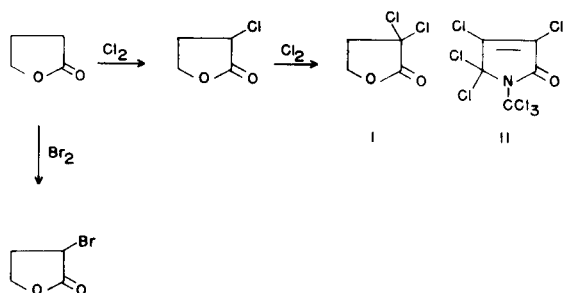


Rohm and Haas Company

Halogenation of 1-(3,4-Dichlorophenyl)-2-pyrrolidinone

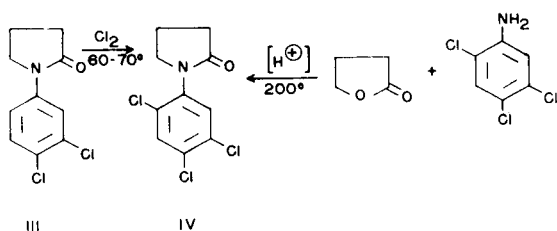
Michael C. Seidel

The halogenation of butyrolactone has been studied by Reppe (1). It leads to α -halo-butyrolactones:

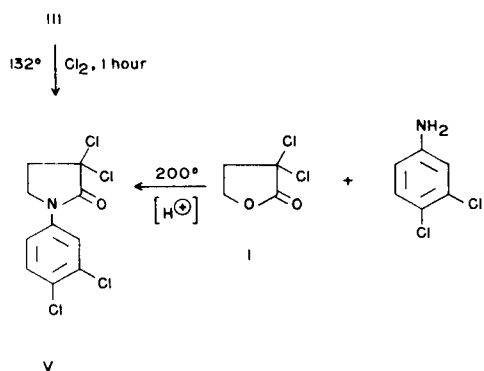


Not much has been reported on the halogenation of pyrrolidinones. Holschmidt (2) on chlorinating *N*-methylpyrrolidinone at 200° isolated II in addition to open chain products.

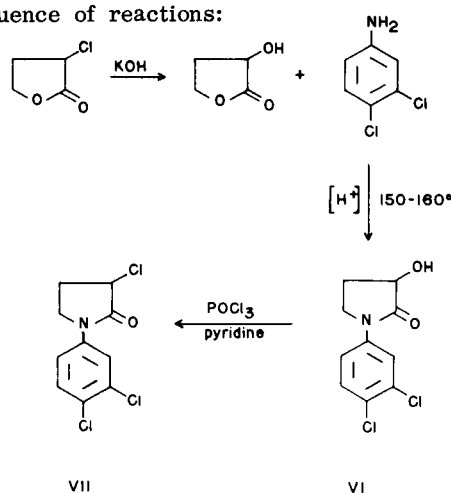
Chlorination of 1-(3,4-dichlorophenyl)-2-pyrrolidinone (III) gave different products depending on the conditions. At 60-70° in carbon tetrachloride in the presence of a small amount of phosphorus trichloride, a 51% yield of IV was obtained, which was prepared independently as shown:



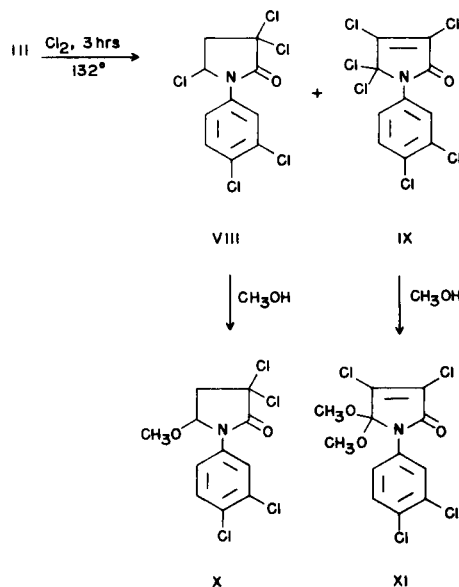
However, in boiling chlorobenzene (132°) also with phosphorus trichloride as catalyst, the reaction took a different course:



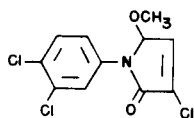
After one hour V could be isolated in 40% yield. It could also be prepared from α,α -dichlorobutyrolactone (I) and 3,4-dichloroaniline. Thin layer chromatography showed the presence of several minor components in the reaction mixture but none of these could be isolated. There was no indication of the presence of the mono-chlorinated compound VII. It could only be prepared by the following sequence of reactions:



When the chlorination at 132° was carried out over three hours two new products were obtained, VIII and IX. These were not isolated as such but were transformed into X and XI by recrystallization from methanol. The latter compounds were obtained in 44% and 3% respectively. It is interesting to note the similarity between IX and II.

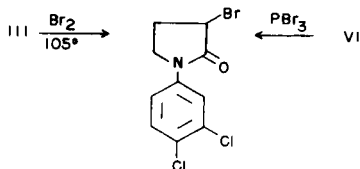


Many attempts were made to dehydrochlorinate V with various pyridine bases at several temperatures, with potassium hydroxide, with sodium methoxide, and with lithium chloride in DMF. All these attempts either led to tars or to the isolation of unchanged starting material. Dehydrochlorination was successful with X. In boiling pyridine XII could be isolated in 15% yield:



XII

Bromination of III occurred at 105° in chlorobenzene on slow addition of bromine.



