522. *Insecticidal Activity and Chemical Constitution. Part II. Synthesis of Some Analogues of " DDT."*

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Several analogues of DDT have been synthesised. All showed little or no activity when tested as contact insecticides against *Calandra granaria*, L.

SINCE the discovery of the outstanding insecticidal activity of 1 : 1 : 1-trichloro-2 : 2-di-*p*-chlorophenylethane (DDT), many related compounds have been synthesised and some correlation between chemical structure and toxicity is apparent; *e.g.*, Busvine (*J. Soc. Chem. Ind.*, 1946, **65**, 356), after examining 41 DDT analogues, emphasised that the most toxic were most similar to DDT in shape and weight, a conclusion also reached by Prill, Synerholm, and Hartzell [*Contr. Boyce Thompson Inst.*, 1946, **14**, (6), 341] in connection with the *p*-substituents, and by Fleck (*J. Amer. Chem. Soc.*, 1948, **70**, 2173). Campbell and West (*Chem. and Ind.*, 1945, 334) suggested that the three β-chlorine atoms were necessary for optimal toxicity owing to a certain steric orientation requirement which also involved the nuclear chlorine atoms in the *p*-positions for maximum effect. Replacement of two or more of the β-chlorine atoms generally has an adverse effect on toxicity.

If the toxicity of DDT is due to its structural resemblance to some essential insect metabolite, then isosteres should presumably act similarly, and replacement of the three β-chlorine atoms by spatially similar atoms or groups of atoms should not destroy activity. The dimensions of the hydroxyl group (radius 1·7 A.) and the methyl group (radius 2·0 A.) agree reasonably well with those of the chlorine atom (radius 1·8 A.) and there are several reported cases of the biological equivalence of CH_3 and Cl. Thus Kuhn and his co-workers (*Ber.*, 1943, **76**, 1044) found that 6 : 7-dichloro-9-ribityl*iso*alloxazine effectively interferes with the action of 6 : 7-dimethyl-9-ribityl*iso*alloxazine (riboflavin) so that the growth of certain bacterial species is prevented. This degree of structural conformity has also been shown by Pauling and Pressman (*J. Amer. Chem. Soc.*, 1945, **67**, 1003) to be well within the limits required for isosteric activity in serological reactions.

$CO_2H\cdot CH(C_6H_4Cl)_2$ (I.)

$COMe\cdot CH(C_6H_4Cl)_2$ (II.)

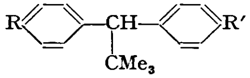
$C(OH)_3\cdot CH(C_6H_4Cl)_2$ (III.)

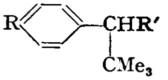
$CMe(OH)_2\cdot CH(C_6H_4Cl)_2$ (IV.)

Erlenmeyer, Bitterli, and Sorkin (*Helv. Chim. Acta*, 1948, **31**, 466) postulated that the compounds (I) and (II) might function biologically as the corresponding tri- (III) and di-hydroxymethyl (IV) compounds. Tested against *Musca domestica, Tinea granella,* and *Dermestes frischii,* both were inactive, though potentially at least isosteric with DDT. However, it is known that whilst replacement of the chlorine atoms in the *p*-positions of DDT by methyl groups reduces the toxicity somewhat, the effect of replacement of the chlorine atoms by polar but lipophobic hydroxyl groups is to produce a compound virtually devoid of insecticidal properties (Martin and Wain, *Ann. Rep. Agric. Hort. Res. Sta., Long Ashton,* 1944, p. 121).

It was thought therefore to be of interest to prepare a series of compounds involving substitution of methyl groups for the chlorine atoms in the DDT molecule. Of the two obvious routes to the structure (V; R = R′ = Cl), that employing the carbinol (VI; R = Cl, R′ = OH) was preferred to the Baeyer condensation using the more difficultly accessible trimethylacetaldehyde. Treatment of *tert.*-butylmagnesium chloride with *p*-chlorobenzaldehyde usually gave a product containing varying amounts of *p*-chlorobenzyl alcohol (cf. Hess and Rheinbolt, *Ber.*, 1921, **54**, 2043; 1924, **57**, 1921), but by carrying out the reaction at *ca.* −30° 1-*p*-chlorophenyl-2 : 2-dimethylpropan-1-ol (VI; R = Cl, R′ = OH) was obtained in 55% yield. Attempts to condense this carbinol with chlorobenzene in the presence of concentrated sulphuric acid and oleum failed to give the required substance (V; R = R′ = Cl). A compound, m. p. 127°, isolated from the distillate was probably (VII).

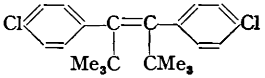
(V.)

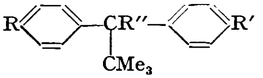




(VI.)

(VII.)





(VIII.)

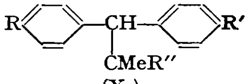
Condensation of *p*-chlorophenylmagnesium bromide with methyl trimethylacetate, however, gave 1 : 1-di-*p*-chlorophenyl-2 : 2-dimethylpropan-1-ol (VIII; R = R′ = Cl, R″ = OH) which in ethyl-alcoholic solution was smoothly reduced by means of amalgamated zinc and dry hydrogen chloride to 1 : 1-di-*p*-chlorophenyl-2 : 2-dimethylpropane (V; R = R′ = Cl). The pentamethyl analogue of DDT (V; R = R′ = Me) was prepared similarly from 1 : 1-di-*p*-tolyl-2 : 2-dimethylpropan-1-ol (VIII; R = R′ = Me, R″ = OH) which had been obtained from *p*-tolylmagnesium bromide.

