Journal of Chromatography, 281 (1983) 95–99
Elsevier Science Publishers B.V., Amsterdam — Printed in The Netherlands

CHROM. 16,206

THERMAL REDUCTION OF CHLORDECONE IN THE PRESENCE OF ALCOHOL

W. H. SOINE*, T. R. FORREST and J. D. SMITH
Department of Pharmaceutical Chemistry, Medical College of Virginia, Virginia Commonwealth University, P.O. Box 581, Richmond, VA 23298-0001 (U.S.A.)
(First received July 11th, 1983; revised manuscript received August 8th, 1983)

SUMMARY

Chlordecone was observed to undergo reduction to chlordecone alcohol when dissolved in primary and secondary alcohols, and analyzed using gas chromatography. Reduction occurred in the injection port and was catalyzed by Na^+, Mg^{2+} and Al^{3+}. It appears that the reduction occurs via a Meerwein-Ponndorf-Verley mechanism.

INTRODUCTION

During recent studies on the synthesis of monohydro- and dihydrochlordecone using Raney nickel, hydrogen and ethanol, the reaction was monitored using gas chromatography (GC). Direct analysis of the reaction mixture indicated that considerable reduction of chlordecone (CD) to chlordecone alcohol (CDOH) (Fig. 1) had occurred; however, when the mixture was analyzed by thin-layer chromatography, no CDOH was detected. This suggested that CD was being reduced to CDOH in the gas chromatograph during the analysis. This observation was unexpected although there were two previous reports in the literature in which CD was reported to be reduced to CDOH in the presence of an alcohol. The first was in a paper by Dilling *et al.*[1] in which the reduction occurred at 200°C in diethylene glycol containing potassium hydroxide. The second was by Harless *et al.*[2] in which they gave an anecdotal report that solutions of CD and methanol could yield CDOH. The latter paper indicated that this observation could be of importance since a benzene and methanol mixture is commonly used in the analysis of CDOH and may cause an unrecognized artifact in CD analysis.

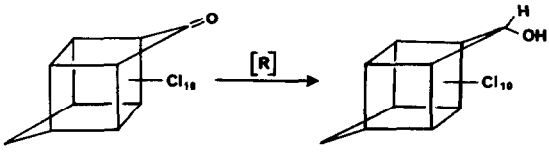

Fig. 1. Reduction of chlordecone to chlordecone alcohol.

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Since the conversion of CD to CDOH in alkanols had already been observed and we also had observed this reduction, this study was directed toward determining what conditions were necessary for CD's reduction. It was desirable to determine the generality of the reaction, what steps were necessary for minimizing or preventing the reaction and if the presence of alkanols could lead to problems using the methods currently reported for the analysis of CD.

EXPERIMENTAL

The analyses were carried out on a Varian Model 3700 gas chromatograph equipped with a flame ionization detector, a Varian Model 9176 strip recorder, a Spectra-Physics autolab minigrator and a glass column, 1.8 m × 2 mm I.D. packed with 3% OV-17 on 100–200 Chromosorb W HP. The carrier gas was nitrogen at a flow-rate of 30 ml/min. The temperature settings were: injection port 250°C (unless otherwise specified), column temperature 240°C and detector temperature 300°C. GC–mass spectrometry (MS) analyses were done on a Hewlett-Packard Model 5993 GC–MS system and were implemented with a coiled glass column, 1.2 m × 2 mm I.D., packed with 3% OV-17 on Gas Chrom Q, 100–200 mesh. Helium (30 ml/min) was used as a carrier gas. The temperature settings were: injection port, 270°C; column, 240°C and splitter, 350°C.

All solvents and chemicals were reagent grade or better. Chlordecone was obtained from Allied Chemical and was purified by converting it to the sodium salt with sodium hydroxide, recrystallization in methanol (2×), neutralization and recrystallization from hexane. Only a single peak corresponding to CD was observed upon analysis of the material by GC using the electron-capture detector[3]. Chlordecone alcohol was prepared as previously described[4]. Monohydromirex, used as the internal standard, was prepared by treatment of CDOH with phosphorus pentachloride[1], purified by recrystallization (2×) from hexane and chromatographed as a single peak upon analysis.

