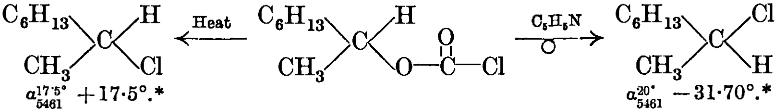
14. *The Conversion of* d-*β-Octyl Chloroformate into Dextrorotatory β-Chloro-octane and the Action of the Chlorides and Oxychloride of Phosphorus on* d-*β-Octanol.*

By Armand Henri Joseph Houssa and Henry Phillips.

d-β-Octyl chloroformate, prepared by the interaction of *d*-β-octanol and carbonyl chloride in the presence of one molecular proportion of a tertiary base (Hunter, J., 1924, **125**, 1391), is a relatively stable compound which can be distilled in a vacuum. From its method of preparation it can be assumed to have the same configuration as *d*-β-octanol. When gently heated in the presence of pyridine (Houssa and Phillips, J., 1929, 2510), it decomposes and yields a lævorotatory β-chloro-octane, the rotatory power of which compares very favourably in magnitude with that of the β-chloro-octane prepared by other methods, such as, for example, the action of thionyl chloride on the *d*-alcohol in the presence of pyridine (McKenzie and Tudhope, *J. Biol. Chem.*, 1924, **62**, 551). It has now been found that when it is heated alone for some hours at 130°, carbon dioxide is evolved, and a dextrorotatory β-chloro-octane is produced with some loss of rotatory power.

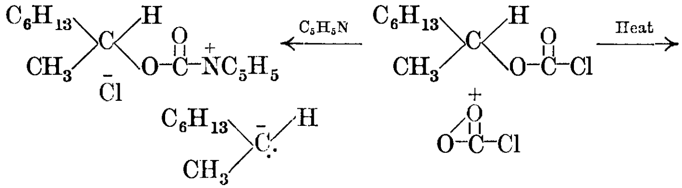


* Observed rotations in 1 dcm. tubes.

This observation is important in that it is the first recorded instance of the preparation of dextrorotatory β-chloro-octane from *d*-β-octanol, the more usual methods of chlorination leading invariably, as they do with all other dextrorotatory aliphatic hydroxy-compounds, to the production of the lævorotatory chloride.

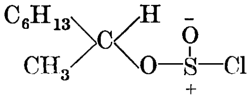
It is suggested that the production of the dextrorotatory chloride from the *d*-chloroformate is unaccompanied by inversion of configuration for the following reasons. The *p*-toluenesulphonate of *d*-β-octanol is converted into the acetate of *l*-β-octanol by interaction with potassium acetate (Phillips, J., 1925, **127**, 2552), whilst the *p*-toluenesulphinate of *d*-β-octanol yields *l*-β-octanol with hypochlorous acid (Houssa, Kenyon, and Phillips, J., 1929, 1700). Both these reactions occur with inversion of configuration. By analogous reactions, namely, the action of lithium chloride on the *d*-sulphonate and of chlorine on the *d*-sulphinate, lævorotatory β-chloro-octane is produced. On the assumption that inversion occurs also during these reactions, lævorotatory β-chloro-octane has the same configuration as *l*-β-octanol and therefore β-chloro-octane is produced without inversion by heating the chloroformate.

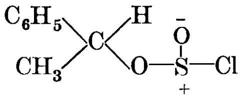
According to the views developed in this series of papers (Kenyon and Phillips, *Trans. Faraday Soc.*, 1930, **26**, 415; Kenyon, Lipscomb, and Phillips, J., 1930, 451) the cause of the production of β-chloro-octanes opposite in sign of rotation from *d*-β-octyl chloroformate, by the two methods employed, is a fundamental difference in the mechanisms of the two reactions. It is assumed that, during the decomposition in the absence of pyridine, the octet of the asymmetric carbon atom remains intact and it possesses, in the β-chloro-octane produced, the same eight valency electrons as it had in the original chloroformate. If, at any stage of the decomposition, the optically active radical becomes free, it must therefore exist as an anion which subsequently unites with a chlorine kation :



