[FROM THE RESEARCH LABORATORIES, ARMY MEDICAL CORPS, ISRAEL DEFENCE FORCES]

On the Fluorination of DDT with Hydrogen Fluoride and Mercuric Oxide

BY SASSON COHEN, ASHER KALUSZYNER AND RAPHAEL MECHOULAM

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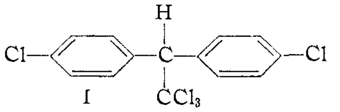
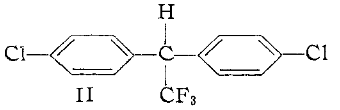
The fluorination of DDT with mercuric oxide and anhydrous hydrogen fluoride does not give II, but V, by a rearrangement reaction. A number of compounds related to DDT have been treated analogously, and the corresponding rearrangement has been observed for 1,1-di-(*p*-chlorophenyl)-1,2,2,2-tetrachloroethane (XI) which gives compounds XII and XIII.

In 1946, Kirkwood and Dacey[1] studied the fluorination of 1,1-di-(*p*-chlorophenyl)-2,2,2-trichloroethane (DDT) (I) with anhydrous hydrogen fluoride in the presence of mercuric oxide. They obtained a compound $C_{14}H_9Cl_2F_3$ melting at 64°, to which they attributed formula II.


I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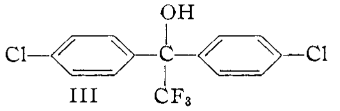
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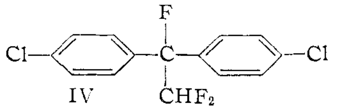
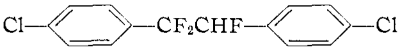

IV


V

Recently,[2] the carbinol III has been prepared and reduced to a compound which undoubtedly has structure II but is different from Kirkwood and Dacey's compound; it melts at 45°. Its structure follows from the presence of the CF_3 bands[3] in its infrared spectrum, its easy conversion into di-(*p*-chlorophenyl)-acetic acid[4] and a second synthesis from (*p*-chlorophenyl)-trifluoromethylcarbinol and chlorobenzene.[2] Kirkwood and Dacey's compound must, therefore, have a different structure.[5]

As we have—repeating the experiment of the Canadian authors—been able to confirm the formula $C_{14}H_9Cl_2F_3$, only two structures (IV and V) appear to be possible, which are isomeric to II. Both these formulas explain the absence of the CF_3 bands in the infrared spectrum of the substance.

The compound has proven very stable to the usual agents employed in degradation experiments (chromic acid in glacial acetic acid, alcoholic sodium hydroxide, sodium methoxide). Refluxing it for 2 hr. with sodium ethoxide solution causes the elimination of hydrogen fluoride, yielding a compound $C_{14}H_8Cl_2F_2$ which must be 1,2-di-(*p*-chlorophenyl)-1,2-difluoroethylene (VI) because of its composition, the similarity of its ultraviolet spectrum with that of 4,4'-dichlorostilbene (see Fig. 1)

VI: 224 (4.34), 294 (4.60), 306 (4.62) (in alc.)

4,4'-Dichlorostilbene:
229 (4.28), 303 (4.53), 317 (4.53) (in alc.)

and its ready oxidation to *p*-chlorobenzoic acid. If one excludes an intramolecular rearrangement in the treatment of Kirkwood and Dacey's compound with sodium ethoxide, the formation of VI proves unambiguously the formula V of 1,2-di-(*p*-chlorophenyl)-1,1,2-trifluoroethane for that compound. It is, indeed, theoretically unlikely that IV would rearrange in a type E_2 elimination reaction. Furthermore, IV should give an intense color reaction with concentrated sulfuric acid, in the same way as di-(*p*-chlorophenyl)-difluoromethyl carbinol[6] or the compounds VII or VIII, which is not the case; V, on the other hand, is not expected to give a carbonium ion.