The solutions used in this study contained 2 μmole CD/ml of alcohol and 1–2 μl was injected for each analysis. Monohydromirex was used as the internal standard for quantitation of both CD and CDOH. A linear response correlation for peak area ratio *versus* concentration was observed from 0.1 to 2 mmole/ml ($r^2 = 0.998$), and the regression line passed through the origin. The FID detector response was greater for CDOH than CD. The sample was injected on-column in the portion of the column in the injection port. This required a 2.8 cm spacer for a 5.3 cm needle.

RESULTS AND DISCUSSION

The observation that CD underwent reduction in the reaction mixture following injection into the gas chromatograph was quite unexpected. However, if this reaction is viewed as an example of a Meerwein-Ponndorf-Verley (M-P-V) reduction[5] as depicted in Fig. 2, it provides a framework to understand and study the reaction. The M-P-V reduction normally utilizes a metal alkoxide catalyst such as aluminum or magnesium, but it has been reported that at temperatures from 200 to 300°C the reduction can take place without a catalyst. Since this temperature range is used in GC analysis, especially in the injection port, the reduction probably occurred in the

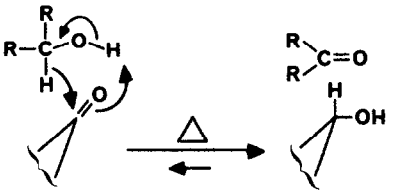

Fig. 2. Mechanism of thermal Meerwein-Ponndorf-Verley reduction.

injection port following injection. To test this hypothesis a methanolic solution of CD was injected and both CD and CDOH were detected. A portion of the sample was evaporated to dryness and redissolved in an equal volume of dichloromethane. The GC analysis of this solution indicated that no CDOH was formed. Further analysis of the original methanolic solution of CD using GC–MS confirmed that CDOH was formed (nine chlorine isotope cluster at *m/z* 453 and a base fragment at *m/z* 218)[2]. To determine if the hydrogen transferred was from methanol, 7 mg of CD was dissolved in 100 μl of d_4-methanol (99.5%), sealed in a pyrex tube and heated to 225–240°C for 3 h. The mixture was cooled, evaporated to dryness, redissolved in methanol, evaporated to dryness, redissolved in dichloromethane and analyzed by GC–MS. Approximately 10% was converted to d_1-CDOH in which the base fragment increased one mass unit to *m/z* 219 and the remaining portions of the spectrum corresponded to standard d_1-CDOH[4].

The extent of reduction was observed to be dependent on previous use of the column and the conversion of CD to CDOH ranged from 0 to 75%. Analysis using a clean, newly conditioned column indicated only trace conversion. This was possibly due to the design of the injection port in that when using a standard 5.8 cm needle, the sample is placed almost directly on the column by-passing the hotter injection port area. When the same sample was injected into the injection port at the head of the column, more conversion was evident, but the area of the CDOH peak was still less than 1% of CD (lower limit of integration). Consistent with the M-P-V mechanism, it would be expected that an increase in injection port temperature should increase conversion. As shown in Table I at temperatures below 300°C conversion increased but not to an amount detected by the integrator, but at 300°C conversion was 3% and increased to 6% at 320°C and remained basically constant to 400°C. The effect of increasing the chain length of the primary alcohol from 1-butanol to 1-octanol (Table I) was evaluated and an increase in conversion was observed with the higher boiling alcohols. This could be due to the CD and alcohol remaining mixed together longer in the hot injection port. An alternative mechanism to the M-P-V would be formation of the alcohol hemiacetal followed by a thermally catalyzed 1,3-hydride shift. The CD 1-butanol hemiacetal was synthesized[6] and under GC conditions in which there was 8% reduction using 1-butanol, only trace conversion was observed for the CD 1-butanol hemiacetal (dissolved in dichloromethane). The effects of branching in the alcohol (not shown) indicated that methanol and ethanol gave comparable conversion while in 2-propanol the conversion decreased and in *tert.*-butanol no reduction was observed. The decreased conversion in 2-propanol was probably due to steric hindrance while no reduction in *tert.*-butanol is consistent with the proposed mechanism. As further evidence to satisfy this mech-

TABLE I

PERCENTAGE CONVERSION OF CHLORDECONE TO CHLORDECONE ALCOHOL DISSOLVED IN ALCOHOL

T = trace conversion, a peak corresponding to chlordecone alcohol was visible on tracing but not quantitated. ND = No conversion to chlordecone alcohol was detected.

