LXXIV.—*The Nitration of Phenyl*cyclo*hexane and of its* p-*Halogeno-derivatives.*

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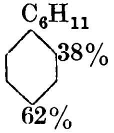
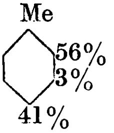
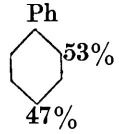
ALTHOUGH Kursanoff (*Annalen*, 1901, **318**, 309) nitrated phenyl*cyclo*hexane, he isolated only one product, which he showed to be *p*-nitrophenyl*cyclo*hexane. In view of the important relationship the hydrocarbon bears to diphenyl on the one hand and to toluene homologues on the other, we have studied its nitration quantitatively, and compared the ortho-directing influence of the *cyclo*hexyl group with those of chlorine and bromine by studying the nitration of the *p*-halogenophenyl*cyclo*hexanes.

Phenyl*cyclo*hexane is nitrated to give 62% of *p*-nitro- and 38% of *o*-nitro-compound, with possibly a trace of a third substance, and it is of value to compare its nitration with those of toluene (Holleman, *Proc. K. Akad. Wetensch. Amsterdam*, 1908, **11**, 248; *Rec.*

trav. chim., 1909, **28**, 408) and diphenyl (Gull and Turner, preceding paper):

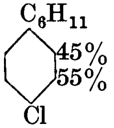


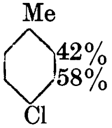


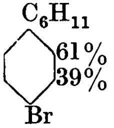


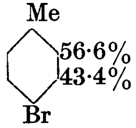
From these figures it is seen that the three *o*/*p* ratios are 0·61, 1·37, and 1·13 respectively. It is by no means clear why phenyl*cyclo*hexane should give so low an *o*/*p* ratio, although, of course, the *cyclo*hexyl radical (like the *tert.*-butyl) may exert a considerable steric effect in opposition to *o*-substitution. This is in interesting contrast to the small steric effect of the phenyl and *o*-nitrophenyl radicals (Gull and Turner, *loc. cit.*).

Numerous experiments were necessary before the conditions for mononitration of p-*chloro*- and p-*bromo-phenyl*cyclo*hexane* could be discovered, but the results ultimately obtained afford an instructive comparison with those recorded by Holleman (*Proc. K. Akad. Wetensch. Amsterdam*, 1908, **11**, 257; *Rec. trav. chim.*, 1915, **34**, 283) for the nitration of *p*-chloro- and *p*-bromo-toluene:









Nitration of *p*-chlorophenyl*cyclo*hexane occurs more in position 2 than in the case of *p*-chlorotoluene, in spite of the relative *o*/*p* ratios for the *cyclo*hexyl and methyl groups. At the moment there is no theory capable of explaining such results. p-*Iodophenyl*cyclo*hexane* cannot be caused to undergo simple nitration, the main product of the action of nitric acid being *p*-iodonitrobenzene. Willgerodt and Hilgenberg (*Ber.*, 1909, **42**, 3832) obtained *p*-di-iodobenzene by treating diphenyl with iodine and nitric acid in light petroleum, and Professor Robinson has directed our attention to a paper by Mrs. Robinson (J., 1916, **109**, 1078) in which similar results were recorded with derivatives of anisole.

Nitration of phenyl*cyclo*hexane may also lead to 2 : 4-dinitrophenyl*cyclo*hexane, readily oxidisable to 2 : 4-dinitrobenzoic acid and reducible to 2 : 4-*diaminophenyl*cyclo*hexane*. The latter is also obtained by reducing 2-*nitro*-4-*aminophenyl*cyclo*hexane*, which is the product of nitrating *p*-aminophenyl*cyclo*hexane in presence of excess of sulphuric acid. These interconversions establish the constitutions of the substances involved.

Dinitration of *p*-chlorophenyl*cyclo*hexane gives a chlorodinitro-compound which is identical with the product obtained by nitrating 4-*chloro-2-nitrophenyl*cyclo*hexane*. The dinitro-compound reacts with piperidine, and must therefore be either the 2 : 3- or the 2 : 5-derivative. Since in this reaction a chlorine atom and not a nitro-group is replaced, the dinitro-compound is probably 4-*chloro-2 : 5-dinitrophenyl*cyclo*hexane* (see note below).

