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STUDIES ON 2,3,5,6-TETRACHLOROPHENYLACTETIC ACID

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The diazotisation of polyhalogenated anilines with nitrosylsulphuric acid at low temperatures in glacial acetic acid is known to proceed very slowly[1], while the conversion of the diazonium salts to the corresponding phenols is usually very poor, due mainly to the formation of resinous materials, formed in the presence of an excess nitrous acid[2]. However, we have found that 2,3,5,6-tetrachloroaniline can be diazotised quite readily by Knoevenagel's procedure[3] and 2,3,5,6-tetrachlorobenzenediazonium hydrogen sulphate (I) is isolated in pure state. The diazonium salt (I) displayed somewhat different behaviors from the usual one, especially a marked different mode was observed in the decomposition of the diazonium salt in a mixture of acetic acid and diluted sulphuric acid.

For example, when a solution containing the crystalline diazonium salt (I) (5g) in a mixture of concd. sulphuric acid (7 ml), water (14 ml) and acetic acid (20 ml), was added dropwise into 70% sulphuric acid at 150 - 160°C, under which the resulting reaction procucts were immediately steam-distilled, we have obtained from the solid acidic component in the distillate a small amount of unknown colourless crystals (II), m.p. 212 - 213°C, but no detectable amount of the expected 2,3,5,6-tetrachlorophenol (III). Meanwhile, 2,3,5,6-tetrachlorobenzene (IV) was also found in the non-acidic portion of the solid distillate, whereas much of the resinous residue remained in the flask.

The compound (II), $C_8H_4Cl_4O_2$, has a remarkable biological activity* and the U.V. spectrum in ethanol shows the absorption maxima (λmax) 295 mμ(ε=445), 285 mμ(ε=419) and 279 mμ(ε=292), while the I.R. spectrum (Fig. 1) contains the characteristic bands at (a) 3000 - 2500 cm^{-1} (OH), (b) 1710, 1420, 1240, and 920 cm^{-1} (-COOH) and (c) 1600 and 870 cm^{-1} (benzene ring). The band at 1410 cm^{-1} seems to indicate the presence of $-CH_2COOH$ group in the molecule[4]. Thus the compound (II) is considered to be 2,3,5,6-tetrachlorophenylacetic acid.

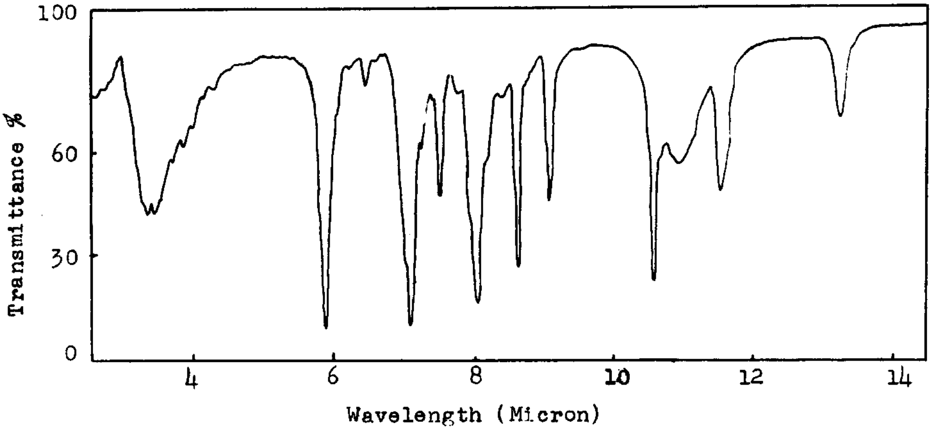

Fig. I Infrared spectrum** of 2,3,5,6-tetrachlorophenylacetic acid.

In a separate experiment, the authentic 2,3,5,6-tetrachlorophenylacetic acid was synthesized by hydrolyzing 2,3,5,6-tetrachlorobenzylcyanide prepared from 2,3,5,6-tetrachlorotoluene[5], and found to have the same m.p. (212 - 213°C) and I.R. spectrum as those of (II).

Recently Weil[6] has claimed to have synthesized 2,3,5,6-tetrachlorophenlylacetic acid by a similar procedure as our's, but reported its melting point as 169 - 170°C. Since Weil isolated none of the intermediates

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* On close investigation of plant response of this substance, this showed very noticeable seed-killing activity to inhibit almost completely the growth of plant root at 1 p.p.m.

