530. *Insecticidal Activity and Chemical Constitution. Part IV.** *Synthesis of 2 : 2-Di-*p*-chlorophenyl-3-methylbutane.*

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A route to substituted 3-methyl-2 : 2-diphenylbutanes of type (I) has been developed. The structure of 2 : 2-di-*p*-chlorophenyl-3-methylbutane (I; R = Cl, R′ = H) obtained in earlier work has been confirmed by comparison with the new synthetic material.

The necessity for an unambiguous synthesis of (I; R = Cl, R′ = H) arose from experiments described in the preceding paper. Initial attempts to achieve the αα-substituted propionic acid (II) involved *C*-methylation of the corresponding acetic acid derivatives. Various workers have reported the formation of a sodio-derivative of methyl or ethyl diphenylacetate (*e.g.*, Schlenk, Hillemann, and Rodloff, *Annalen*, 1931, **487**, 142; Stau-

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* Part III, preceding paper.

dinger and Meyer, *Helv. Chim. Acta*, 1922, **5**, 669) but we were unable to demonstrate this for methyl or ethyl di-*p*-chlorophenylacetate. Methylation of di-*p*-chlorophenylacetonitrile (cf. Klingemann, *Annalen*, 1893, **275**, 85; Neure, *ibid.*, 1889, **250**, 143) was likewise unsuccessful. Finally methyl αα-di-*p*-nitrophenylpropionate (II; $R = NO_2$, $R' = Me$) was obtained by treating a solution of the corresponding acetate in boiling dioxan with excess of methyl iodide and sodium methoxide (cf. von Richter, *Ber.*, 1888, **21**, 2470). Purification of the product was tedious, however, and it was soon found more convenient to proceed to this compound *via* methyl αα-diphenylpropionate (II; R = H, R′ = Me).

$(p\text{-}C_6H_4R)_2CMe{\cdot}CMe_2R'$ (I) $(p\text{-}C_6H_4R)_2CMe{\cdot}CO_2R'$ (II) $(p\text{-}C_6H_4R)_2CMe{\cdot}CMe{:}CH_2$ (III)

Whilst αα-diphenylpropionic acid (II; R = R′ = H) could be obtained in moderate yield, if somewhat erratically, by condensing pyruvic acid with benzene (Böttinger, *Ber.*, 1881, **14**, 1595), in the *p*-chloro-series the only product isolated was α-*p*-chlorophenylacrylic acid. Methyl αα-diphenylpropionate (II; R = H, R′ = Me) and fuming nitric acid at −20°, however, readily gave the dinitro-derivative (II; $R = NO_2$, R′ = Me) which could be converted into the corresponding dichloro-compound by reduction and a subsequent Sandmeyer reaction. This ester with an excess of methylmagnesium iodide gave the alcohol (I; R = Cl, R′ = OH).

Despite the ready conversion of the unsubstituted tertiary alcohol (I; R = H, R′ = OH) into the butene (III; R = H) (see preceding paper), a similar conversion of the dichloro-analogue (I; R = Cl, R′ = OH) proved very difficult. At temperatures up to 165° the compound was recovered unchanged, whilst temperatures high enough to bring about loss of water also caused extensive decomposition. An alternative route to the hydrocarbon (I; R = Cl, R′ = H), involving 3-methyl-2 : 2-diphenylbutane (I; R = R′ = H) obtained from the butene (III; R = H) by catalytic reduction, was finally successful: nitration and a Sandmeyer reaction gave 2 : 2-di-*p*-chlorophenyl-3-methylbutane (I; R = Cl, R′ = H) as a crystalline solid, m. p. 122°.

In an attempt to obtain this hydrocarbon by another route, reaction of *p*-chloroacetophenone and *iso*propylmagnesium iodide gave 2-*p*-chlorophenyl-3-methylbutan-2-ol but this failed to undergo a successful Baeyer condensation with chlorobenzene. Attempts to condense methyl *iso*propyl ketone with benzene or chlorobenzene in the presence of sulphuric acid also proved fruitless.