On the other hand, when the decomposition occurs in the presence of pyridine, a pyridinium chloride is presumably produced and the entering chloro-group takes part in further reaction as an anion, replacing two of the valency electrons of the optically active radical, which must therefore take part in this reaction in the kationic state. An explanation of the occurrence of inversion under these circumstances has been suggested (Kenyon and Phillips, *loc. cit.*). On these assumptions, since *d*-β-octyl chlorosulphinate (I), the unstable intermediate phase in the chlorination of *d*-β-octanol with thionyl chloride (Levene and Mikeska, *J. Biol. Chem.*, 1924, **59**, 45), decomposes with inversion, it can be concluded that the substitution of the more negative sulphoxyl group for the ketonic group of the chloroformate militates against the separation of the *d*-β-octyl radical as an anion. The electron-retaining capacity of the asymmetric carbon atom can, however, be increased by replacing the *n*-hexyl group of (I) by a phenyl group as in (II) : decomposition then again leads to the formation of a chloride without inversion (Kenyon, Phillips, and Taylor, J., 1931, 382) :

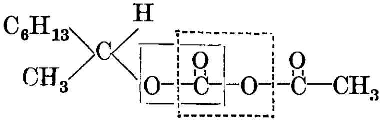
(I.)



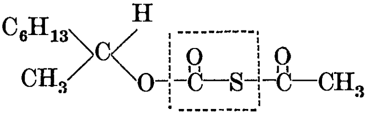


(II.)

The introduction of the conception of an optically active radical which takes part in a reaction as an anion and thereby suffers no configurative change necessitates the confirmation of certain conclusions drawn from previous experimental results (Houssa and Phillips, *loc. cit.*). It was suggested that the formation of *d*-β-octyl acetate by the action of *d*-β-octyl chloroformate on potassium acetate proved that the intermediate mixed anhydride (III) decomposed as indicated by the larger broken square and not as indicated by the smaller continuous square.



(III.)



(IV.)

On the more recently extended hypothesis, if the optically active β-octyl radical separates as a negative ion and retains its octet of valency electrons, a dextrorotatory β-octyl acetate may result in spite of the removal of the octoxy-oxygen atom as indicated by the smaller continuous square. More substantial evidence for the correctness of the original interpretation, *viz.*, that decomposition occurs as indicated by the larger broken square, has, however, been provided by an investigation of the interaction of *d*-β-octyl chloroformate and potassium thioacetate [ethanethiolate]. This interaction presumably proceeds *via* the mixed anhydride (IV) and decomposition occurs as indicated by the broken square, since carbon oxysulphide and *d*-β-octyl acetate are the products of the change : if decomposition had occurred by the alternative route, carbon dioxide and β-octyl thioacetate would have been produced.

The sign of rotation of the β-chloro-octane obtained by the action of the chlorides and oxychloride of phosphorus on *d*-β-octanol has not hitherto been recorded. With all three chlorinating agents, a lævorotatory β-chloro-octane was obtained, in greater yield but with a lower rotatory power in the presence of zinc chloride than in its absence. The rotatory power of the β-chloro-octane was highest when the trichloride was used and lowest with the oxychloride. In the presence of pyridine, only the pentachloride gave an appreciable quantity of lævorotatory β-chloro-octane. The main products of these reactions, isolated after being washed with water, were β-octyl esters of the oxy-acids of phosphorus : the trichloride gave mainly di-β-octyl hydrogen phosphite, together with a little β-octyl dihydrogen phosphite, and the pentachloride and the oxychloride gave mainly β-octyl dihydrogen phosphate, together with a little di-β-octyl hydrogen phosphate.

By the preparation of lævorotatory β-chloro-octane by means of the chlorides and oxychloride of phosphorus, as described, the number of reactions by which *d*-β-octanol has been converted into its lævorotatory chloride has been increased to thirteen; twelve of these reactions have already been referred to in this paper, the remaining one being by the action of hydrogen chloride (Pickard and Kenyon, J., 1911, **99**, 45).

EXPERIMENTAL.

The Conversion of d-β-*Octyl Chloroformate into Dextrorotatory* β-*Chloro-octane.*—A steady evolution of carbon dioxide occurred when *d*-β-octyl chloroformate [1·5 g., $\alpha_{5461}^{17^\circ}$ + 7·13° ($l = 0{\cdot}25$)] was heated at 130° for 14 hours. The product, b. p. 55—56°/10—11 mm., dextrorotatory β-chloro-octane * (Found : Cl, 23·5. Calc., 23·9%), had $n_D^{21^\circ}$ 1·4273 and $\alpha_{5461}^{17^\circ}$ + 4·39° ($l = 0{\cdot}25$).