** Infrared spectrum was measured by the KBr-disk.

in the whole process of the total synthesis of 2,3,5,6-tetrachlorophenylacetic acid, and apparently dealt with crude impure materials.

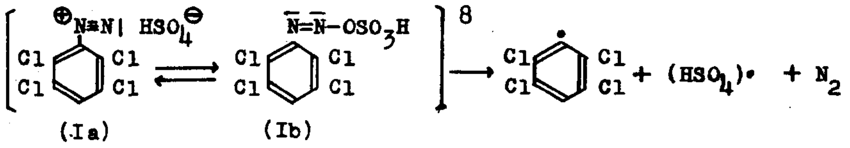
It is interesting that the phenylacetic acid (II) was obtained instead of the phenol (III) in the reaction, since the formation of phenylacetic acids by the decomposition of such diazonium compounds in acetic acid has never been reported.

When the above decomposition was carried out at 150 - 160°C in the presence of ferric chloride[7] as a radical scavenger, no 2,3,5,6-tetrachlorophenylacetic acid was found among the reaction products. In this case, a small amount of the phenol (III) was the only material isolated from the acidic component of the solid distillate.

On the other hand, when the diazonium salt (I) was decomposed at 70°C in a mixture of acetic acid and diluted sulphuric acid, neither the phenylacetic acid (II) nor the phenol (III) were obtained. Instead, yellow explosive needles, m.p. 117 - 118°C (decomp.), I.R. 2150 cm^{-1}, were unexpectedly obtained in a good yield. This was identified as 3,4,6-trichlorobenzene -2-diazo-1-oxide (V). The treatment of the diazo-oxide (V) in a mixture of acetic acid and 70% sulphuric acid at 160°C gave a dark red tar, and no detectable amount of the phenylacetic acid (II) was isolated.

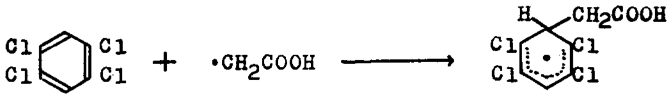
The formation of the phenylacetic acid (II) at high temperatures is considered to proceed through a radical mechanism (eq. 1-4), while the reaction at low temperatures undoubtedly involves the nucleophilic substitution of the ortho chlorine atom to the diazonium group to give the diazo-oxide derivative (V) (eq. 5).

The equilibrium between the diazonium salt (Ia) and the diazo-compound (Ib) is known to be shifted to the right hand side due to the electron-withdrawing effect of the polychloro substituents on the benzene ring. The initial homolysis of the diazo-compound (Ib) seems to favor the formation of the phenylacetic acid (II). Apparently the two reactions undergo through two entirely different paths, namely;

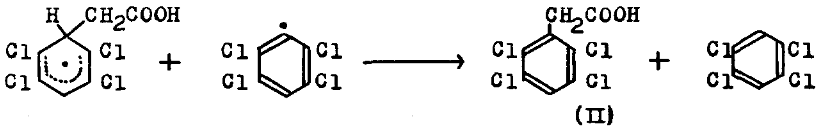


(1)

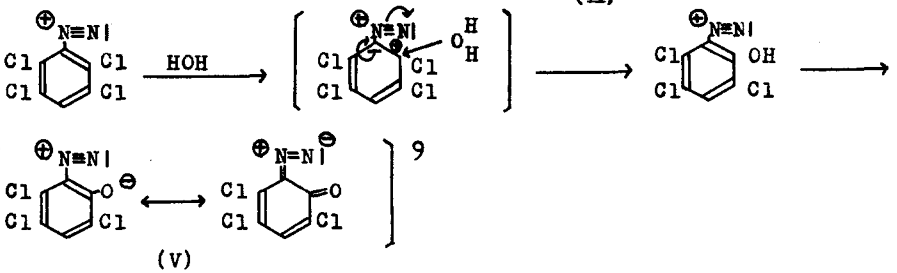
(2)



(3)



(4)



(5)

Perhaps the homolysis is a less energy-consuming process than the heterolysis for this compound, since the 2,3,5,6-tetrachlorophenyl cation presumed to be formed in the heterolysis, would be very highly energetic and unstable due to the strong electron-withdrawing polychloro substituents on the benzene ring.

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