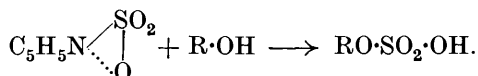


XXXII.—*The Reaction between Diaryloxyisopropyl Alcohols and Phosphorus Oxychloride in the Presence of Pyridine.*

By DAVID RUNCIMAN BOYD and DONALD ERNEST LADHAMS.

$\alpha\gamma$ -DIARYLOXYISOPROPYL alcohols react slowly with phosphorus oxychloride at 100°, and from the reaction product, on treatment with ice, a mixture of mono- and bis-esters of phosphoric acid is obtained. A much more rapid reaction takes place, even at low temperatures, when pyridine is employed as solvent and condensing agent.

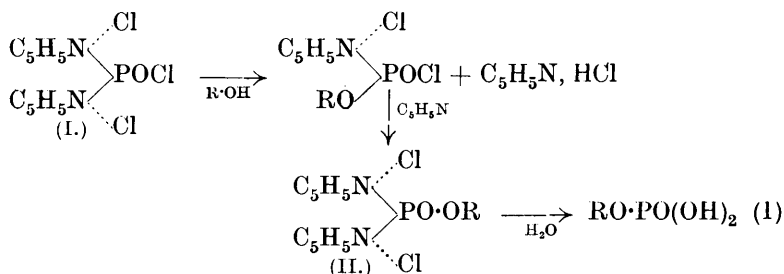
Pyridine has been used by several investigators in the preparation of the esters of inorganic acids. Verley (*Bull. Soc. chim.*, 1901, 25, 46) prepared a series of aryl hydrogen sulphates by means of pyridine and chlorosulphonic acid. These two substances react to give pyridiniumsulphonic acid (Baumgarten, *Ber.*, 1926, 59, 1166), and this compound has recently been used by Lapworth and Burkhardt for the same purpose (*J.*, 1926, 684) :



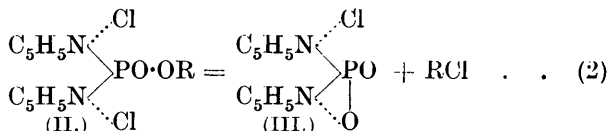
E. Fischer (*Ber.*, 1914, 47, 3194) introduced the use of pyridine with phosphorus oxychloride for the preparation of phosphoric esters, and the method was afterwards employed by Abderhalden (*Ber.*, 1918, 51, 1308). Neither investigator has noted that a crystalline compound of pyridine and phosphorus oxychloride is formed when the two liquids are mixed. The analytical data for this substance, although not decisive, point to the formula $(\text{C}_5\text{H}_5\text{N})_2\cdot\text{POCl}_3$. A number of acyl-pyridinium salts are mentioned in the literature; only in a few cases, however, have they been prepared in analytically pure condition. In those compounds which are derived from the chlorides of monobasic acids one molecule of base is associated with one molecule of acyl chloride, but from sulphuryl chloride and pyridine an addition compound has been obtained which probably

has the formula $(C_5H_5N)_2SO_2Cl_2$ (Baumgarten, *Ber.*, 1927, **60**, 1174).

Since, in the presence of pyridine, $\alpha\gamma$ -diaryloxyisopropyl alcohols react with phosphorus oxychloride at 0° and in less than a fifth of the time that is required when no pyridine is present, it is difficult to suppose that the function of the pyridine is merely to fix the hydrogen chloride which is liberated. The pyridine-phosphorus oxychloride addition compound is, doubtless, the reactant :



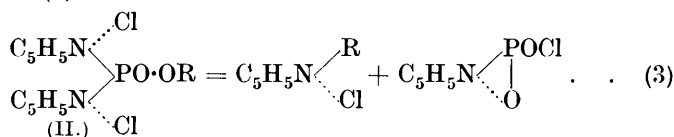
Excellent yields of $\alpha\gamma$ -diaryloxyisopropyl phosphoric esters can be obtained by the pyridine method provided the experimental conditions are suitably regulated. But the unexpected observation has been made that no monophosphoric ester is formed if the reaction mixture, containing excess of phosphorus oxychloride, is heated in a water-bath for a short time. The product under these conditions consists mainly of the diaryloxyisopropyl chloride, accompanied by a comparatively small amount of the corresponding pyridinium compound, which in certain cases can be isolated as the difficultly soluble nitrate. Diaryloxyisopropyl alcohols do not yield chlorides on heating with phosphorus oxychloride alone. The presence of pyridine is a necessary factor in the formation of the chloride, and the reaction is most simply explained by assuming a decomposition of the pyridinium compound (II) under the influence of a rise of temperature :