Oxidation of 1-*p*-chlorophenyl-2 : 2-dimethylpropan-1-ol (VI; R = Cl, R′ = OH) with chromic acid and reaction of the resulting ketone with *p*-tolylmagnesium bromide gave the asymmetrical carbinol (VIII; R = Cl, R′ = CH_3, R″ = OH) which was reduced to the hydrocarbon (V; R = Cl, R′ = CH_3) as already described for the symmetrical compounds.

During preliminary work the reaction of DDT and some of its analogues with methylmagnesium iodide was examined. Reduction to the dichloroethane was general, and from DDT itself some 4 : 4′-dichlorostilbene was also obtained (cf. Forrest, Stephenson, and Waters, *J.*, 1945, 333). A similar case of reduction of the CCl_3 group has recently been reported by Pepper and Kulka (*J. Amer. Chem. Soc.*, 1949, **72**, 1417).

Successive replacement of the β-chlorine atoms of DDT by methyl groups would lead to compounds (IX) and (X; R = R′ = R″ = Cl). An obvious route to the dichloro-compound

$CMeCl_2{\cdot}CH(C_6H_4Cl)_2$
(IX.)



(X.)

$CHMe(OH){\cdot}C(OH)(C_6H_4Cl)_2$
(XI.)

(IX) requires 1 : 1-di-*p*-chlorophenylacetone. Attempts to prepare this compound from di-*p*-chlorophenylacetonitrile were not successful, neither methylmagnesium iodide nor methyllithium showing any tendency to react (cf. Gilman and Kirby, *J. Amer. Chem. Soc.*, 1933, **55**, 1270).

Reaction between *p*-chlorophenylmagnesium bromide and ethyl lactate, however, gave the diol (XI), but removal of the elements of water by refluxing this with acetic anhydride, to give the enolic form of 1 : 1-di-*p*-chlorophenylacetone as described by Stoermer (*Ber.*, 1906, **39**, 2288), could not be achieved; acetic anhydride in the presence of fused sodium acetate gave the diol acetate in the usual way. Finally, 1 : 1-di-*p*-chlorophenylacetone was obtained as a crystalline solid, m. p. 52—53°, by hydrolysis of the condensation product from sodiomalonic ester and di-*p*-chlorophenylacetyl chloride (cf. Erlenmeyer *et al.*, *loc. cit.*). It appeared stable to 2N-sodium hydroxide and the large amounts of 4 : 4′-dichlorobenzophenone isolated in some experiments were probably formed by autoxidation of the intermediate β-keto-γγ-di-*p*-chlorophenyl-*n*-butyric acid (cf. Rigaudy, *Compt. rend.*, 1949, **228**, 253). Treatment with phosphorus pentachloride over a wide range of reaction temperatures gave the chloroethylene (XII; R = Cl) as the main product. If this is formed *via* the enol, the stability of 1 : 1-di-*p*-chlorophenylacetone to alkali is surprising in view of Rigaudy's results (*loc cit.*).

Ethyl di-*p*-chlorophenylacetate reacted smoothly with methylmagnesium iodide, forming the carbinol (X; R = R′ = Cl, R″ = OH) in 92% yield. Treatment with phosphorus pentachloride at room temperature gave 2-chloro-1 : 1-di-*p*-chlorophenyl-2-methylpropane (X; R = R′ = R″ = Cl), a viscous liquid which was readily dehydrochlorinated by boiling alcoholic sodium hydroxide to give 1 : 1-di-*p*-chlorophenyl-2-methylprop-1-ene (XII; R = Me), m. p. 69—70°. It is suggested that the chloro-compound (X; R = R′ = R″ = Cl) results from the decomposition of an intermediate phosphorus-containing complex by the sodium hydrogen carbonate used in the isolation procedure. When the carbinol was treated with phosphorus pentachloride at temperatures above 100°, 1 : 1-di-*p*-chlorophenyl-2-methylprop-2-ene (XIII), m. p. 124°, was obtained in addition to the isomer (XII; R = Me). In this case breakdown of the phosphorus complex is postulated to yield both ethylenes without previous formation of 2-chloro-1 : 1-di-*p*-chlorophenyl-2-methylpropane (X; R = R′ = R″ = Cl) since the latter has been shown to be stable to phosphorus pentachloride at 140°.

$\mathrm{CRMe{:}C(C_6H_4Cl)_2}$
(XII.)

$\mathrm{CH_2{:}CMe{\cdot}CH(C_6H_4Cl)_2}$
(XIII.)

The structures of the isomers (XII; R = Me) and (XIII) were assigned after oxidation by means of chromic acid had been carried out in a stream of carbon dioxide. The higher-melting isomer (XIII) gave formaldehyde, and the lower-melting (XII; R = Me) formed acetone, both isolated as their 2 : 4-dinitrophenylhydrazones. Confirmation of formula (XII; R = Me) was obtained by an unambiguous synthesis. Interaction of ethyl *iso*butyrate and *p*-chlorophenylmagnesium bromide afforded 1 : 1-di-*p*-chlorophenyl-2-methylpropan-1-ol (XV; R = Me, R′ = OH), which was readily converted into (XII; R = Me) by treatment with potassium hydrogen sulphate at 160°. Some early attempts to obtain an ethylene from the carbinol (X; R = R′ = Cl, R″ = OH) by means of potassium hydrogen sulphate at 170—180° gave the ether (XIV).