It was originally hoped to study the nitration of a number of compounds allied to phenyl*cyclo*hexane. Phenyl*cyclo*hexene could not be caused to undergo simple nitration under a very large variety of experimental conditions. Phenyl*cyclo*hexane readily condenses with acetyl chloride in presence of aluminium chloride to give p-*acetylphenyl*cyclo*hexane* (4-cyclo*hexylphenyl methyl ketone*), from which 4-cyclo*hexylbenzoic acid* is readily obtainable by oxidation. The constitution of the acid was established by its synthesis from the nitrile obtained normally from *p*-aminophenyl*cyclo*hexane.

EXPERIMENTAL.

*Phenyl*cyclo*hexane*.—This substance was obtained by Kursanoff's method (*loc. cit.*), excepting that the reaction between *cyclo*hexyl chloride, benzene, and aluminium chloride was completed by a short heating at 100°. The yield of the pure hydrocarbon, b. p. 115°/15 mm. or 132°/30 mm., was 76% (Kursanoff, 50%). The required *cyclo*hexyl chloride was prepared by dissolving *cyclo*hexanol in about 1½ times its volume of concentrated hydrochloric acid, saturating the solution with hydrogen chloride, and heating it under reflux for 2 hours. A little *cyclo*hexene is the only by-product, and the yield is 60—70%.

p-*Chlorophenyl*cyclo*hexane*.—*cyclo*Hexyl chloride (62 g.) was slowly added to a well-shaken mixture of chlorobenzene (160 g.) and aluminium chloride (14 g.), which was not cooled. The yield of p-*chlorophenyl*cyclo*hexane*, a colourless liquid, b. p. 145°/19 mm., 140°/15 mm., and 134°/10 mm., $d_{4^\circ}^{25^\circ}$ 1·065, $n_{D}^{25^\circ}$ 1·5386, was 74 g. (Found: Cl, 18·3. $C_{12}H_{15}Cl$ requires Cl, 18·3%). The constitution of the chloro-compound was shown by oxidation: The compound (2 g.) was stirred with a solution of 20 g. of sodium dichromate in 60 c.c. of water, and 45 c.c. of concentrated sulphuric acid were then added slowly; the temperature rose until oxidation set in, and at this point acid was added at such a rate that the oxidation proceeded smoothly (unless care is exercised, the reaction becomes violent). After addition of the acid, the mixture was stirred for ¼ hour, heated to 100°, and diluted. The precipitated *p*-chlorobenzoic acid was filtered off and crystallised from alcohol. It had m. p. 236°, alone or mixed with an authentic specimen of the acid.

The chloro-compound was also obtained in poor yield from the corresponding amino-compound by the Sandmeyer reaction.

p-*Bromophenyl*cyclo*hexane*.—Using a method similar to that for the chloro-compound, we obtained the *bromo*-compound as a colourless liquid, b. p. 160°/23 mm., $d_{4°}^{25°}$ 1·283, $n_D^{25°}$ 1·5584, in 65% yield (Found : Br, 33·0. $C_{12}H_{15}Br$ requires Br, 33·5%). Oxidation by the dichromate method gave a product containing chromium compounds which could only be removed with considerable difficulty; *p*-bromobenzoic acid was, however, obtained. The bromo-compound was also prepared, although in poor yield, by the Sandmeyer reaction from *p*-aminophenyl*cyclo*hexane; it had $n_D^{25°}$ 1·5579.

p-*Iodophenyl*cyclo*hexane*.—This *substance* was obtained in good yield by adding diazotised *p*-aminophenyl*cyclo*hexane to potassium iodide solution; it is an oil, b. p. 185°/21 mm. or 174°/11 mm., $d_{4°}^{19°}$ 1·448, $n_D^{25°}$ 1·5900 (Found : I, 44·2. $C_{12}H_{15}I$ requires I, 44·4%).