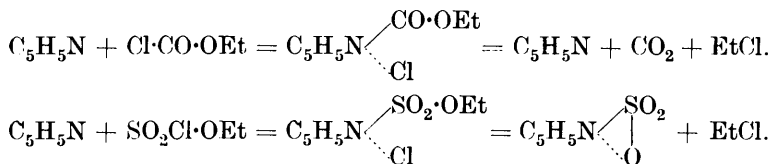
Phosphorus oxychloride has hitherto been regarded as essentially an agent for the introduction of the phosphoric acid radical. Bergmann, in editing a paper by Fischer and Pfähler (*Ber.*, 1920, **53**, 1607), directed attention to the formation of $CH_2Cl \cdot CH_2 \cdot O \cdot PO(OH)_2$ from glycol, pyridine, and phosphorus oxychloride as a noteworthy exception to the general rule. Our experiments show, however,

that phosphorus oxychloride in association with pyridine may, according to the experimental conditions, act either as a reagent for the introduction of the phosphoric acid radical or for the exchange of hydroxyl for chlorine. The experiments of Fischer and Pfähler were carried out at -20° , and their results are interesting as showing that reaction (2) may in some cases occur at low temperatures.

The formation of an alkylpyridinium compound (*e.g.*, $\alpha\gamma$ -di-*p*-tolylxyisopropylpyridinium chloride) along with the alkyl chloride requires explanation. The most obvious hypothesis is that two consecutive reactions occur, the pyridinium salt being formed by the combination of pyridine, always present in excess, with some of the alkyl chloride produced in reaction (2). But if this were so, the yield of pyridinium salt ought to be increased by prolonged heating of the reaction mixture. Actually, the yields of chloride and pyridinium salt are constant and unaffected by an increase in the time of heating. Moreover, direct experiment has shown that $\alpha\gamma$ -di-*p*-tolylxyisopropyl chloride does not form a pyridinium salt on heating with pyridine, even in the presence of phosphorus oxychloride. It would seem, therefore, that the alkylpyridinium salt must be formed by a decomposition of the pyridinium compound (II) proceeding concurrently with the reaction indicated in equation (2):



Reaction (2) is closely analogous to the spontaneous decomposition of the unstable addition compounds which pyridine forms with ethyl chloroformate (Fry, *J. Amer. Chem. Soc.*, 1914, **36**, 259) and ethyl chlorosulphonate (Baumgarten, *Ber.*, 1926, **59**, 1166):



Reaction (3) is novel in type. It offers a method for the preparation of pyridinium compounds in cases where other processes may be inapplicable or less convenient, and experiments are now in progress to ascertain to what extent it is of general application.

$\alpha\gamma$ -Di-*p*-tolylxyisopropylpyridinium nitrate may be crystallised from hot water, and is quite stable towards hot dilute acid. It is

decomposed by cold aqueous alkali into *p*-cresol and products which quickly resinify. The splitting off of *p*-cresol under such mild conditions of hydrolysis is remarkable, in view of the great stability of the diaryloxyisopropyl alcohols towards hydrolysing agents.

EXPERIMENTAL.

The Addition Compound of Pyridine and Phosphorus Oxychloride.—12 G. of pyridine (3 mols.), dissolved in 40 c.c. of dry ether, were added slowly to a solution of 10 g. of phosphorus oxychloride (1 mol.) in about 40 c.c. of ether, atmospheric moisture being excluded as far as possible. The oily precipitate produced quickly crystallised and was then repeatedly washed, by decantation, with dry ether and dried in a current of dry air for some hours; the last trace of ether was removed under diminished pressure. The product (7.4 g.) was dissolved in water, and the solution made up to a definite volume [Found: P, 9.2; Cl, 27.8. $(C_5H_5N)_2.POCl_3$ requires P, 9.9; Cl, 34.1%].

The compound is extremely hygroscopic and very rapidly decomposed by water. The analytical data may be interpreted as indicating that, in spite of the precautions taken to exclude moisture, a part of the substance has been hydrolysed to the compound (III). The pyridine-phosphorus oxychloride compound dissolves readily in chloroform; it is not soluble in carbon tetrachloride.

Preparation of Phosphoric Esters by the Action of Phosphorus Oxychloride and Pyridine.—The method of procedure, and the general properties of the products are exemplified by the case of di-*p*-tolylloxyisopropyl alcohol.

αγ. Di-*p*-tolylloxyisopropyl phosphate, $(C_7H_7 \cdot O \cdot CH_2)_2CH \cdot O \cdot PO(OH)_2$. In order to obtain a good yield of the mono-ester, it is necessary to use a considerable excess of phosphorus oxychloride. The pyridine-phosphorus oxychloride compound, however, is only slightly soluble in pyridine. Its effective concentration is therefore diminished by separation in solid form, and hence the production of the bis-ester is favoured. This difficulty may be obviated by using a mixture of chloroform and pyridine as the solvent.