$\mathrm{[(Cl{\cdot}C_6H_4)_2CH{\cdot}CMe_2]_2O}$
(XIV.)

$\mathrm{CR'(CHR_2)(C_6H_4Cl)_2}$
(XV.)

Replacement of one chlorine atom of the $\mathrm{CCl_3}$ group of DDT by hydrogen leads to 1 : 1-dichloro-2 : 2-di-*p*-chlorophenylethane (DDD) (XV; R = Cl, R′ = H) which still possesses moderate insecticidal activity (Cristol *et al.*, *Science*, 1946, **104**, 343; Busvine, *loc. cit.*; Stringer, *Ann. Appl. Biol.*, 1949, **36**, 206). The isosteric compound (XV; R = Me, R′ = H) obtained by catalytic reduction of either (XII; R = Me) or (XIII) had no such activity.

The seven analogues (V; R = R′ = Cl; R = R′ = Me; R = Cl, R′ = Me) and (X; R = R′ = Cl, R″ = OH; R = R′ = Me, R″ = OH; R = R′ = R″ = Cl; R = R′ = Me, R″ = Cl) which have been prepared showed little or no activity when tested by Mr. A. Stringer as contact insecticides against *Calandra granaria*.* It is suggested that the difference between these and DDT is caused by some intrinsic property of the $\mathrm{CCl_3}$ group, probably its capacity for electron attraction. That 2-chloro-1 : 1-di-*p*-chlorophenyl-2-methylpropane (X; R = R′ = R″ = Cl) is also non-insecticidal though readily capable of losing hydrogen chloride, is also significant in view of Martin and Wain's suggestion (*Nature*, 1944, **154**, 512) that ready dehydrochlorination is a prerequisite of insecticidal activity.

EXPERIMENTAL.

(M.p.s are uncorr. C and H microanalyses are by Drs. Weiler and Strauss.)

1-p-*Chlorophenyl*-2 : 2-*dimethylpropan*-1-*ol* (VI; R = Cl, R′ = OH).—A dry ethereal solution of *tert.*-butylmagnesium chloride, prepared from *tert.*-butyl chloride (46·7 ml.) and magnesium turnings (10·4 g.), was cooled to below −30° (solid carbon dioxide–acetone) and vigorously stirred during the

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* [*Added in proof.*] Brown and Rogers (*J. Amer. Chem. Soc.*, 1950, **72**, 1864) reported that the DDT isostere (V; R = R = OMe) possesses considerable insecticidal activity against several species. Prepared by us this compound was completely non-toxic to *Callandra granaria* L.

cautious dropwise addition of *p*-chlorobenzaldehyde (14 g.) dissolved in ether (25 ml.). After a further 4—5 hours' stirring at the same temperature, the reaction mixture was decomposed with 2N-sulphuric acid and extracted with ether. The extract, after being washed with water, saturated sodium hydrogen sulphite (three times), and sodium hydrogen carbonate, was dried, and the solvent removed. Distillation of the residue gave 1-p-*chlorophenyl*-2 : 2-*dimethylpropan*-1-*ol* as a colourless liquid (10·9 g., 55%), b. p. 90—95°/0·5 mm., n_D^{14} 1·5401 (Found : C, 66·7; H, 7·7; Cl, 17·9. $C_{11}H_{15}OCl$ requires C, 66·5; H, 7·6; Cl, 17·9%). Treatment with phenyl *iso*cyanate in light petroleum (b. p. 80—100°) gave the *phenylurethane*, which crystallised from aqueous methanol in colourless rhombic prismatic plates, m. p. 129° (Found : C, 68·1; H, 6·3; Cl, 11·2. $C_{18}H_{20}O_2NCl$ requires C, 68·0; H, 6·3; Cl, 11·2%). When the above reaction was carried out with only ice-cooling, the final distillate generally partly solidified. The solid, m. p. 72—73°, was identified as *p*-chlorobenzyl alcohol by mixed m. p. with an authentic specimen, and by the preparation of the *phenylurethane*, which crystallised from light petroleum (b. p. 80—100°) in colourless monoclinic prisms, m. p. 93·5° (Found : C, 64·5; H, 4·6; Cl, 13·9. $C_{14}H_{12}O_2NCl$ requires C, 64·3; H, 4·6; Cl, 13·6%). Attempts to separate the carbinol (VI; R = Cl, R′ = OH) and *p*-chlorobenzyl alcohol by fractionation of the acetylated mixture were unsuccessful.

1-*Chloro*-1-p-*chlorophenyl*-2 : 2-*dimethylpropane* (VI; R = R′ = Cl).—A solution of the carbinol (VI; R = Cl, R′ = OH) (4·8 g.) in dry benzene (10 ml.) was added cautiously with shaking to a suspension of phosphorus pentachloride (6·0 g., 1·2 mols.) in dry benzene (10 ml.) After being heated at 100° for 0·25 hour the mixture was diluted with water and extracted with ether, the extract dried, and the solvent removed. Distillation of the residue gave a colourless mobile liquid (4·5 g.), b. p. 80—84°/0·4 mm., n_D^{15} 1·5372 (Found : Cl, 33·0. $C_{11}H_{14}Cl_2$ requires Cl, 32·7%).