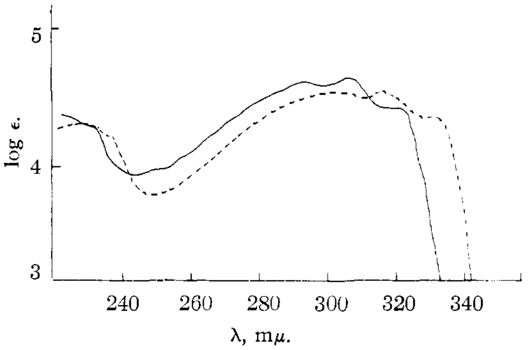


Fig. 1.—Ultraviolet spectra of 1,2-di-(*p*-chlorophenyl)-1,2-difluoroethylene (VI) (———) and 4,4'-dichlorostilbene (......), in alcoholic solution.

In order to substantiate these conclusions by analogies, the reaction of a number of compounds related to DDT with hydrogen fluoride and mercuric oxide has been studied. In 1,1-di-(*p*-chlorophenyl)-1,2,2-trichloroethane (VII), only the tertiary chlorine atom is replaced by fluorine, giving VIII. Its structure follows from its conversion to 1,1-di-(*p*-chlorophenyl)-2,2-dichloroethylene (IX) by means of either concentrated sulfuric acid or alcoholic potassium hydroxide solution. The easy replaceability of the tertiary chlorine atom recalls the

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[1] S. Kirkwood and J. R. Dacey, *Can. J. Res.*, **24B**, 69 (1946).

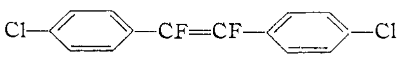
[2] A. Kaluszyner, S. Reuter and E. D. Bergmann, THIS JOURNAL, **77**, 4164(1955).

[3] For literature, see ref. 2, footnote 9.

[4] R. Mechoulam, S. Cohen and A. Kaluszyner, *J. Org. Chem.*, **21**, 801 (1956).

[5] It should be recalled that the insecticidal activity and fat solubility of the compound of Kirkwood and Dacey were used to support a theory of the mode of action of DDT; see, *e.g.*, S. Kirkwood and P. H. Phillips, *J. Pharmacol. Exp. Therap.*, **87**, 375 (1946); E. F. Rogers, H. D. Brown, I. M. Rasmussen and R. E. Heal, THIS JOURNAL, **75**, 2991 (1953).

[6] E. D. Bergmann, *et al.*, THIS JOURNAL, **79**, 4174 (1957).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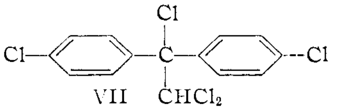
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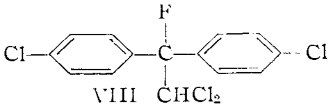
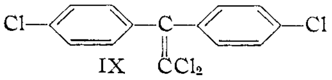

VIII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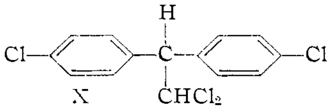
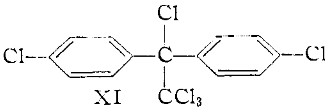

X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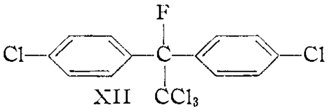
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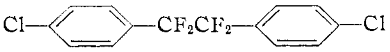
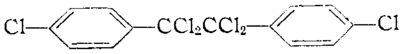