A solution of the alcohol (2.72 g.) in 8 c.c. of pyridine was added, in the course of about 20 minutes, to a solution of 3.6 c.c. of phosphorus oxychloride (4 mols.) in 8 c.c. of pyridine (10 mols.), which had been mixed with 10 c.c. of chloroform. The process was carried out in the absence of atmospheric moisture and at 0°. Each drop caused the appearance of a transient red coloration, and towards the end of the operation a small quantity of crystalline matter separated. After standing a short time in ice and for $\frac{1}{2}$ hour at room temperature, the mixture was decomposed with ice and rendered alkaline

with ammonia. The aqueous layer was filtered from the oily mixture of bis-ester and chloroform and made strongly acid. The emulsion which at first formed soon crystallised to a mass of needles, which, after being washed with dilute hydrochloric acid and dried in a vacuum, weighed 3.99 g. (96%). The crystals melted at 158° after recrystallisation from ethyl acetate–light petroleum (Found : P, 8.6. $C_{17}H_{21}O_6P$ requires P, 8.8%).

Di-p-tolyloxyisopropyl phosphate is soluble in alcohol, ether, and other organic solvents. It is moderately easily soluble in hot water, and readily soluble in dilute ammonia; more concentrated ammoniacal solutions are soapy and, on evaporation, deposit the ammonium salt in oily form. The ester is hydrolysed by warming with hydrochloric acid in aqueous-alcoholic solution; but the sodium salt of the ester is unaffected by boiling with aqueous caustic soda.

Bis- α -di-p-tolyloxyisopropyl phosphate,
 $[(C_7H_7 \cdot O \cdot CH_2)_2CH \cdot O]_2PO \cdot OH$.

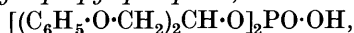
Phosphorus oxychloride was added slowly to an ice-cold solution of the alcohol (1 mol.) in pyridine, the precautions indicated above being taken; the mixture was then heated for about $\frac{1}{2}$ hour in a water-bath. After treatment with ice and ammonia, the pyridine was driven off by heating in the water-bath, and the bis-ester was removed by extraction with ether. The ethereal solution on standing over anhydrous potassium carbonate deposited the potassium salt of the bis-ester, from which the free ester was obtained by treatment with dilute acid. The ester forms needles, m. p. 160°, from acetic acid (Found : P, 4.9. $C_{34}H_{39}O_8P$ requires P, 5.1%). The yield varied considerably. In one experiment it amounted to 94%. When the reaction mixture was not heated before being decomposed with ice, only 20–30% of bis-ester was obtained. The ester is insoluble in water or aqueous caustic alkali. No hydrolysis occurred on boiling a solution of the sodium salt in alcoholic sodium hydroxide.

On evaporating the ethereal solution from which the potassium salt of the bis-ester had separated, there was always obtained a certain amount of a solid substance containing phosphorus, presumably the tri-ester. After recrystallisation from aqueous alcohol it melted at 205–207°. *Di-p-tolyloxyisopropyl chloride* is present along with this product if the reaction mixture has been heated before treatment with ice.

α -Diphenoxyisopropyl phosphate, $(C_6H_5 \cdot O \cdot CH_2)_2CH \cdot O \cdot PO(OH)_2$, m. p. 137–137.5°, crystallises with difficulty. The best solvent is ethyl acetate–light petroleum. The *sodium* salt forms colourless prisms, m. p. 54° (Found : H_2O , 33.0. $C_{15}H_{15}O_6PNa_2 \cdot 10H_2O$

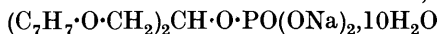
requires H_2O , 32.8%. Found for the salt dried at 110° : Na, 12.1 ; P, 8.5. $\text{C}_{15}\text{H}_{15}\text{O}_6\text{PNa}_2$ requires Na, 12.5 ; P, 8.4%.

Bis- $\alpha\gamma$ -diphenoxyisopropyl phosphate,



forms needles, m. p. 105° from acetic acid (Found : C, 65.4 ; H, 5.8 ; P, 5.7. $\text{C}_{30}\text{H}_{31}\text{O}_8\text{P}$ requires C, 65.4 ; H, 5.7 ; P, 5.6%).

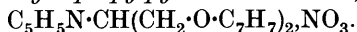
*$\alpha\gamma$ -Di-*o*-tolylxyisopropyl phosphate,* $(\text{C}_7\text{H}_7\cdot\text{O}\cdot\text{CH}_2)_2\text{CH}\cdot\text{O}\cdot\text{PO}(\text{OH})_2$, could not be crystallised, but its solution in warm aqueous sodium hydroxide gave colourless needles of the sodium salt,



(Found : P, 5.35 ; H_2O , 32.9. $\text{C}_{17}\text{H}_{19}\text{O}_6\text{PNa}_2\cdot 10\text{H}_2\text{O}$ requires P, 5.4 ; H_2O , 31.25%).