1 : 1-*Di*-p-*chlorophenyl*-2 : 2-*dimethylpropan*-1-*ol* (VIII; R = R′ = Cl, R″ = OH).—(*a*) *tert.*-Butylmagnesium chloride, prepared from *tert.*-butyl chloride (11·5 g.) and magnesium clippings (3 g.), was refluxed with di-*p*-chlorophenyl ketone (10 g.) in absolute ether (50 ml.) for 1 hour. After cooling and decomposition with 2N-sulphuric acid the product on isolation consisted of unchanged ketone and a little di-*p*-chlorophenylcarbinol.

(*b*) *p*-Chlorophenylmagnesium bromide, prepared from *p*-chlorobromobenzene (38·3 g.) and magnesium turnings (4·8 g.), was vigorously stirred in anhydrous ether (75 ml.) at 0° during the slow dropwise addition of methyl pivalate (11·6 ml.) in anhydrous ether (25 ml.). After refluxing for 16 hours, the reaction mixture was cooled in ice and decomposed with 2N-sulphuric acid. Extraction with ether and distillation of the product left after removal of the dried solvent gave unchanged chlorobromobenzene (3·6 g.) and the tertiary *carbinol* (VIII; R = R′ = Cl, R″ = OH) as a colourless viscous liquid (16·8 g., 54%), b. p. 160—164°/0·4 mm., n_D^{15} 1·5924 (Found : C, 66·2; H, 5·8; Cl, 23·2. $C_{17}H_{18}OCl_2$ requires C, 66·0; H, 5·8; Cl, 23·0%). Attempts to acetylate this and to form its phenyl- and α-naphthylurethanes were unsuccessful. Oxidation in glacial acetic acid with chromic acid gave 4 : 4′-dichlorobenzophenone, m. p. 145—146°, undepressed on admixture with an authentic specimen.

1-*Chloro*-1 : 1-*di*-p-*chlorophenyl*-2 : 2-*dimethylpropane* (VIII; R = R′ = R″ = Cl).—The carbinol (VIII; R = R′ = Cl, R″ = OH) (4·0 g.) failed to react with phosphorus pentachloride (3 g., 1 mol.) at 100°, but when heated at 140° for 2 hours afforded the *trichloro*-compound which, isolated by ether, distilled as a colourless viscous liquid (2·4 g., 56%), b. p. 190—192°/0·5 mm. (Found: Cl, 30·7. $C_{17}H_{17}Cl_3$ requires Cl, 32·5%).

1 : 1-*Di*-p-*chlorophenyl*-2 : 2-*dimethylpropane* (V; R = R′ = Cl).—The carbinol (VIII; R = R′ = Cl, R″ = OH) (7·7 g.) and amalgamated zinc (30 g.) were treated in refluxing ethyl alcohol (40 ml.) with dry hydrogen chloride for 3 hours. The oily layer which had separated on the surface was isolated with ether, and the extract washed with sodium hydrogen carbonate solution and dried. Removal of the solvent and distillation of the residual oil gave the *dichloro*-compound (6·3 g., 86%), b. p. 153°/0·5 mm., n_D^{14} 1·5861 (Found : C, 70·2; H, 6·0; Cl, 24·2. $C_{17}H_{18}Cl_2$ requires C, 69·6; H, 6·1; Cl, 24·2%). Treatment with fuming nitric acid at 0° for 0·5 hour and pouring on ice gave a cream-coloured solid which was collected, washed with water, and dried in a desiccator (Found : Cl, 18·3. $C_{17}H_{16}O_4N_2Cl_2$ requires Cl, 18·5%). This product, which was very soluble in ether and methanol, could not be obtained crystalline and is probably a mixture of isomeric *dinitro*-derivatives. Attempts to form a picrate of (V; R = R′ = Cl) were unsuccessful.

3 : 4-*Di*-p-*chlorophenyl*-2 : 2 : 5 : 5-*tetramethylhex*-3-*ene* (VII).—A mixture of 1-*p*-chlorophenyl-2 : 2-dimethylpropan-1-ol (4·2 g.) and chlorobenzene (2·3 ml.) was vigorously stirred during the addition of concentrated sulphuric acid (4 ml.) and oleum (2 ml.) and for a further 5 hours, then poured on ice; the *hexene* was isolated with ether and distilled. A glassy liquid (2·7 g.), b. p. 185°/0·5 mm., was obtained which after repeated recrystallisation from ethyl alcohol gave prisms, m. p. 127° [Found : C, 73·2; H, 7·1; Cl, 19·8%; *M* (cryoscopic in benzene), 325. $C_{22}H_{26}Cl_2$ requires C, 73·1; H, 7·2; Cl, 19·7%; *M*, 361].