*Nitration of Phenyl*cyclo*hexane*.—Kursanoff (*loc. cit.*) cooled the hydrocarbon in ice and added excess of fuming nitric acid. This procedure is inadvisable, since with too efficient cooling the hydrocarbon solidifies, whereas with inefficient cooling a violent reaction may set in. The following methods were found suitable :

(1) Phenyl*cyclo*hexane (58 c.c.) was slowly added to 210 c.c. of nitric acid (*d* 1·5), kept well stirred and cooled to 0°. Stirring was continued for a short time after the addition was complete, and the solution was then poured on ice, and the semi-solid product extracted with benzene. The extract, after being washed successively with water, alkali, and water, was dried over calcium chloride, and most of the benzene removed at ordinary pressure. The residue, b. p. 205—225°/25 mm., was separated by repeated distillation into two fractions, A and B.

(2) A saturated solution of phenyl*cyclo*hexane (100 g.) in glacial acetic acid (190 c.c.) was slowly added to a mixture of 375 c.c. of nitric acid (*d* 1·5) and 160 c.c. of glacial acetic acid, the temperature being kept at 0°. After addition was complete, the mixture was kept stirred for $\frac{1}{2}$ hour, poured on ice, and worked up as before. Fractional distillation gave two fractions, A and C.

Fraction A, b. p. 198°/16 mm. or 210°/25 mm., solidified on cooling, and after crystallisation from alcohol formed pale yellow plates, m. p. 58·5°. This was identical with Kursanoff's *p*-nitrophenyl*cyclo*hexane, m. p. 57·5—58·5° (Found : N, 7·0. Calc. : N, 6·8%). Kursanoff oxidised his product with dilute nitric acid (35 hours at 135—140°), but the dichromate method has been found to give almost quantitative yields of *p*-nitrobenzoic acid.

Fraction B, b. p. 222°/15 mm., also solidified on cooling, and separated from alcohol in pale yellow platelets, m. p. 57° (Found :

N, 11·9. $C_{12}H_{14}O_4N_2$ requires N, 11·2%). Oxidation with dichromate gave 2 : 4-dinitrobenzoic acid, so the product was 2 : 4-*dinitrophenyl*cyclo*hexane*.

Fraction C, b. p. 174°/16 mm., $d_{4°}^{23°}$ 1·111, $n_D^{25°}$ 1·5472, remained as an oil (Found : N, 7·1. $C_{12}H_{15}O_2N$ requires N, 6·8%). Oxidation caused complete destruction of the molecule, but the oil was shown to be the expected o-*nitrophenyl*cyclo*hexane* by its conversion into 2 : 4-dinitrophenyl*cyclo*hexane, which was also formed from the *p*-isomeride.

*Quantitative Nitration of Phenyl*cyclo*hexane*.—The nitration was effected in acetic acid solution (method 2, above). Over 95% of the product consisted of the *o*, *p*-mixture. Its composition was determined by three methods.

(1) *Fractional distillation.* Repeated distillation under reduced pressure of 380 g. of the mixture gave 230 g. of pure *p*-compound, the proportion of which in the mixture is, therefore, not less than 60%.

(2) *Oxidation.* As stated above, *p*-nitrophenyl*cyclo*hexane is almost quantitatively oxidised to *p*-nitrobenzoic acid, whilst the *o*-isomeride is destroyed. An artificial mixture of 0·740 g. of *o*- with 1·440 g. of *p*-nitro-compound was oxidised by the dichromate method, 1·155 g. of *p*-nitrobenzoic acid being obtained (Calc., 1·170 g.; 98·7% yield). When 2·145 g. and 2·490 g. of the nitration product were similarly oxidised in two different experiments, 1·089 g. and 1·205 g. of *p*-nitrobenzoic acid were obtained, corresponding to 62·4 and 59·4% of *p*-nitrophenyl*cyclo*hexane, or, after correction on the basis of the above 98·7% yield, to 63·2 and 60·2% (mean, 61·7%).