EXPERIMENTAL

M. p.s are uncorr. Microanalyses (C and H) are by Drs. Weiler and Strauss, Oxford.

αα-Diphenylpropionic Acid (II; R = R′ = H).—Böttinger's method (*Ber.*, 1881, **14**, 1595) was modified as follows: Concentrated sulphuric acid (technical; 400 ml.) was vigorously stirred at −14° during the addition of benzene (70 ml.) in 20 minutes, followed by pyruvic acid (20 ml. of 95%) in 25 minutes. The mixture was allowed to warm to 6°, stirred for a further 25 minutes at this temperature, and then poured on ice (3 kg.). The organic matter was extracted with ether, and acidic material isolated by shaking the extract with 5% sodium hydroxide solution (3 × 20 ml.). The combined alkaline washings were acidified with concentrated hydrochloric acid, and the product recovered by extraction with ether. Removal of the solvent, after drying, gave a solid acid (19·7 g., 33%) which crystallised from methyl alcohol in massive rhombic agglomerates, m. p. 173·5—174° (Found: C, 79·3; H, 6·3. Calc. for $C_{15}H_{14}O_2$: C, 79·6; H, 6·2%). In one double-scale preparation, atropic acid (10·8 g.), m. p. 106—107°, was the only product isolated. Methyl αα-diphenylpropionate, prepared by diazomethane, was a colourless liquid, b. p. 144°/1 mm., n_D^{20} 1·5674 (Found: C, 79·6; H, 6·7. Calc. for $C_{16}H_{16}O_2$: C, 80·0; H, 6·7%). Bateman and Marvel (*loc. cit.*) give b. p. 149—152°/3 mm.

*Methyl αα-Di-*p*-nitrophenylacetate.*—(*a*) Methyl αα-diphenylacetate (19·6 g.) was added in small portions during 2 hours to vigorously stirred fuming nitric acid (130 ml.), kept at −30° during the addition and for a further 1 hour. The mixture was poured on crushed ice (1 kg.), the solid product was extracted with chloroform, and the extract washed with water and then dilute sodium hydroxide solution and dried ($CaCl_2$). The solvent was removed and the residual solid crystallised from acetic acid in aggregates of pale yellow rhombic prisms (13·8 g., 50%),

m. p. 162—163°. This procedure gave yields substantially greater than those obtained by Haskelberg and Lavie (*J. Amer. Chem. Soc.*, 1949, **71**, 2580) who reported m. p. 162°. From the mother-liquors was obtained a solid which crystallised from methyl alcohol in yellow hexagonal prisms, m. p. 118·5—119° (Found : C, 56·6; H, 3·7. $C_{15}H_{12}O_6N_2$ requires C, 57·0; H, 3·8%), probably the isomeric *methyl* o-*nitrophenyl*-p-*nitrophenylacetate*.

Ethyl αα-Di-p-*nitrophenylacetate*.—This *ester*, prepared in 36% yield as described for the methyl ester, crystallised from acetic acid in slender yellow rectangular prisms, m. p. 132—132·5° (Found : C, 58·3; H, 4·2. $C_{16}H_{14}O_6N_2$ requires C, 58·2; H, 4·3%).

Methyl αα-Di-p-*nitrophenylpropionate* (II; R = NO_2, R′ = Me).—(*a*) Methyl αα-diphenylpropionate (II; R = H, R′ = Me) (8·2 g.) was added gradually to vigorously stirred fuming nitric acid (53 ml.) at −20° and the mixture was kept at that temperature for a further 1 hour, then poured on crushed ice (1 kg.). The solid product was extracted with ether, and the extract washed free from acid with dilute sodium hydroxide solution and dried (Na_2SO_4). Removal of the solvent left the *nitro-ester* which crystallised from ethyl alcohol–acetic acid, during several days, in large aggregates of pale yellow prisms (5·2 g., 47%), m. p. 107—108° (Found : C, 58·2; H, 4·2. $C_{16}H_{14}O_6N_2$ requires C, 58·2; H, 4·3%).

