# Acylation Reactions Involving Halogenoquinones

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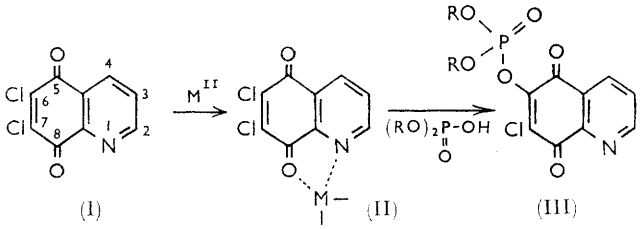
Halogen-substituted quinones activate phosphate and carboxylate anions, promoting acyl transfer; both anhydrides and esters can be produced. The reaction is catalysed to a marked extent by pyridine.

6,7-Dichloroquinoline-5,8-quinone (I) has been used,[1] in the presence of transition metal ions, to convert carboxylic and phosphoric acids into acylating agents. Mixed anhydrides can be produced and the esterification of alcohols achieved. This reaction has been cited [1] as an example of an acylation catalysed by a complex (II) of the quinone (I) and a transition-metal ion. In this complex, C-6 of the quinolinequinone is electron deficient, and hence the displacement of chloride by a carboxylate or phosphate anion readily occurs. Support for this hypothesis was provided (*a*) by the failure of the quinone (I) to promote acylation in the absence of a transition-metal ion, and (*b*) by the instability of the quinone in hydroxylic media in the presence of such ions.




(I) (II) (III)

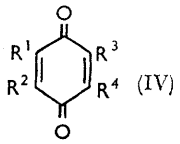
The phosphorylated intermediate (III) is, however, a vinylogous acyl phosphate in the absence of a transition metal ion and should therefore behave as a phosphorylating agent of the P–XYZ type.[2] In consequence it should be possible to promote acylation by use of a

[1] E. J. Corey and H. König, *J. Amer. Chem. Soc.*, 1962, **84**, 4904.

[2] V. M. Clark, D. W. Hutchinson, A. J. Kirby, and S. G. Warren, *Angew. Chem. Internat. Edn.*, 1964, **3**, 678; V. M. Clark and D. W. Hutchinson, *Progr. Org. Chem.*, 1968, **7**, 75.

suitably reactive halogenoquinone in the absence of a metal ion. Such has proved to be the case.

In preliminary experiments,[3] the several tetramethylammonium salts of orthophosphoric acid were treated with the quinone (IV; $R^1 = R^2 = Cl$, $R^3 = R^4 = CN$)


(IV)

in anhydrous dioxan. Varying amounts of inorganic pyrophosphate were formed, depending on temperature, the duration of the reaction, the ratio of quinone to phosphate, and the ionic species of the phosphate. When a solution of tetramethylammonium dihydrogen phosphate was heated under reflux in dry dioxan for 24 hr. with a five fold molar excess of (IV; $R^1 = R^2 = Cl$, $R^3 = R^4 = CN$), the yield of inorganic pyrophosphate was 90%. The yield of pyrophosphate decreased with decreasing ratio of quinone to phosphate and with decreasing time of reaction. At room temperature, no pyrophosphate could be detected after 72 hr. The effect of altering the ionic species of the phosphate was studied by allowing the three tetramethylammonium orthophosphates to react under strictly comparable conditions. The yields of pyrophosphate obtained with the di- and tri-anions were about half that obtained with the mono-anion.

The reaction was extremely sensitive to traces of moisture, and variable yields of pyrophosphate were obtained unless strict precautions to exclude water were taken. The formation of pyrophosphate was reduced to a marked extent by the addition of water (1 equiv.); addition of 4 equiv. resulted in complete inhibition.

Except for disodium hydrogen phosphate, no metal salts of orthophosphoric acid gave pyrophosphate with the quinone (IV; $R^1 = R^2 = Cl$, $R^3 = R^4 = CN$). This may be attributable to the difficulty of obtaining metal phosphates in sufficiently anhydrous condition, and to their insolubility in dioxan. For example, the monohydrate of sodium dihydrogen phosphate loses water only above 170°, a temperature at which thermal conversion into pyrophosphate takes place.

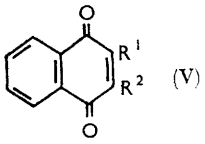
Tetrachloro-*o*-benzoquinone was also capable of promoting acylation in dioxan but was less effective than (IV; $R^1 = R^2 = Cl$, $R^3 = R^4 = CN$). Chloranil (IV; $R^1 = R^2 = R^3 = R^4 = Cl$), bromanil (IV; $R^1 = R^2 = R^3 = R^4 = Br$) and the quinolinequinone (I) did not promote phosphoryl transfer under these conditions.