(3) *Thermal analysis.* Preliminary experiments showed that it would only be necessary to determine half of the freezing-point curve for mixtures of *o*- and *p*-nitrophenyl*cyclo*hexane. The following freezing points were observed, following the procedure described in a previous paper (J., 1928, 691) :

p-Nitro-compound, %	100	77·8	67·7	65·4	60·5
F. p.	56·7°	44·3°	38·3°	35·7°	32·0°

Three different nitration products had f. p. (1) 34·5°, (2) 34·5°, and (3) 32·0°, corresponding respectively to (1) 63·0%, (2) 63·0% and (3) 60·5% of para-compound (mean, 62·2%).

p-*Aminophenyl*cyclo*hexane*.—Kursanoff obtained this compound, m. p. 54—56°, by reducing the nitro-compound with tin and hydrochloric acid. We have found iron, water, and a little hydrochloric acid preferable as a reducing agent, giving a base of m. p. 55° in almost theoretical yield. The *acetyl* derivative melts at 129° (Found : N, 6·6. $C_{14}H_{19}ON$ requires N, 6·5%).

Nitration of p-*Aminophenyl*cyclo*hexane.*—The dry sulphate (11·2 g.) of the base was dissolved in 60 c.c. of concentrated sulphuric acid, the solution cooled to 0°, and 3 c.c. of nitric acid (*d* 1·5) slowly added. The mixture was kept for a further ¼ hour, poured on ice, and the precipitate filtered off. 2-*Nitro*-4-*aminophenyl*cyclo*hexane*, crystallising from alcohol in yellow leaflets, melts at 66° (Found : N, 12·8. $C_{12}H_{16}O_2N_2$ requires N, 12·7%).

2 : 4-*Diaminophenyl*cyclo*hexane.*—Reduction of the corresponding dinitro-compound by the above method with iron gave this *base*, which crystallised from alcohol in colourless needles, m. p. 108° (Found : N, 14·8. $C_{12}H_{18}N_2$ requires N, 14·7%).

Similar reduction of the above nitroamine gave the same diamine. The two specimens of diamine, acetylated separately, gave the same diacetyl compound, separating from alcohol in platelets, m. p. 268°.

Nitration of p-*Chlorophenyl*cyclo*hexane.*—As stated above, the nitration of this compound proved very tedious, owing to the difficulty of securing quantitative mononitration. The comparative insolubility of the compounds themselves, and of the derived nitro-compound, added to the difficulty.

When *p*-chlorophenyl*cyclo*hexane was slowly added to 8 times its weight of nitric acid (*d* 1·5), kept at 0° to −5°, 4-*chloro*-2 : 5-*dinitrophenyl*cyclo*hexane* was obtained in good yield. It crystallises from alcohol in almost colourless plates, m. p. 92° (Found : N, 10·1; Cl, 12·3; *M*, in camphor, 288. $C_{12}H_{13}O_4N_2Cl$ requires N, 9·9; Cl, 12·5%; *M*, 284·5). When warmed with piperidine for a short time, it gave 2 : 5-*dinitro*-4-*piperidinophenyl*cyclo*hexane*, which crystallised from dilute acetic acid in orange-yellow plates, m. p. 108° (Found : N, 12·8. $C_{17}H_{23}O_4N_3$ requires N, 12·6%).