XIII

The 3-bromo derivative (XIII) was isolated in 65% yield. The position of the bromine atom was proven by an independent synthesis from the 3-hydroxy derivative VI.

EXPERIMENTAL

All melting points are uncorrected. The microanalyses were carried out by Mr. C. W. Nash and his associates, Rohm and Haas Company, Bristol, Pa.

The reaction of lactones with anilines for the preparation of III, IV, V and VI was carried out as described in the preceding paper (3).

Chlorination of III in Carbon Tetrachloride (IV).

Into a solution of 23 g. (0.1 mole) of III in 100 ml. of carbon tetrachloride with 1 ml. of phosphorus trichloride added chlorine was bubbled in a slow stream for 4 hours, while the temperature was kept at 60-70°. The solvent was then evaporated and the residue recrystallized twice from methanol, 12.0 g. (51%), m.p. 124-126°.

Anal. Calcd. for $C_{10}H_8Cl_3NO$: C, 45.40; H, 3.05; N, 5.30; Cl, 40.21. Found: C, 45.69; H, 3.05; N, 5.27; Cl, 40.42.

Chlorination of III in Chlorobenzene for 1 Hour (V).

Into a refluxing solution of 34.4 g. (0.15 mole) of III in 100 ml. of chlorobenzene containing 1.5 ml. of phosphorus trichloride 20 g.

of chlorine was bubbled during 1 hour. The mixture was then washed with water and the solution evaporated. The residue was recrystallized twice from methanol, yield, 18 g. (40%), m.p. 110-112°.

Anal. Calcd. for $C_{10}H_7Cl_4NO$: N, 4.68; Cl, 47.44. Found: N, 4.53; Cl, 47.19.

Chlorination of III in Chlorobenzene for 3 Hours (X and XI).

Into a refluxing solution of 23.0 g. (0.1 mole) of III and 1 ml. of phosphorus trichloride in 200 ml. of chlorobenzene a stream of chlorine at 20 g./hour was introduced. After 3 hours the solvent was evaporated and the residue treated with hexane. A crystalline precipitate formed which was taken up in methanol after filtration. A different compound crystallized from the methanol (by IR spectrum), yield, 14.5 g. (44%), m.p. 82-84°.

Anal. Calcd. for $C_{11}H_9Cl_4NO_2$ (X): C, 40.15; H, 2.76; N, 4.26; Cl, 43.11. Found: C, 40.27; H, 2.78; N, 4.23; Cl, 42.99.

From the mother liquors another compound precipitated, yield 1.0 g. (3%), m.p. 168-170°.

Anal. Calcd. for $C_{12}H_9Cl_4NO_3$ (XI): C, 40.36; H, 2.54; N, 3.92. Found: C, 40.03; H, 2.58; N, 3.84.

Dehydrochlorination of X (XII).

A solution of 3.0 g. (0.0091 mole) of X in 50 ml. of pyridine was heated at reflux for 30 minutes. The mixture turned black. The solution was then poured into excess water and the precipitated product recrystallized from methanol, 0.4 g. (15%), m.p. 113-115°.

Anal. Calcd. for $C_{11}H_7Cl_3NO_2$: C, 45.16; H, 2.75; N, 4.79; Cl, 36.36. Found: C, 45.42; H, 2.89; N, 4.75; Cl, 36.16.

Bromination of III (XIII).

A solution of 23.0 g. (0.1 mole) of III and 1.5 ml. of phosphorus trichloride in 100 ml. of chlorobenzene was heated to 105° and 16 g. (0.1 mole) of bromine was added over a period of 1 hour. Hydrogen bromide evolution started visibly after 30 minutes. The reaction mixture was kept at 105° for 5 hours, then the solvent was evaporated and the residue twice recrystallized from methanol and decolorized with charcoal, yield 20.5 g. (65%), m.p. 124-126°.

Anal. Calcd. for $C_{10}H_8BrCl_2NO$: C, 38.90; H, 2.61; N, 4.54. Found: C, 39.21; H, 2.92; N, 4.78.

1-(3,4-Dichlorophenyl)-3-hydroxy-2-pyrrolidinone (VI).

A mixture of 32.4 g. (0.2 mole) of 3,4-dichloroaniline and 20.4 g. (0.2 mole) of 3-hydroxybutyrolactone was heated with 3 drops of concentrated hydrochloric acid at 150-160° for 24 hours. The resulting oil was then exhaustively extracted with cyclohexane, the cyclohexane evaporated and the residue recrystallized from methanol, 22.6 g. (46%), m.p. 124-126°.

Anal. Calcd. for $C_{10}H_8Cl_2NO_2$: Cl, 28.9; N, 5.7. Found: Cl, 28.77; N, 5.52.

1-(3,4-Dichlorophenyl)-3-chloro-2-pyrrolidinone (VII).

To a solution of 12.3 g. (0.05 mole) of VI in 100 ml. of pyridine was added 10 ml. of phosphorus oxychloride with ice cooling. The mixture was left at room temperature over night. The reaction mixture was then poured into water and the product recrystallized from methanol, yield, 10.2 g. (75%), m.p. 115-117°.

Anal. Calcd. for $C_{10}H_6Cl_3NO$: C, 45.40; H, 3.05; N, 5.30. Found: C, 45.35; H, 3.12; N, 5.31.

Acknowledgment.

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