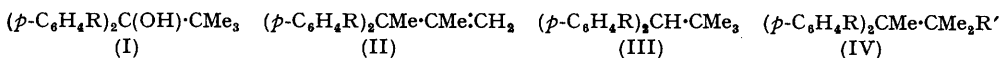


529. Insecticidal Activity and Chemical Constitution. Part III.* A New Synthetic Route to Methyl Analogues of DDT.

By E. JOHN SKERRETT and D. WOODCOCK.

The DDT isosteres $[(p\text{-C}_6\text{H}_4\text{R})_2\text{CHBu}^t$; R = Cl or Me] reported earlier have been shown to contain the corresponding butenes $[(p\text{-C}_6\text{H}_4\text{R})_2\text{CMe}\cdot\text{CMe}\cdot\text{CH}_2$; R = Cl or Me]. New unambiguous syntheses are described and the negligible contact insecticidal activity of these compounds against *Calandra granaria* is confirmed. The rearrangement of the alcohols by acids is discussed and a carbonium-ion mechanism is suggested.

A NUMBER of compounds, including (III; R = Cl or Me), which are isosteric with DDT (Part II* of this series), were completely ineffective as contact insecticides against the grain weevil *Calandra granaria* L. In view of the considerable activity against various insect species reported for the compound (III; R = OMe) (Brown and Rogers, *J. Amer. Chem. Soc.*, 1950, **72**, 1864) it was decided to examine the possibility of rearrangement having occurred during the reduction of the alcohols (I; R = Cl or Me) by ethyl-alcoholic hydrogen chloride and amalgamated zinc.



The ready rearrangement of 2:2-dimethyl-1:1-diphenylpropan-1-ol (I; R = H) and elimination of water under the influence of acidic reagents to form the butene (II; R = H) has been described by various workers (Schlenk and Racky, *Annalen*, 1912, **394**, 212; Ramart-Lucas, *Ann. Chim. Phys.*, 1913, **30**, 390; *Compt. rend.*, 1912, **154**, 1088; Bateman and Marvel, *J. Amer. Chem. Soc.*, 1927, **49**, 2917). We have confirmed that the rearrangement is brought about by toluene-*p*-sulphonic acid (Bateman and Marvel, *loc. cit.*) and have shown that hot ethyl-alcoholic hydrogen chloride is similarly effective. With the dichloro-alcohol (I; R = Cl) the latter treatment also caused loss of the elements of water, to form 3:3-di-*p*-chlorophenyl-2-methylbut-1-ene (II; R = Cl), though at 0° the action of dry ethyl-alcoholic hydrogen chloride was to form the chloro-compound (IV; R = R' = Cl) (cf. Schlenk and Racky, *loc. cit.*). It seemed highly probable, therefore, that the reduction procedure previously described for (I) (Skerrett and Woodcock, *loc. cit.*) would cause rearrangement. Re-examination of the product believed to be (III; R = Cl) showed it to contain some of the butene (II; R = Cl), since 2:2-di-*p*-chlorophenyl-3-methylbutane (IV; R = Cl, R' = H) was isolated after hydrogenation in presence of Raney nickel. Its formation can be explained by assuming a reactive intermediate of carbonium-ion type (cf. Lucas, *J. Amer. Chem. Soc.*, 1930, **52**, 802; Brown and Fletcher, *ibid.*, 1949, **71**, 1845); this can undergo rearrangement to the butene (II) or reduction to the hydrocarbon (III), and the extent to which the latter proceeds will depend on the stability of the carbonium ion. In the case of the unsubstituted alcohol (I; R = H) rearrangement was complete even in the presence of nascent hydrogen, whereas with the dichloro-alcohol (I; R = Cl) reduction to the hydrocarbon (III; R = Cl) predominated, presumably owing to the stabilising influence of the *p*-chlorine atoms on the carbonium ion.

It is interesting that no rearrangement of the tertiary alcohol (IV; R = Cl, R' = OH) was observed in refluxing ethyl-alcoholic hydrogen chloride, but in the presence of amalgamated zinc some reduction to the hydrocarbon took place.

For an unambiguous synthesis of (III; R = Cl), the alcohol (I; R = H) was hydrogenated to the hydrocarbon (III; R = H) under pressure, in presence of copper chromite. Fuming nitric acid at -15° then afforded the dinitro-derivative (III; R = NO₂) which led to the diamine (III; R = NH₂), whence a Sandmeyer reaction gave 1:1-di-*p*-chlorophenyl-2:2-dimethylpropane (III; R = Cl), m. p. 82°; the failure of the earlier product to crystallise was probably due to the presence of the liquid butene.

Similarly, the compound (III; R = Me) (Skerrett and Woodcock, *loc. cit.*) was likely

* Part II, *J.*, 1950, 2718.

to have contained considerable amounts of the butene (II; R = Me). Hydrogenation of (I; R = Me) gave the compound (III; R = Me) as a liquid.