1 : 1-*Di*-p-*tolyl*-2 : 2-*dimethylpropan*-1-*ol* (VIII; R = R′ = Me, R″ = OH).—*p*-Tolylmagnesium bromide, prepared from *p*-bromotoluene (34·2 g.) and magnesium turnings (4·8 g.) in absolute ether (125 ml.), was treated at 0° with a solution of methyl trimethylacetate (11·6 ml.) in absolute ether (25 ml.). After refluxing for 3 hours, the reaction mixture was cooled and the *propanol* isolated as for the analogue (VIII; R = R′ = Cl, R″ = OH). It was a colourless viscous liquid (8·4 g., 31%), b. p. 162—166°/0·5 mm., n_D^{14} 1·5862 (Found : C, 85·2; H, 9·0. $C_{19}H_{24}O$ requires C, 85·1; H, 9·0%). The structure was confirmed by chromic acid oxidation in glacial acetic acid solution to 4 : 4′-dimethylbenzophenone, m. p. 94—95° undepressed on admixture with an authentic specimen.

1 : 1-*Di*-p-*tolyl*-2 : 2-*dimethylpropane* (VI; R = R′ = Me).—Treatment of the carbinol (VIII; R = R′ = Me, R″ = OH) (2·2 g.) with amalgamated zinc (10 g.) in the presence of dry hydrogen chloride, as already described for the corresponding chloro-carbinol (VIII; R = R′ = Cl, R″ = OH),

gave the *propane* as a colourless mobile liquid (1·4 g.), b. p. 120—122°/0·3 mm., n_{D}^{16} 1·5540 (Found: C, 90·8; H, 9·0. $C_{19}H_{24}$ requires C, 90·5; H, 9·5%).

p-*Chlorophenyl* tert.-*Butyl Ketone*.—1-*p*-Chlorophenyl-2 : 2-dimethylpropan-1-ol (VI; R = Cl, R′ = OH) was oxidised by the method of Mosher and Langerak (*J. Amer. Chem. Soc.*, 1949, **71**, 286). A solution of the carbinol (8·8 g.) in glacial acetic acid (10 ml.) was stirred at 0° for 6 hours during the dropwise addition of a solution of chromic trioxide (2·5 g.) in water (2·5 ml.) and glacial acetic acid (5 ml.). The reaction mixture was poured on ice (100 g.), and the product isolated with ether. Distillation of the residue left after removal of the dried solvent gave the *ketone* as a colourless mobile liquid (6·0 g., 69%), b. p. 84—86°/0·7 mm., n_{D}^{16} 1·5309 (Found: C, 66·7; H, 6·7; Cl, 17·9. $C_{11}H_{13}OCl$ requires C, 67·2; H, 6·6; Cl, 18·1%). The *oxime*, prepared in the usual way, crystallised from ethyl alcohol in colourless monoclinic prisms, m. p. 218—219° (Found: C, 63·2; H, 6·6; Cl, 17·0. $C_{11}H_{14}ONCl$ requires C, 62·4; H, 6·6; Cl, 16·8%). The *semicarbazone* crystallised from aqueous ethyl alcohol in monoclinic prisms, m. p. 208—209° (softens at *ca.* 125°) (Found: C, 56·8; H, 6·4; Cl, 13·6. $C_{12}H_{16}ON_3Cl$ requires C, 56·8; H, 6·3; Cl, 14·0%).

1-p-*Chlorophenyl*-1-p-*tolyl*-2 : 2-*dimethylpropan*-1-*ol* (VIII; R = Cl, R′ = Me, R″ = OH).—An ethereal solution of the above ketone (12·9 g.) was added with shaking to an ice-cooled ethereal solution of *p*-tolylmagnesium bromide, prepared from magnesium turnings (2·9 g.) and *p*-bromotoluene (20·5 g.) in ether (50 ml.), and heated under reflux for 4—6 hours. The mixture was cooled in ice and decomposed by 2N-sulphuric acid. The ethereal layer, after being washed with water and sodium hydrogen sulphite and saturated sodium hydrogen carbonate solutions, was dried (Na_2SO_4), and the solvent removed. Distillation of the residue gave a fore-run consisting mainly of *p*-bromotoluene, and finally 1-p-*chlorophenyl*-1-p-*tolyl*-2 : 2-*dimethylpropan*-1-*ol* (12·7 g., 67%), b. p. 158—160°/0·7 mm., n_{D}^{15} 1·5811 (Found: C, 75·3; H, 7·7; Cl, 11·1. $C_{18}H_{21}OCl$ requires C, 74·9; H, 7·3; Cl, 12·3%). Confirmation of the structure was obtained by chromic acid oxidation which gave *p*-chlorophenyl *p*-tolyl ketone, m. p. 126—127°, undepressed by admixture with an authentic specimen.

1-p-*Chlorophenyl*-1-p-*tolyl*-2 : 2-*dimethylpropane* (V; R = Cl, R′ = Me).—This asymmetrical DDT *analogue* was obtained by reduction of the corresponding carbinol (VIII; R = Cl, R′ = Me, R″ = OH) as already described for the symmetrical hydrocarbons (V; R = R′ = Cl or Me). It was isolated as a mobile, water-white liquid (80%), b. p. 138—140°/0·6 mm., n_{D}^{16} 1·5713 (Found: C, 80·3; H, 7·7; Cl, 12·5. $C_{18}H_{21}Cl$ requires C, 79·3; H, 7·7; Cl, 13·0%).