(*b*) A solution of methyl αα-di-*p*-nitrophenylacetate (2 g.) in a mixture of methyl alcohol (5 ml.), dioxan (5 ml.), and methyl iodide (5 ml.) was stirred and refluxed for 4 hours during the dropwise addition of a solution of sodium (0·15 g.) in methyl alcohol (1·5 ml.). After removal of the solvents, the product was extracted with ether and purified as in (*a*) above (yield, 0·65 g., 44%; m. p. 105—106° undepressed by admixture with the above product). Unchanged starting material (0·6 g.) was recovered.

(*c*) When *C*-methylation of ethyl αα-di-*p*-nitrophenylacetate was attempted, simultaneous trans-esterification occurred and the products isolated were methyl αα-di-*p*-nitrophenylacetate, m. p. 163—164°, and methyl αα-di-*p*-nitrophenylpropionate, m. p. 105—106°, both m. p.s being undepressed on admixture with authentic specimens.

Methyl αα-Di-p-*aminophenylpropionate* (II; R = NH_2, R′ = Me).—A solution of the above nitro-ester (II; R = NO_2) (4·6 g.) in dioxan (17 ml.) and ethyl alcohol (17 ml.) was shaken in an atmosphere of hydrogen in the presence of Raney nickel for 4 hours. Removal of the solvents after filtration from the catalyst left the *diamine* as a viscous syrup which crystallised from ethyl alcohol in stout rectangular prisms (3·7 g., 98%), m. p. 145—146° (Found : C, 71·1; H, 6·7. $C_{16}H_{18}O_2N_2$ requires C, 71·1; H, 6·7%). The *diacetyl* derivative crystallised from methyl alcohol in minute prisms, m. p. 224° (Found : C, 67·8; H, 6·6. $C_{20}H_{22}O_4N_2$ requires C, 67·8; H, 6·6%).

Methyl αα-Di-p-*chlorophenylpropionate* (II; R = Cl, R′ = Me).—The amino-ester (3·2 g.) in 2N-hydrochloric acid (32 ml.) was treated at 4—8° with sodium nitrite (1·7 g.) in water (6 ml.). After destruction of the excess of nitrous acid by urea, the solution was run into a stirred boiling solution of cuprous chloride (*ca.* 10 g.) in concentrated hydrochloric acid (32 ml.). After a further 5 minutes' stirring the mixture was poured on ice and the product isolated with ether. The extract, after being washed with dilute sodium hydroxide solution and water, was dried and the solvent was removed. Distillation of the residue gave the *dichloro-ester* (3·4 g., 93%), b. p. 160—162°/0·7 mm. (Found : C, 62·2; H, 4·6. $C_{16}H_{14}O_2Cl_2$ requires C, 62·1; H, 4·6%). Hydrolysis by alcoholic potassium hydroxide gave *αα-di*-p-*chlorophenylpropionic acid*, which crystallised from aqueous methyl alcohol in rosettes of rectangular prisms, m. p. 158—159° (Found : C, 61·0; H, 4·0. $C_{15}H_{12}O_2Cl_2$ requires C, 61·0; H, 4·1%).

Attempts to prepare this acid by the condensation of chlorobenzene and pyruvic acid as described for 2 : 2-diphenylpropionic acid gave only α-*p*-chlorophenylacrylic acid, m. p. 108°, identical with an authentic specimen (see below).

3 : 3-*Di*-p-*chlorophenyl-2-methylbutan-2-ol* (I; R = Cl, R′ = OH).—A solution of methyl αα-di-*p*-chlorophenylpropionate (5·2 g.) in ether (50 ml.) was added to ethereal methylmagnesium iodide (from 2 g. of magnesium and 5·1 ml. of methyl iodide) cooled to 0°. After 16 hours' refluxing the mixture was cooled to 0° and decomposed with 2N-sulphuric acid. The ethereal layer was separated, washed successively with water, aqueous sodium hydrogen sulphite and sodium hydrogen carbonate, and then dried (Na_2SO_4). Distillation gave the *alcohol* (4·5 g., 87%), b. p. 160°/0·2 mm., which slowly solidified. It crystallised from aqueous methyl alcohol in rhombic prismatic plates, m. p. 61—61·5° (Found : C, 66·0; H, 5·6; Cl, 23·0. $C_{17}H_{18}OCl_2$ requires C, 66·0; H, 5·8; Cl, 23·0%). An attempt to prepare the methyl ether by diazomethane was unsuccessful. Oxidation with chromium trioxide in acetic acid gave 4 : 4-dichlorobenzophenone, m. p. 145° undepressed on admixture with an authentic specimen, thus establishing the 4 : 4′-orientation of the nitro-groups in the methyl dinitrophenylpropionate described