The Action of Potassium Thioacetate on d-β-*Octyl Chloroformate.*—When *d*-β-octyl chloroformate (9·6 g.; 1 mol.) was added to potassium thioacetate (5·7 g.; 1 mol.), a gas was evolved which dissolved in potassium hydroxide solution, giving rise to potassium sulphide. After the mixture had been heated under reflux on a steam-bath for 12 hours, it was triturated with dry ether. The high-boiling residue from this ethereal extract distilled almost entirely (5·3 g.) at 80—85°/15 mm. After redistillation, b. p. 77—78°/10 mm., it had $n_D^{18{\cdot}5^\circ}$ 1·4186 and $\alpha_{5461}^{18{\cdot}5^\circ}$ − 1·78° ($l = 0{\cdot}25$) [Found : C, 70·5; H, 11·8. Calc. for $C_{10}H_{20}O_2$ (β-octyl acetate) : C, 69·9; H, 11·6%]. To ensure that this product was almost pure β-octyl acetate and was free from any unforeseen products, it was partially hydrolysed with alcoholic potassium hydroxide. The *l*-β-octanol was separated from the unhydrolysed ester by conversion into its acid phthalic ester, which was dissolved in sodium carbonate solution. On isolation, this *l*-β-octyl hydrogen phthalate had $[\alpha]_{5461}^{19^\circ}$ − 54·6° and was therefore optically pure. The unhydrolysed acetate had b. p. 73—75°/10 mm., $n_D^{17^\circ}$ 1·4178, and $\alpha_{5461}^{18^\circ}$ − 1·43° ($l = 0{\cdot}25$) (Found : C, 69·1; H, 11·4%). It contained a trace of chlorine. From these results it can be concluded that *l*-β-octyl acetate was the main product of the reaction and that no racemisation of the *l*-β-octyl radical had occurred.

The Interaction of Phosphorus Trichloride with d-β-*Octanol.*—(a) *In the presence of ether.* A vigorous evolution of hydrogen chloride occurred when *d*-β-octanol [2·8 g., $\alpha_{5461}^{20^\circ}$ + 9·88° ($l = 1{\cdot}0$)], dissolved in anhydrous ether (2 vols.), was slowly dropped into an ice-cold ethereal solution of phosphorus trichloride (2·95 g.). The mixture was gently warmed until the evolution ceased and was then

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* This and other β-chloro-octanes prepared in the investigation were repeatedly distilled, first and last fractions being rejected, until their rotatory powers remained unaltered.

cooled and poured on ice. The ethereal solution was washed with water and with dilute aqueous sodium carbonate. From the dried solution lævo-β-chloro-octane, b. p. 60°/12 mm., $n_D^{20°}$ 1·4302, $\alpha_{5461}^{20°}$ − 35·5° (l = 1·0), was obtained.

(b) *In the presence of ether and zinc chloride.* A slow evolution of hydrogen chloride occurred when *d*-β-octanol [2·8 g., $\alpha_{5461}^{20°}$ + 9·88° (l = 1·0)], dissolved in anhydrous ether (1 vol.), was slowly added to an ethereal solution of phosphorus trichloride (2·95 g.) covering anhydrous zinc chloride (3·0 g.). After treatment as in (a), the ethereal solution gave lævo-β-chloro-octane, b. p. 60°/12 mm., $n_D^{20°}$ 1·4275, $\alpha_{5461}^{20°}$ − 23·15° (l = 1·0).