Di-p-*chlorophenylacetyl Chloride*.—Di-*p*-chlorophenylacetic acid (42 g.), prepared by the method of Grummitt, Buck, and Egan (*Org. Synth.*, 1946, **26**, 24), was heated under reflux for 3 hours with thionyl chloride (82 g.) which had been freshly distilled after being kept for 18 hours over a little linseed oil. After removal of excess of reagent, the chloride was distilled (41·7 g., 93%); it had b. p. 190°/2 mm. (Found: Cl, 34·8. Calc. for $C_{14}H_9OCl_3$: Cl, 35·5%). Grummitt and Marsh (*J. Amer. Chem. Soc.*, 1949, **71**, 4156) report the isolation of an oily acid chloride which decomposed on attempted distillation at 3—4 mm.; Erlenmeyer *et al.* (*loc. cit.*) give m. p. 57—59°.

Di-p-*chlorophenylacetamide*.—Reid and Hunter's method (*J. Amer. Chem. Soc.*, 1948, **70**, 3515) for diphenylacetamide was employed. The above acetyl chloride (25·8 g.) was added gradually to ammonia solution (*d* 0·88; 250 ml.) and boiled for 10 minutes with occasional shaking. The product (21·8 g.,90%) crystallised from ethyl alcohol in stout rhombs, m. p. 156—157°. Grummitt and Marsh (*loc. cit.*) give m. p. 152—154°.

Di-p-*chlorophenylacetonitrile*.—Reid and Hunter's method (*loc. cit.*) was modified as follows. Di-*p*-chlorophenylacetamide (9·3 g.) and redistilled phosphorus oxychloride (2·2 ml.) were heated at 100° for 2 hours, and then poured on crushed ice. The product (8 g., 92%) isolated with ether crystallised from ethyl alcohol in aggregates of hexagonal prisms, m. p. 88—89° (Found: C, 64·3; H, 3·8; Cl, 27·2. Calc. for $C_{14}H_9NCl_2$: C, 64·1; H, 3·4; Cl, 27·1%). Grummitt and Marsh (*loc. cit.*) give m. p. 85—86°.

Di-p-*tolylacetic Acid*.—1 : 1-Dichloro-2 : 2-di-*p*-tolylethylene (44·4 g.) and powdered potassium hydroxide (27·2 g.) were refluxed for 24 hours in diethylene glycol (350 ml.) and then poured on crushed ice (1 kg.). After extraction of the neutral matter with ether, the solution was acidified with concentrated hydrochloric acid, and the product isolated with ether. Removal of the dried solvent gave the acid (20·4 g., 53%), from which traces of diethylene glycol were removed by boiling with water. Crystallisation from methyl alcohol gave a mass of colourless needles, m. p. 143—144°. Fritsch and Feldmann (*Annalen*, 1899, **306**, 81) give m. p. 144°.

1 : 1-*Di*-p-*chlorophenyl*-2 : 2-*dimethylpropan*-2-*ol* (X; R = R′ = Cl, R″ = OH).—Ethyl di-*p*-chlorophenylacetate (35·2 g.) in absolute ether (50 ml.) was added dropwise to a vigorously stirred ethereal solution of methylmagnesium iodide (from methyl iodide, 17·2 ml., and magnesium turnings, 7·2 g.). After refluxing for 4 hours, the reaction mixture was cooled and decomposed with 2N-sulphuric acid, and the product isolated with ether. Distillation of the residue after removal of the solvent gave a viscous liquid (31 g., 92%), b. p. 175—178°/0·4 mm. After being kept at 0° for 24 hours this liquid solidified and crystallised from light petroleum (b. p. 40°) in massive prisms, m. p. 76—77° (Found: C, 65·1; H, 5·5; Cl, 24·0. $C_{16}H_{16}OCl_2$ requires C, 65·1; H, 5·4; Cl, 24·1%). Attempts to acetylate or *p*-nitrobenzoylate this *propanol* and to prepare a phenyl- or α-naphthyl-urethane were not successful.

1 : 1-*Di*-p-*tolyl*-2 : 2-*dimethylpropan*-2-*ol* (X; R = R′ = Me, R″ = OH).—Ethyl di-*p*-tolylacetate (25·4 g.) reacted with methylmagnesium iodide as described above, and the product was isolated similarly after 18 hours' refluxing. It was obtained as a glassy liquid (23 g., 96%), b. p. 159—162°/0·6 mm., which slowly crystallised. The *propanol* crystallised from light petroleum (b. p. 40°) in large colourless prisms, m. p. 78—79° (Found: C, 84·9; H, 9·0. $C_{18}H_{22}O$ requires C, 85·1; H, 8·7%).

2-*Chloro*-1 : 1-*di*-p-*tolyl*-2-*methylpropane* (X; R = R′ = Me, R″ = Cl).—The foregoing carbinol (2·5 g.) was mixed with phosphorus pentachloride (2·2 g.) and kept overnight. The *chloro*-compound, isolated with ether and washed with sodium hydrogen carbonate solution, remained as a colourless viscous liquid (2·4 g. 89%) after aspiration of the dry solvent (Found, after drying *in vacuo* over P_2O_5 : Cl, 10·3. $C_{18}H_{21}Cl$ requires Cl, 13·0%).