XIII

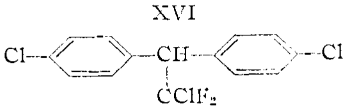
analogous behavior of diphenyldichloromethane and triphenylchloromethane,[7] whilst the stability of the $CHCl_2$ group to fluorination has been confirmed by our inability to obtain a fluorine-containing product from 1,1-di-(*p*-chlorophenyl)-2,2-dichloroethane (X), much polymeric material being formed. From 1,1-di-(*p*-chlorophenyl)-1,2,2,2-tetrachloroethane (XI), on the other hand, and the fluorinating agent two compounds have been obtained of the formulas $C_{14}H_8Cl_2F_4$ and $C_{14}H_8Cl_5F$, respectively, for which we propose—in the light of our experience related here—the structures of 1,1-di-(*p*-chlorophenyl)-1-fluoro-2,2,2-trichloroethane (XII) and 1,2-di-(*p*-chlorophenyl)-1,1,2,2-tetrafluoroethane (XIII). The structure of the former compound is supported by the observation that its treatment with zinc dust and alcohol yields 1,1-di-(*p*-chlorophenyl)-2,2-dichloroethylene (IX). On the other hand, XIII was not affected by this treatment or by heating it with boiling sodium ethoxide. It is equally significant that the chlorinated 1,2-diphenylethane derivatives XIV–XVI did not undergo fluorination, in the first two cases much polymeric product being formed.[8] We do not wish, at this time, to propose a definite mechanism for the formation of V from DDT (I), although one might be tempted to assume—in view of the fact that the fluorination of the CCl group under mild conditions proceeds generally only to the stage of $CClF_2$[9]—that initially XVII is formed; this compound may ionize to XVIII in which the rearrangement (to XIX) takes place, followed by the uptake of a fluoride ion. An analogous explanation would apply to the formation of XIII from XI. An analogy to such a mechanism may be seen in the observations that amongst the reduction products of DDT 4,4′-dichlorostilbene has been found[10] and that 1,1-di-(*p*-chlorophenyl)-2,2-dichloroethane (V) and 1,2,2,2-tetrachloroethane (XI) rearrange under the influence of ferric chloride to 1,2-di-(*p*-chlorophenyl)-1,2-dichloro- and 1,1,2,2-tetrachloroethane (XIV, XVI), respectively.[11,12]

The study of agents similar to mercuric fluoride has shown that DDT (I) is dehydrochlorinated to 1,1-di-(*p*-chlorophenyl)-2,2-dichloroethylene (IX) by mercuric chloride, antimony trifluoride,[13] ferric chloride[14] or aluminum chloride. The observation that IX is not affected by the mixture of mercuric oxide and hydrofluoric acid, incidentally, proves that it cannot be an intermediate in the formation of Kirkwood and Dacey's compound.


XIV


XV


XVI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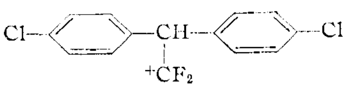
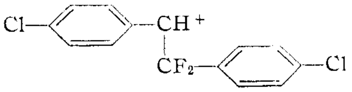

XVIII


XIX

Experimental

1,1-Di-(*p*-chlorophenyl)-2,2,2-trichloroethane (I) (m.p. 107–108°) was obtained from commercial "DDT" by recrystallization from ethanol. Its dehydrochlorination with alcoholic potassium hydroxide gave 1,1-di-(*p*-chlorophenyl)-2,2-dichloroethylene (IX) (m.p. 88–89°). Chlorination of the latter according to Grummitt, *et al.*,[15] yielded 1,1-di-(*p*-chlorophenyl)-1,2,2,2-tetrachloroethane (XI) (m.p. 91–92°).

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(7) A. L. Henne, THIS JOURNAL, **60**, 1569 (1938).

(8) It should be noted that according to W. I. Balon and J. H. Tinker, U. S. Patent 2,238,242 (*C. A.*, **35**, 4779 (1941)), 1,2-diphenyl-1,1,2,2-tetrachloroethane gives 1,2-diphenyl-1,2-dichloro-1,2-difluoroethane under similar conditions; however, the structure of this product has not been proven. With anhydrous hydrogen fluoride alone (at 100°), 1,2-diphenyl-1,2-difluoroethylene has been claimed as product. DDT (I), in our experience, is not affected by anhydrous hydrogen fluoride (in the absence of mercuric oxide).

(9) A. L. Henne, "Organic Reactions," Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1944, p. 56.

(10) J. Forrest, O. Stephenson and W. Waters, *J. Chem. Soc.*, 333 (1946).

(11) E. E. Fleck, *J. Org. Chem.*, **12**, 708 (1947).

(12) W. L. Walton, THIS JOURNAL, **69**, 1544 (1947).

(13) E. Pouterman and A. Giradet (*Experientia*, **2**, 459 (1946)) claim that the treatment of DDT with antimony trifluoride gives 1,1-di-(*p*-chlorophenyl)-2-chloro-2,2-difluoroethane, m.p. 90°. The latter substance has been prepared by E. D. Bergmann, *et al.* (THIS JOURNAL, **79**, 4174 (1957)) by an unambiguous method and has m.p. 54–55°. The compound of Pouterman and Giradet is, in fact, IX, which has a similar C and H content as the product claimed by these authors (C, 52.3; H, 2.8. Cmpd. IX: C, 52.8; H, 2.5).

