

## Synthesis of N-(*p*-Chlorophenyl)-amidophosphoric Acid

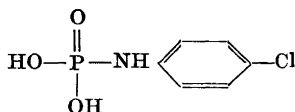
SI-OH LI

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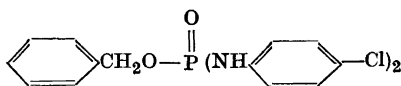
In 1933 Ichihara<sup>1</sup> suggested that N-(*p*-chlorophenyl)-amidophosphoric acid **I** might be used as a substrate for certain enzymatic investigations. The synthesis of this compound had previously been reported by Otto<sup>2</sup>, and Ichihara and later Gomori<sup>3</sup> used his directions for the preparation of a compound which they believed to be **I**. However, Rorig<sup>4</sup> has recently shown that Otto's compound is in fact N-(*p*-chlorophenyl)-diamidophosphoric acid.

The present communication describes the synthesis of **I** by hydrogenolysis of dibenzyl-*p*-chloroanilinophosphonate, which was prepared by a procedure used by Atherton, Openshaw and Todd<sup>5</sup> for the synthesis of similar compounds. **I** could also be synthesized by Otto's method, using sodium hydroxide instead of ammonium hydroxide for the hydrolysis of the dichloride. These routes were found equally convenient for the preparation of **I** and have since been used for the synthesis of other similar compounds.

The hydrogenolysis of dibenzyl-*p*-chloroanilinophosphonate to **I** was carried out with Adams' palladium oxide catalyst. If Adams' platinum oxide catalyst was used, a different compound with the empirical formula  $C_{19}H_{17}O_2PN_2Cl_2$  (408), was obtained. The equivalent weight, found by acidimetric titration was 426. On the basis of this analytical evidence, the structure **II** is proposed for the compound.



(I)



(II)

## EXPERIMENTAL

(Microanalyses by G. Cornali)

Preparation of dibenzyl *p*-chloroanilinophosphonate

Thirteen g of crude dibenzyl hydrogen phosphite (Atherton, Openshaw and Todd<sup>6</sup>) in 15 ml of dry carbon tetrachloride were added at  $-10^{\circ}$  (slowly, with stirring) to a solution of 6 g of *p*-chloroaniline in carbon tetrachloride. After the addition had been completed the reaction mixture was left at room temperature, when some heat was evolved and a precipitate separated out. Next day water was added and the carbon tetrachloride layer separated, washed with dilute hydrochloric acid and with a 10 % solution of sodium hydrogen carbonate and dried with anhydrous sodium sulfate. The solvent was removed under reduced pressure and the residue evaporated with alcohol. After cooling in the ice box the residue crystallized in needles. The crude product was recrystallized from aqueous alcohol; yield 11.1 g = 63 %; m. p.  $92-105^{\circ}$ . A small amount of the sample was recrystallized for analysis. The pure crystals melted partially at  $93^{\circ}$  and totally at  $110.5-111^{\circ}$  (Hershberg apparatus).

$C_{20}H_{19}O_3PNCl$  (387.8) Calc. C 61.9 H 4.94 N 3.61 Cl 9.14 P 7.99  
 Found » 62.6 » 5.19 » 3.88 » 9.23 » 7.59

Hydrogenolysis of dibenzyl-*p*-chloroanilinophosphonate

*Preparation of N-(p-chlorophenyl)-amidophosphoric acid.* Dibenzyl-*p*-chloroanilinophosphonate (7.8 g) was hydrogenated in absolute alcohol (120 ml) with Adams' palladium oxide catalyst (0.180 g) under 1 atmosphere at  $22^{\circ}$ . A little more than the theoretical amount of hydrogen was taken up during 60 minutes. The reaction stopped spontaneously. The catalyst was then filtered off and washed with alcohol. After removal of the solvent in vacuum, the white residue was collected and washed repeatedly and successively with water and ether. Yield 2.5 g = 60 %. For purification the crude product was washed thoroughly with hot water and ether and dried at  $80^{\circ}/0.1$  mm for 15 hours. The compound did not melt sharply but darkened at  $260^{\circ}$  and decomposed at  $292^{\circ}$ .

$C_6H_7O_3PNCl$  (207.6) Calc. C 34.7 H 3.40 N 6.75 Cl 17.1 P 14.9  
 Found » 34.8 » 4.23 » 6.71 » 16.1 » 14.8

*Isolation of a compound m. p.  $128^{\circ}$ .* Ten g of dibenzyl-*p*-chloroanilinophosphonate were hydrogenated in 150 ml of absolute alcohol with 0.20 g of Adams' platinum oxide catalyst under 1 atmosphere at  $22^{\circ}$ . 1395 ml of hydrogen were taken up during 4 hours. The catalyst was then filtered off and washed with alcohol. The solvent was removed in vacuum on a water bath of  $37^{\circ}$ , and the residue evaporated with 20 ml of alcohol. After cooling the residue crystallized. The crude product was recrystallized from aqueous alcohol in small white needles; m. p.  $130-131^{\circ}$ ; yield 2.8 g = 27 %. After a second recrystallization the yield was 1.9 g = 18 %; m. p.  $128^{\circ}$ .

$C_{19}H_{17}O_2PN_2Cl_2$  (408) Calc. C 55.8 H 4.16 N 6.86 Cl 17.4 P 7.59  
 Found » 53.6 » 4.48 » 6.69 » 17.1 » 7.54

Preparation of N-(*p*-chlorophenyl)-amidophosphoric acid  
from *p*-chloroanilidophosphoryl-dichloride

One g of pure *p*-chloroanilidophosphoryl-dichloride, prepared according to Otto<sup>2</sup>, was dissolved in 9 ml of 3 N sodium hydroxide, and N hydrochloric acid was added, whereby a white precipitate was formed. The addition was continued until nothing more separated. The precipitate was then filtered off and washed repeatedly and successively with water and ether. Yield 0.45 g = 53 %. The crude product was purified and dried as described above. When the pure compound was heated in a tube it behaved in the same way as the product obtained by hydrogenolysis. The identity of the two compounds was further ascertained by analysis.

$C_6H_7O_3PNCl(207.6)$	Calc.	C 34.7	H 3.40	N 6.75	Cl 17.1	P 14.9
	Found	» 35.1	» 3.56	» 6.53	» 16.2	» 14.5

SUMMARY

N-(*p*-Chlorophenyl)-amidophosphoric acid has been prepared by two independent methods. A compound melting at 128°, which is believed to be benzyl-di-*p*-chloroanilinophosphonate, was obtained by hydrogenolysis of dibenzyl-*p*-chloroanilinophosphonate with Adams' platinum oxide catalyst.

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