above. Treatment with phosphorus pentachloride at 160° for 1 hour in an attempt to prepare 3-chloro-2 : 2-di-*p*-chlorophenyl-3-methylbutane (I; R = R′ = Cl) gave an unidentified product, m. p. 98·5—99°. Treatment of an ethyl alcoholic solution of the alcohol (I; R = Cl, R′ = OH) with dry gaseous hydrogen chloride at 0° or at the b. p. resulted in recovery of the alcohol unchanged.

2-*Methyl*-3 : 3-*diphenylbutan*-2-*ol* (I; R = H, R′ = OH).—A solution of methyl αα-diphenylpropionate (11·2 g.) in ether (75 ml.) was added to a vigorously stirred solution of methylmagnesium iodide (from 17 g. of magnesium) in ether (200 ml.) at 0°. The mixture was kept at room temperature for 3 days, then cooled to 0° and decomposed with 2N-sulphuric acid. Isolation as above gave the *alcohol* (11·2 g., 100%), b. p. 135—136°/0·6 mm., n_D^{18} 1·5772 (Found: C, 84·9; H, 8·2. $C_{17}H_{20}O$ requires C, 84·9; H, 8·4%). Bateman and Marvel (*loc. cit.*) presumably prepared this compound but did not isolate, purify, or analyse it.

2-*Methyl*-3 : 3-*diphenylbut*-1-*ene* (III; R = H).—The alcohol (I; R = H, R′ = OH) (4·3 g.) was heated with toluene-*p*-sulphonic acid (0·4 g.) at 125° for 20 minutes. The butene, after removal of the acid, distilled as a colourless mobile liquid (4·0 g., 100%), b. p. 116—118°/0·3 mm., n_D^{21} 1·5728 (Found: C, 91·5; H, 8·2. Calc. for $C_{17}H_{18}$: C, 91·8; H, 8·2%). Bateman and Marvel (*loc. cit.*) give b. p. 132—135°/4·5 mm., n_D^{20} 1·5730.

3-*Methyl*-2 : 2-*diphenylbutane* (I; R = R′ = H).—A solution of the above olefin in ethyl alcohol (30 ml.) was reduced by hydrogen in the presence of Raney nickel. Distillation of the filtered solution gave 3-*methyl*-2 : 2-*diphenylbutane* which distilled as a mobile liquid (4·3 g., 100%), b. p. 112°/0·6 mm., n_D^{17} 1·5653 (Found: C, 90·9; H, 9·0. $C_{17}H_{20}$ requires C, 91·0; H, 9·0%).

3-*Methyl*-2 : 2-*di*-p-*nitrophenylbutane* (I; R = NO_2, R′ = H).—A solution of the hydrocarbon (I; R = R′ = H) (7·9 g.) in acetic acid (20 ml.) was added dropwise, with stirring, during 30 minutes, to fuming nitric acid (50 ml.) cooled to −15°. After 2 hours' stirring at the same temperature the mixture was poured into ice-water, and the *butane* collected by filtration. After being washed with sodium hydrogen carbonate solution and water, the residual solid crystallised from aqueous acetone in small yellow waxy prismatic plates (6·5 g., 59%), m. p. 175—175·5° (Found: C, 64·7; H, 5·9. $C_{17}H_{18}O_4N_2$ requires C, 64·9; H, 5·8%).