1 : 1-*Di*-p-*chlorophenyl*-2-*methylpropan*-1-*ol* (XV; R = Me, R′ = OH).—Ethyl *iso*butyrate (5·8 g.) in anhydrous ether (25 ml.) was added with cooling and shaking to a solution of *p*-chlorophenylmagnesium bromide (from *p*-chlorobromobenzene, 19·2 g., and magnesium, 2·4 g., in anhydrous ether, 100 ml.). After being kept overnight, the mixture was decomposed with 2N-sulphuric acid, and the ethereal layer separated and washed with water and sodium hydrogen carbonate, and finally dried (Na_2SO_4). Removal of the solvent and distillation of the residue gave a fraction (2·5 g.), b. p. <80°/0·6 mm., and the tertiary *carbinol* (XV; R = Me, R′ = OH) (8·8 g.), b. p. 175—180°/0·6 mm., which quickly solidified. It crystallised from light petroleum (b. p. 60—80°) in large, colourless, hexagonal plates, m p. 115—116° (Found : C, 65·2; H, 5·5; Cl, 23·5. $C_{16}H_{16}OCl_2$ requires C, 65·1; H, 5·4; Cl, 24·0%). The di-*p*-chlorophenylmethane structure was confirmed by chromic acid oxidation in glacial acetic acid solution, 4 : 4′-dichlorobenzophenone, m. p. 145—147°, being obtained, undepressed on admixture with an authentic specimen.

2-*Chloro*-1 : 1-*di*-p-*chlorophenyl*-2-*methylpropane* (X; R = R′ = R″ = Cl).—The above carbinol (X; R = R′ = Cl, R″ = OH) (3 g.) was mixed with phosphorus pentachloride (2·7 g., 1 mol.) and kept overnight. The product, after isolation with ether and washing with sodium hydrogen carbonate solution, distilled as a colourless viscous liquid (2·6 g.), b. p. 184—186°/1·2 mm. (Found : Cl, 33·3. $C_{16}H_{15}Cl_3$ requires Cl, 34·0%). Treatment of either the crude product or the distilled sample with phosphorus pentachloride at 140° for 2 hours failed to bring about any decomposition.

1 : 1-*Di*-p-*chlorophenyl*-2-*methylprop*-1-*ene* (XII; R = Me).—(*a*) The chloro-compound (X; R = R′ = R″ = Cl) described above (3·7 g.), dissolved in ethyl alcohol (5 ml.), was refluxed for 2 hours with a solution of sodium hydroxide (0·47 g.) in ethyl alcohol (10 ml.). After removal of excess of solvent, water was added and the product extracted with ether and washed with water, and the extract dried (Na_2SO_4). Removal of the ether and distillation of the residue gave the *ethylene* (XII; R = Me) as a viscous liquid (2·9 g.), b. p. 152—156°/0·3 mm. It crystallised from methyl alcohol in prismatic plates, m. p. 69—70° (Found : C, 69·3; H, 5·0; Cl, 25·0. $C_{16}H_{14}Cl_2$ requires C, 69·4; H, 5·0; Cl, 25·6%).

(*b*) 1 : 1-Di-*p*-chlorophenyl-2-methylpropan-1-ol (XV; R = Me, R′ = OH) (1·0 g.), prepared as already described, was heated with an equal weight of anhydrous potassium hydrogen sulphate at 155—160° for 1 hour. On cooling, the product was isolated by trituration with ether, and after removal of the solvent the residual viscous oil crystallised from methyl alcohol in prisms, m. p. 63—65°, undepressed on admixture with the compound prepared as in (*a*).

Oxidation of the ethylene (XII; R = Me) (0·1 g.) in acetic acid (5 ml.) was carried out by refluxing with chromic acid (0·1 g.) for 1 hour in a stream of carbon dioxide. Acetone 2 : 4-dinitrophenylhydrazone, m. p. 123—124°, and 4 : 4′-dichlorobenzophenone, m. p. 146—147°, both undepressed on admixture with authentic specimens, were obtained from the trap and the residue, respectively.

1 : 1-*Di*-p-*chlorophenyl*-2-*methylprop*-2-*ene* (XIII).—The carbinol (X; R = R′ = Cl, R″ = OH) (3 g.) and phosphorus pentachloride (2·7 g., 1 mol.) were heated at 150° for 1 hour. After cooling, the product was isolated with ether, and the extract washed with saturated sodium hydrogen carbonate solution and dried. Removal of the solvent and distillation of the residue gave a viscous liquid (2·4 g.), b. p. 160—165°/0·4 mm., which gradually solidified. Crystallisation from methyl alcohol gave a product (A), m. p. 121—123°, which on recrystallisation from ethyl alcohol gave 1 : 1-*di*-p-*chlorophenyl*-2-*methylprop*-2-*ene* (XIII), (0·35 g.), m. p. 124—124·5° (Found : C, 69·5; H, 4·6; Cl, 25·3. $C_{16}H_{14}Cl_2$ requires C, 69·4; H, 5·0; Cl, 25·6%). Oxidation with chromic acid, as already described for the isomeric compound (XII; R = Me), yielded formaldehyde 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 150—151°. Evaporation of the mother-liquors from (A) gave a product (0·6 g.), m. p. 64—66°, identical with the ethylene (XII; R = Me). Attempts to convert (XIII) into (XII; R = Me) by heating it at 140° for 18 hours either alone or with sodium ethoxide in a sealed tube were not successful In the former case the material was recovered unchanged, and in the latter a brownish amorphous material was obtained which has not yet been fully investigated.