Tetrachloro-*o*-benzoquinone and the quinone (IV; $R^1 = R^2 = Cl$, $R^3 = R^4 = CN$) were also capable of promoting acylation with salts of carboxylic acids. When the quinones were shaken with an ethanolic solution of tetramethylammonium or benzyltrimethylammonium benzoate, ethyl benzoate was formed in low yield. The effect of adding pyridine to the reaction mixture was dramatic; the yield of ester rose to 70%.

[3] V. M. Clark, D. W. Hutchinson, and R. K. Roschnik, *Chem. and Ind.*, 1965, 135.

Addition of pyridine to mixtures of (IV; $R^1 = R^2 = Cl$, $R^3 = R^4 = CN$) and various phosphate ions yielded condensed phosphates. Moreover (I), chloranil, and bromanil, under analogous conditions, gave condensed phosphates. Other tertiary bases enhancing the phosphorylation reaction include isoquinoline, 2,4,6-collidine, and 2,6-lutidine.

In the absence of pyridine, monoesters of phosphoric acid did not give pyrophosphates to any appreciable extent; however, when a monoester (2 equiv.) and the halogenoquinone (IV; $R^1 = R^2 = Cl$, $R^3 = R^4 = CN$) (1 equiv.) were stirred together at room temperature in pyridine–acetonitrile (20%, v/v), complete conversion into the $P^1P^2$-disubstituted pyrophosphate was observed after 1 hr. Other quinones which promote the formation of pyrophosphates in the presence of pyridine include (I), chloranil, bromanil, tetrachloro-*o*-benzoquinone, 2,3-dichloro-1,4-naphthoquinone (V; $R^1 = R^2 = Cl$), 2,3-dichlorobenzoquinone (IV; $R^1 = R^2 = Cl$, $R^3 = R^4 = H$), and 2,5-dichlorobenzoquinone (IV; $R^1 = R^3 = Cl$, $R^2 = R^4 = H$). No pyrophosphate formation could be detected with monochlorobenzoquinone (IV; $R^1 = Cl$, $R^2 = R^3 = R^4 = H$), its trimethyl analogue (IV; $R^1 = Cl$, $R^2 = R^3 = R^4 = Me$), 2,3-dicyanobenzoquinone (IV; $R^1 = R^2 = CN$, $R^3 = R^4 = H$), tetramethoxybenzoquinone (IV; $R^1 = R^2 = R^3 = R^4 = OMe$), 2-chloro-1,4-naphthoquinone (V; $R^1 = Cl$, $R^2 = H$), 2-chloro-3-methyl-1,4-naphthoquinone (V; $R^1 = Cl$, $R^2 = Me$), ubiquinone (0) (IV; $R^1 = R^2 = OMe$, $R^3 = H$, $R^4 = Me$) and ubiquinone (9) (IV; $R^1 = R^2 = OMe$, $R^3 = Me$, $R^4 = C_{45}H_{73}$).


(V)

The pyridine-catalysed phosphoryl transfer reaction promoted by (V; $R^1 = R^2 = Cl$) gave a good yield of the zwitterion 2-oxido-3-(1-pyridinio)-1,4-naphthoquinone (V; $R^1 = O^-$, $R^2 = C_5H_5N^+$) [4] and with (IV; $R^1 = R^2 = Cl$, $R^3 = R^4 = CN$) a black microcrystalline solid (IV; $R^1 = O^-$, $R^2 = C_5H_5N^+$, $R^3 = R^4 = CN$) was produced. A similar product was obtained from the reaction between (V; $R^1 = R^2 = Cl$) and isoquinoline.

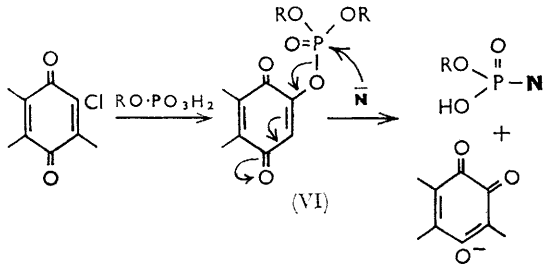
The preparation [1] of bistrimethylene pyrophosphate from (I) and cupric trimethylene phosphate was repeated and a yield of 10% was obtained. When (I) reacted with trimethylene phosphoric acid in acetonitrile–pyridine, complete conversion into $P^1P^2$-bistrimethylene pyrophosphate was observed after 6 hr. at room temperature.

The reaction between phenyl dihydrogen phosphate and chloranil in methanol gave methyl phenyl phosphate, isolated as its cyclohexylammonium salt, in 82% yield. No phosphoryl transfer to phenol could be observed under comparable conditions.

[4] F. Ullmann and M. Ettisch, *Ber*, 1921, **54**, 259.