2 : 2-*Di*-p-*aminophenyl*-3-*methylbutane* (I; R = NH_2, R′ = H).—The above nitro-compound (3·3 g.) in dioxan (50 ml.) was reduced by hydrogen and Raney nickel. The *diamine* crystallised from aqueous methyl alcohol in rosettes of monoclinic prisms (2·4 g., 90%), m. p. 135—135·5° (Found: C, 80·0; H, 8·7. $C_{17}H_{22}N_2$ requires C, 80·3; H, 8·7%). The *diacetyl* derivative crystallised from aqueous methyl alcohol in tiny nacreous plates, m. p. 139—139·5° (Found: C, 74·4; H, 7·7. $C_{21}H_{26}O_2N_2$ requires C, 74·5; H, 7·75%).

2 : 2-*Di*-p-*chlorophenyl*-3-*methylbutane* (I; R = Cl, R′ = H).—The above diamine (3·3 g.) was stirred with warm 2N-hydrochloric acid (32 ml.), cooled to 0°, and diazotised at 5—10° by sodium nitrite (1·6 g.) in water (4 ml.). After 90 minutes' stirring excess of nitrous acid was removed with urea, and the diazonium solution was added during 3 minutes to a stirred boiling solution of cuprous chloride (20 g.) in concentrated hydrochloric acid (50 ml.). After a further 3 minutes the mixture was poured on ice and the product extracted with ether. After the extract had been washed with 5% sodium hydroxide solution and then water, it was dried (Na_2SO_4) and distilled (2·0 g., 64%; b. p. 140°/0·2 mm.). The *chloro*-compound crystallised in aggregates of stout prisms, m. p. 121·5—122° (Found: C, 69·8; H, 6·2; Cl, 24·0. $C_{17}H_{18}Cl_2$ requires C, 69·6; H, 6·2; Cl, 24·2%). Oxidation with chromium trioxide in acetic acid gave 4 : 4′-dichlorobenzophenone, m. p. 145—146°.

α-p-*Chlorophenyl*-α-*hydroxypropionic Acid*.—A solution of pyruvic acid (2 ml. of 95%, ≡ 2·3 g.) in ether (20 ml.) was dried ($CaCl_2$) and added with stirring to an ice-cooled solution of phenylmagnesium bromide [from magnesium turnings (2·3 g.) and *p*-bromochlorobenzene (17 ml.)] in ether (100 ml.). After 48 hours at room temperature the mixture was cooled to 0° and decomposed with 2N-sulphuric acid, and the ethereal layer washed with water, 1% sodium hydrogen sulphite solution, and again with water. The product was isolated by extraction of the ethereal layer with saturated sodium hydrogen carbonate solution, acidification of the combined extracts with concentrated hydrochloric acid, and re-extraction with ether. After being washed twice with water, the ethereal extract was dried (Na_2SO_4), and the solvent was removed. The solid *acid* crystallised from benzene in a mass of monoclinic prisms (3·0 g., 57%), m. p. 136—137° (Found: C, 54·0; H, 4·5; Cl, 17·9. $C_9H_9O_3Cl$ requires C, 53·9; H, 4·5; Cl, 17·7%). The p-*bromophenacyl* ester crystallised from aqueous methyl alcohol in clusters of minute prisms, m. p. 88—90° (Found: C, 51·5; H, 3·6. $C_{17}H_{14}O_4ClBr$ requires C, 51·3; H, 3·6%).

α-p-*Chlorophenylacrylic Acid*.—The above hydroxy-acid (0·13 g.) in ether (1 ml.) was added to concentrated sulphuric acid (20 ml.), and the mixture stirred at room temperature for 1·5 hours and then poured on ice. The organic matter was extracted with ether, the extract washed with water, and the acid recovered by saturated sodium hydrogen carbonate solution (2 × 5 ml.) and acidification. α-p-*Chlorophenylacrylic acid,* isolated with ether, crystallised from aqueous methyl in a mat of fine needles (0·09 g.), m. p. 109—110° (Found: C, 58·9; H, 4·1. $C_9H_7O_2Cl$ requires C, 59·2; H, 3·9%).

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