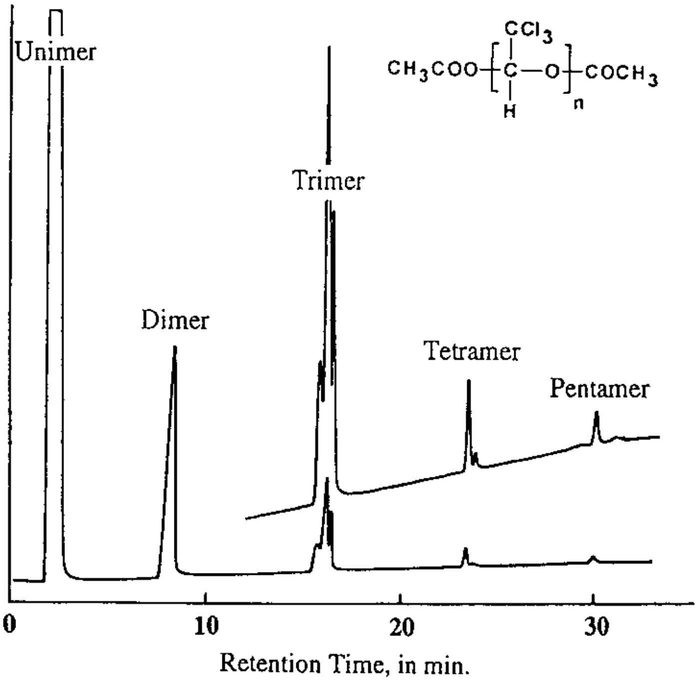


Figure 1. Capillary GC of Strychnine Initiated Chloral Oligomer Diacetates

In order to analyse our oligomers in more detail, especially to establish the exact molecular weight of the individual oligomers, the mixture were subjected to K+IDS mass spectrometry. Figure 2 shows the K+IDS mass spectrum of the mixture of chloral oligomer diacetates (CODA) which were obtained by initiation of chloral with strychnine followed by acetylation. The K+IDS mass spectra of mixtures of CODA's obtained by initiation with other

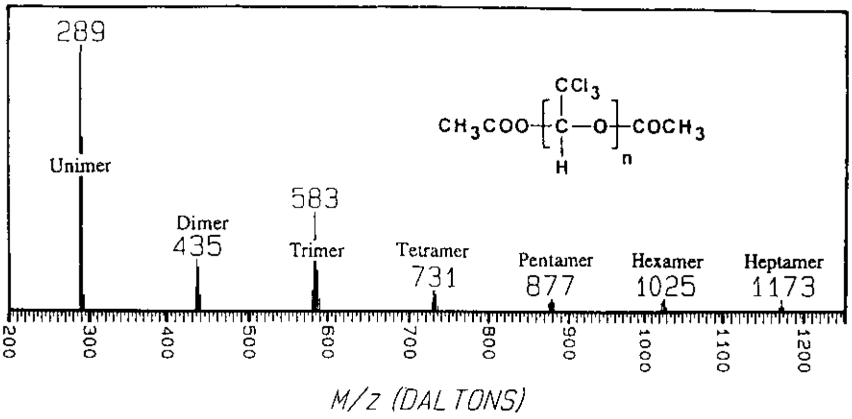


Figure 2. K+IDS Mass Spectrum of Strychnine Initiated Chloral Oligomer Diacetates

heterocyclic tertiary amines were nearly identical. None of the samples has the amine portion incorporated in the chloral oligomers, the oligomers are clearly the CODA's.

Table. Characterization of Strychnine Initiated Chloral Oligomer Diacetates

CODA	[M]K+ in Daltons	Capillary GC Retention Time, in Minutes
Unimer	289	2.0
Dimer	435	7.6
Trimer	583	16.0
Tetramer	731	23.2
Pentamer	877	30.0
Hexamer	1025	-
Heptamer	1173	-

The position of the individual oligomers in the K+IDS mass spectrum and in the gas chromatogram is shown in the Table. The relationship of the oligomers higher than dimers is believed to be accurate.