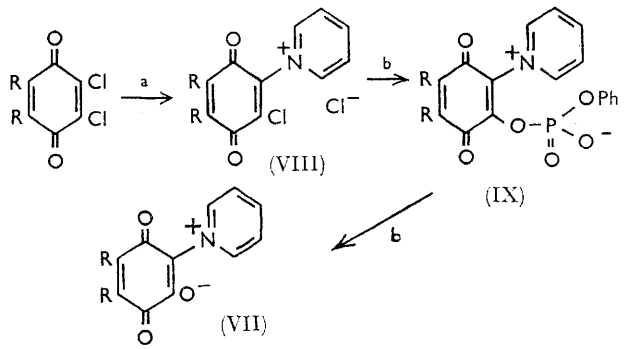
In the absence of pyridine, the reaction probably proceeds in two stages, (*a*) the displacement of halide by phosphate, and (*b*) nucleophilic attack on the intermediate (VI).

The displacement of halide from halogenoquinones is well authenticated for amines,[5] cyanide ion,[6] and *OO*-dialkyl phosphorodithioates.[7] Moreover, with (IV; $R^1$ =




$R^2$ = Cl, $R^3$ = $R^4$ = CN) halide is displaced rather than cyanide and 2,3-dichlorobenzoquinone promotes phosphoryl transfer while 2,3-dicyanobenzoquinone does not.

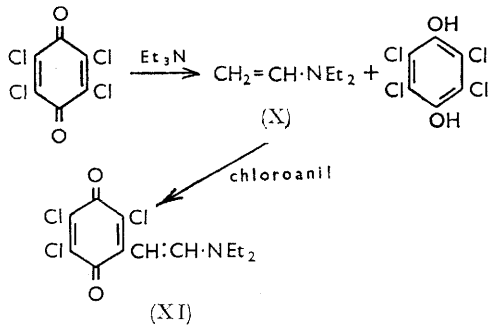
To account for the formation of (VII) when pyridine is used requires attack by phenyl dihydrogen phosphate to displace chloride from the initial adduct (VIII) to give (IX). Attack by a second molecule of phenyl dihydrogen phosphate then gives (VII) and $P^1P^2$-diphenyl pyrophosphate. The formation of (IX) by displacement of a second halide ion can account for the inability of monochloroquinones to promote phosphoryl transfer.




+ $P^1P^2$ — diphenyl pyrophosphate

a = $C_5H_5N$, b = $PhOP{\cdot}O_3H_2$

An alternative pathway leading to (VII) might involve attack by adventitious water on (VIII); a quantitative yield of 2-oxido-3-(1-pyridinio)-1,4-naphthoquinone is produced when pyridine (2 equiv.) is heated with 2,3-dichloro-1,4-naphthoquinone in anhydrous butanol; butyl chloride is eliminated.[8] Support for the initial attack of the tertiary base on the halogenoquinone is provided by comparison of the effects of pyridine, 2,6-lutidine, and triethylamine on the phosphorylation reaction promoted by (V; $R^1$ = $R^2$ = Cl). When 2,6-lutidine is used, only 5% pyrophosphate formation was observed under conditions in which pyridine causes complete conversion into pyrophosphate. Since 2,6-lutidine is a slightly stronger base than pyridine, but has a sterically hindered nitrogen atom, it must act as a specific and not as a general base. When triethylamine was added to a mixture of chloranil and phenyl dihydrogen phosphate, no pyrophosphate was produced. Studies on the reaction between triethylamine and chloranil [9,10] have shown that direct nucleophilic attack by nitrogen on the quinone ring does not take place. Instead, the triethylamine is oxidised to an enamine (X) which displaces chloride ion from another molecule of chloranil to give the dialkylaminovinyl quinone (XI).

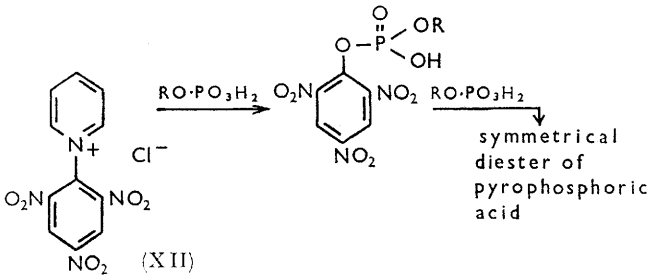



The effectiveness of a halogenoquinone in promoting acyl transfer depends not only on the susceptibility of the quinone nucleus towards nucleophilic attack but also on the ease with which the oxygen atoms can accommodate a negative charge. The latter is a function of the electron affinity of the quinone [11] as determined by the one-electron reduction potential.[12] The presence of substituents on the quinonoid nucleus has a marked effect on the electron affinity; [11] electron-withdrawing substituents raise the potential and activate the quinone towards nucleophilic attack. 2,3-Dichloro-5,6-dicyano-*p*-benzoquinone, with four strongly electronegative substituents, has the highest electron affinity of the quinones investigated, followed by tetrachloro-*o*-benzoquinone and chloranil. In our experiments, this sequence corresponds to the relative effectiveness of these quinones to promote phosphoryl transfer in the absence of pyridine.