1 : 2-*Dichloro*-1 : 1-*di*-p-*chlorophenyl*-2-*methylpropane*.—The ethylene, m. p. 69—70° (XII; R = Me) was dissolved in chloroform (5 ml.) and saturated with chlorine at 0°. Next morning, excess of chlorine was removed by aspiration, and the product extracted with ether, washed with sodium hydrogen carbonate solution, and dried. Removal of the solvent and distillation of the residue gave the *dichloro*-compound as a pale yellow viscous liquid, b. p. 185—188°/0·5 mm. (Found : Cl, 38·8. $C_{14}H_{14}Cl_4$ requires Cl, 40·8%).

1 : 1-*Di*-p-*chlorophenyl*-2-*methylpropane* (XV; R = Me, R′ = H).—Reduction of either of the ethylenes (XII; R = Me) or (XIII) in ethyl-alcoholic solution by means of Raney nickel and hydrogen at atmospheric pressure gave the *hydrocarbon* (XV; R = Me, R = H) as a colourless viscous liquid, b. p. 142—146°/0·8 mm., n_D^{23} 1·5881 (Found : C, 68·5; H, 5·5; Cl, 25·6. $C_{16}H_{16}Cl_2$ requires C, 68·8; H, 5·7; Cl, 25·4%). Attempts to reduce 1 : 1-di-*p*-chlorophenyl-2-methylpropan-1-ol (XV; R = Me, R′ = OH) in ethyl-alcoholic solution by amalgamated zinc and dry hydrogen chloride resulted in loss of water and formation of the ethylene (XII; R = Me).

Bis-1 : 1-*di*-p-*chlorophenyl*-2-*methyl*-2-*propyl Ether* (XIV).—The carbinol (X; R = R′ = Cl, R″ = OH) (2·0 g.) and fused potassium hydrogen sulphate (2·0 g.) were heated together at 170—180° for 1 hour. The *product* (1·6 g.) isolated with ether was a colourless viscous liquid, b. p. 138—140°/0·2 mm., n_D^{14} 1·5941 (Found : C, 67·4; H, 5·2; Cl, 24·0. $C_{32}H_{30}OCl_4$ requires C, 67·2; H, 5·2; Cl, 24·8%).

p-*Chlorophenyl* p-*Tolyl Ketone*.—Toluene (125 ml.) and powdered aluminium chloride (10·4 g.) were cooled in ice and vigorously stirred during the dropwise addition of *p*-chlorobenzoyl chloride (13·75 g.).

The mixture was kept for 3 days and then decomposed by addition of ice and 2N-hydrochloric acid. The organic layer was separated, excess of toluene distilled off under reduced pressure, and the residue extracted with ether. After being washed with 2N-hydrochloric acid, water, and 10% sodium hydroxide solution, the extract was dried, and the solvent removed. Distillation of the residue gave the ketone (13·3 g., 73%), b. p. 170—180°/3 mm., which crystallised from ethyl alcohol in nacreous plates, m. p. 126—127°. Cohen (*Rec. Trav. chim.*, 1919, **38**, 117) gives m. p. 118°. The 2 : 4-*dinitrophenylhydrazone* crystallised from acetic acid–dioxan in small, lustrous, vermilion plates, m. p. 209—210° (Found : C, 58·3; H, 3·8; Cl, 8·5. $C_{20}H_{15}O_4N_4Cl$ requires C, 58·5; H, 3·7; Cl, 8·6%).

Reaction of DDT with Methylmagnesium Iodide.—Methylmagnesium iodide (3 mols.) (from methyl iodide, 10·6 ml., and magnesium, 4·2 g., in absolute ether, 70 ml.) was treated with DDT (20·2 g., 1 mol.) and heated under reflux for 7 hours after being kept overnight. The mixture was acidified with 2N-sulphuric acid, and the products isolated with ether. Removal of the dry solvent and distillation yielded a main fraction (5·0 g.), b. p. 150—160°/0·4 mm. Crystallisation from light petroleum (b. p. 40—60°) gave 1 : 1-dichloro-2 : 2-di-*p*-chlorophenylethane (XV; R = Cl, R′ = H), m. p. 109—110° (Found : C, 52·6; H, 3·1. Calc. for $C_{14}H_{10}Cl_4$: C, 52·5; H, 3·1%) undepressed on admixture with an authentic specimen. 4 : 4′-Dichlorostilbene, m. p. 174—175° (Found : C, 67·3; H, 4·0. Calc. for $C_{14}H_{10}Cl_2$: C, 67·5; H, 4·0%) undepressed by an authentic specimen, was also obtained.

Reaction of 1 : 1 : 1-*Trichloro*-2 : 2-*di*-p-*tolylethane with Methylmagnesium Iodide.*—This was carried out as above for DDT. The product (6·1 g.), b. p. 136—142°/0·2 mm., from the DDT analogue (10 g.) crystallised from light petroleum (b. p. 40°) in agglomerates of rhombic prisms, m. p. 81—82° undepressed on admixture with an authentic specimen of 1 : 1-dichloro-2 : 2-di-*p*-tolylethane. Brand (*Ber.*, 1913, **46**, 2941) gives m. p. 80°. No stilbene derivative was isolated.

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