(c) *In the presence of ether and pyridine.* *d*-β-Octanol [6·5 g. (0·05 mol.), $\alpha_{5461}^{20°}$ + 9·60° (l = 1·0)], in anhydrous ether (2 vols.), was added to dry pyridine (7·9 g.; 0·1 mol.), and the mixture dropped slowly into an ethereal solution of phosphorus trichloride (6·8 g.; 0·05 mol.) in an ice-bath. The reaction mixture was then warmed on a steam-bath for 10 minutes, cooled, and poured on ice. The ethereal extract was washed successively with dilute sodium carbonate solution, water, dilute hydrochloric acid, and water, and dried over potassium carbonate. The washings remained clear as long as they contained excess of sodium carbonate, but when they were acidified an oil was precipitated : this acid product was extracted, washed, and dried (anhydrous sodium sulphate) in ether. The neutral product, on removal of the solvent, when distilled at less than 0·1 mm. yielded only a trace of unchanged β-octanol and no β-chloro-octane : the less volatile neutral residue (3·5 g.) had b. p. 116—118° under less than 0·1 mm., $n_D^{19°}$ 1·4379, $\alpha_{5461}^{20°}$ + 18·84°, $\alpha_{4359}^{20°}$ + 31·40° (l = 1·0), $d_{4°}^{4°}$ 0·9292, $d_{4°}^{15°}$ 0·9218 (Found : C, 62·1 ; H, 11·55 ; P, 9·5, 9·5. *Di-*β*-octyl hydrogen phosphite*, $C_{16}H_{35}O_3P$, requires C, 62·7 ; H, 11·4 ; P, 10·1%). The acid product failed to distil at 150° under less than 0·1 mm. and decomposed above this temperature : a sample, after being maintained for some time at 60—70° under less than 0·1 mm. in order to remove volatile impurities, contained 10·8% of phosphorus and had an equivalent (by titration with *N*/10-sodium hydroxide and phenolphthalein) of 191. These results suggest that the acid product was a mixture of β-octyl dihydrogen phosphite and di-β-octyl hydrogen phosphite.

The Interaction of Phosphorus Pentachloride and d-β-*Octanol.*—(a) *In the presence of ether.* *d*-β-Octanol [6·5 g., $\alpha_{5461}^{20°}$ + 9·62° (l = 1·0)] in ether (10 c.c.) was slowly added to a boiling solution of phosphorus pentachloride (11·5 g.) in ether (20 c.c.). After the evolution of hydrogen chloride had ceased, the mixture was heated under reflux for 15 minutes, cooled, and poured on ice. The ethereal extract was washed and dried with potassium carbonate. On removal of the solvent, lævo-β-chloro-octane (3 g.), b. p. 68°/21 mm., $\alpha_{5461}^{20°}$ − 33·84° (l = 1·0), $n_{D}^{18·5°}$ 1·4276, was obtained. A small quantity of octylene (0·5 g.) was also isolated, but no other product. These products represent a yield of 40% of lævo-β-chloro-octane and 5% of octylene calculated on the original β-octanol.

(b) *In the presence of ether and zinc chloride.* A slow evolution of hydrogen chloride resulted when d-β-octanol [6·5 g., $\alpha_{5461}^{20°}$ + 9·62° (l = 1·0)] in anhydrous ether (1 vol.) was added to a solution of phosphorus pentachloride (10·5 g.) in ether (20 c.c.) covering zinc chloride (6·8 g.), the whole being maintained at 50°. After ½ hour, the reaction had subsided and the mixture was cooled and poured on ice. The ethereal layer was washed and dried as previously described; from it, a trace of octylene and lævo-β-chloro-octane (4·75 g.; 65% yield), b. p. 67—68°/22 mm., $\alpha_{5461}^{20°}$ − 15·04° (l = 1·0), $n_{D}^{18·5°}$ 1·4267, were obtained.

(c) *In the presence of ether and pyridine.* A mixture of d-β-octanol [6·5 g. (0·05 mol.), $\alpha_{5461}^{20°}$ + 9·62° (l = 1·0)] and pyridine (7·9 g.; 0·10 mol.) in ether (20 c.c.) was slowly added to phosphorus pentachloride (10·5 g.; 0·05 mol.) in ether, the whole being maintained at 0°. After being heated under reflux for 30 minutes, the reaction mixture was cooled, poured on ice, and treated in the way described under phosphorus trichloride (c). The washings, on addition of excess of hydrochloric acid, yielded an acid product as an oil, which was extracted, washed, and dried in ether. The neutral product yielded on fractional distillation impure β-chloro-octane, b. p. 60—70°/24 mm., and a viscous liquid which did not distil at 125° under less than 0·1 mm. and decomposed above this temperature. The lævo-β-chloro-octane, when freed by distillation from a small quantity of octylene, had b. p. 69—70°/23—24 mm., $\alpha_{5461}^{23°}$ − 34·86° (l = 1·0), $n_{D}^{20°}$ 1·4265.