Preparation of Diaryloxyisopropyl Chlorides and Pyridinium Salts by the Action of Phosphorus Oxychloride and Pyridine.—Di-*p*-tolylxyisopropyl alcohol was caused to react with phosphorus oxychloride in pyridine solution according to the method described under the preparation of the monophosphoric ester (the use of chloroform as a solvent is not essential). The reaction mixture was then heated in a water-bath for $\frac{1}{2}$ hour. On treatment with ice, $\alpha\gamma$ -di-*p*-tolylxyisopropyl chloride separated in almost pure condition ; m. p. 73° after crystallisation from alcohol. The yield, 77%, was not altered by keeping the reaction mixture at room temperature for $\frac{1}{2}$ hour before heating or by continuing the heating in the water-bath for an additional 3 hours.

*1- $\alpha\gamma$ -Di-*p*-tolylxyisopropylpyridinium nitrate,*



The filtrate from the di-*p*-tolylxyisopropyl chloride (about 200—300 c.c.) was mixed with a large excess of saturated ammonium nitrate solution. The *pyridinium nitrate* thus slowly precipitated (yield, 16%) recrystallised from alcohol or chloroform in colourless plates, m. p. 165° (decomp.) (Found : C, 66.6 ; H, 6.05 ; N, 7.1. $\text{C}_{22}\text{H}_{24}\text{O}_5\text{N}_2$ requires C, 66.7 ; H, 6.1 ; N, 7.1%). The corresponding *chlorate*, prepared from the nitrate and potassium chlorate in hot concentrated aqueous solution, crystallised from chloroform in colourless plates, m. p. 153° (violent decomp.) (Found : N, 3.2 ; Cl, 8.4. $\text{C}_{22}\text{H}_{24}\text{O}_5\text{NCl}$ requires N, 3.35 ; Cl, 8.5%). The thiocyanate, also, is crystalline and sparingly soluble in water. The double compound which the pyridinium chloride forms with mercuric chloride is sticky.

Di-*p*-tolylxyisopropylpyridinium nitrate is decomposed by cold aqueous sodium hydroxide, giving a turbid, brown solution. An alkaline vapour with a peculiar smell is liberated on heating, but no pyridine could be detected. If the resinous matter formed by the action of cold caustic soda is removed by shaking with ether,

p-cresol can be detected in the colourless alkaline solution. From 0.8 g. of the pyridinium salt, treated in this manner, 0.43 g. of *p*-tolyl benzoate was obtained, m. p. 69.5° (mixed m. p. 69°). One of the products of the alkaline fission of the pyridinium nitrate condenses with aniline. A solution of the salt in alcohol, containing aniline (1 mol.) and potassium hydroxide (1 mol.), was kept at 0° for 12 hours. Potassium nitrate was deposited, and from the filtrate on treatment with dilute nitric acid deep red crystals were obtained, m. p. 117—119° (decomp.). The phenomena are similar to those observed by Zincke in the case of the pyridinium salt derived from dinitrochlorobenzene (*Annalen*, 1904, **333**, 296). Pyridine, along with much tarry matter, was obtained on heating the pyridinium nitrate with a 10% aqueous solution of sodium acetate for 4 hours at 160°.

1- α -*Di-o-tolyloxyisopropylpyridinium nitrate* forms colourless leaflets, m. p. 154°, from aqueous alcohol. The yield was 12.5% (Found: C, 66.5; H, 6.2; N, 7.0%). The properties of the substance are very similar to those of the *p*-tolyl compound.

1- α -*Di-p-nitrophenoxyisopropylpyridinium nitrate* was obtained as colourless prisms, m. p. 182°. It is considerably less stable than the tolyl derivatives.

α -*Di-p-nitrophenoxyisopropyl chloride* is very sparingly soluble in most solvents; it crystallises from glacial acetic acid in prisms, m. p. 186°. The yield was 84% (Found: Cl, 9.7. C₁₅H₁₃O₆N₂Cl requires Cl, 10.1%).

The Action of Phosphorus Oxychloride and Pyridine on Diphenoxyisopropyl Alcohol at 100°.—No pyridinium nitrate was isolated in this case; the failure is probably due to the salt being more soluble than the corresponding tolyl compounds. Diphenoxyisopropyl chloride was formed in about 75% yield, and no phosphoric esters were obtained.

The Action of Phosphorus Oxychloride on Diaryloxyisopropyl Alcohols in the Absence of Pyridine.—This action was investigated in this laboratory some years ago by Mr. A. G. King. Mono- and bis-esters of phosphoric acid were obtained from diphenoxyisopropyl alcohol and from di-*p*-tolylloxyisopropyl alcohol; but in neither case could any diaryloxyisopropyl chloride be detected.

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