(14) E. E. Fleck and H. L. Haller, *ibid.*, **66**, 2095 (1944).

(15) O. Grummitt, A. Buck and A. Jenkins, *ibid.*, **67**, 155 (1945); *cf.* A. R. Bader, *et al.*, *ibid.*, **78**, 1709 (1956).

1,1-Di-(*p*-chlorophenyl)-2,2-dichloroethane (X) (m.p. 108–109°) was obtained from a sample of "Rothane" (Rohm and Haas) by recrystallization from ethanol. Its dehydrochlorination with 1 *N* ethanolic potassium hydroxide gave 1,1-di-(*p*-chlorophenyl)-2-chloroethylene (m.p. 62–63°)[16] and chlorination of the latter in carbon tetrachloride solution at room temperature, 1,1-di-(*p*-chlorophenyl)-1,2,2-trichloroethane (VII) as a heavy yellowish oil, b.p. 180–185° (2 mm.).[17] VII gives a cherry red color with concentrated sulfuric acid; from this solution, 1,1-di-(*p*-chlorophenyl)-2,2-dichloroethylene (IX) is isolated.

1,2-Di-(*p*-chlorophenyl)-1,2-dichloroethane (XIV) (m.p. 94–95°) was prepared according to Fleck,[18] 1,2-di-(*p*-chlorophenyl)-1,1,2,2-tetrachloroethane (XVI) (m.p. 198–199°) according to Walton.[12]

Method of Fluorination.—Unless otherwise stated, the general method for the substitution of chlorine by fluorine was as follows: To an intimate mixture of the compound to be fluorinated and red mercuric oxide (at the ratio of 0.5 mole of the oxide for every atom of fluorine to be introduced) in a polyethylene flask, liquid anhydrous hydrogen fluoride was added, so that the mixture was covered by a liquid layer of about 0.5-cm. thickness. The hydrogen fluoride was allowed to evaporate within 2 to 3 hr. Water was then added and the insoluble residue filtered off and dried in air. It was then extracted with hot benzene, the solvent evaporated and the residue either recrystallized or distilled *in vacuo*.

Fluorination of DDT (I).—This compound (9 g.), when fluorinated, gave 1,2-di-(*p*-chlorophenyl)-1,1,2-trifluoroethane (V) (4 g.), b.p. 140–145° (1.5 mm.), m.p. (from ethanol) 64–65°, yield 52%.

Anal. Calcd. for $C_{14}H_9Cl_2F_3$: C, 55.1; H, 2.9. Found: C, 55.4; H, 2.9; ultraviolet spectrum: 224 mμ (4.48), 257 mμ (2.65), 263 mμ (2.80), 269 mμ (2.84); infrared spectrum (KBr pellet): ν_{C-F} 1010, 1088, 1100; ν_{C-F_2} 1150; 1255 cm.$^{-1}$ [19]).

When the experiment was repeated in the *absence* of mercuric oxide, Compound I was recovered in quantitative yield.

When a few mg. of mercuric chloride was added to I at the melting point, a vigorous evolution of hydrogen chloride took place; recrystallization of the product from ethanol gave 1,1-di-(*p*-chlorophenyl)-2,2-dichloroethylene (IX), m.p. 88–89°.

Fluorination of 1,1-**Di**-(*p*-**chlorophenyl**)-1,2,2-**trichloroethane** (**VII**).—This compound (7 g.), when fluorinated, gave 1,1-di-(*p*-chlorophenyl)-1-fluoro-2,2-dichloroethane (VIII) (2.5 g., 37%), m.p. 103–104° after recrystallization from alcohol. VIII gives a cherry-red color reaction with concentrated sulfuric acid. Upon refluxing with 1 *N* potassium hydroxide in alcohol, 1,1-di-(*p*-chlorophenyl)-2,2-dichloroethylene (IX) is obtained.