Another experiment, performed in the same manner with d-β-octanol [9·75 g., $\alpha_{5461}^{20°}$ + 4·0° (l = 1·0)], yielded similar products: the undistillable residue (4·5 g.) was a light yellow oil, $\alpha_{5461}^{20°}$ + 4·68° (l = 1·0). Analytical results obtained with a sample of this product which had been heated at 140°/22 mm. gave no definite information, but suggest that the product is a mixture of di-β-octyl hydrogen phosphate with a little mono-β-octyl dihydrogen phosphate.

The acid product (above) was dissolved in dilute sodium hydroxide solution, non-acid compounds were extracted with ether, and the aqueous liquid was acidified with hydrochloric acid. The precipitated oil was extracted and dried (sodium sulphate) in ether, recovered, and heated for 2 hours in a steam-oven and then kept for 24 hours in a vacuum. The product (3·1 g.) eventually set to a semi-solid mass (Found: C, 45·8; H, 8·9; P, 14·4. Calc. for di-β-octyl hydrogen phosphate, $C_{16}H_{35}O_4P$: C, 59·6; H, 10·9; P, 9·6%. Calc. for mono-β-octyl dihydrogen phosphate, $C_8H_{19}O_4P$: C, 45·1; H, 9·0; P, 14·8%). The product was therefore probably a mixture of these two esters, the latter predominating. This conclusion was confirmed by a titration curve obtained conductometrically by Dr. C. W. Davies, who further reported that the product probably consisted of a mixture of 15% of a monobasic acid, equivalent 322, and 85% of a dibasic acid, equivalent 105, giving an apparent equivalent of 138.

The Interaction of Phosphorus Oxychloride with d-β-*Octanol.*—(a) *In the presence of ether.* A vigorous evolution of hydrogen chloride resulted on the addition of *d*-β-octanol [2·8 g., $\alpha_{5461}^{20°}$ + 9·64° (l = 1·0)] in ether (1 vol.) to an ethereal solution of phosphorus oxychloride (3·3 g.) maintained at 0°. The lævo-β-chloro-octane (1 g.; 30% yield) had b. p. 58—60°/12 mm., $\alpha_{5461}^{20°}$ − 12·77° (l = 1·0), $n_D^{14°}$ 1·4291.

(b) *In the presence of ether and zinc chloride.* A solution of *d*-β-octanol [2·8 g., $\alpha_{5461}^{20°}$ + 9·64° (l = 1·0)] in ether was added to phosphorus oxychloride (3·3 g.) in ether, covering zinc chloride (3·0 g.). The sole product, except a trace of octylene, was lævo-β-chloro-octane (2·3 g.; 70% yield), b. p. 66—67°/23 mm., $\alpha_{5461}^{20°}$ − 3·49° (l = 1·0), $n_D^{21°}$ 1·4293.

(c) *In the presence of ether and pyridine.* A mixture of *d*-β-octanol [6·5 g. (0·05 mol.), $\alpha_{5461}^{20°}$ + 9·16° (l = 1·0)] and pyridine (7·9 g.; 0·10 mol.) in ether was slowly added to an ethereal solution of phosphorus oxychloride (7·6 g.; 0·05 mol.) at 0°. After 30 minutes' heating under reflux on a steam-bath, the products were isolated as described in previous experiments. Only a trace of β-chloro-octane was produced, the main products being a neutral phosphoric ester, which could not be distilled and therefore was not analysed, and a mixture of acid phosphoric esters. 0·2538 G. of this mixture (Found: P, 13·7%) required 0·0381 g. of sodium hydroxide for neutralisation (methyl-orange) and a further 0·0376 g. (phenolphthalein). These results suggest that the mixture consists of 81% of β-octyl dihydrogen phosphate and 19% of di-β-octyl hydrogen phosphate.

In conclusion, the authors wish to thank Miss E. K. Waller, B.Sc., for assistance in some of the experiments with the chlorides and oxychloride of phosphorus, and Dr. J. Kenyon for his interest in the investigation. They are also indebted to the Government Grant Committee of the Royal Society and to Imperial Chemical Industries, Ltd., for grants which have defrayed much of the cost.

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