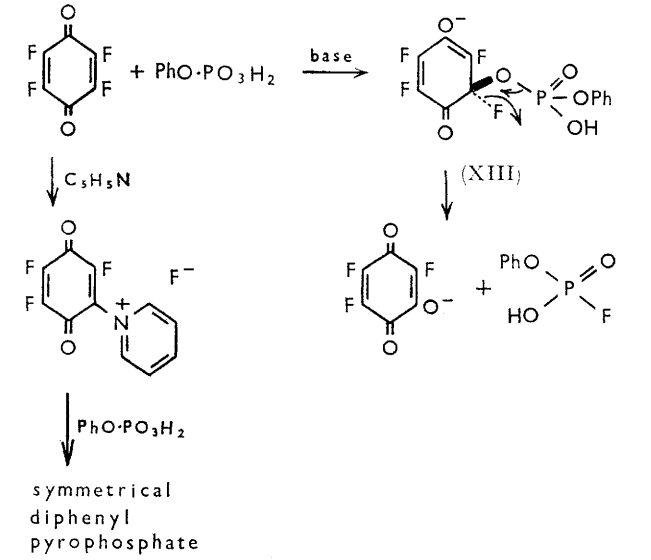
The efficacy of phosphorylation also depends on the relative orientation of the halogen atoms substituted in the quinone nucleus. With the halogen atoms *meta* to one another, acyl transfer is less effective than with the halogen atoms either *ortho* or *para* to each other. Thus, (IV; $R^1$ = $R^2$ = Cl, $R^3$ = $R^4$ = H) and (IV; $R^1$ = $R^3$ = Cl, $R^2$ = $R^4$ = H) are more effective than (IV; $R^1$ = $R^4$ = Cl, $R^2$ = $R^3$ = H).

[5] M. Niemeyer, *Annalen*, 1885, **228**, 322.
[6] K. Wallenfels and G. Bachmann, *Angew. Chem.*, 1961, **73**, 142.
[7] W. Gauss and O. Bayer, G.P. 1,167,838 (*Chem. Abs.*, 1964, **61**, 1841).
[8] J. A. VanAllan and G. A. Reynolds, *J. Org. Chem.*, 1963, **28**, 1019.
[9] D. Buckley, S. Dunstan, and H. B. Henbest, *J. Chem. Soc.*, 1957, 4880.
[10] D. Buckley, H. B. Henbest, and P. Slade, *J. Chem. Soc.*, 1957, 4891.
[11] G. Briegleb, *Angew. Chem. Internat. Edn.*, 1964, **3**, 617.
[12] M. E. Peover, *J. Chem. Soc.*, 1962, 4540.

The acyl transfer reaction in the presence of pyridine is similar to that initiated by picryl chloride.[13,14] The postulated intermediate, *N*-(2,4,6-trinitrophenyl)-pyridinium chloride (XII) is a known compound,[15] and both (XII) and the corresponding picrate [16] have been used to initiate phosphoryl transfer.[14]




2,4-Dinitrofluorobenzene, in the presence of organic bases, has been similarly used;[17] the nature of the products varies with the base employed. With pyridine, a mixture of pyrophosphate and phosphorofluoridate was produced, whereas phosphorofluoridate was the sole product in the presence of triethylamine. A closely analogous reaction occurs with fluoranil; it converts monophenyl phosphoric acid into approximately equal amounts of $P^1P^2$-diphenyl pyrophosphate and monophenyl phosphorofluoridate in the presence of pyridine. With triethylamine, only the phosphorofluoridate was formed. The reaction presumably follows a path similar to that for 2,4-dinitrofluorobenzene.




Fluoranil is particularly susceptible to nucleophiles,[18] and direct attack by monophenyl phosphate can easily occur. The intermediate (XIII) so produced can then give rise to the phosphorofluoridate either by intramolecular rearrangement, or by attack of fluoride ion. In the presence of pyridine there are two competing pathways, the direct attack by monophenyl phosphate and displacement of fluoride by pyridine, giving rise to the two products.