When a solution of 5·3 g. (5 c.c.) of *p*-chlorophenyl*cyclo*hexane in 5 c.c. of glacial acetic acid was added gradually to a mixture of 20 c.c. of nitric acid (*d* 1·5) and 7 c.c. of glacial acetic acid at 5—10°, almost quantitative mononitration occurred. The resulting solution, after being kept at 10° for a short time, was poured on ice, and the whole then extracted with ether. The extract was washed with water, with alkali, and again with water, dried, and freed from solvent by heating at 100°. The residual oil, A, was analysed (Found : Cl, 14·5. $C_{12}H_{14}O_2NCl$ requires Cl, 14·8%). A portion of it was heated for 2—3 hours at 100° with excess of piperidine, which reacted with the 3-nitro- but not with the 2-nitro-compound. The reaction product was treated with water and extracted with benzene; the extract was shaken three times with 60% sulphuric acid to remove piperidine and the piperidino-derivative, then washed with water, dried, and freed from benzene by evaporation. The 4-*chloro*-2-*nitrophenyl*cyclo*hexane* so obtained was dissolved in excess of nitric acid (*d* 1·5), the solution kept for several hours, and then rapidly diluted. The semi-solid precipitate, after being crystallised from alcohol, had m. p. 90·5—91·5°, and when mixed with the above 4-chloro-2 : 5-dinitrophenyl*cyclo*hexane had m. p. 90·5—92°. Further, when it was heated with piperidine, it gave the above dinitropiperidino-compound, m. p. 105—106·5°, a mixture with the specimen obtained as above melting at 105—107·8°. *p*-Chlorophenyl*cyclo*hexane was apparently not nitrated by ordinary nitric acid (*d* 1·42), but slowly darkened in colour. By vigorously stirring the chloro-compound (2·1 g.) with 10 c.c. of nitric acid (*d* 1·48) at 0° for 1¼ hours, a product, B, was obtained containing Cl, 14·7%, corresponding to almost quantitative mononitration.

In order to determine the relative proportions of 2- and 3-nitro-compounds present in A and B, one of two methods was employed. A number of samples corresponding to A and B were actually examined, but the results obtained with one sample of each origin are alone given.

Method 1. A weighed sample of the nitration product was heated with excess of piperidine on a water-bath for 2—3 hours. Distilled water was then added, the mixture thoroughly extracted with benzene, and the aqueous solution of piperidine hydrochloride analysed. This method was more tedious than the following.

Method 2. The nitration product was weighed into a small wide-necked flask, which was fitted with a cork through which passed a soda–lime tube (to prevent formation of piperidine carbonate and carbamate) and a small funnel. Piperidine was added through the funnel, which was then stoppered to prevent ingress of air. The flask was heated for 2—3 hours as before, allowed to cool, and pure dry benzene was added through the funnel. The precipitated piperidine hydrochloride was collected on a Gooch crucible, washed with benzene, and dried at 100°.

Analysis of A. Method 1. 2·2430 G. and 1·6064 g. of the nitration product gave 0·7605 g. and 0·5382 g. of AgCl, whence 3-nitro-compound = 56·6 and 56·0%.

Method 2. 1·0420 G. gave 0·2975 g. of piperidine hydrochloride, whence 3-nitro-compound = 56·3%.

Analysis of B. 0·5727, 0·6209, and 0·5405 G. of B gave respectively 0·1610, 0·1743, and 0·1521 g. of piperidine hydrochloride, whence 3-nitro-compound = 55·4, 55·3, and 55·5%.

A large number of check nitrations, in which incomplete mononitration occurred, gave results which supported the above figures.

Nitration of p-*Bromophenyl*cyclo*hexane.*—5 G. of the bromo-compound were stirred with 20 c.c. of nitric acid (*d* 1·475) for 1¼ hours at 0°. The product, isolated as in the case of the chloro-compound, contained Br, 28·3% (calc. for mononitro-compound: Br, 28·2%). Reactive bromine was determined as piperidine hydrobromide: 0·4190 g. and 0·5600 g. gave 0·0893 g. and 0·1204 g. of the hydrobromide, whence 3-nitro-compound = 36·5 and 36·8%.

In another experiment, 2·55 g. of the bromo-compound were stirred with 10 c.c. of nitric acid (*d* 1·48) for 1¼ hours at 0°. The product contained 28·7% Br, and 0·4100 g. and 0·5010 g. gave respectively 0·0911 g. and 0·1172 g. of piperidine hydrobromide, whence 3-nitro-compound = 38·0 and 40·0%. The most probable value from these experiments is 38%.

As in the case of the chloro-compound, numerous check experiments were performed.