Anal. Calcd. for $C_{14}H_9Cl_4F$: C, 49.7; H, 2.7. Found: C, 49.9; H, 2.9; ultraviolet spectrum: 231 mμ (4.50), 259 mμ (2.82), 266 mμ (2.83); infrared spectrum (KBr pellet): ν_{C-F} *1020*, 1088, *1155* cm.$^{-1}$; ν_{C-Cl_2} 720, 738, 850, *770* cm.$^{-1}$.

Fluorination of 1,1-Di-(*p*-**chlorophenyl**)-1,**2,2,2-tetrachloroethane** (**XI**).—Fluorination of this compound (9.5 g.) and fractional distillation of the resultant mixture *in vacuo* gave two compounds: (a) 1,2-di-(*p*-chlorophenyl)-1,1,2,2-tetrafluoroethane (XIII) (1 g., 13%), b.p. 130–140° (1.5 mm.), m.p. (from methanol) 92–93°.

Anal. Calcd. for $C_{14}H_8Cl_2F_4$: C, 52.0; H, 2.5; F, 23.5. Found: C, 51.7; H, 2.8; F, 22.5; ultraviolet spectrum: 225 mμ (4.48), 256 mμ (2.40), 263 mμ (2.78); infrared spectrum (KBr pellet); ν_{C-F_2} 1025, *1100*, *1140*, *1260* cm.$^{-1}$.

(b) 1,1-Di-(*p*-chlorophenyl)-1-fluoro-2,2,2-trichloroethane (XII) (2 g., 28%), b.p. 160–170° (1.5 mm.), m.p. (from ethanol) 82–83°.

Anal. Calcd. for $C_{14}H_8Cl_5F$: C, 45.1; H, 2.2. Found: C, 45.1; H, 2.7; ultraviolet spectrum: 232 mμ (4.36), 259 mμ (2.80), 266 mμ (2.83); infrared spectrum (KBr pellet): ν_{C-Cl_3} 740, *775;* ν_{C-F} *1020*, 1045, *1050*, *1105* cm.$^{-1}$.

1,2-Di-(*p*-**chlorophenyl**)-1,**2-difluoroethylene** (**VI**).—Refluxing of V (1 g.) for 2 hr. with a 10% ethanolic solution of sodium ethoxide (20 ml.), dilution with water, filtration of the precipitate and recrystallization from ethanol gave VI (0.5 g., 53%), m.p. (from ethanol) 133–134°.

Anal. Calcd. for $C_{14}H_8Cl_2F_2$: C, 58.9; H, 2.8; F, 13.3. Found: C, 59.2; H, 3.1; F, 13.4; ultraviolet spectrum: 224 mμ (4.34), 294 mμ (4.60), 306 mμ (4.62) (in alcohol); infrared spectrum (KBr pellet): ν_{C-F} 1160 cm.$^{-1}$; no band at 1665–1675 cm.$^{-1}$, due to the symmetry of substitution.

The compound VI (0.5 g.) was refluxed with acetic acid (3 cc.) and chromic acid (0.5 g.) for 10 minutes. Dilution with water, extraction with ether, evaporation of the solvent and recrystallization from benzene gave *p*-chlorobenzoic acid (0.2 g., 37%), m.p. 238°. It was identified by a mixed melting point determination with an authentic specimen.

It was not possible to add liquid hydrogen fluoride to VI, nor did we succeed in an attempt to add fluorine to 4,4'-dichlorotolane (m.p. 179–180°) by treating it with a mixture of lead dioxide and liquid hydrogen fluoride at room temperature.

Acknowledgment.—The authors wish to express their thanks to Prof. Ernst D. Bergmann under whose guidance this investigation has been carried out.

TEL-AVIV, ISRAEL

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[16] H. L. Haller, *et al.*, THIS JOURNAL, **67**, 1600 (1945).

[17] P. Muller, *Helv. Chim. Acta*, **28**, 1560 (1946).

[18] E. E. Fleck, THIS JOURNAL, **70**, 2173 (1948).

[19] For comparison, the infrared spectrum of II shows the following peaks: 1002, 1042, 1070, 1180 and 1260 cm.$^{-1}$, and its ultraviolet spectrum the following bands: 227 mμ (4.46), 260 mμ (2.76), 267 mμ (2.81), 275 mμ (2.64).