## EXPERIMENTAL

Paper chromatograms (on Whatman no. 1 or no. 4 paper) were developed with (*a*) propan-2-ol–ammonia–water (7 : 1 : 2) or (*b*) trichloroacetic acid–propan-2-ol–ammonia–water.[19] The relative phosphorus content of the various materials on chromatograms was determined by the method of Usher.[20]

*Preparation of Quinones.*—Chloranil, bromanil, 2,3-dichloro-1,4-naphthoquinone, 2,3-dichloro-5,6-dicyano-*p*-benzoquinone and tetrachloro-*o*-benzoquinone were commercially available and were used without further purification. 6,7-Dichloroquinoline-5,8-quinone and ubiquinone (9) were gifts. 2,3-Dichloro-,[21] 2,5-dichloro-,[21] 2,6-dichloro-,[22] and 2,3-dicyano-benzoquinone,[23] monochlorobenzoquinone,[24] 2-chloro-1,4-naphthoquinone,[25] and 2-chloro-3-methyl-1,4-naphthoquinone [26] were prepared as described in the literature.

*Phosphorylation involving Halogenoquinones.*—The quinone (IV; $R^1 = R^2 = Cl$, $R^3 = R^4 = CN$) (160 mg., 4 mol.) and tetramethylammonium dihydrogen phosphate (30 mg., 1 mol.) (both dried at 50° *in vacuo*) were heated under reflux with exclusion of moisture for 24 hr. in dry dioxan (10 ml.), then cooled. The supernatant (which contained no phosphorus) was discarded, and the precipitate was dissolved in water (10—15 ml.). Paper chromatography in solvent (*b*) revealed the presence of orthophosphate (20%) and pyrophosphate (80%).

*Variation in the Amount of Phosphoryl Transfer with Time and Amount of Quinone.*—The reaction was carried out as above except that aliquot portions were removed and analysed by paper chromatography at different times, as recorded in Tables 1 and 2. When the reaction was carried out at room temperature, no pyrophosphate could be detected after 72 hr.

TABLE 1

Variation in the amount of phosphoryl transfer with time

| Time (hr.) | 1 | 6 | 15 | 24 | 48 |
|---|---|---|---|---|---|
| Yield of pyrophosphate (%) | 0 | 14 | 62 | 80 | 80 |

TABLE 2

Effect of altering the quinone–phosphate ratio

| Ratio | 0·2 | 0·3 | 0·5 | 1·0 | 4·0 | 5·0 |
|---|---|---|---|---|---|---|
| Yield of pyrophosphate (%) after 24 hr. | 3 | 9 | 13 | 31 | 80 | 90 |

*Effect of Altering the Ionic Species of Phosphate.*—The following tetramethylammonium salts of orthophosphoric

[13] J. Stockx, *Bull. Soc. chim. belges*, 1961, **70**, 591.
[14] R. Wittmann, *Chem. Ber.*, 1963, **96**, 2116.
[15] M. Busch and W. Kögel, *J. prakt. Chem.*, 1911, **84**, 507.
[16] F. W. Hodges, *J. Chem. Soc.*, 1926, 2417.
[17] R. Wittmann, *Chem. Ber.*, 1963, **96**, 771.
[18] K. Wallenfels and K. Friedrich, *Chem. Ber.*, 1960, **93**, 3070.
[19] J. P. Ebell, *Mikrochim. Acta*, 1954, 679.
[20] D. A. Usher, *J. Chromatog.*, 1963, **12**, 262.
[21] J. B. Conant and L. F. Fieser, *J. Amer. Chem. Soc.*, 1923, **45**, 2194.
[22] H. van Erp, *Ber*, 1925, **58**, 663.
[23] J. Thiele and F. Gunther, *Annalen*, 1906, **349**, 45.
[24] S. Levy and G. Schultz, *Annalen*, 1881, **210**, 133.
[25] T. Zincke and M. Schmidt, *Ber.*, 1894, **27**, 2753.
[26] K. Fries and W. Lohmann, *Ber.*, 1921, **54**, 2912.

acid were treated with the quinone (IV; $R^1 = R^2 = Cl$, $R^3 = R^4 = CN$) (4 molar equiv.) as described above. Yields are recorded in Table 3. No pyrophosphate formation could be detected when sodium dihydrogen, trisodium, cupric, cobaltic, phenyl dihydrogen, or cyclohexyl dihydrogen phosphate was used with (IV; $R^1 = R^2 = Cl$, $R^3 = R^4 = CN$), nor when duroquinone, bromanil, chloranil or (I), was used instead of the dichlorodicyanoquinone.

TABLE 3

Variation in yield of pyrophosphate with change in initial species

| Anion | $H_2PO_4^-$ | $HPO_4^{2-}$ | $*HPO_4^{2-}$ | $\dagger HPO_4^{2-}$ | $PO_4^{3-}$ | $Na_2HPO_4$ |
|---|---|---|---|---|---|---|
| Yield of pyrophosphate (%) | 80 | 40 | 14 | 0 | 36 | 40 |

* Water (1 mol.) added. † Water (4 mol.) added.