Nitration of p-*Iodophenyl*cyclo*hexane*.—The iodo-compound (2·9 g.; 2 c.c.) was gradually added to 10 c.c. of nitric acid (*d* 1·48), kept stirred at 0°. The dark liquid obtained was poured on ice, the whole was extracted with ether, and the extract washed with alkali, which became red. Routine procedure then gave the nitration product as a dark orange oil which, when kept, deposited crystals. These crystallised from alcohol in very pale yellow needles, m. p. 172°, and were identified as *p*-iodonitrobenzene (analysis, m. p., mixed m. p., and conversion into *p*-nitrophenylpiperidine).

p-*Acetylphenyl*cyclo*hexane*.—Aluminium chloride (11·3 g.) was gradually added to a mixture of 15·8 g. of phenyl*cyclo*hexane, 5 g. of acetyl chloride, and 63 c.c. of carbon disulphide. When the vigorous reaction had abated, the mixture was heated on the water-bath for ½ hour and then treated with dilute hydrochloric acid. The carbon disulphide layer on evaporation gave a solid which crystallised from alcohol in lustrous white plates, m. p. 68—69° (yield, 60%). The *phenylhydrazone*, yellow plates from alcohol, m. p. 105°, became black when kept (Found: N, 9·9. $C_{20}H_{24}N_2$ requires N, 9·6%).

Neutral potassium permanganate was without marked action on the ketone, but when a suspension of 2 g. of the latter in a solution of 3·2 g. of potassium permanganate and 3 g. of sulphuric acid in 200 c.c. of water was boiled, terephthalic acid was formed.

p-cyclo*Hexylbenzoic Acid*.—A suspension of the ketone in excess of dilute aqueous sodium hypobromite was boiled, further hypobromite being added from time to time until the oil present did not solidify on cooling. The cooled mixture was extracted with benzene to remove bromoform, and then concentrated to a small bulk. *Sodium* p-cyclo*hexylbenzoate* separated in white needles (Found: Na, 10·4. $C_{13}H_{15}O_2Na$ requires Na, 10·2%). The free acid crystallised from alcohol in minute plates, m. p. 199°. It was also obtained as follows: *p*-Aminophenyl*cyclo*hexane was diazotised, and the solution added to sodium cuprocyanide; the nitrile so formed was partially purified by distillation in steam and then boiled with alcoholic potassium hydroxide. Acidification of the product gave a solid, which, after two crystallisations from alcohol, was identical with the above acid.

Note, added January 24th, 1929.—Although the constitution of the above dinitro-derivative of *p*-chlorophenyl*cyclo*hexane was not seriously in doubt, the following additional evidence in its favour has now been obtained.

The chlorodinitro-compound was reduced with iron filings, water, and a little acetic acid at 100°. When the reaction was over, excess of precipitated calcium carbonate was added, and the whole was extracted with ether. On evaporation of the ethereal solution, an oil resulted which rapidly solidified; after being crystallised from dilute alcohol, it had m. p. 92—93°, and after being further crystallised from light petroleum (b. p. 60—80°) formed almost colourless needles (tending to form rosettes), m. p. 95—96° (Found : Cl, 15·4. $C_{12}H_{17}N_2Cl$ requires Cl, 15·8%). This substance is therefore 4-chloro-2 : 3 (or 5)-diaminophenyl*cyclo*hexane.

A saturated alcoholic solution of an equimolecular mixture of the diamine and phenanthraquinone was boiled under reflux for 4 hours. The solution darkened considerably, but no separation of solid occurred even after cooling, and this points to the absence of an *o*-diamine structure.

The diamine formed a sparingly soluble hydrochloride, the aqueous solution of which was readily diazotised. The diazo-solution coupled with alkaline β-naphthol to give a purple azo-derivative, thus indicating the presence of a *p*-diamine and the absence of an *o*-diamine.

When the diamine was warmed with either manganese dioxide or potassium dichromate and dilute sulphuric acid, an odour resembling that of a *p*-quinone was developed, affording evidence against an *o*-diamine structure.

The diamine is therefore 4-*chloro*-2 : 5-*diaminophenyl*cyclo*hexane*, and the dinitro-compound has the constitution originally assigned to it.

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