To establish the molecular structure of the individual CODA's compounds, especially the exact chlorine content, we have determined the isotope distribution of each compound. The experimental and calculated values for the oligomers are in excellent agreement and have established beyond any reasonable doubt the molecular structure of the CODA's. It should be pointed out that the unimer could also be formed by direct amine catalyzed acetylation of unreacted chloral. In separate experiments we have shown that uncatalyzed acetylation of chloral is extremely slow.

Figure 3 shows the K+IDS mass spectrum of bromal oligomer diacetates (BODA) prepared by sparteine initiation. The unimer bromal diacetate can be seen at [M]K+=423 Da, the dimer at 701 Da, the trimer at 982 and the tetramer at 1264 Da.

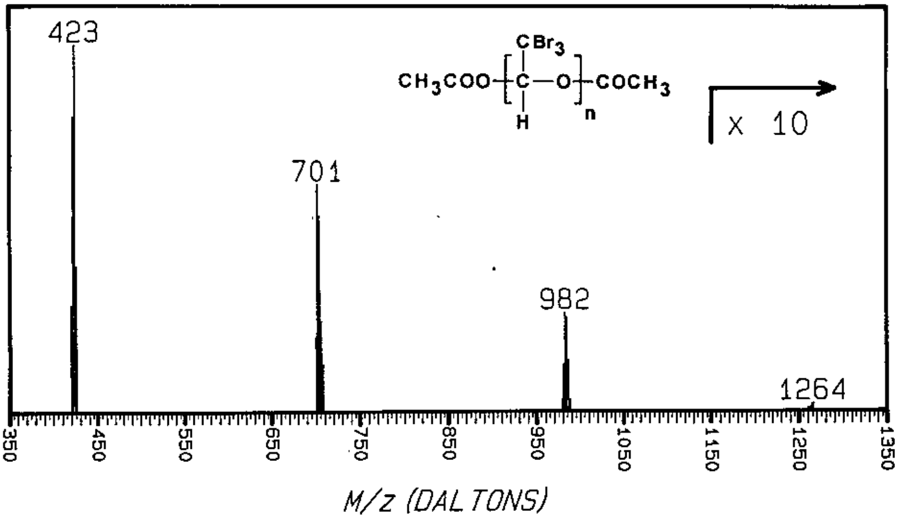
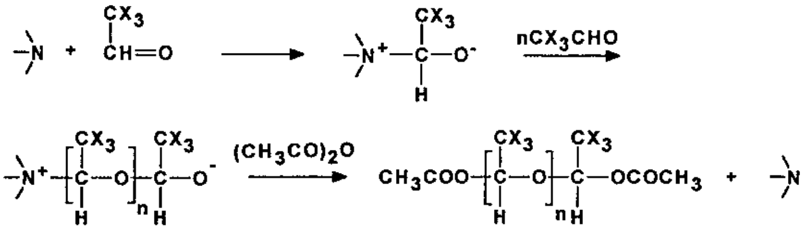


Figure 3. K+IDS Mass Spectrum of Sparteine Initiated Bromal Oligomer Diacetates

The oligomeric chloral alkoxides obtained by initiation of chloral with tertiary amines were also acylated with other anhydrides: propionic anhydride, n-butyric anhydride, isobutyric anhydride, pivalic anhydride, benzoic anhydride, adamantanecarboxylic anhydride and diphenylacetic anhydride. Most of the acylation reactions with the less reactive anhydrides are much slower than the acetylation with acetic anhydride and gave lower yields and even insignificant amounts of higher CODA's.