*Evolution of Hydrogen Chloride from the Reaction with Quinone* (IV; $R^1 = R^2 = Cl$, $R^3 = R^4 = CN$).—Tetramethylammonium dihydrogen phosphate (0·15 g.) and (IV; $R^1 = R^2 = Cl$, $R^3 = R^4 = CN$) (0·8 g.) were heated under reflux for 36 hr. in dry dioxan (40 ml.). A slow stream of nitrogen was passed through the mixture and the outgoing gas was passed into a solution of silver nitrate (5 ml.; saturated at room temperature). The precipitate (72 mg., 57% AgCl) contained no carbon and did not give a blue colour with cupric acetate–benzidine acetate.[27]

*Acylation with Salts of Benzoic Acid.*—Mixtures of the halogenoquinone (*ca.* 50 mg., 1 mol.), the benzoate salt (1 mol.), and naphthalene (25 mg.) as internal standards in either ethanol (5 ml.) or ethanol–pyridine (4 : 1 v/v; 5 ml.) were shaken at room temperature for 24 hr. (There was no increase in yields of ethyl benzoate after that time.) The mixture was then examined by g.l.c. (15% L.A.C. on silanised brickdust column). The results are summarised in Table 4.

TABLE 4

Quinone-promoted acylation with salts of benzoic acid

| Halogeno-quinone | Cation | Solvent | Yield of ethyl benzoate after 24 hr. (%) |
|---|---|---|---|
| None | $PhCH_2\cdot\overset{+}{N}Me_3$ | EtOH | 0 |
| (IV; $R^1 = R^2 =$ Cl, $R^3 = R^4 =$ CN) | $PhCH_2\cdot\overset{+}{N}Me_3$ | EtOH | 1 |
| | $PhCH_2\cdot\overset{+}{N}Me_3$ | EtOH–pyridine | 45 |
| | $Cu^{2+}$ | EtOH–pyridine | <0·4 |
| (V; $R^1 = R^2 =$ Cl) | $PhCH_2\cdot\overset{+}{N}Me_3$ | EtOH–pyridine | 66 |
| | $Li^+$ | EtOH–pyridine | 66 |

*Isolation of Ethyl Benzoate.*—A suspension of 2,3-dichloronaphthoquinone (1·15 g., 1·1 mol.) and lithium benzoate (0·64 g., 1 mol.) in ethanol–pyridine (5 : 1 v/v; 30 ml.) was shaken for 12 hr. at room temperature and then filtered. The filtrate, and ethanol washings of the residue, were concentrated (to *ca.* 5 ml.) *in vacuo* and refiltered. Ethyl benzoate (i.r. and n.m.r. spectra identical to those of an authentic sample) was isolated from the filtrate by g.l.c. (Found: C, 72·2; H, 6·8. Calc. for $C_9H_{10}O_2$: C, 72·0; H, 6·7%).

*Phosphorylation with Halogenoquinones in the Presence of Pyridine.*—A solution of tetramethylammonium dihydrogen phosphate (30 mg., 1 mol.) and (IV; $R^1 = R^2 = Cl$, $R^3 = R^4 = CN$) (160 mg., 4 mol.) in dry dioxan (10 ml.) and pyridine (2 ml.), was heated under reflux for 24 hr., then cooled. The supernatant was discarded and the tarry residue dissolved in aqueous acetic acid (50% v/v; 16 ml.) and examined by paper chromatography. Complete conversion of orthophosphate had occurred; the products were pyrophosphate (37%) and trimetaphosphate (63%). When bistetramethylammonium hydrogen phosphate was treated as above, some orthophosphate (26%) was left after 24 hr.; the products were pyro- (30%) and trimeta-phosphate (44%).

Pyro- and trimeta-phosphate were produced when chloranil, tetrachloro-*o*-benzoquinone or (I) were used in the place of (IV) above.