Injection port temperature (°C)	*Conversion (%)*			
	Methanol	*1-Butanol*	*1-Octanol*	*tert.-Butanol*
260	T	T	T	ND
280	T	T	–	ND
300	3	4	3	ND
320	6	6	8	ND
338	6	8	10	ND
358	7	8	9	ND
378	7	8	10	ND
398	7	7	10	ND

anism, it was necessary to identify the reduced product formed from the alcohol. For this study benzyl alcohol was heated with CD at 200°C allowing the solvent to slowly distill over to a cooled receiver. Analysis of the distillate by GC indicated a substance that co-chromatographed with benzaldehyde and its identity was confirmed by GC–MS. Sufficient quantities of the benzaldehyde were obtained so that the phenylhydrazone derivative could be prepared and its mixed melting point was identical to standard (m.p. 158°C). Since the M-P-V reduction involves an equilibrium between ketone and alcohol, it would be expected that CDOH would be oxidized to CD in the presence of a ketone. To test this hypothesis 5 mg of CD was dissolved in 100 μl of cyclohexanol in a glass tube and 5 mg of CDOH was dissolved in 100 μl of cyclohexanone in a separate tube, the tubes were sealed and heated at 230–240°C for 3 h. Analysis of the reaction mixtures by GC–MS indicated approximately 50% reduction of CD to CDOH in cyclohexanol but only about 2% oxidation of CDOH to CD. It would appear that the reaction strongly favors reduction of the CD carbonyl, possibly due to the positive character of the carbonyl which is evidenced in its hydration in water[1].

Since the extent of conversion of CD was affected by column age and use, we wanted to determine what was responsible for this. Attempts to artificially age the column by injection of 7 μl of 10% HCl had no effect[7]. Following the injection of 5 μl of 25% NaOMe in methanol, neither CD nor CDOH was detectable probably due to their conversion to the sodium salt on injection. Since the M-P-V reaction has been shown to be catalyzed by metals such as sodium, magnesium, aluminum and iron[5], these metals were evaluated for their ability to catalyze the reduction. The metal chloride salt solution was prepared in equimolar concentration with CD and injected directly on the column. As shown in Table II the amount converted was increased significantly in the presence of the metals, *i.e.* there was 12% reduction with magnesium chloride at 250°C and less than 1% at 300°C in the absence of magnesium chloride. In the presence of these metal ions no significant reduction to CDOH was detected in the presence of *tert.*-butanol, although some conversion with sodium chloride was detected. This may have been due to some primary or secondary

TABLE II

PERCENTAGE CONVERSION OF CHLORDECONE TO CHLORDECONE ALCOHOL IN THE PRESENCE OF SALTS

Injection port, 250°C.

Alcohol	*Conversion (%)*			
	NaCl	$MgCl_2$	$AlCl_3$	$FeCl_3$
Methanol	10	12	7	5
Ethanol	11	11	5	5
2-propanol	3	2	ND	2
tert.-Butanol	1	ND	ND	ND

alcohol contaminant in the *tert.*-butanol. The observation that sodium ion was the most effective catalyst was unexpected, however, at high temperature alumina doped with Na^+ was a very effective catalyst for M-P-V reactions using methanol[8]. Finally, CD was found to undergo facile reduction to CDOH (85% yield) under classical M-P-V conditions (aluminium isopropoxide)[5]. It would appear that CD can undergo reduction to CDOH in alcohols that have at least one hydrogen geminal to the hydroxyl group. This reduction appears to go via a form of M-P-V reduction and is catalyzed by heat and cationic metal ions.

A better understanding of the mechanism of this reduction provides additional rational in the design of analytical procedures used for monitoring and detecting CD. Obviously, no reasonable analytical method would use an injection port temperature 50 to 150°C higher than the column temperature or recommend co-injection of a metal ion with CD. However, depending on prior column exposure, conditions could be such that reduction of CD could occur. This is because the current methods for analysis of CD use methanol (1%) as a co-solvent[2,3,10] or isopropanol as a solvent[9] for the injection solution. This would appear to be the basis of the reduction of CD to CDOH observed by Harless *et al.*[2] and was also observed during our early studies. If it is desirable that alcohol solvents continue to be used for CD analysis, adequate controls should be followed to assure that this reduction is not occurring. It also may be preferred to use a solvent other than an alcohol or to substitute *tert.*-butanol for the alcohol. That this type of reduction by alcohol could also occur with other compounds containing a strongly positive carbonyl carbon is currently under investigation.

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