From these results we conclude that the initiation of the (anionic) chloral oligomerization by tertiary amines is caused by the addition of the nucleophilic nitrogen atom of the heterocyclic amine to the carbonyl carbon atom of chloral forming a zwitterion alkoxide. The alkoxide part of the zwitterion is now capable of propagation with more chloral monomer [Scheme]. When the oligomerization is terminated, acid anhydride first acylates the alkoxide oxygen. The remaining acyl anion is then capable of replacing the heterocyclic tertiary amine fragment and liberating the heterocyclic tertiary amine - the originally used alkaloid. The reaction products of the chloral oligomerization are the CODA's.



n = 0 - 6

N = Heterocyclic Tertiary Amine, X = Cl or Br

Scheme

We have measured the optical activity of our CODA mixtures. Some small amount of activity was observed in a few cases, but it could be attributed to trace amounts of the initiator that was not completely removed by the acid washing of the CODA mixture. The possibility of such an artifact always has to be taken into account when a small value of rotation is measured and the rotation has the same sign as the chiral amine used for the initiation. A small amount of optical activity measured could be attributed to the rigid chiral oligomers present in the CODA mixture. The amount of the active ingredient of the oligomer mixture - pentamer and higher oligomers is probably lower than one percent of the total oligomer mixture. We have had established earlier that the optically active pentamer, prepared by chloral initiation with lithium tertiary butoxide followed by acetate endcapping, which was well characterized, has a rotation of $[\alpha]_D^{25}=-23.7°$.[15]

It might be possible that during the acetylation, particularly the removal of the chiral hetereocyclic tertiary amine, racemization of the CODA's occurred. And finally, it could very well be that the acetyl end groups of higher oligomes are too small to stabilize the helical conformation of the CODA's which might also be thermally racemized during the work-up.

This problem of initiating the oligomerization of chloral with tertiary amines is still intriguing and has some very interesting features. Should our mechanism of the termination of the chloral oligomerization be correct, it would allow not only to make symmetrical oligomers of trihaloacetaldehydes such as acylates but also asymmetric oligomers with different end groups using the appropriate capping reagents. If chirality has originally been introduced into the oligomers, it might be retained with the proper end-capping reagent and the proper reaction condition for the end-capping reaction.

EXPERIMENTAL

Measurements. Mass spectrometric determinations of the oligomer mixtures were carried out by K+IDS mass spectrometry and gas chromatography on a capillary column as described previously.[18-21]

Preparations. Chloral oligomers were prepared by tertiary amine initiation of chloral in methylcyclohexane or dichloromethane. A mixture of chloral and the heterocyclic tertiary amine in a molar ratio of 5:1 was prepared at 50 C and then cooled below 0 ℃. This temperature sequence caused the formation of a suspension of soluble oligomeric and solid polymeric alkoxides of chloral. The reaction was then terminated by adding an excess of acetic anhydride. The insoluble polychloral was removed by filtration and the filtrate was repeatedly washed with a 10 % aqueous sulfuric acid solution in order to remove quantitatively the heterocyclic amine. After washing with 5 % aqueous sodium bicarbonate solution and water, the organic phase was dried and concentrated; an oily oligomer mixture was obtained in yields of about 50-60% consisting of 80 - 90 % of the unimer $CH_3COO-CH(CCl_3)-OCOCH_3$. The mixture was analyzed by capillary GC and K+IDS.[9] To identify the higher oligomers, the lower boiling unimer fraction was removed by Kugelrohr distillation and the residue was investigated.

Bromal oligomers were prepared by a procedure similar to that used for the preparation of the chloral oligomers, only the temperature sequence necessary for the bromal oligomerization was much lower. The mixture of bromal and tertiary amine was prepared in dichloromethane at room temperature. After stirring for 30 min the yellow solution was cooled gradually to -60°C over a period of 30 min. The precipitation of insoluble polybromal was noticed and an excess of acetic anhydride (which had been precooled to -78 °C)[22] was added with a cold syringe. The suspension was stirred for 5 h at -70 °C and the temperature was then allowed to raise to room temperature. Solid polybromal was removed from the suspension by filtration and the filtrate was washed, dried and the solvent was removed. The residue was analyzed similarly to the investigations of the chloral oligomers.

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