*Preparation of Biscyclohexylammonium $P^1P^2$-Diphenyl Pyrophosphate.*—A solution of phenyl dihydrogen phosphate (0·35 g., 2 mol.) and chloranil (0·25 g., 1 mol.) in acetonitrile–pyridine (5 : 1 v/v; 12 ml.) was stirred for 1 hr. at room temperature. Paper chromatography in solvent (*a*) showed almost complete conversion into the pyrophosphate ($R_F$ 0·7). Cyclohexylamine (2 ml.) and ether (50 ml.) were added to the mixture; after 15 min. the precipitate which had formed was filtered off, washed with ether, and then crystallised from water containing a little cyclohexylamine to give biscyclohexylammonium $P^1P^2$-diphenyl pyrophosphate (0·36 g., 65%), m.p. 260—261° (Found: C, 54·6; H, 6·4; N, 5·4; P, 12·0. Calc. for $C_{24}H_{38}N_2O_7P_2$: C, 54·4; H, 7·2; N, 5·3; P, 11·7%). Biscyclohexylammonium $P^1P^2$-diphenyl pyrophosphate was isolated (60—70%) when the following quinones were used in the reaction described above: (I), chloranil, bromanil, (IV; $R^1 = R^2 =$ Cl, $R^3 = R^4 =$ CN), (IV; $R^1 = R^3 =$ Cl, $R^2 = R^4 =$ H), and tetrachloro-*o*-benzoquinone. Good yields of pyrophosphate were demonstrated by paper chromatography with (IV; $R^1 = R^2 =$ Cl, $R^3 = R^4 =$ H), (IV; $R^1 = R^2 =$ Cl, $R^3 = R^4 =$ Me), (IV; $R^1 = R^3 =$ Cl, $R^2 = R^4 =$ Me), and (V; $R^1 = R^2 =$ Cl). A slow formation of pyrophosphate was observed with (IV; $R^1 = R^4 =$ Cl, $R^2 = R^3 =$ H) and (IV; $R^1 = R^4 =$ Cl, $R^2 = R^3 =$ Me) when left at room temperature in pyridine–acetonitrile with phenyl dihydrogen phosphate for several days.

No pyrophosphate formation could be detected with (IV; $R^1 =$ Cl, $R^2 = R^3 = R^4 =$ H), (IV; $R^1 = R^2 =$ CN, $R^3 = R^4 =$ H), (IV; $R^1 = R^2 = R^3 = R^4 =$ OMe), (IV; $R^1 = R^2 =$ OMe, $R^3 =$ H, $R^4 =$ Me), and ubiquinone (9).

*Comparison of Different Bases.*—A solution of phenyl dihydrogen phosphate (0·5 mmole) and 2,3-dichloro-1,4-naphthoquinone (0·5 mmole) in acetonitrile (4 ml.) and base (1 ml.) was stirred at room temperature, then examined by paper chromatography in solvent (*a*). The yields of $P^1P^2$-diphenyl pyrophosphate are shown in Table 5.

*Phosphorylation of Solvent Methanol.*—To phenyl dihydrogen phosphate (0·174 g., 1 mol.) dissolved in methanol (5 ml.), acetonitrile (5 ml.), and pyridine (2 ml.) was added a solution of chloranil (0·37 g., 1·5 mol.) in acetonitrile (15 ml.). The mixture was stirred for 1 hr. at room temperature, the solvents were removed under reduced pressure, water (20 ml.) was added, and the mixture shaken with ether (20 ml.). Triethylamine (2 ml.) was added to the aqueous phase and the mixture was evaporated to dryness. The residue was taken up in a large volume of acetone–ether and the solution was filtered and again evaporated to dryness. After the

[27] F. Feigl, 'Spot Tests in Inorganic Analysis,' Elsevier, Amsterdam, 1958, p. 276.

TABLE 5

Yield of $P^1P^2$-diphenyl pyrophosphate with use of various bases

| Base | Yield $P^1P^2$-diphenyl pyrophosphate (%) 1 hr. | 6 hr. | 22 hr. |
|---|---|---|---|
| Isoquinoline | 97 | 95 | 95 |
| Pyridine | 92 | 96 | 97 |
| 2,4,6-Collidine | 5 | 43 | 98 |
| 2,6-Lutidine | 5 | 20 | 40 |
| Triethylamine | 0 | 0 | |

residue had been dissolved in acetone and filtered to remove the last traces of triethylammonium chloride, cyclohexylamine (2 ml.) was added to the filtrate, which was then evaporated to dryness. The residue gave cyclohexylammonium methyl phenyl phosphate (0·24 g., 85%), m.p. 152—153° (from acetonitrile) (Found: C, 55·4; H, 7·7; N, 4·95. Calc. for $C_{13}H_{22}NO_4P$: C, 54·3; H, 7·7; N, 4·9%). When the reaction described above was repeated with phenol in the place of methanol, paper chromatography of the mixture after 1 hr. revealed the presence of phenyl dihydrogen phosphate and $P^1P^2$-diphenyl pyrophosphate, but no diphenyl hydrogen phosphate.

*Preparation of Bistrimethylene Pyrophosphate.*—(a) *By the method of Corey and König.*[1] Bistrimethylene pyrophosphate (m.p. 137—138°) was prepared (10%) from cupric trimethylene phosphate.