Both the pure DDT isosteres (III; R = Cl and Me) have been tested for contact insecticidal potency against *Calandra granaria* and found to possess negligible activity. This further strengthens the view that the toxicity of DDT is not due to its structural resemblance to some insect metabolite (Skerrett, Stringer, and Woodcock, *Biochem. J.*, 1951, **49**, xxviii).

EXPERIMENTAL

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

2 : 2-Dimethyl-1 : 1-diphenylpropan-1-ol (I; R = H).—A solution of methyl pivalate (12 ml., supplied through the courtesy of the Director, Chemical Research Laboratory, Teddington) in anhydrous ether (25 ml.) was added to an ice-cooled solution of phenylmagnesium bromide [from bromobenzene (22 ml.) and magnesium turnings (4.9 g.)] in ether (100 ml.). The mixture was not refluxed owing to the possibility of rearrangement but was kept at room temperature for 3 days, then cooled in ice and decomposed by 2N-sulphuric acid. The ethereal layer was washed successively with water, 1% sodium hydrogen sulphite and saturated sodium hydrogen carbonate solutions, dried (Na_2SO_4), and freed from solvent. Distillation of the residue gave a fore-run (2.5 g.), b. p. $<110^\circ/0.3$ mm., and then the required alcohol (16.9 g., 65%), b. p. $140\text{--}142^\circ/0.3$ mm., n_D^{20} 1.5750. Bateman and Marvel (*loc. cit.*) give b. p. $148\text{--}150^\circ/2.5$ mm., n_D^{20} 1.5748.

2 : 2-Dimethyl-1 : 1-diphenylpropane (III; R = H).—The above alcohol (10.6 g.) was hydrogenated in ethyl alcohol (50 ml.) in the presence of copper chromite (2.0 g.) at $200^\circ/150$ atm. for 10 hours. The cooled solution was filtered and, after removal of the solvent, distillation of the residue gave the hydrocarbon (9.8 g., 99%), b. p. $128\text{--}132^\circ/0.4$ mm., which rapidly solidified. It crystallised from methyl alcohol in monoclinic prisms, m. p. $55\text{--}56^\circ$ (Found : C, 90.9; H, 9.0. $\text{C}_{17}\text{H}_{20}$ requires C, 91.0; H, 9.0%).

Refluxing the alcohol (1.1 g.) in ethyl alcohol for 2 hours with zinc amalgam in the presence of dry gaseous hydrogen chloride gave a mixture (0.7 g.), b. p. $90\text{--}94^\circ/0.2$ mm., n_D^{20} 1.5719 (Found : C, 91.1; H, 8.6. Calc. for $\text{C}_{17}\text{H}_{18}$: C, 91.8; H, 8.2. Calc. for $\text{C}_{17}\text{H}_{20}$: C, 91.0; H, 9.0%), of the propane (III; R = H) and the butene (II; R = H). Presence of the latter was shown by hydrogenation (Raney nickel) and nitration (fuming nitric acid in acetic acid at -20°). The nitro-derivative crystallised from acetone-ethyl alcohol in nacreous plates, m. p. $171\text{--}172^\circ$ alone or mixed with an authentic specimen (following paper).

2 : 2-Dimethyl-1 : 1-di-p-nitrophenylpropane (III; R = NO_2).—A solution of the hydrocarbon (III; R = H) (6.3 g.) in acetic acid (16 ml.) was added dropwise during 0.75 hour to vigorously stirred fuming nitric acid (41 ml.) at -15° . The mixture was allowed to warm to $+3^\circ$ in 1.5 hours and then poured into water. The precipitated solid was extracted with chloroform, and the extract washed with water, followed by saturated sodium hydrogen carbonate solution, and dried (CaCl_2). After removal of the solvent the dinitro-compound crystallised from acetone-ethyl alcohol in fine yellow needles (5.8 g., 66%), m. p. $149.5\text{--}150^\circ$ (Found : C, 64.98; H, 5.8. $\text{C}_{17}\text{H}_{18}\text{O}_4\text{N}_2$ requires C, 64.94; H, 5.8%).

1 : 1-Di-p-aminophenyl-2 : 2-dimethylpropane (III; R = NH_2).—The foregoing compound (4.9 g.) was hydrogenated in dioxan (50 ml.) in the presence of Raney nickel at room temperature and pressure. The solvent was removed from the filtered solution by distillation under reduced pressure and the diamine (4.0 g.) crystallised from aqueous methyl alcohol in rhombic prisms, m. p. $141\text{--}142^\circ$ (Found : C, 80.2; H, 8.8. $\text{C}_{17}\text{H}_{22}\text{N}_2$ requires C, 80.3; H, 8.7%). The diacetyl derivative crystallised from methyl alcohol in sheaves of fine prisms, m. p. $167\text{--}168^\circ$ (Found : C, 74.5; H, 7.7. $\text{C}_{21}\text{H}_{26}\text{O}_2\text{N}_2$ requires C, 74.5; H, 7.7%).