(b) *In the presence of pyridine.* A solution of trimethylene hydrogen phosphate (280 mg., 2 mol.) and (I) (230 mg., 1 mol.) in acetonitrile–pyridine (9 : 1 v/v; 10 ml.) was stirred with the exclusion of moisture for 6 hr. at room temperature. T.l.c. of the mixture on silica showed that conversion into the pyrophosphate was almost complete. The solid formed during the reaction was filtered off and washed with small amounts of acetonitrile. The combined filtrate and washings were evaporated to dryness, acetonitrile (2 ml.) was added to the residue, the solution was filtered, and the filtrate was evaporated *in vacuo*. Trituration of the residual gum with ether gave a crystalline mass which gave bistrimethylene pyrophosphate (113 mg., 42%), m.p. and mixed m.p. 137° (from acetonitrile–ether) (Found: C, 27·3; H, 4·75; P, 24·75. Calc. for $C_6H_{12}O_7P_2$: C, 27·9; H, 4·7; P, 24·05%).

*Reaction of Phenyl Dihydrogen Phosphate and Fluoranil.*—A solution of phenyl dihydrogen phosphate (0·35 g., 2 mol.) and fluoranil (0·18 g., 1 mol.) in acetonitrile–pyridine (5 : 1 v/v; 12 ml.) was stirred for 1 hr. at room temperature. Paper chromatography of the mixture at this stage [solvent (*a*)] showed the presence of phenyl hydrogen phosphorofluoridate (45%; $R_F$ 0·8), $P^1P^2$-diphenyl pyrophosphate (50%, $R_F$, 0·7), and phenyl dihydrogen phosphate (5%, $R_F$ 0·35). When triethylamine was used as described above in the place of pyridine, the mixture contained phenyl hydrogen phosphorofluoridate and phenyl dihydrogen phosphate, but no $P^1P^2$-diphenyl pyrophosphate.

*Isolation of Ammonium Phenyl Hydrogen Phosphorofluoridate.*—A solution of phenyl dihydrogen phosphate (140 mg., 1 mol.) and fluoranil (144 mg., 1 mol.) in acetonitrile–pyridine (5 : 1 v/v; 12 ml.) was stirred for 4 hr. at room temperature. The solvents were removed under reduced pressure, the residue was dissolved in water (30 ml.), and the solution was extracted with ether (3 × 20 ml.). The aqueous phase was concentrated (to *ca.* 10 ml.) and washed on to an ECTEOLA column (2 × 30 cm.; $HCOO^-$). The column was washed with water and then eluted with 0·1M-ammonium formate solution. Phenyl hydrogen phosphorofluoridate came off in the first fractions, which were combined and evaporated to dryness. The ammonium formate was removed under reduced pressure at 50°, and the residue gave *ammonium phenyl hydrogen phosphorofluoridate* (20 mg., 16%), m.p. 208—210° (from aqueous ethanol) (Found: C, 40·3; H, 5·0. $C_6H_9FNO_3P$ requires C, 40·65; H, 5·1%).

*Isolation of 2-Oxido-3-(1-pyridinio)-quinones.*—(a) *From 2,3-dichloro-1,4-naphthoquinone.*—A solution of phenyl dihydrogen phosphate (353 mg.) and 2,3-dichloro-1,4-naphthoquinone (223 mg.) in dry acetonitrile–pyridine (4 : 1 v/v; 10 ml.) was shaken at room temperature for 1 hr. (paper chromatography indicated complete conversion into pyrophosphate) and then set aside for 24 hr.; yellow-orange crystals of 2-oxido-3-(1-pyridinio)-1,4-naphthoquinone (243 mg.), m.p. 303—305° were obtained. A sample was prepared for analysis by vacuum sublimation (<0·001 mm., 230°) (Found: C, 71·2; H, 3·8; N, 5·6. Calc. for $C_{15}H_9NO_3$: C, 71·8; H, 3·6; N, 5·6%), *m/e* 251 ($M^+$), 223 ($M^+$ — CO), 195 ($M^+$ — 2CO), 179 ($M^+$ — 2CO — O), 104, 79, and 76.

(b) *From 2,3-dichloro-5,6-dicyano-p-benzoquinone.* 2,3-Dicyano-5-oxido-6-(1-pyridinio)-*p*-benzoquinone was obtained (53%) from a similar reaction between phenyl dihydrogen phosphate and (IV; $R^1 = R^2 = Cl$, $R^3 = R^4 = CN$) but could not be crystallised or sublimed for analysis. It was identified by its i.r. spectrum and its mass spectrum [*m/e* 251 ($M^+$ — CO), 195 ($M^+$ — 2CO), 179 ($M^+$ — 2CO — O), and 79.

(c) *From 2,3-dichloro-1,4-naphthoquinone and Isoquinoline.*—2-Oxido-3-(2-isoquinolinio)-1,4-naphthoquinone was obtained (88%) as reddish-orange crystals, m.p. 326—328° in an analogous manner; *m/e* 301 ($M^+$), 273 ($M^+$ — CO), 245 ($M^+$ — 2CO), 229 ($M^+$ — 2CO — O), 150·5 ($M^+/2$), 129, 104, and 76.

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