1 : 1-Di-p-chlorophenyl-2 : 2-dimethylpropane (III; R = Cl).—The diamine (III; R = NH_2) (4.0 g.) was suspended in 2N-hydrochloric acid (42 ml.) and stirred at $2\text{--}4^\circ$ during the addition of sodium nitrite (2.5 g.) in water (7.5 ml.) in 10 minutes. Excess of nitrous acid was removed by urea, and the diazonium chloride solution was then added rapidly (5 minutes) to a vigorously stirred boiling solution of cuprous chloride (32 g.) in concentrated hydrochloric acid (70 ml.). The mixture was poured into brine to prevent precipitation of insoluble copper salts, the organic material extracted with ether, and the extract washed with dilute sodium hydroxide solution and then water, and dried (Na_2SO_4). Distillation gave the chloro-compound (2.9 g., 63%), b. p. $150^\circ/1.5$ mm., which slowly solidified and crystallised from methyl alcohol in rosettes of slender prisms, m. p. $81\text{--}82^\circ$ (Found : C, 69.6; H, 6.2; Cl, 24.2. $\text{C}_{17}\text{H}_{18}\text{Cl}_2$ requires C, 69.6; H, 6.1; Cl, 24.2%). The orientation of the chlorine atoms was confirmed by oxidation of the

product with chromium trioxide in glacial acetic acid, which gave 4:4'-dichlorobenzophenone, m. p. 144—145°, undepressed on admixture with an authentic specimen.

2-Methyl-3:3-diphenylbut-1-ene (II; R = H).—A solution of the alcohol (I; R = H) (1.7 g.) in ethyl alcohol (10 ml.) was refluxed for 3 hours during the passage of dry gaseous hydrogen chloride. After addition of water the product was extracted with ether, and the extract washed with sodium hydrogen carbonate solution and dried. Distillation gave a mobile liquid (1.35 g.), b. p. 110—112°/0.7 mm., n_D^{20} 1.5730 (Found: C, 91.8; H, 8.0. 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. and n_D^{20} 1.5730.

3:3-Di-*p*-chlorophenyl-2-methylbut-1-ene (II; R = Cl).—(a) The chloro-alcohol (I; R = Cl) (Part II) (2.0 g.) was treated as described above for the unsubstituted alcohol. The *chlorobutene*, was a viscous liquid (1.5 g.), b. p. 158—162°/0.8 mm. (Found: Cl, 24.8. $C_{17}H_{16}Cl_2$ requires Cl, 24.4%).

(b) The chloro-alcohol (I; R = Cl) (1.2 g.) was heated with toluene-*p*-sulphonic acid (0.3 g.) at 150—160° for 9 hours. The product (0.8 g.), isolated with ether, was a liquid, b. p. 150—160°/0.8 mm. (Found: Cl, 23.9%).

2:2-Di-*p*-chlorophenyl-3-methylbutane (IV; R = Cl, R' = H).—An alcoholic solution of the product from (a) or (b) (1.5 g.) was hydrogenated at room temperature and pressure in the presence of Raney nickel. Absorption of the theoretical amount of hydrogen was rapid and, after removal of the solvent from the filtered solution, the residue was distilled. The product crystallised from ethyl alcohol in aggregates of stout prisms (1.3 g.), m. p. 121—122° alone or mixed with each other or with an authentic specimen (following paper).

3-Chloro-2:2-di-*p*-chlorophenyl-3-methylbutane (IV; R = R' = Cl).—A solution of the alcohol (I; R = Cl) (4.0 g.) in absolute ethyl alcohol was saturated at 0° with dry gaseous hydrogen chloride and kept overnight at the same temperature. After decantation from the sticky material which had been formed, the solution deposited crystals during 2 days at room temperature. This *product* crystallised from ethyl alcohol in rhombic prisms, m. p. 130—132° (decomp.) (Found: C, 62.6; H, 5.1; Cl, 31.5. $C_{17}H_{17}Cl_3$ requires C, 62.3; H, 5.2; Cl, 32.5%).

2:2-Dimethyl-1:1-di-*p*-tolylpropane (III; R = Me).—A solution of 2:2-dimethyl-1:1-di-*p*-tolylpropan-1-ol (I; R = Me) (2.3 g.) in ethyl alcohol (25 ml.) was hydrogenated for 10 hours at 200°/160 atm. in the presence of copper chromite (0.5 g.). The solvent was removed from the filtered solution, and the residue dissolved in ether, washed successively with 2*N*-hydrochloric acid (to remove ether-soluble metallic complexes), water, and saturated sodium hydrogen carbonate solution, and dried. Distillation gave the *hydrocarbon* (1.9 g.), b. p. 138°/4.2 mm., n_D^{20} 1.5510 (Found: C, 90.3; H, 9.7. $C_{19}H_{24}$ requires C, 90.5; H, 9.5%).

The authors thank Professor W. Baker, F.R.S., for making available certain laboratory facilities, and Mr. A. Stringer for the insecticidal testing. One of them (E. J. S.) is indebted to the Bristol Education Committee for a Scholarship.

DEPARTMENT OF AGRICULTURE AND HORTICULTURE,
UNIVERSITY OF BRISTOL, RESEARCH STATION,
LONG ASHTON, BRISTOL.

[Received, March 31st, 1952.]